Thermal and Bromide Ion-Catalyzed Rearrangement of Benzofuran Dioxetanes to 1-Oxaspiro[2.5]octa-5,7-dien-4-ones

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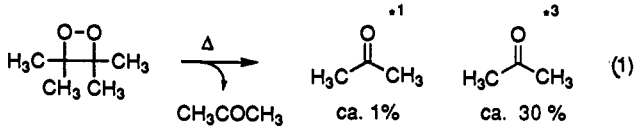
Abstract: The reaction of the tetrasubstituted benzofuran dioxetanes **2** with various nucleophiles, e.g. Br^-, Cl^-, I^-, and $HN(i\text{-}Pr)_2$, was investigated and the unprecedented bromide ion-catalyzed rearrangement to the hitherto unknown 1-oxaspiro[2.5]octa-5,7-dien-4-ones **4** observed. As the mechanism, an S_N2 attack of the bromide ion at the O-3 of the peroxide bond is proposed, in which the resulting hypobromite intermediate **8** rearranges to the spiroepoxide **4** by opening of the furan ring and expulsion of the bromide ion through intramolecular nucleophilic attack of the phenolate ion on the O–Br bond. This unique reaction type is limited to the bromide and the iodide ions, since none of the other nucleophiles led to the spiroepoxide **4**. On thermolysis, the labile spiroepoxides **4** rearrange to the benzodioxoles **5**, and at low temperature, the dimers **6** were formed by the Diels–Alder reaction. 4-Methyl-1,2,4-triazoline-3,5-dione (MTAD) gave with the spiroepoxide **4a** the Diels–Alder product **7a**. The thermolysis of the dioxetanes **2** gave, besides the conventional C–C cleavage products **3**, the dioxoles **5** by rearrangement of the intermediary spiroepoxides **4**. In the latter reaction, electron donors favor the formation of the dioxoles **5** and electron acceptors the C–C cleavage products **3**. The intermediacy of the spiroepoxides **4** in the thermolysis of the dioxetanes **2** was established by trapping of the spiroepoxide **4a** with MTAD in the form of the [4 + 2] cycloaddition product **7a**. For the thermal rearrangement **2** → **4**, the electron-rich arene moiety is proposed to serve as an intramolecular nucleophile which initiates spiroepoxide formation. Both the bromide ion-catalyzed and the thermal rearrangements are unprecedented in dioxetane chemistry.

Introduction

The characteristic property of 1,2-dioxetanes is their thermal decomposition to afford electronically excited carbonyl products, predominantly triplet excited states as illustrated for the simple tetramethyl derivative (eq 1).[1] The triplet excited acetone has



(1)

been utilized to sensitize pyrimidine dimer formation in calf thymus DNA by thermolysis of the above dioxetane in the dark.[2] Since this earliest report on the photobiological application of dioxetanes, we have conducted intensive studies to induce mutagenicity in bacteria and cells by means of these high-energy molecules.[3] While in isolated DNA, besides pyrimidine dimer formation, the major damage caused by dioxetanes entails single strand breaks, base modifications, and apyrimidinic and apurinic sites, little if any mutagenicity was observed in bacteria and cells.[4] Exceptions were the dioxetanes **2** derived from 2,3-dimethylbenzofurans **1**, which exhibited massive mutagenicity in the *Salmonella typhimurium* strain TA 100.[5] ^{32}P postlabeling studiesrevealed adduct formation through alkylation-type activity rather than sensitized photocycloaddition.[6] The former may result from deoxygenation of the dioxetane to its epoxide and subsequent addition of the nucleophilic DNA base.[5] Alternatively, direct S_N2 attack of the base on the peroxide bond should also result in DNA adducts. The feasibility of the latter S_N2 process was recently demonstrated for 3,3-disubstituted dioxetanes, for which the nucleophile attacks the more exposed oxygen atom of the O–O bond on grounds of steric reasons.[7]

In view of the aforementioned, we examined the reaction of the tetrasubstituted benzofuran dioxetanes **2** with a variety of nucleophiles, in order to provide a chemical basis for the mutagenicity of this special class of dioxetanes. In this context we uncovered that catalytic amounts (<5 mol %) of bromide ions induced the transformation of the benzofuran dioxetanes **2** to the cleavage products **3** and the spiroepoxides **4** (Scheme 1). The thermal rearrangement **2** → **4** was already observed for the benzofuran,[5b] naphthofuran,[8] and ketofuran dioxetanes;[9] however, the bromide ion-catalyzed process is unprecedented. We propose that nucleophilic attack by Br^- at the O-3 oxygen atom of the dioxetane peroxide bond initiates this rearrangement.

Results

The benzofurans **1** were obtained according to standard literature procedures,[10–13] the corresponding dioxetanes **2**, by TPP-sensitized photooxygenation (Scheme 1).[14] In the case of benzofuran **1f**, in addition to the dioxetane **2f**, also the allylic hydroperoxide **2f'** was formed in substantial amounts (40%).

Treatment of the benzofuran dioxetanes **2a-l** with catalytic amounts of bromide ions (Et_4NBr or KBr/18-crown-6) led under

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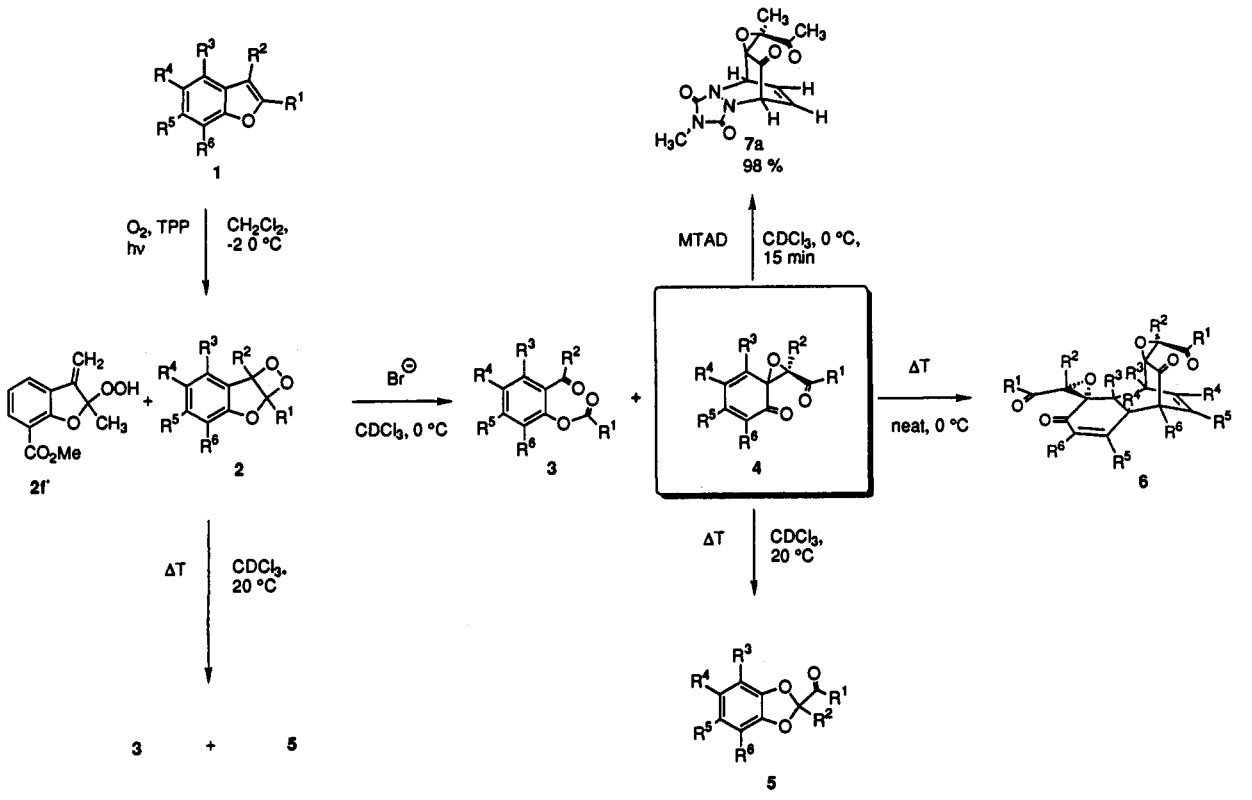
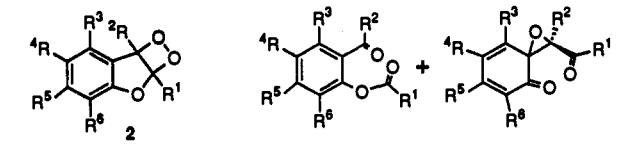
Scheme 1



mild conditions (−10 to 0 °C) to the 2-acetylphenyl acetates **3** as fragmentation products and the spiroepoxides **4** as rearrangement products (Scheme 1). In the absence of bromide ions, less than 5% of conversion only to the cleavage product **3** was found. The results are summarized in Table 1.

The product ratio of **3** *versus* **4** depended strongly on the substitution pattern of the dioxetanes **2**, as exhibited by the data in Table 1. Thus, the dimethyl derivative **2a** (entry 1) and the chloromethyl derivative **2b** (entry 2) afforded the spiroepoxides **4a,b** as the main products (95%). The sterically demanding isopropyl substituent at C-3 of the dioxetane **2c** (entry 3) increased the amount of cleavage product **3c** (35%) compared to the dimethyl derivative **2a**. Substituents at C-4, as in the case of the dioxetanes **2d,h** (entries 4 and 8), inhibit the reaction with bromide ions completely. The variation of the substituents at C-5 and C-7 from electron-withdrawing to -donating, as in the dioxetanes **2e-g,l** (entries 5–7 and 9), did not affect significantly the product distribution. In these cases the corresponding spiroepoxides **4e-g,l** were formed as main products. Phenyl substitution at C-2 as in dioxetane **2j** (entry 10) led to a 52:48 product mixture of the cleavage product **3j** and the spiroepoxide **4j**. The reaction of the 3-phenyl-substituted benzofuran dioxetanes **2k** (entry 11) led with catalytic amounts of bromide ions exclusively to the cleavage products **3k**, whereas for the 6-methoxy-3-phenyl derivative **3l** (entry 12), the spiroepoxide **4l** was obtained in 16% yield.

Table 1. Product Studies of the Bromide Ion-Catalyzed Transformation of Benzofuran Dioxetanes **2** to the Cleavage Products **3** and the Spiroepoxides **4**



entry		R^1	R^2	R^3	R^4	R^5	R^6	3[a]	4[a]
1	**a**	CH_3	CH_3	H	H	H	H	5	95
2	**b**	CH_2Cl	CH_3	H	H	H	H	8	92
3	**c**	CH_3	$CH(CH_3)_2$	H	H	H	H	35	65
4	**d**	CH_3	CH_3	CO_2Et	H	H	H	*b*	
5	**e**	CH_3	CH_3	H	CO_2Et	H	H	12	88
6	**f**	CH_3	CH_3	H	H	H	CO_2Me	6	94
7	**g**	CH_3	CH_3	H	*t*-Bu	H	H	5	95
8	**h**	CH_3	CH_3	*t*-Bu	H	*t*-Bu	H	*b*	
9	**i**	CH_3	CH_3	H	OMe	H	H	10	90
10	**j**	Ph	CH_3	H	H	H	H	52	48
11	**k**	CH_3	Ph	H	H	H	H	>95	
12	**l**	CH_3	Ph	H	H	OMe	H	84	16

[a] Relative yields normalized to 100% determined by ^{1}H NMR analysis (200 MHz, −20 to 0 °C), error limits ± 5% of stated values, conversions in all cases of 100% (except for **2d,h**), mass balance >95%. [b] No conversion after 2 d at 0 °C as determined by ^{1}H NMR analysis (200 MHz).

For comparison, the dioxetane **2a** was treated also with KCl under phase-transfer conditions. At 0 °C, only the cleavage product **3a** was detected. Under these conditions, KI led to the cleavage product **3a** and spiroepoxide **4a** in a 81:19 ratio. Ferrocene and potassium superoxide gave again exclusively the cleavage product **3a**.

The intensive yellow $CDCl_3$ solutions (λ_{max} = 320 for **4a**) of the 1-oxaspiro[2.5]octa-5,7-dien-4-ones **4** exhibited characteristic olefinic proton resonances at δ 4.5–6.8 and epoxide carbon

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Table 2. Product Distribution in the Thermolysis of Benzofuran Dioxetanes **2a,e,g,i**[a]

entry	dioxetane	R^4	**3**[b] (%)	**5**[b] (%)
1	**2e**	CO_2Et	100	0
2	**2a**	H	92	8
3	**2g**	*t*-Bu	80	20
4	**2i**	OMe	37	63

[a] In $CDCl_3$, determined by ^1H NMR analysis on the crude reaction mixture, error ±5% of the stated values, conversion 100%, mass balance >95%. [b] Normalized to 100%.

resonances at δ 65–78, which substantiate the proposed structure of the spiroepoxides **4**. The *cis*-dione functionality of the spiroepoxides **4** was established by low-temperature NOE on derivative **4a** (Scheme 1). Thus, irradiation of the methyl protons of the spiroepoxy ring caused an enhancement of the signal for the vicinal proton (R-3) at the 4-position of the former benzofuran ring and *vice versa*. Moreover, irradiation of the acetyl protons increased the methyl group intensity but not that of the olefinic protons.

Additionally, the chemical transformations displayed in Scheme 1 corroborate the proposed structure for the spiroepoxide **4**. Thus, in $CDCl_3$ at 20 °C, the cases **4a,e,g,i,l** rearranged to the known 1,3-benzodioxole **5a**[5b] and the new derivatives **5e,g,i,l** in high yields (71–95%). Furthermore, on removal of the solvent without warm-up of the freshly prepared spiroepoxides **4a,c,j**, the respective Diels–Alder dimers **6a**,[5b]**c,j** were obtained, the first in as much as 95% and the latter two in 35–39% yields. The structure of the fully characterized dimers **6c,j**[15] was established by comparison of the characteristic spectral data with those of the known dimer **6a**[5b] and similar cyclohexa-2,4-dien-1-one dimerization products.[16] The high diastereoselectivity in the Diels–Alder dimerization of the spiroepoxides **4a,c,j** is similar to that previously observed in the thermolysis of dioxetane **2a**[5b] and in the dimerization of unsubstituted cyclohexa-2,4-dien-1-ones.[16] Finally, in the presence of 4-methyl-1,2,4-triazoline-3,5-dione (MTAD), *in situ* generated spiroepoxide **4a** led to the corresponding Diels–Alder adduct **7a** (Scheme 1) in excellent yield (>98%).

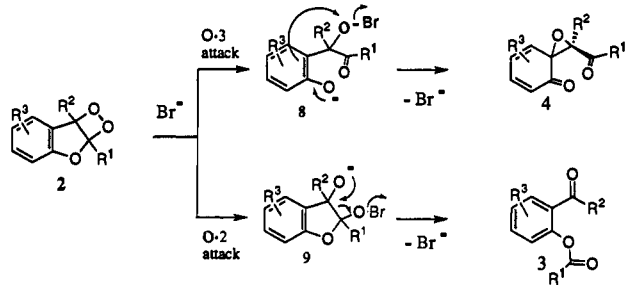
The thermal decomposition of the benzofuran dioxetane **2a** (Table 2, entry 2) led to the cleavage product **3a** and the dioxole **5a** in a ratio of 92:8. In the presence of the dienophile MTAD, the spiroepoxide **4a** was trapped in the form of the Diels–Alder product **7a** (11%) at the expense of the dioxole **5a**; the remainder was the cleavage product **3a** (89%).

To assess the electronic factors in the thermal rearrangement of the benzofuran dioxetanes **2** to the cleavage products **3** and spiroepoxides **4**, the substituted dioxetanes **2e,g,i** were investigated. As the results in Table 2 reveal, the electron-withdrawing COOEt substituent in dioxetane **2e** (entry 1) inhibited the formation of the corresponding dioxole, while for the dioxetane **2g** (entry 3) with the electron-donating *t*-Bu substituent, the ratio of the cleavage product **3g** and the dioxole **5g** was 80:20. For the dioxetane **2i** (entry 4) with the stronger electron-donating OMe substituent, the ratio was 37:63.

Discussion

The thermal rearrangement of benzofuran dioxetanes **2** to spiroepoxides **4** has been previously described,[5b] and analogous transformations have been documented for naphthofuran dioxetanes.[8] That such rearrangements can be catalyzed by bromide ions (Scheme 1) appears to be unprecedented and constitutes a novel dioxetane transformation. For the thermal process, an

Scheme 2



intramolecular electron-transfer process was postulated,[5b] in which an electron is transferred from the electron-rich aromatic moiety to the dioxetane ring with subsequent reorganization of the bonds and final back-transfer of an electron. This is analogous to the intramolecular CIEEL process,[17] except that, in addition to the usual cleavage products **3**, also the novel spiroepoxides **4** are formed. Such a mechanism cannot, however, apply to the bromide ion-catalyzed rearrangement **2** → **4** since deliberate electron transfer to the benzofuran dioxetanes **2** by ferrocene and potassium superoxide generated exclusively the cleavage products **3** and not even traces of the spiroepoxides **4**. Instead, we propose that nucleophilic attack at the O-3 oxygen atom of the peroxide bond in the benzofuran dioxetane **2** initiates this rearrangement, as detailed in Scheme 2. In support of this mechanistic proposal, nucleophilic attack of bromide ions on simple dioxetanes has recently been documented,[7c] in which the peroxide bond is cleaved but the dioxetane C–C bond conserved.

For the unsymmetrical peroxide bond in the benzofuran dioxetanes **2**, the bromide ion has two options for nucleophilic attack, namely, at the O-2 or the O-3 oxygen atom. Stereoelectronic requirements for the S_N2 process dictate that the nucleophile comes in along the dioxetane peroxide bond. Thus, steric effects should dominate the preferred attack at the more exposed oxygen atom.[7c] Several experimental facts (Table 1) substantiate this notion. For example, the 4-substituted derivatives **2d** (entry 4) and **2h** (entry 8) are inert toward bromide ions, even on prolonged exposure. Yet, the 7-substituted case **2f** (entry 6) readily reacts to give a 6:94 mixture of **3f** and **4f**, i.e. the spiroepoxide dominates. Consequently, attack at the O-3 position is conducive for spiroepoxide formation and, when obstructed by *ortho* substitution (position C-4), the rearrangement **2** → **4** does not take place.

In support of this steric argument, another set of examples includes the phenyl-substituted dioxetanes **2j** (entry 10) and **2k** (entry 11), for which the former gives a **3j**:**4j** ratio of 52:48 and the latter exclusively the cleavage product **3k**. Again, the 3-phenyl substituent on the dioxetane ring in **2k**, as well as in the case of the derivative **2l** (entry 12), interferes with the Br^- attack at O-3 and, thus, spiroepoxide formation is suppressed. A similar situation applies to the 3-isopropyl derivative **2c** (entry 3), for which the **3c**:**4c** ratio is 35:65. Yet, the 2-chloromethyl derivative **2b** (entry 2) affords a much higher proportion of spiroepoxide, i.e. the **3b**:**4b** ratio is 8:92, which is essentially the same as that observed for the 2,3-dimethyl case **2a** (entry 1).

The latter comparison also brings out that electronic effects of substituents at the dioxetane ring play no significant role in controlling the ratio of cleavage to rearrangement products. Even more evident is the lack of electronic effects on the bromide ion-catalyzed rearrangement for the substitution in the benzo ring, as exemplified for the dioxetanes **2e** (entry 5), **2f** (entry 6), **2g** (entry 7), and **2i** (entry 9). Thus, irrespective of the ring position and the electronic nature of the substituent, the **3**:**4** ratio varies between 12:88 and 5:95 with no particular trend.

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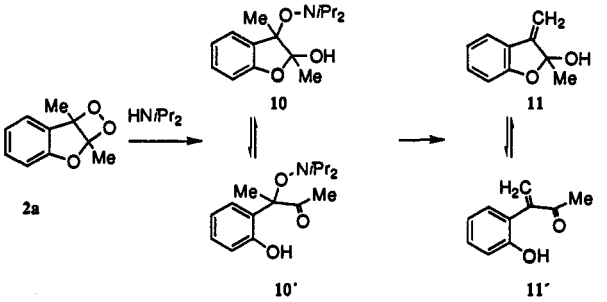
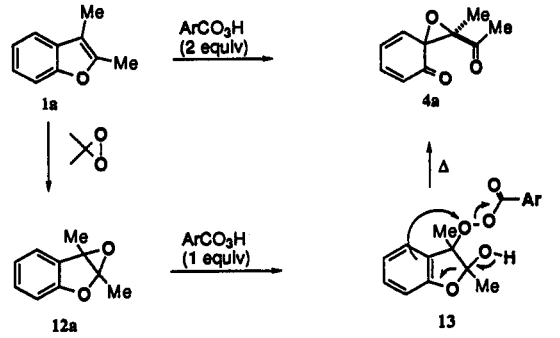
Scheme 3



Scheme 4

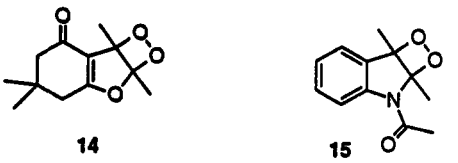


Additional support for preferential nucleophilic attack at the O-3 site of the dioxetane peroxide bond was obtained through the spectral observation of a persistent adduct, analogous to the simpler disubstituted dioxetanes.[7c] For this purpose, the benzofuran dioxetane **2a** was allowed to react with diisopropylamine (Scheme 3). Unfortunately, the initial amine adduct **10** could not be isolated because on attempted low-temperature chromatography it decomposed to the mixture of the allylic alcohol **11** and its ring-opened tautomer **11'**, which are formed by elimination of hydroxylamine, as established in the benzofuran epoxide chemistry.[18] Nevertheless, NMR spectroscopy revealed the intermediacy of the amine adduct **10** and its ring-opened tautomer **10'** (cf. the Experimental Section). The fact that no spiroepoxide **4a** is formed in the amine reaction can be rationalized by concomitant protonation of the incipient alkoxide ion at the O-2 site, which intercepts the subsequent rearrangement.

In analogy to the amine reaction, preferrential attack of the Br^- nucleophile at the O-3 position of the peroxide bond is reasonable. However, an essential step in the formation of the spiroepoxide product **4** is the subsequent nucleophilic attack on the hypobromite bond in the intermediate **8** (Scheme 2), with release of the bromide ion. A precedent for this unusual pathway, which competes favorably with dioxetane C–C bond scission to the cleavage product **3**, is our recent observation[15] that benzofuran epoxide **12a** on reaction with *m*-chloroperbenzoic acid (*m*-CPBA) also affords a mixture of cleavage product **3** and spiroepoxide **4** (Scheme 4). The key intermediate is the perester **13**, formed by nucleophilic addition of *m*-CPBA by the benzofuran epoxide at the C-3 position, which subsequently ejects *m*-chlorobenzoic acid through nucleophilic attack on the perester bond with generation of the spiroepoxide **4a**. Acid elimination by C–C bond scission to the dioxetane cleavage product **3a** operates in competition. The sequence of events displayed in Scheme 4 and the Scheffer–Weitz reaction[19] serve as good analogies for the bromide ion-catalyzed reaction of the benzofuran dioxetanes **2** (Scheme 2).

As to the competition between the rearrangement **2** → **4** *versus* fragmentation **2** → **3** processes, thermodynamic considerations suggest that the formation of the cleavage product **3** should dominate. We speculate that the driving force for the rearrangement derives from concomitant formation of the phenoxide ion on opening of the furan ring at the C-2 acetal center during the nucleophilic attack by Br^- at the O-3 peroxide site. The combined effect of release of dioxetane ring strain and gain of phenolate resonance circumvents the inherent propensity of dioxetanes to undergo C–C bond cleavage.

The subsequent intramolecular S_N2 process with regeneration of bromide ion and formation of the strained spiroepoxide appears to be optimal for the hypobromite intermediate **8** in view of the weak O–Br bond, the good leaving group ability of Br^-, and the high nucleophilicity of the phenolate ion. In this context, it is instructive to compare the efficiency of the bromide ion-catalyzed rearrangement of the benzofuran dioxetanes **2** with those of the related cases **14** and **15**. Thus, like the benzofuran dioxetanes



2, also the furan derivative **14** gives essentially quantitatively (>90% yield) the spiroepoxide.[9] On the other hand, the indole derivative **15**[20] afforded only the corresponding cleavage product. Presumably for this dioxetane the release of the amide ion is not competitive with dioxetane C–C bond cleavage.

It is important to realize that the bromide ion also catalyzes the decomposition of the benzofuran dioxetanes **2** into their cleavage products **3**. This is manifested by the fact that, much below the temperature of self-decomposition, Br^- promotes the **2** → **3** process. In view of the above mechanistic discussion, it is tempting to propose that nucleophilic attack at the O-2 site of the dioxetane peroxide bond to afford the alternative hypobromite intermediate **9** (Scheme 2) is responsible for the catalyzed cleavage. This cleavage represents a Grob-type fragmentation, although the optimal W-shaped transition state for scission of the dioxetane C–C bond is not fulfilled.[21]

As to the direct thermal decomposition of the benzofuran dioxetanes **2**, i.e. in the absence of bromide ions, the spiroepoxides **4** do not survive even at 20 °C and further rearrange to the dioxoles **5** (Scheme 1). Control experiments with authentic spiroepoxides **4** confirmed the thermolysis sequence **2** → **4** → **5**, so that the proportion of the dioxole **5** formed reflects the efficiency of the rearrangement of the dioxetanes **2** to the spiroepoxides **4**.

While for the bromide ion-catalyzed process there was no electronic substituent effect on the **3**:**4** product ratio for the dioxetanes **2a,e,g,i** (Table 1, entries 1, 5, 7, and 9), a pronounced trend was observed in the direct thermolysis (Table 2). Thus, the more electron-rich the aromatic moiety, the higher the amount of spiroepoxide (in terms of dioxole **5**), i.e. for **2e** (entry 1) exclusively cleavage product **3e**, while for **2i** (entry 4) predominantly spiroepoxide **4i** was formed.

Previously[5b] we interpreted such electronic tuning by substituents to reflect intramolecular electron transfer (CIEEL activity). Alternatively, this rearrangement might be triggered though intramolecular S_N2-type attack by the arene π system on the dioxetane peroxide bond, as visualized in Scheme 5.

In support of the latter mechanistic suggestion, we offer the quite analogous rearrangement of the benzofuran epoxides **12** to their quinonemethides **12'** (Scheme 5).[18] In contrast to the dioxetane–spiroepoxide transformation, the epoxide–quinonemethide process is reversible, but again electron donors on the arene moiety promote quinonemethide formation. However, with

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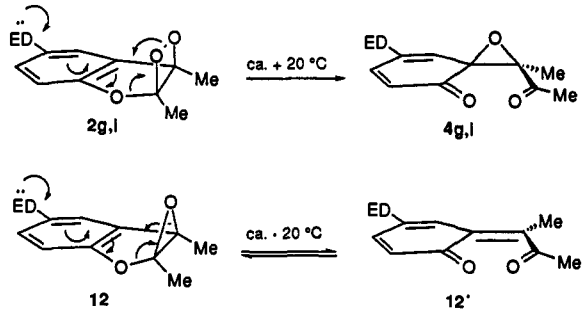
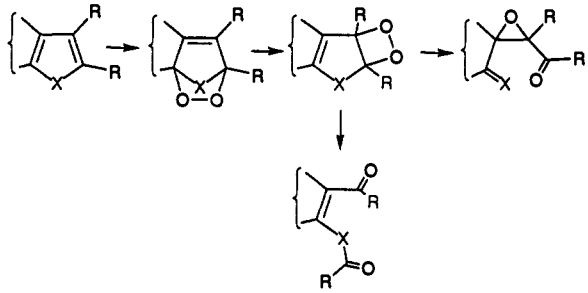
Scheme 5



Scheme 6



electron acceptors, the benzofuran epoxides **12** persist, while the dioxetanes **2** fragment to the cleavage products **3** (Table 2).

The present results display that benzofuran dioxetanes **2** readily rearrange to the quinonemethide spiroepoxides **4**, a process which appears to be of general scope in the photooxygenation of heteroarenes (Scheme 6). Thus, the initially formed heteroarene endoperoxides rearrange to the corresponding dioxetanes, which in turn either afford cleavage products or transpose to the spiroepoxide-type products. The endoperoxide–dioxetane rearrangement has been unequivocally established in the photooxygenation of furans,[9,22b] pyrroles,[23d] and fulvenes,[24] while for imidazoles[25] and oxazoles[26] it was postulated. We propose that the resulting dioxetanes may serve as precursors to epoxide and dioxetane cleavage products when the latter are observed in the photooxygenation of heteroarenes.[22-27]

Experimental Section

General Aspects. The photooxygenation procedure and the purification of the solvents and products were identical to those reported before.[28] Benzofurans **1a,d–f,i–k** were prepared according to literature procedures.[10] *2a,7b-Dihydro-2a,7b-dimethyl-1,2-dioxeto[3,4-b]benzo[d]furan* (**2a**)[5b] and *2a,7b-dihydro-2a-methyl-7b-phenyl-1,2-dioxeto[3,4-b]benzo[d]furan* (**2k**)[15] were prepared by known procedures, and physical and spectral data matched those reported. Benzofuran **1l** was supplied by Dr. M. Sauter, while *2,3-dimethyl-4,6-di-tert-butylbenzo[b]furan* (**1h**) was prepared by J. Bialas, both from the University of Würzburg. The synthesis of the unknown benzofurans **1b,c,g** and the spectral and physical data are given as supplementary material.

Synthesis of the Benzofuran Dioxetanes 2. General Procedure. Into a 15-mL test tube, equipped with gas inlet and outlet tubes, was placed a solution of the particular benzofuran **1** (0.5–1.2 mmol) and ca. 5 mg of tetraphenylporphine (TPP) in 2–5 mL of CH_2Cl_2 [distilled three times from EDTA and passed over basic alumina (activity grade 1)]. The test tube, cooled by means of a methanol bath that was thermostated with a KT 290 S cryostat (Colora Messtechnik GmbH), was irradiated externally with two Osram sodium lamps (NAV-E, 250 W) while a gentle stream of oxygen gas (dried over $CaCl_2$/indicating silica gel/P_2O_5) was allowed to pass through the solution. The progress of the reaction was monitored by TLC, and after completion, the solution was concentrated by distillation (0 °C, 16 Torr) and the residue chromatographed on silica gel (60–230 mesh, substrate/adsorbant ca. 1:100) at the specified temperature.

Dioxetanes **2a,k** were prepared according to literature procedures.[14] The spectral and physical data matched those reported. The synthesis of the dioxetanes **2** and the cleavage products **3** and their spectral and physical data are given as supplementary material.

Thermolysis of the Benzofuran Dioxetanes 2a,e–g,i. General Procedure. A sample of the corresponding dioxetane **2** (0.07–0.60 mmol) was dissolved in 800 μL of $CDCl_3$, which was freshly passed through basic alumina oxide (activity grade 1), and the solution was kept at 20 °C for the required time to form the cleavage product **3** and the dioxolane **5**. The ratio of decomposition product **3** and dioxolane **5** was determined by ^1H NMR analysis (error ±5%). The product distribution is given in Table 2, and the experimental details are given as supplementary material.

Bromide Ion-Catalyzed Rearrangement of Dioxetanes 2a–e. General Procedure. A sample of the required dioxetane **2** (0.1–0.6 mmol) was dissolved in 700 μL of $CDCl_3$, and at −20 to 0 °C, a solution of 1.72 mg (8.18 μmol) of freshly recrystallized (from EtOH) tetraethylammonium bromide (Et_4NBr) in 100 μL of $CDCl_3$ was added. The reaction progress was monitored directly by NMR. The conversion was ca. 100% as indicated additionally by the negative peroxide test (KI/HOAc). Without Et_4NBr, the dioxetanes **2** underwent no significant (<5%) decomposition under these conditions. Isolation and purification procedures of the products are reported individually. The spiroepoxides **4** are too labile or reactive for isolation and rearrange to the dioxoles **5** or dimerize to the Diels–Alder adducts **6**. The product distributions are given in Table 1, the experimental details are given as supplementary material.

Transformations of the Spiroepoxide 4a. *Dimerization.* A solution of 37.2 mg (0.209 mmol) of spiroepoxide **4a**, prepared as reported above, was concentrated at 0 °C and 16 Torr, and crystallization of the residue yielded 35.4 mg (95%) of spirodimer **6a** as the only detectable isomer. The spectral and physical data matched those reported.[5b]

Thermolysis. The yellow solution of 56.7 mg (0.0450 mmol) of spiroepoxide **4a** in 800 μL of $CDCl_3$ was kept at 20 °C until complete decoloration (12 h). After filtration over silica gel and elution with CH_2Cl_2, 52.1 mg (92%) of the benzodioxole **5a** was isolated on removal of the solvent (20 °C, 16 Torr). The spectral and physical data matched those reported in the literature.[5b]

[4 + 2] Cycloaddition of *N*-Methyl-1,2,4-triazoline-3,5-dione (MTAD). A sample of 35.0 mg (0.196 mmol) of dioxetane **2a** was dissolved in 10 mL of absolute CH_2Cl_2 at 0 °C, and 1.50 mg (7.00 μmol) of Et_4NBr and 30.3 mg (0.264 mmol) of MTAD in 1 mL of CH_2Cl_2 were added. The temperature was kept at 0 °C for 1 h, the solvent removed by distillation (20 °C, 16 Torr), and the residue recrystallized from CH_2Cl_2/pentane to give 47.0 mg (81%) of *13-acetyl-4,13-dimethyl-12-oxacyclopropanespiro-2,4,6-triazatricyclo[5.2.2.0^{2,6}]undec-10-ene-3,5,9-trione* (**7a**) as colorless needles, mp 208–209 °C. IR (CCl_4): ν 2960, 2860, 1790, 1740–1710, 1450, 1400, 1360, 1260, 1100, 1010 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.55 (s, 3 H, 17-H), 2.37 (s, 3 H, 16-H), 3.06 (s, 3 H, 14-H), 4.86 (dd, $J_{7,11}$ = 5.9 Hz, $J_{7,10}$ = 1.9 Hz, 1 H, 7-H), 5.30 (dd, $J_{1,10}$ = 5.6 Hz, $J_{1,11}$ = 1.8 Hz, 1 H, 1-H), 6.59 (ddd, $J_{10,11}$ = 8.2 Hz, $J_{10,1}$ = 5.6 Hz, $J_{10,7}$ = 1.9 Hz, 1 H, 10-H), 6.80 (ddd, $J_{11,10}$ = 8.2 Hz, $J_{11,7}$ = 5.9 Hz, $J_{11,1}$ = 1.8 Hz, 1 H, 11-H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.8 (q), 25.9 (q), 26.0 (q), 55.0 (d), 60.6 (d), 64.1 (s, C-13), 70.4 (s, C-8), 128.1 (d), 133.0 (d), 156.0 (s), 156.9 (s), 191.8 (s), 203.9 (s). Anal. Calcd for $C_{13}H_{13}N_3O_5$ (291.2): C, 53.61; H, 4.50; N, 14.43. Found: C, 53.33; H, 4.03; N, 14.92.

Thermolysis of Dioxetane 2a in the Presence of MTAD. A sample of 15.3 mg (0.086 mmol) of dioxetane **2a** dissolved in 800 μL of $CDCl_3$ was heated in the presence of 10.8 mg (0.094 mmol) of MTAD at 20 °C for 24 h. Proton NMR analysis revealed formation of the cleavage product

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3a and the [4 + 2] cycloadduct **7a** in a ratio of 89:11. The spectral data of the cleavage product **3a** matched those reported in the literature,[5b] and those of the [4 + 2] cycloadduct **7a** matched those reported above.

Reactions of Dioxetane 2a with Potassium Halides and Potassium Superoxide. *General Procedure.* A sample of 10.2 mg (56.2 μmol) of dioxetane **2a** and 1.33 mg (5.03 μmol) of 18-crown-6 ether was dissolved in 800 μL of cold $CDCl_3$, and at 0 °C, the required potassium salt was added. The reaction progress was monitored by NMR spectroscopy.

Potassium Chloride. Treatment of the dioxetane **2a** with 5.00 mg of KCl yielded after 6 h the cleavage product **3a** as the only detectable product (47% conversion).

Potassium Bromide. Treatment of the dioxetane **2a** with 5.00 mg of KBr yielded after 10 min the cleavage product **3a** and the spiroepoxide **4a** in a ratio of 8:92 (100% conversion).

Potassium Iodide. Treatment of the dioxetane **2a** with 5.00 mg of KI yielded after 10 min the cleavage product **3a** and the spiroepoxide **4a** in a ratio of 81:19 (100% conversion).

Potassium Superoxide. Treatment of the dioxetane **2a** with 5.00 mg of KO_2 yielded after 5 min the cleavage product **3a** as the only detectable product (100% conversion).

Reaction of Dioxetane 2a with Ferrocene. A sample of 15.4 mg (86.0 μmol) of dioxetane **2a** in 800 μL of cold $CDCl_3$ was treated with 2.89 mg (0.015 μmol) of ferrocene at −20 °C. Immediate NMR analysis revealed 100% conversion exclusively to the cleavage product **3a**.

Reaction of Dioxetane 2a with Diisopropylamine. *N*-[(2,3-Dihydro-2,3-dimethyl-2-hydroxybenzo[*b*]furan-3-yl)oxy]-*N*,*N*-diisopropylamine (10), *N*-[[2′-(Hydroxyphenyl)-3-oxybutan-2-yl]oxy]-*N*,*N*-diisopropylamine (10′), 2,3-Dihydro-3-methylene-2-methylbenzo[*b*]furan-2-ol (11), and 3-(2′-Hydroxyphenyl)-3-buten-2-one (11′). A sample of 250 mg (1.40 mmol) of dioxetane **2a** in 800 μL of cold $CDCl_3$ was treated with 425 mg (4.20 mmol) of diisopropylamine at −25 °C for 3 d until complete conversion of the dioxetane (TLC control). NMR monitoring at −20 °C revealed >95% conversion to the adduct **10** and less than 5% cleavage product **3a**. Upon standing at 20 °C the characteristic carbon resonances of the ring-opened tautomer **10′** could be observed in a mixture with the deoxygenation products **11** and **11′**. Chromatography (CH_2Cl_2, −10 °C) gave 150 mg (65%) of the known[5b] deoxygenation products **11** and **11′**. The spectral data matched those reported.

Adduct 10. ^1H NMR ($CDCl_3$, 200 MHz, −30 °C): δ 0.73 (d, J = 7.0 Hz, 6 H), 1.00 (d, J = 7.0 Hz, 6 H), 1.50 (s, 3 H), 1.52 (s, 3 H), 2.42–2.75 (m, 2 H), 6.60–6.82 (m, 2 H), 7.02–7.26 (m, 2 H), 9.07 (br s, 1 H). ^{13}C NMR ($CDCl_3$, 50 MHz, −30 °C): δ 54.2 (d), 78.6 (s), 110.1 (s), 112.9 (d), 119.6 (d), 125.1 (d), 129.4 (d), 129.8 (s), 156.6 (s). The remaining aliphatic resonances could not be assigned due to severe overlap with those of the ring-opened tautomer **10′**.

Adduct 10′. ^1H NMR ($CDCl_3$, 200 MHz): δ 0.83 (d, J = 7.0 Hz, 6 H), 1.23 (d, J = 7.0 Hz, 6 H), 1.62 (s, 3 H), 2.05 (s, 3 H), 2.42–2.75 (m, 2 H), 6.60–6.82 (m, 2 H), 7.02–7.26 (m, 2 H), 10.31 (br s, 1 H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 27.1 (q), 57.0 (d), 81.6 (s), 118.9 (d), 119.2 (d), 130.3 (d), 130.7 (d), 148.3 (s), 161.8 (s), 204.7 (s). The remaining aliphatic resonances could not be assigned due to severe overlap with those of the ring-opened tautomer **10′** and the deoxygenation products **11** and **11′**.

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Supplementary Material Available: Experimental details and physical and spectral data for **1b,c,g**, **2b–l**, **3b–l**, **4a–c,e–g,i,j,l**, **5e,g,i,l**, and **6c,j** (18 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from ACS; see any current masthead page for ordering information.