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Thermolysis of Disubstituted 1,2-Dioxetanes: Activation Parameters and Chemiexcitation Yields

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ABSTRACT

trans-3-Methyl-4-(p-anisyl)-1,2-dioxetane 1, trans-3-methyl-4-(o-anisyl)-1,2-dioxetane **2**, *3-methyl-3-benzyl-1,2-dioxetane* **3**, *and 3-methyl-3-p-methoxybenzyl-1,2-dioxetane* **4** *were synthesized in low yield by the β-bromo hydroperoxide method. The activation parameters were determined by the chemiluminescence method (for 1* $\Delta G\ddagger = 22.8 \pm 0.3$ *kcal/mol,* $\Delta H\ddagger = 22.2$, $\Delta S\ddagger = -1.7$ *e.u.,* $k_{60} = 7.6 \times 10^{-3}s^{-1}$*; for* **2** $\Delta G\ddagger + 23.6 \pm 0.3$ *kcal/mol,* $\Delta H\ddagger = 22.8$, $\Delta S\ddagger = -2.2$ *e.u.,* $k_{60} = 2.5 \times 10^{-3}s^{-1}$*; for* **3** $\Delta G\ddagger = 24.0 \pm 0.4$ *kcal/mol,* $\Delta H\ddagger = 23.1$, $\Delta S\ddagger = -2.7$ *e.u.,* $k_{60} = 1.2 \times 10^{-3}s^{-1}$*; for* **4** $\Delta G\ddagger = 24.0 \pm 0.2$ *kcal/mol,* $\Delta H\ddagger$, $= 23.2$, $\Delta S\ddagger$, $= -2.4$ *e.u.,* $k_{60} = 1.2 \times 10^{-3}s^{-1}$*). Thermolysis of* **1–4** *produced excited carbonyl fragments (direct production of high yields of triplets relative to excited singlets) [chemiexcitation yields* ϕ^T, ϕ^S, *respectively: for* **1** *0.02, 0.0001; for* **2** *0.02, 0.0001; for* **3** *0.03, 0.0002; for* **4** *0.02, 0.0001]. The effect of para-methoxyaryl substitution was consistent with electronic effects. The ortho substitution in* **2** *resulted in an increase in stability of the dioxetane, opposite that observed for an electronic effect. The results are discussed in relation to a diradical-like mechanism.*

The thermolysis of alkyl and/or phenyl substituted dioxetanes has been shown to produce carbonyl fragments, one of which may be produced in an excited state (direct, high yields of excited triplets) [1]. Historically, two mechanistic extremes have been proposed [1] to describe the thermal decomposition of simply substituted dioxetanes: (a) diradical and (b) concerted (Scheme 1). Electron-transfer type decomposition [2] that occurs for certain peroxides does not occur readily with simply substituted dioxetanes. Most studies have been interpreted to support a diradical-type process. For example, steric effects [3a,b], inverse deuterium isotope effect for CD_3 groups [3c], lack of additional ring-strain effect on Ea [3d], lack of dioxetane ring position deuterium isotope effect [3e], Hammett-type studies [3f,g], insensitivity of Ea to phenyl for methyl substitution [3i], absence of solvent effects [3j], cis/trans isomer stability [3k], and group additivity-type calculations [3l] are consistent with a two-step mechanism. A merged mechanism has also been proposed [4] based on effect of the degree and pattern of methyl substitution. We report here the synthesis and characterization of a series of disubstituted dioxetanes that shows steric effects can be more important than electronic effects with regard to dioxetane stability.

RESULTS

trans-3-Methyl-4-(*p*-anisyl)-1,2-dioxetane **1**, trans-3-methyl-4-(*o*-anisyl)-1,2-dioxetane **2**, 3-methyl-3-benzyl-1,2-dioxetane **3**, and 3-methyl-3-*p*-methoxybenzyl-1,2-dioxetane **4** were synthesized in low yield by the Kopecky method [5], closure of the corresponding β-bromo hydroperoxides with base at low temperature (Scheme 2). The β-bromo hydroperoxides were synthesized by the Kopecky procedure [5], treatment of the corresponding alkenes with an electrophilic bromine source in the presence of concentrated hydrogen peroxide at low

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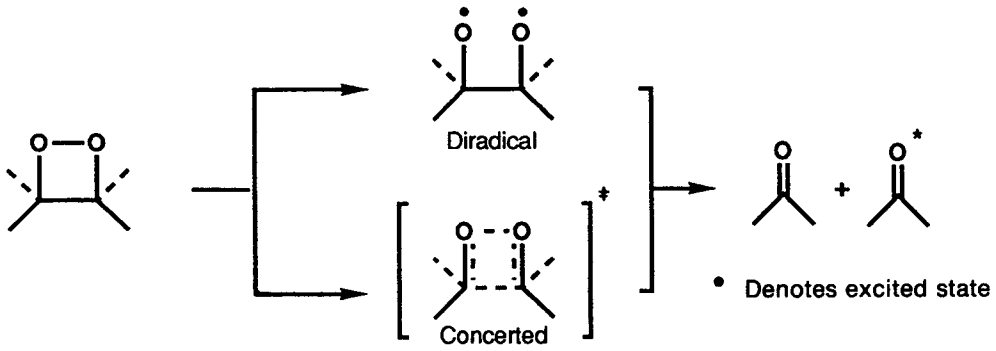
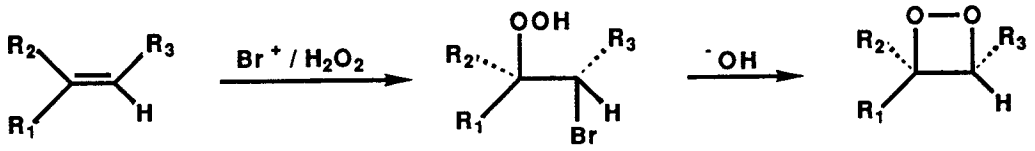


SCHEME 1



1 R_1 = p-$MeOC_6H_4$; R_2 = H; R_3 = CH_3

2 R_1 = o-$MeOC_6H_4$; R_2 = H; R_3 = CH_3

3 R_1 = $C_6H_5CH_2$; R_2 = CH_3; R_3 = H

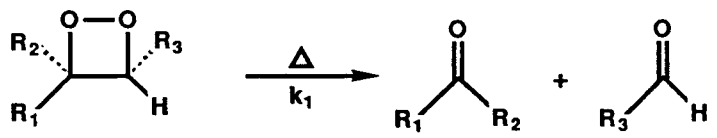
4 R_1 = p-$MeOC_6H_5CH_2$; R_2 = CH_3; R_3 = H

SCHEME 2

temperature (Scheme 2). The method has been shown to be stereospecific; *trans*-alkenes yield *trans*-dioxetanes exclusively [1, 3k]. The dioxetanes were purified by low-temperature column chromatography and characterized by ^1H nuclear magnetic resonance (NMR) spectroscopy. Dioxetanes **1–4** were further characterized by analysis of their thermolysis products; in all cases only the expected cleavage products were produced (Reaction 1).

The rates of thermolysis of dioxetanes **1–4** were monitored by the decay of chemiluminescence intensity in aerated xylenes with or without added fluorescers at constant temperature (±0.2°). The rates of thermal decomposition were cleanly first order for at least three half-lives and showed no dependence on the type or amount of added fluorescer. The first-order rate constants (k_1) were determined over a 50°C temperature range. The activation parameters were determined by the Arrhenius method. Correlation coefficients were 0.995 or greater for all cases. The activation parameter data (95% confidence limits on errors) are shown in Table 1.

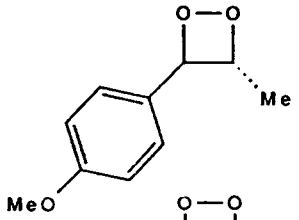
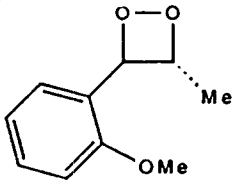
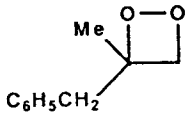
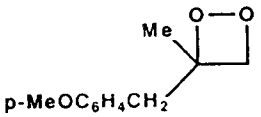
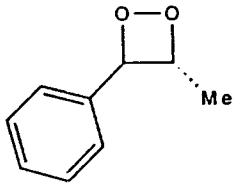
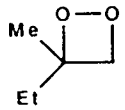
Without the presence of added fluorescers, the thermolyses of dioxetanes **1–4** showed only weak chemiluminescence. Addition of 9,10-dibromoanthracene (DBA) or 9,10-diphenylanthracene (DPA) greatly increased the intensity of chemiluminescence without affecting the kinetics. The yields of chemiexcitation generated during dioxetane thermolysis were determined by the DBA/DPA (chemiluminescence) method. For all four dioxetanes, thermolysis directly produced high yields of excited triplets (ϕ^T) and low yields of excited singlets (ϕ^S). The ϕ^T values were 2%–3%. The results are summarized in Table 2.



(1)

REACTION 1

TABLE 1. Activation Parameters for the Thermolysis of Dioxetanes **1–4** in Xylenes

No.	Dioxetane	Ea (kcal/mol)	logA	ΔH‡[a]	ΔS‡e.u.[a]	ΔG‡ kcal/mol[a]	$k_1 s^{-1}$ (60°C)
1		22.9 ± 0.3[b]	12.9	22.2	−1.7	22.8 ± 0.3[b]	7.6×10^{-3}
2		23.5 ± 0.3	12.7	22.8	−2.2	23.6 ± 0.3	2.5×10^{-3}
3		23.8 ± 0.4	12.7	23.1	−2.7	24.0 ± 0.4	1.2×10^{-3}
4		23.9 ± 0.2	12.8	23.2	−2.4	24.0 ± 0.2	1.2×10^{-3}
5		23.2 ± 0.2[c]	12.8	22.6	−2.4	23.2 ± 0.2	3.4×10^{-3}
6		24.5 ± 0.2[d]	13.1	23.8	−0.9	24.1 ± 0.2	1.0×10^{-3}

[a] Calculated at 60°C
[b] All errors reported at 95% confidence limits.
[c] Lit. [3k].
[d] Lit. [3b].

DISCUSSION

Dioxetane **1** is less stable than the parent compound, *trans*-3-methyl-4-phenyl-1,2-dioxetane **5** by 0.4 kcal/mol (in ΔG‡). The relative stability of **1** can be regarded as a normal electronic effect on the diradical mechanism. For example, 3-methyl-3-(*p*-anisyl)-1,2-dioxetane has been shown [3f] to be less stable than 3-methyl-3-phenyl-1,2-dioxetane by roughly 0.7 kcal/mol (ΔG‡); an electronic effect essentially identical to that observed in the present case. Hammett studies on other less structurally similar dioxetanes also have shown that the electronic effect of a *p*-methoxyaryl group should produce a slight decrease in dioxetane stability [3g,h].

Dioxetane **2** is the first ortho-phenyl substituted compound to be reported. **2** appears to be slightly more stable than the parent compound, **5**, and is clearly more stable (~1 kcal/mol) than the electronically similar para isomer **1**. Since the che-

TABLE 2 Chemiexcitation Yields[a] for the Thermolysis of Dioxetanes **1–4** in Xylenes

Dioxetane	ϕ^T	ϕ^S	ϕ^T/ϕ^S [b]
1	0.02	0.0001	200
2	0.02	<0.0001	200
3	0.03	0.0002	150
4	0.02	0.0001	200

[a] Instrument calibrated with tetramethyl-1,2-dioxetane: ϕ^T = 0.30; ϕ^S = 0.002 (DBA/DPA method).

[b] Estimate of triplet/singlet ratio since light yields are rounded off and the chemiluminescence method has error limits of ±50% of observed values.

miexcitation yields are unaffected, no change in mechanism is likely. The unexpected stability of **2** can not be electronic in nature but must be the result of conformational or steric effects. Previous studies have shown that changes in dioxetane-ring torsion angle can effect dioxetane stability [3d, 6]. However, molecular mechanics calculations (MM2) [7] predicted that the conformations of **1**, **2**, and **5** are essentially identical with dioxetane-ring torsion angles of zero degrees and torsion angles of 52–60° between the planes of the aryl group and that of the dioxetane. Thus, torsion-angle differences are not involved for this case.

The relative stabilities of alkyldioxetanes have been shown [3b] to correlate with the number of formal substitution ("branching") on a 3-"methyl" group, presumably because the increase in steric interactions hinder O—O bond scission. This effect has been shown to be largely due to direct interactions with the oxygen closest to the site rather than interactions with groups across the ring. The molecular mechanics results also rule out this type of steric hindrance (3,3-effect) as a cause of the increased stability of **2**.

However, the MM2 calculations did provide an insight into the origin of the increased stability of **2**. The major structural difference found was a large barrier to rotation around the aryl-dioxetane ring bond in **2** while similar rotation in **1** and **5** showed essentially no unusual barriers. Interestingly, the observed barrier in **2** was due to the interaction of the *o*-methoxy group with the hydrogen on position 4 (O···H distance 1.5 Å). This implies that the increased stability noted for this case is due to a 3,4-buttressing effect. This appears to be the first example of a measurable 3,4-steric effect on simple dioxetane thermolysis. The results predict that dioxetanes with larger ortho-substituents and 2,6-disubstituted phenyl groups should show even larger increases in stability.

The stabilities of dioxetanes **3** and **4** are essentially identical, showing that the electronic effect of the *p*-methoxy group in **4** is negligible as expected. Previous work [3i] had shown that 3-methyl-3-phenyl-1,2-dioxetane had similar properties to those of 3,3-dimethyl-1,2-dioxetane. This indicated that phenyl groups showed about the same steric influences as methyl groups. In agreement with this conclusion, properties of **3** and **4** are indistinguishable from those of 3-methyl-3-ethyl-1,2-dioxetane [3b].

The chemiexcitation yields for the thermolysis of dioxetanes **1–4** were normal for disubstituted dioxetanes, between 2% and 10% [1]. Furthermore, the ϕ^S values were extremely low: around 0.01%. Thus, the chemiexcitation yields and the ratios of excited triplets to excited singlets ($\phi^T/\phi^S \approx 200$) showed no unexpected trends or deviations that could be indicative of a change in mechanism. All the chemiexcitation data suggest that dioxetanes are undergoing thermolysis by the diradical-like mechanism.

EXPERIMENTAL SECTION

All solvents were of reagent grade. ^{1}H NMR spectra were recorded on a Varian 360L spectrometer. Gas chromatography studies were performed on a Varian 920-gas chromatograph with a 6 ft × 0.25 in SE-30 on chromosorb W column. 9,10-Diphenylanthracene (Aldrich) and 9,10-dibromoanthracene (Aldrich) were recrystallized from xylenes (Aldrich) before use. 2-Methyl-3-phenyl-1-propene (Wiley Organics) and E-1-(*p*-anisyl)propene (*trans*-anethole, Aldrich) were commercially available and were used without further purification. 2-Methyl-3-(*p*-anisyl)-1-propene was prepared from 1-(*p*-anisyl)-2-propanone (Wiley Organics) by the Wittig route [8]. E-1-(2-anisyl)propene [9] was prepared by the reaction of 1-(2-hydroxyphenyl)propene (2-propenylphenol, Aldrich) with dimethyl sulfate in the presence of base [10] and distilled (reduced pressure) prior to use. Molecular mechanics calculations were carried out on a micro VAX using the MM2 program MODEL Version KS 2.93 available from Dr. K. Steliou, University of Montreal, Canada.

Dioxetane Synthesis

The following two-step procedure for the synthesis of *trans*-3-methyl-4-(*p*-anisyl)-1,2-dioxetane **1** was employed for the preparation of all the compounds. A 30-mmol sample of *trans*-1-(*p*-anisyl)propene was converted to the β-bromo hydroperoxide by the Kopecky procedure [5]. The β-bromo hydroperoxide, (S*, R*)-1-(*p*-anisyl)-1-hydroperoxy-2-bromopropane, a clear, viscous oil (Caution!) was purified by precipitation from pentane at −78°C (max. yield ~60%): ^{1}H NMR ($CDCl_3$) δ 1.7 (d, J = 7Hz, 3H); δ 3.72 (s, 3H); δ 4.2–4.7 (m, 1H); δ 4.9 (d, J = 6 Hz, 1H); δ 6.6–7.4 (AB, 4H); δ 8.5 (br s, 1H); ^{1}H NMR data for the other hydroperoxides—for (S*, R*)-1-*o*-anisyl-1-hydroperoxy-2-bromopropane: δ 1.6 (d, J = 6Hz, 3H), δ 3.73 (s, 3H), δ 4.2–4.8 (m, 1H),

δ 5.45 (d, J = 5 Hz, 1H), δ 6.65–7.5 (m, 4H), δ 8.4 (s, 1H); for 1-phenyl-2-methyl-2-hydroperoxy-3-bromopropane: δ 1.25 (s, 3H), δ 2.93 (br s, 2H), δ 3.5 (s, 2H), δ 7.2 (br s, 5H), δ 7.7 (s, 1H); for 1-*p*-anisyl-2-methyl-2-hydroperoxy-3-bromopropane: δ 1.25 (s, 3H), δ 2.9 (s, 2H), δ 3.55 (s, 2H), δ 3.8 (s, 3H), δ 6.8–7.4 (AB, 4H); δ 7.7 (s, 1H). Active oxygen content was generally 95%. All the β-bromo hydroperoxides were isolated in approx. 60 ± 5%.

Purified β-bromo hydroperoxide (~14 mmol, caution!) was placed in 5 mL of carbon tetrachloride or methylene chloride with rapid magnetic stirring and cooled by an ice bath. A solution of 2.5 g of potassium hydroxide in 5–10 mL of cold, deionized water was added dropwise (15 min) to the β-bromo hydroperoxide solution in the dark to yield a two-phase mixture. The reaction time for dioxetane synthesis was optimized: for **1**, **2**, and **4**, 24 h while for **3**, 1 h. The extended reaction times required for the closure of the methoxyaryl substituted β-bromo hydroperoxides seemed to be related to their water solubility and a tendency to form emulsions. Additional extractions of the water layer with methylene chloride were required to obtain reasonable yields of dioxetane in these three cases. The pale-yellow organic layers were separated, dried over magnesium sulfate, and filtered. The solvent was removed under reduced pressure and the dioxetane purified by column-chromatography at −78°C using a jacketed 1-cm inside diameter (id) column packed with 20 g of silica gel containing 1% Na_2 EDTA (pentane). The dioxetane in CCl_4 was added to the column and washed with 50 mL of pentane followed by successive 50-mL additions of a 5% methylene chloride/pentane (v/v) step gradient. Fractions were assayed for dioxetane content by placing a small aliquot into a DBA solution in the chemiluminescence apparatus. Fractions containing the most dioxetane were combined and the solvent removed under reduced pressure. The purified dioxetanes (**1–4**) were oils. The purity was checked by ^1H NMR spectroscopy. Dioxetane samples that were less than 95% pure were passed through the column a second time. In general, the major impurities were the corresponding epoxides the presence of which had no effect on dioxetane properties. The overall yield of dioxetane was 1%–2% for all four cases. The dioxetanes were stored in CCl_4 at −30° or lower. Little decomposition was noted even after several months of storage. The ^1H NMR data (CCl_4) are: for **1** δ 1.4 (d, J = 5 Hz, 3H); δ 3.8 (s, 3H), δ 5.5–5.9 (m, 1H, δ 5.97 (d, J = 7 Hz, 1H), δ 6.8–7.6 (AB, 4H); for **2**, δ 1.6 (d, 6 Hz, 6H); δ 3.74 (s, 3H); δ 5.0–5.5 (m, 1H), δ 6.2 (d, 8 Hz, 1H), δ 6.6–7.7 (m, 4H); for **3** δ 1.5 (s, 3H); δ 3.2 (AB, 2H), δ 5.05 (AB, 2H); δ 7.2 (br s, 5H); for **4** δ 1.5 (s, 3H); δ 3.2 (AB, 2H), δ 3.7 (s, 3H), 5.0 (AB, 2H), δ 6.7–7.2 (AB, 4H). The ^1H NMR data for **1** and **2** showed the dioxetanes to be the *trans*-isomers (the 4-methyl groups of *cis*-isomers would show signals at δ 1.1) [3k].

Product Studies

The following general procedure was employed for the thermolysis of dioxetanes **1–4**. A solution of dioxetane (approx. 0.2 M) in CCl_4 was heated at 60°C in a sealed NMR sample tube until the yellow color disappeared. In all cases, the expected carbonyl fragments were the sole products detected by NMR spectroscopy. The formaldehyde generated from the cleavage of **3** and **4** was not observed. The carbonyl products were identified by comparison with authentic samples.

Kinetic Studies

The chemiluminescence monitoring system is essentially identical with that previously described [1]. The reaction cell was jacketed and the temperature maintained by using a constant temperature bath. The temperature in the cell (±0.2°C) was monitored by use of a YSI Model 425C apparatus with a series 400 probe. The cell was pretreated with a conc. aq. Na_2 ethylene diaminetetraacetic acid (EDTA) solution and washed with solvent before use. Kinetic experiments were carried out employing xylenes (mixture of isomers) as solvent. The initial dioxetane concentrations were approx. 10^{-4} M in order to avoid induced decomposition. Experiments carried out without added fluorescer and with low concentration (~10^{-3}) of DBA or DPA were of the first order for at least three half-lives and showed no measurable dependence on the type or amount of added fluorescer.

Chemiexcitation Yields

The instrument was calibrated with tetramethyl-1,2-dioxetane [3d] by taking the triplet yield (ϕ^T) determined by the DBA method as 0.30 at 60°C. All measurements were carried out at 60°C with a constant concentration of dioxetane. The ϕ^T and ϕ^S yields were calculated by a method that has been discussed in detail [1g]. The concentration of dioxetane was determined by ^1H NMR spectroscopy vs concentration of added standard. The experimental error by the DBA/DPA method is estimated to be ±50% of observed value.

Acknowledgment

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