Heteroatom Chemistry
Volume 12, Number 6, 2001

Thermolysis of 3-Alkyl-3-Methyl-1,2-Dioxetanes: Activation Parameters and Chemiexcitation Yields

Alfons L. Baumstark, Sean L. Anderson, Chariety J. Sapp, and Pedro C. Vasquez

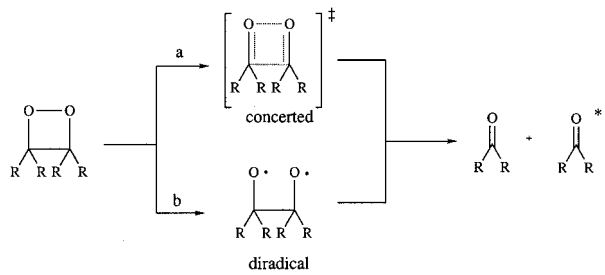
Department of Chemistry, Center for Biotechnology and Drug Design, Georgia State University, Atlanta, GA 30303

Received 02 November 2000; revised 22 January 2001

ABSTRACT: *3-Methyl-3-(3-pentyl)-1,2-dioxetane* **1** *and 3-methyl-3-(2,2-dimethyl-1-propyl)-1,2-dioxetane* **2** *were synthesized in low yield by the α-bromohydroperoxide method. The activation parameters were determined by the chemiluminescence method (for* **1** $\Delta H‡ = 25.0 \pm 0.3$ *kcal/mol,* $\Delta S‡ = -1.0$ *entropy unit (e.u.),* $\Delta G‡ = 25.3$ *kcal/mol,* k_1 *(60°C)* $= 4.6 \times 10^{-4} s^{-1}$*; for* **2** $\Delta H‡ = 24.2 \pm 0.2$ *kcal/mol,* $\Delta S‡ = -2.0$ *e.u.,* $\Delta G‡ = 24.9$ *kcal/mol,* k_1 *(60°C)* $= 9.2 \times 10^{-4} s^{-1}$*. Thermolysis of* **1–2** *produced excited carbonyl fragments (direct production of high yields of triplets relative to excited singlets) (chemiexcitation yields for* **1:** $\phi^T = 0.02$, $\phi \leq 0.0005$*; for* **2:** $\phi^T = 0.02$, $\phi^S \leq 0.0004$*). The results are discussed in relation to a diradical-like mechanism.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:459–462, 2001

INTRODUCTION

The thermolysis of phenyl-substituted and/or alkyl-substituted dioxetanes has been shown to produce carbonyl fragments, one of which may be produced in an excited state (direct production of high yields of excited triplets relative to excited singlets) [1]. Historically, two mechanistic extremes have been proposed [1] to describe the thermal decomposition of simply substituted dioxetanes: (1) concerted and (2) diradical (Scheme 1). The electron-transfer type processes [1,2] that occur for certain peroxides do not occur readily with simply substituted dioxetanes. Most mechanistic studies have been interpreted to support a diradical-type two-step mechanism [3]. A merged mechanism has also been proposed [4] based on effect of the degree and pattern of methyl substitution. Previous results on alkyl dioxetanes have shown that relative stability depended on the steric interactions of the substituents [3]. We report here the synthesis and characterization of two 3,3-disubstituted dioxetanes in which the effective steric size of one substituent is varied.

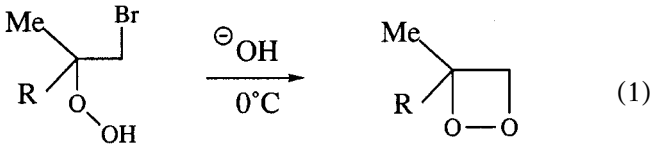


SCHEME 1

Correspondence to: Alfons L. Baumstark.
Contract Grant Sponsor: Ronald E. McNair Post-baccalaureate Program (S.A., C.S.).
Contract Grant Sponsor: Alliance for Minority Participation Program.
Contract Grant Number: OSP-98-01-661-001.

RESULTS

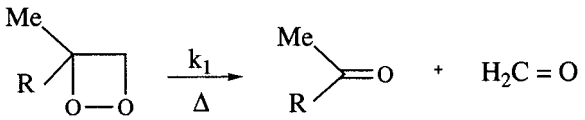
3-Methyl-3-(3-pentyl)-1,2-dioxetane **1** and 3-methyl-(2,2-dimethyl-1-propyl)-1,2-dioxetane **2** were synthesized in low yield by the Kopecky method [1], with closure of the corresponding α-bromohydroperoxides with a base at low temperature (Reaction 1).



(1)

1 R = 3-Pentyl
2 R = Neopentyl

The α-bromohydroperoxides were synthesized by the Kopecky procedure [1], treatment of the corresponding alkenes with an electrophilic bromine source in the presence of concentrated hydrogen peroxide (caution!) at low temperature in fair yield. The dioxetanes were purified by low-temperature column chromatography and characterized by ^{1}H NMR and ^{13}C NMR spectroscopy. Dioxetanes **1–2** were further characterized by analysis of their thermolysis products; in all cases, only the expected cleavage products were produced (Reaction 2).



(2)

The rates of thermolysis of dioxetanes **1–2** were monitored by the decay of chemiluminescence intensity in aerated xylenes with added fluorescers at constant temperature (±0.2°). The rates of thermal decomposition were clearly first order for at least three half-lives and showed no dependence on the type or amount of added fluorescer. At 60°C, the value of k_1 for dioxetane **1** was $4.6 \pm 0.1 \times 10^{-4}$s^{-1}, while that for **2** was $9.2 \pm 0.2 \times 10^{-4}$s^{-1}. The first-order rate constants (k_1) were determined over a 50°C temperature range. Correlation coefficients were 0.995 or greater for all cases. The activation parameters were determined by the Arrhenius method. Dioxetane **1** with the 3-pentyl substituent was found to be more stable than **2** with the neopentyl group. The activation parameter data with 95% confidence limits on errors are shown in Table 1.

Without the presence of added fluorescers, the thermolyses of dioxetanes **1–2** exhibited 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 [1,5]. For both dioxetanes, thermolysis directly produced relatively high yields of excited triplets (ϕ^T) and low yields of excited singlets (ϕ^S). The ϕ^T values for both compounds at 60°C were 2%, while the ϕ^S values were less than or equal to 0.05%. The results are summarized in Table 2.

TABLE 1 Activation Parameters for the Thermolysis of 3-Alkyl-3-Methyl-1,2-dioxetanes **1** and **2** in Xylenes

Dioxetane	*3-Alkyl*	$\Delta H‡^{a,b}$	$\Delta S‡$ *e.u.*^{b}	$\Delta G‡$ *kcal/mol*^{b}	$k_1 s^{-1}$ *(60°C)*
1	3-pentyl	25.0 ± 0.3	-1.0	25.3	4.6×10^{-4}
2	neopentyl	24.2 ± 0.3	-2.0	24.9	9.2×10^{-4}

[a]All errors reported at 95% confidence limits.
[b]Calculated at 60°C.

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

Dioxetane	ϕ^T	ϕ^S
1	0.02	$\leq$0.0005
2	0.02	$\leq$0.0004

[a]Instrument calibrated with tetramethyl-1,2-dioxetane: $\phi^T = 0.30$; $\phi^S = 0.002$ (DBA/DPA method at 60°C); error limits ± 50% of observed values [5].

DISCUSSION

Conformational and steric substituent effects on dioxetane stability have been extensively investigated [1b]. Extensive studies of the relative stability of unsymmetric cis/trans pairs of dioxetanes [3a] and 3,3-cyclic substituted dioxetanes [6] had shown that steric considerations were important to dioxetane properties. A key study [3b] on 3-alkyl-3-methyl-1,2-dioxetanes showed that the relative stability series was: Et **3** < *i*-Pr **4** < *t*-Bu **5** (see Table 3). The major effect showed up in the ΔH‡ terms while little or no observable trends were noted in the $\Delta S‡$ terms. The results showed that the increased stability of the dioxetanes correlated with increased branching of the 3-alkyl substituent in the series. Furthermore, dioxetanes in this series in which the ethyl group was formally replaced by either *n*-propyl or *n*-butyl [3b] were found to be of the same relative stability (kinetically indistinguishable). These were interpreted to be consistent with steric interactions between the 3-alkyl group(s) and oxygen-2 in a diradical process.

TABLE 3 Activation Parameters for the Thermolysis of 3-Alkyl-3-Methyl-1,2-dioxetanes **3–6** in Xylenes[a]

Dioxetane	*3-Alkyl*	$\Delta H^{\ddagger}$[b]	$\Delta S^{\ddagger}$ e.u.[b]	$\Delta G^{\ddagger}$ kcal/mol[b]	$k_1 s^{-1}$ (60°C)
3	Ethyl	23.9 ± 0.2	-2.7	24.8	1.0×10^{-3}
4	Isopropyl	24.3 ± 0.3	-2.6	25.2	5.8×10^{-4}
5	*t*-Butyl	25.7 ± 0.3	-0.2	25.8	2.4×10^{-4}

[a]Recalculated parameter data from reference 3b.
[b]All errors reported at 95% confidence limits; calculated at 60°C.

The effective size of substituents in the previous study was limited [3b]. In the present study, the 3-alkyl substituents are larger both in total number of atoms and effective size. Surprisingly, the larger alkyl groups in dioxetanes **1** and **2** have little or no effect over those of the appropriate model compounds. Thus, dioxetane **1** with a 3-pentyl substituent has activation parameter data essentially identical to that of **4**. Similarly, dioxetane **2** with a neopentyl group has essentially the same stability as that of **3** with an ethyl substituent. Clearly, the larger 3-alkyl groups in **1** and **2** do not lead to increased stabilities. This indicates that buttressing (steric) effects between the large substituents and position-4 groups are not a factor. Furthermore, the correlation of the relative stabilities of **1** and **2** with the degree of branching of the 3-alkyl substituent implies that the conformation of the substituents is such that the extra atoms do not interact sterically with oxygen-2. Molecular mechanics calculations [7] have been shown to be of value in interpreting dioxetane properties [1b,3a,f]. No torsion angle changes seem to be involved in the present cases. The results appear to be consistent with 3,3-interactions.

The chemiexcitation yields ($\sim$2% ϕ^{T}) are as expected for disubstituted dioxetanes [1]. The data suggest that dioxetanes **1** and **2** are undergoing thermolysis by the standard diradical-like mechanism. Work is in progress on dioxetanes with two large substituents.

EXPERIMENTAL

All solvents were of reagent grade. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 300 MHz spectrometer. 9,10-Diphenylanthracene (Aldrich) and 9,10-dibromoanthracene (Aldrich) were recrystallized from xylenes (Aldrich) before use. 3-Ethyl-2-methyl-1-pentene (Wiley Organics) and 2,4,4-trimethyl-1-pentene (Aldrich) were commercially available and were used without further purification. CH analyses were carried out, in house, on the α-bromohydroperoxides.

Dioxetane Synthesis

The following two-step procedure for the synthesis of 3-methyl-3-(3-pentyl)-1,2-dioxetane **1** was employed for the preparation of the two dioxetanes. A 50 mmol sample of 3-ethyl-2-methyl-1-pentene was converted to the α-bromohydroperoxide by the Kopecky procedure [1]. The α-bromohydroperoxide, 1-bromo-3-ethyl-2-hydroperoxy-2-methylpentane, a clear, viscous oil (caution!) was purified by low temperature (-78°C) column chromatography (silica gel, pentane/dichloromethane) (yield $\sim$60%): ^{1}H NMR ($CDCl_3$) δ 0.98 (t, 6H); δ 1.19 (s, 3H); δ 1.22 (m, 4H); δ 1.66 (m, 1H); δ 3.63-3.73 (AB, 2H); δ 7.82 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.31, 13.53, 16.80, 22.06, 23.18, 38.69, 45.20, 85.65; for 1-bromo-2-hydroperoxy-2,3,3-trimethylbutane (yield $\sim$65%): ^{1}H NMR ($CDCl_3$) δ 1.01 (s, 9H), 1.36 (s, 3H), 1.50 (d, 1H), 1.809 (d, 1H), 3.52 (AB, 2H), 7.68 (s, 1H); ^{13}C NMR ($CDCl_3$) δ; 21.32, 31.12, 31.34, 40.57, 46.84, 83.88. Active oxbygen content was determined to be 87 ± 6%.

The purified α-bromohydroperoxide (14 mmol) (caution!) was placed in 20 mL of methylene chloride with rapid magnetic stirring and cooled by an ice bath. A solution of 5.0 g of potassium hydroxide in 10 mL of cold, deionized water was added dropwise (5 minutes) to the α-bromohydroperoxide solution to yield a two-phase mixture. This mixture was stirred in an ice bath ($\sim$0°C) for 2 hr. The progress of the reaction was monitored by the amount of light produced by an aliquot of the organic layer. After the organic phase was separated, additional extractions of the aqueous layer with methylene chloride were required to increase the yields of the dioxetanes. The pale yellow organic layers were combined, dried over magnesium sulfate, and filtered. The solvent was removed under reduced pressure, and the dioxetane was purified by column chromatography (metal-ion free) at -78°C using a jacketed 1 cm i.d. column packed with 20 g of silica gel containing 1% Na_2 EDTA (pentane). The impure dioxetane in approximately 1 mL 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 step gradient. Fractions were assayed for dioxetane content relative to light intensity by placing a small aliquot of each fraction into a DBA solution in the chemiluminescence apparatus at 60°C. Fractions containing the most dioxetane were combined and the solvent removed under reduced pressure. The purified dioxetanes **1–2** were yellow oils. The purity was checked by ^{1}H and ^{13}C NMR spectroscopy. Dioxetane samples that were less than 95% pure were passed through the column a second time. The overall yield of dioxetane was

1–2% in both cases. The dioxetanes were stored in CCl_4 at -30° C or lower. Little decomposition was noted even after several months of storage. The ^{1}H NMR data ($CDCl_3$) are: **1** δ 0.83 (m, 6H); δ 1.17 (m, 4H), δ 1.52 (s, 3H), δ 2.00 (m, 1H), δ 4.71 (d, 1H), δ 5.06 (d, 1H); ^{13}C NMR ($CDCl_3$) δ 12.26, 12.56, 20.02, 20.73, 26.66, 49.81, 82.40, 90.22; for **2**, δ 0.99 (s, 9H); δ 1.84 (s, 3H); δ 1.89 (d, 1H), δ 1.97 (d, 1H), δ 4.80 (d, 1H), δ 5.22 (d, 1H); ^{13}C NMR ($CDCl_3$) δ 26.19, 30.55, 30.57, 52.32, 83.40, 88.49.

Product Studies

The following general procedure was employed for the thermolysis of dioxetanes **1–2**. A solution of dioxetane (ca. 0.2 M) in CCl_4 was heated at 60°C in an 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 **1** and **2** 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 was 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 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 ca. 10^{-4} M to avoid induced decomposition. Experiments carried out without added fluorescer and with low concentration ($\leq 10^{-3}$) 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. Reproducibility of k_1 values was excellent (better than 5% of value). All k_1 determinations had correlation coefficients of greater than 0.999.

Chemiexcitation Yields

The instrument was calibrated with tetramethyl-1,2-dioxetane [5] 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 [1]. The concentration of dioxetane was determined by ^{1}H NMR spectroscopy vs. concentration of added standard. The experimental error by the DBA/DPA method is estimated to be ±50% of observed value.

REFERENCES

[1] (a) For reviews, see: Baumstark, A. L.; Rodriguez, A. In Organic Photochemistry and Photobiology; Horspool, W. M., Song, P.-S., Eds.; CRC Press: New York, 1995; Chapter 27; (b) Baumstark, A. L. In Advances in Oxygenated Processes; Baumstark, A. L., Ed.; JAI Press: Greenwich, CT, 1988, Vol. 1, Chapter 2; (c) Baumstark, A. L. In Singlet Oxygen; Frimer, A., Ed.; Uniscience CRC: Boca Raton, FL, Vol. II, Chapter 1; (d) Adam, W. In The Chemistry of Peroxides; Patai, S., Ed.; Wiley: New York, 1982; Chapter 24; (e) Adam, W.; Zinner, K.; In Chemical and Biological Generation of Electronically Excited States; Cilento, G., Adam, W., Eds.; Academic Press: New York, 1982; Chapter 5; (e) Adam, W. In Chemical and Biological Generation of Electronically Excited States; Cilento, G., Adams, W., Eds.; Academic Press: New York, 1982; Chapter 4; (f) Kopecky, K. R. In Chemical and Biological Generation of Electronically Excited States; Cilento, G., Adams, W. Eds.; Academic Press: New York, 1982; Chapter 3.

[2] (a) Schuster, G. B.; Schmidt, S. P. Adv Phys Org Chem 1982, 18, 187–238; (b) For recent example, see: Adam, W.; Trofimov, A. V. J Org Chem 2000, 65, 6474–6478.

[3] (a) Baustark, A. L.; Retter, C. A.; Tehrani, K.; Kellog, C. J Org Chem 1987, 52, 3308–3311; (b) Bausmtark, A. L.; Dunams, T.; Catalani, L. H.; Bechara, E. J. H. J Org Chem 1983, 48, 3713–3716; (c) Baumstark, A. L.; Vasquez, P. C. J Org Chem 1984, 49, 2640–2642; (d) Schaap, A. P.; Gagnon, S. D.; Zalika, K. A. Tetrahedron Lett 1982, 23, 2943–2946; (e) Richardson, W. H.; Thomson, S. A. J Org Chem 1985, 50, 1803–1810; (f) Baumstark, A. L.; Parker, A. N. J Heterocycl Chem 1992, 29, 791–794.

[4] Adam, W.; Baader, W. J. J Am Chem Soc 1985, 107, 410–416.

[5] Wilson, T.; Golan, D. E.; Harris, M. S.; Baumstark, A. L. J Am Chem Soc 1976, 98, 1086–1091.

[6] Baumstark, A. L.; Niroomand, F.; Vasquez, P. C. J Org Chem 1984, 49, 4497–4500.

[7] Burkert, U.; Allinger, N. L. In Molecular Mechanics, ACS Monograph 177; American Chemical Society: Washington, DC, 1982.