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Synthesis of Sulfanyl-, Sulfinyl-, and Sulfonyl-Substituted Bicyclic Dioxetanes and Their Base-Induced Chemiluminescence

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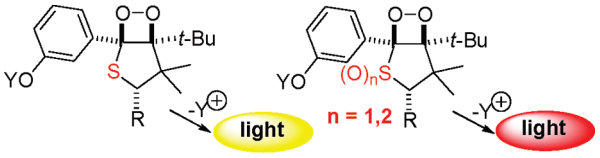

The singlet oxygenation of 4-*tert*-butyl-3,3-dimethyl-5-(3-oxyphenyl)-2,3-dihydrothiophenes **5c**−**e** bearing an acetoxy or methoxy group at the 2-position exclusively gave the corresponding sulfanyl-substituted bicyclic dioxetanes **2c**−**e**, while that of **5a** without 2-substituent mainly gave sulfoxide **11** along with a small amount of dioxetane **2a**. These dioxetanes were sufficiently stable thermally to permit handling at room temperature. Sulfanyl-substituted dioxetanes, **2c** and **2e**, were further oxidized with *m*-chloroperbenzoic acid to afford the corresponding sulfinyl-substituted dioxetanes **3c**, **3e** and sulfonyl-substituted dioxetanes **4c**, **4e**. X-ray single crystallographic analysis was performed for **2c** and **4e**. Base-induced decomposition of the dioxetanes in DMSO gave light with a maximum wavelength λ_{max}^{CL} at 554 nm for **2a** and 565 nm for **2e** in moderate light yields, while sulfinyl-derivative **3e** gave weak light with λ_{max}^{CL} = 795 nm and sulfonyl-derivative **4e** gave very weak light with λ_{max}^{CL} = 848 nm.

Introduction

Enol ethers readily undergo singlet oxygenation to give oxy-substituted dioxetanes, which at room temperature have half-lives ($t_{1/2}^{TD}$: TD = thermal decomposition) that range from shorter than a second to hundreds of years.[1,2] Thus, such dioxetanes, especially those bearing an easily oxidized aryl group, have been developed as high-performance chemiluminescence substrates.[3−8] Sulfur-analogues, e.g. sulfanylethylenes, also smoothly undergo the 1,2-addition of singlet oxygen.[9,10] However, the resulting sulfanyl-substituted

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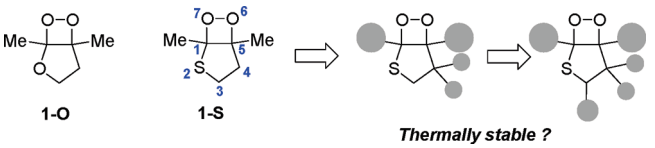
CHART 1. Oxy-Substituted Dioxetane 1-O and Sulfanyl-Substituted Dioxetane 1-S



dioxetanes are in general quite unstable, in contrast to the oxy-analogues, except for polyfluoroalkylsulfanyl-substituted dioxetanes.[11] For instance, a dioxetane fused with a tetrahydrothiophene ring, such as 1,5-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane (**1-S**) has small activation free energy $\Delta G^{\ddagger} = 95$ kJ mol^{-1}, which is much lower (about 25 kJ mol^{-1}) than its oxy-analogue **1-O** for thermolysis (Chart 1).[12,13]

We found that the introduction of bulky substituents in place of two methyls at the 1- and 5-positions and further substitution at the 3- and 4-positions in **1-S** led to sulfanyl-substituted dioxetanes **2** with sufficient thermal stability to permit handling at room temperature (Charts 1 and 2).[14,15] In addition, we synthesized unprecedented sulfinyl- and sulfonyl-substituted dioxetanes, **3** and **4**, and investigated the chemiluminescent decomposition of the thus-realized dioxetanes bearing a sulfur with various oxidation states.

Results and Discussion

1. Synthesis of Sulfanyl-Substituted Bicyclic Dioxetanes and Their Thermal Stability. The synthesis of sulfanyl-substituted dioxetanes **2** was based on the singlet oxygenation of the precursor dihydrothiophenes **5**, the preparation of which included the LDA-mediated cyclization of 7-(3-methoxyphenyl)-6-thiaheptan-3-one **7** into 3-hydroxytetrahydrothiophene **8** as a key step, as shown in Scheme 1. Thiaheptanone **7** was synthesized by condensation of 3-methoxybenzyl chloride with 2,2,4,4-tetramethyl-1-sulfanylpentan-3-ol, prepared from tosylate **6**, and successive oxidation of the condensation product with Ac_2O/DMSO.[16] The thus-synthesized **8** was dehydrated with $SOCl_2$ to give dihydrothiophene **5b** in high yield. Oxidation of **5b** with sodium periodate in aq MeOH gave sulfoxide **9**, the Pummerer rearrangement[17] of which was attained with Ac_2O in hot toluene to give 2-acetoxydihydrothiophene **5c**. 2-Methoxy-derivative **5d** was prepared from **5c** through its hydrolysis giving hydroxy-derivative **5f**. Deprotection of **5b** and **5d** was carried out with EtSNa in hot DMF to give **5a** and **5g**, respectively. Esterification of **5g** with Ac_2O gave acetate **5e**.

When 2-acetoxy-2,3-dihydrothiophene **5c** was irradiated with a Na-lamp in the presence of a catalytic amount of Methylene Blue (MB)[18] in CH_2Cl_2 under an oxygen atmosphere at 0 °C for 2.5 h, singlet oxygenation took place smoothly. ^{1}H NMR analysis of the photolysate showed that dioxetane **2c** was selectively produced, while there was no S-oxygenation product. Chromatographic purification of the photolysate (silica gel/CH_2Cl_2−hexane) gave **2c** as pale yellow columnar crystals (from ether−hexane, mp 98.5−99.5 °C dec). Dioxetane **2c** gave satisfactory ^{1}H NMR, ^{13}C NMR, IR, mass spectral data, and elemental analysis. The stereochemistry of an acetoxy group of **2c** was finally determined to be trans relative to the dioxetane O−O based on X-ray single crystallographic analysis, and the ORTEP view of **2c** is shown in the Supporting Information. The stereoisomer **2c**-*cis* (Chart 2) was not observed even in the crude photolysate of **5c**. This shows that singlet oxygen exclusively attacked the π-face from the less-hindred site for **5c**. Upon heating in toluene-d_8, **2c** decomposed following first-order kinetics to quantitatively give keto thioate **10c** (Chart 3). Thus, the time-course of the thermolysis of **2c** was examined at 60−80 °C in toluene-d_8 and the thermodynamic parameters and half-life were estimated from Arrhenius plots: $\Delta G^{\ddagger} = 113$ kJ mol^{-1}, $\Delta H^{\ddagger} = 111$ kJ mol^{-1}, $\Delta S^{\ddagger} = -5.7$ kJ mol^{-1}, and $t_{1/2}{}^{TD}$ at 25 °C = 210 d.

Singlet oxygenation took place at C=C of the dihydrothiophene ring also for **5d** and **5e** but not at sulfur to selectively give the corresponding dioxetanes **2d** and **2e** without their stereoisomers. The stereochemistry of **2d** and **2e** was tentatively assigned to be trans, as with **2c**, based on the presumption that the π-face selectivity of $^1O_2$ was similar to that for **5c**. In contrast to **5c**−**e**, dihydrothiophene analogue **5a** with no substituent at the 2-position underwent singlet oxygenation to predominantly give sulfoxide **11** (93%) along with a small amount of expected dioxetane **2a** (6%). Singlet oxygen also attacked preferentially the sulfur of methoxyphenyl-analogue **5b** to give **9**, though dioxetane **2b** could not be isolated because of its instability but decomposition product **10b** was produced. These results show that a 2-oxy substituent in 2,3-dihydrothiophenes **5** decisively influences the chemoselectivity to determine whether singlet oxygen preferentially attacks a C=C double bond or sulfur atom. An MO calculation showed for dihydrothiophenes **5a**, **5c**, and **5d** that HOMO electron density at the sulfur decreased and that on the C=C inversely increased when an oxy-substituent was introduced at the adjacent position of the sulfur (Supporting Information). Thus, in addition to the steric effect described above, the 2-oxy substituent is suggested to decrease the reactivity of the sulfur relative to the C=C toward electrophilic $^1O_2$.

Thermolysis of **2a** and **2c**−**e** exclusively gave the corresponding keto thioates **10a** and **10c**−**e** in toluene-d_8. The experimental thermodynamic parameters for the thermolysis of **2a** and **2c**−**e** are summarized in Table 1. They show that an electron-withdrawing group, e.g., acetoxy group, at the 2-position of the tetrahydrothiophene ring apparently acts to improve the thermal stability of bicyclic sulfanyl-substituted dioxetanes **2**.

2. Synthesis of Sulfinyl- and Sulfonyl-Substituted Bicyclic Dioxetanes and Their Thermal Stability. In contrast to sulfanylethylenes (C=CSR), sulfinylethylenes [C=CS(O)R] and sulfonylethylenes [C=CS(O_2)R] are too electron-deficient to undergo 1,2-addition of electrophilic $^1O_2$ to a carbon−carbon double bond, and thus there are no known

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(14) A similar structural modification of **1-O** has been reported to lead to 1-aryl-5-*tert*-butyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptanes with marked thermal stability.[15]
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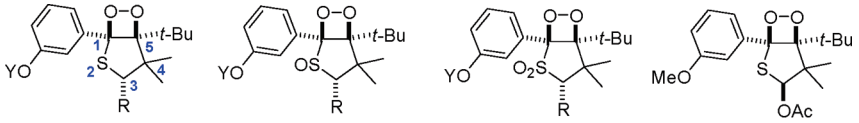
(18) Among various sensitizers, such as TPP, perfluoroTPP, and Rose Bengal, MB gave the desired dioxetanes with the least byproduct.

CHART 2. S-Substituted Dioxetanes 2, SO-Substituted Dioxetanes 3, and SO_2-Substituted Dioxetanes 4



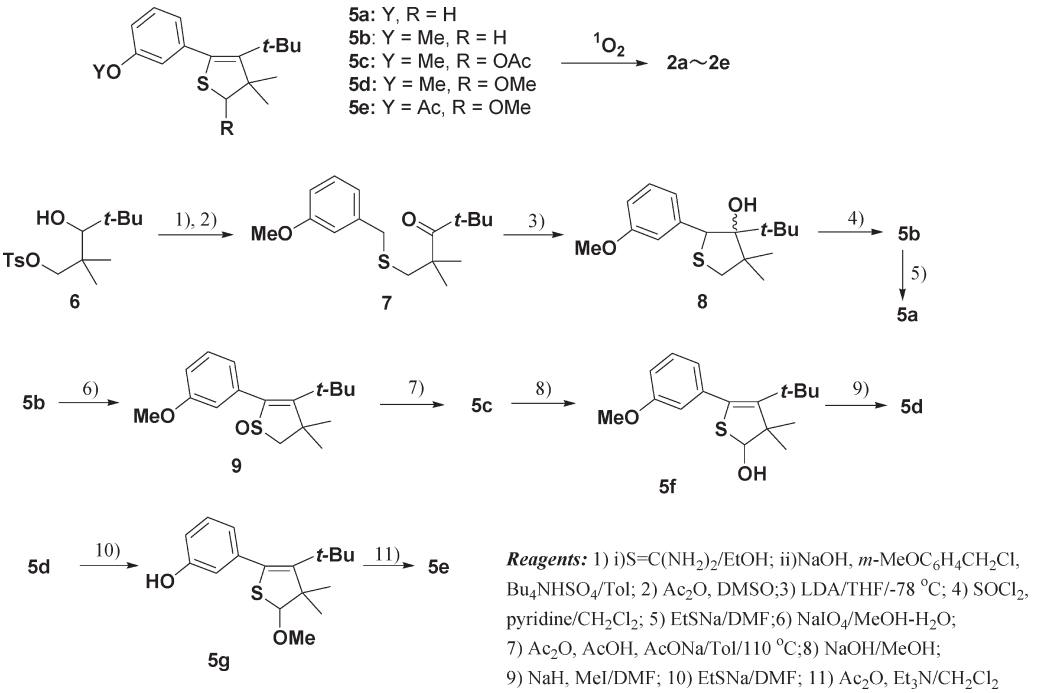
2a: Y, R = H
2b: Y = Me, R = H
2c: Y = Me, R = OAc
2d: Y = Me, R = OMe
2e: Y = Ac, R = OMe

3c: Y = Me, R = OAc
3e: Y = Ac, R = OMe

4c: Y = Me, R = OAc
4e: Y = Ac, R = OMe

2c-*cis*

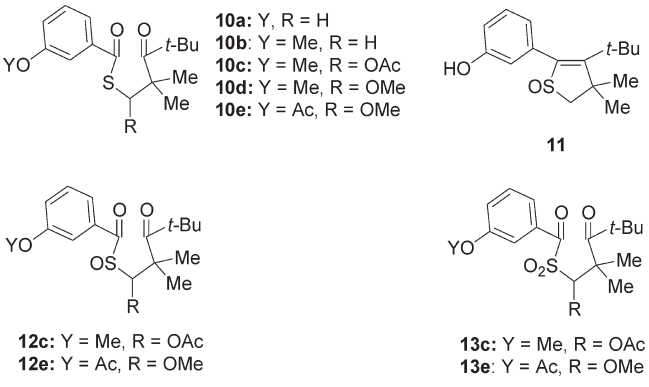
SCHEME 1. Synthetic Pathway of Key Intermediates 5 Leading to Sulfanyl-Substituted Dioxetanes 2



5a: Y, R = H
5b: Y = Me, R = H
5c: Y = Me, R = OAc
5d: Y = Me, R = OMe
5e: Y = Ac, R = OMe

Reagents: 1) i)S=C(NH_2)$_2$/EtOH; ii)NaOH, *m*-MeOC$_6$H$_4$CH$_2$Cl, Bu_4NHSO_4/Tol; 2) Ac_2O, DMSO;3) LDA/THF/-78 °C; 4) $SOCl_2$, pyridine/CH_2Cl_2; 5) EtSNa/DMF;6) $NaIO_4$/MeOH-H_2O; 7) Ac_2O, AcOH, AcONa/Tol/110 °C;8) NaOH/MeOH; 9) NaH, MeI/DMF; 10) EtSNa/DMF; 11) Ac_2O, Et_3N/CH_2Cl_2

CHART 3. Keto Thioates 10, 12, and 13 and Dihydrothiophene *S*-Oxide 11



10a: Y, R = H
10b: Y = Me, R = H
10c: Y = Me, R = OAc
10d: Y = Me, R = OMe
10e: Y = Ac, R = OMe

11

12c: Y = Me, R = OAc
12e: Y = Ac, R = OMe

13c: Y = Me, R = OAc
13e: Y = Ac, R = OMe

examples of dioxetanes bearing a sulfinyl or sulfonyl group.[1,2] In fact, attempts at the singlet oxygenation of dihydrothiophene *S*-oxides **9** and **11** only resulted in recovery of the intact substrates. Thus, we planned to oxidize sulfanyl-substituted dioxetanes and selected **2c** and **2e** as representative substrates. When **2c** was treated with 1 equiv of *m*-chloroperbenzoic acid (MCPBA) in CH_2Cl_2 at room temperature, sulfinyl-substituted dioxetane **3c** was formed selectively. Dioxetane **3c** could only barely be isolated by column chromatography, although its purity was not satisfactory, since it was unstable and decomposed gradually at room temperature. On the other hand, sulfonyl-substituted dioxetane **4c** was thermally stable and obtained by the oxidation of **2c** with >2 equiv of MCPBA (Chart 2). ^{13}C NMR chemical shifts, as a characteristic index of dioxetane ring carbons, were observed in $CDCl_3$ at δ (ppm) 104.9 and 109.4 for **2c**, 102.0 and 104.2 for **3c**, and 100.2 and 101.2 for **4c**. Dioxetane **2e** was similarly oxidized with MCPBA to give **3e** and **4e**: **4e** was obtained as stable

TABLE 1. Thermodynamic Parameters for the Thermolysis of Dioxetanes 2, 3, and 4[a]

	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J mol^{-1}	$\Delta G^{\ddagger}$/kJ mol^{-1}	$t_{1/2}$ at 25 °C/day
2a	107	−6.1	109	50
2c	111	−5.7	113	210
2d	112	9.9	109	54
2e	116	21	110	65
3c	107	26	99	0.8
3e	91	−25	98	0.6
4c	98	−56	115	470
4e	102	−37	113	190

[a]Thermolysis of **2**, **3**, and **4** was carried out in toluene-d_8 at 50−80 °C.

crystals that allowed X-ray single crystallographic analysis (Supporting Information).

^{1}H NMR showed that, on heating in toluene-d_8, **4c** decomposed to give a rather simple product assigned as **13c**, although it could not be isolated but rather gave a degradation product, 3-methoxybenzoic acid, in high yield (94%), during isolation. Thermolysis of **3c** gave a complex mixture instead of the expected product **12c** (Chart 3). However, during the early stage of thermolysis, dioxetanes **3c** and **4c** both disappeared following first-order kinetics. The behaviors of **3e** and **4e** on heating were similar to those of **3c** and **4c**. Thus, the formal activation parameters of thermolysis for **3c**, **3e** and **4c**, **4e** were estimated to be similar to those in the case of **2**. As shown in Table 1, thermal stability increased in the order sulfinyl-substituted dioxetane **3** ≪ sulfanyl-substituted dioxetane **2** < sulfonyl-substituted dioxetane **4**.

3. Base-Induced Chemiluminescent Decomposition of Sulfanyl-, Sulfinyl-, and Sulfonyl-Substituted Dioxetanes. Deprotonation or deprotection of a dioxetane substituted with a phenolic group gives unstable dioxetane bearing an oxidophenyl anion, which undergoes intramolecular charge-transfer-induced decomposition (CTID)[19] with the accompanying emission of light.[3−8] Thus, we investigated the CTID of the present dioxetanes **2e**−**4e** bearing a 3-acetoxyphenyl group and dioxetane **2a** bearing a 3-hydroxyphenyl group. When a solution of **2e** in DMSO (1.0×10^{-5} M, 1 mL) was added to a tetrabutylammonium fluoride (TBAF)[20,21] solution in DMSO (1.0×10^{-2}, 2 mL) at 25 °C, **2e** decomposed following pseudo-first-order kinetics (k^{CTID}, Table 2) to emit yellow light, the spectrum of which is shown in Figure 1. The chemiluminescence properties were as follows: maximum wavelength $\lambda_{max}^{CL} = 565$ nm, chemiluminescence efficiency $\Phi^{CL} = 3.0 \times 10^{-3}$,[22,23] and half-life of decomposition $t_{1/2}^{CTID} = 4.9$ s (Table 2). Although a neutral form of **14e** could not be isolated from the spent reaction mixture presumably because of its instability under the basic conditions, the CTID of **2e** should give excited **14e**, inferring from various CTIDs of hydroxyaryl-substituted dioxetanes reported (Scheme 2).[8] The decomposition of **2a** was similarly induced with TBAF to give chemiluminescence (Figure 1 and Table 2). Notably, sulfanyl-substituted dioxetanes **2a** and **2e** displayed chemiluminescence with λ_{max}^{CL} that was considerably longer than that for a related oxy-substituted dioxetane such as 5-*tert*-butyl-1-(3-hydroxyphenyl)-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptane (λ_{max}^{CL} = 467 nm),[24] and the substituent R at the 3-position of **2** influenced the chemiluminescence spectrum, as illustrated in Figure 1.

TABLE 2. Base-Induced Chemiluminescent Decomposition of Dioxetanes Bearing a Sulfanyl-, Sulfinyl-, or Sulfonyl Group in a TBAF/DMSO System[a]

	R	Y		λ_{max}^{CL}/nm	Φ^{CL}[b]	k^{CTID}/s^{-1}	$t_{1/2}^{CTID}$/s
2a	H	H	S	554	7.9×10^{-3}	4.3×10^{-2}	12
2e	OMe	Ac	S	565	3.0×10^{-3}	1.4×10^{-1}	4.9
3e	OMe	Ac	SO	795			
4e	OMe	Ac	SO_2	848	2.2×10^{-7}	3.3	0.2

[a] All reactions were carried out at 25 °C. [b] Φ^{CL} values were estimated based on the value reported for 3-adamantylidene-4-methoxy-4-(3-siloxyphenyl)-1,2-dioxetane.[22]

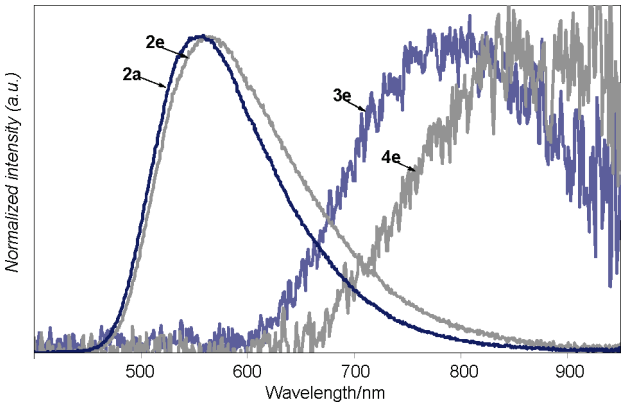
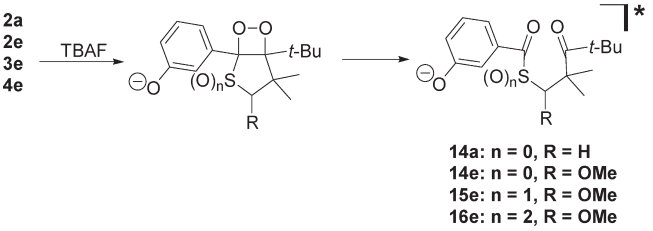


FIGURE 1. Chemiluminescence spectra of sulfanyl-**2a**, **2e**, sulfinyl-**3e**, and sulfonyl-substituted dioxetane **4e**.

SCHEME 2. TBAF-Induced Chemiluminescent Decomposition of Dioxetanes Bearing a Sulfanyl-, Sulfinyl-, or Sulfonyl Group



14a: n = 0, R = H
14e: n = 0, R = OMe
15e: n = 1, R = OMe
16e: n = 2, R = OMe

Next, we attempted to investigate the base-induced decomposition of sulfonyl-substituted dioxetane **4e**. When treated with a large excess of TBAF in DMSO, **4e** decomposed to give very weak dark-red light (λ_{max}^{CL} = 848 nm), the spectrum of which is shown in Figure 1. As shown in Table 2, Φ^{CL} was only 1/14000 of that for sulfanyl-substituted dioxetane **2e**. Although **3e** was unstable as described above, we tried to examine the TBAF-induced decomposition of **3e**. As a result, **3e** gave very weak light with λ_{max}^{CL} = 795 nm (Figure 1), and neither Φ^{CL} nor k^{CTID} was estimated. The tendency for the present dioxetanes to decrease emission energy as increasing oxidation state of the sulfur is apparently elucidated by an MO calculation (B3LYP/6-31G(d)): the energy gap ($\Delta E = E_{LUMO} - E_{HOMO}$) of model emitters, ArCO−X−Me (Ar = *m*-oxidophenyl), decreased in the order of X = O (ΔE = 3.17 eV) > X = S (2.85 eV) > X = SO (2.42 eV) > X = SO_2 (2.27 eV).

(19) The chemiluminescent (CL) decomposition of hydroxyphenyl-substituted dioxetanes has been proposed to proceed by the CIEEL[8] (chemically initiated electron exchange luminescence) mechanism, where an initially formed radical ion pair annihilates by back electron transfer (BET) to afford excited aromatic ester. However, the question as to whether such a CL reaction includes BET as a fundamental process is still being argued and remains unclear. Therefore, we have recently been using the term CTID, which includes the CIEEL and other CT-induced mechanisms.

(20) TBAF has been known to effectively act as a base for hydrolysis of esters and amides.[21]

(21) (a) Namikoshi, M.; Kundu, B.; Rinehart, K. L. *J. Org. Chem.* **1991**, *56*, 5464–5466. (b) Choe, Y. S.; Katzenellenbogen, J. A. *Tetrahedron Lett.* **1993**, *34*, 1579–1580. (c) Kita, Y.; Maeda, H.; Takahashi, F.; Fujii, S.; Ogawa, T.; Hatayama, K. *Chem. Pharm. Bull.* **1994**, *42*, 147–150.

(22) Φ^{CL} was estimated based on the value of 0.29 for chemiluminescent decomposition of 3-adamantylidene-4-methoxy-4-(3-oxidophenyl)-1,2-dioxetane in the TBAF/DMSO system.[23]

(23) Trofimov, A. V.; Mielke, K.; Vasil'ev, R. F.; Adam, W. *Photochem. Photobiol.* **1996**, *63*, 463–467.

(24) Matsumoto, M.; Yamada, K.; Ishikawa, H.; Hoshiya, N.; Watanabe, N.; Ijuin, H. K. *Tetrahedron Lett.* **2006**, *47*, 8407–8411.

Conclusions

The sulfanyl-substituted bicyclic dioxetanes **2** reported here were found to be sufficiently stable thermally to permit handling at room temperature. Among them, **2a** and **2e** underwent TBAF-induced decomposition in DMSO to give yellow light with moderate chemiluminescence yields ($\Phi^{CL} = 3.0 \times 10^{-3}$ to 7.9×10^{-3}). The oxidation of **2c** and **2e** with 1 equiv of MCPBA gave the corresponding sulfinyl-substituted dioxetanes **3c** and **3e**, while their oxidation with >2 equiv of MCPBA gave the corresponding sulfonyl-substituted dioxetanes **4c** and **4e**. Both **3e** and **4e** were also found to undergo TBAF-induced decomposition to give very weak light with $\lambda_{max}{}^{CL}$ values longer than those for **2**.

Experimental Section

Singlet Oxygenation of 2-Acetoxy-4-*tert*-butyl-5-(3-methoxyphenyl)-3,3-dimethyl-2,3-dihydrothiophene (5c): Typical Procedure. A solution of 2-acetoxy-4-*tert*-butyl-5-(3-methoxyphenyl)-3,3-dimethyl-2,3-dihydrothiophene (**5c**) (265 mg, 0.792 mmol) and MB (5.0 mg) in dry CH_2Cl_2 (25 mL) was irradiated externally with a 940 W Na lamp for 2.5 h under an oxygen atmosphere at 0 °C. The photolysate was concentrated in vacuo. The residue was chromatographed on silica gel and eluted with CH_2Cl_2−hexane (1:2) to give 3-acetoxy-5-*tert*-butyl-1-(3-methoxyphenyl)-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane (**2c**) as a pale yellow solid (256 mg, 88% yield).

Dihydrothiophenes **5d** and **5e** were similarly oxygenated with singlet oxygen to give the coresponding dioxetanes **2d** and **2e** both in 85% yields, respectively.

2c: pale yellow columns, mp 98.5−99.5 °C dec (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.09 (s, 9H), 1.16 (s, 3H), 1.41 (s, 3H), 2.19 (s, 3H), 3.81 (s, 3H), 6.69 (s, 1H), 6.86 (d with fine coupling, J = 8.2 Hz, 1H), 7.08−7.30 (m, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 18.3, 20.0, 20.8, 27.8, 39.2, 53.7, 55.3, 83.1, 104.9, 109.4, 113.7 (br), 114.1, 120.4 (br), 128.7, 138.3, 159.0, 169.6 ppm. IR (KBr): $\tilde{\nu}$ 3009, 1762 cm^{-1}. Mass (m/z, %): 366 (M^+, trace), 334 ($M^+ - 32$, 3), 136 (11), 135 (100). HRMS (ESI): 389.1385, calcd for $C_{19}H_{26}O_5SNa$ [$M + Na^+$] 389.1399. Anal. Calcd for $C_{19}H_{26}O_5S$: C, 62.27; H, 7.15. Found: C, 61.88; H, 7.19.

2d: pale yellow columns, mp 86.0−87.5 °C dec (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.07 (s, 9H), 1.20 (s, 3H), 1.32 (s, 3H), 3.59 (s, 3H), 3.81 (s, 3H), 5.61 (s, 1H), 6.85 (d with fine coupling, J = 8.2 Hz, 1H), 7.04−7.32 (m, 2H), 7.26 (dd, J = 8.2 and 7.8 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 17.6, 20.1, 27.9, 39.2, 54.0, 55.3, 60.8, 94.8, 105.9, 108.5, 113.4 (br), 114.0, 120.7 (br), 128.6, 139.2, 158.9 ppm. IR (KBr): $\tilde{\nu}$ 2988, 2933, 2832, 1607, 1581 cm^{-1}. Mass (m/z, %): 338 (M^+, trace), 306 ($M^+ - 32$, 1), 171 (30), 136 (11), 135 (100), 107 (10). HRMS (ESI): 361.1441, calcd for $C_{18}H_{26}O_4SNa$ [$M + Na^+$] 361.1450. Anal. Calcd for $C_{18}H_{26}O_4S$: C, 63.87; H, 7.74. Found: C, 63.79; H, 7.87.

2e: pale yellow granules, mp 98.5−100.5 °C dec (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.06 (s, 9H), 1.20 (s, 3H), 1.31 (s, 3H), 2.30 (s, 3H), 3.59 (s, 3H), 5.61 (s, 1H), 7.06 (ddd, J = 8.1, 2.2, and 0.7 Hz, 1H), 7.30−7.40 (m, 1H), 7.35 (t, J = 8.1 Hz, 1H), 7.42−7.51 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 17.6, 20.0, 21.0, 27.7, 39.2, 53.9, 60.7, 94.9, 105.9, 108.0, 120.8 (br), 121.7, 124.2, and 125.9 (br), 128.5, 139.3, 150.0, 169.0 ppm. IR (KBr): $\tilde{\nu}$ 2981, 2935, 1766, 1589 cm^{-1}. Mass (m/z, %, 20 eV): 366 (M^+, 3), 334 ($M^+ - 32$, 9), 281 (39), 250 (12), 171 (56), 164 (12), 163 (100), 152 (13), 136 (10), 128 (36). HRMS (ESI, 30 eV): 389.1400, calcd for $C_{19}H_{26}O_5SNa$ [$M + Na^+$] 389.1399. Anal. Calcd for $C_{19}H_{26}O_5S$: C, 62.27; H, 7.15. Found: C, 62.26; H, 7.32.

Singlet Oxygenation of 4-*tert*-Butyl-5-(3-hydroxyphenyl)-3,3-dimethyl-2,3-dihydrothiophene (5a). A solution of 4-*tert*-butyl-5-(3-hydroxyphenyl)-3,3-dimethyl-2,3-dihydrothiophene (**5a**) (252 mg, 0.960 mmol) and TPP (1.0 mg) in CH_2Cl_2 (20 mL) was irradiated externally with a 940 W Na lamp for 20 min under an oxygen atmosphere at 0 °C. The photolysate was concentrated in vacuo and the residue was chromatographed on silica gel and eluted with CH_2Cl_2 to give dioxetane **2a** as a pale yellow solid (16 mg, 6% yield). Further elution gave sulfoxide **11** as a colorless solid (249 mg, 93% yield). Sulfoxide **11** was synthesized independently by the oxidation of **5a** with sodium periodate in H_2O/MeOH.

2a: yellow granules ,mp 96.0−97.5 °C dec (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.04 (s, 9H), 1.26 (s, 3H), 1.50 (s, 3H), 2.55 (d, J = 11.6 Hz, 1H), 3.95 (d with fine coupling, J = 11.6 Hz, 1H), 4.86 (br s, 1H), 6.79 (dd, J = 8.9 and 2.4 Hz, 1H), 7.08−7.28 (m, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 22.7, 24.9, 27.7, 38.5, 47.4, 52.2, 106.7, 112.4, 114.9 (br), 115.6, 120.4 (br), 128.9, 139.5, 155.1 ppm. IR (KBr): $\tilde{\nu}$ 3433, 3064, 2985, 2964, 1601 cm^{-1}. Mass (m/z, %): 294 (M^+, 0.9), 262 ($M^+ - 32$, 0.8), 238 (25), 209 (11), 121 (100). HRMS (ESI): 317.1185, calcd for $C_{16}H_{22}O_3SNa$ [$M + Na^+$] 317.1187. Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.27; H, 7.53. Found: C, 65.23; H, 7.62.

11: colorless granules, mp 174.0−175.0 °C (from THF−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.15 (s, 9H), 1.47 (s, 3H), 1.64 (s, 3H), 2.96 (d, J = 12.7 Hz, 1H), 3.29 (d, J = 12.7 Hz, 1H), 6.66−6.72 (m, 2H), 6.76 (br s, 1H), 7.14 (td, J = 7.8 and 2.2 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 30.0, 30.5, 32.1, 37.3, 51.2, 66.4, 115.7, 117.1 (br), 120.5 (br), 129.1, 135.1, 142.7, 156.9, 159.5 ppm. IR (KBr): $\tilde{\nu}$ 3152, 2965, 1588 cm^{-1}. Mass (m/z, %): 278 (M^+, 22), 262 (61), 247 (100), 191 (70), 159 (53), 121 (27). HRMS (ESI): 279.1417, calcd for $C_{16}H_{23}O_2S$ [$M + H^+$] 279.1419, and 301.1217, calcd for $C_{16}H_{22}O_2SNa$ [$M + Na^+$] 301.1238. Anal. Calcd for $C_{16}H_{22}O_2S$: C, 69.02; H, 7.96. Found: C, 68.97; H, 8.14.

Oxidation of 3-Acetoxy-5-*tert*-butyl-1-(3-methoxyphenyl)-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane (2c) with *m*-Chloroperbenzoic Acid (MCPBA): Typical Procedure. MCPBA (65.0%, 135 mg, 0.508 mmol) was added to a solution of 3-acetoxy-5-*tert*-butyl-1-(3-methoxyphenyl)-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane (**2c**) (200 mg, 0.546 mmol) in dry CH_2Cl_2 (4.0 mL) and stirred at room temperature for 1.5 h. The reaction mixture was chromatographed on NH silica gel and eluted with CH_2Cl_2 to remove *m*-chlorobenzoic acid and intact MCPBA. The solid 3-acetoxy-5-*tert*-butyl-1-(3-methoxyphenyl)-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane 2-oxide (**3c**) was recrystallized from ether−hexane to give **3c** as a pale yellow granules (181 mg, 87% yield).

When 4 equiv of MCPMA was used to oxidize **2c** (100 mg) under similar conditions as described above, 3-acetoxy-5-*tert*-butyl-1-(3-methoxyphenyl)-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane 2,2-dioxide (**4c**) was produced. The reaction mixture was chromatographed on NH silica gel and eluted with CH_2Cl_2 to give **4c** as a pale yellow solid (84% yield).

Similar oxidation was applied to 1-(3-acetoxyphenyl)-5-*tert*-butyl-3-methoxy-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane (**2e**) to give 1-(3-acetoxyphenyl)-5-*tert*-butyl-3-methoxy-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane 2-oxide (**3e**) (31%) or 1-(3-acetoxyphenyl)-5-*tert*-butyl-3-methoxy-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane 2,2-dioxide (**4e**) (84%).

3c: pale yellow granules, mp 72.5−74.5 °C dec (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.10 (s, 3H), 1.11 (s, 9H), 1.40 (s, 3H), 2.30 (s, 3H), 3.83 (s, 3H), 6.84−7.30 (m, 4H), 7.37 (t, J = 8.2 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 19.8, 20.5, 20.8, 27.3, 40.0, 48.4, 55.3, 92.7, 102.0, 104.2, 113.2 (br), 115.0, 118.2, and 119.7 (br), 129.7, 135.0, 159.7, 169.2 ppm. IR (KBr): $\tilde{\nu}$ 2976, 1764, 1688, 1584 cm^{-1}.

Mass (m/z, %, 20 eV): 382 (M^+, 0.5), 286 (39), 152 (33), 135 (74), 85 (77), 57 (100). HRMS (ESI): 405.1342, calcd for $C_{19}H_{26}O_6SNa$ [M + Na^+] 405.1348, and 787.2822, calcd for $C_{38}H_{52}O_{12}S_2Na$ [2M + Na^+] 787.2798.

4c: pale yellow granules, mp 120.0−123.0 °C dec (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.16 (s, 9H), 1.18 (s, 3H), 1.51 (s, 3H), 2.35 (s, 3H), 3.83 (s, 3H), 6.67 (s, 1H), 7.00 (d with fine coupling, J = 8.3 Hz, 1H), 7.10 (s with fine coupling, 1H), 7.16 (ddd, J = 7.8, 1.7, and 0.9 Hz, 1H), 7.37 (dd, J = 8.3 and 7.8 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 18.1, 20.4, 21.0, 27.7, 40.7, 46.2, 55.3, 85.1, 100.2, 101.2, 112.7, and 115.0 (br), 115.7, 119.6, and 121.2 (br), 127.6, 128.7, and 129.5 (br), 158.6 and 159.6 (br), 168.8 ppm. IR (KBr): $\tilde{\nu}$ 2975, 1769, 1607, 1582 cm^{-1}. Mass (m/z, %, 20 eV): 398 (M^+, 0.3), 277 (11), 199 (13), 152 (37), 135 (50), 128 (17), 85 (62), 57 (100). HRMS (ESI): 421.1300, calcd for $C_{19}H_{26}O_7SNa$ [M + Na^+] 421.1297, and 819.2687, calcd for $C_{38}H_{52}O_{14}S_2Na$ [2M + Na^+] 819.2696. Anal. Calcd for $C_{19}H_{26}O_7S$: C, 57.27; H, 6.58. Found: C, 57.22; H, 6.58.

3e: pale yellow plates, mp 93.3−95.0 °C dec (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.09 (s, 9H), 1.20 (s, 3H), 1.33 (s, 3H), 2.31 (s, 3H), 3.86 (s, 3H), 5.27 (s, 1H), 7.04−7.55 (m, 2H), 7.15 (d with fine coupling, J = 7.9 Hz, 1H), 7.45 (t, J = 7.9 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 19.3, 20.8, 21.0, 27.3, 40.0, 49.3, 61.1, 102.3, 103.7, 104.2, 122.7, 129.5 (br), 135.6, 150.7 (br), 168.9 ppm. IR (KBr): $\tilde{\nu}$ 2976, 1764, 1206, 1030 cm^{-1}. Mass (m/z, %, 20 eV): 318 (M^+ − 64, 2), 303 (2), 212 (18), 171 (51), 163 (48), 138 (10), 86 (33), 85 (100). HRMS (ESI): 405.1340, calcd for $C_{19}H_{26}O_6SNa$ [M + Na^+] 405.1348.

4e: pale yellow plates, mp 100.0−102.0 °C dec (from AcOEt−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.13 (s, 9H), 1.24 (s, 3H), 1.41 (s, 3H), 2.31 (s, 3H), 3.89 (s, 3H), 5.13 (s, 1H), 7.19−7.24 (m, 1H), 7.30 (br s, 1H), 7.40−7.50 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 17.3, 21.0, 21.3, 27.6, 40.6, 46.7, 61.5, 96.5, 99.6, 101.5, 120.7, and 122.5 (br), 123.1, 124.3, and 126.2 (br), 128.1, 128.4, and 129.3 (br), 149.5 and 150.7 (br), 168.9 ppm. IR (KBr): $\tilde{\nu}$ 2981, 2940, 1769, 1589 cm^{-1}. Mass (m/z, %, 20 eV): 180 ($AcOC_6H_4CO_2H$, 10), 171 (11), 163 (43), 152 (15), 138 (46), 128 (12), 86 (27), 85 (69), 57 (100). HRMS (ESI): 421.1280, calcd for $C_{19}H_{26}O_7SNa$ [M + Na^+] 421.1297. Anal. Calcd for $C_{19}H_{26}O_7S$: C, 57.27; H, 6.58. Found: C, 56.89; H, 6.67.

Thermal Decomposition of 3-Acetoxy-5-*tert*-butyl-1-(3-methoxyphenyl)-4,4-dimethyl-6,7-dioxa-2-thiabicyclo[3.2.0]heptane (2c): Typical Procedure. Dioxetane **2c** (54.6 mg, 0.149 mmol) was stirred in toluene (1.0 mL) for 1 h under a N_2 atmosphere at 110 °C. After the concentration in vacuo, the reaction mixture was chromatographed on silica gel and eluted with AcOEt−hexane (1:9) to give *S*-1-acetoxy-2,2,4,4-tetramethyl-3-oxopentyl 3-methoxybenzenethioate (**10c**) as a colorless solid (47.6 mg, 87% yield). The other dioxetanes **2a**, **2d**, and **2e** were similarly decomposed in hot toluene to give the corresponding arylthioate **10a**, **10d**, and **10e** in 75−92% isolated yield.

10c: colorless needles melted at 94.0−94.5 °C (from ether−hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.29 (s, 9H), 1.41 (s, 3H), 1.42 (s, 3H), 2.05 (s, 3H), 3.85 (s, 3H), 7.12 (ddd, J = 8.3, 2.6, and 1.0 Hz, 1H), 7.12 (s, 1H), 7.35 (dd, J = 8.3 and 7.6 Hz, 1H), 7.48 (dd, J = 2.6 and 1.7 Hz, 1H), 7.58 (ddd, J = 7.6, 1.7, and 1.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 20.9, 22.5, 22.7, 28.3, 45.9, 54.1, 55.5, 81.8, 111.5, 120.2, 120.5, 129.6, 137.5, 159.7, 168.7, 188.8, 214.8 ppm. IR (KBr): $\tilde{\nu}$ 2974, 1753, 1680, 1580 cm^{-1}. Mass (m/z, %): 366 (M^+, trace), 252 (4), 222 (7), 136 (11), 135 (100), 107 (10). HRMS (ESI): 389.1390, calcd for $C_{19}H_{26}O_5SNa$ [M + Na^+] 389.1399. Anal. Calcd for $C_{19}H_{26}O_5S$: C, 62.27; H, 7.15. Found: C, 62.15; H, 7.22.

Time Course for Thermal Decomposition of Dioxetanes 2: General Procedure. A solution of dioxetane **2** (3−5 mg) in toluene-d_8 (0.8 mL) in an NMR sample tube was heated by means of a liquid paraffin bath thermostated at an appropriate temperature range of 50−80 °C. After heating at regular intervals, ^{1}H NMR analysis was conducted on the samples to determine the ratio of the intact **2** vs. the corresponding keto thioester **10**.

Chemiluminescence Measurement: General Procedure. A freshly prepared solution (2 mL) of TBAF (1.0×10^{-2} mol/L) in DMSO was transferred to a quartz cell ($10 \times 10 \times 50$ mm) and the latter placed in the spectrometer, which was thermostated with stirring at 25 °C. After 3−5 min, a solution of the sulfanyl-substituted dioxetane **2a** or **2e** in DMSO (1.0×10^{-5} mol/L, 1 mL) was added by means of a syringe with immediate starting of measurement. The intensity of the light emission time-course was recorded and processed according to first-order kinetics. The total light emission was estimated by comparing it with that of an adamantylidene dioxetane, whose chemiluminescent efficiency Φ^{CL} has been reported to be 0.29 and was used here as a standard.[22] For chemiluminescent decomposition of sulfinyl-substituted dioxetane **3e**, a solution of the dioxetane in DMSO (1.0×10^{-4} mol/L, 1 mL) was used, while for sulfonyl-substituted dioxetane **4e**, a solution of the dioxetane in DMSO (1.0×10^{-3} mol/L, 1 mL) and TBAF (0.1 mol/L) in DMSO were used.

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Supporting Information Available: General method for the Experimental Section, ^{1}H NMR/^{13}C NMR spectra of **2c**−**e**, **2a**, **3c**, **3e**, **4c**, **4e**, **5a**−**g**, $\mathbf{7_{OH}}$, **7**, **8**-*cis*, **8**-*trans*, **9**, **10a**, **10c**−**e**, and **11**, and crystallographic information files for **2c** and **4e**. This material is available free of charge via the Internet at http://pubs.acs.org.