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Base-induced chemiluminescent decomposition of stereoisomeric 5-*tert*-butyl-1-(3-*tert*-butyldimethylsiloxy)phenyl-4,4-dimethyl-3-phenyl-2,6,7-trioxabicyclo[3.2.0]heptanes and their related dioxetanes

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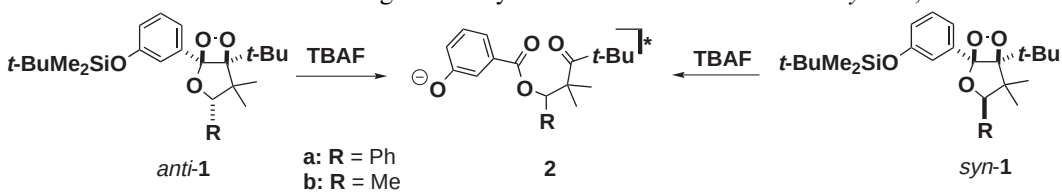
Abstract—Singlet oxygenation of 4-*tert*-butyl-5-(3-*tert*-butyldimethylsiloxy)phenyl-3,3-dimethyl-2-phenyl-2,3-dihydrofuran (**3a**) in dichloromethane at 0°C gave a 95:5 mixture of stereoisomeric dioxetanes (*anti*-**1a**) and (*syn*-**1a**). The isomer (*anti*-**1a**) was more stable thermally than *syn*-**1a**. On treatment with tetrabutylammonium fluoride in DMSO or acetonitrile, both isomeric dioxetanes emitted intense blue light. Chemiluminescence efficiency (Φ_{CL}) of *anti*-**1a** was considerably higher than that of *syn*-**1a**; nevertheless, both of them gave the very same couple of two carbonyl fragments (**2a**). A methyl-analog (**1b**) was also synthesized and its chemiluminescent properties were examined.

Dioxetanes substituted with an aromatic electron donor such as an aryl-O^- moiety display chemically initiated electron exchange luminescence (CIEEL).[1,2] The phenomenon has received a great deal of attention from the viewpoint of mechanistic interests related to bioluminescence and application to chemiluminescent bioassays, and extensive research efforts have been made to elucidate the chemiexcitation pathways, as well as to develop efficient chemiluminescent systems.[3] However, a study of the structural relation of the CIEEL-active dioxetanes to their chemiluminescence efficiency (Φ_{CL}) is still lacking, though there have been several reports on the relationship between the aryl-O^- moiety on dioxetanes and their chemiluminescent properties.[4–7] One difficulty hampering such a study is how to evaluate the difference in the participation of another carbonyl fragment concomitantly formed with an emitter between the CIEEL-active dioxetanes to be compared. We attempted here to examine the CIEEL decay of a pair of stereoisomeric dioxetanes affording the very same couple of two carbonyl fragments as a rudimentary study on the relationship between their structure and chemiluminescence efficiency (Φ_{CL}), while avoiding the difficulty mentioned above.

Our choice of such stereoisomeric dioxetanes were the *anti*-form of 5-*tert*-butyl-1-(3-*tert*-butyldimethylsiloxy)-phenyl-4,4-dimethyl-3-phenyl-2,6,7-trioxabicyclo[3.2.0]-heptane (*anti*-**1a**) and its *syn*-isomer (*syn*-**1a**), both of which decompose by desilylation to afford the same couple of an emitter and the remaining aliphatic carbonyl fragment which join together, i.e. a ketoester (**2a**): the *anti*-**1a** possesses 3-phenyl lying *anti* to the dioxetane ring, and *syn*-**1a** possesses the opposite stereochemistry. When a dihydrofuran (**3a**) (300 mg) and a catalytic amount of tetraphenylporphin (TPP) were irradiated with a 940-W Na lamp in dichloromethane (15 mL) under an oxygen atmosphere at 0°C for 1 h, 1,2-addition of singlet oxygen occurred to give a 95:5 mixture of *anti*-**1a** and *syn*-**1a**, which were separated by



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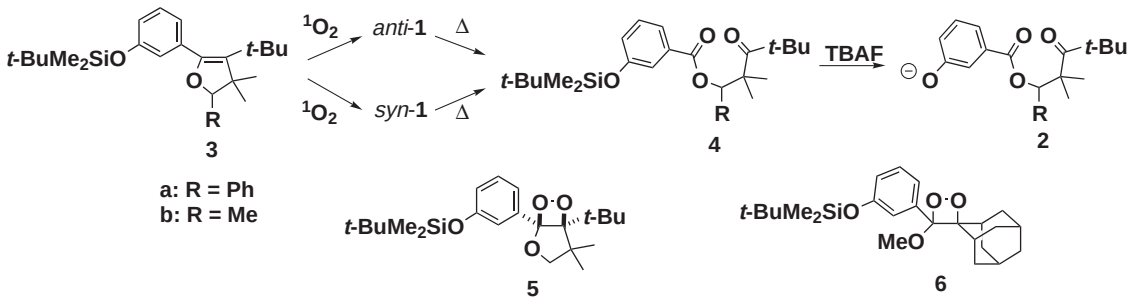
silica gel chromatography. Their structures were determined by ^{1}H NMR, ^{13}C NMR, ^{1}H–^{1}H COSY, ^{13}C–^{1}H COSY, NOE, IR, and mass spectral analysis.[8] Similar singlet oxygenation of a furan bearing a 2-methyl (**3b**) also gave selectively the corresponding mixture of stereoisomeric dioxetanes (*anti*-**1b**:*syn*-**1b**=65:35).[9]

Both of the stereoisomeric dioxetanes (*anti*-**1**) and (*syn*-**1**) decomposed exclusively to the same ketoester (**4**) in hot toluene. These decompositions followed first-order kinetics and their rates were measured at 90–120°C in toluene-d_8 or *p*-xylene-d_{10} to estimate their activation parameters. The results summarized in Table 1 show that all dioxetanes (*anti*- and *syn*-**1a**, *anti*- and *syn*-**1b**) are thermally persistent, and that the *anti*-isomers are more stable than the parent dioxetane (**5**),[10] while the *syn*-isomers show reverse tendency.

The siloxyphenyl-substituted dioxetanes are triggered with tetrabutylammonium fluoride (TBAF) in an aprotic solvent such as DMSO and acetonitrile; their desilylation with fluoride affords an unstable phenolate-substituted dioxetane, which decomposes rapidly by the CIEEL process. It has been reported very recently for the fluoride-triggered CIEEL of 3-adamantylidene-4-(3-*tert*-butyldimethylsiloxyphenyl)-4-methoxy-1,2-dioxetane (**6**) that the CIEEL decay rate depends on both the TBAF concentration and the substrate concentration, though it follows pseudo-first-order kinetics independent of the TBAF concentration when an excess of fluoride concentration is used.[11] To simplify the analysis of fluoride-induced decomposition of the present dioxetanes (**1**) we used also a large excess of TBAF. When solutions of *anti*-**1a** and *syn*-**1a** in DMSO (1.0×10^{-5} mol dm^{-3}, 1 mL) were added to TBAF solutions in DMSO (1.0×10^{-2} mol dm^{-3}, 2 mL) at 25°C, the dioxetanes (*anti*-**1a**) and (*syn*-**1a**) emitted intense blue light with chemiluminescent properties, as shown in Table 2. ^{1}H NMR analysis showed that both spent reaction mixtures from *anti*-**1a** and *syn*-**1a** included exclusively a

Table 1. Thermal decomposition of dioxetanes (**1**)[a]



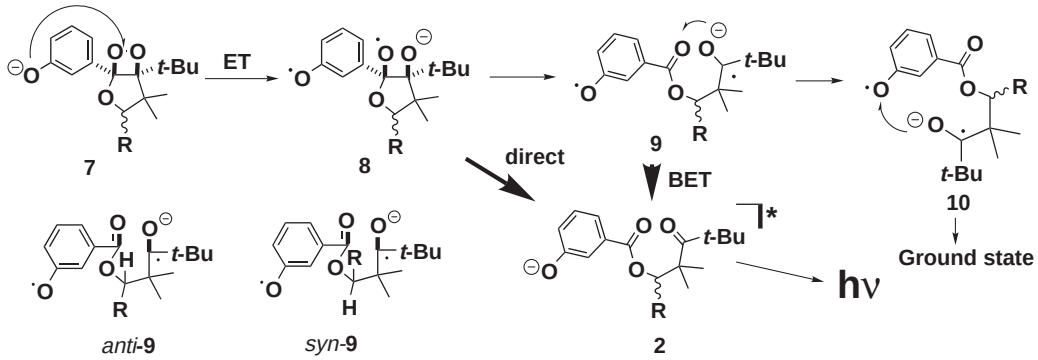
Dioxetane	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal K^{-1} mol^{-1})	$\Delta G^{\ddagger}$ (kcal mol^{-1})	$t_{1/2}$ at 25°C (y)
Anti-**1a**	31.4	5.1	29.9	87.6
Syn-**1a**	28.6	0.5	28.5	8.5
Anti-**1b**	28.8	−1.5	29.2	25.2
Syn-**1b**	25.8	−9.4	28.6	8.6
5[b]	27.1	−6.8	29.1	22.1

[a] Thermal decomposition of **1** was carried out in toluene-d_8 or xylene-d_{10} at 90–120°C, and ratios **1** versus **4** were measured by ^{1}H NMR.
[b] Ref. 10.

Table 2. TBAF-induced chemiluminescent decomposition of (**1a**) and (**1b**) in DMSO and acetonitrile[a,b,c]

Dioxetane	DMSO				Acetonitrile			
	λ_{max} (nm)	Φ_{CL}	Φ_S	$t_{1/2}$ (s)	λ_{max} (nm)	Φ_{CL}	Φ_S	$t_{1/2}$ (s)
Anti-**1a**	466	0.18	0.58	4.0	471	0.075	0.29	11
Syn-**1a**	466	0.12	0.39	1.8	471	0.052	0.20	6.4
Anti-**1b**	466	0.25	0.76	9.8	470	0.077	0.43	38
Syn-**1b**	466	0.21	0.64	16	470	0.077	0.43	80
5	466	0.20	0.63[d]	4.6	469	0.075	0.31[d]	19

[a] Solutions of **1a** and **1b** in DMSO or acetonitrile (1.0×10^{-5} mol dm^{-3}, 1 mL) were added to TBAF solutions in DMSO or acetonitrile (1.0×10^{-2} mol dm^{-3}, 2 mL) at 25°C.
[b] Fluorescence quantum yields (Φ_F) of **2** generated from **4** on treatment with TBAF in DMSO or acetonitrile at 25°C were as follows: **2a** in DMSO=0.31, **2a** in acetonitrile=0.26, **2b** in DMSO=0.33, **2b** in acetonitrile=0.18. Yields (Φ_S) of singlet-excited ester (**2**) were estimated in accord with an equation $\Phi_S=\Phi_{CL}/\Phi_F$.
[c] Chemiluminescent yields (Φ_{CL}) were based on the reported value for **6**: $\Phi_{CL}=0.29$ in DMSO (Ref. 11).
[d] Yields (Φ_S) of a singlet-excited ester produced from **5** were estimated by the use of reported values for Φ_F of the ester: Φ_F in DMSO=0.32, Φ_F in acetonitrile=0.24 (Ref. 14).



Scheme 1.

free form of **4a** as a decomposition product. The fluoride-induced decomposition of **1b** was also carried out and the results are summarized in Table 2.

Both chemiluminescent spectra from *anti*-**1a** and *syn*-**1a** were in good agreement not only with that of **6**, whose emitter has been established to be an oxy-anion of methyl *m*-hydroxybenzoate,[11] but also with the fluorescent spectrum of an oxy-anion of ketoester (**2a**) generated from a silyl-protected ketoester (**4a**) in TBAF/DMSO or acetonitrile. Therefore, an oxy-anion of the *m*-hydroxybenzoate moiety in **2a** is unquestionably the emitter for both the CIEEL decay of *anti*-**1a** and *syn*-**1a**. Based on these results, yields of singlet chemiexcitation ($\Phi_S = \Phi_{CL}/\Phi_F$) for *anti*-**1a** and *syn*-**1a** were estimated from their Φ_{CL} and fluorescence quantum yield (Φ_F) of **2a**, which was measured at 0.31 in TBAF/DMSO and 0.26 in TBAF/acetonitrile. The results in Table 2 reveal that the chemiluminescent yield (Φ_{CL}) as well as the yield (Φ_S) of singlet-excited **2a** are higher for *anti*-**1a** than for *syn*-**1a** both in DMSO and in acetonitrile. A similar tendency in Φ_S was also observed for isomeric methyl-analogs (*anti*-**1b**) and (*syn*-**1b**) in DMSO, as shown in Table 2.

The present results provide the first example that stereoisomeric dioxetanes, giving the same decomposition product, emit light with the different efficiencies for the CIEEL-decay. The phenomenon suggests that the stereochemistry of a starting dioxetane is reflected in the chemiexcitation process, though it cannot be used at present to distinguish between two the main mechanistic alternatives proposed for the CIEEL chemiexcitation process, namely, a stepwise electron transfer (ET)–electron back-transfer (BET) process[1,11–15] and charge transfer (CT)-induced concerted cleavage of dioxetane leading to direct chemiexcitation.[16,17]

As illustrated in Scheme 1, a pertinent feature of the CIEEL process for a phenolate-substituted dioxetane, such as **7** produced from **1**, is that the intramolecular ET from the phenolate moiety to the peroxide bond causes O–O bond cleavage and the reaction proceeds through a transition state as **8**, irrespective of the stepwise ET–BET or the concerted process. For the ET–BET process, **8** leads to a radical ion pair (**9**), in which the ketyl radical functionality is proximate to the ester carbonyl, and its annihilation by a BET from the ketyl radical part to the ester carbonyl results in a singlet-excited ester (**2**). This chemiexcitation channel has very recently been suggested by Adam[15] to compete with another channel giving the ground state product, in which BET occurs from the ketyl radical to the phenoxy group when these two groups approach each other as **10** by conformational motion in **9**. Thus, Φ_S reflects the efficiency of BET (giving an excited state), which would change as the structure of a radical ion pair changes. In the case of **1**, since a steric repulsion between the ketyl radical and a substituent R (=Ph or Me) should be larger for a diradical (*syn*-**9**) from *syn*-**1** than for *anti*-**9** from *anti*-**1**, the ketyl radical of *syn*-**9** should separate from the ester carbonyl more easily than *anti*-**9** so that *syn*-**1** gives light less effectively than *anti*-**1**.

The difference in Φ_S between stereoisomers (*anti*-**1**) and (*syn*-**1**) is most likely rationalized well by the ET–BET chemiexcitation mechanism, as described above. However, the CT-induced direct chemiexcitation mechanism cannot be ruled out because the stereochemistry of the starting dioxetanes (**1**) is retained by means of a tetrahydrofuran ring in a transition state (**8**), which would influence more or less the yield of singlet-excited state when it decomposes directly to give **2**.

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8. Selected data for *anti*-**1a**: colorless needles (from hexane–dichloromethane), mp 113.5–114.0°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.22 (s, 6H), 0.87 (s, 3H), 1.00 (s, 9H), 1.06 (s, 9H), 1.20 (s, 3H), 5.75 (s, 1H), 6.90 (ddd, J=7.5, 2.6, and 1.8 Hz, 1H), 7.22 (d, J=1.8 Hz, 1H), 7.28–7.47 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C −4.19, 18.4, 18.6, 20.4, 25.8, 27.1, 37.3, 48.7, 87.0, 105.9, 114.1, 120.0, 121.3, 121.4, 127.5, 127.8, 128.9, 136.2, 137.3, 155.2. Selected data for *syn*-**1a**: colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.20 (s, 6H), 0.89 (s, 3H), 0.99 (s, 9H), 1.07 (s, 9H), 1.57 (s, 3H), 5.36 (s, 1H), 6.87–6.89 (m, 1H), 7.15 (d, J=1.2 Hz, 1H), 7.26–7.37 (m, 5H), 7.75 (d, J=7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C −4.19, −4.17, 18.3, 20.8, 25.8, 27.0, 29.7, 37.1, 50.6, 98.1, 106.1, 118.1, 120.2, 121.2, 121.5, 127.2, 127.6, 128.3, 128.8, 137.7, 140.3, 155.2.
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