

Fluoride-induced chemiluminescent decomposition of 1,2-dioxetanes bearing a phenyl moiety substituted with a methyl having an electron-withdrawing group†

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Received (in Cambridge, UK) 6th November 2002, Accepted 13th January 2003

First published as an Advance Article on the web 27th January 2003

A new type of dioxetane bearing a 3-(cyanomethyl)phenyl (1a), 3-(methoxycarbonylmethyl)phenyl (1b), 3-(benzoylmethyl)phenyl (1c), or 3-[cyano(methoxycarbonyl)methyl]phenyl group (1d) decomposed through an intermediary dioxetane bearing a benzylic carbanion to afford crimson to yellow light on treatment with TBAF in DMSO.

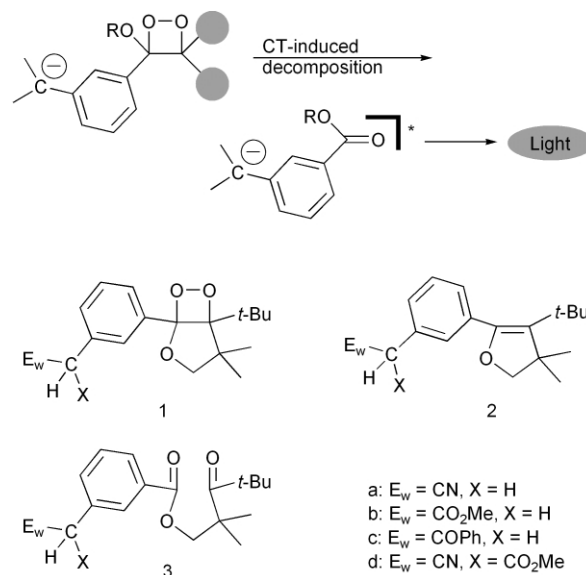
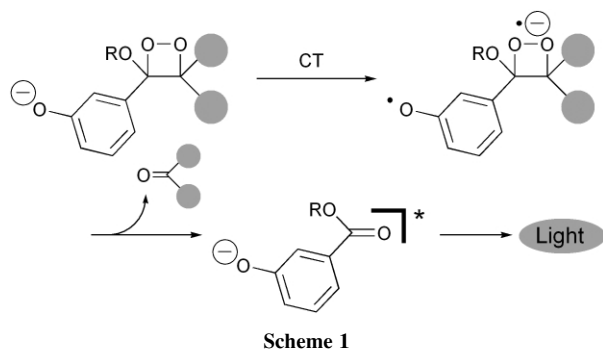
Dioxetanes substituted with an aromatic electron donor such as an oxyanion of a hydroxyarene (aryl-O⁻) moiety undergo intramolecular charge-transfer (CT)-induced decomposition with accompanying luminescence.^{1–5} The phenomenon has received much attention from the viewpoint of mechanistic interest related 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.^{6,7} However, there has been little known of dioxetanes bearing a carbanion such as a benzylic anion (aryl-C⁻) instead of an aryloxy anion (aryl-O⁻), though a benzylic carbanion would play a role of electron donor similar to an aryloxy anion for the intramolecular CT-induced chemiluminescent decomposition (Scheme 1). This situation prompted us to design a new type of dioxetane (1) (Scheme 2) bearing a phenyl moiety substituted with a methyl having an electron-withdrawing group(s) (-CH₂-E_w or X-CH-E_w), of which a proton is easily abstracted with a base to afford a benzylic carbanion, and it was found that these dioxetanes (1) decompose rapidly to afford crimson to yellow light on treatment with tetrabutylammonium fluoride (TBAF) in DMSO.

The designed dioxetanes were 5-*tert*-butyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptanes^{‡8} bearing a 3-(cyanomethyl)phenyl (1a), 3-(methoxycarbonylmethyl)phenyl (1b), 3-(benzoylmethyl)phenyl (1c), or 3-[cyano(methoxycarbonyl)methyl]phenyl group (1d) at the 1-position. When a 4-*tert*-butyl-3,3-dimethyl-2,3-dihydrofuran bearing a 3-(cyanomethyl)phenyl at the 5-position (2a) (200 mg) was irradiated in the presence of tetraphenylporphyrin (TPP, 1 mg) with a 940-W Na lamp in CH₂Cl₂ (10 mL) under O₂ atmosphere at 0 °C for 1 h, the desired dioxetane (1a) was produced as pale yellow granules (mp 99.8–100.6 °C) in 89% yield after chromatographic

purification [SiO₂/hexane-CH₂Cl₂ (1:1)]. The structure of dioxetane (1a) was determined by ¹H NMR, ¹³C NMR, IR, and HRMass spectral analysis.§ Methoxycarbonylmethyl- (1b), benzoylmethyl- (1c), and cyano(methoxycarbonyl)methyl-analogs (1d) were similarly synthesized from the corresponding dihydrofurans (2b–2d) in 86, 90, and 94% isolated yield, respectively. All dioxetanes (1a–1d) synthesized here were stable enough to permit handling at room temperature, though they decomposed to give the corresponding keto-esters (3a–3d) exclusively in refluxing *p*-xylene.

When a solution of a dioxetane (1a) in DMSO (1 × 10⁻³ mol dm⁻³, 1 mL) was added to a solution of tetrabutylammonium fluoride (TBAF)¶ in DMSO (0.1 mol dm⁻³, 2 mL) at 25 °C, 1a decomposed rapidly to emit flash crimson light (maximum wavelength: λ_{max}^{CL} = 702 nm, chemiluminescence efficiency: Φ^{CL} = 3.3 × 10⁻⁵,||¹⁰ half-life: t_{1/2} < 0.02 s).** On treatment with TBAF in DMSO similarly to the case of 1a, the other dioxetanes (1b–1d) also decomposed to exhibit chemiluminescence, of which the properties are summarized together with those for 1a in Table 1. It is noteworthy that a dioxetane (1d) exhibits chemiluminescence with far higher efficiency (Φ^{CL}), far longer half-life (t_{1/2}), and far shorter maximum wavelength of the emission (λ_{max}^{CL}) than those for the others (1a–1c).

The fresh spent reaction mixture of TBAF-induced chemiluminescent decomposition for all dioxetanes (1a–1d) in DMSO was confirmed to include the corresponding keto-esters (3a–3d) exclusively.†† On the other hand, fluorescence of the spent reaction mixture was observed only for 1d, while little was unfortunately observed for the other dioxetanes (1a–1c). The maximum wavelength of the chemiluminescence (λ_{max}^{CL}) for 1d coincided with the maximum wavelength of the fluorescence (λ_{max}^{fl}) for the spent reaction mixture in TBAF-DMSO. The authentic keto-ester (3d), prepared by thermolysis



† Electronic supplementary information (ESI) available: experimental section. See <http://www.rsc.org/suppdata/cc/b2/b210857g/>

of **1d**, showed fluorescence with efficiency $\Phi^f = 0.018$ and its maximum wavelength (λ_{\max}^f)^{‡‡} coincided also with $\lambda_{\max}^{\text{CL}}$ of the chemiluminescence for **1d** in TBAF–DMSO. Furthermore, when a solution of a keto-ester (**3d**) in TBAF–DMSO was treated with methyl iodide, a product methylated at the benzylic position (**6d**) was produced exclusively. These facts reveal that the emitter produced is undoubtedly a carbanion of **3d**, namely **5d**, and thus, the singlet-chemiexcitation efficiency ($\Phi_s = \Phi^{\text{CL}}/\Phi^f$) is estimated to be $\Phi_s = 0.32$ for the TBAF-induced decomposition of **1d**. The emitter would be the respective benzylic carbanion of the keto-ester (**3a–3c**) also for the TBAF-induced chemiluminescent decomposition of the other dioxetanes (**1a–1c**), though little fluorescence was observed even for the authentic keto-ester (**3a–3c**) in TBAF–DMSO.

When TBAF was absent in DMSO, little chemiluminescent decomposition occurred for all dioxetanes (**1a–1d**), while it took place easily also on treatment with a base such as *t*-BuOK instead of TBAF. Considering this fact and that a benzylic carbanion of **3** would be an emitter, it is reasonable to assume that proton-abstraction from **1** with TBAF produces an unstable dioxetane (**4**) bearing a benzylic carbanion, from which CT occurs to induce the decomposition of the dioxetane ring producing an excited carbanion (**5**) of the keto-ester by a mechanism similar to the case of a dioxetane bearing an aryloxy anion,^{1–5} as illustrated in Scheme 3.

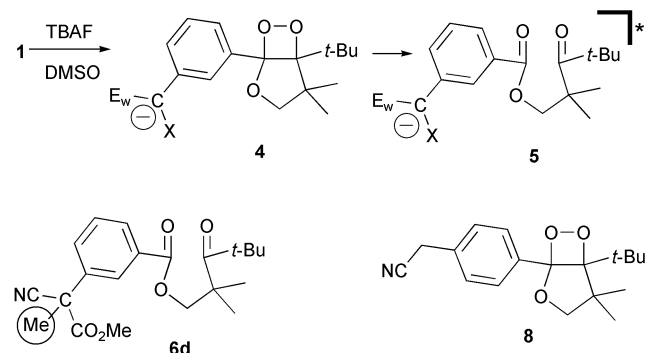
From an analogy of the CT-induced decomposition of a dioxetane bearing an aryloxy anion, it is inferred that chemiluminescent decomposition of a dioxetane (**4**) bearing a benzylic carbanion produced from **1** is expected to occur more easily, as the benzylic carbanion becomes less stable and is more easily oxidized. This idea is apparently consistent with the fact that the half-life of chemiluminescence ($t_{1/2} = \log_e 2/k$; k : rate constant of TBAF-induced decomposition) becomes longer in the order of **1a** < **1b** < **1c** < **1d** (Table 1): considering the order of acidity for the parent carbon acids,¹¹ namely, CH_3CN ($\text{p}K_a = 25$) < $\text{CH}_3\text{CO}_2\text{Me}$ ($\text{p}K_a = 24.5$) < CH_3COPh ($\text{p}K_a = 19$) << $\text{CH}_2(\text{CN})\text{CO}_2\text{Me}$ ($\text{p}K_a = 9$), the acidity of a benzylic position for **1** increases presumably in the order of **1a** < **1b** < **1c** < **1d**, so that the stability of their conjugate carbanions increases in the same order.

Table 1 TBAF-induced chemiluminescent decomposition of dioxetanes (**1a–1d**) in DMSO^a

Dioxetane (1)	<i>E</i> _w	X	λ_{\max} / nm	$t_{1/2}$ s	$\Phi^{\text{CL}b}$
1a	-CN	H	702	< 0.02	3.3×10^{-5}
1b	-CO ₂ Me	H	666	0.42	4.0×10^{-5}
1c	-COPh	H	622	0.43	4.4×10^{-4}
1d	-CN	-CO ₂ Me	530	2300	5.7×10^{-3}

^a A solution of a dioxetane (**1**) in DMSO (1×10^{-3} mol dm⁻³, 1 mL) was added to a solution of TBAF in DMSO (0.1 mol dm⁻³, 2 mL) at 25 °C.

^b Chemiluminescence yields (Φ^{CL}) were based on the reported value for TBAF-induced chemiluminescent decomposition of 1,2-dioxetane in TBAF: $\Phi^{\text{CL}} = 0.29$ (ref. 10).



Scheme 3

The results presented here show a first example that a dioxetane bearing a phenyl group substituted with an acidic methylene or methyne undergoes base-induced chemiluminescent decomposition through an intermediary dioxetane bearing a benzylic carbanion by a mechanism similar to the case of CT-induced chemiluminescent decomposition of a dioxetane bearing an aryloxy anion. Finally, it should be noted here that a dioxetane bearing a 4-(cyanomethyl)phenyl (**8**) decomposed as easily as its 3-(cyanomethyl)phenyl-isomer (**1a**) but gave little light. This tendency resembles the case of dioxetanes bearing an oxyphenyl anion, for which a 4-oxyphenyl-analog has been known to emit light far less effectively than a 3-oxyphenyl-analog.^{6,12}

The authors gratefully acknowledge financial assistance provided by a grant-in-aid for Scientific Research by the Ministry of Education, Science, Sports and Culture.

Notes and references

‡ 1-Aryl-5-*tert*-butyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptane has been recently reported to provide a thermally persistent dioxetane skeleton.⁸

§ Selected data for **1a**: δ_{H} (400 MHz, CDCl₃) 0.98 (s, 9H), 1.16 (s, 3H), 1.39 (s, 3H), 3.79 (s, 2H), 3.83 (d, $J = 8.2$ Hz, 1H), 4.59 (d, $J = 8.2$ Hz, 1H), 7.39 (d, $J = 7.6$ Hz, 1H), 7.44 (t, $J = 7.6$ Hz, 1H), 7.59 (s, 1H), 7.62 (d, $J = 7.6$ Hz, 1H); δ_{C} (100 MHz, CDCl₃) 18.5, 23.7, 25.2, 26.8, 36.7, 45.7, 80.3, 104.9, 116.2, 117.4, 127.8, 128.1, 128.7, 128.9, 129.7, 137.1; Mass (m/z , %) 302 ($M^+ + 1$, 2), 269 (7), 244 (40), 218 (52), 162 (48), 144 (89), 85 (66), 57 (100). Anal. Calcd. for C₁₈H₂₃NO₃: C, 71.73; H, 7.69; N, 4.65. Found: C, 71.86; H, 8.08; N, 4.73.

¶ TBAF has been widely used as a strong base for carbanion-participated reactions such as aldol condensation and Michael addition in an aprotic solvent.⁹

|| Chemiluminescence yields (Φ^{CL}) were based on the reported value for TBAF-induced chemiluminescent decomposition of 3-(2'-spiroadaman-tane)-4-methoxy-4-(3'-*tert*-butyldimethylsiloxy)phenyl-1,2-dioxetane in TBAF: $\Phi^{\text{CL}} = 0.29$.¹⁰

** Preliminary kinetic experiments showed that chemiluminescent decomposition of **1** occurred following pseudo-first-order kinetics independent of the TBAF concentration, when a large excess of TBAF (> 100 eq.) was used.

†† Keto-ester (**3**) changed gradually into a complex mixture including products of aldol and/or Claisen condensation on standing at room temperature in TBAF–DMSO.

‡‡ Quinine bisulfate was used as the fluorescence standard.

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