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Base-induced decomposition of dioxetanes bearing a 3-hydroxyphenyl moiety substituted with a proton-donating group at the 4-position: effect of intramolecular hydrogen bonding on decomposition rate and chemiluminescence efficiency

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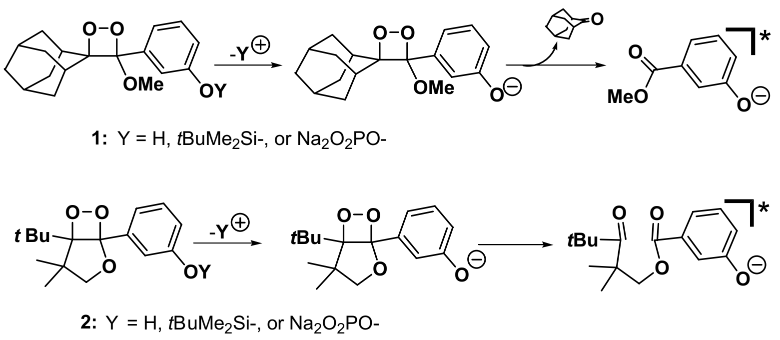
Abstract—Bicyclic dioxetanes bearing a 3-hydroxyphenyl moiety substituted with an amidomethyl group (**3a–c**) or a hydroxymethyl group (**4**) were synthesized. On treatment with tetrabutylammonium fluoride in CH_3CN, they decomposed rapidly with accompanying emission of blue light. Their decomposition rates and chemiluminescence efficiencies were found to be affected by the intramolecular hydrogen bonding between the phenoxy anion and the adjacent proton-donating group.

Deprotonation or deprotection of thermally stable dioxetanes bearing a phenolic moiety such as **1** and **2** produces unstable dioxetanes bearing a phenoxide anion, which decompose rapidly with accompanying efficient emission of light in an aprotic solvent[1–3] by the intramolecular charge-transfer (CT) mechanism as shown in Scheme 1.[4,5] On the other hand, the chemiluminescence efficiency (Φ^{CL}) decreases markedly for their CT-induced decomposition in an aqueous medium.[6,7] The pronounced decrease of Φ^{CL} in the aqueous system has been suggested to be mainly due to the hydrogen bonding of H_2O molecules with intermediary oxyanions of dioxetanes (**1** and **2**), and with the excited emitter produced, which causes significant decrease of singlet-chemiexcitation efficiency (Φ_S) and fluorescence efficiency (Φ^{fl}) of the emitter.[8–10] However, experimental evidence is still lacking to clarify the effect of hydrogen bonding on chemiluminescent efficiency of dioxetanes active toward the intramolecular CT-induced decomposition. Thus, as a clue to know such effect of the hydrogen



Scheme 1.

Keywords: 1,2-Dioxetane; Charge-transfer; Chemiluminescence; Hydrogen bonding.

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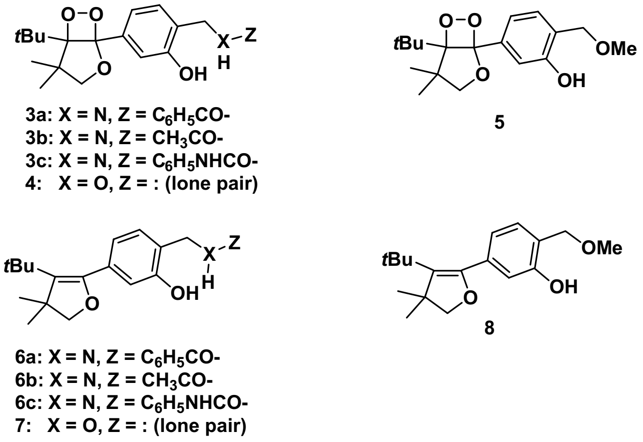


Scheme 2.

bonding, we attempted to examine the CT-induced decomposition of dioxetanes bearing a 3-hydroxyphenyl substituted with an amidomethyl (–CH_2NHCOR) (**3a**–**c**) or a hydroxymethyl (**4**) as a proton-donating group at the 4-position, and of dioxetane (**5**) bearing a 3-hydroxy-4-methoxymethylphenyl group as a reference (Scheme 2).

Dioxetanes (**3a**–**c** to **5**) were synthesized by singlet oxygenation of the corresponding dihydrofurans (**6a**–**c** to **8**). Thus, a solution of dihydrofuran (**6a**) was irradiated together with a catalytic amount of tetraphenylporphin (TPP) with a 940 W Na-lamp in CH_2Cl_2 under oxygen atmosphere at 0 °C for 1 h. The photolysate was concentrated and chromatographed on silica gel with AcOEt–hexane to give dioxetane (**3a**) in 97% yield.[11] The other dihydrofurans (**6b**,**c** to **8**) were similarly oxygenated to afford the corresponding dioxetanes (**3b**,**c** to **5**) in 79–97% yields. All dioxetanes (**3a**–**c** to **5**) synthesized here were thermally stable enough to permit handling at room temperature.

When a solution of dioxetane (**3a**) in CH_3CN (1.0×10^{-5} M, 1 mL) was added to a tetrabutylammonium fluoride (TBAF) solution in CH_3CN (1.0×10^{-2} M, 2 mL), **3a** emitted blue light (λ_{max}^{CL} = 471 nm) with chemiluminescence efficiency Φ^{CL} = 0.02 and half-life $t_{1/2}$ = 170 s ($t_{1/2} = \log_e 2/k^{DICT}$: k^{DICT} is rate constant of CT-induced decomposition of dioxetane following pseudo-first order kinetics). Dioxetanes (**3b**,**c** and **4**) were similarly treated with TBAF in CH_3CN also to emit blue light with chemiluminescent properties (λ_{max}^{CL}, Φ^{CL}, and $t_{1/2}$) as shown in Table 1. Comparing these chemiluminescent properties with those of the parent dioxetane (**2**), one realizes for dioxetanes (**3a**–**c** and **4**) that rates of CT-induced decomposition decrease into 1/1.6–1/6.8 of the rate for **2**, and even chemiluminescence efficiencies decrease into 1/1.1–1/5.5, though the maximum wavelengths of emission are not exactly different from the case of **2**.

The decrease of CT-induced decomposition rate for **3a**–**c** and **4** should not be attributed to the electronic factor of an amidomethyl or a hydroxymethyl group on a phenoxy moiety, but be attributed to their role as a proton-donor for intramolecular hydrogen bonding as illustrated in Scheme 3. This idea was supported by the base-induced decomposition of dioxetane (**5**), in which a 4-methoxymethyl group on a phenolic ring is electron-donating similarly to a hydroxymethyl in **4** but cannot play the role as a proton-donor for the hydrogen bonding. Thus, on treatment with TBAF in CH_3CN, dioxetane (**5**) exhibited emission of blue light similar to the case of dioxetanes (**3a**–**c** and **4**), but its CT-induced decomposition rate was far more rapid than those for dioxetanes (**3a**–**c** and **4**) and even than that of the parent dioxetane (**2**) (see Table 1). The efficiency of light emission (Φ^{CL}) was also higher (1.8–9 times) for **5** than those for **3a**–**c**,**4**, and **2**. These results show that the introduction of a methoxymethyl group at the 4-position on 3-hydroxyphenyl moiety of dioxetane (**2**) effects to increase both Φ^{CL} and k^{DICT}, contrary to the case of **3a**–**c** and **4**.

The ^1H NMR spectra of dioxetanes (**3a**–**c** and **4**) showed that the intramolecular hydrogen bonding exists between a phenolic OH and the adjacent –CH_2–X(H)–Z group, namely amidomethyl (X = N, Z = –COR) or hydroxymethyl (X = O, Z = lone pair): a singlet peak due to the intramolecular hydrogen bonding was observed at δ_H 9.58 for **3a**, 9.55 for **3b**, 9.81 for **3c**, and 7.38 for **4** in $CDCl_3$. This fact suggests that the intramolecular hydrogen bonding presumably participates even in oxyanions of intermediary dioxetanes (**14a**–**d**) produced from the corresponding dioxetanes (**3a**–**c** and **4**) and as well in emitters (**15a**–**d**) (Scheme 3). The CT-induced decomposition would occur rapidly for dioxetane bearing an easily oxidized aromatic electron donor.[8,9] Therefore, it is reasonably understood that the hydrogen bonding to a phenoxy anion of intermediary dioxetane (**14**) should make the phenoxy anion less oxidized and,

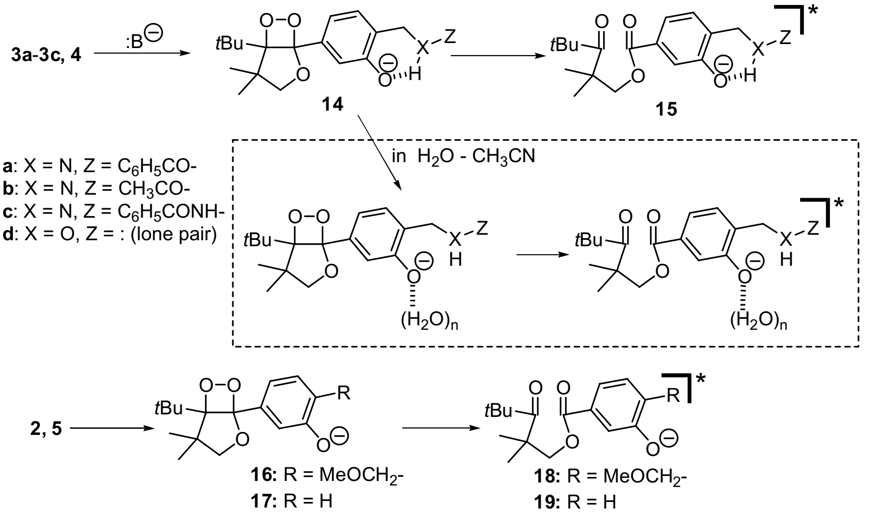
Table 1. Base-induced chemiluminescent decomposition of dioxetanes (**3a**–**c** to **5**)

Dioxetane	TBAF/CH_3CN[a]				NaOH/H_2O–CH_3CN (2:1)[b]			
	λ_{max}^{CL}/nm	Φ^{CL} [c]	k^{DICT}/s^{-1}	$t_{1/2}$/s	λ_{max}^{CL}/nm	Φ^{CL} [c]	k^{DICT}/s^{-1}	$t_{1/2}$/s
3a	471	0.02	4.1×10^{-3}	170	487	5.2×10^{-5}	1.4×10^{-3}	490
3b	470	0.10	1.6×10^{-2}	44	483	5.2×10^{-5}	1.5×10^{-3}	450
3c	469	0.06	1.7×10^{-2}	40	483	2.6×10^{-5}	1.9×10^{-3}	370
4	468	0.10	4.1×10^{-3}	170	487	3.0×10^{-5}	1.8×10^{-3}	390
5	472	0.18	9.0×10^{-2}	7.7	485	6.4×10^{-5}	1.8×10^{-3}	390
2	471	0.11	2.8×10^{-2}	25	483	8.2×10^{-5}	4.1×10^{-4}	1700

[a] A solution of a dioxetane in CH_3CN (1.0×10^{-5} M, 1 mL) was added to a solution of TBAF in CH_3CN (1.0×10^{-2} M, 2 mL) at 25 °C.

[b] A solution of a dioxetane in CH_3CN (1.0×10^{-4} M, 1 mL) was added to a solution of NaOH in H_2O (1.0×10^{-1} M, 2 mL) at 25 °C.

[c] Relative quantum yields based on the value for dioxetane (**1**, Y = $tBuMe_2Si$–) in TBAF/DMSO system (Ref. 2: Φ^{CL} = 0.29).



Scheme 3.

hence, causes the decrease of the CT-induced decomposition rate, comparing with the rate for **16** and **17**, in which an oxyanion center is formally naked in CH_3CN.

Table 1 shows also the chemiluminescent properties of dioxetanes (**3a**–**c** to **5**) together with those of **2** in the NaOH/H_2O–CH_3CN (2:1) system.[12] One characteristic feature noted for chemiluminescent decomposition of all dioxetanes discussed here in the aqueous system is that chemiluminescence efficiencies (Φ^{CL}) decreased significantly and converged into the value for dioxetane (**5**). On the other hand, the decreases in CT-induced decomposition rates (k^{DICT}) from the CH_3CN system to the aqueous system were rather small, though the rates (k^{DICT}) converged also into the value for dioxetanes (**5**) except the case of dioxetane (**2**). For the NaOH/H_2O–CH_3CN system, the difference in k^{DICT} between **5** and **2** is most likely attributed to the electron-donating effect of methoxymethyl group in **5**, considering that the magnitude of decrease in k^{DICT} for **5** was similar to that for **2**. The decrease in k^{DICT} itself for **5** and **2** should be due to the hydrogen bonding of H_2O molecule(s)[13] to oxyanion of **16** and **17**. This effect is presumably applied to the decrease in k^{DICT} for **3a**–**c** and **4** in the NaOH/H_2O–CH_3CN system.

The decrease of chemiluminescence efficiencies (Φ^{CL}) for **3a**–**c** and **4** in the aqueous system should be caused by the intermolecular hydrogen bonding with H_2O molecule(s)[13] not only to **14** but also to **15**: the former causes the decrease of singlet-chemiexcitation efficiency, while the latter leads to the decrease of fluorescence efficiency (Φ^{fl}) of emitter, though it was not confirmed since fluorescence of **15** and **18** could not be unfortunately observed because of rapid hydrolysis of authentic ketoesters corresponding to **15** and **18**, which were prepared easily from the respective dioxetanes (**3a**–**c** to **5**) by thermolysis.

In conclusion, the present results reveal for a dioxetane bearing a phenoxide anion that the hydrogen bonding to the oxyanion causes in fact the decreasing rate of the intramolecular CT-induced decomposition of dioxetane as well as the decreasing chemiluminescence efficiency. However, in addition to the hydrogen bonding of H_2O molecules with the phenoxide anion, other factors such as the hydrogen bonding to carbonyl oxygen of the emitter produced from a dioxetane may participate with the significant decrease of chemiluminescence efficiency in the aqueous system, as suggested already.[10]

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11. Selected data for compound **3a**: colorless needles, mp 183.0–184.0 °C, dec; ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.00 (s, 9H), 1.13 (s, 3H), 1.36 (s, 3H), 3.78 (d, $J = 8.2$ Hz, 1H), 4.52–4.62 (m, 3H), 6.94 (br s, 1H), 7.12 (dd, $J = 7.8$ and 1.8 Hz, 1H), 7.17 (d, $J = 7.8$ Hz, 1H), 7.20 (d, $J = 1.8$ Hz,

1H), 7.46 (t, $J = 7.3$ Hz, 2H), 7.54 (t, $J = 7.3$ Hz, 1H), 7.78 (d, $J = 7.3$ Hz, 2H), 9.59 (s, 1H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C 18.5, 25.0, 26.9, 36.7, 40.8, 45.6, 80.2, 105.0, 116.4, 118.2, 119.8, 125.2, 127.2, 128.8, 130.3, 132.4, 132.6, 138.2, 155.7, 169.7 ppm; HRMS (ESI): 434.1940, calcd for $C_{24}H_{29}NO_5Na$ [M+Na$^+$]: 434.1943. Selected data for compound **3b**: amorphous solid; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H 1.00 (s, 9H), 1.13 (s, 3H), 1.36 (s, 3H), 1.98 (d, $J = 3.4$ Hz, 3H), 3.79 (d, $J = 8.1$ Hz, 1H), 4.22–4.33 (m, 2H), 4.53 (d, $J = 8.1$ Hz, 1H), 6.71 (br s, 1H), 7.03–7.08 (m, 2H), 7.15 (s, 1H), 9.55 (s, 1H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C 18.4, 22.6, 24.9, 26.9, 36.7, 40.2, 45.5, 80.2, 105.0, 116.5, 117.8, 119.6, 125.4, 130.3, 137.8, 155.5, 173.0 ppm; HRMS (ESI): 372.1770, calcd for $C_{19}H_{27}NO_5Na$ [M+Na$^+$]: 372.1787. Selected data for compound **3c**: pale yellow granules, mp 155.0–156.5 °C, dec; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H 0.98 (s, 9H), 1.12 (s, 3H), 1.33 (s, 3H), 3.77 (d, $J = 8.1$ Hz, 1H), 4.13–4.24 (m, 2H), 4.52 (d, $J = 8.1$ Hz, 1H), 5.78 (t, $J = 6.3$ Hz, 1H), 6.96–7.05 (m, 3H), 7.14 (d, $J = 1.6$ Hz, 1H), 7.17–7.23 (m, 4H), 9.81 (br s, 1H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C 18.4, 24.9, 26.8, 36.6, 40.4, 45.5, 80.2, 105.1, 116.7, 117.4, 119.5, 121.0, 124.2, 126.6, 129.1, 130.3, 137.3, 137.6, 155.4, 157.8 ppm; HRMS (ESI): 449.2018, calcd for $C_{24}H_{30}N_2O_5Na$ [M+Na$^+$]: 449.2052. Selected data for compound **4**: colorless needles, mp 146.0–147.0 °C, dec; ^{1}H NMR (400 MHz, CD$_3$Cl) δ_H 1.00 (s, 9H), 1.15 (s, 3H), 1.37 (s, 3H), 2.24 (s with fine coupling, 1H), 3.80 (d, $J = 8.1$ Hz, 1H), 4.54 (d, $J = 8.1$ Hz, 1H), 4.90 (d, $J = 5.7$ Hz, 2H), 7.05 (d, $J = 7.6$ Hz, 1H), 7.13 (d, $J = 7.6$ Hz, 1H), 7.14 (s, 1H), 7.38 (s, 1H) ppm; ^{13}C NMR (125 MHz, CD$_3$COCD$_3$): δ_C 19.1, 25.6, 27.7, 37.8, 46.7, 61.6, 80.9, 105.8, 116.3, 117.6, 120.5, 127.9, 130.2, 137.2, 155.5 ppm; IR (KBr): 3467, 3269, 2995, 2970, 2935, 2906, 1622, 1574 cm^{-1}; mass (*m*/*z*, %): 308 (M$^+$, trace), 291 (4), 253 (23), 252 (17), 152 (11), 151 (100), 150 (19), 149 (15), 135 (11), 134 (26), 133 (26), 57 (49); HRMS (ESI): 331.1511, calcd for $C_{17}H_{24}O_5Na$ [M+Na$^+$]: 331.1521. Selected data for compound **5**: colorless columns, mp 93.0–94.5 °C, dec; ^{1}H NMR (400 MHz, CDCl$_3$): δ_H 1.00 (s 9H), 1.14 (s, 3H), 1.37 (s, 3H), 3.45 (s, 3H), 3.79 (d, $J = 8.2$ Hz, 1H), 4.56 (d, $J = 8.2$ Hz, 1H), 4.69 (s, 2H), 7.03 (d, $J = 8.0$ Hz, 1H), 7.12–7.13 (m, 1H), 7.14 (s, 1H), 7.57 (s, 1H) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C 18.4, 25.0, 26.8, 36.7, 45.5, 58.4, 73.8, 80.2, 104.9, 116.4, 116.6, 119.8, 123.2, 127.5, 137.5, 155.8 ppm; IR (KBr): 3377, 2993, 2962, 2893, 1624, 1579 cm^{-1}; mass (*m*/*z*, %): 322 (M$^+$, 0.4), 290 (1), 266 (21), 265 (13), 166 (11), 165 (100), 150 (14), 133 (15), 57 (26); HRMS (ESI): 345.1665, calcd for $C_{18}H_{26}O_5Na$ [M+Na$^+$]: 345.1678.

12. Base-induced decomposition was not carried out for dioxetanes (**3a**–**c** and **4**) in NaOH/H$_2$O, since **3a**–**c**, **4**, especially **3c**, dissolved slightly in NaOH/H$_2$O.
13. Coordination of sodium ion to an oxyanion probably participates also in the CT-induced decomposition process of dioxetanes in NaOH/H$_2$O–CH$_3$CN system.