New Triggering System for Dioxetane-based Chemiluminescence: Base-induced Decomposition of Bicyclic Dioxetanes Bearing a 3-Aminophenyl or 2-Phenylindol-6-yl Moiety

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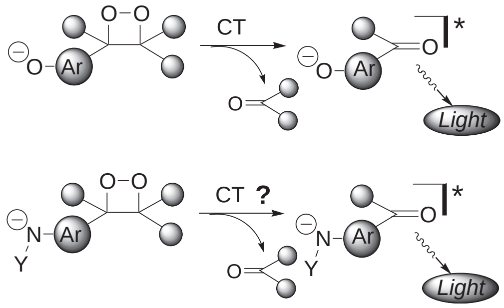
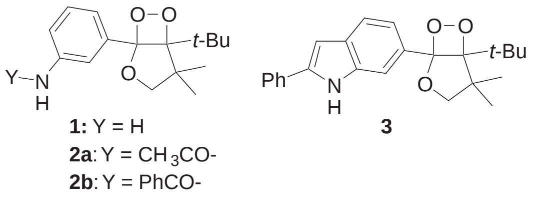
A dioxetane substituted with a 3-aminophenyl group was deprotonated with *t*-BuOK in DMSO to give an unstable dioxetane bearing a phenylamide anion, which decomposed with accompanying emission of flash red light. Dioxetane bearing an indol-6-yl group was synthesized and found to exhibit emission of flash blue light on treatment with tetrabutylammonium fluoride as well as with *t*-BuOK.

Dioxetanes substituted with an aromatic electron donor such as an oxyanion of a hydroxyarene moiety (ArO$^-$) undergo intramolecular charge-transfer (CT)-induced decomposition with accompanying emission of light.[1–4] The phenomenon has received much attention, and extensive research efforts have been made to elucidate the chemiexcitation pathways as well as to develop efficient chemiluminescent systems.[1,2] However, there has been little known of dioxetanes bearing an amide anion such as an arylamide anion (Ar(Y)N$^-$) instead of an aryloxide anion (ArO$^-$), though Ar(Y)N$^-$ would act as an electron donor similar to ArO$^-$ for the intramolecular CT-induced decomposition (Scheme 1). This situation prompted us to design a new type of dioxetane bearing an Ar(Y)NH moiety, from which a proton is abstracted with a base to generate an arylamide anion (Ar(Y)N$^-$).

We chose three types of dioxetanes bearing an Ar–NH–Y moiety to be examined. The first was dioxetane **1** bearing a simple 3-aminophenyl group, synthesis of which has been reported already.[5] The second was dioxetanes bearing a 3-acetylaminophenyl **2a** or 3-benzoylaminophenyl group **2b**, whose synthesis was easily attained by the singlet oxygenation of the corresponding dihydrofurans **4a**, **4b**[6,7] in high yield. The third was dioxetane **3** bearing a 2-phenylindol-6-yl moiety, in which a 2-phenyl group was introduced to decrease the reactivity of the indole ring toward singlet oxygenation used for the synthesis of **3** from a key intermediate **5**. Dihydrofuran having a 2-phenylindol-6-yl moiety **5** was synthesized by intramolecular cyclization of *N*-benzoyl-*o*-toluidine **6**: on treatment with BuLi at 50 °C, **6** was converted into **5** in 55% isolated yield.[8] An amide **6** was synthesized by transformation of a bromophenyl group in dihydrofuran **7** to a benzoylamino group through a toluidine derivative **8** in 86% total yield. When a solution of dihydrofuran **5** and a catalytic amount of tetraphenylporphin in CH_2Cl_2 was irradiated externally with a 940-W Na lamp under an O_2 atmosphere at −78 °C for 2 h, dioxetane **3** was produced exclusively and was isolated as pale yellow granules (mp 223.9–224.9 °C) after chromatographic purification (SiO_2/ether-hexane). The structures of dioxetanes **2** and **3** were determined by ^1H NMR, ^{13}C NMR, IR, HRMass spectral analysis.[9] On heating in hot toluene, these dioxetanes **1**–**3** decomposed exclusively to ketoesters **9**–**11**, respectively, though they were quite stable to permit handling at room temperature.

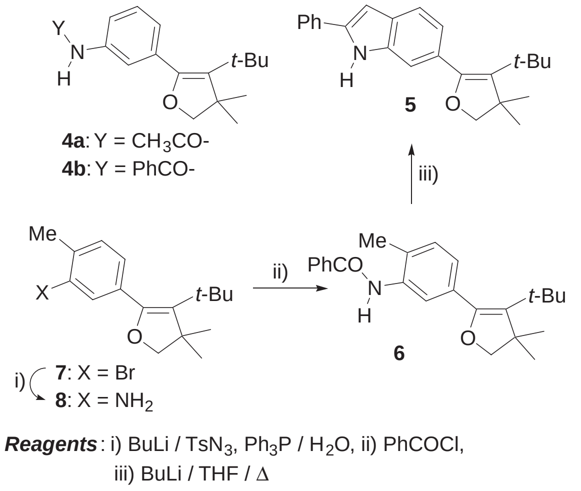


Scheme 1. Intramolecular CT-induced chemiluminescent decomposition of dioxetanes.



Scheme 2. Dioxetanes bearing a 3-aminophenyl or indol-6-yl group.

When a solution of dioxetane **1** in DMSO (1.0×10^{-4} M, 1 mL) was added to a solution of *t*-BuOK in DMSO (1.0×10^{-1} M, 2 mL) at 25 °C, **1** decomposed rapidly to give ketoester **9** with accompanying emission of flash red light with maximum wavelength ($\lambda_{max}{}^{CL}$) = 642 nm, chemiluminescence efficiency



Scheme 3. Synthesis of key intermediate **5** for the synthesis of dioxetane **3**.

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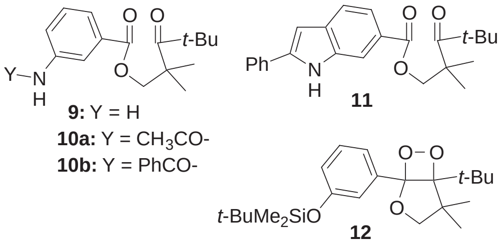
(Φ^{CL}) = 4.8×10^{-6}, and rate constant for CT-induced decomposition following pseudo-first order kinetics (k^{DICT}) = 1.4 s^{-1}. The chemiluminescent properties for **1** were significantly different from those for dioxetane **12** bearing a 3-(*t*-butydimethylsiloxy)phenyl, which emits bright blue light with $\lambda_{max}{}^{CL}$ = 466 nm, Φ^{CL} = 0.20, and k^{DICT} = 0.15 s^{-1}.[10] Furthermore, differently than **12**, decomposition of dioxetane **1** was not induced by treatment with TBAF in DMSO, which is frequently used as a triggering system for dioxetanes active toward the intramolecular CT-induced chemiluminescent decomposition.[4] This difference would be due to the fact that aniline is a very weak acid: pK_a = 30.6 for aniline in DMSO at 25 °C.[11,12]



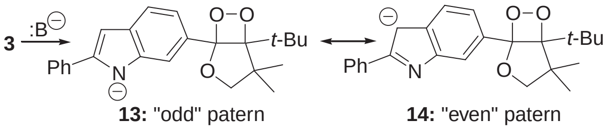
Scheme 4. Ketoesters **9**–**11** and parent dioxetane **12**.

On the other hand, anilides such as acetanilide are presumably a far stronger acid (pK_a = 21.45 for acetanilde)[11] than aniline, so that deprotonation of dioxetanes **2a** and **2b** would take place much more easily than **1** to give the corresponding acylamide anions. However, the expected CT-induced decomposition of **2** itself occurred sluggishly to emit little observable light.

Indole is also an acid as strong as acetanilide (pK_a = 20.95).[11] When dioxetane **3** was treated with a large excess of *t*-BuOK in DMSO similarly to the case of **1**, **3** decomposed to emit flash blue light with $\lambda_{max}{}^{CL}$ = 457 nm, $\Phi^{CL} = 3.4 \times 10^{-5}$, and k^{DICT} = 7.7 s^{-1}. The chemiluminescent decomposition of **3** occurred to give a quite similar result on treatment with TBAF in place of *t*-BuOK in DMSO. The chemiluminescent spectrum of **3** in *t*-BuOK or TBAF/DMSO coincided with the fluorescence spectrum of the spent reaction mixture, from which ketoester **11** was isolated after neutralization in high yield. The fluorescence spectrum of authentic ketoester **11** coincided also with the chemiluminescent spectrum of **3** in TBAF/DMSO.

The chemiluminescent efficiency (Φ^{CL}) was rather lower than that of our expectation. Since the efficiency of fluorescence (Φ^{fl}) for the emitter, namely, ketoester **11**, was estimated to be 0.39 in TBAF/DMSO, the efficiency of singlet-chemiexcitation (Φ_S) was estimated to be only 8.7×10^{-5} for the chemiluminescent decomposition of **3**. This fact is most likely accounted for by the idea that amide anion **13** produced from dioxetane **3** by triggering with a base would be an ambident anion including **13** and carbanion **14** as canonical structures, as is well-known for indoles. Applying dioxetane **3** to the "odd/even" relationship between the substitution pattern of the anion on the aromatic ring and chemiluminescent properties (Φ^{CL}, $\lambda_{max}{}^{CL}$, k^{DICT}) for base-induced decomposition of dioxetanes, the amide anion **13** is "odd" pattern, though the canonical structure of carbanion **14** is unfortunately "even" pattern. It has been known for dioxetanes bearing an aromatic electron donor active toward the intramolecular CT-induced decomposition, that dioxetanes with "odd" pattern tend to exhibit chemiluminescence with higher Φ^{CL}, longer $\lambda_{max}{}^{CL}$ and slower rate (k^{DICT}) than those for dioxetanes with "even" pattern.[4]

In conclusion, the present studies show that a dioxetane substituted with a 3-aminophenyl group can be triggered with a base to give an unstable dioxetane bearing a phenylamide anion, which decomposes with accompanying emission of flash red light. Decomposition of a dioxetane bearing an indol-6-yl group was shown to be induced with a base to give flash blue light. These results provide an entry to dioxetane-based chemiluminescent substrates with a new triggering system.



Scheme 5. Intermediary dioxetane produced from **3**.

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References and Notes

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6 5-Aryl-4-*t*-butyl-3,3-dimethyl-2,3-dihydrofurans **4a**, **4b**, and **7** were synthesized from 7-aryl-2,2,4,4-tetramethyl-6-oxoheptan-3-ones, according to the method reported.[7]
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9 Selected data for **3**: ^{1}H NMR (400 MHz, CDCl3) δ_H 1.01 (s, 9H), 1.18 (s, 3H), 1.43 (s, 3H), 3.85 (d, J = 8.2 Hz, 1H), 4.62 (d, J = 8.2 Hz, 1H), 6.83 (s with fine coupling, 1H), 7.31–7.37 (m, 2H), 7.43–7.48 (m, 2H), 7.62 (d, J = 8.3 Hz, 1H), 7.66–7.70 (m, 2H), 7.79 (s, 1H), 8.50 (broad s, 1H) ppm; ^{13}C NMR (125 MHz, CDCl3) δ_C 18.7, 25.1, 26.9, 36.9, 45.7, 80.1, 99.6, 105.2, 111.7, 117.7, 120.0, 120.2, 125.2, 127.8, 128.9, 129.5, 129.8, 132.0, 136.1, 139.4 ppm; HRMass (ESI) m/z found 400.1889, calcd for $C_{24}H_{27}NaO_3$ [M + Na$^+$] 400.1861.
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12 Amide anion of **9** is most likely the emitter for the chemiluminescent decomposition of **1**, though **9** exhibited little fluorescence with $\lambda_{max}{}^{CL}$ = 642 nm in *t*-BuOK/DMSO, in which the expected amide anion was presumably generated not in sufficient concentration because of very low acidity of **9**.

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