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## Design and Synthesis of Dioxetane-Based Chemiluminescent Substrates with High Efficiency in Aqueous System

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**Abstract:** The chemiluminescent efficiency of hydroxyphenyl-substituted dioxetanes is well known to decrease significantly in an aqueous medium, though more than bioluminescence in an aprotic medium. We investigated here the effect of hydrogen bonding on singlet-chemiexcitation and fluorescence efficiency of the emitter produced for charge-transfer-induced chemiluminescence by the use of dioxetanes bearing a 3-hydroxyphenyl moiety substituted with a proton-donating group at the 4-position as a model substrate. Based on this investigation, four bicyclic dioxetanes bearing a 4-(benzoazol-2-yl)-3-hydroxyphenyl moiety were designed and synthesized. The thus-realized dioxetanes exhibited chemiluminescence with markedly high efficiency in aqueous medium as well as in aprotic medium.

**Keywords:** dioxetane, chemiluminescence, hydrogen bonding

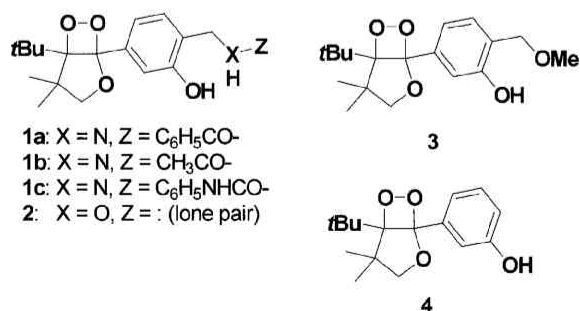
### Introduction

Dioxetanes bearing a phenoxide anion decompose rapidly with accompanying efficient emission of light in an aprotic solvent by the intramolecular charge-transfer-induced chemiluminescence (CTICL) mechanism.<sup>1)</sup> Nowadays, CTICL-active dioxetanes have been designed that exhibit luminescent efficiencies in aprotic solvent as high as most bioluminescences. However, the chemiluminescence efficiency decreases markedly for their CT-induced decomposition in an aqueous medium. We report here a study to identify how water molecule(s) decreases chemiluminescent efficiency for the CTICL of dioxetanes, and a successful attempt to realize a new type of substrates emitting light with high efficiency even in an aqueous medium.

### Result and Discussion

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<sup>2)</sup>

The pronounced decrease of  $\Phi^{CL}$  in the aqueous system has been suggested to be mainly due to the hydrogen bonding of H<sub>2</sub>O molecules with intermediary oxyanions of dioxetanes, and with the excited emitter produced, which causes significant decrease of singlet-chemiexcitation efficiency ( $\Phi_S$ ) and fluorescence efficiency ( $\Phi^f$ ) of the emitter. However, experimental evidence is still lacking to clarify the effect of hydrogen bonding on the chemiluminescent efficiency of dioxetanes active toward intramolecular CT-induced decomposition. Thus, we attempted to examine the CTICL-decomposi-



Scheme 1.

tion of dioxetanes bearing a phenolic moiety capable of forming an intramolecular hydrogen bonding as a clue to elucidate this effect of water. The thus-designed dioxetanes bore a 3-hydroxyphenyl substituted with an amidomethyl ( $-\text{CH}_2\text{NHCOR}$ ), **1a-1c**, or a hydroxymethyl **2** as a proton-donating group at the 4-position, and dioxetane **3** bearing a 3-hydroxy-4-methoxy-methylphenyl group as a reference (Scheme 1).

All these dioxetanes decomposed rapidly with accompanying emission of blue light in TBAF /  $\text{CH}_3\text{CN}$ . Comparing their chemiluminescent properties with those of a parent dioxetane **4**, it is realized that for dioxetanes **1a-1c** and **2** the rates of CTICL-decomposition decrease by  $1/1.6 \sim 1/6.8$  of the rate for **4**, and even chemiluminescence efficiencies decrease by  $1/1.1 \sim 1/5.5$ , though the maximum wavelengths of emission are not exactly different from **4**. The decrease of the CTICL-decomposition rate for **1a-1c** and **2** can be attributed to an amidomethyl or a hydroxymethyl group on a phenoxy moiety as a proton-donor for intramolecular hydrogen bonding.

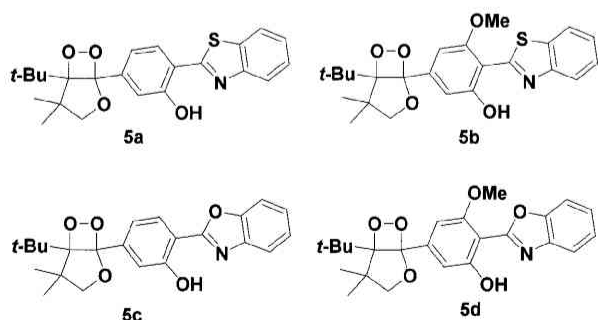
These results reveal that for a dioxetane bearing a phenoxide anion hydrogen bonding to the oxyanion decreases the rate of CTICL-decomposition of dioxetane as well as decreasing chemiluminescence efficiency. However, as reported previously, in addition to the hydrogen bonding of  $\text{H}_2\text{O}$  molecules with the phenoxide anion, other factors such as hydrogen bonding to the carbonyl oxygen of the emitter produced from a dioxetane may participate with the significant decrease of chemiluminescence efficiency in the aqueous system. Bicyclic dioxetanes bearing a 4-(benzoxazol-2-yl)-3-hydroxyphenyl moiety: chemiluminescence profile for base-

induced decomposition in aprotic medium and in aqueous medium<sup>3)</sup>

Four bicyclic dioxetanes, **5a-5d**, bearing a 4-(benzothiazol-2-yl)-3-hydroxyphenyl or 4-(benzoxazol-2-yl)-3-hydroxyphenyl group were synthesized. When dioxetane **5a** was treated with TBAF in acetonitrile, **5a** decomposed to emit blue light with chemiluminescent efficiency  $\phi^{\text{CL}} = 0.39$ , which was twice higher than that from the parent dioxetane **2**. The dioxetane **5a** exhibited markedly effective chemiluminescence even in an  $\text{NaOH} / \text{H}_2\text{O}$  system;  $\phi^{\text{CL}} = 0.12$  was ca 11000 times higher than that from **2**.<sup>4)</sup> It was clarified for the CTICL of **5a** that both singlet chemiexcitation efficiency and fluorescence efficiency of the emitter were very high even in the  $\text{NaOH} / \text{H}_2\text{O}$  system. Dioxetane **5b** displayed chemiluminescence more effective than **5c** in both triggering systems ( $\phi^{\text{CL}} = 0.46$  in TBAF / acetonitrile, and  $\phi^{\text{CL}} = 0.18$  in  $\text{NaOH} / \text{H}_2\text{O}$ ), though the CTICL-decomposition rate was slower than that for **5a**. The other dioxetanes, **5b** and **5d** afforded light less effectively than **5a** and **5c**, without any acceleration of CTICL-decomposition rate.

## References

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Scheme 2