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. 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

The pronounced decrease of $\Phi_{CL}$ in the aqueous system has been suggested to be mainly due to the hydrogen bonding of H$_2$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-
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 (-CH2NHCOR), 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 / CH3CN. 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 ~ 1/6.8 of the rate for 4, and even chemiluminescence efficiencies decrease by 1/1.1 ~ 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 as well as decreasing chemiluminescence efficiency. However, as reported previously, in addition to the hydrogen bonding of H2O 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-(benzothiazol-2-yl)-3-hydroxyphenyl moiety: chemiluminescence profile for base-induced decomposition in aprotic medium and in aqueous medium.

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 $\phi_{CL} = 0.12$ which was twice higher than that from the parent dioxetane 2. The dioxetane 5a exhibited markedly effective chemiluminescence even in an NaOH / H2O system; $\phi_{CL} = 0.12$ was ca 11000 times higher than that from 2. 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 NaOH / H2O system. Dioxetane 5b displayed chemiluminescence more effective than 5c in both triggering systems ($\phi_{CL} = 0.46$ in TBAF / acetonitrile, and $\phi_{CL} = 0.18$ in NaOH / H2O, 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