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Color modulation for chemiluminescence of a dioxetane bearing a 3-(anthracen-9-yl)-5-hydroxyphenyl moiety induced by a complex of crown ether with potassium *tert*-butoxide

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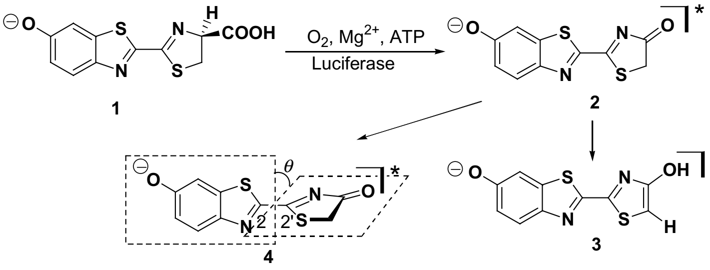
Abstract—Color modulation was first observed for CT-induced chemiluminescent decomposition of a dioxetane bearing a 3-(anthracen-9-yl)-5-hydroxyphenyl induced by a complex of crown ether with potassium *tert*-butoxide in benzene system. The phenomenon is rationalized by conformational change of a biaryl moiety in the emitter, which is induced by steric interaction of anthryl and a plane of crown ether complex.

One marvelous phenomenon in luminous organisms is color modulation observed in the bioluminescence of beetles such as the firefly. Beetle luciferases use the same luciferin (**1**) to display light ranging in color from green to red. An influential proposal to elucidate the phenomenon is that a luciferase-assisted tautomerization of excited-state oxyluciferin (**2**) to an enol (**3**) causes color change of luminescence.[1] Another persuasive elucidation is that color variation relates to TICT (twisted intramolecular charge transfer) excited state[2] due to conformational changes of the keto form of excited-state oxyluciferin (**2**) to a twisted form (**4**),[3] which occurs by rotation about the C2–C2′ bond (Scheme 1). A very recent experimental study using luciferase mutants has supported the latter elucidation including conformational change of **2**,[4] whereas a theoretical study reported recently has taken sides with the former proposal.[5]

On the other hand, there has been little known of the color modulation by the microenvironment for chemiluminescence derived from intramolecular charge-transfer (CT)-induced decomposition of dioxetane bearing an electron donor (Scheme 2),[6] although such type of CT is generally accepted to be responsible for



Scheme 1.

Keywords: 1,2-Dioxetane; Crown ether; Charge transfer; Chemiluminescence; Color modulation.

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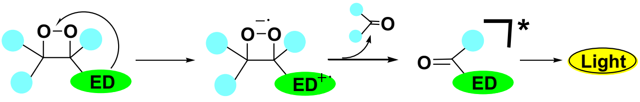


Scheme 2.

the bioluminescence mechanism of the firefly including a high-energy dioxetanone intermediate.[5,7] This situation prompted us to realize a substrate that changes color of chemiluminescence depending on the microenvironment. The designed dioxetanes were 5-*tert*-butyl-4,4-dimethyl-2,6,7-trioxabicyclo[3.2.0]heptane bearing a 1-[3-(anthracen-9-yl)-5-hydroxyphenyl] (**5a**) and its 10-cyanoanthracen-9-yl analog (**5b**). These dioxetanes (**5a**, **5b**) and a parent dioxetane (**6**)[8] were examined for their chemiluminescent behavior in the coordination sphere of a crown ether complex with potassium in benzene[9] (Scheme 3).

Dioxetanes (**5a**, **5b**) were synthesized by singlet oxygenation of the corresponding dihydrofurans (**7a**) and (**7b**). The structures of **5a** (mp 125.0–126.3 °C) and **5b** (mp 195.3–196.2 °C) were determined by ^{1}H NMR, ^{13}C NMR, IR, Mass, and HRMass spectral analysis. X-ray single crystallographic analysis of **5a** was successfully achieved as shown in Figure 1, where the most important point to be noted is that two aromatic rings twist markedly to each other.[10] When a solution of **5a** in benzene (1.0×10^{-3} M, 1 mL) was added to a solution of tetrabutylammonium *tert*-butoxide ($TBA^+\cdot tBuO^-$) in benzene (1.0×10^{-1} M, 2 mL), **5a** decomposed rapidly to give crimson light with maximum wavelength λ^{CL}_{max} = 709 nm, chemiluminescent yield $\Phi^{CL} = 4.0\times10^{-5}$, and half life of decay $t_{1/2}$ = 45 s at 25 °C.[11,12] The chemiluminescent decomposition of **5a** triggered with tetrabutylammonium fluoride (TBAF/DMSO) gave a similar result (λ^{CL}_{max} = 709 nm). The maximum wavelength of chemiluminescence (λ^{CL}_{max}) for **5a** coincided with the maximum wavelength of fluorescence (λ^{fl}_{max}) from the spent reaction mixture as well as λ^{fl}_{max} of an oxyanion (**8a**) of an authentic ketoester, which was easily prepared by thermolysis of **5a**. These results show that **8a** is an emitter for the chemiluminescent decomposition of **5a**.

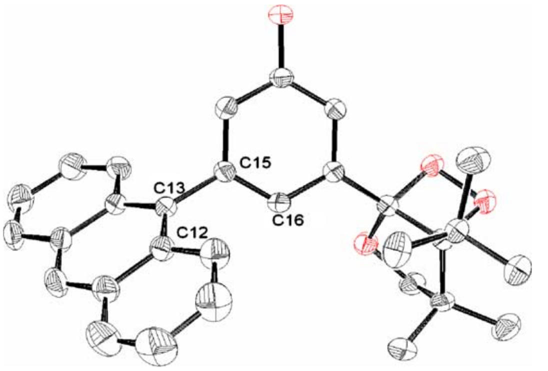
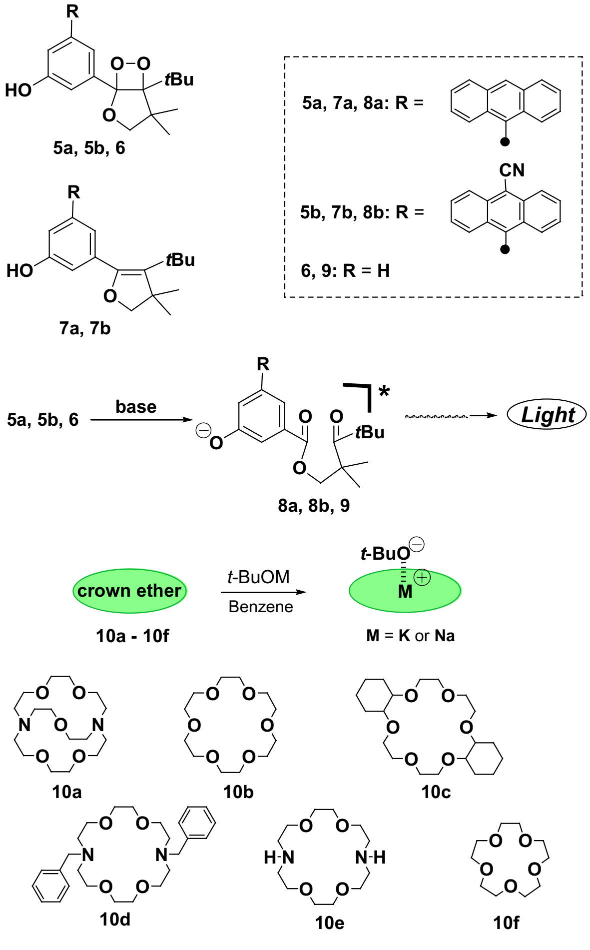


Figure 1. ORTEP view of dioxetene (**5a**) twisted angle (θ): C_{12}–C_{13}–C_{15}–C_{16} = 65.5°.



Scheme 3.

Next, we carried out chemiluminescent decomposition of **5a** by the use of various complexes of crown ether with *t*BuOK, $[K\subset(\text{crown ether})]^+ tBuO^-$, in benzene. Consequently, the color of chemiluminescence from **5a** was found to change significantly depending on the crown ether used as a ligand. Thus, λ^{CL}_{max} from **5a** was 25 nm shorter for triggering with a complex of 18-crown-6 ether (**10b**) ($[K\subset(\mathbf{10b})]^+$) ($\lambda^{CL}_{max}$ = 684 nm) than λ^{CL}_{max} with $TBA^+\cdot tBuO^-$, while it became far shorter (>100 nm) with a complex of *N*,*N*′-dibenzyl-4,13-diaza-18-crown-6 ether (**10d**) ($[K\subset(\mathbf{10d})]^+$) ($\lambda^{CL}_{max}$ = 606 nm). These results are summarized in Table 1 together with those for cryptand[2.2.1] (**10a**), dicyclohexano-18-crown-6 ether (**10c**), and 4,13-diaza-18-crown-6 ether (**10e**). Chemiluminescent decomposition of cyanoanthracene analog (**5b**) exhibited a tendency similar to the case of **5a**, though the emissions from **5b** were observed in longer wavelength region as shown in Table 1. It is noteworthy that the result for **5b** is presumably the first example of emission of near infrared light from a dioxetane-based chemiluminescent substrate.

The stability of $[K\subset(\text{crown ether})]^+$ is well known to vary dramatically with the ligand.[13] Since the interaction between the ligand and the potassium ion can be considered to be purely electrostatic in nature for complexes $[K\subset(\text{crown ether})]^+$, the ionic attraction of potassium for phenoxide (**8**) was assumed to vary with their stability, thereby color change of chemiluminescence from **5**

Table 1. Color change for base-induced chemiluminescence from dioxetanes (**5a**), (**5b**), and (**6**)

Base[a]	log K_s[b]	Maximum wavelength of chemiluminescence (λ_{max}^{CL}) and deviation of maximum wavelength ($\Delta\lambda$)					
		5a		**5b**		**6**	
		λ_{max}^{CL}/nm	$\Delta\lambda$[c]/nm	λ_{max}^{CL}/nm	$\Delta\lambda$[d]/nm	λ_{max}^{CL}/nm	$\Delta\lambda$[c]/nm
$TBA^+ \cdot t BuO^-$[e]	—	709	0	>900[f]	—	478	0
$[K \subset (\mathbf{10a})]^+ t BuO^-$	8.40	680	−29	854	−46	471	−7
$[K \subset (\mathbf{10b})]^+ t BuO^-$	6.09	684	−25	849	−51	486[g]	+8
$[K \subset (\mathbf{10c})]^+ t BuO^-$	5.65	626	−83	767	−133	492[g]	+14
$[K \subset (\mathbf{10d})]^+ t BuO^-$	3.38	606	−103	745	−155	470	−8
$[K \subset (\mathbf{10e})]^+ t BuO^-$	1.83	650[h]	−59	844	−56	472	−6
$[Na \subset (\mathbf{10b})]^+ t BuO^-$	4.32	579	−130	677	−223	451	−27
$[Na \subset (\mathbf{10f})]^+ t BuO^-$	3.48	569	−140	718	−182	460	−18

[a] Unless otherwise stated, a solution of a dioxetane in benzene (1.0×10^{-3} mol dm^{-3}, 1 mL) was added to a solution of a complex of crown ether with alkali metal *t*-butoxide in benzene (0.1 mol dm^{-3}, 2 mL) at 25 °C.

[b] Stability of crown ether complex with alkaline metal in methanol (Ref. 13).

[c] Deviation of maximum wavelength (λ_{max}^{CL}) from the value for $TBA^+ \cdot t BuO^-$ in benzene as a standard.

[d] Deviation of maximum wavelength (λ_{max}^{CL}) from 900 nm for convenience sake.

[e] A solution of a dioxetane in benzene (1.0×10^{-3} mol dm^{-3}, 1 mL) was added to a solution of $TBA^+ \cdot t BuO^-$ in benzene (0.1 mol dm^{-3}, 2 mL) at 25 °C.

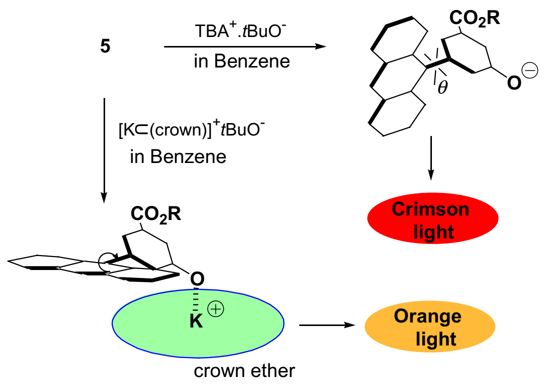
[f] THF was used instead of benzene as a solvent.

[g] A shoulder peak was observed at ca. 450 nm.

[h] A broad spectrum was observed.

relates to the stability of $[K \subset (\text{crown ether})]^+$. However, little obvious correlation was noted between the stability of $[K \subset (\text{crown ether})]^+$ and color change for chemiluminescence of **5**. Moreover, the variation of ligand for $[K \subset (\text{crown ether})]^+$ caused only a little change of emission color from **6** as shown in Table 1. These results suggest that the ionic interaction between a phenoxide ion and potassium ion of $[K \subset (\text{crown ether})]^+$ varies with the ligand not so much as to cause the color change of chemiluminescence. This suggestion is supported by an experiment using complexes of crown ether with a sodium ion, which should attract a phenoxide anion far more strongly than a potassium ion, as the ionic radius of sodium ion is fairly smaller than that of the potassium ion. In fact, when $[Na \subset (\mathbf{10b})]^+ t BuO^-$ and a complex of 15-crown-5 (**10f**), $[Na \subset (\mathbf{10f})]^+ t BuO^-$, were used in benzene, the maximum wavelength (λ_{max}^{CL}) of chemiluminescence from **6** shifted to shorter wavelength ($\Delta\lambda = 18$–27 nm),[14] and, furthermore, marked blue shift was observed for **5a** ($\Delta\lambda = 130$–140 nm) and **5b** ($\lambda = 182$–223 nm), as shown in Table 1.

Hence, the color change of chemiluminescence observed for **5** is most likely attributed to steric interaction of an emitter (**8**) with $[K \subset (\text{crown ether})]^+$. An anthracene ring and a phenolic ring in a stable conformer of **8** lie presumably with large twisted angle ($\theta \approx 66°$) also in a solution, according to the result shown in Figure 1 and estimation by an AM1 MO calculation. If the conformation with large θ is maintained even for **8** coordinated with $[K \subset (\text{crown ether})]^+$, a wing (or terminus) of the anthracen-9-yl ring attached to the *meta*-position of a phenoxide is assumed to come near or into contact with a plane of the coordinated crown ether, referring to structural data reported for several $[K \subset (\text{crown ether})]^+ \cdot ArO^-$ complexes.[15] For such case, the twisted angle (θ) would become smaller to avoid the steric repulsion of the anthracene ring with a plane of crown ether, and the change of θ affects presumably MO energies in a π-electron system of **8**, as illustrated in Scheme 4. This type of steric interaction is little expected for emitter **9** bearing a simple 3-hydroxyphenyl. An AM1 MO calculation illustrates suggestive though qualitative features for the relationship between θ and LUMO/HOMO energies for emitter **8**: a methyl ester analog instead of **8** was used as a model for convenience sake. Thus, the calculation suggests that, as θ decreases from ca. 70° to 30°, the energy gap ($\Delta E = E_{LUMO} - E_{HOMO}$) increases, thereby λ_{max}^{CL} shifts to blue, as shown in Figure 2.



Scheme 4.

Among the complexes of crown ether with potassium, **10c** and **10d**, having fairly bulky substituents, are easily supposed to be conspicuously large sterically, and thus influential toward conformational change of a biaryl system of **8**, so that they should cause color change of chemiluminescence from **5** effectively. In fact, blue shift of λ_{max}^{CL} was far larger for $[K \subset (\mathbf{10c})]^+$ and $[K \subset (\mathbf{10d})]^+$ than the others as shown in Table 1.

The results described here support a proposed elucidation that interactions between luciferase and emitter oxyluciferin (**2**) maintain specific conformers of the excited state thus influencing color variation. However,

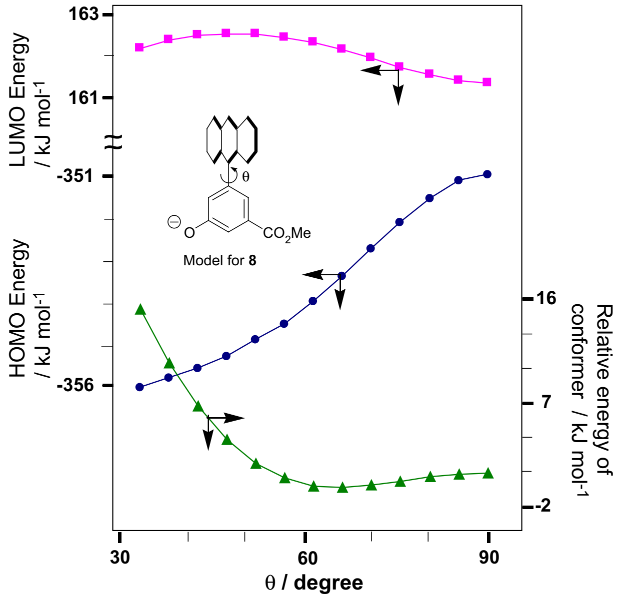


Figure 2. Variation of HOMO energy (●), LUMO energy (■), and relative energy (▲) of conformers with the change of twisted angle (θ) of a biaryl system for methyl 3-(anthracen-9-yl)-5-hydroxybenzoate as a model of **8**.

they do not rule out the other elucidations proposed for the color change of bioluminescence from the beetles. In fact, triggering of **6** as well as **5a** and **5b** with $[\mathrm{Na}\subset(\mathbf{10b})]^+t\mathrm{BuO}^-$ or $[\mathrm{Na}\subset(\mathbf{10f})]^+t\mathrm{BuO}^-$ was found to cause blue shift of chemiluminescence as described already. This phenomenon should be rationalized by ionic attraction of the sodium ion for a phenoxide stronger than that of potassium.

In conclusion, we have shown here a first example that the color of light is modulated by the microenvironment for CT-induced chemiluminescent decomposition of a dioxetane bearing a biaryl moiety, namely, 3-(anthracen-9-yl)-5-hydroxyphenyl. The phenomenon is most likely rationalized by conformational change of a biaryl moiety in the emitter, which is induced by steric interaction of anthryl and a plane of $[\mathrm{K}\subset(\text{crown ether})]^+$. The change of ionic interaction between a phenoxide of the emitter and the alkaline metal ion coordinated with crown ether was found also to cause change of color of dioxetane-based chemiluminescence. These findings suggest that the color modulation of bioluminescence of the firefly may be caused not only by conformational change of oxyluciferin but also by strength of ionic interaction at an oxyanion of the hydroxybenzothiazole part of oxyluciferin (**2**).

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10. Crystal data for compound **5a**: $C_{30}H_{30}O$ ($M_r = 454.56$), pale yellow prism, $0.30 \times 0.30 \times 0.10$ mm, monoclinic, space group $P21/c$ (#14), $a = 10.42(2)$ Å, $b = 18.22(2)$ Å, $c = 13.739(12)$ Å, $\beta = 91.486(11)°$, $V = 2608.1(53)$ Å^3, $Z = 4$, $\rho_{\mathrm{calcd}} = 1.158\,\mathrm{g\,cm^{-3}}$, $T = 173$ K, $2\theta_{\max} = 54.9$, $F(000) = 968.00$, reflections collected/unique 55,936/6120 ($R_{\mathrm{int}} = 0.038$), $\mu(\mathrm{Mo\,K\alpha}) = 0.76\,\mathrm{cm^{-1}}$. Final R indices $R1 = 0.041$ [$I > 2\sigma(I)$], $wR2 = 0.107$ (all data), GOF on $F^2 = 1.001$, and residual electron density 0.48/−0.29 e Å^{-3}. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB21EZ, UK; fax (+44)1223 336 033; or deposit@ccdc.cam.au.uk).
11. Under the reaction conditions using a large excess of a base, the rate of decomposition followed pseudo-first-order kinetics independent of the concentration of the base used. Φ^{CL} was estimated by the use of a value reported for a 3-(3-siloxyphenyl)-1,2-dioxetane as a standard (Ref. 12).
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14. $\Delta\lambda$ means deviation of $\lambda^{\mathrm{CL}}_{\max}$ from the value in $\mathrm{TBA}^+ \cdot t\mathrm{BuO}^-$/benzene system.
15. The Cambridge Structural Database (CSD) was searched by the program ConQuest, and X-ray single crystallographic data for several $[\mathrm{K}\subset(\text{crown ether})]^+\cdot\mathrm{ArO}^-$ complexes were found there.