Chemiluminescence in molecular recognition: base-induced decomposition of optically active dioxetanes bearing a bisnaphthol moiety with a complex of optically active crown ether–potassium *tert*-butoxide†

Masakatsu Matsumoto,* Koji Hamaoka, Yuji Takashima, Mizuki Yokokawa, Kazutaka Yamada, Nobuko Watanabe and Hisako K. Ijuin

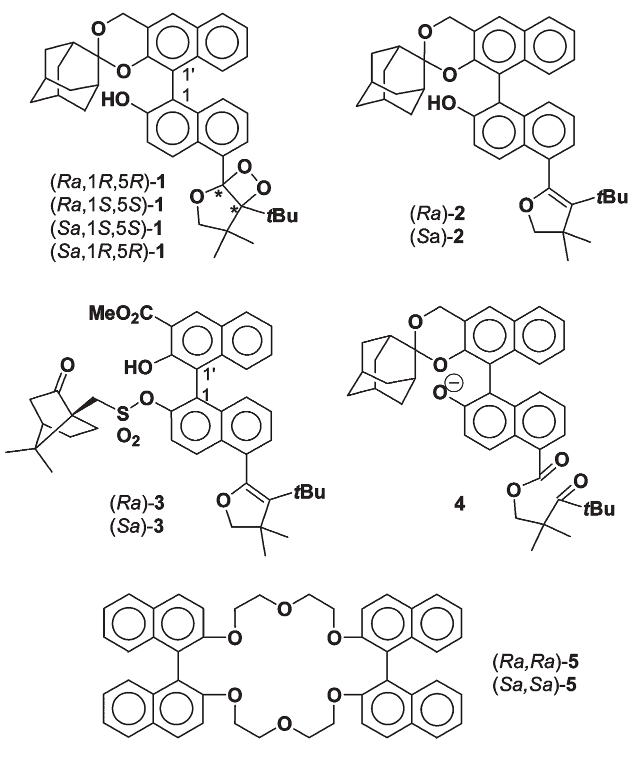
Received (in Cambridge, UK) 13th September 2004, Accepted 15th November 2004
First published as an Advance Article on the web 23rd December 2004
DOI: 10.1039/b414001j

Four optically pure isomers of dioxetane (1) were decomposed by the action of the complex of an optically active crown ether with potassium *tert*-butoxide to afford light with λ_{max}^{CL} and gave four different spectrum shapes.

Dioxetanes substituted with an aromatic electron donor such as an oxyphenyl anion display intramolecular electron transfer (ET)-induced decomposition with an accompanying emission of light. The phenomenon has received much attention from the viewpoints of mechanistic interests related to bioluminescence and application to chemiluminescent bioassays, and a wide variety of dioxetane-based chemiluminescent substrates have been synthesized.[1–4] However, little has been known of optically active dioxetanes, which cause ET-induced chemiluminescent decomposition. We report here the first examples of such dioxetanes and their chemiluminescent properties, which vary depending on the optically active microenvironment.

Dioxetanes synthesized here were stereoisomeric bicyclic dioxetanes (**1**) bearing a substituted binaphthyl moiety, for which axial chirality around the C_1–$C_{1'}$ bond and the chirality of carbon in the dioxetane ring give rise to four optical isomers, namely (*Ra*,1*R*,5*R*), (*Ra*,1*S*,5*S*), (*Sa*,1*S*,5*S*) and (*Sa*,1*R*,5*R*) (Scheme 1). Singlet oxygenation of dihydrofurans bearing an atropisomeric binaphthyl group, (*Ra*-**2**) and (*Sa*-**2**), afforded the corresponding pairs of diastereoisomeric dioxetanes (**1**), which were separated from each other by column chromatography: $[\alpha]_D^{25}$ (c0.335, CH_2Cl_2) = −19.2, +95.2, +19.2 and −95.3 for (*Ra*,1*R*,5*R*), (*Ra*,1*S*,5*S*), (*Sa*,1*S*,5*S*), (*Sa*,1*R*,5*R*)-isomer, respectively. The structures of these dioxetanes were determined by means of ^{1}H NMR, ^{13}C NMR, IR, mass and HR mass spectral analysis,‡ and all of their optical purities were estimated to be >99.5% by HPLC using a chiral column. Their stereochemistry was determined as follows. Optical resolution by the use of (1*S*)-(+)-camphorsulfonyl chloride gave optical isomers of binaphthyl (*Ra*-**3**) and (*Sa*-**3**) in pure form, the stereochemistry of which were determined by X-ray single crystallographic analysis.§ Configuration of the dioxetane ring was determined by the use of data from the X-ray single crystallographic analysis of a racemate [(*Ra*,1*S*,5*S*)-**1** + (*Sa*,1*R*,5*R*)-**1**] synthesized from racemic **2**, which was separated from another racemic diastereoisomer [(*Ra*,1*R*,5*R*)-**1** + (*Sa*,1*S*,5*S*)-**1**], and by comparing the ^{1}H NMR spectra of optically pure isomers with those of the racemates.

When these stereoisomeric dioxetanes (**1**) were individually treated with a large excess of tetrabutylammonium fluoride (TBAF) in DMSO at 25 °C, they decomposed rapidly to the corresponding ketoesters (**4**) with an accompanying emission of flash red light (maximum wavelength λ_{max}^{CL} = 600 nm). As shown in Table 1, the rates of chemiluminescent decomposition (rate constant: k) and chemiluminescent yield (Φ^{CL})¶[5] were different to some extent between a pair of [(*Ra*,1*R*,5*R*)-**1** and (*Sa*,1*S*,5*S*)-**1**] and a pair of [(*Ra*,1*S*,5*S*)-**1** and (*Sa*,1*R*,5*R*)-**1**], though little change in λ_{max}^{CL} was observed among these four



Scheme 1

---

† Electronic supplementary information (ESI) available: synthesis of dioxetanes, analysis of optically active compounds synthesized by HPLC using a chiral column, synthesis of (*Ra,Ra*)-bis(binaphtho)-22-crown-6 ether [(*Ra,Ra*)-**5**] and (*Sa,Sa*)-bis(binaphtho)-22-crown-6 ether [(*Sa,Sa*)-**5**], chemiluminescence measurements, X-ray single crystallographic analysis. See http://www.rsc.org/suppdata/cc/b4/b414001j/

*matsumo-chem@kanagawa-u.ac.jp

Table 1 Base-induced chemiluminescent decomposition of stereoisomeric dioxetanes (**1**)

	TBAF[a]			$[\mathrm{K}\subset(18\mathrm{C}6)]^+\mathrm{BuO}^{-b}$			$\{\mathrm{K}\subset[(Ra,Ra)\text{-}\mathbf{5}]\}^+\mathrm{BuO}^{-c}$			$\{\mathrm{K}\subset[(Sa,Sa)\text{-}\mathbf{5}]\}^+\mathrm{BuO}^{-c}$		
Dioxetane (**1**)	λ_{max}/nm	Φ^{CLd}	k/s^{-1}	λ_{max}/nm	Φ^{CLd}	k/s^{-1}	λ_{max}/nm	Φ^{CLd}	k/s^{-1}	λ_{max}/nm	Φ^{CLd}	k/s^{-1}
(*Ra*,1*R*,5*R*)	600	9.2×10^{-3}	0.36	595	4.7×10^{-3}	0.095	615	9.0×10^{-3}	1.4×10^{-3}	646	5.1×10^{-3}	5.9×10^{-3}
(*Ra*,1*S*,5*S*)	600	8.4×10^{-3}	0.21	595	7.8×10^{-3}	0.15	633	7.4×10^{-3}	2.1×10^{-3}	605	6.9×10^{-3}	1.1×10^{-3}
(*Sa*,1*S*,5*S*)	600	9.2×10^{-3}	0.30	595	4.8×10^{-3}	0.092	646	4.8×10^{-3}	5.4×10^{-3}	615	8.4×10^{-3}	1.4×10^{-3}
(*Sa*,1*R*,5*R*)	600	8.4×10^{-3}	0.24	595	8.7×10^{-3}	0.15	605	5.9×10^{-3}	1.1×10^{-3}	633	7.2×10^{-3}	2.1×10^{-3}

[a] A solution of dioxetane (**1**) in DMSO (1.0×10^{-5} mol dm^{-3}, 1 mL) was added to a solution of TBAF in DMSO (1.0×10^{-2} mol dm^{-3}, 2 mL) at 25 °C. [b] A solution of dioxetane (**1**) in benzene–THF (1 : 1) (1.0×10^{-4} mol dm^{-3}, 1 mL) was added to a solution of $[\mathrm{K}\subset(18\mathrm{C}6)]^+\mathrm{BuO}^-$ in benzene–THF (1 : 1) (1.0×10^{-1} mol dm^{-3}, 2 mL) at 25 °C. [c] A solution of dioxetane (**1**) in benzene–THF (1 : 1) (1.0×10^{-4} mol dm^{-3}, 1 mL) was added to a solution of $\mathrm{K}\subset[\mathbf{5}]^+\mathrm{BuO}^-$ in benzene–THF (1 : 1) (1.0×10^{-2} mol dm^{-3}, 2 mL) at 25 °C. [d] Relative quantum yields based on the value for 3-adamantylidene-4-methoxy-4-(3-siloxyphenyl)-1,2-dioxetane (ref. 5).

isomers. Similar tendencies were also observed for the chemiluminescent decomposition in benzene–THF (1 : 1) using a complex of 18-crown-6 ether with *t*BuOK, $[\mathrm{K}\subset(18\mathrm{C}6)]^+t\mathrm{BuO}^-$ as a base (Table 1).

Next, we examined the chemiluminescent decomposition of **1** by the use of a complex of optically active crown ethers (*Ra,Ra*)-**5** and (*Sa,Sa*)-**5**[6,7] with *t*BuOK in benzene–THF (1 : 1) (Scheme 2). When a dioxetane (*Ra*,1*R*,5*R*)-**1** was treated with a complex of (*Ra,Ra*)-**5**, $[\mathrm{K}\subset(Ra,Ra)\text{-}\mathbf{5}]^+t\mathrm{BuO}^-$, at 25 °C, chemiluminescence was observed with $\lambda_{max}{}^{CL} = 615$ nm, $\Phi^{CL} = 9.0 \times 10^{-3}$, and $k = 1.4 \times 10^{-3}$ s^{-1}. Similar treatment of the other stereoisomers with $[\mathrm{K}\subset(Ra,Ra)\text{-}\mathbf{5}]^+t\mathrm{BuO}^-$ also gave chemiluminescence, the properties of which were different from each other. In particular, it should be noted that each of the four stereoisomers of **1** exhibited different shapes of the chemiluminescent spectrum as well as different maximum wavelengths ($\lambda_{max}{}^{CL}$) (Fig. 1 and Table 1).

When a complex of another enantiomeric crown ether, $[\mathrm{K}\subset(Sa,Sa)\text{-}\mathbf{5}]^+t\mathrm{BuO}^-$, was used for the base-induced decomposition of **1**, each of the four stereoisomers gave light with properties exchanged completely with those for the case using $[\mathrm{K}\subset(Ra,Ra)\text{-}\mathbf{5}]^+t\mathrm{BuO}^-$ between enantiomers, namely, between (*Ra*,1*R*,5*R*)-**1** and (*Sa*,1*S*,5*S*)-**1**, and between (*Ra*,1*S*,5*S*)-**1** and (*Sa*,1*R*,5*R*)-**1** as shown in Fig. 1 and Table 1. These results reveal that each of the four stereoisomeric dioxetanes (**1**) are recognized for coordination with each of the optically active crown ether complexes $[\mathrm{K}\subset(Ra,Ra)\text{-}\mathbf{5}]^+t\mathrm{BuO}^-$ and $[\mathrm{K}\subset(Sa,Sa)\text{-}\mathbf{5}]^+t\mathrm{BuO}^-$, so that their features of coordination are reflected in their chemiluminescent properties being different from each other.

With the color change of chemiluminescence depending on the combination of stereoisomeric dioxetane (**1**) and a stereoisomeric complex, $[\mathrm{K}\subset\mathbf{5}]^+t\mathrm{BuO}^-$ is an unprecedented phenomenon. This phenomenon should be accounted for by the idea that the twisted angle around an axis joining two naphthalene rings should vary with steric interaction between $[\mathrm{K}\subset\mathbf{5}]^+$ and an emitter (**4**) produced from **1**, so that the features of the π-electronic system vary for the excited emitter. The twisted angles of a binaphthyl system are presumably different from each other also for an intermediary dioxetane bearing an oxyanion of naphthol coordinated with $[\mathrm{K}\subset\mathbf{5}]^+$. Hence, it is not surprising that the rate of CT-induced decomposition as well as chemiluminescent yield varies more or less with the combination of stereoisomeric dioxetane (**1**) and a stereoisomeric complex, $[\mathrm{K}\subset\mathbf{5}]^+t\mathrm{BuO}^-$. Another important but rather unnoticed fact observed here is that the color of chemiluminescence was different between diastereoisomers, namely, between (*Ra*,1*R*,5*R*)-**1** and (*Ra*,1*S*,5*S*)-**1** and between (*Sa*,1*S*,5*S*)-**1** and (*Sa*,1*R*,5*R*)-**1**, though the chiral carbons in a

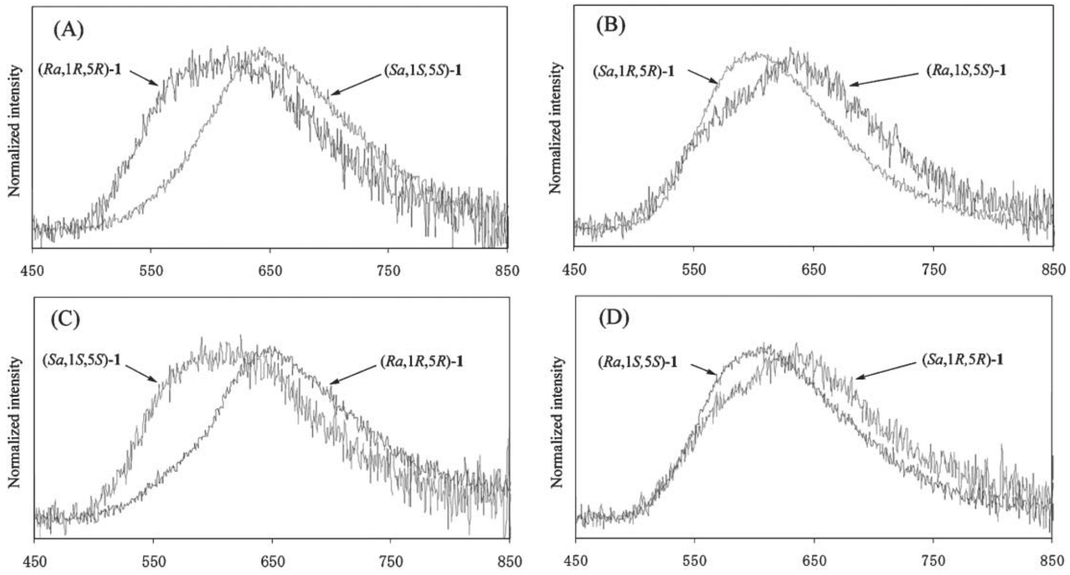
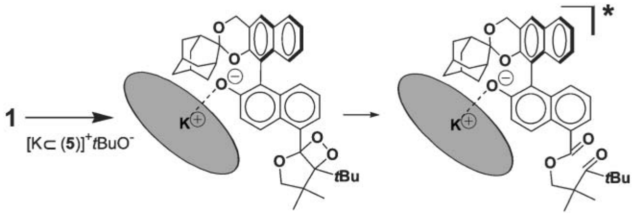


Fig. 1 Chemiluminescent spectra for the decomposition of optically active dioxetanes (**1**) induced by a complex of optically active crown ether (**5**) with a potassium ion. (A), (B): $\{\mathrm{K}\subset[(Ra,Ra)\text{-}\mathbf{5}]\}^+t\mathrm{BuO}^-$/benzene–THF system (C), (D): $\{\mathrm{K}\subset[(Sa,Sa)\text{-}\mathbf{5}]\}^+t\mathrm{BuO}^-$/benzene–THF system.



Scheme 2

dioxetane ring exist no longer in an emitter (**4**). This fact suggests that steric hysteresis of the dioxetane part for **1** coordinated to [K⊂**5**]$^+$ is retained to some extent after ET-induced decomposition into an emitter (**4**), though the details are obscure at present.

We have described here the first example of ET-induced chemiluminescent decomposition of optically active dioxetanes in an optically active microenvironment, namely, in the coordination sphere of an optically active crown ether complex with potassium *tert*-butoxide. The most important finding was that each of the four stereoisomeric dioxetanes (**1**) were recognized for coordination with each of the optically active crown ether complexes [K⊂(*Ra,Ra*)-**5**]$^+$*t*BuO$^-$ and [K⊂(*Sa,Sa*)-**5**]$^+$*t*BuO$^-$, and their features of coordination were reflected in their colors of chemiluminescence being different from each other.

Masakatsu Matsumoto,* Koji Hamaoka, Yuji Takashima, Mizuki Yokokawa, Kazutaka Yamada, Nobuko Watanabe and Hisako K. Ijuin
Department of Materials Science, Kanagawa University, Tsuchiya, Hiratsuka, Kanagawa 259-1293, Japan.
E-mail: matsumo-chem@kanagawa-u.ac.jp

Notes and references

‡ Selected data for (*Ra*,1*R*,5*R*)-**1**: ^{1}H NMR (400 MHz, CDCl$_3$) δ_H = 0.93 (s, 9H), 1.07–1.78 (m, 16H), 1.92–2.12 (m, 4H), 4.05–4.18 (m, 1H), 4.74 (d, *J* = 8.3 Hz, 1H), 4.97 (s, 1H), 5.12 (s, 2H), 7.07 (broad d, *J* = 8.3 Hz, 1H), 7.15–7.38 (m, 5H), 7.66 (s, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.89–8.11 (m, 1H), 8.60–8.90 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ_C = 20.0, 26.1, 26.5, 26.8, 26.9, 32.9, 33.0, 33.4, 33.5, 34.2, 34.6, 36.9, 37.0, 45.7, 59.7, 80.5, 102.7, 106.0, 114.7, 115.0, 117.2, 117.6, 122.2, 124.1, 124.4, 124.7, 124.8, 126.7, 126.8, 127.2, 127.7, 127.9, 128.0, 128.6, 131.1, 133.2, 134.7, 148.2, 150.8 ppm. Selected data for (*Ra*,1*S*,5*S*)-**1**: ^{1}H NMR (400 MHz, CDCl$_3$) δ_H = 0.87 (s, 9H), 1.03 (broad d, *J* = 12.5 Hz, 1H), 1.15 (broad d, *J* = 12.5 Hz, 1H), 1.25–1.35 (m, 2H), 1.32 (s, 3H), 1.47–1.60 (m, 5H), 1.68 (s, 3H), 1.76 (broad s, 1H), 1.90–2.09 (m, 4H), 4.14 (d, *J* = 8.3 Hz, 1H), 4.74 (d, *J* = 8.3 Hz, 1H), 4.93 (s, 1H), 5.06 (d, *J* = 15.1 Hz, 1H), 5.14 (d, *J* = 15.1 Hz, 1H), 7.16–7.38 (m, 6H), 7.64 (s, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 8.04 (broad d, *J* = 6.3 Hz, 1H), 8.67 (broad d, *J* = 9.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ_C = 20.3, 26.3, 26.5, 26.7, 26.8, 32.9, 33.3, 33.5, 33.6, 35.2, 36.8, 37.0, 45.7, 59.7, 80.6, 102.5, 105.7, 114.7, 115.1, 117.2, 117.5, 122.1, 124.2, 124.4, 124.7, 124.8, 126.5, 126.7, 127.1, 127.7, 127.8, 128.0, 128.5, 131.0, 133.1, 134.7, 148.3, 150.8 ppm.

§ CCDC 242157 for (*Ra*-**3**), 242158 for (*Sa*-**3**) and 242975 for the racemate comprised of (*Ra*,1*S*,5*S*)-**1** and (*Sa*,1*R*,5*R*)-**1** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax (+44) 1223-336-033; or deposit@ccdc.cam.au.uk). See http://www.rsc.org/suppdata/cc/b4/b414001j/ for crystallographic data in .cif or other electronic format

¶ Under reaction conditions using a large excess of 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 3-adamantylidene-4-methoxy-4-(3-siloxyphenyl)-1,2-dioxetane as a standard.[5]

1 S. Beck and H. Köster, *Anal. Chem.*, 1990, **62**, 2258–2270.
2 A. Mayer and S. Neuenhofer, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1044–1072.
3 W. Adam, D. Reinhardt and C. R. Saha-Möller, *Analyst*, 1996, **121**, 1527–1531.
4 M. Matsumoto, *J. Photochem. Photobiol., C*, 2004, **5**, 27–53.
5 A. V. Trofimov, K. Mielke, R. F. Vasil'ev and R. W. Adam, *Photochem. Photobiol.*, 1996, **63**, 463–467.
6 E. P. Kyba, G. W. Gokel, F. de Jong, K. Koga, L. R. Sousa, M. G. Siegel, L. Kaplan, G. D. Y. Sogah and D. J. Cram, *J. Org. Chem.*, 1977, **42**, 4173.
7 D. J. Cram and J. M. Cram, *Acc. Chem. Res.*, 1978, **11**, 8–14.