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Marked difference in singlet-chemiexcitation efficiency between *syn-anti* isomers of spiro[1,2-dioxetane-3,1′-dihydroisobenzofuran] for intramolecular charge-transfer-induced decomposition

Masakatsu Matsumoto *, Yuka Takamido, Kana Nomura, Tamaki Shiono, Nobuko Watanabe, Hisako K. Ijuin

Department of Chemistry, Kanagawa University, Tsuchiya, Hiratsuka, Kanagawa 259-1293, Japan

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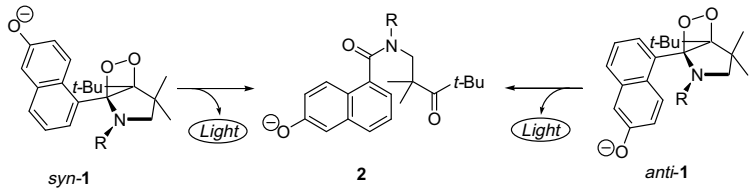
ABSTRACT

Spiro[1,2-dioxetane-3,1′-dihydroisobenzofuran] *syn*-**3** bearing a hydroxy group at the 6-position (as a model *syn*-rotamer of parent dioxetane **4** bearing a 3-hydroxyphenyl group) and its isomer *anti*-**3** (as a model *anti*-rotamer of **4**) were synthesized. When these spiro-dioxetanes were treated with tetrabutylammonium fluoride (TBAF) in DMSO, *anti*-**3** emitted light with high efficiency ($\Phi^{CL} = 0.41$), while the respective value for *syn*-**3** was only 1/10 for *anti*-**3**. This significant difference in Φ^{CL} between *syn*-**3** and *anti*-**3** was attributed to the difference in their singlet-chemiexcitation efficiencies.

The intramolecular charge-transfer-induced decomposition (CTID) of dioxetane bearing an electron donor is believed to strongly contribute to the bioluminescence of organisms such as the firefly as well as to high-performance dioxetane-based chemiluminescence.[1–8] However, it is still unclear how singlet-chemiexcitation occurs and how it is related to the structure of high-energy molecules, that is, dioxetanes. It has very recently been shown that dioxetane **1** bearing a 6-oxidonaphthalen-1-yl group undergoes CTID accompanied by the emission of light, the efficiency of which (Φ^{CL}) is significantly affected by the rotational isomerism of the naphthyl group: Φ^{CL} for *anti*-**1** is 10–20 times higher than that for *syn*-**1**, though both rotamers give the same decomposition product **2** (Scheme 1).[9] Whether or not this phenomenon is common to the CTID of oxidoaryl-substituted dioxetanes is an important point to clarify with regard to the singlet-chemiexcitation process in chemi- and bioluminescence. We report here that singlet-chemiexcitation took place from spiro[1,2-dioxetane-3,1′-dihydroisobenzofuran] *anti*-**3** bearing a hydroxy at the 4-position with markedly higher efficiency than that from 6-hydroxy isomer *syn*-**3** under basic conditions (Scheme 2).

Based on an AM1 MO calculation, a parent dioxetane **4** bearing a 3-hydroxyphenyl group[10,11] should lie in equilibrium between stable rotamers *syn*-**4** and *anti*-**4**, though the ^{1}H NMR spectrum did not show any evidence of these rotamers at around room temperature, presumably because of low rotational barriers (estimated rotational barrier = 35–38 kJ mol^{-1}). Thus, we designed spiro[1,2-dioxetane-3,1′-dihydroisobenzofuran]s **3**, the 6-hydroxy-isomer of which, that is, *syn*-**3**, was likened to a fixed form of *syn*-**4**, while the 4-hydroxy-isomer, that is, *anti*-**3**, was likened to a fixed form of *anti*-**4** (Scheme 2).

Singlet oxygenation of precursor enol ether *syn*-**5** followed by chromatographic purification gave *syn*-**3** as colorless prisms, mp



Scheme 1.

* Corresponding author. Tel.: +81 463 59 4111; fax: +81 463 58 9684.
E-mail address: matsumo-chem@kanagawa-u.ac.jp (M. Matsumoto).

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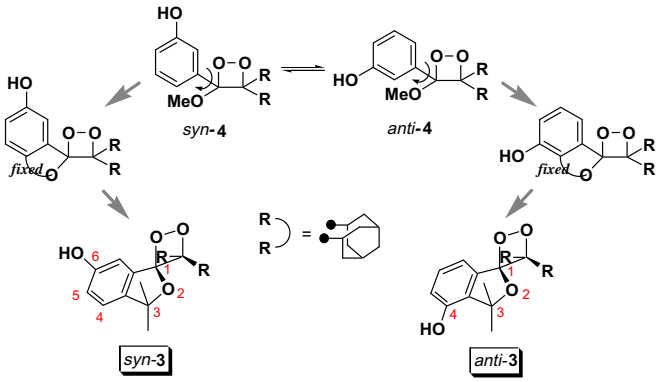
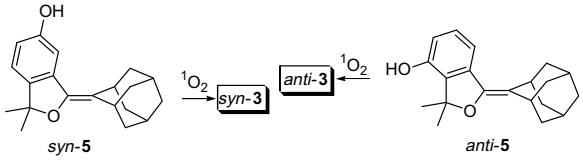


Scheme 2.



Scheme 3.

130.0–131.0 °C, in 93% isolated yield.[12] Similarly, *anti*-**3** was synthesized from *anti*-**5** and obtained as colorless prisms, mp 244 °C (dec.), in 86% isolated yield (Scheme 3).[13] Both dioxetanes gave satisfactory ^{1}H NMR, ^{13}C NMR, IR, and mass spectral data. X-ray single crystallographic analysis was successfully performed for both *syn*-**3** and *anti*-**3**.[14] ORTEP-drawings are shown in Figure 1.

When a solution of dioxetane *syn*-**3** in DMSO (1.0×10^{-5} mol cm^{-3}, 1 mL) was added to a solution of TBAF in DMSO (1.0×10^{-2} mol cm^{-3}, 2 mL) at 25 °C, *syn*-**3** decomposed according to pseudo-first order kinetics to give blue light with maximum wavelength λ_{max}^{CL} = 453 nm and rate constant $k^{CTID} = 3.4 \times 10^{-3}$ s^{-1} (half-life $t_{1/2}$ = 200 s). The chemiluminescence efficiency Φ^{CL} of 0.041 was only 1/6–1/7 of that for parent dioxetane **4** (Φ^{CL} = 0.26).[15] Chemiluminescence spectra of *syn*-**3** and **4** are illustrated in Figure 2. Upon treatment with TBAF/DMSO as in the case of *syn*-**3**, *anti*-**3** decomposed to give violet light with λ_{max}^{CL} = 432 nm (Figure 2) and $k^{CTID} = 4.6 \times 10^{-4}$ s^{-1} ($t_{1/2}$ = 1500 s) (Fig. 2, Table 1). The chemiluminescence efficiency Φ^{CL} of *anti*-**3** was markedly high (Φ^{CL} = 0.41), and may be the highest among those for known dioxetanes bearing a rather simple 3-hydroxyphenyl group.[4] These results are summarized in Table 1, from which we can see a prominent difference in chemiluminescence efficiency Φ^{CL} between *anti*-**3** and *syn*-**3**: Φ^{CL} for *syn*-**3** was only 1/10 of that for *anti*-**3**.

After neutralization, the spent reaction mixtures of *syn*-**3** and *anti*-**3** exclusively gave the corresponding lactones *syn*-**7** and *anti*-**7**. Authentic oxido anion *syn*-**6** prepared from lactone *syn*-**7** in TBAF / DMSO showed fluorescence with maximum wavelength, λ_{max}^{fl} = 453 nm, the spectrum of which coincided with the chemiluminescence spectrum of *syn*-**3**. The fluorescence spectrum of authentic *anti*-**7** was similarly measured and was found to coincide with the chemiluminescence spectrum of *anti*-**3**. These results show that the emitters produced in the CTID of *syn*-**3** and *anti*-**3** were undoubtedly *syn*-**6** and *anti*-**6**, respectively (Scheme 4). Based on the fluorescence efficiencies Φ^{fl} = 0.51 for *syn*-**6** and 0.50 for *anti*-**6**, singlet-chemiexcitation efficiencies $\Phi_s = \Phi^{CL}/\Phi^{fl}$ were estimated to be 0.080 for *syn*-**3** and 0.80 for *anti*-**3**. Thus, these results strongly suggest that the marked difference in chemiluminescence efficiency between *syn*-**3** and *anti*-**3** can be attributed to the difference in their singlet-chemiexcitation efficiency. Tanaka and coworkers will report elsewhere a theoretical elucidation (ab initio calculation by the hybrid DFT method using GAUSSIAN 98 and 03 programs) of how the singlet-chemiexcitation process is affected by stereochemistry of oxidoaryl-subsituted dioxetane.[16]

In conclusion, dioxetane *syn*-**3** as a model *syn*-rotamer of dioxetane **4** bearing a 3-hydroxyphenyl group could not effectively cause singlet-chemiexcitation leading to the emission of light in CTID, whereas dioxetane *anti*-**3** as a model *anti*-rotamer of **4**

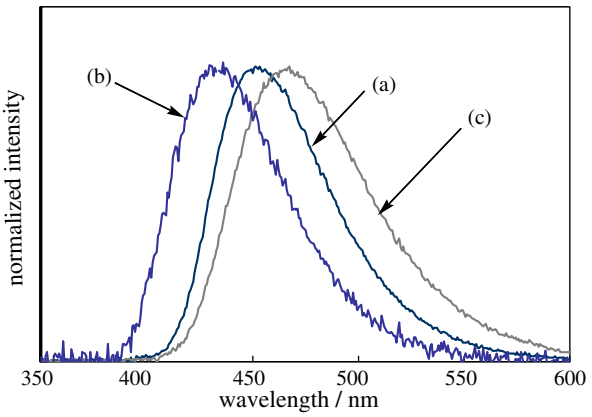


Figure 2. Chemiluminescence spectra of dioxetanes in TBAF/DMSO system. (a): *syn*-**3**, (b): anti-**3**, (c): **4**.

Table 1
TBAF-induced chemiluminescent decomposition of dioxetanes *syn*-**3** and *anti*-**3**

Dioxetane	Solvent	λ_{max}^{CL} (nm)	Φ^{CL} [a]	Φ^{fl} [b]	Φ_s	k^{CTID} (s^{-1})	$t_{1/2}$ (s)
syn-**3**	DMSO	453	0.041	0.51	0.080	3.4×10^{-3}	200
anti-**3**	DMSO	432	0.41	0.50	0.80	4.6×10^{-4}	1500
syn-**3**	Acetonitrile	456	0.017	0.21	0.081	4.0×10^{-4}	1700
anti-**3**	Acetonitrile	435	0.14	0.20	0.70	1.1×10^{-4}	6500
4	DMSO	465	0.26	0.50	0.52	0.14	5.1

[a] Φ^{CL}s were estimated, based on the value for a siloxyphenyl-analog of **4**.[11]
[b] Fluorescence efficiencies of authentic emitters *syn*-**3** and *anti*-**3**.

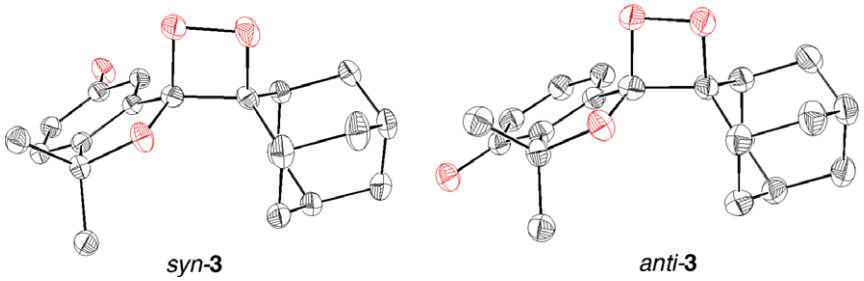
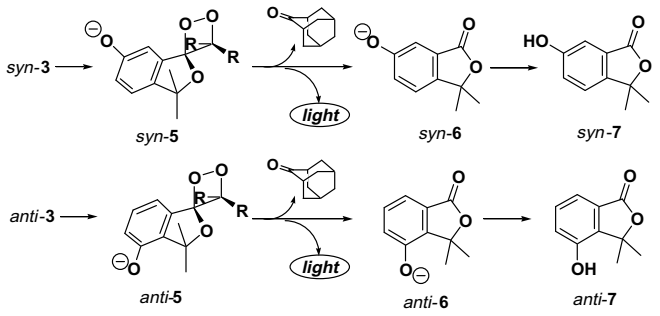


Figure 1. ORTEP views of *syn*-**3** and *anti*-**3**.



Scheme 4.

showed very effective singlet-chemiexcitation. If we suppose that a 1: 1 mixture of *syn*-**3** and *anti*-**3** undergoes CTID, we would observe that chemiluminescence derived predominantly from *anti*-**3** but not from *syn*-**3** with $\Phi^{CL} = 0.23$, that is, the mean of the Φ^{CL}s for *syn*-**3** and *anti*-**3**. This value is quite close to that for parent dioxetane **4** ($\Phi^{CL} = 0.26$, Table 1), for which rotational isomerism of the 3-hydroxyphenyl group presumably occurs very rapidly. If this is not a coincidence, then it is presumed in CTID that only ca. 1/2 of dioxetane **4** would give light effectively, while the rest of **4** would decompose without the emission of bright light.

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12. *Selected data for syn*-**3**: Colorless columns (from ether), mp 130.0–131.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.50 (s, 3H), 1.57 (s, 3H), 1.57–2.00 (m, 12H), 2.98–3.06 (m, 2H), 5.04 (s, 1H), 6.95 (dd, J = 8.3 and 2.2 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 7.36 (d, J = 2.2 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 26.0 (CH), 26.1 (CH), 28.1 (CH_3), 31.4 (CH_3), 31.8 (CH_2), 32.2 (CH_2), 32.7 (CH), 32.7 (CH), 33.6 (CH_2), 34.5 (CH_2), 36.3 (CH_2), 86.7 (C), 97.4 (C), 111.5 (CH), 115.6 (C), 118.7 (CH), 121.3 (CH), 135.4 (C), 141.0 (C), 155.9 (C) ppm; IR (KBr): ν 3464, 2920, 2857, 1622, 1315, 1197 cm^{-1}; mass (*m/z*, %): 178 [M$^+$−150(2-adamantanone), 9], 163 (51), 151 (13), 150 (100), 117 (16), 93 (11), 91 (11), 81 (27), 80 (40), 79 (42), 78 (10), 77 (11); HRMS (ESI): 329.1748, calcd for $C_{20}H_{25}O_4$, [M+H$^+$] 329.1753. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 72.84; H, 7.64.
13. *Selected data for anti*-**3**: Colorless granules (from ether), mp 244 °C (dec.). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.22 (d with fine coupling, J = 13.1 Hz, 1H), 1.56–1.80 (m, 8H), 1.62 (s, 3H), 1.69 (s, 3H), 1.86–2.00 (m, 3H), 3.00–3.07 (m, 2H), 5.00 (s, 1H), 6.78 (d, J = 7.8 Hz, 1H), 7.25 (t, J = 7.8 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 26.0 (CH), 26.1 (CH), 26.2 (CH_3), 28.8 (CH_3), 31.8 (CH_2), 32.2 (CH_2), 32.7 (CH), 32.7 (CH), 33.6 (CH_2), 34.4 (CH_2), 36.4 (CH_2), 86.9 (C), 97.3 (C), 116.1 (C), 116.9 (CH), 117.8 (CH), 129.7 (CH), 134.5 (C), 136.7 (C), 149.4 (C) ppm; IR (KBr): ν 3335, 2978, 2856, 1604 cm^{-1}; Mass (*m/z*, %): 296 (M$^+$−32, 1), 281 (1), 178 (18), 164 (11), 163 (100), 150 (46), 107 (10), 81 (17), 79 (20); HRMS (ESI): 329.1748, calcd for $C_{20}H_{25}O_4$, [M+H$^+$] 329.1753. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 72.78; H, 7.69.
14. *Crystal data for syn*-**3**: $C_{20}H_{24}O_4$ (M_r = 328.41), colorless prism, 0.30 × 0.25 × 0.20 mm, orthorhombic, space group *Pbca* (#61), a = 12.735(4) Å, b = 13.031(9) Å, c = 20.009(6) Å, V = 3320.5(27) Å^3, Z = 8, ρ_{calcd} = 1.314 g cm^{-3}, T = 120 K, $F(000)$ = 1408.00, reflections collected/unique 34750/3768 (R_{int} = 0.029), μ(Mo Kα) = 0.90 cm^{-1}. Final R indices R_1 = 0.036 [$I > 2\sigma(I)$], wR_2 = 0.08 (all data), GOF on F^2 = 1.023, and residual electron density 0.23/−0.14 e Å^{-3} CCDC deposition number: 690664.*Crystal data for anti*-**3**: $C_{20}H_{24}O_4$ (M_r = 328.41), colorless prism, 0.25 × 0.15 × 0.10 mm, orthorhombic, space group *Pbca* (#61), a = 12.86(2) Å, b = 13.261(10) Å, c = 19.589(12) Å, V = 3339.8(59) Å^3, Z = 8, ρ_{calcd} = 1.306 g cm^{-3}, T = 120 K, $F(000)$ = 1408.00, reflections collected/unique 36065/3814 (R_{int} = 0.057), μ(Mo Kα) = 0.90 cm^{-1}. Final R indices R_1 = 0.054 [$I > 2\sigma(I)$], wR_2 = 0.161 (all data), GOF on F^2 = 1.000, and residual electron density 0.14/−0.17 e Å^{-3}. CCDC deposition number: 690663.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 e-mail: deposit@ccdc.cam.au.uk).
15. All Φ^{CL}s presented here were estimated, based on the value reported for the 3-(*tert*-butyldimethylsiloxy)phenyl-analog of **4** (Φ^{CL} = 0.29). 11
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