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Location effect of an OH group on the chemiluminescence efficiency of 4-hydroperoxy-2-(*o*-, *m*-, or *p*-hydroxyphenyl)-4,5-diphenyl-4*H*-isoimidazoles

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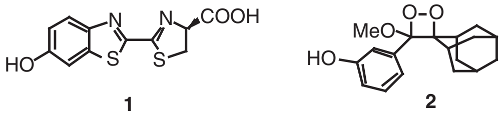
Abstract—In studying the location effect of an OH group on the chemiluminescence efficiency of 4-hydroperoxy-2-(*o*-, *m*-, or *p*-hydroxyphenyl)-4,5-diphenyl-4*H*-isoimidazoles **4**, we found that the efficiency of **4a** with *o*-OH was 0.28 times that of lophine peroxide on initiation with KOH/MeOH. When the trigger base was changed to TBAF/THF, efficiency was 530-fold in dry DMF. The efficiency of **4b** with *m*-OH or **4c** with *p*-OH showed no such dramatic change.

As the first artificial chemiluminescent system, lophine derivatives have been widely studied in chemiluminescence (CL) research.[1,2] A major objective of such research is to maximize CL yield.[3] In the 2-(*p*-X-phenyl)-4,5-diphenylimidazole series, Philbrook et al. observed that efficiency increases with X electron donation in the 2-phenyl group.[4] Kimura et al. found a nonlinear bell-shaped relationship between relative efficiency and Hammet's σ using a series of 2-(*p*-dimethylaminophenyl)-4,5-di(*p*-Y-phenyl)-4-hydroperoxy-4*H*-isoimidazoles, for which CL efficiency was maximized at σ of Y = F.[5] In typical chemiluminescent systems, an electron-donating hydroxyl group plays an important role in enhancing the bioluminescence of firefly luciferin **1** and the chemiluminescence of 1,2-dioxetane having 3-hydroxy phenyl **2**.[6] On the contrary, it has been also known that their CL efficiencies tend to be decreased both by protic solvents and by the introduction of an OH group[6,7] (Scheme 1).



Scheme 1.

Further, it is simply expected that the efficiencies of 2-(*o*- or *p*-hydroxyphenyl)-4,5-diphenylimidazols **3a** and **3c** would be basically equal. In the schematic these structures are shown as **3a** and **3c** where the locations of OH group attached to *o*-position and to *p*-position dictate their *o*- and *p*-directing electron donation properties, respectively. In terms of substituent effect, therefore, same outcome should be observed with *o*- as with the *p*-case. In reality however, the emission in the case of *p*- has been found to increase but in the case of *o*- no emission of any kind is reported.[4,8] This anomaly could be attributed to a number of factors such as solvent dependence, inconceivable *o*-function, and so forth. It is important that this anomaly be pursued further since there maybe some hidden mechanism related to the OH found in fluorescent material and could lead to some fundamental understanding of the luminescence phenomena. Research in areas other than on chemiluminescence has been conducted on the extraordinary effects of *o*-OH on fluorescence efficiency due to a conical intersection through internal hydrogen bonding, which accelerates deactivation to the ground state.[9] This conical intersection may be related to CL efficiency and prompted us to study the relationship between the location of an OH group in 2-phenyl of lophine peroxide and CL efficiency of **4a–c**, 4-hydroperoxy-2-(*o*-, *m*-, and *p*-hydroxyphenyl)-4,5-diphenyl-4*H*-isoimidazoles (**a** = *o*-: **b** = *m*-: **c** = *p*-). We found conditions under

Keywords: Chemiluminescence; Lophine peroxide; Conical intersection; Hydrogen bond.

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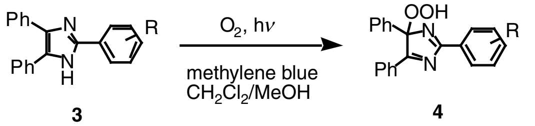


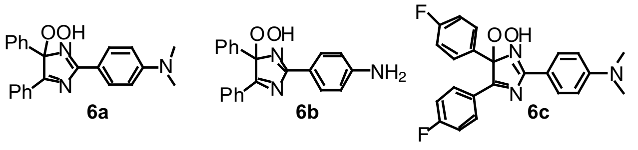
a: R = *o*-OH, **b**: R = *m*-OH, **c**: R = *p*-OH,
d: R = *o*-OMe, **e**: R = *m*-OMe, **f**: R = *p*-OMe, **g**: R = H

Scheme 2.

which *o*-OH peroxide **4a** provided the anticipated efficient chemiluminescence. We report on the location effect of an OH group on CL efficiency and discuss **4a** having an OH group at the *ortho* position in the 2-phenyl group of **4** (Scheme 2).

We prepared peroxides **4a**, **4b**, and **4c** and corresponding methoxy derivatives **4d**, **4e**, and **4f** as references by the method of Kimura and co-workers.[10] CL emission was measured using a photodiode array (Hamamatsu Photonics Model C-2491 Photonic Multichannel Analyzer) to record integrated illumination in photons. Relative CL efficiency Φ/Φ_0 is defined as the relative amount of chemiluminescence of peroxide **4a**–**f** compared to that of lophine peroxide **4g** as the standard. In typical CL measurement, 0.2 mL of 0.5 N potassium hydroxide in methanol was added to a solution consisting of a peroxide derivative in CH_2Cl_2 (5 mM, 1.0 mL). In initiation with a methanol solution of KOH (0.5 N), we calculated CL efficiency Φ/Φ_0 of **4a**–**f** in CH_2Cl_2 (Table 1). Efficiency Φ/Φ_0 of methoxy derivatives **4d**–**f** was higher than that of **4a**–**c** with an OH group. Similar enhancement is seen when $-N(CH_3)_2$ group shown in **6a** takes the place of $-NH_2$ group shown in **6b** (Scheme 3). The efficiency (Φ/Φ_0) of the former group, also referred as dimethylamino, is 61 whereas Φ/Φ_0 of the later group referred simply as amino, 1.62. This observation is in accordance with our previous report that efficiency increase is seen when –O–CH_3 replaces –O–H. In summary an assertion can be made that efficiency increase is possible where a group with –H bond is replaced with a group with $-CH_3$ bond. The relative efficiency of **4a**, **4b**, and **4c** is lower than that of methylated **4d**–**f**.

Dioxetane **2** emits bright illumination on initiation with tetrabutylammonium fluoride (TBAF). This is an example that when the trigger base was changed from NaOH/H_2O to TBAF the CL efficiency in DMSO increased dramatically.[6b,7b] This enhancement in the case of dioxetane **2** having an OH group at the *meta* position of the phenyl group is quite significant and is known as the *meta* substitution effect.[6b,c] When the trigger base was changed to TBAF/THF (1 N), the relative efficiency (Φ/Φ_0) of **4a** with *o*-OH increased to 88.6. When the solvent was changed to dry DMF, the relative efficiency for **4a** increased to 148 on initiation with TBAF/THF. This efficiency is the same as that of *p*-dimethylamino derivative **6c** ($\Phi_{cl}/\Phi_0 = 160$), which is the most efficient of lophine derivatives.



Scheme 3.

The CL spectra of the peroxides **4a**, **4b**, **4c**, and **4g** in aprotic solvents (CH_2Cl_2 and DMF) are exhibited in Figure 1 and CL maxima (λ_{max}) of peroxides **4a**–**g** (CH_2Cl_2) and **4a**–**c**, and **4g** (DMF) are summarized in Tables 1 and 2, respectively. The CL spectral maxima of **4a**–**g** are dependent of the reaction medium and the means of triggering (OH^- or F^-).

The intensity of **4a** with *o*-OH was higher by several orders of magnitude as compared to the rest in the group of peroxide **4a**–**g**. The *meta* substitution effect was anticipated for **4b** and **4e**, but luminescence was not enhanced.

We would like to answer location effect for **4a** with *o*-OH not to perform an efficient chemiluminescent reaction even in the presence of methanol. We propose a mechanism as shown in Scheme 4. Some efficient fluorescent molecules possessing an *o*-OH group are rapidly deactivated through the conical intersection involving the intramolecular hydrogen shift.[9] Use of a polar aprotic solvent and methanol-free base appears to be important for increasing the efficiency. In ^{1}H NMR spectra in

Table 1. Relative CL efficiencies (Φ/Φ_0) and lifetimes (τ/s) of lophine peroxides **4a**–**g** in CH_2Cl_2

Compound	KOH/MeOH[b]			TBAF/THF[c]		
	λ_{max}/nm	Φ/Φ_0[a,d]	τ/s[e]	λ_{max}/nm	Φ/Φ_0[a,d]	τ/s[e]
4a	589	0.28	26.3	564	88.6*	<1
4b	583	0.23	13.5	553	0.99	<1
4c	534	1.02*	35.8	568	1.05*	18.9
4d	554	1.36	8.2	556	3.06	4.7
4e	557	1.32	7.9	558	2.72	1.4
4f	559	1.44	12.8	552	2.64	2.1
4g	553	1.00 ($=\Phi_0/\Phi_0$)	8.5	553	2.46	1.4

[a] The CL intensity (Φ_0) was counted by PMA upon addition of a methanol solution of KOH (0.5 N, 0.2 mL) to a CH_2Cl_2 solution of **4g** (5 mM, 1 mL) as the standard substance.

[b] An ignition base is KOH (0.5 N, 0.2 mL) in MeOH.

[c] An ignition base is TBAF (1 N, 0.2 mL) in THF.

[d] The CL intensity (Φ) was counted by PMA upon addition of an ignition base to a CH_2Cl_2 solution of **4a**–**g** (5 mM, 1 mL) or (1 mM, 1 mL)*.

[e] The CL lifetime (τ/s) was measured by CLD-310 upon addition of an ignition base to a CH_2Cl_2 solution of **4a**–**g** (1 mM, 1 mL).

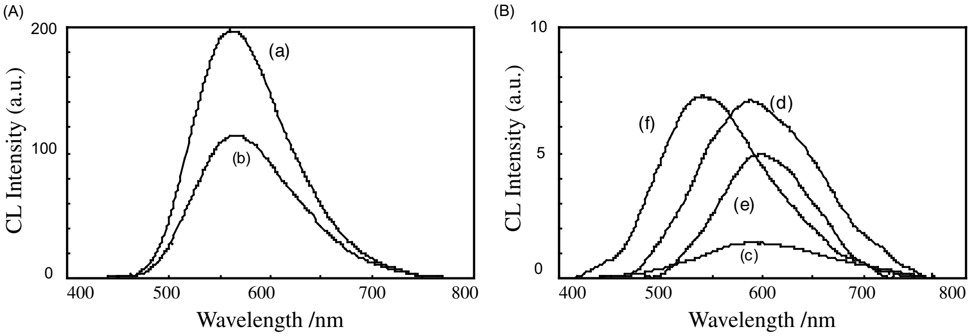


Figure 1. CL spectra of **4a**, **4b**, **4c**, and **4g**. A: (a) peroxide **4a** (1 mM, 1 mL) in DMF; ignition base = TBAF (1 N, 0.2 mL) in THF, (b) peroxide **4a** (1 mM, 1 mL) in CH_2Cl_2; Ignition base = TBAF (1 N, 0.2 mL) in THF. B: (c) peroxide **4a** (5 mM, 1 mL) in CH_2Cl_2; ignition base = KOH (0.5 N, 0.2 mL) in MeOH, (d) peroxide **4b**, (e) peroxide **4c**, and (f) peroxide **4g**. For (d), (e), and (f), common DMF solutions (5 mM, 1 mL) was used and an ignition base was common TBAF (1 N, 0.2 mL) in THF.

Table 2. Relative CL intensities and lifetimes (τ/s) of **4a**, **4b**, **4c**, and **4g** in DMF[b]

Compound	λ_{max}/nm	Φ/Φ_0[a,c]	τ/s[d]
4g	542	1.25	<1
4a (R = *o*-OH)	559	148*	<1
4b (R = *m*-OH)	588	1.30	<1
4c (R = *p*-OH)	599	0.71	<1

[a] Φ_0 is the same as in Table 1.

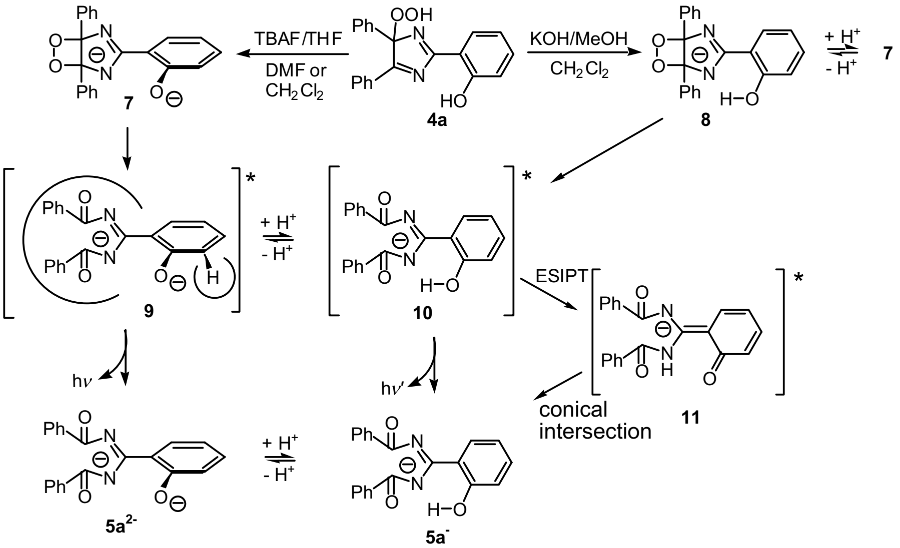
[b] An ignition base is TBAF (1 N, 0.2 mL) in THF.

[c] The CL intensity (Φ) was counted by PMA upon addition of an ignition base to a DMF solution of **4a–c** (5 mM, 1 mL) or (1 mM, 1 mL)*.

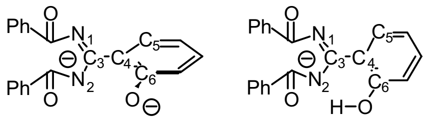
[d] The CL lifetime (τ/s) was measured by CLD-310 upon addition of the ignition base to a DMF solution of **4a–c** (1 mM, 1 mL).

acetone-d_6, the phenol proton of peroxide **4a** was read to be 12.1 ppm and the field-shift on the spectra in this case was lower than the chemical shift of phenol proton of **4c** read at 9.2 ppm. This shift implies the presence of rigid intramolecular hydrogen bonding in the peroxide **4a**. We assume the same intramolecular hydrogen bond formation is probable for amidine **5a** as an anticipated product, which is a most likely emitter but it has not yet been confirmed.[11] We think that the intramolecular hydrogen bonding probably plays an important role in the anomalous CL behavior involving the conical intersection. In a protic solvent, anionic amidine **9*** in an excited state may be trapped by hydrogen of a protic solvent to form intramolecular hydrogen bonding **10***. Enol **10*** is isomerized **11*** by excited-state intramolecular proton transfer (ESIPT). At the conical intersection, **11*** is immediately transferred to the ground state surface of **5a** by intramolecular hydrogen bonding. While in an aprotic solvent, intramolecular hydrogen bond formation is decreased and chemiluminescence may be synchronously increased because an *o*-O^- group formed with free F^- operates as an electron donor as shown in **7** and **9***. One would expect that even **4c** with *p*-OH should have the same efficiency as **4a** with *o*-hydroxy, but in reality it does not. To optimize the system, it should be noted that the CL efficiency of this system might be influenced negatively by dipole–dipole interactions with solvent and proton transfer in polar protic media.

The dihedral angles N1–C3–C4–C5 and N2–C3–C4–C6 predicted with MM 2 calculation for the dianionic form



Scheme 4.



Scheme 5.

of amidine **9** are 39° and 41° those of monoanionic form are 0° and 1° (Scheme 5). In the dianionic form, the dibenzoyl amidine moiety and *o*-hydroxy phenyl group are twisted each other. A naked *m*- or *p*-O^{-} group cannot avoid direct contact with solvents, which probably would accelerate deactivation of emitters in excited states, while an *o*-O^{-} group of amidine **9*** is somewhat protected sterically by adjacent anionic di-benzoyl amidine moieties, that is, a pocket. The twisted dibenzoyl amidine moiety is supportive of the formation of the pocket, in which the 2-phenyl *o*-hydroxy group is likely protected from solvent contact. The electron donation of *o*-O^{-} may thus operate to enhance chemiluminescence in the pocket.

The following statement summarizes the *o*-OH effect on CL efficiency. When the reaction is triggered in an aprotic solvent, intrinsic electron donation of –O^{-} recovers the *ortho* position and enhances efficiency.

Acknowledgements

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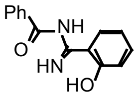
10. (a) Lophine peroxide derivatives were prepared by the method of Kimura et al. Hu, Z. Z.; Takami, S.; Kimura, M.; Tachi, Y.; Naruta, Y. *Acta Crystallogr. C* **2000**, *56*, e465–e466; (b) Tsunenaga, M.; Kimura, M.; Naruta, Y. *ITE Lett. Batter. New Technol. Med.* **2003**, *4*, 633–638.
11. Probable emitters are final products, which are believed to be the corresponding fluorescent amidine derivatives **5**, but any fluorescence related to their chemiluminescene was not observed from resulted solutions of **4**. From the resulted solution of **4a**, monobenzoylamidine **12** was isolated quantitatively. In the chemiluminescent reaction of lophine peroxides, confirmation of emitter is an important work but acylated amidines are occasionally hard to be isolated. An emitter of the case of the standard lophine peroxide **4g** also has not been known. Amidine **5g**, which was synthesized by independent method, was not fluorescent. See Ref. 1b.



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