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A Kinetic Study on the Chemiluminescence of 9-Alkylacridines upon Air Oxidation in Alkaline Aprotic Solvents

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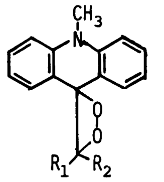
9-Methyl- (**1a**), 9-benzyl- (**1b**), 9-(diphenylmethyl)- (**1c**), and 9-ethylacridine (**1d**) were employed to obtain luminescent features of the acridines. The decay of chemiluminescence (CL) exhibits a pseudo-first order behavior with apparent rate constants 0.10, 3.30, 4.10, and 0.07 min^{-1} at 312 K for **1a**, **1b**, **1c**, and **1d**, respectively. A relatively high CL quantum yield (6.3×10^{-3}) is provided for **1a**, in contrast to low yields for **1b**, **1c**, and **1d** (1.5×10^{-6}, 1.1×10^{-5}, and 1.3×10^{-4}, respectively). A reaction mechanism involving a cleavage of a dioxetane intermediate to give excited singlet acridone anion is plausible for the luminescent reaction. In view of the fact that several dioxetanes decompose to give excited singlet products in high yields, the CL appears to arise from a minor reaction.

A number of acridines and acridinium salts have been reported to chemiluminesce in various reactions.[1)] However, there exists little information as to the chemiluminescence (CL) of 9-alkylacridines on base-catalyzed air oxidation except a short description by White and Harding.[2)] They observed a CL of 9-methylacridine (**1a**) on reaction with potassium *t*-butoxide (*t*-BuOK) and oxygen in dimethyl sulfoxide and proposed a reaction scheme involving a cleavage of a dioxetane intermediate to give the excited singlet acridone anion. Recently, such 1,2-dioxetanes as **2a**, **2b**, and **2c** have been derived and shown to decompose thermally to give excited singlet 10-methylacridone.[3)]



2a: $R_1=R_2=H$
2b: $R_1=H$, $R_2=C_6H_5$
2c: $R_1=R_2=C_6H_5$

According to Lee and Singer,[3c)] the chemiexcitation yield for the generation of excited singlet 10-methylacridone changes with a structural variation at R_1 and R_2 in the dioxetanes, increasing in the order **2a**<**2b**<**2c**. Thus, we anticipated that if dioxetane intermediates like **2b** and **2c** were generated, the CL from air oxidation of 9-benzyl- (**1b**) or 9-(diphenylmethyl)acridine (**1c**) would be more intense than that from **1a**. A preliminary experiment, however, showed that the pattern of the substituent effect was contrary to our expectation; only feeble emission could be detected from **1b** and **1c** in spite of a high yield of ground state of acridone anion being obtained.

In order to study the effect of 9-alkyl substituents on the CL intensity of 9-alkylacridines **1a**—**1c** and 9-ethylacridine (**1d**), we investigated the kinetics for the luminescent air oxidation and determined the CL quantum and chemiexcitation yields for the generation of the excited singlet acridone anion.

Results and Discussion

The luminescent reaction was initiated by adding 0.3 cm^3 of a solution of *t*-BuOK in *t*-butyl alcohol (*t*-BuOK/*t*-BuOH solution, 2×10^{-2} mol/dm^3) to 2.0 cm^3 of an aerated solution of **1a**, **1b**, **1c**, or **1d** in DMF (1×10^{-4} mol/dm^3). CL emissions from each acridine show the same spectral distribution, matching the fluorescence (FL) spectra of the spent reaction mixtures and the FL spectrum of acridone anion under the identical experimental conditions,[4)] as shown in Fig. 1. Actually, 9-acridone was detected and identified by a comparison with an authentic sample (Tokyo Kasei, guaranteed reagent) by means of thin layer chromatography on silica gel.

Under the experimental conditions employed, CL decays showed a pseudo-first order behavior to about 3 half-lives. From the decays, apparent rate constants at several different temperatures were determined. Rates of reactions were also determined by following the increase in the concentration of acridone anion through measurement of its FL-emission intensity at 465 nm. The FL-increasing curves obtained from **1a** and **1b** are illustrated together with the corresponding CL-decay curves in Fig. 2. The rate constants determined from the FL-increasing curves and those from CL-decay curves are shown in Table 1. A fairly good

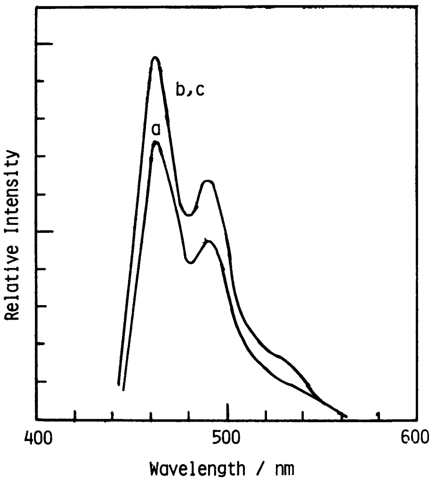


Fig. 1. The CL spectrum of **1a** in DMF (a), and FL spectra of the spent reaction mextures (b) and acridone anion under the identical conditions (c).

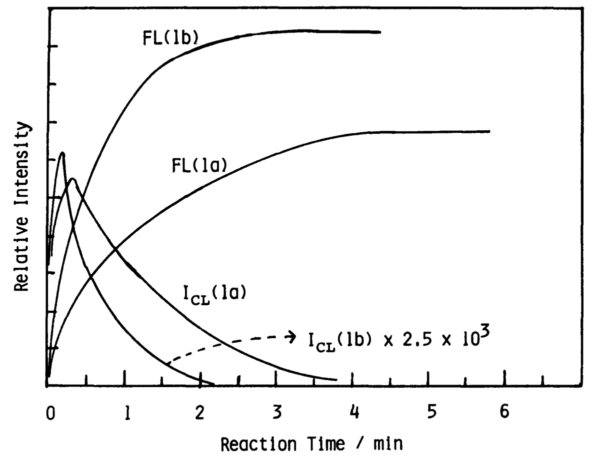


Fig. 2. FL-increasing curves (FL) and CL-decay curves (I_{CL}) in systems of **1a** and **1b** at 307K.

TABLE 1. APPARENT PSEUDO-FIRST ORDER RATE CONSTANTS (k_{obsd}/min^{-1}) FOR THE CHEMILUMINESCENT REACTIONS OF **1a**—**d** AT SEVERAL DIFFERENT TEMPERATURES

Method of measurement	CL decay	FL curve	CL decay	FL curve
Acridine	**1a**		**1b**	
293 K	0.21	0.23	0.78	0.77
289 K	0.34	0.34	0.91	0.91
303 K	0.48	0.51	1.59	1.53
307 K	0.75	0.78	1.95	1.85
312 K	1.00	1.01	3.30	3.26
Acridine	**1c**		**1d**	
312 K	4.10	4.05	0.07	0.07
316 K			0.10	0.10
321 K			0.14	0.16

TABLE 2. APPARENT ACTIVATION ENERGIES (E_a) AND PREEXPONENTIAL FACTORS (A) FOR THE CHEMILUMINESCENT REACTIONS OF **1a**, **1b**, AND **1d**

Acridine	E_a / kJ mol^{-1}	A / min^{-1}
1a	65.2	8.8×10^{10}
1b	58.9	2.4×10^{10}
1d	70.8	4.2×10^{10}

agreement is found between the two, which indicates that the rate of the luminescent reaction is parallel to the rate of generation of acridone anion. The rate constants yield rather good Arrhenius plots, from which apparent activation energies and preexponential factors for **1a**, **1b**, and **1d** were determined. These kinetic data are tabulated in Table 2.

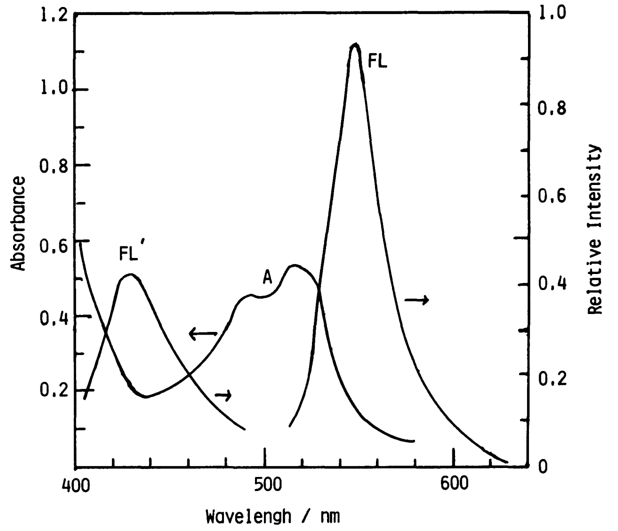


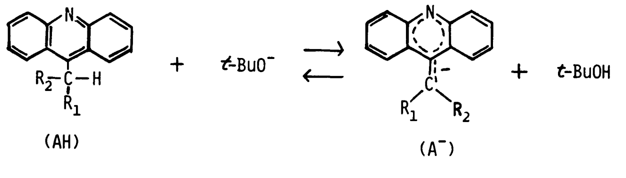
Fig. 3. The spectra of absorption and FL emission of orange-red intermediate in a system of **1b**. A: Absorption; FL: FL emission; FL′: FL emission of **1b**.

When *t*-BuOK/*t*-BuOH solution was added to a degassed solution of **1a** or **1b** *in vacuo*, no CL emission was observed and an orange-red intermediate was found, which was stable in the absence of oxygen. The absorption and FL spectra of this intermediate in a system with **1b** are shown Fig. 3. An admission of air to the system caused CL to appear progressively. Mason and Roberts[5] observed a similar orange-red intermediate when they added aqueous sodium hydroxide to a degassed solution of 4,5-dihydropyrazino[2,1-a:3,4-a′]diisoquinolinediium dibromide in methanol, which chemiluminesced on reaction with oxygen due to generation of excited singlet 1,2-di[2-(1-isoquinolonyl)]-ethane. Heller and coworkers[6] reported that the orange-red color is attributable to a formation of electron-rich olefin *via* a cation radical, which reacts with oxygen to produce excited singlet 1,2-di[2-(1-isoquinolonyl)]ethane, and that the initial step of the change is the abstraction of a proton from the pyrazinodiisoquinolinediium salt.

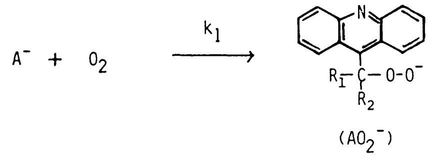
On the analogy of the luminescent reaction of the pyradinodiisoquinolinediium salt, it seems likely that an electron-rich olefin is generated at the initial stage by loss of a proton from acridines. The extremely low magnitude of reaction rate for **1d** is probably due to low concentration of the olefin since no appreciable formation of the orange-red intermidiate was observed.

In view of the experimental results described above, the following reaction scheme, analogous to the one outlined by White and Harding,[2] would be plausible for the luminescent reaction.

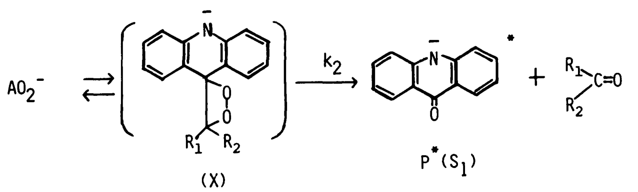
(1) Proton transfer from acridine (AH) to *t*-BuO$^-$ to form an electron-rich olefin (A$^-$):



(2) Reaction of A$^-$ with oxygen to produce a peroxide anion (AO$_2^-$):



(3) Of the decomposition processes of AO_2^-, one is a cleavage *via* a dioxetane intermediate (X) to give excited singlet acridone anion ($P^*(S_1)$):



or to give the ground state of acridone anion ($P(S_0)$):

$$AO_2^- \rightleftarrows (X) \xrightarrow{k_3} P(S_0) + R_1R_2C{=}O.$$

(4) The cleavage processes of AO_2^- *via* acyclic pathways to give $P(S_0)$ and other products (Q) will compete with the above processes:

$$AO_2^- \xrightarrow{k_4} P(S_0),$$

$$AO_2^- \xrightarrow{k_5} Q.$$

(5) FL emission from $P^*(S_1)$:

$$P^*(S_1) \xrightarrow{k_6} P(S_0) + h\nu.$$

(6) Radiationless deactivation of $P^*(S_1)$:

$$P^*(S_1) \xrightarrow{k_7} P(S_0).$$

(7) Intersystem crossing to excited triplet acridone anion ($P^*(T_1)$) followed by radiationless deactivation:

$$P^*(S_1) \xrightarrow{k_8} P^*(T_1) \longrightarrow P(S_0).$$

According to the scheme, the intensity of CL emission is given by

$$I_{CL} = k_6[P^*(S_1)].$$

Using the steady-state approximation formulations $d[P^*(S_1)]/dt=0$ and $d[AO_2^-]/dt=0$, I_{CL} can be written as

$$I_{CL} = (k_2/(k_2+k_3+k_4+k_5))\Phi_F k_1[A^-][O_2],$$

where Φ_F is the apparent FL quantum yield of acridone anion in aerated DMF-*t*-BuOK systems and is given by

$$\Phi_F = k_6/(k_6+k_7+k_8).$$

If $[O_2]$ and [*t*-BuO⁻] are assumed to be maintained constant during the CL emission, I_{CL} is given by

$$I_{CL} = (k_2/(k_2+k_3+k_4+k_5))\Phi_F k_{obsd}[AH],$$

where

$$k_{obsd} = k_1[O_2]K[t\text{-BuO}^-]/[t\text{-BuOH}]$$

and

$$K = [A^-][t\text{-BuOH}]/[AH][t\text{-BuO}^-].$$

Figure 4 shows plots of the logarithm of emission intensity *vs.* time for the CL of **1a** (1.0×10^{-4} mol/dm³) for different concentrations of *t*-BuOK, which indicates that the apparent first-order rate constant for the CL decay (k_{obsd}) is a function of [*t*-BuO⁻] as assumed above.

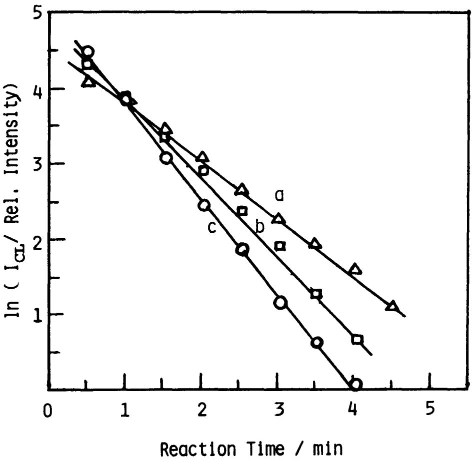


Fig. 4. The plots of ln (CL intensities of **1a** with different *t*-BuOK concentrations) *vs.* reaction time at 321K.
a: [*t*-BuOK]$=2.5\times10^{-3}$ mol/dm³, $k_{obsd}=0.28$ min⁻¹; b: 4.0×10^{-3} mol/dm³, 1.00 min⁻¹; c: 5.0×10^{-3} mol/dm³, 1.30 min⁻¹.

The scheme further gives the following relation:

$$d[P(S_0)]/dt = ((k_2+k_3+k_4)/(k_2+k_3+k_4+k_5))k_{obsd}[AH].$$

Because of the low concentration of A⁻, $d[P(S_0)]/dt$ is approximately written as

$$d[P(S_0)]/dt = ((k_2+k_3+k_4)/(k_2+k_3+k_4+k_5)) \times(-d[AH]/dt),$$

so that $[AH]=[AH]_0\exp(-k_{obsd}t)$, where $[AH]_0$ is the initial concentration of acridine.

Thus, I_{CL} is given by

$$I_{CL} = (k_2/(k_2+k_3+k_4+k_5))\Phi_F k_{obsd}[AH]_0 \exp(-k_{obsd}t), \tag{1}$$

and the concentration of acridone anion at reaction time *t* is given by

$$[P(S_0)]_t = ((k_2+k_3+k_4)/(k_2+k_3+k_4+k_5))[AH]_0 \times(1-\exp(-k_{obsd}t)). \tag{2}$$

From Eqs. 1 and 2, the overall CL quantum yield defined by

$$\Phi_{CL} = \int_0^{t_e} I_{CL}dt/[AH]_0$$

is given by

$$\Phi_{CL} = \Phi^*\Phi_F\Phi_r,$$

where t_e is the duration of CL emission, Φ^* is the chemiexcitation yield for the generation of excited singlet acridone anion from acridine, given by

$$\Phi^* = k_2/(k_2+k_3+k_4+k_5),$$

and Φ_r is the yield of acridone anion from acridine, given by

$$\Phi_r = [P(S_0)]_{t_e}/[AH]_0.$$

Φ_{CL} was determined from the ratio of the total light emitted from the CL of acridine to that from a standard luminol solution in dimethyl sulfoxide containing *t*-BuOK ($\Phi^S_{CL}=1.28\times10^{-2}$)7) by the same method as described in our previous paper.8) Φ_r was determined from

TABLE 3. CHEMILUMINESCENCE QUANTUM YIELD (Φ_{CL}), YIELDS OF ACRIDONE ANION FROM ACRIDINES (Φ_r), AND CHEMIEXCITATION YIELDS FOR THE GENERATION OF EXCITED SINGLET ACRIDONE ANION FROM DIOXETANE INTERMEDIATES (Φ^*) AT SEVERAL DIFFERENT TEMPERATURES

	Φ_{CL}	Φ_r	Φ^*	Φ_{CL}	Φ_r	Φ^*
		1a			**1b**	
293 K	6.3×10^{-3}	0.40	7.5×10^{-2}	1.6×10^{-6}	0.625	1.2×10^{-6}
298 K	6.8×10^{-3}	0.43	7.5×10^{-2}	1.5×10^{-6}	0.63	1.1×10^{-6}
303 K	6.9×10^{-3}	0.43	7.6×10^{-2}	1.5×10^{-6}	0.66	1.1×10^{-6}
307 K	6.3×10^{-3}	0.40	7.5×10^{-2}	1.5×10^{-6}	0.62	1.1×10^{-6}
312 K	6.3×10^{-3}	0.425	7.1×10^{-2}	1.4×10^{-6}	0.625	1.1×10^{-6}
		1c			**1d**	
312 K	1.1×10^{-5}	0.60	7.8×10^{-5}	1.1×10^{-4}	0.21	2.5×10^{-3}
316 K				1.3×10^{-4}	0.24	2.6×10^{-3}
321 K				1.45×10^{-4}	0.34	2.2×10^{-3}

($\Phi_F=0.21$ over the temperature range)

FL assay with known concentrations of acridone anion as internal standard by the method reported by Lee and coworkers (the method of standard addition).[9] Φ_F was determined by comparison of the FL emission of acridone anion in basic DMF[4] with that from a standard solution of quinine sulfate in 0.50 mol/dm^3 H_2SO_4 ($\Phi_F^S=0.50$)[10] and obtained to be 0.21, which was maintained almost constant over the temperature range of 289—321 K. The values of Φ_{CL} and Φ_r at several different temperatures and of Φ^* calculated from Eq. 3 are tabulated in Table 3. The results indicate that neither k_{obsd} nor Φ_r but Φ^* contributes to Φ_{CL}, which means that the ratio of k_2 to $k_3+k_4+k_5$ governs the CL quantum yield. The little dependence of Φ^* (and thus Φ_{CL}) on temperature may be interpreted in terms of the little dependence of k_2, k_3, k_4, and k_5 on temperature due to the low activation energy for the decomposition of unstable peroxide anion (AO_2^-). Our present experimental data do not allow us to decide whether k_3 or k_4+k_5 contributes predominantly to the lowering of the value of Φ_{CL} since the net chemiexcitation yield from dioxetane intermediate, $k_2/(k_2+k_3)$, cannot be determined. In view of the fact that several isolated dioxetanes decompose to give excited singlet product in high yields,[3a,c] it seems likely that the decomposition path *via* the dioxetane intermediate is a minor one, and thus, the extremely high magnitude of k_4 or k_5 lowers the Φ_{CL}-values of **1b** and **1c**.

Two other possibilities to lower the Φ_{CL}-values of **1b** and **1c** are conceivable. One is the direct generation of excited triplet acetophenone (from **1b**) or benzophenone (from **1c**), and the other is the generation of some quenching products. These, however, seem unlikely because neither indirect CL with 9,10-dibromoanthracence (one of triplet monitors) nor cis isomerization of added *trans*-stilbene could be observed, and because the CL of **1a** was not quenched by the addition of **1b** or **1c**. Further investigation is required to clarify the reason why the CL emissions from **1b** and **1c** are by far lower than the one from **1a**.

Experimental

Preparation of 9-Alkylacridines. The acridines were synthesized by heating a mixture of a carboxylic acid and diphenylamine with zinc chloride. The following procedure is representative of the syntheses. A mixture of diphenylamine (5.0 g), acetic acid (5.0 g), and zinc chloride (2.0 g) was heated at 210—220 °C for 10 h. While warm, the mixture was mixed with water (200 cm^3) and the product was extracted with benzene (3×200 cm^3). Evaporation of the extract and subsequent crystallization from benzene gave 9-methylacridine (**1a**) as pale yellow needles (49% yield): mp 117.5—118.5 °C [O. Blum, *Chem. Ber.*, **62**, 881 (1929): mp 117—118 °C]; MS *m/z* 193 (M^+). Found: C, 87.05; H, 5.68; N, 7.20. Calcd for $C_{14}H_{11}N$: C, 87.01; H, 5.74; N, 7.25. In a similar way, the following compounds were synthesized. 9-ethylacridine (**1d**) (58% yield): mp 115.5—116.5 °C [O. Tsuge, M. Nishinohara, and K. Sadano, *Bull. Chem. Soc. Jpn.*, **38**, 2037 (1965): mp 116 °C]; MS *m/z* 207 (M^+). Found: C, 86.59; H, 6.38; N, 6.62. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. 9-benzylacridine (**1b**) (58% yield): mp 173—174 °C [E. H. Huntress and E. N. Show, *J. Org. Chem.*, **13**, 674 (1948): mp 173 °C]; MS *m/z* 269 (M^+). Found: C, 88.93; H, 5.59; N, 5.27. Calcd for $C_{20}H_{15}N$: C, 88.18; H, 5.61; N, 5.20. 9-(diphenylmethyl)acridine (**1c**) (30% yield): mp 195—197 °C (from a 1.1 mixture of benzene and hexane); MS *m/z* 345 (M^+). Found: C, 89.95; H, 5.60; N, 4.15. Calcd for $C_{26}H_{19}N$: C, 90.39; H, 5.55; N, 4.06.

Measurements of Intensity and Spectra of CL and FL Emissions. The reactions were conducted in a quartz cell (1.0×1.0×4.5 cm), which was kept at a constant temperature by means of thermostated cell holder. The intensity and spectrum of CL emission were measured on a Hitachi MPF-2A fluorescence spectrophotometer, with the excitation source off. The intensity and spectrum of FL emission were also measured on the same apparatus.

References

1) F. McCapra and D. G. Richardson, *Tetrahedron Lett.*, **1964**, 3167; F. McCapra, D. G. Richardson, and Y. C. Chang, *Photochem. Photobiol.*, **4**, 1111 (1965); M. M. Rauhut, D. Sheehan, R. A. Clark, B. G. Roberts, and A. M. Semsel, *J. Org. Chem.*, **30**, 3587 (1965); E. Rapaport, M. W. Cass, and E. H. White, *J. Am. Chem. Soc.*, **94**, 3160 (1972); J. Gaglias and J. Nikokavouras, *Monatsch. Chem.*, **110**, 763 (1979); G. Perkizas and J. Nikokavouras, *ibid.*, **114**, 3 (1983).

2) E. H. White and M. J. Harding, *Photochem. Photobiol.*, **4**, 1129 (1965).

3) a) F. McCapra, I. Beheshti, A. Burford, R. A. Hann, and K. A. Zaklika, *J. Chem. Soc., Chem. Commun.*, **1977**, 944; b) E. H. White, N. Suzuki, and W. H. Hendrickson, *Chem. Lett.*, **1979**, 1491; c) C. Lee and L. A. Singer, *J. Am. Chem. Soc.*, **102**, 3823 (1980).

4) The solution of acridone anion was prepared by adding 0.3 cm^3 of a *t*-BuOK/*t*-BuOH solution (2×10^{-2} mol/dm^3) to a solution of 9-acridone in DMF (1.0×10^{-4} mol/dm^3).

5) S. F. Mason and D. R. Roberts, *Chem. commun.*, **1967**, 476.

6) C. A. Heller, R. A. Henry, and J. M. Fritsh, "Chemiluminescence and Bioluminescence," ed by M. J. Cormier, D. M. Hercules, and J. Lee, Plenum Press, New York (1973), p. 249.

7) J. Lee, A. S. Wesley, J. F. Ferguson III, and H. H. Seliger, "Bioluminescence in Progress," ed by F. H. Johnson and Y. Haneda, Princetone Univ. Press, Princetone (1966), p. 35.

8) I. Kamiya and T. Sugimoto, *Bull. Chem. Soc. Jpn.*, **54**, 25 (1981).

9) K.-M. Lee, L. A. Singer, and K. D. Legg, *J. Org. Chem.*, **41**, 2685 (1976).

10) J. N. Demas and G. A. Crosby, *J. Phys. Chem.*, **75**, 991 (1971).