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The Chemiluminescence of Indole Derivatives. IV. Correlation between Chemiluminescence and Structure of 2,3-Dimethylindoles

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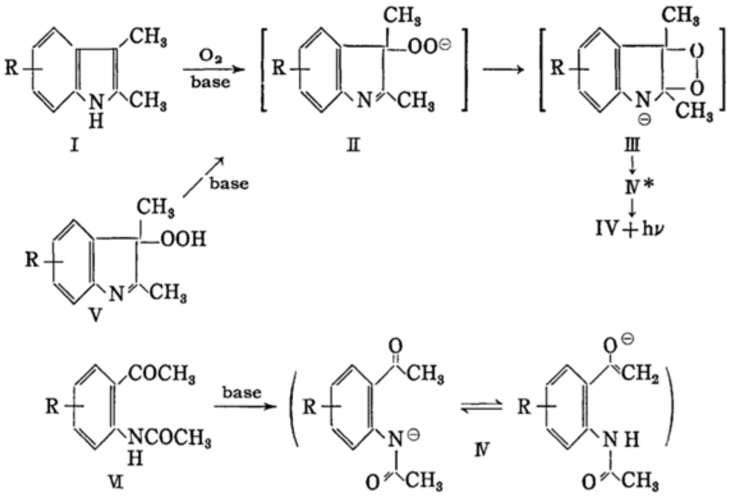
Four 5-substituted and three 6-substituted 2,3-dimethylindoles and unsubstituted 2,3-dimethylindole were synthesized and their light emission was measured in the presence of atmospheric oxygen and potassium *t*-butoxide in dimethyl sulfoxide. It was found that the Hammett equation was applicable to their chemiluminescent reaction with ρ value of -1.24. For the 6-position of indole nucleus σ_p was used, and for the 5-position σ_m was used. Also, four hydroperoxides of 2,3-dimethylindole bearing substituents at the 5- or 6-position, which emitted light in the presence of potassium *t*-butoxide in dimethyl sulfoxide, gave linear Hammett plots with ρ value of -2.04. The relationship between the Hammett equation and the chemiluminescence of these inole derivatives has been discussed further.

Previously we found that forty-one of substituted indoles were chemiluminescent in the presence of atmospheric oxygen and potassium hydroxide in dimethyl sulfoxide.[1] Also, we proposed the mechanism of the chemiluminescence of 2,3-dimethylindole (I) involving the hydroperoxide anion (II) as an intermediate.[2] McCapra *et al.*[3,4] independently suggested the same intermediate and discussed the mechanism of the chemiluminescence from the standpoint of the decomposition of the hydroperoxide.



Scheme 1

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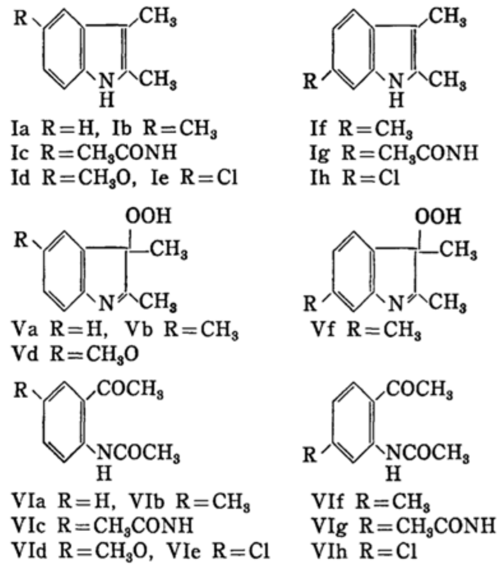
[1] N. Sugiyama, M. Akutagawa, T. Gasha, Y. Saiga and H. Yamamoto, This Bulletin, **40**, 347 (1967).

[2] N. Sugiyama and M. Akutagawa, *ibid.*, **40**, 240 (1967).

[3] F. McCapra, D.G. Richardson and Y.C. Chang, *Photochem. Photobiol.*, **4**, 1111 (1965).

[4] F. McCapra and Y. C. Chang, *Chemical Commun.*, **1966**, 522.



Scheme 2

Furthermore, we speculated the mechanism of the chemiluminescent reaction of I as shown in Scheme 1.[5] The compound I changes to hydroperoxide anion (II), with oxygen and base, while the hydroperoxide (V) requires only base for conversion to II. Then II is converted to four-membered cyclic peroxide (III) which decomposes to an excited *o*-acetamidoacetophenone anion (IV*). And IV* falls to the ground state with an emission of light.

Recently we have prepared some substituted 2,3-dimethylindoles, measured their chemiluminescence, and found that the Hammett equation was applicable to their chemiluminescent reaction. The Hammett relationship was first found to apply to the chemiluminescent reaction of lophine by Philbrook *et al.*[6] There is, however, no example of the application of the Hammett equation to the chemiluminescence of indoles. It is interesting to examine the relationship between the Hammett equation and the chemiluminescence of indole derivatives.

Results and Discussion

We prepared eight 2,3-dimethylindoles, four of which had substituents at the 5-position of indole ring (Ib, Ic, Id and Ie), and three of which had substituents at the 6-position (If, Ig and Ih). Also we synthesized four hydroperoxides of 2,3-dimethylindoles (Va, Vb, Vd and Vf). The chemiluminescence maxima are shown in Table 1 and the fluorescence maxima after the chemiluminescent reaction are shown in Table 2. It can be concluded that the emitting species of the chemiluminescent reaction of I and V are the same and might be *o*-acetamidoacetophenone anion (VI*) in an excited singlet state, because the maxima of the fluorescence spectra of VI under the same condition as the chemiluminescence agreed closely with the maxima of the chemiluminescence spectra of I and V and also with the maxima of their fluorescence spectra after the chemiluminescent reaction.

TABLE 1. CHEMILUMINESCENCE MAXIMA OF 2,3-DIMETHYLINDOLES (I) AND THEIR HYDROPEROXIDES (V)

R of I or V		Chemiluminescence maxima of I	V
a.	H	520 mμ	520 mμ
b.	5-CH_3	532	532
c.	5-CH_3CONH	537	
d.	5-CH_3O	548	546
e.	5-Cl	532	
f.	6-CH_3	519	520
g.	6-CH_3CONH	530	
h.	6-Cl	518	

TABLE 2. FLUORESCENCE MAXIMA OF 2,3-DIMETHYLINDOLES (I), HYDROPEROXIDES (V) AND CHEMILUMINESCENCE PRODUCTS (VI)

R of I, V or VI		Fluorescence maxima of I	V	VI+
a.	H	520 mμ	520 mμ	520 mμ
b.	5-CH_3	531	531	532
c.	5-CH_3CONH	539		539
d.	5-CH_3O	549	546	546
e.	5-Cl	532		533
f.	6-CH_3	521	520	520
g.	6-CH_3CONH	532		530
h.	6-Cl	518		519

+ synthesized product under the same condition as the chemiluminescent reaction.

We found that σ values of para and meta substitution in benzene ring were favorably used for the 6- and 5-positions of indole nucleus respectively. In the cases of eight indoles, Ia, Ib, Ic, Id, Ie, If, Ig and Ih, the plot of log A/A_0 against σ given by McDaniel and Brown,[7] was a straight line, where A and A_0 are the amount of light emitted during the chemiluminescent reaction of substituted 2,3-dimethylindoles and that of 2,3-dimethyl-

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[5] N.Sugiyama, M.Akutagawa and H.Yamamoto, This Bulletin, **41**, 936 (1968).

[6] a) G. E. Philbrook and M. A. Maxwell, *Tetrahedron Letters*, **1964**, 1111.

b) G.E. Philbrook, M.A. Maxwell, R. E. Taylor and J.R.Totter, *Photochem. Photobiol.*, **4**, 1175 (1965).

[7] D.H.McDaniel and H.C.Brown, *J. Org. Chem.*, **23**, 420 (1958).

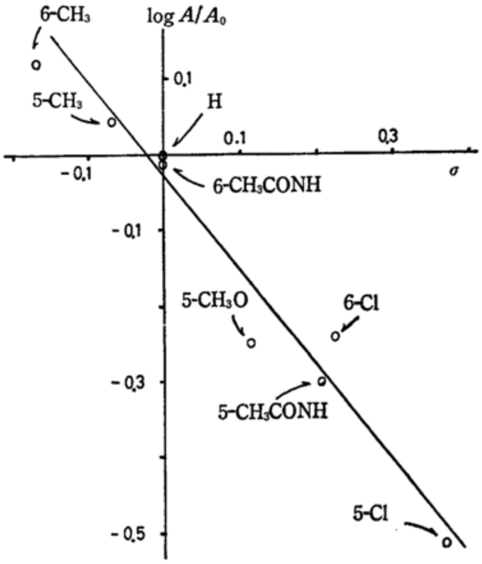


Fig. 1. Hammett plot based on the relative total light emission for substituted 2,3-dimethylindoles.

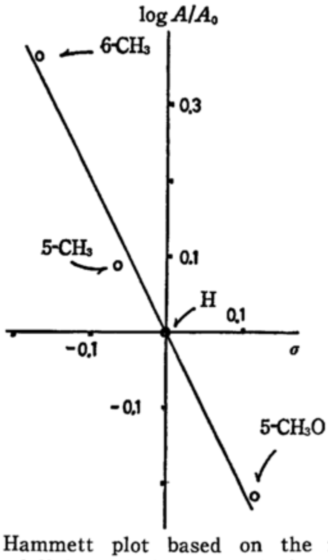


Fig. 2. Hammett plot based on the relative total light emission for substituted 2,3-dimethylindolenyl-3-hydroperoxides.

TABLE 3. RELATIVE TOTAL LIGHT EMISSION (A/A_0) OF 2,3-DIMETHYLINDOLES (I) AND THEIR HYDROPEROXIDES (V)

	R of I or V	I[+]	V[++]
a.	H	1.00	1.00
b.	5-CH_3	1.11	1.22
c.	5-CH_3CONH	0.50	
d.	5-CH_3O	0.56	0.60
e.	5-Cl	0.30	
f.	6-CH_3	1.32	2.34
g.	6-CH_3CONH	0.97	
h.	6-Cl	0.57	

[+] A_0=Total emission of Ia

[++] A_0=Total emssion of Va

TABLE 4. HALF-LIVES OF CHEMILUMINESCENCE OF 2,3-DIMETHYLINDOLES (I) AND THEIR HYDROPEROXIDES (V)

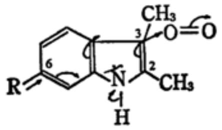
	R of I or V	I	V
a.	H	22 sec	1.6 sec
b.	5-CH_3	21	1.7
c.	5-CH_3CONH	25	
d.	5-CH_3O	31	1.9
e.	5-Cl	82	
f.	6-CH_3	12	1.5
g.	6-CH_3CONH	9.8	
h.	6-Cl	62	

indole, respectively. (Fig. 1) The value of the reaction constant ρ determined by least squares method is -1.24. Also we proved the Hammett relationship in the chemiluminescent reaction of four indole hydroperoxides, Va, Vb, Vd and Vf. The value of ρ is -2.04. (Fig. 2).

The negative values of ρ indicate that these chemiluminescent reactions are facilitated by a high electron density at the reaction site. Both Fig. 1 and Fig. 2 show that an electron-releasing substituent favors the chemiluminescent reaction and the negative slope is consistent with the interpretation described above.

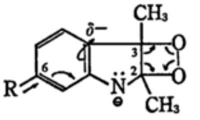
From intensity of chemiluminescence-time curves, decay constants were calculated by the equation $I=I_0\exp(-t/\alpha)$, where I and I_0 are the intensity at time t and zero respectively, and $1/\alpha$ is a decay constant. A plot of $\log I$ *vs.* time t gave α. The half-lives of chemiluminescence calculated by the equation $t_{1/2}=2.303\times\alpha\times\log 2$ for indoles and hydroperoxides are shown in Table 4. The hydroperoxides (V) emitted light instantaneously, the duration being a few seconds, $t_{1/2}=1.5-1.9$ sec, while the parent indoles (I) emitted light more slowly, the duration being from 40 to 170 seconds, $t_{1/2}=9.8-82$ sec. Considering the facts that the reaction rate of the chemiluminescence of V is very fast, and that the amount of the light is different with different substituents, it is tentatively assumed that the quantum yield of the chemiluminescence of V is correlated with the Hammett σ function.

Finally, we attempt to show a reasonable explanation for the slope of the curve in Fig. 1 or in Fig. 2, which is consistent with the reaction mechanism shown in Scheme 1. In the intermediate III an electron-releasing substituent R at the 6-position contributes to an increase of an electron density on the para



position to R. This negative charge will facilitate the homolytic fission of the bond between C-2 and C-3. This is the reason why the reaction from V to IV or from I to II is favored by high electron availability.

Also, we can explain the fact that the absolute value of ρ, 1.24, for the reaction from I to IV is less than that of ρ, 2.04, for the reaction from V to IV. If we assume that the rate from I to II in the reaction from I to IV is slow, the substituent R at the 6-position increases an electron density on the para position to R and it is probably unfavorable for the increase of the electron density at the 3-position of indole nucleus. Then the electron-releasing substituent in the 6-position retards the reaction from I to III, and this makes the absolute value of ρ decrease from 2.04 to 1.24.



Now, we can conclude that the Hammett relationship may be applied to interpret the influence of a substituent on an indole ring upon the quantum yield of the chemiluminescent reaction of 5- or 6-substituted 2,3-dimethylindole hydroperoxides as well as upon the light emission of the parent 2,3-dimethylindoles.

Experimental

5-Acetamido-2,3-dimethylindole (Ic). Powdered 5-amino-2,3-dimethylindole,[8] 0.5 g, was dissolved in 4.7 m*l* of acetic anhydride and kept for 3 hr at room temperature. Then the solution was poured onto crushed ice. White precipitates, 0.52 g, were collected and recrystallized from ethanol-water to give colorless long plates, mp 171.0—171.5 °C.

Found: C, 71.26; H, 6.71; N, 13.95 %. Calcd for $C_{12}H_{14}ON_2$: C, 71.26; H, 6.98; N, 13.85 %.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 245(4.45), 298(3.68, sh.), 310(3.44). IR: ν^{KBr} cm^{-1} 3370, 3250, 1650, 1550, 860, 810.

6-Acetamido-2, 3-dimethylindole (Ig). By the same method as Ic, 6-amino-2,3-dimethylindole was acetylated. Colorless leaflets from ethanol, mp 204—206°C.

Found: C, 71.08; H, 7.08; N, 13.97 %. Calcd for $C_{12}H_{14}ON_2$: C, 71.26; H, 6.98; N, 13.58 %.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 218(4.24), 248(4.37), 294 (4.01). IR: ν^{KBr} cm^{-1} 3290, 3210, 1625, 1525, 860, 810.

2, 3, 6-Trimethylindole (If).[9] White leaflets from ethanol-water, mp 119.5—121.0 °C.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 230(4.55), 280(3.79), 295 (3.69, sh.). IR: ν^{KBr} cm^{-1} 3360, 2950, 2890, 2840, 853, 802.

6-Chloro-2,3-dimethylindole (Ih).[9] White leaflets, from ether-petroleum ether, mp 164.5—165.5 °C.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 235(4.57), 286(3.83), 296 (3.78, sh.). IR: ν^{BKr} cm^{-1} 3360, 848, 804, 740.

2,3,6-Trimethylindolenyl-3-hydroperoxide (Vf). 1f, 200 mg, was dissolved in warm light petroleum (bp 60—80 °C, 30 m*l*) and a trace of benzoyl peroxide was added to the solution in the presence of atmospheric oxygen. After an hour the solution began to deposit the hydroperoxide, 110 mg, as white crystals, mp 112.5—113.0 °C (decomp.).

Found: C, 69.09; H, 6.79; N, 7.24 %. Calcd for $C_{11}H_{13}O_2N$: C, 69.05; H, 6.85; N, 7.33 %.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 218(4.31, sh.), 223(4.37), 230(4.26, sh.), 274(3.43). IR: ν^{KBr} cm^{-1} 3410, 3050, 2920, 2770, 878, 820.

Preparation of 2-Acetamidoacetophenone Derivatives (VI). Corresponding substituted indoles were dissolved in acetic acid and treated with ozonized oxygen at room temperature until the indole spot had disappeared on thin-layer chromatography. The products were isolated by neutralization followed by extraction with ether.

2,4-Diacetamidoacetophenone (VIg). Colorless leaflets from ethanol-water, mp 217—218 °C.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 254(4.42), 296(4.27). IR: ν^{KBr} cm^{-1} 3260, 3180, 1692, 1665, 1640, 1545, 883, 825.

2-Acetamido-4-methylacetophenone (VIf).[10] Colorless crystals, mp 75—76 °C.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 235(4.43), 239(4.44), 266 (4.04), 274(4.02), 325(3.58). IR: ν^{KBr} cm^{-1} 3200, 1680, 1640, 1525, 880, 810.

2-Acetamido-4-chloroacetophenone (VIh).[9] White plates from methanol, mp 146.5—148.0 °C.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 236(4.53, sh.), 240(4.57), 266(4.15), 274(4.11), 323(3.67). IR: ν^{KBr} cm^{-1} 3160, 1680, 1640, 875, 810, 750.

2,5-Diacetamidoacetophenone (VIc).[11] White needles from ethanol, mp 190—191 °C.

UV: $\lambda^{\mathrm{EtOH}}_{\mathrm{max}}$ mμ (log ε), 243(4.43), 276(4.18), 351 (3.40). IR: ν^{KBr} cm^{-1} 3190, 1680, 1650, 882, 820.

Chemiluminescence. In the case of the chemiluminescence of I, 1 m*l* of potassium *t*-butoxide DMSO solution (10^{-2} mol/*l*) was at once added to 1 m*l* of the sample DMSO solution (10^{-3} mol/*l*), continuous tiny bubbles of oxygen being passed through the solution. The change in the intensity of light with time was recorded and total light emission

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[8] E. Shaw and D.W. Woolley, *J. Am. Chem. Soc.*, **75**, 1877 (1958).

[9] D.W. Ockenden and K. Schofield, *J. Chem. Soc.*, **1957**, 3175.

[10] D. W. Ockenden and K. Schofield, *ibid.*, **1953**, 612.

[11] N.J. Leonard and S.N. Boyd, Jr., *J. Org. Chem.*, **11**, 405 (1946).

(A) was determined by the area of emission curve. Then relative total light emission (A/A_0) was calculated. A_0 is the area of Ia which was taken as the reference substance. In the case of V, continuous bubbles of argon was passed through the DMSO solution and the area of emission curve of Va was taken as the reference area. (Table 3).

Chemiluminescence Spectra and Fluorescence Spectra. Chemiluminescence spectra of I and V were measured by the same method as described in the preceeding paper.[5] Fluorescence spectra of substituted 2-acetamidoacetophenone (VI) were measured under the same condition as chemiluminescent reaction of I. Chemiluminescence and fluorescence maxima are shown in Table 1 and Table 2.