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9-Adamantylidene-10-alkyl-9,10-dihydroacridine Oxide as a Novel and Potential Chemiluminescent Precursor: Proximity Effect of the Nitrogen Atom

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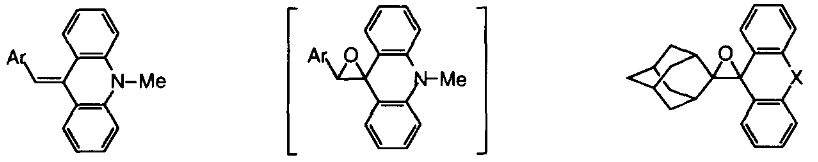
Abstract: An oxirane derivative having acridane and adamantane moieties was prepared and proved to show potential chemiluminescent property on treatment with alkaline hydroperoxide and subsequently with hydrochloric acid, in which the electron-donating property of the nitrogen was experimentally shown to play an important role for the chemiluminescence. © 1997 Elsevier Science Ltd.

An analytic method using chemiluminescent compounds could be one of the most promising tools for detection of a small quantity of biomacromolecules.[1] For such purposes, intensive studies on various chemiluminescent peroxy derivatives such as 1,2-dioxetanes have been reported.[2] Although some 1,2-dioxetane derivatives are known to exhibit high light-emission ability, the level of their physical stability does not permit easy handling. Recently, Sakanishi and his co-workers reported a suggestive work that light emission was observed during the oxidation of 9-arylmethylene-10-methylacridane **1** with an excess of *m*-chloroperbenzoic acid (MCPBA) or dimethyldioxirane (DMD).[3] In these studies, they proposed that β-hydroxyalkyl peroxyesters[3a] or 1,2,4-trioxanes[3b] generated *in situ via* unstable oxiranes **2** are involved as key intermediates and would be decomposed *via* a chemically initiated electron exchange luminescence (CIEEL) mechanism. It occurred to us that an oxirane ring system could be stabilized by introducing a bulky substituent, such as an adamantane moiety,[4] thereby rendering it a more potent precursor for chemiluminescence. As one of our synthetic studies on novel and useful chemiluminescent compounds,[5] we studied the preparation and chemiluminescent property of some oxiranes **3a-e** and experimentally clarified the significant role of the neighboring nitrogen for the chemiluminescence.



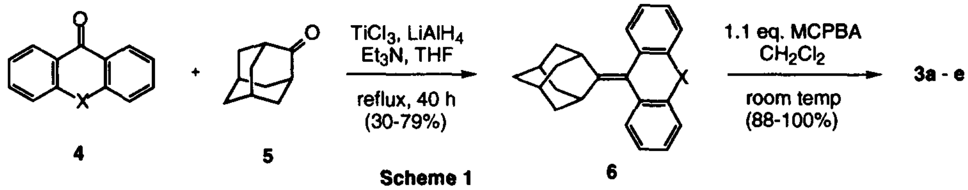
1

2

3a : X = N-Bn, **b** : X = N-Ph,
c : X = N-CH_2CO_2Et,
d : X = CH_2, **e** : X = bond

Fig. 1

Olefins **6** were obtained by the McMurry condensation between aromatic ketones **4** and adamantanone (**5**). On treatment of **6** with a slight excess of MCPBA in dichloromethane at room temperature, oxiranes **3** were isolated in good yields.[6] Although isolation of the oxiranes **2** was reported to be impossible, the oxiranes **3a**-**e** are quite stable to be handled as expected.



Scheme 1

At first, the luminescent property of **3a** was examined and the results are outlined in the Table.[7] According to Sakanishi's report,[3a] oxirane **3a** was further oxidized with MCPBA in various solvent systems. However, remarkable light emission was not detectable under these conditions (Table, entry 1). On treatment of **3a** with an alkaline hydrogen peroxide solution, rapid decomposition was observed on the TLC, but there was no intense chemiluminescence in this case as well (entry 2). On the other hand, when hydrochloric acid was added after 25 sec delay from the alkaline hydrogen peroxide treatment, quick and strong light emission was detectable as shown in Fig. 2 (entry 3) accompanying the formation of ketones **4** (X = N-Bn) and **5**.[8]

Table. Total relative light units for **3** during 120 sec

Entry	Oxirane 3	Additive (at 0 sec)	Amounts of HCl (at 25 sec)	RLU (x 10^4)
1	**3a**	MCPBA in CH_2Cl_2	none	< 10
2	**3a**	alkaline H_2O_2	none	< 10
3	**3a**	alkaline H_2O_2	0.10 M, 0.1 ml	3065
4	**3b**	alkaline H_2O_2	0.10 M, 0.1 ml	320
5	**3c**	alkaline H_2O_2	0.10 M, 0.1 ml	57
6	**3d**	alkaline H_2O_2	0.10 M, 0.1 ml	< 10
7	**3e**	alkaline H_2O_2	0.10 M, 0.1 ml	26

A 1.2 M H_2O_2 solution in a 0.1 M NaOH aqueous solution (0.1 ml) was used.

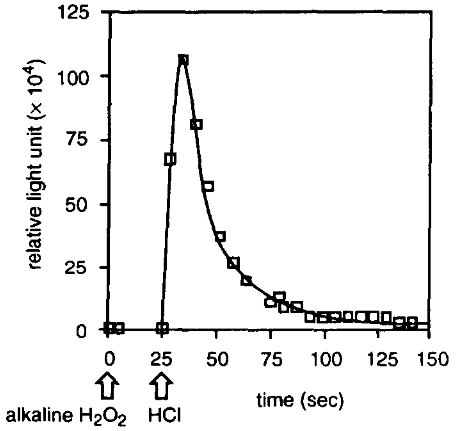


Fig. 2 Light-emission profiles of **3a** by treatment with alkaline H_2O_2 and subsequent with HCl

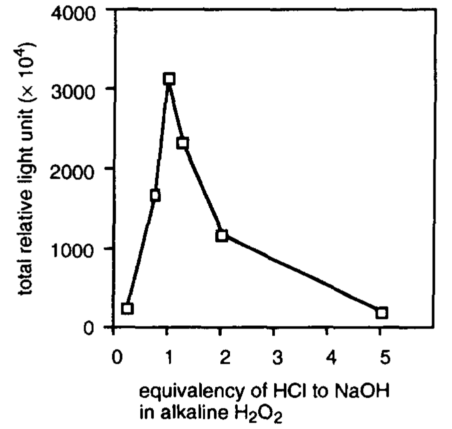
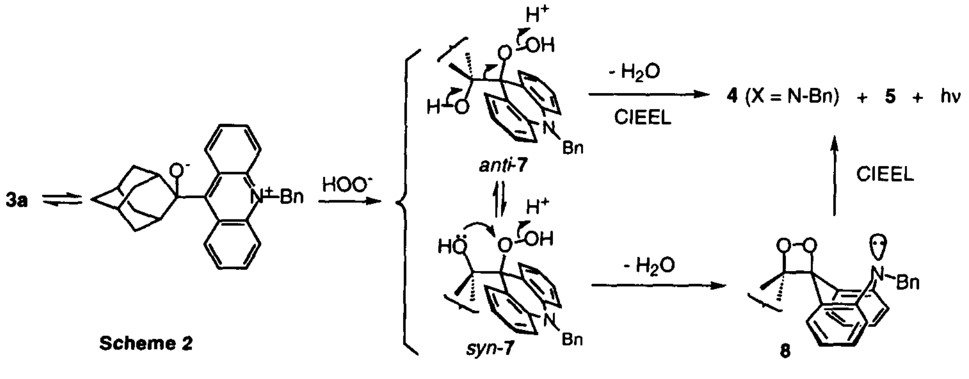


Fig. 3 Relationship between the chemiluminescence for **3a** and the concentration of HCl

In order to investigate the effect of the nitrogen at X, the other oxiranes **3b-e** were also examined under the same conditions (entries 4-7). Although the electron-donating property of the nitrogen at X was expected to facilitate the cleavage of the oxirane ring, **3b-e** were also decomposed rapidly by treatment with alkaline H_2O_2. The introduction of an electron-withdrawing group on the nitrogen (**3b** and **c**) decreased the light emission (entries 4 and 5). The compounds **3d** and **e**, neither of which has a nitrogen, were almost inert (entries 6 and 7). These findings indicate the significant role of the electron-donating property of the nitrogen for the chemiluminescence.

The effect of the amounts of HCl on the intensity of the light emission was studied by using **3a**. When 1 equivalent of acid to the base was added, the strongest light emission was obtained as shown in Fig. 3. The chemiluminescent quantum yield (Φ_{CL}) was estimated to be 0.0018, based on that of luminol ($\Phi_{CL} = 0.011$) and is ca. 4000 times stronger than that of the olefin **1** (Ar = Ph) reported by Sakanishi.[3a] The use of excess HCl dramatically decreased the light emission.

Although the exact mechanism is not clear, we propose the possible pathways for the chemiluminescent decomposition of oxirane **3a** in Scheme 2. At first, the hydroperoxy anion is most likely to attack the epoxide at the benzyl position to form the β-hydroperoxyalcohol **7**, without light emission. Since a *tert*-alkyl perester was reported to be inactive in light emission,[9a] it is suggested the hydroxy group at the β-position plays a significant role in this reaction. The addition of HCl, which specifically induces light emission, appears to facilitate the release of H_2O by protonation of the hydroperoxy group. Taking these into account, the following two pathways from **7** could be proposed: i) decomposition from the *anti*-conformation *anti*-**7** could give ketones with light emission; ii) formation of the dioxetane **8** from the *syn*-conformation *syn*-**7** by participation of the neighboring hydroxy group[10] and subsequent decomposition of **8** could occur similarly.[11] From the fact that the epoxide-cleavage for the other compounds **3b-e** was also rapid enough and the results summarized in the Table, it is apparent that the chemiluminescent step depends on the electron-donating property of the nitrogen at X. This suggests that the decomposition with light emission would be facilitated by the intramolecular electron transfer from the nitrogen, i.e., *via* a CIEEL mechanism.[9] Additionally, this is supported by the characteristic dependency of the luminescence of **3a** on the acid concentration (Fig. 3). The excess acid would protonate the nitrogen of **3a** and, consequently, could inhibit the decomposition *via* a CIEEL mechanism.



Scheme 2

In conclusion, the present work experimentally revealed the significant role of the neighboring nitrogen and also showed that the oxirane having an acridane structure could serve as a stable and potential precursor for intensive light emission by a chemical procedure.

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6. Satisfactory spectral data for all new compounds were obtained. Spectral data for **3a** are as follows. Colorless crystals, mp. 227-229 °C (AcOEt). IR ν_{max}(KBr): 2913, 2849, 1596, 1496, 1464, 1372, 1267 cm^{-1}. UV λ_{max}(MeCN) nm (ϵ): 280 (18000). ^1H NMR (200 MHz, $CDCl_3$) δ: 1.00-1.20 (2H, br d, J = 9 Hz), 1.35-1.50 (2H, br d, J = 9 Hz), 1.50-1.85 (7H, m), 1.90-2.00 (1H, br s), 2.03-2.17 (2H, br d, J = 8 Hz), 5.27 (2H, s), 6.84 (2H, d, J = 8 Hz), 6.97 (2H, t, J = 7 Hz), 7.12 (2H, dd, J = 8, 2 Hz), 7.15-7.32 (5H, m), 7.36 (2H, dd, J = 7, 2 Hz). ^{13}C-NMR (68 MHz, $CDCl_3$) δ_C: 26.6, 27.0, 30.0, 34.9, 36.0, 50.3, 66.1, 96.1, 112.7, 119.9, 122.0, 125.3, 126.6, 127.0, 127.4, 128.6, 136.7, 142.9. *Anal.* Calcd for $C_{30}H_{29}NO$: C, 85.88; H, 6.97; N, 3.34. Found: C, 85.85; H, 6.98; N, 3.30.
7. Some epoxy compounds are known to undergo thermal decomposition with only a weak chemiluminescence: Stauff, J.; Simo, I.; Tsai, W. L. *Naturforsch.* **1978**, *33c*, 769-770.
8. Representative procedure for chemiluminescent decomposition of **3a** is as follows. Alkaline hydrogen peroxide (0.1 M H_2O_2 in 0.1 M NaOH aqueous solution, 0.10 ml) was added to a DMSO solution of oxirane (1.0×10^{-7} M, 0.10 ml), and HCl (0.025-0.2 M, 0.10 ml) was added to the reaction mixture after 25 sec. Light emission was monitored for 120 sec on a photon counter (Berthold Lumat LB 9501).
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10. In contrast to our result, the addition of the base (Et_3N) reportedly increased the intensity of light emission in the reaction with MCPBA.[3a] Although the authors proposed that the addition of Et_3N makes the decomposition by a CIEEL mechanism the main pathway, additionally, it might activate the hydroxy group of the β-hydroxyalkyl perester to form the dioxetane.
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