A RELATIONSHIP BETWEEN CHEMILUMINESCENCE AND REACTIVITY OF WITTIG TYPE REACTIONS OF PHOSPHONATE CARBANIONS

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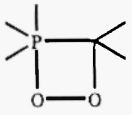
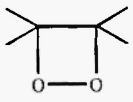
Abstract: The chemiluminescence (CL) quantum yields (Φ_{CL}) of oxygenation of 10-methyl-9,10-dihydroacridine-9-phosphonate carbanions depended on the phosphorus substituents. The acridinephosphonate with electron negative phosphorus substituents such as bis(2,2,2-trifluoroethyl)phosphono group showed higher Φ_{CL}, which was considered comparing the reactivity of the phosphonoacetates in the Horner-Wadsworth-Emmons (HWE) reactions involving the corresponding phosphorus substituents.

Phospha-1,2-dioxetane has been suggested as the most likely common intermediate in autooxidation of phosphonium ylide or phosphonate carbanion (1), albeit it has never been detected so far. This oxidation should proceed through a similar manner to the Wittig reaction, which gives a carbonyl compound by fragmentation (2). Phospha-1,2-dioxetane is a structurally four-membered cyclic peroxide; namely, a phospha-analogue of well-known chemiluminescent 1,2-dioxetanes (3).



phospha-1,2-dioxetane



1,2-dioxetane

Although a few reports (4,5) documented that the postulated phospha-1,2-dioxetanes produced excited carbonyl compounds and showed chemiluminescence (CL) in the suitable systems, such CL has not been well investigated. In this paper we report CL quantum yields (Φ_{CL}) of autooxidation of 10-methyl-9,10-dihydroacridine-9-phosphonate carbanions, comparing the reactivity of the related olefination reaction, the Horner-Wadsworth-Emmons (HWE) reaction (6), with the phosphonoacetates involving the corresponding phosphorus substituents. The outline of the present work is illustrated in Scheme 1.

When 10-methyl-9,10-dihydroacridine-9-phosphonates **1a-d** prepared from the Arbuzov reaction of *N*-methylacridinium iodide and the corresponding phosphites (7), were treated with excess potassium *tert*-butoxide (^{t}BuOK) in aerated dimethylformamide (DMF) or dimethyl sulfoxide (DMSO), weak and pale-blue emission was observed in a dark. The isolation or detection by UV-spectrum of the reaction mixture showed the formation of *N*-methylacridone (NMA) as the chief product. As described previously (5), NMA was isolated in a 69 % yield in the case of **1a** after thorough oxygenation.

Scheme 1

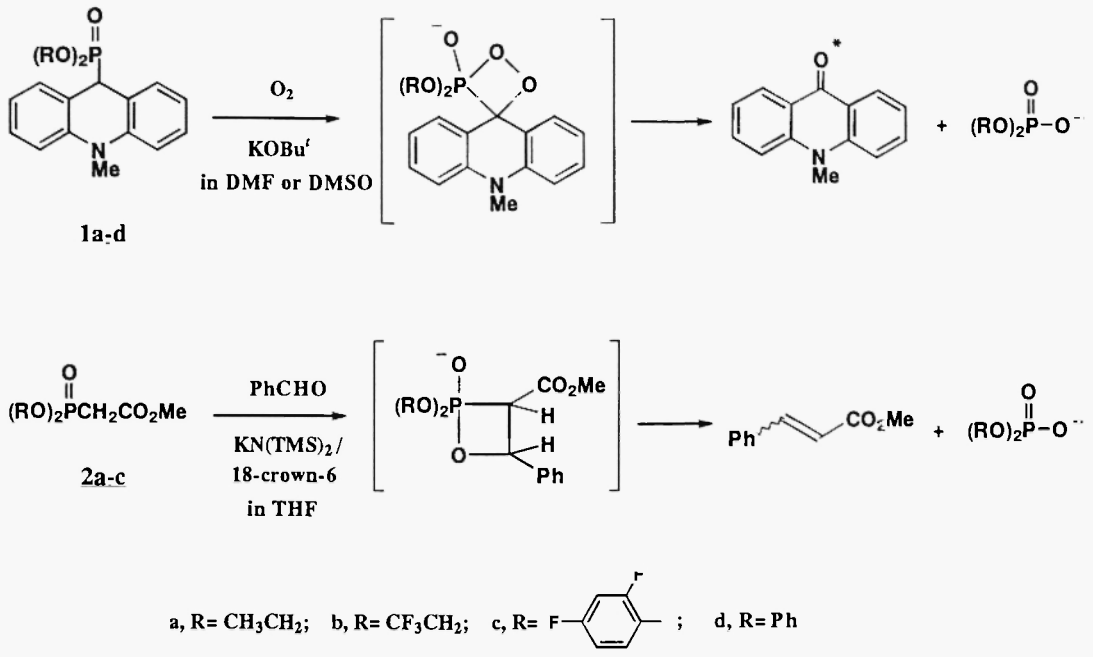


Table 1. CL quantum yield (Φ_{CL}) of 9-phosphoryl-10-methyl-9,10-dihydro-acridines (1a-d)

acridine	Yield of NMA (%) [a]	Φ_{CL} x 10^7 (E mol^{-1}) [b]
1a	68.8	1.62
1b	71.4	26.1
1c	69.8	5.87
1d	69.3	11.0

[a] Determined by UV-spectrum.
[b] Measured by a photocounting method (see Experimental).

The CL quantum yields (Φ_{CL}) for **1a-d** were estimated by a photocounting method in dry DMSO. The results are listed in Table 1. Despite very low Φ_{CL}'s, the difference depending on the phosphorus substituents was observed. While the yields of NMA were almost equal, Φ_{CL} of **1b** with 2,2,2-trifluoroethyl groups was about 16 times efficient compared to **1a**. The aromatic substituents of **1c** and **1d** also increased Φ_{CL}'s. The enhanced Φ_{CL}'s due to the electron negativity of the phosphorus substituents should be induced from these results.

In the HWE reaction with benzaldehyde, the phosphonoacetates **2b** and **2c** bearing fluorine containing phosphorus substituents are known to give more than 98 % *cis*-selectivity under the kinetic reaction condition [$KN(SiMe_3)_2$, 18-crown-6, THF, -78 °C] (7,8). On the other hand, methyl diethylphosphonoacetate **2a** is a typical HWE reagent (9) whose reaction with benzaldehyde gives only methyl *trans*-cinnamate in the same reaction condition. Accordingly, the relative reactivities of **2a** *versus* **2b** or **2c** could be approximately estimated as the ratios of *cis*- and *trans*-isomers under the competition reaction condition. Whereas the competition of the carbanions of **2a** and **2b** with 0.2 equiv. benzaldehyde gave only *cis*-cinnamates under the stated reaction condition, that of **2a** and **2c** gave a mixture of *cis*- and *trans*-cinnamates in the ratio of 33/67. Thus, the order of the reactivity was estimated as **2b>2a>2c**. This order disagrees with that of CL efficiencies described above but the predominance of 2,2,2-trifluoroethyl group in both reactions was established.

Considering these two Wittig type reactions, the common effect on increase of Φ_{CL} and the reactivity in the HWE reaction would be essentially due to the strong electron negativity of 2,2,2-trifluoroethyl group. According to the previously suggested explanation (6) for the *cis*-selectivity of **2b** in the HWE reaction, the strongly electron negative group accelerates the formation of the transient oxaphosphetane and irreversible elimination of the phosphate ion from an equilibrium state of the *threo*- and *erythro*-adducts. Therefore, it is reasonable to consider that such the electron negative phosphorus substituent also promotes the formation of the presumed phospha-1,2-dioxetane to lead to increment of Φ_{CL} in the present oxygenation. The disagreement between the orders of the CL efficiency and the reactivity in the olefination is interesting because a little larger electron negativity of aryloxy groups than ethoxy group (10) was reflected in the CL, while the other fact such as steric effect contributes to the selectivity in the olefination. If the intramolecular CIEEL (chemically initiated electron exchange luminescence) is applicable to the present CL as observed in 10-methylacridan dioxetanes (11), the effect of the electron negative substituents may give another explanation that it might promote the single electron transfer from the nitrogen atom to the LUMO of the O-O bond in the presumed phospha-1,2-dioxetane. This assumption awaits a verification and further investigation is undertaken in our laboratory.

Experimental

Melting points were taken on Mitamura Riken micro melting apparatus and are uncorrected. ^{1}H NMR, HRMS, and UV spectra were recorded on a JOEL PMX-FX 60 (60 MHz), HITACHI M-80B mass spectrometer, and HITACHI U-3210 spectrophotometer, respectively.

Diethyl 10-methyl-9,10-dihydroacridine-9-phosphonate 1a:

Although **1a** has been prepared from the reaction of and 10-methylacridinium methosulfate and diethyl sodiophosphonate (12), the Arbuzov reaction of triethyl phosphite and 10-methylacridinium iodide was also applicable. Thus, a mixture of triethyl phosphite (2.70 g, 16 mmol) and *N*-methylacridinium iodide (5.00 g, 15.6 mmol) in benzene (17 ml) and DMF (33 ml) was heated for 1 hr under reflux. After removal of the solvents by vacuum distillation, water and chloroform were added to the residue and the organic layer was dried on Na_2SO_4. Removal of the solvent gave **1a** (3.83 g, 78 %), mp 88-89 °C (lit. 89-91 °C) (12). The ^{1}H NMR spectrum agreed with that reported.

Bis(2,2,2-trifluoroethyl) 10-methyl-9,10-dihydroacridine-9-phosphonate 1b:
A mixture of 10-methylacridinium iodide (2.27 g, 7.0 mmol) and bis(2,2,2-trifluoroethyl) methyl phosphite (1.84 g, 7.0 mmol) was warmed by heating gun. After red color of acridinium salt disappeared, the residue was treated with petroleum ether to give the white powder. Recrystallization from ether gave **1b** (0.8 g, 26 %), mp 125-126 °C ; δH (60 MHz; $CDCl_3$) 3.29(3H, s, NMe), 3.69-4.27(4H, m, CH_2CF_3), 4.61(1H, d, 9-H, J_{PH}=24.6 Hz), 6.59-7.36(8H, m, ArH); m/z (EI) 439 (M^+) (Found: 439.0748; $C_{18}H_{16}NO_3F_6P$ requires 439.0770).

Bis(2,4-difluorophenyl) 10-methyl-9,10-dihydroacridine-9-phosphonate 1c:
The same procedure described above and purification by column chromatography on silica gel (chloroform as an eluant) afforded **1c** in 18% yield, mp 131-132 °C ; δH (60 MHz; $CDCl_3$) 3.38 (3H, s, NMe), 5.16 (1H, d, 9-H, J_{PH}=25.2 Hz), 6.64-7.72 (14H, m, ArH); m/z (EI) 499 (M^+) (Found: 499.0952; $C_{26}H_{18}NO_3F_4P$ requires 499.0958).

Diphenyl 10-methyl-9,10-dihydroacridine-9-phosphonate 1d:
To a suspension of sodium hydride (50 % in oil, 1.76 g, 44 mmol) in dry THF (60 ml) was added diphenyl phosphite (20.0 ml, 44 mmol) under a nitrogen atmosphere. After hydrogen evolution ceased, this solution of diphenyl sodiophosphonate was added dropwise to a suspension of 10-methylacridinium iodide (14.0 g, 44 mmol) in THF (100 ml) for 45 min. at room temperature. After removal of the solvent and addition of water and chloroform, the organic layer was dried on Na_2SO_4. Removal of the solvent and recrystallization from ether gave **1d** (4.33 g, 24 %), mp 125-128 °C ; δH (60 MHz; $CDCl_3$) 2.71 (3H, s, NMe), 4.93 (1H, d, ring-CHP, J_{PH}=19 Hz), 6.56-7.63 (18H, m, ArH); m/z (EI and FAB) 427 (M^+) (Found: 427.1331; $C_{26}H_{22}O_3NP$ requires 427.1337).

Measurement of Φ_{CL} : The CL quantum yields (Φ_{CL}) of four acridinephosphonates were determined by a photocounting method using a photomultiplier (R464 Hamamatsu Photonics K.K.) connected with photocounting unit (C3866), photocounting board (M3949), and handling software (U3997). The calibration was made by a standard method (13) with luminol chemiluminescence in the presence of ^{t}BuOK in dry DMSO. The quantum efficiency of the photomultiplier (R464) in the range of 450 nm to 500 nm was almost equal within 4 %. The emission λ_{max}'s of luminol (485 nm) and NMA (455 nm) were in this region. All measurements described bellow were done in the same geometry.

A solution (1 mL) of ^{t}BuOK (2.00 x 10^{-2} mol/l in DMSO) was added to each solution (2 mL) of acridinephosphonates **2a-d** (1.00 x 10^{-3} mol/l in DMSO) and photons produced during six minutes were counted, which led to estimation of the corrected photons by comparison with the above described luminol chemiluminescence. The resulting solution was diluted at once with a mixed solution of DMSO (18 mL) and ^{t}BuOH (9 mL) for the UV measurement. The yields of NMA were calculated by comparison of the absorption at 401 nm with the standard solution of NMA (1x10^{-4} mol/l) in the same solvent. The Φ_{CL} was calculated as a quotient of photons per produced NMA.

The competitive HWE reaction of phosphonoacetates: A toluene solution of $KN(SiMe_3)_2$ (0.5 mol/l toluene solution, 2.0 mL, 1.00 mmol) was added dropwise to a solution of **2a** (0.21g, 1.00 mmol),

2b (0.38g, 1.00 mmol), and 18-crown-6 (1.32g 5.00 mmol) in THF (40 mL) at -78°C and the mixture was stirred at this temperature for 1h under N_2. After addition of benzaldehyde (0.02g, 0.20 mmol) in THF (2 mL) and stirring for 1 min., the reaction was quenched with saturated NH_4Cl. The THF layer was separated and the organic materials were further extracted with Et_2O (2 x 20 mL) from the aqueous layer. The combined extracts were washed with brine and dried on Na_2SO_4. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel using benzene as an eluant to give an isomeric mixture of methyl *cis*- and *trans*-cinnamates. Their ratio was determined by ^1H NMR spectrum. The competition of **2a** and **2c** was performed by the exactly same procedure.

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