Development of Novel Color Former Containing Phenoxazine Moiety

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A novel phenoxazine color former, 3,7-bis(*N,N*-diethylamino)-10-(2,2,2-trichloroethoxycarbonyl)phenoxazine (**1**), was synthesized. Acetonitrile solution of colorless **1** was observed to give blue cation **2a** by γ irradiation of 10 Gy. Little absorbance changes were observed when the blue shade solution was kept for 6 d after γ irradiation. Compound **1** showed excellent sensitivity to γ rays and the resulting cation **2a** was stable enough to provide a candidate for a novel dosimetry system.

Keywords: functional dye, phenoxazine, radiation dosimeter, γ rays

1. Introduction

Phenoxazines have been well investigated and used for many purposes[1,2]. But there is no report about radioactive sensing system using these chromophores. Similar system using phenothiazine moiety has already been reported to give little sensitivity to γ rays[3]. In this study, a novel color former 3,7-bis(*N,N*-diethylamino)-10-(2,2,2-trichloroethoxycarbonyl) phenoxazine (**1**) was synthesized. Compound **1** consists of a precursor of phenoxazine coloring moiety **2a** and 2,2,2-trichloroethoxycarbonyl moiety as a blocking group[4]. Color forming scheme of the target molecule **1** is given below.

Scheme 1

2. Experimental

2.1 Materials

Basic Blue 3 (**2a** · Cl⁻) was purchased from Aldrich Co. Ltd. 2,2,2-Trichloroethyl chloroformate was purchased from Tokyo Kasei Kogyo Co. Ltd. Sodium hydroxide, sodium

dithionite and sodium hydrogen carbonate were purchased from Wako Pure Chemical Industries, Ltd. All materials were used without further purification. 3,7-bis(*N,N*-diethylamino)-10-(2,2,2-trichloroethoxycarbonyl)phenoxazine (**1**) was prepared by the similar method for introducing blocking groups to amino groups on amino acids[4,5].

Synthesis of 3,7-bis(*N,N*-diethylamino)-10-(2,2,2-trichloroethoxycarbonyl)phenoxazine (**1**)

Basic blue 3 (**2a** · Cl⁻) (742 mg, 2.06 mmol) was dissolved in water (50 ml). Sodium hydroxide (NaOH, 335 mg, 8.38 mmol), sodium dithionite (Na₂S₂O₄, 1.09 g, 6.27 mmol), and sodium hydrogen carbonate (NaHCO₃, 874 mg, 10.4 mmol) were dissolved in water (30 ml) and reductive solution was prepared. Toluene (50 ml) was added, and then the latter solution was added at once to the Basic Blue 3 mixture and stirred at 0 °C until the blue solution became orange, indicating the reduction of cationic dye **2a** · Cl⁻ to give product **3a** was complete. Toluene (10 ml) solution of 2,2,2-trichloroethyl chloroformate (ClCOOCH₂CCl₃, 1.50 g, 7.09 mmol) was added over a period of 1 h at 0 °C. The mixture was stirred for another 9 h. The toluene layer was separated from water layer and washed with water, then dried over anhydrous sodium sulfate. The sodium sulfate was removed by filtration and the

Scheme 2

solvent was evaporated under reduced pressure. The crude product was recrystallized twice from acetone. The crystal was collected by suction filtration and washed with acetone to give **1**: yield 426 mg (41 %), colorless crystal: ^1H NMR (400 MHz, CDCl_3) δ (ppm) 7.43 (2H, dd, H_a , $J_{ac} = 9.3$ Hz, $J_{ab} \sim 0$ Hz), 6.39 (2H, dd, H_b , $J_{bc} = 3.7$ Hz, $J_{ab} \sim 0$ Hz), 6.36 (2H, dd, H_c , $J_{ac} = 9.3$ Hz, $J_{bc} = 3.7$ Hz), 4.89 (2H, s, H_d), 3.33 (8H, q, H_e , $J_{ef} = 7.0$ Hz), 1.15 (12H, t, H_f , $J_{ef} = 7.0$ Hz); MS (EI, m/z) 499 (M^+), 501 ($\text{M}+2$).

2.2 Method

Electronic absorption spectra were measured with Shimadzu UV-2500 spectrophotometer. NMR spectra were taken by Varian Gemini 2000 Spectrometer and Bruker ARX-400 Spectrometer. MS spectra were measured with Nippondensi JMS-DX303HF. Acetonitrile solutions of **1** were irradiated with ^{60}Co γ rays at room temperature. Irradiation was performed at the absorbed dose rate of 600 Gy/h.

3. Results and Discussion

3.1 Ionization potential of phenoxazine derivatives calculated by PPP (Pariser-Parr-Pople) molecular orbital method.

Intermediate **3a** is oxidized immediately to give colored form **2a** (Scheme 3). The velocity of oxidation depends on the structure of derivatives

Scheme 3

3a-3g. In this case, it can be described as ionization potential (IP)[6]. IP can be evaluated from equation (1) from Koopman's theorem[6].

$$IP = -E_{\text{HOMO}} \quad (1)$$

IP s of phenoxazine derivatives **3a-3g** were obtained by calculating HOMOs using PPP (Pariser-Parr-Pople) molecular orbital software [7-9]. Results are shown in Table 1. The value of IP decreases with the increment of electron-donating property of the substituent R, i.e. the decrease of the substituent constant σ of Hammett's rule. Thus, the derivative **3a** containing diethylamino groups is expected to give most easily the corresponding colored form **2a** due to strong electron-donating group. Because the cation **2a** generated from the oxidation of **3a** is stabilized by electron donation from strong electron-donating groups at both ends on the phenoxazine ring.

Table 1 The *IPs* of phenoxazine derivatives

No.	-R	<i>IP</i> [eV]	substituent constant σ
3a	-NEt ₂	10.45	-0.83
3b	-OH	11.21	-0.37
3c	-OCH ₃	11.36	-0.27
3d	-SH	11.27	0.15
3e	-Cl	11.60	0.23
3f	-CN	11.84	0.66
3g	-NO ₂	12.54	0.78

3.2 Irradiation of γ rays

The electronic absorption spectra of acetonitrile solution of **1** and **2a** · Cl⁻ are shown in Figure 1 ([**1**]₀ = 0.25 mM, [**2a** · Cl⁻]₀ = 0.020 mM). Color former **1** has no absorption between 350 and 750 nm, colored form **2a** · Cl⁻ has absorption maximum at 644 nm ($\epsilon = 1.0 \times 10^5$). When acetonitrile solutions of **1** ([**1**]₀ = 0.25 mM) were

Figure 1 Spectra of **1** and **2a** · Cl⁻ in dry acetonitrile ([**1**]₀ = 0.25 mM, [**2a** · Cl⁻]₀ = 0.020 mM).

irradiated with ⁶⁰Co γ rays at room temperature, absorbance at 644 nm was increased. The obtained spectra change is shown in Figure 2, indicating the cleavage of **1** by γ irradiation to give colored form **2a** ($\lambda_{\max} = 644$ nm). It must be noted that the coloration of **1** in acetonitrile was observed in the absence of acid generators such as *N*-sulfonyloxy phthalimide or diphenyliodonium chloride[10]. In the case of formerly reported color formers such as BDX[11] or leuco crystal violet[12], acid generators were required of their color change by γ rays. Energy transfer[13] from the excited state of solvent acetonitrile to the ground state of **1** may cause the cleavage of **1** to give colored form **2a**.

Figure 2 Spectral changes of **1** to give colored form **2a** ([**1**]₀ = 0.25 mM) in dry acetonitrile by γ irradiation.

Figure 3 Absorbance changes at 644 nm of colored form **2a** ([**1**]₀ = 0.25 mM) vs. absorbed dose in dry acetonitrile by γ irradiation.

Figure 4 Absorbance changes at 644 nm of colored form **2a** vs. initial concentration of **1** ([**1**]₀ = 0.25, 0.50 and 1.0 mM) in dry acetonitrile by γ irradiation.

The absorbance changes at 644 nm for acetonitrile solution of **1** are shown in Figure 3. The coloration to blue could be recognized by the naked eye at an absorbed dose of 10 Gy. In order to investigate the effect with initial concentration of **1**, several acetonitrile solutions ($[1]_0 = 0.25, 0.50$ and 1.0 mM) were prepared and irradiated with γ rays (Figure 4). In every dose, the absorbance increased proportional to the concentration and correlation coefficient R^2 of each plot was quite near to 1.0000. Formerly reported color formers, for example, BDX[11] or diarylethene[14] required hundreds Gy of γ irradiation to cause color changes recognized by the naked eye. On the other hand, only 10 Gy of γ irradiation was enough to coloration of the solution of **1**.

In order to investigate the stability of the color former **1**, absorbance of the γ irradiated sample was measured at 644 nm after 8 h, 1, 2, and 6 d (Figure 5). Little absorbance changes were observed even after 6 d from γ irradiation. The colored form **2a** was more stable in solution than the other color former such as BDX[11]. When colorless form of BDX in chloroform was irradiated with γ rays, red solution of BDX was obtained. After the irradiation was completed, the absorbance of the red solution gradually increased with the passage of time. After 80 h the absorbance reached to 0.4 from 0.1[11].

Figure 5 Absorbance changes at 644 nm of colored form **2a** ($[1]_0 = 0.25$ mM) vs. the passage of time (after 8 h, 1, 2, and 6 d) in dry acetonitrile by γ irradiation.

4. Summary

A novel phenoxazine color former **1** was synthesized. PPP calculation indicated colorless

form **3a** would be immediately oxidized to give colored form **2a**. The results of γ irradiation of color former **1** coincided with this expectation. Acetonitrile solution of **1** changed blue to give colored form **2a** without acid generator at γ irradiation of 10 Gy. Resulting **2a** was stable in acetonitrile. Compared with the former reported color formers such as BDX[11], leuco crystal violet[12] or diarylethene[14], novel color former **1** showed high sensitivity to γ rays.

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