

Synthesis and $^1\text{H-NMR}$ Spectra of Halogenated Spiro[isobenzofuran-1(3*H*),9'(9*H*)-6'-(methylcyclohexylamino)-3'-methyl-2'-anilinoxanthene]-3-ones

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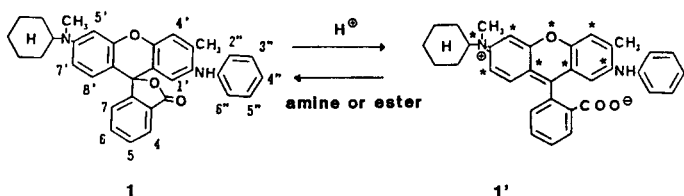
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Reaction of spiro[isobenzofuran-1(3*H*),9'(9*H*)-6'-(methylcyclohexylamino)-3'-methyl-2'-anilinoxanthene]-3-one (**1**), which is typical leuco fluoran dye, with *N*-bromosuccinimide and *N*-chlorosuccinimide leads to halogenated derivatives **2a-2c** and **3**, respectively. Their structures were established by two-dimensional proton-proton (COSY) experiment and their thermal properties examined by means of DSC and compared with commercially available **1**.

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Spiro[isobenzofuran-1(3*H*),9'(9*H*)-6'-(methylcyclohexylamino)-3'-methyl-2'-anilinoxanthene]-3-one (**1**), which is called a leuco fluoran dye, is generally used in thermal recording layers of papers for thermal transfer facsimile [1,2].

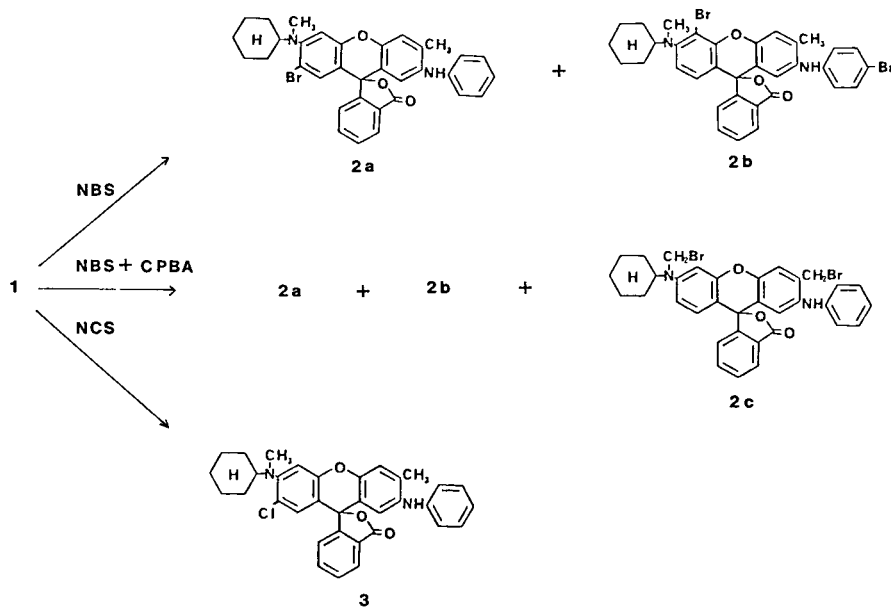
Scheme I



The colorless lactone from **1** readily undergoes ring opening by a developer, such as bisphenol A, under heating to give the black dye **1'**. This dye shows two absorption bands at 594 nm (λ_1) and 452 nm (λ_2) in acetic acid. The λ_1 is complementary to λ_2 , and the color is black. Many substituted leuco fluoran dyes have been prepared to improve the sensitivity of the thermal response and the stability of the developed dye [3,4]. Though leuco fluorans are very important as thermal transfer dyes, little assignment of their aromatic protons in the ^1H nmr spectra is made to determine their chemical structures.

We have attempted to prepare halogenated leuco fluoran dyes to improve their thermal properties. Leuco fluoran dyes are generally prepared by condensation of benzophenone and aniline derivatives [5]. Some halogenated leuco fluorans were similarly prepared [6,7].

Scheme II



We prepared the halogenated leuco fluoran by direct halogenation of **1** with *N*-bromosuccinimide (NBS) and *N*-chlorosuccinimide (NCS). The reaction of **1** with NBS at 50° in benzene gave halogenated products **2a** and **2b** in 15% and 7% yield, each of which could be isolated in a pure form by a column chromatography. The same reaction in the presence of *m*-chloroperbenzoic acid gave **2a** (17%), **2b** (8%) and **2c** (2%). Similar reaction with NCS gave only the mono-chloro product, **3**, in 30% yield. In these reactions, the major product was non-halogenated fluoran dye **1'**, which was formed by opening of the isobenzofuran ring of **1**.

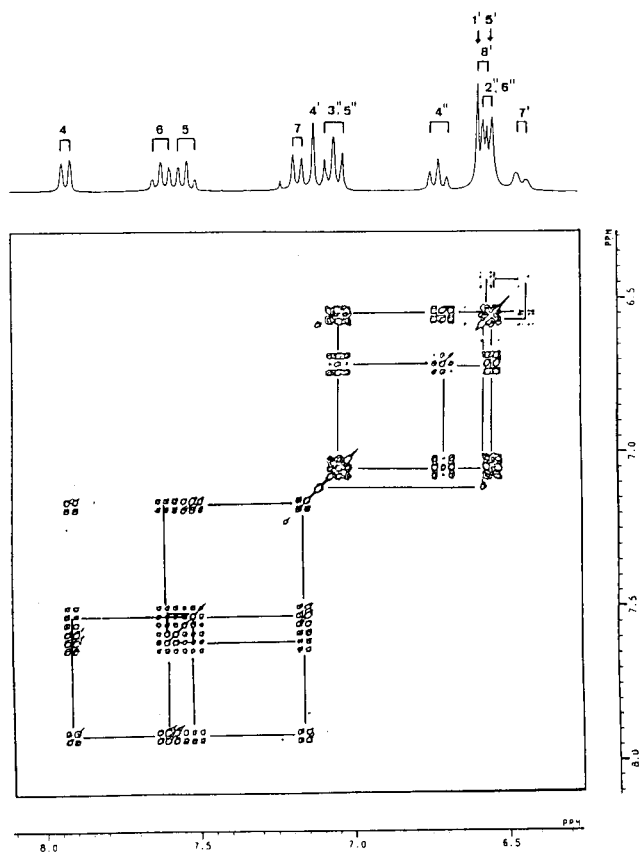


Figure 1. Two-dimensional (270 MHz) homonuclear shift-correlated (COSY) spectrum of **1**. Connectivities of above diagonal data show strong vicinal coupling responses using a Fourier transformation with a 2.5 Hz Gaussian filter. Connectivities of below the diagonal data include long-range coupling responses.

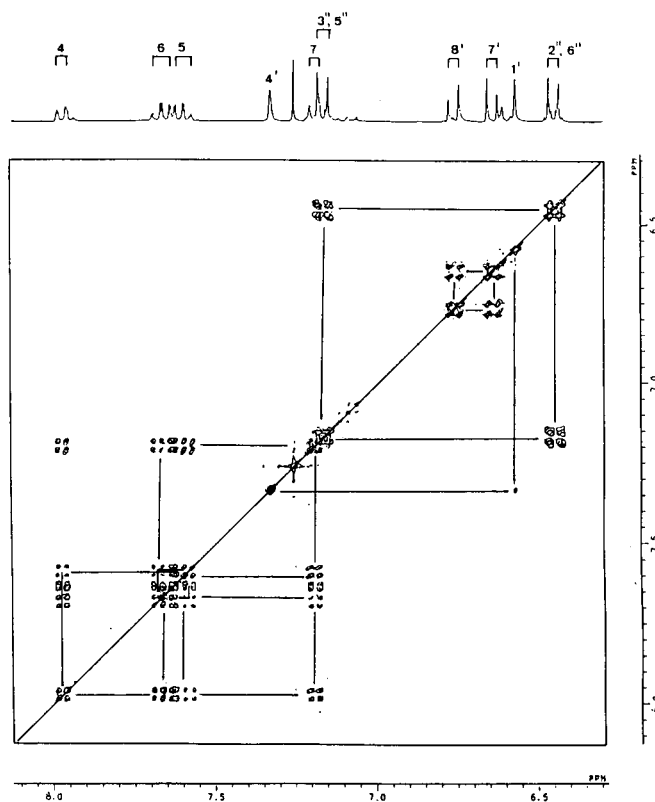


Figure 2. Two-dimensional (270 MHz) homonuclear shift-correlated (COSY) spectrum of **2b**. Connectivities of above diagonal data show strong vicinal coupling responses using a Fourier transformation with a 2.5 Hz Gaussian filter. Connectivities of below the diagonal data include long-range coupling responses.

signed to 7'-halogenated derivatives **2a** and **3**, respectively, as the double-doublet at 6.45 ppm with $J = 8.8$ and $J = 2.8$ Hz of **1**, which was observed in the spectrum in higher concentration and showed typical *o*- and *m*-couplings, assigned to the 7' proton. However, substitution at the 8'-position may be better from comparison of absorption maxima of **1** and **2a** or **3**, as the 8'-position is the unstarred position in fluoran dye **1'** belonging to alternant hydrocarbon system and increasing the electronegativity at unstarred position gives theoretically a bathochromic shift of λ_1 and λ_2 [8,9]. This bathochromic shift may be reflected in steric hindrance between methylcyclohexylamino group at the 6'-position and halogen atom at the 7'-position. The following structure for dibromo derivative was established, on the basis of ^1H nmr spectrum using COSY technique [10]. Their connectivities of aromatic protons for **1** and **2b** are shown in Figures 1 and 2. Assignments of all aromatic protons of these compounds shown in the COSY spectra are performed by connectivities of vicinal coupling responses and long-range coupling responses. The four different aromatic doublets at 6.45, 6.64, 6.76 and 7.17 ppm in the spectrum of **2b**, typical of

Based on an nmr study, the following structures for the mono halogenated leuco fluorans **2a** and **3** were assigned. Compared with the ^1H nmr of **1**, the doublet resonance at 6.45 ppm disappeared, and the singlet resonance appeared at 6.74 ppm in the ^1H nmr spectrum of **2a**. Similar observation was made in the ^1H nmr spectrum of **3**. These results suggest that a halogen atom is substituted at the 7' or 8' position of **1**. Mono halogenated compounds are as-

Table I
Physical and Thermal Properties of Halogenated Leuco Fluoran Dyes

No	Mp °C [a]	Leuco Fluoran Dyes			Recording Materials [e]	
		λ ₁	λ ₂ nm [b]	ΔH kJmol ⁻¹ [c]	Mt °C [d]	ΔH Jg ⁻¹ [c]
1	203	590	455	39.9	87.6	45.1
2a	151	620	484	24.7	86.7	37.1
2b	168	616	485	26.2	86.5	38.4
2c	206	593	466	34.6	86.7	31.2
3	169	610	470	49.0	86.9	39.4

[a] Melting points measured by means of DSC. [b] In acetic acid. [c] Heat of fusion. [d] Molten temperature measured by means of DSC. [e] Leuco dye 1-3/Bisphenol A/Sensitizer: 1/2/2, wt/wt.

p-substituted aniline and *o*-coupling, correspond to the resonances for (2'',6''), (7'), (8') and (3'',5'')-aromatic protons, respectively. Compound **2b** may be formed by the familiar bromination at the 4'' and 5' positions, as bromine is produced in the reaction of NBS with hydrogen bromide.

Thermal properties of leuco fluorans **1-3** and recording materials, which constituted leuco fluoran, bisphenol A as developer and phenyl 1-hydroxy-2-naphthoate as sensitizer, were measured by means of DSC. The results are summarized in Table I. Replacement of hydrogen atom(s) in the phenyl group of **1** with halogen atom(s) leads to a lowering of the melting point of leuco fluoran dyes, except for **2c**, whereas the molten temperature of recording materials is constant at 87-88°. The heat of fusion of leuco dyes with bromine atoms(s) is smaller than that of **1**, and that of the recording materials containing brominated leuco dyes also is smaller, compared with that of commercially available **1**.

From these results, brominated leuco dyes are expected to have higher sensitivity of thermal response, but their sensitivities are practically low when used in practical recording materials. Because the λ₁ and λ₂ of developed **2a**, **2b** and **3** were shifted to longer wavelength, compared with those of **1**, as shown in Table I, and the λ₁ of those compounds is not complementary to the λ₂, their developed colors are not black, but bluish black. The lactone ring of halogenated leuco fluorans is very stable, and it undergoes little ring opening even in acetic acid (*ca.* 0.01 relative to **1**).

EXPERIMENTAL

Elemental microanalyses were recorded on a Yanaco MT-3 corder. Melting points and the heat of fusion of compounds were determined on a Rigaku 8113BS TG-DSC calorimeter with 10°/minute under nitrogen (95 ml/minute). The absorption spectra were obtained on a Shimadzu 265FS. Mass spectra were determined on a Shimadzu LKB 9000 spectrometer at 70 eV. The ¹H-nmr spectra were taken on a JEOL GX-270 spectrometer at 270 MHz in deuteriochloroform with tetramethylsilane

as internal standard. The two dimensional ¹H-¹H shift correlated (COSY) data were acquired at a sweep width 500 Hz (1024 data points) in the F2 and F1 domains, 512 spectra (16 scan each) were accumulated with a relaxation delay between scans of 2 seconds. Connectivities of diagonal data were performed with Fourier transformations using Sinebel wind-function and 2.5 Hz Gaussian function COSY option of a standard program system in JEOL GX-270 spectrometer.

Spiro[isobenzofuran-1(3*H*),9'(9*H*)-6'-(methylcyclohexylamino)-3'-methyl-2'-anilinoxanthene]-3-one (**1**).

Compound **1** is of commercial origin (Shin-nippon Soda Co., PSD150): ¹H-nmr (deuteriochloroform): δ 1.10-1.85 (m, 10H, -CH₂-), 2.21 (s, 3H, CH₃), 2.79 (s, 3H, N-CH₃), 3.56 (m, 1H), 5.24 (s, 1H, NH), 6.45 (dd, J = 8.8 Hz and 2.8 Hz, 1H), 6.54-6.59 (m, 5H), 6.72 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 7.6 Hz, 2H), 7.12 (s, 1H), 7.17 (d, J = 7.20 Hz, 1H), 7.53 (t, J = 7.20 Hz, 1H), 7.62 (t, J = 7.20 Hz, 1H), 7.93 (d, J = 7.20 Hz, 1H).

Brominated Spiro[isobenzofuran-1(3*H*),9'(9*H*)-6'-(methylcyclohexylamino)-3'-methyl-2'-anilinoxanthene]-3-one (**2**).

To a solution of 10 g (19 mmoles) of compound **1** in 100 ml of benzene a solution of 3.45 g of *N*-bromosuccinimide in 150 ml of benzene was added slowly dropwise at 50°. The resultant mixture was stirred at 50° for 2 hours. After cooling, the resulting black fluoran dye **1'** and succinimide were removed by filtration. The filtrate was evaporated *in vacuo*, and the residue was dissolved in ethyl ether (200 ml). After filtration, the filtrate was evaporated *in vacuo*. The products were extracted with *n*-hexane (4 x 500 ml), and chromatographed on silica gel with benzene-acetone (15:1, v/v) to give a mixture of **2a** and **2b**. The mixture was further chromatographed on silica gel with benzene and recrystallization from *n*-hexane to give pure **2a** (1.7 g, 15%) and **2b** (0.9 g, 7%).

Compound **2a** had ¹H-nmr: δ 1.26-1.82 (m, 10H, -CH₂-), 2.27 (s, 3H, CH₃), 2.70 (s, 3H, N-CH₃), 3.26 (m, 1H), 5.23 (s, 1H, NH), 6.58-6.66 (m, 4H), 6.74 (s, 1H), 6.77 (t, J = 7.3 Hz, 1H), 7.10 (t, J = 7.3 Hz, 2H), 7.21 (d, J = 7.3 Hz, 1H), 7.33 (s, 1H), 7.58 (t, J = 7.3 Hz, 1H), 7.64 (t, J = 7.3 Hz, 1H), 7.97 (d, J = 7.3 Hz, 1H); ms: 597 (M⁺ + 2, 77), 595 (M⁺, 76), 554 (43), 552 (57), 473 (43), 472 (100), 471 (40), 470 (38), 461 (62), 459 (63), 441 (42), 439 (38).

Anal. Calcd. for C₂₈H₃₁BrN₂O₃: C, 68.57; H, 5.25; N, 4.70. Found: C, 68.86; H, 5.44; N, 4.45.

Compound **2b** had ¹H-nmr: δ 1.21-1.83 (m, 10H, -CH₂-), 2.25 (s, 3H, CH₃), 2.70 (s, 3H, N-CH₃), 3.27 (m, 1H), 5.21 (s, 1H, NH), 6.45 (d, J = 9.2 Hz, 2H), 6.57 (s, 1H), 6.64 (d, J = 8.6 Hz, 1H), 6.76 (d, J = 9.2 Hz, 1H), 7.17 (d, J = 9.2 Hz, 2H), 7.20 (d, J = 7.3 Hz, 1H), 7.34 (s, 1H), 7.60 (t, J = 7.3 Hz, 1H), 7.68 (t, J = 7.3 Hz, 1H), 7.99 (d, J = 7.3 Hz, 1H); ms: 677 (M⁺ + 4, 60), 675 (M⁺ + 2, 100), 673 (M⁺, 47), 634 (36), 632 (77), 630 (51), 552 (63), 550 (73), 461 (83), 459 (83).

Anal. Calcd. for C₂₈H₃₀Br₂N₂O₃: C, 60.55; H, 4.48; N, 4.15. Found: C, 61.03; H, 4.46; N, 4.03.

The brominated products **2a**, **2b** and **2c** were prepared in 17%, 8% and 2% yields, respectively, in the presence of *m*-chloroperbenzoic acid (1% to *N*-bromosuccinimide), with the procedure described above.

Compound **2c** had ¹H-nmr: δ 1.26-1.82 (m, 10H, -CH₂-), 2.27 (s, 2H, CH₂Br), 2.70 (s, 2H, N-CH₂Br), 3.27 (m, 1H), 5.27 (s, 1H), 6.41 (d, J = 8.7 Hz, 1H), 6.58-6.66 (4H, m), 6.77 (d, J = 8.7 Hz, 1H), 6.97 (t, J = 7.3 Hz, 1H), 7.21 (t, J = 7.3 Hz, 2H), 7.37 (s, 1H), 7.43 (dd, J = 7.9 and 1.2 Hz, 1H), 7.62 (t, J = 7.3 Hz, 1H), 7.68 (t, J = 7.3 Hz, 1H), 7.99 (d, J = 7.3 Hz, 1H); ms: 677 (M⁺ + 4, 13), 675 (M⁺ + 2, 23), 673 (M⁺, 13), 633 (9), 631 (18), 629 (18), 551 (15), 549 (17), 460 (21), 458 (22), 356 (33), 355 (100).

Anal. Calcd. for C₃₄H₃₀Br₂N₂O₃: C, 60.55; H, 4.48; N, 4.15. Found: C, 60.79; H, 4.53; N, 3.83.

Spiro[isobenzofuran-1(3*H*),9'(9*H*)-7'-chloro-6'-(methylcyclohexylamino)-3'-methyl-2'-anilinoxanthene]-3-one (**3**).

The title compound was prepared in 30% yield under reflux for 1 hour using *N*-chlorosuccinimide with the procedure described for the preparation of **2a** and **2b**. No dichloro derivative was obtained. The product **3** was recrystallized from benzene; ¹H-nmr: δ 1.27-1.81 (m, 10H, -CH₂-), 2.26 (s, 3H, CH₃), 2.71 (s, 3H, N-CH₃), 3.27 (m, 1H), 5.24 (s, 1H, NH), 6.57-6.61 (m, 5H), 6.72 (s, 1H), 7.08 (t, J = 7.8 Hz, 2H), 7.20 (d, J = 7.3 Hz, 1H), 7.32 (s, 1H), 7.58 (t, J = 7.3 Hz, 1H), 7.63 (t, J = 7.3 Hz, 1H), 7.95 (d, J = 7.3 Hz, 1H); ms: 552 (M⁺ + 2, 40), 551 (M⁺ + 1, 40), 550 (M⁺, 100), 509 (20), 508 (20), 507 (65), 506 (34), 505 (34), 494 (10), 493 (10), 492 (25), 465 (15), 464 (15), 463 (38).

Anal. Calcd. for C₃₄H₃₁ClN₂O₃: C, 74.10; H, 5.67; N, 5.08. Found: C, 74.61; H, 5.81; N, 4.48.

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