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Reactivities of 9-Phenylxanthylium and 9-Phenylthioxanthylium Salts in Electrophilic and Nucleophilic Reactions. II.[1,2] Structure of Dinitrated 9-Phenylthioxanthylium Perchlorate

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The reaction of 9-phenylthioxanthylium salt (II) with a mixed acid gave dinitrated II in 91% yield. In order to determine the structure of dinitrated II, 4-nitro-9-(*m*-nitrophenyl)thioxanthene (IV), 4-acetamido-9-(*p*-acetamidophenyl)thioxanthene (VI), 2,4-dinitro-9-phenylthioxanthene (XV), and their related compounds were synthesized. And it was confirmed that the dinitration of II gives 4-nitro-9-(*m*-nitrophenyl)thioxanthylium and 4-nitro-9-(*p*-nitrophenyl)thioxanthylium salts in the ratio of formation being 1.0: 1.2. Thus, it was recognized that the nitration of II occurs in the phenyl group at 9-position and then at 4-position in the hetero ring of II.

We reported in the preceding paper[1] that nitration of 9-phenylthioxanthylium perchlorate (II) introduces a nitro group to the *para* or *meta* position of the phenyl group at 9-position, that the derivatives are produced in a ratio of the *meta* compound to the *para* compound of 1.0: 1.25, and that II is much more easily nitrated than the corresponding oxygen compound, 9-phenylxanthylium perchlorate (I). It was thus demonstrated that nitration of II by a mixed acid containing 15 equivalents of nitric acid as was done by Shriner, *et al.*[4] in the case of I introduces two nitro groups. Even when the nitric acid is reduced to 5 equivalents, two nitro groups are also introduced.

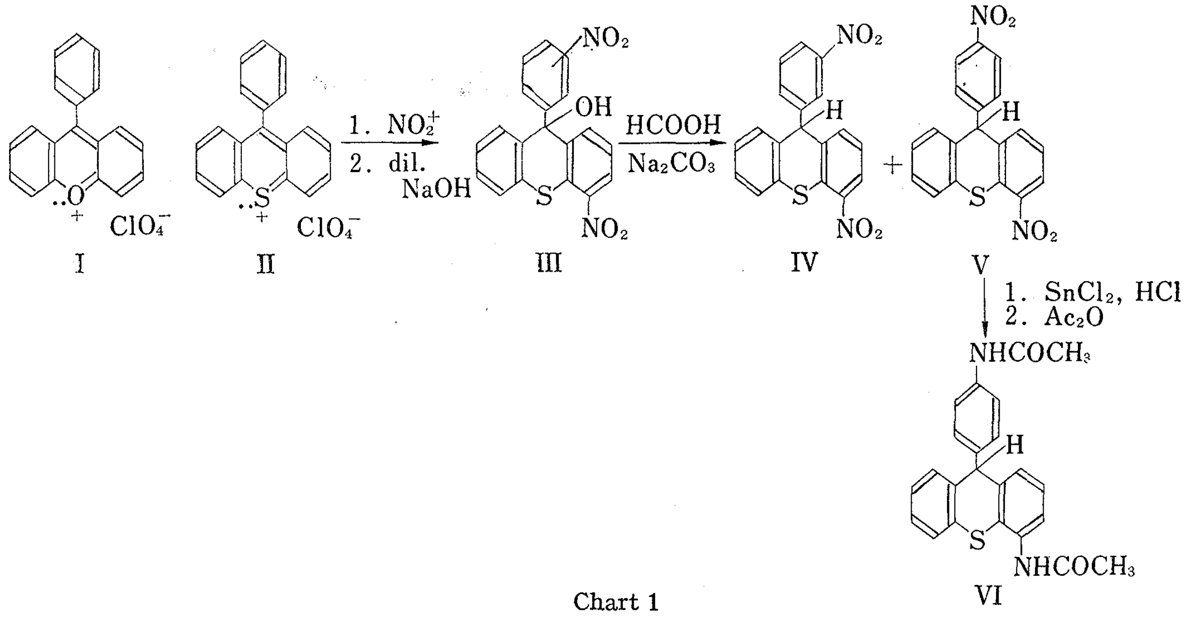

Chart 1

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[1] Part I: M. Hori, T. Kataoka, K. Ohno, and T. Toyoda, *Chem. Pharm. Bull.* (Tokyo), 21, 1272 (1973).

[2] A part of this work was presented at Third Organic Sulfur Symposium, Caen (France), May, 1968. Abstracts of Papers, p. 91 and the International Symposium on the Chemistry of Nonbenzenoid Aromatic Compounds, Sendai, August, 1970. Abstracts of Papers, p. 35.

[3] Location: *492-36, Mitahora, Gifu.*

[4] R.L. Shriner and C.N. Wolf, *J. Am. Chem. Soc.*, 73, 891 (1951).

We would like to report here that the structures of the dinitrated products of II were established and that the ratio of products of both isomers was determined.

Chart 1 shows a synthetic route of the dinitrated products and their derivatives. The compound (II) was treated at 0—10° with a mixed acid containing 5—15 equivalents of nitric acid to give dinitrated 9-phenylthioxanthenol (III) with a yield of 88—91%. The compound (III) was purified by thin-layer chromatography (TLC) or column chromatography. The separation of the isomers and crystallization were unsuccessful. Then the hydroxy group at 9-position was reduced with formic acid and sodium carbonate to produce 9-phenylthioxanthene derivative, which was carefully purified by chromatography using a mixed benzene–hexane solvent (1: 1) with silica gel to separate IV from V. The positions of the nitro groups in IV and V were determined by the comparison of the melting points and the instrumental data such as nuclear magnetic resonance (NMR) spectra and infrared (IR) absorption bands, with those of synthetic samples shown in Chart 2—4. The former was found to be 4-nitro-9-(*m*-nitrophenyl)thioxanthene and the latter, to be 4-nitro-9-(*p*-nitrophenyl)thioxanthene.

The compound (V) could not be synthesized directly and was further reduced with $SnCl_2$ to a diamine derivative, which was identified as a diacetamido derivative (VI) after treatment with acetic anhydride.

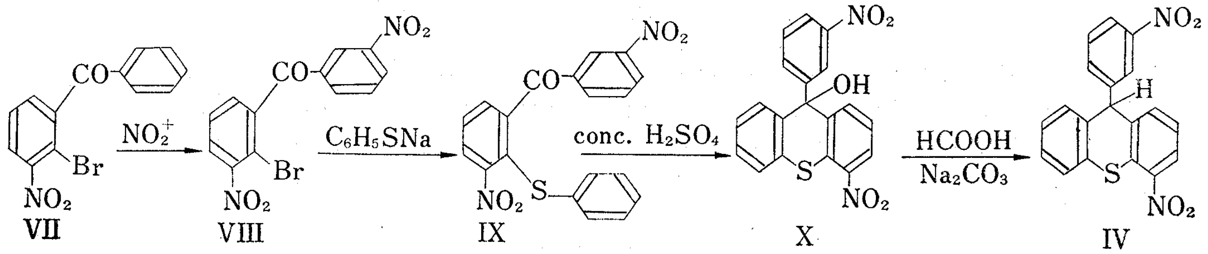

Chart 2

Now, synthetic procedures of authentic samples carried out for the determination of positions of nitro groups will be described. Chart 2 shows a synthetic route of 4-nitro-9-(*m*-nitrophenyl)thioxanthene. The compound (VII) was nitrated with a mixed acid to give 2-bromo-3,3′-dinitrobenzophenone (VIII), in which the bromine at 2-position was replaced by phenylthio group with the formation of IX. Subsequently, IX was treated with concentrated sulfuric acid to yield X by a ring closure reaction, and the hydroxy group at 9-position of X was reduced with formic acid and sodium carbonate to give IV.

2-Nitro-9-(*m*-nitrophenyl)thioxanthene, which was presumably one of the isomers, was synthesized according to the route shown in Chart 3. Nitration of *o*-chlorobenzophenone with a mixed acid afforded a substance, which seemed to be 2-chloro-3,3′-dinitrobenzophenone

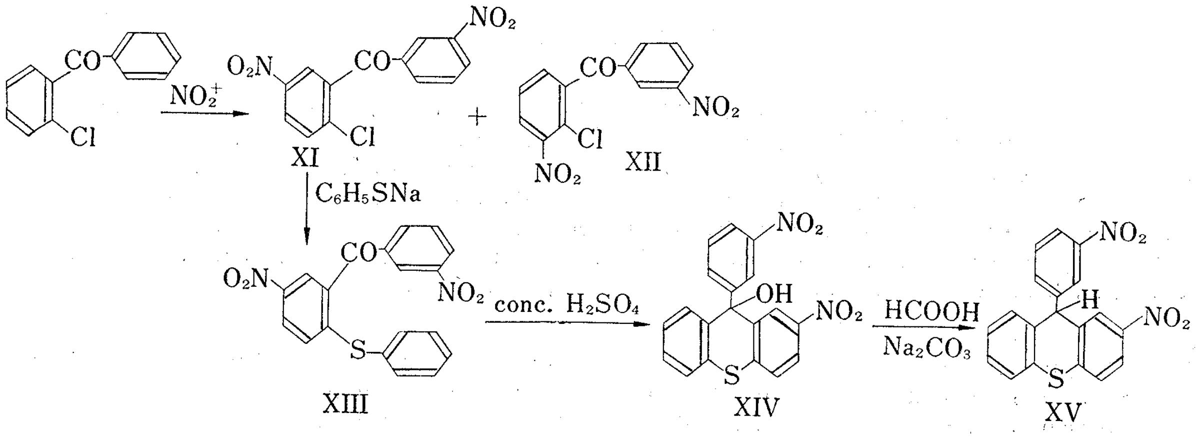

Chart 3

(XII), in addition to 2-chloro-3′,5-dinitrobenzophenone (XI). The substance (XI) was allowed to react with C_6H_5SNa to give XIII, which was treated with concentrated sulfuric acid to yield 2-nitro-9-(*m*-nitrophenyl)thioxanthenol (XIV). Then 2-nitro-9-(*m*-nitrophenyl)thioxanthene (XV) was formed quantitatively by the reduction of XIV with formic acid and sodium carbonate.

An attempt was made to synthesize 4-nitro-9-(*p*-nitrophenyl)thioxanthene (V) on the basis of the fact that the product was 9-(*p*-nitrophenyl)thioxanthene in mononitration of II, but in vain. Hence, synthesis of diacetamido compound (VI) derived from V was carried out as shown in Chart 4.

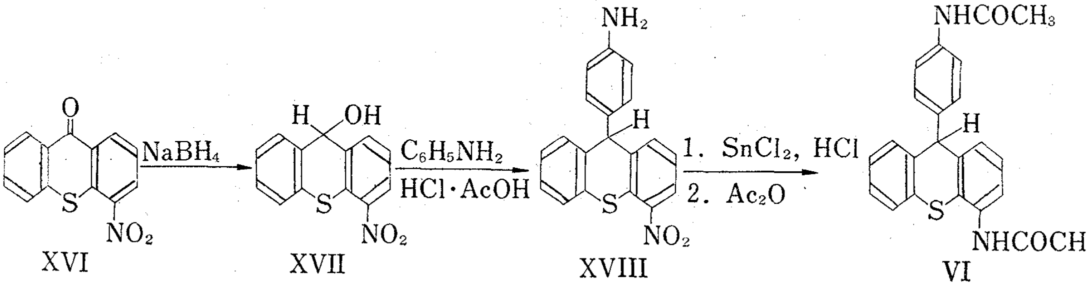

Chart 4

A compound (XVI) was reduced with $NaBH_4$ to 4-nitrothioxanthenol (XVII), which was allowed to react with aniline in acetic acid and hydrochloric acid to form XVIII. The nitro group at 4-position of XVIII was reduced with $SnCl_2$, followed by diacetylation with acetic anhydride, which led to the synthesis of VI.

Result

The syntheses of some dinitro compounds, which were expected to be formed by nitration of II, were attempted. IV, VI, XV, and their related compounds were synthesized as shown in Chart 2, 3, and 4. The structures of dinitrated 9-phenylthioxanthenes were confirmed to be IV and V. The ratio of IV to V was also determined to be 1.0: 1.2. This ratio supports the result reported in the preceding paper that the ratio of the *meta* nitro compound to the *para* nitro compound is 1.0: 1.25 in mononitration of II.

It was thus confirmed that the nitration of II occurs in the phenyl group at 9-position and then at 4-position in the hetero ring of II.

In the next paper, we would like to report on the reaction of I and II with carbanions and to discuss the differences in the reactivities of I and II in the electrophilic and nucleophilic reactions by calculating the electron densities.

Experimental[5]

Nitration of 9-Phenylthioxanthylium Perchlorate (II)——a) To a stirred solution of II[6] (5 g, 13 mmole) in conc. H_2SO_4 (19 ml), HNO_3 (d=1.38) (14.4 ml, 192 mmole) was added at 5—10°. The reaction mixture was made to react with stirring for 20 min in an ice-bath and poured into cold 10% NaOH. The yellow precipitate was extracted with $CHCl_3$, and the extract was dried and evaporated. The residue was chromatographed on silica gel with $CHCl_3$. The pure dinitrated 9-phenylthioxanthenol (III) (4.5 g, 91%) was obtained as a yellow powder, mp 72—73°. *Anal.* Calcd. for $C_{19}H_{12}O_5N_2S$: C, 59.99; H, 3.18; N, 7.36. Found: C, 60.19; H, 3.36; N, 7.10. IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1520 (NO_2), 1350 (NO_2).

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5) Melting points were measured on a Yanagimoto micromelting apparatus and uncorrected. The NMR spectra were recorded on a Hitachi R-20B spectrometer using tetramethylsilane as an internal standard. A Hitachi EPI-S2 spectrometer was used for the IR absorption spectra.

6) C.C. Price, M. Hori, T. Parasaran, and M. Polk, *J. Am. Chem. Soc.*, **85**, 2278 (1963).

b) II (2 g, 5 mmole) was nitrated with a mixed acid of HNO_3 ($d=1.38$) (2.04 ml, 27 mmole) and conc. H_2SO_4 (10.2 ml) at 0—5°. The same treatment of the reaction mixture as method a) gave III (1.7 g, 88%). The IR spectrum was identical with that of the compound prepared by method a).

4-Nitro-9-(*m*-nitrophenyl)thioxanthene (IV) and 4-Nitro-9-(*p*-nitrophenyl)thioxanthene (V)——To a solution of III (1 g) in 80% formic acid (100 ml), Na_2CO_3 (2 g) was added, and the mixture was refluxed for 2 hr. On cooling the mixture a yellow precipitate appeared, which was filtered and washed with water. Recrystallization of the dried solid from MeOH gave yellow crystals (0.7 g), mp 73—74°. Yellow crystals were chromatographed carefully on silica gel using benzene–*n*-hexane (1 : 1) as an eluent to give 4-nitro-9-(*m*-nitrophenyl)thioxanthene (IV), mp 138° and 4-nitro-9-(*p*-nitrophenyl)thioxanthene (V), mp 175°, in the ratio of 1.0 to 1.2. IV: *Anal.* Calcd. for $C_{19}H_{12}O_4N_2S$: C, 62.62; H, 3.32; N, 7.62. Found: C, 62.84; H. 3.63; N, 7.65. IR ν_{max}^{KBr} cm^{-1}: 1520 (NO_2), 1345 (NO_2). This sample was identified with an authentic sample by admixture and by comparison of their IR spectra. V: *Anal.* Calcd. for $C_{19}H_{12}O_4N_2S$: C, 62.62; H, 3.32; N, 7.62. Found: C, 62.88; H, 3.19; N, 7.44. IR ν_{max}^{KBr} cm^{-1}: 1510 (NO_2), 1340 (NO_2).

4-Acetamido-9-(*p*-acetamidophenyl)thioxanthene (VI)——In a solution of $SnCl_2 \cdot 2H_2O$ (4 g) in AcOH (30 ml) saturated with HCl gas, V (0.5 g) was dissolved. After standing overnight, the mixture was warmed on a water–bath, and the solvent was evaporated under reduced pressure. The residue was poured into conc. NaOH and extracted with benzene. The benzene extract was dried and evaporated. A solution of the resulting amine in Ac_2O (5 ml) was permitted to stand for 1 hr and warmed 30 min on a water–bath. After evaporation of Ac_2O, the residue was washed with benzene several times. Recrystallization from EtOH gave colorless needles (0.1 g), mp 298°. *Anal.* Calcd. for $C_{23}H_{20}O_2N_2S$: C, 71.10; H, 5.19; N, 7.21. Found: C, 70.81; H 5.41; N, 6.78. IR ν_{max}^{KBr} cm^{-1}: 3400—3125 (NH), 1660 (CO).

2-Bromo-3,3′-dinitrobenzophenone (VIII)——To a stirred solution of VII[1] (3.1 g) in conc. H_2SO_4 (10 ml), the mixture of HNO_3 ($d=1.42$) (1 ml) and conc. H_2SO_4 (3 ml) was added at 25—35°. The temperature of the mixture was slowly raised to 70°, and the mixture was kept at 70° for 30 min. The cooled mixture was poured into ice-water and the precipitate was filtered with suction, washed thoroughly with water, and dried. In order to remove the starting material, the solid was washed with EtOH and recrystallized from benzene to give colorless prisms (2.7 g), mp 145°. *Anal.* Calcd. for $C_{13}H_7O_5N_2Br$: C, 44.47; H, 2.01; N, 7.98. Found: C, 44.22; H, 4.04; N, 8.04. IR ν_{max}^{KBr} cm^{-1}: 1675 (CO), 1530 (NO_2), 1345 (NO_2).

3,3′-Dinitro-2-phenylthiobenzophenone (IX)——To a hot solution of VIII (2.5 g) in EtOH (150 ml), an EtOH solution of C_6H_5SNa prepared from thiophenol (0.9 g) and Na (0.2 g) was gradually added. The reaction mixture was refluxed for 1.5 hr and removed the solvent. Water was added to the residue, which was extracted with $CHCl_3$. The extract was dried and evaporated. After purification of the brown oil by column chromatography, yellow crystals were obtained. Recrystallization from ether gave yellow prisms (2 g), mp 151°. *Anal.* Calcd. for $C_{19}H_{12}O_5N_2S$: C, 59.99; H, 3.18; N, 7.36. Found: C, 60.14; H, 3.14; N, 7.11. IR ν_{max}^{KBr} cm^{-1}: 1665 (CO), 1520 (NO_2), 1350 (NO_2).

4-Nitro-9-(*m*-nitrophenyl)thioxanthenol (X)——A solution of IX (1 g) in conc. H_2SO_4 (10 ml) was allowed to stand for 10 hr and poured into ice-water and extracted with $CHCl_3$. The extract was washed with dil. Na_2CO_3, dried and evaporated. Recrystallization of the residue from benzene–pet. ether gave yellow prisms (0.8 g), mp 144°. *Anal.* Calcd. for $C_{19}H_{12}O_5N_2S$: C, 59.99; H, 3.18; N, 7.36. Found: C, 59.80; H, 3.28; N, 7.43. IR ν_{max}^{KBr} cm^{-1}: 3375 (OH), 1520 (NO_2), 1340 (NO_2).

4-Nitro-9-(*m*-nitrophenyl)thioxanthene (IV)——A solution of X (5 g) in 85% formic acid (50 ml) containing a small amount of Na_2CO_3 was refluxed for 3 hr. The cold mixture was poured into water and extracted with $CHCl_3$. The extract was washed with dil. Na_2CO_3, dried, and evaporated. The residue was purified by column chromatography. Recrystallization from MeOH gave yellow needles (0.4 g), mp 139°. *Anal.* Calcd. for $C_{19}H_{12}O_4N_2S$: C, 62.62; H, 3.32; N, 7.69. Found: C, 62.83; H, 3.57; N, 7.58. IR ν_{max}^{KBr} cm^{-1}: 1520 (NO_2), 1345 (NO_2).

Nitration of *o*-Chlorobenzophenone——A solution of *o*-chlorobenzophenone[7] (28.5 g) in conc. H_2SO_4 (128 ml) was nitrated at 25—30° with a mixture of HNO_3 ($d=1.50$) (16.5 ml) and conc. H_2SO_4 (32 ml). The solution was slowly heated to 75° and kept at this temperature for 30 min. The cooled solution was poured over crused ice. The precipitate was washed with water until the washings were no longer acidic, dried, and then washed with EtOH carefully. Recrystallization of the residue from methyl ethyl ketone or acetone gave 2-chloro-3′,5-dinitrobenzophenone (XI) as colorless plates (15 g), mp 182° (reported[8] 177°). *Anal.* Calcd. for $C_{13}H_7O_5N_2Cl$: C, 50.92; H, 2.30; N, 9.13. Found: C, 50.97; H, 2.46; N, 9.24. IR ν_{max}^{KBr} cm^{-1}: 1665 (CO), 1535 (NO_2), 1350 (NO_2). Recrystallization of the crystals obtained from EtOH filtrate from EtOH–ether gave 2-chloro-3,3′-dinitrobenzophenone (XII) (1.8 g) as colorless prisms, mp 144°. *Anal.* Calcd. for $C_{13}H_7O_5N_2Cl$: C, 50.92; H, 2.30; N, 9.13. Found: C, 50.76; H, 2.42; N, 9.17. IR ν_{max}^{KBr} cm^{-1}: 1690 (CO), 1515 (NO_2), 1345 (NO_2).

2-Nitro-9-(*m*-nitrophenyl)thioxanthenol (XIV)——A solution of XIII[9] (0.5 g) in cold conc. H_2SO_4 (10 ml) was allowed to stand for 14 hr. The same treatment as X afforded yellow crystals. Recrystallization from

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7) E. Berliner, *J. Am. Chem. Soc.*, **66**, 533 (1944).

8) J.D. Loudon, J.R. Robertson, J.N. Watson, and S.D. Aiton, *J. Chem. Soc.*, **1950**, 55.

9) R.H.B. Galt, J.D. Loudon, and A.D.B. Sloan, *J. Chem. Soc.*, **1958**, 1588.

pet. ether–benzene gave yellow needles (0.4 g), mp 156°. *Anal.* Calcd. for $C_{19}H_{12}O_5N_2S$: C, 59.99; H, 3.18; N, 7.36. Found: C, 60.03; H, 3.33; N, 7.13. IR ν_{max}^{KBr} cm^{-1}: 3575 (OH), 1540 (NO_2), 1510 (NO_2), 1340 (NO_2), 1330 (NO_2).

2-Nitro-9-(*m*-nitrophenyl)thioxanthene (XV)——To a solution of XIV (0.1 g) in 80% formic acid (30 ml), a small amount of Na_2CO_3 was added. The mixture was refluxed for 2 hr. Water was added to the cooled mixture, and the resulting yellow precipitate was isolated by filtration and washed with Na_2CO_3 and then water. After purification by column chromatography, recrystallization from MeOH–$CHCl_3$ quantitatively gave yellow needles, mp 166°. *Anal.* Calcd. for $C_{19}H_{12}O_4N_2S$: C, 62.62; H, 3.32; N, 7.69. Found: C, 62.69; H, 3.43; N, 7.63. IR ν_{max}^{KBr} cm^{-1}: 1515 (NO_2), 1335 (NO_2).

4-Nitrothioxanthenol (XVII)——A suspension of XVI^10) (5 g) in EtOH (150 ml) was reduced with $NaBH_4$ (3 g) in the usual way. The reaction mixture was poured into water and the yellow precipitate was filtered. Recrystallization from benzene–pet. ether gave greenish yellow needles (3.6 g), mp 133—134°. *Anal.* Calcd. for $C_{13}H_9O_3NS$: C, 60.21; H, 3.50; N, 5.40. Found: C, 60.45; H, 3.69; N, 5.63. IR ν_{max}^{KBr} cm^{-1}: 3200—3150 (OH), 1510 (NO_2), 1340 (NO_2).

9-(*p*-Aminophenyl)-4-nitrothioxanthene (XVIII)——A reaction mixture of XVII (3.4 g) and aniline (3 g) in AcOH (30 ml) and conc. HCl (2 ml) was gently refluxed for 4 hr and poured into water and neutralized with Na_2CO_3. The precipitate was filtered and dried. Recrystallization from ether gave yellow prisms (2.5 g), mp 141—142°. *Anal.* Calcd. for $C_{19}H_{14}O_2N_2S$: C, 68.24; H, 4.22; N, 8.38. Found: C, 68.47; H, 4.39; N, 8.24. IR ν_{max}^{KBr} cm^{-1}: 3400 (NH_2), 3350 (NH_2), 1510 (NO_2), 1330 (NO_2).

4-Acetamido-9-(*p*-acetamidophenyl)thioxanthene (VI)——To a solution of $SnCl_2 \cdot 2H_2O$ (2.5 g) in AcOH (30 ml) saturated with HCl gas, XVIII (0.5 g) was added, and diamine was obtained in the same way as VI prepared from V. The diamine was acetylated with Ac_2O (5 ml). Recrystallization from EtOH gave colorless needles (0.2 g), mp 295°. *Anal.* Calcd. for $C_{23}H_{20}O_2N_2S$: C, 71.10; H, 5.19; N, 7.21. Found: C, 70.94; H, 5.27; N, 6.93. IR ν_{max}^{KBr} cm^{-1}: 3400—3125 (NH), 1660 (CO). NMR (DMSO-d_6) τ: 2.5—3.2 (11H, multiplet, aromatic H), 4.50 (1H, singlet, C_9-H), 7.96 (3H, singlet, CH_3), 8.06 (3H, singlet, CH_3).

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10) F. Mayer, *Chem. Ber.*, 42, 3046 (1909).