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Selenoxanthylium Salts. I. Nitration of 9-Phenylselenoxanthylium Perchlorate[1]

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It was confirmed that the nitration of 9-phenylselenoxanthylium salt (III) with a mixed acid (1 equivalent of HNO_3) gave 9-(*p*-nitrophenyl)- and 9-(*m*-nitrophenyl)selenoxanthylium salts in the product ratio of 1.0 to 1.5.

On the other hand, the reaction of III with a mixed acid (5 equivalents of HNO_3 in H_2SO_4) gave 4-nitro-9-(*p*-nitrophenyl)- and 4-nitro-9-(*m*-nitrophenyl)selenoxanthylium salts in the product ratio of 1.0 to 1.25.

Based on these results, the reactivity of III in the nitration has been discussed.

The authors have performed a series on six-membered aromatic compounds containing an element of the VIB group of the periodic table, especially on 9-phenylxanthylium salt (I) and 9-phenylthioxanthylium salt (II). In this series of studies, electrophilic reactions,[3] nucleophilic reactions,[4] and reactions of organometallic reagents[5] were examined in detail. A surprizingly large difference was found between the reactivities of I and II. The authors described in the preceeding report on the reactions between 9-phenylselenoxanthylium salt

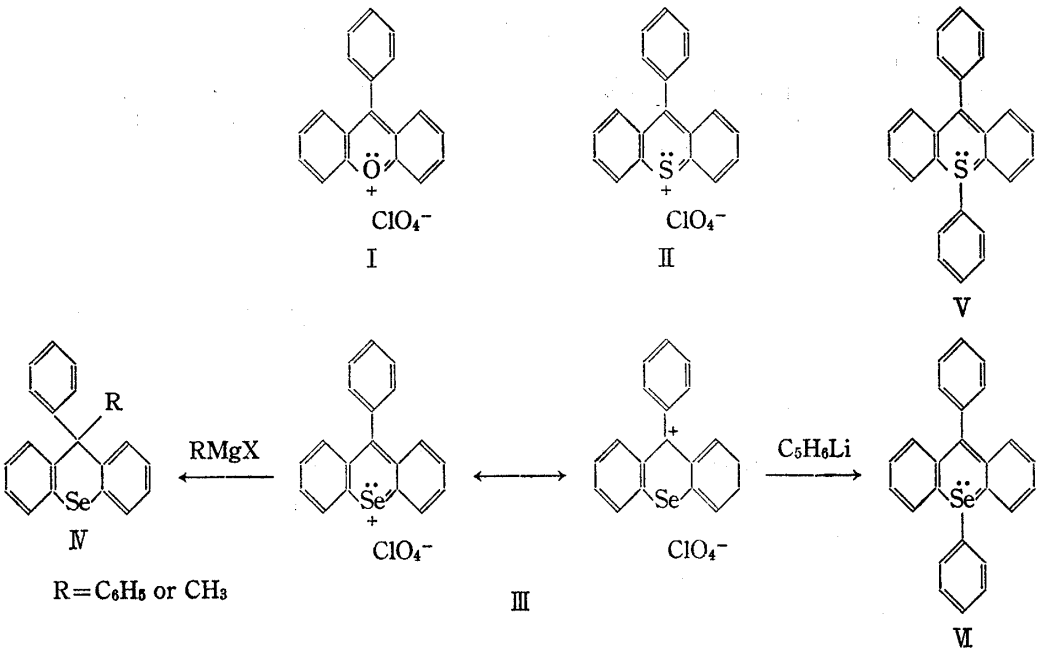

Chart 1

1) A part of this work was presented at International Symposium on the Chemistry of Nonbenzenoid Aromatic Compounds, Sendai, August, 1970. Abstracts of Papers, p. 35.
2) Location: *492–36, Mitahora, Gifu.*
3) *a*) M. Hori, T. Kataoka, K. Ohno, and T. Toyoda, *Chem. Pharm. Bull.* (Tokyo), **21**, 1272 (1973); *b*) M. Hori and T. Kataoka, *ibid.*, **21**, 1282 (1973).
4) M. Hori, T. Kataoka, Y. Asahi, and E. Mizuta, *Chem. Pharm. Bull.* (Tokyo), **21**, 1415 (1973).
5) M. Hori, T. Kataoka, Y. Asahi, and E. Mizuta, *Chem. Pharm. Bull.* (Tokyo), **21**, 1318 (1973); *idem*, *ibid.*, **21**, 1692 (1973).

(III) and organometallic reagents and on the successful synthesis of a selenabenzene analog, 9,10-diphenyl-10-selenaänthracene (VI), which is a novel aromatic heterocycle.[6] The synthesis of the corresponding sulfur compound, thiabenzene analog, 9,10-diphenyl-10-thiaanthracene (V) has been reported by Price, *et al.*, previously.[7] In the present study, the nitration of III was examined in closer detail and was compared with those of I and II reported before.

As shown in Chart 2, III was treated at −70° with a mixed acid containing 1 equivalent of HNO_3 and then neutralized with dilute NaOH. Then mononitrated 9-phenylselenoxanthenol (VII) was obtained at a yield of 54%. Although VII was purified by thin-layer chromatography (TLC) and column chromatography, the isolation of isomers was unsuccessful.

By the reduction of VII with formic acid and sodium carbonate, only the hydroxyl group at 9-position was reduced to give 9-phenylselenoxanthene derivative (VIII). The reduction of the nitro group of VIII with $SnCl_2$–HCl gave amino derivatives. Treatment of these amino derivatives with acetic anhydride gave acetamide compounds, which were successfully separated into two isomers with mp 220° and 228° by preparative TLC on silica gel by the use of $CHCl_3$–ether (3: 10) as an eluent. Identification of these two compounds was carried out by the comparison of melting points and instrumental data with those of authentic samples synthesized by a different way shown in Chart 3. The results indicated that the compound with mp 220° was 9-(*p*-acetamidophenyl)selenoxanthene (IXa) and that with mp 228° was 9-(*m*-acetamidophenyl)selenoxanthene (IXb). The product ratio of the two thus prepared, IXa/IXb was 1.0/1.5.

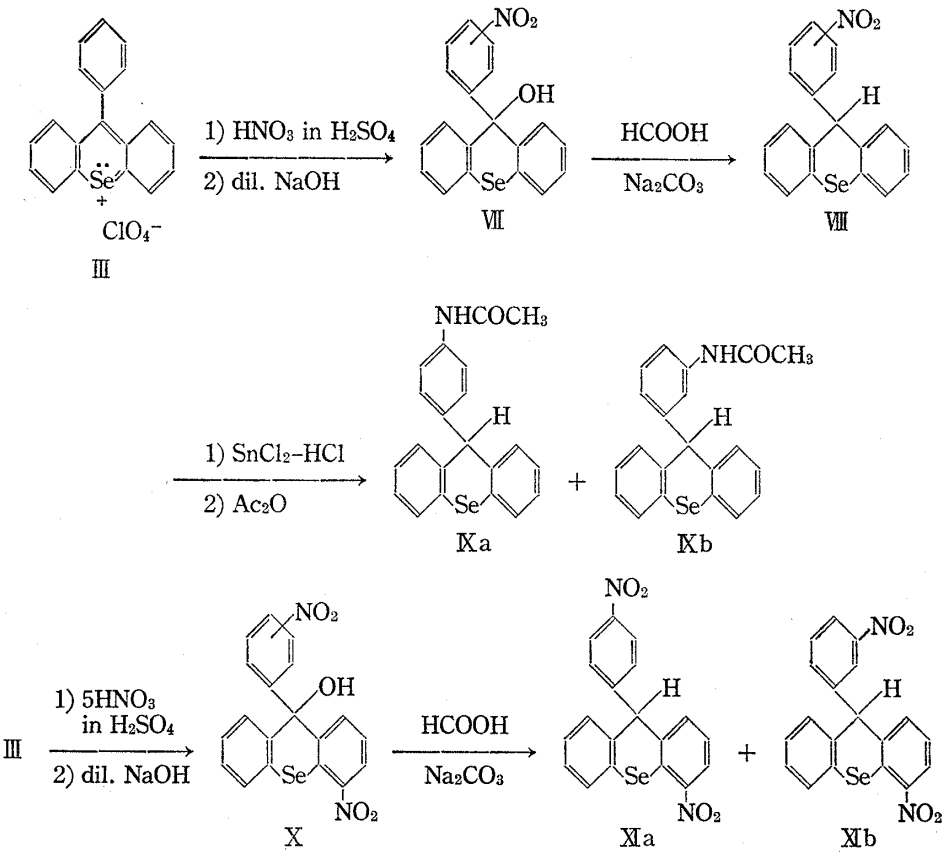

Chart 2

6) M. Hori, T. Kataoka, and Chen-Fu Hsü, *Chem. Pharm. Bull.* (Tokyo), **22**, 15 (1974).
7) C.C. Price, M. Hori, T. Parasaran, and M. Polk, *J. Am. Chem. Sos.*, **85**, 2278 (1963).

On the other hand, III was nitrated under the same conditions as II which was reported in our previous report. Namely, III was nitrated at 0—2° with a mixed acid containing 5 equivalents of HNO_3, and then neutralized with 10% NaOH. Then yellow foam product (X) was obtained in a yield of 19%.[8] It was confirmed by the elemental analysis and various spectral data that X was a mixture of dinitrated 9-phenylselenoxanthenols. The crystallization and the separation of the isomers were unsuccessful. X was treated with HCO_2H–Na_2CO_3 to give 9-phenylselenoxanthene derivative (XI) in which the hydroxy group at 9-position was reduced. XI was then successfully separated into two isomers having melting points 197° and 156° by preparative TLC on silica gel by the use of benzene–petroleum ether (1 : 1) as an eluent. The IR spectra of these two dinitro compounds were very similar to those of the corresponding dinitro sulfur compounds XVIIIa and XVIIIb whose structure was well established.[3b] Thus, the compound with a melting point of 197° and that with a melting point of 156° was identified as 4-nitro-9-(*p*-nitrophenyl)selenoxanthene (XIa) and 4-nitro-9-(*m*-nitrophenyl)selenoxanthene (XIb), respectively, as shown in Fig. 1 and 2 by the comparison of these spectra.

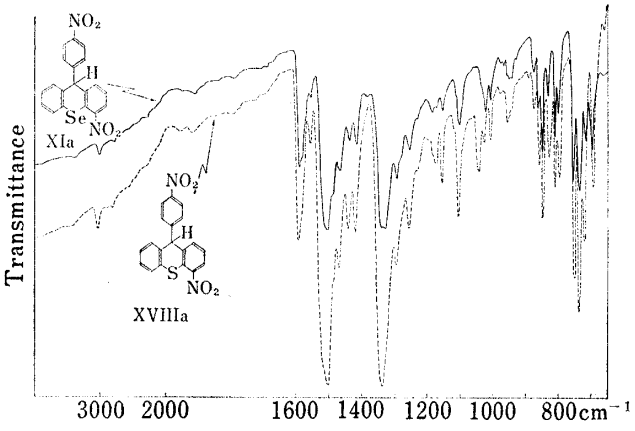

Fig. 1. IR Spectra (KBr) of XIa and XVIIIa

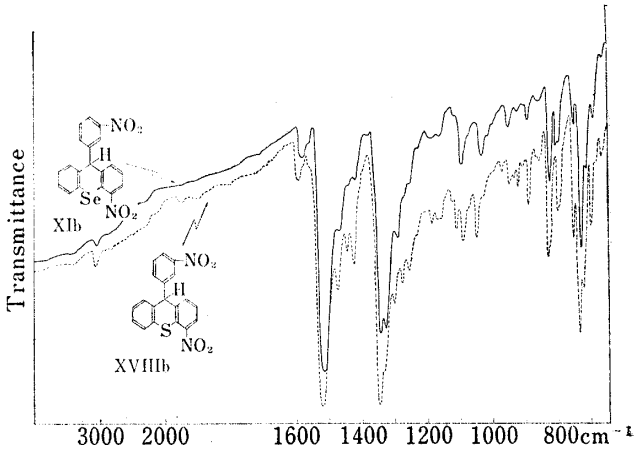

Fig. 2. IR Spectra (KBr) of XIb and XVIIIb

The product ratio of the two isomers thus prepared, XIa/XIb was 1.0/1.25.

Chart 3 shows the route of synthesis of the authentic samples. These were prepared to identify the compounds obtained by mononitration of III, namely, the compounds having melting points of 220° and 228°.

By the reaction with aniline, selenoxanthylium salt (XII) gave 9-(*p*-aminophenyl)-selenoxanthene (XIII) by the Hofmann–Martius rearrangement. It was determined from the following data that an amino group of XIII was present at the *para* position. In the nuclear magnetic resonance (NMR) spectrum, aromatic protons in a phenyl group at 9-position appeared at τ 3.26 and τ 3.5 as a pair of doublet (A_2B_2 pattern). By the acetylation, XIII was converted to an acetamide derivative (IXa), mp 220°.

9-(*p*-Amino-*o*-nitrophenyl)selenoxanthene (XV) was synthesized from *o*-nitroaniline and selenoxanthenol (XIV). 9-(*m*-Nitrophenyl)selenoxanthene (XVI) was obtained by diazotization and deamination of XV with hypophosphorous acid. XVI was reduced to an amino derivative (XVII) with $SnCl_2$ and then converted to an acetamide derivative (IXb), mp 228°.

8) The yield of the nitration compound of III is lower than those of the compounds (I) and (II.) This low yield is attributable to the nature of III, which is easily oxidized by a mixed acid. When III was allowed to react with 2 equivalents of $CuNO_3$ in acetic anhydride, nitration did not proceed. Therefore, mononitration of III mentioned before, was examined at −70° with a mixed acid containing 1 equivalent of HNO_3. The results were satisfactory.

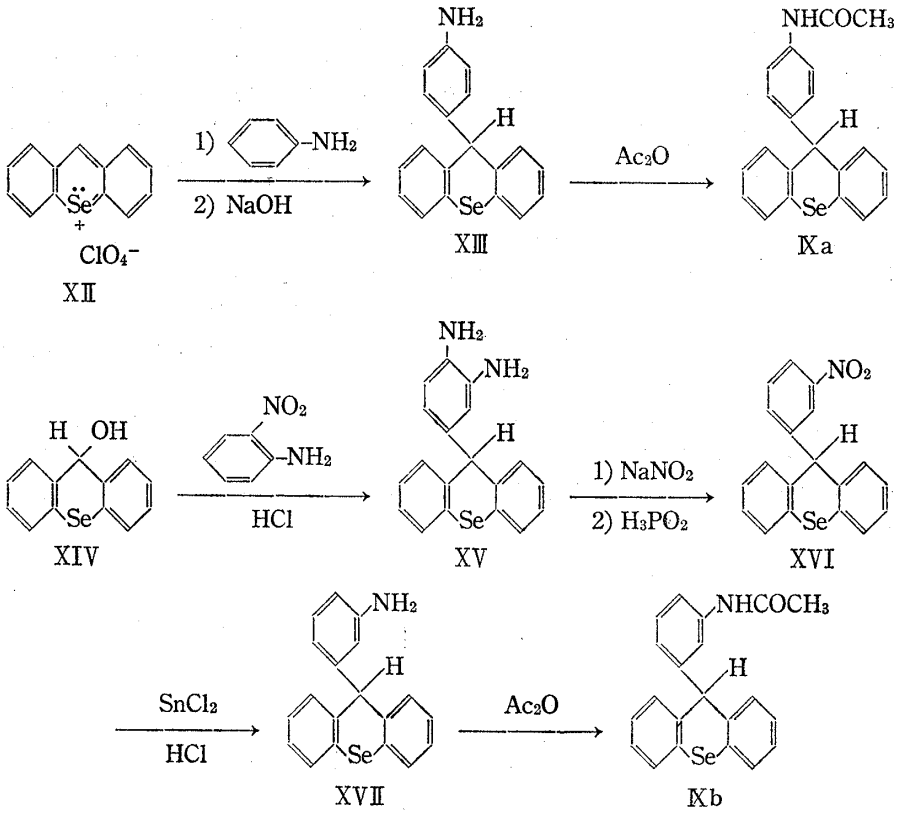

Chart 3

Discussion

The authors reported before following results:

(i) The compound (I) did not give dinitrated compounds by the treatment with 15 equivalents of HNO_3, but formed two isomers in which mononitration occurred at the *para* position (4′ position) and the *meta* position (3′ position) of the phenyl group at 9 position. The product ratio of the two isomers formed by this reaction 4′/3′-mononitrated compounds was 1.0/4.5.

(ii) II easily gave dinitrated compounds when treated with 5 equivalents of HNO_3. The ratio of the two isomers 4′,4/3′,4-dinitrated compounds was 1.2. II gave mononitrated compounds when treated with 1 equivalent of HNO_3. The product ratio of the two isomers 4′/3′-mononitrated compounds was 1.25.

From these results it is concluded that the reactivity of I and II are given by the ratio of 4′/3′-mononitrated compounds.

It was confirmed in the present study for III that the product ratio of the two isomers 4′/3′-mononitrated compounds was 1.0/1.5 and the product ratio of the two isomers, 4′,4/3′,4-dinitrated compounds, was 1.0/1.25. By the comparison of the results of nitration of I, II, and III, it was noticed that the order of reactivity is the reactivity of II (=S̈–⁺)> the reactivity of III (=S̈e–⁺)> the reactivity of I (=Ö–⁺). It is a very remarkable fact that this order does not correspond with the atomic number of the elements of the group in the periodic table.

The results of nitration experiments suggest that similar difference may be present in the reactions of I, II, and III with other electrophiles.

The results of study on the reaction of III with carbanion and the reaction indices of electrophilic and nucleophilic reactions of III will be reported in the following paper.

Experimental[9]

9-Nitrophenylselenoxanthenol (VII)——A mixture of HNO_3 ($d=1.38$) (0.18 ml) and conc. H_2SO_4 (3.05 ml) was added to III[6] (1.0 g) at a temperature of acetone–dry ice bath. After standing for 1.5 hr, the reaction mixture was decomposed with a cold 10% NaOH and extracted with $CHCl_3$. The extract was dried (K_2CO_3) and evaporated. Purification of the residue by column chromatography on silica gel using benzene–pet. ether (2: 1) gave yellow powders. Recrystallization from benzene–pet. ether gave yellow prisms (0.4 g, 54%), mp 192—193°. *Anal.* Calcd. for $C_{19}H_{13}O_3NSe$: C, 59.69; H, 3.43; N, 3.67. Found: C, 59.85; H, 3.61; N, 3.70. IR ν_{max}^{KBr} cm^{-1}: 3475 (OH), 1510, 1340 (NO_2).

9-Nitrophenylselenoxanthene (VIII)——A solution of VII (0.30 g) in 85% HCO_2H (25 ml) containing a small amount of Na_2CO_3 was refluxed for 3 hr. After removal of HCO_2H under reduced pressure, water was added to the residue, and the mixture was extracted with $CHCl_3$. The extract was washed wiht dil. Na_2CO_3, dried (K_2CO_3) and evaporated. The resulting solid was purified by column chromatography on silica gel using benzene–pet. ether (1: 1). Recrystallization from $CHCl_3$–pet. ether gave yellow prisms (0.26 g, 91%), mp 182—183°. *Anal.* Calcd. for $C_{19}H_{13}O_2NSe$: C, 62.31; H, 3.58; N, 3.83. Found: C, 62.17; H, 3.79; N, 3.70. IR ν_{max}^{KBr} cm^{-1}: 1515, 1345 (NO_2).

9-(*p*-Acetamidophenyl)selenoxanthene (IXa) and 9-(*m*-Acetamidophenyl)selenoxanthene (IXb)——An AcOH solution of $SnCl_2$ was prepared by dissolving $SnCl_2 \cdot 2H_2O$ (2 g) in AcOH (15 ml) saturated with HCl gas. VIII (0.195 g) was dissolved in an AcOH solution of $SnCl_2$. The solution was allowed to stand for 24 hr, and then the solvent was evaporated under reduced pressure. The resulting residue was decomposed with conc. NaOH and extracted with benzene. The extract was dried (K_2CO_3) and evaporated. Purification of the residual oil by chromatography on silica gel using $CHCl_3$ as an eluent gave an amine, which has an absorption band of the amino group at 3450 and 3350 cm^{-1} in infrared (IR) spectrum (KBr). A solution of the amine in Ac_2O (5 ml) was warmed for 10 min on a water bath and then allowed to stand for 2 hr. After evaporation of Ac_2O under reduced pressure, the residue was separated into IXa and IXb by preparative TLC on silica gel using $CHCl_3$–ether (3: 10) as an eluent. The substance having a small *Rf* value was found to be *p*-isomer (IXa) by the comparison of the IR spectrum with that of an authentic sample. Recrystallization from $CHCl_3$–pet. ether gave colorless prisms (40.9 mg), mp 220°. *Anal.* Calcd. for $C_{21}H_{17}ONSe$: C, 66.67; H, 4.53; N, 3.71. Found: C, 66.79; H, 4.70; N, 3.26. IR ν_{max}^{KBr} cm^{-1}: 3230 (NH), 1660 (CO). The acetamide having a large *Rf* value was found to be *m*-isomer (IXb) by the comparison of the IR spectrum with that of an authentic sample. Recrystallization from ether–$CHCl_3$ gave colorless plates (83.2 mg), mp 228°. *Anal.* Calcd. for $C_{21}H_{17}ONSe$: C, 66.67; H, 4.53; N, 3.71. Found: C, 66.46; H, 4.66; N, 3.59. IR ν_{max}^{KBr} cm^{-1}: 3250 (NH), 1660 (CO). Separation of the crude acetamide, which was prepared from III without isolation of pure intermediates, in the same way as mentioned above afforded IXa and IXb in the ratio of 1: 1.5.

Dinitrated 9-Phenylselenoxanthenol (X)——To a cold solution of III (1.5 g) in H_2SO_4 (2.6 ml), a cold mixed acid prepared from HNO_3 ($d=1.38$) (0.82 ml) and conc. H_2SO_4 (2.6 ml) was added over 20 min at 0—2°. After stirring for 5 min, the reaction mixture was decomposed with an ice-cold 10% NaOH and extracted with $CHCl_3$, dried (K_2CO_3), and evaporated. Purification by column chromatography on silica gel gave yellow powders (0.3 g, 19%). All attempts for recrystallization were unsuccessful. *Anal.* Calcd. for $C_{19}H_{12}O_5N_2Se$: N, 6.56. Found: N, 6.32.

4-Nitro-9-(*p*-nitrophenyl)selenoxanthene (XIa) and 4-Nitro-9-(*m*-nitrophenyl)selenoxanthene (XIb)——A solution of X (0.1 g) in 85% HCO_2H (30 ml) containing a small amount of Na_2CO_3 was heated under reflux for 3 hr. At the end of the reaction HCO_2H was removed under reduced pressure. The residue was neutralized with dil. Na_2CO_3 and extracted with $CHCl_3$. The extract was dried (K_2CO_3) and evaporated. Dinitrated 9-phenylselenoxanthene was obtained quantitatively. Separation by preparative TLC on silica gel using benzene–pet. ether (1: 1) gave two isomers. The upper part gave yellow prisms, mp 156°, which was recrystallized from benzene–pet. ether. *Anal.* Calcd. for $C_{19}H_{12}O_4N_2Se$: C, 55.48; H, 2.94; N, 6.81. Found: C, 55.69; H, 3.16; N, 6.86. IR ν_{max}^{KBr} cm^{-1}: 1510, 1340 (NO_2). The lower part gave yellow prisms, mp 197°, which was recrystallized from benzene–pet. ether or MeOH. *Anal.* Calcd. for $C_{19}H_{12}O_4N_2Se$: C, 55.48; H, 2.94; N, 6.81. Found: C, 55.64; H, 3.13; N, 6.59. IR ν_{max}^{KBr} cm^{-1}: 1510, 1345, 1330 (NO_2). The product ratio of the former to the latter was 1 to 1.25. It was assumed that the former is 4-nitro-9-(*m*-nitrophenyl)-selenoxanthene (XIb) and the latter is 4-nitro-9-(*p*-nitrophenyl)selenoxanthene (XIa), because they resemble the corresponding sulfur compounds very closely in IR spectra.

9-(*p*-Aminophenyl)selenoxanthene (XIII)——To an ethereal solution of aniline (0.2 g), XII[6] (0.3 g) was gradually added. After stirring for 1 hr, the reaction mixture was washed with dil. NaOH and water and then dried (K_2CO_3). Removal of the solvent gave the crude product, which was purified by column chromatography. Recrystallization from benzene–pet. ether gave colorless prisms (0.2 g, 68.5 %), mp 151°. *Anal.* Calcd. for $C_{19}H_{15}NSe$: C, 67.85; H, 4.50; N, 4.17. Found: C, 68.03; H, 4.76; N, 3.94. IR ν_{max}^{KBr} cm^{-1}:

9) All melting points are uncorrected.

3350, 3300 (NH). NMR ($CDCl_3$) τ: 2.25—3.65 (8H, multiplet, selenoxanthene ring H), 3.26, 3.52 (4H, A_2B_2 pattern, J=9.0 Hz, C_9-phenyl H), 4.73 (1H, singlet, C_9-H), 6.40—7.10 (2H, broad singlet, NH_2).

9-(*p*-Acetamidophenyl)selenoxanthene (IXa)——A solution of XIII (0.1 g) in Ac_2O (2 ml) was allowed to stand for 2 hr and warmed for 30 min on a water bath. After removal of Ac_2O the residue was recrystallized from $CHCl_3$–pet. ether to give colorless needles (0.1 g, 89%), mp 220°. *Anal.* Calcd. for $C_{21}H_{17}ONSe$: C, 66.67; H, 4.53; N, 3.71. Found: C, 66.61; H, 4.77; N, 3.73. IR ν_{max}^{KBr} cm^{-1}: 3250 (NH), 1660 (CO). NMR (DMSO-d_6) τ: 0.10 (1H, broad singlet, NH), 2.10—3.30 (12H, multiplet, aromatic H), 4.40 (1H, singlet, C_9-H), 8.00 (3H, singlet, CH_3).

9-(*p*-Amino-*m*-nitrophenyl)selenoxanthene (XV)——To a solution of XIV[6] (0.8 g) and *o*-nitroaniline (0.5 g) in EtOH (20 ml), conc. HCl (2 ml) was added, and the reaction mixture was refluxed for 2 hr on a water bath. The cooled mixture was poured into an Na_2CO_3 solution and warmed for 30 min on a water bath. After cooling the mixture, a resulting precipitate was filtered and dried. Purification by column chromatography on silica gel using benzene–pet. ether (2: 1) as an eluent gave a yellow solid. Recrystallization from benzene–pet. ether afforded yellow needles (0.9 g, 77%), mp 163°. *Anal.* Calcd. for $C_{19}H_{14}O_2N_2Se$: C, 59.84; H, 3.70; H, 7.34. Found: C, 60.12; H, 3.95; N, 7.10. IR ν_{max}^{KBr} cm^{-1}: 3450, 3325 (NH_2), 1510, 1330 (NO_2).

9-(*m*-Nitrophenyl)selenoxanthene (XVI)——To a solution of XV (0.8 g) in DMF (10 ml) containing conc. HCl (0.5 ml), an aqueous solution of $NaNO_2$ ($NaNO_2$ (0.2 g) in H_2O (1 ml)) was added at −1—3° over 1.5 hr. Then 50% H_3PO_2 (3 ml) was added to the reaction mixture. After standing overnight in a refrigerater, the reaction mixture was poured into water (100 ml) and extracted with $CHCl_3$. The extract was dried (K_2CO_3) and evaporated. After purification of the residue by column chromatography the resulting yellow solid was recrystallized from $CHCl_3$–ether to give yellow needles (0.5 g, 66.5%), mp 143°. *Anal.* Calcd. for $C_{19}H_{13}O_2NSe$: C, 62.31; H, 3.58; N, 3.83. Found: C, 62.44; H, 3.75; N, 3.83. IR ν_{max}^{KBr} cm^{-1}: 1520, 1345 (NO_2).

9-(*m*-Aminophenyl)selenoxanthene (XVII)——In a mixture of $SnCl_2 \cdot 2H_2O$ (2 g) and AcOH (30 ml) saturated with HCl gas, XVI (0.3 g) was dissolved, and the mixture was allowed to stand overnight. Then it was warmed for 1 hr on a water bath. After removal of the AcOH under reduced pressure, the residue was decomposed with conc. NaOH and extracted with benzene. The benzene extract was dried (K_2CO_3) and evaporated. After purification of the crude amine by column chromatography, it was recrystallized from benzene–pet. ether to give colorless prisms (0.2 g, 72.5%), mp 142°. *Anal.* Calcd. for $C_{19}H_{15}NSe$: C, 67.85; H, 4.50; N, 4.17. Found: C, 67.88; H, 4.47; N, 3.98. IR ν_{max}^{KBr} cm^{-1}: 3350, 3300 (NH_2).

9-(*m*-Acetamidophenyl)selenoxanthene (IXb)——A solution of XVII (0.1 g) in Ac_2O (2 ml) was allowed to stand for 2 hr and then warmed for 30 min on a water bath. After removal of the solvent under reduced pressure, the residue was recrystallized from $CHCl_3$–ether to give colorless plates (0.1 g, 89%), mp 228°. *Anal.* Calcd. for $C_{21}H_{17}ONSe$: C, 66.67; H, 4.53; N, 3.71. Found: C, 66.49; H, 4.74; N, 3.59. IR ν_{max}^{KBr} cm^{-1}: 3250 (NH), 1660 (CO). NMR (DMSO-d_6) τ: 0.32 (1H, broad singlet, NH), 2.20—3.60 (12H, multiplet, aromatic H), 4.42 (1H, singlet, C_9-H), 8.06 (3H, singlet, CH_3).