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Synthesis of 3,6-Bis(dimethylamino)thio- and Selenoxanthene (1)

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The only reported synthesis of 3,6-bis-(dimethylamino)thioxanthene (2), IIa, is over sixty-five years old, and by modern standards is inadequately described. Indeed, from the color and melting point of the reported product, it is evident that the leuco-base was contaminated by oxidation products (3). We wish to report an improved synthesis of this compound and the synthesis of the previously unreported 3,6-bis-(dimethylamino)selenoxanthene (IIb). Figure 1 gives the synthetic route developed for the preparation of the described thio- and selenoxanthene derivatives.

The thio- and selenoxanthylium salts (Ia and b) were prepared according to literature methods (4, 5) and were isolated as zinc chloride double salts. These early reports use the older type of nomenclature; *i.e.*, thiopyronine and selenopyronine for the respective thioxanthylium and selenoxanthylium ring system. The preparation of IIa, as reported in the early literature (3), used zinc and hydrochloric acid to reduce the thioxanthylium ring to the thioxanthene ring. The resulting leuco-base was unstable in air. We have found that Ia can be more conveniently reduced to IIa with sodium borohydride in water. Air oxidation was avoided by using deaerated solvents under an inert atmosphere. The corresponding selenium compound, IIb, was similarly prepared by the lithium aluminum hydride reduction of Ib in tetrahydrofuran. Temperatures higher than 30° must be avoided in the work-up of IIb. The selenoxanthene was sublimed to give pure white crystals that can be kept indefinitely without discoloration (oxidation) in darkened, evacuated glass ampoules. The colorless leuco-bases, IIa and IIb, rapidly become red when exposed to air. The ketones, IIIa and IIIb, were obtained by the alkaline permanganate oxidation of the zinc chloride double salts, Ia and b. Numerous attempts to improve the low yields of the selenoxanthone, IIIb, were unsuccessful.

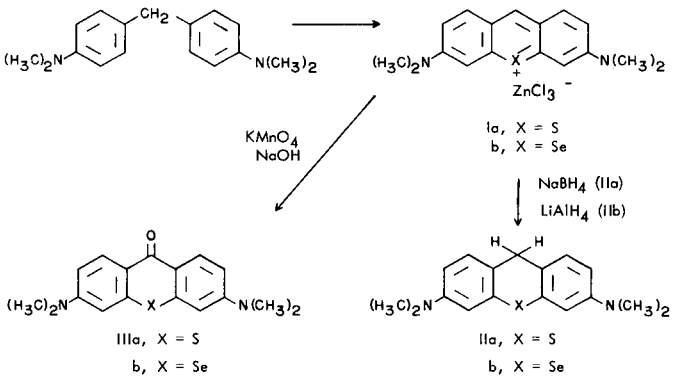


Figure 1

EXPERIMENTAL

Melting points are corrected. Elemental analyses were carried out by Schwarzkopf Microanalytical Laboratories, Inc., Woodside, N. Y. Infrared spectra were determined in potassium bromide pellets on a Perkin-Elmer Model 30 spectrophotometer. Visible and ultraviolet spectra were recorded with a Cary Model 14 spectrophotometer. Nuclear magnetic resonance (n.m.r.) spectra were obtained with a Varian A-60 spectrometer.

3,6-Bis(dimethylamino)thioxanthylium Chloride Zinc Chloride Double Salt (Ia).

Fuming sulfuric acid (20-30% sulfur trioxide) (200 g.) was placed in a 500-ml. Morton flask. Sulfur (20.0 g., 0.65 mole) was added in small portions, with vigorous stirring over a 15 minute period. The reaction flask was placed in an ice bath and 4,4'-bis(dimethylamino)diphenylmethane (20.0 g., 0.079 mole) was added in small portions, at such a rate that the temperature of the reaction mixture was maintained between 25° and 30°. This addition was completed in ten minutes. The ice bath was removed, the dark red mixture was stirred at ambient temperature for 1.5 hours and was then poured into 500 g. of ice. The resulting deep red solution was boiled for 1 hour and was allowed to cool overnight. The solution was filtered through a coarse glass fritted funnel, and a 40% aqueous solution of zinc chloride was added to the filtrate until a greenish reflex was noted (100 ml.). The solution was chilled in an ice bath and was filtered. The dark solid was dried and recrystallized from 3*M* hydrochloric acid (14 ml./g.) to give 2.16 g. of brilliant golden plates, m.p. 269-270°, dec. The mother liquor from the recrystallization was reduced to one-half volume and was cooled slowly for three days with a seed crystal to give an additional 2.59 g. of brilliant gold-green crystals, m.p. 266°, dec. These crystals had an infrared spectrum identical with that of the first crop. The total yield of Ia was 4.75 g. (13.2%). The visible and ultraviolet spectra of Ia showed λ max (EtOH), mμ (ε), 564 (131,000), and 284 (76,700).

3,6-Bis(dimethylamino)selenoxanthylium Chloride-Zinc Chloride Double Salt (Ib).

Fuming sulfuric acid (20-23% sulfur trioxide) (300 ml.) was placed in a 4 neck, 1-liter flask, equipped with a mechanical stirrer, pressure equalizing dropping funnel, and thermometer. A selenous acid solution was prepared by dissolving sodium selenite (10.0 g., 58 mmoles) in distilled water (14 ml.) and carefully adding concentrated sulfuric acid (160 ml.). This solution was placed in the dropping funnel. With ice bath cooling of the reaction flask, the simultaneous addition of 4,4'-bis(dimethylamino)diphenylmethane (50.0 g., 196 mmoles) and the selenous acid solution was begun in small portions and at such a rate that the reaction temperature did not rise above 35°. The addition was completed in 20 minutes. The ice bath was removed. The mixture was stirred at ambient temperature for 2 hours and was then poured onto 1 kg. of ice. The deep red solution was boiled for

2 hours and was cooled and filtered through a coarse glass fritted funnel. To the filtrate was added enough 50% aqueous zinc chloride solution to impart a green reflex to the surface of the filtrate. After 30 hours the solution was filtered and the crude product recrystallized from methanol (60 ml./g.) to give 7.70 g. (26.5%) of brilliant green needles, m.p. 298-300°. The yields of Ib were variable, and the quality of crude product varied from a dark crystalline solid to a tar with a golden reflex. Although large material losses were experienced, methanol was the most suitable solvent for recrystallization. The melting point was unchanged by further recrystallization. The visible and ultraviolet spectrum of Ib showed λ max (EtOH), mμ (ε), 570 (113,000), 285 (53,100).

3,6-Bis(dimethylamino)thioxanthene (IIa).

All solvents were reagent grade, were distilled under nitrogen, and were kept in amber bottles, sealed under nitrogen until used. All operations on the leuco-base (IIa) were performed under a nitrogen atmosphere.

A solution of Ia (1.00 g., 2.2 mmoles) in water (100 ml.) was treated with small amounts of sodium borohydride until the solution was colorless. The solution was stirred 20 minutes, and was then extracted with ether (two 100-ml. portions). The ether extracts were combined and transferred to a flask containing 100-ml. of absolute ethanol. The ether was removed by distillation under nitrogen. The slightly pink color of the residual ethanol solution was removed by adding 1 drop of 30% ammonium sulfide solution. Hot water was slowly added to the warm ethanol solution until a cloudiness persisted. The solution was allowed to cool slowly and then was chilled in an ice bath. The colorless crystals of the leuco-base were filtered and dried to give 0.52 g. (83%) of product, m.p. 150-151.5° (lit. (3) m.p. 130°). Further recrystallization from ethanol-water did not change the melting point.

Anal. Calcd. for $C_{17}H_{20}N_2S$: C, 71.78; H, 7.09; N, 9.85; S, 11.28. Found: C, 72.10; H, 7.17; N, 9.71; S, 11.23.

3,6-Bis(dimethylamino)selenoxanthene (IIb).

All solvents were distilled under nitrogen, and were kept in amber bottles sealed under nitrogen until used. All operations on the leuco-base (IIb) were performed under a nitrogen atmosphere.

To a rapidly stirred solution of lithium aluminum hydride (0.21 g., 5.5 mmoles) in 200 ml. of tetrahydrofuran, in a 500-ml. Morton flask, was added Ib (2.51 g., 5 mmoles), in small portions. The mixture was stirred for 3 hours. Water (10 ml.) was added to the colorless mixture to destroy the excess hydride. The mixture was filtered free of inorganic material, and the precipitate was washed with ethyl ether (two 30-ml. portions). An additional 200 ml. of water and 200 ml. of ethyl ether were added to the filtrate, and the ether layer was separated. The aqueous phase was extracted with ethyl ether (two 150-ml. portions). The ether extracts were combined with the original filtrate, and were dried over magnesium sulfate. The desiccant was removed and the ether solution was transferred to a 1-liter flask, equipped with a thermometer and a distillation head, containing 200 ml. of absolute ethanol. The ether was removed *in vacuo* while the temperature of the solution was maintained between 10° and 30° by means of a water bath. After most of the ether had been removed, 150 ml. of water was added to precipitate the leuco-base. The mixture was chilled in an ice bath and was filtered through a coarse glass fritted funnel. The yellow powder was transferred to a vacuum desiccator where it was dried overnight to yield a crude brownish product that weighed 1.46 g. (83%), m.p. 147-151°, dec. The average yield of six such reactions was 82%. Crude IIb (2.30 g.) was sublimed at 150-160°/0.05 mm Hg to yield 1.68 g. of white solid and a black tar as residue. The sublimate was resublimed at 120-135°/$<10^{-3}$ mm Hg to give 1.28 g. of pure white solid (m.p. 161-162°). No residue remained in the sublimator. The twice-sublimed material was transferred to glass tubes in an oxygen-free dry box. The tubes were evacuated to $<10^{-3}$ mm Hg and were sealed. Each tube was then wrapped in aluminum foil. The leuco-base showed no discoloration over a period of a year.

Anal. Calcd. for $C_{17}H_{20}N_2Se$: C, 61.63; H, 6.08; N, 8.46; Se, 23.83. Found: C, 61.56; H, 5.94; N, 8.31; Se, 24.03.

Spectral Data (leuco-bases, IIa and IIb).

The leuco-bases, IIa and IIb, possessed identical infrared and ^1H n.m.r. spectra. The infrared spectra showed λ max (KBr), (cm^{-1}), 2882, 2786, 1595 and 1493 (saturated and unsaturated C-H stretching), 1437 (methyl group deformation, and 1351 (C-N). ^1H n.m.r. in deuterochloroform showed peaks at (6) 2.83 singlet [6], 3.70 singlet [1] and 7.0 multiplet [3]. These are assigned respectively to the protons of the dimethylamino group, the protons of the 9-position, and the aromatic ring protons.

The ultraviolet and visible spectra of IIb were measured using twice-sublimed material in deaerated absolute ethanol. All necessary dilutions and transfer to cells were done under nitrogen in a darkened room. The ultraviolet spectrum showed λ max (EtOH), mμ (ε), 252 (31,900), and 310 (3,960). A very small peak in the visible spectrum at 571 mμ (ε60) probably resulted from the reaction of the leuco-base with traces of air in the solvent to form the selenoxanthylium cation (see Ib).

3,6-Bis(dimethylamino)thioxanthone (IIIa).

Ia (1.37 g., 3 mmoles) was added to a stirred solution of potassium permanganate (0.63 g., 4 mmoles) and sodium hydroxide (3.0 g., 80 mmoles) in 50 ml. of water. The mixture was refluxed for 2 hours, cooled and filtered. The brownish precipitate (manganese dioxide) was dried and extracted with benzene (500 ml.) in a Soxhlet apparatus for 16 hours. The benzene was removed *in vacuo* and the resulting orange solid was recrystallized from a minimum amount of benzene (charcoal) to give 0.37 g. (41.5%) of orange solid, m.p. 284° (lit. (3) m.p. 288°). Further recrystallization from absolute ethanol (charcoal) gave 0.25 g. (28%) of straw colored crystals, m.p. 292-293°. The ultraviolet spectrum of IIIa showed λ max (EtOH), mμ (ε), 268 (45,400), 384 (40,500).

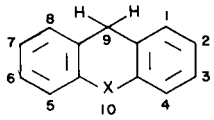
3,6-Bis(dimethylamino)selenoxanthone (IIIb).

Ib, (1.50 g., 2.93 mmoles) was added to a stirred solution of potassium permanganate (0.63 g., 4 mmoles) and sodium hydroxide (7.0 g., 175 mmoles) in 150 ml. of water. The solution was refluxed for 4 hours, cooled and filtered. The brown precipitate (manganese dioxide) was dried and was extracted with benzene (500 ml.) in a Soxhlet apparatus for 16 hours. Removal of benzene *in vacuo* yielded an orange solid that was recrystallized from a minimum amount of absolute ethanol (charcoal) to give 0.22 g. (21%) of dark green crystals, m.p. 261-263° (lit. (4c) m.p. 261°). The ultraviolet spectrum of IIIb showed λ max (EtOH), mμ (ε), 388 (41,700), 277 (34,200) and 260 (30,700).

REFERENCES

(1) This investigation was supported by the Air Force Avionics Laboratory, ASD, Wright-Patterson Air Force Base, Ohio, under contracts AF 33(657)-11430 and AF 33(615)-1343.

(2) Nomenclature and numbering used throughout this paper is in accord with Chemical Abstracts usage as given below.



(xanthene Numbering)

X = O xanthene

X = S thioxanthene

X = Se selenoxanthene

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(4) M. Battegay and G. Hugel, (a) *Bull. Soc. Chim. Belges*, 29, 557 (1920), (b) *ibid.*, 30, 1103 (1921), (c) *ibid.*, 31, 440 (1922).

(5) M. Battegay and P. Fries, *ibid.*, 30, 1098 (1921).

(6) N.m.r. values are in p.p.m. vs. tetramethylsilane. The brackets [ ] enclose the integrated ratio of protons.

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