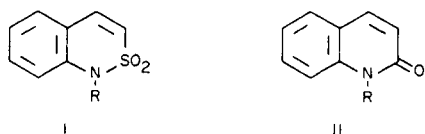


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### Sulfostyryl. III. Reactions

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In a previous paper (1), the synthesis of sulfostyryl (2,1-benzothiazine-2,2-dioxide) (I), the sulfone analog of the carbostyryls (II) was described.



This report deals with some reactions of sulfostyryl, the preparation of various derivatives, and some chemical differences between carbostyryls and sulfostyryls.

The reactions are summarized in Fig. 1.

Sulfostyryl is readily hydrogenated to dihydrosulfostyryl (III). It can be methylated (VII) with methyl sulfate in aqueous alkali, but alkylation with aminoalkyl halides (to give VI,  $n = 2$  and 3) gave satisfactory yields only when carried out using sodium hydride in dimethylsulfoxide. Arylation (IV) was carried out using diphenyliodonium chloride in alkaline methanol solution, catalyzed by cuprous chloride.

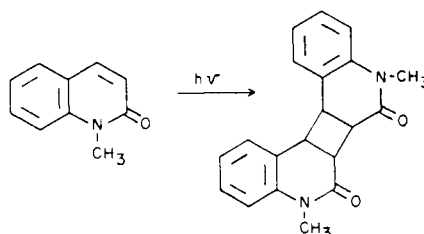
Bromination of 3,4-dihydrosulfostyryl with *N*-bromosuccinimide (NBS) has been shown to give 6-bromo- or 6,8-dibromosulfostyryl depending on whether one or two equivalents of NBS is used (2). In contrast, sulfostyryl even with a limited amount of NBS, gives a complex mixture from which only a tribromo derivative (V) could be isolated. By analogy with the earlier results (2), two of the bromines are in the 6 and 8 positions; the remaining halogen atom is believed to be in the 3 or 4 position.

*N*-Methylsulfostyryl on reaction with *N*-bromosuccinimide gives a monobromosulfostyryl (VIII); the bromine is assumed to be in the 6 position by analogy with the results observed in the dihydrosulfostyryl series, and by analogy with the results observed on brominating *N*-methylcarbostyryl. When this latter compound was reacted with NBS under the same conditions — brief heating in dimethylformamide — a monobromocarbostyryl was obtained, and was shown to be 6-bromo-*N*-methylcarbostyryl (3) by comparison with an authentic sample prepared unambiguously from 6-bromoquinoline.

The sulfostyryls differ chemically from the carbostyryls

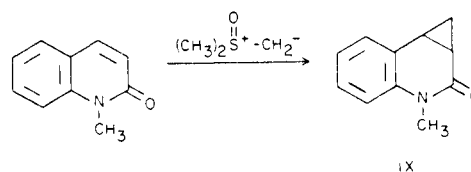
in two important ways:

On exposure to ultraviolet light, carbostyryls readily undergo dimerization in high yield, within a few hours, to form compounds having the structures shown below (4):



In contrast, the sulfostyryls on exposure to ultraviolet light for as long as a week are recovered unchanged.

Carbostyryls react smoothly and clearly with dimethylsulfoxonium ylid to form the tricyclic compounds IX (5) in high yield. *N*-Methylsulfostyryl, under the same conditions, gave a mixture of compounds having the correct elemental analysis for a cyclopropane but which did not show any cyclopropyl absorption in the n.m.r., instead it showed *C*-methyl absorption, and from a comparison with n.m.r. spectra of 3- and 4-substituted *N*-methylsulfostyryls



it was found to be a mixture of the 3 and 4 methyl derivatives.

#### EXPERIMENTAL (6)

##### Dihydrosulfostyryl (III).

Sulfostyryl (1) (I) was hydrogenated in ethanol using a 5% palladium-on-carbon catalyst at 50 p.s.i.g. After the theoretical amount of hydrogen had been absorbed, the catalyst was filtered and the solvent removed, *in vacuo*, giving a 90% yield of dihydrosulfostyryl, m.p. 155-156°, identical with an authentic sample (lit. (2) m.p. 155-156°).

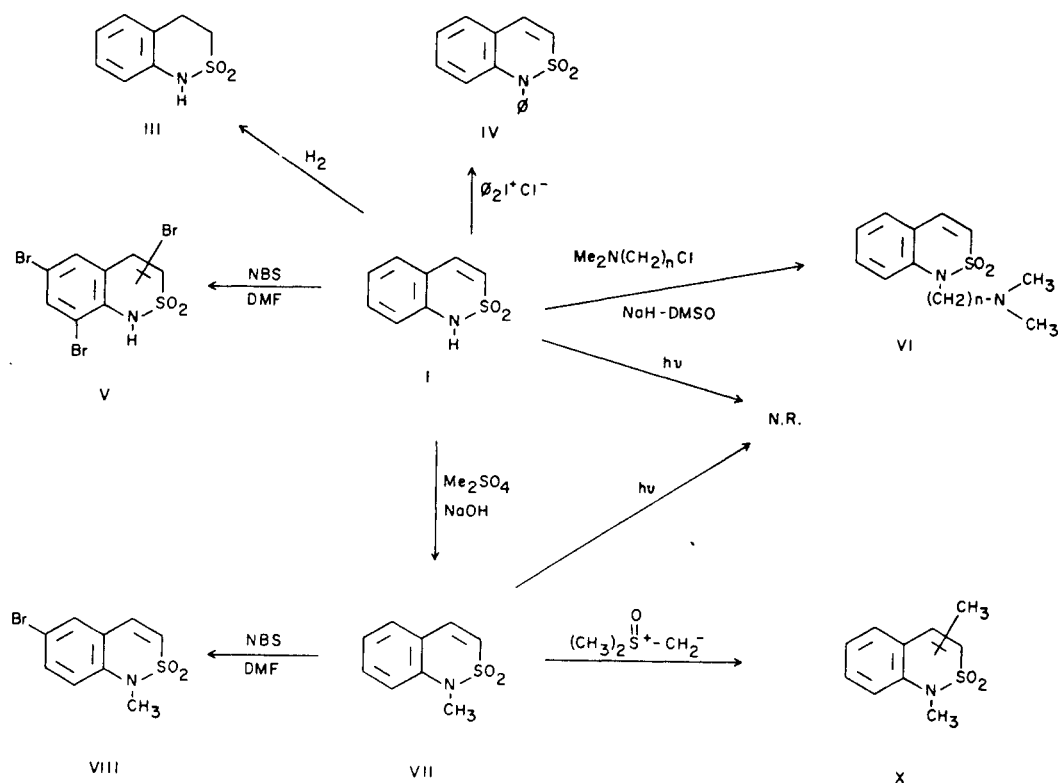


Fig. 1 Reaction of Sulfostyryls

*N*-Methylsulfostyryl (VII).

Sulfostyryl (1) (10 g., 0.053 mole) was dissolved in 10% sodium hydroxide, and 25 ml. of dimethyl sulfate was added. The mixture was warmed and at 40° the reaction became exothermic and an oil separated. On cooling, the oil crystallized and was recrystallized from isopropyl ether, giving 7.3 g. (68% yield), m.p. 70-71°.

*Anal.* Calcd. for  $\text{C}_9\text{H}_9\text{NO}_2\text{S}$ : C, 55.37; H, 4.65; N, 7.17. Found: C, 55.73; H, 4.59; N, 7.08.

*N*-Dimethylaminoethylsulfostyryl (VI, n = 2).

Sodium hydride (0.018 mole, 0.8 g. of a 55% dispersion in mineral oil) was added to a solution of 3.0 g. (0.0166 mole) of sulfostyryl (1) in 50 ml. of dry dimethylsulfoxide. When evolution of hydrogen ceased, a solution of 0.041 mole of dimethylaminoethyl chloride in benzene was added and the mixture was heated on the steam bath for eighteen hours. The volatile materials were removed, *in vacuo*, and water was added to the residue. Extraction with ether and removal of the solvent gave a brown oily material which was dissolved in ether and converted to the hydrochloride with gaseous hydrogen chloride, 78% yield, m.p. 237.5-241° when recrystallized from alcohol-water. The salt was somewhat hygroscopic.

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{17}\text{ClN}_2\text{O}_2\text{S}\cdot 0.3\text{H}_2\text{O}$ : C, 48.99; H, 5.93; N, 9.60. Found: C, 49.35; H, 5.97; N, 9.57.

*N*-Dimethylaminopropylsulfostyryl (VI, n = 3).

Using the same procedure described above and employing 4.0 g. of sulfostyryl (1), 1.1 g. of sodium hydride dispersion, and 6.5 g. of

3-dimethylaminopropyl chloride, there was obtained *N*-(3-dimethylaminopropyl)sulfostyryl hydrochloride, 3.4 g., m.p. 132-135°. After drying, the melting point rose to m.p. 161-162°. The salt was hygroscopic.

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{19}\text{ClN}_2\text{O}_2\text{S}\cdot 0.3\text{H}_2\text{O}$ : C, 50.66; H, 6.41; N, 9.01. Found: C, 50.58; H, 6.46; N, 9.39.

*N*-Phenylsulfostyryl (IV).

A mixture of 10.0 g. (0.0552 mole) of sulfostyryl, 19.9 g. of diphenyliodonium chloride (0.0828 mole) and 3.0 g. of sodium methoxide (0.0552 mole) was dissolved in 200 ml. of methanol. To this slurry was then added 0.5 g. of cuprous chloride and the mixture was heated, with stirring, to reflux, whereupon the solution turned dark and a precipitate formed. The mixture was heated for eighteen hours, then filtered and the filtrate evaporated to dryness, leaving a black semi-solid. Water and dilute base was added and then the suspension was extracted with methylene chloride. The organic layer was dried and concentrated, *in vacuo*, leaving a solid residue of 3.0 g., m.p. 141-153°. The solid was recrystallized from ethyl acetate to give 1.8 g. of product, m.p. 155.5-156.5°.

*Anal.* Calcd. for  $\text{C}_{14}\text{H}_{11}\text{NO}_2\text{S}$ : C, 65.35; H, 4.31; N, 5.44. Found: C, 65.13; H, 4.33; N, 5.34.

*N*-Methyl-6-bromosulfostyryl (VIII).

A mixture of 5.0 g. (0.0256 mole) of *N*-methylsulfostyryl and 4.56 g. (0.0256 mole) of *N*-bromosuccinimide was dissolved in

15 ml. of dimethylformamide and heated on a steam bath for three hours. The solution was poured into water and the brown oil that separated was extracted into hot isopropyl ether and then chilled, giving 2.0 g. of product, m.p. 102-103°.

*Anal.* Calcd. for  $C_9H_8BrNO_2S$ : C, 39.44; H, 2.94; N, 5.11. Found: C, 39.77; H, 2.96; N, 4.85.

#### 6,8, x-Tribromosulfostyryl (V).

A mixture of 5.0 g. (0.0277 mole) of sulfostyryl, and 9.86 g. (0.0554 mole) of *N*-bromosuccinimide was treated with 25 ml. of dimethylformamide, whereupon an immediate vigorous reaction occurred. The resulting brown solution was heated on the steam bath for two hours, cooled, and poured into 300 ml. of water. An oil separated and was extracted with chloroform, then the organic layer was dried and concentrated, giving an oil which slowly partially crystallized. On stirring with ether, a small amount of white solid formed which was discarded. The filtrate was concentrated and the resulting brown oil was chromatographed on alumina, using methanol as solvent. A dark, non-fluorescent band formed on the alumina and was extruded and extracted with hot methanol, giving 1.7 g. of a gum. The gum was treated with dilute sodium hydroxide, and, on acidification, a solid separated, 1.0 g., m.p. 160-169°. Recrystallization from ethanol-water gave 0.5 g. of tribromide, m.p. 179-180°.

*Anal.* Calcd. for  $C_8H_4Br_3NO_2S$ : C, 23.0; H, 0.95; N, 3.35; Br, 57.4. Found: C, 23.08; H, 1.02; N, 3.45; Br, 57.33.

#### *N*-Methyl-6-bromocarbostyryl.

A mixture of 3.2 g. (0.02 mole) of *N*-methylcarbostyryl and 3.6 g. (0.02 mole) of *N*-bromosuccinimide was treated with dimethylformamide. Within a few minutes, the solid dissolved and a mild exothermic reaction occurred. The mixture was heated for five minutes on a steam bath and then poured into water. The solid which separated was filtered, m.p. 110-125°. It was chromatographed on silica gel using chloroform as eluent; two fractions were obtained; one had m.p. 144-146°, 0.9 g., identical by infrared and mixed melting point with authentic *N*-methyl-6-bromocarbostyryl (3). Another material was obtained, 1.0 g., m.p. 142-145°, analyzing as a monobromo derivative, but which depressed the melting point on mixing with *N*-methyl-6-bromocarbostyryl.

*Anal.* Calcd. for  $C_{10}H_8BrNO$ : C, 50.45; H, 3.39; N, 5.88. Found: C, 50.45; H, 3.20. N, 5.60.

#### 1,3 (and 1,4)-Dimethylsulfostyryl (X).

Sodium hydride (7.96 g., 0.185 mole, 55% dispersion in mineral oil) was added portionwise and with cooling to a suspension of 40.5 g. (0.185 mole) trimethylsulfoxonium iodide in 175 ml. of dry dimethylsulfoxide. The mixture was stirred for one hour and then a concentrated solution of 9.0 g. (0.0462 mole) of 1-methylsulfostyryl in dimethylsulfoxide was added. The mixture was heated at 70° for three hours and then was poured into water. A yellow solid precipitated and was extracted with chloroform; the solution was dried and concentrated, giving 9.7 g. of solid, m.p. 69-98°. Attempts were made to separate this mixture into its component by chromatography on alumina, using benzene as solvent, however, all fractions obtained gave a broad melting range. The combined fractions had a melting point range of 78-112° and analyzed correctly for a dimethylsulfostyryl.

*Anal.* Calcd. for  $C_{10}H_{11}NO_2S$ : C, 57.39; H, 5.30; N, 6.69. Found: C, 57.31; H, 5.51; N, 6.42.

#### Attempted Photodimerization of *N*-Methylsulfostyryl.

*N*-Methylsulfostyryl (1.0 g.) was dissolved in 30 ml. benzene in a Vycor flask, and irradiated using a 140 watt Hanovia high pressure mercury vapor lamp without a filter. After seven days exposure, the solution had darkened and a small amount of tar separated. The solution was concentrated and 0.9 g. of starting material was recovered. The same results were observed when 0.5 ml. acetone was used as an activator. Under either of these conditions, *N*-methylcarbostyryl is converted to the dimer in better than 90% yield in 5 hours.

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- (6) All melting points are corrected. Analysis were performed by the Analytical Department of these laboratories.

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