Chemistry of Substituted Styrene Sulfides

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Syntheses of *p*-nitro-, *p*-methoxy-, and the unsubstituted styrene sulfides from the corresponding oxides via the intermediate thiuronium salts are described. Methoxystyrene sulfide is more stable under solvolytic conditions than the corresponding oxide, a fact related to the reduced strain in the sulfide. The strain enthalpies of ethylene oxide and ethylene sulfide are 21.47 and 17.62 kcal. per mole, respectively.

IN CONNECTION with an ultraviolet spectral study of aryl-substituted three-membered ring compounds (*9*), the *p*-nitro- and *p*-methoxystyrene sulfides as well as the already known unsubstituted styrene sulfide were required. The synthesis of *cis*- and *trans*-stilbene sulfide from the oxides was published earlier (*7*); the present report is an extension of this procedure (*1*) to the preparation of these styrene sulfides.

This method and several other procedures had failed earlier to afford substituted stilbene sulfides from any of the following oxides: *trans*-4-methoxystilbene oxide, *trans*-4,4′-dimethoxystilbene oxide, *trans*-4-methoxy-4′-nitrostilbene oxide, *cis*- and *trans*-4-nitrostilbene oxide, and *cis*- and *trans*-4,4′-dinitrostilbene oxide. Attempted preparations of any of the *cis*-4-methoxy substituted stilbene oxides failed.

EXPERIMENTAL

Melting points are corrected. Microanalyses were performed at the Microanalytical Laboratory, Department of Chemistry, University of California, Berkeley, Calif. NMR spectra were recorded on a Varian Associates A-60 high resolution spectrometer with tetramethylsilane as an internal standard.

Preparation of the *S*-(1-Aryl-2-hydroxyethyl)thiuronium Sulfates (IIa, b, c). The procedure is illustrated by the preparation of the *p*-methoxy derivative (IIb). Five grams (0.037 mole) of the oxide (*3*) (Ib) was added (10 min.) to a stirred solution of 20 ml. of water, 3.05 grams (0.04 mole) of thiourea, and 2.0 grams (0.04 equiv.) of concentrated sulfuric acid at 23° C. After 10 hours, the product was filtered and washed with ethanol and then ether. There was obtained 6.7 grams (37%) of S-(1-*p*-methoxyphenyl-2-hydroxyethyl) thiuronium sulfate, m.p. 167–168° C. The NMR spectrum (in trifluoroacetic acid, TFAA) showed a triplet, $\delta = 4.4$ (CH), and a doublet. $\delta = 3.8$. Anal: Calcd. for $C_{10}H_{16}N_2O_6S_2$: S, 19.76. Found: S, 20.58.

p-Nitrostyrene oxide (*2*) (Ic) was converted in 78% yield to the *p*-nitrophenylthiuronium salt (IIc), m.p. 165–167° C. The NMR spectrum (TFAA) showed a triplet, $\delta = 4.6$, and a doublet, $\delta = 3.9$. Anal: Calcd. for $C_{18}H_{24}N_6O_{10}S_3$: S, 16.57. Found: S, 16.72.

S-(1-Phenyl-2-hydroxyethyl) thiuronium sulfate (IIa), m.p. 169–170° C. was prepared in 53% yield from styrene oxide (Ia). The NMR spectrum (TFAA) showed a triplet, $\delta = 4.42$, and a doublet, $\delta = 3.85$. Anal: Calcd. for $C_{18}H_{26}N_4O_6S_3$: S, 19.61. Found: S, 19.77.

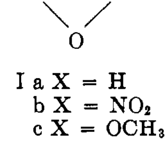
***p*-Methoxystyrene Sulfide (IIIb).** The intermediate (IIb, 10 grams, 0.018 mole) was suspended in 25 ml. of water and made alkaline (pH-9) with 10% sodium carbonate. The mixture was stirred for 10 minutes, and the crude product was collected and washed with water to give 5.3 grams, 33% based on oxide (Ib), m.p. 43–45° C. Crystallization from hexane afforded white needles, m.p. 57–58° C. Anal: Calcd. for $C_9H_{10}OS$: C, 65.02; H, 6.06; S. 19.29. Found: C, 64.88; H, 6.21; S, 19.37.

Styrene Sulfide (IIIa). The salt (IIa, 10.0 grams, 0.0205 mole) was suspended in 20 ml. of water and 30 ml. of peroxide-free ether, and the aqueous phase was made alkaline (pH-9) with sodium carbonate. The product was extracted with ether, and the extract was dried and concentrated under vacuum to give 1.31 grams (49%) of styrene sulfide. The material was crystallized repeatedly from hexane at low temperature to give a product with m.p. −7 to −6° C. This material had ultraviolet and infrared spectra identical to those of styrene sulfide, prepared according to the method of Guss and Chamberlain(*4*).

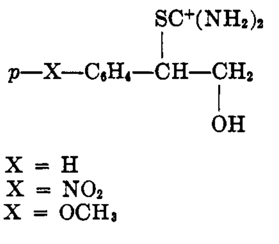
***p*-Nitrostyrene Sulfide (IIIc).** A 3.5-gram (0.006 mole) sample of the thiuronium salt (IIc) was suspended in 30 ml. of peroxide-free ether, and was made alkaline (pH-7.5) with 5% sodium bicarbonate. The mixture was stirred for 30 minutes. The ether phase was separated, dried over anhydrous sodium sulfate, and concentrated under vacuum to yield 1.6 grams (73%, based on oxide) of *p*-nitrostyrene sulfide, m.p. 39–41° C. Crystallization from hexane gave fine white needles m.p. 55-56° C or pale yellow needles, m.p. 63-64° C. Anal: Calcd. for $C_8H_7NO_2S$: C, 53.02; H, 3.89; N, 7.73; S, 17.69. Found: C, 52.78; H, 3.78; N, 7.63; S, 17.55.

RESULTS AND DISCUSSION

In view of the adverse effect of these substituents on the stilbene sulfide synthesis, it was surprising that the styrene sulfides were so easily obtained. Reaction of the corresponding oxide (I) with thiourea and acid (*1*, *7*) gave the intermediate thiuronium salt (II) which, when treated with base (*1*, *7*), gave the sulfide (III).

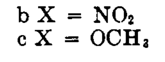


I a X = H
b X = NO_2
c X = OCH_3



$$p\text{—X—}C_6H_4\text{—}\underset{\displaystyle}{\overset{\displaystyle SC^+(NH_2)_2}{\overset{|}{CH}}}\text{—}\underset{\displaystyle OH}{\underset{|}{CH_2}}$$

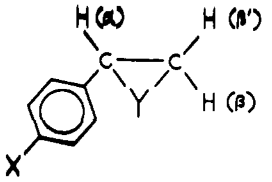
II a X = H
b X = NO_2
c X = OCH_3



III a X = H
b X = NO_2
c X = OCH_3

The only difficulty encountered was conversion of the intermediate nitro-substituted thiuronium salt to the sulfide. The usual procedure afforded a noncrystalline, apparently poly-

Table I. NMR Spectral Data[a] on



		Chemical Shifts[b]			Coupling Constants[c]		
X	Y	α	β	β'	αβ	αβ'	ββ'
OCH_3	O	3.6[d]	2.94	2.66	4.6	2.5	5.5
OCH_3	S	3.6[d]	2.61	2.38	6.5	6.0	1.7
H	O	3.25	2.44	2.15	4	3	6
H	S	3.48	2.33	2.16	7	5.5	1.1
NO_2	O	4.00	3.26	2.80	4	2.5	5.8
NO_2	S	3.9	2.91	2.62	7	5	2

[a] In $CDCl_3$. [b] In δ, p.p.m., downfield from tetramethylsilane, used as an internal standard. [c] In c.p.s. [d] The exact position was obscured by the CH_3O group resonance. Coupling constants were checked by determining the spectrum in pyridine.

Table II. Comparison of Data for Oxiranes and Thiiranes and Unstrained Analogs

Strained Compound	ΔH_1[a] Form.	Unstrained Compound	ΔH_2[a] Form.	ΔH_3[a,b] 2H	ΔH_4[a,c] Strain
$CH_2—CH_2O$	−12.20[d]	CH_3OCH_3	−44.35[d]	−32.15	21.47
$CH_2—CH_2S$	19.30[d]	CH_3SCH_3	−8.99[d]	−28.30	17.62

[a] In kcal./mole. [b] Enthalpy of hydrogenation, $\Delta H_2 - \Delta H_1$. [c] ΔH_n for hydrogenation of an unstrained bond ($C_2—C_3$ in *n*-butane) is −10.68 kcal.,[d] $\Delta H_n - \Delta H_3 = \Delta H_4$, the strain enthalpy of the ring. Compare with ΔH_4 for cyclopropane = 27.60[d]. [d] (*8*).

meric product. However, when the suspension was made basic with sodium bicarbonate in the presence of peroxide-free ether to extract the product as it was formed, a good yield of the sulfide was obtained. The adverse effect of the stronger base must be manifest prior to product formation, since the product, once formed, is stable toward both sodium carbonate and sodium hydroxide. This procedure also resulted in a convenient synthesis of styrene sulfide in which the product was purified by crystallization at reduced temperatures.

One minor ambiguity concerned the structure of the intermediate thiuronium salts. That all of the salts have structure II can be seen from the values and the near identity of the NMR chemical shifts for the CH and CH_2 groups in each compound. The NMR spectra of the styrene sulfides and the substituted styrene oxides are similar to that of styrene oxide (*6*) in that the three structurally unique aliphatic protons represent an ABX system which results in three quartets. These data are given in Table I.

The stability of the styrene sulfides was studied spectroscopically in connection with earlier work (*9*). All of the sulfides were stable in dilute ethanolic sodium hydroxide at room temperature. Under acid conditions *p*-methoxystyrene sulfide was more stable than *p*-methoxystyrene oxide (*3*). The sulfide underwent slow ethanolysis over a 24-hour period. The solvolysis was faster in 50% ethanol. Like the oxygen analog (*5*), *p*-nitrostyrene sulfide was stable to both acid and base in either alcohol or aqueous alcohol.

The increased stability of *p*-methoxystyrene sulfide relative to the oxide is surprising in view of the decreased strength of the carbon-sulfur bond. There appear to be two possible explanations: first, the lower basicity of sulfur may result in a significant decrease in concentration of the protonated form, thus retarding the reaction. The other possibility relates to the expected smaller strain in the thiirane relative to the oxirane ring giving rise to a higher activation energy for carbon-sulfur bond breaking.

There is no reference in the literature to the amount of strain in either thiiranes or oxiranes. However, the data are available from which to calculate these values for the unsubstituted compounds. The enthalpy of hydrogenation for the strained carbon-carbon bond in ethylene oxide can be obtained from the difference in the enthalpy of formation of ethylene oxide and methyl ether. Subtraction of this value from the enthalpy of hydrogenation of an unstrained carbon-carbon bond affords the strain enthalpy of the cyclic system. These data, together with comparable data for ethylene sulfide, are given in Table II. Thus, the strain energy of ethylene sulfide is 4 kcal. per mole less than that of ethylene oxide, which is 6 kcal. per mole less than cyclopropane. It is reasonable to assume that the greater stability of *p*-methoxystyrene sulfide relative to the oxide results partly from its smaller strain.

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