5-Trimethylsilylindole (VI).—A solution of 5-trimethylsilylindoline (8 g, 0.042 mol) in xylene (110 ml) was heated under reflux for 4 hr, in the presence of 10% Pd-C (0.9 g). The reaction mixture was filtered and fractionally distilled. The 5-trimethylsilylindole (6 g, 75%) distilled at 103–105° (1 mm) or at 110–114° (2 mm) and solidified to crystals: mp 42°; λ_{max} 223 mμ (ε 56,000), 274 (5600), and 293 (3500).

Anal. Calcd for $C_{11}H_{15}NSi$: C, 69.78; H, 7.98; N, 7.40; Si, 14.82. Found: C, 69.39; H, 7.89; N, 7.34; Si, 14.35.

5-Trimethylsilylgramine (VII).—A mixture of acetic acid (20 ml), dioxane (20 ml), 37% aqueous formalin solution (1.6 g), and 28% aqueous dimethylamine solution (3.2 g) was cooled to 0° in an ice bath, and 5-trimethylsilylindole (3.8 g, 0.02 mol) was dropped in slowly with stirring during 1 hr and left overnight. The reaction mixture was diluted with water to a volume of 300 ml and filtered. The filtrate was made strongly alkaline with sodium hydroxide solution, and the trimethylsilylgramine separated out as an oil which solidified on standing to yield 4.3 g (87%): mp 113° on recrystallization from petroleum ether; λ_{max} 226 mμ (ε 51,500), 282 (5300), and 292 (4200).

Anal. Calcd for $C_{14}H_{22}N_2Si$: C, 68.24; H, 9.00; N, 11.37; Si, 11.39. Found: C, 68.14; H, 9.13; N, 11.29; Si, 11.51.

5-Trimethylsilyl-3-piperidinomethylindole (VIII).—5-Trimethylsilylgramine (1 g, 0.004 mol) in piperidine (20 ml) was heated under reflux for 3 hr. Excess piperidine was removed *in vacuo*, and petroleum ether was added to the residual oil. The 5-trimethylsilyl-3-piperidinomethylindole (1 g, 86%) crystallized out: mp 126° on recrystallization from petroleum ether; λ_{max} 226 mμ (ε 50,000), 284 (5400), and 294 (4100).

Anal. Calcd for $C_{17}H_{26}N_2Si$: C, 71.27; H, 9.15; N, 9.77; Si, 9.80. Found: C, 71.11; H, 9.20; N, 9.60; Si, 9.62.

5-Trimethylsilylindole-3-acetonitrile (X).—Methyl iodide (4 ml) in petroluem ether (10 ml) was added with stirring into a solution of 5-trimethylsilylgramine (1.23 g, 0.005 mol), stirred for 30 min, and left overnight in the cold. The precipitated methiodide was filtered off, dried, and dissolved in 50% aqueous ethanol (100 ml). Sodium cyanide (3 g, 0.06 mol) was added and the solution was stirred and heated to 70–80° for 2 hr. Water (100 ml) was added and the 5-trimethylsilyl-3-indole acetonitrile was taken up in chloroform, washed with water, dried, and concentrated *in vacuo*. Petroleum ether was then added to the concentrated solution to precipitate the nitrile. A yield of 0.82 g (72%) was obtained: mp 105° on recrystallization from chloroform–petroleum ether; λ_{max} 225 mμ (ε 52,000), 283 (5500), and 283 (4100).

Anal. Calcd for $C_{13}H_{16}N_2Si$: C, 68.37; H, 7.06; N, 12.27; Si, 12.29. Found: C, 68.23; H, 6.85; N, 12.53; Si, 12.44.

5-Trimethylsilylindole-3-acetic Acid (XI).—5-Trimethylsilylindole-3-acetonitrile (1.2 g, 0.0052 mol) in ethanol (25 ml) was hydrolyzed by heating with a solution of potassium hydroxide (4.5 g) in water (15 ml) for 10 hr in a nitrogen atmosphere. The reaction mixture was cooled, diluted with water (200 ml), and filtered. The filtrate was brought to pH 7 with hydrochloric acid and left to crystallize out in the cold for several hours, yielding 1 g (77%) of 5-trimethylsilylindole-3-acetic acid: mp 110° on recrystallization from chloroform–petroleum ether; λ_{max} 229 mμ (ε 49,500), 284 (5200), and 294 (4000).

Anal. Calcd for $C_{13}H_{17}NO_2Si$: C, 63.12; H, 6.93; N, 5.66; Si, 11.34. Found: C, 62.27; H, 7.05; N, 5.39; Si, 11.62.

5-Trimethylsilyltryptamine (XII).—A solution of 5-trimethylsilylindole-3-acetonitrile (0.8 g, 3.5 mmol) in dry ether (50 ml) was added slowly with stirring into lithium aluminium hydride (2 g, 0.053 mol) in ether (80 ml), and the mixture stirred for 10 hr. Excess lithium aluminium hydride was destroyed by addition of ethyl acetate, followed by water and then by 20% sodium hydroxide solution (4 ml). The reaction mixture was filtered, the precipitate was washed thoroughly with ether, and the combined ethereal solutions were washed with water and dried over magnesium sulfate. Upon removal of the ether 5-trimethylsilyltryptamine remained as an oil which solidified on addition of petroleum ether to yield 0.59 g (78%): mp 103° on recrystallization from chloroform–petroleum ether; λ_{max} 227 mμ (ε 48,500), 285 (5000), and 295 (4000).

Anal. Calcd for $C_{13}H_{20}N_2Si$: C, 67.19; H, 8.68; N, 12.06; Si, 12.08. Found: C, 66.98; H, 8.64; N, 12.32; Si, 12.36.

β-(5-Trimethylsilylindolyl)ethanol (XIII).—A solution of 5-trimethylsilylindole-3-acetic acid (1 g, 4×10^{-3} mol) in dry ether (50 ml) was added slowly with stirring into lithium aluminium hydride (1.5 g, 0.04 mol) in ether (50 ml), and the reaction mixture was stirred for 15 hr. Excess lithium aluminium hydride was destroyed by addition of a minimal quantity of water and the reaction mixture was filtered. The precipitate was washed thoroughly with ether and the combined ethereal solutions were washed with bicarbonate solution, followed by water, and dried over magnesium sulfate. The ether was driven off *in vacuo* and the β-(5-trimethylsilylindolyl)ethanol (0.76 g, 82%) distilled at 138–142° (1 mm): λ_{max} 229 mμ (ε 42,500), 285 (4800), and 295 (3700).

Anal. Calcd for $C_{13}H_{19}NOSi$: C, 66.91; H, 8.21; N, 6.00; Si, 12.02. Found: C, 66.81; H, 8.23; N, 6.25; Si, 11.82.

A New Synthesis of 6-Phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole

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A four-step synthesis of the anthelmintic *dl*-6-phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole hydrochloride (tetramisole) from styrene oxide and ethylenimine is described. The key step is the reaction of α-phenyl-2-aziridineethanol with thiocyanic acid to give 2-imino-α-phenyl-3-thiazolidineethanol hydrochloride which proceeds in excellent yield.

The reported[1] broad spectrum anthelmintic activity of 6-phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole hydrochloride (VI) prompted the search for a new and more general synthetic route. The previous major synthesis[2] of VI involved the condensation of a phenacyl halide with 2-aminothiazoline, sodium borohydride reduction of the resultant 3-aroylmethyl-2-iminothiazolidine, and subsequent ring closure. This paper describes a new synthesis of VI starting with styrene oxide and ethylenimine.

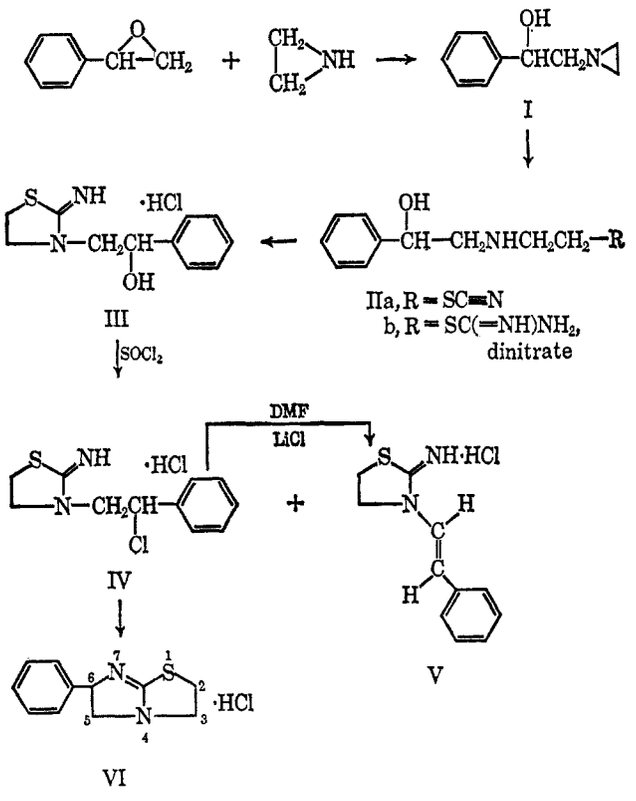
Condensation of ethylenimine and styrene oxide gave α-phenyl-1-aziridineethanol (I), which reacted with thiocyanic acid to provide 2-imino-α-phenyl-3-thiazolidineethanol hydrochloride (III). Reaction of III with thionyl chloride, followed by ring closure gave VI.

Funke and Benoit[3] obtained crystalline I in a 48% yield from the reaction of styrene oxide with ethylenimine and a trace of water in a sealed tube at 100°. Initial results in this laboratory showed that the reac-

(1) (a) D. C. I. Thienpont, O. F. J. Vanparijs, A. H. M. Raeymaekers, J. Vandenberk, P. J. A. Demoen, F. T. N. Allewijn, R. P. H. Marsboom, C. J. E. Niemegeers, K. H. L. Schellekens, and P. A. J. Janssen, *Nature*, **209**, 1084 (1966); (b) J. S. Remders, *Neth. J. Vet. Sci.*, **91**, 967 (1966); (c) J. W. Pankhurst and D. O. Sutton, *Vet. Record*, **79**, 166 (1966); J. K. Walley, *ibid.*, **78**, 406 (1966).

(2) (a) A. H. M. Raeymaekers, F. T. N. Allewijn, J. Vandenberk, P. J. A. Demoen, T. T. T. V. Offenwert, and P. A. J. Janssen, *J. Med. Chem.*, **9**, 545 (1966). (b) The route to tetramisole starting with styrene oxide and ethylenimine was independently discovered in the Research Laboratories of I.C.I.A.N.A.: A. Baklien, *et al.*, submitted for publication in *Aust. J. Chem.*

(3) A. Funke and G. Benoit, *Bull. Soc. Chim. Fr.*, 1021 (1953).



tion could be carried out without a sealed tube, and a study of the effect of solvents, temperatures, and mole ratios on the reaction rate and yield was initiated. For this purpose nmr analyses of the reaction was a convenient and rapid method of screening the effects of a wide range of variables. In the various solvent systems tested, the methine hydrogen or the X portion of an ABX system in styrene oxide appeared in the region of τ 6.2, whereas the methine hydrogen of I appeared near 5.2. Product formation could usually be calculated by integration of these two areas. In cases where the τ 5.0 region was obscured, the integrations of the methylene protons at τ 7.6 of I and of the styrene oxide methine proton were utilized.

Most significant in the variables tested was the mole ratio of ethylenimine to styrene oxide. Increasing the ethylenimine–styrene oxide ratio from equimolar to 4.5:1 resulted in large increases in product formation, with essentially no further increase at a 6:1 ratio. The presence of lower molecular weight alcohols and water in relatively low concentrations gave a definite acceleration to the reaction rate. Ethanol (in concentrations up to *ca.* 16% by weight) was found to be the most effective of these agents in increasing the rate of product formation without appreciable increases in side product formation. However, the final yield of I (as measured by nmr, gas chromatography, and distillation) was quite close to that obtained without alcohol. With other solvent systems such as pyridine, cyclohexane, decalin, chloroform, acetonitrile, acetone, water, and aqueous base the rate of product formation and/or yield was lowered. When benzene was the solvent, no reaction took place.

Similar solvent effects have been observed by Parker[4] for the reaction of styrene oxide and benzylamine. In Parker's study, varying amounts (8–40.5%) of the "abnormal" isomer in the product, resulting from amine attack at the more highly substituted carbon, were obtained. The lowest ratio of "abnormal" isomer was obtained in diethylene glycol dimethyl ether and the highest in methanol. In contrast to the results with benzylamine, the secondary amine piperidine gave only 4% of the "abnormal" isomer on reaction with styrene oxide in ethanol.[5]

In the present work, the presence of small amounts of the "abnormal" isomer, β-phenyl-1-aziridineethanol, in reaction mixtures and impure samples of I was suspected from nmr spectra.

A side reaction which was evident in the formation of I was the production of a viscous, polymeric material. References[6] to the polymerization of aziridines indicate that the reaction is catalyzed by acidic reagents. However, styrene oxide that had been specially freed from possible acidic impurities did not give results different from those obtained with commercial styrene oxide. Examination of the stability of I in various solvents revealed that styrene oxide polymerized the aziridine product. Whereas elemental analyses do not permit the polymeric distillation residue to be a polymer of I alone, they are consistent with a polymer consisting mostly of α-phenyl-1-aziridineethanol units and incorporating a small amount of styrene oxide. The styrene oxide concentration was effectively maintained at a low level by slow addition of the styrene oxide to the refluxing reaction, and by the use of a large excess of ethylenimine.

The formation of β-aminoalkylthiocyanates, which are intermediates for 2-iminothiazolidines, from β-aminoalkyl halides is of limited utility,[7] except where the halide is of the reactivity of benzyl chloride.[8] In contrast, Earley[9] has shown that ring opening of substituted aziridines to give alkyl thiocyanates is a fast reaction. The reported relative rates of thiocyanate and chloride attack on aziridinium ions indicated the feasibility of synthesizing III from I by generating thiocyanic acid from sodium thiocyanate and hydrochloric acid. This was further shown in the present work by a study of the relative rate of reaction of I with thiocyanic acid, hydrochloric acid, and various ratios of sodium thiocyanate and hydrochloric acid (Table I).

TABLE I
ACID RING OPENING OF I

Reactants (mole ratios)	% ring opened[a] after 20 min	% ring opened[a] after 60 min
I and HSCN (1:2.5)	78	>96
I, NaSCN, and HCl (1:1.5:1.5)	65	88
I, NaSCN, and HCl (1:1.5:2.5)	32	67
I and HCl (1:25)	5	10

[a] Ring opening carried out at 0° in ethanol. Residual I was determined, after quenching aliquots with base, by gas chromatography on an Aerograph gas chromatograph, Model A-90-P, with a 2-ft column packed with 6% NaOH, 10% Ucon 510 fluid on Chromosorb W diatomaceous support.

(4) R. E. Parker, *U. S. Dept. Comm., Office Tech. Serv., P B Rept.*, AD 260,659 (1961).

(5) N. B. Chapman, N. S. Isaacs, and R. E. Parker, *J. Chem. Soc.*, 1925 (1959).

(6) P. E. Fanta, "Heterocyclic Compounds with Three- and Four-Membered Rings," part 1, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 557.

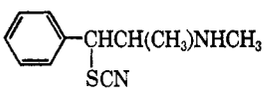
(7) A. Wolf, U. S. Patent 2,558,068 (1951); *Chem. Abstr.*, **46**, 3087e (1952).

(8) D. L. Klayman and G. W. A. Milne, *J. Org. Chem.*, **31**, 2349 (1966).

(9) J. E. Earley, C. E. O'Rourke, L. B. Clapp, J. O. Edwards, and B. C. Lawes, *J. Amer. Chem. Soc.*, **80**, 3458 (1958).

The relative rates of aziridine disappearance were shown to be clearly dependent on the thiocyanate ion concentration. Although the competing reaction of hydrogen chloride opening of I is of slight importance, a large excess of hydrochloric acid decreased the reaction rate, presumably by suppression of thiocyanic acid ionization. For synthetic preparation of III, the ideal situation for the aziridine ring-opening reaction is complete protonation of I to prevent polymerization and a large excess of thiocyanate ion during most of the reaction.

After formation of the alkyl thiocyanate IIa, extremely low pH conditions prevent ring closure to III. This may be more clearly understood by considering the thiocyanate VII which is stable in the completely protonated form, but which rapidly ring closes to give 3,4-dimethyl-5-phenyl-2-iminothiazolidine when a small amount of base is added.[7]



VII

The proper pH conditions for conversion of I into III are met by addition of the aziridine I to excess sodium thiocyanate while adjusting the reaction mixture apparent pH with hydrochloric acid.

Alternatively, the conversion of I into III could be accomplished by the reaction of I with thiourea to give the pseudothiourea IIb and subsequent ring closure of IIb in refluxing water. In this case III was conveniently isolated as the free base.

The reaction of III with thionyl chloride gave crude 3-(β-chlorophenethyl)-2-iminothiazolidine hydrochloride (IV) in good yields. The presence of minor impurity in the crude product, as demonstrated by tlc, was due to the concurrent formation of the elimination product, 2-imino-3-*trans*-styrylthiazolidine hydrochloride (V). Its structure was shown by its synthesis by hydrogen chloride elimination from IV, analyses, and spectra. In particular, the ultraviolet spectrum displayed absorbance at 295 mμ (ε 25,600) and the nuclear magnetic resonance spectrum showed two vinyl proton doublets (J = 14 cps) which confirmed the *trans*-styryl configuration.[10]

Ring closure of the free base of IV was accomplished in good yield to give VI.

Experimental Section[11]

α-Phenyl-1-aziridineethanol (I).—To 387.6 g (9.0 mol) of stirred refluxing ethylenimine was added 360.5 g (3.0 mol) of styrene oxide over a period of 170 min, and the reaction heated at reflux an additional 2 hr. The viscous residue (486.6 g), after evaporation of the ethylenimine under vacuum, was distilled at 0.35 mm to give 388.55 g (79%) of oily crystals in 3 fractions: 3.05 g, bp 25–105°, mp 56–71°; 182.7 g, bp 98–105°, mp 57–73°; 202.8 g, bp 98°, mp 57–71° [lit.[3] bp 116–117° (0.06 mm), mp 73°]. The crude product was crystallized from methyl isobutyl ketone to give 268.9 g (55%) of white crystals, mp 74–75°.

Analysis of the distillate residue from the reaction of 6 mol of ethylenimine, 2 mol of styrene oxide, and 8% ethanol gave an O/N ratio of 1.12.

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58; O, 9.80. Found: C, 74.09; H, 7.99; N, 7.87; O, 10.05 (by difference).

Stability of α-Phenyl-1-aziridineethanol (I).—The stability of I in ethylenimine, chloroform, methanol, *t*-butyl alcohol, and styrene oxide as 25% solutions was measured by nmr at 50°. After 20 hr I was absent from the styrene oxide solution, but essentially unchanged in the other solvents.

2-Imino-α-phenyl-3-thiazolidineethanol Hydrochloride (III).[12]—A solution of 8.11 g (0.10 mol) of sodium thiocyanate in 125 ml of ethanol was prepared in a flask fitted with a condenser, mechanical stirrer, glass electrode, and two dropping funnels. The apparent pH of the reaction was monitored with a Heathkit pH recording electrometer, standardized at pH 7.0 with aqueous buffer. To the thiocyanate solution was added 10 ml of a solution of 18.3 ml (0.22 mol) of concentrated hydrochloric acid in 50 ml of ethanol, followed by the addition of 18.0 g, (0.11 mol) of I in 50 ml of ethanol over a period of 10 min, while maintaining the apparent pH at 1.5–3.0 during the addition of I by the addition of the remainder of the hydrochloric acid solution. After 50 min at 40–45°, the precipitated sodium chloride was filtered; the filtrate was stirred at 40–45° for 1.5 hr and overnight at room temperature. Filtration of the mixture gave 10.45 g of product, mp 201–203°. Concentration of the mother liquor at reduced pressure gave an additional 12.0 g, mp 200–204°. The yield was 87% (based on sodium thiocyanate) or 78% (based on I). The infrared spectrum showed bands at 1610 and 1660 cm^{-1}, and no absorption band in the 2000–2200-cm^{-1} region (no SC≡N).[13]

Hydrolysis of 2-acetylimino-α-phenyl-3-thiazolidineethanol[2] at room temperature for 3 days in dilute hydrochloric acid gave a low yield of analytically pure III, mp 200–201.5°. The infrared spectrum was identical with that of III prepared from I.

Anal. Calcd for $C_{11}H_{15}N_2SClO$: C, 51.06; H, 5.84; N, 10.82; S, 12.39; Cl, 13.70. Found: C, 51.22; H, 5.90; N, 10.80; S, 12.39; Cl, 13.93.

2-{2-[β-Hydroxyphenethyl]aminoethyl}-2-thiopseudourea Dinitrate (IIb).—A modification of the general procedure of Brois[14] was used.

To a stirred slurry prepared by the addition of 29 ml (0.46 mol) of 16 *N* nitric acid to 15.22 g (0.20 mol) of thiourea in 80 ml of methanol, a solution of 32.64 g (0.20 mol) of α-phenyl-1-aziridineethanol in 60 ml of methanol was added over 25 min at 7–10°. After an additional 25 min at 5–10°, the solution was evaporated at reduced pressure to give 81.14 g of yellow solid. Recrystallization from ethanol gave 55.68 g of white crystals, mp 111–118°. Recrystallization from methanol–isopropyl alcohol gave 48.83 g (67% of theory) of analytically pure product, mp 134–137°.

Anal. Calcd for $C_{11}H_{19}N_5SO_7$: C, 36.16; H, 5.24; N, 19.17; S, 8.78. Found: C, 36.41; H, 5.48; N, 19.10; S, 8.49.

2-Imino-α-Phenyl-3-thiazolidineethanol (III Free Base). Method A.—A modification of the procedure of Doherty[15] for the ring closure of S,2-aminoethylisothiouronium bromide hydrobromide was used.

A solution of 6.0 g (0.016 mol) of 2-[2-(β-hydroxyphenethylamino)ethyl]-2-thiopseudourea dinitrate in 150 ml of water was heated at reflux for 4 hr, then cooled in an ice bath and made basic with concentrated ammonium hydroxide. The resultant precipitate was filtered and washed consecutively with water, ethanol, and ether. The dried product weighed 2.1 g (58%), mp 121–123°, and was identical by infrared spectrum with the product prepared by method B.

Method B.—A mixture of 1.29 g (0.005 mol) of III and 15 ml of water was warmed and treated with ammonium hydroxide. The precipitated free base was filtered and dried to give 0.85 g (76%) of crystals, mp 125.5–126.5°.

Recrystallization of the crude product from benzene gave the

(10) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p 85.

(11) Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra were obtained in mineral oil mull on a Perkin-Elmer Infracord spectrometer, and ultraviolet spectra by means of a Cary Model 11M spectrometer. Nuclear magnetic resonance spectra were obtained with a Varian nuclear magnetic resonance spectrometer, Model A-60. Melting points were obtained in open capillaries with a Thomas–Hoover capillary melting point apparatus and are corrected.

(12) The hydrobromide salt of III has been prepared by another route.[2]

(13) D. W. Emerson and J. K. Booth, *J. Org. Chem.*, **30**, 2380 (1965).

(14) S. J. Brois, *U. S. Dept. Comm., Office Tech. Serv., P B Rept.* 135,447; *Chem. Abstr.*, **54**, 12,090*b* (1960).

(15) D. G. Doherty, R. Shapira, and W. T. Burnett, Jr., *J. Amer. Chem. Soc.*, **79**, 5667 (1957).

analytical sample, mp 125–125.5°, which had an infrared spectrum identical with III free base prepared by method A.

Anal. Calcd for $C_{11}H_{14}N_2SO$: C, 59.43; H, 6.35; N, 12.60; S, 14.42. Found: C, 59.93; H, 6.60; N, 12.69; S, 14.73.

3-(β-Chlorophenethyl)-2-iminothiazolidine Hydrochloride (IV).—To a stirred slurry of 40.0 g (0.154 mol) of III and 62 ml of methylene chloride was added 17 ml (28.4 g, 0.238 mol) of thionyl chloride over a period of 2–3 min. The reaction mixture was stirred for 45 min, filtered, washed with methylene chloride and ether, and dried. The crude product weighed 30.0 g (91%): mp 178–182° and 240°; λ_{max}^{MeOH} 295 mμ. Recrystallization of the product from ethanol gave 25.3 g (59%) of white crystals, mp 245–246°. Tlc analysis (silica gel) in the solvent system acetonitrile–ammonium hydroxide (95:5, v/v) revealed a major component at R_f 0.80 and a very minor component at R_f 0.85 in both crude and recrystallized product. The minor component had the same mobility as V.

Anal. Calcd for $C_{11}H_{14}N_2SCl_2$: C, 47.66; H, 5.09; N, 10.11; S, 11.56; Cl, 25.58. Found: C, 47.06; H, 4.67; N, 9.37; S, 10.72; Cl, 23.41.

An aqueous solution of the hydrochloride was treated with sodium perchlorate to give the perchlorate salt, mp 206–207°, homogeneous by tlc.

Anal. Calcd for $C_{11}H_{14}N_2SCl_2O_4$: C, 38.72; H, 4.14; N, 8.21; S, 9.40; Cl, 20.78. Found: C, 38.90; H, 4.19; N, 8.01; S, 9.50; Cl, 21.06.

2-Imino-3-*trans*-styrylthiazolidine Perchlorate and Hydrochloride (V).—The following procedure was adapted from that used for the dehydrobromination of α-bromo ketones.[16]

A mixture of 16.0 g (0.0583 mol) of IV, 4.24 g (0.10 mol) of lithium chloride, and 130 ml of dry dimethylformamide was stirred at 113–120° for 3.5 hr, and then at room temperature for 16 hr. The mixture was poured into 1 l. of water and 450 ml of ether and ammonium hydroxide was added to a pH of 8–9. The aqueous layer was extracted again with 450 ml of ether, the ether extracts were washed with water, and dried over anhydrous potassium carbonate. Removal of the solvent *in vacuo* gave 9.43 g of a colorless oil.

The hydrochloride salt was prepared with ethanolic hydrogen chloride. The crude yellow gummy hydrochloride from evaporation of the solvent was warmed with 700 ml of water and filtered; the filtrate was treated with an aqueous solution of 7.35 g (0.06 mole) of sodium perchlorate to precipitate the perchlorate which, after filtering, washing with water, and drying under vacuum, weighed 5.83 g, mp 210–214°. Two recrystallizations from absolute ethanol gave the analytical sample, mp 232.5–234°.

Anal. Calcd for $C_{11}H_{13}N_2SClO_4$: C, 43.35; H, 4.30; N, 9.19; S, 10.52; Cl, 11.63. Found: C, 43.15; H, 4.31; N, 8.98; S, 10.67; Cl, 11.64.

The perchlorate was converted into the free base with ammonium hydroxide and extracted into chloroform. Evaporation of the chloroform, solution in methanol, and the addition of ethanolic hydrogen chloride gave the hydrochloride as cream-colored crystals, mp 224–225°. Recrystallization from methanol–ethanol gave the analytical sample as white needles, mp 223–224°. This had the same tlc mobility as the minor component of IV.

Anal. Calcd for $C_{11}H_{13}N_2SCl$: C, 54.87; H, 5.44; N, 11.64; S, 13.32; Cl, 14.73. Found: C, 54.84; H, 5.40; N, 11.62; S, 13.62; Cl, 14.96.

6-Phenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole Hydrochloride (VI).—A slurry of IV prepared from 7.77 g (0.030 mol) of III and 3.21 ml (0.045 mol) of thionyl chloride in 68 ml of methylene chloride (see the preparation of IV) was poured into ice and water and made basic by the careful addition of 3 *N* sodium hydroxide solution. The layers were separated, the aqueous layer extracted with 50 ml of methylene chloride, the organic phase washed with water, and the solvent removed at reduced pressure. The residual free base of IV was refluxed in 100 ml of isopropyl alcohol for 50 min to effect ring closure. The resultant hydrochloride precipitate was filtered, washed with ether, and dried to give 3.22 g of light yellow crystals, mp 255–259° (lit.[2] mp 260–270°). The mother liquor upon treatment with isopropyl alcoholic hydrogen chloride and concentration at reduced pressure gave an additional 2.43 g. The total crude yield was 78%. Recrystallization of the combined fractions from ethanol gave 4.30 g (59%) of product, mp 260–262°.

(16) (a) D. Djerassi, N. Finch, R. C. Cookson, and C. W. Bird, *J. Amer. Chem. Soc.*, **82**, 5488 (1960); (b) R. Joly and J. Warnant, *Bull. Soc. Chim. Fr.*, 367 (1958).

Registry No.—I, 15591-40-9; IIb, 15591-46-5; III, 15591-41-0; III free base, 15591-42-1; IV, 15643-70-6; IV perchlorate salt, 15643-71-7; V, 15591-43-2; V perchlorate salt, 15591-44-3; VI, 5086-74-8.

New Heteroaromatic Compounds. XXIX.[1] The Mechanism of Salt Formation in Some Nitroborazarophenanthrenes[2]

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The mechanism of salt formation in 6- and 8-nitro-10-methyl- and -10-hydroxy-10,9-borazarophenanthrene[4] has been studied, using ir and ^{11}B nmr[5] spectroscopy, and their pK_A's have been measured. These borazaro derivatives differ from most other analogous compounds[6] in that they behave as Lewis acids, salt formation involving addition of base to boron rather than loss of a proton from OH or NH. Their pK_A's are surprisingly low, comparable with that of phenol, and their longest wavelength absorption bands show large bathochromic shifts on salt formation.

In the course of another investigation, we noticed that 6- and 8-nitro-10-hydroxy-10,9-borazarophenanthrene (Ia and IIa, respectively) both developed intense colors on treatment with alkali, implying that in their conjugate bases there is an enhanced mesomeric interaction between the imino nitrogen and the nitro group *ortho* or *para* to it.

In a prior paper[4] of this series, we reported studies of salt formation in a number of compounds containing the groups BOH, using ^{11}B nmr. The results established that compounds of this type behave as Lewis acids, rather than protic acids, unless the boron atom forms part of an aromatic ring. When the boron atom does form part of an aromatic ring, as in the case in 10-hydroxy-10,9-borazarophenanthrene (IIIa), salt formation normally involves loss of a proton from the hydroxyl group. These results made it difficult to understand the behavior of Ia and IIa, for loss of a proton from hydroxyl would leave an ion (IV) in which the negative charge should be mainly localized

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(3) Robert A. Welch Postdoctoral Fellow.

(4) M. J. S. Dewar and V. P. Kubba, *Tetrahedron*, **7**, 213 (1959).

(5) M. J. S. Dewar and R. Jones, *J. Amer. Chem. Soc.*, **89**, 2408 (1967).