g-atom) of magnesium turnings in 50 ml of anhydrous ether in a flask fitted with a gas inlet tube, a dropping funnel, stirrer, and a Dry Ice–acetone condenser. To this solution, 20 g (0.196 mole) of phenylacetylene in 30 ml of ether was added slowly. After the mixture was cooled to 15–20°, 12 ml (at −76°, 18.8 g, 0.138 mole) of trifluoromethanesulfenyl chloride was added through the gas-addition tube above the surface of the reaction mixture and allowed to reflux into the reaction mixture. This addition required about 1 hr. The reaction mixture was then poured into large volume of ice water containing an excess of hydrochloric acid. The product was removed by two extractions with 100 ml of ether. The ether extracts were washed once with water, dried over anhydrous magnesium sulfate, and rapidly distilled through a small spinning-band still. There was thus obtained 13.77 g (49%) of crude product distilling at 42.5 (1.75 mm)–56° (2.35 mm), $n^{25}D$ 1.5219–1.5509. Upon redistillation of this fraction, 7.20 g (26%) of phenyl (trifluoromethylthio)-acetylene was obtained distilling at 43° (2.4 mm), $n^{25}D$ 1.5198–1.5203. The infrared spectrum is recorded in Table III.

Anal. Calcd for $C_9H_5F_3S$: C, 53.5; H, 2.5; F, 28.2; S, 15.8. Found: C, 53.6; H, 2.6; F, 28.0; S, 15.7.

26. **Nmr Spectra.**—F^{19} nmr spectra (56.4 Mc) were obtained from 10% solutions of the compounds in fluorotrichloromethane (Freon-11) with an A-56/60 nmr spectrometer manufactured by Varian Associates, Palo Alto, Calif. Chemical shifts are reported in cycles per second (cps) measured from the resonance of fluorotrichloromethane as an internal standard.

H^1 nmr spectra (60 Mc) were obtained with an A-60 nmr spectrometer manufactured by Varian Associated, Palo Alto, Calif. Solutions (10%) in CCl_4 containing tetramethylsilane were used except where indicated.

Registry No.—I, 13003-31-1; II (n = 1), 819-67-0; II (n = 2), 674-64-6; II (n = 3), 13003-34-4; II (n = 5), 13003-35-5; III, 691-69-0; IV, 681-87-8; V, 674-43-1; VI, 688-53-9; VII, 13003-40-2; XI, 762-80-1; XIII, 674-36-2; XIV, 13040-44-3; XV, 1542-22-9; XVII, 13003-43-5; XVIII, 13003-44-6; XIXa, 13003-45-7; XIXb, 13003-46-8; XX, 13003-47-9; XXI, 13003-48-0; XXII, 13003-49-1; XXIII, 2266-81-1; XXV, 2069-87-6; XXVI, 13003-52-6; *cis* XXVII, 13003-53-7; *trans* XXVII, 13003-54-8; XXVIII, 13003-55-9; XXIX, 13003-56-0; XXX, 2002-89-3; trifluoromethanethiol, 1493-15-8; bromo-1,2-bis(trifluoromethylthio)ethane, 673-62-1; $CF_3SO_2C_2H_5$, 13003-57-1; $CF_3SO_2(CH_2)_2SO_2CF_3$, 13040-45-4; $CF_3SO_2(CH_2)_3SO_2CF_3$, 13003-58-2; $CF_3SO_2(CH_2)_5SO_2CF_3$, 13003-59-3.

The Thiazolo[2,3-*b*]thiazolium Cation. A New Aromatic System[1]

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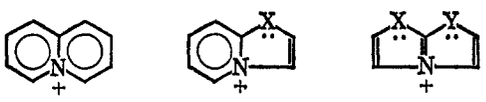
Through cyclization of α-(2-thiazolylthio)aldehydes and ketones, the first simple thiazolo[2,3-*b*]thiazolium salts have been prepared. With a mixture of sulfuric and nitric acids, the 3,5-dimethylthiazolo[2,3-*b*]thiazolium ion undergoes mononitration. With sodium hydroxide, it undergoes ring opening to afford 2-(4-methylthiazol-2-on-3-yl)prop-1-ene-1-thiol.

In an earlier communication,[3] it was pointed out that on the basis of the stability of the quinolizinium ion (1) which may be considered an azonialog[4] of naphthalene, there might exist a whole series of stable azonialogs of well-known bicyclic aromatic heterocyclic systems. To date the thiazolo[3,2-*a*]pyridinium (2, X = S),[3,5,6] the oxazolo[3,2-*a*]pyridinium (2, X = O),[7] and the imidazo[1,2-*a*]pyridinium[8] (2, X = NR) cations have been described. These ions are azonialogs of thianaphthene, benzofuran, and indole, respectively, and each has a 10-π-electron system in a structure formed by the fusion of a five- with a six-membered ring.



1 2 3

It seemed reasonable to expect the existence of stable aromatic cationoid systems having structures like 3 in which there are two, fused five-membered rings and the heteroatoms designated X and Y each have at least one pair of unshared electrons. The present communication describes the first simple[9] thiazolo-[2,3-*b*]thiazolium salts.

By analogy to the synthesis of thiazolo[3,2-*a*]pyridinium salts,[5,6] it would be expected that 2-thiazolyl β-keto sulfides (5) could be cyclized to thiazolothiazolium salts (6). Fortunately, the 2-mercaptothiazoles (4) needed for the preparation of such sulfides are readily available[10,11] by the reaction of α-halo ketones or aldehydes with ammonium dithiocarbamate. Even more fortunate is the earlier observation that ammonium dithiocarbamate can be made to react with 2 moles of an α-halo ketone to afford the required keto sulfide (5, $R_1 = R_3$) directly. The first cyclization attempt was carried out on the known[10] 1-(4-methyl-2-thiazolylthio)propanone (5c). (See Table I.)

Unlike the 1-(2-pyridylthio)propanone, methylthiazolylthiopropanone (5c) did not cyclize readily in concentrated sulfuric acid at room temperature, but on heating for 3 hr at 100° afforded a new salt in 97% yield. The ultraviolet absorption spectrum of the cyclization product showed new maxima at longer wavelengths and the infrared absorption spectrum showed the absence of a carbonyl group. Most convincing evidence that the new product was indeed 6c was afforded by the remarkably simple nmr spec-

(1) A portion of this work was described in a preliminary communication: C. K. Bradsher, D. F. Lohr, Jr., and W. J. Jones, Jr., *Tetrahedron Letters* 1723 (1965).

(2) James B. Duke Fellow, 1964–1966.

(3) C. K. Bradsher and W. F. Lohr, Jr., *Chem. Ind.* (London), 1801 (1964).

(4) The term "azonialog" has been proposed to describe an aromatic compound derived from another by the replacement of a bridgehead carbon atom by a quaternary nitrogen: R. E. Doolittle and C. K. Bradsher, *J. Heterocyclic Chem.*, **2**, 399 (1965).

(5) F. S. Babichev and V. N. Bubnovskaya, *Ukr. Khim. Zh.*, **30**, 848 (1964).

(6) C. K. Bradsher and D. F. Lohr, Jr., *J. Heterocyclic Chem.*, **3**, 27 (1966).

(7) C. K. Bradsher and Mary F. Zinn, *ibid.*, **1**, 219 (1964).

(8) C. K. Bradsher, E. F. Litzinger, Jr., and M. F. Zinn, *ibid.*, **2**, 331 (1965).

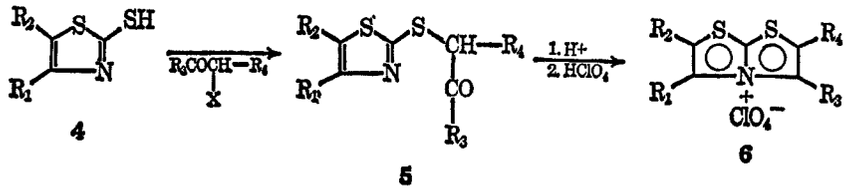
(9) G. F. Duffin and J. D. Kendall [U. S. Patent 2,513,923 (1950)] have described a betaine which has the thiazolo[2,3-*b*]thiazolium nucleus.

(10) I. Ubaldini and A. Firoenza, *Gazz. Chim. Ital.*, **73**, 169 (1943).

(11) W. S. Emerson and T. M. Patrick, *J. Org. Chem.*, **13**, 722 (1948).

TABLE I

PREPARATION OF THIAZOLO[2,3-b]THIAZOLIUM SALTS



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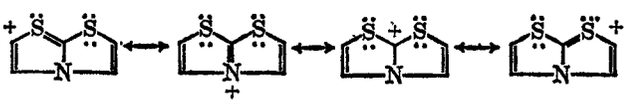
Position	R_1	R_2	R_3	R_4	X	5, yield, %	6, yield, %	λ_{max}, mμ (log ε)
a	...	...	...	...	Cl	22[a]	70	200 (3.94), 210 sh (3.76), 216 (3.80), 222 sh (3.68), 236 sh (2.99), 282 (4.11)
b	...	...	CH_3	...	Cl	22	50	200 (3.98), 220 (3.85), 225 sh (3.76), 286 (4.11)
c	CH_3	...	CH_3	...	Cl	64[b,c]	97	221 (3.84), 226 (3.75), 292 (4.06), 298 (4.04)
d	CH_3	...	C_6H_5	...	Cl	34	80	203 (4.29), 224 (4.08), 227 sh (4.06), 294 (4.05)
e	C_6H_5	...	C_6H_5	...	Cl	40[c,d]	91	196 (4.55), 223 (4.27), 240 sh (4.14), 290 (4.04)
f	C_6H_5	...	CH_3	...	Cl	..[e]	70	...[f]
g	C_6H_5	...	...	...	Br	30[g]	69	198 (4.41), 238 (4.08), 256 sh (3.90), 288 (4.00)
h	C_6H_5	...	C_6H_5	C_6H_5	Cl	79	0[h]	...
i	C_6H_5	...	CH_3	$COCH_3$	Cl	73	86[i]	193 (4.37), 221 sh (4.21), 299 (4.00)
j	CH_3	CH_3	...	...	Br	46[g]	44	203 (4.12), 221 (3.90), 226 sh (3.83), 288 (4.09)
k	CH_3	CH_3	CH_3	...	Cl	58	65	203 (4.08), 222 (3.77), 228 sh (3.73), 296 (4.07)
l	CH_3	CH_3	CH_3	CH_3	Br	47	76	205 (4.12), 297 (4.09)
m	CH_3	CH_3	C_6H_5	...	Cl	88[j]	83	203 (4.31), 224 sh (4.09), 296 (4.04)
n	p-BrC_6H_4	...	p-BrC_6H_4	...	Br	19[c]	70	201 (4.62), 236 (4.45), 293 (4.11)
o	CH_3	$COOC_2H_5$	C_6H_5	...	Cl	76	40[i]	204 (4.28), 213 (4.29), 244 sh (3.97), 298 (4.03)

[a] Alkylation carried out on free thiol rather than anion. The product was isolated as a hydrated hydrochloride. [b] Prepared by directions of Ubaldini and Fiorenza.[10] [c] Yield from reaction of 2 moles of the chloro ketone with 1 mole of ammonium dithiocarbamate. [d] Prepared by directions of Emerson and Patrick.[11] [e] Not isolated as a pure compound. [f] Identical with product from 5d. [g] The diethyl acetal rather than the free bromoacetaldehyde was used in the alkylation, and the alkylation product (5) was an acetal. [h] After 8 hr in concentrated sulfuric acid, a part of the starting material was converted into a tar. The rest was recovered unchanged. [i] The cyclization was carried out in polyphosphoric acid. [j] This compound was prepared earlier but not obtained in an analytically pure form: F. D. Stewart and R. A. Mathes, *J. Org. Chem.*, **14**, 1111 (1949).

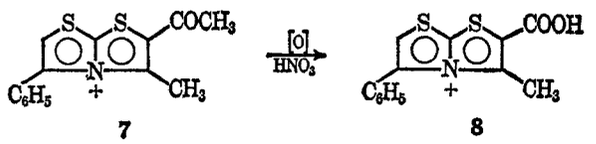
trum, consisting of two singlets at τ 7.06 and 2.43 with areas in an approximate ratio of 3:1. Since the new cation **6c** can be prepared in 62% over-all yield from chloroacetone, with only ammonia and carbon disulfide as additional starting materials, it can be produced inexpensively as well as conveniently. The known[11] 2-(4-phenyl-2-thiazolylthio)acetophenone (**5e**) was cyclized to the 3,5-diphenylthiazolo[2,3-*b*]thiazolium ion in 91% yield. A number of sulfides (**5**, $R_1 \neq R_3$) were prepared for cyclization to unsymmetrical thiazolothiazolium salts. Notable among these were 2-(4-methyl-2-thiazolylthio)acetophenone (**5d**) and 1-(4-phenyl-2-thiazolylthio)propanone (**5f**) both of which gave the same product, 3-methyl-5-phenylthiazolo-[2,3-*b*]thiazolium ion (**6d**), affording chemical evidence for the equivalence of the two five-membered rings.

The unsubstituted cation (**6a**) was prepared by the cyclization of the sulfide (**5a**) obtained by the reaction of chloroacetaldehyde with 2-thiazolethiol (**4a**). The nmr spectrum (in trifluoroacetic acid) of the unsubstituted cation (**6a**) was an AB system containing two doublets of equal area centered at τ 1.33 and 1.79 each with J_{AB} = 4 cps. The resonance of both protons at such low fields suggests that the positive charge is shared by the sulfur atoms, as well as the nitrogen, as would be indicated by the canonical forms represented below.



A number of derivatives of the new heterocyclic system have been prepared; yields and ultraviolet absorption data are given in Table I.

For the synthesis of salts having functional groups (**6i** and **6o**) polyphosphoric acid was found to be superior to sulfuric acid. When sulfuric acid was used in a cyclization expected to lead to the 2-acetyl-3-methyl-5-phenylthiazolo[2,3-*b*]thiazolium (**7**) cation, the chief product (55% yield) was the deacylation product, 3-methyl-5-phenylthiazolo[2,3-*b*]thiazolium



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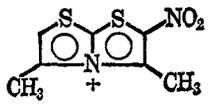
(**6d**). Oxidation of the acyl derivative (**7**) with nitric acid gave the corresponding acid **8**. Efforts to convert the acid to a betaine were unsuccessful.

A preliminary study of the chemistry of the thiazolothiazolium system was made, employing the easily prepared 3,5-dimethyl derivative (**6c**).

Attempted hydrogenation of the dimethyl derivative at atmospheric pressure over a platinum oxide catalyst was ineffective, as were attempts to oxidize the methyl groups with nitric acid, or to effect condensation on the methyl groups using *p*-N,N,-dimethylaminobenzaldehyde in refluxing acetic anhydride.

It would be expected that electrophilic substitution on an aromatic cation in which the positive charge could be so extensively delocalized might be difficult. Treatment of the dimethyl derivative (**6c**) with equal



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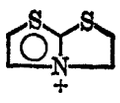

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volumes of concentrated nitric and sulfuric acids did afford a 6% yield of 2-nitro-3,5-dimethylthiazolo-[2,3-*b*]thiazolium cation (**9**) as the perchlorate. This nitration must have been accompanied by side reactions as no starting material could be recovered. The infrared absorption spectrum of the nitration product showed the presence of a nitro group and the nmr spectrum (trifluoroacetic acid) showed that the two methyl groups were no longer equivalent. A multiplet at τ 2.30 was assigned to the C-6 ring proton, a singlet at 6.68 was assigned to the C-3 methyl group, and a doublet (J = 1 cps) at 7.04 was attributed to the methyl at C-5.

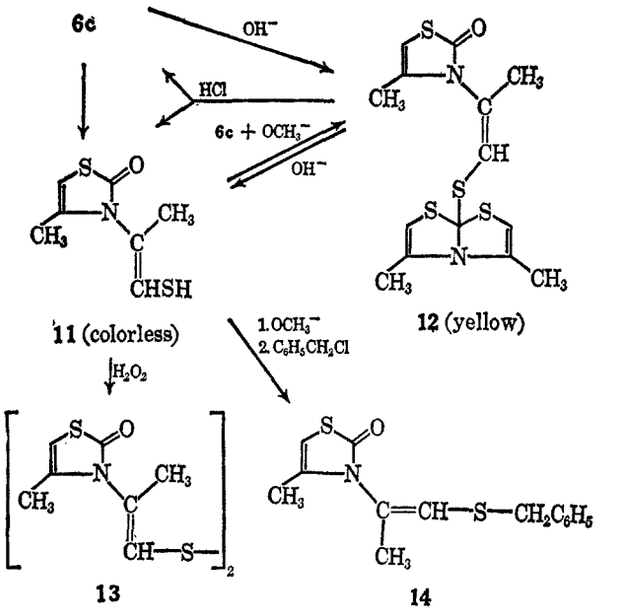
An attempt at chlorination of the nucleus of 3,5-dimethylthiazolo[2,3-*b*]thiazolium bromide using sulfuryl chloride and aluminum chloride failed, as did attempts to brominate the side chains using liquid bromine or N-bromosuccinimide.

Thiazolium salts in alkaline solution undergo changes leading to the destruction of the ring system.[12] A few minutes after a warm, aqueous solution of 3,5-dimethylthiazolo[2,3-*b*]thiazolium bromide (**6c**) was made 2 N in sodium hydroxide, a bright, yellow precipitate began to form, which after 30 min at room temperature was collected. Acidification of the filtrate produced a colorless compound. The same colorless compound could be produced in good yield (86%) if an alkaline solution of the dimethylthiazolothiazolium salt was heated for 4 hr at 100° and then acidified. It could likewise be obtained (88% yield) by dissolving the yellow compound in alkali, followed by neutralization of the solution. Acidification of the yellow compound gave the colorless compound plus the dimethyl thiazolothiazolium cation (**6c**).

Periodic observation of the ultraviolet absorption spectrum of a solution of 3,5-dimethylthiazolo[2,3-*b*]-thiazolium bromide (**6c**) in an aqueous solution made 0.1 N in sodium hydroxide showed that the spectrum after a few minutes was essentially that of the yellow compound, while after 100 hr when reaction appeared complete, the spectrum resembled that of the anion of the colorless compound.

The report by Seto and Ikegami[13] on the ring opening of tetrahydrothiazolo[2,3-*b*]thiazolium chloride (**10**) by alkali provided a useful guide to the understanding of our observations. It is believed that the attack of hydroxide ion on the thiazolo[2,3-*b*]thiazolium system (as in the case of the tetrahydro derivative) occurs at the bridgehead carbon atom and the first product is the salt of 2-(4-methylthiazol-2-on-1-yl)prop-1-ene-1-thiol (**11**). This mercaptide ion should be greatly superior to hydroxide ion as a nucleophile and should attack another mole of the thiazolothiazolium salt at the bridgehead carbon yielding **12**, the yellow compound (Scheme I). The only slightly soluble, yellow compound would undergo hydrolysis at room temperature relatively slowly with the result that, at first, accumulation of precipitated yellow compound would

SCHEME I



occur, followed by its slow disappearance when the thiazolothiazolium ion supply became exhausted.

As one would predict, equimolecular parts of the anion of the colorless compound **11** and the cation of the 3,5-dimethylthiazolo[2,3-*b*]thiazolium salt **6c** react to form the yellow compound, and the yield is too large (88%) for all of the product to have come from the cation.

The vinyl thiol structure (**11**) of the colorless compound is supported by both physical and chemical evidence. The infrared spectrum showed a strong absorption at 2440, characteristic of aliphatic thiols,[14] and a broad and strong absorption at 1640 cm^{-1} observed by Seto and Ikegami[13] for a related cyclic thiocarbamate. The nmr spectrum of the thiol in deuteriochloroform lends strong support to the assignment of **11** as the correct structure. An irregular triplet centered at τ 7.35 (six methyl protons) was probably the result of two overlapping doublets each with J = 1 cps. The two methyl groups are not quite equivalent and each is split by a vinyl proton. A doublet (J = 10 cps) with a weight of one proton, and centered at τ 6.62, was assigned to the thiol proton with the splitting attributed to the presence of a vinyl proton on the carbon to which the thiol group is attached. A one-proton multiplet at τ 3.58 was assigned to the ring vinyl proton while the remaining doublet (J = 10 cps) centered at 3.12, with each peak actually appearing as a multiplet, was assigned to the side-chain vinyl proton. It seems quite reasonable that the singlet for the side-chain vinyl proton would be split into a doublet by the thiol proton and that the peaks forming the doublet would be further split by the adjacent vinyl methyl group.

Oxidation of the thiol with hydrogen peroxide yielded the corresponding disulfide (**13**). The infrared spectrum of the disulfide showed no thiol group absorption at 2450 cm^{-1} and the nmr spectrum likewise showed the absence of a thiol group. The thiol (**11**) was further characterized by alkylation with

(12) A. Schöberl and M. Stock, *Ber.*, **73**, 1240 (1940).

(13) S. Seto and Y. Ikegami, *Bull. Chem. Soc. Japan*, **36**, 730 (1963).

(14) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 351.

TABLE II

SYNTHESIS OF NEW β-KETO SULFIDES (5)

Compd	Ref thiol	Mp or bp[a] (mm), °C	Derivative	Formula[b]	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found
5b	...[c]	90–95 (0.4)	DNP[d]	$C_{12}H_{11}N_5O_4S_2$	40.78	40.81	3.14	3.13	19.82	19.91
5d	...[e]	80–81	...[f]	$C_{12}H_{11}NOS_2$	57.80	57.86	4.45	4.36	5.62	5.73
5f	Ref 11	...[g]	DNP[h]	$C_{18}H_{15}N_5O_4S_2$	50.34	50.62	3.52	3.66	16.31	16.54
5h	Ref 11	134.5–135.5	...[i]	$C_{23}H_{17}NOS_2$	71.28	71.32	4.42	4.42	3.62	3.66
5i	Ref 11	101.5–102.5	...[j]	$C_{14}H_{13}NO_2S_2$	57.71	57.67	4.50	4.71	4.81	4.95
5j	...	115 (0.45)	...[k]	$C_{11}H_{19}NO_2S_2$	50.54	50.26	7.33	7.09	5.36	5.60
5k	...[l]	121–123 (0.8)	DNP[m]	$C_{14}H_{15}N_5O_4S_2$	44.08	43.94	3.96	4.03	18.36	18.48
5l	...[l]	114–117 (3.8)	DNP[n]	$C_{15}H_{17}N_5O_4S_2$	45.55	45.32	4.33	4.38	17.71	17.54
5m	...[l]	58–58.5	...[o]	$C_{13}H_{13}NOS_2$	59.28	59.39	4.97	5.10	5.32	5.25
5o	...[p]	86–87	...[o]	$C_{15}H_{15}NS_2O_3$	56.05	56.06	4.70	4.61	4.36	4.35

[a] Boiling points may be distinguished from melting points by the indication of pressure. [b] The formula is that of the compound actually analyzed. [c] M. O. Kolosova, *J. Appl. Chem. USSR*, **36**, 931 (1963); *Chem. Abstr.*, 59, 6380 (1963). [d] The dinitrophenylhydrazone was obtained from ethanol as an orange powder, mp 119–122°. [e] T. G. Levi, *Gazz. Chim. Ital.*, **61**, 719 (1963). [f] Irregular crystals from ether. [g] Undistilled oil used in cyclization. [h] Orange needles, mp 176–177°, from ethanol–ethyl acetate. [i] Needles from ethanol. [j] Small needles from methanol. [k] The sulfide was diethyl acetal rather than a free aldehyde. [l] Tables I, ref *j*. [m] Red-orange needles, mp 168–169°, from ethanol. [n] Orange–yellow plates, mp 120–121°, from ethanol. [o] Needles from ether. [p] J. J. D'Amico, *J. Am. Chem. Soc.*, **75**, 102 (1953).

benzyl chloride to yield the corresponding benzyl sulfide.

Attempts to bring about the addition of nucleophiles, other than the hydroxyl group, to the 3,5-dimethylthiazolo[2,3-*b*]thiazolium cation (**6c**) were unsuccessful. These nucleophiles included the anions of *p*-toluenethiol, 2-benzothiazolethiol, and phenylacetonitrile.

Experimental Section

The elemental analyses were carried out by the Janssen Pharmaceutical Research Laboratories, Beerse, Belgium, or by Ilse Beetz Mikroanalytisches Laboratorium, Kronach, Germany. All ultraviolet absorption spectra were measured in 95% ethanol using 1-cm quartz cells with a Cary Model 14 spectrometer. Infrared spectra were determined in potassium bromide plates using a Perkin-Elmer Model 137 spectrophotometer. Nmr measurements were made with a Varian A-60 spectrometer using a tetramethylsilane standard and, except as noted, deuteriochloroform as the solvent.

General Procedure for the Preparation of β-Keto Sulfides (5).—A solution of sodium methoxide was prepared by dissolving 0.58 g (0.025 g-atom) of sodium metal in 40 ml of absolute methanol. Next the 2-thiazolethiol (0.025 mole) was added followed by the halo ketone[15] (0.025 mole). The resulting mixture was allowed to stand at room temperature for 12 hr during which the mixture usually darkened and sodium halide precipitated. The mixture was filtered to remove the halide and the methanol was removed under vacuum with a rotary evaporator. Dilute sodium hydroxide and methylene chloride were added to the residue, and the organic layer was separated, washed with water, dried over magnesium sulfate, concentrated, and distilled under reduced pressure. Yields are indicated in Table I, physical constants and analytical data are given in Table II.

4-(*p*-Bromophenyl)-2-thiazolethiol (4n).—The general procedure of Emerson and Patrick[11] was employed. From 18.6 g of 2,4′-dibromoacetophenone and 11.0 g of ammonium dithiocarbamate in 130 ml of water there was obtained 0.81 g (4.5%) of a yellow solid, mp 214–216°. The analytical sample crystallized from ethanol–water as pale yellow needles, mp 215.5–217.5°.

Anal. Calcd for $C_9H_6BrNS_2$: C, 39.71; H, 2.22; N, 5.15. Found: C, 39.90; H, 2.30; N, 4.96.

4′-Bromo-2-(4-*p*-bromophenyl-2-thiazolylthio)acetophenone (5n).—This compound was found in the alkali-insoluble fraction in the preceeding preparation (**4n**) as a light yellow solid, mp 145–146°, yield 5.7 g (19%). The analytical sample crystallized from ethanol as colorless needles, mp 146–147°.

Anal. Calcd for $C_{17}H_{11}Br_2NOS_2$: C, 43.51; H, 2.36; N, 2.99. Found: C, 43.68; H, 2.47; N, 2.86.

Thiazolo[2,3-*b*]thiazolium Salts. A. General Procedure Using Sulfuric Acid.—One gram of the β-keto sulfide (**5**) was dissolved in approximately 10 ml of cold, concentrated sulfuric acid, and after a few minutes the mixture was heated on the steam bath for 3 hr. The sulfuric acid solution was cooled and then poured into 100–150 ml of ice-cold, anhydrous ether. An oil or a solid salt precipitated immediately, but the mixture was kept at 0° until the ether solution was clear. The ethereal solution of sulfuric acid was then decanted and the residue was dissolved in 5–10 ml of water. The water solution was warmed to expel any dissolved ether, treated with Norit, filtered, and cooled, and an excess of 35% perchloric acid was added. The resulting precipitate was recrystallized from methanol, except as noted, and the product crystallized as colorless needles.

B. Using Polyphosphoric Acid.—A solution of 3.0 g of the β-keto sulfide (**5**) in about 25 g of polyphosphoric acid was heated at 100° for 18–20 hr. The solution was cooled, 25 ml of ice water was added, and the acid solution was filtered. Addition of 35% perchloric acid to the filtrate precipitated the perchlorate salt. The salt was recrystallized from an appropriate organic solvent.

Melting points and analyses for all salts are to be found in Table III.

Thiazolo[2,3-*b*]thiazolium Perchlorate (6a).—A solution of 2.34 g of 2-thiazolethiol[16] and 1.92 g of chloroacetaldehyde hydrate in 40 ml of reagent grade acetone was refluxed for 2 hr. The salt (0.94 g) which separated from the cooled solution was dissolved in 10 ml of concentrated sulfuric acid and cyclized in the usual way, affording an over-all yield of 0.75 g (15%) of a tan solid, mp 293–297°. The analytical sample crystallized from water as colorless needles, mp 299–300° dec.

Anal. Calcd for $C_5H_4ClNO_4S_2$: C, 24.85; H, 1.67; N, 5.80. Found: C, 24.90; H, 1.60; N, 5.78.

3-Phenylthiazolo[2,3-*b*]thiazolium Perchlorate (6g).—The general procedure used in the preparation of (**6j**) was used except that the intermediate acetal was not obtained pure. The salt was obtained from the thiol (**4g**) in an over-all yield of 21%. The analytical sample crystallized from water as colorless needles, mp 225–226°.

Anal. Calcd for $C_{11}H_8ClNO_4S_2$: C, 41.58; H, 2.54; N, 4.41. Found: C, 41.67; H, 2.61; N, 4.47.

2-Carboxy-3-methyl-5-phenylthiazolo[2,3-*b*]thiazolium Bromide (6, R_4 = COOH; R_3 = CH_3; R_2 = H; R_1 = C_6H_5).—A solution containing 2.05 g of 2-acetyl-3-methyl-5-phenylthiazolo[2.3-*b*]-thiazolium perchlorate (**9i**) in 35 ml of 8 *M* nitric acid was refluxed for 8 hr. The nitric acid was removed under reduced pressure and the residue was dissolved in 30 ml of warm water. A solution of bromine in 48% hydrobromic acid was added dropwise with stirring and the yellow precipitate, presumably the tribromide precipitate, was collected. The yellow salt was treated with 50 ml of an acetone–methanol mixture (1:1) and the volume of the resulting solution was reduced to about 20 ml. Ethyl acetate was added and the mixture was kept at 0° for 24 hr. The resulting pale yellow solid was collected, yield 1.20 g (61%). Recrystallization of the product from methanol–ether afforded colorless, irregular crystals, mp 263–264°.

(15) The halogen substituent present in the halide is indicated in Table I.

(16) Table II, footnote *c*.

TABLE III

THIAZOLO[2,3-*b*]THIAZOLIUM (6) PERCHLORATES BY CYCLODEHYDRATION

Compd	Mp, °C	Formula	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found
6b[a]	175.5–177	$C_6H_5ClNO_4S_2$	28.18	28.06	2.37	2.32	5.48	5.54
6c[b]	362[c]	$C_7H_8ClNO_4S_2$	31.17	31.14	2.99	2.78	5.19	5.40
6d	252–253[d]	$C_{12}H_{10}ClNO_4S_2$	43.44	43.78	3.04	3.06	4.22	4.47
6e[e]	228.5–229.5[d]	$C_{17}H_{12}ClNO_4S_2$	51.84	52.02	3.07	3.22	3.56	3.80
6i[f]	204–206[d,g,h]	$C_{14}H_{12}ClNO_5S_2$	44.98	45.19	3.24	3.45	3.75	3.67
6j[i,j]	135–136	$C_7H_8ClNO_4S_2$	31.17	31.19	2.99	3.04	5.19	5.13
6k	186–187	$C_8H_{10}ClNO_4S_2$	33.86	33.53	3.55	3.41	4.94	5.07
6l	271–272	$C_9H_{12}ClNO_4S_2$	36.30	36.11	4.06	4.14	4.70	4.73
6m[j]	230.5–231.5	$C_{13}H_{12}ClNO_4S_2$	45.15	45.19	3.50	3.52	4.05	4.07
6n	316.5–317.5	$C_{17}H_{10}Br_2ClNO_4S_2$	37.01	36.78	1.83	1.91	2.54	2.56
6o[f]	178–181[k]	$C_{15}H_{14}ClNO_6S_2 \cdot 0.5H_2O$	43.63	43.80	3.66	3.50	3.39	3.43

[a] This cyclization was carried at room temperature for 19 hr. [b] Keto sulfide (**5c**); ref 10. [c] The analytical sample does not melt, but explodes at the indicated temperature. The corresponding bromide may be prepared by precipitation of the tribromide salt from a solution of the bisulfate or perchlorate, followed by warming the precipitate in methanol–acetone. The bromide crystallized from methanol as colorless needles, mp 355–356° dec. *Anal.* Calcd for $C_7H_8BrNS_2 \cdot H_2O$: C, 31.35; H, 3.76; N, 5.22. Found: C, 31.55; H, 3.80; N, 5.26. [d] From ethanol. [e] Keto sulfide (**5e**); ref 11. [f] Cyclized in polyphosphoric acid. [g] Pale yellow needles. [h] Infrared absorption at 1700 cm^{-1} (carbonyl). [i] The starting material was not the aldehyde but the corresponding diethyl acetal. Preliminary to cyclization, the acetal was allowed to stand in 6 *M* hydrochloric acid solution overnight, the acid was removed under vacuum, and the residue was cyclized in sulfuric acid. [j] Cyclized at room temperature for 36 hr. [k] Irregular crystals from methanol–ether.

Anal. Calcd for $C_{13}H_{10}BrNO_2S_2 \cdot 0.25H_2O$: C, 43.16; H, 2.92; N, 3.87. Found: C, 43.26; H, 2.82; N, 4.14.

2-Nitro-3,5-dimethylthiazolo[2,3-*b*]thiazolium Perchlorate (9).—Four grams of 3,5-dimethylthiazolo[2,3-*b*]thiazolium bromide (**6c**) was added in small portions, with stirring, to a mixture containing 25 ml of concentrated sulfuric acid and 25 ml of concentrated nitric acid. After the addition was complete, the solution was heated on a steam bath for 2 hr and then cooled and diluted with 200 g of an ice–water mixture. The solution which became cloudy as the solution was diluted, was later warmed on the steam bath until it became clear. The clear solution was decanted from some oily residue on the walls of the flask and 35% perchloric acid added. After the mixture had stood for several days at −15° a total of 280 mg (6%) of colorless needles, mp 202–209°, was collected. The analytical sample, crystallized from methanol as prisms, mp 208–209°, showed strong infrared absorptions at 1340 and 1540 cm^{-1} (nitro group).[17]

Anal. Calcd for $C_7H_7ClN_2O_6S_2$: C, 26.71; H, 2.24; N, 8.90. Found: C, 26.46; H, 2.26; N, 8.97.

2-(4-Methylthiazol-2-on-3-yl)prop-1-ene-1-thiol (11).—A solution of 2.68 g of 3,5-dimethylthiazolo[2,3-*b*]thiazolium bromide hydrate in 100 ml of 5% sodium hydroxide solution was heated at 100° for 4 hr. The yellow precipitate which appeared early in the reaction dissolved during the heating period. The resulting pale yellow solution was cooled to 0° and acidified with 6 *M* hydrochloric acid, affording 1.62 g (86%) of a colorless solid, mp 76–78°. The product was recrystallized first from ether–petroleum ether (bp 30–60°) and then from ether, as colorless needles, mp 78.5–80°. On drying at 56° (0.3 mm), the sample showed some tendency to undergo sublimation, λ_{max} 226 mμ (log ε 4.10).

Anal. Calcd for $C_7H_9NOS_2$: C, 44.89; H, 4.84; N, 7.48; S, 34.24. Found: C, 44.83; H, 5.01; N, 7.47; S, 33.92.

Bis[2-(4-methylthiazol-2-on-3-yl)prop-1-en-1-yl] Disulfide (13).—To a solution of 0.53 g of 2-(4-methylthiazol-2-on-3-yl)prop-1-ene-1-thiol (**11**) in 7 ml of ethanol, 7 ml of a 30% solution of aqueous hydrogen peroxide was added dropwise and the mixture was stirred for 18 hr at room temperature at which time a solid had begun to separate. The mixture was cooled and the product was collected, affording 0.19 g (28%) of a pale yellow solid, mp 130–132°. The analytical sample crystallized from ether as pale yellow, irregular crystals, mp 132–133°. The infrared absorption spectrum showed no absorption peak at 2450 cm^{-1} (thiol). The nmr spectrum (deuteriochloroform) showed no thiol proton, while the protons of the methyl groups again appeared as overlapping doublets (J = 1 cps) centered at τ 7.96. A multiplet assigned to the vinyl ring protons appeared at τ 4.15 while the side-chain vinyl protons were assigned a broad multiplet at 3.49. The observed decrease in the splitting of the side-chain vinyl protons (as compared with that observed for **11**) is attributed to the removal of the thiol proton.

(17) Reference 14, p 298.

Anal. Calcd for $C_{14}H_{16}N_2O_2S_4$: C, 45.13; H, 4.33; N, 7.52. Found: C, 45.36; H, 4.35; N, 7.46.

1-Benzylthio-2-(4-methylthiazol-2-on-3-yl)prop-1-ene (14).—To a sodium methoxide solution formed by the addition of 0.17 g of sodium to 20 ml of absolute methanol, 1.38 g of 2-(4-methylthiazol-2-on-3-yl)prop-1-ene-1-thiol (**11**) was added, followed by 0.93 g of benzyl chloride. After 6 hr at room temperature the mixture was filtered (to remove sodium chloride) and concentrated, the residue was taken up in methylene chloride, and the solution was washed, dried, and concentrated. The resulting yellow oil solidified, affording 1.48 g (72%) of a yellow solid, mp 86–92°. The analytical sample crystallized from ether as colorless, square plates, mp 94–96°.

Anal. Calcd for $C_{14}H_{15}NOS_2$: C, 60.62; H, 5.45; N, 5.05. Found: C, 60.52; H, 5.57; N, 5.10.

Formation of the Yellow Compound (12). A. By Action of Sodium Hydroxide on 3,5-Dimethylthiazolo[2.3-*b*]thiazolium Bromide.—To a solution of 26.8 g of the title bromide (monohydrate) in 250 ml of warm water, 550 ml of 10% sodium hydroxide solution was added. A yellow color was immediately apparent and a yellow solid began to precipitate. After 30 min at room temperature the yellow solid was collected, washed with water, and dried to yield 11.9 g (67%) of yellow needles, mp 193–194° dec. Longer reaction times were found to result in a decrease in yield. A small amount of the product was crystallized from methanol as yellow needles, which darken at 190–193° and decompose at 194–195°.

The alkaline filtrate on acidification with hydrochloric acid to pH 6 deposited 2.41 g (13%) of 2-(4-methylthiazol-2-on-3-yl)-prop-1-ene-1-thiol (**11**), mp 78–79°.

B. By Reaction of 3,5-Dimethylthiazolo[2,3-*b*]thiazolium Bromide with 2-(4-Methylthiazol-2-on-3-yl)prop-1-ene-1-thiol (11).—To a solution of sodium methoxide prepared from 0.11 g of sodium and 30 ml of absolute methanol, 0.87 g of the thiol (**11**) was added and a warm solution of 1.25 g of the dimethylthiazolothiazolium bromide (**6c**) in 15 ml of absolute methanol added all at once. There was an immediate precipitation of 1.44 g (88%) of a yellow solid, mp 190–194° dec, identical in infrared spectrum and melting point with the product obtained by procedure A.

Anal. Calcd for $C_{14}H_{16}N_2OS_4$: C, 47.16; H, 4.52; N, 7.86; S, 35.97. Found: C, 47.06; H, 4.47; N, 7.97; S, 35.94.

Reaction of the Yellow Compound (12) with Sodium Hydroxide.—One gram of the yellow compound (**12**) was warmed on a steam bath with 25 ml of 10% sodium hydroxide solution until the solid was completely dissolved (about 3 hr). The solution was cooled to 0° and acidified to give 0.92 g (88%) of buff-colored 2-(4-methylthiazol-2-on-3-yl)prop-1-ene-1-thiol (**11**). This was shown to be identical with the product (**11**) obtained by alkaline hydrolysis of 3,5-dimethylthiazolo[2,3-*b*]thiazolium bromide.

Reaction of the Yellow Compound (12) with Hydrochloric Acid.—To a suspension of 2.0 g of the yellow compound **12** in 50 ml of ethanol, 15 ml of 6 *M* hydrochloric acid was added with stirring. The yellow color disappeared immediately and after 1 hr the colorless solution was concentrated under vacuum and the residue was treated with 25 ml of ether and 25 ml of benzene. The solid remaining was collected and amounted to 1.10 g (96%) of colorless 3,5-dimethylthiazolo[2,3-*b*]thiazolium chloride, (**6c**) mp 316–319°. The infrared spectrum was identical with that of 3,5-dimethylthiazolo[2,3-*b*]thiazolium bromide and a small sample was converted to the perchlorate salt for comparison, mp 357° (explosive decomposition).

The ether–benzene filtrate obtained in this procedure was evaporated under reduced pressure and the residue was taken up in ether. Addition of petroleum ether (bp 30–60°) to the ether solution afforded 0.42 g (40%) of pale yellow 2-(4-methylthiazol-2-on-3-yl)prop-1-ene-1-thiol (**11**), mp 75–78°. Identity of this sample with those obtained previously in this work was demonstrated by mixture melting points and comparison of infrared spectra.

Registry No.—**3** (X = Y = S), 252-07-3; **4n**, 2103-95-9; **5b**, 13056-52-5; DNP of **5b**, 13085-15-9; **5d**, 2591-05-1; DNP of **5f**, 5591-02-6; **5h**, 13056-54-7; **5i**, 13056-55-8; **5j**, 13056-56-9; **5k**, 13056-57-0; DNP of **5k**, 13056-58-1; **5l**, 13056-59-2; DNP of **5l**, 13056-60-5; **5m**, 13056-61-6; **5n**, 13056-62-7; **5o**, 13056-63-8; **6a**, 13056-64-9; **6b**, 13056-65-0; **6c**, 2591-12-0; bromide of **6c**, 13056-67-2; **6d**, 2591-07-3; **6e**, 2591-13-1; **6g**, 13056-70-7; **6i**, 13056-71-8; **6j**, 13056-72-9; **6k**, 13056-73-0; **6l**, 13056-74-1; **6m**, 13056-75-2; **6n**, 13056-76-3; **6o**, 13056-77-4; **6** ($R_4 = CO_2H$; $R_3 = CH_3$; $R_2 = H$; $R_1 = C_6H_5$), 13056-78-5; perchlorate of **9**, 13056-79-6; **11**, 13056-80-9; **12**, 13056-81-0; **13**, 13085-17-1; **14**, 13056-82-1.

The Thiazolo[2,3-*b*]oxazolium Cation. A New Aromatic System

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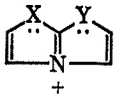
Alkylation products obtained by the reaction of α-halo ketones with oxazolethiols have been cyclized in sulfuric or polyphosphoric acid to produce the first aromatic thiazolo[2,3-*b*]oxazolium salts. The nmr deshielding in the environment of the oxygen and sulfur atoms of the new system resembles that reported earlier for simple oxazolium and thiazolium salts.

In an earlier communication,[2] it was pointed out that there should exist a series of aromatic cations having the general formula I in which X and Y represent hetero-



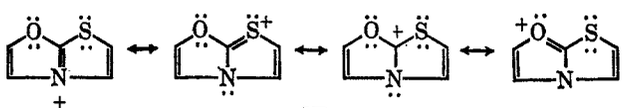
I

atoms having at least one unshared pair of electrons, and the first simple aromatic thiazolo[2,3-*b*]thiazolium salts (I, X = Y = S) were described. The present paper describes the first aromatic thiazolo[2,3-*b*]-oxazolium salts (I, X = O; Y = S). A logical approach to the synthesis of the new system was by an extension of the method which had proved successful in the thiazolothiazolium series. The recent discovery[3] that α-hydroxy ketones react with thiocyanic acid to afford 2-oxazolethiols (II) greatly facilitated the task. The thiols (II) were converted to the corresponding anion and allowed to react with α-halo ketones (III). The resulting sulfides (IV) were cyclized to the thiazolo-[2,3-*b*]oxazolium salts by use of either concentrated sulfuric or polyphosphoric acids. As might have been predicted from the very weak basicity of the oxazole nitrogen atom,[4] the cyclization of the oxazolyl sulfides (IV) proved slightly more difficult than for the thiazole counterparts, but in only one instance, IVg, did it prove impossible. The results are summarized in Table I.

The ultraviolet absorption spectra of the new thiazolooxazolium compounds (V) showed that the long-wavelength maximum occurs at significantly shorter wavelength than in the spectra of the thiazolothiazolium counterparts (I, X = Y = S). Frequently, the long-wavelength maximum of the starting sulfide (IV) would lie so close to that of the cyclization product (V) to make ultraviolet spectroscopy of little value in following the cyclization.

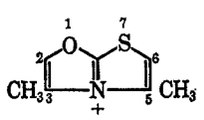
The nmr spectrum (trifluoroacetic acid) of the new compounds afforded evidence that cyclization had occurred and that the resulting ring system had aromatic character. No ring protons gave signals of greater than τ 2.69.

The possibilities for extensive delocalization of the positive charge are represented in incomplete and non-quantitative fashion by VI. It is clear that the new



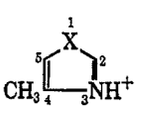
VI

system presents an excellent opportunity for the comparison of the environment adjacent to oxygen and sulfur in an otherwise symmetrical system. The nmr



ClO_4^-

VII



VIII, X = S
IX, X = O

spectrum (trifluoroacetic acid) of 3,5-dimethylthiazolo-[2,3-*b*]oxazolium perchlorate (VII) was particularly interesting. There were two, distinct one-proton peaks at τ 1.99 and 2.68 reflecting the inequality of the environments of the ring protons adjacent to oxygen and sulfur. Haake and Miller[5] have examined the

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