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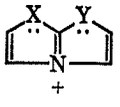
Alkylation products obtained by the reaction of α-halo ketones with oxazolethiols have been cyclized in sulfuric or polyphosphoric acid to produce the first aromatic thiazolo[2,3-*b*]oxazolium salts. The nmr deshielding in the environment of the oxygen and sulfur atoms of the new system resembles that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



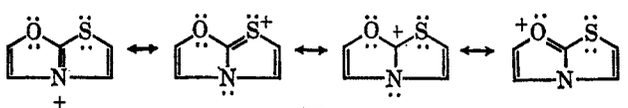
I

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.

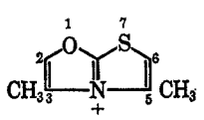
The nmr spectrum (trifluoroacetic acid) of the new compounds afforded evidence that cyclization had occurred and that the resulting ring system had aromatic character. No ring protons gave signals of greater than τ 2.69.

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



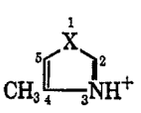
VI

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



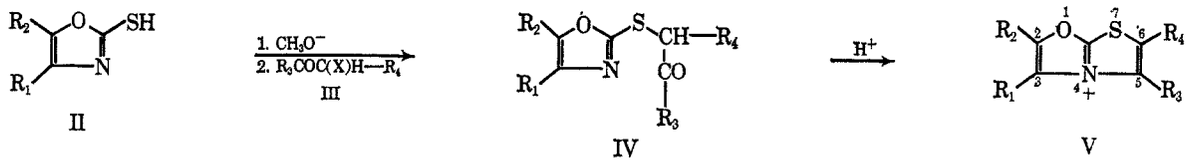
VIII, X = S
IX, X = O

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

(1) James B. Duke Fellow 1964–1966.
(2) C. K. Bradsher and W. J. Jones, Jr., *J. Org. Chem.*, **32**, 2074 (1967).
(3) J. F. Willems and A. Vandenberghe, *Bull. Soc. Chim. Belges*, **70**, 745 (1961).
(4) R. H. Wiley, *Chem. Rev.*, **37**, 401 (1945).
(5) P. Haake and W. B. Miller, *J. Am. Chem. Soc.*, **85**, 4044 (1963).

TABLE I

PREPARATION OF THIAZOLO[2,3-*b*]OXAZOLIUM PERCHLORATES



II IV V

No.	R_1	R_2	R_3	R_4	X	Yield of IV, %	Acid	Temp,[a] °C	Time, hr	Yield of V, %	λ_{max}, mμ (log ε)
a	Me	...	Me	...	Cl	79	S[b]	100	3	71	198 (3.88), 229 sh (3.66), 247 (3.76), 310 sh (2.54)
b	Me	...	Ph	...	Cl	80	S	100	3	44	198 (4.41), 216 sh (4.10), 278 (4.05)
c	Me	...	Me	Me	Br	73	S	100	3	77	201 (3.96), 241 (3.79)
d	Me	Me	Ph	...	Cl	74	P[c]	100	9	45[d]	198 (4.23), 214 sh (4.05), 236 sh (3.83), 267 (3.84)
e	Me	Me	Me	...	Cl	40	S	100	2	38	201 (3.96), 254 (3.71)
f	Me	Me	Me	Me	Br	90	S	100	2	38[e]	198 (4.08), 254 (3.72)
g	Ph	...	Me	...	Cl	59	P	100	9	0[f]	
h	Ph	...	Ph	...	Cl	58	P	150	17	78	200 (4.46), 271 (3.99)
i	Ph	Ph	Me	...	Cl	55	P	150	21	63	199 (4.52), 228 sh (4.12), 245 (4.14), 280 sh (3.73)
j	Ph	Ph	Ph	...	Cl	75	P	150	11	85	200 (4.67), 237 sh (4.23), 247 (4.24)

[a] S = sulfuric acid. [b] All temperatures are centigrade. [c] P = polyphosphoric acid. [d] The yield from sulfuric acid cyclization at 100° was only 26% after 3 hr. [e] Polyphosphoric acid at 100° for 3 hr gave only 25%. [f] Tar or nonsaltlike materials obtained using sulfuric acid. With polyphosphoric acid at 100 or 150°, only tar formation was encountered.

nmr spectra of the 4-methylthiazolium cation (VIII) and the 4-methyloxazolium cation (IX). They found that the resonance of the C-5 proton of the oxazolium salt (IX) occurred at τ 1.88, whereas the analogous proton on the thiazolium salt (VIII) occurred at 2.19. This makes it possible to assign the peak observed at τ 1.99 in 3,5-dimethyl-thiazolo[2,3-*b*]oxazolium perchlorate (VII) to C-2 (adjacent to oxygen) and the peak at 2.68 to C-6 (adjacent to sulfur). Confirmation of the correctness of this assignment was made by examination of the aromatic proton resonance of two trimethylthiazolo[2,3-*b*]oxazolium salts. In the 2,3,5-trimethyl derivative (proton adjacent to sulfur) resonance was observed at τ 2.63, while for the 3,5,6 derivative (proton adjacent to oxygen), it was observed at 2.00. The greater deshielding experienced by the proton adjacent to oxygen is explicable in terms of relative electronegativities of oxygen and sulfur.

The two methyl groups of 3,5-dimethylthiazolo-[2,3-*b*]oxazolium cation (VII) are nonequivalent. The doublet at τ 7.32 (J = 1.4 cps) was assigned to the C-3 methyl group, while that at 7.26 (J = 1.2 cps) was assigned to C-5. This assignment was made on the basis of the observation of Haake and Miller[5] that the methyl group of the 4-methylthiazolium salt (VIII) appeared as a doublet at a lower field and with a smaller coupling constant than was exhibited by its oxazolium counterpart (IX). The infrared spectrum of 3,5-dimethylthiazolo[2,3-*b*]oxazolium perchlorate bears a strong resemblance to that of the analogous 3,5-dimethylthiazolo[2,3-*b*]thiazolium salt.

The thiazolo[2,3-*b*]oxazolium system appears to be even less resistent to alkali than the thiazolo[2,3-*b*]-thiazolium system (I, X = Y = S). The attack of alkali on the 3,5-dimethyl derivative (VII) could be followed easily by the disappearance of the characteristic absorption at 247 mμ. At room temperature, this change occurred after 44 hr with 0.01 M and after 68 hr with 0.001 M sodium hydroxide solution. For comparison, the 3,5-dimethylthiazolo[2,3-*b*]thiazolium system required 0.1 M sodium hydroxide to effect complete reaction in 120 hr at room temperature.

Experimental Section

Elemental analyses were carried out by the Janssen Pharmaceutical Research Laboratories, Beerse, Belgium. All ultraviolet spectra were measured in 95% ethanol using 1-cm quartz cells using a Cary Model 14 spectrometer. Infrared data were obtained with a Perkin-Elmer Model 137 spectrophotometer. Nmr data were obtained with a Varian A-60 spectrometer using an external standard.

4-Methyl-2-oxazolethiol (II, R_1 = CH_3; R_2 = H).—The general method of Willems and Vandenberghe[3] was used. A solution of thiocyanic acid was prepared by dissolving 145.8 g of potassium thiocyanate in 3.2 l. of ethanol and adding 150 ml of concentrated hydrochloric acid, followed by filtration to remove the potassium chloride that precipitated. The ethanolic solution of hydrocyanic acid was refluxed for 24 hr with 74 g of a 95% solution of acetol.[6] The volume of the solution was evaporated under reduced pressure, and the resulting product was crystallized from ethanol affording 81.8 g (77%), mp 145–150°. The analytical sample was crystallized from ethanol as long, colorless needles, mp 150–152°.

Anal. Calcd for C_4H_5NOS: C, 41.72; H, 4.38; N, 12.17. Found: C, 41.80; H, 4.32; N, 12.27.

α-(2-Oxazolylthio) Ketones (IV).—A solution of sodium methoxide was prepared by the reaction of 4.6 g (0.2 g-atom) of sodium metal in 300 ml of absolute methanol, and 0.2 mole of the 2-oxazolethiol was added. To the resulting solution, 0.2 mole of the α-halo ketone was added slowly. After the solution had stood at room temperature for 18 hr, it was filtered to remove sodium chloride and the yellow filtrate was concentrated under reduced pressure. The residue was taken up in methylene chloride and the solution was washed with sodium hydroxide solution and water, dried (magnesium sulfate), and concentrated. The residue was purified by vacuum distillation or crystallized from methanol. Experimental data are summarized in Tables I and II.

Thiazolo[2,3-*b*]oxazolium Perchlorates (V). A. By Cyclization in Sulfuric Acid.—About 20 g of the α-(2-oxazolylthio) ketone (IV) was added to 60 ml of cold, concentrated sulfuric acid. The resulting solution was allowed to warm to room temperature and then heated for 3 hr on a steam bath. The acid solution was cooled to −15° and then poured into 700 ml of cold, anhydrous ether. A solid precipitate or oil formed. After the mixture had been allowed to stand for several hours in the refrigerator, the ether layer was decanted and the residue was taken up in 250 ml of water. The aqueous solution was charcoaled, filtered, and treated with about 10 ml of 35% perchloric

(6) We are indebted to the Jefferson Chemical Co. for a generous gift of acetol.

TABLE II

α-(OXAZOLYLTHIO) KETONES (IV)

IV	Ref[a]	Mp or bp[b] (mm), °C	Derivative[c]	Formula	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found
a	...[d]	78 (0.3)	Base	C_7H_9NOS[e]					8.18	8.18
b	...[d]	147–151 (0.5)[f]	DNP[g,h]	$C_{18}H_{15}N_5O_5S$	52.29	52.33	3.66	3.78	16.94	17.09
c	...[d]	71–73 (0.35)	Base	$C_8H_{11}NO_2S$	51.87	51.68	5.99	5.89	7.56	7.66
d	3	71.5–72.5[i]	Base	$C_{13}H_{13}NO_2S$	63.13	63.14	5.30	5.68	5.66	5.42
e	3	88–92 (0.45)	DNP[j]	$C_{14}H_{15}N_5O_5S$	46.02	45.95	4.14	4.18	19.17	18.99
f	3	76 (0.3)	Base	$C_9H_{13}NO_2S$	54.25	54.06	6.57	6.55	7.03	7.04
g	...[k]	82–83[i]	Base	$C_{12}H_{11}NO_2S$	61.78	61.48	4.75	4.85	6.01	5.95
h	...[k]	114–115[l]	Base	$C_{17}H_{13}NO_2S$	69.13	68.91	4.45	4.44	4.74	4.65
i	3	110–111[m]	Base	$C_{18}H_{15}NO_2S$	69.88	69.48	4.89	4.86	4.53	4.46
j	3	121.5–122[m,n]	Base	$C_{23}H_{17}NO_2S$	74.37	74.44	4.61	4.59	3.77	3.78

[a] Reference to preparation of the required thiol. [b] Boiling points are distinguished from melting points by indication of pressure in millimeters (in parentheses). [c] Derivative actually analyzed. [d] Experimental Section. [e] The 2,4-dinitrophenylhydrazone crystallized from ethanol as orange needles, mp 121–123°. *Anal.* Calcd for $C_{13}H_{13}N_5O_5S$: C, 44.44; H, 3.73; N, 19.94. Found: C, 44.32; H, 4.08; N, 20.09. [f] The oil solidified on standing, mp 27–29°. [g] 2,4-Dinitrophenylhydrazone. [h] From ethanol as small orange plates, mp 146–148°. [i] Colorless prisms. [j] From ethanol as orange needles, mp 145–146.5°. [k] E. D. Sych and Zh. N. Belaya, *J. Gen. Chem. USSR*, **33**, 1471 (1963). [l] Pale pink prisms. [m] Colorless needles. [n] From ethanol.

TABLE III

THIAZOLO[2,3-b]OXAZOLIUM PERCHLORATE SALTS (V)

V	Mp, °C	Crystalline form	Formula	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found
a	330–332[a]	Needles[b]	$C_7H_8ClNO_6S$	33.14	32.94	3.17	3.03	5.52	5.54
b	256–258[c]	Plates[b,d]	$C_{12}H_{10}ClNO_6S$	45.65	45.78	3.19	3.21	4.44	4.42
c	221–222.5	Needles[b]	$C_8H_{10}ClNO_6S$	35.89	35.93	3.77	3.70	5.23	5.25
d	264–265[c]	Plates[b]	$C_{13}H_{12}ClNO_6S$	47.35	47.28	3.67	3.55	4.25	4.35
e	183–185	Prisms[b]	$C_8H_{10}ClNO_6S$	35.89	35.92	3.77	3.75	5.23	5.15
f	173.5–175.5	Needles[b]	$C_9H_{12}ClNO_6S$	38.37	38.26	4.30	4.25	4.97	4.96
h	271–271.5[c]	Needles	$C_{17}H_{12}ClNO_6S$	54.04	54.41	3.20	3.28	3.71	3.64
i	168–170[e]	Prisms	$C_{18}H_{14}ClNO_6S$	55.18	55.09	3.60	3.63	3.58	3.43
j	239–241[c]	Needles	$C_{23}H_{16}ClNO_6S$	60.86	60.71	3.55	3.71	3.09	3.12

[a] Decomposes. [b] From methanol. [c] Melts with decomposition. [d] Light tan. [e] Previous shrinking at 151–153°.

acid. The precipitate obtained on cooling was recrystallized from methanol–ether.

B. By Cyclization in Polyphosphoric Acid.—About 1 g of the oxazolylthio ketone (IV) was heated with 20 g of polyphosphoric acid (time and temperature indicated in Table I), and the mixture was cooled and poured on about 20 g of cracked ice. When the ice had melted, the mixture was filtered to remove some tarry material. Addition of an excess of 35% perchloric acid to the filtrate afforded a precipitate which was recrystallized from methanol–ether. Additional experimental details may be found in Table III.

Registry No.—I (X = O; Y = S), 13016-16-5; II (R_1 = CH_3; R_2 = H), 13016-17-6; IVa, 13016-18-7; DNP of IVa, 13000-68-5; DNP of IVb, 13016-19-8; IVc, 13016-20-1; IVd, 13016-21-2; DNP of IVe, 13016-22-3; IVf, 13016-23-4; IVg, 13016-24-5; IVh, 13016-25-6; IVi, 13016-26-7; IVj, 13016-27-8; Va, 13016-28-9; Vb, 13016-29-0; Vc, 13016-30-3; Vd, 13016-31-4; Ve, 13016-32-5; Vf, 13016-33-6; Vg, 13016-34-7; Vh, 13016-35-8; Vi, 13016-36-9; Vj, 13016-37-0.