decomposition procedures utilized were analogous to those described for the preparation of Ia and Ib from their corresponding amines (*4*). Oxidation of the dihalo-3-picolines in neutral potassium permanganate afforded the desired dihalonicotinic acids.

Elemental analyses (C, H, N) for all new compounds in agreement with theoretical values were obtained and submitted for review. Experimental and physical data for the compounds described are presented in Table I.

EXPERIMENTAL

Elemental analyses were performed by the Heterocyclic Chemical Corp., Harrisonville, Mo. Melting points were taken on a Mel-Temp apparatus and are uncorrected. Infrared spectra were obtained in potassium bromide disks (unless otherwise indicated) on a Perkin-Elmer 337 spectrophotometer. Nuclear magnetic resonance (nmr) spectra were obtained at 60 MHz on either a Varian A-60 or a Jeolco C-60 HL instrument with tetramethylsilane as an internal standard.

2,5- and 5,6-Dihalonicotinic Acids. The appropriate dihalo-3-picoline (0.007 mole) and potassium permanganate (0.02 mole) were added to water (100 ml) and refluxed for 2 hr. After traces of unreacted starting material were removed by steam distillation, the manganese dioxide was removed by filtration, and the clear filtrate was concentrated to a volume of approximately 10 ml on a rotary evaporator. Acidification with concentrated hydrochloric acid afforded the crude dihalonicotinic acid which was recrystallized from water. The yield percentages were calculated on the basis of the amount of reacted starting material.

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Synthesis and Spectral Data for Bithiazole Derivatives

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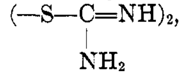
Nine bithiazole derivatives were synthesized by the interaction of rubeanic acid with α-haloketones. Uv, ir, and nmr data for the bithiazoles are presented.

Nine bithiazole derivatives were synthesized by the method of Karrer et al. (*2*), by the interaction of 1 mole of rubeanic acid (dithio-oxamide) with 2 moles of α-haloketones in alcoholic solutions. The α-haloketones used were: 2-bromoacetylfluorene, *p*-hydroxyphenacylbromide, *p*-nitrophenacylbromide, 2-bromo-1-tetralone, 2-bromocyclohexanone, 3-chloroacetylacetone, 5-bromoacetylindane, 3-bromoacetylindole, and 2-bromoacetylfuran. The structure and physical properties of the synthesized bithiazoles are given in Table I.

The direct preparation of substituted bithiazoles from a mixture of the ketone, rubeanic acid, and the oxidizing agent (bromine, iodine, or sulfuryl chloride) was not successful even when employing differing experimental conditions. In the condensation of thiourea with ketones, in the presence of an oxidizing agent, and in the synthesis of 2-aminothiazoles, formamidine disulfide  $(\text{—S—}\underset{\text{NH}_2}{\underset{|}{\text{C}}}\text{=NH})_2$, the oxidation product of thiourea, is thought to be the intermediate, since heating with certain ketones gives 2-aminothiazoles (*5*, *6*). Similarly, one expects that a similar intermediate is formed when rubeanic acid is treated with an oxidizing agent. When it was attempted to prepare such an intermediate, negative results were obtained due to the fact that the expected formamidine disulfide does never appear to be formed as an intermediate compared with the corresponding thiourea. On the contrary, α-bromoketones condensed successfully with rubeanic acid in alcoholic solutions. On the other hand, some α-haloketones, not mentioned in Table I, such as bromoacetone, bromoethylmethylketone, and α-bromoethylacetate, condensed poorly with rubeanic acid even on prolonged heating. 3-Chloroacetylacetone condensed more easily with rubeanic acid than its bromo analog, giving better yields. The uv, ir, and nmr data for the synthesized bithiazoles are given in Tables II and III.

EXPERIMENTAL

Melting points were taken by a Kofler Hot Bench, and are uncorrected. Elemental analyses were performed by Alfred Bernhardt's Laboratories, Ruhr, Germany. Ultraviolet absorption spectra were recorded by a Unicam sp800B ultraviolet spectrophotometer. Infrared spectra were recorded by a Perkin-Elmer Model 137B infracord spectrophotometer as Nujol mulls. Nuclear magnetic resonance spectra were measured on a Varian A60A spectrometer, as solutions in deuterated dimethylsulfoxide (DMSO-d_6) or trifluoroacetic acid (TFA) with tetramethylsilane (TMS) as the internal reference. All τ-values are correct to 0.01 τ unit.

Materials. Rubeanic acid (dithiooxamide) was a British Drug House (BDH) product and was recrystallized from ethanol. α-Haloketones were prepared by the procedure described in an earlier paper (*3*).

General Procedure for Preparation of Bithiazoles. Rubeanic acid (0.1 mole) in ethanol or glacial acetic acid (500 ml) was mixed with an alcoholic solution of α-haloketone (0.2

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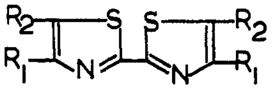
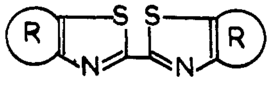
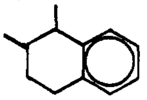
Table I. Physical Properties of Substituted Bithiazoles[a]



I



II

Molecular formula	R_1(or R)	R_2	Mp, °C	Yield, %	Reflux time	Solvent of crystallization
$C_{32}H_{20}N_2S_2$	2-Fluorenyl	H	339–40	50	8	Pyridine
$C_{18}H_{12}N_2O_2S_2$	$C_6H_4.OH$(p)	H	309–10	85	4	Ethanol
$C_{18}H_{10}N_4O_4S_2$	$C_6H_4.NO_2$(p)	H	327–28	75	5	Acetone/pyridine
$C_{12}H_{12}N_2O_2S_2$	Methyl	Acetyl	190–1	72	8	Ethanol
$C_{24}H_{20}N_2S_2$	5-Indanyl	H	220–21	58	1	Benzene/acetone
$C_{22}N_{14}N_4S_2$	3-Indolyl	H	356–8	52	2	Benzene/acetone
$C_{14}H_8N_2O_2S_2$	2-Furyl	H	236–8	50	2	Ethanol
$C_{14}H_{16}N_2S_2$	Cyclohexano	. . .	235–6	60	10	Acetone
$C_{22}H_{16}N_2S_2$		. . .	265–6	64	5	Acetone

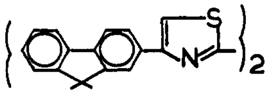
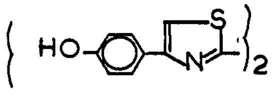
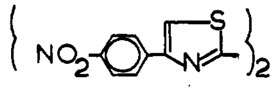
[a] Elemental analysis (C, H, N, S) in agreement with theoretical values were obtained and submitted for review.

Table II. Infrared and Ultraviolet Absorption Data for Bithiazoles[a]

νC=C, C=N	νC—H in-plane deformation	νC—H out-of-plane deformation	λ_{max} mμ (log ε)	Other bands (solvent)
1620(s), 1400(s) 1375(s), 1315(s)	1160(m), 1055(m) 1003(w), 962(s) 930(w)	895(s), 878(s) 855(s), 850(s) 805(s), 775(m) 755(m), 732(s)	303 (4.65)	290, 350 (DMFA)
1635(s), 1535(s)	1250(s), 1180(s) 1116(m), 1065(s) 955(s)	895(s), 855(s) 840(w), 815(w) 768(s), 755(s)	263 (4.56)	205, 351 (Ethanol)
1630(s), 1535(s) 1345(s)	1225(w), 1125(s) 1060(m), 1015(w) 945(s)	890(m), 865(s) 835(s), 782(s) 755(s)	335 (4.61)	265 (DMFA)
1675(s), 1370(s) 1325(s)	1250(s), 1060(s) 1040(w), 1000(w) 967(s)	880(w), 725(m) 705(m)	344 (4.28)	205 227, 253 (Ethanol)
1450(s), 1430(w) 1400(m), 1330(m)	1160(w), 1100(w) 1156(m), 972(w) 960(s)	890(s), 875(m) 850(m), 815(m) 755(s), 730(m)	208 (4.35)	252, 342 (Ethanol)
1575(w), 1335(w)	1235(w), 1100(s) 1055(w), 1010(m) 1005(m), 930(s)	885(s), 880(m) 842(m), 822(w) 768(w), 742(s) 722(w), 685(m)	204 (4.45)	233, 346 (Ethanol)
1640(w), 1530(w)	1200(m), 1088(w) 1062(w), 1008(s) 965(m), 910(s)	890(m), 880(m) 870(m), 815(m) 812(m), 765(s)	263 (4.45)	223, 346 (Ethanol)
1675(w), 1550(s) 1375(s), 1340(w)	1150(m), 1025(m) 960(m), 925(s)	860(m), 838(m) 725(m), 710(m)	332 (4.14)	203, 223 (Ethanol)
1670(w), 1370(m) 1280(w)	1200(w), 1080(m) 1040(w), 1020(m) 950(s), 905(s)	842(m), 788(w) 768(s), 735(m) 710(w), 675(m)	310 (4.52)	285, 352 (Ethanol)

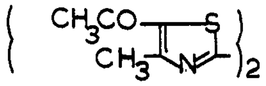
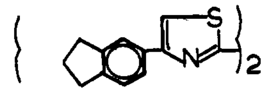
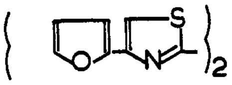
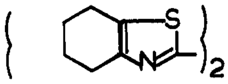
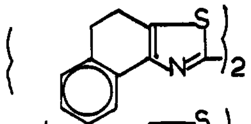
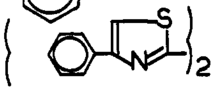
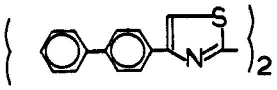
[a] s = strong, m = medium, w = weak, DMFA = *n,n*-dimethylformamide.

Table III. Nuclear Magnetic Resonance Data for Bithiazoles[a]

	Structural formula	Solvent	Aliphatic-H	Aromatic-H	H-5	J_{ab}, c/sec	J_{ac}, c/sec
IA		DMSO	6.6s, 5.8s, CH_2	1.7m, 2.4m	1.46s		
IB		DMSO	6.8b, OH, D_2O disappears	2d, 2.98d	1.87s	8.5	
IC		DMSO		1.5d, 1.85d	1.42s	9	

(*Continued on next page*)

Table III. *(Continued)*

	Structural formula	Solvent	Aliphatic-H	Aromatic-H	H-5	J_{ab}, c/sec	J_{ac}, c/sec
ID		DMSO	7.6s CH_3, 7.5s $COCH_3$				
IE		DMSO	7.64m, 6.8m	1.9m, 2.4m	1.76s		
IG		DMSO		2.18d, 3.18d, 3.33dd	1.94s	3.5	1.6
IIA		TFA	6.92m, 7.9m				
IIB		TFA	6.75m	2.5m			
IH*		DMSO		1.88dd, 2.4m	1.6s	6	2
Ii*		DMSO		2.3dd, 2.1m, 2d, 1.5d	1.34s	8	

[a] s = singlet, d = doublet, dd = double doublet, m = complex multiplet. J_{ab} = coupling constant in all AB systems. J_{ac} = coupling constant for AC part of all ABC systems. * The synthesis, uv, and ir spectra of these compounds have been described in the literature (*1, 4*).

mole in 100 ml of ethanol). The mixture was kept under continuous reflux for several hours (Table I). Excess solvent was removed under reduced pressure, and the precipitated product was recrystallized to give the pure bithiazole derivative. Melting points, yields, time of reflux, and solvent of crystallization for the synthesized bithiazoles are given in Table I.

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