The preparation of the previously undisclosed disulfide, 2,2′-dithio-bis-thiazole (V), was effected using a number of oxidizing agents; the best of these, ammonium persulfate, gave a 93% yield.

Experimental

Formylmethyl Dithiocarbamate (III).—Fifty-eight grams (0.53 mole) of II was dissolved in a solution of 50 cc. of water and 20 cc. ethanol. While stirring this solution and maintaining the temperature at 20°, 43.8 g. (0.5 mole) of I was added in thirty minutes. An oily layer separated but quickly solidified as agitation was continued. After cooling to −3°, the product was recovered by filtration, and upon drying at room temperature, 47 g. (69% yield), melting at 101–103°, was obtained. As a considerable amount of gum precipitated in the filtrate, the recovery of more product was not attempted. After recrystallizing from water, III was obtained as colorless crystals melting at 110°.

Anal. Calcd. for $C_3H_5NOS_2$: C, 26.65; H, 3.73; N, 10.36; S, 47.43; mol. wt., 135. Found: C, 26.74; H, 3.78; N, 10.31; S, 47.51; mol. wt., 138.5.

2-Thiazolethiol (IV).—One hundred and twenty grams (1.1 moles) of II[7] was dissolved in 250 cc. of water and while stirring vigorously 87.5 g. (1 mole) of I dissolved in 150 cc. of ethanol was added rapidly. The temperature rose from 25 to 82° during this reaction. The water solution of the reaction mixture was decanted from a small amount of sticky, yellow gum and was transferred to an evaporating dish. The solution was evaporated at 50° almost to dryness and was then extracted with 200 cc. of chloroform. The chloroform solution, after evaporating to dryness, gave 95 g. of crude product which upon recrystallizing from water yielded 58 g. (50%) as colorless plates, melting at 79–80°.

Anal. Calcd. for $C_3H_3NS_2$: C, 30.75; H, 2.58; N, 11.95; S, 54.72; mol. wt., 117. Found: C, 30.82; H, 2.64; N, 11.88; S, 54.58; mol. wt., 115.5.

A sample of the gum formed in the reaction, after repeated extractions with hot water, gave positive qualitative tests for nitrogen and sulfur. The composition of the gum was not determined because its physical condition made purification difficult.

It was concluded from further experimental work that no improvement in yield is obtained when the following variations in reaction conditions are employed: reversal of the order of addition, length of time of addition, reaction temperatures of 0 to 50°, concentration of reactants, the absence of air and light, the control of *p*H and the use of organic solvents as reaction diluents.[8]

In an attempt to promote ring closure by the addition of sulfuric acid to the solution resulting from the initial interaction of I and II, a colorless, apparently amorphous product melting at 96–98° was precipitated. The composition of this compound was not determined but it slowly undergoes spontaneous decomposition to form IV in rather low yield (38%).

2,2′-Dithio-bis-thiazole (V).—One hundred and fifty-two grams (1.3 moles) of IV was dissolved in a solution of 500 cc. of water and 54.6 g. (1.35 moles) of sodium hydroxide. While vigorously stirring this solution, 163 g. (0.72 mole) of ammonium persulfate, dissolved in 500 cc. of water, was added in one hour at 8°. During the addition of ammonium persulfate, a crystalline solid precipitated. After stirring for thirty minutes, the product was recovered by filtration, washed with water and dried at room temperature to give 141 g. (93% yield), melting at 79–80°. After recrystallizing from *n*-hexane, the disulfide was obtained as fine, light yellow needles melting at 83°.

Anal. Calcd. for $C_6H_4N_2S_4$: C, 31.01; H, 1.74; N, 12.06; S, 55.19; mol. wt., 232. Found: C, 31.13; H, 1.79; N, 12.13; S, 55.27; mol. wt., 236.

The disulfide decomposed slowly on storage. A similar effect has previously been reported for 2,2′-dithio-bis-(4,5-dimethylthiazole).[9]

Summary

The synthesis of 2-thiazolethiol and its intermediate, formylmethyl dithiocarbamate, from the interaction of chloroacetaldehyde and ammonium dithiocarbamate has been described. The oxidation of 2-thiazolethiol, under mild conditions, is shown to proceed normally to give the disulfide, 2,2′-dithio-bis-thiazole.

---

[7] Mathes, U. S. Patent 2,117,619. Ammonium dithiocarbamate was prepared according to Example 2.

[8] In these experiments, chloroacetaldehyde was used both as the hemihydrate and as the anhydrous compound which was prepared by passing hot vapors of the hemihydrate over calcium chloride.

[9] Buchman, Reims and Sargent, *J. Org. Chem.*, **6**, 764 (1941).

AKRON, OHIO RECEIVED OCTOBER 6, 1947

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE B. F. GOODRICH CO.]

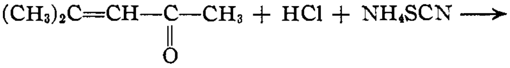
A Synthesis of 2-Pyrimidinethiols

BY ROGER A. MATHES, FLOYD D. STEWART AND FRANK SWEDISH, JR.[1]

In view of the usefulness of heterocyclic thiols as vulcanization accelerators, the authors had occasion to investigate 2-pyrimidinethiols. A new synthesis has been developed which simplifies the preparation, results in improved yields and extends the scope of former methods.

Methods previously employed to prepare 2-pyrimidinethiols include, among others, the interaction of 2-amino-2-methyl-4-pentanone (diacetonamine) and isothiocyanates[2] and the reaction of aliphatic ketones with ammonium thiocyanate.[3]

When mesityl oxide reacts with ammonium thiocyanate in the presence of a strong mineral acid, 2-methyl-2-thiocyano-4-pentanone[4] is formed. When this compound reacts with a primary amine or ammonia and an acid catalyst, a condensation takes place resulting in the formation of a 2-pyrimidinethiol. In the absence of an acid catalyst, ring closure is less readily effected and the intermediate thiourea is formed along with the 2-pyrimidimethiol.



$$(CH_3)_2C{=}CH{-}\underset{\displaystyle \overset{\|}{O}}{C}{-}CH_3 + HCl + NH_4SCN \longrightarrow$$

---

[1] Present address: Marathon Corporation, Rothschild, Wis.

[2] Traube, *Ber.*, **27**, 279 (1894); Traube and Lorenz, *Ber.*, **32**, 3156 (1899).

[3] ter Horst, U. S. Patent 2,234,848, *ibid.*, **35**, 4242[8] (1941).

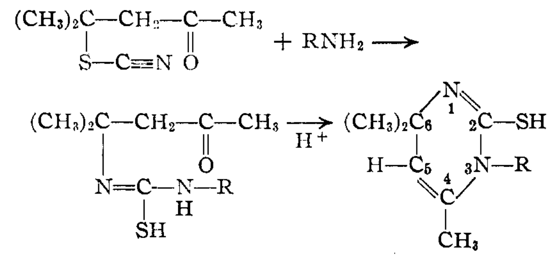
[4] Bruson, U. S. Patent 2,395,453, *ibid.*, **40**, 3467[1] (1946).

TABLE I

2-MERCAPTO-3-SUBSTITUTED-4,6,6-TRIMETHYLPYRIMIDINES

	R[c]	M. p., °C.[a]	Yield, %[b]	Formula	Calcd., % C	H	N	S	Mol. wt.	Found, % C	H	N	S	Mol. wt.
1	Hydro	254–255	90	$C_7H_{12}N_2S$	53.78	7.75	17.94	20.53		53.70	7.84	17.81	20.38	
2	*p*-Tolyl	191	83.5	$C_{14}H_{18}N_2S$	68.29	7.31	11.40	13.00	246	68.22	7.34	11.42	12.97	238
3	α-Naphthyl	216	87	$C_{17}H_{18}N_2S$	72.29	6.43	9.92	11.36	282	72.17	6.45	9.98	11.35	277
4	2-Hydroxyethyl[d]	180	54.5	$C_9H_{16}N_2OS$	53.96	8.05	13.99	16.01	200	54.01	8.05	14.08	16.07	197
5	Isopropyl[e]	267	27	$C_{10}H_{18}N_2S$	60.55	9.15	14.13	16.17	198	60.56	9.14	14.13	16.22	203
6	Cyclohexyl[f]	281-282	[f]	$C_{13}H_{22}N_2S$	65.49	9.30	11.76	13.45	238	65.45	9.28	11.82	13.46	238
7	1,3-Phenylene[g]	202	87	$C_{20}H_{26}N_4S_2$	62.12	6.78	14.50	16.60		62.05	6.77	14.56	16.57	
8	1,4-Phenylene	225	61	$C_{20}H_{26}N_4S_2$	62.12	6.78	14.50	16.60	386	61.76	6.92	14.49	16.64	384

[a] Melting points given are for analytical samples. [b] Yields are based on crude products. [c] Compounds 2, 3, 4, 7 were recrystallized from ethanol; 5, 6, 8 from chloroform; 1 from benzene. [d] During the preparation of this compound, the intermediate, 1-ethanol-3-[2-(2-methyl-4-pentanonyl)]-2-thiourea, was isolated. It melted at 144°. [e] In addition to this compound, 1-isopropyl-2-thiourea (m. p. 168–169°) was recovered from the reaction mixture. [f] This compound was recovered from the reaction mixture in low yield. The principal product of the reaction was 1-cyclohexyl-2-thiourea (m. p. 162°). [g] 1,3-Phenylene-bis-3,3′-(2-mercapto-4,6,6-trimethylpyrimidine).



This method of preparing 2-pyrimidinethiols from 2-methyl-2-thiocyano-4-pentanone and a primary amine or ammonia, in the presence of an acid catalyst, is of quite general application. It can be used successfully to prepare 2-pyrimidinethiols from mono and poly aromatic amines, alicyclic amines, aliphatic amines and hydroxy aliphatic amines. The reactions take place more readily and result in higher yields when aromatic amines are employed.

A second method was developed whereby the reaction can be carried out in one step, thus eliminating the initial preparation of 2-methyl-2-thiocyano-4-pentanone. In this modified procedure, acid is added to an agitated aqueous mixture of ammonium thiocyanate, mesityl oxide and a primary amine. Under the experimental conditions employed, this method was found to be applicable only to aromatic amines. Cyclohexylamine, isopropylamine, *n*-amylamine and ethanolamine were tried but in no case was a reaction product isolated. Apparently amines having dissociation constants greater than about 10^{-9} do not form 2-pyrimidinethiols in the modified procedure.

Experimental[5]

2-Methyl-2-thiocyano-4-pentanone.—Forty-nine grams (0.5 mole) of sulfuric acid dissolved in 50 ml. of water was added over a period of fifteen minutes to 98 g. (1 mole) of mesityl oxide at 15°. Seventy-six grams (1 mole) of ammonium thiocyanate dissolved in 100 ml. of water was added quite rapidly to this mixture at 20°. After stirring for fifteen minutes, the upper, red, oily layer was separated and was washed with water until free from acid. The crude product weighed 145 g., a yield of 92%. An analytical sample boiled at 97° (10 mm.), n^{20}_{D} 1.5030, d^{20}_{20} 1.0363.

Anal. Calcd. for $C_7H_{11}ONS$: C, 53.50; H, 7.00; N, 8.91; S, 20.38; mol. wt., 157. Found: C, 53.47; H, 7.06; N, 8.88; S, 20.30; mol. wt., 161.

The 2,4-dinitrophenylhydrazone derivative was prepared and when purified melted at 204°.

Anal. Calcd. for $C_{13}H_{15}O_4N_5S$: N, 20.77; S, 9.49. Found: N, 20.75; S, 9.45.

2-Mercapto-3-phenyl-4,6,6-trimethylpyrimidine—General Procedure.—A mixture of 78.5 g. (0.5 mole) of 2-methyl-2-thiocyano-4-pentanone, 46.5 g. (0.5 mole) of aniline, 2 g. (0.02 mole) of sulfuric acid and 150 ml. of water was agitated and warmed to refluxing temperature. The buff-colored crystalline product precipitated almost immediately. After cooling to room temperature, filtering, washing with water and drying, 96 g. (82.8% yield) of crude product melting at 188–190° resulted. On recrystallizing twice from alcohol, the melting point was 192–193°.

Anal. Calcd. for $C_{13}H_{16}N_2S$: C, 67.25; H, 6.90; N, 12.05; S, 13.80; mol. wt., 232. Found: C, 67.11; H, 6.98; N, 11.97; S, 13.84; mol. wt., 232.

3-*o*-Tolyl-2-mercapto-4,6,6-trimethylpyrimidine—Modified Procedure.—A mixture of 49 g. (0.5 mole) of mesityl oxide, 38 g. (0.5 mole) of ammonium thiocyanate, 53.5 g. (0.5 mole) of *o*-toluidine and 100 ml. of water was agitated in the reaction flask. Fifty-five grams (0.55 mole) of hydrochloric acid was added in ten minutes at a temperature of 20°. When heated to reflux, the buff-colored, crystalline product precipitated. After cooling to room temperature, filtering, washing with water and drying, 104.6 g. (85% yield) of crude product melting at 199–201° resulted. On recrystallizing twice from alcohol, the melting point was 202°.

Anal. Calcd. for $C_{14}H_{18}N_2S$: C, 68.29; H, 7.31; N, 11.40; S, 13.00; mol. wt., 246. Found: C, 68.08; H, 7.30; N, 11.41; S, 13.08; mol. wt., 253.

Summary

1. A new synthesis for 2-pyrimidinethiols, which consists of the reaction of 2-methyl-2-thiocyano-4-pentanone with primary amines, has been developed.

2. In a modified method it is shown that 3-aryl-2-pyrimidinethiols can be prepared in one step, with no evidence of the intermediate formation of 2-methyl-2-thiocyano-4-pentanone.

3. The preparation by these methods of ten representative compounds is described.

AKRON, OHIO

RECEIVED DECEMBER 6, 1947

---

(5) The melting points given are uncorrected.