three times with benzene; the combined benzene extracts were extracted with sodium bisulfite solution and then the solvent was removed under reduced pressure. The crude cyanohydrin was thus obtained as a colorless oil weighing 11.8 g. (90%). For analyses, a small sample of this product was distilled at 100° under a pressure of three microns.

Anal. Calcd. for C_5H_9NOS: C, 45.8; H, 6.87; N, 10.68. Found: C, 46.0; H, 6.88; N, 10.49.

3. 5(β-Methylmercaptoethyl)-hydantoin. A. From β-Methylmercaptopropionaldehyde.—A mixture of 26 g. (0.25 mole) of β-methylmercaptopropionaldehyde, 113 g. (1.17 moles) of finely divided ammonium carbonate, 24.5 g. (0.5 mole) of sodium cyanide, 335 ml. of ethanol and 335 ml. of water was agitated and heated for four hours at 50–55°. The light yellow reaction mixture was filtered, and the filtrate was concentrated at 60° to a volume of 300 ml., acidified with 50 ml. of concentrated hydrochloric acid and heated for five minutes at 90° to cyclize the hydantoic acid, which was found to be present in small amounts. After crystallization, separation and drying, the hydantoin weighed 34 g. (79% yield) and melted at 103–105°. The melting point remained unchanged after recrystallization from ethanol.

Anal. Calcd. for $C_6H_{10}O_2N_2S$: C, 41.38; H, 5.74. Found: C, 41.36; H, 5.81.

B. From α-Hydroxy-γ-methylmercaptobutyronitrile.—The cyanohydrin was prepared by the method given previously from 2.0 moles of the aldehyde. Removal of the benzene solvent left 255 g. of crude cyanohydrin, which was converted into the hydantoin, 174 g. (50% yield based on β-methylmercaptopropionaldehyde), by reaction with 420 g. of ammonium carbonate in 1000 ml. of 50 volume per cent. methanol for two and one-half hours at 50–55°. The product was isolated by the procedure described above.

4. DL-Methionine. A. From the Hydantoin.—5-(β-Methylmercaptoethyl)-hydantoin, 17.4 g. (0.10 mole) was refluxed for six hours with a solution of 8.8 g. of sodium hydroxide in 75 ml. of water contained in a stainless steel flask; an additional 4.4 g. of sodium hydroxide was added, and refluxing was continued for a total of twenty-four hours. The reaction mixture was decolorized with Norit, neutralized to litmus with concentrated hydrochloric acid, and allowed to crystallize at 5°. The product weighed 10.8 g. (73.5%); m. p. 269° with decomposition. An additional 1.7 g. (11%) of material could be isolated by a procedure involving acidification (hydrochloric acid), concentration to dryness, extraction with ethanol, and neutralization of the filtered ethanol extract to Congo with pyridine. After recrystallization of the combined fractions from aqueous ethanol, 10.6 g. of analytically pure methionine was obtained.

By omitting the isolation of both the β-methylmercaptopropionaldehyde and 5-(β-methylmercapto)-hydantoin, pure methionine was obtained in 50% yield based on the charge of acrolein and methyl mercaptan.

B. From the Cyanohydrin.—Gaseous ammonia was passed into 123 g. (0.94 mole) of the stirred cyanohydrin, maintained at 60° for thirty minutes. The reaction mixture was dissolved in benzene, heated to expel excess ammonia, and extracted with dilute hydrochloric acid. The aqueous layer was made alkaline with ammonia water and extracted with benzene; evaporation of the solvent left 49 g. (40%) of crude methionine nitrile. Several futile attempts were made to purify this intermediate and to obtain a crystalline derivative. The crude aminonitrile (10 g.) was hydrolyzed by heating on the steam-bath for five and one-half hours with 20 ml. of concentrated hydrochloric acid. The reaction mixture was diluted with 50 ml. of water, decolorized with Darco, and the solution concentrated to dryness under vacuum. The resulting solid was extracted with hot ethanol, and the ethanolic solution was filtered and neutralized to Congo with pyridine. Methionine in 75% yield (8.5 g.) was obtained.

Summary

A three-step synthesis of methionine has been devised based on the catalyzed addition of methyl mercaptan to acrolein, followed by the Bücherer hydantoin reaction, and then by hydrolysis.

RAHWAY, NEW JERSEY RECEIVED NOVEMBER 7, 1947

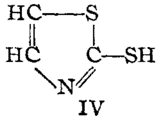
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE B. F. GOODRICH CO.]

A Synthesis of 2-Thiazolethiol and its Disulfide

BY ROGER A. MATHES AND ADOLPH J. BEBER

2-Thiazolethiols, particularly 2-mercaptobenzothiazole, have been used extensively for many years as accelerators for the vulcanization of rubber. The preparation of 2-thiazolethiol (IV), the parent compound of this series, recently has been reported[1] in the patent literature. This synthesis which was effected by treating α-chloroacetaldehyde (I) with ammonium dithiocarbamate (II), has been investigated by us in some detail and under varied conditions. The intermediate, formylmethyl dithiocarbamate (III), was isolated and characterized. The yield of IV was 50% based on I. The synthesis of IV is attended by troublesome side reactions, giving rise to gummy by-products, which apparently result from intermolecular reactions of aldehydes I and III with amino groupings in II and III. Acetaldehyde is known to react with II,[2] and I likewise reacts as a typical aldehyde.[3] Substituted 2-thiazolethiols,[4] on the other hand, can be prepared, usually in high yields,[4c] by the conventional reaction of α-halogen ketones with II. 1,2-Dichloroethyl ether which is known to replace I in thiazole syntheses[5] reacts with II to give a liquid of uncertain composition.[6]

$$\underset{\text{I}}{ClCH_2CHO} + \underset{\text{II}}{NH_2CSSNH_4} \longrightarrow \underset{\text{III}}{NH_2CSSCH_2CHO} \longrightarrow$$



IV

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(1) Jones, U. S. Patent 2,426,397.

(2) Levi, *Gazz. chim. ital.*, **59**, 757 (1929).

(3) Natterer, *Monatsh.*, **3**, 442 (1882); Glinsky, *Z. Chemie*, N. F., **6**, 647 (1870).

(4) (a) Miolati, *Gazz. chim. ital.*, **23**, 575 (1893); (b) Levi, *ibid.*, **61**, 719 (1931); (c) Mathes, U. S. Patent 2,186,419.

(5) Traumann, *Ann.*, **249**, 36 (1888); Hantzsch, *ibid.*, **250**, 271 (1889).

(6) Mathes, U. S. Patent 2,411,219.

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.

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[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.]

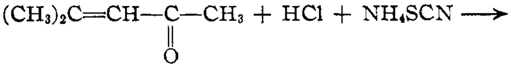
A Synthesis of 2-Pyrimidinethiols

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.



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

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[1] Present address: Marathon Corpoaation, 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).