[CONTRIBUTION FROM RÖHM AND HAAS COMPANY, INC.]

Action of Sulfuric Acid upon Unsaturated Isothiocyanates: Mercaptothiazolines

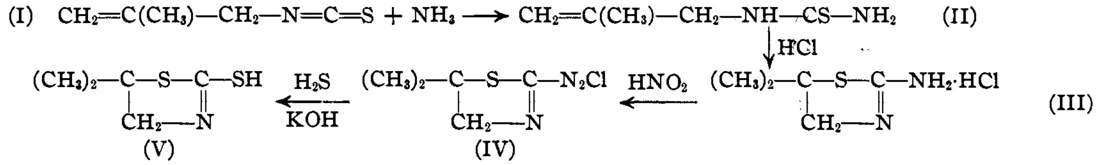
BY HERMAN ALEXANDER BRUSON AND JOHN W. EASTES

The action of concentrated sulfuric acid upon unsaturated aliphatic isothiocyanates has been investigated only slightly. Allyl isothiocyanate is reported to yield allylamine sulfate.[1]

However, we have found that the presence of a double bond carrying a tertiary carbon atom, as in methallyl isothiocyanate (I) or in α-ethyl methallyl isothiocyanate (XII) leads to the formation of more complex substances, namely, mercaptothiazolines.

The main product of the action of concentrated sulfuric acid upon methallyl isothiocyanate in the cold is a crystalline compound melting at 162.5–163° and having the empirical formula $C_5H_9S_2N$. It is a mercaptan the structure of which, as established by two independent syntheses, is 5,5-dimethyl-2-mercaptothiazoline (V). It gives a well-defined crystalline benzoate and acetate. With mercuric chloride, it gives a white mercurated derivative, $C_5H_8S_2NHgCl$.

Methallyl isothiocyanate (I) was converted by means of ammonia into methallylthiourea (II) which was then heated in a sealed tube with concentrated hydrochloric acid to form the cyclic compound, 5,5-dimethyl-2-aminothiazoline hydrochloride (III). The latter was diazotized and the diazonium salt (IV) treated with alkali and hydrogen sulfide to yield the corresponding mercaptan (V), which was identical with the specimen prepared by the action of concentrated sulfuric acid on methallyl isothiocyanate.

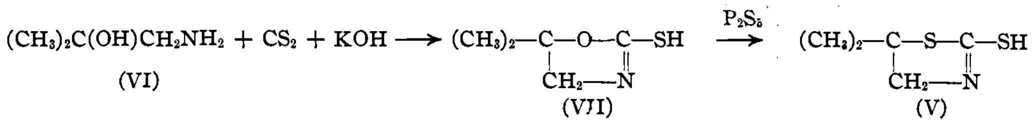


$$\text{(I)}\ CH_2{=}C(CH_3)\text{—}CH_2\text{—}N{=}C{=}S + NH_3 \longrightarrow CH_2{=}C(CH_3)\text{—}CH_2\text{—}NH\text{—}CS\text{—}NH_2\ \text{(II)}$$

$$\underset{\text{(V)}}{\begin{array}{l}(CH_3)_2\text{—C—S—C—SH}\\ \qquad\quad\ |\qquad\ \ \|\\ \qquad\quad CH_2\text{—N}\end{array}} \xleftarrow[KOH]{H_2S} \underset{\text{(IV)}}{\begin{array}{l}(CH_3)_2\text{—C—S—C—}N_2Cl\\ \qquad\quad\ |\qquad\ \ \|\\ \qquad\quad CH_2\text{—N}\end{array}} \xleftarrow{HNO_2} \begin{array}{l}(CH_3)_2\text{—C—S—C—}NH_2\cdot HCl\\ \qquad\quad\ |\qquad\ \ \|\\ \qquad\quad CH_2\text{—N}\end{array}\ \text{(III)}$$

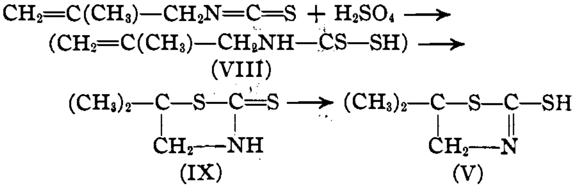
(II) $\xrightarrow{HCl}$ (III)

Another synthesis consisted in heating isobutanolamine (VI) in alkaline solution with carbon disulfide to form 5,5-dimethyl-2-mercapto oxazoline (VII) which, upon treatment with phosphorus pentasulfide, was converted to the corresponding thiazoline identical with (V).



$$\underset{\text{(VI)}}{(CH_3)_2C(OH)CH_2NH_2} + CS_2 + KOH \longrightarrow \underset{\text{(VII)}}{\begin{array}{l}(CH_3)_2\text{—C—O—C—SH}\\ \qquad\quad\ |\qquad\ \ \|\\ \qquad\quad CH_2\text{—N}\end{array}} \xrightarrow{P_2S_5} \underset{\text{(V)}}{\begin{array}{l}(CH_3)_2\text{—C—S—C—SH}\\ \qquad\quad\ |\qquad\ \ \|\\ \qquad\quad CH_2\text{—N}\end{array}}$$

The formation of 5,5-dimethyl-2-mercaptothiazoline by the action of concentrated sulfuric acid in the cold upon methallyl isothiocyanate can be explained by assuming that the first step in the reaction is the formation of a dithiocarbamic acid (VIII) which is unstable and immediately undergoes cyclization to the compound (IX), which tautomerizes to the mercaptan form (V).



$$CH_2{=}C(CH_3)\text{—}CH_2N{=}C{=}S + H_2SO_4 \longrightarrow \underset{\text{(VIII)}}{(CH_2{=}C(CH_3)\text{—}CH_2NH\text{—}CS\text{—}SH)} \longrightarrow$$

$$\underset{\text{(IX)}}{\begin{array}{l}(CH_3)_2\text{—C—S—C=S}\\ \qquad\quad\ |\qquad\ \ |\\ \qquad\quad CH_2\text{—NH}\end{array}} \longrightarrow \underset{\text{(V)}}{\begin{array}{l}(CH_3)_2\text{—C—S—C—SH}\\ \qquad\quad\ |\qquad\ \ \|\\ \qquad\quad CH_2\text{—N}\end{array}}$$

This explanation fits in well with the mechanism of the formation of thiazoline phenols by the action of concentrated sulfuric acid upon a mixture of phenol and allyl or methallyl isothiocyanate, recently described by Niederl, Hart and Scudi.[2]

Concentrated sulfuric acid also was found to act upon α-ethyl methallyl isothiocyanate (XII) in an analogous manner, to yield a mercaptothiazoline, thus indicating that the reaction is probably a general one for β,γ-unsaturated isothiocyanates in which the double bond carries a tertiary carbon atom.

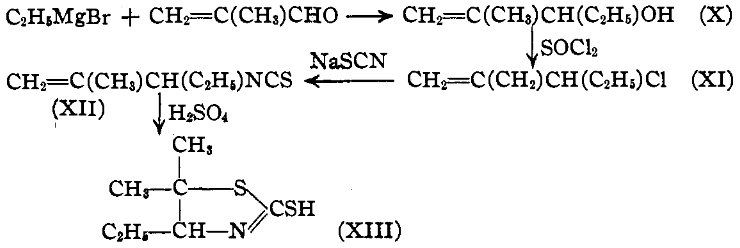
The α-ethyl methallyl isothiocyanate was prepared by condensing ethylmagnesium bromide with methacrolein to obtain the alcohol (X) which was converted to the chloride (XI) by means of thionyl chloride in pyridine. The chloride (XI)

---

(1) Hofmann, *Ber.*, **1**, 183 (1868).

(2) Niederl, Hart and Scudi, THIS JOURNAL, **58**, 707 (1936). A product having the composition $C_5H_9S_2N$, apparently identical with our compound, has been isolated from the products of the action of sulfuric acid on phenol and methallyl isothiocyanate by Niederl and his co-workers (private communication from Dr. J. B. Niederl).

was treated with sodium thiocyanate and the resultant isothiocyanate (XII) was treated with concentrated sulfuric acid, giving a mercaptothiazoline (XIII).



According to views proposed by Billeter,[3] concerning the rearrangement of thiocyanates to isothiocyanates, the structure of this product would be 5-methyl-5-propyl-2-mercaptothiazoline, instead of the structure (XIII) shown.

Experimental

I. **Methallyl Isothiocyanate.**—Four hundred and twenty-six grams (6 moles) of sodium thiocyanate was dissolved in 1.6 liters of boiling methanol and 547 g. (6 moles) of methallyl chloride (b. p. 71–72°) gradually added to the refluxing solution. The mixture was boiled under reflux for three hours after the addition of the methallyl chloride, then cooled, and the sodium chloride filtered off by suction. Upon fractionating the filtrate through an 8″ (20-cm.) column *in vacuo*, 640 g. of methallyl isothiocyanate was obtained; yield 94–95%; colorless liquid of onion-like odor. It showed the following boiling points: 56–59° (5 mm.), 64° (10 mm.), 78° (25 mm.), 85° (36 mm.), 89–90° (50 mm.), 169–170° (760 mm.).

Anal. Calcd. for C_5H_7NS: N, 12.38. Found: N, 12.00.

II. **N-Methallyl Thiourea.**—Thirty-four grams of methallyl isothiocyanate (I) and 400 cc. of 27% ammonium hydroxide were shaken together and allowed to stand for twenty-four hours. The white crystalline precipitate was purified by crystallization from water, using Norite to decolorize, m. p. 92–94°.

Anal. Calcd. for $C_5H_{10}N_2S$: C, 46.12; H, 7.75; N, 21.53; S, 24.60. Found: C, 46.59; H, 7.77; N, 21.40; S, 24.15.

III. **5,5-Dimethyl-2-aminothiazoline Hydrochloride.**—Thirty-seven grams of methallyl thiourea (II) and 30 cc. of 35% aqueous hydrochloric acid were heated in a sealed tube at 140° for eight hours. The resultant solution was extracted with ether, heated with Norite, filtered, and concentrated on steam-bath to crystallization. The crystals were recrystallized from acetone and dried in a desiccator over calcium chloride; m. p. 127–129.5°.

Anal. Calcd. for $C_5H_{11}N_2SCl$: C, 36.02; H, 6.66; N, 16.81; S, 19.21; Cl, 21.30. Found: C, 36.06; H, 6.58; N, 16.80; S, 19.44; Cl, 21.90.

IV. **5,5-Dimethylthiazoline Diazonium Chloride-2.**—Thirteen and five-tenths grams of 5,5-dimethyl-2-aminothiazoline hydrochloride (III) and 12 g. of sodium nitrite were dissolved in 400 cc. of water, the solution cooled to about 10°, and made acid with hydrochloric acid while stirring and allowing to come to room temperature. The bright yellow crystalline diazonium salt which separated was filtered off with suction, washed with cold water and dried in the air. It is fairly stable at ordinary temperature, but decomposes sharply and violently at about 140°.

V. (a) **5,5-Dimethyl-2-mercaptothiazoline.**—The 5,5-dimethylthiazoline diazonium chloride (IV) prepared as above from 13.5 g. of 5,5-dimethyl-2-aminothiazoline hydrochloride after filtration, but without drying, was dissolved in 200 cc. of water, which contained 5 g. of potassium hydroxide, to give a clear solution. This solution was saturated with hydrogen sulfide at 5°, resulting in the formation of a yellow precipitate. The mixture was then heated to boiling, while hydrogen sulfide was passing in, causing the yellow precipitate to turn white and then dissolve in the solution. Upon cooling, the solution deposited 4 g. of white crystals which were filtered off, dissolved in 25% sodium hydroxide solution, heated with Norite, filtered, and the clear, colorless filtrate made acid with hydrochloric acid, giving a white, crystalline product, m. p. 162.5–163°.

Anal. Calcd. for $C_5H_9NS_2$: C, 40.79; H, 6.17; N, 9.52; S, 43.52. Found: C, 40.90; H, 6.32; N, 9.05; S, 42.77.

V. (b) The same product was obtained from the action of sulfuric acid upon methallyl isothiocyanate, as follows: 500 cc. of 95% sulfuric acid was stirred and kept below 5° with an ice–salt bath, while 200 g. of methallyl isothiocyanate (I) was dripped in at such a rate that the temperature could be kept below 5°. After stirring for two hours at 5°, subsequent to the addition, the reaction mixture was poured into 2 liters of finely chipped ice, with stirring. The light yellow precipitate was filtered off, dissolved in 10% sodium hydroxide solution, heated with Norite, and the clear, colorless filtrate made acid with hydrochloric acid to give 95 g. of snow-white precipitate. If desired, the product may be purified further by recrystallization from alcohol or benzene. The pure product melted at 162.5° and gave no melting point depression in admixture with V-a.

Anal. Calcd. for $C_5H_9NS_2$: C, 40.79; H, 6.17; N, 9.52; S, 43.52. Found: C, 40.68; H, 6.49; N, 9.20; S, 43.50.

(V-b) **Benzoate.**—Bright yellow crystals, m. p. 91°, made by boiling V-b with sodium hydroxide solution and benzoyl chloride.

Anal. Calcd. for $C_{12}H_{13}NS_2O$: C, 57.35; H, 5.22; N, 5.58; S, 25.80. Found: C, 57.60; H, 5.40; N, 5.45; S, 25.57.

(V-b) **Acetate.**—Lemon yellow crystals, m. p. 69.5°, made by boiling V-b and acetic anhydride.

Anal. Calcd. for $C_7H_{11}S_2NO$: C, 44.18; H, 5.87; S, 33.84; N, 7.40. Found: C, 45.34; H, 6.15; S, 33.26; N, 7.65.

---

(3) Billeter, *Helv. Chim. Acta*, **8**, 337 (1925).

(V-b) **Mercuric Chloride.**—White crystalline powder made by mixing dilute alcoholic solutions of mercuric chloride and V-b.

Anal. Calcd. for $C_5H_8S_2NHgCl$: Hg, 52.42. Found: Hg, 52.90.

V. (c) A mixture consisting of 25 g. of phosphorus pentasulfide, 65 g. of 5,5-dimethyl-2-mercapto-oxazoline (VII) and 250 cc. of dry benzene, was refluxed for twenty-four hours. The benzene was distilled off and the residue extracted with 25% sodium hydroxide solution. This extract was treated with Norite, filtered, and acidified with hydrochloric acid, giving a white precipitate (5 g.) which, after recrystallization from boiling water, and then from alcohol, formed colorless crystals, m. p. 161.5°, which gave no depression of the melting point when mixed with the products obtained in (a) or (b) above.

Anal. Calcd. for $C_5H_9NS_2$: C, 40.79: H, 6.17; N, 9.52; S, 43.52. Found: C, 41.02; H, 6.30; N, 9.33; S, 43.07.

VII. **5,5-Dimethyl-2-mercapto-oxazoline.**—Twenty-five grams of 1-amino-2-hydroxyisobutane ("isobutanolamine" of b. p. 151° (760 mm.) obtained from the Shell Development Company) and 38 g. of carbon disulfide were mixed while cooling, and then a solution of 28 g. of potassium hydroxide in 150 cc. of alcohol and 20 cc. of water, was added. The reaction mixture was boiled under reflux for six hours, evaporated to dryness on the steam-bath, taken up in as little water as possible, and the solution made acid with dilute sulfuric acid; 38 g. of colorless crystals separated. These were purified by recrystallization from water and by throwing out of benzene solution by the addition of petroleum ether; m. p. 107–109°.

Anal. Calcd. for C_5H_9NOS: C, 45.77; H, 6.92; N, 10.68; S, 24.41. Found: C, 46.10; H, 7.16; N, 10.14; S, 24.30.

X. **1-Ethyl-2-methylallyl Alcohol.**—Twenty-four grams of magnesium turnings was treated with 109 g. of ethyl bromide in 300 cc. of anhydrous diethyl ether. The resultant ethylmagnesium bromide solution was treated with 70 g. of methacrolein and the reaction mixture decomposed with water. The ether layer was separated, dried over sodium sulfate, and distilled. The crude 1-ethyl-2-methyl allyl alcohol distilled at 129–140°; yield 54.5 g. It was not further purified, but was converted to the chloride directly.

XI. **1-Ethyl-2-methylallyl Chloride.**—Fifty-four and five-tenths grams of (X) above and 10 g. of pyridine were heated with 70 g. of thionyl chloride at 65° for four hours. The product was washed with water, taken up in ether, dried over sodium sulfate, and distilled. The yield was 38 g. of product boiling at 120–124°.

XII. **1-Ethyl-2-methylallyl Isothiocyanate.**—Thirty grams of sodium thiocyanate was dissolved in 300 cc. of hot methanol, and 38 g. of (XI) added. The mixture was refluxed for four hours, filtered, the filtrate diluted with water, and the oil layer separated, dried, and distilled. The yield of isothiocyanate was 20 g., boiling at 75–90° (10 mm.), 190–200° (760 mm.).

XIII. **4-Ethyl-5,5-dimethyl-2-mercaptothiazoline** (or **5-Methyl-5-propyl-2-mercaptothiazoline**).—Ten grams of 1-ethyl-2-methyl allyl isothiocyanate (XII) was added slowly to 70 g. of 95% sulfuric acid at 0°, and the mixture left at this temperature for thirty-six hours. The solution was poured into 600 cc. of finely chipped ice, giving a pink precipitate which was filtered off, dissolved in 10% sodium hydroxide solution, treated with Norite, and the resultant cleared solution made acid with hydrochloric acid. The product crystallized upon standing overnight, in the form of colorless plates which, after recrystallization from alcohol, melted at 115–118°.

Anal. Calcd. for $C_7H_{13}NS_2$: C, 47.97; H, 7.48; N, 8.00; S, 36.55. Found: C, 48.55; H, 7.47; N, 7.84: S, 36.70.

Summary

The action of concentrated sulfuric acid in the cold upon methallyl isothiocyanate and its α-ethyl homolog was investigated. In each case, a mercaptothiazoline was found to be the main product. The compound obtained from methallyl isothiocyanate was found to be 5,5-dimethyl-2-mercaptothiazoline, the structure of which was established by two synthetic methods.

PHILADELPHIA, PA.

RECEIVED AUGUST 4, 1937