4. Phenylbutadiene chlorohydrin readily absorbs a molecule of chlorine to give 1-phenyl-1,2,4-trichloro-3-hydroxybutane.

5. Phenylbutadiene chlorohydrin absorbs a molecule of hypochlorous acid to give a dichlorohydrin. In the same way phenylbutadiene bromohydrin absorbs a molecule of hypobromous acid to give a dibromohydrin

6. On treating with powdered potassium hydroxide, both phenylbutadiene chlorohydrin and bromohydrin lose a molecule of hydrogen chloride and hydrogen bromide, respectively, to give a monoxide of phenylbutadiene, $C_6H_5CH{=}CHCH{-}CH_2$ (with O bridging the CH and CH_2). This is the first time a monoxide of a conjugated compound has been reported.

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RESEARCHES ON PYRIMIDINES. CXIV. THE REARRANGEMENT OF 2-ETHYLMERCAPTO-5-CARBETHOXY-6-THIOCYANPYRIMIDINE INTO ITS ISOTHIOCYANATE MODIFICATION[1]

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The behavior of several chloropyrimidines toward potassium thiocyanate has been described in previous papers from this Laboratory,[2] but of all the different pyrimidine halides thus far studied in our thiocyanate researches no one has proved to be more interesting than 2-ethylmercapto-5-carbethoxy-6-chloropyrimidine, II, which was first described by Wheeler and Johns.[3] They prepared it by the action of phosphorus oxychloride on 2-ethylmercapto-5-carbethoxy-6-oxypyrimidine, I.

$\overline{\overline{NHC(SC_2H_5){=}NCH{=}C(COOC_2H_5)}CO}$ I

$\overline{\overline{NC(SC_2H_5){=}NCH{=}C(COOC_2H_5)}CCl}$ II

$\overline{\overline{NC(SC_2H_5){=}NCH{=}C(COOC_2H_5)}CSCN}$ III

$\overline{\overline{NC(SC_2H_5){=}NCH{=}C(COOC_2H_5)}CNCS}$ IV

$\overline{\overline{NC(SC_2H_5){=}NCH{=}C(COOC_2H_5)}CNH_2}$ V

2-Ethylmercapto-5-carbethoxy-6-chloropyrimidine, II, is another example of a halide in the pyrimidine series which interacts in a characteristic manner with potassium thiocyanate, giving a normal thiocyanate deriva-

[1] Constructed from part of a dissertation presented by Yuoh Fong Chi to the Faculty of the Graduate School of Yale University in June, 1928, in partial fulfilment of the requirements for the Ph.D. degree.

[2] Wheeler and Bristol, THIS JOURNAL, **23**, 287 (1901); Johnson and McCollum, *Am. Chem. J.*, **36**, 136 (1906); Johnson and Storey, *ibid.*, **40**, 138 (1908).

[3] Wheeler and Johns, *Am. Chem. J.*, **38**, 594 (1907).

tive, III. The rhodanide which is formed represents, however, a more stable structure than that revealed by any of the combinations previously studied. While the thiocyanate III can be distilled without decomposition, and without conversion to its isomeric isothiocyanate form, IV, its stability is influenced by the presence of certain reagents and a molecular rearrangement to the isothiocyanate can be accomplished at temperatures much below that of its boiling point. The conditions under which this change is brought about are discussed in the experimental part of this paper.

It has previously been shown in our paper on pyrimidine thiocyanates that chloropyrimidines corresponding in structure to II interact with potassium thiocyanate in absolute alcohol to give their corresponding pyrimidine thionurethans. In such reactions the first product of change is the thiocyanate, which then undergoes rearrangement to give the isothiocyanate modification. This latter compound, however, has a momentary existence only under the conditions of reaction and interacts immediately with the alcohol, when formed, to give the corresponding thionurethan derivative.

The thiocyanate III does not undergo a rearrangement to IV at the temperature of boiling alcohol. When heated with alcohol at 150°, however, the normal conversion is brought about, but the yield of thionurethan obtained under such conditions is only about 40% of the theoretical. We now find that this low yield of thionurethan can be accounted for by the formation of 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine, V. Not only does this latter compound account for the remainder of the reaction products, but we also have been able to show that, if the heating with alcohol is continued for a prolonged period (six hours) the thiocyanate is transformed almost completely into the corresponding amino compound. In other words, the thionurethan is destroyed by the prolonged action of alcohol. This is the first case so far observed in which we have been able to obtain directly from a thiocyanate an aminopyrimidine in good yield by interaction with alcohol. The mechanism of the change may be explained in the following manner: by interaction of the pyrimidine chloride II with potassium thiocyanate in alcohol solution, the rhodanide III is first formed, and is rearranged to the isothiocyanate or mustard oil, IV. This in turn then combines with a molecule of ethyl alcohol, giving a thionurethan, which under the conditions of the experiment reacts with alcohol to form the aminopyrimidine, V.

This interesting behavior of absolute alcohol toward the pyrimidine thiocyanate III opens up a new method of preparing amino compounds in the pyrimidine series by direct replacement of an SCN radical by NH_2 without the use of ammonia. A corresponding change was observed early in our researches on pyrimidines by Wheeler and Bristol,[4] who obtained 2-ethylmercapto-5-bromo-6-thiopyrimidine and the corresponding 6-aminopy-

[4] Wheeler and Bristol, *Am. Chem. J.*, **33**, 452 (1905).

rimidine in small amount by digesting 2-ethylmercapto-5-bromo-6-chloropyrimidine in alcohol solution with potassium thiocyanate. This reaction will probably prove of value for synthesis in cases where it is impossible to introduce an amino group in place of a halogen by heating with ammonia, without replacing other radicals or groupings at the same time.

Experimental Part

2-Ethylmercapto-5-carbethoxy-6-chloropyrimidine, II.—This pyrimidine was prepared according to the directions of Wheeler and Johns.[3] The yield from 13 g. of the mercapto-oxypyrimidine was 10 g. of the chloride boiling at 203° under a pressure of 20 mm.

2-Ethylmercapto-5-carbethoxy-6-thiocyanpyrimidine, III.—This thiocyanate can be obtained by the action of potassium thiocyanate on the above chloride in boiling alcohol, benzene, xylene, toluene or acetone solutions. Ten grams of the chloropyrimidine, boiling at 203° at 20 mm. pressure, and 4 g. of potassium thiocyanate are dissolved in 200 cc. of 95% alcohol and the solution refluxed on a steam-bath for one hour, when the reaction is complete. The solution is then filtered while hot and chilled, when the thiocyanate separates immediately in the form of colorless plates. The yield was 9 g. or 82% of the theoretical. After purification by crystallization from alcohol, it melted at 104–105° to a colorless oil and distilled at 204–205° under a pressure of 4 mm. The thiocyanate is insoluble in alkali, but soluble in benzene, toluene and xylene, very soluble in hot alcohol, and insoluble in petroleum ether.

Anal. Calcd. for $C_{10}H_{11}O_2N_3S_2$: N, 15.61. Found: N, 15.90, 15.60, 15.91.

The alcohol filtrate remaining after the separation of the above thiocyanate was evaporated to complete dryness and the residue obtained then triturated with cold dilute sodium solution. On acidifying this alkaline solution with acetic acid, 0.6 g. of a yellow compound separated in crystalline condition. After recrystallization from 95% alcohol, this melted at 180–181° with decomposition. The analytical values for nitrogen indicated that we are dealing here with 2-ethylmercapto-6-thionethylurethan-pyrimidine-5-carboxylic acid, $\overline{NC(SC_2H_5)=NCH=C(COOH)CNHCSOC_2H_5}$ (see below).

Anal. Calcd. for $C_{10}H_{13}O_3N_3S_2$: N, 14.63. Found: N, 14.38.

Proof of Structure of the Thiocyanate.—That the compound described above (melting at 104–105°) is to be represented by a normal rhodanide or thiocyanate structure is established by the following experimental facts: (1) it does not undergo any change leading to formation of a thiourea when exposed to the action of concentrated aqueous ammonia; (2) it can be crystallized from hot alcohol without conversion to a thiourethan, and (3) the compound interacts with thioacetic acid[5] to form the dithiourethan described below.

2-Ethylmercapto-5-carbethoxypyrimidine-6-acetyldithiourethan, $\overline{NC(SC_2H_5)=NCH=C(COOC_2H_5)CSCSNHCOCH_3}$.—Two grams of 2-ethylmercapto-5-carbethoxy-6-thiocyanopyrimidine was dissolved in 10 cc. of thioacetic acid and the solution warmed on a steam-bath for eight to ten hours. The solution was then evaporated to dryness to remove the excess of the thio-acid and the sirupy residue brought to crystallization by trituration with alcohol. This product was purified by crystallization from boiling 95% alcohol and it separated on cooling in the form of yellow plates melting at 142–143°.

Anal. Calcd. for $C_{12}H_{15}O_3N_3S_3$: N, 12.17. Found: N, 12.20.

[5] Wheeler and Merriam, THIS JOURNAL, **23**, 283 (1901).

The compound exhibited all the properties of a dithiourethan. It dissolved in cold alkali solution and was reprecipitated unaltered from such solutions by addition of acetic acid.

The Molecular Rearrangement of 2-Ethylmercapto-5-carbethoxy-6-thiocyanpyrimidine into its Isomeric Form, IV

2-Ethylmercapto-5-carbethoxy-6-isothiocyanpyrimidine, IV.—The best procedure for preparing this mustard oil is as follows. Five grams of the above thiocyanate is dissolved in 50 cc. of benzene and the solution heated at 190° for seven and one-half hours. When the tube was examined the solution was colored dark red. After evaporating the benzene, in which the isothiocyanate is very soluble, the latter was then extracted with petroleum ether, the solution concentrated and finally chilled, when the isothiocyanate separated in the form of prisms melting at 32–33° to an oil. The yield obtained was about 75%.

Anal. Calcd. for $C_{10}H_{11}O_2N_3S_2$: N, 15.61. Found: N, 15.68, 15.62.

Proof of Structure of the Isothiocyanate, IV. Reactivity toward Amines with Formation of Thioureas

2-Ethylmercapto-5-carbethoxy-6-thiourea-pyrimidine.—Two grams of the thiocyanate III was rearranged to the isothiocyanate IV as described above and the latter then separated in petroleum ether solution. On passing dry ammonia gas into this solution two grams of the above thiourea precipitated in crystalline form. After purifying by crystallization from ether, it melted at 165–168°.

Anal. Calcd. for $C_{10}H_{14}O_2S_2N_4$: N, 19.58. Found: N, 19.72, 19.60.

2-Ethylmercapto-5-carbethoxy-6-phenylthiourea-pyrimidine.—This is formed in quantitative yield by the action of aniline on the isothiocyanate in cold petroleum ether solution. It crystallizes from 95% alcohol in prisms which melt at 134–135° to an oil.

Anal. Calcd. for $C_{16}H_{18}O_2S_2N_4$: N, 15.47. Found: N, 15.36, 15.40.

2-Ethylmercapto-6-thionethylurethan-pyrimidine-5-carboxylic Acid.—One gram of the thiocyanate was rearranged to the isothiocyanate modification, then dissolved in 10 cc. of absolute alcohol and the solution boiled for one hour. On cooling, the urethan separated. This was then dissolved in dilute sodium hydroxide solution to saponify the ester grouping, and the alkaline solution then acidified with acetic acid, when 0.7 g. of the above thionurethan-carboxylic acid separated. After crystallization from alcohol it melted at 180–181°.

Anal. Calcd. for $C_{10}H_{13}O_3N_3S_2$: N, 14.63. Found: N, 14.45, 14.55.

Conditions Affecting the Rearrangement of the Thiocyanate, III.—While the thiocyanate can be distilled under diminished pressure without change into its isothiocyanate modification, IV, it can be rearranged at a temperature much lower than its boiling point. Rearrangement can be brought about by prolonged heating at 160–170°, but below this temperature the change is very slow. At 180–190° rapid change takes place, but the rearrangement is accompanied by secondary changes which lead to a reaction product which is very hard to purify. Dry heating is not recommended for accomplishing the thiocyanate rearrangement. Heating in benzene solution at 150° for six hours produced no change. At 160° partial rearrangement had taken place after heating for seven hours, and from the solution both the thiocyanate and isothiocyanate were separated, melting at 32–33 and 104°, respectively. Heating at 190° in either toluene or benzene solution leads to a complete molecular rearrangement. A specimen

of the thiocyanate III which had been preserved in a bottle for over two years was found to have suffered no change and melted at 104–105°.

Rearrangement by Heating in Alcohol.—At the boiling point of ethyl alcohol the thiocyanate III undergoes no rearrangement and can be recrystallized repeatedly from this solvent without alteration. On the other hand, when heated in alcohol at 150° (54° below its boiling point) the rhodanide is transformed completely into its isothiocyanate form, IV. This is formed as an intermediate product of reaction which then combines with the solvent, giving **2-ethylmercapto-5-carbethoxy-6-thionurethan-pyrimidine,** $\overline{NC(SC_2H_5)=NCH=C(COOC_2H_5)}CNHCSOC_2H_5$.

Ten grams of the thiocyanate III dissolved in 100 cc. of absolute alcohol was heated at 150° for two hours. When the tube was opened, 5 g. of a crystalline compound had separated. This crystallized from boiling alcohol in the form of prisms and melted at 119° to an oil. It gave the analytical results recorded below when analyzed for nitrogen and sulfur, indicating that the above thionurethan was the compound with which we were dealing.

Anal. Calcd. for $C_{12}H_{17}O_3N_3S_2$: N, 13.33; S, 20.34. Found: N, 13.23, 13.11, 13.22; S, 19.95, 20.18.

The alcohol filtrate from filtration of the above thionurethan was evaporated to dryness and the residue obtained triturated with dilute hydrochloric acid. Neutralization of the acid solution with ammonia produced an immediate crystalline precipitate weighing 3.5 g. which crystallized from dilute alcohol (50%) in plates melting at 101–102°. The compound gave no test for sulfur and it was identified as **2-ethylmercapto-5-carbethoxy-6-aminopyrimidine,** $\overline{NC(C_2H_5)=NCH=C(COOC_2H_5)}CNH_2$.

Conversion to this aminopyrimidine to the extent of 90% of the theoretical was accomplished by heating 10 g. of the thiocyanate III in alcohol at 150° for six hours. It crystallized in rectangular plates melting at 101–102° and when mixed with the aminopyrimidine prepared according to the method of Wheeler and Johns,[8] the melting point was not altered. A mixture of this pyrimidine and the thiocyanate III melted at 78°. This pyrimidine is moderately soluble in cold alcohol, and insoluble in water.

Anal. Calcd. for $C_9H_{13}O_2N_3S$: N, 18.50; S, 14.11. Found: N, 18.40, 18.47; S, 14.40, 14.42, 14.05.

Summary

1. 2-Ethylmercapto-5-carbethoxy-6-chloropyrimidine interacts normally with potassium thiocyanate to form a true thiocyanate derivative, 2-methylmercapto-5-carbethoxy-6-thiocyanpyrimidine.

2. This thiocyanate can be rearranged smoothly under certain experimental conditions into its isomeric isothiocyanate. Both the thiocyanate and isothiocyanate can be obtained as crystalline compounds.

3. The 2-ethylmercapto-5-carbethoxy-6-isothiocyanopyrimidine interacts with ethyl alcohol, at its boiling point, to form the corresponding thiourethan derivative. If the latter is heated, however, with alcohol at 150° for several hours, there is formed in almost quantitative yield 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine. This is a new method for converting pyrimidine thiocyanates into their corresponding aminopyrimidines, or for replacing a —SCN group by —NH_2.

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