

tallization from absolute methyl alcohol-ether mixtures, it separates in the form of very fine white needles which melt at 180-180.5° with the evolution of a gas.

Anal. Calcd. for $C_{13}H_{21}O_6N \cdot HCl$: N, 3.69; Cl, 9.37. Found: N, 3.67, 3.68; Cl, 9.32, 9.29.

The dimethyl ester hydrochloride is extremely soluble in absolute methyl alcohol, dissolving in less than its own volume, and is insoluble in ether. While stable in alcohol-ether mixtures, it readily dissociates hydrochloric acid when dissolved in water. Solution in this solvent is accompanied by the immediate separation of an oil and the water layer when decanted gives a precipitate of silver chloride when tested in the usual way.

Summary

An improved method for separating and purifying tyrosine-N-phenyl-acetic acid is described. Two distinct hydrogen chloride addition products of this acid have been prepared, together with the hydrochlorides of the corresponding methyl and ethyl esters.

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RESEARCHES ON PYRIMIDINES. CXXVIII. THE REARRANGEMENT OF 2-ETHYLMERCAPTO-4-METHYL-6-THIOCYANOPYRIMIDINE INTO ITS ISOTHIOCYANATE MODIFICATION^{1,2}

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Since Wheeler, Johnson and their co-workers began the study of the chemistry of thiocyanopyrimidine compounds,³ no specific change has proved to be more interesting to the writers than the rearrangement of 2-ethylmercapto-5-carbethoxy-6-thiocyanopyrimidine into its isomeric isothiocyanate modification, a transformation which was described recently in a paper by Johnson and Chi.⁴ They found that this thiocyanate could be distilled without decomposition and without molecular conversion to the isothiocyanate form, while its molecular rearrangement into the isothiocyanate form could be accomplished easily, under specific experimental conditions, at a temperature much below that of its boiling point.

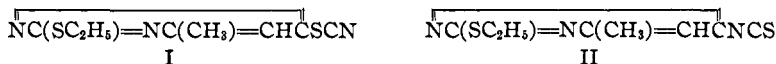
¹ This publication is a report of one phase of a research program dealing with the chemistry of certain pyrimidine thiocyanates, which was started originally in the Sterling Chemistry Laboratory of Yale University under the direction of Professor Treat B. Johnson.

² This research has been accomplished and arranged for publication through the support of a grant of \$750 from the Rockefeller Foundation. The authors desire to express here their appreciation and heartiest thanks for this liberal assistance.

³ Wheeler and Bristol, *Am. Chem. J.*, **33**, 450 (1905); Johnson and McCollum, *ibid.*, **36**, 143 (1906); Johnson and Storey, *ibid.*, **40**, 131 (1908).

⁴ Johnson and Chi, *THIS JOURNAL*, **52**, 1580 (1930).

This behavior was so interesting that the writers decided to examine the stability of another pyrimidine representative which has not been investigated. We now find that a similar behavior is observed in the case of the molecular rearrangement of 2-ethylmercapto-4-methyl-6-thiocyanopyrimidine (I) into its isomeric form represented by formula II.



This thiocyanopyrimidine I exhibits a chemical behavior similar to Johnson and Chi's 2-ethylmercapto-5-carbomethoxy-6-thiocyanopyrimidine. It can be distilled under diminished pressure (b. p. 155–158° at 5 mm.) without decomposition and without conversion into its isothiocyanate form II. The stability of the pyrimidine I, however, is greatly influenced by the presence of other reagents, and a molecular rearrangement to the isothiocyanate II can be accomplished easily at a temperature very much below that of the boiling point of the thiocyanate. This instability of molecular structure is quite remarkable. The conditions under which the transformation is brought about are described in the experimental part of this paper.

It has been the previous experience in the pyrimidine thiocyanate researches that thiocyanates corresponding to I may lead to the formation of polymeric forms of the thiocyanate after continued distillation.⁵ These new constructions result from the polymerization of the isothiocyanate modification resulting by molecular rearrangement. In the case of the thiocyanate I, this polymerized form is not produced directly by distillation, but it is formed by prolonged heating of the rearranged form II. The polymer is distinguished from the isothiocyanate form by its non-reactivity toward ammonia, aniline and ethyl alcohol.

Experimental Part

2-Ethylmercapto-4-methyl-6-thiocyanopyrimidine. I.—This pyrimidine is easily prepared as follows: 20 g. of the corresponding chloropyrimidine⁶ and 11 g. of potassium thiocyanate are dissolved in 120 cc. of 95% alcohol and the solution heated to boiling for one hour. The solution is then filtered hot to separate potassium chloride and then cooled, when the thiocyanate separates immediately in the form of colorless crystals. The yield was 19 g. or 81%. It was purified by crystallization from alcohol, melts at 69–70° to a clear liquid, and boils at 155–158° under 5 mm. pressure. The thiocyanate is insoluble in alkali, soluble in benzene, toluene and xylene. It is very soluble in hot alcohol, and insoluble in ether.

Anal. Calcd. for C₈H₉N₃S₂: N, 19.90. Found: N, 20.01, 19.62, 19.63.

This same thiocyanate compound I is likewise formed by refluxing 2-ethylmercapto-4-methyl-6-chloropyrimidine with potassium thiocyanate in both toluene and xylene solutions for one hour. The thiocyanate can be crystallized repeatedly from alcohol

⁵ Johnson and Storey, *Am. Chem. J.*, **40**, 131 (1908).

⁶ Johns, *ibid.*, **40**, 350 (1908).

without conversion to a thionurethan; it does not undergo any change leading to the formation of thioureas when exposed to the action of ammonia and aniline.

Molecular Rearrangement of the Thiocyanate I

2-Ethylmercapto-4-methyl-6-isothiocyanopyrimidine. II.—Four grams of the thiocyanate I was refluxed in 10 cc. of xylene for eight hours, giving a red colored solution. After distilling off the xylene, the isothiocyanate residue was triturated with cold ether and the ether finally evaporated, leaving behind the crude isothiocyanate as a red oil. This showed no signs of solidifying, and the yield corresponded to 67% of the theoretical. When this oil was subjected to distillation under diminished pressure, it slowly underwent a profound decomposition. A fraction distilling at 146–158° at 1 to 3 mm. exhibited all the properties of a true isothiocyanate. This reacted immediately with aniline, ammonia and alcohol in accordance with its isothiocyanate structure. Notwithstanding this characteristic behavior the oil did not respond to a good analysis for nitrogen and it could not be purified by further distillation.

Anal. Calcd. for $C_8H_9N_3S_2$; N, 19.90. Found: N, 21.00, 21.05.

Formation of the Polymerized Form of the Isothiocyanate.—Twenty grams of the thiocyanate I was treated as in the previous experiment to accomplish rearrangement to the isothiocyanate form. Attempts to purify the rearrangement product by distillation under diminished pressure led to the formation of a mixture of compounds. At 150–180° under a pressure of 4 to 10 mm., the impure isothiocyanate was collected. The distillation was then continued until the temperature rose to 220°, when a viscous oil was obtained which solidified almost immediately in the receiver. This dissolved in boiling benzene and separated on cooling in colorless crystals melting at 108–109°. The same crystalline compound was also obtained by redistillation of the crude isothiocyanate fraction boiling at 150–180° (see above). This substance is apparently a polymerized form of the isothiocyanate II. It can be recrystallized from alcohol without change, and does not combine with aniline and ammonia to form the corresponding thiourea derivatives.

Anal. Calcd. for $(C_8H_9N_3S_2)_2$; N, 19.90; S, 30.3. Found: N, 20.2, 20.00; S, 30.4.

Proof of Structure of the Isothiocyanate II

2-Ethylmercapto-4-methyl-6-thioureapyrimidine, $C_8H_{12}N_4S_2$.—The thiocyanate I was rearranged into the isothiocyanate form II, and an ether solution of the latter combined with an excess of concentrated aqueous ammonia. The corresponding thiourea was formed immediately and 1.8 g. of this was obtained from 2 g. of the thiocyanate. It was purified by crystallization from alcohol and melted at 229–231°.

Anal. Calcd. for $C_8H_{12}N_4S_2$; N, 24.55. Found: N, 24.35, 24.42.

2-Ethylmercapto-4-methyl-6-phenylthioureapyrimidine, $C_{14}H_{16}N_4S_2$.—Two grams of the rearranged thiocyanate gave 2.8 g. of this compound by treatment with aniline at ordinary temperature. This was purified by crystallization from 95% alcohol and separated in prisms melting at 209–210°.

Anal. Calcd. for $C_{14}H_{16}N_4S_2$; N, 18.41. Found: N, 18.28, 18.32.

2-Ethylmercapto-4-methyl-6-thionethylurethan Pyrimidine, $C_{10}H_{15}ON_3S_2$.—This is formed by warming the crude isothiocyanate II with absolute alcohol. The urethan separates from alcohol in the form of flat prisms melting at 97–98°.

Anal. Calcd. for $C_{10}H_{15}ON_3S_2$; N, 16.33. Found: N, 16.27, 16.31.

2-Ethylmercapto-4-methyl-6-thionmethylurethan Pyrimidine, $C_9H_{13}ON_3S_2$.—Prepared by the action of methyl alcohol on the crude isothiocyanate II. It crystallizes from ethyl alcohol in the form of needles melting at 84–86°.

Anal. Calcd. for $C_9H_{13}ON_3S_2$; N, 17.28. Found: N, 17.30.

Experimental Conditions Influencing the Rearrangement of the Pyrimidine Thiocyanate I

A.—Heating of the thiocyanate I at 115–120° for four hours and at 100° for eight hours did not give any detectable amount of the isothiocyanate modification.

Digestion of the pyrimidine thiocyanate I in toluene did not produce a rearrangement but the change was brought about by refluxing in xylene solution.

B. Rearrangement of the Thiocyanate I by Heating with Alcohol.—At the boiling point of ethyl alcohol the pyrimidine thiocyanate I undergoes no change and can be recrystallized repeatedly from this solvent without structural alteration. On the other hand, when heated in alcohol solution at 100° for six hours (55° below its boiling point), the thiocyanate is transformed completely into the isothiocyanate II, and the latter combines with the alcohol, giving the corresponding thionurethan. The yield is excellent, and the thionurethan melts sharply after one crystallization at 97–98°.

Summary

1. 2-Ethylmercapto-4-methyl-6-thiocyanopyrimidine is formed by interaction of potassium thiocyanate with 2-ethylmercapto-4-methyl-6-chloropyrimidine in boiling ethyl alcohol solution.

2. This thiocyanate distills at 155–158° at 5 mm. and is rearranged to its isomeric form, the isothiocyanate, (1) by heating with alcohol at 100° and (2) by digestion in boiling xylene.

3. 2-Ethylmercapto-4-methyl-6-isothiocyanopyrimidine cannot be distilled without decomposition. It is slowly transformed into a polymeric modification.

4. The thiocyanate does not react with alcohols, ammonia or aniline. The isothiocyanate interacts with these same reagents to form the corresponding thionurethans and thioureas, respectively.

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THE PARA-PHENYLPHENACYL ESTERS OF CERTAIN ORGANIC ACIDS¹

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The advantages of *p*-phenylphenacyl bromide as a reagent for identifying organic acids have been previously described by Bronitsky and one of us.² We have made frequent use of the reagent in this Laboratory in research and in a course in organic qualitative analysis, and because of the success we have experienced in its use, we have deemed it desirable to report the melting points and solubility behavior of certain *p*-phenylphenacyl esters not prepared in the earlier work.

¹ From a thesis submitted to the Graduate School of the University of Maryland by J. P. Sweeney in partial fulfillment of the requirements for the degree of Master of Science.

² Drake and Bronitsky, *THIS JOURNAL*, **52**, 3715 (1930).