hexyl 2-carbamylcyclohexylamine hydrochloride in 37% hydrochloric acid in a sealed Carius tube at 180° for 10 hr. resulted only in complete decomposition of the product. Attempts to isomerize either cyclohexyl 2-carbamylcyclohexylamine hydrochloride or cyclohexyl 2-carboxycyclohexylamine hydrochloride in 37% hydrochloric acid at 180° for 1 hr. also resulted in decomposition. When cyclohexyl 2-carboxycyclohexylamine hydrochloride (0.5 g.) in 37% hydrochloric acid was heated at 130° for 1 hr., starting material was recovered in 64.2% yield (0.32 g., m.p. 240–241°).

Attempts to prepare trans-cyclohexyl 2-substituted cyclohexylamines (a). A mixture of 1-cyanocyclohex-1-ene (5 g., 0.046 mole), cyclohexylamine (7 g., 0.07 mole) and a few crystals of hydroquinone was sealed in a Carius tube and heated at 150° for 50 hr. The mixture on distillation *in vacuo* gave 6.19 g. (88.5%) of unchanged cyclohexylamine and 4.4 g. (88.7%) of 1-cyanocyclohex-1-ene. No other products could be identified.

(b). A solution of cyclohex-1-enecarboxylic acid (2.5 g., 0.0198 mole) and cyclohexylamine (7.85 g., 0.080 mole) in water (12.5 ml.) was heated in a Carius tube at 180° for 66 hr. The solution was evaporated to dryness and the residue was dissolved in 10% hydrochloric acid. Extraction of the acid solution with ether gave 2.4 g. (96%) of unchanged acid which was identified by a mixed melting point determination.

LaSalle, Quebec

[Contribution from the Department of Chemistry of the University of Buffalo]

Reactions of Ethoxymethylenemalononitrile with Thioureas[1]

STEVE G. COTTIS[2] AND HOWARD TIECKELMANN

Received April 19, 1960

Ethoxymethylenemalononitrile is hydrolyzed in alkaline aqueous solvents to hydroxymethylenemalononitrile, malononitrile, or tetracyanopropene, depending on conditions. 2-Amino-3,5-dicyano-6-alkoxypyridines are formed in alkaline aqueous alcohols. 2-Amino-3,5-dicyano-6-alkylthiopyridines are formed in solutions containing mercaptans or alkylthioureas. Ethoxymethylenemalononitrile condenses with 2-alkyl-2-thiopseudoureas to give 2-alkylthio-4-amino-5-cyanopyrimidines in alkaline aqueous solvents if the nitrile is added to the thiourea.

The condensation of ethoxymethylenemalononitrile (I) with amidines, guanidine, and thioureas in anhydrous solvents to form 2-substituted-4-amino-5-cyanopyrimidines is well known.[3,4] Aqueous solvents usually are not used in these condensations although 2-methyl-4-amino-5-cyanopyrimidine has been prepared in good yield from I in an aqueous medium.[5] Because of the observations that thioureas (II) often condense well to form 2-alkylthiopyrimidines in solvents containing water, we have investigated reactions of I with thioureas in alkaline aqueous solutions.

Preliminary experiments indicated that the yields of pyrimidines in aqueous solution sometimes were low but that pyridines were also formed and that the nature of the products depended, to some extent, on the ratio of starting materials, the solvent, and the order of addition of the reagents. For example, the addition of I in acetone to a solution of 2-methyl-2-thiopseudourea (II, R = CH_3) in aqueous acetone gave a good yield of 2-methylthio-4-amino-5-cyanopyrimidine (III, R = CH_3). However, when a mixture of I and II (R = CH_3) in aqueous acetone or alcohol was brought slowly to neutrality with ammonium hydroxide, the addition of more base after one hour gave a 47% yield of 2-amino-3,5-dicyano-6-methylthiopyridine (VIII).

It was not apparent immediately that some of our products were pyridines. However, a study of the behavior of I in the presence of bases, and in the absence of thioureas was informative. When a solution of I in alcohol was added slowly to an equivalent quantity of potassium hydroxide, the potassium salt of hydroxymethylenemalononitrile (VI) was formed (80%). If a solution containing one half an equivalent of potassium hydroxide in alcohol was added slowly to I in alcohol, the salt of 1,1,3,3-tetracyanopropene (VII) was formed and an odor of ethyl formate was detected. Intermediate procedures such as the addition of potassium hydroxide in one portion to I gave mixtures of VI and VII. An excess of potassium hydroxide in water added to I in methanol gave some 2-amino-3,5-dicyano-6-methoxypyridine (XI). This latter substance was more conveniently prepared from VII, which, in turn, was prepared in quantity from anilinomethylenemalononitrile and malononitrile by the method of Strell.[6]

The above observations can be explained by considering two competing reactions of I in base through a Claisen type intermediate IV. The intermediate can lose alcohol to give VI or undergo a reverse Claisen condensation to give ethyl formate

(1) Supported by a grant CY-2857 from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

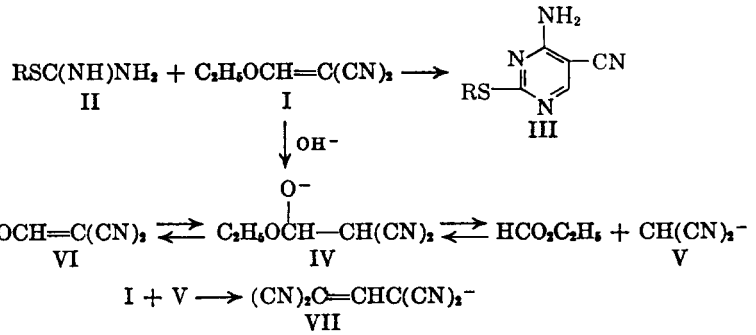
(2) In part from a thesis submitted by Steve G. Cottis to the Graduate School of Arts and Sciences, the University of Buffalo, in partial fulfillment of the requirements for the degree of Master of Arts, February 1959.

(3) R. Grewe, *Z. physiol. Chem.*, **242**, 89 (1936).

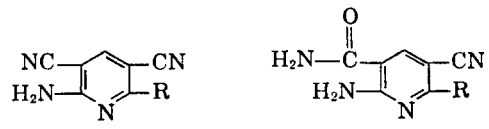
(4) W. Huber and H. A. Holsher, *Ber.*, **71B**, 87 (1938).

(5) Y. Sawa, F. Osawa, and H. Kaneko, *J. Pharm. Soc. Japan*, **67**, 204 (1947); *Chem. Abstr.*, **45**, 9063 (1951).

(6) M. Strell, W. B. Braunbuck, W. F. Fuhler, and O. Huber, *Ann.*, **587**, 177 (1954).



and the malononitrile anion (V). If I is present in excess it reacts readily with V to form VII.



	R		R
VIII	CH_3S—	XII	C_2H_5O—
IX	C_2H_5S—	XIII	HO—
X	$C_6H_5CH_2S$—	XIV	CH_3S—
XI	CH_3O—	XV	C_2H_5S—

The possibility was considered that VI was an intermediate in the formation of VII and of pyrimidines. Experiments indicated that under the conditions employed for the formation of these substances, the potassium salt of VI did not react with I or V to form VII or with II to form pyrimidines.

Pyrimidines were formed from I and II if an excess of I was avoided during the condensation, most easily accomplished by slow addition of a solution of I in acetone to a solution of II in aqueous acetone. An excess of base led to an only slightly lower yield. The use of alcohol as the solvent led to lower yields.

The formation of VII from I and V is well known.[7,8] Furthermore, it has been demonstrated that although VII is formed in high yield when the reaction is carried out at 0°, if the reagents are mixed without cooling, 2-amino-3,5-dicyano-6-ethoxypyridine is formed.[8] 6-Chloropyridines of this series have been formed from hydrogen chloride and VII. 6-Alkoxypyridines have been prepared from the 6-chloropyridine and by treatment of quaternary ammonium salts of VII, with alcohols in the presence of sulfuric acid.[8]

In the present work when the potassium salt of VII was heated in a basic solution of aqueous methanol, 2-amino-3,5-dicyano-6-methoxypyridine (XI) was formed but under similar conditions, when aqueous ethanol was the solvent, 2-amino-5-cyano-6-ethoxy-3-pyridinecarboxamide (XII) resulted. The structure of XII was established by conversion to 4-hydroxy-6-cyano-7-ethoxypyrido-(2,3-d)pyrimidine on treatment with formamide.

When XII was refluxed in dilute potassium hydroxide it gave a hydrate of the potassium salt of 2-amino-5-cyano-6-hydroxy-3-pyridinecarboxamide (XIII). A nitrile band in the infrared spectrum at 2220 cm.$^{-1}$ indicated this substance was a hydrated cyanocarboxamide rather than the dicarboxamide. In addition, XIII was prepared by heating VII in alkaline solution and from 2-amino-3,5-dicyano-6-chloropyridine by a similar procedure.

Although 6-alkylthiopyridines are formed by the addition of base to solution of I and II in alcohol or from VII and the corresponding mercaptan, in most cases it was more convenient to prepare members of this series from VII and 2-alkyl-2-thiopseudoureas. The structure of 2-amino-3,5-dicyano-6-ethylthiopyridine (IX) was confirmed by its synthesis from 2-amino-3,5-dicyano-6-chloropyridine.

The dicyanopyridines were readily hydrolyzed to cyanocarboxamidopyridines (XIII, XIV, XV) and under more vigorous conditions to the dicarboxylic acids (XVI, XVII). On heating with 10*N* potassium hydroxide, XIV gave 2-amino-6-hydroxy-3,5-pyridinedicarboxylic acid (XVIII).

EXPERIMENTAL[9]

Potassium 1,1,3,3-tetracyanopropene. A solution of 4.6 g. (0.082 mole) of potassium hydroxide in 50 ml. of alcohol was added slowly to 20.0 g. (0.165 mole) of ethoxymethylenemalononitrile in 20 ml. of alcohol at below 5°. After addition of 20 ml. of ether, the precipitate was collected and recrystallized from *n*-butyl alcohol–methanol to give 12.0 g. (82%) of yellow needles which decomposed at 319–320°. (Lit.: A decomposition, beginning at 250° has been reported.[5] Prepared by this method an impure material was formed which decomposed above 250°. Recrystallized several times from alcohol, long white needles were formed which decomposed sharply at 319–320°.)

Anal. Calcd. for C_7HN_4K: C, 46.65; H, 0.55; N, 31.09; K, 21.69. Found: C, 47.09; H, 0.38; N, 31.40; K, 21.67.

The potassium salt of hydroxymethylenemalononitrile. A cold solution of 5.0 g. (0.41 mole) of I in 20 ml. of alcohol was added slowly to 2.3 g. of potassium hydroxide in 5 ml. of water at below 5°. After stirring for 15 min. the precipitate was collected, washed with *n*-butyl alcohol, and

(7) Y. Urushibara, *Bull. Chem. Soc. Japan*, 2, 278 (1927).

(8) E. L. Little, Jr., W. J. Middleton, D. D. Coffman, V. A. Engelhardt, and G. N. Sausen, *J. Am. Chem. Soc.*, 80, 2832 (1958).

(9) Microanalyses by Geller Laboratories, Bardonia, N. Y., and Schwartzkopf Microanalytical Laboratories, Woodside, N. Y. Melting points are uncorrected.

recrystallized from alcohol–butyl alcohol to give 4.3 g. (79%) of yellow needles which decomposed with melting at 270–271° (lit.[10] m.p. 268°).

Anal. Calcd. for C_4N_2HOK: C, 36.35; H, 0.76; N, 21.20. Found: C, 36.08; H, 0.52; N, 21.55.

2-Amino-3,5-dicyano-6-methylthiopyridine (VIII). *Method A.* An acetone solution of 7.3 g. (0.06 mole) of I was added to a solution of 8.0 g. (0.029 mole) of 2-methyl-2-thiopseudourea sulfate in 150 ml. acetone and 20 ml. water. Concentrated ammonium hydroxide was added dropwise to neutrality. After standing for 1 hr., 200 ml. water was added. Ammonium hydroxide was again added and precipitation occurred. After standing 12 hr. the precipitate was collected, washed with water, and recrystallized from methanol to give 2.6 g. (47%) of white granules which melted to a yellow oil at 270–271°.

Method B. A solution of 9.0 g. (0.050 mole) of potassium 1,1,3,3-tetracyanopropene in 100 ml. of water was added to 10.0 g. (0.035 mole) of 2-methyl-2-thiopseudourea sulfate in 100 ml. of 1*N* potassium hydroxide. After standing overnight in a refrigerator, the precipitate was collected, washed with cold water, and recrystallized from methanol to give 8.5 g. (90%) of white granules which melted to a yellow oil at 270–271°.

Anal. Calcd. for $C_8H_6N_4S$: C, 50.51; H, 3.18; N, 29.45; S, 16.86. Found: C, 50.67; H, 3.11; N, 29.07; S, 16.90.

2-Amino-3,5-dicyano-6-ethylthiopyridine (IX). *Method A.* Ten grams (0.055 mole) of potassium 1,1,3,3-propenetetracarbonitrile in 100 ml. of 50% alcohol was added to 4.0 g. of ethyl mercaptan in 20 ml. of 4*N* potassium hydroxide. The yellow precipitate which formed on standing was collected, washed with water, and recrystallized from alcohol; yield 9.0 g. (80%), m.p. 203–205°.

Method B. One gram of ethyl mercaptan (0.016 mole), and 1.0 g. of potassium hydroxide in 5 ml. water was added to 0.5 g. (0.003 mole) of 2-amino-3,5-dicyano-6-chloropyridine[8] in 10 ml. of alcohol. After the addition of 10 ml. of water the solution was warmed to 40° and allowed to stand. The white solid, recrystallized from alcohol (0.34 g., 60%), melted at 202–204°. A mixed melting point with material from methods A and B gave no depression.

Anal. Calcd. for $C_9H_8N_4S$: C, 52.92; H, 3.95; S, 15.70. Found: C, 52.98; H, 4.01; S, 15.21.

2-Amino-3,5-dicyano-6-benzylthiopyridine (X). With method B, used for VIII, 9.0 g. of potassium 1,1,3,3-tetracyanopropene and 13.5 g. (0.067 mole) of 2-benzyl-2-thiopseudourea hydrochloride gave 6.1 g. (45%) of X, after recrystallization from benzene-methanol, m.p. 205–206°.

Anal. Calcd. for $C_{14}H_{10}N_4S$: C, 63.13; H, 3.78; S, 12.04. Found: C, 63.61; H, 3.83; S, 12.16.

2-Amino-3,5-dicyano-6-methoxypyridine (XI). *Method A.* One gram of potassium hydroxide in 15 ml. water was added to 1.0 g. (0.0055 mole) of potassium 1,1,3,3-tetracyanopropene in 50 ml. of methanol. After a 10-min. reflux the solution was cooled and 100 ml. of water was added. The precipitate was collected, washed with water, and recrystallized from methanol to give 0.81 g. (85%) of long white needles, m.p. 258–259°.

Anal. Calcd. for $C_8H_6N_4O$: C, 55.17; H, 3.47; N, 32.17. Found: C, 55.27; H, 3.72; N, 32.25.

Method B. Ten grams of potassium hydroxide in 15 ml. of water was added in one portion to 10.0 g. (0.082 mole) of I in 75 ml. of methanol. The reaction was exothermic. After cooling, the mixture was diluted with 150 ml. of water. The precipitate was recrystallized from methanol to give 2.1 g. (29%), m.p. 258–259°. A mixed melting point with material from method A gave no depression.

2-Amino-5-cyano-6-ethoxy-3-pyridinecarboxamide (XII). *Method A.* A solution of 1.6 g. of potassium hydroxide in 25 ml. of water was added to 5.0 g. of potassium 1,1,3,3-tetracyanopropene in 50 ml. of alcohol. After a 5-min. reflux the solution was cooled and diluted with 200 ml. of water. The precipitate was collected, washed with water, and recrystallized from alcohol to give 4.1 g. (69%) of long, pale green needles, m.p. 272–273°.

Method B. One gram (0.0053 mole) of 2-amino-3,5-dicyano-6-ethoxypyridine[8] in 100 ml. of 0.1*N* potassium hydroxide was refluxed 0.5 hr. and then allowed to stand at room temperature 12 hr. The precipitate was collected, washed with water, and recrystallized from alcohol to give 0.80 g. (73%), m.p. 272–273°.

Method C. A solution of 3.5 g. of XI and 3.5 g. of potassium hydroxide in 50 ml. of ethyl alcohol was heated to boiling for 3 min. After cooling and diluting with 100 ml. water the precipitate was collected, washed with water, and recrystallized from ethyl alcohol to give 3.2 g. (74%) of pale green needles, m.p. 272–274°. Mixed melting point of material from the above preparations gave no depression.

Anal. Calcd. for $C_9H_{10}N_4O_2$: C, 52.42; H, 4.89; N, 27.17. Found: C, 52.09; H, 5.16; N, 27.25.

2-Amino-5-cyano-6-methylthio-3-pyridinecarboxamide (XIV). A mixture of 1.0 g. (0.0053 mole) of 2-amino-3,5-dicyano-6-methylthiopyridine in 50 ml. of 0.1*N* potassium hydroxide was refluxed 1.5 hr. and filtered while hot. The precipitate which formed on cooling was collected, washed with water, and recrystallized from methanol-water to give 0.31 g. (33%), white solid, m.p. 294–295°.

Anal. Calcd. for $C_8H_8N_4OS$: C, 46.14; H, 3.87; N, 26.91. Found: C, 45.80; H, 4.11; N, 26.63.

2-Amino-5-cyano-6-ethylthio-3-pyridinecarboxamide (XV). A mixture of 1.0 g. of 2-amino-3,5-dicyano-6-ethylthiopyridine (0.005 mole) and 50 ml. of 0.1*N* potassium hydroxide was refluxed 1 hr. and filtered while hot. The precipitate which formed on cooling was collected, washed with water, and recrystallized from methanol-benzene to give 0.74 g. (68%), m.p. 254–256°.

Anal. Calcd. for $C_9H_{10}N_4OS$: C, 48.63; H, 4.54; N, 25.21. Found: C, 49.10; H, 4.63; N, 25.60.

2-Amino-6-methylthio-3,5-pyridinedicarboxylic acid (XVI). A mixture of 3.0 g. (0.16 mole) of VIII in 200 ml. of 6*N* potassium hydroxide was refluxed until most of the solid had dissolved and filtered while hot. The filtrate was cooled to 5° and acidified with cold acetic acid. The precipitate was collected, washed with water, and recrystallized from water to give 2.1 g. (58%) of a white powder which decomposed at 315–316°.

Anal. Calcd. for $C_8H_8N_2O_4S$: C, 42.10; H, 3.53; N, 12.28. Found: C, 41.98; H, 3.61; N, 12.38.

2-Amino-6-ethylthio-3,5-pyridinedicarboxylic acid (XVII). With the method used for XVI, 2.0 g. (0.0098 mole) of IX in 100 ml. of 6*N* potassium hydroxide gave 1.3 g. (55%) of XVII recrystallized from aqueous acetic acid, dec. 268–270°.

Anal. Calcd. for $C_9H_{10}N_2O_4S$: C, 44.62; H, 4.16; N, 11.57. Found: C, 44.30; H, 4.58; N, 11.50.

2-Amino-6-hydroxy-3,5-pyridinedicarboxylic acid (XVIII). A mixture of 5.0 g. (0.024 mole) of XII and 100 ml. of 10*N* potassium hydroxide was refluxed 2 hr. After filtering while hot the filtrate was cooled to 5° and acidified with acetic acid. The precipitate after recrystallization from water (2.1 g., 41%) decomposed at 218–220°.

Anal. Calcd. for $C_7H_6N_2O_5$: C, 42.43; H, 3.05; N, 14.14. Found: C, 42.03; H, 3.32; N, 14.24.

Potassium 2-amino-5-cyano-6-hydroxy-5-pyridinecarboxamide hydrate. Method A. Four grams of potassium hydroxide and 3.5 g. of VII dissolved in 75 ml. water was boiled in an open vessel until crystals formed. After cooling to 5° the precipitate was collected and recrystallized from water to give 2.4 g. (53%) of long white needles which decomposed at 327–332°.

Method B. One gram (0.005 mole) of 2-amino-5-cyano-6-ethoxy-3-pyridinecarboxamide was refluxed with 130 ml. of 1*N* potassium hydroxide until the solid dissolved (about 1.5 hr.). After cooling the solution was acidified with

(10) H. Schenk, M. Finken, Fr. Pleuger, and P. Michaelis, *Ann.*, 462, 158 (1928).

glacial acetic acid. The precipitate was collected and treated with 10 ml. of 1*N* potassium hydroxide and the solution heated to boiling. The solid formed on cooling was recrystallized from water to give 0.53 g. (47%) of white needles which decomposed at 327–330°.

Method C. A mixture of 0.5 g. of 2-amino-3,5-dicyano-6-chloropyridine[8] in 25 ml. of 1*N* potassium hydroxide was refluxed until the solid dissolved. Method B was then followed to give 0.47 g. (71%).

Anal. Calcd. for $C_7H_7N_4O_3K$: C, 35.87; H, 3.01; N, 23.92. Found: C, 35.84; H, 2.84; N, 23.82.

7-Ethoxy-4-hydroxy-6-cyanopyrido(2,3-d)pyridine. Three grams (0.015 mole) of 2-amino-5-cyano-6-ethoxy-3-pyridinecarboxamide in 25 g. formamide was heated to 160–170° and maintained at this temperature for 2 hr. The compound slowly went into solution. Upon cooling, crystals formed which were filtered and washed with water. The filtrate was cooled to 5° in an ice bath and a second crop was obtained. Then the combined crops were shaken for a few minutes with 100 ml. of 0.1*N* potassium hydroxide and 50 ml. of water. The solution was filtered and the filtrate acidified with glacial acetic acid to yield 2.1 g. (67%) of a yellow powder which decomposed at 260–270°. An analytical sample was obtained by recrystallizing from dimethylformamide-water, m.p. 274–275°.

Anal. Calcd. for $C_{10}H_8N_4O_2$: C, 55.55; H, 3.73; N, 25.92; C_2H_5O, 20.85. Found: C, 55.50; H, 3.97; N, 25.93; C_2H_5O, 21.02.

2-Methylthio-4-amino-5-cyanopyrimidine. A solution of 8.0 g. of sodium hydroxide in 20 ml. of water was added to a mixture of 27.8 g. (0.100 mole) of 2-methyl-2-thiopseudourea sulfate in 100 ml. of acetone. Ethoxymethylenemalononitrile (24.4 g., 0.200 mole) in 150 ml. acetone was then added. After stirring for 2 hr. 200 ml. water was added; a precipitate formed. After standing for 12 hr. the precipitate was collected, washed with cold water, and recrystallized from alcohol-water to give 21.5 g. (65%) of fine white needles, m.p. 240–241°.

Anal. Calcd. for $C_6H_6N_4S$: C, 43.35; H, 3.64; N, 33.71. Found: C, 43.53; H, 3.54; N, 33.67.

2-Ethylthio-4-amino-5-cyanopyrimidine. A solution of 8.0 g. of sodium hydroxide in 20 ml. water was added to a mixture of 31.0 g. (0.100 mole) of 2-ethyl-2-thiopseudourea sulfate and 100 ml. of acetone. Ethoxymethylenemalononitrile (24.4 g., 0.200 mole) in 150 ml. of acetone was then added. The mixture was allowed to stand 12 hr. The precipitate was filtered, washed with cold water, and recrystallized from alcohol-water to give 25.0 g. (70%) of fine white needles, m.p. 140° [lit. m.p. 141° (16.5%),[4] 147° (56%)].[11]

4-Amino-2-benzylthio-5-cyanopyrimidine. Ten grams (0.08 mole) of ethoxymethylenemalononitrile in 50 ml. of acetone was added slowly, with stirring, to a solution of 16.6 g. (0.080 mole) of 2-benzyl-2-thiopseudourea hydrochloride and 3.3 g. of sodium hydroxide in 50 ml. water. After all the ethoxymethylenemalononitrile solution had been added, the mixture was stirred for 0.5 hr. Then 100 ml. of water was added and the mixture cooled overnight in the refrigerator. The solid was then filtered and washed with water. Recrystallization from alcohol-water gave 15.5 g. (72%) of yellow needles, m.p. 174–176° (lit.[11] 86%, m.p. 171°).

4-Amino-2-thio-5-cyanopyrimidine. Ethoxymethylenemalononitrile (10 g., 0.080 mole) was added slowly to 7.0 g. (0.09 mole) of thiourea in a mixture of 70 ml. of water, 50 ml. of acetone, and 3.3 g. of sodium hydroxide. The solution was stirred for 0.5 hr. and 250 ml. of water added. The solution was acidified with glacial acetic acid and placed in the refrigerator overnight. A precipitate formed which was collected by filtration, washed with water, and dried. The yield of crude was 1.5 g. (12%). The infrared spectrum of this product was identical with that of 4-amino-2-thio-5-cyanopyrimidine prepared in an 85% yield by a method similar to that of Suter and Habicht.[11]

BUFFALO, N. Y.

(11) H. Suter and E. Habicht, U. S. Patent 2,698,326, December 1954.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLLEGE OF PHARMACY, UNIVERSITY OF ILLINOIS]

Addition of Thiourea to 2- and 4-Vinylpyridines[1]

LUDWIG BAUER AND LIBERO A. GARDELLA, JR.

Received April 26, 1960

The acid-catalyzed addition of thiourea to 2- and 4-vinylpyridines readily afforded *S*-[2-(2- and 4-pyridinium)ethyl]-isothiuronium salts, II and IV, in excellent yields. In a cognate experiment, 2-methyl-5-vinylpyridine did not add thiourea. A mechanism is postulated to explain these phenomena. The isothiuronium salts, II and IV, were characterized by the corresponding thiols, disulfides and sulfonic acids.

Among the numerous nucleophilic reagents which have been added to the β-carbon of the side chain of 2- and 4-vinylpyridine are hydrogen cyanide,[2a] active methylene compounds (ketones,[2b] malonic esters,[2a] phenylacetonitriles,[2c] nitroalkanes[2d]), indole,[2f] imides,[2g] amides,[2c] amines[2c,2e] and phosphite esters.[2h] To establish a carbon-sulfur bond at the β-carbon of the vinyl side chain, mercaptans[3] and sodium bisulfite[2a] have been treated to form the corresponding 2-(2- and 4-pyridyl)ethyl sulfides and

(1) This work was sponsored by the Office of the Surgeon General, U. S. Army, Contract DA-49-193-MD-2047. This assistance is gratefully acknowledged.

(2) (a) W. E. Doering and R. A. N. Weil, *J. Am. Chem. Soc.*, 69, 2461 (1947); (b) V. Boekelheide and J. H. Mason, *J. Am. Chem. Soc.*, 73, 2356 (1951); R. Levine and M. H. Wilt, *J. Am. Chem. Soc.*, 74, 342 (1952) and 75, 1368 (1953); G. Magnus and R. Levine, *J. Org. Chem.*, 22, 270 (1957); (c) G. Magnus and R. Levine, *J. Am. Chem. Soc.*, 78, 4127 (1956); (d) E. Profft, *Chem. Techn.*, 8, 705 (1956); (e) A. P. Phillips, *J. Am. Chem. Soc.*, 78, 4441 (1956) and literature cited therein; E. Profft, *Chem. Ber.*, 90, 1738 (1957); 91, 958 (1958); (f) A. P. Gray and W. L. Archer, *J. Am. Chem. Soc.*, 79, 3554 (1957); (g) A. P. Gray, W. L. Archer, E. E. Spinner, and C. J. Cavallito, *J. Am. Chem. Soc.*, 79, 3805 (1957); S. L. Shapiro, I. M. Rose, E. Roskin, and L. Freedman, *J. Am. Chem. Soc.*, 80, 1648 (1958); (h) E. Maruszewska-Wieczorkowska and J. Michalski, *J. Org. Chem.*, 23, 1886 (1958).

(3) W. H. Vinton, U. S. Patent 2,607,776, August 1952; *Chem. Abstr.*, 47, 6989 (1953).