about 20 cc. On cooling more of the same material separated. This was identified as the mercaptoaldehyde and melted at 145°. It crystallized in elongated prisms which were soluble in hot water and dilute hydrochloric acid and sparingly soluble in alcohol. The aldehyde reduced silver nitrate in ammoniacal solution and gave a crystalline hydrazone. Analysis:

Calc. for $C_7H_8O_2N_2S$: N, 15.16. Found: N, 15.06.

Uracil-4-aldehyde (V).—This aldehyde has not been subjected to investigation and consequently we shall only mention here a single experiment in which the pyrimidine was obtained. One gram of the above 2-ethylmercaptopyrimidineacetal was heated with boiling hydrochloric acid for one-half hour and the solution then evaporated practically to dryness. On cooling the remaining liquid, this pyrimidine separated as a white powder which was crystallized from dilute hydrochloric acid. It separated in small distorted prisms arranged in rosets which did not melt at 300°. It did not respond to a test for sulfur and contained a molecule of water of crystallization, which was removed by heating the pyrimidine at 130°.

Calc. for $C_5H_4O_3N_2$: N, 17.7; H_2O, 11.39. Found: N, 17.45; H_2O, 11.30.

This pyrimidine will be subjected to a thorough investigation.

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON PYRIMIDINES. LXXVI. NEW METHODS OF SYNTHESIZING 2-KETOPYRIMIDINES AND THEIR SULFUR ANALOGS.

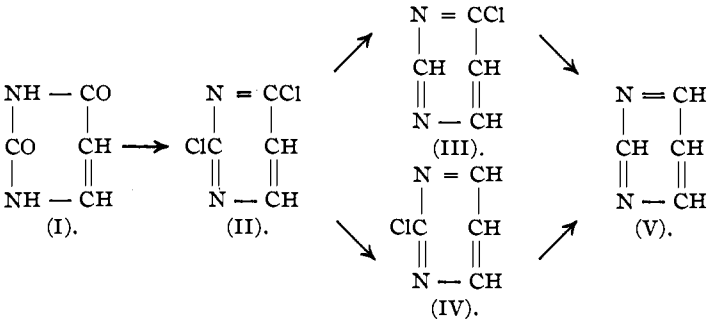
BY TREAT B. JOHNSON AND A. WILLARD JOYCE.

Received July 5, 1915.

Although the chemistry of the 2,6-dioxypyrimidines, of which uracil (I), is the prototype, has been the subject of extended investigation largely on account of the ready accessibility of such substances and their biochemical interest, that of the *mono*-ketopyrimidines and the simple pyrimidine compounds has received comparatively little attention, and it was with the view of filling this gap and partly with definite synthetical aims that the preliminary work discussed in this paper was instituted.

The 2,6-dioxypyrimidines (I) are easily transformed into their corresponding dichloropyrimidines (II) by interaction with phosphorus pentachloride and phosphorus oxychloride. The yields of these dihalides are good and consequently they are available in quantity for synthetical purposes. When such halogenated pyrimidines are subjected to reduction, different intermediate products can theoretically be formed before complete removal of the halogen is effected. For example, reduction

can take place in the 2- or 6-positions of the pyrimidine ring with formation of two isomeric compounds, namely, a 6-chloro- or a 2-chloropyrimidine corresponding to Formulas III and IV, respectively. Which product



will be formed cannot be foretold and, consequently, the structure of each reduction product must be determined in each case examined. During the course of an investigation now in progress in this laboratory, we had occasion to apply such a reduction process with 2,6-dichloro-5-ethoxypyrimidine and obtained a crystalline monochloro derivative. It was not until we undertook to establish experimentally the structure of this substance that we realized the want of a simple and practical method of proving the constitution of such compounds. An account of a new method of proving structure, which fulfils the needs of our work, is now given below.

A dioxypyrimidine is obtained, by our method of synthesis, from its corresponding 2-thio- or 2-mercapto-6-oxypyrimidine by desulfurization with boiling chloroacetic acid or strong hydrochloric acid. For example, 2-ethylmercapto-5-ethoxy-6-oxypyrimidine[1] (VIII) and the 5-ethoxyuracil[2] (IX) represent such a pair of compounds and the latter is easily prepared from the mercaptopyrimidine by the action of chloroacetic acid. Both of these pyrimidines interact with phosphorus halides to form the corresponding chlorides (XI) and (X). The mercaptohalide (XI) has been described by Johnson and McCollum[3] and the dihalide (X) by Johnson and Guest.[4] We now find that this mercaptopyrimidine (XI) undergoes reduction smoothly with zinc dust in dilute alcohol, giving the reduced pyrimidine (XIV), and it is on this observation that our method of proving structure is based. The dichloropyrimidine (X) is reduced according to the same procedure giving an excellent yield of a monochloro compound. With this data in hand it was only necessary to convert our chloropyrimidine into its corresponding ethylmercapto

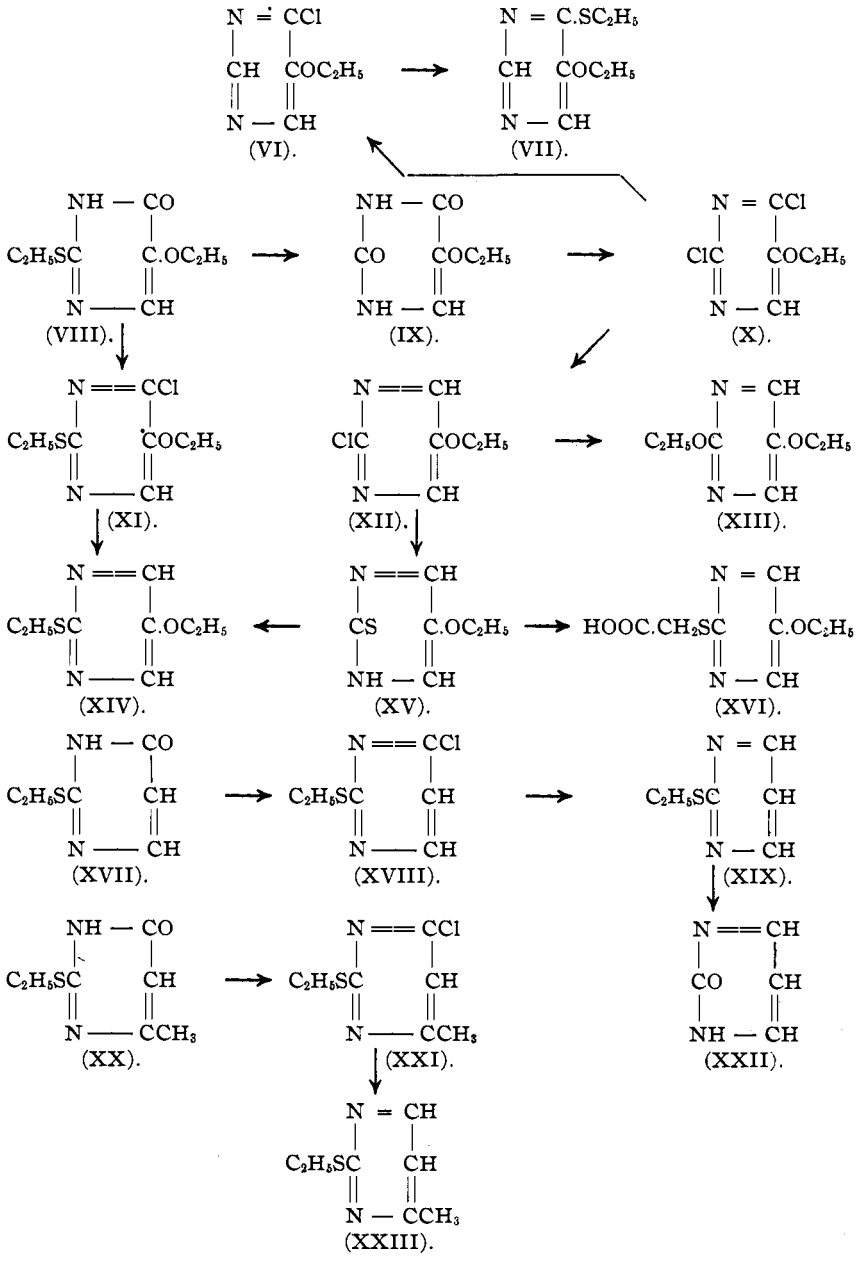
[1] Johnson and McCollum, *J. Biol. Chem.*, **2**, 441 (1906).

[2] Johnson and McCollum, *loc. cit.*

[3] *Loc. cit.*

[4] *Am. Chem. J.*, **42**, 284 (1909).

derivative in order to establish its constitution. Either the mercapto-pyrimidine (XIV), or its isomer represented by Formula VII, should be formed. This change we have now accomplished. The chloropyrimidine



was found to interact almost quantitatively with potassium hydrogen sulfide with formation of the potassium salt of the 2-thiopyrimidine represented by Formula XV. When the latter was warmed with ethyl bromide in alcohol solution it underwent alkylation smoothly, giving the same 2-ethylmercapto-5-ethoxypyrimidine (XIV) as was obtained by reduction of the chloride (XI) with zinc dust. Therefore, the dichloropyrimidine (X) undergoes reduction in the 6-position of the ring with formation of the 2-chloro-5-ethoxypyrimidine (XII). We obtained no evidence of the formation of any 6-chloro-5-ethoxypyrimidine (VI). This method of proving constitution is characterized by its simplicity and is apparently of general application. The study of pyrimidine dihalides will be continued, and it will be interesting to determine what influence the character of the groupings substituted in positions 4 and 5 will have upon their reactivity towards reducing agents.

Having shown that the mercaptopyrimidine (XI) can be reduced with zinc dust it was important to determine whether the reaction is applicable with other mercaptopyrimidines of this type. We have now investigated the behavior towards zinc dust of 2-ethylmercapto-6-chloropyrimidine[1] (XVIII), and the corresponding 4-methylpyrimidine[2] (XXI), and find that both compounds are reduced smoothly to their corresponding mercaptopyrimidines represented by Formulas XIX and XXIII. In other words, these mercaptohalides behave in a similar manner towards zinc dust as their corresponding 2-anilino- and 2-methylamino representatives, which have been investigated by Johnson and Heyl[3] and Johnson and Mackenzie.[4]

It is of interest to note here that Wheeler[5] observed that 2,6-dichoropyrimidine (II) is reduced by hydriodic acid and phosphorus with formation of 6-oxypyrimidine (XXIV). In this reaction the imido-acid chloride grouping in the 1,6 positions of the ring underwent hydrolysis, while the chlorine between the two nitrogen atoms in position 2 was removed by reduction. He also made the observation that 2-amino-6-chloropyrimidine (XXV), is reduced by zinc dust to the pyrimidine (XXVI), while the isomeric 2-chloro-6-aminopyrimidine (XXVII) is not changed by this reagent. On the other hand this pyrimidine is reduced smoothly by the action of hydriodic acid giving 6-aminopyrimidine (XXVIII). Hydriodic acid cannot be used for the reduction of 2-mercaptochloropyrimidines because the mercapto radicle is destroyed by hydrolysis in the presence of this reagent.

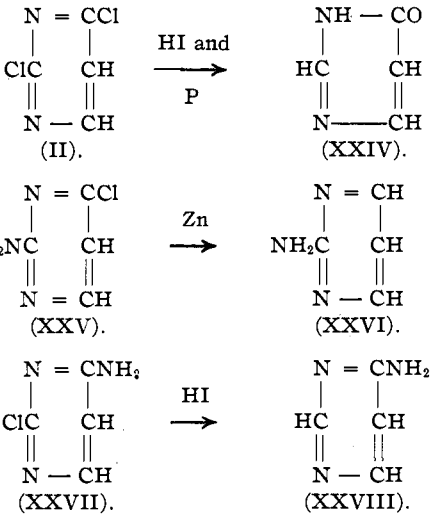
[1] Wheeler and Johnson, *Am. Chem. J.*, **29**, 497 (1903); Wheeler and Bristol, *Ibid.*, **33**, 450 (1905).

[2] Johns, *Am. Chem. J.*, **40**, 351 (1908).

[3] *Am. Chem. J.*, **38**, 236 (1907).

[4] *Ibid.*, **42**, 355 (1909).

[5] *J. Biol. Chem.*, **3**, 289 (1907).



(II). (XXIV). (XXV). (XXVI). (XXVII). (XXVIII).

2-Mercaptopyrimidines can be obtained by condensation of 1,3-diketones with pseudothioureas. Wheeler[1] and Jamieson prepared, for example, 2-methylmercapto-4,6-dimethylpyrimidine (XXIX) by condensing methylpseudothiourea with acetylacetone. The yield, however, was only 24.4% of the theoretical. It has been our experience that this method of synthesis is limited in its application. Many of the 1,3-diketones are extremely difficult to obtain in quantity and many of them, which we have examined, have failed to condense with pseudoureas. By reduction of the mercaptochlorides it should be possible to obtain new pyrimidine combinations which it would be practically impossible to synthesize easily by other known methods. Certain unknown representatives of this class of pyrimidines should be very valuable for further important synthesis.

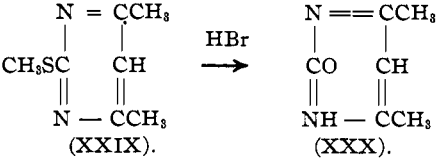
1,3-Diketones of the type of acetylacetone condense with urea and thiourea giving the corresponding 2-keto- and 2-thiopyrimidines[2] (XXX and XXXI). Complications are, however, met with here unless special conditions are adopted, and a new method of synthesizing these types of compounds is desirable. It seems not improbable that their preparation from the 2-mercaptopyrimidines will prove to be a feasible method. Wheeler and Jamieson[3] have shown that 2-methylmercapto-4,6-dimethylpyrimidine (XXIX) is convertible into 2-oxy-4,6-dimethylpyrimidine (XXX), by hydrolysis with hydrobromic acid. We now find that the 2-ethylmercaptopyrimidine represented by Formula XIX is transformed

[1] *Am. Chem. J.*, **32**, 356 (1904); Hale, THIS JOURNAL, **37**, 594 (1915).

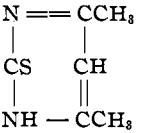
[2] Evans, *J. prakt. Chem.*, [2] **48**, 489 (1893); de Haen, *Rec. trav. chim.*, **27**, 162 (1908); Hale, THIS JOURNAL, **36**, 104 (1914); **37**, 594 (1915); **37**, 1544 (1915).

[3] *Loc. cit.*

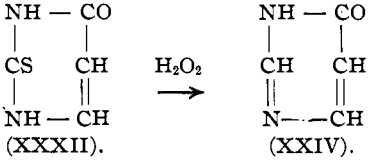
into the hitherto unknown 2-oxypyrimidine (XXII), by hydrolysis with hydrochloric and also hydrobromic acid. The isomeric 6-oxypyrimidine (XXIV) has been described by Wheeler[1] and was prepared by reduction of 2,6-dichloropyrimidine (II), with hydriodic acid, and also by the interaction of 2-thiouracil (XXXII) with hydrogen peroxide. Wheeler's ketone (XXIV) was a basic substance melting at 164–165°, and was characterized by its great solubility in water and alcohol. 2-Ketopyrimidine (XXII) in likewise a basic pyrimidine and forms stable salts with hydrochloric and hydrobromic acids. The free base, however, does not melt below 300° and is insoluble in water and the common organic reagents.



(XXIX). (XXX).

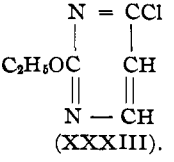


(XXXI).



(XXXII). (XXIV).

This investigation of 2-keto and 2-thiopyrimidines will be continued. We shall also continue our work on the reduction of mercaptochloropyrimidines, and their corresponding oxygen compounds, of which the compound (XXXIII) is a typical representative.



(XXXIII).

Experimental Part.

2-Ethylmercapto-5-ethoxy-6-oxypyrimidine (VIII).—This mercaptopyrimidine, which was used in this investigation, was prepared by condensing ethyl α-ethoxy-β-hydroxylacrylate with pseudoethylthiourea according to the directions of Johnson and McCollum.[1]

2,6-Dioxy-5-ethoxypyrimidine (IX).—This pyrimidine was formed smoothly by digesting 50 g. of the above mercaptopyrimidine with 58

[1] *Loc. cit.*

g. of chloroacetic acid (2 molecular proportions) in 200 cc. of water for 6 hours. Ethylmercaptan was evolved copiously with gradual solution of the mercaptopyrimidine. After the reaction was complete the aqueous solution was filtered quickly and cooled, when the dioxypyrimidine crystallized out. It melted at 275° with decomposition and the yield was 35 g. or 90% of the theoretical. This pyrimidine has previously been prepared by Johnson and McCollum[1] by hydrolyzing the mercaptopyrimidine with hydrochloric acid. Its formation, however, was not smooth under such conditions and the yield was small, due to the formation of the corresponding hydroxy compound—isobarbituric acid. None of the latter is formed when the hydrolysis is effected with chloroacetic acid.

2-Ethylmercapto-5-ethoxy-6-chloropyrimidine (XI) was prepared according to the directions of Johnson and McCollum[1] by the action of an excess of phosphorus oxychloride on the above mercaptopyrimidine. It was purified by distillation under diminished pressure and the yield was 85% of the theoretical.

2,6-Dichloro-5-ethoxypyrimidine (X).—Thirty-four grams of 2,6-dioxy-5-ethoxypyrimidine were placed in a distilling flask with 140 g. of phosphorus oxychloride and the mixture heated at 120–130° for 3 hours. The resulting dark-colored liquid was then subjected to distillation under diminished pressure and the excess of phosphorus oxychloride removed by heating at 100°. The crude chloride was then poured upon crushed ice to destroy any phosphorus halide present and the pyrimidine extracted with ether. The yield was 37 g. or 90% of the theoretical. The melting point of this compound is 51° and not 41–2° as previously recorded.[2] This pyrimidine is insoluble in water and is not decomposed by boiling water. If a strong acid is present (HCl) hydrolysis takes place at once and the dioxypyrimidine is formed.

Reaction Applied with 2-Ethylmercapto-5-ethoxy-6-chloropyrimidine (XI).—(*1*) *Action of Chloroacetic Acid:* This pyrimidine is not desulfurized smoothly by digestion with chloroacetic acid. Three grams of the pyrimidine were mixed with 3 g. of chloroacetic acid (2 molecular proportions) in 50 cc. of water and the mixture heated for several hours at 130–150°. No mercaptan was evolved and the liquid assumed a dark color indicating decomposition. On cooling, a black, viscous product was obtained, from which no definite compound could be isolated.

(*2*) *Reduction with Zinc Dust:* A mixture of 10 g. of the mercaptochloropyrimidine, 25 g. of zinc dust, 75 cc. of water and 75 cc. of 95% alcohol was boiled under a reflux condenser for 3 hours. Frequent agitation of the mixture is essential in order to prevent caking of the zinc on the bottom of the flask. When the reduction was complete the unchanged

[1] *Loc. cit.*

[2] Johnson and Guest, *loc. cit.*

zinc was separated by filtration and the excess of alcohol and water removed by heating at 100° under diminished pressure. A dark-colored oil separated. This was extracted with ether and the solution dried over calcium chloride (aqueous filtrate was saved). After removal of the solvent the pyrimidine was obtained as an oil which soon solidified. It was purified by crystallization from petroleum ether and separated in the form of thin, transparent plates or prisms, which melted at 31–32° to a clear oil. The yield was 6.0 g. or 71% of the theoretical. The compound was identified as *2-ethylmercapto-5-ethoxypyrimidine* (XIV).

Calc. for $C_8H_{12}ON_2S$: N, 15.19 Found: N, 15.19, 15.10.

This pyrimidine is soluble in ether, benzene and alcohol and insoluble in water. The compound is a weak base, dissolving in acids and is reprecipitated by alkali. It forms a stable hydrochloride which easily undergoes hydrolysis in the presence of water. Molecular weight determination in benzene solution by the cryoscopic method:

Calc. for $C_8H_{12}ON_2S$: M. W., 184. Found: M. W., 180 and 182.

After the extraction of the above pyrimidine with ether, the aqueous filtrate was made strongly alkaline with concentrated sodium hydroxide solution. Sufficient alkali was added to dissolve the precipitated zinc hydroxide, when we obtained an insoluble, crystalline precipitate. This was separated by filtration, washed with water and finally crystallized from dilute alcohol. It separated from this solvent in the form of bunches of needles. The yield was 0.6 g. This compound, whose structure has not been established, was insoluble in alkali solutions and cold water and soluble in alcohol and hot water. It crystallized from dilute alcohol in beautiful needles which melted at 126–127°. Molecular weight determinations in benzene solution by the cryoscopic method gave the values 202 and 204. Whether we are dealing here with a stereoisomer of 2-ethylmercapto-5-ethoxypyrimidine or a different reduction product remains to be established.

Attempts were made to reduce 2-ethylmercapto-5-ethoxy-6-chloropyrimidine (XI) by digesting with zinc dust in the presence of boiling water, but under no condition could a smooth reduction be effected. The pyrimidine underwent partial decomposition with evolution of mercaptan and tarry products were formed with production of very poor yields of the reduced pyrimidine (XIV), melting at 31–32°.

Hydrochloride of 2-Ethylmercapto-5-ethoxypyrimidine.—This is easily prepared by saturating an ether solution of the pyrimidine with hydrochloric acid gas. It separated as stout prisms which melted at 120–121°.

Calc. for $C_8H_{12}ON_2S.HCl$: N, 12.69. Found: N, 12.64, 12.76.

Platinum Salt.—Prepared by adding chloroplatinic acid to a hydrochloric acid solution of the mercaptopyrimidine. It crystallized in golden-yellow prisms which melted at 165–166°.

Calc. for $(C_8H_{12}ON_2S)_2.H_2PtCl_6$: Pt, 24.86. Found: Pt, 25.09.

Action of Chloroacetic Acid on 2-Ethylmercapto-5-ethoxypyrimidine (XIV).—One gram of the mercaptopyrimidine and 1 g. of the halogenated acid were heated together in an oil bath for 10 hours. No mercaptan was evolved. One gram more of chloroacetic acid was added and the heating continued for 8 hours. Still no mercaptan was evolved. Water was then added and the solution extracted with ether. On evaporating the ether the unaltered mercaptopyrimidine melting at 31–32° was recovered.

Digestion of 2-Ethylmercapto-5-ethoxypyrimidine with Zinc Dust.—One gram of the pyrimidine was digested in a mixture of 25 cc. of water and 25 cc. of alcohol with 1 g. of zinc dust for one hour. No further reduction was accomplished by this treatment and the unaltered pyrimidine was recovered.

Action of Alcoholic Ammonia on 2-Ethylmercapto-5-ethoxypyrimidine.—Two grams of the pyrimidine were sealed in a bomb tube with 30 cc. of strong alcoholic ammonia (saturated solution) and the mixture then heated at 100° for 24 hours. After cooling, and opening of the tube there was no odor of mercaptan. The tube was sealed again and heated for 10 hours at 130–150°. Under these conditions there was no reaction. The contents of the tube were again heated for 4 hours at 140–170° and finally for 10 hours at 175–185°. After this vigorous treatment there was no formation of mercaptan and the pyrimidine was recovered unaltered.

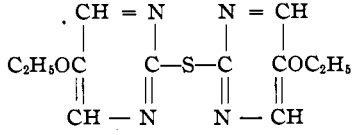
Reduction of 2,6-Dichloro-5-ethoxypyrimidine (X) with Zinc Dust: 2-Chloro-5-ethoxypyrimidine (XII).—Twenty grams of the dichloropyrimidine and 40 g. of zinc dust were suspended in a mixture of 100.0 cc. of alcohol and 100.0 cc. of water. This was then heated to boiling for 1.5 hours and the unchanged zinc separated by filtration. After removing the alcohol by heating under diminished pressure, the monochloropyrimidine separated in a crystalline condition. The yield was 13 g. or 80% of the theoretical. It was observed that the best results were always obtained by using a large excess of zinc dust and digesting for a limited period with equal parts of water and alcohol. A smaller proportion of zinc was tried, as was also longer boiling, but the yields of monochloropyrimidine were not so good. An attempt to reduce the dichloropyrimidine to its monochloro derivative by digestion with zinc dust and acetic acid was unsuccessful. This new pyrimidine is soluble in ether, alcohol and benzene and also in acids. It is insoluble in alkalis and in water. It can best be recrystallized from dilute alcohol and separates, on cooling, in thin, transparent plates, which melt at 70° to an oil. The compound possesses no odor, but is characterized by its peculiar effect when placed on the tongue. A cooling sensation is experienced and in small quantities it has a sweet taste.

Calc. for $C_6H_7ON_2Cl$: N, 17.66. Found: N, 17.65, 17.70.

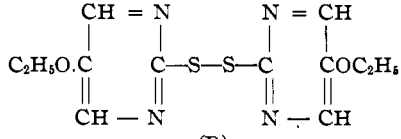
Action of Potassium Hydrogen Sulfide on 2-Chloro-5-ethoxypyrimidine with Formation of 2-Thio-5-ethoxypyrimidine (XV).—Eight and four-tenths grams of potassium hydroxide were dissolved in 60 cc. of 95% alcohol and the solution thoroughly saturated with hydrogen sulfide. Six grams of the 2-chloropyrimidine were then dissolved in the solution and the mixture heated on the steam bath for 5 hours. It was then cooled and the potassium chloride separated by filtration. The solution was evaporated to dryness to remove the alcohol and the yellow residue acidified with dilute hydrochloric acid, when the 2-thio-5-ethoxypyrimidine (XV) separated as a bright, golden-yellow solid. It was purified by crystallization from about 20 parts of glacial acetic acid and separated in small, yellow columns. They melted at 192–193°. The yield of crude material was 5 g. This pyrimidine is sparingly soluble in alcohol and benzene, insoluble in water, ether and acid solution (HCl). When digested with basic lead acetate solution, or mercury oxide suspended in water, metallic sulfides are formed. The pyrimidine dissolves in alkaline solutions and is reprecipitated by addition of acids.

Calc. for $C_6H_8ON_2S$: N, 17.95. Found: N, 17.85, 17.83.

After crystallization of this pyrimidine, the acetic acid filtrates were diluted with water, when a small amount of crystalline material separated. After crystallization from dilute alcohol this substance melted constant at 125°. It gave a strong test for sulfur. It was insoluble in both acids and alkalis, indicating one of the two sulfides below (A and B). Nitrogen



(A).



(B).

determinations agreed with the calculated value for the disulfide B.

Calc. for $C_{12}H_{14}O_2N_4S_2$: N, 17.90. Found: N, 17.87, 18.01.

Conversion of 2-Thio-5-ethoxypyrimidine into 2-Ethylmercapto-5-ethoxypyrimidine (XIV).—Two and five-tenths grams of the thiopyrimidine were converted into its potassium salt by dissolving the pyrimidine in 75 cc. of alcohol containing in solution 1 g. of potassium hydroxide. Fifteen grams of ethylbromide were then added and the heating continued for 3 hours. There was an immediate reaction with separation of potassium bromide. After filtering from potassium bromide, the alcohol was evaporated, when we obtained an oil, which was insoluble in water. It dissolved immediately in ether and on evaporation of the ether, deposited in long prisms melting at 31–32°. It was identified as the mercaptopyrimidine which has been described in a previous experiment. A mix-

ture of the two substances melted at 31°. It formed a platinum salt which melted at 165–166°.

Action of Chloroacetic Acid on 2-Thio-5-ethoxypyrimidine, 5-Ethoxypyrimidine-2-thioglycollic Acid (XVI).—Two and eight-tenths grams of the thiopyrimidine were suspended in a solution of 2 g. of chloroacetic acid in 50 cc. of water. On boiling the solution the pyrimidine gradually dissolved and after heating for 5 hours the reaction was considered complete. There was no change of color. On cooling the acid solution, the thioglycollic acid separated in the form of needles. They were purified by crystallization from 95% alcohol and melted at 137–138° to an oil. The yield was 2.5 g. The compound gave a strong test for sulfur and was soluble in alkaline but insoluble in acid solutions.

Calc. for $C_8H_{10}O_3N_2S$: N, 13.08. Found: N, 13.02, 13.3.

Attempts to Hydrolize the Thioglycollic Acid by Digesting with Hydrochloric Acid.—One and five-tenths grams of the thioglycollic acid were digested with hydrochloric acid (50 cc. concentrated acid) for 3.5 hours. The mixture assumed a dark, reddish brown color. The acid was removed by evaporation and the residue neutralized with sodium hydroxide to destroy any hydrochloride. After evaporating to dryness again, the residue was then extracted with alcohol and benzene, but nothing but tarry, indefinite products were obtained. The pyrimidine had apparently undergone complete decomposition.

The experiment was repeated using 10% hydrochloric acid. After boiling for 4 hours, the solution was evaporated under diminished pressure and the residue triturated with pure water. The unaltered pyrimidine was recovered in a crystalline condition. It crystallized from alcohol and melted at 137–138°.

2,5-Diethoxypyrimidine (XIII).—This pyrimidine was prepared by interaction of 2-chloro-5-ethoxypyrimidine, in alcohol, with the required amount of sodium ethylate. The reaction was rendered complete by heating for one hour on the steam bath. After filtering off the sodium chloride and evaporating the alcohol under diminished pressure at 40°, the pyrimidine was then extracted with ether and the solution dried over sodium sulfate. Calcium chloride could not be used because it formed a double combination with the pyrimidine. After removal of the ether we obtained 18 g. of the pyrimidine which boiled at 142° under a pressure of 24 mm. This compound crystallizes in beautiful, large, transparent plates, which melt at 19°. One of the crystals measured 1.375 inches on its longest axis and was 0.125 inch in thickness. The pyrimidine is insoluble in water and alkaline solutions but soluble in concentrated acids, ether, alcohol and benzene. It forms a hydrochloride which is easily hydrolized by moisture, and also forms an insoluble platinum salt.

Calc. for $C_8H_{12}O_2N_2$: N, 16.66. Found: N, 16.73, 16.50.

Hydrochloric Acid Salt.—This was prepared by saturating an ether solution of the base with hydrochloric acid gas. It separated in the form of colorless needles.

Calc. for $C_8H_{12}O_2N_2.HCl$: N, 13.69. Found: N, 13.81, 13.71.

Double Platinum Salt.—This crystallizes in golden-yellow prisms which melt at 176° with decomposition.

Calc. for $(C_8H_{12}O_2N_2)_2.H_2PtCl_6$: Pt, 26.16. Found: Pt, 26.12.

Reduction of 2-Ethylmercapto-6-chloropyrimidine (XVIII): 2-Ethylmercaptopyrimidine (XIX).—The chloropyrimidine was prepared according to directions already described in papers from this laboratory.[1] Our product boiled at 131–132° under 20 mm. pressure and at 135° under 24 mm. The yield was 84% of the theoretical.

Fifteen grams of this chloride, together with 25 g. of zinc dust, were placed in a flask with 75 cc. of water and an equal volume of 95% alcohol. This mixture was then heated to boiling for one hour, the mixture being shaken occasionally to prevent caking of the zinc. During the reduction, the odor of mercaptan was noticeable. After the reduction was complete the zinc was separated by filtration and the filtrate evaporated under diminished pressure. A dark-colored oil separated as well as a small amount of crystalline material which proved to be uracil. The latter was separated by filtration and the oily 2-mercaptopyrimidine extracted with ether and its solution dried over calcium chloride. After removal of the ether the oil was purified by distillation under diminished pressure. It distilled at 115° at 20 mm. pressure. The oil was colorless and was characterized by its unpleasant, pungent odor. On exposure to the air it gradually assumed a dark color. The yield was 9 g. or 75% of the theoretical.

This pyrimidine does not solidify at 0°. It possesses basic properties and dissolves in concentrated acids. It is soluble in ether, alcohol and benzene, and is insoluble in water and alkaline solutions.

Calc. for $C_6H_6N_2S$: N, 20.00. Found: N, 19.93, 19.90.

Hydrochloride.—This was prepared by saturating an ether solution of the base with dry hydrochloric acid gas. The salt separated in colorless crystals and was dried, for analysis in a vacuum over sulfuric acid. It melted at 98–99°. The salt is unstable in damp air and dissociates into the free base and hydrochloric acid.

Calc. for $C_6H_8N_2S.HCl$: N, 15.86. Found: N, 15.85, 15.87.

Double Platinum Salt.—This salt deposits as clusters of golden-yellow needles when chloroplatinic acid is added to a solution of the base in concentrated hydrochloric acid. It melts at 166°.

Calc. for $(C_6H_8N_2S)_2.H_2PtCl_6$: Pt, 28.27. Found: Pt, 28.22.

[1] Wheeler and Johnson, *Am. Chem. J.*, 29, 497; Wheeler and Bristol, *Ibid.*, 33, 450 (1905).

2-Oxypyrimidine (XXII).—Seven grams of the 2-mercaptopyrimidine were digested with 50 cc. of concentrated hydrochloric acid for 5.5 hours. The solution turned dark in color and ethylmercaptan was evolved. After the reaction was complete the solution was then evaporated to dryness, when we obtained a residue almost black in color, but crystalline in appearance. This was dissolved in water and the solution decolorized with bone-coal. The latter was then concentrated until crystals began to deposit when it was allowed to stand. The hydrochloride of the pyrimidine separated. This was purified by crystallization from 97% alcohol and melted at 203–205°.

Calc. for $C_4H_4ON_2.HCl$: N, 21.13. Found: N, 21.13.

The hydrobromide of the 2-oxypyrimidine was obtained by hydrolysis of the mercaptopyrimidine with hydrobromic acid. The hydrolysis, however, is not so smooth as when hydrochloric acid is used.

Calc. for $C_4H_4ON_2.HBr$: N, 15.82. Found: N, 15.77.

The free 2-oxypyrimidine can be prepared from its hydrochloride by dissolving the latter in water and exactly neutralizing the hydrochloric acid with dilute sodium hydroxide solution. Under these conditions the free pyrimidine separated as a light yellow, amorphous substance which did not melt at 320°. It possesses both acid and basic properties. It is sparingly soluble in water, alcohol, benzene and acetic acid, and practically insoluble in ether and ligroin. It is more soluble in a solution of ammonium chloride or ammonium bromide than in pure water.

2-Ethylmercapto-4-methylpyrimidine (XXIII).—The 2-ethylmercapto-4-methyl-6-chloropyrimidine (XXI), used in this experiment was prepared according to the directions of Johns.[1] Our product boiled at 142° under 15 mm. pressure. In order to convert this into the above pyrimidine, 25 g. of the chloride and 50 g. of zinc dust were suspended in a mixture of equal volumes of water and alcohol (100 cc.) and the mixture boiled for 2.5 hours. The excess of zinc was then separated by filtration and the solution evaporated at a temperature of 30–40° under diminished pressure. The pyrimidine separated as an oil, together with a little 4-methyluracil. The oil was dissolved in ether, dried over calcium chloride and finally distilled. It boiled at 123–124° at a pressure of 18–19 mm. It would not solidify at 0°. The yield was 15 g. or 72% of the theoretical. This compound has a pungent odor. It is a basic substance and is insoluble in alkalis. It is insoluble in water and soluble in ether, alcohol and benzene.

Calc. for $C_7H_{10}N_2S$: N, 18.17. Found: N, 18.05, 17.95.

Hydrochloride.—This crystallizes in prisms which melt at 141–142°. The salt is dissociated by water.

Calc. for $C_7H_{10}N_2S$: N, 14.70. Found: N, 14.71, 14.86.

[1] *Am. Chem. J.*, **40**, 351 (1908).

Double Platinum Salt.—This crystallizes in needles which melt at 165–166°.

Calc. for $(C_7H_{10}N_2S)_2.H_2PtCl_6$: Pt, 27.17. Found: Pt, 27.14, 27.26.

A description of the products obtained by hydrolysis of this pyrimidine will be given in a future paper.

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

STUDIES ON NITRATED PROTEINS. II. THE SYNTHESIS OF 3,5-DINITROTYROSINE.[1]

BY TREAT B. JOHNSON AND EDWARD F. KOHMANN.

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In his paper entitled "Über das Tyrosin," Städeler[2] states that if special precautions are not taken in the preparation of *mono*-nitrotyrosine[3] from tyrosine, and the proper proportions of nitric acid, water and tyrosine are not used, the nitrate of *mono*-nitrotyrosine will not separate from the acid solution. If such a condition develops and the resulting solution is allowed to stand and is then evaporated at a low temperature a new amino acid is obtained which crystallizes from boiling water in golden yellow plates. He concluded that this acid is *dinitrotyrosine*. The same amino acid is also obtained, according to him, by treatment of *mono*-nitrotyrosine with a mixture of equal parts of water and nitric acid (sp. gr. 1.3) at ordinary temperature, and then evaporating the acid solution at a low temperature. This transformation, however, was not quantitative because of the secondary formation of a large amount of oxalic acid and also a secondary nitrogenous substance which Städeler did not examine. According to this investigator the same dinitro compound is also formed by saturating tyrosine, suspended in water, with gaseous nitrous acid. Städeler described this amino acid as a yellow compound which crystallizes in plates that are difficultly soluble in cold and hot water, but easily soluble in alcohol and moderately soluble in ether. It possessed a sour taste and was characterized by the property of staining the skin, linen and other objects intensely yellow. No melting point was assigned to the compound, but Städeler states that at 100–115° it loses no weight, and when heated at a higher temperature decomposes with effervescence. He found by analysis 39.30% of carbon and 3.40% of hydrogen while the calculated values for these two elements are 39.85% and 3.32%, respectively. The percentage of nitrogen was not determined. Städeler

[1] Part of a dissertation presented by Mr. Edward F. Kohmann to the Faculty of the Graduate School of Yale University, 1915, in candidacy for the Degree of Doctor of Philosophy.

[2] *Ann.*, **116**, 82 (1860).

[3] Johnson and Kohmann, THIS JOURNAL, **37**, 1863 (1915).