

Summary.

1. Very few characteristic color reactions for papaverine are known, the most satisfactory being the deep rose produced by Marquis' reagent.

2. By treating papaverine ferricyanide with Marquis' reagent a blue color is produced which passes through violet and green stages to a dirty, brownish yellow.

3. By treating a mixture of the alkaloid, papaverine, and potassium ferricyanide with Marquis' reagent an essentially identical reaction is produced, although the initial color is generally greenish blue.

4. Many other oxidizing agents may be used in place of potassium ferricyanide, the shades of color produced varying somewhat with the reagent employed.

5. The reaction is best observed by intimately mixing a very small quantity of papaverine with a very small quantity of an oxidizing agent, such as cerium oxide, phosphomolybdic acid or potassium permanganate, and stirring the mixture with a few drops of sulfuric acid containing a little formaldehyde.

6. Of thirty-nine alkaloids tested but one (unnamed alkaloidal separate from sanguinaria) gave colors which in any way simulated the reaction with papaverine.

7. By using selenious acid as the oxidizing agent the unnamed sanguinaria alkaloid (or alkaloids) may be differentiated readily from papaverine.

The thanks of the author are due to Professor John Uri Lloyd for specimens of alkaloids from gelsemium, tobacco, sanguinaria and veratrum kindly furnished by Professor Lloyd for the investigation. Also to Dr. Willis S. Hilpert for verifying some of the reactions.

CHICAGO, ILL.

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

RESEARCHES ON HYDANTOINS. XXXIV. THE INTERACTION OF HIPPURIC ACID WITH THIOCYANATES.

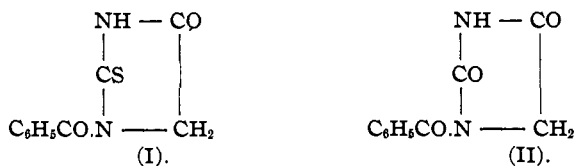
BY TREAT B. JOHNSON, ARTHUR J. HILL AND BERNARD H. BAILEY.

Received July 19, 1915.

Hippuric acid and dry ammonium thiocyanate interact very smoothly in the presence of acetic anhydride forming 2-thio-3-benzoylhydantoin¹ (I). Potassium thiocyanate likewise interacts to give the same hydantoin, but the yield is about 50% less than that obtained when ammonium thiocyanate is used.² Neither ammonium cyanate nor potassium cyanate interact with hippuric acid under similar conditions to give the corresponding 3-benzoylhydantoin (II).

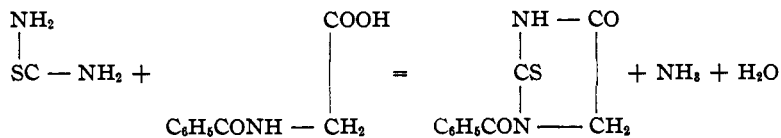
¹ Johnson and Nicolet, *THIS JOURNAL*, **33**, 1973 (1911).

² Johnson, *Am. Chem. J.*, **49**, 68 (1913); Johnson and Nicolet, *Ibid.*, **49**, 197 (1913).



Brunner¹ has recently investigated the behavior of potassium cyanate and potassium thiocyanate towards acetic anhydride and finds that both salts interact with this reagent in a characteristic manner forming diacetamide $(\text{CH}_3\text{CO})_2\text{NH}$. The best yield of this compound was obtained by employing potassium cyanate and applying the reaction at ordinary temperature in ether. Furthermore, Brunner showed that this same salt likewise interacted with propionic, butyric, isobutyric and benzoic anhydrides forming the corresponding diacylamides. In the case of the potassium thiocyanate no statement is made regarding any transformations of the sulfur atom in this salt during the treatment with the anhydride. The behavior of ammonium thiocyanate towards acetic anhydride under similar conditions was not investigated.

Since the publication of our results on the abnormal behavior of potassium thiocyanate towards hippuric acid, as compared to that of the ammonium salt,² we have received, by correspondence and otherwise, several suggestions of possible explanations for this unique difference in reactivity. In our previous paper we did not attempt to offer an explanation, and stated that efforts would be made to obtain new data which would enable us to draw a more definite conclusion as to the mechanism of the reaction. One of the explanations that has been proposed is that the ammonium thiocyanate undergoes a normal rearrangement, when heated with acetic anhydride, giving primarily thiourea, which then interacts with the hippuric acid forming the 2-thiohydantoin (I). Such a condensation might be expressed as follows: There are three fundamental reasons



why this interpretation is not tenable. Firstly, such an explanation would necessitate the conception of an entirely different reaction-mechanism to explain the formation of the thiohydantoin (I) from an inorganic thiocyanate. The interpretation of this interesting transformation, which we have already proposed,³ is of general application and is based on the conception that thiocyanic acid is formed by action of the acetic

¹ *Ber.*, **47**, 2677 (1914).

² Johnson and Nicolet, *Am. Chem. J.*, **49**, 197 (1913).

³ Johnson and Scott, *THIS JOURNAL*, **35**, 1136 (1913).

anhydride and acetic acid on the thiocyanate. Secondly, ammonium thiocyanate does not undergo a rearrangement to thiourea when warmed with acetic anhydride and, thirdly, if thiourea was actually formed under such conditions it would not condense with hippuric acid, but interact immediately with the acetic anhydride at 100° giving acetylthiourea, $\text{CH}_3\text{CONHC(S)NH}_2$.¹ Kohmann² has recently shown that thiourea interacts with acetic anhydride, in the presence of hippuric acid, forming the monoacyl derivative $\text{CH}_3\text{CONHC(S)NH}_2$. He obtained no evidence of the formation of 2-thio-3-benzoylhydantoin.

We have investigated very carefully the behavior of acetic anhydride towards ammonium thiocyanate. According to the directions given by Nencki and Leppert³ and Klason,⁴ acetylpersulfocyanic acid is formed. We now find that if these two reagents (NH_4SCN and $(\text{CH}_3\text{CO})_2\text{O}$) are allowed to interact for a shorter time and at a slightly higher temperature, an entirely different result is obtained and *isodithiocyanic* acid is formed. A description of this interesting reaction is given in the experimental part of this paper. In no case did we observe the formation of monoacetyl- or diacetylthiourea,⁵ $\text{CH}_3\text{CONHC(S)NHCOCH}_3$. The results are all in accord with the assumption that thiocyanic acid is first formed when acetic anhydride and acetic acid interact with ammonium thiocyanate.⁶

Another suggestion to explain the difference in behavior between ammonium and potassium thiocyanates is that ammonium thiocyanate first interacts with acetic anhydride to form acetylpersulfocyanic acid,⁷ which then combines with hippuric acid to form the hydantoin (I). We are now able to state that such a change is not involved. No acetylpersulfocyanic acid is formed under the conditions of our experiments. Furthermore, if it was actually formed it would not interact with hippuric acid to form the thiohydantoin (I). Acetylpersulfocyanic acid is a very stable substance in the presence of acetic anhydride and no thiohydantoin (I) was formed after heating this compound with hippuric acid in acetic anhydride solution for 21 hours. In fact, practically all of the acetylpersulfocyanic acid used was recovered unaltered after such a vigorous treatment.

We have stated above that Brunner⁸ observed potassium cyanate to interact with a series of anhydrides to form the corresponding diacid-amides. In the light of this interesting observation it seemed of special

¹ Nencki, *Ber.*, **6**, 599, 905 (1872); Prätorius, *J. prakt. Chem.*, [2] **21**, 147 (1880).

² THIS JOURNAL, **37**, 2130 (1915).

³ *Ber.*, **6**, 902 (1873).

⁴ *J. prakt. Chem.*, [2] **38**, 368 (1888).

⁵ Kohmann, *Loc. cit.*

⁶ Johnson and Scott, *Loc. cit.*

⁷ Nencki and Leppert, *Loc. cit.*; Klason, *Loc. cit.*

⁸ *Loc. cit.*

interest to us to determine whether other anhydrides besides acetic anhydride might be employed to effect a thiohydantoin condensation with hippuric acid. We have now applied the reaction with propionic and benzoic anhydrides and obtained with both reagents the thiohydantoin (I). In fact, propionic anhydride is just as efficient in producing the condensation as the acetic anhydride. We did not observe the formation of any propionylthiourea $C_2H_5CONHCSNH_2$. On the other hand, when benzoic anhydride was used only a small yield of the thiohydantoin was obtained, but a second product was formed which proved to be very interesting.

We now find that while part of the ammonium salt reacts as expected to form the thiohydantoin (I) the remainder undergoes a normal molecular rearrangement into thiourea, which then interacts with the benzoic anhydride giving benzoylthiourea,¹ $C_6H_5CONH.CSNH_2$. In fact, fully 50% of the ammonium thiocyanate undergoes the latter transformation. This interesting change is not due to the catalytic influence of the hippuric acid. We find that ammonium thiocyanate and benzoic anhydride interact smoothly at 100° , giving the same benzoylthiourea as is obtained when hippuric acid is incorporated. Therefore, we are dealing here with a normal rearrangement of the ammonium thiocyanate into thiourea, which then undergoes acylation, forming benzoylthiourea. In other words, *the benzoic anhydride acts catalytically*.

So far as the writers are aware no one has hitherto shown that ammonium thiocyanate can be rearranged to thiourea below 100° . It is a well-known fact that ammonium cyanate will change to urea at the temperature of boiling water but Reynolds² has shown that ammonium thiocyanate remains unchanged when subjected to such a treatment. He was the first to show that a rearrangement is produced by heating the thiocyanate at 170° . In fact, Reynolds³ states that ammonium thiocyanate changes very slowly when heated at its melting point ($148-149^\circ$) and gives only 15.2% of its weight in thiourea after heating for 40 minutes. He has shown experimentally that the maximum proportion formed at a single operation is only 24.76% of the theoretical and that this is reached after heating at 170° for about 45 minutes. At 182° both the thiourea and ammonium thiocyanate begin to undergo decomposition and guanidine thiocyanate is formed with evolution of ammonia and hydrogen sulfide.

Dunstan and Mussell⁴ have recently reported data which they believe indicates that ammonium thiocyanate may rearrange to thiourea at a temperature below the melting point of this salt ($148-9^\circ$). These investi-

¹ Pike, *Ber.*, 6, 755, 1107 (1873).

² Reynolds, *Ann.*, 150, 224 (1869).

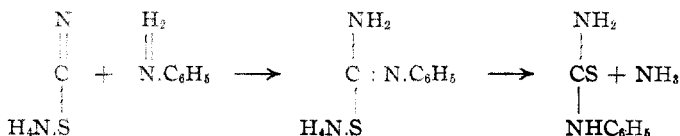
³ *J. Chem. Soc.*, 83, 1 (1903).

⁴ *Ibid.*, 99, 567 (1911).

gators observed that this salt and an excess of aniline interact at 130° forming phenylthiourea, $C_6H_5NHCSNH_2$, and state, in their paper, that the probable cause of the reaction is the primary formation of thiourea by rearrangement, which then reacts with the aniline giving the phenyl derivative. Such an interpretation, however, is not in accord with the known facts. Apparently Dunstan and Mussell¹ were unaware that Rathke had already investigated the behavior of both ammonium thiocyanate and thiourea towards aniline 26 years before the publication of their paper. Rathke wrote as follows:²

“Sodann habe ich jetzt beobachtet, dass eine concentrirte Lösung des gewöhnlichen Schwefelharnstoffs beliebig lange mit Anilin gekocht werden kann ohne dass eine Einwirkung stattfindet, während Rhodanammonium in gleicher Weise behandelt mit Leichtigkeit grosse Mengen des gewünschten Productes (Phenylthioharnstoff) liefert.”

In fact, Rathke gave an interpretation of the mechanism of this transformation which is expressed by the following equation:



In other words, the formation of the phenyl derivative does not necessarily involve the primary rearrangement of the thiocyanate.

The latest contribution on this interesting problem is a recent paper by Sohn³ in which he describes the remarkable observation that aniline and ammonium thiocyanate do not interact in boiling, glacial acetic acid solution to form either *mono*-phenyl or *di*-phenylthioureas. On the other hand, diphenylurea is formed quantitatively with evolution of hydrogen sulfide. *The acetic acid therefore acts catalytically.* Urea and aniline likewise interacted in acetic acid solution forming the same substituted urea. Sohn also observed that the two reagents (thiourea and aniline) do not interact in the presence of acetic acid to produce phenylthioureas. Acetanilide only was formed under these conditions. In other words, this observation is in accord with that made by Rathke.⁴

In the case of this unique aniline-ammonium thiocyanate reaction, the evidence, so far obtained, therefore indicates that we are dealing here with a reaction-mechanism which does not involve a normal molecular rearrangement of the thiocyanate. We consider Rathke's and Sohn's observations of importance in their bearing on our speculations⁵ regarding the mechanism of our hydantoin reaction.

¹ *Loc. cit.*

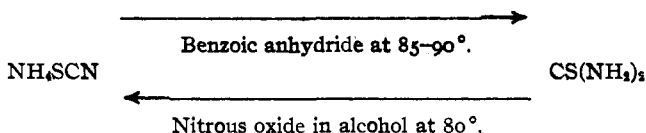
² *Ber.*, 18, 3105 (1885).

³ *Ibid.*, 47, 2438 (1914).

⁴ *Loc. cit.*

⁵ Johnson and Scott, *Ibid.*

The reverse change— $\text{CS}(\text{NH}_2)_2 \rightarrow \text{NH}_4\text{SCN}$ —is brought about by heating thiourea with water at 140° and also under the influence of catalytic agents. Claus¹ made the interesting observation several years ago that thiourea can be transformed into ammonium thiocyanate by saturation of an alcoholic solution of the urea with nitrous oxide. He found urea to be stable under similar conditions. Therefore, both ammonium thiocyanate and thiourea are susceptible to catalytic influence and their interconversion can be effected below 100° .



The study of these rearrangements will be continued.

We have now investigated further the behavior of inorganic thiocyanates towards hippuric acid in acetic anhydride solution. Ten different salts have been examined, namely, the four thiocyanates of the alkali metals NH_4 , Li , Na and K , the four thiocyanates of the alkali earths Mg , Ca , Sr and Ba and finally the two thiocyanates of Mn and Zn . Every one of these salts, with the exception of zinc thiocyanate, interacted normally with hippuric acid with formation of the thiohydantoin (I). The yields obtained, however, were not concordant. No salt examined reacted to give a yield of thiohydantoin (I) anywhere nearly equivalent to that obtained by application of the reaction with ammonium thiocyanate. The only combination besides the ammonium salt, that interacted to give a yield of thiohydantoin greater than 50% of the theoretical, was magnesium thiocyanate. The yield obtained in this case was 77% of theory while the yield of hydantoin was 93.4% when ammonium thiocyanate was used. The results of these experiments are recorded in the experimental part of this paper.

Experimental Part.

Acetylpersulfocyanic Acid, $\text{C}(\text{S}.\text{COCH}_3) = \text{N} - \text{S} - \text{C}(\text{S}.\text{COCH}_3) = \text{N}$.—

This cyclic compound was prepared by heating ammonium thiocyanate with acetic anhydride according to the directions given by Nencki and Leppert² and also by Klason.²

Reactions with Hippuric Acid in Presence of Acetic Anhydride.

Action of Acetylpersulfocyanic Acid.—Two grams of hippuric acid (finely pulverized) and 2 g. of acetylpersulfocyanic were suspended in a mixture of 9 cc. of acetic anhydride and 1 cc. of glacial acetic acid, and the mixture heated for 1 hour at 100° . There was no interaction of the

¹ *Ann.*, 179, 128 (1875).

² *Loc. cit.*

cyanic acid under these conditions. Nine cubic centimeters of acetic anhydride were then added and the heating continued for 20 hours at 100°. The liquid was then cooled and filtered when we recovered 1.7 g. of acetylpersulfocyanic acid, or 85.0% of the original amount taken. The acid filtrate was poured into 50 cc. of cold water and the solution evaporated to dryness. We obtained a semisolid substance which dissolved in warm sodium hydroxide solution. After filtering, in order to separate a little gummy material, the solution was acidified with hydrochloric acid. A crystalline substance deposited which melted at 121°. It was identified as benzoic acid. Acetylpersulfocyanic acid, therefore, does not interact with hippuric acid in acetic anhydride solution to form 2-thio-3-benzoylhydantoin.¹

Action of Potassium Cyanate on Aceturic and Hippuric Acids.—It has been shown that the *mono*-potassium salt of cyanic acid, $C_3H_2O_3N_3K$, is formed by the action of dilute acetic acid on potassium cyanate.² In order to determine whether a hydantoin would result by interaction of cyanic acid with hippuric acid in acetic anhydride solution, 2 g. of hippuric acid and 2 g. of potassium cyanate were suspended in a mixture of 9 cc. of acetic anhydride and 1 cc. of glacial acetic acid and this then heated on the steam bath. There was an immediate reaction on heating and a clear, yellow solution was obtained within a few minutes. On continued heating the mixture assumed an orange color and we obtained a thin magma of colorless crystalline material. After warming for 15 minutes the reaction product was poured into about 3 volumes of water, when a crystalline product separated. This crystallized from hot water in beautiful, rhombic prisms which did not melt at 300°. It did not contain potassium and was hydrolyzed by hydrochloric acid with formation of ammonium chloride. When digested with strong, hot alkali, ammonia was evolved. It sublimed when heated on a platinum foil. The compound was identified as cyanuric acid, $C_3H_3O_3N_3$. The filtrate above was evaporated and the residue recrystallized from water. Benzoic acid separated and melted at 121°. We obtained no evidence of the formation of 3-benzoylhydantoin. The similar behavior was observed when aceturic acid and glycocholl were used instead of hippuric acid. Cyanuric acid was formed in both cases. We did not obtain 3-acetylhydantoin (m. p. 148°) which has previously been described by Harries and Weiss.³ It is of interest to note here that Brunner⁴ did not observe the formation of cyanuric acid when potassium cyanate was allowed to interact with acetic anhydride in ether solution.

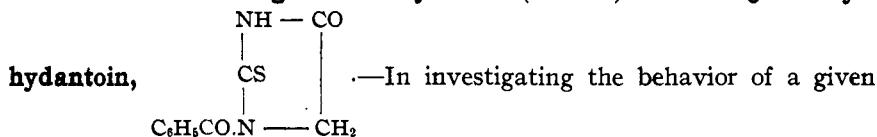
¹ Johnson and Nicolet, *THIS JOURNAL*, **33**, 1973 (1911).

² Richter's "Organ. Chem.," I, 512.

³ *Ann.*, **327**, 355 (1903)

⁴ *Loc. cit.*

The Action of Inorganic Thiocyanates (R.SCN). 2-Thio-3-benzoyl-



thiocyanate towards hippuric acid our procedure was consistent and was as follows: Two grams of the anhydrous rhodanide and 2 g. of hippuric acid were suspended in a mixture of 9 cc. of acetic anhydride and 1 cc. of glacial acetic acid. We then heated the mixture on the steam bath for one hour (in each case) and poured the resulting product into 50 cc. of cold water to decompose the acetic anhydride. Whenever the thiohydantoin was produced, it separated after pouring into water. This was dried and weighed. After separation of the thiohydantoin, the aqueous solution was then evaporated to dryness and benzoic acid separated from the residue by treatment with alkali. Whenever a small yield of thiohydantoin was obtained we found a corresponding large amount of benzoic acid in the filtrate. This resulted from hydrolysis of the unaltered hippuric acid with alkali. Ten inorganic salts were examined and the results, which we obtained, are recorded in the following table:

TABLE I.

| Salt. | Weight of thiohydantoin (g.). | Percentage of theory. | Filtrate. |
|----------------------------|-------------------------------|-----------------------|------------------------------------|
| NH ₄ SCN..... | 2.3 | 93.4 | |
| LiSCN..... | 1.1 | 44.7 | C ₆ H ₅ COOH |
| NaSCN..... | 0.1 | ... | C ₆ H ₅ COOH |
| KSCN..... | 1.1 | 46.7 | C ₆ H ₅ COOH |
| Mg(SCN) ₂ | 1.9 | 77.2 | |
| Ca(SCN) ₂ | 0.6 | 0.24 | C ₆ H ₅ COOH |
| Sr(SCN) ₂ | 1.2 | 47.8 | C ₆ H ₅ COOH |
| Ba(SCN) ₂ | 0.6 | 0.24 | C ₆ H ₅ COOH |
| Mn(SCN) ₂ | 1.0 | 40.6 | C ₆ H ₅ COOH |
| Zn(SCN) ₂ | | ... | C ₆ H ₅ COOH |

Ammonium thiocyanate, as has been emphasized in a previous paper,¹ reacts to give the maximum yield of 2-thio-3-benzoylhydantoin. It is also an interesting fact that magnesium thiocyanate interacts the most smoothly of the thiocyanates of the alkali earth metals. No salt examined, with the exception of magnesium thiocyanate, reacted to give a yield of the thiohydantoin greater than 48% of the theoretical. No hydantoin was formed when zinc thiocyanate was used.

Action of Thiourea.—This experiment was conducted in the usual manner by warming 2 g. of thiourea and hippuric acid, respectively, with acetic anhydride and a small amount of acetic acid for 1 hour at 100°. After cooling and pouring into 50 cc. of cold water no thiohydantoin separated. The aqueous solution was evaporated to 100°, when we

¹ Johnson and Nicolet, *Loc. cit.*

obtained a semi-solid residue which dissolved easily in a small volume of 95% alcohol. On cooling, stout prisms separated which melted at $166-7^{\circ}$. This substance was identified as acetylthiourea. It dissolved in dilute sodium hydroxide solution and was precipitated unaltered by addition of hydrochloric acid. The substance gave a strong test for sulfur. The yield of purified material was 1.3 g.

Calc. for $C_5H_6ON_2S$: N, 23.7. Found: N, 23.4.

Action of a Mixture of Ammonium Thiocyanate and Thiourea.---

Two grams of a mixture, containing equal parts by weight of ammonium thiocyanate and thiourea, and 2 g. of hippuric acid were treated in the usual manner with 9 cc. of acetic anhydride and 1 cc. of glacial acetic acid. After heating for 0.5 hour the resulting fluid was then poured into 50 cc. of cold water, when 0.9 g. of 2-thio-3-benzoylhydantoin separated. This is a yield of 81.0% of the theoretical. It crystallized from 95% alcohol in prisms and melted at 165° .

After filtering off the thiohydantoin, the acid filtrate was evaporated to dryness and the residue triturated with a small volume of cold water to dissolve ammonium thiocyanate. A product was obtained here which was insoluble in water. This crystallized from alcohol in prisms which melted at 167° . This material contained sulfur and was identified as acetylthiourea. A mixture of this substance with some acetylthiourea melted at the same temperature. The yield was 0.9 g. A theoretical yield would have been 1.5 grams.

Action of Ammonium Thiocyanate on Hippuric Acid in Propionic Anhydride Solution.

In this experiment the following proportions were used: 2 g. of the thiocyanate, 2 g. of hippuric acid and 10 cc. of pure distilled propionic anhydride. On heating the mixture at 100° the hippuric acid dissolved at once and the solution assumed a yellow color, which finally developed into a deep red. After one hour's treatment the solution was then poured into 50 cc. of water when the 2-thio-3-benzoylhydantoin separated. The yield of crude hydantoin was 2.4 g. It crystallized from alcohol in prisms which melted at 165° . In other words the thiohydantoin was formed just as smoothly in the presence of propionic anhydride as when acetic anhydride was used.

The Action of Potassium Thiocyanate.

An attempt to prepare the thiohydantoin by the action of potassium thiocyanate on hippuric acid in propionic anhydride solution was unsuccessful. On pouring the reaction mixture into water only a gum was obtained. This refused to crystallize, and on trituration with alkali gave a small amount (0.5 gram) of benzoic acid.

The Action of Benzoic Anhydride on Ammonium Thiocyanate.

Two grams of the thiocyanate and the same quantity of benzoic anhydride were heated together for an hour on the steam bath (temperature

of solution 85–90°). The anhydride, on melting, dissolved the thiocyanate forming a light yellow solution without evolution of hydrogen sulfide. On pouring the resulting mixture into 50 cc. of water a yellow, crystalline substance separated. This was separated by filtration and triturated with a small volume of dilute, aqueous ammonia when only part of the material dissolved. The insoluble material (0.6 g.) contained sulfur and crystallized from hot water in prisms which melted at 176°. This substance was identified as benzoylthiourea. A mixture of this product with some benzoylthiourea¹ melted at the same temperature.

The ammoniacal solution was acidified with hydrochloric acid when benzoic acid separated. This melted at 121°.

The Action of Benzoic Anhydride on Ammonium Thiocyanate in the Presence of Hippuric Acid.

The following proportions were used in this experiment: 10 g. of benzoic anhydride, 2 g. of hippuric acid and 2 g. of dry ammonium thiocyanate. The three substances were thoroughly mixed and then heated in a water bath at 100°. The mixture completely liquefied, giving a clear solution which became red on prolonged heating. A slight effervescence was also observed and benzoic acid sublimed from the solution. After heating for 1 hour the mixture was poured into 50 cc. of water when a semi-solid substance separated (filtrate was saved). This was dark red in color and dissolved in ether with the exception of a very small amount of material which was not examined further. After evaporation of the ether the residue was then triturated with dilute aqueous ammonia when only part of the material dissolved. This contained sulfur and crystallized from water in small prisms which melted at 176°. It was identified as benzoylthiourea. The yield was 1.0 g.

The ammoniacal solution was acidified with hydrochloric acid, when benzoic acid, melting at 121°, separated. The filtrate mentioned above was evaporated to dryness and the residue was crystallized from water. The only substances isolated in a state of purity were ammonium thiocyanate and benzoic acid. We obtained here 0.7 g. of this acid. We did not obtain evidence of the formation of any 2-thio-3-benzoyl hydantoin.²

The Formation of Isodithiocyanic Acid by the Action of Acetic Anhydride on Dry Ammonium Thiocyanate.

Isodithiocyanic Acid, NH.CS.NH.CS .—Ten grams of ammonium thiocyanate (previously dried at 110°) were suspended in 14 g. of acetic anhydride in an 8 oz. flask. The latter was connected with a return condenser and the mixture protected from moisture while it was heated on the steam bath. There was an immediate reaction on heating with solution of the thiocyanate and constant evolution of gaseous products

¹ *Loc. cit.*

² Johnson and Nicolet, *Loc. cit.*

among which hydrogen sulfide was identified. A clear solution resulted. Within two or three minutes, however, this commenced to become quite turbid, and within 15 minutes a considerable quantity of orange-colored material had deposited. Heating was discontinued at the end of 3 hours and the reaction mixture allowed to stand at room temperature for 12 hours. The orange-colored product, weighing 1.8 g., was then filtered off and the anhydride solution concentrated to a small volume and poured into cold water. After standing a short time this aqueous solution deposited 0.5 g. of material which afterwards proved to be identical with the substance which separated from the original anhydride solution. This compound was quite soluble in sodium hydroxide solution, from which it was precipitated unchanged by dilute hydrochloric acid. It was very difficultly soluble in cold water, but somewhat soluble in hot, and separated on cooling in characteristic yellow balls. It was more soluble in ethyl and amyl alcohol than in water. A cold, aqueous solution of the acid was unaffected by addition of ferric chloride solution, while the solution on warming turned brown. When heated in a capillary tube, the substance did not melt, but underwent partial decomposition when heated above 200° . Nitrogen and sulfur determinations agreed with the calculated values for the isodithiocyanic acid. For the purposes of identification this acid was synthesized in accordance with given directions.¹ The two compounds proved to be identical in every respect. We did not obtain any evidence of the formation of acetylpersulfocyanic acid or acetylthiourea.

Calc. for $C_2H_2N_2S_2$: N, 23.77; S, 54.24. Found: N, 23.88, 23.93; S, 53.86.

The above experiment was also carried out under somewhat altered conditions. The heating period was shortened to one hour and the reaction mixture then poured into cold water. A granular precipitate formed immediately. It weighed 2.4 g. and proved to be isodithiocyanic acid. The yield, therefore, was practically the same as in the first experiment.

NEW HAVEN, CONN.

[CONTRIBUTION FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]
**RESEARCHES ON HYDANTOINS. XXXV. A NEW METHOD OF
SYNTHESIZING GLYCOCYAMIDINE COMPOUNDS, AND
THE CONVERSION OF GLYCOCYAMIDINE
INTO ISOMERS OF CREATININE.**

BY TREAT B. JOHNSON AND BEN H. NICOLET.

Received July 31, 1915.

If we disregard amidine and keto-enol tautomerism, there are only five structurally isomeric monomethyl derivatives of glycoxyamide (I) theoretically possible. Three of these are nitrogen substituted com-

¹ *Ann.*, **179**, 204 (1875).