Summary

1. Three monophenyl biurets, in which the phenyl group is attached to nitrogen, are described in the literature. These may be designated, according to their melting points, as the 156–165°, the 190° and the 197° substances. According to the accepted theory of structure, only two should exist.

2. The wide variation in the reported melting points of the 156–165° substance is due to the fact that it decomposes on melting, but without charring, rapid evolution of gas or other obvious evidences of decomposition.

3. Results having to do with the 190° substance will be reserved for a later communication.

4. The third substance, melting at 197°, was found to be a molecular compound of three moles of the 156–165° phenylbiuret with two moles of phenylisocyanuric acid. A peculiar property of this molecular compound is that it forms continuous series of solid solutions with each component. Other of its physical properties are very interesting and were investigated in some detail.

STANFORD UNIV., CALIF. RECEIVED NOVEMBER 10, 1933

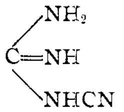
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF STANFORD UNIVERSITY]

The Tautomerism of Cyanourea with Guanyl Isocyanate[1]

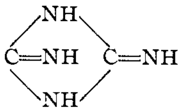
BY J. S. BLAIR AND G. E. P. SMITH, JR.

A striking peculiarity of carbonic acid, H_2CO_3, is that it lacks the property of forming pyro acids, analogous to the pyro silicic and pyro phosphoric acids, by dehydration at elevated temperatures or by interaction with the anhydride. On the other hand, one of the most interesting features of the ammono carbonic acids[2] is that they all, except cyanamide and guanidine, possess structures and properties which entitle them to be called pyro acids.

Consider the substance dicyanodiamide as a typical pyro carbonic acid. Both chain and ring structures have been advanced for this substance.[3]



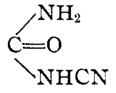
I



II

As a matter of fact, three chain and two ring structures were considered by the early workers with this long known substance but nowadays it is to be assumed that the chain structures or the ring structures would be tautomeric among themselves. But from the standpoint that the substance is a pyro acid it would seem reasonable to inquire as to the possibility that all carbonic acid structures of the formula $H_4C_2N_4$ are intertautomeric, just as one assumes that all possible phosphoric acid structures of the formula $H_4P_2O_7$ are inter-tautomeric. This postulate involves the assumption that ring–chain tautomerism exists between Formulas I and II, above, a possibility which, we believe, has not been considered by any previous investigator. For this assumption there is at present no evidence other than the fact that two isomeric dicyanodiamides are not known to exist. If the ring and chain formulas are not tautomeric, then the addition reactions of the substance[3] bespeak for it, more probably, the chain structure, but it is extremely difficult to outline experiments with dicyanodiamide which would bring unambiguous testimony to bear on the matter.

We have therefore turned to the mixed aquo ammono pyro carbonic acid[4] cyanourea (also called amidodicyanic acid), which, like dicyanodiamide, has been represented both by a chain[5] and by a ring[6] structure



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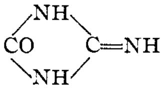

IV

In choosing between such formulas, or in considering the question of tautomerism between them, the situation is closely analogous to that involving dicyanodiamide, and the earlier work affords no basis for a conclusion. However, we wish to offer for consideration a new formula V, which may be referred to as the guanyl isocyanate structure, and

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[1] Read at the Chicago meeting of the American Chemical Society, September, 1933.

[2] Franklin, THIS JOURNAL, **44**, 486 (1922).

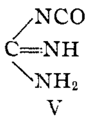
[3] For literature references see (a) Hale and Vibrans, *ibid.*, **40**, 1046 (1918); (b) G. B. L. Smith, Kane and Mason, *ibid.*, **51**, 2522 (1929).

[4] Blair, *ibid.*, **48**, 87 (1926).

[5] Baumann, *Ber.*, **8**, 709 (1875); Wunderlich, *ibid.*, **19**, 448 (1886).

[6] Hallwachs, *Ann.*, **153**, 293 (1870).

which represents equally well with the cyanourea structure, all the properties of the substance called cyanourea with the exception of the hydrolysis to biuret in sulfuric acid solution.[5] Such a substance as guanyl isocyanate could not give biuret by hydrolysis but would be expected to hydrolyze, at least in part, to guanidine. On the other hand, the cyanourea structure (III) could not in any way react with water to give guanidine. Both (III) and (V) could with equal plausibility be considered as tautomeric with the ring structure (IV).

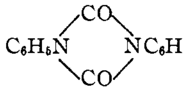

V

In the present work cyanourea was prepared and purified by the method of Hallwachs and hydrolyzed in sulfuric acid solution exactly as described by Baumann. The biuret which was formed was isolated according to Baumann's directions. Then the mother liquor was examined for guanidine by the Vozarik method[7] with positive results.

The formation of both biuret and guanidine by the acid hydrolysis of the substance called cyanourea or amidodicyanic acid cannot be explained by either chain structure, alone. One of two assumptions must be made. (1) The substance has the ring structure, which is easily broken by hydrolysis. The two chain structures are then simply symbolic of the two ways in which the ring structure may react. (2) Molecules having the ring structure exist in tautomeric equilibrium with molecules having the cyanourea chain structure as well as with molecules having the guanyl isocyanate chain structure.

A basis for a choice between the two hypotheses is afforded by the probability that cyanourea and dicyanodiamide (cyanoguanidine) should have analogous structures. But when ring-chain tautomerism is left out of consideration, the reactions of cyanourea require the ring structure and those of dicyanodiamide require the chain structure. It would therefore appear that the most reasonable assumption is that ring-chain tautomerism occurs in both cases. There is no direct evidence, whatever, against this assumption.

As a further test of the authenticity of such a ring structure, we have made a series of molecular weight determinations, using the boiling point method in benzene and carbon tetrachloride as solvents, of the substance considered by Hofmann,[8] on the basis of its chemical properties alone, to be a dimer of phenyl isocyanate. Our results confirm this assumption; the substance is in fact a dimer. In this case no chain structure is possible and the substance in all probability has the ring structure which was assigned to it by Hofmann



Cyanourea is a moderately strong acid in only the first of the three possible stages of its ionization, and therefore previous investigators, working with aqueous solutions, have prepared only the di-hydrogen salts. In liquid ammonia, however, it has been found possible to prepare not only the mono-potassium salt but also the di- and tri-potassium salts, and these are described herewith.

Experimental

Preparation of Pure Cyanourea.—The fundamental reaction of the Hallwachs method may be well expressed by the equation

$$H_2NCN + CNO^- + H_2O = H_3C_2ON_3 + OH^-$$

Cyanourea is a much weaker acid than cyanic acid, and in accordance with this fact an initially neutral (to phenolphthalein) solution of equimolecular proportions of potassium cyanate and cyanamide becomes alkaline as the reaction proceeds. This reaction of ion with free molecule is analogous to that which characterizes the polymerization of cyanamide.[9] The reaction does not appear to go to completion even under the most favorable conditions of hydrogen-ion concentration. The silver test for cyanamide and the Werner[10] test for cyanate remain positive. In a typical experiment following the Hallwachs procedure, the silver salt of cyanourea was obtained in 67% yield. The yield of free acid was 52% of that theoretically obtainable from the silver salt. The material at this point was quite pure but for analysis a portion was further purified by conversion to the copper salt and reconversion to the free acid by means of hydrogen sulfide.

Anal. Calcd. for $H_3C_2ON_3$: N, 49.41. Found (Dumas): N, 49.31.

Hydrolysis of Cyanourea.—Five grams of cyanourea (recrystallized, but not purified through the copper salt) was heated for three hours at 60–65° with 20 cc. of 6 *N* sulfuric acid. The cyanourea dissolved completely, but rather slowly. During the heating cyanic acid was evolved, detected by its characteristic odor.

On cooling, a small quantity of crystals formed in the strongly acid solution, and a quantity of acid was added just sufficient to bring them again into solution. Test portions of this solution gave the following results.

1. Addition of silver nitrate gave a copious white precipitate, completely soluble in ammonia. Unchanged cyanourea was therefore present and cyanamide was absent.

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(7) Vozarik, *Z. angew. Chem.*, **15**, 670 (1902).

(8) Hofmann, *Ann.*, Suppl. I, 57 (1861); *Ber.*, **3**, 765 (1870); *ibid.*, **4**, 246, 266 (1871).

(9) Grube and Krüger, *Z. physik. Chem.*, **86**, 65 (1914).

(10) E. A. Werner, *J. Chem. Soc.*, **123**, 2577 (1923).

2. The biuret test was strongly positive.
3. Made alkaline with sodium hydroxide, a portion tested by the nickel method[11] showed the absence of guanylurea.
4. The Werner test for cyanates was negative.
5. The urease test showed that urea was present.
6. The Vozarik test showed the presence of guanidine.

The main portion of the solution was neutralized with calcium carbonate, filtered and evaporated to a volume of about 20 cc. On cooling crystals appeared which weighed 1.8 g., melted at 187–188° and were identified as biuret. The filtrate contained a good deal of ammonium salt, and was therefore made alkaline with a few drops of 10% sodium hydroxide and aerated for an hour. To the resulting clear solution, measuring 20 cc., 50 cc. of Vozarik reagent was added. The typical microcrystalline precipitate of guanidinium picrate appeared, but on standing some ammonium picrate also separated as larger needles, in spite of the previous aeration. However, on filtering and thorough washing the ammonium picrate readily dissolved leaving the guanidinium picrate which when dry weighed 0.15 g. This material melted with decomposition at 311–315° and when mixed with authentic guanidinium picrate, m. p. 311–312°, the melting point was unchanged. All the samples showed some darkening at 300° or thereabouts, but with no signs of liquefaction, and the melting (decomposition) point was quite sharp.

In two other similar experiments guanidine was similarly identified as a product of the acid hydrolysis of cyanourea, though always in similarly small yield. In one case the picrate was compared under the microscope with authentic guanidinium picrate, and with the description and drawings of Emich,[12] and the results leave no room for doubt as to the identity of the substance.

Salts of Cyanourea.—The potassium salts of cyanourea were prepared and analyzed as described in many previous papers from this Laboratory.[13] Cyanourea, while only slightly hygroscopic, is very ammonoscopic, forming a liquid phase even at atmospheric pressure and room temperature. The mono-potassium salt was quite soluble, while the di- and tri-potassium salts are quite insoluble.

Monopotassium Cyanourea.—The potassium amide solution formed from 0.092 g. of metallic potassium was added to a solution of 0.40 g. of cyanourea. No precipitate appeared until the solution was concentrated. The mother liquor was decanted off, the crystals carefully washed five times with fresh ammonia, and the sample dried *in vacuo* for analysis.

Anal. Calcd. for $KH_2C_2ON_3$: N, 34.11; K, 31.76. Found: N, 34.2, 34.6; K, 31.65.

Dipotassium Cyanourea.—The potassium amide from 0.091 g. of metallic potassium was added to a solution of 0.10 g. of cyanourea. The salt was thrown down immediately as a white flocculent precipitate. Care was necessary to prevent its being formed on the inner walls of the tube, since it adheres thereto so firmly that it cannot be well washed. The precipitate was washed and dried *in vacuo* for analysis.

Anal. Calcd. for $K_2HC_2ON_3$: N, 26.09; K, 49.13. Found: N, 25.7, 26.02; K, 48.91.

Tripotassium Cyanourea.—In this case an excess of potassium amide (from 0.152 g. of metallic potassium) was added to a solution of 0.10 g. of cyanourea. The appearance and behavior of the precipitate was very similar to that of the dipotassium salt. When the potassium amide had all been added, a large part of the ammonia was distilled off and the precipitate left in contact overnight with the concentrated solution of excess potassium amide. The precipitate was then washed with fresh ammonia, but rather sparingly so as to lessen the chance for a possible ammonolysis. The sample was then prepared for analysis in the usual way.

Anal. Calcd. for $K_3C_2ON_3$: N, 21.51; K, 59.86. Found: N, 21.85, 21.60; K, 60.3.

The Molecular Weight of Diphenyldiisocyanate.—In the preparation of this substance a modification of the method of Snape[14] was used. Equimolecular quantities of dry, redistilled pyridine and of phenyl isocyanate were mixed and allowed to stand overnight. A good deal of heat was evolved and some crystals appeared almost immediately. After a few hours the system was practically solid. The crystals were dissolved in hot benzene, filtered from the small amount of diphenylurea which seemed to be unavoidably formed in spite of all attempts to exclude moisture and further purified by recrystallization from benzene or carbon tetrachloride. When pure the crystals melted at 175–176° with decomposition. The usual technique of the Kjeldahl method for nitrogen failed because of the apparently complete insolubility of the substance in concentrated sulfuric acid, together with its volatility at the temperature of the acid, so that most of the sample distilled out of the flask. This difficulty was overcome by diluting the acid with water, fitting the flask with an efficient reflux condenser and hydrolyzing the substance as the first stage of the analysis. Complete hydrolysis required about seventy hours. The condenser was then removed, the water distilled out and the analysis carried out as usual.

Anal. Calcd. for $C_{14}H_{10}N_2O_2$: N, 11.78. Found: N, 11.90, 11.68.

The identity of the substance was further established by the preparation of the diphenylallophanic ethyl ester and the asymmetrical diphenylbiuret described by Hofmann. The melting point and nitrogen contents of these substances agreed with his description.

For determining the molecular weight it was hard to find a solvent in which diphenyl diisocyanate is sufficiently soluble without reaction. Benzene and carbon tetrachloride were finally chosen but in both cases the solubility at low temperatures was too small to permit the use of the freezing point method. Recourse was therefore had to the boiling point method, but even at the boiling points solubility was so restricted that the highest concentration that could be used in any of the experiments was about 2.5%, which corresponded to a boiling point elevation of less than 0.3°. This fact constituted one of the principal limitations to the accuracy of the results.

Use was made of the apparatus and method of Cottrell

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[11] Buchanan, *Ind. Eng. Chem.*, **15**, 637 (1923).

[12] Emich, *Monatsh.*, **12**, 24 (1891).

[13] Leading reference, Franklin, THIS JOURNAL, **35**, 1460 (1913).

[14] Snape, *J. Chem. Soc.*, **49**, 254 (1886).

as modified by Washburn and Read.[15] Simultaneous readings (two observers) were made of the temperatures in two similar apparatus, one containing the solution and the other the pure solvent. This eliminated very well the effect of fluctuating atmospheric pressure on Δt_B, for which values constant within a 0.005° range could be obtained readily. It is believed that the principal source of error and uncertainty in the method as so far developed lies in the correction of the concentration of the boiling solution, to allow for the amount of solvent present in the vapor phase and as liquid in the condenser. Washburn and Read determined the actual concentration of the boiling solution by withdrawing a sample and determining its density, followed by an experimental correlation of density with concentration. This method, however, could not be applied to solutions so dilute as ours. In the present experiments use was therefore made of the alternative method suggested but not used by Washburn and Read, according to which the same apparatus is used to determine Δt_B for solutions of reference solutes. In the present work naphthalene was used as the reference solute for the benzene solutions and benzil for the solutions in carbon tetrachloride. The concentrations of the reference solutions were such as to give boiling point elevations of the same order of magnitude as those which characterized the diphenyl diisocyanate solutions.

In view of the various limitations to accuracy the results of the present work are presented as calculated by the approximation for dilute solutions (Washburn and Read's Equation 14) in which molecular weight of solute is directly proportional to solvent concentration. The "apparent molecular weights" so calculated for diphenyl diisocyanate and for the two reference solutes take no account of the concentration error discussed above. Then values for an "adjusted molecular weight" for diphenyl diisocyanate are given in which this error, as well as other constant errors, are eliminated by the use of a factor equal to the error of the "apparent molecular weight" of the reference substance.

Solvent	Benzene	Benzene	CCl_4	CCl_4
Solute	Naphthalene	Diphenyl diisocyanate	Benzil	Diphenyl diisocyanate
Experiments, no.	6	4	2	2
Apparent mol. wt.	120.8	218.3	193.1	204.7
Av. dev. from mean, %	4.4	2.7	5.6	4.2
Adjusted mol. wt.		231.5		222.2
Max. probable error		±16.5		±21.8

The maximum probable error is given as the effect, on the "adjusted molecular weight" of diphenyl diisocyanate, of the sum of the two average deviations. It is believed that while the results are not of high accuracy, they are dependable within this range. The calculated value for a dimer of phenyl isocyanate is 238.2. The uniformly negative deviation (in the case of no single experiment was the value of the "adjusted molecular weight" greater than 238.2) would seem to indicate the probability of a certain small degree of dissociation of the diphenyl diisocyanate at the temperature of the boiling solutions.

Summary

1. It has been known since 1875 that the substance called cyanourea, or amidodicyanic acid, reacts with water in the presence of acid to yield biuret. It is now found that guanidine is simultaneously formed under these conditions.

2. From this and other considerations it appears that the chemistry of cyanourea is best explained by the assumption of tautomerism between a four-membered ring and two different chain structures for the substance.

3. The validity of such a ring structure as that postulated for cyanourea is attested by the results of work with Hofmann's diphenyl diisocyanate.

4. All three of the hydrogen atoms of cyanourea are dissociable, as attested by the fact that the substance behaves as a tribasic acid in liquid ammonia solution.

5. The labile structure and acid character of cyanourea are in accord with the point of view that cyanourea should be regarded as a mixed aquo ammono pyro carbonic acid.

STANFORD UNIV., CALIF. RECEIVED NOVEMBER 10, 1933

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(15) Cottrell, THIS JOURNAL, **41**, 721 (1919); Washburn and Read, *ibid.*, **41**, 729 (1919).