and the filtrate acidified. The precipitate was dissolved in acetic acid and the solvent allowed to evaporate. The material, 4'-hydroxydiphenylphthalide, was recrystallized from acetic acid; mixed m. p. 165–167°.[12]

A solution was made of 5 g. of the lower melting compound in 25 cc. of concd. sulfuric acid; after one-half hour the solution was poured onto ice, the cold mixture filtered, the granular product dissolved in benzene, the solution shaken with sodium carbonate solution and then extracted with 10% sodium hydroxide. Upon acidification of the latter 4 g. of 4'-hydroxydiphenylphthalide was obtained of m. p. 165–166°.

Summary

The interaction of the acid chloride of 2-benzoylbenzoic acid with (a) the potassium derivative of various phenols, with (b) the phenols alone and with (c) the phenols in the presence of pyridine was studied. In general it may be stated that three isomeric compounds are produced—two compounds which are presumably the aryl ester of benzoylbenzoic acid and the phenylaryloxyphthalide, respectively, and the hydroxydiarylphthalide.

ANN ARBOR, MICH. RECEIVED NOVEMBER 10, 1933

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[12] Baeyer [*Ann.*, **354**, 173 (1907)] recorded the melting point as 167°.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF STANFORD UNIVERSITY]

The Monophenyl Nitrogen Esters of Biuret

BY J. S. BLAIR

Biuret is one of the most familiar mixed aquo ammono pyrocarbonic acids.[1]

The commonly accepted structural formula for this substance, $H_2NCONHCONH_2$, postulates the existence of two isomeric mono-esters, in which the substituting group is attached to nitrogen. The phenyl mono-esters are the only ones which have been thoroughly studied, and discrepancies appear in the literature which seem strange in the case of such simple derivatives of so common a substance.

One well-defined substance has found general acceptance as the unsymmetrical phenyl biuret, and has been prepared by several investigators using several different methods. However, some investigators[2] cite temperatures in the neighborhood of 156° as the melting point of the substance, while others[3] give values in the neighborhood of 165°. Dains and Wertheim[4] observed both melting points according to the sample.

Since this state of affairs would almost make it appear that two substances might be involved, the preparative methods of Lakra and Dains, of Gatewood (Reference a) and of Dains and Wertheim were followed in obtaining samples for comparison. It was found that the discrepancy is due to the decomposition of the substance, without charring, and with such slow evolution of gas that it may easily be unobserved. Dr. G. E. P. Smith, formerly of this Laboratory, has found that this type of behavior is general for this class of compounds, and has worked out a "decomposition curve" method for examination of such substances which will be described in a forthcoming paper and which has some advantages over the Maquenne block. The point of principal importance in the present instance is that complete liquefaction at constant temperature is not a sufficient criterion of purity. Indeed, it was found that samples prepared by the method of Lakra and Dains would, as first obtained, liquefy more rapidly at a given temperature than those prepared by the method of Dains and Wertheim, and these in turn more rapidly than those prepared by the method of Gatewood. Yet any of the three materials would appear to "melt" as a pure substance. However, after repeated recrystallization from hot water, practical coincidence in the "decomposition curves" of samples from the three sources was ultimately attained. That these samples were identical was then further established by mixed "melting points" determined simultaneously with "melting points" on the pure components of the mixtures, so that the rate of heating would be identical. No lowering, due to mixing, was observed, and the conclusion

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[1] Blair, THIS JOURNAL, **48**, 87 (1926); Blair and Smith, *ibid.*, **56**, 907 (1934).

[2] Pickard and Carter, *J. Chem. Soc.*, **79**, 843 (1900); McKee, *Am. Chem. J.*, **26**, 254 (1901); Lakra and Dains, THIS JOURNAL, **51**, 2222 (1929).

[3] Schiff, *Ann.*, **352**, 79 (1907); Fromm and Wenzl, *Ber.*, **55**, 812 (1922); Gatewood (a) THIS JOURNAL, **45**, 146 (1923); (b) *ibid.*, **47**, 410 (1925); Davis and Blanchard, *ibid.*, **51**, 1809 (1929).

[4] Dains and Wertheim, *ibid.*, **42**, 2307 (1920).

is that the 156–165° phenylbiuret is a single substance.[5]

A second phenylbiuret has been described[6] which is stated to melt at 190° and to have the symmetrical phenylbiuret structure. However, these results have been called into question by other investigators.[7] A good deal of work has been done in this Laboratory which has shown that these reactions, which were largely incidental to the main interests of the earlier investigators, were very imperfectly studied by them. The results of this study will be reserved for a later communication.

The uncertainty as to the status of the 190° substance encouraged Moore and Gatewood[8] to attribute, tentatively, the symmetrical phenylbiuret structure to a third substance, melting at 197°, which was obtained by the combined action of potassium hydroxide and hydrogen peroxide on 9-phenyluric acid. Certain general considerations having to do with the chemistry of the purines had led these investigators to expect that the symmetrical phenylbiuret, rather than the unsymmetrical one, would be formed in this reaction. The fact that the 156–165° substance, generally accepted as unsymmetrical, was also a product of the reaction, was apparently explained by the discovery that the 197° substance would yield the 156–165° substance on treatment with potassium hydroxide and hydrogen peroxide. Potassium or sodium hydroxides, alone, were not found to bring about this reaction, which appeared to be an "isomerization" of the symmetrical to the unsymmetrical phenylbiuret. However, this 197° substance has been identified, in the present investigation, as a molecular compound of three moles of the 156–165° phenylbiuret with two moles of phenylisocyanuric acid. That phenylisocyanuric acid should be a product of oxidation and alkaline hydrolysis of a phenyluric acid is not surprising in view of the fact that cyanuric acid is formed from uric acid under similar conditions.[9]

An extremely interesting property of this molecular compound is that it forms continuous series of solid solutions with each component. This type of behavior is of rare occurrence, but is found in the magnesium–cadmium system.[10]

The 9-phenyluric acid was prepared according to the references cited by Miss Gatewood (Ref. 3a). It was oxidized exactly according to her procedure, and the results as to yield and properties of the 156–165° substance and of the 197° substance tallied closely with her description. The peculiar hemispherical crystalline aggregates of the 197° substance persistently retain a brown tarry impurity (one constituent of which is nitrobenzene) at their nuclei, even after repeated crystallization. This can be eliminated, however, by the use of animal charcoal. A further peculiar property is the slowness with which solution in and crystallization from water take place. In purification the substance was boiled for half an hour with the minimum quantity of water required to effect solution, and then five days were allowed for crystallization to become complete. This was repeated three times until the constancy of the "decomposition curve" left little doubt as to the fact that a pure substance of constant properties was being dealt with. Two such samples (different preparations) were analyzed. Calculated for a phenylbiuret; C, 53.61; H, 5.06; N, 23.46. Calculated according to the formula $(C_8H_9O_2N_3)_3\cdot(C_9H_7O_3N_3)_2$ later found by other means to represent the substance: C, 53.21; H, 4.36; N, 22.18. Found: (I) C, 53.3; H, 4.6; N, 22.16, 22.36; (II) N, 22.23, 22.26, 22.17.

Since the ultimate analysis showed that the substance could not be a phenylbiuret, it became of particular interest to ascertain the nature of the "isomerization" reaction. It was found that sodium hydroxide alone would bring about this change.

Forty cc. of 0.997 *N* sodium hydroxide was heated to boiling, 0.2175 g. of the 197° substance was added and the mixture stirred until solution was complete. The clear solution was then quickly cooled in an ice-bath (to minimize hydrolytic decomposition), allowed to stand one hour, and the crystals collected, washed with water and dried. The product weighed 0.0397 g., and was found to be a very pure sample of the 156–165° phenylbiuret. The filtrate was acidified and slowly deposited 0.07 g. of crystalline aggregates which "melted" over the range 205–240°. On partial evaporation and longer standing the mother liquor gave a further crop weighing 0.05 g. This "isomerization" reaction was several times repeated in an endeavor to isolate the high-melting component in a pure state, but the highest-melting fraction ever obtained

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[5] However, McKee (*loc. cit.*) states that the substance prepared by his method (not repeated in the present work) is insoluble in ether, while all three samples just described are readily and completely soluble in ether.

[6] Schiff, *Ann.*, **352**, 73 (1907); Biltz and Jeltsch, *Ber.*, **56**, 1925 (1923).

[7] Böeseken and Couvert, *Rec. trav. chim.*, [ii] **14**, 291 (1910); Scott and Cohen, *J. Chem. Soc.*, **121**, 2036 (1922).

[8] Moore and Gatewood, THIS JOURNAL, **45**, 135 (1923).

[9] Venable and Moore, *ibid.*, **39**, 1750 (1917).

[10] Bruni and Sandonnini, *Z. anorg. Chem.*, **78**, 273 (1912).

melted (with decomposition) over the range 288–302°, and was not analyzed.

This was sufficiently close to the melting point of phenylisocyanuric acid (305°), however, to indicate that this substance might well be the higher-melting component. This acid was accordingly prepared in the pure state[11] by the method of Dains, Greider and Kidwell.[12] Intimate and finely powdered mixtures of the 156–165° phenylbiuret (B) and phenylisocyanuric acid (C) were prepared, in proportions corresponding to the formulas B_2C, B_3C_2, B_4C_3 and BC. The melting points of these samples were taken simultaneously, so as to equalize the rate of heating. A sample of the 197° substance was also present in the bath. The B_2C mixture began to liquefy at 193° and was all liquid at 196°, while the others all began to liquefy at 197°. The B_3C_2 mixture liquefied completely at this temperature, while the B_4C_3 mixture left a residue to 210° and the BC mixture to 225°. The B_3C_2 mixture is practically indistinguishable from the "197° phenylbiuret" in its thermal behavior, and when mixed with it this behavior is unaffected. When the B_3C_2 mixture is dissolved in hot water and the solution is cooled and allowed to stand, hemispherical crystalline aggregates slowly appear which are indistinguishable in every way from the "197° phenylbiuret."

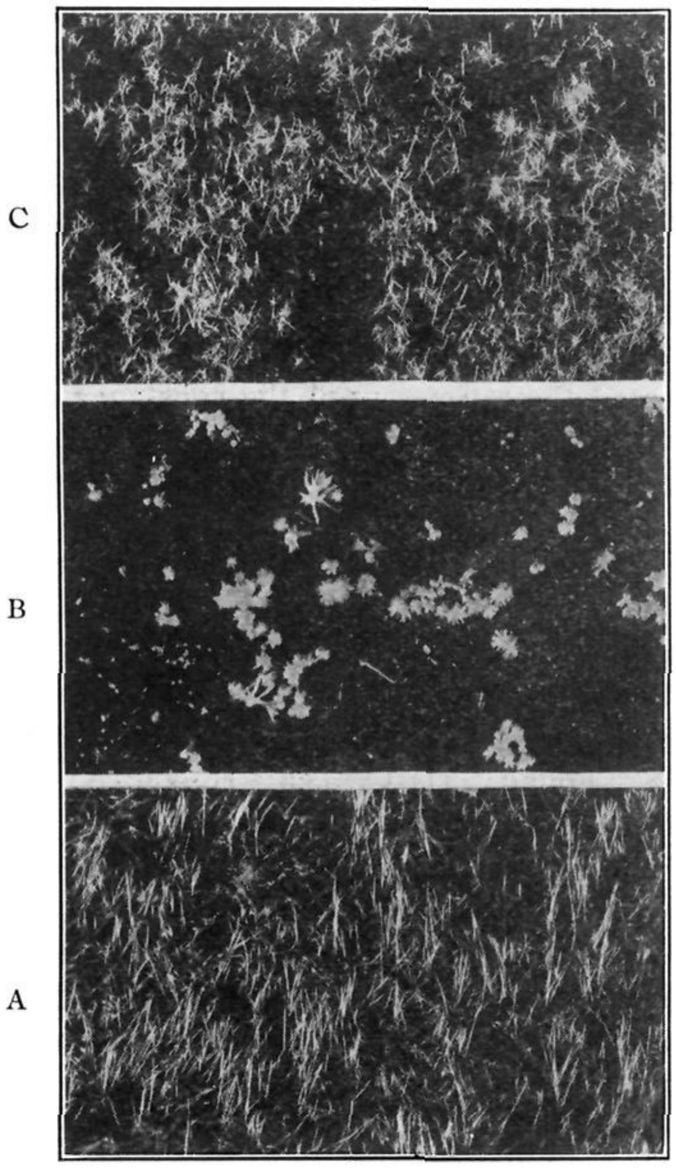

Fig. 1.

The "isomerization" reaction may now be explained as follows. Both components of the 197° substance are acids, but the phenylisocyanuric acid is much the stronger acid and its solubility is much more enhanced by adding a base than is the solubility of the phenylbiuret. This was established by direct experiment. Under proper conditions, therefore, the phenylbiuret will crystallize out alone, and in a pure state though in small yield, on cooling the alkaline solution. It may be said, however, that when ammonia is used for the "isomerization" rather than a stronger base, there are definite indications that the 156–165° phenylbiuret so obtained is contaminated with the 197° compound. This probably explains the high "melting points" mentioned above as characteristic of the 156–165° phenylbiuret prepared by the method of Gatewood.

It was definitely established by repeated comparative "melting point" determinations (pure sample and mixture heated at the same rate) that admixture of the "197° phenylbiuret" does not lower, in the slightest degree, the melting point of the 156–165° phenylbiuret, and also that admixture of phenylisocyanuric acid does not lower the melting point of the 197° substance. It may, therefore, be stated definitely that the system is characterized by lack of eutectics. Further than to establish this fact no attempt was made to carry out an accurate thermal analysis of the system. Such an analysis would be rendered difficult, though perhaps not impossible, by the fact that all substances concerned melt with decomposition.

To test out the possibility that the "197° phenylbiuret" might be a solid solution, or system of congruent solid solutions rather than a definite compound, search was made for a solvent which would dissolve, in the cold, one of the components to a much larger extent than the other. Absolute alcohol was found to serve this purpose admirably. All experiments were carried out at a temperature ranging from 22 to 24°. The solubility of the 156–167° phenylbiuret was found to be 33.96 g. per liter of solution, while that of the phenylisocyanuric acid was 4.75 g. per liter of solution. In each case the solution was continuously agitated for twelve hours in contact with excess of the solute.

A sample of the 197° molecular compound, prepared from 9-phenyluric acid and weighing 0.4306 g., was agitated with 20.0 cc. of absolute alcohol in this same temperature range for forty-five hours. The weight of undissolved solute was 0.27 g. Fifteen cc. of the saturated solution gave, on evaporation to dryness, 0.1136 g. of solute, indicating a solubility of 7.57 g. per liter of solution. The 0.27 g. of undissolved solute was investigated after simply drying in a current of warm air and then in a desiccator. Its thermal behavior as to melting point and "decomposition curve" was identical with that of the original material.

The fact thus established, that the composition of the "197° phenylbiuret" is not altered by leaching with a solvent in which one of its components is seven times as soluble as the other, would seem to establish beyond reasonable doubt that the substance is a definite compound.

Photographs are presented showing the crystalline habit of the 156–165° phenylbiuret (Fig. 1A); of the molecular compound (Fig. 1B), and of phenylisocyanuric acid (Fig. 1C).

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[11] Thanks are due to Dr. G. E. P. Smith for aid at this point.

[12] Dains, Greider and Kidwell, This Journal, **41**, 1004 (1919).

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.

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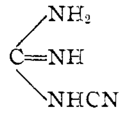
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF STANFORD UNIVERSITY]

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]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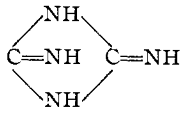
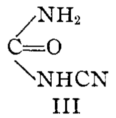

II

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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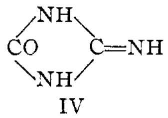
IV

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).