[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN.]

# FOUR-MEMBERED CYCLIC UREAS. III. THE CONDENSATION OF ISOCYANIC ACID WITH ALKYL SCHIFF BASES AND RELATED COMPOUNDS.[1]

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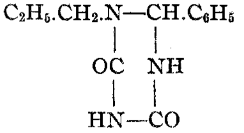
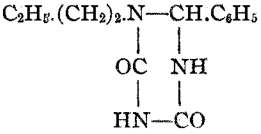
In our previous communication[2] attention was drawn to the fact that the addition of isocyanic acid to a Schiff base, where an ethyl group was attached to a nitrogen of the —N : C : complex, resulted in the formation of a diketocyanidine. Two molecules of isocyanic acid were found to enter into condensation with one molecule of Schiff base. The reaction is exactly analogous to the polymerization of isocyanic acid to cyanuric acid and finds its counterpart in the work of Staudinger,[3] who showed that two molecules of isocyanic acid condense in similar fashion with one molecule of a ketene.

For the further study of this reaction just mentioned, we have prepared the benzylidene derivatives of 3 normal primary alkyl amines by condensation of the latter with benzaldehyde. These alkyl Schiff bases were made thus to condense with isocyanic acid and to yield the expected triazines: from benzylidene propylamine, 1-propyl-6-phenyl-2,4-diketohexahydrocyanidine (I); from benzylidene butylamine, the corresponding 1-butyl derivative (II); and from benzylidene amylamine, the corresponding 1-amyl derivative (III). When, on the other hand an aryl group is attached to the nitrogen of the —N : C : complex of a Schiff base we have shown that the base now reacts with only one molecule of isocyanic acid to the production of a 4-membered cyclic urea or uretidone (see Papers I and II of this series).[4] The reaction is now being studied in more detail.

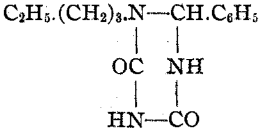
(I).



(II).



(III).



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[1] The work described in this article forms part of a thesis submitted by Norbert A. Lange, in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

[2] THIS JOURNAL, **41**, 379 (1919).

[3] *Ann.*, **374**, 11 (1911); *Ber.*, **50**, 1042 (1917).

[4] THIS JOURNAL, **41**, 370, 379 (1919).

We have thought now to apply this study to other compounds containing the —N : C : complex or, as we shall call it, the carbimino nucleus. With Schiff bases the nitrogen of this nucleus is attached directly to an alkyl or aryl group. We have endeavored to condense isocyanic acid with compounds containing this carbimino nucleus where the nitrogen is attached to amino derivatives. For example, the compounds benzylidene-phenylhydrazone, ($C_6H_5.CH : N.NH.C_6H_5$), benzylidene *as*-diphenylhydrazone, ($C_6H_5.CH : N.N(C_6H_5)_2$), and also benzylidene-benzylhydrazone, ($C_6H_5.CH : N.NH.CH_2.C_6H_5$), were each investigated in this direction. Of these compounds neither the first nor second showed any tendency to add cyanic acid at low temperature and in glacial acetic acid solution. The first, however, is reported[1] as adding phenyl-isocyanate to the imino position during warming to 170° after the manner of the Wöhler synthesis, producing 1-benzylidene-2,4-diphenyl-semicarbazone. The imino hydrogen in the last named of the 3 semicarbazone compounds offers indeed a ready point of attack for isocyanic acid itself, as has just recently been demonstrated by Bailey and Moore,[2] and the products resulting, or 1-benzylidene-2-benzyl-semicarbazone, ($C_6H_5.CH : N.N(CONH_2).CH_2.C_6H_5$), no longer is able to add isocyanic acid. This general type of condensation of isocyanic acid with imino hydrogen has been investigated in detail by Busch and Walter[3] and by Bailey and Read.[4] It would seem possible to effect the addition of isocyanic acid to a disubstituted N-amino derivative of the carbimino nucleus (*i. e.*, to the type $R_2N—N : CHR$) but more than likely phenyl isocyanate or other ethers of this acid will constitute the proper means of attack. Bailey and Moore already have reported the addition of isocyanic acid to benzalazine, a compound possessing two carbimino nuclei ($C_6H_5.CH : N-N : CH.C_6H_5$).

Though the work of these authors cannot at this time be discussed in detail, it has seemed advizable to us to investigate this tendency for imino hydrogen on the one hand and the carbimino nucleus on the other to enter into condensation with isocyanic acid. Thus, as just stated, Bailey and Moore prepared 1-benzylidene-2-benzyl-semicarbazone (V) by the action of isocyanic acid upon benzylidene-benzylhydrazone. Their description of the work, however, coupled with the statement that the product did not undergo hydrolysis when subjected to distillation with steam in the presence of a small amount of sulfuric acid raised considerable doubt in our minds as to the exact manner in which the isocyanic acid had attached itself. From our earlier publication it may be

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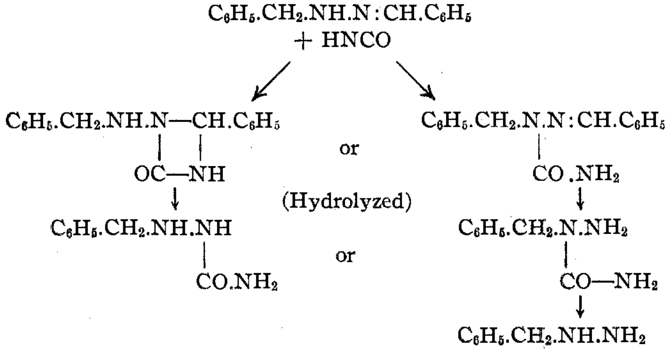
[1] Busch and Walter, *Ber.*, 36, 1360 (1903).

[2] THIS JOURNAL, 39, 290 (1917).

[3] *Ber.*, 36, 1359 (1903).

[4] THIS JOURNAL, 37, 935 (1915).

inferred that isocyanic acid could add directly to the carbimino nucleus and result in a compound of structure (IV). If, on the other hand, the attack took place on the imino hydrogen we should obtain the compound V as reported by Bailey and Moore. In either case the product should be capable of hydrolysis with liberation of benzaldehyde and a semicarbazide, 1-benzyl-semicarbazide (VI) if from a compound of Formula IV and 2-benzyl-semicarbazide (VII) if from a compound of Formula V.



$$\begin{array}{ccccc} & & C_6H_5.CH_2.NH.N{:}CH.C_6H_5 + HNCO & & \\ & \swarrow & & \searrow & \\ (IV). & \begin{array}{c} C_6H_5.CH_2.NH.N{-}CH.C_6H_5 \\ \quad\;\; | \quad\;\; | \\ OC{-}NH \end{array} & \text{or} & \begin{array}{c} C_6H_5.CH_2.N.N{:}CH.C_6H_5 \\ | \\ CO.NH_2 \end{array} & (V). \\ & \downarrow & \text{(Hydrolyzed)} & \downarrow & \\ (VI). & \begin{array}{c} C_6H_5.CH_2.NH.NH \\ | \\ CO.NH_2 \end{array} & \text{or} & \begin{array}{c} C_6H_5.CH_2.N.NH_2 \\ | \\ CO{-}NH_2 \end{array} & (VII). \\ & & & \downarrow & \\ & & & C_6H_5.CH_2.NH.NH_2 & (VIII). \end{array}$$

The semicarbazides (VI) and (VII) have both been reported in the literature. The first (VI) was prepared by Kessler and Rupe[1] by the reduction of benzylidene-semicarbazone ($C_6H_5.CH:N.NH.CO.NH_2$) through the action of sodium amalgam and alcohol. The pure product melts at 155° and its hydrochloride at 178–180°. The second (VII) was prepared by Curtius[2] through the action of isocyanic acid upon benzylhydrazine. The compound which Curtius obtained melted not sharply at 135°. He assigned to it the formula of a 1-benzyl-semicarbazide (identical with VI). Its strong basic properties, however, led Busch, Opfermann and Walther[3] to identify it as a 2-benzyl-semicarbazide (VII), which they reported as melting at 127–128°. Later the work of Kessler and Rupe[4] eliminated all possibility of the Curtius formula for this compound in that they actually prepared the 1-benzyl-semicarbazide (see above) whose properties in no wise tallied with those reported by Curtius. We must conclude, therefore, that isocyanic acid attacks preferably the imino hydrogen in benzylhydrazine (*i. e.*, at the α-nitrogen position). This has appeared to be a general conclusion for alkyl hydrazines, but for aryl hydrazines the β-position (*i. e.*, the amino hydrogen) affords also a likely point of attack, the more stable type of compound thus resulting. If, as is common, the α-position is first attacked the more or less labile product may be transformed by gentle heat into the stable

[1] *Ber.*, **45**, 26 (1912).

[2] *J. prakt. Chem.*, [2] **62**, 97 (1900).

[3] *Ber.*, **37**, 2325 (1904).

[4] *Loc. cit.*

$\beta$-form. According to Busch, Opfermann and Walther,[1] if a benzoyl hydrazine is subjected to the action of mustard oil or an alkyl isocyanate this strongly negative aroyl group forces the point of attack altogether upon the $\beta$-nitrogen position. The distinctly active character of the imino hydrogen as against the amino hydrogen may further be seen in the action of chloroacetic acid upon hydrazino-acetic acid ($H_2N.NH.CH_2.COOH$) to give hydrazinodiacetic acid ($H_2N.N(CH_2COOH)_2$).[2] Phenylhydrazine and chloroacetic acid react similarly to give *as*-phenylhydrazinoacetic acid ($H_2N.N(C_6H_5).CH_2.COOH$).

From the consideration just stated we may easily interpret the action of isocyanic acid upon benzylhydrazine as attacking the $\alpha$-nitrogen position and leading to 2-benzyl-semicarbazide as reported by Busch *et al.* No statement, however, is made by these authors as to the possibility of transforming their 2-benzyl-semicarbazide into a 1-benzyl-semicarbazide. Their general rule indeed would seem to eliminate this possibility in that they state that methyl- or benzylhydrazine takes up mustard oil or alkyl isocyanates exclusively upon the $\alpha$-nitrogen and the resulting 2,4-substituted compound (*e. g.*, $C_2H_5.\overset{4}{N}H.\overset{3}{C}O.\overset{2}{N}(CH_2.C_6H_5).\overset{1}{N}H_2$) does not suffer transformation into the 1,4-substituted compound (*e. g.*, $C_2H_5.\overset{4}{N}H.\overset{3}{C}O.\overset{2}{N}H.\overset{1}{N}H.CH_2.C_6H_5$). In such examples as phenyl-isocyanate upon phenylhydrazine the 1,4-type of compound above results as may be gathered from one of the preceding statements.[3] In our experiments upon the 2-benzyl-semicarbazide of Curtius and also Busch, *et al.*, we now find that a transformation of this carbazide into the 1,4-substituted form (*i. e.*, 1-benzyl-semicarbazide) takes place simply upon melting of the former. In those cases where allyl isocyanates were employed by Busch, *et al.*, it may be assumed that the alkyl radical in the carbamino group affords greater stability to the molecule with the lack of any tendency to suffer this transformation. We prepared the 2-benzyl-semicarbazide by carefully adding potassium cyanate to a cold aqueous solution of benzylhydrazine hydrochloride. The crystalline product thus separating was dried *in vacuo* and found to melt between 130° and 135°. The slight solubility of 1-benzyl-semicarbazide in cold chloroform and the ready solubility in this same solvent of the greater part of this product melting at 130–35° offered a simple means for the separation of the two semicarbazides. That part of this 130–35° product which could be taken up in cold chloroform was immediately precipitated therefrom, by the addition of ligroin, in small flattened prisms melting at 135–6°. The minute portion remaining undissolved by the chloroform consisted chiefly of the higher melting

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[1] *Loc. cit.*, p. 2330.

[2] *J. prakt. Chem.*, [2] **83**, 271 (1911); THIS JOURNAL, **36**, 1747 (1914).

[3] *Ber.*, **36**, 1362 (1903).

semicarbazide, but its presence was just sufficient to render difficult any attempts to determine the correct melting point of the 130–35° product. Curtius, however, possibly by repeated and careful crystallizations, actually isolated the pure compound (m. p. 135°), whereas Busch, Opfermann and Walther undoubtedly had a compound slightly contaminated with a little of the 1-benzyl-semicarbazide and hence the lower and inexact melting point, 127–8°.

When condensed with benzaldehyde at ordinary temperatures the pure 2-benzyl-semicarbazide yielded the well known 1-benzylidene-2-benzyl-semicarbazone (V) melting at 155.5°, the same compound as reported by Busch *et al.*, but with slightly lower melting point (153–154°). When the 2-benzyl-semicarbazide was melted and the cooled product crystallized from alcohol beautiful, glistening leaflets of 1-benzyl-semicarbazide, melting at 155–6°, were obtained. This final product was now shown to be identical with the 1-benzyl-semicarbazide prepared by Kessler and Rupe;[1] its hydrochloride also, both when alone and when mixed with samples of the hydrochloride of the compound prepared by Kessler and Rupe, melted at the recorded point 178–180°. There remains, therefore, no further question concerning the transformation of 2-benzyl-semicarbazide into 1-benzyl-semicarbazide at the point of fusion of the former. This transformation was, of course, accomplished in the case of the pure product (m. p. 135–6°) as well as for the more or less impure mixture which one first obtains in the action of isocyanic acid upon benzylhydrazine (130–135°). Any chance that the two semicarbazides might have been formed simultaneously is thus eliminated.

With the matter thus cleared concerning the structure and isolation of 2-benzyl- and 1-benzyl-semicarbazides (VII and VI), we saw at once the impossibility of proving anything concerning the structure of that addition product of isocyanic acid upon benzylidene-benzylhydrazone. Through the negative results obtained by us in our attempts to acetylate this addition product we were forced to the conclusion that a cyclic urea structure as a uretidone (shown in IV) cannot likely be present. In our earlier work we have remarked on the ease with which this latter type of compound undergoes acetylation. Further than this we may consider the hydrolysis which the compound suffers as not sufficiently speedy to indicate the presence of a uretidone.

The hydrolysis of the addition product (now to be considered as of structure V) as carried out by Bailey and Moore, was accompanied by a slight oxidation in the presence of sulfuric acid and neither benzaldehyde nor other products could be detected. We accomplished the hydrolysis by mixing the compound with dil. hydrochloric acid and subjecting this mixture to distillation with steam. The requisite quantity of benzalde-

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[1] *Loc. cit.*

hyde (1 mol.) is slowly liberated during long boiling, and the contents of the flask, upon evaporation and recrystallization from alcohol gave a product melting at 110°. As it proved not to be the 2-benzyl-semicarbazide (VII) which we anticipated we had only to look to the slight loss in carbon dioxide and ammonia during the distillation to anticipate yet another hydrolytic step with the final product easy of identification—that of benzylhydrazine (VIII) in the form of its hydrochloride. A slight contamination of this hydrochloride with a dihydrochloride was noted; the latter is removed by its lesser degree of solubility in absolute alcohol. Pure benzylhydrazine hydrochloride is reported to melt at 111°. The pure product and that obtained by us when mixed melt at 110–11°. We identified our product conclusively by causing it to react with isocyanic acid in aqueous solution. The product of course proved to be 2-benzyl-semicarbazide (VII), m. p. 135–36°.

The addition of isocyanic acid to benzylidene-benzylhydrazone is, therefore, to be interpreted in accordance with Formula V, which Bailey and Moore have proposed. The hydrolysis of this 1-benzylidene-2-benzyl-semicarbazone, however, is now seen to be possible and through its study we have come to a clear understanding concerning the stability of 1-benzyl-semicarbazide over that of the corresponding 2-benzyl-semicarbazide. The tendency of isocyanic acid to select an inimo or amino hydrogen in hydrazino derivatives is more and more clearly shown to depend upon the nature of the substituents on the nitrogen atoms of the hydrazines; the more strongly negative substituents force the attack to the $\beta$-nitrogen position. In the case of individual amino derivatives a primary amine naturally takes preference over a secondary amine when open to action with isocyanic acid. In the carbimino nucleus again we note the great influence of a substituent either upon the nitrogen or upon the carbon atoms in directing the action of isocyanic acid. With an alkyl substituent upon the nitrogen atom only ketocyanidines result. When an aryl group is attached to the nitrogen atom only the uretidone is produced. None of these condensations, however, is likely to proceed when a simple amino group is attached to the nitrogen atom; no matter whether the hydrogen atoms of the amino group are entirely replaced by aryl groups as seen above in the case of benzylidene-*as*-diphenylhydrazone, or only one of the hydrogen atoms is so substituted, as in benzylidene-phenylhydrazone. The conditions which will make for a uretidone formation from a carbimino nucleus even when the nitrogen is attached to amino derivatives are now under investigation.

## Experimental Part.

The alkyl Schiff bases employed in this work were prepared by adding an equimolecular quantity of benzaldehyde to the alkyl amine in question (*n*-propyl, *n*-butyl, and *n*-amyl) at 5–10° and drying the product over anhydrous potassium carbonate.

**1 - Propyl - 6 - phenyl - 2,4 - diketo-hexahydrocyanidine,** $C_3H_7.C_3H_3O_2N_3.C_6H_5$ (I).—To a well-cooled solution of benzylidene-*n*-propylamine in glacial acetic acid is slowly added, during constant stirring, small quantitites of potassium cyanate until a slight excess over two molecules have been used. The mixture is then set aside in a cool place for several days, after which it is transferred to a flask containing water and a few cubic centimeters of hydrochloric acid and subjected to distillation with steam. When no further trace of benzaldehyde is detectable in the distillate the solution in the flask is filtered, evaporated to small volume and then allowed to stand; crystals of the cyanidine derivative are soon deposited. Several crystallizations from alcohol gave fine, colorless, flaky needles melting at 211°. This propyl-phenyl-diketocyanidine is readily soluble in acetic acid; fairly soluble in alcohol, chloroform, acetone, ethyl acetate; slightly soluble in ether, benzene or water; and insoluble in ligroin. The solubilities partake closely after those of the corresponding ethyl derivative as reported in the previous publication.[1] The ethyl derivative is also slightly soluble in benzene—a point of correction for the description given in the earlier paper.

Calc. for $C_{12}H_{15}O_2N_3$: C, 61.77; H, 6.48; N, 18.03. Found: C, 61.76; H, 6.58; N, 18.38.

**1 - Propyl - 6 - phenyl - 1 - acetyl - 2, 4 - diketo - hexahydrocyanidine,** $C_3H_7.C_3H_2O_2N_3(COCH_3).C_6H_5$.—When the propyl-phenyl-diketocyanidine obtained above is boiled for a few minutes with acetic anhydride and fused sodium acetate and the mixture poured upon ice a crystalline mono-acetyl derivative is readily obtained. The compound may be purified by crystallization from 80% alcohol. The small colorless prisms melt at 120°. It is readily soluble in almost all of the organic solvents; only fairly soluble in ligroin and insoluble in water. The determination of percentage of carbon and hydrogen could not lead to definite conclusions. A nitrogen determination, however, sufficed to show the presence of only one acetyl group, more than likely in the 3-position.

Calc. for $C_{14}H_{17}O_3N_3$: N, 15.27. Found: 15.43.

**1 - Butyl - 6 - phenyl - 2, 4 - diketo - hexahydrocyanidine,** $C_4H_9.C_3H_3O_2N_3.C_6H_5$ (II).—Benzylidene-*n*-butylamine was digested with potassium cyanate in a cold glacial acetic acid solution in exactly analogous manner to that described above for the preparation of propyl-phenyl-diketocyanidine. The final crystalline product crystallized from alcohol melts at 188°. It is readily soluble in acetic acid; fairly soluble in alcohol, chloroform, acetone, ethyl acetate; slightly soluble in ether, benzene, or water; and insoluble in ligroin.

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[1] *Loc. cit.*

The preparation of acetyl derivatives was not undertaken either here or in the succeeding case, as one instance seemed sufficient to establish the constitutions proposed.

Calc. for $C_{13}H_{17}O_2N_3$: C, 63.13; H, 6.93; N, 17.00. Found: C, 63.41; H, 7.03; N, 17.10.

**1 - Amyl - 6 - phenyl - 2,4 - diketo - hexahydrocyanidine,** $C_5H_{11}$-$C_3H_3O_2N_3.C_6H_5$ (III).—Benzylidene-*n*-amylamine was here digested with potassium cyanate in cold, glacial, acetic acid solution and the operation carried out exactly as described for the two preceding ketocyanidines. Amylphenyl-diketocyanidine was purified by crystallization from alcohol and melts at 202°. It is readily soluble in acetic acid, chloroform or acetone; fairly soluble in alcohol or ethyl acetate; slightly soluble in ether, benzene or water; and insoluble in ligroin.

Calc. for $C_{14}H_{19}O_2N_3$: C, 64.34; H, 7.33; N, 16.09. Found: C, 64.49; H, 7.43; N, 16.37.

**Hydrolysis of 1 - benzylidene - 2 - benzyl - semicarbazone,** $C_6H_5$.-$CH_2$.N(.CO.$NH_2$).N : CH.$C_6H_5$.—This compound was prepared according to the directions of Bailey and Moore[1] by first reducing benzalazine with sodium amalgam and then treating the reduced product, benzylidenebenzylhydrazone, with potassium cyanate in cold, glacial, acetic acid solution. The substance thus separating out may be crystallized from ether and melts at 155.5°, or practically 156°, as reported by Bailey and Moore. It is readily soluble in most organic solvents, but only slightly soluble in ligroin. When placed in a flask containing a little water and hydrochloric acid and subjected to distillation with steam the product is slowly hydrolyzed. This process was continued until the distillate no longer contained benzaldehyde, after which the contents of the flask was filtered and finally evaporated to dryness upon a water bath. The dry residue was next boiled with a small amount of absolute alcohol and the clear filtrate from the insoluble portion (the dihydrochloride of benzylhydrazine), allowed to stand. The crystals of benzylhydrazine hydrochloride appeared in glistening leaflets melting at 110°. Pure benzylhydrazine hydrochloride melts at 111°; a mixture of the latter and the sample we obtained in the hydrolysis melted at 110–11°. In all respects the hydrolytic product checked with the properties of pure benzylhydrazine hydrochloride. The hydrolysis, therefore, may be interpreted as proceeding in the manner previously indicated, (V) ⟶ (VII) ⟶ (VIII).

When the final hydrolytic product (*i. e.*, the benzylhydrazine hydrochloride) was dissolved in a very small amount of water and a little more than an equimolecular quantity of potassium cyanate added to the solution there precipitated, after a short time, colorless crystals melting at 130–35°, and thus in agreement with the results found by Busch *et al.*,[1]

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[1] *Loc. cit.*

when isocyanic acid was allowed to condense with benzylhydrazine to give 2-benzyl-semicarbazide (m. p. 135–36°). A sample prepared according to the method of Busch *et al.*, melted at 130–35°, and when mixed with our product above the mixture likewise melted at 130–35°. There would seem to be no doubt concerning the identity of the two compounds—that prepared according to Busch and that obtained by the action of isocyanic acid upon the hydrolytic product.

Calc. for $C_8H_{11}ON_3$: C, 58.15; H, 6.71; N, 25.45. Found: C, 58.39; H, 6.87; N, 25.23.

**Preparation of Pure 2 - Benzyl - semicarbazide,** $C_6H_5.CH_2N(.NH_2).CO.NH_2$ (VII).—The action of potassium cyanate upon an aqueous solution of benzylhydrazine is reported by Curtius[1] to give a 1-benzyl-semicarbazide melting at 135°. The product of this same reaction as carried out by Busch, Opfermann and Walther[1] is construed as a 2-benzyl-semicarbazide melting at 127–28°. Kessler and Rupe[1] prepared the pure 1-benzyl-semicarbazide (m. p. 155°) as described in our theoretical considerations. When potassium cyanate is added to an ice-cold concentrated aqueous solution of benzylhydrazine (in equimolecular quantities), the crystals of 2-benzyl-semicarbazide are at once precipitated. Filtered off and dried *in vacuo* the product melts at 126–135°. These crystals are now mixed with ice-cold chloroform and the mixture filtered immediately by suction, pouring a little chloroform also upon the filter to insure removal of last traces of the soluble material. Upon the addition of ligroin to this chloroform filtrate small glistening colorless flat prisms of 2-benzyl-semicarbazide appear. The product may be again taken up in chloroform and precipitated by ligroin, but the melting point is not changed—135–36°. 2-Benzyl-semicarbazide is readily soluble in alcohol, acetone, chloroform, ethyl acetate or glacial acetic acid; fairly soluble in benzene or water; slightly soluble in ether; and insoluble in ligroin. This semicarbazide does not reduce Fehling's solution in the cold, even after several days' standing, but upon warming the reduction is accomplished slowly. At the temperature of its melting point it is transformed into 1-benzyl-semicarbazide.

**Preparation of 1 - Benzyl - semicarbazide,** $C_6H_5.CH_2.NH.NH.CO.NH_2$ (VI).—When 2 benzyl-semicarbazide is heated in an air bath to the point of melting for a few minutes and the cooled product then crystallized from 20% alcohol, colorless prisms of 1-benzyl-semicarbazide are obtained. These crystals are not so flattened nor so small as those of 2-benzyl-semicarbazide. Both the melting point (155°) and the physical properties of this product are identical with that compound prepared by Kessler and Rupe. 1-Benzyl-semicarbazide is readily soluble in alcohol, acetone or glacial acetic acid; fairly soluble in chloroform, ethyl acetate,

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[1] *Loc. cit.*

or water; slightly soluble in benzene or ether; and insoluble in ligroin. These solubilities differ somewhat from those of the 2-benzyl-semicarbazide. In cold chloroform very little of the product dissolves and hence a means of separating the two semicarbazides is afforded. This semicarbazide begins to reduce Fehling's solution even in the cold and reduces it readily upon warming, as recorded by Busch *et al.* A sample of this semicarbazide and an equal quantity of 2-benzyl-semicarbazide melted as low as 120–4°, hence an explanation of the indefinite results obtained by other investigators.

### Action of Isocyanic Acid upon N-Amino Derivatives of Carbimino Nucleus.

As previously stated, the compounds here subjected to the action of isocyanic acid failed to condense with the latter at low temperatures either in glacial acetic or propionic acid. Benzylidene-*as*-diphenylhydrazone ($C_6H_5.CH : N.N : (C_6H_5)_2$) was brought into reaction under these conditions and also in a mixture of benzene and acetic acid in order to increase somewhat its solubility. No reaction could be detected. In a similar manner benzylidene-phenylhydrazone ($C_6H_5.CH : N.NH.C_6H_5$) was found to be unreactive toward isocyanic acid, but as discussed in our theoretical considerations, this compound does condense with phenyl isocyanate at high temperature. 1-Benzylidene-2-benzyl-semicarbazone as also previously discussed, failed to condense further with isocyanic acid. Though the carbimino nucleus is a favored complex for condensation with isocyanic acid, we note further that certain substituents on the nitrogen atom may considerably retard this tendency for condensation.

MIDLAND, MICH.

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[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY, U. S. DEPARTMENT OF AGRICULTURE.]

# THE OCCURRENCE OF MELEZITOSE IN HONEY.

BY C. S. HUDSON AND S. F. SHERWOOD.

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We recently[1] called attention to the abundant occurrence of the rare trisaccharide melezitose in a manna that forms upon Douglas fir trees in British Columbia during summer droughts. Since bees often collect manna and honey-dew in times of drought when the preferred floral nectar is scarce it would appear to be possible that honey from the particular region of British Columbia where this Douglas fir manna occurs would contain melezitose. An occurrence of melezitose in honey would not only be of general scientific interest but would require the attention of the food analyst because melezitose may readily be confused with cane sugar,

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[1] THIS JOURNAL, 40, 1456–60 (1918).