Analyses. Calc. for $C_{18}H_{28}O_2N_4$: C, 65.06; H, 8.43; N, 16.87. Found: C, 65.09; H, 8.55; N, 17.21.

Summary

1. Conditions are given for obtaining good yields of hydro-aromatic semicarbazides by catalytic reduction of the corresponding semicarbazones.
2. The catalytic reduction of acetone semicarbazone to *iso*-propyl semicarbazide has been simplified.
3. It is made probable that for the first time a method of general application has been found in catalytic reduction for the conversion of semicarbazones to the corresponding semicarbazides.
4. Terpene semicarbazides being now readily available, a pharmacological study of the heterocyclic compounds that can be made from these should prove of interest.

Austin, Texas

[Contribution from the Chemical Laboratory, University of Texas]

THE BEHAVIOR OF SEMICARBAZIDES AT ELEVATED TEMPERATURES

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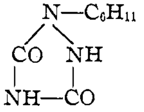
Received August 8, 1923

Introduction

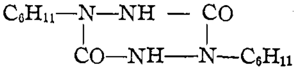
Hexahydrophenyl semicarbazide, described in the preceding article decomposes at elevated temperatures, forming dihexahydrophenyl carbazide (I), hexahydrophenyl urazole (II), and dihexahydrophenyl urazine (III),

$CO(NHNHC_6H_{11})_2$

I



II



III

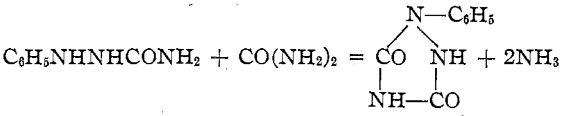
substances described in the experimental part of this paper. It is evident that in the formation of I, a molecule of urea is split out between two molecules of the semicarbazide, and that II results from the interaction of this urea with a third molecule of the semicarbazide, while if the structure of our urazine is correctly interpreted by Formula III, its formation is entirely independent of the reactions involved in connection with I and II.

Pinner[1] studied the effect of heat on phenyl semicarbazide and reported that at a temperature of 160–170° there are given off carbon dioxide, carbon monoxide and benzene, while the nonvolatile residue consists of unchanged phenyl semicarbazide, phenyl urazole, and diphenyl urazine. In repeating the experiment of Pinner, we find that ammonia, nitrogen and carbon dioxide, but not carbon monoxide, are evolved. What is more important

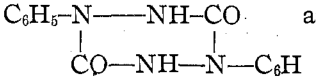
[1] Pinner, *Ber.*, **21**, 1224 (1888).

is the proof that diphenyl carbazide[2] is also formed, although its isolation and analysis here were not effected. Through the remarkable color reactions of this substance reported by Cazeneuve[3] it can now be identified in the minutest traces and, furthermore, as observed by Skinner and Ruhemann, this carbazide imparts through atmospheric oxidation to ammonium hydroxide solution within a short time a deep red color due to the formation of the so-called diphenyl carbazone,[4] $C_6H_5N{=}NCONHNH\text{-}C_6H_5$. We find that phenyl semicarbazide, on the other hand, imparts to ammonium hydroxide solution a yellow color and gives none of the Cazeneuve color reaction of the carbazide. That diphenyl carbazide is formed at least in small amount, even on fusion of phenyl semicarbazide, can be demonstrated in a simple way by heating a very small sample of the latter substance in an ordinary melting-point tube to liquefaction, then immediately removing the tube from the bath, and carrying out the color tests referred to above. As is evident from the following equations, the formation of diphenyl carbazide, as a decomposition product of phenyl semicarbazide, clears up the mechanism of the simultaneous formation here of phenyl urazole.

$$2\ C_6H_5NHNHCONH_2 + \delta = (C_6H_5NHNH)_2CO + CO(NH_2)_2 \qquad (1)$$



(2)

The structure of Pinner's so-called diphenyl urazine was first correctly interpreted by Heller[5] as  and this formula has been confirmed by the work of other investigators.[6]

As might be expected, dihexahydrophenyl carbazide does not give color reactions analogous to diphenyl carbazide. An explanation of this difference in behavior of the two carbazides is evident from the following considerations. All the color reactions of diphenyl carbazide depend primarily on the oxidation of this hydrazo body to a mixed hydrazo-azo compound containing the group, $—N{=}N—CO—NHNH—$. In the hydrazo complex of this group the imido hydrogens are replaceable by metals with the formation of colored salts that possess the unusual property of being soluble in organic solvents. On the other hand, dihexahydrophenyl carbazide contains the group $CO(NHNHCH{=})_2$, and it is well known that the stable oxidation product expected here would be of hydrazono and not azo structure.[7]

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[2] Skinner and Ruhemann, *J. Chem. Soc.*, **53**, 550 (1888).

[3] Cazeneuve, *Chem.-Ztg.*, **24**, 557, 684 (1900).

[4] Heller, *Ann.*, **263**, 274 (1891).

[5] Ref. 4, p. 282.

[6] Freund and Kuh, *Ber.*, **23**, 2831 (1890). Rolla, *Gazz. chim. ital.*, **38**, 344 (1908).

[7] Poth and Bailey, THIS JOURNAL, **45**, 3003 (1923).

It is probable that the system, 2 mols. of semicarbazide $\rightleftarrows$ 1 mol. of carbazide + 1 mol. of urea, represents a reversible reaction. In conformity with this view is the observation of Skinner and Ruhemann[8] that phenyl semicarbazide is formed on heating a mixture of diphenyl carbazide and urea. In the case of the phenyl compounds the equilibrium shifts to the left, while with hexahydrophenyl compounds it shifts to the right, so that in the latter case conditions have been established for obtaining a fairly good yield of carbazide by heating the semicarbazide.

The very unexpected observation was made that hexahydrophenyl semicarbazide on heating with urethan forms the carbazide in good yield. Apparently, the action of the urethane is either catalytic or, what is more probable, the urethan simply exerts a solvent action, causing a liquefaction of the semicarbazide at a temperature lower than its melting point. This latter view is in accordance with our observation that protracted heating of the semicarbazide melt or the urethan-semicarbazide melt has a marked influence in decreasing the yield of carbazide, due probably to its gradual decomposition at elevated temperatures. This method of preparing dihexahydrophenyl carbazide, applied to *i*-propyl and phenyl semicarbazides, showed that here urethan has no effect on the carbazide formation, at least under the conditions of our experiments.

Experimental Part

The Decomposition of Hexahydrophenyl Semicarbazide at Elevated Temperatures.—The semicarbazide, heated for 1$^1/_2$ hours at 180–185°, decomposes, giving a strong odor of ammonia and an aromatic odor resembling cyclohexanol. The melt, of a slightly yellow color, is extracted with 50 cc. of boiling water and filtered. From the filtrate there separates a white crystalline product, which is filtered off, and the filtrate is again used for extracting the residue. In all, three extractions are made with the same solution. The water-soluble material is leached out with a little chloroform to remove carbazide and urazine present only in small amounts, the residue dissolved in ammonia, and the urazole precipitated from the filtered solution with acetic acid. For further purification it is recrystallized from water. The yield of urazole is about 13.8% of that calculated theoretically. The water-insoluble product obtained above dissolves in ammonia, thus showing the absence of unchanged semicarbazide, and reprecipitates with acetic acid. It is purified by recrystallization from alcohol. The yield of urazine is about 34%. The carbazide, which under the above conditions is formed in very small amount, is dissolved in acetic acid and reprecipitated with ammonia with subsequent recrystallizations from water and acetic ether. Complete analyses of the above products agree closely in each case with the formula assigned.

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[8] Skinner and Ruhemann, *Ber.*, **20**, 3373 (1887).

If the semicarbazide is quickly heated up to 200°, 12 minutes being consumed in the operation, all the water-soluble material dissolves in dil. hydrochloric acid, thus showing the absence of urazole, and the carbazide is obtained from the acid solution by precipitation with ammonia in a yield of 41%. As the water-insoluble material is completely soluble in acid, it contains no urazine, but is unchanged semicarbazide. The amount recovered amounted to 19.5% of that originally used in the experiment.

Dihexahydrophenyl Carbazide.—The carbazide is readily soluble in cold chloroform or alcohol. Recrystallized from water, it is obtained in plates that melt at 187°. Acetic ether is also well adapted for recrystallizing the carbazide, which is difficultly soluble in benzene and sparingly soluble in ether. This substance acts as a strong reducing agent.

Analyses. Calc. for $C_{13}H_{26}ON_4$: C, 61.42; H, 10.23; N, 22.05. Found: C, 61.38; H, 10.34; N, 22.19.

Dihexahydrophenyl carbazide hydrochloride separates on dissolving the carbazide in methyl alcoholic hydrochloric acid in the form of thin plates, melting with gas evolution at 217°.

Analyses. Calc. for $C_{13}H_{28}ON_4Cl_2$: N, 17.12; Cl, 21.47. Found: N, 17.18; Cl, 21.76.

The most satisfactory method of preparing dihexahydrophenyl carbazide from the corresponding semicarbazide is to heat the latter mixed with $^1/_2$ its weight of urethan at 160° until liquefaction ensues and then maintain a temperature of 150° for 15 minutes. In this way an almost completely water-soluble melt is obtained which, worked up in the way described, gives a yield of 73% of carbazide. In an experiment where the mixture of semicarbazide and urethan was heated at 165° for $1^1/_2$ hours, only a 20% yield of carbazide was obtained.

Phenyl semicarbazide and *i*-propyl semicarbazide, heated with urethan under conditions similar to those employed in the case of hexahydrophenyl semicarbazide do not give the corresponding carbazides.

Hexahydrophenyl Urazole, or 3,5-Dihydroxy-1-Hexahydrophenyl Triazole.—The urazole is readily soluble in hot water and crystallizes on cooling in characteristic, thin, prismatic plates which melt at 271°. It is readily soluble in alcohol and sparingly soluble in the other common organic solvents. It does not give a color reaction with ferric chloride, shows an acid reaction to litmus, and acts as a strong reducing agent.

Analyses. Calc. for $C_8H_{13}O_2N_3$: C, 52.46; H, 7.10; N, 22.95. Found: C, 52.71; H, 7.25; N, 23.12.

The urazole is obtained in a yield of 74.5% by heating hexahydrophenyl semicarbazide and urea in molecular proportions. The mixture in a glycerol bath at 200° quickly liquefies with vigorous evolution of gas with the melt at a temperature of 150°. After 10 minutes the melt at a temperature of 190° becomes solid only to liquefy again after a few minutes. Toward the end of the operation, which consumes $^1/_2$ hour in all, the reaction mixture again becomes solid. During the entire operation the mixture is stirred. The urazole prepared in this way acquires its ready solubility in hot water only after it has been dissolved in ammonium hydroxide and reprecipitated with acetic acid. The above method of preparing urazoles was originally used by Pinner[9] in the preparation of the corresponding phenyl urazole from phenyl semicarbazide.

Dihexahydrophenyl Urazine or 3,6-Dihydroxy-1,4-dihexahydrophenyl-1,2,4,5-Tetrazine.—The urazine is very soluble in chloroform or alcohol, more difficultly soluble

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[9] Ref. 1, p. 1220.

in water, acetic ether, or benzene, and very difficultly soluble in ether. It can be recrystallized from acetic ether in the form of a network of fine needles, or from alcohol in slender prisms, which begin to soften at 187° and melt at 197°. Compared with the corresponding urazole, the urazine is less soluble in water and alcohol and more soluble in chloroform, benzene, and acetic ether. It acts as a strong reducing agent and gives no color reaction with ferric chloride.

Analyses. Calc. for $C_{14}H_{24}O_2N_4$: C, 60.00; H, 8.57; N, 20.00. Found: C, 60.32; H, 8.81; N, 20.03.

Dihexahydrophenyl carbazide and urea, heated in molecular proportions at 180° for 30 minutes, do not yield urazine, at least not in an amount sufficient for identification. This is in conformity with the structural formulas assigned here.

The most satisfactory method of preparing dihexahydrophenyl urazine is through the decomposition of the hydrochloride of the corresponding semicarbazide. When this salt is heated for $^1/_2$ hour at 200–210°, there is very little evolution of gas and the product without liquefying becomes viscous. For isolation of the urazine, the ammonium chloride, along with a small amount of carbazide, is leached out with boiling water, the residue dissolved in ammonium hydroxide, the solution filtered from tarry matter, and the urazine precipitated with acetic acid. This method of preparation gives a 70% yield of urazine.

The Gaseous Products Evolved on Heating Phenyl Semicarbazide.—As stated above, Pinner found among the decomposition products of phenyl semicarbazide, ammonia, carbon dioxide and carbon monoxide. In testing for carbon dioxide, it should be observed that this combines with the ammonia given off to form ammonium carbamate. To determine whether carbon monoxide is formed in the decomposition of the semicarbazide, 5 g. was heated at 109° for 5 hours in an atmosphere of carbon dioxide. The gas, collected in the usual way over 30% sodium hydroxide, measured 21.5 cc. at 26° and 746 mm. No reduction of this volume was effected by scrubbing the gas with cuprous chloride, which proves quite conclusively that nitrogen and not carbon monoxide was the gas under investigation.

Summary

1. Diphenyl carbazide is formed together with phenyl urazole and diphenyl urazine when phenyl semicarbazide is heated. The carbazide was identified by its characteristic color reactions.

2. Hexahydrophenyl semicarbazide, like phenyl semicarbazide, decomposes when heated with the formation of the corresponding carbazide, urazole and urazine. These were all isolated and analyzed.

3. Special methods are given in each case for the preparation in good yields of hexahydrophenyl urazole, dihexahydrophenyl carbazide and dihexahydrophenyl urazine from hexahydrophenyl semicarbazide.

AUSTIN, TEXAS