

solution to equilibrium with the salt. The solubilities so found are expressed in grams of salt per hundred grams of solvent.

In the preceding tables are recorded several of the properties, the results of analysis and the solubilities of the neutral ammonium salts of the acids listed.

Summary

Fifteen neutral ammonium salts of organic acids have been prepared by the action of dry ammonia on solutions of the respective acids.

The stabilities in dry and moist air and some of the solubilities have been determined.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TEXAS]

REDUCTION OF SEMICARBAZONES

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Introduction

The Skita method of reduction with colloidal platinum as catalyst, as shown in a previous communication from this Laboratory,¹ is of service in converting semicarbazones to the corresponding semicarbazides where other methods of reduction have produced only negative results.² Certain semicarbazones, such as glyoxylic acid semicarbazone³ and benzal semicarbazone,⁴ are readily reduced with sodium amalgam without molecular cleavage, but it has been quite definitely determined that reduction in the desired way with sodium amalgam succeeds only when an electronegative radical is joined to the carbon of the C=N complex. From the experiments described in this paper it appears probable that catalytic reduction with colloidal platinum is of general application in the conversion of semicarbazones to the corresponding semicarbazides.

Conditions have been established for obtaining excellent yields of semicarbazides with a minimum amount of platinum; for example, carvone semicarbazone and hexanone semicarbazone can be reduced with a yield of 80% where the semicarbazone and 10% platinic chloride solution are employed in the ratio of 10 g. to 1 cc. It is necessary in the case of camphor and fenchone, terpene ketones of similar structure, to employ for the reduction of their semicarbazones a much larger amount of platinic chloride. Camphor

¹ Neighbors, Foster, Clark, Miller and Bailey, *THIS JOURNAL*, **44**, 1557 (1922).

² Rupe and Oestreicher, *Ber.*, **45**, 30 (1912).

³ Darapsky and Prabhakar, *Ber.*, **45**, 2625 (1912). Bailey and Read, *THIS JOURNAL*, **36**, 1751 (1914).

⁴ Kessler and Rupe, *Ber.*, **45**, 26 (1912).

semicarbazone and platinum chloride are employed in the ratio of 1 g. to 1 cc., while in the case of fenchone semicarbazone the ratio is 1 g. to 4 cc.

It has been found in the catalytic reduction of the C=N complex to form basic products that the reduction is greatly facilitated by the presence of an acid for salification,⁵ but the reductions described on different semicarbazones, as shown in the experimental part of this article, give maximum yields with great variations in the amount of hydrochloric acid present. In the reduction of hexanone semicarbazone the hydrochloric acid, liberated from the platinum chloride used, suffices for a completion of the reaction, although this represents only a small fraction of the acid required for converting the hexahydrophenyl semicarbazide formed to its hydrochloride. With carvone, camphor and menthone semicarbazones maximum yields are obtained when only half of the calculated amount of hydrochloric acid is present, whereas in the case of acetone and fenchone semicarbazones it is necessary to employ the calculated amount of hydrochloric acid. The advantage of using a minimum amount of hydrochloric acid, in the case of the semicarbazones that readily hydrolyze, is apparent but, on the other hand, where the semicarbazide is difficultly, and its hydrochloride readily, soluble, a sufficiency of the mineral acid has the advantage of effecting clear solution at the end of the reduction. In order to keep down the acid concentration, it will frequently be found advisable to add the hydrochloric acid gradually at different stages of the reduction. Of the semicarbazones investigated, the velocity of hydrogenation is greatest in the case of those of hexanone, carvone and acetone, and slowest in that of fenchone, while camphor and menthone semicarbazones, in the order named, follow fenchone semicarbazone in their slowness of reduction. The effect of temperature here has not been studied, but it is quite evident that at higher temperatures there would be danger of increased hydrolysis of the semicarbazones.

The reduction of carvone semicarbazone is of interest because it contains two double bonds between carbons and a third between a carbon and a nitrogen. It is certain that the reduction of the C=N complex does not precede that of the C=C complexes, because, with one-third of the calculated hydrogen consumed, there remains, even with one molecular equivalent of hydrochloric acid present, a large amount of insoluble semicarbazone. The indications are that the difference in velocities of the reduction of the unsaturated complexes is not sufficient to allow of isolation of partial reduction products of carvone semicarbazone, at least with satisfactory yields. However, no experiments were made in this direction.

The aliphatic and hydro-aromatic semicarbazides, in contrast to the aryl

⁵ Compare A. Skita, *Ber.*, **52**, 1521 (1919). Lochte, Bailey and Noyes, *This Journal*, **43**, 2599 (1921).

semicarbazides, form stable salts that do not lose hydrochloric acid on standing. However, the hydrochlorides in aqueous solution react acid to methyl orange. All semicarbazides add a molecule of phenyl isocyanate and with acid chlorides yield acyl derivatives which with caustic alkalis lose a molecule of water to form triazoles.⁶ They apparently react with phenyl mustard oil, but the products could not be made to crystallize. The hydro-aromatic semicarbazides react with nitrous acid, but crystalline nitroso compounds were not isolated. On oxidation this type of semicarbazides yields azo compounds that cannot be isolated because of the ease with which they invariably transpose to the isomeric, colorless semicarbazones.⁷ All of the hydro-aromatic semicarbazides investigated give water-insoluble condensation products with formaldehyde⁸ which possess various solubilities in organic solvents and are neutral to both acids and alkalis. In no instance was a way of recrystallizing these substances found. Experiments aimed at acid and alkali hydrolysis of the hydro-aromatic semicarbazides to the corresponding hydrazino compounds did not produce the desired results: The decomposition of hexahydrophenyl semicarbazide at elevated temperatures is discussed in the succeeding article.

Experimental Part

General Conditions for Reduction of Semicarbazones.—In the case of most semicarbazones, it is advisable to prepare the colloidal platinum solution before the addition of the substance to be reduced. To a mixture of 200 cc. of water, 100 cc. of methyl alcohol, 5 cc. of 10% chloroplatinic acid and a few drops of seeding solution is added 0.4 g. of gum arabic, and the mixture is shaken in the usual way with hydrogen under pressure until a deep black color develops. A grayish, colloidal solution at this stage indicates a catalyst of poor efficiency and should not be used, since the physical state of the colloid has a pronounced effect on the rate of hydrogenation and the yield of semicarbazide. The semicarbazone is next added to the platinum solution, followed by the requisite amount of hydrochloric acid, and the reduction carried out with agitation in the usual way with an initial pressure of hydrogen registering $2\frac{1}{3}$ atmospheres (35 lbs.). It is advisable to hydrogenate semicarbazones with a pressure never lower than $1\frac{2}{3}$ atmospheres (25 lbs.). In the reductions described, 33% alcohol was employed as solvent with the ratio of solvent to platinic chloride of 60 cc. to 1 cc. In all cases except that of benzal semicarbazone 1 g. of semicarbazone was reduced in 6 cc. of the colloidal solution. As a rule, semicar-

⁶ Compare Widman, *Ber.*, **29**, 1946 (1896). Bailey and Acree, *ibid.*, **33**, 1520 (1900). Ref. 2, p. 32.

⁷ Compare Elbers, *Ann.*, **227**, 354 (1885). E. Fischer, *Ber.*, **29**, 894 (1896). Thiele, *Ann.*, **376**, 267 (1910). Ref. 1, p. 1561.

⁸ Compare Rassow, *J. prakt. Chem.*, [2] **64**, 131 (1901). Knorr and Weidel, *Ber.*, **42**, 3525 (1909).

bazones and, unless present as hydrochlorides, many semicarbazides are not completely soluble in this concentration of alcohol. A higher concentration is objectionable because, frequently, it breaks the colloid and in any event has a tendency to inactivate the catalyst.

The general method of procedure in carrying out the reduction of semicarbazones and the isolation of the semicarbazide formed is given under the preparation of fenchyl semicarbazide. The additional data in the following table are self-explanatory.

TABLE I
HYDROGENATION EXPERIMENTS

Semicarbazide formed	Semicarbazone G.	Methyl alcohol Cc.	Water Cc.	HCl ^a	Pt sol. Cc.	Time Hours	Yield %
Fenchyl.....	10	50	10	calc.	43	24	100
Carvomethyl.....	50	100	200	1/2 calc.	5	5	80
Hexahydrophenyl.....	50	100	200	trace	5	3	80
Menthyl.....	50	100	200	1/2 calc.	5	2.75	80
<i>iso</i> Propyl.....	50	100	200	calc. ^b	5	6	76
Benzyl.....	25	100	200	calc.	5	2.5	50
Bornyl.....	10	20	40	1/2 calc.	10	20	100

^a Concd. hydrochloric acid was used so as to keep the volume of solution a minimum.

^b The acid was added in three equal portions, one at the beginning and the other two when the hydrogen absorbed equalled 1/3 and 2/3, respectively, of the amount required.

^c This semicarbazone was not isolated, but benzaldehyde and semicarbazide hydrochloride, in calculated amounts, were added to the reduction mixture.

In all the reduction experiments 0.4 g. of gum arabic was used as a protective colloid for each 300 cc. of colloidal solution.

Fenchyl Semicarbazide.—To 43 cc. of 10% chloroplatinic acid, in a pressure bottle, are added 0.5 g. of gum arabic in 10 cc. of water, a few drops of seeding colloid, 50 cc. of methyl alcohol, 1 cc. of hydrochloric acid (d., 1.2) and 10 g. of fenchone semicarbazone,⁹ and the mixture is then shaken at over 2 atmospheres' pressure until the theoretical amount of hydrogen is absorbed. Finally, the colloid is broken with acetone, the filtered solution evaporated in a vacuum on a water-bath, and the fenchyl semicarbazide precipitated with ammonium hydroxide. Conditions have not been established for isolating salts of fenchyl semicarbazide which, so far as examined, do not possess good crystallizing properties. Fenchyl semicarbazide is practically insoluble in water, ether and petroleum ether, readily soluble in dilute mineral acids, chloroform and ethyl alcohol, slightly soluble in benzene and moderately soluble in acetic ether. It dissolves in glacial acetic acid but precipitates on dilution. For purification, it can be recrystallized from ethyl acetate in short needles, melting at 181° with decomposition.

Analyses. Calc. for C₁₁H₂₁ON₃: C, 62.56; H, 9.95; N, 19.91. Found: C, 62.51; H, 10.25; N, 20.02.

Benzoyl-fenchyl Semicarbazide, C₁₀H₁₇N(COC₆H₅)NHCONH₂.—To 5 g. of fenchyl semicarbazide, dissolved in 300 cc. of dry benzene, are added 4 cc. of benzoyl chloride and 5.3 g. of sodium bicarbonate. After the mixture has been refluxed for four hours on a

⁹ Wallach, *Ann.*, **353**, 211 (1907).

boiling water-bath, the benzoyl derivative separates as a gelatinous mass. The solvent is then distilled and the residue extracted with 95% alcohol. From the alcoholic solution, the benzoyl derivative is precipitated on dilution. On recrystallization from glacial acetic acid containing a few drops of water, it is obtained as a fine, crystalline powder which softens at 223° and decomposes at 226°. Like the other benzoyl derivatives described in this paper, it has neither acidic nor basic properties. An analysis of a sample, dried at 106°, indicates that the product obtained was not pure.

Analyses. Calc. for $C_{18}H_{25}O_2N_3$: C, 68.57; H, 7.94; N, 13.33. Found: C, 68.02; H, 8.39; N, 13.31, 13.36.

3-Hydroxy-1-fenchyl-5-phenyltriazole.—When 2.85 g. of benzoyl-fenchyl semicarbazide is boiled for one-half hour with 40 cc. of 30% potassium hydroxide, the triazole in the form of its potassium salt separates as an oil and redissolves on dilution. The triazole is liberated with hydrochloric acid and extracted with ether. It is readily soluble in water, alcohol or glacial acetic acid, slightly soluble in acetic ether or benzene, and insoluble in the other common solvents. Recrystallized from 95% ethyl alcohol, the triazole forms thick, triangular plates, which soften at 230° and melt at 234° to a clear, light brown liquid.

Analyses. Calc. for $C_{18}H_{23}ON_3$: C, 72.73; H, 7.74; N, 14.14. Found: C, 72.57, 72.79, 72.60; H, 8.00, 8.06, 7.67; N, 14.36, 14.38.

α -Phenylcarbamyl-fenchyl Semicarbazide, $C_{10}H_{17}N(CONHC_6H_5)-NHCONH_2$.—A solution of 4 g. of fenchyl semicarbazide and 2.4 cc. of phenyl isocyanate in 80 cc. of dry benzene is refluxed on a water-bath for one hour. The urethan separates and is recrystallized from 95% ethyl alcohol in the form of thin, shaft-like plates with arched end-faces, melting to a clear liquid at 192°. Like the other carbamyl derivatives described in this paper, it has neither acidic nor basic properties.

Analyses. Calc. for $C_{18}H_{25}O_2N_4$: C, 65.45; H, 7.88; N, 16.97. Found: C, 65.33; H, 7.93; N, 17.23.

Carvomenthyl Semicarbazide.—This semicarbazide prepared from carvone semicarbazone,¹⁰ is readily soluble in the common solvents with the exception of water, ether, and petroleum ether. It separates from ethyl acetate in thin plates melting with slow gas evolution at 126°.

Analyses. Calc. for $C_{11}H_{23}ON_3$: C, 61.97; H, 10.79; N, 19.72. Found: C, 62.06; H, 11.02; N, 19.98.

Carvone semicarbazone is obtained in a yield of 73% by adding 7 cc. of carvone in 25 cc. of ethyl alcohol to a solution of 5 g. of semicarbazide hydrochloride and 5 g. of anhydrous sodium acetate in 10 cc. of water. After 12 hours the semicarbazone is filtered off and washed with water, alcohol, and ether.

Carvomenthyl Semicarbazide Hydrochloride.—The hydrochloride separates from the reduction mixture of carvone semicarbazone on concentration. Recrystallized from 95% alcohol, it is obtained in the form of short needles that decompose at 186°. This salt is readily soluble in alcohol and water, and very difficultly soluble in the other common solvents.

Analyses. Calc. for $C_{11}H_{24}ON_3Cl$: N, 16.83; Cl, 14.23. Found: N, 17.13; Cl, 13.99.

Benzoyl-carvomenthyl Semicarbazide.—The procedure here is the same as in the case of the corresponding fenchyl compound, except that only 70 cc. of benzene is employed to 5 g. of the semicarbazide. When the reaction is completed, one-half of the solvent is distilled, and after the addition of 200 cc. of petroleum ether the mixture is

¹⁰ Rupe and Dorschky, *Ber.*, 39, 2113 (1906).

refluxed for one hour. In this way the benzoyl compound is obtained in a suitable state for filtering. Recrystallized from glacial acetic acid containing a few drops of water, it melts to a clear liquid at 235°. It is either difficultly soluble or insoluble in the common solvents.

Analyses. Calc. for $C_8H_7O_2N_3$: C, 68.14; H, 8.51; N, 13.25. Found: C, 67.82; H, 8.70; N, 13.35.

3-Hydroxy-1-carvomenthyl-5-phenyltriazole.—This triazole, prepared in the usual way, can be isolated, in the form of an oil, by means of extraction with chloroform. When this oil is taken up in alcohol and diluted with water, the triazole separates in a crystalline form by allowing the solution to evaporate at room temperature. It has solubilities similar to those of the corresponding fenchyl triazole, and crystallizes from absolute alcohol in thin plates that begin to soften at 180°, and melt completely at 187°.

Analyses. Calc. for $C_{15}H_{25}ON_3$: C, 72.24; H, 8.36; N, 14.05. Found: C, 72.14; H, 8.63; N, 14.27.

α -Phenylcarbonyl-carvomenthyl Semicarbazide, prepared in benzene solution under the same conditions as the corresponding fenchyl derivative is, after removal of the greater part of the solvent, refluxed with petroleum ether, filtered off, and recrystallized from acetic acid containing a few drops of water. It is thus obtained in clusters of radiating needles that begin to soften at 202°, and melt at 205° with gas evolution. This derivative is readily soluble in glacial acetic acid and difficultly soluble in other common solvents.

Analyses. Calc. for $C_{18}H_{28}O_2N_4$: C, 65.06; H, 8.43; N, 16.87. Found: C, 65.21; H, 8.79; N, 17.05.

The Action of Formaldehyde on Carvomenthyl Semicarbazide Hydrochloride.—When an aqueous solution of carvomenthyl semicarbazide is treated with an excess of formalin, a white crystalline product separates immediately that is very soluble in the common organic solvents with the exception of petroleum ether. Since no method of purifying this substance by recrystallization was found, the sample for analysis was thoroughly washed with water and dried at room temperature in a vacuum. It begins to decompose with evolution of ammonia at about 125° and melts with further decomposition at 150°. The analysis indicates that in the above reaction a molecule of water is split out between one molecule of formaldehyde and two molecules of the semicarbazide. A probable structure of this substance is, therefore, $CH_2(N(NHCONH_2)C_{10}H_{16})_2$.

Analyses. Calc. for $C_{20}H_{40}O_2N_6$: C, 63.01; H, 10.50; N, 19.18. Found: C, 62.79; H, 10.21; N, 18.41.

Hexahydrophenyl Semicarbazide.—After the solution obtained in the reduction of hexanone semicarbazone has been concentrated and chilled,¹¹ hexahydrophenyl semicarbazide hydrochloride separates as large acicular crystals, or the free base may be precipitated with ammonia. The base is readily soluble in alcohol, slightly soluble in ethyl acetate or benzene, and difficultly soluble in the other common solvents. Recrystallized from 95% ethyl alcohol, as fine needles, it softens at 183° and decomposes at 185° with evolution of gas.

Analyses. Calc. for $C_7H_{13}ON_3$: C, 53.50; H, 9.55; N, 26.75. Found: C, 53.46; H, 9.85; N, 26.87.

The hydrochloride recrystallizes from alcohol in long, slender needles melting at 176° to 178°.

Analyses. Calc. for $C_7H_{13}ON_3Cl$: N, 21.70; Cl, 18.35. Found: N, 21.85; Cl, 18.53.

¹¹ Zelinsky, *Ber.*, 30, 1541 (1897).

Benzoyl-hexahydrophenyl Semicarbazide.—The conditions employed in the preparation and isolation of benzoyl-carvomenthyl semicarbazide are followed in this preparation. This benzoyl derivative is readily soluble in glacial acetic acid, moderately soluble in alcohol, chloroform or acetone, and difficultly soluble in the other common solvents. It can be recrystallized from 95% acetic acid in the form of fine needles, which begin to soften at 260°, and melt with slow evolution of gas at 267°.

Analyses. Calc. for $C_{14}H_{19}O_2N_3$: C, 64.33; H, 7.33; N, 16.08. Found: C, 64.30; H, 7.61; N, 16.28.

3-Hydroxy-1-hexahydrophenyl-5-phenyltriazole.—This triazole is prepared and isolated as was the corresponding carvomenthyl compound. It is very soluble in chloroform, less soluble in alcohol, slightly soluble in ethyl acetate, and very difficultly soluble in the other common solvents. It separates from alcohol in radiating clusters of slender prisms with pyramidal end-faces, and melts to a light brown liquid at 232–234°.

Analyses. Calc. for $C_{14}H_{17}ON_3$: C, 69.13; H, 7.00; N, 17.28. Found: C, 69.15; H, 7.33; N, 17.23.

α -Phenylcarbamyl-hexahydrophenyl Semicarbazide, prepared in benzene solution under conditions analogous to those for the corresponding carvomenthyl derivative, is recrystallized from 95% alcohol as short microscopic needles, which decompose with vigorous gas evolution at 236°. It is slightly soluble in ethyl acetate, chloroform, and acetone.

Analyses. Calc. for $C_{14}H_{20}O_2N_4$: C, 60.87; H, 7.25; N, 20.29. Found: C, 60.80; H, 7.55; N, 20.53.

Benzyl Semicarbazide.—Benzyl semicarbazide was originally prepared by Kessler and Rupe by reducing benzal semicarbazone with sodium amalgam.¹² It can be made in a simple way by catalytic reduction of a mixture of semicarbazide hydrochloride and benzaldehyde in molecular proportions. However, the yield under the conditions employed is only 50% of that calculated.

*iso*Propyl, Bornyl, and Menthyl Semicarbazides¹³

Under the conditions given above for reducing acetone semicarbazone, only $1/30$ as much platinum is required as recommended by Neighbors and Bailey, with a slight increase in yield of *iso*-propyl semicarbazide. In the isolation of this semicarbazide with chloroform, continuous extraction is recommended. Our method of reducing camphor semicarbazone gives a quantitative yield of bornyl semicarbazide and employs only one-third of the amount of platinum used by Miller and Bailey. In reducing menthone semicarbazone, $1/27$ of the platinum employed by Clark and Bailey is used, and the time consumed in the process is appreciably shortened. Attention is directed to the fact that menthyl semicarbazide hydrochloride is difficultly soluble in the common solvents. It is, therefore, advisable at the end of the reduction to filter off the hydrochloride before breaking the colloid. Any dissolved menthyl semicarbazide is recovered in the usual way.

Benzoyl Menthyl Semicarbazide.—This benzoyl derivative has poor crystallizing properties. For analysis it was purified by precipitation from its alcoholic solution with ethyl acetate as a crystalline powder melting with gas evolution at 216°.

Analysis. Calc. for $C_{18}H_{27}O_2N_3$: N, 13.25. Found: N, 13.50.

α -Phenylcarbamyl-menthyl Semicarbazide, prepared like the corresponding carvomenthyl compound, crystallizes from alcohol in clusters of radiating needles, which decompose at 184°.

¹² Ref. 4, p. 26.

¹³ Ref. 1, pp. 1559, 1563.

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.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TEXAS]

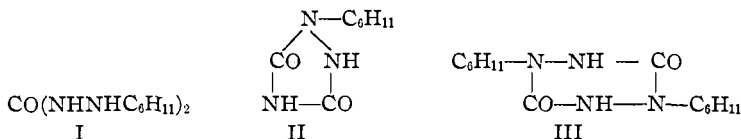
THE BEHAVIOR OF SEMICARBAZIDES AT ELEVATED TEMPERATURES

BY E. J. POTH AND J. R. BAILEY

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Introduction

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

Pinner¹ 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).