

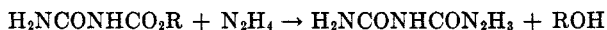
HYDRAZINE DERIVATIVES OF THE CARBONIC AND THIO-
CARBONIC ACIDS. V. ALLOPHANYL HYDRAZIDE
AND ITS DERIVATIVES^{1, 2}

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Although allophanyl hydrazide (1-aminobiuret) (VIII) was first prepared by Thiele and Uhlfelder (1) in the form of the hydrochloride by the zinc-hydrochloric acid reduction of 1-nitrobiuret, no attempt was made to isolate the parent substance. Only the benzaldehyde and acetone derivatives in addition to the hydrochloride, nitrate, and picrate salts of allophanyl hydrazide were characterized. The hydrochloride and the nitrate were found to cyclize to urazole (XIV) at their melting points; treatment of the hydrochloride in cold aqueous medium with sodium nitrite led to the isolation of allophanyl azide (XIII).

Excellent yields of allophanyl hydrazide can be obtained by the hydrazinolysis of methyl and ethyl allophanates (VII), if the solvolytic reactions are carried out in a low boiling solvent such as methanol.



The product is obtained directly, by concentrating and cooling the reaction mixture, as a white crystalline compound, melting at 166° with decomposition. It is a relatively non-hygroscopic substance and thermally unstable when heated at 110° for 24 hours.

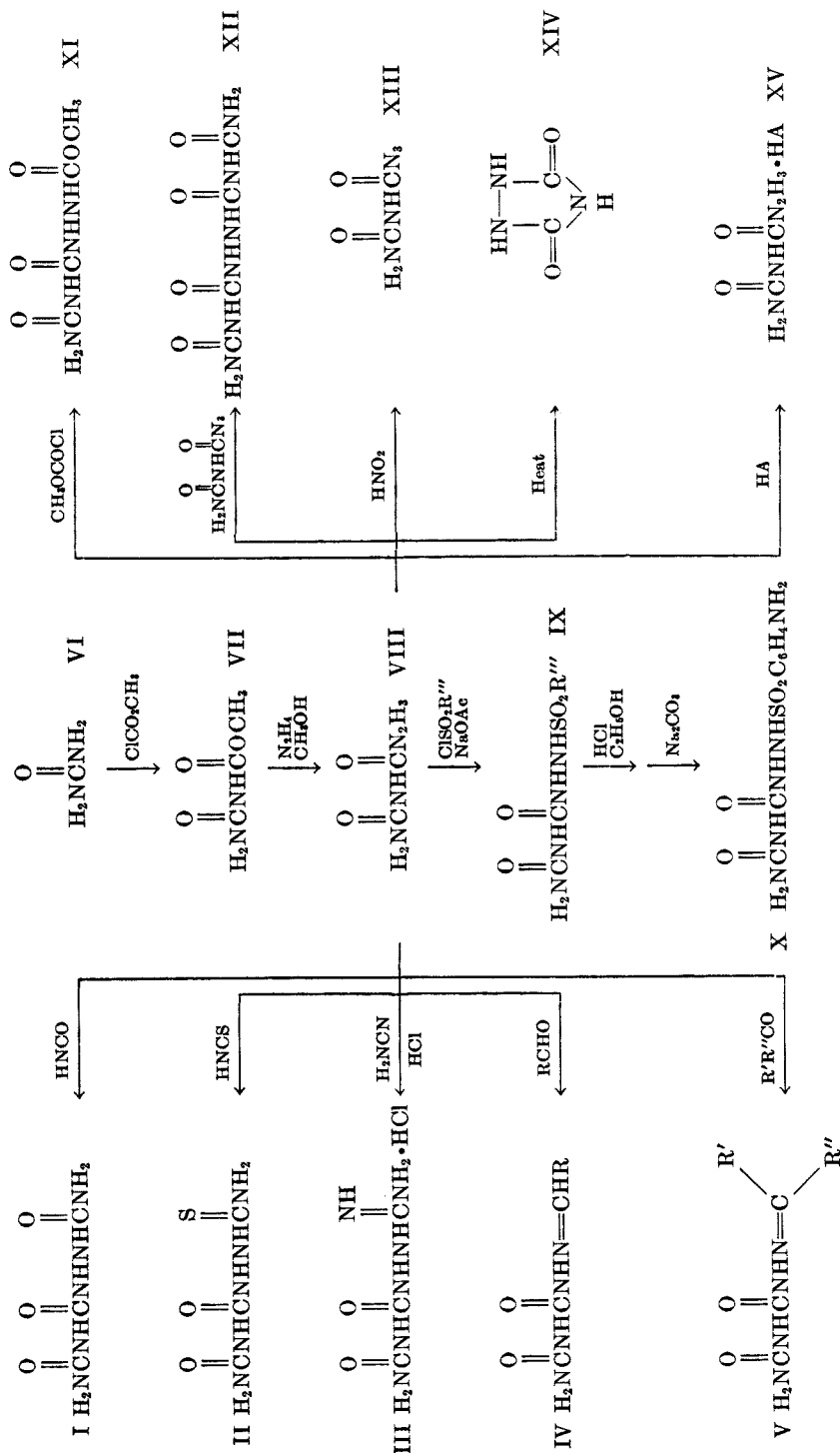
It has been found that allophanyl hydrazide forms well defined aldehyde (IV) and ketone (V) derivatives (allophanylhydrazones); it also undergoes characteristic condensation (solvation) reactions with cyanic acid to produce 1-allophanyl semicarbazide (I), with thiocyanic acid to produce 1-allophanyl thiosemicarbazide (II), and with aqueous cyanamide to form 1-allophanyl-aminoguanidine hydrochloride (III). Allophanyl hydrazide also undergoes condensation with chlorocarbonic esters to yield 3-allophanyl carbazinic acid esters (XI) and with *p*-acetamidobenzenesulfonyl chloride to give an intermediate which yields 1-sulfanilamidobiuret (X) upon hydrolysis.

Although the diazotization of allophanyl hydrazide to allophanyl azide (XIII), had been reported by the original investigators (1), usefulness of the latter as an agent for the introduction of the allophanyl group had not previously been demonstrated. It reacts readily with a variety of substances to form compounds

¹ For the previous article of this series see Scott and Audrieth, *J. Org. Chem.*, **19**, 1231 (1954).

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R = C₆H₅; *o*-HOC₆H₄; *p*-CH₃OC₆H₄;
 R', R'' = CH₃, CH₃; -CH₂CH₂CH₂CH₂CH₂; CH₃; *p*-ClC₆H₄;
 R''' = CH₃CONHC₆H₄;
 HA = HCl; HNO₃; HOC₆H₄(NO₂)₃; $\frac{1}{2}$ H₂C₂O₄

FIG. 1. SYNTHESIS AND REACTIONS OF ALLOPHANYL HYDRAZIDE

TABLE I
 ALLOPHANYL HYDRAZONES

Formula	M.P., °C.	Analytical Data					
		C		H		N	
		Calc'd	Found	Calc'd	Found	Calc'd	Found
H ₂ NCONHCONHN:CHC ₆ H ₅	209	52.42	52.42	4.89	5.09	27.17	27.38
H ₂ NCONHCONHN:CHC ₆ H ₄ OH- <i>o</i>	198	48.65	48.82	4.54	4.43	25.22	25.33
H ₂ NCONHCONHN:CHC ₆ H ₄ OCH ₃ - <i>p</i>	215	50.84	50.99	5.12	5.09	23.72	23.82
H ₂ NCONHCONHN:C(CH ₃) ₂ ^a	192	37.97	38.13	6.37	6.49	35.43	35.49
	dec.						
H ₂ NCONHCONHN: <u>CCH₂CH₂CH₂CH₂CH₂</u> ^b ...	200	48.47	48.59	7.12	6.95	28.27	28.26
H ₂ NCONHCONHN:C(CH ₃)C ₆ H ₄ Cl- <i>p</i> ^c	216	47.16	47.11	4.35	4.21	22.00	21.92

^a Acetone was used as the solvent; refluxed for two hours. ^b Reactants were warmed on a steam bath for two hours without solvent. ^c Reactants were refluxed 2½ hours in 500 ml. of methanol.

which may be looked upon as N-substituted biuret derivatives. With ammonia, biuret is obtained; with hydrazine, the hydrazide is reformed. Significant, however, is the reaction between allophanyl azide and allophanyl hydrazide which results in the formation of 1,2-diallophanyl hydrazine (or bi-biuret) (XII), representing an unusually long chain carbon-nitrogen compound, H₂NCONHCONHNHCONHCONH₂.

Reactions leading to the preparation of allophanyl hydrazide by the new and superior method involving the hydrazinolysis of allophanyl esters and the chemistry and reactions of this interesting new hydrazide are presented schematically in Figure 1.

EXPERIMENTAL

Allophanyl hydrazide (VIII) from methyl allophanate. The methyl and ethyl esters of allophanic acid were prepared as recommended by Dains and Wertheim (2). A mixture of 118 g. (1.0 mole) of methyl allophanate,⁴ 100 ml. (3.0 moles) of 95% hydrazine, and 1.5 liters of methanol was refluxed for six hours. The reaction mixture was chilled overnight in a freezer (-14°) to yield 95 g. (80.5%) of allophanyl hydrazide, m.p. 166° with decomposition. Concentration of the filtrate to 100 ml. under reduced pressure and chilling produced an additional 4.4 g. of hydrazide to bring the over-all yield to 84% of theory. The compound was recrystallized from hot water using 7 ml. of solvent per gram of hydrazide.

Anal. Calc'd for C₂H₆N₄O₂: C, 20.34; H, 5.12; N, 47.45.

Found: C, 20.40; H, 5.56; N, 47.23.

The base dissociation constant of allophanyl hydrazide was found to be of the magnitude 10⁻¹¹ by a pH titration of a 0.1 M solution with 0.1 N hydrochloric acid. The compound undergoes weight loss and decomposition when heated for an extended period of time at 110°. Allophanyl hydrazide was found to be non-hygroscopic when exposed to 90% relative humidity (saturated ZnSO₄ solution) at room temperature for two days.

⁴ Ethyl allophanate (132 g., 1.0 mole) may be used, but the reaction time must be increased (eight hours). An 81% yield (95.8 g.) was obtained in this manner, but the product was not as pure as that obtained from the methyl ester.

Allophanyl hydrazones (IV, V). The hydrazones were prepared by interaction of equimolar quantities of VIII with benzaldehyde, salicylaldehyde, anisaldehyde, acetone, cyclohexanone, and *p*-chloroacetophenone, respectively. The allophanyl hydrazide was dissolved in warm water. A few drops of hydrochloric acid were added followed by an equimolar quantity of the carbonyl compounds after which the reaction mixture was stirred for one-half to one hour at room temperature unless otherwise specified. (See Table I). All compounds were recrystallized from 95% ethanol.

1-Allophanyl semicarbazide (I). To a solution containing 11.8 g. (0.1 mole) of allophanyl hydrazide and 8.3 ml. (0.1 mole) of concentrated hydrochloric acid dissolved in 225 ml. of water there was added with stirring 9.75 g. (0.12 mole) of finely ground potassium cyanate. The white precipitate which formed after a few minutes was removed by filtration and found to weigh 14 g. (89%), m.p. 201–202° with decomposition. Recrystallization from hot water raised the melting point to 205°.

Anal. Calc'd for $C_5H_7N_3O_2$: C, 22.36; H, 4.38; N, 43.47.

Found: C, 22.76; H, 4.43; N, 43.21.

1-Allophanyl thiosemicarbazide (II). The hydrazide (VIII), (10 g., 0.085 mole), 7 ml. (0.085 mole) of concentrated hydrochloric acid, and 8.1 g. (0.10 mole) of sodium thiocyanate were dissolved in a mixture of 500 ml. of methanol and 100 ml. of water and refluxed for two hours. The reaction mixture was concentrated to 75 ml. over an infrared lamp and chilled overnight in a freezer (–14°) to give 3 g. (20%) of a light yellow crystalline product. The compound gave no precipitate with benzaldehyde, a negative test for thiocyanate ion with ferric chloride, reduced ammoniacal silver solution, and was shown to contain sulfur. Four recrystallizations from water finally yielded a product which decomposed at 193–194°.

Anal. Calc'd for $C_5H_7N_3O_2S$: C, 20.33; H, 3.98; N, 39.53.

Found: C, 20.39; H, 4.28; N, 39.30.

1-Allophanylaminoguanidine hydrochloride (III). The hydrazide (VIII) hydrochloride (15.4 g., 0.1 mole), 20 ml. (0.1 mole) of an aqueous cyanamide solution (3), and 75 ml. of water were heated for eight hours at 60°. The reaction mixture was chilled in a refrigerator overnight to give a white crystalline substance which was removed by filtration and washed with ethanol. The product, weighing 7.4 g. (38%) was purified by dissolving it in hot water (3 ml./g), adding ethanol to turbidity and chilling; m.p. 217–218°. The compound reduces ammoniacal silver solution, but gives no precipitate with benzaldehyde.

Anal. Calc'd for $C_5H_9ClN_3O_2$: C, 18.33; H, 4.61; N, 42.75.

Found: C, 19.05; H, 4.94; N, 42.42.

The *picrate* was prepared as a characterizing derivative by mixing equivalent quantities of the hydrochloride and an alcoholic picric acid solution. The product was recrystallized from hot water and decomposed at 189–190°.

Anal. Calc'd for $C_9H_{11}N_3O_9$: C, 27.77; H, 2.85; N, 32.39.

Found: C, 27.54; H, 2.63; N, 32.24.

Allophanyl azide (XIII). A solution containing 47.3 g. (0.4 mole) of VIII and 36.4 ml. (0.44 mole) of concentrated hydrochloric acid in 800 ml. of water was chilled to 0°. A cold solution containing 30.3 g. of sodium nitrite (0.44 mole) in 112 ml. of H_2O was added to the allophanyl hydrazide hydrochloride solution with stirring and at such a rate that the temperature remained between 0° and 5°. The resulting white precipitate was filtered and washed with water, ethanol, ether, and finally air-dried; weight, 46.1 g. (89%), m.p. 190° with decomposition (1). A sample dissolved in warm water gave no precipitate with benzaldehyde, but did give a red color with ferric chloride solution indicating the presence of the azide ion. The compound was not purified by recrystallization because of its insolubility and instability in warm solvents. A sample was obtained by sublimation at 150°, the analysis of which is given below. The product obtained by sublimation melts in a capillary tube at 193–194° with decomposition.

Allophanyl azide⁵ is non-hygroscopic at 90% R.H. at room temperature. Continued

⁵ Allophanyl azide reacts with ammonia to give biuret [Lipschitz, *J. Am. Chem. Soc.*, **66**, 658 (1944)]; it undergoes solvolysis with hydrazine to reform allophanyl hydrazide.

heating at 110° brings about decomposition and weight loss through volatilization. Impact sensitivity tests carried out at Picatinny Arsenal indicate that the azide is not shock sensitive.

Anal. Calc'd for $C_2H_2N_6O_2$: C, 18.61; H, 2.34; N, 54.26.

Found: C, 19.19; H, 2.81; N, 53.79.

1,2-Diallophanyl hydrazine (XII). A solution containing 3 g. (0.02 mole) of XIII and 2.75 g. (0.02 mole) of VIII in 200 ml. of water was stirred for 19 hours at room temperature. The white precipitate was filtered, and washed with water, ethanol, and ether; weight, 2.9 g. (61%); m.p. 213° with decomposition. Recrystallization from hot water yields a product which decomposes at 211–212°, gives no precipitate with benzaldehyde, reduces ammoniacal silver solution and gives a deep blue color with ferric chloride solution.

Anal. Calc'd for $C_4H_8N_6O_4$: C, 23.53; H, 3.95; N, 41.17.

Found: C, 23.58; H, 3.56; N, 40.80.

3-Allophanyl methyl carbazinate (XI). A mixture of 23.6 (0.2 mole) of VIII and 45.8 ml. (0.6 mole) of methyl chlorocarbonate was refluxed for five hours after which the crude reaction product was dissolved in 250 ml. of hot water and chilled to obtain white crystals; weight, 13.3 g. (76.8%); m.p. 193–194° with decomposition.

Anal. Calc'd for $C_4H_4N_4O_4$: C, 27.27; H, 4.58; N, 31.81.

Found: C, 27.32; H, 4.63; N, 32.35.

1-Sulfanilamidobiuret (X). An intimate mixture consisting of 11.8 g. (0.1 mole) of allophanyl hydrazide, 23.3 g. (0.1 mole) of *p*-acetamidobenzenesulfonyl chloride, and 40.8 g. (0.3 mole) of sodium acetate trihydrate was made into a paste with water and then heated for one-half hour at 60°. The reaction product was washed well with water, ethanol, and ether; weight, 15.8 g. (50%); m.p. 203–204°. The crude 1-(*N*⁴-acetylsulfanilamido)biuret (IX) was suspended in 600 ml. of hot water and filtered to obtain 15.6 g. of an insoluble product, m.p. 208° with decomposition.

Hydrolysis of the acetyl group was accomplished by refluxing 15.6 g. (0.05 mole) of IX with 48 ml. (0.575 mole) of concentrated hydrochloric acid in 160 ml. of 95% ethanol for three hours. The yellow reaction mixture was chilled to obtain 4.63 g. of light pink crystals, m.p. 212° with decomposition; this product was insoluble in water, soluble in dilute hydrochloric acid and sodium hydroxide, and gave a negative Beilstein test for halogen. The filtrate was neutralized with sodium carbonate to yield 2.68 g. of crystals, m.p. 214–215° with decomposition. Purification from hot water raised the decomposition point to 216–217°. The over-all yield of 1-sulfanilamidobiuret based on the starting material was 7.43 g. (27%) or 54% based on the amount of acetyl derivative which had been subjected to hydrolysis.

Anal. Calc'd for $C_8H_{11}N_3O_4S$: C, 35.16; H, 4.06; N, 25.63.

Found: C, 35.43; H, 4.08; N, 25.70.

Salts of allophanyl hydrazide. The hydrochloride, nitrate, and picrate of allophanyl hydrazide, all three of which have been reported previously by Thiele and Uhlfelder as well as the oxalate, were prepared by dissolving the hydrazide in a minimum amount of warm water, neutralizing with corresponding acid, and chilling. They can be purified by recrystallization from the minimum amount of hot water.

Analytical results for the normal *oxalate* are presented herewith:

Anal. Calc'd for $C_8H_7N_4O_4$: C, 22.09; H, 4.33; N, 34.35.

Found: C, 22.18; H, 4.43; N, 34.55.

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SUMMARY

Allophanyl hydrazide (1-aminobiuret) has been prepared by the hydrazinolysis of the methyl or ethyl esters of allophanic acid in methanolic solution. The parent compound reacts (a) with aldehydes and ketones to form the corresponding allophanyl hydrazones; (b) with cyanic acid, thiocyanic acid, and cyanamide to yield the respective condensation products, 1-allophanyl semicarbazide, 1-allophanyl thiosemicarbazide, and 1-allophanylaminoguanidine; (c) with methyl chlorocarbonate to form 3-allophanyl methyl carbazinate; and (d) with *p*-acetamidobenzenesulfonyl chloride to produce, after hydrolysis of the intermediate, 1-sulfanilamidobiuret. Diazotization effects conversion to allophanyl azide which has been used to introduce the allophanyl group onto hydrazine and allophanyl hydrazide to yield allophanyl hydrazide and 1,2-diallophanyl hydrazine, respectively.

URBANA, ILLINOIS

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