[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Preparation of N-Substituted Hydrazines by Modification of the Raschig Synthesis

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Chloramine, produced by interaction of equimolar quantities of hypochlorite and ammonia in alkaline solution, will react with various primary amines to form the corresponding N-substituted hydrazines. As in the Raschig synthesis the yield of alkyl hydrazine depends upon the following factors: (a) presence of gelatin as an inhibitor, (b) ratio of amine to chloramine, (c) presence of a permanent base. The amine–chloramine reaction differs from the corresponding ammonia–chloramine reaction in that smaller mole ratios of amine/chloramine are required to achieve maximum yields, and that the rate of reaction is much greater. Preparation of the following hydrazines has been achieved: methyl-, ethyl-, *n*-propyl-, isopropyl-, *n*-butyl-, isobutyl- and *t*-butyl. These have been isolated as the hydrogen sulfates, $RN_2H_3 \cdot H_2SO_4$.

Introduction

Chloramine, produced by the reaction of equimolar quantities of hypochlorite and ammonia in alkaline aqueous solutions, was shown by Raschig[1,2] to be capable of reacting with further quantities of ammonia to produce hydrazine. It has been postulated[3] that this reaction involves formation of either the $NHCl^-$ ion or the imide molecule, NH, as the active intermediate. The Raschig procedure for the synthesis of hydrazine is thus similar in many respects to the well-known Hofmann reaction.[4] The formation of hydrazine from chloramine may then be regarded as a reaction between ammonia and the imide molecule, represented as an electron-deficient structure, to give a tautomeric form of hydrazine, $[H_3N \rightarrow NH]$. Other Lewis bases may be expected to react with chloramine in strongly alkaline solutions, or in basic non-aqueous solvents, in accordance with the general equation

$$[H\ddot{N}] + B \longrightarrow [B \longrightarrow \underset{\cdot\cdot}{\ddot{N}}H]$$

where B = Lewis base (H_2O, NH_3, RNH_2, R_2NH)

The present investigation was undertaken to determine whether amines would react with chloramine in alkaline solution to yield N-substituted hydrazines. It was anticipated that the more strongly basic amines should react more rapidly with chloramine than ammonia. Practical considerations served as a further incentive, since no simple general method for the preparation of N-substituted hydrazines, specifically methylhydrazine, has been disclosed in the literature.

Alkyl hydrazines have been prepared previously by the following methods: (a) the direct alkylation of hydrazine,[5,6] (b) the alkylation of benzalazine and hydrolysis of the resultant quaternary salt,[7,8] (c) the reduction and subsequent hydrolysis of a nitrosoalkyl urea,[9-11] (d) the nitrosation of an amine followed by reduction of the nitrosamine[12] and (e) by the reaction of an amine with O-hydroxylaminosulfonic acid.[13,14]

It has been found that chloramine does in fact react with various amines to produce the corresponding N-substituted hydrazines. Conditions leading to the formation of alkyl hydrazines are similar in many respects to those which apply to the Raschig synthesis. The yield of N-substituted hydrazine has been found to depend upon the following factors: (a) the mole ratio of amine to chloramine, (b) the presence of a metal deactivator such as gelatin, (c) the presence of a permanent base and (d) the temperature. However, significant differences also were observed. First, the molar ratio of amine to chloramine necessary for maximum yields is much smaller than the ammonia to chloramine ratio necessary to obtain maximum yields of hydrazine and, secondly, the temperature required for the formation of the alkyl hydrazine in good yields is considerably lower than that necessary for the formation of hydrazine. Thus, for instance, in carrying out the reaction of methylamine with chloramine appreciable quantities of methylhydrazine were formed even at 0° and at molar ratios of $CH_3NH_2 : NH_2Cl = 5$.

Experimental

Materials and Solutions.—All chemicals were of reagent grade; the gelatin used as metal deactivator was Schaar pure gelatin powder. Commercial methylamine (40% aqueous solution) and ethylamine (70% aqueous solution) were used without further purification. Other amines were purified by fractionation through an efficient column packed with glass helices. Aqueous ammonia was prepared by dilution of concentrated ammonia. Sodium hypochlorite was prepared as described in reference 15.

Analytical Methods.—Ammonia content was determined by comparison with standard hydrochloric acid. Purified and recrystallized potassium iodate was used as a primary oxidimetric standard. Thiosulfate was standardized against a potassium iodate solution, starch being used as the indicator. Sodium hypochlorite and chloramine were determined iodometrically, using starch as an indicator.

Although no analytical method is recorded specifically for N-substituted monoalkyl hydrazines, several modifications of the Andrews–Jamison iodate titration have been applied to other hydrazine derivatives.[16] The hydrazines were determined as follows: A 5-ml. aliquot of the reaction mixture containing the alkyl hydrazine was dissolved in 60 ml. of 9.0 *N* hydrochloric acid, 15 ml. of chloroform was added and the solution cooled. Standard potassium iodate (0.025*f*) was then added until the color of the chloro-

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[12] J. Thiele and C. Meyer, *Ber.*, **29**, 961 (1896).

[13] F. Sommer, O. F. Schultz and M. Nassau, *Z. anorg. u. allgem. Chem.*, **147**, 142 (1925).

[14] G. Gever and K. Hayes, *J. Org. Chem.*, **14**, 813 (1949).

[15] H. S. Booth, "Inorganic Syntheses," Vol. I, McGraw-Hill Book Co., New York, N. Y., 1939, p. 60.

[16] W. R. McBride, R. A. Henry and S. Skolnik, *Anal. Chem.*, **23**, 890 (1951); **25**, 1043 (1953).

form layer changed from dark brown to a light pink. At this point the iodate was added dropwise and the solution shaken after the addition of each drop. Disappearance of the iodine color in the chloroform layer served for the determination of the end-point.

Effect of Variables on the Yield of Methylhydrazine.—A standardized experimental procedure was adopted to study the influence of such variables as (a) the addition of gelatin and (b) the methylamine–chloramine ratio upon the yield of methylhydrazine from methylamine and chloramine.

To study the effect of gelatin, 50 ml. of a gelatin solution containing 0 to 1.00 g. of gelatin and 100 ml. of 1.15 *M* sodium hypochlorite were placed in a three-neck flask fitted with a thermometer, dropping funnel and an outlet vent. The apparatus was placed in an ice-bath and cooled to 0°. One hundred ml. of cold 1.15 *M* ammonium hydroxide was added dropwise to the solution. After the addition of the ammonium hydroxide the flask was shaken cautiously, care being taken to avoid excessive gas evolution. Solutions prepared in this manner were found to contain no hypochlorite when tested with aniline water, and to be 0.16 *M* with respect to their chloramine content. Ten and three-tenths grams (0.33 mole) of methylamine (30.6 ml. of a 39% solution) diluted to 40 ml. was added to 250 ml. of 0.16 *M* chloramine and the reaction mixture stirred at 0°. The methylamine–chloramine ratio (8.3:1) was held constant in all runs. The reaction mixture was allowed to warm to room temperature during a two-hour interval, after which an aliquot was removed and analyzed for methylhydrazine. The yields of methylhydrazine based upon chloramine are plotted in Fig. 1 as a function of the amount of added gelatin.

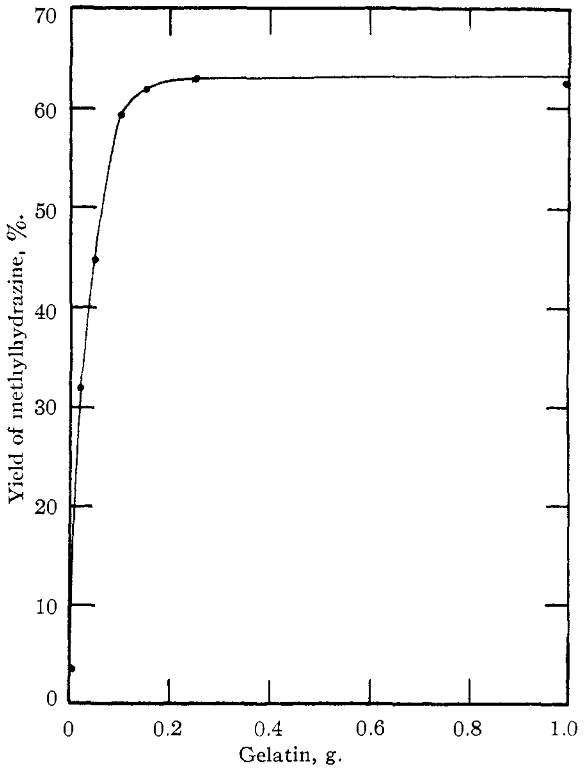

Fig. 1.—Effect of gelatin on the yield of methylhydrazine; mole ratio, CH_3NH_2/NH_2Cl = 8.3.

To evaluate the effect of the molal ratio of methylamine to chloramine upon the yield of methylhydrazine a method similar to that described above was employed. Methylamine (0.04 to 0.40 mole) diluted to 40 ml. was added to 250 ml. of a cold 0.16 *M* chloramine solution containing 0.25 g. of gelatin. The above values represent molal ratios of methylamine to chloramine varying from 1:1 to 10:1. After allowing the reaction mixture to warm to room temperature, an aliquot was removed and analyzed for methylhydrazine. The yield of methylhydrazine as a function of the methylamine–chloramine ratio is depicted graphically in Fig. 2.

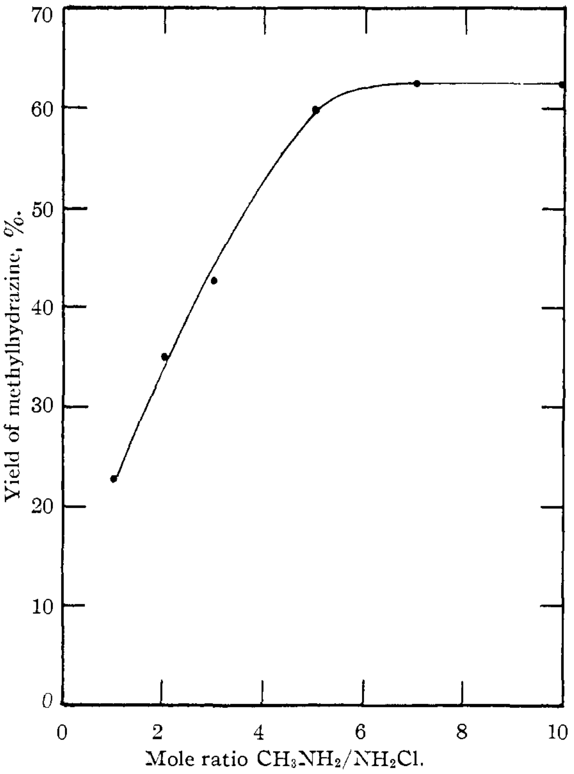

Fig. 2.—Effect of mole ratio CH_3NH_2/NH_2Cl on yield of methylhydrazine; amount of gelatin constant at 0.25 g./290 ml. of solution.

The effect of permanent base (in the form of sodium hydroxide) upon the formation of methylhydrazine was not demonstrated directly. Sodium hydroxide is formed in an amount at least equivalent to the chloramine content in the preparation of chloramine from sodium hypochlorite and ammonia.[17] However, when methylamine gas that had previously been condensed and dried over sodium was passed into an anhydrous ethereal solution of chloramine, no methylhydrazine could be detected even after a 48-hour period. Furthermore, the solution still gave a strong test for presence of chloramine. Only after the addition of aqueous sodium hydroxide to the ether–methylamine–chloramine solution could the formation of methylhydrazine be demonstrated.

Methylhydrazine Sulfate.—Methylhydrazine was isolated and analyzed as methylhydrazine hydrogen sulfate. The reaction mixture containing methylhydrazine was fractionated in an atmosphere of oxygen-free nitrogen. Methylhydrazine was found to concentrate in the final portions of the distillate, indicating the formation of a maximum boiling azeotrope. In a typical run, the final 25 ml. of distillate containing 1.10 g. of methylhydrazine was recovered from the fractionation of 280 ml. of a solution containing 1.17 g. of methylhydrazine. The aqueous solution of methylhydrazine was neutralized with 50 ml.

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(17) Solutions of sodium hypochlorite invariably contained an excess of sodium hydroxide. They were analyzed for their hydroxide content by a *p*H titration with 0.100 *N* hydrochloric acid. The first break in the *p*H curve, occurring at *p*H 10.5–10.1, is equivalent to the amount of hydroxide present in the hypochlorite. Solutions of 1.15 *M* sodium hypochlorite that were 0.05, 0.5 and 1.5 *M* in sodium hydroxide were used in a series of comparative experiments for preparation of chloramine. It was found that the amount of excess sodium hydroxide present in the hypochlorite had no effect on the yield of methylhydrazine. It is entirely possible that presence of a strongly basic amine in aqueous solution makes addition of a "permanent base" unnecessary.

TABLE I

MONOALKYL HYDRAZINE HYDROGEN SULFATES

$RN_2H_3 \cdot H_2SO_4$ R	Yield,[a] %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
CH_3	64	142	$CH_6N_2 \cdot H_2SO_4$[8]	8.33	8.41	5.59	5.69	19.43	19.52
C_2H_5	67	125	$C_2H_8N_2 \cdot H_2SO_4$	15.19	15.32	6.37	6.60	17.71	17.90
n-C_3H_7	62	122	$C_3H_{10}N_2 \cdot H_2SO_4$	20.92	20.85	7.02	7.10	16.27	16.08
i-C_3H_7	55	68	$C_3H_{10}N_2 \cdot H_2SO_4$	20.92	21.41	7.02	7.04	16.27	16.33
n-C_4H_9	68	141	$C_4H_{12}N_2 \cdot H_2SO_4$	25.80	25.73	7.60	7.59	15.04	15.08
i-C_4H_9	59	145	$C_4H_{12}N_2 \cdot H_2SO_4$	25.80	25.56	7.60	7.66	15.04	15.03
t-C_4H_9[b]	71	187	$C_4H_{12}N_2 \cdot HCl$[c]	38.61	38.45	10.45	10.44	22.48	22.73

[a] Based upon the amount of chloramine. [b] *t*-Butylhydrazine was isolated as the hydrochloride, since *t*-butylhydrazine sulfate was found to be so hygroscopic that is could not be prepared in a satisfactory crystalline form for analysis. [c] Reported by O. Westphal, *Ber.*, **74B**, 759 (1941).

of 1.0 *N* sulfuric acid and evaporated to a small volume. Methylhydrazine sulfate separated upon cooling; it was recrystallized from 80% ethanol. See Table I for analytical data.

Preparation of Alkyl Hydrazines.—To further study the applicability of the chloramine–amine reaction, a series of monoalkyl hydrazines was prepared from chloramine and the corresponding amines. The procedure was analogous to that used in preparation of methylhydrazine. An excess of the alkylamine, *ca.* 8:1, was added to a cold solution of chloramine in the presence of gelatin and the reaction mixture stirred at 0°. The solution was allowed to warm to room temperature over a two-hour period and subsequently analyzed for its alkyl hydrazine content. In the preparation of isobutylhydrazine and *t*-butylhydrazine it was necessary to warm the reaction mixtures upon a steam-bath for an additional 10 minutes to effect completion of the reaction. The monoalkyl hydrazine was separated from the excess of the lower-boiling amine by fractionation under nitrogen at atmospheric pressure. The distillate containing the alkyl hydrazine was treated with an excess of sulfuric acid and evaporated to a small volume. The alkyl hydrazine sulfate separated upon the addition of ether. The compounds were recrystallized from a minimum amount of methanol with the addition of ether. The yields, analytical data and melting points of the hydrogen sulfates of the N-substituted hydrazines prepared by a modification of the Raschig synthesis are presented in Table I.

Discussion of Results

It is evident from the data presented graphically in Fig. 1 that an inhibitor, such as gelatin, is necessary in order to obtain good yields of methylhydrazine from chloramine and methylamine. This finding leads to the conclusion that conditions which permit the formation of methylhydrazine from methylamine and chloramine are strikingly similar to those which have been found to affect the yield of hydrazine in the Raschig synthesis. It is known that the gelatin functions to complex and to remove from solution the heavy metal ions, particularly copper, which catalyze a secondary reaction between hydrazine and chloramine. It is therefore quite probable that the yield of alkyl hydrazine is reduced by a reaction between the desired product and chloramine and that such a reaction is subject to metal ion catalysis. This problem is being subjected to further study.

The methylamine–chloramine ratio necessary for maximum yields of methylhydrazine is much smaller than the ammonia–chloramine ratio required to achieve good yields of hydrazine (see Fig. 2). Yields of methylhydrazine in excess of 60% may be realized with methylamine–chloramine ratios as small as 5:1, the yield being essentially constant even with larger excesses of methylamine. This is in striking contrast to the twenty-fold excess of ammonia needed to obtain hydrazine in satisfactory yields.

It has previously been demonstrated that the presence of a permanent base, such as sodium hydroxide, is necessary for the realization of substantial yields of hydrazine from ammonia and hypochlorite. Only in alkaline solution does chloramine react with ammonia to produce hydrazine. Although methylamine (pK_b 3.36) is a stronger base than ammonia (pK_b 4.74) the presence of permanent base would appear to be necessary for the formation of methylhydrazine from chloramine and methylamine. It is significant that the reaction between chloramine and methylamine in anhydrous ether takes place slowly, if at all; this is in agreement with earlier observations by Wiberg and Schmidt[18] to the effect that chloramine and ammonia do not react in ether solution, but some hydrazine is formed when such mixtures are brought in contact with water.

The reaction of methylamine with chloramine takes place more rapidly than does the reaction leading to formation of hydrazine. Methylhydrazine forms rapidly even at 0°; at room temperature the reaction is essentially complete in 20 minutes. Substantial yields of hydrazine are formed only after heating ammonia–hypochlorite solutions to temperatures above 60°. It would appear on the basis of evidence presented thus far that substances more basic than ammonia will react with chloramine more rapidly than will ammonia itself.

The experimental material presented in this paper suggests that the mechanism advanced for the Raschig synthesis involving the chloramide ion with transient formation of the imide molecule is consistent with the facts and has already served a useful purpose in pointing the way to a new and technically important procedure for the synthesis of a wide variety of substituted hydrazines.

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