Discussion

The data obtained from these reactions may be regarded as further substantiating the condensation theory of vesicant action, but they entirely eliminate thiazane formation as an important factor and appear to demand a new limitation, that of a reactive halogen on the beta carbon atom. That the formation of ring compounds of the thiazane type is not essential is demonstrated by the reaction of mono-halogen substituted alkyl sulfides and of bis-(β-chloropropyl) sulfide with benzylamine to form open-chain derivatives. The limitation to a reactive halogen attached to the beta carbon atom appears necessary in view of the condensation of both bis-(chloromethyl) sulfide and of ethyl γ-chloropropyl sulfide with benzylamine. Neither of these compounds is vesicant, yet both undergo reaction with amino compounds of the type of benzylamine.

The author is exceedingly grateful to Dr. Walter E. Lawson, who offered much valuable assistance during the course of this work.

Summary

1. The preparation of ethyl allyl sulfide and fifteen halogen substituted aryl, alkyl and di-alkyl sulfides is described, three of which have not previously been recorded in the literature.

2. The viscosity and the density of each have been determined.

3. The preparation of a new series of benzylaminoaryl, alkyl and dialkyl sulfides together with their hydrochlorides is described.

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RECEIVED NOVEMBER 18, 1932
PUBLISHED MAY 6, 1933

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE STATE UNIVERSITY OF IOWA]

The Reaction of Monobromoamine with Grignard Reagents

BY GEORGE H. COLEMAN, HAROLD SOROOS AND CHARLES B. YAGER

Previous work in this Laboratory has shown that monochloroamine reacts with Grignard reagents to form primary amines and ammonia.[1]

The present investigation was prompted by the thought that monobromoamine should undergo a reaction with Grignard reagents similar to that of monochloramine and that a comparison of the results obtained in the two cases would be of interest.

Monobromoamine has been prepared by Moldenhauer and Burger[2] by the reaction of ammonia with bromine in ether solution at 0°. The reaction is represented by the equation

$$2NH_3 + Br_2 = NH_2Br + NH_4Br \qquad (1)$$

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[1] Coleman and Hauser, THIS JOURNAL, **50**, 1193 (1928); Coleman and Yager, *ibid.*, **51**, 567 (1929).

[2] Moldenhauer and Burger, *Ber.*, **62**, 1615 (1929).

No direct analysis of the ethereal solution of the monobromoamine for nitrogen and bromine is given.

Attempts to adapt this method to the preparation of ethereal solutions of monobromoamine led at first to products in which the bromine to nitrogen ratio was considerably greater than 1.0.

Owing to the instability of the bromoamine solution at 0°, the monobromoamine was prepared at the temperature of solid carbon dioxide in an apparatus illustrated in Fig. 1. By using a large excess of ammonia over that required by equation 1, products with a bromine to nitrogen ratio of about 1.2 were obtained. The analysis indicates that a little dibromoamine is formed at the same time, which would account in part for the excess of bromine over nitrogen after the removal of the excess of ammonia. Decomposition of some of the monobromoamine by the use of calcium chloride for removing excess of ammonia would also increase the bromine to nitrogen ratio.

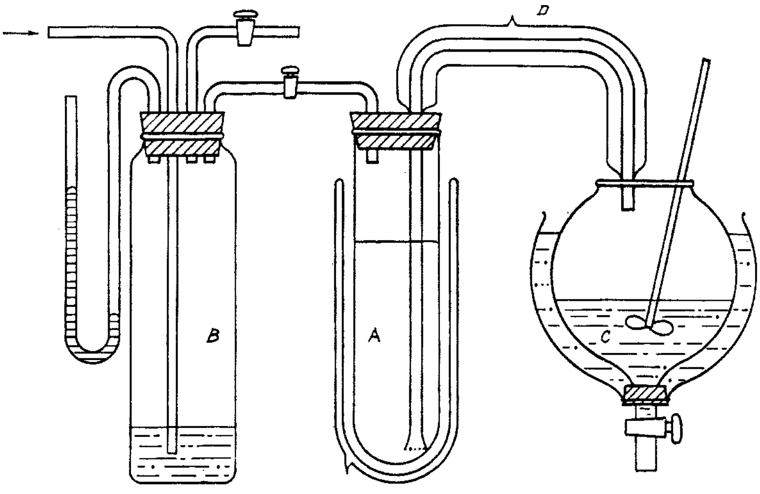

Fig. 1.—Apparatus for the preparation of monobromoamine.

The addition of a few cubic centimeters of cyclohexene to the ether solution of the bromine and ammonia just after mixing yielded a product with a bromine to nitrogen ratio only slightly above 1.0.

The reaction of monobromoamine with Grignard reagents is similar to that of monochloroamine in that primary amines and ammonia are formed. The formation of these products may be represented by the equations

$$NH_2Br + RMgX = RNH_2 + MgXBr \qquad (2)$$

$$NH_2Br + RMgX = RBr + MgXNH_2 \qquad (3)$$

The reaction differs from that of monochloroamine in that lower yields of amines and higher yields of ammonia are usually obtained, and in that an appreciable amount of nitrogen is liberated during the reaction.

In the case of monochloroamine only a negligible quantity of nitrogen is formed.

The results obtained with ten Grignard reagents are given in Table I.

Table I

Percentage Yield of Amines, Ammonia and Nitrogen from Monobromoamine and Grignard Reagents

Reagents	RNH_2	NH_3	N_2	Total	Reagents	RNH_2	NH_3	N_2	Total
n-C_4H_9MgCl	29	64	15	108	t-C_4H_9MgBr	8	78	12	98
n-C_4H_9MgBr	9	78	7	94	t-C_4H_9MgI	5	85	3	93
n-C_4H_9MgI	3	89	8	100	$C_6H_5CH_2MgCl$	63	30	12	105
s-C_4H_9MgCl	46	42	15	103	$C_6H_5C_2H_4MgCl$	34	51	6	91
t-C_4H_9MgCl	45	22	5	72	C_6H_5MgCl	4	85	11	100

The percentage yields are calculated on the basis of the nitrogen content of the bromoamine solutions. An excess of the Grignard reagent was always used. The fact that the sum of the percentage yields differs from 100% in most cases is probably due to experimental error. The greatest error doubtless occurs in the estimation of the nitrogen gas evolved.

The variation in yields of amines with reagents prepared from chlorides, bromides and iodides which is characteristic of monochloroamine was also observed in this work. The yields of primary amines obtained both in this work and in that with monochloroamine from Grignard reagents containing the same halogen, are, with one or two possible exceptions, in the same order as the relative electronegativities of the respective radicals as given by Kharasch and Flenner.[3]

The formation of ammonia in the reaction of monochloroamine or monobromoamine with Grignard reagents is essentially a reduction. It was thought that there might be a connection between the amount of ammonia formed in these reactions and the per cent. of dialkylmagnesium in the Grignard reagents. A comparison of the percentages of dialkylmagnesium in several Grignard reagents as given by Noller and Hilman[4] with the yields of ammonia obtained in this work and in that with monochloroamine shows, however, no significant relationships.

Experimental

Preparation of Monobromoamine.—About 300 cc. of anhydrous ether was placed in a tube of 700 cc. capacity and cooled to −60° by placing the tube in a Dewar flask containing a mixture of solid carbon dioxide and acetone. The calculated quantity of ammonia gas and about 50% excess required to react with 2 cc. of bromine was allowed to pass slowly into the cold ether. Two cc. of bromine was dissolved in 250 cc. of anhydrous ether in another tube cooled to −60°. The latter solution was then allowed to drop from a separatory funnel into the ethereal ammonia solution at the rate of about 3 cc. per minute. The reaction mixture was stirred continuously. After the addition of the ethereal bromine solution 2 cc. of cyclohexene was added.

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(3) Kharasch and Flenner, This Journal, **54**, 674 (1932).

(4) Noller and Hilman, *ibid.*, **54**, 2503 (1932).

The apparatus used to separate the solid ammonium bromide and excess ammonia from the ether solution of monobromoamine is illustrated in Fig. 1. Tube A containing the reaction mixture was surrounded by solid carbon dioxide and acetone. The separatory funnel C, containing a calcium chloride solution (sp. gr. 1.20), was fitted with an outer jacket. The calcium chloride solution was cooled to −25° by placing acetone in the outer jacket and adding carbon dioxide until the desired temperature was reached. For transferring the cold ether solution of monobromoamine use was made of the vacuum jacketed tube D. The lower end of this tube which extended nearly to the bottom of tube A was enlarged and perforated. A filter paper was tied over the end. Air pressure was applied to the surface of the reaction mixture by allowing water to run into the bottle B. During the addition of the reaction mixture, the calcium chloride solution was agitated vigorously by means of a mechanical stirrer and the stirring was continued for about one-half minute after all the solution had been added. The stirring was then stopped and as soon as the two layers had separated the aqueous layer was withdrawn. The ether solution of monobromoamine was collected in a cold graduated tube and cooled to −60° to cause the separation of any water in the form of ice. Ether solutions prepared by this method contained from 14 to 18 mg. moles of monobromoamine in 350 cc. of solution.

Analysis of the Monobromoamine Solution.—A filter paper was tied over one end of a large glass tube which after having been cooled in ether at −60° was lowered into the monobromoamine solution. When a sufficient quantity of the pale straw colored solution had filtered into the tube, 5-cc. samples were withdrawn with a previously cooled pipet. For the determination of nitrogen a sample was added to 15 cc. of cold concentrated hydrochloric acid. The small flask containing the sample was allowed to stand until the color of the bromine, which was formed at first, disappeared. Excess sodium hydroxide was then added and the ammonia determined by distillation into standard acid. For the determination of bromine a sample was added to excess cold sodium sulfite solution. After completion of the reaction, the ether was removed by gentle heating and the solution acidified with dilute nitric acid. The excess sulfite was oxidized with potassium permanganate and the bromine determined by the Volhard method. The results of a number of determinations showed that the ratio of bromine to nitrogen was only slightly greater than 1.

Preparation of the Grignard Reagents.—The methods used in the preparation and analysis of the Grignard reagents were essentially those described by Gilman and his co-workers.[5]

Reaction of Monobromoamine with Grignard Reagents.—The apparatus used is represented in Fig. 2. The Grignard reagent was prepared in the two-liter flask C, equipped with a mechanical stirrer and mercury seal. The monobromoamine was contained in the tube A surrounded by a mixture of solid carbon dioxide and acetone. For transferring the cold ether solution of monobromoamine, use was made of the vacuum jacketed tube D described above. A filter paper was tied over the end to prevent ice from entering the reaction flask. In order to determine the volume of monobromoamine solution added to the Grignard reagent, the tube A was graduated and the level of the solution in it was noted before and after the transfer to the reaction flask.

The flask containing the Grignard reagent was cooled to 0° by means of an ice-bath, the vacuum jacketed tube was attached and connection was made to the gasometer E; the reaction flask was then cooled to −5°. Water was allowed to flow into the bottle, forcing the clear straw colored monobromoamine solution into the reaction flask. The flow of water was so regulated that about one hour was required for the addition of the monobromoamine solution. When air bubbles appeared in the vacuum jacketed tube,

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[5] Gilman, Wilkinson, Fishel and Meyers, THIS JOURNAL, **45**, 150 (1923); Gilman and Meyers, *ibid.*, **45**, 159 (1923); Gilman and Zoellner, *ibid.*, **50**, 425 (1928).

the addition was stopped, the reaction mixture was warmed very slowly to 0° and the total volume of gas collected was noted.

The temperature in the reaction flask usually rose 2 or 3° during the addition. When the ether solution of monobromoamine came in contact with the Grignard reagent, a vigorous reaction took place with the formation of a precipitate which was white in the case of the chlorides and bromides. A brown coloration appeared immediately upon the addition of monobromoamine to the iodides.

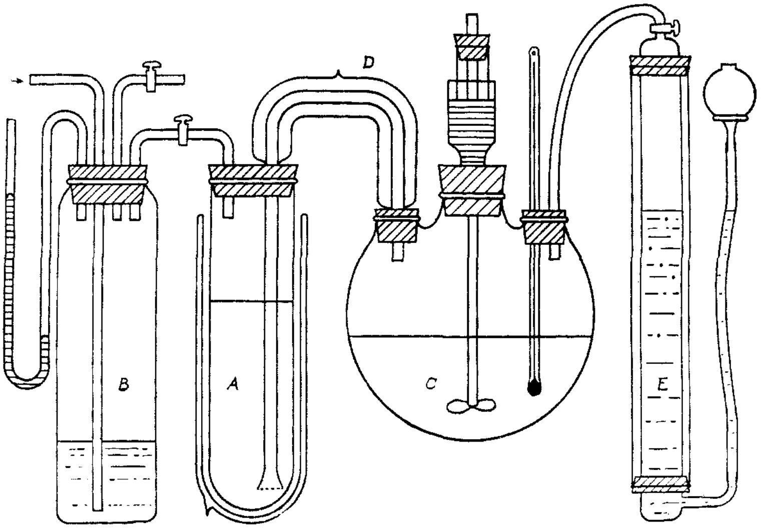

Fig. 2.—Apparatus for reaction of monobromoamine with Grignard reagents.

In order to determine the volume of nitrogen evolved during the reaction a blank run was made using a typical Grignard reagent and a solution of bromine in ether under the same experimental conditions as described above. The volume of nitrogen evolved in a run was determined by difference. It was found advisable to introduce a wash bottle containing a little concd. sulfuric acid between the reaction flask and the gasometer in order to remove ether vapor from the gas.

After the addition of the monobromoamine solution, the reaction mixture was treated with a slight excess of dilute sulfuric acid. The ether layer was separated and washed with dilute sulfuric acid. The original aqueous layer was combined with the washings, excess alkali was added and the product steam distilled into dilute hydrochloric acid. After evaporation of the distillate to dryness, the amine hydrochloride and ammonium chloride were separated with *n*-butyl alcohol as previously described by Coleman and Hauser.[1] The amine hydrochlorides were obtained in pure form by dissolving them in absolute alcohol and reprecipitating with anhydrous ether.

Summary

Monobromoamine reacts with Grignard reagents to form primary amines, ammonia and nitrogen.

The yields of amines are greatest with organomagnesium chlorides, less with bromides, and least with iodides.

The reaction differs from that of monochloroamine in that lower yields

of amines and higher yields of ammonia are usually obtained, and in that an appreciable amount of nitrogen is liberated during the reaction.

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RECEIVED NOVEMBER 21, 1932
PUBLISHED MAY 6, 1933

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Preparation and Properties of 2,4-Dimethoxyphenyl Alkyl Sulfides[1]

BY C. M. SUTER AND HAROLD L. HANSEN

Since *p*-hydroxyphenyl alkyl sulfides have been found to be active germicides[2] it became of interest to study some analogous dihydroxy compounds. Although the present attempts to prepare 2,4-dihydroxyphenyl alkyl sulfides were unsuccessful the results obtained are of some interest.

Compounds of the type under consideration may obviously be made by alkylation of 2,4-dihydroxythiophenol or of a related derivative which contains groups convertible into hydroxyls. Three possible synthetic methods have been investigated. The action of cold chlorosulfonic acid upon dicarbethoxyresorcinol did not give appreciable amounts of a monosulfonyl chloride which is in contrast to the behavior of carbethoxyphenol[3] with this reagent. A sulfonyl chloride of this type could presumably be reduced to the thiol, alkylated, and the carbethoxy groups removed by hydrolysis. Since thiocyanates can be readily reduced to thiols, direct thiocyanation of resorcinol was attempted according to the method of Kaufmann.[4] No thiocyanoresorcinol could be isolated from the reaction mixture. A non-phenolic compound of unknown structure and a red tar were the only products. The third method of preparation studied involved the demethylation of 2,4-dimethoxyphenyl alkyl sulfides which were prepared by the following series of reactions.

$$(CH_3O)_2C_6H_4 \longrightarrow (CH_3O)_2C_6H_3SO_3K \longrightarrow (CH_3O)_2C_6H_3SO_2Cl \longrightarrow$$
$$(CH_3O)_2C_6H_3{-}SH \longrightarrow (CH_3O)_2C_6H_3{-}S{-}R$$

That the sulfonation product of resorcinol dimethyl ether has the structure indicated was shown by chlorinating it in aqueous solution to the 4,6-dichlororesorcinol dimethyl ether whose structure is known,[5] replacement of the sulfo group by chlorine occurring readily. The 2,4-dimethoxythiophenol has been previously[6] obtained in small amounts as a by-product in the reduction of resorcinol dimethyl ether disulfonyl chloride.

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(1) A portion of a paper presented before the Medicinal Division of the American Chemical Society at the Denver Meeting, August, 1932.

(2) Suter and Hansen, THIS JOURNAL, **54**, 4100 (1932).

(3) Gebauer-Fuelnegg and Schlesinger, *Ber.*, **61**, 781 (1928).

(4) Kaufmann, *ibid.*, **62**, 390 (1929).

(5) Jacobs, Heidelberger and Rolf, THIS JOURNAL, **41**, 463 (1919).

(6) Pollak and Wienerberger, *Monatsh.*, **35**, 1489 (1914).