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ALKYLATION OF PHENYLHYDRAZINE IN LIQUID AMMONIA

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Preliminary experiments had shown that phenylhydrazine is extremely soluble in liquid ammonia and that the resulting solutions react rapidly with alkali metals and alkali amides to give soluble alkali metal derivatives (equations I and II).

$$\text{I.}\qquad C_6H_5N_2H_3 + Na \rightarrow C_6H_5(Na)NNH_2 + \tfrac{1}{2}H_2$$

$$\text{II.}\qquad C_6H_5N_2H_3 + NaNH_2 \rightarrow C_6H_5(Na)NNH_2 + NH_3$$

This immediately suggested that the process of alkylation of phenylhydrazine in liquid ammonia might possess advantages over the conventional procedure which involves heterogeneous reaction between the alkali metal derivative and the alkyl halide in some inert solvent (1). The experimental work outlined in this paper is based upon the results of a study of the reactions of a typical aryl hydrazine, phenylhydrazine, with alkali metals and alkali amides in liquid ammonia, and the subsequent alkylation of these intermediates with alkyl halides to give the unsymmetrical disubstituted α-alkyl arylhydrazines (N,N-alkylphenylhydrazines).

EXPERIMENTAL

1. Reaction of phenylhydrazine with sodium in liquid ammonia. The principal reaction which occurs when sodium is added to a solution of phenylhydrazine is given in equation I. The addition of metallic sodium is accompanied by the rapid evolution of hydrogen and the formation of an orange-yellow solution. As the amount of sodium added approaches that required by the above equation the reaction slows down markedly, so that the blue color of metallic sodium persists for more than a few minutes. Quantities of sodium in excess of that required by the equation can then be added, inducing further reaction and involving reduction to aniline. Thus, if phenylhydrazine is added to a large excess of sodium dissolved in liquid ammonia complete reduction to aniline takes place.[1]

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[1] That the preparation of sodium phenylhydrazine, using only one mole of sodium per mole of phenylhydrazine, involves some simultaneous reduction is furthermore indicated by the fact that the yields of N,N-alkylaryl hydrazine obtainable upon subsequent alkylation are always low, whereas yields approaching theoretical are obtained when the alkali metal compounds are prepared using the metal amides.

In a typical experiment 9.2 g. of sodium (0.4 mole) was dissolved in 500 cc. of liquid ammonia and 10.8 g. (0.1 mole) of phenylhydrazine was added. The solution was allowed to stand for one-half hour, after which the blue color of the excess sodium was discharged by the addition of 2.6 g. (0.0486 mole) of ammonium chloride. This indicates a ratio of approximately 3.5 moles of sodium per mole of phenylhydrazine, somewhat in excess of that required by equation III. The formation of aniline was

$$\text{III.} \qquad C_6H_5N_2H_3 + 3Na \rightarrow C_6H_5NNa_2 + NaNH_2$$

confirmed by isolation of the product and conversion into benzanilide, m.p. 159–160°.

2. Preparation of N,N-ethylphenylhydrazine. (a) Using the sodium-phenylhydrazine procedure. Twenty-seven grams of phenylhydrazine (0.25 mole) was dissolved in 400 cc. of liquid ammonia contained in a transparent one-liter Pyrex Dewar flask. Sodium metal was added in small pieces until the blue color no longer disappeared rapidly. Ethyl bromide (0.25 mole) was then added slowly with continuous agitation to the solution and the mixture allowed to stand until the ammonia had evaporated. The residue left after evaporation was extracted with chloroform and filtered to remove sodium bromide. The extract was dried over anhydrous sodium sulfate and then saturated with dry hydrogen chloride gas. A slight precipitate of phenylhydrazine hydrochloride was removed and the residual solution concentrated to a small volume, treated with ether, and cooled, thus facilitating the precipitation of N,N-ethylphenylhydrazine hydrochloride. After repeated crystallization of the product from chloroform-ether, 12 g. (28%) of the hydrochloride, m.p. 146–147° (2) was obtained.

In a duplicate run the crude hydrochloride was treated with aqueous sodium hydroxide and the N,N-ethylphenylhydrazine was extracted with ether. After removal of the ether, the residue was distilled under reduced pressure and the fraction boiling at 115–119° at 19–21 mm. was collected. For identification, a portion was treated with benzaldehyde yielding the crystalline benzylidene derivative, melting at 46–47°, as compared with the previously recorded melting point of 49° (3).

(b) Using the sodium amide-phenylhydrazine procedure. The method of Vaughn, Vogt, and Nieuwland (4) was used to convert 6.9 g. (0.3 mole) of sodium into sodium amide. To the dark gray suspension of finely divided iron (catalyst) and sodium amide in 500 cc. of liquid ammonia was added slowly 27 g. (0.25 mole) of phenylhydrazine. An excess of ethyl bromide (35 g., 0.32 mole) was then added dropwise. The solution was agitated during the addition of both phenylhydrazine and ethyl bromide. Afther the reaction was completed the ammonia was allowed to evaporate and the residue extracted with ether. The ether solution was washed with water and dried over sodium hydroxide. After removal of the ether the residue was distilled under reduced pressure. The fraction boiling at 120–127° at 25 mm. was redistilled, yielding 30 g. (88%) of pure N,N-ethylphenylhydrazine.

3. Preparation of N,N-benzylphenylhydrazine. (a) Using the sodium-phenylhydrazine method. Phenylhydrazine (27 g., 0.25 mole) was converted into the sodium derivative using metallic sodium. Benzyl chloride (35.4 g., 0.28 mole) was added slowly, after which the reaction mixture was treated as in 2a to give the hydrochloride. A total yield of 24 g. (41%) was obtained, melting at 164–169°. Michaelis and Philips (5) reported the melting poing 167° for this compound. Titration of the hydrochloride with standard base gave a neutral equivalent of 235, in agreement with the theory.

(b) Using the sodium amide-phenylhydrazine method. Sodium phenylhydrazine (0.334 mole), prepared as in 2b, was treated with a slight excess of benzyl chloride to effect alkylation. After purification, 48 g. (73%) of N,N-benzylphenylhydrazine, distilling at 157-159° at 4 mm. was obtained. This material gave an acetyl derivative, m.p. 120–121°, agreeing with that reported previously (5).

4. Preparation of N,N-propylphenylhydrazine. (a) Using the sodium-phenylhydrazine method. Sodium phenylhydrazine, prepared by adding 6 g. (0.26 mole) of sodium to 27 g. (0.25 mole) of phenylhydrazine in 400 cc. of liquid ammonia, was allowed to react with 34 g. (0.27 mole) of propyl bromide. A yield of 13.3 g. (36%) of crude N,N-propylphenylhydrazine, boiling at 120–132° at 20 mm. was recovered from the reaction mixture.

(b) Using the potassium amide-phenylhydrazine method. A solution of 13 g. (0.33 mole) of potassium in liquid ammonia was converted to the amide using a rusty iron wire as the catalyst. Phenylhydrazine (0.25 mole) was added and the resulting orange-yellow solution was treated with 36 g. (0.29 mole) of propyl bromide. Extraction of the residue with ether, subsequent drying, and fractionation gave 35.4 g. (94%) of N,N-propylphenylhydrazine distilling at 122–130° at 20 mm. No lower-boiling fractions were obtained at in the previous case in which the sodium phenylhydrazine was prepared from metallic sodium. The product was characterized by conversion into the hydrochloride, m.p. 135° (6); the benzylidene derivative, m.p. 64°;

Anal. Calc'd for $C_{16}H_{18}N_2$: N, 11.77. Found: N, 11.69; and the *p*-nitrobenzoate, m.p. 153–154°;

Anal. Calc'd for $C_{16}H_{17}N_3O_3$: N, 14.05. Found: N, 14.09.

5. Reduction of N,N-propylphenylhydrazine with sodium in liquid ammonia. The absence of any N′-propyl-N-phenylhydrazine in the product obtained in 4b was confirmed by reduction with excess sodium in liquid ammonia. The N-propyl derivative should yield propylaniline, whereas the N′-propyl derivative should give aniline as one of the products.

Twelve and one-half grams of the product was dissolved in 400 cc. of liquid ammonia and 5 g. of sodium was added. After standing for one hour the solution was decolorized by adding ammonium chloride. The product was isolated in the usual manner and distilled *in vacuo* giving 7.5 g. (69%) of propylaniline boiling at 97–99° at 7 mm. The product was shown to consist exclusively of secondary amine by reaction with *p*-toluenesulfonyl chloride. It was identified by boiling point (micro) 221°, and by conversion (85% yield) to the acetyl derivative, melting at 48–49°.

These observations leave little doubt that alkylation of the alkali metal phenylhydrazine compounds under the given conditions yields only the unsymmetrical α-substituted phenylhydrazines (N,N-alkylphenylhydrazines).

SUMMARY

The alkylation of phenylhydrazine to give the unsymmetrical α-substituted phenylhydrazines (N,N-alkylphenylhydrazines) can be carried out conveniently in liquid ammonia as solvent. The following advantages may be gained by the use of this procedure: 1. The alkali metal phenylhydrazine compounds can be prepared readily by direct reaction of the primary hydrazine with the alkali metal or alkali amide. The latter is preferred in order to avoid reduction. 2. The alkali metal phenylhydrazine compounds and the alkyl halides are soluble in liquid ammonia, thus facilitating complete reaction. The preparation of N-ethyl-, N-benzyl-, N-propyl-, N-phenylhydrazines by this new technique is described.

Cleavage of the N—N bond in primary and unsymmetrical disubstituted hydrazines takes place in liquid ammonia upon treatment with an excess of sodium.

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