

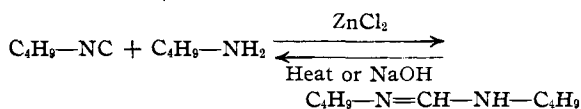
[CONTRIBUTION NO. 154 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Addition of Butylamine to Butyl Isocyanide

BY TENNEY L. DAVIS AND WILLIAM E. YELLAND

Hofmann¹ reported in 1867 that on distilling phenyl isocyanide to free it from aniline he obtained a compound which boiled at 230° and crystallized on cooling. Weith² in 1876 showed that the substance is N,N'-diphenylformamidine, formed by the addition of aniline to phenyl isocyanide, and Nef³ later repeated the experiments, securing a 30% yield of product, and prepared N,N'-di-*o*-tolylformamidine by a similar process. No similar reaction has heretofore been reported in the aliphatic series.

We find that *n*-butylamine combines with *n*-butyl isocyanide to form N,N'-di-*n*-butylformamidine if the two substances are heated together with anhydrous zinc chloride in a sealed tube at 100 to 120°. Bromoform and chloroform heated with an excess of *n*-butylamine yield the same substance along with *n*-butyl isocyanide and unidentified tarry material, and the yields are increased if anhydrous zinc chloride is present in the reaction mixtures. We have isolated the N,N'-di-*n*-butylformamidine in the form of its picrate, and have identified our products by comparison of the picrates with a picrate prepared from N,N'-di-*n*-butylformamidine synthesized by the interaction of *n*-butylamine and *n*-butylformamide in the presence of phosphorus oxychloride. The picrate decomposes to produce perceptible quantities of *n*-butyl isocyanide when it is heated above its melting point, and to produce larger quantities when fused with sodium hydroxide. The combination of the amine and isocyanide to produce the formamidine derivative is therefore a reversible reaction.



Since both the isocyanide and the formamidine derivative are produced by the interaction of the amine with chloroform, and since either of these substances in the reaction mixture may be converted into the other, the evidence leaves us unable to decide which of them, if either, is the first product of the interaction.

(1) Hofmann, *Ann.*, **144**, 119 (1867).

(2) Weith, *Ber.*, **9**, 454 (1876).

(3) Nef, *Ann.*, **270**, 274 (1892).

Experiments

Reaction of Bromoform with *n*-Butylamine.—Ten and one-half grams (0.04 *M*) of 96% bromoform (4% alcohol) was refluxed with 12 g. (0.16 *M*) of *n*-butylamine in a flask sealed to a condenser equipped with a drying tube. After half an hour the mixture began to turn yellow, and after twenty-one hours it was light brown in color. The mixture, which had a very strong isocyanide odor, was diluted with 100 cc. of water, acidified slightly, filtered for the removal of a small quantity of tar, and extracted with chloroform for the removal of a further amount. The aqueous solution was treated with an excess of a saturated water solution of picric acid. After chilling, the yellow precipitate was removed, dissolved in warm methyl alcohol and recrystallized by adding water and allowing to evaporate spontaneously: yield 0.5 g., identified as N,N'-di-*n*-butylformamidine by melting point and by mixed melting point with a known sample.

Preparation of *n*-Butyl Isocyanide.—The refluxing together of *n*-butylamine, chloroform, and aqueous sodium hydroxide gave a powerful isocyanide odor, but apparently very poor yields of the material, and we have not been able to obtain better than a 5% yield by this process. The reaction of silver cyanide with *n*-butyl iodide was found to provide a much better method of preparation.

Seventy-five grams (0.56 *M*) of dry silver cyanide and 51.5 g. (0.28 *M*) of *n*-butyl iodide were heated together under reflux for an hour and a half in an oil-bath at 125–130°. The mixture became a sticky brown mass. After cooling, it was treated with enough aqueous potassium cyanide solution (80 g. of cyanide in 400 cc. of water) to cause all solid matter to go into solution. The oil which separated was collected and dried with anhydrous sodium sulfate; it amounted to about 10 g. (40% yield) of crude isocyanide. On fractionation through a small Vigreux column it yielded about 8 g. of *n*-butyl isocyanide, b. p. 124–125° at 761.5 mm. Analysis for nitrogen: found 16.31, 16.82%; calcd. 16.86%.

n-Butyl isocyanide proved to be so disagreeable to manipulate that none of its physical constants except boiling point were determined. Even when a hood with an extra forced draft was used, the odor pervaded the laboratory and adjoining rooms, deadening the sense of smell and producing in the operator, and in others, severe headaches and nausea which usually persisted for several days.

Effect of Zinc Chloride.—Sealed tubes containing, respectively: I, 1 g. (0.0120 *M*) of *n*-butyl isocyanide and 1.7 g. (0.0233 *M*) of *n*-butylamine; II, 1 g. (0.0120 *M*) of *n*-butyl isocyanide, 0.9 g. (0.0123 *M*) of *n*-butylamine and 1.7 g. (0.0109 *M*) of *n*-butylamine hydrochloride; III, 1 g. (0.0120 *M*) of *n*-butyl isocyanide, 1.7 g. (0.0233 *M*) of *n*-butylamine and 0.15 g. (0.011 *M*) of freshly fused and powdered zinc chloride; and IV, 5 g. (0.0849 *M*) of *n*-butylamine, 3 g. (0.025 *M*) of chloroform and 0.31 g. (0.0028 *M*) of zinc chloride were heated at 100–105° for

twenty-four hours. When the tubes were opened, all of them except III were found to have strong isocyanide odors. The liquid in III had become very viscous. The contents of I and II were transferred to new tubes each containing 1.6 g. of freshly fused zinc chloride and the tubes were sealed, IV was resealed, and the three tubes were heated again for twenty-four hours. At the end of that time all of the tubes contained viscous liquids none of which smelled of isocyanide. Many experiments were carried out in order to isolate the products of these reactions. Those described below are typical of our best results.

Reaction of Chloroform with *n*-Butylamine in the Presence of Zinc Chloride.—Six grams (0.05 *M*) of chloroform, 20 g. (0.27 *M*) of *n*-butylamine and 0.5 g. (0.004 *M*) of freshly fused and powdered zinc chloride were sealed together in a Pyrex tube and heated at 115–120° for one hundred and sixty-eight hours. On cooling, the contents of the tube solidified to a mass of transparent waxy crystals in a brown oil. Earlier experiments had shown that both the crystals and the oil contained zinc chloride and the hydrochlorides of butylamine and dibutylformamidine. The contents of the tube was accordingly treated with water enough to dissolve the crystals (15 cc.) and with a saturated solution of ammonium picrate until no further precipitation occurred. The filtrate from the precipitate on slow evaporation yielded crystals of *n*-butylamine picrate, m. p. 141–144°. The yellow precipitate, rinsed with water and washed with warm alcohol until no more dissolved, left a residue of zinc picrate which was discarded. The alcohol extract, on evaporation to a small volume and dilution with water, yielded yellow crystals of the crude picrate, about 5 g., and these, dissolved in warm alcohol and recrystallized by the addition of water, yielded pure *N,N'*-di-*n*-butylformamidine picrate, about 2 g. (10%), identified by melting point and by mixed melting point with a known sample.

Reaction of *n*-Butyl Isocyanide with *n*-Butylamine in the Presence of Zinc Chloride.—One gram (0.0120 *M*) of *n*-butyl isocyanide, 1.7 g. (0.0233 *M*) of *n*-butylamine and 0.1 g. (0.00073 *M*) of freshly fused and powdered zinc chloride, heated in a sealed tube for sixteen hours at 105–110°, and worked up as described for the preceding experi-

ment, yielded 0.9 g. (18.4%) of pure *N,N'*-di-*n*-butylformamidine picrate, identified by melting point and by mixed melting point with a known sample.

Preparation of *N,N'*-Di-*n*-Butylformamidine. *n*-Butylformamide was prepared by mixing 14.6 g. (0.2 *M*) of *n*-butylamine and 25 g. (0.435 *M*) of formic acid, sp. gr. 1.20, refluxing gently for thirty minutes, distilling and fractionating: yield 14 g. (70%), b. p. 124–126°. Analysis for nitrogen: found 13.8, 14.2%; calcd. 13.98%.

Five grams (0.05 *M*) of *n*-butylformamide and 6 g. (0.059 *M*) of *n*-butylamine hydrochloride were made into a paste which was cooled while 15 g. (0.1 *M*) of phosphorus oxychloride was added rapidly with stirring. A vigorous reaction ensued and an isocyanide odor was evolved. The mixture was warmed cautiously for a few minutes until it turned dark orange, then cooled and treated with a saturated solution of ammonium picrate until no further precipitation occurred. The precipitate was a brownish oil which solidified in the ice box to a sticky mass. This, worked up by dissolving in warm alcohol and recrystallizing by the addition of water, yielded 0.2 g. of pure *N,N'*-di-*n*-butylformamidine picrate, bright yellow transparent prisms and needles, m. p. 114.5–116.5°. Analysis for nitrogen: found 18.03, 18.09%; calcd. 18.18%.

Summary

n-Butylamine combines with *n*-butyl isocyanide in the presence of zinc chloride to form *N,N'*-di-*n*-butylformamidine.

The picrate of this substance, heated above its melting point or fused with sodium hydroxide, breaks down to form *n*-butyl isocyanide.

Chloroform reacts with an excess of *n*-butylamine to form both *n*-butyl isocyanide and *N,N'*-di-*n*-butylformamidine, either one of which may be the primary product, but the latter substance results exclusively if zinc chloride is present and if the heating is continued sufficiently.

CAMBRIDGE, MASS.

RECEIVED AUGUST 7, 1937