

uct. The latter method worked very well with γ -allylaminopropanol and γ -amylaminopropanol but was not very good for γ -methylaminopropanol and β -allylamino-ethanol, due to their great solubility in water. In all cases better yields would be obtained by working with larger amounts.

All of the amino alcohols were colorless liquids when freshly prepared but darkened on standing. All had a characteristic odor. All were soluble in water, alcohol, ether, chloroform, ethyl acetate and acetone. The solubility in water decreased with increase in molecular weight, for, although all dissolved readily, amylaminopropanol was salted out readily with potassium carbonate, allylaminopropanol was salted out a little less readily and methylaminopropanol and allylamino-ethanol could scarcely be salted out. In carbon disulfide and petroleum ether amylaminopropanol was readily soluble, while the lower molecular weight amino alcohols went into solution with difficulty.

Summary

1. Allylamine was condensed with β -chloro-ethylchloroformate to yield β -chloro-ethylallyl carbamate. The latter compound, refluxed with 1.5 moles of alcoholic potash, yielded 3-allyl-2-oxazolidone, and with 4 moles of alcoholic potash, yielded β -allylamino-ethanol.

2. Allyl-, methyl-, and *n*-amylamines condensed with γ -chloropropylchloroformate to yield the corresponding γ -chloropropyl alkyl carbamates. These carbamates, refluxed with 4 moles of alcoholic potash, yielded the corresponding γ -alkyl aminopropanols.

GEORGETOWN, KENTUCKY

[CONTRIBUTION FROM THE GATES CHEMICAL LABORATORY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 156]

THE PREPARATION OF 2-BROMO-*p*-CRESOL FROM *p*-NITROTOLUENE

BY HOWARD J. LUCAS AND NATHAN F. SCUDDER

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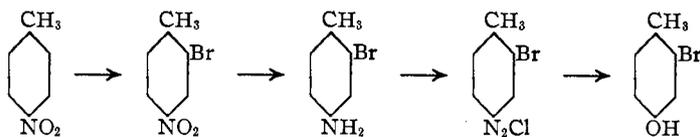
The usefulness of 2-bromo-*p*-cresol in standardizing bromide-bromate solutions¹ makes desirable a convenient method of preparation. It has been obtained from 2-amino-*p*-cresol through the diazo reaction² and its use as a dye intermediate has been suggested.³

In this work it has been found that the desired compound may be conveniently obtained in satisfactory yield from *p*-nitrotoluene by the following operations.

¹ Buxton and Lucas, *THIS JOURNAL*, **50**, 249 (1928).

² Plummer, Melamed and Puttfarcken, *Ber.*, **55B**, 3116 (1922).

³ D. R. P. 156,333; *Chem. Cent.*, **1904**, II, 1673.



Bromination of *p*-Nitrotoluene

In the usual method of brominating *p*-nitrotoluene⁴ the materials, including iron bromide, are sealed in a tube and heated to 170°. We have found that, using iron filings as the source of the iron bromide, the reaction proceeds with moderate rapidity at 50–60° and, although some bromine is lost in the process, the yield obtained is satisfactory.

To 300 g. (2.2 moles) of *p*-nitrotoluene (Eastman) and 10 g. of iron filings in a flask fitted with a return cooler is slowly added 370 g. (2.3 moles) of cold bromine. The flask is surrounded by an ice-bath in order to moderate the reaction, which is quite rapid at first and continues vigorously for about one hour. The next day it is slowly heated by means of a warm water-bath and finally to 150° by means of an oil-bath until the evolution of hydrogen bromide ceases. This requires about three hours.

The mass, after cooling, is shaken with an aqueous solution of sodium bisulfite, in order to remove hydrogen bromide and unchanged bromine, and then leached out with cold alcohol in order to remove any unchanged nitrotoluene. Crystallization from hot alcohol gave 358 g. of 2-bromo-4-nitrotoluene (76% yield). Although the yield is lower than that obtained by Scheufelen,⁴ the superiority of this method lies in the greater convenience and saving of time.⁵

Reduction of 2-Bromo-4-Nitrotoluene

Although 2-bromo-4-aminotoluene has been prepared in other ways,^{5,6} the reduction of the corresponding nitro compound seems to be the most practicable. Neville and Winther⁷ reduced with tin and hydrochloric acid, while Blanksma⁵ reduced with sodium bisulfide in alcohol solution, obtaining not only the expected bromotoluidine but also 2-bromo-4-amino-benzaldehyde. In this work ammonium sulfide in alcohol was used as the reducing agent and gave a satisfactory yield (85%) of the expected amine, which was easily purified from a small amount of another substance which may have been the compound observed by Blanksma. The following method was employed. An alcoholic solution of ammonium sulfide was prepared by passing anhydrous ammonia into 1 liter of alcohol until the gain in weight was 108 g. (6.35 moles), followed by hydrogen sulfide until no more was absorbed, 90 g. (2.65 moles). When about half of the hydrogen sulfide had been added, white plate-like crystals came

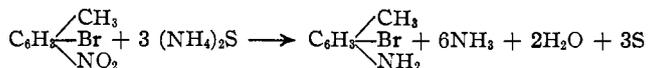
⁴ Scheufelen, *Ann.*, **231**, 171 (1885); Cohen and Dutt, *J. Chem. Soc.*, **105**, 505 (1914); a 94% yield is claimed.

⁵ The desired compound may also be obtained from 2-amino-4-nitrotoluene by the Sandmeyer method, Blanksma, *Chem. Weekblad*, **6**, 899 (1909).

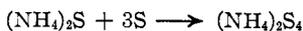
⁶ Hafner, *Ber.*, **22**, 2903 (1899), obtained 2-bromo-4-aminotoluene along with some of the 3-isomer by brominating the sulfate of *p*-toluidine.

⁷ Neville and Winther, *ibid.*, **14**, 418 (1891). No yield is given.

down and by the time saturation was reached the mixture had become mushy due to the separation of ammonium sulfide. The amount of 2-bromo-4-nitrotoluene, 150 g. (0.66 mole), was so chosen that there would be about 30% excess⁸ of ammonium sulfide needed for the reduction according to the equation



The unchanged ammonium sulfide (30%) would react with the sulfur to form the poly-sulfide, as follows



The characteristic brown color of the polysulfide which develops as the operation proceeds is useful in indicating the extent of the reaction. Soon after mixing there was a small heating effect which was taken care of by placing the flask in an ice-bath. At first the color of the solution was unaffected but later on it changed rapidly from yellow to red-brown. After standing overnight the flask was heated on a steam-bath under a reflux condenser in order to drive out the ammonium sulfide, which was absorbed by another portion of alcohol preparatory for a subsequent run. By passing a slow stream of air through the system the troublesome condensation of solid ammonium sulfide in the condenser could be avoided. After heating for some hours, the ammonium sulfide was largely removed from the alcoholic liquid, which had lost all but a trace of the brown color and was mixed with much precipitated sulfur. The liquid was filtered hot to remove sulfur and then the alcohol was evaporated on the steam-bath to small volume, leaving a brown oil.⁹ The oil was heated with sufficient 6 *N* hydrochloric acid to dissolve it hot; the resulting solution was filtered from a small amount of sulfur and allowed to cool. Long, slender crystals having a pale brown tint separated, weight 130 g. Evaporation of the filtrate to small volume and cooling gave a small amount of yellow amorphous solid but no crystals. The yield of the hydrochloride of 2-bromo-4-aminotoluene is 84%.

This salt was obtained in fine, snow-white needles by crystallizing 25 g. from hot absolute alcohol (300 cc.) in which dry hydrogen chloride was dissolved. After washing with absolute alcohol, the crystals were dried for thirty-six hours in a vacuum desiccator containing both concentrated sulfuric acid and solid sodium hydroxide. Two analyses for chloride ion by precipitation as silver chloride gave 15.95 and 15.97%; the theoretical is 15.94%. The melting point in a sealed tube was 271°.

Treatment of the purified salt with concentrated ammonium hydroxide

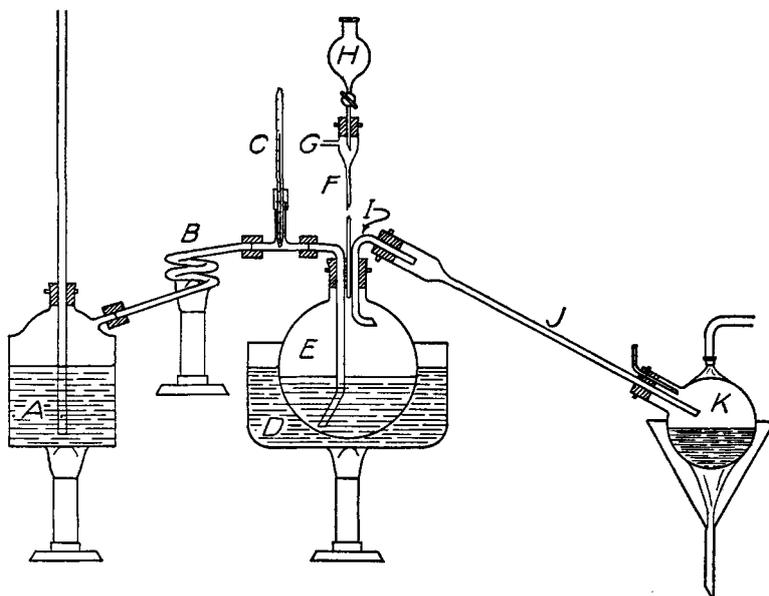
⁸ With 100% excess of ammonium sulfide the yield was much lower (56%).

⁹ A more convenient method of working up the reaction mixture would consist in distilling off alcohol and ammonium sulfide together, leaving behind the crude amine.

gave the free base, which after drying over solid sodium hydroxide was slightly brown in color and melted at 27.3–27.5° (corr.).

2-Bromo-*p*-Cresol from the Amine

Attempts to convert the amine into the corresponding hydroxyl compound by the usual method of heating the diazotized solution of the amine led to the formation of much tar, from which only small amounts of the cresol could be extracted. However, by heating the diazo solution rapidly and distilling out the product as soon as it formed, a satisfactory yield



A, Steam generator; B, steam heater; C, thermometer; D, oil-bath, 130–140°; E, balloon flask, 3 liter; F, tube, internal diameter 2 mm., length 30–40 cm.; G, side arm for compressed air; H, container for diazotized amine; I, exit tube, internal diameter 10–12 mm.; J, condenser tube, length 60 cm.; K, flask, 2 liter, cooled by water.

Fig. 1.—Apparatus for converting diazotized bromotoluidine into bromocresol.

was obtained. This was accomplished in the apparatus shown in the figure by the following method. The hydrochloride of the amine, 90 g. (0.4 mole), was dissolved in a hot solution of 55 cc. of concentrated hydrochloric acid and 350 cc. of water. This was cooled to 2–3° and diazotized with a solution of 31 g. of sodium nitrate (5% excess) in 120 cc. of water in the usual way. To the diazotized solution, now about 500 cc., was added 150 cc. of cold, dilute sulfuric acid (approximately 65%, from equal volumes of acid and water), keeping the temperature at all times below 8°. This cold, diazotized solution was placed in the dropping funnel H, and introduced rapidly in portions of 10–15 cc. into the flask

E which contained a hot mixture of 750 g. of anhydrous sodium sulfate, 300 cc. of concentrated sulfuric acid and 300 cc. of 6 *N* sulfuric acid,¹⁰ and was heated by the oil-bath D kept at 130–140°. Steam heated to 160–180° in the heating coil B was passed into the flask, thus removing the cresol as soon as it formed and preventing a coupling reaction between it and the diazonium salt.

By adding the diazo solution rapidly and blowing off the last few drops from the tube F by a jet of air through G, it cannot become warm and undergo reaction before it enters the flask. The distillate of approximately 600 cc. was shaken twice with about 200 cc. of benzene and the benzene solution then extracted with 1000 cc. of 2 *N* sodium hydroxide. The alkaline solution after filtering and acidifying with sulfuric acid gave an oil which solidified in the ice box overnight. The crude 2-bromo-*p*-cresol was filtered off and after drying in a vacuum desiccator over sulfuric acid weighed 91 g. (yield, 80.5%).

The bromocresol was purified by washing with some cold redistilled petroleum ether, b. p. 40–63°, to remove most of the colored impurity, and then crystallized from another portion, b. p. 40–75°, giving white, silky, slender needles. Since the temperature coefficient of solubility is high, slow cooling was necessary in order to avoid excessive supersaturation and the formation of a liquid instead of the desired solid phase. The first crop when dissolved in petroleum ether gave an almost colorless solution and crystallized out as before. The recrystallized material melted at 55.2–55.4° (corr.) to a colorless liquid.¹¹ By proper evaporation of the filtrate the greater part of the 2-bromo-*p*-cresol is recovered. Thus from a total of 142 g. of crude material there was obtained 131 g. (92% recovery) of the purified cresol. On this basis the best yield of purified 2-bromo-*p*-cresol calculated back to nitrotoluene is 47% for the three operations, whereas that obtained by Plummer² from 2-amino-*p*-cresol through the diazo reaction in one operation was 18.5%.

Analyzed for bromine by the Carius method, 0.2031 g. of 2-bromo-*p*-cresol gave 0.2066 g. of AgBr, and 0.2447 g. gave 0.2457 g. of AgBr, equivalent to 43.3 and 42.7% of bromine, compared to the calculated value of 42.7%.

The cresol is exceedingly soluble in benzene and in methyl, ethyl and propyl alcohols and does not crystallize readily from these solvents. It is readily soluble in ligroin, from which it separates as a liquid phase. Petroleum ether, b. p. 40–75°, is the most satisfactory solvent for purification purposes.

The Benzoate of 2-bromo-*p*-cresol.—This compound was easily obtained from the cresol by the Schotten-Baumann reaction. After treatment with sodium hydroxide solution, followed by two crystallizations from absolute alcohol, it separates in the form of large, white needles melting at 74.6–75.1° (corr.), a value unchanged by further crystallization.

Summary

Starting with *p*-nitrotoluene, 2-bromo-*p*-cresol has been obtained in yields of 47% by the operations of bromination, reduction and replacement of the diazonium group.

¹⁰ A mixture of this composition, which is in reality largely sodium acid sulfate with smaller amounts of sulfuric acid and water, has a boiling point of 135°.

¹¹ Previous observers, Plummer, ref. 2, gave 54–55°, and D. R. P., ref. 3, 55–56°.

Replacement of the diazonium group by hydroxyl is best accomplished by running the diazotized amine into a solution of sulfuric acid and sodium sulfate at 130–140°, and continually distilling out the cresol with superheated steam.

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[CONTRIBUTION FROM THE GATES CHEMICAL LABORATORY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 157]

THE ANALYSIS OF BROMINATED CRESOLS

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Previously described methods which were being employed for analyzing mixtures of brominated cresols were found to be troublesome enough to justify further investigation in the hope that improvements could be made. In the bromide-bromate titration method of Francis and Hill¹ there is, after acidification, a slow reaction between the standard solution and the alcohol used as solvent. In the method of halogen determination proposed by Robertson² the end-point of the final titration is difficult to determine because hydrogen peroxide present in the solution reacts with the thiocyanate.

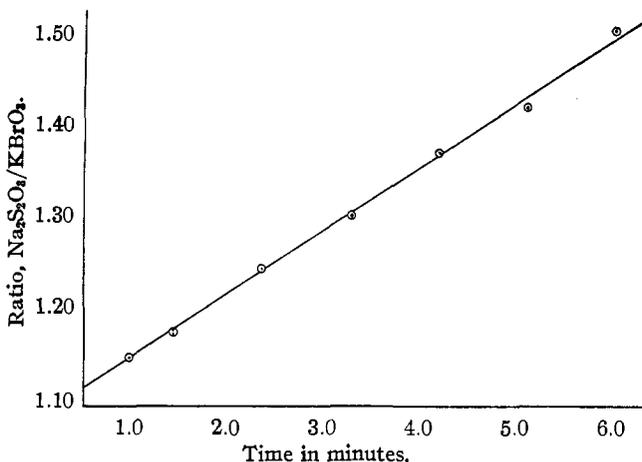


Fig. 1.—Effect of alcohol upon standard bromate solution in 1 *N* H₂SO₄.

The Bromide-Bromate Titration.—In the method of Francis and Hill it was found that the reaction between alcohol and bromate in acid solution decreased the amount of thiosulfate required for back titrations. Fig. 1 shows how the ratio of 0.1005 *N* thiosulfate to 0.091 *N* bromate changes

¹ Francis and Hill, *THIS JOURNAL*, **46**, 2499 (1924).

² Robertson, *J. Chem. Soc.*, 107, 902 (1912).