Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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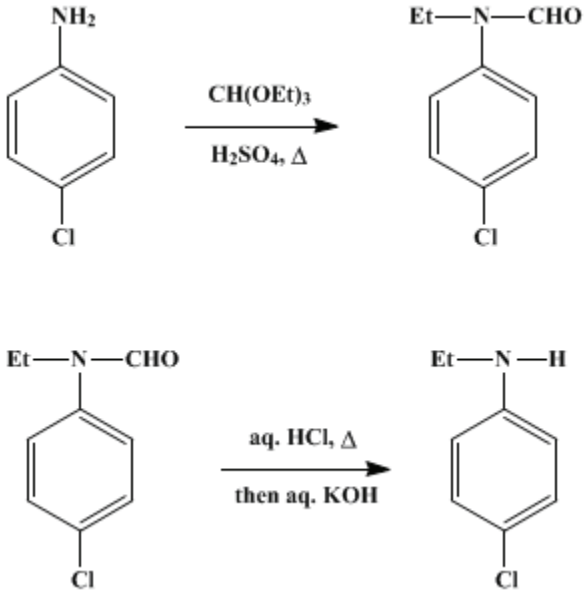
N-ETHYL-*p*-CHLOROANILINE

[Aniline, *p*-chloro-N-ethyl-]



Submitted by Royston M. Roberts and Paul J. Vogt[1].
Checked by James Cason and Milton Finger.

1. Procedure

A. *N-Ethyl-p-chloroformanilide.* In a 300-ml. round-bottomed flask, equipped with a side tubulature just large enough to accommodate a thermometer, are placed 63.8 g. (0.50 mole) of *p*-chloroaniline and 111 g. (0.75 mole) of triethyl orthoformate (Note 1), and then 2.0 g. (0.02 mole) of concentrated sulfuric acid is added with mixing. The flask is attached to a 30-cm. column 2 cm. in diameter packed with glass helices (Note 2), which is surmounted by a distillation head equipped with a thermometer and condenser. A thermometer is connected through a slip joint made from a short section of rubber tubing to the side tubulature so that its bulb is in the reaction mixture; then the flask is heated in an oil bath. When the temperature of the oil bath reaches 115–120°, the reaction mixture begins to boil, and ethanol soon begins to distil at a vapor temperature of 78–80° at the top of the column. During the course of about 1 hour the bath temperature is raised to about 175°. This promotes a steady distillation of ethanol at a rate which begins to decrease after 30 minutes. The amount of ethanol that distils (70–75 ml.) is always in excess of the stoichiometric amount. Finally, the reaction mixture is kept in the oil bath at 175–180° for 30 minutes (Note 3); an additional small amount of volatile material distils during this time.

After the reaction mixture has cooled somewhat the flask is disconnected from the column, a Claisen head is attached, and the product is distilled at reduced pressure (Note 4). After a fore-run of about 20 g. (not readily condensed below 40 mm. pressure), the faintly yellow product is collected at 124–126°/3 mm., weight 73–79 g. (80–86%), n_D^{25} 1.5525–1.5540 (Note 4).

B. *N-Ethyl-p-chloroaniline.* In a 500-ml. round-bottomed flask are placed 70 g. (0.38 mole) of N-ethyl-*p*-chloroformanilide and 170 ml. of 10% hydrochloric acid. The mixture is heated under reflux for 1 hour, cooled, then neutralized, and finally made basic with 15% potassium hydroxide solution. The lower layer of N-ethyl-*p*-chloroaniline is separated, and the aqueous layer is saturated with potassium carbonate and extracted with two 200-ml. portions of ether. The ether extracts are combined with the bulk of the product, washed with two 100-ml. portions of water, and then dried over calcium chloride. After the ether has been removed by distillation, the residue is distilled at reduced pressure from a 125-

ml. Claisen flask. N-Ethyl-*p*-chloroaniline is collected at 108–110°/5 mm. or 149–150°/40 mm., n_D^{25} 1.5650–1.5661, weight 52–55 g. (87–92%) (Note 5).

2. Notes

1. The checkers used, without purification, white label grades of *p*-chloroaniline and triethyl orthoformate from Eastman Organic Chemicals; the submitters used triethyl orthoformate from Kay-Fries Chemicals Inc., New York.
2. It is most convenient to make connections with standard taper joints. The checkers used with equal satisfaction a 50-cm. column randomly packed with short sections of glass tubing.
3. The submitters report that during this heating period the temperature of the reaction mixture may rise as high as 185–190° on account of an exothermic reaction; however, the checkers did not observe this temperature rise of the reaction mixture. The submitters also report that in some of the preparations mentioned in Note 5 the reaction is more exothermic and the temperature may rise as high as 244°, but this does not cause difficulty.
4. The submitters distilled the product through the 30-cm. packed column which was wrapped with a heating tape for this purpose. If this is done, there are collected about 20 g. of recovered triethyl orthoformate at 65–67°/40 mm. and about 2 g. of ethyl N-*p*-chlorophenylformimidate at 82–83°/40 mm., followed by the product, which has n_D^{25} 1.5559. The checkers obtained the same results when this distillation was carried out through a fractionating column; however, the yield and properties of N-ethyl-*p*-chloroaniline obtained from this material were the same as those of amine obtained from material distilled through a Claisen head.
5. This method is suitable for the mono-N-alkylation of other primary aromatic amines. Trimethyl and triethyl orthoformate are commercially available, and other alkyl orthoformates can be obtained readily from them by transesterification.[2] The following have been prepared in a similar manner by the submitters.[3]

Product	Yield,%	B.P., °C./mm.	n_D (t, °C)
N-Methylaniline	44	104–105/40	1.5701 (22)
N-Ethylaniline	66	92–93/16	—
N-Isoamylaniline	58	149–151/40	1.5212 (25)
N-Methyl-*m*-toluidine	67	120–121/40	1.5557 (25)
N-Ethyl-*m*-toluidine	69	125–127/40	1.5451 (23)
N-Methyl-*p*-chloroaniline	77	141–142/40	1.5799 (25)

3. Discussion

N-Ethyl-*p*-chloroaniline has been prepared by alkylation of *p*-chloroaniline with ethyl bromide[4,5] and by reduction of aceto-*p*-chloroanilide with lithium aluminum hydride.[6] The present procedure, which is based on the results of an investigation by Roberts and Vogt,[3] is a convenient general method for preparation of pure N-alkyl aromatic amines.

References and Notes

1. University of Texas, Austin, Texas.
2. Alexander and Busch, *J. Am. Chem. Soc.*, **74**, 554 (1952); Roberts, Higgins, and Noyes, *J. Am. Chem. Soc.*, **77**, 3801 (1955).
3. Roberts and Vogt, *J. Am. Chem. Soc.*, **78**, 4778 (1956).
4. Hofmann, *Ann.*, **74**, 143 (1850).
5. Crowther, Mann, and Purdie, *J. Chem. Soc.*, **1943**, 58.
6. Bory and Mentzer, *Bull. soc. chim. France*, **1953**, 814.

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

amine

Trimethyl and triethyl orthoformate

aceto-p-chloroanilide

ethanol (64-17-5)

calcium chloride (10043-52-4)

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ether (60-29-7)

Ethyl bromide (74-96-4)

potassium hydroxide (1310-58-3)

triethyl orthoformate (122-51-0)

N-Methylaniline (100-61-8)

lithium aluminum hydride (16853-85-3)

N-Ethylaniline (103-69-5)

N-Isoamylaniline

p-chloroaniline (106-47-8)

N-Ethyl-m-toluidine (102-27-2)

N-Ethyl-p-chloroaniline,
Aniline, p-chloro-N-ethyl- (13519-75-0)

N-Ethyl-p-chloroformanilide (26772-93-0)

ethyl N-p-chlorophenylformimidate

N-Methyl-m-toluidine (696-44-6)

N-Methyl-p-chloroaniline (932-96-7)