Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

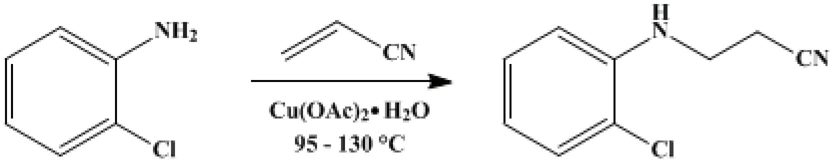
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.038.0014

Organic Syntheses, Coll. Vol. 4, p.146 (1963); Vol. 38, p.14 (1958).

3-(*o*-CHLOROANILINO)PROPIONITRILE

[Propionitrile, 3-*o*-chloroanilino-]



Submitted by S. A. Heininger[1]
Checked by John C. Sheehan and Alma M. Boston.

1. Procedure

A 500-ml. three-necked flask equipped with a stirrer, reflux condenser, and thermometer is charged with 255 g. (2.0 moles) of *o*-chloroaniline, 106 g. (2.0 moles) of acrylonitrile, and 10.2 g. (4.0% by weight of the amine) of cupric acetate monohydrate (Note 1). The mixture is then stirred and heated to reflux, beginning at about 95°. Refluxing is continued for 3 hours (Note 2), with the pot temperature rising to about 130° (Note 3).

The dark mixture is then transferred to a 500-ml. distilling flask fitted with a 15.2-cm. modified Vigreux column and the unchanged acrylonitrile (17–20 g.) collected at 100 mm. (water pump). The distillation is continued (vacuum pump) and the unchanged *o*-chloroaniline (110–120 g.), b.p. 57–60°/0.5 mm., is recovered. The 3-(*o*-chloroanilino) propionitrile (182–192 g.) is obtained as a colorless, somewhat viscous liquid, b.p. 139–141°/0.3 mm., n_D^{25} 1.5728–1.5735 (Note 4).

A pot residue of 30–35 g. remains (Note 5). The conversion of *o*-chloroaniline to 3-(*o*-chloroanilino) propionitrile is 50.5–53%, with a yield of 90–95% based on *o*-chloroaniline, and 53–65% based on acrylonitrile (Note 6).

2. Notes

1. The commercially available monohydrate form of cupric acetate was used. Anhydrous cupric acetate gives the same results. From 2% to 5% of catalyst by weight of the amine employed gives good yields of cyanoethylated products from a variety of anilines.
2. Slightly improved yields may be obtained by use of longer reaction times.
3. Maintaining the temperature at 100–110° for the same period of time gives equivalent results.
4. Physical constants for pure 3-(*o*-chloroanilino) propionitrile are: b.p. 139–141°/0.3 mm., n_D^{25} 1.5734, d_{25}^{25} 1.2103.
5. The residue consists mainly of polyacrylonitrile and copper or copper salts. It is slowly soluble in acetone, more readily soluble in polyacrylonitrile solvents such as dimethylformamide or dimethyl sulfoxide, especially when warmed.
6. An attempt to prepare 3-(*o*-chloroanilino) propionitrile by the Cymerman-Craig procedure (*o*-chloroaniline hydrochloride, diethylamine, and acrylonitrile) (p. 205) gave no isolable product, with recovery of 75% of the *o*-chloroaniline as its acetyl derivative, m.p. 86–87°; reported m.p. 87–88°.[2] Thus representative *ortho*-substituted anilines can be cyanoethylated in much better yields by use of the cupric acetate catalyst than by the Cymerman-Craig route, which is known to be subject to steric interferences.[3] Comparative yields for cyanoethylation of *o*-toluidine substantiate this conclusion; cupric acetate gave 62%, whereas Cymerman-Craig reported 25%.[3] Bulky N-substituents appear to affect yields similarly: methyl-, ethyl-, *n*-propyl-, and isopropylanilines gave yields of 65%, 41%, 17.5%, and 0.5% by the exchange reaction,[3] whereas, with cupric acetate, *n*-butylaniline was cyanoethylated in 68% yield.

3. Discussion

Cupric acetate is an efficient catalyst for the cyanoethylation of all but nitro-substituted aromatic amines. It is particularly effective with anilines which give poor yields by known methods, i.e., those with substituents on the nitrogen atom or in the *ortho* position.[4]

Other known catalysts for cyanoethylation of aromatic amines include acetic acid,[5,6] acetic acid-cuprous chloride mixtures,[7,8] aniline salts,[9] and choline.[10] 3-Anilinopropionitriles may also be prepared by an exchange reaction between the aniline hydrochloride and diethylaminopropionitrile (p. 205).[3]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 4, 205

References and Notes

1. Research Department, Research and Engineering Division, Monsanto Chemical Company, Dayton, Ohio.
2. Beilstein and Kurbatow, *Ann.*, **182**, 100 (1876).
3. Bates, Cymerman-Craig, Moyle, and Young, *J. Chem. Soc.*, **1956**, 388; and earlier papers.
4. Heininger, *J. Org. Chem.*, **22**, 1213 (1957).
5. Braunholtz and Mann, *J. Chem. Soc.*, **1952**, 3046.
6. Cookson and Mann, *J. Chem. Soc.*, **1949**, 67.
7. Smith and Yu, *J. Am. Chem. Soc.*, **74**, 1096 (1952).
8. Braunholtz and Mann, *J. Chem. Soc.*, **1953**, 1817.
9. Bekhli and Serebrennikov, *J. Gen. Chem. U.S.S.R.*, **19**, 1553 (1949); [*C. A.*, **44**, 3448 (1950)].
10. Pietra, *Gazz. chim. ital.*, **86**, 70 (1956).

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

acetic acid (64-19-7)

aniline hydrochloride (142-04-1)

copper (7440-50-8)

acetone (67-64-1)

cupric acetate (142-71-2)

diethylamine (109-89-7)

acrylonitrile (107-13-1)

dimethylformamide (68-12-2)

cupric acetate monohydrate (6046-93-1)

dimethyl sulfoxide (67-68-5)

acetic acid-cuprous chloride

choline (62-49-7)

diethylaminopropionitrile (5351-04-2)

o-toluidine (95-53-4)

o-chloroaniline (95-51-2)

3-(o-Chloroanilino)propionitrile,
Propionitrile, 3-o-chloroanilino-,
3-(o-chloroanilino) propionitrile (94-89-3)

o-chloroaniline hydrochloride (137-04-2)

n-butylaniline (1126-78-9)