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.

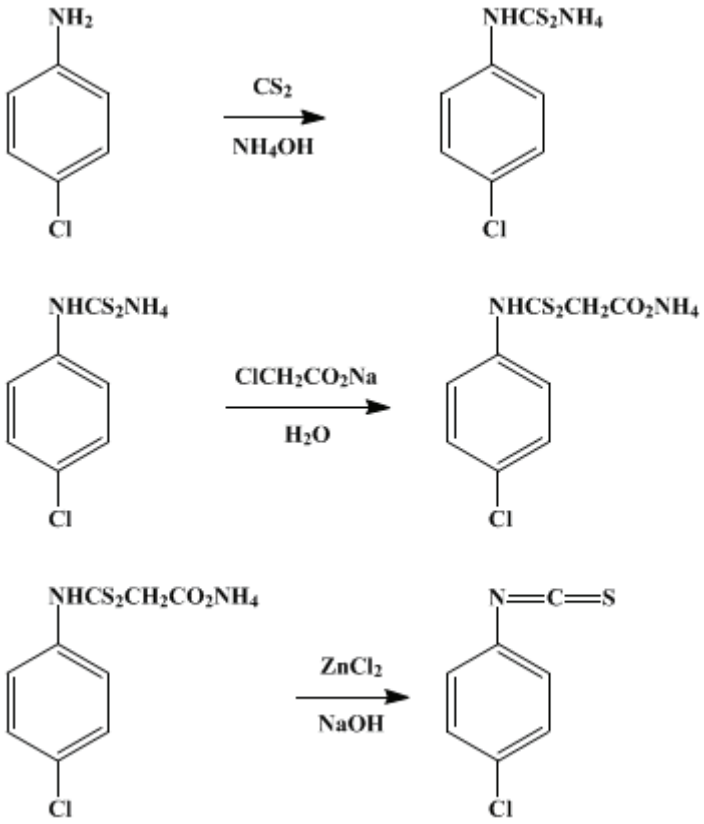
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.045.0019

Organic Syntheses, Coll. Vol. 5, p.223 (1973); Vol. 45, p.19 (1965).

p-CHLOROPHENYL ISOTHIOCYANATE

[Isothiocyanic acid, *p*-chlorophenyl ester]



Submitted by G. J. M. van der Kerk, C. W. Pluygers, and G. de Vries[1].
Checked by W. S. Wadsworth, Jr. and William D. Emmons.

1. Procedure

Caution! p-Chlorophenyl isothiocyanate may cause severe dermatitis if allowed to come in contact with the skin. This preparation should be carried out in a good hood, and rubber gloves should be worn throughout.

In a 250-ml. round-bottomed flask fitted with mechanical stirrer, reflux condenser, and thermometer are placed 38.3 g. (0.30 mole) of *p*-chloroaniline (Note 1), 41 ml. (0.6 mole) of concentrated aqueous ammonia (sp. gr. 0.9), and 21 ml. (0.35 mole) of carbon disulfide. The mixture is stirred vigorously, and when it is heated to 30° the reaction starts. The temperature is maintained at 30–35° by external cooling (Note 2). The reaction mixture turns into a deep-red turbid solution within a few minutes, and then suddenly a heavy yellow precipitate of ammonium *p*-chlorophenyldithiocarbamate separates. To the mixture 15 ml. of water is added, and stirring is continued for 1 hour. The mixture is filtered with suction, and the residue is washed with two 30-ml. portions of a 3% aqueous solution of ammonium chloride and with two 15-ml. portions of 96% ethanol.

The ammonium *p*-chlorophenyldithiocarbamate obtained is transferred immediately to a 1-l. beaker fitted with an efficient mechanical stirrer. Water (250 ml.) is added, and the temperature is raised to 30°. A solution of 28.4 g. (0.30 mole) of chloroacetic acid in 30 ml. of water is neutralized with sodium carbonate [18.6 g. (0.15 mole) of $Na_2CO_3 \cdot H_2O$ in 70 ml. of water] and is added to the well-stirred

dithiocarbamate suspension over a 10-minute period (Note 3). In the beginning the suspension gradually becomes less viscous, but at the end of the addition it rapidly turns into a creamy mass. Another 250 ml. of water is added to facilitate stirring, which is continued for 1 hour after the addition at about 30°.

The creamy suspension is allowed to cool to room temperature, and the electrodes of a pH meter are inserted (Note 4). A solution of 20.5 g. (0.15 mole) of zinc chloride (Note 5) in 75 ml. of water is added dropwise with vigorous stirring over a period of 45 minutes, while the pH is maintained at 7 by the simultaneous dropwise addition of a 4*N* aqueous solution of sodium hydroxide (Note 6). The mixture is stirred for 1 hour and is then filtered with suction; the solid product is dried under reduced pressure over phosphorus pentoxide. The dry material is slurried with 200 ml. of petroleum ether (b.p. 30–60°), and the solvent is decanted. This process is repeated five times, and the combined extract is evaporated at reduced pressure. The yield of almost pure *p*-chlorophenyl isothiocyanate, obtained as a readily crystallizing oil with a pleasant anise-like odor, is 33–35 g. (65–68%), m.p. 44–45°. The product can be recrystallized from the minimum amount of ethanol at 50°.

2. Notes

1. A commercial grade (Eastman Organic Chemicals, white label) of *p*-chloroaniline was used without further purification.
2. The reaction is conveniently started by dipping the flask in a hot-water bath. The reaction temperature is easily maintained by occasional dipping of the flask in a cold-water bath.
3. Any free chloroacetic acid leads to the formation of N-*p*-chlorophenylrhodanine.
4. A Beckman pH meter (Model N) was used.
5. The anhydrous zinc chloride used was obtained from Baker and Adamson, reagent grade.
6. The pH must not drop below 7, although a slightly higher pH does no harm; addition of the zinc chloride in a shorter time lowers the yield.

3. Discussion

The procedure given here is essentially that described previously by the submitters.[2] *p*-Chlorophenyl isothiocyanate has been prepared from *sym*-di-*p*-chlorophenyl thiourea with iodine in alcoholic solution,[3] from ammonium *p*-chlorophenyldithiocarbamate and lead nitrate[4] [cf. also *Org. Syntheses*, Coll. Vol. **1** 447 (1932)], by the action of thiophosgene on *p*-chloroaniline[5] and from *p*-chloroaniline with thiocarbonyl tetrachloride in the presence of stannous chloride.[6]

4. Merits of the Preparation

The present method has the advantage that the whole process can be carried out in aqueous medium at low temperatures. The procedure is also attractive because of the reagents used and the relatively simple isolation procedure employed. The only restriction observed is that the formation of the aromatic dithiocarbamate must be possible.

Other isothiocyanates obtained by this method are: phenyl isothiocyanate (65%), *p*-phenylene diisothiocyanate (71%), *p*-acetylaminophenyl isothiocyanate (73%), *p*-ethoxyphenyl isothiocyanate (64%), and *p*-bromophenyl isothiocyanate (55%).

References and Notes

1. Organisch Chemisch Instituut T.N.O., Utrecht, Nederland.
2. G. J. M. van der Kerk, C. W. Pluygers, and G. de Vries, *Rec. Trav. Chim.*, **74**, 1262 (1955).
3. S. M. Losanitsch, *Ber.*, **5**, 156 (1872).
4. F. B. Dains, R. Q. Brewster, and C. P. Olander, *Univ. Kansas Sci. Bull.*, **13**, 1 (1922) [*C.A.*, **17**, 543 (1923)].
5. G. M. Dyson, *Org. Syntheses*, Coll. Vol. **1**, 165 (1932).
6. J. M. Connolly and G. M. Dyson, *J. Chem. Soc.*, 679 (1935).

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

petroleum ether

sym-di-p-chlorophenyl thiourea

ethanol (64-17-5)

ammonia (7664-41-7)

ammonium chloride (12125-02-9)

sodium hydroxide (1310-73-2)

sodium carbonate (497-19-8)

stannous chloride

chloroacetic acid (79-11-8)

iodine (7553-56-2)

lead nitrate (10099-74-8)

carbon disulfide (75-15-0)

zinc chloride (7646-85-7)

Thiophosgene (463-71-8)

PHENYL ISOTHIOCYANATE (103-72-0)

p-Chlorophenyl isothiocyanate,
Isothiocyanic acid, p-chlorophenyl ester (2131-55-7)

thiocarbonyl tetrachloride

p-chloroaniline (106-47-8)

phosphorus pentoxide (1314-56-3)

ammonium p-chlorophenyldithiocarbamate

p-bromophenyl isothiocyanate (1985-12-2)

N-p-chlorophenylrhodanine

p-phenylene diisothiocyanate (4044-65-9)

p-acetylaminophenyl isothiocyanate

p-ethoxyphenyl isothiocyanate (3460-49-9)