



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.

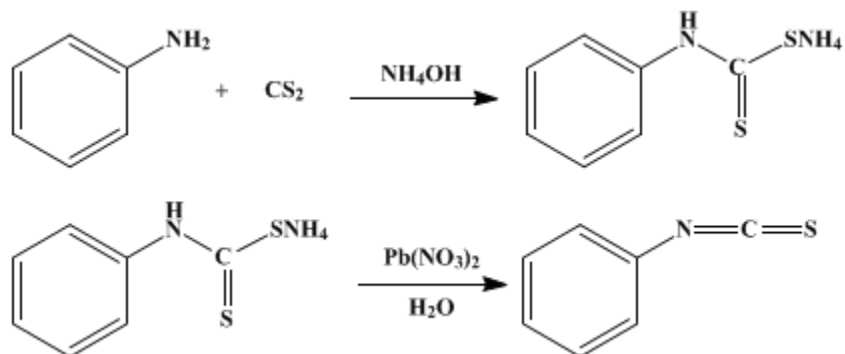
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.447 (1941); Vol. 6, p.72 (1926).

PHENYL ISOTHIOCYANATE

[Isothiocyanic acid, phenyl ester]



Submitted by F. B. Dains, R. Q. Brewster, and C. P. Olander.
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1. Procedure

In a 500-cc. round-bottomed flask (Note 1), fitted with a mechanical stirrer and surrounded by an ice-salt cooling bath, are placed 54 g. (43 cc., 0.71 mole) of carbon disulfide and 90 cc. (1.3 moles) of concentrated aqueous ammonia (sp. gr. 0.9). The stirrer is started, and 56 g. (0.6 mole) of aniline (Note 2) is run into the mixture from a separatory funnel at such a rate that the addition is complete in about twenty minutes. The stirring is continued for thirty minutes after all the aniline has been added, and then the reaction mixture is allowed to stand for another thirty minutes. During this time a heavy precipitate of ammonium phenyldithiocarbamate separates and may even stop the stirrer.

The salt is dissolved in 800 cc. of water (Note 3) and transferred to a 5-l. round-bottomed flask. To the solution is added with constant stirring a solution of 200 g. (0.6 mole) of lead nitrate in 400 cc. of water. Lead sulfide separates as a heavy brown precipitate which soon turns black. The mixture is then distilled with steam into a receiver containing 5–10 cc. of 1 *N* sulfuric acid as long as any oil comes over (Note 4). About 2–3 l. of distillate is collected. The product is separated from the water and weighs 63–66 g.

The oil is dried over a little calcium chloride and distilled under reduced pressure. The yield of phenyl isothiocyanate boiling at 120–121°/35 mm. is 60–63 g. (74–78 per cent of the theoretical amount) (Note 5) and (Note 6).

2. Notes

1. If the reaction is carried out in a beaker, so much ammonia is lost by volatilization that the crystalline ammonium phenyldithiocarbamate is not formed. The temperature should be from 0° to 10° to avoid loss of ammonia.
2. Ordinary technical aniline was used in these experiments.
3. The transfer of the salt to the 5-l. flask is conveniently made by the addition of four successive 200-cc. portions of water to the flask containing the salt.
4. The sulfuric acid is added to react with any ammonia that may be carried over. Otherwise the ammonia may react with the product to give phenylthiourea.
5. Larger runs give somewhat lower percentage yields; thus 280 g. of aniline gives about 250 g. (61 per cent of the theoretical amount) of redistilled phenyl isothiocyanate.
6. The following slightly modified procedure is generally applicable to the preparation of aryl isothiocyanates.
To a solution of 90 g. (0.50 mole) of *p*-bromoaniline, 60 g. (0.78 mole) of carbon disulfide and 90 cc. of

95 per cent alcohol at 10–15° is added 81.6 g. (0.63 mole) of concentrated aqueous ammonia. The milky suspension, in a stoppered flask covered with a towel, is shaken occasionally until a clear solution is obtained. Considerable heat is evolved, and crystals of the intermediate dithiocarbamate soon separate. After standing overnight the crystals are filtered, washed with ether, dissolved in 3 l. of cold water, and stirred while a solution of 174 g. (0.5 mole) of lead nitrate is slowly added. Stirring is continued for fifteen to twenty minutes, and then the *p*-bromophenylisothiocyanate is steam-distilled into a flask acidified with sulfuric acid. The product, which solidifies, is separated and dried. It weighs 30.5 g. (a yield of 27 per cent) and melts at 60–61°.

In this procedure the use of alcohol is essential; without it no isothiocyanate is obtained. It is also advisable with very reactive aromatic amines to add the ammonia in small portions so as to avoid a too vigorous reaction and to keep the temperature of the contents of the stoppered flask below 35°. With some substituted anilines the intermediate dithiocarbamate does not crystallize although the heat evolved indicates that a reaction has taken place. When this happens the solution can be diluted with water and treated with lead nitrate, but the yield will usually be small.

Using this procedure the following isothiocyanates have been prepared with the percentage yields indicated: *p*-iodophenyl, 26–50; *p*-isopropylphenyl, 34; *m*-(trifluoromethyl) phenyl, 50; *p*-acetylphenyl, trace; *m*-bromophenyl, 20; β -naphthyl, 8; *p*-dimethylaminophenyl, 13; 2-methyl-4-isopropylphenyl, 5. The reaction did not work with 2-aminopyridine. (C. J. Kibler, private communication.)

3. Discussion

Phenyl isothiocyanate can be prepared from thiocarbanilide by the action of phosphorus pentoxide,¹ hydrochloric acid,² iodine,³ phosphoric acid,⁴ acetic anhydride,⁵ and dilute sulfuric acid;⁶ from ammonium phenyldithiocarbamate by the action of ethyl chlorocarbonate,⁷ copper sulfate,⁸ ⁹ lead nitrate,⁹ ferrous sulfate,⁹ and zinc sulfate;⁹ and from methylene aniline by heating with sulfur.¹⁰

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 165
- Org. Syn. Coll. Vol. 3, 312
- Org. Syn. Coll. Vol. 4, 700
- Org. Syn. Coll. Vol. 5, 223

References and Notes

1. Hofmann, Jahresber. 349 (1858).
2. Weith and Merz, Z. Chem. 589 (1869).
3. Hofmann, Ber. 2, 453 (1869); Rudnev, J. Russ. Phys. Chem. Soc. 10, 184 (1878).
4. Hofmann, Ber. 15, 985 (1882).
5. Werner, J. Chem. Soc. 59, 396 (1891).
6. Bly, Perkins and Lewis, J. Am. Chem. Soc. 44, 2896 (1922).
7. Kaluza, Monatsh. 33, 367 (1912).
8. Losanitsch, Ber. 24, 3021 (1891).
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10. Kawaoka, J. Soc. Chem. Ind., Japan 43, No. 2, Suppl. binding 53 (1940) [C. A. 34, 6131 (1940)].

Appendix

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

β -naphthyl isothiocyanate

alcohol (64-17-5)

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

ether (60-29-7)

acetic anhydride (108-24-7)

aniline (62-53-3)

lead sulfide

copper sulfate (7758-98-7)

sulfur (7704-34-9)

ferrous sulfate (13463-43-9)

iodine (7553-56-2)

phosphoric acid (7664-38-2)

lead nitrate (10099-74-8)

carbon disulfide (75-15-0)

zinc sulfate (7733-02-0)

PHENYL ISOTHIOCYANATE,
Isothiocyanic acid, phenyl ester (103-72-0)

ammonium phenyldithiocarbamate

phenylthiourea (103-85-5)

dithiocarbamate

2-aminopyridine (504-29-0)

thiocarbanilide (102-08-9)

ethyl chlorocarbonate (541-41-3)

methylene aniline (100-62-9)

phosphorus pentoxide (1314-56-3)

p-bromoaniline (106-40-1)

p-bromophenylisothiocyanate (1985-12-2)

p-iodophenyl isothiocyanate

p-isopropylphenyl isothiocyanate

m-(trifluoromethyl) phenyl isothiocyanate

p-acetylphenyl isothiocyanate

m-bromophenyl isothiocyanate

p-dimethylaminophenyl isothiocyanate

2-methyl-4-isopropylphenyl isothiocyanate