



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.

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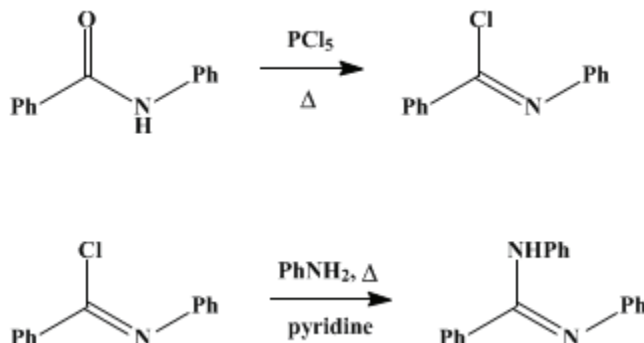
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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N,N'-DIPHENYLBENZAMIDINE

[Benzamidine, N,N'-diphenyl-]



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Checked by R. S. Schreiber and Wm. Bradley Reid, Jr..

1. Procedure

In a 1-l. three-necked round-bottomed flask (Note 1) are placed 90.0 g. (0.456 mole) of [benzanilide](#)² (Note 2) previously dried in an oven at 120° (Note 3) and 95 g. (0.456 mole) (Note 4) of [phosphorus pentachloride](#). The solids are mixed by shaking, and lumps are reduced by manipulation with a rod. A short reflux condenser and a small dropping funnel are attached.

The mixture is heated in an electric mantle or oil bath at 110° for 30 minutes and heated under reflux at 160° for 90 minutes or until active evolution of [hydrogen chloride](#) ceases (Note 5). To the mixture are added slowly through a dropping funnel first 36.4 g. (0.46 mole) of [pyridine](#) (Note 6) previously dried over pellet-form [potassium hydroxide](#), and then 42.4 g. (0.456 mole) of freshly distilled [aniline](#). The contents of the flask are mixed by swirling. The mixture is heated at 160° for about 20 minutes or until the red color is discharged, at which point the flask is removed from the source of heat. The mixture is cooled to about 90°, and 250 ml. of water is added slowly through the dropping funnel with agitation to ensure separation of the solid product in granular form. After the mixture has cooled to room temperature, the solid is collected on a Büchner funnel and air-dried.

The crude [diphenylbenzamidine hydrochloride](#) is transferred to a 1-l. beaker and treated with 500 ml. of 28% ammonia water (hood). The mixture is stirred mechanically and warmed very gently for an hour. The [diphenylbenzamidine](#) is collected on a Büchner funnel and air-dried. The melting point of the product at this stage is 130–136°.

To purify the product it is recrystallized from 80% [ethanol](#) (Note 7), using 8–10 ml. per gram of [diphenylbenzamidine](#). The small insoluble residue of unconverted hydrochloride which may remain (Note 8) is removed by filtering the hot solution. The solution is chilled in an ice-salt bath, and the crystalline product is collected on a Büchner funnel, pressed dry, and finally dried in the air or in an oven at 100°. The yield is 91–100 g. (73–80%) (Note 9) of product having a melting point of 142–144° (Note 10) and (Note 11). Recrystallization of 100 g. of this material from 800 ml. of 80% [ethanol](#) gives 87 g. (87% recovery) of pure [N,N'-diphenylbenzamidine](#), m.p. 144–145°.

2. Notes

1. An all-glass apparatus is desirable as cork connections are attacked during formation of the imido chloride. The checkers used mechanical stirring.
2. The [benzanilide](#) should be of good quality, or tarry material will form and interfere with purification of the product. [Benzanilide](#) is readily made by the Schotten-Baumann procedure from [aniline](#), 10% aqueous [sodium hydroxide](#), and [benzoyl chloride](#) in the proportions 6:30:5, and after crystallization

from 95% ethanol is sufficiently pure.

3. The use of benzanilide dried by fusion³ did not improve the yield.

4. The use of one-fourth an equivalent of phosphorus pentachloride, in an attempt to utilize fully the dehydroxylating capacity of both phosphorus pentachloride and the derived phosphorus oxychloride, led to a low yield of diphenylbenzamidine (50%) and to formation of tarry material that interfered with purification. By use of phosphorus oxychloride⁴ instead of the pentachloride, a temperature of 170° was required to keep the mixture liquid, tarry material was considerable, and the operation was generally unsatisfactory.

5. Isolation of the imido chloride by distillation under reduced pressure offers no advantage.

6. Pyridine serves to make all the aniline available. It does not prevent combination of hydrogen chloride with the N,N'-diphenylbenzamidine even when two equivalents of pyridine are used. In the presence of pyridine the reaction mixture is a suspension and is easily handled. In the absence of pyridine it solidifies to a cake, which must be pulverized to permit liberation of the amidine from the hydrochloride.

7. A series of tests showed ethanol of 78–82% by weight (sp. gr. 0.8344–0.8442 at 25.5°; 84–87% by volume) to be the best solvent. To dissolve 1.0 g. of N,N'-diphenylbenzamidine at the boiling point required 15.5 ml. of 94% (by weight) ethanol, 7.24 ml. of 80% ethanol, and 11 ml. of 71% ethanol, and the recoveries on chilling were respectively 45%, 73%, and 45%; ten intermediate concentrations of ethanol gave results consistent with these. The solubility of N,N'-diphenylbenzamidine in methanol is greater than in ethanol, but recovery is relatively low.

8. The undissolved residue is unchanged hydrochloride and is usually small. If considerable it may be re-treated with ammonia and the free base recovered.

9. By chilling to 20° the yield is about 68% of pure material that melts at 144–145°. A second crop of less pure material can be obtained from the mother liquor by concentrating and chilling. By chilling in a Dry Ice-ethanol bath the yield is about 80% but the product is less pure. Admixed tarry material may be removed in large part by extraction with cold ether, in which the tar dissolves readily.

10. The checkers used a Fisher-Johns block.

11. This method is capable of extension to the preparation of other N,N'-disubstituted amidines.⁵ In some preparations it may be advantageous to remove phosphorus oxychloride by distillation under reduced pressure before addition of the amine. The method is not wholly satisfactory for preparation of N,N'-diarylformamidines, which are better made by the orthoformic ester method⁶ During preparation of diphenylacetamidine considerable gluey material formed by decomposition of the intermediate N-phenylacetimidochloride⁷ is an impediment to the isolation of the product.⁸ This amidine is better prepared by the method of Sen and Ray.⁹

3. Discussion

N,N'-Diphenylbenzamidine and closely related amidines have been made by several procedures which involve interaction of amines with N-substituted imido chlorides either preformed¹⁰ or formed *in situ* from an acylamine by action of phosphorus trichloride,¹¹ phosphorus oxychloride,⁴ or phosphorus pentachloride.⁵ Diphenylbenzamidine is formed from aniline and benzanilidochloroiodide,¹² from aniline and phenyl benzimido ether,¹³ and from aniline hydrochloride and N-phenylbenzamidine.¹⁴ It is obtained also from carbanilide and benzoyl chloride,¹⁵ from carbodiphenylimide and phenylmagnesium bromide,¹⁶ from aniline hydrochloride and benzonitrile at 220–240°,¹⁷ and from benzanilide and phenyl isocyanate.¹⁸ Amidines, including diphenylbenzamidine, are obtainable from nitriles by heating with ammonium or amine salts of sulfonic acids,¹⁹ by heating benzotrichloride with amines,²⁰ and from Schiff bases by action of *tert*-amyl hypochlorite.²¹ Good yields are claimed for a patented process using an acylamine, benzenesulfonyl chloride, and amine in the presence of pyridine.²² The method described is based on the procedures of Wallach³ and Hill and Cox.⁵

References and Notes

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

ammonia water

N-phenylacetimidochloride

phenyl benzimido ether

carbodiphenylimide

ethanol (64-17-5)

hydrogen chloride (7647-01-0)

ammonia (7664-41-7)

methanol (67-56-1)

ether (60-29-7)

aniline (62-53-3)

benzotrile (100-47-0)

sodium hydroxide (1310-73-2)

phosphorus pentachloride (10026-13-8)

aniline hydrochloride (142-04-1)
Benzanilide (93-98-1)
benzoyl chloride (98-88-4)
Benzenesulfonyl chloride (98-09-9)
Phosphorus Oxychloride (21295-50-1)
pyridine (110-86-1)
potassium hydroxide (1310-58-3)
benzotrichloride (98-07-7)
phosphorus trichloride (7719-12-2)
Phenylmagnesium bromide (100-58-3)
Carbanilide (102-07-8)
phenyl isocyanate (103-71-9)
diphenylacetamidine
diphenylbenzamidine hydrochloride
diphenylbenzamidine,
N,N'-Diphenylbenzamidine,
Benzamidine, N,N'-diphenyl- (2556-46-9)
benzanilidochloroiodide
N-Phenylbenzamidine (1527-91-9)
tert-amyl hypochlorite