



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](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.

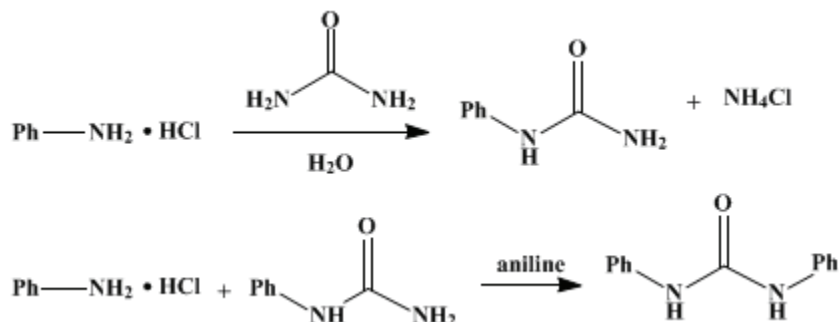
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries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

*Organic Syntheses, Coll. Vol. 1, p.453 (1941); Vol. 3, p.95 (1923).*

## PHENYLUREA and *sym.*-DIPHENYLUREA

[Urea, phenyl-, and Carbanilide]



Submitted by Tenney L. Davis and K. C. Blanchard.  
Checked by C. S. Marvel and W. B. King.

### 1. Procedure

A solution of 390 g. (3 moles) of [aniline hydrochloride](#) and 190 g. (3.2 moles) of [urea](#) in 1500 cc. of water is boiled in a 3-l. flask under a reflux condenser ([Note 1](#)) and ([Note 2](#)). After about one hour, crystals begin to separate; at the end of one and one-half to two hours, the mixture, which bumps considerably, is filtered rapidly by suction, and the crystals of [carbanilide](#) washed with 100 cc. of boiling water. The filtrate is chilled, and the [phenylurea](#) which crystallizes out is filtered off and rinsed with a little cold water, the washings being discarded. The filtrate is again boiled under a reflux condenser for one and one-half to two hours, or until it begins to bump, and the process is repeated. The above operations are repeated a third time, and each time the [phenylurea](#) is collected from the cold filtrate. The mother liquor is finally evaporated to one-half its original volume, and additional crops of [carbanilide](#) and [phenylurea](#) are so obtained. Further evaporation is not profitable.

The crude [carbanilide](#) (symmetrical [diphenylurea](#)) is practically pure, and may be obtained in large colorless needles melting at 235° by recrystallization from [alcohol](#) with the use of [decolorizing carbon](#); 1 l. of [alcohol](#) is required for every 25 g. of product ([Note 3](#)). The weight of the crude [carbanilide](#) is 122–128 g. (38–40 per cent of the theoretical amount).

The crude [phenylurea](#) is somewhat colored and contains a little [carbanilide](#). It may be purified by dissolving in a minimum quantity of boiling water, adding a little [decolorizing carbon](#), and filtering. When the filtrate first begins to cool, a flocculent precipitate of [carbanilide](#) is deposited; this must be filtered off while the liquid is still hot. The filtrate, on cooling, yields colorless stout needles or flakes of [phenylurea](#) melting at 147° ([Note 4](#)). The total weight of pure product is 212–225 g. (52–55 per cent of the theoretical amount).

### 2. Notes

1. The reaction can undoubtedly be explained by the formation of an equilibrium mixture of [urea](#) and [ammonium cyanate](#) in boiling solution; the [ammonium cyanate](#) reacts at the moment of its formation with [aniline hydrochloride](#), yielding [phenylurea](#). [Phenylurea](#) also undergoes a secondary reaction, involving the intermediate formation of [phenyl isocyanate](#), which reacts with [aniline hydrochloride](#), forming [carbanilide](#); so that in order to obtain the best yield it is necessary to interrupt the process from time to time and remove the [phenylurea](#) first formed.

That the reaction proceeds to completion under the above conditions is shown by the fact that although the mixture ultimately becomes faintly alkaline (on account of the formation of [ammonia](#) by hydrolysis of the excess of [urea](#)) at no time does the mixture appear to contain [aniline](#).

2. In the above directions the concentration is as high as it is safe to make it; if less water is used the

yield of [phenylurea](#) decreases and there is grave danger of loss due to the sudden heating of the mixture by rapid separation of crystals. This phenomenon has been observed with a more concentrated mixture even on heating on the steam bath.

3. The [carbanilide](#) can also be obtained in long needles from glacial [acetic acid](#) or preferably [ethyl acetate](#).

4. If the solution of [phenylurea](#) is allowed to cool slowly, the product separates in needles several centimeters in length.

### 3. Discussion

[Phenylurea](#) can be prepared from aniline salts with [potassium cyanate](#) in aqueous solution,<sup>1</sup> a method which suffers from the disadvantage that [potassium cyanate](#) is not easily prepared in the laboratory and rapidly undergoes spontaneous decomposition in storage; by heating [aniline](#) with [urea](#),<sup>2</sup> whereby [carbanilide](#) is formed in rather larger proportion than [phenylurea](#); and from [aniline](#) and [nitrourea](#) in aqueous solution.<sup>3</sup> A method analogous to the procedure described has been patented for the preparation of *p*-phenetylurea,<sup>4</sup> in which *p*-phenetidine is heated with [urea nitrate](#) (or *p*-phenetidine [hydrochloride](#) with [urea](#)) in aqueous solution. This reaction appears to be generally applicable to aromatic primary amines; it does not, however, appear to be so well suited to the preparation of the corresponding derivatives of secondary amines.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 1, 450](#)

---

### References and Notes

1. Hofmann, *Ann.* **57**, 265 (1846); Weith, *Ber.* **9**, 820 (1876).
  2. Fleischer, *Ber.* **9**, 995 (1876); Davis and Underwood, *J. Am. Chem. Soc.* **44**, 2600 (1922).
  3. Davis and Blanchard, *J. Am. Chem. Soc.* **51**, 1790 (1929).
  4. Riedel, *Ger. pat.* 76,596 [*Frdl.* **4**, 1268 (1894–97)].
- 

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

aniline salts

aromatic primary amines

secondary amines

sym.-DIPHENYLUREA

*p*-phenetylurea

[alcohol](#) (64-17-5)

[acetic acid](#) (64-19-7)

[ammonia](#) (7664-41-7)

ethyl acetate (141-78-6)

aniline (62-53-3)

aniline hydrochloride (142-04-1)

decolorizing carbon (7782-42-5)

urea (57-13-6)

Nitrourea (556-89-8)

urea nitrate

Phenylurea,  
Urea, phenyl- (64-10-8)

diphenylurea (603-54-3)

Carbanilide (102-07-8)

ammonium cyanate

phenyl isocyanate (103-71-9)

potassium cyanate (590-28-3)

p-phenetidine (156-43-4)

p-phenetidine hydrochloride (637-56-9)