



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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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.

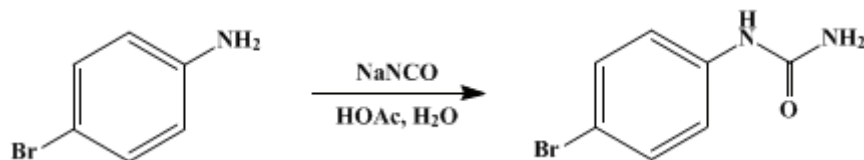
Organic Syntheses, Coll. Vol. 4, p.49 (1963); Vol. 31, p.8 (1951).

ARYLUREAS

I. CYANATE METHOD

p-BROMOPHENYLUREA

[Urea, (*p*-bromophenyl)-]



Submitted by Frederick Kurzer¹

Checked by Richard T. Arnold and Lester C. Krogh.

1. Procedure

In a 2-l. beaker, 86 g. (0.5 mole) of *p*-bromoaniline is dissolved in 240 ml. of glacial acetic acid and 480 ml. of water at 35°. This solution is treated with a solution of 65 g. (1 mole) of sodium cyanate (Note 1) in 450 ml. of water at 35° (Note 2). About 50 ml. of the sodium cyanate solution is added slowly with stirring until a white crystalline precipitate of the product appears. The rest is then added quickly with vigorous agitation (Note 3). The very rapid separation of the product is accompanied by a rise in the temperature to 50–55°. The thick, paste-like suspension is stirred for another 10 minutes, allowed to stand at room temperature for 2–3 hours, and diluted with 200 ml. of water. After cooling to 0°, the material is filtered with suction, washed with water, drained thoroughly, and dried. The yield of crude *p*-bromophenylurea, a white crystalline powder, is 95–100 g. (88–93%). The product is sufficiently pure for further synthetic work, but it can be recrystallized from aqueous ethanol (12 ml. of ethanol and 3 ml. of water per gram of crude material) to give a 65% recovery of lustrous white prisms of *p*-bromophenylurea, m.p. 225–227° (Note 4). This method is suitable for the preparation in excellent yields of a large number of arylureas (Note 5).

2. Notes

1. Comparable results are obtained with an equivalent quantity (81 g.) of potassium cyanate.
2. Instead of the solution, a well-stirred suspension of the cyanate in 150 ml. of water may be used with equal success.
3. Considerable frothing occurs with loss of some isocyanic acid (faint smell resembling that of sulfur dioxide). The foam collapses readily on stirring.
4. Melting points varying between 220° and 278° have been reported for *p*-bromophenylurea (see Methods of Preparation). It has been shown² that the thermal conversion of arylureas to the corresponding diarylureas takes place extremely rapidly, even below the melting point. This is particularly true of arylureas containing certain substituents in the *para* position to the ureido grouping. Melting points of such compounds are therefore liable to be indefinite and correspond to mixtures of the *mono* and *sym* disubstituted urea, especially if the temperature is raised slowly. Reproducible values for the melting points of such compounds, including *p*-bromophenylurea, have now been determined by the following simple procedure: After the approximate softening temperature or melting range of the urea derivative has been found, the bath temperature of the apparatus is raised a further 10–20° above that point and samples are inserted into the slowly cooling bath until a temperature is reached at which a specimen just fails to liquefy. Insertion of a further specimen at a temperature 1° higher causes instantaneous fusion and can be taken as the "melting point" of the urea derivative under examination. Under these conditions practically no conversion to a diarylurea occurs, and samples withdrawn immediately after fusion show nitrogen contents corresponding to the original arylurea. This method gives reproducible physical constants for urea derivatives whose properties preclude slow heating.

5. A list of substituted arylureas prepared by the method above is given in the accompanying table, which records slight variations in the quantities of starting materials employed and in the yields obtained.

The quantities of water recorded in column III are used for preparing the arylamine acetate solutions. The sodium cyanate is dissolved or suspended in the appropriate volume of water as detailed in the synthesis of *p*-bromophenylurea. The yields refer to the quantity of crude product. The substituted ureas thus obtained are usually sufficiently pure for further syntheses but can be recrystallized from ethanol.

SUBSTITUTED ARYLUREAS

I Arylurea	II Arylamine, moles	III Water, ml.	IV Acetic Acid, ml.,	V Sodium Cyanate moles,	VI Initial Temperature, °C	VII Yield, %
<i>p</i> -Tolylurea	0.5	500	50	1.0	25	96
<i>m</i> -Tolylurea	0.5	400	75	1.0	30	86
<i>o</i> -Tolylurea	0.5	400	75	1.0	30	94
1-(4-Biphenyl) urea	0.3	500	350	0.6	40	80
1-(2-Biphenyl) urea	0.25	400	400	0.5	30	75
<i>p</i> - Methoxyphenylurea	0.3	150	30	0.6	40	94
<i>p</i> -Ethoxyphenylurea	0.5	500	75	1.0	25	95
<i>m</i> -Ethoxyphenylurea	0.3	500	120	0.6	20	54
<i>o</i> -Ethoxyphenylurea	0.5	500	170	1.0	20	88
<i>m</i> -Bromophenylurea	0.5	300	150	1.0	20	90
<i>o</i> -Bromophenylurea	0.5	100	250	1.0	25	92
<i>o</i> -Chlorophenylurea	0.5	100	200	1.0	25	92

3. Discussion

p-Bromophenylurea has been prepared by the bromination of phenylurea, using glacial acetic acid,^{3,4} ethanol,⁴ or chloroform⁵ as solvents; by the action of potassium cyanate on *p*-bromoaniline hydrochloride;^{4,6} and by the interaction of *p*-bromoaniline and ethyl allophanate.⁷

References and Notes

1. University of London, London, England.
2. Kurzer, *J. Chem. Soc.*, **1949**, 2292.
3. Pinnow, *Ber.*, **24**, 4172 (1891).
4. Wheeler, *J. Am. Chem. Soc.*, **51**, 3653 (1929).
5. Desai, Hunter, and Khalidi, *J. Chem. Soc.*, **1934**, 1186.
6. Scott and Cohen, *J. Chem. Soc.*, **121**, 2034 (1922).
7. Dains and Wertheim, *J. Am. Chem. Soc.*, **42**, 2303 (1920).

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

ethanol (64-17-5)

acetic acid (64-19-7)
chloroform (67-66-3)
sulfur dioxide (7446-09-5)
nitrogen (7727-37-9)
Phenylurea (64-10-8)
potassium cyanate (590-28-3)
isocyanic acid (75-13-8)
sodium cyanate (917-61-3)
1-(4-Biphenyl)urea
1-(2-Biphenyl)urea
ethyl allophanate (626-36-8)
p-bromoaniline (106-40-1)
p-bromoaniline hydrochloride
p-Bromophenylurea,
Urea, (p-bromophenyl)- (1967-25-5)
p-Tolylurea (622-51-5)
m-Tolylurea (63-99-0)
o-Tolylurea (614-77-7)
p-Methoxyphenylurea (1566-42-3)
p-Ethoxyphenylurea (150-69-6)
m-Ethoxyphenylurea (13142-86-4)
o-Ethoxyphenylurea
m-Bromophenylurea (2989-98-2)
o-Bromophenylurea (13114-90-4)
o-Chlorophenylurea (114-38-5)