



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.

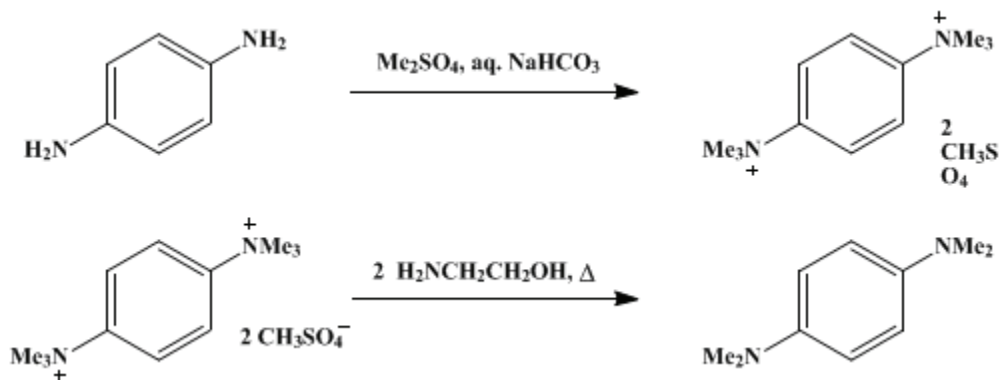
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries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

Organic Syntheses, Coll. Vol. 5, p.1018 (1973); Vol. 49, p.107 (1969).

TETRAMETHYL-*p*-PHENYLENEDIAMINE

[*p*-Phenylenediamine, N,N,N',N'-tetramethyl]



Submitted by S. Hünig, H. Quast, W. Brenninger, and E. Frankenfeld¹.
Checked by R. A. Schwartz and K. B. Wiberg.

1. Procedure

*Caution! Tetramethyl-*p*-phenylenediamine may induce a painful dermatitis when brought into contact with the skin.² Suitable precautions should be taken to avoid such contact.*

In a 2-l. three-necked flask fitted with a stirrer, thermometer, and pressure-compensated dropping funnel are placed 54 g. (0.5 mole) of powdered *p*-phenylenediamine (Note 1), 310 g. (3.7 mole) of sodium bicarbonate, and 250 ml. of water. The temperature of the solution is maintained at 18–22° using an ice bath while 320 ml. (3.4 mole) of dimethyl sulfate (Note 2) is added with stirring over a 30- to 50-minute period. Carbon dioxide is evolved vigorously and a transient purple color is developed; it changes to a brown tinge later on.

When the addition of dimethyl sulfate is complete, stirring is continued for 1 hour at 20–25°. Then the temperature is raised to 60–65° during 10 minutes (Note 3) and is kept at this value until the evolution of carbon dioxide ceases. After the addition of 250 ml. of cold water, the reaction flask is cooled rapidly in an ice bath and 100 ml. of ethanolamine (Note 4) is added. The resultant crystalline slurry is removed from the flask, and the apparatus is rearranged as indicated in (Note 5), using an upright condenser between the dropping funnel (Note 6) and the receiving flask.

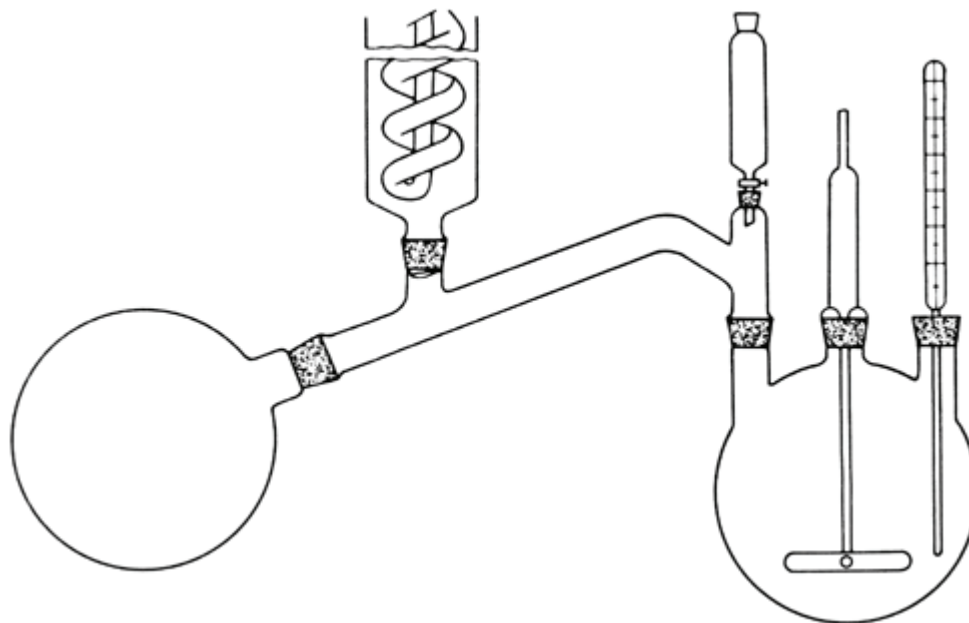
To the reaction flask is added 200 ml. of ethanolamine, and it is heated to 140° with stirring. The slurry above is added in moderate portions over a 40- to 50-minute period (Note 7). When the heating bath is maintained at 230–240°, the addition of the slurry should provide an inner temperature at 120–140° as the water and oily product distill. After the addition is complete, the dropping funnel is rinsed with 100–150 ml. of water. As soon as the inner temperature has reached 160°, 50 ml. of ethanolamine is added and the temperature is maintained at 160–170° for 20 minutes. Water (50 ml.) is added through the dropping funnel to initiate a rapid steam distillation. Steam distillation is continued by the addition of 50-ml. portions of water at an inner temperature of 120–140° and a bath temperature of 230–240° until no more oil appears in the distillate (Note 8).

The oily product solidifies on cooling to about 20°, forming white lumps. After filtration by suction, the lumps are crushed, filtered, and washed four times with 50-ml. portions of ice water. Drying over silica gel in a vacuum gives 62–72 g. (82–88%) of white glistening scales, m.p. 51°.

2. Notes

1. A technical grade of *p*-phenylenediamine was used.
2. Dimethyl sulfate was distilled, b.p. 73–75° (13 mm.).
3. At this temperature the excess of dimethyl sulfate is destroyed.
4. Ethanolamine was distilled, b.p. 74–75° (13 mm.).
5. The apparatus shown in Fig. 1 is suitable for this step. It is essential that the condenser be very effective since the steam distillation is very rapid. If vapor is lost from the top of an internal coil condenser, cold towels placed on the outside of the condenser will provide additional cooling.

Fig. 1



6. The dropping funnel should have a stopcock bore as large as possible.
7. Stirring and addition of only 40–50 ml. of the slurry into the dropping funnel should avoid obstruction of the stopcock. The use of a thin metal wire is sometimes helpful.
8. Transient blue colors in the distillate result from autoxidation. They do not, however, affect the purity of the final product.

3. Discussion

Tetramethyl-*p*-phenylenediamine has been obtained in low yield by the reaction of *p*-phenylenediamine with various alkylating agents such as methyl iodide,³ methanol in the presence of hydrochloric acid at 170–200°,⁴ or formaldehyde and formic acid.⁵ In addition it has been prepared by methylating *p*-dimethylaminoaniline using methanol in the presence of hydrochloric acid at 170–200°,^{6,7} followed by treatment of the resulting salts with aqueous ammonia at 180–190°. In the most recent procedure, *p*-phenylenediamine was alkylated with sodium chloroacetate. Decarboxylation of the *p*-phenylenediaminetetraacetic acid at 180° gave 28% of tetramethyl-*p*-phenylenediamine based on the starting diamine.⁸

The present procedure⁹ combines two general methods described earlier.^{10,11} It is conveniently carried out and gives a substantially higher yield than previous methods. Dimethyl sulfate in the presence of aqueous sodium bicarbonate selectively methylates aromatic amines under mild conditions to give quaternary salts without affecting phenolic hydroxy groups present in the molecule. If the quaternization step is sterically hindered, the reaction stops at the tertiary amine stage.¹⁰ Heterocyclic compounds may also be converted to quaternary salts in high yield, two or more methyl groups being introduced in one step.¹² The rate of reaction may conveniently be followed by observing the carbon dioxide evolution.

Dealkylation of quaternary ammonium salts using ethanolamine is more convenient than the use of aqueous ammonia in sealed tubes at high temperatures.¹⁰ Ethanolamine may be replaced by other

ethanolamines.¹³ The reaction leads to preferential removal of methyl groups.

References and Notes

1. Chemisches Institut der Universität Würzburg, Germany.
 2. Private communication from H. T. Clarke.
 3. A. W. Hofmann, *Compt. Rend.*, **56**, 994 (1863); *Jahresber. Fortschr. Chem.*, 422 (1863).
 4. R. Meyer, *Ber.*, **36**, 2979 (1903).
 5. J. N. Ashley and W. G. Leeds, *J. Chem. Soc.*, 2706 (1957).
 6. C. Wurster, *Ber.*, **12**, 522 (1879).
 7. J. Pinnow, *Ber.*, **32**, 1401 (1899).
 8. J. R. Cox, Jr., and B. D. Smith, *J. Org. Chem.*, **29**, 488 (1964).
 9. S. Hünig, H. Quast, W. Brenninger, and E. Schmitt, *Ber.*, **102**, 2874 (1969).
 10. S. Hünig, *Ber.*, **85**, 1056 (1952).
 11. S. Hünig and W. Baron, *Ber.*, **90**, 395 (1957).
 12. H. Quast and E. Schmitt, *Ber.*, **101**, 4012 (1968).
 13. K. Menzel, Ger. Patent 953170 (1953) [*Chem. Abstr.*, **53**, 8071 (1959)].
-

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

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

methanol (67-56-1)

formaldehyde (50-00-0)

sodium bicarbonate (144-55-8)

formic acid (64-18-6)

carbon dioxide (124-38-9)

dimethyl sulfate (77-78-1)

sodium chloroacetate (3926-62-3)

hydroxy (3352-57-6)

Methyl iodide (74-88-4)

ethanolamine (141-43-5)

Tetramethyl-p-phenylenediamine (3102-87-2)

p-dimethylaminoaniline (99-98-9)

[p-phenylenediamine \(106-50-3\)](#)

[p-Phenylenediamine, N,N,N',N'-tetramethyl \(100-22-1\)](#)

[p-phenylenediaminetetraacetic acid \(1099-02-1\)](#)