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.
3,3'-DIHYDROXYBIPHENYL
[m,m'-Biphenol]

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1. Procedure

3,3'-Dimethoxybiphenyl (8 g., 0.037 mole) is dissolved in 120 ml. of methylene chloride in a 250-
ml. conical flask, and the flask is placed in an acetone-dry ice bath at −80°. The flask is fitted with an air
condenser. A solution of 15.9 g. (6.0 ml., 0.063 mole) of boron tribromide (Note 1), (Note 2) in 40 ml.
of methylene chloride (Note 3), (Note 4) is added carefully to the stirred solution through the condenser.
When the addition is complete, a calcium chloride tube is fitted to the top of the air condenser in order
to protect the reaction mixture from moisture. As the solution of boron tribromide is added, a white
precipitate is formed. The reaction mixture is allowed to attain room temperature overnight with
stirring, when a clear, brownish yellow solution is obtained. The reaction mixture is then hydrolyzed by
careful shaking with 130 ml. of water, thus precipitating a white solid which is dissolved by the addition
of 500 ml. of ether. The organic layer is separated and extracted with 240 ml. of 2N sodium hydroxide;
the alkaline extract is neutralized with dilute hydrochloric acid, extracted with 300 ml. of ether, and the
ether extract is dried over anhydrous magnesium sulfate. On removal of the ether under reduced
pressure, a brownish yellow oil remains which soon crystallizes to give an off-white solid; this is
recrystallized twice from hot benzene, the first time with the addition of charcoal, and gives 3,3'-
dihydroxybiphenyl as white needles with a pinkish tint, m.p. 126–127° (Note 5). The yield is 5.4–6.0 g.
(77–86%).

2. Notes

1. Boron tribromide of 99.9% purity, from Koch-Light Laboratories Ltd., Colnbrook, Bucks, England,
was used.
2. Boron tribromide is a heavy, colorless liquid ($d = 2.6$) when pure but begins to decompose on
exposure to light, liberating free bromine. It fumes vigorously in air, being rapidly hydrolyzed to boric
acid, with the evolution of considerable heat.
3. Demethylation reactions proceed equally well using dry n-pentane or dry methylene chloride as the
solvent for both the ether and the boron tribromide; methylene chloride, having by far the more
powerful solvent action, is to be preferred.
4. When making up the solution of boron tribromide in methylene chloride, it has been found best to
stand the vessel containing the solvent in an acetone-dry ice bath at −80° and to add the required amount
(it is difficult to measure accurately) to the methylene chloride as rapidly as possible.
5. In order to obtain a perfectly white product, recrystallization from water is necessary;\textsuperscript{3,4} prismatic
needles several centimeters long are obtained. The compound is moderately soluble in boiling water and
slightly soluble in cold water.

3. Discussion

The above preparation of 3,3'-dihydroxybiphenyl is a good example of the utility of boron
tribromide for the cleavage of aryl methyl ethers; it is based on the method of McOmie, Watts, and
West.\textsuperscript{5} 3,3'-Dihydroxybiphenyl has been prepared previously by diazotization\textsuperscript{1} of 3,3'-diaminobiphenyl
and subsequent boiling with water, by the fusion of biphenyl-3,3'-disulfonic acid with potassium
hydroxide, and by heating 3,3′-dimethoxybiphenyl with hydriodic acid.

Almost all the methods previously employed for the demethylation of aromatic methyl ethers have involved fairly high temperatures, e.g., hydrogen halides in water or acetic acid at reflux temperature, whereas the present method is effective at, or well below, room temperature although in a few cases it has been found necessary to boil the solution (b.p. of methylene chloride, 40°). Boron tribromide does not effect cleavage of methylenedioxy groups nor of diphenyl ethers. It can be used for the demethylation of aryl methyl ethers in the presence of many functional groups without affecting these. It is especially valuable for the demethylation of iodinated ethers and of methoxy biphenylenes where the usual reagents are either ineffective or else cause decomposition. Boron tribromide was the reagent of choice for the final (demethylation) step in the synthesis of the naturally occurring macrolide, Zearalenone.

References and Notes


Appendix

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

m,m′-Biphenol

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

Benzene (71-43-2)

ether (60-29-7)

sodium hydroxide (1310-73-2)

bromine (7726-95-6)

potassium hydroxide (1310-58-3)

hydriodic acid (10034-85-2)
n-PENTANE (109-66-0)
methylene chloride (75-09-2)
boric acid (10043-35-3)
magnesium sulfate (7487-88-9)
boron tribromide (10294-33-4)

3,3'-DIMETHOXYBIPHENYL (6161-50-8)
3,3'-dihydroxybiphenyl (612-76-0)
3,3'-diaminobiphenyl
biphenyl-3,3'-disulfonic acid