Organic Syntheses

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.

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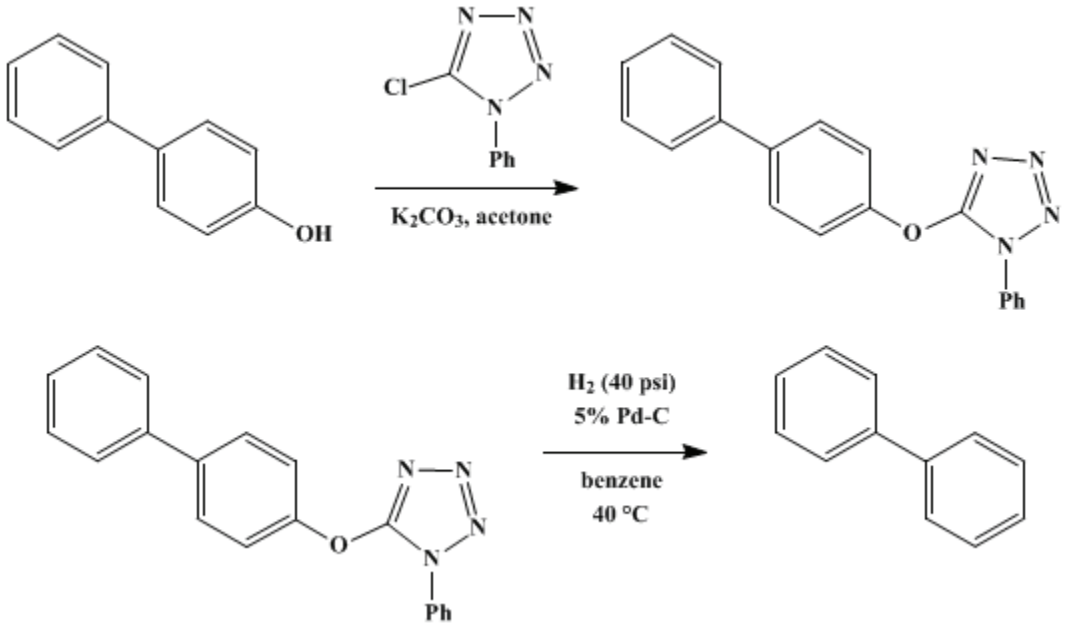
DEHYDROXYLATION OF PHENOLS; HYDROGENOLYSIS OF PHENOLIC ETHERS: BIPHENYL



Submitted by Walter J. Musliner and John W. Gates Jr[1].
Checked by D. Robert Coulson and Richard E. Benson.

1. Procedure

Caution! Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A. 4-(1-*Phenyl-5-tetrazolyloxy)biphenyl*. A 1-l., round-bottomed flask fitted with an efficient condenser and a magnetic stirring bar is charged with 17 g. (0.10 mole) of 4-phenylphenol, 18.1 g. (0.100 mole) of 1-phenyl-5-chlorotetrazole (Note 1), 27.6 g. (0.200 mole) of anhydrous potassium carbonate, and 250 ml. of acetone. The mixture is stirred and heated under reflux for 18 hours (Note 2). Water (250 ml.) is added to the hot mixture producing a clear solution that is chilled in ice. After 1 hour, the solid is collected by filtration and dried in air, giving 32–33 g. of the crude product, m.p. 151–153°, which is then dissolved in 250 ml. of hot ethyl acetate. The solution is filtered while hot to remove a small amount of insoluble material and cooled on ice, yielding 25 g. of 4-(1-phenyl-5-tetrazolyloxy) biphenyl, as white crystals, m.p. 150–153°. An additional 2–3 g. of product is recovered from the filtrate by concentration to 125 ml. bringing the total yield to 27–28 g. (86–89%).

B. *Biphenyl*. Added to a solution of 10 g. (0.032 mole) of the product from Part A in 200 ml. of benzene is 2 g. of 5% palladium-on-charcoal, and the mixture is shaken with hydrogen in a Parr apparatus at 40 p.s.i. and 35–40° for 8 hours (Note 3). The mixture is filtered, and the insoluble residue is washed with three 100-ml. portions of hot ethanol (Note 4). The filtrates are combined, and the solvent is removed with a rotary evaporator at 60° (12 mm.), leaving a solid residue, which is dissolved in 100 ml. of benzene. After adding 100 ml. of 10% aqueous sodium hydroxide the mixture is shaken, and the layers separated. The aqueous layer is extracted with 100 ml. of benzene, and the original benzene layer is washed with 100 ml. of water (Note 5). The benzene solutions are combined and dried over magnesium sulfate. Removal of the benzene by distillation yields 4.0–4.7 g. (82–96%) of biphenyl as a white powder, m.p. 68–70° (Note 6). The IR spectrum is identical with that of an authentic sample,

and a purity of at least 99.5% was indicated by GC analysis.

2. Notes

1. 4-Phenylphenol and 1-phenyl-5-chlorotetrazole were obtained from Eastman Organic Chemicals.
2. A reflux period of 18 hours was chosen because it represents an overnight reaction time; the reaction is essentially completed in 8 to 10 hours.
3. The hydrogenolysis can also be carried out in ethanol or tetrahydrofuran. An amount of catalyst equivalent to 10–20% by weight of tetrazolyl ethers is most satisfactory for this reaction. Platinum oxide also catalyzes this hydrogenolysis.
4. A large portion of 1-phenyl-5-tetrazolone (and a small amount of biphenyl) remains mixed with and adsorbed to the catalyst and is removed by the ethanol treatment.
5. 1-Phenyl-5-tetrazolone can be recovered from the combined aqueous solutions by acidification with dilute hydrochloric acid. The yield is 4.2–4.7 g. (82–92%), m.p. 190–191°.
6. Benzoxazolyl ethers can also be used in this reaction sequence but an amount of catalyst equivalent to 20–40% by weight of ether is necessary in the hydrogenolysis step. 2-Chlorobenzoxazole is available from Eastman Organic Chemicals.

3. Discussion

The preparation is essentially that described by the submitters[2] and is cited as an example of this general procedure for replacement of phenolic hydroxyl groups by hydrogen.

The reaction sequence, which involves the conversion of the phenolic hydroxyl groups to a phenyltetrazolyl ether (see (Note 6)) followed by reduction to effect removal of the phenolic hydroxyl group, illustrates a mild, efficient, general, and convenient procedure. It has been applied successfully by the submitters[2] to a variety of substituted phenols, as shown in Table I.

TABLE I
HYDROGENOLYSIS OF PHENOLIC ETHERS

Substituted Phenol	Yield of Tetrazolyl Ether, %	Hydrogenolysis Time, hours	Hydrogenolysis Product	Hydrogenolysis Yield, %
Guaiacol	94	15	Anisole	86[a]
3-Methoxyphenol	95	16	Anisole	85[a]
4-Methoxyphenol	97	6	Anisole	83[a]
2-Phenylphenol	98	8	Biphenyl	82
4-Aminophenol	86	9	Aniline	46[b]
4-Carbethoxyphenol	91	16	Ethyl benzoate	89[a]
Thymol	93	15	*p*-Cymene	72[a]
1-Naphthol	88	7	Naphthalene	50
2-Naphthol	94	17	Naphthalene	65
4-Chlorophenol	92	18	Benzene[c]	70[a]

[a]Filtered solution analyzed directly by gas chromatography with toluene as internal standard.
[b]Isolated as the hydrochloride salt.
[c]From hydrogenolysis of carbon-chlorine bond.

Phenols having a variety of substituents including alkyl, alkoxyl, aryl, amino, and carbalkoxyl have been successfully converted to the desired product in good yield. The only limitation yet found is in the hydrogenolysis of the halogen–carbon bond. Thus 4-chlorophenol was converted to benzene using this procedure.

Other procedures include zinc-dust distillation, not generally useful except for exhaustive degradation of phenols to hydrocarbons, and various sodium and liquid ammonia cleavages of phenol ethers.[3,4,5,6,7] These latter reactions lack generality and are often unpredictable. They require conditions too harsh for certain aromatic substituents, and the yields are frequently low.

References and Notes

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

palladium-on-charcoal

efficient condenser

ethanol (64-17-5)

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

Benzene (71-43-2)

ethyl acetate (141-78-6)

ether (60-29-7)

aniline (62-53-3)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

phenol (108-95-2)

1-Naphthol (90-15-3)

2-naphthol (135-19-3)

platinum oxide

Anisole (100-66-3)

acetone (67-64-1)

toluene (108-88-3)

sodium (13966-32-0)

Biphenyl (92-52-4)

Naphthalene (91-20-3)

Guaiacol (90-05-1)

ethyl benzoate (93-89-0)

thymol (89-83-8)

p-cymene (99-87-6)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

4-Carbethoxyphenol (120-47-8)

4-Methoxyphenol (150-76-5)

4-phenylphenol (92-69-3)

1-phenyl-5-chlorotetrazole (14210-25-4)

4-(1-Phenyl-5-tetrazolyloxy)biphenyl (17743-27-0)

1-phenyl-5-tetrazolone

2-Chlorobenzoxazole (615-18-9)

phenyltetrazolyl ether

Tetrazolyl Ether

3-Methoxyphenol (150-19-6)

2-Phenylphenol (90-43-7)

4-Aminophenol (123-30-8)

4-Chlorophenol (106-48-9)