



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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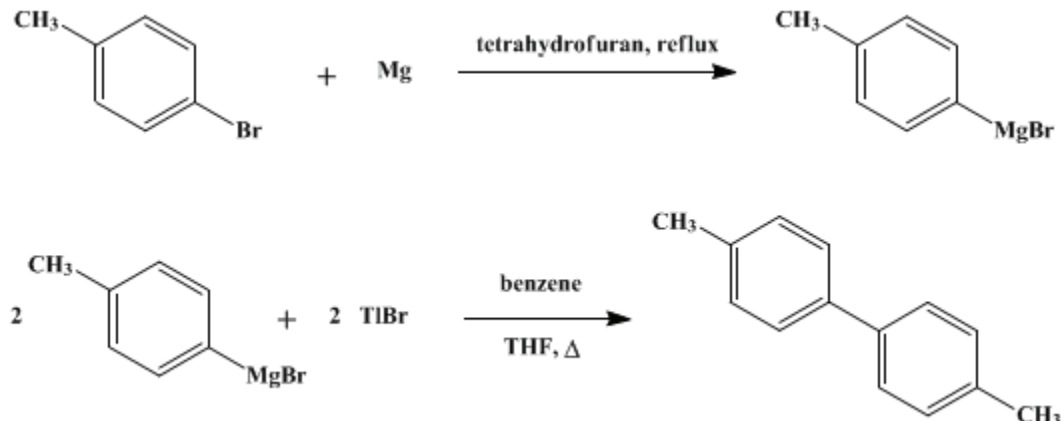
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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4,4'-DIMETHYL-1,1'-BIPHENYL



Submitted by L. F. Elsom, Alexander McKillop¹, and Edward C. Taylor².
 Checked by Ronald F. Sieloff and Carl R. Johnson.

1. Procedure

*Caution! Thallium salts are very toxic. This preparation should be carried out in a well-ventilated hood. The operator should wear rubber gloves. For disposal of thallium wastes, see (Note 1) in *Org. Synth.*, Coll. Vol. 6, 791 (1988).*

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-methylphenyl)magnesium bromide*. A 500-ml., three-necked, round-bottomed flask equipped with a reflux condenser protected by a drying tube, a mercury-sealed mechanical stirrer, and a 250-ml., pressure-equalizing dropping funnel fitted with a gas-inlet tube is thoroughly purged with dry nitrogen (Note 1) and charged with 6.25 g. (0.256 g.-atom) of magnesium turnings and 50 ml. of anhydrous tetrahydrofuran (Note 2). The dropping funnel is charged with a solution of 42.7 g. (30.5 ml., 0.250 mole) of 4-bromotoluene (Note 3) in 100 ml. of anhydrous tetrahydrofuran. Approximately 10 ml. of the 4-bromotoluene solution is added to the flask, and the contents are stirred until the Grignard reaction commences (Note 4). When the initial vigorous reaction has subsided the remainder of the 4-bromotoluene solution is added at a rate such that the mixture refluxes gently. Generally the addition is complete at the end of 1 hour, and almost all of the magnesium has dissolved. The mixture is refluxed for a further hour and cooled. The yield of (4-methylphenyl)magnesium bromide is about 95% (Note 5).

B. *4,4'-Dimethyl-1,1'-biphenyl*. A 1-l., three-necked, round-bottomed flask equipped with a reflux condenser protected by a drying tube, a mercury-sealed mechanical stirrer, and a gas-inlet tube is charged with 101 g. (0.356 mole) of thallium(I) bromide and 400 ml. of anhydrous benzene. The slurry is stirred vigorously while a stream of dry nitrogen is passed through the apparatus. The reflux condenser is temporarily removed, and the solution of (4-methylphenyl)magnesium bromide is added to the flask as rapidly as possible through a large filter funnel fitted with a loose plug of glass wool (Note 6). A black solid precipitates almost immediately from solution. The reflux condenser is replaced, and the contents of the flask are refluxed with stirring for 4 hours under a nitrogen atmosphere. The reaction mixture is then cooled, filtered, and the metallic thallium washed with 200 ml. of diethyl ether. The organic layer is washed once with 100 ml. of 0.1 N hydrochloric acid and once with 100 ml. of water, then dried over anhydrous sodium sulfate.

The organic solvent is removed by distillation under reduced pressure, giving 4,4'-dimethyl-1,1'-biphenyl contaminated with a small amount of bis(4-methylphenyl)thallium bromide. The crude product is dissolved in 30 ml. of benzene, and the solution is filtered through a short column of alumina (Note 7) using 250 ml. of benzene as eluent. Distillation of the benzene under reduced pressure leaves 19–21 g. (80–83%) of 4,4'-dimethyl-1,1'-biphenyl as a colorless solid, m.p. 118–120° (Note 8).

2. Notes

1. Nitrogen is dried by passage through two Drechsel bottles containing concentrated sulfuric acid and potassium hydroxide pellets, respectively.
2. Tetrahydrofuran was dried as described in *Org. Synth.*, **Coll. Vol. 4**, 259 (1963).
3. 4-Bromotoluene (purchased from Aldrich Chemical Company, Inc.) was distilled before use, b.p. 71–72° (15 mm.).
4. The Grignard reaction starts within a few minutes and should not require the use of a catalyst. If the reaction has not commenced within 5 minutes, the flask should be gently heated with a hot water bath until reaction starts.
5. The Grignard reagent may be standardized by the general procedure described for cyclohexylmagnesium chloride in *Org. Synth.*, **Coll. Vol. 1**, 187 (1932).
6. A loose plug of glass wool prevents any unreacted magnesium metal from being added to the reaction mixture. Care must be taken to ensure that the plug is loose enough to allow rapid addition of the Grignard reagent.
7. The dimensions of the alumina column are not critical. A column approximately 2.5 cm. × 12.5 cm. is recommended. The small amount of bis(4-methylphenyl)thallium bromide formed in the reaction remains on the top of the column.
8. The reaction may be conducted on two or three times the scale described with no decrease in yield.

3. Discussion

4,4'-Dimethyl-1,1'-biphenyl has been prepared by a wide variety of procedures, but few of these are of any practical synthetic utility. Classical radical biaryl syntheses such as the Gomberg reaction or the thermal decomposition of diaryl peroxides give complex mixtures of products in which 4,4'-dimethyl-1,1'-biphenyl is a minor constituent. A radical process may also be involved in the formation of 4,4'-dimethyl-1,1'-biphenyl (13%) by treatment of 4-bromotoluene with hydrazine hydrate.³ 4,4'-Dimethyl-1,1'-biphenyl has been obtained in moderate to good yield (68–89%) by treatment of either dichlorobis(4-methylphenyl)tellurium or 1,1'-tellurobis(4-methylbenzene) with degassed Raney nickel in 2-methoxyethyl ether.⁴

All of the useful procedures described for the preparation of 4,4'-dimethyl-1,1'-biphenyl involve coupling of either a 4-halotoluene by a metal or the corresponding Grignard reagents by a metal halide. 4-Halotoluenes can be coupled directly by treatment with lithium,⁵ sodium,^{6,7,8} magnesium,⁹ or copper^{10,11}; yields are, however, very low in the first three cases (5–15%) and only moderate (54–60%) when copper is employed, as in the Ullmann synthesis. Bis(1,5-cyclooctadiene)nickel(0) has also been used to couple 1-iodo-4-methylbenzene, giving the biaryl in 63% yield.¹²

The present method of preparation of 4,4'-dimethyl-1,1'-biphenyl is that described by McKillop, Elsom, and Taylor,¹³ has the particular advantages of high yield and manipulative simplicity, and is, moreover, applicable to the synthesis of a variety of symmetrically substituted biaryls. 3,3'- and 4,4'-Disubstituted and 3,3',4,4'-tetrasubstituted 1,1'-biphenyls are readily prepared, but the reaction fails when applied to the synthesis of 2,2'-disubstituted-1,1'-biphenyls. The submitters have effected the following conversions with the present procedure (starting aromatic bromide, biphenyl product, % yield): bromobenzene, biphenyl, 85; 1-bromo-4-methoxybenzene, 4,4'-dimethoxy-1,1'-biphenyl, 99; 1-bromo-3-methylbenzene, 3,3'-dimethyl-1,1'-biphenyl, 85; 4-bromo-1,2-dimethylbenzene, 3,3',4,4'-tetramethyl-1,1'-biphenyl, 76; 1-bromo-4-chlorobenzene, 4,4'-dichloro-1,1'-biphenyl, 73; 1-bromo-4-fluorobenzene, 4,4'-difluoro-1,1'-biphenyl, 73.

Related procedures, in which treatment of (4-methylphenyl)magnesium halides with halides of copper(II),¹⁴ silver(I),¹⁵ cobalt(II),¹⁶ or chromium(III)¹⁷ also lead to the formation of 4,4'-dimethyl-1,1'-

biphenyl, are either experimentally more difficult than, or do not give yields comparable to, the present method.

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 6, 468](#)

References and Notes

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Appendix

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

[sulfuric acid](#) (7664-93-9)

[hydrochloric acid](#) (7647-01-0)

[Benzene](#) (71-43-2)

[diethyl ether](#) (60-29-7)

[magnesium](#) (7439-95-4)

[sodium sulfate](#) (7757-82-6)

[nitrogen](#) (7727-37-9)

[copper](#) (7440-50-8)

[Raney nickel](#) (7440-02-0)

[potassium hydroxide](#) (1310-58-3)

sodium (13966-32-0)

bromobenzene (108-86-1)

Biphenyl (92-52-4)

cyclohexylmagnesium chloride

hydrazine hydrate (7803-57-8)

lithium (7439-93-2)

Tetrahydrofuran (109-99-9)

2-methoxyethyl ether (111-96-6)

4,4'-Dimethyl-1,1'-biphenyl (613-33-2)

copper(II)

cobalt(II)

Thallium (7440-28-0)

4-bromotoluene (106-38-7)

(4-Methylphenyl)magnesium bromide (4294-57-9)

thallium(I) bromide

bis(4-methylphenyl)thallium bromide

dichlorobis(4-methylphenyl)tellurium

1-iodo-4-methylbenzene (624-31-7)

1-bromo-4-methoxybenzene (104-92-7)

1-bromo-3-methylbenzene (591-17-3)

4-bromo-1,2-dimethylbenzene (583-71-1)

1-bromo-4-chlorobenzene (106-39-8)

1-bromo-4-fluorobenzene (460-00-4)

silver(I)

chromium(III)

4,4'-Dimethoxy-1,1'-biphenyl (2132-80-1)

[4,4'-difluoro-1,1'-biphenyl \(398-23-2\)](#)

[3,3'-dimethyl-1,1'-biphenyl \(612-75-9\)](#)

[1,1'-tellurobis\(4-methylbenzene\)](#)

[3,3',4,4'-tetramethyl-1,1'-biphenyl](#)

[4,4'-dichloro-1,1'-biphenyl](#)

[Bis\(1,5-cyclooctadiene\)nickel\(0\)](#)