



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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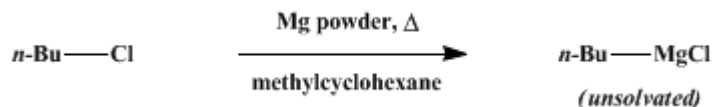
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 5, p.1141 (1973); Vol. 47, p.113 (1967).

UNSOLVATED *n*-BUTYLMAGNESIUM CHLORIDE



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1. Procedure

In a 250-ml. round-bottomed flask fitted with a glass-link or Teflon, stirrer, thermometer, reflux condenser with outlet to an oil seal, dropping funnel, and inlet for nitrogen (Note 2), (Note 3) are placed 3.22 g. of magnesium powder (0.132 mole) (Note 4) having a particle size of 64–76 μ (Note 5), (Note 6), and 60 ml. of methylcyclohexane (Note 7). The apparatus is flushed with nitrogen. A slow stream of nitrogen is introduced, and the methylcyclohexane is heated to reflux temperature (Note 8).

About one-fifth of a solution of 9.26 g. of 1-chlorobutane (0.1 mole) (Note 9), (Note 10) in 20 ml. of methylcyclohexane is added to the vigorously stirred refluxing mixture. Reaction commences (gray turbidity) within 2–8 minutes (Note 5), (Note 11), and the remainder of the halide solution is then added steadily over about 12 minutes to the heated mixture, the rate being adjusted so that the inner temperature of the refluxing mixture does not fall appreciably below 99–100°. Stirring and heating under reflux are continued for an additional 15 minutes. The resulting product contains approximately 0.073 mole (73% yield) of *n*-butylmagnesium chloride as determined either by hydrolysis to *n*-butane (Note 12), (Note 13) or by titration (Note 14).

2. Notes

1. The empirical formula of *n*-butylmagnesium chloride prepared in methylcyclohexane cannot readily be determined because of the virtual insolubility of the reagent in this medium. The reagent is somewhat more soluble in aromatic media such as toluene or isopropylbenzene, and, although the empirical formula of the solute may initially approach C₄H₉MgCl, there is a tendency for precipitation of magnesium chloride from solution. This process appears to be catalyzed by traces of alkoxides, which are liable to be formed after contact of oxygen with the solution. In practice, products will tend to contain less halogen than is required by the simple formula C₄H₉MgCl. The reagents are associated (see reference ² for a fuller discussion).

2. The nitrogen used (British Oxygen Co., White Spot) contained about 10 p.p.m. of oxygen and was dried by passage through a glass spiral cooled in acetone and solid carbon dioxide. For the most precise work, the submitters reduced the proportion of oxygen to about 0.1 p.p.m. by scrubbing the nitrogen with chromous chloride solution in a Nilox apparatus (Southern Analytical Ltd., Camberley, Surrey, England).

3. The apparatus should preferably be baked at 120° for several hours immediately before use. The uppermost region of condensing methylcyclohexane should not be cloudy; if it is, a few milliliters should be allowed to distil.

4. The yield of *n*-butylmagnesium chloride is increased to 80% (analyzed by evolution of *n*-butane) if twice the stated amount of magnesium is used.

5. Magnesium powder (grade 4, Magnesium Elektron Ltd., Manchester, England) was used within 6 months of its grinding by the manufacturer, and was sieved to the stated particle size. The use of unsieved material often gives results nearly as good, but exact reproducibility is more difficult because of variations of the particle size distribution from sample to sample. In general, the more freshly ground the magnesium, the shorter are the induction periods before reaction and, to a limited extent, the higher are the yields of organomagnesium product.

6. Fresh magnesium turnings for Grignard reaction can be used if suitable powder is unavailable, but initiation of reaction is likely to be prolonged, and the subsequent addition of the halide solution should

occupy at least 30 minutes, longer if possible.

7. **Methylcyclohexane** is purified by shaking with 3 portions of concentrated **sulfuric acid**, washing successively with water, **sodium carbonate** solution, and water, drying over calcium sulfate (Drierite), and distilling. The material boiling at 100–101° is used. Other nonsolvating media which can be used are **toluene**, xylenes, **cumene**, **tetralin**, light petroleum (b.p. 80°), **decalin**, and kerosene; aliphatic media are preferred, for reasons given in references ^{2, 3, and 4}.

8. The rate of flow of **nitrogen** should be just sufficient to maintain a positive pressure in the apparatus. Too rapid a flow leads to loss of **1-chlorobutane**.

9. **1-Chlorobutane** is purified with **sulfuric acid** as for **methylcyclohexane** (Note 7), dried over **calcium chloride**, and fractionated. A middle fraction is collected.

10. The yield of product is increased to 81% (analyzed by evolution of *n*-butane) if 0.67 g. (0.0033 mole) of **aluminum isopropoxide** is added to the suspension of **magnesium** before addition of the halide solution. Alternatively, an equivalent amount of **2-propanol** and **iodine** (giving 0.01 mole of C₃H₇OMgI) may be added. These modified procedures (particularly the second) also shorten the induction periods and render unnecessary any special drying of the reagents and apparatus and the use of fresh **magnesium**.

The products in such cases contain complexes between *n*-butylmagnesium chloride and the particular alkoxide employed. With the stated low proportions of alkoxides, these complexes broadly resemble the alkoxide-free materials, but increased proportions of the alkoxide component give complexes having generally decreased chemical reactivity (see references ^{3 and 4}).

11. The reaction generally starts without addition of **iodine** as an initiator, but the use of a crystal of **iodine** (no stirring) may occasionally be necessary with "old" **magnesium** or insufficiently dried materials or apparatus. A slower rate of addition of **1-chlorobutane** gives slightly higher yields; for example, addition over a period of 60 minutes gave yields of 82–87%.

12. The reflux condenser was connected by an adaptor and Teflon tube to a trap of known weight which was cooled by a mixture of **acetone** and solid **carbon dioxide**. The flow of **nitrogen** was stopped, and an excess of water (about 15 ml.) was added dropwise through the dropping funnel to the stirred reaction product. The resulting mixture was heated at the reflux temperature, and the **butane** was collected in the trap. The weight of **butane**, b.p. –1° to 0°, was 4.23–4.35 g. (73–76% yield).

13. The submitters have detected traces of *trans*-butene-2 and **propylene** among the gases (mainly *n*-butane and **hydrogen**) formed on hydrolysis.

14. Sufficient dry **ether** (approximately 100 ml.) is added to bring the organomagnesium products into solution. Aliquot portions of the solution are then added to a known volume of standard **hydrochloric acid**, and the excess acid is determined by titration with standard base. Yields determined in this way tend to be a few percent higher than those determined by collection of *n*-butane (Note 12).

3. Discussion

The method is an extension of the well-known Grignard synthesis in ethers to the use of nonsolvating media, and is a development of procedures previously reported.^{2,3,4,5,6} A version of it has been employed with straight-chain primary alkyl chlorides, bromides, and iodides from C₂ to C₁₄,^{5,6,7} and in solvents (or an excess of the halide) which permit reaction temperatures above 120°, with simple aryl halides such as **chlorobenzene** and **1-chloronaphthalene**. Branched-chain primary, secondary, and tertiary alkyl halides, allyl, vinyl, and benzyl halides either fail to react or give extensive side reactions. Better results are reported to be obtained in such cases with the use of catalytic quantities of a mixture of an alkoxide and an **ether** such as **diethyl ether** or **tetrahydrofuran** in a hydrocarbon medium, but the products are not, of course, completely unsolvated.⁴

4. Merits of the Preparation

Unsolvated organomagnesium compounds have been recommended for the synthesis of organometallic derivatives of **mercury**, **boron**, **aluminum**, **silicon**, **germanium**, **tin**, **phosphorus**, **arsenic**, and **antimony**^{3,6,8} and have been used in procedures for the alkylation of aromatic rings and for the production of various polymerization catalysts.^{4,6,9}

References and Notes

1. Chemistry Department, The University, Reading, England.
 2. D. Bryce-Smith and G. F. Cox, *J. Chem. Soc.*, 1175 (1961).
 3. E. T. Blues and D. Bryce-Smith, *Chem. Ind. (London)*, 1533 (1960); Brit. Patent 955,806 (1964).
 4. D. Bryce-Smith, *Bull. Soc. Chim. France*, 1418 (1963).
 5. L. I. Zakharkin, O. Yu. Okhlobystin, and B. N. Strunin, *Tetrahedron Lett.*, 631 (1962).
 6. D. Bryce-Smith and G. F. Cox, *J. Chem. Soc.*, 1050 (1958).
 7. F. J. Buescher, A. H. Frye, G. J. Goepfert, and V. G. Soukup, Abstracts of Papers presented at the Symposium on Current Trends in Organometallic Chemistry, University of Cincinnati, June, 1963, p. 10.
 8. L. I. Zakharkin, O. Yu. Okhlobystin, and B. N. Strunin, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 2002 (1962).
 9. E. T. Blues and D. Bryce-Smith, *Proc. Chem. Soc.*, 245 (1961); Brit. Patent 955,807 (1964).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

calcium sulfate (Drierite)

light petroleum

calcium chloride (10043-52-4)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ether,
diethyl ether (60-29-7)

hydrogen (1333-74-0)

magnesium,
magnesium turnings,
magnesium powder (7439-95-4)

propylene (115-07-1)

sodium carbonate (497-19-8)

PHOSPHORUS (7723-14-0)

oxygen (7782-44-7)

nitrogen (7727-37-9)

tin (7440-31-5)

aluminum (7429-90-5)

mercury (7439-97-6)

carbon dioxide (124-38-9)

iodine (7553-56-2)

acetone (67-64-1)

chlorobenzene (108-90-7)

toluene (108-88-3)

2-propanol (67-63-0)

aluminum isopropoxide

1-chlorobutane (109-69-3)

methylcyclohexane (108-87-2)

antimony (7440-36-0)

cumene,
isopropylbenzene (98-82-8)

Tetralin (119-64-2)

boron (7440-42-8)

butane,
n-butane (106-97-8)

magnesium chloride (7786-30-3)

Tetrahydrofuran (109-99-9)

arsenic

1-chloronaphthalene (90-13-1)

chromous chloride (10049-05-5)

germanium

decalin (91-17-8)

silicon

n-BUTYLMAGNESIUM CHLORIDE (693-04-9)

trans-butene-2 (624-64-6)

