



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.

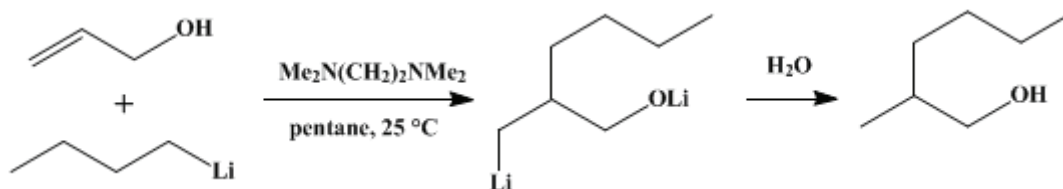
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ADDITION OF ORGANOLITHIUM REAGENTS TO ALLYL ALCOHOL: 2-METHYL-1-HEXANOL

[1-Hexanol, 2-methyl-]



Submitted by J. K. Crandall¹ and A. C. Rojas.

Checked by D. E. Berthet and G. Büchi.

1. Procedure

A 500-ml., three-necked, round-bottomed flask is fitted with a gas-inlet tube, a rubber septum, a reflux condenser connected to a mineral oil bubbler, and a sealed mechanical stirrer. The system is flamed with a Bunsen burner as it is flushed with dry nitrogen. The reaction vessel is cooled under nitrogen in an ice bath, and 7.25 g. (0.125 mole) of 2-propen-1-ol (Note 1), 70 ml. of pentane (Note 2), and 1.16 g. (0.0100 mole) of *N,N,N',N'*-tetramethyl-1,2-ethanediamine (Note 3) are added successively through the rubber septum with a syringe. While maintaining a positive nitrogen pressure, 180 ml. of 1.5 *M* (0.270 mole) *n*-butyllithium in pentane (Note 4) is added from a syringe over a 20-minute period (Note 5). The ice bath is removed, and the reaction mixture is stirred for an additional hour (Note 6). The ice bath is then restored, the gas-inlet tube replaced with a pressure-equalizing dropping funnel, and 70 ml. of water is added, cautiously at first, and then more rapidly after the exothermic reaction ceases. The resulting mixture is transferred to a separatory funnel, the aqueous layer is separated and discarded, and the pentane layer is washed with a 10-ml. portion of 3 *N* hydrochloric acid, then two 10-ml. portions of water. The organic layer is dried over anhydrous magnesium sulfate and filtered. The solvent is removed by distillation through a 20-cm. Vigreux column. Distillation of the residual oil through a short-path distillation apparatus yields 9.3–9.6 g. (64–66%) (Note 7) of 2-methyl-1-hexanol, b.p. 166–167° (Note 8) and (Note 9).

2. Notes

1. Commercial 2-propen-1-ol was purchased from Aldrich Chemical Company, Inc., and was distilled prior to use (b.p. 94.5–95°).
2. Technical grade pentane was distilled from concentrated sulfuric acid.
3. Commercial *N,N,N',N'*-tetramethyl-1,2-ethanediamine was obtained from Aldrich Chemical Company, Inc., and distilled prior to use (b.p. 119.5°).
4. Commercial solutions of *n*-butyllithium were obtained from Foote Mineral Company.
5. During the addition of *n*-butyllithium, a gel forms. If the solution is not well agitated during this period, the yield is somewhat lower.
6. Extending the reaction time did not increase the yield.
7. The checker's yield was 10.5–10.7 g. (72–74%) (see Note 5).
8. The purity of the product is greater than 99% as determined by GC analysis using a 6-m. column of 30% Carbowax 20M on 60–80 Chromosorb W. The major impurity (<1%) was shown to be 3-heptanol by comparison of GC retention times and mass spectral fragmentation patterns with those of an authentic sample.
9. The spectral properties of the product are as follows; IR (neat) cm^{-1} : 3268, 1377, 1037; ¹H NMR (CCl₄), δ (multiplicity, number of protons): 0.88 (m, 6H), 1.38 (m, 7H), 3.33 (unresolved d, 2H), 5.14 (broad s, 1H).

3. Discussion

This procedure illustrates a convenient method of converting allyl alcohol to 2-substituted-1propanols by the addition of an organolithium reagent.² A variety of organolithiums have given moderate to high yields of the corresponding alcohols. The indicated organolithium species is a demonstrated intermediate which can, in principle, be employed in a host of further synthetic conversions.² Substituted allylic alcohols, however, do not undergo analogous conversions efficiently, except when the substituent is at the carbinol carbon.²

2-Methyl-1-hexanol has also been prepared by the reaction of 2-hexylmagnesium halides with formaldehyde,³ the reduction of 2-methylhexanoic acid or its ester,^{4,5} and by hydroformylation of 1hexene^{6,7,8} among others.

References and Notes

1. Department of Chemistry, Indiana University, Bloomington, Indiana 47401.
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4. P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **84**, 571 (1929).
5. M. Leclercq, J. Billard, and J. Jacques, *Mol. Cryst. Liq. Cryst.*, **8**, 367 (1969).
6. I. Wender, R. Levine, and M. Orchin, *J. Am. Chem. Soc.*, **72**, 4375 (1950).
7. T. Asahara, H. Sekiguchi, and C. Kimura, *Yuki Gosei Kagaku Kyokai Shi*, **10**, 538 (1952) [*Chem. Abstr.*, **47**, 11123i (1953)].
8. British Petroleum Company Ltd., Fr. Pat. 1,549,414 (1968) [*Chem. Abstr.*, **72**, 2995p (1970)].

Appendix

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

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

formaldehyde (50-00-0)

Allyl alcohol,
ALLYLIC ALCOHOLS,
2-propen-1-ol (107-18-6)

nitrogen (7727-37-9)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

n-butyllithium (109-72-8)

1-hexene (592-41-6)

2-Methyl-1-hexanol,
1-Hexanol, 2-methyl- (61949-26-6)

3-heptanol (589-82-2)

2-methylhexanoic acid (4536-23-6)

N,N,N',N'-tetramethyl-1,2-ethanediamine (110-18-9)