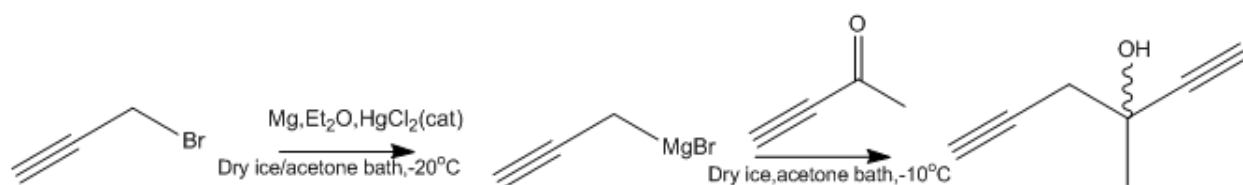


Diacetylenic alcohols by in situ Grignard reaction with acetylenic aldehydes or ketones; 3-methyl-1,5-hexadiyn-3-ol

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Chemicals Used

Propargyl bromide (3-bromopropyne), Manchester Chemicals, freshly distilled, N34375.

Magnesium turnings, chip, 99.8%, Sigma-Aldrich, 25,411-8.

Ether, anhydrous, 99.8%, Sigma-Aldrich, unless fresh material, dry just before use over sodium wire or lithium aluminum hydride, 29,608-2.

Mercuric chloride, 98% or better, Sigma-Aldrich, 41,344-5.

3-Butyn-2-one, 99.5%, Sigma-Aldrich, 161314, or Manchester Chemicals, Y10022, redistill before use.

Ammonium chloride, 99.5%, ACS reagent, Sigma-Aldrich, 21,330-0.

Tetrahydrofuran, 99.5%, HPLC grade, Sigma-Aldrich, 27,038-5.

Procedure

An oven-dried one liter three-neck flask was equipped with a mechanical stirrer, heating mantle, dropping funnel, nitrogen inlet, Friedrich water condenser and calcium chloride drying tube. The flask was charged with 0.1 g of mercuric chloride, 24 g (1 mol) of magnesium turnings, 200 ml of dry diethyl ether and 4 g redistilled propargyl bromide. The mixture was stirred, then gently warmed, until reaction commenced after 10 minutes, as evidenced by a white solution and moderate ether reflux. The flask was then immersed in a dry ice/acetone bath maintained at approximately -20 °C. A solution of 56 g redistilled propargyl bromide (total 0.50 mol) and 23 g (0.34 mole) 3-butyn-2-one (0.34 mole) in 200 ml dry ether was then added drop-wise, with vigorous stirring, over a

four hour period. The bath was maintained at approximately $-10\text{ }^{\circ}\text{C}$. After the addition was complete, 10ml dry THF was added to dissolve precipitated Grignard complex. The mixture was allowed to come to room temperature over one hour and the contents of the flask were poured into a two liter beaker containing a well mixed slurry of $\sim 500\text{g}$ crushed ice and $\sim 500\text{g}$ ammonium chloride. The mixture was stirred manually with the mechanical stirrer until two clear layers were present, and all excess magnesium chips and salts had dissolved. The upper ether layer was separated in a separatory funnel and the aqueous layer extracted three times in the separatory funnel with 10 ml ether portions. The combined ether layers were shaken three times with 20 ml deionized water portions and dried over 5g anhydrous magnesium sulfate for one hour. Evaporation of the ether on a steam bath in a fume hood yielded 40.5 g of a light yellow oil. Careful fractionation of the crude material in an oil bath under water vacuum pressure ($\sim 80^{\circ}\text{C}$ bath temperature) with a short path distillation column yielded 36.8 g of product in three fractions (66% based on the amount of 3-butyn-2-one used), which were $>97\%$ pure on both SE-30 and Triton-X-305 columns, and which contained no isomeric internal acetylenic or allenic alcohols. Infrared spectra showed no trace of a characteristic strong allenic stretch at $\sim 1950\text{ cm}^{-1}$ and proton n.m.r. was devoid of peaks due to internal acetylenic and allenic products.

Author's Comments

In order to avoid an internal rearrangement of the propargyl Grignard reagent, a modification of the procedure reported by Sondheimer (other reference 1), was utilized. Without this modification, a room temperature standard Grignard synthesis of 1-hexen-5-yne-3-ol (see lead reference), gave an approximate 50/50 mixture of desired product and the rearranged internal alkyne product 1-hexen-4-yn-3ol. This reaction gives yields in the 50-70% range as long as the instructions below are followed.

As with all Grignard syntheses, glassware should be dried in an oven before use, and the diethyl ether must be 99.9% or dried before use over sodium wire or lithium aluminum hydride.

Unsaturated carbonyl reactants should be distilled before use.

Mercuric chloride is toxic, and although used in very small quantities in these reactions latex gloves should be used when manipulating this material.

Propargyl bromide is toxic and a potent lacrimator, as is 3-butyn-2-one. Work in an efficient fume hood

Diethyl ether is extremely flammable and open flames must be avoided near this material.

Other di acetylenic alcohols were prepared in fair to excellent yield by this procedure. See: http://www.ccl.net/cca/documents/MacMillan_Papers/Acetylenic_Alcohols.pdf and secondary reference 3.

No trace of product alcohols resulting from rearrangement of propargyl Grignard to

internal acetylenic or allenic species could be detected under these conditions. In contrast, room temperature reactions gave alcohol product mixtures resulting from the rearrangement of propargyl Grignards to internal alkynyl or allenyl Grignards. This synthetic modification is of great utility in preparation of alcohol precursors for annulene synthesis or acetylenic oxy-Cope rearrangements.

Data

b.p. 50 °C (10 mmHg), n_D^{25} 1.4628, d_4^{28} 0.9288

Anal. Calc. For C_7H_8O : C, 77.78; H, 7.46.

Found: C, 77.59; H, 7.30

IR (neat film), 3400(s), 3300 (spike, s), 2900 (m), 2120 (w), 1450 (s), 1420 (m), 1380 (s), 1360 (s), 1260 (m), 1160 (m), 1130 (s), 1090 (s), 950 (m), 940 (m), 910 (w), 875 (m), and 650 (s) cm^{-1} .

1H NMR (60 Mhz, $CDCl_3$) δ 1.65 (s, 3H, methyl) 2.25 (t, 1H, acetylenic), 2.65 (d, 2H, aliphatics), 3.30 (s, broad, 1H, hydroxyl)

Lead Reference

A. Viola and J.H. MacMillan, J. Amer. Chem. Soc., 90, 6141, (1968).

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Other References

1) F. Sondheimer, Y. Amiel, and Y. Gaoni, J. Amer. Chem. Soc., 84, 270-274, (1962).
DOI: [10.1021/ja00861a029](https://doi.org/10.1021/ja00861a029)

2) Chemspider <http://www.chemspider.com/Chemical-Structure.29332401.html>

3) John H. MacMillan and Alfred Viola "The Acetylenic-Oxy-Cope Rearrangement of 1,5-Hexadiyne-3-ol and Methyl Substituted Derivatives", Internet Archive, 2012

http://www.ccl.net/cca/documents/MacMillan_Papers/The_Acetylenic-Oxy-Cope_Rearrangement_of_1_5-Hexadiyne-3-ol_and_Methyl_Substituted_Derivatives.pdf

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