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Working with Hazardous Chemicals

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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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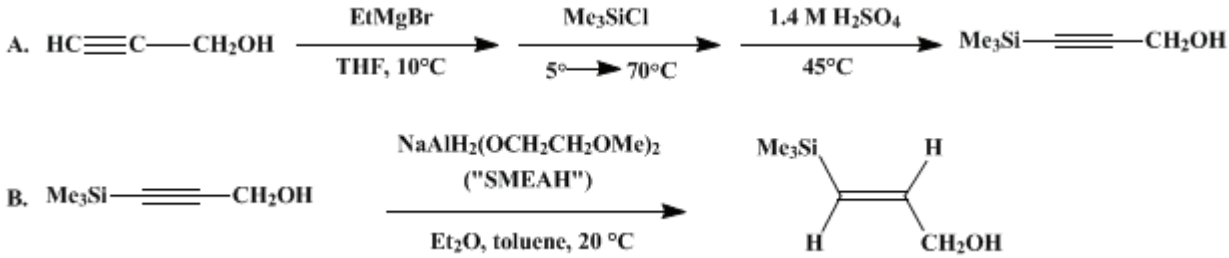
STEREOSPECIFIC REDUCTION OF PROPARGYL ALCOHOLS: (*E*)-3-TRIMETHYLSILYL-2-PROPEN-1-OL

[2-Propen-1-ol, 3-(trimethylsilyl)-, (*E*)-]



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Checked by Steven M. Viti and K. Barry Sharlpess.

1. Procedure

A. *3-Trimethylsilyl-2-propyn-1-ol.* A 3-L, three-necked, round-bottomed flask (equipped with a mechanical stirrer and a thermometer) is fitted with a Claisen adapter on which is mounted a 250-mL pressure-equalizing addition funnel and a reflux condenser (Note 1). The apparatus is flushed with nitrogen and then charged with 48.7 g (2.0 mol) of magnesium turnings and 1 L of dry tetrahydrofuran (Note 2). To the stirred suspension is added dropwise 149.5 mL (218.3 g, 2.0 mol) of bromoethane over 3 hr while maintaining the temperature at 50°C or less. After complete addition, the gray–green solution is heated at 50°C for 1 hr and then cooled to 5°C on ice. A solution of 41.6 mL (40.5 g, 0.72 mol) of propargyl alcohol (Note 3) in 42 mL of tetrahydrofuran is cautiously added dropwise to the gray suspension over 2.25 hr while maintaining the temperature at 10°C or less (Note 4). The addition funnel is rinsed with 25 mL of tetrahydrofuran and the gray–green suspension is stirred overnight. The resulting solution is cooled to 5°C on ice and the addition funnel is charged with 254 mL (217 g, 2.0 mol) of chlorotrimethylsilane (Note 5). This is added dropwise to the stirred solution over 1 hr while maintaining the temperature at 25°C or less by external cooling with ice. After complete addition, the mixture is heated to reflux for 2 hr with a heating mantle (Note 6). The suspension is cooled to 20°C on ice and then 800 mL of 1.4 *M* aqueous sulfuric acid is cautiously added over 0.75 hr so that the temperature remains below 45°C. The resulting solution is stirred for 5 min and then 600 mL of ether is added. Both phases are transferred to a 4-L separatory funnel and the layers are separated. The aqueous phase is extracted twice with 400-mL portions of ether and all ether layers are individually washed in series with two 1-L portions of water and once with 800 mL of saturated sodium chloride solution. The combined organic extracts are dried over magnesium sulfate and concentrated by rotary evaporation. The yellow–brown residue is purified by short path distillation to afford 82–86 g (91–94% yield) of 3-trimethylsilyl-2-propyn-1-ol as a clear, colorless liquid (Note 7), bp 76°C (20 mm) (Note 8).

B. *(E)-3-Trimethylsilyl-2-propen-1-ol.* A three-necked, 2-L, round-bottomed flask fitted with a thermometer, nitrogen inlet, 250-mL pressure-equalizing addition funnel, and magnetic stirring bar is charged with 147 mL of a 3.4 *M* solution of sodium bis(2-methoxyethoxy)aluminum hydride (SMEAH, (Note 9)) and 200 mL of anhydrous ether (Note 10). The SMEAH solution is cooled to 3°C on ice and then treated dropwise from the addition funnel with a solution of 40 g (0.31 mol) of 3-trimethylsilyl-2-propyn-1-ol in 180 mL of ether over 1.25 hr, while maintaining the temperature at 5°C or less. Then 10 min after complete addition, the ice bath is removed and the reaction is complete within 1 hr (Note 11). The mixture is cooled to 0°C and then quenched by the addition of 1 L of 3.6 *M* aqueous sulfuric acid (Note 12). The layers are separated in a separatory funnel and the aqueous phase is extracted twice with 200-mL portions of ether. All ether layers are individually washed in series with two 200-mL portions of water and once with 200 mL of saturated sodium chloride. The combined organic extracts are dried over magnesium sulfate and concentrated by rotary evaporation. Distillation of the yellow residue with a capillary bleed affords 27.7–29.0 g (68–71%) of (*E*)-3-trimethylsilyl-2-propen-1-ol (Note 13) as a clear,

colorless liquid, bp 73–75°C (20 mm) (Note 14).

2. Notes

1. It is not necessary to flame or oven-dry this apparatus, but a nitrogen inlet on the reflux condenser is desirable. The size of the stirring paddle is critical because of the viscous nature of the solution during this protection step. A paddle at least 11 cm in length is recommended to ensure complete mixing.
2. Magnesium turnings and bromoethane are Mallinckrodt AR grade and are used without purification. Tetrahydrofuran is Aldrich Gold Label and is distilled from sodium benzophenone ketyl prior to use.
3. Propargyl alcohol is obtained from Aldrich Chemical Company, Inc. and is distilled from potassium carbonate.
4. Evolution of ethane can conveniently be monitored with a Nujol bubbler in the nitrogen line by turning off the nitrogen flow.
5. Chlorotrimethylsilane is purchased from Silar and used as received.
6. The progress of the reaction can be monitored by gas chromatography. Column: 5% Carbowax 12 M on acid-washed Chromosorb W, 6 ft × one-eighth in; temperature program: 70°C (2 min), 20°C/min, 200°C (5 min). Retention times: propargyl alcohol, 2.4 min; 3-trimethyl-2-propyn-1-ol, 4.8 min.
7. *Caution! The distillation pot may ignite if it is exposed to air before it is allowed to cool.* The product thus obtained is 94–98% pure by GC analysis and is of suitable purity for reduction. Further purification can be effected by distillation through a 6-in. Vigreux column.
8. The product has the following spectral characteristics: ^{1}H NMR (90 MHz, $CDCl_3$) δ: 0.27 [s, 9 H, $(CH_3)_3Si$], 1.65 (s, 1 H, OH), 4.28 [s, 2 H, 2 H-C(1)].
9. Sodium bis(2-methoxyethoxy)aluminum hydride is obtained as a 70% solution in toluene from Aldrich Chemical Company, Inc. (Red-Al). Iodometric titration gives a 3.6 *M* concentration.
10. Anhydrous ether is obtained from Mallinckrodt, Inc. (AR grade) and used without purification.
11. The reaction can be monitored by gas chromatography (Note 6), temperature program: 70°C (2 min), 20°C/min, 150°C (2 min). Retention times: (*E*)-3-trimethylsilyl-2-propen-1-ol, 4.2 min; 3-trimethylsilyl-2-propyn-1-ol, 6.1 min.
12. A vigorous evolution of hydrogen accompanies the addition of the first milliliters of sulfuric acid. The reaction mixture becomes gelatinous and unstirable but clarifies on further addition of acid.
13. The product is 100% E geometry by GC analysis.
14. The product has the following spectral characteristics: ^{1}H NMR(90 MHz, $CDCl_3$) δ: 0.23 [s, 9 H, $(CH_3)_3Si$], 1.5 (t, 1 H, J = 6, OH), 4.22 [d of d, 2 H, J = 6 and 4, 2 H-C(1)], 5.93 [d, 1 H, J = 18, H-C(3)], 6.23 [d of t, 1 H, J = 18 and 4, H-C(2)].

3. Discussion

The silylation of propargyl alcohol dianion[2] described here is a further modification of the procedure recently reported.[3] By replacing ether with tetrahydrofuran the reaction mixture is more manageable and the silyl ether can be hydrolyzed in situ obviating an unnecessary workup and distillation. The yield correspondingly improves by up to 91–94%. Silylation of the dilithium salt in ether is reported[4] to proceed in 86% yield.

Reduction of 3-trimethylsilyl-2-propyn-1-ol exemplifies the problem of stereoselectivity in hydride reduction of acetylenic alcohols to *E*-allyl alcohols.[5,6] Early reports[7,8] that lithium aluminum hydride stereoselectively reduced acetylenic alcohols gave way to closer scrutiny, which revealed a striking solvent dependence of the stereochemistry.[9] Specifically, the percentage of trans reduction is seen to increase with increasing Lewis basicity of solvent. Similarly, the addition of less Lewis acidic cations to the reducing mixture leads to improved trans : cis ratios.[10,11] Sodium bis(2-methoxyethoxy)aluminum hydride (SMEAH)[12,13,14] makes use of these phenomena simultaneously (even in ether–toluene mixtures) and leads to completely stereospecific trans reduction where lithium aluminum hydride in various solvents or with sodium methoxide is less selective.[3,15,16,17] The use of SMEAH to reduce stereospecifically other acetylenic alcohols has been reported.[18,19]

(*E*)-3-Trimethylsilyl-2-propen-1-ol is a versatile intermediate used to introduce organosilicon functional groups into organic molecules.[15,20] The corresponding aldehyde has found use in the preparation of β-silyl divinyl ketones[21,22,23,24] and as a precursor for 1-trimethylsilyl-substituted

dienes.[16,17,25]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 9, 510

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

sodium benzophenone ketyl

PROPARGYL ALCOHOLS

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

ether (60-29-7)

hydrogen (1333-74-0)

magnesium turnings (7439-95-4)

sodium chloride (7647-14-5)

bromoethane (74-96-4)

nitrogen (7727-37-9)

sodium methoxide (124-41-4)

toluene (108-88-3)

magnesium sulfate (7487-88-9)

ethane (74-84-0)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

acetylenic alcohols (32038-79-2)

propargyl alcohol (107-19-7)

CHLOROTRIMETHYLSILANE (75-77-4)

3-Trimethylsilyl-2-propyn-1-ol (5272-36-6)

sodium bis(2-methoxyethoxy)aluminum hydride

3-trimethyl-2-propyn-1-ol (590-38-5)

(E)-3-Trimethylsilyl-2-propen-1-ol,
2-Propen-1-ol, 3-(trimethylsilyl)-, (E)- (59376-64-6)