Organic Syntheses

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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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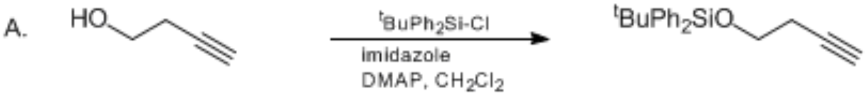
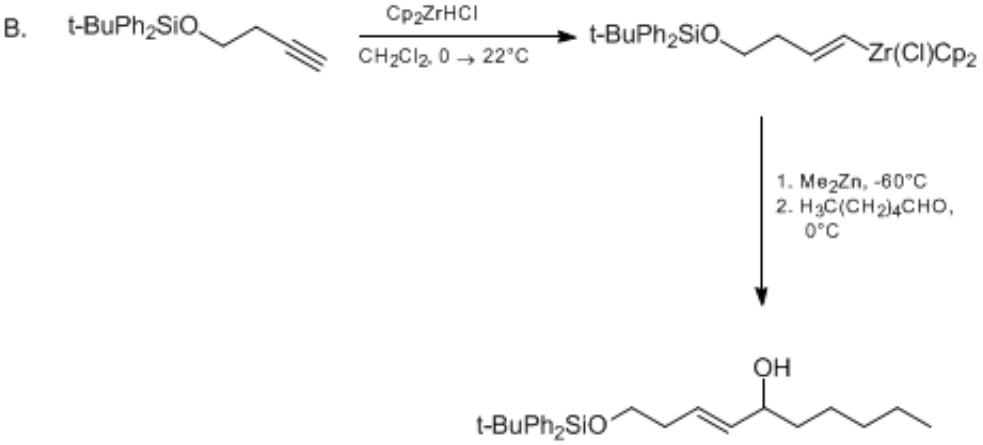
ALLYLIC ALCOHOLS BY ALKENE TRANSFER FROM ZIRCONIUM TO ZINC: 1-[(tert-BUTYLDIPHENYLSILYL)OXY]-DEC-3-EN-5-OL





Submitted by Peter Wipf and Wenjing Xu[1].
Checked by Thomas Wynn and Louis S. Hegedus.

1. Procedure

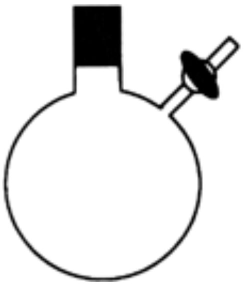
Caution! Dialkylzinc compounds, especially in undiluted form, are pyrophoric and must not be allowed to come into contact with air or moisture. These compounds should only be handled by individuals trained in their proper and safe use. [Note added January 2011]

A. *tert-Butyl(but-3-ynyloxy)diphenylsilane*. A dry, 250-mL, round-bottomed flask is fitted with a rubber septum and a magnetic stirring bar. The flask is charged with 3-butyn-1-ol (2.1 g, 30 mmol) (Note 1) and dry dichloromethane (60 mL) (Note 2). After addition of 8.5 g (31 mmol) of tert-butyldiphenylchlorosilane (Note 3), the reaction flask is immersed in a water bath and imidazole (2.86 g, 42 mmol) is added in one portion followed by 4-dimethylaminopyridine (0.37 g, 3 mmol). The water bath is removed and the reaction mixture is stirred at room temperature overnight. The white precipitate is filtered through a sintered glass funnel (`M' frit). The precipitate is washed with cold dichloromethane (50 mL). The combined filtrates are transferred to a 500-mL separatory funnel and washed with 1 M aqueous hydrochloric acid solution (50 mL) and water (100 mL), successively. The organic layer is dried over magnesium sulfate and concentrated by rotary evaporator. Bulb-to-bulb distillation of the residue (bp 150–152°C/1 mm) gives 8.90 g (96%) of tert-butyl(but-3-ynyloxy)diphenylsilane as a colorless oil (Note 4).

B. *1-[(tert-Butyldiphenylsilyloxy)]-dec-3-en-5-ol*. A flame-dried, 250-mL, round-bottomed flask equipped with a gas inlet stopcock (Figure 1) is fitted with a rubber septum and a magnetic stirring bar, and flushed with nitrogen. The flask is charged with tert-butyl(but-3-ynyloxy)diphenylsilane (5.55 g, 18 mmol) and dry dichloromethane (60 mL), immersed in a cold water bath and stirred. Within 20 min, 5.10

g (19.8 mmol) of zirconocene hydrochloride (Note 5) is added in five portions. The water bath is removed and the reaction mixture is stirred at room temperature until a homogenous solution forms. The resulting golden-yellow solution is stirred for another 20 min (Note 6) and then cooled to −60°C. By syringe, dimethylzinc (2.0 M solution in toluene, 10.4 mL, 20.8 mmol) (Note 1) is added dropwise over 45 min while the bath temperature is kept at −60°C. The resulting orange-yellow solution is stirred for an additional 10 min at −60°C after the addition is completed. The reaction flask is immersed in an ice bath, and a solution of 2.16 g (21.6 mmol) of hexanal (Note 1) in dry dichloromethane (10 mL) is added via syringe over 45 min. The reaction mixture is stirred at 0°C for another 6 hr. The yellow solution is poured slowly into a beaker containing ice-cold aqueous 5% sodium bicarbonate solution (200 mL) and vigorous stirring is continued at room temperature until gas evolution subsides. The mixture is transferred to a 1-L separatory funnel and is extracted with diethyl ether (3 × 200 mL) (Note 7). The combined extracts are washed with a saturated aqueous sodium chloride solution (300 mL) and dried over sodium sulfate. The cloudy solution is filtered through a pad of Florisil (Note 8) loaded on a sintered glass funnel (`M' frit). The clear filtrate solution is concentrated by rotary evaporator. The residue is layered on a column of silica gel (150 g, column diameter: 6.0 cm) and eluted (ethyl acetate/hexane, 1:30 to 1:15 as eluents) to give 4.90 g (66%) of 1-[(tert-butyldiphenyl-silyl)oxy]-dec-3-en-5-ol as a colorless oil (Note 9).

Figure 1



2. Notes

1. 3-Butyn-1-ol, dimethylzinc and hexanal were obtained from Aldrich Chemical Company, Inc., and used without purification.
2. Solvent grade dichloromethane was dried over calcium hydride, refluxed and distilled freshly before use.
3. tert-Butyldiphenylchlorosilane was obtained from United Chemical Technologies, Inc. or Aldrich Chemical Company, Inc., and used without purification.
4. The product has the following spectral properties: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.06 (s, 9 H), 1.95 (t, 1 H, J = 2.6), 2.45 (dt, 2 H, J = 7.1, 2.7), 3.79 (t, 2 H, J = 7.1), 7.36–7.46 (m, 6 H), 7.67–7.70 (m, 4 H).
5. Zirconocene hydrochloride was prepared according to Buchwald's procedure[2] and stored in a Schlenk filter flask under argon in a freezer at −20°C or obtained from Aldrich Chemical Company, Inc., and used without further purification.
6. The reaction is conveniently monitored by TLC (silica gel, 4:1 hexane-ethyl acetate) with anisaldehyde stain (alkyne stains as a red spot, while the hydrozirconation product shows a blue color).
7. Significant amounts of white foam form between the ether and aqueous layers during extraction. Separation of these layers can be improved by the addition of 1–2 spoonfuls of solid sodium chloride.
8. Florisil (100–200 mesh) was obtained from Fisher Scientific Company.
9. The product has the following spectral data: IR (neat) cm^{-1}: 3350, 2912, 1454, 1417, 1099, 733, 698, 609; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.88 (t, 3 H, J = 6.7), 1.05 (s, 9 H), 1.34–1.51 (m, 9 H), 2.26–2.33 (m, 2 H), 3.71 (t, 2 H, J = 6.6), 4.00–4.03 (m, 1 H), 5.49 (dd, 1 H, J = 15.5, 6.8), 5.64 (dt, 1 H, J = 15.5, 6.7), 7.35–7.46 (m, 6 H), 7.66–7.69 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ: 14.1, 19.2, 22.6, 25.2, 26.9, 31.8, 35.6, 37.2, 63.6, 73.1, 127.7, 128.2, 129.6, 133.9, 135.2, 135.6; MS (EI) m/e (relative intensity) 353 ([M-tert-butyl]+, 4), 335 (20), 229 (25), 199 (100), 135 (20), 91 (15), 57 (10); HRMS (EI) m/e calcd. for

$C_{22}H_{29}O_2Si$ (M-C_4H_9): 353.1937, found: 353.1833.

Waste Disposal Information

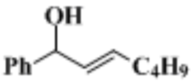
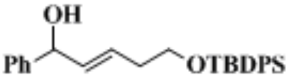
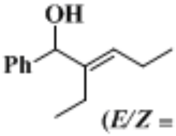
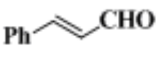
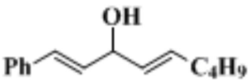
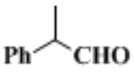
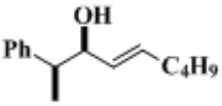
All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

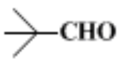
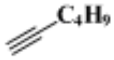
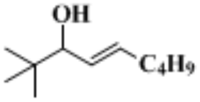
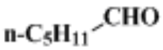
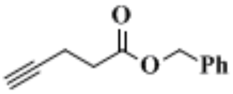
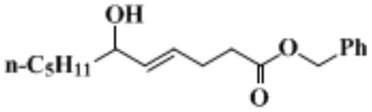
3. Discussion

Organometallic derivatives of zirconium(IV) are readily obtained by hydrozirconation of alkenes and alkynes with Cp_2ZrHCl (Schwartz reagent). Because of the relatively low reactivity of the resulting organozirconocenes, transmetalation protocols are frequently applied for further carbon-carbon formation.[3] [4] Transmetalation of alkenylzirconocenes to the corresponding organozinc compounds occurs rapidly at low temperature in the presence of stoichiometric amounts of commercially available dimethyl- or diethylzinc. Subsequent addition of aldehydes provides an in situ protocol for the conversion of alkynes into allylic alcohols in good to excellent yields.[5] Compared to standard organometallic methods applying lithium or Grignard reagents for this transformation, the use zirconocenes tolerates the presence of a wide range of functional groups in the substrate (Table). The zirconium → zinc transmetalation is related in scope to the boron → zinc transmetalation, which can also be applied for the conversion of alkynes to allylic alcohols.[6] [7]

TABLE I

REACTION OF *IN SITU* GENERATED ALKENYLALKYLZINC REAGENTS WITH ALDEHYDES

Aldehyde	Alkyne	Time (h)	Product	yield (%)
PhCHO		1		93
PhCHO		2		89
PhCHO		5	 (*E/Z* = 2.5:1)	78
		1.5		94
		1.5	 (*syn:anti* = 85:15)	92

		2		54
		2		72#

On 5 g scale, this product was isolated in 68% yield.

References and Notes

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7. Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593.

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

zirconocene hydrochloride

dimethyl- or diethylzinc

hydrochloric acid (7647-01-0)

ethyl acetate (141-78-6)

ether,
diethyl ether (60-29-7)

sodium bicarbonate (144-55-8)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

PhCHO (100-52-7)

toluene (108-88-3)

zinc (7440-66-6)

dichloromethane (75-09-2)

lithium (7439-93-2)

magnesium sulfate (7487-88-9)

Imidazole (288-32-4)

hexane (110-54-3)

zirconium

argon (7440-37-1)

carbon-carbon

calcium hydride (7789-78-8)

3-butyn-1-ol (927-74-2)

Hexanal (66-25-1)

4-dimethylaminopyridine (1122-58-3)

tert-butyldiphenylchlorosilane (58479-61-1)

1-[(tert-Butyldiphenylsilyloxy)]-dec-3-en-5-ol,
1-[(tert-butyldiphenyl-silyl)oxy]-dec-3-en-5-ol,
1-[(tert-BUTYLDIPHENYLSILYL)OXY]-DEC-3-EN-5-OL (190072-44-7)

tert-Butyl(but-3-ynyloxy)diphenylsilane

dimethylzinc (544-97-8)

zirconium(IV)