



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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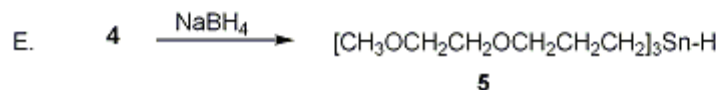
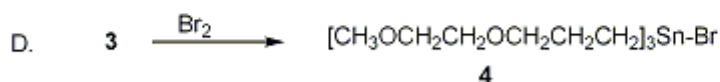
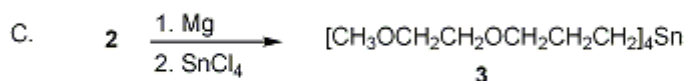
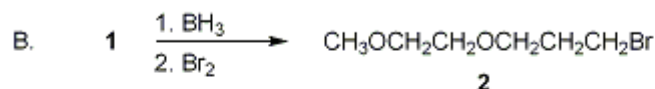
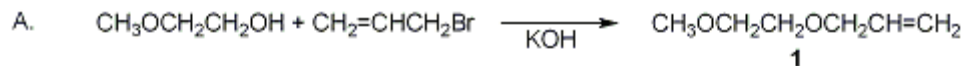
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions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

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A WATER-SOLUBLE TIN HYDRIDE: TRIS[3-(2-METHOXYETHOXY)PROPYL]STANNANE

[2,5,13,16-Tetraoxa-9-stannaheptadecane, 9-[3-(2-methoxyethoxy)propyl]-]



Submitted by James Light and Ronald Breslow¹.

Checked by Scott R. Breining and Robert K. Boeckman, Jr..

1. Procedure

A. *3-(2-Methoxyethoxy)propene* (1). A three-necked, 1000-mL flask equipped with a thermometer, mechanical stirrer, and dropping funnel is charged with 51 g (0.9 mol) of potassium hydroxide (KOH, (Note 1)) and 65 mL (62.3 g, 0.82 mol) of dry 2-methoxyethanol (Note 2). The resulting mixture is cooled in an ice bath, efficient stirring is begun, and 72 mL (100 g, 0.82 mol) of allyl bromide (Note 3) is added dropwise, keeping the internal temperature below 10°C (Note 3). After the solution is stirred overnight, the sticky white solid is collected by suction filtration and the collected solids are washed with 300 mL of hexanes. The combined yellow filtrate and washings are dried thoroughly over sodium sulfate (Na₂SO₄), and the whole mixture is distilled from calcium hydride (CaH₂) through a 6-in. Vigreux column (Note 4). The product (67–69 g, 70–73%) is collected from 115–129°C with the bulk of the material distilling at bp 117–127°C, and is 94% pure (as judged by gas chromatography, (Note 5), (Note 6), (Note 7)).

B. *1-Bromo-3-(2-methoxyethoxy)propane* (2). A flame-dried, three-necked, 1000-mL flask that is equipped for magnetic stirring, and has a dry addition funnel and a thermometer, is placed under an inert atmosphere and charged with 209 mL (250 g, 0.209 mol) of a 1.0 M solution of borane-tetrahydrofuran complex (Note 2). The resulting solution is cooled to –10°C using a dry ice/ethylene glycol bath and 3-(2-methoxyethoxy)propene (1, 60 g, 0.52 mol) is added dropwise over ~1 hr keeping the internal temperature of the reaction mixture at or below 0°C. Methanol (1.5 mL) is added to destroy any excess borane, and the reaction mixture is stirred an additional 1 hr below 10°C.

After the reaction mixture is recooled to –15°C (internal temperature), 35 mL (107.8 g, 0.67 mol) of bromine (Br₂) is added dropwise over 1 hr, keeping the reaction temperature between –10° and 0°C. The mixture is stirred a further 1.5 hr at 0°C then recooled to –15°C. While cooling is maintained, 210 mL of a 4 M solution of sodium methoxide (0.84 mol) in methanol (freshly prepared from sodium metal) is added dropwise over 1.5 hr, keeping the reaction temperature between –15° and 0°C. The resulting orange brown solution and white precipitate are slowly warmed to room temperature and stirred overnight (16 hr).

Hexane (100 mL) is added to the reaction mixture causing more white precipitate to form. The mixture is filtered by suction, and the collected solids are washed with two 50-mL portions of hexane. The combined filtrate and washings are partitioned with 200 mL of a mixture (1:3 v/v) of saturated potassium carbonate solution and water (Note 8). The aqueous phase is extracted with three 200-mL portions of hexane. The combined organic phases are partitioned with 100 mL of saturated sodium chloride, dried thoroughly over anhydrous sodium sulfate and concentrated under reduced pressure to afford 65–75 g of crude product. A small amount of additional crude material can be isolated by continuously extracting the combined aqueous layers with hexane for 3 hr.

Distillation of the crude product through a 6-in. Vigreux column at 0.6 mm into a dry ice/acetone-cooled receiver affords 55–70 g of material bp $>40^{\circ}\text{C}/0.6$ mm that is $\sim 83\%$ pure (as judged by gas chromatography, (Note 6)). To obtain material of greater purity (94%) suitable for further transformation, a second distillation through a 6-in. Vigreux column packed with glass beads is required to afford 53–57 g (52–56%) of the bromide as a colorless liquid, bp $55\text{--}65^{\circ}\text{C}/0.6$ mm (Note 9).

C. *Tetra[3-(2-methoxyethoxy)propyl]stannane (3)*. A 500-mL, three-necked flask is fitted with a thermometer and a dried addition funnel, charged with 9.1 g (0.375 mol) of magnesium metal turnings (Note 2) and heated with a flame or heat gun while purging with argon. After the flask is cooled, 50 mL of dry tetrahydrofuran (THF) and a crystal of iodine are added, and the addition funnel is charged with 40 mL (52 g, 0.264 mol) of 1-bromo-3-(2-methoxyethoxy)propane (2, (Note 10)). Approximately 2 mL of the bromide is added to the reaction mixture, and the internal temperature of the mixture is monitored. When the temperature rises slightly ($\sim 3^{\circ}\text{C}$) and the iodine color is discharged indicating that formation of the Grignard reagent has begun, the reaction mixture is immediately cooled to -15°C in a dry ice/ethylene glycol bath, 100 mL of dry THF (Note 10) is added to the addition funnel, and 150 mL of dry THF (Note 10) is directly added to the reaction mixture. The bromide solution is added dropwise over 2 hr while keeping the reaction temperature between -15° and 5°C (Note 11).

The concentration of the Grignard reagent solution is determined by titration. An oven-dried, 10-mL flask with septum is charged with 1 mg of phenanthroline and 3.0 mL of the reaction mixture. 2-Methylpropanol is added until the red-purple color is dissipated and a yellow endpoint is reached. The yield of Grignard reagent is 0.184 mol (70%).

A dry, 1000-mL flask is placed under a nitrogen atmosphere, charged with 4.9 mL (0.042 mol) of tin(IV) chloride (SnCl_4 , (Note 1)), and cooled to -78°C in a dry ice/acetone bath with swirling. After the SnCl_4 solidifies on the walls of the flask, the flask is equipped for magnetic stirring. The previously prepared Grignard solution is added to the SnCl_4 as a slow stream via cannula and the reaction mixture is allowed to warm to room temperature with stirring overnight (20 hr). After the solution is stirred at room temperature for ~ 20 hr, the addition funnel is replaced by a reflux condenser, and the reaction mixture is heated at reflux for 4 hr by means of a heating mantle (Note 12). After the solution is cooled, the solvent is removed under reduced pressure, 300 mL of water is added, and the resulting mixture (a heavy precipitate results) is continuously extracted with 750 mL of hexane for 12–24 hr. The hexane solution is dried over magnesium sulfate (MgSO_4), and the volatile material is removed under reduced pressure, to afford 23.6–24 g (96–97% based on SnCl_4) of the tetraalkylstannane that is not homogeneous as judged by NMR integration. Pure stannane suitable for further transformation is obtained by removal of a low boiling impurity (bp $90\text{--}100^{\circ}\text{C}/0.6$ mm) under high vacuum to afford 21–23 g of purified stannane. Stannane (bp $210\text{--}215^{\circ}\text{C}$ at 0.005 mm) of even higher purity can be obtained by short-path distillation with some loss due to decomposition (Note 13).

D. *Bromotris[3-(2-methoxyethoxy)propyl]stannane (4)*. A dry, 50-mL, round-bottomed flask is placed under a nitrogen atmosphere and charged with 8.25 g (14.0 mmol) of tetra[3-(2-methoxyethoxy)propyl]stannane (3), and 40 mL of dry carbon tetrachloride (CCl_4) (Note 1). After the mixture is cooled to $\sim 0^{\circ}\text{C}$ in an ice-water bath, 14 mL of a 1 M solution of bromine (0.014 mol) in CCl_4 is added dropwise (Note 14). The mixture is allowed to warm slowly to room temperature and stand overnight. The solvent is removed under reduced pressure, and the residual brown liquid is purified by Kugelrohr distillation at 0.1 mm. A low boiling fraction (bp $<70^{\circ}\text{C}$) that contains alkyl bromide is discarded, and the residual material is distilled to afford 6.9–7.4 g (90–96%) of the bromotrialkylstannane (bp $100\text{--}110^{\circ}\text{C}$) as a pale tan viscous oil that is homogeneous as judged by NMR spectroscopy and of sufficient purity for further transformation (Note 15), (Note 16), (Note 17).

E. *Tris[3-(2-methoxyethoxy)propyl]stannane* (**5**). A 100-mL, round-bottomed flask equipped for magnetic stirring is placed under an inert atmosphere and charged with 5.0 g (4.5 mmol) of freshly distilled bromotris[3-(2-methoxyethoxy)propyl]stannane (**4**) and 40 mL of dry 1,2-dimethoxyethane (Note 10). To the stirred solution is added 2.0 g (54 mmol) of sodium borohydride (NaBH₄) (Note 2) at room temperature in portions at such a rate as is required to control foaming. The resulting white suspension is stirred at room temperature for 2.5 hr (the reaction appears complete nearly instantaneously) and then concentrated under reduced pressure. The residue is taken up in 50 mL of ether, suction filtered through a bed of Celite, and concentrated under reduced pressure to afford 3.47–3.64 g (82–86%) of the trialkyltin hydride as a clear colorless oil that is homogeneous by NMR. The trialkyltin hydride is pure enough for most purposes, but further purification is possible by short-path distillation to afford pure trialkyltin hydride bp 100–120°C (pot temperature) at 0.005–0.01 mm (Note 18).

2. Notes

1. Potassium hydroxide was A.C.S. reagent grade obtained from J. T. Baker Chemical Company and used as received.
2. 2-Methoxyethanol was research grade obtained from Aldrich Chemical Company, Inc., and used as received.
3. The reaction is exothermic, and temperature control is required for control of the reaction. Good agitation is essential to avoid occlusion of unreacted starting materials in the sticky precipitate.
4. Substantial amounts (grams) of CaH₂ may be required (care should be taken on addition because of foaming) if predrying with Na₂SO₄ is incomplete.
5. The boiling range is broad because of codistillation of the product with small amounts of allyl bromide and 2-methoxyethanol.
6. Analysis was performed on a 25-m fused silica capillary column with DX-3 (polymethylsiloxane) stationary phase and a temperature program from 50°C–150°C.
7. The spectra are as follows: ¹H NMR (300 MHz, CDCl₃) δ: 3.39 (s, 3 H), 3.59–3.61 (m, 4 H), 4.03 (dt, 2 H, J = 5.7, 1.6), 5.18 (dq, 1 H, J = 10.3, 1.6), 5.28 (dq, 1 H, J = 17.2, 1.6), 5.92 (ddt, 1 H, J₁ = 17.2, J₂ = 10.3, J₃ = 5.7); ¹³C NMR (75.43 MHz, CDCl₃) δ: 58.64, 69.03, 71.70, 71.95, 116.62, 134.55.
8. Three phases may result. If three phases are present, add the minimum amount of additional water that affords two phases. Addition of large amounts of water should be avoided because of the significant water solubility of the product.
9. The spectra are as follows: ¹H NMR (300 MHz, CDCl₃) δ: 2.18 (quintet, 2 H), 3.42 (s, 3 H), 3.54–3.68 (m, 8 H); ¹³C NMR (75.4 MHz, CDCl₃) δ: 30.57, 32.71, 58.99, 68.61, 70.23, 71.81. The checkers noted a larger variability in yield (38–56%).
10. Tetrahydrofuran and 1,2-dimethoxyethane were dried and deoxygenated by distillation from sodium benzophenone ketyl under argon.
11. Inadequate temperature control leads to the formation of by-products resulting from elimination.
12. Magnetic stirring is difficult because of the formation of a sticky precipitate. A very vigorous reaction ensues upon heating the mixture to reflux if inadequate agitation occurs during addition of the Grignard reagent or if the SnCl₄ is allowed to solidify in a pool in the bottom of the flask.
13. The spectra are as follows: ¹H NMR (300 MHz, CDCl₃) δ: 0.77 (m, 8 H, apparent t within a doublet), 1.78 (m, 8 H), 3.39 (s, 12 H), 3.39 (t, 8 H), 3.55 (AA'BB' m, 16 H); in D₂O, d₄-TSP ref. δ: 0.89 (m, 8 H), 1.84 (m, 8 H), 3.64 (m, 16 H), 3.53 (t, 8 H), 3.40 (s, 12 H); ¹³C NMR (75.4 MHz, CDCl₃) δ: 4.44, 26.69, 59.00, 69.95, 71.90, 74.82 (apparent ¹³C-¹¹⁹Sn ¹J = 322, ²J = 19, ³J = 66); ¹¹⁹Sn NMR 111.86 MHz (200 mg/mL) CDCl₃, Me₄Sn ref. δ: –3.8 ppm (inverse gated decoupled).
14. Discharge of the yellow color is instantaneous until >13 mL of the bromine solution is added. A persistent yellow color was not observed until 1 equiv of bromine had been added.
15. No unreacted tetraalkylstannane is observed when a full equivalent of bromine is employed.
16. The bromotrialkylstannane is stable to storage under argon in the freezer, and can be converted to the tin hydride as needed.
17. The spectra are as follows: ¹H NMR (300 MHz, C₆D₆) δ: 1.38 (br t, 6 H), 1.95 (br quintet, 6 H), 3.14 (s, 9 H), 3.25 (m, 12 H), 3.35 (m, 6 H); ¹³C NMR (75.4 MHz, CDCl₃) δ: 15.06 ppm (apparent ¹³C-¹¹⁹Sn ¹J = 413, ³J = 64), 26.04, 58.90, 70.06, 71.71, 73.44; ¹¹⁹Sn NMR 111.86 MHz (200 mg/mL), Me₄Sn ref. δ: +60.0 ppm (inverse gated decoupled). CI MS with NH₃ gave peaks at m/e 471 (base peak) and m/e 433 with the isotopic distribution expected for Sn and Br.

18. The spectra are as follows: ^1H NMR (300 MHz, C_6D_6) δ : 0.94 (td, 6 H, $J = 8$, $J_{\text{HSnCH}} = 1.8$), 1.85 (quintet, 6 H, $J_{\text{avg}} = 7$), 3.15 (s, 9 H), 3.36 (t, 6 H, $J = 6.4$), 3.40–3.52 (m, AA'BB', 12 H), 5.17 (br septet, 1 H, $J < 2$); ^{13}C NMR (75.4 MHz, C_6D_6) δ : 4.87, 27.54, 58.28, 70.00, 71.97, 74.03, (apparent ^{13}C - ^{119}Sn $^1J = 354$, $^2J = 22$, $^3J = 52$, apparent ^{13}C - ^{117}Sn $^1J = 336$, $^2J = 22$, $^3J = 52$); ^{119}Sn NMR 111.86 MHz (200 mg/mL), C_6D_6 , Me_4Sn standard δ -82.4 ppm (d of septets, $^1J_{\text{Sn-H}} = 1612$, $^2J_{\text{Sn-H}} = 55$); IR (film on NaCl) cm^{-1} : 3500 weak, 2970–2930 strongest absorption, $\nu_{\text{Sn-H}}$ 1810, 1452, 1358, 1300, 1285, 1245, 1200, 1140–1100 broad, 1040, 985, 925, 885, 850, 715, 685.
Anal: Calcd for $\text{C}_{18}\text{H}_{40}\text{SnO}_6$, MW 471.19: C, 45.88; H, 8.56; Sn, 25.19. Found: C, 45.74, 45.76; H, 8.71, 8.36; Sn, 25.08, 25.17.

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

Tributyltin hydride is a common reagent, used extensively in free radical chemistry.² However, it is soluble only in typical organic solvents. The tin hydride reagent prepared here³ can be used in free radical chemistry in many solvents. It is soluble in organic media, but also has sufficient water solubility (30 mM at room temperature, more on warming) to be useful in aqueous reactions. This reagent is not only of interest for use with water-soluble biomolecules but there is also increasing interest in the special effects of water as solvent on organic reactions.^{4,5,6} In addition, the reaction product of this reagent is the corresponding tin oxide species that can be easily recovered and recycled, and that is sometimes more easily removed from organic products than is the corresponding product from tributyltin hydride. Most notably, this reagent is non-volatile and odorless.

This procedure illustrates the bromopropylation of an alcohol by allylation and then hydroboration/bromination,⁷ a clean, selective procedure compared with other approaches via 3-substituted propyl bromide derivatives. Conversion to the tetraalkyl tin, then brominative cleavage, is the standard sequence for preparation of trialkyl tin derivatives.⁸ The standard lithium aluminum hydride (LiAlH_4) reduction of the tin bromide was not usable here because of contamination of the product by LiAlH_4 by-products that were not easily separated, and the polymethylhydrosiloxane reduction method⁹ was not successful. However, use of NaBH_4 in 1,2-dimethoxyethane was effective and convenient.¹⁰

References and Notes

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Appendix

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

D₂O

sodium benzophenone ketyl

potassium carbonate (584-08-7)

methanol (67-56-1)

ether (60-29-7)

magnesium (7439-95-4)

sodium chloride (7647-14-5)

bromine (7726-95-6)

Allyl bromide (106-95-6)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

nitrogen (7727-37-9)

iodine (7553-56-2)

sodium methoxide (124-41-4)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

2-Methylpropanol (78-83-1)

magnesium sulfate (7487-88-9)

borane (7440-42-8)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

hexane (110-54-3)

2-methoxyethanol (109-86-4)

argon (7440-37-1)

tributyltin hydride (688-73-3)

calcium hydride (7789-78-8)

1,2-dimethoxyethane (110-71-4)

phenanthroline

tin oxide

TIN HYDRIDE

Tris[3-(2-methoxyethoxy)propyl]stannane,
2,5,13,16-Tetraoxa-9-stannaheptadecane, 9-[3-(2-methoxyethoxy)propyl]- (130691-03-1)

1-Bromo-3-(2-methoxyethoxy)propane (59551-75-6)

3-(2-Methoxyethoxy)propene (18854-48-3)

Tetra[3-(2-methoxyethoxy)propyl]stannane (130691-01-9)

Bromotris[3-(2-methoxyethoxy)propyl]stannane (130691-02-0)

borane-tetrahydrofuran complex (14044-65-6)