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.

SYNTHESIS OF TRIS(2-PERFLUOROHEXYLETHYL)TIN HYDRIDE: A HIGHLY FLUORINATED TIN HYDRIDE WITH ADVANTAGEOUS FEATURES OF EASY PURIFICATION

[Stannane, tris-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)-]
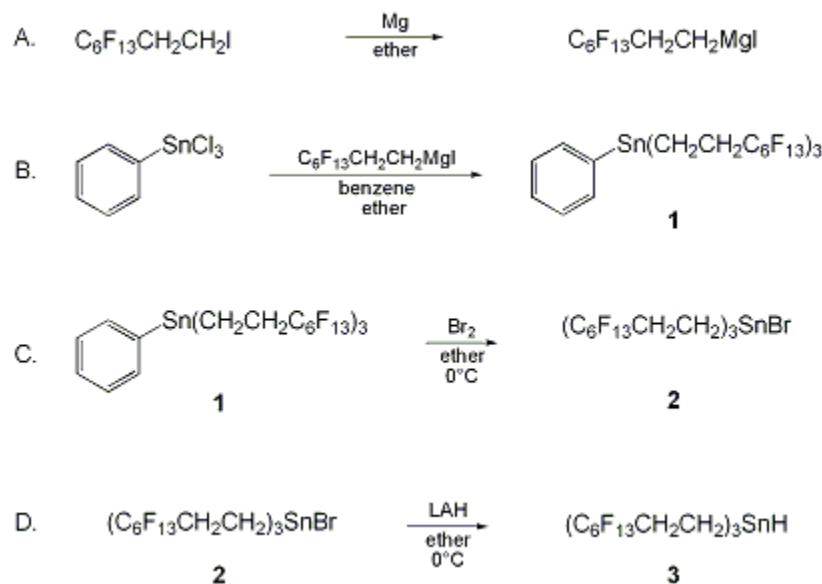
Submitted by Aimee Crombie, Sun-Young Kim, Sabine Hadida, and Dennis P. Curran[1] .
Checked by Peter Ranslow and Louis S. Hegedus.

1. Procedure

A. (Perfluorohexyl)ethylmagnesium iodide . A 500-mL, three-necked flask equipped with a stirring bar and a reflux condenser is dried in an oven overnight and then cooled under argon. Dry ether (20 mL) and 2-perfluorohexyl-1-iodoethane (1 mL) are added to magnesium (2.91 g, 120 mmol) in the dried flask equipped with a reflux condenser, thermometer and an outlet to argon gas (Note 1). The reaction is initiated by sonication for 30 min. Additional dry ether (70 mL) is added to the mixture while stirring. In a separate, dry, 100-mL, round-bottomed flask cooled under argon, dry ether (45 mL) is combined with 2-perfluorohexyl-1-iodoethane (13.70 mL, total of 60 mmol). This separate mixture is slowly added to the reaction mixture over 1 hr with stirring. The addition rate is adjusted to keep a constant temperature of about 30°C. The reaction mixture is heated at reflux for 2.5 hr in an oil bath at 50°C and allowed to stand after removal from the bath until it reaches room temperature.

B. Tris(2-perfluorohexylethyl)phenyltin . Phenyltin trichloride (2.46 mL, 15 mmol) is dissolved in dry benzene (30 mL) in a 100-mL, round-bottomed flask under argon at room temperature. The solution is slowly added to the 500-mL, three-necked flask containing the Grignard reagent at room temperature over 1 hr while stirring. The addition rate is adjusted to keep a constant temperature of about 25°C. The reaction mixture is heated at reflux overnight in an oil bath at 50°C, removed from the bath, and allowed to stand at ambient temperature for 4.5 hr with stirring. The reaction mixture is diluted with ether (100 mL), vacuum filtered into a 1-L Erlenmeyer flask, and hydrolyzed with saturated ammonium chloride solution (300 mL). Excess magnesium solid is also hydrolyzed with saturated ammonium chloride (100 mL) separately (Note 2). The mixture is transferred to a 1-L separatory funnel. The water layer is removed, and the organic layer is washed three times with 3% sodium thiosulfate (3 × 200 mL). The organic layer is dried over magnesium sulfate and filtered under vacuum. The solvent is evaporated to dryness under reduced pressure using a rotovap. The impure product is redissolved in ether (20 mL) and transferred to a 50-mL pear-shaped flask. The ether is removed under reduced pressure. Kugelrohr

distillation is peformed to remove a dimer impurity of ($C_6F_{13}CH_2CH_2CH_2CH_2C_6F_{13}$) at 0.02 mm, 100-120°C for 5 hr (Note 3). The residue is further purified by column filtration over silica (30 g) under pressure with hexane (1 L) (Note 4). The solvent is evaporated under reduced pressure to leave 17.2 g (13.9 mmol, 93%) of pure compound as a colorless oil (Notes 5 and 9).

C. Bromotris[2-(perfluorohexyl)ethyl]tin . The fluorous phenyltinproduct (17.2 g, 13.9 mmol) and dry ether (80 mL) are transferred to a 250-mL, three-necked flask that had been dried in an oven and cooled to 0°C under argon. Bromine (0.71 mL, 14 mmol) is added dropwise over 30 min to the mixture. The addition rate is adjusted to keep the temperature between 0° and 1°C. The mixture is warmed to 25°C and stirred for 7 hr. The reaction mixture is transferred to a 250-mL, round-bottomed flask. The ether and excess bromine are removed under reduced pressure to leave a yellow oil. The oil is dissolved in FC-72 (75 mL) and transferred to a 250-mL separatory funnel. The bromine and bromobenzene by-products are removed by washing three times with methylene chloride (3 × 75 mL) leaving the fluorous layer colorless. The FC-72 is removed under reduced pressure to provide 15.8 g (12.7 mmol, 92%) of a colorless oil (Note 6).

D. Tris[(2-perfluorohexyl)ethyl]tin hydride (Note 7). A 1-L, three-necked flask and a stirring bar are dried in an oven. The fluorous tin bromide (13.8 g, 11.1 mmol) is dissolved in dry ether (275 mL) and transferred to the dried three-necked flask equipped with a thermometer, stirring bar, and an outlet to argon. The solution is cooled to 0°C. A 1 M solution of lithium aluminum hydride (LAH) in ether (11.1 mL, 11.1 mmol) is added dropwise over 45 min to the solution. The addition rate is adjusted to maintain a temperature between 0° and 1°C. The reaction mixture is stirred for 6 hr at 0°C. Water (75 mL) is slowly added (initially dropwise) with stirring to the ice-cold mixture. Sodium potassium tartrate (20%) (250 mL) is added and the mixture is transferred to a 1-L separatory funnel. The ethereal layer is separated and the aqueous layer is extracted three times with ether (3 × 100 mL). The combined extracts are dried with magnesium sulfate and vacuum filtered into a 1-L, round-bottomed flask. The solvent is evaporated under reduced pressure. The crude product is distilled under a reduced pressure of 0.02 mm at 133-140°C to provide 11.3 g (9.69 mmol, 87%) of the pure product as an oil (Notes 8 and 9).

2. Notes

1. Ether and benzene were distilled with sodium/benzophenone prior to use. The 2-perfluorohexyl-1-iodoethane was purchased from Lancaster and the FC-72 was purchased from 3M . Magnesium (powder, 50 mesh) and all other reagents were purchased from Aldrich Chemical Company, Inc.
2. The mixture can be hydrolyzed without filtration. However, it is more convenient to remove the solid magnesium and hydrolyze the two components separately.
3. A cooled collection flask and a guard collection flask were used during the Kugelrohr distillation so that the dimer impurity (white solid) would not contaminate the vacuum pump. Periodic heating of the neck of the guard flask was performed with a heat gun to prevent any blockage from the impurity. A high vacuum pump was used to reduce the pressure. Although simple distillation has been used in the past, the Kugelrohr distillation is more advantageous and more convenient.
4. Short column chromatography can be performed to purify the compound further if desired.
5. The spectral properties of product **1** are as follows: ^1H NMR ($CDCl_3$) δ:1.31 [t, 6 H, J = 8.3, $^2J(^{119}Sn-H)$ = 53.4], 2.31 (m, 6 H), 7.41 (s, 5 H) ; ^{119}Sn NMR ($CDCl_3$) − 11.7 ppm; IR (thin film) cm^{-1}: 3100, 2950, 1238, 1190, 1144, 655 ; MS (m/z) 1161 (M+ - Ph), 891 (M+ - $CH_2CH_2C_6F_{13}$).
6. The spectral properties of product **2** are as follows: ^1H NMR ($CDCl_3$) δ: 1.56 [t, 6 H, J = 8.3, $^2J(^{119}Sn-H)$ = 53.4], 2.42 (m, 6 H) ; ^{119}Sn NMR (hexane-C_6D_6) 109.2 ppm; IR (thin film) cm^{-1}: 3600, 1250, 1227, 1145, 534 ; MS (m/z): 1161 (M+ - Br), 893 (M+ - $CH_2CH_2C_6F_{13}$).
7. Reactions on a smaller scale tended to give better yields for the reduction of the fluorous tin bromide to fluorous tin hydride.
8. The spectral properties of product **3** are as follows (Note 10): ^1H NMR ($CDCl_3$) δ: 1.16 [t, 6 H, J = 8.1, $^2J(^{119}Sn-H)$ = 53.4], 2.35 (m, 6 H), 5.27 (s, 1 H) ; ^{119}Sn NMR ($CDCl_3$) − 84.5 ($^1J(^{119}Sn-H)$ = 1835) ; IR (thin film) cm^{-1}: 1842, 1197 ; MS (m/z)1161 (M+ - H), 813 (M+ - $CH_2CH_2C_6F_{13}$).
9. Thin layer chromatography was performed using silica plates and eluting with hexane . Potassium permanganate was used to visualize the spots. The R_f values for products **1** and **3** were 0.38 and 0.37, respectively.
10. All NMR samples were dissolved in chloroform . The fluorous tin hydride is only slightly soluble in

chloroform . Therefore it is necessary to saturate this NMR sample. The NMR spectrum must be recorded quickly since the tin hydride reduces chloroform on standing in the light.

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

Trialkyltin hydrides represent an important class of reagents in organic chemistry because of their utility in radical reactions.[2] However, problems of toxicity and the difficulty of product purification made trialkyltin hydrides less than ideal reagents.[3] Several workup procedures[4] and structurally modified trialkyltin hydrides[5] have been developed to facilitate the separation of tin residues from the reaction mixture. Tris(trimethylsilyl)silicon hydride [6a] has also been synthesized and is often used successfully in radical reactions. However, its reactivity is different from that of trialkyltin hydrides in a number of important respects. Other tin hydride surrogates are also available.[6b]

On the heels of work by Zhu[7] and Horváth and Rábai,[8a] perfluorocarbon solvents and fluorous reagents have been used increasingly in organic syntheses.[9] Fluorous compounds often partition preferentially into a fluorous phase in organic/fluorous liquid-liquid extraction, thus providing easy separation of the compounds. Tris[(2-perfluorohexyl)ethyl]tin hydride [9b-9e] combines the favorable radical reaction chemistry of trialkyltin hydrides with the favorable separation features of fluorous compounds.

Tris[(2-perfluorohexyl)ethyl]tin hydride has three perfluorinated segments with ethylene spacers and it partitions primarily (> 98%) into the fluorous phase in a liquid-liquid extraction. This feature not only facilitates the purification of the product from the tin residue but also recovers toxic tin residue for further reuse. Stoichiometric reductive radical reactions with the fluorous tin hydride **3** have been previously reported and a catalytic procedure is also well established.[9b-9e] The reduction of adamantyl bromide in BTF (benzotrifluoride) [10,11] using 1.2 equiv of the fluorous tin hydride and a catalytic amount of azobisisobutyronitrile (AIBN) was complete in 3 hr (Scheme 1). After the simple liquid-liquid extraction, adamantane was obtained in 90% yield in the organic layer and the fluorous tin bromide was separated from the fluorous phase. The recovered fluorous tin bromide was reduced and reused to give the same results. Phenylselenides, tertiary nitro compounds, and xanthates were also successfully reduced by the fluorous tin hydride. Standard radical additions and cyclizations can also be conducted as shown by the examples in Scheme 1. Hydrostannation reactions are also possible,[9e] and these are useful in the techniques of fluorous phase switching.[10] Carbonylations are also possible.[9p] Rate constants for the reaction of the fluorous tin hydride with primary radicals and acyl radicals have been measured; it is marginally more reactive than tributlytin hydrides.[9c,e]

Scheme 1
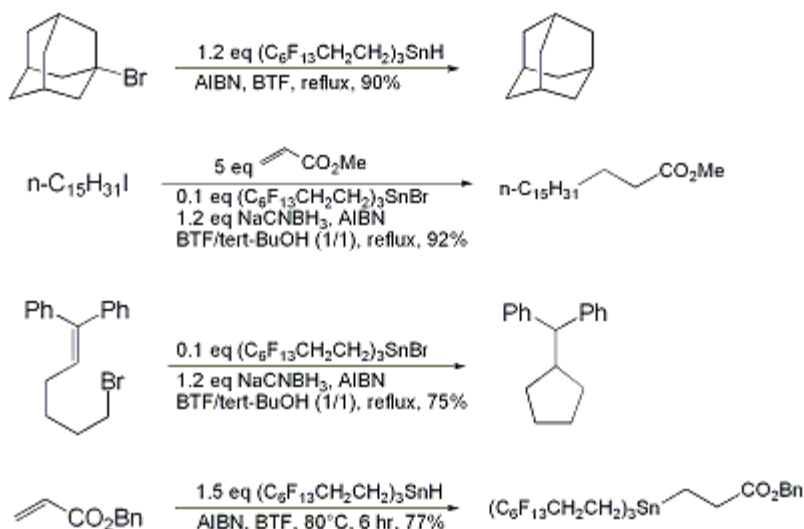
The preparation method reported here can be applied to the synthesis of a variety of related fluorous tin compounds. Seven more fluorous tin hydrides with the general formula of $[CF_3(CF_2)_n(CH_2)_m]_3SnH$ (n = 3, m = 2,3, n = 5, m = 3, and n = 9, m = 2) and $[CF_3 (CH_2)_m CH_2CH_2]SnMe_2H$ (m = 5, 7, 9) were synthesized using this method and used for radical reactions.[9e] The fluorous phenyl tin compound **1** and related compounds have been successfully reacted in Stille coupling reactions[9f-k] demonstrating the easy purification feature of fluorous compounds. Fluorous tin bromide **2** is an important intermediate for the synthesis of various reagents including tin azide and allyl tin compounds.[9g,h] Fluorous silanes are made by similar routes.[9m-o]

Recently, the submitters have developed new separation procedures based on fluorous silica gel,[12] and the separation of fluorous compounds by solid phase extraction has become another option for compounds that are not easy to separate by liquid-liquid extraction.

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

Tris[(2-perfluorohexyl)ethyl]tin hydride:
Stannane, tris(3,3,4,4,5,5,6,6,7,7,8,8,-tridecafluorooctyl)- (13); (175354-32-2)

2-Perfluorohexyl-1-iodoethane:
Octane, 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-8-iodo- (9); (2043-57-4)

Tris[(2-perfluorohexyl)ethyl]phenyl tin:
Stannane, phenyltris(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)- (13); (175354-30-0)

Phenyltin chloride: Aldrich:
Phenyltin trichloride:
Stannane, trichlorophenyl- (8,9); (1124-19-2)

Bromotris[(2-perfluorohexyl)ethyl]tin:
Stannane, bromotris(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)- (13); (175354-31-1)

Bromine (8,9); (7726-95-6)

Lithium aluminum hydride:
Aluminate (1-), tetrahydro-, lithium;
aluminate (1-), tetrahydro-, lithium, (T-4)- (9); (16853-85-3)

Magnesium (8,9); (7439-95-4)