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A novel reduction reaction for the conversion of tributyl(trifluoromethyl)stannane into tributyl(difluoromethyl)stannane

Alexander S. Golubev, Petr N. Ostapchuk

A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
Vavilov St. 28, 119991, GSP-1, Moscow, Russian Federation
E-mail: golubev@ineos.ac.ru

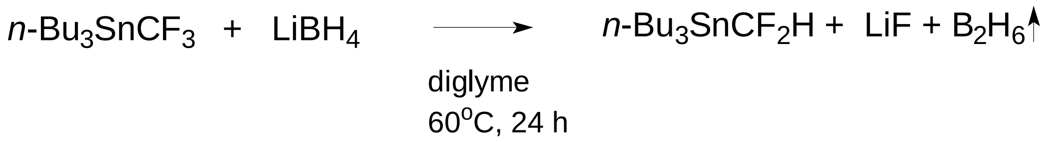
Abstract: A new method for obtaining tributyl(difluoromethyl)stannane n-Bu_3SnCF_2H by reduction of n-Bu_3SnCF_3 with lithium borohydride in diglyme has been developed.

Keywords: tributyl(difluoromethyl)stannane, tributyl(trifluoromethyl)stannane, lithium borohydride, reduction.

The introduction of a difluoromethyl group into organic molecules is often used in the development of new pharmaceuticals and agrochemicals [1]. Several years ago, a method for difluoromethylation of aryl, heteroaryl and *β*-styryl iodides using tributyl(difluoromethyl)stannane *n*-Bu_3SnCF_2H was developed. The synthesis of *n*-Bu_3SnCF_2H was accomplished by the reaction of tributyltin hydride with trifluoromethyltrimethylsilane Me_3SiCF_3, with column chromatography being used to purify *n*-Bu_3SnCF_2H [2].

As part of an ongoing project on the synthesis of difluoromethyl-containing physiologically active compounds, we needed *n*-Bu_3SnCF_2H free of *n*-Bu_3SnCF_3. In experiments on the synthesis of n-Bu_3SnCF_2H according to the protocol given in [2], we have always observed the formation of tributyl(trifluoromethyl)stannane *n*-Bu_3SnCF_3 as a by-product. Column chromatography could indeed significantly reduce the content of *n*-Bu_3SnCF_3 impurity. Nevertheless, it was possible to completely get rid of *n*-Bu_3SnCF_3 only at the expense of a significant loss of the target *n*-Bu_3SnCF_2H. To obtain *n*-Bu_3SnCF_2H not containing *n*-Bu_3SnCF_3, we have developed a new reduction reaction for the conversion of *n*-Bu_3SnCF_3 to *n*-Bu_3SnCF_2H.

We found that tributyl(trifluoromethyl)stannane *n*-Bu_3SnCF_3 reacted with lithium borohydride $LiBH_4$ in diglyme to form tributyl(difluoromethyl)stannane *n*-Bu_3SnCF_2H (scheme 1).



$$n\text{-}Bu_3SnCF_3 + LiBH_4 \xrightarrow[\text{60}^{o}\text{C, 24 h}]{\text{diglyme}} n\text{-}Bu_3SnCF_2H + LiF + B_2H_6\uparrow$$

Scheme 1.

Application of 1.5 equivalents of $LiBH_4$ and moderate heating (60 °C) brought about a complete conversion of the starting *n*-Bu_3SnCF_3 and a good yield of the target *n*-Bu_3SnCF_2H (60-70%) in a reasonable time (24 h). The formation of *n*-Bu_3SnCF_2H was also observed at room temperature, but the conversion did not exceed 50% in 24 hours. The completion of the reaction was monitored by $^{19}F\{^1H\}$ NMR spectroscopy (*n*-Bu_3SnCF_3 showed a singlet at -45.13 ppm with ^{119}Sn satellites: ^2J (^{19}F,^{119}Sn) = 214 Hz; *n*-Bu_3SnCF_2H showed a singlet at -124.62 ppm with ^{119}Sn satellites: ^2J (^{19}F,^{119}Sn) = 212 Hz) and ^{119}Sn NMR spectroscopy (a quartet with at -22.7 ppm with a coupling constant ^2J (^{19}F,^{119}Sn) = 218 Hz for *n*-Bu_3SnCF_3; a triplet at -49.4 ppm with a coupling constant ^2J (^{19}F,^{119}Sn) = 214 Hz for *n*-Bu_3SnCF_2H).

The main byproduct of the reaction was bis(tributyltin) oxide. Its formation apparently occurs due to traces of water in the reagents ($LiBH_4$ is extremely hygroscopic).

Only one hydride ion of the $LiBH_4$ molecule was involved in the reduction reaction. Since diborane was released during the reaction, the reduction process had to be carried out under a continuous flow of nitrogen flow. The gas stream leaving the reaction vessel was bubbled through a column of water or acetone.

By the end of the reaction, clear partitioning of the reaction solution into two phases was observed. The study of the phases showed that *n*-Bu_3SnCF_2H was almost completely in the lower phase. Unreacted $LiBH_4$ and the remaining diborane were in the upper phase. Their interaction, as is known [3,4], leads to the formation of LiB_2H_7. Lithium diborohydride binds diglyme (DG) in the form of a solvate complex of the $LiB_2H_7 \times 2DG$ structure, which was apparently the reason for partitioning of the reaction solution.

Treatment of the reaction with water required special attention. It is recommended to pour the reaction into ice water. Adding water to the reaction in one of the experiments caused a vigorous reaction, which led to the splashing of the contents of the reaction flask.

Our attempts to use sodium borohydride $NaBH_4$ in diglyme for the reduction of *n*-Bu_3SnCF_3 by analogy with the reduction of trifluoromethyltrimethylsilane Me_3SiCF_3 to difluoromethyltrimethylsilane Me_3SiCF_2H [5] met no success. We observed the formation of *n*-Bu_3SnCF_2H, however, we failed to achieve a significant conversion in the temperature range of 20-50 °C. Interestingly, when reducing Me_3SiCF_3 to Me_3SiCF_2H with sodium borohydride, at least 3 hydride ions of the $NaBH_4$ molecule are involved in the process [5].

Thus, we have developed a new method for obtaining tributyl(difluoromethyl)stannane n-Bu_3SnCF_2H by reduction of n-Bu_3SnCF_3 with lithium borohydride in diglyme. The new method avoids the use of unsafe and prone to oxidation tributyltin hydride. An advantage of the method is the possibility of obtaining Bu_3SnCF_2H that does not contain n-Bu_3SnCF_3.

Experimental part

^1H, ^{19}F, ^{119}Sn NMR spectra were recorded on a Bruker Avance™400 spectrometer (400.13 MHz for ^1H, 376.50 MHz with proton decoupling for ^{19}F, 149.21 MHz for ^{119}Sn). The proton chemical shifts were measured relative to the residual solvent signal (δ ($CDCl_3$) 7.28 ppm) and recalculated from the $SiMe_4$ signal. The ^{19}F NMR chemical shifts were measured relative to trifluoroacetic acid (an internal standard) and referenced to $CFCl_3$. ^{119}Sn NMR chemical shifts were determined relative to Me_4Sn as an internal standard (δ 0.0 ppm).

Tributyl(trifluoromethyl)stannane n-Bu_3SnCF_3 was prepared from bis(tributyltin) oxide and trifluoromethyltrimethylsilane Me_3SiCF_3 according to the procedure described in [6].

The reaction was carried out in a 3-necked round bottom flask under a stream of dry nitrogen. The flask was equipped with a dry nitrogen inlet tube, a dropping funnel and an outlet connected to an absorption column with water or acetone. To a solution of 7.0 g (19.5 mol) tributyl(trifluoromethyl)stannane in 30 ml of dry diglyme was added lithium borohydride (0.64 g, 29.3 mmol) as a solution in diglyme (9.8 ml of a 3M solution in diglyme). The addition of $LiBH_4$ was accompanied by a rapid rise in the temperature of the reaction mixture to 35 °C. The reaction mixture was heated with stirring at 60 °C for 24 hours. Reaction control (^{19}F NMR) showed complete conversion of the starting n-Bu_3SnCF_3. The reaction was poured into ice water (200 ml), extracted with toluene (50 ml + 30 ml). The combined organic phases were evaporated in vacuo on a rotary evaporator. The residue was distilled, and 4.2 g (63%) of the liquid with b.p. 89-93 °C/0.3 Torr was obtained, which was tributyl(difluoromethyl)stannane n-Bu_3SnCF_2H and about 6 mol. % diglyme. Tributyl(difluoromethyl)stannane n-Bu_3SnCF_2H can be further purified through a small pad of silica gel, eluent petroleum ether: ethyl acetate 100: 1, to detect cerium molybdate (Hanessian's Stain).

^{1}H NMR ($CDCl_3$) δ 6.45 (t, J = 44.9 Hz, 1H), 1.70 – 1.44 (m, 6H), 1.44 – 1.24 (m, 6H), 1.21 – 0.97 (m, 6H), 0.93 (t, J = 7.3 Hz, 9H).

$^{19}F\{^1H\}$ NMR ($CDCl_3$) δ -124.62 s with ^{119}Sn satellites: ^2J (^{19}F,^{119}Sn) = 212 Hz).

^{119}Sn NMR ($CDCl_3$) δ -51.94 (t, J = 214.4 Hz) (see, also [2]).

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Literature

1. Yerien D. E., Barata-Vallejo S., Postigo A., Difluoromethylation reactions of organic compounds, Chemistry–A European J., **2017**, 23(59), 14676-14701.
2. Prakash G. K. S., Ganesh S. K., Jones J.-P., Kulkarni A., Masood K., Swabeck J. K., Olah G. A. Copper-mediated difluoromethylation of (hetero)aryl iodides and β-styryl halides with tributyl(difluoromethyl)stannane, Angewandte Chemie, **2012**, 124(48), 12256-12260.
3. Brown H. C., Stehle P. F., Tierney P. A., Singly-bridged compounds of the boron halides and boron hydrides., J. Am. Chem. Soc., **1957**, 79(8), 2020-2021.
4. Titov L. V., Gavrilova L. A., Borohydrides of the alkali and alkaline-earth metals., Russ. Chem. Bull., **1976**, 232-235.
5. Tyutyunov A. A., Boyko V. E., Igoumnov S. M. The unusual reaction of (trifluoromethyl)-trimethylsilane with sodium borohydride., Fluorine Notes, **2011**, № 1(74).
6. Prakash G. K. S., Yudin A. K., Deffieux D., Olah G. A., Synthetic methods, Part 197, Facile preparation of (trifluoromethyl)tributyltin and transtrifluoromethylation of disilyl sulfides to the corresponding trifluoromethylsilanes, Synlett, **1996**, 2, 151-153.