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A simple and effective procedure for removal of tri-*n*-butyltin halides from reaction mixtures

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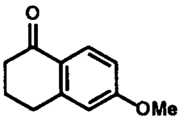
Abstract

A mixture of powdered 2:1, CsF:CsOH (solid solution) and silica gel can be used conveniently to remove Bu_3SnHal from non-polar organic coproducts.

Several very useful synthetic reactions involve the use of tri-*n*-butyltin reagents (especially Bu_3SnH)[1] to generate an organic product and tri-*n*-butyltin halide or other salt.[2,3] In many of these reactions, for example Bu_3Sn radical induced cyclization or deoxygenation, it is frequently difficult to obtain pure product because of similar solubilities and chromatographic mobility of the organic product and Bu_3SnX. We describe herein a convenient new method of removal of tri-*n*-butyltin salts from such reaction mixtures.

We have recently described the preparation of a 1:1 solid solution of CsF and CsOH and its application as a highly reactive F^- source for desilylation of various substrates.[4] A similar 2:1, CsF:CsOH mixture is made simply by fusing the components in a nickel crucible, cooling and pulverizing. When Bu_3SnCl in CH_2Cl_2 is stirred with ca. 1.5 parts by weight 2:1, CsF:CsOH and 1 part by weight of silica gel for ca. 30 min and then filtered through a short plug of silica gel, the tin compound is completely removed from the solution. Using this method 6-methoxy-1-tetralone (**1**) was quantitatively recovered in pure form from a 1:1 mixture with Bu_3SnCl using the following procedure: To a solution of 6-methoxy-1-tetralone (**1**, 50 mg, 0.284 mmol) in dichloromethane (1 mL, 0.284 M) was added tributyltin chloride (77 μL, 0.284 mmol), followed by 2:1, CsF:CsOH fused salt (129 mg, 0.568 mmol fluoride ion), and silica gel (60 mg). The mixture was stirred at room temperature for 25 min, and transferred to a short (2 cm) plug of silica gel with dichloromethane (5 mL). Elution with hexanes:EtOAc (2:1, 15 mL) afforded pure tetralone **1** in quantitative yield.



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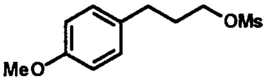

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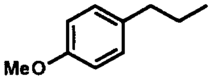

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A specific application of this method to the removal of Bu_3SnI from an organic coproduct of similar polarity is the deoxygenation of mesylate **2** to form 4-*n*-propylanisole (**3**). The deoxygenation was carried out using SmI_2 in catalytic amount along with LiI and Bu_3SnH in THF containing hexamethylphosphorictriamide (HMPA) at 35°C. Under these conditions, mesylate **2** is converted to the corresponding iodide in situ. SmI_2 serves as an iodine atom abstractor forming the 4-methoxyphenylpropyl radical which then undergoes the usual free radical chain reaction with Bu_3SnH to form the reduction product **3**. The effectiveness of the reaction and the process of tin removal is illustrated by the following experimental procedure for the conversion of **2**→**3**: To a flask containing dry LiI (137 mg, 1.025 mmol) and mesylate **2** (50 mg, 0.205 mmol) was added THF (200 μL, 1.0 M), Bu_3SnH (95 μL, 0.353 mmol), and HMPA (71 μL, 0.410 mmol). The mixture was treated at room temperature with three portions of SmI_2 (200 μL each, 0.1 M in THF) over the time course of 1 h. The purple solution, which turned colorless over the course of 1 h, was then heated to 35°C for 20 h, cooled to 0°C, and poured into cold 0.1N HCl (6 mL). The layers were separated, and the aqueous layer extracted with pentane:ether (5:1, 2×10 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$, and the solvents evaporated in vacuo (10°C) to afford a clear colorless oil. The crude product was titrated with iodine solution (0.05 M in ether) to iodinate any excess Bu_3SnH until the iodine color persisted. After stirring for 45 min, the solution was concentrated and treated sequentially with pentane:ether (5:1, 1 mL), 2:1 CsF:CsOH fused salt (240 mg, 1.06 mmol fluoride ion), and silica gel (75 mg). The mixture was stirred at room temperature for 25 min and filtered through silica, which was washed with pentane:ether (2:1, 20 mL) to give pure **3** (29.2 mg, 95%) as colorless crystals.

The conversion of mesylate **2** to the deoxygenation product **3** takes place by way of the primary iodide corresponding to **2**, as shown by time course studies of the reaction using chromatographic and in situ FTIR analysis. The transformation of mesylate to iodide is accelerated by Li^+ and also Sm^{+3} (e.g., relative to R_4N^+) which appear to function as Lewis acids to assist in the departure of mesylate ion in a medium (THF) that is a poor anionic solvator. In the absence of added SmI_2, the conversion of **2**→**3** is much slower.

In summary, we have developed a simple, non-aqueous, mild procedure for the physical removal of alkyl tin salts from organic coproducts.[5] The utilization of a fused CsF:CsOH salt for this purpose adds to a growing list of uses for these interesting anhydrous fluoride ion sources.

Acknowledgements

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