Tetrabutylammonium Difluorotriphenylstannate [Bu₄N][Ph₃SnF₂]: Delivering Carbon or Fluorine Ligands via Hypercoordination

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Abstract: The reagent, tetrabutylammonium difluorotriphenylstannate, was easily prepared on a multigram scale (~100 g). Several of its applications are presented, either as a soluble, thermally stable and anhydrous nucleophilic fluorinating agent or as a synthetic equivalent to PhMgX or PhLi species under aqueous and aerobic conditions. The proposed methodologies emphasize the concept of hypercoordination and its usefulness for improving selectivity, reactivity and shelf-stability of reagents.

Key words: fluorination, tin, carbanions, sulfur, hypercoordination



Scheme 1

In 1991, one of us described the first hypercoordinated organotin 3 acting as an anhydrous nucleophilic fluorinating agent.¹ Among many advantages, its thermal stability, its solubility in less polar solvents and its anhydrous nature (even after many years), led to a synthetic equivalent to tetrabutylammonium fluoride (TBAF) with improved properties. For instance, it was shown that drying TBAF was almost impossible and gradually lead to its decomposition.² More importantly, the concept of hypercoordination for modulating the properties of a reagent was put forward. Recently, this demonstration went further when hypercoordination helped in stabilizing carbanionic species for making synthetic equivalents to PhMgX or to Ph-Li, albeit without their disadvantages (such as titration, strict anhydrous and inert conditions, pyrophoric or flammable properties).³

Due to the usefulness of this ambivalent reagent, either as synthetic equivalents to TBAF or to PhMgX/PhLi species under aqueous and aerobic conditions, a plethora of publications followed, which clearly indicated its usefulness

SYNTHESIS 2006, No. 1, pp 0182–0185 Advanced online publication: 16.12.2005 DOI: 10.1055/s-2005-921747; Art ID: Z09605SS © Georg Thieme Verlag Stuttgart · New York and importance. This reagent has found its way in the fine chemicals industry under the name 'Gingras Reagent', but its cost discouraged an extensive use. The purpose of this article is threefold: a) to describe a reliable and multigram preparative procedure of the reagent (~100 g), which was checked several times,⁴ b) to report a detailed characterization and analysis of purity of **3** and c) to demonstrate two classes of synthetic applications such as enol silyl ether C-alkylations and selective sulfurations of organotins.

Procedures

Procedure 1 depicts for the first time a large-scale preparation of triphenyltin fluoride **2** and its conversion to tetrabutylammonium difluorotriphenylstannate (**3**) (Scheme 1). In the first step, commercial triphenyltin chloride (**1**) dissolved in ethyl acetate was rapidly converted into polymeric triphenyltin fluoride **2** within minutes at 20 °C after addition of an aqueous solution of potassium fluoride. Ethyl acetate played a major role to ensure an almost complete precipitation of **2** as a white powder, which was further rinsed with water. A trituration with diethyl ether and filtration helped to remove the bulk

of water. The crude product was dried under vacuum at about 50 °C until constant weight and was used as such in the next step. Triphenyltin fluoride (2) quickly reacted at 20 °C with commercial tetrabutylammonium fluoride trihydrate in dichloromethane. After two recrystallizations, the expected product 3 was obtained. Practical aspects of those procedures were a quick reactivity at 20 °C (within minutes) for both steps and simple precipitations or recrystallizations. Finally, it was shown that 100 g of pure product was easily obtained without chromatography or special purification techniques. This reagent could be kept for years without protection from moisture. The overall yield of sufficiently pure product (92.6 g, 66%) represents an improvement over the first report (53%).¹ A detailed multigram preparative procedure of 3 has never been previously disclosed.

Procedure 2 presents a selective C-alkylation of enol silyl ether **4**, probably through a nucleophilic enol stannate generated via a fluoride ion ligand exchange from Sn to Si atoms¹ (Scheme 1). An interesting feature was again a prompt reactivity at 20 °C and selectivity for a mono Calkylation of cyclopentanone; the latter compound being known to often generate polyalkylated products. It is noteworthy that no O-alkylation reaction was observed. The simplicity of the procedure was demonstrated when reagent **3** was added in one portion to a solution of enol silyl ether **4** and benzyl bromide (**5**) in THF at low temperature. The mixture was immediately warmed at 20 °C for a few hours and an almost quantitative yield of benzylated product **6** was obtained, after removing organotin by-products over silica gel column by chromatography.

Applications

Reagent **3** has found several uses in synthesis such as: a) nucleophilic fluorinations for making alkyl fluorides^{1,5} and gem-difluoroalkanes,⁶ b) trifluoromethylations,^{7,8a} c) difluoroalkylations,⁹ d) Stille couplings,¹⁰ e) enol silyl ether alkylations^{1,8} and f) Ar–S bond formations.¹¹

As shown in Procedure 2 (Scheme 1), enol silyl ethers were activated with reagent 3 and then C-alkylated, possibly through organotin enolates (experimentally unverified). Some examples of this reaction are shown in Scheme 2.

Not only fluoride ion ligand could be delivered from reagent **3**, but a 'nucleophilic' phenyl ligand (or a Sn–C bond) reacted with elemental sulfur or sulfur-transfer re-



agents for making Ar–S bonds, under aqueous and aerobic conditions (Scheme 3). It emphasized the versatile use of reagent **3** or hypercoordinated organotin fluoride species, generated in situ, to transfer either a fluorine or a carbon ligand. It was a clear demonstration of the usefulness of hypercoordination to drive the control of selectivity and reactivity. More importantly, previous sulfurations of organotins with elemental sulfur provided a mixture of sulfurated products and organotin sulfides at higher temperatures near 200 °C.³ In our case, selective disulfide formation was observed with most sulfur transfer agents in the presence of water and air at 150 °C and within a few minutes only. The presence of fluorine ligands was thus crucial for selectivity and reactivity.



2)

3)





(R-S-R or R-SH not usually observed)

Scheme 3

Sulfuration of reagent 3 is an example of a somewhat broad method that could be applied to a wide variety of organotins, even though the procedure was more efficient with aryltins, compared to alkyltins. In short, optimization of the process indicated that 10% of water in DMF increased the selectivity for disulfide formation, the relative molar ratio sulfur/organotin was best at 3.1. Coordinating solvents such as DMF, DMSO, MeCN and 1,3-dimethyl-2-imidazolidinone (DMI) were chosen, but DMF gave overall the best results. A convenient compromise between temperature and reaction time was found at 150 °C within 25 minutes for triphenyltin chloride. Electron rich aryltins reacted faster than electron-poor aryltins. Finally, it was observed that tetraaryltins and triaryltins reacted faster than mono- and diaryltins. Some examples are described in Scheme 3.

¹H and ¹³C and ¹⁹F NMR spectra were recorded in CDCl₃ (referenced to TMS or PhCF₃) with Bruker instruments AC 200 (200 MHz) and AC 500 (500 MHz). FT-IR spectra were recorded with a Perkin-Elmer 883 or Perkin-Elmer Spectrum 1000 instrument with dry KBr disks (about 1% w/w of sample). Melting points (uncorrected) were determined in an open capillary with an Electrothermal SMP3 (0.2 °C/min) apparatus. MS (EI, 70 eV) were recorded on a Kratos MS-80RFA (University of Wisconsin-Madison, USA).

Triphenyltin Fluoride (2)

To a 3-L, three-necked flask, fitted with a mechanical stirrer, was added Ph₃SnCl (1; 101.2 g, 0.263 mol, an inert atmosphere was not needed). EtOAc (500 mL, laboratory grade) was poured into the flask to dissolve the Ph₃SnCl. An aqueous solution of KF·2H₂O (37.1 g, 0.394 mol) was prepared in warm distilled H₂O (50 mL). This solution was slowly poured into the main flask within a few min and the mixture was mechanically stirred at 20 °C. Insoluble

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Scheme 2

polymeric Ph₃SnF (**2**) instantly precipitated. After stirring for 1 h (less time might be needed), the mixture was filtered using a 1000-mL fritted funnel. The resulting solid was washed with EtOAc (150 mL), distilled H₂O (300 mL) and Et₂O (100 mL, laboratory grade). The product was partially dried in open air and was further dried under vacuum until a constant weight (50 °C/0.1 mmHg). A white powder was obtained (97.0 g, 99%) and used without any further purification in the next step.

Tetrabutylammonium Difluorotriphenylstannate (3)

To a 3-L, three-necked flask, fitted with a mechanical stirrer, was added the above prepared Ph₃SnF (2; 82.4 g, 0.223 mol, an inert atmosphere was not needed). n-Bu₄NF·3H₂O (70.4 g, 0.223 mol, hygroscopic) was added in one portion to the flask, followed by CH₂Cl₂ (250 mL, laboratory grade). More CH₂Cl₂ (50 mL) was used to rinse the glassware. The mixture was mechanically stirred at 20 °C for 35 min. The solids partly dissolved after 5 min but a fine precipitate remained. Anhyd Na₂SO₄ (20 g) was then added in order to remove some residual H2O and stirring was continued for about 10 min. The mixture was filtered through a 1000 mL fritted funnel and the filtrate was collected in a 3-L Erlenmeyer flask. CH₂Cl₂ (50 mL) was used to wash the residual solid. To the combined filtrates, was slowly added Et₂O from a dropping funnel. After adding about 700 mL of Et₂O, the first crystals appeared. More Et₂O (300 mL) was continuously added within 10 min while stirring with a stirring bar. The flask was placed in a fridge at -20 °C (or at 0-3 °C in an ice-bath) for about 1 h and the crystals were collected in a 1000-mL fritted funnel. The solid was washed further with Et₂O (300 mL) and dried in open air overnight (moist solid, 123.9 g). It was then vacuum-dried at 20 °C (0.1 mm Hg) until constant weight. The resulting white solid (102.8 g, mp 181.3 \pm 0.5 °C) was not sufficiently pure and was recrystallized from CH2Cl2 (150 mL) with slow addition of Et_2O (450 mL). The mixture was left in the cold at -20 °C for 1 h. The solid formed was filtered and washed with Et_2O (200 mL). [Note: both the mother liquors from the above two filtrations were combined, evaporated and the residue was recrystallized from a mixture of acetone (60 mL) and Et₂O (250 mL), followed by addition of EtOAc (100 mL), see below]. After vacuum drying, the reagent 3 was obtained as white crystals (93.0 g, 66%); mp 186.4 \pm 0.4 °C. This first crop obtained was recrystallized by dissolving it in warm acetone (500 mL, laboratory grade), followed by filtration before adding n-hexane (750 mL, laboratory grade) via a dropping funnel. Two phases appeared and Et₂O (500 mL) was slowly poured into the mixture. The crystals were formed at 20 °C. After collecting and drying them (0.1 mmHg), pure tetrabutylammonium difluorotriphenylstannate (3) was obtained (76.6 g); mp 191.0 \pm 0.5 °C (Lit.¹ mp 189.5 \pm 0.5 °C). The solvents from the mother liquors were evaporated and the residual solid was combined with the crop obtained from the earlier mother liquors (see above). The residual solids from the combined mother liquors were recrystallized as above (100 mL acetone, 200 mL Et₂O, 200 mL n-hexane). The crystals formed were collected (21.7 g) and recrystallized to provide an additional material (16.0 g); mp 184.0 \pm 0.5 °C. Even this last crop was sufficiently pure for most purposes; overall yield: 92.6 g (66%).

¹H NMR (500 MHz, CDCl₃/TMS): δ = 8.09 (d, *J* = 5.0 Hz, 6 H), 7.25 (m, 9 H), 2.46 (t, *J* = 7.0 Hz, 8 H), 1.07 (m, 16 H), 0.88 (t, *J* = 7.0 Hz, 12 H).

¹³C NMR (125.77 MHz, CDCl₃/TMS): δ = 13.99 (CH₃), 19.74 (CH₂), 23.88 (CH₂), 58.05 (CH₂N), 127.65 (CH), 128.07 (CH), 138.05 (CH).

¹⁹F NMR (282.2 MHz, CDCl₃/PhCF₃): δ = -95.24 (s), Sn satellites (d, *J*[¹¹⁹Sn,¹⁹F] = 1971 Hz, d, [¹¹⁷Sn,¹⁹F] = 1887 Hz).

¹¹⁹Sn NMR (111.82 MHz, CD₂Cl₂/Me₄Sn_{ext}): $\delta = -342.4$ (t, J[¹¹⁹Sn,¹⁹F] = 1971 Hz).

Anal. Calcd for $C_{34}H_{51}F_2NSn$ (630.48): C, 64.77; H, 8.15. Found: C, 64.92; H, 8.11.

Enol Silyl Ether Alkylations; 2-Benzylcyclopentanone (6); Typical Procedure

Freshly distilled 1-(trimethylsilyloxy)cyclopentene (**4**; 1.41 mmol) was added via a syringe to a solution of pure distilled benzyl bromide (**5**, 2.12 mmol) in anhyd (dried over Na/benzophenone) THF (5.0 mL). After cooling to -78 °C for 15 min, reagent **3** (1.55 mmol) was added in one portion with the help of a lateral Gooch tube (cooling might not be needed in some cases). The cooling bath was removed whereupon the solid dissolved at 20 °C. Stirring was continued for 6 h and a filtration over a short column of silica gel (CH₂Cl₂) removed most of the organotins and salts. After evaporation of solvents and drying under vacuum (0.1 mm Hg) overnight, crude product **6** was obtained (293 mg, theory: 243 mg). A flash chromatography over silica gel (acetone–hexane, 1:10) afforded pure **6** (243 mg, 99%).

¹H NMR (200 MHz, CDCl₃): δ = 7.40–7.10 (m, 5 H), 3.17 (dd, *J* = 3.9, 13.6 Hz, 1 H), 2.52 (dd, *J* = 13.6, 9.5 Hz, 1 H), 2.48–2.25 (m, 2 H), 2.25–1.88 (m, 3 H), 1.88–1.45 (m, 2 H).

¹³C NMR (67.92 MHz, CDCl₃): δ = 219.76, 139.79, 128.68, 128.20, 125.94, 50.78, 37.96, 35.38, 28.92, 20.34

HRMS (EI): *m/z* calcd for : 174.1052; found: 174.1045 [M⁺].

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