Organic/Fluorous Phase Extraction: A New Tool for the Isolation of Organometallic Complexes

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*Summary: Strategies for isolating and purifying organometallic complexes are limited. The use of the unique solubility properties of fluorous reagents allows for purification by fluorous/organic phase extraction. An 85% yield of pure $(R_{fh})_3SnCp^*$ (**1**, $R_{fh} = (CH_2)_2(CF_2)_5CF_3$) was isolated by filtration and extraction with FC-72 (fluorinated hexanes) of the reaction of $(R_{fh})_3SnBr$ with Cp*Li. The reaction of **1** with $TaCl_5$ and $NbCl_5$ gave the alkylated products Cp^*TaCl_4 and Cp^*NbCl_4, respectively. These products were isolated from the reaction mixtures in good yields by simple extraction with a biphasic combination of FC-72 and a nonfluorinated solvent.*

Strategies for the isolation and purification of air- and water-sensitive organometallic compounds are extremely limited. The reactive nature and high boiling points of most interesting organometallic compounds generally preclude the use of common purification techniques such as chromatography, organic/aqueous phase extraction, and distillation. Of the methods used in organic synthesis, only crystallization and sublimation are routinely applicable. In this paper, we describe the application of a new, more facile purification strategy, organic/fluorous phase extraction, to the synthesis of *nonfluorinated* complexes of the type Cp^*MCl_4 (M = Nb, Ta; Cp* = C_5Me_5).[1]

These pentamethylcyclopentadienyl complexes, which are important starting materials in group V chemistry,[2] are typically prepared by a sequence of two organometallic reactions.[3] The alkylating agent $Cp^*Sn(n\text{-}Bu)_3$ is first prepared by reaction of Cp*Li with $(n\text{-}Bu)_3SnX$ (X = Cl, Br). Isolation is accomplished by filtration followed by vacuum distillation. The tin reagent is then reacted stoichiometrically with $TaCl_5$ or $NbCl_5$ to give Cp^*MCl_4. The isolation by crystallization relies on the relative insolubility of the products in the $(n\text{-}Bu)_3SnX$-containing mother liquor.

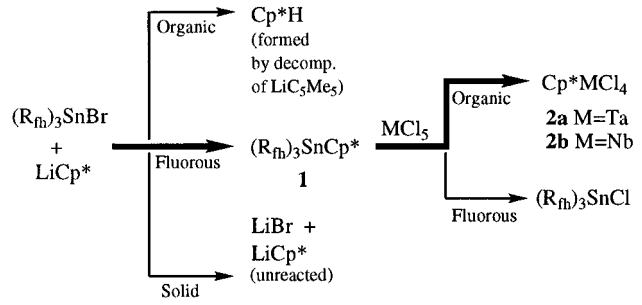

Figure 1. Summary of reactions and product isolations by fluorous/organic phase extraction.

Our alternative preparation for these pentamethylcyclopentadienyl group V halides utilizes the same synthetic strategy but rather than using ancillary butyl substituents $-(CH_2)_2(CF_2)_5CF_3$ (abbreviated R_{fh}) that have recently been employed in fluorinated approaches to synthetic organic purifications.[4,5] Reaction of $(R_{fh})_3SnBr$[5] with 1.2 equiv of LiCp* in refluxing Et_2O for 1 day produced $(R_{fh})_3SnCp^*$, **1**, in 85% yield based on tin (Figure 1).[6] Isolation of the pale yellow liquid product was accomplished by filtration, removal of Et_2O, and a biphasic extraction with a mixture of FC-72 (a mixture of perfluorohexanes) and benzene. The removal of solvent from the fluorous phase gave the Cp*Sn reagent **1**. The ^1H NMR spectrum of **1** consists of a singlet at δ 1.79 with tin satellites ($^3J_{Sn-H}$ = 10.8 Hz) for the equivalent cyclopentadienyl methyls and two multiplets at δ 2.15 and 0.99 that are attributed to the hydrocarbon methylene spacer groups. The ^{119}Sn NMR spectrum exhibits a single resonance at δ 9.02.

The reaction of tin reagent **1** with a slight deficiency of $TaCl_5$ for less than 1 h produced the product Cp^*TaCl_4, **2a**, in a quantitative yield.[7] In this case, the product was recovered by extraction of the byproduct $(R_{fh})_3SnCl$

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(6) Preparation of **1**: A suspension of LiCp* (47.0 mg, 0.33 mmol) in 20 mL of Et_2O was treated with $(R_{fh})_3SnBr$ (400.0 mg, 0.32 mmol) dissolved in 20 mL of Et_2O. The reaction mixture was refluxed for 24 h, cooled to 25 °C, concentrated to ~5 mL, and filtered. The Et_2O was removed *in vacuo*, and the residue was extracted with a biphasic system consisting of FC-72 (purchased from 3M; distilled from CaH_2) and benzene. Upon removal of the fluorous solvent, **1** (353 mg, 85%) was obtained as a yellowish oil. ^1H NMR (300 MHz, $CDCl_3$): δ 0.99 (m, CH_2CH_2Sn, 6H), 1.79 (s, C_5Me_5, $^3J_{Sn-H}$ = 10.8 Hz, 15H), 2.15 (m, $CF_2CH_2CH_2$, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −1.71 (CH_2CH_2Sn), 11.72 (C_5Me_5), 27.64 (t, $CF_2CH_2CH_2$, $^2J_{C,F}$ = 25 Hz), 109−111 (m, CF_2, CF_3), 119.75 (C_5Me_5). ^{119}Sn NMR (186 MHz, $CDCl_3$): δ 9.02. EI-MS (*m*/*z*): 1296 (M^+), 1161 ($M^+ - C_5Me_5$), 949 ($M^+ - CH_2CH_2C_6F_{13}$).

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into the fluorous phase. Removal of the solvent from the organic phase gave pure **2a** as a yellow solid in 99% yield. The less stable niobium derivative was prepared similarly, although 12−15 h was required to reach completion and it was necessary to combine the reagents at low temperature (−35 °C) in order to prevent side reactions. Using this procedure, a 97% yield of powdery red Cp^*NbCl_4, **2b**, contaminated with ∼5% of unidentified fluorine-containing impurites, was isolated. Although the yield is reduced to 70−80%, the compound can be freed of the fluorinated impurities by recrystallization.[8] Conventional preparations of **2b** gave isolated yields of 70% or less.[9] The ^{1}H NMR spectra of both **2a** and **2b** were identical to those reported in the literature.[3a,9]

This fluorous strategy for the preparation of Sn-reagent **1** is superior to that reported for the preparation of $(n\text{-Bu})_3SnCp^*$ in that the tedious, high-temperature vacuum distillation is not required; the fluorinated reagent **1** is >98% pure after the described workup. Using **1**, Cp^*NbCl_4 and Cp^*TaCl_4 were then prepared in yields that are equivalent to the best reported literature values for nonfluorinated tin *or* silicon reagents.[3c,9] It is also important to note that the fluorous phase recovered after the transmetalation of Cp* contains pure $(R_{fh})_3SnCl$ that can be easily recycled, thereby reducing the overhead costs associated with using the fluorinated side chains. Such recycling has been successful in the Stille couplings that employ this reagent.[1d]

The potential advantages of the fluorous purification strategy extend beyond its application to the preparation of the title compounds. The most global of these advantages is that this approach need not be limited to tin reagents. One can envision that in any system that employs a reagent that donates a substituent, such as the increasingly important atom/group-transfer reagents, the use of fluorinated spectator ligands will allow for facile purification of the reaction products by fluorous extraction. Obviously, fluorination will not prove practical for all systems, but given the paucity of purification methods currently available to the organometallic chemist, the potential for application is significant.

The second, more immediately appreciable, advantage of the fluorous approach described in this report is the potential increase in the utility of tin alkylating reagents for organometallic synthesis. Crystallization, the isolation procedure normally employed for organometallic compounds prepared using hydrocarbon tin reagents, is impractical for compounds that are significantly more soluble than the monoperalkylcyclopentadienyl compound featured herein since $(n\text{-Bu})_3SnX$, a viscous oil, is always present in the mother liquor. The fluorous extraction technique, in contrast, would be expected to be more versatile in that it is suitable for products with a wide range of solubilities.

In summary, we have shown that by using a fluorinated tin reagent in combination with fluorous/organic extraction we can prepare the highly reactive organometallic compounds Cp^*TaCl_4 and Cp^*NbCl_4 more simply but in comparable yields to conventional strategies. Furthermore, it is clear that this approach is not limited to this system. Fluorous phase extraction in similarly designed reaction sequences can significantly expand the limited repertoire of organometallic purification techniques.

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Supporting Information Available: ^{1}H NMR spectra for all compounds (5 pages). Ordering information is given on any current masthead page.

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(7) Preparation of **2a**: A suspension of $TaCl_5$ (54.9 mg, 0.15 mmol) in 5 mL of CH_2Cl_2 was treated with $(Rfh)_3SnCp^*$ (200.0 mg, 0.15 mmol) dissolved in 5 mL of CH_2Cl_2. The solution immediately turned yellow. After 1 h, the solution was extracted with FC-72 (2 × 5 mL). Upon removal of the CH_2Cl_2 in vacuo, 69.2 mg (98.6%) of Cp^*TaCl_4 was isolated. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.74 (s, C_5Me_5, 15H).

(8) Preparation of **2b**: A suspension of $NbCl_5$ (40.1 mg, 0.15 mmol) in 5 mL of CH_2Cl_2 at −35 °C was treated with $(Rfh)_3SnCp^*$ (174.0 mg, 0.13 mmol) dissolved in 5 mL of CH_2Cl_2 at −35 °C. The color of the reaction changed to red-brown instantly. The reaction mixture was stirred at 25 °C for 15 h. The solution was filtered and extracted with FC-72 (2 × 5 mL). Upon removal of the CH_2Cl_2 in vacuo, 48.1 mg (96.8%) of Cp^*NbCl_5 was isolated. **2b** was contaminated with ∼5% of unidentified fluorine-containing impurities. The material was further purified by recrystallization from CH_2Cl_2/hexanes. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 2.50 (s, C_5Me_5, 15H). A ^{19}F NMR of the recrystallized product showed no evidence of incorporation of fluorine into the niobium complex.

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