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Stille Reactions Catalytic in Tin: A "Sn−F" Route for Intermolecular and Intramolecular Couplings†

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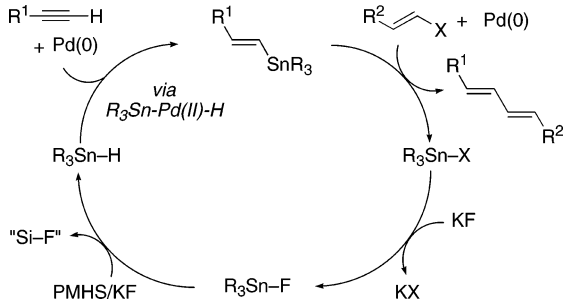

Polymethylhydrosiloxane (PMHS) made hypercoordinate by $KF_{(aq)}$ allows Me_3SnH to be recycled during a Pd(0)-catalyzed hydrostannation/Stille cascade. Starting with a variety of alkynes, in situ vinyltin formation is followed by Stille reaction with aryl, styryl, benzyl, or vinyl electrophiles present in the reaction mixture. Both inter- and intramolecular versions of the process are possible with tin loads of approximately 6 mol %. Regeneration of the organotin hydride is believed to proceed through a Me_3SnF intermediate. Given the aggregated nature of organotin fluorides and the ability to use these organotins in substoichiometric quantities, the hazards and purification problems associated with the removal of organotin wastes from reaction mixtures are minimized.

Introduction

The palladium-catalyzed cross-coupling of organostannanes with a variety of organic electrophiles is commonly referred to as the Stille reaction.[1] Due to its versatility and functional group compatibility, the Stille reaction has long been a popular method for the construction of sp^2−sp^2 carbon−carbon bonds via σ bond formation.[2] That said, Stille reactions typically demand the management of stoichiometric amounts of tin before, during, and after the cross-couplings. This is unattractive because of troubles associated with the cost and toxicity of organotins as well as the general difficulty of their removal from reaction mixtures.[3] Such problems have, in part, driven the development of cross-coupling reactions that replace the tin with other metals, boron, silicon, zinc, and indium among them.[4] Despite the clear value of these other cross-coupling methods, recognition of the aforementioned positive features of the tin-mediated process has prompted the invention of more appealing organostannane derivatives for use in Stille reactions[5] and better methods for the removal of tin-containing byproducts.[6] We too have

† Dedicated to Professor Amos B. Smith, III, in honor of his 60th birthday and 40 years in organic chemistry.

(1) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−523. (b) Farina, V.; Krishnamurthy, V.; Scott, W. J. *The Stille Reaction*; John Wiley & Sons: New York, 1998.

(2) For some recent examples of the employment of the Stille reaction in medicinal chemistry, materials science, and natural product synthesis, see: (a) Elzein, E.; Palle, V.; Wu, Y.; Maa, T.; Zeng, D.; Zablocki, J. *J. Med. Chem.* **2004**, *47*, 4766−4773. (b) Romo, D.; Choi, N. S.; Li, S.; Buchler, I.; Shi, Z.; Liu, J. O. *J. Am. Chem. Soc.* **2004**, *126*, 10582−10588. (c) Liu, J.; Kadnikova, E. N.; Liu, Y.; McGehee, M. D.; Frechet, J. M. J. *J. Am. Chem. Soc.* **2004**, *126*, 9486−9487. (d) Zhang, X.; Kohler, M.; Matzger, A. J. *Macromolecules* **2004**, *37*, 6306−6315. (e) Durham, T. B.; Blanchard, N.; Savall, B. M.; Powell, N. A.; Roush, W. R. *J. Am. Chem. Soc.* **2004**, *126*, 9307−9317. (f) Stangeland, E. L.; Sammakia, T. *J. Org. Chem.* **2004**, *69*, 2381−2385.

(3) (a) Krigman, M. R.; Silverman, A. P. *Neurotoxicology* **1984**, *5*, 129−140. (b) *Chemistry of Tin*; Smith, P. J., Ed.; Blackie Academic & Professional: New York, 1998. (c) Davies, A. G. In *Organotin Chemistry*; VCH: New York, 1997.

(4) Boron: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. Silicon: (b) Hatanaka, T.; Hiyama, T. *Synlett* **1991**, 845−853. (c) Denmark, S. E.; Sweis, R. F. *Chem. Pharm. Bull.* **2002**, *50*, 1531−1541. Zinc: (d) Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719−2724. Indium: (e) Perez, I.; Sestelo, J. P.; Sarandeses, L. A. *J. Am. Chem. Soc.* **2001**, *123*, 4155−4160.

(5) (a) Stannatranes: Yang, C.; Jensen, M. S.; Conlon, D. A.; Yasuda, N.; Hughes, D. L. *Tetrahedron Lett.* **2001**, *41*, 8677−8681 and references cited therein. (b) Alkyltrichlorostannanes: Bumagin, N. A.; Roshchin, A. I. *Russ. J. Gen. Chem.* **2000**, *70*, 57−63 and references cited therein. (c) Monoorganostannanes: Fouquet, E.; Rodriguez, A. L. *Synlett* **1998**, 1323−1324. (d) Polymer-bound organotins: Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Murphy, F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2534−2537.

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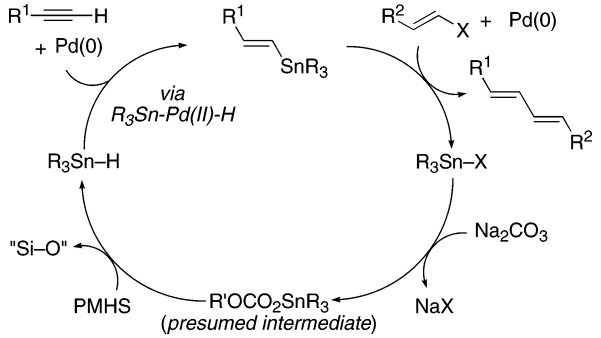
SCHEME 1. Tin-Catalyzed Stille Reactions: The "Sn−O" Approach



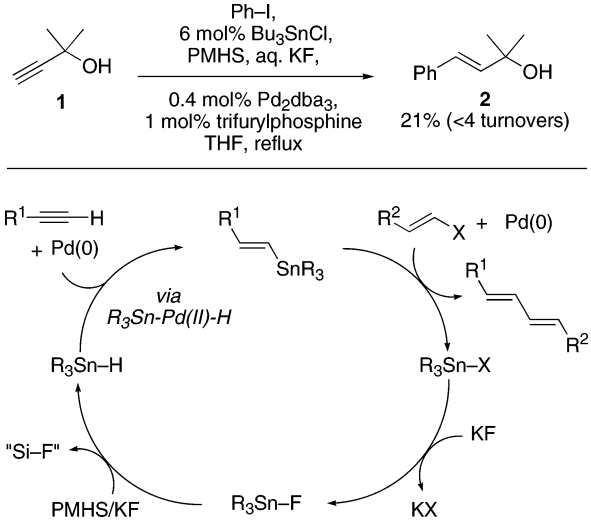
focused on this more direct approached to the "tin problem" by developing a Stille reaction that is catalytic in tin.[7,8]

Results and Discussion

Our early efforts toward such a process focused on connecting a one-pot Pd-mediated alkyne hydrostannation and cross-coupling sequence by recycling the organotin halide Stille byproduct back to tin hydride via polymethylhydrosiloxane (PMHS) reduction of a putative tin carbonate intermediate (Scheme 1).[8] While this first-generation protocol proved to be reasonably successful, improvements were sought by others and us. Kilburn and co-workers nicely addressed the continuing issue of tin residue removal by employing polymer-supported dialkyltin chlorides in the cycle.[9] Similarly, Shay has explored adapting our protocol for operation in room-temperature ionic liquids.[10] In contrast, our development efforts centered on replacing the ill-defined "Sn−O" species in the catalytic cycle.

Early on, the use of fluoride in Stille reactions was investigated by Stille himself,[11] who showed that the use of CsF allowed ~80% of the tin waste to be removed by filtration. It is now common practice to perform a fluoride workup to remove any tin byproducts by converting them to easily filterable organotin fluorides. Moreover, as aggregated solids that are sparingly insoluble in most solvents, organotin fluorides are neither volatile nor easily absorbed through the skin. Given organotin fluoride's lowered health risk and ease of removal and our awareness of more recent studies demonstrating that fluoride-activation of vinylstannanes facilitates their cross-coupling,[12] we decided to investigate a "Sn−F" vs "Sn−O" approach to recycling the tin during our reaction sequence.

SCHEME 2. Tin-Catalyzed Stille Reactions: The "Sn−F" Approach



In initiating this study, we immediately focused on prior work from our labs that showed how a combination of Bu_3SnCl, aqueous KF, and PMHS produced Bu_3SnH in high yield[13] and how organotin hydrides prepared in this way could efficiently hydrostannylate alkynes in situ when formed in the presence of a palladium catalyst.[14] We also knew that aqueous KF and PMHS could regenerate Bu_3SnH from Bu_3SnX produced during dehalogenations, thus rendering those reactions catalytic in tin.[13] Finally, as all evidence pointed to Bu_3SnF as the primary intermediary for these reactions, we hypothesized that the appropriate combination of R_3SnX, PMHS, and fluoride would enable a one-pot hydrostannation/Stille cascade requiring only catalytic amounts of tin (Scheme 2).

In practice, mixing a THF solution of 2-methyl-3-butyn-2-ol (**1**) and iodobenzene with PMHS, aqueous KF and catalytic amounts of Pd_2dba_3, tri-2-furylphosphine, and 6 mol % Bu_3SnCl, for 48 h, produced the cross-coupled product in 21% yield (Scheme 2).[13] The results of this experiment indicated that the tin was being recycled, albeit in unacceptably low turnover numbers. While disappointing, the relatively poor performance of this reaction was not surprising in light of earlier observations. During our "Sn−O" studies,[8] the use of Me_3SnCl instead of Bu_3SnCl proved to be essential for the success of the reaction sequence. Thus, rather than exploring higher tin loads or modifying other reaction conditions, we moved immediately to experiments with Me_3SnCl.

This proved to be rather successful,[15] as reacting alkyne **3** in the presence of KF, catalytic TBAF, catalytic Pd(0), bromostyrene, and 6 mol % Me_3SnCl afforded diene **4** in 90% yield, representing a minimum of 15 tin turnovers (Scheme 3). Examination of other reaction parameters also revealed aqueous KF as the best fluoride

(6) (a) Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 7200−7201. (b) Saloman, C. J.; Danelon, G. O.; Mascaretti, O. A. *J. Org. Chem.* **2000**, *65*, 9220−9222.

(7) Maleczka, R. E., Jr.; Terstiege, I. *J. Org. Chem.* **1998**, *63*, 9622−9623.

(8) (a) Maleczka, R. E., Jr.; Gallagher, W. P.; Terstiege, I. *J. Am. Chem. Soc.* **2000**, *122*, 384−385. (b) Gallagher, W. P.; Maleczka, R. E., Jr.; Terstiege, I. *J. Am. Chem. Soc.* **2001**, *123*, 3194−3204.

(9) Hernán, A. G.; Guillot, V.; Kuvshinov, A.; Kilburn, J. D. *Tetrahedron Lett.* **2003**, *3*, 8601−8603.

(10) Shay, W. R.; Ngwendson, J. N.; Mawo, R. 226th National Meeting of the American Chemical Society, Sept 7−11, 2003, New York; American Chemical Society: Washington, DC, 2003; ORGN 455.

(11) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033−3040.

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(13) (a) Maleczka, R. E., Jr.; Terstiege, I. *J. Org. Chem.* **1999**, *64*, 342−343. (b) Maleczka, R. E., Jr.; Terstiege, I. *J. Org. Chem.* **2000**, *65*, 930.

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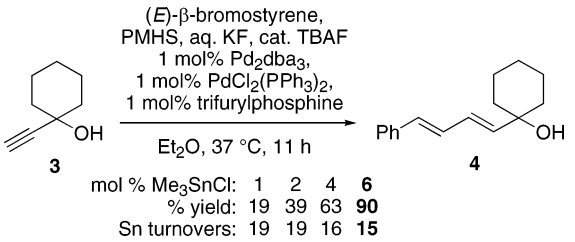
(15) Maleczka, R. E., Jr.; Gallagher, W. P. *Org. Lett.* **2001**, *3*, 4173−4176.

SCHEME 3

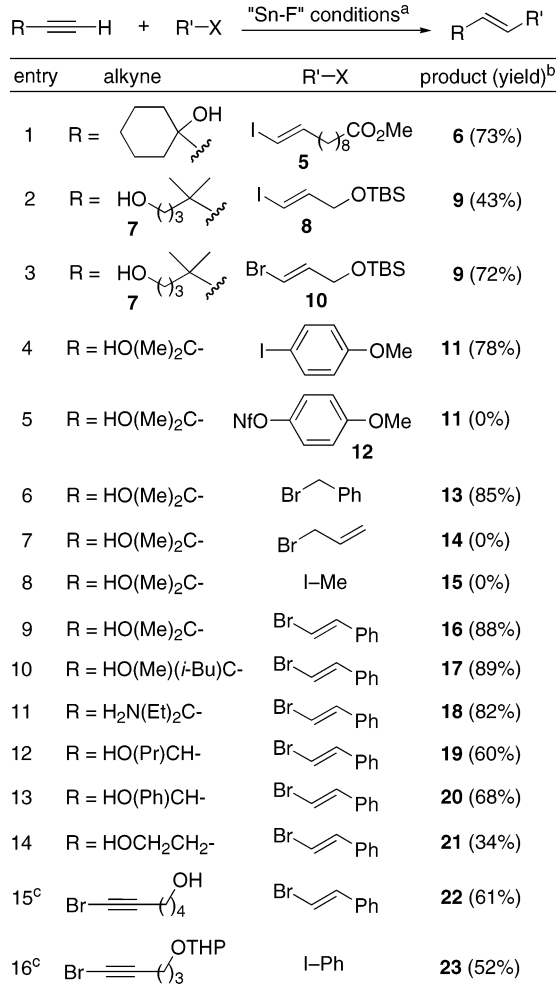


source. Replacing KF with CsF or a CsF:CsOH fused salt afforded high yields of Sonogashira-like enynes instead of the desired Stille products.[16] TBAF also could not be used as the sole fluoride source since reaction of stoichiometric TBAF with R_3SnH affords intrusive amounts of R_3SnSnR_3[17] in what is a terminating event for the catalytic cycle. Despite previous successes with microwave-accelerated one-pot hydrostannation/Stille reactions using stoichiometric amounts of R_3SnH,[18] reactions with catalytic quantities of tin carried out in a conventional microwave oven afforded low yields of the expected dienes. Finally, while higher loads of Me_3SnCl led to little improvement, loadings below 6 mol % resulted in fairly significant reductions in yield (Scheme 3). Thus, 6 mol % would become the standard amount of organotin employed in subsequent explorations of the reaction sequence.

In an effort to gain an appreciation of the reaction's scope, a variety of alkynes and electrophiles were subjected to the hydrostannation/Stille sequence (Table 1). Vinyl and aryl iodides and bromides acted as good electrophiles, as did benzyl bromide (entry 6). In contrast, methyl iodide, allyl bromide, and an aryl nonaflate did not couple under these conditions (entries 5, 7, and 8). Importantly, despite the presence of fluoride, the electrophilic partners could possess TBS ethers (entries 2 and 3). As with our "Sn−O" protocol,[8] α-trisubstituted alkynes (entries 1−11) and α-disubstituted alkynes (entries 12 and 13) coupled well, but reactions with monosubstituted alkynes proceeded poorly (entry 14). To efficiently couple these substrates they were transformed into their bromoalkyne derivatives.[19] These 1-bromoalkynes proved to be successful, giving us the coupled products in modest 61 and 52% yields, respectively (entries 15 and 16).

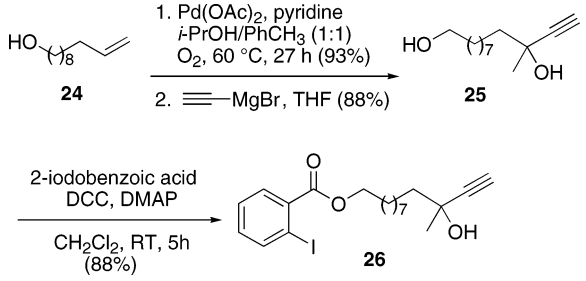
Of course the Stille reactions detailed in Table 1 are all intermolecular in nature. Over the past decade the intramolecular Stille reaction has emerged as a mild and useful way to form variously sized rings.[20] Thus, we wondered if our protocol could be made amenable to a one-pot Pd-mediated hydrostannation/*intramolecular* Stille coupling. To answer this question we first needed to obtain a suitable starting compound. Alkyne-aryl iodide

TABLE 1. Scope and Limitations Studies



[a] "Sn−F" conditions: 6 mol % Me_3SnCl, aq KF, ca. 0.8 mol % TBAF, PMHS, 1 mol % $PdCl_2(PPh_3)_2$, 1 mol % Pd_2dba_3, 4 mol % $(2\text{-furyl})_3P$, Et_2O, 37 °C, 11 h. [b] Average isolated yield of three runs. [c] See Supporting Information for preparation of the starting 1-bromoalkyne.

SCHEME 4



26 was targeted for this purpose; its synthesis being shown in Scheme 4.

10-Undecenol (**24**) was subjected to a Wacker-type oxidation[21] to afford the keto-alcohol in 93% yield. Treatment with ethynylmagnesium bromide afforded the desired alkynol **25** in 88% yield. Finally, DCC-mediated coupling of **25** with 2-iodobenzoic acid produced the target alkyne-aryl iodide **26** in 88% yield.

(16) Use of CsF in combination with PMHS has been explored to produce enynes; see: (a) Gallagher, W. P.; Maleczka, R. E. *Synlett* **2003**, 537−541. (b) Gallagher, W. P.; Maleczka, R. E. *J. Org. Chem.* **2003**, *68*, 6775−6779 and references cited therein.

(17) Kawakami, T.; Shibata, I.; Baba, A. *J. Org. Chem*. **1996**, *61*, 82−87.

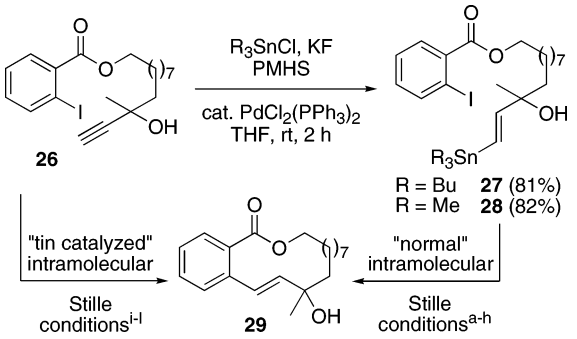
(18) Maleczka, R. E.; Lavis, J. M.; Clark, D. H.; Gallagher, W. P. *Org. Lett*. **2000**, *2*, 3655−3658.

(19) Boden, C. D. J.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2417−2419.

(20) (a) Duncton, M. A. J.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1235−1246. (b) Pattenden, G.; Sinclair, D. J. *J. Organomet. Chem.* **2002**, *653*, 261−268.

(21) Nishimura, T.; Kakiuchi, N.; Onoue, T.; Ohe, K.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, *11*, 1915−1918.

SCHEME 5[a]



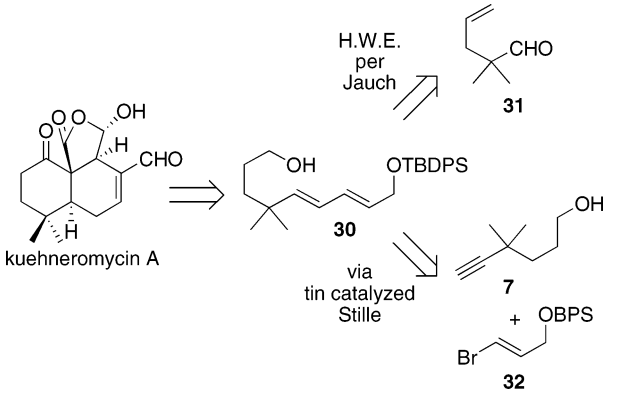
[a] All Stille reactions were carried out with 3 mol % Pd_2dba_3 and 12 mol % ligand at a concentration of 0.005 M. For the "normal" intramolecular Stille conditions: (a) R = Bu, $AsPh_3$, NMP, 60 °C, 22 h, (60% yield); (b) R = Bu, $AsPh_3$, THF, 70 °C, 28 h, (52% yield); (c) R = Bu, $(2\text{-furyl})_3P$, NMP, 60 °C, 24 h, (61% yield); (d) R = Bu, $(2\text{-furyl})_3P$, THF, 70 °C, 27 h, (63% yield). (e) R = Me, $AsPh_3$, NMP, 60 °C, 14 h, (72% yield); (f) R = Me, $AsPh_3$, THF, 70 °C, 15 h, (63% yield); (g) R = Me, $(2\text{-furyl})_3P$, NMP, 60 °C, 10 h, (74% yield); (h) R = Me, $(2\text{-furyl})_3P$, THF, 70 °C, 12 h, (73% yield). For the "tin-catalyzed" intramolecular Stille conditions: (i) 5 mol % Me_3SnCl, aq KF, PMHS, THF, 70 °C, 14 h, (23% yield); (j) same as conditions i except for the addition of **26** by syringe pump over 8 h (29% yield); (k) 5 mol % Me_3SnF, aq Na_2CO_3, PMHS, THF, 70 °C, 12 h, (41% yield); (l) same as conditions k except for the addition of **26** by syringe pump over 8 h (47% yield).

Although Grigg[22] had previously demonstrated the hydrostannation of an alkyne in the presence of an aryl iodide, it was deemed prudent to learn if **26** could be converted into its vinyltin without reduction of the iodide moiety.[23] Furthermore, as intramolecular Stille reactions tend to be more substrate dependent than their intermolecular counterparts, we also thought it sensible to sort out efficient cross-coupling conditions with any vinyltin-aryl iodides prepared from **26**.

In practice, Pd-mediated hydrostannation with PMHS/KF/R_3SnCl generated tin hydride afforded vinylstannanes **27** and **28**[24] in excellent yield (Scheme 5) *and without* hydrodehalogenation of the aryl iodide. Next, a survey of catalyst/ligand combinations and conditions was conducted. On the basis of this assessment, Pd_2dba_3/TFP in THF was chosen as the catalyst/ligand/solvent mix for attempts at the tin-catalyzed one-pot hydrostannation/intramolecular Stille sequence (Scheme 5).

Thus, first experiments were carried out under these Pd-catalyst conditions in union with the general "Sn−F" conditions noted in Table 1. When all reagents were added at once to a 70 °C 0.005 M THF solution (Scheme 5) and the ensuing reaction was allowed to proceed for 14 h, a 23% yield of macrocycle **29** was obtained along with traces of the dehalogenated starting material (GC-MS). Adding **26** via a syringe pump over 8 h slightly improved the process, as **29** was produced in 29% yield and no dehalogenated starting material was detected. Interestingly, and in contrast to the intermolecular results, a modified version of our original "Sn−O" approach (see Scheme 1) to Stille reactions catalytic in tin were superior in the intramolecular version as applied to **26**. A 0.005 M THF solution of 5 mol % Me_3SnF,[25] Pd-catalyst, ligand, PMHS, and Na_2CO_3 with all of **26** added at the beginning of the reaction afforded a 41% yield of **29** after 12 h at 70 °C. Again, the slow addition of **26** netted a small gain in yield (47%). It should also be noted that the Na_2CO_3-based conditions did not produce any detectable amounts of dehalogenated material. Furthermore, in the absence of tin, only starting material was recovered, thus ruling out the occurrence of Heck-type reaction pathways to **29**.

SCHEME 6. Intersecting Jauch's Retrosynthesis of Kuehneromycin A



To conclude our evaluation of scope and synthetic utility, we sought to apply our "Sn−F" method to the synthesis of a literature target molecule, namely, diene **30**. Several years ago, Jauch reported the synthesis of the reverse transcriptase inhibitor kuehneromycin A.[26] His total synthesis proceeds through diene **30**, which was formed via a Horner−Wadsworth−Emmons olefination of aldehyde **31** (Scheme 6). Thus, the synthesis of diene **30** from 4,4-dimethylhex-5-yn-1-ol (**7**) became our test case.

Alkyne **7**[27] had been synthesized before, but in our hands the prior preparation proved too time consuming. Thus, we chose to investigate a dianion alkylation[28] route to this molecule. After some experimentation (Table 2), we found that treating isopropylacetylene **33** with 2 equiv of *n*-BuLi and 1 equiv of TMEDA in Et_2O at 50 °C resulted in the formation of a red dianion solution. This solution was then treated with oxetane,[29] followed by slow addition of $BF_3{\cdot}Et_2O$ at −78 °C. The oxetane was thus ring opened, and alkyne **7** was formed in a synthetically useable 35% yield.

(22) Casaschi, A.; Grigg, R.; Sansano, J. M.; Wilson, D.; Redpath, J. *Tetrahedron* **2000**, *56*, 7541−7551.

(23) Combination of PMHS/aq KF and Pd are known to facilitate dehydrohalogenations. Studies are ongoing in our labs. For recent work, see: (a) Maleczka, R. E., Jr.; Rahaim, R. J., Jr.; Teixeira, R. *Tetrahedron Lett.* **2002**, *43*, 7087−7090. (b) Pri-Bar, I.; Buchman, O. *J. Org. Chem.* **1986**, *51*, 734−735. (c) Maleczka, R. E., Jr.; Rahaim, R. J., Jr. *Tetrahedron Lett.* **2002,** *43*, 8823−8826.

(24) Both **27** and **28** were also prepared via a separate route to confirm their structure: (1) hydrostannation of **25** followed by (2) DCC coupling with 2-iodobenzoic acid. See Supporting Information for full details.

(25) Similar results were observed when, per our original protocol, Me_3SnCl was used as the starting material.

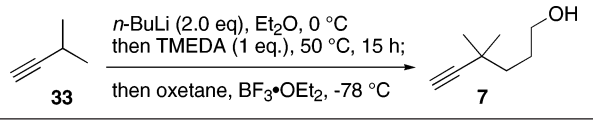
(26) (a) Jauch, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2764−2765. For the isolation, see: Erkel, G.; Lorenzen, K.; Anke, T.; Velten, R.; Gimenez, A.; Steglich, E. *Z. Naturforsch. C.* **1995**, *50*, 1−10.

(27) Harada, T.; Iwazaki, K.; Otani, T.; Oku, A. *J. Org. Chem.* **1998**, *63*, 9007−9112.

(28) (a) Bhanu, S.; Scheinman, F. *J. Chem. Soc., Chem. Commun.* **1975**, 817. (b) McMurry, J. E.; Matz, J. R.; Kees, K. L. *Tetrahedron* **1987**, *43*, 5489−5498.

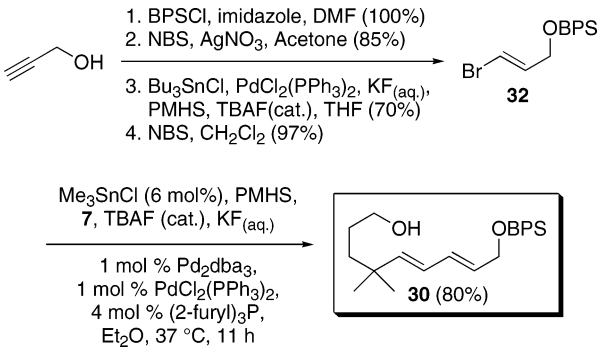
(29) Yamaguchi, M.; Nobayashi, Y.; Hirao, I. *Tetrahedron* **1984**, *40*, 4261−4266 and references cited therein.

TABLE 2. Modified Synthesis of Alkyne 7



entry	method of addition	yield
1	addition of oxetane to dianion followed by BF_3·OEt_2 dropwise at -78 °C	35%
4	addition of dianion to a solution of oxetane/BF_3·OEt_2 at -45 °C	22%
3	addition of dianion to a solution of oxetane/BF_3·OEt_2 at -78 °C	27%
2	addition of oxetane to dianion followed by BF_3·OEt_2 in one portion at −78 °C	20%

SCHEME 7



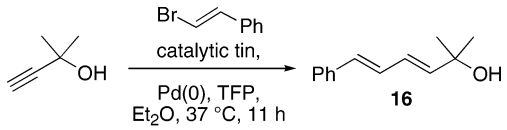
The electrophile for our key tin-catalyzed Stille process was synthesized by first protecting propargyl alcohol as its *tert*-butyldiphenylsilyl (BPS) ether (Scheme 7). To enhance the selectivity during the subsequent Pd(0)-catalyzed hydrostannation,[19] the BPS propargyl ether was converted to its 1-bromoalkyne. Hydrostannation under our standard conditions[14] provided the corresponding (*E*)-vinylstannane and a trace of its proximal isomer (∼95:5). After chromatography, treatment of the vinyltin with NBS afforded (3-bromoallyloxy)-*tert*-butyldiphenylsilane **32** in 58% combined yield from propargyl alcohol. Subjecting vinyl bromide **32**[30] and alkyne **7** to our Me_3SnF-catalyzed protocol afforded diene **30** in 80% yield. In addition to providing a very modest example of the method's performance in target synthesis, the preparation of **30** again highlights this chemistry's tolerance toward silyl ethers.

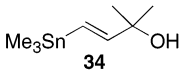
Experiments were also carried out with the intention of providing support for our putative catalytic cycle (Scheme 2). For the reaction described in entry 1 of Table 1, we could start the reaction with 6 mol % of any of the proposed tin intermediates. Indeed, using Me_3SnCl, Me_3SnF, Me_3SnH, or vinylstannane **34** as the initial tin source had very little effect on the outcome of the reaction (Table 3).[31] Stoichiometric experiments that were followed by ^{1}H NMR indicated that the reduction of Me_3SnCl (δ 0.06 ppm in CD_3OD) to Me_3SnH (δ 0.14 ppm) proceeds through Me_3SnF (δ 0.45 ppm). We believe that the spectroscopic and chemical data suggest the sequence to be proceeding via a cycle like that illustrated in Scheme 2. However, it must be stated that the presence

(30) The corresponding vinyl iodide gave intrusive amounts of homocoupling under traditional Stille conditions.

(31) See Supporting Information for full experimental details.

TABLE 3. Evaluating Different Initial Sources of Tin



entry	tin source	yield
1	Me_3SnCl	88%
2	Me_3SnF	85%
3[a]		87%
4	Me_3SnH	86%

[a] See Supporting Information for preparation of vinylstannane **34**.

of multiple aggregates of Me_3SnF, [Me_3SnF(Cl)]K or related "ate" intermediates cannot be completely ruled out.

ICP Analysis. Finally, we scrutinized the end of the reaction to determine the final fate of the tin. During the course of the reaction, a solid material was always present. Filtration and analysis suggested this material to be Me_3SnF, but somewhat surprisingly this recovered solid accounted for only ∼20% of the possible tin. ICP analysis of the organic and aqueous phases separated from the reaction mixture indicated that ∼75% of the tin used in the reaction could be accounted for in the aqueous phase. The crude organics contained ∼0.5% of the reaction's tin or 4.8 ppb.[32] Significantly, after column chromatography, ICP analysis of the purified product measured no detectable amounts of tin.

Summary

In conclusion, we have developed a complementary method for performing one-pot hydrostannation/Stille reactions with catalytic amounts of tin. In addition to lowering the typical tin requirements of these reactions by ∼94%, the use of the organotin fluorides allows for removal of most tin byproducts by a straightforward combination of filtration and extraction. Moreover, after column chromatography, the cross-coupled products can be completely isolated from any measurable amounts of tin.

Experimental Section

General Procedure for the Me_3SnCl-Catalyzed One-Pot Hydrostannation/Stille Coupling. Tri-2-furylphosphine (9.3 mg, 0.04 mmol) was added to a solution of Pd_2bda_3 (9.2 mg, 0.01 mmol) in Et_2O (5 mL). After the solution was stirred at room temperature for 15 min, electrophile (1.5 mmol), Me_3SnCl (0.06 mL, 0.06 mmol; 1 M solution in THF), aq KF (0.1743 g, 3 mmol, 1 mL H_2O), TBAF (1 drop of a 1 M solution in THF (ca. 8 μL or 0.8 mol %)), and $PdCl_2(PPh_3)_2$ (7.0 mg, 0.01 mmol) were all added to the solution. The solution was heated to reflux, and then a solution of alkyne (1 mmol) and PMHS (0.09 mL, 1.5 mmol) in Et_2O (4 mL) was added via a syringe pump over 11 h. The phases were separated and the organics washed with brine, dried over $MgSO_4$, filtered, and concentrated. The resulting residue was purified by column chromatography. Full experimental details are given in Supporting Information.

(32) The remaining ∼4.5% of the tin was unaccounted for.

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Supporting Information Available: Experimental procedures for Schemes 2−5 and 7 and Tables 1 and 2, additional experimental details for the preparations of compounds **5**, **8**, **10**, **27**, **28**, and **34**, descriptions of control experiments and ligand surveys, and ^{1}H and ^{13}C NMR spectra for all reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

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