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# Stille Couplings Catalytic in Tin: The “Sn−O” Approach

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**Abstract:** A one-pot tandem Pd-catalyzed hydrostannylation/Stille coupling protocol for the stereoselective generation of vinyltins and their subsequent union, employing only catalytic amounts of tin, is described. By recycling the organotin halide Stille byproduct back to organotin hydride, a hydrostannylation/cross-coupling sequence can be carried out with catalytic amounts of tin. Such a process is most effective with $Me_3SnCl$ serving as the tin source. This protocol allows a 94% reduction of the tin requirement, while maintaining good yields (up to 90%) for a variety of Stille products. Furthermore, since one cycle requires the tin to undergo at least four transformations, each moiety of trialkyltin is experiencing a minimum of 60 reactions over the course of the hydrostannylation/Stille sequence.

## Introduction

Beginning in the late 1970s and continuing throughout most of the 1980s, studies by the late J. K. Stille helped to establish the palladium-catalyzed cross-coupling reaction of organotin reactants with a variety of organic electrophiles as a highly useful method for carbon−carbon $\sigma$-bond construction.[1,2] Today, Stille reactions commonly represent a key step in the preparation of natural products,[3] new materials,[4] medicinal agents,[5] etc. Although the Stille reaction can be viewed as a routine synthetic tool, its study continues.[1d] Recent advances include adaptation of the method to aqueous,[6] combinatorial,[7] solid phase,[7b,c,8] fluorous phase,[9] and super critical environments.[10] Recent work has also provided a greater mechanistic understanding of the reaction,[11] expanded its scope,[12] and improved existing Stille protocols.[13]

Many of the newly reported improvements to the Stille reaction offer greater ease in the separation of the cross-coupled product from the organotin byproducts. Difficulties in purification along with cost and toxicity issues associated with using stoichiometric amounts of organostannanes[14] have long been considered problematic features of these reactions. Solutions to the “tin problem” have largely focused on either derivatizing

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the organotin[5b,6b,8f,i,9,13b−d] or inventing reaction workups[1d,15] aimed at aiding removal of the tin byproducts.[16]

A complementary approach to this problem would be to develop a Stille cross-coupling protocol catalytic in tin. The development of such a catalytic process would involve the design of a catalytic process where the organotin species is the reactant;[17] that is to say, where the tin moiety is fixed to the organic substrate via a stable, covalent bond.[18]

## Results and Discussion

Early work in pursuit of a tin-catalyzed Stille protocol focused on the fact that, in addition to the Stille reaction, the hydrostannylation of terminal alkynes can also be catalyzed by palladium(0).[19] Thus, a Stille reaction catalytic in tin could be achieved if organotin hydride could undergo an in situ chemoselective sequence of Pd(0)-catalyzed vinyltin generation and cross coupling and then be regenerated from the organotin halide byproduct (Figure 1). Realization of such a catalytic cycle would require the address of several issues including (a) regioselectivity during the Pd(0)-mediated hydrostannylation, (b) finding catalyst and solvent conditions which will allow both hydrostannylation and cross coupling, while at the same time minimizing unwanted side reactions (vide infra), and (c) uncovering appropriate methods for recycling the $R_3SnX$ back to $R_3SnH$.

To avoid regiochemical complications, the first group of alkynes studied were all trisubstituted at the propargylic position. Such sterically hindered alkynes are known to heavily favor formation of the terminal (distal) (*E*)-isomer over the internal (proximal) isomer.[19,20]

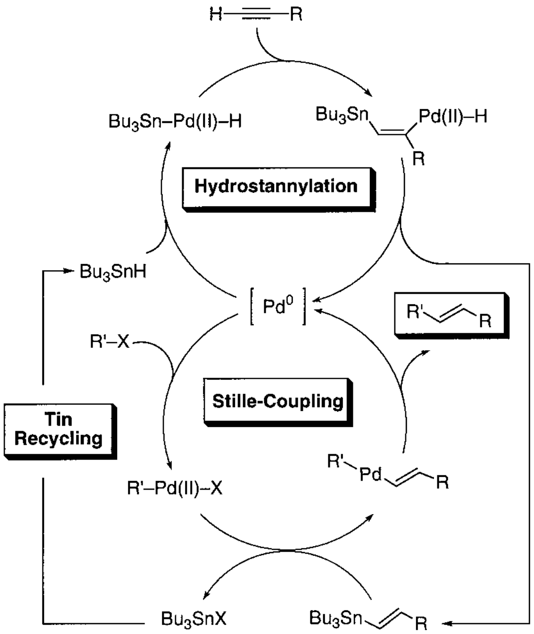

**Figure 1.**

Although the regiochemical outcome of the hydrostannylation was assured, the feasibility of carrying out Pd-catalyzed hydrostannylations in the presence of a Stille electrophile was not. A balance would need to be struck between the catalyst requirements for high-yielding hydrostannylations (strong $\sigma$-donor ligands such as $PPh_3$) and efficient cross couplings (weaker $\sigma$-donor ligands).[1d] Equally important was the need to minimize side reactions, especially Pd-mediated $Bu_3SnH$ dimerization[21] and/or reduction of the organohalides.[22] To address the dimerization issue, we examined the palladium-mediated hydrostannylation under a variety of “Stille-like” catalyst and solvent conditions. After investigating the performance of several Pd catalysts ($Pd_2dba_3$/P(2-furyl)$_3$, $(PPh_3)_2PdCl_2$, $(MeCN)_2PdCl_2$) in various solvents ($Et_2O$, THF, DMF, NMP), $(PPh_3)_2PdCl_2$ and $Pd_2dba_3$/P(2-furyl)$_3$ in ethereal solvents (THF or $Et_2O$) emerged as most proficient. Other Pd/solvent combinations promoted bistributyltin formation to such an extent that the rate of the hydrostannylation reactions could no longer compete.

With suitable catalyst and solvent conditions secured, the next step was to combine the hydrostannylation and Stille coupling into a single-pot reaction sequence.[23] Initially operating with stoichiometric amounts of tin,[24] tributyltin hydride was added to a solution of alkyne, bromostyrene, and Pd catalyst in THF. Although reaction times were relatively long (1−5 days), the one-pot hydrostannylation/Stille sequence gave cross-coupled products in yields comparable to those of the stepwise protocol (Table 1).[25,26] Furthermore, GC analysis of the reaction mixture

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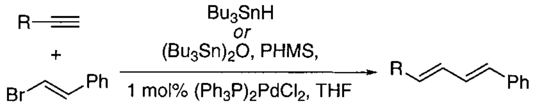
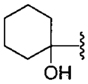
**Table 1**



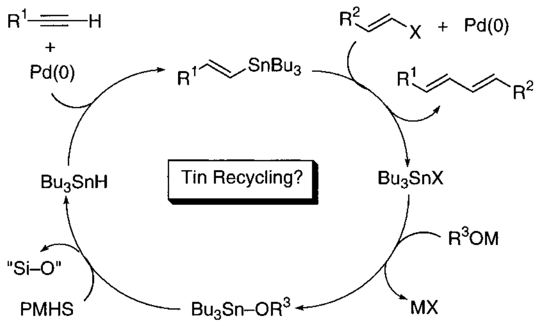
| entry | alkyne | | product yields[a] | | |
|---|---|---|---|---|---|
| | | | $Bu_3SnH$ | PMHS/ $(Bu_3Sn)_2O$ | stepwise |
| 1 | R = HO(Me)$_2$C– (**1**) | **2**: | 87% | 66% | 49% |
| 2 | R = *t*-Bu– (**3**) | **4**: | 89% | 52% | 19%[c] |
| 3 | R =  OH (**5**) | **6**: | 51% | 52% | 42% |
| 4 | R = HO(Me)(Ph)C– (**7**) | **8**: | 75% | 69% | 56% |
| 5 | R = HO(Me)(Et)C– (**9**) | **10**: | 86% | 60% | 56% |
| 6 | R = HO(Me)(*i*-Bu)C– (**11**) | **12**: | 76% | 58% | 35% |
| 7 | R = H$_2$N(Et)$_2$C– (**13**) | **14**: | 47%[b] | – | 36% |

[a] Unless otherwise stated, all yields refer to isolated products. [b] On the basis of 37% recovered vinylstannane. [c] The low yield was in part due to difficulties in purifying the nonpolar vinyltin inermediate.

showed that no Pd-mediated reduction of bromostyrene had occurred.[22,27]

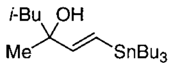
With these results in hand, methods for recycling the $Bu_3SnX$ byproduct back to $Bu_3SnH$ were considered. Strong hydride donors such as $LiAlH_4$ or $NaBH_4$[14,28] were less than ideal as they are known to reduce Pd(II) intermediates[29] and would severely curtail the broad functional group tolerance normally associated with the Stille reaction. Hayashi et al.[30] had shown that tributyltin hydride can be generated via reduction of $(Bu_3Sn)_2O$ by the cheap, nontoxic, and relatively mild hydride donor, polymethylhydrosiloxane (PMHS).[31] Furthermore, the $(Bu_3Sn)_2O$/PMHS mixture had been shown to work well as an in situ source of $Bu_3SnH$ in free radical hydrostannylations of 1-alkynes,[32] while the elegant work of Fu and co-workers[17a,b] demonstrated that PMHS and other silanes can serve as the stoichiometric reducing agent in reactions catalytic in tin. Although PMHS does not reduce organotin halides,[33] numerous methods exist for converting the Sn−X bond into a Sn−O bond.[14] Thus, an "Sn−O" approach to the development of a Stille reaction catalytic in tin was pursued (Scheme 1).

**Scheme 1**

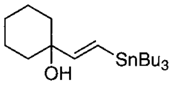


The $(Bu_3Sn)_2O$/PMHS method of $Bu_3SnH$ formation was successfully applied to the one-pot hydrostannylation/Stille sequence (Table 1). Importantly, palladium-mediated hydrosilylation of the alkyne or alkene[34] was not observed.[35] However, a 2-fold excess of $(Bu_3Sn)_2O$ was required since generation of two full equivalents of $Bu_3SnH$ from one molecule of $(Bu_3Sn)_2O$ occurs only at elevated temperatures (80−110 °C).[30]

With these results in place, a method of converting the tin halide into an Sn−O species that would be amenable to the sequence of reactions and reagents was sought. Various methods of effecting such a transformation were studied. Since treatment of $Bu_3SnCl$ with $NH_4OH$ had been previously reported to afford $(Bu_3Sn)_2O$,[36] $Bu_3SnCl/NH_4OH$/PMHS as a potential in situ source of $Bu_3SnH$ was studied. However, when ammonium hydroxide was added to an ethereal solution of tin chloride **11**, Pd(0), and PMHS dimer, formation of a white precipitate was observed (presumably ammonium chloride) and, after 2.5 h reaction time, only a 1:1 ratio of product (**15**) to starting material was obtained. Heating the reaction mixture in toluene/EtOH for 6.5 h increased the ratio to 1.7:1; however, it was not possible to drive this reaction to completion. Thus, direct conversion of the tin halide byproduct into bis(tributyltin) oxide appeared impractical.



**15**



**16**

Since organotin halides can be converted to organotin alkoxides,[37] attention turned to tributyltin methoxide as a tributyltin hydride precursor. Hydrostannylation of alkyne **5** using $Bu_3SnOMe$ and PMHS as the in situ tin hydride source produced a small amount of product after 20 min at 0 °C; however, upon stirring at room temperature for an additional 1.5 h, the vinylstannane (**16**) could be isolated in 52% yield.[38] Furthermore, a $Bu_3SnX$ to $Bu_3SnOMe$ to $Bu_3SnH$ sequence also worked in a hydrostannylation reaction. Reaction of tributyltin bromide with sodium methoxide at 0 °C, followed by **5**, PMHS, and Pd(0), was complete in only 15 min,[39] again affording the vinylstannane in 52% yield.[40] The reaction sequence could also be carried out by mixing all the reagents at once, and if run below 0 °C, the yield could be improved to 74%.

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(26) As a check on our hydrostannylation experiments, we carried out the one-pot sequence in the better Stille solvent DMF (ref 1c). In these experiments a larger excess of tin hydride (~2.5 equiv) was required to consume the alkyne affording the Stille product (~35%), recovered stannane (~38%), and a fairly large amount (17%) of styrene dimer.

(27) It is possible that styrene is not stable under the reaction conditions and therefore could not be detected. However as bromostyrene was used in only very small excess (with respect to the alkyne) and the Stille products were often isolated in high yields (86−89%), it could be concluded that reduction occurs in only a very small extent, if at all.

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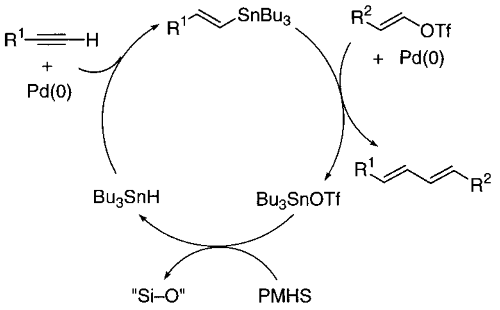
(36) Sawyer, A. K. In *Organotin Compounds*; Marcel Deccer: New York, 1971; Vol. 1.

(37) Alleston, D. L.; Davies, A. G. *J. Chem. Soc.* **1962**, 2051−2052.

(38) In theory $Bu_3SnH$ could be generated from $Bu_3SnOMe$ without PMHS via $\beta$-hydride elimination of a $Bu_3Sn−Pd(II)−OMe$ species: (a) Palucki, M.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 3395−3396. (b) Zask, A.; Helquist, P. *J. Org. Chem.* **1978**, *43*, 1619−1620. However, hydrostannylation experiments performed in the absence of PMHS did not produce any product, thus arguing against such a mechanism.

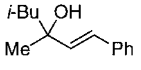
**Scheme 2**



Unfortunately, attempts at carrying out the same sequence with catalytic amounts of tin failed. Stirring NaOMe, PMHS, alkyne **11**, bromostyrene, catalytic Pd(0), and 20 mol % of $(Bu_3Sn)_2O$[41] in THF at 60 °C for 18 h only afforded 3% of the cross-coupled product (**12**). Under low concentrations, the NaOMe reacts with PMHS rather than the organotin species, resulting in gas evolution[40] and formation of an insoluble gel.[42]

In theory, the problematic halide to oxide step could be circumvented through the employment of vinyl or aryltriflates as Stille electrophiles (Scheme 2). However, attempts to generate vinylstannanes with tributyltin hydride derived from PMHS reduction of $Bu_3SnOTf$ gave no observable reaction until prolonged stirring/heating decomposed all reactants. On the basis of these results, this approach was abandoned in favor of finding a PMHS-compatible oxo-nucleophile for converting the organotin halide into an organotin alkoxide.

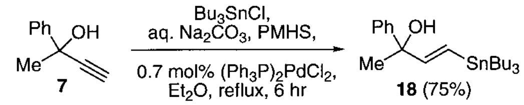
In this regard, alkoxides which are less basic/nucleophilic than NaOMe were examined. Although a solution of NaOPh and PMHS in $Et_2O$/THF polymerized within 15 min, qualitatively the reaction was slow as compared to that with NaOMe. Given the reactivity difference, NaOPh was tested in a $Bu_3SnX$ to $Bu_3SnOPh$ to $Bu_3SnH$ to vinyltin sequence. Treatment of $Bu_3SnX$ with NaOPh in THF,[43,44] followed by alkyne **11**, $(Ph_3P)_2PdCl_2$, and finally PMHS, resulted in complete disappearance of the alkyne within 15 min at room temperature, and ultimately allowed isolation of the vinylstannane (**15**) in 71% yield. Adding phenyl iodide to the reaction provided **17** in 54% yield.[45]



**17**

During attempts at carrying out the sequence with catalytic amounts of tin, the only suggestion of tin turnover came when the reactions were carried out in a repetitive stepwise fashion. In these experiments, 1 equiv of $Bu_3SnCl$ in the presence of 1 equiv of **11** was first reacted with NaOPh and then PMHS. Upon complete consumption of the alkyne (approximately 30 min), the temperature was raised, 4 equiv of phenyl iodide was added, and the cross coupling proceeded. Consumption of the vinylstannane then constituted completion of the first cycle, at which time another equivalent of **11** and NaOPh followed by more PMHS were added. This allowed formation of the Stille product (**17**) in near quantitative yield based on tin (55% based on alkyne).

**Scheme 3**



Organotin formates and acetates[46] were also explored as potential reaction intermediates. Prolonged heating of reaction mixtures containing a tributyltin halide, PMHS, Pd(0) catalyst, alkyne **7**, and either NaOAc or $HCO_2NH_4$ did indeed effect hydrostannylation of the alkyne. However, crude NMR and TLC showed the reactions also contained significant amounts of the starting alkyne or protiodestannylated material.[47]

Following the failure of carboxylates, we turned to carbonates. When THF solutions of alkyne **7** and $Bu_3SnCl$ were treated with PMHS, Pd catalyst, and a 3-fold excess of the partially organic soluble $Cs_2CO_3$, only small amounts of vinylstannane were detected accompanied by a large amount of decomposition products. On the other hand, with a mixture of aqueous $Na_2CO_3$ in refluxing $Et_2O$,[48] vinylstannane **18** was afforded as a 15:1 ratio of (*E*)/internal isomers (Scheme 3).[49] The hydrostannylation probably proceeds through a tin carbonate; however, the exact structures of triorganotin carbonates remains a subject of debate.[50] In fact, the possibility that $Bu_3SnCl$ is hydrolyzing in the aqueous media,[51] with the resultant tin hydroxide (or oxide) being reduced by the PMHS, has not been ruled out. However, reactions run in carbonate-free water showed only trace amounts of **18** by TLC.

Experiments aimed at incorporating the cross-coupling step into the sequence identified $Pd_2dba_3$ and $P(2\text{-furyl})_3$(TFP) as a better palladium ligand combination. Furthermore, we experimented with the order and time over which reactants were added. Thus, syringe pump addition of alkyne, bromostyrene, and PMHS to a solution of $Bu_3SnCl$, aqueous $Na_2CO_3$, and Pd(0) produced the Stille product (**8**) in 47% yield[52] or an average of 84% for each of the four reaction steps involved (tin carbonate formation, tin hydride formation, hydrostannylation, Stille

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(39) The shorter reaction time when starting with $Bu_3SnBr$ is interesting as this approach includes one more transformation. We do not believe $Bu_3SnBr$ is reduced directly by PMHS, as treatment of $Bu_3SnBr$ and $Bu_3SnCl$/NaI with PMHS in the absence of NaOMe did not produce any product. That said we cannot rule out the possibility that $NaOCH_3$ activates the PMHS via a pentacoordinated silane intermediate (Chuit, C.; Corriu, R. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371−1448), making it more reactive than the nonactivated PMHS toward either $Bu_3SnBr$ or $Bu_3SnOCH_3$.

(40) The reaction was accompanied by gas evolution, presumably $H_2$.

(41) On the basis of the observations by Fu et al. (Hays, D. S.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 4−5. Lopez, R. M.; Hays, D. S.; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 6949−6950), we expected NaOMe would also react with $(Bu_3Sn)_2O$ and the in situ formed $Bu_3SnOSiR_3$ allowing $(Bu_3Sn)_2O$ to produce 2 equiv of $Bu_3SnH$ despite the relatively low reaction temperatures.

(42) In a control experiment, PMHS and NaOR (R = Me or Et) were admixed and within minutes an insoluble gel was formed under heavy gas evolution.

(43) Running the reaction in dioxane/THF afforded the vinyltin in 46% yield along with the stannane homocoupled product, whereas DMF/THF as solvent and $(MeCN)_2PdCl_2$ as catalyst only gave $Bu_3SnSnBu_3$.

(44) The reaction slowed when run in toluene/THF and led to unidentified byproduct formation. This is consistent with reports by Fu et al. (ref 17b) that PMHS reduction of $Bu_3SnOPh$ requires the addition of BuOH which presumably transforms the tin phenoxide into the more reactive butoxide. Our results suggest that PMHS can easily reduce $Bu_3SnOPh$ as long as THF is used as the solvent.

(45) Running the reaction in dioxane (higher boiling point) yielded 40% of the Stille product.

(46) Bähr, G.; Pawlenka, S. *Methoden der Organischen Chemie*; Thieme Verlag: Stuttgart, 1978; pp 295−296.

(47) The protiodestannylated material may actually be the result of Pd(0)/$HCO_2NH_4$-mediated hydrogenolysis of the alkyne (Tsuji, J.; Yamakawa, T. *Tetrahedron Lett.* **1979**, 613−616).

(48) For reasons that remain unclear, reactions run in THF were often not as clean as those run in $Et_2O$. See ref 19c for further discussion.

(49) Attempts to optimize this reaction via the use of aqueous $K_2CO_3$ in MeOH proved unproductive.

(50) Kümmerlen, J.; Sebald, A. *J. Organomet. Chem.* **1992**, *427*, 309−323 and references therein.

(51) (a) Das Sarma, K.; Maitra, U. *Tetrahedron* **1998**, *54*, 4965−4976. (b) Maitra, U.; Das Sarma, K. *Tetrahedron Lett.* **1994**, *35*, 7861−7862.

**Scheme 4**

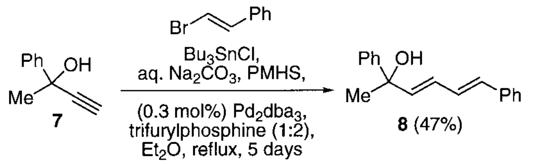
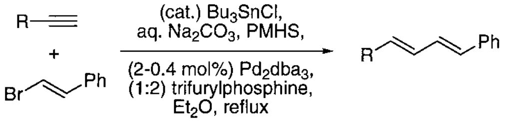
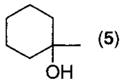


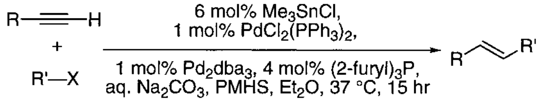
**Table 2**

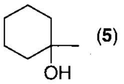
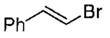
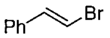
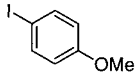
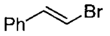
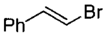
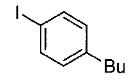
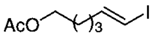
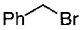
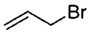
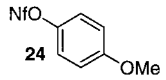


| entry | alkyne | $Bu_3SnCl$ [mol%] | Sn turnovers | product yield |
|---|---|---|---|---|
| 1 | R = HO(Me)(Ph)C– (**7**) | 20 | 2 | **8**: 40% |
| 2 | R = HO(Me)(Ph)C– (**7**) | 4 | 5 | **8**: 22%[a] |
| 3 | R = $HO(Me)_2C$– (**1**) | 10 | 2 | **2**: 24% |
| 4 | R =  OH (**5**) | 10 | 2.5 | **6**: 26% |

[a] 1 mol % $Pd(Ph_3P)_2Cl_2$ was also added to the reaction.

**Table 3**



| entry | alkyne | R'—X | product yield |
|---|---|---|---|
| 1 | R =  OH (**5**) |  | **6**: 90% |
| 2 | R = HO(Me)(Ph)C– (**7**) |  | **8**: 85% |
| 3 | R = HO(Me)(Ph)C– (**7**) |  | **19**: 80% |
| 4 | R = $H_2N(Et)_2C$– (**13**) |  | **14**: 86% |
| 5 | R = $HO(Me)_2C$– (**1**) |  | **2**: 91% |
| 6 | R = $HO(Me)_2C$– (**1**) |  | **20**: 75% |
| 7 | R = $HO(Me)_2C$– (**1**) |  **21** E/Z 4:1 | **22**: 80% |
| 8 | R = $HO(Me)_2C$– (**1**) |  | **23**: 85% |
| 9 | R = $HO(Me)_2C$– (**1**) |  | no Stille product |
| 10 | R = $HO(Me)_2C$– (**1**) | Me–I | no Stille product |
| 11 | R = $HO(Me)_2C$– (**1**) |  **24** | no Stille product |

coupling) (Scheme 4). With this result in hand, reactions were attempted with catalytic amounts of tin.

Again experimenting with the rate and order of addition, several alkynes were mixed with bromostyrene, catalytic $Pd_2dba_3$/TFP, aqueous $Na_2CO_3$, and substoichiometric quantities of $Bu_3SnCl$. As illustrated in Table 2, such a blend of reactants afforded the first clear examples of Stille reactions catalytic in tin. With tin loads ranging from 20 to 3.7 mol %, the dienes were produced in yields representing two–five tin turnovers.[53]

While the results of Table 2 established proof-of-principle, the modest to poor yields were less than practical. In part, the long reaction times (up to 72 h) offered ample time for the tin to react down nonproductive avenues. Attempts to accelerate the reaction through the use of polar solvents (DMF or NMP) or more active catalysts such as $(MeCN)_2PdCl_2$ resulted in overall diminished yields, as Pd-catalyzed conversion of $Bu_3SnH$ into hexabutylditin predominated the reaction.[21] Furthermore, the addition of copper salts provided little or no improvement in the catalytic process.[13a,g,54] In contrast, switching from tributyltins to the less sterically demanding trimethyltins accelerated and, in turn, significantly improved the efficiency of the catalytic cycle.[55,56] As illustrated in Table 3 (entries 1–8), syringe pump addition of 1.1 equiv of vinyl, aryl, or benzyl bromides or iodides to a 37 °C ethereal mixture of various α-trisubstituted alkynes, aqueous $Na_2CO_3$, PMHS, $Pd_2dba_3$, trifurylphosphine, $PdCl_2(PPh_3)_2$,[57] and 0.06 equiv of $Me_3SnCl$[58] over a period of 15 h afforded the corresponding cross-coupled products in 75–91% yields representing an average of ~15 tin turnovers. Allyl bromide and methyl iodide failed under these conditions, and somewhat consistent with our earlier experience with triflates, nonaflate **24** also gave no Stille products (Table 3, entries 9–11).

To more fully address regiochemical issues, sterically less demanding alkynes were applied to the protocol. Two α-disubstituted alkynes[59] afforded the anticipated dienes (Table 4, entries 1–2) but in lower yields presumably due to diminished regiocontrol during the hydrostannylation portion of the reaction sequence.[19]

α-Monosubstituted alkynes performed poorly (Table 4, entries 3–4). For example, reaction of **31** resulted in the formation of **32** (16% yield) and the cross-coupled product derived from the proximal vinyltin (3% yield). These results were not entirely surprising as unhindered alkynes are known to undergo non-

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(52) In comparison, preparing and isolating the vinyltin (via $Bu_3SnH$ and $Pd_2dba_3$/$(P(2\text{-furyl})_3$ and then subjecting that material to the Stille reaction (via $Pd_2dba_3$/$(P(2\text{-furyl})_3)$) gave the cross-coupled product in 63% (56% with $(PPh_3)_2PdCl_2$), whereas a one-pot hydrostannylation/Stille with $Bu_3SnH$ and $(PPh_3)_2PdCl_2$ afforded the diene in 75% yield.

(53) The same reaction sequence *absent* tin produced no Stille coupling products, ruling out the Pd-mediated coupling of a transient vinylsilane with the halide [(a) Hosimi, A.; Kohra, S.; Tominaya, Y. *Chem. Pharm. Bull.* **1988**, *36*, 4622–4625. (b) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918–923].

(54) Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C. J.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905–5911.

(55) Maleczka, R. E., Jr.; Gallagher, W. P.; Terstiege, I. *J. Am. Chem. Soc.* **2000**, *122*, 384–385.

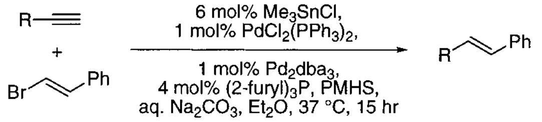
(56) Previous work suggests a only a small increase in the rate-determining transmetalation rate for trimethyl- vs tributylstannanes (Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129–6137), thus in this case substituting $Me_3Sn$ for $Bu_3Sn$ may also facilitate formation of more reactive hypervalent tin species.

(57) :1 $Pd_2dba_3$, $(2\text{-furyl})_3P$, and $PdCl_2(PPh_3)_2$ gave the best yields. In situ reduction of $PdCl_2(PPh_3)_2$ gives the coordinatively unsaturated Pd(0)-$(PPh_3)_2$ (ref 1c). This species, along with the 1:1 mixture of $Pd_2dba_3$ and $(2\text{-furyl})_3P$, affords Pd(0) which is capable of complexing with a $PPh_3$ and/or $(2\text{-furyl})_3P$. We speculate that this combination of ligands provides a good compromise between activity toward cross coupling and $Bu_3SnH$ dimerization. However, simply adding the appropriate quantities of $PPh_3$ and/or $(2\text{-furyl})_3P$ to a solution of either $Pd_2dba_3$ or $PdCl_2(PPh_3)_2$ did not prove as effective. Thus the reason for the optimal performance of the mixed palladium system remains unclear.

(58) Since $Me_3SnCl$ is more prone to hydrolysis than $Bu_3SnCl$, we repeated the experiment aimed at determining the necessity of $Na_2CO_3$. As before, reacting **7** with water, $Me_3SnCl$, Pd catalyst, and PMHS in refluxing $Et_2O$ failed to provide measurable quantities of the vinyltin.

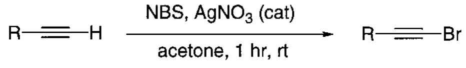
(59) But-3-yn-2-ol was also studied, but did not afford any of the anticipated diene. Rather two unidentified more polar compounds were observed. Analogous compounds were not detected when reacting **25** or **27**.

**Table 4**



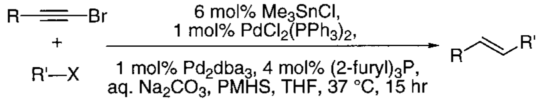
| entry | alkyne | product yield |
|---|---|---|
| 1 | R = HO($n$-Pr)CH– (**25**) | **26**: 59% |
| 2 | R = HO(Ph)CH– (**27**) | **28**: 69% |
| 3 | R = $HOCH_2CH_2$– (**29**) | **30**: 36% |
| 4 | R = $MeOCH_2$– (**31**) | **32**: 16% |

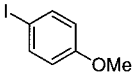
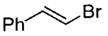
**Table 5**



| entry | 1-alkyne | product yield |
|---|---|---|
| 1 | R = $HOCH_2CH_2$– (**29**) | **33**: 95% |
| 2 | R = $HO(CH_2)_3CH_2$– (**34**) | **35**: 95% |
| 3 | R = $THPO(CH_2)_2CH_2$– (**36**) | **37**: 97% |

**Table 6**



| entry | 1-alkyne | R'—X | product yield |
|---|---|---|---|
| 1 | R = $HOCH_2CH_2$– (**33**) | <br>I<br>OMe | **38**: 52% |
| 2 | R = $HO(CH_2)_3CH_2$– (**35**) | <br>Ph Br | **39**: 51% |
| 3 | R = $THPO(CH_2)_2CH_2$– (**37**) | Ph—I | **40**: 52% |

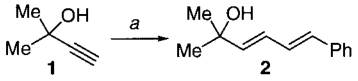
regioselctive palladium-mediated hydrostannylation.[60] Furthermore, Stille coupling of internal (proximal) isomers is very sluggish, thus prohibiting efficient tin turnover.[61]

To circumvent problems associated with unhindered alkynes, the employment of 1-bromoalkynes was examined. Guibé[19a] and more recently Pattenden[23] have shown that palladium-mediated hydrostannylations of 1-bromoalkynes proceed with a high bias toward the (*E*)-vinylstannanes. Since these reactions produce the $R_3SnBr$ as a byproduct, we rationalized that 1-bromoalkynes should be amenable to our chemistry.

Following the general procedure of Pattenden,[23] several 1-bromoalkynes were prepared (Table 5). Despite adding a fifth tin reaction to the sequence, these substrates cleanly afforded dienes in ~50% yield (Table 6).[62]

The effect of tin loading was also studied. While higher loads of $Me_3SnCl$ saw little improvement, loadings below 6 mol % of tin resulted in fairly significant reductions in yield (Scheme 5). For example, at 1 mol % of $Me_3SnCl$ the 1,3-diene was formed in only 18% yield.

**Scheme 5**

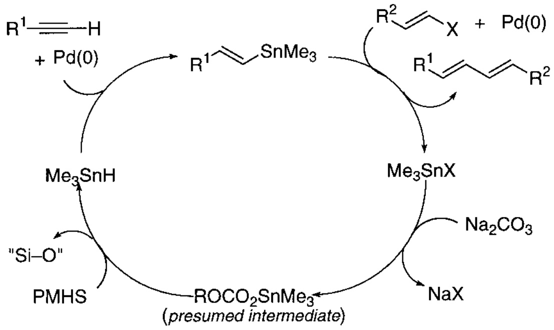


**1** **2**

$^a$ (cat.) $Me_3SnCl$,1 mol% $PdCl_2(PPh_3)_2$, 1 mol% $Pd_2dba_3$, 4 mol% $(2\text{-furyl})_3P$, PMHS, aq. $Na_2CO_3$, bromostyrene, $Et_2O$, 37 °C, 15 hr

| $Me_3SnCl$ [mol%] | Sn turnovers | yield |
|---|---|---|
| 6 | 15 | 91% |
| 4 | 17 | 67% |
| 1 | 18 | 18% |

**Scheme 6**



## Conclusions

The limitations and problems associated with the stoichiometric tin requirement of traditional Stille reactions has been addressed. Studies have demonstrated the feasibility of a one-pot tandem Pd-catalyzed hydrostannylation/Stille coupling with either $Bu_3SnH$ or $(Bu_3Sn)_2O$ and PMHS serving as the tin hydride source. Furthermore, by in situ conversion of the organotin halide Stille byproduct into an intermediate tin carbonate and then back to organotin hydride, it is possible to conduct a hydrostannylation/cross-coupling sequence with catalytic amounts of tin. Such a sequence is most effective with $Me_3SnCl$ serving as the tin source. While trimethyltins carry the burden of increased toxicity,[14,63] their use can allow for a 94% reduction of the tin requirement while maintaining good yields (up to 90%) for a variety of Stille products. Furthermore, since one cycle requires the tin to undergo at least four transformations (Scheme 6), each molecule of organostannane is experiencing a minimum of 60 reactions over the course of the hydrostannylation/Stille sequence.

For optimal efficiency, the hydrostannylation/Stille sequence is best run with α-trisubstituted alkynes so as to avoid regiochemical mixtures during the hydrostannylation step and beyond. This limitation can be mitigated by the employment of 1-bromoalkynes which provide a good level of regiocontrol in the hydrostannylation step and thereby enable the formation of the Stille product, albeit in more modest yields (50–55%).

## Experimental Section[64]

**Representative Procedure for a Stepwise Hydrostannylation/Stille Cross Coupling (Table 1). Preparation of 5-Methyl-1-phenyl-1,3-hexadien-5-ol (2).** $(Ph_3P)_2PdCl_2$ (28 mg, 0.04 mmol) and 3-methyl-1-butyn-1-ol (**1**) (0.40 mL, 4 mmol) were added to 20 mL of THF. The solution was cooled to 0 °C with an ice bath, and then $Bu_3SnH$ (1.18 mL, 4.4 mmol) was added dropwise. The reaction was stirred for 1 h and then concentrated. The resulting residue was then purified by column chromatography (silica gel; pentane/EtOAc 90:10, 1% $Et_3N$) to afford 1.12 g (75%) of 1-(tributylstannyl)-3-methyl-1-(*E*)-buten-3-ol[65] as a clear oil. A solution of the 1-(tributylstannyl)-3-methyl-1-(*E*)-buten-3-ol (1.13 g, 3 mmol), (*E*)-*β*-bromostyrene (0.42 mL, 3.3 mmol), and $(Ph_3P)_2PdCl_2$ (7 mg, 0.01 mmol) in dry THF (5 mL) was heated

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[60] For example, hydrostannylation of **29** affords a 2.3/1 mixture of (*E*)/internal vinylstannanes, whereas hydrostannylation of **31** favors the internal stannane ((*E*)/internal = 1/2.5).

[61] Surprisingly, the overwhelming balance of the reaction material was not unreacted alkyne, but rather multiple multicomponent cross-coupling products. Product determination and further investigation of these multicomponent cross couplings is underway.

[62] Reactions with 1-bromoalkynes proved more efficient if THF was substituted for $Et_2O$ and if both the Stille electrophile and the 1-bromoalkyne were syringe pumped into the reaction vessel simultaneously. Addition of the 1-bromoalkyne at once gave multiple products.

[63] (a) Scott, W. J.; Moretto, A. F. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. Ed.; Wiley: New York, 1995; Vol. 7, pp 5327–5328. (b) Dyer, R. S.; Walsh, T. J.; Wonderlin, W. F.; Bercegeay, M. *Neurobehav. Toxicol. Teratol.* **1982**, *4*, 127–133.

[64] For a description of the general materials and methods employed, see the Supporting Information and ref 19c.

[65] For previous preparation and spectroscopic data, see ref 19c.

for 6 days to 50 °C. A concentrated aqueous KF solution (5 mL) was added to the reaction mixture, which was stirred for 3 h. The phases were separated, the aqueous layer was extracted with Et$_2$O, and the combined organic phases were dried over MgSO$_4$. Evaporation of the solvent afforded the crude product, which was purified by radial chromatography (silica gel; petroleum ether/EtOAc 90:10) to afford 5-methyl-1-phenyl-1,3-hexadien-5-ol (**2**) (363 mg, 65%; 49% from alkyne). IR (CHCl$_3$) 3598, 3451 cm$^{-1}$; $^{1}$H NMR (300 MHz, CDCl$_3$) $\delta$ 0.90 (t, $J$ = 7.4 Hz, 3 H), 1.31 (s, 3 H), 1.60 (q, $J$ = 7.4 Hz, 2 H), 5.86 (d, $J$ = 15.4 Hz, 1 H), 6.38 (ddd, $J$ = 15.4, 10.4, 0.6 Hz, 1 H), 6.53 (d, $J$ = 15.7 Hz, 1 H), 6.76 (ddd, $J$ = 15.7, 10.4, 0.6 Hz, 1 H), 7.16−7.39 (m, 5 H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 8.3, 27.4, 35.2, 77.0, 126.2, 127.3, 127.8, 128.5, 128.6, 131.9, 137.2, 140.8; HRMS (EI) *m*/*z* 188.1204 [(M)$^+$; calcd for C$_{13}$H$_{16}$O 188.1201].[66]

**Preparation of (5,5-Dimethylhexa-1,3-dienyl)benzene (4).** Applying the hydrostannylation procedure above to 3,3-dimethyl-1-butyne (**3**) (0.492 g, 6 mmol) afforded after column chromatography (silica gel; pentane, 1% Et$_3$N) 970 mg (44%) of tributyl(3,3-dimethyl-but-1-enyl)stannane.[65] Applying the Stille conditions above to tributyl(3,3-dimethyl-but-1-enyl)stannane (980 mg, 2.6 mmol) and (*E*)-$\beta$-bromostyrene (530 mg, 2.9 mmol) afforded after a 5 day reaction time and column chromatography (silica gel; petroleum ether/EtOAc 95:5) (5,5-dimethylhexa-1,3-dienyl)benzene (**4**)[66,67] (199 mg, 43%; 19% from alkyne).

**Preparation of 1-(4-Phenylbuta-1,3-dienyl)cyclohexanol) (6).** Applying the hydrostannylation procedure above to 1-ethynylcyclohexanol (**5**) (124 mg, 1 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 95:5, 1% Et$_3$N) 290 mg (70%) of 1-(2-tributylstannylvinyl)cyclohexanol[20] as a clear oil. Applying the Stille conditions above to 1-(tributylstannyl)-2-(cyclohexanol)-1-ethene (252 mg, 0.6 mmol) and (*E*)-$\beta$-bromostyrene (0.15 mL, 1.2 mmol) afforded after a 30 h reaction time and column chromatography (silica gel; petroleum ether/EtOAc 95:5, 1% Et$_3$N) 1-(4′-phenyl-1′,3′-butadienyl)cyclohexan-1-ol (**6**)[66] (83 mg, 60%; 42% from alkyne).

**Preparation of 2,6-Diphenylhexa-3,5-dien-2-ol (8).** Applying the hydrostannylation procedure above to 2-phenylbut-3-yn-2-ol (**7**) (292.0 mg, 2 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 95:5, 1% Et$_3$N) 752 mg (86%) of 2-phenyl-4-tributylstannylbut-3-en-2-ol[65] as a clear oil. Applying the Stille conditions above to 1-(tributylstannyl)-3-phenyl-1-(*E*)-buten-3-ol (480 mg, 1.1 mmol) and (*E*)-$\beta$-bromostyrene (0.14 mL, 1.1 mmol) afforded after a 5 day reaction time and column chromatography (silica gel; petroleum ether/EtOAc 95:5) 1,5-diphenyl-1,3-hexadien-5-ol (**8**)[66,68] (180 mg, 65%; 56% from alkyne).

**Preparation of 3-Methyl-7-phenylhepta-4,6-dien-3-ol (10).** Applying the hydrostannylation procedure above to 3-methylpent-1-yn-3-ol (**9**) (0.23 mL, 2 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 95:5, 1% Et$_3$N) 624 mg (80%) of 3-methyl-1-tributylstannylpent-1-en-3-ol[69] as a clear oil. Applying the Stille conditions above to 1-(tributylstannyl)-3-methyl-1-(*E*)-penten-3-ol (540 mg, 1.4 mmol) and (*E*)-$\beta$-bromostyrene (0.23 mL, 1.8 mmol) afforded after a 5 day reaction time and column chromatography (silica gel; petroleum ether/EtOAc 90:10) 5-methyl-1-phenyl-1,3-hetadien-5-ol (**10**)[66] (199 mg, 70%; 56% from alkyne).

**Preparation of 2,4-Dimethyl-8-phenylocta-5,7-dien-4-ol (12).** Applying the hydrostannylation procedure above to 3,5-dimethyl-1-hexyn-1-ol (**11**) (757 mg, 6 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 90:10, 1% Et$_3$N) 1.94 g (77%) of 3,5-dimethyl-1-tributylstannylhex-1-en-3-ol[65] as a clear oil. Applying the Stille conditions above to 3,5-dimethyl-1-tributylstannylhex-1-en-3-ol (1.30 g, 3.0 mmol) and (*E*)-$\beta$-bromostyrene (620 mg, 3.3 mmol) in dry THF (5 mL) afforded after a 5 day reaction time and column chromatography (silica gel; petroleum ether/EtOAc 95:5) 2,4-dimethyl-8-phenylocta-5,7-dien-4-ol (**12**)[66] (306 mg, 45%; 35% from alkyne).

**Preparation of 1,1-Diethyl-5-phenylpenta-2,4-dienylamine (14).** Applying the hydrostannylation procedure above to 1,1-diethylpropargylamine (**13**) (667 mg, 6 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 80:20, 1% Et$_3$N) 1.90 g (80%) of 1,1-diethyl-3-tributylstannylallylamine as a clear oil. $^{1}$H NMR (300 MHz, CDCl$_3$) $\delta$ 0.79 (m, 6 H), 0.87 (m. 15 H), 1.21−1.36 (m, 9 H), 1.38−1.57 (m, 9 H), 5.84 (d, $J$ = 19.5 Hz, 1 H), 5.96 (d, $J$ = 19.5 Hz, 1 H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 7.9, 9.5, 13.9, 27.3, 29.1, 33.7, 58.4, 123.0, 155.0. Applying the Stille conditions above to 1,1-diethyl-3-tributylstannylallylamine (1.30 g, 3.0 mmol) and (*E*)-$\beta$-bromostyrene (0.60 g, 3.3 mmol) in dry THF (5 mL) afforded after a 5 day reaction time and column chromatography (silica gel; petroleum ether/EtOAc 95:5) 1,1-diethyl-5-phenylpenta-2,4-dienylamine (**14**)[66] (305 mg, 47%; 36% from alkyne).

**Representative Procedure for a Tandem One-Pot Hydrostannylation/Stille Coupling with Bu$_3$SnH (Table 1). Preparation of (5,5-Dimethylhexa-1,3-dienyl)benzene (4).** Tributyltin hydride (0.89 mL, 3.3 mmol) was added dropwise at 0 °C to a solution of 3,3-dimethylbut-1-yne (**3**) (0.37 mL, 3 mmol), (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol), and (PPh$_3$)$_2$PdCl$_2$ (7 mg, 0.01 mmol) in THF (2 mL). The solution was allowed to warm to room temperature overnight and stirred at this temperature for an additional 2 days. The reaction mixture was then treated with a 10% aqueous NH$_4$OH solution (3 mL) and stirred for 4 h. The phases were separated, the aqueous layer was extracted with Et$_2$O, and the combined organic phases were dried over MgSO$_4$. Evaporation of the solvent afforded the crude product, which was purified by column chromatography (silica gel; petroleum ether) to yield (5,5-dimethylhexa-1,3-dienyl)benzene (**4**)[66] (496 mg, 89%).

**Preparation of 5-Methyl-1-phenyl-1,3-hexadien-5-ol (2) with Bu$_3$SnH.** Applying the conditions from above to 2-methylbut-3-yn-2-ol (**1**) (0.29 mL, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol) afforded after column chromatography (silica gel; petroleum ether/EtOAc 95:5) 5-methyl-1-phenyl-1,3-hexadien-5-ol (**2**)[66] (490 mg, 87%).

**Preparation of 1-(4-Phenylbuta-1,3-dienyl)cyclohexanol (6) with Bu$_3$SnH.** The conditions from above were applied to 1-ethynylcyclohexanol (**5**) with the following modifications: After the addition of tributyltin hydride (0.89 mL, 3.3 mmol), the solution was allowed to warm to room temperature overnight and then heated for an additional 2 days to 45 °C. The reaction mixture was then treated with a 10% aqueous NH$_4$OH solution (3 mL) and stirred for 4 h. The phases were separated, the aqueous layer was extracted with Et$_2$O, and the combined organic phases were dried over MgSO$_4$. Evaporation of the solvent afforded the crude product, which was purified by column chromatography (silica gel; petroleum ether/EtOAc 95:5) to afford 1-(4′-phenyl-1′,3′-butadienyl)cyclohexan-1-ol (**6**)[66] (349 mg, 51%).

**Preparation of 1,5-Diphenyl-1,3-hexadien-5-ol (8) with Bu$_3$SnH.** Applying the conditions from above to 2-phenylbut-3-yn-2-ol (**7**) (146 mg, 1 mmol) and (*E*)-$\beta$-bromostyrene (0.13 mL, 1 mmol) afforded after column chromatography (silica gel; petroleum ether/EtOAc 90:10) 1,5-diphenyl-1,3-hexadien-5-ol (**8**)[66] (188 mg, 75%).

**Preparation of 3-Methyl-7-phenylhepta-4,6-dien-3-ol (10) with Bu$_3$SnH.** Applying the conditions from above to 3-methylpent-1-yn-3-ol (**9**) (0.34 mL, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol) afforded after column chromatography (silica gel; petroleum ether/EtOAc 95:5) 3-methyl-7-phenylhepta-4,6-dien-3-ol (**10**)[66] (520 mg, 86%).

**Preparation of 2,4-Dimethyl-8-phenylocta-5,7-dien-4-ol (12) with Bu$_3$SnH.** Applying the conditions from above using 3,5-dimethylhex-1-yn-3-ol (**11**) (0.44 mL, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol) afforded after column chromatography (silica gel; petroleum ether/EtOAc 95:5) 2,4-dimethyl-8-phenylocta-5,7-dien-4-ol (**12**)[66] (523 mg, 76%).

**Preparation of 1,1-diethyl-5-phenylpenta-2,4-dienylamine (14) with Bu$_3$SnH.** Applying the conditions from above to 1,1-diethylprop-2-ynylamine (**13**) (0.40 mL, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol) afforded after column chromatography (silica gel; petroleum ether/EtOAc 80:20) 1,1-diethyl-5-phenylpenta-2,4-dienylamine (**14**)[66] (190 mg, 29%) and recovered stannane (450 mg, 37%).

**Representative Procedure for One-Pot Hydrostannylation/Stille Coupling with in Situ Generated Tin Hydride (Bistributyltin Oxide and Polymethylhydrosiloxane) (Table 1). Preparation of (5,5-**

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(66) See Supporting Information for additional spectroscopic data.

(67) For previous preparations see: (a) Yuan, T. M.; Luh, T. Y. *J. Org. Chem.* **1992**, *57*, 4550−4552. (b) Tamura, R.; Saegusa, K.; Kakihana, M.; Oda, D. *J. Org. Chem.* **1988**, *53*, 2723−2728.

(68) For previous preparations see: Mikhailov, B. M.; Ter-Sarkisyan, G. S.; Tutorskaya, F. B. *Iz. Akad. Nauk. SSSR Ser. Khim.* **1959**, 804−810.

(69) For previous preparations see: Hanson, R. N.; Franke, L.; Murphy, F. *Nucl. Med. Biol.* **1996**, *23*, 585−588.

**Dimethylhexa-1,3-dienyl)benzene (4).** A solution of 3,3-dimethylbut-1-yne (**3**) (0.37 mL, 3 mmol), $(Bu_3Sn)_2O$ (1.86 mL, 3.6 mmol), PMHS (0.42 mL, 7.2 mmol), (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol), and $(PPh_3)_2$ $PdCl_2$ (7 mg, 0.01 mmol) in dry THF (2 mL) was stirred at room temperature for 5 days and then heated to reflux for 5 more days. Then a concentrated aqueous KF solution was added to the reaction mixture, which was stirred for 3 h. The phases were separated, the aqueous layer was extracted with $Et_2O$, and the combined organic phases were dried over $MgSO_4$. Evaporation of the solvent afforded the crude product, which was purified by radial chromatography (silica gel; petroleum ether) to yield (5,5-dimethylhexa-1,3-dienyl)benzene (**4**)[66] (288 mg, 52%).

**Preparation of 5-Methyl-1-phenyl-1,3-hexadien-5-ol (2) with $(Bu_3Sn)_2O$/PMHS.** Applying the conditions from to 2-methylbut-3-yn-2-ol (**1**) (0.29 mL, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol) afforded after radial chromatography (silica gel; petroleum ether/EtOAc 95:5) 5-methyl-1-phenyl-1,3-hexadien-5-ol (**2**)[66] (370 mg, 66%).

**Preparation of 1-(4-Phenylbuta-1,3-dienyl)cyclohexanol (6) with $(Bu_3Sn)_2O$/PMHS.** Applying the conditions from above to 1-ethynylcyclohexanol (**5**) (375 mg, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.4 mL, 3.1 mmol) afforded after column chromatography (silica gel; petroleum ether/EtOAc 95:5) 1-(4-phenylbuta-1,3-dienyl)-cyclohexanol (**6**)[66] (354 mg, 52%).

**Preparation of 1,5-Diphenyl-1,3-hexadien-5-ol (8) with $(Bu_3Sn)_2O$/PMHS.** Applying the conditions from above to 2-phenylbut-3-yn-2-ol (**7**) (438 mg, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.43 mL, 3.3 mmol) afforded after radial chromatography (silica gel; petroleum ether/EtOAc 95:5) 1,5-diphenyl-1,3-hexadien-5-ol (**8**)[66] (518 mg, 69%).

**Preparation of 3-Methyl-7-phenylhepta-4,6-dien-3-ol (10) with $(Bu_3Sn)_2O$/PMHS.** Applying the conditions from above to 3-methylpent-1-yn-3-ol (**9**) (0.35 mL, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.4 mL, 3.1 mmol) afforded after radial chromatography (silica gel; petroleum ether/EtOAc 95:5) 3-methyl-7-phenylhepta-4,6-dien-3-ol (**10**)[66] (364 mg, 60%).

**Preparation of 2,4-Dimethyl-8-phenylocta-5,7-dien-4-ol (12) with $(Bu_3Sn)_2O$/PMHS.** Applying the conditions from to 3,5-dimethylhex-1-yn-3-ol (**11**) (0.44 mL, 3 mmol) and (*E*)-$\beta$-bromostyrene (0.4 mL, 3.1 mmol) afforded after column chromatography (silica gel; petroleum ether/EtOAc 95:5) 2,4-dimethyl-8-phenylocta-5,7-dien-4-ol (**12**)[66] (400 mg, 58%).

**Pd(0)-Mediated Hydrostannylation with $Bu_3SnCl/NH_4OH$/PMHS Generated $Bu_3SnH$. Preparation of 3,5-Dimethyl-1-tributylstannylhex-1-en-3-ol (15) (Scheme 5, eq 1).** To a mixture of $Bu_3SnCl$ (2 mmol, 0.46 mL) and aqueous $NH_4OH$ (2 mL) in $Et_2O$ were added 3,5-dimethylhex-1-yn-3-ol (**11**) (2 mmol, 0.29 mL), PMHS dimer (2 mmol, 0.66 mL), and $(PPh_3)_2PdCl_2$ (14 mg, 0.02 mmol). The solution was stirred at room temperature for 1.5 h and then heated overnight. TLC showed a greater than 1:1 ratio for alkyne/stannane; however, upon column chromatography (silica gel; pentane/EtOAc 95:5) only 117 mg (14%) of 3,5-dimethyl-1-tributylstannylhex-1-en-3-ol (**15**)[65] was isolated.

**Pd(0)-Mediated Hydrostannylation with $Bu_3SnCl/NH_4OH$/PMHS Generated $Bu_3SnH$. Preparation of 3,5-Dimethyl-1-tributylstannylhex-1-en-3-ol (15).** Aqueous $NH_4OH$ (5 mL) was added to a solution of 3,5-dimethylhex-1-yn-3-ol (**11**) (0.29 mL, 2 mmol), $Bu_3SnCl$ (0.46 mL, 2 mmol), PMHS dimer (0.33 mL, 1 mmol), $(PPh_3)_2PdCl_2$ (3.5 mg, 0.005 mmol) in EtOH (1 mL), and toluene (2 mL). The reaction mixture was heated to 55 °C for 30 min; TLC showed only formation of tin dimer and stannane and a small amount of unreacted alkyne. The solution was heated for an additional 6 h, but the composition did not change any further. The mixture was then washed with water, and the organic phase was washed with brine and dried over $MgSO_4$. Evaporation of the solvent yielded the crude product. $^1H$ NMR showed a 1.7:1 ratio of stannane/alkyne and a 21:1 ratio of (*E*)/int-stannane. Column chromatography (silica gel; hexane/EtOAc 96:4) afforded 3,5-dimethyl-1-tributylstannylhex-1-en-3-ol (**15**)[65] (177 mg, 21%).

**Pd(0)-Mediated Hydrostannylation with $Bu_3SnOMe$/PMHS Generated $Bu_3SnH$. Preparation of 1-(2-Tributylstannylvinyl)cyclohexanol (16).** PMHS (0.06 mL, 1.1 mmol) was added dropwise at 0 °C under $N_2$ to a solution of 1-ethynylcyclohexanol (**5**) (124 mg, 1 mmol), $Bu_3SnOCH_3$ (0.29 mL, 1 mmol), and $(PPh_3)_2PdCl_2$ (3.5 mg, 0.005 mmol) in THF (2 mL). The solution was stirred for 1.5 h until GC showed a 13:1 ratio of stannane/$Bu_3SnOCH_3$. The solvent was evaporated, and column chromatography (silica gel; petroleum ether/EtOAc 95:5) of the crude product yielded 1-(2-tributylstannylvinyl)-cyclohexanol (**16**)[66] (220 mg, 52%).

**Pd(0)-Mediated Hydrostannylation with $Bu_3SnBr$/NaOMe/PMHS Generated $Bu_3SnH$. Preparation of 1-(2-Tributylstannylvinyl)cyclohexanol (16) Using $Bu_3SnBr$.** To a solution of 1-ethynylcyclohexanol (**5**) (124 mg, 1 mmol), $Bu_3SnBr$ (90%, 0.31 mL, 1 mmol), and $(PPh_3)_2PdCl_2$ (3.5 mg, 0.005 mmol) in dry THF (1 mL) were added $NaOCH_3$ (162 mg, 3 mmol) and PMHS (0.06 mL, 1.1 mmol) at 0 °C under $N_2$. GC analysis after 15 min showed complete conversion of $Bu_3SnBr$. The mixture was washed with water; the organic phase was washed with brine and dried over $MgSO_4$. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel; petroleum ether/EtOAc 95:5) to yield 1-(2-tributylstannylvinyl)cyclohexanol (**16**)[66] (220 mg, 52%).

**Pd(0)-Mediated Hydrostannylation with $Bu_3SnCl/NH_4OH$/PMHS Generated $Bu_3SnH$. Preparation of 3,5-Dimethyl-1-tributylstannylhex-1-en-3-ol (15).** $NaOCH_3$ (54 mg, 1 mmol) was added at −7 °C to a solution of 3,5-dimethylhex-1-yn-3-ol (**11**) (0.145 mL, 1 mmol), PMHS (0.06 mL, 1.1 mmol), $Bu_3SnCl$ (0.27 mL, 1 mmol), and $(PPh_3)_2PdCl_2$ (3.5 mg, 0.005 mmol) in THF (1 mL). After stirring for 1.5 h at 0 °C, the reaction mixture was cooled to −7 °C again, treated with PMHS (0.06 mL, 1.1 mmol) and $NaOCH_3$ (110 mg, 2 mmol), and allowed to warm to 0 °C within 1 h. The solvent was then evaporated and the crude product purified by column chromatography (silica gel; petroleum ether/EtOAc 95:5) to yield 3,5-dimethyl-1-tributylstannylhex-1-en-3-ol (**15**)[65] (306 mg, 74%).

**Attempted Tandem One-Pot Hydrostannlyation/Stille Cross Coupling Using Substoichiometric Amounts of Tin (20 mol % of $(Bu_3Sn)_2O$ and $NaOCH_3$ and PMHS]. Preparation of 2,4-Dimethyl-8-phenylocta-5,7-dien-4-ol (12).** A solution of 3,5-dimethylhex-1-yn-3-ol (**11**) (0.15 mL, 1 mmol), (*E*)-$\beta$-bromostyrene (0.13 mL, 1 mmol), $(Bu_3Sn)_2O$ (0.1 mL, 0.2 mmol), PMHS (0.07 mL, 1.2 mmol), and $(PPh_3)_2PdCl_2$ (7 mg, 0.01 mmol) in THF was treated with $NaOCH_3$ (65 mg, 1.2 mmol). Gas evolution occurred, and the reaction mixture was heated to 60 °C. After 5 h additional PMHS (0.07 mL, 1.2 mmol) and $NaOCH_3$ (65 mg, 1.2 mmol) were added. The solution was heated overnight, additional PMHS (0.07 mL, 1.2 mmol) was added, and after an additional 3 h at 60 °C, a 10% aqueous $NH_4OH$ solution was added. The aqueous phase was extracted with $Et_2O$, and the combined organic phases were washed with brine and dried over $MgSO_4$. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel; petroleum ether/EtOAc 95:5) to yield 2,4-dimethyl-8-phenylocta-5,7-dien-4-ol (**12**)[66] (8 mg, 3%).

**Pd(0)-Mediated Hydrostannylation with $Bu_3SnCl$/NaOPh/PMHS Generated $Bu_3SnH$. Preparation of 3,5-Dimethyl-1-tributylstannylhex-1-en-3-ol (15).** Phenol (188 mg, 2 mmol) and Na (46 mg, 2 mmol) were stirred in dry THF until the sodium was dissolved. This solution was added to a mixture of 3,5-dimethylhex-1-yn-3-ol (**11**) (0.145 mL, 1 mmol), $Bu_3SnCl$ (0.27 mL, 1 mmol), $(PPh_3)_2PdCl_2$ (3.5 mg, 0.005 mmol), and THF. A very fine precipitation of NaCl formed, and TLC indicated complete conversion of $Bu_3SnCl$ into the phenoxide. PMHS (0.09 mL, 1.5 mmol) was added at room temperature, and after 15 min TLC showed complete conversion of the alkyne. The solvent was evaporated, and $^1H$ NMR of the crude product showed a 14:1 ratio for (*E*)/int-stannane. Column chromatography (silica gel; pentane/EtOAc 95:5) afforded 3,5-dimethyl-1-tributylstannylhex-1-en-3-ol (**15**)[65] (250 mg, 71%). See above for spectroscopic data.

**$Bu_3SnCl$/NaOPh/PMHS Mediated Tandem One-Pot Hydrostannylation/Stille Coupling. Preparation of 3,5-Dimethyl-1-phenylhex-1-en-3-ol (17).** To a solution of $Pd_2dba_3$ (9.2 mg, 0.01 mmol), TFP (9.3 mg, 0.04 mmol), $Bu_3SnCl$ (0.27 mL, 1 mmol), and NaOPh (0.5 mL of 4 M solution in THF, 2 mmol) in THF (2 mL) were added 3,5-dimethylhex-1-yn-3-ol (**11**) (0.145 mL, 1 mmol) and PMHS (0.09 mL, 1.5 mmol). The reaction mixture was stirred until TLC showed complete consumption of the alkyne. Iodobenzene (0.33 mL, 3 mmol) was added, and the solution was heated to reflux for 5 h. During this time additional iodobenzene (0.05 mL, 0.45 mmol) was added. A saturated aqueous KF solution was added, and the reaction mixture was stirred for additional 3 h. The organic phase was washed with water and brine and dried over $MgSO_4$. After evaporation of the solvent, column chromatography (silica gel; pentane/EtOAc 95:5) of the crude product yielded of 3,5-dimethyl-1-phenylhex-1-en-3-ol (**17**)[66] (110 mg, 54%). IR ($CHCl_3$) 3594 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.91−0.99 (m, 6 H), 1.34 (s, 3 H), 1.35−1.81 (m, 3 H), 6.27 (d, $J$ = 16.2 Hz, 1 H), 6.57 (d, $J$ = 16.2 Hz, 1 H), 7.20−7.39 (m, 5 H), (OH not observed); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 24.4, 24.5, 24.6, 29.22, 51.5, 73.7, 126.3, 126.42, 127.2, 128.5, 137.1, 137.2; HRMS (EI) *m/z* 204.1465 [$(M)^+$; calcd for $C_{14}H_{20}O$ 204.1412].

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.36; H, 9.85.

**Attempted Tandem One-Pot Hydrostannylation/Stille Coupling with Substoichiometric Amounts of $Bu_3SnCl$/NaOPh/PMHS Generated $Bu_3SnH$. Preparation of 3,5-Dimethyl-1-phenylhex-1-en-3-ol (17).** A NaOPh solution in THF (prepared from PhOH (94 mg, 1 mmol) and Na (23 mg, 1 mmol) was added to a solution of $Bu_3SnCl$ (0.14 mL, 0.5 mmol), 3,5-dimethylhex-1-yn-3-ol (**11**) (0.07 mL, 0.5 mmol), $Pd_2dba_3$ (13 mg, 0.014 mmol), and TFP (13 mg, 0.06 mmol) in dry THF (2 mL). After stirring at room temperature for 15 min, PMHS (0.03 mL, 0.5 mmol) and iodobenzene (0.1 mL, 1 mmol) were added and the mixture was heated to 60 °C. After 30 min, an additional 2 equiv of iodobenzene was added and the solution was heated for an additional 2 h. 3,5-Dimethylhex-1-yn-3-ol (0.07 mL, 0.5 mmol) and a NaOPh solution in THF (0.25 mL, 4 M) were added. After stirring at room temperature for 15 min, PMHS (0.03 mL, 0.05 mmol) was added and the reaction mixture was heated until TLC showed complete consumption of stannane. The reaction mixture was extracted with water, and the organic phase was dried over $MgSO_4$, concentrated, and purified by column chromatography (silica gel; pentane/EtOAc 97:3) to yield 3,5-dimethyl-1-phenylhex-1-en-3-ol (**17**)[66] (112 mg, 55%). See above for spectroscopic data.

**Pd(0)-Mediated Hydrostannylation with $Bu_3SnCl/Na_2CO_3$/PMHS Generated $Bu_3SnH$. Preparation of 2-Phenyl-4-tributylstannylbut-3-en-2-ol (18) (Scheme 3).** A mixture of 2-phenylbut-3-yn-2-ol (**7**) (125 mg, 0.85 mmol), $Bu_3SnCl$ (0.27 mL, 1 mmol), PMHS (0.12 mL, 2 mmol), $(PPh_3)_2PdCl_2$ (4.6 mg, 0.006 mmol), and $Na_2CO_3$ (318 mg, 3 mmol) in $H_2O$ (0.5 mL) and $Et_2O$ (5 mL) was heated to reflux for 30 min before additional PMHS (0.12 mL, 2 mmol) and $Na_2CO_3$ (159 mg, 1.5 mmol) were added. After heating the solution for an additional 5.5 h, water was added and the phases were separated. The organic phase was washed with brine and dried over $MgSO_4$. After evaporation of the solvent the crude product was purified by column chromatography (silica gel; petroleum ether/EtOAc 95:5) to yield 2-phenyl-4-tributylstannylbut-3-en-2-ol and 2-phenyl-3-tributylstannylbut-3-en-2-ol (**18**)[65] (278 mg, 75%).

**One-Pot Hydrostannylation/Stille Cross Coupling with $Bu_3SnCl$ and $Na_2CO_3$/PMHS Generated $Bu_3SnH$. Preparation of 2,6-Diphenylhexa-3,5-dien-2-ol (8) (Scheme 4).** A mixture of $Pd_2dba_3$ (9.2 mg, 0.01 mmol) and TFP (9.3 mg, 0.04 mmol) in $Et_2O$ (5 mL) was stirred at room temperature for 15 min before $Bu_3SnCl$ (0.84 mL, 3 mmol), $Na_2CO_3$ (638 mg, 6 mmol), and $H_2O$ (2 mL) were added. Over a period of 18 h a solution of 2-phenylbut-3-yn-2-ol (**7**) (438 mg, 3 mmol), (*E*)-$\beta$-bromostyrene (0.67 mL, 5 mmol), and PMHS (0.3 mL, 5 mmol) in $Et_2O$ (5 mL) was added with a syringe pump to the refluxing solution. The solution was stirred for an additional 4 days; then a saturated aqueous KF solution was added and the reaction mixture was stirred for an additional 3 h. The organic phase was washed with water and brine and dried over $MgSO_4$. After evaporation of the solvent, radial chromatography (silica gel; pentane/EtOAc 95:5) of the crude product yielded 2,6-diphenylhexa-3,5-dien-2-ol (**8**)[66] (354 mg, 47%).

**Tandem Hydrostannlyation/Stille Cross Coupling Using Substoichiometric Amounts of Tin (20 mol % of $Bu_3SnCl$ and PMHS). Preparation of 2,6-Diphenylhexa-3,5-dien-2-ol (8) (Table 2).** A mixture of $Pd_2dba_3$ (9.2 mg, 0.01 mmol) and TFP (9.3 mg, 0.04 mmol) in $Et_2O$ (5 mL) was stirred for 15 min at room temperature. 2-Phenylbut-3-yn-2-ol (**7**) (146 mg, 1 mmol), $Bu_3SnCl$ (0.05 mL, 0.2 mmol), (*E*)-$\beta$-bromostyrene (0.13 mL, 1 mmol), $Na_2CO_3$ (560 mg, 5 mmol), PMHS (0.15 mL, 2.5 mmol), and $H_2O$ (1 mL) were added, and the mixture was heated to reflux. After 1 h additional $Na_2CO_3$ (560 mg, 5 mmol) and after 2 h and 3.5 h additional PMHS (2×, 0.15 mL, 2.5 mmol) were added. The reaction mixture was refluxed for a total of 7.5 h and filtered, and the filtrate was washed with ether. After evaporation of the solvent, the residue was purified by column chromatography (silica gel; petroleum ether/EtOAc 90:10) to yield 2,6-diphenylhexa-3,5-dien-2-ol (**8**)[66] (100 mg, 40%). See above for spectroscopic data.

**Tandem Hydrostannlyation/Stille Cross Coupling Using Substoichiometric Amounts of Tin (4 mol % of $Bu_3SnCl$ and PMHS). Preparation of 2,6-Diphenylhexa-3,5-dien-2-ol (8) (Table 2).** A solution of $Pd_2dba_3$ (9.2 mg, 0.01 mmol) and TFP (9.3 mg, 0.04 mmol) in ether (5 mL) was stirred for 15 min before (*E*)-$\beta$-bromostyrene (0.67 mL, 5 mmol), $Bu_3SnCl$ (0.05 mL, 0.185 mmol), $(PPh_3)_2PdCl_2$ (7 mg, 0.01 mmol), $Na_2CO_3$ (425 mg, 4 mmol), and $H_2O$ (1 mL) were added. While the solution was stirred at room temperature, a solution of 2-phenylbut-3-yn-2-ol (**7**) (730 mg, 5 mmol) and PMHS (0.45 mL, 7.5 mmol) in $Et_2O$ (3 mL) was added with a syringe pump. After 5.5 h additional $Na_2CO_3$ (425 mg, 4 mmol) in $H_2O$ (1 mL) were added. After 3 days at room temperature, an aqueous $NH_4OH$ solution (10%, 2 mL) was added to the reaction mixture, which was then stirred for 30 min and extracted with ether. The organic phase was washed with water and brine and dried over $MgSO_4$. After evaporation of the solvent, column chromatography (silica gel; petroleum ether then petroleum ether/EtOAc 90:10) of the residue afforded 2,6-diphenylhexa-3,5-dien-2-ol (**8**)[66] (250 mg, 22%).

**Tandem Hydrostannlyation/Stille Cross Coupling Using Substoichiometric Amounts of Tin (10 mol % of $Bu_3SnCl$ and PMHS). Preparation of 5-Methyl-1-phenyl-1,3-hexadien-5-ol (2) (Table 2).** A mixture of $Pd_2dba_3$ (18.4 mg, 0.02 mmol) and TFP (18.6 mg, 0.08 mmol) in $Et_2O$ (5 mL) was stirred for 15 min at room temperature. 2-Methylbut-3-yn-2-ol (**1**) (0.1 mL, 1 mmol), $Bu_3SnCl$ (0.056 mL, 0.2 mmol), $Na_2CO_3$ (212 mg, 2 mmol), PMHS (0.12 mL, 2 mmol), (*E*)-$\beta$-bromostyrene (0.15 mL, 1.15 mmol), and $H_2O$ (1 mL) were added, and the reaction mixture was heated to reflux for 1 h before additional alkyne (0.1 mL, 1 mmol) was added. After refluxing for 23 h, a saturated aqueous KF solution was added and the mixture was stirred for 3 h. The phases were separated; the organic phase was washed with brine and dried over $MgSO_4$. Evaporation of the solvent and radial chromatography (silica gel; pentane/EtOAc 97:3) of the residue yielded 5-methyl-1-phenyl-1,3-hexadien-5-ol (**2**)[66] (90 mg, 42% ((*E*)-$\beta$-bromostyrene as limiting reagent), 2.4 cycles).

**Tandem Hydrostannlyation/Stille Cross Coupling Using Substoichiometric Amounts of Tin (10 mol % of $Bu_3SnCl$ and PMHS). Preparation of 1-(4-Phenylbuta-1,3-dienyl)cyclohexanol (6) (Table 2).** A mixture of $Pd_2dba_3$ (18.4 mg, 0.02 mmol) and TFP (18.6 mg, 0.08 mmol) in $Et_2O$ (5 mL) was stirred for 15 min at room temperature. 1-Ethynylcyclohexanol (**5**) (124 mg, 1 mmol), $Bu_3SnCl$ (0.056 mL, 0.2 mmol), $Na_2CO_3$ (212 mg, 2 mmol), PMHS (0.12 mL, 2 mmol), (*E*)-$\beta$-bromostyrene (0.15 mL, 1.15 mmol), and $H_2O$ (1 mL) were added, and the reaction mixture was heated to reflux for 1 h before additional alkyne (0.1 mL, 1 mmol) was added. After refluxing for 12 h, additional (*E*)-$\beta$-bromostyrene (0.15 mL, 1.15 mmol) was added together with PMHS (0.12 mL, 2 mmol). The solution was heated for an additional 24 h; then saturated aqueous KF solution was added and the mixture was stirred for 3 h. The phases were separated, and the organic phase was washed with brine and dried over $MgSO_4$. Evaporation of the solvent and radial chromatography (silica gel; pentane/EtOAc 97:3) of the residue yielded 1-(4-phenylbuta-1,3-dienyl)cyclohexanol (**6**)[66] (117 mg, 26%).

**Representative Procedure for the Tandem One-Pot Hydrostannylation/Stille Cross Coupling with Catalytic Amounts of tin Using $Me_3SnCl$. Preparation of 1-(4′-Phenyl-1′-3′-butadienyl)cyclohexan-1-ol (6) (Table 3, entry 1).** Tri-2-furylphosphine (9.3 mg, 0.04 mmol) was added to a solution of $Pd_2dba_3$ (9.2 mg, 0.01 mmol) in dry diethyl ether (5 mL). After 15 min of stirring the solution at room temperature, 1-ethynyl-1-cyclohexanol (**5**) (124 mg, 1.0 mmol), PMHS (0.1 mL, 1.5 mmol), $Me_3SnCl$ (0.06 mL of a 1 M solution in THF, 0.06 mmol), $Na_2CO_3$ (85 mg, 0.8 mmol), $H_2O$ (0.5 mL), and $(PPh_3)_2PdCl_2$ (7 mg, 0.01 mmol) were added. The reaction was heated to reflux, and a solution of (*E*)-$\beta$-bromostyrene (275 mg, 1.5 mmol) in diethyl ether (4 mL) was added dropwise via a syringe pump (0.24 mL/h). When the addition was complete, an aqueous $NH_4OH$ solution (10%, 2 mL) was added and the reaction mixture stirred for 30 min. The reaction was then filtered and separated, and the aqueous phase was extracted with diethyl ether. The organics were combined, washed with water and then brine, dried over MgSO$_4$, and filtered. The solvent was evaporated, and the residue was purified by column chromatography (silica gel; pentane/EtOAc 90:10, 1% Et$_3$N) to afford 1-(4′-phenyl-1′-3′-butadienyl)cyclohexan-1-ol (**6**)[66] (205 mg, 90%) as an oil.

**Preparation of 1,5-Diphenyl-1,3-hexadien-5-ol (8) (Table 3, entry 2).** Applying the conditions above to 2-phenyl-3-butyn-2-ol (**7**) (146 mg, 1.0 mmol) and (*E*)-$\beta$-bromostyrene (275 mg, 1.5 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 80:20, 1% Et$_3$N) 1,5-diphenyl-1,3-hexadien-5-ol (**8**)[66] (211 mg, 85%) as an oil.

**Preparation of 2-Phenyl-4-(*p*-methoxyphenyl)-3-buten-2-ol (19) (Table 3, entry 3).** Applying the conditions above to 2-phenyl-3-butyn-2-ol (**7**) (292 mg, 2.0 mmol) and *p*-iodoanisole (702 mg, 3.0 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 90:10, 1% Et$_3$N) 2-phenyl-4-(*p*-methoxyphenyl)-3-buten-2-ol (**19**)[70] (204 mg, 80%) as an oil.

**Preparation of 5-Amino-5-ethyl-1-phenyl-1,3-heptadiene (14) (Table 3, entry 4).** Applying the conditions above to 1,1-diethylpropargylamine (**13**) (111 mg, 0.14 mL, 1.0 mmol) and (*E*)-$\beta$-bromostyrene (275 mg, 1.5 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 50:50, 1% Et$_3$N) 5-amino-5-ethyl-1-phenyl-1,3-heptadiene (**14**)[66] (170 mg, 86%) as an oil.

**Preparation of 5-Methyl-1-phenyl-1,3-hexadien-5-ol (2) (Table 3, entry 5).** Applying the conditions above to 2-methyl-3-butyn-2-ol (**1**) (84 mg, 0.10 mL, 1.0 mmol) and (*E*)-$\beta$-bromostyrene (275 mg, 1.5 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 90:10, 1% Et$_3$N) 5-methyl-1-phenyl-1,3-hexadien-5-ol (**2**)[66] (173 mg, 91%) as an oil which gave spectroscopic data consistent with that previously reported.

**Preparation of 2-Methyl-4-(*p-n*-butylphenyl)-3-buten-2-ol (20) (Table 3, entry 6).** Applying the conditions above to 2-methyl-3-butyn-2-ol (**1**) (168 mg, 0.20 mL, 2.0 mmol) and *p-n*-butyliodobenzene (780 mg, 3 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 90:10, 1% Et$_3$N) 2-methyl-4-(*p-n*-butylphenyl)-3-buten-2-ol (**20**)[66] (328 mg, 75%) as an oil.

**Preparation of 2-Methyl-4-(6-aceto-1-(*E*)-hexene)-3-buten-2-ol (22E) and 2-Methyl-4-(6-aceto-1-(*Z*)-hexene)-3-buten-2-ol (22Z) (Table 3, entry 7).** Applying the conditions above to 2-methyl-3-butyn-2-ol (**1**) (84 mg, 0.10 mL, 1.0 mmol) and a 3:1 mixture of 6-aceto-1-iodo-1-(*E*)-hexene (**21E**) and 6-aceto-1-iodo-1(*Z*)-hexene (**21Z**) (402 mg, 1.5 mmol; experimental preparation provided below) afforded after column chromatography (silica gel; pentane/EtOAc 80:20, 1% Et$_3$N) 180 mg (80%) of an oily inseparable 4:1 mixture of 2-methyl-4-(6-aceto-1-(*E*)-hexene)-3-buten-2-ol (**22E**)[66] and 2-methyl-4-(6-aceto-1-(*Z*)-hexene)-3-buten-2-ol (**22Z**).[66]

**Preparation of 2-Methyl-5-phenylpent-3-en-2-ol (23) (Table 3, entry 8).** Applying the conditions above to 2-methyl-3-butyn-2-ol (**1**) (0.10 mL, 1.0 mmol) and benzyl bromide (0.18 mL, 1.5 mmol) afforded after flash chromatography (silica gel; pentane/EtOAc, 1% Et$_3$N) 2-methyl-5-phenylpent-3-en-2-ol (**23**)[66,71] (151 mg, 85%) as a thick yellow oil.

**Preparation of 8-Phenylocta-5,7-dien-4-ol (26) (Table 4, entry 1).** Applying the conditions above to 1-hexyn-3-ol (**25**) (0.12 mL, 1.0 mmol) and (*E*)-$\beta$-bromostyrene (275 mg, 1.5 mmol) afforded after column chromatography (silica gel; pentane/EtOAc 90:10, 1% Et$_3$N) to afford 120 mg (59%) of 8-phenylocta-5,7-dien-4-ol (**26**)[66] as a yellow oil.

**Preparation of 1,5-Diphenylpenta-2,4-dien-1-ol (28) (Table 4, entry 2).** Applying the conditions above to 1-phenyl-2-propyn-1-ol (**27**) (0.25 mL, 2.0 mmol) and (*E*)-$\beta$-bromostyrene (549 mg, 3.0 mmol) afforded after flash chromatography (silica gel; pentane/EtOAc 90:10, 1% Et$_3$N) 1,5-diphenylpenta-2,4-dien-1-ol (**28**)[66,72] (320 mg, 68%) as an oil.

**Preparation of 6-Phenylhexa-3,5-dien-1-ol (30) (Table 4, entry 3).** Tri-2-furylphosphine (9.3 mg, 0.04 mmol) was added to a solution of Pd$_2$dba$_3$ (9.2 mg, 0.01 mmol) in dry diethyl ether (5 mL). After 15 min of stirring the solution at room temperature, 3-butyn-1-ol (**29**) (0.08 mL, 1.0 mmol), PMHS (0.09 mL, 1.5 mmol), Me$_3$SnCl (0.06 mL of a 1 M solution in THF, 0.06 mmol), Na$_2$CO$_3$ (85 mg, 0.8 mmol), H$_2$O (0.5 mL), and (PPh$_3$)$_2$PdCl$_2$ (7 mg, 0.01 mmol) were added, respectively. The reaction was heated to reflux, and a solution of (*E*)-$\beta$-bromostyrene (274.5 mg, 1.5 mmol) in diethyl ether (4 mL) was added dropwise via a syringe pump (0.24 mL/h). When the addition was complete, an aqueous NH$_4$OH solution (10%, 2 mL) was added and the reaction mixture stirred for 30 min. The reaction was then filtered and separated, and the aqueous phase was extracted with diethyl ether. The organics were combined, washed with water and then brine, dried over MgSO$_4$, and filtered. The solvent was evaporated, and the residue was purified by column chromatography (silica gel; pentane/EtOAc 80:20, 1% Et$_3$N) to afford 62 mg (36%) of 6-phenylhexa-3,5-dien-1-ol (**30**)[66] as a white solid (mp = 63−64 °C).

**Preparation of (5-Methoxypenta-1,3-dienyl)benzene (32) (Table 4, entry 4).** Tri-2-furylphosphine (9.3 mg, 0.04 mmol) was added to a solution of Pd$_2$dba$_3$ (9.2 mg, 0.01 mmol) in dry diethyl ether (5 mL). After 15 min of stirring the solution at room temperature, methyl propargyl ether (**31**) (0.08 mL, 1.0 mmol), PMHS (0.09 mL, 1.5 mmol), Me$_3$SnCl (0.06 mL of a 1 M solution in THF, 0.06 mmol), Na$_2$CO$_3$ (85 mg, 0.8 mmol), H$_2$O (0.5 mL), and (PPh$_3$)$_2$PdCl$_2$ (7 mg, 0.01 mmol) were added, respectively. The reaction was heated to reflux, and a solution of (*E*)-$\beta$-bromostyrene (275 mg, 1.5 mmol) in diethyl ether (4 mL) was added dropwise via a syringe pump (0.24 mL/h). When the addition was complete, an aqueous NH$_4$OH solution (10%, 2 mL) was added and the reaction mixture stirred for 30 min. The reaction was then filtered and separated, and the aqueous phase was extracted with diethyl ether. The organics were combined, washed with water and then brine, dried over MgSO$_4$, and filtered. The resulting residue was purified by column chromatography (silica gel; pentane/EtOAc 95:5, 1% Et$_3$N) to afford 54 mg (16%) of (5-methoxy-penta-1,3-dienyl)benzene (**32**).[73]

**Representative Procedure for the Tandem One-Pot Hydrostannylation/Stille Cross Coupling with Catalytic Amounts of Me$_3$SnCl Using 1-Bromoalkynes. Preparation of 4-(4-Methoxyphenyl)but-3-en-1-ol (38) (Table 6).** To 10 mL of THF were added Pd$_2$dba$_3$ (9.2 mg, 0.01 mmol) and tri-2-furylphosphine (9.3 mg, 0.04 mmol), and the mixture was allowed to stir for 15 min. Me$_3$SnCl (0.06 mL of a 1 M solution in THF, 0.06 mmol), Na$_2$CO$_3$ (0.0852 g, 0.80 mmol), 1 mL of H$_2$O, PMHS (0.09 mL, 1.5 mmol), and (PPh$_3$)$_2$PdCl$_2$ (7 mg, 0.01 mmol) were all added, respectively. The mixture was then heated to reflux, and a solution of 4-bromobut-3-yn-1-ol (**33**) (149 mg, 1.0 mmol) and *p*-iodoanisole (351 mg, 1.5 mmol) in 4 mL of Et$_2$O was added via a syringe pump (0.024 mL/h). When addition was complete, 2 mL of 10% NH$_4$OH (aqueous) was added and the mixture was stirred for an additional 30 min. The reaction was then filtered and separated, and the aqueous layer was extracted with ether. All organics were combined, washed with H$_2$O and brine, dried over MgSO$_4$, filtered, and concentrated. The resulting residue was then purified by flash chromatography (silica gel; pentane/EtOAc 80:20, 1% Et$_3$N) to give 91 mg (51%) of 4-(4-methoxyphenyl)but-3-en-1-ol (**38**)[66,74] as an oil.

**Preparation of 8-Phenylocta-5,7-dien-1-ol (39) (Table 6).** Applying the conditions from above using 6-bromo-hex-5-yn-1-ol[19c] (**35**) (177 mg, 1.0 mmol) and (*E*)-$\beta$-bromostyrene (275 mg, 1.5 mmol) afforded a residue which was purified by flash chromatography (silica gel; pentane/EtOAc 80:20, 1% Et$_3$N) to give 98 mg (49%) of 8-phenylocta-5,7-dien-1-ol (**39**)[75] as a white solid (mp = 38−39 °C). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 1.51 (m, 2 H), 1.61 (m, 2 H), 1.73 (br s, 1 H), 2.19 (q, $J = 7.9$ Hz, 2 H), 3.65 (t, $J = 6.6$ Hz, 2 H), 5.83 (dt, $J = 7.5$, 15.5 Hz,

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1 H), 6.23 (dd, $J = 10.4$, 15.9 Hz 1 H), 6.46 (d, $J = 15.9$ Hz, 1 H), 6.76 (dd, $J = 10.2$, 15.7 Hz 1 H), 7.14−7.46 (m, 5 H);$^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 137.5, 135.2, 130.9, 130.2, 129.3, 128.5, 127.1, 126.1, 62.7, 32.5, 32.2, 25.3.

**Preparation of 2-(5-Phenylpent-4-enyloxy)tetrahydropyran (40) (Table 6).** Applying the conditions above to 2-(5-bromo-pent-4-ynyloxy)-tetrahydropyran[19c] (**37**) (143 mg, 0.58 mmol) and *p*-iodobenzene (0.17 mL, 1.5 mmol) afforded a residue which was purified by flash chromatography (silica gel; pentane/EtOAc 95:5, 1% $Et_3N$) to give 75 mg (52%) of 2-(5-phenylpent-4-enyloxy)tetrahydropyran (**40**)[66,76] as an oil.

**Preparation of 6-Aceto-1-iodo-1-(*E*)-hexene (21E) and 6-Aceto-1-iodo-1(*Z*)-hexene (21Z).** A solution containing a 3:1 *E*/*Z* mixture of 6-aceto-1-(tributylstannyl)-1-hexene[65] (1.0 g, 2.31 mmol) in anhydrous dichloromethane (10 mL) was cooled to 0 °C. Iodine (586 mg, 2.31 mmol) in anhydrous dichloromethane (6 mL) was slowly added to the reaction mixture being careful not to let the purple color persist. The reaction was quenched by the addition of aqueous sodium thiosulfate. The reaction mixture was diluted with diethyl ether and water, and the layers were separated. The organic phase was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude iodide was purified by flash silica gel chromatography (silica gel; pentane/EtOAc 95:5) to afford 610 mg (98%) of an oily inseparable 4:1 mixture of 6-aceto-1-iodo-1-(*E*)-hexene (**21E**) and 6-aceto-1-iodo-1(*Z*)-hexene (**21Z**).[66] IR (neat) 1734 $cm^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.40−1.725 (m, 8 H), 2.00−2.23 (m, 10 H), 4.00−4.10 (m, 4 H), 6.02 (d, $J = 14.3$, 1 H, (*E*)), 6.11−6.25 (m, 2 H, (*Z*)), 6.42−6.56 (m, 1 H (*E*));$^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 20.9, 24.3, 24.7, 27.8, 27.9, 34.2, 35.5, 64.1, 64.2, 75.0, 82.9, 140.6, 145.9, 171.1; HRMS (EI) *m*/*z* 267.9958 [$(M)^+$ calcd for $C_8H_{13}IO_2$ 267.9960].

**Preparation of 1,1,2,2,3,3,4,4,4-Nonafluorobutane-1-sulfonic Acid 4-Methoxyphenyl Ester (24).** Following the general procedure of Corey,[13a] to a solution of *p*-methoxyphenol (1.24 g, 10 mmol) and $Et_3N$ (1.70 mL, 12 mmol) in $CH_2Cl_2$ (80 mL) at room temperature was added perfluoro-1-butanesulfonyl fluoride (2.16 mL, 12 mmol) dropwise. The resulting solution was stirred for 2 h. The reaction mixture was then washed with 5% NaOH (2 × 100 mL), $H_2O$ (2 × 100 mL), and brine (2 × 100 mL) and then dried over $MgSO_4$ and concentrated. The resulting residue was purified by column chromatography (silica gel; pentane/EtOAc 95:5, 1% $Et_3N$) to afford 3.28 g (81%) of 1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonic acid 4-methoxyphenyl ester (**24**)[77] as a clear oil.

**Preparation of 4-Bromobut-3-yn-1-ol (33) (Table 5).** *N*-Bromosuccimide (9.78 g, 55 mmol) and $AgNO_3$ (0.750 g, 4.4 mmol) were added to a solution of 3-butyn-1-ol (**29**) (3.78 mL, 50 mmol) in dry acetone (150 mL). The reaction was stirred at room temperature until complete by TLC (1 h). The reaction was quenched by the addition of 200 mL of pentane and then washed with $H_2O$. The layers were separated, the aqueous layer was back extracted with $Et_2O$/pentane (1:1), and the organics were combined, dried over $MgSO_4$, filtered, and concentrated. The resulting residue was then purified by flash chromatography (silica gel; pentane/EtOAc 90:10, 1% $Et_3N$) to give 7.45 g (94%) of 4-bromobut-3-yn-1-ol (**33**).[78]

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**Supporting Information Available:** Spectroscopic data for all new compounds pictured, as well as detailed experimental procedures. This material is available free of charge via the Internet at http:/pubs.acs.org.

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[77] For spectroscopic data see: Subramanian, L. R.; Martinez, A. G.; Fernandez, A. H.; Alvarez, R. M. *Synthesis* **1984**, 481−485.

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