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# Stereoselective Synthesis of Stannyl Enones via Palladium-Catalyzed and Free Radical Hydrostannation of Alkynyl Ketones with Trineophyltin Hydride

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A study on the addition of trineophyltin hydride (**1**) to alkynones under free radical (AIBN and $Et_3B$) and palladium-catalyzed [$(PPh_3)_2PdCl_2$] conditions is reported. The results obtained indicate that the addition of **1** to eight ynones catalyzed by bis(triphenylphosphine)palladium(II) chloride led in all cases to addition products in very high yields (80−96%). These additions take place with excellent regio- and stereochemistry, leading to the α adducts as major products in seven out of the eight cases studied. Also the *E* adducts, resulting from a *syn* attack, were the only (seven cases) or the predominant (one case) products. The radical hydrostannations initiated by AIBN of ynones **2**−**5** with **1** led to addition products in good yields (60−88%); with the more hindered ketones **6** and **7**−**9** the yields obtained were lower. The radical additions initiated by triethylboron to ynones **2**−**6** follow a similar pattern but with lower yields; no addition products in the hydrostannation of ynones **7**−**9** were detected. The new acyl-substituted vinylstannanes, owing to their greater stability compared with that of their tributyl- and trimethylstannyl analogues, can be purified by column chromatography using neutral alumina (in all cases) or silica gel 60 (in most cases) as adsorbents. Full $^1H$, $^{13}C$, and $^{119}Sn$ NMR data are given.

## Introduction

Stannyl enones are compounds of importance in organic synthesis, for example, in the synthesis of natural products of pharmacological interest.[1] α-Stannyl enones are considered synthetic equivalents of the anions of α,*β*-enones. Hydrostannation of alkynyl ketones is the shortest route to stannyl enones. Thus, the synthesis of α-stannyl enones has been carried out by palladium(0)- and palladium(II)-catalyzed hydrostannation of alkynones with trimethyl- and tributyltin hydride.[2,3] It should be pointed out that the synthesis of these compounds presents difficulties because of their instability; thus it has been reported that some α-stannyl enones are temperature-labile and so sensitive to acid conditions that during the workup they tend to decompose and could not be isolated pure.[2,3] Among other methods, the synthesis of α- and *β*-stannyl enones has been carried out, mostly in more than one step, by hydrostannation of propargyl alcohols followed by oxidation of the vinyltin adducts,[4] the photooxygenation of vinyl stannanes followed by dehydration of the resulting hydroperoxides,[5] the conjugate addition of the cuprate derived from copper(I) thiophenoxide and $Bu_3SnLi$ to an ynone,[1a] and the coupling of (*E*)-1,2-bis(tributylstannyl)ethene with acid chlorides in the presence of palladium catalysts.[6] We could not find any reference to radical addition of organotin hydrides to alkynones in the literature.

In previous work,[7] we have shown that hydrostannation of substituted alkynes with trineophyltin hydride (**1**) leads stereoselectively and in high yields to vinylstannanes that showed enhanced stability in comparison with that of vinylstannanes resulting from the additions of the more common triorganotin hydrides (Me, Bu, and Ph). We thus considered it of interest to carry out a study on the free radical and palladium-catalyzed addition of trineophyltin hydride (**1**) to various alkynyl ketones. It should be noted that, taking into account both the regio-

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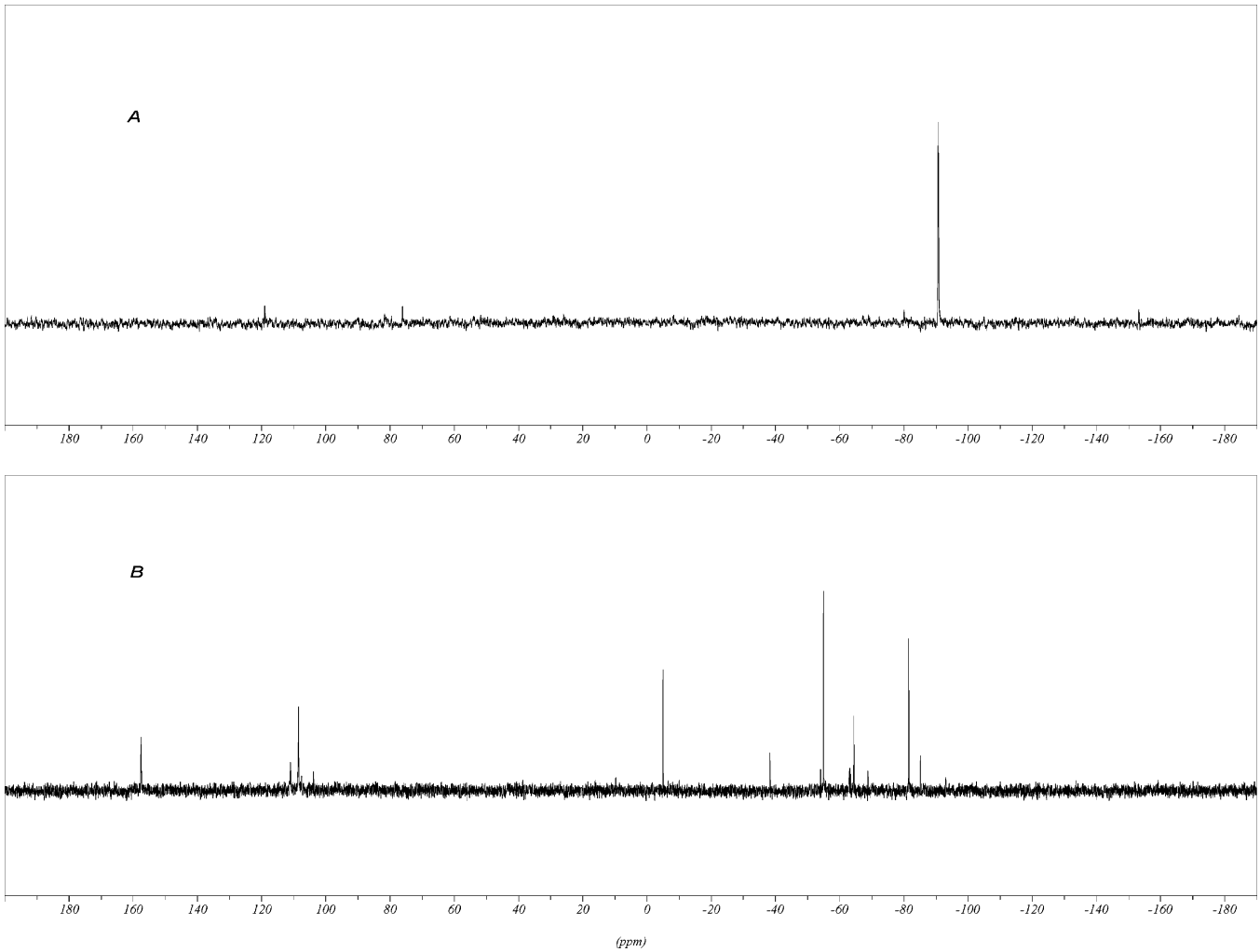
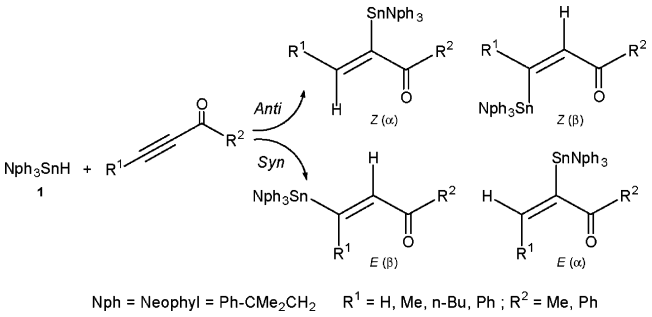



**FIGURE 1.** Hydrostannation of 3-butyn-2-one under radical conditions. $^{119}$Sn NMR spectra: (A) addition of $Nph_3SnH$ (**1**), (B) addition of $Bu_3SnH$.

**SCHEME 1. *syn* and *anti* Additions of Trineophyltin Hydride to Alkynyl Ketones**




and stereochemistry of the addition of tin hydride **1**, these reactions could lead to four stereoisomers as shown in Scheme 1.

## Results and Discussion

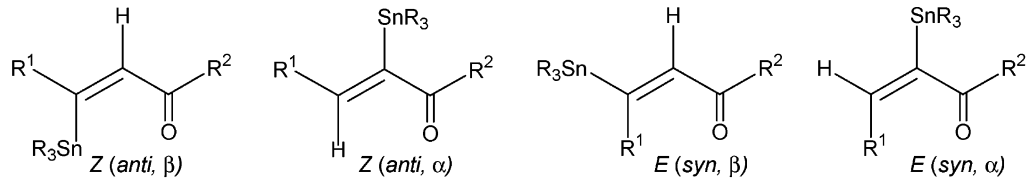
Because of the lack of information on the radical additions of other organotin hydrides to alkynones, we initially compared the addition of tributyltin hydride and of trineophyltin hydride (**1**) to 3-butyn-2-one. The $^{119}$Sn NMR spectra of the crude products resulting from these additions (Figure 1) clearly show that the hydrostannation using hydride **1** (spectrum A) is more efficient and selective than the addition of tributyltin hydride (spectrum B).

These spectra show that whereas the addition of hydride **1** is very selective, giving a mixture of two products in a ratio 96/4 (later we determined that they were the *Z*-addition products), the addition of tributyltin hydride leads to a mixture of various vinylstannanes: not only vinyl ketones but also allyl alcohols, tin alkoxides, and hexabutylditin (−81.7 ppm).

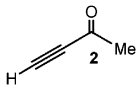
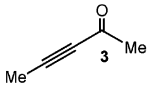
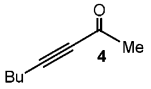
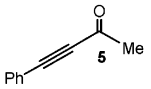
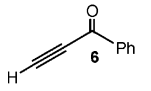
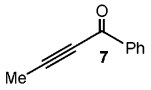
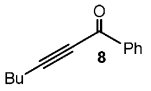
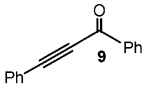
We then carried out a study on the addition of trineophyltin hydride (**1**) to the following ynones: 3-butyn-2-one (**2**), 3-pentyn-2-one (**3**), 3-octyn-2-one (**4**), 4-phenyl-3-butyn-2-one (**5**), 1-phenyl-2-propyn-1-one (**6**), 1-phenyl-2-butyn-1-one (**7**), 1-phenyl-2-heptyn-1-one (**8**), and 1,3-diphenyl-2-propyn-1-one (**9**). First we studied the additions under radical conditions (Table 1, Methods A and B) of **1** to the above-mentioned alkynes; the results obtained are summarized in Table 1.

The *Z* geometry was assigned on the basis of the large $^3J$(Sn,H) coupling constants, all of them over 112 Hz (see Experimental Section, Table 2), which indicate the existence of *trans* H−C−C−Sn linkages in these compounds.

**TABLE 1. Trineophyltin Hydride (1) Additions to Alkynyl Ketones**



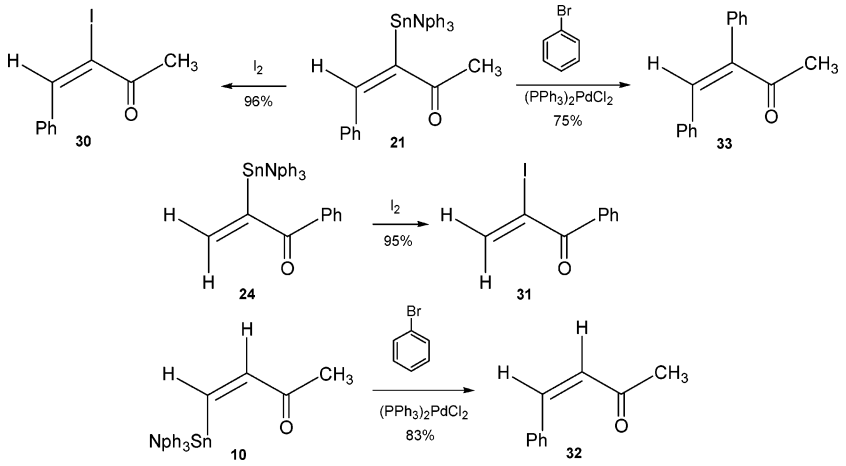

R = Neophyl = $PhMe_2CCH_2$

| Comp. Nº | Alkynone | Meth.[a] | Temp (ºC) | Time (h) | Yield[b] (%) | *Z* ( ) (%) (Nº) | *Z* ( ) (%) (Nº) | *E* ( ) (%) (Nº) | *E* ( ) (%) (Nº) | $^{119}Sn$[c] (ppm) |
|---|---|---|---|---|---|---|---|---|---|---|
| **10** & **11** |  | A | 60 | 3 | 66 | 96 (**10**) | 4[d] (**11**) | -- | (4)[d] | **10**: -89.0<br>**11**: -78.3[g] |
| **10** | | B | 25 | 3 | 79 | 100 | -- | -- | -- | |
| **10**, **11** & **12** | | C | 25 | 1 | 94[e] | 20 (**10**) | (58)[d] | 22 (**12**) | 58[d](**11**) | **12**: -80.5[g] |
| **13**, **14** & **15** |  | A | 80 | 3.3 | 60 | 28 (**13**) | 31 (**14**) | -- | 41 (**15**) | **13**: -90.3<br>**14**: -94.6<br>**15**: -67.1 |
| **13** | | B | 25 | 17 | 2.5[e] | 100 | -- | -- | -- | |
| **15** | | C | 25 | 1 | 90 | -- | -- | -- | 100 | |
| **16** & **17** |  | A | 80 | 3 | 68 | -- | 33 (**16**) | -- | 67 (**17**) | **16**: -89.1<br>**17**: -66.5 |
| **16**, **18** & **19** | | B | 25 | 24 | 5[e] | 23 (**18**) | 33 (**16**) | 44 (**19**) | -- | **18**: -97.8[g]<br>**19**: -56.4[g] |
| **17** | | C | 25 | 1 | 90 | -- | -- | -- | 100 | |
| **20** & **21** |  | A | 90 | 8 | 88 | 6 (**20**) | -- | -- | 94 (**21**) | **20**: -92.9[g]<br>**21**: -54.7 |
| **21** | | B | 25 | 4 | 1[e] | -- | -- | -- | 100 | |
| **21** & **22** | | C | 25 | 1 | 96[e] | -- | -- | 62 (**22**) | 38 (**21**) | **22**: -62.9[g] |
| **23** & **24** |  | A | 65 | 2.5 | 43 | 17 (**23**) | 83[d] (**24**) | -- | (83)[d] | **23**: -91.1<br>**24**: -66.3 |
| **23** & **24** | | B | 25 | 3 | 41 | 87 (**23**) | 13[d] (**24**) | -- | (13)[d] | |
| **24** & **25** | | C | 25 | 1 | 86 | -- | (94)[d] | 6 (**25**) | 94[d] (**24**) | **25**: -80.6[g] |
| **26** |  | A | 110 | 8 | 9[e] | -- | -- | -- | 100 | **26**: -63.2 |
| -- | | B | 25 | 24 | [f] | -- | -- | -- | -- | -- |
| **26** | | C | 26 | 1 | 80 | -- | -- | -- | 100 | |
| **27** |  | A | 90 | 6 | 25[e] | -- | -- | -- | 100 | **27**: -62.5 |
| -- | | B | 25 | 24 | [f] | -- | -- | -- | -- | -- |
| **27** | | C | 25 | 1 | 89 | -- | -- | -- | 100 | |
| **28** |  | A | 90 | 5 | 6[e] | -- | -- | 100 | -- | **28**: -66.7[g] |
| -- | | B | 25 | 24 | [f] | -- | -- | -- | -- | -- |
| **28** & **29** | | C | 25 | 1 | 88 | -- | -- | 7 (**28**) | 93 (**29**) | **29**: -49.1 |

[a] The reactions were carried out under a nitrogen atmosphere; ratio **1**/alkyne = 1. Method A: AIBN 0.01 equiv, without solvent. Method B: triethylboron 0.1 equiv, in ethyl ether. Method C: $(PPh_3)_2PdCl_2$ 2% in THF. [b] Yields of products isolated from chromatography except when otherwise stated. [c] In $CDCl_3$; in ppm with respect to $Me_4Sn$. [d] In these cases $Z(\alpha) = E(\alpha)$. [e] From the $^1H$ and/or $^{119}Sn$ NMR spectra of the crude products. [f] No adduct formation was detected. [g] From the spectra of the mixture.

On the other hand, the *E* stereochemistry was assigned taking into account that the observed $^3J(Sn,H)$ coupling constants were mostly around 65 Hz and, in one case, 82.6 Hz (Supporting Information, Table 2), clearly indicating a *cis* arrangement of the proton attached to one of the vinyl carbons and the trineophyltin moiety attached to the other vinyl carbon of these adducts. These structures were confirmed by a detailed analyses of the $^1H$ and $^{13}C$ NMR data (Supporting Information, Tables 2 and 3).

**SCHEME 2. Iododestannylations and Stille Reactions of Some Acyl-Substituted Vinylstannanes**




In Table 1, it can be seen that whereas the radical hydrostannations initiated by AIBN (Method A) of ynones **2**−**5** with the organotin hydride **1** lead to addition products in good to very good yields (60−88%), the yields obtained with the more hindered ketones **6** (43%) and **7**−**9** (6−25%) are lower. In Table 1 it can also be seen that the radical additions initiated by triethylboron (Method B) to ynones **2**−**6** follow a similar pattern with, in general, substantially lower yields. We could not detect addition products in the hydrostannations of ynones **7**−**9** with hydride **1** using Method B.

It should be mentioned that although these radical additions led in most cases to mixtures of trineophyltin adducts, we were able to separate and purify these by column chromatography. This suggests that trineophyltin adducts are more stable than their trimethyl- and tributyltin analogues, which have been reported to decompose during chromatographic purification[2] or to isomerize.[8]

The addition of **1** catalyzed by bis(triphenylphosphine)-palladium(II) chloride to the same ynones **2**−**9** (Table 1, Method C) led in all cases to addition products in very high yields (80−96%). It should be noted that the yields obtained in the palladium-catalyzed hydrostannations of ynones using trimethyl- and tributyltin hydrides[2] were between 30% and 37% lower than the yields obtained in the additions of hydride **1**.

In the case of the radical additions initiated by AIBN, in only three cases (Table 1, ynones **2**, **3**, **6**) do the *Z* adducts, resulting from an *anti* addition, predominate over the *E* adducts. As in previous studies we have demonstrated that the stereochemistry of these additions is *anti*;[7] the mixtures of *E* and *Z* isomers obtained in the additions to some of these carbonyl conjugated alkynes probably arise from configurational instability of the principally formed *Z* isomers. As for the regiochemistry, a clear predominance of the α adducts (six out of eight cases) over the $\beta$ adducts is observed. The fact that the bulk of the substituents $R^1$ and $R^2$ do not apparently have any influence on the orientation of the addition suggests that the predominance of the α adducts could be connected with electronic factors.

On the other hand, the results obtained in the radical additions initiated by triethylboron (Method B), although disappointing from the point of view of the yields, showed that in those cases where the addition took place (Table 1, ynones **2**−**6**) in four out of five cases the predominant products were those with the *Z* configuration. Also, in four out of five cases the products of $\beta$ regiochemistry were obtained in higher proportion.

As shown in Table 1, the palladium-catalyzed reactions took place with excellent regio- and stereochemistry. Thus, the α adducts were the major products in seven out of the eight cases studied, and the *E* adducts, resulting from a *syn* attack, were the only (seven cases) or the predominant (one case) products of the hydrostannations using trineophyltin hydride (**1**).

To test the chemical reactivity of the new trineophylstannylenones, we carried out iododestannylations and Stille reactions with some of them (Scheme 2). We found that the reactions between iodine and adducts **21** and **24** lead selectively and almost quantitatively to the corresponding iodovinyl ketones **30** and **31**, respectively.[9] On the other hand, whereas the $PdCl_2(PPh_3)_2$-catalyzed Stille reaction between adduct **10** and bromobenzene led to (*Z*)-benzylideneacetone (**32**)[10] in 83% yield, the reaction of adduct **21** with bromobenzene gave (*Z*)-3,4-diphenyl-3-buten-2-one (**33**) (75%).[11] These results clearly indicate that the reactivity of the new trineophylstannylenones is similar to that of the tributyl- and trimethylstannylenones reported previously by other authors.

The major advantages of the hydrostannation of ynones with trineophyltin hydride are not only the higher yields but the greater stability of the resulting adducts compared with that of their tributyl- and trimethylstannyl analogues. The stability of the trineophylstannylenones enable their separation and purification by column chromatography either using neutral alumina (in all cases) or silica gel 60 (in most cases) as adsorbents, this resulting in a dramatic improvement of the yields of pure isolated compounds.

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## Experimental Section

NMR spectra were recorded on a 300-MHz instrument, using $CDCl_3$ as solvent; chemical shifts ($\delta$) are reported in ppm with respect to TMS ($^1H$ and $^{13}C$) and with respect to $Me_4Sn$ in the case of $^{119}Sn$ NMR spectra. IR spectra were recorded on a FT spectrometer. Mass spectra were obtained using a 70-eV mass spectrometer. Irradiations were conducted in a reactor equipped with four 250-W lamps with peak emition at 350 nm. All the solvents and reagents used were analytical reagent grade. Trineophyltin hydride (**1**) was prepared as described previously.[12] 3-Butyn-2-one (**2**) was purchased, and 3-pentyn-2-one (**3**), 3-octyn-2-one (**4**), 4-phenyl-3-butyn-2-one (**5**), 1-phenyl-2-propyn-1-one (**6**), 1-phenyl-2-butyn-1-one (**7**), 1-phenyl-2-heptyn-1-one (**8**), and 1,3-diphenyl-2-propyn-1-one (**9**) were prepared following known techniques.[13]

**Addition of Trineophyltin Hydride (1) to Ynones under Radical Conditions. Typical Procedures. Method A.** A mixture of 1-phenyl-2-propyn-1-one (**6**) (0.130 g, 1 mmol), hydride **1** (0.519 g, 1 mmol), and AIBN as a catalyst, under nitrogen, was heated at 65 °C during 2.5 h. (This optimal time of reaction and temperature was indicated in earlier experiments in which the reaction was monitored by taking samples at intervals and observing the disappearance of the Sn−H absorption by IR and products formation by $^1H$ NMR.) The $^{119}Sn$ NMR spectrum of the crude product showed that it consisted of two compounds: (*Z*)-3-(trineophylstannyl)-1-phenyl-2-propen-1-one (**23**), peak at −91.1 ppm (17%), and 2-(trineophylstannyl)-1-phenyl-2-propen-1-one (**24**), peak at −66.3 ppm (83%). Column chromatography (silica gel 60) of the mixture afforded compounds **23** (0.043 g, 0.07 mmol, 7%) and **24** (0.234 g, 0.36 mmol, 36%) in the fractions eluted with hexanes−ethyl ether (90:10).

**Method B.** To a solution of 3-butyn-2-one (**2**) (0.052 g, 0.77 mmol) and tin hydride **1** (0.400 g, 0.77 mmol) in dry ethyl ether (3 mL) under nitrogen was added triethylboron (0.077 mmol, 0.077 mL of a 1 M solution in hexane), and the mixture was stirred for 3 h at room temperature. The $^{119}Sn$ NMR spectrum of the product showed that it consisted of only one compound, (*Z*)-4-(trineophylstannyl)-3-buten-2-one (**10**), peak at −89.0 ppm. Column chromatography (neutral alumina) of the crude product gave compound **10** pure (0.357 g, 0.608 mmol, 79%) in the fraction eluted with hexanes−ethyl ether (95:5).

**Addition of Trineophyltin Hydride (1) to Ynones Catalyzed by Bis(triphenylphosphine)palladium(II) Chloride. Method C.** To a solution of 3-octyn-2-one (**4**) (0.124 g, 1 mmol) and bis(triphenylphosphine)palladium(II) chloride (0.011 g, 0.02 mmol) in dry THF (4 mL) under nitrogen was added hydride **1** (0.519 g, 1 mmol), and the mixture was stirred at room temperature for 1 h. The solution was diluted with hexane (5 mL) and cooled in the refrigerator, and then the residual Pd(0) was filtered through a porous plate. The solvent was then distilled off under reduced pressure, and the $^{119}Sn$ NMR spectrum of the product showed that it consisted of only one compound, (*E*)-3-(trineophylstannyl)-3-octen-2-one (**17**), peak at −66.5 ppm. Column chromatography (silica gel 60) of the crude product gave compound **17** pure (0.580 g, 0,9 mmol, 90%) in the fraction eluted with hexanes−ethyl ether (98:2).

**Representative Stille Coupling Reaction: Synthesis of (*Z*)-4-Phenyl-3-buten-2-one (32).**[14] To a mixture of bromobenzene (0.083 g, 0.53 mmol), $PdCl_2(PPh_3)_2$ (0.014 g, 2%), and some crystals of 2,6-di-*tert*-butyl-4-methylphenol under nitrogen was added a solution of **10** (0.340 g, 0.58 mmol) in dry toluene (1.3 mL) at room temperature, and the mixture was stirred for 30 h under reflux, with monitoring by TLC. Column chromatography with silica gel 70−230 of the product gave compound **32**[9] (0.064 g, 0.44 mmol, 83%) in the fraction eluted with hexanes−ethyl ether (94:6).

**Representative Iododestannylation Reaction: Synthesis of 1-Iodovinylphenyl Ketone (31).**[3] To a solution of 2-(trineophylstannyl)-1-phenyl-2-propen-1-one (24) (0.085 g, 0.13 mmol) in dry $CH_2Cl_2$ (1.5 mL) under nitrogen was added iodine (1.1 equiv, 0.04 g, 0.144 mmol). The mixture was stirred at room temperature for 30 min, with monitoring of the reaction by TLC. The iodovinyl ketone **31**[8] was purified by column chromatography with silica gel 70−230 eluting with hexane (0.032 g, 0.12 mmol, 95%).

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**Supporting Information Available:** Characterization data for the products including full $^1H$ and $^{13}C$ NMR spectra, as well as mass spectra of the isolated pure compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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