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On the Stereospecific Conversion of Proximally-Oxygenated Trisubstituted Vinyltriphenylstannanes into Stereodefined Trisubstituted Alkenes

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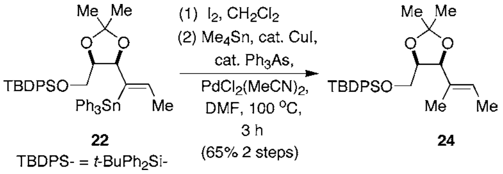
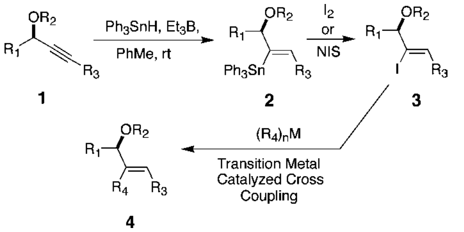
ABSTRACT



Allylically oxygenated vinyl α-triphenylstannanes such as 22 can be readily converted into vinyl iodides and thereafter stereodefined trisubstituted alkenes with retention of configuration.

For the *O*-directed, Ph_3SnH-mediated, free-radical hydrostannation of disubstituted acetylenes to emerge as a reaction of true practical significance for the preparation of trisubstituted olefins, its vinyltriphenylstannane products must be readily transformable into stereodefined vinyl iodides to allow transition-metal-catalyzed cross-coupling processes to complete the final alkene elaboration step (Scheme 1).[1]

Scheme 1 *O*-Directed Alkyne Hydrostannation and the Subsequent Elaboration into Target Trisubstituted Alkenes



At the outset of our studies on the aforesaid sequence, we did not anticipate that the conversion of our vinyltriphenylstannane products into vinyl iodides would be especially problematic. However, not long after we commenced our studies on the *O*-directed hydrostannation reaction with Ph_3SnH and cat. Et_3B, we came across a report by Marco-Contelles and Malacria[2] in which they showed that the iododemetalation of vinyltriphenylstannanes could take a most unexpected course when an allylic *O*-substituent was in close proximity to the Ph_3Sn moiety. Specifically, they demonstrated that when the vinyltriphenylstannanes **5** and **6** were reacted with molecular I_2 in CH_2Cl_2, a separable mixture of the chloro(diphenyl)stannylidenes **7** and **8** was obtained, as opposed to the two vinylic iodides that were expected (see Scheme 2).

In light of their results, we conducted an exhaustive search of the literature to find examples of other allylically oxygenated β- and α-vinyl triarylstannanes that had been successfully converted to vinyl halides by the action of electrophilic halogen sources. To our surprise, virtually all of the work that had previously been published had focused

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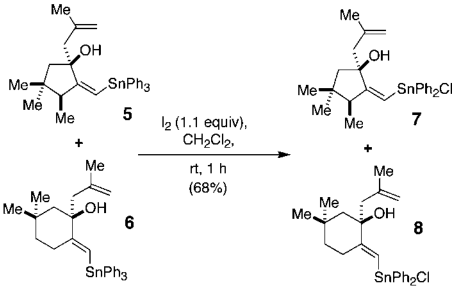
[1] (a) Part 1: Dimopoulos, P.; Athlan, A.; Manaviazar, S.; George, J.; Walters, M.; Lazarides, L.; Aliev, A. E.; Hale, K. J. *Org. Lett.* **2005**, *7*, 5369. (b) Part 3: Dimopoulos, P.; George, J.; Tocher, D. A.; Manaviazar, S.; Hale, K. J. *Org. Lett.* **2005**, *7*, 5377.

[2] Marco-Contelles, J.; Mainetti, E.; Fensterbank, L.; Malacria, M. *Eur. J. Org.* Chem. **2003**, 1759.

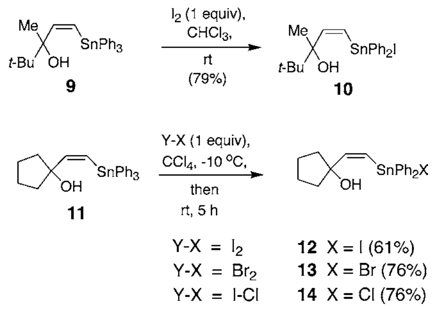
10.1021/ol051935t CCC: $30.25

Scheme 2. Unexpected Course to Iododestannylation



on (Z)-disubstituted β-triarylstannyl allyl alcohols,[3] which invariably react with halogens (Scheme 3) to give vinyl diarylhalostannyl alcohols as the preferred reaction products.

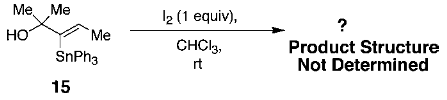
Scheme 3. Attempted Halodemetalation of Various β-Triphenylstannyl Allyl Alcohol Systems



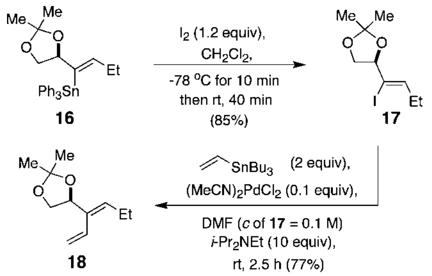
X-ray crystallographic studies on a significant number of (Z)-disubstituted β-triarylstannylated allyl alcohols have given valuable insights into this observed pattern of reactivity. It appears that in such systems, the central tin atom always adopts a distorted trigonal bipyramidal geometry due to strong internal coordination between the allylic OH and the tin. Apparently, the latter greatly weakens the C−Sn bond to the apical phenyl substituent, enabling it to be preferentially cleaved by the halogen.

Surprisingly, only one α-triarylstannylated allylic alcohol has ever been examined in the halodemetalation process viz. (Z)-2-methyl-3-triphenylstannyl-3-penten-2-ol **(15)** with I_2 in $CHCl_3$ (Scheme 4).[4] Unfortunately, a structure was never assigned to the major alkene product of this reaction, notwithstanding a claim being made that its triphenyltin substituent had been successfully cleaved. Given that this product was never isolated from the crude reaction mixture, nor its spectroscopic or analytical data ever reported, it remained unclear as to whether a vinyl iodide had ever actually been produced in this process.

Scheme 4. Iododemetalation of Vinylstannane **15**



Scheme 5. Tin−Iodine Exchange of Vinyltriphenylstannane **16** and the Stille Coupling of **17**



Because the propargylic-O atom of an alkylacetylene is capable of coordinating to a Ph_3Sn radical during its addition to the acetylenic system, we became concerned that this very same O-atom might strongly coordinate internally to the tin center in our product α-vinyltriphenylstannanes. If this were the case, then by analogy, one could expect the halogen−tin exhange process to be potentially troublesome and possibly yield vinyldiarylhalostannane products rather than the desired vinylic halides.

In view of the enormous importance of this transformation to the overall success of our new trisubstituted olefin synthesis, we thought it essential that we unambiguously determine the outcome of iododestannylation in α-triphenylstannylalkene systems with an allylic O-substituent. The present paper documents our findings in this respect and provides, for the very first time, unambiguous proof that vinyl iodides are indeed the favored products of iododestannylation in such systems. We would also like to record here the successful elaboration of these vinyl iodides into a range of target trisubstituted alkenes by an assortment of Pd(0)-catalyzed cross coupling techniques. As a result of the present work, we can now claim to have successfully demonstrated the great scope and worth of the O-directed, Ph_3SnH-mediated, alkyne hydrostannation reaction.

Our iododestannylation studies began with the vinylstannane **16** (Scheme 5), which was dissolved in CH_2Cl_2, cooled to −78 °C, and treated with 1.2 equiv of solid I_2. After the reaction mixture was warmed to rt and stirred for a further 40 min, TLC analysis revealed that a single faster moving product had formed. After extractive workup and purification by SiO_2 flash chromatography, the alkene product was isolated in 85% yield and was shown to be **17** by detailed spectroscopic analysis. To confirm that **17** could be suc-

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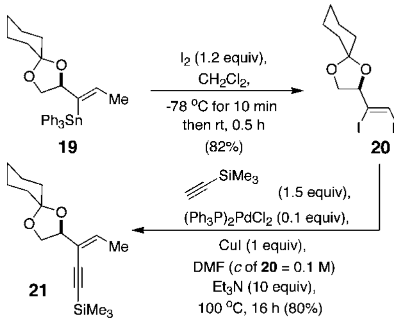
(3) (a) Pan, H.; Willem, Meunier-Piret, J.; Gielen, M. *Organometallics* **1990**, *9*, 2199. (b) Gielen, M.; Lelieveld, P.; de Vos, D.; Pan, H.; Willem, R.; Biesemans, M.; Fiebig, H. H. *Inorg. Chim. Acta* **1992**, *196*, 115. (c) Kayser, F.; Biesemans, M.; Pan, H.; Gielen, M.; Willem, R. *J. Chem. Soc., Perkin Trans. 2* **1994**, 297. (d) Kayser, F.; Biesemans, M.; Delmotte, A.; Verbruggen, I.; De Borger, I.; Gielen, M.; Willem, R.; Tiekink, E. R. T. *Organometallics* **1994**, *13*, 4026. (e) Dai, H. C.; Ying, Q. H.; Wang, X. H.; Yue, S. M.; Pan, H. D.; Chen, X. *Polyhedron* **1998**, *17*, 2503.

(4) Willem, R.; Delmotte, A.; De Borger, I.; Biesemans, M.; Gielen, M.; Kayser, F.; Tietink, E. R. T. *J. Organomet. Chem.* **1994**, *480*, 255.

Scheme 6. Tin−Iodine Exchange of Vinyltriphenylstannane **19** and the Sonogashira Coupling of **20**



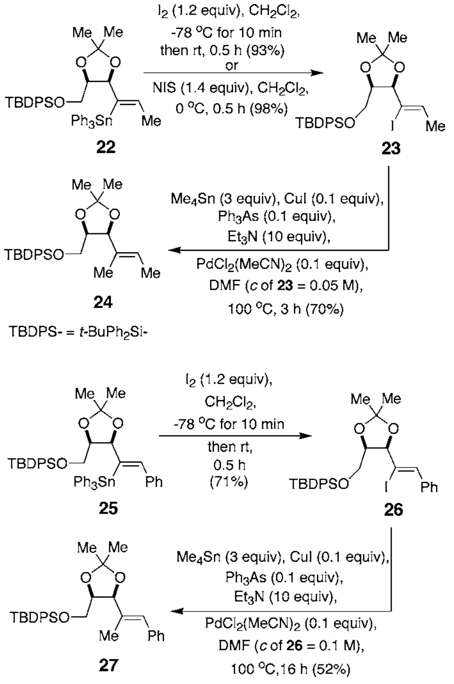
cessfully converted into a representative target alkene, with retention of olefin geometry, we examined its Stille coupling[5] with vinyltri-*n*-butylstannane and catalytic $(MeCN)_2PdCl_2$ in DMF at rt and observed that **18** was formed very cleanly in 77% yield.

We next addressed the iododestannylation of vinylstannane **19**, whose sterically more encumbered 1,3-dioxolane system was now derived from cyclohexanone (Scheme 6). As previously, the desired tin−iodine exchange reaction with I_2 proceeded efficiently and with complete retention of configuration; vinyl iodide **20** being isolated in 82% yield. The latter was coupled to trimethylsilylacetylene, under Pd(0)/Cu(I)-mediated Sonogashira conditions,[6] using Et_3N as the base in DMF at 100 °C for 16 h. A single cross-coupling product **21** emerged in 80% yield.

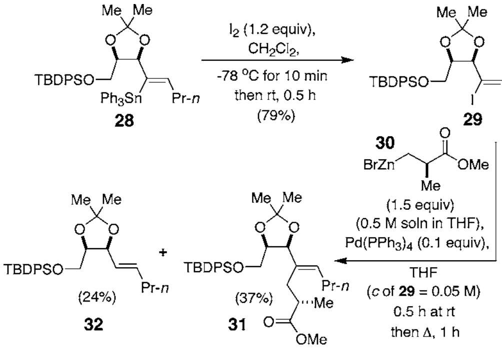
Encouraged by these successes, we extended our iododemetalation studies to vinyl-α-triphenylstannanes in which the 1,3-dioxolane system was branched. With the methyl- and phenyl-substituted vinyltriphenylstannanes **22** and **25** (Scheme 7), the expected vinyl iodides **23** and **26** were again formed after I_2 treatment and alkene geometry was preserved. We also found that **22** could equally well be converted into **23** by the action of *N*-iodosuccinimide (NIS) in CH_2Cl_2 at 0 °C (98%), although clearly this is a more expensive option than I_2. Happily, reasonable results were later obtained in the Pd(0)-mediated sp^3/sp^2-Stille cross couplings that were performed on **23** and **26** with Me_4Sn, so long as both reactions were effected in the presence of copper(I) iodide and triphenylarsine in DMF at 100 °C.[7]

Given the present very high level of interest in sp^3/sp^2 cross couplings between vinyl halides and alkylzinc halides, we iododestannylated **28** to obtain **29** and examined its Negishi coupling[8] with **30** (Scheme 8). Apart from obtaining the desired cross-coupling product **31** in 37% yield, the dehalogenated product **32** was also coproduced in 24% yield. Presumably, **32** arises from protonation of the vinylzinc bromide that is generated after metal−halogen exchange between **29** and **30**.

Scheme 7. Tin−Iodine Exchange of Vinyltriphenylstannane **22** and **25** and Their Subsequent Stille Couplings To Give **24** and **27**



Scheme 8. Iododestannylation of Vinyltriphenylstannane **28** and the Negishi Coupling of **29**



Having confirmed that 1,3-dioxolane-containing vinyl α-triphenylstannanes could successfully be converted into representative trisubstituted alkenes in reasonable yield, we

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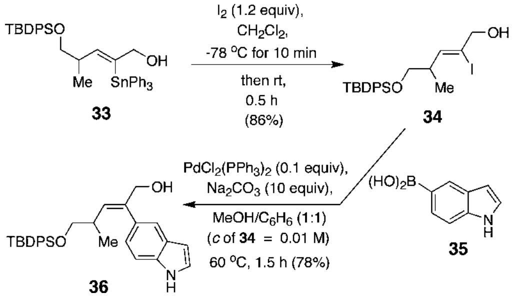
[5] Farina, V.; Krishnamurthy, V.; Scott, W. J. *The Stille Reaction*; John Wiley & Sons: New York, 1998; p 1.

[6] (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4465. (b) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 3, p 521.

[7] For a previous example of the $Ph_3As/CuI/(MeCN)_2PdCl_2$ being used to mediate a Stille coupling, see; Gibbs, R. A.; Krishnan, U.; Dolence, J. M.; Poulter, C. D. *J. Org. Chem.* **1995**, *60*, 7821.

[8] (a) Negishi, E.; Zhang, Y.; Cederbaum, F. E.; Webb, M. B. *J. Org. Chem.* **1986**, *51*, 4080. (b) Negishi, E.; Ay, M.; Gulevich, Y. V.; Noda, Y. *Tetrahedron Lett.* **1993**, *34*, 1437. (c) McMurry, J. E.; Bosch, G. K. *J. Org. Chem.* **1987**, *52*, 4885. (d) Asao, K.; Iio, H.; Tokoroyama, T. *Tetrahedron Lett.* **1989**, *30*, 6401. (e) Nakamura, E.; Sekiya, K.; Kuwajima, I. *Tetrahedron Lett.* **1987**, *28*, 337. (f) Jackson, R. F. W.; Turner, D.; Block, M. H. *J. Chem. Soc., Chem. Commun.* **1995**, 2207. (g) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445. (h) Negishi, E.; Liu, F. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; VCH: Weinheim, 1998; p 1.

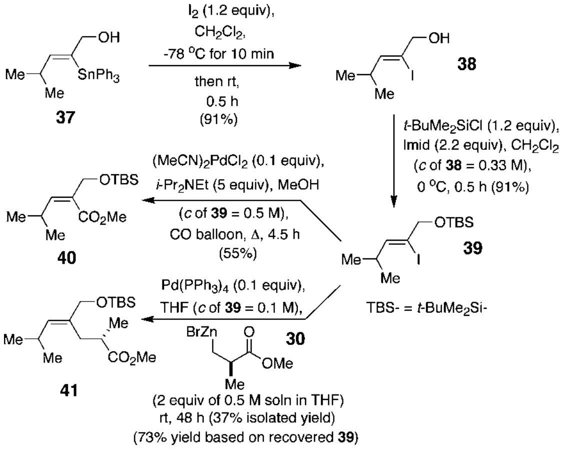
Scheme 9. Conversion of Vinylstannane **33** into **36**



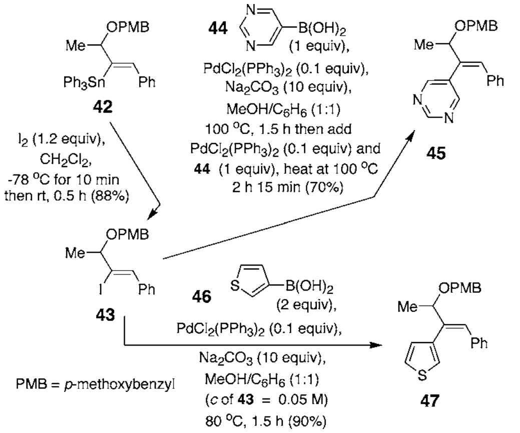
next examined the iodinolysis of α-triphenylstannyl alkenes with an allylic OH. The first system we investigated was the vinyltriphenylstannane **33**; it smoothly iododestannylated in 86% yield (Scheme 9). Vinyl iodide **34** was subsequently employed for a Suzuki coupling[9] with **35**, which furnished **36** in 78% yield.

In like fashion, the branched allylic alcohol **37** (Scheme 10) could be readily iododestannylated (91% yield), *O*-silylated (91% yield), and carbonylated (55% yield) to obtain the enoate **40** as a single product. Negishi coupling[9] of **39** with **30** also occurred cleanly (37%) but was slow due to steric hindrance.

Scheme 10. Iododestannylation of Vinyltriphenylstannane **37** and the Pd(0)-Mediated Carbonylation and Negishi Coupling of **39**



Scheme 11. Conversion of **42** into **43**, **45**, and **47**



Finally, the iododemetalation of a vinyl α-triphenylstannane with an allylic OPMB (PMB = *p*-methoxybenzyl) group was studied (Scheme 11). As expected, **42** reacted readily. The resulting vinyl iodide **43** also successfully engaged in Suzuki reactions[9] to give **45** and **47**, respectively, in 70% and 90% yield.

In conclusion, we have demonstrated for the first time that vinyl triphenylstannanes, with an allylic *O*-substituent α to the tin residue, can successfully be converted into vinyl iodides in good yield with retention of configuration by two methods. We have also shown that the iodoalkene products can be readily transformed into a variety of trisubstituted alkenes through a range of Pd (0) catalyzed cross-coupling techniques. As a result of our work, we have now demonstrated the great synthetic worth of the *O*-directed, Ph_3SnH-mediated, free-radical hydrostannation process for stereodefined trisubstituted olefin construction.

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Supporting Information Available: Full experimental procedures, 500 MHz ^1H and 125 MHz ^{13}C spectra, and HRMS spectra for all new compounds are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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[9] Reviews: (a) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; p 49. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.