Pergamon

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Tetrahedron Letters 44 (2003) 1087–1089

TETRAHEDRON LETTERS

Directed Pd(0)-catalyzed hydrostannations of internal alkynes

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Received 18 October 2002; revised 21 November 2002; accepted 22 November 2002

Abstract—Hydrostannations of primary propargylic alcohols with Bu_3SnH catalyzed by $Pd(PPh_3)_2$ yield (*E*) allylic alcohols in which the Bu_3Sn group is affixed to the carbon proximal to the CH_2OH substituent, suggestive of an OH directing effect. Hydrostannations of the related propargylic acetates show no such effect.

The hydrostannation of alkynes is a well-established route to vinylstannanes. These intermediates have proven quite useful as precursors to olefins, vinyl halides, cuprates and other organometal reagents.[1] They also can serve as partners in Stille coupling reactions.[1b] Terminal alkynes have been studied most extensively. Both free radical and Pd(0)-catalyzed additions to these alkynes typically proceed efficiently and stereoselectively to afford (*E*)-vinyl stannanes.[2a] Haloalkynes have also been shown to undergo efficient Pd(0)-catalyzed hydrostannation, often with higher stereoselectivity than the nonhalogenated analogue.[2a,b] Hydrostannations of internal alkynes have proven less satisfactory owing to diminished reactivity and low regioselectivity. An early study by Guibé and co-workers showed that conjugated alkynones, alkynoic esters and diynes afford α-stannylated (*E*) adducts regioselectively upon Pd(0)-catalyzed hydrostannation with Bu_3SnH.[2a] Subsequently, in work mainly directed at stannylcupration, Pancrazi and co-workers noted that the Pd(0)-catalyzed hydrostannation of 2-butyn-1-ol afforded a 3:1 mixture of (*E*) 2- and 3-tributylstannyl-2-buten-1-ols suggestive of an OH directing effect.[3] However, the tertiary alcohol 1-ethynyl cyclohexanol yielded only the terminal vinylstannane under these conditions.

The possibility of an OH directing effect in Pd(0)-catalyzed hydrostannations was explored in greater detail by Maleczka and co-workers.[4] They examined a series of unbranched terminal alkynols of the type $HC{\equiv}C(CH_2)_nCH_2OH$ (**A**) in which an increasing number of methylenes separate the CH_2OH and alkyne groups (Fig. 1). Propargyl alcohol ($n=0$) afforded a 1.3:1 mixture of proximal **B** and distal **C** hydrostannation products. However, the next three higher homologues ($n=1$–3) all gave mixtures favoring the latter regioisomers.

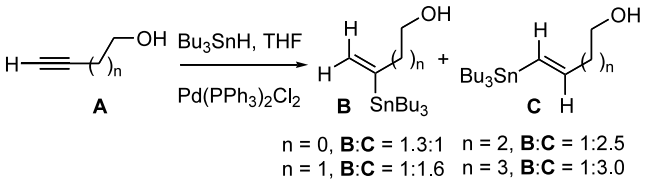

Figure 1. Evaluation of a possible OH directing effect in hydrostannations of terminal alkynes (Ref. 4).

Our interest in the hydrostannation of internal alkynes was motivated by a possible application of this reaction to the synthesis of trisubstituted alkenes related to polyketide natural products (Fig. 2).[5] However our efforts to effect these additions to internal alkynes such as **D** were unpromising. The reactions were slow and proceeded in less than 20% yield. Remarkably, under the same conditions, the hydroxymethyl and acetoxymethyl analogues **G** and **H** afforded the *syn* adducts **I** and **J** with complete regioselectivity (Fig. 3).[6] Subsequent hydrogenolysis of the alcohol **I**, via the derived allylic bromide, afforded the vinylstannane **E**. The success of this sequence prompted our additional investigations into the possible directing effect of CH_2OH and CH_2OAc substituents in hydrostannations of internal alkynes.

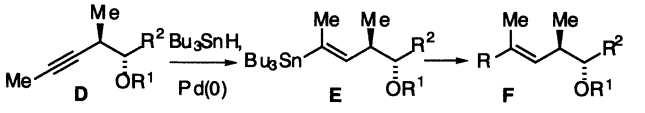

Figure 2. Synthetic plan for trisubstituted alkenes related to polypropionate segments of polyketide natural products.

Keywords: hydrostannation; vinylstannae; poyketide; directing effects.
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0040-4039/03/$ - see front matter
PII: S0040-4039(02)02660-6

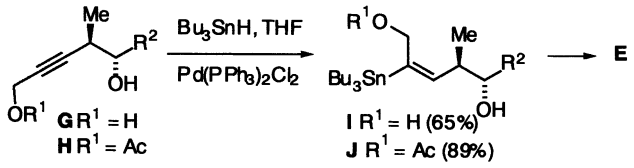
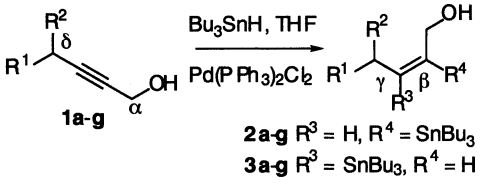


Figure 3. An alternative route to polypropionate segments of polyketide natural products.

The first alkynes examined were the propargylic alcohols **1a–d** prepared by addition of formaldehyde to lithiated 1-octyn-3-ol and the corresponding ether derivatives.[7,8] The hydrostannations were effected in THF with Bu_3SnH in the presence of 10 mol% of the precatalyst, $Pd(PPh_3)_2Cl_2$. Additions to the OTBS and OBOM-substituted propargylic alcohols **1a** and **1b** proceeded rapidly at room temperature to afford the (*E*)-vinyl stannanes **2a** and **2b** as the only detectable products (Table 1). Analogous reactions of the methyl ether **1c** and alcohol **1d**, though highly stereoselective, were less regioselective.

The *sec*-butyl-substituted propargylic alcohol **1e**[9] yielded the proximal regioisomer **2e** as the sole adduct, whereas the propyl analogue **1f** reacted less selectively affording a 7:1 mixture of regioisomers favoring **2f**. As previously noted, 2-butyn-1-ol (**1g**) has been reported to give a 3:1 mixture of the two (*E*)-adducts **2g** and **3g**.[3,10]

Table 1. Hydroxyl-directed hydrostannations of γ-substituted propargylic alcohols

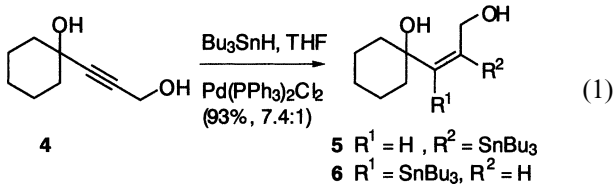


R^1	R^2	Series	Yield (%)	**2**:**3**
C_5H_{11}	OTBS	**a**	69	>20:1
C_5H_{11}	OBOM	**b**	70	>20:1
C_5H_{11}	OMe	**c**	66	6.3:1
C_5H_{11}	OH	**d**	71	2.9:1
C_2H_5	CH_3	**e**	75	>20:1
C_3H_7	H	**f**	73	7:1
H	H	**g**	58	3:1[a]

[a] See Ref. 3.

The general trend of Table 1 can be explained by a steric effect stemming from the δ-propargylic substituent reinforced by a cooperative OH-directing effect. Accordingly, branching at the γ position by OTBS, OBOM or CH_3 directs the regioselectivity of the addition to the β-position and this effect is further augmented by the proximal OH substituent. The directing influence of the OH substituent is apparent from the hydrostannation of the unbranched propyl-substituted propargyl alcohol **1f** in which a distinct preference for the proximal (β) product **2f** is found. The lower selectivity observed for the diol **1d** may reflect a moderate opposing directing effect by the secondary alcohol. The methyl ether substituent of **1c** would lack this opposing directing effect and exert a larger steric effect than OH, in accord with the more favorable ratio of isomeric adducts from **1c** versus **1d**.

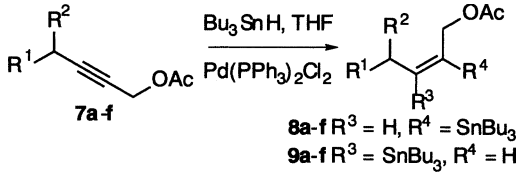
Hydrostannation of the cyclohexanol derivative **4**[11] led to a 7.4:1 mixture of the two regioisomers **5** and **6** (Eq. (1)). This selectivity is considerably better than the 2.9:1 preference observed for the secondary alcohol **1d** in accord with an enhanced steric effect for **4** and a diminished competing directing effect of the tertiary OH.



(1)

The next hydrostannation experiments were conducted on the acetate derivatives **7a–f** (Table 2). In this series only the *sec*-butyl-substituted alkyne **1e** gave rise to a single adduct. Furthermore, the trend in regioselectivity for the γ-oxygenated compounds **7a–d** was quite different from that of their alcohol counterparts **1a–d**. Notably hydrostannation of the TBS and BOM ethers **7a** and **7b** proceeded with the lowest regioselectivity. The ordering of **7c**>**7d**>**7b**>**7a** is not easily explained. However, it is clear that the acetoxymethyl group exerts a relatively modest directing effect at best.

Table 2. Hydrostannations of γ-substituted propargylic acetates



R^1	R^2	Series	Yield (%)	**8**:**9**
C_5H_{11}	OTBS	**a**	73	3:1
C_5H_{11}	OBOM	**b**	63	3.2:1
C_5H_{11}	OMe	**c**	73	6.3:1
C_5H_{11}	OH	**d**	62	4:1
C_2H_5	CH_3	**e**	79	>20:1
C_3H_7	H	**f**	73	7:1

The present findings, together with our earlier studies, more clearly define the role of propargylic alcohol and acetate substituents in directing the regioselectivity of hydrostannations. It should be noted that certain internal alkynes substituted by a secondary propargylic hydroxyl grouping afford mainly β-stannylated allylic

alcohols.[12] These results, and the trends noted for diols **1d** and **4**, indicate that a primary alcohol function more effectively directs regioselectivity than a secondary or tertiary. The origin of this effect is not clear. Bäckvall et al. have formulated a four-membered oxapalladacycle complex in connection with a methoxy-directed carbonylation.[13] An analogous intermediate could account for the present additions. However, at present such explanations must be regarded as highly speculative. Nonetheless, our findings extend the list of synthetically useful hydrostannation reactions and provide a route to vinylstannanes such as **2a**/**b**/**e**/**f** and analogues thereof.

Acknowledgements

Support for these investigations was provided through Grant R01 GC10547 from the National Cancer Institute.

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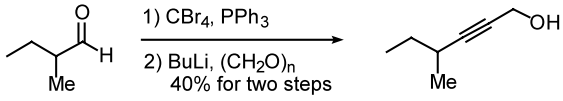
8. Satisfactory analytical and/or spectral data were obtained for all new compounds.
9. The intermediate **1e** was prepared by the following sequence:



10. In an earlier reported study of Pd(0)-catalyzed hydrostannations Miyake and Kimiaki obtained a 5:1 mixture of these two regioisomers. Miyake, H.; Kimiaki, Y. *Chem. Lett.* **1989**, 981.
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