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Synthesis of substituted allylic alcohols *via* palladium-catalized hydrostannation

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Introduction

The problem of stereoselective construction of some unsaturated fragments required for total synthesis of natural products has been resolved in many cases making use of vinyl- and dienylstannanes. Therefore, these tin derivatives occupy a key position as synthetic intermediates especially when having a well defined stereochemistry. In the literature, there are numerous synthetic applications based on the use of stannylated allylic alcohols. Hydrostannation of propargylic alcohols is a simple and economical route for preparing them.

Miyake (Miyake and Yamamura, 1989) and Guibé (Zhang *et al.*, 1990) were the first to publish studies related with hydrostannation of propargylic alcohols and ethers. They found that in the case of ethers without substituents at propargylic position, the addition of tributyltin hydride takes place with moderate α–regioselectivity, probably due to electronic and/or coordinative effects. However, the introduction of substituents results in a change in addition regioselectivity, thus showing a preference for formation of the β–adduct. The palladium-catalyzed reaction leads efficiently and stereoselectively to (*E*)-vinylstannanes (thermodynamic product). Such additions, as consequence of their mechanism, usually take place with *syn* stereochemistry (Fig. 1), and in many cases with good regioselectivity due to a combination of steric and electronic factors (Smith *et al.*, 2000). It is considered that these reactions take place through a catalytic cycle, which involves an oxidative addition followed by hydrometalation and reductive elimination. It is also possible that a stannylmetalation directly occurs followed by reductive elimination leading to reaction adducts.

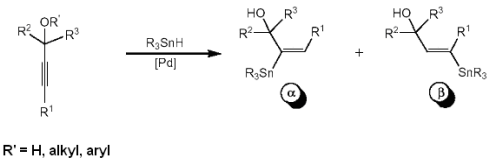

Figure 1

Taking into account the synthetic importance of these compounds, and based on experimental evidence, we consider of interest to expand the study of hydrostannations with trineophyltin hydride (Dodero *et al.*, 2002) to a series of substituted propargylic alcohols in order to assess the stereochemical behaviour of the palladium-catalyzed additions.

Methodology

A method used to carry out hydrostannation reactions catalyzed by *bis*(triphenylphosphine) palladium (II) chloride is described in general terms. To a solution of propargylic alcohol (1 equiv.) in dry THF, $(PPh_3)_2PdCl_2$ (0.02 equiv.) was added under inert atmosphere, followed by trineophyltin hydride (1 equiv.). The mixture was stirred at room temperature until the initially orange-coloured solution turned to dark brown colour (within 30 min and 2 h). Reaction was monitored by IR spectroscopy observing the disappearance of the Sn-H absorption band (approx. 1800 cm^{-1}), and by TLC. Solvent was

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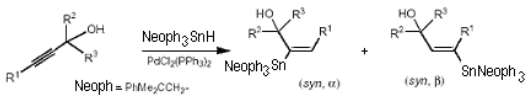
removed at reduced pressure without warming. Purification of all organotin adducts was carried out by column chromatography, using silicagel 60 as stationary phase.

Structural characteristics of the new organotin adducts were determined by IR spectroscopy, multinuclear magnetic resonance, *e.g.*, ^{1}H-, ^{13}C- and ^{119}Sn -NMR.

Discussion of results

Results obtained upon addition of trineophyltin hydride to different propargylic alcohols, at room temperature in THF containing 2% *bis*(triphenylphosphine)palladium (II) dichloride are shown in Table 1.

Table 1. Palladium-catalyzed additions of trineophyltin hydride to substituted propargylic alcohols.[a]



Nr.	Compnd.	R	R^1	R^2	R^3	*Syn*-Adducts (α) (%)	(β) (%)	^{119}Sn (ppm)[b]
1	**1 and 2**	Neoph	H	H	H	70 (**1**)	30 (**2**)	**1**: -85.6 **2**: -84.7
2	**3 and 4**	Neoph	Me	H	H	53 (**3**)	47 (**4**)	**3**: -82.5 **4**: -76.4
3	**5 and 6**	Neoph	Ph	H	H	67 (**5**)	33 (**6**)	**5**: -77.2 **6**: -77.6
4	**7 and 8**	Neoph	H	Me	H	34 (**7**)	66 (**8**)	**7**: -84.2 **8**: -82.4
5	**9 and 10**	Neoph	H	H	Ph	40 (**9**)	60 (**10**)	**9**: -79.1 **10**: -82.0
6	**11 and 12**	Neoph	H	Me	Ph	24 (**11**)	76 (**12**)	**11**: -77.7 **12**: -79.3
7	**13 and 14**	Neoph	Me	Me	H	12 (**13**)	88 (**14**)	**13**: -82.5 **14**: -73.4

[a] 2% $(PPh_3)_2PdCl_2$ in dry THF; alkyne/hydride ratio = 1.
[b] In $CDCl_3$; in ppm with respect to Me_4Sn.

In all cases, these reactions led in less than 2 hours to mixtures of adducts accounting for two posible regioisomers from a *syn* attack. Yields were good to excellent (60-90%), and in all cases isomers were separated successfully. The structures of the new organostannic compounds were determined by spectral characteristics (^{1}H-, ^{13}C- and ^{119}Sn-NMR).

The stereochemistry of stannylated allylic alcohols was assigned taking into account ^{n}J coupling constants (^{119}Sn, ^{1}H) and ^{n}J (^{119}Sn, ^{13}C).

Usually, results obtained in palladium-catalyzed hydrostannations can be rationalized considering a *syn* addition. Additions to propargylic alcohols can show two cases: I- When the α–position of the alcohol is not substituted, and in turn, may contain a substituent in γ–position (Fig. 2).

II- When the α–position of the alcohol contains one or more substituents, and in turn, can have another substituent at γ–position (Fig. 3).

In the first case, when the CH_2OH group does not contain substituents, but may have a substituent in γ–position (Fig. 2) the reaction would lead to the intermediate **A** complex, thus obtaining the *proximal* stannylated derivative as main isomer. Predominance of α–adducts accounting for regioisomers **1**, **3** and **5** is shown in Table 1 (entries 1-3).

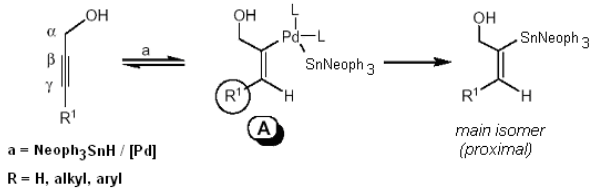


Figure 2

In the second case (Fig. 3) due to steric effects in the intermediate **B**, palladium with its ligands adopts the *distal* position to minimize interaction with substituent R_2. Therefore, the *distal* allylic alcohol is preferably obtained as main isomer even though alkyne function contains another substituent (R_1). Main adducts **8**, **10**, **12** and **14** account for β– regioisomers as can be observed in Table 1 (entries 4-7).

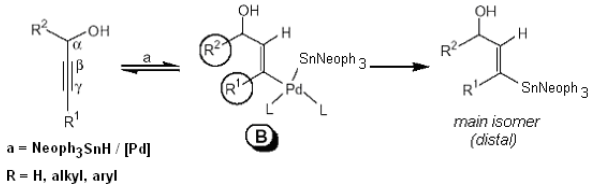


Figure 3

Conclusions

Results show that the addition of trineofyltin hydride catalyzed by $(PPh_3)_2PdCl_2$ to the examined propargylic alcohols takes place stereoselectively, leading in all cases to products of a *syn* attack.

Stannylated allylic alcohols were obtained in very good average yields, achieving in all cases regioisomer separation. Studies carried out so far suggest that α/β regioselectivity observed in the

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hydrostannation of substituted propargylic alcohols is more influenced by the steric volume of proximal substituents than electronic effects.

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