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Regio- and Stereoselective Synthesis of (*E*)-2-Methyl-1-Alkenyltrimethylstannanes from 1-Alkynes

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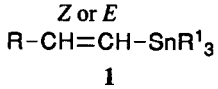
Abstract: Several procedures, which are based on the zirconium-catalyzed methylalumination of 1-alkynes (**5**), have been tested for the regio- and stereoselective synthesis of (*E*)-2-methyl-1-alkenyltrimethylstannanes (**4**). The best one among these procedures as regards simplicity and mildness is that based on the water-accelerated methylalumination of compounds **5**, followed by treatment with a THF solution of Me_3SnCl. This procedure allows the preparation of (*E*)-2-aryl-2-methylethenyltrimethylstannanes, (*E*)-2-benzyl-2-methylethenyltrimethylstannanes and (*E*)-2-(1-cycloalkenyl)-2-methylethenyltrimethylstannanes in quite high yields. On the other hand, (*E*)-2-alkyl-2-methylethenyltrimethylstannanes having high regio- and stereoisomeric purities have been effectively and conveniently synthetized by a reaction sequence involving the zirconium-catalyzed methylalumination of compounds **5** according to a standard protocol and the conversion of the alkenyldimethylalanes (**7**) so obtained into the corresponding methylalanates (**10**), followed by treatment with a THF solution of Me_3SnCl.

Stereodefined 2-substituted ethenylstannanes of general formula **1** are intermediates widely used in organic synthesis[1]. They serve as stable stereochemically defined 1-alkenyl units that may be used for carbon-carbon bond forming reactions via Pd[2], Li[3], and Cu[4] chemistry.



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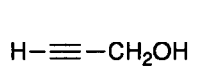
Several methods for the preparation of compounds **1** have been developed[5-18]. On the contrary, much less attention has been paid to the synthesis of stereodefined 2-substituted 1-alkenylstannanes. In fact, to the best of our knowledge, only one general method for the preparation of these compounds has been reported[12], which involves the reaction between 1-alkynes and $Bu_3SnMgCH_3$, in the presence of CuCN, followed by treatment with electrophiles. However, this method, which has been used to prepare an (*E*)-2-methyl-1-alkenylstannane[12], is quite complicated and in our hands afforded 2-substituted 1-alkenylstannanes contaminated by not negligble amounts of undesired isomers. Moreover, it must be mentioned that crude (*Z*)-3-*t*-butyldimethylsilyloxy-2-methyl-1-propenyl-trimethylstannane (**3b**) has been recently synthesized by a

long reaction sequence involving the conversion of propargyl alcohol (**2**) into (*Z*)-1-iodo-3-*t*-butyldimethylsilyloxy-2-methyl-1-propene (**3a**) and treatment of this iodide with 2 equiv of butyllithium in THF at -78°C, followed by reaction with an Et_2O solution of 2 equiv of Me_3SnCl[19].

As a consequence of several ongoing synthetic projects in our laboratory, we had need for a simple synthetic method which permitted the preparation of gram quantities of (*E*)-2-methyl-1-alkenyltrimethylstannanes of general formula **4** having very high stereo- and regioisomeric purities, where R is an alkyl, aryl, benzyl, 1-cycloalkenyl or a functionalized alkyl group. In this paper we describe new simple entries into these compounds, which are based on the zirconium-catalyzed carboalumination of 1-alkynes[20].



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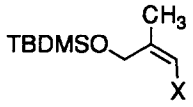
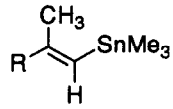


3a: X = I
3b: X = $SnMe_3$



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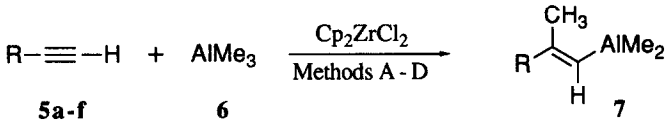
RESULTS AND DISCUSSION

At least in principle, compounds **4** could be synthetized by methylcupration of 1-alkynes (**5**), followed by treatment of the (*E*)-2-methyl-1-alkenylcopper species so obtained with an HMPA solution of chlorotributylstannane. However, we take into account that lithium dimethylcuprate is not able to transfer a methyl group to 1-alkynes to give the corresponding (*E*)-2-methyl-1-alkenylcopper derivatives[21] and that similar organometallic species could be only obtained either by reaction with a very large excess of the homocuprate $(CH_3)_2CuMgCl{\cdot}LiBr$ with 1-alkynes[21], or by a very slow reaction between the complex $CH_3Cu{\cdot}Me_2S{\cdot}MgBr_2$ and 1-alkynes in a mixture of Et_2O and Me_2S at -25 °C[22]. Therefore, because of the shortcomings of these two procedures, we preferred to develop a different synthetic method for compounds **4**, which was based on the methylalumination of compounds **5** with trimethylalane (**6**), in the presence of zirconocene dichloride[20,23] [eq. (1)].



5a-f **6** **7**

(1)

a: R = *n*-C_4H_9 **d**: R = $TBDMSO(CH_2)_3$
b: R = *n*-C_6H_{13} **e**: R = 1-cyclohexenyl
c: R = Ph **f**: R = 4-F-$C_6H_4CH_2$

The 1-alkynes used in this study were: 1-hexyne (**5a**), 1-octyne (**5b**), phenylacetylene (**5c**), 5-*t*-butyldimethylsilyloxy-1-pentyne (**5d**), 1-ethynylcyclohexene (**5e**) and 3-(4-fluorophenyl)-1-propyne (**5f**).

Four different procedures (methods A - D) were employed to convert compounds **5** into the

corresponding (*E*)-2-methyl-1-alkenyldimethylalanes (**7**) (Table 1). Methods A, B and C, which were used for the preparation of compounds **7a**, **7d** and **7a-e**, respectively, involved the methylalumination of the corresponding 1-alkynes by the procedure described by Negishi[20b-d, 23] and differred from one another in the 1-alkyne/zirconocene dichloride/$AlMe_3$ molar ratio. In fact, this was 1.0 : 1.0 : 2.0, 1.0 : 0.51 : 2.0 and 1.0 : 0.32 : 2.78 for the methods A, B and C, respectively. On the other hand, method D, which was employed for the preparation of compounds **7b**, **7c**, **7e** and **7f**, involved the methylalumination of the corresponding 1-alkynes in the presence of water[24] (entries 8 - 11, Table 1). In particular, to a 2 M hexane solution of 3.1 equiv of Me_3Al and 0.22 equiv of Cp_2ZrCl_2 in CH_2Cl_2 cooled to -23 °C were slowly added 1.55 equiv of water. After stirring for 10 min at -23 °C, a CH_2Cl_2 solution of 1.0 equiv of compound **5** was added and the mixture was further stirred . The acceleration by water of the carboalumination of compounds **5b**, **5c**, **5e** and **5f** was impressive. In fact, compounds **7b**, **7e** and **7f** were obtained in quantitative yields after 0.5 h at -23 °C and also compound **7c**, which had been obtained in 95.5 % yield after 161 h using method C, was obtained in quantitative yield after 4.5 h. Moreover, the regioisomeric purities of these alanes were comparable or higher than those obtained using the standard protocols (methods A - C).

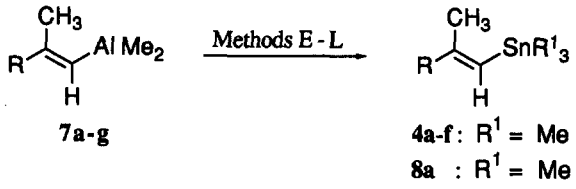
Table 1. Zirconium-catalyzed methylalumination of 1-alkynes (**5**)

Entry	1-Alkyne		Method [a]	Reaction time / Temperature	Product	Yield	Regioisom. purity
	5	R		(h / °C)	**7**	(%) [b]	(%)
1	**5a**	*n*-C_4H_9	A	21/20	**7a**	100	96
2	**5a**	*n*-C_4H_9	C	22/20	**7a**	100	96
3	**5d**	TBDMSO$(CH_2)_3$	B	7/20	**7d**	97	93
4	**5b**	*n*-C_6H_{13}	C	16/20	**7b**	100	96
5	**5c**	C_6H_5	C	161/20	**7c**	96	96
6	**5d**	TBDMSO$(CH_2)_3$	C	41/20	**7d**	98	94
7	**5e**	1-cyclohexenyl	C	40/20	**7e**	98	96
8	**5b**	*n*-C_6H_{13}	D	0.5/-23	**7b**	100	97
9	**5c**	C_6H_5	D	4.5/-23	**7c**	100	98
10	**5e**	1-cyclohexenyl	D	0.5/-23	**7e**	100	97
11	**5f**	4-F-$C_6H_4CH_2$	D	0.5/-23	**7f**	100	98

[a] Method A: 1.0 equiv of **5**, 1.0 equiv of Cp_2ZrCl_2 and 2.0 Equiv of Me_3Al in $ClCH_2CH_2Cl$ at room temperature; Method B: 1.0 equiv of **5**, 0.51 equiv of Cp_2ZrCl_2 and 2.0 equiv of Me_3Al in $ClCH_2CH_2Cl$ at room temperature; Method C: 1.0 equiv of **5**, 0.32 equiv of Cp_2ZrCl_2 and 2.78 equiv of Me_3Al in CH_2Cl_2 at room temperature (for details, see: Experimental); Method D: 1.0 equiv of **5**, 0.22 equiv of Cp_2ZrCl_2, 3.1 equiv of Me_3Al and 1.55 equiv of H_2O in CH_2Cl_2 at -23 °C (for details, see: Experimental). [b] Evaluated by GLC of the protolysis products.

Several procedures (methods F - L) were then tested to convert organoalanes **7a-f** so prepared into the

corresponding (*E*)-2-methyl-1-alkenyltrimethylstannanes **4a-f** [eq. (2)].



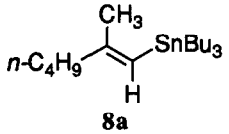
7a-g

4a-f: R^1 = Me
8a : R^1 = Me

(2)

The results obtained using these different protocols as well as that obtained in an attempt to prepare (*E*)-2-methyl-1-hexenyltributylstannane (**8a**) from the corresponding organoalane **7a** are summarized in Table 2.

A preliminary experiment involving (*E*)-2-methyl-1-octenyldimethylalane (**7d**) was carried out using a protocol similar to that reported for the direct transmetallation of (*E*)-1-alkenyldiisobutylalanes with Me_3SnCl[25] (method E). Thus, the reaction mixture, which derived from the methylalumination of **5d** according to method B, was concentrated *in vacuo* and the residue, which was diluted with toluene, hexane and THF was treated at -23 °C with a THF solution of 3.2 equiv of LiCl and 3.2 equiv of Bu_3SnCl and stirred for 30 h at 20 °C and for 4 h at 50 °C (entry 1, Table 2). However, this reaction did not provide compound **8a**, but gave methyltributylstannane (**9**) in 65 % yield.

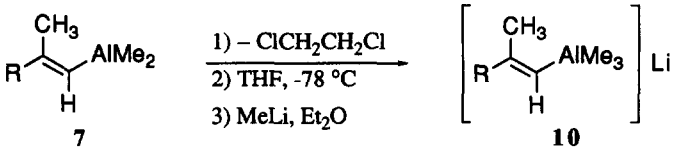


8a

9

A quite unsatisfactory result was also obtained when the reaction mixture, which derived from the zirconium-catalyzed methylalumination of **5b** according to method C, was concentrated *in vacuo*, the residue was cooled to -60 °C, diluted with CH_2Cl_2, treated at -23 °C with 3.0 equiv of Me_3SnCl in THF solution and the mixture was stirred for 21 h at -23 °C, for 23 h at room temperature and for 24 h under reflux (method F). In fact, this reaction gave the desired organostannane **4b** in 28 % GLC yield (entry 2, Table 2).

On the other hand, a significative improvement of the yield of the transmetallation reaction was obtained when alkenylalanes **5** were converted into the corresponding alkenylmethylalanates **10** prior reaction with Me_3SnCl [eq. (3)] (entries 5 - 8, Table 2).



7 **10**

(3)

In fact, when the reaction mixtures, which derived from the carboalumination of **5b, 5c, 5d** and **5e** according to method C, were concentrated *in vacuo*, cooled to -78 °C, diluted with THF and treated with 1.1 equiv of methyllithium in Et_2O and the alanates so obtained were reacted with 2.53 equiv of Me_3SnCl in THF

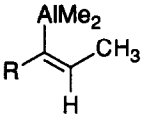
Table 2. Synthesis of (*E*)-2-methyl-1-alkenyltrialkylstannanes **4a-f** and **8a** from the corresponding (*E*)-2-methyl-1-alkenyldimethylalanes **7a-f**

Entry	Alane		Method for the prepn. of **7**	Method for the prepn. of **4** or **8** [a]	Reaction time / Temperature (h / °C)	Product	Yield (%) [b]	Regioisom. purity (%)	Stereoisom. purity (%)
	7	R							
1	**7d**	TBDMSO(CH_2)$_3$	B	E	30/20; 4/50	CH_3SnBu_3 (**9**)	65	—	—
2	**7b**	*n*-C_6H_{13}	C	F	21/-23; 24/20; 24/65	**4b**	28 [c]	91	99
3	**7a**	*n*-C_4H_9	A	H [d]	2/-78 to 0; 15.5/20	**8a** [e]	14	n.d.	n.d.
4	**7a**	*n*-C_4H_9	C	I [f]	0.5/-78; 2/-78 to 20; 63.5/20	**4a** [g]	51	99	99
5	**7b**	*n*-C_6H_{13}	C	G	0.25/-78; 1/-78 to 0; 39/65	**4b**	70	97	97
6	**7c**	C_6H_5	C	G	0.66/-78 to 0; 16/65	**4c**	54	>99	82
7	**7d**	TBDMSO(CH_2)$_3$	C	G	0.5/-78; 0.5/-78 to 20; 23/65	**4d**	61	>95	>95
8	**7e**	1-cyclohexenyl	C	G	2/-30 to 20; 15/65	**4e**	64	100	80
9	**7b**	*n*-C_6H_{13}	C	I [f]	0.5/-78; 21.5/-78 to 0	**4b** [h]	17	98	>99
10	**7b**	*n*-C_6H_{13}	C	I [i]	1/-78; 2/-78 to 0; 125/20; 5/40	**4b**	—	—	—
11	**7b**	*n*-C_6H_{13}	D	L	90.5/-23; 7.5/0; 17/20; 47/0	**4b**	48	95	>99
12	**7c**	C_6H_5	D	L	46/-23 to 0; 75/20; 16/0	**4c**	83	>99	100
13	**7e**	1-cyclohexenyl	D	L	19/-23; 15/20; 53/0	**4e**	57	100	98
14	**7f**	4-F-$C_6H_4CH_2$	D	L	15/-23; 8/20; 22/0	**4f**	74	>99	>99

[a] Chlorotrimethyltin was used as electrophile unless otherwise noted. For the description of methods E - L, see: Experimental. [b] Isolated yields based on the alkyne unless otherwise noted. [c] GLC yield. [d] Reaction carried out using a THF solution of Bu_3SnI. [e] Methyltributylstannane (**9**) was also obtained in 45 % yield. [f] Reaction carried out using a THF solution of Me_3SnI. [g] The crude reaction mixture contained **2a** and 4-iodo-1-butanol (**12**) in *ca.* 5.9 :1 molar ratio, respectively. [h] Compound **4b** was obtained together with iodoalcohol **12**, which was isolated in 17 % yield. [i] Reaction carried out using an Et_2O solution of Me_3SnI.

solution for 15 - 39 h under reflux (method G), compounds **4b**, **4c**, **4d** and **4e** were obtained in 70, 54, 61 and 64 % isolated yields, respectively.

The improvement of the yields was not surprising, since it has been previously reported that the reactivity of alkenylalanes towards electrophiles is enhanced by their conversion into the corresponding alkenylalanates[26]. On the other hand, the fact that compounds **4b**, **4c**, **4d** and **4e** had regioisomeric purities higher than those of the corresponding alkenylalanes **7b**, **7c**, **7d** and **7e**, respectively, could be explained on the basis of the expected higher reactivity of these last compounds in comparison with that of their more hindered regioisomers **11b**, **11c**, **11d** and **11e**, respectively.



11b: R = *n*-C_6H_{13} **11d**: R = TBDMSO$(CH_2)_3$

11c: R = C_6H_5 **11e**: R = 1-cyclohexenyl

I–$(CH_2)_4$OH

12

On the contrary, quite surprising was the fact that, whereas compounds **4b** and **4d** had stereoisomeric purities higher than 95 %, compounds **4c** and **4e** were 82 and 80 % stereoisomerically pure.

We also attempted to improve the yields of method G using iodotrialkylstannanes instead of the corresponding chlorotrialkylstannanes. Nevertheless, the results obtained using this new procedure (method H) were not completely satisfactory. In fact, when a THF solution of alanate **10a** (R = *n*-Bu) was treated at -78 °C with 1.5 equiv of Bu_3SnI in THF solution and the mixture was warmed up to 0 °C for 2.5 h and then stirred at room temperature for 15.5 h, a crude reaction mixture containing methyltributylstannane (**9**), (*E*)-2-methyl-1-hexenyltributylstannane (**8a**) and unreacted Bu_3SnI was obtained. This mixture was then treated with a large excess of a semisaturated aqueous KF solution, filtered, extracted with Et_2O and the organic extract was purified by MPLC on silica gel to give compounds **9** and **8a** in 45 and 14 % isolated yields, respectively (entry 3, Table 2). On the other hand, when alanate **10a** prepared from **5a** according to method C was reacted with a THF solution of 1.67 equiv of Me_3SnI (method I) using reaction conditions similar to those employed for entry 3, a crude reaction mixture containing (*E*)-2-methyl-1-hexenyltrimethylstannane (**4a**) and 4-iodo-1-butanol (**12**) in a *ca.* 5.9 : 1 molar ratio, respectively, was obtained. Purification of this mixture by distillation allowed to isolate compound **4a** in 51 % yield (entry 4, Table 2).

Unfortunately, when a similar procedure involving the use of 2.53 equiv of Me_3SnI was employed for the synthesis of (*E*)-2-methyl-1-octenyltrimethylstannane (**4b**), compounds **4b** and **12** were obtained in quite low yields (entry 9, Table 2).

It must be noted that compound **12** did not derive from a direct reaction between Me_3SnI and THF. In fact, a THF solution of this organostannane proved to be stable when maintained for 56 h at room temperature. However, since compound **12** very probably derived from a ring-opening reaction of THF or a its complex during the reaction which afforded compound **4b**, in the hopes of improving the yield of this last compound and in order to prevent the formation of **12** we carried out the transmetalation between compound **8b** and Me_3SnI in Et_2O solution. Nevertheless, under these reaction conditions compound **10b** was proved to be

unable to react with Me_3SnI also using very long reaction times (entry 10, Table 2).

Finally, we developed a simpler and quite efficient protocol to convert (*E*)-2-methyl-1-alkenyldimethylalanes **7** into the corresponding organostannanes **4** which avoided the transformation of compounds **7** into the corresponding alanates **10** and afforded compounds **4** having regioisomeric purities which ranged from 95.0 to 100 % and stereoisomeric purities which ranged from 98 to 100 %. This protocol (method L) involved treatment of the reaction mixtures, which derived from the carboalumination of the 1-alkynes **5** according to method D, with a THF solution of 2.5 equiv of Me_3SnCl at -23 °C and stirring the resulting reaction mixtures at temperatures which ranged from 0 to 20 °C (entries 11 - 14, Table 2). Purification by MPLC on reversed - phase of the crude reaction products, which were obtained starting from 1-alkynes **5b**, **5c**, **5e** and **5f**, allowed to isolate compounds **4b**, **4c**, **4e** and **4f** in 48, 83, 57 and 74 % yields, respectively.

CONCLUSIONS

In conclusion, various procedures have been tested for the stereoselective synthesis of compounds **4** from the corresponding 1-alkynes **5**. The best one as regards simplicity and mildness as well as the stereoisomeric purities of compounds **4** is that based on the water-accelerated methylalumination of compounds **5**, followed by treatment with a THF solution of Me_3SnCl. Such method is especially well suited for the preparation of (*E*)-2-aryl-2-methylethenyltrimethylstannanes, (*E*)-2-benzyl-2-methylethenyltrimethylstannanes and (*E*)-2-(1-cycloalkenyl)-2-methylethenyltrimethylstannanes. On the other hand, (*E*)-2-alkyl-2-methylethenyltrimethylstannanes can be prepared in quite high yields and high regio- and stereoisomeric purities by a reaction sequence involving the zirconium-catalyzed methylalumination of the corresponding 1-alkynes according to a standard method (method C) and the conversion of the so obtained alkenylalanes into the corresponding methylalanates, followed by treatment with a THF solution of Me_3SnCl.

Applications of these procedures to the synthesis of some bioactive naturally-occurring products will be reported in due course.

EXPERIMENTAL

All boiling points are uncorrected. Precoated silica gel plates Merck F-254 and RP-18 $F_{254}S$ were used for TLC analyses. GLC analyses were performed on a Dani 6500 gas-chromatograph with a PTV injector and equipped with a Dani data station 86.01. Two types of capillary columns were used: a SE-30 bonded FSOT column (30 m × 0.25 mm i.d.) and a AT-35 bonded FSOT column (30 m × 0.25 mm i.d.). Purifications by MPLC were performed on a Büchi instrument, using a Bischoff 8100 differential refractometer as detector. GLC/MS analyses were performed using a Q-mass 910 spectrometer interfaced with a Perkin-Elmer 8500 gas-chromatograph. ^1H NMR spectra were recorded on a Varian Gemini 200 MHz spectrometer using TMS as an internal standard.

All air and water sensitive reactions were performed in flame dried glassware under an atmosphere of

argon or nitrogen. Air and water sensitive solutions were transferred with hypodermic syringes or double ended needles. Solvents were dried and distilled before use.

1-Hexyne (**5a**), 1-octyne (**5b**), phenylacetylene (**5c**), 1-ethynylcyclohexene (**5e**), and zirconocene dichloride were commercially available. 5-*t*-Butyldimethylsilyloxy-1-pentyne (**5d**) [b.p. 83-4 °C/13 Torr; lit[27] b.p. 65 °C/9 Torr] was synthetized in 87 % yield according to the literature[27] starting from commercially available 4-pentyn-1-ol. 3-(4'-Fluorophenyl)-1-propyne (**5f**) [b.p. 52 °C/52 Torr] was synthetized in 68 % overall yield starting from 4-fluorobenzyl chloride according to a general procedure for the synthesis of 3-(hetero)aryl-1-propynes[28]. The physical and spectral properties of this compound were in very good agreement with those previously reported[28].

Procedures for the synthesis of (E)*-2-methyl-1-alkenyldimethylalanes* ***7a-f***

Four different protocols (methods A - D) were used for ther preparation of the title compounds. The results obtained are summarized in Table 1.

Method A. To a stirred suspension of Cp_2ZrCl_2 (5.85 g, 20.0 mmol) in dry 1,2-dichloroethane (47 ml) was added a 2 M hexane solution of Me_3Al (20 ml, 40 mmol) under argon at room temperature. After few minutes a solution of an alkyne **5** (20.0 mmol) in dry 1,2-dichloroethane (30 ml) was added and the reaction mixture was stirred at room temperature for the period of time reported in Table 1. The reaction was periodically monitored by GLC/MS of its samples hydrolyzed with a dilute and cold aqueous HCl solution under argon.

Method B. This method, which was used for the preparation of compound **7d** (entry 3, Table 1), was very similar to method A, but the **5**/Cp_2ZrCl_2/$AlMe_3$ molar ratio was 1 : 0.51 : 2.0 instead of 1.0 : 1.0 : 2.0. Compound **7d**, which was so obtained in 97 % yield after 7 h at 20 °C (as evaluated by GLC/MS analysis of an hydrolyzed sample of the reaction mixture), had 93 % regioisomeric purity.

Method C. This method, which was used for the preparation of compounds **7a**, **7b**, **7c**, **7d**, and **7e**, was very similar to method A, but the **5**/Cp_2ZrCl_2/$AlMe_3$ molar ratio was 1 : 0.32 : 2.78. Moreover, $AlMe_3$ and **5** were sequentially added to a suspension of Cp_2ZrCl_2 in 1,2 dichloroethane maintained at 0 °C. The resulting solution was then stirred at room temperature for the period of time reported in Table 1. The yields and regioisomeric purities of compounds **7a-c** are also reported in this table (entries 4 - 7).

Method D. A 2 M hexane solution of $AlMe_3$ (12.4 ml, 24.8 mmol) was added to a stirred suspension of Cp_2ZrCl_2 (0.51 g, 1.76 mmol) in dry CH_2Cl_2 (30 ml) cooled to 0 °C. The reaction mixture was stirred for 10 minutes and then cooled to -23 °C. Water (0.22 ml, 12.4 mmol) was cautiously added under vigorous stirring. After 10 minutes a solution of the 1-alkyne (8.0 mmol) in dry CH_2Cl_2 (13 ml) was slowly added and the mixture was stirred at -23 °C for the period of time reported in Table 1. Compounds **7b**, **7c**, **7e** and **7f** were so obtained in quantitative yields. They had 97, 98, 97 and 98 % regioisomeric purities, respectively (entries 8 - 11, Table 1).

Procedures for the preparation of (E)-2-methyl-1-alkenyltrialkylstannanes of general formula 4 and 8

Six different protocols (methods E - L) were tested for the preparation of the title compounds.

Method E. This method, which was used in an attempt to prepare (*E*)-5-*t*-butyldimethylsilyloxy-2-methyl-1-pentenyltributylstannane (**8d**) (entry 1, Table 2), involved removal *in vacuo* of the solvent of the reaction mixture obtained in the zirconium-catalyzed methylalumination of 5-*t*-butyldimethylsilyloxy-1-pentyne (**5d**) (4.16 g, 21.0 mmol) according to method B. The residue was diluted with toluene (42 ml), hexane (84 ml) and THF (84 ml) and the resulting mixture was cooled to -23 °C. A solution of Bu_3SnCl (21.59 g, 66.3 mmol) and LiCl (2.81 g, 66.3 mmol) in THF (72 ml) was dropwise added and the mixture was allowed to warm to room temperature and stirred for 30 h at 20 °C and for 4 h at 50 °C. After this period the reaction mixture, which had been periodically monitored by GLC analysis, was quenched into a cold solution of saturated NH_4Cl and extracted with Et_2O. The organic extract was washed with a saturated aqueous NH_4Cl solution, dried, filtered on Celite and concentrated *in vacuo*. The residue was purified by MPLC on silica gel using hexane as eluant to give methyltributylstannane (**9**) (13.16 g, 65 % yield).

Method F. This method was used for the preparation of (*E*)-2-methyl-1-octenyltrimethylstannane (**4b**) (entry 2, Table 2). In particular, the reaction mixture, which was obtained by the zirconium-catalyzed methylalumination of 1-octyne (**5b**) (1.32 g, 12.0 mmol) according to method C, was concentrated *in vacuo* to remove the solvent as well as unreacted Me_3Al. The residue was cooled at -60 °C and then diluted with CH_2Cl_2 (75 ml) and the mixture was warmed up to -23 °C. A solution of Me_3SnCl (7.17 g, 36.0 mmol) in THF (36 ml) was added and the mixture was stirred for 21 h at -23 °C, 24 h at 20 °C and for 24 h under reflux. It was then cooled to room temperature, slowly added to a large excess of a 10 % aqueous NH_4OH solution cooled to -10 °C and extracted with hexane. The organic extract was filtered, washed with a 10 % aqueous NH_4OH solution, dried, filtered and concentrated at reduced pressure. GLC/MS analysis of the residue showed the presence of a new compound, which was subsequently identified as **4b** by comparison with an authentic sample of this substance prepared according to method L. Compound **4b** was obtained in 28 % GLC yield.

Method G. This method was used for the preparation of compounds **4b**, **4c**, **4d** and **4e** (entries 5 - 8, Table 2). Thus, the reaction mixtures, which derived from the zirconium-catalyzed methylalumination of compounds **5b**, **5c**, **5d** and **5e** (23.0 mmol) according to method C, were concentrated *in vacuo* and the residues were cooled to -78 °C, diluted with THF (70 ml) and stirred for 10 minutes. A 1.93 M Et_2O solution of methyllithium (13.1 ml, 25.3 mmol) was dropwise added to the yellow solutions so obtained, which were maintained at 0 °C. The resulting mixtures were stirred for 10 minutes at this temperature, for 3 h at room temperature and then cooled to -78 °C. A solution of Me_3SnCl (11.6 g, 58.2 mmol) in THF (56 ml) was added dropwise and the mixtures were stirred at the temperatures and for the period of time reported in Table 2 (entries 5 - 8). They were then cooled to room temperature and slowly added to a large excess of a 10 % aqueous NH_4OH solution cooled to -10 °C. The mixtures were extracted with hexane and the organic extracts were filtered on Celite, dried, filtered and the filtrates were concentrated *in vacuo*. The residue obtained in the preparation of compound **4b** starting from **5b** was purified by fractional distillation, but those obtained in the

preparations of compounds **4c**, **4d** and **4e** were purified by MPLC on LiChroprep RP-18 (25 - 40 μm) using acetonitrile as eluant. Yields and regio- and stereoisomeric purities of compounds **4b**, **4c**, **4d** and **4e** so obtained are reported in Table 2. The regio- and stereoisomeric purities were evaluated by GLC/MS analysis and were confirmed by ^1H NMR analysis.

Method H. This method was employed for the synthesis of (*E*)-2-mehyl-1-hexenyltributylstannane (**8a**) (entry 3, Table 2). In particular, the reaction mixture, which derived from the methylalumination of **5a** (1.64 g, 20.0 mmol) according to method A, was concentrated *in vacuo* and the residue was cooled to -78 °C and diluted with THF (60 ml). A 1.72 M Et_2O solution of methyllithium (11.6 ml, 20.0 mmol) was dropwise added to the solution so obtained, which was maintained at 0 °C, and the resulting mixture was stirred for 2 h at room temperature and then cooled to -78 °C. A solution of Bu_3SnI (12.51 g, 30.0 mmol) in THF (30 ml) was dropwise added and the mixture was warmed up to 0 °C within 2.5 h and then stirred at room temperature for 15.5 h. After this period the mixture was cooled to 0 °C, cautiously quenched with a large excess of a saturated aqueous NH_4Cl solution and extracted with Et_2O. The organic extract was filtered on Celite, washed with a saturated aqueous $NaHCO_3$ solution and water, dried filtered and concentrated *in vacuo*. The residue, which was analyzed by GLC/MS, was diluted with Et_2O (115 ml) and stirred with a large excess of a semisaturated aqueous KF solution (225 ml) for 2.5 h. The mixture was filtered and extracted with Et_2O and the organic extract was dried and concentrated *in vacuo*. The residue was purified by MPLC on LiChroprep RP-18 (25 - 40 μm), using a mixture of acetonitrile and CH_2Cl_2 (9 : 1 *v/v*) as eluant, to give compound **8a** (1.08 g, 14 % yield).

Method I. This method, which was used for the preparation of compounds **4a** and **4b** (entries 4 and 9, Table 2), was quite similar to method H, but Me_3SnI (1.67 equiv) was used as stannylating agent. In particular, the reaction mixtures, which derived from the methylalumination of compounds **5a** and **5b** (25.0 mmol) according to method C, were concentrated *in vacuo* and the residues were cooled to -78 °C and diluted with THF (75 ml). A 1.89 M Et_2O solution of methyllithium (13.2 ml, 25.0 mmol) was added to the solutions so obtained, which were maintained at 0 °C, and the resulting mixtures were stirred for 3 h at room temperature and then cooled to -78 °C. A solution of Me_3SnI (12.12 g, 41.7 mmol) in THF (40 ml) was dropwise added and the mixtures were stirred at the temperature and for the period of time reported in Table 2. They were then cooled to -30 °C and quenched with methanol (5 ml) and subsequently treated with a solution of saturated NH_4Cl/NH_4OH (9 : 1 *v/v*). The resulting mixtures were extracted with hexane and the organic extracts were washed with water, dried, filtered and concentrated at reduced pressure. GLC/MS analysis of the residues showed that each of them was constituted of the desired organostannane and a compound subsequently identified as 4-iodo-1-butanol (**12**). In particular, the residue obtained in the preparation of compound **4a**, contained compounds **4a** and **12** in a 5.9 : 1 molar ratio, respectively. Compound **12**, which was identified by comparison with an authentic sample of 4-iodo-1-butanol prepared by reaction of commercially available 4-chloro-1-butanol with a molar excess of LiI in acetone solution, was insoluble in crude compounds **4a** and **4b** and therefore it was easily separated from these organostannanes. Compound **12** was obtained in 17 % yield in the preparation of compound **4b**. On the other hand, compounds **4a** (3.33 g, 51 % yield) and **4b** (1.19 g,

17 % yield) having high regio- and stereoisomeric purities, were obtained by fractional distillation of the residues obtained from the corresponding preparations after their purification from compound **12** (entries 4 and 9, Table 2).

It must be noted that in an attempt to prepare compound **4b** by this procedure, but using Et_2O instead of THF as reaction solvent (entry 10, Table 2), we observed that methylaluminate **10b** involved in this preparation was unable to react with Me_3SnI also using very long reaction times.

Method L. This method was used for the preparation of compounds **4b**, **4c**, **4e** and **4f** (entries 11 - 14, Table 2). In particular, the reaction mixtures, which derived from the methylalumination of compounds **5b**, **5c**, **5e** and **5f** (11.0 mmol) according to method D, were maintained under stirring at -23 °C while a solution of Me_3SnCl (5.48 g, 27.5 mmol) in THF (28 ml) was added dropwise. The resulting mixtures were stirred at the temperature and for the period of time reported in Table 2, then cautiously added to a 10 % aqueous NH_4OH solution (100 ml) cooled to -20 °C, and extracted with hexane. The organic extracts were filtered, washed with 10 % aqueous NH_4OH solution, dried, filtered and concentrated at reduced pressure. The residues, which were analyzed by TLC and GLC/MS, were purified by MPLC on LiChroprep RP-18 (25 - 40 μm) using acetonitrile as eluant. Yields, regio- and stereoisomeric purities of compounds **4b**, **4c**, **4e** and **4f** so obtained are reported in Table 2.

Some physical and spectroscopic properties of compounds **4a-f**, **8a** and **9** prepared by these methods are reported below.

*(E)-2-Methyl-1-hexenyltrimethylstannane (**4a**).* B.p. 90 - 91 °C/15 Torr. MS, *m/z* (%): 247 (61), 245 (47), 151 (30), 135 (33), 55 (63), 41 (100). ^1H NMR ($CDCl_3$), δ: 5.45 (1 H, s, $^2J_{Sn-H}$ = 82 Hz, H-1), 2.12 (2 H, t, J = 7.3 Hz, H-3), 1.63 (3 H, s, =C-CH_3), 1.54 - 1.18 (4 H, m, H-4 and H-5), 0.90 (3 H, t, J = 7.1 Hz, H-6), 0.13 ppm (9 H, s, $SnMe_3$). Anal. Calcd. for $C_{10}H_{22}Sn$: C, 46.02 ; H, 8.50. Found: C, 46.58; H, 8.56.

*(E)-2-Methyl-1-octenyltrimethylstannane (**4b**).* B.p. 107 °C/5 Torr. MS, *m/z* (%): 275 (42), 273 (31), 151 (31), 135 (45), 55 (39), 41 (100). ^1H NMR ($CDCl_3$), δ: 5.45 (1 H, s, $^2J_{Sn-H}$ = 82 Hz, H-1), 2.11 (2 H, t, J = 7.3 Hz, H-3), 1.76 (3 H, s, =C-CH_3), 1.52 - 1.15 (8 H, m, H-4, H-5, H-6 and H-7), 0.88 (3 H, t, J = 6.5 Hz, H-8), 0.13 ppm (9 H, s, $SnMe_3$). Anal. Calcd. for $C_{12}H_{26}Sn$: C, 49.87; H, 9.07. Found: C, 49.69; H, 9.21.

*(E)-2-Phenyl-1-propenyltrimethylstannane (**4c**).* MS, *m/z* (%): 267 (100), 265 (81), 227 (32), 197 (37), 135 (35), 117 (22). ^1H NMR ($CDCl_3$), δ: 7.50 -7.10 (5 H, m, C_6H_5), 6.26 (1 H, s, $^2J_{Sn-H}$ = 71 Hz, H-1), 2.22 (3 H, s, H-3), 0.23 ppm (9 H, s, $SnMe_3$). Anal. Calcd. for $C_{12}H_{18}Sn$: C, 51.30; H, 6.46. Found: C, 51.69; H, 6.83.

*(Z)-2-Phenyl-1-propenyltrimethylstannane (**4c**):* MS, *m/z* (%): 267 (92), 266 (94), 265 (72), 117 (26), 115 (41), 39 (100). ^1H NMR ($CDCl_3$), δ: 7.50 - 7.10 (5 H, m, C_6H_5), 5. 89 (1 H, q, J = 1.3 Hz, H-

1), 2.25 (3 H, d, J = 1.3 Hz, =C-CH_3), -0.14 ppm (9 H, s, $SnMe_3$).

(E)-2-Methyl-5-t-butyldimethylsilyloxy-1-pentenyltrimethylstannane (4d). MS, *m/z* (%) : 363 (7), 321 (4), 165 (100), 135 (23), 81 (21), 59 (31). ^1H NMR ($CDCl_3$), δ: 5.48 (1 H, s, $^2J_{Sn-H}$ = 81 Hz, H-1), 3.60 (2 H, t, J = 6.6 Hz, H-5), 2.16 (2 H, t, J = 7.5 Hz, H-3), 1.77 (3 H, s, =C-CH_3), 1.81 - 1.48 (2 H, m, H-4), 0.90 (9 H, s, *t*-Bu), 0.13 (9 H, s, $SnMe_3$), 0.05 ppm (6 H, s $SiMe_2$). Anal. Calcd. for $C_{15}H_{34}OSiSn$: C, 47.76; H, 9.09. Found: C, 47.49; H, 9.39.

(E)-2-(1'-Cyclohexenyl)-1-propenyltrimethylstannane (4e). MS, *m/z* (%): 271 (45), 269 (37), 121 (21), 93 (27), 55 (23), 41 (100). ^1H NMR ($CDCl_3$), δ: 5.97 - 5.87 (1 H, m, H-2'), 5.88 (1 H, s, H-1), 2.29 - 2.10 (4 H, m, H-3' and H-6'), 1.97 (3 H, s, =C-CH_3), 1.75 - 1.48 (4 H, m, H-4' and H-5'), 0.17 ppm (9 H, s, $SnMe_3$). Anal. Calcd. for $C_{12}H_{22}Sn$: C, 50.57; H, 7.78. Found: C, 50.72; H, 8.20.

(E)-2-Methyl-3-(4'-fluorophenyl)-1-propenyltrimethylstannane (4f). MS, *m/z* (%): 299 (72), 297 (55), 165 (41), 149 (100), 135 (75), 109 (87). ^1H NMR ($CDCl_3$): δ: 7.20 - 7.05 (2 H, m, H-2' and H-6'), 7.02 - 6.85 (2 H, m, H-3' and H-5'), 5.49 (1 H, s, H-1), 3.39 (2 H, s, H-3), 1.72 (3 H, s, =C-CH_3), 0.14 ppm (9 H, s, $SnMe_3$). Anal. Calcd. for $C_{13}H_{19}FSn$: C, 49.89; H, 6.12. Found: C, 49.78 ; H, 6.56.

(E)-2-Methyl-1-hexenyltributylstannane (8a). MS, *m/z* (%): 331 (22), 329 (16), 219 (57), 121 (35), 55 (21), 41 (100). ^1H NMR ($CDCl_3$), δ: 5.42 (1 H, br s, $^2J_{Sn-H}$ = 75 Hz, H-1), 2.13 (2 H, t, J = 7.2 Hz, H-3), 1.74 (3 H, s, =C-CH_3), 1.60 - 1.15 (16 H, m, H-4, H-5, H-2' and H-3'), 0.98 - 0.70 ppm (18 H, m, H-6, H-1' and H-4'). Anal. Calcd. for $C_{19}H_{40}Sn$: C, 58.93; H, 10.41. Found:C, 59.12; H, 10.78.

Methyltributylstannane (9): B.p. 120 °C/10 Torr. MS, *m/z* (%): 291 (1), 269 (54), 213 (33), 155 (41), 57 (42), 41 (100). ^1H NMR ($CDCl_3$), δ: 1.67 - 1.17 (12 H, m, H-2' and H-3'), 0.98 - 0.62 (15 H, m, H-1' and H-4'), -0.03 ppm (3 H, s, CH_3). Lit[29] b.p. 122 - 124 °C/12 Torr.

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