Solvent Assisted Addition of Tetraallylic, Tetraallenic and Tetrapropargylic Stannanes to Aldehydes and Acetals

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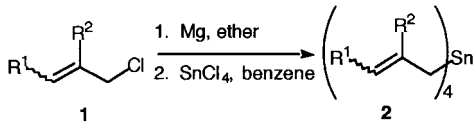
Abstract: Tetraallylic, tetraallenic and tetrapropargylic stannanes (0.25 eq) react with aldehydes in methanol to provide unsaturated alcohols. These reactions proceed exclusively with allylic rearrangement for tetra(2-butenyl)tin **2b** and tetra(1,2-butadienyl)tin **5e** and predominantly with allylic rearrangement for tetrapropadienyltin **5c** and tetra(2-butynyl)tin **6e**. The corresponding TFA catalysed reactions of dimethyl acetals with **5c** and **6e** are highly regioselective with allylic rearrangement.

The allylation of carbonyl groups provide homoallylic alcohols which possess useful functionality for further elaboration.[1] A large number of protocols have been developed which allow this transformation to be achieved with high levels of regio- and stereocontrol.[2] The related propargylation and allenylation of aldehydes has also received considerable attention over the past decade, particularly by Marshall and coworkers.[2a] This group has developed a variety of methods to achieve regio- and stereocontrol which they have employed for the asymmetric synthesis of complex natural products.[3] We recently reported a particularly mild and convenient procedure for the chemoselective allylation of aldehydes and some ketones with commercially available tetraallyltin.[4] The carbonyl compound and stannane (0.25 eq) react quantitatively in methanol at room temperature (aldehydes) or at reflux (ketones) over approximately 4 to 20 h. The resulting homoallyl alcohol can be easily separated from insoluble tin methoxide salts. Unlike the corresponding reactions of allyltrialkylstannanes, this procedure does not require anhydrous conditions, the use of expensive catalysts or chromatography to remove organotin by-products. Acetals are also allylated with this reagent, but require the addition of TFA or SiO_2.[5] This latter procedure is particularly suited to the reaction of unstable amino aldehydes which are more conveniently handled as the corresponding acetals.

We have previously suggested that the methanol promoted allylation of carbonyl compounds might be concerted with the activating influence of the solvent primarily a result of hydrogen bonding to the carbonyl oxygen.[4b] If this is the case, then allylation should be regiospecific with addition of the aldehyde or ketone to the γ- position of the allylic triad. We now report an investigation of the regiochemistry of this reaction and extend it to the analogous propargylation and allenylation reactions.

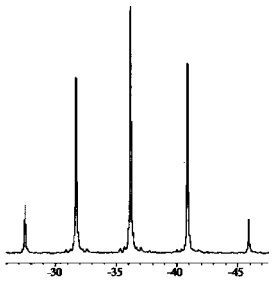
Methyl substituted tetraallylic stannanes **2a** and **2b** were prepared from the corresponding allylic chlorides **1** by a Grignard reaction (Scheme 1).[6] Chloride **1b** (*E : Z* = 90 : 10) yielded a mixture of tetraorganostannanes which isomerised to an almost perfect binomial distribution of the five diastereomers of **2b** on standing (Figure 1).[7] Stereochemical assignments were based on comparisons with the corresponding ^{13}C and ^{119}Sn NMR data for 2-butenyltributylstannane.[8]

Tetrapropargylic and tetraallenic stannanes were prepared from the corresponding propargylic chlorides **3** and bromides **4** by a Grignard reaction in the presence of a catalytic amount of $HgCl_2$ (*ca* 2 mol%) (Scheme 2).[9] Each tetraorganostannane was obtained as a single regioisomer determined by the substitution pattern of starting propargylic halide (Table 1). Thus, propargylic halides **3e** and **4e** with a



a: $R^1 = H, R^2 = CH_3$
b: $R^1 = CH_3, R^2 = H$

Scheme 1

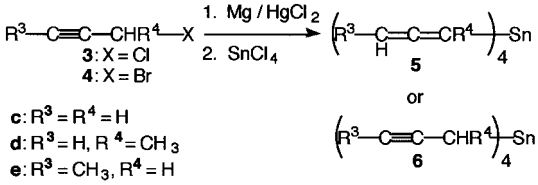


assignments (from L to R):

cis, cis, cis, cis (7.2%)
cis, cis, cis, trans (26.6%)
cis, cis, trans, trans (37.2%)
cis, trans, trans, trans (23.9%)
trans, trans, trans, trans (5.1%)

Figure 1. $^{119}Sn\ \{^1H\}$ NMR spectrum of **2b** in $CDCl_3$

methyl group at the terminal position yielded tetrapropargylic stannane **6e** while the other propargylic halides not substituted at this position provided tetraallenic stannanes **5c** or **5e** exclusively. Propargylic triarylstannanes are reported to isomerise in methanol to the corresponding allenyl isomer depending on the substitution pattern.[10] No isomerisation of **5c**, **5e** or **6e** was observed in methanol after 48 h at room temperature suggesting that the Grignard reaction yields the thermodynamically favoured product in each case.



c: $R^3 = R^4 = H$
d: $R^3 = H, R^4 = CH_3$
e: $R^3 = CH_3, R^4 = H$

Scheme 2

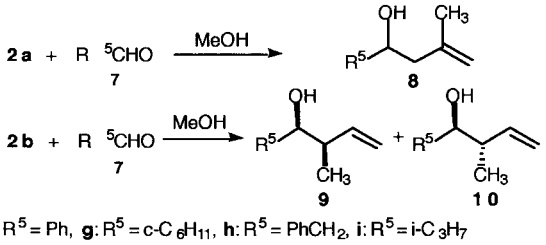
Tetraallylic stannanes **2a** and **2b** (0.25 eq) were reacted with aldehydes in methanol at room temperature (*ca* 25°C) for 24 h (Scheme 3) and provided the corresponding homoallylic alcohols cleanly in 60 - 83% yield after distillation (Table 2). Aldehyde addition to stannane **2b** was highly regioselective proceeding with allylic rearrangement, but with low diastereoselectivity in favour of the *erytho* isomer **9** over the *threo* isomer **10** (d.e. = 0 - 30%).

The corresponding reactions of tetraallenic stannanes **5c** and **5e** and tetrapropargylic stannane **6e** with aldehydes **7** (Scheme 4) in methanol (4 - 24 h, *ca* 30°C) also proceeded cleanly and in good yield (74 - 88%, Table 2). The addition of aldehydes to tetrapropadienyltin **5c** was regioselective in favour of the allylically rearranged homopropargylic alcohols **13**, but contaminated with up to 30% of the isomeric allenyl

Table 1. Synthesis of tetra- allylic, allenic and propargylic stannanes

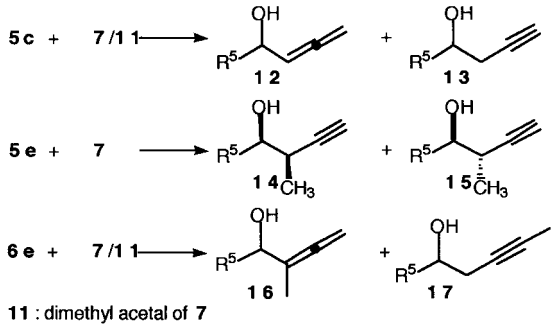
propargyl halide	tetraorganostannane	yield (%)
1a	**2a**	50
1b	**2b**[a]	94
3c	**5c**	61
4c	**5c**	61
3d	**5e**[b]	59
4d	**5e**[b]	63
3e	**6e**	61
4e	**6e**	62

[a]Consists of five diastereomers (Figure 1). [b]Consists of three diastereomers in the ratio 50 : 37 : 13 as determined by ^{119}Sn NMR spectroscopy



Scheme 3

alcohols **12**. Tetra(1,2-butadienyl)tin **5e**, however, reacted exclusively with allylic rearrangement to provide diastereomeric homopropargylic alcohols **14** (*erythro*) and **15** (*threo*) with a predominance of the former (d.e. = 26 - 70%). Tetra(2-butynyl)tin **6e** yielded a mixture of regioisomers favouring the allylically rearranged allenyl alcohols **16** over the homopropargylic alcohols **17**.



Scheme 4

We have also briefly examined the TFA catalysed addition of dimethyl acetals **11** to tetraallenic stannane **5c** and tetrapropargylic stannane **6e**. In all cases the reactions were highly regioselective with **5c** yielding homopropargylic alcohols **13** and **6e** yielding allenic alcohols **16** exclusively. While these results suggest a concerted S_E' process for reactions of both stannanes under these conditions, we have observed that a mixture of **12f** and **13f** (prepared from **5c** and **7f** in methanol) isomerises under the influence of TFA in methanol to yield **13f**. It may be, therefore, that alcohols **13** are the thermodynamic, rather than kinetic, products of the addition of acetals to **5c**.[11]

We have demonstrated that the methanol promoted allylation of aldehydes with tetraallyltin can be extended to substituted tetraallylic stannanes and also to tetraallenic and tetrapropargylic stannanes. These reactions proceed exclusively with allylic rearrangement for tetra(2-butenyl)tin **2b** and tetra(1,2-butadienyl)tin **5e** and predominantly with allylic rearrangement for tetrapropadienyltin **5c** and tetra(2-butynyl)tin **6e**. This outcome is consistent with our proposition of a concerted,

Table 2. Reactions of tetra- allylic, allenic and propargylic stannanes with aldehydes and acetals

stannane	aldehyde / acetal	reaction conditions	products	product ratio[a]	yield (%)
2a	**7f**	MeOH, 24 h	**8f**	--	68
2a	**7g**	MeOH, 24 h	**8g**	--	76
2a	**7h**	MeOH, 24 h	**8h**	--	60
2b	**7f**	MeOH, 24 h	**9f : 10f**	50 : 50	83
2b	**7g**	MeOH, 24 h	**9g : 10g**	65 : 35	67
2b	**7h**	MeOH, 24 h	**9h : 10h**	56 : 44	71
5c	**7f**	MeOH, 4 h	**12f : 13f**	25 : 75	79
5c	**7g**	MeOH, 20 h	**12g : 13g**	30 : 70	78
5c	**7h**	MeOH, 14 h	**12h : 13h**	27 : 73	79
5c	**7i**	MeOH, 24 h	**12i : 13i**	30 : 70	77
5c	**11f**	TFA, 16 h	**12f : 13f**	0 : 100	74
5c	**11h**	TFA, 16 h	**12h : 13h**	0 : 100	78
5e	**7f**	MeOH, 24 h	**14f : 15f**	63 : 37	84
5e	**7g**	MeOH, 24 h	**14g : 15g**	85 : 15	88
5e	**7h**	MeOH, 24 h	**14h : 15h**	74 : 26	80
6e	**7f**	MeOH, 6 h	**16f : 17f**	83 : 17	87
6e	**7g**	MeOH, 20 h	**16g : 17g**	90 : 10	85
6e	**7h**	MeOH, 14 h	**16h : 17h**	94 : 6	77
6e	**11f**	TFA, 16 h	**16f : 17f**	100 : 0	81
6e	**11h**	TFA, 16 h	**16h : 17h**	100 : 0	79

[a] Determined by ^{1}H and ^{13}C NMR spectroscopy

eight-membered transition state involving methanol coordination to tin and hydrogen bonding to the carbonyl oxygen,[4b] although the small loss of regiospecificity for reactions of **5c** and **6e** suggest the possible intervention of some other mechanism(s) also. The modest *erythro* stereoselectivity observed for reactions of **2b** and **5e** is not surprising given that both substrates are mixtures of diastereomers and that each transfer of an organic group from tin generates a different reactive species.

The benefits of these solvent promoted organometallic reactions are the simplicity of the method (both to conduct and for product isolation), the relatively mild conditions under which they are performed and the productive use of all four organic groups on the metal. While lacking the stereo- and, in some cases, regiocontrol available with more elaborate protocols they constitute, we believe, a convenient class of carbon-carbon bond forming reactions which should have applications in synthesis.

Typical Experimental Procedure for Methanol Promoted Allylation, Allenylation and Propargylation of Aldehydes:

***erythro and threo* 3-methyl-1-phenyl-4-pentyn-2-ol 14h and 15h** Phenylacetaldehyde (**7h**, 0.48 g, 4.0 mmol) and tetra(1,2-butadienyl)tin (**5e**, 0.33 g, 1.0 mmol) were dissolved in methanol (5 mL) and stirred at room temperature (*ca* 25 ^{o} C) for 24 h. Water (10 mL) was then added and the resulting white precipitate allowed to settle. The solvent was decanted and the solid washed with CH_2Cl_2. The aqueous methanol was then extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic extracts dried (Na_2SO_4), concentrated *in vacuo* and kugelrohr distilled (oven temp 120 ^{o}C, 2 mm Hg) to provide a mixture of the diastereomeric alcohols **14h** and **15h** (0.57 g, 80%) as a clear oil. Anal. $C_{12}H_{14}O$. Found C = 82.31 %, H = 8.04 %. Calc. C = 82.72 %, H = 8.10 %. ^{1}H NMR (200 MHz, $CDCl_3$) **14h**: δ 1.28 (3H, d, J = 7.0 Hz), 2.10 (1H, s), 2.22 (1H, d, J = 2.6 Hz), 2.61 (1H, m), 2.92 (2H, dd, J = 5.7 Hz, 4.2 Hz), 3.73 (1H, m), 7.25 - 7.34 (5H, m); **15h**: δ 1.30 (3H, d, J = 6.9 Hz), 2.07 (1H, s), 2.61 (1H, m), 2.92 (2H, dd, 5.7 Hz, 4.2 Hz), 3.73 (H, m), 7.25 - 7.34 (5H, m). ^{13}C NMR (50 MHz, $CDCl_3$) **14h**: δ 17.44, 31.68, 41.69, 71.45, 75.17, 84.99, 126.58, 128.62, 128.88, 129.45,

129.14, 138.33; **15h**: δ 16.47, 32.22, 40.58, 70.77, 75.17, 86.31, 126.58, 127.73, 128.41, 129.07, 129.58, 140.19.

Typical Experimental Procedure for TFA Promoted Allenylation and Propargylation of Aldehydes:

To a solution of benzaldehyde dimethylacetal **11f** (152 mg, 1.0 mmol) in methanol (5 mL) was added tetrapropadienyltin **5c** (70 mg, 0.25 mmol) in methanol (5 ml) followed by the dropwise addition of TFA (125 mg, 1.1 mmol). The reaction was stirred at room temperature for 16 h, poured onto water (50 mL) and extracted with CH_2Cl_2 (3 x 25 mL), the organic extracts were dried ($MgSO_4$), condensed and eluted through a short bed of silica with ethyl acetate / hexane (1 : 1) to provide **13f** (108 mg, 74%) as a clear oil. The ^{1}H NMR spectrum was identical to that previously reported.[12] ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.42, 72.07, 72.38, 80.05, 125.87, 127.72, 128.54, 142.97.

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