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Reactivity of (*E*)-1-(*tert*-Butyldimethyl)silyloxy-3,3-bis(tributylstannyl)-Propene : *Syn* Selective S_E' Addition to Aldehydes

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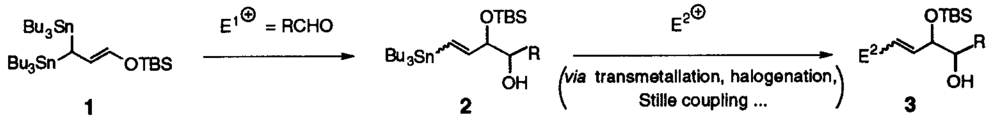
Abstract : The reactivity of (*E*)-1-(*tert*-butyldimethyl)silyloxy-3,3-bis(tributylstannyl)propene **1** as potential 1,3 dianion equivalent has been investigated. Condensation with aldehydes **4a-h**, in presence of $BF_3{\cdot}OEt_2$, afforded in high yields the mono-protected diols **5a-h** exhibiting an exclusive *E* configuration of the vinyltin residue. Good to high *syn* selectivities have been measured, in agreement with an S_E' addition mechanism. Further transformation of the resulting vinyltin moiety of these diols into various functionalities has been successfully tested. © 1997 Elsevier Science Ltd.

In the preceding paper [1] is described a synthesis of the new gem-distannyl derivative **1** which can be claimed to exhibit interesting synthetic potentialities, especially in the field of (di)enediynes antitumor agents.[2] In a first set of reactions, this 1-silyloxy-3,3-bis(tributylstannyl)propene can be expected to behave as a classical allyl mono-tin silyl enol ether to give, when added to carbonyl reagents, the corresponding dihydroxyvinylstannanes **2** (Scheme 1).[3] Interestingly for synthetic purposes, the latter vinylstannanes are likely to be utilized in a great number of transformations widely used in the synthesis of complex natural compounds.[4]



Scheme 1

According to precedents from the well studied chemistry of analogous allylic substrates bearing a single tin residue, [5] allyl bis-stannanes such as **1** can be expected to exhibit, under Lewis acid conditions, high reactivities towards aldehydes which might lead to mono-protected diols **2** according to a *syn* selective S_E' mechanism.[6] More recent investigations showed that 1,1-hetero-Sn,Si- or 1,1-homo-Si,Si-alk-2-enes derivatives led, in presence of $BF_3{\cdot}Et_2O$, to similar *syn* selective S_E' condensation reactions with different electrophiles including several aldehydes.[7] However, to date, nothing is known about the reactivity of **1** when subjected to Lewis acid-promoted condensations and this paper deals with the results of the preliminary investigations on the reactivity of **1** with aldehydes as well as further transformations of the resulting adducts **2** in view of synthetic applications.

(*E*)-1-(*tert*-Butyldimethyl)silyloxy-3,3-bis(tributylstannyl)propene **1** has been condensed on different aldehydes **4a-h** in presence of $BF_3{\cdot}OEt_2$ in dichloromethane and the results are summarised on the Table. In all reported cases, a solution of **1** (1.0 eq) in CH_2Cl_2 was added at -78°C to a premixed solution containing the required aldehyde **4a-h** (1.1 eq) and $BF_3{\cdot}OEt_2$ (1.1 eq). After completion of the addition of **1** to the reaction mixture, 3.0 supplementary equivalents of. $BF_3{\cdot}OEt_2$ were added. After complete disparition of the starting material, the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$ to give after

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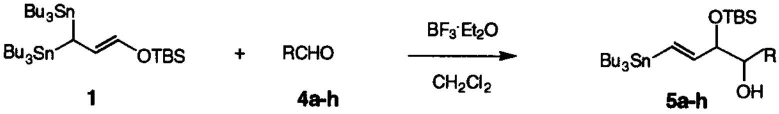
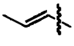
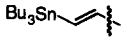
subsequent flash-chromatography, the mono-protected 1,2-diols **5a-h** in 81-100% yields.[8] The additional 3 equivalents of Lewis acid are essential for the efficiency of the reaction; otherwise, the condensation revealed sluggish and upon longer reaction times, notable amounts of hydrodestannylated derivatives were isolated.

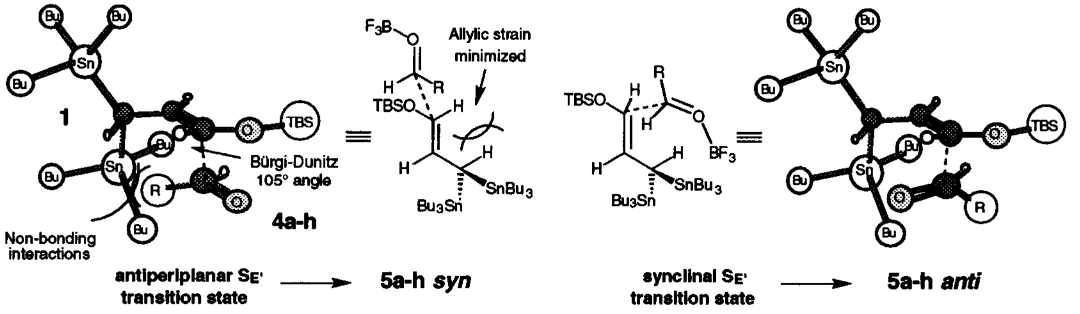


	Aldehyde, R =	Product	Yield (%)	Diastereomeric ratio *syn/anti* (%)*
4a	Et	**5a**	quant.	87:13
4b	^{i}Pr	**5b**	quant.	> 95:5
4c	C_6H_{11}	**5c**	95%	93:7
4d	Ph	**5d**	96%	95:5
4e		**5e**	90%	90:10
4f	 Bu3Sn	**5f**	97%	88:12
4g	^{n}Bu—≡—	**5g**	96%	75:25
4h	TMS—≡—	**5h**	97%	66:33

* determined by ^{1}H NMR

Table

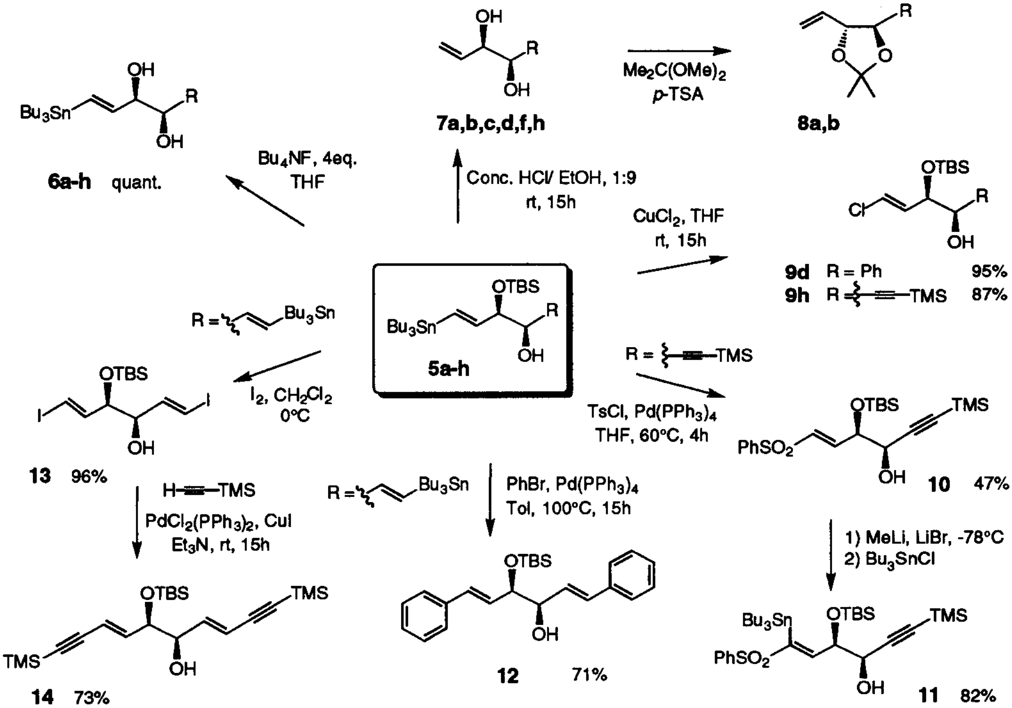
All the yields obtained throughout these assays are good to excellent. In all cases, as already observed in the case of 1,1-hetero-Sn,Si ou 1,1-homo-Si,Si by M. Lautens *et al*, [5] the configuration of the double bond is *E* with no trace of the *Z* isomer, in agreement with the $S_{E'}$ antiperiplanar transition state depicted on Scheme 2. Although synclinal dispositions leading to *syn* adducts cannot be excluded,[9] the depicted disposition, which is in agreement with previous hypotheses for the crotyl mono-tin analogues of **1**,[10] minimises 1,3-allylic strain.



Scheme 2

The *syn/anti* diastereomeric ratio of isomers ranges from 66:33/75:25 in the case of the sterically less demanding diols **5h** or **5g** respectively up to 95:5 in the case of the most encumbered isobutyraldehyde **5b**. These ratios are significantly lower than those obtained in the case of the corresponding γ-silyloxy crotyl mono-stannanes by Marshall *et al.*[5a] Modeling the approach of the reactants according to an antiperiplanar $S_{E'}$ transition state show that steric repulsions may exist between the axially disposed non-reacting tin residue of **1** and the R group of aldehydes. These steric biases can partially counterbalance the OTBS repulsion which is claimed to favor the formation of the *syn* mono-protected diol. Release of these interactions can be accomplished, at least partly, when the depicted synclinal $S_{E'}$ transition state is developed, leading to *anti* isomers of **5a-h**.

For the unambiguous assignment of the *syn* stereochemistry, a series of transformations was carried out on most of the diols in order to correlate their NMR data with those of thoroughly described compounds as shown on Scheme 3 (all the transformations have been carried out on the purified syn/anti mixtures of diastereomers obtained in the ratios described on the Table). Aliphatic mono-protected diols **5a,b** have been transformed into acetonides **8a,b** *via* diols **7a,b**.[11] ^{1}H NMR data for *syn* diol **7d** obtained after HCl/EtOH treatment of **5d** were in full agreement with the literature.[12] *Syn* configuration assignment of **7c** obtained after acidic treatment of **5c** has been deduced from comparison with ^{1}H NMR data reported for the corresponding *anti* isomer.[13] The bis-vinyltin derivative **5f**, when treated with HCl/EtOH, cleanly gave the known *syn* hexa-1,5-diene-3,4-diol **7f**.[14] The acetylenic mono-protected diol **5h** has been converted under the same acidic conditions into the *syn* trimethylsilylacetylenic diol **7h** which exhibits ^{1}H NMR signals identical with those of its known desilylated analogue.[15] The major *syn* relative configuration of the other products has been tentatively deduced from the above ones.



Scheme 3

Another set of reactions has been carried out to investigate the synthetic potentialities of these mono-protected diols. Chlorination of **5d** and **5h** took place smoothly to give, in presence of $CuCl_2$, the chloroalcohols **9d** and **9h** in high yield.[16] According to a published procedure,[17] vinylstannane **5h** has been transformed, in 47% yield, into the vinylic sulfone **10** which could be efficiently metalled to give the Z vinyltin derivative **11** without isomerization of the double bond.[18] Perhaps more interestingly, the symmetrically disposed bis-vinyltin mono-protected diols **5f** were submitted to two types of cross-coupling reactions. A Stille coupling reaction between **5f** and iodobenzene cleanly gave the expected bis-styryl derivative **12** in 71% yield after purification.[19] On another hand, a Sonogashira coupling reaction [20] was carried out on the bis-iodovinyl derivative **13** (prepared in high yield from **5f** through tin-iodine exchange)[21] to give the bis-enyne **14** in 73% yield.

initial allylation step gave the *syn* adducts **5a-h** in high-yield with exclusive formation of the 1,3-addition products exhibiting the *E* configuration of the vinyltin double bond. We are currently applying these results in the field of neocarzinostatin.

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8. All new compounds have been fully characterized by ^{1}H NMR, ^{13}C NMR, IR, mass spectrometry and combustion analysis All $^3J_{H\text{-}H}$ vinylic coupling constants range from 19.0 to 19.5 Hz. Typical protacol for preparation of (*E*)-1,6-bis-(tributylstannyl)-4-(*tert*-butyldimethyl)silyloxy-1,5-butadiene-3-ol **5f**. To a solution of (*E*)-3-(tributylstannyl)-2-propenal **4f** (1.01 g, 2.94 mmol, 1.10 eq) in dichloromethane (20 mL) at -78°C was added dropwise $BF_3.OEt_2$ (370 µL, 2.94 mmol, 1.10 eq). The mixture was stirred for 5 min and successively added at -78°C with a solution of 1-(*tert*-butyldimethyl)silyloxy-3,3-bis(tributylstannyl)propene 1 (2.00 g, 2.67 mmol) in dichloromethane (30 mL) then $BF_3.OEt_2$ (990 µL, 8.0 mmol, 3.0 eq). The reaction mixture was stirred for 15 min at -78°C and quenched at this temperature by addition of 30 mL of a satured aqueous $NaHCO_3$ solution. The resulting mixture was allowed to warm at room temperature and, after decantantion, the aqueous layer was extracted with 3x50 mL diethyl ether. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by silica gel flash-chromatography (diethyl ether/petoleum ether 95:5) to give 2.09 g of **5f** (97% yield, *E/Z* = 88:12). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) : 6.27 (d, 1H, *J* = 19.1 Hz), 6.19 (d, 1H, *J* = 19.1 Hz), 6.01 (dd, 1H, *J* = 19.1, 4.4 Hz), 5.96 (dd, 1H, *J* = 19.1, 5.8 Hz), 3.93 (m, 2H), 2.60 (d, 1H, *J* = 4.4 Hz), 1.48 (m, 12H), 1.30 (m, 12H), 0.90 (m, 39H), 0.09 (s, 3H), 0.06 (s, 3H). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ (ppm) : 148.0 (CH), 147.1 (CH, $J_{Sn\text{-}C}$ = 39 Hz), 131.2 (CH, $J_{Sn\text{-}C}$ = 41 Hz)), 129.6 (CH), 80.4 (CH, $J_{Sn\text{-}C}$ = 64 Hz), 77.8 (CH, $J_{Sn\text{-}C}$ = 43 Hz), 29.2 (CH_2, $J_{Sn\text{-}C}$ = 19 Hz), 27.4 (CH_2, $J_{Sn\text{-}C}$ = 54 Hz), 26 (CH_3), 18.3 (C), 13.8(CH_3), 9.6 (CH_2, $J_{^{117}Sn\text{-}C}$ = 329 Hz, $J_{^{119}Sn\text{-}C}$ = 343 Hz), -3.9 (CH_3), -4.7 (CH_3). MS (CI, NH_3) : *m/z* = 791 (M^++1-18), 777, 749, 675, 617, 443, 405, 347, 291, 235, 57. IR (Film), cm^{-1} : 3568, 2955, 2926, 2869, 2854, 1602, 1463, 1376, 1251, 1080, 991, 863, 778. Anal. Calcd for $C_{36}H_{76}O_2SiSn_2$, 806.45, C : 53.62, H : 9.50. Found : C : 53.74, H : 9.51.
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