Communication

Remote stereocontrol using (E)-6-hydroxy-4-methylhex-2-enyl(tri-n-butyl)stannane

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Abstract

Reactions of (E)-6-hydroxy-4-methylhex-2-enyl(tributyl)stannane (**11**) with aldehydes, when promoted by tin(IV) bromide, proceed with effective 1,5-stereocontrol to give (Z)-1,5-*anti*-5-methylhept-3-ene-1,7-diols (**23**), suitable precursors for the stereoselective synthesis of eight-membered lactones.
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1. Introduction

Allylstannanes with heteroatom functionality at the 4-, 5- and 6-positions are transmetallated stereoselectively by tin(IV) halides to give allyltin trihalides which react with aldehydes with useful levels of 1,5-, 1,6- and 1,7-stereocontrol [1]. In particular, the 5-benzyloxy-4-methylpent-2-enylstannane (**1**) and the 6-hydroxy-5-methylhex-2-enylstannane (**3**) are transmetalled by tin(IV) chloride or bromide and by tin(IV) bromide, respectively, to give intermediates which react with aldehydes to give products **2** and **4** with effective 1,5- and 1,6-*anti*-(Z)-stereocontrol [2,3]. However, in anticipation of a proposed natural product synthesis, it was necessary to establish the stereoselectivity of the analogous reactions of the 6-hydroxy-4-methylhex-2-enylstannane (**11**), a regioisomer of stannane **3**, and the results of this investigation are outlined in this paper.
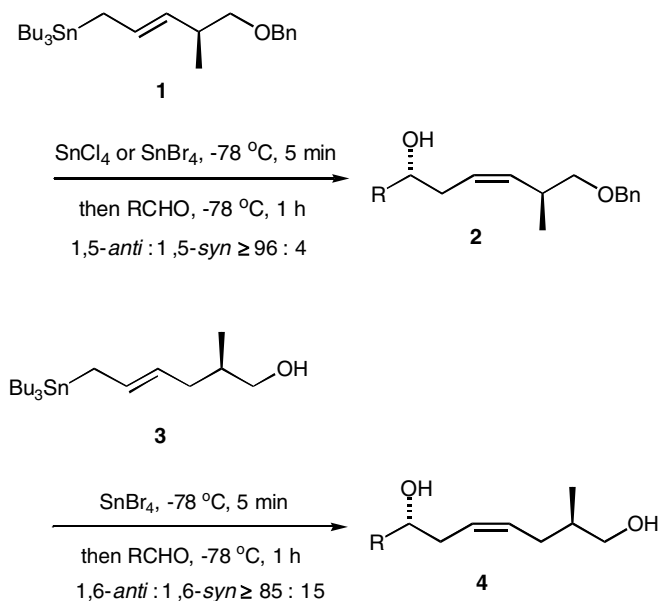
2. Results and discussion

The stannane **11** was synthesised as outlined in Scheme 1. *O*-silylation of racemic citronellol **5** gave the *tert*-butyl-

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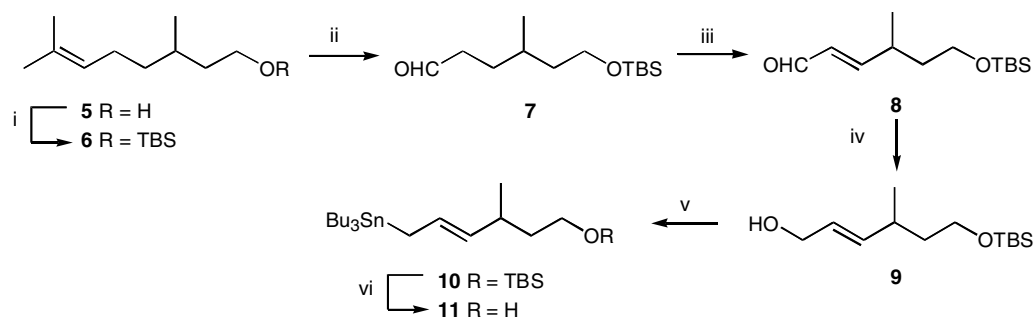
Scheme 1. *Reagents and conditions:* i, TBSCl, imid., CH$_2$Cl$_2$, 0 °C to r.t., 16 h (90%); ii, O$_3$, CH$_2$Cl$_2$, −78 °C, then PPh$_3$ (71%); iii, Pd(OAc)$_2$, allyl diethyl phosphate, NaHCO$_3$, THF, reflux, 72 h (90%); iv, DIBAL-H, THF, −78 to −45 °C (84%); v, (a) MsCl, Et$_3$N, CH$_2$Cl$_2$, −7 °C to r.t.; (b) Bu$_3$SnLi, THF, −78 °C to r.t. (52%); vi, TBAF, THF, r.t. (80%).

dimethylsilyl ether **6** which was ozonolysed to give the aldehyde **7**. Palladium catalysed dehydrogenation using palladium(II) acetate and allyl diethyl phosphate [4] gave the α,β-unsaturated aldehyde **8** which was reduced to the alcohol **9** using DIBAL-H. Conversion of the alcohol into the stannane **11** was then carried out via mesylation and in situ displacement of the mesylate by tributyltin lithium to give the stannane **10** which was deprotected to give the required 6-hydroxy-4-methylhex-2-enylstannane (**11**).

Treatment of the stannane **11** with tin(IV) bromide at −78 °C followed by addition of benzaldehyde gave the (3Z)-1,5-*anti*-hept-3-ene-1,7-diol **12** with excellent stereoselectivity, 1,5-*anti* (**12**):1,5-*syn* (**13**) ⩾99:1 (65% yield), with no (E)-isomer **14** being isolated, see Scheme 2. The use of tin(IV) chloride was slightly less satisfactory since the 1,5-*anti*:1,5-*syn* ratio was ca. 95:5 (40% yield) and approximately 5% of the (E)-isomer **14** was also obtained. With indium(III) chloride the (E)-isomer **14** was the major prod-
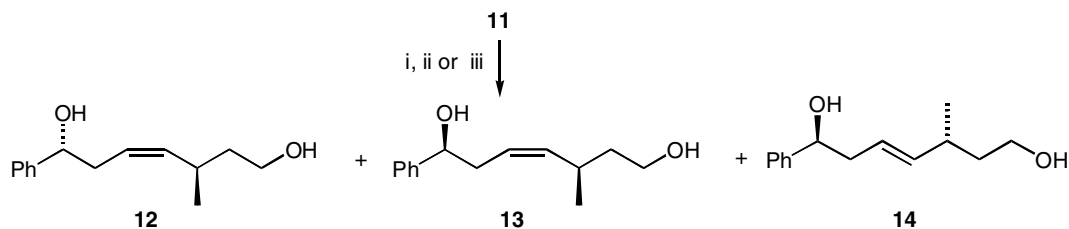
Scheme 2. *Reagents and conditions:* i, SnBr$_4$, −78 °C, 5 min then PhCHO, −78 °C, 45 min (65%; **12**: **13** ⩾99:1); ii, SnCl$_4$, −78 °C, 5 min then PhCHO, −78 °C, 45 min (**12/13**, 40%; **12:13** = 95:5; **14**, 5%); iii, InCl$_3$, PhCHO, CH$_2$Cl$_2$, MeCN, r.t. 45 min (65%, **14:12** = 60:40).
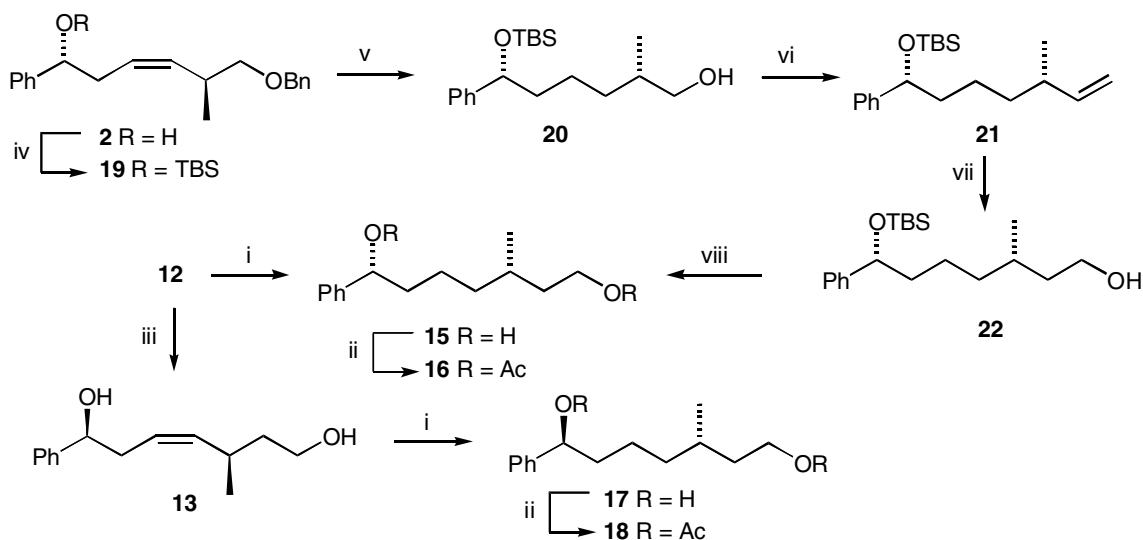
Scheme 3. *Reagents and conditions:* i, TsNHNH$_2$, Et$_2$O then NaOAc, H$_2$O, reflux (**15**; 72%: **17**, 68%); ii, AcCl, py., DMAP, CH$_2$Cl$_2$, r.t. (**16, 18** both ca. 100%); iii, (a) TBSCl, imid., CH$_2$Cl$_2$, r.t.; (b) EtO$_2$CN=NCO$_2$Et, PPh$_3$, p-O$_2$NC$_6$H$_4$CO$_2$H; (c) NaOH, MeOH, r.t., 1 h; (d) TBAF, THF, r.t., 2 h (48% from **12**); iv, TBSCl, imid., CH$_2$Cl$_2$, 1 h, r.t. (83%); v, H$_2$, 10% Pd/C, MeOH, r.t., 1 h (62%); vi, (a) Dess Martin periodinane, NaHCO$_3$, CH$_2$Cl$_2$, r.t., 1 h; (b) Ph$_3$PMeBr, ^{t}BuOK, THF, r.t., 18 h (82%); vii, BH$_3$·THF, r.t., 18 h, then H$_2$O$_2$/NaOH (85%); viii, TBAF, THF, r.t., 1 h (85%).

uct, although the stereoselectivity was only modest [ca. 60:40 in favour of the (E)-heptenediol **14**], and with bismuth(III) iodide at room temperature, a complex mixture of products was obtained [5].

The 1,5-*anti*-stereochemistry was assigned to the major product **12** by correlation with known compounds, see Scheme 3. Reduction using diimide gave the heptanediol **15** which was converted into its diacetate **16**, and selective protection of the diol **12**, followed by a Mitsunobu inversion [6], saponification and deprotection gave the 1,5-*syn*-diastereoisomer **13**. The 1,5-*anti*- and 1,5-*syn*-diastereoisomers **12** and **13** were distinguishable by NMR, the *syn*-isomer **13** corresponding to the minor product from the tin(IV) bromide promoted reactions of the stannane **11** with benzaldehyde. Diimide reduction of the 1,5-*syn*-isomer **13** gave diol **17** which was converted into the diacetate **18**. The diols **15** and **17** and the diacetates **16** and **18** were distinguishable by NMR and their configurations were established as shown by comparison with authentic samples of the diol **15** and diacetate **16** prepared from the 1,5-*anti*-product **2** (R = Ph) [1,2]. Protection of the secondary alcohol **2** (R = Ph) as its silyl ether **19**, hydrogenation and hydrogenolysis gave the primary alcohol **20**. This was taken through to the alkene **21** by oxidation and a Wittig condensation, and hydroboration/oxidation gave the homologated alcohol **22**. Deprotection and acetylation then gave the diol **15** and diacetate **16** which were identical to samples prepared from the major product isolated from the tin(IV) halide promoted reactions between benzaldehyde and stannane **11**. The (Z)-double-bond geometry in **12** was established by ^{1}H NMR ($J_{3,4} = 10.5$ Hz).

The tin(IV) bromide promoted reactions of the stannane **11** with several aldehydes were then investigated, see Table 1. In all cases they proceeded with useful stereoselectivity in favour of the 1,5-*anti*-products **23**.

The stereoselectivity of these reactions is consistent with stereoselective transmetallation of the allylstannane **11** to give the allyltin tribromide **25** in which the methyl and vinyl substituents are *trans*-disposed, i.e. pseudo-equatorial, with respect to the six-membered ring formed by coordination of the electron deficient tin by the hydroxyl group. Subsequent reaction with the aldehyde then generates a second intermediate which reacts via the six-membered, chair-like, transition structure **26** in which the group next to tin is in the axial position [7], to give the (Z)-1,5-*anti*-product **23**.
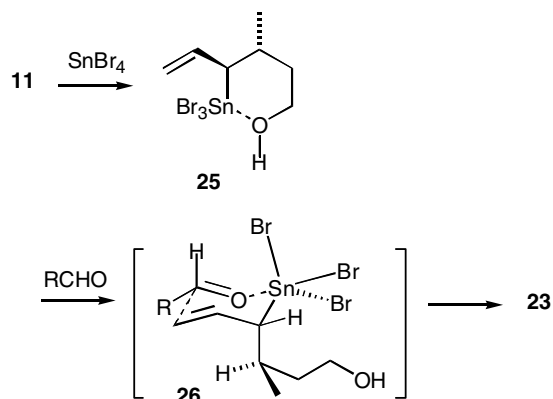

Finally, further aspects of the chemistry of the (Z)-1,5-*anti*-diol **12** were investigated. This was converted into the mono-silyl ether **27** by bis-silylation followed by selective deprotection of the primary hydroxyl group, see Scheme 4. Oxidation into the carboxylic acid **28** was carried out via the aldehyde and desilylation gave the hydroxy-acid **29**. Lactonisation was then accomplished using the modified Yamaguchi procedure [10] to give the unsaturated eight-membered ring lactone **30** which was isolated essentially as a single diastereoisomer.

To summarise, in this work, the remote *anti*-stereocontrol observed for the allylstannanes **1** and **3** has been shown to apply to the new stannane **11** which was transmetallated by tin(IV) bromide with good stereocontrol to generate the allyltin tribromide **25** which reacted stereoselectively with aldehydes to give the (Z)-1,5-*anti*-hept-3-ene-1,7-diols (**12**)

Table 1
Tin(IV) bromide promoted reactions of stannane **11** with aldehydes

R	Yield (%)	1,5-*anti*-**23**:1,5-*syn*-**24**
Ph	65	99:1
Me$_2$CH	63	91:9
nPr	67	96:4
(E-MeCH=CH)	76	97:3
p-MeOC$_6$H$_4$	61	99:1
p-O$_2$NC$_6$H$_4$	62	99:1
p-ClC$_6$H$_4$	74	98:2
m-ClC$_6$H$_4$	64	99:1
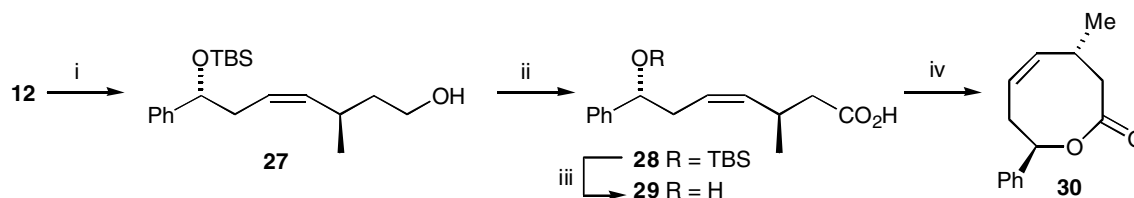
Scheme 4. *Reagents and conditions:* i, (a) TBSCl, imid., DMAP, CH$_2$Cl$_2$, r.t., 18 h (83%); (b) HF, py., THF, r.t., 18 h (72%); ii, (a) Dess Martin periodinane, CH$_2$Cl$_2$, r.t., 1 h; (b) NaClO$_2$, 2-methylbut-2-ene, NaH$_2$PO$_4$, ^{t}BuOH, H$_2$O, r.t., 2 h (76%); iii, HCl, MeOH, r.t., 2 h (80%); iv, 2,4,6-trichlorobenzoyl chloride, Et$_3$N, THF, r.t., 2 h, then DMAP, toluene, reflux, 4.5 h (60%).

and (**23**) with useful overall 1,5-stereocontrol [11]. Applications of this chemistry to the stereoselective synthesis of natural products will be investigated.

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[11] Representative experimental for the tin(IV) bromide promoted reactions of stannane **1** with aldehydes: tin(IV) bromide (110 mg, 0.19 mmol) in dichloromethane (1 cm^3), cooled to −78 °C, was added to a solution of stannane **11** (100 mg, 0.19 mmol) in dichloromethane (1 cm^3) at −78 °C. The resulting solution was stirred for 5 min then benzaldehyde (0.07 cm^3, 0.57 mmol) in dichloromethane (0.5 cm^3) was added. The solution was stirred at −78 °C for 45 min then methanolic ammonium chloride was added and the mixture allowed to warm to room temperature. The aqueous phase was extracted with dichloromethane and the combined organic extracts washed with brine, dried and concentrated under reduced pressure. Flash column chromatography of the residue using light petroleum:diethyl ether:triethylamine (19:80:1) as eluent gave the (*Z*)-1,5-*anti*-5-methylhept-3-ene-1,7-diol **12** (**23**, R = Ph) (36 mg, 65%) (Found: [M + NH$_4$]$^+$, 238.1806. C$_{14}$H$_{24}$NO$_2$ requires *M*, 238.1802); ν_{max}/cm^{-1} 3349, 1453, 1050, 739; δ_H (CDCl$_3$, 300 MHz): 0.96 (3H, d, *J* = 7 Hz, 5-CH$_3$), 1.36 (1H, m, 6-H), 1.70 (1H, m, 6-H), 2.36 (1H, m, 5-H), 2.76 (2H, m, 2-H$_2$), 3.05 (2H, bs, 2 × OH), 3.65 (2H, m, 7-H$_2$), 4.74 (1H, dd, *J* = 3.5, 5.5 Hz, 1-H), 5.35 (1H, t, *J* = 10.5 Hz, 4-H), 5.51 (1H, m, 3-H) and 7.36 (5H, m, ArH); δ_C (CDCl$_3$, 75 MHz): 21.9, 28.6, 38.1, 40.0, 60.9, 74.2, 125.2, 125.9, 127.8, 128.7, 138.7, 144.9; *m/z* (CI) 238 ([M$^+$ + 18], 100%), and 220 ([M$^+$], 80).