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Chemoselectivity in the Chromium(II)-Mediated Synthesis of *E*-Alkenylstannanes from Aldehydes and $Bu_3SnCHBr_2$

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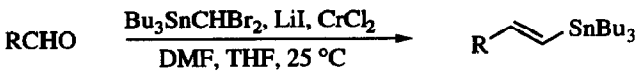
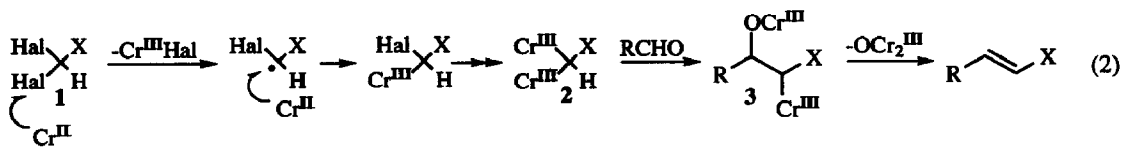
Abstract: *The synthesis of functionalised E-alkenylstannanes from aldehydes and a mixture of $Bu_3SnCHBr_2$, LiI and $CrCl_2$ is described.*

We recently reported a direct method for the preparation of *E*-alkenylstannanes from simple aldehydes using $Bu_3SnCHBr_2$ and $CrCl_2$ (Eq. 1).[1]



(1)

By analogy with the chromium(II)-mediated reduction of other substituted *gem*-dihalides **1** (Eq. 2, X = Hal, alkyl, $SiMe_3$, SPh, $SnBu_3$),[2] the reaction is believed to proceed *via* two successive halogen atom transfers[3] to $CrCl_2$ where the intermediate radicals are immediately reduced to give ultimately a *gem*-dichromium species **2** which adds to the aldehyde to give **3**. β-Elimination from **3** then occurs to provide predominantly or exclusively the *E*-alkene.



(2)

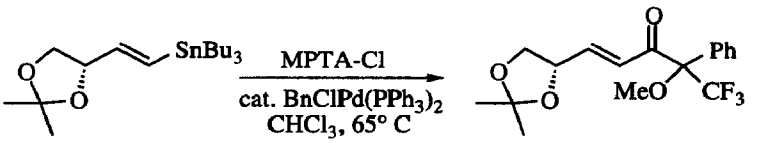
Here we communicate our results concerning the chemoselectivity of the process shown in Eq. 1, since this will be one of the major factors determining the utility of the reaction in synthesis. In particular, knowledge of compatibility with functional groups that are also tolerated when using alkenylstannanes in Pd-catalysed cross-coupling reactions[4] and higher-order cyanocuprate-based transmetallation sequences[5] will be of value. The susceptibility of an α-chiral aldehyde to epimerisation during the reaction is also examined.

Ester, cyano and ketal groups are unaffected during alkenylstannane formation (Table 1, entries 1, 2 and 5). A keto-aldehyde gave mainly the homologated stannyl enone (entry 3), and a small amount (10%) of the alkenylstannane with the ketone also methylenated. Thus, although cyclododecanone is partially methylenated under the reaction conditions in Eq. 1 (45%, 73% based on recovered ketone),[1] a ketone is reasonably well tolerated in a competitive reaction with an aldehyde.

Table 1. Synthesis of Functionalised *E*-Alkenylstannanes

Entry	Aldehyde[6]	Alkenylstannane[7]	Yield,[8] %	Alkene[9]	Yield,[8] %
1.	$MeO_2C(CH_2)_4CHO$	$MeO_2C(CH_2)_4$ SnBu$_3$	61	$MeO_2C(CH_2)_4$	34
2.	$NC(CH_2)_6CHO$	$NC(CH_2)_6$ SnBu$_3$	58	$NC(CH_2)_6$	41
3.	$MeCO(CH_2)_{10}CHO$	$MeCO(CH_2)_{10}$ SnBu$_3$	53	$MeCO(CH_2)_{10}$	36
4.	CHO	SnBu$_3$	58	—	
5.	CHO	SnBu$_3$	63	—	

1,2-Attack on an α,β-unsaturated aldehyde (entry 4) indicates that the reaction provides a simple route to 1-tributylstannyl dienes, however in this case a mixture of geometrical isomers (83:17, *E*:*Z*) was obtained. The e.e. of the stannane derived from *R*-glyceraldehyde acetonide (entry 5) was determined to be ≥ 95% by Pd-catalysed cross-coupling with both racemic and *S*-Mosher's acid chlorides and inspection of the ^{1}H nmr alkenyl regions of the resulting enones (Eq. 3).[10]

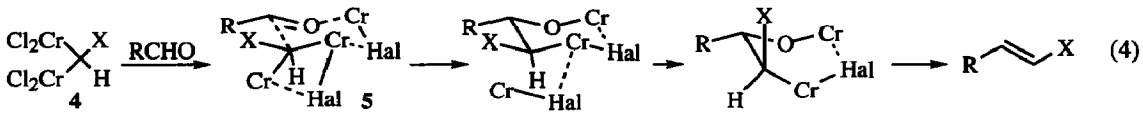


(3)

In entries 1-3, the non-volatile alkenes[9] resulting from methylenation of the aldehyde were also detected and easily separated chromatographically from the *E*-alkenylstannanes. Shortened reaction times (1-2 h instead of 24 h), or buffered work-up conditions, did not significantly alter the *E*-alkenylstannane:alkene ratio, whereas addition of I_2 just prior to work-up gave, in the case of nonanal,[1] 1-iodo-1-decene[11] (49%) exclusively as the *E*-isomer. Therefore, it is possible that the alkene forms competitively alongside the *E*-alkenylstannane.

We suggest a general mechanism to explain the preference for *E*-geometry in the chromium(II)-mediated homologation of aldehydes to alkenes (Eq. 2). This mechanism is based on our results, the importance of bridging halide ions in chromium chemistry,[12] the fact that deoxygenations of both *E*- and *Z*-2-butene epoxides with chromium complexes gave the same *E*:*Z* ratio of 2-butene (~55:45)[13] and that treatment of 1,1-diiodo-2-tridecanol with $CrCl_2$ produced a 1:1 mixture of *E*- and *Z*-1-iodo-1-tridecenes.[14] These last three observations suggest that *E*-alkene formation is not inherently favoured in the β-elimination step (Eq. 2), but must be dependant on the relative *vic*-stereochemistry in **3**. That is, the carbon-chromium linkage in **3** is sufficiently stable to maintain stereochemical integrity until stereospecific β-elimination occurs.[13]

Our mechanism (Eq. 4, other ligands on chromium omitted for clarity, X = Hal, alkyl, $SiMe_3$, SPh, $SnBu_3$) involves stereoselective addition of a substituted *gem*-dichromium reagent **4** to an aldehyde followed by a stereospecific elimination step, which is likely to be a *syn* process.[13] The minor *Z*-alkene, or methylenated by-product when X = $SnBu_3$, then arises from a less favourable transition state **5** (X and H interchanged) which, when X = $SnBu_3$, generally prefers to eliminate by a tin Peterson-type process[15] and generate an *E*-alkenyl chromium (which abstracts a H-atom from the solvent), rather than form the more hindered *Z*-alkenylstannane.



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7. Selected data - for entry 5: R_f 0.30 [3% ether/light petroleum (b.p. 40-60 °C)]; $[\alpha]_D^{20}$ +39.0 (*c* 1.25 in benzene); found: $(M\text{-Bu})^+$, 361.1189, $C_{15}H_{29}O^{120}Sn$ requires 361.11896); ν_{max}(neat)/cm^{-1} 2958s, 2927s, 2871s and 2854s; δ_H(400 MHz; $CDCl_3$; $SiMe_4$; *J*/Hz) 6.23 (1 H, dd, *J* 19 and 1, $J_{^{119}Sn\text{-}H}$ 66, $J_{^{117}Sn\text{-}H}$ 63, =CHSn), 5.89 (1 H, dd, *J* 19 and 7, $J_{^{119}Sn\text{-}H}$ 60, $J_{^{117}Sn\text{-}H}$ 57, C*H*=CHSn), 4.40 (1 H, m, C*H*CH=), 4.03 (1 H, dd, *J* 8 and 6, H of OCH_2), 3.53 (1 H, t, *J* 8, H of OCH_2), 1.49-1.10 [18 H, m, 3 x CH_2CH_2Me, incl. at 1.37 (3 H, s, Me) and 1.32 (3 H, s, Me)], 0.91-0.76 [15 H, m, $Sn(CH_2)_3$, incl. at 0.88 (9 H, t, *J* 7, 3 x Me)]; δ_C(100 MHz; $CDCl_3$, *J*/Hz) 145.2 (HC=), 133.2 ($J_{^{119}Sn\text{-}C}$ 360, $J_{^{117}Sn\text{-}C}$ 343, =CSn), 109.2 (Me_2C), 80.0 ($J_{Sn\text{-}C}$ 66, *C*HCH=), 69.3 (OCH_2), 29.0 ($J_{Sn\text{-}C}$ 20, $Sn(CH_2CH_2)_3$), 27.2 ($J_{Sn\text{-}C}$ 55, 3 x CH_2Me), 26.7 (Me), 25.9 (Me), 13.7 (3 x Me) and 9.4 ($J_{^{119}Sn\text{-}C}$ 348, $J_{^{117}Sn\text{-}C}$ 331, $Sn(CH_2)_3$); *m/z* (EI) 361 (75%), 308 (50), 291 (100) and 247 (20).
8. Isolated total yields of chromatographically homogeneous, spectroscopically pure products.
9. Assigned by comparison with: Nakatani, M.; Fukunaga, Y.; Haraguchi, H.; Taniguchi, M.; Hase, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3535-3539 (entry 1). Giese, B.; Kretzschmar, G. *Chem. Ber.* **1984**, *117*, 3160-3164 (entry 2). Cottier, L.; Descotes, G. *Bull. Chim. Soc. Fr.* **1972**, 1072-1076 (entry 3).
10. Whilst the cross-coupling yields are modest (35% and 49% respectively), racemic Mosher's acid chloride gave a 1:1 diastereomeric mixture of enones which indicated that during the reactions there was no preference for the formation (or destruction) of a particular diastereomer.
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