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Convenient Preparation of α–Trimethylsilyloxy- and α–Hydroxystannanes from Aldehydes

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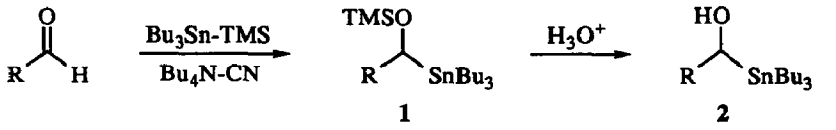
Abstract: Aldehydes, but not ketones, are converted to α–hydroxystannanes via the corresponding silyl ethers in good to excellent yields by Bu_4NCN catalyzed addition of $Bu_3SnSiMe_3$ and hydrolytic isolation. Modest asymmetric induction was observed using a chiral quaternary ammonium cyanide catalyst.

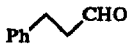
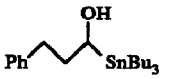
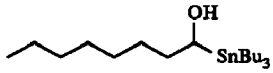
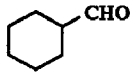
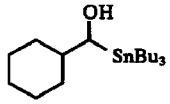
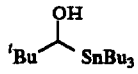
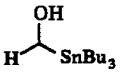
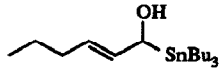
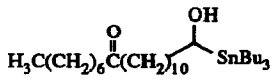
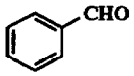
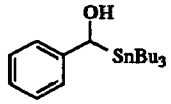
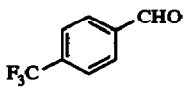
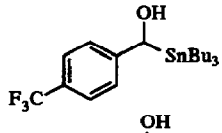
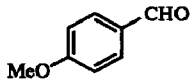
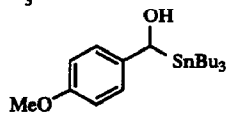
α–Alkoxystannanes have found numerous synthetic applications, *inter alia*, in the generation of configurationally stable α–alkoxyorganolithium and copper reagents,[1] as precursors to chiral tetraalkylstannanes and secondary alcohols,[2] and in Lewis acid induced S_E' aldol condensations.[3] Recently, we[4] and others[5] have exploited α–alkoxystannanes in stereospecific Stille-type cross-couplings mediated by transition metals. The parent α–hydroxystannanes **2** are most commonly prepared by addition of stoichiometric lithium or magnesium stannyl anions to carbonyls[6] or by hydride reduction of labile acyl stannanes.[3,7] However, since the aforementioned preparative methodology is not always compatible with base sensitive or polyfunctional substrates, we report herein a mild and convenient synthesis of **2** from aldehydes via the intermediate TMS ether **1** (eq 1).



1 **2** (eq 1)

The results obtained with representative aldehydes are summarized in Table 1 and serve to define the scope of the transformation. Under the influence of tetrabutylammonium cyanide (3 mole %), simple aliphatic aldehydes (entries 1 and 2) reacted smoothly with commercial $Bu_3SnSiMe_3$[8] (1.5 equiv) in THF at ambient temperature in 2-3 h. Quenching with saturated NH_4Cl solution, extractive isolation and SiO_2 chromatographic purification afforded **2** and its silylated counterpart **1** in good to excellent combined yield.[9] Alternatively, **2** could be obtained as the sole product in comparable yields by *in situ* hydrolytic desilylation with dilute acid during work-up. Stannylations in other solvents, e.g., benzene, dichloromethane, acetonitrile, and N,N-dimethylformamide, were characterized by poor conversions. Likewise, reactions catalyzed by Lewis acids [BF_3•Et_2O, $ZnCl_2$, $Ti(iPrO)_4$] were uniformly unsatisfactory as were additions mediated by Bu_4NF, KCN/18-crown-6, $P(NMe_2)_3$, Et_3N, and Me_3SiCN. Replacement of $Bu_3SnSiMe_3$ by $Bu_3SnSiMe_2{}^tBu$ resulted in a very sluggish reaction even under forcing conditions and gave low yields of adduct.

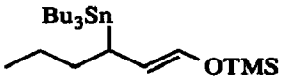
Table 1. Preparation of α-Alkoxystannanes from Aldehydes.

Entry	Aldehyde	Ratio 1 / 2	Adduct	Rxn Cond Solvent/Temp,°C/Time,h	Isolated Yield(%)
1		3 : 1		THF / 23 / 3	82
2		3 : 1		THF / 23 / 2	80
3		>50 : 1		THF / -20 / 1	68
4	^{t}Bu– CHO	>50 : 1		THF / -78 / 5	71
5	–(HCHO)$_n$–	1 : >50		THF / 23 / 48	80[a]
6		>50 : 1		THF / -78 / 0.3	20
7		>50 : 1		THF / -20 / 1	74
8		4.6 : 1		PhH / 10 / 0.6	85
9		1 : >50		PhH / 23 / 24	15
10		>50 : 1		PhH / 10 / 0.75	98

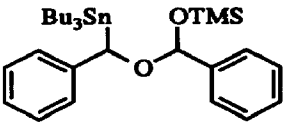
[a]Isolated and characterized as the acetate (Ac_2O, DMAP, Et_3N, CH_2Cl_2, 23°C, 4 h).

Branched aldehydes such as cyclohexanecarboxaldehyde (entry 3) and pivalaldehyde (entry 4) were also well behaved, but in contrast to the preceding examples, gave rise exclusively to α–silyloxystannane 1; subsequent hydrolysis led quantitatively to the corresponding α–hydroxy adduct 2. The simplest aldehyde, introduced into the reaction as paraformaldehyde (entry 5), on the other hand, required 48 h for complete reaction and evolved 2 only. Yields for α,ß-unsaturated aldehydes (entry 6)

were modest, due primarily to competitive 1,4- addition.[8] This produced silyl enol ethers of type **3** which in some instances, e.g., in benzene at 10°C, became the major product (61%). Significantly, cyclic and acyclic ketones were refractory under all conditions. The exploitation of this differential reactivity for the selective functionalization of aldehydes was cogently illustrated in entry 7.

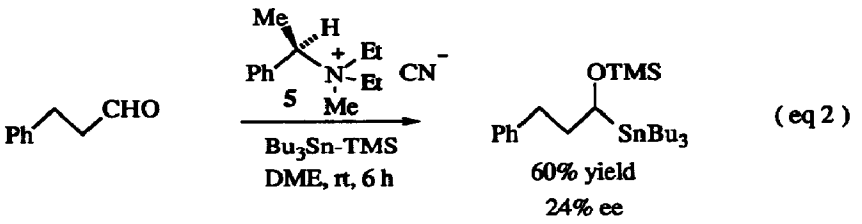


3



4

Additions to aromatic aldehydes showed a unique solvent dependency. For instance, benzaldehyde reacted rapidly in THF at 0°C, but the combined yield of **1** and **2** was relatively low (40-50%) compared with that in benzene (85%, entry 8). In THF at -78°C, there was a shift in the mode of attack; **1** was isolated in 50% yield along with 40% of the "mixed dimer" **4**. A comparison of benzaldehydes with opposite inductive effects (entry 9 vs. 10) revealed the carbonyl carbon experiences an electron deficiency during the rate limiting step which is ameliorated by electron donating substituents.



(eq 2)

Chiral induction was demonstrated using ammonium cyanide salt **5**, prepared from R-(+)-N-methyl-α–phenethylamine,[10] following the general procedure (*vide infra*) using dimethoxyethane as solvent (eq 2). ^{1}H NMR analysis of the adduct, following conversion to the Mosher ester [R-(+)-MTPA, DCC, DMAP, CH_2Cl_2, 23°C], indicated the stannylation achieved 22% ee. Improvements to this modification and their application to natural products total synthesis are under active investigation.

General Procedure: To a solution of aldehyde (2 mmol) and $Bu_3SnSiMe_3$ (3 mmol) in THF or benzene (4 ml) was added a solution of Bu_4NCN (0.06 mmol, 0.1 M in the reaction solvent). After stirring at the temperature and for the time indicated in Table 1, the reaction mixture was quenched with saturated NH_4Cl solution (4 ml), or 1 N hydrochloric acid if only **2** was desired, and extracted with Et_2O (2 x 5 ml). The combined ethereal extracts were washed with H_2O (2 x 5 ml), brine (5 ml), and concentrated under reduced pressure. Purification of the residue by flash column chromatography on SiO_2 using hexane/EtOAc afforded **1** and/or **2**.

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References and Notes

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8. For other synthetic applications of $Me_3SiSuBu_3$ see, Mori, M.; Kaneta, N.; Isono, N.; Shibasaki, M. *J. Organomet. Chem.* **1993**, *455*, 255-260.
9. Satisfactory spectral data (^1H, ^{13}C, MS) were obtained for all stable compounds using chromatographically homogeneous samples.
10. Salt **5** was prepared from commercial R-(+)-N-methyl-α-phenethylamine by exhaustive alkylation (EtI, K_2CO_3, EtOH, 78°C, 24h), ion exchange of the product over Amberlite IRA-400 (CN^-) eluted with water, and drying in vacuo. ^1H NMR ($CDCl_3$, 250 MHz): δ 1.41-1.53 (m, 6H), 1.90 (d, 3H, J=7 Hz), 3.07 (s, 3H), 3.23-3.33 (m, 1H), 3.42-3.56 (m, 2H), 3.70-3.78 (m, 1H), 4.95 (q, 1H, J=7Hz), 7.46-7.51 (m, 3H), 7.56-7.60 (m, 2H).

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