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A Convenient Preparation of Triisopropylsilyl Acyl Silanes

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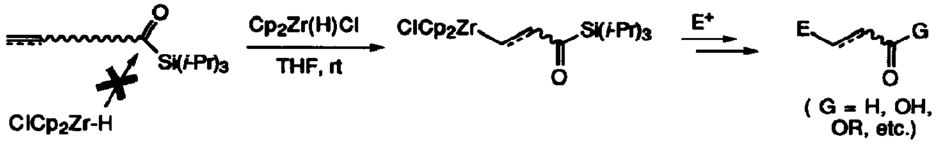
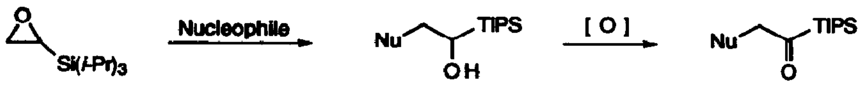
Abstract. *Treatment of α-epoxytriisopropylsilane with selected nucleophiles leads to α-silyl alcohols which are readily oxidized to the corresponding TIPS acyl silanes in good overall yields.*

In a recent *Letter* we described the inert nature of a triisopropylsilyl (TIPS) acyl silane toward hydride addition by Schwartz's reagent ($Cp_2Zr(H)Cl$).[1] In educts that also contain an ω-alkene or alkyne, hydrozirconation thus occurs cleanly, the trialkylsilyl moiety ultimately being converted to alternative functionality (Scheme 1). The versatility of acyl silanes has led to a number of methods for their generation,[2] most commonly involving simpler silanes (*e.g.*, Me_3Si); rarely are they applied to the TIPS series.[3] These routes also tend to involve several steps,[4] and due to the increased steric demands of the TIPS group, overall efficiencies in our hands appear to be modest at best.[5] We now describe a method for preparing TIPS acyl silanes based on the ready availability of silyl epoxide **1** (Scheme 2).[6]

Scheme 1



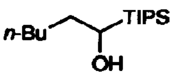
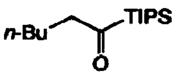
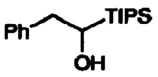
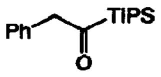
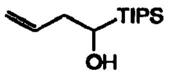
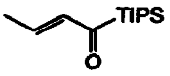
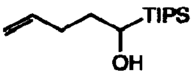
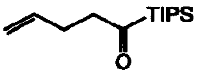
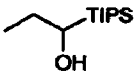
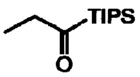
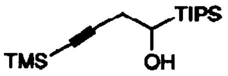
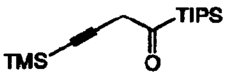
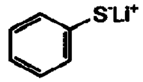
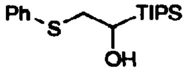
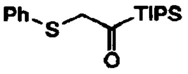
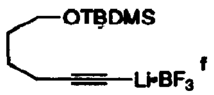
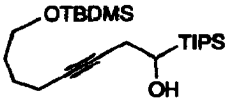
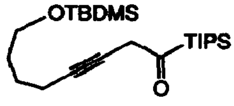
Scheme 2



1 **2** **3**

Although well-precedented that nucleophiles[7] (in particular, cuprate reagents)[8] tend to attack epoxy silanes at carbon bearing silicon,[2] it was anticipated that the TIPS moiety would reverse the

Table 1. Prepartion of TIPS acyl silanes 3 starting with epoxide 1.

Entry	Nucleophile[a]	Conditions[b]	Product 2 (yield, %)[c]		Acyl silane 3 (yield, %)[c]	
1	n-Bu$_2$Cu(CN)Li$_2$	Et$_2$O, -78°, 4 h[d]		(91)		(87)
2	Ph$_2$Cu(CN)Li$_2$	Et$_2$O, -78°, 4 h[d]		(84)		(85)
3		Et$_2$O, -78°, 4 h[d]	 6	(89)		(78)
4	 20 mol % CuCN	Et$_2$O:THF (3:1),[d] -78°, 3 h		(80)		(86)
5	MeMgBr 20 mol % CuCN	Et$_2$O:THF (3:1),[d] -78°, 3 h		(87)		(86)
6	TMS—≡—Li[e] Et$_2$AlCl	PhCH$_3$, 110°, 24 h		(71)		(72)
7		THF, 0°, 2 h		(90)		(84)
8		THF, -78° 4 h		(83)		(82)

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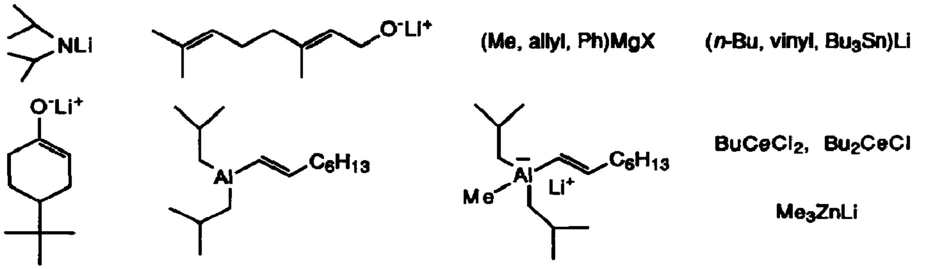
[a] 1-1.2 eq used *vs.* epoxide 1. [b] Reactions were run at 0.2-0.3 M in nucleophile. [c] All compounds were fully characterized by NMR, IR, LR and HRMS. [d] BF$_3$•Et$_2$O (1.5 equiv) was added prior to addition of the epoxide. [e] 1 eq of the Lewis acid was used. [f] 1 eq of BF$_3$•Et$_2$O was added to the lithio acetylide.

regiochemistry of addition.[6b] A single example in the literature by Chong[6c] suggested that this might be a general phenomenon worthy of further inspection. As illustrated in Table 1, cyanocuprates[9] react to afford excellent yields of α-silyl alcohols upon workup (entries 1-3). Reactions usually occur at -78° in a few hours, and by capillary GC appear to be regiospecific. CuCN-catalyzed Grignard additions, likewise, give comparable results (entries 4,5). Metallated acetylenic reagents also readily participate (entries 6 and 8). In one case involving a heteroatom nucleophile (*i.e.*, thiophenoxide, entry 7), the desired adduct was realized in high yield.

Several other nucleophiles were screened, albeit with far less success. Outlined in Figure 1, these include an alkoxide, amide, Grignard reagents, organolithiums, organoceriums, zincates, vinyl alanes and alanates, and enolates. Yields for all were <35%, with most of the remaining mass being recovered as starting material.

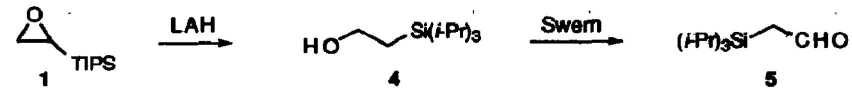
Figure 1



Oxidation of the intermediate α-silyl alcohols **2** was straightforward using Swern conditions,[6c,10] although homoallylic alcohol **6** led to olefin migration *en route* to product (entry 3). The homopropargylic α-silyl alcohol derivatives (*cf.* Table 1, entries 6 and 8), however, were uniformly problematic. Fortunately, while attempts with, *e.g.*, PDC[11a] and TPAP[11b] were marginally successful, Dess-Martin oxidation[11c] gave good results.

Oxirane **1** could also be smoothly reduced to the β-TIPS ethanol, **4** (Scheme 3),[12a] the regiochemistry of which to be anticipated from early work by Eisch.[12b] Swern oxidation afforded previously unknown α-triisopropylsilylacetaldehyde **5** as an uncharacteristically stable oil in 75% overall yield. Thus, whereas α-trimethylsilylacetaldehyde must be formed and immediately used *in situ*,[13] **5** is isolable and storable,[14] thereby presenting interesting opportunities for further elaboration (*e.g.*, conversion to allylic silanes, Peterson olefinations, etc.).[2]

Scheme 3



In summary, a simple 2-step sequence has been developed which allows for generation of TIPS acyl silanes from epoxide **1**. These previously difficult-to-come-by materials should extend the usefulness of this class of organic substrate.

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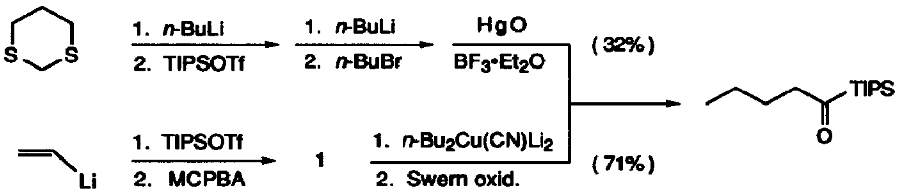
5. By way of comparison, use of dithiane according to the sequence below gave the acyl silane in 32% overall yield, *vs.* a yield of 71% starting with vinyllithium.



6. (a) As shown above, **1** is prepared in 90+% overall yield starting with vinyllithium; all attempts to substitute vinyl Grignard in this first step were totally unsuccessful. Epoxide **1** is a colorless liquid, bp 104° at 4.25 mmHg (Kugelrohr); (b) See ref. 9 in 6c; (c) Chauret, D.C., Chong, J.M., *Tetrahedron Lett.*, **1993**, *34*, 3695.

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14. Aldehyde **5** is a pale yellow oil; ν_{CO} 1709 cm^{-1}; ^1H NMR δ 9.75 (1H, t, J = 4.4 Hz); HRMS calcd for $C_8H_{17}SiO$: 157.1054; found 157.1049 (M^+ - *i*-Pr).

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