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Expanding the Versatility of Schwartz' Reagent: Hydrozirconation of Vinylic and Acetylenic Acyl Silanes

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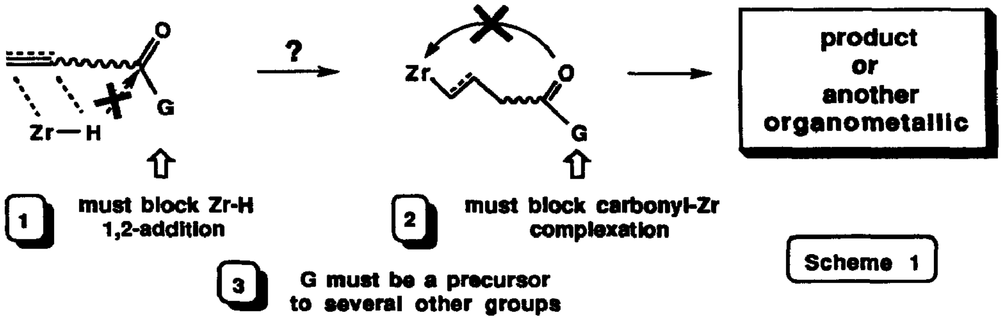
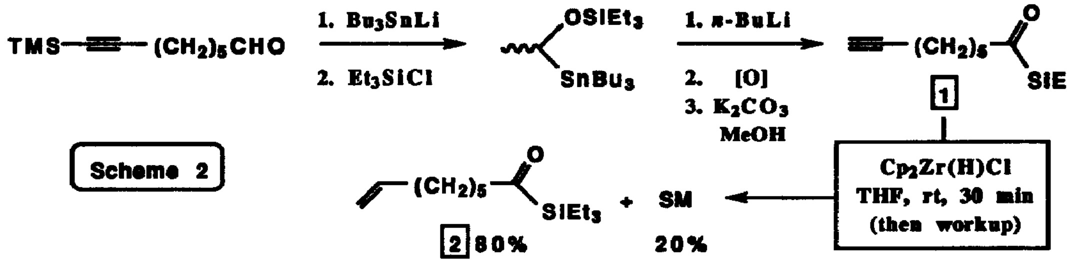
Summary. *By virtue of a triisopropylsilyl acyl silane contained within a substrate undergoing hydrozirconation, chemospecificity can be realized favoring addition across the alkene or alkyne, rather than competitive 1,2-addition of hydride to the carbonyl portion of the molecule.*

Hydrozirconation reactions of alkenes and alkynes are especially valuable processes in that the addition of $Cp_2Zr(H)Cl$ (*i.e.*, 'Schwartz' reagent') to the carbon-carbon multiple bond is highly regio- and (for acetylenes) stereoselective.[1] Moreover, both alkyl and vinyl zirconocenes are highly prone toward transmetalations with various Cu(I) species (*e.g.*, Cu(I) salts,[2] higher order cyanocuprates,[3] etc.), which result in reactive cuprate complexes capable of transferring the desired ligand to a variety of electrophiles. Since much of our work in this area of late relies on an initial hydrozirconation, we are particularly cognizant of the limitations associated with this powerful reagent, for these would necessarily establish minimum constraints on any subsequent chemistry envisioned to derive from an initial zirconocene intermediate. Those limitations identified include (1) competing 1,2-additions of hydride to aldehyde/ketone-containing alkenes/alkynes;[4] and (2) the facility with which carbonyl-containing substrates participate in intra- or intermolecular acid-base complexation,[3,5] which can completely inhibit any second-stage cuprate-assisted transmetalation (Scheme 1).[3] In order to circumvent these problems, we considered use of a group 'G' which not only prevents both (1) and (2) from occurring, but (3) adds considerable flexibility as to the nature of the substituent which could be inserted in its place. We now report a solution to these issues based on the chemistry of acyl silanes.[6]



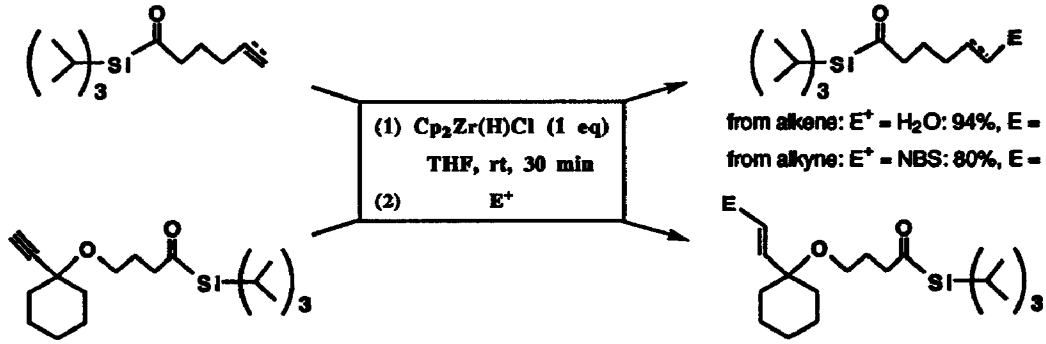
Scheme 1

Selection of an acyl silane was governed by its well-established use[6] as a synthetic equivalent to precisely the carbonyl-containing functional groups not tolerant to $Cp_2Zr(H)Cl$, their availability *via* several known routes, and the numerous opportunities to vary (sterically and stereoelectronically) the groups on silicon. The concept was initially tested with the triethylsilyl derivative **1**, prepared *via* a reverse Brook rearrangement strategy according to Linderman.[7] Treatment of **1** with $Cp_2Zr(H)Cl$ (1 equiv) afforded an 80% yield of the desired olefin **2**, with no detectable amount (by capillary GC) of the carbonyl 1,2-adduct. Unfortunately, the remaining material consisted entirely of unconsumed **1** which could *not* be cleanly driven to completion by time or additional reagent[8] (Scheme 2).



Scheme 2

By switching to the triisopropylsilyl (TIPS) analog,[9] however, hydrozirconation fully consumes the alkene or alkyne substrate to ultimately afford products of subsequent trapping by electrophiles E^+ (Equations 1, 2).



(Eq. 1)

from alkene: $E^+ = H_2O$: 94%, E = H

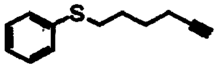
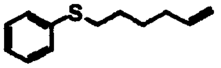
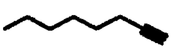
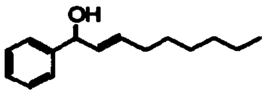
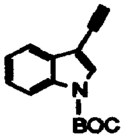
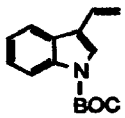
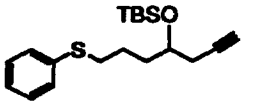
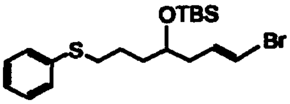
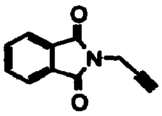
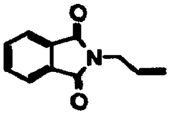
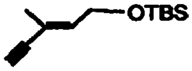
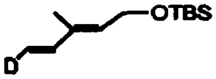
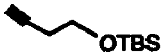
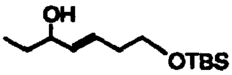
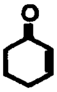
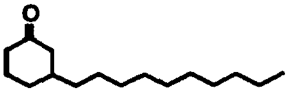
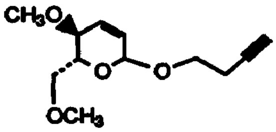
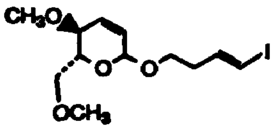
from alkyne: E^+ = NBS: 80%, E = Br

(Eq. 2)

$E^+ = H_2O$: 83%, E = H

To test the compatability of various functionalized olefins/acetylenes toward hydrozirconation in the presence of a standard TIPS acyl silane **3**, numerous competition experiments were conducted, as illustrated in Table 1. From these examples, which include sulfides (entries 1,4), nitrogen-containing educts (entries 3,5), a conjugated enyne (entry 6), and a carbohydrate (entry 9), among others, together with an array of trapping agents (E^+), it seems safe to conclude that competitive 1,2-addition as well as acid-base chemistry [*cf.* limitation (2); *vide supra*, and entry 8 in Table 1 which involves a transmetalation to copper] are eliminated using this structural unit. Indeed, even exposure of acyl silane **3b**[10] alone (*i.e.*, with no alkene or alkyne present) to *excess* $Cp_2Zr(H)Cl$ over time led to no observed reaction (Equation 3).

Table 1. Competition study between an alkene/alkyne and acyl silane 3 for $Cp_2Zr(H)Cl$[1]

	SUBSTRATE	E+	PRODUCT(S)[2]	YIELD(%)[3]	recov'd(%) acyl silane[3,4]
[1]		H_2O		85	89
[2]		PhCHO cat $AgClO_4$[5]		85	90
[3]		H_2O		92	90
[4]		NBS		83	90
[5]		H_2O		60	91
[6]		D_2O		94	96
[7]		 cat $AgClO_4$[6]		70	95
[8]		 cat CuCN[7]		77	91
[9]	[8]	NIS		81	92

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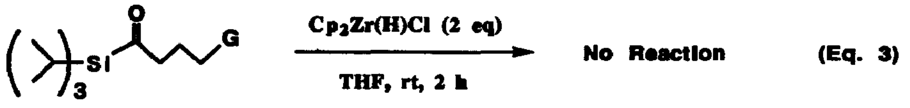
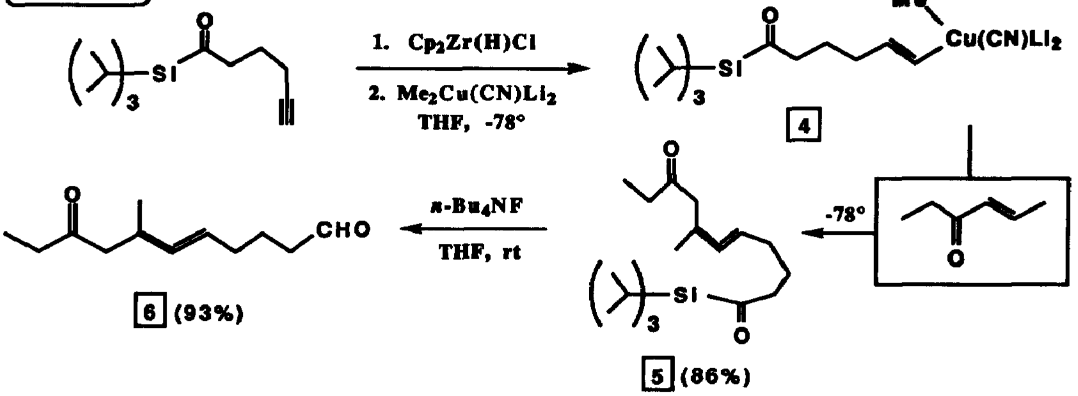
[1] Ratio of reactants is 1:1:1. [2] Fully characterized by spectral and mass spec (LR, HR) data. [3] Isolated. [4] Entries 1-5 used silane 3a; entries 6-9 used 3b. [5] See Maeta, H., Hashimoto, T., Hasegawa, T., Suzuki, K., *Tetrahedron Lett.*, 1992, 33, 5965. [6] Wipf, P., Xu, W., *J. Org. Chem.*, 1993, 58, 825. [7] Wipf, P., Smitrovich, J.H., *ibid.*, 1991, 56, 6494. [8] An 8:1 mix of α:β anomers.



3 a, G = H; b, G = Cl

Notwithstanding the heartiness of this group in resisting reduction by Schwartz' reagent, or its reluctance to serve as a Lewis base toward zirconocene intermediates, its manipulation to other valued functionality is quite straightforward.[6] Thus, following hydrozirconation, transmetalation, and Michael addition of cuprate **4** to arrive at ketone **5**, exposure of **5** to *n*-Bu_4NF in THF[11] smoothly affords the keto aldehyde **6** in 93% yield (Scheme 3).

Scheme 3



In summary, it has been demonstrated that carbonyl surrogate TIPS acyl silanes are resistant to 1,2-addition by $Cp_2Zr(H)Cl$, thereby allowing for the hydrozirconation of an alkene or alkyne present within the molecule to be carried out chemospecifically.

Acknowledgement. Financial support provided by the NSF is gratefully acknowledged.

References and Notes

1. Schwartz, J., Labinger, J.A., *Angew. Chem. Int. Ed. Engl.*, **1976**, 15, 333; Negishi, E., Takahashi, T., *Synthesis*, **1988**, 1.
2. See Table 1, footnote 7 for a representative example.
3. Lipshutz, B.H., Keil, R., *J. Am. Chem. Soc.*, **1992**, 114, 7919.
4. Acetone is used to titrate $Cp_2Zr(H)Cl$; *cf.* Buchwald, S.L., LaMaire, S.J., Nielsen, R.B., Watson, B.T., King, S.M., *Tetrahedron Lett.*, **1987**, 28, 3895.
5. Erker, G., Aulbach, M., Mena, M., Pfaff, R., Sosna, F., *Chem. Scripta*, **1989**, 29, 451.
6. Cirillo, P.F., Danek, F.S., *Org. Prep. Proc. Int.*, **1992**, 24, 553; Bulman Page, P.C., Klair, S.S., Rosenthal, S., *Chem. Soc. Rev.*, **1990**, 19, 147; Ricci, A., Degl' Innocenti, A., *Synthesis*, **1989**, 647.
7. Linderman, R.J., Ghannam, A., *J. Org. Chem.*, **1988**, 53, 2878.
8. Reagent used in excess of 1 eq leads to the 1,2-hydride reduction product of **1**.
9. Yanagisawa, A., Habaue, S., Yamamoto, H., *J. Org. Chem.*, **1989**, 54, 5198.
10. Made by procedures analogous to those in: Corey, E.J., Seebach, D., Freedman, R., *J. Am. Chem. Soc.*, **1967**, 89, 434.
11. Schinzer, D., Heathcock, C.H., *Tetrahedron Lett.*, **1981**, 22, 1881.

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