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COMMUNICATIONS

Published on Web 06/17/2002

A Chemoselective Reduction of Alkynes to (*E*)-Alkenes

Barry M. Trost,* Zachary T. Ball, and Thomas Jöge

Department of Chemistry, Stanford University, Stanford, California 94305-5080

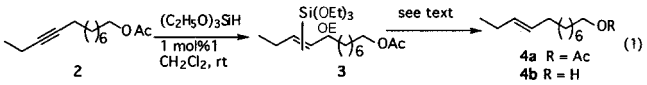
Received April 8, 2002

Alkynes are useful building blocks in organic synthesis because of the ease with which they can be elaborated. Among their most important applications is their controlled reduction to cis alkenes which is a reliable and general synthetic method because of its chemoselectivity and high degree of control of geometry. On the other hand, the complementary process—trans addition of hydrogen to afford (*E*)-alkenes—remains an elusive goal. Metal hydrides,[1] dissolving metal reductions,[2] and low-valent chromium salts[3] have all been employed for such reductions, even in the context of complex molecule synthesis.[3a] However, all of these methods suffer from chemoselectivity drawbacks. Furthermore, these methods generally require an alcohol, amine, or carbonyl functionality in the propargylic position for reactivity. A mild general trans reduction for all types of alkynes including isolated alkynes remains an unsolved problem.

One approach is a two-stage trans hydrometalation and subsequent protodemetalation.[4] Our recent discovery that the complex $[Cp^*Ru(MeCN)_3]PF_6$ (**1**) catalyzes the hydrosilylation of a wide variety of alkynes under mild conditions with good functional group tolerance and complete selectivity for the unusual trans addition led us to consider the possibility of coupling this transformation with a protodesilylation to achieve a two-step net trans reduction of alkynes as shown in eq 1.[5] While simple protonation with typical strong acids does effect protodesilylation with retention of olefin geometry, the harshness of the reaction conditions compromises its chemoselectivity and induced us to seek a milder protocol.[6a] Our goal became the development of a desilylation protocol with high chemoselectivity.

Alkyne **2** (eq 1) represents a reasonable test with a common functionality which cannot survive many of the reduction methods if the alkyne reduces well. As expected, hydrosilylation of **2** with triethoxysilane (1.2 equiv) proceeds cleanly in the presence of ruthenium complex **1** (1.0 mol %) to afford vinylsilane **3** in 89% yield as a nearly 1:1 mixture of (*Z*)-regioisomers. Protodesilylation of vinylsilanes is well studied for monoalkoxyvinylsilane substrates, and generally requires treatment with TBAF at elevated temperatures (≥80 °C).[6b] We had initially hoped that by employing trialkoxysilane substrates such as **3** we might enhance the reactivity of our vinylsilane toward nucleophilic protodesilylation. However, we found that **3** behaved similar to monoalkoxyvinylsilanes and required treatment with TBAF at 80 °C in DMF to effect protonation of the vinylsilane. Perhaps not surprisingly, under these conditions the acetate was hydrolyzed prior to vinylsilane protonation. Additionally, vinylsilane **3** proved inert to acidic desilylation conditions (anhydrous HCl, TsOH/MeCN/H_2O, or HF·pyridine), giving only decomposition upon prolonged heating.

Seeking a more general solution to the problem at hand, we envisioned transmetalation of the vinylsilane followed by protonation of the new vinylmetal as a potentially catalytic solution.[7] Intrigued by recent work employing copper *tert*-butoxide for the allylation of trialkylsilanes bearing an allylic alcohol, we investigated copper as a promoter of protodesilylation.[8] Although copper alkoxides failed to bring about the desired desilylation, cuprous iodide (1.5 equiv) in the presence of TBAF in THF effected clean protodesilylation of **3** to give **4a** with no observable cleavage of the acetate (**4b**). Although TLC analysis indicated complete



2 3 (1)

conversion at room temperature, evidence for vinylsilanes remained by ^1H NMR, presumably as polysiloxane polymers. Complete protodesilylation could be induced through gentle heating to 35 °C wherein the *trans*-acetate **4a** was isolated in 89% yield. Use of other cuprous salts were either significantly less effective (cuprous cyanide) or failed (cuprous chloride).

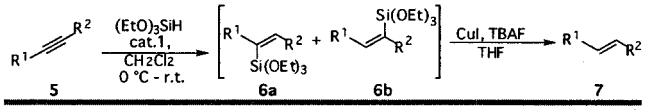
The copper-mediated desilylation proceeds cleanly when only catalytic CuI (0.2 equiv) is employed. However, under these conditions with **3** as substrate the labile acetate is also cleaved, so that *trans*-alcohol **4b** was the sole product isolated in 85% yield. Therefore, whenever sensitive functionality is present, stoichiometric amounts of cuprous iodide are utilized. These observations allow us to postulate that cuprous iodide actually serves two distinct roles in the protodesilylation reaction. First, the copper salt facilitates the desilylation reaction, allowing the cleavage of the C−Si bond at much lower temperatures than those required with TBAF alone. Second, the cuprous ion tempers (buffers) the reactivity of TBAF, making it less active in noncatalyzed pathways such as acetate cleavage. The exact nature of the copper salt has not been established, but it is possible that a soluble complex of the elusive cuprous fluoride is being generated in situ under these conditions.[9]

As shown in Table 1, the cuprous iodide-induced protodesilylation allows a net trans alkyne reduction for a wide variety of alkynes. Experimentally, the intermediate vinylsilanes were not isolated, but were filtered through a pad of florisil to remove the ruthenium catalyst and then concentrated under reduced pressure to remove excess silane. The crude silane was directly subjected to the new protodesilylation method. The two-stage procedure proved effective for conjugated esters and ketones as well as for propargyl alcohols. Additionally, an isolated ketone, a primary alkyl chloride and even a particularly acid labile acetal proved compatible with the mild reaction conditions. The compatibility of a secondary hydroxyl group that is both benzylic and allylic in the product is also noteworthy. With internal alkynes, regioselectivity of the hydrosilylation is irrelevant since the silicon is ultimately replaced by hydrogen. Nevertheless, as we noted,[6] it may be highly regioselective. In contrast to the facility of the protodesilylation of the triethoxysilanes, trialkylvinyl silanes do not react under the conditions described. We have generally filtered the ruthenium catalyst and exchanged solvent prior to protodesilylation. However,

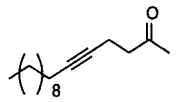
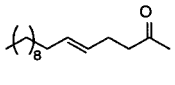
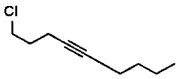
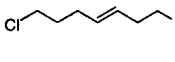
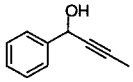
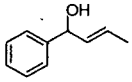
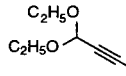
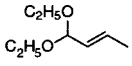
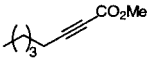
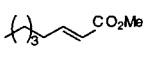
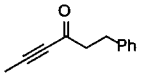
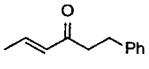
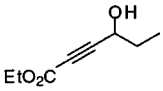
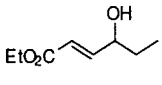
* To whom correspondence should be addressed. E-mail: bmtrost@stanford.edu.

10.1021/ja026457l CCC: $22.00

Table 1. Trans Alkyne Reduction by Hydrosilylation−Protodesilylation[a]

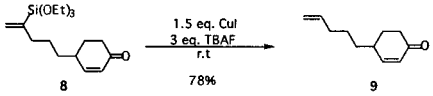


5 6a 6b 7

entry	alkyne	mol% 1	eq. CuI	product	yield[b]
a[c]		1.0	1.5		96
b[c]		2.0	1.5		59[d]
c[c,e]		3.0	0.2		76
d[c]		1.0	0.2		67[d]
e		1.0	0.1		83
f		1.0	1.5		68
g[e]		2.0	0.2		80

[a] Hydrosilylations performed at 0.5 M in CH_2Cl_2 under Ar and were generally complete within 1 h. Vinylsilanes were not purified and in several cases were formed as regiomeric mixtures. Desilylation was performed at rt for 16 h under Ar with 2.0 equiv (cat. CuI) or 3.0 equiv (1.5 equiv CuI) TBAF unless otherwise noted. [b] Isolated yield. [c] Desilylation performed at 35 °C. [d] Modest yield due at least in part to volatility of product olefin. [e] Me_2(EtO)SiH used as silane.

entry e afforded 65% of the desired *trans*-olefin when, cuprous iodide and TBAF in THF were added directly to the hydrosilylation reaction mixture.



8 9 (2)

It has been noted that 1,1-disubstituted vinylsilanes are difficult protodesilylation substrates, presumably because olefin protonation requires formation of a primary carbocation.[10] We became interested to see if our cuprous iodide-mediated conditions would succeed for this substrate class as well and were gratified to find that under the same conditions utilized above, vinylsilane **8** was smoothly cleaved to the terminal olefin **9** at ambient temperature (eq 2).

The cuprous iodide/TBAF system outlined above permits facile protodesilylation of vinylsilanes under conditions much milder than previously reported. The reaction proceeds with a catalytic amount of CuI. For sensitive substrates, the use of stoichiometric CuI moderates the reactivity of TBAF with respect to other nucleophilic or basic processes and permits more selective reactivity. To the extent that the hydrosilylation is regioselective, this method also allows selective introduction of hydrogen isotopes. The intriguing mechanism of this activation of the vinylsilane remains elusive. Because new synthetic applications may derive from its understanding, probing the mechanism is the subject of our continuing studies. Presently, together with the ruthenium-catalyzed trans hydrosilylation, the process represents an efficient chemoselective trans reduction of all types of alkynes to permit selective synthesis of *trans*- as well as *cis*-olefins.

A general procedure for the synthesis of methyl (*E*)-2-octenoate (Table 1, entry e) follows. To methyl 2-octynoate (105 mg, 0.68 mmol) in CH_2Cl_2 (1.4 mL) under an Ar atmosphere was added triethoxysilane (0.150 mL, 0.82 mmol). $[Cp^*Ru(MeCN)_3]PF_6$ (**1**) (3.4 mg, 0.0068 mmol) was added after cooling to 0 °C. The flask was immediately allowed to warm to ambient temperature, where it was stirred for 30 min. The solution was diluted with ether (5 mL), filtered through a plug of florisil (1−2 cm), and washed with additional ether (15 mL). The filtrate was concentrated under reduced pressure and taken up in THF (3.4 mL) under Ar at ambient temperature. To the solution was added CuI (13 mg, 0.068 mmol) followed by dropwise addition of TBAF (1.3 mL, 1.3 mmol), and the resulting orange slurry was stirred for 20 h. The mixture was then filtered through a plug of silica gel, concentrated, and purified by silica gel column to afford 89 mg (83%) of the desired methyl (*E*)-2-octenoate.

Acknowledgment. We acknowledge the National Science Foundation and the National Institutes of Health for their generous support of our programs. Z.T.B. thanks Stanford University for a Stanford Graduate Fellowship. T.J. acknowledges receipt of a fellowship from the German Academic Exchange Service (DAAD). Mass spectra were provided by the Mass Spectrometry Facility, University of San Francisco, supported by the NIH Division of Research Resources.

Supporting Information Available: Characterization data for vinylsilanes **3** and **8** as well as for all olefin products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org

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JA026457L