

Rhenium-Catalyzed Coupling of Propargyl Alcohols and Allyl Silanes

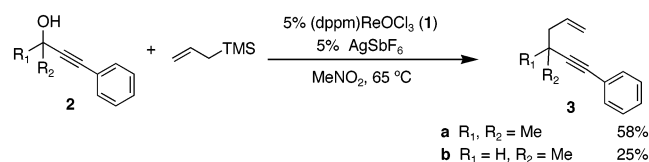
Michael R. Luzung and F. Dean Toste*

Center for New Directions in Organic Synthesis, Department of Chemistry, University of California, Berkeley, California 94720

Received October 19, 2003; E-mail: fdtoste@uclink.berkeley.edu

Transition metal-catalyzed coupling of aryl and vinyl halides or pseudohalides with organometallic nucleophiles has become an important and powerful method for the formation of carbon–carbon bonds.¹ In contrast, related transition metal-catalyzed coupling reactions of alkyl halides, for the formation of aliphatic carbon–carbon bonds, are relatively rare.² Addition of organometallic reagents to propargylic halides/pseudohalides provides an attractive alternative for the construction of sp³–sp³ C–C bonds. In addition to allowing access to the saturated products by hydrogenation, the alkyne moiety provides a handle for transformation into a variety of other functional groups. Unlike transition metal-catalyzed allylic alkylation,^{3,4} propargylic substitution has been dominated by the reaction of nucleophiles with propargyl cations stabilized by stoichiometric transition metal complexes.^{5,6} We have recently reported that rhenium(V)-oxo complex **1** serves as an air- and moisture-tolerant catalyst for the formation of aliphatic ethers by the coupling of simple alcohols and propargyl alcohols.⁷ Herein, we describe the application of this catalyst system to the formation of carbon–carbon bonds by the coupling of allylsilanes⁸ and propargyl alcohols.

Our preliminary attempts at rhenium-catalyzed coupling of propargyl alcohols and allyl trimethylsilane were complicated by competing Meyer–Schuster rearrangement.⁹ Gratifyingly, we found that 5 mol % (dppm)ReOCl₃ (**1**) and 5 mol % ammonium hexafluorophosphate in nitromethane, at 65 °C, cleanly produced the substituted 1,5-enyne in excellent yields (Table 1) and without competing rearrangement to the enone. The reaction could be carried out with lower catalyst loadings (compare entries 1 and 2) without significant deterioration in yield by increasing the reaction temperature to 80 °C. Similarly, the reaction temperature could be lowered to room temperature (compare entries 5 and 6) by extending the reaction time from 2 to 8 h. Substitution was carried out on electron-rich and electron-poor (entry 9) aromatic substrates. Halogenated aromatic substrates (entries 9–11) that may subsequently participate in transition metal-catalyzed cross-coupling reactions and acid labile ketals (entries 10 and 11) survive the reaction conditions. Sterically encumbered *ortho*-disubstituted phenyl groups (entry 12) do not affect the course of the carbon–carbon bond formation. Notably, substitution of a propargyl alcohol occurs preferentially to reaction with a propargyl aryl ether (entry 15). Variation of the alkynyl substituent is also well tolerated; however, larger alkynyl substituents require slightly longer reaction times, but maintain high yields. Additionally, chemoselective propargylic substitution occurs in preference to conjugate addition, when an alkynoate ester is employed as a substrate (entry 7).



Nonbenzylic propargyl alcohols also participate in the substitution reaction; however, silver hexafluoroantimonate is required as the

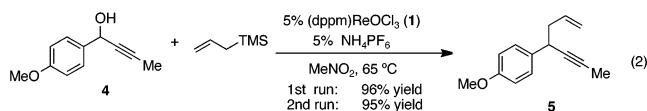
Table 1. Rhenium-Oxo-Catalyzed Synthesis of 1,5-Enynes^a

Entry	R ₁	R ₂	R ₃	temp (°C)	mol% (1)	Yield ^b	
1		Ph	H	65	5	79	
2		Ph	H	80	1	75	
3		TMS	H	65	1	82	
4		<i>n</i> -Bu	H	65	5	90	
5		Me	H	65	4	95	
6		Me	H	rt	4	96	
7		CO ₂ Et	H	65	5	73	
8		Me		65	5	99	
9		Me	H	65	5	65	
10		X = H	Me	H	65	5	89
11		X = Br	TMS	H	65	5	89
12		Me	H	65	5	89	
13		Me	H	65	5	90	
14		Me	H	65	5	87	
15		Me	H	65	5	82	

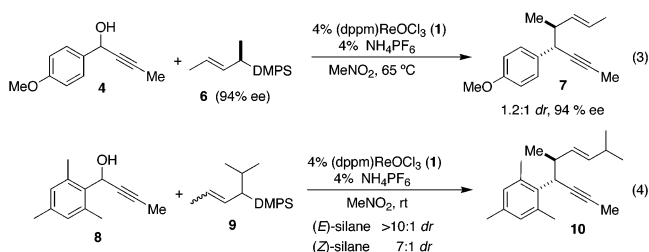
^a Reaction conditions: 0.25 M propargyl alcohol in MeNO₂, 3.0 equiv of allylsilane, 2 h. ^b Isolated yield after chromatography.

cocatalyst (eq 1). Rhenium-catalyzed coupling with tertiary alcohol **2a** allows for the construction of a quaternary carbon without competing formation of the allene product.¹⁰ Secondary aliphatic alcohol **2b** also participates in our rhenium-catalyzed reaction, albeit with diminished yield.

The stability of our high oxidation state complexes allows for catalyst recovery in some cases (eq 2). For example, coupling of **4** and allyltrimethylsilane, catalyzed by 5 mol % **1**, affords the desired adduct (**5**) in 96% yield. Approximately 70% of the initial catalyst was recovered by removal of MeNO₂ in vacuo, followed by precipitation of the catalyst with hexanes or ether. After filtration of the solid, NH₄PF₆ was removed from the catalyst by a simple aqueous wash. The recovered rhenium complex can be reused in the coupling reaction without a noticeable deterioration in activity.



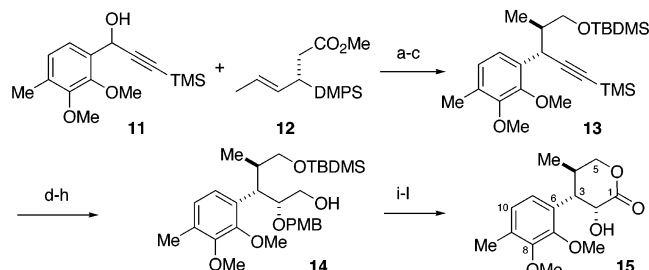
We also examined the effect of variation in the allylsilane. For example, chloromethyl-substituted allylsilane participated well in the reaction (Table 1, entry 8). Additionally, the diastereoselectivity of the substitution was investigated using enantioenriched crotylsilane **6** as the nucleophile. In temperatures ranging from 50 to 65 °C, our rhenium-catalyzed coupling consistently afforded propargyl adduct **7** as a 1.2:1 mixture of diastereomers with complete fidelity in the chirality transfer (eq 3). The presence of *ortho*-dimethyl groups on the aryl ring significantly increased the diastereoselectivity (eq 4). Rhenium-catalyzed coupling of (*E*)- and (*Z*)-crotylsilanes (**9**),¹¹ at room temperature, produced **10** and *ent*-**10**¹² in >10:1 dr and 7:1, respectively.



To establish the absolute and relative stereochemistry of the coupling of propargyl alcohols with chiral allylsilanes, we undertook a synthesis of δ -lactone, 7,8-di-*O*-methylcalopin (**15**) (Scheme 1).¹³ Two of the three stereocenters in **15** were set by the rhenium-catalyzed allylation of propargyl alcohol **11** with chiral allyl silane **12**.¹⁴ Ozonolysis of the major diastereomer followed by reductive workup and then protection gave protected alcohol **13** in 68% yield over three steps. Desilylation and hydrogenation of the acetylene to the olefin allowed for installation of the C1–C2 oxygens by dihydroxylation. The hydroxyl groups were differentiated by formation of the *para*-methoxybenzyl acetal followed by regioselective reduction with Dibal-H to afford **14**. Oxidation of the primary alcohol with Dess–Martin periodinane and deprotection of the silyl ether provided a lactol that was oxidized to the lactone using catalytic TPAP and NMO. Deprotection of the PMB ether afforded (–)-7,8-di-*O*-methylcalopin **15**, whose stereochemistry was assigned from nOe measurements and comparison of the optical rotation.^{13,15}

In conclusion, we have developed the first transition metal-catalyzed coupling of propargyl alcohols and allylsilanes. This method allows for the preparation of a variety of 1,5-enynes by formation of propargylic sp³–sp³ carbon–carbon bonds. A wide

Scheme 1. Synthesis of (–)-Di-*O*-Me-calopin^a



^a (a) 5 mol % (dppm)ReOCl₃, 5 mol % NH₄PF₆, CH₃NO₂, 82% (1.2:1 dr); (b) O₃, MeOH, then NaBH₄; (c) TBDMS–Cl, imidazole, 68% over two steps; (d) K₂CO₃, MeOH, quant.; (e) H₂, cat. Pd(BaSO₄), quinoline, quant.; (f) cat. OsO₄, NMO, 69% (1.2:1 dr); (g) (MeO)₂CHC₆H₄-*p*-OMe, PPTS; (h) Dibal-H, CH₂Cl₂, 73% over two steps; (i) Dess–Martin periodinane, 80%; (j) TBAF, CH₂Cl₂; (k) 5% TPAP, NMO, 4 Å MS, CH₂Cl₂, 66% over two steps; (l) H₂, Pd–C, EtOH, 49%.

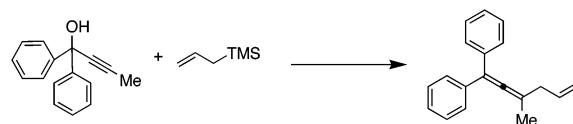
range of silanes and propargyl alcohols, including simple aliphatic, are viable coupling partners. Additionally, rhenium-catalyzed reaction of chiral crotylsilanes allows for the enantioselective synthesis of two adjacent stereocenters. The catalyst is both air and moisture stable, allowing for the recovery and reuse of the rhenium complex. This exemplifies the potential and advantages of high oxidation transition complexes as catalysts for organic reactions.

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Supporting Information Available: Experimental procedures and compound characterization data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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