J. Am. Chem. Soc. **2001,** *123,* 2897−2898

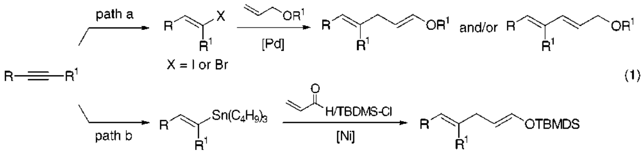
An Atom-Economical Three-Carbon Chain Extension of Alkynes to Form *E*-Enol Silanes

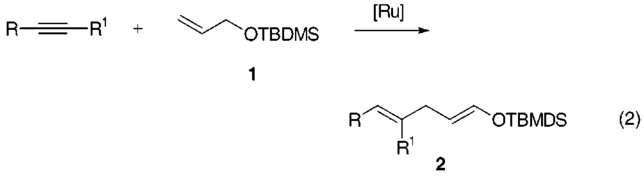
Barry M. Trost,* Jean-Philippe Surivet, and F. Dean Toste

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

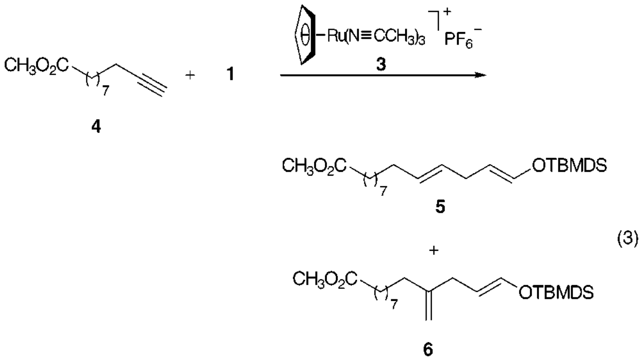
Received November 6, 2000

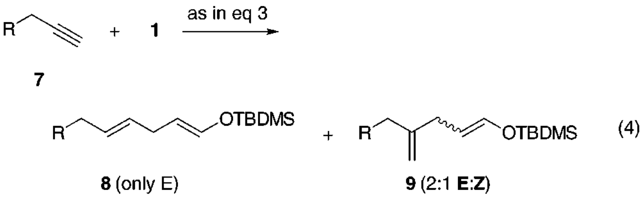
Enol silyl ethers are important synthetic intermediates.[1] Because the alkene geometry can influence the stereochemistry of subsequent events, obtaining geometrically defined enol silyl ethers is an important goal.[1,2] Simultaneously, chain extension methods represent an important protocol. Three-carbon chain extension of alkynes to geometrically defined enol silyl ethers requires stoichiometric conversion to a vinyl halide followed by a Heck reaction (eq 1, path a)[3] or to a vinyl organometallic followed by conjugate addition, an example of which is illustrated in eq 1, path b.[4] Moreover, Heck vinylations of allyl alcohols is reported to be problematic.[5] We report a simplified protocol to effect a direct catalytic three-carbon chain extension of alkynes to *E*-enol silanes (**2**) according to eq 2 using allyl silyl ether **1**.[6,7]

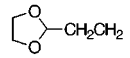




Initial results examined the use of a terminal alkyne **4** using ruthenium complex **3**[8,9] as catalyst (eq 3). Subjecting a 1:1 mixture of alkyne and alkene to 10 mol % **3** in acetone at 0.1 M led within 1 h to a 66% yield of a 3.2:1.0 mixture of **5**:**6**.[10] Interestingly, the major product **5** was produced exclusively as the *E*-alkene; whereas, the minor regioisomer was formed as a 2:1 *E:Z* ratio. The *E*-geometry of the enol silyl ether is characterized by $J = 12$ Hz for the vinyl hydrogens. Decreasing the catalyst load to 5 mol % but increasing the concentration to 0.5 M led to a similar result. However, at this lower catalyst loading and 0.2 M in 1:4 acetone−THF, the yield increased to 75% with unchanged selectivity. Application of these very mild conditions to a series of substrates **7** to produce mainly the linear products **8**[10] and to test the chemoselectivity is illustrated in eq 4. In all cases, reactions were performed using 1:1 ratios of the two reactants. Normally, reactions were complete between 0.5 and 3 h. For substrates **7a** and **7b**, reactions benefited by performing them using 5 mol % of **3** at 0.2 M rather than 10 mol % of **3** at 0.1 M. The reaction of the ketone substrate was performed only with 10 mol % catalyst at 0.1 M. In contrast to the above cases, the sulfonamide substrate **7d** saw a decrease in yield from 83 to 63% upon decreasing the catalyst load from 10 mol % at 0.1 M to 5 mol % at 0.2 M. The BOC derivative **7e**, however, reversed this behavior and gave excellent results at 5 mol % of **3** at 0.2 M using a 1:4 acetone−THF mixed solvent system. In this latter solvent system, the catalyst load could be decreased to 2.5 mol % (0.3 M) with almost no change in yield (72%), but a further decrease to 1 mol % (0.4 M) decreased the conversion so that only a 49% yield of product was obtained. In all cases, the linear products **8** were produced exclusively as the *E,E*-alkene isomers.





a) R = 	76%	**8:9**	3.4:1
b) R = $NCCH_2CH_2$	82%	**8:9**	3.6:1
c) R = CH_3COCH_2	51%	**8:9**	3.6:1
d) R = $TsNHCH_2$	83%	**8:9**	2.3:1
e) R = $\text{Ts}\overset{\text{Boc}}{\text{N}}\text{CH}_2$	79%	**8:9**	3.4:1

Introduction of branching had a most interesting effect as shown in eq 5. In each case, the linear isomer **11**[10] was virtually to exclusively the only product as the *E,E* geometric isomer. The success of the propargyl alcohol substrate **10c** is most interesting because of its propensity to form allenylidene complexes with

---

[1] Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; Wiley-Interscience: New York, 2000; pp 215−239; Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983; Chapters 12−16, pp 206−272.

[2] Gennari, C. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 2.4, pp 629−660.

[3] Compare reaction with allyl alcohol, Jeffery, T. *Chem. Commun.* **1991**, 324; Jeffery, T. *Tetrahedron Lett.* **1990**, *31*, 6641.

[4] Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 5160.

[5] Kao, L. C.; Stakem, F. G.; Patel, B. A.; Heck, R. F. *J. Org. Chem.* **1982**, *47*, 1267.

[6] For reactions of lithiated allyl silyl ethers with electrophiles to form enol silyl ethers, see: Evans, D. A.; Takacs, J. M.; Hurst, K. M. *J. Am. Chem. Soc.* **1979**, *101*, 371; Hosomi, A.; Hashimoto, H.; Sakurai, H. *J. Org. Chem.* **1978**, *43*, 2551; Still, W. C. *J. Org. Chem.* **1976**, *41*, 3062; Still, W. C.; Macdonald, T. L. *J. Am. Chem. Soc.* **1974**, *96*, 5561.

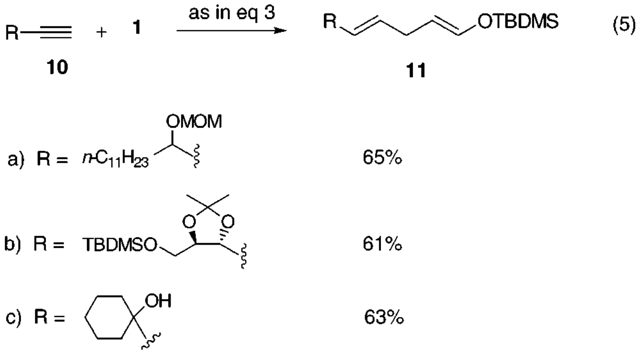
[7] For isomerization of allyl silyl ethers to enol silyl ethers, see: Baudry, D.; Ephritikhine, M.; Felkin, H. *Chem. Commun.* **1979**, 694; Suzuki, H.; Koyama, Y.; Moro-oka, Y.; Ikawa, T. *Tetrahedron Lett.* **1979**, 1415; Ohmura, T.; Shirai, Y.; Yamamoto, Y.; Mujaura, N. *Chem. Commun.* **1998**, 1337.

[8] Gill, T. P.; Mann, K. R. *Organometallics* **1982**, *1*, 485.

[9] For its use in Alder ene-type processes, see: Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 9728; Trost, B. M.; Toste, F. D. *Tetrahedron Lett.* **1999**, *40*, 7739.

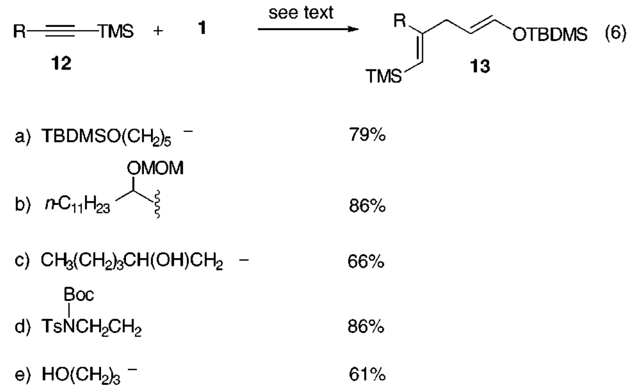
[10] New compounds have been satisfactorily characterized by spectroscopy and elemental composition established by high-resolution mass spectrometry and/or combustion analysis.

10.1021/ja003870p CCC: $20.00



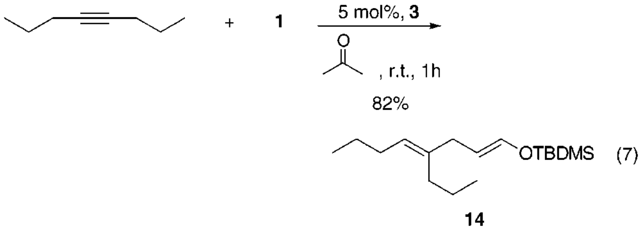
Ru catalysts.[11,12] Performing this reaction in acetone using 10 mol % of **3** gave a 57% yield which improved to 63% by switching to 1:4 (v:v) acetone−THF and decreasing the catalyst to 5 mol %.

To obtain branched isomers selectively, a TMS group was used as a proton surrogate in the terminal alkynes as shown in eq 6.[13]



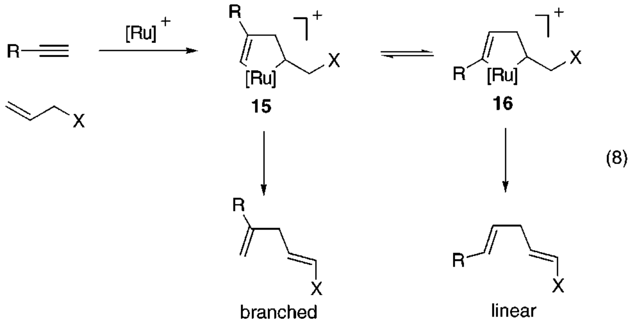
For substrates **12a**, **12d**, and **12e**, the reactions were performed using 10 mol % **3** at 0.1 M in acetone; whereas, the reactions of **12b** and **12c** were performed with 5 mol % **3** at 0.2 M in 1:4 THF−acetone. In all cases, only one geometry of the vinyl silane was observed. For **13a**−**d**,[10] the products were exclusively the *E*-enol silyl ethers. Only in the case of **13e**[10] was a small amount of the *Z*-isomer detected (96:4 *E*:*Z*).

The success of silylalkynes **12** suggests that disubstituted alkynes are satisfactory partners. Indeed, 4-octyne is an excellent substrate as shown in eq 7 where only a single product, **14**,[10] was isolated in 82% yield.



14

This simple three-carbon chain extension simultaneously provides a geometrically controlled synthesis of enol silyl ethers under remarkably mild conditions, usually within 1 h at room temperature. Furthermore, it constitutes a convenient strategy to geometrically defined di- and trisubstituted alkenes with an appendage nicely functionalized for further elaboration. Underlying the atom economy of the method is the concept that maintaining the same overall oxidation level of the starting materials and products is more efficient. Thus, earlier methods relying on conjugate addition to acrolein, as in eq 1, by necessity require some accompanying stoichiometric reduction. This reaction contrasts with the reaction of α-substituted allyl alcohols and alkynes catalyzed by CpRu(COD)Cl which is not successful with allyl alcohol.[14] Conversely, the silyl ether **1** fails to react successfully using the CpRu(COD)Cl catalyst. An attractive aspect of this chain extension is the ability to obtain both regioisomers from terminal alkynes—the linear isomer (e.g., **8**, **11**) by direct use of the terminal alkyne or the branched (e.g., **13** followed ultimately by protodesilylation after elaboration of the enol silyl ether) by use of the trimethylsilyl group as a regiochemical control element. The preference for the linear isomers compared to alkenes without substituents such as allylic oxygen raises an intriguing mechanistic question. A possible rationale is illustrated in eq 8. Because of the steric bulk of the substituents on ruthenium, kinetically ruthenacycle **15** is favored over **16**. If β-hydrogen elimination and subsequent reductive elimination is fast, then the branched product dominates. On the other hand, if β-hydrogen elimination is slowed by the X substituent[15] (as in the case of siloxy or similar groups), then equilibration to the ruthenacycle **16**, which is either more stable or more reactive toward β-hydrogen reductive elimination, competes, thereby favoring the linear product. Indeed, increasing the size of the Cp group on ruthenium to Cp* shifts the linear-to-branched ratio to 1:1.2 in accord with this interpretation. It should be noted that substitution of the vinylsilanes also provides a geometrically defined approach to trisubstituted alkenes. The excellent atom economy is highlighted by the fact that only stoichiometric amounts of the two reactants are required.



Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for their generous support of our programs. Rhône-Poulenc graciously provided a postdoctoral fellowship for J.P.S. Mass spectra were obtained from the Mass Spectrometry Regional Center of the University of California-San Francisco, supported by the NIH Division of Research Resources.

Supporting Information Available: Experimental procedures for **13**−**15**, **24**, **26**, **27**, **30**−**34** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA003870P

---

[11] Cadierno, V.; Gamasa, M. P.; Gimeno, J.; Borge, J.; Garcia-Granda, S. *Organometallics* **1997**, *16*, 3178; Touchard, D.; Pirio, N.; Dixneuf, P. H. *Organometallics* **1995**, *14*, 4920; Selegue, J. R.; Young, B. A.; Logan, S. L. *Organometallics* **1991**, *10*, 1972 and references therein.

[12] Conversion of the propargyl alcohol to the allenylidene would not be anticipated if **3** exists as a 14-electron complex (see ref 11). However, because several species are present which could act as ligands, the existence of 16-electron Ru complexes cannot be excluded.

[13] Trost, B. M.; Machacek, M.; Schnaderbeck, M. J. *Org. Lett.* **2000**, *2*, 1761.

[14] Trost, B. M.; Martinez, J. A.; Kulawiec, R. J.; Indolese, A. F. *J. Am. Chem. Soc.* **1993**, *115*, 10402. However, Cp*Ru (COD)Cl catalyzes the coupling of alkynes and allyl alcohols: Dérien, S.; Jan, D.; Dixneuf, P. H. *Tetrahedron* **1996**, *52*, 5511; Dérien, S.; Ropartz, L.; Le Paih, J.; Dixneuf, P. H. *J. Org. Chem.* **1999**, *64*, 3524.

[15] Cf. corresponding process in Pd-catalyzed reactions, Trost, B. M.; Chung, J. Y. L. *J. Am. Chem. Soc.* **1985**, *107*, 4586; Trost, B. M.; Lee, D. C. *J. Org. Chem.* **1989**, *54*, 2271; Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255; Trost, B. M.; Romero, D. L.; Rise, F. *J. Am. Chem. Soc.* **1994**, *116*, 4268.