ORGANIC LETTERS

2003
Vol. 5, No. 10
1725−1728

$W(CO)_5(L)$-Catalyzed Endo-Selective Cyclization of Allenyl Silyl Enol Ethers: An Efficient Method for the Cyclopentene Annulation onto α,*β*-Unsaturated Ketones

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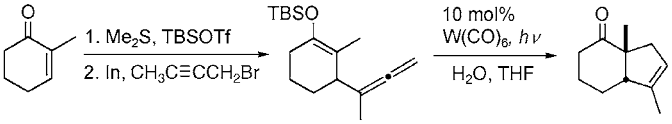
Received March 1, 2003

ABSTRACT



Indium-mediated allenylation of α,*β*-unsaturated ketones in the presence of *tert*-butyldimethylsilyl triflate and dimethyl sulfide gives 6-siloxy-1,2,5-trienes, which undergo $W(CO)_5(L)$-catalyzed 5-endo cyclization to give the corresponding cyclopentene derivatives in good yield. Furthermore, this novel $W(CO)_5(L)$-catalyzed cyclization of allenyl silyl enol ethers proceeds in a 6-endo manner when 5-siloxy-1,2,5-trienes are employed as a substrate. In these reactions, effective electrophilic activation of allenyl compounds for attack by silyl enol ethers is achieved using a catalytic amount of $W(CO)_6$.

Allenyl compounds play an important role in synthetic reactions due to their unique structure and high reactivity.[1] Although π-allyl palladium(II) complex formation by the carbopalladation of allenyl compounds with palladium(II) compounds, followed by attack on the complex by nucleophiles, has been studied extensively (eq 1),[2,3] simple transition metal-catalyzed electrophilic activation of allenyl compounds for attack by carbon nucleophiles has remained relatively unexplored despite its high potential as a method for the construction of carbon frameworks (eq 2).[2,4−6]

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(1) (a) *The Chemistry of Ketenes, Allenes, and Related Compounds*; Patai, S., Ed; John Wiley & Sons: New York, 1980; Part 1. (b) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley & Sons: New York, 1984.

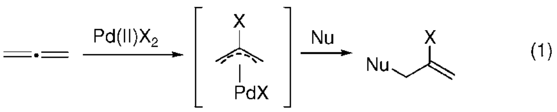
(2) For a review on the palladium-catalyzed reaction of allenes, see: Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067−3125.

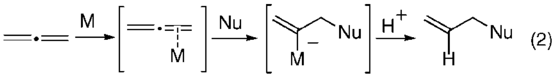
(3) For recent examples of the palladium-catalyzed carbocyclization of allenyl compounds, see: (a) Ma, S.; Zhao, S. *Org. Lett.* **2000**, *2*, 2495−2497. (b) Kang, S.-K.; Baik, T.-G.; Kulak, A. N.; Ha, Y.-H.; Lim, Y.; Park, J. *J. Am. Chem. Soc.* **2000**, *122*, 11529−11530. (c) Shin, S.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2001**, *123*, 8416−8417. (d) Kang, S.-K.; Ha, Y.-H.; Ko, B.-S.; Lim, Y.; Jung, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 343−345. (e) Franzén, J.; Löfstedt, J.; Dorange, I.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **2002**, *124*, 11246−11247.

(4) For a review on the transition-metal catalyzed nucleophilic cyclization of allenyl compounds, see: Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12−21.

(5) Transition metal-catalyzed cyclizations of allenyl compounds by heteronucleophiles have been reported. For recent examples of 5-endo-selective cyclization by oxygen nucleophiles, see: (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285−2288. (b) Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537−2538. (c) Ma, S.; Yu, Z. *Angew. Chem., Int. Ed.* **2002**, *41*, 1775−1778.

10.1021/ol034365a CCC: \$25.00





We recently reported a concise method for cyclopentene annulation onto α,*β*-unsaturated ketones utilizing indium-mediated propargylation in the presence of *tert*-butyldimethylsilyl triflate and dimethyl sulfide, followed by W(CO)$_5$(thf)-catalyzed 5-endo-dig cyclization of the silyl enol ether generated onto the terminal alkyne.[7] One specific feature of this reaction is that cyclopentene derivatives having a double bond at the *β*,*γ*-position of the carbonyl group are obtained selectively. We expected that by finding an appropriate method for 1,4-allenylsilylation of α,*β*-unsaturated ketones, followed by transition metal-catalyzed 5-endo cyclization of the silyl enol ether generated onto the transition metal-activated allenyl moiety, another useful cyclopentene annulation could be achieved where the double bond of the product is situated at the *γ*,*δ*-position of the carbonyl group. Thus, these two procedures would constitute complementary methods for cyclopentene annulation with control of double bond position (Figure 1).

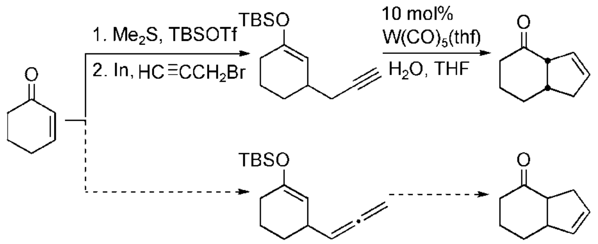
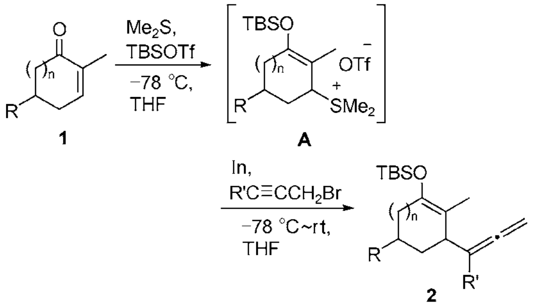


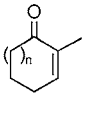
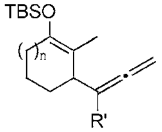
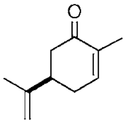
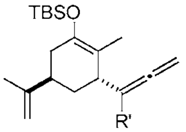
Figure 1. Cyclopentene Annulation onto Cyclic α,*β*-Unsaturated Ketones.

In the first place, allenylation in the presence of silyl triflate and dimethyl sulfide was examined.[8] As it is known that indium reagents prepared from propargyl bromides having a substituent on the terminal alkyne react with aldehydes or ketones to give allenyl compounds as the major product,[9] we expected that 1,4-allenylsilylation could be achieved by employing indium reagents prepared from substituted propargyl bromides and indium metal.

Thus, to a THF solution of 2-methylcyclohex-2-en-1-one **1a** were added in succession *tert*-butyldimethylsilyl triflate and dimethyl sulfide to afford in situ 3-*tert*-butyldimethylsiloxycyclohex-2-enylsulfonium salt **A**, which was treated at −78 °C with the indium reagent prepared from 1-bromo-2-butyne and indium metal. The mixture was slowly warmed to room temperature overnight to give the desired allenylated silyl enol ether **2a** in 77% yield. As summarized in Table 1, the present preparative method was found to be generally applicable to 1,4-allenylsilylation of cyclic α,*β*-unsaturated ketones when propargyl bromides having a substituent on the terminal alkyne were employed.

Table 1. Indium-Mediated 1,4-Allenylsilylation of Cyclic α,*β*-Unsaturated Ketones



substrate	propargyl bromide	product	yield/%
			
1a: n = 1	R' = Me	**2a**	77
1b: n = 0	R' = Me	**2b**	61
			
1c	R' = Me	**2c**	86
1d	R' = *n*-Bu	**2d**	49
1e	R' = Ph	**2e**	44

We next examined the cyclization reaction using the 6-siloxy-1,2,5-trienes generated as a substrate. When **2a** was treated with an equimolar amount of preformed W(CO)$_5$(thf) in the presence of 3 molar equiv of H_2O, **2a** was completely consumed at room temperature within 3 days to give the 5-endo-cyclized ketone **3a** as a single product in 71% yield. Furthermore, the reaction time was greatly diminished (4 h) by carrying out the reaction with an equimolar amount of W(CO)$_6$ under direct photoirradiation at 40 °C to give the same product **3a** in 94% yield.[10] This reaction could be carried out successfully even with a catalytic amount (as little as 10 mol %) of W(CO)$_6$ under

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(6) For recent examples of 5-endo-selective cyclization by nitrogen nucleophiles, see: (a) Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Osawa, E.; Yamaoka, Y.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1999**, *64*, 2992−2993. (b) Rutjes, F. P. J. T.; Tjen, K. C. M. F.; Wolf, L. B.; Karstens, W. F. J.; Schoemaker, H. E.; Hiemstra, H. *Org. Lett.* **1999**, *1*, 717−720.

(7) Iwasawa, N.; Miura, T.; Kiyota, K.; Kusama, H.; Lee, K.; Lee, P. H. *Org. Lett.* **2002**, *4*, 4463−4466.

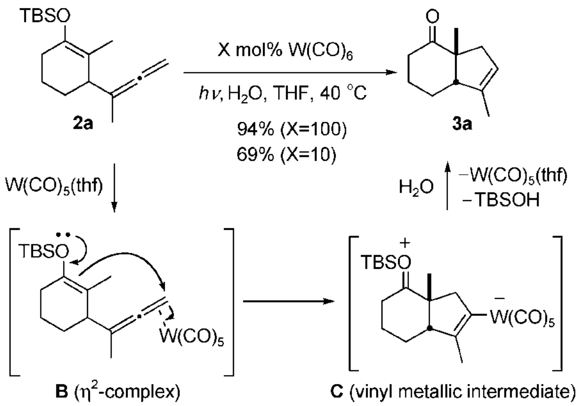
(8) For another example of 1,4-addition with indium reagents in the presence of *t*-butyldimethylsilyl triflate and dimethyl sulfide, see: Lee, P. H.; Lee, K.; Kim, S. *Org. Lett.* **2001**, *3*, 3205−3207.

(9) For an example of In-mediated propargylation or allenylation, see: (a) Isaac, M. B.; Chan, T.-H. *J. Chem. Soc., Chem. Commun.* **1995**, 1003−1004. (b) Yi, X.-H.; Meng, Y.; Hua, X.-G.; Li, C.-J. *J. Org. Chem.* **1998**, *63*, 7472−7480. (c) Nair, V.; Jayan, C. N.; Ros, S. *Tetrahedron* **2001**, *57*, 9453−9459. (d) Lee, K.; Seomoon, D.; Lee, P. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3901−3903.

(10) It is known that photoirradiation enhances ligand substitution on the W(CO)$_5$(L) complex; see: Kirtley, S. W. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds; Pergamon Press: Oxford, UK, 1982; Vol. 3, pp 1079−1148.

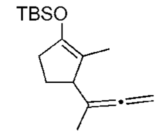
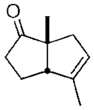
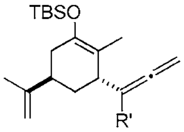
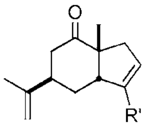
photoirradiation to give **3a** in 69% yield. Other metal complexes such as Pd(OAc)$_2$, PdCl$_2$, and PtCl$_2$, failed to give better results.[11] When **2c** was reacted in the presence of 3 molar equiv of D_2O instead of H_2O, the degree of deuterium incorporation at the olefinic proton of **3c** was more than 90%.[12] On the basis of these results, the reaction is assumed to proceed as follows: treatment of **2a** with W(CO)$_6$ under photoirradiation would give the allene−W(CO)$_5$ η^2 complex **B**. Next, intramolecular attack of the silyl enol ether occurs on the distal carbon of the allene moiety to give the vinylmetallic intermediate **C**. Finally, the carbon−tungsten bond is protonated to give the 5-endo-cyclized ketone **3a**, with regeneration of the W(CO)$_5$(thf) (Scheme 1).

Scheme 1



We then examined the generality of this reaction employing a variety of 6-siloxy-1,2,5-trienes as summarized in Table 2. The five-membered substrate **2b** also gave the 5-endo-cyclized ketone **3b** in good yield. Varying the substituent on the allene moiety (**2c**−**e**) did not lower the yield. Thus, this 5-endo-trig cyclization of 6-siloxy-1,2,5-trienes constitutes another useful method for cyclopentene annulation onto α,*β*-unsaturated ketones utilizing a novel W(CO)$_5$(L)-catalyzed electrophilic activation of the allene moiety toward attack by neutral carbon nucleophiles.

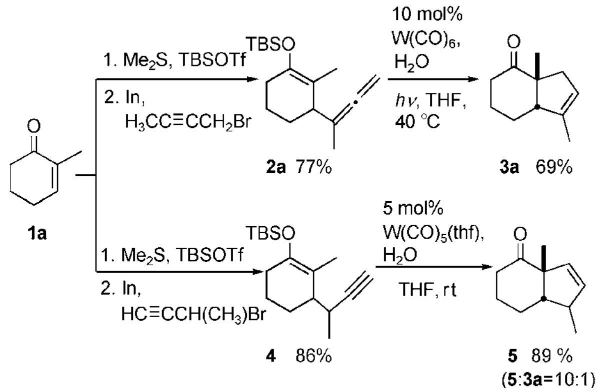
Table 2. Stoichiometric and Catalytic Endo-Selective Cyclization of 6-Siloxy-1,2,5-trienes[a]

substrate	product	yield(%) W(CO)$_6$ 100 mol%	10 mol%
 TBSO **2b**	 O **3b**	83	74
 TBSO R'	 O R'		
2c R' = Me	**3c**	93	74
2d R' = *n*-Bu	**3d**	80	51
2e R' = Ph	**3e**	99	86

[a] General procedure: a THF solution of the substrate, W(CO)$_6$, and 3 molar equiv of H_2O was irradiated at ambient temperature for 4−20 hours.

The following two reactions clearly demonstrate the synthetic utility of these protocols. Thus, starting from isomeric propargyl bromides, that is, 1-bromo-2-butyne and 3-bromo-1-butyne, either 6-siloxy-1,2,5-triene **2a** or 6-siloxy-5-en-1-yne **4** could be synthesized selectively, and subsequent W(CO)$_5$(L)-catalyzed reaction gave either regioisomer of the cyclopentene annulated products **3a** or **5** with good to perfect control of the position of the double bond (Scheme 2).[13]

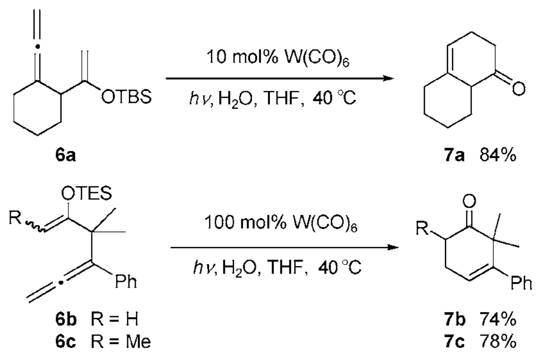
Scheme 2



We next applied this novel reaction to other types of allenyl silyl enol ethers. Thus, the reaction of 5-siloxy-1,2,5-triene **6a** with 10 mol % W(CO)$_6$ under photoirradiation in toluene proceeded smoothly to give the 6-endo cyclized ketone **7a** in good yield. The same type of 6-endo cyclization reaction was found to proceed similarly with acyclic substrates **6b** and **6c**, although an equimolar amount of W(CO)$_6$ was required to obtain a good yield of the products **7b** and **7c** (Scheme 3).

In conclusion, we have developed a novel method for the cyclization of allenyl silyl enol ethers in an endo manner

Scheme 3



using a catalytic amount of $W(CO)_6$ and realized an efficient method for cyclopentene annulation onto α,β-unsaturated ketones. In this reaction, effective activation of the allene moiety is achieved by complexation with $W(CO)_5$, allowing attack by neutral carbon nucleophiles. Further studies to expand the utility of this reaction are in progress in our laboratory.

Acknowledgment. This research was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan, Grant R02-2002-000-00046-0 of the Basic Research Program of the Korea Science & Engineering Foundation, and the CMDS at KAIST. T. M. has been granted a Research Fellowship of the Japan Society for the Promotion of Science for Young Scientists.

Supporting Information Available: Preparative methods and spectral and analytical data of compounds **2a**−**7c** and ^1H and ^{13}C NMR spectra for compounds **2a** and **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Use of $Pd(OAc)_2$ or $PdCl_2$ did not give **3a** at all. When $PtCl_2$ was employed, a low yield of **3a** was obtained along with a complex mixture of unidentified products.

(12) Vinylmetallic intermediate underwent efficient deuteration at the carbon−tungsten bond by means of D_2O; see: Barluenga, J.; Ballesteros, A.; Rúa, R. B.; Santamaría, J.; Rubio, E.; Tomás, M. *J. Am. Chem. Soc.* **2003**, *125*, 1834−1842.

(13) While **3a** was obtained as a single product, **5** was accompanied by a small amount (about 10% of the product) of the olefinic regioisomer **3a**. The reason for the formation of this compound is not yet obvious.