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W(CO)$_5$·THF-Catalyzed Endo-Selective Cyclization of ω-Acetylenic Silyl Enol Ethers

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The development of new types of cyclization reaction for the construction of carbocycles is an important focus of synthetic organic chemistry.[1] One problem requiring fresh approaches is the achievement of reactions proceeding selectively through the endo mode, which remains relatively unexplored compared with exo cyclizations.[1,2] It is known that terminal alkynes and carbonyl complexes of low-valent group 6 metals such as M(CO)$_5$·L (M = Cr, Mo, W; L = THF, Et$_3$N, etc.) are in equilibrium with their η^2-alkyne complexes and/or their vinylidene complexes.[3] Although these complexes are expected to have electrophilic character, their use in synthetic reactions has been quite limited.[4,5] We thought of employing a substrate having both a terminal alkyne and a nucleophilic group in the molecule, expecting that a formal endo mode of cyclization could be achieved via its vinylidene complex, the central carbon of which has high electrophilicity.[4] In this paper, we report an endo-selective cyclization of ω-acetylenic silyl enol ethers by the *catalytic use* of W(CO)$_5$·THF or related species.

First, the reaction was examined employing silyl enol ether **1** as substrate and using a stoichiometric amount of W(CO)$_5$·THF. When **1** was treated with 1.5 equiv of preformed W(CO)$_5$·THF[6] at room temperature for 2 days, it was completely consumed and a cyclopentene derivative **2**, produced by intramolecular attack of the silyl enol ether on the terminal alkyne in an endo manner, was obtained in moderate yield. Other group 6 metal complexes such as Cr(CO)$_5$·THF and Mo(CO)$_5$·THF failed to give better results, but the reaction did proceed in better yield in the presence of a proton source such as methanol or H_2O. Thus, the cyclopentene derivative **2** was obtained in 80% yield when the same reaction was carried out at room temperature in the presence of 2 equiv of H_2O. At present the reaction is assumed to proceed as follows: treatment of the silyl enol ether **1** with W(CO)$_5$·THF generates a small amount of the η^2-alkyne complexes **A** and/or the vinylidene complex **B**. When this complex is formed, the alkyne part becomes electron deficient due to the electron-withdrawing nature of W(CO)$_5$ and intramolecular attack of the silyl enol ether occurs to give the vinyl metallic intermediate **C** or **D**, which is finally protonated to give the cyclopentene **2**[7,16] (Scheme 1).

Although transition-metal-promoted, intramolecular attack of silyl enol ethers on alkenes or alkynes has several precedents,[8] in most cases a stoichiometric amount of palladium(II)[9] or mercuric(II)[10] compounds has been employed. On the other hand, this W(CO)$_5$·THF-promoted reaction proceeds in the presence of H_2O, and hence, it was expected that W(CO)$_5$·THF would be regenerated on protonation of the vinyl metallic intermediate **C** or **D**. In practice, the reaction was found to proceed even with a catalytic amount of W(CO)$_5$·THF. For example, treatment of **1** with 30 mol % of W(CO)$_5$·THF[11] in the presence of 2 equiv of H_2O at room temperature for 3 days gave the same product **2** in 73% yield. Even 10 mol % of W(CO)$_5$·THF gave the product in 56% yield, although in this case about 40% of the starting material **1** was recovered. Reactions of representative substrates are summarized in Table 1. Several features of the reaction are as follows:

(1) In every case, the reaction proceeds at room temperature in the presence of H_2O or methanol to give cyclized β,γ-unsaturated ketones in good yield without isomerization of the double bond,[12] even using only 10 mol % of W(CO)$_5$·THF.

(2) At present, the reaction is specific for terminal alkynes. Although the reaction of *o*-ethynylacetophenone derivative **3a** proceeds cleanly to give silylated 1-naphthol derivative **4** in high yield, the corresponding reaction of **3b** containing an internal alkyne gave no cyclized product under similar reaction conditions.

(3) The most characteristic feature of this reaction is that the endo mode of cyclization occurs more readily than in other related

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[1] (a) Thebtaranonth, C.; Thebtaranonth, Y. *Cyclization Reactions*; CRC Press: Boca Raton, FL, 1994. (b) Giese, B.; Kopping, B.; Göbel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. *Org. React.* **1996**, *48*, 301. (c) Grigg, R.; Sridharan, V. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 299.

[2] For recent examples of endo cyclization, see: (a) Albrecht, U.; Wartchow, R.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 910. (b) Hoffmann, H. M. R.; Herden, U.; Breithor, M.; Rhode, O. *Tetrahedron* **1997**, *53*, 8383. (c) Bruyere, D.; Gaignard, G.; Bouyssi, D.; Balme, G. *Tetrahedron Lett.* **1997**, *38*, 827.

[3] (a) Landon, S. J.; Shulman, P. M.; Geoffroy, G. L. *J. Am. Chem. Soc.* **1985**, *107*, 6739. (b) Szymańska-Buzar, T.; Downs, A. J.; Greene, T. M.; Marshall, A. S. *J. Organomet. Chem.* **1995**, *495*, 163.

[4] (a) McDonald, F. E.; Zhu, H. Y. H. *Tetrahedron* **1997**, *53*, 11061. (b) Cosset, C.; Del Río, I.; Péron, V.; Windmüller, B.; Le Bozec, H. *Synlett* **1996**, 435. (c) Hoye, T. R.; Suriano, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 1154. (d) Parlier, A.; Rudler, H. *J. Chem. Soc., Chem. Commun.* **1986**, 514.

[5] For the review of vinylidene complexes, see: Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197. Bruce, M. I.; Swincer, A. G. *Adv. Organomet. Chem.* **1983**, *22*, 59. For synthetic use of vinylidene or η^2-alkyne intermediates of other transition metals, see: Trost, B. M. *Chem. Ber.* **1996**, *129*, 1313. Bruneau, C.; Dixneuf, P. H. *J. Chem. Soc., Chem. Commun.* **1997**, 507. Merlic, C. A.; Pauly, M. E. *J. Am. Chem. Soc.* **1996**, *118*, 11319. Ohe, K.; Kojima, M.; Yonehara, K.; Uemura, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1823.

[6] W(CO)$_5$·THF was prepared just before use by irradiating a slurry of W(CO)$_6$ in dry THF (concentration about 0.1 mol/L) under Ar for 4 h with a high-pressure Hg lamp.

[7] We monitored the reaction by NMR by carrying it out in THF-d_8. During the course of the reaction, only the starting material and the cyclized product were observed and none of the possible intermediates could be detected.

[8] For the reaction of transition-metal−alkene or −alkyne complexes with nucleophiles, see: (a) McDaniel, K. F. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 601. (b) Hegedus, L. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 4, p 571.

[9] For the reactions of silyl enol ethers with alkenes promoted by palladium(II) complexes, see: (a) Ito, Y.; Aoyama, H.; Hirao, T.; Mochizuki, A.; Saegusa, T. *J. Am. Chem. Soc.* **1979**, *101*, 494. (b) Ito, Y.; Aoyama, H.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 4519. (c) Kende, A. S.; Roth, B.; Sanfilippo, P. J. *J. Am. Chem. Soc.* **1982**, *104*, 1784. (d) Kende, A. S.; Roth, B.; Sanfilippo, P. J.; Blacklock, T. J. *J. Am. Chem. Soc.* **1982**, *104*, 5808.

[10] For the reactions of silyl enol ethers with alkynes promoted by mercury(II) compounds, see: (a) Drouin, J.; Boaventura, M. A.; Conia, J. M. *J. Am. Chem. Soc.* **1985**, *107*, 1726. (b) Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1995**, *60*, 2773. (c) Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1995**, *60*, 5746. (d) Frontier, A. J.; Raghavan, S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 6686.

[11] Based on the amount of W(CO)$_6$ employed.

[12] Products were isolated by SiO_2 (deactivated with 10% H_2O) column chromatography without a detectable isomerization of the double bond.

[13] It has been reported that the $HgCl_2$-promoted reaction of **5** gave no cyclized products. See ref 10a.

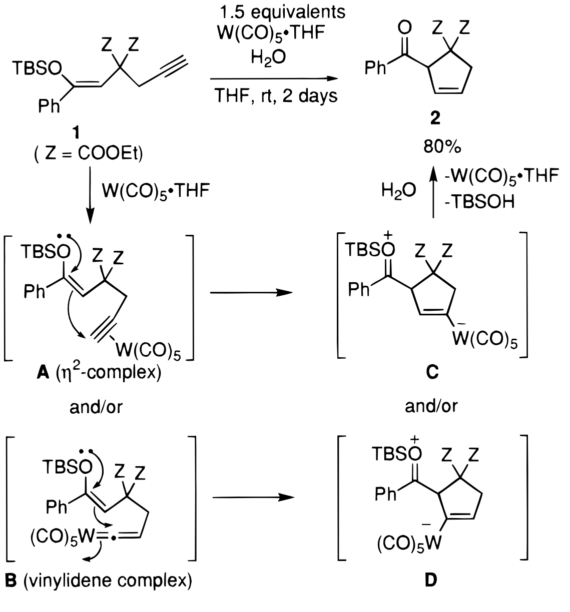
[14] Conia, J. M.; Le Perchec, P. *Synthesis* **1975**, 1.

[15] At present we have no explanation for this solvent effect. The difference of the reaction procedure (the reaction mixture was directly irradiated due to the instability of W(CO)$_5$·L (L = Et_2O or CH_2Cl_2)) is not the main reason for this effect, because the reaction in THF with direct irradiation still gave the exo-cyclized product with high selectively.

[16] To obtain information on the mechanism of this reaction, we have carried out several D_2O experiments and obtained the following results. The reaction of **1** and **5** in the presence of 2 equiv of D_2O revealed that both of the olefinic protons are partially deuterated with the degree of deuteration dependent on the substrate. Furthermore the reaction of **1** and **5** in the presence of 10 equiv of D_2O revealed that the degree of deuterium incorporation at the two olefinic protons was total of about 50%. This result removes the possibility that H−D exchange occurs rapidly during the reaction. On the basis of these results, we at present propose that the reaction proceeds in both ways (through η^2-complex and vinylidene complex) and that the ratio of the two reaction pathways is substrate dependent (for **1**, η^2-complex vs vinylidene complex about 1:1; for **5**, about 3:7 based on the deuterium incorporation).

S0002-7863(97)03317-9 CCC: $15.00

Scheme 1

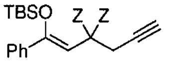
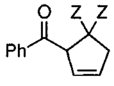
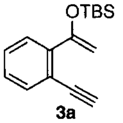
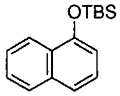
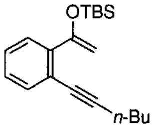
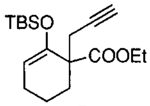
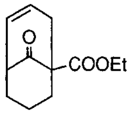
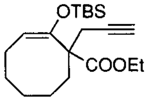
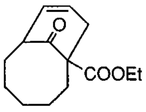
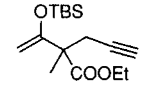
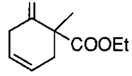
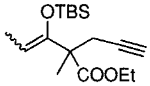
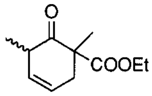


cyclization reactions. For comparison, we ran the $HgCl_2$-promoted reaction using substrates **1**, **3a**, and **9** according to the Conia method.[13] The results were that **1** and **9** did not give any cyclized product but rather the products of alkyne hydration in good yield and the reaction of **3a** gave a moderate yield of 3-methylene-1-indanone, an exo-cyclized product, accompanied by a hydrated derivative, but with no detectable trace of any 1-naphthol compounds. These results indicate that in this $W(CO)_5$•THF-catalyzed reaction the endo mode of cyclization occurs preferentially compared to the $HgCl_2$-promoted reaction.

According to the Conia classification,[14] the cyclizations of **3a**−**11** in Table 1 belong to the α'-type for which the exo mode of cyclization is relatively slower than for α-type substrates in reactions leading to five-membered ring formation.[14] We next examined the reaction of an α-type substrate **13**, and in this case, the exo-cyclized product **14**, thought to be obtained via the η^2-alkyne complex, was obtained in high yield with a catalytic amount of $W(CO)_5$•THF. To obtain the endo-cyclized product selectively, we further examined the reaction of **13** under several different conditions and found that the reaction in less-donating solvents favored the formation of the endo-cyclized product.[15] For example, when the reaction was carried out in diethyl ether under irradiation, a mixture of exo- and endo-cyclized products (**14** and **15**) was obtained in 52% yield in the ratio of 1:1.5. Furthermore, the reaction in CH_2Cl_2 gave the products in 60% yield in good endo selectivity (**14**:**15** = 1:5) (Scheme 2). Thus, even for **13**, which of the substrates examined is thought to be the most susceptible to exo cyclization, we can obtain the endo-cyclized product as the major product by choosing appropriate reaction conditions.

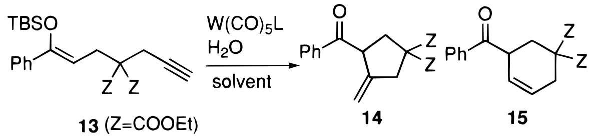
In conclusion, we have developed a new endo-selective cyclization of silyl enol ethers derived from ω-acetylenic ketones requiring only a catalytic amount of $W(CO)_5$•THF complex. Further studies to elucidate the mechanism of this reaction and to expand further its utility are in progress in our laboratory.[16,17]

Table 1. Stoichiometric and Catalytic Cyclization of ω-Acetylenic Silyl Enol Ethers[a]

Starting Material	Product	Yield(%) Amount of $W(CO)_5$•THF		
		1.2-1.5 eq	0.3 eq	0.1 eq
 **1** (Z=COOEt)	 **2**	80	73	56[b]
 **3a**	 **4**	93	93	96
 **3b**		No Reaction		
 **5**	 **6**	88	90	90
 **7**	 **8**	90	93	97
 **9**	 **10**	74	77	64[c]
 **11**	 **12**	80	82	83

[a] General procedure: about 0.1 mol/L THF solution of $W(CO)_5$•THF was prepared by irradiating a THF suspension of $W(CO)_6$ for 4 h with a high-pressure Hg lamp. For the stoichiometric reactions, 2 equiv of H_2O and a substrate were added successively, and the mixture was stirred at room temperature (rt) for 1−2 days. For the catalytic reaction, required amounts of the preformed $W(CO)_5$•THF solution was added to the substrate and then 2 equiv of H_2O were added. The mixture was stirred at rt for 3−5 days (0.3 equiv), or 1 week (0.1 equiv). [b] Compound **1** was recovered in about 40% yield. [c] Acetylenic ketone was recovered in about 15% yield.

Scheme 2



0.1 equiv. of preformed $W(CO)_5$•THF/THF	94% **14** only
1.2 equiv. of $W(CO)_6/Et_2O$, Hg lamp	52% **14** : **15** = 1 : 1.5
1.3 equiv. of $W(CO)_6/CH_2Cl_2$, Hg lamp	60% **14** : **15** = 1 : 5

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Supporting Information Available: Experimental procedures and spectral data for compounds **1**−**15** (82 pages). See any current masthead page for ordering information and Web access instructions.

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(17) After submission of this manuscript, a paper has appeared describing an intramolecular endo-favored cyclization of active methylene compounds onto terminal alkyne using $Mo(CO)_5$•NEt_3 and NaH. See: McDonald, F. E.; Olson, T. C. *Tetrahedron Lett.* **1997**, *38*, 7691.