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W(CO)$_5$-Amine Catalyzed *Exo*- and *Endo*-Selective Cyclizations of ω-Alkynyl Silyl Enol Ethers: A Highly Useful Method for the Construction of Polycyclic Compounds

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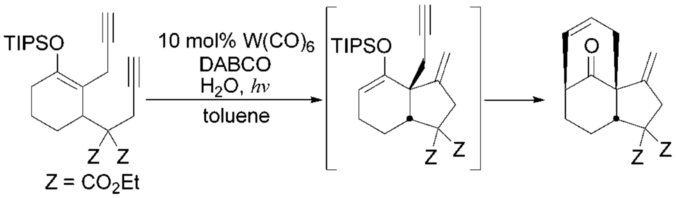
ABSTRACT



A highly useful method for the construction of polycyclic compounds based on the amine-controlled *exo*- and *endo*-selective cyclizations of ω-alkynyl silyl enol ethers catalyzed by W(CO)$_5$(L) is reported. When bis-alkynyl silyl enol ethers were treated with a catalytic amount of W(CO)$_6$, DABCO, and water under photoirradiation, synthetically useful tricyclic ketones were obtained in good yield.

We report herein a highly useful method for the construction of polycyclic compounds based on the amine-controlled *exo*- and *endo*-selective cyclizations of ω-alkynyl silyl enol ethers catalyzed by W(CO)$_5$(L).[1]

Recently, we reported that in the presence of H_2O even a catalytic amount of pentacarbonyltungsten(0) complex promotes cyclization of ω-alkynyl silyl enol ethers. A noteworthy feature of this reaction is that when 7-siloxy-6-en-1-yne derivatives are employed as substrates the competitive cyclization modes (5-*exo* vs. 6-*endo*) could be controlled by choosing the appropriate reaction solvent: use of THF gives *exo*-cyclized products selectively, while use of toluene favors formation of the *endo*-cyclized products.[2,3] The principal reaction pathway is assumed to be as follows: complexation of a tungsten(0) species with the terminal alkyne moiety generates the corresponding π-alkyne complex **A**, making the alkynyl part sufficiently electrophilic to enable *exo*- or *endo*-mode intramolecular nucleophilic attack of the silyl enol ether on an alkynyl carbon to give zwitterionic intermediate **B** or **C**. An additional pathway is also possible: π-alkyne complex **A** may isomerize to vinylidene complex **D**, then nucleophilic attack of the silyl enol ether on the highly electrophilic vinylidene carbon affords the *endo*-cyclized product through the intermediate **E** (Scheme 1).

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[1] For recent examples of the use of M(CO)$_5$(L) in synthesis (M = Cr, Mo, W), see; (a) Dötz, K. H.; Sturm, W. *Organometallics* **1987**, *6*, 1424. (b) McDonald, F. E.; Chatterjee, A. K. *Tetrahedron Lett.* **1997**, *38*, 7687. (c) Cutchins, W. W.; McDonald, F. E. *Org. Lett.* **2002**, *4*, 749. (c) Painter, J. E.; Quayle, P. *Tetrahedron Lett.* **1995**, *36*, 8089. (e) Ohe, K.; Yokoi, T.; Miki, K.; Nishino, F.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 526.

[2] (a) Iwasawa, N.; Maeyama, K.; Kusama, H. *Org. Lett.* **2001**, *3*, 3871. (b) Maeyama, K.; Iwasawa, N. *J. Am. Chem. Soc.* **1998**, *120*, 1928. See also: (c) Maeyama, K.; Iwasawa, N. *J. Org. Chem.*, **1999**, *64*, 1344. (d) Iwasawa, N.; Shido, M.; Kusama, H. *J. Am. Chem. Soc.* **2001**, *123*, 5814. (e) Miura, T.; Iwasawa, N. *J. Am. Chem. Soc.* **2002**, *124*, 518.

[3] For recent examples of nucleophilic *endo*-selective cyclization onto alkynes, see: (a) Kim, K.; Okamoto, S.; Sato, F. *Org. Lett.* **2001**, *3*, 67. (b) Imamura, K.; Yoshikawa, E.; Gevorgyan, V.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 4081. (c) Imamura, K.; Yoshikawa, E.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 5339.

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Scheme 1

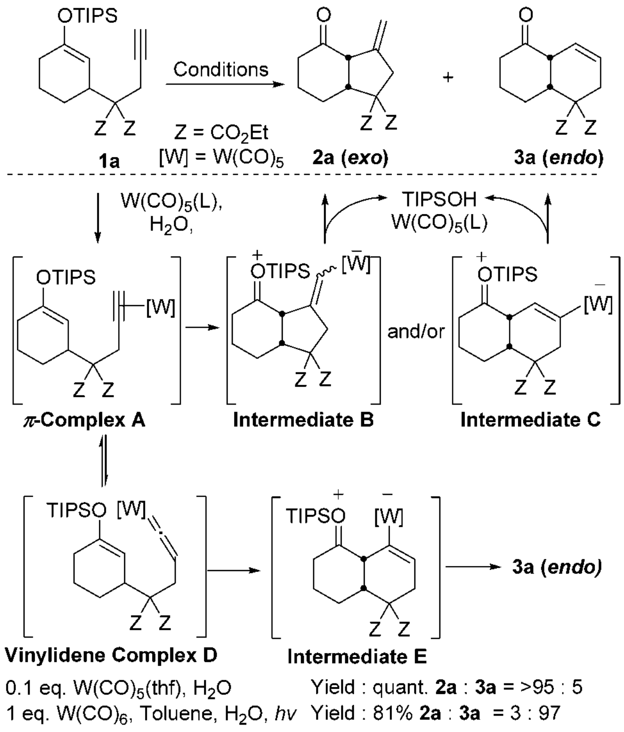
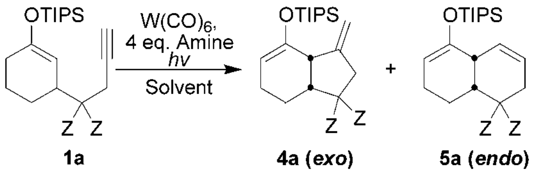


Table 1. Influence of the Amine and the Reaction Solvent on the *Exo* vs. *Endo* Selectivity with **1a** as Substrate



entry	loading of $W(CO)_6$ (equiv)	solvent	amine	yield (%)	**4a**:**5a**
1	1	THF	DABCO	97	95:5
2	0.1	THF	DABCO[b]	92	94:6
3	1	THF	Et_3N	80	91:9
4	1	toluene	DABCO	97	94:6
5	1	toluene	Et_3N	96	53:47
6	1	toluene	n-Bu_3N	98	18:82
7	0.1	toluene	n-Bu_3N	92	17:83

[a] The reactions were usually carried out until **1a** was completely consumed (20 min to 5 h). [b] 2 equiv of DABCO was used.

The zwitterionic intermediates **B**, **C**, and **E** in Scheme 1 contain a silyloxonium moiety, which is hydrolyzed to the corresponding ketone by H_2O. We expected that by carrying out the reaction *in the presence of an amine* instead of H_2O, these silyloxonium intermediates could be converted to silyl enol ethers by deprotonation, and that the generated silyl enol ethers would be available for further carbon−carbon bond-forming reactions. This led to the discovery of novel amine-controlled *exo*- and *endo*-selective cyclizations, and these reactions were further applied to the preparation of synthetically useful polycyclic compounds.

First, *exo*-cyclization of **1a** was investigated by using a stoichiometric amount of $W(CO)_6$ in the presence of various amines (4 equiv) in THF under photoirradiation conditions. Gratifyingly, the presence of tertiary amines did not suppress the reaction, and the expected silyl enol ether, which is produced from the zwitterionic intermediate **B**, **C**, or **E** by deprotonation of the α-proton of the silyloxonium moiety followed by protonation of the tungsten−carbon bond, was obtained as a mixture of 5-*exo*- and 6-*endo*-cyclized products, **4a** and **5a**. In addition, the steric bulk of the amine was found to have a significant effect on *exo* vs. *endo* selectivity, and the use of DABCO, the least sterically demanding amine examined, gave the desired silyl enol ether **4a** with the highest *exo*-selectivity (97% yield, *exo*:*endo* = 95:5, Table 1, Entry 1).[4,5] Importantly, this reaction proceeded even with a catalytic amount of $W(CO)_6$ without significantly decreasing the yield or selectivity.

The results of our examination of the *endo*-cyclization in toluene are summarized in Entries 4−7. In this case, the dependence of *exo*−*endo* selectivity on steric bulkiness of the amine is more explicit. While use of DABCO gave the *exo*-cyclized product **4a** with high selectivity regardless of the solvent used, *endo*-cyclized product **5a** was produced with good selectivity by using bulky tributylamine (98% yield, *exo*:*endo* = 18:82, Entry 6). Again, the reaction proceeded catalytically without loss of chemical yield or selectivity. Thus, both the *exo*- and *endo*-cyclized silyl enol ethers could be obtained in good yield by the appropriate choice of amine.

The reactions of several substrates **1a** to **1e** under both the *exo*- and *endo*-selective conditions described above were examined. As summarized in Table 2, all the *exo*-cyclizations proceeded in high yield with high selectivity by use of a catalytic amount of $W(CO)_6$. For the *endo*-cyclization, a modest to good level of selectivity was realized in most cases.[6] The reaction of 2-methyl-substituted substrate **1b** gave the *endo*-cyclized product as a tetracyclic ketal **6b**.[7]

On the basis of the above results, we next examined the possibility of realizing a tandem cyclization. Bis-alkynyl silyl

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(4) No reaction occurred with amines such as DBU and pyridine, probably because of their strong coordination to tungsten.

(5) When a stoichiometric amount of isolated $W(CO)_5$(dabco) complex was employed at room temperature without photoirradiation, the reaction proceeded with much slower rate at room temperature than the corresponding photoirradiation reaction. It is known that photoirradiation enhances dissociation of an amine from $W(CO)_5$(amine) complexes, see; Kirtley, S. W. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds; Pergamon Press: Oxford, UK, 1982; Vol. 3, p 1079.

(6) We are currently pursuing research to clarify the effect of the amines on the *exo* vs. *endo* selectivity.

(7) The tetracyclic ketals **6b** and **6e** were produced as follows: nucleophilic attack of the ester carbonyl on the silyloxonium moiety results in the tricyclic intermediates **F**. Then the alkenyl tungsten attacks the oxonium moiety to give carbene intermediates, which finally give **6** by a 1,2-hydrogen shift.

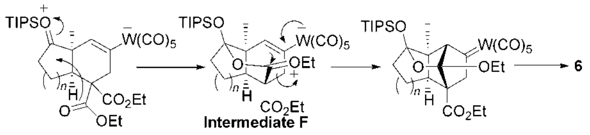
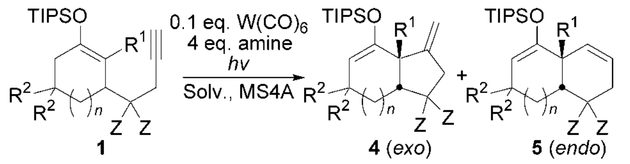
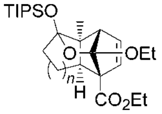


Table 2. *Exo*- and *Endo*-Selective Cyclization of Cyclic Silyl Enol Ethers **1**



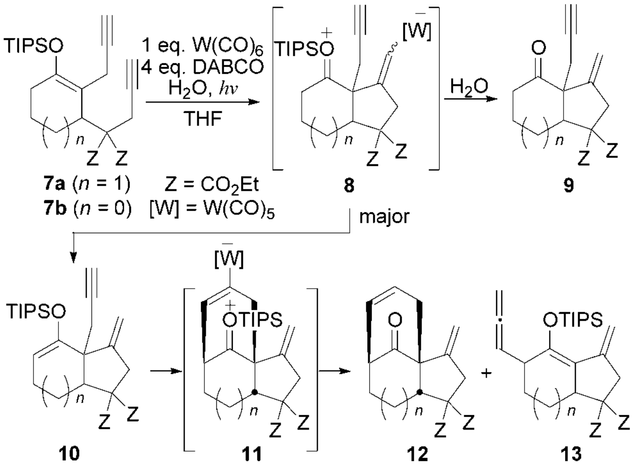
substrate			conditions A[a]		conditions B[b]	
n	R^1	R^2	yield (%)	*exo*:*endo*	yield (%)	*exo*:*endo*
1	H	H (**1a**)	92[c,d]	94:6	92[c,d]	17:83
1	Me	H (**1b**)	quant	>99:1	73[e]	11:89[f]
1	H	Me (**1c**)	95[c,g]	95:5	83[c]	20:80
0	H	H (**1d**)	88	90:10[h]	97	16:84[h]
0	Me	H (**1e**)	quant	>99:1	90	10:90[i]

[a] Conditions A: DABCO, THF, *hν*, 1 to 18.5 h. For the details of the reaction time, see the Supporting Information. [b] Conditions B: *n*-Bu$_3$N, toluene, *hν*, 2 to 21 h. For the details of the reaction time, see the Supporting Information. [c] Without MS4A [d] 2 equiv of DABCO was used. [e] *Exo*-cyclized ketone (**2b**) was also isolated in 13% yield. [f] *Endo*-cyclized product was obtained as **6b**. **5b** was not detected. [g] 0.3 equiv of W(CO)$_6$ was used. [h] **4** and **5** were obtained as a regioisomeric mixture. [i] The *endo*-cyclized product was a mixture of **5e** and **6e** in the ratio of 8:1.



6b *n* = 2
6e *n* = 1

Table 3. Tandem Cyclization of Bis-Alkynyl Silyl Enol Ethers **7**



substrate	loading of H$_2$O (equiv)	reaction time	yield (%) **10**	**12 (9)**[a]	**13**
7a	none	30 min	32	15	19
7a	1	2 h		85	10
7a	5	2 h		70 (17)	9
7a[b]	10	11 h		80	10
7b	5	8 h		69 (10)	

[a] **9** and **12** were obtained as an inseparable mixture. Numbers in parentheses represent the yield of **9** determined by integration of the ^{1}H NMR spectra. [b] The reaction was carried out with 0.1 equiv of W(CO)$_6$ and 1 equiv of DABCO in toluene.

enol ethers **7** were chosen as substrates, expected to give tricyclic compounds **12**, having a carbon skeleton commonly found in naturally occurring compounds. In this case, a possible difficulty lies in the fact that the second cyclization requires H$_2$O to hydrolyze the zwitterionic intermediate **11**,[8] while the presence of H$_2$O could potentially cause hydrolysis of the first zwitterionic intermediate **8** to give ketone **9**. Thus the amount of H$_2$O might be crucial for the success of this tandem cyclization. When **7a** was irradiated in THF in the presence of W(CO)$_6$ and DABCO without adding H$_2$O, the expected tricyclic ketone **12a** was obtained in 15% yield, accompanied by 19% of the allene **13a**, which was produced via C−C bond cleavage of the zwitterionic intermediate **11a**.[9] The same reaction was next examined in the presence of H$_2$O. Although excess water (5 equiv) gave the monoalkynyl ketone **9a** generated by hydrolysis of the first zwitterionic intermediate **8**, reaction with 1 equiv of H$_2$O and 4 equiv of DABCO gave tricyclic ketone **12a** in 85% yield. Furthermore, this tandem cyclization could be performed under catalytic conditions without lowering the yield of **12a** by carrying out the reaction in toluene. Five-membered substrate **7b** also gave the corresponding tricyclic ketone **12b** having the basic carbon skeleton of the cedranes. Thus we can prepare synthetically useful, tricyclic compounds utilizing this W(CO)$_5$(L)-catalyzed tandem cyclization in the presence of DABCO.

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Supporting Information Available: Preparative methods and spectral and analytical data of compounds **1**−**12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Deprotonation of the intermediate **11** would violate Bredt's rule.
(9) The allene **13** is thought to be produced as shown below.