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Efficient Control of π-Alkyne and Vinylidene Complex Pathways for the $W(CO)_5(L)$-Catalyzed Synthesis of Two Types of Nitrogen-Containing Bicyclic Compounds

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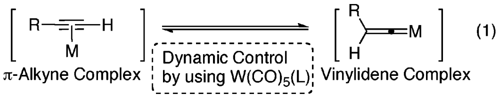
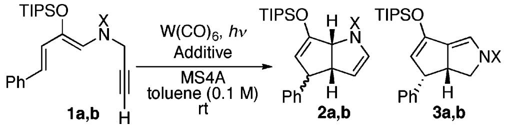
Recently, electrophilic activation of alkynes through π-complex formation has extensively been studied for the construction of useful cyclic carbon skeletons using a variety of transition-metal complexes such as Au(I),[1a−e] Au(III),[1a,c,e] Pt(II),[1a,b, 1d,e] Ru(II),[1a,b, 1e] and so on.[2] Utilization of vinylidene complexes generated from terminal alkynes has also emerged as an attractive method for the unique transformations of terminal alkynes,[3] however, a limited number of examples have been reported of their use for catalytic C−C bond formations.[4,5] Moreover, control of these two reaction pathways of terminal alkynes simply by slightly changing the reaction conditions has rarely been achieved, in particular, for the catalytic construction of carbon skeletons (eq 1).[6] In this paper is described successful control of π-alkyne- and vinylidene-complex pathways in the $W(CO)_5(L)$-catalyzed cyclization of terminal alkynes bearing the siloxy diene moiety for the construction of synthetically useful 2-aza- and 3-azabicyclo[3.3.0]octane skeletons, respectively.



(1)

According to the previously established protocol for the $W(CO)_5$-(L)-catalyzed geminal carbofunctionalization,[7] we first examined the reaction of ω-acetylenic dienol silyl ether **1a** containing NTs part in the tether. When the reaction was carried out with 10 mol % of $W(CO)_6$ in toluene in the presence of MS 4A under photo-irradiation, the desired 2-azabicyclo[3.3.0]octane **2a** was obtained in 68% yield as a mixture of diastereomers (Table 1, entry 1). Quite interestingly, treatment of **1a** with 100 mol % of $W(CO)_6$ in the presence of 100 mol % of NEt_3 under the same reaction conditions gave another bicyclic compound **3a**, which was found to have 3-azabicyclo[3.3.0]octane skeleton, in 80% yield without formation of **2a** (entry 2). Other amines such as n-Bu_3N and DABCO were also effective for this reaction (entries 3, 4). However, when the amount of $W(CO)_6$ was reduced to 10 mol %, the yield of the 3-aza derivative **3a** became considerably lower (entries 5, 6). Further examination of several reaction parameters revealed that use of *N*-Ms derivative **1b** instead of *N*-Ts derivative **1a** improved the yield of the products considerably. Thus, either reaction in the absence or presence of n-Bu_3N proceeded efficiently even with 10 mol % of $W(CO)_6$ to give 2-aza- or 3-azabicyclo[3.3.0]octane in high yield (entries 7, 9). The latter reaction proceeded even with 3 mol % of $W(CO)_6$ without significantly decreasing the yield (entry 10). The structure of **3b** was confirmed by X-ray analysis after hydrolysis of the silyl enol ether moiety.

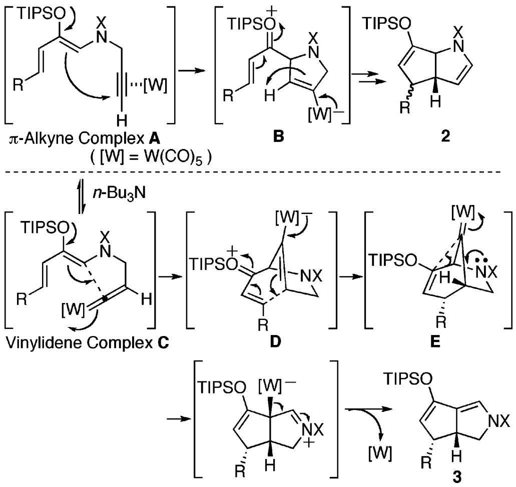
Table 1. $W(CO)_5(L)$-Catalyzed Reaction of Dienol Silyl Ethers **1a**,**b**



entry	X		$W(CO)_6$ (mol %)	additive (100 mol %)	time	yield (%) 2 (α-Ph/β-Ph)	yield (%) 3
1	Ts	**1a**	10	−	1.5 h	68 (67:33)	0
2			100	Et_3N	15 min	0	80
3			100	n-Bu_3N	1 h (15 min)[a]	0 (4)[a]	57 (73)[a]
4			100	DABCO[b]	40 min	0	81
5			10	Et_3N	2 h	0	0
6			10	n-Bu_3N	2 h	0	32
7	Ms	**1b**	10	−	1.5 h	85 (60:40)	0
8			10	Et_3N	2 h	0	61
9			10	n-Bu_3N	2 h	0	93
10			3	n-Bu_3N[c]	3.5 h	0	92

[a] Dilution conditions (0.01 M). [b] Run using 50 mol %. [c] Run using 30 mol %.

Scheme 1. Proposed Reaction Mechanism



The proposed reaction mechanism is shown in Scheme 1. The reaction in the absence of the amine is thought to proceed in a similar manner as previously proposed.[7] Thus, the alkenyl metallic moiety in the zwitterionic intermediate **B**, produced by 5-endo nucleophilic cyclization of the enol silyl ether part to the π-alkyne complex **A**, attacked the α,β-unsaturated silyloxonium moiety at the position β to the metal to generate bicyclic unstabilized carbene complex, which underwent a 1,2-hydrogen shift to give 2-azabicyclo[3.3.0]octane **2**. On the other hand, formation of 3-azabicyclo[3.3.0]octane derivative **3** by the reaction in the presence of the amine is more complex and could be explained as follows: the amine facilitated isomerization of π-alkyne complex **A** to their vinylidene complex **C**,[8] and then, nucleophilic attack of the enol silyl ether part to the vinylidene carbon occurred to afford zwitterionic intermediate **D**. Then, the resulting alkenyl metallic species reacted with the α,β-unsaturated silyloxonium moiety at the position β to the metal to generate the bridged-carbene complex intermediate **E**, which further underwent 1,2-alkyl migration assisted by electron donation from the nitrogen atom to give 3-azabicyclo[3.3.0]octane

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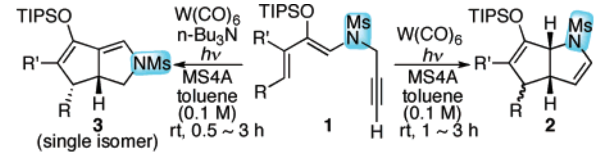
Table 2. $W(CO)_5(L)$-Catalyzed Reaction of Dienol Silyl Ethers (**1b**−**g**)

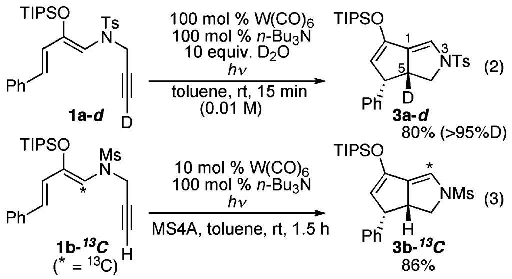


entry	R	R′		$W(CO)_6$ (mol %)	n-Bu_3N (mol %)	yield (%) (α-R/β-R)
1	Ph	H	**1b**	10	−	**2b**: 85 (60:40)
				3	30	**3b**: 92
2	2-furyl	H	**1c**	5	−	**2c**: 70 (60:40)
				5	50	**3c**: 82
3	1-naphthyl	H	**1d**	30	−	**2d**: 64 (40:60)
				10	100	**3d**: 74
4	Ph	Me	**1e**	30	−	**2e**: 65 (47:53)
				5	50	**3e**: 80
5	*i*-Pr	H	**1f**	10	−	**2f**: 67 (60:40)[a]
				10	10	**3f**: 50 (**2f**: 10%)[b]
6	*c*-hexyl	H	**1g**	10	−	**2g**: 74 (60:40)[a]
				10	10	**3g**: 59 (**2g**: 11%)[b]

[a] Dilution conditions (0.01 M). [b] Dilution conditions (0.01 M) in hexane.

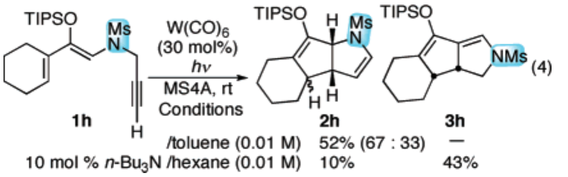
derivative **3**. $W(CO)_5(L)$ was regenerated at the last step, and thus the reaction proceeded catalytically.

To support this proposed mechanism in the presence of the amine, we carried out deuterium- and ^{13}C-labeling experiments. When the deuterated substrate **1a-*d*** was subjected to the same reaction conditions, 3-azabicyclo[3.3.0]octane derivative **3a-*d*** with the deuterium at the 5-position (46% D incorporation) was obtained in 82% yield (other positions were not deuterated). The reaction in the presence of 10 equiv of D_2O was also examined to prevent H−D exchange of the terminal alkyne proton, and the degree of deuterium incorporation increased to >95% (80% yield) (eq 2). More significantly, when the reaction of ^{13}C-labeled substrate **1b-^{13}*C*** was examined, 3-azabicyclo[3.3.0]octane derivative **3b-^{13}*C*** with the ^{13}C at the 2-position was obtained in 86% yield (eq 3). These results are consistent with the proposed mechanism; that is, the reaction proceeded via vinylidene complex formation and 1,2-alkyl migration from intermediate **E**.



Next, generality of this control of π-alkyne and vinylidene complex pathways was examined with several substrates, with the results being summarized in Table 2. When substrates having an aryl group at the diene terminus were employed, the corresponding 2-azabicyclo[3.3.0]octanes **2** and 3-azabicyclo-[3.3.0]octanes **3** were obtained in good yield by carrying out the reaction in the absence or presence of n-Bu_3N, respectively (entries 1−3). Even the reaction of a tetrasubstituted diene **1e** proceeded smoothly to afford the corresponding substituted 2- and 3-azabicyclo[3.3.0]octane in good yield (entry 4). Alkyl-substituted dienes could also be employed to give the corresponding bicyclic compounds in reasonable yield (entries 5 and 6). In these cases, small amounts of 2-aza derivatives were obtained in the amine-promoted reaction.

Additionally, the reaction could be applied to a dienol silyl ether **1h** having a cyclohexenyl group at the diene moiety, and two types of tricyclic product were obtained in reasonable yield without problem (eq 4).



In summary, we have succeeded in controlling the π-alkyne and vinylidene complex pathways by using a catalytic amount of $W(CO)_5(L)$ and an amine. Very rare control of these two catalytic reaction pathways simply by slightly changing the reaction conditions was achieved. Control of π-alkyne and vinylidene complex pathways can be a new method for the catalytic transformation of alkyne to afford two types of products starting from the same terminal alkynes.

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Supporting Information Available: Preparative methods and spectral and analytical data of compounds **1**−**3** (PDF) and X-ray data for the derivatives of **2a** and **3b** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For recent reviews of electrophilic activation of alkynes, see; (a) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (b) Bruneau, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 2328. (c) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (d) Nieto-Oberhuber, C.; López, S.; Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 5916. (e) Echavarren, A. M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431.

(2) For recent reviews of electrophilic activation of alkynes by using other transiton-metal complexes, (a) Yamamoto, Y. *J. Org. Chem.* **2007**, *72*, 7817. (b) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079. (c) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285.

(3) For reviews on metal vinylidene chemistry, see: (a) Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197. (b) Bruce, M. I.; Swincer, A. G. *Adv. Organomet. Chem.* **1983**, *22*, 59. (c) Wakatsuki, Y. *J. Organomet. Chem.* **2004**, *689*, 4092.

(4) For recent reviews on the catalytic C−C bond formations utilizing vinylidene complex as a key intermediate, see: (a) Bruneau, C.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 2176. (b) Varela, J. A.; Saá, C. *Chem. Eur. J.* **2006**, *12*, 6450. (c) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695. (d) Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311.

(5) For recent examples on the catalytic C−C bond formations utilizing vinylidene complex, see: (a) Kim, H.; Goble, S. D.; Lee, C. *J. Am. Chem. Soc.* **2007**, *129*, 1030. (b) Odedra, A.; Datta, S.; Liu, R.-S. *J. Org. Chem.* **2007**, *72*, 3289. (c) Bigeault, J.; Giordano, L.; de Riggi, I.; Gimbert, Y.; Buono, G. *Org. Lett.* **2007,** *9*, 3567.

(6) We have already succeeded in controlling π-alkyne- and vinylidene-complex pathways in the $W(CO)_5(L)$-promoted reaction of *o*-ethynylphenyl ketone derivatives, but the reaction via vinylidene complex was stoichiometric: from π-alkyne complex, see: (a) Iwasawa, N.; Shido, M.; Kusama, H. *J. Am. Chem. Soc.* **2001**, *123*, 5814. (b) Kusama, H.; Funami, H.; Shido, M.; Hara, Y.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2005**, *127*, 2709. From vinylidene complex, see: (c) Iwasawa, N.; Shido, M.; Maeyama, K.; Kusama, H. *J. Am. Chem. Soc.* **2000**, *122*, 10226. Ohe and Uemura also have reported the same control of π-alkyne- and vinylidene-complex pathways, see: (d) Miki, K.; Uemura, S.; Ohe, K. *Chem. Lett.* **2005**, *34*, 1068. (e) Miki, K.; Yokoi, T.; Nishino, F.; Ohe, K.; Uemura, S. *J. Organomet. Chem.* **2002**, *645*, 228.

(7) Kusama, H.; Yamabe, H.; Onizawa, Y;, Hoshino, T.; Iwasawa, N. *Angew. Chem., Int. Ed.* **2005**, *44*, 468. See also, Kusama, H.; Onizawa, Y; Iwasawa, N. *J. Am. Chem. Soc.* **2006**, *128*, 16500.

(8) A similar effect of an amine has been proposed, see: (a) Ohe, K.; Yokoi, T.; Miki, K.; Nishino, F.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 526. See also, ref 6e. (b) Alcázar, E.; Pletcher, J. M.; McDonald, F. E. *Org. Lett.* **2004**, *6*, 3877. See also: (c) Kim, H.; Lee, C. *J. Am. Chem. Soc.* **2006**, *128*, 6336. (d) Barluenga, J.; Diéguez, A.; Rodríguez, F.; Fañanás, F. J.; Sordo, T.; Campomanes, P. *Chem. Eur. J.* **2005**, *11*, 5735.

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