Homogeneous Catalysis

Rhenium(I)-Catalyzed Intramolecular Geminal Carbofunctionalization of Alkynes: Tandem Cyclization of ω-Acetylenic Dienol Silyl Ethers**

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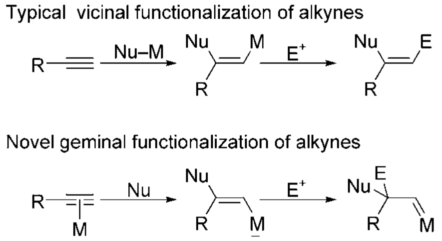
1,2-Vicinal functionalization of alkynes can readily be carried out by carbometalation using various kinds of organometallic reagents, such as Cu, Al, Zr, etc., followed by reaction of the resulting alkenyl metallic species with electrophiles (Scheme 1).[1] However, geminal functionalization, and in particular geminal carbofunctionalization of alkynes, has remained unexplored despite its high potential as a synthetic method.[2,3]



Scheme 1. Vicinal- or geminal-functionalization of alkynes.

We have already reported that $[W(CO)_5(L)]$ can effectively activate terminal alkynes towards the intramolecular nucleophilic attack of enol silyl ethers to give various kinds of carbocycles catalytically.[4] The aim of these studies was to realize geminal carbofunctionalization of alkynes by using this strategy. Thus, by appropriate choice of the metallic reagent, the alkenyl metallic species produced by addition of carbo-nucleophiles to the electrophilically activated alkynes would react with carbo-electrophiles not at the α-position but at the β-position to the metal center to give carbene complex intermediates, in a similar way to the anions of Fischer-type carbene complexes[5] (Scheme 1). Further reaction of the

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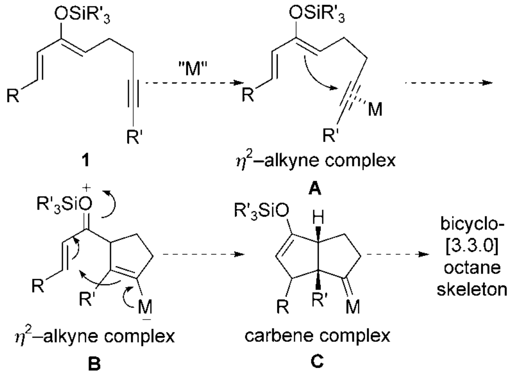
carbene moiety to release the reactive metallic species would constitute a catalytic method for the geminal carbofunctionalization of alkynes.

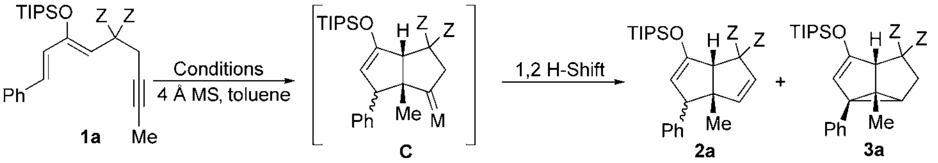
On the basis of the above considerations we designed the system shown in Scheme 2. Thus, treatment of acetylenic dienol silyl ethers **1** with an appropriate metallic reagent should give zwitterionic intermediates **B** by 5-*endo* nucleophilic cyclization of the enol silyl ether to the electrophilically activated η^2-alkyne complexes **A**. The alkenyl metallic moiety produced should then undergo an intramolecular attack at the β-position of the metal center to the α,β-unsaturated silyloxonium moiety to generate bicyclic unstable carbene complexes **C**. Finally, the destabilized carbene complex moiety would undergo a typical carbene reaction, such as 1,2-hydrogen migration, to give the products with regeneration of the reactive metallic species.[6]



Scheme 2. Tandem cyclization of dienol silyl ethers.

We first examined the reaction of ω-acetylenic dienol silyl ether **1a** with 10 mol% of $[\text{W(CO)}_6]$ under photoirradiation in toluene in the presence of molecular sieves (4 Å) (Table 1). Although the tungsten-catalyzed cyclization reaction of enol silyl ethers with an internal alkyne moiety has not been examined before,[7] the reaction proceeded as expected and the desired bicyclic enol silyl ether **2a** was obtained in high yield as a mixture of diastereomers accompanied by a small amount of tricyclic compound **3a**.[8] Since geminal carbofunctionalization was found to proceed as expected, we further examined the possibility of using other transition-metal complexes. PtCl_2[2b,c,e,f] (67% yield) and AuBr_3[2d,e] (79% yield) also showed moderate catalytic activity towards this transformation, and furthermore $[\text{ReCl(CO)}_5]$ was found to have an extremely high activity. The reaction proceeded even with 0.5 mol% of $[\text{ReCl(CO)}_5]$ to give the cyclized products **2a** and **3a** in 92% yield in a ratio of 86:14 by carrying out the reaction in toluene under photoirradiation.[9,10] Formation of the tricyclic compound **3a** explicitly implicates the presence of the intermediate carbene complex **C**, in which the carbene moiety inserts into the neighboring benzylic C–H bond.

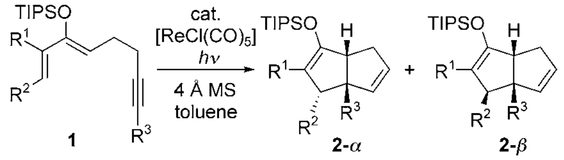
Table 1: Reaction of dienol silyl ether **1a**.



Conditions	*t* [h]	Yield (**2a**+**3a**) [%]	**2a**(α:β):**3a**
$[\text{W(CO)}_6]$ (10 mol%), *hν*	4	88	86(9:1):14
$[\text{PtCl}_2]$ (10 mol%), 70°C	48	67	59(1.3:1):41
$[\text{AuBr}_3]$ (10 mol%), RT	24	79	65(7.7:1):35
$[\text{ReCl(CO)}_5]$ (10 mol%), *hν*	3	98	91(12.5:1):9
$[\text{ReCl(CO)}_5]$ (0.5 mol%), *hν*	16	92	86(4.2:1):14

Z = CO_2Me, TIPS = triisopropylsilyl, MS = molecular sieves.

Table 2: Rhenium-catalyzed reaction of dienol silyl ethers (**1b–j**).



Entry	R^1	R^2	R^3		$[\text{ReCl(CO)}_5]$ [mol%]	Yield [%]	**2-α**:**2-β**
1	H	Me	Me	**1b**	0.5	92	67:33
2	H	Et	Me	**1c**	0.5	92	70:30
3	H	*i*Pr	Me	**1d**	1.0	86	70:30
4	H	Ph	Me	**1e**	1.0	73	50:50
5	Me	Me	Me	**1f**	3.0	68	22:78
6	Me	Ph	Me	**1g**	1.0	76	32:68
7	H	H	Me	**1h**	1.0	51	–
8	Me	H	Me	**1i**	1.0	81	–
9	H	Ph	H	**1j**	3.0	74	85:15

Once we established that $[\text{ReCl(CO)}_5]$ catalyzed the geminal carbofunctionalization reaction very efficiently, the reaction of several substrates was examined (Table 2). The trisubstituted dienes (**1b–e**)[11] with a methyl, primary, or secondary alkyl group as well as a phenyl group at the β-position (R^2) were cyclized to afford the corresponding bicyclic enol silyl ethers in high yield (Table 2, entries 1–4). Even the reaction of the tetrasubstituted dienes (**1f**, **1g**)[11] proceeded to afford the corresponding substituted bicyclic enol silyl ethers in high yield. The $[\text{ReCl(CO)}_5]$-catalyzed reaction gave superior results in most cases relative to that catalyzed by $[\text{W(CO)}_5\text{(L)}]$.[12] In particular, the rhenium-catalyzed reaction of dienyl silyl ethers **1h** and **1i** with no substituent at the β-position (R^2 = H) afforded the desired bicyclic enol silyl ethers in moderate to high yields. However, the corresponding tungsten-catalyzed reaction proceeded in very low yield (17%) even with a stoichiometric amount of $[\text{W(CO)}_5\text{(L)}]$ for **1i**. In addition, a substrate possessing a terminal alkyne moiety **1j**[11] could also be employed for this reaction (Table 2, entry 9). The use of low-valent rhenium complexes in catalytic synthetic reactions, in particular for C–C bond forming reactions, is quite limited.[13] The extremely high activity of a rhenium(I)–carbonyl complex for the electrophilic activation of alkynes towards attack of carbo-nucleophiles observed here should be noted as a new potential use of rhenium complexes in organic synthesis.[14]

In summary, we have developed a geminal carbofunctionalization reaction of alkynes catalyzed by $[\mathrm{ReCl(CO)_4(L)}]$. Utilization of this intermediate carbene moiety for further C–C bond formations will enable the construction of up to four C–C bonds onto an alkyne in a single operation.

Experimental Section

Cyclization of **1a**: Compound **1a** (292 mg, 0.60 mmol) was added to a mixture of $[\mathrm{ReCl(CO)_5}]$ (1.1 mg, 0.0030 mmol, 0.5 mol%) and activated 4-Å molecular sieves in degassed toluene (1.0 mL). The mixture was photoirradiated (250 W super high-pressure Hg lamp) for 16 h, and then the reaction mixture was directly passed through silica gel deactivated with 5 wt% of water (10% ethyl acetate in hexane) to give the crude product, which was purified by preparative thin-layer chromatography (10% ethyl acetate in hexane) to give 269 mg (0.55 mmol, 92%) of **2a** and **3a** (**2a**-α:**2a**-β:**3a** = 69:17:14).

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[7] The $[\mathrm{W(CO)_5(L)}]$-catalyzed cyclizations are assumed to proceed through both a η^2-alkyne complex and a vinylidene complex as determined by deuterium experiments on the cyclization of an ω-acetylenic enol silyl ether.[4a]

[8] The tricyclic enol silyl ether **3** was not obtained when the substrates without a *gem*-diester (**1b**–**i**) were employed.

[9] The reaction of **1a** with 0.5 mol% of $[\mathrm{W(CO)_6}]$ under photoirradiation in toluene proceeded to only a small extent after 16 h to give < 5% of cyclized product **2a**.

[10] It has already been reported that coordinatively unsaturated species $[\mathrm{ReX(CO)_4(L)}]$ was generated by thermal liberation of carbon monoxide from $[\mathrm{ReX(CO)_5}]$ and acted as a Lewis acid for a Friedel–Crafts type acylation.[13a] The reactions of **1b** with 1.0 mol% $[\mathrm{ReCl(CO)_5}]$ in refluxing toluene without photoirradiation also gave bicyclic product **2b** in 47% yield. On the basis of these results, we currently believe that $[\mathrm{ReCl(CO)_4(L)}]$ is the active species in this reaction.

[11] The geometry of the major isomer is shown in the scheme; see the Supporting Information for details of the isomeric ratio of the starting materials.

[12] The reactions of **1a**–**g** and **1j** gave bicyclic silyl enol ethers in high yield (67–81% yield) with 5–20 mol% $[\mathrm{W(CO)_6}]$ under photoirradiation in toluene. The $[\mathrm{W(CO)_5(L)}]$-catalyzed reactions of **1e** and **1g** gave slightly better results than the corresponding rhenium-catalyzed reactions, but they required a larger amount of tungsten complex (for **1e**, 5 mol% of $[\mathrm{W(CO)_6}]$ gave **2e** in 81% yield; for **1g**, 10 mol% of $[\mathrm{W(CO)_6}]$ gave **2g** in 79% yield).

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