

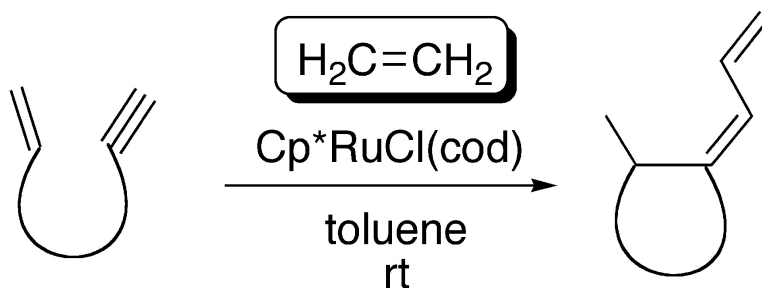
Communication

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Novel Alkenylative Cyclization Using a Ruthenium Catalyst

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The ruthenium-catalyzed metathesis reaction is one of the most unique and significant reactions discovered in recent years in synthetic organic chemistry.¹ A second-generation ruthenium carbene complex² is very effective for the metathesis reaction of highly substituted olefins or electron-deficient olefins.^{2c,3} During the course of our reinvestigation of a metathesis reaction⁴ of an enyne having a di- or trisubstituted alkene or disubstituted alkyne,⁵ we found that the reaction of simple enyne **1a** with **2b** gave metathesis product **3a** in low yield (Scheme 1, Table 1, run 1). It is known that ethylene gas is very effective^{6a} in metathesis of enyne **1a** having a terminal alkyne using a first-generation ruthenium carbene complex **2a**⁷ (run 2), although under argon gas, **3a** was obtained in low yield.^{6b} When a toluene solution of **1a** was warmed at 80 °C under ethylene gas (1 atm) in the presence of **2b**, **1a** was consumed after 1.5 h, and the yield of **3a** slightly increased (run 3). Surprisingly, a small amount of ethylenative cyclization product **4a**, whose structure was confirmed by the spectral data, was obtained.

Scheme 1. Reinvestigation of Enyne Metathesis Using **2a** or **2b**

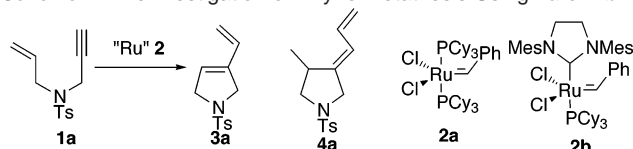
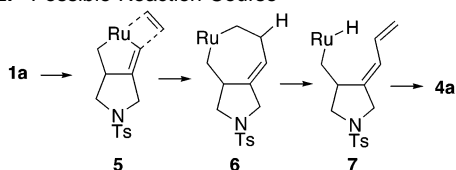


Table 1. Reinvestigation of Enyne Metathesis of **1a**

run	Ru (mol %)	atmosphere	solvent	time (h)	3a (%)	4a (%)
1	2b (5)	argon	toluene	1.5	23	—
2	2a (1)	ethylene	CH ₂ Cl ₂	22	90	—
3	2b (5)	ethylene	toluene	1.5	38	12

Presumably, **4a** would be obtained by the following mechanism. Oxidative cyclization of enyne **1a** gives ruthenacyclopentene **5**, and then insertion of ethylene into **5** gives ruthenacycloheptene **6**. β -Hydrogen elimination from **6** gives hydride–ruthenium complex **7**, and reductive elimination would give **4a** (Scheme 2).

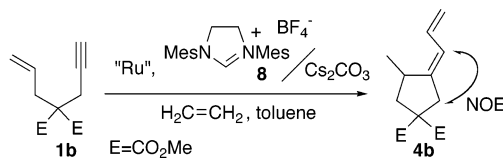
Scheme 2. Possible Reaction Course



Ruthenium-catalyzed cyclization of ene-yne via ruthenacyclopentene was well studied by Trost.⁸ Insertion of alkyne,^{9a} alkene,^{9b–d} or carbon monoxide^{9e–f} into them followed by reductive elimination gave the cyclized compound. Our reaction is very interesting because β -hydrogen elimination occurs from **6**, not reductive elimination to form a six-membered ring compound. If our reaction proceeds via the above process, the low-valent ruthenium catalyst formed from **2b** should act in this reaction.

Thus, a ruthenium catalyst that would effectively induce this reaction was sought. Compound **1b** was used as a substrate. The use of [RuCl₂(CO)₃]₂ and Ru₃(CO)₄ in the presence or in the absence of imidazolium salt **8** and Cs₂CO₃¹⁰ (an equimolar amount of **8**) did not afford the desired product **4b**. When 5 mol % of [RuCl₂(*p*-cymene)]₂¹¹ was used in the presence of **8** and Cs₂CO₃, a relatively large amount of **4b** was obtained (Table 2, run 1). However an increase in the amount of the catalyst did not give a good result (run 2). The effect of the heterocyclic carbene ligand generated from **8** and Cs₂CO₃ was not found (run 3). On the other hand, the reaction of enyne **1b** with ethylene in the presence of 10 mol % of Cp*RuCl(cod)¹² proceeded smoothly to give cyclized compound **4b** after only 20 min in high yield, and the lower reaction temperature gave good results (runs 5–7). Using 5 mol % of catalyst, the reaction proceeded at room temperature, and **4b** was obtained in 85% yield after 3 h (run 8). The results of an NOE experiment of **4b** showed that *Z*-olefin was formed in this reaction.

Table 2. Search for a Ruthenium Catalyst



run	"Ru" (mol %)	8 (mol %)	temp (°C)	time (h)	yield (%)
1	[RuCl ₂ (<i>p</i> -cymene)] ₂ (2.5)	5	80	24	33
2	[RuCl ₂ (<i>p</i> -cymene)] ₂ (5)	10	80	8	31
3	[RuCl ₂ (<i>p</i> -cymene)] ₂ (5)	0	80	1.6	28
4	Cp*RuCl(cod) (10)	0	80	0.3	71
5	Cp*RuCl(cod) (10)	0	60	0.3	76
6	Cp*RuCl(cod) (10)	0	40	0.6	81
7	Cp*RuCl(cod) (10)	0	25	1.5	84
8	Cp*RuCl(cod) (5)	0	25	3	85

Various enynes were treated in a similar manner, and the results are shown in Table 3. Carbo- and heterocyclic compounds were formed from enynes **1** under ethylene gas in high yields (runs 1–6). It was interesting that even in the presence of an amino group in a chain, the ethylenative cyclization proceeded smoothly and the desired compound **4g** was obtained in good yield (run 6).

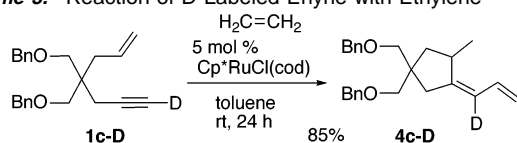
Next, the substituents effects on the multiple bonds were examined. The reaction of enynes **1k** or **1l** having internal alkyne or 1,2-disubstituted alkene with ethylene did not proceed, but enyne **1h** having 1,1-disubstituted alkene afforded the desired cyclized compound **4h** in 51% yield (run 7). The reaction of enyne **1i** or **1j** having an electron-withdrawing group on the alkene or alkyne gave **4i** or **4j** in high yield (runs 8 and 9). The results are interesting because the carbomethoxy group can be converted into the various functional groups.

When the enyne **1c–D** (D content, 91%) having deuterated alkyne was treated under similar conditions, deuterated cyclized

Table 3. Alkenylative Cyclization of Various Enynes Using Cp*RuCl(cod)^a

run	substrate	time (h)	product	yield (%)
1		24		78
2		22		90
3		1		83
4		3		70
5		4		49
6		18		74
7		5		51 ^b
8		8		89
9		19		72

^a All reactions were carried out using 5 mol % of Cp*RuCl(cod) at room temperature. ^b 10 mol % of Cp*RuCl(cod). Temp 60 °C.

Scheme 3. Reaction of D-Labeled Enyne with Ethylene

compound **4c-D** (D content, 90%) was obtained in high yield. It means that ruthenacycloheptene **6** is formed as an intermediate (Scheme 3).

The novel alkenylative cyclization was realized. The reaction procedure is very simple, and the reaction conditions are very mild: a toluene solution of enyne is stirred under ethylene gas (1 atm) in the presence of a catalytic amount of Cp*RuCl(cod) at room temperature. Further studies on alkenylative cyclization are now in progress.

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Supporting Information Available: Experimental procedure and the spectral data for **4** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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