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Ruthenium-Catalyzed [2 + 2 + 2] Cocyclization of Diene-yne

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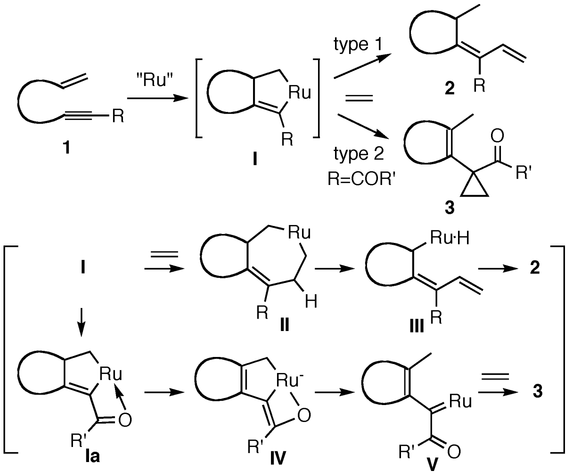
Transition metal-catalyzed cyclizations are useful methods for the synthesis of carbo- and heterocycles.[1] Among them, [2 + 2 + 2] cocyclization is a unique and an atom-economical method. It has been shown that [2 + 2 + 2] cocyclization of α,ω-diyne and an alkyne or intramolecular cocyclization of triyne using a cobalt, rhodium, iridium, or ruthenium complex is a useful method for the synthesis of benzene derivatives.[2] However, there are a few reports of [2 + 2 + 2] cocyclization of enyne and an alkene or intramolecular reaction of diene-yne.[3] Recently, we reported two types of ruthenium-catalyzed cyclization of enyne accompanying ethylene insertion (Scheme 1).[4] The first reaction is alkenylative cyclization of enyne, where ethylene is inserted into ruthenacyclopentene **I** to afford cyclic compound **2** having a diene moiety via **II** (type 1). The other is cyclization accompanying the formation of a cyclopropane ring when the keto-carbonyl group is placed on the alkyne. In this case, ruthenium carbene **V** should be formed to afford cyclic compound **3** having a cyclopropane ring (type 2).

For confirmation of the formation of ruthenium carbene complex **V**, intramolecular cyclization of enyne **1a** was carried out and cyclic compound **3a** having a fused 3,6-membered ring was obtained.[4b] During the course of further investigation, we obtained an interesting result. When a toluene solution of diene-yne **4a**, whose tether was shortened to five carbons, was stirred in the presence of 5 mol % of Cp*RuCl(cod)[5] at room temperature for 2 h, tricyclic compound **5a** was obtained in quantitative yield instead of compound **3b**. It means that [2 + 2 + 2] cocyclization of two alkenes and alkyne occurred. The intermediate should be ruthenacyclopentene **Ib**, and insertion of an alkene part of **4a** into **Ib** occurs to give ruthenacycloheptene **IIb**. Reductive elimination gives tricyclic compound **5a** (Scheme 2).

To examine whether a keto-carbonyl group on an alkyne is essential to this novel [2 + 2 + 2] cocyclization, compounds **4b** and **4c** were treated in a similar manner. As a result, tricyclic compounds **5b** and **5c** were obtained in high yields (Table 1). This means that carbonyl oxygen is not required and that an appropriate carbon-chain length is important.

Scheme 1. Two Types of Ruthenium-Catalyzed Cyclization



Scheme 2

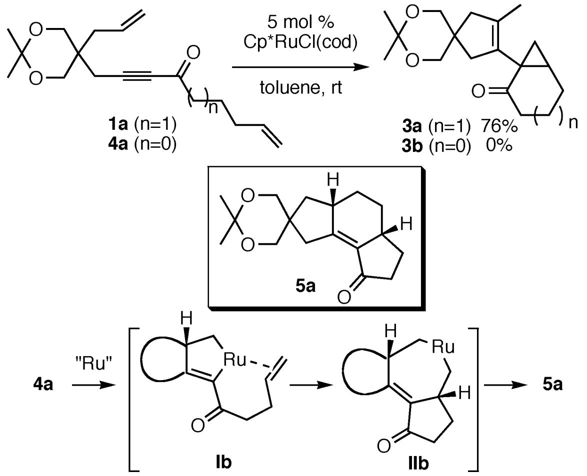
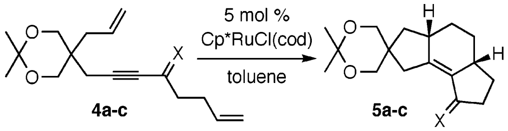


Table 1. Effect of Carbonyl Group on Alkyne



entry	X	dieneyne	conditions	product	yield (%)
1	O	**4a**	room temp, 2 h	**5a**	quantitative
2	OAc, H	**4b**	room temp, 24 h	**5b**	97
3	H_2	**4c**	reflux, 24 h	**5c**	quantitative

Various 1,11-diene-6-ynes were treated in a similar manner (Table 2). Diene-ynes **4e**−**j** having heteroatoms in a chain also afforded tricyclic compounds **5e**−**j** in high yields (entries 2−7). It was interesting that indoline derivative **5k** with a fused five-membered ring was obtained from diene-ynamide **4k** in moderate yield (entry 8). To determine the stereochemistry of the protons on the ring junctions, X-ray crystallographic analysis of **5j** was carried out and these protons are placed on the same side.[6] Furthermore, the substituent effects on the alkene were examined. Diene-yne **4l** having 1,1-disubstituted alkene and terminal alkene gave tricyclic compound **5l** in quantitative yield after only 2 h at room temperature (entry 9). The reaction of **4m** having two 1,1-disubstituted alkenes at room-temperature gave desired tricyclic compound **5m** in 25% yield along with compound **6m**,[7] which has two fused 5,3-membered rings. The yields of these compounds **5m** and **6m** were improved to 40% and 45%, respectively, when a toluene solution of **4m** was warmed at 60 °C (entry 10). A similar

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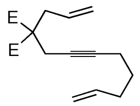
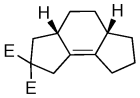
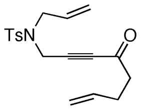
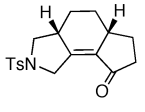
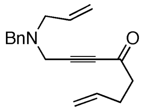
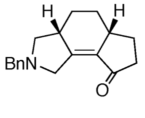
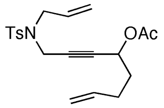
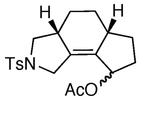
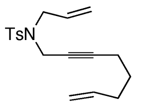
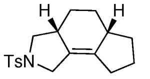
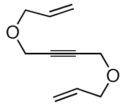
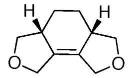
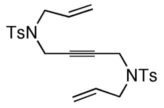
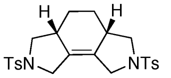
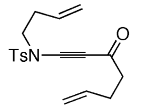
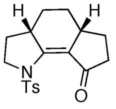
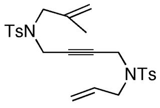
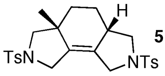
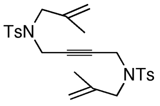
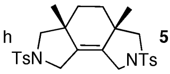
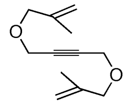
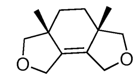
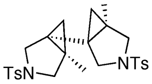
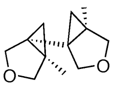
Table 2. Ruthenium-Catalyzed Cocyclization of Diene-yne[a]

entry	dienyne	conditions	products	yields (%)
1		**4d** reflux, 2 h E=CO$_2$Ne	 **5d**	92%
2		**4e** rt, 2 h	 **5e**	95%
3		**4f** rt, 20 h	 **5f**	77%
4		**4g** rt, 2 h	 **5g**	99%[b]
5		**4h** rt, 48 h	 **5h**	quant.
6		**4i** rt, 15 h	 **5i**	93%
7		**4j** rt, 30 h	 **5j**	84%
8		**4k** rt, 24 h	 **5k**	42%
9		**4l** rt, 2 h	 **5l**	quant.
10		**4m** 60 °C, 24 h	 **5m**	40%[c]
11		**4n** 60 °C, 1 h	 **5n**	50%[d]



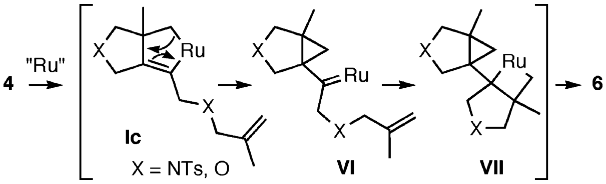
6m



6n

[a] All reactions were carried out using 5 mol % of Cp*RuCl(cod) under argon gas. [b] A single product is formed. [c] **6m** was obtained in 45% yield. When the reaction was carried out at room temperature for 48 h, **5m** was obtained in 25% yield along with **6m** in 17% yield, and **4m** was recovered in 55% yield. [d] **6n** was obtained in 27% yield.

Scheme 3. Reaction Course for Formation of **6**



result was obtained in the reaction of **4n**, which has oxygen in a tether and has two 1,1-disubstituted alkenes, to give **5n** in 50% yield along with **6n** in 45% yield (entry 11). It was interesting that **4j** and **4l** gave only tricyclic compounds **5j** and **5l**, in high yields, while in the reaction of **4m**, starting material **4m** was recovered in 55% yield after 48 h at the same temperature, and two products **5m** and **6m** were formed. In the reactions of **4m** and **4n** having two disubstituted alkenes, ruthenacyclopentene **Ic** would be formed.[8] Since the reaction rate of insertion of 1,1-disubstituted alkene into ruthenacycle **Ic** would be not fast, ring opening of **Ic** occurs to form ruthenium carbene complex **VI**, the ruthenium carbene of which reacts with the alkene moiety intramolecularly to form ruthenacyclobutane **VII**, and it affords compound **6** (Scheme 3).

A novel ruthenium catalyzed [2 + 2 + 2] cocyclization of 1,-11-diene-6-yne was developed. The remarkable feature is that [2 + 2 + 2] cocyclization proceeds between two alkenes and one alkyne using Cp*RuCl(cod). The reaction conditions are mild and tricyclic carbo- and heterocyclic compounds were formed in one step from the straight-chain compounds in high yields. Further studies are in progress.

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Supporting Information Available: Experimental details and the spectral data of **4a**−**n**, **5a**−**n** and **6m**−**n**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) Crystallographic data of **5j** have been deposited to the Cambridge Crystallographic Data Center (CCDC). The stereochemistry of other cyclic products was assigned by analogy with those spectral data. See Supporting Information.

(7) The structure of **6m** was confirmed by X-ray crystallography whose crystallographic data have been deposited to the CCDC.

(8) Tricyclic compound **5l** would be formed by insertion of terminal alkene into ruthenacycle having a methyl group on the ring junction.

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