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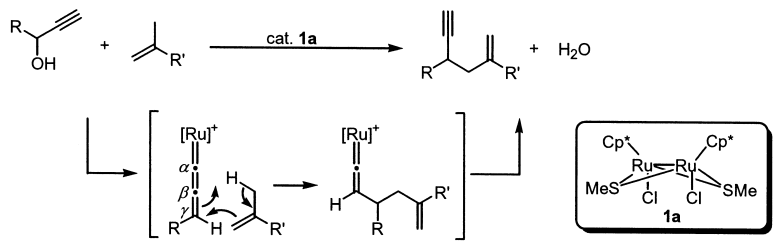

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Ruthenium-Catalyzed Carbon−Carbon Bond Formation between Propargylic Alcohols and Alkenes via the Allenylidene-Ene Reaction

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Transition metal allenylidene complexes ($M{=}C{=}C{=}CR_2$), which belong to a series of unsaturated carbene derivatives, have attracted a great deal of interest in recent years as a new type of organometallic intermediate.[1] Although remarkable developments of the reactivity of allenylidene complexes have been attained,[1,2] only a few examples of catalytic reactions via allenylidene intermediates are reported until now.[3−6] We have recently disclosed the ruthenium-catalyzed efficient propargylic substitution reactions of propargylic alcohols[7] with various heteroatom- and carbon-centered nucleophiles to afford the corresponding propargylic products in high yields.[8] Interestingly, the reactions are catalyzed only by thiolate-bridged diruthenium complexes[9] such as [Cp*RuCl(μ_2-SR)$_2$RuCp*Cl] (Cp* = η^5-C_5Me_5; R = Me (**1a**), ^{n}Pr (**1b**), ^{i}Pr (**1c**)) and [Cp*RuCl(μ_2-S^{i}Pr)$_2$RuCp*(OH_2)]OTf (OTf = OSO_2CF_3; **1d**). During our continuous study on the catalytic reactions via allenylidene complexes, we have now found a novel carbon−carbon bond formation between propargylic alcohols and alkenes via the unprecedented allenylidene-ene reaction (Chart 1) providing a novel catalytic coupling reaction between alkynes and alkenes. Preliminary results are described here.

Chart 1

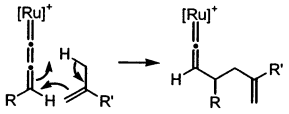
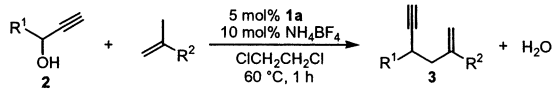


Table 1. Reaction of Propargylic Alcohols (**2**) with Alkenes in the Presence of **1a**[a]



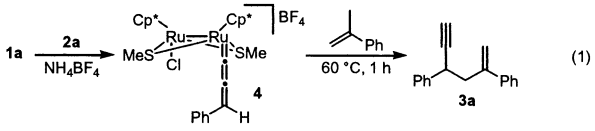
run	propargylic alcohol	alkene	yield of **3**, %[b]
1	**2a**, R^1 = Ph	R^2 = Ph	**3a**, 46 (34)[c]
2	**2b**, R^1 = *p*-MeC_6H_4	R^2 = Ph	**3b**, 56
3	**2c**, R^1 = *p*-$MeOC_6H_4$	R^2 = Ph	**3c**, 13
4	**2d**, R^1 = *p*-ClC_6H_4	R^2 = Ph	**3d**, 27
5	**2e**, R^1 = *p*-FC_6H_4	R^2 = Ph	**3e**, 42
6	**2a**, R^1 = Ph	R^2 = *p*-MeC_6H_4	**3f**, 50
7	**2b**, R^1 = *p*-MeC_6H_4	R^2 = *p*-MeC_6H_4	**3g**, 67
8	**2c**, R^1 = *p*-$MeOC_6H_4$	R^2 = *p*-MeC_6H_4	**3h**, 40
9	**2d**, R^1 = *p*-ClC_6H_4	R^2 = *p*-MeC_6H_4	**3i**, 35
10	**2e**, R^1 = *p*-FC_6H_4	R^2 = *p*-MeC_6H_4	**3j**, 60
11	**2a**, R^1 = Ph	R^2 = *p*-ClC_6H_4	**3k**, 30

[a] All the reactions of **2** (0.50 mmol) with α-methylstyrene (10 mmol) were carried out in the presence of **1a** (5 mol %) and NH_4BF_4 (10 mol %) in $ClCH_2CH_2Cl$ (12 mL) at 60 °C for 1 h. [b] Isolated yield. [c] At room temperature for 1 h.

Treatment of 1-phenyl-2-propyn-1-ol (**2a**) with α-methylstyrene in $ClCH_2CH_2Cl$ in the presence of **1a** (5 mol %) at 60 °C for 1 h afforded 2,4-diphenyl-1-hexen-5-yne (**3a**) in 46% isolated yield (Table 1, run 1). Neither other products nor regioisomers of **3a** were detected by GLC and ^{1}H NMR. The reaction at room temperature proceeded slowly, **3a** being produced in 34% isolated yield for 1 h. Other di- and monoruthenium complexes except **1** were ineffective for this carbon−carbon bond-forming reaction (see the Supporting Information for experimental details).

Typical results using various propargylic alcohols (**2**) are shown in Table 1. Thus, carbon−carbon bond-forming reactions between propargylic alcohols (**2b**−**e**) and alkenes at 60 °C for 1 h proceeded to afford the corresponding 2,4-disubstituted-1-hexen-5-ynes (**3b**−**k**) in moderate yields. Unfortunately, when 1,1-diphenyl-2-propyn-1-ol was used, the reaction did not proceed under the same reaction conditions. *p*-Methyl-α-methylstyrene (Table 1, runs 6−10) exhibited a slightly higher reactivity as compared to α-methylstyrene (Table 1, runs 1−5). On the other hand, *p*-chloro-α-methylstyrene exhibited a low reactivity (Table 1, run 11).

To elucidate the reaction mechanism of the present reaction, the following stoichiometric and catalytic reactions were investigated. Treatment of the allenylidene complex (**4**), which could be prepared from the reaction of **1a** with 1 equiv of **2a** in the presence of NH_4BF_4 in tetrahydrofuran (THF) at room temperature for 30 min,[8a] with 20 equiv of α-methylstyrene in $ClCH_2CH_2Cl$ at 60 °C for 1 h led to the formation of **3a** in 89% GLC yield (eq 1).

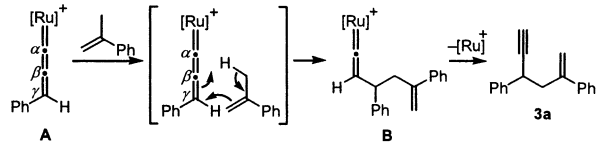


(1)

Furthermore, reaction of **2a** with α-methylstyrene in the presence of 5 mol % **4** at 60 °C for 1 h afforded **3a** in 90% GLC yield. These results indicate that the carbon−carbon bond formation between propargylic alcohols and alkenes should proceed via allenylidene intermediates such as **4**.

On the basis of these findings, a pathway for this catalytic reaction is proposed in Scheme 1. The C_β−C_γ double bond of an

Scheme 1



allenylidene complex (**A**) reacts with α-methylstyrene, where complex **A** works as an enophile, to afford a vinylidene complex (**B**) via the allenylidene-ene reaction with α-methylstyrene. This scheme is strongly supported by the finding that 2,4-diphenyl-1-hexen-5-yne-d_3 was formed with a high deuterium incorporation (53%) at the C-6 position when **2a** was treated with 20 equiv of α-methylstyrene-methyl-d_3 in the presence of **1a** (eq 2). A substantial isotope effect (k_H/k_D = 4) was observed when the reaction was carried out at 60 °C. This result indicates that the

[†] Kyoto University.
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Scheme 2

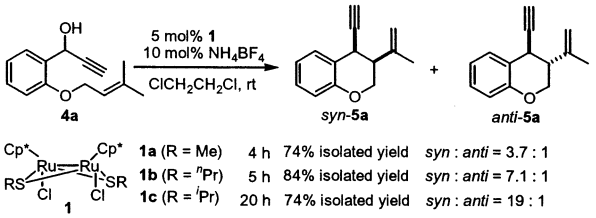
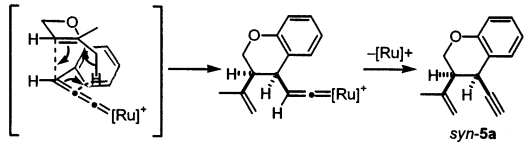
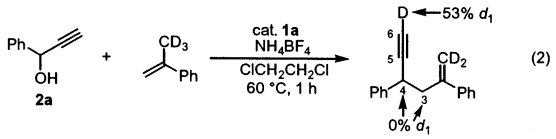


Chart 2



C−H bond breaking at the allylic position of α-methylstyrene is involved in the rate-determining step.



Esteruelas and co-workers have already reported the stoichiometric Diels−Alder-type addition of dienes to the $C_\beta-C_\gamma$ double bond of allenylidene complexes to give the corresponding substituted vinylidene complexes,[10] but the allenylidene-ene reaction described here is the first example of the use of the $C_\beta-C_\gamma$ double bond of allenylidene complexes as an enophile in the catalytic process.

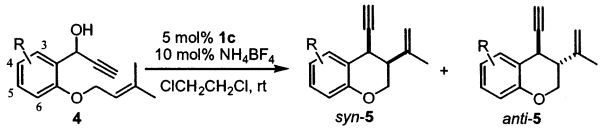
Next, we investigated the intramolecular version of this reaction. Thus, by stirring propargylic alcohol bearing the alkene moiety (**4a**) in $ClCH_2CH_2Cl$ in the presence of **1a** (5 mol %) at room temperature for 4 h, we obtained 4-ethynyl-3-(1-methylethenyl)-chromane (**5a**) in 74% isolated yield as a mixture of two diastereomers of **5a**, the syn isomer (*syn*-**5a**) being major (*syn*-**5a**:*anti*-**5a** = 3.7:1).[11] Interestingly, the use of the complexes bearing sterically more demanding groups such as ^{n}Pr (**1b**) and ^{i}Pr (**1c**) dramatically increased the diastereoselectivity of **5a**, although a prolonged reaction time was required (Scheme 2).

The results of intramolecular cyclization of various propargylic alcohols (**4**) at room temperature in the presence of **1c** to afford the corresponding substituted chromanes (**5b**−**g**) are shown in Table 2. Irrespective of the kind of functional groups such as methyl, methoxy, chloro, and bromo, this catalytic intramolecular cyclization proceeded smoothly with a quite high diastereoselectivity.

This intramolecular cyclization seems to proceed through such a transition state as shown in Chart 2 to afford *syn*-**5**. The transition state leading to the formation of *anti*-**5** may be inhibited by the steric bulkiness of thiolate-bridged ligands in **1**. Tyrrell and co-workers have already reported a diastereoselective intramolecular cyclization of **4** using the Nicholas reaction to give *anti*-**5**,[12] where a stoichiometric amount of $Co_2(CO)_8$ was used and several steps were necessary.[13] The diastereoselectivity of the produced **5** using the Nicholas reaction is in sharp contrast to that of **5** obtained in the present reaction.

In summary, we have found a novel ruthenium-catalyzed carbon−carbon bond formation between propargylic alcohols and alkenes via the allenylidene-ene reaction, disclosing a new reactivity of allenylidene complexes. As a synthetic application, intramolecular cyclization using this carbon−carbon bond-forming reaction has been developed to give the corresponding *syn*-substituted chromanes in high yields with excellent diastereoselectivity.

Table 2. Intramolecular Cyclization of Propargylic Alcohols (**4**) in the Presence of **1c**[a]



run	propargylic alcohol	reaction time (h)	yield of **5**, %[b]	syn:anti[c]
1	**4a**, R = H	20	**5a**, 74	19:1
2	**4b**, R = 4-Me	24	**5b**, 75	16:1
3	**4c**, R = 4-OMe	20	**5c**, 79	16:1
4	**4d**, R = 4-Br	20	**5d**, 82	19:1
5	**4e**, R = 4-Cl	10	**5e**, 74	20:1
6	**4f**, R = 6-Me	3	**5f**, 81	25:1
7	**4g**, R = 6-OMe	20	**5g**, 80	25:1

[a] All the reactions of **4** (0.60 mmol) were carried out in the presence of **1c** (5 mol %) and NH_4BF_4 (10 mol %) in $ClCH_2CH_2Cl$ (15 mL) at room temperature. [b] Isolated yield. [c] Determined by ^{1}H NMR.

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Note Added after ASAP: Version published on Web 4/29/2003 contained an error in Table 1. Version published on Web 4/30/2003 and print version are correct.

Supporting Information Available: Experimental procedures and spectral data for all of the new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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