

Cp*Ru(cod)Cl-Catalyzed [2 + 2 + 2] Cycloaddition of 1,6-Heptadiynes with Allylic Ethers. A Decisive Role of Coordination to the Ether Oxygen Atom

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Received August 11, 1998

Transition-metal-catalyzed cyclotrimerization of alkynes has been extensively investigated as a feasible method to construct substituted aromatic nuclei.¹ Related cyclocotrimerization of two molecules of an alkyne with an alkene is a straightforward route to substituted cyclohexadiene derivatives, which is a highly valuable synthetic intermediate.¹ Stoichiometric reactions of CpCo(CO)₂ with enediynes have been employed for the syntheses of polycyclic natural products by Vollhardt and co-workers.²

Catalyzed intermolecular version of such couplings, however, is successful only when an *electron-deficient alkene* is employed with a neutral alkyne³ or an *electron-deficient alkyne* with a neutral alkene.⁴ Therefore, the cyclocotrimerization between a neutral alkyne and a neutral alkene has received less attention. Some sporadic examples gave only limited results.^{3b,5} Herein, we wish to report a novel Cp*Ru(cod)Cl-catalyzed cycloaddition of 1,6-heptadiynes with allylic ethers as an electronically nonactivated alkyne-alkene coupling.

Previously, we have reported that an indenylruthenium(II) complex, (η⁵-C₇H₅)Ru(PPh₃)₂Cl (**1a**) catalyzes the tandem [2 + 2 + 2]/[4 + 2] cycloaddition of 1,6-heptadiyne derivatives with norbornene.⁶ In the presence of **1a**, diyne **2a** was reacted similarly with cyclopentene **3** to give a tandem adduct **4a** (X = CH₂) albeit in low yield (25%) even when **3** was used in large excess (Scheme 1). This result shows the ring strain of norbornene being essential to our tandem cycloaddition. In contrast, a cyclic ether, 2,5-dihydrofuran (**5**), gave a considerable amount of [2 + 2 + 2] cycloadduct **6a** (23%) along with a corresponding tandem adduct **4b** (X = O, 18%) (Scheme 1). Thus, 2,5-dihydrofuran obviously behaves in a different manner. Moreover, the simple [2 + 2 + 2] cycloadduct **6a** was selectively obtained in 87% yield by use of bulkier Cp*Ru(cod)Cl (**1b**). Typically, in the presence of **1b** (1 mol %), diyne **2a** (1 mmol) was stirred at 40 °C in 3 mL (ca. 40 equiv) of degassed **5** under N₂ for 24 h. After excess **5** was recovered under reduced

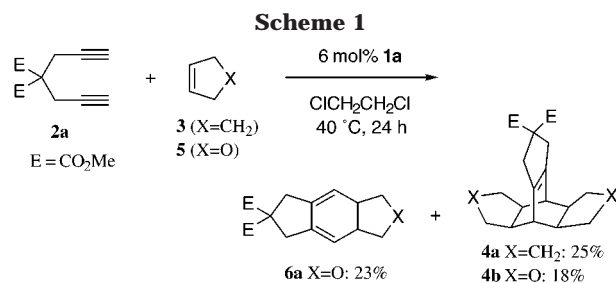


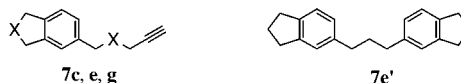
Table 1. [2 + 2 + 2] Cycloaddition of Diyne **2a–g** with **5**^a

diyne	[2 + 2 + 2] cycloadduct	yield (%)
		87%
		67%
		68% ^b
		90%
		50% ^c
		74%
		70% ^b

^a Conditions: 1 mol% Cp*Ru(cod)Cl, 1 mmol of **2**, 3 mL of **5**, 40 °C, 24 h.

^b Dimer **c**, and **g** were isolated in 14, and 8% yields, respectively.

^c A mixture of the dimer **7e** and trimer **7e'** was obtained in ca. 28%.



pressure, purification by silica gel chromatography gave **6a** in excellent yield (Table 1).⁷ Diyne self-cycloaddition was completely suppressed by use of commercially available **5** as the solvent.

In the same manner, other diynes were subjected to the catalyzed coupling with **5** as summarized in Table 1. Diynes having a tertiary center at the 4-position (**2b–d**) gave the desired cycloadducts **6b–d** in good yields. A simple diyne **2e** having no tertiary center also gave a corresponding product **6e** (50%) despite being expected to have low cyclizability without the Thorpe–Ingold effect.⁸ Interesting heterotricycles **6f** and **6g** were obtained from propargyl ether **2f** and *N,N*-dipropargylsulfonamide **2g** in 74 and 70% yields, respectively.

(7) Spectral data for **6a**: mp 51–52 °C; IR (CHCl₃) 1739, 1254, 1047 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.89 (2 H, d, *J* = 16.5 Hz), 2.97 (2 H, s), 2.99 (2 H, d, *J* = 16.5 Hz), 3.46 (2 H, m), 3.71 (3 H, s), 3.72 (3 H, s), 4.11 (2 H, m), 5.41 (2 H, s); ¹³C NMR (125 MHz, CDCl₃) δ 38.7, 38.8, 52.8, 52.9, 58.6, 75.2, 117.3, 134.6, 171.5; MS (EI) *m/z* (rel intensity) 278 (M⁺, 19), 247 (6), 218 (24), 188 (37), 157 (9), 129 (100). Anal. Calcd for C₁₅H₁₈O₅: C, 64.74; H, 6.52. Found: C, 64.76; H, 6.50.

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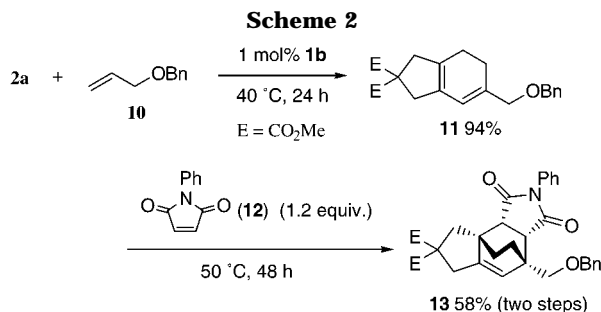
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Obviously, the oxygen atom on the furan ring plays a key role: i.e. the corresponding cyclopentene gave no cycloadduct at all under the same reaction conditions.⁹ Another important aspect of the present catalytic cycloaddition is that the ring strain of the olefin counterpart does not affect the yield and the selectivity. In fact, acyclic allyl benzyl ether (**10**) reacted with **2a** to produce cyclohexadiene **11** as a major regioisomer via concomitant 1,5-H shift (Scheme 2). The structure of **11** was deduced by the following facts. In the ¹H NMR spectrum, only one vinyl proton absorption was observed at δ 5.86 together with the absorption of the two vicinal methylene protons on the cyclohexa-1,3-diene ring at δ 2.15–2.35. In addition, another possibility of a cyclohexa-1,4-diene structure was denied by Diels–Alder cycloaddition of **11** with *N*-phenylmaleimide (**12**), leading to **13** (vide infra). According to the above results, the bidentate coordination of the allylic ether moiety seems essential to the selective coupling. This agrees with the observation that 3-methoxycyclohexene (**14**), which has the allylic ether moiety fixed as the *s*-trans orientation, showed no reactivity under the same reaction conditions. The insertion mechanism via a cationic ruthenacycle¹⁰ **15** depicted in Figure 1 is reasonable, although no cycloadduct was observed when AgOTf was employed as additive (85% of **2a** was recovered).¹¹

In conclusion, the present cycloaddition of 1,6-heptadiynes with allylic ethers is a novel and practical protocol for the synthesis of functionalized bicyclic cyclohexadienes. It is highly advantageous that no environmentally harmful sol-

(9) For examples of heteroatom-directed regio- and stereochemical control, see: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.

(10) Related ruthenacyclopentadiene was recently synthesized from Cp^{*}Ru(PPh₃)₂Cl and ethylene, and the isolated complex catalyzes the linear coupling of acetylene and acrylonitrile (Yi, C. S.; Torres-Lubian, J. R.; Liu, N.; Rheingold, A. L.; Guzei, I. A. *Organometallics* **1998**, *17*, 1257).

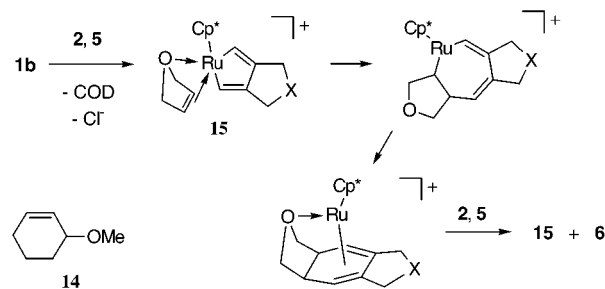


Figure 1.

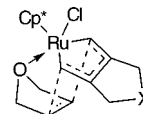
vents such as halogenated alkanes or benzene derivatives are required, and instead, allylic ethers are used as a solvent and readily recovered by simple distillation. Cp^{*}Ru(cod)Cl is a catalyst of choice since the bulkiness of the Cp^{*} ligand facilitates the dissociation of the produced cyclohexadiene. The synthetic utility of this method was further demonstrated by the one-pot construction of a complex tetracycle **13** via sequential [2 + 2 + 2]/[4 + 2] cycloaddition (Scheme 2). Furthermore, our method is not only the first example of ruthenium-catalyzed version, but also a rare case of cyclocotrimerization between electronically nonactivated alkynes and alkenes with both extreme chemoselectivity and high product yields under the mild conditions (40 °C, atmospheric pressure) in addition to the recently reported Rothwell's titanium-catalyzed method.¹²

Acknowledgment. We gratefully acknowledge financial support (09305059, 10132222) from the Ministry of Education, Science Sports and Culture, Japan.

Supporting Information Available: Experimental procedures and spectral data for selected compounds (5 pages).

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(11) The coordinated ether oxygen-assisted Diels–Alder mechanism as shown below might be an alternative explanation for the efficiency of the present system.



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