Ru(II)-Catalyzed Cycloadditions of 1,6-Heptadiynes with Alkenes: New Synthetic Potential of Ruthenacyclopentatrienes as Biscarbenoids in Tandem Cyclopropanation of Bicycloalkenes and Heteroatom-Assisted Cyclocotrimerization of 1,6-Heptadiynes with Heterocyclic Alkenes

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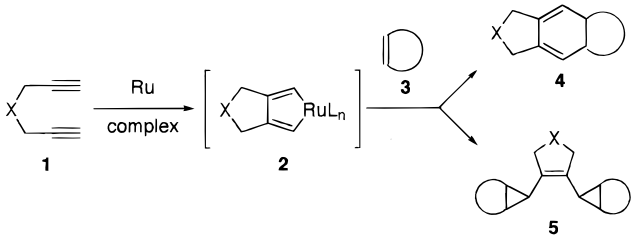
Abstract: The ruthenium(II)-catalyzed tandem cycloaddition of 1,6-heptadiynes with bicyclic alkenes, such as bicyclo[3.2.1]heptenones and norbornene derivatives, furnishes the 1:2 adducts between the diynes and two molecules of the bicycloalkenes together with common [2 + 2 + 2] cyclocotrimerization products. The structure of a representative tandem 1:2 adduct between dimethyl dipropargylmalonate and 2,4-dimethylbicyclo[3.2.1]-oct-6-en-3-one was unequivocally determined by X-ray analysis and was concluded to involve an unusual 1,2-dicyclopropylcyclopentene skeleton. On the basis of the spectroscopic analogy, the previously communicated structures of the tandem cycloadducts between the diynes and norbornene derivatives were corrected. The formation of the tandem double-cyclopropanation products from the diynes is chemical evidence of a biscarbenoid hybrid structure, 1,3,5-metallacyclopentatriene, of the corresponding 2,4-metallacyclopentadiene intermediates. The selectivity for the formation of the tandem cyclopropanation adducts was increased in the order of (η^5-C_9H_7)Ru(PPh_3)$_2$Cl > CpRu(cod)Cl > Cp*Ru(cod)Cl, indicative of the $\eta^5 \rightarrow \eta^3$ ring slippage of the cyclopentadienyl type ligands playing a key role in the tandem cyclopropanation. On the other hand, the normal [2 + 2 + 2] cyclocotrimerization between 1,6-heptadiynes and alkenes was selectively catalyzed by Cp*Ru(cod)Cl, in the case of cyclic or linear alkenes possessing heteroatoms at the allylic position. The latter heteroatom-assisted cyclocotrimerization was also catalyzed by a paramagnetic dinuclear ruthenium(III) complex, [Cp*$RuCl_2$]$_2$, at lower temperature.

Introduction

Metallacyclopentadiene complexes have received considerable attention because they react with unsaturated molecules such as alkynes, alkenes, nitriles, CO, etc. to give valuable cyclic products.[1] The reactions of ruthenacyclopentadiene complexes with unsaturated molecules, however, have drawn less attention;[2] a ruthenacyclopentadiene intermediate in the cyclotrimerization of acetylene dicarboxylic acid esters has so far been isolated and characterized by X-ray analysis.[3] Only recently, a ruthenacyclopentadiene having a pentamethylcyclopentadiene ligand has also been isolated and used for the catalytic linear cotrimerization of two molecules of acetylene with acrylonitrile.[4] Catalytic cyclocarbonylations of alkynes or diynes are also claimed to involve a ruthenacyclopentadiene intermediate.[5] In this conjunction, we have independently explored the ruthenium-catalyzed cyclocotrimerization of two alkyne components with one or two molecules of a cyclic alkene (Scheme 1).[6] To make the ruthenacycle formation entropically favorable, a 1,6-heptadiyne derivative **1** was particularly useful as the alkyne component. If the resultant bicyclic ruthenacyclopentadiene intermediate **2a** is effectively trapped by an alkene component **3**, a Ru-catalyzed cyclocotrimerization becomes viable to afford a fused cyclohexadiene **4**. On the basis of this idea, we examined

Scheme 1



† Research Center for Materials Science, Department of Chemistry

(1) Shore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol 5. p 1129.

(2) (a) Naota, T.; Takaya, H.; Murahashi, S. *Chem. Rev.* **1998**, *98*, 2599. (b) Butenschön, H. In *Organic Synthesis Highlights III*; Mulzer, J., Waldman, H., Eds; Wiley-VCH: Weinheim, 1998; p 96.

(3) Lindner, E.; Jansen, R.-M.; Mayer, H. A.; Hiller, W.; Fawzi, R. *Organometallics* **1989**, *8*, 2355.

(4) Yi, C. S.; Torres-Lubian, J. R.; Liu, N.; Rheingold, A. L.; Guzei, I. A. *Organometallics* **1998**, *17*, 1257.

(5) (a) Bruce, M. I.; Knight, J. R. *J. Organomet. Chem.* **1968**, *12*, 411. (b) Chatani, N.; Fukumoto, Y.; Ida, T.; Murai, S. *J. Am. Chem. Soc.* **1993**, *115*, 11614.

(6) (a) Yamamoto, Y.; Kitahara, H.; Hattori, R.; Itoh, K. *Organometallics* **1998**, *17*, 1910. (b) Yamamoto, Y.; Kitahara, H.; Ogawa, R.; Itoh, K. *J. Org. Chem.* **1998**, *63*, 9610.

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the reaction of **1** and strained bicyclic alkenes. As a result, we have found that various organoruthenium complexes having a cyclopentadienyl-based ligand gave the unexpected tandem cyclopropanation product **5** involving one molecule of a heptadiyne **1** and two molecules of an alkene **3**, together with the expected simple [2 + 2 + 2] cyclocotrimerization product **4**. The product ratio clearly depends on the cyclopentadienyl-type ligand in the Ru(II) catalysts; the selectivity for the tandem cyclopropanation increased in the order of η^5-indenyl > cyclopentadienyl (Cp) > pentamethylcyclopentadienyl (Cp*). In contrast, alkenes possessing a heteroatom at the allylic position afforded substantial amounts of cyclohexadienes **4** despite using the indenyl complex. This fact obviously indicates that the coordination of the ruthenium center to the heteroatom plays a key role in the selection of the reaction mode. In this paper, we wish to reveal the nature of the alkene components and how two different modes of cycloadditions, that is, tandem cyclopropanation and cyclocotrimerization, are selected by the Ru(II)-based catalytic system.

Results and Discussion

Ru(II)-Catalyzed Tandem Cycloaddition of 1,6-Heptadiynes with Bicycloalkenes Revisited. Transition-metal-catalyzed [2 + 2 + 2] cyclocotrimerization of two molecules of an alkyne with an alkene has been studied less than the parent alkyne cyclotrimerization,[7] although the resultant cyclohexadiene is a valuable synthetic intermediate such as a diene component for the Diels−Alder reaction.[8] This is because a 2:1 coupling of an alkyne and an alkene has difficulty competing with the more facile alkyne trimerization.[9] The success of the selective coupling depends on the electronic balance between the alkyne and alkene components; the combination of an *electron-deficient alkene* with a neutral alkyne[10] or an *electron-deficient alkyne* with a neutral alkene[11] were successful in the previous examples. Therefore, the intermolecular coupling employing electronically non-activated alkene and alkyne components has remained a challenging subject.[12] With this perspective, we previously investigated the Ru-catalyzed cycloaddition of 1,6-heptadiynes

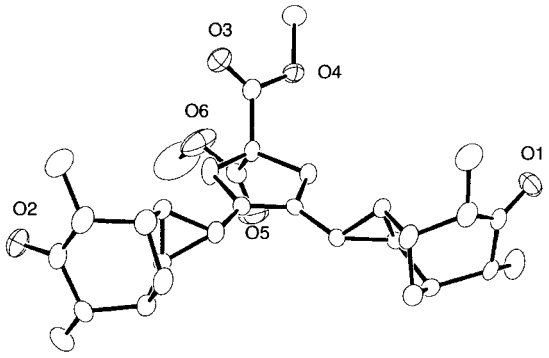
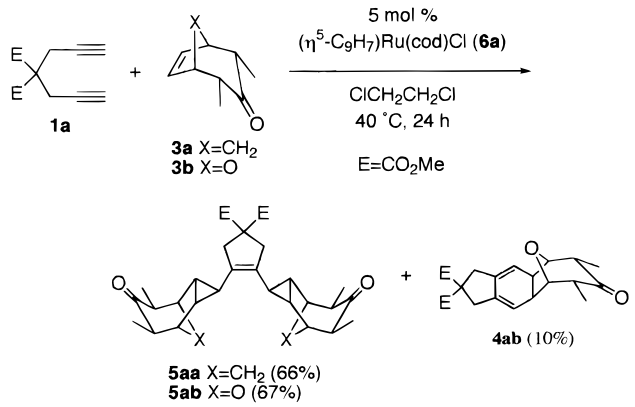


Figure 1. ORTEP diagram of the structure of **5aa**. All hydrogen atoms are omitted for clarity.

Scheme 2



1 with a strained cycloalkene, norbornene, and found that unexpected 1:2 cycloadducts were obtained together with the desired cyclocotrimerization products.[6a] Along this line, we next applied this novel cycloaddition to a bicyclo[3.2.1]cyclooctene system (Scheme 2). The reaction of dimethyl dipropargylmalonate (**1a**) and 20 equiv of 2,4-dimethylbicyclo[3.2.1]oct-6-en-3-one (**3a**) was carried out in the presence of an indenylruthenium(II) complex, (η^5-C_9H_7)Ru(PPh_3)$_2$Cl (**6a**),[13] at 40 °C in 1,2-dichloroethane for 24 h. The purification of the crude reaction mixture by silica gel column chromatography afforded a cycloadduct **5aa** as a colorless crystal. The ^{1}H and ^{13}C NMR analyses of the adduct showed similar spectral patterns with those reported for the 1:2 adduct between **1a** and norbornene. The molecular ion peak (MH^+, 509) and the elemental analysis indicated that **5aa** is the 1:2 adduct of **1a** and **3a**. In the ^{13}C NMR spectrum, there are three sp^2 peaks (δ 212.6, 172.1, and 131.4) assigned to the ester and the ketone carbonyl groups and the alkene moiety of the cyclopentene ring, respectively, together with nine other sp^3 peaks, indicating its highly symmetrical structure. The absence of the vinylic signal of the expected cyclohexadiene ring in its ^{1}H NMR spectrum initially allows us to assign **5aa** to the [2 + 2 + 2]/[4 + 2] cycloadduct involving a bicyclo[2.2.2]octene framework.[6] The ^{13}C NMR peak appearing at δ 12.8, however, seems slightly too far upfield and was originally assigned to the bridge carbon of the expected bicyclo[2.2.2]octene skeleton. Finally, both the correct structure and the stereochemistry of **5aa** were unequivocally determined by an X-ray analysis. As shown in Figure 1, the tandem adduct **5aa** has a symmetrical 1,2-dicyclopropylcyclopentene skeleton. Each two cyclopropane rings are fused by the bicyclo[3.2.1]-octane at the *exo*-face. In the ^{13}C spectrum of **5aa**, a resonance shown at δ 16.4 and 21.7 was reasonably assigned to the

(7) (a) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, p 741. (b) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: California, 1990; Chapter 8. (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (d) Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635.

(8) Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Tetrahedron Organic Chemistry Series, Vol. 8; Pergamon Press: Oxford 1990.

(9) (a) Carbonaro, A.; Greco, A.; Dall'Asta, G. *Tetrahedron Lett.* **1968**, 5129. (b) Singleton, D. M. *Tetrahedron Lett.* **1973**, 1245. (c) Mitsudo, T.; Naruse, H.; Kondo, T.; Ozaki, Y.; Watanabe, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 580.

(10) (a) Chalk, A. J. *J. Am. Chem. Soc.* **1972**, *94*, 5928. (b) Grigg, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1365. (c) Zhou, Z.; Battaglia, L. P.; Chiusoli, G. P.; Nardelli, M.: Pelizzi, C.; Predieri, G. *J. Chem. Soc., Chem. Commun.* **1990**, 1632. (d) Zhou, Z.; Costa, M.; Chiusoli, P. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1399. (e) Tsuda, T.; Mizuno, H.; Takeda, A.; Tobisawa, A. *Organometallics* **1997**, *16*, 932. (f) Ikeda, S.; Mori, N.; Sato, Y. *J. Am. Chem. Soc.* **1997**, *119*, 4779. (g) Ikeda, S.; Watanabe, H.; Sato, Y. *J. Org. Chem.* **1998**, *63*, 7026. (h) Mori, N.; Ikeda, S.; Sato, Y. *J. Am. Chem. Soc.* **1999**, *121*, 2722. (i) Sambaiah, T.; Li, L.-P.; Huang, D.-J.; Lin, C.-H.; Rayabarapu, D. K.; Cheng, C.-H. *J. Org. Chem.* **1999**, *64*, 3663.

(11) (a) Suzuki, H.; Itoh, K.; Ishii, Y.; Simon, K.; Ibers, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 8494. (b) Brown, L. E.; Itoh, K.: Suzuki, H.; Hirai, K.; Ibers, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 8232. (c) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1987**, *109*, 4753.

(12) (a) Thorn, M. G.; Hill, J. E.; Waratuke, S. A.; Johnson, E. S.; Fanwick, P. E.; Rothwell, I. P. *J. Am. Chem. Soc.* **1997**, *119*, 8630. (b) Johnson, E. S.; Balaich, G. J.; Rothwell, I. P. *J. Am. Chem. Soc.* **1997**, *119*, 7685.

(13) Oro, L. A.; Ciriano, M. A.; Campo, M. *J. Organomet. Chem.* **1985**, *289*, 117.

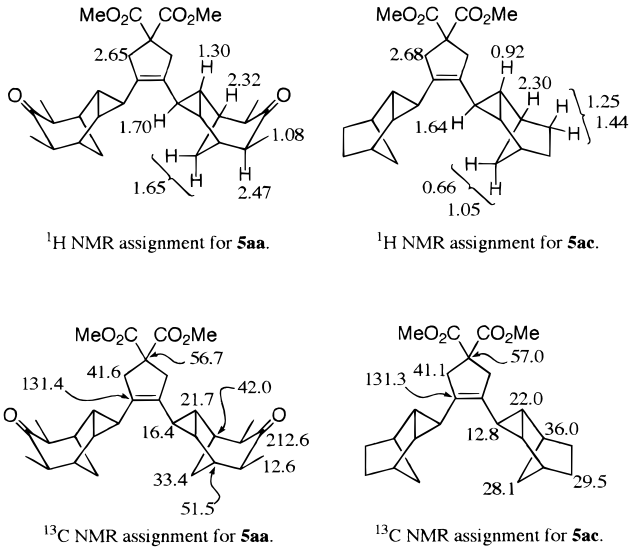


Figure 2. Comparison of ^{1}H and ^{13}C NMR data of the tandem adducts **5aa** and **5ac**.

cyclopropane carbon α to the cyclopentene ring. In the same manner, a double cyclopropanation product **5ab** was obtained from **1a** and a 2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**3b**) in 67% yield together with a cyclocotrimerization adduct **4ab** (10%). It is noteworthy that both the ^{1}H and ^{13}C NMR spectra of the well-defined **5aa** were quite analogous to those of the previously reported tandem adduct **5ac** between **1a** and norbornene (**3c**) as summarized in Figure 2. Unfortunately, a number of attempts to obtain suitable single crystals of the tandem cyclopropanation adducts derived from the norbornene derivatives **3c**−**h** or the simple monocyclic alkenes **3i**,**j** were unsuccessful, and therefore, the X-ray structural determinations were impossible. As summarized in Table 1, our corrected structural assignment of the tandem adducts **5**, however, is strongly supported by the following spectroscopic observations. A pair of slightly upfield signals typical of the cyclopropane moiety was observed at δ 12−24 in the ^{13}C NMR spectra of all these tandem products. Interestingly, the ^{13}C shift corresponding to the carbon α to the cyclopentene moiety (C_α) was directly influenced by the ring strain of the fused alkene moiety: the C_α peak appearing at around δ 12 for the norbornene adducts moved downfield to δ ∼16 for the less strained bicyclo[3.2.1]octene adducts. Moreover, the peaks were observed at δ 18.2 and 19.3 for the least strained cyclopentene and dihydrofuran adducts, respectively. This fact suggests that the ring strain of the fused cyclic system is concentrated at the C_α of the cyclopropane. In contrast, the olefinic ^{13}C signals of the cyclopentene part appeared in the narrow region (δ 130.3−131.7). According to the spectroscopic analogy summarized in Figure 2 and Table 1 (also see, Supporting Information), the previously reported structure of the tandem cycloadduct between **1a** and norbornene (**3c**) should be corrected to be **5ac** (vide infra).

Table 2 summarizes the results of the reaction of **1a** and norbornene (**3c**) conducted using various ruthenium complexes having a planar auxiliary ligand (Scheme 3). Entry 1 shows the best results under the conditions used above. Comparable yield and selectivity were attained with a higher amount of the catalyst (10 mol %) (entry 2). Surprisingly, the indenyl complex **6a** in refluxing dichloromethane gave both cycloadducts only in lower yields (entry 3). In contrast, the parent cyclopentadienyl complex, CpRu(cod)Cl (**6b**),[14] was effective in dichloromethane, but the ratio of **5ac** was lowered. In the presence of **6b** (10 mol %), **1a** and **3c** were refluxed for 7 h to afford the tandem adduct **5ac** in 45% yield together with the [2 + 2 + 2] cyclocotrimerization product **4ac** in 20% yield (entry 4). A cationic system "[CpRu]$^+$" (10 mol % of **6b** with 20 mol % of NH_4-

Table 1. Representative ^{13}C NMR Data for Cyclopropane Moiety of Tandem Adducts **5**

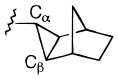
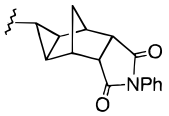
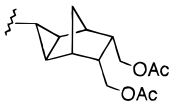
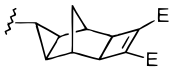
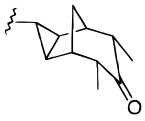
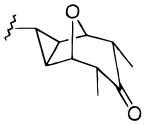
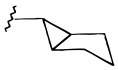
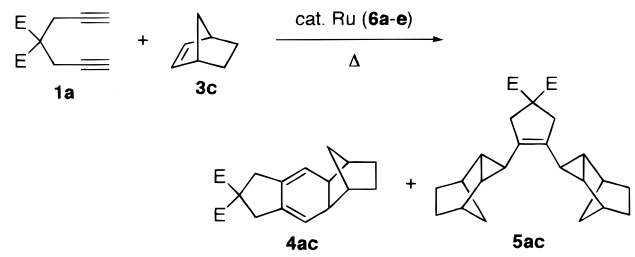
entry	tandem adducts	cyclopropane moieties	C_α (δ, ppm)	C_β (δ, ppm)
1	**5ac**		12.8	22.0
2	**5ad**		12.1	18.0
3	**5ad**		12.2	16.9
4	**5ah**		15.7	20.4
5	**5aa**		16.4	21.7
6	**5ab**		15.9	21.7
7	**5ai**		18.2	20.9
8	**5aj**		19.3	23.5

Table 2. Cycloaddition of 1,6-Heptadiyne **1a** with Norbornene (**3c**)

entry	catalysts (mol %)	conditions	time (h)	isolated yields **4ac** (%)	isolated yields **5ac** (5%)
1	**6a** (5)	$ClCH_2CH_2Cl$, 40 °C	24	12	77
2	**6a** (10)	$ClCH_2CH_2Cl$, 40 °C	24	10	78
3	**6a** (10)	CH_2Cl_2, reflux	24	9	32
4	**6b** (10)	CH_2Cl_2, reflux	7	20	45
5	**6b** (10)[a]	CH_2Cl_2, reflux	72	10	47
6	**6c** (10)	CH_2Cl_2, reflux	17	47	15
7	**6d** (10)	CH_2Cl_2, reflux	48	10	19
8	**6e** (10)	CH_2Cl_2, reflux	42	13	14

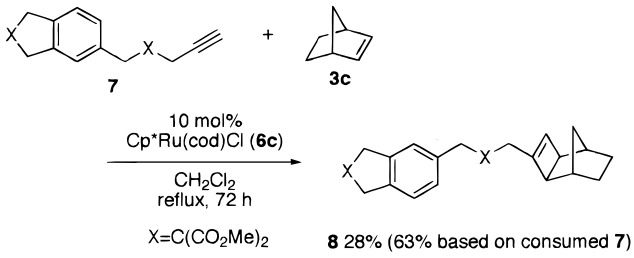
[a] NH_4PF_6 (20 mol %) was added.

Scheme 3



(14) (a) Albers, M. O.; Robinson, J. D.; Shaver, A.; Singleton, E. *Organometallics* **1986**, *5*, 2199. (b) Masuda, K.; Nakano, K.; Fukahori, T.; Nagashima, H.; Itoh, K. *J. Organomet. Chem.* **1992**, *428*, C1.

Scheme 4

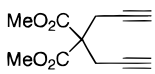
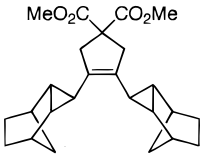
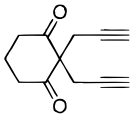
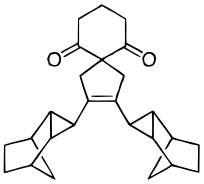
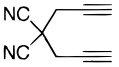
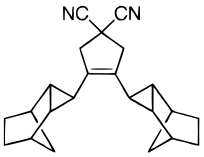
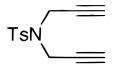
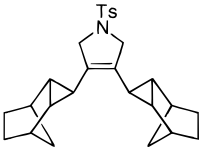
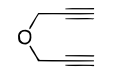
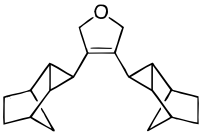


PF_6), which is effective for linear trimerization of butadienes,[15] improved the selectivity but the total yield was somewhat lower (entry 5). The product selectivity was reversed using Cp*Ru(cod)Cl (**6c**; Cp* = pentamethylcyclopentadienyl),[16] having a more electron-donating but bulkier Cp* ligand instead of a Cp ligand (entry 6). In this case, the [2 + 2 + 2] cycloadduct **4ac** became the major product (47%). This indicates that the rigidly coordinated Cp* ligand suppressed the reaction path via the ruthenacyclopentatriene intermediate **2b** (vide infra). In addition, a [2 + 2] cycloadduct **8** was also obtained in 21% yield. The formation of **8** is explained in terms of a Mitsudo-type [2 + 2] cycloaddition between the remaining alkyne terminus of the self-cyclodimerization product **7** and norbornene.[17] In fact, the treatment of **7** and **3c** with 10 mol % **6c** in refluxing dichloromethane afforded **8** in 63% yield based on the consumed **7** (Scheme 4).

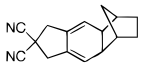
The cyclopentadienyl phosphine complex, $CpRu(PPh_3)_2Cl$ (**6d**),[18] was far less reactive and less selective than the corresponding indenyl complex **6a** (entry 7). In the associative ligand substitution, the η^5-indenyl complexes are generally more active than the corresponding cyclopentadienyl analogues due to the facile η^5-to-η^3 slippage of the indenyl ligand.[19] It is noteworthy that the η^5-indenyl ligand combined with PPh_3 improved not only the yield but also the product selectivity. In contrast to the above Ru(II) complexes, a Ru(0) complex, $(C_6Me_6)Ru(cod)$ (**6e**),[20] was found to be ineffective for the present cycloaddition even though **6e** contains both a planar auxiliary ligand (C_6Me_6) and a good leaving ligand (cod) (entry 8). This fact suggests that tandem cyclopropanation does not proceed through a Ru(0) ↔ R(II) channel but through a Ru(II) ↔ Ru(IV) one.

The transformations of α,β-unsaturated cyclopropanes have received continuous attentions in organic synthesis.[21] In particular, the vinylcyclopropane rearrangement is a powerful protocol to construct unsaturated five-membered rings. In this context, 1,2-dicyclopropylcyclopentene is a quite interesting molecule as a potential precursor for this type of transformation, if it can generally be synthesized from a wide variety of diynes and alkenes. Under the optimized reaction conditions, a series of 1,6-heptadiynes **1b-e** were subjected to the tandem cyclopropanation (Table 3). For cyclohexanedione diyne derivative **1b** (entry 2) and malononitrile derivative **1c** (entry 3), a longer reaction time (48 h) was required to complete the reaction. Thus, **1b** gave exclusively a corresponding dicyclopropylcyclopentene **5bc** in 64% yield, while a substantial amount of [2 + 2 + 2] adduct **4cc** (35%) was also formed from **1c** together with a tandem adduct **5cc** (50%). Furthermore, diynes having a heteroatom at the 4-position, **1d** and **1e**, also gave pyrroline derivative **5dc** and dihydrofuran derivative **5ec** selectively in 47 and 36% yields, respectively (entries 4 and 5). The lower yield of **5ec** may be ascribable to its thermal instability, because the isolated **5ec** was confirmed to decompose slowly even at −15 °C. In contrast to the above diynes, a parent 1,6-heptadiyne **1f** having neither a tertiary center nor a heteroatom at the 4-position gave only trace amounts of the expected cycloadduct under the same reaction conditions. An octadiyne **1g** also failed to react with **3c**, although it has two tertiary carbon centers, with 59% recovery of **1g**. This shows that five-membered ring formations from **1a**−**e** are much more favorable than the corresponding six-membered ring formation from **1g**. Furthermore, internal diynes **1h** and **1i** showed no reactivity toward our catalytic system. Starting diynes were recovered intact in 83 and 93%, respectively. Therefore, terminal substituents on a diyne com-

Table 3. $(\eta^5\text{-}C_7H_9)Ru(PPh_3)_2Cl$-Catalyzed Cycloaddition of 1,6-Heptadiynes **1a**−**e** with Norbornene (**3c**)[a]

entry	diynes	products (isolated yields)[b]
1	 **1a**	 **5ac** (77%)
2	 **1b**	 **5bc** (64%)
3	 **1c**	 **5cc** (50%)
4	 **1d**	 **5dc** (47%)
5	 **1e**	 **5ec** (36%)

[a] Conditions: Norbornene (20 equiv.), $(\eta^5\text{-}C_7H_9)Ru(PPh_3)_2Cl$ (**6a**) (5 mol %), $ClCH_2CH_2Cl$, 40 °C, 24 h (48 h for **1b** and **1c**). [b] [2 + 2 + 2] cyclocotrimerization products **4ac** (entry 1) and **4cc** (entry 3) were obtained in 12 and 35% yields, respectively.



4cc

(15) (a) Masuda, K.; Nakano, K.; Fukahori, T.; Nagashima, H.; Itoh, K. *J. Organomet. Chem.* **1992**, *428*, C21. (b) Masuda, K.; Ohkita, H.; Kurumatani, S.; Itoh, K. *Organometallics* **1993**, *12*, 2221.

(16) Oshima, N.; Suzuki, H.; Moro-oka, Y. *Chem. Lett.* **1984**, 1161.

(17) For Cp*Ru(cod)Cl-catalyzed [2 + 2] cycloaddition of an acetylene with norbornene, see: Mitsudo, T.; Naruse, H.; Kondo, T.; Ozaki, Y.; Watanabe, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 580.

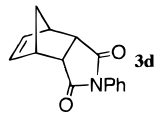
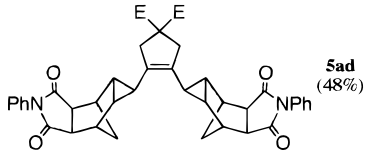
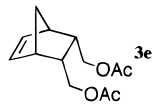
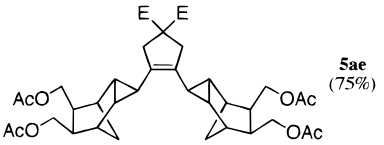
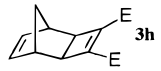
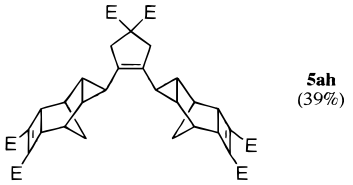
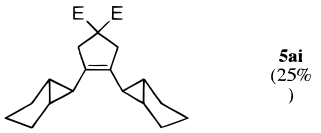
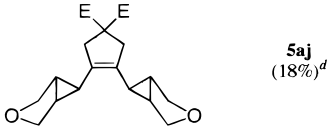
(18) Bruce, M. I.; Windsor, N. J. *Aust. J. Chem.* **1977**, *30*, 1601.

(19) (a) Bönnemann, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 248. (b) Borrini, A.; Diversi, P.; Ingrosso, G.; Lucherini, A.; Serra, G. *J. Mol. Catal.* **1985**, *30*, 181. (c) Trost, B. M.; Kulawiec, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 2027. (d) Gamasa, M. P.; Gimeno, J.; Gonzalez-Bernardo, C.; Martín-Vaca, B. M.; Monti, D.; Bassetti, M. *Organometallics* **1996**, *15*, 302.

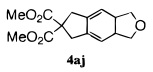
(20) Bennett, M. A.; Huang, T.-N.; Matheson, T. W.; Smith, A. K. *Inorg. Synth.* **1982**, *21*, 74.

(21) Hudlicky, T.; Reed, J. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol 5. p 899.

Table 4. (η^5-C_7H_9)Ru(PPh_3)$_2$Cl-Catalyzed Cycloaddition of 1,6-Heptadiynes **1a** with Alkenes **3d,e,h**−**j**[a,b]

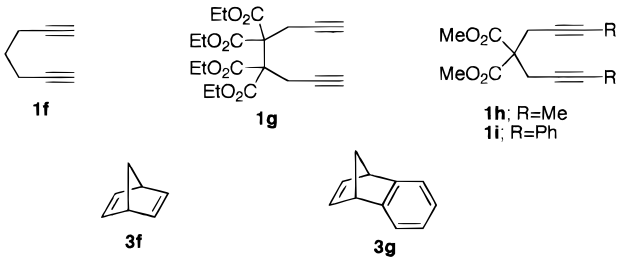
entry	alkenes	products (isolated yields)
1	 **3d**	 **5ad** (48%)
2	 **3e**	 **5ae** (75%)
3	 **3h**	 **5ah** (39%)
4	 **3i**[c]	 **5ai** (25%)
5	**3j**[c]	 **5aj** (18%)[d]

[a] Conditions: (η^5-C_7H_9)Ru(PPh_3)$_2$Cl (**6a**) (5 mol %), diyne **1a** (1 mmol), alkene (20 equiv.), $ClCH_2CH_2Cl$ (5 mL) 40 °C, 24 h. [b] E = CO_2Me. [c] Reactions were carried out in alkene (4 mL)/$ClCH_2CH_2Cl$ (2 mL). [d] A [2 + 2 + 2] cycloadduct **4aj** was obtained in 23% yield.



4aj

pletely inhibit the ruthenacycle formation, or the formed ruthenacyclopentatriene was too stable to react with **3c**.



1f **1g** **1h**; R=Me **1i**; R=Ph

3f **3g**

In the next step, we examined the influence of the structure of the olefin component (Table 4). Norbornenes **3d** and **3e** with substituents at the 5- and 6-positions gave the corresponding tandem adducts **5ad** and **5ae** in 48 and 75% yields, respectively (entries 1 and 2). The tandem cyclopropanation of norbornadiene **3f** was expected to furnish a linear polymer; **3f**, however, gave no product at all (97% recovery of **1a**). Similarly, benzonorbornadiene **3g** did not give the expected tandem adduct, but instead, the dimer and trimer of **1a** were obtained in 77 and 17% yields, respectively. Thus, unsaturation at the C5−C6 position in the norbornene system prevented the tandem cyclopropanation. On the other hand, a cyclobutene-fused norbornene **3h**, prepared by the Mitsudo procedure,[22] selectively reacted on the norbornene ring to afford the desired tandem adduct **5ah** in 39% yield (entry 3). The importance of the ring strain of alkene substrates was clearly shown by the examples of simple monocyclic alkenes. The expected tandem cyclopropanation products **5ai** and **5aj** were obtained in only low yields even when cyclopentene (**3i**) or its oxa-analogue, 2,5-dihydrofuran (**3j**), was used in large excess (entries 4 and 5). Instead, [2 + 2 + 2] cycloadduct **4aj** became the major product in the reaction of 2,5-dihydrofuran (**3j**). This result suggests again that the ether oxygen atom on the alkene affects the product selectivity to a large extent (vide infra).[6b]

Heteroatom-Assisted Selective Cyclocotrimerization of 1,6-Heptadiynes with Cyclic and Linear Alkenes Possessing a Heteroatom in the Allylic Position. As described above, diyne **1a** was reacted similarly with cyclopentene (**3i**) to give a tandem adduct **5ai,** albeit in low yield (25%), even when **3i** was used in large excess. This result shows that the ring strain of bicycloalkenes is essential for our tandem cyclopropanation. Moreover, a cyclic ether, 2,5-dihydrofuran (**3j**), gave the [2 + 2 + 2] cycloadduct **4aj** as the major product, indicative of the ether oxygen at the allylic position playing an important role in the product selection.[23,24] This fact prompted us to develop a novel heteroatom-assisted cyclocotrimerization of 1,6-heptadiynes with 2,5-dihydrofuran because the selective cyclocotrimerization between electronically neutral alkynes and alkenes has been a challenging theme (vide supra). Thus, we next attempted the selective formation of tricyclic cyclohexadiene **4aj** from **1a** and **3j**. Toward this end, the pentamethylcyclopentadienylruthenium(II) complex **6c** is the catalyst of choice; the rigidly coordinated Cp* ligand suppressed the tandem cyclopropanation even in the reaction with norbornene (**3c**). In the presence of **6c** (1 mol %), diyne **1a** (1 mmol) was stirred at 40 °C in 3 mL (∼40 equiv) of degassed **3j** under N_2 for 24 h. After recovering excess **3j** under reduced pressure, purification by silica gel chromatography gave the desired **4aj** in excellent yield (87%) (entry 1, Table 5). Diyne self-dimerization was completely suppressed using commercially available **3j** as the solvent. In the same manner, other diynes were subjected to the catalyzed coupling with **3j** as summarized in Table 5. Diynes **1b**,**j**−**l** having a tertiary center at the 4-position gave the desired cycloadducts **4** in moderate to good yields (entries 2−5). In sharp contrast to the reaction with norbornene (**3c**), a simple diyne **1f** having no tertiary center at the 4-position also gave a corresponding cycloadduct **4fj** (50%) despite being expected to have low cyclization ability without the Thorpe−Ingold effect.[25] Encouraged by this result, we carried out the reactions with diynes **1d** and **1e** possessing a heteroatom at the 4-position to afford heterotricycles **4dj** and **4ej** in 70 and 74% yields, respectively. The

(22) (a) Mitsudo, T.; Kokuryo, K.; Takegami, Y. *J. Chem. Soc., Chem. Commun*. **1976**, 722. (b) Mitsudo, T.; Kokuryo, K.; Shinsugi, T.; Nakagawa, Y.; Watanabe, Y.; Takegami, Y. *J. Org. Chem*. **1979**, *44*, 4492.

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

(24) For heteroatom-directed transition-metal-mediated cycloadditions, see: (a) Kraft, M. E. *J. Am. Chem. Soc*. **1988**, *110*, 968. (b) Kraft, M. E.; Juliano, C. A.; Scott, I. L.; Wright, C.; McEachin, M. D. *J. Am. Chem. Soc*. **1991**, *113*, 1693. (c) Kraft, M. E.; Juliano, C. A. *J. Org. Chem*. **1992**, *57*, 5106. (d) Kraft, M. E.; Scott, I. L.; Romero, R. H. *Tetrahedron Lett*. **1992**, *33*, 3829. (e) Kraft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Pelt, C. E. V. *J. Am. Chem. Soc*. **1993**, *115*, 7199. (f) Montenegro, E.; Poch, M.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett*. **1998**, *39*, 335. (g) Bhatarah, P.; Smith, E. H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2603. (h) Bhatarah, P.; Smith, E. H. *J. Chem. Soc., Chem. Commun*. **1991**, 277. (i) Bhatarah, P.; Smith, E. H. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2163. (j) Duckworth, D. M.; Lee-Wong, S.; Slawin, A. M. Z.; Smith, E. H.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 815.

(25) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc*. **1915**, *107*, 1080.

Scheme 5

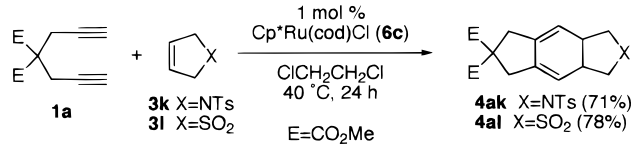
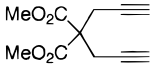
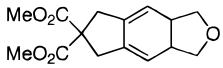
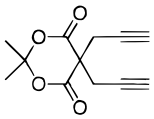
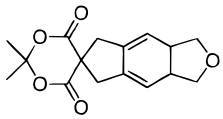
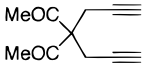
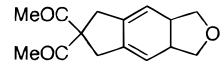
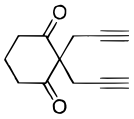
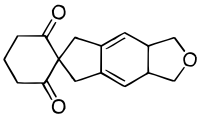
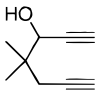
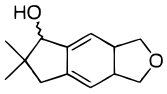
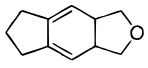
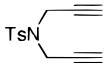
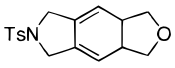
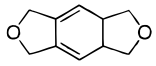
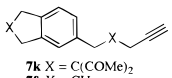
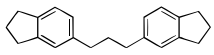


Table 5. Cp*Ru(cod)Cl-Catalyzed [2 + 2 + 2] Cycloaddition of Diynes **1** with 2,5-Dihydrofuran (**3j**)[a]

entry	diynes	products (isolated yields)
1	 **1a**	 **4aj** (87%)
2	 **1j**	 **4jj** (67%)
3	 **1k**	 **4kj** (68%)[b]
4	 **1b**	 **4bj** (90%)
5	 **1l**	 **4lj** (83%)[c]
6	 **1f**	 **4fj** (50%)[d]
7	 **1d**	 **4dj** (70%)[b]
8	 **1e**	 **4ej** (74%)

[a] Conditions: Cp*Ru(cod)Cl (**6c**) (1 mol %), diyne **1** (1 mmol), 2,5-dihydrofuran **3j** (3 mL), 40 °C, 24 h. [b] Dimers **7k** and **7d** were isolated in 14 and 8% yields, respectively. [c] 1:1 Diasteromer mixture. [d] A mixture of dimer **7f** and trimer **7f′** was obtained in ∼28%.

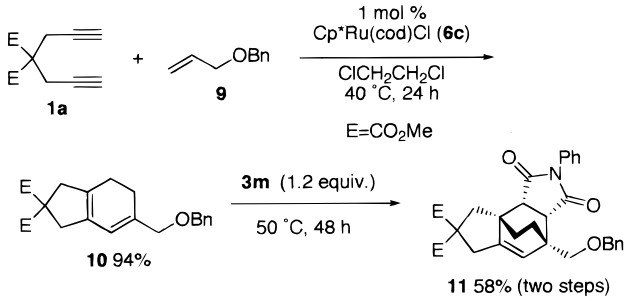




present cycloaddition is tolerant of a wide variety of functional groups, although malononitrile-derived diyne **1c** hardly gave the corresponding adduct.

To extend the scope of the heteroatom-assisted [2 + 2 + 2] cycloaddition, we then applied this protocol to other cycloalkenes possessing a hetero functionality (Scheme 5). The reactions of *N*-tosyl pyrroline (**3k**) and 3-sulfolene (**3l**) with diyne **1a** were carried out in a manner similar to that of **3j** to afford the expected tricyclic pyrrolidine derivative **4ak** and sulfone derivative **4al** in 71 and 78% yields, respectively. Obviously, the heteroatoms on the cycloalkene ring play a key role: that is, the corresponding cyclopentene (**3i**) gave no cycloadduct under the same reaction conditions. Another important aspect of the heteroatom-assisted cycloaddition is that the ring strain of the olefin component does not affect the yield and the selectivity. In fact, acyclic allyl benzyl ether (**9**) reacted with **1a** to produce cyclohexadiene **10** as a major regioisomer via a concomitant

Scheme 6



1,5-H shift (Scheme 6). The structure of **10** was deduced from the following facts. In the ^{1}H 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 **10** with maleimide **3m**, leading to **11**. The complex tetracycle **11** can also be obtained in 58% yields by the one-pot, sequential [2 + 2 + 2]/[4 + 2] cycloaddition.

During the screening of the catalyst system, we unexpectedly found that an analogous dinuclear pentamethylcyclopentadienylruthenium(III) complex, $[Cp^*RuCl_2]_2$ (**6f**),[16] is a much superior catalyst for the heteroatom-assisted [2 + 2 + 2] cyclocotrimerization. The Ru(III) complex **6f** is the important precursor for the syntheses of a variety of pentamethylcyclopentadienylruthenium complexes such as $[Cp^*RuCl]_4$,[26] $Cp^*Ru(diene)Cl$,[16,27] $Cp^*Ru(phosphine)_2$,[16] $Cp^*Ru(CO)_2Cl$,[16] $[Cp^*Ru]_2(\mu\text{-}H)_4$,[28] and $Cp^*Ru(allyl)Cl_2$.[29] Among them, Cp*Ru(cod)Cl (**6c**) has recently been used in interesting catalytic organic transformations.[17,30] On the other hand, the parent **6f** itself has not been used as such a C−C bond-forming catalyst except for a few examples: Trost et al. claimed that **6f** was less effective than a related Ru(II) complex, CpRu(cod)Cl (**6b**), in the catalyzed coupling of 1-octyne and ethyl 4-hydroxy-5-methyl-2-hexynoate.[31] Moreover, **6f** was also reported to be 5 times less active than its osmium analogue, $[Cp^*OsBr_2]_2$, in the ring-opening methathesis polymerization of norbornene.[32] To our surprise, the reaction of **1a** with **3j** was completed within 2 h at room temperature in the presence of **6f** (0.5 mol %), although **1a** was not completely consumed after 24 h using the Ru(II) catalyst **6c**. The purification of the crude mixture by silica gel chromatography gave the desired cyclohexadiene **4aj** in 81% yield (TOF = 81 h^{-1}; entry 1, Table 6). In a similar manner, both *N*,*N*-dipropargyltosylamide **1d** and propargyl ether **1e** gave

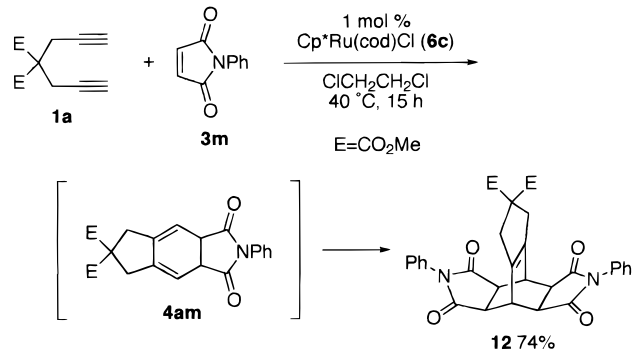
(26) Fagan, P. J.; Mahoney, W. S.; Calabrese, J. C.; Williams, I. D. *Organometallics* **1990**, *9*, 1843 and references.
(27) Masuda, K.; Ohkita, H.; Kurumatani, S.; Itoh, K. *Organometallics* **1993**, *12*, 2221.
(28) Suzuki, H.; Omori, H.; Lee, D. H.; Yoshida, Y.; Moro-oka, Y. *Organometallics* **1988**, *7*, 2243.
(29) Nagashima, H.; Mukai, K.; Shiota, Y.; Yamaguchi, K.; Ara, K.; Fukahori, T.; Suzuki, H.; Akita, M.; Moro-oka, Y.; Itoh, K. *Organometallics* **1990**, *9*, 799.
(30) (a) Itoh, K.; Masuda, K.; Fukahori, T.; Nakano, K.; Aoki, K.; Nagashima, H. *Organometallics* **1994**, *13*, 1020. (b) Dérien, S.; Dixneuf, P. H. *J. Chem. Soc., Chem. Commun.* **1994**, 2551. (c) Dérien, S.; Jan, D.; Dixneuf, P. H. *Tetrahedron* **1996**, *52*, 5511. (d) Dérien, S.; Ropartz, L.; Paih, J. L.; Dixzeuf, P. H. *J. Org. Chem.* **1996**, *64*, 3524. (e) Paih, J. L.; Dérien, S.; Dixneuf, P. H. *Chem. Commun.* **1999**, 1437. (f) Kondo, T.; Uenoyama, S.; Fujita, K.; Mitsudo, T. *J. Am. Chem. Soc.* **1999**, *121*, 482. (g) Kondo, T.; Morisaki, Y.; Uenoyama, S.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **1999**, *121*, 8657.
(31) Trost, B. M.; Müller, T. J. J.; Martinez, J. *J. Am. Chem. Soc.* **1995** *117*, 1888.
(32) Brumaghim, J. L.; Girolami, G. S. *Organometallics* **1999**, *18*, 1923.

Table 6. $[Cp^*RuCl_2]_2$-Catalyzed [2 + 2 + 2] Cycloaddition of Diynes **1** with Heterocyclic Alkenes **3**[a]

entry	diynes	alkenes	time (h)	products (isolated yields)
1	**1a**	**3j**	2	**4aj** (81%)
2	**1d**	**3j**	2	**4dj** (70%)
3	**1e**	**3j**	2	**4ej** (70%)
4	**1a**	**3k**	2	**4ak** (71%)
5	**1a**	**3l**	15	**4al** (55%)

[a] Conditions: diyne **1** (1 mmol), alkene **3** (5 mL), $[Cp^*RuCl_2]_2$ (**6f**) (0.005 mmol), rt.

Scheme 7



the corresponding products **4dj** and **4ej** in 70% yield (entries 2 and 3). *N*-Tosyl-3-pyrroline (**3k**) and 3-sulfolene (**3l**) could also be employed as cycloalkene components. The excess pyrroline **3k** and **1a** were reacted in 1,2-dichloromethane to furnish the pyrrolidine **4ak** in 71% yield (entry 4). The sulfolene **3l** was less reactive than other heterocyclic alkenes. The reaction with **1a** required 15 h for completion and gave the sulfone **4al** in moderate yield (55%; entry 5).

Heteroatom-Assisted [2 + 2 + 2]/[4 + 2] Cycloaddition with Electron-Deficient Cycloalkenes. The selective cyclocotrimerization of electronically neutral alkyne and alkene components was successfully realized by the combination of heterocyclic alkenes and the ruthenium(II) complex **6c** or the dinuclear ruthenium(III) complex **6f** having a rigidly coordinated Cp* ligand. Moreover, electron-deficient *N*-phenylmaleimide (**3m**) can be employed as the alkene component. In this case, an unexpected 1:2 cycloadduct **12** was, however, obtained in good yield (84%) despite using a smaller amount (5 equiv) of **3m** (Scheme 7). The mass measurement (MH^+, 555) and the elemental analysis obviously showed that **12** is the 1:2 adduct of diyne **1a** and maleimide **3m**. In the ^{13}C NMR spectrum, only five sp^3 signals and seven sp^2 signals (two are carbonyl carbons and five are aromatic and vinylic carbons) were observed, indicating that **12** has a highly symmetrical structure. The absence of a vinylic proton signal in the ^1H NMR spectrum and a pair of upfield shifts of a cyclopropane in the ^{13}C NMR spectum shows that **12** is a [2 + 2 + 2]/[4 + 2] cycloadduct having a symmetrical bicyclo[2.2.2]octene core skeleton. Chalk also reported that similar [2 + 2 + 2]/[4 + 2] cycloadducts were obtained in low yield in the Ni(0)-catalyzed reaction of phenylacetylene or 1-hexyne with *N*-methylmaleimide.[10a] In our work, the second [4 + 2] cycloaddition of a tricyclic cyclohexadiene intermediate **4am** and **3m** took place via the thermal Diels−Alder cycloaddition and exclusively furnished the highly symmetrical 1:2 adduct **12**. To obtain further insight into this cascade reaction, the Diels−Alder reaction of the [2 + 2 + 2] cycloadduct **4aj** with maleimide **3m** or maleic anhydride (**3n**) was examined in the absence of the catalyst as depicted in Scheme 8. As expected, the desired bicyclo[2.2.2]octene derivatives **13** and **14** were successfully obtained in 75 and 69% yields, respectively. To confirm the bicyclo[2.2.2]octene framework as well as the stereochemistry in the second Diels−Alder cycloaddition, the X-ray analysis of **14** was undertaken as shown in Figure 3. The normal *endo*-selective [4 + 2] cycloadditions proceeded, avoiding the steric repulsion between the tetrahydrofuran moiety and the cycloalkene component via a transition state **15** to realize the *exo*-orientation of both the tetrahydrofuran and the succinic anhydride or the succinimide rings. According to the spectral similarities, the [4 + 2]/[2 + 2 + 2] cycloadduct **12** is considered to have a similar bicyclo[2.2.2]octene skeleton with the *exo*-oriented succinimide moieties.

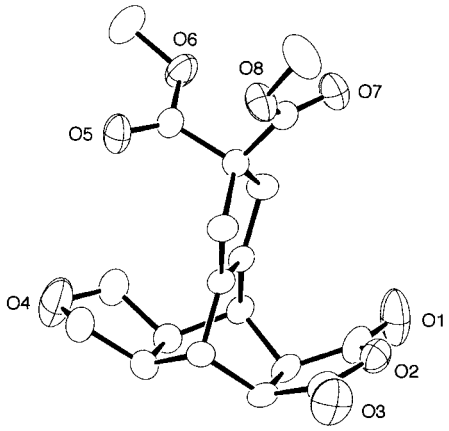
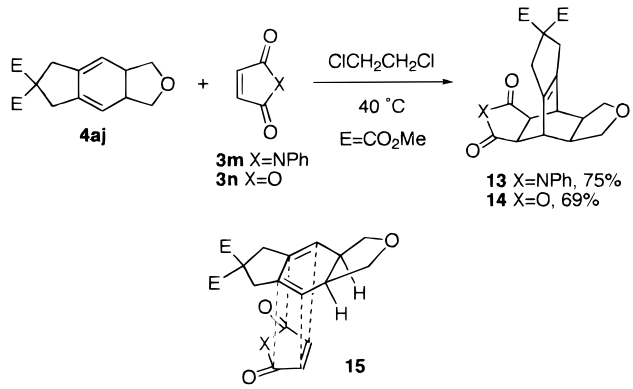


Figure 3. ORTEP diagram of the structure of **11**. All hydrogen atoms are omitted for clarity.

Scheme 8

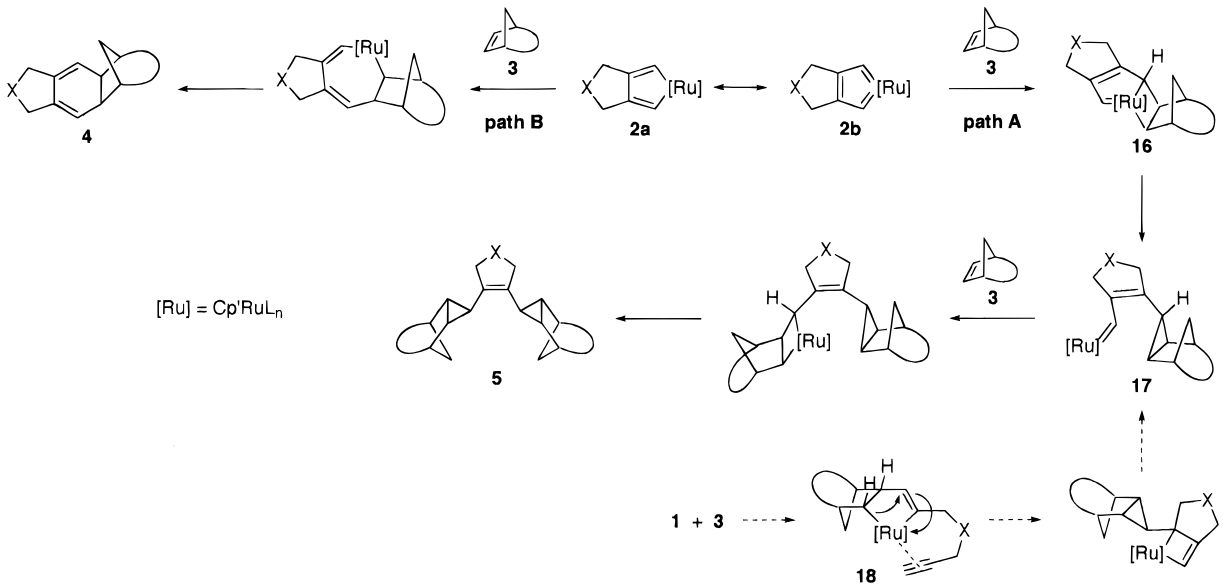


Reaction Mechanisms. The detailed reaction mechanism of the tandem cyclopropanation is not clear at present, but a ruthenacyclopentatriene intermediate **2b** is believed to be a key intermediate (Scheme 9). Some metallacyclopentatriene complexes have so far been isolated and characterized by X-ray analyses.[33] The related cyclopentadienylruthenacyclopentatriene has also been isolated by Singleton and co-workers.[34] The chemical reactivities of metallacyclopentatriene complexes, however, are hardly known although they have a fascinating cyclic biscarbene structure. Taube et al. have reported the reaction of an osmacyclopentatriene complex with *tert*-butylamine leading to a ring-opening dienylcarbene complex.[33e]

(33) (a) Hirpo, W.; Curtis, M. D. *J. Am. Chem. Soc.* **1988**, *110*, 5218. (b) Kerschner, J. L.; Fanwick, P. E.; Rothwell, I. P. *J. Am. Chem. Soc.* **1988**, *110*, 8235. (c) Bruce, M. I.; Koutsantonis, G. A. *Aust. J. Chem.* **1991**, *44*, 207. (d) Pu, L.; Hasegawa, T.; Parkin, S.; Taube, H. *J. Am. Chem. Soc.* **1992**, *114*, 2712. (e) Pu, L.; Hasegawa, T.; Parkin, S.; Taube, H. *J. Am. Chem. Soc.* **1992**, *114*, 7609. (f) Pu, L.; Hasegawa, T.; Parkin, S.; Taube, H. *J. Am. Chem. Soc.* **1993**, *115*, 2545.

(34) Albers, M. O.; de Waal, D. J. A.; Liles, D. C.; Robinson, D. J.; Singleton, E.; Wiege, M. B. *J. Chem. Soc., Chem. Commun.* **1986**, 1680.

Scheme 9



Bicyclic ruthenacyclopentatrienes were also considered as key intermediates by Kirchner et al. in their synthesis of ruthenium allyl carbene complexes.[35] In addition, a ruthenacyclopentatriene intermediate was very recently postulated by Dixneuf's group in their catalytic coupling of terminal alkynes and carboxylic acids.[30e] The reaction of the ruthenium(II) complex with a diyne **1** produces a fused ruthenacyclopentatriene **2b**. The following stereoselective cyclopropanation via a ruthenacyclobutane **16** produced a vinylcarbene complex **17**, which undegoes the second stereoselective cyclopropanation to afford **5** (path A). An alternative mechanism via a ruthenacyclopentene **18** (path B), which might be involved in the ruthenium-catalyzed skeletal reorganization of 1,6- and 1,7-enynes,[36] seems less likely, because the formation of a ruthenacyclopentadiene **2a** from a diyne **1** is entropically more favorable than that of a ruthenacyclopentene **18** intermolecularly from **1** and an alkene **3**.[37] Moreover, Mitsudo et al. reported that similar ruthenacyclopentene intermediates gave [2 + 2] cycloaddition products, cyclobutenes, rather than cyclopropanes.[17,22] In contrast, the ruthenium-catalyzed cyclopropanation of norbornene with alkynes were recently reported by Takahashi and co-workers.[38] This cyclopropanation, however, proceeds only when propargyl alcohol and its derivatives are employed as an alkyne component. In addition, cationic complexes having Cp or a substituted Cp ligand are active catalysts, although neutral complexes such as **6b** and **6c** were inactive.

The metallacyclopentatriene mechanism also agrees with the difference in reactivity between **1a**−**e** and the parent 1,6-heptadiyne **1f**. The 1,6-heptadiyne **1f** having no tertiary center at the 4-position gave only trace amounts of the expected cycloadduct under the same reaction conditions. This is because the metallacycle formation is far less favorable without the aid of the Thorpe−Ingold effect.[25] The slippage of the cyclopentadienyl ligands[39] is essential for the selective formation of the tandem adducts **5**; an $\eta^5 \rightarrow \eta^3$ haptotropic shift can open a vacant site in the coordinatively saturated *18-electron* intermediate **2b** prior to the coordination of the second molecule of a bicyclic alkene **3** to the ruthenium center. Therefore, the most flexible indenyl complex **19** gave the tandem adduct **5** with the highest yield and excellent selectivity via η^3-indenyl complex **20**, although a rigidly coordinated pentamethylcyclopentadienyl ligand in **21** gave the normal [2 + 2 + 2] cycloadduct **4** as the major product (Scheme 10). In this case, a ruthenacyclopentadiene structure **2a** becomes predominant, and the insertion of **3** into the Ru−C bond in **2a** is followed by the reductive elimination of the Cp*RuCl fragment to furnish **4** (path B in Scheme 9).

In contrast to the strained bicycloalkenes, 2,5-dihydrofuran (**3j**) gave the [2 + 2 + 2] cycloadducts as the major product even using the indenyl complex **6a**. The bidentate coordination of the allylic ether moiety in **3j** seems to be unfavorable for the formation of the ruthenacyclopentatriene intermediate. In turn, this allylic ether effect plays a key role in Cp*Ru(cod)Cl-catalyzed [2 + 2 + 2] cycloaddition. This agrees with the observation that cyclopentene (**3i**) and 3-methoxycyclohexene (**3o**), which have the allylic ether moiety fixed in *s*-trans orientation, showed no reactivity under the same reaction conditions. The insertion mechanism via a cationic ruthenacycle **22** depicted in Scheme 11 is reasonable, although no cycloadduct was observed when AgOTf was employed as an additive (85% of **1a** was recovered). The coordinated ether oxygen-assisted Diels−Alder mechanism via a transition state **23** might be an

(35) Mauthner, K.; Soldouzi, K. M.; Mereiter, K.; Schmid, R.; Kirchner, K. *Organometallics* **1999**, *18*, 4681.

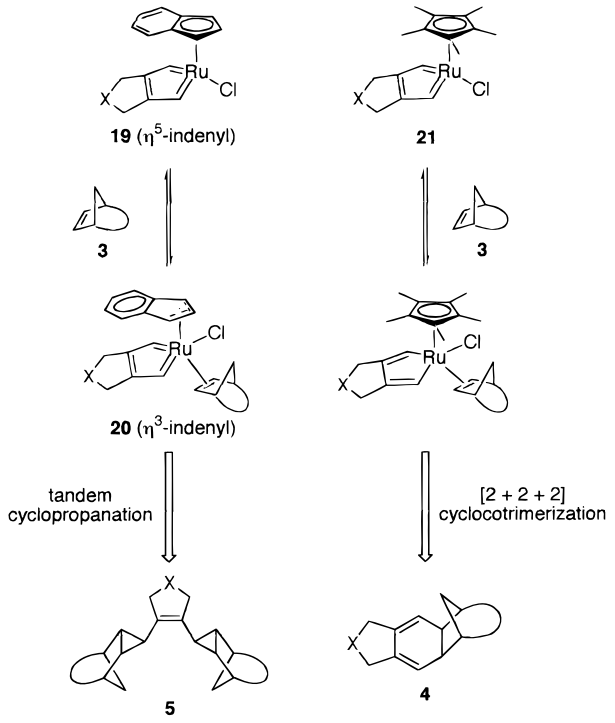
(36) (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049. (b) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901. (c) Chatani, N.; Kataoka, K.; Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 9104 and references therein.

(37) Ruthenacyclopentene formations were proposed to be a key step in the Ru-catalyzed reactions of alkynes and alkenes or of enynes, see: (a) Trost, B. M.; Imi, K.; Indolese, A. F. *J. Am. Chem. Soc.* **1993**, *115*, 8831. (b) Trost, B. M.; Müller, T. J. J. *J. Am. Chem. Soc.* **1994**, *116*, 4985. (c) Trost, B. M.; Indolese, A. F.; Müller, T. J. J.; Treptow, B. *J. Am. Chem. Soc.* **1995**, *117*, 615. (d) Trost, B. M.; Müller, T. J. J.; Martinez, J. *J. Am. Chem. Soc.* **1995**, *117*, 1888. (e) Trost, B. M.; Portnoy, M.; Kurihara, H. *J. Am. Chem. Soc.* **1997**, *119*, 836. (f) Trost, B. M.; Roth, G. J. *Org. Lett.* **1999**, *1*, 67. (g) Morimoto, T.; Chatani, N.; Fukumoto, Y.; Murai, S. *J. Org. Chem.* **1997**, *62*, 3762. (h) Mitsudo, T.; Zhang, S.-W.; Nagao, M.; Watanabe, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 598. (i) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **1997**, *119*, 6187 and also see refs 17 and 29b−d.

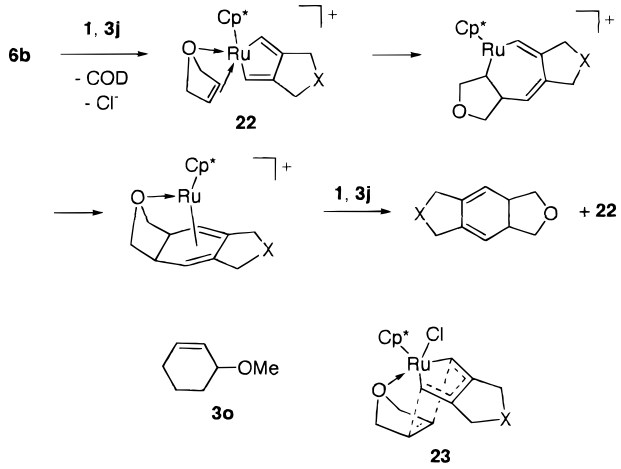
(38) Kikuchi, H.; Uno, Mitsunari, Takahashi, S. *Chem. Lett.* **1997**, 1273.

(39) (a) Schuster-Woldan, H. G.; Basolo, F. *J. Am. Chem. Soc.* **1966**, *88*, 1657. (b) Cramer, R.; Seiwell, L. P. *J. Organomet. Chem.* **1975**, *92*, 245. (c) Rerek, M. E.; Basolo, F. *J. Am. Chem. Soc.* **1984**, *106*, 5908. (d) Abdulla, K.; Booth, B. L.; Stacey, C. *J. Organomet. Chem.* **1983**, 293, 103. (e) Rerek, M. E.; Basolo, F. *Organometallics* **1983**, *2*, 372. (f) Arthurs, M.; Karodia, H.; Seddwick, M. *J. Organomet. Chem.* **1985**, *291*, 231. (g) Cheong, M.; Basolo, F. *Organometallics* **1988**, *7*, 2041. (h) Vest, P.; Anhaus, J.; Bajaj, H. C.; van Eldik, R. *Organometallics* **1991**, *10*, 818.

Scheme 10



Scheme 11



alternative explanation for the efficiency of the present system. Moreover, the higher catalytic activity of the Ru(III) complex **6f** might be ascribable to the dinuclear character of this complex. Tilley et al. have obtained a dinuclear ruthenium complex containing a ruthenacyclopentadiene from tetranuclear $[Cp^*RuCl]_4$ with acetylene.[40] The X-ray analysis of the dinuclear complex revealed that a Ru(IV) metallacyclopentadiene moiety is coordinated as a diene by the neighboring Ru(II) species to fulfill the electron count of both the Ru(IV) and the Ru(II) centers.

Conclusions

We have found a novel Ru(II)-catalyzed tandem cyclopropanation between 1,6-heptadiynes and strained bicycloalkenes. The catalytic cycle possibly starts with the formation of a ruthenacyclopentatriene from a ruthenium(II) intermediate and a diyne. Therefore, the present tandem cyclopropanation is the first typical example of chemical evidence of a bis-carbenoid hybrid structure, 1,3,5-metallacyclopentatriene, of the corresponding 2,4-metallacyclopentadiene intermediates, leading to the C−C bond formation. The tandem cyclopropanation was accompanied by the competitive [2 + 2 + 2] cyclocotrimerization via the ruthenacyclopentadiene. The selectivity for the formation of the tandem adduct was increased in the order of $(\eta^5\text{-}C_9H_7)Ru(PPh_3)_2Cl$ > CpRu(cod)Cl > Cp*Ru(cod)Cl, reflecting the increasing order of the haptotropic flexibility of the cyclopentadienyl type ligands. The rigidity of the Cp* ligand favorable for the [2 + 2 + 2] cyclocotrimerization mode was successfully exploited in the heteroatom-assisted [2 + 2 + 2] cyclocotrimerization. The pentamethylcyclopentadienylruthenium complexes, Cp*Ru(cod)Cl or $[Cp^*RuCl_2]_2$ effectively catalyzed the cycloaddition of the 1,6-heptadiynes with cyclic or linear alkenes possessing heteroatoms at the allylic position. This novel cycloaddition of 1,6-heptadiynes with heterocyclic alkenes is a practical protocol for the synthesis of functionalized bicyclic cyclohexadienes. Furthermore, our method is not only the first example of ruthenium-catalyzed cyclocotrimerization between two molecules of an alkyne and an alkene but also a rare case of cyclocotrimerization between electronically non-activated alkynes and alkenes with both good chemoselectivity and high product yields under the mild conditions.

Experimental Section

General. ^1H and ^{13}C NMR spectra were obtained for samples in $CDCl_3$ solution. Flash chromatography was performed with a silica gel column (Merck Silica gel 60) eluted with mixed solvents [hexane/ethyl acetate]. Elemental analyses were performed by the Microanalytical Center of Kyoto University. Melting points were obtained in sealed capillary tubes and are uncorrected. 1,2-Dichloroethane was distilled from CaH_2, and degassed. $RuCl_3 \cdot xH_2O$ was purchased from N. E. Chemcat Corporation.

Starting Materials. $(\eta^5\text{-}C_9H_7)Ru(PPh_3)_2Cl$ (**6a**),[13] Cp*Ru(cod)Cl (**6c**),[16] $CpRu(PPh_3)_2Cl$ (**6d**),[18] $(C_6Me_6)Ru(cod)$ (**6e**),[20] $[Cp^*RuCl_2]_2$ (**6f**),[16] 2,4-dimethylbicyclo[3.2.1]oct-6-en-3-one (**3a**),[41] and 2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (**3b**)[41] were obtained according to the literature procedures. CpRu(cod)Cl (**6b**) was prepared from $CpRu(\eta^3\text{-}C_3H_5)Cl_2$ with 1,5-cyclooctadiene according to the established methods.[14b]

Typical Procedure for Ru-Catalyzed Tandem Cyclopropanation of 1,6-Heptadiynes with Cycloalkenes. $(\eta^5\text{-}C_9H_7)Ru(PPh_3)_2Cl$-Catalyzed Reaction of Diyne 1a with Norbornene (3c). To a solution of $(\eta^5\text{-}C_9H_7)Ru(PPh_3)_2Cl$ (**6a**) (34.4 mg, 0.044 mmol) in dry degassed 1,2-dichloroethane (20 mL) were added norbornene (**3c**) (1.67 g, 17.8 mmol) and diyne **1a** (185 mg, 0.89 mmol) under Ar atmosphere at room temperature. The reaction mixture was stirred at 40 °C for 24 h. The solvent was removed, and the products were extracted with ethyl acetate (10 mL × 3). The extract was concentrated, and the residue was purified by silica gel flash column chromatography (eluent hexane−AcOEt 30:1) to give tandem adduct **5ac** (271 mg, 77%) as a white solid. Further elution gave [2 + 2 + 2] adduct **4ac** (31 mg, 12%) as a white solid. Other reactions of diynes **1b−e** with norbornene, and diyne **1a** with alkenes **3b−j** were carried out in similar manners. The yields and conditions are summarized in Tables 2−4.

Analytical Data for 5aa: mp 206−210 °C (eluent hexane−AcOEt 5:1); IR ($CHCl_3$) 2974, 1730, 1704 cm^{-1}; ^1H NMR (300 MHz) δ 1.08 (6 H, d, J = 6.6 Hz), 1.30 (4 H, d, J = 3.0 Hz), 1.65 (4 H, m), 1.70 (2 H, t, J = 3.0 Hz), 2.32 (4 H, m), 2.47 (4 H, dq, J = 6.6, 2.4 Hz), 2.65 (4 H, s), 3.68 (6 H, s); ^{13}C NMR (75 MHz) δ 12.6, 16.4, 21.7, 33.4, 41.6, 42.0, 51.5, 52.8, 56.7, 131.4, 172.1, 212.6; MS (EI) *m/z* (rel intensity) 509 (MH^+, 86), 460 (100); Anal. Calcd for $C_{31}H_{40}O_6$: C, 73.20; H, 7.93. Found: C, 73.26; H, 7.87.

Cp*Ru(cod)Cl-Catalyzed Reaction of Dimer 7 with Norbornene (3c). A solution of Cp*Ru(cod)Cl (**6c**) (17 mg, 0.045 mmol), norbornene (227 mg, 2.25 mmol) and dimer **7** (187 mg, 0.45 mmol) in

(40) Campion, B. K.; Hetn, R. H.; Tilley, T. D. *Organometallics* **1990**, *9*, 1106.

(41) Rawson, D. I.; Carpenter, B. K.; Hoffmann, H. M. R. *J. Am. Chem. Soc.* **1979**, *101*, 1786.

dry degassed dichloromethane (1 mL) was refluxed for 72 h under Ar atmosphere. The solvent was removed, and the residue was purified by silica gel flash column chromatography (eluent hexane−AcOEt 5:1) to give **8** (64 mg, 28%) as an oil together with recovered **7** (106 mg, 57%).

Analytical Data for 8: IR (neat) 1736 cm^{-1}; ^1H NMR (500 MHz) δ 0.93 (1 H, d, $J = 10$ Hz), 0.98 (2 H, m), 1.37 (1 H, d, $J = 10$ Hz), 1.52 (2 H, m), 1.89 (2 H, d, $J = 17$ Hz), 2.36 (2 H, s), 2.46 (1 H, d, $J = 16$ Hz), 2.51 (1 H, d, $J = 16$ Hz), 3.20 (1 H, d, $J = 14$ Hz), 3.30 (1 H, d, $J = 14$ Hz), 3.54 (4 H, d, $J = 2$ Hz), 3.68 (3 H, s), 3.70 (3 H, s), 3.74 (6 H, s), 5.73 (1 H, s), 6.87 (1 H, d, $J = 8$ Hz), 6.91 (1 H, s), 7.07 (1 H, d, $J = 8$ Hz); ^{13}C NMR (125 MHz) δ 27.6, 28.2, 30.2, 31.6, 32.8, 34.3, 37.7, 40.2, 40.4, 47.0, 51.3, 52.3, 52.4, 53.0, 57.7, 60.3, 123.9, 125.7, 128.6, 132.4, 134.9, 138.5, 139.9, 145.1, 171.2, 171.4, 172.0; MS (EI) *m*/*z* (rel intensity) 510 (M^+, 26), 479 (13), 450 (5), 376 (32), 344 (100); Anal. Calcd for $C_{29}H_{34}O_8$: C, 68.22; H, 6.71. Found: C, 67.93; H, 7.00.

Typical Procedure for Cp*Ru(cod)Cl-Catalyzed Cycloaddition of 1,6-Heptadiynes with Heterocyclic Alkenes. The Reaction of Diyne 1a with 2,5-Dihydrofuran (3j). To a solution of Cp*Ru(cod)Cl (**6c**) (3.8 mg, 0.01 mmol) in dry degassed 2,5-dihydrofuran (**3j**) (3 mL) was added diyne **1a** (208 mg, 1.0 mmol) under Ar atmosphere at room temperature. The reaction mixture was stirred at 40 °C for 24 h. The solvent was removed, and the products were extracted with ethyl acetate (10 mL × 3). The extract was concentrated, and the residue was purified by silica gel flash column chromatography (eluent H−A 10:1) to give [2 + 2 + 2] adduct **4aj** (242 mg, 87%) as a white solid. In a similar manner, other reactions of diynes with heterocyclic alkenes or allyl benzyl ether (**9**) were carried out. The yields and conditions are summarized in Tables 5 and 6.

Analytical Data for 4aj: mp 51−52 °C (eluent Hexane-AcOEt 30:1); IR ($CHCl_3$) 1739, 1254, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.89 (2 H, d, $J = 16.5$ Hz), 2.97 (2 H, m), 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.76; H, 6.50.

Analytical Data for 10: oil (eluent H−A 10:1); IR (neat) 1739, 1092 cm^{-1}; ^1H NMR (300 MHz) δ 2.17−2.33 (4 H, m), 3.04 (4 H, s), 3.74 (6 H, s), 3.99 (2 H, s), 4.49 (2 H, s), 5.86 (1 H, s), 7.27−7.35 (5 H, m); ^{13}C NMR (75 MHz) δ. 23.4, 24.9, 41.4, 43.3, 52.9, 58.5, 71.7, 73.3, 116.4, 118.2, 119.6, 127.4, 127.5, 127.6, 128.3, 129.8, 132.1, 134.8, 172.5; MS (EI) *m*/*z* (rel intensity) 356 (M^+, 76), 265 (47), 205 (100), 175 (65); Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.77; H, 6.79.

One-Pot Synthesis of Tetracycle 11. To a solution of Cp*Ru(cod)Cl (**6c**) (3.8 mg, 0.01 mmol) in dry degassed allyl benzyl ether (**9**) (3 mL) was added diyne **1a** (208 mg, 1.0 mmol) under Ar atmosphere at room temperature. The reaction mixture was stirred at 40 °C for 24 h. To the resultant reaction mixture was added *N*-phenylmaleimide (**3m**) (208 mg), and the mixture was stirred at 50 °C for 2 days. The solvent was removed, and the products were extracted with ethyl acetate (10 mL × 3). The extract was concentrated, and the residue was purified by silica gel flash column chromatography (eluent H−A 2:1) to give **11** (310 mg, 58%) as a white solid (mp 55−57 °C); IR ($CHCl_3$) 1732, 1713 cm^{-1}; ^1H NMR (300 MHz) δ 2.59 (1 H, d, $J = 14.1$ Hz), 2.87 (1 H, dd, $J = 17.1$, 2.7 Hz), 2.91 (12 H, d, $J = 8.1$ Hz), 3.10 (1 H, d, $J = 17.1$ Hz), 3.17 (1 H, d, $J = 8.1$ Hz), 3.540 (1 H, d, $J = 14.1$ Hz), 3.71 (3 H, s), 3.73 (3 H, s), 3.85 (1 H, d, $J = 6$ Hz), 4.08 (1 H, d, $J = 6$ Hz), 4.58 (1 H, d, $J = 12$ Hz), 4.68 (1 H, d, $J = 12$ Hz), 5.73 (1 H, d, $J = 2.7$ Hz); ^{13}C NMR (75 MHz) δ 29.4, 32.5, 37.9, 38.4, 43.4, 47.0, 47.2, 47.3, 53.0, 60.8, 72.7, 60.8, 72.7, 73.4, 121.8, 126.5, 127.4, 127.5, 128.2, 128.4, 131.6, 138.4, 147.2, 171.0, 172.3, 176.0, 176.2; MS (EI) *m*/*z* (rel intensity) 530 (MH^+, 36), 512 (36), 498 (100), 438 (64); Anal. Calcd for $C_{31}H_{31}NO_7$: C, 70.31; H, 5.90; N, 2.64. Found: C, 70.50; H, 5.92; N, 2.53.

Cp*Ru(cod)Cl-Catalyzed [2 + 2 + 2]/[4 + 2] Cycloaddition of Diyne 1a with *N*-Phenylmaleimide (3m). To a solution of Cp*Ru(cod)Cl (**6c**) (3.8 mg, 0.01 mmol) in dry degassed 1,2-dichloromethane (3 mL) were added diyne **1a** (208 mg, 1.0 mmol) and maleimide **3m** (866 mg, 5 mmol) under Ar atmosphere at room temperature. The reaction mixture was stirred at 40 °C for 15 h. The solvent was removed, and the products were extracted with ethyl acetate (10 mL × 3). The extract was concentrated, and the residue was purified by silica gel flash column chromatography (eluent H−A 1:1) to give [2 + 2 + 2]/[4 + 2] adduct **12** (413 mg, 74%) as a white solid (mp >270 °C); IR ($CHCl_3$) 1732, 1716 cm^{-1}; ^1H NMR (300 MHz) δ 3.11 (4 H, s), 3.26 (4 H, m), 3.58 (6 H, s), 4.04 (2 H, m), 7.19−7.46 (10 H, m); ^{13}C NMR (75 MHz) δ 35.4, 42.5, 43.9, 53.0, 58.7, 126.4, 128.7, 129.0, 131.1, 137.1, 171.3, 175.0; MS (EI) *m*/*z* (rel intensity) 555 (MH^+, 10), 523 (17), 495 (36), 463 (100); Anal. Calcd for $C_{31}H_{26}N_2O_8$: C, 67.14; H, 4.73; N, 5.06. Found: C, 67.00; H, 4.39; N, 5.49.

Typical Procedure for Thermal Reaction of [2 + 2 + 2] Cycloadduct with Electron-Deficient Alkenes. The Reaction of Cyclohexadiene 4aj with *N*-Phenylmaleimde (3m). A solution of cyclohexadiene **4aj** (224 mg, 0.81 mmol) and maleimide **3m** (173 mg, 1.0 mmol) in dry 1,2-dichloromethane (5 mL) was stirred at 40 °C for 18 h. The solvent was removed, and the products were extracted with ethyl acetate (10 mL × 3). The extract was concentrated, and the residue was purified by silica gel flash column chromatography (eluent H−A 1:1) to give [4 + 2] adduct **13** (201 mg, 75%) as a white solid. The reaction of **4aj** and meleic anhydride (**3n**) was carried out in the same manner.

Analytical Data for 13: mp 178−179 °C (eluent H−A 1:1); IR ($CHCl_3$) 1777, 1746, 1713 cm^{-1}; ^1H NMR (300 MHz) δ 2.65 (2 H, m), 3.08 (4 H, s), 3.12 (4 H, m), 3.34 (2 H, s), 3.63 (3 H, s), 3.73 (3 H, s), 3.93 (2 H, m), 7.34−7.47 (5 H, m); ^{13}C NMR (75 MHz) δ 36.0, 43.5, 44.7, 45.0, 52.9, 53.1, 59.5, 71.6, 126.5, 128.6, 129.0, 131.4, 137.3, 171.5, 176.6; MS (EI) *m*/*z* (rel intensity) no molecular ion peak 425 (14), 382 (95), 322 (100); Anal. Calcd for $C_{25}H_{25}NO_7$: C, 66.51; H, 5.58; N, 3.10. Found: C, 66.41; H, 5.25; N, 3.52.

Crystallographic Structural Determination. A suitable crystal of **5aa** was mounted on the end of a quartz fiber using Apiezon grease. The crystal was transferred to an Rigaku AFC7 equipped with a MSC/ADSC Quantum1 CCD detector with Mo Kα radiation and cooled to −100 °C under a cold nitrogen stream previously calibrated by a thermocouple placed in the same position. After the crystal had been carefully optical centered within the X-ray beam, 4 data frames measured at 0.5 ° increments of ω were collected to assess the crystal quality. To correct for high-energy background events in the images, data frames were collected as the sum of two 15-s exposures and non-correlating events were eliminated. A total of 149 reflections with $I > 3\sigma(I)$ were selected and utilized to calculate a preliminary unit cell. The intensity images were measured at 0.5 ° intervals of ω for a duration of 82 s each. Frame data were integrated using the d*TREK program package, and an absorption correction was performed using the REQAB program. The 17895 integrated reflections were averaged in point group 2/m to give 6260 unique reflections.

All calculations were performed with TEXSAN. The structure was solved by direct methods, completed by subsequent difference Fourier syntheses, and refined by full-matrix least-squares procedues. There are two independent molecules in an asymmetric unit. All non-hydrogen atoms were refined anisotropically, while the hydrogen atoms were located at calculated positions.

The X-ray analysis of **14** was carried out in a similar manner.

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Supporting Information Available: Analytical data of the cycloadducts, tables of crystallographic data and data collection details, positional parameters with *B*(eq), anisotropic displacement parameters, bond distances and angles, and a figure containing the atom-numbering schemes for **5aa** and **14** (PDF). This material is available free of charge via the Internet at http://pubs.asc.org.

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