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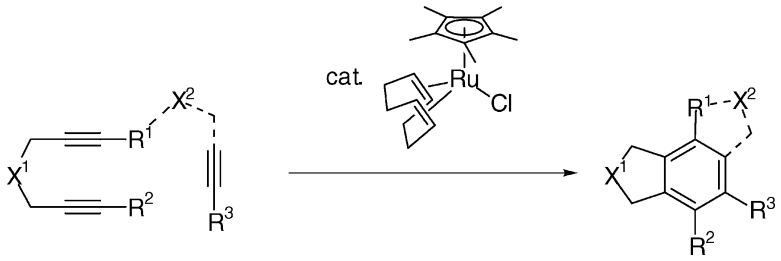

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Ruthenium(II)-Catalyzed Selective Intramolecular [2 + 2 + 2] Alkyne Cyclotrimerizations

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Abstract: In the presence of a catalytic amount of Cp*RuCl(cod), 1,6-diynes chemoselectively reacted with monoalkynes at ambient temperature to afford the desired bicyclic benzene derivatives in good yields. A wide variety of diynes and monoynes containing functional groups such as ester, ketone, nitrile, amine, alcohol, sulfide, etc. can be used for the present ruthenium catalysis. The most significant advantage of this protocol is that the cycloaddition of unsymmetrical 1,6-diynes with one internal alkyne moiety regioselectively gave rise to meta-substituted products with excellent regioselectivity. Completely intramolecular alkyne cyclotrimerization was also accomplished using triyne substrates to obtain tricyclic aromatic compounds fused with 5−7-membered rings. A ruthenabicycle complex relevant to these cyclotrimerizations was synthesized from Cp*RuCl(cod) and a 1,6-diyne possessing phenyl terminal groups, and its structure was unambiguously determined by X-ray analysis. The intermediary of such a ruthenacycle intermediate was further confirmed by its reaction with acetylene, giving rise to the expected cycloadduct. The density functional study on the cyclotrimerization mechanism elucidated that the cyclotrimerization proceeds via oxidative cyclization, producing a ruthenacycle intermediate and subsequent alkyne insertion initiated by the formal [2 + 2] cycloaddition of the resultant ruthenacycle with an alkyne.

Introduction

The transition-metal-catalyzed [2 + 2 + 2] cyclotrimerization of alkynes has received continuous attention as a straightforward route to substituted benzenes.[1] Because of its atom-economical[2] and convergent nature, the cyclotrimerization approach is considerably advantageous in the construction of substituted benzene rings in comparison with conventional strategies depending on the sequential substitutions of a benzene ring by way of electrophilic aromatic substitutions or orthometalation techniques.[3] Although the chemoselective cocyclotrimerizations of two or three different alkyne components were accomplished using *stoichiometric* transition metal reagents,[4−6] the *catalytic* control of both chemo- and regiochemistry has still been a formidable challenge.[7] To address this issue, partial or complete intramolecular approaches, the intermolecular cycloaddition of diynes with monoalkynes, or the intramolecular cyclization of triynes have been developed as a promising tool to assemble polycyclic aromatic frameworks from simple acyclic precursors (Figure 1).[8,9] The prototype diyne−monoalkyne coupling protocol was first developed by Müller and co-workers in their work using stoichiometric $RhCl(PPh_3)_3$,[8a,b] and subsequently, catalytic versions have been realized by Vollhardt,[9a−c] Grigg,[9d,e] and Chiusoli.[9f] While the diyne−monoalkyne coupling has the advantage of utilizing readily accessible diynes and monoalkynes, chemo- and regioselectivity issues remain to be solved. Facile dimerization of the diyne component is a serious drawback, and a large excess of the monoalkyne component is generally employed to prevent such a side reaction. In addition, the precedent

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(1) (a) Shore, N. E. In *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1129−1162. (b) 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, pp 741−770. (c) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901−2915.
(2) (a) Trost, B. M. *Science* **1991**, *254*, 1471−1477. (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259−281. (c) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695−705.
(3) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, 3rd ed.; Plenum Press: New York, 1990; Part B, Chapter 11, pp 571−614.
(4) (a) Wakatsuki, Y.; Kuramitsu, T.; Yamazaki, H. *Tetrahedron Lett.* **1974**, 4549−4552. (b) Yamazaki, H.; Wakatsuki, Y. *J. Organomet. Chem.* **1977**, *139*, 157−167.
(5) (a) Takahashi, T.; Kotora, M.; Xi, Z. *J. Chem. Soc., Chem. Commun.* **1995**, 361−362. (b) Takahashi, T.; Xi, Z.; Yamazaki, A.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1998**, *120*, 1672−1680. (c) Takahashi, T.; Tsai, F.-Y.; Li, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1999**, *121*, 11093−11100.
(6) (a) Suzuki, D.; Urabe, H.; Sato, F. *J. Am. Chem. Soc.* **2001**, *123*, 7925−7926. (b) Tanaka, R.; Nakano, Y.; Suzuki, D.; Urabe, H.; Sato, F. *J. Am. Chem. Soc.* **2002**, *124*, 9682−9683.
(7) Gevorgyan, V.; Radhakrishnan, U.; Takeda, A.; Rubina, M.; Rubin, M.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 2835−2841.
(8) For *stoichiometric* intramolecular alkyne cyclotrimerizations, see: (a) Müller, E.; Thomas, R.; Sauerbier, M.; Langer, E.; Streichfuss, D. *Tetrahedron Lett.* **1971**, 521−524. (b) Müller, E. *Synthesis*, **1974**, 761−774 and references. (c) Bhatarah, P.; Smith, E. H. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2603−2606. (d) Bhatarah, P.; Smith, E. H. *J. Chem. Soc., Chem. Commun.* **1991**, 277−278. (e) Bhatarah, P.; Smith, E. H. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2163−2168. (f) Duckworth, D. M.; Lee-Wong, S.; Slawin, A. M. Z.; Smith, E. H.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 815−821. (g) Hara, R.; Guo, Q.; Takahashi, T. *Chem. Lett.* **2000**, 140−141.

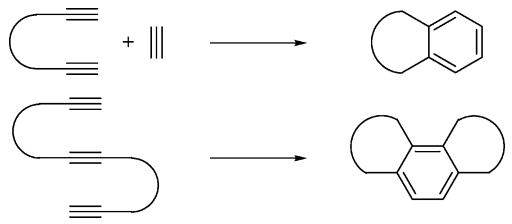


Figure 1. Intramolecular [2 + 2 + 2] alkyne cyclotrimerizations.

catalytic systems have hardly been evaluated in terms of regioselectivity. On the other hand, the intramolecular [2 + 2 + 2] cyclization of triynes afforded the desired product with complete chemo- and regioselectivity, but the preparation of a triyne substrate equipped with required substituents or functional groups at the desired positions often needed lengthy synthetic operations. Aside from such scope and limitations, the synthetic potential of these intramolecular approaches has been extensively demonstrated in the syntheses of natural products,[10] pharmaceutically important molecules,[11] and functional materials.[12]

The development of a milder catalytic process for the cyclotrimerization would also bring a significant advance. Although most of known catalytic systems require heating or irradiation, a simple room-temperature reaction is desirable from the practical point of view. Moreover, a catalytic system compatible with a wide range of functional groups is highly valuable in terms of the synthesis of fine chemicals. With these issues in mind, we developed the new catalytic protocol for the alkyne cyclotrimerizations using a ruthenium(II) complex, Cp*RuCl(cod) (**1a**: Cp* = pentamethylcyclopentadienyl, cod = 1,5-cyclooctadiene),[13] as a catalyst precursor. Significantly, the cycloaddition of unsymmetrical 1,6-diynes with monoalkynes proceeded at ambient temperature to chemo- and regioselectively to afford the desired coupling adducts in good yields. The present ruthenium catalysis is also applicable to the cyclization of triynes, constructing tricyclic benzene derivatives involving 5−7-membered rings. In this article, we wish to present full details of our study on ruthenium(II)-catalyzed intramolecular alkyne cyclotrimerizations using diynes and triynes as alkyne substrates.[14]

Results and Discussion

Cyclotrimerization of Monoalkynes. Since the first discovery of Reppe,[15] numerous transition-metal elements have been found to promote alkyne cyclotrimerizations.[1] Especially, most attention has focused on groups 9 and 10 transition elements such as Co, Rh, Ni, and Pd. With respect to group 8 triads, some stoichiometric and catalytic cyclotrimerizations with limited scope have been reported to date. There exists several examples of *catalytic* cyclotrimerization of highly reactive electron-deficient alkynes at elevated temperatures.[16] On the other hand, the catalytic reaction with *electronically neutral* alkynes is quite rare. Pertici and co-workers only recently reported the iron(0)-catalyzed cyclotrimerization of monoalkynes with aliphatic-, phenyl-, and trimethylsilyl-substituents or the dimerization of 1,7-octadiyne at room temperature.[17] In striking contrast, no example of the ruthenium catalysis for cyclotrimerization of *electronically neutral* alkynes under mild conditions has been precedent except for our preliminary results[14] as well as the recently developed alkyne metathesis cascade catalyzed by Grubbs' carbene complex.[18]

(9) For *catalytic* intramolecular alkyne cyclotrimerizations, see: (a) Vollhardt, K. P. C.; Bergman, R. G. *J. Am. Chem. Soc.* **1974**, *96*, 4996−4998. (b) Hillard, R. L., III; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 712−713. (c) Hillard, R. L., III; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1977**, *99*, 4058−4069. (d) Grigg, R.; Scott, R.; Stevenson, P. *Tetrahedron Lett.* **1982**, *23*, 2691−2692. (e) Grigg, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1357−1364. (f) Chiusoli, G. P.; Pallini, L.; Terenghi, G. *Transition Met. Chem.* **1983**, *8*, 189−190. (g) Williams, A. C.; Sheffels, P.; Sheehan, D.; Livinghouse, T. *Organometallics* **1989**, *8*, 1566−1567. (h) Du Toit, C. J.; Du Plessis, J. A. K.; Lachmann, G. *J. Mol. Catal.* **1989**, *53*, 67−78. (i) Badrieh, Y.; Blum, J.; Amer, I.; Vollhardt, K. P. C. *J. Mol. Catal.* **1991**, *66*, 295−312. (j) Sato, Y.; Nishimata, T.; Mori, M. *J. Org. Chem.* **1994**, *59*, 6133−6135. (k) Sato, Y.; Nishimata, T.; Mori, M. *Heterocycles* **1997**, *44*, 443−457. (l) Nishida, M.; Shiga, H.; Mori, M. *J. Org. Chem.* **1998**, *63*, 8606−8608. (m) Yamamoto, Y.; Nagata, A.; Itoh, K. *Tetrahedron Lett.* **1999**, *40*, 5035−5038. (n) Yamamoto, Y.; Nagata, A.; Arikawa, Y.; Tatsumi, K.; Itoh, K. *Organometallics* **2000**, *19*, 2403−2405. (o) Ozerov, O. V.; Patrick, B. O.; Ladipo, F. T. *J. Am. Chem. Soc.* **2000**, *122*, 6423−6431. (p) Takeuchi, R.; Tanaka, S.; Nakata, Y. *Tetrahedron Lett.* **2001**, *42*, 2991−2994. (q) Slowinski, F.; Aubert, C.; Malacria, M. *Adv. Synth. Catal.* **2001**, *343*, 64−67. (r) Jeevanandam, A.; Korivi, R. P.; Huang, I.; Cheng, C.-H. *Org. Lett.* **2002**, *4*, 807−810. (s) Nishiyama, H.; Niwa, E.; Inoue, T.; Ishima, Y.; Aoki, K. *Organometallics* **2002**, *21*, 2572−2574.

(10) (a) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1976**, *98*, 6755−6757. (b) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1977**, *99*, 5483−5484. (c) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1979**, *101*, 215−217. (d) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1980**, *102*, 5245−5253. (e) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1980**, *102*, 5253−5261. (f) Hillard, R. L., III; Parnell, C. A.; Vollhardt, K. P. C. *Tetrahedron* **1983**, *39*, 905−911. (g) Halterman, R. L.; Nguyen, N. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1985**, *107*, 1379−1387. (h) Lecker, S. H.; Nguyen, N. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1986**, *108*, 856−858. (i) Neeson, S. J.; Stevenson, P. J. *Tetrahedron Lett.* **1988**, *29*, 813−814. (j) Neeson, S. J.; Stevenson, P. J. *Tetrahedron* **1989**, *45*, 6239−6248. (k) McDonald, F. E.; Zhu, H. Y. H.; Holmquist, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 6605−6606. (l) Bradley, A.; Motherwell, W. B.; Ujjainwalla, F. *Chem. Commun.* **1999**, 917−918. (m) Petit, M.; Chouraqui, G.; Phansavath, P.; Aubert, C.; Malacria, M. *Org. Lett.* **2002**, *4*, 1027−1029. (n) Witulski, B.; Zimmermann, A.; Gowans, N. D. *Chem. Commun.* **2002**, 2984−2985.

(11) (a) Kotha, S.; Brahmachary, E. *Tetrahedron Lett.* **1997**, *38*, 3561−3564. (b) Kohta, S.; Mohanraja, K.; Durani, S. *Chem. Commun.* **2000**, 1909−1910. (c) Witulski, B.; Stengel, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 2426−2430. (d) Witulski, B.; Alayrac, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3281−3284. (e) Witulski, B.; Zimmermann, A. *Synlett* **2002**, 1855−1859. (f) Sun, Q.; Zhou, X.; Islam, K.; Kyle, D. J. *Tetrahedron Lett.* **2001**, *42*, 6495−6497. (g) Turek, P.; Kotota, M.; Hocek, M.; Císarová, I. *Tetahedron Lett.* **2003**, *44*, 785−788.

(12) (a) Helson, H. E.; Vollhardt, K. P. C.; Yang, Z.-Y. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 114−115. (b) Diercks, R.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 266−268. (c) Hirthammer, M.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1986**, *108*, 2481−2482. (d) Diercks, R.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1986**, *108*, 3150−3152. (e) Blanco, L.; Helson, H. E.; Hirthammer, M.; Mestdagh, H.; Spyroudis, S.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1246−1247. (f) Schmidt-Radde, R. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1992**, *114*, 9713−9715. (g) Boese, R.; Matzger, A. J.; Mohler, D. L.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1478−1481. (h) Eickmeier, C.; Junga, H.; Matzger, A. J.; Scherhag, F.; Shim, M.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2103−2108. (i) Eickmeier, C.; Holmes, D.; Junga, H.; Matzger, A. J.; Scherhag, F.; Shim, M.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 800−804. (j) Holms, D.; Kumaraswamy, S.; Matzger, A. J.; Vollhardt, K. P. C. *Chem.−Eur. J.* **1999**, *5*, 3399−3412. (k) Bong, D. T.-Y.; Gentric, L.; Holms, D.; Matzger, A. J.; Scherhag, F.; Vollhardt, K. P. C. *Chem. Commun.* **2002**, 278−279. (l) Stará, I. G.; Stary, I.; Kollárovic, A.; Teply, F.; Saman, D.; Tichy, M. *J. Org. Chem.* **1998**, *63*, 4046−4050. (m) Stará, I. G.; Stary, I.; Kollárovic, A.; Teply, F.; Vyskocil, S.; Saman, D. *Tetrahedron Lett.* **1999**, *40*, 1993−1996. (n) Sato, Y.; Ohashi, K.; Mori, M. *Tetrahedron Lett.* **1999**, *40*, 5231−5234. (o) Fletcher, J. T.; Therien, M. J. *J. Am. Chem. Soc.* **2000**, *122*, 12393−12394. (p) Fletcher, J. T.; Therien, M. J. *Inorg. Chem.* **2002**, *41*, 331−341. (q) Fletcher, J. T.; Therien, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 4298−4311. (r) McDonald, F. E.; Smolentsev, V. *Org. Lett.* **2002**, *4*, 745−748.

(13) Oshima, N.; Suzuki, H.; Moro-oka, Y. *Chem. Lett.* **1984**, 1161−1164.

(14) Preliminary results have been reported: Yamamoto, Y.; Ogawa, R. Itoh, K. *Chem. Commun.* **2000**, 549−550.

(15) Reppe, W.; Schweckendiek, W. J. *Justus Liebigs Ann. Chem.* **1948**, *560*, 104−116.

(16) (a) Lindner, E.; Jansen, R.-M.; Mayer, H. A.; Hiller, W.; Fawzi, R. *Organometallics* **1989**, *8*, 2355−2360. (b) Lindner, E.; Kühbauch, H. *J. Organomet. Chem.* **1991**, *403*, C9−14. (c) Ren, C. Y.; Cheng, W. C.; Chan, W. C.; Yeung, C. H.; Lau, C. P. *J. Mol. Catal.* **1990**, *59*, L1−8. (d) Bohanna, C.; Esteruelas, M. A.; Herrero, J.; López, A. M.; Oro, L. A. *J. Organomet. Chem.* **1995**, *498*, 199−206.

(17) Breschi, C.; Piparo, L.; Pertici, P.; Caporusso, A. M.; Vitulli, G. *J. Organomet. Chem.* **2000**, *607*, 57−63.

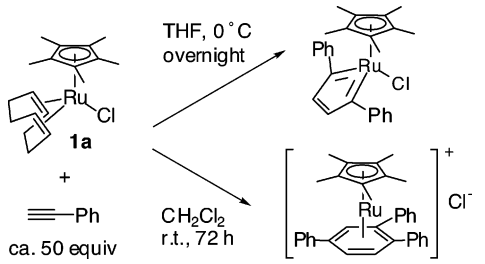
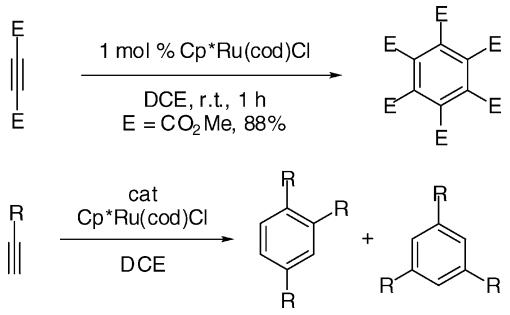


Figure 2. Dinjus' synthesis of ruthenacyclopentatriene and cationic arene complexes.

With these backgrounds in mind, we began to explore the ruthenium-catalyzed alkyne cyclotrimerization. As opposed to the precedents with zerovalent, group 8 complexes,[16] we chose a ruthenium(II) complex, Cp*RuCl(cod) (**1a**),[13] as a catalyst precursor because (1) the cod ligand can be easily replaced by alkyne substrates, (2) the electron donation from Cp* ligand to the ruthenium(II) center enhances the oxidative cyclization step leading to a ruthenacycle key intermediate, and finally, (3) the bulky Cp* ligand provides a compact coordination space, which might control chemo- and regiochemistry. Indeed, Dinjus and co-workers reported that the oxidative cyclization of two molecules of phenylacetylene with **1a** regioselectively took place even at 0 °C in THF to afford a ruthenacyclopentatriene complex (Figure 2).[19b] The same complex was also synthesized by Kirchner et al.,[19a] and the parent cyclopentadienyl (Cp) analogue was first reported by Singleton and co-workers in 1986.[20] Dinjus et al. also reported that a cationic sandwich complex having a 1,2,4-triphenylbenzene ligand as well as the Cp* ligand was formed upon treatment of **1a** with excess phenylacetylene at room temperature in CH_2Cl_2 for 72 h.[19b] The coordinated trisubstituted benzene might be produced via the reaction of the ruthenacyclopentatriene complex with phenylacetylene. These facts suggest that the catalytic cyclotrimerization using Cp*RuCl(cod) as a precatalyst might be achieved with more reactive alkynes, although such a catalytic process was not realized by Dinjus because of the formation of the stable cationic arene complex, which cannot be restored under catalytic conditions. As expected, **1a** proved effective for the cyclotrimerization of highly active electron-deficient alkynes (Scheme 1). In the presence of 1 mol %, **1a**, the cyclotrimerization of dimethyl acetylenedicarboxylate (DMAD), proceeded even at room temperature to give hexamethyl mellitate in 88% yield. Similarly, ethyl propiolate gave both 1,3,4- and 1,3,5-isomers of triethyl benzenetricarboxylate in 61 and 28% yields, respectively. The practical advantage of the present ruthenium(II) catalysis is elucidated by these cyclotrimerizations proceeding without heating.[16] Encouraged by these results, we further attempted the cyclotrimerization of methyl propagyl ether, but the Ru(II) catalysis proved far less effective for such an unactivated alkyne. No regioselectivity was observed, and the yield was moderate (total 39%) even with a higher catalyst loading and elevated temperature of 50 °C. This inferior efficacy might be ascribed to the inefficient oxidative cyclization of propargyl methyl ether with electron-accommodating capability lower than those of DMAD or ethyl propiolate. To improve the oxidative cyclization step, we further employed 1,6-diynes, in which two alkyne moieties are connected with a three-atom tether to make the oxidative cyclization entropically favorable.

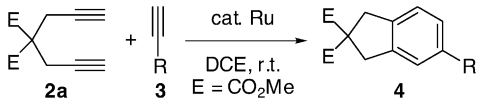
Scheme 1



Cycloaddition of α,ω-Diynes with Terminal Monoalkynes. Previously, we reported that 1,6-diynes possessing a quarternary center at the 4-position are excellent substrates for the Ru(II)-catalyzed [2 + 2 + 2] cycloadditions with alkenes,[21] nitriles,[22] isocyanates,[23a] isothiocyanates,[23b] and tricarbonyl compounds.[24] To realize the cyclotrimerization of unactivated alkynes, we embarked on the initial study on the Ru(II)-catalyzed intramolecular cyclotrimerization using a malonate-derived diyne **2a** as a diyne substrate (Table 1). In the presence of 1 mol % **1a**, a solution of **2a** in dry degassed 1,2-dichloroethane (DCE) was added dropwise over 15 min to 2 equiv of 1-hexyne **3a** in dry degassed DCE at room temperature. After 15 min, the complete consumption of **2a** was confirmed by TLC analysis of the reaction mixture. The chromatographic purification afforded the desired indane derivative **4aa** in 89% yield (run 1). It is noteworthy that only 2 equiv of 1-hexyne effectively suppressed the concomitant formation of a diyne dimer **5a** and a trimer **6a** (total 11% yield). A similar ruthenium(III) complex, $[Cp^*RuCl_2]_2$ (**1b**),[25] was less effective, but gave **4aa** in good yield with prolonged reaction time (run 2). Increased amounts of 1-hexyne to 4 equiv gave a slightly better yield of 94% (run 3). In the same manner, the cycloaddition of **2a** with a variety of monoalkynes was examined as summarized in Table 1. Alkynes bearing a variety of functionalities such as an ether (**3b**), an alcohol (**3c**), an amine (**3d**), and a chloride (**3e**) gave the expected cycloadducts **4ab**, **4ac**, **4ad**, and **4ae**, respectively, in

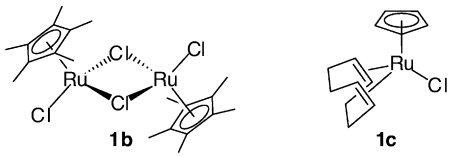
(18) (a) Peters, J.-U.; Blechert, S. *Chem. Commun.* **1997**, 1983−1984. (b) Das, S. K.; Roy, R. *Tetrahedron Lett.* **1999**, *40*, 4015−4018. (c) Witulski, B.; Stengel, T.; Fernández-Hernández, J. M. *Chem. Commun.* **2000**, 1965−1966. (d) Hoven, G. B.; Efskind, J.; Rømming, C.; Undheim, K. *J. Org. Chem.* **2002**, *67*, 2459−2463.
(19) (a) Gemel, C.; LaPensée, A.; Mauthner, K.; Mereiter, K.; Schmid, R.; Kirchner, K. *Monatsh. Chem.* **1997**, *128*, 1189−1199. (b) Ernst, C.; Walter, O.; Dinjus, E. *J. Prakt. Chem.* **1999**, *341*, 801−804. (c) Ernst, C.; Walter, O.; Dinjus, E. *J. Organomet. Chem.* **2001**, *627*, 249−254. (c) Yamada, Y.; Mizutani, J.; Kurihara, M.; Nishihara, H. *J. Organomet. Chem.* **2001**, *637*−*639*, 80−83.
(20) 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**, 1680−1682.
(21) Yamamoto, Y.; Kitahara, H.; Ogawa, R.; Kawaguchi, H.; Tatsumi, K.; Itoh, K. *J. Am. Chem. Soc.* **2000**, *122*, 4310−4319.
(22) (a) Yamamoto, Y.; Ogawa, R.; Itoh, K. *J. Am. Chem. Soc.* **2001**, *123*, 6189−6190. (b) Yamamoto, Y.; Okuda, S.; Itoh, K. *Chem. Commun.* **2001**, 1102−1103.
(23) (a) Yamamoto, Y.; Takagishi, H.; Itoh, K. *Org. Lett.* **2001**, *3*, 2117−2119. (b) Yamamoto, Y.; Takagishi, H.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 28−29.
(24) Yamamoto, Y.; Takagishi, H.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 6844−6845.
(25) The ruthenium(III) complex (**1b**) is commercially available and easily prepared by the literature procedure (see ref 13).

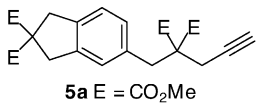
Table 1. Ru(II)-Catalyzed Cycloaddition of Diyne **2a** with Monoalkynes **3a**−**h**[a]

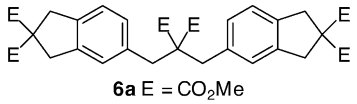


run	R	**3** (equiv)	**1** (mol %)	t	**4**, yield[b] (%)
1	*n*Bu	**3a** (2)	**1a** (1)	15 min	**4aa**, 89
2	*n*Bu	**3a** (2)	**1b** (0.5)	2 h	**4aa**, 75
3	*n*Bu	**3a** (4)	**1a** (1)	15 min	**4aa**, 94
4	CH_2OMe	**3b** (4)	**1a** (1)	15 min	**4ab**, 83
5	CH_2OH	**3c** (4)	**1a** (5)	4 h	**4ac**, 92
6	CH_2NMe_2	**3d** (4)	**1a** (1)	1 h	**4ad**, 77
7	$(CH_2)_3Cl$	**3e** (4)	**1a** (2)	1 h	**4ae**, 96
8	*t*Bu	**3f** (4)	**1a** (1)	1.5 h	**4af**, 34
9	Ph	**3g** (4)	**1a** (5)	15 min	**4ag**, 90
10	H	**3h**[c]	**1a** (1)	1 h	**4ah**, 84

[a] A solution of **2a** (0.5 mmol) in DCE (3 mL) was added dropwise to a solution of **1** and **3** in DCE (2 mL) for 15 min, and the reaction mixture was stirred for the time specified above at room temperature. [b] Isolated yields. [c] Under acetylene atmosphere (1 atm) at 0 °C.



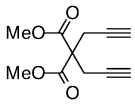
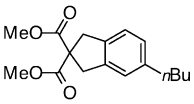
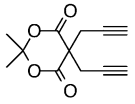
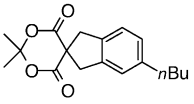
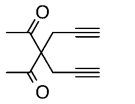
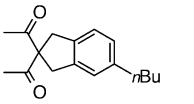
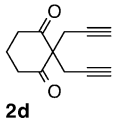
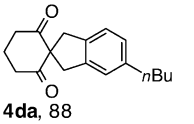
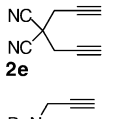
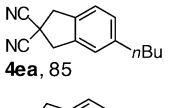
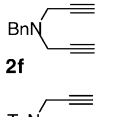
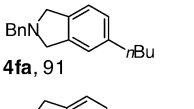
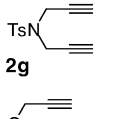
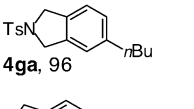
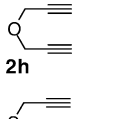
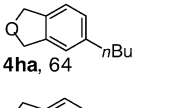
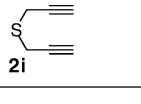
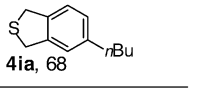




good yields (runs 4−7), although increased catalyst loadings were required for **3c** (5 mol %) and **3e** (2 mol %). The sterically demanding *tert*-butyl group retarded the incorporation of **3f** to afford **4af** only in moderate yield (run 8). Consequently, the oligomerization of the diyne itself predominantly proceeded to give the oligomers **5a** and **6a** in total 47% yield. A phenyl substituent also retarded the cycloaddition of **3g**, but 5 mol % **1a** gave a biphenyl derivative **4ag** in 90% yield (run 9). The ruthenium catalysis can be applied to a gaseous substrate. Under 1 atm acetylene gas, **2a** was converted into **4ah** at 0 °C in 84% yield (run 10).

Given the success of the ruthenium(II)-catalyzed cycloaddition of **2a** with various terminal monoalkynes, we then examined the functional group compatibility of the ruthenium catalysis with respect to 1,6-diyne substrates bearing a variety of functionalities at their 4-positions (Table 2). No deteriorative effects on the reaction rates as well as the yields were observed for diynes **2b**−**g** containing cyclic and acyclic diesters and diketones, a dicyanide, a tertiary amine, and a sulfonamide (runs 2−7). It is noteworthy that a malononitrile-derived diyne **2e** predominantly afforded an arene product **4ea** in 85% yield without forming pyridine byproduct via [2 + 2 + 2] cycloaddition between its 1,6-diyne and dicyanide moieties, as previously reported by our group.[22a] *N*-Benzyl and *N*-tosyl isoindoline derivatives **4fa** and **4ga** were obtained from the corresponding dipropargylamine derivatives **2f** and **2g** in high yields (runs 6 and 7). In contrast, dipropargyl ether **2h** was found to be less

Table 2. Ru(II)-Catalyzed Cycloaddition of Diynes **2a**−**i** with 1-Heyne **3a**[a]

run	diyne **2**	*t*	**4**, yield (%)[b]
1	 **2a**	15 min	 **4aa**, 94
2	 **2b**	15 min	 **4ba**, 83
3	 **2c**	15 min	 **4ca**, 90
4	 **2d**	15 min	 **4da**, 88
5	 **2e**	15 min	 **4ea**, 85
6	 **2f**	15 min	 **4fa**, 91
7	 **2g**	15 min	 **4ga**, 96
8	 **2h**	6 h	 **4ha**, 64
9	 **2i**	1 h	 **4ia**, 68

[a] A solution of **2** (0.5 mmol) in DCE (3 mL) was added dropwise to a solution of **1a** (1 mol % for **2a**−**g**, 5 mol % for **2h**−**i**) and **3a** (4 equiv) in DCE (2 mL) for 15 min and stirred for the time specified above at room temperature. [b] Isolated yields.

efficient (run 8). The prolonged reaction with an increased catalyst loading gave a phthalan derivative **4ha**, albeit in moderate yield. Organosulfur compounds generally behaved as a catalyst poison because of the strong coordination to a catalytically active species. Remarkably, the ruthenium catalysis effectively converted a dipropargyl sulfide **2i** into a 2-thiaindane derivative **4ia** in 68% yield (run 9).

On the contrary to the above 1,6-diynes, a 1,7-diyne **7a**, which is a simple homologue of **2a**, hardly participated in the ruthenium-catalyzed cycloaddition with 1-hexyne **3a** (Scheme 2). This result shows that the only one-atom homologation of the tether chain deteriorates the oxidative cyclization efficiency of the diyne substrate. In accord with this observation, two quarternary centers on the tether chain significantly improved the cycloaddition of a 1,7-diyne because of the kinetic Thorpe−Ingold effect.[26] With the aid of an additional malonate moiety on the tether chain, 10 mol % **1a** effectively catalyzed the reaction of a 1,7-diyne **7b** with **3a** to give a tetrahydronaphthalene derivative **8** in 67% yield.

Scheme 2

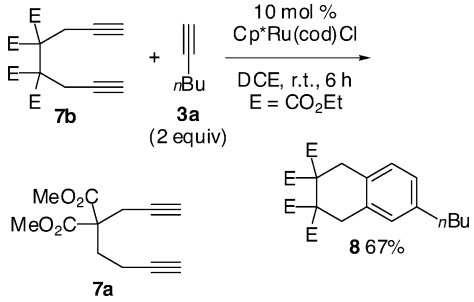
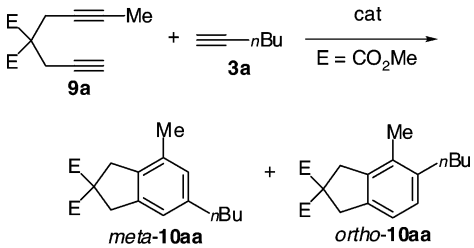


Table 3. Ru(II)-Catalyzed Cycloaddition of Unsymmetrical Diyne **9a** with 1-Hexyne **3a**



run	precatalyst (mol %)	t (h)	**10aa** yield (%)[b] (meta:ortho)[c]
1	Cp*RuCl(cod) **1a** (1)[a]	1	85 (93:7)
2	$[Cp^*RuCl_2]_2$ **1b** (0.5)[a]	2	81 (94:6)
3	CpRuCl(cod) **1c** (1)[a]	24	76 (87:13)
4	$RhCl(PPh_3)_3$ (5)[d]	72	61 (63:37)
5	$Ni(cod)_2/4PPh_3$ (15)[e]	4	83 (30:70)
6	CpCo(cod) (20)[f]	15	70 (54:46)

[a] A solution of **9a** (0.5 mmol) in DCE (3 mL) was added dropwise to a solution of **1** and **3a** (2 equiv) in DCE (2 mL) for 15 min and stirred for the time specified above at room temperature. [b] Isolated yields. [c] Isomer ratios were determined by GC analysis of isolated products. [d] In EtOH at 60 °C. [e] In THF at room temperature. [f] The reaction was carried out with 10 equiv of **3a** in a sealed xylene solution at 150 °C.

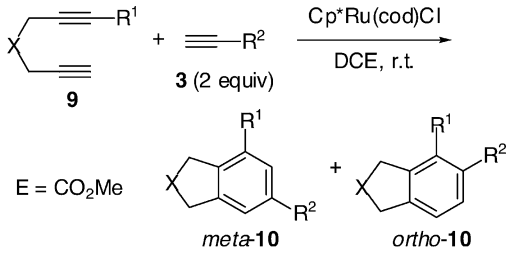
Regiochemistry in Cycloaddition of Unsymmetrical 1,6-Diynes with Terminal Monoalkynes. With the ruthenium catalysis tolerant of a wide range of functionalities in hand, we turned our attention to the regiochemistry in the cycloaddition of unsymmetrical 1,6-diynes. In a similar manner, malonate-derived 1,6-octadiyne **9a** and 2 equiv of **3a** were reacted in the presence of 1 mol % **1a** at room temperature for 1 h (Table 3, run 1). As a consequence, the desired cycloadduct **10aa** was obtained in 85% yield, and remarkably, the excellent isomer selectivity of *meta*-**10aa**/*ortho*-**10aa** = 93:7 was disclosed by the inspection of the isolated sample by GC. A similar yield and regioselectivity were obtained when the ruthenium(III) complex **1b** was employed (run 2). The replacement of the Cp* ligand in **1a** to a less sterically demanding and less electron-releasing Cp ligand in **1c** decreased the isomer selectivity as well as the reactivity (run 3). In addition to these ruthenium complexes, readily available, familiar cyclotrimerization pre-catalysts were examined in terms of the regioselectivity. Wilkinson's complex, $RhCl(PPh_3)_3$, has been introduced as a stoichiometric promoter to the diyne−monoyne coupling chemistry by Müller et al.,[8a,b] and subsequently, its catalytic use has been reported by Grigg and co-workers.[9d,e] There are some examples of regioselective cycloaddition using this precatalyst, but most of these were limited to alkyne substrates possessing a hydroxy group, which might assist the regioselection by its coordination to the rhodium center.[10k,11c,18c] Without resorting to such a directing effect, the cycloaddition partners having no Lewis basic functionality might result in low selectivity. Indeed, the reaction of **9a** and **3a** was conducted in the presence of the 5 mol % Rh complex at 60 °C for 72 h to give **10aa** with much lower selectivity than those observed for **1a**−**c** (run 4). Nickel(0) phosphine complexes have also been reported as efficient promotors for both stoichiometric[8d−f] and catalytic[9f,12n] diyne−monoalkyne couplings. In particular, asymmetric cyclotrimerizations utilizing a nickel(0) precursor with a chiral phosphine are of significance in the syntheses of optically active nitrogen heterocycles[9j,k] and a helicene derivative.[12m] The selectivity given by $Ni(cod)_2/2PPh_3$ was, however, moderate in favor of the ortho-isomer (run 5). These results suggested that the Cp-type planar spectator ligands play an import role in the regioselection event. In this respect, cobalt(I) complexes with a Cp-type ligand are expected to be a suitable catalyst precursor. Yamazaki, Wakatsuki, and co-workers reported the transformation of a phosphine analogue, $CpCo(PPh_3)_2$, into the corresponding cobaltacyclopentadiene complexes, which further reacted with a variety of unsaturated molecules to afford cyclotrimerization products.[27] Intramolecular versions of those Co-mediated cyclotrimerizations have been developed by Vollhardt and co-workers using a corresponding carbonyl analogue, $CpCo(CO)_2$.[9a−c] The highly ortho-selective benzocyclobutene synthesis from 1-trimethylsilyl-1,5-hexadiyne and trimethylsilylacetylene was accomplished by the same authors, but no result for substrates possessing simple alkyl substituents in place of the bulky trimethylsilyl group was presented.[9c] Alkene complexes, $Cp'Co(alkene)_2$, have also been investigated extensively in the alkyne−nitrile cocyclotrimerization by Bönnemann and co-workers.[28] We finally examined the regioselectivity of the cobalt catalysis using a diene complex, CpCo(cod), which is closely relevant to our ruthenium system, **1a** and **1c**. Because the cobalt complex hardly promoted the cycloaddition below 120 °C in accordance with the report from Bönnemann's group, a xylene solution containing 20 mol % CpCo(cod), the unsymmetrical **9a**, and 1-hexyne (10 equiv was used to ensure the complete consumption of **9a**) was heated at 150 °C for 15 h in a sealed glass tube. As a result, **10aa** was obtained in 70% yield with the isomer selectivity of meta/ortho = 54:46 (run 6). With these results, we concluded that the present excellent regioselectivity predominatly furnishing the meta-isomer is the significant merit of the [Cp′RuCl] fragment species (vide infra).

The generality of the regioselection with the ruthenium catalysis was confirmed by the inspection of the cycloaddition between various unsymmetrical diynes and the monoalkynes, as summarized in Table 4. In the same manner as above (run 1), the malonate-derived diyne **9a** and methyl propargyl ether **3b** gave **10ab** in a similar yield and a meta-selectivity with **10aa** (run 2). Phenylacetylene **3g** again retarded the cycloaddition rate, but an increased catalyst loading of 3 mol % and prolonged reaction time afforded **10ag** in 82% yield with slightly lower regioselectivity of meta/ortho = 88:12 (run 3). Similarly, under

(26) (a) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc.* **1915**, *107*, 1080−1106. (b) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224−232.

(27) Wakatsuki, Y.; Yamazaki, H. *J. Chem. Soc., Chem. Commun.* **1973**, 280.
(28) Bönnemann, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 248−262.

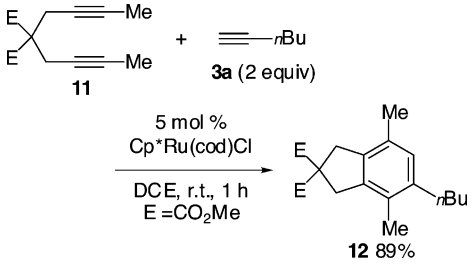
Table 4. Ru(II)-Catalyzed Cycloaddition of Unsymmetrical Diynes **9a**−**f** with Monoalkynes **3a**,**b**,**g**,**i**[a]



run	**9**:X, R^1 **3**:R^2	**1a** t	**10** yield[b] meta:ortho[c]
1	**9a**: CE_2, Me	1 mol %	**10aa**, 85%
	3a: *n*Bu	1 h	93.7
2	**9a**: CE_2, Me	1 mol %	**10ab**, 86%
	3b: CH_2OMe	3 h	94:6
3	**9a**: CE_2, Me	3 mol %	**10ag**, 82%
	3g: Ph	24 h	88:12
4	**9a**: CE_2, Me	3 mol %	**10ai**, 80%
	3i: Me[d]	18 h	94.6
5	**9b**: CE_2, CH_2OMe	3 mol %	**10ba**, 78%
	3a: *n*Bu	12 h	92:8
6	**9c**: CE_2, Ph	10 mol %	**10ca**, 80%
	3a: *n*Bu	24 h	95:5
7	**9d**: CE_2, $SiMe_3$	5 mol %	**10da**, 94%
	3a: *n*Bu	7 h	98:2
8	**9a**: NTs, Me	1 mol %	**10ea**, 82%
	3a: *n*Bu	10 min	93:7
9	**9f**: O, Me	1 mol %	**10fa**, 75%
	3a: *n*Bu	30 min	95:5

[a] A solution of **9** (0.5 mmol) in DCE (3 mL) was added dropwise to a solution of **1a** and **3** (2 equiv) in DCE (2 mL) for 15 min and stirred for the time specified above at room temperature. [b] Isolated yields. [c] Isomer ratios were determined by GC analysis of isolated products. [d] Under propylene atmosphere (1 atm).

Scheme 3

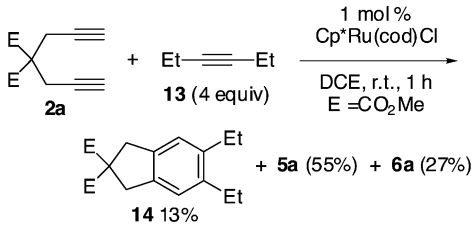


1 atm propyne atmosphere, **9a** was converted into **10ai** in 80% yield with the regioselectivity of 94:6 (run 4).

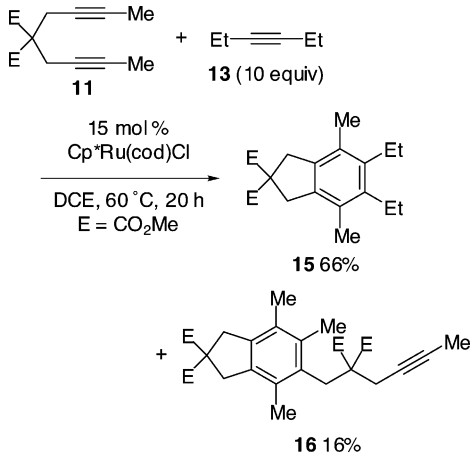
Unsymmetrical diynes possessing methoxymethyl, phenyl, and trimethylsilyl terminal substituents **9b**−**d** required increased catalyst loadings ranging from 3 to 10 mol % (runs 5−7). The reactions of these diynes with 1-hexyne gave the desired cycloadducts **10ba**, **10ca**, and **10da** in 78−94% yields with high regioselectivity. Especially, the trimethylsilyl analogue **10da** was obtained in the highest yield with an excellent meta-selectivity of 98:2 (run 7). In addition to these malonate-derived diynes, diynes **9e** and **9f** having a nitrogen- or an oxygen tether selectively furnished isoindoline and phthalan derivatives, respectively, in good yields (runs 8 and 9).

Cycloaddition of Internal 1,6-Diynes and Monoalkynes. In the presence of 5 mol % **1a**, a 2,7-heptadiyne **11** possessing two internal alkyne termini similarly reacted with 1-hexyne **3a** without difficulty at ambient temperature (Scheme 3). A pentasubstituted benzene **12** was obtained in 89% yield. In striking contrast, the cycloaddition of an internal monoalkyne, 3-hexyne

Scheme 4



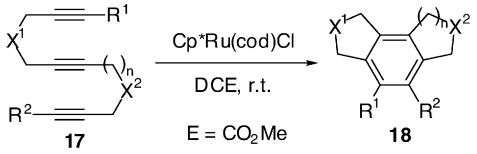
Scheme 5

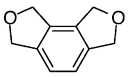
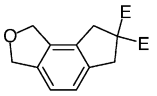
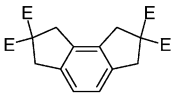
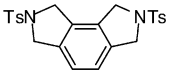
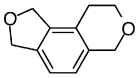
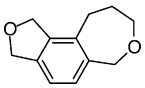
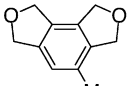
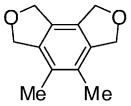


(**13**), resulted in the low-yield formation of a tetrasubstituted **14** (Scheme 4). Consequently, the diyne oligomers **5a** and **6a** were predominately obtained in 55 and 27% yields, respectively, together with only a 13% yield of **14**. To obtain a cycloaddition product from **13**, we employed the internal diyne **11**, which is resistant to oligomerization (Scheme 5). The reaction of **11** with **13** (4 equiv) was, however, not completed within 20 h even with an increased amount of **1a** (10 mol %) at 60 °C. The desired adduct **15** was obtained in 33% yield together with a diyne dimer **16** (20%), and 24% of the diyne **11** was recovered intact. Higher loadings of **1a** (15 mol %) and **13** (10 equiv) improved the conversion and the selectivity. As a result, the fully substituted benzene **15** and the dimer **16** were formed in 66 and 16% yields, respectively.

Completely Intramolecular [2 + 2 + 2] Cyclotrimerization of Triynes. Ruthenium-catalyzed, completely intramolecular alkyne cyclotrimerization of various triyne substrates was next explored, as compiled in Table 5. To avoid intermolecular side reactions, the cyclization of a readily available triyne **17a** was conducted in 0.1 M solution containing 1 mol % **1a** at ambient temperature to afford a tricyclic product **18a** in 82% isolated yield (run 1). Triynes **17b** and **17c** including at least one malonate moiety on their tether chain were converted into **18b** and **18c**, respectively, in good yields with higher catalyst loadings and elongated reaction time (runs 2 and 3). The inferior efficacy of these malonate-derived triynes compared to **17a** might be ascribed to a putative resting state **19a** depicted in Figure 3. The ester carbonyl oxygen was considered to be coordinated by the ruthenium center to form the stable resting state **19a**, which may be in equilibrium with a ruthenacyclopentadiene(alkyne) intermediate **19b**. A bis(tosylamide) derivative **17d** also furnished a nitrogen heterocycle **18d** in 87% yield, although a higher dilution condition of 0.05 M was required because of the lower solubility of **17d** in DCE (run 4). In addition to the above 1,6,11-triynes, a 1,6,12-triyne **17e** and a

Table 5. Ru(II)-Catalyzed Cyclization of Triynes **17a**−**h**



run	**17**	conditions	**18** yield (%)[a]
1	**17a**: n = 1 $X^1 = X^2 = O$ $R^1 = R^2 = H$	1 mol % 0.1 M 2 h	 **18a**, 82
2	**17b**: n = 1 $X^1 = O$, $X^2 = CE_2$ $R^1 = R^2 = H$	5 mol % 0.1 M 3 h	 **18b**, 82
3	**17c**: n = 1 $X^1 = X^2 = CE_2$ $R^1 = R^2 = H$	5 mol % 0.1 M 6 h	 **18c**, 89
4	**17d**: n = 1 $X^1 = X^2 = NTs$ $R^1 = R^2 = H$	1 mol % 0.05 M 5 h	 **18d**, 87
5	**17e**: n = 2 $X^1 = X^2 = O$ $R^1 = R^2 = H$	5 mol % 0.01 M 18 h	 **18e**, 89
6	**17f**: n = 3 $X^1 = X^2 = O$ $R^1 = R^2 = H$	5 mol % 0.01 M 20 h[b]	 **18f**, 53
7	**17g**: n = 1 $X^1 = X^2 = O$ $R^1 = H$, $R^2 = Me$	1 mol % 0.1 M 18 h	 **18g**, 84
8	**17h**: n = 1 $X^1 = X^2 = O$ $R^1 = R^2 = Me$	5 mol % 0.1 M 24 h[c]	 **18h**, 60

[a] Isolated yields. [b] A solution of **17f** in DCE was added by syringe pump for 19 h, and then the solution was stirred for 1 h. [c] The reaction was carried out in refluxing PhCl.

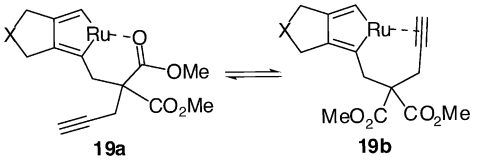
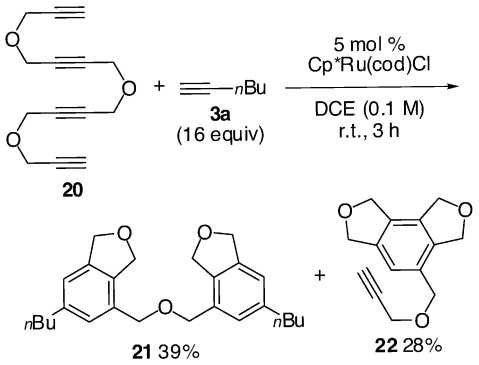


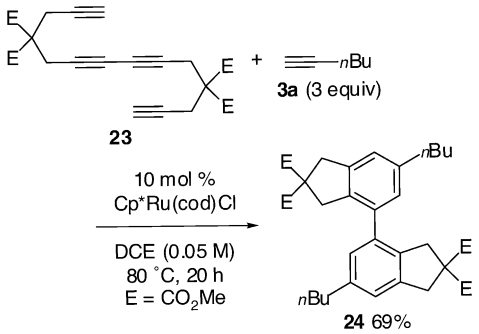
Figure 3.

1,6,13-triyne **17f** were further submitted to the ruthenium-catalyzed cyclization (runs 5 and 6). A 6-membered ring formation was successfully realized in 89% yield, when a higher dilution condition (0.01 M) as well as a catalyst loading of 5 mol % was applied to **17e** (run 5). Although slow addition of **17f** to the catalyst solution by a syringe pump was required to ensure the intramolecular cyclization, the desired 7-membered ring formation was achieved in 53% yield (run 6). A triyne substrate with one internal alkyne terminus **17g** also gave the desired product **18g** without difficulty (run 7), whereas the cyclization of **17h** possessing two internal alkyne termini called for refluxing in chlorobenzene (run 8).

Scheme 6



Scheme 7

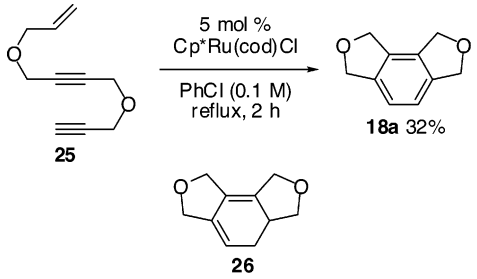


Tandem Cycloaddition of Tetraynes with Monoalkynes. Having examined both the cycloaddition of diynes with the terminal alkynes and the cyclization of the triynes, we next turned our attention to the tandem cycloaddition of a 1,6,11,-16-tetrayne **20** with 1-hexyne **3a** (Scheme 6). If the cycloaddition of the two 1,6-diyne moieties with **3a** is faster than the intramolecular cyclization of the 1,6,11-triyne moiety in **20**, the desired tandem cycloaddition product **21**, in which two bicyclic benzenes are connected by an ether tether, would preferably be obtained. But against our expectation, the intramolecular process leading to **22** competed with the tandem cycloaddition even in the presence of 16 equiv of **3a**. The selectivity was slightly in favor of the tandem product **21** (39%) over the intramolecular cyclization side product **22** (28%). In the absence of **3a**, **22** was solely isolated in 51% yield.

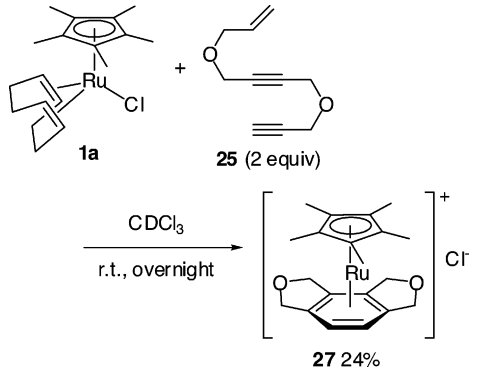
With these results in mind, we devised another tetrayne substrate **23**, which never cyclizes in an intramolecular fashion (Scheme 7).[22a] Upon treatment with 10 mol % **1a** at 80 °C in DCE, the 1,6,8,13-tetrayne **23** reacted with only 3 equiv of **3a** to selectively afford a symmetrical biphenyl derivative **24** in 69% yield.

Intramolecular [2 + 2 + 2] Cocyclotrimerization of Enediyne. We have reported that Cp*RuCl(cod) (**1a**) effectively catalyzes the selective intermolecular [2 + 2 + 2] coupling of 1,6-diynes with cyclic or linear alkenes possessing a heteroatom at the allylic position.[21] To extend such diyne−alkene couplings to an intramolecular version, we attempted the cyclization of an enediyne substrate **25** consisting of a 1,6-diyne moiety and an alkene terminus. The cyclization of **25**, however, never takes place even at 80 °C. To promote the cyclization, **25** was then

Scheme 8



Scheme 9



heated in refluxing chlorobenzene for 2 h in the presence of 5 mol % **1a** to give a dehydroaromatization product **18a** in 32% yield instead of the expected cyclohexadiene **26** (Scheme 8). Such a resistance of the enediyne **25** against cyclization is in striking contrast to the previous report that the diyne **2a** easily reacted with allyl benzyl ether at 40 °C.[21a] It is also surprising that no byproduct via intermolecular reactions was observed. This fact implies that there is some deactivation of catalytic species. This was elucidated by the careful inspection of the reaction of **1a** with 2 equiv of **25** in $CDCl_3$ solution at ambient temperature (Scheme 9). In its ^1H NMR spectrum, an absorption corresponding to the Cp* ligand of **1a** at δ 1.56 ppm slowly disappeared, but instead, a new singlet signal emerged at δ 1.90 ppm and gradually increased. In addition, a singlet peak at δ 6.75 ppm assignable to aromatic protons as well as two pairs of doublet peaks at δ 4.96 (J = 12.9 Hz), 4.88 (J = 13.2 Hz), 4.83 (J = 13.2 Hz), and 4.65 (J = 12.9 Hz) ppm were observed as new peaks. To our delight, the obtained compound **27** was isolated as single crystals and submitted to X-ray diffraction study. As a consequence, the solid-state structure of **27** was unambiguously determined as shown in Figure 4. A cationic sandwich complex **27** consists of the tricyclic benzene **18a** as a η^6-arene ligand as well as a Cp* ligand, and the counteranion is a chloride ion. Therefore, the observed singlet absorption at δ 1.90 ppm and the two sets of doublet peaks were assigned to the Cp* ligand and the methylene protons of the dihydrofuran rings, respectively.

The arene ligand in **27** might be strongly coordinated in η^6-fashion on the cationic ruthenium center. This is why the catalytic cyclization of **25** requires temperature over 100 °C to open coordination sites via dissociation of the arene ligand. This was also substantiated by the fact that the cyclization of the triyne **17a** never proceeded at all in the presence of the isolated **27**. Therefore, this is another evidence that a coordinatively unsaturated, neutral **14e** fragment [Cp*RuCl] is a catalytically active species.

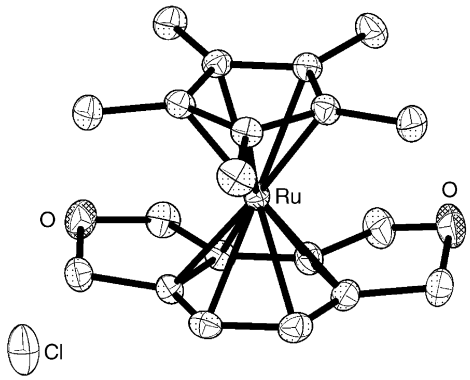


Figure 4. ORTEP drawing of **27**. All hydrogen atoms are omitted for clarity.

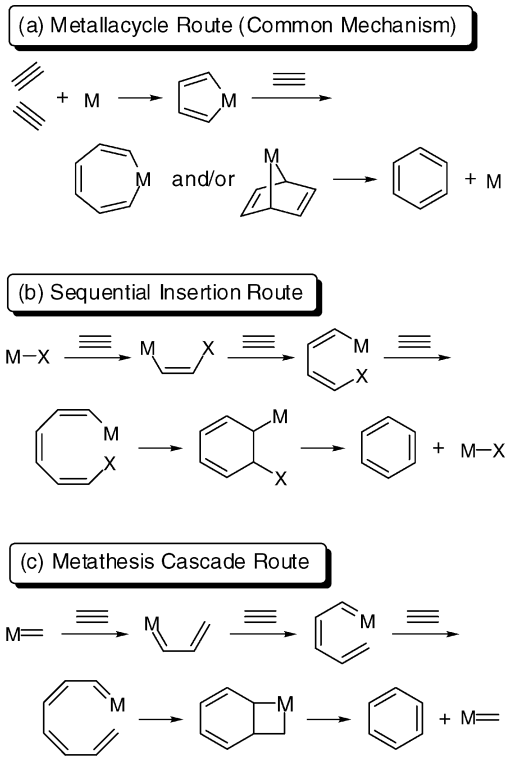


Figure 5. Possible mechanisms of alkyne cyclotrimerization.

Synthesis, Characterization, and Reactivity of Ruthenabicycle Complex. Transition-metal-catalyzed alkyne cyclotrimerizations can be broadly divided into the following three categories on the basis of their reaction mechanisms. The most widely accepted mechanistic picture is the so-called the "common mechanism", in which a metallacyclopentadiene intermediate is produced in the first place by the oxidative cyclization of two alkyne molecules on a low-valent metal center, and it further reacts with an another alkyne molecule to finally afford aromatic products (Figure 5a).[1a] A myriad of metallacyclopentadiene complexes relevant to cyclotrimerization have been isolated to date, and some of them actually gave aromatic products upon treatment with alkynes. On the other hand, a sequential carbometalation mechanism operates in cyclotrimerizations catalyzed by transition-metal hydrides or halides M−X (Figure 5b).[29−31] In addition to these well-known precedents, a meta-

(29) (a) Dietl, H.; Reinheimer, H.; Moffat, J.; Maitlis, P. M. *J. Am. Chem. Soc.* **1970**, *92*, 2276−2285. (b) Li, J.; Jiang, H.; Chen, M. *J. Org. Chem.* **2001**, *66*, 3627−3629.

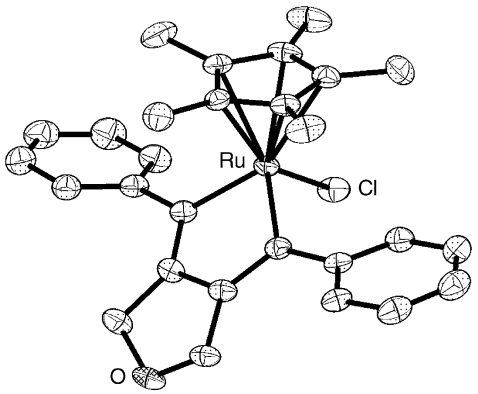


Figure 6. ORTEP drawing of **29**. All hydrogen atoms are omitted for clarity.

thesis cascade using Grubbs' ruthenium carbene complex quite recently proved to be effective for the cyclization of triyne, regioselective coupling of diyne with monoyne, and the trimerization of carbohydrate-derived monoynes (Figure 5c).[18]

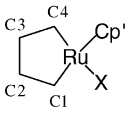
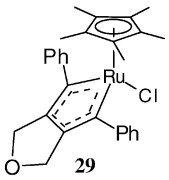
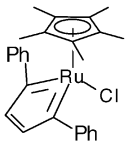
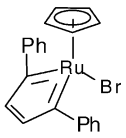
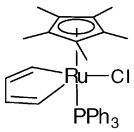
The present catalytic intramolecular alkyne cyclotrimerizations probably proceeded via a ruthenacycle intermediate similar to the aforementioned ruthenacyclopentatriene complex reported by Dinjus (Figure 2).[19b] Highly reactive ruthenacycle complexes, which might be derived from the diyne **2a** or **2h**, however, could not be detected because of the facile oligomerization of such terminal diynes. In striking contrast, an internal diyne **28** possessing phenyl terminal groups slowly reacted with a stoichiometric amount of **1a** in $CDCl_3$ at ambient temperature without forming oligomeric byproducts. After 4 days, a new complex **29** was isolated in 51% yield as single crystals (Scheme 10). The ruthenabicycle structure of **29** was unambiguously confirmed by X-ray diffraction study (Figure 6). Table 6 collects the selected bond lengths and angles of **29** together with those of related ruthenacycles **A**−**C**. The Ru−C1 and Ru−C4 bond distances of 1.995(3) and 1.985(3) Å, respectively, were intermediate between those of the precedent ruthenacyclopentatrienes **A**[19b] and **B**[20] and those of a related ruthenacyclopentadiene(phosphine) complex **C**,[32] indicative of these bonds having double-bond character in part. In accord with this observation, the ^{13}C NMR spectrum (125 MHz, $CDCl_3$) showed the characteristic carbene resonance of C1 and C4 at δ 245.80 ppm. The C−C bond lengths of the ruthenacycle (1.425(4), 1.387(4), and 1.412(4) Å for C1−C2, C2−C3, and C3−C4, respectively) are closer to that of the delocalized bond in benzene (1.40 Å) rather than those of the typical Csp^2-Csp^2 single bond (1.48 Å) or the typical $Csp^2{=}Csp^2$ double bond (1.32 Å). These facts indicate that **29** has a highly delocalized structure, as depicted in Table 6.

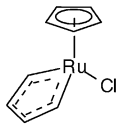
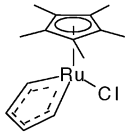
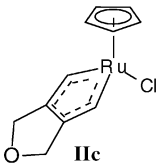
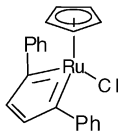
A ruthenabicycle complex similar to **29** is a potential intermediate of the present cycloadditions of diynes and monoynes. In fact, the isolated **29** was heated in $CDCl_3$ at 40 °C under the acetylene atmosphere for 5 days to give the expected terphenyl **30** in 32% isolated yield (Scheme 10). Whereas the intermediary of the ruthenabicycle complex was rationalized, the detailed mechanism for the conversion of the ruthenacycle into an arene product is still not clear at this stage. The insertion/reductive elimination sequence can be assumed as a plausible route according to the "common mechanism",[1a] although a ruthenacycloheptatriene intermediate was not detected. On the other hand, Bercaw, Bergman, and co-workers previously claimed that the arene formation from a coordinatively saturated cobaltacyclopentadiene(trimethylphosphine) complex and DMAD occurs with the direct Diels−Alder cycloaddition mechanism on the basis of an observed second-order rate.[33] In this case, the combination of the electron-rich metallacyclopentadiene moiety and the highly electron-deficient DMAD as an excellent dienophile is indispensable. In addition, recent density functional calculations on the CpCo-catalyzed acetylene cyclotrimerization showed that the transformation of a cobaltacyclopentadiene(alkyne) complex into a η-arene cobalt complex occurs via an indirect Diels−Alder type [4 + 2] cycloaddition mechanism with a very small activation energy (0.5 kcal/mol).[34] For our ruthenium-catalyzed intramolecular cyclotrimerization reactions, a similar indirect mechanism seems operative because the ruthenium precatalyst, Cp*RuCl(cod), has a very similar ligand field to the [CpCo] system. To examine whether or not this is the case, we carried out a density functional study on alkyne cyclotrimerizations catalyzed by [Cp′RuCl] fragments.

Density Functional Study on Cyclotrimerization Mechanism. At the outset, the geometries of three model ruthenacycle complexes **IIa**−**c** were optimized by the Becke's three-parameter hybrid density functional method (B3LYP) with the LACVP* basis set. This basis set uses a double-ζ basis set with the relativistic effective core potential of Hay and Wadt[35,36] for Ru and the 6-31G(d) basis sets[37] for other elements. As shown in Table 6, the structural optimizations of the simplest model **IIa** and its Cp* analogue **IIb** gave quite similar ruthenacycle geometries to both the Dinjus' complex **A**[19b] and the Singleton's complex **B**,[20] except for the ruthenium−halogen bond distances. The Ru−C1 bonds in **IIa** and **IIb** have intermediate lengths between those of **A** and **B**. On the other hand, the calculation on the bicyclic model **IIc** possessing a Cp ligand gave the slightly smaller Ru−C1−C2 angle than those of the monocyclic models. In turn, the C1−Ru−C4 and C1−C2−C3 angles are slightly larger than those in **IIa** and **IIb**. The same trend in the bond angles is also observed for the X-ray data (**29** vs **A** and **B**). It is interesting to note that the C1−C2 bond is shorter than the C2−C3 bond in model complexes, whereas the real complexes have the longer C1−C2 and the shorter C2−C3 bonds. This discrepancy in the bond lengths may be ascribed to the α-phenyl substituents in **A** and **B**. Actually, a phenyl-substituted model complex **IId** possessing Cp and chlorine

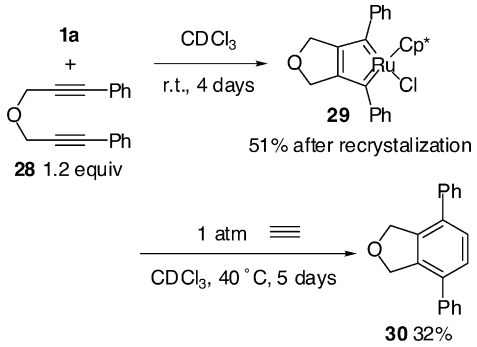
(30) (a) Negishi, E.; Harring, L. S.; Owczarczyk, Z.; Mohamud, M. M.; Ay, M. *Tetrahedron Lett.* **1992**, *33*, 3253−3256. Also see: (b) Meyer, F. E.; de Meijere, A. *Synlett* **1991**, 777−778. (c) Torii, S.; Okumoto, H.; Nishimura, A. *Tetrahedron Lett.* **1991**, *32*, 4167−4168. (d) Negishi, E.; Ay, M.; Sugihara, T. *Tetrahedron* **1993**, *49*, 5471−5482.
(31) Ojima, I.; Vu, A. T.; McCullagh, J. V.; Kinoshita, A. *J. Am. Chem. Soc.* **1999**, *121*, 3230−3231.
(32) Yi, C. S.; Torres-Lubian, J. R.; Liu, N. *Organometallics* **1998**, *17*, 1257−1259.
(33) McAlister, D. R.; Bercaw, J. E.; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 1666−1668.
(34) Hardesty, J. H.; Koerner, J. B.; Albright, T. A.; Lee, G.-Y. *J. Am. Chem. Soc.* **1999**, *121*, 6055−6067.
(35) (a) Kohn, W.; Becke, A. D.; Parr, R. G. *J. Phys. Chem.* **1996**, *100*, 12974−12980. (b) Stephen, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *Phys. Chem. Lett.* **1994**, *98*, 11623−11627. (c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. (d) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098−3100. (e) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789.
(36) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299−310.
(37) (a) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257−2261. (b) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213−222. (c) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654−3665.

Table 6. Selected Bond Lengths (Å) and Angles (deg) for Ruthenacycles

	X-ray			
				
	29	**A** (ref. 19b)	**B** (ref. 20)	**C** (ref. 32)
Ru-C1 [Ru-C4]	1.995(3) [1.985(3)]	1.969(4)	1.942(6)	2.059(5) [2.092(4)]
Ru-X	2.3608(7)	2.365(2)	2.493(1)	2.4398(14)
C1-C2 [C3-C4]	1.425(4) [1.412(4)]	1.402(7)	1.403(8)	1.338(7) [1.321(6)]
C2-C3	1.387(4)	1.37(1)	1.377(12)	1.414(8)
Ru-C1-C2 [Ru-C4-C3]	114.88(19) [115.23(19)]	116.6(4)	117.6(5)	118.6(4) [118.6(4)]
C1-Ru-C4	80.19(11)	78.9(3)	78.7(4)	74.1(2)
C1-C2-C3[C2-C3-C4]	114.0(2) [115.0(2)]	113.7(3)	112.8(6)	114.5(5) [113.8(5)]

	Calculations (RB3LYP/LACVP*)			
				
	IIa	**IIb**	**IIc**	**IId**
Ru-C1 [Ru-C4]	1.952	1.958	1.959	1.967 [1.972]
Ru-X	2.363	2.381	2.366	2.380
C1-C2	1.395	1.393	1.391	1.413
C2-C3	1.404	1.406	1.400	1.387
Ru-C1-C2 [Ru-C4-C3]	117.82	118.18	115.96	115.60 [115.76]
C1-Ru-C4	78.50	78.15	79.88	80.37
C1-C2-C3 [C2-C3-C4]	112.47	112.40	113.63	114.12 [114.14]

Scheme 10

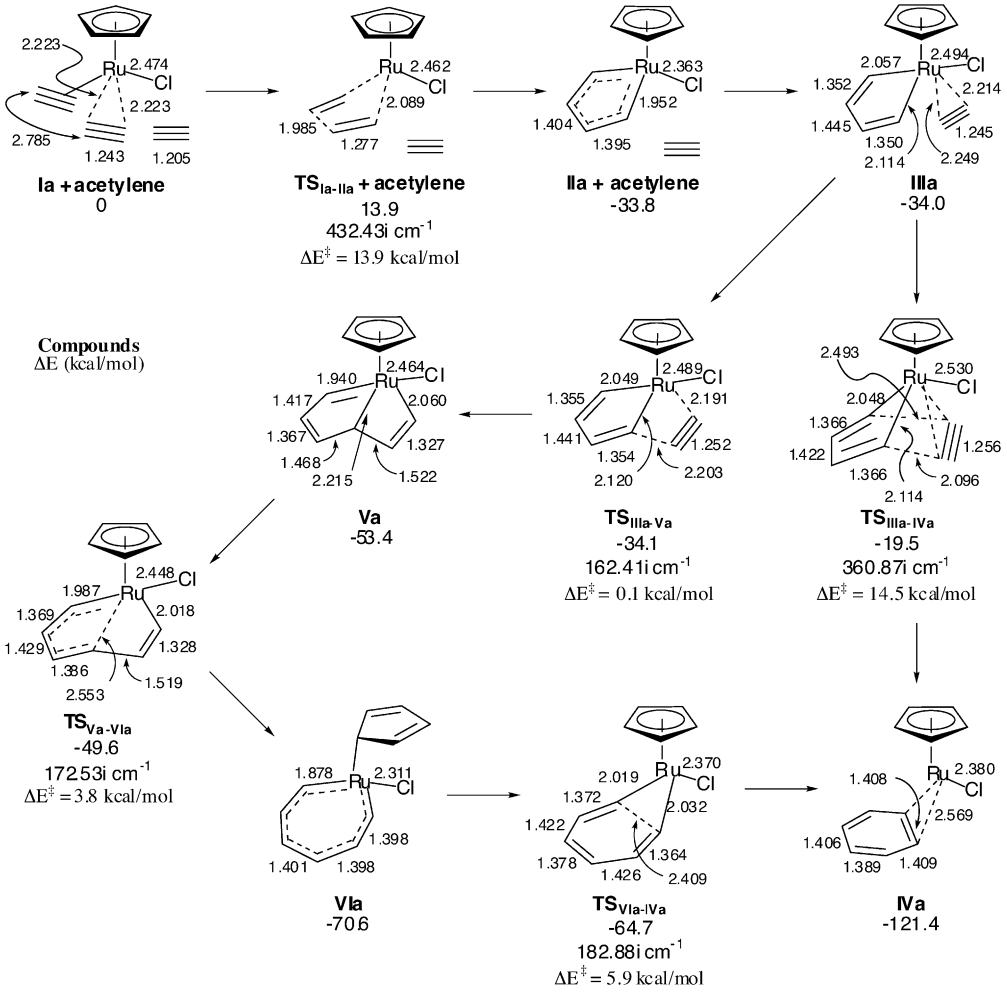


ligands proved to have a quite similar ruthenacycle geometry to that of **A**.

Having obtained the reliable geometries for the model ruthenacycle key intermediates, we next investigated the alkyne cyclotrimerization pathway by exploring individual elementary steps. Initially, the smallest CpRuCl−acetylene combination was chosen as a model for computational efficiency. The energies of all complexes were obtained by the single-point energy calculations for geometries optimized at the B3LYP/LACVP* level. The energy calculations were performed at the B3LYP level using the basis sets consisting of a [6s5p3d2f1g]-contracted valence basis set with the Stuttgart−Dresden−Bonn energy-consistent pseudopotential[38] for Ru and the 6-311++G(d,p) basis sets[39] for other elements. As shown in Scheme 11, the conversion of a bisacetylene complex **Ia** into the ruthenacycle **IIa** proceeds via a transition state $\mathbf{TS_{Ia-IIa}}$ with an activation energy of 13.9 kcal/mol. This value is similar to that estimated for the oxidative cyclization from $CpCo(acetylene)_2$ (12.8 kcal/mol) by Albright and co-workers at the B3LYP level,[34] whereas this process is less exothermic than the ruthenacycle formation ($\Delta E = -13.1$ vs -33.8 kcal/mol). This is clearly ascribed to the difference in stability between the resultant metallacycles. A coordinatively unsaturated cobaltacyclopentadiene is produced in the cobalt system, whereas the ruthenium system gives the highly delocalized ruthenacycle **IIa**. Its C−C bond lengths (1.395 and 1.404 Å) are very similar to that of benzene (1.40 Å), and the short Ru−C bond distance of 1.952 Å suggests that they have a double-bond character. Therefore, **IIa** can be regarded as a 5-membered aromatic compound rather than a metallacyclopentatriene. Such an extensive delocalization formally makes **IIa** coordinatively saturated **18e** species and thus energetically more favorable. Moreover, the chlorine ligand also plays some role in the stabilization of **IIa**. The Ru−Cl bond distance is shortened from 2.474 Å in **Ia** to 2.363 Å in **IIa** with concomitant decrease in the negative charge on the chlorine atom (for NPA charges, see the Supporting Information). These

(38) (a) Andrae, D.; Häussermann, U.; Dolg, M.; Stoll, H.; Preuss, H. *Theor. Chim. Acta* **1990**, *77*, 123−141. (b) Martin, J. M. L.; Sundermann, A. *J. Chem. Phys.* **2001**, *114*, 3408−3420.
(39) (a) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650−654. (b) Clark, T.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Comput. Chem.* **1983**, *4*, 294−301.

Scheme 11



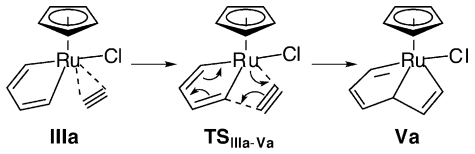
facts suggest that the **16e** ruthenium complex is somewhat stabilized by the chlorine ligand donating its nonbonding electron to the Ru center.

Next, we examined the reaction pathways from the ruthenacycle **IIa** and acetylene to a coordinated benzene as the final product. Upon coordination of one molecule of acetylene, the aromatic ruthenacycle **IIa** is converted into a ruthenacycle(alkyne) complex **IIIa** with a distorted square pyramidal geometry. Its metallacycle moiety is considered to be a normal metallacyclopentadiene with the distinct C−C single and double bonds. The Ru−C bonds have typical single bond distances of 2.057 and 2.114 Å. With the similarity in ligand fields between the CpRuCl and CpCo fragments in mind, we first expected that the indirect Diels−Alder mechanism is also operative for the present ruthenium catalysis. The recent DFT calculations expected that such a transformation from a cobaltacyclopentadiene(alkyne) complex into a η^4-benzene complex occurs with a very small activation energy of 0.5 kcal/mol. A considerably larger activation energy of 14.5 kcal/mol was, however, estimated for the isomerization of **IIIa** via a transition state **TS$_{IIIa-IVa}$**, although the formation of a η^2-benzene complex **IVa** from **IIIa** is a thermodynamically favorable process with an large exothermicity of 87.4 kcal/mol.

Shore's "common mechanism" involving a metallacycloheptatriene intermediate is an alternative route.[1a] Quite recently, a relevant iridacycloheptatriene complex was obtained upon treatment of a Ir(I) complex possessing hydrotris(3,5-dimethylpyrazolyl)borate as a spectator ligand with DMAD and unambiguously characterized by X-ray analysis.[40] We further examined this possibility and found a novel stepwise alkyne insertion mechanism via a putative ruthenabicyclo[3.2.0]-heptatriene intermediate **Va**. The isomerization of ruthenacycle(alkyne) complex **IIIa** to **Va** occurs with an activation energy of only 0.1 kcal/mol. Such a small kinetic barrier is in accord with the least geometry change upon progression to the transition state **TS$_{IIIa-Va}$** from **IIIa**. This is in sharp contrast to the Diels−Alder type route requiring the coordinated acetylene to rotate by ca. 90° around its bond axis with Ru to maximize the overlap between the coordination-free acetylene π-bond and the ruthenacycle π-system. On the basis of the obtained ruthenacycle geometry in **TS$_{IIIa-Va}$**, this process is better described as the formal [5 + 2] cycloaddition of the ruthenacyclopentadiene with acetylene rather than the [2 + 2] cycloaddition of **IIa** as a cyclic biscarbene complex (Scheme 12). The bicyclic complex **Va** has a cyclic monocarbene structure with the Ru=C bond distance of 1.940 Å, which is shorter than those in the biscarbene **IIa**. The central Ru−C single bond (2.215 Å) is considerably elongated, probably due to the ring strain of the ruthenabicyclo[3.2.0]heptatriene framework. Despite having such a strained

(40) Álvarez, E.; Gómez, M.; Paneque, M.; Posadas, C. M.; Poveda, M. L.; Rendón, N.; Santos, L. L.; Rojas-Lima, S.; Salazar, V.; Mereiter, K.; Ruiz, C. *J. Am. Chem. Soc.* **2003**, *125*, 1478−1479.

Scheme 12



structure, the formation of **Va** is estimated to be exothermic ($\Delta E = -19.4$ kcal/mol).

Subsequent scission of the central Ru−C single bond in **Va** proceeds via $\mathbf{TS_{Va-VIa}}$ to give a 7-membered ruthenacycle **VIa**. The activation energy was calculated as 3.8 kcal/mol. The C−C bond distances in the ruthenacycle moiety of ca. 1.40 Å and the short Ru−C bond distance of 1.878 Å clearly indicate that **VIa** again has an aromatic character similar to **IIa**. This is also supported by the completely planar geometry of the 7-membered ring, which is in sharp contrast to the tub-shaped conformation of the reported iridacycloheptatriene.[40] As a consequence of such a delocalized structure, this step is also thermodynamically favorable with an exothermicity of 17.2 kcal/mol.

The final ring closure leading to the benzene complex **IVa** was expected to be highly exothermic because of the formation of a benzene ring. Actually, the exothermicity was estimated as 56.7 kcal/mol. The activation energy of 5.9 kcal/mol is the largest in the consecutive insertion/reductive elimination steps, but is smaller than those of the oxidative cyclization step or the indirect Diels−Alder type route via $\mathbf{TS_{IIIa-IVa}}$. The benzene ligand weakly bound to the Ru center in η^2-fashion is almost planar. This is in contrast to the η^4-coordinated benzene being folded in the DFT-optimized CpCo(benzene).[34]

The geometries of the Cp and chlorine ligands in **VIa** deserve some comments. The Ru−Cl distance of 2.311 Å is the shortest among all calculated complexes **Ia**−**IVa**. This means that the electron donation of the chlorine atom to the ruthenium center is the strongest in **VIa**, and as a consequence, the natural charge on the chlorine center is significantly decreased (see the Supporting Information). On the other hand, the Cp ligand is bound to the ruthenium center in η^1-fashion, indicative of its electron-donating ability being decreased compared with those of its η^5- or η^3-forms. Such a ring slippage of Cp type ligands is well-known to play an important role in ligand substitution reactions.[41] Whereas we could locate such a η^1-cyclopentadienyl complex, the corresponding η^1-pentamethylcyclopentadienyl complex might not be involved in the catalytic cycle because the electron-donating methyl substituents on the Cp* ligand make ring slippage less favorable. In fact, a ruthenacycloheptatriene complex having a slightly slipping Cp* ligand **VIb** was obtained as a local minimum (Figure 7). In this case, the ruthenacycle moiety is not planar and unsymmetrical. The Ru−C bond lengths of 1.963 and 1.940 Å are ca. 0.062−0.085 Å longer than that of **VIa**. A considerably small activation barrier of 1.5 kcal/mol estimated for the reductive elimination step **VIb** → **IVb** implies that the highly symmetrical flat ruthenacycle complex with the η^1-Cp ligand **VIa** is a resting state. The Ru−Cl bonds in **VIb**, $\mathbf{TS_{VIb-IVb}}$, and **IVb** are elongated by ca. 0.03−0.08 Å compared to the corresponding Cp complexes on account of the strong electron donation from the Cp* ligand.

The overall reaction profile is shown in Figure 8. The insertion/reductive elimination mechanism is more favorable than the formal [4 + 2] mechanism. All elementary steps are estimated as exothermic. The rate-determining step is the oxidative cyclization to form the ruthenacycle key intermediate **IIa**, and the bisalkyne complex might be in equilibrium with solvated species CpRuCl(solvent)$_n$(acetylene)$_{2-n}$ and the starting olefin complex. In this respect, 1,6-diynes are excellent substrates compared to monoalkynes for the Ru-catalyzed alkyne cyclotrimerization because the formation of a diyne complex such as **Ic** is entropically more favorable than that of a bisalkyne complex such as **Ia** (Figure 9). Moreover, the activation barriers for the oxidative cyclization of 1,6-diynes were expected to be smaller than those for monoalkynes, because the three-atom tether places the alkyne termi in closer proximity to each other. As shown in Figure 9, the C2−C3 distance is shorter in **Ic** (2.748 Å) than that in **Ia** (2.785 Å). The calculated activation energy of 12.2 kcal/mol for **Ic** → $\mathbf{TS_{Ic-IIc}}$ is smaller than that of the parent **Ia** by 1.7 kcal/mol. Consequently, the diyne substrate is kinetically favorable for both the formation of bisalkyne complex and the oxidative cyclization event leading to the ruthenacycle key intermediate.

Regioselectivity of Cyclotrimerization. On the basis of the above results, we then evaluated the regioselectivity in the ruthenium-catalyzed cyclotrimerization by computing the formal [2 + 2] cycloaddition step of an unsymmetrical model ruthenacycle **IIe** with propyne (**IIe** → **Ve**), as summarized in Figure 10. At first, four possible regio-isomers of a ruthenacycle-(propyne) complex **IIIe** were located at the B3LYP/LACVP* level of theory. In $\mathbf{IIIe_{cis-anti}}$ and $\mathbf{IIIe_{cis-syn}}$, the alkyne ligand is placed cis to the secondary alkyl terminus of the ruthenacycle ring. The methyl substituent of propyne is oriented toward the Cp ligand in $\mathbf{IIIe_{cis-syn}}$ and $\mathbf{IIIe_{trans-syn}}$. The single-point energy calculations of these geometries revealed that the formations of all these isomers were endothermic and that the thermodynamic stability decreased in the order of $\mathbf{IIIe_{cis-anti}} > \mathbf{IIIe_{trans-anti}} \geq \mathbf{IIIe_{cis-syn}} > \mathbf{IIIe_{trans-syn}}$. The syn-isomers are located 0.52−0.62 kcal/mol above the corresponding anti-isomers. This suggests that there exist unfavorable interactions between the propyne methyl terminus and the Cp ligand, as well as the chlorine atom in the syn-isomers. On the other hand, the trans-isomers lie 0.47−0.57 kcal/mol above the corresponding cis-isomers, probably because of the repulsion between the chlorine ligand and the ruthenacycle methyl substituent, as shown by the space-filling models (Figure 11). In the subsequent C−C bond-forming event, however, the trans-isomers become predominant over the cis-isomers. The activation energies of ca. 0.7 kcal/mol estimated for the trans-isomers are comparable to that for the parent transformation from **IIIa** to **Va**. In contrast, the cis-isomers must overcome a barrier of ca. 2 kcal/mol to produce bicyclic intermediates **Ve**. In addition, the formation of $\mathbf{Ve_{trans-syn}}$ and $\mathbf{Ve_{trans-anti}}$ is more exothermic than that of $\mathbf{Ve_{cis-syn}}$ and $\mathbf{Ve_{cis-anti}}$. On going from **IIIe** to $\mathbf{TS_{IIIe-Ve}}$ to **Ve**, the methyl group on the ruthenacycle ring moves up toward the Cp ligand in the cis-isomers, and the steric repulsion between

(41) (a) O'Connor, J. M.; Casey, C. P. *Chem. Rev.* **1987**, *87*, 307−318. (b) Cheong, M.; Basolo, F. *Organometallics* **1988**, *7*, 2041−2044. (c) Vest, P.; Anhaus, J.; Bajaj, H. C.; van Eldik, R. *Organometallics* **1991**, *10*, 818−819. (d) Gamasa, M. P.; Gimeno, J.; Gonzalez-Bernardo, C.; Martín-Vaca, B. M.; Monti, D.; Bassetti, M. *Organometallics* **1996**, *15*, 302−308. (d) Simanko, W.; Tesch, W.; Sapunov, V. N.; Mereiter, K.; Schmid, R.; Kirchner, K. *Organometallics* **1998**, *17*, 5674−5688. (e) Calhorda, M. J.; Veiros, L. F. *Coord. Chem. Rev.* **1999**, *185*−*186*, 37−51. (f) Veiros, L. F. *Organometallics* **2000**, *19*, 3127−3136. (g) Veiros, L. F. *Organometallics* **2000**, *19*, 5549−5558. (h) Fan, H.-J.; Hall, M. B. *Organometallics* **2001**, *20*, 5274−5730.

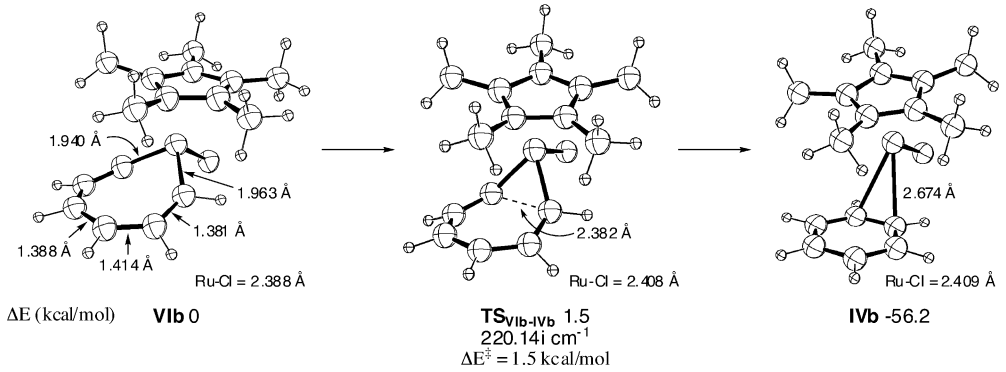


Figure 7. Transformation of ruthenacycloheptatriene complex **VIb** into benzene complex **IVb**.

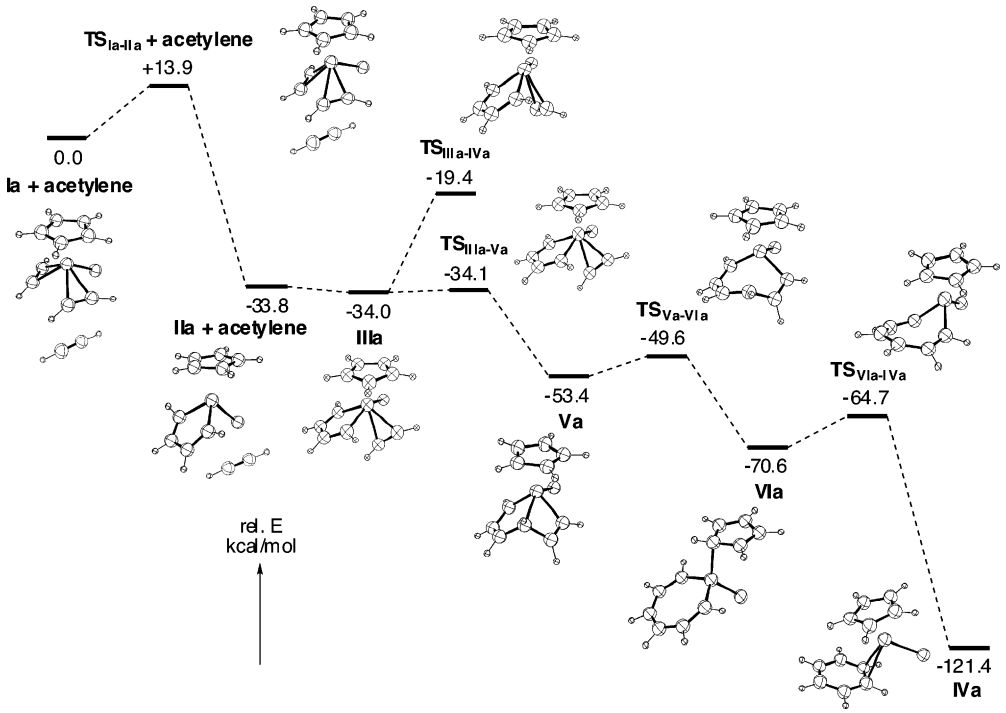


Figure 8. Reaction profile for CpRuCl-catalyzed acetylene cyclotrimerization.

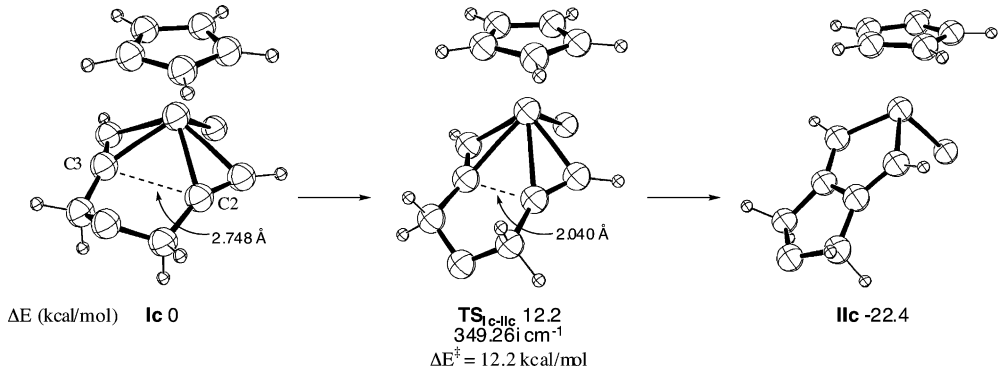


Figure 9. Transformation of diyne complex **Ic** into ruthenabicyclo complex **IIc**.

these moieties makes the cis-isomers unfavorable. As a whole, the pathway leading to a meta-product via the lowest energy trans−anti transition state is considered as both kinetically and thermodynamically most favorable, whereas the initial ruthenacycle(propyne) complex $\mathbf{IIIe}_{\mathbf{trans-anti}}$ is not the most stable isomer. The other three routes might become much less accessible by introducing the bulkier Cp* ligand in place of the Cp ligand.

Relevance to Tandem Cyclopropanation of 1,6-Diynes with Bicycloalkenes. Although the ruthenacyclopentatriene complexes have the interesting cyclic biscarbenoid structure, their reactivity especially toward unsaturated organic molecules such as alkynes or alkenes has been almost unexplored.[42] This is because the coordination of such molecules to the ruthenium center converts the ruthenacyclopentatrienes into the corresponding coordinatively saturated ruthenacyclopentadienes.[20]

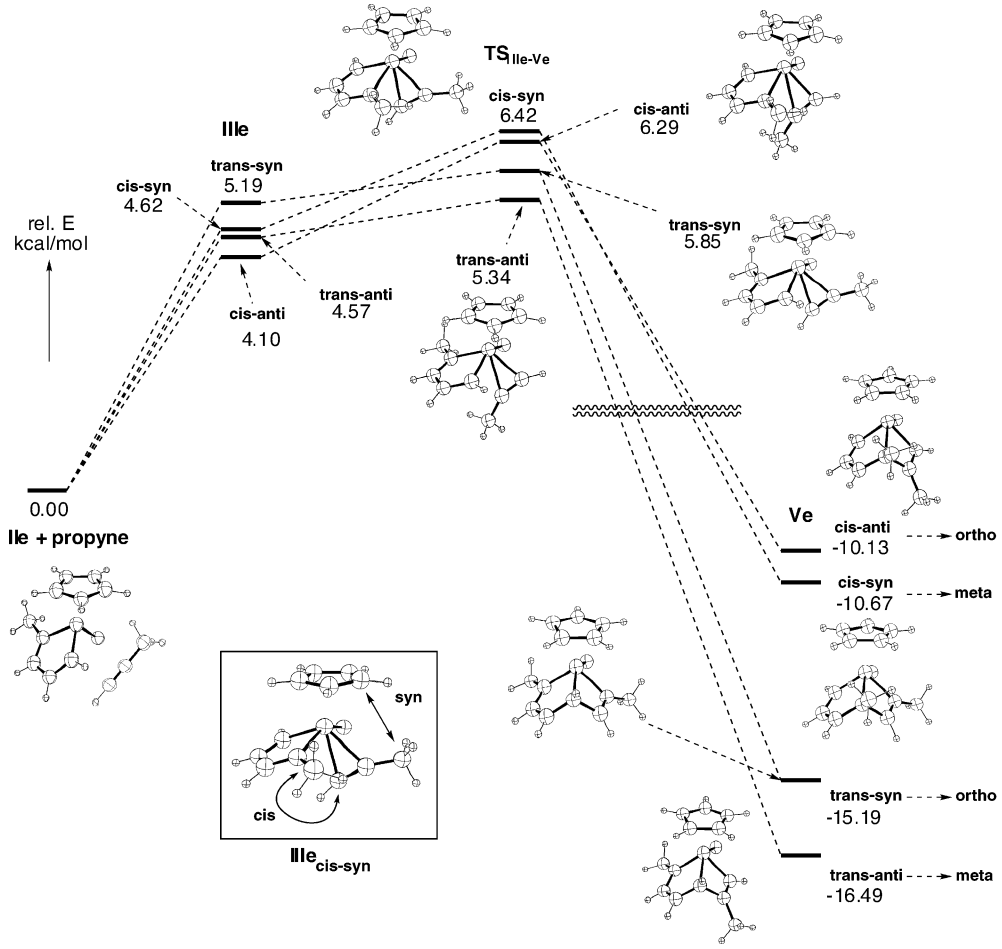


Figure 10. Reaction profile for reaction of unsymmetrical ruthenacycle **IIe** with propyne.

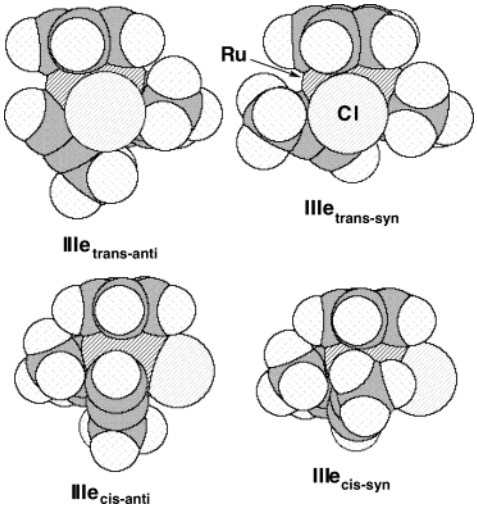
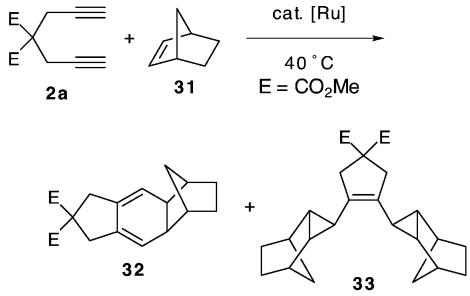


Figure 11. Space-filling representation of ruthenacycle(alkyne) complexes **IIIe**.

Scheme 13

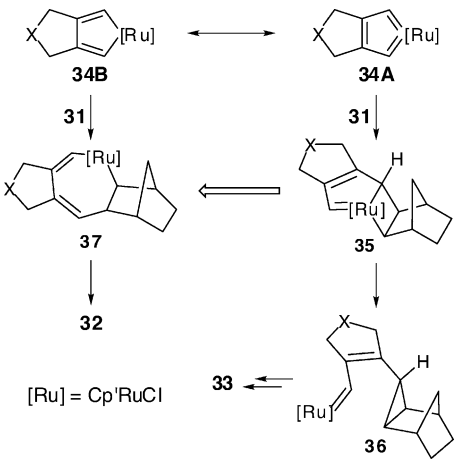


[Ru] (mol %)	solvent	*t* (h)	yield (%)[a] **32** / **33**
1a (10)	CH_2Cl_2	17	47 / 15
1c (10)	CH_2Cl_2	7	20 / 45
1d[b] (5)	DCE	24	12 / 78

[a] Isolated yield. [b] **1d**: $(\eta^5\text{-}C_9H_7)RuCl(PPh_3)_2$.

Therefore, it seems quite difficult to obtain the clear evidence for the behavior of the ruthenacyclopentatrienes as cyclic biscarbenoids. We have previously disclosed that the Ru(II)-catalyzed reaction of some 1,6-diynes with strained bicycloalkenes such as norbornene **31** gave rise to unprecedented tandem cyclopropanation products as a result of the carbenoid behavior of the bicyclic ruthenacyclopentatriene intermediate (Scheme 13).[21] When the pentamethylcyclopentadienyl complex **1a** was used as a precatalyst, the reaction of the diyne **2a** with **31** in dichloromethane at 40 °C gave rise to the normal [2 + 2 + 2] cycloadduct **32** as a major product. On the other hand, a tandem cyclopropanation product **33** was predominantly obtained using the corresponding cyclopentadienyl complex **1c** or indenyl complex **1d**, indicative of the ring slippage of the Cp-type ligands playing an important role. We considered that these two cycloadducts were independently produced from a ruthenacyclopentatriene and a ruthenacyclopentadiene intermediate as

Scheme 14



outlined in Scheme 14. The tandem cyclopropanation might start with the [2 + 2] cycloaddition of the cyclic biscarbene form of the ruthenacycle intermediate (**34A**) and the bicycloalkene **31**, which produces a bicyclic complex **35**. The following reductive elimination of a cyclopropane moiety gives a vinyl carbene **36**, which reacts with another molecule of **31** to finally furnish **33**. On the other hand, the normal alkene insertion into a ruthenacyclopentadiene intermediate **34B** gives rise to a ruthenacycloheptadiene **37**, from which a Cp′RuCl fragment was reductively eliminated to give **32**. The formation of **32**, however, can be explained on the basis of an alternative mechanism similar to one for the above alkyne cyclotrimerization. The cleavage of the central Ru−C bond in **35** followed by the reductive elimination event in **37** might afford **32**.

To elucidate this possibility, we finally carried out density functional calculations on the model reaction of acetylene and norbornene using the same level of theory (Scheme 15). The cycloaddition might start with the oxidative cyclization of two acetylene molecules on the [CpRuCl] fragment to give rise to the ruthenacycle **IIa** as already shown in Scheme 11. The coordination of one norbornene molecule by **IIa** affords a ruthenacyclopentadiene(alkene) complex **VII** with the endothermicity of 4.5 kcal/mol. This is in contrast to the slightly exothermic coordination of acetylene. The isomerization of **VII** into **VIII**, a formal [2 + 2] cycloadduct between **IIa** and norbornene, occurs with an activation energy larger than that of the formation of **Va** from **IIIa**. In addition, the former process was revealed to be less exothermic (8.7 kcal/mol). The ruthenabicyclo[3.2.0]heptadiene geometry in **VIII** resembles the ruthenabicyclo[3.2.0]heptatriene moiety in **Va**. The ring expansion of the ruthenabicycle moiety via cleavage of the central Ru−C bond might give a ruthenacycloheptadiene **IX**, which is the key intermediate of the cocyclotrimerization of acetylene with norbornene. This step is estimated to have a relatively large activation barrier of 12.7 kcal/mol compared to that for the corresponding isomerization of **Va** leading to **VIa**, although the Ru−C bond to cleave in **VIII** is 0.056 Å longer than that in **Va**. The resultant ruthenacycloheptadiene **IX** is only 1.3 kcal/mol more stable in energy than **VIII**. The final reductive elimination of a cyclohexadiene takes place with an activation energy of 11.4 kcal/mol to afford a η^2-cyclohexadiene complex **X** with a favorable exothermicity of 36.3 kcal/mol.

On the other hand, the cyclopropane reductive elimination from **VIII** was calculated to have an activation barrier 3.4 kcal/mol larger than that estimated for the ring opening leading to **IX**. On the basis of these data, the [2 + 2 + 2] cocyclotrimerization is considered to predominate over the competitive tandem cyclopropanation. Such an expectation deduced from the theoretical calculations is, however, inconsistent with the experimental results: the cycloaddition of **2a** with norbornene using CpRuCl(cod) as a precatalyst gave the corresponding biscyclopropane **33** predominantly over the cyclohexadiene **32** (Scheme 13). The exact cause for such a discrepancy is not clear at this stage, but the participation of a second norbornene molecule into the cyclopropane reductive-elimination event (**VIII** → $\mathbf{TS_{VIII-XI}}$ → **XI**) probably lowers the activation barrier by reducing the electron density of the ruthenium center through the back-donation to the coordinated norbornene. Apart from the product selectivity, the present DFT calculations show that the two seemingly quite different processes, the tandem cyclopropanation and the [2 + 2 + 2] cocyclotrimerization, can proceed via the common intermediate **VIII**. The overall reaction profile is summarized in Figure 12.

Conclusion

In conclusion, we developed new ruthenium-catalyzed intramolecular alkyne cyclotrimerizations of diynes and triynes, which proceed under mild conditions with excellent selectivity as well as wide functional group compatibility. A ruthenium(II) complex possessing a bulky planar Cp* ligand, Cp*RuCl(cod), proved to be the most efficient precatalyst. Neither a cationic Cp*Ru(arene) nor the combination of Cp*RuCl(cod) with AgOTf catalyzed the cycloaddition, indicative of a neutral **16e** fragment [Cp*RuCl] being the catalytically active species.

A ruthenabicycle complex relevant to the present cyclotrimerization was synthesized by the stoichiometric reaction of Cp*RuCl(cod) with a 1,6-diyne possessing phenyl terminal groups. The X-ray analysis revealed that it has a bicyclic biscarbene structure similar to the precedent examples derived from phenylacetylene and its analogues. The intermediary of such a ruthenacycle intermediate was confirmed by the observation that the reaction of the obtained ruthenacycle complex and acetylene gave rise to the expected terphenyl derivative.

Density functional calculations of model complexes showed that the Ru(II)-catalyzed alkyne cyclotrimerization proceeds via oxidative cyclization producing a ruthenacycle intermediate and subsequent alkyne insertion/reductive elimination route rather than an alternative pathway involving the indirect [4 + 2] cycloaddition of the ruthenacyclopentadiene moiety with an alkyne. Significantly, the alkyne insertion proved to take place as a result of the formal [2 + 2] cycloaddition of a ruthenacyclopentatriene with an alkyne leading to a ruthenabicyclo[3.2.0]-heptatriene intermediate and its ring enlargement triggered by the cleavage of the central Ru−C bond. The rate-determining step of the overall process was determined as the initial oxidative cyclization event, and therefore, intramolecular process is suitable for the present catalyst system.

Furthermore, DFT calculations suggested that both tandem cyclopropanation and competitive [2 + 2 + 2] cocyclotrimer-

(42) (a) Le Paih, J.; Dérien, S.; Dixneuf, P. H. *Chem. Commun.* **1999**, 1437−1438. (b) Mauthner, K.; Soldouzi, K. M.; Mereiter, K.; Schmid, R.; Kirchner, K. *Organometallics* **1999**, *18*, 4681−4683. (c) Rüba, E.; Mereiter, K.; Schmid, R.; Kirchner, K. *Chem. Commun.* **2001**, 1996−1997. (d) Rüba, E.; Mereiter, K.; Schmid, R.; Sapunov, V. N.; Kirchner, K.; Schottenberger, H.; Calhorda, M. J.; Veiros, L. F. *Chem.−Eur. J.* **2002**, *8*, 3948−3961.

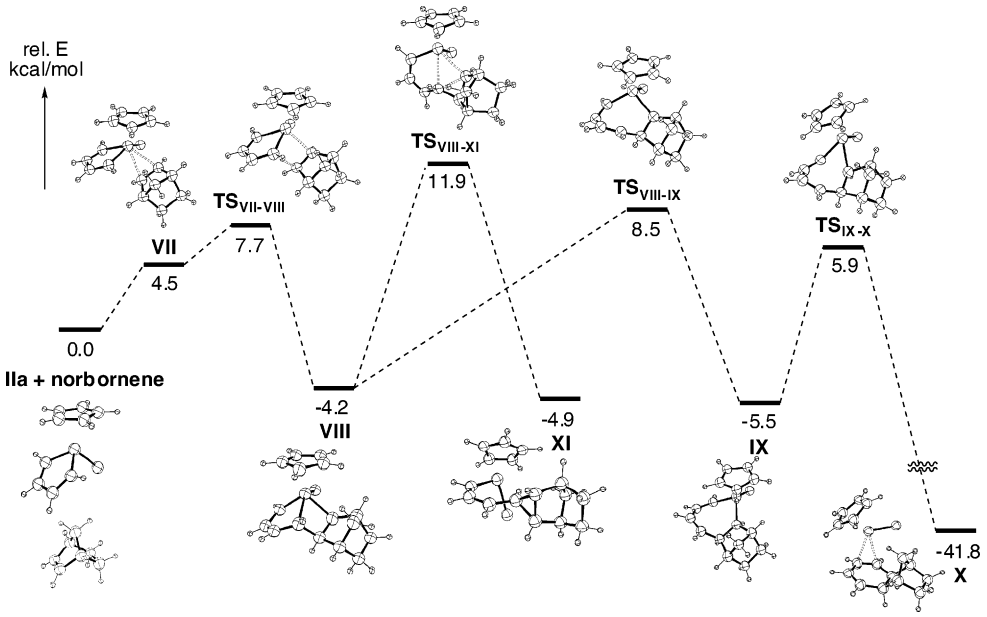
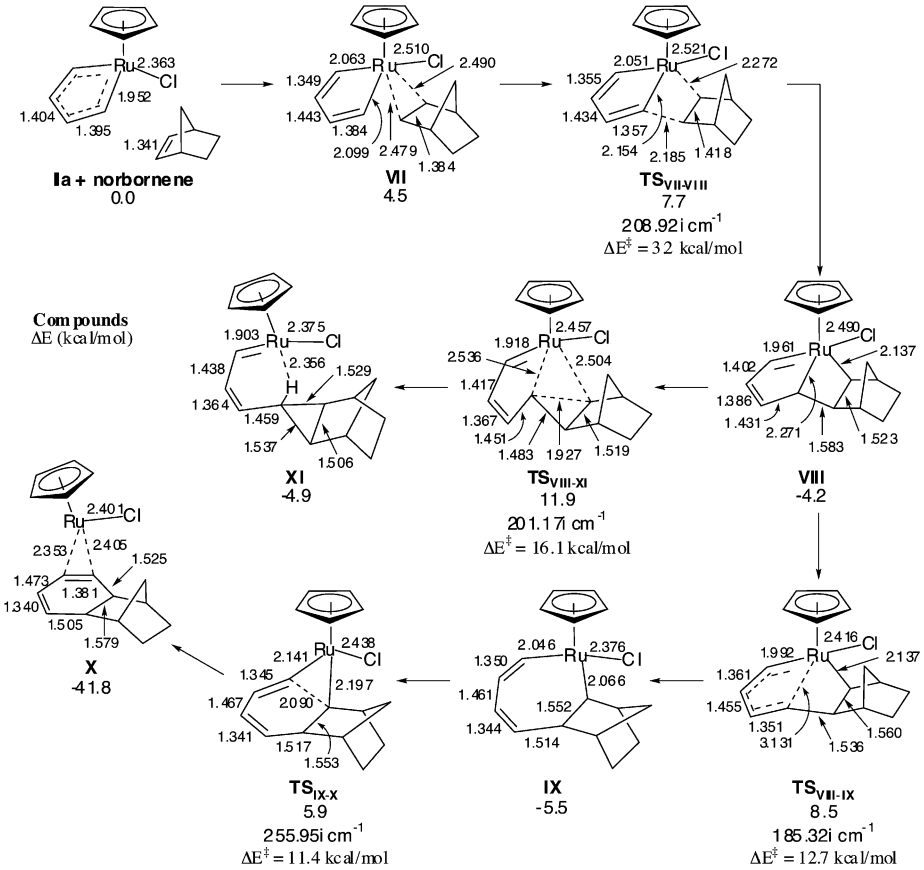


Figure 12. Reaction profile for CpRuCl-catalyzed cycloaddition of acetylene with norbornene.

Scheme 15



ization products from the previously reported cycloaddition of 1,6-diynes with norbornene can be produced via a common intermediate, ruthenabicyclo[3.2.0]heptadiene complex, which is formed by the formal [2 + 2] cycloaddition of the ruthenacyclopentatriene with norbornene.

Experimental Section

General Considerations. ^{1}H 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 capillary tubes and are uncorrected. 1,2-Dichloroethane and chlorobenzene were distilled from CaH_2 and degassed before use.

Representative Procedure for Cp*RuCl(cod)-Catalyzed Cycloaddition of Diynes with Monoalkynes: Synthesis of Indane 4aa from 1,6-Diyne 2a and 1-Hexyne 3a. To a solution of 1-hexyne **3a** (168.1 mg, 2.0 mmol) and Cp*RuCl(cod) **1a** (1.9 mg, 0.005 mmol) in dry

degassed 1,2-dichloroethane (2 mL) was added a solution of a diyne **2a** (98.8 mg, 0.47 mmol) in dry degassed 1,2-dichloroethane (3 mL) for 15 min under Ar atmosphere at room temperature. The reaction mixture was stirred for 15 min. The solvent was evaporated, and the crude product was purified by silica gel flash column chromatography (hexane-AcOEt 20:1) to give an indane **4aa** (129.3 mg, 94%) as pale yellow oil. IR (neat): 1737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.92 (t, $J = 7.2$ Hz, 3 H), 1.28−1.41 (m, 2 H), 1.51−1.62 (m, 2 H), 2.56 (t, $J = 7.5$ Hz, 2 H), 3.57 (s, 4 H), 3.74 (s, 6 H), 6.98 (d, $J = 7.5$ Hz, 1 H), 7.01 (s, 1 H), 7.09 (d, $J = 7.5$ Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 14.06, 22.49, 33.91, 35.56, 40.34, 40.61, 52.93, 56.48, 123.76, 124.07, 127.09, 136.87, 139.76, 141.68, 172.01; MS (FAB) *m*/*z* (%): 291 (100) [MH^+], 230 (100) [$MH^+ - CO_2Me$], 187 (97) [$M^+ - CO_2Me - CH_3CH_2CH_3$], 129 (94) [$M^+ - 2CO_2Me - CH_2CH_2CH_3$]; EA calcd (%) for $C_{17}H_{22}O_4$ (290.35): C, 70.32; H 7.64. Found: C, 70.11; H, 7.73.

Representative Procedure for Cp*RuCl(cod)-Catalyzed Cyclization of Triynes: Synthesis of 18a from 1,6,11-Triyne 17a. To a solution of Cp*RuCl(cod) **1a** (2.0 mg, 0.005 mmol) in dry degassed 1,2-dichloroethane (3 mL) was added a solution of a triyne **17a** (85.8 mg, 0.53 mmol) in dry degassed 1,2-dichloroethane (2 mL) for 15 min under Ar atmosphere at room temperature. The reaction mixture was stirred for 2 h. The solvent was evaporated, and the crude product was purified by silica gel flash column chromatography (hexane-AcOEt 6:1) to give **18a** (70.6 mg, 82%) as pale yellow oil. The analytical data for **18a** was consistent with those reported in the literature.[31]

Tandem Cycloaddition of Tetrayne 20 with 1-Hexyne 3a. To a solution of a 1-hexyne **3a** (660 mg, 8.0 mmol) and Cp*RuCl(cod) **1a** (9.4 mg, 0.025 mmol) in dry degassed 1,2-dichloroethane (2 mL) was added a solution of a tetrayne **20** (125.5 mg, 0.54 mmol) in dry degassed 1,2-dichloroethane (3 mL) for 15 min under Ar atmosphere at room temperature. The reaction mixture was stirred for 3 h. The solvent was evaporated, and the crude product was purified by silica gel flash column chromatography (hexane-AcOEt 22:1) to give a tandem adduct **21** (85.4 mg, 39%) as pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.94 (t, $J = 7.2$ Hz, 6 H), 1.30−1.43 (m, 4 H), 1.55−1.65 (m, 4 H), 2.63 (t, $J = 7.5$ Hz, 4 H), 4.47 (s, 4 H), 5.09 (s, 8 H), 7.01 (s, 2 H), 7.02 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 14.01, 22.41, 33.92, 35.47, 70.57, 72.61, 73.37, 120.15, 126.83, 131.09, 135.09, 139.69, 142.54; MS (FAB) *m*/*z* (%): 393 (100) [$M^+ - H$], 189 (100) [$1/2M^+ - O$]; EA calcd (%) for $C_{26}H_{34}O_3$ (394.55): C, 79.15; H, 8.69. Found: C, 79.18; H, 8.65.

Further elution (hexane-AcOEt 17:1) gave a tricyclic benzene **22** (35.2 mg, 28%) as pale yellow oil: ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ 2.48 (t, $J = 2.5$ Hz, 6 H), 4.17 (d, $J = 2.5$ Hz, 2 H), 4.57 (s, 2 H), 5.02 (s, 2 H), 5.03 (s, 2 H), 5.12 (s, 2 H), 5.17 (s, 2 H), 7.12 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 57.29, 69.53, 72.11, 72.20, 72.67, 73.26, 74.95, 119.60, 130.16, 131.97, 132.59, 137.79, 139.20; MS (FAB) *m*/*z* (%): 229 (100) [$M^+ - H$], 189 (30) [$M^+ - 2H - CH_2C{\equiv}CH$]; EA calcd (%) for $C_{14}H_{14}O_3$ (230.26): C, 73.03; H, 6.13. Found: C, 72.77; H, 6.38.

Tandem Cycloaddition of Tetrayne 23 with 1-Hexyne 3a. To a solution of a 1-hexyne **3a** (56.5 mg, 0.69 mmol) and Cp*RuCl(cod) **1a** (9.8 mg, 0.026 mmol) in dry degassed 1,2-dichloroethane (2 mL) was added a solution of a tetrayne **23** (106 mg, 0.26 mmol) in dry degassed 1,2-dichloroethane (3 mL) for 15 min under Ar atmosphere at room temperature. The reaction mixture was stirred at 80 °C for 20 h. The solvent was evaporated, and the crude product was purified by silica gel flash column chromatography (hexane-AcOEt 5:1) to give a tandem adduct **24** (102.5 mg, 69%) as pale yellow oil. IR ($CHCl_3$) 1737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.92 (t, $J = 6.9$ Hz, 6 H), 1.29−1.43 (m, 4 H), 1.54−1.65 (m, 4 H), 2.59 (t, $J = 7.8$ Hz, 4 H), 3.37 (s, 4 H), 3.62 (s, 4 H), 3.72 (s, 12 H), 6.88 (s, 2 H), 7.00 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 14.07, 22.51, 33.79, 35.50, 39.60, 40.80, 52.86, 60.21, 123.07, 127.54, 135.15, 136.91, 140.08, 141.88, 171.94; MS (FAB) *m*/*z* (%): 579 (14) [MH^+], 487 (100) [$M^+ - CO_2Me - HOMe$]; EA calcd (%) for $C_{34}H_{42}O_8$ (578.69): C, 70.57; H, 7.32. Found: C, 70.58; H, 7.30.

Table 7. Crystal Data and Structure Refinement for **27**·(H_2O) and **28**

	27·(H_2O)	**28**
empirical formula	$C_{20}H_{27}ClO_3Ru$	$C_{28}H_{29}ClORu$
formula weight	451.94	518.03
temperature (K)	173(2)	173(2)
wavelength (Å)	0.71073	0.71073
crystal system	monoclinic	orthorhombic
space group	$P2_1/n$ (No. 14)	*Pbca* (No. 61)
unit cell dimensions		
a (Å)	9.3721(6)	16.559(2)
b (Å)	16.7911(10)	7.3310(9)
c (Å)	11.9364(7)	38.161(5)
β (deg)	98.0280(10)	
volume ($Å^3$)	1860.0(2)	4632.6(10)
Z	4	4
density (calcd) (Mg/m^3)	1.614	0.743
absorption coefficient (mm^{-1})	1.003	0.405
F(000)	928	1064
crystal size (mm^3)	0.1 × 0.2 × 0.4	0.2 × 0.4 × 0.6
θ range for data collection (deg)	2.11−29.16	1.07−29.12
index ranges	$-12 \le h \le 12$	$-22 \le h \le 14$
	$-22 \le k \le 23$	$-10 \le k \le 10$
	$-10 \le l \le 16$	$-51 \le l \le 52$
reflections collected	14 172	33 668
independent reflections [*R*(int)]	4955 [0.0481]	6194 [0.0855]
data/restraints/parameters	4955/0/239	6194/0/285
goodness-of-fit on F^2	1.077	1.202
final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0318$	$R_1 = 0.0437$
	$wR_2 = 0.0855$	$wR_2 = 0.1118$
R indices (all data)	$R_1 = 0.0344$	$R_1 = 0.0464$
	$wR_2 = 0.0871$	$wR_2 = 0.1179$
largest diff. peak and hole (e $Å^{-3}$)	1.631, −0.749	1.173, −0.956

Stoichiometric Reaction of Cp*RuCl(cod) (1a) with Enediyne 25. A solution of Cp*RuCl(cod) **1a** (114 mg, 0.30 mmol) and an enediyne **25** (96.8 mg, 0.59 mmol) in $CDCl_3$ (5 mL) was left at room-temperature overnight. The solution was concentrated in vacuo, and the crude product was purified by recrystallization from $CHCl_3/Et_2O$ to afford a cationic arene complex **27**·H_2O (32.3 mg, 24%) as colorless single crystals. mp 159.2−161.3 °C; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ 1.90 (s, 15 H), 2.63 (br s, 2 H), 4.65 (d, $J = 12.9$ Hz, 2 H), 4.83 (d, $J = 13.2$ Hz, 2 H), 4.88 (d, $J = 13.2$ Hz, 2 H), 4.96 (d, $J = 12.9$ Hz, 2 H), 6.75 (s, 2 H); MS (FAB) *m*/*z* (%): 399 (100) [$M^+ - Cl$]; EA calcd (%) for $C_{20}H_{27}ClO_3Ru{\cdot}H_2O$ (451.95): C, 53.15; H, 6.02. Found: C, 53.23; H, 5.94.

Stoichiometric Reaction of Cp*RuCl(cod) (1a) with Diyne 28. A solution of Cp*RuCl(cod) **1a** (376.2 mg, 0.99 mmol) and a diyne **28** (303.6 mg, 1.23 mmol) in $CDCl_3$ (8 mL) was left at room temperature for 4 days. The solution was concentrated in vacuo, and the crude product was purified by recrystallization from $CHCl_3/Et_2O$ to afford a ruthenacycle complex **29** (263.7 mg, 51%) as dark green single crystals. mp 167.5−168.1 °C; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ 1.22 (s, 15 H), 4.22−4.30 (m, 2 H), 4.51−4.58 (m, 2 H), 7.05−7.15 (m, 8 H), 7.57 (tt, $J = 7.2$, 1.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ 9.88, 70.12, 106.10, 126.23, 129.21, 157.08, 173.94, 245.77; MS (FAB) *m*/*z* (%): 517 (94) [$M^+ - H$], 485 (100) [$MH_2^+ - Cl$]; EA calcd (%) for $C_{28}H_{29}ClORu$ (518.05): C, 64.92; H, 5.64. Found: C, 64.97; H, 5.59.

Reaction of Ruthenacycle Complex 28 with Acetylene. A solution of **28** (238.8 mg, 0.46 mmol) in $CDCl_3$ (11 mL) was heated at 40 °C under acetylene atmosphere (1 atm) for 5 days. The solution was concentrated in vacuo, and the crude product was purified by silica gel flash column chromatography (hexane-AcOEt 30:1) to give a terphenyl **30** (40.3 mg, 32%) as a solid. The analytical data for **30** was consistent with those reported in the literature.[43]

Crystallographic Structural Determination of 27·H_2O and 28. Single crystals of **27**·H_2O and **28** suitable for X-ray analysis were

obtained by recrystallization from $CHCl_3$/ether. Single crystals were mounted on a quartz fiber, and diffraction data were collected in the θ range of 2.11−29.16° for **27**·(H_2O) and 1.07−29.12° for **28** at 173 K on a Brucker SMART APEX CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). An absorption correction was made using SADABS. The structure was solved by direct methods and refined by full-matrix least squares on F^2 by using SHELXTL. All nonhydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in calculated positions. Final refinement details are compiled in Table 7.

Computational Methods: The Q-chem 2.0 program[44] in the Spartan '02 software package[45] was used for geometry optimizations, and the single-point energy calculations for the obtained geometries were performed with the Gaussian 98 program package.[46] All geometries of intermediates and transition states were fully optimized at the B3LYP/LACVP* level of theory. The LACVP* basis set uses a double-ζ basis set with the relativistic effective core potential of Hay and Wadt (LanL2 ECP)[36] for Ru and the 6-31G(d) basis sets[37] for other elements. The vibrational frequencies and zero-point energy (ZPE) were calculated at the same level of theory. The obtained structures were characterized by the number of imaginary frequencies (one or zero for transition or ground states, respectively). Visual inspection of imaginary vibrational modes was also performed with Spartan '02 software package.

Single-point energies were calculated at the B3LYP level using the basis sets consisting of a [6s5p3d2f1g]-contracted valence basis set with the Stuttgart−Dresden−Bonn energy-consistent pseudopotential (SDD)[38] for Ru and the 6-311++G(d,p) basis sets[39] for other elements. The 6-311++G(d,p) and SDD basis sets were used as stored in the Gaussian program. The *f* and *g* exponents for Ru were used as reported in the literature.[38b] Relative energies were corrected with unscaled ZPE. Atomic charges were computed at the B3LYP/LACVP* level using the natural population analysis method as implemented in Gaussian 98.[47]

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Supporting Information Available: Analytical data for the cycloadducts, Cartesian coordinates, total electronic and vibrational energies for all calculated structures (CIF and PDF). This material is available free of charge via the Internet at http://pubs.acs.org. The supplementary crystallographic data for this paper [CCDC 207925 (**27**·(H_2O)) and CCDC 207926 (**28**)] can be obtained via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033; or e-mail: deposit@ccdc.cam.ac.uk).

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(43) Scheller, A.; Winter, W.; Müller, E. *Liebigs Ann. Chem.* **1976**, 1448−1454.
(44) Kong, J.; White, C. A.; Krylov, A. I.; Sherrill, D.; Adamson, R. D.; Furlani, T. R.; Lee, M. S.; Lee, A. M.; Gwaltney, S. R.; Adams, T. R.; Ochsenfeld, C.; Gilbert, A. T. B.; Kedziora, G. S.; Rassolov, V. A.; Maurice, D. R.; Nair, N.; Shao, Y.; Besley, N. A.; Maslen, P. E.; Dombroski, J. P.; Daschel, H.; Zhang, W.; Korambath, P. P.; Baker, J.; Byrd, E. F. C.; Voorhis, T. V.; Oumi, M.; Hirata, S.; Hsu, C.-P.; Ishikawa, N.; Florian, J.; Warshel, A.; Johnson, B. G.; Gill, P. M. W.; Head-Gordon, M.; Pople, J. A. *J. Comput. Chem.* **2000**, *21*, 1532−1548.
(45) *Spartan '02*, version 1.0.2; Wavefunction, Inc.: Irvine, CA, 2002.
(46) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Andres, J. L.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, revision A.11; Gaussian, Inc.: Pittsburgh, PA, 2001.
(47) Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F. *Gaussian NBO*, version 3.1; Gaussian, Inc.: Pittsburgh, PA, 2001.