

Highly Efficient Intra- and Intermolecular [4 + 2] Cycloaddition Reaction Catalyzed by Rhodium Complex

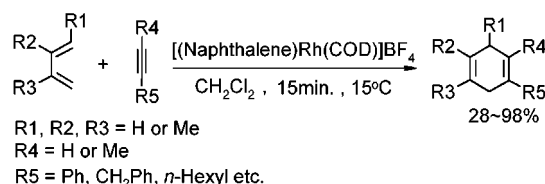
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ABSTRACT



A cationic Rh(I) complex, $[(\eta^6\text{-C}_{10}\text{H}_8)\text{Rh}(\text{cod})]\text{BF}_4$, has been found to be a quite useful catalytic system for both the intermolecular [4 + 2] cycloaddition reaction of 1,3-dienes with nonactivated acetylenes and the intramolecular [4 + 2] cycloaddition of dienyne under very mild reaction conditions (CH_2Cl_2 , 15 °C, 15 min).

The remarkable versatility of the Diels–Alder reaction for the stereoregulated construction of six-membered rings has made this reaction one of the most widely studied synthetic methods in organic chemistry.¹ However, cycloaddition reactions between electronically similar dienes and dienophiles usually require extreme reaction conditions.² This has severely limited their use in organic synthesis until the relatively recent discovery of metal-catalyzed cycloaddition. A number of excellent catalysts have been discovered, and transition metal-catalyzed [4 + 2] cycloadditions are emerging as synthetically useful processes.³ However, in many cases, a transition-metal catalytic system is effective for either intermolecular or intramolecular cycloaddition reaction usu-

ally in the presence of additives. In our continuing efforts in developing efficient catalytic reactions using naphthalene transition-metal complexes,⁴ we have devised a new, highly effective catalyst for the [4 + 2] cycloaddition reaction. Herein we report on the development of a new catalyst system that proceeds under very mild reaction conditions to give the [4 + 2] cycloaddition products in excellent yields.

Our new process has been successfully achieved by introducing (naphthalene)Rh(cod)]BF₄ (**1**)⁵ as a catalyst precursor. Complex **1** is stable and can be stored for a long time under nitrogen. Complex **1** is a practically quite useful

(1) For reviews on Diels–Alder reaction, see: (a) Danishefsky, S. *Aldrichimica Acta* **1986**, 19, 59. (b) Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, p 315. (c) Kagan, H.; Riant, O. *Chem. Rev.* **1992**, 92, 1007. (d) Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, 93, 741. (e) Delox, L.; Srebnik, M. *Chem. Rev.* **1993**, 93, 763. (f) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, 33, 497. (g) Fringuelli, F.; Taticchi, A. *Dienes in the Diels–Alder Reaction*; Wiley: New York, 1990. (h) Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon: Oxford, 1990.

(2) (a) Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1966**, 5, 211. (b) Ciganik, E. *Org. React.* **1984**, 32, 1. (c) Fallis, A. G. *Can. J. Chem.* **1984**, 62, 183. (d) Murakami, M.; Ubukata, M.; Itami, K.; Ito, Y. *Angew. Chem., Int. Ed.* **1998**, 37, 2248.

(3) For intramolecular [4 + 2] cycloaddition reactions, see: (a) Wender, P. A.; Jenkins, T. E. *J. Am. Chem. Soc.* **1989**, 111, 6432. (b) Jolly, R. S.; Luedtke, G.; Sheehan, D.; Livinghouse, T. *J. Am. Chem. Soc.* **1990**, 112, 4965. (c) Wender, P. A.; Smith, T. E. *J. Org. Chem.* **1996**, 61, 824. (d) McKinstry, L.; Livinghouse, T. *Tetrahedron* **1994**, 50, 6145. (e) O'Mahony, D. J. R.; Belanger, D. B.; Livinghouse, T. *Synlett* **1998**, 443. (f) Gilbertson, S. R.; Hoge, G. S. *Tetrahedron Lett.* **1998**, 39, 2075. (g) Gilbertson, S. R.; Hoge, G. S.; Genov, D. G. *J. Org. Chem.* **1998**, 63, 10077. (h) Kumar, K.; Jolly, R. S. *Tetrahedron Lett.* **1998**, 39, 3047. For intermolecular [4 + 2] cycloaddition reactions, see: (i) tom Dieck, H.; Diercks, R. *Angew. Chem., Int. Ed. Engl.* **1983**, 22, 778. (j) Mach, K.; Antropiusová, H.; Petrusová, L.; Turecek, F.; Hanus, V. *J. Organomet. Chem.* **1985**, 289, 331. (k) Matsuda, I.; Shibata, M.; Sato, S.; Izumi, Y. *Tetrahedron Lett.* **1987**, 28, 3361.

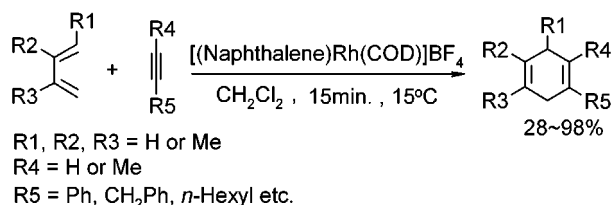
(4) Son, S. U.; Paik, S.-J.; Chung, Y. K. *J. Mol. Catal.* In press.

(5) Scotti, M.; Valderrama, M.; Ganz, R.; Werner, H. *J. Organomet. Chem.* **1985**, 286, 399.

catalytic system for both the intermolecular [4 + 2] cycloaddition reaction of 1,3-dienes with nonactivated acetylenes and intramolecular [4 + 2] cycloaddition reaction of dienyne.

Treatment of phenylacetylene and 2,3-dimethyl-1,3-butadiene with $[(\eta^6\text{-C}_{10}\text{H}_8)\text{Rh}(\text{cod})]\text{BF}_4$ (**1**) (1 mol %) in CH_2Cl_2 at 15 °C for 15 min afforded (4,5-dimethyl-1,4-cyclohexadien-1-yl)benzene in 83% yield without any noticeable amounts of byproducts (Scheme 1).

Scheme 1



No isomerization was observed. The generality of the catalyst was tested with several substrates (Table 1).

Table 1 gives details on the amounts of reagents and conditions of each catalytic run. An important feature of this system is its experimental simplicity. Terminal acetylenes

Table 1. $[(\text{Naphthalene})\text{Rh}(\text{cod})]\text{BF}_4$ -Catalyzed Intermolecular [4 + 2] Cycloaddition^a

entry	substrate	product	diene/alkyne (mole ratio)	yield (%) ^b
1			2	83
2			2	98
3 ^c			2	55
4 ^d			6	71
5			2	94
6			2	82
7			2	86
8 ^{d,e}			2	71
9			2	98(3:1)
10			2	98(3:1)
11 ^f			2	50(2.3:1)
12 ^f			2	50(2.3:1)
13 ^f			2	28(3.5:1)

^a CH_2Cl_2 , 15 °C, 1 mol % of catalyst, 15 min. ^b Isolated yield. ^c 1 h. ^d 2 mol % of catalyst used. ^e 40 °C, 18 h. ^f 15 °C, 8 h.

bearing benzyl (entry 2), *n*-alkyl chains (entry 3), diynes (entry 4), trimethylsilyl (entry 5), protected propargyl alcohol (entry 6), and ferrocenylmethylene (entry 7) gave excellent yields of cycloaddition products. With 1,7-octadiyne (entry 4), a double [4 + 2] cycloaddition reaction occurred. Reactions involving internal alkynes did not proceed well at 15 °C, but the reaction went smoothly at 40 °C (entry 8). It has been reported³ⁱ that in the presence of $[\text{Rh}(\text{cod})(\text{dppb})]\text{-PF}_6$ 1-phenyl-1-propyne gave no cycloaddition products. In contrast with $[\text{Rh}(\text{cod})(\text{dppb})]\text{PF}_6$, treatment of **1** at 40 °C for 18 h gave the corresponding cycloaddition product in 71% yield (turnover number: 35.5). When isoprene was used as a diene, a 3:1 mixture of [4 + 2] cycloaddition products **A** and **B** was obtained in 98% yield (entries 9 and 10). Thus **1** is a quite effective catalyst for the intermolecular [4 + 2] cycloaddition reaction of 1,3-butadienes with nonactivated alkynes.

Treatment of internal dienes and phenylacetylene with **1** in CH_2Cl_2 at 15 °C led to the cyclotrimerization of phenylacetylene. However, when 3-phenyl-1-propyne was used as an alkyne substrate, a mixture of 2.3–3.5:1 of [4 + 2] cycloaddition products **A** and **B** was obtained in 28–50% yields (entries 11–13).

The scope of the catalytic reaction was examined for the intramolecular [4 + 2] cycloaddition reaction (Table 2).

Table 2. $[(\text{Naphthalene})\text{Rh}(\text{cod})]\text{BF}_4$ -Catalyzed Intramolecular [4 + 2] Cycloaddition^a

entry	substrate	product	yield (%) ^b
1			94
2			98
3			98

^a CH_2Cl_2 , 15 °C, 1 mol % of catalyst, 15 min. ^b Isolated yield.

The reaction of 4,4-bis(carbomethoxy)-6,8-decadien-1-yne gave a bicyclic diene derivative in 94% yield. The present reaction can be extended to the use of an oxygen-containing analogue. Subjecting 4-oxo-6,8-decadien-1-yne to the same reaction condition provided the oxabicyclic diene in 98% yield. In the same way, the nitrogen-containing substrate produced azabicyclic diene in 98% yield. Thus, the intramolecular cycloaddition reaction was also extremely effective as an intermolecular cycloaddition reaction and was found to proceed with excellent levels of diastereoselection.

The following observations may provide some insights into the catalytic reaction mechanism. Complex $[(\eta^6\text{-C}_6\text{Me}_6)\text{Rh}(\text{cod})]\text{BF}_4$ has no catalytic activity in the [4 + 2] cycloaddition of 2,3-dimethyl-1,3-butadiene with phenylacetylene. In the reaction of **1** and 2,3-dimethyl-1,3-butadiene, $[(2,3\text{-dimethyl-1,3-butadiene})\text{Rh}(\text{cod})]\text{BF}_4$ was observed as a

product.⁶ Thus, naphthalene acts as a better leaving group than C₆Me₆ does. The easy displacement of naphthalene by diene may be due to the facile ring-slippage.⁷ Hence, we envision that [(diene)Rh(cod)]BF₄ was generated in the first step of the catalytic cycle. The cationic charge on **1** can provide a notable rate enhancement as in other Rh(I)- or Pd(II)-catalyzed [4 + 2] cycloaddition.⁸ Thus, the presence of a formal positive charge on the rhodium and the ease of displacement of the naphthalene ligand may help **1** to be an excellent catalyst system in the [4 + 2] cycloaddition.

In conclusion, we have found a practically useful catalyst

system that is active especially for the inter- and intramolecular [4 + 2] cycloaddition between 1,3-butadiene and nonactivated alkyne. Tables 1 and 2 demonstrate that the method shows considerable promise as a synthetic tool. We are currently investigating asymmetric catalysts based on this system.

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Supporting Information Available: NMR and mass spectroscopy data for new compounds synthesized in this study. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(6) ¹H NMR (CD₃NO₂): δ 5.30 (m, 2 H), 4.96 (m, 2 H), 3.83 (s, 2 H), 2.54 (s, 6 H), 2.24 (s, 2 H), 2.16 (s, 8 H) ppm. FAB-HRMS (M⁺): calcd 293.0776, obsd 293.0741.

(7) (a) Jonas, K. *Pure Appl. Chem.* **1990**, 62, 1169. (b) Kündig, E. P.; Jeger, P.; Bernardinelli, G. *Angew. Chem., Int. Ed. Engl.* **1995**, 34, 2161.

(8) (a) O'Mahony, D. J. R.; Belanger, D. B.; Livinghouse, T. *Synlett* **1998**, 443. (b) Oi, S.; Kashiwagi, K.; Inoue, Y. *Tetrahedron Lett.* **1998**, 39, 6253.