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Highly Chemo- and Regioselective Intermolecular Cyclotrimerization of Alkynes Catalyzed by Cationic Rhodium(I)/Modified BINAP Complexes

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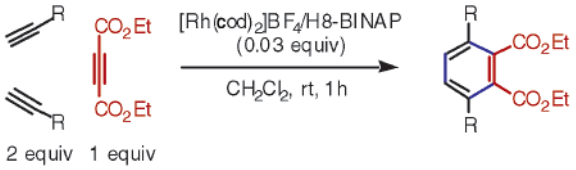
ABSTRACT



Cationic rhodium(I)/modified BINAP complexes are effective catalysts for highly regioselective intermolecular cyclotrimerization of terminal alkynes and highly chemo- and regioselective intermolecular cocyclotrimerization of diethyl acetylenedicarboxylate (DEAD) and terminal alkynes. It is a noteworthy example of intermolecular cocyclotrimerization of two different alkynes in terms of catalytic activity, chemo- and regioselectivity, scope of substrates, and ease of operation. The wide applicability of this new cocyclotrimerization procedure is demonstrated in the one-step synthesis of [6]metacyclophane.

Highly regiocontrolled synthesis of arenes is attractive because arenes are important building blocks in organic synthesis. Cyclotrimerization of alkynes to yield substituted benzenes is a possible method for their synthesis. Although various transition metals catalyze alkyne cyclotrimerization, it has been difficult to carry out that intermolecular reaction in a highly regioselective manner.[1] In particular, catalytic chemo- and regioselective intermolecular cocyclotrimerization of two different alkynes has not been established yet.[2−5] In general, a partially intramolecular reaction between an α,ω-diyne and excess monoynes and a completely intramolecular reaction have been employed to overcome this problem.[6] The present study describes highly regioselective intermolecular cyclotrimerization of terminal alkynes and highly chemo- and regioselective intermolecular cocyclotrimerization of diethyl acetylenedicarboxylate (DEAD) and terminal alkynes catalyzed by cationic rhodium(I)/modified BINAP complexes (Figure 1).

Although a neutral rhodium(I) complex is an effective catalyst for partial or complete intramolecular cyclotrimer-

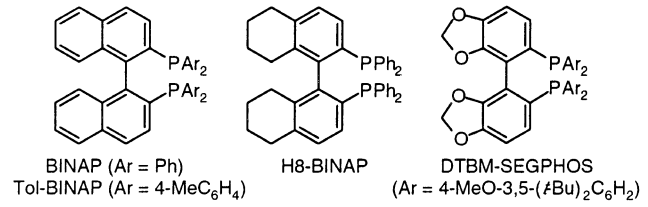


Figure 1. Structures of modified BINAP ligands.

(1) For reviews, see: (a) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901−2915. (b) Frühauf, H.-W. *Chem. Rev.* **1997**, *97*, 523−596. (c) Ojima, I.; Tzamarioudaki, M.; Zhaoyang, L.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635−662. (d) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 46−92. (e) Boese, R.; Sickle, A. P. V.; Vollhardt, K. P. C. *Synthesis* **1994**, 1374−1382. (f) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081−1119. (g) Vollhardt, K. P. C. *Angew. Chem., Int. Ed.* **1984**, *23*, 536−556. (h) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Hegedus, L., Eds.; Pergamon Press: Oxford, 1995; Vol. 12, pp 741−770.

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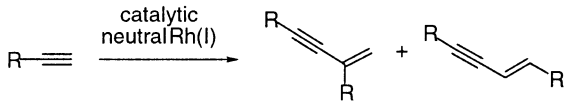
ization of alkynes,[7,8] it generally reacts with terminal alkynes to give linear dimers (Scheme 1).[9,10] On the other hand,

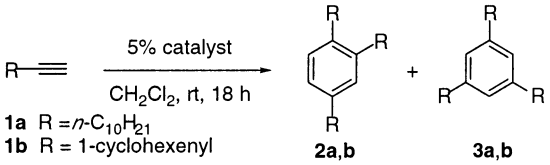
Scheme 1



application of a cationic rhodium(I) complex in oligomerization of terminal alkynes remains unexplored.[11]

We examined the reaction of 1-dodecyne (**1a**) first using 5 mol % of $[Rh(cod)_2]BF_4$/10 mol % PPh_3 at room temperature. The reaction was very slow, but a small amount of cyclotrimerization products was detected (Table 1, entry 1). Although the use of various monodentate or bidentate phosphine ligands (Ph_3P, *n*-Bu_3P, dppe, and dcpe) furnished cyclotrimerization products, the catalytic activities were low (entries 1−4).

Table 1. Cationic Rh(I) Complex-Catalyzed Intermolecular Cyclotrimerization of Terminal Alkynes[a]



entry	catalyst[b]	alkyne	yield (%) (**2** + **3**)[c]	ratio of **2**/**3**[c]
1	$[Rh(cod)_2]BF_4$/2 Ph_3P	**1a**	5	
2	$[Rh(cod)_2]BF_4$/2 *n*-Bu_3P	**1a**	3	
3	$[Rh(nbd)_2]BF_4$/dppe	**1a**	3	
4	$[Rh(cod)_2]BF_4$/dcpe	**1a**	<2	
5	$[Rh(cod)_2]BF_4$/Tol-BINAP	**1a**	>95	64:36
6	$[Rh(cod)Cl]_2$/Tol-BINAP	**1a**	<2	
7	$[Ir(cod)_2]BF_4$/Tol-BINAP	**1a**	<2	
8[e]	$[Rh(cod)_2]BF_4$/DTBM-SEGPHOS	**1a**	91[d]	83:17
9	$[Rh(cod)_2]BF_4$/DTBM-SEGPHOS	**1b**	89[d]	97:3

[a] Rh or Ir complex (0.005 mmol), phosphine (0.005 or 0.01 mmol), 1-dodecyne (0.1 mmol), and CH_2Cl_2 (1 mL) were employed. [b] The active catalysts were prepared by mixing Rh or Ir complex and phosphine in CH_2Cl_2 followed by hydrogenation (1 atm, rt, 0.5 h). [c] Determined by ^1H NMR. [d] Isolated yield. [e] Reaction time = 24 h.

Surprisingly, the use of Tol-BINAP dramatically improved catalytic activity and cyclotrimerization products were obtained in almost quantitative yield with moderate regioselectivity (entry 5). The use of cationic Rh(I) complex is essential for this reaction. The use of neutral Rh(I)/Tol-BINAP complex or cationic Ir(I)/Tol-BINAP complex significantly decreased the activity (entries 6 and 7). Both high activity and regioselectivity were achieved by use of the cationic Rh(I)/DTBM-SEGPHOS[12] complex. Both nonconjugated (**1a**) and conjugated (**1b**) terminal alkynes were good substrates yielding 1,2,4-trisubstituted benzenes **2** in high yield with high regioselectivity (entries 8 and 9).

Next, we investigated intermolecular cocyclotrimerization of two different alkynes. After screening various alkynes and cationic Rh(I)/modified BINAP complexes, we found that the cationic Rh(I)/H8-BINAP[13] complex catalyzed chemo- and regioselective intermolecular cocyclotrimerization of DEAD (**4**) and terminal alkynes. Table 2 shows that two molecules of **1** cleanly reacted with one molecule of **4** to yield 3,6-disubstituted diethyl phthalate **5** in high yield with high regioselectivity upon treatment with catalytic amount of cationic Rh(I)/H8-BINAP complex.[14] Alkyl- (**1a**, entry 1), chloroalkyl- (**1c**, entry 2), methoxymethyl- (**1d**, entry 3), aryl- (**1e**, entry 4 and **1f**, entry 5), and alkenyl-substituted (**1b**, entry 6) terminal alkynes were suitable substrates for this reaction. Although the reaction of sterically demanding trimethylsilylacetylene (**1g**) furnished **5g** in moderate yield, excellent regioselectivity of **5g** was observed (entry 7).

(2) Ni(0)-catalyzed cocyclotrimerization of methyl propiolate and terminal alkynes was reported. Although the regioselectivity is high, chemoselectivity is moderate, and the reaction requires slow addition of methyl propiolate (over 5−60 min) and a substoichiometric amount of zinc(II) phenoxide: Mori, N.; Ikeda, S.-I.; Odashima, K. *Chem. Commun*. **2001**, 181−182.

(3) For Ni(0)-catalyzed cocyclotrimerization of alkynes using a large excess of acetylene gas, see: Sato, Y.; Ohashi, K.; Mori, M. *Tetrahedron Lett*. **1999**, *40*, 5231−5234.

(4) Palladacyclopentadiene-mediated cocyclotrimerization of two molecules of dimethyl acetylenedicarboxylate and one molecule of diphenylacetylene was reported (76% yield), but this reaction proceeded in low yield (40% yield) under catalytic conditions (regioselectivity is not relevant to this case): Dieck, H. T.; Munz, C.; Müller, C. *J. Organomet. Chem*. **1990**, *384*, 243−255.

(5) Stoichiometric zirconium- and copper-mediated cocyclotrimerization of alkynes, see: Takahashi, T.; Xi, Z.; Yamazaki, A.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc*. **1998**, *120*, 1672−1680.

(6) For papers on catalytic intramolecular cyclotrimerization of alkynes, see: (a) Yamamoto, Y.; Nagata, A.; Nagata, H.; Ando, Y.; Arikawa, Y.; Tatsumi, K.; Itoh, K. *Chem. Eur. J*. **2003**, *9*, 2469−2483. (b) Jeevanandam, A.; Korivi, R. P.; Huang, I.; Cheng, C.-H. *Org. Lett*. **2002**, *4*, 807−810. (c) Sugihara, T.; Wakabayashi, A.; Nagai, Y.; Takao, H.; Imagawa, H.; Nishizawa, M. *Chem. Commun*. **2002**, *9*, 576−577. (d) Slowinski, F.; Aubert, C.; Malacria, M. *Adv. Synth. Catal*. **2001**, *343*, 64−67. (e) Ozerov, O. V.; Patrick, B. O.; Ladipo, F. T. *J. Am. Chem. Soc*. **2000**, *122*, 6423−6431. (f) Yamamoto, Y.; Ogawa, R.; Itoh, K. *Chem. Commun*. **2000**, *9*, 549−550. (g) Hillard III, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc*. **1977**, *99*, 4058−4069.

(7) For recent papers on the rhodium-catalyzed intramolecular cyclotrimerization of alkynes, see: (a) Kinoshita, H.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc*. **2003**, *125*, 7784−7785. (b) Nishiyama, H.; Niwa, E.; Inoue, T.; Ishima, Y.; Aoki, K. *Organometallics* **2002**, *21*, 2572−2574. (c) Witulski, B.; Zimmermann, A. *Synlett* **2002**, 1855−1859. (d) McDonald, F. E.; Smolentsev, V. *Org. Lett*. **2002**, *4*, 745−748. (e) Witulski, B.; Stengel, T. *Angew. Chem., Int. Ed*. **1999**, *38*, 2426−2430. (f) Kotha, S.; Brahmachary, E. *Tetrahedron Lett*. **1997**, *38*, 3561−3564. (g) McDonald, F. E.; Zhu, H. Y. E.; Homquist, C. R. *J. Am. Chem. Soc*. **1995**, *117*, 6605−6606.

(8) For pioneering work of the rhodium-catalyzed intramolecular cyclotrimerization of alkynes, see: Grigg, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1357−1364.

(9) (a) Field, L. D.; Ward, A. J.; Turner, P. *Aust. J. Chem*. **1999**, *52*, 1085−1092. (b) Ohshita, J.; Furumori, K.; Matsuguchi, A.; Ishikawa, M. *J. Org. Chem*. **1990**, *55*, 3277−3280.

(10) For rhodium clusters catalyzed intermolecular cyclotrimerization of terminal alkynes, see: Baidossi, W.; Goren, N.; Blum, J. *J. Mol. Catal*. **1993**, *85*, 153−162.

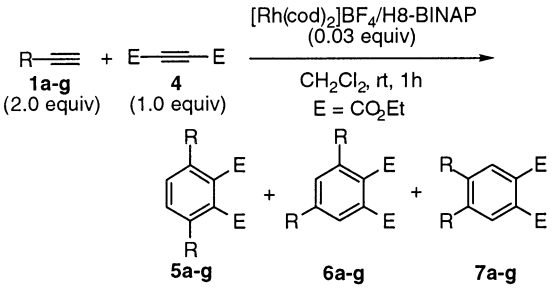
(11) For recent papers on the cationic rhodium(I) complex-catalyzed reaction of alkynes, see: (a) Tanaka, K.; Fu, G. C. *J. Am. Chem. Soc*. **2003**, *125*, 8078−8079. (b) Chakrapani, H.; Liu, C.; Widenhoefer, R. A. *Org. Lett*. **2003**, *5*, 157−159. (c) Tong, X.; Zhang, Z.; Zhang, X. *J. Am. Chem. Soc*. **2003**, *125*, 6370−6371. (d) Hartung, C. G.; Tillack, A.; Trauthwein, H.; Beller, M. *J. Org. Chem*. **2001**, *66*, 6339−6343. (e) Jeong, N.; Sung, B. K.; Choi, Y. K. *J. Am. Chem. Soc*. **2000**, *122*, 6771−6772.

(12) Saito, T.; Yokozawa, T.; Zhang, X.; Sayo, N. EP 850945A, 1998; US 5872273, 1999.

(13) Zhang, X. Mashimo, K.; Koyano, K.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Takaya, H. *Tetrahedron. Lett*. **1991**, *32*, 7283−7286.

(14) In this reaction, major byproducts are 1:2 (= **1**/**4**) cocyclotrimerization products.

Table 2. Cationic Rh(I)/H8-BINAP Complex-Catalyzed Intermolecular Cocyclotrimerization of DEAD and Terminal Alkynes[a]

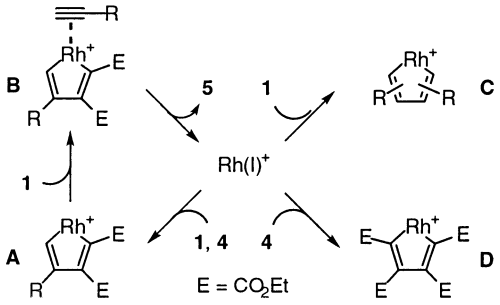


entry	R	yield (%) (**5** + **6** + **7**)[b]	ratio of **5**/**6**/**7**[c]
1	*n*-$C_{10}H_{21}$ (**1a**)	88	92:6:2
2	$Cl(CH_2)_3$ (**1c**)	92	91:8:1
3	$MeOCH_2$ (**1d**)	61	86:10:4
4	Ph (**1e**)	90	89:9:2
5	*o*-Tol (**1f**)	77	89:9:2
6	1-cyclohexenyl (**1b**)	90	91:4:5
7	Me_3Si (**1g**)	57	99:1:0

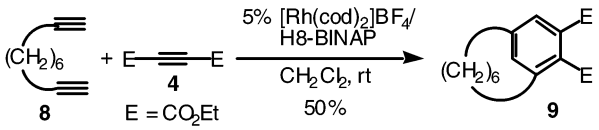
[a] See the Supporting Information for reaction conditions. [b] Isolated yield. [c] Determined by ^1H NMR.

Scheme 2 depicts a plausible mechanism of this cationic rhodium(I)/H8-BINAP complex-catalyzed intermolecular cocyclotrimerization. Chemo- and regioselectivity is determined by preferential formation of metallacycle **A** instead of **C** and

Scheme 2



Scheme 3



D followed by the coordination of terminal alkynes to form complex **B**.[15] Reductive elimination of rhodium gives **5** and regenerates the rhodium catalyst.

The wide applicability of this new cocyclotrimerization procedure is demonstrated in the synthesis of metacyclophane (Scheme 3). The reaction of commercially available 1,9-decadiyne (**8**) and **4** gave a [6]metacyclophane **9** in 50% yield. This is the shortest (one-step) synthesis of a metacyclophane starting from commercially available reagents.[16]

In conclusion, we discovered that cationic rhodium(I)/modified BINAP complexes are versatile new catalysts for highly regioselective intermolecular cyclotrimerization of terminal alkynes, and highly chemo- and regioselective intermolecular cocyclotrimerization of DEAD and terminal alkynes. This catalyst system is the first example of efficient rhodium(I)-catalyzed intermolecular cyclotrimerization of terminal alkynes. It is a noteworthy example of intermolecular cocyclotrimerization of two different alkynes in terms of catalytic activity, chemo- and regioselectivity, scope of substrates, and ease of operation. Work toward developing an asymmetric variant of this process is underway and will be reported in due course.

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Supporting Information Available: Experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) The use of rhodium(I)/DTBM-SEGPHOS complex for the cocyclotrimerization of **1** and **4** significantly lowered the yield of **5** as a result of the generation of **2** and **3** as byproducts. The use of rhodium(I)/Tol-BINAP complex significantly decreased the regioselectivity of **5**.

(16) For the formation of cyclophanes by cyclotrimerization of bisterminal diynes with nitriles, see: Moretto, A. F.; Zhang, H.-C.; Maryanoff, B. E. *J. Am. Chem. Soc*. **2001**, *123*, 3157−3158.