

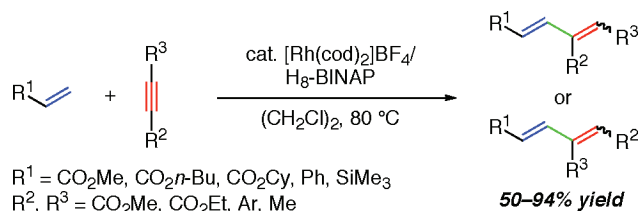
Rhodium-Catalyzed Regio- and Stereoselective Codimerization of Alkenes and Electron-Deficient Internal Alkynes Leading to 1,3-Dienes

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Received April 30, 2008

ABSTRACT



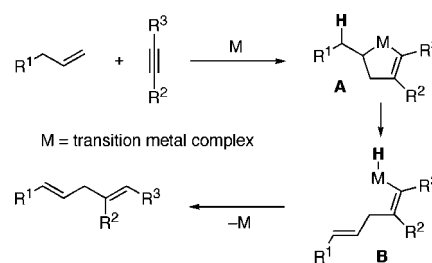
A cationic rhodium(I)/H₈–BINAP complex catalyzes codimerization of alkenes bearing no α -hydrogen and electron-deficient internal alkynes, leading to 1,3-dienes in good yields with moderate to excellent regio- and stereoselectivity. The same complex also catalyzes codimerization of an acrylate and phenyl-substituted electron-rich internal alkynes, leading to 1,3-dienes.

Transition-metal-catalyzed intermolecular codimerization of alkenes and alkynes is an attractive method for the synthesis of substituted dienes in a highly atom-economical fashion.^{1,2} For example, Trost and co-workers have extensively studied the ruthenium-catalyzed intermolecular Alder–ene reaction for the synthesis of substituted 1,4-dienes.^{3,4} Recently, Hilt and Treutwein reported a cobalt-catalyzed variant of this

reaction.⁵ The mechanism for the transition-metal-catalyzed intermolecular Alder–ene reactions is proposed as shown in Scheme 1. A transition-metal complex reacts with an alkene and an alkyne to generate metallacyclopentene **A**. β -Hydride elimination to vinylmetal hydride **B** followed by reductive elimination furnishes a 1,4-diene.

On the other hand, transition-metal-catalyzed intermolecular codimerization of alkenes bearing no α -hydrogen and alkynes giving substituted 1,3-dienes is scarce.^{6–8} A possible

Scheme 1



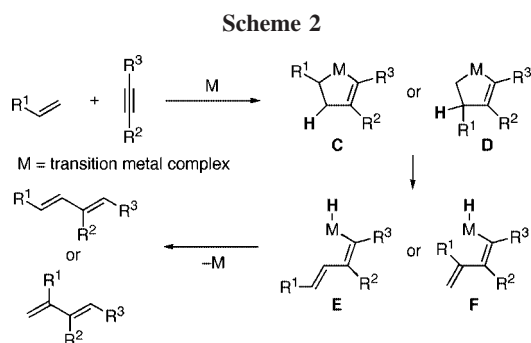
(1) For reviews, see: (a) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813. (b) Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev.* **2001**, *101*, 2067. (c) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Hegedus, L., Eds.; Pergamon Press: Oxford, 1995; Vol. 12, p 741. (d) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081.

(2) For a review of ruthenium-catalyzed alkene–alkyne coupling reactions, see: Trost, B. M.; Frederiksen, M. U.; Rudd, M. T. *Angew. Chem., Int. Ed.* **2005**, *44*, 6630.

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mechanism for the formation of 1,3-dienes is shown in Scheme 2. β -Elimination of the methylene or methine proton



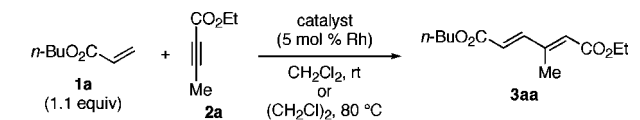
in metallacyclopentene **C** or **D** to dienylnmetal hydride **E** or **F** followed by reductive elimination would furnish a 1,3-diene.⁹ However, β -hydride elimination from a cyclic intermediate is difficult due to the geometrical constraints, which might deter the formation of a 1,3-diene. Mitsudo, Watanabe, and co-workers reported one notable success in achieving such a reaction. They developed the ruthenium-catalyzed intermolecular codimerization of acrylic acid derivatives and *electron-rich* internal alkynes and proposed β -elimination of the methylene proton in a ruthenacyclopentene intermediate.⁶ Murakami, Ito, and co-worker also realized the ruthenium-catalyzed 1,3-diene formation from alkenes and *electron-rich* terminal alkynes by a mechanistically different approach and proposed the formation of a vinylidene complex as a key intermediate.⁷ However, *electron-deficient* internal alkynes may not be included in these ruthenium-catalyzed codimerization reactions.

Our research group has demonstrated that a cationic rhodium(I)/H₈-BINAP complex is a highly effective catalyst for chemo- and regioselective cotrimerization of two terminal alkynes and one *electron-deficient* internal alkyne leading to tetrasubstituted benzenes.^{10,11} This result prompted our investigation into reactions of alkenes and *electron-deficient* internal alkynes in the presence of a cationic rhodium(I)/BINAP-type bisphosphine complex. Herein, we describe a

cationic rhodium(I)/H₈-BINAP complex-catalyzed regio- and stereoselective codimerization of alkenes bearing no α -hydrogen and internal alkynes including *electron-deficient* ones giving substituted 1,3-dienes.

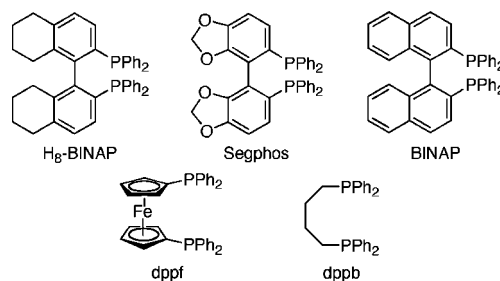
The reaction of *n*-butyl acrylate (**1a**, 1.1 equiv) with ethyl 2-butynoate (**2a**) was first examined in the presence of 5 mol % of the cationic rhodium(I)/H₈-BINAP complex as a catalyst, but no reaction was observed at room temperature (Table 1, entry 1). Fortunately, 1,3-diene **3aa** was obtained

Table 1. Screening of Rh Catalysts for Codimerization of Acrylate **1a** and Electron-Deficient Internal Alkyne **2a**^a



entry	catalyst	conditions	yield (%) ^b
1	[Rh(cod) ₂]BF ₄ /H ₈ -BINAP	rt, 16 h	0
2	[Rh(cod) ₂]BF ₄ /H ₈ -BINAP	80 °C, 3 h	50
3	[Rh(cod) ₂]BF ₄ /Segphos	80 °C, 3 h	35
4	[Rh(cod) ₂]BF ₄ /BINAP	80 °C, 3 h	9
5	[Rh(cod) ₂]BF ₄ /dppf	80 °C, 3 h	0
6	[Rh(cod) ₂]BF ₄ /dppb	80 °C, 3 h	0
7	[RhCl(cod)] ₂ /2H ₈ -BINAP	80 °C, 3 h	0
8 ^c	[Rh(cod) ₂]BF ₄ /H ₈ -BINAP	80 °C, 8 h	71

^a Catalyst (0.010 mmol), **1a** (0.22 mmol), **2a** (0.20 mmol), and CH₂Cl₂ or (CH₂Cl)₂ (2.0 mL) were used. ^b Isolated yield. ^c **1a**: 2 equiv.



in 50% yield with excellent stereoselectivity at elevated temperature (80 °C, entry 2). Thus, various BINAP-type bisphosphine ligands were screened (entries 2–4), which revealed that the use of H₈-BINAP furnished **3aa** in the highest yield (entry 2) in accordance with the cotrimerization of alkynes.¹⁰ A cationic rhodium(I) complex and the BINAP-type bisphosphine ligand are essential to promote this reaction. The use of a cationic rhodium(I)/dppf or dppb complex and a neutral rhodium(I)/H₈-BINAP complex failed to catalyze this reaction (entries 5–7). Further improved yield of **3aa** was achieved by using 2 equiv of **1a**, although the reaction time required for completion was prolonged (entry 8).

Next, the scope of this reaction was examined with respect to both acrylates and internal alkynes as shown in Table 2. With respect to internal alkynes, not only ethyl 2-butynoate (**2a**, entry 1) but also ethyl phenylpropiolate (**2b**, entry 2) reacted with **1a** to give the corresponding 1,3-diene **3ab** in high yield with excellent regio- and stereoselectivity. Sterically demanding 2-methoxynaphthyl-substituted propiolate

(5) Hilt, G.; Treutwein, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 8500.

(6) Mitsudo, T.; Zhang, S.-W.; Nagao, M.; Watanabe, Y. *Chem. Commun.* **1991**, 598.

(7) Murakami, M.; Ubukata, M.; Ito, Y. *Tetrahedron Lett.* **1998**, *39*, 7361.

(8) Recently, ruthenium-catalyzed co-oligomerization of *N*-vinylamides with alkenes or alkynes (*electron-rich* internal alkynes) was reported, and the authors proposed the formation of a ruthenium hydride species through activation of sp² C–H bonds in alkenes or a dmfm ligand, see: Tsujita, H.; Ura, Y.; Matsuki, S.; Wada, K.; Mitsudo, T.; Kondo, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 5160.

(9) The formation of 1,3-dienes from 1,6-enynes presumably through β -elimination of the methine proton in the metallacyclopentene is a well-known side reaction in the rhodium-catalyzed Pauson–Khand-type reactions, see: Schmid, T. M.; Consiglio, G. *Chem. Commun.* **2004**, 2318.

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(11) For our accounts of the cationic rhodium(I)/BINAP-type bisphosphine complex-catalyzed [2 + 2 + 2] cycloaddition reactions, see: (a) Tanaka, K. *Synlett* **2007**, 1977. (b) Tanaka, K.; Nishida, G.; Suda, T. *J. Synth. Org. Chem. Jpn.* **2007**, *65*, 862.

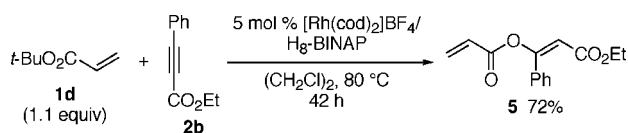
Table 2. Rh(I)⁺/H₈-BINAP-Catalyzed Codimerization of Alkenes **1a–h** and Electron-Deficient Internal Alkynes **2a–d**^a

entry	1 (R ¹ , equiv)	2 (R ² , CO ₂ R ³)	% yield ^b (2 <i>E</i> /2 <i>Z</i>)	
			3	4
1	1a (CO ₂ <i>n</i> -Bu, 2.0)	2a (Me, CO ₂ Et)	71 (2 <i>E</i>)	– ^c
2	1a (CO ₂ <i>n</i> -Bu, 1.1)	2b (Ph, CO ₂ Et)	87 (2 <i>Z</i>)	
3	1b (CO ₂ Me, 1.1)	2b (Ph, CO ₂ Et)	85 (2 <i>Z</i>)	
4	1c (CO ₂ Cy, 1.1)	2b (Ph, CO ₂ Et)	91 (2 <i>Z</i>)	
5 ^d	1a (CO ₂ <i>n</i> -Bu, 1.1)	2c (Ar ^e , CO ₂ Et)	94 (2 <i>Z</i>)	
6	1a (CO ₂ <i>n</i> -Bu, 5.0)	2d (CO ₂ Me, CO ₂ Me)	76 (1:3)	
7	1e (Ph, 2.0)	2a (Me, CO ₂ Et)	52 (2 <i>E</i>) ^f	19 (–) ^f
8	1e (Ph, 2.0)	2b (Ph, CO ₂ Et)	50 (2 <i>Z</i>)	– ^c
9	1e (Ph, 2.0)	2d (CO ₂ Me, CO ₂ Me)	81 (1:2)	
10	1f (SiMe ₃ , 5.0)	2a (Me, CO ₂ Et)	44 (2 <i>E</i>) ^f	21 (–) ^f
11	1g (<i>t</i> -Bu, 5.0)	2a or 2b	0 (–) ^h	
12	1h (<i>n</i> -C ₆ H ₁₃ , 5.0)	2a or 2b	0 (–) ^h	

^a [Rh(cod)₂]BF₄ (0.015 mmol), H₈-BINAP (0.015 mmol), **1** (0.33–1.50 mmol), **2** (0.30 mmol), and (CH₂Cl)₂ (1.5 mL) were used. ^b Isolated yield. ^c A separable unidentified mixture of olefins was generated as byproduct. ^d Catalyst: 20 mol %. ^e Ar = 2-MeO-1-naphthyl. ^f Isolated as a mixture of **3** and **4**. ^g Not determined. ^h No reaction was observed.

(**2c**, entry 5) could also participate in this reaction, although high catalyst loading was required. The reaction of **1a** with dimethyl acetylenedicarboxylate (**2d**, entry 6) proceeded in good yield, while moderate stereoselectivity was observed. With respect to acrylates, not only *n*-butyl acrylate (**1a**, entry 2) but also methyl (**1b**, entry 3) and cyclohexyl (**1c**, entry 4) acrylates reacted with **2b** to give the corresponding 1,3-dienes in high yields with excellent regio- and stereoselectivity. Interestingly, the reaction of *tert*-butyl acrylate (**1d**) with **2b** furnished alkenyl acrylate **5** in good yield, presumably through formation of acrylic acid followed by its addition to **2b** (Scheme 3). The use of *electron-rich* alkenes

Scheme 3



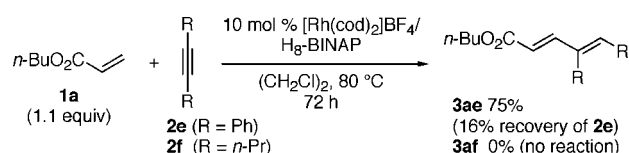
bearing no α-hydrogen was also examined.¹² The reactions of styrene (**1e**) with **2a**, **2b**, and **2d** proceeded in good yields (entries 7–9), while moderate regioselectivity was observed (entries 7 and 8). Vinyltrimethylsilane (**1f**) also reacted with

(12) Although no reaction was observed in entries 11 and 12, the reactions of **1g** and **1h** with dimethyl acetylenedicarboxylate (**2d**) at room temperature furnished cotrimerization products. The structures of monoenes and monoynes determine the selectivity between codimerization vs cotrimerization; see: Shibata, Y.; Noguchi, K.; Hirano M.; Tanaka, K. *Org. Lett.* **2008**, *10*, 2825

2a, giving two regioisomers in good yield (entry 10), while 3,3-dimethyl-1-butene (**1g**) failed to react with **2a** and **2b** (entry 11).¹² The reaction of 1-octene (**1h**) bearing α-hydrogen with **2a** and **2b** was also examined, but both intermolecular Alder–ene reaction leading to a 1,4-diene and linear codimerization leading to a 1,3-diene did not proceed at all (entry 12).¹²

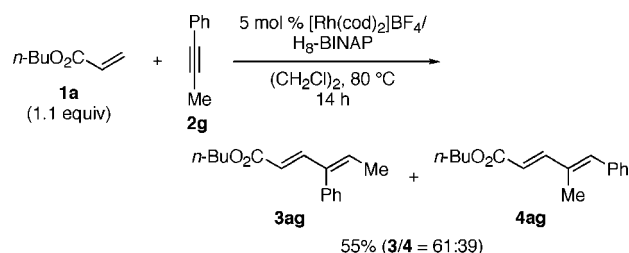
Finally, the reactions of acrylate **1a** with *electron-rich* internal alkynes were also examined. Although high catalyst loading and prolonged reaction time were required, the reaction of **1a** with diphenylacetylene (**2e**) proceeded in good yield with excellent stereoselectivity (Scheme 4). Unfortun-

Scheme 4



nately, 4-octyne (**2f**) failed to react with **1a** (Scheme 4). Unsymmetrical alkyne **2g** bearing phenyl and methyl at each alkyne terminus reacted with **1a** in moderate yield, although two regioisomeric 1,3-dienes were obtained (Scheme 5).

Scheme 5



In conclusion, we have demonstrated that a cationic rhodium(I)/H₈-BINAP complex is an effective catalyst for the regio- and stereoselective codimerization of alkenes bearing no α-hydrogen (acrylates, styrene, and vinyltrimethylsilane) and internal alkynes, including *electron-deficient* ones, leading to 1,3-dienes. Future studies will focus on expanding the scope and elucidation of the precise mechanism.

Acknowledgment. This work was supported partly by a Grant-in-Aid for Scientific Research [Nos. 20675002 and 19028015 (Chemistry of Concerto Catalysis)] from the Ministry of Education, Culture, Sports, Science and Technology, Japan. We thank Takasago International Corp. for the gift of H₈-BINAP and Segphos.

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

OL800995R