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

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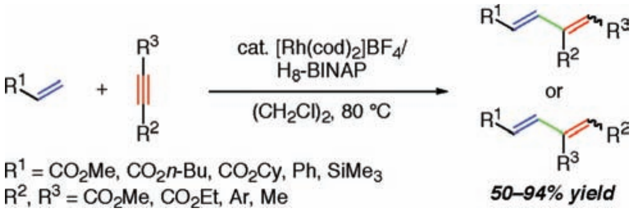
ABSTRACT

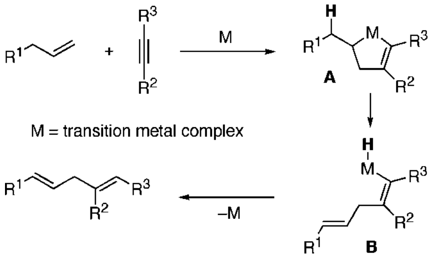


A cationic rhodium(I)/H_8−BINAP complex catalyzes codimerization of alkenes bearing no α-hydrogen and electron-deficient internal alkynes, leading to 1,3-dienes in good yields with moderate to excellent regio- and stereoselectivity. The same complex also catalyzes codimerization of an acrylate and phenyl-substituted 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



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(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.

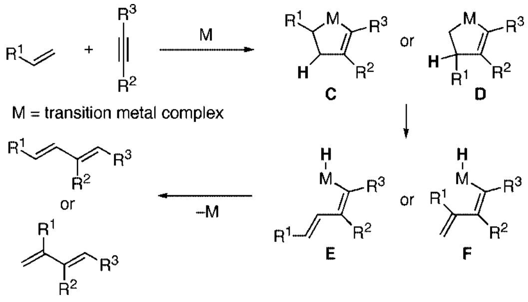
(3) (a) Trost, B. M.; Indolese, A. *J. Am. Chem. Soc.* **1993**, *115*, 4361. (b) Trost, B. M.; Indolese, A. F.; Müller, T. J. J.; Treptow, B. *J. Am. Chem. Soc.* **1995**, *117*, 615. (c) Trost, B. M; Müller, T. J. J.; Martinez, J. *J. Am. Chem. Soc.* **1995**, *117*, 1888. (d) Trost, B. M.; Machacek, M.; Schnaderbeck, M. J. *Org. Lett.* **2000**, *2*, 1761. (e) Trost, B. M.; Shen, H. C.; Pinkerton, A. B. *Chem.*−*Eur. J.* **2002**, *10*, 2341. (f) Trost, B. M.; Machacek, M. R. *Angew. Chem., Int. Ed.* **2002**, *41*, 4693. (g) Trost, B. M.; Machacek, M. R.; Ball, Z. T. *Org. Lett.* **2003**, *5*, 1895.

(4) For a ruthenium-catalyzed Alder−ene reaction of di- and triynes, see: Hansen, E. C.; Lee, D. *J. Am. Chem. Soc.* **2005**, *127*, 3252.

10.1021/ol800995r CCC: $40.75

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 dienylmetal 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.

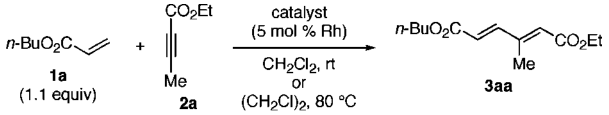
Scheme 2



Our research group has demonstrated that a cationic rhodium(I)/H_8−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)/H_8−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.

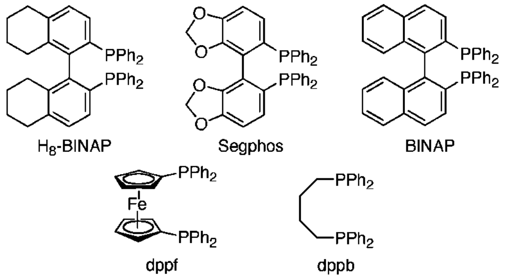
The reaction of *n*-butyl acrylate (**1a**, 1.1 equiv) with ethyl 2-butynoate (**2a**) was first examined in the presence of 5 mol % of the cationic rhodium(I)/H_8−BINAP complex as a catalyst, but no reaction was observed at room temperature (Table 1, entry 1). Fortunately, 1,3-diene **3aa** was obtained 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 H_8−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)/H_8−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).

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 CH_2Cl_2 or $(CH_2Cl)_2$ (2.0 mL) were used. [b] Isolated yield. [c] **1a**: 2 equiv.



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

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[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.

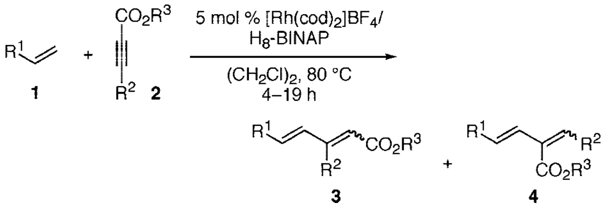
[8] Recently, ruthenium-catalyzed co-oligomerization of *N*-vinylamides with alkenes or alkynes (*electron-rich* internal alkynes) was reported, and the authors proposed the formation of a ruthenium hydride species through activation of sp^2 C−H bonds in alkenes or a dmfm ligand, see: Tsujita, H.; Ura, 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.

[10] (a) Tanaka, K.; Shirasaka, K. *Org. Lett.* **2003**, *5*, 4697. (b) Tanaka, K.; Toyoda, K.; Wada, A.; Shirasaka, K.; Hirano, M. *Chem.*−*Eur. J.* **2005**, *11*, 1145.

[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)$^+$/H$_8$−BINAP-Catalyzed Codimerization of Alkenes **1a**−**h** and Electron-Deficient Internal Alkynes **2a**−**d**[a]

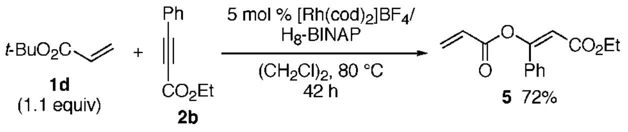


			% yield[b] (2*E*/2*Z*)	
entry	**1** (R^1, equiv)	**2** (R^2, CO$_2$R^3)	3	4
1	**1a** (CO$_2$*n*-Bu, 2.0)	**2a** (Me, CO$_2$Et)	71 (2*E*)	-[c]
2	**1a** (CO$_2$*n*-Bu, 1.1)	**2b** (Ph, CO$_2$Et)	87 (2*Z*)	
3	**1b** (CO$_2$Me, 1.1)	**2b** (Ph, CO$_2$Et)	85 (2*Z*)	
4	**1c** (CO$_2$Cy, 1.1)	**2b** (Ph, CO$_2$Et)	91 (2*Z*)	
5[d]	**1a** (CO$_2$*n*-Bu, 1.1)	**2c** (Ar[e], CO$_2$Et)	94 (2*Z*)	
6	**1a** (CO$_2$*n*-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*E*)[f]	19 (-[g])[f]
8	**1e** (Ph, 2.0)	**2b** (Ph, CO$_2$Et)	50 (2*Z*)	-[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*E*)[f]	21 (-[g])[f]
11	**1g** (*t*-Bu, 5.0)	**2a** or **2b**	0 (−)[h]	
12	**1h** (*n*-C$_6$H$_{13}$, 5.0)	**2a** or **2b**	0 (−)[h]	

[a] [Rh(cod)$_2$]BF$_4$ (0.015 mmol), H$_8$−BINAP (0.015 mmol), **1** (0.33−1.50 mmol), **2** (0.30 mmol), and (CH$_2$Cl)$_2$ (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.

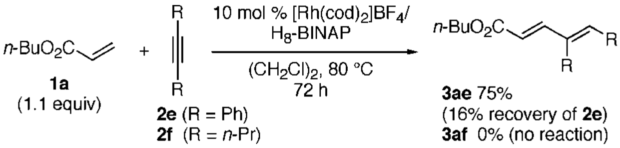
(**2c**, entry 5) could also participate in this reaction, although high catalyst loading was required. The reaction of **1a** with dimethyl acetylenedicarboxylate (**2d**, entry 6) proceeded in good yield, while moderate stereoselectivity was observed. With respect to acrylates, not only *n*-butyl acrylate (**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 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 **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]

Scheme 3

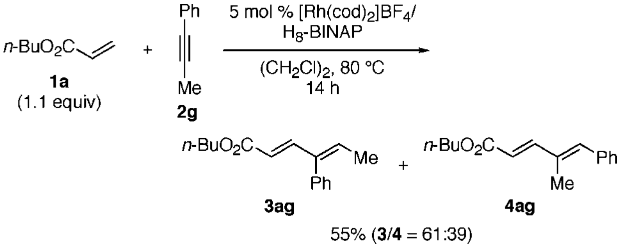


Finally, the reactions of acrylate **1a** with *electron-rich* internal alkynes were also examined. Although high catalyst loading and prolonged reaction time were required, the reaction of **1a** with diphenylacetylene (**2e**) proceeded in good yield with excellent stereoselectivity (Scheme 4). Unfortunately,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



Scheme 5



In conclusion, we have demonstrated that a cationic rhodium(I)/H$_8$−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.

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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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[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