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Cationic Rh(I)/Modified-BINAP-Catalyzed Reactions of Carbonyl Compounds with 1,6-Diynes Leading to Dienones and Ortho-Functionalized Aryl Ketones

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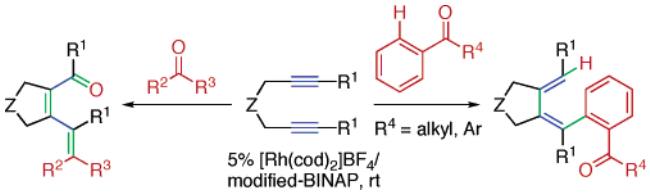
ABSTRACT



We have determined that a cationic rhodium(I)/H_8-BINAP complex catalyzes a [2 + 2 + 2] cycloaddition of both activated and unactivated carbonyl compounds with 1,6-diynes leading to dienones in high yields. On the other hand, unactivated aryl ketones react with 1,6-diynes in the presence of a cationic rhodium(I)/Segphos complex to give ortho-functionalized aryl ketones in high yields.

Transition-metal-catalyzed [2 + 2 + 2] cycloadditions of diynes with C_{sp}-heteroatom multiple bonds such as nitriles and heterocumulenes are valuable methods to construct various heterocycles.[1] On the other hand, analogous cycloadditions involving C_{sp^2}-heteroatom multiple bonds such as aldehydes and ketones have been reported in a limited number of examples.[2−10] The pioneering work for such catalytic [2 + 2 + 2] cycloadditions was reported in a Ni(0)/monophosphine-catalyzed reaction of diynes with unactivated aldehydes.[4] After this report, a Ru(II)-catalyzed reaction involving electron-deficient ketones[5,6] and a Ni(0)/imidazolylidene-catalyzed reaction involving unactivated aldehydes and ketones were reported.[7,8] A [2 + 2 + 2 + 1] cycloaddition of diynal with CO using $[Rh(cod)Cl]_2$ as a catalyst furnished an intramolecular [2 + 2 + 2] cycloaddition product as a byproduct (18−33% yield).[9] Recently, cationic Rh(I)/BIPHEP [2,2′-bis(diphenylphosphino)-1,1′-biphenyl]-catalyzed carbonyl *Z*-dienylation via multicomponent reductive coupling of aldehydes and α-ketoesters

† Department of Applied Chemistry.
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(1) For recent reviews, see: (a) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307. (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (c) Varela, J. A.; Saá, C. *Chem. Rev.* **2003**, *103*, 3787.

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(7) Tekevac, T. N.; Louie, J. *Org. Lett.* **2005**, *7*, 4037.

(8) For Ni-catalyzed [4 + 2 + 2] cycloaddition of 1,6-diynes with cyclobutanones, see: Murakami, M.; Ashida, S.; Matsuda, T. *J. Am. Chem. Soc.* **2006**, *128*, 2166.

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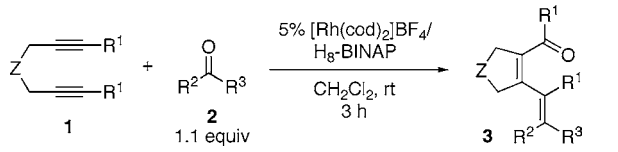
mediated by hydrogen in the presence of a catalytic amount of triphenylacetic acid, which involves carbonyl insertion into cationic rhodacyclopentadienes, was reported.[10,11] Our research group recently reported cationic Rh(I)/modified-BINAP-catalyzed [2 + 2 + 2] cycloadditions of both activated and unactivated C_{sp}-heteroatom multiple bonds with alkynes.[12] In this Communication, we describe a cationic Rh-(I)/H_8-BINAP[13] [2,2′-bis(diphenylphosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl]-catalyzed [2 + 2 + 2] cycloaddition of both activated and unactivated carbonyl compounds with 1,6-diynes leading to dienones and an unprecedented cationic Rh(I)/Segphos[14] [(4,4′-bi-1,3-benzodioxole)-5,5′-diylbis(diphenylphosphine)]-catalyzed ortho-functionalization of aryl ketones.

We first investigated the reaction of malonate-derived 1,6-diyne **1a** with diethyl ketomalonate (**2a**). After screening various Rh catalysts, we found that $[Rh(cod)_2]BF_4$/H_8-BINAP catalyzed this reaction to give dienone **3aa** in high yield via common electrocyclic ring opening[15] of the expected fused α-pyran (Table 1, entry 1). Thus, we explored the scope of

Table 1. Rh(I)$^+$/H_8-BINAP-Catalyzed Reactions of 1,6-Diynes with Carbonyl Compounds

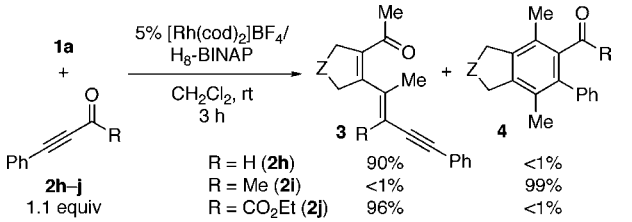


entry	R^1, Z(**1**)	R^2, R^3 (**2**)	% yield (*E*:*Z*)[a]
1[b]	Me, C(CO$_2$Me)$_2$ (**1a**)	CO$_2$Et, CO$_2$Et (**2a**)	95
2	Me, C(CO$_2$Me)$_2$ (**1a**)	CO$_2$Et, Ph (**2b**)	98 (1:2)
3[c]	Me, C(CO$_2$Me)$_2$ (**1a**)	CO$_2$Et, Me (**2c**)	99 (6:1)
4	Me, C(CO$_2$Me)$_2$ (**1a**)	H, Ph (**2d**)	97 (9:1)
5[d]	Me, C(CO$_2$Me)$_2$ (**1a**)	H, CH=CH$_2$ (**2e**)	55 (>20:1)
6[e]	Me, C(CO$_2$Me)$_2$ (**1a**)	Me, Me (**2f**)	51[f]
7	Me, C(CO$_2$Me)$_2$ (**1a**)	H, *n*-C$_7$H$_{15}$ (**2g**)	<5
8	Me, NTs (**1b**)	CO$_2$Et, CO$_2$Et (**2a**)	88
9	Et, O (**1c**)	CO$_2$Et, CO$_2$Et (**2a**)	84

[a] Isolated yield. [b] At 50 °C. [c] **2c**: 1.5 equiv. [d] **2e**: 5 equiv and reaction time of 8 h. [e] Ligand, tol-BINAP and solvent, **2f**. [f] Product exists as an equilibrium mixture of dienone (major) and ether (minor).

this process with respect to carbonyl compounds and 1,6-diynes. Both phenyl and methyl substituted ketoesters **2b** and **2c** reacted with **1a** to give the corresponding dienones in excellent yields (entries 2 and 3). Not only activated

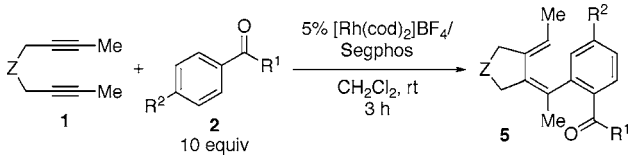
Scheme 1



carbonyl compounds but benzaldehyde (**2d**), acrolein (**2e**), and acetone (**2f**) could also participate in this reaction (entries 4−6), but the reaction of 1-octanal (**2g**) with **1a** led to a complex mixture of products presumably because of the competitive C−H bond activation of the aldehyde moiety (entry 7). With regard to 1,6-diynes, tosylamide and ether linked 1,6-diynes **1b** and **1c** could be employed for this reaction (entries 8 and 9).

As we already demonstrated that cationic Rh(I)/modified-BINAP complexes are highly effective catalysts for the [2 + 2 + 2] cycloaddition of alkynes,[16] chemoselective cycloadditions involving alkynyl carbonyl compounds are of interest. Carbonyl groups of alkynyl aldehyde **2h** and alkynyl ketoester **2j** exclusively reacted with **1a**, but the alkyne moiety exclusively reacted with **1a** in the case of alkynyl ketone **2i** (Scheme 1).

Table 2. Rh(I)$^+$/Segphos-Catalyzed Reactions of 1,6-Diynes with Aryl Ketones



entry	Z(**1**)	R^1, R^2 (**2**)	yield (%)[a]
1	C(CO$_2$Me)$_2$ (**1a**)	Me, H (**2k**)	88
2	C(CO$_2$Me)$_2$ (**1a**)	Me, MeO (**2l**)	89
3[b]	C(CO$_2$Me)$_2$ (**1a**)	Me, CF$_3$ (**2m**)	<5
4	C(CO$_2$Me)$_2$ (**1a**)	Et, H (**2n**)	94
5[b]	C(CO$_2$Me)$_2$ (**1a**)	*i*-Pr, H (**2o**)	82
6	C(CO$_2$Me)$_2$ (**1a**)	Ph, H (**2p**)	97
7	NTs (**1b**)	Me, H (**2k**)	84
8[c]	O (**1d**)	Me, MeO (**2l**)	69

[a] Isolated yield. [b] At 80 °C. [c] At 15 °C.

The present catalytic system enables reactions involving unactivated aliphatic ketone **2f**, so reactions involving

(11) For examples of carbonyl insertion into a Rh−C bond, see: (a) Krug, C.; Hartwig, J. F. *J. Am. Chem. Soc*. **2002**, *124*, 1674. (b) Fujii, T.; Koike, T.; Mori, A.; Osakada, K. *Synlett* **2002**, 298.

(12) (a) Tanaka, K.; Wada, A.; Noguchi, K. *Org. Lett*. **2005**, *7*, 4737. (b) Tanaka, K.; Wada, A.; Noguchi, K. *Org. Lett.* **2006**, *8*, 907. (c) Tanaka, K.; Suzuki, N.; Nishida, G. *Eur. J. Org. Chem*. **2006**, 3917. (d) Wada, A.; Noguchi, K.; Hirano, M.; Tanaka, K. *Org. Lett.* **2007**, *9*, 1295.

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

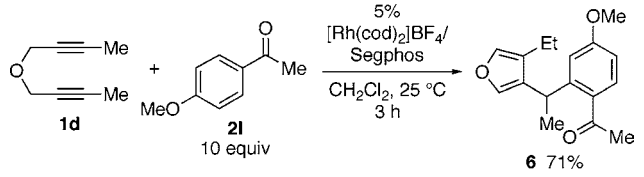
(14) Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal*. **2001**, *343*, 264.

(15) Marvell, E. N.; Caple, G.; Gosink, T. A.; Zimmer, G. *J. Am. Chem. Soc.* **1966**, *88*, 619.

(16) (a) Tanaka, K.; Shirasaka, K. *Org. Lett*. **2003**, *5*, 4697. (b) Tanaka, K.; Nishida, G.; Wada, A.; Noguchi, K. *Angew. Chem., Int. Ed*. **2004**, *43*, 6510. (c) Tanaka, K.; Toyoda, K.; Wada, A.; Shirasaka, K.; Hirano, M. *Chem.—Eur. J*. **2005**, *11*, 1145. (d) Tanaka, K.; Nishida, G.; Ogino, M.; Hirano, M.; Noguchi, K. *Org. Lett*. **2005**, *7*, 3119. (e) Nishida, G.; Suzuki, N.; Noguchi, K.; Tanaka, K. *Org. Lett*. **2006**, *8*, 3489. (f) Tanaka, K.; Takeishi, K.; Noguchi, K. *J. Am. Chem. Soc*. **2006**, *128*, 4586. (g) Tanaka, K.; Sagae, H.; Toyoda, K.; Noguchi, K; Hirano, M. *J. Am. Chem. Soc*. **2007**, *129*, 1522.

unactivated aryl ketones were also investigated (Table 2). Interestingly, unprecedented ortho-functionalization of acetophenone (**2k**) with **1a** proceeded in good yield. In this transformation, Segphos is more effective than H_8-BINAP, and the ortho-functionalized aryl ketone was obtained in 88% yield (entry 1). Importantly, although para substitution of the aromatic ring (R^2) with an electron-donating group (**2l**) did not affect the yield of product (entry 2), an electron-withdrawing group (**2m**) completely shut down the reaction (entry 3). The reactions involving both alkyl and aryl substituted (R^1) aryl ketones **2n**−**p** and tosylamide-derived 1,6-diyne **1b** proceeded in high yields (entries 4−7). In the case of ether linked 1,6-diyne **1d**, the reaction temperature is critical. Diene **5** was obtained at 15 °C (entry 8), but the corresponding double bond isomerization product **6** was obtained at 25 °C (Scheme 2).[17] The structure of ortho-

Scheme 2



functionalized aryl ketone **5bk** was unambiguously determined by X-ray crystallographic analysis (Figure 1).

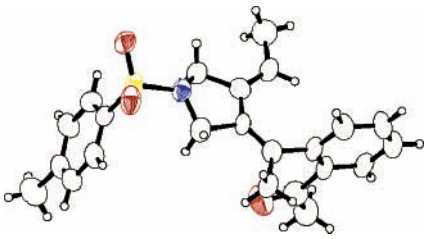
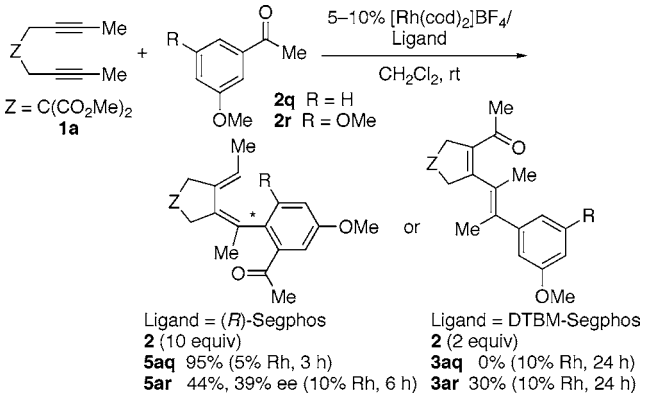


Figure 1. ORTEP diagram of **5bk**.

The regio- and enantioselectivity of this reaction was also investigated (Scheme 3). 3-Methoxyacetophenone (**2q**) reacted with **1a** at the para position to give **5aq** as a single regioisomer.[18] The reaction of 3,5-dimethoxyacetophenone (**2r**) with **1a** furnished axially chiral aryl ketone **5ar** with moderate enantioselectivity.[18] Interestingly, the use of sterically demanding DTBM-Segphos [(4,4′-bi-1,3-benzodioxole)-5,5′-diylbis{di(3,5-di-*tert*-butyl-4-methoxyphenyl)-phosphine}][14] as a ligand promoted the dienone formation from **1a** and **2r**.

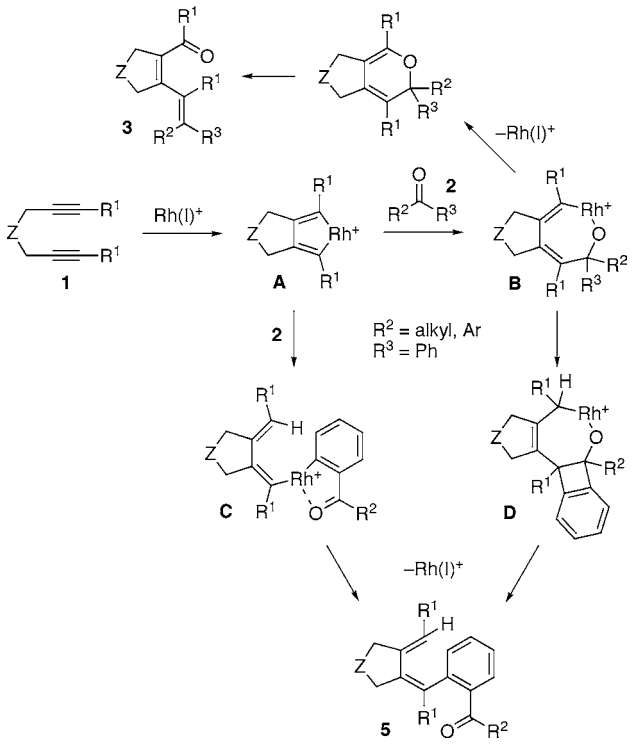
Scheme 4 depicts a possible mechanism of these reactions. Rhodacyclopentadiene **A**, generated through the reaction of

Scheme 3



1,6-diyne **1** with rhodium, reacts with carbonyl compound **2** to form rhodacycle **B**. Reductive elimination of rhodium followed by electrocyclic ring opening furnishes dienone **3**. Although the mechanism remains unknown in the case of

Scheme 4



unactivated aryl ketones, aryl C−H bond activation or electrophilic aromatic substitution with Rh(III) complex **A** may furnish intermediate **C** followed by reductive elimination to give ortho-functionalized aryl ketone **5**.[19−21] Alternatively,

(17) The use of (*R*)-Segphos as a ligand furnished **6** with <10% ee.

(18) For Rh-catalyzed C−H arylation of anisole and 1,3-dimethoxybenzene with an aryl iodide, see: Yanagisawa, S.; Sudo, T.; Noyori, R.; Itami, K. *J. Am. Chem. Soc*. **2006**, *128*, 11748.

(19) For recent reviews of transition-metal-catalyzed C−H bond activation, see: (a) Dyker, G., Ed. *Handbook of C-H Transformations*; Wiley-VCH: Weinheim, Germany, 2005. (b) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (c) Kakiuchi, F.; Chatani, N. *Adv. Synth. Catal*. **2003**, *345*, 1077. (d) Miura, M.; Nomura, M. *Top. Curr. Chem*. **2002**, *219*, 211.

ortho-substitution may proceed through intermediate **D**. Monoalkynes failed to react with acetophenone (**2k**) in the presence of 5% $[Rh(cod)_2]BF_4$/Segphos, so direct *o*-C−H bond activation of aryl ketone **2** may not be included in the formation of **5**.[22]

In conclusion, we have developed a cationic Rh(I)/H_8-BINAP-catalyzed [2 + 2 + 2] cycloaddition of 1,6-diynes with both activated and unactivated carbonyl compounds leading to dienones and an unprecedented cationic Rh(I)/Segphos-catalyzed ortho-functionalization of aryl ketones. Detailed mechanistic studies and scope expansion are currently underway in our laboratory.

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

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(21) Aryl C−H activation, electrophilic aromatic substitution, and carbopalladation with a Pd(II) complex are proposed in the Pd-catalyzed direct *o*-C−H functionalization of α-chloroacetanilides: Hennessy, E. J.; Buchwald, S. L. *J. Am. Chem. Soc*. **2003**, *125*, 12084.

(22) For Ru-catalyzed direct *o*-C−H activation of aryl ketones, see: (a) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529. (b) Kakiuchi, F.; Murai, S. *Acc. Chem. Res*. **2002**, *35*, 826.