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Rh-Catalyzed [4 + 2] Carbocyclization of Vinylarylaldehydes with Alkenes and Alkynes Leading to Substituted Tetralones and 1-Naphthols

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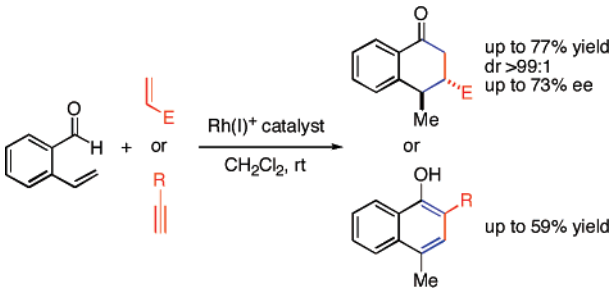
ABSTRACT



Regio-, diastereo-, and enantioselective intermolecular [4 + 2] carbocyclizations of vinylarylaldehydes with alkenes and alkynes leading to substituted tetralones and 1-naphthols have been developed by using a cationic rhodium(I)/dppb or dppp complex as a catalyst.

Carbocyclizations are valuable tools for the construction of complex carbocycles.[1] In particular, [4 + 2] carbocyclizations of five-membered acylmetal intermediates, generated through reactions of transition metal carbonyl complexes with alkynes[2,3] and carbon−carbon bond cleavage of cyclobutenones[4,5] or cyclobutanones,[6,7] with alkenes or alkynes are useful methods for the synthesis of six-membered carbonyl compounds. An alternative, more convenient generation of five-membered acylmetal intermediates was realized by intramolecular cis addition of a rhodium acyl hydride to a metal-bound triple bond of 4-alkynals.[8−10] These intermediates cleanly react with alkynes,[8] alkenes,[9] and isocyanates[10] to give substituted six-membered carbonyl compounds in

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(5) For synthesis of five-membered rings by rhodium-catalyzed [3 + 2] cycloaddition of cyclopropenones with alkynes, see: Wender, P. A.; Paxton, T. J.; Williams, T. J. *J. Am. Chem. Soc.* **2006**, *128*, 14814.

(6) Murakami, M.; Itahashi, T.; Ito, Y. *J. Am. Chem. Soc.* **2002**, *124*, 13976.

(7) For synthesis of eight-membered rings from cyclobutanones, see: (a) Wender, P. A.; Correa, A. G.; Sato, Y.; Sun, R. *J. Am. Chem. Soc.* **2000**, *122*, 7815. (b) Matsuda, T.; Fujimoto, A.; Ishibashi, M.; Murakami, M. *Chem. Lett.* **2004**, *33*, 876.

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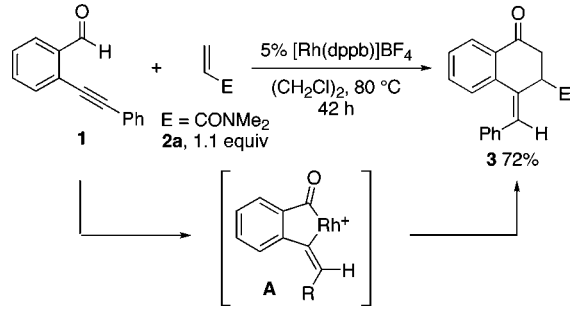
high yields with high regio- and enantioselectivity. We have demonstrated that benzofused five-membered acylrhodium intermediates, generated from 2-alkynylbenzaldehydes, react with alkenes to give tetralone derivatives in higher yield than those obtained from 4-pentynal derivatives.[9] This result prompted our investigation into [4 + 2] carbocyclizations using 2-alkenylbenzaldehydes instead of 2-alkynylbenzaldehydes. In this Letter, we have established that a cationic rhodium(I)/dppb or dppp complex catalyzes intermolecular [4 + 2] carbocyclizations of vinylarylaldehydes with alkenes and alkynes, leading to substituted tetralones and 1-naphthols, respectively.

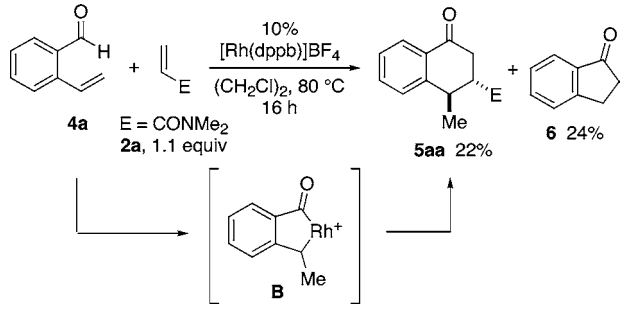
In our previous report, the reaction of 2-alkynylbenzaldehyde **1** with *N*,*N*-dimethylacrylamide (**2a**) in the presence of 5% [Rh(dppb)]BF_4 [dppb = 1,4-bis(diphenylphosphino)-butane] at 80 °C furnished the corresponding tetralone **3** in good yield (Scheme 1).[9] Under similar reaction conditions,

Scheme 1



2-vinylbenzaldehyde (**4a**) reacted with **2a** to give 3,4-disubstituted tetralone **5aa** in 22% yield as a single diastereomer along with indanone (**6**) (Scheme 2).[11]

Scheme 2



The intermolecular [4 + 2] carbocyclization of **4a** with **2a** was examined using various bidentate phosphine ligands

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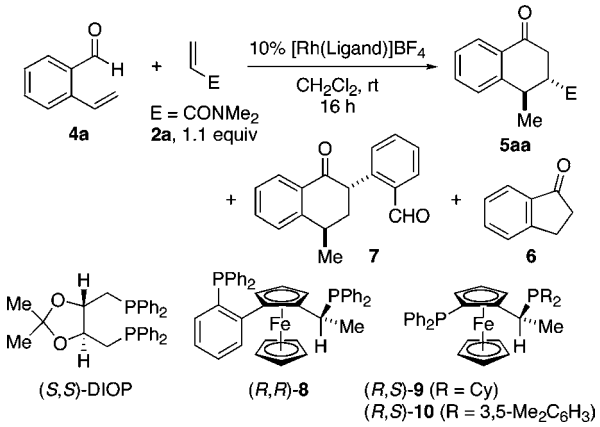
(11) Morehead and co-workers reported that this dimer formation can be decreased by decreasing the concentration of the aldehyde; see: Kundu, K.; McCullagh, J. V.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **2005**, *127*, 16042.

Table 1. Screening of Ligands for Rh-Catalyzed [4 + 2] Carbocyclization of 2-Vinylbenzaldehyde (**4a**) with *N*,*N*-Dimethylacrylamide (**2a**)[a]



entry	ligand	conversion (%)[b]	yield (%)[b] 5aa	7	6	ee (%) 5aa
1	dppb	100	78	0	15	
2	dppp	100	74	0	18	
3	dppe	100	30	20	22	
4	dppf	39	0	0	8	
5	(*R*)-BINAP	52	0	0	40	
6	(*S*,*S*)-DIOP	29	16	13	0	
7	(*R*,*R*)-**8**	23	<1	22	0	
8	(*R*,*S*)-**9**	100	46	54	0	59
9	(*R*,*S*)-**10**	94	89	4	0	64

[a] [Rh(ligand)]BF_4 (0.010 mmol), **4a** (0.10 mmol), **2a** (0.11 mmol), and CH_2Cl_2 (1.0 mL) were used. [b] Determined by ^1H NMR.

to improve the yield of tetralone **5aa** (Table 1). The study revealed that the use of dppb or dppp [1,3-bis(diphenylphosphino)propane] as a ligand at room temperature furnished **5aa** in high yield with perfect regio- and diastereoselectivity (entries 1 and 2). On the other hand, the use of dppe [1,2-bis(diphenylphosphino)ethane] significantly lowered the yield of **5aa** as a result of the formation of 2,4-disubstituted tetralone **7** through an intermolecular homo-[4 + 2] carbocyclization of **4a** (entry 3). Recently, Morehead and coworkers reported that the reaction of **4a** in the presence of a catalytic amount of [Rh(dppe)]ClO_4 furnished **6** along with the same dimer **7**.[11] In the cases of dppf [1,1′-bis(diphenylphosphino)ferrocene] and BINAP, **6** was obtained as a major product (entries 4 and 5). Then the enantioselective [4 + 2] carbocyclization of **4a** with **2a** was examined using various chiral bidentate phosphine ligands, which have large P−M−P natural bite angles. The use of (*S*,*S*)-DIOP and the Walphos ligand [(*R*,*R*)-**8**] was ineffective (entries 6 and 7), but we were pleased to find that the use of the Josiphos ligand PPF-Pcy_2 [(*R*,*S*)-**9**] furnished **5aa** in moderate yield and ee (entry 8). Further improved yield and ee were achieved by using the Josiphos ligand PPF-$Pxyl_2$ [(*R*,*S*)-**10**] (entry 9).

We explored the scope of this process with respect to both aldehydes and alkenes by employing the above optimal reaction conditions (Table 2). Not only *N*,*N*-dimethylacrylamide (**2a**, entry 1) but sterically demanding (**2b**, entry 2)

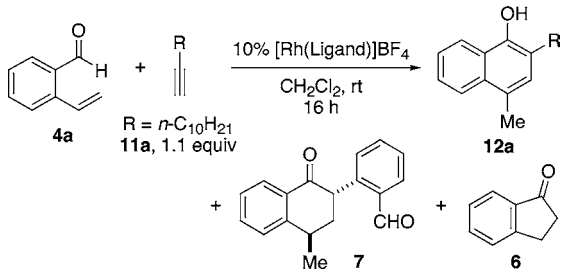
Table 2. Rh-Catalyzed Regio-, Diastereo-, and Enantioselective [4 + 2] Carbocyclization of Vinylarylaldehydes **4a**−**c** with Electron-Deficient Alkenes **2a**−**d**[a]

entry	aldehyde	alkene	product	yield (%)[b]	ee (%)
1	**4a**	**2a** E = $CONMe_2$	**5aa**	77	64
2[c]	**4a**	**2b** E = $CONi\text{-}Pr_2$	**5ab**	65	66
3	**4a**	**2c** E = CON	**5ac**	65	68
4[d]	**4a**	**2d** E = $CO_2t\text{-}Bu$	**5ad**	70	73
5	**4b**	**2a** E = $CONMe_2$	**5ba**	64	46
6	**4c**	**2a** E = $CONMe_2$	**5ca**	<10	–

[a] Reactions were conducted using [Rh((*R*,*S*)-**10**)]BF_4 (0.030 mmol), **4** (0.30 mmol), **2** (0.33 mmol, 1.1 equiv), and CH_2Cl_2 (3.0 mL) at rt for 24−48 h. [b] Isolated yield. [c] Temperature = 80 °C and solvent = $(CH_2Cl)_2$. [d] **2d**, 15 mmol (50 equiv).

or cyclic (**2c**, entry 3) *N*,*N*-dialkylacrylamides could also participate in this reaction. Acrylate **2d** reacted with **4a** to give the corresponding tetralone **5ad** in good yield with improved ee, although a large excess (50 equiv) of **2d** was required, presumably due to the low coordination ability of **2d** (entry 4).[12] With respect to aldehydes,[13] 2-vinyl-1-naphthaldehyde (**4b**) reacted with **2a** to give the corresponding tetralone **5ba** in good yield, although enantioselectivity decreased (entry 5). Unfortunately, the reaction of 1-vinyl-2-naphthaldehyde (**4c**) and **2a** furnished the corresponding tetralone **5ca** in <10% yield (entry 6).

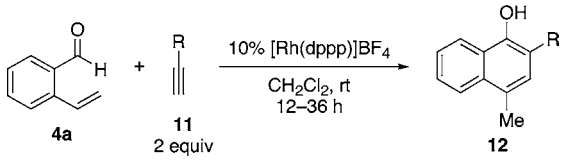
Table 3. Screening of Ligands for Rh-Catalyzed [4 + 2] Carbocyclization of 2-Vinylbenzaldehyde (**4a**) with 1-Dodecyne (**11a**)[a]



entry	ligand	conversion (%)[b]	yield (%)[b] **12a**	**7**	**6**
1	dppb	96	18	0	38
2	dppp	100	63	15	21
3	dppe	100	11	60	12
4	dppf	39	0	0	12
5	BINAP	100	0	0	71

[a] [Rh(ligand)]BF_4 (0.010 mmol), **4a** (0.10 mmol), **11a** (0.11 mmol), and CH_2Cl_2 (1.0 mL) were used. [b] Determined by ^1H NMR.

Table 4. Rh-Catalyzed Regioselective [4 + 2] Carbocyclization of 2-Vinylbenzaldehyde (**4a**) with Terminal Alkynes **11a**−**f**[a]

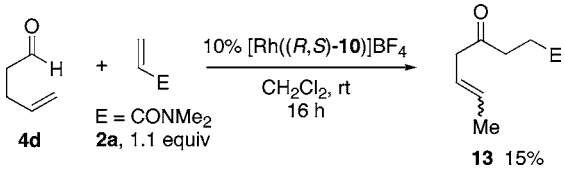


entry	**11**	R	**12**	yield (%)[b]
1	**11a**	$n\text{-}C_{10}H_{21}$	**12a**	52
2	**11b**	$Cl(CH_2)_3$	**12b**	59
3	**11c**	Bn	**12c**	55
4	**11d**	Ph	**12d**	51
5	**11e**	$4\text{-}F_3CC_6H_4$	**12e**	55
6	**11f**	$2\text{-}MeOC_6H_4$	**12f**	48

[a] [Rh(dppp)]BF_4 (0.030 mmol), **4a** (0.30 mmol), **11** (0.60 mmol), and CH_2Cl_2 (1.0 mL) were used. [b] Isolated yield.

Next, the intermolecular [4 + 2] carbocyclization of 2-vinylbenzaldehyde (**4a**) with alkynes was investigated. In the presence of 10% [Rh(dppb)]BF_4 at room temperature, terminal alkyne **11a** reacted with **4a** to give 2,4-disubstituted 1-naphthol **12a** in low yield (Table 3, entry 1).[14] Fortunately, the use of dppp as a ligand dramatically improved the yield of **12a** (entry 2). Like the reaction of **4a** with alkene **2a**, the use of dppe furnished dimer **7** as a major product, and that of dppf and BINAP furnished indanone (**6**) as a major product (entries 3−5).

Scheme 3

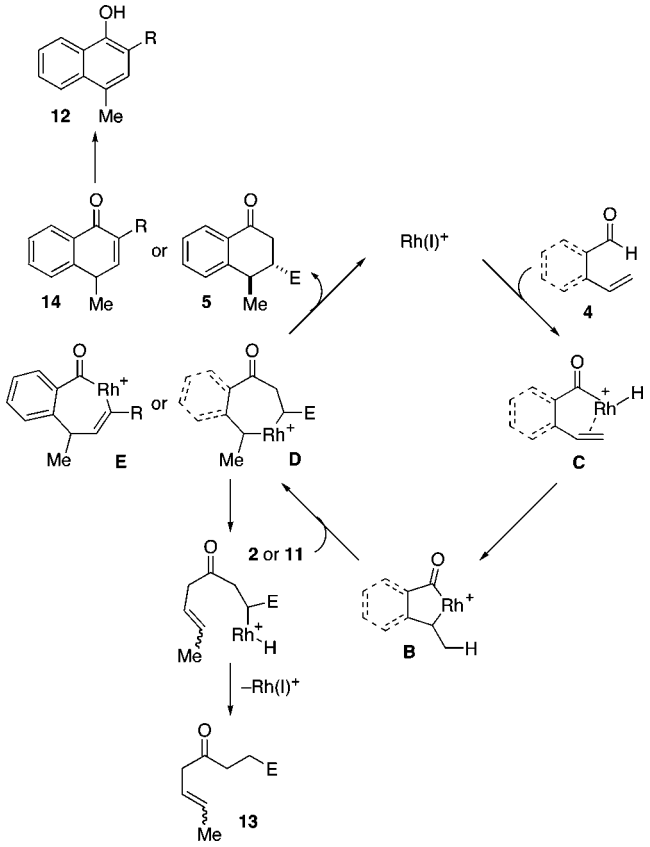


A series of terminal alkynes **11a**−**f** was subjected to the above optimal reaction conditions (Table 4).[15] The reactions of alkyl-substituted terminal alkynes **11a**−**c** with **4a** afforded the corresponding 1-naphthols in good yield as a single

(12) Electron-rich alkenes such as styrene, and substituted electron-deficient alkenes such as *N*,*N*-dimethylmethacrylamide and 1-pyrrolidinyl-2-buten-1-one failed to react with **4a**.

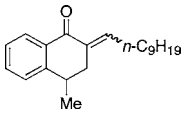
(13) The reaction of a substituted vinylbenzaldehyde such as 2-(1-phenylvinyl)benzaldehyde did not furnish the corresponding carbocyclization product.

Scheme 4



regioisomer (entries 1−3). Not only alkyl-substituted terminal alkynes, but phenylacetylene (**11d**) could also participate in this reaction (entry 4). Electronic and steric effects of the substituents on the aromatic rings on yields of the corresponding carbocyclization products appear to be small, as indicated by entries 5 and 6.

(14) 4-Methyl-2-alkylidenetetralone was generated as a major product (ca. 39% NMR yield), although this compound could not be isolated in pure form by silica gel chromatography.



The reaction of 4-pentenal (**4d**) was also investigated. In the presence of 10% [Rh((*R*,*S*)-**10**)]BF_4 at room temperature, **4d** reacted with alkene **2a** to give acyclic alkenyl ketone **13** in 15% yield (Scheme 3). The reaction of **4d** with alkyne **11d** in the presence of 10% [Rh(dppp)]BF_4 at room temperature led to a complex mixture of products.

A possible mechanism for these [4 + 2] carbocyclizations is shown in Scheme 4. The rhodium catalyst oxidatively inserts into the aldehyde C−H bond, providing a rhodium acyl hydride **C**. Cis addition of the rhodium hydride to the metal-bound double bond then provides the five-membered acylrhodium intermediate **B**. Complexation of the alkene or alkyne followed by insertion forms metallacycle **D** or **E**. Reductive elimination regenerates the Rh catalyst and furnishes tetralone **5** or enone **14**, which is isomerized to 1-naphthol **12**. On the other hand, β-hydride elimination from metallacycle **D** can furnish the acyclic alkenyl ketone **13**.

In conclusion, we have developed a cationic rhodium(I)/dppb or dppp complex-catalyzed regio-, diastereo-, and enantioselective intermolecular [4 + 2] carbocyclizations of vinylarylaldehydes with alkenes and alkynes leading to substituted tetralones and 1-naphthols. Expanding the scope and detailed mechanistic studies are currently underway in our laboratory.

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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) Both electron-rich and electron-deficient internal alkynes such as 4-octyne and ethyl 2-butynoate failed to react with **4a**. Synthesis of substituted phenols by [4 + 2] annulation of cyclobutenones with alkynes or alkenes, see: (a) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1991**, *113*, 2771. (b) Kondo, T.; Niimi, M.; Nomura, M.; Wada, K.; Mitsudo, T. *Tetrahedron Lett.* **2007**, *48*, 2837.