Homogeneous Catalysis

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Rhodium-Catalyzed Cross-Cyclotrimerization and Dimerization of Allenes with Alkynes

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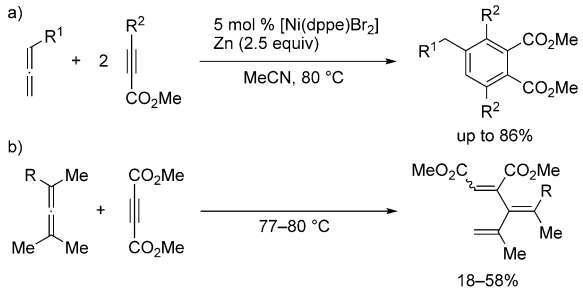
Abstract: *It has been established that a cationic rhodium(I)/binap complex catalyzes the cross-cyclotrimerization of two molecules of a monosubstituted allene with one molecule of a functionalized alkyne to give 3,6-dialkylidenecyclohex-1-enes. In contrast, the reactions involving di- or trisubstituted allenes and/or unfunctionalized alkynes afforded cross-dimerization products, substituted dendralenes, through β-hydrogen elimination from the corresponding rhodacycles.*

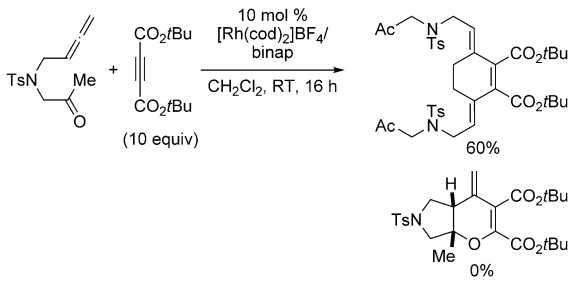
Transition-metal-catalyzed intermolecular cross-cyclotrimerization and cross-dimerization reactions of alkynes with alkenes are efficient and atom-economical methods for the synthesis of substituted six-membered carbocycles and dienes, respectively.[1] In contrast, similar transformations using allenes in place of alkenes have been reported in a limited number of examples.[2] As examples of the cross-cyclotrimerization of alkynes with allenes,[3–5] the nickel-catalyzed reactions of one molecule of a monosubstituted allene with two molecules of an electron-deficient internal alkyne followed by aromatization through olefin isomerization, which affords the corresponding pentasubstituted benzenes, has been reported (Scheme 1 a).[3a] However, the usable alkynes are limited to electron-deficient alkynoates, and electron-rich alkynes cannot be employed.[3a] Furthermore, a selective and general method for the cross-cyclotrimerization of two molecules of an allene and one molecule of an alkyne has not been reported to date.[5] As examples of the cross-dimerization of allenes with alkynes, thermal reactions giving substituted dendralenes have been reported (Scheme 1 b).[6–8] However, the usable alkynes are limited to electron-deficient dimethyl acetylenedicarboxylate and (trifluoromethyl)acetylene.[6] Herein, we disclose the cross-cyclotrimerization of two molecules of a monosubstituted allene with functionalized alkynes, and cross-dimerization of di- or trisubstituted allenes with both functionalized and unfunctionalized alkynes.



Scheme 1. Previously reported cross-cyclotrimerization and cross-dimerization of allenes with alkynes. dppe = 1,2-bis(diphenylphosphino)-ethane.

Recently, our research group reported the rhodium-catalyzed enantioselective [2+2+2] cycloaddition of tosylamide-linked 5-allenals and 5-allenones with internal alkynes.[9] In this study, we found that the reaction of the tosylamide-linked 5-allenone with di-*tert*-butylacetylenedicarboxylate in the presence of a cationic rhodium(I)/binap catalyst does not afford the expected [2+2+2] cycloaddition product, but instead delivers an unexpected cross-cyclotrimerization product, 3,6-dialkylidenecyclohex-1-ene derivative, in good yield (Scheme 2).

Thus, we examined the reaction of the monosubstituted allene **1a** with di-*tert*-butylacetylenedicarboxylate (**2a**) in the presence of the same rhodium catalyst (Table 1). Pleasingly, the cross-cyclotrimerization proceeded at room temperature to give the corresponding 3,6-dialkylidenecyclohex-1-ene **3aa**, although the regioisomer **4aa** was generated as a minor product (entry 1). The effect of biaryl bis(phosphine) ligands was then examined (entries 1–5). Increasing the dihedral angle of ligands improved the ratio of **3aa** to **4aa** (dihedral angle:[10] H_8-binap > binap > segphos, ratio of **3aa** to **4aa**: H_8-binap > binap > segphos). Increasing the steric



Scheme 2. Unexpected discovery of rhodium-catalyzed cross-cyclotrimerization of an allenone with di-*tert*-butylacetylenedicarboxylate. cod = 1,5-cyclooctadiene.

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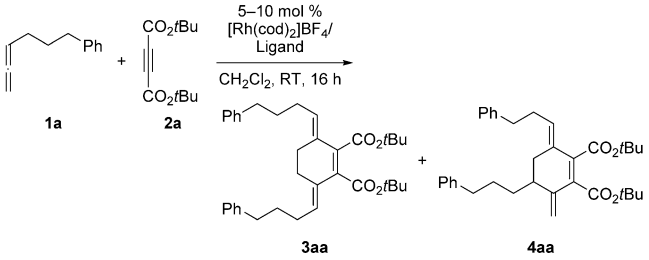
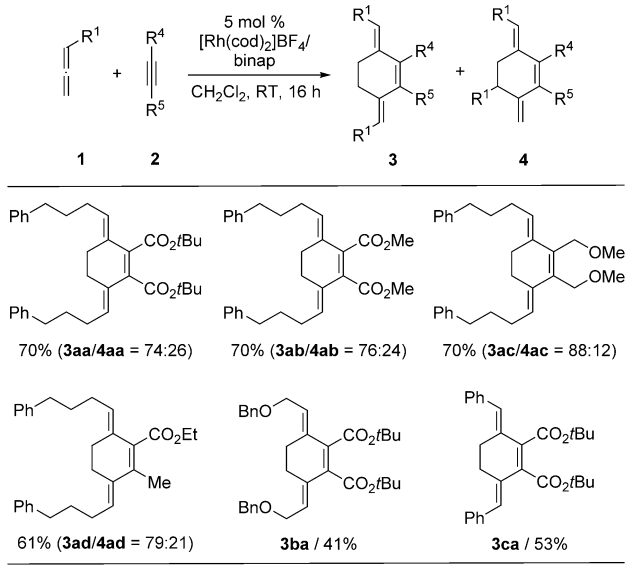
Table 1: Optimization of reaction conditions for rhodium-catalyzed cross-cyclotrimerization of **1a** with **2a**.[a]



Entry	Ligand	Catalyst (mol%)	**1a**/**2a**	Conv [%]	Yield [%][b] (**3aa**/**4aa**)
1	binap	10	1:1	>99	68 (74:26)
2	segphos	10	1:1	>99	69 (71:29)
3	H_8-binap	10	1:1	>99	52 (83:17)
4	tol-binap	10	1:1	>99	51 (79:21)
5	xyl-binap	10	1:1	46	18 (85:15)
6[c]	binap	10	1:2	>99	57 (74:26)
7[d]	binap	10	2:1	>99	47 (74:26)
8[e]	binap	10	4:1	>99	45 (74:26)
9[f]	binap	5	1:1	>99	70 (74:26)

[a] $[Rh(cod)_2]BF_4$ (0.010 mmol), ligand (0.010 mmol), **1a** (0.10 mmol), **2a** (0.10 mmol), and CH_2Cl_2 (2.0 mL) were used. [b] Yield of isolated product. [c] **1a** (0.10 mmol) and **2a** (0.20 mmol) were used. [d] **1a** (0.10 mmol) and **2a** (0.05 mmol) were used. [e] **1a** (0.20 mmol) and **2a** (0.050 mmol) were used. [f] $[Rh(cod)_2]BF_4$ (0.010 mmol), ligand (0.010 mmol), **1a** (0.20 mmol), **2a** (0.20 mmol), and CH_2Cl_2 (2.0 mL) were used. Binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, H_8-binap = 2,2′-bis(diphenylphospino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, segphos = 5,5′-bis(diphenylphosphino)-4,4′-bi-1,3-benzodioxole, tol-binap = 2,2′-bis[di(2,2′-*p*-tolyl)phosphino]-1,1′-binaphthyl, xyl-binap = 2,2′-bis[di(3,5-xylyl)phosphino]-1,1′-binaphthyl.

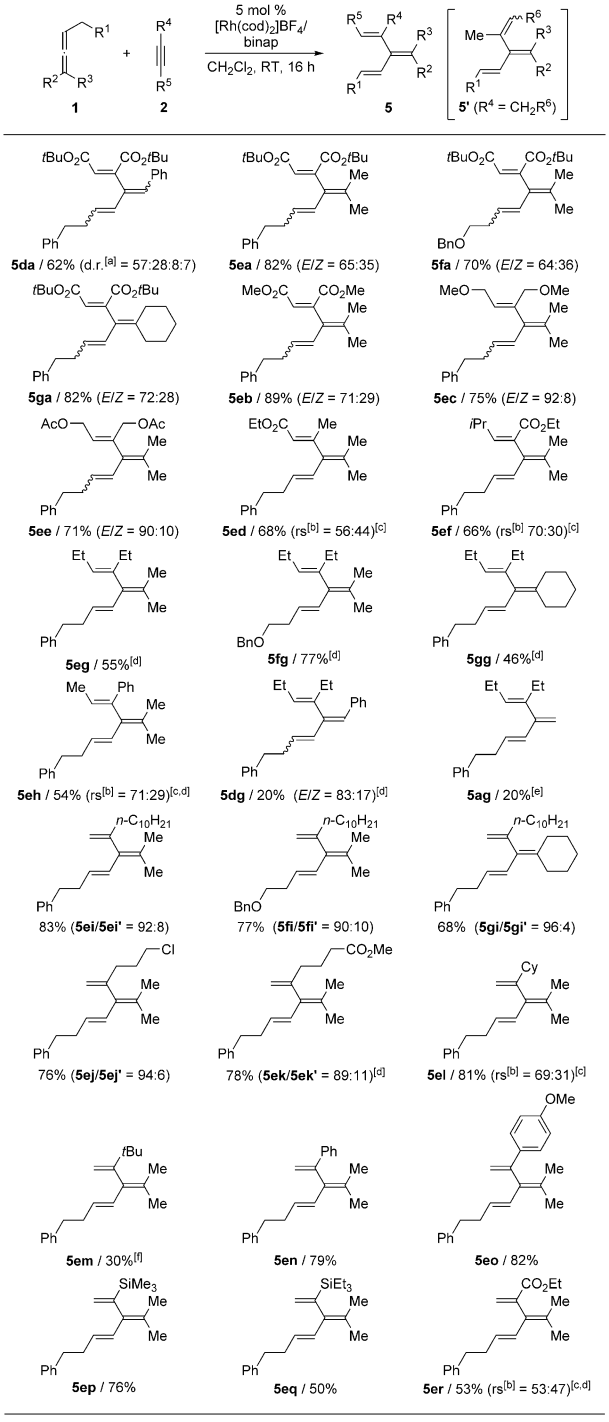


Scheme 3. Rhodium-catalyzed cross-cyclotrimerization of allenes (**1**) with functionalized alkynes (**2**). $[Rh(cod)_2]BF_4$ (0.010 mmol), binap (0.010 mmol), **1** (0.20 mmol), **2** (0.20 mmol), and CH_2Cl_2 (2.0 mL) were used. The cited yields are of the isolated products.

bulk of aryl groups on the phosphorus improved the ratio of **3aa** to **4aa** (steric bulk: xyl-binap > tol-binap > binap, ratio of **3aa** to **4aa**: xyl-binap > tol-binap > binap). The use of binap afforded **3aa** in the highest yield, although the ratio of **3aa** to **4aa** was moderate (entry 1). The ratio of **1a** to **2a** was then examined (entries 1 and 6–8), and revealed that a 1:1 ratio afforded **3aa**/**4aa** in the highest yield (entry 1). In this reaction, the homo-cyclotrimerization of **2a** and the cross-cyclotrimerization of one molecule of **1a** with two molecules of **2a** were not observed. Finally, the catalyst loading could be reduced to 5 mol% without erosion of the product yield (entry 9).

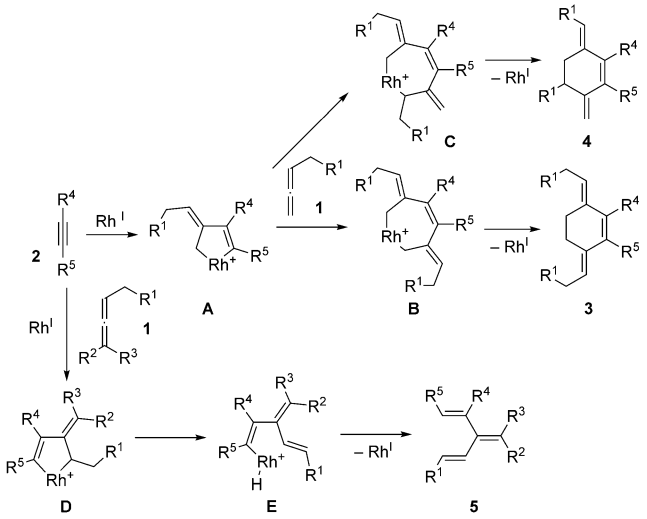
The substrate scope of the rhodium-catalyzed cross-cyclotrimerization is shown in Scheme 3. With respect to alkynes, both electron-deficient and electron-rich symmetrical alkynes (**2a-c**) participated in this reaction to give the corresponding cyclohexenes **3aa–ac**/**4aa–ac** in good yields. Not only symmetrical alkynes but also the unsymmetrical alkyne **2d** reacted with **1a** to give the corresponding cyclohexenes **3ad**/**4ad** in good yield. Unfortunately, terminal alkynes could not be employed because of their rapid homo-cyclotrimerization. With respect to allenes, not only the aliphatic allene **1a** but also functionalized and aromatic ones (**1b**,**c**) reacted with **2a** to give the corresponding cyclohexenes **3ba** and **3ca** in moderate yields. Although the reason is not clear, the reactions employing allenes **1b**,**c** did not afford the regioisomers **4** at all.

Interestingly, the reaction of the disubstituted allene **1d** with **2a** in the presence of the same rhodium catalyst did not afford a cyclotrimerization product, but instead the dimerization product, the tetrasubstituted dendralene[11] **5da**, in good yield (Scheme 4). The use of the trisubstituted allene **1e** significantly increased the yield of the corresponding **5ea**. The substrate scope of this cross-dimerization was then examined. With respect to allenes, not only **1e** but also the functionalized **1f** reacted with **2a** to give the corresponding dendralene **5fa** in good yield. Not only dimethyl but also the cyclohexyl derivative **1g** could be employed. With respect to alkynes, both electron-deficient and electron-rich symmetrical alkynes (**2a–c** and **2e**) participated in this reaction to give the corresponding dendralenes in high yields. Unsymmetrical alkynes (**2d** and **2f**) could also be employed, although regioselectivity was moderate. It is worthy of note that the unfunctionalized alkynes **2g** and **2h** smoothly react with both functionalized and unfunctionalized trisubstituted allenes (**1e–g**) to give the corresponding dendralenes in moderate to good yields. Furthermore, the di- and monosubstituted unfunctionalized allenes (**1d**,**a**) were capable of reacting with **2g**, although the product yields were low. Not only internal alkynes but also terminal alkynes could be employed for this cross-dimerization with allenes. 1-Dodecyne (**2i**) reacted with **1e–g** to give the corresponding dendralenes **5ei–gi** in high yields. Not only 1-dodecyne (**2i**) but also a variety of alkyl and aryl acetylenes (**2j–o**) could be employed, although olefin isomerization products (**5′**) were generated in small amounts when employing primary-alkyl-substituted alkynes (**1i–k**). In addition, the silyl acetylenes **2p**,**q** and ethyl propiolate (**2r**) were capable of reacting with **1e** to give the corresponding dendralenes **5ep–er**.



Scheme 4. Rhodium-catalyzed cross-dimerization of allenes (**1**) with internal alkynes (**2**). $[Rh(cod)_2]BF_4$ (0.010 mmol), binap (0.010 mmol), **1** (0.20 mmol), **2** (0.20 mmol), and CH_2Cl_2 (2.0 mL) were used. The cited yields are of the isolated products. [a] d.r. = diastereomer ratio. See the Supporting Information for details. [b] rs = regioselectivity. [c] Major regioisomer is shown. [d] **2** (0.60 mmol) was used. [e] **1** (0.10 mmol) and **2** (0.10 mmol) were used. [f] **2** (0.30 mmol) was used.

Possible reaction mechanisms for the formation of the 3,6-dialkylidenecyclohex-1-enes **3** and **4**, and dendralene **5** from **1** and **2** are shown in Scheme 5. The reaction of **1** and **2** with



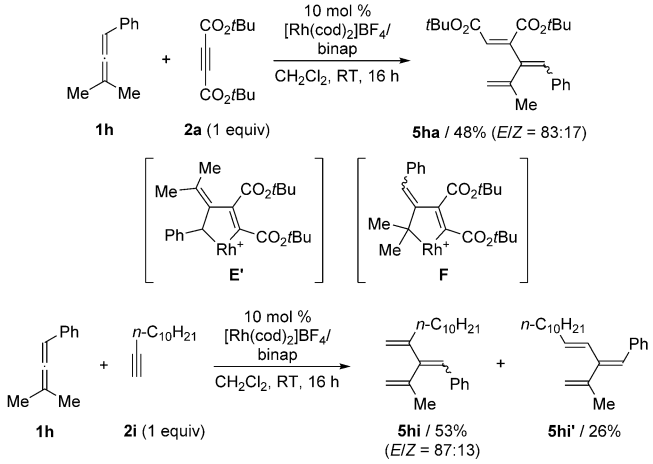
Scheme 5. Possible mechanisms for cross-cyclotrimerization and dimerization.

rhodium generates the rhodacyclopentene **A**. Insertion of another molecule of **1** into **A** generates the intermediate **B**, and then reductive elimination furnishes **3**. The minor regioisomer **4** may be generated from the intermediate **C** through insertion of the internal double bond of **1** into **A**. As **4ad** was obtained as a single regioisomer, the formation of **A** may be regioselective for the unsymmetrical alkyne **2d** (R^4 = CO_2Et, R^5 = Me). In contrast, the reaction of a di- or trisubstituted allene (**1**) and **2** with rhodium generates the rhodacyclopentene **D**. β-Hydrogen elimination affords the intermediate **E** and subsequent reductive elimination furnishes **5**. Avoiding steric repulsion between the allene substituent and ligand on rhodium might account for the observed regioselective formation of **A**, **B**, and **D**.

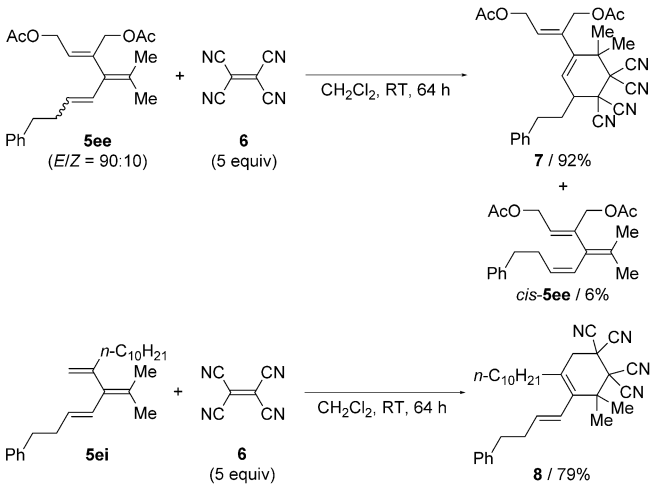
It was anticipated that the reaction of the phenyl-substituted allene **1h** and **2a** with rhodium would afford rhodacyclopentene **E′**, in which no β-hydrogen atoms exist (Scheme 6). However, the reaction of **1h** with **2a** afforded the dendralene **5ha** with a different substitution pattern, presumably through β-hydrogen elimination from the rhodacyclopentene **F**. Similarly, **1h** reacted with **2i** to give the regioisomeric dendralenes **5hi** and **5hi′** in high yield.

As dendralenes serve as good cycloaddition partners in Diels–Alder reactions,[12] the reactions of **5** with tetracyanoethylene (**6**) were examined (Scheme 7). The reaction of an *E*/*Z* mixture of the pentasubstituted dendralene **5ee** with **6** afforded the corresponding vinylcyclohexene **7** in high yield, and *cis*-**5ee** was recovered. The tetrasubstituted dendralene **5ei** also reacted with **6** to give the corresponding vinylcyclohexene **8** in high yield.

In conclusion, we have established that a cationic rhodium(I)/binap complex catalyzes the cross-cyclotrimerization of two molecules of monosubstituted allenes with one molecule of functionalized alkynes to give 3,6-dialkylidenecyclohex-1-enes. In contrast, the reactions involving di- or trisubstituted allenes and/or unfunctionalized alkynes afforded the cross-dimerization products, substituted dendralenes, through β-hydrogen elimination from the correspond-



Scheme 6. Rhodium-catalyzed cross-dimerization of **1h** with **2a,i**.



Scheme 7. Diels–Alder reactions of **5ee** and **5ei** with **6**.

ing rhodacycles. Future work will focus on further exploration of the cationic rhodium(I) complex-catalyzed C–C bond-forming reactions involving allenes.

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