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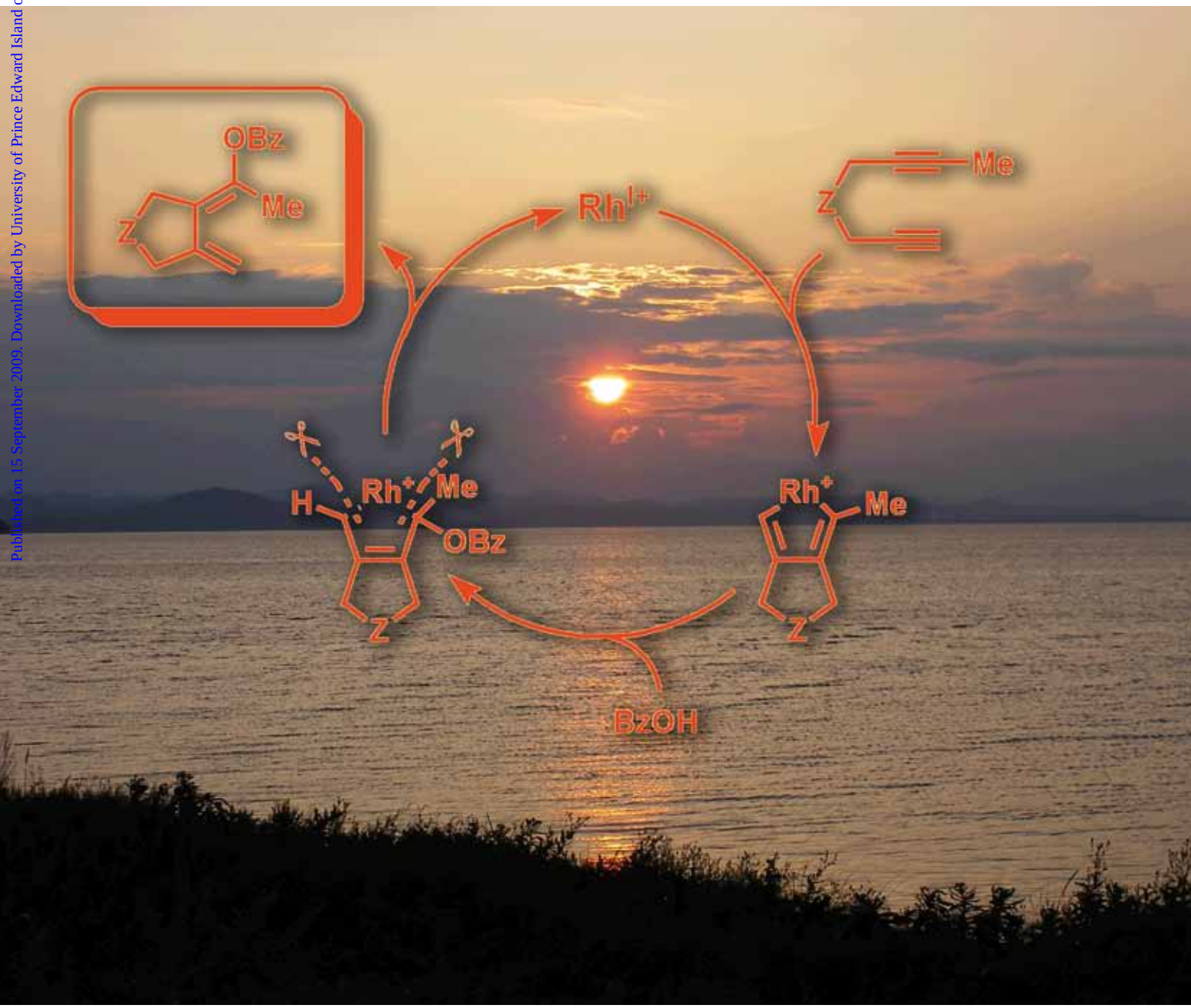

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Cationic rhodium(I)/bisphosphine complex-catalyzed cyclization of 1,6-diynes with carboxylic acids†‡

Ken Tanaka,* Shunsuke Saitoh, Hiromi Hara and Yu Shibata

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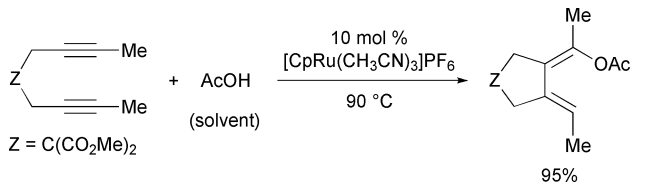
A cationic rhodium(I)/bisphosphine complex catalyzes carboxylative cyclizations of 1,6-diynes, leading to cyclic dienyl carboxylates, in high yields with high chemo-, regio-, and stereoselectivities under mild reaction conditions.

Addition reactions of heteroatom-hydrogen bonds to metallacyclopentadienes are potentially attractive methods for the synthesis of functionalized dienes.[1–9] Wakatsuki and Yamazaki reported that N-H bonds of thioacetanilide and thiourea, and a S-H bond of thiocresol react with cobaltacyclopentadienes to furnish nitrogen- and sulfur-substituted dienes.[1] Vollhardt and co-workers reported that N-H bonds of 2- and 4-pyridones,[2] and various NH-amides and imides[3] react with the cobaltacyclopentadiene to furnish nitrogen-substituted dienes. The addition reactions of O-H bonds to the metallacyclopentadienes have been accomplished by using a catalytic amount of ruthenium complexes. Dixneuf and co-workers reported ruthenium-catalyzed carboxylative dimerizations of arylacetylenes to form dienyl carboxylates through ruthenacyclopentatriene intermediates.[4,5] Trost and Rudd reported ruthenium-catalyzed cyclizations of internal 1,6- and 1,7-diynes with water and methanol.[6] Carboxylative cyclizations of 1,6- and 1,7-diynes catalyzed by a cationic ruthenium(II) complex were reported by Saá and co-workers.[7] The reaction of an internal 1,6-diyne in acetic acid solvent at 90 °C furnished the corresponding five-membered dienyl carboxylates[8] in high yield (eqn (1)).[7] However, 1,6-diynes containing a terminal alkyne moiety reacted with acetic acid to yield decarbonylative cyclization products presumably due to the formation of vinylidene intermediates (eqn (2)),[7] although 1,7-diynes containing a terminal alkyne moiety could furnish the desired dienyl carboxylates.[7] In the case of terminal 1,6-diynes, Lee and co-workers reported carboxylative cyclizations leading to six-membered dienyl carboxylates presumably through the formation of similar vinylidene intermediates (eqn (3)).[9] Thus, the ruthenium-catalyzed carboxylative cyclizations of diynes are limited to internal 1,6-diynes. Furthermore, a large excess of acetic acid and elevated reaction temperature are required.



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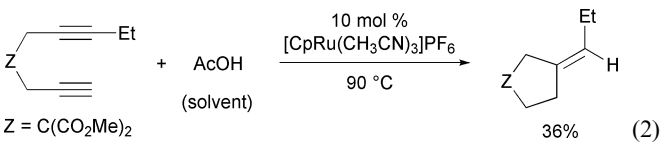

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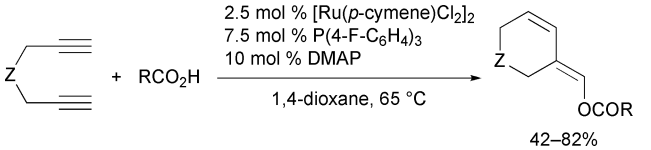


(3)

On the other hand, our research group demonstrated that cationic rhodium(I)/biaryl bisphosphine complexes are highly effective catalysts for [2 + 2 + 2] cycloadditions of both terminal and internal alkynes presumably through rhodacyclopentadiene intermediates.[10,11] In this Communication, we describe chemo-, regio-, and stereoselective cyclizations of both terminal and internal 1,6-diynes with only a slight excess of carboxylic acids under mild reaction conditions catalyzed by a cationic rhodium(I)/bisphosphine complex.

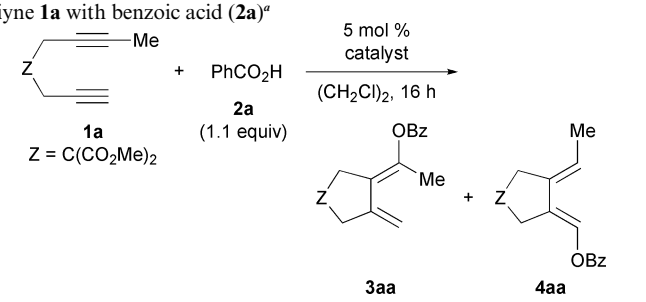
We first investigated the reaction of unsymmetrical 1,6-diyne **1a**, possessing a methyl group and hydrogen at each alkyne terminus, and benzoic acid (**2a**, 1.1 equiv) in the presence of a cationic rhodium(I)/BIPHEP complex (5 mol %). We were pleased to find that the reaction proceeded at room temperature to give the desired cyclic dienyl benzoate **3aa** in quantitative yield with high regioselectivity (Table 1, entry 1). Thus, various rhodium(I)/bisphosphine (Fig. 1) complexes were screened. Cationic rhodium(I) complexes with biaryl bisphosphine ligands showed high catalytic activity (entries 1–4), and BIPHEP was the ligand of choice for both the product yield and regioselectivity (entry 1). Sterically demanding biaryl bisphosphine ligands were not effective (entries 5 and 6). Among non-biaryl bisphosphine ligands examined (entries 7–9), dppb was the best for the product yield and regioselectivity (entry 9). Although the catalytic activity of the dppb complex was low, complete conversion of **1a** could

Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184-8588, Japan. E-mail: tanaka-k@cc.tuat.ac.jp; Fax: +81 42 388 7037; Tel: +81 42 388 7037

† Electronic supplementary information (ESI) available: Compound characterization data including ^{1}H and ^{13}C NMR spectra of all new compounds and reaction products. See DOI: 10.1039/b913344e

‡ **Typical Procedure** (Table 2, **entry 5**): Under an Ar atmosphere, BIPHEP (7.8 mg, 0.015 mmol) and $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) were dissolved in $(CH_2Cl)_2$ (2.0 mL) and the mixture was stirred at room temperature for 30 min. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 1 h, the resulting mixture was concentrated to dryness. To the residue was added a solution of **1a** (66.7 mg, 0.300 mmol) and **2d** (33.7 mg, 0.330 mmol) in $(CH_2Cl)_2$ (2.0 mL) at room temperature. The mixture was stirred at room temperature for 16 h. The resulting solution was concentrated and purified by a silica gel chromatography (hexane/EtOAc = 2:1), which furnished **3ad** (97.4 mg, 0.291 mmol, 97% isolated yield) as a pale yellow oil.

Table 1 Screening of catalysts for rhodium-catalyzed cyclization of 1,6-diyne **1a** with benzoic acid (**2a**)[a]



Entry	Catalyst	Temp/°C	Convn (%)[b]	% yield[b] (**3aa**/**4aa**)
1	$[Rh(cod)_2]BF_4$/BIPHEP	rt	100	>99 (95:5)
2	$[Rh(cod)_2]BF_4$/Segphos	rt	100	99 (95:5)
3	$[Rh(cod)_2]BF_4$/BINAP	rt	91	91 (87:13)
4	$[Rh(cod)_2]BF_4$/H_8-BINAP	rt	92	92 (68:32)
5	$[Rh(cod)_2]BF_4$/xyl-H_8-BINAP	rt	5	5 (>99:1)
6	$[Rh(cod)_2]BF_4$/DTBM-Segphos	rt	0	0
7	$[Rh(cod)_2]BF_4$/dppf	rt	26	25 (>99:1)
8	$[Rh(nbd)_2]BF_4$/dppe	rt	50	11 (>99:1)
9	$[Rh(cod)_2]BF_4$/dppb	rt	36	35 (>99:1)
10	$[Rh(cod)_2]BF_4$/dppb	60	100	96 (>99:1)
11	$[Rh(cod)Cl]_2$/2dppb	rt	0	0
12[c]	$[Rh(cod)_2]BF_4$/dppb	rt	0	0

[a] Rh complex (0.0050 mmol of Rh), ligand (0.0050 mmol), **1a** (0.10 mmol), **2a** (0.11 mmol), and $(CH_2Cl)_2$ (1.5 mL) were used. The active catalyst was generated in situ by hydrogenation. [b] Convn and yield were determined by ^{1}H NMR using 1,4-dimethoxybenzene as an internal standard. [c] Without hydrogenation.

be realized by increasing the reaction temperature to 60 °C without erosion of the regioselectivity (entry 10). The use of the cationic rhodium(I) complex and the treatment of the catalyst with hydrogen were essential as demonstrated in entries 11 and 12.

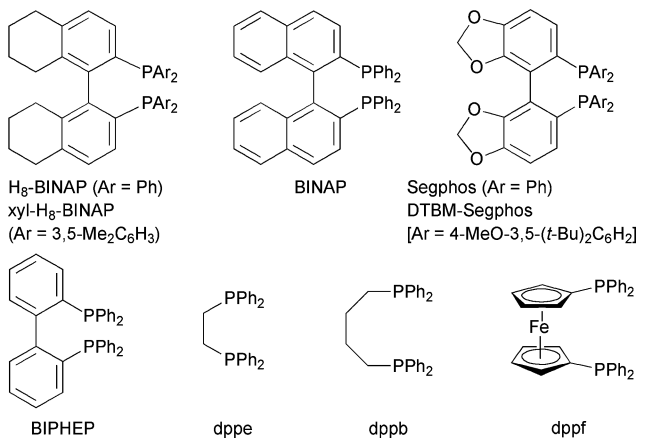
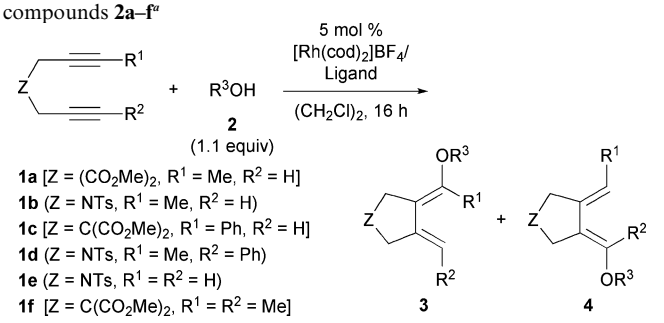


Fig. 1 Structures of bisphosphine ligands.

Thus, we explored the scope of hydroxy compounds and 1,6-diynes by using 5 mol % of the cationic rhodium(I)/bisphosphine complex as shown in Table 2. With respect to hydroxy compounds, not only benzoic acid (**2a**, entries 1 and 2) but also various aliphatic carboxylic acids (**2b–d**, entries 3–5) reacted with **1a** to furnish the corresponding dienyl carboxylates in high yields with perfect regioselectivity.[12] Importantly, the rhodium-catalyzed diyne cyclizations are specific to carboxylic

Table 2 Rhodium-catalyzed cyclizations of 1,6-diynes **1a–f** with hydroxy compounds **2a–f**[a]

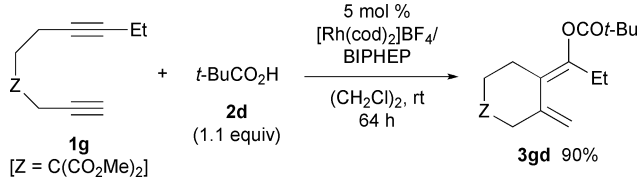


Entry	**1**	**2** (R^3)	Ligand, Temp/°C	% **3**/**4** (% yield)[b]
1	**1a**	**2a** (Bz)	dppb, 60	**3aa** (84)
2	**1a**	**2a** (Bz)	BIPHEP, rt	**3aa**/**4aa** = 95:5 (90)
3[c]	**1a**	**2b** (Ac)	BIPHEP, rt	**3ab** (90)
4	**1a**	**2c** (CyCO)	BIPHEP, rt	**3ac** (84)
5	**1a**	**2d** (*t*-BuCO)	BIPHEP, rt	**3ad** (97)
6	**1a**	**2e** (Ph)	BIPHEP, rt	**3ae**/**4ae** (0)
7	**1a**	**2f** (Me)	BIPHEP, rt	**3af**/**4af** (0)
8	**1b**	**2d** (*t*-BuCO)	BIPHEP, rt	**3bd** (63)
9	**1c**	**2d** (*t*-BuCO)	BIPHEP, rt	**3cd**/**4cd** = 85:15 (87)
10	**1d**	**2a** (Bz)	BIPHEP, rt	**3da** (88)
11	**1e**	**2a** (Bz)	H_8-BINAP, rt	**3ea** (73)
12	**1f**	**2a** (Bz)	H_8-BINAP, 40	**3fa** (87, E/Z = 95:5[d])

[a] $[Rh(cod)_2]BF_4$ (0.015 mmol), ligand (0.015 mmol), **1a–f** (0.30 mmol), **2a–f** (0.33 mmol), and $(CH_2Cl)_2$ (2.0 mL) were used. The active catalyst was generated in situ by hydrogenation. [b] Isolated yield. [c] **2b**: 2 equiv. [d] Stereochemistry of the enol double bond.

acids, which is in sharp contrast to the rhthenium-catalyzed diyne cyclizations.[5,6] Thus, phenol (**2e**, entry 6) and methanol (**2f**, entry 7) failed to react with **1a**.[13,14] With respect to 1,6-diynes, not only malonate- (**1a**) but also tosylamide-linked 1,6-diyne (**1b**, entry 8) could participate in this reaction. Although unsymmetrical 1,6-diyne **1c**, possessing a phenyl group and hydrogen at each alkyne terminus, furnished the desired dienyl carboxylate with moderate regioselectivity (entry 9), unsymmetrical 1,6-diyne **1d**, possessing methyl and phenyl groups at each alkyne terminus, furnished the desired dienyl carboxylate with perfect regioselectivity (entry 10). Both terminal and internal symmetrical 1,6-diynes **1e** and **1f** reacted with **2a** to give the corresponding dienyl carboxylates in good yields by using H_8-BINAP as a ligand (entries 11 and 12).

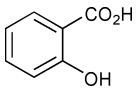
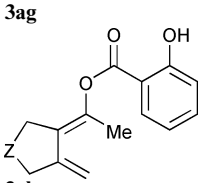
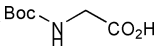
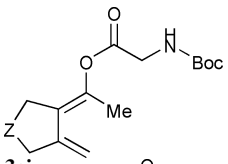
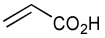
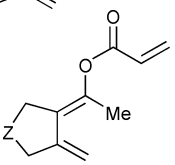
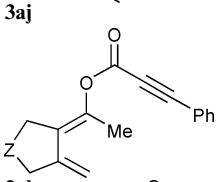
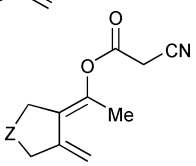
Furthermore, the carboxylative cyclization of unsymmetrical 1,7-diyne **1g** with **2d** also proceeded at room temperature to give the corresponding six-membered cyclic dienyl carboxylate **3gd** in high yield with perfect regio- and stereoselectivity (eqn (4)).



(4)

The reactions of electron-deficient 1,6-diynes **1h**[15] and **1i**,[16] and 1,6-enynes **5a**[17] and **5b**[17] with benzoic acid (**2a**, 1.1 equiv) were also examined under the same reaction conditions for entry 2 of Table 2 (5 mol % $[Rh(cod)_2]BF_4$/BIPHEP at room temperature for 16 h), while a rapid homo-[2 + 2 + 2] cycloaddition of **1h** proceeded

Table 3 Rhodium-catalyzed cyclizations of 1,6-diyne **1a** [Z = $C(CO_2Me)_2$] with bifunctional carboxylic acids **2g–k**[a]

Entry	2	3	Yield (%)[b]
1[c]	**2g** 	**3ag** 	54
2[d]	**2h** 	**3ah** 	92
3	**2i** 	**3ai** 	92
4	**2j** 	**3aj** 	65
5	**2k** 	**3ak** 	79

[a] Reactions were conducted using $[Rh(cod)_2]BF_4$ (0.015 mmol), BIPHEP (0.015 mmol), **1a** (0.30 mmol), **2g–k** (0.33 mmol), and $(CH_2Cl)_2$ (2.0 mL) at rt for 16 h. The active catalyst was generated in situ by hydrogenation. [b] Isolated yield. [c] Catalyst: 10 mol %. For 64 h. [d] For 20 h.

quantitatively and no conversions of **1i**, **5a**, and **5b** were observed (Fig. 2).

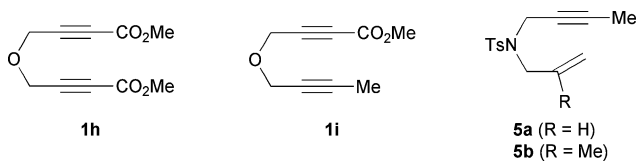
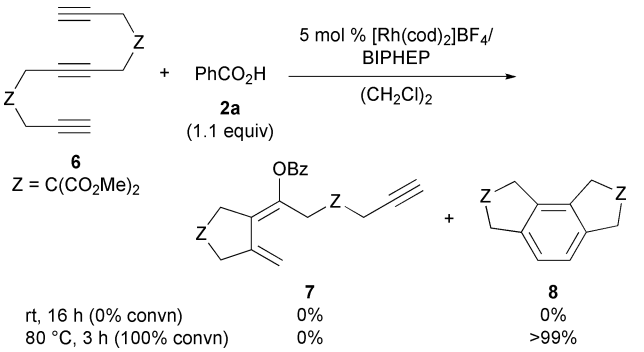


Fig. 2 Unsuitable substrates for the carboxylative cyclization.

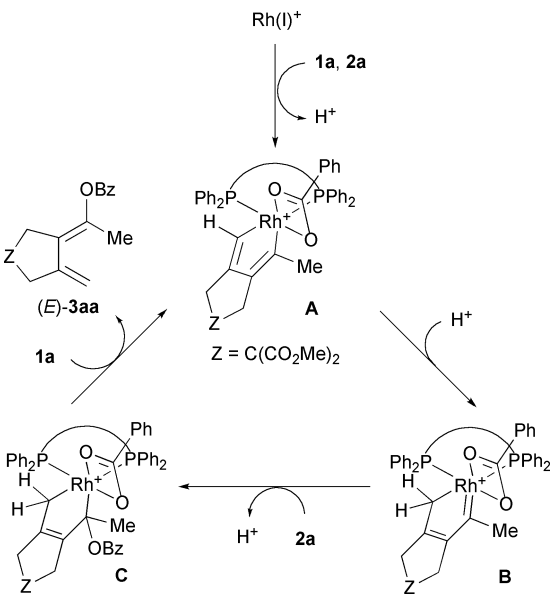
Next, chemoselective cyclizations of 1,6-diyne **1a** with bifunctional carboxylic acids were examined as shown in Table 3. In terms of the chemoselectivity between a carboxyl O-H group and a phenolic O-H or an amidic N-H group, the carboxyl O-H groups of salicylic acid (**2g**, entry 1) and *N*-Boc glycine (**2h**, entry 2) selectively reacted with **1a** to furnish the corresponding dienyl carboxylates. In terms of the chemoselectivity between the carboxyl O-H group and various multiple bonds, the carboxyl O-H groups of acrylic acid (**2i**, entry 3), phenylpropiolic acid (**2j**, entry 4), and cyanoacetic acid (**2k**, entry 5) selectively reacted with **1a** to furnish the corresponding dienyl carboxylates without formation of [2 + 2 + 2] cycloaddition products.

In the present rhodium-catalyzed addition reactions of carboxylic acids to diynes, homo-cyclotrimerizations of diynes are effectively suppressed, which might suggest strong coordination of the carboxylic acid to the cationic rhodacyclopentadiene. Therefore, we anticipated that the reaction of triyne **6** with benzoic acid (**2a**) would furnish carboxylative cyclization product **7**. Contrary to our expectation, no reaction was observed at room temperature and cyclotrimerization product **8** was obtained in quantitative yield at 80 °C (eqn (5)).



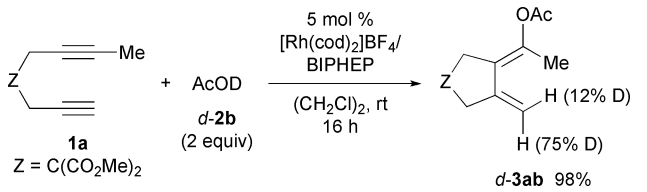
(5)

A possible mechanism for the selective formation of dienyl benzoate **3aa** is shown in Scheme 1. 1,6-Diyne **1a** and benzoic acid (**2a**) react with the cationic rhodium(I) complex furnishing rhodacyclopentadiene intermediate **A**, bearing a chelating carboxylate ligand. Regioselective protonation of the sterically less demanding carbon forms intermediate **B**. Carboxylate addition to **B** generates intermediate **C**. Elimination of (*E*)-dienyl benzoate (*E*)-**3aa** followed by the reaction of 1,6-diyne **1a** regenerates the rhodacyclopentadiene intermediate **A**.[18] As the rapid homo-[2 + 2 + 2] cycloaddition of **1a** proceeded at room temperature in the presence of $[Rh(cod)_2]BF_4$/BIPHEP (5 mol %) and methyl benzoate (1.1 equiv), strong deprotonative chelation of benzoic acid (**2a**) in the intermediate **A** might be important to suppress the homo-[2 + 2 + 2] cycloaddition of **1a**.



Scheme 1 Possible mechanism for the formation of **3aa**.

Consistent with this pathway, the reaction of 1,6-diyne **1a** and AcOD (*d*-**2b**) led to 87% incorporation of deuterium in the product *d*-**3ab** (eqn (6)).[18]



(6)

In conclusion, we have demonstrated cationic rhodium(I)/bisphosphine complex-catalyzed chemo-, regio-, and stereoselective cyclizations of 1,6-diynes with carboxylic acids, leading to cyclic dienyl carboxylates. Importantly, the present rhodium-catalyzed diyne cyclization allows the use of both terminal and internal diynes, proceeds under mild reaction conditions, and is specific to carboxylic acids.

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12 The reactions of 1,6-diyne **1a** and formic acid in the presence of the catinonic rhodium(I)/BIPHEP complex (5 mol %) proceeded at room temperature to yield the corresponding dienyl carboxylates in *ca.* 30% NMR yield, while the product could not be isolated due to its instability. The reaction of **1a** and oxalic acid was also examined, but the corresponding addition products were not obtained at all.
13 Intramolecular addition reactions of phenol to acylrhodacycles were reported; see: M. Murakami, T. Tsuruta and Y. Ito, *Angew. Chem., Int. Ed.*, 2000, **39**, 2484.
14 Intermolecular addition reactions of phenol, methanol, and water to acylrhodacycles were also reported; see: K. Tanaka and G. C. Fu, *Angew. Chem., Int. Ed.*, 2002, **41**, 1607.
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18 The stereoselectivity might be determined at the step of intermediate **C** to the product, and the sterically less demanding (*E*)-isomers [(*E*)-**3aa** and (*E*)-*d*-**3ab**] are generated preferentially.

