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A New Route to Substituted Phenols by Cationic Rhodium(I)/BINAP Complex-Catalyzed Decarboxylative [2 + 2 + 2] Cycloaddition

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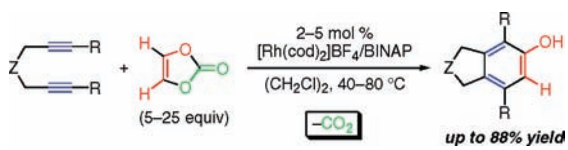
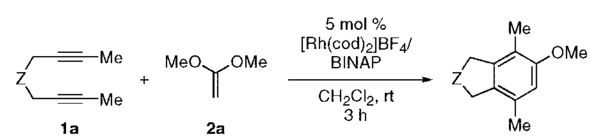
ABSTRACT



A new route to substituted phenols has been developed by cationic rhodium(I)/BINAP complex-catalyzed decarboxylative [2 + 2 + 2] cycloadditions of 1,6- and 1,7-diynes with commercially available vinylene carbonate.

Transition-metal-catalyzed [2 + 2 + 2] cycloadditions of tethered diynes with alkynes have been widely employed for the regioselective synthesis of substituted aromatic compounds.[1] Instead of alkynes, alkenes possessing a leaving group can be employed as alkyne equivalents. As such, Takeuchi and co-workers first reported a neutral iridium(I)/dppe complex-catalyzed [2 + 2 + 2] cycloaddition of a 1,6-diyne with *n*-butyl vinyl ether at elevated temperature (70 °C), which furnishes a tetrasubstituted benzene through elimination of *n*-butanol in moderate yield.[2−5] Following this pioneering report, our research group recently reported cationic rhodium(I)/BINAP complex-catalyzed [2 + 2 + 2] cycloadditions[6−9] of 1,6-diynes with enol ethers.[10] The high Lewis acidity of the cationic rhodium(I)/BINAP complex facilitates the elimination of an alcohol even at room temperature, which significantly improved the yields of the desired tetra- and pentasubstituted benzenes. Furthermore, the use of the cationic rhodium(I)/BINAP complex as a catalyst enabled a [2 + 2 + 2] cycloaddition of 1,6-diyne **1a** with ketene acetal **2a** at room temperature, which furnished the corresponding bicyclic methoxybenzene **3aa** in quantitative yield (Scheme 1).[10,11]

Scheme 1



1a Z = C(CO$_2$Me)$_2$ **2a** (5 equiv) **3aa** >99%

Takeuchi and co-workers also reported that the neutral iridium(I)/dppe complex catalyzes a [2 + 2 + 2] cycloaddition of a 1,6-diyne with a cyclic enol ether (2,3-dihydrofuran) instead of an acyclic enol ether (*n*-butyl vinyl ether)

(1) For recent reviews of transition-metal-catalyzed [2 + 2 + 2] cycloadditions, see: (a) Tanaka, K. *Chem. Asian J.* **2009**, *4*, Epub ahead of print, DOI: 10.1002/asia.200800378. (b) Varela, J. A.; Saá, C. *Synlett* **2008**, 2571. (c) Shibata, T.; Tsuchikama, K. *Org. Biomol. Chem.* **2008**, 1317. (d) Heller, B.; Hapke, M. *Chem. Soc. Rev.* **2007**, *36*, 1085. (e) Agenet, N.; Buisine, O.; Slowinski, F.; Gandon, V.; Aubert, C.; Malacria, M. In *Organic Reactions*; Overman, L. E., Ed.; John Wiley & Sons: Hoboken, 2007; Vol. 68, p 1. (f) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307. (g) Gandon, V.; Aubert, C.; Malacria, M. *Chem. Commun.* **2006**, 2209. (h) Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem.* **2005**, 4741. (i) Gandon, V.; Aubert, C.; Malacria, M. *Curr. Org. Chem.* **2005**, *9*, 1699. (j) Yamamoto, Y. *Curr. Org. Chem.* **2005**, *9*, 503. (k) Varela, J.; Saá, C. *Chem. Rev.* **2003**, *103*, 3787.

(2) Kezuka, S.; Tanaka, S.; Ohe, T.; Nakaya, Y.; Takeuchi, R. *J. Org. Chem.* **2006**, *71*, 543.

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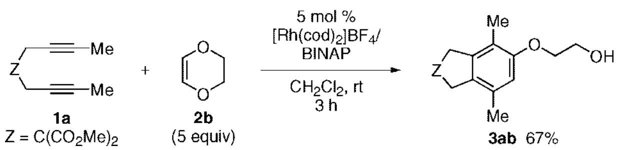
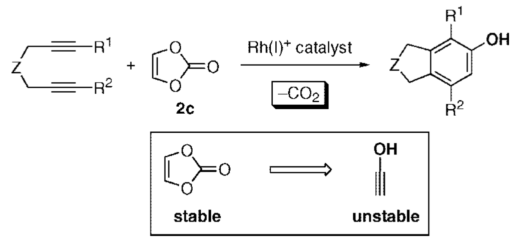
to furnish an aromatic alcohol in high yield.[3,12,13] Thus, a [2 + 2 + 2] cycloaddition of 1,6-diyne **1a** with a 2,3-dihydro-1,4-dioxin (**2b**) was examined in the presence of the cationic rhodium(I)/BINAP complex (5 mol %). Pleasingly, the reaction proceeded at room temperature to furnish the expected ethyleneglycol monoaryl ether **3ab** in good yield (Scheme 2).

Scheme 2



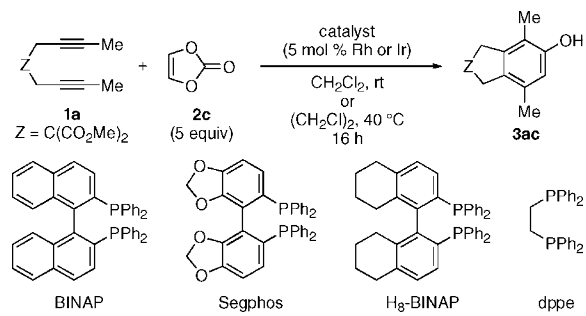
We anticipated that the use of commercially available vinylene carbonate (**2c**) instead of 2,3-dihydro-1,4-dioxin (**2b**) would furnish substituted bicyclic phenols through elimination of carbon dioxide.[14−16] If this new route to phenol derivatives is realized, vinylene carbonate (**2c**) can be used as a stable equivalent of unstable hydroxyacetylene (Scheme 3).

Scheme 3



We first investigated the reaction of 1,6-diyne **1a** and vinylene carbonate (**2c**, 5 equiv) in the presence of the cationic rhodium(I)/BINAP complex (5 mol %). We were pleased to find that the expected decarboxylative [2 + 2 + 2] cycloaddition proceeded at room temperature to give the corresponding bicyclic phenol **3ac** in 64% yield (Table 1, entry 1). Thus, various rhodium(I)/bisphosphine complexes were screened. Cationic rhodium(I) complexes with bisphosphine ligands (BINAP, Segphos, H_8-BINAP, and dppe) were able to catalyze this reaction (entries 1−4), and BINAP was the best for the product selectivity (entry 1).[17] On the other hand, a neutral rhodium(I)/BINAP complex and both cationic and neutral iridium(I)/BINAP complexes were not able to catalyze this reaction at all (entries 5−7). The neutral

Table 1. Screening of Reaction Conditions for [2 + 2 + 2] Cycloaddition of 1,6-Diyne **1a** with Vinylene Carbonate (**2c**)[a]



entry	catalyst	temp (°C)	convn (%)[b]	yield (%)[b]
1	$[Rh(cod)_2]BF_4$/BINAP	rt	85	64
2	$[Rh(cod)_2]BF_4$/Segphos	rt	83	29
3	$[Rh(cod)_2]BF_4$/H_8-BINAP	rt	100	54
4	$[Rh(nbd)_2]BF_4$/dppe	rt	48	18
5	$[Rh(cod)Cl]_2$/2BINAP	rt	0	0
6	$[Ir(cod)_2]BF_4$/BINAP	rt	0	0
7	$[Ir(cod)Cl]_2$/2BINAP	rt	0	0
8	$[Ir(cod)Cl]_2$/2dppe	rt	0	0
9	$[Rh(cod)_2]BF_4$/BINAP	40	100	76

[a] $[Rh(cod)_2]BF_4$ (0.0075 mmol), ligand (0.0075 mmol), **1a** (0.150 mmol), **2c** (0.750 mmol), and CH_2Cl_2 or $(CH_2Cl)_2$ (0.8 mL) were used. [b] Determined by ^{1}H NMR.

(3) For the first discovery of a neutral iridium(I)/bisphosphine complex-catalyzed [2 + 2 + 2] cycloaddition of alkynes, see: (a) Takeuchi, R.; Tanaka, S.; Nakaya, Y. *Tetrahedron Lett.* **2001**, *42*, 2991. For their related reports, see: (b) Takeuchi, R.; Nakaya, Y. *Org. Lett.* **2003**, *5*, 3659. (c) Kezuka, S.; Okado, T.; Niou, E.; Takeuchi, R. *Org. Lett.* **2005**, *7*, 1711. (d) Onodera, G.; Matsuzawa, M.; Aizawa, T.; Kitahara, T.; Shimizu, Y.; Kezuka, S.; Takeuchi, R. *Synlett* **2008**, 755.

(4) For a review of neutral iridium(I)/bisphosphine complex-catalyzed enantioselective [2 + 2 + 2] cycloadditions, see ref 1c.

(5) Although palladium-catalyzed [2 + 2 + 2] cycloadditions of dimethyl acetylenedicarboxylate with vinyl ethers and esters were reported, the reactions required a large excess of the vinyl compounds and a long reaction time; see: Stephan, C.; Munz, C.; Dieck, H. T. *J. Organomet. Chem.* **1993**, *452*, 223.

(6) For the first discovery of a cationic rhodium(I)/biaryl bisphosphine complex-catalyzed [2 + 2 + 2] cycloaddition of alkynes, see: (a) Tanaka, K.; Shirasaka, K. *Org. Lett.* **2003**, *5*, 4697. See also: (b) Tanaka, K.; Toyoda, K.; Wada, A.; Shirasaka, K.; Hirano, M. *Chem. Eur. J.* **2005**, *11*, 1145.

(7) For our accounts of cationic rhodium(I)/biaryl bisphosphine complex-catalyzed [2 + 2 + 2] cycloadditions, see: (a) Tanaka, K. *Synlett* **2007**, 1977. (b) Tanaka, K.; Nishida, G.; Suda, T. *J. Synth. Org. Chem. Jpn.* **2007**, *65*, 862.

(8) For a review of rhodium-catalyzed [2 + 2 + 2] cycloadditions, see: Fujiwara, M.; Ojima, I. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH: Weinheim, 2005; p 129.

(9) For cationic rhodium(I)/biaryl bisphosphine complex-catalyzed [2 + 2 + 2] cycloadditions involving monoenes, see: (a) Tsuchikama, K.; Kuwata, Y.; Shibata, T. *J. Am. Chem. Soc.* **2006**, *128*, 13686. (b) Tanaka, K.; Nishida, G.; Sagae, H.; Hirano, M. *Synlett* **2007**, 1426. (c) Shibata, T.; Kawachi, A.; Ogawa, M.; Kuwata, Y.; Tsuchikama, K.; Endo, K. *Tetrahedron* **2007**, *63*, 12853. (d) Shibata, Y.; Noguchi, K.; Hirano, M.; Tanaka, K. *Org. Lett.* **2008**, *10*, 2825. (e) Tanaka, K.; Takahashi, M.; Imase, H.; Osaka, T.; Noguchi, K.; Hirano, M. *Tetrahedron* **2008**, *64*, 6289.

(10) (a) Hara, H.; Hirano, M.; Tanaka, K. *Org. Lett.* **2008**, *10*, 2537. (b) Hara, H.; Hirano, M.; Tanaka, K. Submitted for publication.

(11) For cationic rhodium(I)/BINAP complex-catalyzed [2 + 2 + 2] cycloadditions of diynes with alkynyl ethers en route to aryl ethers, see: Clayden, J.; Moran, W. J. *Org. Biomol. Chem.* **2007**, *5*, 1028.

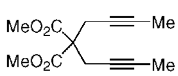
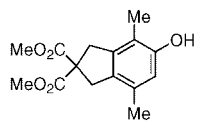
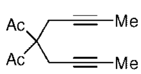
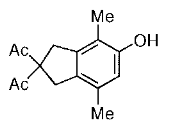
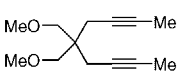
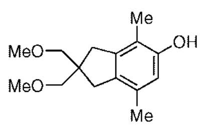
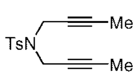
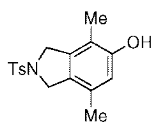
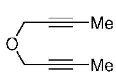
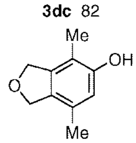
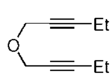
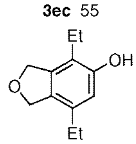
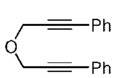
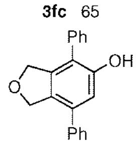
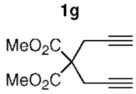
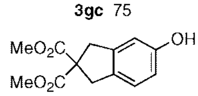
(12) A cobalt-mediated [2 + 2 + 2] cycloaddition of an alkynylboronic pinacolate ester with 2,3-dihydrofuran was reported. Not the corresponding aromatic alcohol but the corresponding diborylated cyclohexadiene was obtained as a major product; see: Geny, A.; Leboeliguf, D.; Rouquié, G.; Vollhardt, K. P. C.; Malacria, M.; Gandon, V.; Aubert, C. *Chem. Eur. J.* **2007**, *13*, 5408.

(13) For transition-metal-catalyzed [2 + 2 + 2] cycloadditions of 1,6-diynes with 2,5-dihydrofuran to form substituted bicyclic cyclohexadienes, see: (a) Yamamoto, Y.; Kitahara, H.; Ogawa, R.; Itoh, K. *J. Org. Chem.* **1998**, *63*, 9610. (b) Varela, J. A.; Rubin, S. G.; González-Rodríguez, C.; Castedo, L.; Saá, C. *J. Am. Chem. Soc.* **2006**, *128*, 9262.

iridium(I)/dppe complex, which was employed for the [2 + 2 + 2] cycloaddition of a 1,6-diyne with enol ethers,[3] showed no catalytic activity (entry 8). Increasing the reaction temperature to 40 °C realized complete conversion of **1a**, which improved the yield of **3ac** to 76% (entry 9).

Thus, we explored the scope of 1,6-diynes by using 5 equiv of vinylene carbonate (**2c**) and 5 mol % of the cationic rhodium(I)/BINAP complex as shown in Table 2. With respect to tethers, not only malonate- (**1a**, entry 1) but also acetylacetone- (**1b**, entry 3), dimethoxypropane- (**1c**, entry 4), tosylamide- (**1d**, entry 5), and oxygen-linked (**1e**, entry 6) internal 1,6-diynes could be employed for this reaction. With respect to substituents at alkyne termini, not only methyl- (**1a**−**e**, entries 1−6) but also ethyl- (**1f**, entry 7) and phenyl-substituted (**1g**, entry 8) internal 1,6-diynes could participate in this reaction.[18] Unfortunately, terminal 1,6-diyne **1h** reacted with **2c** to give the corresponding bicyclic phenol **3hc** in low yield even using a large excess of **1h** (25 equiv) due to the rapid homo-[2 + 2 + 2] cycloaddition of **1h** (entry 9). Although elevated temperature (80 °C) was necessary, the catalyst loading could be reduced to 2 mol % with only a slight erosion of the product yield (entry 2).

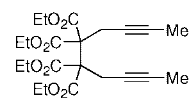
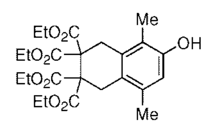
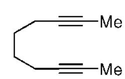
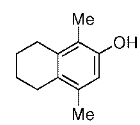
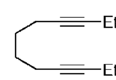
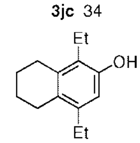
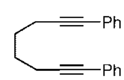
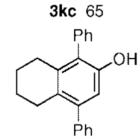
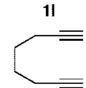
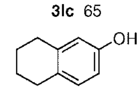
Table 2. Cationic Rh(I)/BINAP-Catalyzed Decarboxylative [2 + 2 + 2] Cycloadditions of 1,6-Diynes **1a**−**h** with **2c**[a]

entry	1	2c (equiv)	3 / yield (%)[b]
			
1	1a	5	3ac 66
2[c]	1a	5	3ac 61
			
3	1b	5	3bc 58[d]
			
4	1c	5	3cc 65
			
5	1d	5	3dc 82
			
6	1e	5	3ec 55
			
7	1f	5	3fc 65
			
8	1g	25	3gc 75
			
9	1h	25	3hc 14

[a] Reactions were conducted using $[Rh(cod)_2]BF_4$ (0.015 mmol), BINAP (0.015 mmol), **1a**−**h** (0.300 mmol), **2c** (1.50 or 7.50 mmol), and $(CH_2Cl)_2$ (2.0 mL) at 40 °C for 16 h. [b] Isolated yield. [c] Catalyst: 2 mol %. At 80 °C for 20 h. [d] Isolated as a mixture of **3bc** and dimer of **1b**. Yield of **3bc** was determined by ^1H NMR.

Next, the reactions of 1,7-diynes and vinylene carbonate (**2c**) were investigated as shown in Table 3. The reaction of ethanetetracarboxylate-linked 1,7-diyne **1i** and **2c** (5 equiv) proceeded in high yield (entry 1), whereas that of 2,8-decadiyne **1j** and **2c** proceeded in low yield even using excess **2c** (25 equiv, entry 2). With respect to substituents at the alkyne termini, the reaction with ethyl-substituted internal 1,7-diyne **1k** (entry 3) proceeded in higher yield than that with methyl-substituted internal 1,7-diyne **1j** because of the slow homo-[2 + 2 + 2] cycloaddition of **1k** (entry 3). In the case of phenyl-substituted 1,7-diyne **1l**, the corresponding bicyclic phenol **3lc** was obtained in good yield at elevated temperature (80 °C, entry 4). Like the reaction with terminal 1,6-diyne **1h**, terminal 1,7-diyne **1m** was not a suitable

Table 3. Cationic Rh(I)/BINAP-Catalyzed Decarboxylative [2 + 2 + 2] Cycloadditions of 1,7-Diynes **1i**−**m** with **2c**[a]

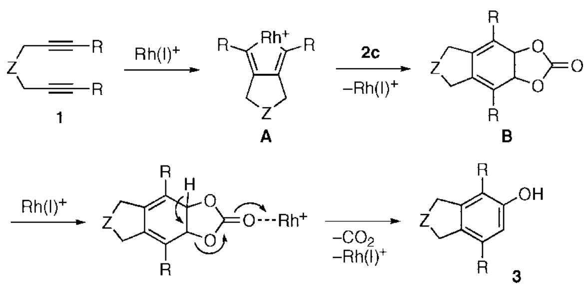
entry	1	2c (equiv)	3 / yield (%)[b]
			
1	1i	5	3ic 88
			
2	1j	25	3jc 34
			
3	1k	25	3kc 65
			
4[c]	1l	25	3lc 65
			
5	1m	25	3mc <5

[a] Reactions were conducted using $[Rh(cod)_2]BF_4$ (0.015 mmol), BINAP (0.015 mmol), **1i**−**m** (0.300 mmol), **2c** (1.50 or 7.50 mmol), and $(CH_2Cl)_2$ (2.0 mL) at 40 °C for 16 h. [b] Isolated yield. [c] At 80 °C for 40 h.

coupling partner for **2c** due to the rapid homo-[2 + 2 + 2] cycloaddition of **1m**, and thus the corresponding cycloadduct **3mc** was obtained in only a trace amount (entry 5).

A possible mechanism for the present decarboxylative [2 + 2 + 2] cycloaddition of 1,6- and 1,7-diynes **1** with vinylene carbonate (**2c**) is shown in Scheme 4. Diyne **1** reacts

Scheme 4



with rhodium to form rhodacyclopentadiene intermediate **A**. Subsequent insertion of **2c** followed by reductive elimination of rhodium furnishes carbonate **B**.[19] Coordination of the cationic rhodium(I) complex to the carbonyl group of carbonate **B** would facilitate the elimination of carbon dioxide to form bicyclic phenol **3**.

In conclusion, we have developed a new route to substituted phenols by cationic rhodium(I)/BINAP complex-catalyzed decarboxylative [2 + 2 + 2] cycloadditions of 1,6- and 1,7-diynes with commercially available vinylene carbonate. Application of the present decarboxylative cycloaddition approach to various annulation reactions and developing asymmetric variants of this reaction are 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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(14) Transition-metal-catalyzed syntheses of substituted phenols through benzannulation by means of ring-closing methathesis have been reported; see: (a) Yoshida, K.; Imamoto, T. *J. Am. Chem. Soc.* **2005**, *127*, 10470. (b) Yoshida, K.; Horiuchi, S.; Iwadate, N.; Kawagoe, F.; Imamoto, T. *Synlett* **2007**, 1561. (c) Yoshida, K.; Narui, R.; Imamoto, T. *Chem. Eur. J.* **2008**, *14*, 9706. (d) Yoshida, K.; Kawagoe, F.; Hayashi, K.; Horiuchi, S.; Imamoto, T.; Yanagisawa, A. *Org. Lett.* **2009**, *11*, 515.

(15) A platinum-catalyzed intramolecular reaction of furans with alkynes, leading to substituted phenols, was reported; see: Martin-Matute, B.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 4754.

(16) A synthesis of substituted 1-naphthols through Diels−Alder reaction of 3-silylbenzynes with substituted furans followed by acid-mediated aromatization was reported; see: Akai, S.; Ikawa, T.; Takayanagi, S.-I.; Morikawa, Y.; Mohri, S.; Tsubakiyama, M.; Egi, M.; Wada, Y.; Kita, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 7673.

(17) Other than the desired phenol product **3ac**, the homo-[2 + 2 + 2] cycloaddition product of **1a** was obtained as a by-product in 13% isolated yield.

(18) An ether-linked 1,6-diyne, possessing methoxycarbonyl groups at the alkyne termini, failed to react with **2c** as a result of its rapid homo-[2 + 2 + 2] cycloaddition.

(19) Isolation and ^{1}H NMR observation of intermediate **B** have not been accomplished at the present stage.