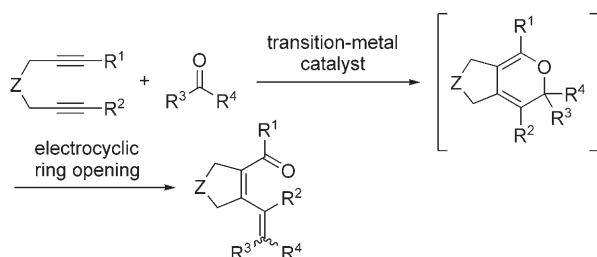


Highly Regio-, Diastereo-, and Enantioselective [2+2+2] Cycloaddition of 1,6-Enynes with Electron-Deficient Ketones Catalyzed by a Cationic $\text{Rh}^{\text{I}}/\text{H}_8\text{-binap}$ Complex**

Ken Tanaka,* Yousuke Otake, Hiromi Sagae, Keiichi Noguchi, and Masao Hirano

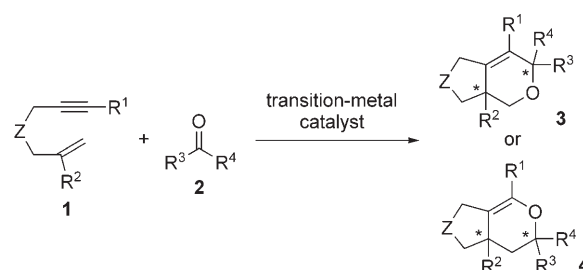
Transition-metal-catalyzed [2+2+2] cycloaddition reactions are efficient methods for the construction of six-membered carbocycles and heterocycles.^[1] For the synthesis of six-membered oxygen heterocycles, [2+2+2] cycloaddition reactions involving carbonyl compounds are potentially attractive. Catalytic [2+2+2] cycloaddition reactions of diynes with carbonyl compounds^[2] in the presence of various transition-metal complexes have been reported, for example, with Ni,^[3] Ru,^[4] and Rh.^[5] However, these reactions frequently failed to produce oxygen heterocycles, and instead dienones were obtained as the major products as a result of electrocyclic ring opening of the initially formed fused α -pyrans (Scheme 1). In



Scheme 1. Transition-metal-catalyzed [2+2+2] cycloaddition of 1,6-diynes with carbonyl compounds.

contrast, a transition-metal-catalyzed [2+2+2] cycloaddition of enynes **1** to ketones **2** would furnish fused dihydropyrans **3** or **4** with two quaternary carbon centers,^[6] bicyclic compounds that would not be converted into ring-opened

products (Scheme 2). Although a $\text{Ni}^0/\text{imidazolyldiene}$ -catalyzed reaction of a 1,7-enyne with benzaldehyde has been reported, poor regioselectivity and β -hydride elimination



Scheme 2. Transition-metal-catalyzed [2+2+2] cycloaddition of 1,6-enynes with ketones.

prior to reductive elimination from the corresponding nickelacycle were observed.^[3b,7] Our research group recently reported the reaction of 1,6-diynes with carbonyl compounds to give dienones and *ortho*-functionalized aryl ketones under the catalysis of cationic complexes of Rh^{I} with modified binap ligands (binap = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl).^[8,9] Herein, we describe the [2+2+2] cycloaddition of 1,6-enynes with electron-deficient ketones to give fused dihydropyrans with two quaternary carbon centers under the catalysis of a cationic $\text{Rh}^{\text{I}}/\text{H}_8\text{-binap}$ complex, as well as the *ortho* functionalization of aryl ketones with 1,6-enynes in the presence of the same catalyst. Both reactions proceed with excellent regio-, diastereo-, and enantioselectivity.

We first investigated the reaction of the tosylamide-linked 1,6-enyne **1a**, which contains a geminally disubstituted alkene moiety, with ethyl pyruvate (**2a**) in the presence of cationic $\text{Rh}^{\text{I}}/\text{binap}$ -type bisphosphane complexes (Table 1). The reaction proceeded at 80°C to give the desired fused dihydropyran **3aa** as a single regioisomer and a single diastereomer in excellent yield and with high enantioselectivity in the presence of the catalyst $[\text{Rh}(\text{cod})_2]\text{BF}_4/(\text{R})\text{-binap}$ (10 mol %; Table 1, entry 1). The use of the sterically demanding binap-type bisphosphane ligands (*R*)-tol-binap and (*R*)-xyl-binap led to a significant decrease in the yield of **3aa** (Table 1, entries 2 and 3). Although the use of (*R*)-segphos led to an improvement in the enantioselectivity, the yield of **3aa** decreased to 58% (Table 1, entry 4). Both high yield and high enantioselectivity were observed with the ligand (*R*)- $\text{H}_8\text{-binap}$ (Table 1, entry 5).

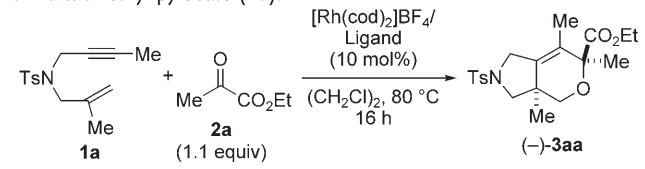
[*] Prof. Dr. K. Tanaka, Y. Otake, H. Sagae, Dr. M. Hirano
Department of Applied Chemistry, Graduate School of Engineering,
Tokyo University of Agriculture and Technology, Koganei,
Tokyo 184-8588 (Japan)
Fax: (+81) 42-388-7037
E-mail: tanaka-k@cc.tuat.ac.jp

Prof. Dr. K. Noguchi
Instrumentation Analysis Center, Tokyo University of Agriculture
and Technology, Koganei, Tokyo 184-8588 (Japan)

[**] This research was partly supported by a Grant-in-Aid for Scientific Research on Priority Areas (No. 19028015, Chemistry of Concerto Catalysis) from the Ministry of Education, Culture, Sports, Science and Technology (Japan). We thank Yusuke Aida (TUAT) for his experimental assistance and Takasago International Corporation for the gift of modified binap ligands. $\text{H}_8\text{-binap}$ = 2,2'-bis(diphenylphosphanyl)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl.

Supporting information for this article is available on the WWW under <http://www.angewandte.org> or from the author.

Table 1: Screening of ligands for the Rh-catalyzed [2+2+2] cycloaddition of **1a** with ethyl pyruvate (**2a**).

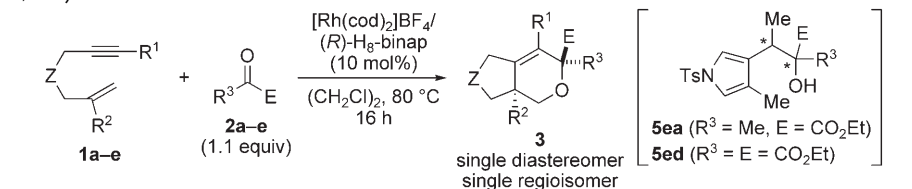


Entry	Ligand	Yield [%] ^[a]	ee [%]
1	(R)-binap	> 99	91
2	(R)-tol-binap ^[b]	22	92
3	(R)-xyl-binap ^[c]	< 10	–
4	(R)-segphos ^[d]	58	96
5	(R)-H ₈ -binap ^[e]	> 99	95

[a] Yield of the isolated product. [b] 2,2'-Bis(di-*p*-tolylphosphanyl)-1,1'-binaphthyl. [c] 2,2'-Bis(di(3,5-xylyl)phosphanyl)-1,1'-binaphthyl. [d] (4,4'-Bi-1,3-benzodioxole)-5,5'-diylbis(diphenylphosphane). [e] 2,2'-Bis(diphenylphosphanyl)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl. cod = 1,5-cyclooctadiene, Ts = *p*-toluenesulfonyl.

We then explored the scope of this process with respect to the two substrates (Table 2). Not only ethyl pyruvate (**2a**; Table 2, entry 1), but also 2,3-butanedione (**2b**; entry 3) and diethyl ketomalonate (**2d**, entry 5), underwent the desired reaction with **1a** to furnish the expected dihydropyran in high yield; however, the reaction of ethyl phenylglyoxylate (**2c**) with **1a** gave the expected dihydropyran **3ac** in low yield (Table 2, entry 4), and acetone (**2e**) failed to react with **1a**

Table 2: Rh⁺/(R)-H₈-binap-catalyzed regio-, diastereo-, and enantioselective [2+2+2] cycloaddition of 1,6-enynes **1** with ketones **2**.



Entry	1 (Z, R ¹ , R ²)	2 (R ³ , E)	3	Yield [%] ^[a]	ee [%]
1	1a (NTs, Me, Me)	2a (Me, CO ₂ Et)	(–)- 3aa	> 99	95
2 ^[b,c]	1a (NTs, Me, Me)	2a (Me, CO ₂ Et)	(–)- 3aa	91	> 99
3	1a (NTs, Me, Me)	2b (Me, Ac) ^[d]	(3 <i>R</i> ,6 <i>S</i>)-(–)- 3ab ^[e]	73	98
4	1a (NTs, Me, Me)	2c (Ph, CO ₂ Et)	(+)- 3ac	24	97
5	1a (NTs, Me, Me)	2d (CO ₂ Et, CO ₂ Et)	(–)- 3ad	89	97
6	1a (NTs, Me, Me)	2e (Me, Me) ^[f]	3ae	< 1	–
7	1b (C(CO ₂ Me) ₂ , Ar ^[g] , Me)	2a (Me, CO ₂ Et)	(+)- 3ba	49	98
8	1b (C(CO ₂ Me) ₂ , Ar ^[g] , Me)	2b (Me, Ac) ^[d]	(+)- 3bb	33	92
9 ^[b,c]	1b (C(CO ₂ Me) ₂ , Ar ^[g] , Me)	2a (Me, CO ₂ Et)	(+)- 3ba	82	> 99
10	1c (O, Ph, Me)	2a (Me, CO ₂ Et)	(+)- 3ca	67	> 99
11	1c (O, Ph, Me)	2d (CO ₂ Et, CO ₂ Et)	(+)- 3cd	64	96
12	1d (O, CO ₂ Me, Me)	2a (Me, CO ₂ Et)	(–)- 3da	17	98
13	1d (O, CO ₂ Me, Me)	2d (CO ₂ Et, CO ₂ Et)	(–)- 3dd	61	93
14 ^[b,h]	1e (NTs, Me, H)	2a (Me, CO ₂ Et) ^[d]	(–)- 3ea	25 (30 ^[i])	94
15 ^[b,h]	1e (NTs, Me, H)	2d (CO ₂ Et, CO ₂ Et) ^[d]	3ed	< 1 (70 ^[i])	– (52 ^[j])

[a] Yield of the isolated product. [b] Catalyst: 20 mol %. [c] The reaction was carried out at 25 °C in CH₂Cl₂. [d] Compound **2**: 2 equivalents. [e] The absolute configuration of (–)-**3ab** was determined by X-ray crystallographic analysis (Figure 1). [f] Acetone (**2e**) was used as both substrate and solvent. [g] Ar = 4-BrC₆H₄. [h] Ligand: (R)-binap. [i] Data for **5ea** (d.r. 2.8:1). [j] The ee value of the major diastereomer. [k] The ee value of the minor diastereomer. [l] Data for **5ed**.

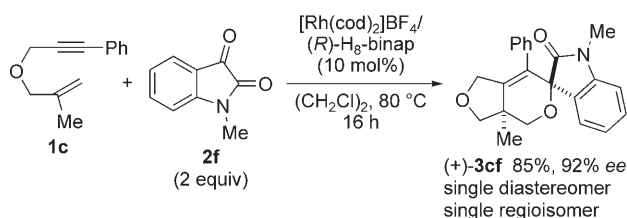
(entry 6).^[10] When the reaction of **1a** with **2a** was carried out at 25 °C with 20 mol % of the Rh catalyst, almost complete enantioselectivity was observed (Table 2, entry 2).

We found that 1,6-enynes with tosylamide (**1a**; Table 2, entries 1–5), malonate (**1b**, entries 7–9), and oxygen (**1c** and **1d**, entries 10–13) linkages could be used in the cycloaddition. With respect to the substituent R¹ at the alkyne terminus, 1,6-enynes substituted not only with methyl (**1a**; Table 2, entries 1–5), but also with phenyl and 4-bromophenyl groups (**1c** and **1b**, entries 7–11), participated in the reaction. In the case of the 4-bromophenyl-substituted 1,6-enyne **1b**, improved yield and enantioselectivity were observed when the reaction was carried out at 25 °C with 20 mol % of the Rh catalyst (Table 2, entry 9). The reaction of the methoxycarbonyl-substituted 1,6-enyne **1d** with **2a** furnished the corresponding dihydropyran **3da** in low yield as a result of the rapid [2+2+2] homocycloaddition of **1d** (Table 2, entry 12); however, when the highly electron deficient ketone **2d** was used, the corresponding dihydropyran **3dd** was obtained in good yield (entry 13). Although the 1,6-enyne **1e** with a monosubstituted alkene moiety reacted with **2a**, the alcohol **5ea** was obtained as the major product along with the expected dihydropyran **3ea** (Table 2, entry 14). Furthermore, the use of diethyl ketomalonate (**2d**) instead of **2a** led to the almost exclusive formation of the alcohol **5ed** (Table 2, entry 15).^[11,12]

We applied this regio-, diastereo-, and enantioselective [2+2+2] cycloaddition to the synthesis of the enantiomerically enriched spirocyclic compound **3cf** by using 1-methylisatin (**2f**) as the carbonyl substrate (Scheme 3).^[13] Importantly, neither the regioisomer **4** nor the other diastereomer was detected in the crude product mixture for this reaction or any of those described in Table 2. The absolute configuration of the dihydropyran product (–)-**3ab** was determined by the anomalous dispersion method (Figure 1).^[14]

Scheme 4 depicts a possible mechanism for the selective formation of the dihydropyran (3*R*,6*S*)-**3ab**: The 1,6-enyne **1a** reacts with the rhodium center of the catalyst to form the rhodacyclopentene **A** as a result of a steric interaction between the Rh-CH₂ moiety and the equatorial P-Ph group of (R)-H₈-binap. Subsequently, 2,3-butanedione (**2b**) coordinates to **A** to form complex **B**. The insertion of **2b** followed by the reductive elimination of rhodium then furnishes (3*R*,6*S*)-**3ab**.

Next, we examined the reaction of 1,6-enynes with electron-rich aryl ketones (Table 3). In analogy with



Scheme 3. Synthesis of the enantiomerically enriched spirocyclic compound (+)-3cf.

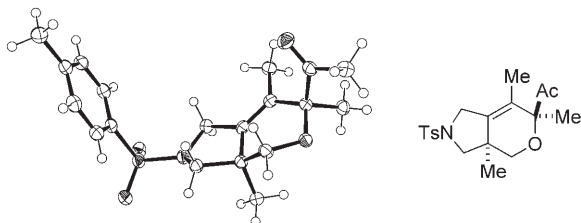
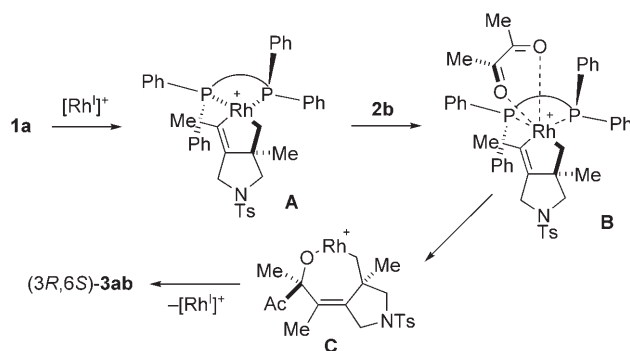


Figure 1. ORTEP drawing of (3R,6S)-(-)-3ab drawn at the 50% probability level.



Scheme 4. Possible mechanism for the selective formation of the dihydropyran (3R,6S)-3ab.

the reactions of 1,6-diynes with electron-rich aryl ketones,^[8a] when the 1,6-enyne **1e** was added over 5 min to a solution of benzophenone (**2g**) and the $[\text{Rh}(\text{cod})_2]\text{BF}_4/(\text{R})\text{-H}_8\text{-binap}$ catalyst (5 mol%) in CH_2Cl_2 at 25 °C, the *ortho*-functionalized aryl ketone **6eg** was isolated in 55% yield (Table 3, entry 1).^[15–17] Although the desired product was obtained in comparable yield when the ligand (*R*)-segphos was used (Table 3, entry 2), the use of (*R*)-binap led to a significantly lower yield of **6eg** (entry 3).^[18] These reactions proceeded with perfect regioselectivity and high enantioselectivity. Acetophenone (**2h**) also participated in the reaction with **1e** (Table 3, entry 4). Although **2i**, in which the *meta* substituent R^3 is an electron-donating group, reacted with **1f** to provide the expected product **6fi** as a single regioisomer (Table 3, entry 5), the presence of an electron-withdrawing group at the *meta* position (in **2j**) led to a complete shutdown of the reaction (entry 6). Furthermore, the 1,6-enyne **1a** with a geminally disubstituted alkene moiety failed to react with **2g**. Instead, **1a** underwent [2+2+2] homocycloaddition (Table 3, entry 7). The absolute configuration of the *ortho*-

Table 3: Rh-catalyzed regio- and enantioselective *ortho* functionalization of aryl ketones **2** with 1,6-enynes **1**.^[a]

Entry	1	2 (R^2 , R^3)	Ligand	6	Yield [%] ^[b]	ee [%]
1	1e	2g (Ph, H)	(<i>R</i>)- $\text{H}_8\text{-binap}$	(+)- 6eg	55	96
2	1e	2g (Ph, H)	(<i>R</i>)-segphos	(+)- 6eg	59	95
3	1e	2g (Ph, H)	(<i>R</i>)-binap	(+)- 6eg	26	97
4	1e	2h (Me, H)	(<i>R</i>)- $\text{H}_8\text{-binap}$	(<i>R</i>)-(+)- 6eh ^[c]	34	98
5	1f	2i (Me, OMe)	(<i>R</i>)- $\text{H}_8\text{-binap}$	(+)- 6fi	34	94
6	1f	2j (Me, CF_3)	(<i>R</i>)- $\text{H}_8\text{-binap}$	6fj	< 1	–
7	1a	2g (Ph, H)	(<i>R</i>)- $\text{H}_8\text{-binap}$	6ag	< 1	–

[a] The enyne **1** was added over a period of 5 min (see the Supporting Information). [b] Yield of the isolated product. [c] The absolute configuration of (+)-**6eh** was determined by X-ray crystallographic analysis (Figure 2).

functionalized aryl ketone (+)-**6eh** was determined by the anomalous dispersion method (Figure 2).^[14]

In conclusion, a cationic $\text{Rh}^I/(\text{R})\text{-H}_8\text{-binap}$ complex catalyzes the [2+2+2] cycloaddition of 1,6-enynes with

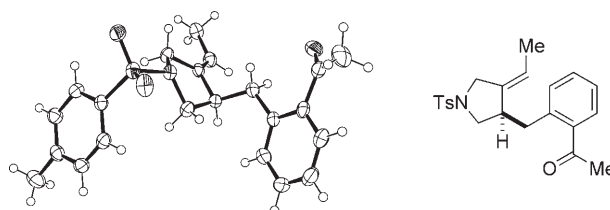


Figure 2. ORTEP drawing of (*R*)-(+)-**6eh** drawn at the 50% probability level.

electron-deficient ketones to give fused dihydropyrans containing two quaternary carbon centers with excellent regio-, diastereo-, and enantioselectivity. Electron-rich aryl ketones react with 1,6-enynes in the presence of the same catalyst to give *ortho*-functionalized aryl ketones with excellent regio- and enantioselectivity. Further studies to expand the scope of the two reactions and elucidate the reaction mechanisms are in progress.

Experimental Section

Representative procedure: (*R*)- $\text{H}_8\text{-binap}$ (18.9 mg, 0.030 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (12.2 mg, 0.030 mmol) were dissolved in CH_2Cl_2 (2.0 mL) in a Schlenk tube under an argon atmosphere, and the

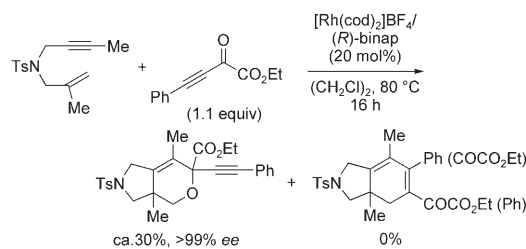
mixture was stirred at room temperature for 5 min. H_2 was introduced into the resulting solution, which was then stirred at room temperature for 0.5 h, concentrated to dryness, and dissolved in $(CH_2Cl)_2$ (0.5 mL). A solution of **1c** (55.9 mg, 0.300 mmol) and **2f** (96.7 mg, 0.600 mmol) in $(CH_2Cl)_2$ (1.5 mL) was added at room temperature, and the resulting mixture was stirred at 80 °C for 16 h. The reaction mixture was then concentrated, and the product was purified by preparative TLC (hexane/ethyl acetate 2:1) to furnish (+)-**3cf** (88.8 mg, 0.256 mmol, 85 %, 92 % ee, single diastereomer) as a pale yellow oil. $[\alpha]_D^{25} = +52.8$ deg $cm^3 g^{-1} dm^{-1}$ ($c = 2.04 \times 10^{-2}$ g cm^{-3} acetone; 92 % ee); 1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.29$ (d, $J = 7.5$ Hz, 1H), 7.20 (t, $J = 7.5$ Hz, 1H), 7.15–6.99 (m, 4H), 6.87–6.75 (m, 2H), 6.57 (d, $J = 7.5$ Hz, 1H), 4.59 (d, $J = 10.5$ Hz, 1H), 4.45 (d, $J = 13.8$ Hz, 1H), 4.09 (d, $J = 13.8$ Hz, 1H), 3.93 (d, $J = 10.5$ Hz, 1H), 3.91 (d, $J = 8.1$ Hz, 1H), 3.62 (d, $J = 8.1$ Hz, 1H), 3.00 (s, 3H), 1.58 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 175.6$, 144.3, 144.1, 135.3, 129.9, 128.7, 128.6, 128.0, 127.5, 127.2, 124.4, 122.9, 108.2, 79.1, 77.0, 69.7, 68.3, 41.4, 25.8, 23.0 ppm; IR (neat): $\tilde{\nu} = 2964$, 1715, 1090, 1052, 705 cm^{-1} ; HRMS (FAB): m/z calcd for $C_{22}H_{21}NO_3$: 380.1532; found: 380.1562 $[M+H]^+$; HPLC (chiralcel OD-H, hexane/iPrOH 90:10, 1.0 mL min^{-1}): t_R (major isomer): 8.5 min, t_R (minor isomer): 12.9 min.

Received: October 15, 2007

Published online: January 8, 2008

Keywords: asymmetric catalysis · cycloaddition · enynes · ketones · rhodium

- For recent reviews on [2+2+2] cycloaddition, see: a) B. Heller, M. Hapke, *Chem. Soc. Rev.* **2007**, 36, 1085; b) P. R. Chopade, J. Louie, *Adv. Synth. Catal.* **2006**, 348, 2307; c) V. Gandon, C. Aubert, M. Malacria, *Chem. Commun.* **2006**, 2209; d) S. Kotha, E. Brahmachary, K. Lahiri, *Eur. J. Org. Chem.* **2005**, 4741; e) Y. Yamamoto, *Curr. Org. Chem.* **2005**, 9, 503; f) J. A. Varela, C. Saá, *Chem. Rev.* **2003**, 103, 3787; g) N. Agenet, O. Buisine, F. Slowinski, V. Gondon, C. Aubert, M. Malacria, *Organic Reactions*, Vol. 68 (Ed.: L. E. Overman), Wiley, Hoboken, **2007**, p. 1.
- For the use of stoichiometric Co reagents, see: a) D. F. Harvey, B. M. Johnson, C. S. Ung, K. P. C. Vollhardt, *Synlett* **1989**, 15; b) R. Gleiter, V. Schehlmann, *Tetrahedron Lett.* **1989**, 30, 2893; for the use of stoichiometric zirconacyclopentadienes, see: c) T. Takahashi, Y. Li, T. Ito, F. Xu, K. Nakajima, Y. Liu, *J. Am. Chem. Soc.* **2002**, 124, 1144.
- For pioneering work on Ni catalysis, see: a) T. Tsuda, T. Kiyoi, T. Miyane, T. Saegusa, *J. Am. Chem. Soc.* **1988**, 110, 8570; for the use of Ni^0 /imidazolyldiene complexes, see: b) T. N. Tekevac, J. Louie, *Org. Lett.* **2005**, 7, 4037; for the Ni-catalyzed [4+2+2] cycloaddition of 1,6-diynes with cyclobutanones, see: c) M. Murakami, S. Ashida, T. Matsuda, *J. Am. Chem. Soc.* **2006**, 128, 2166.
- For pioneering work on Ru catalysis, see: a) Y. Yamamoto, H. Takagishi, K. Itoh, *J. Am. Chem. Soc.* **2002**, 124, 6844; for the Ru^{II} -catalyzed hydrative cyclization and [4+2] cycloaddition of yne-enones, see: b) B. M. Trost, R. E. Brown, F. D. Toste, *J. Am. Chem. Soc.* **2000**, 122, 5877.
- For the $[Rh(cod)Cl]_2$ -catalyzed intramolecular [2+2+2] cycloaddition of diynals (cod = 1,5-cyclooctadiene), see: a) B. Ben-nacer, M. Fujiwara, S.-Y. Lee, I. Ojima, *J. Am. Chem. Soc.* **2005**, 127, 17756; for a Rh^+ /biphenyl-catalyzed carbonyl Z dienylations involving carbonyl insertion into cationic rhodacyclopentadienes (biphenyl = 2,2'-bis(diphenylphosphanyl)-1,1'-biphenyl), see: b) J. R. Kong, M. J. Krische, *J. Am. Chem. Soc.* **2006**, 128, 16040.
- For recent reviews of catalytic asymmetric methods for the generation of quaternary carbon centers, see: a) B. M. Trost, C. Jiang, *Synthesis* **2006**, 369; b) C. J. Douglas, L. E. Overman, *Proc. Natl. Acad. Sci. USA* **2004**, 101, 5363; c) I. Denissova, L. Barriaud, *Tetrahedron* **2003**, 59, 10105.
- For the Au-catalyzed diastereoselective intermolecular addition of carbonyl compounds to 1,6-enynes to give fused [5,5] ring systems, see: M. Schelwies, A. L. Dempwolff, F. Rominger, G. Helmchen, *Angew. Chem.* **2007**, 119, 5694; *Angew. Chem. Int. Ed.* **2007**, 46, 5598.
- a) K. Tanaka, Y. Otake, A. Wada, K. Noguchi, M. Hirano, *Org. Lett.* **2007**, 9, 2203; a similar publication appeared soon afterwards: b) K. Tsuchikama, Y. Yoshinami, T. Shibata, *Synlett* **2007**, 1395.
- For selected reports by our research group of [2+2+2] cycloaddition reactions of alkynes under the catalysis of cationic Rh^I /modified-binap complexes, see: a) K. Tanaka, K. Shirasaka, *Org. Lett.* **2003**, 5, 4697; b) K. Tanaka, G. Nishida, A. Wada, K. Noguchi, *Angew. Chem.* **2004**, 116, 6672; *Angew. Chem. Int. Ed.* **2004**, 43, 6510; c) K. Tanaka, K. Toyoda, A. Wada, K. Shirasaka, M. Hirano, *Chem. Eur. J.* **2005**, 11, 1145; d) K. Tanaka, K. Takeishi, K. Noguchi, *J. Am. Chem. Soc.* **2006**, 128, 4586; e) K. Tanaka, H. Sagae, K. Toyoda, K. Noguchi, M. Hirano, *J. Am. Chem. Soc.* **2007**, 129, 1522; f) G. Nishida, K. Noguchi, M. Hirano, K. Tanaka, *Angew. Chem.* **2007**, 119, 4025; *Angew. Chem. Int. Ed.* **2007**, 46, 3951, and references therein; for similar reactions of nitriles, see: g) K. Tanaka, N. Suzuki, G. Nishida, *Eur. J. Org. Chem.* **2006**, 3917; h) A. Wada, K. Noguchi, M. Hirano, K. Tanaka, *Org. Lett.* **2007**, 9, 1295; for similar reactions of isocyanates and isothiocyanates, see: i) K. Tanaka, A. Wada, K. Noguchi, *Org. Lett.* **2005**, 7, 4737; j) K. Tanaka, A. Wada, K. Noguchi, *Org. Lett.* **2006**, 8, 907; for similar reactions of alkenes, see: k) K. Tanaka, G. Nishida, H. Sagae, M. Hirano, *Synlett* **2007**, 1426.
- We investigated the chemoselectivity of the present cycloaddition with respect to the reactivity of a carbonyl group in the presence of an alkyne moiety and found that the carbonyl group of an alkynyl ketoester reacted with a 1,6-enyne, although the cycloadduct could not be isolated in pure form. For the [2+2+2] cycloaddition of 1,6-enynes with monoalkynes under the catalysis of cationic complexes of Rh^I with modified binap ligands, see: a) P. A. Evans, K. W. Lai, J. R. Sawyer, *J. Am. Chem. Soc.* **2005**, 127, 12466; b) T. Shibata, Y. Arai, Y. Tahara, *Org. Lett.* **2005**, 7, 4955.



- When the ligand (*R*)-binap was used, the cycloaddition products were obtained in higher yields than with (*R*)-H₈-binap.
- Similar heterocycle formation during the transition-metal-catalyzed cycloisomerization of enynes was reported; for Ru, see: a) M. Mori, Y. Kozawa, M. Ishida, M. Kanamaru, K. Onozuka, M. Takimoto, *Org. Lett.* **2000**, 2, 3245; for Co, see: b) O. Buisine, C. Aubert, M. Malacria, *Chem. Eur. J.* **2001**, 7, 3517; for Rh, see: c) H. Kawai, S. Oi, Y. Inoue, *Heterocycles* **2006**, 67, 101; d) K. Tanaka, Y. Otake, M. Hirano, *Org. Lett.* **2007**, 9, 3953.
- For the synthesis of chiral spirocyclic compounds through a [2+2+2] cycloaddition catalyzed by a cationic Rh^I /modified-binap complex, see: K. Tsuchikama, Y. Kuwata, T. Shibata, *J. Am. Chem. Soc.* **2006**, 128, 13686.

- [14] CCDC-662606 (**3ab**) and CCDC-662607 (**6eh**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [15] For the Rh- or Ir-catalyzed dienylation of aromatic C–H bonds with alkynes, see: a) M. C. Comstock, J. R. Shapley, *Organometallics* **1997**, *16*, 4816; b) J. Müller, T. Akhnoukh, P. Escarpa Gaede, A. Guo, P. Moran, K. Qiao, *J. Organomet. Chem.* **1997**, *541*, 207; c) S. A. Gardner, P. S. Andrews, M. D. Rausch, *Inorg. Chem.* **1973**, *12*, 2396.
- [16] For the Co-mediated dienylation of aromatic C–H bonds with alkynes, see: a) C. Aubert, P. Betschmann, M. J. Eichberg, V. Gandon, T. J. Heckrodt, J. Lehmann, M. Malacria, B. Masjost, E. Paredes, K. P. C. Vollhardt, G. D. Whitener, *Chem. Eur. J.* **2007**, *13*, 7443; b) H. Pelissier, J. Rodriguez, K. P. C. Vollhardt, *Chem. Eur. J.* **1999**, *5*, 3549; c) R. Boese, D. F. Harvey, M. J. Malaska, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1994**, *116*, 11153; d) D. B. Grotjahn, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1986**, *108*, 2091; e) Y. Wakatsuki, H. Yamazaki, *J. Organomet. Chem.* **1978**, *149*, 385; f) H. Yamazaki, Y. Wakatsuki, *J. Organomet. Chem.* **1978**, *149*, 377; for theoretical studies, see: g) C. Aubert, V. Gandon, A. Geny, T. J. Heckrodt, M. Malacria, E. Paredes, K. P. C. Vollhardt, *Chem. Eur. J.* **2007**, *13*, 7466; h) V. Gandon, N. Agenet, K. P. C. Vollhardt, M. Malacria, C. Aubert, *J. Am. Chem. Soc.* **2006**, *128*, 8509.
- [17] For selected examples of the Rh-catalyzed chelation-assisted intermolecular hydroarylation of alkynes and alkenes, see: a) J. C. Lewis, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2007**, *129*, 5332; b) C.-H. Jun, C. W. Moon, J.-B. Hong, S.-G. Lim, K.-Y. Chung, Y.-H. Kim, *Chem. Eur. J.* **2002**, *8*, 485; c) C. P. Lenges, M. Brookhart, *J. Am. Chem. Soc.* **1999**, *121*, 6616; d) U. R. Aulwurm, J. U. Melchinger, H. Kisch, *Organometallics* **1995**, *14*, 3385, and references therein.
- [18] Recently, the *ortho* functionalization of aryl ketones with 1,6-enynes in the presence of a cationic Rh^I/(*R*)-binap catalyst was reported. However, the use of (*R*)-binap required the very slow addition (over a period of 30 min) of the enyne substrate; furthermore, neither the absolute configuration of the product nor electronic effects on the reaction were determined: K. Tsuchikama, Y. Kuwata, Y. Tahara, Y. Yoshinami, T. Shibata, *Org. Lett.* **2007**, *9*, 3097.