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[10] In the deprotonated form, *trans*-[$Os^{IV}(tpy)(Cl)_2(NSC_6H_3Me_2)$], the angle Os1-N1-S1 (129.5(2)°) and bond Os1-N1 (1.890(3) Å) are relatively unchanged while there are significant changes in the angle N1-S1-C41 (104.3(2)°), and the bonds N1-S1 (1.596(4) Å), and S1-C41 (1.784(4) Å cf. with Os1-Cl1 (2.4139(10), Os1-Cl_2 (2.4007(10), Os1-N11 (2.057(3), Os1-N21 (2.012(3), Os1-N31 (2.065(3)) Å in [**1A**]$^+$). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-141160 (**1A**) and -149866. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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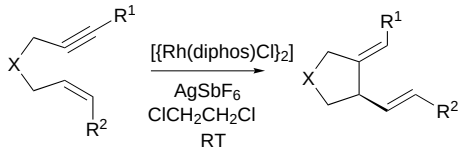
The First Highly Enantioselective Rh-Catalyzed Enyne Cycloisomerization**

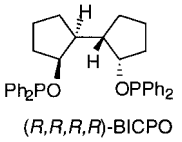
Ping Cao and Xumu Zhang*

The development of efficient asymmetric cyclizations is of great interest in organic synthesis due to the existence of many biologically active and naturally occurring cyclic compounds.[1] However, efficient enantioselective transition metal catalyzed cyclization reactions are rare and remain relatively unexplored.[2, 3] In contrast, the racemic variants of these reactions have been extensively studied. For example, transition metal catalyzed cycloisomerization of 1,6-enynes have been explored in depth.[4] An asymmetric variant of this transformation would be significant for the synthesis of enantiomerically pure five-membered carbo- and heterocycles. So far, only limited progress has been made in this important enantioselective transformation.[5] We reasoned that a key to developing such highly enantioselective metal-catalyzed reaction is to find a highly active catalyst for cycloisomerization under mild conditions. Recently, we made a significant advance in developing the first Rh^I-catalyzed enyne cycloisomerization reaction at room temperature. Excellent chemo-, regio-, and diastereoselectvities were achieved (Scheme 1).[6] Here we report on the first asymmetric Rh-catalyzed enyne cycloisomerizations facilitated by Rh^I



Scheme 1. Rh-catalyzed enyne cycloisomerization.

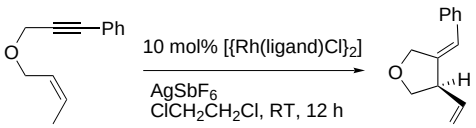
complexes with Me-DuPhos (DuPhos = 1,2-bis(phospholano)benzene),[7] BICP (2*R*,2′*R*)-bis(diphenylphosphanyl)-(1*R*,1′*R*)-dicyclopentane (**1**) [8] and the phosphinite (*R*,*R*,*R*,*R*)-BICPO ligands.[9]



(*R*,*R*,*R*,*R*)-BICPO

Using some commercially available chiral phosphane ligands and ligands developed in our laboratory, we screened the asymmetric enyne cycloisomerization reaction with **1a** as a prototypical substrate (Table 1). The highest *ee* was achieved with a Rh/Me-DuPhos catalyst, while no reactivity was observed with a Rh/BINAP system (BINAP = 2,2′-bis(diphenylphosphanyl)-1,1′-dinaphthyl). We found that both the activity and enantioselectivity of this asymmetric

Table 1. Ligand effects on Rh-catalyzed enantioselective enyne cycloisomerization [Eq. (1)].[a]



1a **2a** (1)

Entry	Ligand	Conversion [%][b]	*ee* [%][c]
1	Me-DuPhos	100	95
2	Et-DuPhos	< 5	63
3	BICP	100	74
4	Me-PennPhos	100	71
5	BINAP	0	–
6	Et-BPE	< 5	5

[a] All reactions were carried out with 10 mol% [{Rh(ligand)Cl}$_2$] in $ClCH_2CH_2Cl$ with 0.1 M enyne substrate at room temperature for 2 – 12 h. The cationic Rh^I catalyst was generated by adding $AgSbF_6$ to the solution of [{Rh(ligand)Cl}$_2$] in the presence of the substrate. [b] Conversion was determined by GC. [c] The *ee* was determined by GC on a 15 m Supelco β-390 column with a chiral phase.

C–C bond-forming reaction are sensitive to the structure of the chiral ligand. For example, both activity and enantioselectivity were low with the Et-BPE (BPE = 1,2-bis(phospholano)ethane) ligand, and the enantioselectivity dropped significantly on changing from Me-DuPhos to Et-DuPhos. Good enantioselectivities were also obtained with BICP and Me-PennPhos (Me-PennPhos = *P*,*P*′-1,2-diphenylenebis(endo-2,5-dimethyl-7-phosphabicyclo[2.2.1]heptane).

On the basis of these results, Me-DuPhos was selected as the preferred ligand for the Rh-catalyzed cycloisomerization of **1a**. We found that the optimal catalyst loading for achieving high reactivity and enantioselectivity is 5 – 10 mol%. The cationic Rh^I catalyst must be generated in situ by adding one equivalent of $AgSbF_6$ to the reaction mixture after the substrate has been introduced. Higher catalyst loading

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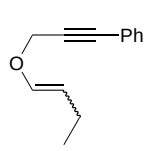

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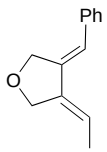

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(>20 mol%) leads to the formation of the rearrangement product **3**. After the substrate was consumed, the desired 1,4-diene **2a** isomerized to the more stable conjugated 1,3-diene **4** in the presence of the Rh^I catalyst. Therefore, the reaction was usually quenched as soon as the substrates were consumed to avoid this isomerization reaction.

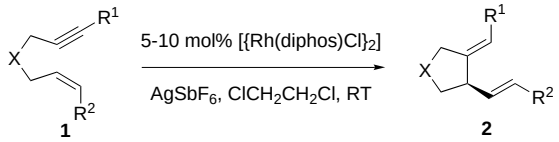
Under the optimal reaction conditions, a variety of enyne substrates **1** were tested for cycloisomerization with Rh/Me-DuPhos, Rh/BICP, and Rh/BICPO catalysts (Table 2). For those substrates with an aryl terminal group on the acetylene (**1a**–**1f**), enantioselectivities achieved with Me-DuPhos were typically higher than those obtained with BICP (Table 2, entries 1–11). However, when R^1 was an alkyl or cyclic alkyl group, no reaction occurred with the Rh/Me-DuPhos catalyst. On the other hand, enantioselectivities with the Rh/BICP catalyst were excellent (Table 2, entries 12–15). Therefore, it appears that the Rh-catalyzed asymmetric enyne isomerization is highly sensitive to subtle variations in substrate substituents. While the detailed reasons for this observation are unknown, a possible explanation is that this catalyst system is responsive to the electronic nature of the ligands and substrates.[6] For the electron-donating Me-DuPhos system, enyne substrates with aryl groups on the acetylenic terminal are better π acceptors than those with alkyl groups in this position. Higher reactivities and enantioselectivities were observed with less electron-donating substrates (Table 2, entry 4 vs entry 10). For a more electron-donating enyne substrate bearing an alkyl group on the acetylenic terminal, the strong *trans* effect of an electron-donating phosphane (i.e., Me-DuPhos) may prevent strong bonding of the enyne to Rh and thus inhibit the subsequent oxidative cyclization. However, enynes with alkyl groups on the acetylenic terminal may confer the right electronic properties for enyne binding and oxidative cyclization when a less electron-donating phosphane (e.g., BICP) is used. These subtle changes in activities and enantioselectivities indicate that screening of a variety of chiral chelating ligands is needed to identify a highly active and enantioselective enyne cycloisomerization catalyst for a given substrate. A further demonstration of this substrate dependence is illustrated by cycloisomerization of enynes bearing a nitrogen linker (**1i**–**1k**). A phosphinite-modified Rh catalyst (BICPO/Rh) successfully facilitated the cyclization and gave good enantioselectivities (69–82% *ee*, Table 2, entries 16–18), while Rh/Me-DuPhos and Rh/BICP catalysts were inactive for these transformations.

In conclusion, we have developed the first highly enantioselective Rh-catalyzed enyne cycloisomerization reaction. This asymmetric C–C bond-forming reaction is highly substrate dependent. Our future studies will focus on expanding the substrate scope and exploring the synthetic utility of this asymmetric reaction.

Experimental Section

[{Rh(BICP)Cl}$_2$]: BICP (0.3 g, 0.6 mmol) was added to [Rh(C_8H_{12})Cl]$_2$ (0.15 g, 0.3 mmol) in deoxygenated toluene (5.0 mL) at room temperature. The mixture was stirred for 5 h, and then hexane (4 mL) was added. The solution was cooled to −78 °C for 1 h. Orange crystals formed and were collected by filtration and washed with hexane (6 × 15 mL) to give [{Rh(BICP)Cl}$_2$] (0.22 g, 85% yield). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 8.52 (br s, 8H), 7.42 (m, 8H), 7.14 (m, 8H), 7.08 (m, 8H), 6.88 (m, 8H),

Table 2. Rhodium-catalyzed enantioselective cycloisomerization of 1,6-enynes [Eq. (2)].[a]



1 2 (2)

Entry	Substrate	X	R^1	R^2	Ligand	Cat. loading [mol%]	Time [h]	Yield [%]	*ee* [%] (config.)[b]
1	**1a**	O	Ph	Me	(*R*,*R*)-Me-DuPhos	5	2	62	96 (−)
2					(*R*,*R*,*R*,*R*)-BICP	5	2	73	74 (−)
3					(*R*,*R*,*R*,*R*)-BICPO	10	1.5	81	65 (+)
4	**1b**	O	C_6H_4(*p*-Me)	Me	(*R*,*R*)-Me-DuPhos	10	4	38	77 (−)
5					(*R*,*R*,*R*,*R*)-BICP	10	7	58	87 (−)
6	**1c**	O	C_6H_4(*p*-Cl)	Me	(*R*,*R*)-Me-DuPhos	5	2	60	95 (−)
7					(*R*,*R*,*R*,*R*)-BICP	10	0.25	24	83 (−)
8	**1e**	O	C_6H_4(*m*-Cl)	Me	(*R*,*R*)-Me-DuPhos	10	0.5	68	93 (−)
9					(*R*,*R*,*R*,*R*)-BICP	10	7	39	79 (−)
10	**1f**	O	C_6H_4(*p*-CF_3)	Me	(*R*,*R*)-Me-DuPhos	5	1	60	96 (−)
11					(*R*,*R*,*R*,*R*)-BICP	10	7	47	91 (−)
12	**1g**	O	cyclopentyl	Me	(*R*,*R*)-Me-DuPhos	10	12	–	–
13					(*R*,*R*,*R*,*R*)-BICP[c]	5	2	43	95 (−)
14	**1h**	O	C_4H_9	Me	(*R*,*R*)-Me-DuPhos	10	12	–	–
15					(*R*,*R*,*R*,*R*)-BICP	5	1	67	98 (−)
16	**1i**	$PhSO_2N$	Me	Me	(*R*,*R*,*R*,*R*)-BICPO	3	13	98	82 (−)
17	**1j**	$PhSO_2N$	Et	Me	(*R*,*R*,*R*,*R*)-BICPO	3	13	99	80 (−)
18	**1k**	$PhSO_2N$	Me	Et	(*R*,*R*,*R*,*R*)-BICPO	3	13	99	69 (−)

[a] All reactions were carried out in $ClCH_2CH_2Cl$ at room temperature with 0.2 mmol substrate at 0.1 M concentration. [{Rh(diphos)Cl}$_2$]/$AgSbF_6$ = 1/1 (diphos = 1,2-bis(diphenylphosphanyl) ethane). $AgSbF_6$ was added to the solution of [{Rh(diphos)Cl}$_2$] after the substrate had been added. [b] The *ee* value was determined by GC on a Supelco β-390 column with a chiral phase and by HPLC. [c] $AgPF_6$ was used.

2.56 (m, 8H), 0.76–1.16 (m, 24H); ^{13}C NMR (90 MHz, $CDCl_3$): $\delta = 21.92$, 24.51, 30.07, 30.47, 32.93, 45.52, 126.02, 127.46, 127.91, 127.99, 128.94, 129.75, 130.67, 133.01, 137.92; ^{31}P NMR (145 MHz, $CDCl_3$): $\delta = 47$ (d, $J = 187$ Hz).

General method for enyne cycloisomerization: The enyne (0.4 mmol), [{Rh(BICP)Cl}$_2$] (5 mol%), and $ClCH_2CH_2Cl$ (2 mL) were introduced into a 25-mL Schlenk tube in a glovebox. The mixture was stirred for 1 min. To this mixture $AgSbF_6$ (5 mol%) was added, and a precipitate was observed. The mixture was stirred at room temperature, and the course of the reaction was monitored by TLC. The cyclization was normally complete within 2–6 h. The crude mixture was diluted with diethyl ether and filtered to remove silver chloride before purification by flash chromatography.

1e: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.20$ (m, 1H), 7.11 (m, 1H), 7.06 (m, 1H), 6.95 (m, 1H), 6.14 (m, 1H), 5.63 (m, 1H), 5.18 (m, 1H), 5.14 (m, 1H), 4.50–4.63 (m, 2H), 4.06 (dd, $J = 7.4$, 7.4 Hz), 3.49 (dd, $J = 8.4$, 8.4 Hz), 3.42 (m, 1H); ^{13}C NMR (90 MHz, $CDCl_3$): $\delta = 51.20$, 70.61, 72.74, 118.41, 121.32, 126.33, 127.12, 128.35, 130.12, 134.12, 136.72, 139.34, 145.92. MS: *m/z*: 220 [M^+]; HRMS (APCI) calcd for $C_{14}H_{13}ClO$ [M^++H]: 221.0733; found: 221.0724.

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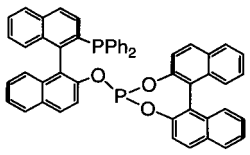
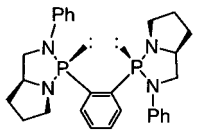
Rhodium-Mediated Asymmetric Hydroformylation with a Novel Bis(diazaphospholidine) Ligand**

Simon Breeden, David J. Cole-Hamilton, Douglas F. Foster, Gary J. Schwarz, and Martin Wills*

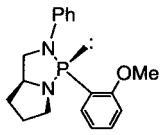
Asymmetric catalytic hydroformylation of alkenes is one of the most efficient and atom-economic of all the known processes for the synthesis of high-value chiral compounds. In one step, three readily available components (alkene, carbon monoxide, hydrogen) are combined in a C–C bond-forming process with no by-products other than unconverted reagents.[1] Asymmetric hydroformylation of vinyl acetate would convert this inexpensive bulk chemical in one step into a three-carbon synthetic building block which could be employed as an intermediate for the synthesis of many more complex molecules. Despite the scientific and commercial attractiveness of this process, few efficient catalysts are available for this reaction. Of those reported to date, BINAPHOS (**1**) and the closely related BIPHEMPHOS (**8**) are among the most efficient (Scheme 1).[2] As little as 0.20–0.25 mol% of a Rh^I complex of **1** facilitates the asymmetric



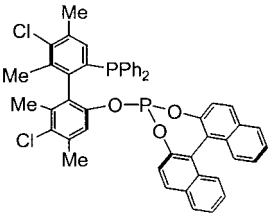
(*R*,*S*)-BINAPHOS (**1**)



ESPHOS (**6**)



SEMI-ESPHOS (**7**)



(*S*,*R*)-BIPHEMPHOS (**8**)

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Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

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