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**Electronic and Steric Effects of Atropisomeric Ligands SYNPHOS[®],
and DIFLUORPHOS[®] vs BINAPs in Rh(I)-Catalyzed Asymmetric
Pauson-Khand Reaction†**

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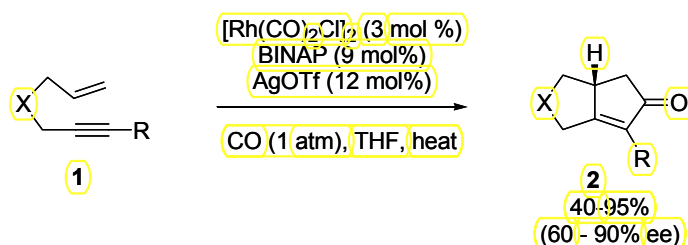
Abstract: The electronic and steric effects of chiral biaryl diphosphine ligands on the Rh(I) catalyzed asymmetric Pauson-Khand type reaction were examined. We demonstrated that enantioselectivity and reaction yield were influenced by the electronic density on phosphorus, the dihedral angle of ligands and the electronic density of the alkyne substrate. Ligands bearing a narrower dihedral angle than Binap, such as Synphos (L4) and Difluorphos (L5), were found to increase substantially the enantioselectivity of the reaction, compared to Binap-type ligands. Ligands having deshielded phosphine, such as *p*-CF₃-Binap (L3) and Difluorphos (L5) provided better enantioselectivity than Binap, with reduced formation of side products, especially with electron-poor alkyne substrates.

Key Words; Pauson-Khand reaction, enantioselective, atropisomeric ligands, electronic effects, steric effects

Introduction

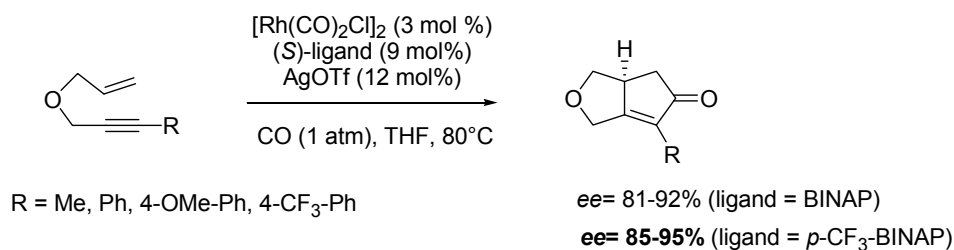
In recent years, a great deal of research has been devoted to the asymmetric catalytic Pauson-Khand reaction (denoted as the PKR hereafter),¹ which is defined as the transition metal mediated [2+2+1] cycloaddition of an alkyne, an alkene and CO.² Various versions of the enantioselective PK type reaction using cobalt,³ titanium,⁴ rhodium⁵ and iridium⁶ together with chiral ligands have been published.³ Several years ago, we described the first rhodium catalyzed enantioselective PKR under a CO atmosphere in the presence of an atropisomeric ligand (Scheme 1).⁵ These early results were promising in terms of enantioselectivity, but they also exhibited some limitations with certain classes of substrates.

Efforts to optimize this methodology were reported,⁷ but improvements in terms of enantioselectivity and chemical yield still need to be realized. In a previous paper,⁸ we performed a systematic screening of twelve different classical PKR 1,6-enyne substrates and six



Scheme 1. The Rh(I) catalyzed asymmetric PKR

Binap-type ligands displaying different electronic properties. Accurate interpretation of the results showed a clear tendency: for a given Binap ligand, the more electron-rich the alkyne, the better the enantioselectivity (but the lower the yield); for a given substrate, the more electron-poor the Binap ligand, the higher the enantioselectivity (almost no influence on the yield). Especially enantioselectivities obtained with *p*-CF₃-Binap ligand, bearing a far lower electronic density on phosphorus than Binap, were 2 to 5% higher than those obtained with Binap, as shown on Scheme 2.



Scheme 2.

In the present study, we wished to get a deeper insight in designing an optimized Rh(I)/ligand catalyst for enantioselective PKR under CO atmosphere, by evaluating the performance of Synphos⁹ and Difluorphos¹⁰ ligands in this reaction, comparatively to Binap family ligands.

Results and Discussion

We have eliminated our mechanistic proposition from here. Instead, we wish to describe our previous results.



The biaryl diphosphine ligands used in this study were chosen to permit distinct examination of their steric and electronic influence on the stereochemical outcome of the

reaction. Binap ligand (**L2**) was chosen as reference. *p*-OMe-Binap (**L1**) and *p*-CF₃-Binap (**L3**) ligands were selected because they have geometric properties similar to Binap, but different electronic features. Synphos (**L4**) and Difluorophos (**L5**) ligands proved to give better selectivities than Binap in several enantioselective transition-metal catalyzed reactions of C-H¹⁰ or C-C¹¹ bond formation, using Ru, Rh or Ag catalysts. As far as Ru(II)-mediated asymmetric hydrogenation of prochiral α - or β -ketoesters is concerned, we showed in a previous study^{10b} that a smaller dihedral angle (θ in Figure 1) of the biaryl backbone in the geometrical structure of **L4** and **L5** was responsible for their better performance in this particular reaction, compared to Binap. Thus we wished to evaluate the influence of steric and electronic properties of these five ligands **L1-L5** on the yield and enantioselectivity in Rh-mediated PKR.

The quantification of steric properties of atropisomeric diphosphines is conveniently achieved by measuring the dihedral angle θ of the biaryl backbone using Molecular Modeling techniques, as shown in Table 1. Although the biaryl moiety is a flexible backbone, allowing atropisomeric ligands to adapt their geometrical structure to the coordination sphere of the metal, the relative order of θ for **L1-L5** is independent of the type of molecular structure containing the diphosphine (free ligand, Pd or Rh complexes): $\theta(\mathbf{L1}) \sim \theta(\mathbf{L2}) \sim \theta(\mathbf{L3}) > \theta(\mathbf{L4}) > \theta(\mathbf{L5})$. The tetraoxygenated biaryl core of Synphos (**L4**) and Difluorophos (**L5**) confers to these ligands a narrower dihedral angle than binaphthyl-based diphosphines **L1**, **L2** and **L3**.

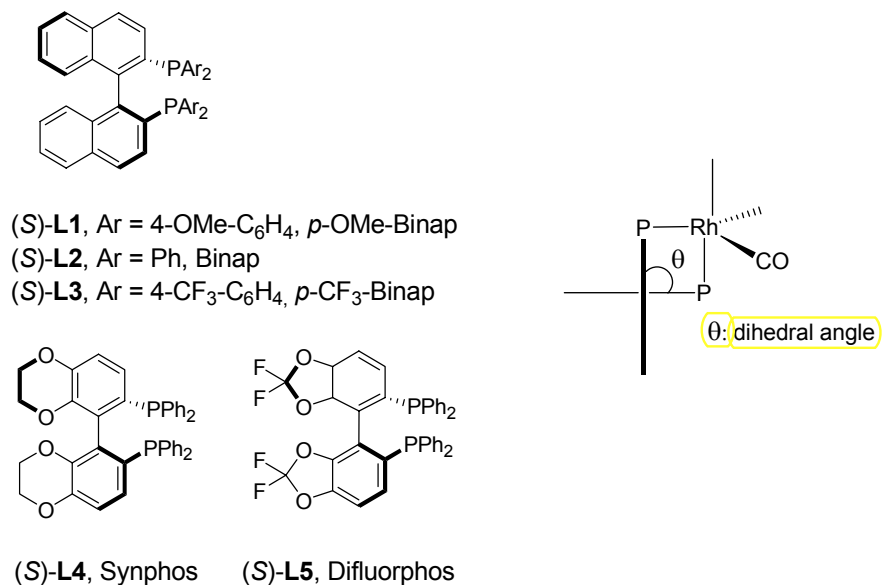


Figure 1. The ligands used in this study.

Ligand (L*)	dihedral angle of free ligand ^b	Dihedral angle of ligand (L*) in [PdCl ₂ (L*)] ^a	Dihedral angle of ligand (L*) in [RhCl(CO)(L*)] ^a
L1 <i>p</i> -OMe-Binap	85.2	79.2	78.3
L2 Binap	86.2	79.2	78.3
L3 <i>p</i> -CF ₃ -Binap	83.8	79.0	78.0
L4 Synphos	70.7	73.6	73.0
L5 Difluorphos	67.6	73.0	72.2

a. Structures minimized by Molecular Mechanics calculations (CACHÉ MM2 program)¹²

Table 1. Steric properties of biaryl diphosphine ligands **L1-L5**
 (key steric parameter = dihedral angle of biaryl backbone θ)

Regarding the comparative electronic profiles of the diphosphines **L1-L5**, this can be evaluated by several described methods.¹³ First we quantified the electronic density on phosphorus through ³¹P NMR spectra of free ligands (Table 2): the higher the ³¹P chemical shift, the more electron-poor the ligand. Synphos (**L4**) and Binap (**L2**) free ligands seem to have similar electronic properties (-14.3 and -14.4 ppm respectively), *p*-CF₃-Binap (**L3**) and

Difluorphos (**L5**) reveal a less basic profile than Binap (-13.8 and -12.5 ppm respectively), Difluorphos (**L5**) being the most electron-poor ligand of the series. As expected, *p*-OMe-Binap **L1** is the most electron-rich ligand of the series, displaying a chemical shift of -16.9 ppm. In order to complete this electronic evaluation with data relative to chelated diphosphines, we synthesized the [Rh(CO)Cl(ligand)] complexes according to reported procedure^{13b} and evaluated the IR stretching frequency of carbonyl ligand in these complexes for **L1** through **L5**: the higher the frequency, the higher the π -acidic character of the chelated diphosphine. As reported in Table 2, the five diphosphines ordered by decreasing π -acidity are as follows: *p*-CF₃-Binap (**L3**, $\nu(\text{CO}) = 2022\text{cm}^{-1}$) > Difluorphos (**L5**, $\nu(\text{CO}) = 2014\text{cm}^{-1}$) > Binap (**L2**, $\nu(\text{CO}) = 2003\text{cm}^{-1}$) > Synphos (**L4**, $\nu(\text{CO}) = 2000\text{cm}^{-1}$) > *p*-OMe-Binap (**L1**, $\nu(\text{CO}) = 1998\text{cm}^{-1}$). These results confirm that Lewis acidity of the catalyst is not a merely a reflection of electronic effects, instead it is influenced by geometrical factors as well. Thus, Synphos **L4** makes the catalyst more Lewis-basic than Binap when chelated to a transition metal, whereas *p*-CF₃-Binap **L3** and Difluorphos **L5** are far more electron-poor.



Ligand (L*)	NMR chemical shift of ³¹ P (CDCl ₃) (δ , ppm)	IR carbonyl stretching frequency in [RhCl(CO)(L*)] from THF ($\nu(\text{CO})$, cm ⁻¹) ^a
L1 <i>p</i> -OMe-Binap	-16.9	1998
L2 Binap	-14.4	2003
L3 <i>p</i> -CF ₃ -Binap	-13.8	2022
L4 Synphos	-14.3	2000
L5 Difluorphos	-12.5	2014

^a. This parameter quantifies the electronic donor-acceptor properties of the diphosphine ligand (L*) when chelated to a transition metal: the higher the carbonyl stretching frequency, the higher the π -acidic character of the diphosphine.^{13b}

Table 2. Electronic properties of biaryl diphosphine ligands **L1-L5**

Figure 2 summarizes the comparative steric and electronic profiling of ligands **L1-L5**: two ligands (*p*-OMe-Binap **L1** and Synphos **L4**) are more electron-rich than Binap (**L2**); whereas geometric properties of **L1** are identical to Binap, Synphos **L4** bears a narrower dihedral angle than Binap, making the steric hindrance of diphenylphosphino groups around the metal more important. The two remaining diphosphines **L3** (*p*-CF₃-Binap) and **L5** (Difluorpos) are both more electron-poor than Binap but display different steric features: dihedral angle of Difluorpos (**L5**) is narrower than Binap (**L2**) and *p*-CF₃-Binap (**L3**).

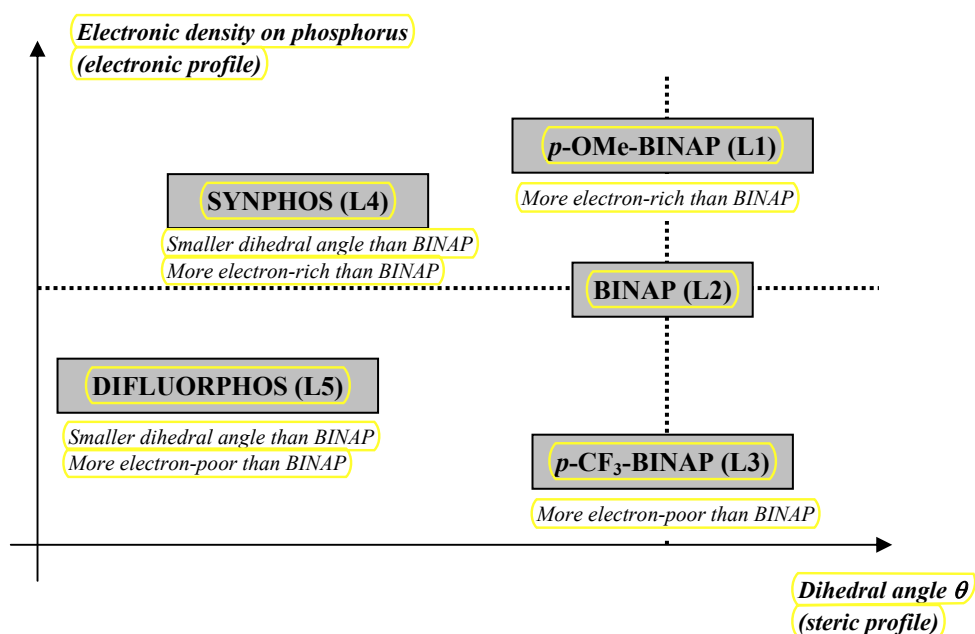
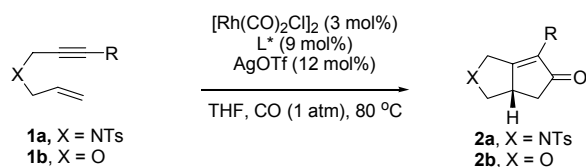


Figure 2. Comparative stereoelectronic profiles of ligands **L1-L5**



Having in hand quantitative steric and electronic evaluation of the diphosphine ligands **L1** to **L5**, we investigated their performances as chiral inductors in asymmetric Rh-mediated PKR under CO atmosphere. Representative substrates for the study were selected in order to reflect

the effects of electronic character on alkynes. These can be divided into the alkyl-substituted alkynes (**1a-1** and **1b-1**) and the aryl-substituted alkynes, which were further differentiated electronically by the substituents on the *para* position of the phenyl ring (**1a-2**, **1a-3**, **1a-4** for *N*-tosyl tethered substrates and **1b-2**, **1b-3** and **1b-4** for *O*-tethered substrates). A typical reaction was carried out with catalyst prepared by mixing tetracarbonyldi- μ -chlorodirhodium $\{[\text{Rh}(\text{CO})_2\text{Cl}]_2\}$ and selected diphosphine ligand in tetrahydrofuran for 30 minutes at ambient temperature under an argon atmosphere. The substrate was introduced into the mixture, the argon atmosphere was replaced by carbon monoxide (1 atm) and the mixture was heated to 80 °C until complete conversion of starting material. The results are summarized in Table 3.



entry	ligand	R	Me (1)			4-MeOC ₆ H ₄ (2)			C ₆ H ₅ (3)			4-CF ₃ C ₆ H ₄ (4)			
		X	<i>t</i> ^c (h)	yield (%)	ee (%) ^a	<i>t</i> ^c (h)	yield (%)	ee (%) ^b	<i>t</i> ^c (h)	yield (%)	ee (%) ^a	<i>t</i> ^c (h)	yield (%)	ee (%) ^b	
1	(<i>S</i>)- L1 <i>p</i> -OMe-Binap	NTs	0.5	53	81	0.5	70	70	0.5	99	60	1.5	95	60	
2	(<i>S</i>)- L2 Binap		0.5	70	83	4	92	71	3	99	65	4	99	63	
3	(<i>S</i>)- L3 <i>p</i> -CF ₃ -Binap		0.5	65	84	3	97	75	2.5	97	67	4	98	68	
4	(<i>S</i>)- L4 Synphos		(1a)	0.5	57	93	1.5	74	89	2.5	98	65	4	93	68
5	(<i>S</i>)- L5 Difluorphos		0.5	62	89	0.5	90	75	2	90	70	3.5	90	71	
6	(<i>S</i>)- L1 <i>p</i> -OMe-Binap	O	0.5	33	85	0.5	65	73	0.5	67	64	1	81	69	
7	(<i>S</i>)- L2 Binap		0.5	42	92	2	75	85	1.5	72	85	1	82	81	
8	(<i>S</i>)- L3 <i>p</i> -CF ₃ -Binap		0.5	44	95	4	84	87	3	89	90	1	85	85	
9	(<i>S</i>)- L4 Synphos		(1b)	0.5	42	98	1.5	56	89	1	75	85	1.5	82	85
10	(<i>S</i>)- L5 Difluorphos		0.5	38	94	0.5	70	91	1	81	87	0.5	80	90	

^a (*S*)-**2a** is a major product when the absolute configuration of ligand employed is (*S*).^{5a}

^b The absolute configuration of these products has not been determined.

^c Time for the complete consumption of starting materials.



Table 3. Rh(I)-catalyzed enantioselective PKR with various ligands **L1-L5**

(preferred ligand/sustrate pairs shown in shaded boxes)

As we noticed in our previous study,⁸ for a given ligand, the more electron-poor the substrate, the poorer the enantioselectivity (but the better the yield). This clear tendency can be checked in any entry of Table 3, as illustrated for example in entry 2 for Binap ligand: *ee*(**2a-1**)=83% > *ee*(**2a-2**)=71% > *ee*(**2a-3**)=65% > *ee*(**2a-4**)=63%. As a result, only electron-rich cyclopentenone compounds **2a-1** and **2b-1** could be obtained with *ee* > 92%. For these two PKR products, but also for compound **2a-2**, the preferred ligand/substrate pairs were obtained with Synphos (**L4**)

as illustrated by shaded boxes in Table 3 ($ee=89-98\%$ compared to $71-92\%$ with Binap), which represent a significant increase in enantioselectivity of $+6\%$ (for substrate **1b-1**) to $+18\%$ (for substrate **1a-2**), compared to Binap. However these enhancements in selectivity are tainted by significant loss of chemical yield with Synphos ligand, as illustrated for example with substrate **1a-1** and **1a-2** (entry 4), which were converted into **2a-1** and **2a-2** in only 57% and 74% yield, respectively (to be compared with 70% and 92% yield obtained with Binap – entry 2). This decrease in chemical yield with electron-rich alkynes **1a-1** and **1a-2** is also observed with *p*-OMe-Binap **L1** (53% and 70% yield respectively for the same substrates – entry 1); therefore one could argue that the use of electron-rich ligands is detrimental to the yield for these substrates, which means that the competitive formation of side products became more significant.¹⁴

This result deserves to have a brief look at the reaction mechanism proposed in Scheme

3. Step b, which consists of the oxidative formation of metallacyclopentene **7** is considered to be the rate- and stereo-determining step of the reaction.⁸ Therefore two diastereoisomeric transition state can lead to complex **7**. In asymmetric catalysis, it is usually admitted that improvement of enantioselectivity would be the result of an increased difference in energy between these two competing diastereomeric transition states. Nevertheless, if Rh/Synphos complex is associated with electron-rich PKR substrates, there is a significant relationship between enantioselectivity and yield (increase in selectivity at the expense of yield), so one

cannot rule out completely the possibility of a kinetic differentiation during the reaction. In

other words, one diastereomeric intermediate of **7** is mostly prone to follow the pathway giving

Pauson–Khand reaction products **2** (through intermediate **8**, Scheme 3), whereas the other

diastereomeric intermediate of **7** is prone to give products derived from **3** by taking other

reaction pathway through intermediate **9**. Thus, the reaction provides the higher

enantioselectivity only with the sacrifice of chemical yield of desired PKR product **2**. In

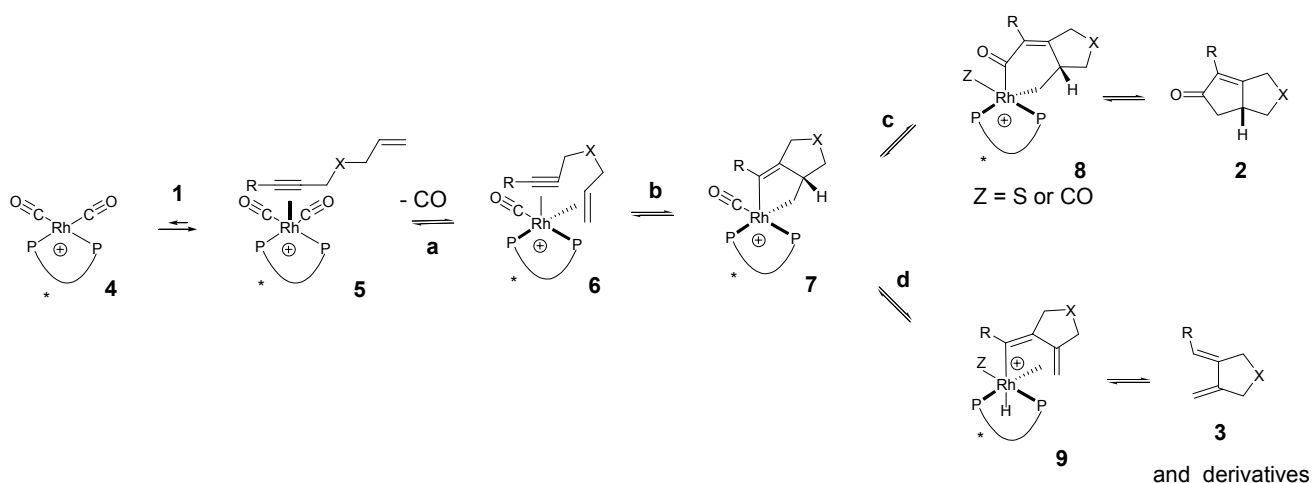
summary it seems that kinetic differentiation occurs preferably with electron rich alkyne

substates **1a-1**, **1a-2**, **1b-1** and **1b-2** and with Synphos ligand (**L4**) exclusively. Indeed, using

electron-richer *p*-OMe-Binap (**L1**) instead of Binap (**L2**) with these substrates makes the yield

decrease significantly but has almost no positive influence on the enantioselectivity, which

reveals a rather different behavior than Synphos.



Scheme 3. A proposed mechanism for the Rh(I) catalyzed asymmetric Pauson-Khand type reaction under CO atmosphere

As mentioned earlier, electron-deficient *N*-tosylated alkynes **1a-3** and **1a-4** are considered as challenging PKR substrates, in that Rh complexes bearing ligands **L1**, **L2** or **L3** (Binap-type) failed to catalyze the reaction with high enantioselectivity (*ee* = 60-68%, entries 1, 2 and 3). For these substrates, dihedral angle of the ligand is not a critical parameter to design the best enantioselective catalyst, in that Synphos (**L4**) gives results comparable to Binap (*ee*=65% for substrate **1a-3**) and *ee*'s are more sensitive to the electronic properties of the ligand: the more electron-poor the ligand, the better the enantioselection. Therefore electron-poor diphosphines give the best selectivities for product **2a-3** (*ee* = 67% with *p*-CF₃-Binap (**L3**), *ee* = 70% with Difluorphos (**L5**)). Extrapolating this observation, one could expect that biaryl diphosphines bearing more electron-deficient substituents than Difluorphos would improve this mild result further.

As underlined by grey boxes in Table 3, Difluorphos (**L5**) and *p*-CF₃-Binap (**L3**) ligands display the best performances with this catalytic system in terms of chemical yield and enantioselectivity (see entries 5, 8 and 10), especially preferred ligand/substrate pairs were obtained with compounds **1a-3**, **1a-4** (*ee* = 70-71%) and more remarkably with *O*-tethered 1,6-enynes **1b-2** (~~**1b-4**~~), for which very good *ee*'s of 90-91% could be reached (only 81-85% *ee* with Binap). For these substrates, the electronic profile of Difluorphos (**L5**) and *p*-CF₃-Binap (**L3**) (with a lower electronic density on phosphorus than Binap) is responsible for the improved enantioselectivity from Synphos **L4** and Binap ligands (**L1** and **L2**). Noticeably, and contrary to

what we observed with Synphos and electron-rich alkynes, this increase in enantioselectivity with these ligands is not accompanied with a loss of chemical yield. Good to excellent yields were obtained ranging from 70% for **2b-2** (*ee*=91%) and 90% for **2a-4** (*ee* = 71%) with Difluorphos **L5**. Even better chemical yields (+7% for **2a-2** and **2b-2** to +14% for **2b-3**) with somewhat inferior enantioselectivities (-3 to -5%) were obtained by *p*-CF₃-Binap (**L3**) with exception of **2b-3**. For example, 84% yield for **2b-2** with 87% *ee* and 98% yield for **2a-4** with 68% *ee* were obtained with **L3**.

It is also evident that the ligands having narrower dihedral angle accelerated the reaction significantly more than Binap-based ligands. Synphos **L4**, which has narrower dihedral angle than Binap **L2** but with chemical shift of phosphorus similar to, completed the reaction in a shorter period. In addition, Difluorphos (**L5**), whose phosphorus is more deshielded than *p*-CF₃-Binap (**L3**), makes the reaction completed in a shorter time. However, this acceleration is often associated with a loss of chemical yield in certain cases (for **2a-2**, **2a-3**, **2b-2** and **2b-3**).

Conclusion

We demonstrated that the enantioselectivity and yield of the catalytic Pauson-Khand reaction depends on both the electronic density and dihedral angle of diphosphine ligand, as well as on the electronic density of the alkyne moiety of the 1,6-enyne PKR substrate. As we considered as utopical to design a universal Rh-catalytic system for Pauson-Khand reaction

under CO atmosphere, we targeted and identified preferred ligand/substrate correspondences providing the best yields and enantioselectivities, and identified general trends to optimize the methodology. As an important complement to our previous study in this area,⁸ we found that steric properties of the biaryl backbone of the ligand, especially the value of its dihedral angle θ , play a crucial role in the stereochemical outcome of Rh-mediated PKR: Synphos **L4** and Difluorphos **L5**, with a narrower dihedral angle than Binap-type ligands, give the improved reactivities and enantioselectivities for most substrates (*ee*'s up to 98% for Synphos ligand and up to 91% for Difluorphos ligand). However, this increase in selectivity is often reached at the expense of chemical yield, certainly explained by a preferential kinetic differentiation pathway. Electronic adequation between substrate and ligand was confirmed as a crucial point to reach high enantioselectivities: electron-rich alkyne substrates **1a-1**, **1a-2** and **1b-1** were converted in moderate yield (42-74%) but excellent enantioselectivities (89-98%) to their corresponding PKR product using electron-rich Rh/Synphos complexes; on the contrary electron-deficient enynes **1a-3**, **1a-4**, **1b-3** and **1b-4** provided the best yields (80-90%) and enantioselectivities (70-91%) when Difluorphos (**L5**) or *p*-CF₃-Binap (**L3**) were used as chiral inductors, essentially because of their low electronic density on phosphorus.

Experimental Section

Representative Procedure; The catalytic enantioselective Pauson-Khand reaction

6-Methyl-2-(toluene-4-sulfonyl)-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**2a-1**)⁵

[Rh(CO)₂Cl]₂ (1.3 mg, 0.003 mmol, 3 mol%) and (*S*)-Synphos (6.6 mg, 0.010 mmol, 9 mol%) were placed in THF (1 mL) and the mixture was stirred for 30 minutes at 20 °C under atmospheric pressure of argon. A solution of AgOTf (3.5 mg, 0.014 mmol, 12 mol%) in THF (1 mL) was added, and the resultant reaction mixture was stirred for another 30 minutes at 20°C. The argon atmosphere was replaced with CO (1 atm), and then a solution of **1a-1** (30 mg, 0.114mmol) in THF (1 mL) was introduced. The reaction mixture was heated at 80°C. After completion of the reaction, the reaction mixture was cooled to room temperature and the carbon monoxide was released in the hood. The crude reaction mixtures were directly purified by column chromatography on silica gel using n-hexane/ethyl acetate mixture as the eluent to afford PKR product **2a-1** (19 mg, 0.065 mmol, 57%). The enantiomeric excess of the product **2a-1** was determined by HPLC analysis using Daicel columns (CHIRALPAK AD-H, 0.46mm I.D. x 25 cm, *n*-Hex/IPA=4/1, flow 0.8mL/min, 254nm): *t*_R = 13.08 min (minor) and 13.94 min (major). Ee was determined to be 93% when (*S*)-Synphos was used.

Determination of Enantiomeric Purity; The enantiomeric excess of other products were determined by chiral HPLC analysis using Daicel columns (0.46mm I.D. x 25cm) as specified.

6-(4-Methoxy-phenyl)-2-(toluene-4-sulfonyl)-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (2a-2)

The ee value was determined by HPLC analysis using a chiral column (DAICEL CHIRALPAK AD, *n*-Hex/IPA=3/1, 1.2mL/min, 254nm): t_R = 17.16 min (minor) and 19.06 min (major). Ee was determined to be 89% when (*S*)-Synphos was used.

$[\alpha]_D^{21} = -4.50$ (c 1.3, CH₂Cl₂).

IR (KBr): 1705 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 2.22 (dd, J = 18.0 and 3.0 Hz, 1 H), 2.40 (s, 3 H), 2.58 (dd, J = 18.0 and 15.0 Hz, 1 H), 2.76 (dd, J = 18.0 and 6.0 Hz, 1 H), 3.07 – 3.22 (m, 1 H), 3.82 (s, 3 H), 4.04 (dd, J = 18.0 and 6.0 Hz, 1 H), 4.07 (d, J = 18.0 Hz, 1H), 4.60 (d, J = 18.0 Hz, 1 H), 6.92 (d, J = 8.5 Hz, 2 H), 7.30 (d, J = 8.0 Hz, 2 H), 7.42 (d, J = 8.5 Hz, 2 H), 7.71 (d, J = 8.0 Hz, 2 H).

¹³C NMR (75 MHz, CDCl₃): δ = 21.8, 40.9, 41.9, 48.7, 52.3, 55.6, 114.3, 122.7, 127.6, 129.8, 130.2, 133.9, 135.7, 144.3, 160.3, 170.0, 206.1.

HRMS (FAB⁺): m/z [M + Na]⁺ calcd for C₂₁H₂₁NO₄SNa: 406.1089; found: 406.1078.

6-Phenyl-2-(toluene-4-sulfonyl)-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (2a-3)^{5a}

The ee value was determined by HPLC analysis using a chiral column (DAICEL CHIRALPAK AD-H, *n*-Hex/IPA=3/1, 1.2mL/min, 254nm): t_R = 11.15 min (minor) and 13.00 min (major). Ee was determined to be 70% when (*S*)-Difluorophos was used.

2-(Toluene-4-sulfonyl)-6-(4-trifluoromethyl-phenyl)-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (2a-4)

The ee value was determined by HPLC analysis using a chiral column (DAICEL CHIRALPAK AD-H, *n*-Hex/IPA=3/1, 1.2mL/min, 254nm): t_R = 24.07 min (major) and 25.77 min (minor). Ee was determined to be 71% when (*S*)-Difluorophos was used.

$[\alpha]_D^{21} = +42$ (c 0.5, CH₂Cl₂).

IR (KBr): 1710 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 2.29 (dd, J = 18.0 and 3.7 Hz, 1 H), 2.41 (s, 3 H), 2.64 (dd, J = 12.0 and 9.6 Hz, 1 H), 2.83 (dd, J = 18.0 and 6.6 Hz, 1 H), 3.20 - 3.33 (m, 1 H), 4.08 (dd, J = 18.0 and 6.0 Hz, 1 H), 4.10 (d, J = 15.0 Hz, 1H), 4.66 (d, J = 15.0 Hz, 1 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.62 (d, J = 8.2 Hz, 2 H), 7.66 (d, J = 8.2 Hz, 2 H), 7.72 (d, J = 8.0 Hz, 2 H).

¹³C NMR (75 MHz, CDCl₃): δ = 21.8, 40.9, 42.4, 48.5, 52.1, 124.2 (q, J = 272 Hz), 125.8 (q, J = 8.3 Hz), 128.5, 130.6 (q, J = 30 Hz), 133.8, 134.2, 179.9, 206.5

HRMS (FAB+): m/z $[M + Na]^+$ calcd for $C_{21}H_{18}F_3NO_3SNa$: 444.0857; found: 444.0863.

6-Methyl-3a,4-dihydro-1H,3H-cyclopenta[c]furan-5-one (2b-1)^{5a}

The ee value was determined by HPLC analysis using a chiral column (DAICEL CHIRALPAK AS-H, *n*-Hex/IPA=9/1, 1.0mL/min, 254nm): t_R = 12.69 min (major) and 12.48 min (minor). Ee was determined to be 98% when (*S*)-Synphos was used.

6-(4-Methoxyphenyl)-3a,4-dihydro-1H,3H-cyclopenta[c]furan-5-one (2b-2)

The ee value was determined by HPLC analysis using a chiral column (DAICEL CHIRALPAK AD-H, *n*-Hex/IPA=4/1, 1.0mL/min, 254nm): t_R = 11.53 min (minor) and 12.50 min (major). Ee was determined to be 91% when (*S*)-Difluorophos was used.

$[\alpha]_D^{21} = + 1.97$ (c 1.1, CH_2Cl_2).

IR (KBr): 1701 cm^{-1} .

¹H NMR (300 MHz, $CDCl_3$): δ = 2.32 (dd, J = 17.7 and 3.2 Hz, 1 H), 2.82 (dd, J = 17.7 and 6.0 Hz, 1 H), 3.21 (dd, J = 12.0 and 6.0 Hz, 1 H), 3.25 – 3.35 (m, 1 H), 3.82 (s, 3H), 4.36 (dd, J = 12.0 and 9.0 Hz, 1 H), 4.57 (d, J = 16.8 Hz, 1 H), 4.91 (d, J = 16.8 Hz, 1 H), 6.93 (d, J = 8.8 Hz, 2 H), 7.48 (d, J = 8.8 Hz, 2 H).

¹³C NMR (75 MHz, $CDCl_3$): δ = 40.5, 43.4, 55.5, 66.6, 71.6, 114.3, 123.5, 129.6, 134.4, 160.0, 175.5, 207.5.

HRMS (EI+): m/z calcd for $C_{14}H_{14}O_3$: 230.0943; found: 230.0944.

6-Phenyl-3a,4-dihydro-1H,3H-cyclopenta[c]furan-5-one (2b-3)^{5a}

The ee value was determined by HPLC analysis using a chiral column (DAICEL CHIRALPAK AD-H, *n*-Hex/IPA=4/1, 0.8mL/min, 254nm): $t_R = 9.99$ min (minor) and 12.13 min (major). Ee was determined to be 90% when (*S*)-*p*-CF₃-Binap was used.

6-(4-Trifluoromethyl-phenyl)-3a,4-dihydro-1H,3H-cyclopenta[c]furan-5-one (2b-4)

The ee value was determined by HPLC analysis using a chiral column (DAICEL CHIRALPAK AS-H, *n*-Hex/IPA=9/1, 1.0mL/min, 254nm): $t_R = 11.83$ min (major) and 13.83 min (minor). Ee was determined to be 90% when (*S*)-Difluorophos was used.

$[\alpha]_D^{21} = + 12.75$ (c 1.1, CH₂Cl₂).

IR (KBr): 1693 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): $\delta = 2.38$ (dd, $J = 17.9$ and 3.3 Hz, 1 H), 2.88 (dd, $J = 17.9$ and 6.3 Hz, 1 H), 3.27 (dd, $J = 12.0$ and 6.0 Hz 1 H), 3.33 – 3.43 (m, 1 H), 4.40 (t, $J = 12.0$ and 7.4 Hz, 1 H), 4.60 (d, $J = 16.8$ Hz, 1 H), 4.97 (d, $J = 16.8$ Hz, 1 H), 7.62 – 7.67 (m, 4 H).

¹³C NMR (75 MHz, CDCl₃): $\delta = 40.5, 43.9, 66.4, 71.5, 125.7, 124.0$ (q, $J = 272$ Hz), 125.6 (q, $J = 3.8$ Hz), 128.9, 130.0 (q, $J = 33$ Hz), 134.5, 134.6, 170.8, 171.6, 181.2, 206.8.

HRMS (EI⁺): m/z calcd for C₁₄H₁₁F₃O₂: 268.0711; found: 268.0723.

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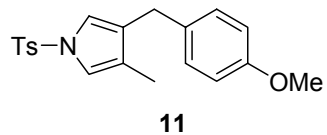
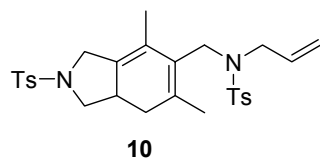
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12. All molecular geometries incorporating diphosphine ligands (free L*, PdCl₂(L*) and Rh(CO)Cl(L*) complexes) were optimized with the same molecular mechanics program (CAChE Worksystem Pro 5.0), using the same parameter set : force field parameters, MM2; calculation type, structure optimization; optimisation method, conjugate gradient for no more than 3 000 updates or until convergence to 10⁻⁴ kcal.mol⁻¹.
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14. Undesired side products were often obtained as an inseparable mixture of compounds derived from diene **3** (see Scheme 3). In case of reaction with **1a-1** and **1a-b**, analytically pure

products were obtained. **10** and **11** were obtained from **1a-1** and **1a-2** as side products, respectively.



Graphic Abstract

Electronic and Steric Effects of Atropisomeric Ligands SYNPHOS[®], DIFLUORPHOS[®] vs BINAPs in Rh(I) Catalyzed Asymmetric Pauson-Khand Reaction

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The electronic and steric effects of chiral biaryl diphosphine ligands on the Rh(I) catalyzed asymmetric Pauson-Khand type reaction were examined. We demonstrated that enantioselectivity and reaction yield were influenced by the electronic density on phosphorus, the dihedral angle of ligands and the electronic density of the alkyne substrate. Ligands bearing a narrower dihedral angle than Binap, such as Synphos (**L4**) and Difluorphos (**L5**), were found to increase substantially the rate and the enantioselectivity of the reaction, compared to Binap-type ligands. Ligands having deshielded phosphine, such as *p*-CF₃-Binap (**L3**) and Difluorphos (**L5**) provided better enantioselectivity than Binap, with reduced formation of side products, especially with electron-poor alkyne substrates.

