DOI: 10.1002/adsc.200700145

PuPHOS and CamPHOS Ligands in the Intermolecular Catalytic Pauson–Khand Reaction

Agustí Lledó,[a] Jordi Solà,[a] Xavier Verdaguer,[a,*] Antoni Riera,[a,*] and Miguel A. Maestro[b]

[a] Unitat de Recerca en Síntesi Asimètrica (URSA-PCB), Institute for Research in Biomedicine (IRB Barcelona) and Departament de Química Orgànica, Universitat de Barcelona, c/Josep Samitier 1–5, 08028 Barcelona, Spain
Fax: (+34)-9-3403-7095; e-mail: xverdaguer@pcb.ub.cat
[b] Departamento de Química Fundamental, Universidade da Coruña, 15071 A Coruña, Spain

Received: March 21, 2007; Published online: September 11, 2007

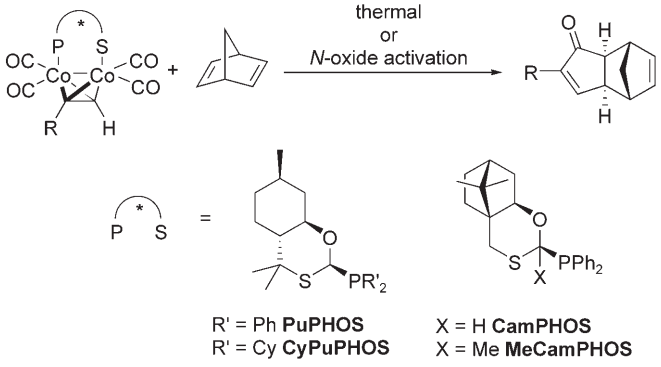
Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: The first asymmetric intermolecular cobalt-catalyzed Pauson–Khand reaction is described. The use of the hemilabile CamPHOS ligand provides good conversions and selectivity up to 28% *ee*. The catalytic process was studied by *in situ* FT-IR and it was found that both bridged and non-bridged complexes were present in the reaction mixture. Our results suggest that recognition between the alkyne substrate and the ligand is essential to attain stereocontrol in the catalytic cyclization.

Keywords: asymmetric catalysis; cobalt; hydrogen bonds; P,S ligands; Pauson–Khand reaction

Introduction

The use of chiral bidentate (P,S) PuPHOS and CamPHOS ligands in the stoichiometric asymmetric Pauson–Khand reaction (PKR) has been extensively explored by our group.[1–3] Coordination of these ligands to a terminal alkyne dicobalt complex affords two diastereomeric bridged complexes in variable ratios. While the use of non-functionalized terminal alkynes results in modest diastereoselectivities (up to 50% *de*), the use of a hydrogen bond acceptor (a sulfonyl or an amide moiety) on the alkyne moiety leads to a significant increase in coordination selectivity as a result of the presence of a non-classical C–H···O stabilizing interaction with the strongly polarized CH-OPS methine group of the ligand.[4–6] In both cases, when each of these isolated diastereomeric complexes reacts with norbornadiene it affords the corresponding Pauson–Khand cycloadducts in high *ee* (Scheme 1). This process has been successfully applied to the enantioselective synthesis of deoxyphytoprostanes.[7]



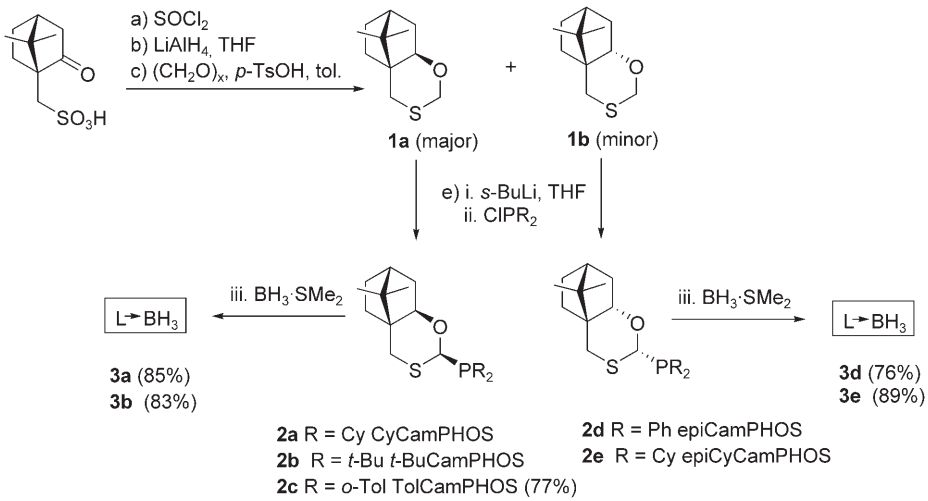
Scheme 1. Bidentate P,S ligands in the asymmetric PKR.

A step further in this research would be to make this process catalytic both in metal and ligand. A number of intramolecular catalytic asymmetric PKRs or Pauson–Khand-type reactions have been described.[8–14] In contrast, a reliable methodology for the catalytic asymmetric *intermolecular* PKR has yet to be reported.[15] This fact encouraged us to explore the use of our ligands in the catalytic reaction with norbornadiene. Thus, here we report on the use of PuPHOS- and CamPHOS-type ligands in the intermolecular cobalt-catalyzed Pauson–Khand reaction.

Results and Discussion

Preparation of Ligands

PuPHOS and CamPHOS ligands are prepared from pulegone and camphorsulfonic acid.[2,3] To further ex-



Scheme 2. Synthesis of camphor-derived ligands.

plore the whole potential of the camphor skeleton, new ligands derived from camphorsulfonic acid were prepared. Reduction of camphorsulfonic acid chloride and reaction with formaldehyde provides two epimeric oxathianes (Scheme 2). The major isomer **1a** can be purified by crystallization. In contrast, the minor component **1b** was obtained in pure form by chromatography of the corresponding mother liquors. From oxathianes **1a** and **1b**, metallation and substitution with the appropriate chlorophosphine provided ligands **2a–e** (Scheme 2). The new phosphine ligands were protected *in situ* as their borane complexes to prevent oxidation of the phosphorus atom, thereby providing protected ligands **3a**, **3b**, **3d** and **3e** in good overall yield. TolCamPHOS (**2c**) could not be protected with $BH_3{\cdot}SMe_2$ and was isolated as a free phosphine in good yield. The greater steric hindrance around the phosphorus atom caused by the *ortho*-tolyl groups may explain why the protection step failed. In this case, this is not an inconvenience since; even in solution, the resulting phosphine **2c** is resistant to oxidation.

Preparation of Bridged Dicobalt Complexes

To obtain defined catalysts for the PKR, the corresponding bridged alkyne complexes were prepared. The new ligands **2a–e** obtained were subjected to exchange reactions with several alkyne dicobalt complexes; the results are shown in Table 1 along with data for previously reported ligands. Ligand exchange was carried out by heating (65 °C) a toluene mixture of the borane-protected ligand and the corresponding hexacarbonyldicobalt complex in the presence of DABCO as a borane-deprotecting agent. The diastereomeric ratios observed for the bridged complexes are the result of a thermodynamic equilibrium.[4] Initial selectivity improved on heating over time to reach a final diastereomeric ratio.

Reaction with trimethylsilylacetylene dicobalt hexacarbonyl complex afforded mixtures with low to modest diastereomeric ratios, as ascertained by ^{1}H NMR analysis of the final reaction mixtures (Table 1, entries 1–8). Only in the case of MeCamPHOS was a good selectivity observed (Table 1, entry 3). In sharp contrast, a high diastereoselectivity was observed when an amide was present in the alkyne moiety (Table 1, entries 9–17). This result is due to the stabilizing effect of the intramolecular C–H···O contact. In these cases, diastereomeric ratios up to 200:1 were obtained with CamPHOS and TolCamPHOS (Table 1, entries 11, 15 and 17). Unusually low selectivities were attained with CyCamPHOS and *t*-BuCamPHOS ligands with diethylpropynamide (Table 1, entries 12 and 13). This behavior could be attributed to the electron-releasing nature of these phosphines, which may reduce the hydrogen bond donor capacity of the ligand while at the same time hamper the isomerization of the bridged complexes.

Suitable crystals for X-ray analysis for the major and minor isomers of the complex with diethylpropynamide and CyCamPHOS (**15a** and **15b**) were obtained. For the major complex **15a** the corresponding ORTEP plot show the close proximity (2.41 Å) of the methine proton to the carbonyl oxygen atom (O1), thus providing the stabilizing hydrogen bond (Figure 1). The structure of the minor isomer **15b** shows how the hydrogen-bond donor and acceptor are on opposite sides of the molecule and thus the stabilizing C–H···O=C cannot be realized. In this case, the ligand and the alkyne substituent (amide) adopt an *anti* conformation to minimize steric repulsions.[16]

Table 1. Ligand exchange reaction with various alkyne precursors.

Entry	R	Ligand	Complex (yield)	*dr*[a]	*de*	Ref.
1	TMS	PuPHOS	**4a/4b** (91%)	3:1	50%	[1,3]
2		CamPHOS	**5a/5b** (90%)	5:1	66%	this study
3		MeCamPHOS	**6a/6b** (64%)	12:1	85%	[2]
4		CyCamPHOS	**7a/7b** (84%)	1.5:1	20%	this study
5		*t*-BuCamPHOS	**8a/8b** (84%)	1.3:1	13%	this study
6		TolCamPHOS	**9a/9b** (93%)	1:1	0%	this study
7		epiCamPHOS	**10a/10b** (86%)	2:1	33%	this study
8		epiCyCamPHOS	**11a/11b** (44%)	3.4:1	55%	this study
9	$CONEt_2$	PuPHOS	**12a/12b** (68%)	32:1	94%	[6]
10		CamPHOS	**13a/13b** (74%)	19:1	90%	[6]
11		TolCamPHOS	**14a/14b** (74%)	200:1[b]	99%	[6]
12		CyCamPHOS	**15a/15b** (66%)	3.1:1	51%	[6]
13		*t*-BuCamPHOS	**16a/16b** (78%)	3.1:1	51%	this study
14	$CON(i\text{-}Pr)_2$	PuPHOS	**17a/17b** (70%)	19:1	90%	[6]
15		CamPHOS	**18a/18b** (74%)	4.3:1	96%	[6]
16	$CON(CH_2)_5$	PuPHOS	**19a/19b** (74%)	7.3:1	76%	[6]
17		CamPHOS	**20a/20b** (73%)	200:1[b]	99%	[6]

[a] Diastereomeric ratio was determined by ^1H NMR analysis.
[b] Formation of minor isomer was not detected by TLC analysis.

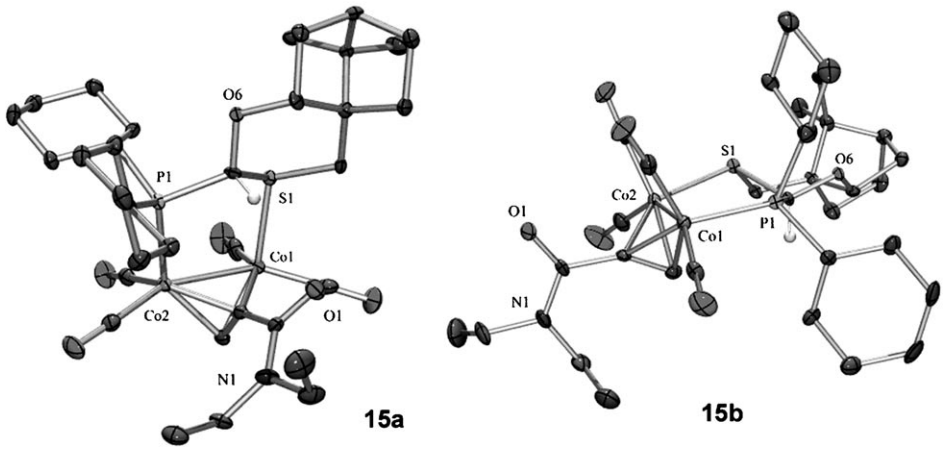


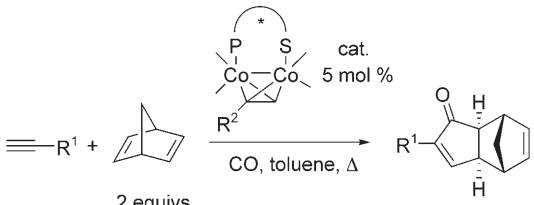
Figure 1. ORTEP plot of **15a** (*left*, major diastereomer) and **15b** (*right*, minor diastereomer) showing 50% probability ellipsoids. Only the hydrogen that can participate in the stabilizing contact is shown.

Catalytic PKRs

With all these complexes in hand we examined the catalytic PKRs with several alkynes: trimethylsilylacetylene and 2-methyl-3-butyn-2-ol are commercially available. Diethylpropynamide and diisopropylpropynamide were prepared from commercial propynoic acid following reported procedures.[17] Reactions were carried out under carbon monoxide pressure in Schlenk glass tubes, each fitted with a pressure-resistant Teflon screw cap. A 5% molar ratio of the corresponding bridged complex as a catalyst and a 1-fold excess of norbornadiene over the alkyne were used.

Soon it became clear that using a single diastereomeric complex or a mixture of them as catalyst had a negligible effect on the outcome of the reaction, since equilibration between them occurred readily under the reaction conditions employed. This phenomenon could be clearly observed by TLC monitoring of the reaction of $TMSC_2H$ with the PuPHOS ligand

Table 2. Catalytic PKRs using PuPHOS and CamPHOS ligands.



21 – 24

Entry	R^1	Catalyst	Ligand	Conditions	Time	Product	Yield[a]	*ee*[b]
1	TMS	**4a** ($R^1=R^2$)	PuPHOS	1 bar CO/toluene/90 °C	20 h	(+)-**21**	70 %	3 %
2	TMS	**5a/5b**	CamPHOS	2 bar CO/toluene/70 °C	20 h	(+)-**21**	98 %	0 %
3	"	**6a/6b** ($R^1=R^2$)	MeCamPHOS	1 bar CO/toluene/90 °C	18 h	(+)-**21**	60 %	5 %
4	"	**7a/7b** ($R^1=R^2$)	CyCamPHOS	2 bar CO/toluene/90 °C	3 d	(+)-**21**	10 %	15 %
5	"	**10a/10b** ($R^1=R^2$)	epiCamPHOS	2 bar CO/toluene/90 °C	16 h	(+)-**21**	22 %	4 %
6	"	**11a/11b** ($R^1=R^2$)	epiCyCamPHOS	2 bar CO/toluene/90 °C	16 h	(−)-**21**	6 %	5 %
7	$CONEt_2$	**13a** ($R^1=R^2$)	CamPHOS	0.5 bar CO/toluene/90 °C	24 h	(+)-**22**	12 %	40 %
8	"	**13a** ($R^1=R^2$)	CamPHOS	2 bar CO/toluene/70 °C	24 h	(+)-**22**	90 %	16 %
9	$CON(i\text{-}Pr)_2$	**18a** ($R^1=R^2$)	CamPHOS	2 bar CO/toluene/70 °C	24 h	(+)-**23**	91 %	23 %
10	$CON(i\text{-}Pr)_2$	**7a/7b** (R^2=TMS)	CyCamPHOS	2 bar CO/toluene/70 °C	48 h	(+)-**23**	34 %	8 %
11	"	**8a/8b** (R^2=TMS)	*t*BuCamPHOS	2 bar CO/toluene/70 °C	70 h	(+)-**23**	25 %	1 %
12	"	**9a/9b** (R^2=TMS)	TolCamPHOS	2 bar CO/toluene/70 °C	48 h	(+)-**23**	20 %	0
13	"	**9a/9b** (R^2=TMS)	TolCamPHOS	3 bar CO/toluene/70 °C	48 h	(+)-**23**	80 %	1 %
14	"	**4a/4b** (R^2=TMS)	PuPHOS	2 bar CO/toluene/70 °C	48 h	(+)-**23**	20 %	1 %
15	"	**5a/5b** (R^2=TMS)	CamPHOS	2 bar CO/toluene/70 °C	24 h	(+)-**23**	90 %	20 %
16	"	**5a/5b** (R^2=TMS)	CamPHOS	3 bar CO/toluene/70 °C	48 h	(+)-**23**	91 %	17 %
17	"	**5a/5b** (R^2=TMS)	CamPHOS	CO atm P/toluene/70 °C	48 h	(+)-**23**	45 %	28 %
18	"	**5a/5b** (R^2=TMS)	CamPHOS	2 bar CO/toluene/55 °C	48 h	(+)-**23**	30 %	20 %
19	CMe_2OH	**5a/5b** (R^2=TMS)	CamPHOS	2 bar CO/toluene/70 °C	48 h	(+)-**24**	40 %	4 %

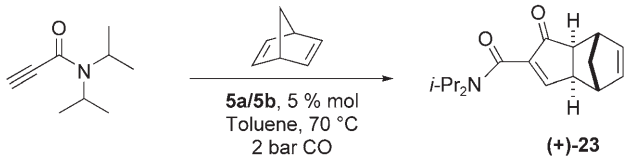
[a] Flash chromatography isolated yield.
[b] Determined by chiral HPLC analysis.

(Table 2, entry 1). In concordance with the low or modest complexation diastereoselectivity observed with trimethylsilylacetylene, very low *ee*s were obtained when this alkyne was used as substrate for catalytic PKR (Table 2, entries 1–6). Only for CyCamPHOS was a modest excess observed, although at the expense of very low conversion (Table 2, entry 4). However, when propynamides were used, a significant selectivity was observed with CamPHOS, although the *ee*s were still modest (Table 2, entries 7–9). A maximum 40 % *ee* was obtained at 0.5 bar of CO despite low conversion numbers (Table 2, entry 7), while 16 % *ee* was achieved when the reaction reached completion (Table 2, entry 8). Slightly higher *ee*s (23 %) with excellent yield were obtained for the corresponding diisopropylamide substrate (Table 2, entry 9).

We also carried out the reaction with an alkyne complex distinct from that used as substrate (Table 2, entries 10–19). This procedure prevented a contribution of the initial catalytic cycle to the final *ee* when a pure diastereomer was used as catalyst. For practical reasons, the complex with trimethylsilylacetylene (mixture of diastereomers **5a**:**5b**) was used as catalyst; this did not affect the results (compare Table 2, entries 9 and 15). A negative effect on the catalytic activity was observed when electron-rich phosphines were used (Table 2, entries 10 and 11). After some experimentation, we observed that lowering the CO pressure had a positive effect on the *ee* (Table 2, entry 16) although at the expense of lower yields, probably as a result of catalyst decomposition. Lowering the temperature reaction did not significantly affect the selectivity but again had a detrimental effect on yields, as the reactions slowed down (Table 2, entry 18). Finally, when a poorer hydrogen bond acceptor such as the 2-methyl-3-butyn-2-ol was used the *ee* obtained was very low (Table 2, entry 19). This observation supports the hypothesis that the origin of selectivity is due to the occurrence of the weak hydrogen-bond when a propynamide substrate is used.

FT-IR Reaction Monitoring

To gain further insight into the metallic species involved in the catalytic process, the reaction between diisopropylpropynamide and norbornadiene catalyzed



Scheme 3. Catalytic PKR studied by *in situ* FT-IR.

by CamPHOS complex **5a**/**5b** was monitored by *in-situ* FT-IR spectroscopy (Scheme 3). Infrared spectra acquired at regular intervals allowed us to follow the course of the reaction by the appearance of the characteristic C–O stretching band of the enone formed at around 1698 cm^{-1}. Interesting mechanistic information was obtained from the region between 1950 and 2100 cm^{-1} where the C–O stretching bands of the complex CO ligands appeared. Figure 2 shows this region at the beginning of the reaction and its evolution over time. Four characteristic bands were distinguished, corresponding to free propynamide (**A**), the open pentacarbonylic complex (**B**) and the initial bridged tetracarbonylic complex (**C** and **D**). Figure 3 shows the absorbance profiles of cobalt species in the reaction mixture. Thus, bands **C** and **D**, corresponding to the initial bridged tetracabonyl complex, rapidly decreased while band **B**, diagnostic of a pentacarbonylic species, grew proportionally. These data show that both tetracarbonyl and pentacarbonyl species are present in the catalytic reaction mixture. Thus, we may attribute the decrease in selectivity in the catalytic process to the presence of the non-bridged complex.

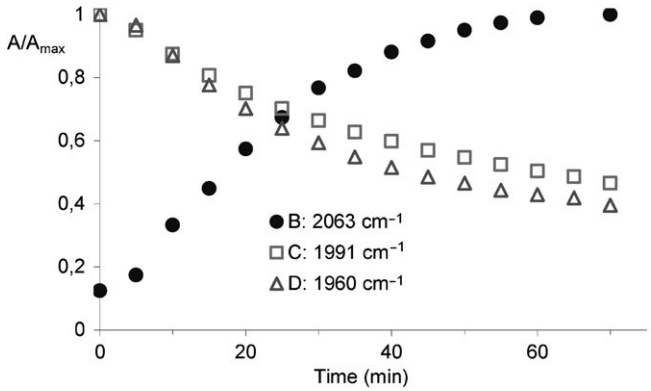


Figure 3. IR absorbance profile of the tetra- and pentacarbonyldicobalt species during the catalytic PKR.

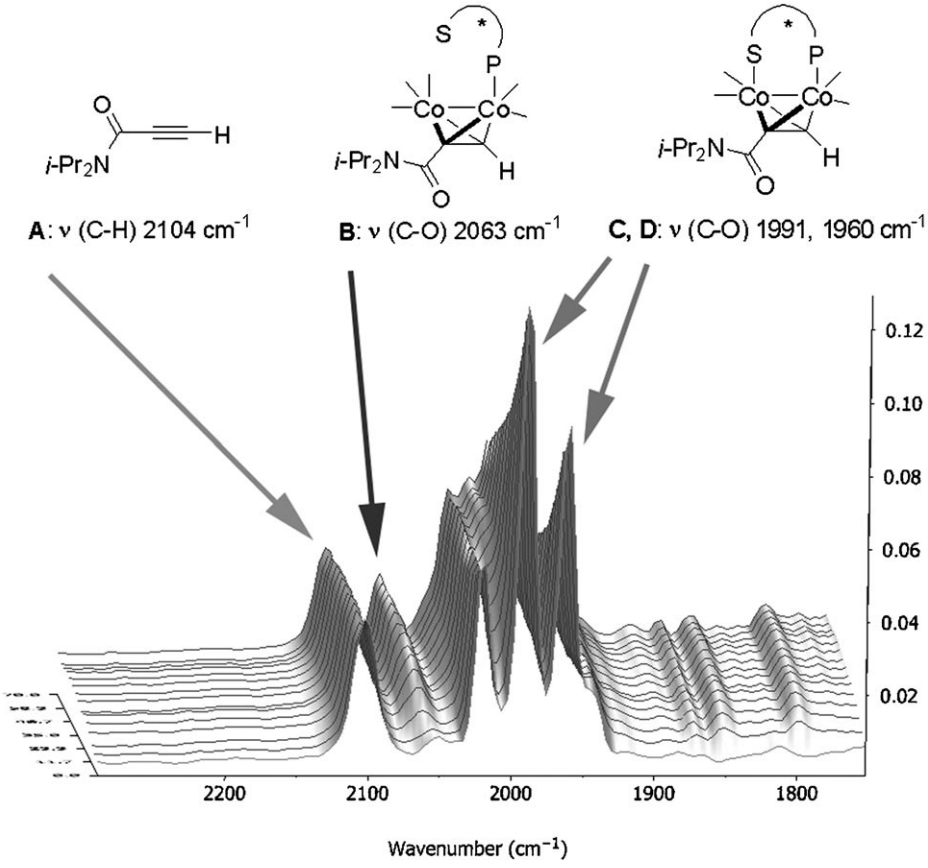
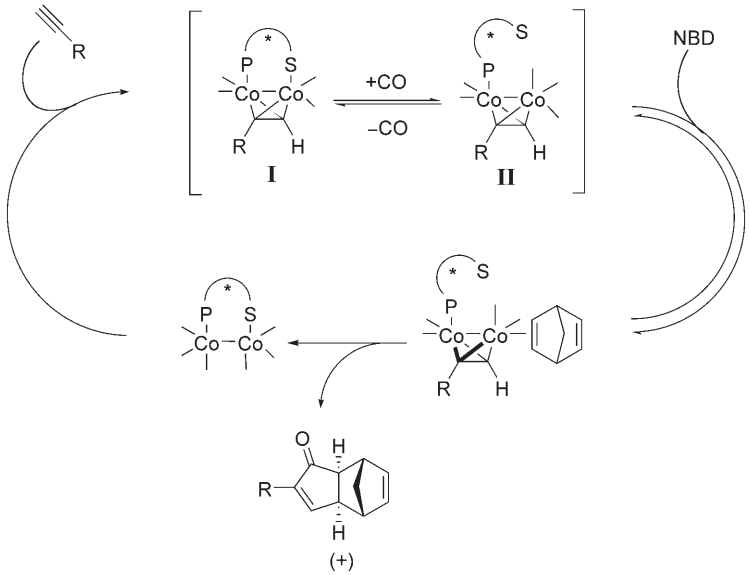


Figure 2. FT-IR stack plot of the metal carbonyl region during the catalytic Pauson–Khand reaction. Visible IR species implied are indicated.



Scheme 4. Feasible catalytic cycle for the intermolecular PKR with bridged P,S ligands. Carbonyl ligands are omitted for the sake of clarity.

As we have previously demonstrated, in the stoichiometric reaction, a high stereoselectivity/specificity was observed when a diastereomerically pure bridged complex reacted with norbornadiene. FT-IR monitoring of the catalytic process revealed that under CO pressure, equilibrium between the bridged tetracarbonyl complexes **I** and the open complexes **II** takes place (Scheme 4). While a high diastereomeric bias operates for bridged complexes, low selectivity is expected in the equilibration of non-bridged complexes **II**. In this situation, PKR through **I** is expected to occur with elevated selectivity while reaction through **II** will provide poor stereocontrol. In addition, for the catalytic process we must take into account the step in which the alkyne enters the catalytic cycle (Scheme 4). Alkyne coordination to the dicobalt-ligand moiety may also occur with a range of selectivity levels.

Noteworthy, despite the multiple species in equilibrium in the reaction mixture, which may lead to opposite enantiomers, significant selectivity was observed when propynamides were used as substrates. This observation illustrates how the weak, non-classical hydrogen bond interaction operating in this system significantly shifts these equilibriums to the major bridged complex **I**. The fact that the same enantiomer of the corresponding enone (+)-**23** was obtained for the catalytic and stoichiometric process supports this hypothesis.[5,6]

Conclusions

Here we have described the first intermolecular asymmetric cobalt-catalyzed PKR. The bridged P,S ligand-dicobaltcarbonyl system is an efficient catalyst for the intermolecular process and provides good conversions and yields. The occurrence of an intramolecular hydrogen bond between the ligand and the substrate is essential to attain selectivity in the reaction. FT-IR monitoring of the reaction mixture revealed that under CO pressure the bridged complex coexists with the open pentacarbonylic species. Thus, reaction through the non-bridged complex is thought to be responsible for the low selectivity observed. Further tuning of the P,S ligand system should provide enhanced stereocontrol in the catalytic intermolecular Pauson–Khand reaction.

Experimental Section

General Remarks

Solvents were generally distilled under an N_2 atmosphere just before use. Diethyl ether and THF were distilled over Na/benzophenone, toluene was distilled over molten Na and dichloromethane was distilled over CaH_2. DMF was distilled over CaH_2 at 15 mm Hg and was stored under N_2 over molecular sieves. Butyllithium (1.6 M or 2.5 M in hexanes) and *sec*-butyllithium (1.7 M in cyclohexane) solutions were purchased from Aldrich and were titrated prior to use with *p*-phenylbenzyl alcohol. Flash column chromatography was generally used for purification of compounds, using SiO_2 (35–70 μm) as stationary phase. For purification of cobalt complexes the stationary phase was washed once with diethyl ether to remove moisture and then with hexane before use. See the Supporting Information for the full characterization and analytical data of new compounds.

General Procedure for the Preparation of Bidentate Ligands.

To a solution of the required thioisoborneol oxathiane **1a**/**1b** (400 mg, 2.0 mmol) in 5 mL of THF at −78 °C were added dropwise 1.6 mL (2.2 mmol) of *sec*-BuLi solution (1.4 M in cyclohexane). The flask was allowed to warm to −20 °C and after 20 min a solution of 2.02 mmol of the corresponding chlorophosphine in 2 mL of THF were added *via* cannula. After 2 h the reaction mixture was allowed to warm to 0 °C and 0.35 mL (3.7 mmol) of $BH_3{\cdot}SMe_2$ were added. Then the flask was left to reach room temperature for one hour and the mixture was diluted with Et_2O. The flask was cooled again to 0 °C and water was carefully added (gas may evolve violently). The phases were separated and the aqueous layer was washed with Et_2O. The combined organic extracts were washed with saturated NaCl solution and dried over $MgSO_4$. The solvent was removed under reduced pressure and the resulting crude purified by flash chromatography. Yields are usually over 70%.

(−)-(1*S*,4*S*,6*R*,8*R*)-4-Dicyclohexylphosphino-11,11-dimethyl-5-oxa-3-thiatricyclo[6.2.1.0^{1,6}]undecane Borane Complex, CyCamPHOS·BH$_3$ (3a): Prepared according to the general procedure using 388 mg (1.96 mmol) of oxathiane **1a**, 1.46 mL (2.1 mmol) of *sec*-BuLi 1.4 M in cyclohexane, 0.47 mL (2.2 mmol) of chlorodicyclohexylphosphine and 0.24 mL (2.5 mmol) of $BH_3{\cdot}SMe_2$. The crude product was purified by flash chromatography (SiO_2, hexanes/Et_2O, 95:5) and complex CyCamPHOS·BH_3 was obtained as a colorless oil; yield: 649 mg (1.7 mmol, 85%).

(−)-(1*S*,4*S*,6*R*,8*R*)-4-Di-*tert*-butylphosphino-11,11-dimethyl-5-oxa-3-thiatricyclo[6.2.1.0^{1,6}]undecane Borane Complex, *t*-BuCamPHOS·BH$_3$ (3b): Prepared according to the general procedure using 1.05 g (5.0 mmol) of oxathiane **1a**, 5.3 mL (5.3 mmol) of *sec*-BuLi 1.0 M in cyclohexane, 1.1 mL (5.5 mmol) of di-*tert*-butylchlorophosphine and 0.86 mL (6.6 mmol) of $BH_3{\cdot}SMe_2$. The crude product was purified by flash chromatography (SiO_2, hexanes/Et_2O, 95:5) and complex *t*-BuCamPHOS·BH_3 was obtained as white crystals; yield: 1.50 g (4.2 mmol, 83%).

(−)-(1*S*,4*S*,6*R*,8*R*)-11,11-Dimethyl-5-oxa-3-thia-4-di-*o*-tolylphosphinotricyclo[6.2.1.0^{1,6}]undecane, TolCamPHOS (2c): Prepared according to the general procedure using 400 mg (2.02 mmol) of oxathiane **1a**, 2.2 mL (2.2 mmol) of *sec*-BuLi 1.0 M in cyclohexane, 500 mg (2.0 mmol) of di-*o*-tolylchlorophosphine and 0.35 mL (3.7 mmol) of $BH_3{\cdot}SMe_2$. The crude product was purified by flash chromatography (SiO_2, hexanes/Et_2O, 99:1) and then recrystallized from hot AcOEt under N_2; the free ligand TolCamPHOS was obtained as white crystals; yield: 640 mg (1.6 mmol, 77%).

(+)-(1*S*,4*R*,6*S*,8*R*)-4-Diphenylphosphino-11,11-dimethyl-5-oxa-3-thiatricyclo[6.2.1.0^{1,6}]undecane Borane Complex, epiCamPHOS·BH$_3$ (3d): Prepared according to the general procedure using 307 mg (1.53 mmol) of oxathiane **1b**, 1.3 mL (1.84 mmol) of *sec*-BuLi 1.4 M in cyclohexane, 0.35 mL (1.84 mmol) of chlorodiphenylphosphine and 0.20 mL (1.99 mmol) of $BH_3{\cdot}SMe_2$. The crude product was purified by flash chromatography (SiO_2, Hexanes/AcOEt, 95:5 to 90:10) and the complex epiCamPHOS·BH_3 was obtained as a white solid which can be recrystallized in hexanes/AcOEt mixtures; yield: 459 mg (1.16 mmol, 73%).

(+)-(1*S*,4*R*,6*S*,8*R*)-4-Dicyclohexylphosphino-11,11-dimethyl-5-oxa-3-thiatricyclo[6.2.1.0^{1,6}]undecane Borane Complex, epiCyCamPHOS·BH$_3$ (3e): Prepared according to the general procedure using 341 mg (1.72 mmol) of oxathiane **1b**, 1.6 mL (2.24 mmol) of *sec*-BuLi 1.4 M in cyclohexane, 0.49 mL (2.24 mmol) of chlorodicyclohexylphosphine and 0.23 mL (2.30 mmol) of $BH_3{\cdot}SMe_2$. The crude product was purified by flash chromatography (SiO_2, hexanes/AcOEt, 95:5 to 90:10) and the complex epiCamPHOS·BH_3 was obtained as a white solid after recrystallization from hexanes/AcOEt; yield: 624 mg (1.53 mmol, 89%).

General Procedure for the Preparation of Cobalt Complexes

Into a Schlenk tube were weighed 0.24 mmol of the desired starting alkyne-dicobalt hexacarbonyl complex, 0.24 mmol of the required ligand-borane complex (L-BH_3) and 0.36 mmol of DABCO (1,4-diazabicyclo[2.2.2]octane). The tube was purged with argon and 3 mL of toluene were added, then the mixture was heated to 65 °C for the adequate time while CO was periodically removed by means of vacuum and argon refilling. The solvent was removed under reduced pressure and the resulting crude is purified by flash column chromatography.

Co_2(μ-Et_2NCOC_2H)(CO)$_4$(μ-$C_{19}H_{35}$OPS) (16a) and (16b): Prepared according to the general procedure using 100 mg (0.24 mmol) of dicobalt complex Co_2(μ-Et_2NCOC_2H)(CO)$_6$, 85 mg (0.24 mmol) of the complex *t*-BuCamPHOS·BH_3 **3g**, 40 mg (0.36 mmol) of DABCO and 3 mL of toluene, reaction time 9 h. After chromatographic purification (SiO_2, hexane/AcOEt 90:10 to 60:40) 100 mg (0.14 mmol, 60%) of the major complex **16a** and 30 mg (0.04 mmol, 18%) of the minor complex **16b** were obtained.

Co_2(μ-TMS-C_2H)(CO)$_4$(μ-$C_{23}H_{39}$OPS) (7a) and (7b): Prepared according to the general procedure using 100 mg (0.26 mmol) of dicobalt complex Co_2(μ-TMS-C_2H)(CO)$_6$, 100 mg (0.24 mmol) of the complex CyCamPHOS·BH_3 **3e**, 40 mg (0.36 mmol) of DABCO and 4 mL of toluene, reaction time 16 h. After chromatographic purification (SiO_2, hexane/AcOEt 95:5) 100 mg (0.20 mmol, 84%) of a 1.5:1 mixture of diastereomeric complexes **7a/7b** was obtained.

Co_2(μ-TMS-COC_2H)(CO)$_4$(μ-$C_{19}H_{35}$OPS) (8a) and (8b): Prepared according to the general procedure using 150 mg (0.39 mmol) of dicobalt complex Co_2(μ-TMS-C_2H)(CO)$_6$, 142 mg (0.39 mmol) of the complex *t*-BuCamPHOS·BH_3 **3f**, 65 mg (0.58 mmol) of DABCO and 3 mL of toluene, reaction time 18 h. After chromatographic purification (SiO_2, hexane) 220 mg (0.33 mmol, 84%) of a 1.3:1 mixture of diastereomeric complexes **8a/8b** was obtained as a red oil that further crystallizes in the fridge.

Co_2(μ-TMS-C_2H)(CO)$_4$(μ-$C_{25}H_{33}$OPS) (9a) and (9b): Prepared according to the general procedure using 100 mg (0.26 mmol) of dicobalt complex (μ-TMS-C_2H)(CO)$_6$, 100 mg (0.24 mmol) of TolCamPHOS **1g**, 40 mg (0.36 mmol) of DABCO and 4 mL of toluene, reaction time 16 h. After chromatographic purification (SiO_2, hexane/AcOEt 95:5) 165 mg (0.22 mmol, 93%) of a 1:1 mixture of diastereomeric complexes **7a/7b** was obtained as a red foam.

Co_2(μ-TMS-C_2H)(CO)$_4$(μ-$C_{23}H_{27}$OPS) (10a) and (10b): Prepared according to the general procedure using 100 mg (0.26 mmol) of dicobalt complex (μ-TMS-C_2H)(CO)$_6$, 95 mg

(0.24 mmol) of the complex epiCamPHOS·BH_3 **3h**, 40 mg (0.36 mmol) of DABCO and 4 mL of toluene, reaction time 16 h. After chromatographic purification (SiO_2, hexane/AcOEt 95:5) 147 mg (0.21 mmol, 86%) of a 2:1 mixture of diastereomeric complexes **10a/10b** was obtained as a red oil.

Co_2(μ-TMS-C_2H)(CO)$_4$(μ-$C_{23}H_{39}$OPS) (11a) and (11b): Prepared according to the general procedure using 100 mg (0.26 mmol) of dicobalt complex (μ-TMS-C_2H)$(CO)_6$, 95 mg (0.24 mmol) of the complex epiCyCamPHOS·BH_3 **3i**, 40 mg (0.36 mmol) of DABCO and 4 mL of toluene, reaction time 16 h. After chromatographic purification (SiO_2, hexane/AcOEt 95:5) 76 mg (0.11 mmol, 44%) of a 3.4:1 mixture of diastereomeric complexes **11a/11b** is obtained as a red oil.

General Procedure for the Catalytic Pauson–Khand Reaction

In a pressure Schlenk tube (total volume) fitted with a teflon screw cap (Kontes HI-VAC) were dissolved 0.650 mmol of alkyne and 0.0325 mmol of the dicobalt complex in 3 mL of toluene. Norbornadiene (132 mL, 1.30 mmol) was then added and the tube quickly purged with CO. The required working pressure was set up and the tube closed and heated in an oil bath. After the required reaction time the volatile components were evaporated and the crude product was directly purified by flash chromatography and analyzed by chiral HPLC (for detailed chromatographic conditions see Ref.[6]).

Crystallographic Data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre and allocated the deposition no. CCDC-636614 and 636615. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax.: (internat.) (+44)-1223/336-033; e-mail: mailto:deposit@ccdc.cam.ac.uk].

Acknowledgements

This work was supported by MEC (CTQ2005–623). X.V. thanks the DURSI for a "Distinció per a la Promoció de la Recerca Universitària". A. L. thanks the MEC for a fellowship; J.S. thanks the DURSI and Universitat de Barcelona for a fellowship.

References

[1] X. Verdaguer, A. Moyano, M. A. Pericàs, A. Riera, M. A. Maestro, J. Mahia, *J. Am. Chem. Soc.* **2000**, *122*, 10242.
[2] X. Verdaguer, M. A. Pericàs; A. Riera, M. A. Maestro, J. Mahia, *Organometallics* **2003**, *22*, 1868.
[3] X. Verdaguer, A. Lledó, C. Lopez-Mosquera, M. A. Maestro, M. A. Pericàs, A. Riera, *J. Org. Chem.* **2004**, *69*, 8053.
[4] J. Solà, A. Riera, X. Verdaguer, M. A. Maestro, *Organometallics* **2006**, *25*, 5795.
[5] J. Solà, A. Riera, X. Verdaguer, M. A. Maestro, *J. Am. Chem. Soc.* **2006**, *128*, 13312.
[6] J. Solà, A. Riera, X. Verdaguer, M. A. Maestro, *J. Am. Chem. Soc.* **2005**, *127*, 13629.
[7] M. Iqbal, P. Evans, A. Lledó, X. Verdaguer, M. A. Pericàs, A. Riera, C. Loeffler, A. K. Sinha, M. J. Mueller, *ChemBioChem.* **2005**, *6*, 276.
[8] a) T. Shibata, *Adv. Synth. Catal.* **2006**, *348*, 2328; b) J.-M. Muller, A. Rickers, W. Leitner, *Adv. Synth. Catal.* **2007**, *349*, 287.
[9] S. Laschat, A. Becheanu, T. Bell, A. Baro, *Synlett* **2005**, 2547.
[10] S. E. Gibson, A. Stevenazzi, *Angew. Chem.* **2003**, *115*, 1844; *Angew. Chem. Int. Ed.* **2003**, *42*, 1800.
[11] S. E. Gibson, N. Mainolfi, *Angew. Chem.* **2005**, *117*, 3082; *Angew. Chem. Int. Ed.* **2005**, *44*, 3022.
[12] F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 7026.
[13] N. Jeong, B. K. Sung, Y. K. Choi, *J. Am. Chem. Soc.* **2000**, *122*, 6771.
[14] K. Hiroi, T. Watanabe, R. Kawagishi, I. Abe, *Tetrahedron Lett.* **2000**, *41*, 891.
[15] Shibata described the only case of asymmetric intermolecular PKR catalyzed by Ir, see: T. Shibata, K. Takagi, *J. Am. Chem. Soc.* **2000**, *122*, 9852.
[16] The dicobalt alkyne-bridged complexes present fluxionality and may be present in two distinct conformations, *syn* and *anti*, through rotation about the Co-Co bond. See: Ref.[6] and references cited therein.
[17] G. Coppola, *Synth. Commun.* **1993**, *23*, 2003.

