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Rhodium/tris-binaphthyl chiral monophosphite complexes: Efficient catalysts for the hydroformylation of disubstituted aryl olefins

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ABSTRACT

A family of threefold symmetry phosphite ligands, P(O–BIN–OR)$_3$ (BIN = 2,2′-binaphthyl; R = Me, Bn, CHPh$_2$, 1-adamantyl), derived from enantiomerically pure (*R*)-BINOL, was developed. Cone angles within the range 240–270° were calculated for the phosphite ligands, using the computational PM6 Hamiltonian. Their rhodium complexes formed *in situ* showed remarkable catalytic activity in the hydroformylation of hindered phenylpropenes, under relatively mild reaction conditions, with full chemoselectivity for aldehydes, high regioselectivity, however with low enantioselectivity. The ether substituents at the ligand affected considerably the catalytic activity on the hydroformylation of 1,1- and 1,2-disubstituted aryl olefins. The kinetics of the hydroformylation of *trans*-1-phenyl-1-propene, using tris[(*R*)-2′-benzyloxy-1,1′-binaphthyl-2-yl]phosphite as model ligand, was investigated. A first order dependence in the hydroformylation initial rate with respect to substrate and catalyst concentrations was found, as well as a positive order with respect to the partial pressure of H_2, and a slightly negative order with respect to phosphite concentration and CO partial pressure.

1. Introduction

Hydroformylation is among the most significant C–C bond forming reactions and represents an important synthetic tool for the manufacture of aldehydes [1–4]. There is a significant interest in the catalytic hydroformylation of vinylarenes [5–12], since aryl alkanals are important intermediates with high synthetic value, namely in pharmaceutical industry [6,7]. Although it is well known that the hydroformylation of disubstituted or internal double bounds is troublesome and usually requires harsh reaction conditions [13], remarkable exceptions are Rh(I)/bulky monophosphite catalysts that are able to promote the hydroformylation of sterically hindered substrates, under relatively mild conditions [14–19]. Bulky phosphite ligands proved to enhance rhodium-catalyzed hydroformylation reaction rates, when compared to rhodium/phosphine systems [20], due to steric and electronic effects. Despite the recent interest in chiral monodentate ligands in asymmetric catalysis [21–24], there are only a few reports concerning the use of chiral monophosphite [25,26] and phosphoramidite [27] ligands in the asymmetric rhodium-catalyzed hydroformylation. Furthermore, the kinetics and mechanistic studies on catalytic hydroformylation are essentially limited to terminal and/or cyclic olefins [15,16,19,20,28–35]. In fact, the asymmetric hydroformylation of disubstituted olefins has received much less attention than their monosubstituted counterparts [8–12]. The synthesis and characterization of C_3-symmetric binaphthyl-based chiral monophosphites, of general formula P(O–BIN–OR)$_3$ (BIN=(*R*)-2,2′-binaphthyl; R = Me, Bn, CHPh$_2$), has been recently developed by our group [36]. Similar phosphite ligands of type P(O–BIN–O$_2$CR)$_3$ (R = Bn, 1-adamantyl) have been also reported, as well as their efficient application in the asymmetric Rh-catalyzed hydrogenation of homoallylic alcohols [37].

Herein, we report the synthesis and characterization of a new monophosphite P(O–BIN–OR)$_3$, (*R* = 1-adamantyl) and the catalytic evaluation of a set of phosphite ligands (R = Me, Bn, CHPh$_2$, 1-adamantyl) in the asymmetric Rh-catalyzed hydroformylation of disubstituted aryl olefins, in our endeavour to recognize the effect of the ligand's ether substituent in catalysts activity and selectivity.

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The ligand's cone angles were calculated using the semi-empirical PM6 Hamiltonian, and ^{31}P NMR spectroscopic studies in solution were performed for Rh/phosphite complexes. Furthermore, kinetic studies were carried out for the hydroformylation of *trans*-1-phenyl-1-propene with the Rh/tris[(*R*)-2′-benzyloxy-1,1′-binaphthyl-2-yl]phosphite catalyst, whereas the effects of reaction parameters in reaction rate and selectivity are discussed.

2. Experimental

2.1. Material and methods

^{1}H, ^{13}C and ^{31}P NMR spectra were recorded in $CDCl_3$ solutions on a Bruker Avance 400 MHz spectrometer. Chemical shifts for ^{1}H and ^{13}C are expressed in ppm, relatively to an internal standard of TMS, while for ^{31}P, a solution of phosphoric acid 85% was used as external standard. GC–MS was carried out on HP-G1800A mass selective detector apparatus, equipped with capillary HP-5 column and ESI detector. GC was carried out on Agilent-6890 and Konik HRGC–3000C apparatus equipped, respectively, with capillary column HP-5 and chiral capillary column Supelco β-Dex 120, both with FID detectors. Enantiomerically pure (*R*)-BINOL (99% ee) and all reagents were from commercial origin.

2.2. Ligands synthesis

2.2.1. Chiral mono-alkyl ethers

(*S*) or (*R*)-BINOL (**1**) was dried azeotropically with toluene. To a stirred solution of **1** (5.0 g, 17 mmol), PPh_3 (4.5 g, 17 mmol) and the desired alcohol **2a**–**d** (20 mmol) in dry THF (100 mL), diethyl azodicarboxylate (DEAD) (40% in toluene, 7.5 mL, 17 mmol) was dropwise added at 0 °C. After 48 h at room temperature, the solvent was evaporated and the *mono*-alkyl ethers **3a**–**d** were isolated by silica gel column chromatography, using dichloromethane/*n*-hexane (1:1) as eluent, and the products were further purified by recrystallization from toluene/*n*-hexane. Spectroscopic data of **3a**–**c** were in good agreement with those previously reported [38]

(Note: DEAD is highly toxic, so the appropriate safety procedures were taken for its manipulation. R: 5-11-20-36/37/38-48/20-63-65-67; S: 26-36/37-62).

*(R)-2′-(adamantyloxy)-1,1′-binaphthyl-2-ol (**3d**).* The product was obtained as a white solid (yield: 52%, 3.71 g); mp: 85–87 °C; $[\alpha]_D^{25}$: −130 (*c* 2.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)]1.20 (d, *J* = 12.0 Hz, 3H), 1.31 (d, *J* = 12.4 Hz, 3H), 1.46 (br s, 6H), 1.80 (br s, 3H), 5.53 (s, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 7.04–7.25 (m, 6H), 7.33 (d, *J* = 9.2 Hz, 1H), 7.69–7.76 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)]30.9, 35.9, 43.0, 80.6, 117.0, 118.4, 123.1, 123.9, 124.9, 124.9, 125.9, 126.0, 126.4, 126.6, 128.0, 128.2, 129.0, 129.1, 129.5, 129.7, 130.9, 133.8, 133.9, 151.7, 151.9. HRMS (ESI) (*m*/*z*): calcd for $C_{30}H_{28}O_2Na$ $[M + Na]^+$, 443.1982; found, 443.1988.

2.2.2. Chiral tris-binaphthyl monophosphites

A dried Schlenk flask was charged with the desired monoprotected BINOL ether **3a**–**d** (6.9 mmol), then placed under nitrogen atmosphere and dry triethylamine (15 mL) was added. The solution was cooled to 0 °C and PCl_3 (0.2 mL, 2.3 mmol) was slowly added. After stirring for 3 h, the solvent was evaporated, the phosphites **4a**–**d** were isolated through silica gel column chromatography using dichloromethane/*n*-hexane (1:1) as eluent, and further purified by recrystallization in ethyl ether/*n*-hexane. Spectroscopic data of **4a**–**c** were in good agreement with those previously reported [36].

*Tris[(R)-2′-(adamantyloxy)-1,1′-binaphthyl-2-yl]phosphite ((R)-**4d**).* The product was obtained as a white solid (yield: 76%, 2.25 g); mp: 158–160 °C; $[\alpha]_D^{25}$:−160 (*c* 2.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm)]1.32–1.42 (m, 33H), 1.80 (br s, 12H), 6.44 (d, *J* = 8.8 Hz, 3H), 6.77 (d, *J* = 8.4 Hz, 3H), 6.89–7.22 (m, 18H), 7.29 (d, *J* = 8.8 Hz, 3H), 7.64 (d, *J* = 8.4 Hz, 3H), 7.68 (d, *J* = 7.6 Hz, 3H), 7.70 (d, *J* = 8.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)]29.9, 35.0, 42.1, 77.7, 119.2, 119.3, 122.3, 122.3, 122.8, 122.9, 123.4, 124.3, 124.5, 124.8, 125.4, 125.5, 126.5, 126.6, 127.1, 127.5, 128.9, 129.0, 132.7, 133.0, 146.7, 146.7, 150.9; ^{31}P NMR (161 MHz, $CDCl_3$): δ (ppm)] 132.17; HRMS (ESI): (*m*/*z*) calcd for $C_{90}H_{81}O_6PNa$ $[M + Na]^+$, 1311.5663; found, 1311.5628.

*Tris[(S)-2′-(benzyloxy)-1,1′-binaphthyl-2-yl]phosphite ((S)-**4b**).* The product was obtained as a white solid (yield: 87%, 2.315 g); mp: 112–114 °C; $[\alpha]_D^{25}$: −15 (*c* 1.0, toluene).

2.3. General hydroformylation procedure

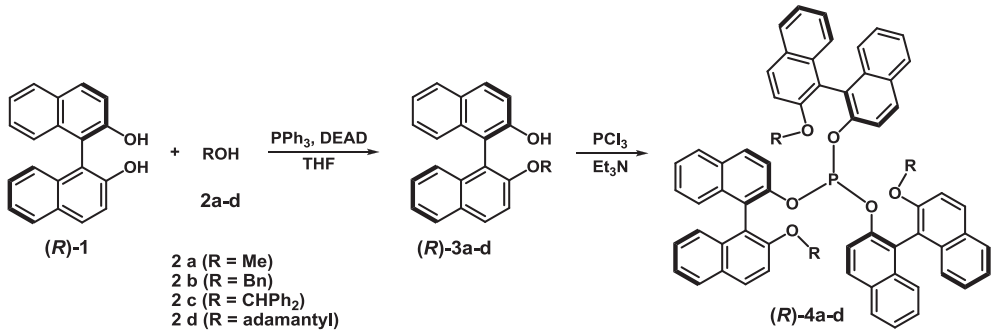
The autoclave was charged with the appropriate amount of phosphite ($14.5 \cdot 10^{-3}$ mmol) and the system was purged by three cycles of vacuum and *syngas*. A solution of $[Rh(CO)_2(acac)]$ (0.75 mg, $2.9 \cdot 10^{-3}$ mmol) in toluene was introduced, under vacuum. Then, the reactor was pressurized with 40 bar of an equimolar mixture of CO/H_2, and kept at 80 °C for 1 h to ensure the formation of the Rh/phosphite complex. After this incubation period, the autoclave was slowly depressurized and set to the working temperature. The substrate (2.32 mmol), previously passed through an aluminium oxide (grade I) column was introduced through the inlet *cannula*. Then, pressure was set to the desired value for each catalytic experiment. For kinetic studies, samples were taken at no more than 20% conversions of alkenes into aldehydes in order to determine the initial rates, without product interferences. The conversion, chemo- and regioselectivity throughout the reactions were determined by gas chromatography analysis of aliquots from the reaction mixture. Enantiomeric excesses (ee) were determined by GC equipped with a chiral capillary column, through the injection of the aldehydes or the respective carboxylic acids obtained from aldehydes oxidation, with potassium permanganate. Final products of all catalytic reactions were identified by the appropriate analytical techniques.

2.4. Computational calculation of monophosphite ligand cone angles

In order to measure the monophosphite cone angles, the MOPAC2009 [39] semi-empirical molecular modelling software and the molecular editors AVOGADRO [40] and MOLDEN [41] were used. The first step was the optimization of the monophosphite ligands **4a**–**d** molecular geometries for *anti* conformations, *i.e.* with the OR substituents positioned straight opposite to the phosphorus lone electron pair. After the geometric optimization for a large number of possible *anti* conformers, the most stable was selected, using the PM6 semi-empirical Hamiltonian [42] in all calculations. The structure was then read by the molecular editor, in which a reference point (X) was defined at a distance of 2.28 Å from the P atom, corresponding to the centre of the apex angle of Tolman's [43] cylindrical cone. Since we were dealing with symmetrical ligands, this point lied along their C_3 axis of symmetry. The farthest H atom from the C_3 axis was used to measure the P-X-H angles (α), using the atomic centres. In order to convert them into cone angles (θ), consistent with Tolman's definition [43], considering the van der Waals surfaces, the half cone angle (θ/2) was calculated by the expression:

$$(\theta/2) = \alpha + 180/\pi \times \sin^{-1}(r_H/d) \quad (1)$$

where r_H is the van der Waals radius of hydrogen and d is the distance X–H [44].



Scheme 1. Synthesis of tris-binaphthyl monophosphite ligands.

3. Results and discussion

3.1. Synthesis of chiral tris-binaphthyl monophosphite ligands

The synthetic strategy for chiral monophosphites of general formula P(O–BIN–OR)$_3$, (R = Me, Bn, CHPh$_2$), (*R*)-**4a**–**c** has been previously optimized [36], through the mono-etherification of (*R*)-BINOL **1**, *via* modified Mitsunobu reaction [38], using primary and secondary alcohols, followed by PCl$_3$ phosphorylation (Scheme 1). In order to expand the study of the effect of the size and structure of the ligand R group, the monophosphite **4d** (*R* = 1-adamantyl), was also synthesized following the same approach.

Reactions of BINOL with methanol **2a** or benzyl alcohol **2b**, gave good yields (84–87%) of the desired BINOL *mono*-ethers **3a**–**b**. The reaction proceeded at a much slower rate with diphenylmethanol **2c** than with primary alcohols, but the *mono*-ether **3c** was obtained in a satisfactory yield (63%), with full recovery of the non-reacted BINOL. However, with 1-adamantanol **2d**, the etherification took place very slowly to give the BINOL ether **3d** in 50% isolated yield. Therefore, as expected, the nature of the R substituent strongly affects the rate of etherification. In all cases, the formation of BINOL *bis*-ethers was negligible (less than 4%). In the second step of the synthesis, the phosphorylation of *mono*-ethers **3a**–**d** with PCl$_3$ was performed in triethylamine, yielding 83%, 81%, 77% and 76% of the corresponding phosphites, respectively. The use of Et$_3$N as solvent and, simultaneously, as base in this reaction, rendered clean and reproducible syntheses.

Table 1
Calculation of ligand cone angles for optimized *anti* conformers.

Ligand	Calculated θ (Lit. *)
P(OMe)$_3$	96° (107°)
P(OPh)$_3$	123° (121°)
P(O–o–^{t}BuPh)$_3$	188° (175°)
(***R***)-**4a**	239°
(***R***)-**4b**	253°
(***S***)-**4b**	252°
(***R***)-**4c**	271°
(***R***)-**4d**	249°

*Literature values [43].

3.2. Ligand cone angles

The cone angles (θ) of the new tris-binaphthyl phosphite ligands were determined, using computational chemistry software and involving Tolman's standard definition, as described in section 2.4. Firstly, the cone angles (θ) of trimethyl phosphite P(OMe)$_3$, triphenylphosphite P(OPh)$_3$ and tris(*o*-tertbutylphenyl)phosphite P(O–*o*–^{t}BuPh)$_3$ were determined, using the described methodology, with the results being consistent with those values previously reported in the literature [43]. Therefore, the described strategy was applied to estimate the cone angles (θ) of phosphite ligands (*R*)-**4a**–**d**, always assuming their *anti* conformations and threefold symmetry with *P* helical orientation [45]. Furthermore, in the case of ligand (*S*)-**4b**, computational calculations were also performed assuming *M* helical orientation.

The results in Table 1 show that there is only a slight influence of the relatively remote OR substituents in the calculated cone angle for the optimized *anti* geometries of monophosphite ligands **4a**–**d**, attaining values higher than 200° in all cases (239–271°). In Fig. 1, the front and back views of PM6 optimized

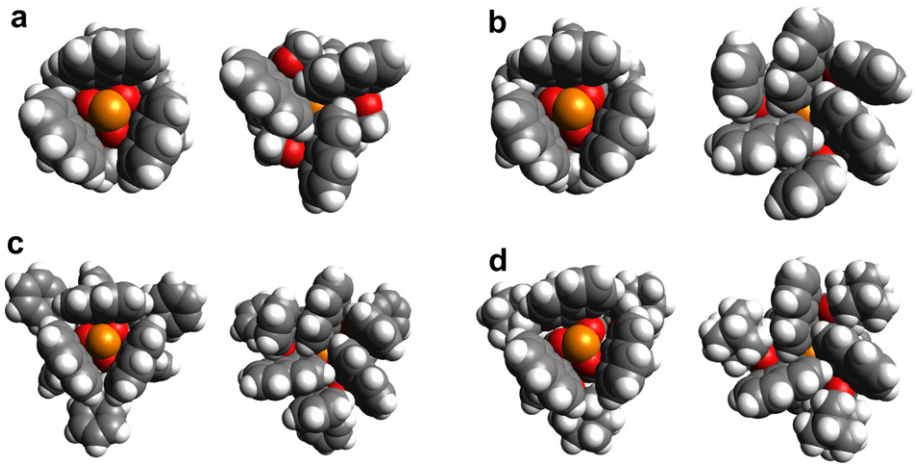


Fig. 1. Front and back views of PM6 optimized structures for monophosphites **4a**–**d** *anti* conformers. a) P(O-BIN-OMe)$_3$; b) P(O-BIN-OBn)$_3$; c) R = P(O-BIN-OCHPh$_2$)$_3$; d) P(O-BIN-OAdamantyl)$_3$.

structures for *anti* conformers of monophosphites **4a**–**d** are illustrated.

Ligands **4a** and **4b**, with considerable conformational flexibility on their OR groups, present cone angles of 239 and 253°, respectively, with the binaphthyl scaffold being the main feature that determines the ligand cone angle, as it is shown in Fig. 1a and b. The highly restraining bulkiness of the diphenylmethoxy groups in ligand **4c** push the binaphthyl groups towards the P atom, Fig. 1c, which causes an increased cone angle of 271°. The adamantyloxy groups of monophosphite **4d** can easily accommodate opposite to P atom, with the cone angle (249°) being also controlled by the binaphthyl framework.

3.3. NMR studies of [Rh(acac)(CO)(phosphite)] complexes in solution

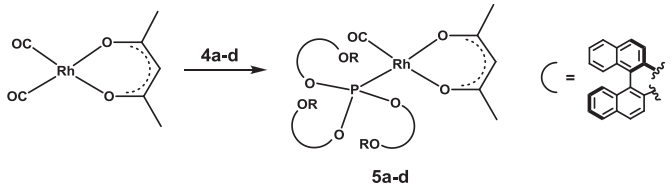
The NMR studies in solution, carried out with equimolar amounts of $[Rh(CO)_2(acac)]$ and phosphites **4a**–**d** in $CDCl_3$, at 298 K, revealed in all cases the presence of one major species, presenting a ^{31}P NMR doublet in the range 120–125 ppm, with $^1J(^{103}Rh–^{31}P$ = 289–292 Hz) attributed to [Rh(acac)(CO)(phosphite)] (**5a**–**d**) (Scheme 2), and a non-identified minor component (<10%), showing a doublet in the range δ = 131–134 ppm and J_{Rh-P} within 260–265 Hz. When a twofold excess of ligand was used, the NMR spectra of the complexes remained unchanged, and only the typical signal of the non-coordinated phosphite ligand, as a singlet in the range 131–134 ppm, was observed. Furthermore, when Rh/**4a** and Rh/**4b** complexes were isolated, only the main doublet was observed in the ^{31}P NMR spectra at 120–125 ppm, a single IR signal at 2005 ± 2 cm^{-1} was found, and the exact mass analysis indicated the presence of rhodium complexes with one carbonyl group and a single phosphite ligand, HRMS-ESI $[M\text{-acac}]^+$ = 1059.1914 (Rh/**4a**); $[M\text{-acac}]^+$ = 1287.2882 (Rh/**4b**). These results are consistent with those obtained from the previously reported related complex $Rh(acac)(CO)(P(OPh)_3)$ (δ = 122.1 ppm; $^1J(^{103}Rh, ^{31}P)$ = 293 Hz; IR(CO) = 2006 cm^{-1}) [46] and the similar Rh/phosphite complexes of type $[Rh(P(O–BIN–O_2CR)_3)(COD)]OTf$ [37].

3.4. Hydroformylation of hindered phenylpropenes with Rh/chiral monophosphite catalysts

Catalysts prepared *in situ* from rhodium precursor $[Rh(CO)_2(acac)]$ and ligands **4a**–**d**, in the presence of *syngas*, were evaluated in the hydroformylation of 2-phenyl-1-propene **6** and *trans*-1-phenyl-1-propene **7** (Scheme 3).

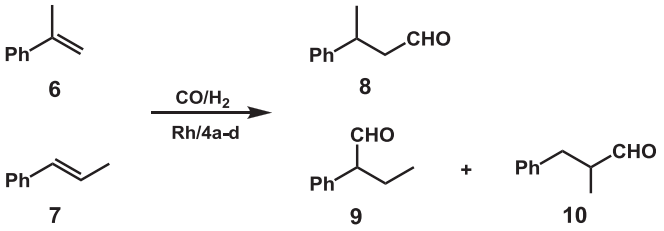
Table 2 collects the results of the hydroformylation of substrates **6** and **7**.

In the hydroformylation of 2-phenyl-1-propene **6**, at 80 °C and 30 bar of *syngas*, Rh/**4a**–**d** catalysts reached conversions of 78, 71, 47 and 94%, respectively, after 18 h of reaction, while a conversion of 41% was obtained without addition of ligand (Table 2, entries 1–5). Thus, a significant ligand effect was observed on the reaction rates, being the most active catalyst the one with ligand **4d** (R = adamantyl), which was twice as fast as catalyst with ligand **4c**



5a-d

Scheme 2.



Scheme 3.

(R = $CHPh_2$). The rates achieved with catalytic systems Rh/**4a** and Rh/**4b** were within those obtained with Rh/**4d** and Rh/**4c**. Complete chemoselectivity was reached for aldehydes, together with a substrate controlled regioselectivity (≥99% to the linear aldehyde **8**), while the stereoselectivity was low (equal or below 15% in all cases). The Rh/phosphite catalysts were then applied to the hydroformylation of *trans*-1-phenyl-1-propene **7**, using the same reaction conditions (Table 2, entries 7–10). From these results, we observed that the 1,2-disubstituted olefin **7** hydroformylates faster than the 1,1-disubstituted olefin **6**, which is in agreement with the established relative reactivity of olefins [47], with catalyst Rh/**4d** being again the one that achieved the highest rate, with TOF = 256 h^{-1}; 96% of conversion in 3 h (Table 2, entry 10). The rates shown for Rh/**4a**–**d** catalysts followed the same trend for the substrate **7** (*i.e.* **4d** > **4a** ≈ **4b** > **4c**).

This result becomes evident in Fig. 2 that shows the evolution of the hydroformylation of **7** along the time, catalyzed with Rh/**4a**–**d**. Despite the similar conversions observed using Rh/**4c** system and the unmodified Rh catalyst (Table 2, entries 6 and 9) the concomitant increased regioselectivity in the presence of the ligand suggests the formation of a complex with a high sterical hindrance caused by the diphenylmethoxy groups, which may enclose the metal, making difficult the olefin approach. Slight differences were observed in the regioselectivity for 2-phenylbutanal **9** in the range 84–90% with all catalytic systems and, independently of the OR substituent at the ligand, the enantiomeric excesses were equal or below 20% (*R*). As it was expected, the use of phosphite (*S*)-**4b** as ligand in the hydroformylation of **7**, produced similar results to those obtained with its (*R*)-BINOL based counterpart, however with

Table 2
Evaluation of Rh/monophosphite catalysts in hydroformylation of 2-phenyl-1-propene **6** and *trans*-1-phenyl-1-propene **7**.

Entry	Substrate	Ligand	time (h)	Conv.[a] (%)	TOF[b] (h^{-1})	Regio. (%)	ee (%)
1	**6**	no ligand	18	41	18	98[c]	–
2		(***R***)-**4a**	18	78	35	99[c]	10 (*R*)[e]
3		(***R***)-**4b**	18	71	32	100[c]	15 (*R*)[e]
4		(***R***)-**4c**	18	47	21	100[c]	8 (*R*)[e]
5		(***R***)-**4d**	18	94	42	99[c]	10 (*R*)[e]
6	**7**	no ligand	3	25	67	62[d]	–
7		(***R***)-**4a**	3	81	216	84[d]	16 (*R*)[f]
8		(***R***)-**4b**	3	72	192	88[d]	20 (*R*)[f]
9		(***R***)-**4c**	3	33	88	90[d]	11 (*R*)[f]
10		(***R***)-**4d**	3	97	259	84[d]	12 (*R*)[f]
11		(***S***)-**4b**	3	74	197	89[d]	20 (*S*)[f]

Reaction conditions: $[Rh(CO)_2(acac)]$ = 0.193 mM, 15 mL toluene; substrate/Rh/ligand = 800:1:5; P (CO/H_2) = 30 bar; *T* = 80°C.
[a] % of substrate converted at the indicated time.
[b] Turnover frequency: mol of substrate converted per mol of Rh per hour.
[c] Regioselectivity: % of **8** with respect to the total amount of aldehydes.
[d] Regioselectivity: % of **9** with respect to the total amount of aldehydes.
[e] % Enantiomeric excesses measured for **8**.
[f] % Enantiomeric excesses measured for **9**; Chemoselectivity was always ≥99% for aldehydes.

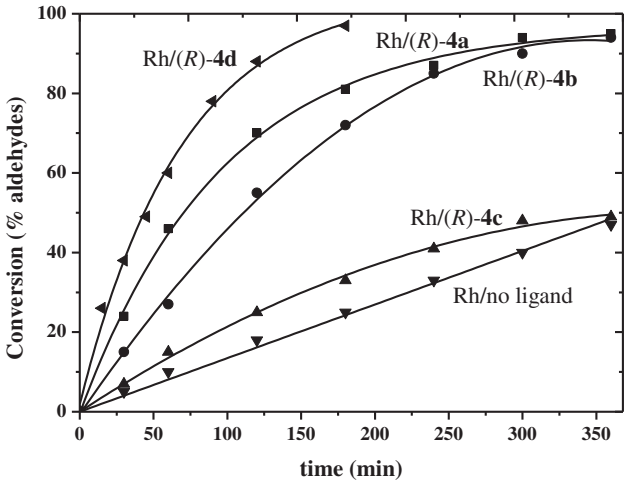


Fig. 2. Evolution on the hydroformylation of **7** catalyzed by Rh/**4a**–**d**. Reaction conditions: $[Rh(CO)_2(acac)]$ = 0.193 mM, 15 mL toluene; **7**/Rh/ligand = 800:1:5; P = 30 bar (CO/H_2); T = 80 °C.

inverse absolute configuration of the products (Table 2, entry 11). In order to evaluate the catalysts performance in the hydroformylation of a terminal aryl olefin, the Rh/**4a**–**d** catalytic systems were also applied to styrene. At a temperature of 40 °C and *syngas* pressure of 25 bar, regardless of the phosphite used, complete conversions (>90%) were achieved after 3 h reaction, with TOF's in the order of 260 h^{-1}, full chemoselectivity for aldehydes and 96% of regioselectivity for the branched aldehyde. It should be noticed that the OR substituent at the ligand did not affect the catalytic activity, contrarily to the results using substituted olefins as substrates. Furthermore, using (*R*)-**4b** as model ligand, the hydroformylation of styrene was also performed at 80 °C and 25 bar, achieving complete conversion after 25 min, with a TOF of $1.9 \cdot 10^3$ h^{-1}, which is within the order of the most active catalytic systems reported so far [16]. Despite this remarkable activity, enantiomeric excesses were in the range 12–20% in all cases. The monodentate nature of the rhodium/phosphite complexes, as well as the possible equilibrium between *P* and *M* conformations of the ligands in solution [37], which causes the loss of C_3 symmetry and the subsequent chirality, might explain the low enantiodiscrimination of the catalytic species.

3.5. Kinetic study of hydroformylation of trans-1-phenyl-1-propene with Rh/*4b* catalyst

As mentioned above, hydroformylation kinetic studies are mainly focused on a limited number of model olefins, like styrene and various terminal linear or cyclic internal alkenes. Nevertheless, the hydroformylation of disubstituted aryl olefins is actually much less studied and most of the described catalytic systems require the use of severe reaction conditions [8–12]. In this context, the olefin *trans*-1-phenyl-1-propene **7** was chosen as model substrate and **4b** as model ligand from this threefold symmetry phosphite family, in order to investigate the effects of the reaction parameters (temperature, P/Rh ratio, concentrations of substrate and catalyst and partial pressures of H_2 and CO) on the hydroformylation initial rate and selectivity.

To study the effect of temperature, experiments were performed in the range 50 to 90 °C, keeping constant the rest of reaction parameters. Results presented in Table 3 show a sharp increase of the reaction rate (3.5 times) when the temperature is raised from 50 to 60 °C. Above 60 °C, the rate steadily increases linearly with temperature. This non-Arrhenius behaviour might be attributed to

Table 3
Effect of temperature in the catalytic hydroformylation of *trans*-1-phenyl-1-propene **7** with Rh/**4b**

T (°C)	TOF[a] (h^{-1})	Regio.[b] (%)
50	40	97
60	144	95
70	176	91
80	208	89
90	232	80

Reaction conditions: $[Rh(CO)_2(acac)]$ = 0.193 mM, 15 mL toluene; **7**/Rh = 800, **4b**/Rh = 5; P = 30 bar (CO/H_2).
[a] Turnover frequency calculated until *ca.* 20% conversion.
[b] Regioselectivity for 2-phenylbutanal **9**. Chemoselectivity was always ≥99% for aldehydes.

the occurrence of a required stage for formation/regeneration of the active catalytic species after the first incubation period, or simply due to scarce catalytic activity of Rh/**4b** to carry out the hydroformylation of the disubstituted olefin at temperatures below 60 °C. The regioselectivity for **9** increased from 80 to 97% when the temperature was diminished from 90 to 50 °C, similar to the results reported by Lazzaroni *et al.* [48] in rhodium-carbonyl catalyzed hydroformylation of styrene, and attributed to slower β-elimination. Furthermore, the chemoselectivity was ≥99% for aldehydes in all cases.

The effect of the ligand/Rh molar ratio in the catalyst performance was also investigated. The molar ratio was changed from 1 to 20, keeping the rest of parameters in the standard conditions of this study.

The results summarized in Table 4 indicate that the formation of the active catalytic species requires from 2.5 to 5 mol of phosphite per Rh, since in this interval the maximum rate is achieved. Further increase of the phosphite concentration leads to a drop in the rate. Remarkably, the regioselectivity for aldehyde **9** scarcely changes when the phosphite/Rh ratio was increased from 5 to 20. Other reports of Rh(I) catalysts, modified with naphthyl [18] and biphenyl [19] based monodentate phosphites, showed a dependence on the ligand concentration in the reaction rate and selectivity.

The effect of *trans*-1-phenyl-1-propene concentration on the rate of the hydroformylation reaction was studied varying the substrate initial concentration from 38.7 to 309.3 mM, while the rest of reaction conditions were kept constant. Results are shown in Fig. 3, where the plot of the TOF *versus* the initial concentration of substrate nicely fits with a straight line, indicating that the reaction is first order with respect to the substrate. Moreover, the chemoselectivity for aldehydes was always up to 99% and nearly constant regioselectivity (88–89%) for **9** was observed in all experiments.

Next, the effect of catalyst concentration on hydroformylation initial rate was analysed. A substrate concentration of 154.7 mM was used, keeping constant the standard conditions for this study.

Table 4
Effect of **4b**/Rh molar ratio in the catalytic hydroformylation of *trans*-1-phenyl-1-propene **7**.

L/Rh	[ligand] (mM)	TOF[a] (h^{-1})	Regio.[b] (%)
1	0.193	184	85
2.5	0.483	216	88
5	0.965	208	89
15	2.895	160	90
20	3.860	144	90

Reaction conditions: $[Rh(CO)_2(acac)]$ = 0.193 mM, 15 mL toluene; **7**/Rh = 800; P = 30 bar (CO/H_2); T = 80 °C.
[a] Turnover frequency calculated until *ca.* 20% conversion.
[b] Regioselectivity for 2-phenylbutanal **9**. Chemoselectivity was always ≥99% for aldehydes.

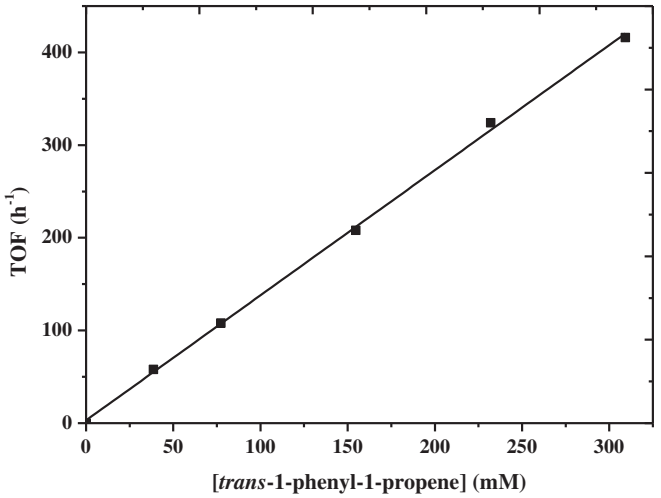


Fig. 3. Effect of the initial substrate concentration on hydroformylation TOF with Rh/**4b**. Reaction conditions: $[Rh(CO)_2(acac)]$ = 0.193 mM, 15 mL toluene; **4b**/Rh = 5; P = 30 bar (CO/H_2); T = 80 °C.

The results collected in Table 5 show that the reaction is also first order with respect to the catalyst concentration. Also no considerable changes were observed in regioselectivity with variation of initial catalyst concentration, while chemoselectivity was always ≥99% for aldehydes.

The effects of CO and H_2 partial pressures were then appraised in the initial rate and selectivity of the reaction, using the Rh/**4b** catalyst and the results are summarized in Table 6.

The results show a linear dependence of the reaction rate with the partial pressure of H_2, for constant partial pressures of CO, at both 10 and 20 bar (Table 6, entries 1–8). The regioselectivity for aldehyde **9** does not depend on $p(H_2)$ when a partial pressure of CO of 10 bar is used (Table 6, entries 1–4) however, when a higher p(CO) of 20 bar is used, an increase from 82 to 90% is observed in the regioselectivity, varying $p(H_2)$ from 2 to 20 bar (Table 6, entries 5–8).

A more complex effect was observed for CO partial pressure on the reaction rate. At a constant H_2 partial pressure of 10 bar, the increase of p(CO) from 5 to 25 bar produced a decrease in reaction rates (Table 6, entries 2,7,9,10). At a constant H_2 partial pressure of 20 bar, the increase of p(CO) from 2 to 10 bar caused a slight increase in reaction rates (Table 6, entries 3,11,12), however a slight decrease in the rate was observed varying CO partial pressure from 10 to 20 bar (Table 6, entries 3 and 8). Moreover, significant increase in the regioselectivity for aldehyde **9** was observed when p(CO) was raised, for both H_2 partial pressures of 10 and 20 bar (Table 6, entries 2,7,9,10 and entries 3,8,11,12). Since both H_2 and CO partial pressures have a significant effect in the reaction regioselectivity, the complex effects depicted in Table 6 may be explained by the different isomeric aldehydes **9** and **10** formation rates dependence with $p(H_2)$ and p(CO). Thus, considering the experiments involving p(CO) = 10 bar and varying $p(H_2)$ from 10 to 30 bar (Table 6, entries 2–4), as well as $p(H_2)$ = 10 bar and varying p(CO) from 10 to 25 bar (Table 6, entries 2,7 and 10), the experimental rate expression **(2)** for the hydroformylation of *trans*-1-phenyl-1-propene with the Rh/phosphite **4b** catalyst, obtained from the plots of log (TOF) as function of the several parameters, can be written as:

$$d[\text{aldehyde}]/dt = k[\text{Rh}][\text{phosphite}]^{-0.3}[\text{substrate}][H_2][\text{CO}]^{-0.3} \quad (2)$$

This expression applies exclusively to the standard conditions used in this study, [Rh] = 0.2–0.6 mM, phosphite/Rh ≥ 5, [substrate] = 30–300 mM and CO and H_2 pressures ≥ 10 bar. The partial negative orders for the CO pressure and ligand, combined with a positive order with respect to the substrate are reminiscent of the expressions found for the hydroformylation of 1-alkenes with Rh/PPh_3 catalysts [33–35,49]. However, the most striking result of the kinetic expression for the hydroformylation of *trans*-1-phenyl-1-propene with the Rh/phosphite **4b** catalyst is the positive order for both the substrate and the H_2 pressure, suggesting that either the olefin coordination/insertion or the oxidative addition of H_2 to the Rh/acyl intermediate may be the rate determining step. This ambiguous behaviour may be attributed to an intermediate situation, implying that there is not a clear rate limiting step, since two of more steps proceed at similar rate, or rather due to the presence of dinuclear metal resting state species, whose fast equilibrium with the active catalytic species depends on H_2 pressure [50–52].

Table 5
Effect of Rh concentration in the catalytic hydroformylation of *trans*-1-phenyl-1-propene **7** with Rh/**4b**

$[Rh(CO)_2(acac)]$ (mM)	Initial rate[a] (mmol substrate·h^{-1})	Regio.[b] (%)
0.193	0.603	89
0.386	1.253	92
0.580	1.810	91

Reaction conditions: [**7**] = 154.7 mM, 15 mL toluene; **4b**/Rh = 5; P = 30 bar (CO/H_2); T = 80 °C.
[a] Initial rate in mmol of substrate converted into aldehydes per hour until *ca.* 20% conversion.
[b] Regioselectivity for 2-phenylbutanal **9**. Chemoselectivity was always ≥99% for aldehydes.

Table 6
Effects of H_2 and CO partial pressures on the catalytic hydroformylation of *trans*-1-phenyl-1-propene **7** with Rh/**4b**

Entry	P(CO) (bar)	$P(H_2)$ (bar)	TOF[a] (h^{-1})	Regio.[b] (%)
1	10	5	102	84
2	10	10	200	85
3	10	20	376	88
4	10	30	552	88
5	20	2	66	82
6	20	5	112	88
7	20	10	176	88
8	20	20	360	90
9	5	10	277	81
10	25	10	156	95
11	2	20	313	81
12	5	20	340	86

Reaction conditions: $[Rh(CO)_2(acac)]$=0.193mM, 15 mL toluene; **7**/Rh=800, **4b**/Rh=5; T=80°C.
[a] Turnover frequency calculated until *ca.* 20% conversion.
[b] Regioselectivity for 2-phenylpropanal **9**. Chemoselectivity was always ≥99% for aldehydes.

4. Conclusions

An efficient and clean two-step synthesis of a family of chiral bulky monophosphite ligands was developed, and the cone angles for PM6 optimized *anti* structures were calculated based on original Tolman's definition, achieving values in the range 239–271°. The rhodium/phosphite complexes, prepared *in situ*, showed remarkable catalytic activity in the hydroformylation of hindered phenylpropenes, under relatively mild reaction conditions, with full chemoselectivity for aldehydes. A significant effect of the ether substituent R at the ligand was observed in the catalytic activity, following the trend R = adamantyl > R = Me ≈ R = Bn > R = $CHPh_2$, when both 1,1- and 1,2-substituted aryl olefins were used as substrates. Regardless of the ligands' structure, regioselectivities in

the order of 90% were obtained with all catalytic systems. Despite the noteworthy catalytic activity and regioselectivity, the achievement of high enantioselectivities remains a challenge, since enantiomeric excesses below 20% were obtained with these ligands. The experimental rate expression for the hydroformylation of *trans*-1-phenyl-1-propene with the catalyst Rh/tris[(*R*)-2′-benzyloxy-1,1′-binaphthyl-2-yl]phosphite, in the studied range of catalyst concentrations used and exclusively applicable for H_2 and CO partial pressures above 10 bar, showed a first order dependence on the substrate concentration, together with a positive order with respect to the H_2 partial pressure, and slight negative order on CO partial pressure and phosphite ligand concentration.

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References

[1] P.W.N.M. van Leeuwen, C. Claver (Eds.), Rhodium Catalyzed Hydroformylation, Kluwer Academic Publishers, Dordrecht, The Netherlands, 2000.
[2] A. Gual, C. Godard, S. Castillón, C. Claver, Tetrahedron: Asymmetry 21 (2010) 1135–1146.
[3] J. Klosin, C. Landis, Acc. Chem. Res. 40 (2007) 1251–1259.
[4] A.T. Axtell, J. Klosin, G.T. Whiteker, C.J. Cobley, M.E. Fox, M. Jackson, K.A. Abboud, Organometallics 28 (2009) 2993–2999.
[5] A.F. Peixoto, M.M. Pereira, A.A.C.C. Pais, J. Mol. Catal. A: Chem. 267 (2007) 234–240.
[6] P. Uriz, E. Fernández, N. Ruiz, C. Claver, Inorg. Chem. Commun. 3 (2000) 515–519.
[7] K.B. Rajurkar, S.S. Tonde, M.R. Didgikar, S.S. Joshi, R.V. Chaudhari, Ind. Eng. Chem. Res. 46 (2007) 8480–8489.
[8] K. Nozaki, H. Takaya, T. Hiyama, Top. Catal. 4 (1997) 175–185.
[9] L. Kollár, E. Farkas, J. Bâtiu, J. Mol. Catal. A: Chem. 115 (2002) 283–288.
[10] R. Lazzaroni, R. Settambolo, G. Uccello-Barretta, A. Caiazzo, S. Scamuzzi, J. Mol. Catal. A: Chem. 143 (1999) 123–130.
[11] A.C. Silva, K.C.B. Oliveira, E.V. Gusevskaya, E.N. Santos, J. Mol. Catal. A: Chem. 179 (2002) 133–141.
[12] M.R. Axet, S. Castillon, C. Claver, Inorg. Chim. Acta 359 (2006) 2973–2979.
[13] H. Siegel, W. Himmele, Angew. Chem. Int. Ed. Engl. 19 (1980) 178–183.
[14] P.W.N.M. van Leeuwen, C.F. Roobeek, J. Organomet. Chem. 258 (1983) 343–350.
[15] T. Jongsma, G. Challa, P.W.N.M. van Leeuwen, J. Organomet. Chem. 421 (1991) 121–128.
[16] A. van Rooy, E.N. Orij, P.C.J. Kamer, P.W.N.M. van Leeuwen, Organometallics 14 (1995) 34–43.
[17] A.F. Peixoto, M.M. Pereira, A.M.S. Silva, C.M. Foca, J.C. Bayón, M.J.S.M. Moreno, A.M. Beja, J.A. Paixão, M.R. Silva, J. Mol. Catal. A: Chem. 275 (2007) 121–129.
[18] A.A. Dabbawala, H.C. Bajaj, R.V. Jasra, J. Mol. Catal. A: Chem. 302 (2009) 97–106.
[19] O. Saidi, J. Ruan, D. Vinci, X. Wu, J. Xiao, Tetrahedron Lett. 49 (2008) 3516–3519.
[20] A. van Rooy, J.N.H. de Bruijn, K.F. Roobeek, P.C.J. Kamer, P.W.N.M. van Leeuwen, J. Organomet. Chem. 507 (1996) 69–73.
[21] J.-H. Xie, Q.-L. Zhou, Acc. Chem. Res. 41 (2008) 581–593.
[22] K.N. Gavrilov, S.E. Lyubimov, S.V. Zheglov, E.B. Benetsky, P.V. Petrovskii, E.A. Rastorguev, T.B. Grishina, V.A. Davankov, Adv. Synth. Catal. 349 (2007) 1085–1094.
[23] B.D. Chapsal, Z. Hua, I. Ojima, Tetrahedron 17 (2006) 642–657.
[24] M.T. Reetz, G. Mehler, Angew. Chem. Int. Ed. 39 (2000) 3889–3890.
[25] M. Yan, X. Li, A.S. Chan, Chin. Sci. Bull. 48 (2003) 2188–2192.
[26] C.J. Cobley, K. Gardner, J. Klosin, C. Praquin, C. Hill, G.T. Whiteker, A. Zanotti-Gerosa, J.L. Petersen, K.A. Abboud, J. Org. Chem. 69 (2004) 4031–4040.
[27] Z. Hua, V.C. Vassar, H. Choi, I. Ojima, Proc. Natl. Acad. Sci. U. S. A. 101 (2004) 5411–5416.
[28] M. Rosales, G. Chacón, A. González, I. Pacheco, P.J. Baricelli, L.G. Melean, J. Mol. Catal. A: Chem. 287 (2008) 110–114.
[29] V.K. Srivastava, S.K. Sharma, R.S. Shukla, N. Subrahmanyam, R.V. Jasra, Ind. Eng. Chem. Res. 44 (2005) 1764–1771.
[30] I. del Rio, O. Pàmies, P.W.N.M. van Leeuwen, C. Claver, J. Organomet. Chem. 608 (2000) 115–121.
[31] T. Horiuchi, E. Shirakawa, K. Nozaki, H. Takaya, Organometallics 16 (1997) 2981–2986.
[32] C. Bergounhou, D. Neibecker, R. Mathieu, J. Mol. Catal. A: Chem. 220 (2004) 167–182.
[33] D.Y. Murzin, A. Bernas, T. Salmi, J. Mol. Catal. A: Chem. 315 (2010) 148–154.
[34] V.S. Nair, S.P. Mathew, R.V. Chaudhari, J. Mol. Catal. A: Chem. 143 (1999) 99–110.
[35] B.M. Bhanage, S.S. Divekar, R.M. Deshpande, R.V. Chaudhari, J. Mol. Catal. A: Chem. 115 (1997) 247–257.
[36] R.M.B. Carrilho, A.R. Abreu, G. Petöcz, J.C. Bayón, M.J.S.M. Moreno, L. Kollár, M.M. Pereira, Chem. Lett. 38 (2009) 844–845.
[37] M.T. Reetz, H. Guo, J.-A. Ma, R. Goddard, R.J. Mynott, J. Am. Chem. Soc. 131 (2009) 4136–4142.
[38] M. Takahashi, K. Ogasawara, Tetrahedron 8 (1997) 3125–3130.
[39] J.J.P. Stewart, Stewart Computational Chemistry. MOPAC, Colorado Springs, CO, USA, 2009. http://OpenMOPAC.net/.
[40] Avogadro. Version 1.01, http://avogadro.openmolecules.net/.
[41] G. Schaftenaar, MOLDEN 4.7. CMBI, 1996. http://www.cmbi.ru.nl/molden/molden.html.
[42] J.J.P. Stewart, J. Mol. Model. 13 (2007) 1173–1213.
[43] (a) C.A. Tolman, J. Am. Chem. Soc. 92 (1970) 2956–2965;
(b) C.A. Tolman, Chem. Rev. 77 (1977) 313–346.
[44] T.E. Müller, D.M.P. Mingos, Transit. Met. Chem. 20 (1995) 533–539.
[45] V. Prelog, G. Helmchen, Angew. Chem. Int. Ed. Engl. 21 (1982) 567–583.
[46] W. Simanko, K. Mereiter, R. Schmid, K. Kirchner, A.M. Trzeciak, J.J. Ziolkowski, J. Organomet. Chem. 602 (2000) 59–64.
[47] (a) C. Botteghi, R. Ganzerla, M. Lenarda, G. Moretti, J. Mol. Catal. 40 (1987) 129–182;
(b) M. Haumann, H. Yildiz, H. Koch, R. Schomäcker, Appl. Catal. A: Gen. 236 (2002) 173–178.
[48] R. Lazzaroni, A. Raffaelli, R. Settambolo, S. Bertozzi, G. Vitulli, J. Mol. Catal. 50 (1989) 1–9.
[49] P.C. d'Oro, L. Raimondi, G. Pagani, G. Montrasi, G. Gregorio, A. Andreetta, Chim. Ind. (Milan) 62 (1980) 572–579.
[50] A. Castellanos-Páez, S. Castillón, C. Claver, P.W.N.M. van Leeuwen, W.G.J. de Lange, Organometallics 17 (1998) 2543–2552.
[51] C. Bianchini, H.M. Lee, A. Meli, F. Vizza, Organometallics 19 (2000) 849–853.
[52] E. Fernández, A. Ruiz, C. Claver, S. Castillón, P.A. Chaloner, P.B. Hitchcock, Inorg. Chem. Commun. 2 (1999) 283–287.