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Selective hydroformylation of various olefins using diphosphinite ligands

Shoeb R. Khan and Bhalchandra M. Bhanage*

Novel diphosphinite ligands are synthesized by the reaction of various derivatives of 1,3-diols with chlorodiphenylphosphine. The synthesized ligands exhibited considerable impact on hydroformylation of various olefins with excellent regioselectivity toward branched aldehyde. The effect of solvent, temperature, pressure and catalyst loading on the hydroformylation reaction is also described. The synthesized diphosphinite ligands with rhodium precursor works under milder reaction conditions as compared to traditional phosphine and phosphite-based ligands. Copyright © 2013 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

Keywords: hydroformylation; olefins; bis(phosphinite) ligand; regioselective; homogeneous catalysis

Introduction

Hydroformylation reaction has attracted considerable attention for the synthesis of aldehydes from olefins and finds large applications in fine chemical and pharmaceutical industries.[1] The reaction was first discovered by Otto Roelen in 1938 during investigations on the formation of oxygenated products in cobalt-catalyzed Fisher–Tropsch reactions. Based on homogeneous catalysis, it is one of the largest industrially applied, clean and atom-efficient processes.[2,3] Worldwide, several million tons of aldehyde are produced via hydroformylation reactions, most of which are reduced to alcohols or oxidized to carboxylic acids or esters.[4,5] Nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen (2-arylpropanoic acid) is also synthesized via hydroformylation followed by oxidation of aldehyde using styrene derivative as a substrate.[6,7]

Several transition metal-based catalysts involving Rh, Pt, Co and Ru have been used for this reaction; however, Rh-based catalysts works at lower temperature and pressure and hence are generally preferred for hydroformylation reactions.[8,9] Usually, phosphorus donor ligands employing transition metal complexes are able to act efficiently under mild conditions and are extensively used ligands in homogeneous catalysis, whereas selectivity of desired product can be tuned by varying the ligands attached to the metal centre.[10]

The literature reveals that in the case of hydroformylation processes catalysts based on phosphite/phosphinite (weak σ-donors and strong π-acceptors) ligands are more effective than the conventional Rh-triphenyl phosphine based catalyst.[11–13] Moreover, phosphite and phosphinite ligands are less prone to oxidation compared to phosphine-based ligands.[14,15] However, in spite of their high activity and performance there are very few reports on diphosphinite ligands. Some of the best results with diphosphinite ligands have been obtained using the family of calixarenes, which are known as sophisticated molecular cages and claw-like ligands,[16] pyranoside[17] and furanoside[18] ligands. However, difficulties in preparation of these ligands limit their application.

Thus the development of new ligands to obtain highly active and selective catalysts is always a key issue in the case of the hydroformylation reaction. As hydroformylation seems to be attainable only with synthetic catalysts, much attention has been paid to developing new phosphinite-based ligands. In this regard we have synthesized and characterized a new class of diphosphinite ligands based on 1,3-diol as a backbone and applied to the rhodium-catalyzed hydroformylation of aryl olefins (Scheme 1).

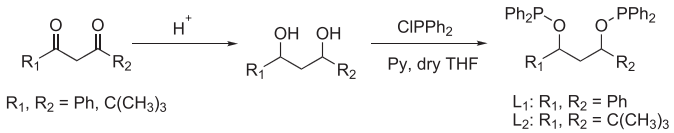
Results and Discussion

The initial studies were conducted using $\mathbf{L_1}$ as a choice of ligand with $Rh(acac)(CO)_2$ for the hydroformylation of styrene as a model reaction (Scheme 2).

A series of experiments were performed to optimize various reaction parameters such as effect of temperature, solvent, catalyst loading, CO/H_2 pressure and time on a model reaction. The results obtained are summarized in Table 1. Initially, the reaction was studied at different temperatures in the range of 50–100°C (Table 1, entries 1–5). High temperature significantly promotes the side reaction of the hydrogenation process with containment of α-formylation and thus provides higher β-aldehyde formation while, lowering the reaction temperature to 50°C, regioselectivity toward branched aldehyde product increased at the expense of reaction rate. Thus further studies were carried out at 60°C, which was found to provide maximum conversion and selectivity toward the desired product (Table 1, entry 4). Next we studied the effect of solvent on hydroformylation reaction. Solvents such as tetrahydrofuran (THF) and methanol provide lower conversion and selectivity of

* *Correspondence to: Bhalchandra M. Bhanage, Department of Chemistry, Institute of Chemical Technology, Matunga, Mumbai 400019, India. E-mail: bm.bhanage@gmail.com*

Department of Chemistry, Institute of Chemical Technology, Matunga, Mumbai 400019, India



Scheme 1. Schematic representation of diphosphinite ligand synthesis.

expected product (Table 1, entries 6 and 7). In the case of methanol as a solvent a considerable amount of acetal formation was observed. It was observed that the reaction was more favourable using toluene as a solvent (Table 1, entry 4). Furthermore, the effect of syngas (CO/H_2) pressure on reaction rate and selectivity was studied (Table 1, entries 4 and 8–10). We observed that lowering the CO/H_2 pressure from 35 to 25 bar did not have any prominent effect on the reaction outcome but with further decrease in pressure decreased the conversion as well as selectivity of the desired product. Thus syngas at 25 bar was found to be the optimized pressure for styrene hydroformylation.

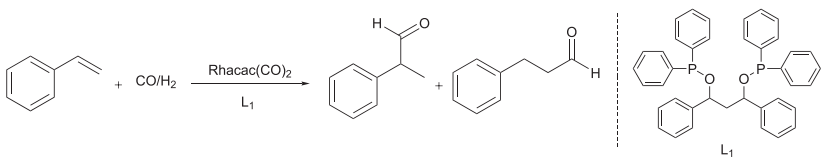
We further studied the substrate:rhodium molar ratio and observed that with increasing molar ratio from 1000:1 to 2000:1 decreased the conversion and selectivity of desired product (Table 1, entry 11); this decrease in conversion and selectivity was due to a decrease in the amount of catalyst from 0.1 mol% (Sub/Rh molar ratio 1000:1) to 0.05 mol% (Sub/Rh molar ratio 2000:1). Subsequently, we also investigated the effects of ligand/Rh molar ratio and it was observed that on increasing the P/Rh molar ratio from 4 to 8 the selectivity for branched aldehyde increased at the expense of conversion (Table 1, entries 4 and 12). The influence of reaction time ranging from 6 h to 3 h was also studied, and it was found that within 4 h the reaction provides maximum yield and selectivity for branched aldehyde formation (Table 1, entries 4, 13 and 14).

Hence the optimized reaction conditions for the hydroformylation of styrene were: styrene (5 mmol), $Rh(acac)(CO)_2$ (0.1 mol%), ligand ($\mathbf{L_1}$) (0.2 mol%), 25 bar CO/H_2 (1:1) at a temperature of 60°C for 4 h in toluene (15 ml) as solvent.

In order to compare the activity and selectivity of the developed diphosphinite ligands, various phosphite and phosphine ligands were screened for hydroformylation of styrene under optimized reaction conditions. It is well known that, especially, ligands that are good electron acceptors have been found to be effective ligands for hydroformylation reactions. Since these ligands decrease the electron density of rhodium and weaken the π-back donation from rhodium to CO, resulting in rapid CO dissociation, this swift mechanistic step in hydroformylation accelerates the rate of reaction.[19,20] The synthesized diphosphinite ligands used in the present study are good electron acceptors and show little difference in their electronic and steric properties. However, it was observed that the conversion continues to decrease from $\mathbf{L_1}$ to $\mathbf{L_2}$ because of different substituents at the 1,3-diol backbone, though $\mathbf{L_2}$ shows very good selectivity towards branched aldehyde but gave low conversion (Table 2, entries 1 and 2). Screened phosphite ligands such as $P(OPh)_3$ and $P(OEt)_3$ showed quite low conversion in comparison with the developed phosphinite ligands under optimized reaction conditions (Table 2, entries 3 and 4). As the phosphine ligands are more basic than their phosphinite counterparts, they provided less conversion and selectivity toward the desired product (Table 2, entries 5–9). Compared with bidentate phosphine ligands, monodentate phosphine (PPh_3) gave better conversion (Table 2, entry 5). In the case of bidentate phosphine ligands, conversion goes on increasing from dppm to dppb (Table 2, entries 4–9). Among all the screened phosphine ligands, dppe offered excellent regioselectivity (97%) for iso aldehyde, whereas low conversion (36%) confines its applications to hydroformylation reactions (Table 2, entry 7). A bulky bidentate phosphine ligand like Xantphos provided a hydroformylation product with very low conversion (7%) and aldehyde selectivity (35%), even after a prolonged reaction period of 8 h (Table 2, entry 10). The reaction was also studied in the absence of ligand using only $Rh(acac)(CO)_2$; however, low conversion and poor selectivity of the desired product address the importance of the ligand in hydroformylation reaction (Table 2, entry 11). Hence, among several screened ligands, diphosphinite ligand $\mathbf{L_1}$ with $Rh(acac)(CO)_2$ precursor was found to be the best catalytic combination for hydroformylation reaction of styrene, providing admirable conversion and selectivity for the desired product.

In order to examine the general applicability of the developed protocol, we studied the range of substrates for this process. Table 3 shows the results from the hydroformylation of a variety of olefins using optimized reaction conditions.

The model reaction of styrene under optimized reaction conditions provided excellent conversion and very good selectivity (91%) toward branched aldehyde (Table 3, entry 1). Substituted styrenes like *p*-*tert*-butylstyrene and 3-methylstyrene were found to react smoothly, furnishing good yields and selectivity of the corresponding product (Table 3, entries 2 and 3). Styrene with an electron-donating group, such as *p*-chlorostyrene, also provides almost complete conversion and immense selectivity for branched aldehyde formation (Table 3, entry 4). It was observed that the regioselectivity for branched product faintly increases with electron-withdrawing substituent on a phenyl ring in the order $p\text{-}(CH_3)_3CPh < m\text{-}CH_3Ph < HPh < ClPh$. This might be due to increase in π-electron density on the α-carbon of styrene, which favours the attack of electropositive Rh metal, providing higher selectivity for branched aldehyde.[21] Allylbenzene and 4-methoxy allylbenzene offered good selectivity for aldehyde formation with almost 100% conversion. As these olefins having an isolated olefinic CC bond form a phenyl



Scheme 2. Hydroformylation of styrene.

Table 1. Effect of reaction parameters on hydroformylation of styrene using L_1 as a ligand[a]

Entry	Temp. (°C)	Solvent	Sub/Rh (molar ratio)	Pressure (bar)	Time (h)	Conv.[c] (%)	Aldehyde (%)	Iso:linear[c] (%)	Reduction(%)
1	100	Toluene	1000	35	6	100	92	64:36	8
2	80	Toluene	1000	35	6	100	94	73:27	6
3	70	Toluene	1000	35	6	100	95	81:19	5
4	60	Toluene	1000	35	6	100	99	90:10	1
5	50	Toluene	1000	35	6	47	99	96:4	1
6	60	THF	1000	35	6	79	95	88:12	5
7	60	MeOH	1000	35	6	85	64:27*	83:17	9
8	60	Toluene	1000	30	6	99	98	88:12	2
9	60	Toluene	1000	25	6	100	99	89:11	1
10	60	Toluene	1000	20	6	92	97	87:13	3
11	60	Toluene	2000	25	6	81	93	85:15	7
12[b]	60	Toluene	1000	25	6	87	99	92:8	1
13	60	Toluene	1000	25	4	100	99	91:9	1
14	60	Toluene	1000	25	3	93	98	93:7	2

[a]Reaction conditions: styrene (5 mmol), $Rhacac(CO)_2$ (0.1 mol%), L_1 (0.2 mol%), 800 rpm; *acetal formation.
[b]P/Rh (8/1).
[c]Conversion and selectivity (iso/linear) were determined by GC analysis.

ring they gave three structural aldehydes due to isomerization reaction (Table 3, entries 5 and 6). Moreover, linear aliphatic alkenes such as 1-hexene gave a remarkable yield of the desired product as well (Table 3, entry 7). Cyclic olefins such as cyclopentene and cyclohexene also provided a satisfactory yield of expected products (Table 3, entries 8 and 9).

Conclusion

Novel diphosphinite ligands have been synthesized and applied in a rhodium-catalyzed hydroformylation reaction. The catalyst systems were optimized with respect to various parameters and enabled hydroformylation of different olefins with electron-rich and electron-deficient substituent. In all cases the developed system afforded excellent yields and high regioselectivity toward branched aldehyde under mild reaction conditions. Thus the wider substrate applicability and high regioselectivity make this catalyst system attractive for further investigations.

Experimental

Materials and Instruments

All chemicals, e.g. olefins, chlorodiphenylphosphine, $[Rh(acac)(CO)_2]$ and phosphorus ligands, were purchased from Sigma-Aldrich and Alfa Aesar. All other reagents were of analytical grade and were used without further purification. Syngas (CO and H_2, 1:1) with a purity of 99.9%, was obtained from Rakhangi Gases Ltd, Mumbai, India.

The 1,3-diol backbones were synthesized from their corresponding 1,3-dione according to the literature procedure.[22] Diphosphinite ligands were also prepared by the reported methods[23–25] under an atmosphere of dry nitrogen or argon using standard Schlenk techniques. Solvents were dried and distilled by conventional methods prior to use.

The ^1H and ^{13}C NMR (δ in ppm) spectra were recorded on a Varian VXR 300 spectrometer at operating frequencies of 300 MHz and 75 MHz, respectively, in $CDCl_3$ solvent using tetramethylsilane as

Table 2. Effect of ligands on hydroformylation of styrene[a]

Entry	Ligand (P/Rh = 4)	Conversion[c] (%)	Aldehyde (%)	Iso:linear[c] (%)	Reduction (%)
1	L_1	100	99	91:9	1
2	L_2	84	100	96:4	—
3	$P(OPh)_3$	83	98	95:5	2
4	$P(OEt)_3$	88	97	74:26	3
5	PPh_3	85	100	86:14	—
6	dppm	29	97	91:9	3
7	dppe	36	96	97:3	4
8	dppp	66	98	81:19	2
9	dppb	84	97	73:27	3
10[b]	Xantphos	07	35	26:74	65
11	—	65	98	56:44	2

[a]Reaction conditions: styrene (5 mmol), $Rhacac(CO)_2$ (0.1 mol%), ligand (0.2 mol%), CO/H_2 (1:1) 25 bar, temperature 60°C, time 6 h, 800 rpm;
[b]time (8 h).
[c]Conversion and selectivity (iso/linear) were determined by GC analysis.

Table 3. Hydroformylation of different olefins using $Rhacac(CO)_2$ with $\mathbf{L_1}$ ligand[a]

Entry	Substrate	Conversion[c] (%)	Aldehyde selectivity[d] (%)	Iso:linear[c] (%)	Reduction (%)
1	Ph-CH=CH_2	100	99	91:9	1
2	*p*-tBu-Ph-CH=CH_2	100	99	87:13	1
3	*m*-CH_3-Ph-CH=CH_2	99	98	89:11	2
4	*p*-Cl-Ph-CH=CH_2	100	99	92:8	1
5	Ph-CH_2-CH=CH_2	97	99	1:40:59	1
6	*p*-OMe-Ph-CH_2-CH=CH_2	99	100	2:37:61	—
7	CH_3-$(CH_2)_3$-CH=CH_2	100	99	4:33:63	1
8[b]	Cyclopentene	87	100	—	—
9[b]	Cyclohexene	72	100	—	—

[a]Reaction conditions: olefin (5 mmol), $Rhacac(CO)_2$ (0.1 mol%), ligand $\mathbf{L_1}$ (0.2 mol%), toluene (15 ml), CO/H_2 (1:1) 25 bar, temperature 60°C, time 4 h, 800 rpm;

[b]temperature 80°C.

[c]Conversion and selectivity (iso/linear) were determined by GC analysis.

[d]Chemoselectivity for aldehyde product to total reaction product.

internal standard. ^{31}P NMR spectra were obtained at an operating frequency of 162 MHz on a Varian VXR 400 spectrometer.

Preparation of 1,3-Bis((diphenylphosphino)oxy)-1,3-diphenylpropane ($\mathbf{L_1}$)

A solution of PPh_2Cl (1.32 g, 6 mmol) in dry THF (5 ml) was added slowly, with stirring, to a mixture of 1,3-diphenylpropane-1,3-diol (0.68 g, 3 mmol) and pyridine (0.47 g, 6 mmol) in dry THF (15 ml) at 0°C. Following the addition, the reaction mixture was left to warm at room temperature and stirred overnight. The pyridine hydrochloride was filtered off under nitrogen atmosphere, the filtrate evaporated to dryness and the residue dissolved in 7 ml diethyl ether. When this solution was cooled to −5°C, the product separated in the form of white crystals and was stored under nitrogen atmosphere: yield 1.5 g (2.52 mmol, 84%).

NMR spectra of $\mathbf{L_1}$: ^1H NMR (300 MHz, $CDCl_3$, 25°C): $\delta = 7.68–7.75$ (m, 8H, *Ph*P), 7.24–7.47 (m, 12H, *Ph*P), 7.31–7.37 (m, 10H, *Ph*CHOP), 4.98 (t, 2H, $J = 5.8$ Hz, *CH*OP), 2.17 (t, 2H, $J = 5.8$ Hz, CH_2CHOP); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): $\delta = 144.3$ (d, $^1J_{p,c} = 18.6$ Hz, C_{ipso} PhP), 133.7 (s, C_{ipso} Ph), 131.3 (d, $^2J_{p,c} = 7.8$ Hz, C_o PhP), 129.6 (s, C_o Ph), 128.9 (d, $^3J_{p,c} = 5.7$ Hz, C_m PhP), 128.1 (s, C_p PhP), 127.3 (s, C_m Ph), 125.7 (s, C_p Ph), 71.5 (d, $^2J_{p,c} = 22.8$ Hz, *CH*OP), 46.9 (d, $^3J_{p,c} = 8.7$ Hz, CH_2CHOP); ^{31}P NMR (162 MHz, $CDCl_3$, 25 °C): $\delta = 111.66$ ppm.

Preparation of ((2,2,6,6-Tetramethylheptane-3,5-diyl)bis(oxy))bis(diphenylphosphine)($\mathbf{L_2}$)

A solution of PPh_2Cl (1.32 g, 6 mmol) in dry THF (5 ml) was added slowly, with stirring, to a mixture of 2,2,6,6-tetramethylheptane-3,5-diol (0.56 g, 3 mmol) and pyridine (0.47 g, 6 mmol) in dry THF (15 ml) at 0°C. Further procedures were the same as discussed earlier. The product was obtained as a white solid: yield 1.3 g (2.3 mmol, 79%).

Characterization results of ligands are in accordance with literature data.[23,26,27]

NMR spectra of $\mathbf{L_2}$: ^1H NMR (300 MHz, $CDCl_3$, 25°C): $\delta = 7.66–7.75$ (m, 8H, *Ph*P), 7.25–7.51 (m, 12 H, *Ph*P), 3.42 (t, 2H, $J = 6.2$ Hz, *CH*OP), 1.68 (t, 2H, $J = 6.2$ Hz, CH_2CHOP), 0.89 (s, 18H, $C(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$, 25°C): $\delta = 141.4$ (d, $^1J_{p,c} = 17.9$ Hz, C_{ipso} PhP), 131.4 (d, $^2J_{p,c} = 7.6$ Hz, C_o PhP), 128.3 (d, $^3J_{p,c} = 5.2$ Hz, C_m PhP), 127.6 (s, C_p PhP), 81.4 (d, $^2J_{p,c} = 22.2$ Hz, *CH*OP), 35.02 (d, $^3J_{p,c} = 11.4$ Hz, *C*CHOP), 31.6 (d, $^3J_{p,c} = 8.3$ Hz, CH_2CHOP), 25.6 (s, $(CH_3)_3C$); ^{31}P NMR (162 MHz, $CDCl_3$, 25°C): $\delta = 110.42$ ppm.

Procedure for Hydroformylation Reaction of Styrene

In a typical experiment, to a high pressure reactor of 100 ml capacity, $Rhacac(CO)_2$ (0.1 mol%), ligand $\mathbf{L_1}$ (0.2 mol%), styrene (5 mmol) and toluene (15 ml) were added. The reactor was then flushed with nitrogen, followed by syngas (1:1 mixture of CO and H_2 gas) at room temperature; next, the reaction was pressurized to 25 bar syngas and heated to 60°C at a stirring speed of 800 rpm for 4 h. After completion of the reaction, the reactor was cooled to room temperature and remaining syngas was carefully released. The reaction mixture was analysed by gas chromatography (GC; Clarus 400, PerkinElmer) equipped with a capillary column (30 m × 0.25 mm × 0.25 μm) and a flame ionization detector (FID). All products obtained are well known in the literature and were confirmed by GC-MS analysis on a Shimadzu GCMS-QP 2010 instrument (Rtx-17, 30 m × 25 mm ID, film thickness 0.25 μm df) (column flow 2 ml min^{-1}, 80–240°C at 10°/min^{-1} rise) see supporting information.

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