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Asymmetric hydroformylation of styrene catalyzed by furanoside phosphine–phosphite–Rh(I) complexes

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Abstract—A series of phosphine–phosphite ligands, derived from inexpensive D-(+)-xylose, were tested in the Rh-catalyzed asymmetric hydroformylation of styrene. Systematic variation of the phosphite moiety revealed a remarkable effect on the selectivity of the hydroformylation catalysts. High regioselectivities for 2-phenylpropanal (up to 95%) and moderate enantioselectivity were found under mild reaction conditions (25–40°C, 25 bar of syn gas). The hydroformylation results are explained by the solution structures of the intermediate species formed under hydroformylation conditions. © 2002 Published by Elsevier Science Ltd.

1. Introduction

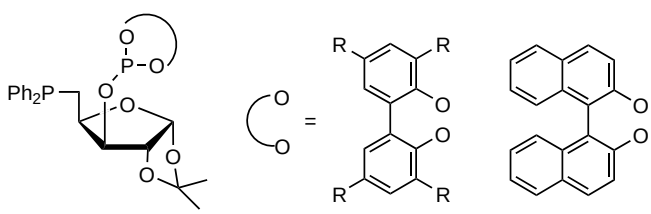
Asymmetric hydroformylation is an attractive route for synthesising enantiomerically pure aldehydes,[1] which can be used as precursors for the synthesis of high value compounds such as pharmaceuticals, agrochemicals, biodegradable polymers and liquid crystals. Rhodium and platinum/tin catalytic systems modified with phosphine ligands have been widely used in asymmetric hydroformylation.[1] However, the enantioselectivity for rhodium systems[2] and the activity and regioselectivity for platinum/tin systems[3] have been highly disappointing. During the last decade, two new types of ligand—diphosphite[4] and phosphine–phosphite[5] ligands—have emerged as suitable ligands for asymmetric hydroformylation, overcoming the limitations of the phosphine-based catalytic systems. Most of the research published to date has been dedicated to diphosphite ligands.[1e] Thus, despite the early success of the phosphine–phosphite Binaphos ligand in the hydroformylation of styrene and the fact that Binaphos is the only ligand with a wide scope in asymmetric hydroformylation,[5] reports on the use of phosphine–phosphite ligands are rare.[5,6]

Encouraged by the success of Binaphos[5] and the excellent combination of regio- and enantioselectivities obtained with diphosphite ligands with furanoside backbone in the asymmetric hydroformylation of olefins,[4c–d] we report herein the use of a series of furanoside phosphine–phosphite ligands derived from inexpensive D-(+)-xylose (Fig. 1) in the asymmetric Rh-catalyzed hydroformylation of styrene.[7] We also discuss the solution structures of the intermediate species formed under the hydroformylation conditions.

2. Results and discussion

2.1. Asymmetric hydroformylation of styrene

Phosphine–phosphite ligands **1**–**4** were tested in the rhodium-catalyzed asymmetric hydroformylation of styrene under different reaction conditions. Styrene was chosen as a substrate because this reaction has been performed with a wide range of ligands with several donor groups, enabling direct comparison of the



1 R = *t*-Bu
2 R = H
3 S_{ax}
4 R_{ax}

Figure 1.

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efficiency of the different catalytic systems.[1] The catalysts were prepared in situ by adding the corresponding phosphine–phosphite ligand to $Rh(acac)(CO)_2$ as a catalyst precursor, 16 h before the styrene was added. The conversion and selectivity results are summarized in Table 1. In all cases hydrogenated or polymerized products of styrene were not observed.

The effects of different reaction parameters (i.e. CO/H_2 pressure ratio, ligand-to-rhodium ratio and temperature) were investigated for the catalytic precursor containing ligand **1**. After identical catalyst preparation, hydroformylation experiments were carried out under different CO and H_2 partial pressures (entries 1, 3 and 4). The results clearly show that higher partial pressures of H_2 lead to higher initial turnover frequencies. Moreover, comparison of entries 1, 3 and 4 shows that both the regio- and enantioselectivity are hardly affected by varying the partial H_2 pressure.

Varying the ligand-to-rhodium ratio shows that these catalyst systems are highly stable under hydroformylation conditions and no excess of ligand is needed (entry 2). This is an important advantage over the rest of the phosphine–phosphite ligands, for which a greater excess of ligand is needed.[5,6] However, at higher ligand-to-rhodium ratios, the turnover frequencies are slightly lower (entries 1 versus 2). This is probably due to competition between the active species $HRh(CO)_2$(**1**) and other less active species that have more than one ligand coordinated to the rhodium centre.

Lowering the temperature of the reaction to room temperature resulted in an increase in enantioselectivity (up to 49%) (entry 5).

The use of ligand **2**, which results from removing the bulky *tert*-butyl groups at the *ortho* and *para* positions of the biphenyl moiety in ligand **1**, leads to slightly higher activity and lower regio- and enantioselectivity than the catalyst system Rh/**1** (entry 4 versus 6). This behaviour is similar to that observed for diphosphite ligands for which the presence of bulky substituents in the *ortho* positions of the biphenyl moieties are crucial to obtain good regio- and enantioselectivities.[4]

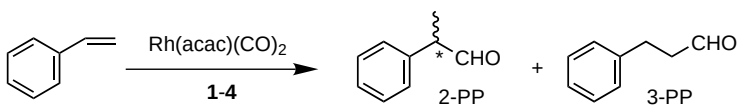
The use of ligand **3**, containing enantiopure (*S*)-binaphthyl moiety, showed better activity and similar enantioselectivity than the catalyst precursor containing ligand **1** (entry 7). However, the regioselectivity is similar to that observed for the Rh/**2** catalyst system (entry 6 versus 7).

The catalyst precursor containing ligand **4**, with an enantiopure (*R*)-binaphthyl moiety, induced much higher reaction rate and a lower enantioselectivity than **3** (entry 7 versus 8). Monodentate coordination of the ligand could explain its higher activity and lower enantioselectivity but this can be excluded from the spectroscopic data obtained under hydroformylation conditions (vide infra). A more plausible explanation is that the conformation adopted by ligand **4** probably causes less steric hindrance at the rhodium complexes than the $HRh(CO)_2$(**3**) and, therefore, it is more reactive and less enantioselective.

2.2. Characterization of $HRh(PP)(CO)_2$ complexes

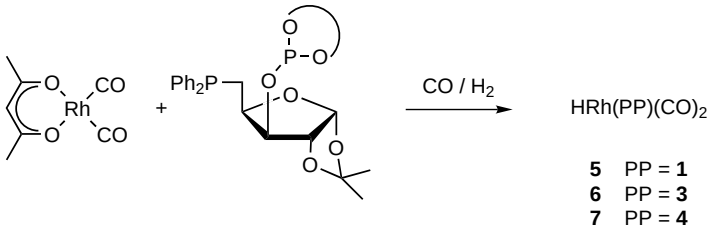
In order to obtain information about the $HRh(PP)(CO)_2$ species, which are known to be responsible for the catalytic activity, we studied by HP NMR spectroscopy the solution structures of hydridorhodium dicarbonyl catalysts ($HRh(PP)(CO)_2$, PP = phosphine–phosphite ligand). They were prepared in situ under hydroformylation conditions by adding 1.1 equivalent of phosphine–phosphite ligand to the catalyst precursor

Table 1. Asymmetric hydroformylation of styrene catalysed by $Rh(acac)(CO)_2$/phosphine–phosphite **1–4**[a]



Entry	Ligand	CO/H_2[b]	T (°C)	TOF[c]	% Conv.[d]	% 2-PP[e]	%ee[f]
1	1	1	40	54	23	94	35 (*S*)
2[g]	1	1	40	49	19	94	33 (*S*)
3	1	2	40	28	15	94	36 (S)
4	1	0.5	40	67	32	94	35 (*S*)
5	1	0.5	25	9	58[h]	95	49 (*S*)
6	2	0.5	40	75	36	89	7 (*S*)
7	3	0.5	40	87	41	90	38 (*S*)
8	4	0.5	40	164	81	91	20 (*S*)

[a] Reaction conditions: P = 25 bar, styrene (13 mmol), $Rh(acac)(CO)_2$ (0.013 mmol), ligand/Rh = 1.1, toluene (15 mL).
[b] pCO/pH_2 ratio.
[c] TOF in mol styrene×mol $Rh^{-1}\times h^{-1}$ determined after 1 h reaction time by GC.
[d] % Conversion of styrene after 5 h.
[e] Regioselectivity in 2-phenylpropanal.
[f] % Enantiomeric excess measured by GC.
[g] Ligand/Rh = 2.
[h] Conversion after 72 h.



Scheme 1. Preparation of complexes **5**–**7**.

Table 2. Selected ^{1}H and ^{31}P NMR data for $HRh(PP)(CO)_2$ complexes **5**–**7**[a]

Complex	δP_1	δP_2	$^{1}J_{Rh-P1}$	$^{1}J_{Rh-P2}$	$^{2}J_{P1-P2}$	δH	$^{2}J_{H-P1}$	$^{2}J_{H-P2}$	$^{1}J_{H-Rh}$
5	8.25	158.2	115	225	11	−9.61 (ddd)	75.9	32.7	8.4
6	7.87	169.3	112	221	38	−9.53 (ddd)	74.4	57.4	9.1
7	7.32	174.1	109	217	42	−9.42 (ddd)	78.2	68.1	9.3

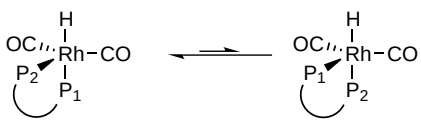
[a] Prepared in toluene-d_8. δ in ppm. Coupling constants in Hz. P_1 = phosphine phosphorus. P_2 = phosphite phosphorus.

$Rh(acac)(CO)_2$ (Scheme 1). No $HRh(CO)_2$(**2**) complexes were prepared because the expected formation of mixtures of diastereoisomeric complexes made this unattractive for an in situ NMR study.[4b,8] The spectroscopic data are summarized in Table 2.

The $^{31}P\{^{1}H\}$ NMR spectrum of $HRh(CO)_2$(**1**), **5** showed two double doublets at 8.25 and 158.2 ppm, which we attributed to the phosphine (P_1) and phosphite (P_2) phosphorus, respectively. The ^{1}H NMR spectrum of **5** revealed a double double doublet in the hydride region, due to the coupling with rhodium and the two non-equivalent phosphorus atoms. The magnitude of the $^{1}J_{H-Rh}$ is typical of an equatorial-axial (ea) coordination for the phosphine–phosphite moieties (i.e. $^{1}J_{H-Rh}$ with the phosphorus atom *trans* to the hydride is around 9 Hz, whereas $^{1}J_{H-Rh}$ with a carbonyl group *trans* to the hydride is less than 4 Hz).[6c] Small *cis* phosphorus–hydride coupling constants (typically between 1 and 10 Hz) are reported in $HRh(PP)(CO)_2$ complexes with diequatorially (ee) coordinating diphosphine and diphosphite ligands.[1e,4b,4d] In contrast, relatively large phosphorus–hydride coupling constants (between 150 and 180 Hz for phosphites[1e,4b] and between 90 and 110 Hz for phosphines[9]) are reported when phosphorus is located *trans* to the hydride atom. The intermediate values for the $^{2}J_{H-P1}$ and $^{2}J_{H-P2}$ indicate a rapid equilibrium between two equatorial-axial (ea) diastereoisomers, which are in fast exchange on the NMR time-scale (Scheme 2). Taking into account the typical values of $^{2}J_{H-P}$ for phosphine and phosphite in an equatorial and axial position, it seems clear that the diastereoisomer with the phosphine in an axial position and the phosphite in an equatorial position is much more stable under hydroformylation conditions. This contrasts with the coordination mode found for HRh(-Binaphos)$(CO)_2$ in which the phosphine occupies an equatorial position and the phosphite moiety the axial position,[5a] which may explain why the enantioselectivities obtained with these catalysts were only moderate. Similar behavior has been observed for complexes **6** and **7**. Interestingly, the coupling constants, $^{2}J_{H-P2}$ for these complexes were higher than those of complex **5**, which indicates that the relative amount of diastereoisomer containing the phosphite in the axial position is higher for these complexes than for complex **5**.

3. Conclusions

A series of phosphine–phosphite ligands **1**–**4**, derived from inexpensive D-(+)-xylose, were screened in the Rh-catalyzed asymmetric hydroformylation of styrene. Good regioselectivities in 2-phenylpropanal (up to 95%) and moderate enantioselectivities (up to 49%) were obtained. The results show that bulky substituents in the *ortho* positions of the biphenyl moiety have a positive effect on the regio- and enantioselectivity of the reaction. The enantioselectivity and activity were also affected by the configuration of the binaphthyl at the phosphite moiety. We used HP NMR to characterise the rhodium complexes formed under CO/H_2. The results indicate that $HRh(PP)(CO)_2$ complexes exist in two diastereoisomeric equatorial-axial forms in fast exchange. In the most stable diastereoisomer, the phosphine occupies an axial position, while the phosphite, the best π-acceptor, occupies an equatorial position. These results contrast with the coordination mode found for HRh(Binaphos)$(CO)_2$ in which the phosphine occupies an equatorial position and the phosphite moiety is in the axial position, and this could explain why the enantioselectivities obtained with these catalysts are moderate.



Scheme 2. Equatorial-axial phosphorus exchange.

4. Experimental

All experiments were carried out under an argon atmosphere. All solvents were dried using standard methods and distilled prior to use. Compounds **1**–**4** were prepared as previously described.[7] ^{1}H and ^{31}P{^{1}H} NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer. Chemical shifts are relative to $SiMe_4$ (^{1}H) as internal standard or H_3PO_4 (^{31}P) as external standard. All assignments in NMR spectra were determined by COSY spectra. Gas chromatographic analyses were run on a Hewlett–Packard HP 5890A instrument (split/splitless injector, J&W Scientific, Ultra-2 25 m column, internal diameter 0.2 mm, film thickness 0.33 mm, carrier gas: 150 kPa He, F.I.D. detector) equipped with a Hewlett–Packard HP 3396 series II integrator. Hydroformylation reactions were carried out in a home-made 100 mL stainless steel autoclave. Enantiomeric excesses were measured after the aldehydes had been oxidised to their corresponding carboxylic acids with a Hewlett–Packard HP 5890A gas chromatograph (split/splitless injector, J&W Scientific, FS-Cyclodex β-I/P 50 m column, internal diameter 0.2 mm, film thickness 0.33 mm, carrier gas: 100 kPa He, F.I.D. detector). The absolute configuration was determined by comparing the retention times with enantiomerically pure (*S*)-(+)-2-phenylpropionic and (*R*)-(−)-2-phenylpropionic acids.

4.1. Hydroformylation of styrene

In a typical experiment, the autoclave was purged three times with CO. The solution was formed from $Rh(acac)(CO)_2$ (0.013 mmol) and the phosphine–phosphite (0.014 mmol) in toluene (10 mL). When the autoclave was pressurized with syn gas and heated to the reaction temperature, the reaction mixture was stirred for 16 h to form the active catalyst. The autoclave was depressurized and a solution of styrene (13 mmol) in toluene (5 mL) was placed in the autoclave and pressurized again. During the reaction, several samples were taken out of the autoclave. After the desired reaction time, the autoclave was cooled to room temperature and depressurized. The reaction mixture was analyzed by gas chromatography.

4.2. In situ HP NMR hydroformylation experiments

In a typical experiment, a sapphire tube ($\phi = 10$ mm) was filled under argon with a solution of $Rh(acac)(CO)_2$ (0.030 mmol) and ligand (molar ratio PP/Rh = 1.1) in toluene-d_8 (1.5 mL). The HP-NMR tube was purged twice with CO and pressurized to the appropriate pressure of CO/H_2. After a reaction time of 16 h shaking at the desired temperature, the solution was analyzed.

4.2.1. [HRh(CO)$_2$(1)], 5. ^{31}P NMR, δ: 8.25 (dd, 1P, P_1, $^1J_{P1-Rh} = 115$ Hz, $^2J_{P-P} = 11$ Hz), 158.2 (dd, 1P, $^1J_{P2-Rh} = 225$ Hz, $^2J_{P-P} = 11$ Hz). ^{1}H NMR, δ: −9.61 (ddd, 1H, $^2J_{P1-H} = 75.9$ Hz, $^2J_{P2-H} = 32.7$ Hz, $^1J_{Rh-H} = 8.4$ Hz), 1.12 (s, 3H, CH_3), 1.23 (s, 18H, CH_3, *t*-Bu), 1.46 (s, 12H, CH_3, CH_3, *t*-Bu), 1.48 (s, 9H, CH_3, *t*-Bu), 2.94 (m, 1H, H-5), 3.01 (m, 1H, H-5′), 3.25 (m, 1H, H-4), 4.09 (d, 1H, H-2, $^3J_{2-1} = 3.3$ Hz), 5.16 (dd, 1H, H-3, $^3J_{3-4} = 2.1$ Hz, $^3J_{3-P} = 13.5$ Hz), 5.44 (d, 1H, H-1, $^3J_{1-2} = 3.3$ Hz), 6.8–7.6 (m, 14H, CH=).

4.2.2. [HRh(CO)$_2$(3)], 6. ^{31}P NMR, δ: 7.87 (dd, 1P, P_1, $^1J_{P1-Rh} = 112$ Hz, $^2J_{P-P} = 38$ Hz), 169.3 (dd, 1P, $^1J_{P2-Rh} = 221$ Hz, $^2J_{P-P} = 38$ Hz). ^{1}H NMR, δ: −9.53 (ddd, 1H, $^2J_{P1-H} = 74.4$ Hz, $^2J_{P2-H} = 57.4$ Hz, $^1J_{Rh-H} = 9.1$ Hz), 1.09 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 3.11 (m, 2H, H-5, H-5′), 3.78 (m, 1H, H-4), 4.28 (m, 1H, H-2), 5.24 (m, 1H, H-3), 5.39 (d, 1H, H-1, $^3J_{1-2} = 3.6$ Hz), 6.8–8.0 (m, 22H, CH=).

4.2.3. [HRh(CO)$_2$(4)], 7. ^{31}P NMR, δ: 7.32 (dd, 1P, P_1, $^1J_{P1-Rh} = 109$ Hz, $^2J_{P-P} = 42$ Hz), 174.1 (dd, 1P, $^1J_{P2-Rh} = 217$ Hz, $^2J_{P-P} = 42$ Hz). ^{1}H NMR, δ: −9.42 (ddd, 1H, $^2J_{P1-H} = 78.2$ Hz, $^2J_{P2-H} = 68.1$ Hz, $^1J_{Rh-H} = 9.3$ Hz), 1.11 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 3.03 (m, 2H, H-5, H-5′), 3.89 (m, 1H, H-4), 4.32 (m, 1H, H-2), 5.21 (m, 1H, H-3), 5.43 (d, 1H, H-1, $^3J_{1-2} = 3.6$ Hz), 6.8–8.0 (m, 22H, CH=).

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