DALTON COMMUNICATION

Rhodium catalyzed asymmetric hydroformylation of vinylarenes with a diphosphite ligand forming a large chelating ring †

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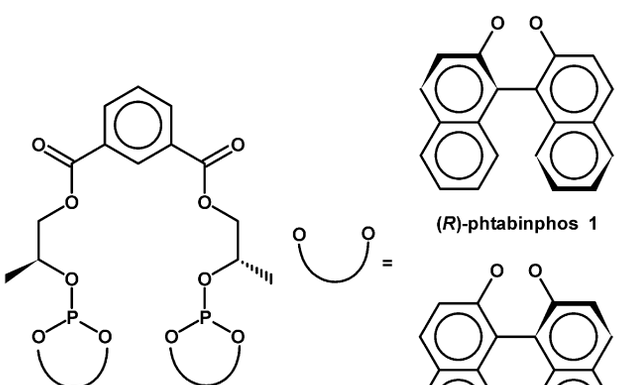
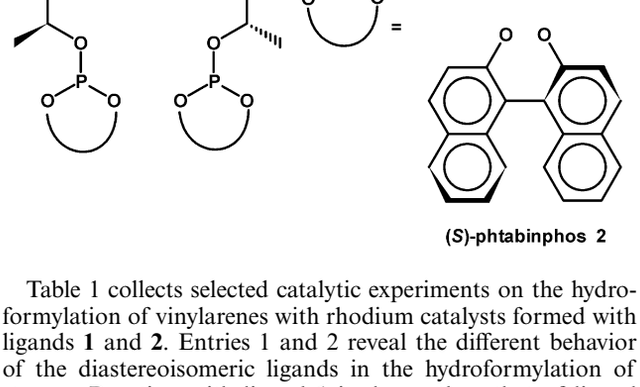
A rhodium complex containing a sixteen membered chelated diphosphite, with the appropriate combination of stereogenic centers, produces ee's above 70% in the hydroformylation of vinylarenes, while a related diastereoisomeric ligand renders very low ee's because it does not form a chelated species.

Asymmetric hydroformylation catalyzed by transition metal catalysts is a method for the synthesis of homochiral aldehydes.[1] Both, platinum and rhodium catalysts, containing bidentate P-donor ligands, have been extensively used in this reaction. However, while Pt–$SnCl_2$ catalysts produce the best stereoselectivities with diphosphine ligands containing four carbon atoms in the backbone (*i.e.* seven membered chelates),[2] in the case of rhodium catalysts, phosphine–phosphite[3] or diphosphite[4] ligands forming eight membered chelates render the best results. Catalysts forming larger chelate rings are reported to produce poor results in enantioselective hydroformylation,[5] although they have been used successfully in other asymmetric reactions.[6] We report here the first results on the enantioselective rhodium catalyzed hydroformylation of vinylarenes using a diphosphite ligand forming a very large, sixteen membered chelate.

Ligands (*R*)-phtabinphos **1** and (*S*)-phtabinphos **2** were prepared by reaction of (2*S*)-hydroxypropyl isophthalate[7] with (*R*)- and (*S*)-binaphthol phosphorochlorhidites and NEt_3.[8]

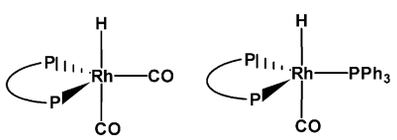


(*R*)-phtabinphos **1**

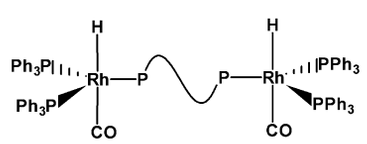


(*S*)-phtabinphos **2**

Table 1 collects selected catalytic experiments on the hydroformylation of vinylarenes with rhodium catalysts formed with ligands **1** and **2**. Entries 1 and 2 reveal the different behavior of the diastereoisomeric ligands in the hydroformylation of styrene. Reaction with ligand **1** is slower than that of ligand **2**, but the latter shows very low stereoselectivity. Matching–mismatching effects between the stereogenic centers of the ligands have been previously observed in asymmetric hydroformylation.[3b,4b,9] In order to get some insight into the nature of this effect in ligands **1** and **2**, the structure of the catalytic species formed by reacting them with $[Rh(\mu\text{-}OMe)(cod)]_2$ under CO/H_2 was studied by HPNMR. For ligand **1**, ^1H- and ^{31}P-NMR spectra show the formation of the species $[RhH(CO)_2(\mathbf{1})]$ **3**, where the diphosphite coordinates the metal in equatorial positions.[10] Very broad spectra, which could not be resolved, were obtained with ligand **2** in the explored temperature range (−40 to 90 °C). These spectra likely correspond to a fluxional species or a mixture of species in dynamic equilibrium.



3 **4**



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More conclusive results were obtained by NMR analysis of the reactions of ligands **1** and **2** with $[RhH(CO)(PPh_3)_3]$ in a ligand/rhodium ratio of 0.5 : 1. Ligand **1** forms the expected species $[RhH(CO)(PPh_3)(\mathbf{1})]$ **4**, with the characteristic 16 (phosphite) plus 8 (phosphine) lines spectrum, again with the diphosphite occupying equatorial positions.[11] However, the reaction with ligand **2** produces a binuclear species $[Rh_2H_2(CO)_2(PPh_3)_4(\mathbf{2})]$ **5**, in which the diphosphite is acting as a bridge between two metal atoms, as indicated by the 8 (phosphite) plus 16 (phosphine) lines ^{31}P-NMR spectrum.[12] These NMR results reveal that the low enantioselectivity observed with diphosphite **2** is due to the tendency of this ligand to act in a bridging or monodentate fashion, which creates a very loose chiral environment on the catalysts. Species of this type are known to be poorly enantioselective in asymmetric hydroformylation.[13] Furthermore, the remarkably different tendency of diastereoisomeric ligands **1** and **2** to form chelating species can be considered as an extreme case of the matching–mismatching effect.

In the case of the catalyst containing ligand **1**, an increase in the temperature (entries 3 and 1 in Table 1) produces an improvement in the activity of the system, but with a drop in the regio- and enantio-selectivity. By increasing the syngas (CO/H_2) pressure (entries 3 and 6) a decrease in the activity of the system was observed with almost no change in the selectivity. A significant increase in the activity (TOF = 31 h^{-1}) and a slight improvement of the ee was achieved by running the reaction at a higher concentration of substrate (entries 3 and 7). Finally, the catalyst Rh/(*R*)-phtabinphos shows higher activity and stereoselectivity in the hydroformylation of vinylnaphthalene than in styrene (entries 5 and 3). However, a decrease in

† Electronic supplementary information (ESI) available: experimental details, NMR data for **1** and **5** and NMR spectra of **3**, **4** and **5**. See http://www.rsc.org/suppdata/dt/b1/b105208j/

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Table 1 Hydroformylation of vinylarenes using (*R*)- and (*S*)-phtabinphos (ligands **1** and **2**) and $[Rh(\mu\text{-}OMe)(cod)]_2$

Entry	L[a]	Substrate[b]	*T*/°C	*P*/bar	Conv. (%) (*t*/h)[c]	regio[d] (%)	ee (%) (conf)[e]
1	**1**	$PhCH{=}CH_2$	50	15	78 (15)	75	62 (*R*)
2	**2**	$PhCH{=}CH_2$	50	15	99 (21)	83	11 (*S*)
3	**1**	$PhCH{=}CH_2$	40	15	30 (36)	80	70 (*R*)
4	**1**	$p\text{-}^tBuC_6H_4CH{=}CH_2$	40	15	53 (115)	66	72 (*R*)
5	**1**	$NaphCH{=}CH_2$	40	15	89 (23)	81	75 (*R*)
6	**1**	$PhCH{=}CH_2$	40	30	25 (69)	80	73 (*R*)
7[f]	**1**	$PhCH{=}CH_2$	40	15	17 (16)	80	76 (*R*)

Reaction conditions: 1.25×10^{-2} mmol Rh, 2.5×10^{-2} mmol ligand and 5.0 mmol substrate (substrate/catalyst = 400) in 7.5 ml of toluene; $P(CO){=}P(H_2)$. [a] Diphosphite. [b] Substrates: styrene; 4-*tert*-butylstyrene, and vinylnaphthalene. [c] Substrate consumed in the time indicated in parentheses. [d] Regioselectivity in the branched aldehyde. [e] Enantiomeric excess of the isomer indicated in parentheses. [f] 2.5×10^{-2} mmol Rh, 5.0×10^{-2} ligand and 45 mmol substrate (substrate/catalyst = 1800) in 4.0 ml of toluene; TOF is 31 h^{-1}.

activity as well as in the regioselectivity was observed in the hydroformylation of 4-*tert*-butylstyrene with respect to styrene (entries 4 and 3).

In conclusion, diphosphite **1** provides the first example of a ligand forming a chiral macrochelate, which produces a fairly good stereoselective catalyst for asymmetric hydroformylation. Furthermore, the modular structure of this ligand allows an easy modification of its stereochemical properties. This approach is currently under investigation.

Acknowledgements

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8 Selected data: **1** δ_P ($CDCl_3$) 145.8; **2** δ_P ($CDCl_3$) 148.6.

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10 NMR data: **3** δ_P ($CDCl_3$, 121.6 MHz) 177.6 (d, $J_{Rh\text{-}P} = 231$ Hz). δ_H ($CDCl_3$, 300 MHz) −9.90 (hydride, q br, $J_{P\text{-}H} = J_{Rh\text{-}H} = 4$Hz).

11 NMR data: **4** δ_P ($CDCl_3$, 101.3 MHz) 180.6 (P1 phosphite, ddd, $J_{Rh\text{-}P1} = 251$ Hz, $J_{P2\text{-}P1} = 271$ Hz, $J_{P3\text{-}P1} = 172$ Hz); 175.3 (P2 phosphite, ddd, $J_{Rh\text{-}P2} = 237$ Hz, $J_{P3\text{-}P2} = 109$ Hz); 37.7 (P3 phosphine, ddd, $J_{Rh\text{-}P3} = 134$ Hz). δ_H ($CDCl_3$, 250 MHz) −10.25 (hydride, dddd, $J = 13.0$ Hz, 6.5 Hz, 2.7 Hz).

12 NMR data: **5** δ_P ($CDCl_3$, 101.3 MHz) 37.8 (P1 phosphine, ddd, $J_{Rh\text{-}P1} = 143$ Hz, $J_{P2\text{-}P1} = 86$ Hz, $J_{P3\text{-}P1} = 167$ Hz); 40.8 (P2 phosphine, ddd, $J_{Rh\text{-}P2} = 148$ Hz, $J_{P3\text{-}P2} = 191$ Hz); 174.7 (P3 phosphite, ddd, $J_{Rh\text{-}P3} = 258$ Hz).

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