



Catalysis  
Science &  
Technology

**A modular family of phosphine-phosphoramidite ligands and their hydroformylation catalysts: Steric tuning impacts upon the coordination geometry of trigonal bipyramidal complexes of type  $[\text{Rh}(\text{H})(\text{CO})_2(\text{P}^{\wedge}\text{P}^*)]$**

Journal:	<i>Catalysis Science &amp; Technology</i>
Manuscript ID:	CY-ART-06-2015-000886.R2
Article Type:	Paper
Date Submitted by the Author:	27-Jul-2015
Complete List of Authors:	How, Rebecca; University of St Andrews, School of Chemistry Hembre, Robert; Eastman Chemical Company, Ponasik, James; Eastman Chemical Company, Tolleson, Ginette; Eastman Chemical Company, Clarke, Matt; University of St. Andrews, School of Chemistry

SCHOLARONE™  
Manuscripts



Journal Name

ARTICLE

## A modular family of phosphine-phosphoramidite ligands and their hydroformylation catalysts: Steric tuning impacts upon the coordination geometry of trigonal bipyramidal complexes of type $[\text{Rh}(\text{H})(\text{CO})_2(\text{P}^{\wedge}\text{P}^*)]$

Received 00th January 20xx,  
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Rebecca C. How<sup>a</sup>, Robert Hembre<sup>b</sup>, James A. Ponasik<sup>b</sup>, Ginette S. Tolleson<sup>b</sup>, and Matthew L. Clarke<sup>a\*</sup>

Four new phosphine-phosphoramidite bidentate ligands have been synthesised and studied in rhodium-catalysed hydroformylation. Variable temperature NMR studies have been used along with HPIR to investigate the coordination mode of the trigonal bipyramidal complexes formed from  $[\text{Rh}(\text{acac})(\text{CO})_2]$ , ligand and syngas. It was found that small changes to the ligand structure have a large effect on the geometry of the active catalytic species. The rhodium catalysts of these new ligands were found to give unusually high *iso*-selectivity in the hydroformylation of propene and 1-octene.

### Introduction

Ligands that respond to subtle structural modification by changing coordination mode or metal geometry are of significant interest to coordination chemists and catalysis chemists. The ability to control geometry and coordination chemistry of a ligand in a predictable manner can help understand structure-performance relationships in catalysis. This can lead to improved ligand design and subsequently developments in applied catalysis. One area where such studies are of particular significance is the study of Rh(I) complexes of phosphine ligands, which are used as pre-catalysts or catalysts for alkene hydroformylation, one of the most important applications of transition metal catalysis in the world. With one or two notable exceptions,<sup>1,2</sup> most hydroformylation catalysts show at least some selectivity towards the linear aldehyde isomers.<sup>3</sup> In the last thirty years, large bite angle diphosphine ligands have been shown to give excellent linear selectivity in this respect (high *n/iso* ratios). These large bite angle ligands, such as BISBI<sup>4,5</sup> and XantPhos,<sup>6</sup> BISBI = 2,2'-*bis*(diphenylphosphinomethyl)-1,1'-biphenyl; Xantphos = 4,5-*bis*(diphenylphosphino)-9,9-dimethylxanthene) always form trigonal bipyramidal Rh(I) complexes where the diphosphine is *bis*-equatorial. Some ligands with smaller bite

angles form complexes with the diphosphine occupying axial-equatorial positions. There is not enough data to make any correlations between axial-equatorial coordination mode and selectivity, although catalysts with axial-equatorial coordinating ligands are rarely or never highly linear selective in the hydroformylation of terminal alkyl alkenes. This led us to study a family of ligands that might be finely balanced between *bis*-equatorial and axial-equatorial coordination modes. Our objective was to understand how ligand structure controls the selectivity for *bis*-equatorial/axial-equatorial isomers and whether the isomer formed has any implications on rate, selectivity, stability or activation times in hydroformylation catalysis. Our ultimate long-term aim is to gain sufficient understanding that we would be able to design a series of catalysts that could access all possible linear to branched ratios in the industrially important hydroformylation of propene. Here we show a readily accessed family of phosphine-phosphoramidite ligands, use low temperature NMR to characterise their Rh(I) hydroformylation catalysts, and demonstrate their unusually high *iso*-selectivity in the hydroformylation of propene and 1-octene.

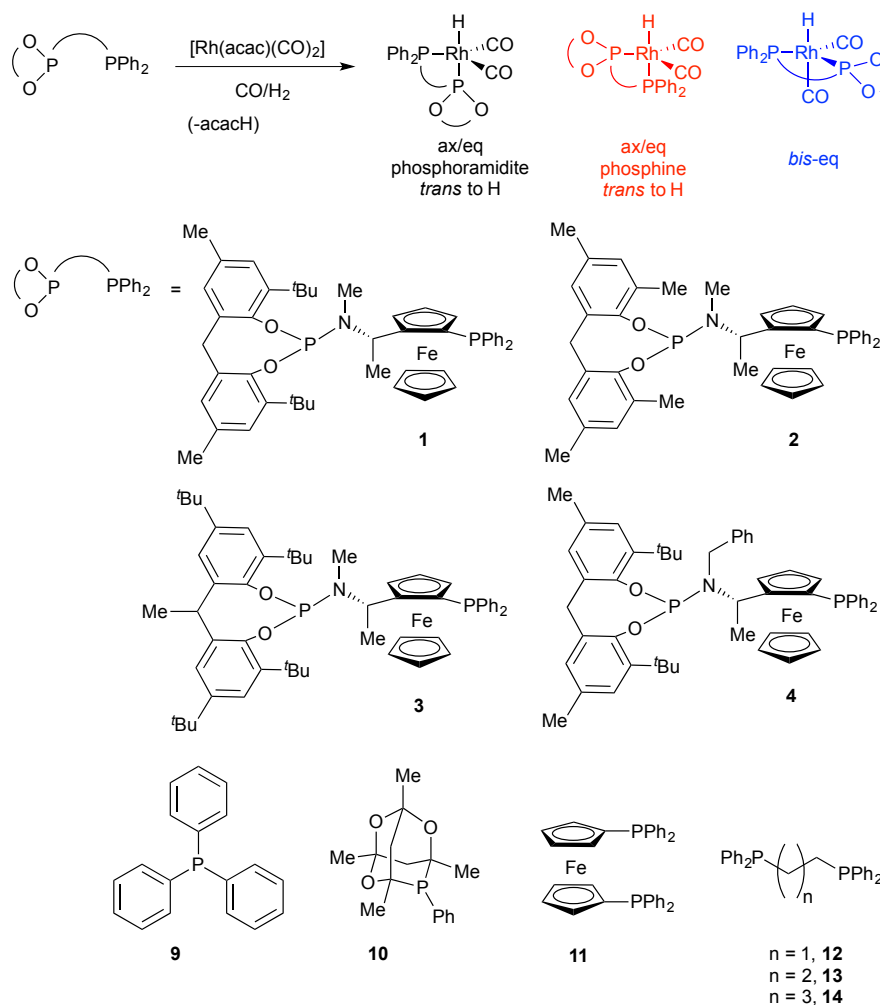
Non-symmetric *bis*-phosphorus ligands with a ferrocenyl amine backbone make up a successful series of asymmetric hydrogenation catalysts invented by researchers at Eastman Chemical Company.<sup>7,8</sup> In this case, we were not particularly interested in exploiting the ligands in enantioselective catalysis, but were attracted to the backbone, since it tends to give catalysts that are rigid and stable and a 7 membered chelate could easily form both *bis*-equatorial and axial-equatorial isomers of catalyst. In addition, ligands with electronically quite different donor sets such as phosphine-

<sup>a</sup> School of Chemistry, University of St Andrews, EaSTCHEM, St Andrews, Fife, KY16 9ST. email: mc28@st-andrews.ac.uk

<sup>b</sup> Eastman Chemical Company, Kingsport, Tennessee, 37662

† Electronic Supplementary Information (ESI) available: [A range of control/additional hydroformylation experiments including unselective attempts at asymmetric hydroformylation, HPIR, analytical data and spectra, please consult the supporting information]. See DOI: 10.1039/x0xx00000x

phosphite<sup>2,9,10</sup> and phosphine-phosphoramidite<sup>11-13</sup> have yielded important catalysts for hydroformylation,<sup>14</sup> which led us to consider phosphine-phosphoramidite **1** to **4** as targets.



**Scheme 1** Catalyst structures for non-symmetric ligands (**1-4**)

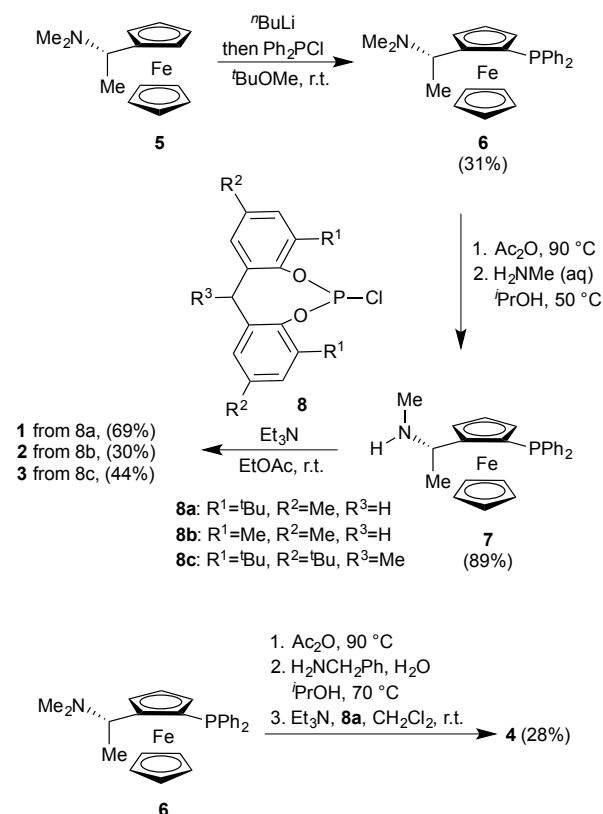
## Results and discussion,

The novel ligands **1-4** were accessed readily from Ugi's amine,<sup>15</sup> **5**, in 4 steps (**Scheme 2**).

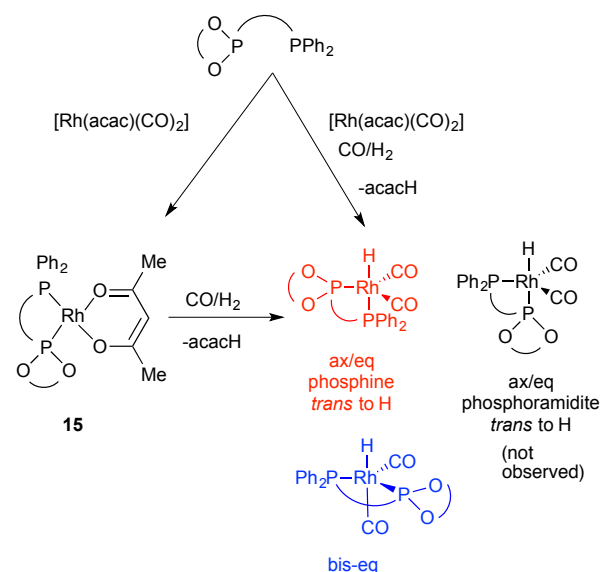
The ligands react with  $[\text{Rh}(\text{acac})(\text{CO})_2]$  under a syngas atmosphere to form the expected complexes of type  $[\text{Rh}(\text{H})(\text{CO})_2(\text{P}^*\text{P}^*)]$  as monitored by low temperature NMR and HPIR (**Scheme 3**). Since the active pre-catalysts are fairly stable for many hours under a nitrogen atmosphere, we generated the active hydroformylation catalysts by treating either  $[\text{Rh}(\text{acac})(\text{CO})_2]$  and ligand or isolated complex **15** with syngas (**Scheme 3**), and then subjecting the newly formed complex to NMR spectroscopy under a  $\text{N}_2$  atmosphere. In a control experiment, the NMR spectrum with ligand **3** was acquired under a pressurised syngas atmosphere; this gave spectra that were the same as those run under a  $\text{N}_2$  atmosphere.

Comparison of room temperature NMR with low temperature NMR spectra for the activated catalyst formed from ligand **1**

(see ESI) shows the peaks are much sharper at  $-70^\circ\text{C}$  in both the  $^1\text{H}$  NMR and  $^{31}\text{P}\{^1\text{H}\}$  NMR spectra. In the low temperature  $^{31}\text{P}\{^1\text{H}\}$  NMR spectrum there were two distinct species, each with a peak in the phosphine [ $\delta$  16-20 range] and phosphoramidite [ $\delta$  155-180 range] regions. There was also a third species of low intensity in the  $^{31}\text{P}\{^1\text{H}\}$  NMR, but this was too small to characterise. In the low temperature  $^1\text{H}$  NMR of the Rh complex of ligand **1**, the major Rh-hydride signal has a  $^2J_{\text{H-P}}$  of 119 Hz. This is very similar to the 117 Hz coupling that Nozaki and co-workers<sup>9,16</sup> observed for a phosphine group *trans* to a rhodium-hydride bond. The minor Rh-hydride signal features a  $^2J_{\text{H-P}}$  of  $\leq 13$  Hz; which is suggestive of a *bis*-equatorial species. There is a  $\sim 9:1$  ratio between the size of the peaks assigned to axial-equatorial (phosphine axial, in red) and *bis*-equatorial species (in blue, See **Scheme 3** and **Table 1**).



Scheme 2: Ligand synthesis



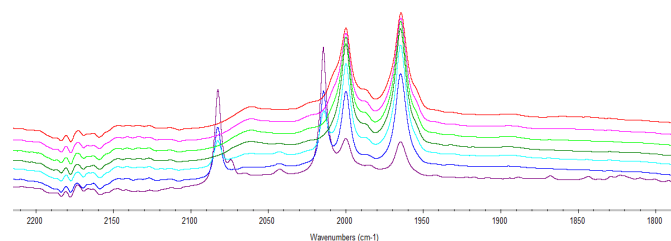
Scheme 3: Activation of the catalyst

$^2J_{\text{P-H}}$  could be easily measured in the  $^1\text{H}$  NMR, but not the  $^{31}\text{P}$  NMR. However, the  $^{31}\text{P}\{^1\text{H}\}$  NMR and  $^{31}\text{P}$  NMR spectra were compared for all peaks. In three of the signals there were no major changes in the appearance of the signal. However, for the major phosphine signal, the peak shape changes due to a large  $J_{\text{P-H}}$  coupling (119 Hz). This confirms that the phosphine is in the axial position and *trans* to the rhodium hydride. The

Electronic Supporting Information contains all the relevant NMR spectra.

The activated catalysts were then studied for other ligands. Ligand **2** gave only an axial-equatorial species where the phosphine was axial. This was found to give sharp peaks in the NMR at both room temperature and low temperature. Remarkably, when ligand **3** reacted with  $[\text{Rh}(\text{acac})(\text{CO})_2]$  and syngas, only a *bis*-equatorial isomer is formed. At room temperature the phosphoramidite peak was very broad, but the peak sharpens so that coupling constants could be resolved at  $-70$  °C. For ligand **4** there is a  $\sim 3:1$  ratio between *bis*-equatorial and axial-equatorial isomers (phosphine axial). Of the *bis*-equatorial species, it appears that both diastereomers are present in almost equal levels (see ESI). These NMR studies show profound changes to the active catalyst geometry are possible just from altering alkyl substituents in the periphery of the ligand structure. These seemingly quite remote substituents might be located close to the coordination sphere of the Rh catalysts. Other workers have seen significant electronic changes to *bis*-eq/eq-axial ratios from 1:1 to 9:1.<sup>17a</sup>

We also studied the formation of the active hydroformylation catalyst of type  $[\text{Rh}(\text{H})(\text{CO})_2(\text{P}^*\text{P}^*)]$  using HPIR. Hexane was used as solvent since it has no absorbance in the carbonyl region of the spectrum. The sample was heated to  $70$  °C, and a spectrum was recorded every 15 minutes to measure the formation of the active catalytic species. The formation of the catalyst requires coordination of the ligand to  $[\text{Rh}(\text{acac})(\text{CO})_2]$  and reaction with  $\text{CO}/\text{H}_2$ , or formation of  $\text{RhH}(\text{CO})_4$  from  $[\text{Rh}(\text{acac})(\text{CO})_2]$  and coordination of the ligand.  $\text{RhH}(\text{CO})_4$  can be formed rapidly from  $[\text{Rh}(\text{acac})(\text{CO})_2]$  and syngas if ligand coordination is slow (carbonyl stretching adsorptions at  $2082$  and  $2015$   $\text{cm}^{-1}$ ). The catalyst was deemed to have fully formed when the spectrum was constant. Bulky ligands **3** and **4** were found to take longer to activate than ligands **1** and **2**.



**Fig.1:** Catalyst activation with ligand **4**. One spectra recorded every 15 minutes,  $\text{RhH}(\text{CO})_4$  was detected in early spectra (purple: 0 minutes, dark blue: 15 min., light blue: 30 min., dark green: 45 min., light green: 60 min., pink: 75 min., red: 90 min.); spectra recorded from 45-90 minutes did not change.

Ligand **2** gave only axial-equatorial species by NMR and was found to have only two carbonyl stretches by HPIR. These stretching adsorptions appeared at  $2002$  and  $1954$   $\text{cm}^{-1}$  and can be unequivocally assigned as an axial-equatorial species with a phosphine *trans* to the rhodium-hydride bond.<sup>17</sup> No unmodified catalyst was noted after 15 minutes.

Table 1: Coupling constants derived from the NMR spectra of the active catalysts

Catalyst	Ligand	Phosphorus	$^1J_{P-Rh}$ (Hz)	$^2J_{P-P}$ (Hz)	$^2J_{P-H}$ (Hz)	<i>ax/eq</i> : <i>bis-eq</i>
1a	1	Major Phosphoramidite	215	45	<10	89 : 11
1a		Major Phosphine	92	45	119	
1b		Minor Phosphoramidite	223	167	10	
1b		Minor Phosphine	140	167	10	
2a	2	Only Phosphoramidite	216	27	<10	100 : 0
2a		Only Phosphine	100	27	113	
3a	3	Only Phosphoramidite	219	164	<10	0 : 100
3a		Only Phosphine	140	164	<10	
4a	4	1 <sup>st</sup> Major Phosphoramidite	223	169	<10	25 : 75
4a		1 <sup>st</sup> Major Phosphine	140	169	<10	
4b		2 <sup>nd</sup> Major Phosphoramidite	199	35	<10	
4b		2 <sup>nd</sup> Major Phosphine	116	35	<10	
4c		Minor Phosphoramidite	218	49	10-20	
4c		Minor Phosphine	94	49	120	

NMR spectra recorded in toluene- $d_6$  at  $-70$  °C.  $^1H$  NMR at 500 MHz,  $^{31}P\{^1H\}$  and  $^{31}P$  NMR at 202 MHz.

Ligand **3** gave only a single *bis*-equatorial species detectable by NMR spectroscopy. Three carbonyl stretching adsorptions were observed by HPIR. However, there may have been a fourth peak hidden under one of the others. The three bands appeared at 2061, 2000 and 1965  $cm^{-1}$ . Some unmodified catalyst was noted until 60 minutes. Kamer and co-workers<sup>17b</sup> reported carbonyl stretching adsorptions at 2049 and 1970  $cm^{-1}$  for a *bis*-equatorial catalyst with DPEphos; and bands at 2052 and 1980  $cm^{-1}$  for a *bis*-equatorial catalyst with a phosphine-phosphite bidentate ligand. The signals at 2061 and 1965  $cm^{-1}$  were tentatively assigned as the *bis*-equatorial species on this basis. We also propose that at 70 °C, the axial equatorial isomer with CO stretching adsorptions at 2000 and 1965 (coincident with *bis*-equatorial) is also present.

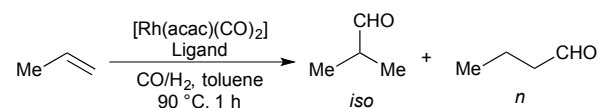
The HPIR spectra for ligands **1** and **4** showed a number of peaks: both axial-equatorial and *bis*-equatorial species, as expected from the NMR studies. For ligand **1** no unmodified catalyst was noted after 15 minutes, but for ligand **4**, it was only after 45 minutes that all the unmodified catalyst is converted to the  $[Rh(H)(L)(CO)_2]$  species. Overall, the HPIR data show there is a strong steric impact on the speed of coordination and that it is likely that broadly similar species are formed at  $+70$  °C under pressure as those detected at  $-70$  °C under an  $N_2$  atmosphere. The conditions of the IR experiment are fairly close to those used in hydroformylation (and the same carbonyl stretching adsorptions are observed for ligand **1** at 90 °C and 70 °C). The HPIR data also confirms that the hydroformylation results stem from purely ligand-modified catalysts.

The hydroformylation of propene is one of the most important examples of industrial hydroformylation catalysis. Propene can be considered somewhat distinct from most other terminal alkenes in that the regioselectivity is not influenced by isomerisation in the same way as, for example, 1-octene. Much effort has been expended into optimising the ratio towards linear aldehyde formation to around 95% or higher. However, the branched aldehyde has many markets and uses, and there is significant interest in increasing the range of *n/iso* ratios that are available (currently around 50-95%). This needs to be accomplished using catalysts that are stable and selective at the typical temperatures needed for industrial application. The unusually high branched selectivities for alkyl alkene hydroformylation recently reported<sup>2,18</sup> required low temperatures for good results to be achieved. The hydroformylation of propene with high *iso*-selectivity under industrially realistic reaction conditions is a formidable challenge. It appears the highest ever branched aldehyde ratio at high temperatures is around 55% *iso*-selective (*n/iso* 0.8) using dppp.<sup>19</sup>

Ligands **1-4** were compared against a range of ligands (Table 2); particularly those that have been previously noted to give significant branched regioselectivity in the hydroformylation of either propene or another alkyl-alkene. Rh catalysts were prepared *in situ* and the reactions were carried out in a sealed vessel pressurised with a  $CO/H_2$  and  $C_3H_6$  mixture with one hour reaction time. The average TOF are therefore a TON after one hour reaction, not initial rates. The activity data served our purpose of showing that there were no huge differences in activity between the ligands and that their rates are of the

same magnitude as those using Rh/PPh<sub>3</sub> under these conditions. Dppp ligand **13** (entry 5) gave lower *iso*-selectivity than literature results, under the reaction conditions tested here. As expected, dppe, **12**, and dppb, **14**, (entry 4 and 6) gave lower *iso*-selectivity than dppp with the dpfp (entry 3) ligand, **11**, giving the lowest *iso*-selectivity. The cage phosphine, **10**, (entry 2) also gave low *iso/n* ratio, though as expected,<sup>20</sup> with high activity.

**Table 2:** Propene hydroformylation using catalysts derived from ligand **1-4** and **9-14**.



Entry	Ligand	Average TOF	iso %	n/i
1	9	903	37.3	1.7
2	10	1013	41.4	1.4
3	11	1082	38.8	1.6
4	12	433	41.4	1.4
5	13	720	48.4	1.1
6	14	513	45.9	1.2
7	1	671	50.8	1.0
8	2	872	45.3	1.2
9	3	602	50.6	1.0
10	4	550	55.0	0.8

Catalyst prepared from [Rh(acac)(CO)<sub>2</sub>] (5.12x10<sup>-3</sup> mmol) and ligand by stirring at 20 bar CO/H<sub>2</sub> (1:1) at 90 °C for 1 hour in toluene (20 mL) prior to running reactions for 1 hour at 20 bar using propene/H<sub>2</sub>/CO mixture in a 1:4.5:4.5 ratio. For monodentate ligands, 0.02 mmol ligand (Rh:L 1:4) was used; for bidentate ligands, 6.30x10<sup>-3</sup> mmol ligand (Rh:L 1:1.25) was used. Products determined by GC using 1-methylnaphthalene as an internal standard. TOFs are average TOF over a 1 hour reaction time (mol/mol/h) in a sealed batch reaction.

The new ligands **1**, **3**, and **4** were found to favour the formation of the desired *iso*-product. Ligand **4** performed the best, with an *iso*-selectivity of 55/45 (Table 2, Entry 10) which is comparable to the best current literature reports. Less bulky ligand, **2**, shows significantly less *iso*-selectivity. This loss of selectivity may be due to direct steric effects between the phosphoramidite part of the ligand and the substrate and not the equatorial-axial arrangement of the ligand on the metal; both ligands **1** and **2** primarily or solely form the equatorial-axial isomer.

The parent ligand, **1**, was also tested using a variety of different solvents (Table 3). It was found that the selectivity for the branched product could be improved with a number of solvents, though this was often met with a decrease in average TOF. However, octafluorotoluene was found to give a small increase in activity as well as an increase in *iso*-selectivity. The

increase in activity is proposed to be at least partly due to the known increased solubility of gases in fluorinated solvents.

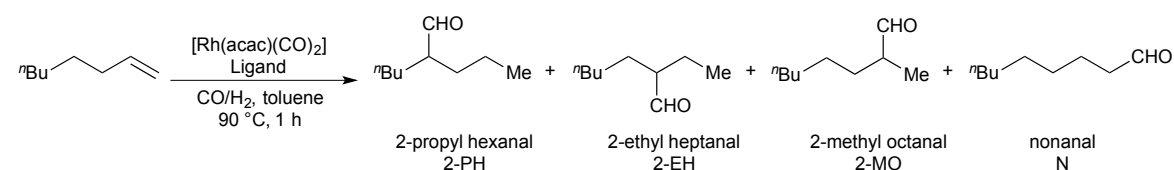
**Table 3:** Effect of solvent in for propene hydroformylation using [Rh(acac)(CO)<sub>2</sub>]/ ligand **1** as catalyst system

Entry	Solvent A	Average TOF	iso %	n/i
1	Toluene	671	50.8	1.0
2	Hexane	743	52.4	0.9
3	Ethyl Acetate	260	54.1	0.8
4	CF <sub>3</sub> C <sub>6</sub> H <sub>5</sub>	585	54.9	0.8
5	Octafluorotoluene	911	55.9	0.8

Catalyst prepared from [Rh(acac)(CO)<sub>2</sub>] (5.12x10<sup>-3</sup> mmol) and ligand **1** (6.30x10<sup>-3</sup> mmol (Rh:L 1:1.25)) by stirring at 20 bar CO/H<sub>2</sub> (1:1) at 90 °C for 1 hour in desired solvent mix (19.35 mL solvent A, 0.65 mL toluene) prior to running reactions for 1 hour at 20 bar using propene/H<sub>2</sub>/CO mixture in a 1:4.5:4.5 ratio. Products determined by GC using 1-methylnaphthalene as an internal standard. TOFs are average TOF over a 1 hour reaction time in mol/mol/h.

The four new ligands were also tested in 1-octene hydroformylation (Table 4). Catalysts derived from both ligands **1** and **2** proceeded rapidly to complete conversion in 17 hours, while catalysts derived from ligands **3** and **4** were found to be slower for the hydroformylation of 1-octene (Entries 1-4).

The catalysts derived from all four ligands were found to give high *iso*-selectivity (Table 4, entries 1-4). However, this does not represent especially high selectivity for 2-aldehydes, since a range of *iso*-aldehydes are formed. This is in contrast to the results obtained using PPh<sub>3</sub> under the same reaction conditions, which lead to almost no apparent isomerisation of the 1-octene (entry 5). The selectivity observed using Rh / ligands **1-4** is due to the isomerisation of 1-octene to internal olefins. This is indeed a very fast reaction, since when the reaction using the Rh/ligand **1** catalyst was repeated with a reaction time of just 30 minutes, almost no 1-octene remains. Isomers of octene were detected, and the higher n:i ratio indicates that the hydroformylation of the terminal alkene favours the formation of nonanal. In a separate experiment, the gas uptake at constant pressure was measured in the reaction catalysed by Rh/ligand **1**; the reaction was found to be first order with respect to substrate (see ESI). The initial turnover frequency measured at 20% conversion was 951 h<sup>-1</sup>

**Table 4:** 1-Octene hydroformylation using catalysts derived from ligand **1-4** and **9**.

Entry	Ligand	Time (h)	Conversion (%)	2-PH (%)	2-EH (%)	2-MO (%)	N (%)	n/i
1	<b>1</b>	17	99	11	14	35	40	0.7
2	<b>2</b>	17	99	9	14	34	43	0.8
3	<b>3</b>	42	97	12	14	35	39	0.6
4	<b>4</b>	44	97	12	14	35	39	0.6
5	<b>9</b>	4	96	<1	2	28	69	2.3
6	<b>1</b>	0.5	18	0	2	30	68	2.1
7	<b>1</b>	2	35	4	7	35	54	1.2

Catalyst prepared from  $[\text{Rh}(\text{acac})(\text{CO})_2]$  (0.010 mmol) and ligand by stirring at 20 bar  $\text{CO}/\text{H}_2$  (1:1) at  $90^\circ\text{C}$  for 1 hour in toluene (20 mL) prior to running reactions with 1-octene (16 mmol) at 20 bar using  $\text{CO}/\text{H}_2$  (1:1) until at or near full conversion. For monodentate ligands, 0.04 mmol ligand (Rh:L 1:4) was used; for bidentate ligands, 0.013 mmol ligand (Rh:L 1:1.25) was used. Products determined by GC using 1-methylnaphthalene as an internal standard.

## Conclusions

Four novel phosphine-phosphoramidites have been prepared and fully characterised. The active Rh hydroformylation catalysts derived from these ligands have been studied using NMR and IR. While we envisaged that this ligand structure may well be finely poised between *bis*-equatorial and axial-equatorial coordination geometries, it was found that making minor changes to ligand structure completely switched the coordination mode from 100% *bis*-equatorial to 100% axial-equatorial. Of the ligands synthesised and tested; it was found that the least bulky ligand **2** leads to only an axial-equatorial species. Increasing steric bulk leads to an increase in the *bis*-equatorial species until only the *bis*-equatorial isomer was detected by NMR with the more bulky ligand **3**. These catalysts were then tested in the hydroformylation of propene and 1-octene and were found to be amongst the most successful catalysts for maximising the branched product at industrially applicable temperatures. The differences in selectivity within the ligand family is very small, limiting the scope of the conclusions that can be drawn. Differences in selectivity between ligand **2**, which forms less *iso*-aldehyde and ligand **3** are more likely ascribed to steric interactions in the transition states for Rh-alkene>Rh-alkyl or Rh-alkyl>Rh-acyl species. Ligands **1** and **3** show very different catalyst geometries but very similar selectivities in hydroformylation, which means there is no strong correlation between coordination mode (alone) and *iso*-selectivity in propene hydroformylation. While this is not entirely unexpected, confirming that there is no isomeric preference towards *iso*-selectivity focuses attention on the design of a coordination sphere that can promote the formation of branched intermediates. Highly *iso*-selective

hydroformylation of propene is clearly a formidable challenge and our studies continue. It is hoped that the knowledge gained here will lead us to the rational design of catalysts that form a single isomer and can lead to even higher *iso*-selective catalysts in the future.

## Experimental

### General information

Full experimental details are available in ESI. All manipulations were carried out under an inert atmosphere of nitrogen or argon using standard Schlenk techniques. Solvents were dried and degassed before use, with the exception of octafluorotoluene which was degassed only.

### General procedure for propene hydroformylation

Ligand (6.40  $\mu\text{mol}$  (Rh:L 1:1.25)) was added to a schlenk tube, which was then purged with  $\text{N}_2$ .  $[\text{Rh}(\text{acac})(\text{CO})_2]$  (5.12  $\mu\text{mol}$ ) was added in a toluene stock solution (2 mg/mL). Toluene was then added to make up to 20 mL total volume, followed by the addition of internal standard 1-methylnaphthalene (0.2 mL). The solution was transferred via syringe to the pressure vessel (which had been purged with  $\text{CO}/\text{H}_2$ ) through the injection port.  $\text{CO}/\text{H}_2$  (1:1) (20 bar) was added and the heating jacket set to  $90^\circ\text{C}$  while stirring. Once the temperature reached  $90^\circ\text{C}$ , the reaction was stirred for 1 hour to fully activate the catalyst. Then pressure was then slowly released and replaced with propene/ $\text{CO}/\text{H}_2$  (20 bar). The reaction was then run for 1 hour before immediate analysis by GC.

**General procedure for ligand synthesis**

Synthesis and characterisation of ferrocenyl-ligand precursors, chlorophosphites and phosphine-phosphoramidite ligands is available in ESI. General synthesis of ligand **1** is given from amine precursor **7** and chlorophosphite **8a**.

**Synthesis of phosphine-phosphoramidite ligand 1:**

Amine **7** (0.30 g, 0.70 mmol) was dissolved in ethyl acetate (1.5 mL) and *N*-methylpyrrolidine (0.11 mL, 1.07 mmol) under Ar. The solution was cooled to 0 °C and was purged with argon for 15 minutes then chlorophosphite **8a** (0.340 g, 0.85 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was added and stirred at 0 °C for 1 hour. The solution was warmed to room temperature and stirred for 16 hours. The solution was concentrated *in vacuo* to afford a crude solid. The solid was purified by flash column chromatography (pre-treated with a solution of 95:5 toluene:Et<sub>3</sub>N) using 30:1 hexane:ethyl acetate as eluent under N<sub>2</sub> to give phosphoramidite **1** as an orange solid (0.38 g, 0.48 mmol, 69%).

**Acknowledgements**

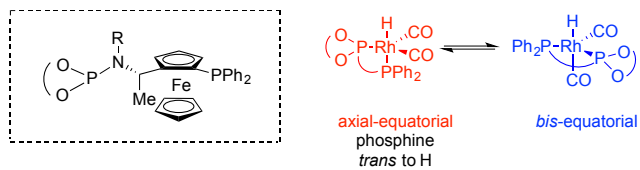
We thank the Eastman Chemical Company for funding, the EPSRC for the use of the national mass spectrometry service, and all the technical staff in the School of Chemistry for their assistance.

**Notes and references**

- (a) T. Besset, D. W. Norman, J. N. H. Reek, *Adv. Synth. Catal.*, 2013, **355**, 348-352; (b) V. F. Slagt, J. N. H. Reek, P. C. J. Kamer and P. W. N. M. van Leeuwen, *Angew. Chem. Int. Ed.* 2001, **40**, 4271-4274; (c) V. F. Slagt, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. N. H. Reek, *J. Am. Chem. Soc.* 2004, **126**, 1526-1536; (d) M. Kuil, T. Soltner, P. W. N. M. van Leeuwen, J. N. H. Reek, *J. Am. Chem. Soc.* 2006, **128**, 11344.
- a) G. M. Noonan, J. A. Fuentes, C. J. Cobley, M. L. Clarke, *Angew. Chem. Int. Ed.*, 2012, **51**, 2477-2480; b) G. M. Noonan, C. J. Cobley, T. Mahoney and M. L. Clarke, *Chem. Commun.* 2014, **50**, 1475-1478.
- a) M. L. Clarke, *Curr. Org. Chem.* 2005, **9**, 701-718. b) van Leeuwen, P. W. N., & Claver, C., (Eds.) *Rhodium Catalysed Hydroformylation*; Kluwer Academic Publishers: Netherlands, 2000.
- T. J. Devon, G. W. Phillips, T. A. Puckette, J. L. Stavinoha, J. J. Vanderbilt, US Pat. 4694109, 1987.
- C. P. Casey, G. T. Whiteker, M. G. Melville, L. M. Petrovich, J. A. Gavney, D. R. Powell, *J. Am. Chem. Soc.*, 1992, **114**, 5535-5543.
- M. Kranenburg, Y. E. M. van der Burgt, P. C. J. Kamer, P. W. N. M. van Leeuwen, K. Goubitz, J. Fraanje, *Organometallics*, 1995, **14**, 3081-3089.
- N. W. Boaz, S. D. Debenham, E. B. Mackenzie, S. E. Large, *Org. Lett.*, 2002, **4**, 2421-2424.
- (a) N. W. Boaz, E. B. Mackenzie, S. D. Debenham, S. E. Large, J. A. Ponasik, *J. Org. Chem.*, 2005, **70**, 1872-1880; (b) See also: X. P. Hu, Z. Zheng, *Org. Lett.* 2004, **6**, 3585-3588.
- K. Nozaki, N. Sakai, T. Nanno, T. Higashijima, S. Mano, T. Horiuchi, H. Takaya, *J. Am. Chem. Soc.*, 1997, **119**, 4413-4423.
- M. Rubio, A. Suárez, E. Álvarez, C. Bianchini, W. Oberhauser, M. Peruzzini, A. Pizzano, *Organometallics*, 2007, **26**, 6428-6436.
- J. Wassenaar, J. N. H. Reek, *Dalton Trans.*, 2007, 3750-3753.
- R. Bellini, J. N. H. Reek, *Chem. Eur. J.*, 2012, **18**, 13510-13519.
- Y. Yan, X. Zhang, *J. Am. Chem. Soc.*, 2006, **128**, 7198-7202.
- S. H. Chikkali, J. I. van der Vlugt, J. N. H. Reek, *Coord. Chem. Rev.*, 2014, **262**, 1-15.
- D. Marquarding, H. Klusacek, G. Gokel, P. Hoffmann, I. Ugi, *J. Am. Chem. Soc.*, 1970, **92**, 5389-5393.
- D. A. Castillo Molina, C. P. Casey, I. Mueller, K. Nozaki, C. Jaekel, *Organometallics*, 2010, **29**, 3362-3367.
- a) L. A. van der Veen, M. D. K. Boele, F. R. Bregman, P. C. J. Kamer, P. W. N. M. van Leeuwen, K. Goubitz, J. Fraanje, H. Schenk, C. Bo, *J. Am. Chem. Soc.* 1998, **120**, 11616-11626; (b) C. F. Czauderna, D. B. Cordes, A. M. Z. Slawin, C. Müller, J. I. van der Vlugt, D. Vogt, P. C. J. Kamer, *Eur. J. Inorg. Chem.* 2014, 1797-1810; (c) S. Schmist, G. Abkai, T. Rosendahl, F. Rominger, P. Hofmann, *Organomet.* 2013, **32**, 1044; (d) I. del Río, W. G. J. de Lange, P. W. N. M. van Leeuwen, C. Claver, *Dalton Trans.* 2001, 1293; (e) I. del Río, O. Pàmies, P. W. N. M. van Leeuwen, C. Claver, *J. Organomet. Chem.* 2000, **608**, 115.
- D. W. Norman, J. N. H. Reek, T. R. M. L. Besset, US Pat. 8710275B2, 2014.
- G. W. Phillips, T. J. Devon, T. A. Puckette, J. L. Stavinoha, J. J. Vanderbilt, US Pat. 4760194, 1988.
- R. A. Baber, M. L. Clarke, K. M. Heslop, A. C. Marr, A. G. Orpen, P. G. Pringle, A. Ward, D. E. Zambrano-Williams, *Dalton Trans.*, 2005, 1079-1085.



## Table of contents



Ligand family can be tuned:  
from axial-equatorial / bis-equatorial = from >50:1 to 1:50

Branched aldehyde selectivity above 50% in hydroformylation of propene and 1-octene