Supramolecular control of regioselectivity in the hydroformylation reaction

Substrate preorganization and second coordination sphere catalysis

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Chapter 4

Regioselective Hydroformylation of $\omega$-Unsaturated Acids via Supramolecular Control Using a 1,3,-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand
Introduction

Achieving highly selective chemical transformations is one of the great challenges chemists face in order to use resources more efficiently and make processes more economically beneficial.[1,2] One of the strategies to engineer highly selective catalysts that has recently gained considerable attention in the field of homogeneous catalysis relies on ditopic binding of substrates to the catalytic center, thereby pre-organizes the substrate by restricting the movement of the reactive group.[3–7] This can be achieved using a supramolecular directing group that binds to a recognition site of the catalyst (Figure 1).

Figure 1 Schematic drawing of the concept of supramolecular substrate preorganization, M = metal center, Do = donor atom, RS = Recognition site, DG = Directing group, RG = reactive group

Successful examples using the ditopic binding of a substrate shows that certain reaction pathways become inaccessible which is often the mechanism underlying the increase in selectivity. Using this strategy, selectivity control has been reported that would otherwise be impossible using traditional transition metal catalysts and has been applied successfully by various research groups for a variety of reactions. Examples include the asymmetric hydrogenation,[8,9] epoxidation[10–12], enantioselective aziridination,[13] sulfoxidation,[14] C-H activation reactions[15–22] as well as in the hydroformylation reaction.[23–31]

In the hydroformylation reaction, a syngas mixture (H₂:CO) is reacted with an alkene in the presence of a transition metal catalyst to form an aldehyde moiety (Figure 2).[32–34]

Figure 2 General scheme of the hydroformylation reaction.

For a number of substrates, it is difficult to obtain a single aldehyde product under commonly used hydroformylation conditions.[33–36] To control the regioselectivity, the aforementioned supramolecular substrate preorganization strategies can be used to
control the regioselectivity for substrates that contain a (supramolecular) directing group.\textsuperscript{[3,4,6]} Using carboxylic acids as supramolecular directing groups, our group and the group of Breit were able to control the regioselectivity of terminal and internal alkenes in the hydroformylation reaction.\textsuperscript{[23–31,37]}

**Figure 3 a)** Regioselectivity control in the hydroformylation reaction of unsaturated carboxylates using diamidodiindolyl methane anion receptor functionalized bisphosphines and phosphites (DIMPhos) b) Investigation into 1,3 benzenedicarboxamide functionalized bisphosphines and bisphosphites.

The substrate preorganization catalysts reported by our group were based on bisphosphine and bisphosphate bidentate ligands (DIMPhos) which contained a diamidodiindolyl methane anion receptor (the DIM pocket) in the backbone (Figure 3a).\textsuperscript{[25–28,30,38]} This diamidodiindolyl methane anion receptor strongly binds deprotonated carboxylic acids allowing for ditopic binding of the carboxylate containing alkenes.\textsuperscript{[12,24]} DFT calculations in Chapter 2 have established that the ditopic binding of the substrate hinders geometries leading to the aldehyde product closest to the directing group. This results in a selectivity enhancement to the outermost product.

The current DIMPhos catalysts are generally difficult to synthesize and require column chromatography steps which impairs the scalability of the synthesis of these ligands.
Therefore, it is desirable to investigate whether novel bidentate bisphosphine and bisphosphite hydroformylation catalysts containing an anion receptor in the backbone are also able to control the regioselectivity \emph{via} ditopic substrate binding.

Indeed, many anion receptors have been published, of which several are easy to synthesize and can potentially be turned into a bisphosphorous ligand.\textsuperscript{[39–49]} The 1,3-benzenedicarboxamide carboxylate receptor, which was initially reported by Crabtree et al. (Figure 3, b)\textsuperscript{[50,51]} was chosen a platform for the synthesis of novel bisphosphine and bisphosphite ligands. This receptor motif finds widespread application in the field of supramolecular chemistry as an anion receptor and many variants are known.\textsuperscript{[44,52–61]} In DCM, these receptors have a binding constant for acetate of ~ 20000 M\textsuperscript{-1}. However, to the best of our knowledge, this anion receptor has not yet been converted into bisphosphorous ligands. The readily available building blocks and the facile synthesis result in a lower overall cost of the ligands, allowing for broader applicability of this type of ligands.

\textbf{Results and discussion}

\textbf{Ligand design, synthesis and anion binding studies}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{ligands.png}
\caption{Novel designed bidentate ligands based on the 1,3 benzenedicarboxamide anion receptor.}
\end{figure}

To study if bisphosphine ligands with a 1, 3-benzenedicarboxamide anion receptor in the backbone could form bidentate chelating coordination complexes with rhodium, DFT calculations were conducted with the ADF modeling suite (BLYP-D3, DZP, ZORA).\textsuperscript{[62–65]} These calculations resulted in the design of L\textsubscript{1}, L\textsubscript{2} and L\textsubscript{3} (Figure 4) as the catalytically relevant [Rh(H)(CO)\textsubscript{2}(L\textsubscript{1})], [Rh(H)(CO)\textsubscript{2}(L\textsubscript{2})] and [Rh(H)(CO)\textsubscript{2}(L\textsubscript{3})] species displayed a similar binding enthalpy as the previously reported [Rh(H)(CO)\textsubscript{2}(DIMphos)] complexes (Figure 5).
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 5 DFT modelled structures of [Rh(H)(CO)₂(L1)], [Rh(H)(CO)₂(L2)] and [Rh(H)(CO)₂(L3)] (BLYP-D3, DZP).

All ligands could be prepared in high yields ranging from 60 to 92% by reacting isophthaloyl chloride with the appropriate amine to form the 1,3-benzenedicarboxamide anion receptor motif. For the phosphine-based ligand, L₁, 4-(diphenylphosphino)benzenemethanamine was used and directly yielded the ligand. To generate bidentate phosphite ligands L₂ and L₃, we first synthesized N¹,N³-bis(4-hydroxyphenyl) 1,3-benzenedicarboxamide and N¹,N³-bis(3-hydroxyphenyl) 1,3-benzenedicarboxamide. Subsequently, the alcohols were reacted with (S)-(binol)P-Cl to ultimately yield the novel bisphosphate ligands. All new ligands were fully characterized by ¹H NMR, ³¹P NMR ¹³C NMR and high-resolution mass spectrometry (see experimental section).

Following the successful synthesis, binding studies were conducted in CD₂Cl₂ to investigate whether these ligands can still effectively bind carboxylates when functionalized when phosphorous moieties have been introduced. Titration of tetrabutylammonium acetate of a solution of L₁ reveals the typical amide N-H peak shifts downfield (from 6.5 ppm to 10.0 ppm) in the ¹H-NMR spectra. The binding isotherm was fitted assuming a 1:1 binding revealing an acetate binding constant of ~ 19000 M⁻¹ for L₁ (see experimental section). This shows the bisphosphate ligand displays a similar binding constant to the parent anion receptor. Analogous to L₁, binding studies were conducted for L₂ and L₃ with tetrabutylammonium acetate in CD₂Cl₂, which gave binding constants of 16000 M⁻¹ and 14000 M⁻¹ for L₂ and L₃, respectively. This shows that these ligands bind acetate in a similar fashion to the parent the 1,3 benzenedicarboxamide core.

Catalytic studies

With these three new anion receptor functionalized ligands in hand, we investigated whether the novel phosphine and phosphites, L₁-L₃, can be used to control the regioselectivity in the hydroformylation reaction of unsaturated carboxylates. Previous studies have shown that DIMPhos based rhodium complexes are able to control the
regioselectivity of deprotonated ω-unsaturated carboxylic acids, forming predominantly the linear product, which is reflected in the high linear/branched ratios (l/b ratios). Control experiments showed that the selectivity for the linear product was significantly lower for the protonated analogs that do not bind in the receptor of the DIMPhos ligands. For the current catalytic experiments, using similar conditions, in which L1, L2 and L3 were mixed with [Rh(acac)(CO)2] in separate vials in DCM, which under syngas pressure (20 bar) form the active hydroformylation catalysts. As substrates, the ω-unsaturated carboxylic acids 3-butenolic acid (n = 1) up to 7-octenoic acid (n = 5) were hydroformylated in the presence and absence of the base, DIPEA. For L1 and L2 the obtained selectivities (l/b) are presented in Figure 6 and Figure 7 for each substrate in the presence (blue) and absence (orange) of the base DIPEA. Since the protonated acids cannot bind to the receptor, these entries serve as control experiments. The differences in selectivities observed in these experiments are reflecting the effect of substrate pre-organization by carboxylate binding. For L1 and L2, the regioselectivity was similar for the protonated and the deprotonated entries, which shows that these ligands are not effective in controlling the regioselectivity via ditopic substrate binding. Only for 3-butenolic acid, a significant regioselectivity difference was observed for the reactions carried out in the presence or absence of base. It should be noted that the deprotonated and protonated entries have an intrinsic difference in regioselectivity due to inductive effects.

Figure 6 Hydroformylation of different omega-unsaturated acids using the [Rh(L1)]. Reagents and conditions: [substrate] = 0.2 M, DIPEA (1.5 equiv. (blue bars)), [Rh(CO)2(acac)] (1 mol %), L1 (1.1 mol %) or L2 (1.1 mol%), 20 bar CO/H2 (1:1), 40°C, 24 h. Conversion and regioselectivity determined by 1H NMR analysis of the crude reaction mixture. For full experimental details, see the experimental section. The blue bars are experiments in presence of base, and the orange bars are in absence of base as control experiment.
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 7 Hydroformylation of different ω-unsaturated acids using the [Rh(L2)] catalyst. Reagents and conditions: [substrate] = 0.2 M, DIPEA (1.5 equiv. (blue bars)), [Rh(CO)₂(acac)] (1 mol %), L₂ (1.1 mol%), 20 bar CO/H₂ (1:1), 40°C, 24 h. Conversion and regioselectivity determined by ¹H NMR analysis of the crude reaction mixture. For full experimental details, see the experimental section. The blue bars are experiments in presence of base, and the orange bars are in absence of base as control experiment.

Gratifyingly, for complexes based on L₃, the selectivity for the linear product is significantly higher for the deprotonated entries compared to the protonated entries (Figure 8). As a control experiment, the [RhL₃] catalyst was used to convert 1-octene in the presence and absence of DIPEA as the base. This was done to study the effect of DIPEA on the selectivity of this [RhL₃] hydroformylation catalyst for substrates that do not have a carboxylate function. Similar regioselectivities are observed for 1-octene in presence and absence of base. These results show the deprotonation of the 3-butenolate substrates to 7-octenoate is responsible for the selectivity enhancement observed. This shows [RhL₃] catalyst is able to control the regioselectivity via anion binding, which confirms our hypothesis that other anion receptor-based ligands can also control the regioselectivity of unsaturated carboxylates in the hydroformylation reaction.
Figure 8 Hydroformylation of different ω-unsaturated acids using the [Rh(L2)] catalyst. Reagents and conditions: [substrate] = 0.2 M, DIPEA (1.5 equiv. (blue bars)), [Rh(CO)\textsubscript{2}(acac)] (1 mol %), L\textsubscript{3} (1.1 mol %), 20 bar CO/H\textsubscript{2} (1:1), 40°C, 24 h. Conversion and regioselectivity determined by \textsuperscript{1}H NMR analysis of the crude reaction mixture. For full experimental details, see the experimental section. The blue bars are experiments in presence of base, and the orange bars are in absence of base as control experiment.

Coordinaiton studies

To understand the catalytic behavior of these three catalysts, coordination and binding studies were conducted on rhodium complexes of \textbf{L1, L2, and L3} (Figure 9). In separate experiments, these three ligands were mixed with [Rh(acac)(CO)\textsubscript{2}] in a 1:1 ratio in CD\textsubscript{2}Cl\textsubscript{2} using the same catalyst concentrations as during the catalytic experiments, and the \textsuperscript{1}H and \textsuperscript{31}P NMR spectra were measured to identify the complexes that were formed.
Regioselective Hydroformylation of \( \omega \)-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 9 Coordination studies with Rh(acac) complexes and proposed mononuclear complexes.

For the \([\text{Rh(acac)}]/\text{L1}\), \([\text{Rh(acac)}]/\text{L2}\) and \([\text{Rh(acac)}]/\text{L3}\) complexes, \(^1\text{H}\) NMR spectra displayed broader peaks compared to the respective free ligands \(\text{L1-L3}\), complicating straightforward analysis of these complexes. The \(^{31}\text{P}\) NMR spectra of the solution containing \([\text{Rh(acac)}]/\text{L1}\) displayed a broad doublet with a coupling constant of 140 Hz and the \([\text{Rh(acac)}]/\text{L3}\) complex gave a similar doublet, but with a coupling constant of 293 Hz. In contrast, the solution containing the \([\text{Rh(L2)(acac)}]\) complex displays no clear peaks in the \(^{31}\text{P}\) NMR spectra even when spectra were recorded with an increased number of scans, which suggests no single species is present in large quantities as this would be observable as a large peak. For all these complexes and their respective ligands, 2D DOSY NMR experiments were conducted to estimate their hydrodynamic size in solution (Table 1). These 2D DOSY experiments reveal stark differences between the \([\text{Rh(L1)(acac)}]\), \([\text{Rh(L2)(acac)}]\) and \([\text{Rh(L3)(acac)}]\) complexes. DFT-optimized (BLYP, DZP) structures of the mononuclear \([\text{Rh(acac)}(\text{L1})]\), \([\text{Rh(acac)}(\text{L2})]\) and \([\text{Rh(acac)}(\text{L3})]\) species give a 5.7 Å, 9.0 Å and 8.3 Å radii for these complexes, respectively (see Table 1). For the \([\text{Rh(acac)}]/\text{L1}\) the measured hydrodynamic radius is slightly smaller than the free ligand and similar to the size of the calculated mononuclear \([\text{Rh(acac)}(\text{L1})]\) complex. This decrease in size measured is presumably caused by a conformational change of the ligand \(\text{L1}\) following complexation with rhodium. In contrast, the \([\text{Rh(acac)}]/\text{L2}\) and \([\text{Rh(acac)}]/\text{L3}\) complexes display an increase in the average hydrodynamic radius compared to the respective free ligands. Also the average hydrodynamic radius is larger than the calculated hydrodynamic radii of \([\text{Rh(acac)}(\text{L2})]\) and \([\text{Rh(acac)}(\text{L3})]\) suggesting that these complexes are likely to be dimeric/oligomeric species. When the dimeric complexes;\([\text{Rh(acac)}(\text{L1})]_2\), \([\text{Rh(acac)}(\text{L2})]_2\) and \([\text{Rh(acac)}(\text{L3})]_2\) are calculated, the hydrodynamic radius is calculated at 11.2 Å, 15.1 Å, and 14.6 Å, respectively. For the \([\text{Rh(acac)}]/\text{L2}\) complex, the measured average hydrodynamic radius on 2D DOSY is larger than both the monomer and the dimer with a hydrodynamic radius that is more than 200% than the measured radius of free ligand \(\text{L2}\). Moreover, this \([\text{Rh(acac)}]/\text{L2}\) complex gave no well-defined peaks in \(^1\text{H}\) NMR. When \(^{31}\text{P}\) NMR was measured of the \([\text{Rh(acac)}]/\text{L2}\) complex, no peaks could be detected. These results show that most of the complex is not the monomeric \(\text{M}_1\text{L}_1\) species. For the \([\text{Rh(acac)}]/\text{L3}\) complex, the \(^1\text{H}\) spectrum displayed
more defined peaks than the [Rh(acac)]/L2 complex and a hydrodynamic radius of [Rh(acac)]/L3 was determined to be 13.2 Å by 2D DOSY NMR spectroscopy that falls between the radius of the monomer and the dimer species (Table 1).

The addition of 5 equivalents of tetrabutylammonium acetate to [Rh(acac)]/L1 displays no shifts of the N-H protons in the 1H NMR spectra, suggesting that acetate is not strongly bound in the pocket of the ligand when it is coordinated to the rhodium. In contrast, the addition of tetrabutylammonium acetate to the [Rh(acac)]/L2 and [Rh(acac)]/L3 complexes leads to downfield N-H peaks in the 1H NMR spectra, characteristic for the binding of acetate. However, due to the broad peaks in the 1H NMR spectra a clear assessment of the binding constant could not be made for these complexes.

**Coordination studies of under syngas conditions**

Next the [Rh(acac)]/L1, [Rh(acac)]/L2 and [Rh(acac)]/L3 complexes were pressurized with syngas (5 bar, H2:CO) in CD2Cl2. Pressurization of these complexes leads to major changes in the 1H and 31P NMR spectra, which shows that the Rh(acac)/L1-L3 complexes are successfully activated by the syngas mixture, forming the catalytically active rhodium catalysts.[69–73]

![Figure 10 Conversion of [Rh(acac)]/L1, [Rh(acac)]/L2 and [Rh(acac)]/L3 complexes under syngas pressure in the absence or the presence of acetate.](image)

The signals of the [RhL1] complex change when it is under syngas pressure and two broad peaks appear in 31P NMR (28–29 ppm). Also, in the 1H NMR spectrum a rhodium-hydrido signal (δ = -9.5 ppm) is observable, providing further evidence for the successful conversion of the [Rh(acac)(L1)] complex to the catalytically active rhodium hydride complex (Figure 11, top). For the [RhL2] and [RhL3] syngas complexes, the 31P NMR spectra reveal no discernible peaks that could be analyzed. Additionally, for all three complexes, the hydrido signal is observed but the signal is not well-defined and therefore coupling constants could not be analyzed from these signals. Next, for these complexes that formed under syngas pressure, 2D DOSY measurements were conducted. These measurements reveal that for all three complexes, the average hydrodynamic radius is larger than observed for the respective free ligands. Additionally, the calculated radii of the mononuclear [Rh(H)(CO)2(L1)], [Rh(H)(CO)2(L2)] and [Rh(H)(CO)2(L3)] species give a 5.7, 0 Å, 9.0 Å and 8.3 Å radii for these complexes, respectively. The calculated dimeric complexes of [Rh(H)(CO)2(L1)]2, [Rh(H)(CO)2(L2)]2 and [Rh(H)(CO)2(L3)]2 are similar to the dimeric [Rh(acac)(Lx)]2 species with calculated radii of 11.2 Å, 15.1 Å and 14.6 Å respectively. For the [RhL1] and [RhL3] syngas complexes, the average hydrodynamic radius determined with 2D DOSY is between the calculated sizes of the monomeric
complex of the ligand and the dimeric rhodium complex of the ligand. For the [RhL2]
complex, the average hydrodynamic size is larger than the calculated dimer and monomer.

In the next series of experiments, solutions of the [Rh(acac)]/L1, [Rh(acac)]/L2 and
[Rh(acac)]/L3 complexes were prepared to which 2 equivalents tetrabutylammonium
acetate was added before converting the Rh(acac) species to the catalytically active
species under syngas pressure. Interestingly, for the [RhL1] syngas complex the addition
of acetate resulted in appearance of downfield peaks that are characteristic of acetate
binding by the 1,3 benzene dicarboxamide core. This is different from the non-pressurized
[Rh(acac)]/L1 precursor complex, which does not display binding of acetate in CD2Cl2
(vide supra).

Moreover, a well-defined rhodium-hydrido species appears following the addition of
acetate in the [RhL1] complex (Figure 11, bottom). This effect is not observed with the
[RhL2] and [RhL3] syngas complexes. Previous studies have shown that for DIMPhos
phosphite ligands the carboxylate can coordinate to rhodium under catalytic conditions,
whereas phosphine based DIMPhos ligands do not display carboxylate coordination,
which forms an explanation for why the rhodium-hydrido signal does not become well
defined following the addition of acetate for phosphite ligands.[26,28,74,75]

Figure 11 Rhodium-hydride region of 1:1 mixture of L1 and [Rh(acac)(CO)2] under syngas
pressure (H2: CO, 5 bar) in CD2Cl2(top) and with two equivalents of tetrabutylammonium
acetate(bottom).

For all three [RhL1], [RhL2] and [RhL3] complexes measured under syngas
in the presence of acetate, more well defined peaks in the aromatic region of
the $^1$H NMR spectra were observed compared to the acetate free spectra under otherwise identical conditions. Also, the presence of acetate results in the appearance of multiple downfield peaks between 8-10 ppm, which is characteristic of carboxylate binding.$^{[50,51]}$ The fact that there are multiple peaks present indicate the formation of multiple species, as for the parent ligands we only found one set of signals. The presence of multiple complexes is also in accordance with the 2D DOSY spectra of these complexes that reveal a higher average hydrodynamic radius than the free ligands L1-L3 (Table 1). In particular, for the [RhL2] complexes the measured average size was larger than the calculated dimeric and monomeric species, which shows most of this ligand is involved in complexes that are in the polymeric/oligomeric state.

<table>
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<th></th>
<th>L1 Hydrodynamic radius$^a$</th>
<th>Increase$^b$</th>
<th>L2 Hydrodynamic radius$^a$</th>
<th>Increase$^b$</th>
<th>L3 Hydrodynamic radius$^a$</th>
<th>Increase$^b$</th>
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<td>Free Ligand</td>
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<td>-</td>
<td>8.1 Å</td>
<td>-</td>
<td>8.1 Å</td>
<td>-</td>
</tr>
<tr>
<td>[Rh(acac)]</td>
<td>5.5 Å</td>
<td>-13%</td>
<td>26 Å</td>
<td>221%</td>
<td>13.2 Å</td>
<td>63%</td>
</tr>
<tr>
<td>Rh syngas</td>
<td>9.3 Å</td>
<td>48%</td>
<td>26 Å</td>
<td>221%</td>
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<td>59%</td>
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<tr>
<td>Rh syngas + acetate$^c$</td>
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<td>48%</td>
<td>42 Å</td>
<td>419%</td>
<td>10.8 Å</td>
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Table 1 Comparison of hydrodynamic radii of L1, L2 and L3 and their respective rhodium complexes in CD$_2$Cl$_2$. Note: For the [RhL2] complexes, a precipitate formed after several hours and 2D DOSY shift was broad, therefore the precise hydrodynamic radius was more difficult to determine than with the other two complexes. $^a$ Hydrodynamic radius determined by performing a 2D DOSY and calculating the radius based on the Stokes-Einstein equation.$^{[67]}$ $^b$ increase in average hydrodynamic radius compared to the free ligand $^c$ Two equivalents acetate added to the reaction mixture prior to pressurization with syngas.

For the [RhL1] and [RhL3] complexes that form under syngas, the average hydrodynamic radius is between the size of the monomeric complex and the dimeric complex. In particular for the [RhL3] complex in the presence of acetate the average hydrodynamic radius is ~30 % larger than the measured free ligand size. If we assume that the [RhL3] complex is only in the monomeric and dimeric state, we estimate that ~60% of the complex is in the monomeric state. However, also larger species may be present, which have a greater impact on the average hydrodynamic radius. These results suggest that the monomeric [RhL3] complex is actually more selective than what is currently observed with the catalytic experiments (vide supra). Through optimization of the conditions the
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Regioselectivity control may be improved by ensuring a higher portion of the [RhL3] catalyst is in the monomeric state.

Since the regioselectivity in the hydroformylation reaction seems to be controlled by substrate pre-organization when complexes based on L3 are used, we conducted variable temperature studies with the complexes formed under syngas conditions, in presence and absence of acetate. In these experiments the temperature was varied from 40 °C to -40°C, however, in this temperature window only minor variations in the ¹H NMR spectra were observed and well-defined peaks in both ³¹P NMR and ¹H NMR were still lacking.[²⁸]

Figure 12. Dimeric/oligomeric rhodium species cannot bind substrate in a ditopic fashion, leading to lower overall selectivity control.

Based on the 2D-DOSY spectra conducted with acetate under syngas conditions, we conclude a larger proportion of the rhodium catalyst based on L3 is in the monomeric state compared to the rhodium catalysts based on L1 and L2. The larger portion of this [RhL3] catalyst being in the monomeric state may explain why this catalyst is able to control the regioselectivity of unsaturated carboxylates, whereas the [RhL1] and [RhL2] catalysts do not convert the ω-unsaturated carboxylates with high levels of regioselectivity. For the [RhL1] and [RhL2] catalysts a large portion is in the dimeric/oligomeric state and such complexes cannot bind the substrates in a ditopic fashion. As a result, the regioselectivity is poorly controlled (Figure 12). Previous studies
have also shown that only when a large portion of the anion receptor functionalized rhodium catalyst is in the M$_1$L$_1$ state, a significant regioselectivity effect is observed.[31]

**Conclusions and outlook**

In conclusion, we report a new class of bidentate ligands based on a 1,3-benzenedicarboxamide anion receptor, L$_1$-L$_3$. We demonstrate that these ligands bind carboxylate substrates and that these can be used as ligands in the hydroformylation reaction. Complexes based on ligand L$_3$ show higher selectivity in the rhodium catalyzed hydroformylation reaction of unsaturated carboxylates, leading to more linear aldehyde, as a result of substrate pre-organization. These results show the approach of controlling the regioselectivity in the hydroformylation reaction with a bidentate phosphorous ligand containing an anion receptor in the backbone can be extended from previously reported DIMPhos to other anion receptor-based ligands. Two other ligands L$_1$ and L$_2$, which also contained the 1,3-benzenedicarboxamide motif in the backbone were successfully synthesized and applied in the hydroformylation of ω-unsaturated carboxylates. In contrast to L$_3$, the resultant rhodium complexes of L$_1$ and L$_2$ do not selectively convert ω-unsaturated carboxylates with higher levels of regioselectivity than the control experiments. This shows these ligands cannot control the regioselectivity via ditopic substrate binding. Mechanistic studies show all three ligands do not selectively form mononuclear complexes and also dimeric/oligomeric complexes are formed under catalytic conditions. The more well-defined spectra observed combined with lower average hydrodynamic radii under of the spectra conducted with acetate under syngas conditions show that a larger portion of the [RhL$_3$] complex is in the monomeric state compared to the [RhL$_1$] and [RhL$_2$] complexes. This explains why the [RhL$_3$] catalyst displays higher regioselectivity than the control experiments. As dimeric/oligomeric transition metal complexes also convert the substrates and since these complexes cannot bind the substrates in a ditopic fashion, the regioselectivity is not controlled by the dimeric/oligomeric rhodium complexes. These insights provide further evidence that the selective formation of a M$_1$L$_1$ species is crucial for attaining high levels of regioselectivity in the hydroformylation for substrate preorganization catalysis. We are using these insights in our pursuit for novel catalysts that are both facile to synthesize and lead to high levels of regioselectivity control in the hydroformylation reaction.
Experimental section

Materials and Methods
All manipulations were conducted under inert atmosphere (argon or nitrogen) using oven-dried or flame dried glassware and pre-dried and degassed. Reactions were carried out under \( \text{N}_2 \) atmosphere using standard Schlenk techniques. THF, pentane, hexane and diethyl ether were distilled from sodium benzophenone ketyl under nitrogen; \( \text{CH}_2\text{Cl}_2 \), methanol and \( \text{Et}_3\text{N} \) were distilled from CaH2 under nitrogen and toluene was distilled from sodium under nitrogen. NMR spectra were measured on a Bruker DRX 300 or a Bruker AMX 400. Measurements were done at room temperature (rt) unless otherwise stated. High resolution mass spectrometry was carried out using the AccuTOF GC v 4g, JMS-T100GCV mass spectrometer (JEOL, Japan). \( \text{CD}_2\text{Cl}_2 \), and DIPEA were dried with activated molecular sieves and degassed using three freeze-pump thaw cycles and stored in young valve Schlenks. All reagents were purchased from commercial suppliers and used without any further purification unless otherwise stated. Tetrabutylammonium acetate was stored in a glovebox.

Ligand Synthesis

\[
\text{F} \quad \text{NH}_2 \quad \text{K} \quad \text{THF} \quad \text{H}_2\text{N} \quad \text{PPh}_2
\]

3 was synthesized according to a previously reported procedure.\cite{76} A 100 ml Schlenk equipped with a reflux condenser was charged with 2.5 mL of 4-fluorobenzylamine and 44 mL of a 0.5 M solution of KPPh2. The reaction mixture was refluxed overnight. After heating the reaction mixture overnight, the reaction was quenched with 2 ml of methanol. Next, the solvents were evaporated and redissolved in dry and degassed DCM (40 ml) and washed in with degassed water (2x 40 ml). Next the reaction mixture was washed 3 times with degassed water and dried with MgSO4. After filtration, all solvents were evaporated and the reaction mixture was purified by column chromatography using a DCM:MeOH (19:1 → 9:1 ) to yield the pure product (2.68 g, 9.2 mmol, 42% yield).
4-(diphenylphosphino)-benzenemethanamine 3 (0.291 g, 1 mmol) was dissolved in a CH₂Cl₂ (15 ml) and Et₃N (0.2 ml) mixture. Next, isophthaloyl chloride 4 (0.100 g, 0.5 mmol) was dissolved in a separate Schlenk in CH₂Cl₂ (2 ml). The dissolved isophthaloyl chloride solution added dropwise to the phosphine mixture. After 1 hour, the full conversion of the starting material was observed with TLC. Following full conversion, the reaction mixture was washed with degassed water and dried with MgSO₄. After filtration, all solvents were evaporated and the reaction mixture was purified using column chromatography DCM:MeOH (20:1) to yield the pure product (0.330 g, 0.46 mmol, 93% yield).

**1H NMR (400 MHz, Chloroform-d)** δ 8.23 (s, 1H), 7.96 (d, J = 7.7 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.44 – 7.22 (m, 28H), 6.54 (t, J = 5.7 Hz, 2H), 4.67 (d, J = 5.7 Hz, 4H).

**13C NMR (126 MHz, DMSO-d₆)** δ 166.32, 141.04, 137.30, 137.20, 134.93, 134.00, 133.85, 133.68, 133.52, 130.38, 129.38, 129.18, 128.16, 42.92

**31P NMR (162 MHz, Chloroform-d)** δ -6.01

Predicted mass: 712.24085 Measured mass: 712.24066

4-(Benzylxoy)aniline hydrochloride 5 (2.35 g, 1.0 mmol) was dissolved in a mixture of dry DCM (40 ml) and Et₃N (5 ml). Next isophthaloyl chloride 4 (1.0 g, 0.5 mmol) was dissolved in 20 ml of dry DCM. Subsequently the solution of 4 was added to the solution of 5. After 10 minutes, a white solid crashed out of solution. The suspension was filtered using vacuum filtration and the solid was washed thoroughly with DCM, which was the pure product (2.45 g, 0.46 mmol, 95% yield).

**1H NMR (400 MHz, DMSO-d₆)** δ 10.32 (s, 2H), 8.53 (s, 1H), 8.12 (d, J = 7.8 Hz, 2H), 7.88 – 7.56 (m, 6H), 7.51 – 7.28 (m, 10H), 7.07 – 6.96 (m, 5H), 5.11 (s, 4H).

**13C NMR (126 MHz, DMSO-d₆)** δ 165.10, 155.15, 137.64, 135.69, 132.80, 130.85, 129.35, 128.86, 128.66, 128.25, 128.15, 122.37, 115.23, 69.83
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Predicted mass: 528.20491 Measured mass: 528.20666

\[
\text{N}^1,\text{N}^3\text{-bis(4-hydroxyphenyl)isophthalamide 8}
\]

7 (1.02 g, 0.2 mmol) was dissolved/suspended in a MeOH:THF 1:3 (150 ml) mixture. Next Pd/C (0.1 g) was added to the reaction mixture. A balloon of H₂ was added and the solution was flushed with hydrogen after which the solution was heated to 40°C and the reaction mixture was stirred vigorously overnight. The next day, a small sample was taken from the crude reaction mixture which was evaporated and measured with NMR spectroscopy. This revealed full conversion of the starting material to the product. Next, the reaction mixture was filtered over celite and the solvents were evaporated to yield the pure product (0.66 g, 0.018 mmol, 94% yield).

\[\text{^1H NMR (400 MHz, DMSO-\text{d}_6)} \delta = 10.18 \text{ (s, 2H), 9.27 (s, 2H), 8.48 (s, 1H), 8.09 (d, J = 7.6 Hz, 2H), 7.65 (t, J = 7.6 Hz, 1H), 7.56 (d, J = 8.4 Hz, 4H), 6.76 (d, J = 8.4 Hz, 4H).}\]

\[\text{^13C NMR (126 MHz, DMSO-\text{d}_6)} \delta = 164.93, 154.25, 135.76, 131.08, 130.71, 128.90, 127.16, 122.65, 115.46\]

Predicted mass: 348.11101 Measured mass: 348.11121

\[\text{(S)-Binol PCl 10}\]

10 was synthesized according to a previously reported procedure.[30]
Note: In order to achieve selective formation of the phosphite product \( L_2 \), extreme caution needs to be taken to work water-free and all steps were carried out using Schlenk techniques. Furthermore, all glassware was flame-dried under vacuum or oven dried and strictly dry and degassed solvents were used. \( 9 \) (0.50 g, 1.43 mmol) was azeotropically dried with (3 x 10 mL) toluene. \( 9 \) was dissolved in 60 ml of THF, to which 2.0 ml Et\(_3\)N was added. In another Schlenk (S)-BinolPCl \( 10 \) (1.02 gram, 2.88 mmol) was dissolved in 10 mL THF. The solution of \( 9 \) in THF was added dropwise to the solution of \( 10 \) at -78 °C. After 30 min the reaction mixture was allowed to warm up until room temperature was reached. The reaction continued at room temperature overnight. Crude \(^{31}\text{P} \) NMR revealed product formation combined with minor amounts of hydrolysis products. The suspension was filtered over basic alumina (activated in the oven at 130 °C) to remove the salts and the hydrolysis product. Next, the product was purified dissolving the compound in a minimum of THF and subsequent precipitation with pentane to yield the pure product (950 mg, 0.97 mmol, 67% yield).

\(^1\text{H} \) NMR (400 MHz, DMSO-\( d_6 \)) \( \delta = 10.53 \) (s, 2H), 8.55 (s, 1H), 8.32 – 8.04 (m, 10 H), 7.87 (d, \( J = 8.6 \) Hz, 4H), 7.75 (m, 4H), 7.55 (q, \( J = 7.0 \) Hz, 5H), 7.41 (t, \( J = 9.2 \) Hz, 4H), 7.27 (m, 8 H).

\(^{13}\text{C} \) NMR (126 MHz, DMSO-\( d_6 \)) \( \delta = 165.42, 147.43, 147.07, 146.85, 136.44, 135.53, 132.48, 132.25, 131.85, 131.58, 131.41, 130.92, 129.14, 127.42, 126.07, 123.90, 122.20, 122.09, 121.12.

\(^{31}\text{P} \) NMR (162 MHz, DMSO-\( d_6 \)) \( \delta = 144.87 \)

Predicted mass: 976.21034 Measured mass: 976.21418

\( N_1^1,N_3^1\)-bis(3-(benzyloxy)phenyl)isophthalamide \( 12 \)

\( 11 \) (2.00 gram, 10 mmol) was dissolved in a mixture of dry DCM (20 ml) and dry Et\(_3\)N (2 ml). Next \( 4 \) (1.00 gram, 5 mmol) was dissolved in 10 ml of DCM. Subsequently the solution of \( 4 \) was added to the solution of \( 5 \). After 10 minutes, a white solid crashed out of solution. The
Regioselective Hydroformylation of \( \omega \)-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Suspension was filtered using vacuum filtration and the solid was washed with DCM to yield the pure product (2.42 gram, 0.46 mmol, 92% yield).

\(^1H\) NMR (400 MHz, DMSO-\( d_6 \)) \( \delta \) 10.39 (d, \( J = 3.9 \) Hz, 2H), 8.51 (s, 1H), 8.13 (d, \( J = 7.8 \) Hz, 2H), 7.70 (t, \( J = 7.7 \) Hz, 1H), 7.59 (d, \( J = 2.3 \) Hz, 2H), 7.51 - 7.18 (m, 14H), 6.79 (dd, \( J = 8.1, 2.6 \) Hz, 2H), 5.12 (s, 4H).

\(^13\)C NMR (126 MHz, DMSO-\( d_6 \)) \( \delta \) 165.55, 159.00, 140.71, 137.51, 135.63, 131.13, 129.95, 129.10, 128.91, 128.29, 128.12, 127.42, 113.28, 110.56, 107.45, 69.62

Predicted mass: 528.20491 Measured mass: 528.20666

\( N^1, N^3 \)-bis(3-hydroxyphenyl)isophthalamide 13

\( N^1, N^3 \)-bis(3-(benzyloxy)phenyl)isophthalamide 12 (2.00 gram, 3.8 mmol) was dissolved/suspended in a MeOH:THF 1:3 (150 ml) mixture in a Schlenk. Next, Pd/C (0.2 gram) was added to the reaction mixture. A balloon of \( H_2 \) was added and the solution was flushed with hydrogen after which the solution was heated to 40°C and the reaction mixture was stirred vigorously overnight. The next day, a small sample was taken from the reaction mixture for NMR analysis, which displayed full conversion to the alcohol product. The reaction mixture was subsequently filtered over celite and the solvents were evaporated to yield the pure product (1.23 gram, 3.5 mmol, 93% yield).

\(^1H\) NMR (400 MHz, DMSO-\( d_6 \)) \( \delta \) 10.27 (s, 2H), 9.43 (s, 2H), 8.47 (s, 1H), 8.11 (d, \( J = 7.8 \) Hz, 2H), 7.67 (t, \( J = 7.7 \) Hz, 1H), 7.38 (s, 2H), 7.16 (dt, \( J = 15.7, 8.1 \) Hz, 4H), 6.53 (d, \( J = 7.9 \) Hz, 2H).

\(^13\)C NMR (101 MHz, DMSO-\( d_6 \)) \( \delta \) 165.27, 157.82, 140.36, 135.86, 130.83, 129.55, 128.00, 127.25, 111.37, 111.22, 107.74

Predicted mass: 348.11101 Measured mass: 348.11020
(bis-4'((S)-1,1'-binaphthyl-2,2-diyl phosphito) 3-bisphenyl N\textsubscript{1}\textsubscript{1},N\textsubscript{3} isophthalamide \textbf{L3}  

Note: In order to achieve selective formation of the phosphite product \textbf{L3}, extreme caution needs to be taken to work water-free and all steps were carried out using Schlenk techniques. Furthermore, all glassware was flame-dried under vacuum or oven dried and strictly dry and degassed solvents were used. \textbf{12} (1.00 g, 2.85 mmol) was azeotropically dried with (3 x 10 mL) toluene. \textbf{12} was dissolved in 60 mL of THF, to which 2.0 mL \text{Et}_3\text{N} was added. In another Schlenk, (S)-BinolPCl \textbf{10} (2.1 gram, 5.8 mmol) was dissolved in 10 mL THF. The solution of \textbf{12} in THF was added dropwise to the solution of \textbf{10} at -78 °C. After 30 min the reaction mixture was allowed to warm up until r.t. was reached. The reaction continued at room temperature overnight. Crude $^{31}$P NMR revealed product formation combined with hydrolysis products. The suspension was filtered over basic alumina (activated in the oven at 130 °C) to remove the salts and the hydrolysis product. Next, the product was purified dissolving the compound in a minimum of THF and subsequent precipitation with pentane to yield the pure product (1.6 g, 1.8 mmol, 63% yield).

\textbf{H NMR} (300 MHz, DMSO-$d_6$) $\delta$ 10.64 (s, 2H), 8.59 (s, 1H), 8.33 – 7.92 (m, 10H), 7.91 (s, 2H), 7.80 – 7.14 (m, 21H), 7.04 (d, $J$ = 4.0 Hz, 2H).

\textbf{C NMR} (126 MHz, DMSO-$d_6$) $\delta$ 165.76, 151.35, 147.40, 146.80, 141.19, 135.45, 132.49, 132.26, 131.87, 131.62, 131.42, 130.81, 129.24, 127.44, 126.50, 125.88, 123.93, 122.58, 122.07, 116.92, 112.44.

\textbf{P NMR} (162 MHz, CD$_2$Cl$_2$) $\delta$ 145.44

Predicted mass: 976.21034 Measured mass: 976.21210

\textbf{Coordination and Anion Binding Studies}

\textbf{Binding studies of free ligands L1 – L3}

For the binding studies of the free ligands \textbf{L1}, \textbf{L2} and \textbf{L3}, two solutions were made which contained a 0.002M concentration of the respective ligands in a Schlenk under nitrogen. To one of the two solutions, several equivalents of tetrabutyl ammonium acetate was added. Next, 0.5 mL of the solution without tetrabutyl ammonium acetate was transferred to a screw cap NMR tube under inert conditions and subsequently equivalents of tetrabutyl ammonium acetate were added until no shift of the N-H species was observed anymore.
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 13 Binding constant determination of free L1 in CD2Cl2; fit based on the N-H proton

Figure 14 Binding constant determination of free L1 in CD2Cl2; fit based on the C-H proton
Chapter 4

Figure 15 Binding constant determination; fit based on the N-H proton of free L2

Figure 16 Binding constant determination; fit based on the C-H proton of free L2
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 17 Binding constant determination in CD₂Cl₂; fit based on the N-H proton of free L₃

\[ K_a = 14000.00 \pm 1060.77 \text{ M}^{-1} \] (7.58\%) \( r = 0.99749 \)

Figure 18 Binding constant determination in CD₂Cl₂; fit based on the C-H proton of free L₃

\[ K_a = 14000.00 \pm 1060.77 \text{ M}^{-1} \] (7.58\%) \( r = 0.99749 \)
Catalytic studies

A stock solution containing [Rh(acac)(CO)$_2$], ligand, DIPEA, internal standard (1,3,5-trimethoxybenzene), and solvent (DCM) was prepared in a flame-dried Schlenk. The substrates are added to GC vials equipped with Teflon stirring bars, after which 1 mL of stock solution is added. The vials are placed in an insert capable of holding 8 vials. This insert is placed in a stainless-steel autoclave. The autoclave was purged three times with 20 bar syngas and then pressurized with 20 bar syngas. The autoclave was heated to the appropriate temperature and the reaction mixture were stirred for the necessary amount of time. After the required time, the pressure was released and the samples were analyzed to obtain the regioselectivity and (conversion) by NMR and/or GC. The terminal alkenes and the internal alkenes that contained a methyl group next to the double bond could be analyzed via $^1$H NMR.

General procedure for preparation of NMR samples

For $^1$H NMR analysis 75 μL from each sample was taken and the volatiles were evaporated using a rotary evaporator (400 mbar, 40 °C). The samples were then diluted with approximately 0.7 mL CDCl$_3$ in an NMR tube. For substrates with a double bond at position 4 from the carboxylate, DIPEA or triethylamine (TEA) (~50 μL) was added in order to allow for analysis of the branched aldehyde as this signal is broadened due to intermolecular interactions.

Coordination studies

For all three ligands, L$_1$ - L$_3$, coordination studies were conducted with rhodium. A flame-dried Schlenk flask equipped with a Teflon stirring bar was charged with a ligand and with [Rh(acac)(CO)$_2$] (1:1 ratio). This is followed by addition of an appropriate amount of CD$_2$Cl$_2$ to obtain a desired concentration of the solution of a Rh-ligand complex. The solution was stirred at room temperature for approximately 10 minutes. Next, $^1$H and $^{31}$P NMR analysis at room temperature was performed in a screw cap NMR tube under inert conditions. Furthermore, $^1$H 2D-DOSY spectroscopy was conducted on the [Rh(Lx)(acac)] complexes as well as the free ligands L$_1$-L$_3$. As an internal standard 1,3,5 trimethoxybenzene was added. From the 2D-DOSY, the average hydrodynamic radii were calculated using the Stokes–Einstein equation, $D = k \cdot T \cdot (6 \pi \eta \cdot r_H)^{-1}$ ($k$ = the Boltzmann constant, $T$ = the absolute temperature, $\eta$ = the fluid viscosity, $r_H$ = the hydrodynamic radius)[67,68,77] Note: For the [RhL2] complexes, a precipitate formed after several hours and 2D DOSY shift was broad, therefore the precise hydrodynamic radius was more difficult to determine than with the other two complexes.
Figure 19 1H NMR spectra (400 mHz, CD2Cl2) of 1:1 mixture with [Rh(acac)(CO)2] and L1 (top), L2 (middle) and L3 (bottom) (0.002M), aromatic region
Figure 20 2D DOSY of [Rh(acac)(CO)\(\text{2}\)]: L1 (1:1 ratio) reaction mixture (0.002M) in CD\(\text{2}\)Cl\(\text{2}\). Average hydrodynamic radius determined at 5.5 Å, determined via Stokes–Einstein equation\[67\] 

Figure 21 2D DOSY of 1:1 mixture of L2 and [Rh(acac)(CO)\(\text{2}\)] (0.002 M) in CD\(\text{2}\)Cl\(\text{2}\). Average hydrodynamic radius determined at 26 Å, determined via Stokes–Einstein equation\[67\]. Average hydrodynamic radius is larger than the free ligand, L2, which shows the oligomeric species are formed.
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 22 2D DOSY of 1:1 mixture of [Rh(acac)(CO)] and L3 (0.002M) in CD2Cl2 Average hydrodynamic radius determined at 13.2 Å. determined via Stokes–Einstein equation[67]

**Binding studies of [Rh(acac)]/L1, [Rh(acac)]/L2 and [Rh(acac)]/L3**

In order to confirm the anion binding properties of the [Rh(acac)]/Lx complexes, tetrabutylammonium acetate was added. For each rhodium complex, two stock solutions were prepared. One contained the rhodium complex in dry and degassed CD2Cl2 and the other solution contained the rhodium complex and 2,1 equivalents of tetrabutyl ammonium acetate. Several screw cap NMR tubes were prepared that contained several equivalents of acetate with respect to the ligand by mixing the appropriate amounts of the two stock solutions under inert conditions. Next, the NMR tubes were vigorously shaken before NMR analysis. Due to the presence of broad peaks, an accurate binding constant could not be assessed.

**NMR complexation experiments under CO/H2 pressure**

Also, the [Rh(acac)]/Lx complexes were pressurized with H2:CO in a high-pressure NMR tube and studied with NMR. In CD2Cl2, both the 1H and the 31P-NMR spectra presented broad signals for all ligand complexes studied. Subsequently 2D DOSY spectroscopy was conducted for all three complexes, which displayed increased hydrodynamic radii compared to the [Rh(acac)]/Lx complexes, which indicates coordination polymers/oligomers are formed. Furthermore, also the complexes that contained two equivalents of acetate were pressurized and studied with NMR spectroscopy. These complexes displayed downfield NH shifts on 1H NMR compared
to the complexes in absence of acetate, which is characteristic of acetate binding. The syngas complexes in the presence of acetate were studied with 2D DOSY spectroscopy. Note: For the [RhL2] complexes, a precipitate formed after several hours and 2D DOSY shift was broad, therefore the precise hydrodynamic radius was more difficult to determine than with the other two complexes

L1

Figure 23\textsuperscript{1}H NMR spectrum (400 mHz, CD\textsubscript{2}Cl\textsubscript{2}) of top 1:1 mixture of L1 and [Rh(acac)CO\textsubscript{2}] (0.002M) 5 bar of syngas (CO/H\textsubscript{2}, 1:1) and bottom: 1:1 mixture of L1 and [Rh(acac)(CO)\textsubscript{2}] (0.002M) with 2 equivalents of tetrabutyl ammonium acetate 5 bar of syngas (CO/H\textsubscript{2}, 1:1)
Regioselective Hydroformylation of $\omega$-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 24 2D DOSY of [RhL1] complex (0.002 M solution), formed in situ under 5 bar of syngas (CO/H$_2$, 1:1) measured in CD$_2$Cl$_2$ Average hydrodynamic radius determined at 9.3 Å determined via Stokes–Einstein equation.$^{[67]}$

Figure 25 2D DOSY of 1:1 mixture of L1 and [Rh(acac)CO$_2$] (0.002M) under 5 bar syngas (H$_2$:CO, 1:1 ratio) in CD$_2$Cl$_2$ with 2 equivalents of tetrabutyl ammonium acetate. Average hydrodynamic radius determined at 8.7 Å determined via Stokes–Einstein equation.$^{[67]}$ Average hydrodynamic radius is larger than the free ligand, L1, indicating the formation of dimeric/oligomeric species.
Figure 26 top: $^1$H NMR spectrum (400 mHz, CD$_2$Cl$_2$) of 1:1 mixture of L2 and [Rh(acac)(CO)$_2$](0.002M) under syngas conditions. Bottom: 1:1 mixture of L2 and [Rh(acac)(CO)$_2$](0.002M) with 2 equivalents of tetrabutyl ammonium acetate under syngas conditions.
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3,-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure 27 2D DOSY of [Rh(L2)(CO)2H] complex (0.002 M solution), formed in situ under 5 bar of syngas (CO/H2, 1:1) measured in CD2Cl2. Average hydrodynamic radius determined at 26 Å, determined via Stokes–Einstein equation[67]. Average hydrodynamic radius is larger than the free ligand, L2, indicating the formation of oligomeric species. Note: due to the broadness of the peaks an accurate assessment of the average hydrodynamic radii could not be made.

Figure 28 2D DOSY of 1:1 mixture of L2 and [Rh(acac)(CO)2] with 2 equivalents of tetrabutyl ammonium acetate under syngas (CO/H2, 1:1) conditions. Average hydrodynamic radius determined at 42 Å, determined via Stokes–Einstein equation[67]. Average hydrodynamic radius is larger than the free ligand, L2, indicating the formation of oligomeric species. Note: due to the broadness of the peaks an accurate assessment of the average hydrodynamic radii could not be made.
Figure 29 top: $^1$H NMR spectrum (400 mHz, CD$_2$Cl$_2$) of 1:1 mixture of L3 and [Rh(acac)(CO)$_2$](0,002M) under syngas conditions bottom: 1:1 mixture of L3 and [Rh(acac)(CO)$_2$] (0,002M) with 2 equivalents of tetrabutyl ammonium acetate under syngas conditions.
Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

Figure S 1 2D DOSY of Rh\textbf{L3} complex (0.002 M solution), formed in situ under 5 bar of syngas (CO/H\textsubscript{2}, 1:1) measured in CD\textsubscript{2}Cl\textsubscript{2}. Average hydrodynamic radius determined to be 12.9 Å. determined via Stokes–Einstein equation\cite{67} Average hydrodynamic radius is larger than the free ligand, \textbf{L3}, indicating the formation of dimeric/oligomeric species.

Figure 30 2D DOSY of Rh\textbf{L3} complex (0.002 M solution), formed in situ under 5 bar of syngas (CO/H\textsubscript{2}, 1:1) with 2 equivalents of tetrabutylammonium acetate measured in CD\textsubscript{2}Cl\textsubscript{2}. Average hydrodynamic radius determined at 10.8 Å. determined via Stokes–Einstein equation\cite{67} Average hydrodynamic radius is larger, \textbf{L3}, which shows oligomeric/dimeric species are formed.

129
DFT calculations

All DFT calculations were performed with the Amsterdam Density Functional (ADF) program\cite{62,63,65}. The BLYP-D3(BJ) density functional was used together with a small core DZP basis set. Relativistic effects were accounted for by running calculations with zeroth-order regular approximation (ZORA)\cite{64}. Complexation enthalpies were calculated from the geometry optimized \([\text{Rh}(\text{Lx})(\text{H})(\text{CO})_2]\) complexes minus the energies of the free ligands and the \([\text{Rh}(\text{H})(\text{CO})_2]\) and these were compared to the complexation enthalpies of the DIMPhos phosphine and phosphite ligands. For all three ligands \(\text{L1-L3}\) the binding enthalpy was lower than the DIMPhos ligands.

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Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

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Regioselective Hydroformylation of ω-Unsaturated Acids via Supramolecular Control Using a 1,3-Benzenedicarboxamide Receptor Functionalized Bidentate Ligand

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