2012

Studies of a dirhodium tetraphosphine catalyst for hydroformylation and aldehyde-water shift catalysis

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STUDIES OF A DIRHODIUM TETRAPHOSPHINE CATALYST FOR HYDROFORMYLATION AND ALDEHYDE-WATER SHIFT CATALYSIS

A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
In partial fulfillment of the
Requirements for the degree of
Doctor of Philosophy

In

The Department of Chemistry

by

Aaron Rider Barnum
B.S. Loyola University New Orleans, 2007
December 2012

ACKNOWLEDGEMENTS

I would like to thank my family, for without their encouragements and support I would not be where I am today. To my parents, Otis and Cindy Barnum, thank you for everything throughout the years. To my grandmother Teruko, you are responsible for two things I hold very dear to my heart: inspiring me to become the scientist and chemist I am today and also for keeping me in touch with my Japanese heritage. You have had a more profound impact on my life than you will ever know, and I will never forget that. To my wife Pearce, thank you for always being by my side, and there is no one else with whom I would rather share the insanity that is our lives. I love you more than anything.

To my advisor, George Stanley, it has been a privilege working with you over these years of research. Hopefully my research and my contributions towards the chemistry demonstration outreach program will continue to help things along in the years to come. To the Stanley Research group, it was a pleasure working with you all. To Marc Peterson and Catherine Alexander, thank you for showing me synthesis techniques and hydroformylation/autoclave techniques when I first began this research. To Darina Polakova and Ciera Duronslet, you two have been great friends over these years of research, and thank you for all the conversations bouncing research ideas back-and-forth. To my undergraduate assistant Kathryn Chabaud, you have become a very skilled chemist over the years, and I wish you the best of luck.

To my committee members: Dr. Julia Chan, Dr. Andrew Maverick, Dr. William Crowe, and Dr. Charles Lindau, thank you for your advice and guidance.

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ABSTRACT

Research into the dirhodium tetraphosphine catalyst precursor [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ shows it is capable of forming a highly active and regioselective hydroformylation catalyst *in situ* when using an acetone or acetone/water solvent. Hydroformylation experiments (using 1-hexene), FT-IR studies, and acid-base studies were performed to better understand the various complexes of the dirhodium catalyst cycle. These studies lead to the newly proposed catalyst mechanism when performed in an acetone/water solution, using the monocationic [*rac*-$Rh_2(\mu\text{-}CO)_2(CO)(H)$(et,ph-P4)]$^+$ as the proposed active catalyst complex for hydroformylation. For the conversion of 1-hexene to heptanal, it is capable of performing an initial rate of 30 turnovers per min, 33:1 linear-to-branched aldehyde regioselectivity, and less than 0.5% isomerization/hydrogenation.

A remarkable new catalytic reaction, termed Aldehyde-Water Shift Catalysis, can occur under the proper conditions only when water is added to the acetone solvent. Under mild hydrogen deficient conditions the reaction of aldehyde and water can produce carboxylic acid and H_2. The net stoichiometry of hydroformylation combined with this unusual aldehyde-water shift catalysis is that of hydrocarboxylation, an extremely difficult reaction to perform selectively or under mild conditions. DFT calculations and experimental studies indicate [$Rh_2(\mu\text{-}CO)_2(CO)_2$(et,ph-P4)]$^{2+}$ as the likely active catalyst for this aldehyde-water shift catalysis. We believe bimetallic cooperativity plays an important role in this catalysis as it does in hydroformylation. Various designs of autoclave reactors were built in order to maintain and monitor the new reaction conditions, including pressure, temperature, and gas flow rate. The best tandem catalysis results yielded a rate of 50 turnovers per hour with a regioselectivity of 60:1 linear-to-branched carboxylic acid, operating at 50 psig (3.4 atm) and 90°C.

CHAPTER 1: BACKGROUND AND INTRODUCTION TO HYDROFORMYLATION

Hydroformylation, or oxo synthesis, is the largest homogeneous industrial process for converting alkenes, CO, and H_2 into aldehydes and associated products which total over fifteen billion pounds produced every year. The generated aldehydes are usually converted to other useful chemicals via processes like hydrogenation (forming the corresponding alcohols) and oxidation (forming the corresponding carboxylic acids). Commercial products using these chemicals as starting materials include polyvinyl chloride (PVC) plastics, detergents, surfactants, solvents, lubricants, and many others.

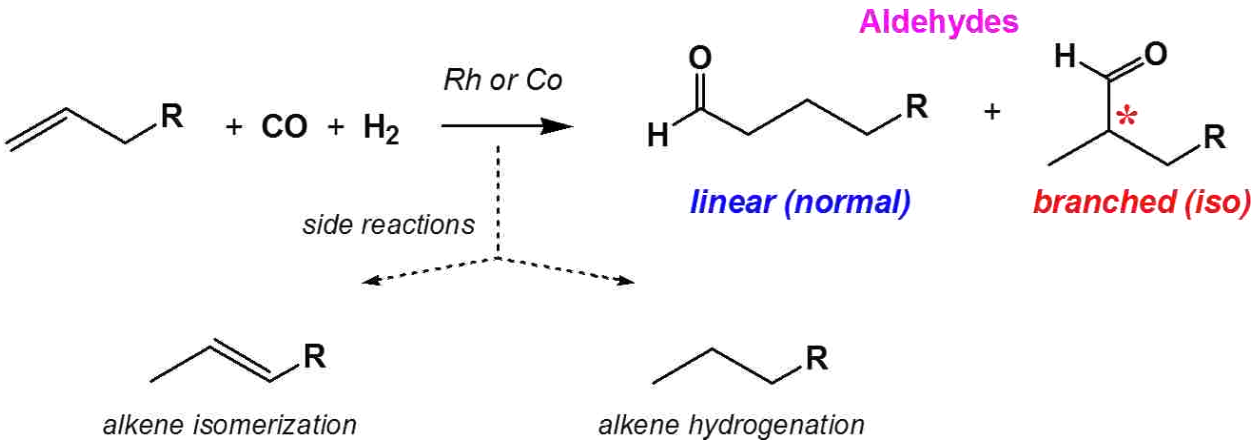

Figure 1.1. Hydroformylation process and products diagram.

The catalysts often used for hydroformylation reactions are usually cobalt or rhodium hydrido carbonyl complexes, often modified with phosphine ligands. These catalysts are used to react terminal alkenes with a mixture of CO and H_2 gases (also known as synthesis gas or "syn-gas") to produce the corresponding aldehyde, as shown in the diagram above. The regioselectivity of the catalyst is determined by the amounts of linear aldehyde (the desired product) produced versus the amounts of branched aldehyde (the often undesired byproduct).

The catalyst used may also cause undesired side reactions, usually the isomerization of the terminal alkene and hydrogenation of the alkene.

Whether hydroformylation catalysts are designed for academic or industrial research, they all use similar terminology to compare results and properties with one another. The turnover number (TON) refers to the number of moles of alkene converted to aldehyde by the catalyst. The turnover frequency (TOF) is the rate of the conversion as calculated by the number of turnovers divided by a unit of time (e.g. turnovers per minute). The selectivity of a hydroformylation catalyst can be indicated by its linear aldehyde to branched aldehyde ratio (L:B ratio). In regards to the possible side reactions, the alkene isomerization percentage (I%) and the hydrogenation percentage (H%) are often shown to indicate the amount of starting terminal alkene consumed by the corresponding side reaction. An ideal catalyst will be very active (high TON and TOF), very selective to the desired product (high L:B ratio and low percentage of side reactions), and have a long lifetime.

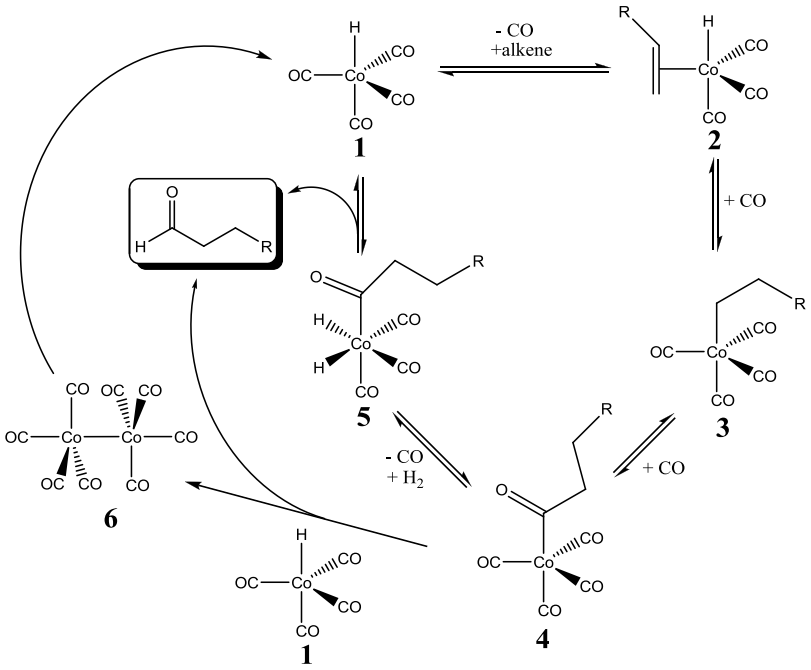

Figure 1.2. The accepted general hydroformylation mechanism proposed by Heck and Breslow.[1]

The process was discovered by Otto Roelen in 1938, and it is generally accepted mechanism was proposed by Heck and Breslow in 1960 and 1961 (Figure 1.2).[1] Using metallic cobalt which dissolved under pressurized H_2/CO gas, Roelen generated the active catalyst, $HCo(CO)_4$ (**1**). The catalytic cycle begins by substituting a carbonyl for a bonded alkene (**2**). A migratory insertion of the alkene and hydride then forms an alkyl ligand, while the newly opened coordination site is filled by an available carbonyl, keeping the complex saturated (**3**). A second migratory insertion combines the alkyl ligand with a carbonyl to yield an acyl ligand (**4**). The reaction then branches off into two different paths: the monometallic (favored) and bimetallic pathway (disfavored). The favored monometallic pathway involves an oxidative addition of H_2 and addition of CO, resulting in a saturated Co(III) complex with an octahedral geometry (**5**). The acyl group readily undergoes a reductive elimination, generating the aldehyde product, and returns to the original active catalyst.

The disfavored bimetallic pathway proposed that **4** will react with the original active catalyst (**1**) via an intermolecular hydride transfer to release the aldehyde product and form the metal-metal bonded $Co_2(CO)_8$ (**6**). Upon the breaking of the metal-metal bond, via reaction with H_2, the original catalyst is generated to begin the cycle again. This method, named the "High Pressure Unmodified Cobalt process", involved using very high pressures (200-300 bar / 2900-4350 psi) at temperatures between 150-300°C. This is in a large part due to the thermal instability of the $HCo(CO)_4$ catalyst complex, which precipitates out metallic cobalt if the CO partial pressure is not high enough.[2]

Since then, the only modification to this process has been the incorporation of phosphine ligands to the hydridocobalt carbonyl catalyst. Research conducted at Shell by Slaugh and Mullineaux showed that adding a trialkylphosphine ligand to the aforementioned catalyst, now

the $HCo(CO)_3(PR_3)$ complex, caused a dramatic change in the rate and regioselectivity of the catalyst.[3] This is due to the difference in the electron donating/withdrawing effects of each ligand. Replacing one of the complex's carbonyl ligands (electron withdrawing) with the trialkylphosphine ligand (electron donating) causes the metal center to become more electron rich, thus strengthening the remaining Co–CO bonds. This stronger binding of the carbonyl ligands means that lower CO partial pressures are required to stabilize the catalyst species. However, the stronger CO binding also reduces the activity of the catalyst by hindering the necessary dissociation of CO required to open a coordination site for the alkene or H_2. The phosphine-modified catalyst, $HCo(CO)_3(PR_3)$, could perform hydroformylation at only 50-100 bar pressures instead of the previous 200-300 bar pressures, as well as showing higher thermal stability.

The next major step for hydroformylation research was the usage of rhodium-phosphine catalysts. In 1965, Osborn, Young, and Wilkinson discovered that Rh(I)-PPh_3 complexes were active hydroformylation catalysts and highly regioselective, even at ambient conditions.[4] The

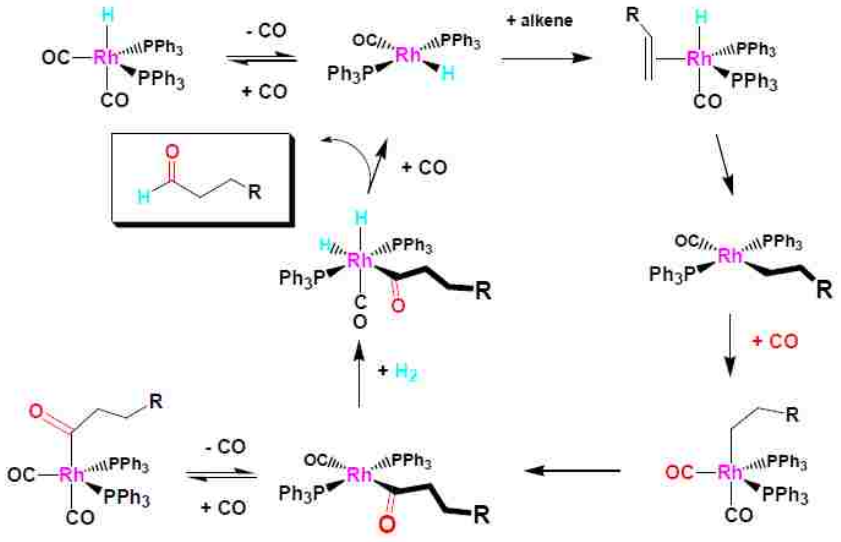

Figure 1.3. Rh/PPh_3 catalyst hydroformylation mechanism.

complex was then modified to $HRh(CO)(PPh_3)_3$ due to the halide ligands inhibiting the hydroformylation reaction, and the currently accepted mechanism is shown above (Figure 1.3).

This process was further improved when Pruett (at Union Carbide) and Booth (at Union Oil) found that adding an excess of phosphine ligand (0.4 M minimum concentration for a 1 mM Rh catalyst system) to the $HRh(CO)(PPh_3)_3$ complex created an active, selective, and stable catalyst system at 80-150 psig and 90-125°C.[5] Due to the labile triphenylphosphine ligand, the excess allows for the stabilization of the rhodium complex which could otherwise result in degradation via the formation of a $14e^-$ complex capable of Rh-induced P-Ph bond cleavage to generate inactive phosphide bridged rhodium dimers and clusters. Dissociation of the PPh_3 from the rhodium complex can initially generate a more active catalyst, however the downside is decreased regioselectivity and increased phosphine fragmentation reactions.

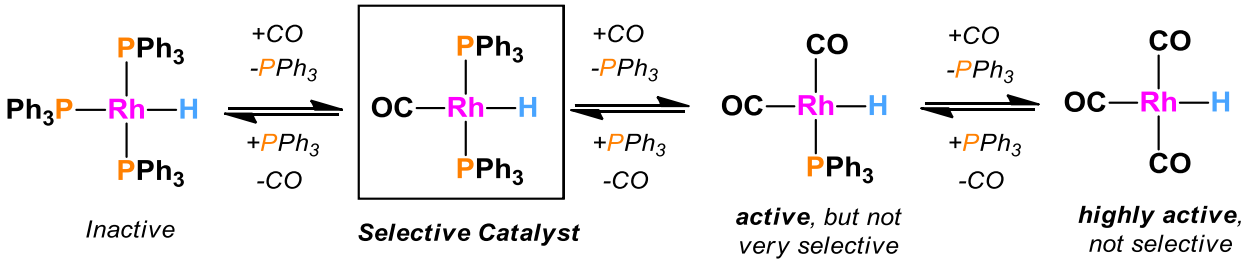

Figure 1.4. CO vs. PPh_3 concentration effects on the Rh/PPh_3 catalyst system.

The excess triphenylphosphine shifts the equilibrium reaction above towards a more selective catalyst, but without the presence of a carbonyl ligand, the catalyst is inactive. Increasing the partial pressure of the CO gas will increase the activity of the catalyst at the expense of selectivity. When this catalyst system is used in industry for hydroformylation, too high of a H_2 partial pressure (or too low of a CO partial pressure) in the syn-gas will increase

alkene hydrogenation and isomerization side reactions. It is truly a balancing act when performing catalysis to achieve the optimal reaction conditions.

Chelating ligands (especially phosphines) are heavily used for research into hydroformylation catalysts. Since most metal-ligand bonds are weak compared to carbon-carbon bonds, they can be more easily broken causing ligand dissociation. The chelation effect is when one ligand is able to coordinate/bind to two or more metal centers. With chelating ligands, if one of the binding sites becomes dissociated, the remainder of the ligand (still attached to the metal center) will keep the site near the metal center to promote re-coordination. Chelating phosphines have interesting effects on hydroformylation reactions. Those with large, bulky phenyl rings provide good steric effects and a large bite angle, resulting in a positive effect on catalyst stability and activity. However, most hydroformylation catalyst systems still require an excess of the chelating phosphine ligand (or another phosphine like triphenylphosphine) to generate an active and selective species. In the figure below (Figure 1.5), three examples of chelating phosphine ligands used for research into hydroformylation catalysts are given.

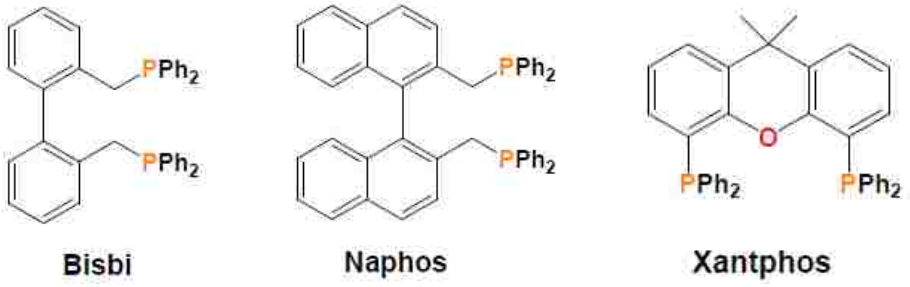

Figure 1.5 Commonly used chelating phosphine ligands.

Bimetallic complexes being used for catalysis is far less common than monometallic complexes, and during the early history of the hydroformylation reaction, the only mention of such a system was suggested in the mechanism derived by Heck and Breslow, as mentioned earlier.[1a] After the aldehyde released, the $HCo(CO)_4$ complex can couple together to form

$Co_2(CO)_8$. However, it is believed that this dicobalt complex is not capable of performing the hydroformylation reaction alone, thus upon breaking the metal-metal bond when reaction with H_2, the original $HCo(CO)_4$ catalyst complex is reformed to complete the cycle. Interest in bimetallic catalyst systems has grown over the years, due to the potential for multielectron transfers and multi-center metal-to-ligand bonds to stabilize or activate catalysts. Even the prospect of using mixed metal systems gives rise to numerous other factors that would affect the catalyzed reaction.

Hydroformylation catalysts and methods have improved over the last few decades in terms of activity, rate, and selectivity. Phosphine ligands currently play a major role in current cobalt and rhodium catalysts. Nitrogen mono or bidentate ligands can also be used, but hydroformylation catalysts much more often use phosphines because nitrogen ligands dissociate too easily from rhodium hydride carbonyls.

One of the best examples of a catalyst complex utilizing bimetallic cooperativity is shown by the research of Stanley and coworkers.[6] They designed the novel binucleating tetraphosphine ligand $(Et_2PCH_2CH_2)(Ph)(PCH_2P)(Ph)(CH_2CH_2PEt_2)$, (abbreviated as "et,ph-P4"), to strongly chelate and bridge to two metal centers, while having a single, conformationally flexible methylene bridging group, to study bimetallic cooperativity in hydroformylation reactions. The two internal phosphines are each chiral centers, leading to the two diastereomers of the et,ph-P4 ligand as shown below (Figure 1.5). This tetraphosphine ligand was used to form the dirhodium catalyst precursor used for both their research and the research described in this dissertation: [*rac*-Rh_2(nbd)(et,ph-P4)]$(BF_4)_2$ (nbd = norbornadiene).

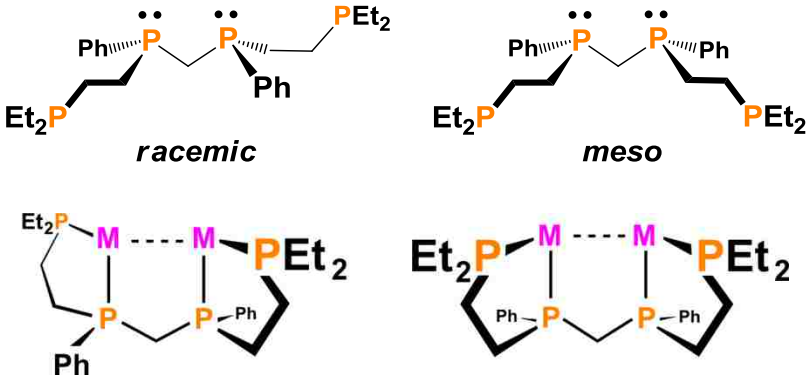

Figure 1.6. *racemic* and *meso* diastereomers of the et,ph-P4 ligand

The active form of this catalyst is generated *in situ* during reaction, and it is capable of highly active and regioselective hydroformylation of terminal alkenes under mild reaction conditions to produce the corresponding aldehydes. The *racemic* form of this catalyst, as shown in the figure below, has been shown to be far more active than the *meso* form.

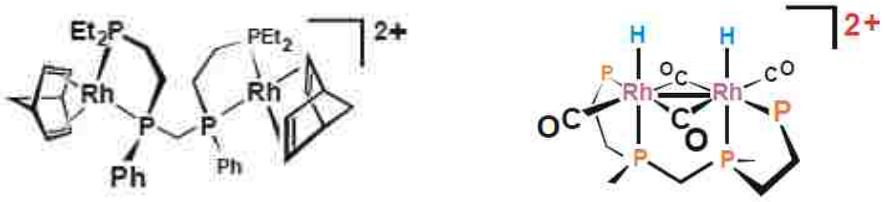

Figure 1.7. The *rac*-Rh_2(P4) catalyst precursor and the proposed active catalyst form, [*rac*-$Rh_2H_2(\mu\text{-}CO)_2(CO)$(et,ph-P4)]$^{2+}$, (Et and Ph groups omitted for clarity).

Table 1.1. Comparison between [*rac*-Rh_2(P4)]$^{2+}$ catalyst and selected Rh monometallic catalysts.

Catalyst (1 mM)	Initial TOF (min^{-1})	Aldehyde L:B ratio	Isomerization %
[*rac*-Rh_2(P4)]$^{2+}$	20	25 : 1	2.5 %
[*rac*-Rh_2(P4)]$^{2+}$ (in 30% H_2O / acetone soln)	30	33 : 1	< 0.5 %
Rh / PPh_3 (1:400)	13	9 : 1	< 0.5 %
Rh / Bisbi (1:5)	25	70 : 1	< 0.5 %
Rh / Naphos (1:5)	27	120 : 1	1.5 %
Rh / Xantphos (1:5)	13	80 : 1	5.0 %

Table 1.1 shows the comparison in terms of rate and regioselectivity of the *rac*-Rh_2(P4) catalyst vs. some of the best monometallic rhodium catalysts used for hydroformylation.

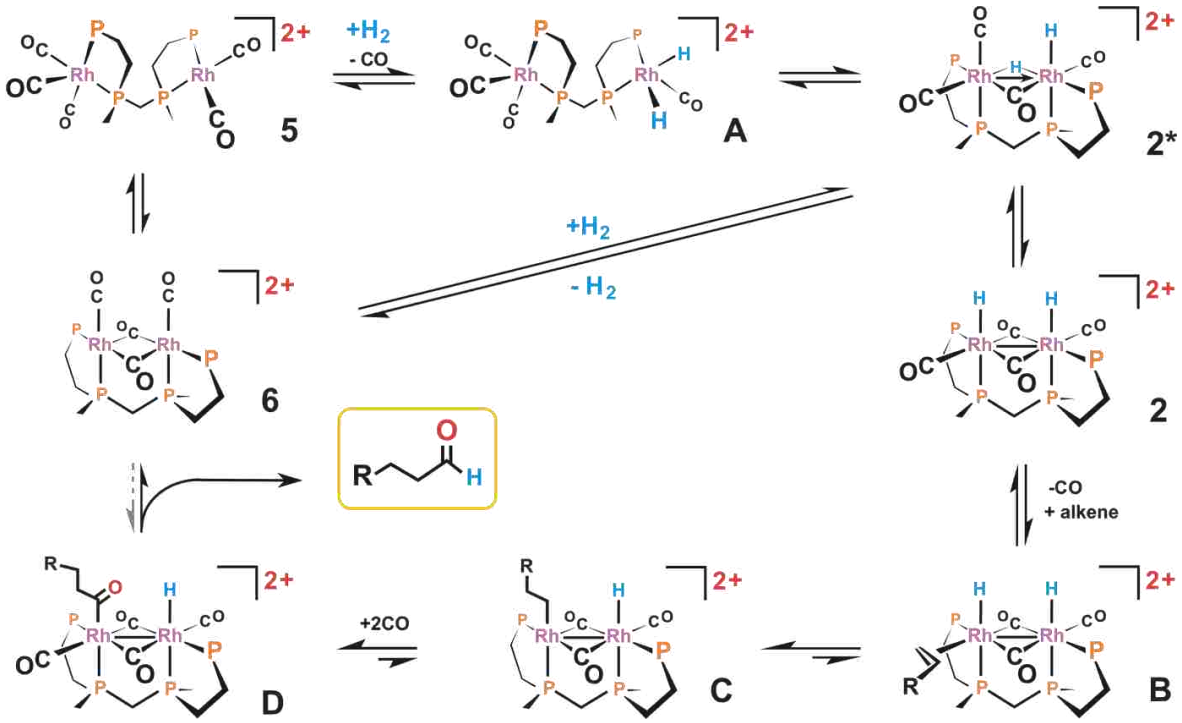

Figure 1.8. Proposed mechanism for hydroformylation using a racemic dirhodium tetraphosphine catalyst. The tetraphosphine ligand is referred to as (et,ph-P4). (Note: complexes **A**,**B**,**C**, and **D** have not been observed spectroscopically)[7]

The dirhodium tetraphosphine catalyst (**5**) was synthesized via methods published by Stanley et. al.[6] The oxidative addition of hydrogen gas followed by the dissociation of a carbonyl ligand begins the catalytic cycle (**A**). To increase stability this complex undergoes an intramolecular hydride transfer from **A** to **2***. This transfer is accomplished by forming two bridging ligands from a carbonyl ligand from the Rh(I) center and a hydride ligand from the Rh(III) center (**2***). The bimetallic complex further stabilizes itself by forming a metal-metal bond (dative or covalent), facilitating the intramolecular hydride transfer, which effectively balances the oxidation states of the two d^7 rhodium cations (each at +2). This bimetallic

complex, $[Rh_2(H)_2(\mu\text{-}CO)_2(et,ph\text{-}P4)]^{2+}$ (**2**), is believed to be the key catalyst species that reacts with the alkene. Ligand substitution of a carbonyl for the alkene (**B**) is followed by a migratory insertion of the equatorial-alkene to the axial-hydride (made possibly due to the previous intermolecular hydride transfer), forming an axial-alkyl ligand (**C**). The complex rapidly reacts with two equivalents of CO to fill the coordination site opened up by the previous migratory insertion and to cause another migratory insertion with the alkyl ligand to form an acyl ligand. (**D**) Finally the aldehyde product is generated by the intramolecular reductive elimination of the acyl and hydride ligands, reducing each metal center, now d^8, to an oxidation state of +1 (**6**). The bimetallic complex then has two possible paths to enter back into the catalytic cycle. The first pathway occurs when reacted with CO, that breaks the CO bridged complex back to the open-mode complex (**5**). The second pathway occurs due an oxidative addition with molecular hydrogen to one metal center, formation of a Rh–Rh bond (dative or covalent), a bridging hydride, and shifting one of the two bridging carbonyls to the other metal center (**2***).

The *racemic*-dirhodium tetraphosphine catalyst (complexes **2 or B**) is in a dicationic +2 charged state, which is an unusual oxidation state for rhodium, but this compensates for the alkylated, strongly donating phosphine ligand that would normally deactivate the Rh center for hydroformylation. The fact that we form a highly active, selective catalyst provides evidence for the bimetallic cooperativity mechanism proposed above. The strong σ-donation of the tetraphosphine ligand increases the electron density of the rhodium metal centers, thus increasing the carbonyl π-backbonding (M-CO bond strength). This σ-donation is partially counteracted by the dicationic charge on the complex, which lowers electron density and M-CO bond strength, resulting in a complex with carbonyl ligands labile enough to readily dissociate. The catalyst was found to be highly selective towards linear aldehydes in experimental hydroformylation

reactions (33:1 linear:branched ratio using 1-hexene in acetone/water).[8] The high regioselectivity is due to the Rh–Rh bond and bridging carbonyls which result in a highly defined square-planar-like bridging site that does not distort when the alkene coordinates to make a 5-coordinate complex (similar to a trigonal bipyramidal geometry). Similar monometallic rhodium diphosphine catalysts were essentially inactive for hydroformylation, indicating that bimetallic cooperativity plays a critical role in the catalysis.

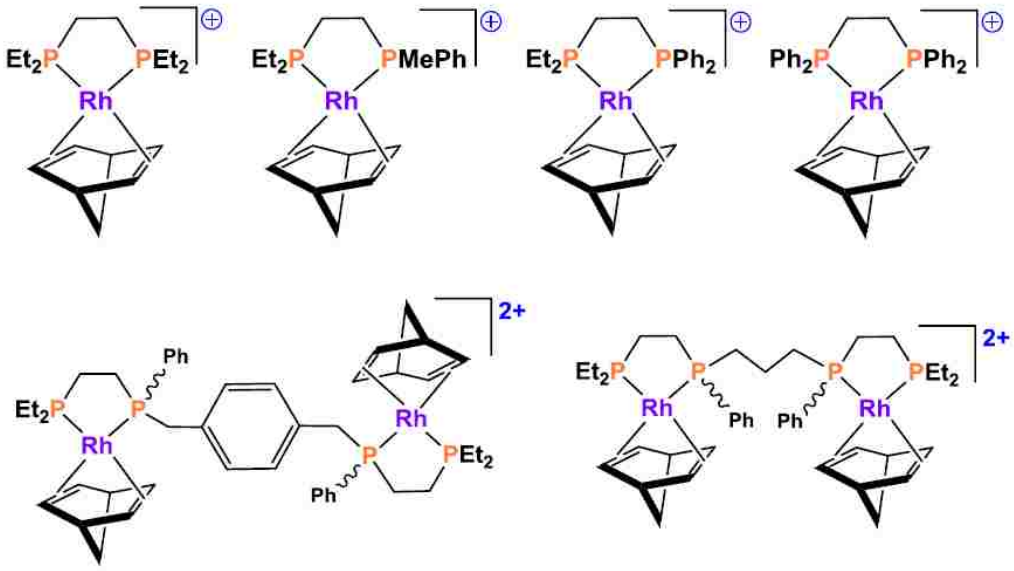

Figure 1.9. Monometallic and other bridging analogs of Stanley's [rac-Rh_2(P4)]$^{2+}$ catalyst.

Also, FT-IR *in situ* spectroscopic studies have clearly indicated the importance of dicationic bimetallic complexes in the hydroformylation, with the activity of the catalyst directly related to the presence and intensity of the bridging carbonyl bands around 1835 cm^{-1} and terminal CO bands between 2000 – 2090 cm^{-1} in the IR spectrum.[9]

The *meso*-$Rh_2(nbd)_2$(et,ph-P4) catalyst, while still superior than similar monometallic rhodium phosphine catalysts, was found in past experimental hydroformylation runs to be considerably less active and less selective than its racemic counterpart. The lower selectivity, in this case, leads to an increase in alkene isomerization and hydrogenation side reactions. An

explanation for this difference in catalytic performance was derived from SYBYL molecular modeling studies of both racemic and meso enantiomers.

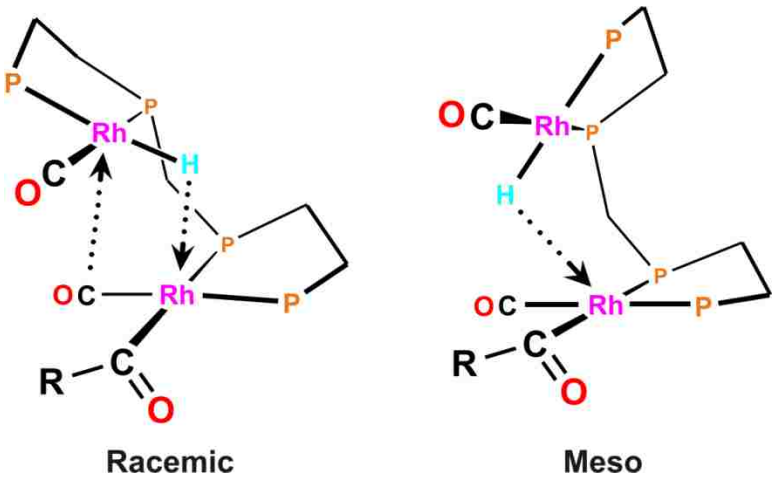

Figure 1.10. *Racemic* vs. *Meso* closed-mode catalyst structures as derived using SYBYL molecular modeling program.

When beginning the intramolecular hydride transfer process, (**8**) to (**9**), the racemic form can rotate around the CH_2 bridge to make both the carbonyl and hydride bridging ligands. This bridging helps facilitate the formation of a metal-metal bond and the hydride transfer to balance out the oxidation states on the two rhodium cations. However, the meso form has more difficulty in rotating around the CH_2 bridge and can only form a single hydride or carbonyl bridge. While the metal-metal bond might still form, it is probable that the lack of the two bridging ligands hinders the intramolecular hydride transfer, thereby reducing the performance of the catalyst. This hindrance results in a higher energy reaction pathway than its racemic enantiomer.[6]

The Stanley group's dirhodium tetraphosphine catalyst is still not fully understood, despite the advances made so far. Research is still being conducted to understand its improved activity and regioselectivity when using a 30% water-acetone solution, as well as into new tetraphosphine ligand designs, synthesis routes, diastereomer separation techniques, and fragmentation studies. It is currently believed that the mechanism for the hydroformylation

catalysis using a water/acetone solvent, is very different than when being run using a pure acetone solvent. FT-IR *in situ* studies show a difference in the rate and frequency of the carbonyl stretching bands in the IR spectra when using a water/acetone versus just an acetone solvent. The chemistry occurring behind the scenes is clearly more complicated than originally believed. While the current design results in an amazing hydroformylation catalyst, further work is still needed before it is ready for possible commercial applications.

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CHAPTER 2: BIPHASIC HYDROFORMYLATION – THE EFFECTS OF WATER ON A DIRHODIUM CATALYST

2.1 Biphasic Hydroformylation

Novella Bridges and David Aubry began the research into using a biphasic system for the hydroformylation of olefins using the dirhodium tetraphosphine catalyst. It was believed that using a polar solvent system would allow for the starting olefin (1-hexene) and the product aldehyde (heptanal) to separate out into an organic layer, while the catalyst remained in the polar aqueous layer. Being able to separate out the product is an important issue in industrial homogeneous catalytic reactions. However this concept led to several unexpected results.

Table 2.1 Addition of water to acetone solvent for hydroformylation reactions of 1-hexene (90°C, 90 psig H_2:CO).[1]

% H_2O	TOF (min^{-1})	Aldehyde L:B	Isomerization %	Hydrogenation %
0	20	25	2.5	3.4
10	23	30	1.5	0.2
20	25	26	< 0.5	0.2
30	30	33	< 0.5	0.1
40	24	32	< 0.5	0.1
50	18	33	2.3	0.2

They found that the addition of 30% water (by volume) to the acetone catalyst solution improved the activity (an increase from 20 to 30 turnovers/min TOF) and regioselectivity (an increase in L:B ratio from 25:1 to 33:1) of the catalyst, while also showing a reduced amount of isomerization and hydrogenation side reactions.[2] Various other water-acetone solution percentages were also tested. The catalytic activity and regioselectivity both increased as the water content increased up to 30%, but they both began to decrease as the water content rose

above that value. It is believed that while the stability of the active catalyst increases with higher water content, simultaneously the solubility of the olefin in the acetone/water layer decreases. The best balance between the two competing factors was found to be at the aforementioned ratio.

While the olefin reagent and aldehyde product did separate out into a separate organic layer as hoped, it turned out that the catalyst was actually more soluble in the organic layer than the new aqueous acetone/water layer. This can be easily seen by the intensity of color in the layers due to the dirhodium catalyst's solubility. The image below (Figure 2.1) clearly shows the biphasic catalyst solution extracted from the autoclave during reaction. The organic product layer on top is significantly darker, indicating a larger quantity of catalyst in solution.

Figure 2.1. A vial of the hydroformylation reaction solution when using an acetone/water solvent, causing the biphasic system.

When performing hydroformylation in pure acetone, the catalyst system suffered severe fragmentation problems. As mentioned previously, phosphine ligand fragmentation issues were a common occurrence when using the monometallic rhodium complexes. It is believed that bimetallic rhodium tetraphosphine complexes fragmented, however, in a different way, as the proposed mechanism shows below.

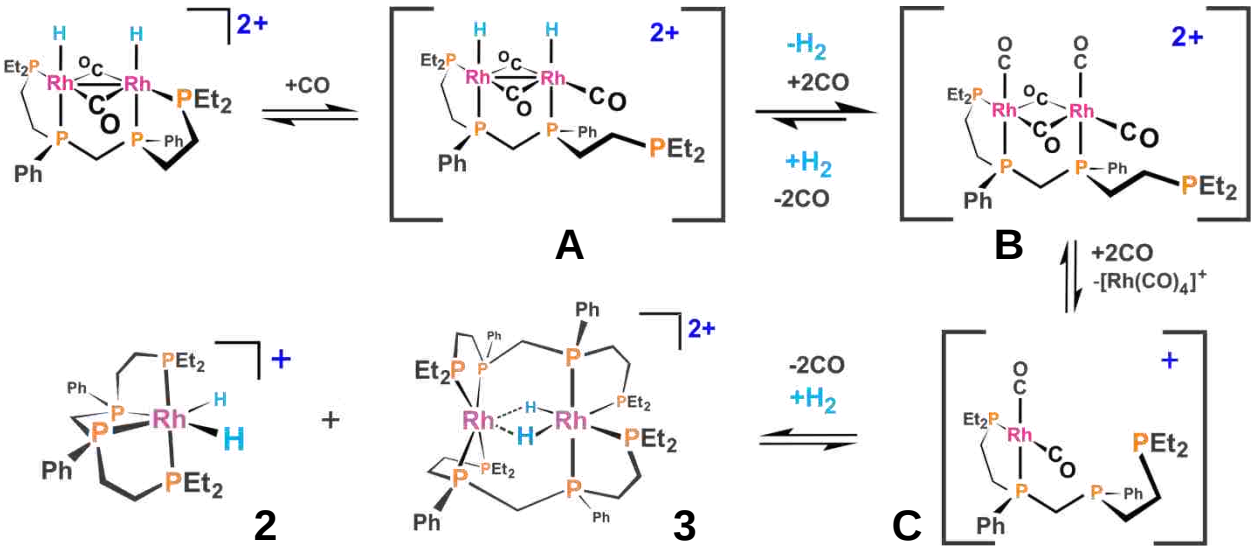

Figure 2.2. The fragmentation mechanism for the bimetallic rhodium tetraphosphine catalyst in an acetone solution.

The mechanism begins with the proposed active catalyst of the hydroformylation reaction in acetone solution. Fragmentation begins when one arm of the tetraphosphine ligand dissociates from a rhodium center and is replaced by a CO ligand, forming complex **A**. This complex is now more electron deficient and will favor reductive elimination of the two hydrides, producing H_2. The hydrides are replaced by two carbonyl ligands, forming complex **B**. At this point, the single phosphine-coordinated rhodium center is not bound strongly enough, allowing it to dissociate. Once complex **C** is formed, the catalyst finishes its degradation/fragmentation by either forming the monometallic tetraphosphine complex (**2**) or dimerize to form the double-P4 ligand dirhodium complex (**3**). The exact structure of structure **3** is not certain, but our best guess based on many high pressure NMR studies is shown.

2.2 Acidity of Catalyst Solution

Given that the new reaction solution uses a 30% water-acetone composition and because the dirhodium tetraphosphine catalyst is dicationic, it was decided that experimentation with the effects of acids and bases should be run. While it was originally believed that the catalyst

solution could be acidic, it was only recently discovered to be acting more like a strong acid, dissociating one proton per equivalent of catalyst added to the water-acetone reaction solution. These readings were collected reaction solutions collected via sample ejection from the autoclave and also directly from the vessel post-reaction during the disassembly of the autoclave.

Table 2.2 Acidity/pH of water-acetone dirhodium hydroformylation reaction solutions.

Concentration	pH
1 mM	3.1
10 mM	2.2

Much of the recent acid-base experiments on the dirhodium tetraphosphine catalyst used for hydroformylation reactions in a 30% water/acetone solution was a collaboration between myself and Darina Polakova.[3] Standard hydroformylation reactions of 1-hexene were performed in the Parr modified autoclaves (Mark II design) with the additions of tetrafluoroboric acid (HBF_4) and triethylamine (NEt_3). These experiments were performed in a similar manner to former researcher Spencer Train's work testing the acid and base effects of the dirhodium tetraphosphine catalyst in an acetone solution.[4] The conditions used for the following acid and base effects on hydroformylation reactions of 1-hexene are as follows: 1 mM catalyst, 1 M 1-hexene, 30% water-acetone solution (with additive), 90°C, 90 psig H_2:CO gas, 2 hrs reaction time. The results obtained were compared to those previously collected in order to understand the differences between acid-base effects on a 30% water/acetone solvent versus a pure acetone solvent.

Table 2.3 The Acid-Base Catalyst Effects on the Hydroformylation of 1-hexene in an Acetone solution[4] and in a 30% Water-Acetone solution.[3]

Additive	Solvent	Initial Rate (min^{-1})	Aldehyde L:B	Isomerization (%)
None	Acetone	10.6	28 : 1	8%
2-4 eq HBF_4		–	21 : 1	12%
2 eq NEt_3		3.6	> 30 : 1	< 1.5
None	30% water-acetone	24	29 : 1	2.7%
5 eq HBF_4		12.5	23 : 1	8.8%
2 eq NEt_3		4.2	15 : 1	1.3%

In Table 2.3 shown above, the acid-base addition experiments using a catalyst solution in acetone (performed by Spencer Train) are shown in the top section, and those experiments using a catalyst in a 30% acetone-water solution (performed by Darina Polakova) are shown in the bottom section. The addition of HBF_4 acid caused a significant decrease in performance of the catalyst and thus the hydroformylation reaction for both the acetone and water-acetone catalyst solutions; the rate of reaction was lowered, the regioselectivity decreased, and the isomerization byproducts increased. The results of the addition of triethyl amine base had even more detrimental effect on the rate of the catalyst. While there seems to be some difference as to its effect on the regioselectivity results (an increase is seen for the acetone experiments while a decrease is seen in the water-acetone experiments), the isomerization byproducts significantly decreased in both cases. Regardless of the few positive effects, the overall performance of the catalyst seems to be affected negatively when either acid or base is added to the reaction mixture.

2.3 FT-IR Studies

Fourier transform infrared spectroscopy (FT-IR) is an very useful tool when studying the structure of metal-carbonyl catalysts, such as our dirhodium tetraphosphine catalyst (when

activated using H_2:CO gas). Depending on the wavenumbers of the metal-carbonyl (M-CO) stretching frequencies (generally found between 1700 cm^{-1} and 2100 cm^{-1})[5] in a given spectrum, information can be obtained regarding the catalyst's structure, such as the presence of terminal and/or bridging carbonyl ligands, as well as indicators of the electron density of the metal centers (via the attached carbonyls). Many researchers have used FT-IR techniques to study the structures of metal-carbonyl catalysts, including *in-situ* cobalt-carbonyls, phosphine modified cobalt-carbonyls,[6] rhodium-carbonyls, phosphine modified rhodium-carbonyls,[7] and a myriad of other phosphorus containing ligands attached to cobalt/rhodium metal centers.[8] FT-IR has also been used to study bimetallic cooperativity on dirhodium complexes with bridging thiolate ligands.[9]

In the case of our dirhodium tetraphosphine catalyst, FT-IR spectroscopy was used to gain insight into the mechanism of the hydroformylation reaction when performed in a 30% water-acetone solution. Please refer to Chapter 3 – Generations of Autoclave Reactor Designs for a more thorough explanation of the high pressure FT-IR autoclave reactor designs (specifically the ReactIR autoclave design) used to collect the IR spectral data of this section. The initial results of the FT-IR studies analyzing IR spectra differences between acetone and water-acetone solvent systems were performed by Catherine Alexander.[10] All current FT-IR investigations into the dirhodium catalyst were performed as joint research conducted between myself and Darina Polakova.

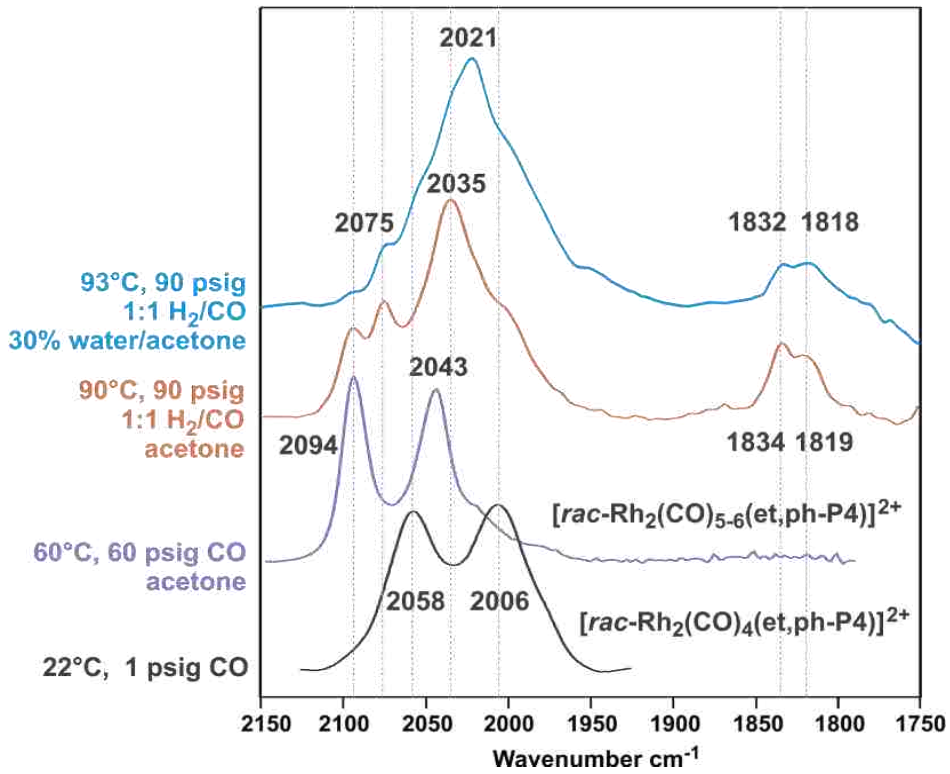

Figure 2.3 [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ activation using H_2:CO gas mix, as obtained from the dissertation of Catherine Alexander.[10]

The top two spectra of Figure 2.3 show the catalyst activation in acetone and the other in a 30% water-acetone solvent. Alexander reported that both spectra contain terminal CO bands at 2094, 2075, and 2035 cm^{-1} (shifted to 2021 cm^{-1} in water-acetone). The bridging CO bands can be seen at 1834 and 1818 cm^{-1} for both spectra. Past experiments have shown a direct relationship between bridging carbonyl bands and catalytic activity for hydroformylation catalysis. She determined that the active dirhodium catalyst species (as indicated by IR spectra) are identical in both acetone and water-acetone solvents when using 90 psig H_2:CO gas (1:1 mixture) at 90°C.

The difference between the IR spectra taken of catalyst (when exposed to CO gas) in acetone/water and acetone is that the pure acetone leads to a higher concentration of penta/hexacarbonyl dirhodium tetraphosphine complex, $[Rh_2(CO)_{5\text{-}6}$(*rac*-et,ph-P4)$]^{2+}$, which can

be seen in spectra as a peak at 2095 cm^{-1} (see Figure 2.3 and also in the activated 90°C spectra of Figure 2.4 and Figure 2.5). The results of past spectra collected by Alexander agree with those collected by myself and Polakova. This is proposed to be the open-mode resting state of the catalyst, which is unable to directly perform hydroformylation. The far lower concentration of the penta/hexa carbonyl complex in the water-acetone solvent suggests something radically different is occurring in the catalyst equilibria or species being generated.

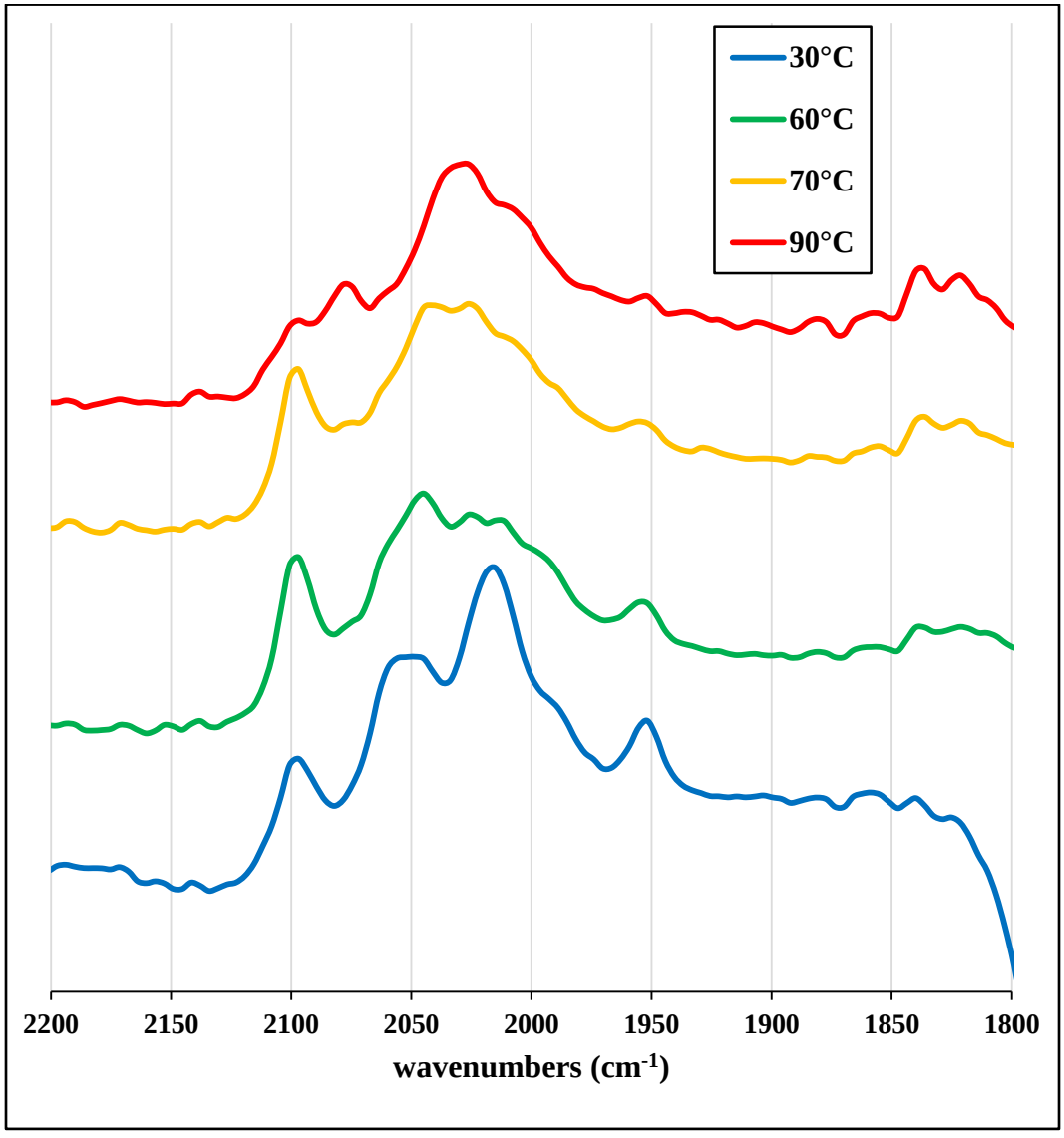

Figure 2.4 IR Spectra of [*rac*-$Rh_2(nbd)_2$(et,ph-P4)$^{2+}$ catalyst species in acetone solvent.

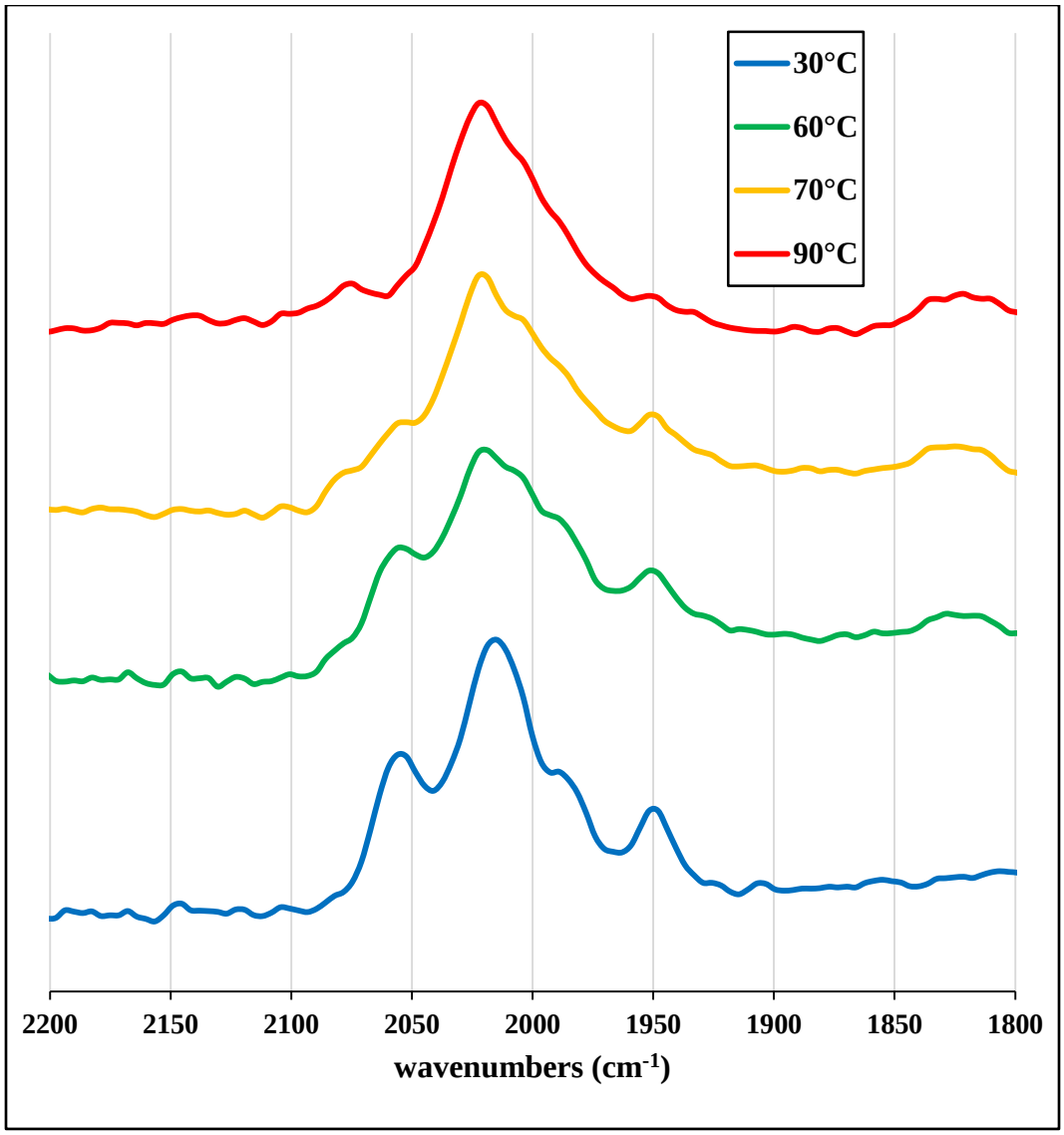

Figure 2.5 IR Spectra of [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$^{2+}$ catalyst species in a 30% water-acetone solvent.

To check the validity of this finding, the catalyst precursor [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ was dissolved in a 30% water-acetone solution, injected into the ReactIR autoclave cell, and exposed to pressurized CO gas (with heating). The catalyst complex undergoes noticeable changes in solution, specifically around 2095 and 2022 cm^{-1}. Over the course of 15 minutes, the peak intensifies, indicating carbonyl replacement of the norbornadiene ligands. As

the pressure and temperature increase, the peak begins to broaden out, which is more characteristic of water-acetone catalyst spectra compared to acetone catalyst spectra (Figure 2.6).

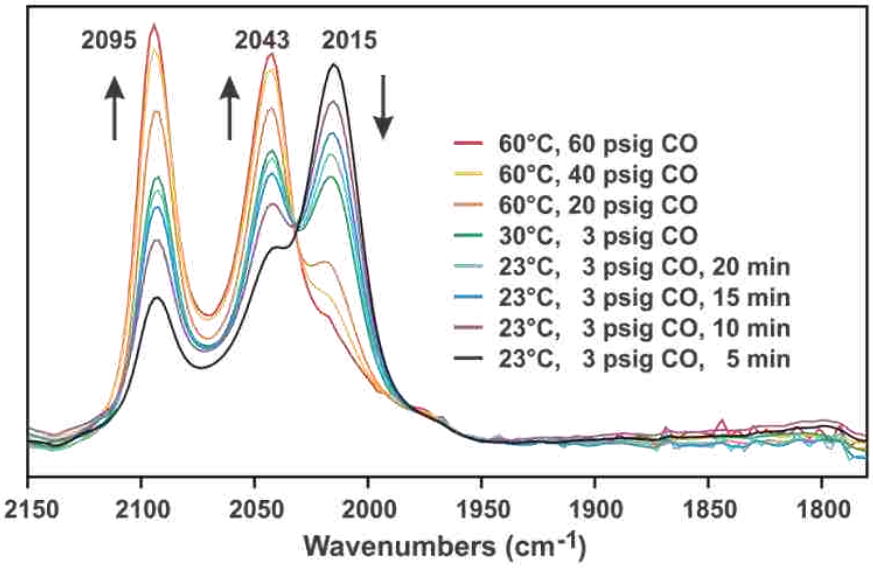

Figure 2.6 Pressure and temperature effects of [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ exposed to CO gas in acetone solution. Spectra collected by Catherine Alexander.[10]

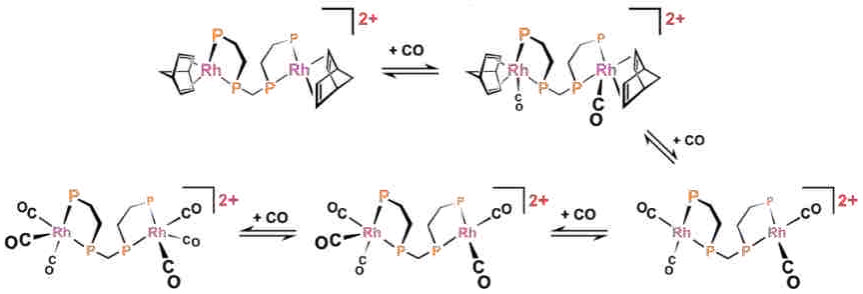

Figure 2.7 Mechanism of carbonyl coordination for the [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$^{2+}$ complex.

In Figure 2.5, the peaks at 2095, 2043, and 2015 cm^{-1} are monitored for changes depending on temperature and pressure of CO gas present in the reactor. The trend seen is that over time, the increase in both temperature and CO pressure causes the peaks at 2095 and 2043 cm^{-1} to increase in intensity, while the peak at 2015 cm^{-1} decreases. The 2015 cm^{-1} peak has been identified as the bis(norbornadiene)dicarbonyl complex. When looking at the proposed mechanism in Figure 2.7, upon further carbonyl coordination, the norbornadiene ligands are

readily substituted off forming the tetra-, penta-, and hexacarbonyl dirhodium complexes (which are represented by the peaks at 2095 and 2043 cm^{-1}). As stated previously, without the presence of hydrogen gas the complex will not form the closed-mode CO-bridging complex capable of hydroformylation.

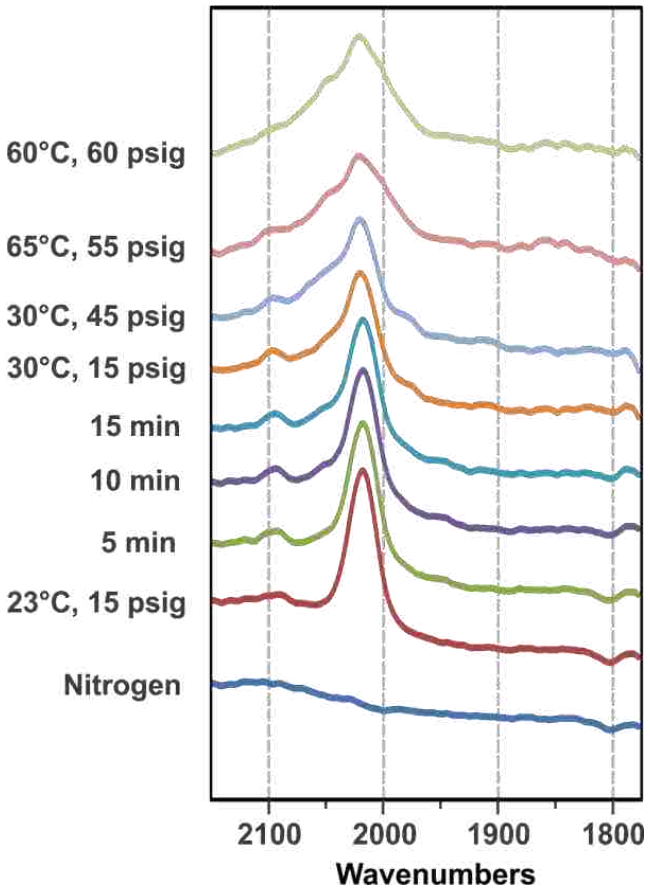

Figure 2.8 Pressure and temperature effects of [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ exposed to CO gas in 30% water-acetone solution

When the same conditions for the dirhodium catalyst precursor were run using the 30% water-acetone solution, there is a significant change in the IR spectra. Instead of three peaks, only one main peak at 2022 cm^{-1} forms as a result of the pressurized CO gas. The norbornadiene seems to be replaced far slower than in pure acetone solution, most likely due to the hydrophobic nature of the organic norbornadiene. There is a small peak at 2100 cm^{-1} seen on some of the

spectra, and this is believed to be the same penta- or hexacarbonyl catalyst complex as the 2095 cm^{-1} peak in Figure 2.6. This greatly diminished peak in the water-acetone solution gives evidence as to one of the reasons for the higher hydroformylation catalyst activity, as the higher carbonyl complex must dissociate carbonyl ligands to perform the oxidative addition of H_2 necessary to form the closed-mode active form. These results are also validated by the findings of the high-pressure NMR studies performed by Darina Polakova.[3]

It is believed that the reason for reduced formation of the pentacarbonyl and hexacarbonyl species is due to the presence of water hindering the coordination of CO by donating electron density to the electron deficient rhodium center(s) (due to the other carbonyl ligands), effectively blocking the remaining coordination sites. Density functional theory (DFT) calculations performed by Dr. George Stanley found a lone pair of electrons on the water's oxygen atom has an energy of -8.13 eV, which is lower than a lone pair on acetone's oxygen atom at -6.88 eV. Thus, acetone is a better donor than water and should coordinate easier to a metal center.

This contradicts our belief that the improved catalytic activity is due to water binding to the dirhodium carbonyl complex and blocking coordination sites from further CO additions, while not binding so strongly that water dissociation is inhibited. In theory, acetone should be just as capable of blocking coordination sites from CO additions, yet the presence of water improves the catalytic activity and regioselectivity. Other effects have been postulated on water's electronic effects, such as water's ability to draw electron density from the CO ligands to facilitate CO dissociation, but DFT calculations have not been performed for this as of yet. The effect of water on the dirhodium catalyst is still not fully understood, and further investigation is needed.

2.4 New Proposed Hydroformylation Mechanism in an Acetone/Water Solution

When considering the findings by the acidity of the catalyst solution, it becomes clear that the dicationic dihydride catalyst acts as a strong acid, releasing an equivalent number of protons per dirhodium catalyst complex. This cannot be explained using the former mechanism proposed for the hydroformylation reaction using the [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$^{2+}$ catalyst precursor in an acetone solution. Taking into consideration the acidity findings along with FT-IR spectra data on dirhodium carbonyl complexes generated *in situ*, a new mechanism was proposed for the hydroformylation reaction using the [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ catalyst precursor in a 30% water/acetone solution.

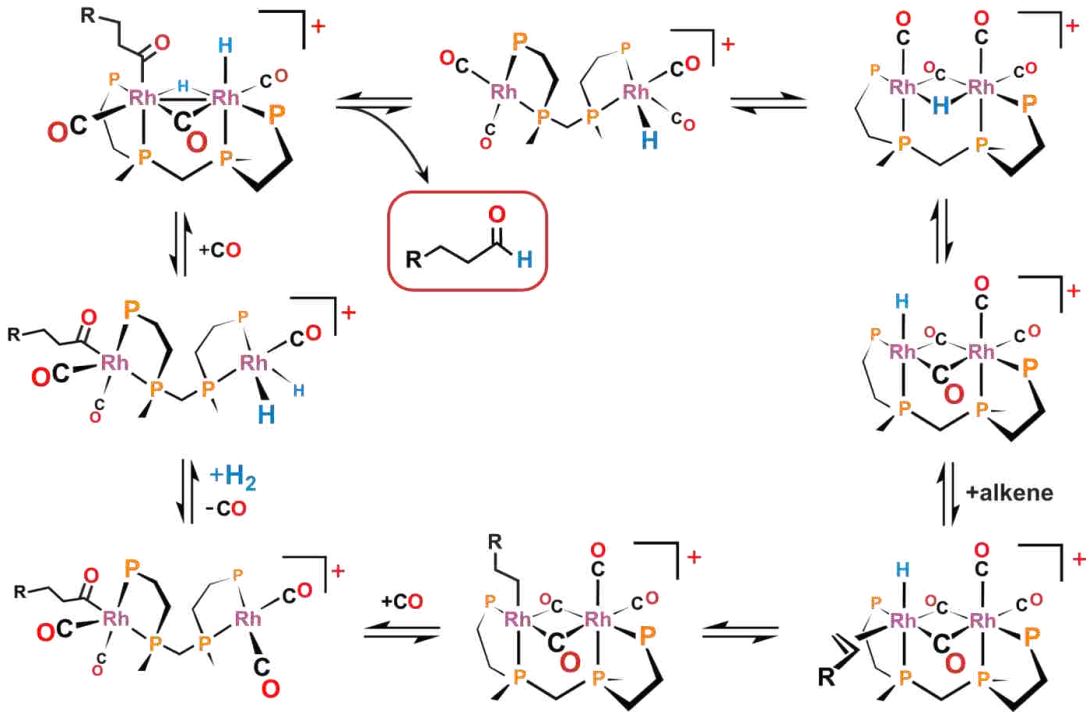

Figure 2.9 The proposed mechanism for hydroformylation using the [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ catalyst precursor.

The mechanism begins by the catalyst precursor, [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$, substituting the norbornadiene ligands for CO ligands, then adding the H_2 in such a way to

coordinate one hydride ligand and generate one H^+ into the solution (whether via oxidative addition or heterolytic cleavage). These steps described so far happen prior to entering the catalytic cycle shown in Figure 2.9. With the now formed [*rac*-$Rh_2(H)(CO)_4$(et,ph-P4)]$^+$ (top-center position of Figure 2.9), the complex achieves a more stable orientation by switching from the open-mode to the closed-mode structure with bridging hydride and carbonyl ligands. The migration of the bridging hydride ligand to a terminal hydride ligand increases the probability of migratory insertion to take place upon coordination of the alkene to an adjacent equatorial binding site on the same rhodium center. Migratory insertion of the hydride and alkene ligands forms an alkyl ligand, followed by the addition of another CO. DFT calculations of the dicationic catalyst mechanism structures suggest that a similar monocationic tetracarbonyl alkyl complex can also "crack open", forming the open-mode species. In order to achieve further stabilization, the alkyl and an adjacent carbonyl ligand perform a migratory insertion to yield an acyl ligand. An oxidative addition of H_2 causes the reformation the more stable closed-mode catalyst species, [*rac*-$Rh_2(\mu\text{-}H)(\mu\text{-}CO)(H)(acyl)(CO)_2$(et,ph-P4)]$^+$. Similar to the hydroformylation mechanism using pure acetone solvent, the acyl and hydride ligands are in close proximity together enabling an intermolecular reductive elimination of aldehyde. Then the dirhodium complex reopens, bringing the cycle back to the starting point.

One of the primary differences between the proposed hydroformylation mechanism in acetone/water versus pure acetone is that the dirhodium species overall has a monocationic charge. The resting state of the catalyst (for this mechanism) is believed to be shifting between the two closed-mode carbonyl-hydrido dirhodium complexes (Figure 2.9 top-right and right complexes). However, DFT calculations of the dicationic compounds indicate that the bridging-hydride ligand is lower in energy and heating is required to shift it into a terminal hydride

position. If the monocationic dirhodium complex behaves similarly, the closed-mode tricarbonyl complex with a terminal hydride may actually be the true resting state of this catalyst system. Despite the improved hydroformylation activity, regioselectivity, and lifetime of the catalyst in an acetone/water solution, calculations suggest the dicationic dirhodium complex (formed in pure acetone) is actually more active towards hydroformylation. However due to the greatly increased catalyst stability and lifetime in an acetone/water solution, there is a significantly higher concentration of active catalyst present (monocationic dirhodium complex) during reaction than when using pure acetone, thus resulting in a higher overall activity.

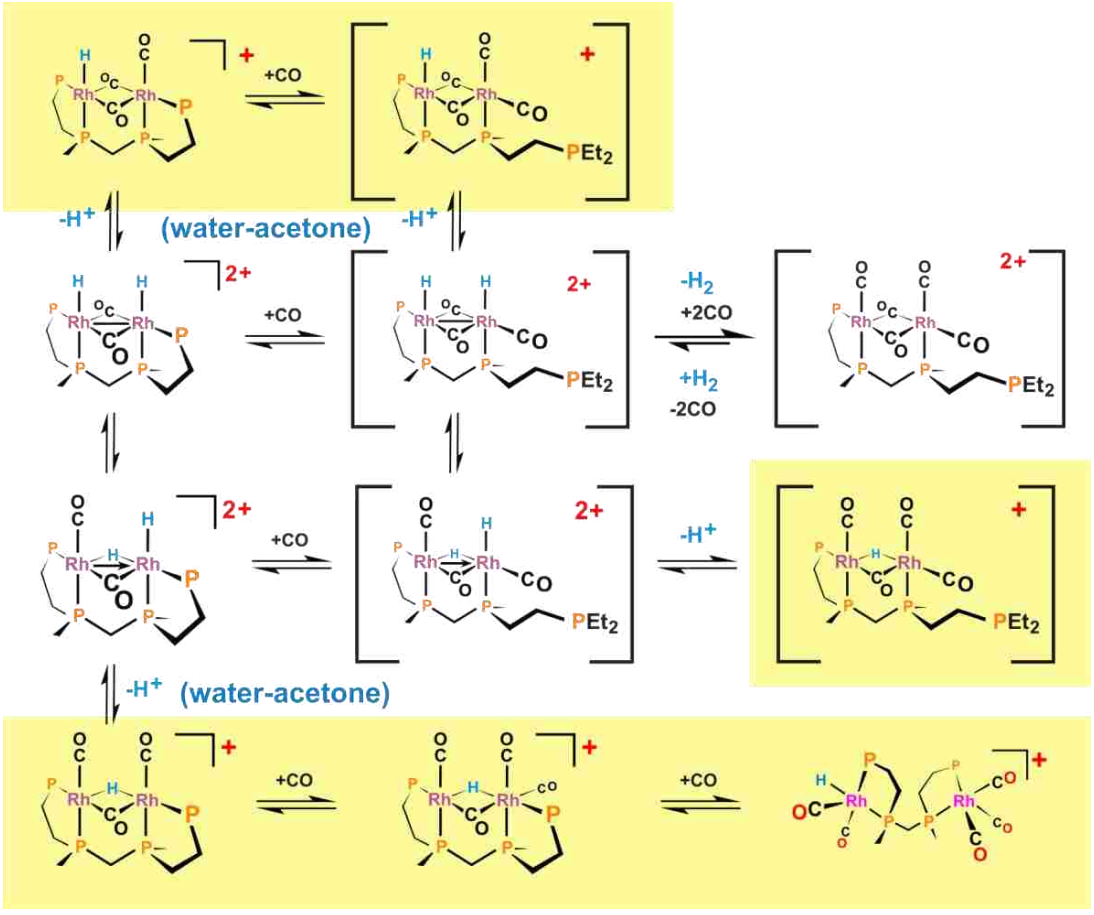

Figure 2.10 Water, H_2, and CO effects on the dirhodium tetraphosphine catalyst

The presence of water plays a significant role in altering the nature of the dirhodium catalyst by promoting proton dissociation. Figure 2.10 shows several of the reaction possibilities, including the ones specific to the newly proposed mechanism for hydroformylation in a 30% water/acetone solvent (shown in the shaded/tinted regions). The proposed active catalyst for the aldehyde-water shift catalysis (discussed further in the Aldehyde-Water Shift Catalysis chapter) is not shown in the above figure, but it can be formed in two ways. The first possibility is the acidic proton performing an electrophilic attack on the hydride ligand, emitting H_2 gas and being replaced by CO ligands. The second possibility is via the intermolecular reductive elimination of H_2, then being replaced by CO ligands. The labile nature of the tetraphosphine ligand allows for relatively easy dissociation and association of the outer phosphines as needed. The presence of these monocationic species show the versatile capabilities of the dirhodium tetraphosphine catalyst, most of which are heavily dependent on the conditions being controlled during hydroformylation using the autoclave reactor system.

There are currently no DFT calculations studies that have been performed on the proposed monocationic dirhodium hydroformylation mechanism (Figure 2.9), but investigations into the proposed monocationic catalyst complexes and the overall mechanism are planned for the near future. These theoretical models will hopefully yield valuable evidence supporting the newly proposed hydroformylation mechanism when using a water-acetone solvent. Catalyst complex stability and energy states are always key when attempting to support or refute a catalysis mechanism cycle.

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CHAPTER 3: GENERATIONS OF AUTOCLAVE REACTOR DESIGNS

3.1 Introduction

All reactions being run for the hydroformylation and aldehyde-water shift require both high pressure and high temperature conditions. Our reactions are run in modified 160 mL stainless steel Parr high pressure reactors (autoclaves). The autoclave reactors need to fulfill the following minimum requirements for our research: chemically inert/resistant material, easily cleaned between reactions, controlled heating, controlled pressure, controlled stirring, able to inject reagent while at high pressure/temperature, and the ability to extract samples from the reactor without interrupting the reaction. So far there have been three generations of high pressure/temperature autoclave reactors modified for our research over the years.

3.2 Original Modified Autoclave Design (Mark I)

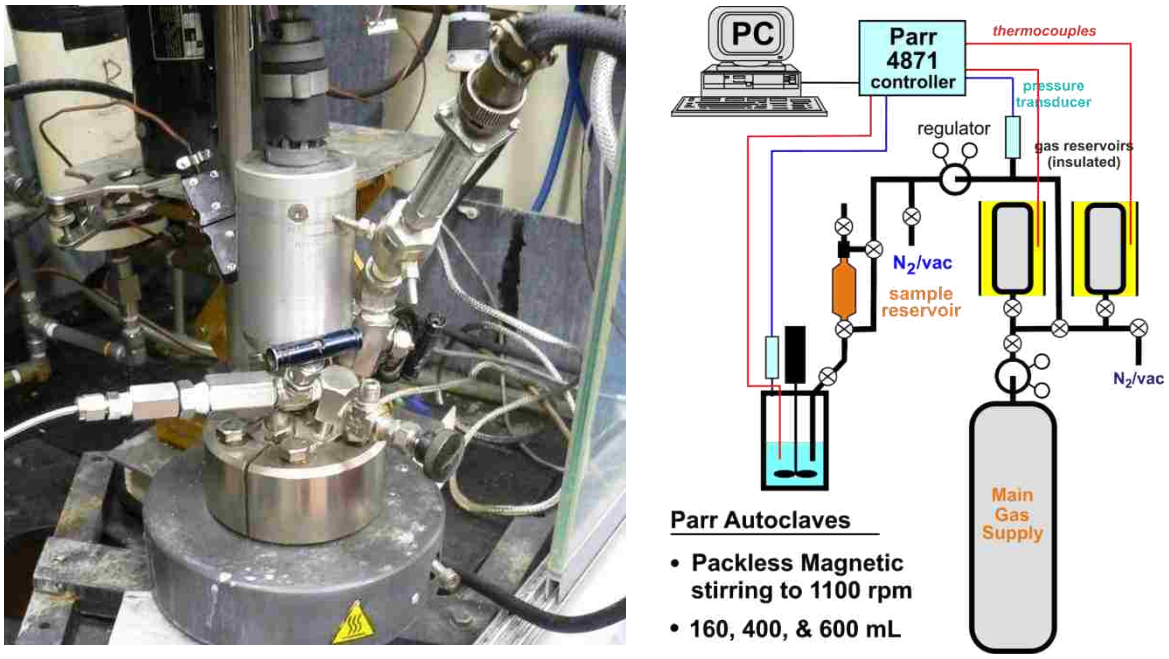

Figure 3.1. The original autoclave modified for our hydroformylation reaction studies.

Figure 3.1 shows the original modified autoclave reactor (image on the left and diagram on the right) for the Stanley research lab's investigation into hydroformylation catalysts. The diagram to the right of the image depicts the controller, reactor, and gas reservoir system, all used when performing and monitoring hydroformylation reactions. The system featured a stainless steel combination gas and olefin injection reservoirs connected to the autoclave using 1/8" stainless steel tubing. Thermocouples and pressure transducers were fitted to the autoclave and gas reservoirs to monitor temperature and pressure, and the readings were recorded on a computer connected to the controller. A packless, magnetic stirrer was used to stir the reaction solution up to 1100 revolutions per minute (RPM). Heating and stirring were controlled by a Parr 4871 process controller which was controlled by a computer. During the reaction, temperature and pressure data were automatically collected from the autoclave and gas reservoirs every 30 seconds, then stored in a spreadsheet. The data was then used to calculate the number of turnovers and the turnover frequency of the reaction using the Ideal Gas law.[1]

The method used for preparing the autoclave reactor was quite different for the first generation of the autoclave design compared to the current method. The olefin and gas injection lines (including all tubing) were connected to a vacuum line for at least 15 minutes to remove any air present. The unassembled autoclave reactor was brought into a nitrogen atmosphere glove box to be charged with 80 mL of 1mM catalyst solution and assembled/sealed. The olefin was filtered through neutral alumina and collected in a separate vial and sealed (usually enough to result in a 1 M concentration of the reaction solution). Once removed from the glove box, the autoclave reactor was connected to the injection and gas reservoirs, and the olefin was transferred via cannula (double ended stainless steel needle). The injection reservoir featured a bypass loop allowing gas to be delivered to the autoclave without passing through the olefin

injection reservoir, in order to pressurize the autoclave without injecting the olefin. The autoclave was then purged with syn-gas to remove any air, but also to saturate the reactor's headspace and catalyst solution with H_2 and CO gases. The reactor was pressurized to 45 psig and stirred at 1000 rpm, then heated to 90°C over the course of 20 minutes. This heating and stirring of the catalyst solution in the presence of H_2 and CO gases is meant to activate the catalyst species, and it is known as the "Soaking Period". After the soaking period, the pressure in the autoclave was vented to 45 psig, and the 90 psig pressure was pushed through the injection reservoir and into the reactor vessel, which added the olefin reactant into the catalyst solution. The reaction was held at 90 psig pressure, 90°C temperature, and 1000 rpm stirring until the end of the reaction/experiment (minimum 2 hrs).[1] Samples were also analyzed via gas chromatography.

After each run, the autoclave was disassembled and cleaned with acetone. Acetone was also injected into the olefin injection reservoir and tubing to rinse any remaining residue. The autoclaves could also be more thoroughly cleaned by being charged with 100 mL acetone, sealed, then heated with stirring for a few hours.

3.3 Mark II Autoclave Design

Over time, catalyst activity and selectivity were decreasing, and it was determined to be due to contamination from past reactions. The autoclave reactor and gas/olefin injection system were effective but not easily cleaned. The new design facilitated easier, more thorough cleaning of the autoclave system, as well as being able to assemble the reactor outside of the glove box. In 2006, Catherine Alexander was responsible for this redesign of the autoclave reactor and gas system. This is most common design of autoclaves currently used in the Stanley research lab.

Figure 3.2. Autoclave Mark II Reactor arms: Olefin Pressure Injection Arm (left), Sampling Arm (middle), and Purge Arm with Pressure Transducer (right).

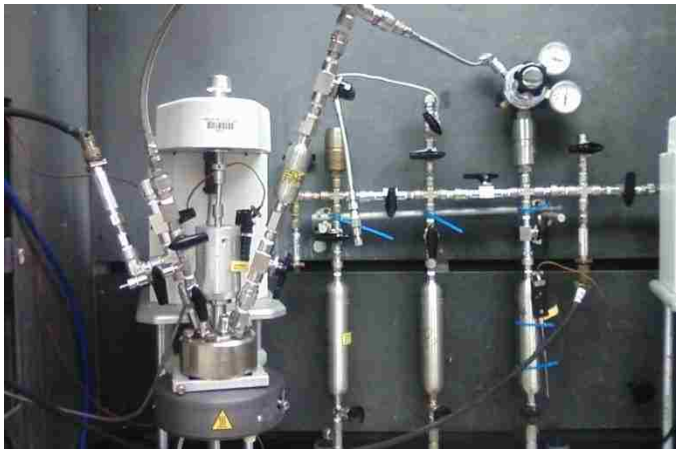

Figure 3.3. Assembled Autoclave Mark II Reactor and Gas Reservoir System

The new design of the autoclave was modified from the original 160 mL Parr stainless steel autoclave reactor. Two of the key differences between the old and new designs are the three detachable reactor arms and the multi-reservoir gas manifold system. All of the autoclave arms, as well as several connection points in the gas reservoir system use Swagelok quick-connect adapters equipped with solvent-resistant Markez o-rings to facilitate easier and more thorough cleaning in-between reactions. The olefin pressure injection arm allows for a short, direct-path addition of the olefin into the catalyst solution as well as a pathway to inject gas directly into the solution. The Sampling Arm design also allows for the injection of gases directly into the reaction solution, similar to the pressure injection arm, but it can also be used to pull a sample of reaction solution without stopping the reaction or risking air contamination of

the entire reaction solution. The purge arm contains a valve used both for the addition of catalyst solution into the reactor vessel and to vent/purge out pressurized gases. It also has a pressure transducer attached which allows monitoring of the reactor pressure on the computer in real-time. Unchanged was the thermocouple probe attached to the autoclave head (to monitor the temperature of the reaction solution) and the packless, magnetic stirrer atop the autoclave head (Figures 3.2 and 3.3).

Figure 3.4. New/current gas manifold system. Source gas cylinders (left) and the manifold gas reservoirs supplying gas to the autoclave (right).

The new gas manifold system allows for faster changing of gas types and easier mixing of gases (if needed). All fittings, gas reservoirs/cylinders, and quick-connect adapters used are stainless steel and Swagelok products. The first section of the manifold can house up to four large gas cylinders at one time used as the source for gases used in our chemical reactions. In the image above (Figure 3.4 (left)) the gases shown are hydrogen, argon, carbon monoxide, and syn-gas (50.00% H_2 and 50.00% CO mix). From here, regulators and valves can be opened to fill/pressurize any of the three 300 mL stainless steel gas reservoirs with any mixture of gas (pressure rating of up to 1800 psig) from the source gas cylinders. Each of the four autoclaves has its own separate regulator to control the pressure in the corresponding reactor. The original

autoclave reactor system only had one gas reservoir, meaning that if an experiment required changing gas feed mixtures, the gas reservoir would have to be closed off, vented, and refilled with the new gas mixture. With the new gas manifold, switching gas feeds into the autoclave takes only a few seconds without any risk of air contamination.

The procedure for performing hydroformylation reactions using this new design is as follows. The autoclave reactor (including all arms) was assembled and a vacuum line was connected for at least 15 minutes. In a nitrogen atmosphere glove box, 80 mL of a 1mM catalyst solution was prepared in a flask and sealed with a septum. Also in the glove box, the olefin was filtered through neutral alumina, collected in a vial, and sealed with a septum (enough to result in a 1 M concentration of the reaction solution). Both the olefin and catalyst solution were removed from the glove box. The olefin was transferred via cannula into the autoclave's olefin pressure inject reservoir arm, and the catalyst solution was transferred via cannula into the autoclave reaction vessel. Using the sampling arm to push gas into the autoclave (similar to the previous model's "bypass loop"), the pressure was increased to 90 psig (the operating pressure), then vented to 45 psig. This was repeated two more times to ensure a pure atmosphere and saturate the catalyst solution with H_2 and CO gases. The soaking period was initiated to heat and stir the catalyst solution over 20 minutes. After soaking, the pressure in the autoclave was vented to 45 psig, and the 90 psig pressure was pushed through the alkene injection reservoir and into the reactor vessel, thus adding the alkene into the catalyst solution. The reaction was held at 90 psig pressure, 90°C temperature, and 1000 rpm stirring until the end of the reaction/experiment (minimum 2 hrs).[1] Samples were also analyzed via Gas Chromatography-Mass Spectrometry (GC-MS).

Some other modification and experimentation was conducted on using protective liners for the autoclave vessels. The hypothesis was that the stainless steel surface of the autoclave vessel was somehow promoting the degradation of the dirhodium catalyst and possibly increasing the percentage of side reactions when performing hydroformylation reactions. Switching to a glass or Teflon lined vessel would allow for a more chemically inert system. The glass liners inserted into the vessels caused issues dealing with reaction solution spilling into the gaps between the liner and the stainless steel vessel walls, regardless of how close the liner's fit was to the vessel's dimensions. Also, if the glass liner was too close of a fit to the vessel, it was found to jam and cause difficulty removing. Teflon liners were tested next for two reasons. First, they provided superior chemical resistance, thus decreasing any effects on the catalyst or other reaction components. Second, the thermal expansion for Teflon (80-300 ppm/°C between 0-140°C) is significantly higher than that of borosilicate glass (3.25 ppm/°C between 0-300°C).[2] This would mean that a Teflon liner closely fitting the autoclave vessel could be used, and the heat during reaction might even cause some expansion, further closing the gap between the liner and the vessel wall. This however caused problems when controlling the heating of the reaction solution, due to the thickness of the new liner.

Finally, a Teflon coating was applied to one of the autoclave vessels by Parr, significantly thinner than the previous insert liner. The new Teflon lined autoclave vessel has been successfully used in hydroformylation reaction studies, with only a minimal delay/lag-time occurring when heating the autoclave. During testing, side by side hydroformylation reactions in both the Teflon lined and bare stainless steel vessels were run using identical catalyst batch, olefin, solvents, and reaction conditions. The hydroformylation reaction using the Teflon lined autoclave vessel did in fact reduce the percentage of isomerization and hydrogenation, but only

slightly, and there was no indication that the lifetime of the catalyst was extended from the average durations. While the longevity and selectivity of the catalyst was not improved using this new autoclave vessel, these experiments did show that prolonged contact with the bare stainless steel was not causing significant catalyst degradation and side reactions.

3.4 Mark III Autoclave Design: Flow-Control Autoclave Reactor

The research being conducted on the Aldehyde-Water Shift catalysis, both tandem with hydroformylation and by itself, required a new design of autoclave reactor. According to the work of past researcher David Aubry, the direct aldehyde-water shift catalysis converting reagent aldehyde into the corresponding carboxylic acid would not initiate without a steady flow/purge of gas through the reactor. This was first seen via the accidental reactor gas leak by Novella Bridges, which under the right conditions, caused the first aldehyde-water shift reaction converting heptanal to heptanoic acid. The current design of the autoclave reactor is a sealed system with the only flow of gas being that amount used up in reaction. A new design of reactor was needed to allow for the usual uptake of syn-gas in a sealed system during a hydroformylation reaction, while being able to switch to a system allowing for a controlled flow of gas through the reactor without loss of reaction solution and reagents. In addition, the new design also needs to be able to vent off any gas possibly produced in reaction (aldehyde-water shift catalysis) while maintaining a constant reactor pressure. The following design modifications were made to Catherine Alexander's autoclave model (Mark II autoclave design).

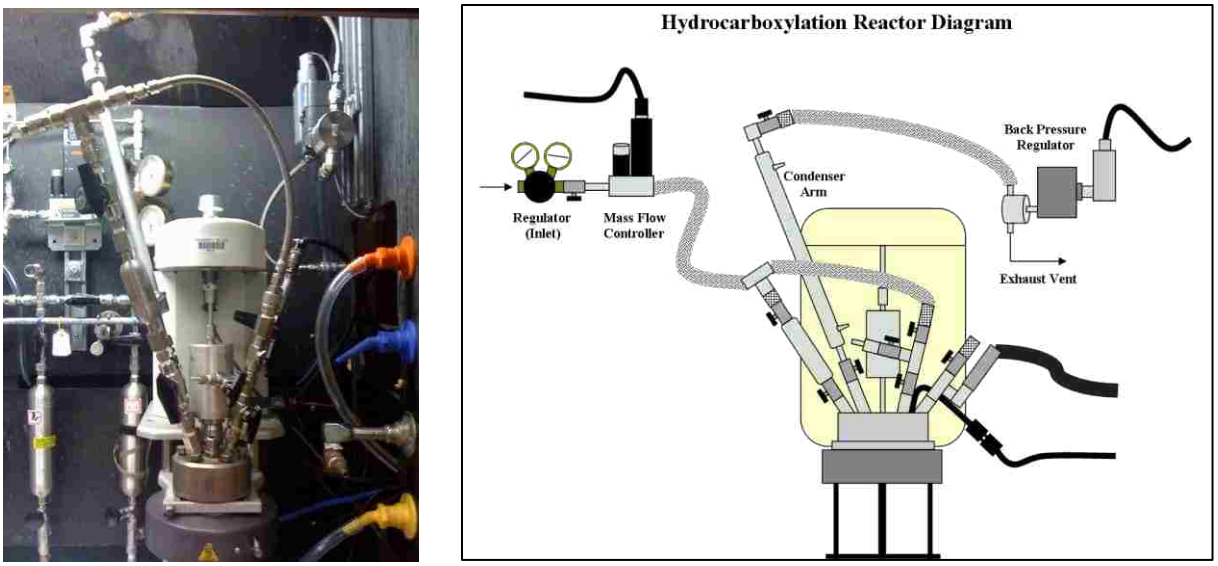

Figure 3.5. Flow-control Autoclave Reactor design

I designed, assembled, and programmed our Parr 4848 Reaction Controller and SpecView software to work with and control all the components. It involved several additions to the overall autoclave system and an additional gas feed line separate from the manifold system. These parts include the mass flow controller (MFC), the autoclave's condenser arm, and the current-to-pressure transducer with back pressure regulator combination (I/P-BPR).

Figure 3.6. The Mass Flow Controller (left) and the I/P–Back Pressure Regulator (right).

The Brooks Smart Digital Mass Flow Controller (Model 5800S series) is designed to regulate the gas flow in a much more accurate and standardized way than was done in previous

experimental trials of the aldehyde-water shift reactions (Figure 3.6). In the past, the gas flow rate was measured in units of psig per minute. This provided consistent values recorded for gas flow rate, since the measurements were taken from the high pressure side of a two-stage regulator feeding the autoclave reactor, but if the volume of the gas reservoirs were incorrect or ever changed due to modifications, all those values would be off when trying to duplicate the experimental results. The mass flow controller pushes into the autoclave a steady stream of gas whose flow rate is measured in units of standardized cubic centimeters per minute (sccm), with this model's flow rate range being 0 – 200 sccm. The standard volume of the gas reservoir used for the Mark II and Mark III autoclave design was 318 cm^3 (close to the gas reservoir volume used in the original Mark I autoclave design), and the conversion of units for the gas flow rate is approximately "10 sccm = 0.47 psig/min" when using a 318 cm^3 volume gas reservoir. If experimental results used this method and units of measurement instead of the previous psig/min, the same gas flow rate can be achieved regardless of the volume and pressure of the source gas reservoirs or cylinders. Larger gas reservoirs or even the source gas cylinders could be used during reaction while still being able to accurately monitor and control flow rates, meaning that reactions can be run for much longer times than before. This also means that the flow rate can be computer controlled, instead of using the needle valve atop the condenser arm. This new method using the mass flow controller allows for higher accuracy and greater ease of reproducing certain reaction conditions.

It is worth mentioning that this design also requires a bypass loop for the MFC. If the hydroformylation reaction is running, the MFC bypass loop is required, allowing for the regulator to directly control the pressure inside the autoclave (the same as the previous design). This is because of two reasons. First, the MFC cannot output a flow rate fast enough to maintain

a 90 psig pressure inside the reactor (+200 sccm). The *rac*-Rh_2(P4) catalyst is the most active during the first ~30 minutes of the hydroformylation reaction, and syn-gas is consumed too rapidly during that time. Secondly, because the catalytic activity and rate of reaction for hydroformylation keep changing, a constant rate of syn-gas flowed into the autoclave cannot be used while maintaining a constant reaction pressure. The only way that the MFC could be used for hydroformylation reactions would be to output a flow rate higher than the syn-gas was being consumed (which is not possible using this model of MFC anyways) then control the pressure inside the reactor using the I/P-BPR. This method would not be a closed system, thus the turnover number of the hydroformylation reaction could not be determined by pressure drop of H_2 and CO gases consumed. Using the bypass loop, the regulator can deliver the syn-gas directly into the autoclave in a closed system, so the turnover number can be determined by gas reservoir pressure drop (also by GC-MS analysis of the reaction solution). If the reaction conditions needed to be switched to allow a fixed flow or purge of gas through the reaction solution, then the bypass loop can be closed off and MFC used to initiate a controlled flow rate.

The condenser arm is made of stainless steel, fitted with Swagelok quick-connect fittings equipped with chemically resistant Markez O-rings, and a needle valve atop the arm. It was designed so that gas could bubble through the reaction solution via the sampling and pressure inject arms, then flow up the condenser and out through the needle valve on top. The outer jacket of the condenser is also stainless steel and is commonly cooled via air or water flow (though other liquids could theoretically be used). The needle valve atop the condenser could be slightly opened to vent the gases out into the chemical hood, or when connected to the back pressure regulator, the valve can be completely opened, and the flow controlled via the I/P-BPR.

As stated before, the I/P-BPR has two parts to it (Figure 3.6). The first section is the current (I) to pressure (P) transducer (ControlAir AH-500 I/P Transducer). Using the computer, the Parr controller sends a signal (4 – 20 mA current) to the I/P Transducer to output a specific pressure of gas from the source. In this case the source gas is supplied using a separate nitrogen gas cylinder (though air or any inert gas could be used since this gas provides the force to control the autoclave's pressure from the outside only). This separate source gas line had to be specially designed and built, as it could not be coupled together with the existing gas manifold system. The I/P Transducer continuously vents out gas from its source feed so that it can raise and lower its pressure accordingly and at a moment's notice. The loss of source gas is large enough, that a separate large gas cylinder was needed. The controlled output of the I/P transducer is what power/controls the back pressure regulator. The second section is the back pressure regulator (BPR) which is simply a stainless steel body with a lubricated piston acting as a valve opening/closing as a purge for the autoclave reactor.

The computer and Parr controller use combination of the mass flow controller, the pressure transducer attached to the purge arm, and the I/P-BPR in order to manage the overall autoclave pressure, as opposed to using a standard gas regulator. The MFC is set to output a specific flow rate of gas into the autoclave, which bubbles through the reaction solution while being heated, stirred, and pressurized. The pressure builds as the gas flows into the autoclave. When the pressure inside the autoclave vessel exceeds the set value for the I/P-BPR on the computer, the I/P transducer lowers its output pressure so that the autoclave can vent the excess pressure into the chemical hood. The air (or water) being pushed through the jacket of the condenser arm is used to ensure that minimal solvent is lost during the continuous purge of the autoclave. Once the target reactor pressure is reached, the I/P transducer increases its output to

maintain a pressurized system. This balance is maintained throughout the reaction to create a stable system allowing for an accurate, controlled flow of gases through the autoclave reactor for extended periods of time without loss of reaction solution, while still maintaining the necessary pressures and temperatures for hydroformylation and aldehyde-water shift reactions.

3.5 High Pressure FT-IR Autoclave Reactor Designs

The dirhodium catalyst system needed to be studied using infrared (IR) spectroscopy techniques. Given that the reaction conditions require a system to be pressurized and heated, a autoclave reactor had to be designed for the purposes of both studying the scans taken from the catalyst solution while in reaction while being similar to the standard autoclaves used in the hydroformylation reactions performed for our research. The high pressure *in-situ* circle reaction FT-IR cell was designed previously by SpectraTech, Inc. and modified by both George Stanley and myself. Since then a newer IR autoclave cell was designed by and purchased from Mettler Toledo International, Inc., with the autoclave arms/attachments, controllers, and gas manifold all designed and assembled by myself.

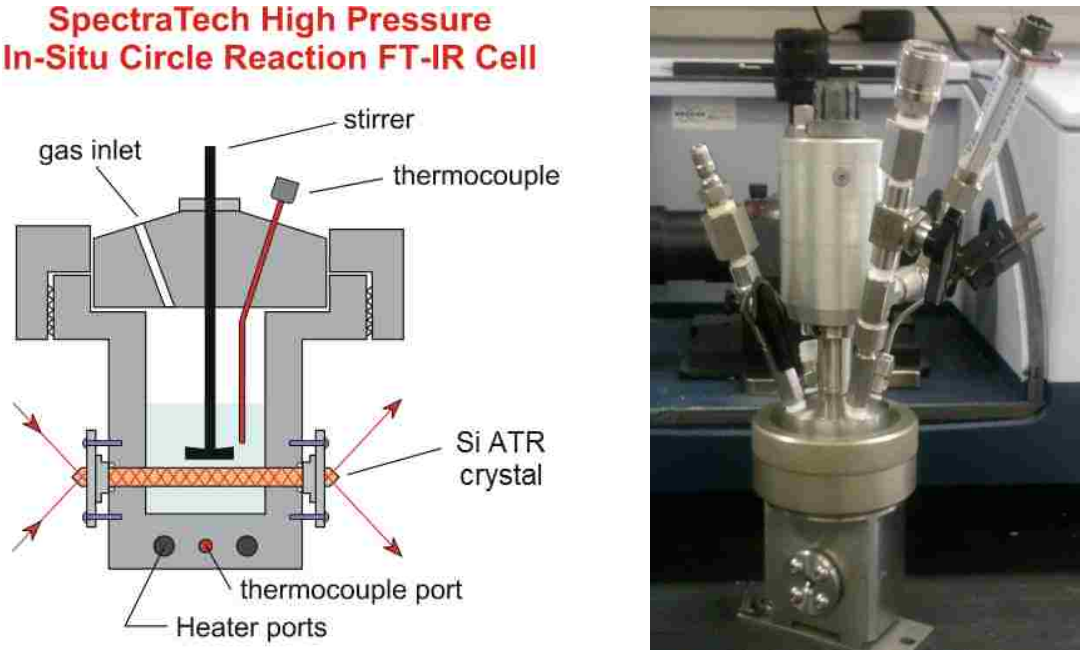

Figure 3.7 SpectraTech High Pressure *In-Situ* Circle Reaction FT-IR Cell

The figure above shows both a diagram and an image of the SpectraTech high pressure *in-situ* autoclave FT-IR cell. The majority of the autoclave is made of 316 stainless steel (similar to the all of our autoclaves), with a silicon attenuated total reflectance (Si ATR) crystal fixed through the middle of the reaction vessel. We previously used a ZnSe crystal rod but found that it reacted with our catalyst solution and deposited what appeared to be rhodium metal onto the ZnSe rod. The use of the Si ATR crystal has worked much better despite its lower IR throughput. We replaced the somewhat corroded reflection mirrors with a new set, and this has significantly boosted the IR intensity at the detector when using the Si ATR rod. This crystal allows for IR monitoring the reaction mixture with the active catalyst. The autoclave reaction cell is placed into a Bruker Tensor 27 fourier transform infrared spectrometer (FT-IR) which then transmits and receives the infrared radiation sent through the crystal.

Similar to the other autoclaves used in our hydroformylation research, there are a few arms and attachments to make the reactions possible. Nitrogen gas is used to purge the system of any air present in the reactor's arms and headspace. The catalyst solution can be injected into the autoclave vessel through the vent arm, which also has a pressure transducer attached (the vent arm is not shown in the diagram of Figure 3.7). The selected gas (usually CO gas or H_2:CO gas mix) can be pushed into reactor vessel through the gas inlet arm, thus saturating the catalyst solution. The packless magnetic stirrer is then activated to stir the reaction solution, and through the use of both the thermocouple and pressure transducer, the reaction's temperature and pressure can be monitored and recorded for further analysis. A controlled heater is built into the reactor vessel.

The new Mettler Toledo ReactIR high pressure *in-situ* autoclave reaction FT-IR cell was modified to be similar to the current hydroformylation autoclaves currently used in our research (designs Mark II and Mark III).

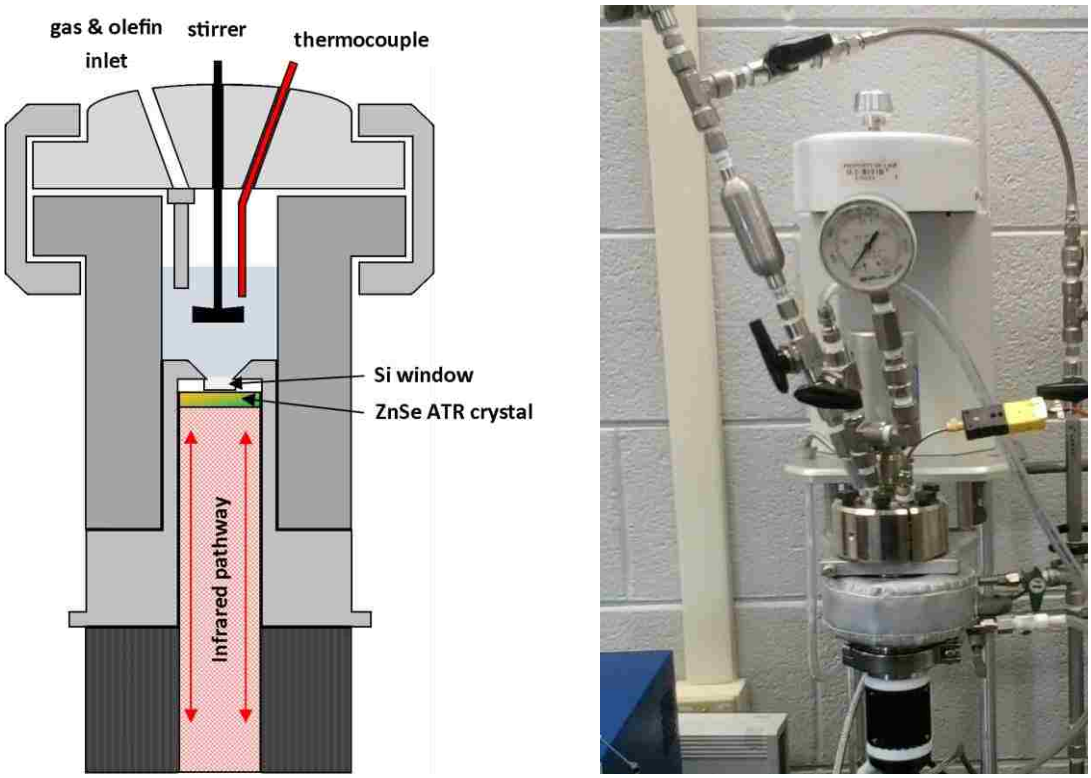

Figure 3.8 High Pressure *In-Situ* ReactIR Autoclave Design

This design uses a different interface to connect to the FT-IR instrument. The ZnSe ATR crystal is fused behind a silicon window surrounded by stainless steel. The IR emitter fires upwards into the hollow stainless steel column (continuously purged using a nitrogen gas flow), through the ZnSe crystal and Si window, thus coming in contact with the reaction solution touching the Si surface, and finally reflected back towards the source where the detector is located. This method of IR signal detection reduces the effect that carbon dioxide gas in the atmosphere has on the resulting spectrum, since the pathway from emitter to crystal/solution to detector is entirely purged of any water or carbon dioxide gases.

Similar to the previous SpectraTech IR autoclave cell, this model includes a stirrer, thermocouple, and a vent port/arm (with attached pressure transducer). The gas inlet port is improved from the SpectraTech design, because it was designed to actually deliver the gas directly into the catalyst solution, as well as able to pressure inject an olefin to test the hydroformylation reaction conditions much closer than previously able. When looking at the picture taken of the ReactIR autoclave (Figure 3.8), the longer arm on the left side is a similar olefin pressure inject reservoir (and valve system) of the mark II and mark III autoclave designs. If an olefin is being used in the experiment, during setup a septum can be placed over the opening of the valve on top so that the olefin can be injected into the reservoir to await pressure injection into the catalyst solution.

Finally, it is worth mentioning that this autoclave model does not have a sampling arm, as does the other hydroformylation autoclave reactors. This is because of the reduced volume of this vessel compared to the other autoclave vessels (20 mL capacity vs. 160 mL). A standard sample taken from the autoclaves using the sampling arm is typically 2-3 mL of reaction solution, which is a far larger percentage of the total solution for the ReactIR autoclave (10-15% vs. 1-2%). Regardless, this feature is not necessary since the predominant method of analysis will be the scans taken using the ReactIR FT-IR spectrometer instead of the usual GC-MS solution analysis.

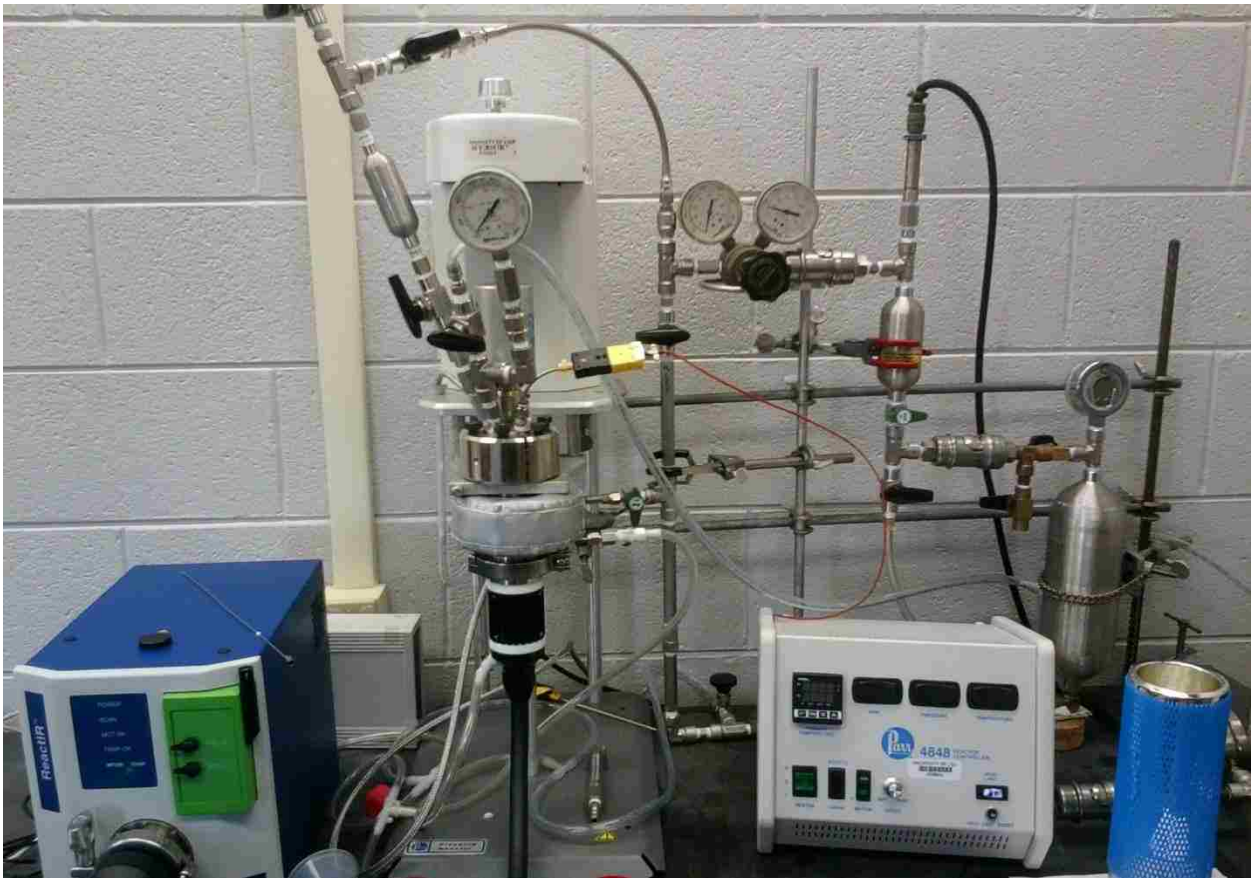

Figure 3.9 The Mettler Toledo ReactIR spectrometer (left), Autoclave FT-IR reactor cell (center), gas manifold system (back/right), and temperature/stirring controller (front/right).

The gas manifold system is shown to the back right of the ReactIR autoclave image (Figure 3.9). The gas source used for this system is a specially designed portable 1L stainless steel gas cylinder (all parts used are available from Swagelok Co.), and these cylinders were built for the purpose of transporting pressurized gases (pressure rated up to 2500 psig) for research use. These can be detached (via Swagelok quick-connect adapters), pressurized from a large gas cylinder, then reattached to the manifold without any other disassembly needed. These portable gas cylinders can also be used to charge the gas reservoirs used by the other autoclave reactors, if a specific gas is needed that is not currently one of the four cylinders attached to our main gas manifold (see Figure 3.4).

The gas manifold was designed so that there is both a nitrogen gas feed (house nitrogen) and a reaction gas feed (portable gas cylinder). Once the autoclave is assembled (as shown in Figure 3.9), a nitrogen gas flow is initiated into the pressure inject arm and out through the vent arm. This is necessary as there is no vacuum pump to evacuate any oxygen present that may poison the catalyst in reaction, and the nitrogen purge is left to flow for at least 30 minutes to ensure an inert atmosphere. During this time, the ReactIR spectrometer detector must be cooled down using liquid nitrogen, followed by a series of configuration tests and background scans. From this point on, IR spectra can be collected during anytime during preparation, soaking, or reaction.

Once purged, the nitrogen is shut off, and the catalyst solution is injected via syringe into the reaction IR cell vessel via the vent arm capped off with a septum. The regulator controlling the reaction gas is set to the desired output pressure and opened to pressurize the entire autoclave. The vent arm is slightly opened to allow a slow purge of gas through the reaction solution to ensure that the reaction gas has bubbled through and saturated the solution. The vent is closed off, and if an olefin is used in the experiment, this is the time to add it. This can be done by using the valves to close the pressure inject arm off from both the regulator and the vessel. The arm is then vented through the valve on top, capped off with a septum, and charged with the olefin via injection using a syringe (top valve closed afterwards). Finally, the heating and stirring are initiated using a Parr 4848 Reaction Controller.

Many different IR spectra were taken throughout the soaking period in order to monitor the changes in spectra corresponding to changes that the dirhodium catalyst was going through due solely to the presence of CO and/or H_2 gases. In other experiments, the olefin (usually 1-hexene) was pressure injected into the ReactIR autoclave, followed by several IR scans taken, in

order to monitor similar changes to the dirhodium catalyst throughout the entire hydroformylation catalytic cycle. Spectra could be collected manually, at specific intervals throughout the remainder of the experiment (i.e. one spectrum every five minutes), or even at varying time intervals in a set profile (i.e. one spectrum every five minutes for the first hour, then one every fifteen minutes for the remaining 3 hours). For these and other similar catalytic reactions requiring high pressure and high temperature conditions, the high pressure *in-situ* ReactIR autoclave is a very effective tool for the continuous collection of IR spectra of reaction solution while maintaining almost identical conditions to that of larger autoclave reactors.

References

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2. Optik, P. G. PYREX Borosilicate Glass - Specifications. http://www.pgo-online.com/intl/katalog/pyrex.html (accessed August 15, 2012).

CHAPTER 4: ALDEHYDE–WATER SHIFT CATALYSIS

4.1 Introduction and Background

As mentioned previously, hydroformylation uses a terminal alkene, reacted with H_2 and CO gases using a hydrido rhodium or cobalt catalyst, to form linear and branched aldehydes. Aldehyde-Water Shift catalysis is a new reaction that can be initiated on its own or tandem to a hydroformylation reaction. Using the same dirhodium tetraphosphine catalyst precursor, an aldehyde can be reacted with the water from the catalyst solution to form a corresponding carboxylic acid and also produce hydrogen gas. This is currently the only known method of producing a carboxylic acid from an aldehyde without the use of oxygen gas while also being able to produce hydrogen gas via a water molecule. When the hydroformylation and aldehyde-water shift reactions are run tandem, the combined process is results in hydrocarboxylation (also known as hydrocarbonylation). This is the conversion of an alkene, water, and carbon monoxide gas into a carboxylic acid.

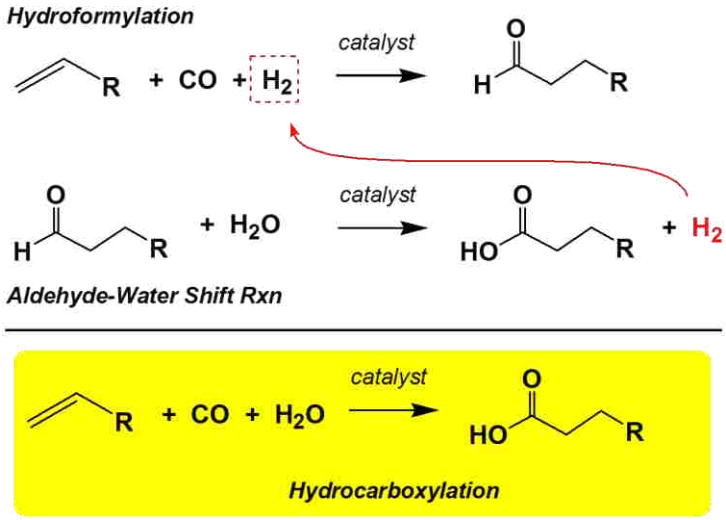


Figure 4.1 Hydrocarboxylation via tandem catalysis.

Most methods of generating carboxylic acids from aldehydes require the presence of oxygen or other oxidizing agents such as H_2O_2. This reaction is unique because it is performed in oxygen-free conditions, while also being able to produce hydrogen gas. The catalytic activation of water has only been previously accomplished under more extreme reaction conditions often with very poor rates and selectivities. The implications of this for chemical hydrogen storage cells could be significant. If the aldehyde-water shift reaction works with formaldehyde, the smallest of the aldehydes, it would be capable of one of the highest H_2 storage capacity per gram of fuel or starting material (8.3% by weight, just under the 9% goal set by the Department of Energy for 2015). Formaldehyde (in an aqueous solution) would be a cheap source of fuel, ideally capable of producing two moles of hydrogen gas per every mole consumed. All products and possible byproducts of this reaction are relatively non-toxic, making this process all the more ideal. The final products would be two equivalents of hydrogen gas and one carbon dioxide. The aldehyde-water shift reaction is essentially without precedent and represents a breakthrough in catalysis due to its rate and selectivity, no requirement for promoters, and use of water as a source of the hydrogen gas.

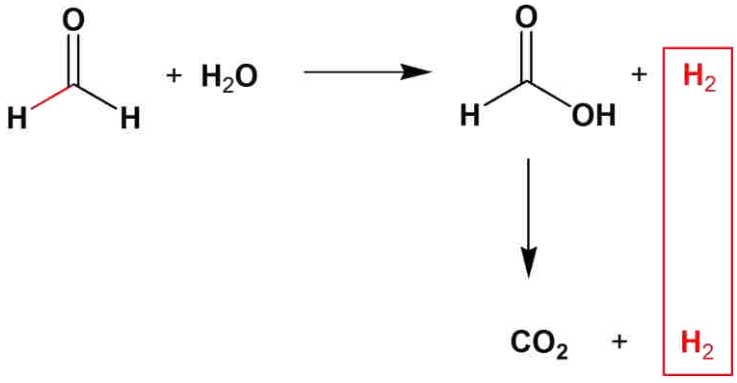


Figure 4.2. The Aldehyde-Water Shift reaction of formaldehyde and water.

The original discovery of the hydrocarboxylation (the conversion of alkenes to carboxylic acids) was due to the work by Walter Reppe.[1] Using a $Ni(CO)_4$ catalyst precursor, he was able

to generate smaller carboxylic acids, such as propionic acid generated from ethylene as the starting olefin. Simple nickel and cobalt systems like these require high temperatures (200-300°C), high pressures (200-300 atm / 2925-4394 psig) of CO gas, and a H-X strong acid promoter (usually X = iodide) to generate the active $HMX(CO)_2$ catalyst complex. Even when using these extreme reaction conditions, the resulting reactions exhibited poor chemo/regio-selectivity and low turnover frequency.

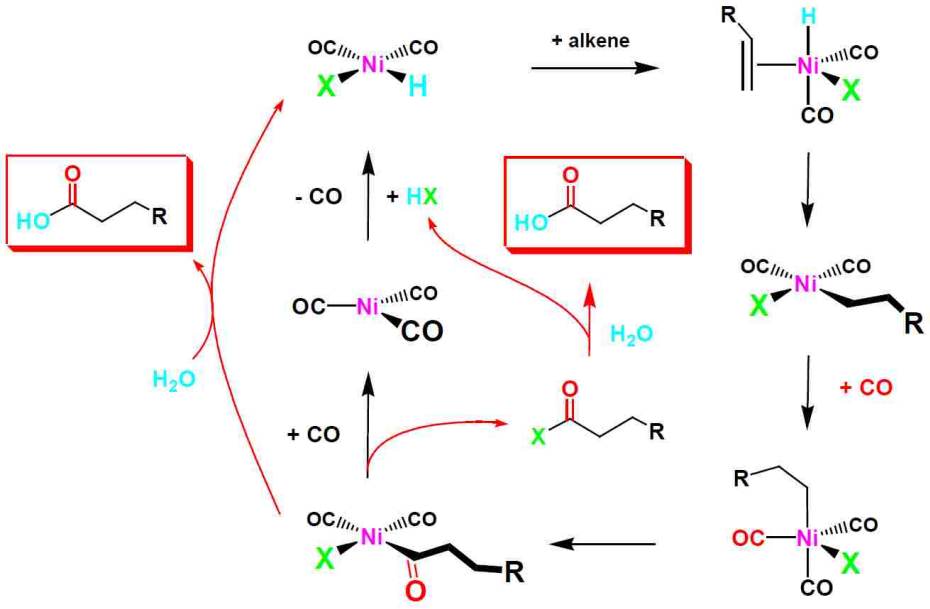


Figure 4.3 Heck's proposed mechanism for hydrocarboxylation using a $Ni(CO)_4$ catalyst precursor.[2]

The above image (Figure 4.3) shows Richard Heck's proposed mechanism for the hydrocarboxylation reaction when using $Ni(CO)_4$ as a catalyst precursor (the active catalyst being $HNiX(CO)_2$)[2]. The starting precursor $Ni(CO)_4$ loses a carbonyl ligand to enter the cycle shown above. The active $HNiX(CO)_2$ is then formed by the oxidative addition of the HX acid and the loss of another carbonyl ligand. Now the alkene can be coordinated to the Ni complex, involved in a migratory insertion with the hydride, and another migratory insertion with a carbonyl, resulting in an acyl ligand. These steps, so far, to generate the aldehyde from the

starting alkene are very similar to Heck's mechanism for Roelen's hydroformylation using $HCo(CO)_4$, but then things take a different turn. The halide (X) and acyl ligands perform a reductive elimination, forming an acyl halide, which reacts with the water in solution to both regenerate the HX acid and to form the carboxylic acid product.

The popular Monsanto Acetic Acid Process utilized similar chemistry to produce acetic acid via the carbonylation of methanol. This process uses Rh or Ir catalyst complexes with a HI acid promoter, and it operates under reaction conditions of 150-200°C temperatures and 30-60 atm (426-867 psig) pressures of CO gas.

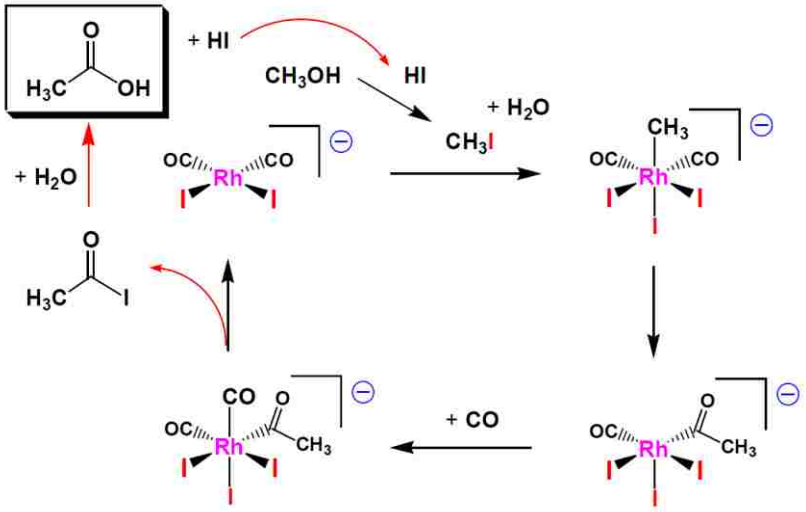


Figure 4.4 The Monsanto Acetic Acid Process proposed mechanism.

The mechanism proposes $[RhI_2(CO)_2]^-$ as the active catalyst species. After the methanol reacts with HI to form methyl iodide intermediate, an oxidative addition and migratory insertion take place, as well as an association of a carbonyl to hinder back-reaction. The resulting acyl ligand is reductively eliminated with an iodide ligand, reforming the active catalyst and kicking off acetyl iodide. The acetyl iodide reacts with water to produce the product acetic acid and regenerate the HI acid needed to continue the cycle.

4.2 Discovery of the Aldehyde-Water Shift Catalysis

The aldehyde-water shift reaction was discovered by Novella Bridges, a former researcher in the Stanley research lab. An accidental gas leak in the autoclave reactor's attached fittings (original Mark I design) along with a few other unspecified conditions, resulted in the formation of heptanoic acid during the hydroformylation of 1-hexene.[3] This was very unexpected, as the typical method for the production of heptanoic acid from heptaldehyde is via oxidation using a catalyst in the presence of oxygen gas or other oxidizing agents.

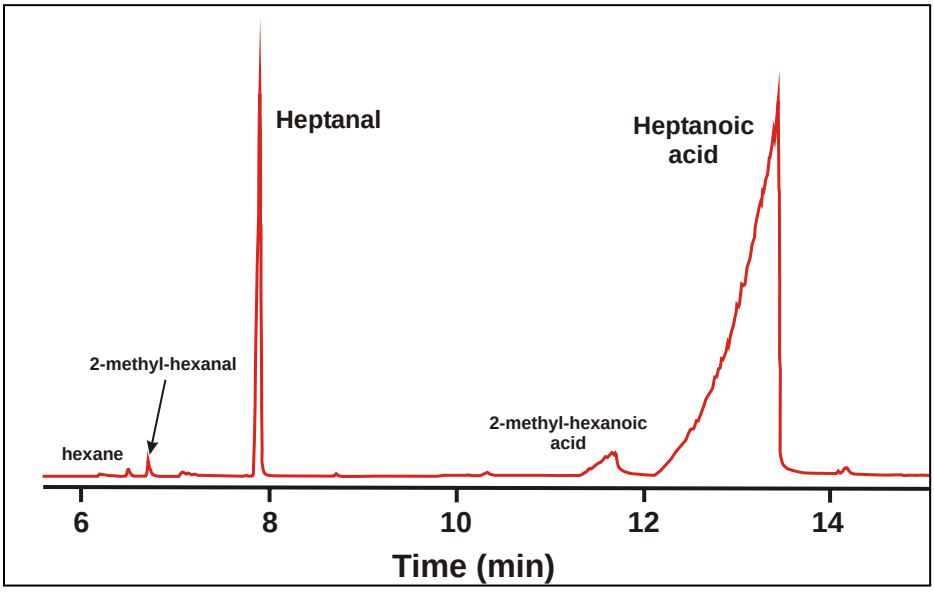


Figure 4.5 Gas chromatograph of Bridges's accidental production of heptanoic acid.

The production of carboxylic acids under such mild conditions (90°C, 90 psig H_2:CO, 1000 rpm stirring, 1 M olefin, 1 mM [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ catalyst precursor) is unprecedented. These results sparked an interest in a new direction of research regarding our dirhodium tetraphosphine catalyst. The results needed to be replicated under more controlled conditions, but when the gas leak in the autoclave was repaired, there was only hydroformylation to produce aldehyde and no production of heptanoic acid. Even with the leak, contamination of

O_2 in the autoclave was ruled out, as the pressurized nature of the system would not allow any external gases to be introduced into the reaction solution.

It is believed that the specific size of the gas leak in the autoclave was crucial in allowing the hydrogen deficient gas conditions to develop. According to Graham's Law of Effusion, the rate of effusion of a gas is inversely proportional to the square root of its molecular weight.[4] The small leak in the reactor would purge out more hydrogen gas, due to its smaller molecular mass, than the carbon monoxide. The rate of gas effusion is approximately 3.7x greater for hydrogen gas than that of carbon monoxide.

$$\frac{Rate\ H_2}{Rate\ CO} = \sqrt{\frac{MM\ CO}{MM\ H_2}} = \sqrt{\frac{28.010\ g/mol}{2.016\ g/mol}} = \mathbf{3.727}$$

More syn-gas would be added to maintain the 90 psig reaction pressure, and as this cycle continues, the atmosphere inside the reactor becomes hydrogen deficient, while allowing a continuous purge of gas through the reactor.

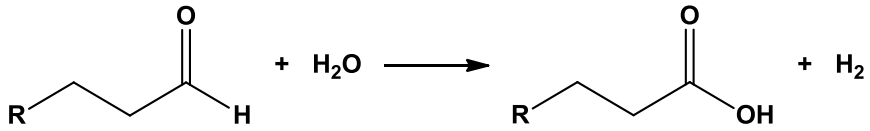
Once the ideal gas mixture was achieved (either mostly or entirely carbon monoxide), the aldehyde-water shift reaction could start. Le Chatelier's principle states that if a chemical equilibrium is disturbed, then the components of the equilibrium shift in a way to counteract the imposed disturbance and a new equilibrium is established.[5] Thus, purging out hydrogen gas, which inhibits the reaction, from the reactor headspace would help drive the aldehyde-water shift reaction. Similarly, the purging of the hydrogen gas via the leak could also prevent any back hydrogenation of heptanoic acid to possibly reform heptanal.

It is also believed that the presence of too much alkene in the reaction solution also hinders the aldehyde-water shift reaction. For the tandem hydrocarboxylation reaction, alkene is necessary for the first phase to produce the aldehyde needed for the second phase. However,

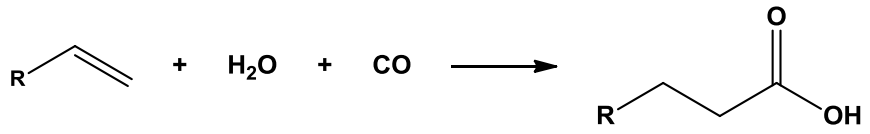
given that an alkene is likely to coordinate stronger to a rhodium center than an aldehyde, the available coordination site would be blocked if too much alkene remained. Thus, both the alkene and H_2 gas levels need to be reduced to initiate the aldehyde-water shift catalysis.

4.3 Thermodynamics, Proposed Mechanism, and DFT Calculations

The thermodynamics of aldehyde-water shift catalysis was studied, and the reaction is favorable. The enthalpy of reaction is exothermic (ΔH_{rxn} = – 9.6 kJ), entropy is increasing (ΔS_{rxn} = +51.9 J/mol*K), and the Gibbs free energy at 90°C is spontaneous (ΔG_{rxn} = –28.4 kJ/mol).



Aldehyde-Water Shift reaction
ΔH_{rxn} = –9.6 kJ/mol (–2.3 kcal/mol)
ΔS_{rxn} = +51.9 J/mol*K
ΔG_{rxn} (@ 90°C) = –28.4 kJ/mol (–6.8 kcal/mol)



Tandem Hydroformylation/Aldehyde-Water Shift (Hydrocarboxylation)
ΔH_{rxn} = –166.9 kJ/mol (–39.9 kcal/mol)
ΔS_{rxn} = –296 J/mol*K
ΔG_{rxn} (@ 90°C) = –59.3 kJ/mol (–14.2 kcal/mol)

Figure 4.6 Thermodynamics of the Aldehyde-Water Shift and tandem hydrocarboxylation reactions.[3]

Each of these values suggest that the aldehyde-water shift catalysis is possible, and the results seen[3] were not just a glitch in the GC-MS software or an oxygen contamination of the reaction solution. When the thermodynamics are viewed for the tandem hydroformylation / aldehyde-water shift reaction, the enthalpy of reaction is exothermic (ΔH_{rxn}= – 166.9 kJ), entropy is

decreasing (ΔS_{rxn} = –296 J/mol*K), and the Gibbs free energy indicates at 90°C it is spontaneous (ΔG_{rxn} = –59.3 kJ/mol).

The only other chemical reaction that is similar is the well-known water-gas shift reaction, hence the reason for naming our reaction the aldehyde-water shift reaction. The process uses a catalyst to react carbon monoxide gas and water forming carbon dioxide and hydrogen gases.[6] Our aldehyde-water shift reaction is still significantly different since it uses an aldehyde in place of the carbon monoxide gas, representing a far more difficult reaction.

The mechanism for the aldehyde-water shift reaction, proposed by Professor Stanley, is shown in the figure below.

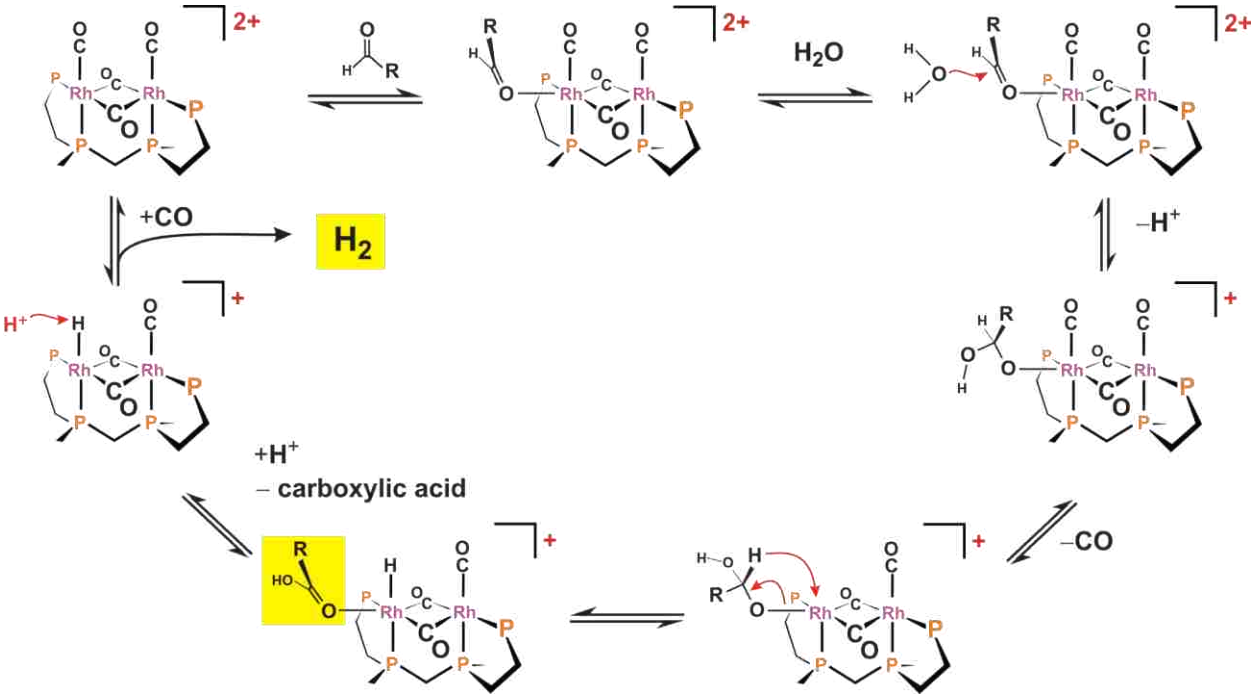


Figure 4.6 The proposed mechanism of the Aldehyde-Water Shift catalysis cycle.

This mechanism shares one dirhodium complex with the hydroformylation mechanism in acetone (Figure 1.7), [*rac*-$Rh_2(\mu\text{-}CO)_2(CO)_2$(et,ph-P4)]$^{2+}$. This will be called the "nexus complex"; the point where the hydroformylation catalytic cycle crosses over with the aldehyde-

water shift catalytic cycle. From the nexus complex, the aldehyde oxygen is coordinated to one of the unsaturated $16e^-$ Rh(+1) centers. Due to the donation by aldehyde's oxygen atom to the rhodium, the carbon's electron density is lowered, thus initiating a nucleophilic attack by H_2O. The loss of a proton from the water molecule causes aldehyde-water ligand to change from neutral to anionic (due to forming an alkoxide ligand), thus making the overall complex monocationic. The additional loss of a terminal carbonyl ligand opens up a binding site for a β-hydride elimination to occur, which generates the carboxylic acid and terminal hydride ligand on the rhodium center. Rhodium is not oxophilic and will readily dissociate the carboxylic acid. The proton (lost during the splitting of the water molecule) can then attack the terminal hydride ligand (protonation of a relatively basic ligand), which releases molecular hydrogen regenerating the dicationic complex. Finally, the carbonyl previously lost can recoordinate to the rhodium center, reforming the dicationic nexus complex. The suggested rate determining steps for this mechanism are either the coordination of the aldehyde to the dirhodium complex or the deprotonation (splitting) of the water molecule, but further study is needed to be certain.

Past researcher, Zakiya Wilson, performed Density Functional Theory (DFT) calculations using Gaussian 98 on the complex $[rac\text{-}Rh_2(\mu\text{-}CO)_2(CO)_2(me,me\text{-}P4)]^{2+}$. This complex (which replaced the ethyl and phenyl groups on the tetraphosphine ligand with methyl groups) was used as a theoretical analog for studying the proposed nexus complex for the aldehyde-water shift reaction, $[rac\text{-}Rh_2(\mu\text{-}CO)_2(CO)_2(et,ph\text{-}P4)]^{2+}$ in order to simplify the calculations while having minimal effects on the results.[7] The lowest unoccupied molecular orbital (LUMO) diagram for this complex is shown below (Figure 4.7). The top and bottom images are two separate views of the same complex.

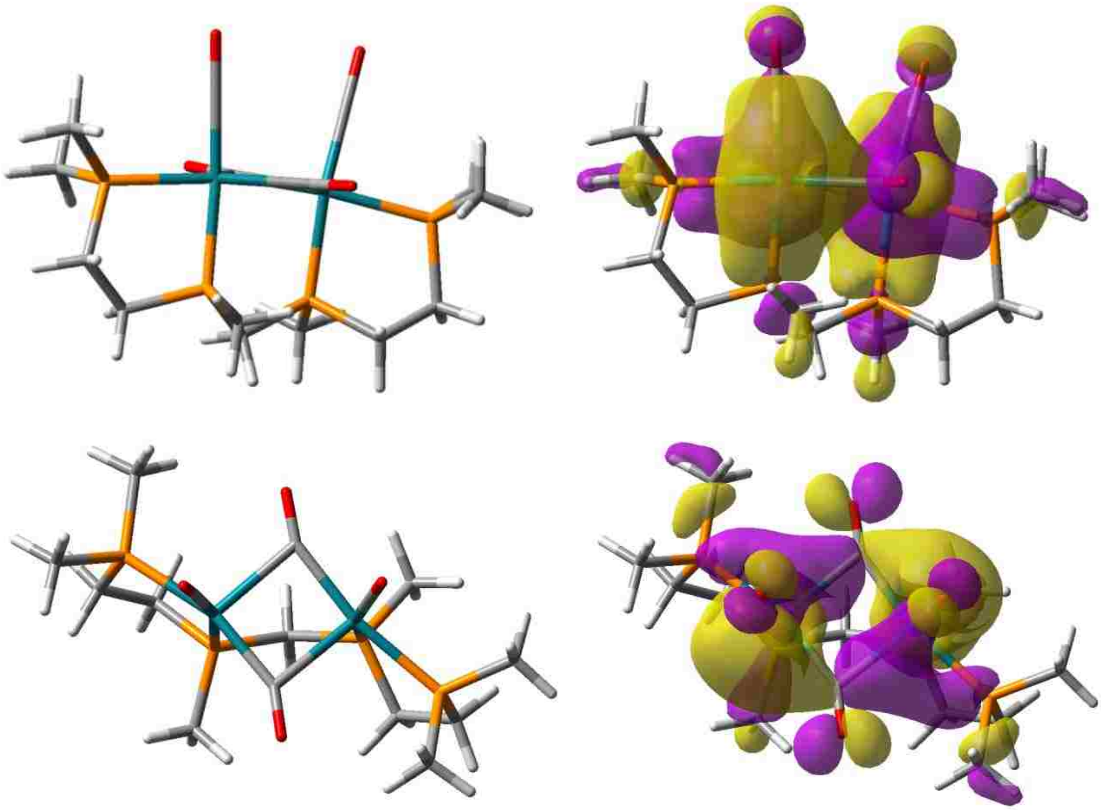


Figure 4.7 Gaussian 98 DFT LUMO calculations for [*rac*-$Rh_2(\mu\text{-}CO)_2(CO)_2$(me,me-P4)]$^{2+}$. (color coding for stick diagrams: Rh = blue, P = orange, O = red, C = grey, H = white)

The LUMO is composed of an empty Rh p_z orbital (the xy plane defined by the terminal CO ligands and the two internal phosphines) strongly bonding with the π^* molecular orbitals for both the terminal and bridging carbonyls.

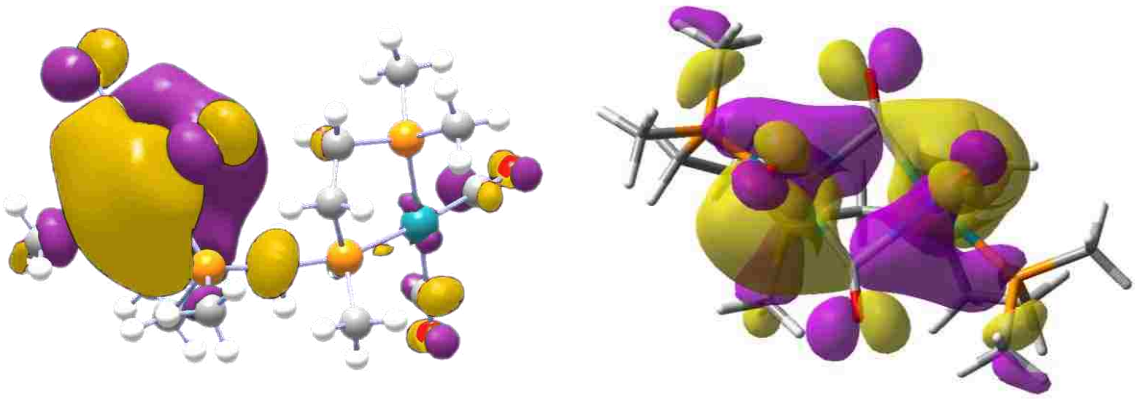


Figure 4.8 Gaussian 98 DFT LUMO calculations for the open (left) and closed (right) modes of the dirhodium tetracarbonyl catalyst complexes.

The unification of the four CO *p** orbitals (the LUMO regions) is made possible by the bridging CO ligands between the two rhodium centers, as shown in Figure 4.8. The closed mode of this complex, [*rac*-$Rh_2(\mu\text{-}CO)_2(CO)_2$(me,me-P4)]$^{2+}$, has a stabilized LUMO that is 0.8 eV lower in energy than its opened mode, [*rac*-$Rh_2(CO)_4$(me,me-P4)]$^{2+}$.[8]

The combined effects of the cationic rhodium centers and the bonding involvement of the carbonyl ligands, bridging and terminal, effectively increase the electron accepting ability of this catalyst complex. This will allow the aldehyde to more easily coordinate to one of the rhodium centers. This electron accepting ability also pulls electron density from the aldehyde to the rhodium, thus promoting the electrophilic attack of the water on the aldehyde. Experimental results by David Aubry agree with these findings given that the opened-mode of the tetracarbonyl complex, [*rac*-$Rh_2(CO)_4$(et,ph-P4)]$^{2+}$, was not capable of initiating aldehyde-water shift catalysis when placed in a similar 30% water-acetone solution, heated/stirred, then pressurized with CO gas.[8] The use of H_2 gas to form the closed-mode of the catalyst structure is crucial in the initial phases of the reaction. But H_2 also hinders the aldehyde-water shift catalysis, hence the need for the continuous gas purge as mentioned previously.

The enhanced electron accepting ability of the closed-mode tetracarbonyl catalyst complex also increases the bonding strength of the alkene coordination if there is too much remaining in the reaction solution. This means that the alkene can block coordination of the aldehyde to the catalyst. Similar to the concentration of H_2 gas, the alkene needs to be depleted in order for the aldehyde bind to the catalyst and initiate the aldehyde-water shift catalysis cycle. Given that the hydroformylation process consumes equivalent amounts of alkene and H_2 gas, as an alternative to the reactor gas leak, it should also be possible to initiate the aldehyde-water shift catalysis by starting the hydroformylation process then switching the syn-gas (H_2:CO) feed to a

pure CO gas feed at a specific time so that the H_2 present in the reactor's headspace and the reaction solution is depleted at the same time the alkene is depleted, though getting the timing of the switch was rather tricky.

4.4 Past Aldehyde-Water Shift Experiments

David Aubry was responsible for much of the previous work investigating the aldehyde-water shift catalysis and the conditions necessary to duplicate the results.[8] To date, the initial few accidental heptanoic acid productions (due to the gas leak in the autoclave) have the highest turnover numbers and highest turnover frequency, though David Aubry was able to replicate the results to some extent.

The original discovery of the aldehyde-water shift catalysis involved the accidental tandem hydrocarboxylation experiment. The reaction conditions used were 1000 eq 1-hexene, 1mM catalyst, 90°C, 90 psig H_2:CO, 30% water/acetone catalyst solution, and 1000 rpm stirring (Figure 4.9).[3] The conditions that are somewhat unknown are the length of soaking time, exact gas leak rate, and location of the autoclave's gas leak. It is currently unknown to what degree these last few conditions affected the results, but under these conditions, a gas leak was absolutely required to initiate the production of heptanoic acid from the heptanal (produced from 1-hexene in the same reaction solution).

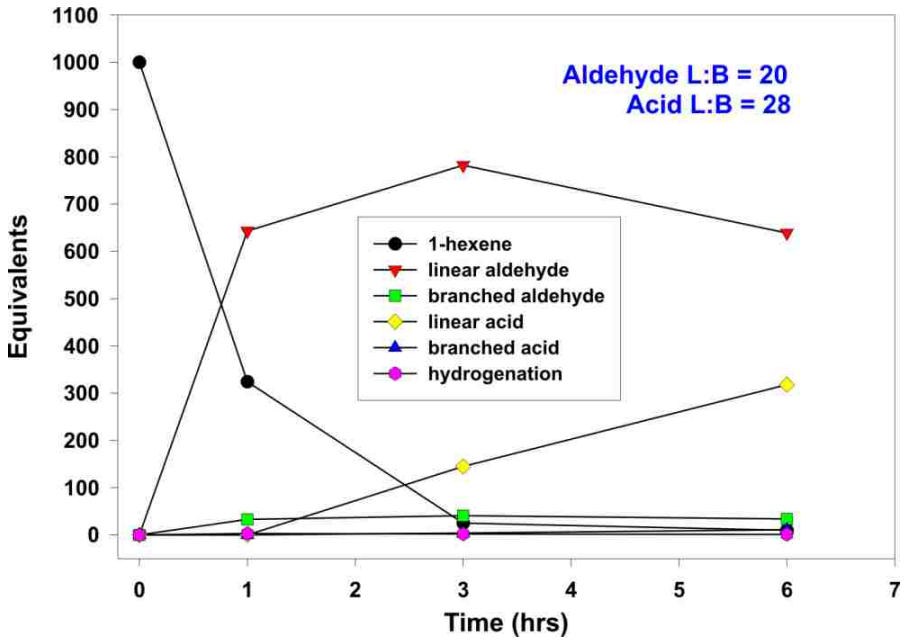


Figure 4.9 The initial tandem hydrocarboxylation reaction by Novella Bridges.[3]

Results showed that after 1 hr, the hydroformylation reaction had completed 675 turnovers, resulting in 325 eq of 1-hexene and 650 eq of heptanal in solution. By the 3 hr mark, 150 eq of heptanoic acid had been produced, almost all of the 1-hexene had been depleted, and 800 eq of heptanal remained. By the final sample at the 6 hr mark, almost all that remained in the reaction solution was 650 eq heptanal and 300 eq of heptanoic acid. The regioselectivity (L:B ratio) of carboxylic acid was actually higher than the L:B ratio of the originally synthesized aldehyde product. This is likely due to the greater difficulty of the branched aldehyde to coordinate to the catalyst. Once the gas leak was detected in the autoclave, it was repaired, but this also caused the production of heptanoic acid to cease.

Based on Prof. Stanley's suggestions, Novella Bridges attempted to replicate the generation of heptanoic acid in a well-sealed autoclave by switching the feed gas during the hydroformylation reaction. A 30% water/acetone hydroformylation run was started for 10 minutes, then stopped the H_2:CO gas feed, flushed the reservoir with pure CO gas, and opened

the CO gas feed to the autoclave. This successfully allowed the aldehyde-water shift catalysis to take place without the presence of a gas leak in the reactor.

David Aubry's work sought to continue the investigation into the reaction conditions required to initiate the aldehyde-water shift catalysis. Initially he attempted a similar method to Novella Bridges, only switching the reaction feed gas from syn-gas to pure CO at the ideal time, which he later determined to be approximately 10 minutes of hydroformylation reaction. This would allow the remaining 1-hexene to react with the remaining H_2 in the reaction solution and head space, in order for them both to be consumed evenly until completion. The conditions used in the first 10 minutes were identical to those used for hydroformylation reactions.

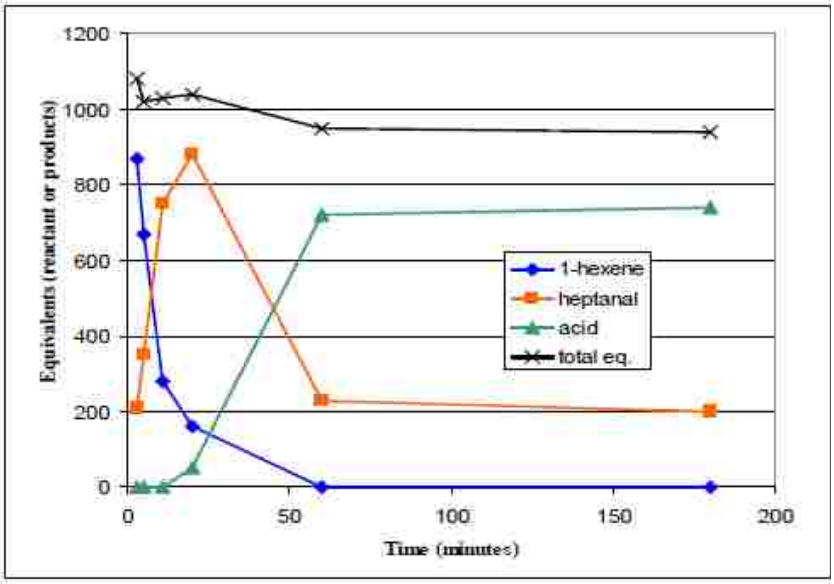


Figure 4.10 Quantitative GC Analysis of David Aubry's Hydrocarboxylation Experiment.[8]

The reaction was a success. The results showed that the initial 10 min TOF hydroformylation step was approximately 75 min^{-1}, as reflected by syn-gas consumption, with a regioselectivity of 28:1 L:B ratio. After the first 10 min of reaction, the gas feed was switched to pure CO gas (just as previously done). The resulting aldehyde-water shift step had an initial rate of 28.3 min^{-1} (via GC analysis) with a regioselectivity of 60:1 L:B carboxylic acid ratio.

The tandem hydrocarboxylation reaction was not as reproducible as the standard hydroformylation reaction performed by our research group. While in all cases some of the alkene charged in the reactor was converted via hydroformylation to heptanal, approximately 25% of these reactions (where the gas switch was performed at 10 min) failed to produce any heptanoic acid, while the other 75% produced approximately 700 turnovers of heptanoic acid, as shown in Figure 4.10. The inconsistencies indicated that the conditions being used were not yet optimized, but this does not explain why reactions only showed either high turnover values or almost no turnovers without any intermediate results. Regardless, it is still believed that the conditions necessary for this reaction to be initiated are very specific.

David Aubry also attempted the aldehyde-water shift catalysis as the direct aldehyde to carboxylic acid, in order to further investigate the conditions necessary to initiate and optimize the mysterious reaction. The dirhodium catalyst precursor, [rac-Rh_2(nbd)$_2$(et,ph-P4)](BF_4)$_2$, was soaked under 1:1 H_2/CO at 90°C with stirring (assumed 20 min soaking time but unknown) to generate the active catalyst. Then, the feed gas was switched to pure CO gas, and a needle valve was attached to the reactor to employ a continuous purge of the reaction vessel. A purge rate of 4-5 psig/min was able to initiate the aldehyde-water shift catalysis and resulted in a conversion of 75% of the heptanal reagent into heptanoic acid with a TOF of 16.7 min^{-1} and undetectable side products. The direct aldehyde-water shift reaction is extremely sensitive to the reaction conditions, timing, and purge rates.

Since 2004, a few researchers have attempted to replicate these results, however no one has been able to yield any production of heptanoic acid using either 1-hexene (via tandem hydrocarboxylation) or heptanal (using direct aldehyde-water shift) until my results described in the following sections.

4.5 Controlled Conditions for Aldehyde-Water Shift Experiments

The difficulty in getting the aldehyde-water shift catalysis to work is most likely tied into very specific reaction conditions needed. Both Aubry and Bridges found that running the initial hydroformylation reaction for 5 min or 15 min would not produce any carboxylic acid. Since that time, the design of the autoclave has greatly changed (Mark II autoclave design) as well as the gas manifold design. Through extensive testing, it has been determined that the new autoclave design has performed equal to or better than the previous design in hydroformylation test runs, so the issue must lie in the exact conditions to which the reaction solution is subjected. All reactions run in the autoclaves control/record (via computer controller) the reactor pressure, reactor temperature, gas reservoir pressure, gas reservoir pressure, and stirring speed, and if using the Mark III autoclave design, the conditions of gas flow rate into the reactor and from the reactor can also be controlled.

Using a combination of these recorded values and GC-MS data collected via reaction solution sampling, the tandem hydrocarboxylation reactions (hydroformylation reaction then switched to aldehyde-water shift conditions during reaction) were monitored/tested on the following conditions: hydroformylation reaction results (including number of turnovers, initial turnover frequency, and reaction time), catalyst solution soaking, reactor vessel purge, reaction gas feed (gas composition and flow rate), controlled reactor vent/purge rate, olefin concentration remaining during reaction switch, catalyst batch, reactor number, additives, and aldehyde-water shift reaction results (number of turnovers, turnover frequency, and reaction time). During the performance of the straight aldehyde-water shift reaction (using reagent aldehyde to produce carboxylic acid and hydrogen gas) the same reaction conditions above were used, though

conditions such as hydroformylation reaction results and remaining olefin concentration were not applicable.

The hydroformylation reaction results are very important to consider when performing the tandem hydrocarboxylation reactions. The timing of the syn-gas feed being switched to pure CO gas was crucial in being able to achieve the ideal amounts of remaining hydrogen gas and olefin so that they deplete each other evenly and completely. The amount of hydroformylation is also critical for determining when the reaction gas switch happens. The number of turnovers is important because, similar to controlling the moment of gas switch using time, it is often a more consistent method of ensuring the proper amount of remaining alkene in the reaction solution. Since the turnover frequency may vary between catalyst samples, switching times may need to be adjusted to achieve optimum results for aldehyde-water shift catalysis.

The catalyst solution soaking, as previously mentioned, is the 20 minute time span where the 30% water-acetone catalyst solution is heated and stirred under pressurized H_2:CO gas in order to generate the active form of the catalyst species *in situ*. Without any H_2 gas, the catalyst precursor, [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$, will not activate, and none of the reactions performed will work. Upon exposure to H_2:CO gas, almost immediately the catalyst precursor begins to displace the norbornadiene ligands in favor of CO ligands, followed by the formation of the closed-mode dirhodium catalyst species. However, heating is required to shift the bridging hydride into the terminal position, which is then capable of reacting with the alkene upon pressure injection into the catalyst solution. The 20 min span is stretched out to ensure the autoclave temperature stabilizes properly (at 90°C). For almost all reactions soaking was performed, although there were a few times it was not, in order to show that it was a necessary

process for the straight aldehyde-water shift reaction, since the reaction does not use H_2 gas, but it is required for the catalyst to activate.

In all cases, the arms and attached hoses of the autoclave reactor were purged during the gas switch to better replicate the conditions experienced by the original Mark I autoclave which had no reactor arms and therefore, less headspace. This additional space filled with pressurized H_2:CO would not have been a factor in the previous results, and so to have the reaction conditions as identical as possible using the Mark II and Mark III autoclave designs, the reactor arms and attached hoses needed to be purged. In some experiments, the reactor vessel was purged for some experiments between the soaking process and initiating the controlled gas flow/purge (the start of the aldehyde-water shift reaction step). If this was not done, then the reactor vessel was left to remove the remaining hydrogen gas via hydroformylation with the remaining olefin or to continuously purge during reaction (if a gas flow was initiated). Each option was explored during these investigations.

The reaction gas composition and flow rate is the most important variable set that was tested during all the experiments on the aldehyde-water shift catalysis. Several different kinds of gases and mixtures were used to pressurize the reactor and flow through the reaction solution. The most common gases tested were pure and mixture compositions of CO, H_2, and/or Ar. Experiments using reaction conditions at 90 psig and 50 psig were also used, in the hopes that a reduced pressure would promote the production of H_2 gas during the aldehyde-water shift catalysis. Given that all of the previous successful attempts at the aldehyde-water shift reaction (both as a standalone reaction and as part of a tandem reaction) utilized standard hydroformylation reaction conditions, most of the experimental conditions that will be tested are modifications of those conditions. One significant difference used for gas flow rates is the use of

standardized units. Bridges and Aubry used the units of "psig per minute" to record the flow rate of gases through their reaction solution. Using the new mass flow controller and the I/P-BPR, the new flow rates are recorded as units of standard cubic centimeters per minute (sccm). The problem with using non-standardized units (psig/min) is that if the volume of the source gas reservoir is ever changed (whether using a different gas manifold or using a large gas cylinder for the source) then the psig/min values are not transferrable or consistent. Using sccm units to record the flow rate of the gases keeps the values constant and accurate regardless of the gas reservoir or cylinder's volume. For our autoclave setup, the volume of the gas reservoir used for the Mark III flow control autoclave was 318 cm^3 (close to the volume used in the original Mark I autoclave design). The conversion of units for the gas flow rate is approximately "10 sccm = 0.47 psig/min". This would be extremely valuable when published, and if there was any hope in trying to duplicate these results using a different autoclave system setup.

The remaining alkene concentration in the reaction solution at the time of the reaction gas switch (the start of the aldehyde-water shift step) is an important variable to know, and it is similarly tied in with the number of hydroformylation turnovers calculated via pressure drop. This is just another way to determine the exact point when the gas switch should happen. If the amount of alkene in the reactor is too high at the point of the gas switch from syn-gas to pure CO gas, then it will inhibit coordination of the aldehyde to the catalyst. If there is no continuous flow/purge of pure CO through the reactor, then the reaction will also not work due to hydrogen gas still being present even after all the alkene is consumed. With a continuous gas purge through the reactor, it may be possible for the reaction to succeed if the olefin concentration is equal to or lower than the H_2 present in the system capable of performing hydroformylation. We know the gas switch should happen under hydrogen deficient conditions, but it is currently

unknown what amount of hydrogen gas remaining (if any) is ideal to initiate the aldehyde-water shift catalysis.

The catalyst batch and reactor number are just two conditions monitored in the event that a contamination could possibly be affecting the results of the catalytic runs. If a specific set of reaction conditions were able to successfully run one time and not on another, these two variables could be checked for any differences or chances. Considerations like this may have been unnecessary, but given the difficulty in the past of reproducing the aldehyde-water shift catalysis, every angle was considered when recording these aldehyde-water shift investigations. The additives variable was just in case any extra chemicals were included in an experimental trial to see if it promoted or diminished the success of the aldehyde-water shift catalysis. The use of an additive in our work is very uncommon, and most of those times the "additive" was heptanoic acid, to see what effect it had on the catalytic solution prior to the injection of 1-hexene or heptanal reagents.

Finally, the results for the aldehyde-water shift reaction, including the number of turnovers, turnover frequency, and reaction time, were recorded to determine the success or failure of the tested set of conditions. Ideally, we would like to get the number of turnovers and the turnover frequency as high as possible, while limiting the reaction time to only a few hours. Experimental trial reaction times ranged from 3 hrs to 18 hrs, while most reaction times were approximately 6 hrs. In all cases, the Mark III autoclave reactor design was used to allow for a controlled purge of gas through the reaction vessel.

4.6 Aldehyde-Water Shift Catalysis Experiments

The experiments run on the aldehyde-water shift reaction (both as a tandem hydrocarboxylation reaction and as a direct aldehyde to carboxylic acid) mostly focused on

altering gas switching times, reactor pressure, reaction gas composition, and gas flow rate. In all cases the reagent used (whether 1-hexene or heptanal) was always 1000:1 equivalents to the catalyst precursor used, [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$. All reactions used the Mark II or Mark III autoclave designs to pressurize the catalyst solution (in 30% water/acetone solution) while heating to 90°C and stirring at 1000 rpms. The experiments were deemed successful if ≥ 0.02 M heptanoic acid concentration (greater than 22.5 turnovers for the aldehyde-water shift catalysis) was detected in the reaction solution via GC-MS sample analysis. This amount was selected after exposing the reaction solution to a 3:1 CO/O_2 gas mixture for 15 minutes, which resulted in the production of ≤ 0.02 M heptanoic acid (a high estimate for the possible oxygen contamination effects during sampling).

4.6.1 Activation of catalyst precursor using CO gas

A few experiments were performed to attempt an unlikely activation of the catalyst precursor, [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$, using pure CO gas and H_2O. In no case was any hydroformylation or aldehyde-water shift activity seen via GC-MS analysis. This agrees with past research that indicated H_2 gas is necessary for the catalyst to form the closed-mode species, and CO gas alone is not enough. However, high-pressure NMR experiments by Darina Polakova have indicated that some activated catalyst species is formed under exposure to pure CO gas and water.[9] This has been attributed to a small amount of H_2 gas being formed via the water-gas shift reaction (CO gas and H_2O reacting to form H_2 and CO_2 gases). While spectroscopically some of the activated catalyst species is formed, the amount is far too low to perform much hydroformylation or any aldehyde-water shift catalysis. The overall result determined that in all reactions involving the aldehyde-water shift catalysis, prior soaking of the catalyst solution using syn-gas (H_2:CO) with heating and stirring is necessary.

4.6.2 Tandem hydrocarboxylation experiments using 90 psig CO gas

The following series of experiments were attempted performing the aldehyde-water shift catalysis as tandem to the hydroformylation reaction. After the soaking of the catalyst solution, 1-hexene was pressure injected, initiating the hydroformylation catalysis. The reaction time used for the hydroformylation step was varied between 10 minutes and 65 minutes (5 minute intervals), thus altering the concentrations of produced heptanal and remaining 1-hexene in the solution. The gas feed was then switched to 90 psig CO in order to allow the remaining H_2 gas in the reaction vessel to be consumed along with the remaining 1-hexene in solution, while still maintaining a pressurized atmosphere. After the gas switch, a continuous purging of the reactor was initiated (in some experiments) with flow rates ranging between 0 – 50 sccm (10 sccm intervals), at 100 sccm, at 150 sccm, and at 200 sccm. Some of these reaction conditions would hopefully initiate the aldehyde-water shift catalysis.

Aubry's reaction conditions were attempted several times (gas switch to pure CO after 10 min hydroformylation reaction time), however no heptanoic acid was ever produced. While there is some controversy as to the TOF achieved by Aubry's experiments, as his tandem hydrocarboxylation data shows, for the hydroformylation step, an initial TOF of 75 min^{-1} (Figure 4.10 shows an initial TOF) while his other hydroformylation experiments show an initial TOF of 30 min^{-1} (Table 2.1, which is more similar to the frequency seen during reaction runs by Alexander, Polakova and myself). Due to this uncertainty, a series of experiments tested several gas switch times between 10 min and 65 min (using 5 minute intervals). The conditions yielding some heptanoic acid production was the gas switch at 45 and 50 minutes (only resulting in ~35 turnovers), which happened to be approximately 800 turnovers of conversion to aldehyde,

similar to Aubry's findings if the gas-switch point is determined by TON instead of reaction time.

When attempting using a continuous gas purge to initiate the aldehyde-water shift catalysis, the experiments ran the hydroformylation step between 40 – 120 min reaction times (10 and 15 minute intervals) of completion before a CO gas purge was initiated with flow rates of 10 – 50 sccm (10 sccm intervals), at 100 sccm, at 150 sccm, and at 200 sccm. It is believed that gas-switch times after the 45 – 50 min mark (more importantly after 800 turnovers), the remaining 1-hexene is too low in concentration to deplete the remaining H_2 to a level low enough to initiate the aldehyde-water shift catalysis. However, initiating a controlled CO gas purge would maintain the autoclave pressure while removing any H_2 present in the vessel and any that may be produced by the aldehyde-water shift reaction. Successful purge rates by past researchers during the accidental reactor leak of syn-gas are ~0.17 psig/min (equivalent to ~5 sccm), a syn-gas purge of 2 – 5 psig/min (equivalent to 43 – 106 sccm), and for a direct aldehyde to carboxylic acid conversion, a CO gas purge of 4 – 5 psig/min (equivalent to 85 – 106 sccm) following catalyst solution soaking.[3, 8]

Despite several attempts using the various gas-switch times and purge rates, the most successful experiments used a 35 sccm CO gas flow rate initiated after ~950 turnovers hydroformylation (120 min reaction time), resulting in 45 turnovers of heptanoic acid after 4 hrs. The high conversion rates of heptanal previously achieved were not seen. The only reaction conditions that produced heptanoic acid used a gas flow rate almost 3 times lower than Aubry's flow rate for CO gas.

In the case that some of the previous catalytic runs truly experienced an initial TOF of 75 min^{-1}, it would be possible that a small amount of catalyst degradation could be hindering the

initiation of the aldehyde-water shift step due to the longer successful gas-switch times (40 min vs. 10 min). A few experiments, a 1-hexene/heptanal mixtures were used as reagents (50/950 eq, 150/850 eq, and 200/800 eq) in an attempt to perform a small amount of hydroformylation (thus ensuring all the same catalyst complexes formed for the hydroformylation reaction), then be able to perform the gas-switch to pure CO at the original 10 min mark with similar amounts of 1-hexene remaining in solution. In most cases, the gas was simply switched to pure CO, but in a few cases, a controlled CO gas purge was used. Unfortunately, all of the 1-hexene/hepanal mix reagent experiments failed to perform any aldehyde-water shift catalysis.

4.6.3 Direct aldehyde-water shift experiments using 90 psig CO gas

Based on previous work, it is also possible to perform the aldehyde-water shift reaction as the direct conversion of aldehyde (heptanal) to carboxylic acid (heptanoic acid).[8] The catalyst solution underwent the soaking process using syn-gas while heating and stirring. In previous experiments, it is unclear as to whether or not the heptanal was added to the pressure inject reservoir (added after catalyst soaking) or added to the reaction vessel prior to soaking, so both scenarios were tested. After soaking, the heptanal reagent was added to the catalyst solution (if not already done so), and the reaction gas feed was switched to 90 psig CO gas with a controlled purge rates ranging between 0-60 sccm (10 sccm intervals), 100 sccm, 150 sccm, and 200 sccm.

None of these reaction conditions tests successfully produced any heptanoic acid. This furthered our belief that there were more factors affecting the initiation and success of the aldehyde-water shift catalysis than previously believed.

4.6.4 Direct aldehyde-water shift experiments using 50 psig CO gas

Experimentation continued to attempt optimization of the reaction conditions. Due to the aldehyde-water shift catalysis generating an equivalent amount of heptanoic acid and H_2 gas

from heptanal and water, lowering the pressure inside the reactor should favor the products in the reaction equilibrium and increase the number of turnovers. High pressure is more important for hydroformylation since it consumes gases, but this reaction should not require high pressures to force gas into the solution. Although the Mark III autoclave design has a high pressure condenser attached, the reaction solution should not be allowed to boil, thus ensuring a constant water/acetone ratio. The boiling point of the catalyst solution was found to be approximately the boiling point of its main component, acetone. Using the vapor-pressure curve for acetone,[10] it was determined that at 90°C the catalyst solution would begin to boil if the pressure dropped to 42 psig. For these experimental reaction runs, 50 psig was used to maximize the pressure lowering effect while safely keeping the solution in the liquid phase. Similar conditions to the previous aldehyde-water shift experiments were tested using an autoclave pressure of 50 psig CO after venting to the operating pressure from the soaking process.

The lowering of the autoclave pressure did successfully produce some heptanoic acid for the experiments where a 20 sccm flow rate using 50 psig CO was initiated following the catalyst solution soaking. The tests where the aldehyde was added directly to the reaction solution prior to soaking yielded more turnovers (45 TON) than if pressure injected (33 TON), so these conditions are certainly a step in the right direction. This gas flow rate is far lower than those used by Aubry (4 – 5 times lower), but when similar flow rates were used, no increase in heptanoic acid concentration could be detected. Due to the positive results seen for these experimental aldehyde-water shift conditions, the lower reaction pressure was then applied to the tandem hydrocarboxylation reaction.

4.6.5 Tandem hydrocarboxylation experiments using 50 psig CO gas

Based on all the past successful reaction conditions for the tandem hydrocarboxylation and direct aldehyde-water shift reactions, the conditions showing any detectable increase in heptanoic acid concentration were retested using 50 psig CO atmosphere for the aldehyde-water shift step of the tandem reaction. In all cases, the catalyst solution would be activated using the soaking process, followed by the pressure injection of the olefin (1-hexene). The hydroformylation step would continue until the desired amount of 1-hexene was consumed (ranging between 750 – 900 turnovers), then the reactor was vented to 50 psig and the feed gas switched to 50 psig CO (in the cases where a continuous gas purge was used, the flow rate was 20 sccm).

The experiments utilizing a 50 psig pressure for tandem hydrocarboxylation reactions yielded the highest production values of heptanoic acid (150 turnovers) since the results obtained by Aubry and Bridges (700 turnovers). Over half of the experiments performed, where the gas was switched to 50 psig CO after most of the 1-hexene was consumed and using no continuous gas purge, successfully generated heptanoic acid. The experiments with the gas-switch performed at 850 and 950 turnovers for the hydroformylation reaction produced between 80 – 150 turnovers of heptanoic acid. In this case, just like all other reaction results, only the linear carboxylic acid (heptanoic acid) was produced with no detectable amount of branched carboxylic acid (2-methylhexanoic acid). Unfortunately no tandem hydrocarboxylation reaction attempt using 20 sccm continuous purge of 50 psig CO gas was able to successfully perform any aldehyde-water shift catalysis.

4.6.6 Aldehyde-water shift experiments using argon gas

In Chapter 2 it was discussed that too high of a CO gas pressure could result in the deactivation and degradation of the catalyst complex (Figure 2.2). The nexus complex, [*rac*-$Rh_2(\mu\text{-}CO)_2(CO)_2$(et,ph-P4)]$^{2+}$, is proposed to be the active catalyst for aldehyde-water shift, and DFT calculations indicate that the coordination of another carbonyl ligand can crack open the closed-mode species. Since this catalysis does not consume any net amount CO gas, the reaction may be improved by the use of an inert gas (pure or mixed with CO gas) to initiate the production of heptanoic acid and H_2.

A series of experiments were conducted for the direct aldehyde-water shift reaction. Following the soaking of the catalyst solution, the heptanal reagent was pressure injected into the activated catalyst solution, followed by a continuous 50 psig Ar gas purge at flow rates ranging between 0 – 60 sccm. Unfortunately, these conditions yielded only minimal success. The only successful reaction conditions used a 20 sccm gas flow and only performed 22 turnovers after 5 hrs of reaction time. The argon gas flow experiments also caused the unexpected side effect of darkening the reaction solution color from a rich orange-red to a dark red-brown color. For lower flow rates (0 – 30 sccm), the color darkening would happen around between 60 – 120 min of reaction, while for the higher flow rates (40 – 60 sccm), the color darkening happened at or before 30 min of reaction. No detectable amount of heptanoic acid was seen produced after the solution's color change. It is believed that this color change is due to the formation of a new catalyst degradation rhodium complex caused by the removal of CO gas from the autoclave thus destabilizing the tetracarbonyl nexus complex. Attempts to grow/collect crystals from the organic layer (for x-ray crystallography analysis) of the post-reaction catalyst complexes failed.

Attempts using FT-IR spectroscopy via the ReactIR autoclave to gain insight into the new degradation complex also failed due to the significant loss of solvent during purging.

Due to this new catalyst deactivation issue, the previous argon gas flow experiments were repeated using argon/CO gas mixtures (2:1 and 9:1 ratios) were used for direct aldehyde-water shift reactions. The small amount of CO gas present throughout the reaction should prevent the deactivation seen from the previous argon gas flow, and the argon gas keeps the overall reactor pressure higher without having to risk the possible degradation from excess CO. While the argon/CO gas mixtures did succeed in preventing the dark color change seen previously, none of the experiments produced any detectable amounts of heptanoic acid. Overall, since only one of the argon gas experiments was capable of producing a small amount of heptanoic acid under aldehyde-water shift conditions, it is not being considered as a viable route to optimizing this catalysis.

4.6.7 Tandem hydrocarboxylation experiments using a syn-gas (H_2:CO) purge

The discovery of the aldehyde-water shift catalysis was due to an accidental gas leak in the autoclave reactor, resulting in the slow purge of syn-gas. It was believed that due to Graham's law of effusion, the lighter H_2 gas was leaving the reactor faster than the heavier CO gas, and as the gas feed continued to inject a 1:1 mixture of H_2:CO, the resulting atmosphere inside the reactor vessel was almost pure CO gas. As mentioned previously (Chapter 4.6.2), the only reported successful syn-gas purge rates to initiate the tandem hydrocarboxylation reaction (without using a gas-switch) are Bridges's accidental reactor leak of syn-gas ~0.17 psig/min (equivalent to ~5 sccm) and Aubry's syn-gas purge of 2 – 5 psig/min (equivalent to 43 – 106 sccm).

These reaction conditions were tested several times using either the digital MFC or a needle valve atop the condenser arm (ensuring a continuous purge despite the changing rate of syn-gas consumption) to control the purge rates. Syn-gas purge rates were tested ranging from ~0.45 psig/min (10 sccm) up to ~4.0 psig/min (85 sccm) while maintaining a 90 psig pressure inside the autoclave. In no case so far has any heptanoic acid been produced using a continuous purge of H_2:CO gas.

4.6.8 Overall aldehyde-water shift experimental results

For the first time in 8 years, since Aubry reported his findings in his dissertation,[8] the aldehyde-water shift catalysis (both direct and tandem reactions) was successfully performed using controlled reaction conditions. Replication of past results have been made more difficult due to autoclave and gas manifold design modifications, process controller upgrades, and lack of detailed raw experimental data from previous work. Despite the lower number of turnovers and turnover frequency of these results, they represent the first reproducible, successful attempts at the aldehyde-water shift catalysis using our current generation of the autoclave reactors.

In all cases, the catalyst must be activated *in situ* by placing the catalyst precursor solution ([*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ dissolved in a 30% water-acetone solution) in the autoclave reaction vessel, then pressurizing it with H_2:CO gas with heating (90°C) and stirring for 20 minutes. For the tandem hydrocarboxylation reactions, the best results were achieved by proceeding with the hydroformylation reaction until 75 – 90% of the 1-hexene has been consumed, then followed by the venting of the autoclave to 50 psig and switching the gas feed to 50 psig CO. After allowing the reaction to continue for 8 hrs, 150 turnovers (~0.13 M concentration) of heptanoic acid were detected via GC-MS, with no detectable amounts of the branched carboxylic acid side product. For the direct aldehyde-water shift reaction, the best

results were achieved by maintaining a 50 psig autoclave pressure using pure CO gas and initiating a 20 sccm gas immediately following the catalyst soaking process. These conditions yielded 45 turnovers (0.04 M concentration) of heptanoic acid, as detected via GC-MS, after a reaction time of 6 hrs.

4.7 Conclusions

While the results of this research into the aldehyde-water shift catalysis are far from matching the number of turnovers and turnover frequency seen by Bridges and Aubry, the reproducibility and plethora of variables controlled/monitored are of key importance to finally understanding and optimizing this extremely valuable catalytic process. Given the high number of reaction condition variables controlled and monitored for these experiments, the number of possible combinations is vast. But given its unprecedented nature and the possible applications for this process, the optimization of reaction conditions for the aldehyde-water shift catalysis is definitely a goal worth pursuing.

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CHAPTER 5: EXPERIMENTAL

5.1 Synthesis of Phenylphosphine

In a 500 mL Schlenk flask, dichlorophenylphosphine (55.5 mL, 409 mmol) and 302 mL of t-glyme were added to yield a colorless solution. To a second 1000 mL Schlenk flask, lithium aluminum hydride (19.93 mL, 478 mmol) (aka: LAH) and 517 mL of t-glyme were added to yield a grey solution. Both flasks were cooled to -5°C and maintained at that temperature for at least 30 minutes. The dichlorophenylphosphine solution was then added slowly to the LAH mixture via a large bore cannula at a rate of ~1 drop per second while the temperature maintained below 0°C the entire time. Upon completion of the addition, the reaction mixture is allowed to warm to room temperature and stir at least 1 hour. The phenylphosphine product is removed via a trap-to-trap distillation. Isolated Yield: 80%. ^{31}P NMR: -121 ppm.

5.2 Synthesis of Bis(phenylphosphino)methane (aka: Bridge)

A 500 mL Schlenk flask with a stir bar was charged with phenylphosphine (20.0 g, 182 mmol), dichloromethane (5.91 mL, 92 mmol), and DMF (133 mL) to give a colorless solution (solution A). The solution was placed in an ice bath and allowed to stir for at least 30 min. A potassium hydroxide solution (35.8 g, 638 mmol) (solution B) was then slowly added dropwise to solution A over a 30 min period (minimum) to give an orange/yellow solution with a ppt. The solution was allowed to stir under nitrogen at room temperature until it became colorless with a white ppt. Distilled water (~50 mL) was then added to the solution to dissolve any solid KCl. The product was extracted with pentane (3 x 150 mL) via cannula into a clean Schlenk flask. The pentane/product solution was then heated to 80°C in a water bath under reduced pressure to

remove pentane and impurities, yielding a viscous, slightly yellow product. Isolated Yield: 50%. ^{31}P NMR: -53 ppm (racemic), -54 ppm (meso)

5.3 Synthesis of Chlorodiethylphosphine

A 1000 mL Schlenk flask with a stirbar was charged with Phosphorous trichloride (100.0 g, 730 mmol) and t-glyme (double the volume of PCl_3) to give a colorless solution. A 500 mL Schlenk flask was charged with Diethylzinc (99.3 g, 804 mmol) and t-glyme (double the volume of $ZnEt_2$) to give a colorless solution. Both flasks were then placed in ice baths for ~30 min. With vigorous stirring, the diethylzinc solution was slowly added dropwise via cannula to the PCl_3 solution. After addition, the reaction mixture was allowed to stir at room temperature for 1 hour. The product was then collected via trap-to-trap distillation with heating into a clean pre-weighed Schlenk flask. Yield: ~70%. ^{31}P NMR: 112 ppm (PEt_2Cl product), 66 ppm (PCl_2Et, acceptable in small amounts)

5.4 Synthesis of Diethylvinylphosphine

A 500 mL Schlenk flask with a stir bar is charged with vinylmagnesium bromide (226 mL, 226 mmol) in THF and t-glyme (200 mL) to give a brown solution with a white ppt. A second 500 mL Schlenk flask is charged with chlorodiethylphosphine (25.55 g, 205 mmol) and t-glyme (225 mL) to give a colorless solution. At least 95% of the THF is removed under reduced pressure with heating and stirring. Both flasks are then placed in an ice bath for at least 30 min. The chlorodiethylphosphine solution is then added dropwise via cannula to the vinylmagnesium bromide solution with stirring. The reaction turns light yellow with a white ppt.

The solution is heated to 90°C, and the product is collected into a clean, pre-weighed Schlenk flask via trap-to-trap distillation. Yield: ~85%. ^{31}P NMR: -18 ppm

5.5 Synthesis of et,ph-P4 ligand (mixed *racemic* and *meso*)

A small Schlenk flask with a stir bar is charged with bis(phenylphosphino)methane (1.0 mol eq) (aka: "Bridge") and vinyldiethylphosphine (2.2 mol eq). The solution is then exposed to UV light with stirring for at least 8 hours (generally overnight). The reaction mixture becomes vicous as the reaction occurs. The flask is then placed under reduced pressure with heating (~90°C hot water bath) to remove the excess vinyldiethylphosphine. Yield (mixed *rac*/*meso*): >85%. 31P NMR: -17 ppm (arms), -25 ppm (racemic), -26 ppm (meso)

5.6 Hexane Separation of *racemic* and *meso* et,ph-P4 ligands

Add hexane to the mixed *rac/meso*-et,ph-P4 product, then place in the freezer for at least 6 hours or overnight. The meso product will crystallize out with hexane while the racemic product remains in solution with hexane. The solution layer is transferred into a separate Schlenk flask, leaving behind the meso-product/hexane frozen mixture. The hexane can be removed under reduced pressure. This process is repeated until the product mixture is ≤ 80% racemic.

5.7 Racemization of et,ph-P4 ligand

This procedure can be used to racemize pure meso or racemic et,ph-P4 ligand and return it to the original diastereomer mixture (~52% racemic / 48% meso). The ligand is placed in a Schlenk flask under nitrogen atmosphere. The flask is then heated in an oil bath at 120°C with stirring for 12 hrs or overnight. See Appendix A.14.

5.8 Synthesis of mixed Ni_2Cl_4(et,ph-P4)

The ligand solution, in ethanol, was added dropwise to a rapidly stirring solution of $NiCl_2$ in ethanol and allowed to at least 12 hours or overnight. This mixture was then filtered to remove the orange precipitate, mainly *meso*-Ni_2Cl_4(et,ph-P4). This precipitate was then rinsed three times with ethanol (30 mL portions). The filtrate was then concentrated under vacuum to yield a dark tarry amorphous solid, mainly *rac*-Ni_2Cl_4(et,ph-P4).

5.9 Cyanolysis of Filtrate Residue

A Schlenk flask containing *rac*-Ni_2Cl_4(et,ph-P4) (4.2 g, 6.26 mmol) was charged with 40.83 g NaCN (0.833 mol, 133 equiv.) in 250 mL of water and 100 mL methanol. The solution was allowed to slowly stir for approximately three hours while the solution turned from orange to red. The solution was then charged with 46.1 g (0.94 mol, 150 equiv.) of NaCN, then stirred slowly until all the NaCN dissolves (~30 minutes). The free ligand was then extracted in three 100 mL aliquots of benzene, yielding a light yellow solution. The solution was then passed through a neutral alumina column and the solvent removed to yield 2.00 g of 70% pure rac-et,ph-P4.

5.10 Cyanolysis of *meso*-Ni_2Cl_4(et,ph-P4)

Meso-Ni_2Cl_4(et,ph-P4) (6.9 g) was added to a Schlenk flask with 140 mL degassed deionized water and allowed to stir for 2 hours to yield a dark red solution. A solution of 2.4 g NaCN in 69 mL of water was then added dropwise very slowly (1 drop per 5 seconds) with slow stirring. Following, 138 mL of methanol was then added followed by 24.2 g NaCN and allowed to stir rapidly causing a bright red solution. The free ligand was then extracted with four 100 mL

aliquots of benzene, yielding a bright red solution. The red color is removed by passing the solution through two 12 inch fritted columns of neutral alumina, and the benzene is removed yielding 1.0 g of free ligand, in a 3:1 ratio of racemic to meso.

5.11 Synthesis of $Rh(CO)_2(acac)$

A 250 mL Schlenk flask is charged with $Rh(CO)_2(acac)$ (3.00 g, 11.54 mmol) and norbornadiene (85 mL, 836 mmol) forming a dark green solution. The solution is refluxed at 90°C overnight forming a yellow solution. The solution is filtered, and excess nbd is removed under pressure yielding a yellow solid. The product is then recrystallized by adding THF and hexane and placing the mixture in the freezer overnight. Isolated yield: ~90%. ^1H NMR: 1.2-2.0 ppm (CH_2 of nbd, CH_3 of acac), 3.8-4.0 ppm (CH of nbd), 5.3 ppm (CO-CH-CO of acac), 6.2 and 6.7 ppm (olefinic CH of nbd).

5.12 Synthesis of $[Rh(nbd)_2](BF_4)$

Rh(nbd)(acac) (1 equiv) is dissolved in THF forming a yellow solution, and cooled to -20°C. HBF_4*OEt_2 (2 equiv) is added dropwise with stirring producing a dark red solution. This addition is then followed by the dropwise addition of norbornadiene (4.5 equiv) which produces an orange precipitate. The flask is placed in the freezer for 1 hr 45 min[†], and the precipitate is collected by filtration. The product is washed with ~150 mL of hexane. Isolated Yield: ~90%. ^1H NMR: 1.7 ppm (CH_2 of nbd), 4.3 ppm (CH of nbd), 5.3 and 5.6 ppm (olefinic CH of nbd).

[†]Note: Cool flask 105 min (1 hr 45 min) exactly. Reaction will not complete properly if not left in freezer long enough, however the product may polymerize if left longer than 2 hours.

5.13 Synthesis of [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$

5.13.1 (method #1)

[Rh(nbd)](BF_4) (2 equiv) and >80% *rac*-et,ph-P4 (1 equiv) are dissolved separately in CH_2Cl_2 (~20mL each) and placed in separate Schlenk flasks. The rac-et,ph-P4 solution is added dropwise to the rhodium complex solution with stirring. The CH_2Cl_2 is removed under reduced pressure. Acetone is then added to the solid allowing the pure racemic product to recrystallize. Any meso product will not recrystallize in acetone, and will remain in solution. Isolated Yield: ~85%.

5.13.2 (method #2)

[Rh(nbd)](BF_4) (2 equiv) and >80% rac-et,ph-P4 (1 equiv) are placed in separate 50 mL Erlenmeyer flasks and are dissolved in CH_2Cl_2 (~10mL each). In the glovebox under nitrogen atmosphere, the rac-et,ph-P4 solution is added dropwise to the rhodium complex solution while continuously swirling the flask. The reaction mixture is then added dropwise to ~150 mL diethyl ether while continuously swirling the ether flask. The contents are immediately filtered and dried. Just enough acetone is then added to dissolve the solid, and then left in the freezer overnight to recrystallize out the racemic product (leaving any meso product in solution). The product was filtered and dried via vacuum. Isolated Yield: ~80%. ^{31}P NMR: 58.7 ppm (doublet) and 46.9 ppm (doublet).

5.14 Hydroformylation Reactions

**Note: Unless otherwise stated, this are the standard reaction conditions used for all hydroformylation reactions performed for this research.*

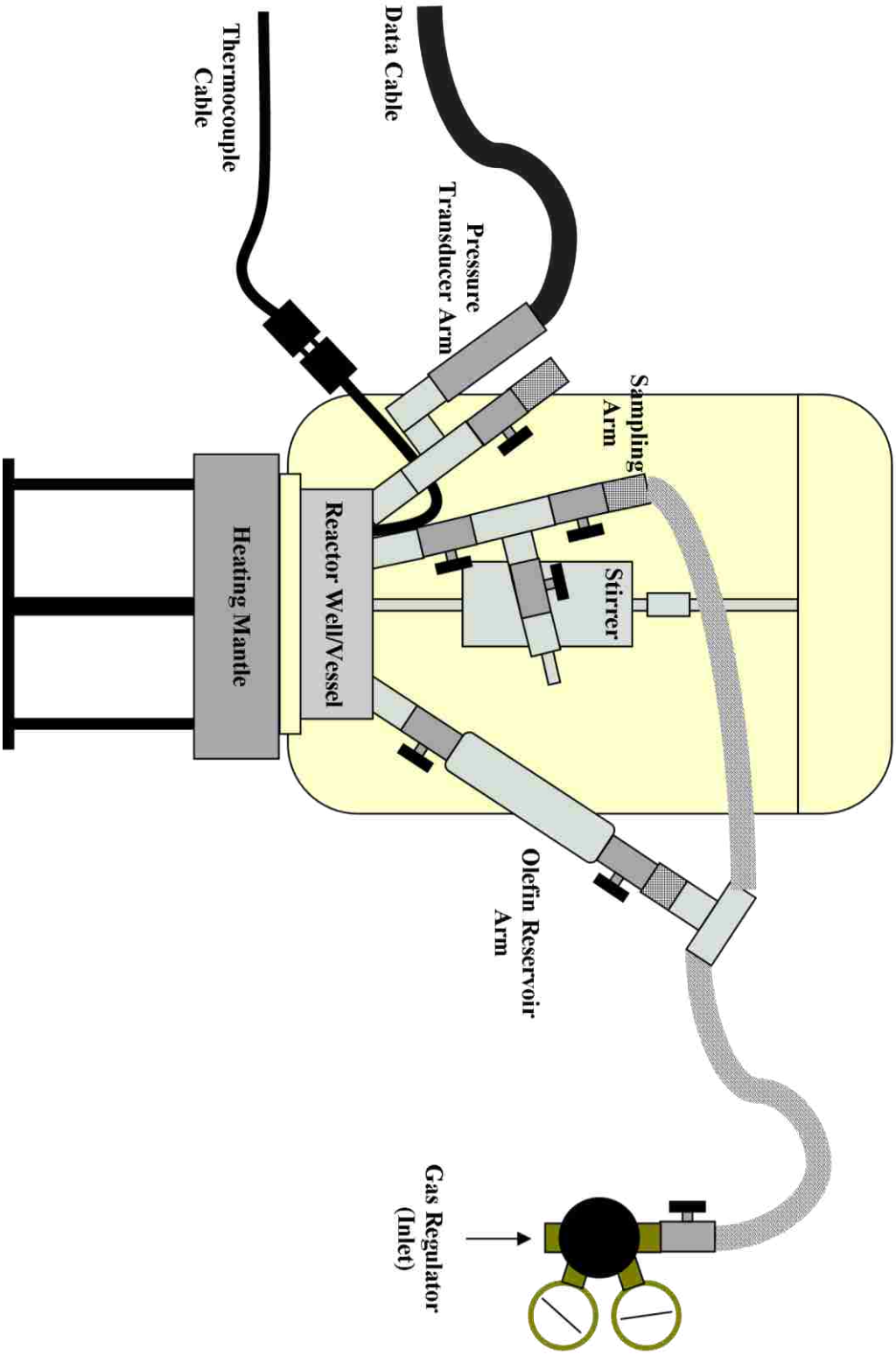
Reactions were performed in modified Parr stainless steel autoclaves, each equipped with a packless magnetic stirrer, thermocouple (temperature monitoring), and electronic pressure transducer (pressure monitoring). The reactor is assembled and evacuated via vacuum for at least 15 minutes. Under glove box inert atmosphere, [*rac*-$Rh_2(nbd)_2$(et,ph-P4)]$(BF_4)_2$ (90 mg, 0.08 mmol) was added to an Erlenmeyer flask, along with 80 mL of 30% water/acetone solution (including 2 mL of toluene as a GC internal standard), then sealed with a septum. In a finger vial, 1-hexene is passed through an alumina column and collected in a finger vial (6.73 g, 10 mL, 80 mmol) sealed with a septum. Via separate cannulas, the 1-hexene was transferred into the reactor's pressure inject reservoir and the catalyst solution was transferred into the main reactor vessel. The autoclave was pressurized to 90 psig with H_2:CO gas mixture ("syn-gas"), then vented to 45 psig. The autoclave is then heated to 90°C with 1000 rpm stirring over a total of 20 minutes (this is known as the Soaking process). Finally, the pressure is vented to 45 psig, and the 1-hexene is pressure injected to the operating pressure of 90 psig. The reaction progress is monitored by syn-gas consumption and GC-MS analysis of reaction solution samples.

5.15 Aldehyde-Water Shift Reactions / Tandem Hydrocarboxylation Reactions

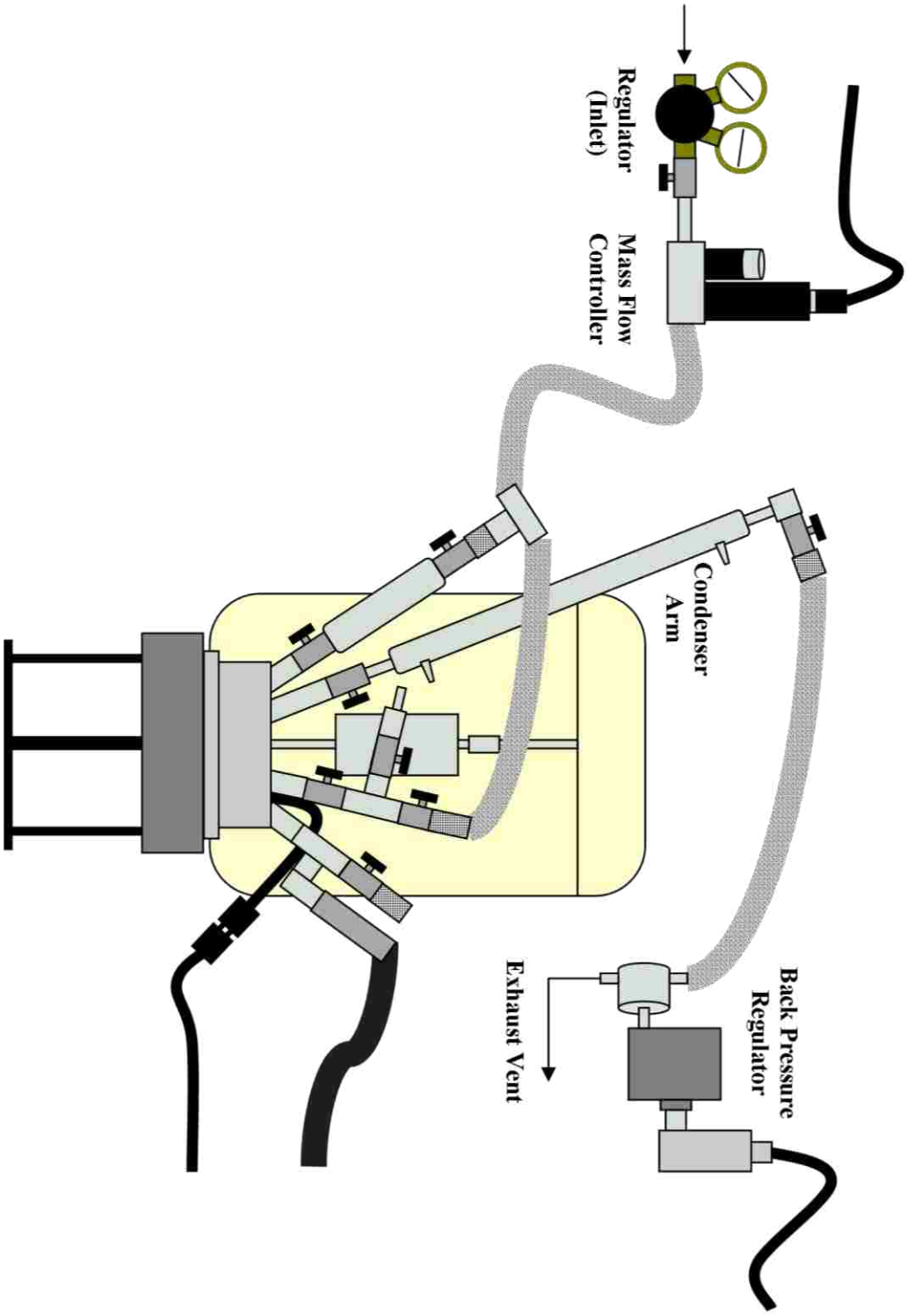
See Chapter 4.6: Aldehyde-Water Shift Catalysis Experiments

APPENDIX

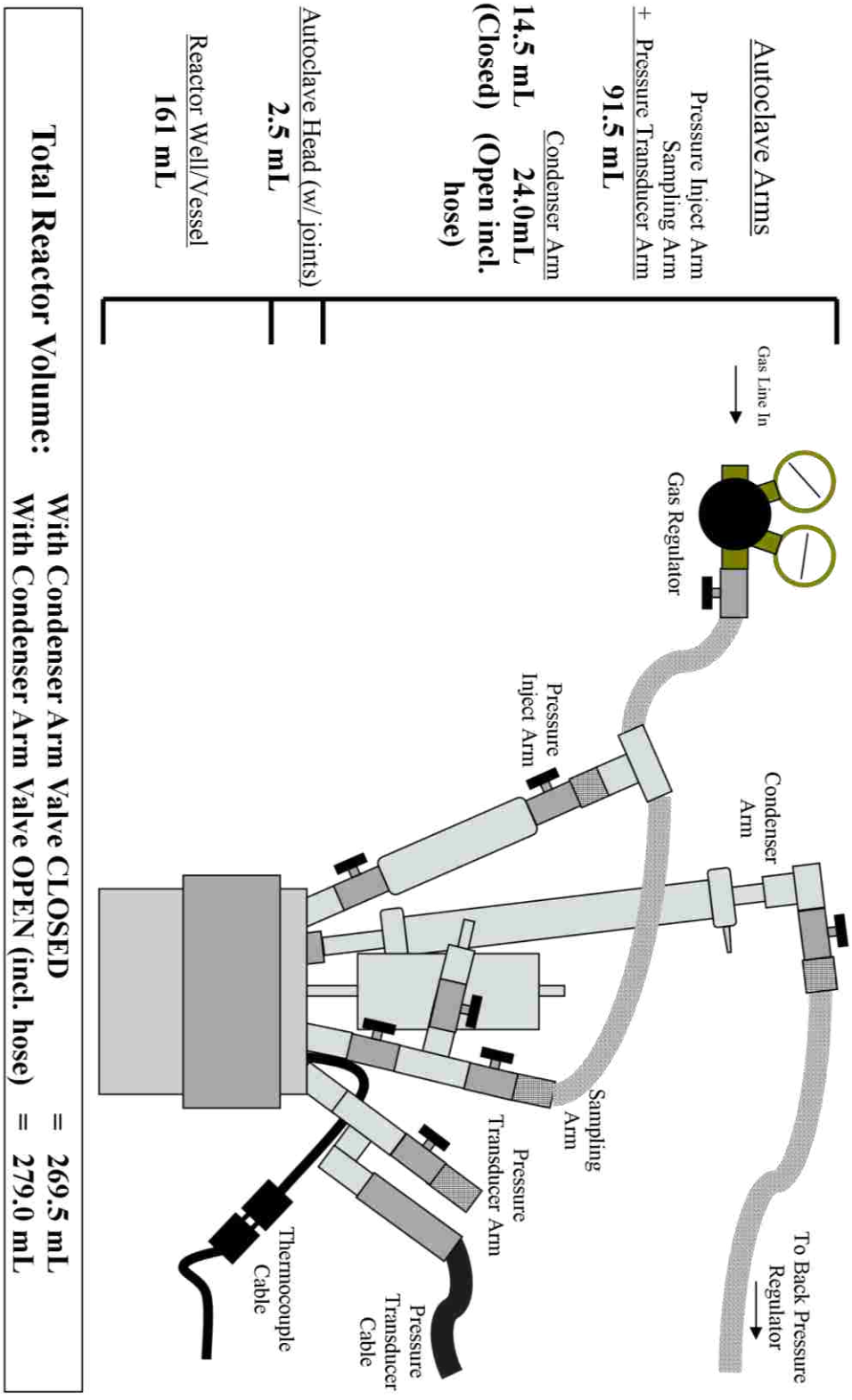
A.1 Mark II Autoclave Reactor Diagram



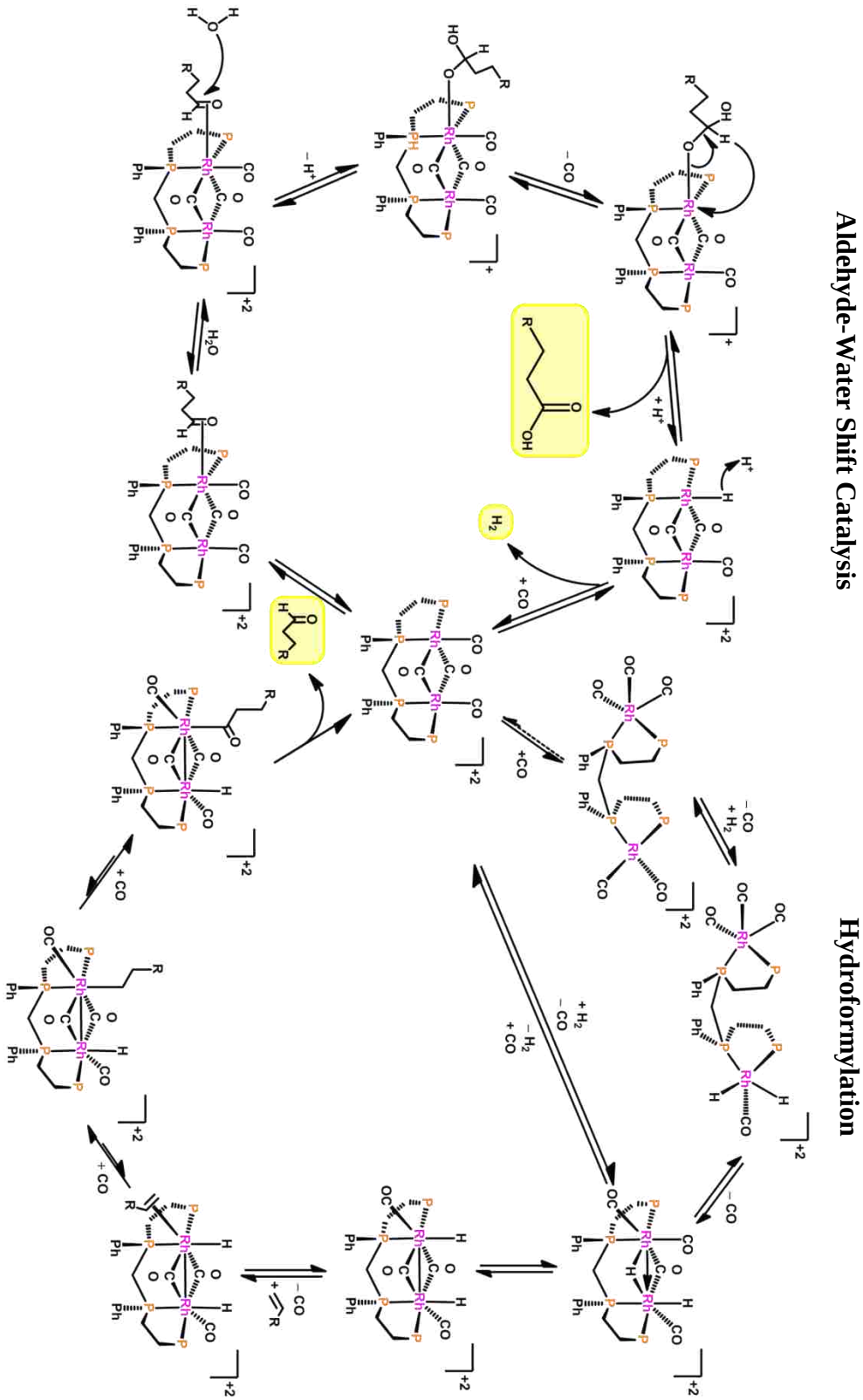
A.2 Mark III Flow-Control Autoclave Reactor Diagram



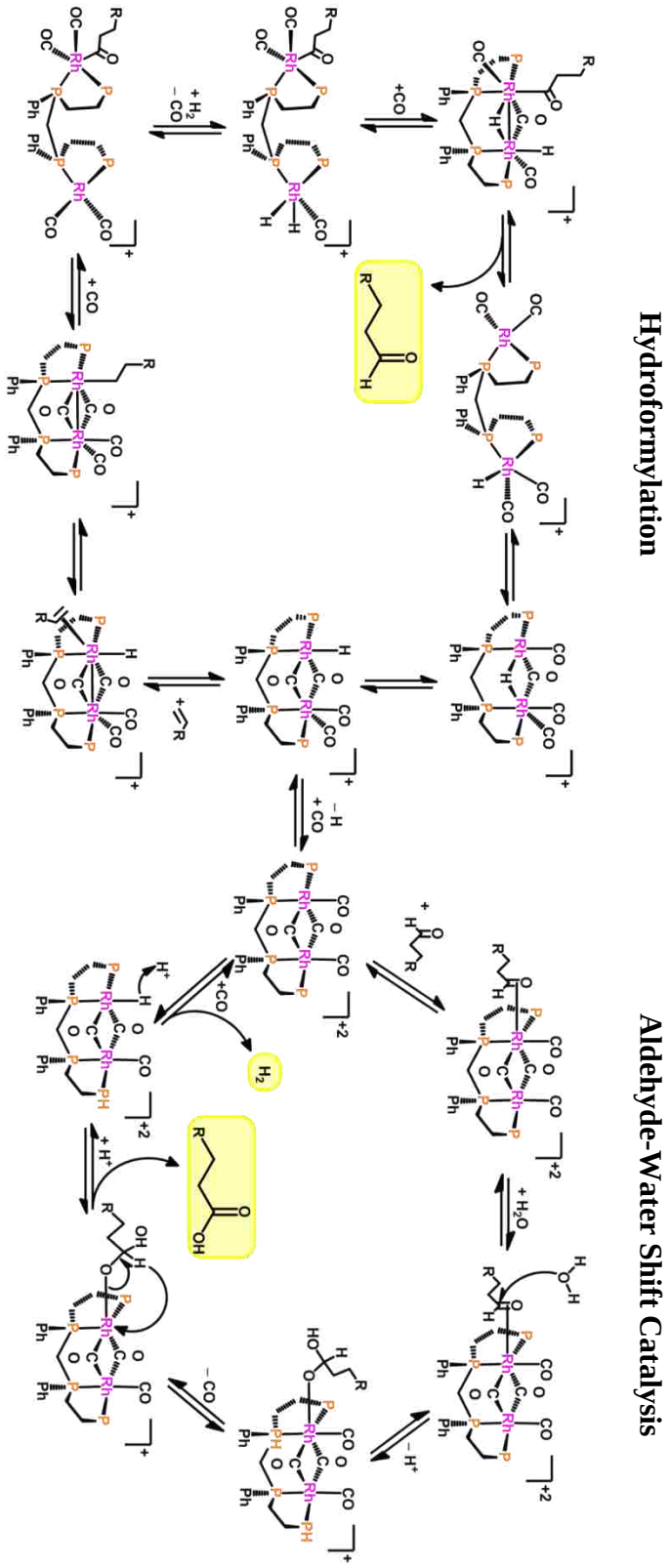
A.3 Mark III Flow-Control Autoclave Reactor Design with Volume Measurements



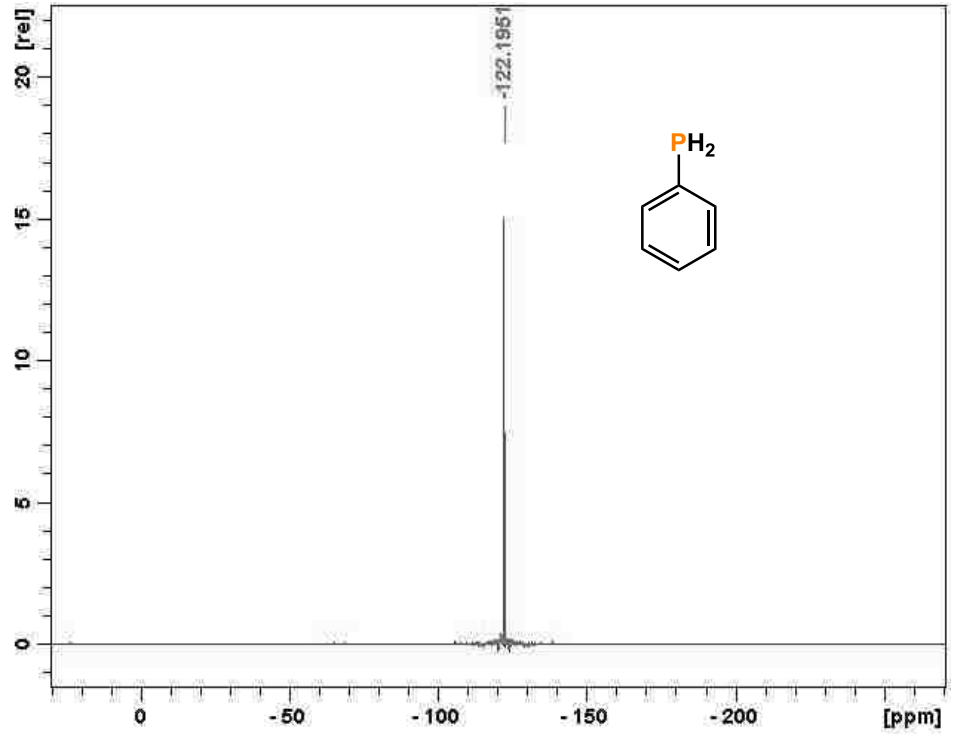
A.4 Proposed Tandem Hydroformylation / Aldehyde-Water Shift Dual Cycle (using the previous dicationic hydroformylation mechanism)



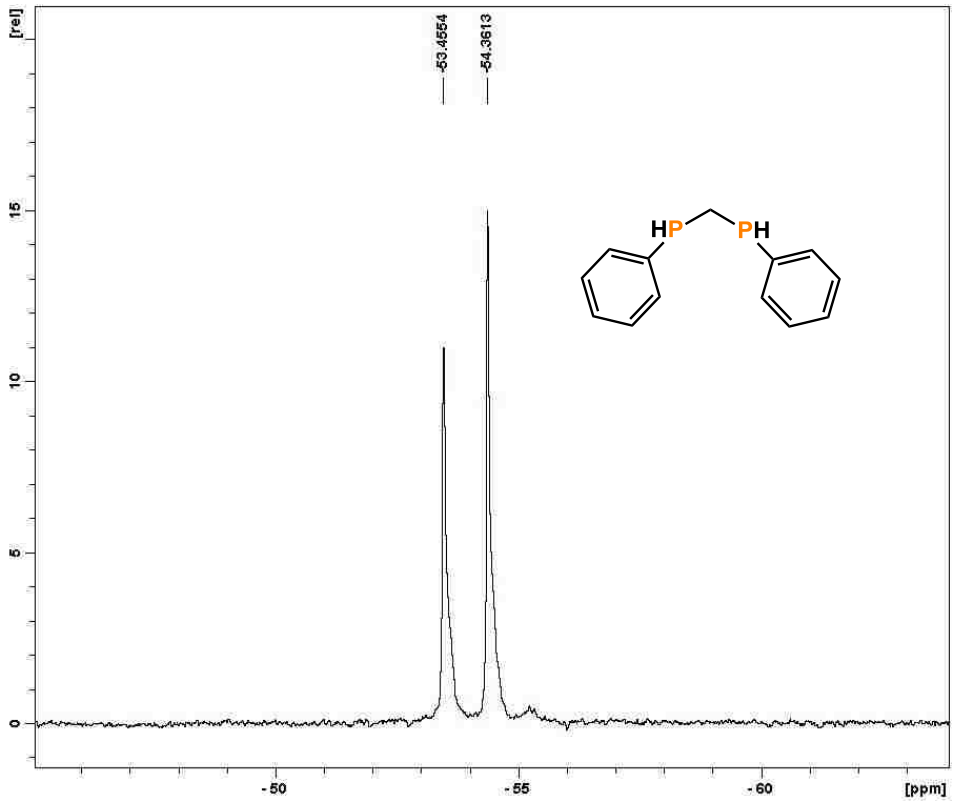
A.5 Proposed Tandem Hydroformylation / Aldehyde-Water Shift Dual Cycle (using the new monocationic hydroformylation mechanism)



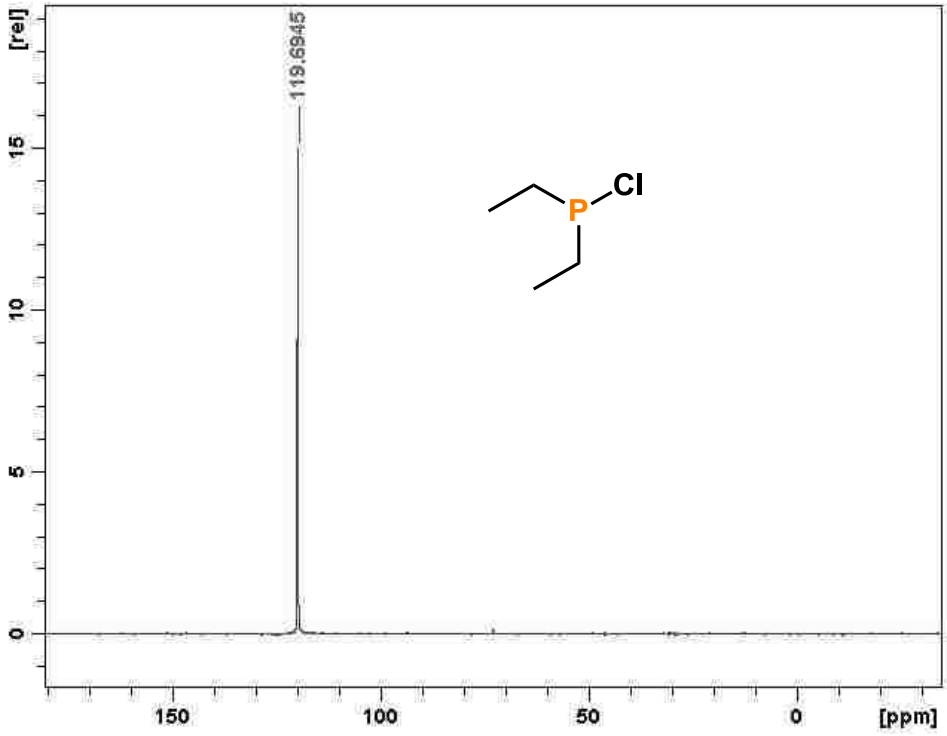
A.6 Phenylphosphine (^{31}PNMR spectrum)



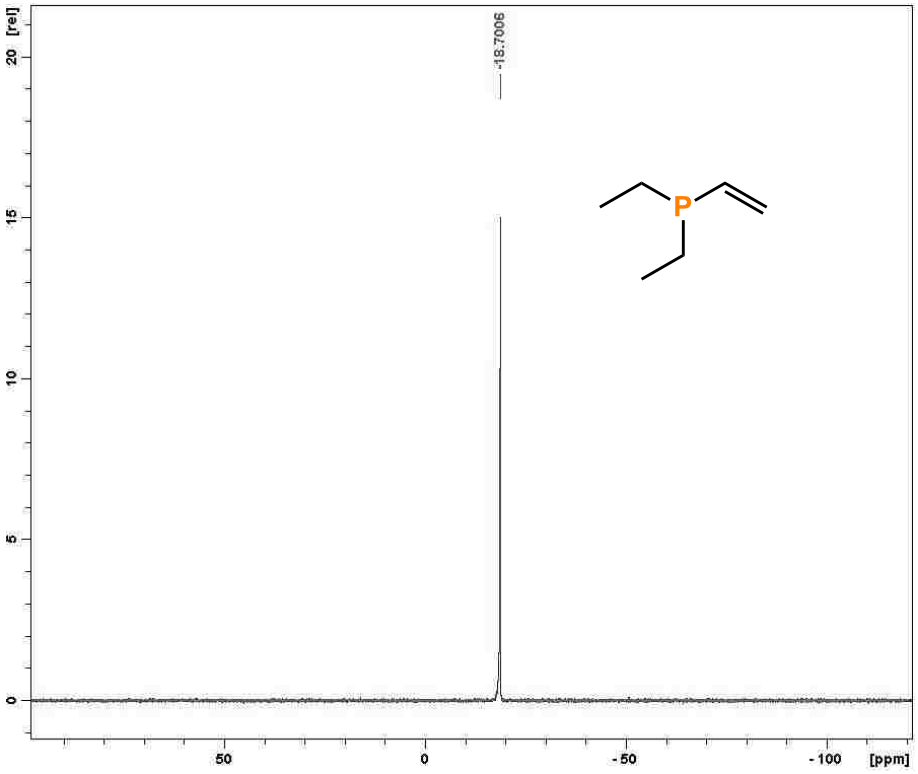
A.7 Bis(phenylphosphino)methane (aka: "bridge") (^{31}PNMR spectrum)



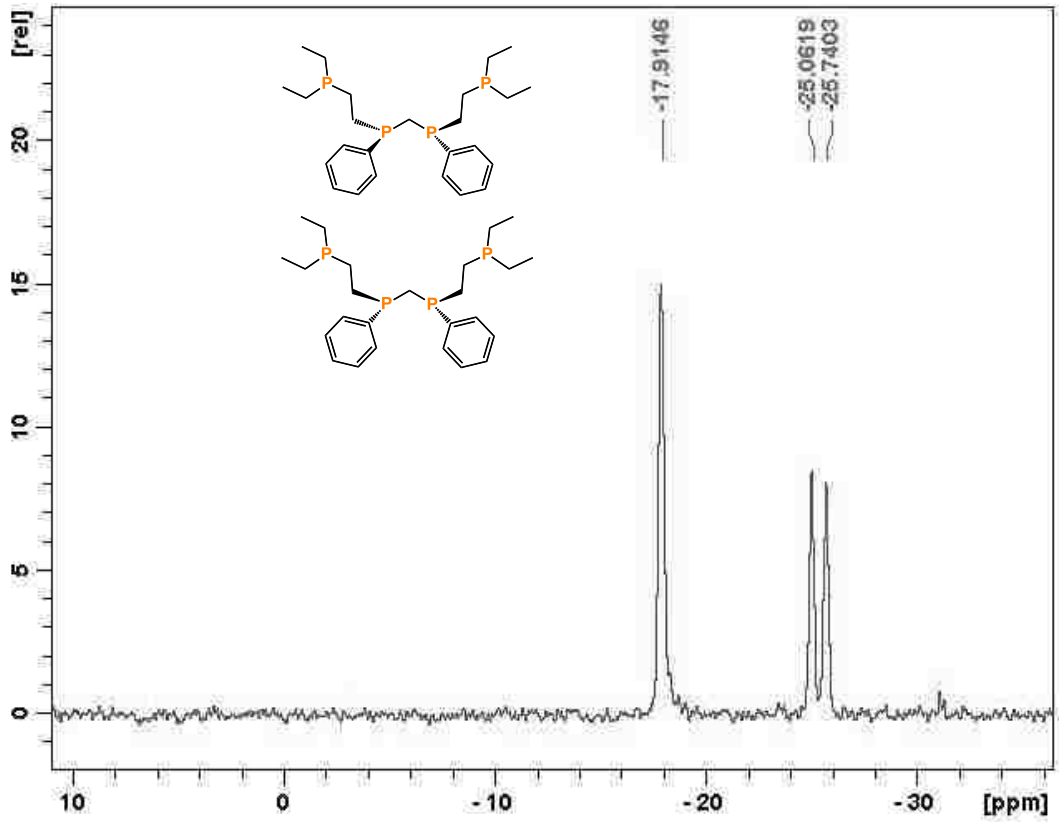
A.8 Chlorodiethylphosphine (^{31}PNMR spectrum)



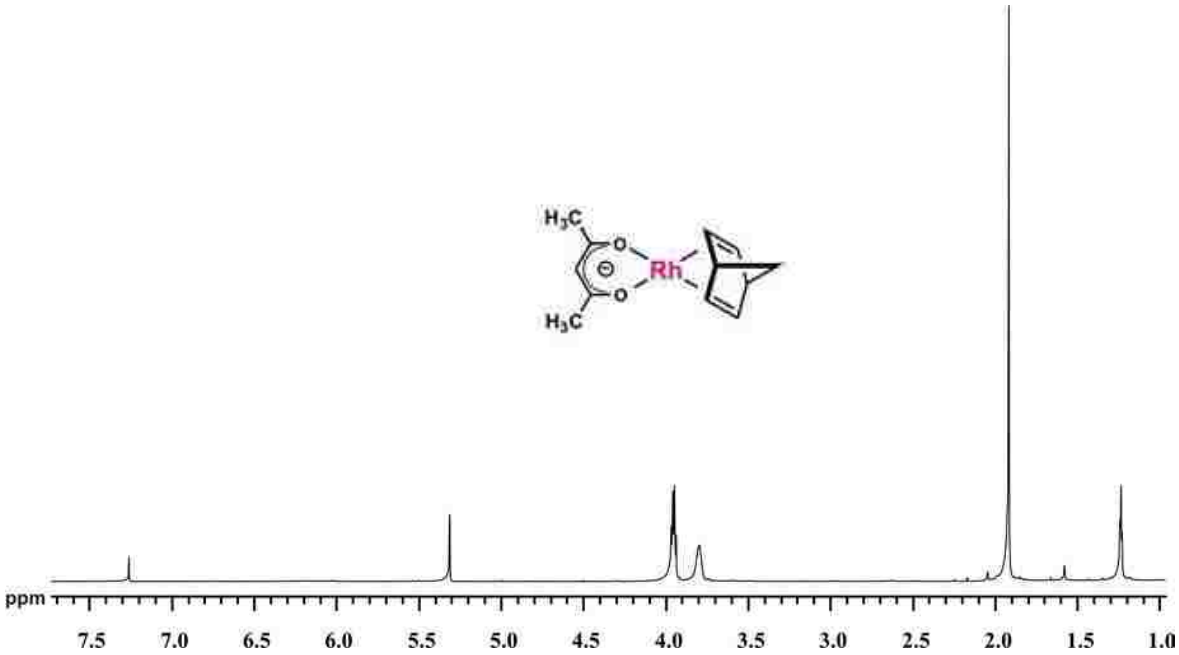
A.9 Diethylvinylphosphine (^{31}PNMR spectrum)



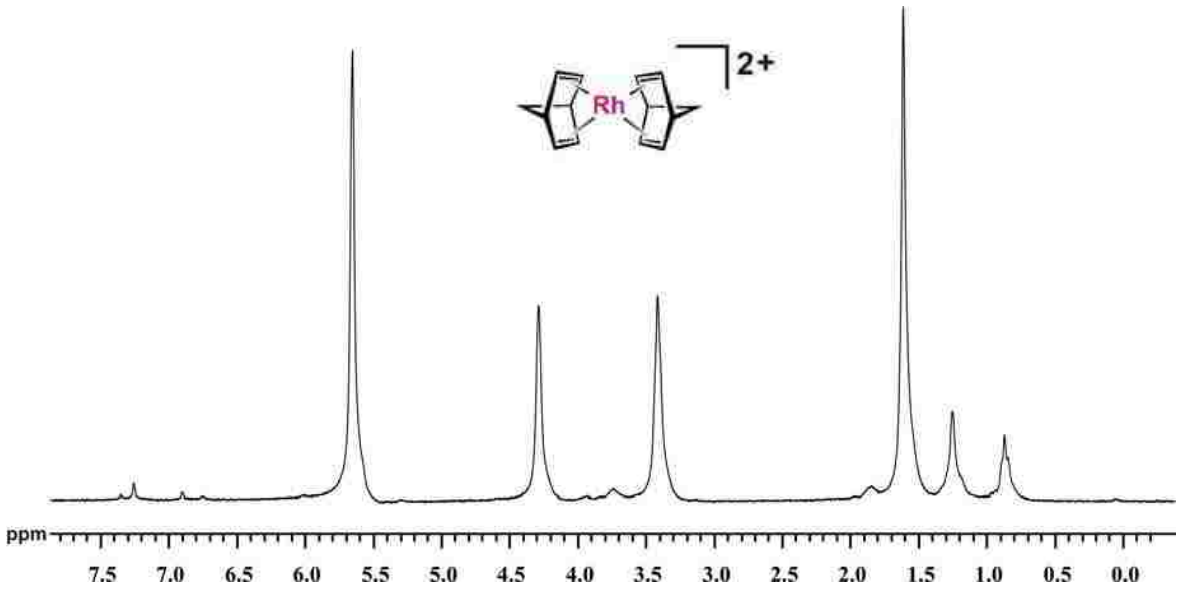
A.10 et,ph-P4 ligand (mixed *racemic*/*meso* diastereomers) (^{31}PNMR spectrum)



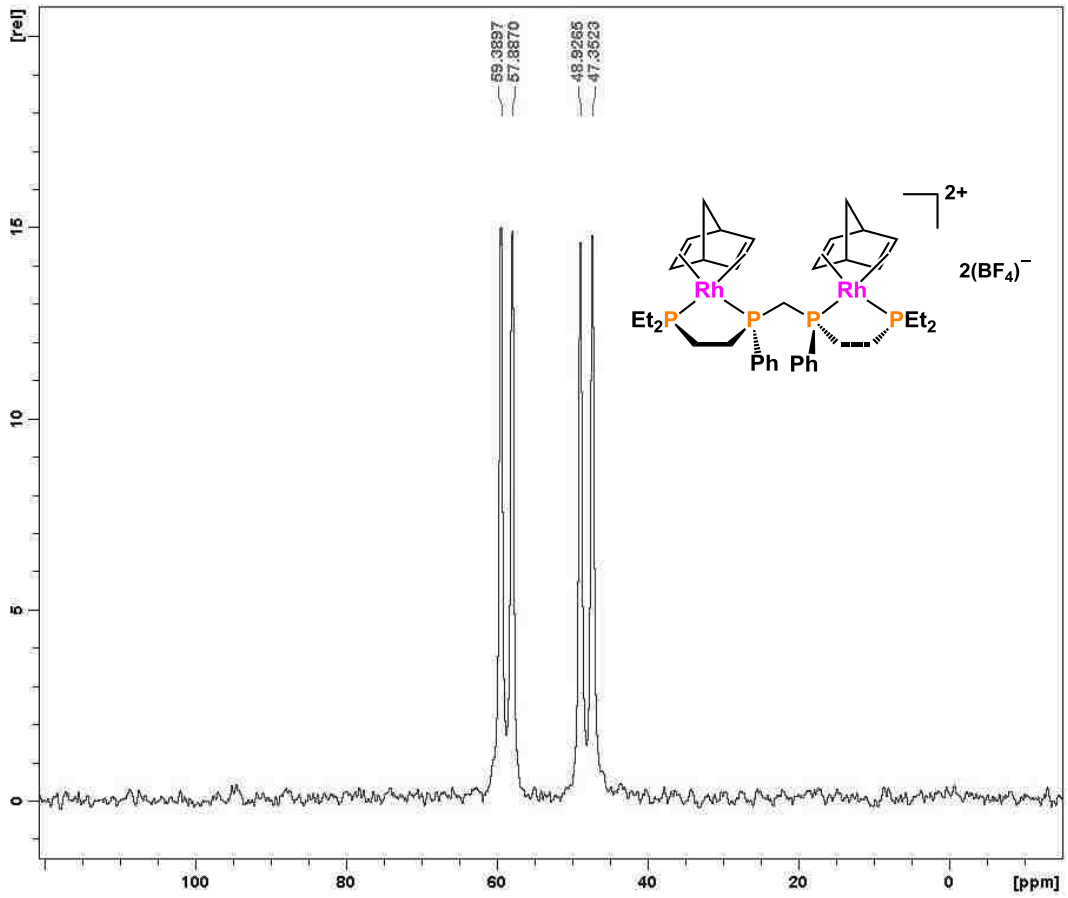
A.11 Rh(nbd)(acac) (^{1}HNMR spectrum)



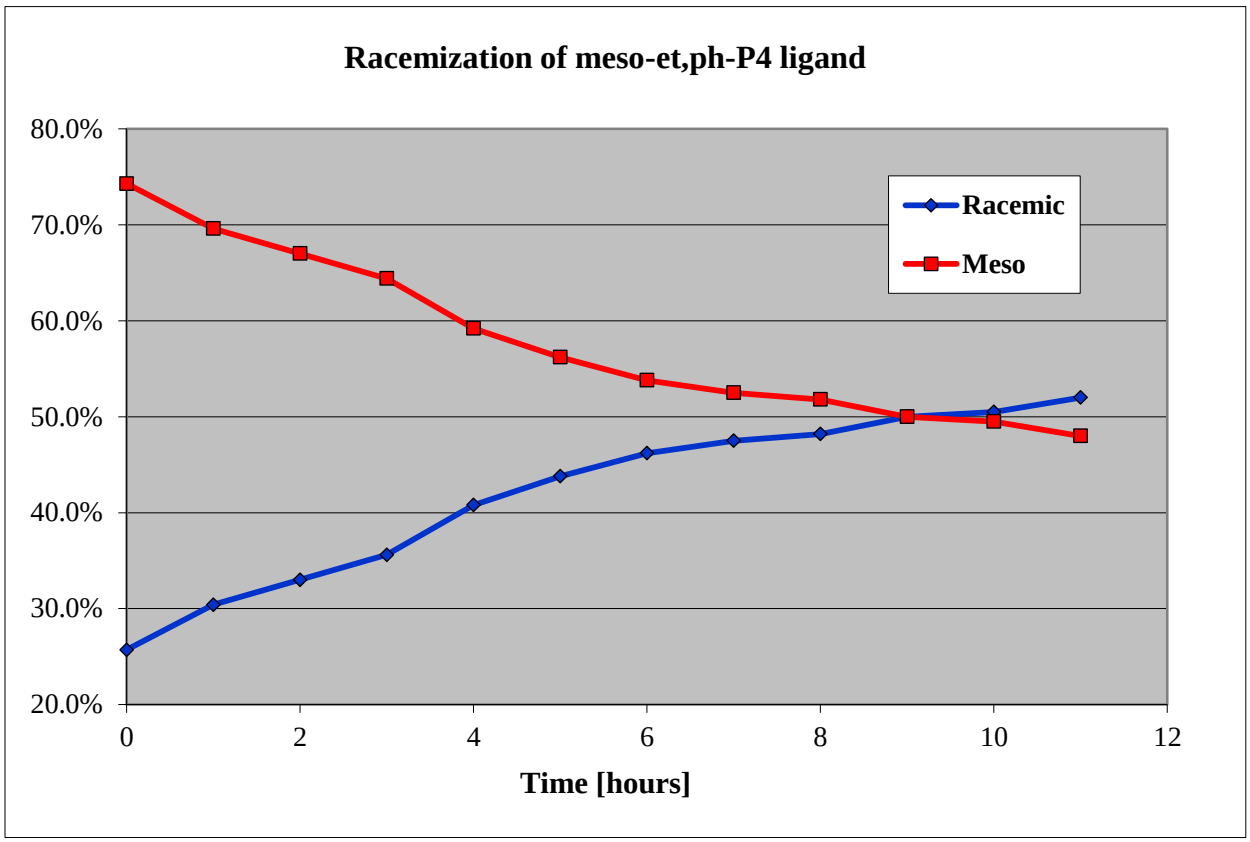
A.12 $[Rh(nbd)_2](BF_4)$ (^{1}HNMR spectrum)



A.13 $[rac\text{-}Rh_2(nbd)_2(et,ph\text{-}P4)](BF_4)_2$ catalyst precursor (^{31}PNMR spectrum)



A.14 Racemization of meso-et,ph-P4 ligand



Time [hr]	% Racemic	% Meso
0	25.7%	74.3%
1	30.4%	69.6%
2	33.0%	67.0%
3	35.6%	64.4%
4	40.8%	59.2%
5	43.8%	56.2%
6	46.2%	53.8%
7	47.5%	52.5%
8	48.2%	51.8%
9	50.0%	50.0%
10	50.5%	49.5%
11	52.0%	48.0%

Vita

A. Rider Barnum attended Loyola University of New Orleans in New Orleans, Louisiana and received a Bachelor of Science degree in Chemistry with minor studies in Theatre/Drama in May of 2007. He attended Louisiana State University in Baton Rouge, Louisiana from August of 2007 until present. He produced this document in partial fulfillment of the requirements for a Doctor of Philosophy degree in Chemistry.