CHAPTER 5
HYDROFORMYLATION
(OXO PROCESS)

Hydroformylation
Introduction

- Largest homogeneous catalytic process
- > 15 billion pounds of aldehydes (alcohols) per year
- Commercial catalysts are complexes of Co or Rh
- Selectivity to linear (normal) or branched (iso) products is important

Hydroformylation
Introduction

- Cobalt catalysts completely dominated industrial hydroformylation until the early 1970's when rhodium catalysts were commercialized.
- In 2004, ~75% of all hydroformylation processes are based on rhodium triarylphosphine catalysts, which excel with C₅ or lower alkenes and where high regioselectivity to linear aldehydes is critical.
- Most aldehydes produced are hydrogenated to alcohols or oxidized to carboxylic acids.
- Esterification of the alcohols with phthalic anhydride produces dialkyl phthalate plasticizers that are primarily used for polyvinyl chloride plastics.
Synthesis Roelen's original research into hydroformylation involved the use of cobalt salts that, under H₂/CO pressure, produced HCo(CO)₄ as the active catalyst.

In 1960 and 1961 Heck and Breslow proposed what is now accepted as the general mechanism for hydroformylation:

A common starting material for HCo(CO)₄ catalyzed hydroformylation, Co₂(CO)₈, is well known to react with H₂ under catalysis reaction conditions to form two equivalents of HCo(CO)₄.

The bimetallic hydride transfer mechanism is operational for stoichiometric hydroformylation with HCo(CO)₄ and has been proposed to be a possibility for slower catalytic hydroformylation reactions with internal alkenes.
The reaction conditions for $\text{HCo(CO)}_4$ hydroformylation are largely governed by the thermal instability of $\text{HCo(CO)}_4$, which produces metallic cobalt if the CO partial pressure is not kept high enough.

As the reaction temperature is increased, the CO partial pressure required to maintain the stability of $\text{HCo(CO)}_4$ increases in a logarithmic fashion (Fig. 1).

Thus, the temps needed for reasonable reaction rates (110-180°C) require rather high CO partial, and hence, total H$_2$/CO pressures of 200-300 bar.

Increasing the CO partial pressure decreases the hydroformylation reaction rate and the amount of alkene isomerization side reactions, while increasing the aldehyde linear to branched product ratio.

Pino proposed that the apparent marked difference between $\text{HCo(CO)}_3$ catalyzed hydroformylation at low and high CO partial pressures was due to the existence of two active catalyst species, $\text{HCo(CO)}_3$ and $\text{HCo(CO)}_4$, formed from the CO association/dissociation equilibrium:

$$\text{HCo(CO)}_3 + \text{CO} \rightleftharpoons \text{HCo(CO)}_4$$
But the active catalyst is most likely the 16e- HCo(CO)$_3$ complex.

The low probability of direct alkene reaction with the 18e-saturated HCo(CO)$_4$ catalyst is consistent with the reduced activity at higher CO partial pressures.

One can also explain the lower regioselectivity at lower CO pressure by proposing that alkene isomerization is more facile with the resulting 16e- RCo(CO)$_3$ species that results after reaction with alkene as shown below:

Under lower CO partial pressures an unsaturated 16e-RCo(CO)$_3$ will have a long enough lifetime to allow reverse $\beta$-hydride elimination and increase the possibility for alkene reinsertion to the branched alkyl species, which is slightly more favored thermodynamically.

At this point CO addition and insertion will yield a branched aldehyde, or another $\beta$-hydride elimination can give alkene isomerization.

This second mechanistic explanation is in line with more recent results from Rh/PPh$_3$ catalyzed hydroformylation studies.
The regioselectivity of HCo(CO)₄ [or HCo(CO)₃] for producing the more valuable linear aldehydes varies with reaction conditions and alkene substrates used. With 1-alkenes one can typically get linear to branched aldehyde ratios of 3-4 to 1. High CO partial pressure slows the rate of catalysis, but increases the linear to branched aldehyde product ratio. Higher CO partial pressures also lower alkene isomerization side reactions. Higher temperatures increase the reaction rate, but lower the linear aldehyde product regioselectivity and increase various undesirable side reactions.

Some aldehyde hydrogenation to alcohols is usually observed (5-12%), although alkene hydrogenation is usually quite low (~ 1%), particularly under higher CO partial pressures. Aldehyde hydrogenation is not considered to be a negative side reaction because the aldehyde products are usually hydrogenated to alcohols in a later reaction step. The aldehyde hydrogenation, however, consumes additional H₂, so H₂/CO ratios greater than 1:1 are used (1-1.5:1 is common).

High linear product regioselectivity is not, however, the major concern for most HCo(CO)₄ catalyzed industrial plants. Exxon Chemical Co. built the first United States hydroformylation plant in 1948 in Baton Rouge, LA using the high pressure HCo(CO)₄ technology confiscated from the Germans after WWII. This plant produced over 540 million lbs of alcohols each year, and a new plant came on line in 1994 which pushed the capacity to over 800 million lbs of alcohols a year.
Exxon uses propylene dimerization/oligomerization to produce a C7 to C12 mixture of branched internal alkenes. This branched, internal alkene mixture is then hydroformylated and hydrogenated to a C8 to C13 alcohol mixture.

The alkene isomerization ability of HCo(CO)₄ is quite important in this situation. HCo(CO)₄ under the proper reaction conditions is good at isomerizing double bonds to essentially all possible locations. This can be clearly seen from the data shown below that shows the % of aldehyde formed at each site for the HCo(CO)₄ catalyzed hydroformylation of 1-octene and 4-octene (150°C; 200 bar 1/1 H₂/CO).

<table>
<thead>
<tr>
<th>Hydroformylation</th>
<th>Cobalt Catalysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>% formyl group addition to indicated carbon</td>
<td></td>
</tr>
<tr>
<td>65%</td>
<td>7%</td>
</tr>
<tr>
<td>22%</td>
<td>12%</td>
</tr>
<tr>
<td>59%</td>
<td>11%</td>
</tr>
</tbody>
</table>

Under these conditions, the linear to branched aldehyde ratio for the hydroformylation of 1-octene was 1.9:1. Starting with 4-octene one still gets a 1.2:1 linear to branched ratio.

Thus, one can start with a considerably less expensive mixture of terminal and internal alkenes and get a product distribution favoring the linear aldehyde.

The product distribution above can be nicely explained by invoking facile alkene isomerization with the fastest hydroformylation occurring for double bonds in the 1-position.

Data for two methylheptenes and % of aldehyde formed at each site is shown below:

<table>
<thead>
<tr>
<th>Hydroformylation</th>
<th>Cobalt Catalysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>% formyl group addition to indicated carbon</td>
<td></td>
</tr>
<tr>
<td>72%</td>
<td>4%</td>
</tr>
<tr>
<td>8%</td>
<td>15%</td>
</tr>
<tr>
<td>18%</td>
<td>1%</td>
</tr>
<tr>
<td>38%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

Alkene branching has a large effect on isomerization and hydroformylation. Very little hydroformylation at the carbon center with the branch, even if it was part of the double bond.

Data for two methylheptenes and % of aldehyde formed at each site is shown below:
Side reactions of the product aldehydes to form heavier products generally occur, particularly at higher reaction temperatures, and usually account for ~9% of the product distribution.

Aldol condensations, aldols, trimerizations, and dimerizations of product alcohols are some of the more common ways to form heavy byproducts.

These side reactions occur to various extents for all long term hydroformylations (Co or Rh).

One advantage of the HCo(CO)₄ technology is that catalyst separation and recycling is well established.

BASF oxidizes HCo(CO)₄ with O₂ to form water soluble Co³⁺ salts that are extracted from the product stream. These Co³⁺ salts are recycled and reduced under H₂/CO to reform HCo(CO)₄.

Exxon uses aqueous NaOH to deprotonate HCo(CO)₄ after catalysis to make Na[Co(CO)₄], which is extracted into an aqueous stream. The active HCo(CO)₄ catalyst is regenerated via use of H₂SO₄ and H₂/CO.
**Hydroformylation**  
**Cobalt Phosphine-Modified Catalysts**

- The electronic effect of substituting an electron donating alkylated phosphine for one of the carbonyl ligands to produce HCo(CO)$_3$(PR$_3$)$_2$, results in stronger Co-CO bonding.
- This causes a dramatic reduction in the CO partial pressures required to stabilize the catalyst and prevent formation of Co metal.
- Instead of 200-300 bars of H$_2$/CO pressure needed for HCo(CO)$_4$, the monophosphine substituted HCo(CO)$_3$(PR$_3$)$_2$ only needed 50-100 bars of pressure, and could be run at higher temperatures without any decomposition of catalyst to cobalt metal.

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**Hydroformylation**  
**Cobalt Phosphine-Modified Catalysts**

- Another electronic effect is that the electron-donating phosphine increases the hydridic nature of the hydride ligand (HCo(CO)$_4$ is quite acidic) and dramatically increases the hydrogenation capabilities of the HCo(CO)$_3$(PR$_3$)$_2$ catalyst.
- This means that the aldehydes produced are subsequently hydrogenated by HCo(CO)$_3$(PR$_3$)$_2$ to make alcohols. Less e-rich phosphines, such as PPh$_3$, give less hydrogenation to alcohol, and lower linear regioselectivities.
- The better hydrogenation ability, however, also results in increased alkene hydrogenation side-reactions producing alkanes that can range from 10-20% of the product distribution.
The final electronic effect of phosphine substitution is that the higher stability of the HCo(CO)₃(PR₃) catalyst, due to stronger Co-CO bonding, means that this catalyst is less active than HCo(CO)₄ (about 5-10 times slower).

Just as with the unmodified cobalt catalyst, CO dissociation from the saturated 18e- species is needed to open up an empty coordination site on the cobalt to allow coordination of alkene and H₂.

From a steric viewpoint the bulkier trialkylphosphine ligand favors formation of linear products.

While linear to branched ratios of only 2-3:1 are typically found for HCo(CO)₄, higher regioselectivities of 7-8:1 occur for HCo(CO)₃(PR₃).

There is a phosphine cone angle cutoff at about 132°, after which the phosphine ligand's steric effects do not increase the product linear regioselectivity any further.

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### Table 1. Hydroformylation of 1-hexene using Co₂(CO)₈/2P as catalyst precursor. 160°C, 70 atm, 1:2:1 H₂/CO

<table>
<thead>
<tr>
<th>PR₃</th>
<th>pKa</th>
<th>Tolman ν (cm⁻¹)</th>
<th>Cone Angle °</th>
<th>kr x 10⁻³ (min⁻¹)</th>
<th>% Linear Prod</th>
<th>Aldehyde to alcohol</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(Ph)₂</td>
<td>9.4</td>
<td>2659.2</td>
<td>160</td>
<td>2.8</td>
<td>85.0</td>
<td>--</td>
</tr>
<tr>
<td>PEt₂</td>
<td>8.7</td>
<td>2661.7</td>
<td>132</td>
<td>2.7</td>
<td>89.6</td>
<td>0.9</td>
</tr>
<tr>
<td>PPh₂</td>
<td>8.6</td>
<td>2660.9</td>
<td>132</td>
<td>3.1</td>
<td>89.5</td>
<td>1.0</td>
</tr>
<tr>
<td>PBr₂</td>
<td>8.4</td>
<td>2660.3</td>
<td>136</td>
<td>3.3</td>
<td>89.6</td>
<td>1.1</td>
</tr>
<tr>
<td>PEt₂Ph</td>
<td>6.3</td>
<td>2663.7</td>
<td>136</td>
<td>5.5</td>
<td>84.6</td>
<td>2.2</td>
</tr>
<tr>
<td>PEEP₂</td>
<td>4.9</td>
<td>2666.7</td>
<td>140</td>
<td>8.8</td>
<td>71.7</td>
<td>4.3</td>
</tr>
<tr>
<td>PFP₂</td>
<td>2.7</td>
<td>2668.9</td>
<td>145</td>
<td>14.1</td>
<td>62.4</td>
<td>11.7</td>
</tr>
</tbody>
</table>
The initial catalyst system was derived from Wilkinson's catalyst, RhCl(PPh3)3, but it was rapidly discovered that halides were inhibitors for hydroformylation.

It was best, therefore, to start with halide-free rhodium starting complexes. HRh(CO)(PPh3)2 and Rh(acac)(CO)2 (acac = acetoacetonate) are two commonly used starting materials for hydroformylation.

The currently accepted mechanism for Rh/PPh3 hydroformylation is shown. The steps are directly analogous to Heck's mechanism for HCo(CO)4.

Wilkinson noted that HRh(CO)(PPh3)2 was very selective to aldehyde products (no alcohol formation, no alkene hydrogenation or isomerization) and that very high linear to branched aldehyde selectivities of 20:1 for a variety of 1-alkenes could be obtained under ambient conditions (25°C, 1 bar 1:1 H2/CO).

At higher temperatures, the rate increased, but the regioselectivity dropped (9:1 at 50°C).

Running under 80-100 bars of H2/CO decreased the linear to branched aldehyde selectivity to only 3:1.
Loss of PPh₃ from HRh(CO)(PPh₃)₂ generates considerably more active, but less regioselective hydroformylation catalysts.

The addition of excess phosphine ligand shifts the phosphine dissociation equilibrium back towards the more selective HRh(CO)(PPh₃)₂ catalyst.

This explains why higher CO partial pressures lower the product regioselectivity, in marked contrast to what is observed for HCo(CO)₄-catalyzed hydroformylation.

The regioselectivity of HRh(CO)(PPh₃)₂ is strongly related to the concentration of PPh₃ in solution (up to a certain point) and the H₂/CO ratio used.

Commercial hydroformylation reactions are run using solutions that have PPh₃ concentrations of 0.3 M or higher (typical Rh concentration around 1 mM).

This corresponds to PPh₃ weight percentages of 8-50% of the total solution in commercial reactors.
Hydroformylation
Rhodium Phosphine Catalysts

Table 2. Rate constants and Regioselectivities for the Hydroformylation of 1-Hexene using Rh(acac)(CO)₂ with Different PPh₃ Concentrations.

<table>
<thead>
<tr>
<th>[Rh] (mM)</th>
<th>[PPh₃] (M)</th>
<th>PPh₃/Rh ratio</th>
<th>kobs (min⁻¹ mM Rh⁻¹)</th>
<th>l:b ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.41</td>
<td>820</td>
<td>0.032</td>
<td>11</td>
</tr>
<tr>
<td>1</td>
<td>0.82</td>
<td>820</td>
<td>0.016</td>
<td>17</td>
</tr>
</tbody>
</table>

The complexity of the phosphine/CO ligand dissociation/association processes and the many catalytically active rhodium complexes present was most clearly pointed out by Tolman and Faller.

The other important reason for adding excess phosphine ligand is to minimize ligand fragmentation reactions that lead to catalyst deactivation.

If a 14e, highly unsaturated species such as HRh(CO)(PPh₃) is formed the very electrophilic metal center can attack the PPh₃ ligand (either intra- or intermolecularly).

This leads to cleavage of the P-Ph bond and formation of either alkyl(diphenyl) phosphines or phosphide-bridged dimers which are inactive for hydroformylation:

```
\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{Rh} & \quad \text{Ph} \\
\text{Rh} & \quad \text{Ph}
\end{align*}
\]
\[\rightarrow \quad + \text{H₂} \quad - \text{benzene}\]
```

```
\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
\text{Rh} & \quad \text{Ph} \\
\text{Rh} & \quad \text{Ph}
\end{align*}
\]
\[\rightarrow \quad \text{Ph} \\
\text{Rh} & \quad \text{Ph} \\
\text{Rh} & \quad \text{Ph}
\]
```
Chelating phosphines have interesting effects on hydroformylation. $R_2P(CH_2)xPR_2$ (x = 2-4) ligands with alkyl or aryl substituents generally form terrible catalysts that give poor rates and selectivities, as well as extensive alkene isomerization and hydrogenation side reactions.

Tridentate tripodal phosphine ligands, such as MeC(CH_2PPh_2)_3, also generate catalysts with very poor rates and regioselectivities.

High pressure NMR studies have shown that an arm-on, arm-off equilibrium is operational to generate the active unsaturated 16e-catalyst species HRh(CO)(MeC(CH_2PPh_2)_3).

Use of dppb either by itself, or in quantities higher than 2 equivalents, leads to catalyst deactivation and/or poor activities and selectivities.

ARCO Chemical licensed the Kuraray technology to build the first plant in 1990 for the hydroformylation of allyl alcohol to produce 1,4-butanediol:

It is not exactly understood how the mixed ligand Rh/dppb/PPh_3 catalyst system functions. Matsumoto proposed that the arm-on, arm-off equilibrium shown below is operational.

A species such as (2) would function much like a normal HRh(CO)(PPh_3) catalyst, but the ability to reform the chelate to form a slightly more electron-rich complex (3) would tend to inhibit alkene isomerization and/or degradation reactions which require 16e-unsaturated species.
By using a sulfonated PPh₃ ligand, P(Ph₉m-SO₃⁻ Na⁺)₃ (TPPTS), a highly water soluble catalyst is generated: HRh(CO)(P(Ph₉m-SO₃⁻ Na⁺))₃.

In aqueous solution the catalyst essentially has a -9 charge, making it totally insoluble in all but the most polar organic solvents.

Excess phosphine ligand is required for good L:B selectivities, as with conventional Rh/PPh₃ catalysts, but lower concentrations are required because the TPPTS phosphine dissociation equilibrium in water is shifted towards the Rh-phosphine coordinated complexes.

Shorter chain alkenes (C₂-C₄) are water soluble enough that migration into the aqueous catalyst phase occurs to allow hydroformylation.

Remigration of the aldehyde product back into the more soluble organic phase allows easy separation of product from catalyst.

Rather high linear to branched regioselectivities of 16-18:1 for propylene can be obtained via this water soluble catalyst.
Rates are slower than with conventional Rh/PPh₃ catalysts due to lower alkene concentrations in the water phase and higher amounts of the inactive tris-phosphine Rh complex.

The process is limited to the shorter chain alkenes that have some appreciable water solubility.

Alkenes higher than 1-pentene are not soluble enough in water. Celanese-Ruhrchemie currently operates several hydroformylation plants based on this water soluble rhodium catalyst technology.

Propylene is the largest single alkene hydroformylated to produce butyaldehyde, which can be hydrogenated to produce butanol, or dimerized by an aldol condensation and then hydrogenated to form 2-ethyl-1-hexanol (2EH), the largest single product produced by hydroformylation (over 5 billion lbs a year).

2-ethyl-1-hexanol is usually reacted with phthalic anhydride to produce dialkyl phthalic esters that are used as plasticizers to keep polyvinyl chloride plastics soft and flexible.
### Industrial Propylene Hydroformylation Processes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Co</th>
<th>Co / phosphine</th>
<th>Rh / phosphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reaction pressure (bar)</td>
<td>200-300</td>
<td>50-100</td>
<td>7.25</td>
</tr>
<tr>
<td>Reaction temperature (°C)</td>
<td>140-180</td>
<td>180-200</td>
<td>90-125</td>
</tr>
<tr>
<td>Selectivity C₂ (%)</td>
<td>&gt;85</td>
<td>&gt;85</td>
<td>&gt;90</td>
</tr>
<tr>
<td>α/ω-mono-Aldehyde</td>
<td>80/20</td>
<td>up to 90/10</td>
<td>up to 95/15</td>
</tr>
<tr>
<td>Catalyst</td>
<td>[HCo(CO)₂]</td>
<td>[HCo(CO)₂(PPh₃)]</td>
<td>[HRh(CO)(PPh₃)]</td>
</tr>
<tr>
<td></td>
<td>FPP₃ up to 1:500</td>
<td>FPP₃ up to 1:500</td>
<td>FPP₃ up to 1:500</td>
</tr>
<tr>
<td>Main products</td>
<td>aldehydes</td>
<td>alcohols</td>
<td>aldehydes</td>
</tr>
<tr>
<td>Hydrogenation to alkane (%)</td>
<td>1</td>
<td>15</td>
<td>0.9</td>
</tr>
</tbody>
</table>