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Metals in Hydroformylation

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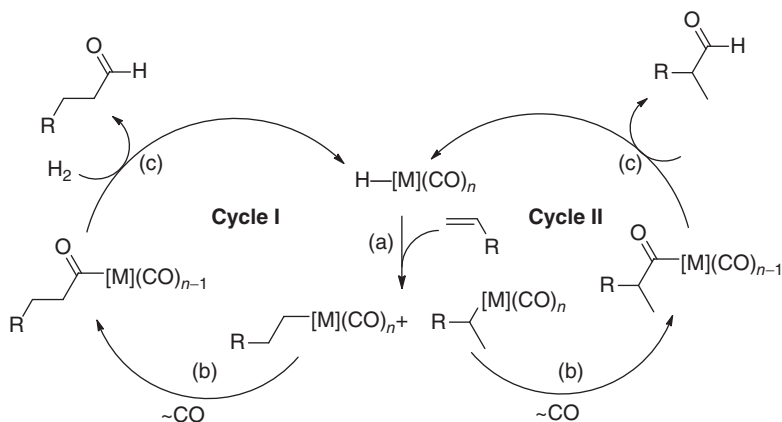
The Pivotal Role of Hydrido Complexes

There are very many investigations in the literature concerning the evaluation of different metals and associated organic ligands in hydroformylation. In 2013, Franke and Beller [1] provided a concise summary about the applicability of alternative metals in hydroformylation. In the same year, another survey was assembled by a joint French/Italian cooperation [2]. In order to avoid a full repetition, only some basic conclusions will be mentioned here, which are not in the focus of the reviews cited above.

Several hydrido metal carbonyl complexes are able to catalyze the hydroformylation reaction (Scheme 1.1). Preconditions are the ability for the formation of the relevant intermediates and the passage of crucial steps, such as a metal–alkyl complex by addition of the M–H bond to an olefin (a), subsequent insertion of CO into the M–alkyl bond by migration of a ligated CO ligand (b), and the final hydrogenolysis of the M–acyl bond to liberate the desired aldehyde and to reconstruct the catalyst (c). The type of the transient M–alkyl complex is responsible for the formation of isomeric aldehydes, here distinguished as Cycle I and II. For the successful passage of these catalytic events, besides the reaction conditions the choice of the appropriate metal and its coordinated ligands are pivotal.

In the early (mainly patent) literature, besides Co and Rh, Ni, Ir, and other metals of the VIII group, also Cr, Mo, W, Cu, Mn, and even Ca, Mg, and Zn were suggested or claimed for hydroformylation [3]. However, several of them do not exhibit any activity.

Adequate hydroformylation activity of the hydrido carbonyl complexes is attributed to the polarity of the M–H bond [4]. It is assumed that high acidity facilitates the addition to an olefin and the hydrogenolysis of the transient metal–acyl complex in a later stage of the catalytic cycle. In this respect, $\text{HCo}(\text{CO})_4$ is a much stronger acid than $\text{H}_2\text{Ru}(\text{CO})_4$, $\text{H}_2\text{Fe}(\text{CO})_4$, $\text{H}_2\text{Os}(\text{CO})_4$, or $\text{HMn}(\text{CO})_5$ [5]. Moreover, anionic hydrido complexes, such as $[\text{HRu}(\text{CO})_4]^-$, behave as strong bases [6]. The conversion of the latter into $\text{H}_2\text{Ru}(\text{CO})_4$ is probably a precondition for



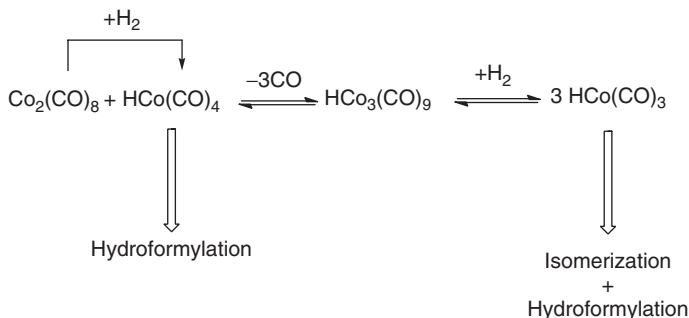
Scheme 1.1 Simplified catalytic cycle for hydroformylation.

the success of the hydroformylation and one explanation why $\text{Ru}_3(\text{CO})_{12}$ is more active than $[\text{HRu}(\text{CO})_4]^-$. The former reacts with H_2 to form $\text{H}_2\text{Ru}(\text{CO})_4$ [7]. Low activity was likewise observed for $[\text{HOS}_3(\text{CO})_{11}]^-$ associated with a low thermal stability [8]. Also, $[\text{Co}(\text{CO})_4]^-$ is a poor hydroformylation catalyst [9]. However, with the addition of strong acids, the active species $\text{HCo}(\text{CO})_4$ can be generated.

Noteworthy, the instability of $\text{HCo}(\text{CO})_4$ under the formation of $\text{Co}_2(\text{CO})_8$ can be attributed in part to the fast intermolecular elimination of H_2 . In this manner, also the formation of alkanes can be explained as a key step in the hydrogenation of olefins. On the other hand, the acidic properties of $\text{HCo}(\text{CO})_4$ allow the convenient separation of product and catalyst after hydroformylation by conversion into water-soluble Co salts (“decobalting”) [10].

Strong acidic metal hydrido complexes such as $\text{HCo}(\text{CO})_4$ or complexes with Lewis acid properties, such as $\text{Rh}_2\text{Cl}_2(\text{CO})_4$, $[\text{Ru}(\text{MeCN})_3(\text{triphos})](\text{CF}_3\text{SO}_3)_2$, $[\text{Pt}(\text{H}_2\text{O})_2(\text{dppe})](\text{CF}_3\text{SO}_3)_2$, $[\text{Pd}(\text{H}_2\text{O})_2(\text{dppe})](\text{CF}_3\text{SO}_3)_2$, or $[\text{Ir}(\text{MeCN})_3(\text{triphos})](\text{CF}_3\text{SO}_3)_3$, are able to act in alcohols as acetalization catalysts, which means they can mediate the transformation of the newly formed aldehydes into acetals (see Section 5.3).

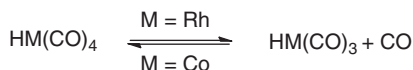
The number of CO ligated to the same metal may affect the catalytic properties (Scheme 1.3) [11]. With cobalt (but also with rhodium) both the tetra and tricarbonyl complexes are considered as catalysts (Scheme 1.2). It is thought that the coordinatively unsaturated complex $\text{HCo}(\text{CO})_3$ is more active than $\text{HCo}(\text{CO})_4$. Moreover, because of different steric congestions of the metal center, it is assumed that both complexes have different regiodiscriminating propensities for the formation of transient alkyl complexes and, consequently, for the formation of isomeric aldehydes. Therefore, the effects that have been observed at different CO partial pressures can be best explained by assuming the formation of $\text{HCo}_3(\text{CO})_9$ in a solution containing $\text{HCo}(\text{CO})_4$ and its precursor $\text{Co}_2(\text{CO})_8$ under hydrogen [12]. $\text{HCo}_3(\text{CO})_9$ reacts with hydrogen to form $\text{HCo}(\text{CO})_3$ [13]. The latter is more



Scheme 1.2 Competition between isomerization and hydroformylation in relation to CO pressure.

active in isomerization and, consequently, forms more isomeric aldehyde as a final product.

In comparison to $\text{HCo}(\text{CO})_4$, the rhodium congener has a greater tendency to liberate one CO ligand [14]. In other words, the equilibrium in Scheme 1.3 is less markedly displaced to the left-hand side in comparison to the cobalt-based system.

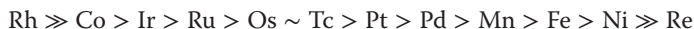


Scheme 1.3 Equilibrium of catalytically active hydrido carbonyl complexes.

Bearing in mind the greater atomic radius of Rh, it becomes apparent why an unmodified rhodium catalyst generates a greater amount of branched aldehydes in comparison to the cobalt congener. For example, in the hydroformylation of 1-pentene, an *l/b* ratio of only 1.6:1 was found, while with the cobalt complex a ratio of 4:1 resulted. A similar correlation has been qualitatively deduced from reactions mediated by the metal clusters $\text{Ru}_3(\text{CO})_{12}$, $\text{Os}_3(\text{CO})_{12}$, and $\text{Ir}_4(\text{CO})_{12}$. Because of the larger atomic radii of the metals, in hydroformylation these catalysts produce more branched aldehydes than observed in the reaction with $\text{Co}_2(\text{CO})_8$. Unfortunately, most of these results were achieved under different reaction conditions or are difficult to interpret because of low reaction rates and are therefore not strictly comparable.

Polynuclear metal clusters may behave differently in catalysis in comparison to their mononuclear species [15]. Thus, the catalytic activity of $[\text{HRu}(\text{CO})_4]^-$ is superior to that of $[\text{HRu}_3(\text{CO})_{11}]^-$ [6]. Noteworthy, $\text{H}_4\text{Ru}_4(\text{CO})_{12}$ is particularly active in hydroformylation with CO_2 [16].

Currently, with unmodified metal carbonyl complexes, the following trend of hydroformylation activity is accepted (ordered by decreasing activity) [17]:



In subsequent chapters, only hydroformylations with Co, Rh, Ru, Pd, Pt, Ir, and Fe will be discussed in detail. Occasionally also molybdenum complexes (e.g., *mer*-Mo(CO)₃(*p*-C₅H₄N-CN)₃) [18] or osmium complexes (e.g., HOs(κ^3 -O₂CR)(PPh₃)₂) have been investigated [19]. Only recently, HOs(CO)(PPh₃)₃Br was evaluated for the hydroformylation of several olefins [20]. A main concern was the high isomerization tendency (up to 39%) noted.

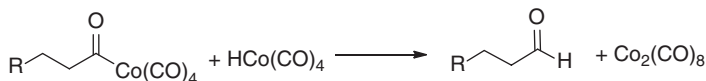
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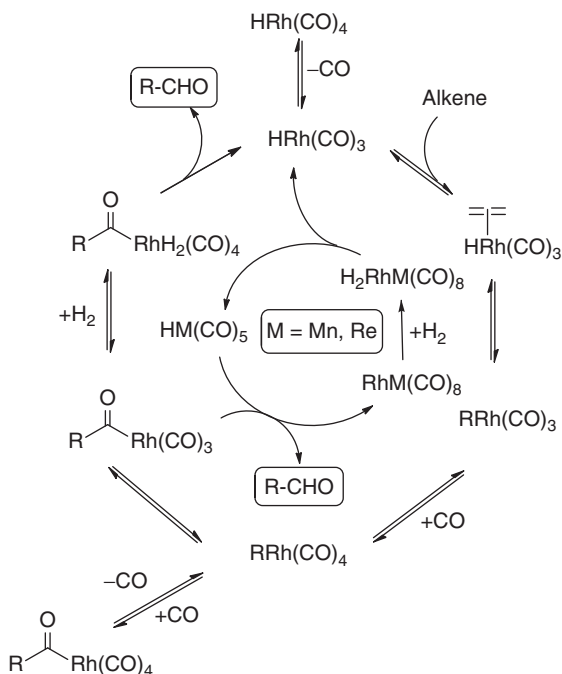
Bimetallic Catalysts

Early investigations with stoichiometric reaction of Co–acyl complexes in the absence of CO or at low CO pressure provided evidence that hydrogenolysis can be assisted by a second cobalt complex (Scheme 1.4) [1].



Scheme 1.4 Support of the hydrogenolysis step by a second catalyst.

This led in turn to the idea to also use combinations of different metals (e.g., Co/Rh, Co/Pt, Co/Fe, Co/Mo, Rh/Fe, Rh/Mn, Rh/Re, Rh/W, Rh/Mo) with the aim of creating synergy effects [2]. In the last decade, especially Garland and coworkers accumulated much evidence through spectroscopic measurements and density functional theory (DFT) calculations that in rhodium-catalyzed hydroformylation of “non-isomerizable” olefins (cyclopentene or 3,3-dimethylbut-1-ene), carbonyl complexes, which are less active in hydroformylation, such as HMn(CO)_5 or HRe(CO)_5 [3], can support the reductive elimination of the aldehyde from



Scheme 1.5 Cooperative effects by means of bimetallic catalysis.

the Rh–acyl intermediate in a second catalytic cycle proceeding in parallel (Scheme 1.5) [4]. As a consequence, the overall rate of hydroformylation is greatly enhanced.

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Effect of Organic Ligands

Organic ligands allow virtually unlimited alteration of the electronic and steric properties of the original carbonyl complex. The σ -donor and π -acceptor properties of the ligand are decisive for the stability of the metal–ligand interactions. Moreover, other ligands at the metal center (CO, H, alkyl, or acyl) can be stabilized or destabilized [1]. In particular, the trans effect of a properly placed counter ligand governs the strength of the opposite M–H or M–CO bond [2]. Therefore, determination of the geometrical structure of catalysts and transient catalytic species is an invaluable advantage and also the subject of numerous studies.

For example, replacement of one CO by stronger σ -acceptor ligands $\text{P}(\text{OPh})_3$ or PPh_3 in the complex $\text{HCo}(\text{CO})_4$ reinforces the Co–H bond and causes a marked decrease in the $\text{p}K_{\text{a}}$ value [3]. In this respect, $\text{HCo}(\text{CO})_3\text{PPh}_3$ ($\text{p}K_{\text{a}} = 6.96$) is comparable with the second dissociation of phosphoric acid ($\text{p}K_{\text{a}} = 6.92$). $\text{HCo}(\text{CO})_3\text{P}(\text{OPh})_3$ ($\text{p}K_{\text{a}} = 4.95$) is similarly acidic to acetic acid ($\text{p}K_{\text{a}} = 4.95$). In spite of the problems in the exact determination of the $\text{p}K_{\text{a}}$ values in several solvents [4], $\text{HCo}(\text{CO})_4$ is by far the most acidic compound among these complexes, comparable with some mineral acids such as HI, HBr, or H_2SO_4 [5]. As a beneficial side effect, phosphorus-modified Co complexes are thermally more stable than $\text{HCo}(\text{CO})_4$.

A similar effect was attributed to the SnCl_3^- ligand in platinum-catalyzed hydroformylation. Because of its inherent trans effect, SnCl_3^- activates the Pt–H bond and thus facilitates its insertion into the olefin [6]. The same, but less pronounced effect was found by quantum chemical calculations for the migratory insertion of CO into the Pt–alkyl bond [7].

Because of the properties of organic ligands, the whole catalytic cycle can be accelerated or, in the worst case scenario, totally blocked. Consecutive or side reactions may be favored. Modification of cobalt catalysts with phosphines not

only improves thermal stability but also decreases hydroformylation activity. Moreover, hydrogenation of the olefin becomes a serious issue. Also, phosphorus ligands in rhodium catalysts contribute to the stability, but, in contrast to cobalt, a generally dramatic enhancement of the hydroformylation rate results. Trialkylphosphines support the formation of alcohols as major hydroformylation products.

The number of coordinated organic ligands decisively influences the space in the environment of the metal. This situation affects not only the activity but also the regiodiscriminating ability of the catalyst. Stereodifferentiation can be achieved with the proper choice of the chiral ligand. In hydroformylation, trivalent phosphorus ligands have been used preferentially (see Section 2.1) [8]. Broad academic research was also dedicated to the use of carbenes (see Section 2.5) [9]. Occasionally, also arsines and, less often, stibines have been tested or claimed in patents [10]. Special N ligands, such as amines or nitrogen-bearing heterocycles (e.g., 2,2'-bipyridines, 1,10'-phenanthroline), have been employed to modify the catalytic properties of $\text{Ru}_3(\text{CO})_{12}$ [11] or $\text{Mo}(\text{CO})_6$ [12]. In a few instances, η^5 -cyclopentadienyl and η^6 -arene ligands have been likewise utilized successfully [13]. A striking example is the replacement of one of the ligated hydrogens by cyclopentadienyl ligands (Cp or Cp^*) in Ru(II) complexes, leading to reduced hydrogenation activity of the resulting complex (Figure 1.1) [14].

The effect of ligand modification depends not only on the electronic and steric properties but also on the number of organic ligands in the coordination sphere of the metal. Appropriate organic ligands can displace coordinated CO in a stepwise manner [15]. The whole complexity is shown by means of the best studied system, namely rhodium catalysts based on trivalent phosphorus ligands (Scheme 1.6). A “volcano” curve lucidly describes the dependence of the reaction rate on the phosphor/rhodium ratio [16].

The shift of equilibria depends on the concentration of the ligand, its coordination properties, and the CO partial pressure. For each catalytic system, an optimum has to be identified, in order to avoid catalysis by the unmodified catalyst $\text{HRh}(\text{CO})_4$ (I). On the other hand, with an excess of the organic ligand, CO can be almost completely expelled, and/or the required vacant coordination sites are blocked (V). As a consequence, the rate of hydroformylation decreases. Complexes with one (II) or two phosphorus ligands (III) are considered to be the most active catalysts in hydroformylation. In contrast, three monodentate and one tridentate, respectively, or even two bidentate diphosphorus ligands on rhodium can be efficient in related reactions, such as decarbonylation (see Chapter 8).

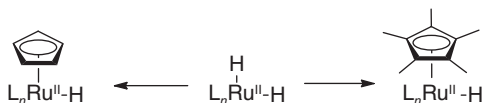
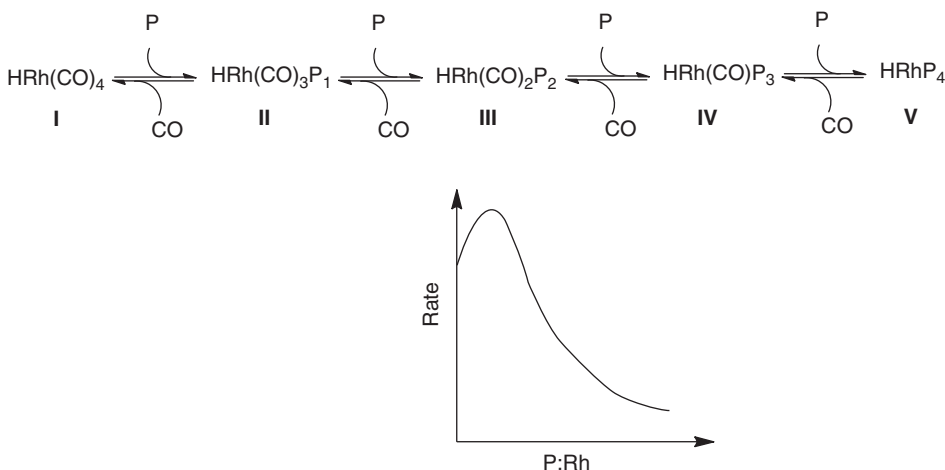


Figure 1.1 Replacement of H by Cp or Cp^* in ruthenium complexes.



Scheme 1.6 Equilibria of hydrido rhodium complexes with different numbers of P ligands and a typical “volcano” curve.

Chelating ligands enhance the tendency for the binding of two ligands at the metal center. By coordinating tridentate ligands, hydroformylation activity may proceed only by dissociation of one ligating group (“arm-off mechanism”) [17].

In general, trivalent phosphorus compounds, arsines, stibenes and several amines improve the thermal stability of hydrido metal–carbonyl complexes because of superior σ -donor and weaker π -acceptor properties [18]. This feature enhances the electron density at the metal center, and hence the metal–CO bond is strengthened as a result of enhanced electron backdonation. However, the special effect of a ligand on the activity and selectivity may be entirely different from one metal to another, and therefore conclusions should be drawn only in close relation to the metal that is used. Only some selected observations will be detailed here, showing the uniqueness of each catalytic system.

Typical examples of different behavior in relation to the metal are trivalent phosphorus ligands. Thus, trials to modify cobalt complexes with PPh_3 proved rather problematic, due to the shift of the equilibrium to the left-hand side, especially under increased CO pressure (Scheme 1.7). As a consequence, the hydroformylation is catalyzed by the unmodified Co complex. Diphosphines of the type $\text{Ph}_2\text{PZPPh}_2$ ($\text{Z} = (\text{CH}_2)_2$, $(\text{CH}_2)_4$, $\text{CH}=\text{CH}$) cause a dramatic decrease in reactivity [19]. Also, phosphites do not form active hydroformylation catalysts with cobalt. It seems that only basic trialkyl phosphines are suitable for the generation of stable Co phosphine hydroformylation catalysts.



Scheme 1.7 Under elevated CO pressure a PPh_3 modified Co catalyst is not stable.

In strong contrast, with rhodium as the metal, not only most triarylphosphines but also even less σ -donating P-ligands, like phosphinites, phosphonites, phosphites, and phosphoramidites, are ideal candidates to form highly efficient catalysts. Under typical hydroformylation conditions, CO does not replace the organic ligand. Monodentate, bidentate, as well as potentially polydentate phosphorus ligands have been tested. Frequently, ligating trivalent phosphorus units have been combined with other ligating groups such as phosphine oxides, ether, and amines in order to achieve hemilabile behavior [20]. The following order of activity in hydroformylation has been concluded with corresponding Rh catalysts in relation to the ligand used [21]:



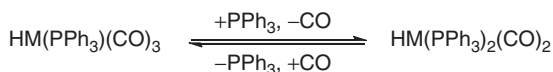
These ligands influence not only the activity and regioselectivity but also chemoselectivity. Rhodium catalysts based on trialkylphosphines exhibit high hydrogenation activity, which allows one-pot hydroformylation–hydrogenation (see Section 5.2). Besides the lower activity in comparison to phosphines, also amines as ligands cause lower chemoselectivity; alkanols as well as alkanes are formed [22]. In a few instances, bridging thiolate ligands have also been used in dinuclear Rh complexes with the hope of generating cooperative effects between both metal centers [23], but it is highly probable that the sulfur ligands do not remain coordinated in the active catalysts [24].

By a comparison of ligands in ruthenium-catalyzed hydroformylation based on elements of the fifth row of the periodic table, the following order of yields was found [25]:



When PPh_3 is coordinated to an appropriate ruthenium precursor, strong hydrogenation activity toward the olefin and the aldehyde is the result [24]. Also heterocyclic N ligands enhance the tendency for the reduction of the aldehyde [26]. In contrast, replacing the phosphine with P(OPh)_3 produces the corresponding aldehydes [27]. The more basic PtBu_3 as a ligand disrupts the hydroformylation almost entirely. Besides mono- and bidentate phosphines, also ruthenium complexes with polydentate phosphines of the type RuCl_2 (tripod) or RuCl_2 (tetraphos), (tetraphos = 1,2-bis[(2-(diphenylphosphino)ethyl)(phenyl)phosphine]ethane) were investigated [28]. As found with ruthenium, but in contrast to rhodium, platinum catalysts with trivalent arsines induce a higher reactivity than the corresponding phosphine ligands [29].

An Ir catalyst hosting only one PPh_3 ligand is more active in hydroformylation than the corresponding complex with two PPh_3 (Scheme 1.8) [30]. Therefore, even a slight excess of PPh_3 or the application of bidentate diphosphines may inhibit the reaction. In contrast, the Rh catalyst operates also fine with two PPh_3 ligands and therefore a reversed dependence on the CO pressure has been found [31]. The relatively high activity of rhodium catalysts with bidentate ligands is eventually the preconditions to run hydroformylation with high *n*-regio- and stereoselectivity.



M = Ir, Rh

Scheme 1.8 Influence of an excess of CO or PPh₃ on the shift of Ir and Rh complexes.

A ruthenium catalyst based on PnBu_3 proved to be less active than the unmodified complex [32]. In contrast, and as found with rhodium, a modification with PPh₃ or P(OPh)₃ led to a dramatic increase in reactivity. Addition of PPh₃ to the intrinsically poorly active $\text{Fe}(\text{CO})_5$ markedly increases the yield of aldehydes [33]. The same effect could be achieved by the direct use of $\text{Fe}(\text{CO})_3(\text{PPh}_3)_2$ or $\text{Fe}(\text{CO})_4\text{PPh}_3$.

Also, homo and heterometallic carbonyl clusters can benefit from the presence of phosphine ligands. A catalyst generated from $\text{Ru}_3(\text{CO})_{12}$ and bulky diphosphines was more active in the hydroformylation of ethylene or propylene than $\text{Ru}_3(\text{CO})_{12}$ [34]. A mixed Rh/Ru cluster modified with chelating diphosphines led to improved regioselectivity [35]. The precondition for successful hydroformylation with $\text{Os}_3(\text{CO})_{12}$ is the specially designed P₂O ligands [12].

By incorporating ligating groups in dendrimers or polymers and subsequent metal catalyst formation, new structures are formed with sometimes less assignable constructions. It should be remembered that inorganic or organic matrices can also alter the catalytic properties of an embedded catalyst.

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1.4

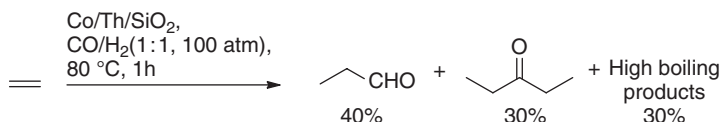
Cobalt-Catalyzed Hydroformylation

1.4.1

History and General Remarks

The cobalt-catalyzed reaction is directly linked to the discovery of the hydroformylation (“oxo-reaction”) by Otto Roelen. In a patent filed in the year 1938, titled “Verfahren zur Herstellung von sauerstoffhaltigen Verbindungen” [1],

which was published in the German version only in 1951 [2], Roelen claimed the reaction of ethylene with syngas in the presence of a silica-based cobalt–thorium contact, which was pretreated with hydrogen (Scheme 1.9). As main products, propionaldehyde and diethylketone were obtained. Moreover, in the same patent the conversion of propylene, acetylene, turpentine, oleyl alcohol, and oleic acid with the same heterogeneous cobalt catalyst and water gas was described.



Scheme 1.9 Discovery of the hydroformylation by Otto Roelen.

Already in 1953, the first plant for the production of butyraldehyde through Co-catalyzed hydroformylation of propylene went on stream at Ruhrchemie AG in Germany. To this time, the focus of the hydroformylation research mainly in industry was dedicated to cobalt carbonyls as catalysts. A first and to date one of the most comprehensive reviews on this issue was given by Cornils in 1980 [3]. Attention was given to various attempts to establish a complete catalytic cycle including characterization of potential intermediates. Moreover, the dependence of activity and regioselectivity of the hydroformylation of unfunctionalized olefins on typical reaction parameters such as temperature, H_2 and CO partial pressures, solvent effects, promoters, poisons as well as concentration of the catalyst and substrates were analyzed. Also, first conclusions on the effect of modifying ligands, mainly phosphines, phosphites, arsines, and pyridines, were drawn. Some methods of heterogenization were also considered. Because of the great competence of the author in the interface between academic and applied research, several industrial approaches were analyzed together with their particular features such as the generation of the catalyst and final removal of the metal. Also, some comparisons to the behavior of other catalytically active metals can be found in this survey.

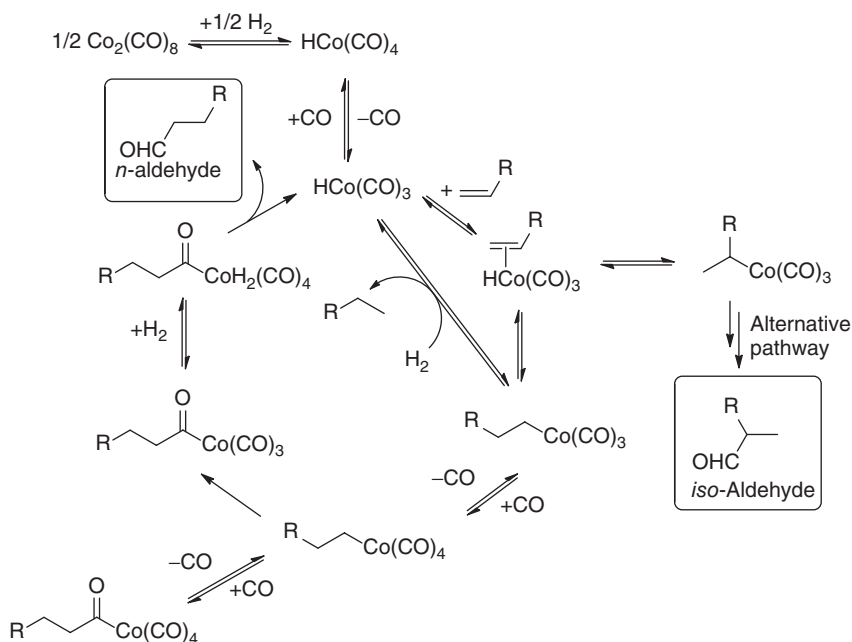
Because of the steadily increasing importance of the rhodium-catalyzed reaction, later reviews on hydroformylation mentioned the cobalt-based version only at the edge. Nevertheless, investigations concerning the mechanism fascinate chemists even now. In 2004, researchers of Sasol reviewed the tendencies and new findings concerning the investigation of the mechanism via high pressure *in situ* nuclear magnetic resonance (NMR) and infrared (IR) spectroscopy [4]. An overview of the mechanistic aspects was given by Hebrard and Kalck in 2009 [5].

1.4.2

The Mechanism, Catalysts, and Ligands

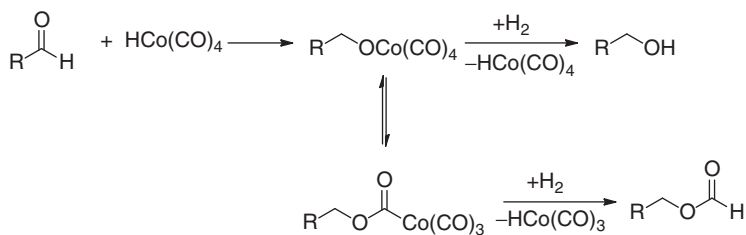
It is interesting to note that the original mechanism for the hydroformylation of monoolefins (1-pentene, methyl acrylate) suggested by Heck and Breslow [6]

in 1960 is still valid (Scheme 1.10). Single steps were refined mainly by spectroscopic and theoretical methods and by considering alternative substrates (e.g., 1,3-butadiene or propene) [7]. In the first step, the catalytically active $16e^-$ species $\text{HCo}(\text{CO})_3$ is formed from $\text{HCo}(\text{CO})_4$ by loss of one CO. Subsequent coordination of the olefin leads reversibly to the formation of two isomeric Co–alkyl complexes [7c,d]. The branched alkyl intermediate affords finally the branched (*iso*) aldehyde, whereas the linear Co–alkyl complex leads directly to the linear product. Upon the effect of hydrogen, the transient alkyl complexes can undergo as a side reaction Co–C bond hydrogenolysis to afford the alkane. In the desired continuation of the hydroformylation mechanism, a fourth CO is ligated to the cobalt center to give a penta-coordinated alkyl complex. CO insertion leads to the corresponding Co–acyl complex. In the presence of an excess of CO, a penta-coordinated acyl complex is formed, which can be considered as a “dormant state” of the catalytic cycle [8]. Addition of hydrogen leads to a cobalt dihydride, which collapses under the liberation of the product aldehyde and catalyst. Under typical catalytic reaction conditions, only $\text{Co}_2(\text{CO})_8$ and $\text{HCo}(\text{CO})_4$ are observable.



Scheme 1.10 Mechanism of cobalt-catalyzed hydroformylation with an unmodified Co catalyst. (Adapted from Ref. [6, 7e].)

Co-catalyzed hydroformylation is closely associated with the fast hydrogenation of the formed aldehyde to give the relevant alcohol (see Section 5.2.2.5.1) (Scheme 1.11) [9]. Its formation can be explained by the addition of $\text{HCo}(\text{CO})_4$ to the aldehyde, followed by reaction of the formed alkoxy–Co complex with



Scheme 1.11 Formation of alcohols and formate esters in Co-catalyzed hydroformylation.

hydrogen. CO insertion into the alkoxy-metal bond and the subsequent hydrogenolysis yields the corresponding formate ester as side product [10].

$\text{HCo}(\text{CO})_4$ can be prepared directly from $\text{Co}_2(\text{CO})_8$ under hydroformylation conditions [11]. Alternatively, other precursors, particularly water-soluble salts such as $\text{Co}(\text{OAc})_2$, $\text{Co}(\text{HCOO})_2$, or $\text{Co}(\text{ethylhexanoate})_2$, have been suggested for technical scale processes. These Co^{2+} salts are reduced to Co^+ under the effect of H_2 . The catalyst formation can be accelerated by the addition of aqueous non-miscible alcohols such as 2-ethylhexanol or isononanol [12]. The generation from water-soluble Co^{2+} salts is especially useful for the preparation of cobalt catalysts anchored on heterogeneous surfaces [13].

In technical processes, the Co catalyst is frequently oxidized after completion of the hydroformylation with oxygen or air to give Co^{2+} salts [14]. The latter can be easily extracted with water (“decobalting”) [15].

In general, the mechanism depicted in Scheme 1.10 is also valid for phosphine-modified Co catalysts [4, 5, 16]. Noteworthy, the formation of the prototypic catalyst $\text{HCo}(\text{CO})_3\text{L}$ from $\text{Co}_2(\text{CO})_6\text{L}_2$ [with $\text{L} = \text{P}(n\text{Bu}_3)$] is less favored than the hydrogenation of (unmodified) $\text{Co}_2(\text{CO})_8$ under hydroformylation conditions at $75\text{--}175^\circ\text{C}$ [17].

In general, organic ligands such as phosphines, phosphites, or arsines diminish the hydroformylation activity of Co catalysts but allow simultaneously a higher degree of linear regioselectivity in comparison to the unmodified catalyst. Moreover, phosphine ligands enhance the hydrogenation activity of the catalyst and, consequently, the hydrogenation of aldehydes to alcohols takes place. This is frequently desired. A high CO pressure displaces the phosphorus ligand and shifts thus the equilibrium in favor of the unmodified Co catalyst with its typical catalytic properties (Scheme 1.12).



Scheme 1.12 Shift of the equilibrium in dependence of the presence of phosphines or enhanced CO partial pressure.

In terms of complex stability, phosphines with strong σ -donor properties are advantageous. Noteworthy, the pK_a value of tertiary phosphines correlates indirectly with the rate of the hydroformylation [18]. Thus, the coordination of

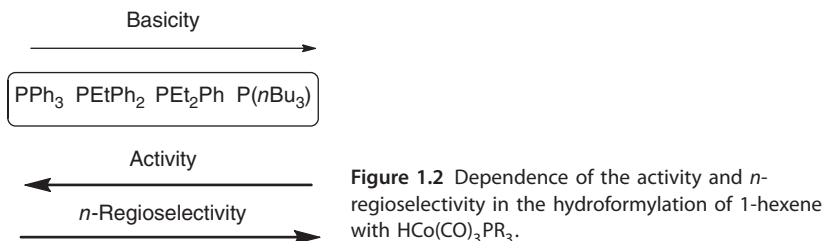


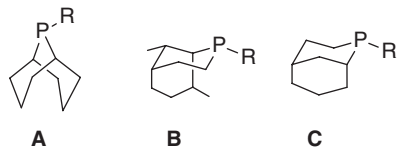
Figure 1.2 Dependence of the activity and *n*-regioselectivity in the hydroformylation of 1-hexene with $\text{HCo}(\text{CO})_3\text{PR}_3$.

PPh_3 leads to the most active Co catalyst (Figure 1.2). On the other hand, the *l/b* ratio of the relevant catalyst is inferior. In order to counteract the drop in activity and to benefit from the superior regioselectivity of strong basic phosphines, a higher temperature must be applied for the hydroformylation, which is possible due to the higher thermal stability of ligand-modified Co catalysts. In this respect, $\text{P}(n\text{Bu}_3)$ has emerged as one of the most favored ligands also on the technical scale (Shell process).

More stable and selective alternatives for such simple trialkylphosphines are isomeric or homologous phosphabicyclo[3.3.1]nonanes of types **A–C** (Figure 1.3), intensively investigated by researchers at Shell and Sasol [19–21]. Such bulky phosphines assist in the generation of the active catalyst from the precatalyst as well as at the level of the Co–acyl complex by enhancement of the dissociation of one CO ligand due to the relief of steric congestion [22].

Diphosphines of the type $\text{Ph}_2\text{PZPPh}_2$ ($\text{Z} = (\text{CH}_2)_2$, $(\text{CH}_2)_4$, $\text{CH}=\text{CH}$) cause a drastic decrease in reactivity [23]. Interestingly, the concomitant isomerization of the olefin is suppressed almost exclusively. Recently, also phobanes have been synthesized, bearing a phosphine oxide moiety as a second weakly coordinating ligating group [24]. For lab-scale applications, the required modified precatalyst can be prepared by the reaction of $\text{Co}_2(\text{CO})_8$ with the phosphine in a mixture of 2-ethylhexanoic acid and a solution of KOH/ethanol under syngas [25]. This method gives a mineral spirit-free Co–ethylhexanoate as the intermediate, which is the cobalt source usually employed in industrial applications.

The hydroformylation with Co catalysts modified with sulfonated phosphines (e.g., TPPTS (trisodium salt of 3,3',3''-phosphinidynetris(benzenesulfonic acid))) in water may be advantageously utilized for the recycling of the metal [26]. Residual cobalt concentrations of 6–70 ppm are left in the organic phase finally. Such

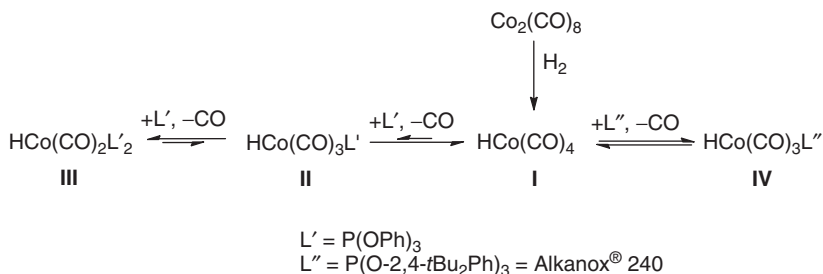


A = 9-Phosphabicyclo[3.3.1]nonanes (Phobanes)
B = 8,9-Dimethyl-2-phosphabicyclo[3.3.1]nonanes (LIM)
C = 2-Phosphabicyclo[3.3.1]nonanes (VCH)

Figure 1.3 Bicyclic phosphines used as standard ligands in Co-catalyzed hydroformylation.

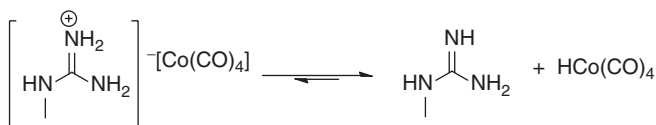
water-soluble Co precatalysts have been prepared by mixing $\text{Co}_2(\text{CO})_8$ and double the amount of the phosphorus ligands. Alternatively, $\text{CoCl}_2(\text{TPPTS})$ has been used [27], which can be synthesized from CoCl_2 and TPPTS in hot ethanol [28]. For a better solubilization of longer olefins, chemically modified cyclodextrines have been suggested by the Monflier group [29].

$\text{HCo}(\text{CO})_2[\text{P}(\text{OPh})_3]_2$ (**III**, Scheme 1.13), which can be prepared starting from $\text{Co}_2(\text{CO})_8$ by treatment with H_2 and subsequent addition of two phosphite ligands to $\text{HCo}(\text{CO})_4$ (**I**), was able to isomerize 1-pentene into 2-pentene [30]. Surprisingly, the corresponding complex $\text{HCo}(\text{CO})_3[\text{P}(\text{OPh})_3]$ (**II**), which was observed only in small amounts in the equilibrium, displayed a poor hydroformylation activity. By the application of the sterically more demanding ligand Alkanox[®] 240, the complex **IV** bearing only one phosphite could be selectively generated [31]. But also this complex turned out to be a very sluggish hydroformylation catalyst. This is in remarkable difference to rhodium-catalyzed hydroformylation where such monophosphites induce superior activities.



Scheme 1.13 Formation of phosphite-based cobalt complexes.

Rieger and coworkers [32] based ionic liquids on $[\text{Co}(\text{CO})_4]^-$ as anion. Preconditions for the success of the subsequent hydroformylation was the presence of strong Brønsted acids in the cation, such as *N*-methyl guanidinium, which are able to shift the protonation equilibrium in favor of $\text{HCo}(\text{CO})_4$ (Scheme 1.14).



Scheme 1.14 Generation of an active hydroformylation catalyst by protonation of $[\text{Co}(\text{CO})_4]^-$ with the cation of an ionic liquid.

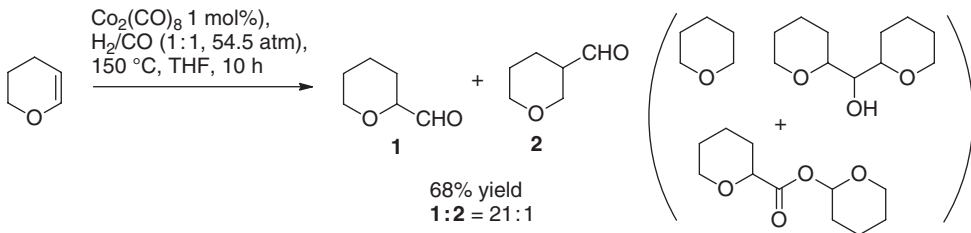
1.4.3

Some Recent and Special Applications

Besides the hydroformylation of common olefins in a large technical scale, also some special applications account for the use of cobalt catalysts. Occasionally, the

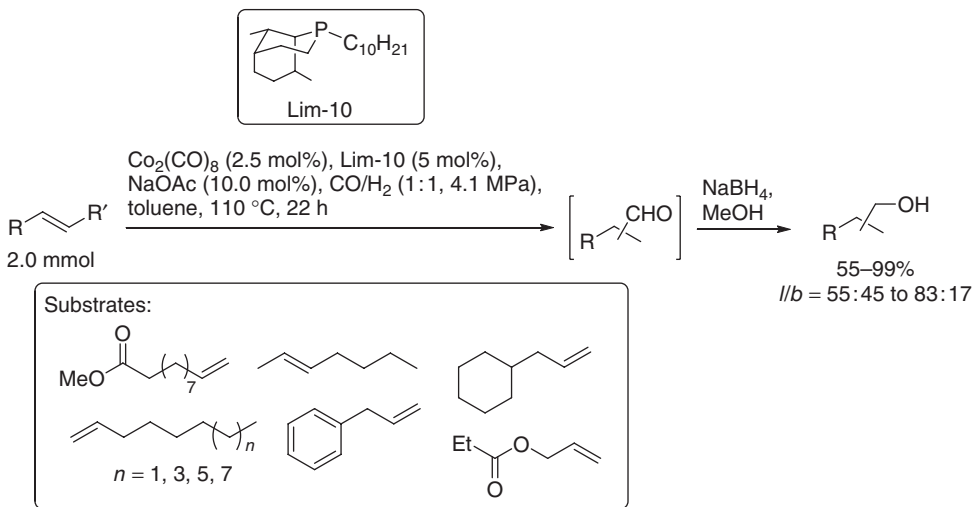
acidic properties of hydrido cobalt complexes have been used for the generation of substrates for hydroformylation.

In 2013, Arias *et al.* [33] investigated the hydroformylation of 3,4-dihydro-2H-pyran (Scheme 1.15). Mainly the 2-formyl product was formed. 3-Formyl-tetrahydropyran and some other side products, such as tetrahydropyran or bis(tetrahydro-2H-pyran-2-yl)methanol, also were formed in much less amounts. Interestingly, no alcohol was found. Addition of PPh₃ decelerated the reaction.



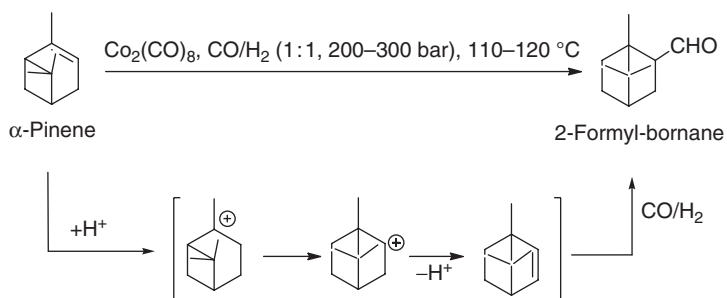
Scheme 1.15 Hydroformylation of dihydropyran with an unmodified Co catalyst.

In a recent study, the group of Alper gave an optimized protocol for the one-pot hydroformylation–hydrogenation reaction of several olefins under less severe pressure conditions (Scheme 1.16) [25]. Yields of up to 99% and moderate regioselectivities were achieved.



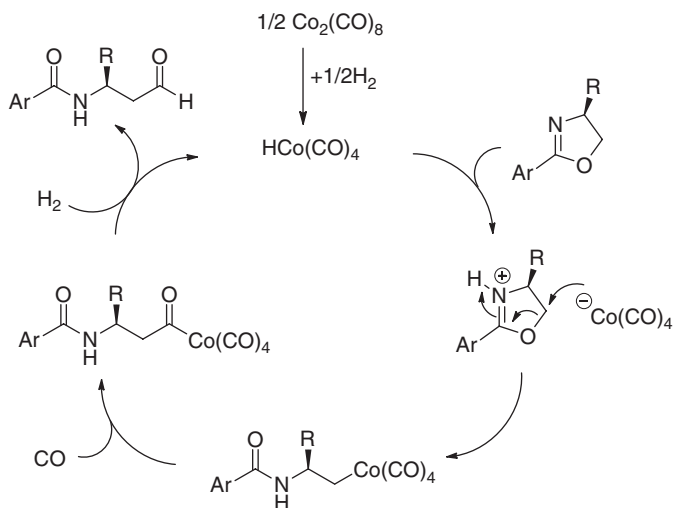
Scheme 1.16 One-pot cobalt-catalyzed hydroformylation–hydrogenation.

The acidic properties of $\text{HCo}(\text{CO})_4$ may lead to rearrangement reactions prior to hydroformylation. Thus, treatment of optically pure α -pinene with syngas gave mainly 2-formyl-bornane (Scheme 1.17) [34]. The Wagner–Meerwein rearrangement can be rationalized by the effect of the acid.



Scheme 1.17 Acid-catalyzed isomerization and subsequent hydroformylation of α -pinene (in the original reference, optical rotations (–) and (+) are not correct and therefore not indicated here).

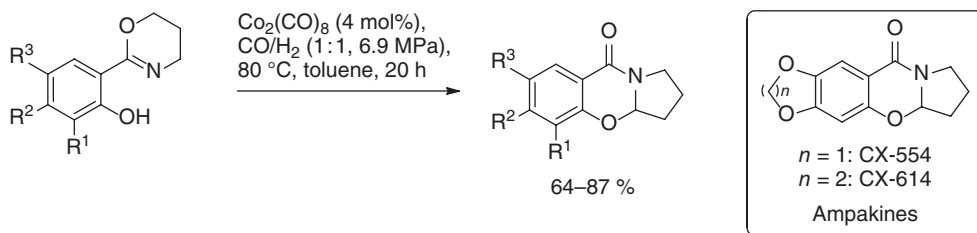
Another method drawing likewise benefit from the acidic properties of $\text{HCo}(\text{CO})_4$ was developed by the group of Coates over the past years (Scheme 1.18) [35]. In the first step, the hydrido complex protonates the nitrogen atom of 2-aryl-1,3-oxazoline. Ring opening and subsequent establishment of a Co–alkyl bond leads to a common metal–alkyl complex. Upon migratory insertion of CO, the Co–acyl complex is formed, which undergoes hydrogenolysis to deliver β -aminoaldehydes. Simultaneously the catalyst is regenerated.



Scheme 1.18 Ring-opening hydroformylation of 1,3-oxazolines.

Recently, this methodology was extended to the synthesis of ampakines, a group of compounds for treatment of Alzheimer's or Parkinson's disease starting from related dihydrooxazines (Scheme 1.19) [36].

Noteworthy, $\text{Co}_2(\text{CO})_8$ gives also promising results in the hydroformylation of ethylene oxide under the conditions where amines, diamines, or amides



Scheme 1.19 Hydroformylation of dihydrooxazines as a method for the preparation of ampakines.

were added [37]. Especially, the Co-catalyzed hydroformylation of oxiranes with $\text{HCo}(\text{CO})_4$ came again in the focus of research recently (see Section 6.3).

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1.5

Rhodium-Catalyzed Hydroformylation

1.5.1

History and Technical Importance

Rhodium, besides cobalt, is the only metal that is used in technical-scale hydroformylation. Because of the classification of industrial hydroformylation processes made by Cornils [1], with rhodium, the third generation, after two generations of Co-based hydroformylation, process was ushered. The first plants went on stream in the 1970s (1974: Ruhrchemie (nowadays Celanese); 1976: Union Carbide Corporation (nowadays Dow); 1978: Mitsubishi Chemical Corporation). These units operate with P-ligand-modified Rh catalysts at low

syngas pressure (1.8–6.0 MPa) and medium temperatures (85–130 °C). These low-pressure oxo-processes (LPOs) are still state of the art and are carried out at numerous large companies. Preferentially, short, unfunctionalized olefins are used as substrates. About 70% of the total hydroformylation capacity, which concerns the transformation of ethylene, propene, and butenes, is based on LPOs with rhodium.

One of the main differences is the technology used to separate the product and the catalyst with the aim of reusing the metal. Wiese and Obst have estimated the annual financial loss in a 400 kt plant when just 1 ppm Rh/kg product is lost at several million euros [2]; therefore efficient catalyst recycling is indispensable. It may be achieved by stripping off the low-boiling product with an excess of syngas (“gas recycling”). The technology is limited to the hydroformylation of alkenes up to pentene. An alternative, more recently developed separation process is based on the destillative removal of the products (“liquid recycling”). The catalyst remains in the residue, consisting of high-boiling condensation products, and is used for the next run. This technology can also be employed in the work-up procedure in the hydroformylation of alkenes with chain lengths greater than C_6 . The lifetime of a catalyst charge may exceed 1 year if sufficient purity of the feed and careful process control are guaranteed.

An aqueous two-phase hydroformylation went on stream at Ruhrchemie AG in 1984 (fourth generation) at their site in Oberhausen/Germany with an annual capacity of 100 kt/a [1]. The current capacity is 500 kt/a. The Rh catalyst is immobilized in the aqueous phase. A sulfonated phosphine ligand (TPPTS, trisodium salt of 3,3',3''-phosphinidynetris(benzenesulfonic acid)) confers the metal catalyst with high solubility in water. The catalyst is removed into the aqueous phase before distillation of the product, which avoids thermal stress. The loss of rhodium is in the range of parts per billion.

Homogeneous unmodified or ligand-modified rhodium catalysts are predominantly utilized for the transformation of olefins with a chain length $\leq C_{10}$. Such Rh catalysts can be up to 1000 times more active than Co catalysts. The major advantages of rhodium catalysis are the reduced syngas pressure and lower reaction temperatures. These features have also been recognized by the chemical industry. Thus, in 1980 less than 10% of hydroformylation was conducted with rhodium, and by 1995 this had been increased to about 80% [3]. In some cases, a combination of Co and Rh can be advantageous [4].

The main problem of rhodium has been its high and very volatile price over the years. The price on the world market is dictated by the automotive industry, which consumes approximately 80% of the metal in catalytic converters for vehicles.

Because of the large success of the technical application of rhodium-based hydroformylation, the associated industrial and academic research is also mainly focused on this metal. By a rough estimate of the publishing activities over the last decade, it can be concluded that more than 80% of all publications and patent activities summarized under the keyword “hydroformylation” are connected in any form with the use of rhodium.

1.5.2

Catalyst Precursors

Unmodified and ligand-modified rhodium complexes are used even today [5]. As precursors for catalysts, numerous complexes use rhodium in the oxidation states 0, I, II, or III.

Especially in earlier times, the cheapest rhodium salt RhCl_3 was employed. Occasionally, also Rh_2O_3 [6], $\text{Rh}(\text{OAc})_3$ [7], $\text{Rh}(\text{2-ethyl hexanoate})_3$ [8], $\text{Rh}_2(\text{SO}_4)_3$ [9], and $\text{Rh}(\text{NO}_3)_3$ [10] have been suggested (or at least claimed in patents) among others for the preparation of water-soluble or heterogenized catalysts.

Rhodium(III) chloride is derived from Na_3RhCl_6 , a product directly obtained in the separation process of rhodium from the other platinum-group metals (Scheme 1.20). The sodium salt is converted into H_3RhCl_6 by ion exchange chromatography. Recrystallization of the salt from water affords the hydrated trichloride, sometimes called *soluble rhodium trichloride* because of its superior solubility in comparison to anhydrous RhCl_3 [11]. The reaction of RhCl_3 with substituted 1,3-ketones yields the corresponding 1,3-oxopropenolate complexes [12], for example, $\text{Rh}(\text{acac})_3$ (acac = acetylacetonate) [13]. Stepwise replacement of the chloro ligands by acac and acetate seems to be likewise possible [14]. Dimeric rhodium(II) acetate can be prepared under reducing conditions by heating rhodium(III) chloride in acetic acid (Scheme 1.20) [15].



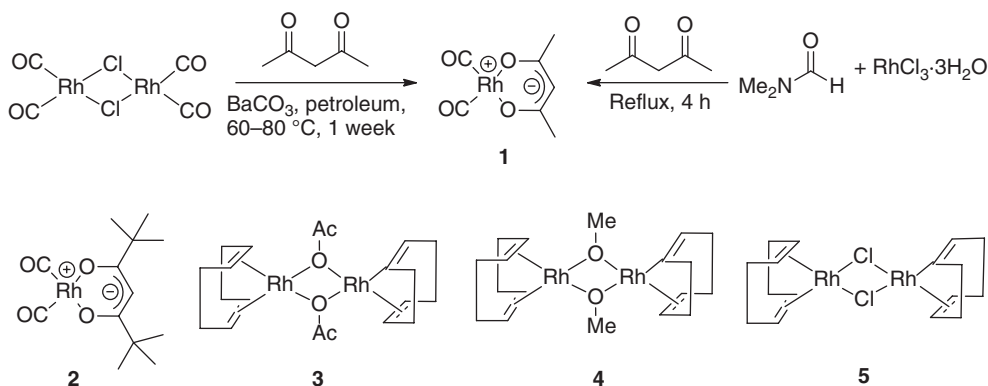
Scheme 1.20 Preparation of rhodium catalyst precursors via RhCl_3 .

Especially in comparison to the later developed $\text{Rh}(\text{I})$ precatalysts, the corresponding catalysts generated from $\text{Rh}(\text{III})$ sometimes turned out to be less active and were characterized by a strong isomerization activity toward the starting olefin [16]. In general, the replacement of chloro ligands by hydrogen is not favored, and therefore the use of amines is usually recommended as scavenger for the formed HCl . Only recently the potential of $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ for the generation of $\text{Rh}(\text{0})$ nanoparticles in the framework of asymmetric hydroformylation or for the immobilization on silicates was rediscovered [17].

Sometimes, also polynuclear clusters such as $\text{Rh}_4(\text{CO})_{12}$ or $\text{Rh}_6(\text{CO})_{16}$ were submitted to the formation of rhodium catalysts [18]. Metallic rhodium embedded in inorganic materials (carbon, Al_2O_3) was tested for mini-plant manufacturing. In this context, the frequently phosphorus ligands [PPh_3 , $\text{P}(\text{OPh})_3$] were added with the intention to detach rhodium from the heterogeneous layer (activated rhodium catalyst = ARC) [19, 20]. More recently, ligand (Xantphos, PPh_3 , BIPHEPHOS)-modified or unmodified rhodium(0) nanoparticles were used as catalyst precursors for solventless hydroformylation [21]. It is assumed that under the reaction conditions these metal nanoparticles decompose and merge into soluble mononuclear Rh species, which in turn catalyze the hydroformylation.

Today, for technical-scale hydroformylation, besides rhodium(II) acetate [18, 22], other carboxylates are recommended, including rhodium formate [23], isobutyrate [24], octanoate [25], or nonanoate [26]. These salts can be manufactured by anion exchange from rhodium(II) acetate. In particular, the corresponding bis(2-ethyl hexanoate) is a frequently employed precursor [27]. The anion can be derived in almost unlimited quantity by the oxidation of 2-ethyl hexanol (2-EH) [28], one of the largest products manufactured via a hydroformylation process.

Currently, in most lab-scale hydroformylation reactions, $\text{Rh}(\text{acac})(\text{CO})_2$ (**1**, Scheme 1.21) is employed, which is particularly useful for the generation of phosphorus-modified catalysts [29]. It can be prepared either from a CO-containing precursor such as $[\text{Rh}(\mu\text{-Cl})(\text{CO})_2]_2$ in the reaction with acetylacetone in the presence of a base [30] or by refluxing $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ in acetylacetone with *N,N*-dimethylformamide (DMF) as the CO donor [31]. The latter reaction may benefit from the effect of ultrasound [32]. By the subsequent addition of phosphorus, ligand-modified precatalysts are obtained [32, 33]. Noteworthy, studies by Poliakoff and George gave evidence that also $\text{Rh}(\text{acac})(\text{CO})_2$ alone reacts with olefins in the absence or presence of hydrogen to give complexes of the type $\text{Rh}(\text{acac})(\text{CO})(\text{alkene})$ [34]. $\text{Rh}(\text{acac})(\text{alkene})_2$ complexes are likewise known [35]. Under enhanced CO pressure, both complex types undergo, even in the solid state, irreversible formation of $\text{Rh}(\text{acac})(\text{CO})_2$ [34]. For mechanistic studies, occasionally $\text{Rh}(\text{acac})(\text{ethylene})_2$ have been used [36].



Scheme 1.21 Preparation modes of $\text{Rh}(\text{acac})(\text{CO})_2$ and other typical rhodium precatalysts.

Recently, Breit and coworkers [37] showed an influence of activity and enantioselectivity on the metal catalyst precursor employed in the asymmetric hydroformylation of styrene. $[\text{Rh}(\text{NBD})_2]\text{BF}_4$ (NBD = norbornadiene) or $[\text{Rh}(\text{OMe})(\text{COD})]_2$ (COD = 1,5-cyclooctadiene) immediately developed high activity, whereas only with the latter the enantioselectivity could be kept constant. By the application of $\text{Rh}(\text{acac})(\text{CO})_2$, a pre-formation time of several hours was

recommended. Unfortunately, under these conditions a slight loss of optical purity in the product was noted.

Nolte suggested the use of rhodium dicarbonyl dipivaloylmethanate (TMHD = 2,2,6,6-tetramethyl-3,5-heptanedionate, (2)) instead of $\text{Rh}(\text{acac})(\text{CO})_2$, which has a longer shelf-life in solution (Scheme 1.21) [38]. Alternatively, $[\text{Rh}(\mu\text{-OAc})(\text{COD})]_2$ (3) or $[\text{Rh}(\mu\text{-OMe})(\text{COD})]_2$ (4) has been used for the generation of rhodium precatalysts [39, 40]. Numerous pieces of evidence were given that also $[\text{Rh}(\mu\text{-Cl})(\text{COD})]_2$ (5), representing a typical precatalyst for hydrogenation, is suitable, for example, for several tandem reactions as well as for heterogenization of rhodium catalysts [41–43]. It should be noted that under hydroformylation conditions the formation of the hydrido rhodium catalyst from the precursors can take considerable time especially at ambient temperature (below 40 °C: 5–10 h); therefore sometimes an incubation time is recommended [44].

The groups of Kalck [45], Pérez-Torrente and Oro [46], Claver [47], and Gladioli [48] investigated binuclear rhodium complexes with bridging thiolate ligands with the hope of generating cooperative effects between both metal centers (Figure 1.4). Because of the variation of the dithiolate ligands, different geometries (a–c) were assumed, which could be beneficial for the regio- and stereoselective discrimination of the catalyst. However, the coordination of the S-ligands throughout the whole catalytic cycle is controversial in the literature due to the strong competition with CO [49]. Moreover, it should be borne in mind that the use of such malodorous sulfur compounds can be disadvantageous, in particular in the production of aroma compounds. Another problematic aspect is that sulfur compounds may affect the rhodium-catalyzed hydroformylation with heterogenized Rh catalysts [50]. In contrast, studies of the Rosales group with homogeneous complexes $[\text{HRh}(\text{CO})_4]$, $[\text{HRh}(\text{CO})_2(\text{PPh}_3)_2]$, $[\text{HRh}(\text{CO})_2(\text{dppe})]$, and $[\text{Rh}(\text{CO})(\mu\text{-Pz})(\text{TPPTS})_2]$ ($\text{dppe} = 1,2\text{-bis}(\text{diphenylphosphino})\text{ethane}$) did not show any deceleration of the rate in the presence of sulfur compounds in a concentration of up to 2500 ppm [51].

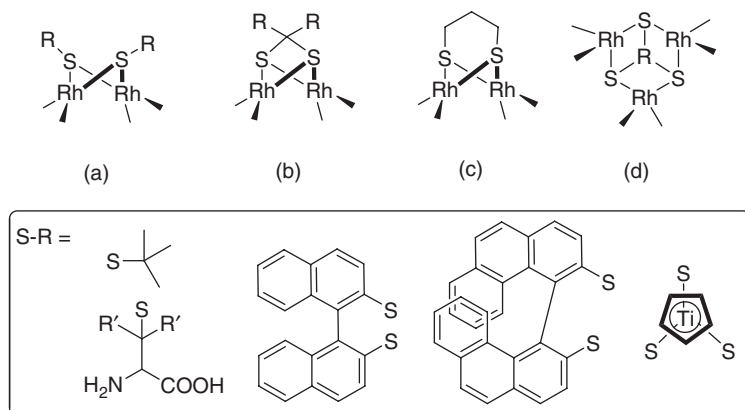
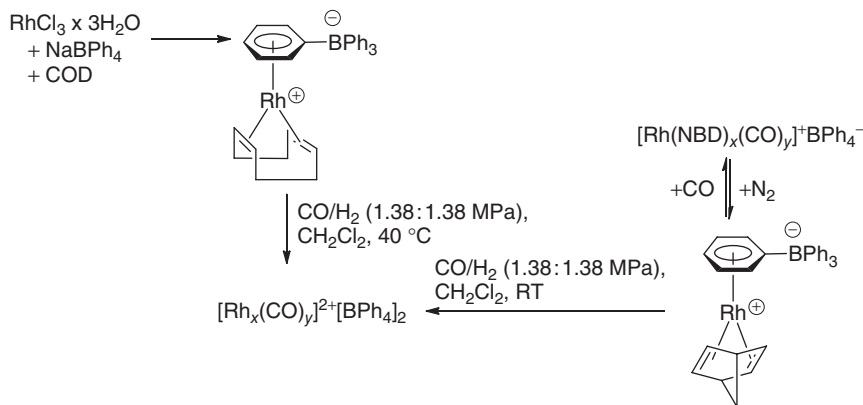


Figure 1.4 Sulfur-bridged polynuclear rhodium clusters and types of thiolate bridges.

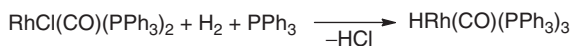
Alper utilized in several investigations zwitterionic Rh complexes (Scheme 1.22). They can be simply prepared by the reaction of rhodium chloride with sodium tetraphenylborate and a cyclic diene in aqueous methanol [52]. Upon the effect of syngas, the diene (COD or NBD) is replaced by CO [53]. NBD is superseded already at room temperature, whereas the substitution of COD required gentle heating. Especially, the COD-based precatalyst was tested in a large variety of hydroformylation reactions [54].



Scheme 1.22 Formation of carbonyl complexes from zwitterionic Rh(BPh₄) complexes.

Usually, ligand-modified precatalysts are generated by the reaction of the metal catalyst precursor with the organic ligand (trivalent phosphorus ligands, N ligands, carbenes). The number of coordinated ligands depends on the nature of the ligands (steric and electronic properties), the ligand/Rh ratio, and the CO partial pressure during hydroformylation. In the catalyst, appropriate bidentate ligands coordinate mainly in a chelating manner at the rhodium center, adopting an equatorial/equatorial (*ee*) or equatorial/axial (*ea*) geometry [55].

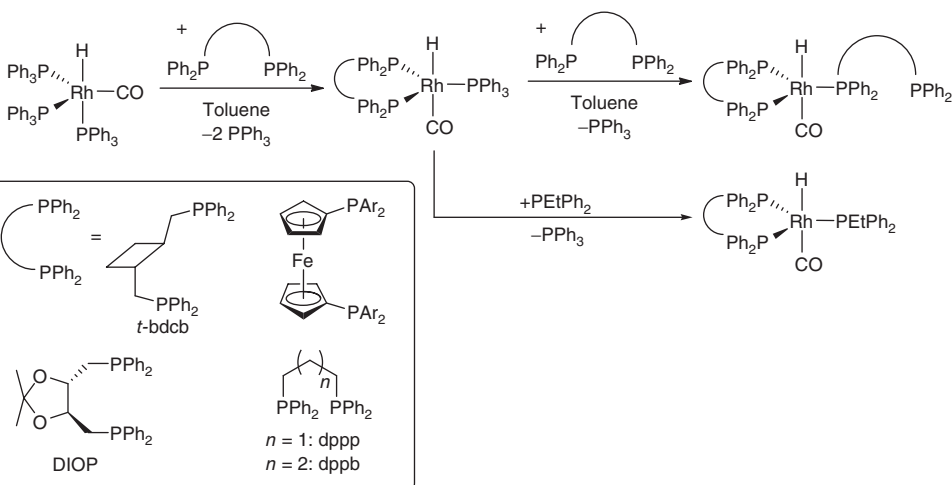
For the catalytic reaction, phosphorus and nitrogen ligands are mostly added in excess to a suitable metal complex. The excess can be avoided with carbene ligands (see Section 2.4). In the presence of syngas, phosphine-modified CO-free rhodium compounds such as the Wilkinson catalyst RhCl(PPh₃)₃ or HRh[(P(OPh₃)₃)₃] can add CO under simultaneous loss of coordinated P ligands [56, 57]. Also, complexes of the type RhX(CO)(PPh₃)₂ (X = Cl, Br, I) are suitable precursors, as exemplarily shown in Scheme 1.23 [58]. Upon the effect of hydrogen/syngas, they are converted into the relevant precatalysts. Hydrogen halide acceptors reduce the



Scheme 1.23 Formation of a phosphine-modified hydrido rhodium complex from RhCl(CO)(PPh₃)₂.

pre-formation time. $\text{HRh}(\text{CO})(\text{PPh}_3)_3$ can be directly submitted to the catalytic reaction [59]. Of course, instead of PPh_3 or $\text{P}(\text{O}i\text{Pr})_3$, also other trivalent phosphorus ligands (e.g., TPPTS) have been used in this connection [60].

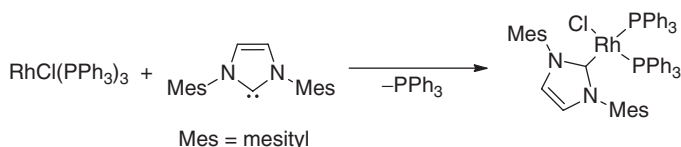
Because of the chelate effect, appropriate diphosphines can replace monodentate phosphines. This method was applied in the framework of hydroformylation to generate the corresponding chelate complexes from $\text{HRh}(\text{CO})(\text{PPh}_3)_3$ (Scheme 1.24) [61]. Noteworthy, also strong basic monophosphines such as PEtPh_2 can substitute ligated PPh_3 .



Scheme 1.24 Replacement of PPh_3 by chelating diphosphines or a strong basic monophosphine.

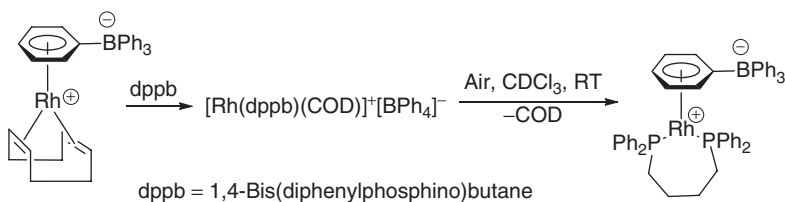
For the decarbonylation of aldehydes, including formaldehyde or paraformaldehyde, occasionally $[\text{Rh}(\text{P}-\text{P})_2]\text{Cl}$ complexes have been suggested (see Chapter 3 and 8) [62]. They can be prepared by mixing $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ with double the amount of the diphosphine. For the same purpose, Rh catalysts bearing tridentate triphosphines were used, which are obtained by the exchange of one coordinated NBD in $[\text{RhCl}(\text{NBD})]_2$ with triphos [63].

Carbenes are able to substitute a ligated PPh_3 in the Wilkinson complex (Scheme 1.25) [64].



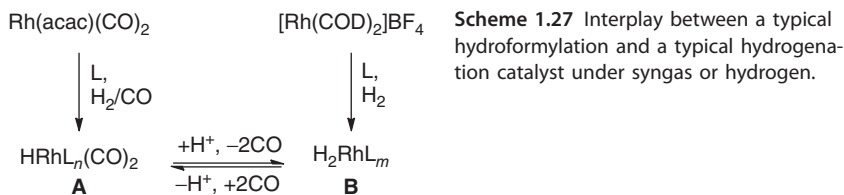
Scheme 1.25 Generation of a carbene complex by substitution of one PPh_3 .

Dioléfins in zwitterionic rhodium complexes can likewise be replaced by chelating phosphines. NMR studies have revealed that cationic rhodium complexes, formed with diphosphines in the first step, lose under air COD and a new zwitterionic complex is formed, as exemplarily shown in Scheme 1.26 [52]. Such complexes have been frequently screened in hydroformylation [65].



Scheme 1.26 Replacement of the diolefin by a chelating diphosphine in a zwitterionic rhodium complex.

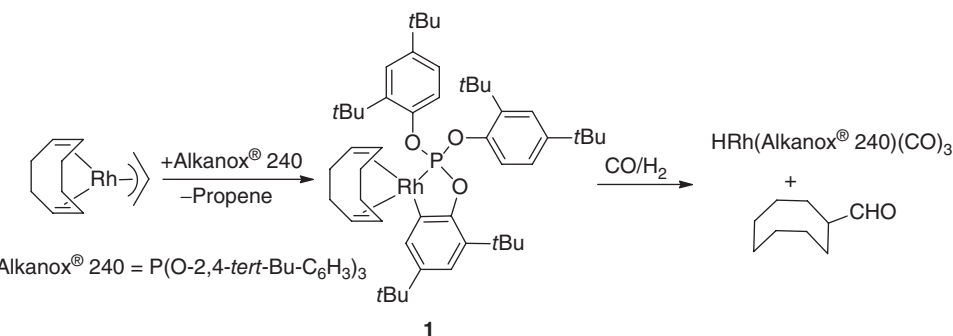
In hydroformylation reactions coupled with a hydrogenation step (e.g., hydroaminomethylation, Section 5.4), the simultaneous use of $\text{Rh}(\text{acac})(\text{CO})_2$ and $[\text{Rh}(\text{COD})_2]\text{BF}_4$ together with a single modifying ligand can be advantageous [66]. The first rhodium complex forms the active hydroformylation catalyst **A**, whereas the second is a precursor of the hydrogenation catalyst **B**. Both are in equilibrium (Scheme 1.27).



Scheme 1.27 Interplay between a typical hydroformylation and a typical hydrogenation catalyst under syngas or hydrogen.

The generation of the catalyst from the precatalyst may lead to the formation of acidic compounds (Hacac, acids, alcohols), which afterward may contribute to the decomposition of ligands bearing P–O bonds. This problem can be circumvented by the use of ortho-metallated rhodium complexes [67]. The organometallic compound **1** based on the monodentate phosphite Alkanox® 240 depicted in Scheme 1.28 is crystalline and can be conveniently stored and handled [68]. Only under syngas (H_2) the desired precatalyst is rapidly liberated through breakage of the Rh–C bond by hydrogenolysis [69]. During the pre-formation reaction, the COD ligand is hydroformylated once, and the second double bond is hydrogenated to produce cyclooctane carbaldehyde.

The ortho-metallation reaction of hydroformylation catalysts has been found to occur also during the distillation of the reaction mixture of a continuously driven hydroformylation reaction. Especially in the presence of excess of olefin and after stripping hydrogen with pure carbon monoxide, the formation of ortho-metallated



Scheme 1.28 Preparation of a modified rhodium catalyst from an ortho-metalated precursor.

rhodium complexes is favored [70]. In this manner, possible decomposition pathways of the catalyst are blocked.

1.5.3

Summary and Conclusions

Currently, a wide range of methods are available to generate active rhodium hydroformylation catalysts from catalyst precursors based on rhodium in oxidation states of 0–III. Because of the almost unmanageable amount of protocols concerning the rhodium-based hydroformylation in the literature, a clear conclusion about the efficiency and duration of catalyst formation processes prior to the hydroformylation is hard to draw. A deeper understanding of these processes occurring prior to the hydroformylation would be of interest in order to distinguish between different catalyst precursors.

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1.6

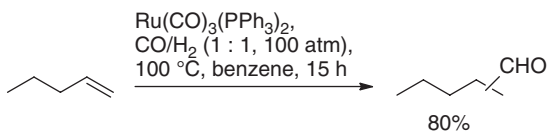
Ruthenium-Catalyzed Hydroformylation

1.6.1

General Aspects

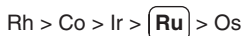
Because of the technical success of rhodium based hydroformylations, it is understandable that since the 1970s the vast majority of academic and industrial investigations in this area dealt with the development of new rhodium catalysts. However, the worldwide demand of rhodium for chemical and technical processes and its enormous price stimulate the search for alternative transition-metal catalysts up to now [1]. A particular focus was given to ruthenium [2].

Pioneering experiments for the application of ruthenium catalysts in homogeneous hydroformylation reactions were published by Wilkinson and coworkers already in 1965 [3]. They tested phosphine-modified Ru complexes in the hydroformylation of 1-pentene in benzene as solvent, such as the insoluble complex $\text{RuCl}_2(\text{CO})_2(\text{PPh}_3)_2$ and the more soluble complex $\text{RuCl}_3(\text{PPh}_3)_3(\text{MeOH})$. Best results were achieved with $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ at 100 atm syngas pressure and 100 °C (Scheme 1.29). Isomeric hexanal was obtained in 80% yield, and the precatalyst could be recovered unchanged after the reaction.



Scheme 1.29 First attempts of Ru-catalyzed hydroformylation.

A comparison of Rh and Ru catalysts in the hydroformylation of linear butenes [4] or the strong electron-deficient substrate 3,3,3-trifluoropropene led to the conclusion that the latter are less active [5]. Moreover, in the hydroformylation of propene in comparison with Co and Rh catalysts, an inferior selectivity was noted [6]. In a competition experiment with the iridium-catalyzed hydroformylation of several α -olefins at 13 bar syngas pressure and 100 °C, a related PPh_3 -modified Ru complex revealed no activity [7]. On the other hand, unmodified ruthenium based catalysts were shown to be more active than osmium complexes [8], thus the following rough order of reactivity results:



Noteworthy, the hydroformylation with cobalt catalysts can draw benefit from the addition of ruthenium [9]. For example, the initial rate of the reaction with cyclohexene was 19 times faster with $\text{Co}_2(\text{CO})_8/\text{Ru}_3(\text{CO})_{12}$ in comparison to the monometallic Co system [10]. By combining the superior hydroformylation properties of a rhodium catalyst with the excellent hydrogenation activity of

a ruthenium catalyst, an excellent hydroformylation/hydrogenation catalyst resulted that produced alcohols [11]. However, because of this pronounced hydrogenation activity the production of alkanes in the hydroformylation reaction may become a serious issue. In order to manage this challenge, a careful choice of the metal precursor, ligand, and reaction conditions is necessary. Because of the varying conditions chosen in the reported hydroformylation protocols, a clear forecast about the reaction products is not possible. In general, elevated temperatures and a high H_2/CO ratio force the hydrogenation.

1.6.2

Catalyst Precursors

As precatalysts, neutral and ionic ruthenium–carbonyl complexes have been tested for hydroformylation. Ru(0), Ru(II), and Ru(III) are suitable depending on the solvent used [3, 12]. Today, the trinuclear cluster $Ru_3(CO)_{12}$ is the most common precursor for the generation of the active catalyst. Replacement of CO by nitrogen or phosphorus ligands allows the modification of the intrinsic catalytic properties of the central metal. Previously, cationic complexes such as $[HRu(CO)(NCMe)_2(PPh_3)_2]BF_4$ have been employed, affording, besides minor amounts of aldehydes, mainly alkanes and alcohols [13]. By the reaction of the latter with carboxylic acid salts, complexes of the type $HRu(\kappa^3-O_2CR)(PPh_3)_2$ are formed. Their hydroformylation activity increased with the pK_a value of the corresponding acid in the order [8]



In the reaction with 1-hexene (cat. (3.3 mol%), $CO/H_2 = 15$ atm, $120^\circ C$, THF (tetrahydrofuran)) a turnover frequency (TOF) of up to $180 h^{-1}$ could be achieved. Occasionally, also cyclopentadienyl complexes such as $[Ru(CO)_2(\eta^5-Cp)]_2$ have been used [14]. Recently, they have seen a renaissance for the optimization of the reductive hydroformylation (see below). For the isomerization–hydroformylation–hydrogenation tandem reaction of internal olefins, the use of $Ru(\text{methylallyl})_2(COD)$ ($COD = 1,5$ -cyclooctadiene) has been shown to be beneficial [15]. In these investigations, $RuCl_3$, $RuCl_2(PPh_3)_3$, $[RuCl_2(CO)_3]_2$, and $[RuCl_2(COD)]_n$ displayed a high hydrogenation activity toward the olefinic substrate.

Neutral $Ru_3(CO)_{12}$ shows a more extended tendency for the isomerization of terminal olefins to 2-alkenes in comparison to the anionic complexes $[HRu(CO)_4]^-$ or $[HRu_3(CO)_{11}]^-$ [16]. The formed aldehydes were immediately reduced to the corresponding alcohols.¹⁾ In contrast, a clean conversion to *n*-butyraldehyde has been observed in the reaction with propene as substrate by

1) With styrene, preferentially the *n*-aldehyde was formed. In the reaction with ethyl acrylate, significant amounts of the dimers, diethyl 2-formyl-2-methylglutarate, and 4-ethoxycarbonyl-4-methyl- δ -valerolactone were obtained.

the assistance of the anionic cluster $[\text{NEt}_4][\text{HRu}_3(\text{CO})_{11}]$ [17]. No alcohol was formed and the catalyst remained after the reaction unchanged in the solution.

Binuclear ruthenium complexes such as $[\text{Ru}_2(\mu\text{-O}_2\text{CR})_2(\text{CO})_4\text{L}_2]$ have been prepared starting from di- μ -acetato diruthenium carbonyls [18]. In the hydroformylation, the presence of an excess of NEt_3 or PPh_3 was mandatory. Superior results were achieved by adding small amounts of water.

Studies comparing the hydroformylation activity of mono- and dinuclear cyclopentadienyl metal complexes, $(\eta^5\text{-Cp})\text{Ru}(\text{CO})_2\text{X}$ ($\text{X} = \text{Cl}, \text{Br}, \text{I}$) and $[(\eta^5\text{-Cp})\text{Ru}(\text{CO})_2]_2$, respectively, emphasized a significant influence of the complex nuclearity on both overall activity and selectivity [19].

There have also been a few attempts to heterogenize ruthenium on solid supports, mainly with the aim to recover the catalyst after the reaction. A heterogeneous hydroformylation catalyst was prepared from $[\text{RuCl}_2(\text{CO})_3]_2$ encapsulated in poly(4-vinylpyridine) (P4VP) and cross-linked with 25% divinylbenzene (DVB) [20]. The hydroformylation of 1-hexene proceeded at 150°C in a solution of NMP (*N*-methylpyrrolidone). Although a high conversion rate of 93% was achieved, only 44% of aldehydes were formed. In addition, 26% of the corresponding alcohol and hexene isomers were obtained as major side products. The microencapsulated catalyst could be reused with only minor loss of activity. Unfortunately, almost no regiocontrol was determined (*l/b* up to 1.1) and the reaction proceeded only with slow overall conversion ($\text{TON} = 2.1\text{--}2.8$, $\text{TOF} = 0.13\text{--}0.17\text{ h}^{-1}$).

1.6.3

Ligands

Organic ligands modify the hydroformylation properties of ruthenium complexes and may suppress the high activity of unmodified Ru catalysts toward the hydrogenation of the starting olefin. Moreover, unmodified Ru complexes tend to isomerize the substrate olefin in an undesired manner [11]. However, N as well as P ligands may enhance the tendency for the reduction of the aldehyde [21]. Typical N ligands tested were aromatic amines such as pyridine, 2,2'-bipyridine, 2,2'-bipyrimidine, 1,10'-phenanthroline, and saturated cyclic amines (Figure 1.5), but also aliphatic amines like Et_3N or simple amides like *N,N*-dimethylacetamide have found application.

It seems that the nature of the products depends strongly on the type of the catalyst and the N ligand used. Thus, a bipyridine-modified $\text{Ru}_3(\text{CO})_{12}$ catalyst supported on glass, inorganic, or organic resins produced mainly alcohols [22]. In contrast, the same but homogeneous catalyst afforded exclusively the aldehyde

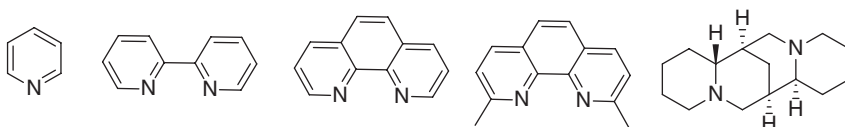


Figure 1.5 Typical N ligands used for the modification of Ru hydroformylation catalysts.

with high *n*-regioselectivity [23]. Exceptionally, under the same conditions with quinuclidine as ligand, the corresponding alcohols were formed [23b]. Aldehydes were obtained likewise when a homogeneous catalyst $\text{Ru}(\text{CO})_2(\text{MeCO}_2)(4,7\text{-dimethylphenanthroline})$ was utilized [24]. With bidentate ligands, preferentially *n*-aldehydes and *n*-alcohols, respectively, were formed [21, 25].

Up to now, besides N ligands also trivalent phosphines have been tested as ancillary ligands for ruthenium. By a comparison of ligands based on elements of the fifth row of the periodic table, the following order of yields in the hydroformylation of 1-hexene was found [26]:



With the PPh_3 -modified Ru catalyst, a strong activity for the undesired hydrogenation of the substrate was noted (60%) [26]. No isomerization of the olefin was observed irrespective on the ligand used.

In the reaction of the strong electron-deficient substrate 3,3,3-trifluoropropene, the addition of PPh_3 to $\text{Ru}_3(\text{CO})_{12}$ diminished the activity of the catalyst [5]. Noteworthy, the hydrogenation activity was lowered simultaneously.

In the Ru-catalyzed hydroformylation of 1-heptene and 1-octene, respectively, replacement of PPh_3 by $\text{P}(\text{O}^i\text{Pr})_3$ afforded the hydrogenated substrate and 2-isomers in minor amounts along with high yields of the corresponding aldehydes [18a]. In contrast, the more basic PtBu_3 disrupted the hydroformylation almost entirely. An excess of PPh_3 ($\text{P/Ru} = 5:1$) led to an enhanced *n*-regioselectivity. Additionally, the higher phosphine concentration prevented isomerization of the starting material. The only attempt to use the prominent ligand Alkanox[®] 240 [tris(2,4-di-*tert*-butylphenyl)phosphite] in the Ru-catalyzed hydroformylation–hydrogenation led to isomerization of the substrate [15].

In strong contrast, electron-rich imidazole-substituted dialkylphosphines assist in the formation of the desired aldehydes from α -olefins in high yields and excellent chemo- and regioselectivity under the precondition that a low P/Ru ratio ($<2:1$) was chosen (Figure 1.6) [27a]. At a higher H_2/CO ratio (20:5 bar), also *n*-regioselective isomerizing hydroformylation of 2-octene was possible. NMR investigations provided evidence that in the active catalyst only a single ligand is coordinated to the metal. One nitrogen atom adopts probably the role of a hemilabile ligand by the establishment of a temporary interaction with ruthenium (A) [27b].

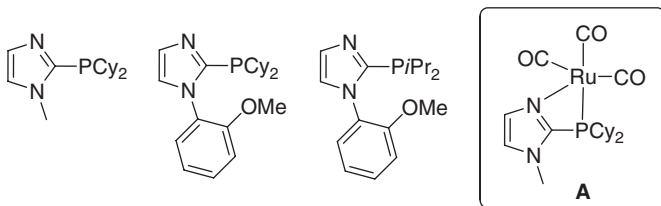


Figure 1.6 Phosphorus ligands suitable for Ru-catalyzed hydroformylation and a possible transient catalytic species.

Bulky diphosphine ligands, for example, bis(dicyclohexylphosphino)methane and bis[bis(pentafluorophenyl)phosphino]ethane (Figure 1.7), form with $\text{Ru}_3(\text{CO})_{12}$ trinuclear ruthenium clusters of different stoichiometry mainly with $\mu_1\text{-}\eta^2$ -coordination [28]. In the hydroformylation of ethylene and propylene, aldehydes were formed with superior activity in comparison to the use of dppe (1,2-bis(diphenylphosphino)ethane). Excellent *l/b* selectivities were also noted by the use of Xantphos as ligand [11]. In general, bidentate ligands provide higher yields than monodentate phosphines.

Besides mono- and bidentate phosphines, also ruthenium complexes with polydentate phosphines of the type $\text{RuCl}_2(\text{triphos})$ (**A**) or $\text{RuCl}_2(\text{tetraphos})$ (tetraphos = 1,2-bis[(2-(diphenylphosphino)ethyl)(phenyl)phosphine]ethane) (**B**) have been investigated (Figure 1.8) [29]. In the reaction with 1-hexene at a temperature of 150 °C and 100 atm syngas pressure, the formation of aldehydes as well as alcohols was observed.

When a TPPTS [$m\text{-C}_6\text{H}_4\text{SO}_3\text{Na}$]₃-modified cationic complex $[\text{HRu}(\text{CO})(\text{CH}_3\text{CN})(\text{TPPTS})_3]\text{BF}_4$ was screened in the aqueous-biphasic hydroformylation in a methoxyethanol–water mixture, the following order of activity was noted, which correlates with the results obtained with the Rh-based congener [30]:

1-hexene \gg allylbenzene > 2,3-dimethyl-1-butene > styrene > cyclohexene

1-Hexene was transformed into *n*-heptanal with a relatively low *l/b* ratio of 2:1. Noteworthy, up to a thiophene concentration of 500 ppm no intoxication effect was observed in the catalytic reaction. Alternatively, for the aqueous biphasic hydroformylation of 1-hexene, the complex $\text{RuCl}_2(\text{DMSO})_2(\text{PySO}_3\text{Na})_2$ was utilized. Remarkably, it converted cleanly also technical naphtha containing thiophene impurities of up to 50 ppm [31].

In early attempts, $[(\eta^5\text{-Cp})\text{Ru}(\text{CO})_2]_2$ revealed only poor hydroformylation capability [14]. More interesting, the cyclopentadienyl ring was not displaced from the metal even at temperatures of up to 150 °C. Under the applied reaction

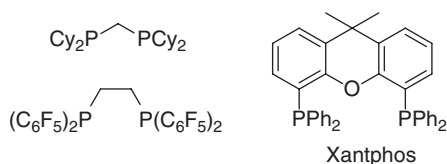


Figure 1.7 Diphosphines screened in the Ru-catalyzed hydroformylation.

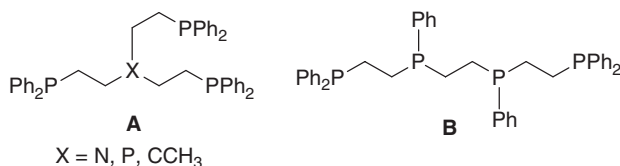
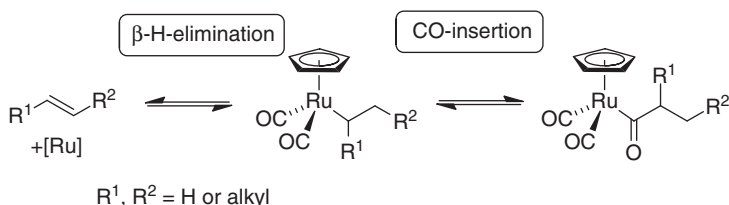


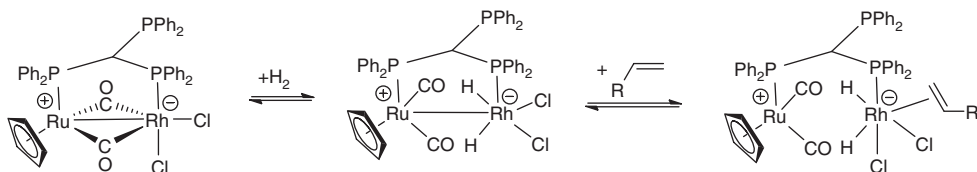
Figure 1.8 Polydentate phosphines employed in the Ru-catalyzed hydroformylation.

conditions, olefin isomerization was found to be predominant, formally indicating the ability to form a metal–alkyl species but rather inhibited acyl formation (Scheme 1.30).



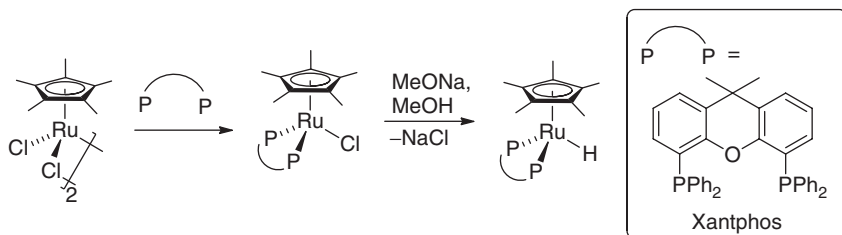
Scheme 1.30 β -H elimination versus CO insertion in cyclopentadienyl ruthenium complexes.

A hemilabile behavior was attributed to a cationic $Ru(Cp)$ unit in the hydroformylation of 1-octene using a heterobimetallic Rh – Ru catalyst linked by a tripod ligand (Scheme 1.31) [32]. In comparison to a related Rh – Ru complex, but with bis(diphenylphosphino)methane as ligand, much higher n -regioselectivities were obtained. This was attributed to the dangling effect of the diphenylphosphino group.



Scheme 1.31 Hemilabile behavior of a “ $Ru(Cp)$ ligand” in a bimetallic Rh – Ru complex.

Only recently the use of cyclopentadienyl ligands for Ru -catalyzed hydroformylation was re-evaluated. Thus, in order to block the undesired hydrogenation activity, which is attributed to formation of dihydrido-ruthenium species, both cyclopentadienyl ligands (Cp , Cp^* , Indenyl) and diphosphines were suggested [11]. A typical precatalyst was generated by the reaction of a dimeric dichloro $Ru(Cp^*)$ complex with Xantphos (Scheme 1.32). Treatment with $NaOMe$ in



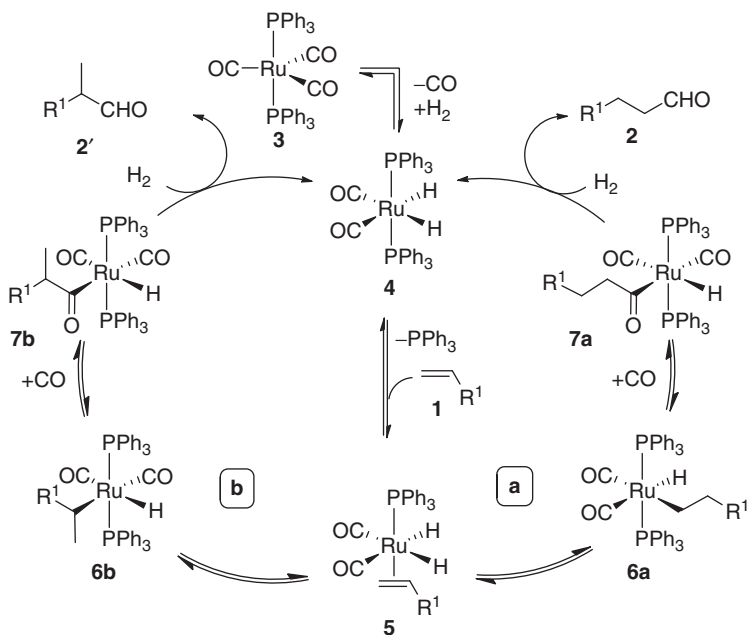
Scheme 1.32 Formation of a Xantphos-modified $(Cp^*)Ru$ hydride complex.

MeOH afforded the desired monohydrido complex, which is presumably the active catalyst.

1.6.4

Mechanistic Considerations

Detailed studies by Wilkinson and colleagues [33] led to the establishment of a catalytic cycle involving $\text{H}_2\text{Ru}(\text{CO})_2(\text{PPh}_3)_2$ (**4**) as the active catalytic species (Scheme 1.33). The oxidative addition of hydrogen to the metal center is accompanied by dissociation of one CO and appears to be the rate-determining step of the reaction. Dissociation of a phosphine ligand allows the coordination of the alkene (**1**) to form the π -complex **5**. Subsequent insertion of the CO into the transient metal–alkyl bond of **6** leads to the corresponding acyl species **7**. Eventually, transfer of a second hydrogen atom forms the desired product and regenerates the catalyst **4**. The coordination of phosphine ligands increases the electron density on the metal center and enforces the polarization of the M–H bond. As a consequence, *anti*-Markovnikov addition is favorable, leading to increasing *n*-selectivity (path **a** over path **b**). Hence, both electronic and steric effects of the phosphine ligand favor the formation of the linear alkyl–metal complex **6a**. An excess of CO is helpful in accelerating the CO migration step (**6**–**7**), which is considerably faster than the competitive β -hydride elimination. When the mononuclear complex $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ was used, isomerization of the alkenes was observed to a minor extent.

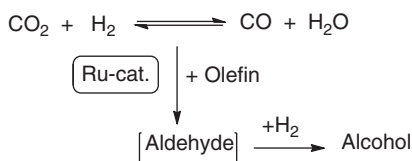


Scheme 1.33 Catalytic cycle for $\text{Ru}(\text{CO})_3(\text{PPh}_3)_2$ -catalyzed hydroformylation.

1.6.5

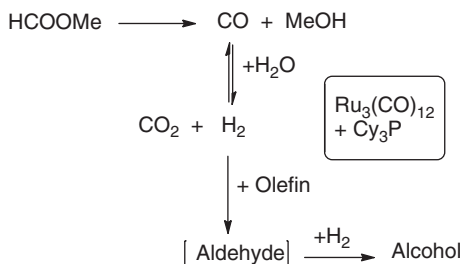
Hydroformylation Using the Reversed Water Gas Shift (RWGS) or Methyl Formate

Ruthenium complexes are particularly attractive as catalysts in the reversed water gas shift (RWGS) reaction [34]. In this respect, under the effect of hydrogen on carbon dioxide, besides water CO is formed. With an excess of hydrogen, a syngas mixture is generated, which can be directly used for hydroformylation (Scheme 1.34) [35]. With those Ru complexes, as discussed above, such as $\text{Ru}_3(\text{CO})_{12}$, $\text{Ru}_6(\text{CO})_{16}$, $\text{H}_4\text{Ru}_4(\text{CO})_{12}$, $[\text{Ru}(\text{bpy})(\text{CO})_2\text{Cl}]_2$ (bpy = bipyridine), or $(\text{PPN})\text{Ru}(\text{CO})_3\text{Cl}_3$ (PPN = bis(triphenylphosphine)nitrogen $\text{N}(\text{PPh}_3)_2$), simultaneously RWGS and hydroformylation of olefins can be realized, as thoroughly investigated by groups of Tominaga and Haukka [36, 37]. Regioselectivities achieved can significantly exceed those obtained with the related Rh catalysts [35]. In general, increasing the total pressure of H_2 and CO_2 promotes RWGS, and the yield of the hydroformylation product is enhanced [38]. Additives such as LiCl , Li_2CO_3 , or ionic liquids ($[\text{BMIM}]\text{Cl}$, BMIM = 1-butyl-3-methylimidazolium) prevent the hydrogenation of the alkene. Usually, due to the high hydrogenation activity of the Ru catalysts, aldehydes that are formed are immediately reduced to the corresponding alcohols. This can be avoided by an increase of the CO_2 pressure [38].



Scheme 1.34 Hydroformylation using CO from RWGS.

Alternatively, paraformaldehyde [39] or aqueous methyl formate has been suggested as non-gaseous sources for the generation of syngas (Scheme 1.35) [39, 40]. A catalyst prepared by the reaction of $\text{Ru}_3(\text{CO})_{12}$ and tricyclohexylphosphine is able to decarbonylate methyl formate and assist in the subsequent water gas shift (WGS) reaction. Finally, the mixture of CO and H_2 formed can react with the olefin. In this manner, several cycloalkenes (cyclopentene,



Scheme 1.35 Ru-catalyzed hydroformylation using syngas generated from methyl formate and WGS.

cyclooctene, cycloheptene, 1-methyl-cyclohexene, norbornene) and linear alkenes could be converted into the corresponding alcohols. The addition of $\text{Pd}(\text{acac})_2$ (acac = acetylacetonate) enhanced the selectivity in favor of the desired products. Hydrogenation of the olefin was a serious side reaction.

An intrinsic problem that has to be overcome in the future is posed by the low partial concentration of CO. This leads to low reaction rates of hydroformylation.

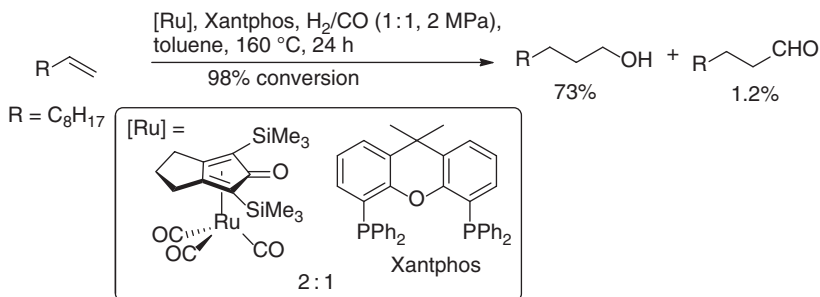
1.6.6

Domino Reactions with Ru Catalysts

Tandem or domino reactions using hydroformylation as the first step allow the immediate transformation of the formed aldehydes into other valuable chemical compounds (see Chapter 5) [41]. As discussed previously, the hydrogenation of olefinic substrates or product aldehydes is a commonly observed side reaction in the hydroformylation with Ru complexes. On the other hand, the reduction of the aldehydes can be desired.

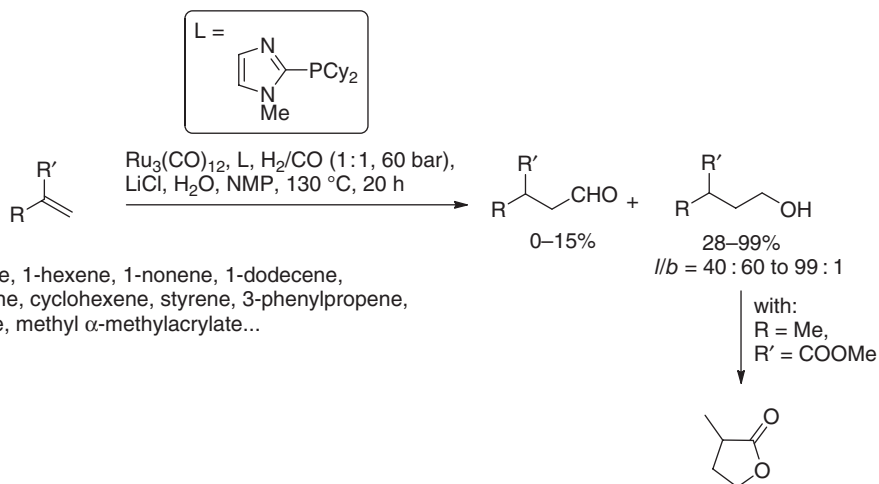
Bell and coworkers showed that both reactions can be mediated by the same Ru catalyst in a one-pot manner. It may be advantageous to adapt the conditions to each reaction. In order to draw benefit from the whole hydrogenation activity of a $\text{RuCl}_2(\text{PPh}_3)_3$ catalyst, removal of traces of CO was mandatory [42]. Thus it was found that in the batch hydroformylation of 1-hexene with stoichiometric amount of carbon monoxide, the residual CO poisoned the Ru catalyst. Only utilization of sub-stoichiometric quantities of CO and a conversion of nearly 100% or venting the hydroformylation gases allowed the subsequent efficient hydrogenation.

A modified Shvo complex with Xantphos as ligand catalyzes the selective hydroformylation–hydrogenation one-pot reaction, as shown by the Nozaki group (Scheme 1.36) [11]. In the best case, only traces of the aldehyde were found in the final product.



Scheme 1.36 Hydroformylation–hydrogenation with a $\text{Ru}(\text{Cp})$ catalyst.

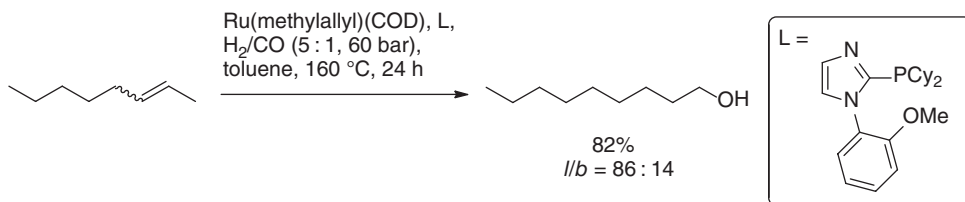
In 2013, Beller *et al.* converted a range of acyclic and cyclic olefins into the corresponding C_1 prolonged alcohols by the application of a Ru catalyst based on imidazole phosphines (Scheme 1.37) [43]. Best results were obtained with linear α -olefins as substrates. Noteworthy, also styrene gave the desired alcohol in



Scheme 1.37 Hydroformylation–hydrogenation with an imidazole phosphine modified Ru catalyst.

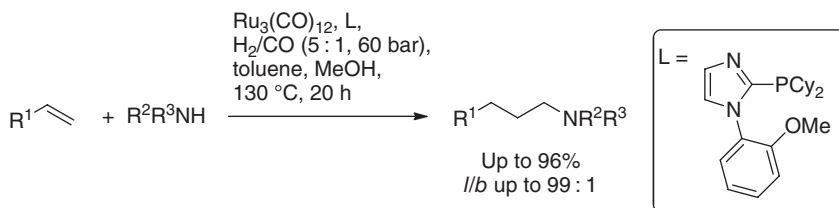
good yield. Isoprene was converted into the saturated monohydric alcohol. Methyl α -methylacrylate reacted further to give the corresponding lactone.

A similar catalytic system was applied for the isomerizing hydroformylation–hydrogenation sequence using an excess of hydrogen (Scheme 1.38) [15]. Preferentially, linear 2-olefins gave corresponding linear alcohols with l/b selectivities up to 86 : 14. Under these conditions, also 2,5-dihydrofuran and 2,3-dihydropyrrol were cleanly converted. The highest selectivity was noted in the reaction with 1-methyl-4-(prop-1-en-2-yl)cyclohex-1-ene, where only the exocyclic double bond reacted.



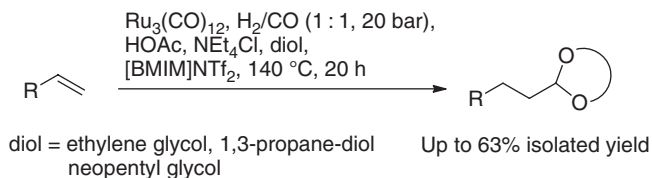
Scheme 1.38 Isomerizing hydroformylation–hydrogenation with an imidazole phosphine-modified Ru catalyst.

The same catalytic system mediates also the hydroaminomethylation of olefins (Scheme 1.39) [44]. Besides piperidine, several other cyclic and linear primary and secondary amines could be utilized. Terminal and internal olefins were equally suitable for the reaction. With enamines and enamides, respectively, 1,3-diamines were formed in moderate to good yields.



Scheme 1.39 Hydroaminomethylation with an imidazole phosphine-modified Ru catalyst.

The intermediary aldehydes derived from the Ru-catalyzed hydroformylation can be trapped as acetals, as shown by Börner and colleagues (Scheme 1.40) [45]. Only traces of alcohols or aldehydes could be detected. The tandem reaction proceeded exclusively with diols that formed thermodynamically stable 1,3-dioxolane and 1,3-dioxane rings. Methanol as the acetalization reagent failed. As olefins, terminal aliphatic olefins as well as styrene derivatives reacted. The catalyst could be recycled and reused at least twice.



Scheme 1.40 Ru-catalyzed hydroformylation–acetalization reaction.

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1.7

Palladium-Catalyzed Hydroformylation

1.7.1

General Aspects

Up to now, palladium complexes do not play a significant role in the hydroformylation of olefins [1]. However, because of their widespread use in the related hydrocarboxylation, hydroesterification, and olefin copolymerization with CO [2], occasionally their utility for hydroformylation was elucidated [3]. Moreover, palladium catalysts have been used for the hydroformylation of aryl and enol triflates to produce the corresponding unsaturated aldehydes [4].

1.7.2

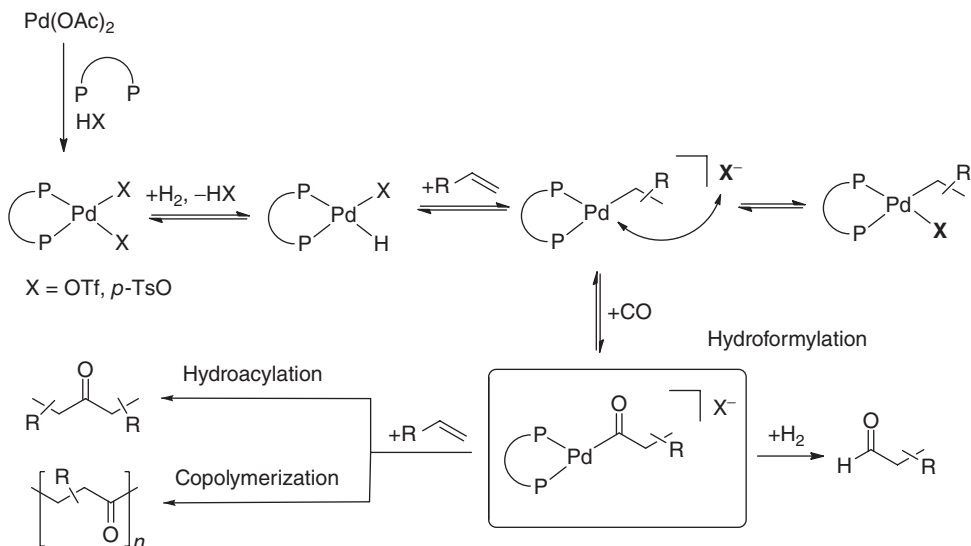
Mechanistic Investigations, Complexes, and Ligands

Commonly, $\text{Pd}(\text{OAc})_2$ is used as a precatalyst precursor. Alternatively, $\text{Pd}(\text{acac})_2$ (acac = acetylacetonate) can be employed as Pd(II) species. Upon *in situ* reaction with a bidentate diphosphine and an acid, the catalyst precursor is formed (Scheme 1.41). In the presence of syngas, binuclear and trinuclear Pd(I) clusters could be detected [5].

The mechanism of the hydroformylation has been intensively investigated by Drent and Budzelaar [6], who analyzed the competition between alternative reactions once a Pd–acyl complex was formed from a Pd–hydride species. The reaction with a second olefin leads to ketones (hydroacylation) and polyketones (copolymerization), respectively, whereas upon hydrogenolysis of the Pd–acyl bond, an aldehyde is released and thus a catalytic hydroformylation cycle is finally closed. Because of the high hydrogenation activity of palladium complexes, the aldehydes formed may be immediately converted into the corresponding alcohols.

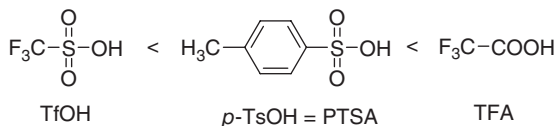
The type of the actually observed reaction pathway is mainly determined by [6]

- 1) The nature of the anionic ligand X^-
- 2) The electrophilicity of the metal
- 3) The addition of substoichiometric amounts of halide anions [7].



Scheme 1.41 Mechanism of the Pd-catalyzed hydroformylation and alternative reaction routes.

- 1) Only weakly coordinating ligands allow the CO insertion into the Pd–C bond and subsequent reactions [6]. The chemoselectivity for the hydroformylation decreases with increasing acid strength. The addition of HCl or HOAc blocked entirely the reaction. The following order of activity with respect to the acid has been established in the hydroformylation of propene and 1-octene:



Addition of urea, which forms hydrogen bonds with the anion, enhances the hydroacylation over the hydroformylation route as a result of decreased coordination strength [8].

- 2) A highly electrophilic Pd center can be generated by strong basic phosphine ligands [6]. Moreover, bidentate cis-chelating ligands are considered to be essential for placing intermediate Pd–H and Pd–C bonds cis to the fourth coordination side, which has to accommodate the substrate in a subsequent step. Bulky P substituents can be used to adjust the steric environment of the Pd center. These requirements are fulfilled by the diphosphines 1,3-bis[(di-*sec*-butyl)phosphino]propane (DsBPP), 1,3-bis[(di-*tert*-butyl)phosphino]propane (DtBPP), and bis(9-phosphabicyclo[3.3.1]nonyl)ethane (BCOPE) (Figure 1.9) [7]. The less basic diphosphines, such as 1,3-bis(diphenylphosphino)propane, were inferior. Sterically demanding

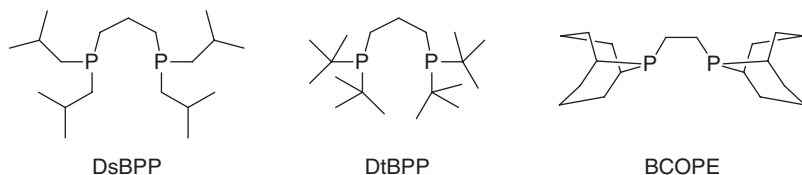


Figure 1.9 Dialkylphosphines suitable for Pd-catalyzed hydroformylation.

substituents at the phosphorus atom increased the formation of the linear aldehyde. Strong acids afforded lowered product linearity.

- 3) Halide anions affect the rate of the hydroformylation of internal olefins as well as its chemo- and regioselectivity [7]. The rate of hydroformylation of thermally equilibrated internal higher alkenes increased by a factor of $\sim 6-7$ by the addition of substoichiometric amounts (with respect to palladium) of Cl^- or Br^- and about a factor of $3-4$ with I^- . Moreover, the selectivity toward the formation of the alcohol was dramatically increased. Highest yields of alcohols were noted with the assistance of iodide. Only traces of alkanes were formed. Up to now, a general explanation of the effect could not be given, but it seems that it is also dependent on the diphosphine ligand used.

The insertion of CO in the Pd–C bond to form an acylpalladium species can be supported by $\text{Co}_2(\text{CO})_8$ as co-catalyst [9]. This finding helped improve the chemoselectivity of the Pd-catalyzed hydroformylation of alkynes [10]. Under the conditions shown in Scheme 1.42, almost no hydrogenation products, such as saturated aldehydes or nonfunctionalized olefins, were formed.

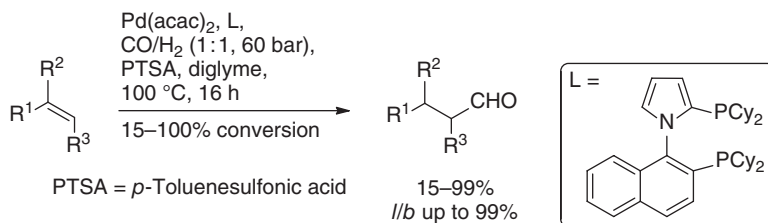


Scheme 1.42 Pd-catalyzed hydroformylation of alkynes by addition of $\text{Co}_2(\text{CO})_8$.

1.7.3

Some Applications

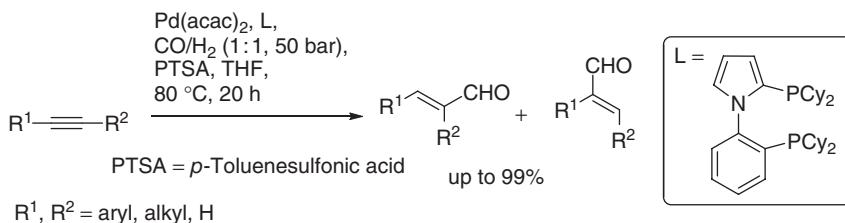
The Pd-catalyzed hydroformylation of several terminal (styrene, 1-octene, *N*-vinylphthalimide, 3,3-dimethyl-1-butene) and internal olefins (*cis*-stilbene, 1-phenylstyrene, cyclooctene, cyclohexene) was investigated at 60 bar syngas pressure and at 100°C by the Beller group [11]. As indicated in Scheme 1.43, an unsymmetric diphosphine ligand was used. With *cis*-stilbene, the corresponding aldehyde was quantitatively formed, whereas cyclic olefins, in particular cyclohexene, gave low yields. Remarkably, in the reaction with styrene, the



Scheme 1.43 Pd-catalyzed hydroformylation of alkenes.

l/b-ratio was 85 : 15, which widely differed from that commonly obtained with Rh catalysts.

The reaction has been extended to internal alkynes as substrates (Scheme 1.44) [12]. Under slightly milder conditions, almost full conversion was noted. Most of the α,β -unsaturated aldehydes formed were obtained in good to excellent yields. Interestingly, with the terminal alkyne 1-octyne, α -hexyl acrolein was obtained only in 17% yield. In unsymmetrically substituted alkyl-aryl-alkynes, the formyl group was predominantly linked to the neighboring aryl substituent. Bulky alkyl groups forced the C–C bond formation reaction in the β position.



Scheme 1.44 Pd-catalyzed hydroformylation of alkynes.

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1.8

Platinum-Catalyzed Hydroformylation

1.8.1

General Aspects

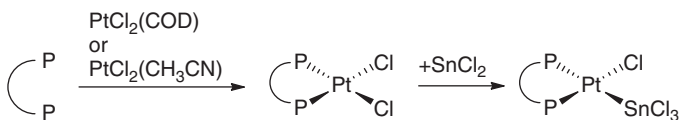
In spite of the large academic effort expended, up to now platinum complexes do not play a role in industrial hydroformylation. However, continuous academic research in this area can be traced back till the middle of 1970 [1]. Especially in the asymmetric hydroformylation, chiral platinum catalysts have long been in the focus [2]. The first platinum-catalyzed hydroformylations were claimed by Shell in 1966 [3]. The catalyst was generated by the reaction of PtCl_2 and $\text{P}(\text{nBu})_3$. At a reaction temperature of 195 °C and a syngas pressure of 500 psi (about 34 bar), it converted 1-pentene into hexanal with rather poor *n*-regioselectivity and in only moderate yield (<50%). The addition of sodium acetate forced the formation of isomeric hexanols. In a patent by Johnson Matthey in the same year, a catalyst of the structure $\text{PtCl}_2(\text{AsPh}_3)_2$ was prepared from PtCl_4 and AsPh_3 in ethanol. In the presence of this catalyst, under a syngas pressure of 40–45 bar and a temperature of 70 °C, 1-hexene reacted to give isomeric heptanals [4].

A breakthrough in the application of platinum catalysts in hydroformylation was the discovery of Knifton at Texaco that the addition of tin(II) chloride allowed much milder reaction conditions and enhanced yield and regioselectivity simultaneously [5]. The rate of the hydroformylation of 1-pentene with $\text{HPt}(\text{SnCl}_3)(\text{CO})(\text{PPh}_3)$ at 100 °C and a syngas pressure of 1500 psi (about 103 bar) was about 5 times compared to that with the $\text{Co}_2(\text{CO})_8$ catalyst [6]. A SnCl_2 -modified Pt catalyst was also successfully employed for the hydrogenation and the regioselective methoxycarbonylation of olefins with CO and methanol [7]. The competition between alkoxy carbonylation and hydroformylation depends on the solvent used. Ketones force the hydroformylation route [8], whereas polar solvents such as DMF (*N,N*-dimethylformamide), THF (tetrahydrofuran), or acetonitrile may inhibit the reaction [9]. Hydrogenation of the olefinic substrate may become a serious side reaction. Worthy of note in this regard is the activity of Pt/Sn catalysts in the selective hydrogenation of multiple double bonds in fatty acids [10]. In this transformation, they also force the *cis/trans* isomerization as well as the migration of the olefinic groups.

1.8.2

Mechanistic Investigations, Complexes, and Ligands

In the most cases, Pt/Sn catalyst are prepared prior to the hydroformylation by the reaction of $\text{PtCl}_2(\text{COD})$ ($\text{COD} = 1,5\text{-cyclooctadiene}$) or $\text{PtCl}_2(\text{CH}_3\text{CN})_2$ with a stoichiometric amount of a preferentially bidentate phosphorus ligand (P_2). Sometimes, refluxing is recommended. Upon addition of SnCl_2 , the activated bimetallic precatalyst is formed by a “carbene-like” insertion of tin(II) into the Pt–Cl bond (Scheme 1.45).



Scheme 1.45 Generation of a bimetallic Pt/Sn precatalyst.

In early attempts, an excess of SnCl_2 was applied. Later studies revealed that an equimolar amount is sufficient and, simultaneously, the formation of byproducts (e.g., alkanes by hydrogenation of the starting olefin) can be diminished [11, 12]. Most complexes are stable even beyond 120°C , but under hydroformylation conditions above 150°C , all activity can be completely lost [13]. An excess of phosphine is beneficial for the insertion of SnCl_2 [14]. Replacement of SnCl_2 by SnF_2 leads to a catalyst that is much more stable [15]. It gave in the asymmetric hydroformylation even at 200°C constantly high enantiomeric excess (ee) values. Moreover, the hydrogenation activity reclaimed with the related SnCl_2 system could be reduced. SnBr_2 and SnI_2 formed less active catalysts [9, 16]. Addition of silver triflate also affected the rate; an excess of this additive poisoned the catalyst [17]. Platinum–tin chloride catalysts have been anchored to silica and used for the hydroformylation in supercritical carbon dioxide [18]. Alternatively, chiral catalysts were attached to linear and cross-linked polymer supports and used in the asymmetric hydroformylation [19].

The rarely investigated tin(II) halide-free systems have been generated from $(\text{P ligand})_2\text{Pt}(\text{CH}_3)_3$ and $\text{B}(\text{C}_6\text{H}_5)_3$, BF_3 , or BPh_3 [20]. Heterobimetallic dithiolate-bridged complexes of the type $[(\text{P-ligand})_2\text{Pt}(\mu\text{-BDT})\text{Rh}(\text{COD})]\text{ClO}_4$ ($\text{BDT} = ^-\text{S}(\text{CH}_2)_4\text{S}^-$) (**1**) developed, after split-off in mononuclear species, considerable activity in the hydroformylation of styrene when monodentate phosphines were used as ancillary ligands (Figure 1.10) [21]. In this case, the hydroformylation result has to be unambiguously attributed to the mononuclear rhodium complex. The reaction in water in the presence of micelles has been mediated starting with a cationic precatalyst of the type $[(\text{P-ligand})_2\text{Pt}(\text{H}_2\text{O})_2](\text{OTf})_2$ (**2**) [22]. Remarkably, with this catalytic system with styrenes as substrates, mainly the linear aldehydes were formed. Unexpectedly, benzaldehydes were observed as side products (up to 17%) deriving from β -aryl elimination. Diphenylphosphinous acid also rendered platinum catalytically active by formation of a pseudo-chelating ligand in the

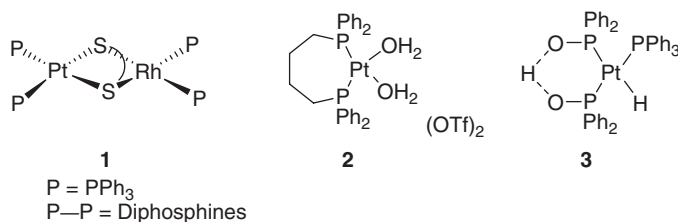
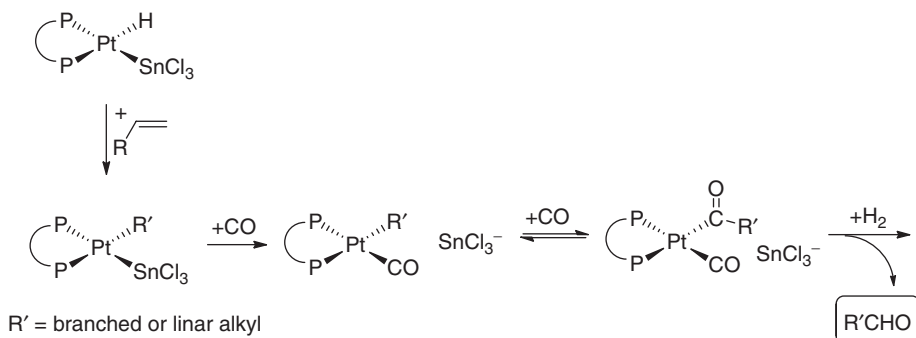


Figure 1.10 Tin(II) halide-free systems used in Pt-catalyzed hydroformylation.

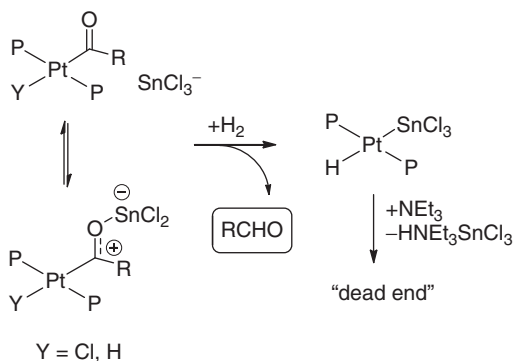
backbone of the metal (**3**) [23]. The hydrogen bond makes the geometry of the catalyst center more rigid, leading to a beneficial effect on the regiodiscrimination of the hydroformylation [24].

The role of $SnCl_2$ is not fully clarified, although, in particular, Kollár and colleagues have performed numerous excellent spectroscopic studies. It may act as a Lewis acid, as a counter-ion ($SnCl_3^-$), or as a $SnCl_3$ ligand directly bonded to the metal. Presumably, it intervenes in different steps of the catalytic cycle. One beneficial effect is clearly the stabilization of the intermediary Pt–alkyl complex, which is formed by olefin insertion into the Pt–H bond in the first stage (Scheme 1.46) [25]. In the next step, trichlorostannate serves as a leaving group and can be thus replaced by CO. In this regard, it assists the CO insertion and facilitates the subsequent formation of a Pt–acyl complex. [26] Whether the olefin insertion or the subsequent carbonylation is the regiochemistry determining step is still unclear [27, 28].



Scheme 1.46 Important elementary steps in the hydroformylation with a Pt/Sn catalyst.

As found with trans-coordinated $Pt(PPh_3)_2$ complexes, tin chloride may also support the final hydrogen activation and cleavage of the aldehyde from the metal center, thus regenerating the catalyst (Scheme 1.47) [29]. The hydrogenolysis is considered as rate-determining step [27, 28]. Addition of strong bases, such as NEt_3 , stops the catalytic reaction by abstracting $H-SnCl_3$ from the active Pt complex [30].



Scheme 1.47 Hydrogenolysis of the Pt-acyl intermediate.

Hydroformylation of internal olefins proceeds in a *cis* manner [31].

As ligands, numerous phosphines have been tested in the Pt/Sn-catalyzed version of hydroformylation. In general, the use of bidentate diphosphines showed superiority to monodentate ligands [32]. Within a series of α,ω -diphosphines, optimum activity in the hydroformylation of 1-pentene, reaching a TOF (turnover frequency) of 2253 h^{-1} , was observed with 1,4-bis(diphenylphosphino)butane (dppb, $n = 4$) (Figure 1.11). PPh_3 and 1,3-bis(diphenylphosphino)propane (dppp, $n = 3$) induced lower activity. Also, the performance of diphosphines forming larger chelate rings ($n = 5$ or 6) was inferior.

The highest activity and regioselectivity ($i/b = 99 : 1$) was observed with *trans*-1,2-bis(diphenylphosphinomethyl)cyclobutane (**1**, Figure 1.12) [32]. This result stimulated the screening of similar, but now also chiral bidentate diphosphines, such as (*R,R*)-DIOP (**2**) [31].

In comparison with enantiopure DIOP, (*S,S*)-Chiraphos (**3**) induced a lower activity but enabled higher optical yield in the reaction of linear olefins or styrene [33]. Noteworthy, both Pt/Sn catalysts rivaled the chiral Rh congener. Probably, π -stacking plays a role in the stereodiscriminating step when the vinyl aromat acts as a substrate [34]. In the hydroformylation of styrene with a Pt/Sn catalyst based on (*S,S*)-2,4-bis(diphenylphosphino)pentane (BDPP, **4**), interesting temperature effects were observed [13,15,35]. At low temperature ($\sim 40^\circ\text{C}$), (*S*)-phenylpropan-2-al was formed, whereas above 90°C the (*R*)-enantiomer was obtained as the dominant product. Moreover, a strong influence on the para substituent of styrenes on temperature was found [36]. Also, this feature may lead in the ultimate case to a reversal of the enantioselectivity in the product. Rigid and bulky dibenzophosphol units such as, for example, diphosphines **5**

Activity: $(n = 1) < (n = 2) < \text{PPh}_3 < (n = 3) < (n = 4) > (n = 5) > (n = 6)$
n-Regioselectivity: $\text{PPh}_3 < (n = 2) < (n = 3) \approx (n = 4) \approx (n = 5) \dots$

Figure 1.11 Dependence of activity and *n*-regioselectivity on the phosphine ligand employed in the hydroformylation of 1-pentene.

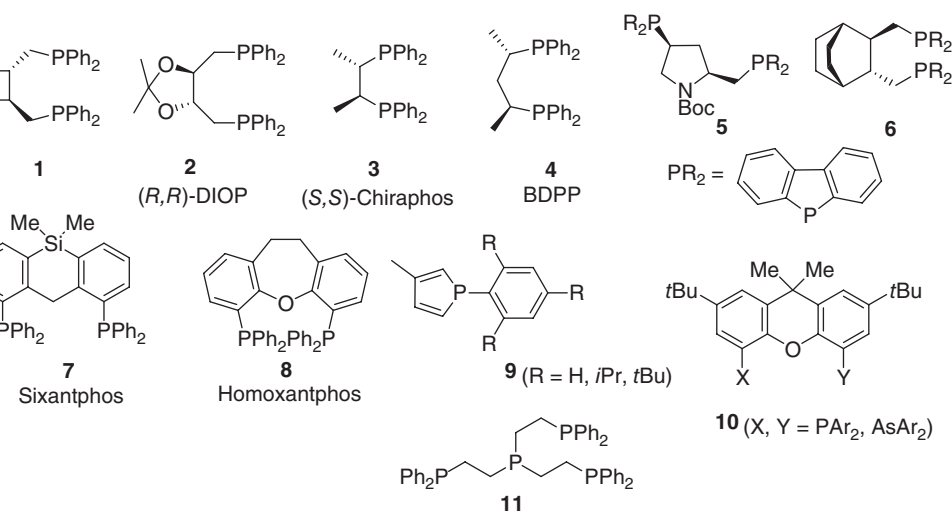


Figure 1.12 Various phosphines investigated as ligands in the Pt/Sn-catalyzed hydroformylation.

or **6** can contribute to the enhancement of the stereodifferentiating ability of the catalyst in the hydroformylation of vinyl arenes [37–39]. With Sixantphos (**7**), superior *n*-regioselectivities were noted in comparison to diphosphines with a smaller bite angle [11]. The same ligand was tested in the isomerizing hydroformylation of 4-octenes [40]. The concept of “large bite angle” [41] was successfully broadened with the employment of Homoxantphos (**8**), which produced in the hydroformylation of 1-octene a TOF of 720 h^{−1} [42, 43]. This is ~40 times larger than the TOF obtained with the parent ligand Xantphos. The latter may coordinate to the platinum in a *cis* or *trans* manner [44]. Alkyl substitution (*iso*-Pr, *tert*-Bu) in P-aryl phospholes **9** lowered the conversion and isoselectivity in the hydroformylation of styrenes [45]. Replacement of one or both phosphine groups by AsPh₂ in Xantphos (ligand **10**) induced, in contrast to the rhodium congeners, in the Pt/Sn-catalyzed hydroformylation higher activities (initial TOF = 350 h^{−1}) and regioselectivity (*l/b* = 200 : 1) [46]. Also, the polydentate phosphine **11** has been evaluated, which, however, did not form a particularly active catalyst [14]. Probably, one of the phosphine groups assists in the insertion of SnCl₂ in the Pt–Cl bond and acts so as a hemilabile ligand.

Also, aminophosphine-phosphinites **1** (AMPPs), originally developed as ligands for asymmetric hydrogenation by the Lyon group of Agbossou-Niedercorn and Mortreux [47, 48], have been tested in asymmetric hydroformylation with a tin-free Pt catalyst (Figure 1.13).

Chiral phosphites such as **2** gave in the asymmetric hydroformylation of styrene only moderate enantiomeric excess values (up to 39% ee, *b/l* = 84 : 16) [49]. Interestingly, with a Pt/Sn catalyst based on binaphthol diphosphites, such as **3**, about 30–40% higher ee values were reported by the Bakos group in

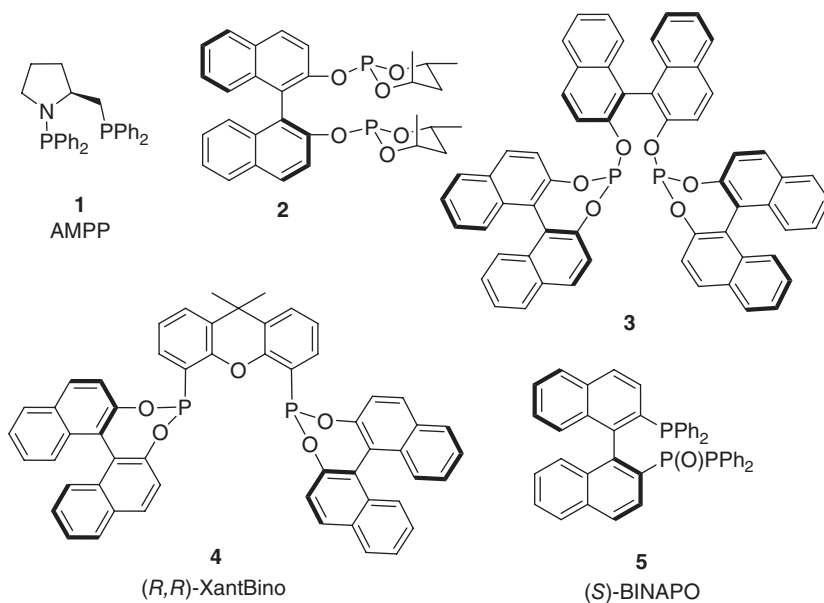


Figure 1.13 Chiral phosphorus ligand investigated in the asymmetric Pt-catalyzed hydroformylation.

comparison with the corresponding Rh catalysts in the same transformation [50]. A rare example of a diphosphonite ligand is chiral (*R,R*)-XantBino (**4**), which gave along with styrene as substrate up to 30% ee [51]. More success in terms of enantioselectivity was found with the same catalyst with allyl acetate and vinyl acetate as substrates (58–80% ee). Noteworthy, with both these substrates, preferentially the (achiral) terminal aldehydes were obtained. Hydroformylation was, in all cases, accompanied by hydrogenation of the substrate. Enhancement of the temperature from 20 to 100 °C led finally to 78% ethyl benzene in the product mixture. BINAPO (**5**), a ligand with a potentially hemilabile coordinating diphenylphosphino oxide group, was also tested with moderate success (styrene: 30% ee) [52].

1.8.3

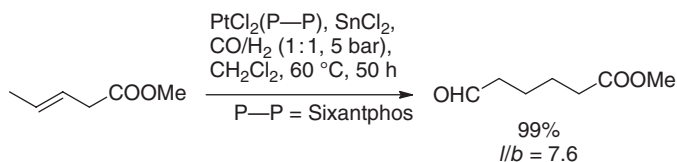
Some Applications

The range of olefins screened in platinum-catalyzed hydroformylation is rather narrow. As seen already above, mostly styrene or 1-olefins were investigated in mechanistic studies with the aim of establishing the structure of catalytic intermediates or to find structure–activity–regio/stereoselectivity relationships. Usually, Pt/Sn catalysts operate under rather mild conditions (10–100 bar syngas, 50–130 °C) [53]. Pt/S ratios of up to 2000:1 have been realized.

In the iso-regioselective hydroformylation of styrenes, in the best cases up to 87% ee was induced [15, 19b, 37]. Rarely, also other olefins (*E*- or *Z*-2-butenes,

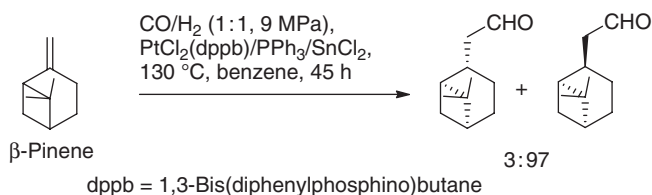
2,3-dimethyl-1-butene, 2-phenylpropene, norbornene) were screened, but only moderate ee values resulted (up to 68% ee) [37]. In a few cases, also isomerizing hydroformylation of internal olefins was in the focus [23b]. A few investigations involved the comparison of platinum-based hydroformylation catalysts with other metals [54]. For example, a striking dependence on the nature of the catalytic system was noted in the hydroformylation of vinyltrimethylsilane [55]. The platinum catalyst gave exclusively the terminal aldehyde, whereas the unmodified rhodium catalyst yielded a mixture of isomeric aldehydes.

In the hydroformylation of ethyl 3-butenate with a PPh_3 -modified Pt/Sn catalyst at 5 MPa syngas pressure, 96% of aldehyde was formed with a dominance of the branched aldehyde [56]. In contrast, in the reaction of methyl 2-pentenoate with a Pt/Sn–Sixantphos catalyst, high regioselectivity in favor of the terminal aldehyde was noted (Scheme 1.48) [11, 45]. Hydrogenation of the olefin or the product aldehyde was not observed.



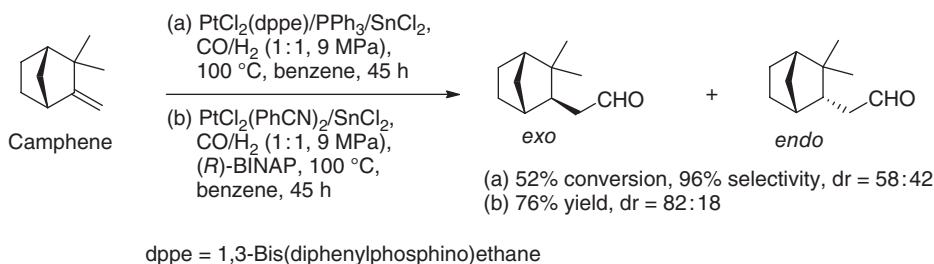
Scheme 1.48 Hydroformylation of ethyl 3-butenate.

Several investigations with Pt/Sn hydroformylation catalysts were conducted by Gusevskaya's group in the field of terpenes. β -Pinene reacted with syngas at 90 bar in the presence of a Pt/Sn catalyst to give the diastereomeric formylpinanes in the ratio 3:97 in favor of the trans stereoisomer (Scheme 1.49) [57]. This is in contrast to Rh or Co catalysts, where this diastereomer is usually obtained in minor amounts. Moreover, the isomerization of β -pinene to α -pinene is rather slow. The isomerization is forced, however, with an excess of the Lewis acid SnCl_2 or by use of PPh_3 as ligand. With dppp, hydrogenation of the olefin became dominant.



Scheme 1.49 Hydroformylation of β -pinene.

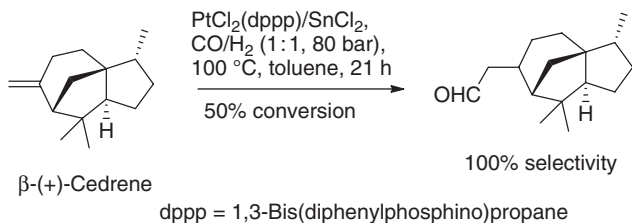
Camphene has been transformed with a syngas pressure of 9 MPa (Scheme 1.50) [58]. The chemoselectivity for the formation of the desired aldehyde was excellent and independent of whether PPh_3 or chelating diphosphines such as dppe (1,2-bis(diphenylphosphino)ethane), dppb (1,4-bis(diphenylphosphino)butane),



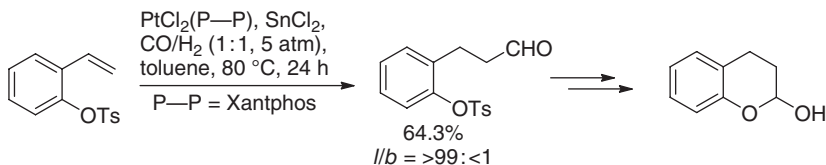
Scheme 1.50 Hydroformylation of camphene.

or dppp (1,3-bis(diphenylphosphino)propane) were used as ligands. Interestingly, only a small diastereomeric excess (de) of the thermodynamically more stable *exo* compound was noted with achiral P ligands [57, 58]. A higher de value (~60%) could be realized using chiral diphosphines such as *(R)*- or *(S)*-BINAP [58]. When an excess of SnCl_2 was added, hydrogenation and isomerization of the starting monoterpene became a problem.

The hydroformylation of the exocyclic terminal double bond in β -cedrene gave the corresponding aldehyde with high chemo- and regioselectivity (Scheme 1.51) [59].

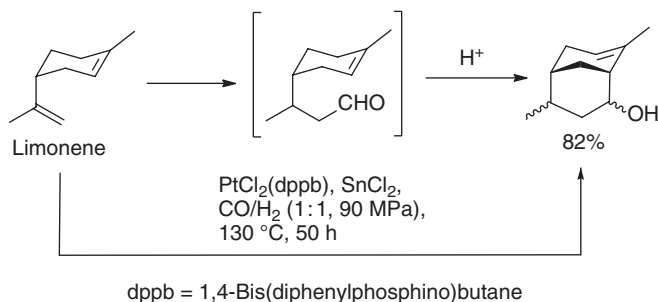
Scheme 1.51 Hydroformylation of β -cedrene.

2-Tosyloxystyrene was reacted in the presence of a Pt/Sn(Xantphos) catalyst with equal parts of CO and H_2 to give, besides some hydrogenation product, exclusively the corresponding linear aldehyde (Scheme 1.52) [12]. In comparison to several Rh catalysts likewise tested, the Pt/Sn-based approach gave the best regioselectivity. The product may be converted into 2-chromanol, which is an important building block for a range of pharmaceutically active compounds.



Scheme 1.52 Hydroformylation of 2-tosyloxystyrene.

Limonene was reacted with syngas to give a bicyclic alcohol in a hydroformylation–cyclization tandem reaction (Scheme 1.53) [60]. In this approach, there was no need to isolate the intermediate aldehyde. Diastereomers were formed in nearly equal amounts (47:53).



Scheme 1.53 Hydroformylation/cyclization of limonene.

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1.9

Iridium-Catalyzed Hydroformylation

1.9.1

General Aspects

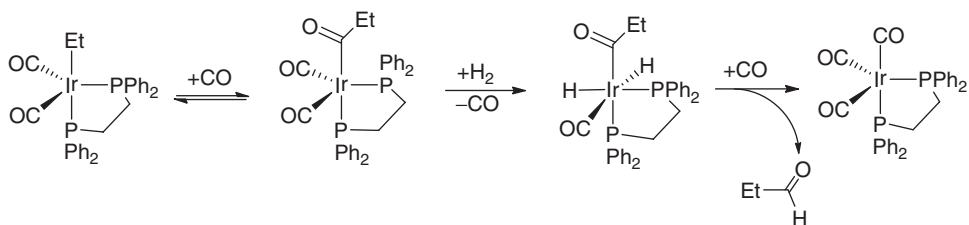
Iridium is another transition metal of group 9 in the periodic table. Therefore it attracts special attention in particular in comparison with the corresponding rhodium catalysts [1, 2]. In general, in all investigations a lowered activity of Ir catalysts was stated. Already in early attempts the high hydrogenation activity of Ir catalysts was complained about [3].

1.9.2

Mechanistic Investigations, Complexes, and Ligands

Rhodium and iridium have closely related chemical properties, and their metal complexes adopt similar coordination geometries. Therefore, occasionally iridium congeners were used as models to study the catalytic properties of rhodium complexes, which are less stable under catalytic conditions [4, 5]. Unfortunately, in comparison to rhodium, only a few studies with quite different catalytic systems exist, and therefore general conclusions are hard to draw.

In 1990, Deutsch and Eisenberg [6] were able to establish a full catalytic cycle on the basis of NMR experiments and X-ray structural analysis of selected intermediates. They found that, in the considered example, the oxidative addition of H₂ to the corresponding Ir–acyl intermediate was the rate-determining step (Scheme 1.54). Therefore, they concluded that the desired aldehyde



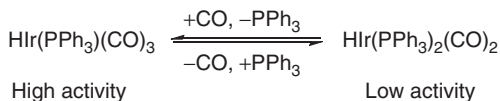
Scheme 1.54 Important intermediates in Ir-catalyzed hydroformylation with an Ir(dppe, 1,2-bis(diphenylphosphino)ethane) catalyst.

should be released finally only at a higher pressure and by using an excess of hydrogen.

In 2004, a similar study with *para*-hydrogen was performed by the group of Duckett starting with $\text{Ir}(\text{CO})(\text{PPh}_3)_2(\eta^3\text{-C}_3\text{H}_5)$ as a catalyst precursor [7]. A main conclusion was that a CO-deficient atmosphere favors hydrogenation over hydroformylation.

Kinetic investigations by Rosales *et al.* [8] on the hydroformylation of 1-hexene with a catalyst generated from Ir(acac)(COD) (acac = acetylacetonate, COD = 1,5-cyclooctadiene) and an excess of PPh₃ indicated several similarities with the Rh-catalyzed reaction (CO/H₂ = 1 : 1, 2.5 bar, 60 °C for Rh and 100 °C for Ir). With both metals, the transfer of the hydride to the olefin was found to be the rate-determining step. Since under the chosen conditions no hydrogenation product was detected, it was assumed that the CO insertion in the metal–alkyl bond proceeded faster than the reductive elimination of the corresponding alkane from the metal center.

Based on quantum chemical calculations, and correlated with results of IR measurements, Franke and coworkers [9] argued that with a PPh₃-modified iridium catalyst a slight excess of CO (CO/H₂ = 2 : 1) should have a positive effect on the catalytic activity (Scheme 1.55). In other words, the Ir catalyst with only one PPh₃ ligand but three ligated CO is more active and, consequently, an excess of PPh₃ may retard the catalytic activity.



Scheme 1.55 Influence of an excess of CO or PPh₃ on the reactivity of an Ir catalyst.

Indeed, these calculations correspond to the experimental results of Beller's group with monodentate phosphine ligands and may explain to some extent the lower reactivity for iridium in comparison to rhodium catalysts found in the past [10]. By comparing the efficiency of trivalent phosphorus ligands on the aldehyde yield, the following order was established (Figure 1.14).

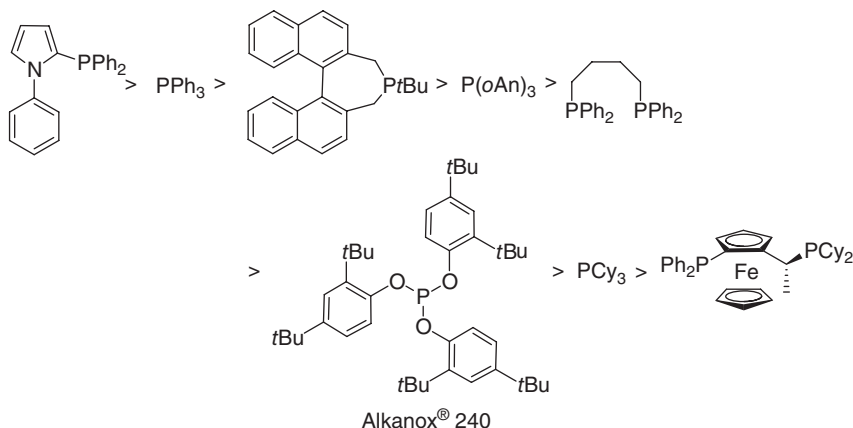


Figure 1.14 Activity in the hydroformylation of 1-octene of the corresponding iridium catalyst in relation to the phosphorus ligand used.

The order leads to the conclusion that monodentate phosphines should be superior to bidentate ligands. Strong basic alkylphosphines reduce the hydroformylation reactivity.

These conclusions confirm the results with Ir(Xantphos) complexes by Eisenberg's group from 2006 [11]. For some of these H_2Ir complexes, a trans coordination of the diphosphine was found. The hydrido complexes $\text{HIr}(\text{CO})_2(\text{Xantphos})$ and $\text{H}_3\text{Ir}(\text{CO})(\text{Xantphos})$ exhibited only modest hydroformylation activity for the transformation of 1-hexene and styrene ($\text{H}_2/\text{CO} = 2:1$, 3 atm; 75°C). The aldehydes were produced in a yield of $\sim 10\%$. More than 50% 1-hexene isomerization was observed. Complete inhibition of the reaction took place in the presence of a twofold excess of the bidentate ligand. It was speculated that in some cases dissociation of Xantphos could be a precondition for catalysis to occur.

In contrast to the relevant Rh complexes, Ir phosphino–enolate complexes (Figure 1.15) were not active in the hydroformylation of styrene until 80°C and 1000 psi (~ 69 bar) syngas pressure [12]. When in the Vaska complex PPh_3 was replaced by Ph_2PPy , the poor hydroformylation activity of the former could be significantly improved [13]. The authors assumed hemilabile coordination of the P-pyridine unit on iridium during the catalytic cycle, which is supported by a protonation/deprotonation equilibrium of the pyridine nitrogen.

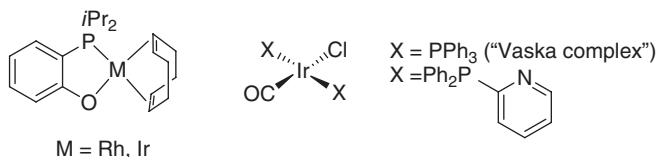


Figure 1.15 Some iridium complexes screened in hydroformylation.

Siloxide complexes of iridium complexes, such as $[\text{Ir}(\text{COD})(\text{OSiMe}_3)_2]$ and $\text{Ir}(\text{COD})(\text{OSiMe}_3)(\text{PCy}_3)$, were tested for the hydroformylation of vinyl silanes [14]. Besides isomeric aldehydes, mainly hydrogenation was observed.

As already noted, a special concern in Ir-catalyzed hydroformylation is the high hydrogenation activity, which leads to the formation of undesired alkanes. With unmodified Ir catalysts, this could be overcome by the addition of inorganic salts (LiCl and CaCl_2 performed best) as suggested by Haukka [15]. In this manner, also the formation of alcohols could be almost suppressed. The chemoselectivity for the formation of the aldehyde with unmodified Ir catalyst increased in the following order:

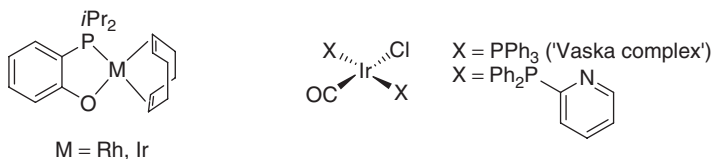


When $\text{Ir}(\text{acac})(\text{COD})$ was reacted with PPh_3 , a superior chemoselective catalyst was generated [8]. In strong contrast, PCy_3 as a ligand induced the formation of more than 50% alkane [10]. Interestingly, a similarly high hydrogenation activity was found with Alkanox[®] 240 as a ligand, which is one of the most preferred modifiers in Rh-catalyzed hydroformylation. No explanation for this disparate behavior has been given to date.

1.9.3

Some Applications

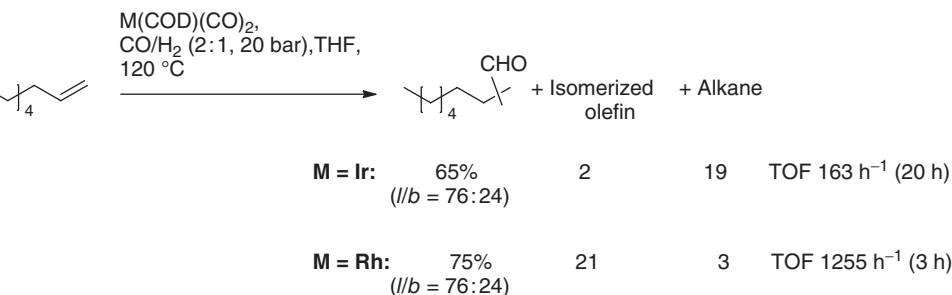
Crudden and Alper [16] investigated the hydroformylation of vinylsilane and observed remarkable differences in selectivity between rhodium and iridium (Scheme 1.56). While $[\text{Rh}(\text{COD})]\text{BPh}_4$ produced at ~ 14 bar the branched aldehyde with 70% selectivity, all tested iridium complexes afforded 3-(trialkylsilyl)propanal as the main product. The highest *n*-regioselectivity was reported when preactivated (160°C) IrCl_3 was employed. Likewise, the cationic complex $[\text{Ir}(\text{COD})_2]\text{BF}_4$ was able to produce linear aldehydes with up to 97% *n*-selectivity and 75–80% yield at ~ 48 bar. It is noteworthy that an excess of CO ($\text{CO}/\text{H}_2 = 7:1$) was necessary in order to prevent olefin hydrogenation. Addition of an excess of PPh_3 completely suppressed any hydroformylation ability of the iridium-based system, which is clearly not the case with rhodium catalysts.



Scheme 1.56 Hydroformylation of vinyl silane with Rh or Ir catalysts.

In 2011, Beller's group utilized an Ir hydroformylation catalyst [10] generated from $\text{Ir}(\text{acac})(\text{COD})$ and a 10-fold excess of PPh_3 for the conversion of various terminal olefins (styrene, 3-propenylarenes, cyclic octenes, linear α -olefins) into

aldehydes. A CO/H₂ ratio of 2:1 was applied. With the exception of styrene, an average regioselectivity of 3:1 in favor of the straight-chain aldehyde was found. Cooling down the reaction mixture after a preliminary run led to the precipitation of a metal salt, which was characterized by X-ray structural analysis as the dinuclear complex [Ir(CO)₃(PPh₃)₂]₂. This complex still showed moderate activity (46%) in the hydroformylation of 1-octene with no change in the *l/b* ratio (74:26). In order to evaluate the catalyst's performance in terms of cost efficiency, a corresponding Rh-based system was subjected to identical reaction conditions (Scheme 1.57). The comparison provided evidence that the activity of iridium catalysts did not differ dramatically from rhodium catalysts as assumed previously.



Scheme 1.57 Ir versus Rh catalysts for the hydroformylation of 1-octene.

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1.10

Iron-Catalyzed Hydroformylation

1.10.1

General Aspects

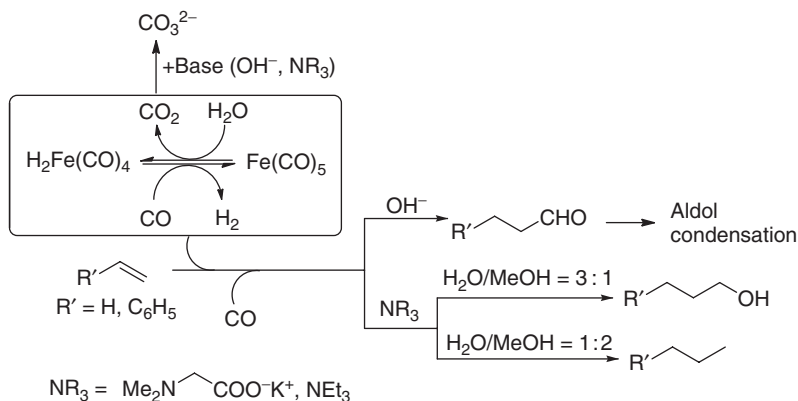
Iron is one of the most abundant metals on earth. It occurs in ~6 wt% in the lithosphere and can be easily obtained from the corresponding ores. Because of the widespread occurrence and broad availability of iron, catalysts made from this material can be exceptionally cheap. Several attempts are described in the literature to use iron as a catalytically active metal in hydroformylation and related reactions. Unfortunately, up to now relevant catalysts have shown extremely low reactivity and the results do not suggest a suitable application. Two main approaches can be distinguished:

- 1) Use of monometallic iron catalysts
- 2) Addition of iron complexes to rhodium or ruthenium hydroformylation catalysts in order to achieve synergistic effects.

1.10.2

Monometallic Iron Catalysts

Because of the poor hydroformylation activity of iron complexes, such as $\text{Fe}(\text{CO})_5$ [1], by using molecular hydrogen, their use is mainly associated with hydroformylation under “Rippe conditions” (Scheme 1.58) [2, 3]. In this context, $\text{H}_2\text{Fe}(\text{CO})_4$ reacts with carbon monoxide to form molecular hydrogen and iron pentacarbonyl. The starting iron complex is regenerated by addition of water and is thus reintroduced into the catalytic cycle. The addition of a base is necessary to remove CO_2 from the equilibrium as carbonate (“Hieber base reaction”) [4]. Under these

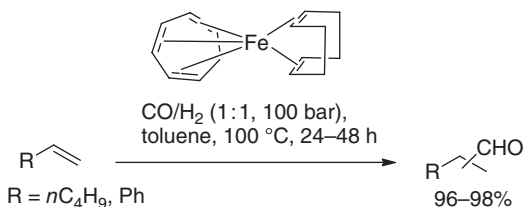


Scheme 1.58 Iron-catalyzed hydroformylation under Reppe conditions.

conditions, olefins are isomerized [5] or converted into oxo products. Potassium dimethyl glycinate [2] or NEt_3 proved to be particularly effective as the base for hydroformylation [6].

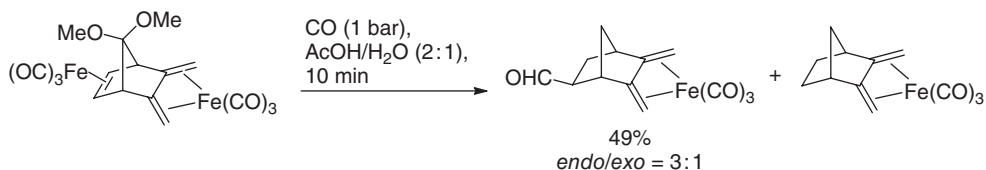
By using aqueous alkaline solutions, aldehydes can be formed, which instantly undergo aldol condensation. In strong contrast, in the presence of amines, alcohols as products of aldehyde hydrogenation are formed. As observed by Markó, the formation of alcohols is also favored in a $\text{MeOH}/\text{H}_2\text{O}$ mixture with high water content [6]. Lowering of the water concentration resulted mainly in the formation of alkanes. The reactions have been carried out at syngas pressures of 100–200 bar and temperatures between 60 and 140 °C. In general, the yields of the oxo products did not exceed 30%.

Much higher yields were reported by Pertici and coworkers [7] using syngas and an iron precatalyst stabilized by the polyolefins 1,3,5-cycloheptadiene and 1,5-cyclooctadiene (Scheme 1.59). Isomeric aldehydes were formed almost quantitatively, but with only moderate *l/b* selectivities.



Scheme 1.59 Hydroformylation with an iron catalyst.

Stoichiometric hydroformylation of a polyolefin iron complex was reported by Ioset and Roulet [8], which preferentially afforded the *endo*-formyl isomer together with the hydrogenation product (Scheme 1.60).



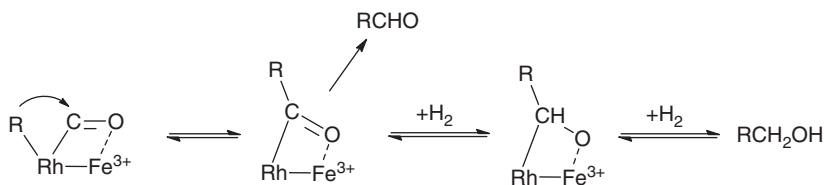
Scheme 1.60 Stoichiometric hydroformylation of an iron–polyolefin complex.

1.10.3

Iron Complexes as Additives to Conventional Hydroformylation Catalysts

The screening of heterobimetallic hydroformylation catalysts with iron as one constituent received more attention than the use of monometallic Fe catalysts [9]. Earlier attempts were encouraged by the assumption that iron carbonyls, which can be formed in steel autoclaves under carbon monoxide, act as poisons for cobalt or rhodium catalysts [10]. Especially, the property of Fe(CO)_5 to catalyze the aldol condensation of product aldehydes was considered to be detrimental to hydroformylation. Usually, this problem is solved either by technological means (fast separation of the product) or by the addition of chelating agents for iron [11].

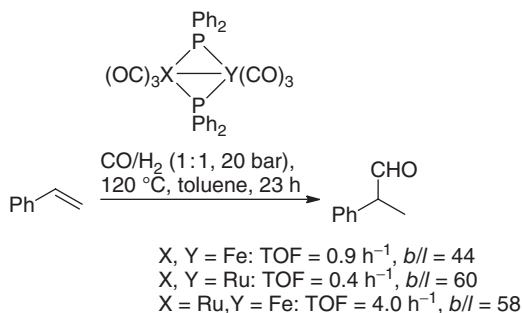
However, iron complexes may also display a beneficial effect. Thus, a promoting effect on hydroformylation was observed with SiO_2 -supported Rh-Fe^{3+} bimetallic carbonyl clusters (Scheme 1.61) [12]. Based on Mössbauer spectroscopy, it was proposed that iron assists during the insertion reaction of CO into the Rh-C bond. Likewise, the hydrogenation of the intermediary alkoxy rhodium species to produce the alcohols may benefit from this bi-site interaction.



Scheme 1.61 Supporting role of Fe^{3+} in Rh-catalyzed hydroformylation.

A heterobimetallic Ru-Fe cluster was 5–10 times more active than its homobimetallic congeners in the hydroformylation of styrene (Scheme 1.62) [13]. The dominance for the formation of the branched aldehyde was in the range of the Ru-Ru catalyst.

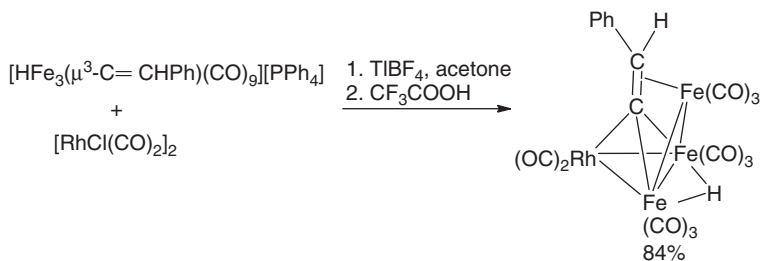
A similar effect was observed with mixed iron–rhodium carbidocarbonyl clusters on oxide supports [14]. Trzeciak and Ziółkowski added Fe(CO)_5 to Rh(acac)(CO)L (acac = acetylacetonate) [$\text{L} = \text{PPh}_3$, P(OPh)_3 , $\text{P(N(C}_4\text{H}_9)_3)$] and achieved in the hydroformylation of 1-hexene at a syngas pressure of 10 atm and 80°C an increase of up to 70% in the yield of the aldehyde [15]. The



Scheme 1.62 Comparison of hetero- and homobimetallic catalysts in hydroformylation.

heterobimetallic complex $\text{H}(\text{PPh}_3)_3\text{Rh}(\mu\text{-CO})_2\text{Fe}(\text{CO})_4$ was identified with spectroscopy, and is probably responsible for these interesting results.

The vinylidene cluster $\text{Fe}_3\text{Rh}(\text{CO})_{11}(\text{C}=\text{CH}(\text{Ph}))$, which was prepared by Mathieu and coworkers started from a trinuclear Fe cluster by reaction with $[\text{RhCl}(\text{CO})_2]_2$ in the presence of TlBF_4 and subsequent protonation, which exhibited the same activity in the hydroformylation of 1-pentene as $\text{Rh}_4(\text{CO})_{12}$ (Scheme 1.63) [16, 17].



Scheme 1.63 Preparation of an iron–rhodium cluster as a catalyst for hydroformylation.

Besides interstitial carbon atoms, nitride groups have also been used to stabilize the cluster structure of iron–rhodium and iron–iridium hydroformylation catalysts [18].

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