Part I
Introduction, Organometallic Aspects
and Mechanism of Homogeneous Hydrogenation

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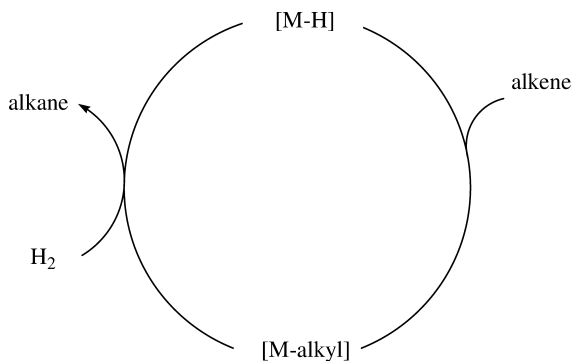# Rhodium

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1.1
Introduction

Homogeneous hydrogenation constitutes an important synthetic procedure and is one of the most extensively studied reactions of homogeneous catalysis. The homogeneous hydrogenation of organic unsaturated substrates is usually performed with molecular hydrogen, but it is also possible to derive hydrogen from other molecules acting as hydrogen donors, such as alcohols; these are termed hydrogen transfer reactions. The impressive developments of coordination and organometallic chemistry have allowed the preparation of a wide variety of soluble metal complexes active as homogeneous hydrogenation catalysts under very mild conditions. These complexes are usually derived from transition metals, especially late transition metals with tertiary phosphine ligands, having partially filled d electron shells. These transition metal complexes present the ability to stabilize a large variety of ligands with a variability of the coordination number and oxidation state. Among those ligands are unsaturated substrates containing π-electron systems, such as alkenes or alkynes, as well as key σ-bonded ligands such as hydride or alkyl groups.

Although the reaction of hydrogen with alkenes is exothermic, the high activation energy required constrains the reaction. Thus, the concerted addition of hydrogen to alkenes is a forbidden process according to orbital symmetry rules. In contrast, transition metals have the appropriate orbitals to interact readily with molecular hydrogen, forming metal hydride species, allowing the transfer of the hydride to the coordinated alkene. Rhodium is a good example of such transition metals, and has played a pivotal role in the understanding of homogeneous hydrogenation, providing clear examples of the two types of homogeneous hydrogenation catalysts that formally can be considered, namely monohydride and dihydride catalysts.

[M-H]

alkene

alkane

H$_2$

[M-alkyl]

Scheme 1.1

1.1.1
Monohydride Hydrogenation Catalysts

Monohydride (MH) catalysts, such as [RhH(CO)(PPh$_3$)$_3$], react with substrates such as alkenes, according to Scheme 1.1, yielding rhodium–alkyl intermediates which, by subsequent reaction with hydrogen, regenerate the initial monohydride catalyst. This mechanism is usually adopted by hydrogenation catalysts which contain an M–H bond.

1.1.2
Dihydride Hydrogenation Catalysts

Many of these catalysts are derived from metal complexes which, initially, do not contain metal hydride bonds, but can give rise to intermediate MH$_2$ (alkene) species. These species, after migratory insertion of the hydride to the coordinated alkene and subsequent hydrogenolysis of the metal alkyl species, yield the saturated alkane. At first glance there are two possibilities to reach MH$_2$ (alkene) intermediates which are related to the order of entry of the two reaction partners in the coordination sphere of the metal (Scheme 1.2).

[M]

alkene

alkane

H$_2$

[M-H$_2$]

[M(alkene)]

alkene

H$_2$

[MH$_2$(alkene)]
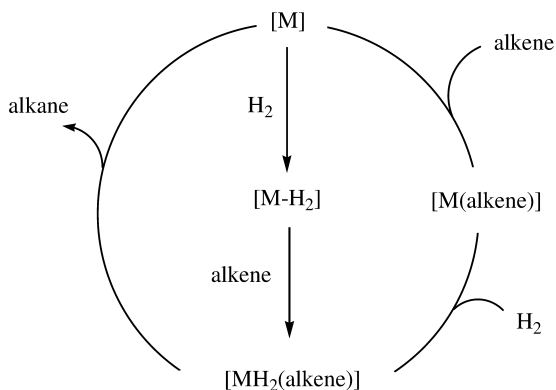
Scheme 1.2

The hydride route involves the initial reaction with hydrogen followed by coordination of the substrate; the well-known Wilkinson catalyst [RhCl(PPh$_3$)$_3$] is a representative example. A second possible route is the alkene (or unsaturated) route which involves an initial coordination of the substrate followed by reaction with hydrogen. The cationic catalyst derived from [Rh(NBD)(DIPHOS)]$^+$ (NBD = 2,5-norbornadiene; DIPHOS = 1,2-bis(diphenyl)phosphinoethane) is a well-known example. The above-mentioned rhodium catalysts will be discussed, in the detail, in the following sections.

Homogeneous hydrogenation reactions by metal complexes have been investigated extensively during previous years. The first authoritative book on this subject, containing interesting and detailed historical considerations, was written by James, and appeared in 1973 [1]. Following this, other monographs [2, 3] were published, as well as several reviews and book chapters [4], reporting on the rapid and impressive development of this field.

1.2
The Early Years (1939–1970)

Calvin made the first documented example of homogeneous hydrogenation by metal compounds in 1938, reporting that quinoline solutions of copper acetate, at 100 °C, were capable of hydrogenating unsaturated substrates such as *p*-benzoquinone [5]. One year later, Iguchi reported the first example of homogeneous hydrogenation by rhodium complexes. A variety of organic and inorganic substrates were hydrogenated, at 25 °C, by aqueous acetate solutions of RhCl$_3$, [Rh(NH$_3$)$_5$(H$_2$O)]Cl$_3$, or [Rh(NH$_3$)$_4$Cl$_2$]Cl, whilst more inert complexes [Rh(NH$_3$)$_6$]Cl$_3$ and [Rh(en)$_3$]Cl$_3$, were inactive [6]. The initial hydrogen reduction of these and other related rhodium(III) complexes with nitrogen donor ligands seems to proceed via hydride rhodium intermediates formed by the heterolysis of hydrogen [1, 7]. In the case of the Iguchi rhodium(III) catalysts, however, after some time, partial autoreduction to rhodium metal occurred. Another seminal contribution of Iguchi, which appeared few years later in 1942, was the observation of the ready absorption of hydrogen by cobalt cyanide aqueous solutions; the formed cobalt hydride, [CoH(CN)$_5$]$^-$, was seen to be highly selective for the hydrogenation of conjugated dienes to monoenes [8].

During this period, the most significant advances in homogeneous hydrogenation catalysis have been the discovery of rhodium phosphine complexes. The hydridocarbonyltris(triphenylphosphine)rhodium(I) complex, [RhH(CO)(PPh$_3$)$_3$], was reported in 1963 [9], and its catalytic activity was studied in detail by Wilkinson and coworkers a few years later [10–13]. The most important rhodium catalyst, the chlorotris(triphenylphosphine)rhodium(I) complex, was prepared during the period 1964–1965 by several groups [14]. It is easily synthesized by treating RhCl$_3 \cdot$3H$_2$O with triphenylphosphine in ethanol. It can also be prepared by displacement of the coordinated diene 1,5-cyclooctadiene from [RhCl(diene)]$_2$ complexes [15]. Wilkinson and coworkers extensively studied the remarkable catalytic properties of this complex, which is usually known as Wilkinson's catalyst. It was

the first practical hydrogenation system to be used routinely under very mild conditions – usually room temperature and atmospheric pressure of hydrogen. This compound catalyzes the chemospecific hydrogenation of alkenes in the presence of other easily reduced groups such as NO_2 or CHO, and terminal alkenes in the presence of internal alkenes [14 b, 16]. The remarkable success of this catalyst inspired the incorporation of chiral phosphines, which in turn prompted the birth of the catalytic enantioselective hydrogenation with pioneering contribution from the groups of Knowles and Horner (see [38, 39, 45 b] in Section 1.1.6).

The synthesis of cationic rhodium complexes constitutes another important contribution of the late 1960s. The preparation of cationic complexes of formula $[Rh(diene)(PR_3)_2]^+$ was reported by several laboratories in the period 1968–1970 [17, 18]. Osborn and coworkers made the important discovery that these complexes, when treated with molecular hydrogen, yield $[RhH_2(PR_3)_2(S)_2]^+$ (S = solvent). These rhodium(III) complexes function as homogeneous hydrogenation catalysts under mild conditions for the reduction of alkenes, dienes, alkynes, and ketones [17, 19]. Related complexes with chiral diphosphines have been very important in modern enantioselective catalytic hydrogenations (see Section 1.1.6).

Rhodium(II) acetate complexes of formula $[Rh_2(OAc)_4]$ have been used as hydrogenation catalysts [20, 21]. The reaction seems to proceed only at one of the rhodium atoms of the dimeric species [20]. Protonated solutions of the dimeric acetate complex in the presence of stabilizing ligands have been reported as effective catalysts for the reduction of alkenes and alkynes [21].

It is noteworthy to comment that the remarkable advances of experimental techniques made during the past few decades has allowed, in many cases, information to be obtained about key intermediates. As a consequence, detailed mechanistic studies have now firmly established reaction pathways.

1.3
The [RhH(CO)(PPh$_3$)$_3$] Catalyst

This complex was first prepared by Bath and Vaska in 1963 [9], and studied in detail by Wilkinson and coworkers some years later [10] as an active catalyst for hydrogenation [11], isomerization [12], and hydroformylation [13] reactions.
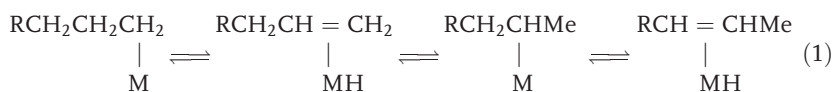
The crystal structure of the [RhH(CO)(PPh$_3$)$_3$] complex [22] shows a bipyramidal structure with equatorial phosphines. This coordinatively saturated 18-electron complex should be considered strictly as a precatalyst (or catalyst precursor) which, after dissociation of PPh$_3$ and creation of a vacant coordination site, yields the real catalytic species, [RhH(CO)(PPh$_3$)$_2$]. It should be remembered at this point that homogeneous mechanisms involve multistep processes, characteristic of coordination and organometallic chemistry (e.g., ligand dissociation or substitution, oxidative addition, reductive elimination), and therefore several types of intermediates are involved. The intermediates proposed by Wilkinson and coworkers in 1968 [11], based on kinetic studies, are shown in Scheme 1.3. Thus, the first step is the *ligand dissociation* of PPh$_3$ (step a), yielding
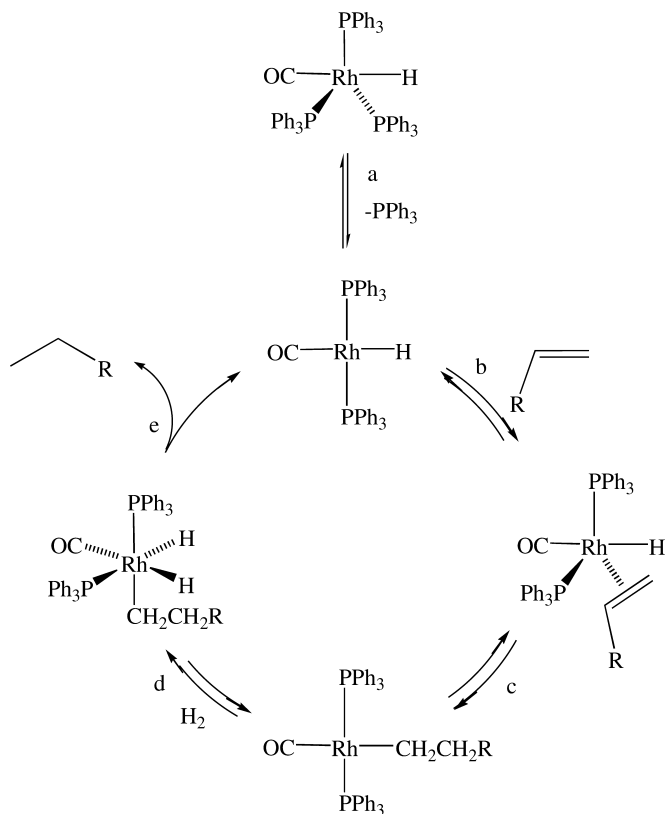
Scheme 1.3

[RhH(CO)(PPh$_3$)$_2$]. A vacant coordination site has been created and *coordination* of the 1-alkene substrate to the [RhH(CO)(PPh$_3$)$_2$] catalyst is feasible (step b). This is followed by the *migratory insertion* of the hydride to the coordinated alkene (step c), and then *hydrogenolysis* of the metal alkyl species to yield the saturated alkane. This hydrogenolysis proceeds, in this case, through two steps – *oxidative addition* of H$_2$ (step d), followed by *reductive elimination* to regenerate the [RhH(CO)(PPh$_3$)$_2$] catalyst (step e). Further support for steps c and d has been obtained by studying the reaction of [RhH(CO)(PPh$_3$)$_2$] with tetrafluoroethylene that yields the stable *trans*-[Rh(C$_2$F$_2$H)(CO)(PPh$_3$)$_2$] that, under reaction with hydrogen and in the presence of phosphine, gives C$_2$F$_2$H$_2$ and [RhH(CO)(PPh$_3$)$_3$] [13].

Rhodium species in oxidation states I and III are involved in the process. Rhodium-catalyzed hydrogenations generally involve oxidative addition reactions, followed by the reverse process of reductive elimination in the final step. Another common elimination process is the so-called *β-elimination*, which accounts for the frequent side reaction of isomerization of alkenes, according to Eq. (1):

$$\begin{array}{cccc}
\text{RCH}_2\text{CH}_2\text{CH}_2 & \text{RCH}_2\text{CH}=\text{CH}_2 & \text{RCH}_2\text{CHMe} & \text{RCH}=\text{CHMe} \\
\mid \rightleftharpoons & \mid \rightleftharpoons & \mid \rightleftharpoons & \mid \qquad (1) \\
\text{M} & \text{MH} & \text{M} & \text{MH}
\end{array}$$

This reversibility explains the frequent isomerization of alkenes by metal hydride complexes, even in the absence of hydrogen. The formation of the secondary alkyl should be unfavored when bulky ligands are present. This steric argument explains why internal alkenes are isomerized by $[\text{RhH(CO)(PPh}_3)_2]$ but are not competitively hydrogenated, as well as the high selectivity of this catalyst for the hydrogenation of terminal alkenes compared to 2-alkenes due to the lowered stability of the secondary alkyl species. The formation of the real catalyst $[\text{RhH(CO)(PPh}_3)_2]$ requires the dissociation of PPh_3 from the rhodium precatalyst. Thus, an addition of excess PPh_3 prevents the dissociation and inhibits alkene hydrogenation. On the other hand, at very low concentrations, the $\text{RhH(CO)(PPh}_3)$ intermediate, which is still more active, is formed by further dissociation of $\text{RhH(CO)(PPh}_3)_2$ according to Eq. (2).
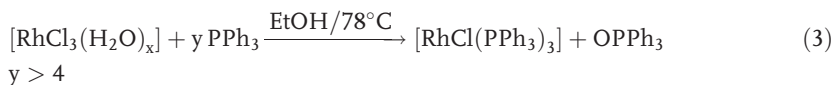
$$[\text{RhH(CO)(PPh}_3)_3] \xrightarrow{-\text{PPh}_3} [\text{RhH(CO)(PPh}_3)_2] \xrightarrow{-\text{PPh}_3} [\text{RhH(CO)(PPh}_3)] \quad (2)$$

1.4
The [RhCl(PPh₃)₃] Complex and Related Catalysts

The widely studied $[\text{RhCl(PPh}_3)_3]$ complex, usually known as Wilkinson's catalyst, was discovered independently in 1965 by Wilkinson (a recipient of the Nobel Prize in 1973) and other groups [14]. This compound catalyzes the chemospecific hydrogenation of alkenes in the presence of other easily reduced groups such as NO_2 or CHO, and terminal alkenes in the presence of internal alkenes [16]. The rate of hydrogenation parallels their coordination ability (Scheme 1.4), but tetrasubstituted alkenes are not reduced.

This burgundy-red compound can be easily prepared by reacting $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ with triphenylphosphine in refluxing ethanol. In this reaction, rhodium(III) is reduced to the rhodium(I) complex $\text{RhCl(PPh}_3)_3$, whilst the phosphine is oxidized to phosphine oxide according to Eq. (3).

$$[\text{RhCl}_3(\text{H}_2\text{O})_x] + y\,\text{PPh}_3 \xrightarrow{\text{EtOH/78°C}} [\text{RhCl(PPh}_3)_3] + \text{OPPh}_3 \qquad (3)$$
$$y > 4$$

The most accepted mechanism for alkene hydrogenation is mainly due to Halpern [23], and is supported by careful kinetic and spectroscopic studies of cyclo-
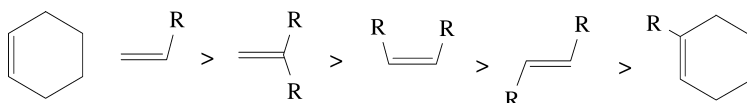
Scheme 1.4

hexene hydrogenation. This mechanism is shown in Scheme 1.5, where the route dominating the catalytic cycle is surrounded by the dotted line. According to this scheme, the predominant hydride route consists of oxidative addition of a hydrogen molecule prior to alkene coordination. Both the associative pathway *via* a 16-electron complex [RhCl(PPh₃)₃] and the dissociative pathway *via* a 14-electron species RhCl(PPh₃)₂ could function for hydrogenation, depending on the concentration of free PPh₃. However RhCl(PPh₃)₂ reacts with H₂ at least 10 000-fold faster than [RhCl(PPh₃)₃], and is therefore the active intermediate. Thus, the hydride path is much more efficient than the alkene path. However, in the absence of hydrogen, RhCl(PPh₃)₂ showed a remarkable tendency to dimerize, yielding [(PPh₃)₂Rh(μ-Cl)Rh(PPh₃)₂] species with bridging chloro ligands; the formation of alkene complexes of general formula [RhCl(alkene)(PPh₃)₂] can also be observed. The addition of small amounts of free phosphine inhibits the formation of these dimers, thereby enhancing the catalytic activity of the complex.

The rapid oxidative addition of hydrogen to RhCl(PPh₃)₂, followed by alkene coordination, affords the 18-electron octahedral dihydride alkene complex [RhH₂Cl(alkene)(PPh₃)₂]. The unsaturated [RhH₂Cl(PPh₃)₂] intermediate is also capable of ligand association with PPh₃, being in equilibrium with [RhH₂Cl(PPh₃)₃]. The rate-determining step for the whole process is the intramolecular alkene insertion into the rhodium–hydride bond of [RhH₂Cl(alkene)(PPh₃)₂], to produce the alkyl hydride intermediate, [RhH(alkyl)Cl(PPh₃)₂]. The next step, the reductive elimination of alkane from this alkyl hydride intermediate to regenerate RhCl(PPh₃)₂, occurs rapidly. The proposed cycle implies changes in the oxidation state (I and III) in the oxidative addition and reductive elimination
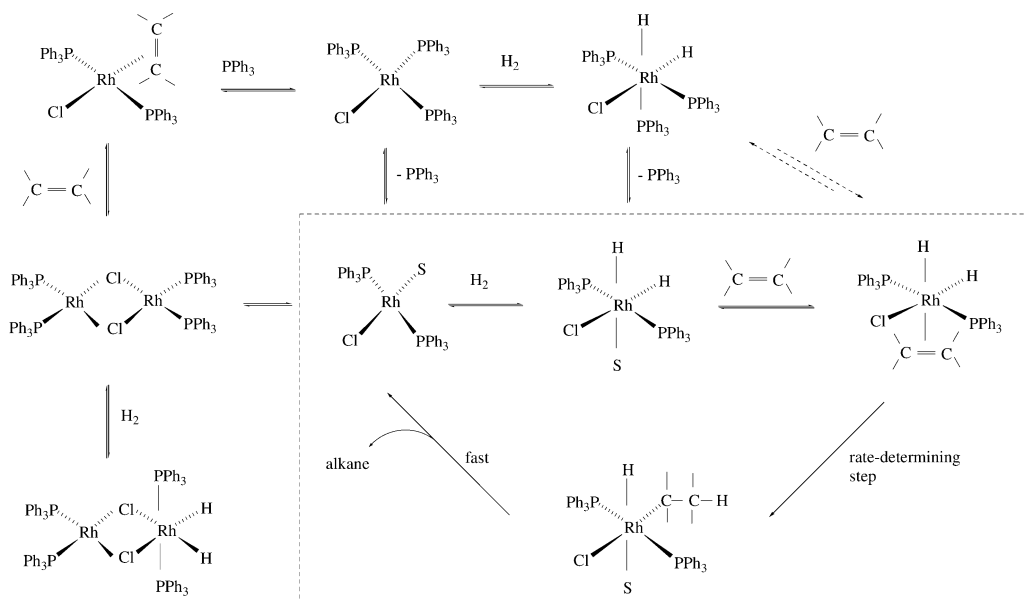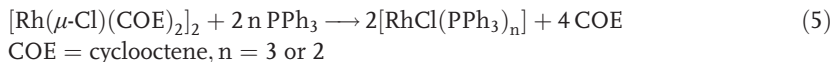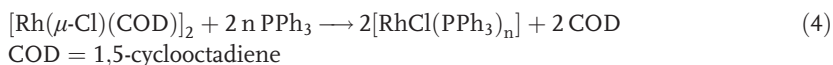

Scheme 1.5

steps, as well as changes in the electronic environment (14-, 16-, and 18-electron species) and coordination numbers, from 3 to 6. Nevertheless, in some cases, some coordination vacancies could be occupied by polar solvent molecules, such as ethanol, which are frequently added to the usual aromatic organic solvents.

This cycle was pieced together from the results of a variety of experiments. The complexes $[RhCl(PPh_3)_3]$, $[RhCl(alkene)(PPh_3)_2]$, $[RhH_2Cl(PPh_3)_3]$, $[(PPh_3)_2Rh(\mu\text{-}Cl)_2Rh(PPh_3)_2]$ and $[(PPh_3)_2Rh(\mu\text{-}Cl)_2RhH_2(PPh_3)_2]$ were directly observed, but the species of Scheme 1.5 which are inside the dashed line, and are thus responsible for the hydrogenation process, were not observable. Furthermore, when styrene was used as substrate, a further path involving the coordination of two styrene molecules was found to be operating. It seems important to remember that, in some catalytic reactions, those compounds that are readily isolable might not be the true intermediates in the catalytic cycle.

Recently [24], using parahydrogen-induced polarization (PHIP) NMR techniques, it has been possible to observe the dihydride $[Rh(H)_2Cl(styrene)(PPh_3)_2]$, which is involved in the hydrogenation process. Although traditionally it has been depicted with *trans* phosphines, this technique shows that the two phosphines are arranged in a *cis* fashion. When PHIP NMR was used to examine the reaction of $[Rh(\mu\text{-}Cl)(PPh_3)_2]_2$ with parahydrogen, the dinuclear hydride complexes $[Rh(H)_2(PPh_3)_2(\mu\text{-}Cl)_2Rh(PPh_3)_2]$ and $[Rh(H)_2(PPh_3)_2(\mu\text{-}Cl)]_2$ were detected and characterized [25]. The same reaction, when carried out in the presence of an alkene, revealed signals corresponding to new dinuclear dihydrides of the type $[Rh(H)_2(PPh_3)_2(\mu\text{-}Cl)_2Rh(PPh_3)(alkene)]$. Kinetic data showed that hydrogenation *via* this intermediate may be significant [26].

Related triarylphosphine complexes of formula $[RhCl(P(C_6H_4\text{-}4\text{-}X)_3)_3]$ are also active hydrogenation catalysts. Studies on cyclohexene hydrogenation show an increase in the relative rates when the basicity of the triarylphosphine increases: $P(C_4H_4\text{-}4\text{-}Cl)_3$ $(1.8) < P(C_6H_5)_3$ $(41) < P(C_6H_4\text{-}4\text{-}Me)_3$ $(86) < P(C_6H_4\text{-}4\text{-}OMe)_3$ (100). However, complexes with more basic tertiary phosphines, such as PEt_3 or $PPhEt_2$, are practically inactive.

A simple method for the *in-situ* preparation of Wilkinson-type catalysts consists of the addition of the appropriate amount of the triarylphosphine to the rhodium dimers, $[Rh(\mu\text{-}Cl)(diene)]_2$ or $[Rh(\mu\text{-}Cl)(cyclooctene)_2]_2$, according to Eqs. (4) and (5). The best results are usually obtained for a rhodium/phosphine ratio of 1:2.

$$[Rh(\mu\text{-}Cl)(COD)]_2 + 2\,n\,PPh_3 \longrightarrow 2[RhCl(PPh_3)_n] + 2\,COD \tag{4}$$
$$COD = 1,5\text{-cyclooctadiene}$$

$$[Rh(\mu\text{-}Cl)(COE)_2]_2 + 2\,n\,PPh_3 \longrightarrow 2[RhCl(PPh_3)_n] + 4\,COE \tag{5}$$
$$COE = cyclooctene, n = 3 \text{ or } 2$$

The water-soluble analogue of Wilkinson's catalyst, $[RhCl(TPPMS)_3]$ $[TPPMS = PPh_2(C_6H_4SO_3Na)]$, prepared *in situ* from $[Rh(\mu\text{-}Cl)(diene)]_2$ and TPPMS, reacts with hydrogen in aqueous solution to yield $[RhH(TPPMS)_3]$, instead of $[RhH_2(TPPMS)_3]$, according to Eq. (6):

$$[RhCl(TPPMS)_3] + H_2 \longrightarrow [RhH(TPPMS)_3] + Cl^- + H^+ \qquad (6)$$
$$TPPMS = PPh_2(C_6H_4SO_3Na)$$
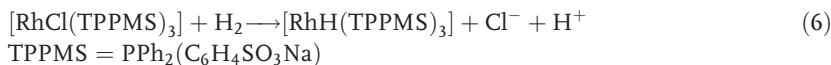
The presence of $[RhH(TPPMS)_3]$ causes substantial changes in the mechanism of hydrogenation, that most probably follows a conventional monohydride mechanism as shown in Scheme 1.1. This is also reflected in the rates and the hydrogenation selectivities [27].

1.5
### The Cationic[Rh(diene)(PR₃)ₓ]⁺ Catalysts

The catalytic potential of $[Rh(diene)L_n]^+$ (n=2 or 3; L=phosphine, phosphite or arsine) complexes as hydrogenation catalysts was discovered by Osborn and co-workers during the period 1969 to 1976 [19, 28]. Under a hydrogen atmosphere the diene is hydrogenated, generating the reactive $[RhH_2S_xL_n]^+$ species which, in some cases such as in $[RhH_2(solvent)_2L_2]^+$ intermediates, can be isolated relatively easily from coordinating solvents such as acetone or ethanol. In contrast to Wilkinson's catalyst, a large number of donor ligands can be used and several easy preparative routes are available. NBD was the preferred diene for the $[Rh(diene)L_n]^+$ catalyst precursors, but other dienes such as 1,5-cyclooctadiene (COD) or tetrafluorobenzobarrelene (TFB) have also been used [28, 29]. The dihydride complexes $[RhH_2S_2L_2]^+$ (S=Me₂CO, EtOH) have two solvent molecules bound through their oxygen lone pairs in the coordination sphere. They are excellent hydrogenation catalysts, and some unusual properties seem to depend on its ionic character.

The dihydride complexes $[RhH_2S_xL_n]^+$ are in equilibrium with monohydride species according to Eq. (7).

$$[RhH_2S_xL_n]^+ \rightleftharpoons [RhHS_yL_n] + H^+ \qquad (7)$$
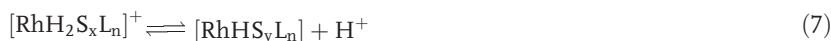
The equilibrium can be shifted by the addition of acid or base, and is also sensitive to the nature of the ligands and solvents. Scheme 1.6 qualitatively accounts for the experimental observations involving three possible pathways by which an unsaturated substrate can be hydrogenated.

Path A involves a neutral monohydride species which both extensively isomerizes and also hydrogenates alkenes, and is favored in the presence of NEt₃ or when the catalyst contains basic phosphine ligands. In path B, which is favored in the presence of acids, cationic dihydride species are the active catalyst; they hydrogenate alkenes less efficiently, but with limited isomerization. Path C involves formation of $[RhH_2S_x(alkene)L_n]^+$ from $[RhS_xL_n]^+$ by intermediacy of $[RhS_x(alkene)L_n]^+$. In the proposed cycles the substrate enters the coordination sphere by displacing a solvent molecule. The experimental observations suggest that the neutral monohydride species $RhHS_yL_n$ are considerably more efficient hydrogenation
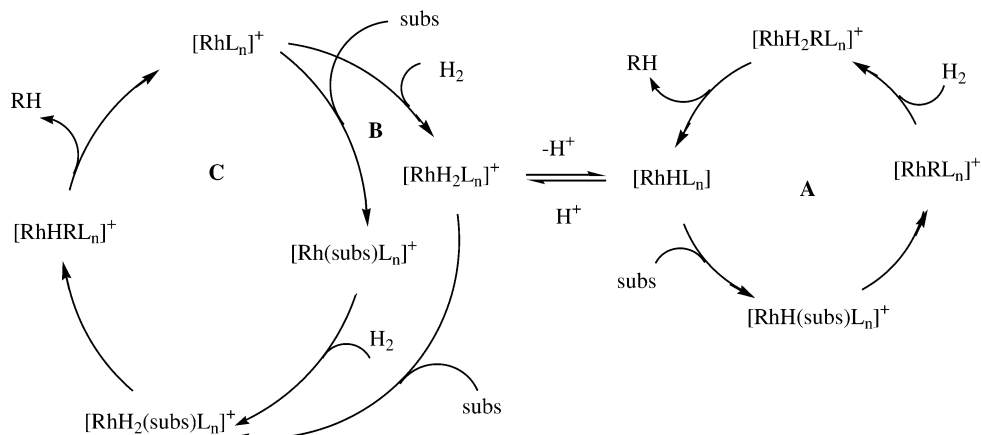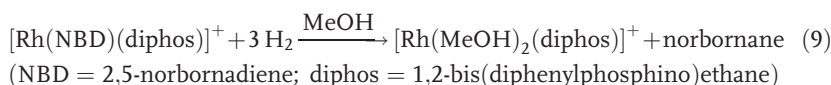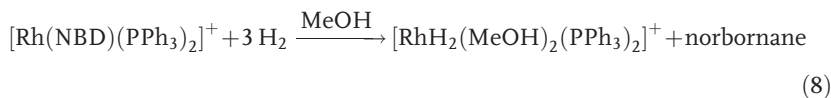
Scheme 1.6

catalysts than the dihydrides $[RhH_2S_xL_n]^+$. However, in order to hydrogenate an alkene without concomitant isomerization, path A must be suppressed; thus, hydrogenation under acidic conditions (path B) becomes operative due to the presence of the cationic $[RhH_2S_xL_n]^+$ dihydrides. The mechanism for hydrogenation via path B shows a close analogy to the proposed mechanism involving the Wilkinson catalyst (Scheme 1.5). The equilibrium illustrated in Eq. (7) offers considerable flexibility, and it is possible to identify appropriate conditions for the selective hydrogenation of alkynes to *cis* alkenes following pathways A and B. However, the rate of hydrogenation with the monohydride species is at least twice that with the dihydride species. It has been proposed that the origin of the selective reduction of 2-hexyne to *cis*-2-hexene seems to arise from the fact that the coordinated *cis*-2-hexene, formed by hydrogenation, is immediately displaced by 2-hexyne, before it can be isomerized or hydrogenated to hexane. Almost exclusive *cis*-addition of hydrogen to the alkyne was observed [28 b].

The selective hydrogenation of dienes to monoenes can also be accomplished by using these rhodium cationic catalysts with proper choice of the phosphine ligand [28 c]. Path C seems to be dominant, where the strongly coordinated dienes were hydrogenated selectively to monoenes, with hydrogen adding both 1,2 and 1,4 to conjugated dienes. The hydrogenation process follows the unsaturated route; in fact, the only detectable species are $[Rh(diene)L_2]^+$ which, after reaction with hydrogen, yield the alkyl–hydride complex. It should be noted that the latter species are common to both pathways B and C, the only difference being the sequence of substrate coordination and previous or posterior reaction with molecular hydrogen. The hydrogenation activity of catalysts derived from $[Rh(TFB)(P(C_6H_4\text{-}4\text{-}X)_3)_2]^+$ species depends on the electron-releasing ability of the X-substituent [29, 30].

Cationic $[Rh(diene)L_2]^+$ species are also catalyst precursors for the hydrogenation of ketones and aldehydes [19]. The mechanism presents some analogies

with that proposed for alkene hydrogenation, with formation of alkoxy species by insertion.

The catalytic activity of cationic rhodium precursors of formula [Rh(diene)(diphosphine)]⁺ was also explored by Schrock and Osborn [28]. Halpern and co-workers made very detailed mechanistic studies of olefin hydrogenation by [RhS₂(diphos)]⁺ species (diphos=1,2-bis(diphenylphosphino)ethane; S=solvent) [31]. Significant differences have been observed in the reaction of the catalyst precursors [Rh(NBD)(PPh₃)₂]⁺ and [Rh(NBD)(diphos)]⁺ in methanol, as shown in Eqs. (8) and (9):

$$[Rh(NBD)(PPh_3)_2]^+ + 3\,H_2 \xrightarrow{\text{MeOH}} [RhH_2(MeOH)_2(PPh_3)_2]^+ + \text{norbornane}$$

$$(8)$$

$$[Rh(NBD)(diphos)]^+ + 3\,H_2 \xrightarrow{\text{MeOH}} [Rh(MeOH)_2(diphos)]^+ + \text{norbornane} \quad (9)$$
(NBD = 2,5-norbornadiene; diphos = 1,2-bis(diphenylphosphino)ethane)

Although the latter product is a solvated mononuclear [Rh(MeOH)₂(diphos)]⁺ cation, in the solid state it is isolated as a binuclear complex of formula [Rh₂(diphos)₂](BF₄)₂, in which each rhodium center is bonded to two phosphorus atoms of a chelating bis(diphenylphosphino)ethane ligand, and to a phenyl ring of the bis(diphenylphosphino)ethane ligand of the other rhodium atom. This dimer reverts to a mononuclear species on redissolving. The mechanism of hydrogenation of the prochiral alkene methyl(Z)-α-acetamidocinnamate, studied in detail by Halpern [31], is depicted in Scheme 1.7.

The hydrogenation process follows the unsaturated route, the rate-determining step being the reaction of [Rh(alkene)(diphos)]⁺ with hydrogen. The proposed mechanism corresponds to pathway C of Scheme 1.6. Analogous cationic rhodium complexes with chiral diphosphines have allowed remarkable progress to be made on the subject of enantioselective hydrogenations, as will be discussed in the following section.

Several heteroaromatic compounds can be hydrogenated by [Rh(COD)(PPh₃)₂]⁺ species. Thus, this cationic complex has been reported to be a catalyst precursor for the homogeneous hydrogenation of heteroaromatic compounds such as quinoline [32] or benzothiophene [33]. Detailed mechanistic cycles have been proposed by Sánchez-Delgado and coworkers. The mechanism of hydrogenation of benzothiophene by the cationic rhodium(III) complex, [Rh(C₅Me₅)(MeCN)₃]²⁺, has been elucidated by Fish and coworkers [34].
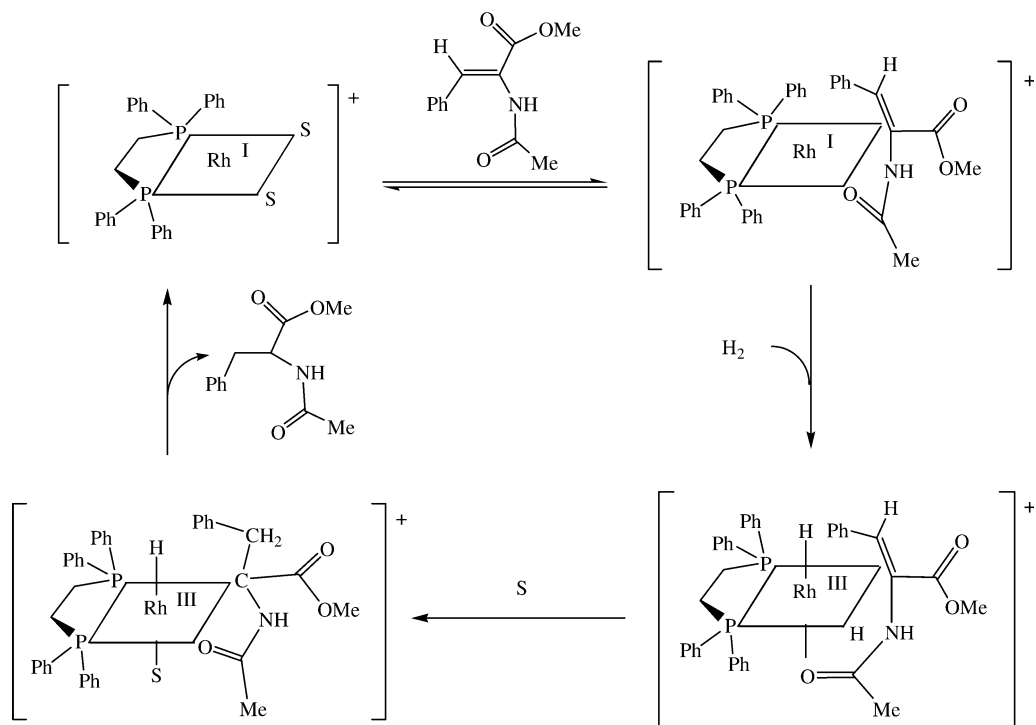
Scheme 1.7

1.6
Enantioselective Rhodium Catalysts

1.6.1
Hydrogenation of Alkenes

Following Wilkinson's discovery of [RhCl(PPh$_3$)$_3$] as an homogeneous hydrogenation catalyst for unhindered alkenes [14b, 35], and the development of methods to prepare chiral phosphines by Mislow [36] and Horner [37], Knowles [38] and Horner [15, 39] each showed that, with the use of optically active tertiary phosphines as ligands in complexes of rhodium, the enantioselective asymmetric hydrogenation of prochiral C=C double bonds is possible (Scheme 1.8).

Knowles reported the hydrogenation of α-phenylacrylic acid and itaconic acid with 15% and 3% optical purity, respectively, by using [RhCl$_3$(P*)$_3$] [P*=(*R*)-(–)-methyl-*n*-propylphenylphosphine] as homogeneous catalyst [38]. Horner found that α-ethylstyrene and α-methoxystyrene can be hydrogenated to (*S*)-(+)-2-phenylbutane (7–8% optical purity) and (*R*)-(+)-1-methoxy-1-phenylethane (3–4% optical purity), respectively, by using the complex formed *in situ* from [Rh(1,5-hexadiene)Cl]$_2$ and (*S*)-(–)-methyl-*n*-propylphenylphosphine as catalyst [39].

R = Ph, 15% *ee*
R = CH₂CO₂H, 3% *ee*

R = Et, 7 - 8% *ee*
R = OMe, 3 - 4% *ee*   **Scheme 1.8**
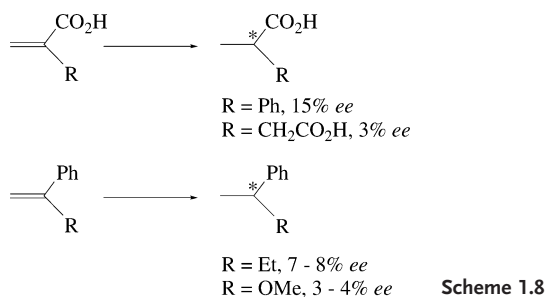
These were the first examples of metal-catalyzed enantioselective hydrogenation. The ee-values achieved were modest [40], but they established the validity of the hydrogenation method. Furthermore, the inherent generality of the method offered enormous opportunities for optimization of the results. It is interesting to note that, in these examples, the chirality of the ligands resides in the phosphorus atom.

The degree of enantioselective bias was improved shortly after this time. In 1971, Morrison et al. reported that the rhodium(I) complex [RhCl(NMDPP)₃] (NMDPP = neomethyldiphenylphosphine) reduces (*E*)-*β*-methylcinnamic and (*E*)-*α*-methylcinnamic acids with 61 and 52% ee, respectively (Scheme 1.9) [41]. NMDPP is a monodentate phosphine derived from (–)-menthol, and its asymmetry lies at carbon atoms.

An important breakthrough was the finding, by Kagan and Dang, that a rhodium complex containing the chiral diphosphine (–)-DIOP ((–)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane, derived from (+)-ethyl tartrate) efficiently catalyzed the enantiomeric reduction of unsaturated prochiral acids. In particular, *α*-acetamidocinnamic acid and *α*-phenylacetamidoacrylic acid were reduced quantitatively with 72 and 68% ee, respectively (Scheme 1.10) [42]. Two assumptions were presented by Kagan as being necessary to achieve a high degree of stereoselectivity in enantioselective catalysis:

- the ligand conformations must have maximum rigidity;
- in order to avoid epimerization equilibria, ligands must stay firmly bonded to the metal.

61% *ee*
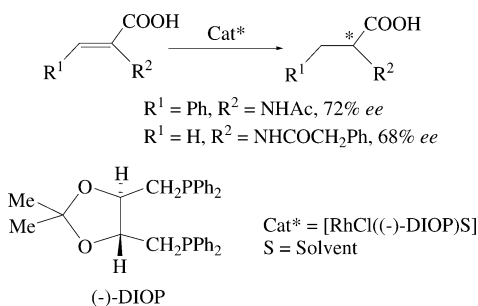
52% *ee*

(-)-NMDPP
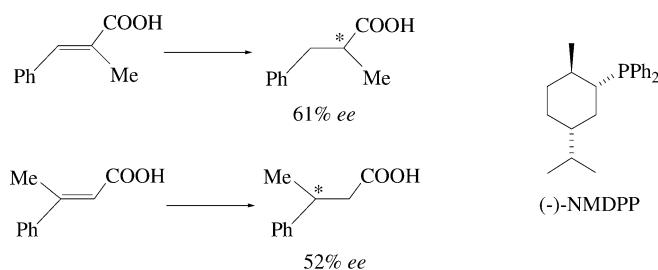
Scheme 1.9

Kagan concluded that diphosphines fulfill both of these conditions. In addition, it is desirable to avoid the possibility of geometric isomerism by choosing diphosphine having two equivalent phosphorus atoms [43]. These conditions strongly conditioned the subsequent development of the field, with the greater research effort being subsequently laid on metallic compounds with chiral diphosphines with C_2 symmetry as ligands. Additionally, Kagan introduced amino acid precursors as benchmark in enantioselective hydrogenation reactions.

At the same time, Knowles' team concentrated their efforts on the use of chiral at phosphorus ligands. Four years after the first report, these authors obtained 88% ee in the reduction of *α*-acylaminoacrylic acids by incorporating cyclohexyl and *ortho*-anisyl substituents [44] (Scheme 1.11).
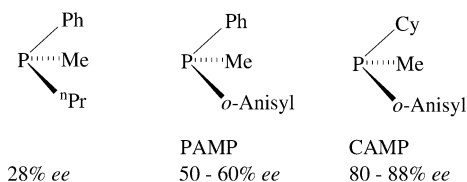
A crucial achievement significantly stimulated the development of the investigation in the field of homogeneous enantioselective catalysis. The Knowles group established a method for the industrial synthesis of *L*-DOPA, a drug used for the treatment of Parkinson's disease. The key step of the process is the enantiomeric hydrogenation of a prochiral enamide, and this reaction is efficiently catalyzed by the air-stable rhodium complex [Rh(COD)((R_P)-CAMP)$_2$]BF$_4$ (Scheme 1.12).

This achievement was unique in two respects: 1) it was the first example of industrial application of a homogeneous enantioselective catalysis methodology; and 2) it represented a rare example of very quick convergence of basic knowledge into commercial application. The monophosphine ligand CAMP was shortly replaced by the related diphosphine ligand DIPAMP which improved the selectivity for the *L*-DOPA system up to 95% ee [45].

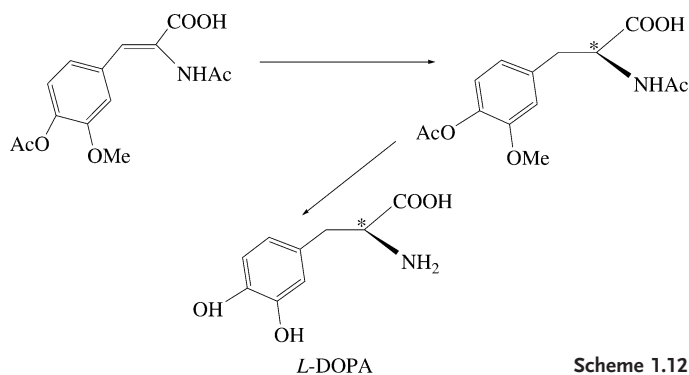The following years witnessed the development of a plethora of new diphosphine ligands with chiral carbon backbones, and at a very impressive pace [46]. Among these, two examples were of particular interest.
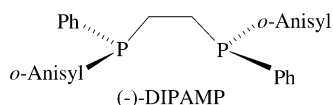

R^1 = Ph, R^2 = NHAc, 72% *ee*
R^1 = H, R^2 = NHCOCH$_2$Ph, 68% *ee*

(-)-DIOP

Cat* = [RhCl((-)-DIOP)S]
S = Solvent

Scheme 1.10

PAMP
50 - 60% *ee*

CAMP
80 - 88% *ee*

28% *ee*

Scheme 1.11
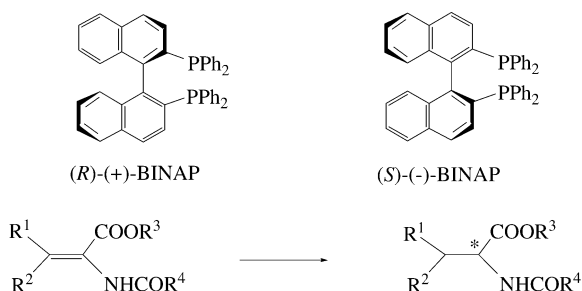
Scheme 1.12

(-)-DIPAMP

Scheme 1.13

The first example was the 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BI-NAP) ligand synthesized by Noyori and Takaya in 1980 [47]. BINAP is an atropoisomeric C_2 diphosphine that forms a seven-membered chelate ring through coordination to metals. The λ or δ conformations of this chelate determine the chiral disposition of the phenyl rings and, in this way, the chirality of BINAP is transmitted to the metal environment. BINAP complexes exhibit high enantios-electivity in various catalytic reactions, including hydrogenation. Thus, BINAP rhodium complexes [48] readily catalyze the hydrogenation of prochiral α-acyla-minoacrylic acids with up to 100% ee (Scheme 1.14).

The second example was the bis(phospholanyl)ethanes (BPE) and bis(phos-pholanyl)benzenes (DuPHOS) ligands developed by Burk some years later [49]. These ligands are electron-rich diphosphines that contain two phospholanes *trans*-substituted in the 2,5 position, and in which the phosphorus atoms are connected by 1,2-ethano or 1,2-phenylene backbones. Chirality lies in the carbon atoms adjacent to the phosphorus atoms and therefore, in the derived catalysts, it lies in the immediacy of the rhodium atoms (Scheme 1.15). By choosing the appropriate R substituent, a large variety of substrates, including α-(acylamino) acrylic acids, enamides, enol acetates, β-keto esters, unsaturated carboxylic acids and itaconic acids, are efficiently hydrogenated by cationic rhodium complexes of the type [Rh(COD)(bisphospholane)]X (X=weakly coordinating anion) with exceedingly high enantioselectivities [50].

Subsequently, it was shown that rhodium complexes derived from diphosphi-nites, diphosphonites, and diphosphites – as well as hybrid ligands – are simi-larly active and selective to diphosphines [46i].
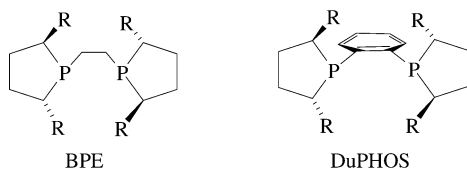
Enantioselective hydrogenation catalysts with chiral nitrogen ligands have been rather neglected, however. Until now, it seems that ligands containing only

(*R*)-(+)-BINAP   (*S*)-(-)-BINAP

R^1	R^2	R^3	R^4	*ee* (%)
H	Ph	H	Ph	100
Ph	H	H	Ph	87
H	Ph	Me	Ph	93
H	Ph	H	Me	84
H	*m*–OMe, *p*–OH– C_6H_2	H	Ph	79
H	H	H	Ph	98

Scheme 1.14

BPE   DuPHOS

Scheme 1.15

nitrogen donor atoms are not well suited for this purpose. Nevertheless, there are some examples of rhodium-based catalysts containing mixed P,N-chiral chelating ligands active for the reduction of C=C double bonds [51].

Since 1999 [52], the potential of monophosphorus ligands in the area has been reconsidered. The commonly accepted rule that bidentate ligands are necessary to achieve high enantioselectivity in hydrogenation reactions has been countered by the discovery that enantiopure monodentate P ligands may provide optical yields comparable to those obtained with chelating diphosphines [46i, 53]. This mostly occurs when two ligands on rhodium strongly restrict each other's conformational freedom [54]. In fact, monodentate P ligands containing biaryl, spirobiindane, oxaphosphinane, or carbohydrate building blocks have been used to efficiently hydrogenate *α*- and *β*-dehydroamino acids, itaconic acid derivatives and enamides with an ee systematically greater than 99% [46j, 53]. Recently, Reetz's group has demonstrated that mixtures of two different monodentate phosphorus ligands can be used in a combinatorial approach [53d–f]. Notably it has been shown that, in several cases, monodentate catalytic

ligands induce higher enantioselectivity and lead to faster asymmetric hydrogenations than bidentate analogues [54, 55].

1.6.2
Hydrogenation of Ketones

Enantioselective hydrogenation of unfunctionalized ketones is promoted only by a limited number of transition metal catalysts. Among these, a few reports dealing with rhodium catalysts have appeared [46 a, b, e, g, i, j, m, 56]. In 1980, Markó et al. reported on the enantioselective catalytic reduction of unfunctionalized ketones, for the first time. In the presence of NEt$_3$, a neutral rhodium complex (prepared from [RhCl(NBD)]$_2$ and (+)-DIOP) hydrogenated methyl, α-naphthyl ketone to give the corresponding chiral alcohol in 84% ee [57]. Another important contribution to the field was the communication by Zhang et al. that alkyl methyl ketones can be efficiently hydrogenated by the *in-situ*-prepared catalyst from [RhCl(COD)]$_2$ and the conformational rigid chiral bisphosphines P,P'-1,2-phenylenebis(*endo*-2,5-dialkyl-7-phosphabicyclo[2.2.1] heptanes (PennPhos; Scheme 1.16). Enantiomeric excesses of up to 94% ee for the *tert*-butyl methyl ketone and 92% ee for cyclohexyl methyl ketone were observed, with the R=Me PennPhos ligand [58].

The hydrogenation of ketones with O or N functions in the α- or β-position is accomplished by several rhodium compounds [46 a, b, e, g, i, j, m, 56]. Many of these examples have been applied in the synthesis of biologically active chiral products [59]. One of the first examples was the asymmetric synthesis of pantothenic acid, a member of the B complex vitamins and an important constituent of coenzyme A. Ojima et al. first described this synthesis in 1978, the most significant step being the enantioselective reduction of a cyclic α-keto ester, dihydro-4,4-dimethyl-2,3-furandione, to *D*-(–)-pantoyl lactone. A rhodium complex derived from [RhCl(COD)]$_2$ and the chiral pyrrolidino diphosphine, (2S,4S)-N-*tert*-butoxycarbonyl-4-diphenylphosphino-2-diphenylphosphinomethyl-pyrrolidine ((S,S)-BPPM; Scheme 1.17) was used as catalyst [60]. The enantioselective hydrogenation of functionalized ketones was also efficiently achieved by a series of rhodium(I) aminophosphine- and amidophosphine-phosphinite complexes [61].

R = Me, *i*Pr
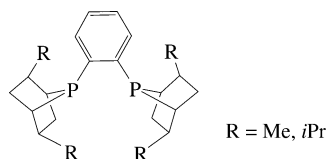
PennPhos   **Scheme 1.16**
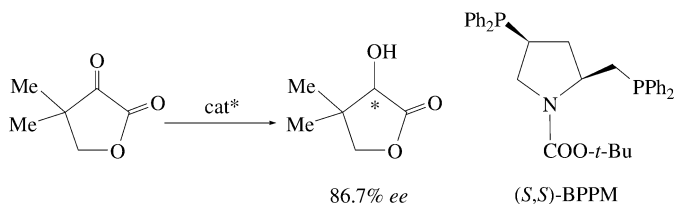
Scheme 1.17

1.6.3
Hydrogenation of Imines

To date, catalyzed enantioselective reductions of C=N double bonds have only led to relatively limited success. Currently, only a few efficient chiral catalytic systems are available for the hydrogenation of imines. Hydrogenation of functionalized C=N double bonds such as *N*-acylhydrazones, sulfonimides, and *N*-diphenylphos-phinylketimines has also been attempted, with some relevant results [46 b, g, i, j, 50, 62]. The first report on enantioselective homogeneous reduction of C=N double bonds mediated by rhodium complexes appeared in 1975. Kagan et al. reported that *N*-benzyl-*α*-phenyl ethylamine was prepared by hydrosilylation with 65% optical purity, using a chiral rhodium complex with (+)-DIOP [63]. Some years later, the Markó group reported that using catalysts prepared *in situ* from [RhCl(NBD)]$_2$ and chiral phosphines of the type Ph$_2$PCHRCH$_2$PPh$_2$ (R = Ph, *i*Pr, PhCH$_2$), optical yields up to 77% were achieved, although reproducibility of the results was poor [64]. Subsequently, some rhodium complexes have shown good ee values, among which two cases are remarkable. Acyclic *N*-alkylimines ArC(Me)=NCH$_2$Ph (Ar = Ph, 2-MeOC$_6$H$_4$, 3-MeOC$_6$H$_4$, 4-MeOC$_6$H$_4$) were hydrogenated in a two-phase system, with ee values up to 96%, using [RhCl(COD)]$_2$ together with sulfonated (*S*,*S*)-(−)-2,4-bis(diphenylphosphino)pentane ((*S*,*S*)-BDPP$_{sulf}$; Scheme 1.18) [65]. Similarly, the C=N group of *N*-acylhydrazones can be reduced by [Rh(COD)(DuPHOS)] (CF$_3$SO$_3$) as catalyst precursor. Enantioselectivities up to 97% were achieved (Scheme 1.19). The N–N bond of the resulting *N*-benzoylhydrazines is cleaved by SmI$_2$ to afford the corresponding amines [66].

Scheme 1.18
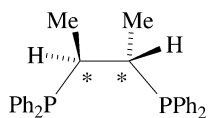
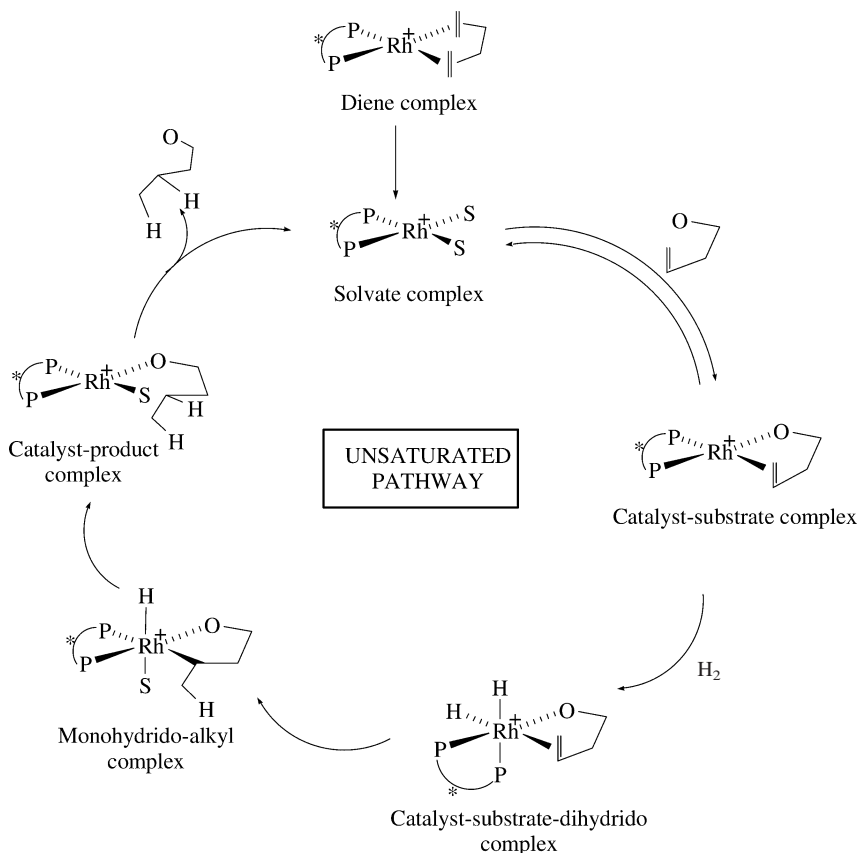cat* = [Rh(COD)(Et-DuPHOS)](CF$_3$SO$_3$)
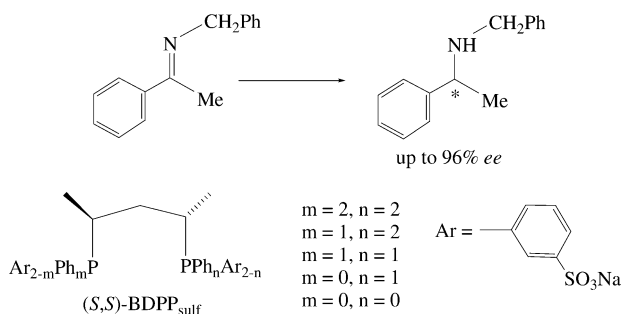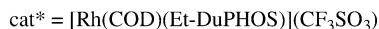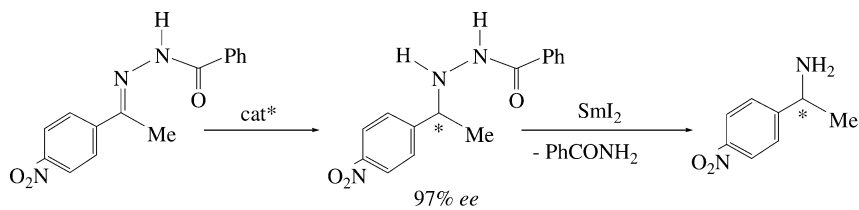
Scheme 1.19

1.6.4
Mechanism of Rhodium-Catalyzed Enantioselective Hydrogenation

The mechanism of rhodium-catalyzed enantioselective hydrogenation is one of the most thoroughly studied mechanisms of all metal-catalyzed processes [46 b, c, h, i, k, 23, 50, 67]. Studies have been focused on cationic rhodium chiral diphosphine complexes as catalyst precursors, and on prochiral enamides as hydrogenation substrates. Early mechanistic studies were conditioned by the case of achiral hydrogenation of alkenes by Wilkinson's catalyst. In the catalytic cycle proposed for Wilkinson's catalyst, dihydride rhodium(III) complexes [14 b, 35] are obtained by reversible oxidative addition of dihydrogen to the active species RhCl(PPh$_3$)$_2$ [23] (see Section 1.4). Thus, the formation of similar intermediates was expected upon hydrogenation of the catalyst precursors employed in asymmetric hydrogenation. However, Halpern et al. showed that [Rh(DIPHOS) (NBD)]$^+$ reacted with 2.0 mol of H$_2$/Rh yielding norbornane and the solvate complex [Rh(DIPHOS)S$_2$]$^+$ which was isolated as the dimer compound [Rh$_2$(DIPHOS)$_2$](BF$_4$)$_2$ (see Section 1.5) [31 a, 68]. Further investigations showed that the formation of [Rh(PP*)S$_2$]$^+$ (PP*=chiral diphosphine; S=solvent molecule) complexes by hydrogenation of the catalyst precursors is a general behavior of *cis*-chelating diphosphine rhodium complexes [46 c, 70]. It has been concluded that, under catalytic conditions, a molecule of the prochiral alkene coordinates to the rhodium atom, affording a bischelate catalyst–substrate complex (see Scheme 1.21). In fact, in 1978, for the first time, Brown and Chaloner provided ^{31}P-NMR-based evidence for the formation of such a type of compound [72], whilst shortly afterwards Halpern et al. reported the first X-ray molecular structure determination for a catalyst–substrate species, namely [Rh{(*S,S*)–CHIRAPHOS}{(*Z*)-EAC}]ClO$_4$ (EAC=ethyl-*α*-acetamidocinnamate) [73]. For C$_2$-symmetrical diphosphines – the most commonly used in enantioselective hydrogenation – two diastereomeric catalyst–substrate complexes can be formed, depending on the alkene enantioface that coordinates with the metal. However, only a single diastereomer of [Rh{(*S,S*)-CHIRAPHOS}{(*Z*)-EAC}]ClO$_4$ was detected in solution by NMR (Scheme 1.20); therefore, the second diastereomer must be present to the extent of less than 5%. Subsequently, numerous catalyst–substrate complexes have been described, and all have demonstrated stereodifferentiation in solution [67 d].

Me   Me

H'''''   H

Ph₂P   *   *   PPh₂

(*S,S*)-CHIRAPHOS

Scheme 1.20

Diene complex

Solvate complex

Catalyst-product
complex

UNSATURATED
PATHWAY

Catalyst-substrate complex

Monohydrido-alkyl
complex

Catalyst-substrate-dihydrido
complex

Scheme 1.21

From all the above observations, it was concluded that, for diphosphine chelate complexes, the hydrogenation stage occurs after alkene association; thus, the unsaturated pathway depicted in Scheme 1.21 was proposed [31 a, c, 74]. The monohydrido-alkyl complex is formed by addition of dihydrogen to the enamide complex, followed by transfer of a single hydride. Reductive elimination of the product regenerates the active catalysts and restarts the cycle. The monohydrido-alkyl intermediate was also observed and characterized spectroscopically [31 c, 75], but the catalyst–substrate–dihydrido complex was not detected.
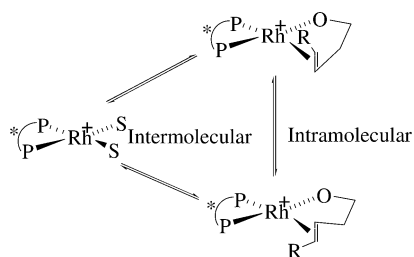
Scheme 1.22

The catalyst–substrate complexes deserve some additional comments. The two possible diastereomers for C_2-symmetrical diphosphines interconvert inter- and intramolecularly, the latter being the dominant mechanism [76] (Scheme 1.22). A second property – at least of some catalyst–substrate complexes – is that the reactivity of the minor diastereomer toward H_2 is notably higher than that of the major diastereomer.

Consequently, the stereochemistry of the hydrogenation is regulated by this relative reactivity rather than by the relative thermodynamic stability of the diastereomers [73, 75, 77]. Halpern and Landis accomplished detailed kinetic measurements on the hydrogenation of methyl-(Z)-α-acetamidocinnamate [(Z)-MAC] enamide catalyzed by Rh(DIPAMP) species. These authors studied the influence of temperature and pressure on the interconversion of catalyst–substrate complexes, on their reaction with H_2 and, as a consequence, on the ee achieved. The oxidative addition of H_2 is the enantio-determining and the turnover-limiting step, and it was concluded that the ee increased with decreasing temperature, because the concentration of the minor diastereomer increased, whereas it decreased with increasing pressure because hydrogenation of the major diastereomer became significant [78].

Extensive computational calculations have been performed by using molecular mechanics (MM) [79], quantum mechanics (QM) [80], or combined MM/QM methods [81]. As major contributions, these theoretical studies predict the greater stability of the major isomer, explain the higher reactivity of the minor diastereomer, introduce the formation of a dihydrogen adduct as intermediate in the oxidative addition of H_2 to the catalyst–substrate complexes, and propose the migratory insertion, instead of the oxidative addition, as a turnover-limiting step.

A new insight into the mechanism of enantioselective hydrogenation was achieved when the elusive dihydride intermediates were detected and characterized spectroscopically [82]. Bargon, Selke et al. detected, through parahydrogen-induced polarization (PHIP), NMR experiments [83, 84], the formation of a dihydride in the hydrogenation of dimethylitaconate with an enantiomerically pure bis(phosphinite)rhodium(I) catalyst (see Scheme 1.23). The structural assignment was not complete: it was not proven that the itaconate is in the coordination sphere of the metal (no ^{13}C-labeled experiments were performed) and there is a supposed *trans* $^2J_{PH}$ of only 4 Hz, far from the usual values for this coupling. However, the presence of

Dimethylitaconate   Bis(phosphinite)rhodium complex   **Scheme 1.23**

PHANEPHOS   **Scheme 1.24**
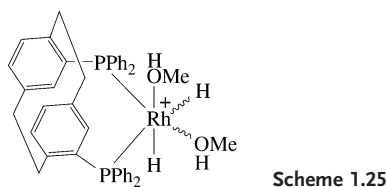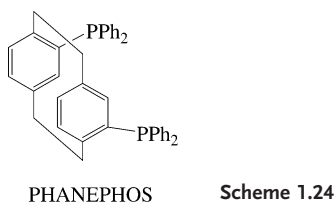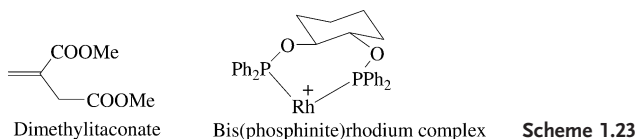
Scheme 1.25

some transient rhodium dihydride is definitive from the experimental evidences [84].

The use of the diphosphine PHANEPHOS (see Scheme 1.24) permitted Bargon, Brown and colleagues to detect and characterize a dihydrido intermediate in the hydrogenation of the enamide MAC by a rhodium-based catalyst. The PHIP NMR technique was employed, and showed one of the hydrogen atoms to be agostic between the rhodium center and the β-carbon of the substrate [85]. By using the same diphosphine and technique it was also possible to detect two diastereomers of the dihydride depicted in Scheme 1.25, which may also be detected using conventional NMR measurements [86].

Following a preparative method developed by Evans [87], Imamoto et al. prepared the C_2-symmetric electron-rich diphosphines BisP* with two stereogenic phosphorus centers [88] (Scheme 1.26). Further, Gridnev and Imamoto carried out detailed mechanistic investigations on the hydrogenation of α-dehydroamino acids and other unsaturated substrates such as enamides, (*E*)-β-dehydroamino acids or 1-benzoyloxyethenephosphonate using the rhodium complexes [Rh(diene)(*t*-Bu-BisP*)]$^+$ (diene=COD, NBD) as catalyst precursors [46h, 67c, d, 89]. These authors showed that hydrogenation of the diene precursors at –20 °C gives the expected solvate complexes [Rh(*t*-Bu-BisP*)S$_2$]$^+$, but at –90 °C affords two diastereomers of the catalysts–solvate dihydrido complex [RhH$_2$(*t*-Bu-BisP*)S$_2$]$^+$. The formation of these dihydrides is reversible [89a]. Similar dihydrides were prepared for the other BisP* ligands [89b]. The catalysts–solvate–dihydrido reacts with α-dehydroamino acids, giving monohydride intermediates
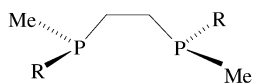
R = *t*-Bu, 1-adamantyl, 1-methylcyclohexyl,
Et₃C, *c*-C₅H₉, *c*-C₆H₁₁, *i*-Pr

(*S*,*S*)-BisP*

Scheme 1.26
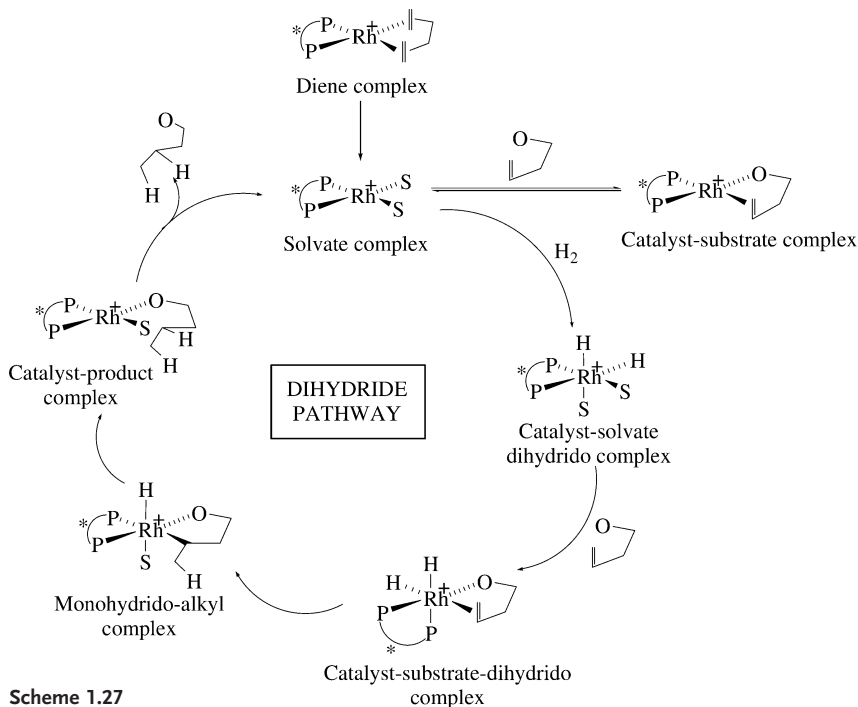
Scheme 1.27

and, eventually, the hydrogenation product with the same configuration and ee value (99%) as obtained in the catalytic reaction. On the other hand, the catalyst–substrate complexes were easily prepared by adding the substrates to the solvates. Hydrogenation of the catalyst-substrate complexes gives, in general, the hydrogenation product, but only at higher temperatures and with a lower ee. From the comparison of their results, the authors concluded that in this case the dihydride mechanism depicted in Scheme 1.27 was operating. The catalyst–substrate complexes dissociate, yielding the solvate complex that is hydrogenated to the solvate–dihydride complex. This dihydride reacts with the substrate, giving the monohydride–alkyl complex as the next observable species. The hydrogenation product is obtained after the reductive elimination step.

Notably, under catalytic conditions, reaction steps preceding catalyst–substrate–dihydrido formation are shown to be in rapid equilibrium. Therefore, stereoselec-

tion must occur at a later step in the catalytic cycle, and the authors suggested the migratory insertion as an enantio-determining and turnover-limiting irreversible step of enantioselective hydrogenation. As a major consequence, following the Gridnev and Imamoto contribution, the boundaries between unsaturated pathway and dihydride pathway are blurred. At least in some cases, both mechanisms are operating, joining in a single pathway before stereoselection occurs.

1.7
Some Dinuclear Catalyst Precursors

Several dinuclear rhodium complexes such as the above-mentioned [$Rh_2(OAc)_4$] have been used as hydrogenation catalysts [22, 23]. Maitlis and coworkers have studied the chemistry and catalytic activity of the [$Rh(C_5Me_5)Cl_2$]$_2$ complex and related complexes. Kinetic studies suggested that cleavage into monomer occurs in the most active catalysts [90].

Muetterties has suggested that the dimeric hydride [$RhH(P\{OiPr\}_3)_2$]$_2$ catalyzes alkene and alkyne hydrogenation *via* dinuclear intermediates [91]. However, no kinetic evidence has been reported to prove the integrity of the catalysts during the reactions. On the other hand, studies of the kinetics of the hydrogenation of cyclohexene catalyzed by the heterodinuclear complexes [H(CO)(PPh$_3$)$_2$Ru(μ-bim)M(diene)] (M = Rh, Ir; bim = 2,2′-biimidazolate) suggested that the full catalytic cycle involves dinuclear intermediates [92].

1.8
Concluding Remark

Throughout the history of homogeneous catalysis – and especially of homogeneous hydrogenation – rhodium complexes have played a crucial role due to the combination of excellent coordinative properties, remarkable activity and selectivity, the adequate redox characteristics of the couple Rh(I)/Rh(III) as well as NMR properties (100% abundance, spin 1/2). The selection of results presented in this chapter show that homogeneous hydrogenation by rhodium complexes represents not only a rich past, as indicated by the exponential growth of the past forty years, but also a bright future.

Abbreviations

BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
BPE	bis(phospholanyl)ethane
COD	1,5-cyclooctadiene
DIPHOS	1,2-bis(diphenyl)phosphinoethane
DuPHOS	bis(phospholanyl)benzene
MH	monohydride

MM   molecular mechanics
NBD   2,5-norbornadiene
NMDPP   neomethyldiphenylphosphine
PHIP   parahydrogen-induced polarization
QM   quantum mechanics
TFB   tetrafluorobenzobarrelene
(*Z*)-MAC   methyl-(*Z*)-*α*-acetamidocinnamate

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