8.1. HYDROGENATION AND RELATED REACTIONS

Of all the reactions promoted by transition metal complexes, the hydrogenation of unsaturated compounds has attracted most attention.[1] It could even be argued that the attention is disproportionately high. A monograph containing almost 2000 references specifically related to hydrogenation appeared in 1973,[1a] and an updated review by the same author five years later quoted an additional 500 papers.[1b]

The earliest observation of the homogeneous activation of molecular hydrogen was reported by Calvin in 1938[2] and concerned the reduction of benzoquinone to hydroquinone. In the following year Iguchi discussed the hydrogenation of fumarate with rhodium complexes, but the significance of this work was not recognized until many years later.[3] Perhaps the most influential article, after Halpern and other researchers[1c] set the stage through their pioneering work for understanding the mechanism of olefin hydrogenation, is that of Wilkinson and his co-workers.[4] It appeared in 1965 after the phenomenon of reversible binding of molecular hydrogen and ethylene by Vaska's complex had been established in 1962.[5] Wilkinson's elegant work combined kinetic studies with physicochemical observations (especially NMR studies) of the interaction of small molecules with complexes, thus enabling fundamental steps such as hydrogen activation and olefin coordination to be studied. In contrast, mechanistic studies of the mode of action of heterogeneous catalysts are severely limited by the lack of such direct experimental evidence.

a. Basic Concept of Olefin Hydrogenation

Figure 8.1 shows the mechanism of olefin hydrogenation by Wilkinson's catalyst, $RhCl(PPh_3)_3$.[6] It is somewhat different in detail from that originally proposed by Wilkinson; side reactions in which dinuclear complexes are formed have been omitted for simplicity.

The complex $RhCl(PPh_3)_3$ dissociates one of its PPh_3 ligands L in solution to give complex [A], which has a coordinated solvent S. Oxidative addition of H_2 to [A] gives a dihydride complex [B]. The same dihydride can also be produced, though much less rapidly, by direct oxidative addition of H_2 to undissociated $RhCl(PPh_3)_3$, giving [E] and subsequent dissociation of triphenylphosphine. The octahedral complex [C] is formed by displacement of S from [B] by an olefin. Wilkinson originally proposed that in the next step the two hydride ligands attack the coordinated olefin in a concerted manner.[1c] However, it is now generally accepted that there is a two-step process in which the olefin inserts into the Rh–H bond to give the hydride–alkyl species [D], and alkane is reductively eliminated to regenerate [A]. The coordinatively unsaturated complex [A] reacts further with H_2 to continue the catalytic cycle. It should be noted that both the initial complex $RhCl(PPh_3)_3$ and [A], con-

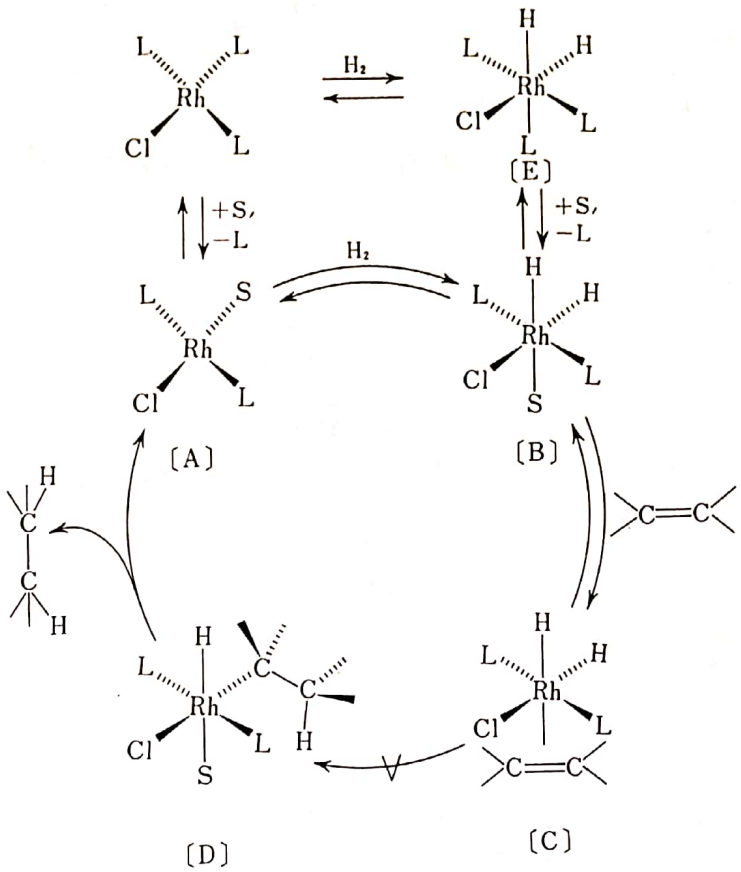


FIGURE 8.1. Mechanism of olefin hydrogenation by Wilkinson's complex.

whereas the octahedral complexes have an 18-electron configuration. The catalytic cycle thus involves coordinatively unsaturated d^8 square planar Rh(I) and coordinatively saturated d^6 octahedral Rh(III) species. In none of the intermediate species is the 18-electron configuration exceeded.

In this mechanism the first step is assumed to be addition of H_2 to [A]. However, the Rh(I) complex may first form a π complex with the olefin and then undergoes oxidative addition of H_2 to give the hydrido-olefin complex. This process does occur in some catalytic reactions. Which alternative is favored depends on the complex and its affinity for the olefin and H_2 and on the relative concentrations of the reactants. Figure 8.2 illustrates the generalized mechanisms of olefin hydrogenation taking both routes into consideration.

In cycle A, H_2 first oxidatively adds to a coordinatively unsaturated species L_nM, step (a). Complexation of an olefin in step (b) gives the dihydrido-olefin complex [M]. The ensuing olefin insertion into one of the two M–H bonds [step (e)] gives a hydrido-alkyl complex that on reductive elimination in step (f) liberates alkane with regeneration of the coordinatively unsaturated L_nM. This reacts further with H_2 to drive the catalytic cycle A in an anticlockwise direction. Figure 8.2 also illustrates cycle B, involving initial olefin complexation [step (c)] to L_nM. Molecular hydrogen oxidatively adds to the olefin complex in step (d) to give the dihydrido-olefin species [M] that undergoes

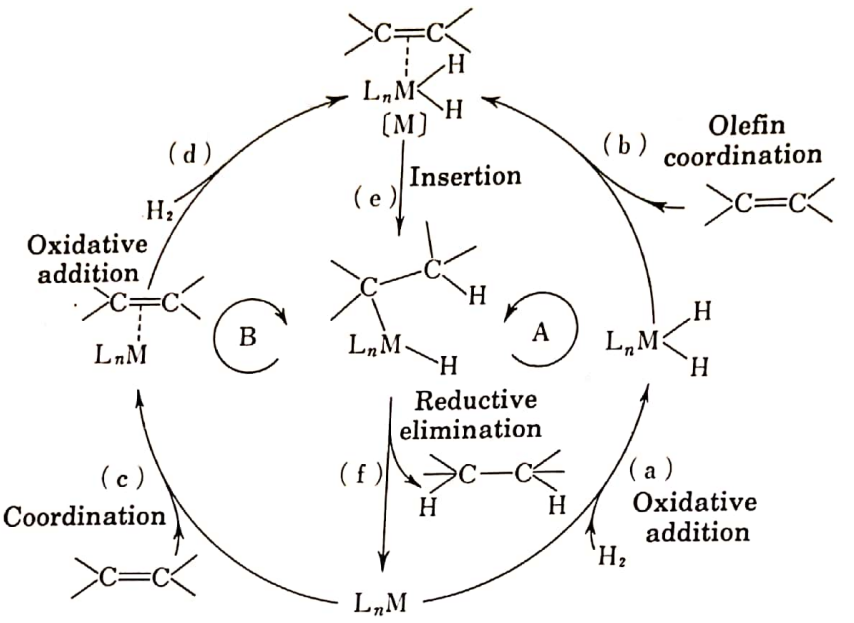
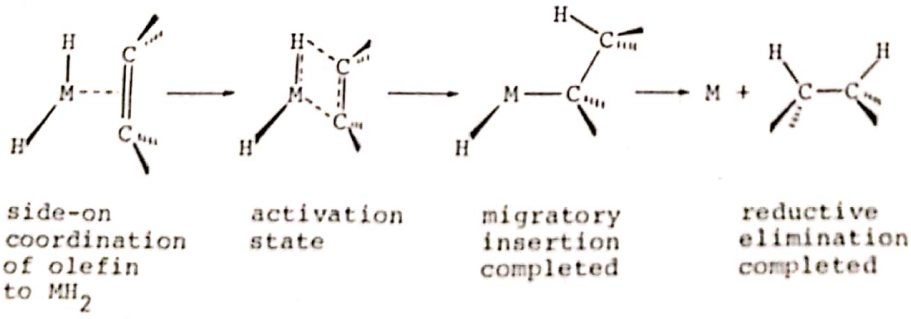


FIGURE 8.2. Two possible catalytic cycles in olefin hydrogenation with a transition metal complex catalyst.

olefin insertion and reductive elimination of alkane. This regenerates L_nM and thus drives the catalytic cycle B in a clockwise direction.

It is not easy in real catalytic systems to establish which cycle is operating, but pertinent information can often be obtained by carrying out kinetic studies on the individual elementary steps of the cycle and by examining the rates of addition of olefin and H_2.

The stereochemistry of the hydrogenation products of various olefins has been established as cis. This is consistent with a process in which the olefin coordinates initially in a side-on manner and undergoes migratory insertion into the M–H bond; the resulting hydrido-alkyl then eliminates alkane in a concerted manner.

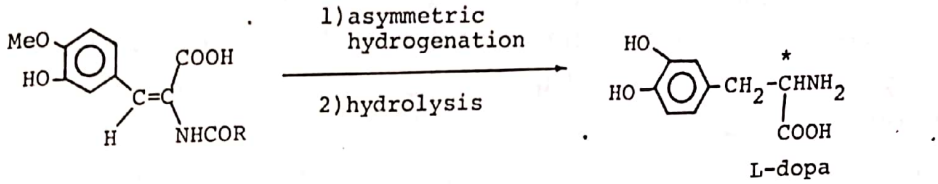


(8.1)

In addition to Wilkinson's catalyst, a variety of other hydrogenation catalysts have been reported, including $[Co(CN)_5]^{3-}$, a platinum–tin(II) chloride complex $[Pt(SnCl_3)_5]^{3-}$, combinations of various transition metal compounds with alkylaluminum compounds (Ziegler type catalysts), and various poly-

b. Asymmetric Hydrogenation

Many naturally occurring organic compounds, such as amino acids and carbohydrates, display optical activity with only one of the enantiomers that show physiological activity. For example, L-glutamic acid markedly enhances the taste of food, whereas D-glutamic acid does not. Proteins are composed of sequential combinations of L-amino acids only. The importance of asymmetric synthesis should be obvious from these few examples alone. Although extensively used in industry, heterogeneous catalysts are not as effective as homogeneous ones for asymmetric synthesis where optical yields of almost 100% have been achieved. An asymmetric hydrogenation with a rhodium complex having chiral phosphine ligands led to the first industrial process for the production of L-DOPA, L-dihydroxyphenylalanine, a compound that is active against Parkinson's disease.



A variety of chiral tertiary phosphine ligands have been prepared and examined for effectiveness in this reaction. Representative examples are shown in Figure 8.3.

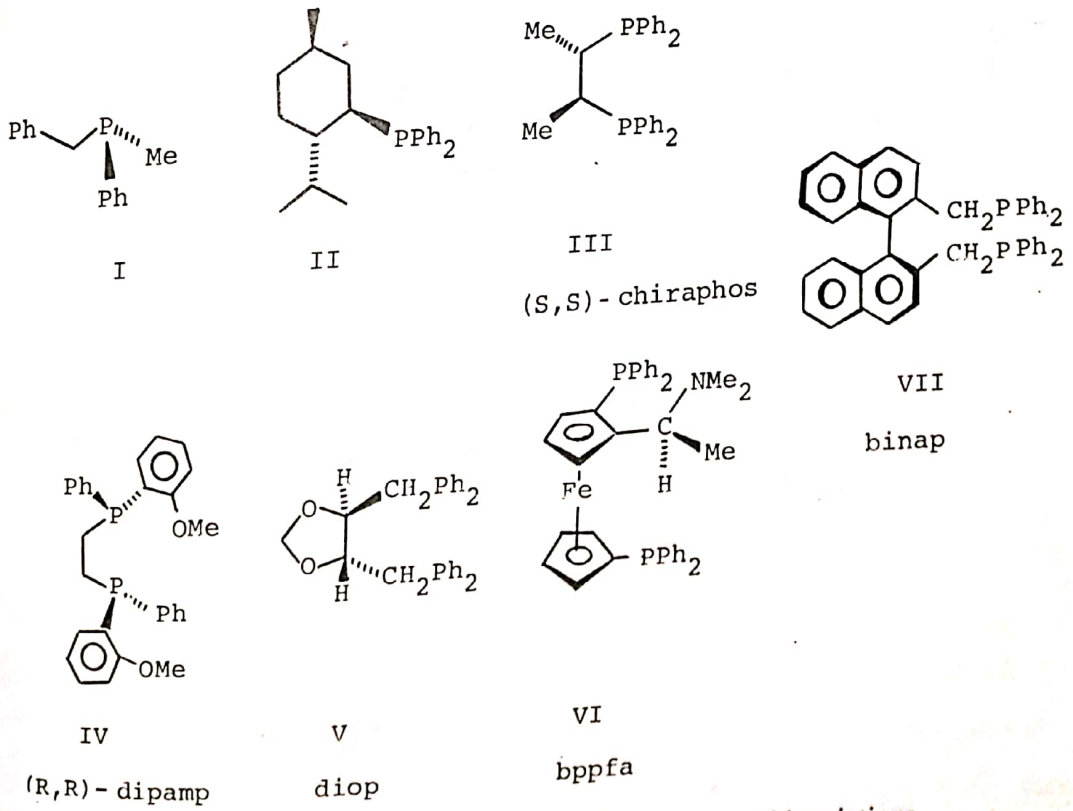


FIGURE 8.3. Some chiral phosphines with common abbreviations.

The asymmetry of the monophosphines may be associated with the phosphorus atom, as in I, or with a substituent, as in II, or both. The bidentate phosphines may form metal chelates with five-membered rings (III and IV), seven-membered rings (V and VI), or even a nine-membered ring, as is the case with binap (VII), which has an axial chirality element.

In general, the unidentate chiral phosphines used in earlier work gave low and variable optical yields. The bidentate ditertiary phosphines are more rigidly coordinated to the metal and result in a larger constraint on the coordinated substrate.

The nature of the substrate also affects the stereoselectivity. Substrates in which a coordinating polar group is adjacent to the double bond usually give higher optical yields than do simple olefins. The α-*N*-acylaminoacrylic acids and their derivatives give particularly high optical yields because they combine with the metal through both the double bond and the carbonyl group.[7] Figure 8.4 illustrates coordination of (*Z*)-α-acetamidocinnamate with a rhodium complex containing a chiral bidentate diphosphine ligand (P—*—P).

On coordination of the olefin asymmetry is induced at the α carbon atom of the olefin so that two diastereomers (A and B) are formed. In the former the rhodium atom is bound to the si face and in the latter to the re face (for the conventions used in stereochemistry see ref. 8a). When (*S,S*)-chiraphos (see Fig. 8.3) was used in combination with ethyl (*Z*)-α-acetamidocinnamate, a rhodium complex corresponding to B in Figure 8.4 was isolated and its structure was determined by X-ray analysis. It was also shown by NMR spectroscopy to be the predominant species in solution.[9]

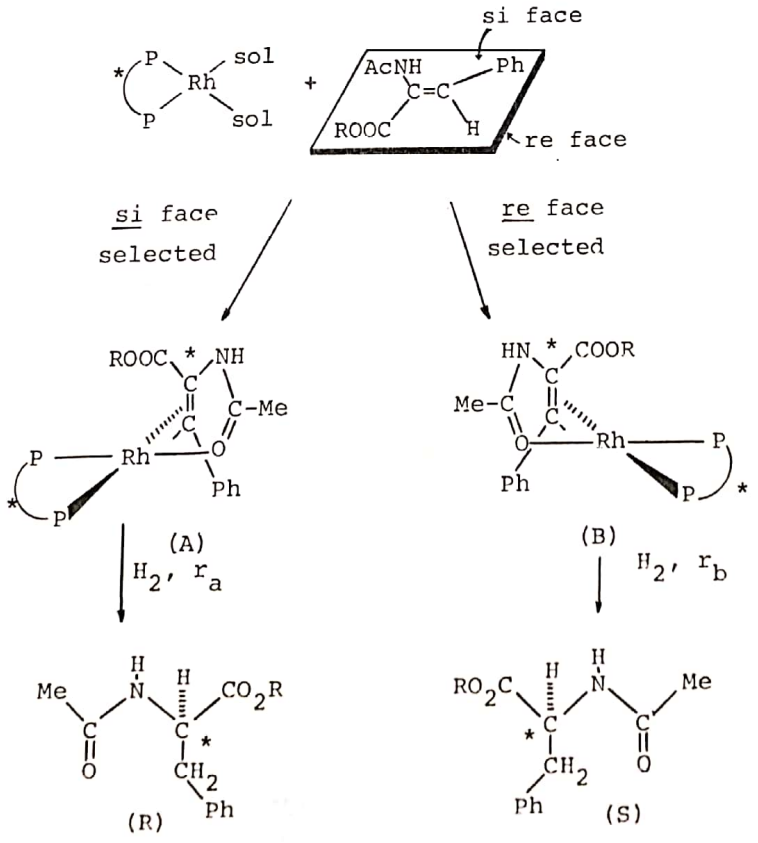


FIGURE 8.4. Two pathways in asymmetric hydrogenation of (*Z*)-α-acetamidocinnamate catalyzed by a rhodium complex having a chiral bidentate ligand.

It is expected that cis addition of H_2 to the re face of the olefin coordinated to the metal would yield *N*-acetyl-(*S*)-phenylalanine ester, as shown in Figure 8.4. However, it was found that the predominant product of hydrogenation with the rhodium complex having the (*S,S*)-chiraphos was the *R* isomer with over 95% enantiomeric excess. [The enantiomeric excess is a currently used measure of optical yield and is defined as the quantity $(X_R - X_S)/(X_R + X_S) \times 100$, where X_R and X_S are the relative quantities of *R* and *S* enantiomers. If 98% of one isomer and 2% of the other are produced, the enantiomeric excess (e.e.) is 96%.]

The result was interpreted by assuming that H_2 adds more rapidly to the minor diastereomer A than to the major diastereomer B ($r_a > r_b$). A similar conclusion was reached for the asymmetric hydrogenation of the same substrate using a rhodium complex containing the (*R,R*)-dipamp ligand, although in this case the chirality of the principal product was opposite to the product obtained with (*S,S*)-chiraphos. NMR investigations revealed that the minor diastereomer was hydrogenated at a much faster rate than the predominant diastereomer.[8i,10]

These results are schematically illustrated in Figure 8.5.

The figure shows that despite its smaller concentration the minor diastereomer will be hydrogenated more rapidly, provided the activation energy, $\Delta G^{\ddagger}_{\text{minor}}$, for H_2 addition to the minor diastereomer is much smaller than that for the major diastereomer.

The crucial question in asymmetric hydrogenation is the stereochemical arrangement of the chiral phosphine in the transition state for hydrogenation. Although this question is difficult to answer, the arrangement of the diphosphine ligands in the substrate–catalyst adduct is known with considerable certainty. Figure 8.6 illustrates the preferred arrangement of the four phenyl rings in [Rh(*S,S*-chiraphos)]$^+$ and [Rh((*R,R*)-dipamp)]$^+$ viewed from the side of the rhodium atom, looking toward the chiral phosphine ligands, that is, the substrate approaches from the viewer's side.