CHAPTER 3

REACTIONS OF OLEFINs AND DIENES – HYDROGENATION AND HY ADDITIONS

CHAPTER 3

OBJECTIVES

- HYDROGENATION OF SIMPLE OLEFINs
- MECHANISMS OF OLEFINs HYDROGENATION
- SELECTIVE HYDROGENATION OF PLOYENES
- ASYMmETRIC HYDROGENATION
- HYDROSILYLATION
- HYDROCYANATION OF OLEFINs AND DIENES

HYDROGENATION OF SIMPLE OLEFINs

- Some of the best studied homogeneous catalytic processes are the additions of H₂, HSiR₃ and HCN to the C=C bond.
- In the past, hydrogenation with soluble catalysts was primarily of academic interest because heterogeneous catalysts such as Pd/C were so flinch more convenient.
- Recently, however, enantioselective hydrogenations with soluble chiral catalysts have become important to the pharmaceutical industry and to the organic synthesis chemist.
HYDROGENATION OF SIMPLE OLEFINS

- The hydrosilylation and hydrocyanation reactions have been applied industrially for over 20 years.
- The synthesis of adiponitrile, a nylon intermediate, by hydrocyanation of butadiene is carried out on a scale of almost 500,000 tons per year.

As evidenced by hundreds of publications, including monographs and reviews the homogeneous hydrogenation of olefins has been studied extensively, perhaps more so than any other reaction catalyzed by a soluble metal complex.
- This intensive study seems anomalous because heterogeneous catalysts are usually more active and more convenient for practical applications such as the hydrogenation of cyclododecatriene to cyclododecane or of dicyanobutene to adiponitrile.

Until the mid-1980s, the sole commercial use of a soluble catalyst for olefin hydrogenation was Monsanto’s reduction of an unsaturated amino acid to a precursor of the drug L-dopa.
- This operation, begun in 1970, pioneered the commercial use of asymmetric induction by an optically active catalyst.
HYDROGENATION OF SIMPLE OLEFINs

- The reduction of a sterically accessible C=C bond is usually simple experimentally.
- One mixes hydrogen, olefin, and catalyst in an organic solvent at 25-100°C and 1-3 atmospheres pressure.
- The reaction is usually clean, and the products are separated from catalysts by conventional techniques such as distillation or washing with water.

HYDROGENATION OF SIMPLE OLEFINs

- Soluble transition metal complexes catalyze hydrogenation of olefins, but four classes are preferred for practical hydrogenation:
  - Wilkinson's catalyst, RhCl(PPh₃)₃, and the related [Rh(diene)(PR₃)₂]+ complexes.
  - Mixtures of platinum and tin chlorides.
  - Anionic cyanocobalt complexes.
  - Ziegler catalysts prepared from a transition metal salt and an alkylaluminum compound.

HYDROGENATION OF SIMPLE OLEFINs

- The best studied soluble catalyst for olefin hydrogenation is Wilkinson's catalyst, RhCl(PPh₃)₃.
- This moderately stable, commercially available compound catalyzes the hydrogenation of many sorts of olefins under mild conditions.
- Terminal olefins such as 1-hexene are rapidly hydrogenated at room temperature and atmospheric pressure.
The hydrogenation of internal olefins proceed slowly, but excellent results are often attained. The stereochemistry of the proceed may differ horn that obtained with heterogeneous catalysis. This catalyst selectively reduces C=C bonds in he presence of other easily reduced functions such as nitro and –CH=O.

It adds H₂ or D₂ cleanly cis to the C=C bond and usually produces little HD scrambling when it is used to introduce deuterium. Its application in synthesis is illustrated by the Organic Syntheses procedure for the hydrogenation of carvone:

In this particular application, a 1,1-disubstituted double bond is hydrogenated in preference to a trisubstituted olefin and a ketone.
HYDROGENATION OF SIMPLE OLEFINS

- Wilkinson's catalyst is slow for the hydrogenation of internal double bonds, but as illustrated above, its selectivity can make it useful in organic synthesis.
- Other potential applications include steroid hydrogenation and the hydrogenation of dicyanobutenes to adiponitrile.

\[ \text{NCCH}_2\text{CH} = \text{CHCH}_2\text{CN} \xrightarrow{\text{H}_2, \text{RhCl(PPh}_3)_2} \text{N} = \text{C(CH}_2)_2\text{CN} \]

HYDROGENATION OF SIMPLE OLEFINS

- In contrast to Wilkinson's catalyst, the closely related catalysts \([\text{Rh(diene)}(\text{PR}_3)_2]^+\) developed by Schrock and Osborn, give respectable rates with highly substituted olefins.
- These cationic catalysts are employed in most systems for the asymmetric hydrogenation of olefins.

HYDROGENATION OF SIMPLE OLEFINS

- The results obtained vary significantly with the reaction conditions.
- In acidic media, the active catalytic species appears to be a cationic dihydride, \([\text{RhH}_2(\text{PR}_3)_2(\text{solvent})_2]^+\) which hydrogenates olefins with little concomitant isomerization.
- In nonacidic media, the dihydride appears to deprotonate to form a neutral complex, which catalyzes both olefin isomerization, and hydrogenation.
HYDROGENATION OF SIMPLE OLEFINs

Another family of catalysts suitable for hydrogenation of C=C in the presence of C=O is generated by mixing platinum and tin chlorides. The commercially available H₂PtCl₆ and SnCl₂·2H₂O react in methanol to form deep red solutions which contain species such as [Pt(SnCl₃)₅]⁴⁻. These solutions catalyze hydrogenation of simple linear olefins and have been extensively studied for hydrogenation of vegetable oils to remove excessive unsaturation which is responsible for flavor instability. Other ligands such as phosphines are often added to modify the catalytic activity.

HYDROGENATION OF SIMPLE OLEFINs

For hydrogenations in water with an inexpensive catalyst, solutions containing cobalt salts and excess cyanide ion are useful. These solutions contain complex anions such as [Co(CN)₅]³⁻ and [HCo(CN)₅]³⁻. The catalysts are selective for hydrogenation of C=C bonds, which are conjugated with one another or with C=O, C≡N, or phenyl groups. In contrast to other diene hydrogenation catalysts, the cobalt cyanides are relatively unreactive with unconjugated dienes such as 1,5-cyclooctadiene.

HYDROGENATION OF SIMPLE OLEFINs

Industrial hydrogen at inn of unsaturated polymers is usually carried out with Ziegler-type systems like those used in arene hydrogenation. These systems are prepared by mixing a hydrocarbon-Soluble complex of a first-row transition metal with an alkane solution of an alkylaluminum compound. Typically, cobalt acetylacetonate or 2-ethylhexanoate is used with triethyl or trisobutylaluminum.
HYDROGENATION OF SIMPLE OLEFINS

The mixtures are dark, air-sensitive solutions, which may contain some colloidal metal. Because of the highly reactive alkyl-metal bonds these catalysts are affected by functional groups such as OH, C=O, and C≡C-H. In a typical application, a 75:25 butadiene-styrene block copolymer is hydrogenated with a catalyst prepared from reaction of a CoCl₂ complex with triisobutylaluminum in hexane.

The C=C bonds in the polybutadiene segments, which contain both internal double bonds and pendant vinyl groups, are completely hydrogenated. The process gives a tough oxidation-resistant rubber of the kind ordinarily found in shoe soles and heels. One of the virtues of soluble catalysts in the hydrogenation of polymers is that the catalyst can diffuse to lie site of the C=C bond in the polymer chain.

In contrast, a heterogeneous catalyst would require that the polymer unfold to gain access to the catalytic site. This virtue of the molecular catalysts is not confined to polymer solutions. It has been shown that RhCl(PPh₃)₃ can diffuse to amorphous regions in 1,2-polybutadiene at 60°C and affect saturation of most of the pendant vinyl groups. This process is not used commercially, but it has some practical potential as a hydrogen sequestrant in nuclear applications.
HYDROGENATION OF SIMPLE OLEFINS

- In addition to the catalyst families described above, 
  Co₂(CO)₈ and [Co(CO)₃(PBu₃)]₂ are useful hydrogenation 
  catalysts.
- The latter is relatively stable and shows excellent 
  selectivity in the hydrogenation of polyenes to monoolefins.
- Other carbonyls such as Cr(CO)₆ and Fe(CO)₅ are also 
  useful.
- They are less active, but become effective when activated 
  by heating or radiation to expel a carbonyl ligand and 
  create a vacant coordination site.

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MECHANISMS OF OLEFINS HYDROGENATION

- Most soluble catalysts add hydrogen to a C=C bond very 
  simply. The olefin and H₂ are brought together as ligands 
  in the coordination sphere of the metal.
- A rearrangement of the hydrido olefin metal complex to a 
  metal alkyl is followed by some sort of M-C bond 
  cleavage process.
- Catalysts differ in the mode of cleaving H₂ to form the 
  metal-hydride ligand and in the mechanism of cleavage 
  of the metal alkyl bond to form alkane.
Three different H₂ cleavage mechanisms are observed for the rhodium(I) platinum-tin and cobalt-cyanide catalysts.

The last system may differ quite fundamentally in its hydrogenation mechanism.

At least three mechanistic pathways have been demonstrated for Wilkinson’s catalyst.
The kinetically dominant mechanism is shown in Figure 3.1.
The Rh(I) species shown at the top of the catalyst cycle is probably a solvated three coordinate complex formed by dissociation of a triphenylphosphine ligand from the parent compound.

\[ \text{RhCl(PPPh₃)₃} \rightleftharpoons \text{RhCl(PPPh₃)₂ + PPPh₃} \]
This Rh(I) species is very coordination-deficient, with a formal electron count of 14. It readily undergoes oxidative addition of an H-molecule to form a dihydride which is formally Rh(III) if the H ligands are regarded as H. In the presence of triphenylphosphine, RhH₂Cl(PPh₃)₃ is detected in solution by NMR.

When the concentration of triphenylphosphine is limited, the dihydride coordinates an olefin to form the complex 1. This complex in turn, undergoes migratory insertion to produce the alkylrhodium-hydride complex 2. The alkylrhodium-hydride complex rapidly eliminates alkane and regenerates the catalytically active Rh(I) species to complete the cycle.

A similar cycle probably operates for the [Rh(diene)(PR₃)₂]⁺ catalysts which have been studied intensively because of their use in asymmetric hydrogenation. In this instance, the Rh(I) species is solvated which is formed by hydrogenation of the diene ligand. The sequence of reaction with H and olefin is reversed with this catalyst.
The olefin coordinates before the oxidative addition of hydrogen, which is the rate-limiting step. It the hydrogenation of an acetamidocinnamic acid, the alkyl hydride complex has been detected by NMR at low temperatures. The hydrogenation catalyst prepared by mixing $\text{H}_2\text{PtCl}_6$ or $\text{K}_2\text{PtCl}_4$ with stannous chloride follows a different reaction pathway.

The catalyst solutions contain several anionic complexes of which the best characterized is $[\text{Pt(SnCl}_3\text{)}_5]^{3-}$. The $\text{SnCl}_3$ ligands in this anion are very labile and dissociate to give vacant coordination sites for reaction with $\text{H}_2$ and with olefins. Time ligands also inhibit reduction of the Pt(II) ion to metallic platinum. The $\text{SnCl}_3$ ligand appears to be a weak a-donor and a good π-acceptor like carbon monoxide. These ligand-metal bond characteristics seem to favor stability of low-valent metal centers.

A major difference from Wilkinson’s catalyst is the mechanism of hydrogen activation. With the anionic platinum catalyst, it occurs by heterolytic cleavage of $\text{H}_2$.

$$\text{H}_2 + [\text{Pt(SnCl}_3\text{)}_3]^{1-} \rightarrow \text{H}^+ + [\text{Hpt(SnCl}_3\text{)}_4]^{1-} + \text{SnCl}_3$$

The anionic platinum hydride, which can be isolated as a tetraalkylammonium salt, reacts with an olefin to give an alkyl complex $[\text{Rpt(SnCl}_3\text{)}_3]^{2-}$. Presumably the coordination of the olefin and the insertion reaction with the Pt-H bond occur much as indicated for Wilkinson catalyst.
The second major difference between the two systems lies in the cleavage of the metal-alkyl. In the platinum system, protonolysis by the acid formed in \( \text{H}_2 \) is the most likely reaction:

\[
\text{[RPt(SnCl)\text{d}_4]^+} + \text{H}^+ \rightarrow \text{RH} + \text{[Pt(SnCl)\text{d}_3]^+}
\]

The third major mechanism is based on homolytic cleavage of the dihydrogen molecule by metal-metal bonded species or by a paramagnetic complex. Two important examples are found in cobalt chemistry:

\[
\text{Co}_2(\text{CO})_4 + \text{H}_2 \rightleftharpoons 2 \text{HCo(\text{CO})}_4
\]

\[
2 \text{[Co(\text{CN})\text{d}_3]^+} \rightleftharpoons [\text{Co}_2(\text{CN})_4]^{6-} + \text{H}_2 \rightleftharpoons 2 \text{[HCo(\text{CN})\text{d}_3]^+}
\]

The kinetics of the cobalt cyanide system are those expected if \( \text{H}_2 \) cleavage is the slow step. It is interesting that the two hydrogen cleavage reactions shown above occur with different oxidation states of the metal. The carbonyl reaction involves a formal transition from Co(0) to Co(1), whereas the cyanide complex changes from Co(II) to Co(III).
The reaction of the cobalt hydride with an olefin such as styrene is proposed to occur without precoordination.

If this proposal is correct, it is an exception to the general rule that olefin insertion reactions involve a coordinated C=C bond.

The rate and course of styrene hydrogenation change little with changes in cyanide ion concentration, whereas major effects would be expected if CN⁻ dissociation were required to free a coordination site for the olefin.

Cyanide concentration does change the stereochemistry of diene hydrogenation, presumably by regulating formation of a π-ally intermediate.

With either alkyl or allyl intermediates, the reduced organic product is released from the metal by reaction with a second cobalt hydride anion:
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SELECTIVE HYDROGENATION OF POLYENES

- The hydrogenation of dienes and trienes to monoolefins has several potentially useful applications in industry.
- Heterogeneous catalysts are used commercially for selective hydrogenation of polyunsaturated vegetable oils to give shortenings with better physical properties.
- Typically, a linolenate ester with three C=C bonds per C_{18} chain may be reduced to a linoleate with two double bonds or an oleate with only one double bond per chain.

SELECTIVE HYDROGENATION OF POLYENES

- In applications of this type, in which only moderate selectivity is required, heterogeneous catalysts excel because they are easy to separate from reaction products by decantation or filtration.
- Soluble catalysts are very difficult to separate from high-boiling materials such as vegetable oils except when the catalyst can be extracted into a polar solvent.
- Homogeneous catalysts are preferred over their heterogeneous analogs when high selectivity is required.
SELECTIVE HYDROGENATION OF POLYENES

- One industrial example is the hydrogenation of 1,5-cyclooctadiene to cyclooctene.
- This selective hydrogenation converts a readily available butadiene dimer to a precursor of specialty dienes and of polyoctenamer rubber.
- Another similar hydrogenation is not operated industrially, but may have considerable potential.
- This is the hydrogenation of 1,5,9-cyclododecatriene, a butadiene trimer, to cyclododecene, a precursor of dodecanedioic acid and laurolactam.

Although heterogeneous catalysts such as palladium on alumina can be used for this hydrogenation, higher selectivity is available with soluble catalysts (Table 3.1).

The two soluble catalysts prepared from nonprecious metals, [Co(CO)3(PBu3)]2 and NiI2(PPh3)2, are interesting because they are inexpensive and give very high yields of the desired cyclododecene.

Similar results are obtained in the hydrogenation of 1,5-cyclooctadiene to cyclooctene with some of the same catalysts.

The catalysts listed in Table 3.1 effect partial hydrogenation of either conjugated or unconjugated dienes and trienes.

In contrast, a second group of catalysts hydrogenate only conjugated dienes.

Catalysts such as [Co(CN)5]3- and [Cr(CO)3 (methyl benzoate)] reduce 1,3,7-octatriene, a linear butadiene dimer, to mixtures of octadienes by selective H2 addition to the 1,3-diene function.
SELECTIVE HYDROGENATION OF POLYENES

- The unconjugated diene products are hydrogenated slowly, if at all, under standard reaction conditions.

### Table 3.1 Hydrogenation of 1,5,9-Cyclododecatrione (CDT) to Cyclododecene (CDE) at Full Conversion.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Temp. (°C)</th>
<th>Pressure (atm)</th>
<th>Time (hr)</th>
<th>Yield of CDE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ni(AlC3)2</td>
<td>150</td>
<td>1.5</td>
<td>1.7</td>
<td>C2H6</td>
</tr>
<tr>
<td>[Co(CO)3(PPh3)2]</td>
<td>140</td>
<td>30</td>
<td>1.7</td>
<td>C2H6</td>
</tr>
<tr>
<td>Ni2(PPh3)2</td>
<td>160</td>
<td>80</td>
<td>6</td>
<td>C2H6</td>
</tr>
<tr>
<td>[Pd(CN)2]Cl2</td>
<td>160</td>
<td>100</td>
<td>10</td>
<td>C2H6</td>
</tr>
<tr>
<td>RuCp2(CO)2(PPh3)</td>
<td>25</td>
<td>10</td>
<td>30</td>
<td>C2H6</td>
</tr>
<tr>
<td>RuCp2(CO)2(PPh3)</td>
<td>140</td>
<td>5</td>
<td>1</td>
<td>C2H6</td>
</tr>
<tr>
<td>RuCl3(pyz)3(NH2)H2</td>
<td>75</td>
<td>0.1</td>
<td>0.1</td>
<td>DMF</td>
</tr>
</tbody>
</table>

* Most of the hydrogenations employed commercially available cis, trans, trans-1,5,9-cyclododecatrione and purified a mixture of cis- and trans-cyclododecene.

### SELECTIVE HYDROGENATION OF POLYENES

- A major distinction between the two classes of catalysts is that those in Table 3.1 are isomerization catalysts while the cobalt cyanide and chromium carbonyl catalysts are not.
- The more versatile catalysts can convert unconjugated dienes or trienes to conjugated systems through double-bond migration.
- Since most of the catalysts in this class are hydride complexes or form hydrides when treated with H2, it is likely that the isomerization occurs by an M-H addition-elimination process.
The selectivity for hydrogenation of dienes in the presence of monoolefins usually arises from the exceptional stability of π-allyl complexes.

Regardless of the H2 cleavage mechanism, M-H addition to a conjugated diene can generate a π-allyl intermediate.

In a hydrogenation mixture that contains diene, monoolefin, and a platinum-tin chloride catalyst, the following reactions are believed to be in competition.

The reaction pathway involving the π-allyl intermediate is favored, especially when the olefin or diene must compete with excess ligand such as R3P, CO, or SnCl3- for a coordination site.

Consequently, the diene in the reaction mixture is almost completely hydrogenated before the concentration of olefin increases to the point that olefin gains access to the catalyst.

Similar competition for catalyst sites is believed to be responsible for selectivity in hydrogenation of dienes by heterogeneous catalysts.
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CHAPTER 3

ASYMMETRIC HYDROGENATION

- Synthesis of optically active organic compounds from nonchiral starting materials is perhaps the most elegant application of homogeneous catalysis.
- This asymmetric induction can occur in many reactions catalyzed by transition metal complexes, but the first commercial application was the enantioselective hydrogenation involved in Monsanto’s synthesis of L-dopa, a drug used in the treatment of Parkinson’s disease.

ASYMMETRIC HYDROGENATION

- One characteristic feature for selective synthesis of one optical isomer of a chiral substance is an asymmetric catalyst site that will bind a prochiral olefin preferentially in one conformation.
- This recognition of the preferred conformation is achieved by using a chiral ligand, which creates a "chiral hole" in the coordination sphere of the metal.
In general, the ligands used in practical applications are chelating diphosphines. The chirality may reside either at the phosphorus or in the organic groups bound to the phosphorus. In general, some of the groups bound to the P atom are aryl, but recently good results have been reported with aliphatic groups that impart chirality. Considerable understanding of the basis for this enantioselectivity has come from studies performed during the past 15 years.

Realization of the dream of synthetic catalysts with enzyme-like stereoselectivity came about through the convergence of three factors in the late 1960s: – Development of highly active and selective catalysts for olefin hydrogenation. – Synthesis of asymmetrically substituted phosphines that would serve as ligands to create a chiral catalyst site. – Evolution of a need to manufacture pharmaceuticals as specific optical isomers.

The last requirement was met through medical research that provided moderate relief for Parkinsonism patients through the administration of L-3,4-dihydroxyphenylalanine (Levodopa, 3). Subsequently, needs have developed for enantioselective commercial processes for phenylalanine and for Naproxen®, a highly effective anti-inflammatory drug.
The industrial synthesis of Levodopa is shown in Figure 3.2. Vanillin 4 is converted to an oxazolidinone 5 by reaction with N-acetylglycine in the presence of sodium acetate and acetic anhydride. The heterocyclic ring in 5 is then hydrolyzed with aqueous acetone to give enamide 6.

This acetamidocinnamic acid is the prochiral substrate in the enantioselective hydrogenation, which is the key step in the overall process. The subsequent hydrolysis of the hydrogenation product 7 to give Levodopa 3 appears to be straightforward, although cares needed to avoid epimerization to a racemate.
The catalyst used in the hydrogenation is prepared by the Schrock-Osborn method of reacting the \([\text{Rh9COD})_2\]^+ cation (COD = 1,5-cyclooctadiene) with the chiral phosphine in aqueous ethanol or isopropanol.

Initially, a monodentate phosphine was used, but subsequent research showed much better enantioselectivity with the chelating diphosphine DIPAMP:

![DIPAMP](image)

The hydrogenation is carried out at about 50°C and 3 atmospheres pressure by adding the amine 6 to the catalyst solution.

It slowly dissolves and reacts, after which the chiral aryl acetamidopropionic acid 7 crystallizes.

It can be filtered away from the catalyst solution, which contains a little racemic product.

The optical yield is high (ca. 95% ee) and about a 90% yield of the desired enantiomer 7 is isolated.

Technology somewhat similar to that employed in the L-dopa synthesis has been commercialized to make phenylalanine in Europe.

The demand for this amino acid has increased substantially as a result of the commercial success of the synthetic sweetener aspartame:

![Apartame](image)
The dipeptide can be prepared by reaction of L-phenylalanine with N-acetylated aspartic anhydride in glacial acetic acid. After removal of the acetyl protecting group, the dipeptide is converted to the methyl ester. The hydrogenation of α-acetamidocinnamic acid 8 is carried out in ethanol with a cationic rhodium catalyst.

As in the L-dopa synthesis, hydrogen is transferred stereospecifically to one face of the olefin to produce N-acetyl-L-phenylalanine in high optical yield. The catalyst appears to be a [Rh(PNNP)(norbornadiene)]⁺ salt, a type of catalyst that has received extensive study.

The PNNP ligand (shown below), in contrast to the P-chiral DIPAMP ligand used by Monsanto, has its chirality centered on the α-phenethyl groups two atoms removed from the phosphorus atoms, which bind to the rhodium ion. Nevertheless the enantioselectivity is good in this reaction. The commercial viability of this phenylalanine process has been challenged by new fermentation technology commercialized by Ajinomoto.
This scientific and technological potential of enantioselective catalysis has stimulated extensive research and the discovery of many new catalyst systems that are effective. Perhaps the most important of these is the BINAP ligand, which has been used with both Rh(I) and Ru(II) catalyst systems.

The rhodium system has limited utility, but complexes such as Ru(BINAP)(O₂CR)₂ catalyze the asymmetric hydrogenation of α-amidocinnamic acids, allylic alcohols, and acrylic acids. The latter capability seems likely to be applied in an industrial process for manufacture of the anti-inflammatory drug Naproxen. A particularly useful characteristic of the ruthenium system is the ability to hydrogeniate β-ketoesters stereoselectively.

Substrates such as the hcnzainidomethyl-3-oxobutanoates 9 yield desirable precursors to the β-lactam antibiotics.
The preferred catalyst is a cationic Ru(II) complex, [Ru(BINAP)(arene)]^+.

Such halide-containing complexes see most effective for hydrogenation of the C=O function, whereas the Ru(BINAP)(O2CR)2 complexes are best for allylic alcohols and amines.

Much of the other scouting for effective ligands for asymmetric hydrogenation catalysts has employed the cationic rhodium system.

The general procedure is illustrated by an Organic Syntheses example employing a substituted acrylic ester as the substrate.

Many give optical yields, expressed as enantiomeric excesses over 90%.

Considerable effort has been devoted to the development of catalytic systems that facilitate separation of the catalyst from the product mixture.

One useful approach is attachment of the catalyst to an insoluble support such as polystyrene or silica gel so that it may be simply filtered from the reaction mixture.

Another approach involves sulfonation of the chiral phosphine ligand to make it water soluble, as in the Ruhrchemie hydroformylation process.

This technique permits decantation of an aqueous catalyst-containing phase from a nonpolar organic phase that contains product and any unreacted starting material.
One limitation of all the catalyst systems discussed to this point is that they do not produce good optical yields with simple olefins; optimum results require the presence of a nearby functional group to help orient the C=C bond when it binds to the catalytic complex.

An exception to this requirement is found with a family of Ziegler-Natta catalysts that catalyze both enantioselective polymerization and hydrogenation of olefins such as styrene and 1-pentene.

The optical yields are not exceptional (up to 65% ee with styrene), but the results provide an interesting research lead. The enantioselectivity results from the use of a chelating chiral ligand derived from Iron, coupling two tetrahydroindenyl groups.

The ligand is coordinated to zirconium in a Zr(CH₃)(ligand) complex used in conjunction with a methylaluminoxane catalyst modifier. The hydrogenation is carried out under mild conditions (25°C, 1-20 atmospheres hydrogen pressure).

One of the world’s largest-selling prescription drugs is the anti-inflammatory Naproxen 10. It is sold as the pure S-isomer because the R-isomer is a liver toxin. Currently the desired isomer is obtained by a conventional optical resolution of the racemate.

Production by an enantioselective synthesis appears to offer a good commercial opportunity, especially since the original patent on the drug expires in 1993. Many enantioselective routes have been explored, but it seems likely that the new industrial process will employ an asymmetric hydrogenation, as outlined in Figure 3.3.
The proposed synthesis employs an innovative electrochemical reduction (aluminum anode, lead cathode) of the acetylnaphthalene derivative 11 in the presence of CO₂.

The resulting α-hydroxypropionic acid 12 is dehydrated over an acidic catalyst to produce the α-naphthylacrylic acid 13.

This compound is the substrate for enantioselective hydrogenation employing an (S)-BINAP ruthenium(II) chloride complex.

For optimal results, the reaction is carried out at low temperatures and high hydrogen pressure in the presence of excess triethylamine.

Optical yields are reported to be in the range of 96-98% ee.

The scientific challenge associated with understanding the enzyme-like specificity of enantioselective hydrogenation has led to intensive study, particularly of the rhodium (I) catalysts bearing chelating diphosphine ligands.

A deep understanding of the mechanism of olefin hydrogenation has resulted.

The mechanism proposed for operation of [Rh(DIPAMP)(solvent)₂]⁺ the catalyst 14 used in L-dopa synthesis is sketched in Figure 3.4.

The initial step, as with most [Rh(PR₃)₂]⁺ catalysts, is coordination of the olefinic substrate.
In these studies methyl Z-acetamidocinnamate 15 is used as a substrate rather than the actual L-dopa precursor. The chirality of the R,R-DIPAMP ligand permits two diastereomeric olefin complexes 16 and 17 to form. Because the following step, H₂ addition to Rh(I), has a significant activation energy and is often rate-limiting, detectable quantities of lie more stable olefinic complex 16 accumulate in solution. The substrate 15 is bound to the metal by coordination of both the C=C bond and the amide oxygen.

Perhaps the most surprising and significant result of this study is that the major product 20 arises from the less-stable initial olefin complex 17. Evidently the rate limiting reaction of 17 with hydrogen is sufficiently faster than that of 16 that it dominates the kinetics of the overall process. Hence, it determines the chirality of the final product. (The oxidative addition of H₂ and subsequent steps appear to be essentially irreversible.)

The chirality of 18 determines that of the product because a hydride ligand transfers to the Rh-bound face of the coordinated olefin to produce the hydrido alkyl complex 19. The subsequent reductive elimination of Rh-H and Rh-C bonds forms the major organic product 20 and regenerates the original catalyst 14. At low temperatures, the reductive elimination step becomes rate limiting and it has been possible to isolate a [Rh(DIPHOS)(S)₂]⁺ hydrido alkyl complex analogous to 19.
CHAPTER 3

OBJECTIVES

- Hydrogenation of Simple Olefins
- Mechanisms of Olefins Hydrogenation
- Selective Hydrogenation of Ployenes
- Asymmetric Hydrogenation
- Hydrosilylation
- Hydrocyanation of Olefins and Dienes

Hydrosilylation of Olefins

- The addition of an Si-H bond to a C=C function has been explored intensively as a route to alkylsilanes.
- In addition to its use in laboratory syntheses, the hydrosilylation reaction is used in many ways in the manufacture of silicone polymers.
- Probably the broadest application is the "curing" of silicone rubbers, a step that converts a syrupy polymer to a gum rubber.
Similarly a putty-like polymer may be converted to a hard material such as dental cement. This toughening process is accomplished by forming crosslinks between polymer chains. Commonly, an SiH function of one chain is added to a vinyl group of another chain.

Typically the crosslinking reaction is carried out by mixing two components:
- (a) a syrupy vinylsilicone polymer containing a trace of a platinum complex, and
- (b) a small amount of an Si-H functional compound such as \([\text{CH}_3\text{SiH-O}]_4\).

Such mixtures are stable for several hours at room temperature, and react rapidly at 50-100°C to form a crosslinked network.

This reaction may be carried out in a mold to produce a tough or hard molded object directly in a process known as reaction injection molding (RIM). The vinyl silanes that provide the crosslinking sites are often made by adding an Si-H function to acetylene. Long-chain alkyl substituents are introduced by adding an Si-H group to a C=C bond of a terminal olefin. For addition of silane Si-H bonds to unactivated olefin as, the usual catalyst of choice is chloroplatinic acid, \(\text{H}_2\text{PtCl}_6\cdot\text{H}_2\text{O}\), often designated as Speier’s catalyst.
HYDROSILYLATION OF OLEFINS

- Transition metal complexes catalyze the addition, the stable, easily available platinum compound is preferred.
- It catalyzes Si-H addition in the presence of many kinds of functional groups.
- A strong steric influence is noted since the silicon almost always attaches to the less-crowded end of a C=C bond.
- Terminal olefins are hydrosilylated in preference to internal olefins.
- Internal olefins often isomerize to form terminal products.

If the silane is optically active, it retains its configuration.
- Asymmetric induction has been observed in hydrosilylation of olefins with catalysts that bear chiral ligands.
- In a typical hydrosilylation, the olefin and the silane are mixed with a solution of Speier's catalyst (10^{-5} mole Pt/mole Si) in a polar solvent such as 2-propanol.
- After a brief induction period a vigorous exothermic reaction occurs.

The mixture is commonly heated to complete the reaction and the product is isolated by distillation.
- The induction period can be reduced or eliminated by using a preformed zero-valent platinum compound.

This compound, known as Karstedt's catalyst produces extremely rapid hydrosilylation of alkenes and alkynes.
- Careful study of Speier's catalyst has shown that H_2PtCl_6 and other platinum chlorides are rapidly reduced to metallic platinum colloids by SiH compounds.
HYDROSILYLATION OF OLEFINS

Figure 3.5 Proposed mechanism for catalytic addition of a silane Si-H bond to an olefin.

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HYDROSILYLATION OF OLEFINS

O₂ Platinum colloid catalyzes the hydrosilylation of an olefin by a mechanism like that shown in Figure 3.5.

A surface atom of the colloid, designated Pt in the Figure, reacts with the Si-H bond of the silane to form an complex 21 or, perhaps an alternative product R₃Si-Pt-H, formed by formal oxidative addition of the Si-H bond.

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HYDROSILYLATION OF OLEFINS

Insertion of the olefin into the coordinated Si-H may be a concerted step, as indicated by 22, or may involve discrete insertion into an H-Pt bond to give a species such as R'CH₂CH₂-Pt-SiR₃.

Either way, elimination of the R'CH₂CH₂SiR₃ product regenerates zero-valent Pt for another catalytic cycle.

Most truly homogeneous hydrosilylation catalysts such as RhCl(PPh₃)₃ are believed to function via discrete oxidative addition, insertion, and reductive elimination mechanisms.

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Another application of hydrosilylation is for the synthesis of siloxane precursors bearing polar substituents such as CN or CF₃. These materials are used to synthesize silicone gums and rubbers with good resistance to gasoline and other hydrocarbon solvents.

The resulting dichlorosilanes may be hydrolyzed alone or with Me₂SiCl₂ to give silicones. The reaction with trifluoropropene may be carried out with one of the platinum catalysts described above. The reaction of acrylonitrile with hex silane is catalyzed by a mixture of cuprous chloride, tetramethylethylenediamine, and a trialkylamine. The chelating diamine probably solubilizes the copper(I) salt. When all three components are present, 75-80% yields of the β-cyanoethylsilane result.

CHAPTER 3

OBJECTIVES

- Hydrogenation of Simple Olefins
- Mechanisms of Olefins Hydrogenation
- Selective Hydrogenation of Polyenes
- Asymmetric Hydrogenation
- Hydrosilylation
- Hydrocyanation of Olefins and Dienes
HYDROCYANATION OF OLEFINS AND DIENES

The ease with which C groups may be converted to other functional groups has made organic nitriles commercially important intermediates.

For example, acrylonitrile, the largest volume organonitrile, is an important monomer both for plastics and synthetic fibers.

Hydrogenation of nitriles to amines provides important intermediates both for polyurethanes (by way of isocyanates) and polyamides (nylons).

Adiponitrile, after hydrogenation to the diamine and reaction with adipic acid, accounts for more than 4 billion pounds per year of nylon-6,6.

HYDROCYANATION OF OLEFINS AND DIENES

The addition of HCN to an unsaturated substrate is not the only method of producing an organonitrile, but it is often the easiest and most economical.

The addition of HCN to aldehydes and ketones is readily accomplished with simple base catalysis, as is the addition to activated olefins (Michael addition).

However, the addition of HCN to unactivated olefins and the regioselective addition to dienes is best accomplished with a transition metal catalyst.

HYDROCYANATION OF OLEFINS AND DIENES

Safety in HCN Use

The lack of reported incidents despite the widespread commercial use of volatile and toxic HCN points to the respect and care with which it is treated within the industry. In a laboratory, HCN should be used only in small quantities in a well-ventilated fume hood.

Vapors may be scrubbed or small samples (up to a few milliliters) may be disposed of by treatment with an equimolar mixture of NaOH and hypochlorite (NaOCl, bleach).

Larger samples or vapor streams should be burned. The use of a “buddy system” and “first response” training is essential when using HCN.
The DuPont adiponitrile (ADN) process involves nickel-catalyzed anti Markovnikov hydrocyanation of butadiene according to eqs. 1 to 4. All the reactions are catalyzed by air- and moisture-sensitive triarylphosphite-nickel (0) complexes. The first HCN addition (eq. 1) occurs at practical rates above 70°C under sufficient pressure to keep butadiene condensed in solution and produces the 1,4- and 1,2-addition products (3-pentenenitrile, 3PN, and 2-methyl-3-butenenitrile, 2M3BN) in a 2 to 1 ratio.

Fortunately thermodynamics favors 3PN (about 9:1) and 2M3BN may be isomerized to 3PN (eq 2) in the presence of the nickel catalyst. The isomerization of 2M3BN goes through a relatively rare C-C cleavage reaction.

The selective anti-Markovnikov addition of the second HCN to provide ADN requires the concurrent isomerization of 3PN to 4-pentenenitrile (4PN) (eq. 3), and HCM addition to 4PN (eq. 4).
HYDROCYANATION OF OLEFINS AND DIENES

Commercial Use

- A Lewis acid promoter is added to control selectivity and increase rate in these latter steps.
- Temperatures in the second addition are significantly lower and practical rates are achieved above 20°C at atmospheric pressure. 2-Methylgutaronitrile (MGN), ethylsuccinonitrile (ESN), and 2-pentenenitrile (2PN) are byproducts of this process.

Similar catalyst systems permit selective HCN addition to many other unsaturated substrates.

α-Olefins such as those obtained from Shell’s Higher Olefin Process (SHOP) are readily hydrocyanated under conditions similar to that described for eq. 4.

The products may be converted to primary amines, amides, and acids containing odd numbers of carbons.

Addition of HCN to styrene and other vinylarenes gives high yields of 2-aryl-propionitriles, which are excellent intermediates for 2-arylpropionic acids, a class of nonsteroidal anti-inflammatory drugs, which include ibuprofen and Naproxen.

The hydrocyanation of dienes, trienes, and other polyenes leads to polyfunctional systems that have many potential applications including polymers and lubricants.
HYDROCYANATION OF OLEFINS AND DIENES  

**Mechanism**

- Though most chemical and mechanistic studies related to the 20-year-old Du Pont ADN process have been published only recently, many of the fundamental studies that advanced the understanding of organometallic catalysis occurred during the development of this process.
- Some of the identifiable concepts to arise from this work include the proposal that many catalytic processes occur through discrete 16- and 18-electron intermediates the elucidation and quantification of important steric effects (ligand cone-angle) in ligand coordination and dissociation.

**HYDROCYANATION OF OLEFINS AND DIENES**  

**Mechanism**

- Added to these are pioneering studies on the mechanism of olefin isomerization in the presence of metal hydride species (hydride addition and elimination mechanism).
- Studies suggest that ligand dissociation from NiL₄ complexes precedes addition of HCN to generate hydrido nickel cyanide complexes.
- Butadiene complexation and insertion into the metal-hydride bond affords π-allylnickel cyanide species, observable by NMR spectroscopy at ambient temperature, which may reductively eliminate 3PN (or 2M3BN) according to eq. 5.

**HYDROCYANATION OF OLEFINS AND DIENES**  

**Mechanism**

- The reaction is reversible and provides the mechanism for the isomerization of 2M3BN to 3PN.
- The addition of DCN to cyclohexadiene has been shown to be stereospecifically cis.
**HYDROCYANATION OF OLEFINS AND DIENES**

*Mechanism*

- The isomerization of 3PM to 4PN is catalyzed by a cationic nickel hydride generated by removal of cyanide by a Lewis acid promoter (designated A in eq. 6).

\[
\text{HN}([\text{CN}+\text{A}]_{2}) \quad \rightarrow \quad \text{HN}[\text{CN}+\text{A}]_{2}^{-} \quad (6)
\]

- A remarkable feature of this isomerization is the kinetic control that allows 4PN to be made more than 70 times faster than the thermodynamically favored 2PN.

- The ability of the nitrile group to coordinate to the catalyst and direct the insertion (Figure 3.6) is believed responsible.

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**HYDROCYANATION OF OLEFINS AND DIENES**

*Mechanism*

- The insertion of an olefin (3PN) into the Ni-H bond, followed by reductive elimination from the resulting alkynickel cyanide complex, are the principle features of the second RICN addition in the ADN process.

- It is clear that the Lewis acid binds preferentially to the nickel-cyanide moiety and that the size of the Lewis acid has direct bearing on product selectivity.

- Bulkier Lewis acids favor the production of linear nitriles as shown in Figure 3.7.

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**Figure 3.6** Isomerization of 3-penten-1-cyano by a nickel hydride catalyst

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The exact nature of the complex from which the final reductive elimination occurs is subject to speculation. The involvement of a five-coordinate nickel complex appears likely based on the observation on the reductive elimination of benzonitrile from \((\text{Et}_3\text{P})_2\text{Ni}(\text{CN})\text{Ph}\) is promoted by triethyl phosphite and that reductive elimination of propionitrile from \([\text{(o-tolyl)}_3\text{P}](\text{C}_2\text{H}_4)\text{Ni}(\text{CN})\text{Et}\) is first order in phosphate concentration.

**Figure 3.7** Stereochemistry of 4-PN insertion into an Ni-H bond \((A = \text{Lewis acid})\).
Asymmetric Hydrocyanation

Catalytic asymmetric carbon-carbon forming reactions are potentially valuable.
Three groups have reported asymmetric hydrocyanation of norbornene (or derivatives) with enantiomeric excesses up to 40%.
These additions are catalyzed by nickel or palladium complexes containing chiral chelating diphosphine or diphosphinite ligands.
High optical yields have been attained in the hydrocyanation of a vinylnaphthalene to a Naproxen precursor.

The versatility of HCN as a building block for complex organic molecules coupled with the growing need for optically pure pharmaceuticals and agrochemicals makes this a rewarding area for research.