# CHAPTER 2

## ISOMERIZATION OF OLEFINS

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## CHAPTER 2 OBJECTIVES

- INTRODUCTION
- ISOMERIZATION OF SIMPLE OLEFINS
- OLEFIN ISOMERIZATLON MECHANISMS
  - Hydride Addition-Elimination
  - 1,3-Hydrogen Shift
- ENANTIOSELECTIVE ISOMERIZATIONS
- ISOMERIZATION OF FUNCTIONAL OLEFINS
  - Fragrance Chemicals
  - Food Additives

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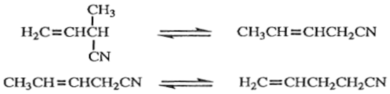
## INTRODUCTION

- Double-bond migration in olefins is one of the simplest and most thoroughly studied catalytic reactions.
- Soluble catalysts are used industrially to isomerizes olefins that are involved as intermediates in other homogeneous catalytic processes.
- For example, Du Pont’s synthesis of adiponitrile from butadiene and HCN includes two olefin isomerization steps:



$$H_2C{=}CH\underset{CN}{\overset{CH_3}{CH}} \rightleftharpoons CH_3CH{=}CHCH_2CN$$

$$CH_3CH{=}CHCH_2CN \rightleftharpoons H_2C{=}CHCH_2CH_2CN$$

## INTRODUCTION

- The first step, conversion of a branched chain to a linear chain, involves cleavage of a C-C bond.
- The second step is a more common type in which an internal olefin equilibrates with a terminal olefin by hydrogen migration without disruption of the carbon skeleton of the olefin.
- This example is notable in that the C-C isomerization occurs in the presence of another potentially reactive, functional group.
- In recent years, several isomerizations of functionally substituted olefins have become important in the manufacture of specialty chemicals.

## INTRODUCTION

- Isomerization of unconjugated to conjugated polyenes appeals to be a key step in the selective hydrogenation of compounds such as l,5-cyclooctadiene to monoenes (e.g., cyclooctene).
- The isomerization mechanisms are believed to be analogous to those of simple olefins.

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# ISOMERIZATION OF SIMPLE OLEFINS

- The double-bond migration of simple olefins may be exemplified by the isomerization of 1-octene to a mixture of predominately internal isomers:

$$C_6H_{13}CH{=}CH_2 \longrightarrow \begin{array}{rl} 2\% & \text{1-octene} \\ 36\% & \text{2-octene} \\ 36\% & \text{3-octene} \\ 26\% & \text{4-octene} \end{array}$$

# ISOMERIZATION OF SIMPLE OLEFINS

- This conversion of a terminal olefin to a near-equilibrium mixture of internal olefins (both cis and trans isomers) is carried out on a massive scale as one step in the SHOP process.
- In industrial practice, a heterogeneous catalyst (potassium supported on alumina) is used, but a wide variety of soluble catalysis are effective for isomerization of simple olefins.

# ISOMERIZATION OF SIMPLE OLEFINS

- The SHOP process which produces both linear α-olefins and linear detergent alcohols, also involves equilibration of internal and terminal olefins by a soluble catalyst.
- Linear aldehydes call be prepared from internal olefins such as 2-decene by using a catalyst that is active for both isomerization and hydroformylation of olefins.
- If the catalyst generates a terminal olefin rapidly and hydroformylates the terminal olefin preferentially, respectable yields of linear aldehyde form by the sequence.

$$C_7H_{15}CH{=}CHCH_3 \rightleftharpoons C_8H_{17}CH{=}CH_2 \xrightarrow[CO]{H_2} C_8H_{17}CH_2CH_2CHO$$

# ISOMERIZATION OF SIMPLE OLEFINS

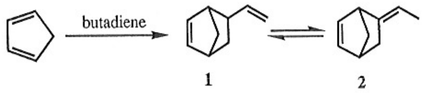
- The linear aldehyde undecanal is of interest both as a perfume intermediate and as a precursor to the $C_{11}$ fatty alcohol, which is an intermediate in detergent manufacture.
- A standard hydroformylation catalyst, $HCo(CO)_4$, is moderately effective in the sequential isomerization and hydroformylation of olefins.

# ISOMERIZATION OF SIMPLE OLEFINS

- This catalyst can also isomerize olefins without hydroformylation when the partial pressures of CO and $H_2$ are reduced to the minimum amount necessary to stabilize the complex.
- In the SHOP process practiced by Shell, it appears that a modified catalyst, $HCo(CO)_4$ is used to effect hydrogenation of the product aldehyde as well as isomerization and hydroformylation.

# ISOMERIZATION OF SIMPLE OLEFINS

- The industrial synthesis of ethylidenenorbornene **2**, a widely used comonomer for ethylene / propylene elastomers also involves olefin isomerization. The monomer synthesis comprises two major steps:

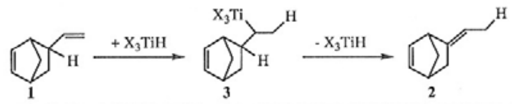


# ISOMERIZATION OF SIMPLE OLEFINS

- Vinylnorbornene **1** is produced by the uncatalyzed Diels-Alder reaction of butadiene with cyclopentadiene, which collies from thermolysis of dicyclopentadiene, a refinery by-product.
- The isomerization of **1** to **2** is catalyzed either with a strong base (Na on $Al_2O_3$ or potassium-tert-butoxide) or with a Ti-based Ziegler catalyst.
- The desired product **2** is formed to the extent of 98% or inure at equilibrium.
- It is likely that the basic catalysts abstract an allylic proton from **1** to a delocalized anion that is reprotonated to give **2**.

# ISOMERIZATION OF SIMPLE OLEFINS

- The Ziegler-type catalysts are prepared by reducing $TiCl_4$ or $Ti(OR)_4$ with $LiAlH_4$ or $R_2AlH$ to form a titanium hydride species.
- The isomerization is presumed to occur by an M-H addition/elimination reaction like those discussed in the next section.
- Addition of a Ti-H bond to i forms an alkyltitanium compound **3**. β-Hydrogen elimination from **3** either regenerates **1** or yields the desired product **2**.



# ISOMERIZATION OF SIMPLE OLEFINS

- Double-bond migration catalyzed by soluble metal complexes is also useful in laboratory scale organic synthesis. Some difficultly accessible unsaturated steroids have been prepared by $RhCl_3$ isomerization reactions.
- This salt forms a soluble hydrate, $RhCl_3.3H_2O$, which is probably the most convenient olefin isomerization catalyst for laboratory use. It is air-stable, commercially available, and easy to use.
- Typically, the olefin is heated with an ethanol solution of $RhCl_3.3H_2O$. After several hours, the mixture is cooled and diluted with water and the olefin is isolated by conventional means.

# ISOMERIZATION OF SIMPLE OLEFINS

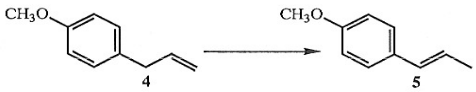
- Another commercially available isomerization catalyst is Wilkinson's compound, $RhCl(PPh)_3$.
- It has been used in several syntheses of natural products and is faster than the simple $RhCl_3$ system.
- A closely related rhodium complex bearing a chiral ligand is used commercially in an commercially isomerization of an allylic amine.

# ISOMERIZATION OF SIMPLE OLEFINS

- Other commercially available materials such as $Fe(CO)_5$, $Fe_3(CO)_{12}$ and $PdCl_2$ are also useful isomerization catalysts for the synthesis laboratory.
- These compounds catalyze double-bond migration by a different mechanism than do the rhodium or nickel catalysts and, hence, different products may be isolated in kinetically controlled experiments.
- Iron pentacarbonyl is the catalyst in a potentially attractive synthesis of anethole, a licorice fragrance chemical.

# ISOMERIZATION OF SIMPLE OLEFINS

- The isomerization of estragole **4** (p-allylanisole) to the arene-conjugated olefin anethole **5** is accomplished by simply heating **4** with a catalytic amount of $Fe(CO)_5$ at 140°C.
- A conversion of 96-99% is attained in eight hours.
- The desired trans isomer of anethole predominates over cis by approximately 87:13.



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# OLEFIN ISOMERIZATLON MECHANISMS

- Extensive studies of olefin isomerization catalysis in the 1960s and 1970s identified two major families of catalysts which function by different reaction mechanisms.
- The largest family is that of transition **metal hydrides**, which may be either preformed catalysts or catalytic species generated in situ.
- These species catalyze C=C bond migration by addition and elimination of an M-H bond, as described for the Ti-based Ziegler catalyst.
- A less common, but well documented, alternative mechanism involves a metal-mediated **1,3-hydrogen shift**, which may involve allylic intermediates.

# OLEFIN ISOMERIZATLON MECHANISMS

- In addition to isomerizing olefins by moving hydrogens, metal ions can also catalyze olefin isomerization by moving a substituent such as Cl, OH, OAc, or CN.
- If reactions are allowed to proceed to completion, equilibrium mixtures of olefins form.
- For instance, the ultimate product of 1-butene isomerization is an equilibrium mixture of 69% trans-2-butene, 25% cis-2-butene, and 6% 1-butene.

## OLEFIN ISOMERIZATLON MECHANISMS

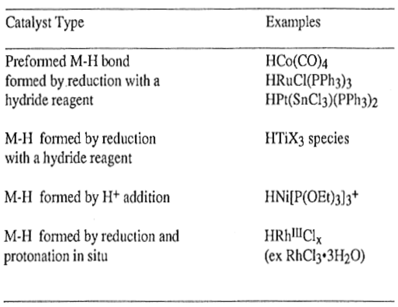
- With many catalysts, however, the cis-2-butene is formed more rapidly than the trans isomer and can be isolated as a major product early in the reaction.
- Some of the more active catalysts facilitate equilibration of cis and trans isomers of olefins such as stilbene for which double-bond migration is impossible.

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

- The most common mechanism for moving a C=C bond involves addition of all M-H bond to give an alkylmetal complex that then undergoes nondegenerate β-hydrogen elimination to form a new C=C bond.
- The function may be a preformed metal hydride complex such as $HCo(CO)_4$ mentioned earlier, or it may be formed in the reaction mixture.
- Some of the more important catalytic species are tabulated in Table 2.1.

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

**Table 2.1 Isomerization Catalysts Based o Metal Hydrides**



| Catalyst Type | Examples |
|---|---|
| Preformed M-H bond formed by reduction with a hydride reagent | $HCo(CO)_4$<br>$HRuCl(PPh_3)_3$<br>$HPt(SnCl_3)(PPh_3)_2$ |
| M-H formed by reduction with a hydride reagent | $HTiX_3$ species |
| M-H formed by $H^+$ addition | $HNi[P(OEt)_3]_3^+$ |
| M-H formed by reduction and protonation in situ | $HRh^{III}Cl_x$<br>(ex $RhCl_3 \cdot 3H_2O$) |

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

- Cationic nickel species formed by protonation of nickel(0) complexes are also commercially significant.
- Du Pont’s hydrocyanation technology is based on isomerization and HCN addition reactions catalyzed by $HNiL_3^+$ and $HNiCNL_3$ species in which L is a triaryl phosphite ligand.
- Studies of the analogous triethyl phosphite complex have shed much light on the mechanism of olefin isomerization.

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

- A catalytic reaction of potential industrial importance is the selective reduction of a molecule containing multiple C=C bonds to monoolefins (e.g., 1,5,9-cyclododecatriene to cyclododecene or linolenic acid esters to oleate esters).
- An initial step in the reaction is believed to be isomerization of the unconjugated polyene to a conjugated polyene, which undergoes hydrogenation in preference to an isolated C=C bond.
- The ruthenium and platinum hydrides are good catalysts for this kind of reaction and, as expected, are good isomerization catalysts.

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

- The metal hydride addition-elimination mechanism is nicely illustrated by $RuHCl(PPh_3)$ a hydrogenation catalyst that catalyzes isomerization of simple olefins as well as polyenes.
- The mechanism of isomerization of 1-pentene by this catalyst is shown in Figure 2.1.
- A coordinatively unsaturated complex labeled H-Ru in the figure reacts with 1-pentene to form the olefin complex **6**.
- Migratory insertion can occur in either of two ways.

# OLEFIN ISOMERIZATLON MECHANISMS

## *Hydride Addition-Elimination*

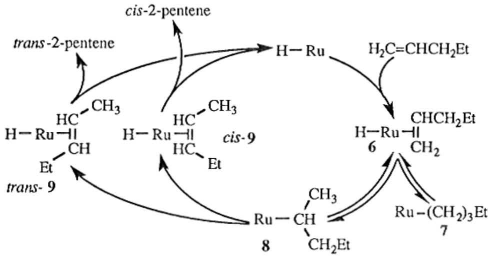


**Figure 2.1** Catalytic cycle for isomerization of 1-pentene to cis- and trans-2-pentene by RuH (The phosphine and chloride ligands are omitted for clarity)

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# OLEFIN ISOMERIZATLON MECHANISMS

## *Hydride Addition-Elimination*

- Addition of Ru-H to the olefin to form the 1-pentyl derivative **7** is nonproductive side reaction.
- Addition in the opposite sense to give the 2-pentyl derivative **8** opens pathways to isomerization (although β-hydrogen elimination from the methyl group leads back to 1-pentene).
- β-Hydrogen elimination from C-3 can occur in two ways to give either cis- or trans-2-pentene as in the complexes **9**. Dissociation of the 2 ligand completes the catalytic cycle.

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# OLEFIN ISOMERIZATLON MECHANISMS

## *Hydride Addition-Elimination*

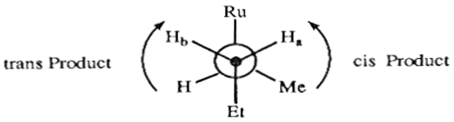
- Readditions of Ru-H to 2-pentene can occur to give a 3-pentyl complex.
- This step is unproductive for pentenes because the 3 group can only yield 2 hut, for long-chain olefins, repeated addition and elimination steps can move the double bond along the chain at random.

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

- The β-hydrogen elimination to give cis-2-pentene is faster than that which gives the trans isomer.
- Early in the reaction (50°C in benzene), a 60:40 ratio of cis- and trans-2-pentene is observed.
- The factor that determines which isomer is formed in a single catalytic cycle is almost certainly the conformation of the 2-pentyl group at the time that α-hydrogen elimination occurs.

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

- The view along the C-2/C-3 bond axis may be represented as (C-3 in front):



- If the C-3 substituents in front rotate counterclockwise to place the Ru on C-2 and $H_a$ on C-3 adjacent in eclipsed positions, cis elimination of Ru-H should yield cis-2-pentene.
- Rotation in the opposite sense would give the trans isomer.

## OLEFIN ISOMERIZATLON MECHANISMS
### *Hydride Addition-Elimination*

- These mechanistic principles seem to apply to metal hydride-based catalysts generally, but the details will vary with the catalyst species.
- In particular, the kinetic distribution of cis and trans isomers will depend on the steric and electronic factors that c the β-hydride elimination process.

# OLEFIN ISOMERIZATLON MECHANISMS

## *1,3-Hydrogen Shift*

- A second major mechanism for olefin isomerization is a metal-assisted shift of an allylic hydrogen from the 3-position of an olefin to the 1-position as illustrated for 3,3-dideutero-1-pentene:

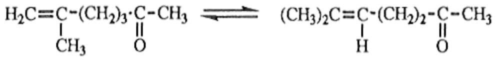
$$EtCD_2CH{=}CH_2 \rightleftharpoons EtCD{=}CHCH_2D$$

- Experimental criteria for diagnosing the occurrence of this mechanism are:
  - High (ca. 4) cis:trans ratios of isomerized olefin early in the reaction.
  - 1,3-Deuterium shift in deuterated olefins with little or no deuterium on C-2 early in the reaction.

# OLEFIN ISOMERIZATLON MECHANISMS

## *1,3-Hydrogen Shift*

- The palladium(2+) catalysts have been studied extensively because their stability to air and moisture make them attractive for kinetic investigation and for practical application.
- This kind of catalyst appears to be used in the industrially significant isomerization of 6-methyl-6-hepten-2-one **10** to the internal olefin **11**.



$$H_2C{=}\underset{CH_3}{\underset{|}{C}}-(CH_2)_3-\underset{O}{\underset{\|}{C}}-CH_3 \rightleftharpoons (CH_3)_2C{=}\underset{H}{\underset{|}{C}}-(CH_2)_2-\underset{O}{\underset{\|}{C}}-CH_3$$

**10** **11**

# OLEFIN ISOMERIZATLON MECHANISMS

## *1,3-Hydrogen Shift*

- The terminal olefin **10** is prepared on a large scale by BASF via condensation of isobutylene, acetone, and formaldehyde.
- **10** and **11** are versatile intermediates for a wide range of flavors and fragrances as well as Vitamin.
- Several detailed mechanisms have been proposed for the 1,3-hydrogen shift mechanism.
- The simplest is a 1,3-suprafacial shift in which a hydrogen ion migrates from C-3 to C-1 in a coordinated terminal olefin without any direct metal-hydrogen interaction.

## OLEFIN ISOMERIZATLON MECHANISMS
### *1,3-Hydrogen Shift*

- Another conceptually simple proposal, metal-assisted proton migration, is shown in Figure 2.2.
- This mechanism is proposed to operate in $Pd^{2+}$ catalyzed isomerization in nonpolar media such as benzene, the solvent chosen for mechanistic study.
- Coordination of the chosen olefin (1-pentene) to the metal brings the allylic C-3 hydrogens close to the metal atom in an initial complex **12**.

## OLEFIN ISOMERIZATLON MECHANISMS
### *1,3-Hydrogen Shift*

- Transfer of hydrogen to the metal gives a π-allyl palladium hydride **13**.
- The metal-bound hydrogen may return to C-3 to reform 1-pentene, or it may migrate to C-1 to form 2-pentene.
- With this catalyst, the trans isomer **14** shown in Figure 2.2 is favored kinetically as well as thermodynamically.

## OLEFIN ISOMERIZATLON MECHANISMS
### *1,3-Hydrogen Shift*

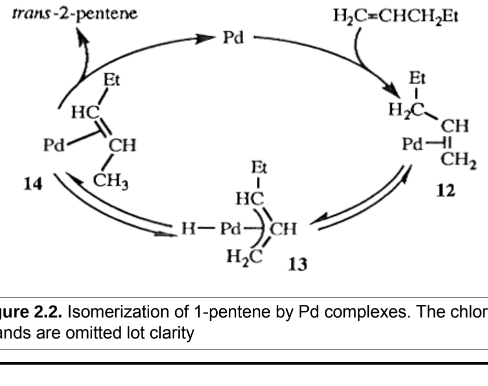
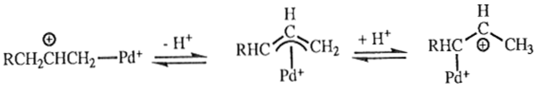


**Figure 2.2.** Isomerization of 1-pentene by Pd complexes. The chloride ligands are omitted lot clarity

## OLEFIN ISOMERIZATLON MECHANISMS
### *1,3-Hydrogen Shift*

- One objection to this π-allylic mechanism is that it involves oxidative addition of a C-H bond to a Pd(II) complex to form a species **13** that is formally Pd(IV), all uncommon oxidation state.
- This consideration, as well as differences in the relative isomerization rates with various Pd(II) catalysts, has led to proposal of an alternative mechanism.
- The alternative involves electrophilic attack of $Pd^{2+}$ on the olefin to give an incipient carbonium ion **15**.

## OLEFIN ISOMERIZATLON MECHANISMS
### *1,3-Hydrogen Shift*



$$\mathrm{RCH_2\overset{\oplus}{C}HCH_2{-}Pd^+} \xrightleftharpoons{-\,\mathrm{H}^+} \mathrm{RHC}\overset{\mathrm{H}}{\underset{\mathrm{Pd^+}}{\mathrm{C}}}\mathrm{CH_2} \xrightleftharpoons{+\,\mathrm{H}^+} \underset{\mathrm{Pd^+}}{\mathrm{RHC}}\overset{\mathrm{H}}{\mathrm{C}}\oplus\mathrm{CH_3}$$

**15** **16** **17**

## OLEFIN ISOMERIZATLON MECHANISMS
### *1,3-Hydrogen Shift*

- This species rearranges via a heterolytic cleavage of a C-H bond to form an allylic intermediate **16**, which is in equilibrium with **17** Compound.
- **17** may be regarded as a partial carbonium ion that at is in equilibrium with the isomerized olefin.
- Clearly, solvent polarity will be a factor in determining whether this mechanism or that of Figure 2.2 will operate in a given situation.

## OLEFIN ISOMERIZATLON MECHANISMS
### *1,3-Hydrogen Shift*

- A 1,3-hydrogen shift with a somewhat different intimate mechanism has been demonstrated for the [Rh(diphosphine)(solvent$_2$]$^+$ catalyst system.
- This type of catalyst is valuable for the isomerization of allylic alcohols to enols and of allylic amines to enamines.
- The latter reaction proceeds via 1,3-shift, if done with a chiral catalyst and a prochiral allylamine, it permits synthesis of a single optical isomer of the enamine.

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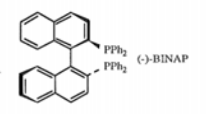
## ENANTIOSELECTIVE ISOMERIZATIONS

- One of the major driving forces for the practical use of soluble catalysts is the need to make specific optical isomers of biologically active compounds.
- One of the most striking examples is the development of enantioselective catalysts for isomerization of olefins.
- In principle, a metal complex, which is coordinated preferentially to one face of a prochiral olefin should be able to effect a stereoselective 1,3-hydrogen shift to produce specifically one of the two optical isomers of the product olefin.

# ENANTIOSELECTIVE ISOMERIZATIONS

- Work at the Takasago Perfumery first showed the possibility of enantioselective isomerization of an allylic amine.
- The catalyst, prepared by reducing a cobalt(II) compound with an organoaluminum in the presence of a chiral ligand, gave only modest enantioselectivity, but subsequent work with rhodium catalysts gave spectacular results.
- A key to success was use of the BINAP ligand, which has also been useful in enantioselective hydrogenations of olefins and ketones.



# ENANTIOSELECTIVE ISOMERIZATIONS

- The most important commercial application of this chemistry is shown in Figure 2.3.
- β-Pinene, an abundant natural terpene, is pyrolyzed to form myrcene **18**.
- Myrcene, in turn, is treated with diethylamine in the presence of lithium diethylamide to form diethylgeranylamine **19** and its Z-isomer, diethylnerylamine.
- Either of these allylic amines may be isomerized to R(-)-diethyl-E-citronellalenamine **20**, but the "handedness" of the product depends on the chirality of the BINAP ligand present ill the catalytic rhodium complex.

# ENANTIOSELECTIVE ISOMERIZATIONS

- For example, **19** is boiled in tetrahydrofuran containing 0.1 mole % [Rh(-)-BINAP(COD(]($ClO_4$) for **21** hours to give a 94% yield of **20**.
- If one starts with the isomeric nerylamine, it is necessary to use the R(+)-BINAP complex. Hydrolysis of 20 with cold aqueous acetic acid gives R(+)-citronellal 21 in 91% chemical yield with an optical purity of about 95%.
- The Lewis-acid-catalyzed ring closure to form **22** accomplishes formation of two more chiral centers, the stereochemistries of which are determined by the chirality at the carbon 3 to the aldehyde function.
- Hydrogenation of the remaining C=C bond in **22** over a Raney nickel catalyst generates L-menthol.

## ENANTIOSELECTIVE ISOMERIZATIONS

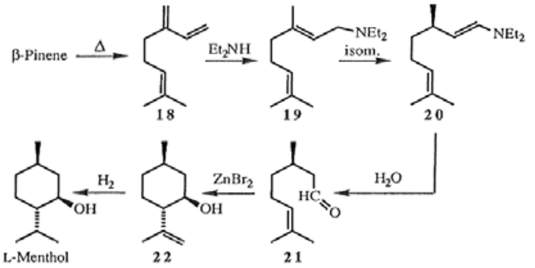


**Figure 2.3** Synthesis of L-menthol by enantioselective isomerizalion of allylic amines

## ENANTIOSELECTIVE ISOMERIZATIONS

- This menthol synthesis is remarkable in that three chiral centers are created, all of which are necessary to produce the characteristic menthol odor and local anesthetic action.
- Even more remarkable is the fact that this complex multistep synthesis can be economically competitive with production of menthol from natural sources.
- The key seems to lie in the enantioselective isomerization, which creates the first chiral center.

## ENANTIOSELECTIVE ISOMERIZATIONS

- The mechanism of the enantioselective isomerization has been studied extensively.
- As shown in Figure 2.4, it is critically dependent on the presence of the amine function, which provides the initial binding of the substrate to the catalyst.
- An allylic amine such as diethylgeranylamine coordinates to the BINAP rhodium(I) complex through N, as shown in 23.

# ENANTIOSELECTIVE ISOMERIZATIONS

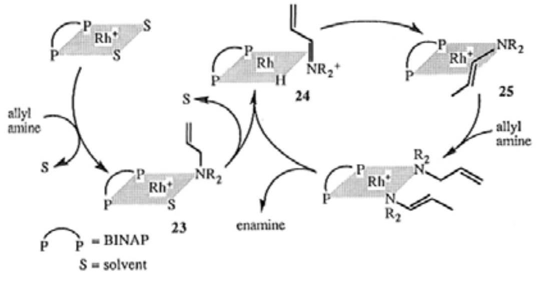


**Figure 2.4** Mechanism of enantioselective isomerization of allylic amines

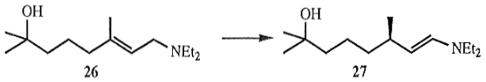
# ENANTIOSELECTIVE ISOMERIZATIONS

- Dissociation of a solvent molecule permits transfer of a hydrogen from the $\alpha$ carbon of the amine to rhodium, formally oxidizing the metal to Rh(III).
- The product of C-H cleavage may be viewed either as an iminium complex **24**, as written, or as an allyl complex bearing a $NR_2$ substituent on C-1.
- If viewed as a π-ally complex, it must have syn stereochemistry because return of H from Rh to C gives the trans enamine in compound **25**.

# ENANTIOSELECTIVE ISOMERIZATIONS

- Displacement of the enamine from **25** by fresh allyl amine completes the catalytic cycle by reforming **24**.
- Stereochemical analysis of the transition slates leading to cleavage has rationalized the role of the BINAP ligand in determining which of the two α-hydrogens migrates to rhodium.
- The enantioselective isomerization reaction appears to have numerous applications in fragrance chemistry.
- In a reaction closely related to the L-menthol synthesis, lie allylic amine **26** is isomerized to the enamine **27** using a BINAP rhodium catalyst:

# ENANTIOSELECTIVE ISOMERIZATIONS



- The enamine can be hydrolyzed to an aldehyde with a ‘lily of the valley” fragrance.
- As in the citronellal synthesis, the (-)-BINAP ligand gives rise to the desired R-stereochemistry at the new chiral center in **27**.
- The enamine again forms with the trans configuration.

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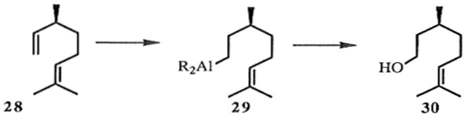
# ENANTIOSELECTIVE ISOMERIZATIONS

- It should be noted that the process of Figure 2.3 is not the only industrial synthesis of L-menthol that employs organometallic chemistry.
- In another commercial process, L-citronellene **28**, derived fro pyrolysis of cis-pinane, is treated with *tris*(isobutyl) aluminum at 125-150ºC in a stoichiometric reaction to form **29** and isobutylene:



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# ENANTIOSELECTIVE ISOMERIZATIONS

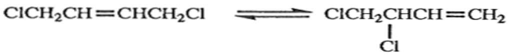
- Oxidation and hydrolysis of the Al-C bond in **29** yields (+)-citronellol **30**, which is convened to L-menthol by conventional organic reactions.
- This oxidative hydrolysis of an organoaluminum compound closely parallels that used in the Conoco process to convert an Al-terminated ethylene oligomer to a fatty alcohol.
- Citronellol **30**, in addition to being a menthol intermediate, is also useful as a component of rose scent.

## CHAPTER 2 OBJECTIVES

- INTRODUCTION
- ISOMERIZATION OF SIMPLE OLEFINS
- OLEFIN ISOMERIZATLON MECHANISMS
  - Hydride Addition-Elimination
  - 1,3-Hydrogen Shift
- ENANTIOSELECTIVE ISOMERIZATIONS
- ISOMERIZATION OF FUNCTIONAL OLEFINS
  - Fragrance Chemicals
  - Food Additives

## ISOMERIZATION OF FUNCTIONAL OLEFINS

- The location of a C bond within an organic molecule can be shifted by moving substituents other than hydrogen.
- the isomerization of an allylic cyanide by CN migration from C-3 to C-1 in the allyl function affects olefin isomerization.
- Another major process, the isomerization of 1,4-dichloro-2-butene, involves an analogous C-1 ←→ C-3 migration of chlorine.



$$ClCH_2CH{=}CHCH_2Cl \rightleftharpoons ClCH_2\underset{\displaystyle Cl}{CH}CH{=}CH_2$$

## ISOMERIZATION OF FUNCTIONAL OLEFINS

- In addition to these two isomerizations, conducted on a scale of many thousands of tons per year, there are many small-scale specialized applications of allylic isomerization.
- In general, they involve the use of a soluble catalyst to move a hydroxyl or carboxylate group in the production of a biologically active compound.
- For example, in the BASF synthesis of vitamin **A**, there is all isomerization of a diacetoxybutene exactly analogous to the 1,4-dichloro-2-butene isomerization mentioned above.

$$AcOCH_2CH{=}CHCH_2OAc \rightleftharpoons AcOCH_2\underset{\displaystyle OAc}{CH}CH{=}CH_2$$

# ISOMERIZATION OF FUNCTIONAL OLEFINS

- A mixture of cis- and trans-diacetoxy-2-butene is heated with a $PtCl_4$ catalyst.
- A slow feed of oxygen and chlorine is added presumably to keep the catalyst in a high oxidation state, while the mixture is slowly distilled, distillate is enriched in the lower boiling 3,4-diacetoxy-1-butene, which is formed in 95% yield with 98-99.5% purity.

# ISOMERIZATION OF FUNCTIONAL OLEFINS

## *Fragrance Chemicals*

- Allylic isomerization is applied to a variety of terpenoid substrates in the perfume industry.
- These $C_{10}$ compounds which are nominally isoprene dimers, are produced industrially both from natural products such as turpentine and from petrochemicals.
- Linalool **32**, a key intermediate in making a number of fragrance alcohols, is obtained both from pinenes and from the 6-methylheptenones **10** and **11**.

# ISOMERIZATION OF FUNCTIONAL OLEFINS

## *Fragrance Chemicals*

- The network of chemistry involving linalool is sketched in Figure 2.5.
- Ethynylation of **11** with acetylene and a metal acetylide catalyst gives dehydrolinalool **31**, which is of interest as a precursor to linalool **32**, citral **33**, and vitamin A.
- The conversion of **31** to **32** involves selective hydrogenation of the bond with a heterogeneous catalyst.

## ISOMERIZATION OF FUNCTIONAL OLEFINS
## *Fragrance Chemicals*

- The isomerization of propargylic alcohols (**31→ 33**) and allylic alcohols (**32 ←→ 34 + 35**) is catalyzed by alkyl vanadate esters.
- In the isomerization of dehydrolinalool **31**, the starting alcohol is heated at 140-160°C with tricyclohexyl vanadate in a paraffin solution.

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## ISOMERIZATION OF FUNCTIONAL OLEFINS
## *Fragrance Chemicals*

- Migration of the OH group from C-3 to C-1 presumably gives a transient enol, which spontaneously tautomerizes to citral **33**.
- In typical examples, the aldehyde is formed in 60-80% yield at 20-33% conversion. Tris(trialkylsilyl) vanadates also catalyze this reaction.

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## ISOMERIZATION OF FUNCTIONAL OLEFINS
## *Fragrance Chemicals*

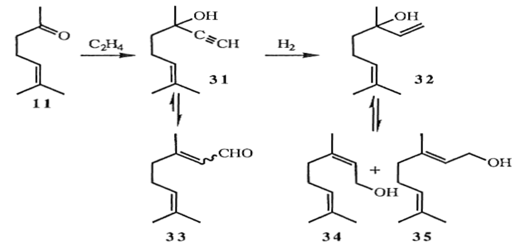


**Figure 2.5.** The role of linalool in fragrance chemistry

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Fragrance Chemicals*

- The equilibrium nature of the isomerization process is more evident in the vanadium-catalyzed reaction of linalool **32**.
- When linalool is heated at 160°C with tris(tetrahydrolinalyl) or tris(triphenylsilyl) vanadate, the mixture that forms contains approximately 30% of the primary alcohols, geraniol **34** and nerol **35**, along with unchanged linalool.
- Starting from the other side of the equation, another vanadate-based catalyst system converts either geraniol or nerol to a mixture that contains 68-70% linalool.

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Fragrance Chemicals*

- The equilibrium mixtures obtained in the linalool isomerization are not altogether satisfactory for perfumery use because separation of the desired geraniol (a rose scent constituent) is difficult.
- The reaction employs a trick to shift the equilibrium in favor of the terminal alcohols. The linalool is convened to a borate ester by ester exchange with tributyl borate. Equilibration of the borate esters yields 75-80% of the primary alcohols.

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Fragrance Chemicals*

- The vanadium-catalyzed isomerization appears to occur within the coordination sphere of the metal as sketched in Figure 2.6.
- The allylic alcohol such as linalool enters the coordination sphere by ester exchange with the trialkyl vanadate catalyst.
- The fundamental rearrangement of the allylic vanadate ester **36** resembles the classical Claisen rearrangement.

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Fragrance Chemicals*

- The transition state may be rather like **37** in which C-1 is forming a bond to the V=O oxygen while the VO-C bond to C-S is breaking.
- The rearrangement produces the new allylic vanadate ester **38** derived from the primary alcohol.
- Ester exchange with free tertiary alcohol (linalool) releases the isomerized product (geraniol or nerol).
- All steps in the process are reversible; hence, the composition of the equilibrated product mixture is determined by the relative thermodynamic stabilities of the products.

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Fragrance Chemicals*

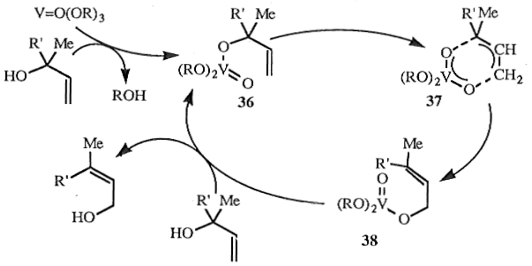


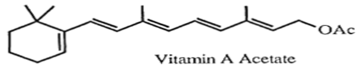
**Figure 2.6** Proposed mechanism for isomerization of allylic alcohols

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Fragrance Chemicals*

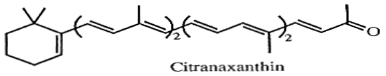
- The vanadate-catalyzed isomerization of allylic alcohols contrasts with the rhodium-catalyzed isomerization mentioned earlier in that vanadium produces a 1,3-oxygen shift while rhodium shifts a hydrogen.
- This mechanistic difference leads to a difference in product. Vanadium makes an isomeric allyl alcohol, but rhodium produces an enolate of an aldehyde or ketone.

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Food Additives*

- The 1,3-shift of a hydroxyl or acetoxyl group may also be catalyzed by copper salts or copper powder.
- BASF makes extensive use of this chemistry in the production of vitamin A and citranaxanthin, a food colorant.



Vitamin A Acetate



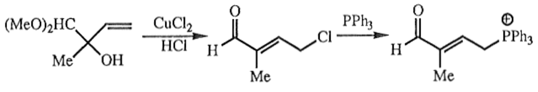
Citranaxanthin

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Food Additives*

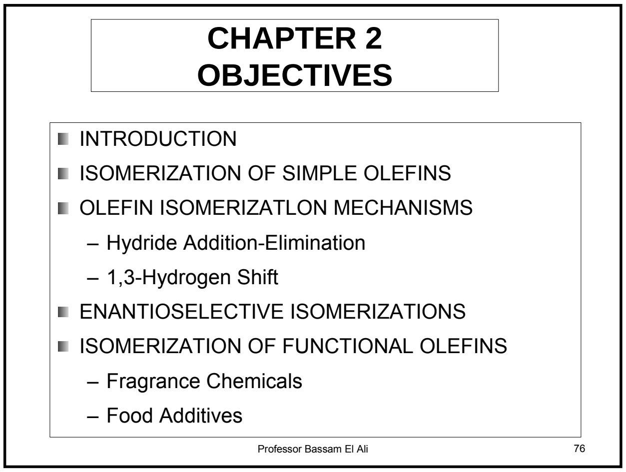
- One example of this reaction is the isomerization of the isoprenoid tertiary alcohol **39** to the primary chloride **40**.
- (Under the acidic reaction conditions, the acetal function is hydrolyzed to the aldehyde.)
- The allylic chloride is then converted to a triphenylphosphonium salt **41** which, in turn, provides Wittig reagent used in building the unsaturated side chains in vitamin A and citranaxanthin.

## ISOMERIZATION OF FUNCTIONAL OLEFINS
### *Food Additives*

- The high chloride concentration in the reaction medium for isomerization of **39** makes it likely that the tertiary alcohol is first convened to the tertiary allylic chloride which then isomerizes by a copper-assisted 1,3-chlorine shift.
- The acetate corresponding to **39** undergoes an analogous isomerization to 4-acetoxy-2- methyl-2-butenal on treatment with $Cu(OAc)_2$ in acetic acid.



**39** **40** **41**



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