Lecture 11

Organic Chemistry 1

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What is the product(s) of the following reaction?

H
CH₃
CH₃
Br
CH₃
→
KOC(CH₃)₃
DMSO, 40°C
H
CH₃
CH₃
OC(CH₃)₃
CH₃
CH₃
CH₃
H
C
H
CH₃
CH₃
CH₃
H
CH₃
CH₃
CH₃

A
B
C
D
E
Addition Reactions of Alkenes

Section 6.1-6.10

You are responsible for Section 6.11.
Addition Reactions of Alkenes

\[
\text{C} = \text{C} \quad + \quad \text{X} - \text{Y} \quad \Rightarrow \quad \text{X} - \text{C} - \text{C} - \text{Y}
\]

- **addition**

\[
\text{C} = \text{C} \quad + \quad \text{H} - \text{H} \quad \Rightarrow \quad \text{H} - \text{C} - \text{C} - \text{H}
\]

- **hydrogenation**

\[
\text{C} = \text{C} \quad + \quad \text{H} - \text{X} \quad \Rightarrow \quad \text{H} - \text{C} - \text{C} - \text{X}
\]

- **hydrogen halide addition**

\[
\text{C} = \text{C} \quad + \quad \text{H} - \text{Br} \quad \Rightarrow \quad \text{H} - \text{C} - \text{C} - \text{Br}
\]

- **free radical bromine addition**

\[
\text{C} = \text{C} \quad + \quad \text{H} - \text{O} - \text{S} - \text{O} - \text{H} \quad \Rightarrow \quad \text{H} - \text{C} - \text{C} - \text{OSO}_3\text{H}
\]

- **sulfuric acid addition**

\[
\text{C} = \text{C} \quad + \quad \text{H} - \text{OH} \quad \Rightarrow \quad \text{H} - \text{C} - \text{C} - \text{OH}
\]

- **hydration**
Hydrogenation

- Exothermic reaction (-ΔH°), but high E_{act} - catalyst required
- Catalysts are heterogeneous transition metals (Pd, R)
- Solvent is typically an alcohol (e.g. ethanol, CH₃CH₂OH)
- Metals are insoluble (heterogeneous mixture)
- Heat of hydrogenation = -ΔH°
Heat of Hydrogenation (-ΔH°)

- **Alkene**: H₂C=CHCH₂CH₃
- **1-Butene**: H₃C\(\text{C}═\text{C}\)H H
- **cis-2-Butene**: H₃C\(\text{C}═\text{C}\)CH₃
- **trans-2-Butene**: H₃C\(\text{C}═\text{C}\)CH₃

Potential energy

\[ \Delta H° \]

+H₂

\[ \text{CH₃CH₂CH₂CH₃} \]
Since only the double bond is undergoing the reaction, heat of hydrogenation is independent of the number of carbon atoms in the molecule.

<table>
<thead>
<tr>
<th>Alkene</th>
<th>$\Delta H^\circ$ (kJ/mol)</th>
<th>example</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethylene</td>
<td>136</td>
<td><img src="image" alt="ethylene" /></td>
</tr>
<tr>
<td>monosubstituted</td>
<td>126</td>
<td><img src="image" alt="monosubstituted" /></td>
</tr>
<tr>
<td>cis-disubstituted</td>
<td>119</td>
<td><img src="image" alt="cis-disubstituted" /></td>
</tr>
<tr>
<td>terminally disubstituted</td>
<td>117</td>
<td><img src="image" alt="terminally disubstituted" /></td>
</tr>
<tr>
<td>trisubstituted</td>
<td>112</td>
<td><img src="image" alt="trisubstituted" /></td>
</tr>
<tr>
<td>tetrasubstituted</td>
<td>110</td>
<td><img src="image" alt="tetrasubstituted" /></td>
</tr>
</tbody>
</table>
General Mechanism for Heterogenous Hydrogenation

reaction takes places at the surface of the catalyst (many metal atoms combined)
Step 1: Oxidative Addition

- Hydrogen ($H_2$) is added to metal.
- Metal is oxidized from $M^0$ to $M^{II}$.

\[ \text{H} \quad \text{H} \quad \xrightarrow{\text{oxidative addition}} \quad \text{H} \quad \text{Pd}^{II} \quad \text{H} \]
Step 2: Coordination

- metal is a Lewis acid (electron acceptor)
- π-bond is a Lewis base (electron donor)
- coordination = Lewis acid/base complex

H–Pd\textsuperscript{II}–H \rightarrow \text{coordination} \rightarrow H–Pd\textsuperscript{II}–H

catalyst surface

H–Pd\textsuperscript{II}–H \rightarrow \text{coordination} \rightarrow H–Pd\textsuperscript{II}–H

catalyst surface
Step 3: Insertion

- two carbon atoms inserted between Pd-H
- formation of a weak metal-carbon σ-bond
- formation of a strong C-H σ-bond
- break a weak metal-H σ-bond
Step 4: Reductive Elimination

- Metal is reduced from $M^{\text{II}}$ to $M^0$.
- Last $\sigma$ C-H bond is formed from the same face of alkene as previous.
- Metal is a catalyst; it is regenerated.
Complete Mechanism

H

H

H—Pd

H—Pd

H—H

: Pd

oxidative addition

reductive elimination

insertion

coordination
Syn Addition of Hydrogen

- as a consequence of mechanism, both hydrogens are added to the same face of the π-bond: *syn* addition
- no *anti*-addition products are formed (addition of hydrogen to opposite faces)
Hydrogenation is Stereoselective

- both products are arise from syn additions of hydrogen to alkene
- stereoselective: preference for one stereoisomer when two or more are possible

This methyl group sterically hinders hydrogen from approaching the \( \pi \)-bond from the top face
Example of Syn Addition

1. Diatomic hydrogen and alkene are present in solution phase. No reaction occurs.
3. \(\pi\)-System of alkene coordinates catalyst surface.
4. One hydrogen atom is transferred to alkene, forming C-catalyst bond.
5. Second hydrogen atom is transferred, breaking substrate-catalyst bond. Alkane diffuses away from catalyst.
6. Steps 1-5 are repeated.
Self Test Question

What is the major product of the following hydrogenation reaction?

A. 

B. 

C. 

D.
Addition of Electrophiles to Alkene

- **Hydrogenation**
  \[ \text{C} = \text{C} + \text{H-H} \rightarrow \text{C} - \text{C} - \text{H} \]

- **Hydrogen halide addition**
  \[ \text{C} = \text{C} + \text{H-X} \rightarrow \text{C} - \text{C} - \text{X} \]

- **Free radical bromine addition**
  \[ \text{C} = \text{C} + \text{H-Br} \rightarrow \text{C} - \text{C} - \text{Br} \]

- **Sulfuric acid addition**
  \[ \text{C} = \text{C} + \text{H-O-SO-OH} \rightarrow \text{C} - \text{C} - \text{OSO}_3\text{H} \]

- **Hydration**
  \[ \text{C} = \text{C} + \text{H-OH} \rightarrow \text{C} - \text{C} - \text{OH} \]
Electrophilic Addition of HX

C= C + δ+ δ- H−X → H−C−C−X

| nucleophile | electrophile |

Hydrogen halide addition

Increasing reactivity of hydrogen halides in addition to alkenes

HF << HCl < HBr < HI

Slowest rate of addition; weakest acid

Fastest rate of addition; strongest acid
Reaction Conditions

- hydrogen halide: HX
- common solvents: chloroform (CHCl₃), dichloromethane (CH₂Cl₂), pentane, acetic acid
- generally performed at low temperature (below 0 °C)
- generally a fast reaction
Electrophilic Addition (AdE) Mechanism

- electrophilic addition: AdE
- RDS = protonation of carbon
- rate = $k[\text{alkene}][\text{hydrogen halide}]$
- unlike oxygen and nitrogen, protonation of carbon is slow
- proceeds through carbocation intermediate
**Regioselectivity**

Preferential reaction at one site of a single functional group over other sites that could undergo the same reaction.

\[
\text{R} - \text{H} - \text{H} \quad \xrightarrow{\text{H-X}} \quad \text{R} - \text{H} - \text{X} - \text{H} \quad \text{rather than} \quad \text{R} - \text{H} - \text{H} - \text{X} \\
\text{R} - \text{H} - \text{H} \quad \xrightarrow{\text{H-X}} \quad \text{R} - \text{H} - \text{X} - \text{H} \quad \text{rather than} \quad \text{R} - \text{H} - \text{H} - \text{X} \\
\text{R} - \text{H} - \text{H} \quad \xrightarrow{\text{H-X}} \quad \text{R} - \text{H} - \text{X} - \text{H} \quad \text{rather than} \quad \text{R} - \text{H} - \text{H} - \text{X} \\
\text{R} - \text{H} - \text{H} \quad \xrightarrow{\text{H-X}} \quad \text{R} - \text{H} - \text{X} - \text{H} \quad \text{rather than} \quad \text{R} - \text{H} - \text{H} - \text{X} \
\]
addition of HX to an unsymmetrically substituted alkene proceeds so that hydrogen (H) adds to the least substituted carbon and the halide (X) adds to the most substituted carbon atom.
Predict the product when 2,4-dimethyl-2-pentene is treated with HCl?

A. 3-chloro-2,4-dimethylpentane
B. 2-chlorooctane
C. 2,3-dichloro-2,4-dimethylpentane
D. 2-chloro-2,4-dimethylpentane
E. 1-chloro-2,4-dimethylpentane
Mechanistic Basis for Markovnikov’s Rule

- curved arrows do not indicate which carbon is protonated
- fastest protonation leads to more stable (more substituted) carbocation
- more substituted carbocation = more substituted alkyl halide
Hammond Postulate: *transition state structure resembles closest energy intermediate*

- transition state resembles carbocation for endothermic RDS (late transition state)
- what stabilizes carbocation also stabilizes transition state
- lowest energy transition state leads to more substituted carbocation
Rearrangement Can Precede Addition

H - Br

\[ \text{H} \quad \text{Br} \quad \text{H} \quad \text{Br} \quad \text{H} \]

2º carbocation

\[ \text{H} \quad \text{Br} \quad \text{CH}_2\text{H} \]

3º carbocation

\[ \text{Br} \quad \text{CH}_2\text{H} \]

hydride shift
Stability of Carbocations (Lecture 8)

2. Hyperconjugation

stabilizing interaction that results from the interaction of the electrons in a $\sigma$-bond (C–H or C–C bond) with an adjacent empty (or partially filled) orbital. Leads to the formation of an extended molecular orbital that increases the stability of the system.

- stabilization results from $\sigma$-donation to empty $p$ orbital of planar carbocation
- electron donation through $\sigma$-bonds toward carbocation delocalizes charge (spreads out)
- methyl cations cannot be stabilized by hyperconjugation since $\sigma$-bonds are perpendicular to the empty $p$ orbital
2. Hyperconjugation

Filling of the C-H bond orbital causes a decrease in the energy of the C-H bond, resulting in stabilization of the carbocation.
Rearrangement Can Precede Addition

\[
\begin{align*}
\text{H-Br} & \quad \rightarrow \\
\text{2}\text{o carbocation} & \quad \rightarrow \\
\text{3}\text{o carbocation} & \\
\text{Normal Addition} & \\
\text{Abnormal Addition} &
\end{align*}
\]
Reversal of Addition Regioslectivity

**The Peroxide Effect**

- alkyl peroxides easily formed from alkanes/alkenes by reaction with \( \text{O}_2 \) in the air
- presence of peroxides leads to anti-Markovnikov product (least substituted alkyl bromide)
- peroxide effect only operates when \( \text{HBr} \)
Mechanistic Rationale for Peroxide Effect

peroxides are radical initiators: they undergo homolysis to generate alkoxy radicals, which begin the chain mechanism

\[ \text{initiation} \quad \begin{array}{c}
\text{heat (}\Delta\text{)} \\
\text{or light (}h\nu\text{)}
\end{array} \]

\[ 2 \text{ R} = \text{O} \cdot \quad \text{alkoxy radical} \]

\[ \text{initiation} \quad \begin{array}{c}
\text{H} - \text{Br} \\
\text{ROH} + \text{Br} \cdot \quad \text{bromine radical}
\end{array} \]
Mechanistic Rationale for Peroxide Effect

- bromine radical **adds** to the **least** substituted carbon of alkene
- this generates the **most substituted** and most stable alkyl radical
- alkyl radical undergoes hydrogen abstraction from HBr to generate a new bromine radical (chain mechanism)
Addition of Sulfuric Acid to Alkenes

\[ \text{alkene} + \text{H}_2\text{SO}_4 \xrightarrow{\text{sulfuric acid addition}} \text{H} = \text{C} - \text{C} - \text{OSO}_3\text{H} \xrightarrow{\text{hydrolysis}} \text{H} = \text{C} - \text{C} - \text{OH} \]

alkyl hydrogen sulfate (ester of sulfuric acid)

compare to:

\[ \text{HO} + \text{H}_2\text{SO}_4 \xrightarrow{80 \, ^\circ\text{C}} \text{alkene(s)} + \text{alkyl hydrogen sulfate} \]

alcohol

elimination
Sulfuric Acid Addition: \( \text{Ad}_E \) Mechanism

- Markovnikov’s rule applies
- Protonation occurs to provide most stable (most substituted) carbocation
- Leads to formation of most substituted alkyl hydrogen sulfate

\[
\begin{align*}
\text{Cation Capture (fast)} & \quad \text{Protonation (slow)} \\
\text{H}_2\text{C} & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

\[
\begin{align*}
\text{H} & \quad \text{C} \quad \text{C} \quad \text{O} \quad \text{SO}_3\text{H} \\
\text{H} & \quad \text{H} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]
Hydrolysis of Alkyl Hydrogen Sulfates

alkyl hydrogen sulfate (ester of sulfuric acid)

hydrolysis

\[ \text{H}_2\text{O} \]

\[ \text{alkyl hydrogen sulfate} \rightarrow \text{alcohol} + \text{sulfuric acid} \]

- don’t worry about mechanism for hydrolysis
- only requires hot water
- cleavage of the O-S bond
- substitution of S with H
Examples of Alkene Hydration

Mixture of 1-butene, cis-2-butene, and trans-2-butene

2-Butanol

Cyclohexene

Cyclohexanol (75%)
Hydration of Alkenes (Addition of Water)

\[
\text{alkene} + \text{H}_2\text{O} \rightarrow \text{alcohol}
\]

compare to:

\[
\text{alcohol} \xrightarrow{\text{H}_2\text{SO}_4, 80 \, ^\circ\text{C}} \text{alkene(s)}
\]
Hydration: $\text{Ad}_E$ Mechanism

Principle of Microscopic Reversibility

In an equilibrium, the forward mechanism is identical to the reverse mechanism
Principle of Microscopic Reversibility

*in an equilibrium, the forward mechanism is identical to the reverse mechanism*
Quiz This Next Week

- Topic = Chapter 5
- Alkenes Nomenclature
- Alkenes: Structure, Bonding & Stability
- Geometrical Isomerism of Alkenes (E vs. Z)
- Mechanism of E1 Eliminations
- Zaitsev’s Rule (E1 & E2) & Stereoselectivity
- Rearrangement During Elimination
- Mechanism of E2 Eliminations
Next Lecture. . .
Chapter 6: Sections 6.12-6.22