CHEM 221 section 01

LECTURE #20 Thurs., Nov.10, 2005

ASSIGNED READINGS:

TODAY'S CLASS: finish Ch.5, start Ch.9

NEXT LECTURE: start Ch.10

http://artsandscience.concordia.ca/facstaff/P-R/rogers

5.19 Stereochemistry of electrophilic additions

Stereochemical outcome depends on the fact that…

- Alkene π-bonds are planar
  - ⇨ Equal probability of rxn at either "face" of π-bond
  - ⇨ Always have possibility of forming > 1 stereoisomer (must analyze products to see if molecules are actually same)
- Carbocation & radical intermediates have an open-shell sp^2 atom
  - ⇨ Attack is equally likely from both faces…
- Possibility of forming 1 or 2 new chiral centres, depending on rxn…

To predict stereochemistry, consider nature of rxn's mechanism:

1. **Concerted attack of E^+ & Nu^-:** *e.g.,* hydroboration, (hydrogenation)
   - no intermediate formed
   - stereochemistry results only from: syn addition to alkene

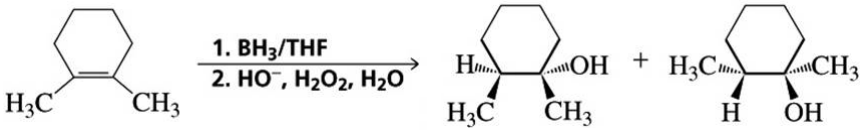
   OR
2. **Step-wise attack of E^+ & Nu^-:** *e.g.,* rest of electrophilic additions
   - intermediate forms, then reacts with nucleophile
   - E^+ atom in intermediate can be attacked from either face

GENERAL STRATEGY: always analyze alkene reactant 1st

- if an sp^2 C has 3 different groups: if is 1 step away from being a chiral center (*i.e.*, is "prochiral")
- if not: addition will not result in formation of chiral centres

⇨ **Do not memorize outcomes: just picture mechanism happening!**

1A. Stereochemistry of Hydroboration–Oxidation



- Concerted attack of π e⁻s on B-H bond: **Always syn addition**
- In 1st step: H-B can add to either side of C=C initially, so get <u>both</u> possible syn products
- Subsequent steps to replace B by OH: stereochemistry defined is 1st step is unaffected (configurations of carbon atoms remain unchanged) ⇨ described as proceeding with "retention of configuration"

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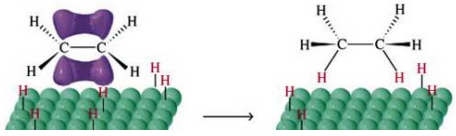
1B. Stereochemistry of hydrogenation

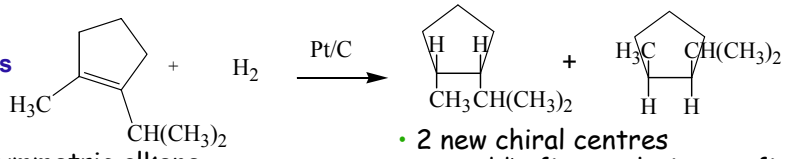
- Alkene "docks" onto metal surface: **Always syn addition**

since H atoms replace bonds between Cs & metal surface

- note: 2 new stereocentres may be formed…



Cyclic alkenes

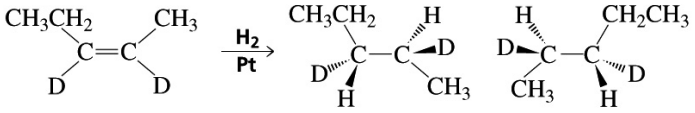


- Asymmetric alkene
- 2 C's one step away from being chiral centres ("prochiral")

- 2 new chiral centres
- syn add'n fixes relative config's

⇨ enantiomers

***cis*-2,3-dideuterio-2-pentene**



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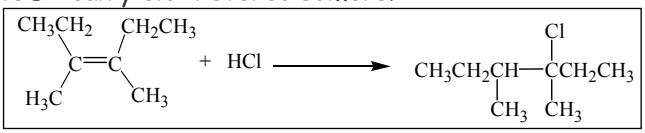
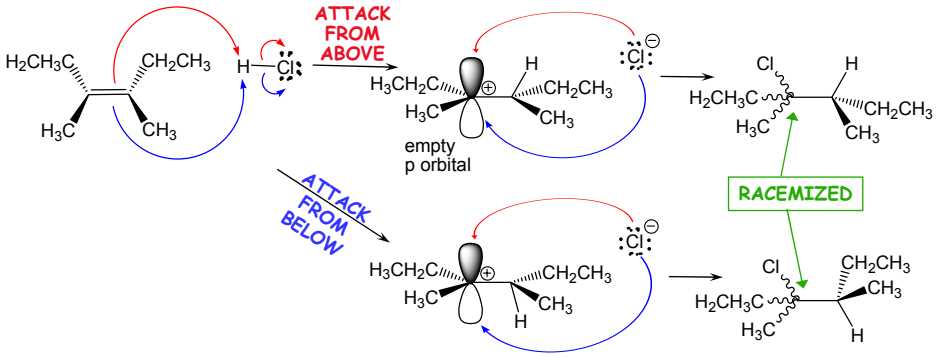
2A. Stereochemistry of hydrohalogenation

- H^+ can bond to either side of alkene ⇨ **1st C is racemized**
- Nucleophile can attack planar carbocationic centre from either side
  ⇨ **2nd C also racemized**!

THUS: can yield 4 stereoisomers!



without showing stereochem (∴ incomplete!)



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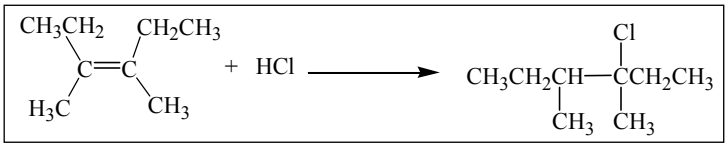
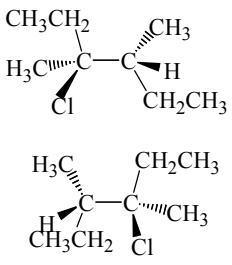


without showing stereochem (∴ incomplete!)

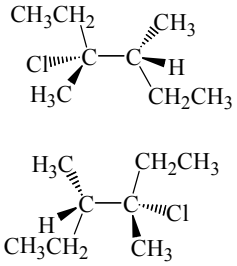
Recall descriptive terms:

If it looks like both groups added to the same side of C=C: "syn addition"

If…added to opposite sides of C=C: "anti addition"



syn addition



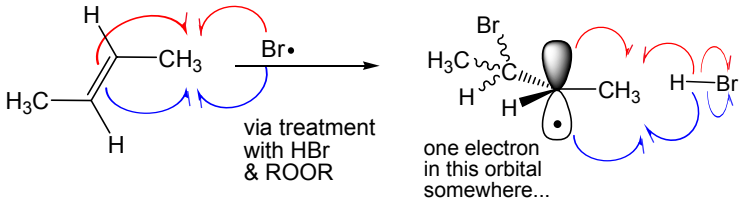
anti addition

Complete description of products
INCLUDES STEREOCHEMISTRY OF ALL.

(6)

2B. Stereochemistry of radical hydrobromination

- bromine radical can add to either side of C=C ⇨ 2 possible config's
- then: alkyl radical intermediate can react with H from either side
  (*i.e.,*: R• abstracts H• via attack from either top or bottom face of C…)



THUS: can form 2 new asymmetric centers, both racemized

- **1st C is racemized** (attack from either face of C=C)
- **2nd C is racemized** (attack by either face of R•)

⇨ can form maximum of 4 stereoisomers

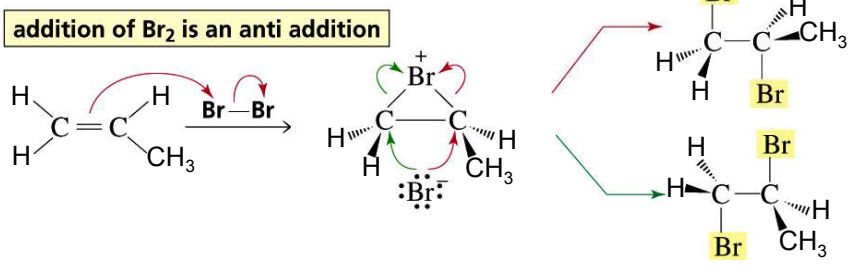
(7)

2C. Stereochemistry of halogenation of alkenes

- 1st halide atom can add to either side of C=C ⇨ 2 possible config's
- then: one face of C-C is blocked by large halogen atom
  so halide nucleophile must add from other side **(ANTI ADDITION)**

THUS: can form 2 new asymmetric centers

- **always 2 possible products:** ***1st X can go on either side…***
- **AND always have ANTI addition of halogens**
- if 2 C*'s just created are the only ones present in molecule
  ⇨ products will be enantiomers *(unless meso…)*
- if other chiral centers were already present in the molecule
  ⇨ products will be diastereomers



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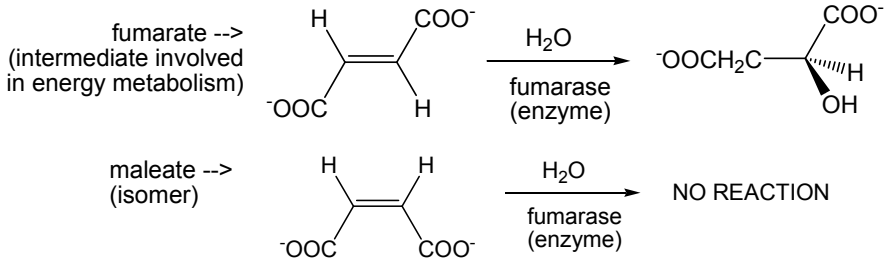
5.20: Stereochemistry of enzyme reactions

Biochemistry = study of reactions in biological systems
- nucleic acids, carbohydrates, …
- proteins (*e.g.*, enzymes): composed of chiral amino acids

Biological reactions involve: *(not additions of HX, X_2, BH_3…)*
- aqueous environment
- acidic (RCOOH) & basic (RNH_2) groups present in proteins
  - ⇨ acid-catalyzed reactions of many kinds occur!
- catalysis by enzymes (which are chiral!)
  - ⇨ thus: rxns have preferred reactant stereochemistry AND product stereochemistry



Chapter 9: Reactions of Alkanes

Chapter Goals

Appreciate the general unreactive nature of alkanes, plus the conditions that can lead to alkanes reacting.

- Understand mechanism of radical halogenation – *including stereochem.*

Chapter Outline: **(responsible for level of detail presented in the notes)**

[You are not responsible at all for 9.5, 9.8, 9.9]

9.1 The low reactivity of alkanes

Can we predict the typical reactivity of alkanes?

- nonpolar, with only C-C and C-H σ-bonds
  ⇨ high pK_as, not electrophilic, not nucleophilic…
- unreactive towards most other substances
- they only react with highly reactive species (or at very high T.)

1. **Combustion reactions:** oxidation via complex radical mechanism
   large activation energy (needs a spark…)

$$C_xH_y + {}^{y}/_{2}\, O_2 \rightarrow xCO_2 + {}^{y}/_{2}\, H_2O$$

2. **Catalytic cracking:** breakdown into shorter branched chains
   → important in petroleum refining
   → sort of like alkene hydrogenation in reverse, then back again
   → requires high temperatures & catalysts (*i.e.,* hard to do!)

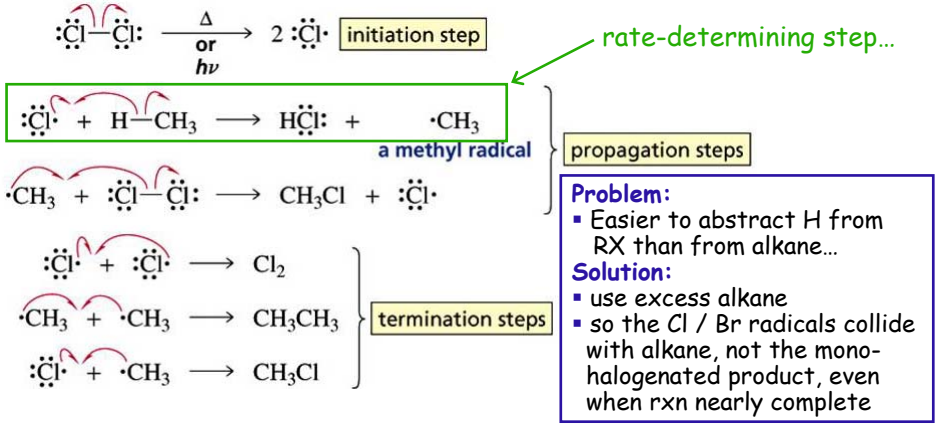
3. **Radical halogenation reactions:** not-so-complex radical mechanism

$$C_xH_y + \tfrac{1}{2}\, X_2 \rightarrow C_xH_{y-1}X + HX$$

9.2 Radical halogenation of alkanes (by Cl_2, Br_2)

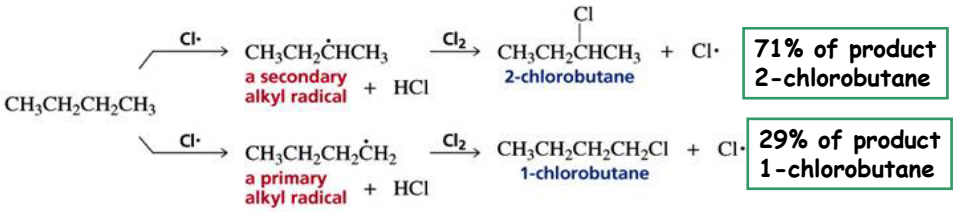
- Cl_2 & Br_s are synthetically useful *(F_2 too dangerous; I_2 too slow)*
- High temperature or light needed: to homolytically cleave the X_2 bond
- Use excess alkane (X_2 as L.R.) to minimize dihalogenated product

Mechanism: radical chain reaction *(similar to alkene HBr/ROOR rxn)*



9.3 Factors that determine product distribution
9.4 The reactivity-selectivity principle

1. **Radical intermediate involved:** *(produced in rxn's rate-limiting step)*
   - more stable radical intermediates will form faster *(lower E ‡)*
   - rearrangements do not occur for radicals
   - ⇨ REGIOCHEMISTRY:
     X• prefers to abstract H• from (∴ X• later adds to…)
     the most highly substituted carbon



Relative rate of formation of R• by Cl• at RT: tertiary (5.0) > secondary (3.8) > primary (1.0)

(13)

2. **Chlorine atoms (radicals) are more reactive than bromine atoms**
   - Smaller atom, higher effective nuclear charge
     ⇨ Cl• has more driving forcer for abstracting H•
     ⇨ Cl• is more reactive, thus "less selective", than Br•

REGIOSELECTIVITY BASED ON:
Reactivity towards that type of H
i.e., Relative rates of R• formation:

Cl• at RT: tertiary (5.0) > secondary (3.8) > primary (1.0)

Chlorine radicals are fast, but **unselective**!
→ lower yields since many products formed
→ lots of extra work separating products

Br• at 125°C: tertiary (1600) > secondary (82) > primary (1)

increasing rate of formation

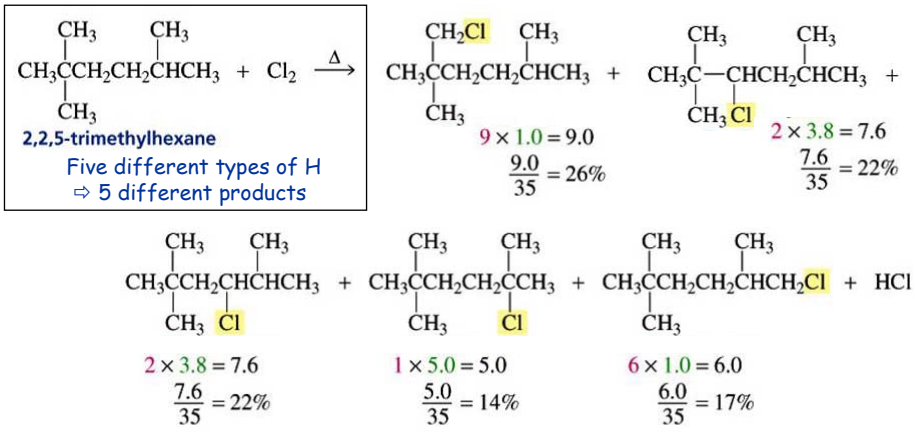
Bromine radicals require higher T, but **very useful**
→ Higher yield of one product

(14)

Relative rates can be used to predict product yields:

- **Statistics:** How many H's of each type (1°,2°,3°…) is present?
- **Selectivity:** What is X·'s relative rate of abstraction of each H type?

Approach: Percentage of product halogenated at site of interest
= (number of Hs at that type of site) x (reactivity)



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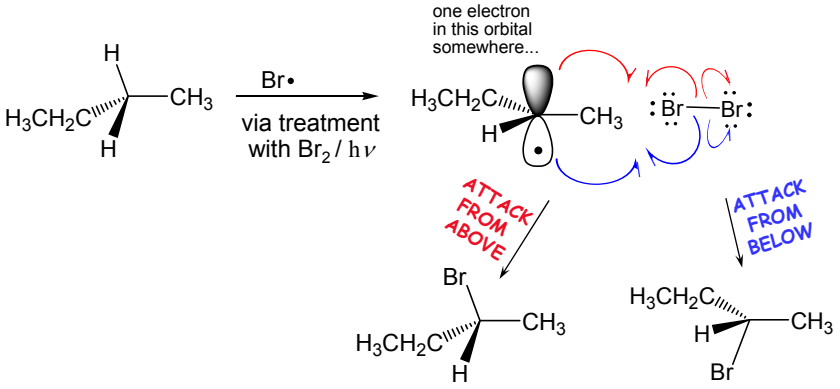
9.6 Stereochemistry of radical substitution

- halogen radical attacks C-H bond ⇨ planar radical intermediate
- then: alkyl radical intermediate can react with X· from either side
  (*i.e.,*: R· abstracts X· via attack from either top or bottom face of C…)



THUS: can form 1 new asymmetric center, but racemized
⇨ Form maximum of 2 stereoisomers (enantiomers here…)

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ASSIGNED READINGS

BEFORE NEXT LECTURE:

Read: Ch.9 material

Practice: predicting products & stereochemistry