Lecture 9
Organic Chemistry 1

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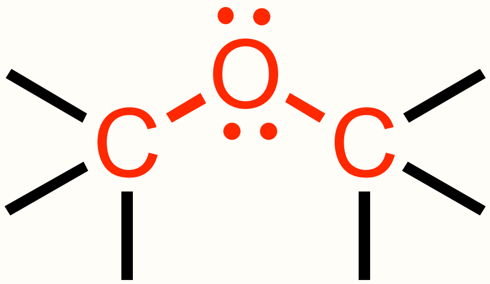
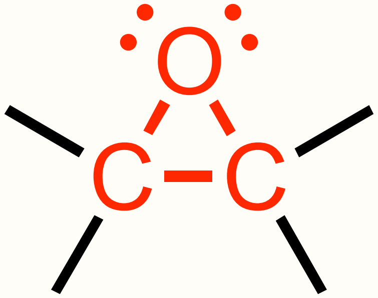
Functional Group Clarification

Although they can be viewed as ethers, epoxides are classified as distinct, three-atom functional groups........



Ether



Epoxide

q. Why?

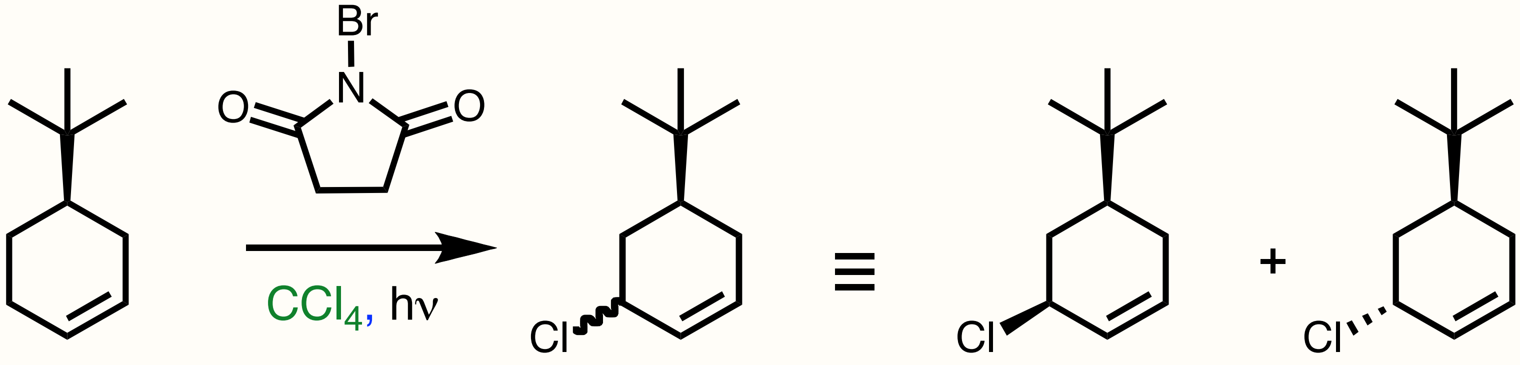
a. Epoxides display distinctly different reactivity to ethers, which arises from their considerable ring strain.

Defining Regioselectivity

Regioselectivity (regioselective)

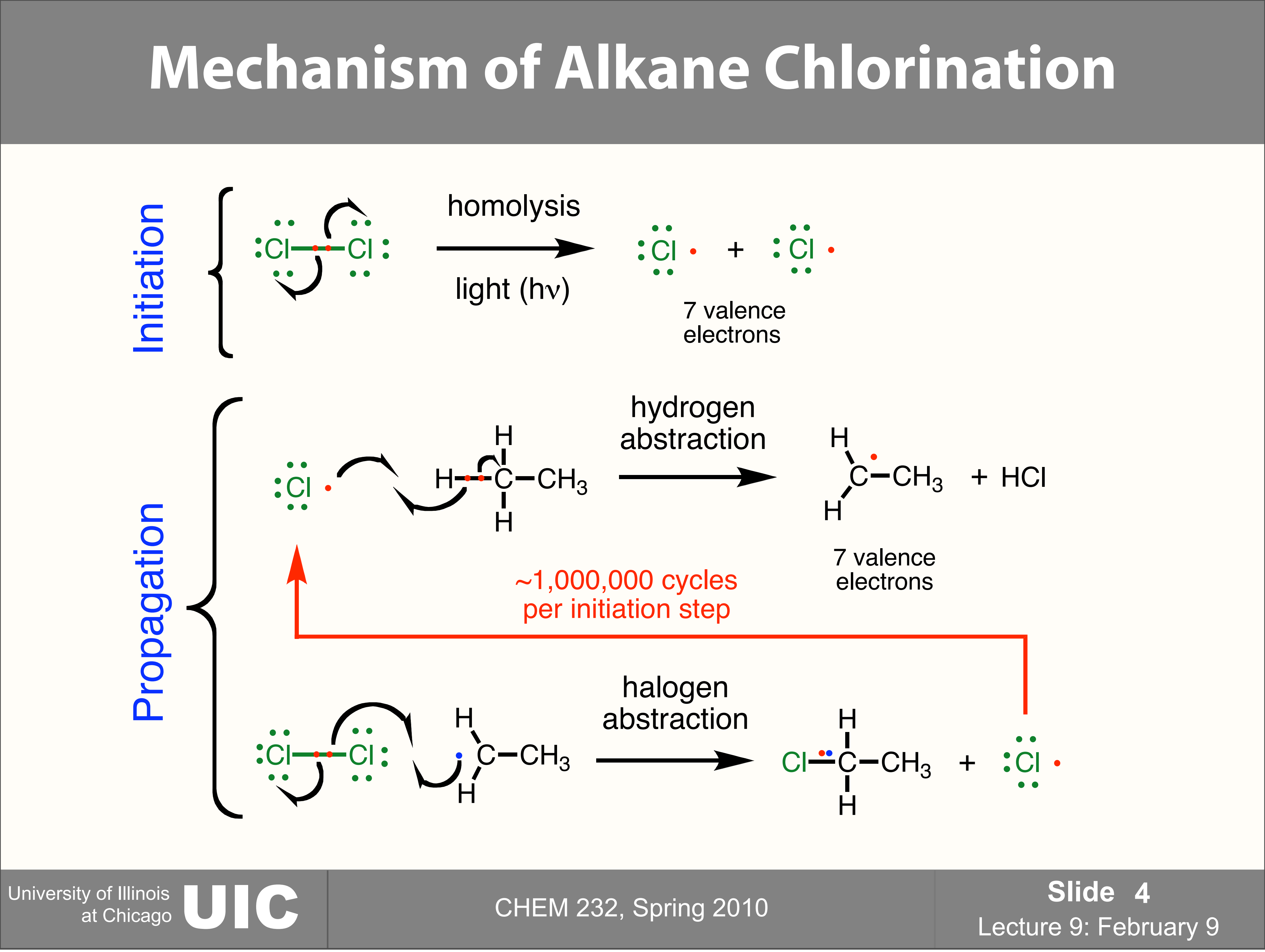
A regioselective reaction is one in which one direction of bond making or breaking occurs preferentially over all other possible directions. Reactions are termed completely (100%) regioselective if the discrimination is complete, or partially (<100%), if the product of reaction at one site predominates over the product of reaction at other sites. The discrimination may also semi-quantitatively be referred to as high or low regioselectivity.

IUPAC Compendium of Chemical Terminology 2nd Edition (1997)



Regioselective Chlorination........

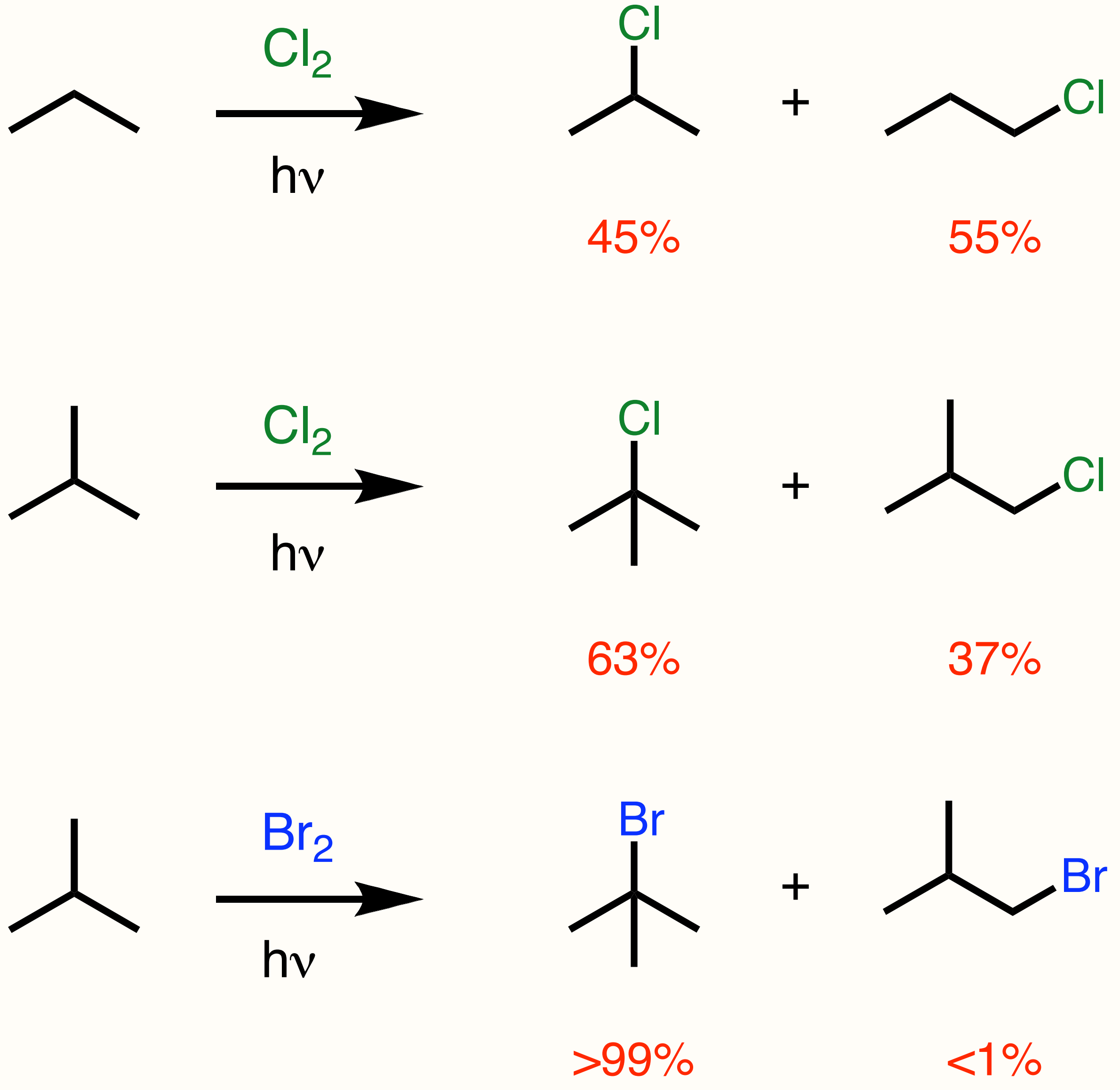
.......not stereoselective!



Mechanism of Alkane Chlorination

Note that typically, this type of chain reaction can continue for 1,000,000 steps for each initiation event.

Factors Governing Regioselectivity

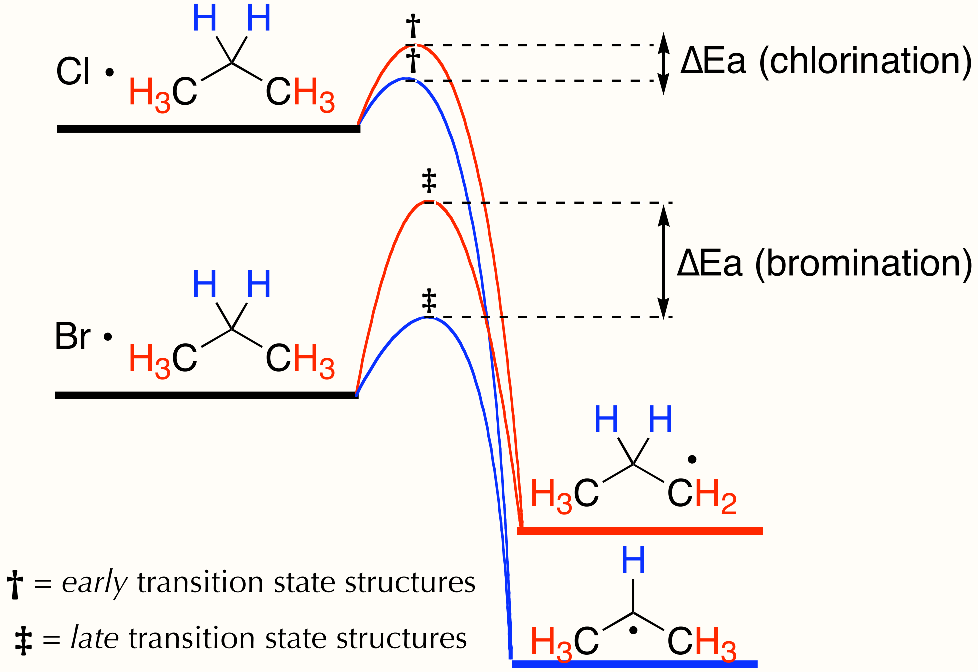


- Strength of C-H Bond Broken
- Number & Type of Substrate C-H Bonds
- Strength of C-X Bond Formed and X-X Bond Broken

Remember that regioselectivity is only an issue in those substrates that more than one type of C–H bond. Cyclohexane, for example, undergoes monochlorination to yield on cyclohexyl chloride.

Useful Bond Dissociation Energies: C–H (1°; 423 kJ/mol); C–H (2°; 410 kJ/mol); C–H (3°; 397 kJ/mol); H–Cl (431 kJ/mol); H–Br (366 kJ/mol); Br–Br (192 kJ/mol)

Bromination is More Selective Than Chlorination



ΔEa (bromination) > ΔEa (chlorination)
Bromination is <u>more</u> selective.

Relative Rates (k_{rel}) of Halogenation

	R_3CH (tertiary, 3°)	R_2CH_2 (secondary, 2°)	RCH_3 (primary, 1°)
chlorination	***5.2***	***3.9***	***1.0***
bromination	***1640***	***82***	***1.0***

Hammond Postulate

- chlorine radicals are higher in energy than bromine radicals =
- transition states in chlorination are earlier =
- look <u>more like</u> reactants =
- less difference in TS energy =
- less selective =
- greater mixture

* * *

- bromine radicals are lower in energy than chlorine radicals =
- transition states in bromination are later =
- look <u>more like</u> products (radical interm.) =
- greater difference in TS energy =
- more selective =
- less of a mixture

Quantifying Selectivity of Halogenation

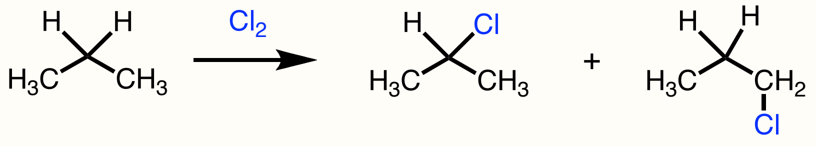
Relative Rates (k_{rel}) of Halogenation

	R_3CH (tertiary, 3°)	R_2CH_2 (secondary, 2°)	RCH_3 (primary, 1°)
chlorination	***5.2***	***3.9***	***1.0***
bromination	***1640***	***82***	***1.0***

$$\% = \frac{(k\text{rel}) \times (\text{statistical factor})}{\text{total}}$$

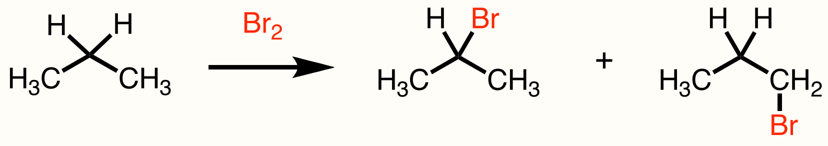
Predicted Product Ratios

	Product	Relative Yield	Absolute Yield
chlorination	**A** (2 2° H's)	2 x ***3.9*** = 7.8	7.8/13.8 = 57%
	B (6 1° H's)	6 x ***1*** = 6.0	6.0/13.8 = 43%
	Sum	13.8	100%
bromination	**A** (2 2° H's)	2 x ***82*** = 164	164/170 = 96%
	B (6 1° H's)	6 x ***1*** = 6.0	6.0/170 = 4%
	Sum	170	100%



A: 57%

B: 43%

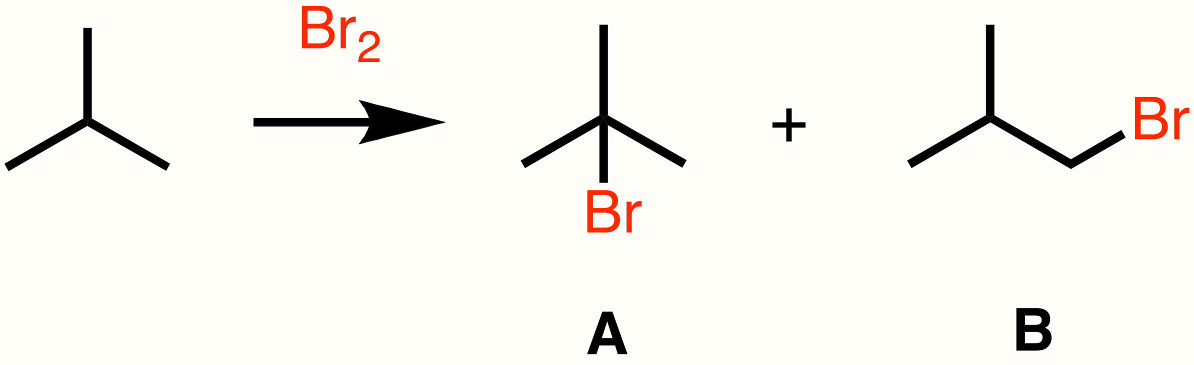


A: 96%

B: 4%

Self Test Question

Determine the predicted product distribution for **A** in the following chlorination.



A. >99%

B. 97%

C. 95%

D. 93%

E. 91%

Relative Rates (k_{rel}) of Halogenation

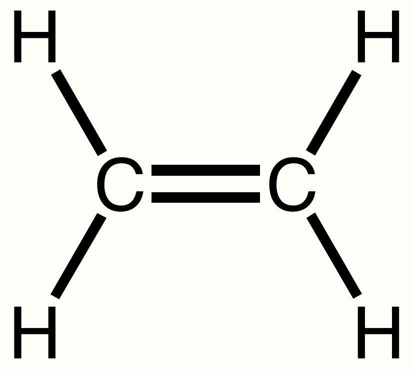
	R_3CH (tertiary, 3°)	R_2CH_2 (secondary, 2°)	RCH_3 (primary, 1°)
chlorination	***5.2***	***3.9***	***1.0***
bromination	***1640***	***82***	***1.0***

Relative Rates for 3° and °1 positions = 1640 and 9, respectively. Absolute yields = 99.4% and 0.6%. **The Answer is A.**

Chapter 5
Nomenclature & Stereoisomerism in Alkenes

Section 5.1-5.11

The Terms Alkene and Olefin are Synonymous

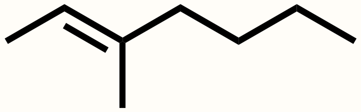


ethylene
C_2H_4

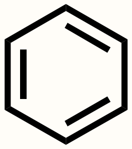
- Alkenes are hydrocarbons that are characterized by a C-C double bond
- Also called “olefins”
- General molecular formula $= C_nH_{2n}$
- Described as *unsaturated* since they have two fewer H atoms than equivalent alkanes

Index of Hydrogen Deficiency (IHD)

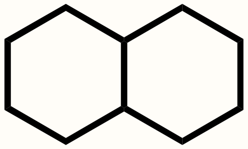
IHD is synonymous with *degrees of unsaturation* and indicates the number of double/triple bonds and/or rings in a molecule



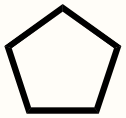
IHD = 1 (1 double bond)



IHD = 4 (3 double bonds & 1 ring)



IHD = 2 (2 rings)



IHD = 1 (one ring)

Calculating IHD

1. Hydrocarbons (C_nH_x) and Oxygenates ($C_nH_xO_y$): Ignore O

$$IHD = \frac{(2n+2) - X}{2}$$

2. Compounds with N ($C_nH_xN_y$): Subtract # N from # H

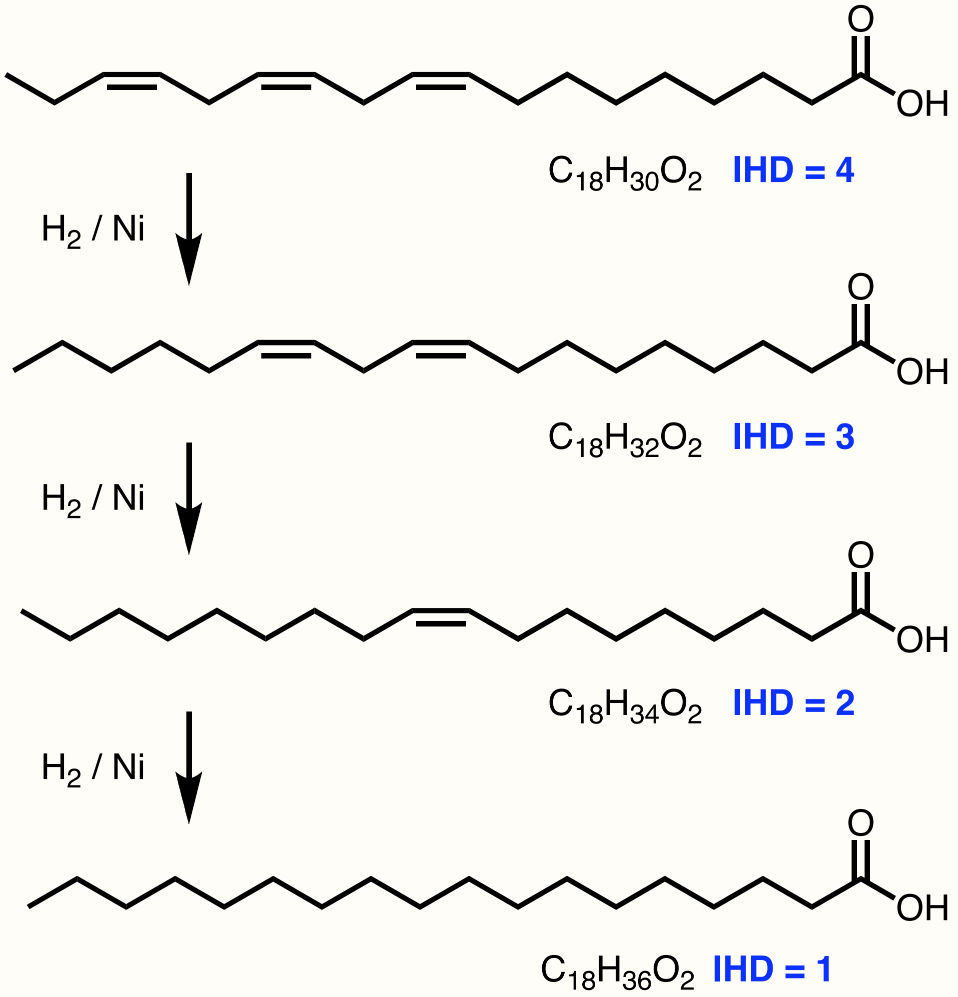
$$IHD = \frac{(2n+2) - (X-Y)}{2}$$

3. Halogens ($C_nH_xX_y$): Add # Halogens to # H

$$IHD = \frac{(2n+2) - (X+Y)}{2}$$

IHD & The Chemistry of Margarine

Employing equation 1 (slide 12)........



H_2 / Ni

$C_{18}H_{30}O_2$ **IHD = 4**

linolenic acid
m.p. -11 °C

$C_{18}H_{32}O_2$ **IHD = 3**

linoleic acid
m.p. -5 °C

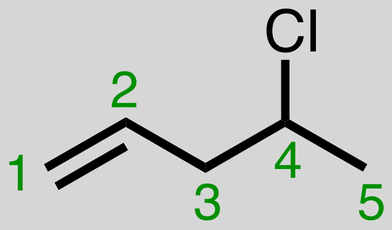
$C_{18}H_{34}O_2$ **IHD = 2**

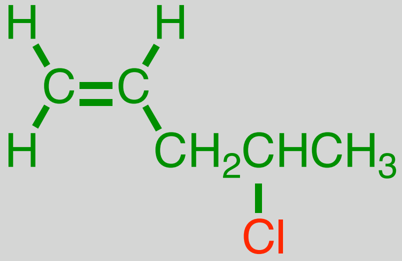
oleic acid
m.p. 16 °C

$C_{18}H_{36}O_2$ **IHD = 1**

stearic acid
m.p. 71 °C

IUPAC Naming of Alkenes





4-chloro-1-pentene or 4-chloropent-1-ene

Steps:

1. Number longest chain that includes both alkene carbons so that they have the lowest locants.
2. Replace -ane ending of parent alkane with -ene (alkene).
3. In the name, list the locant of only the first alkene carbon.

Conventions/Rules:

- alkenes have higher priority over alkane and halide substituents when numbering the longest chain
- alcohols have higher priority over alkenes when numbering the longest chain
- locant may be placed in front of parent name (e.g. 2-pentene) or in front of suffix (e.g. pent-2-ene).

locant — **substituent 1st alphabetically** **parent base** — **alkene locant** — **“ene”**

IUPAC Naming of Alkenols

4-hexen-2-ol or hex-4-en-2-ol

Steps:

1. Number longest chain that contains both the alkene and the alcohol and so that the alcohol group has lowest locant value.
2. Replace -ane ending of parent alkane with -ene (alkene).
3. In the name, list the locant of only the first alkene carbon.

Conventions/Rules:

- alkenes have higher priority over alkane and halide substituents when numbering the longest chain
- alcohols have higher priority over alkenes when numbering the longest chain
- locant may be placed in front of parent name (e.g. 2-pentene) or in front of suffix (e.g. pent-2-ene).
- when “ene” does not occur at the end of a name, drop the last “e”

parent base — **alkene locant** — **“en”** — **-OH locant** — **“ol”**

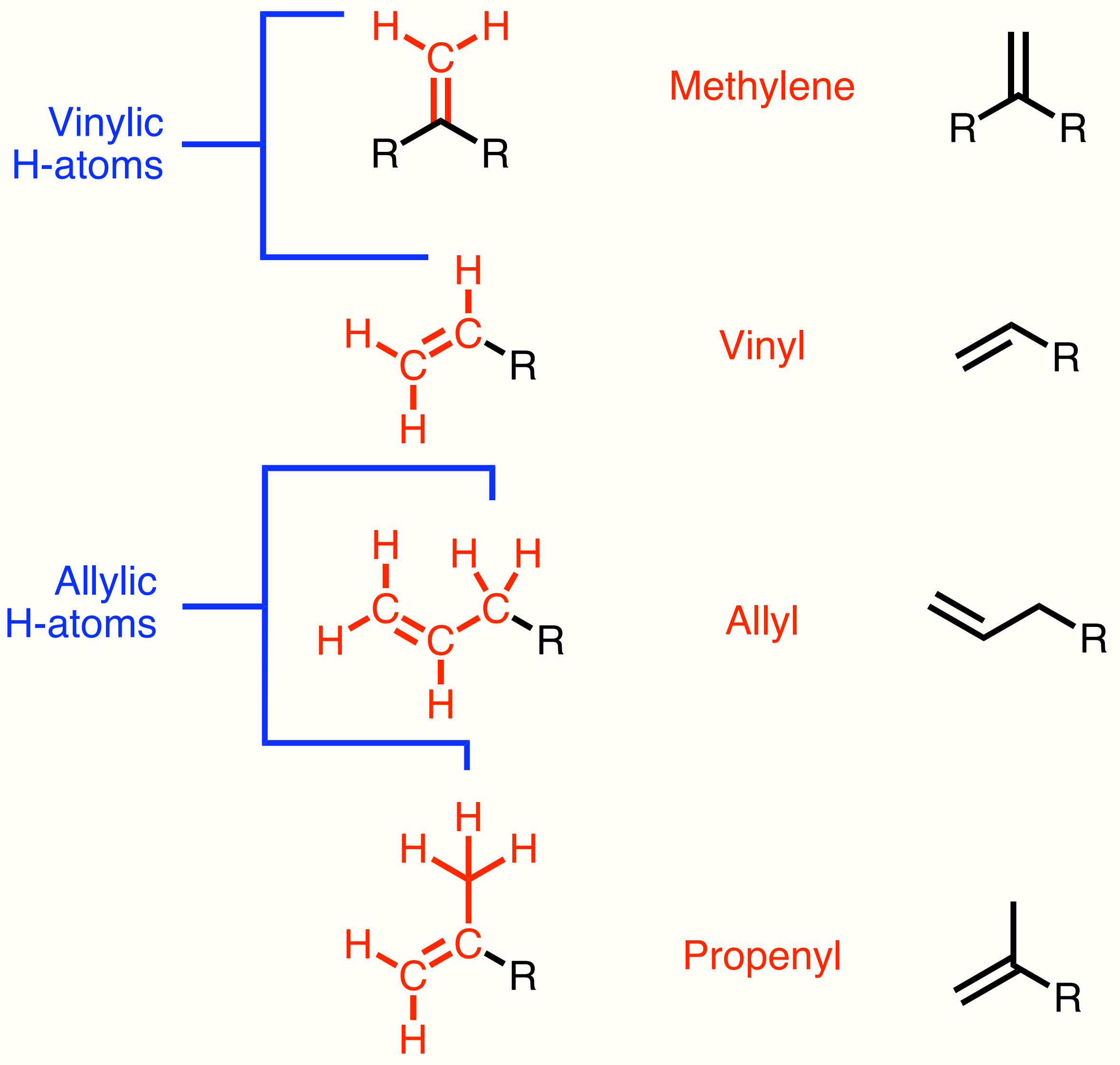
IUPAC Functional Group Priorities for Numbering Longest Chains

Increasing Priority

Priority	Functional Group	Suffix	Substituent Name
3	halide	n.a.	halo
3	alkane	-ane	alkyl
2	alkene	-ene	-en (or alkenyl)
1	alcohol (-OH)	-ol	hydroxy

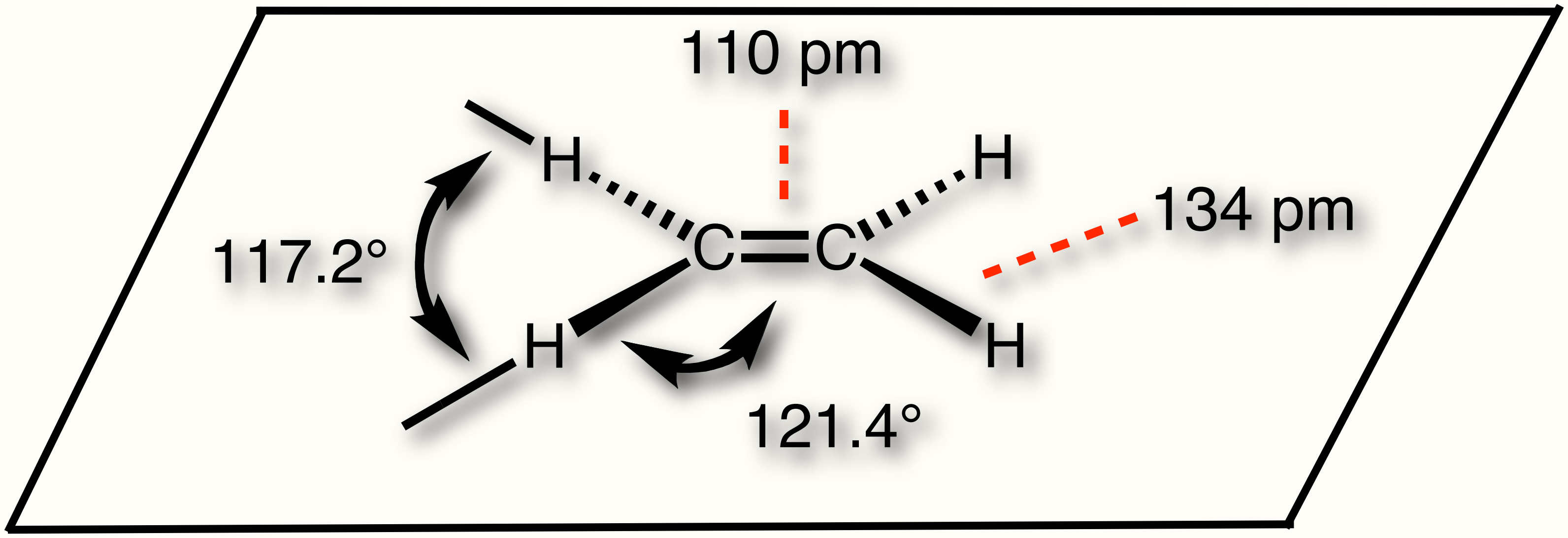
We will add to this table as we encounter more functional groups in IUPAC nomenclature.

Common Alkenyl Group Names

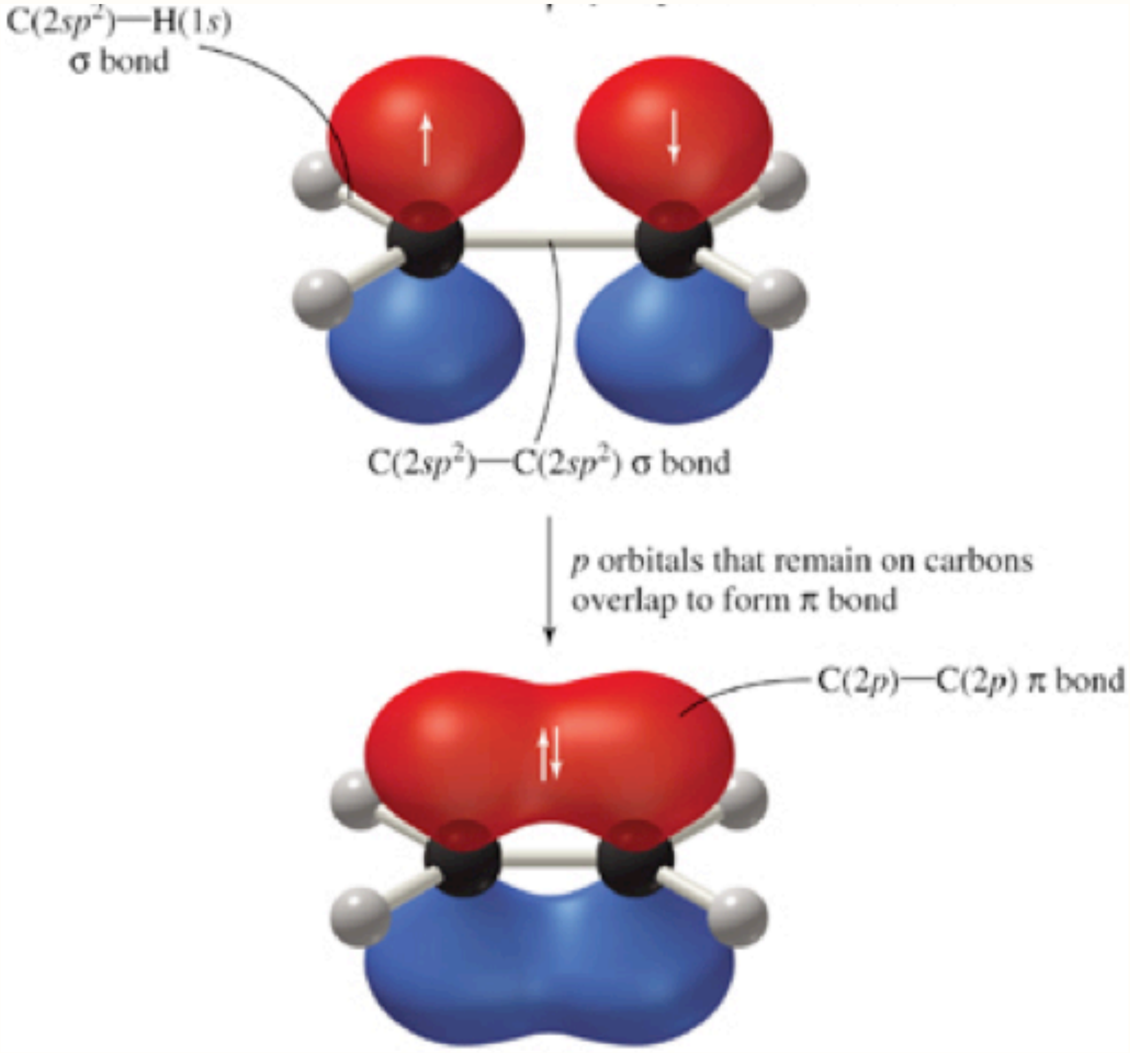


Alkene Structure & Bonding

- carbons in an alkenes are sp^2 hybridized
- bond angles are ~120° around sp^2 hybridized carbons
- geometry around sp^2-carbons is planar (flat)



Double Bond = 1 π-Bond + 1 σ-Bond

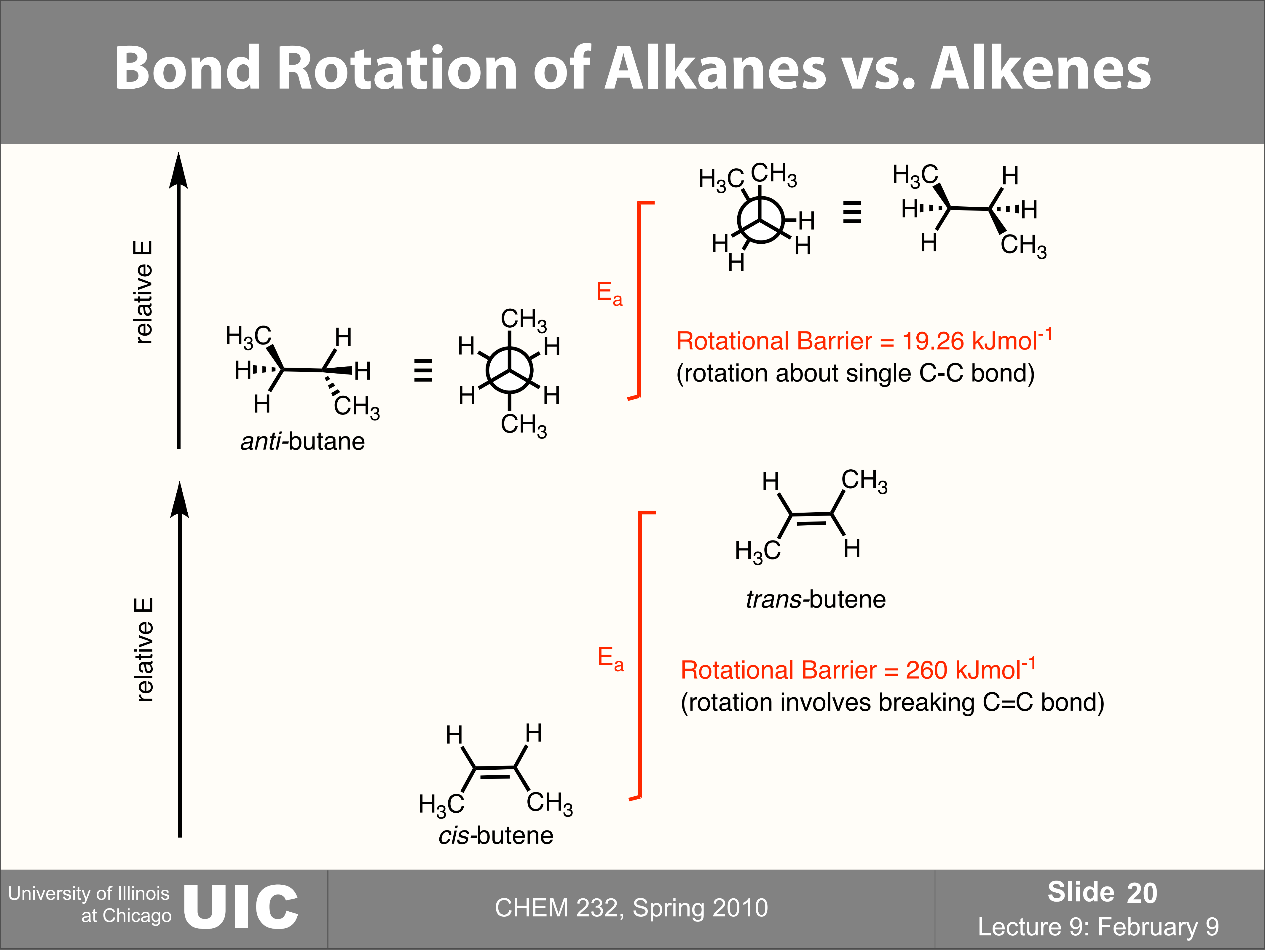


A double bond is formed by two orbital overlaps

1 pi (π) bond
side-to-side overlap
of two p-orbitals;
2 π-electrons

1 sigma (σ) bond
head-to-head overlap
of two sp^2-orbitals

Bond Rotation of Alkanes vs. Alkenes



anti-butane

Rotational Barrier = 19.26 $kJmol^{-1}$
(rotation about single C-C bond)

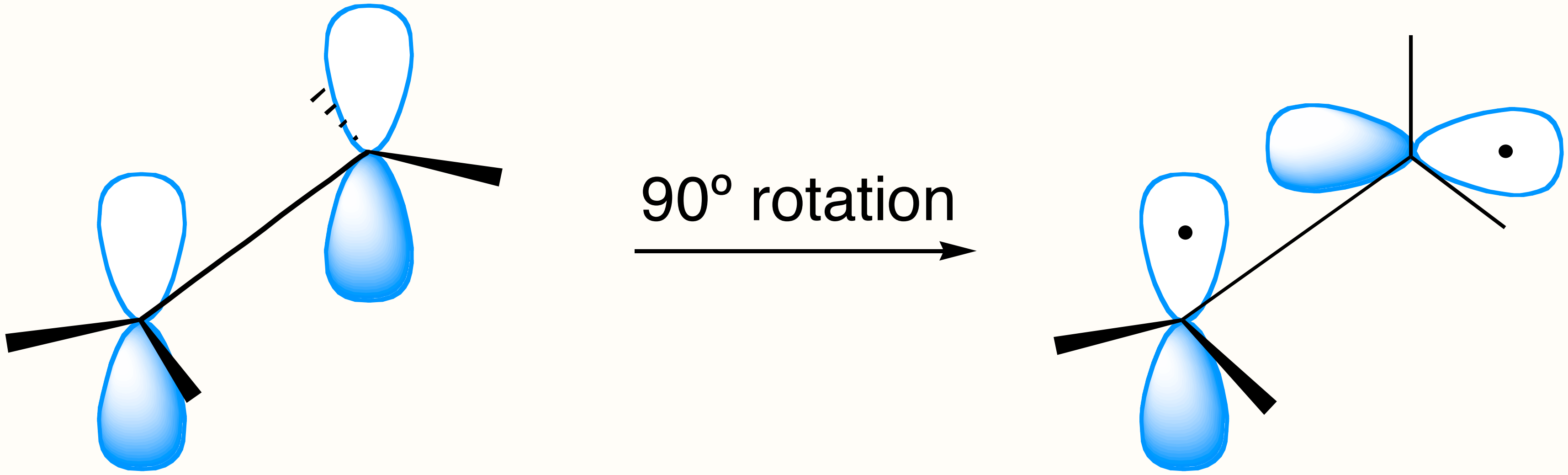
trans-butene

Rotational Barrier = 260 $kJmol^{-1}$
(rotation involves breaking C=C bond)

cis-butene

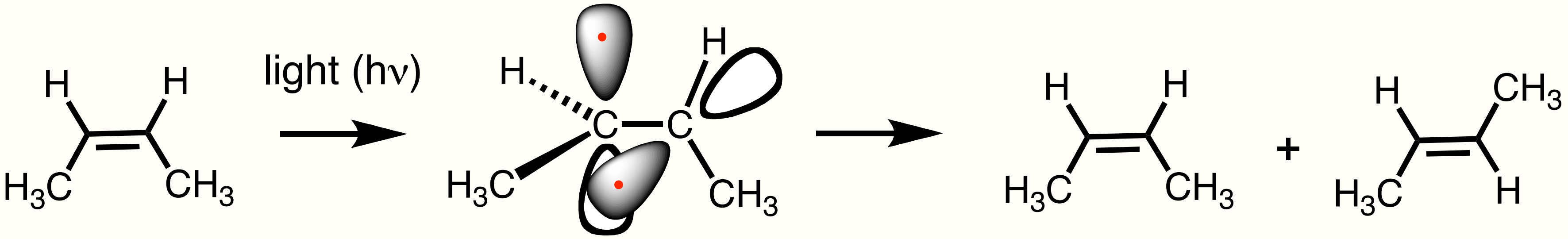
Note that while rotation around C=C bonds is restricted, rotation about the C–H and C–C single bonds is not.

Alkenes Resist Rotation Round C=C Bond



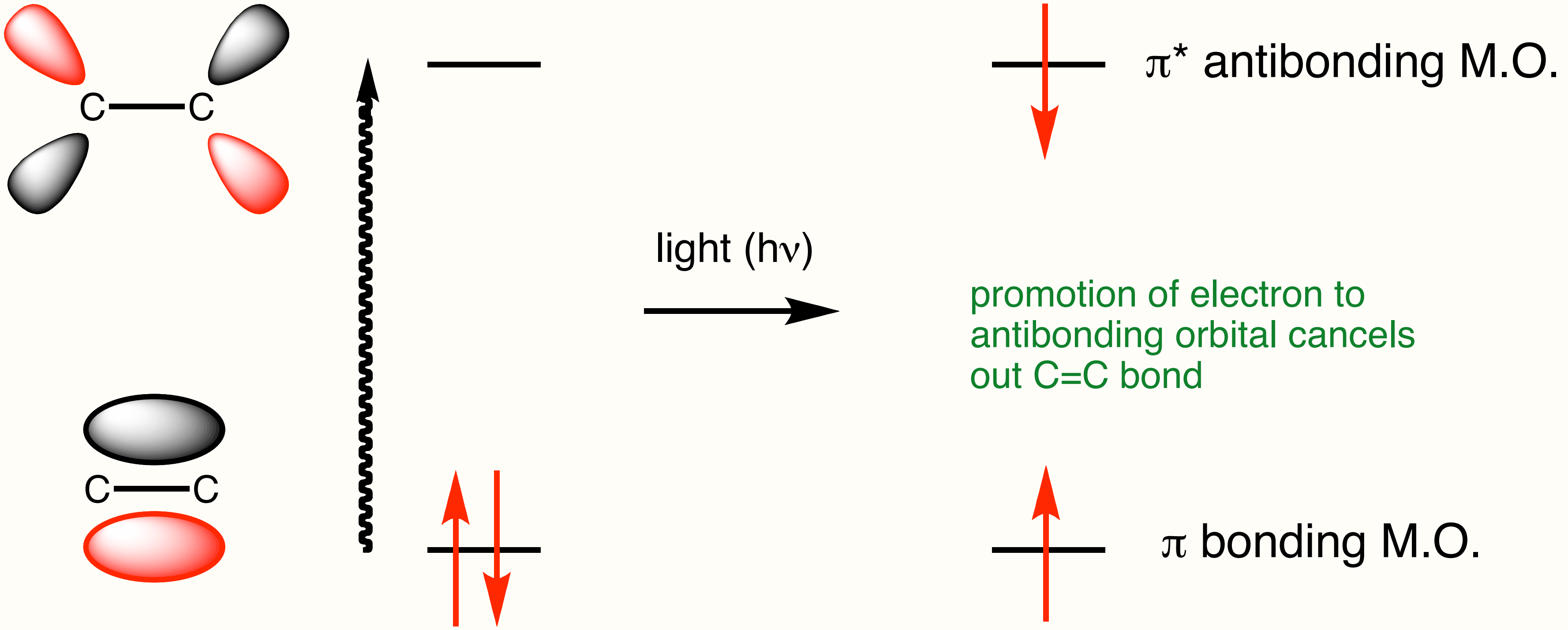
- π-bond prevents full rotation around double bond
- 90° rotation would break π-bond to generate *diradical*
- substituents on alkene "locked" in spacial relationships
- some rotation is possible through pyramidalization (more on this topic later)

Photolysis Mediates C=C Bond Rotation



diradical has C-C single bond

mixture of *cis* and *trans*



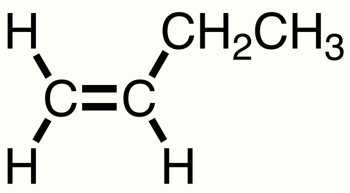
π* antibonding M.O.

light (hν)

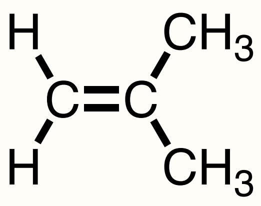
promotion of electron to antibonding orbital cancels out C=C bond

π bonding M.O.

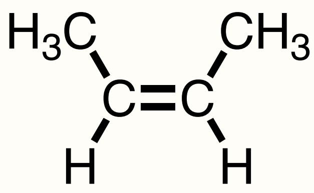
Geometrical Stereoisomers of Alkenes



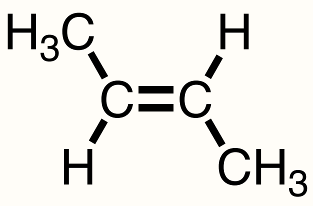
1-Butene



2-Methylbutene

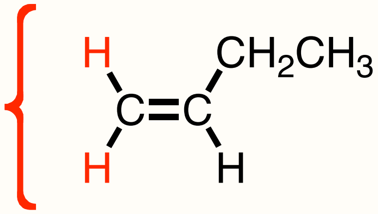


cis-2-Butene



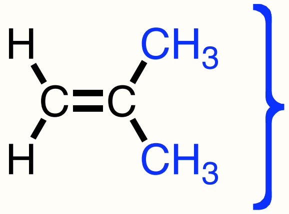
trans-2-Butene

Identical



1-Butene

No possible stereoisomers

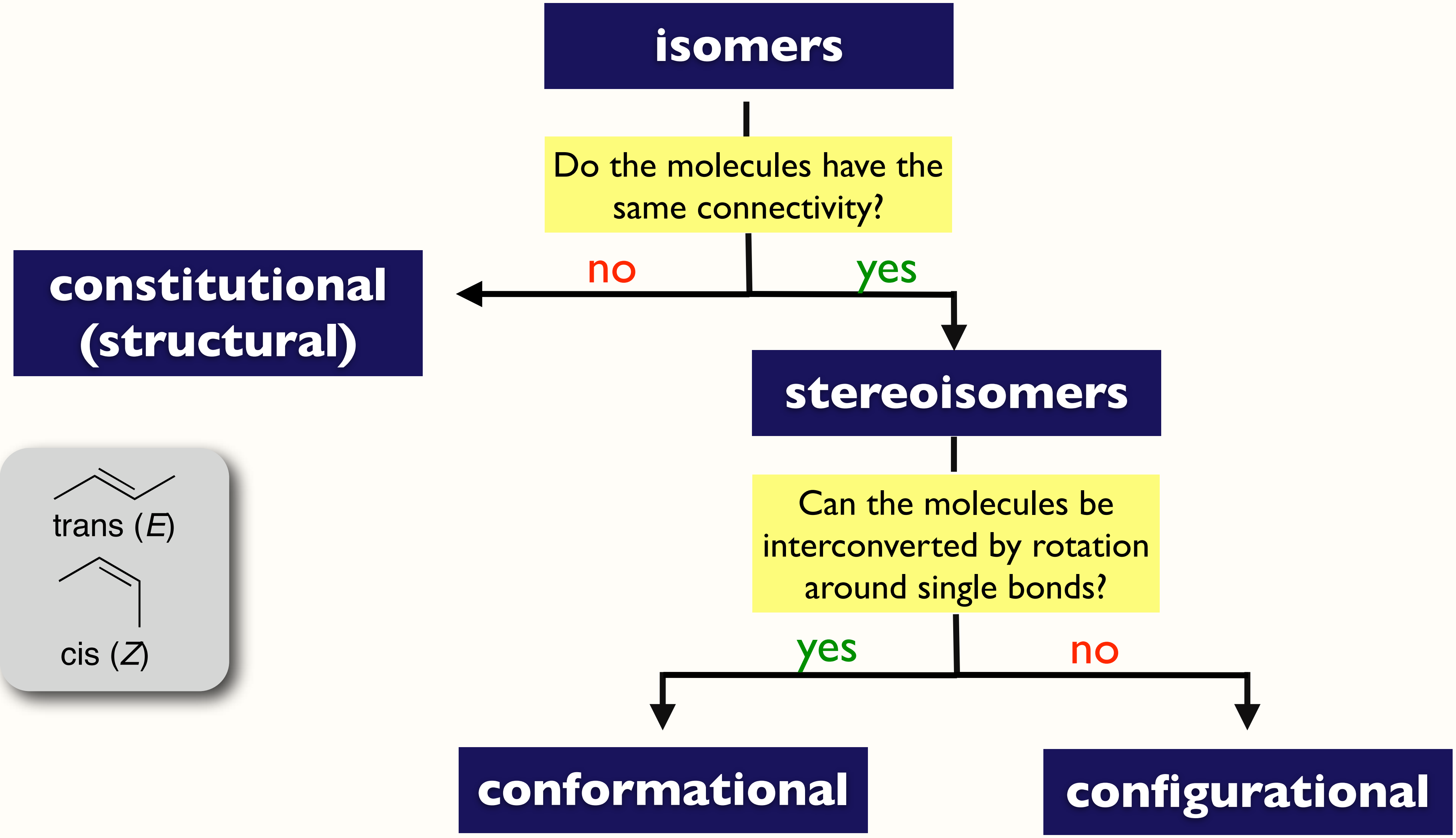


2-Methylbutene

Identical

- restricted rotation around double bond gives *cis* and *trans* geometrical isomers (stereoisomers)
- *cis* and *trans*: relationship between <u>two</u> vicinal groups on alkene
- *cis*: same side; *trans*: opposite sides

Constitutional vs. Configurational Isomers



isomers

Do the molecules have the same connectivity?

no

constitutional (structural)

yes

stereoisomers

Can the molecules be interconverted by rotation around single bonds?

yes

conformational

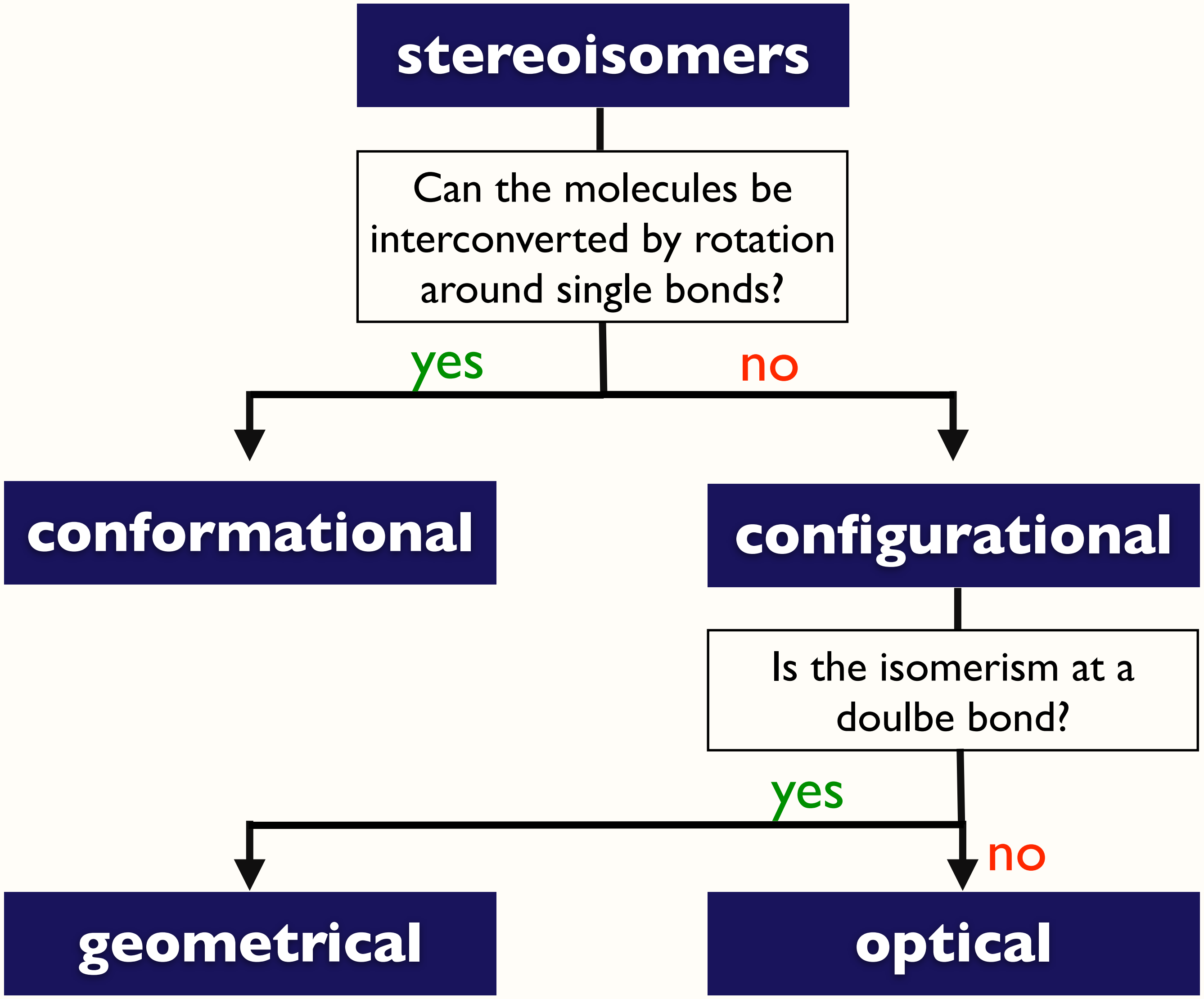
no

configurational

trans (*E*)

cis (*Z*)

Stereoisomers



stereoisomers

Can the molecules be interconverted by rotation around single bonds?

yes

no

conformational

configurational

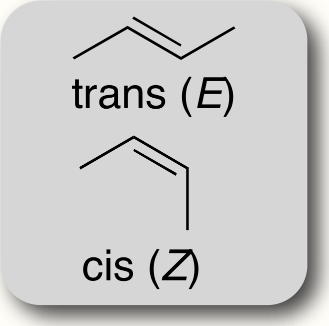
Is the isomerism at a doulbe bond?

yes

no

geometrical

optical

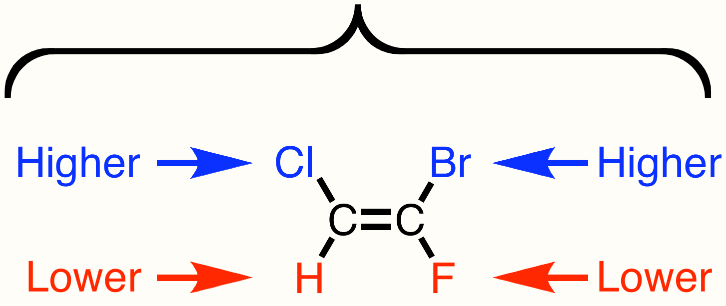


trans (*E*)

cis (*Z*)

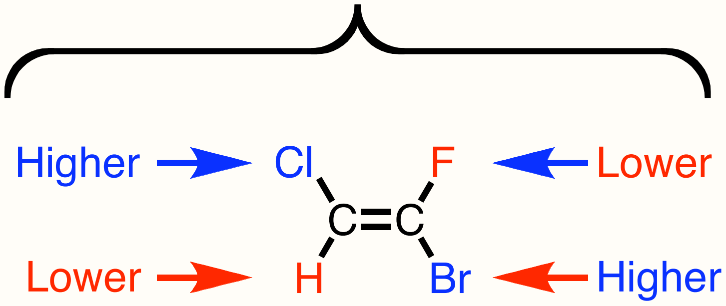
E-*Z* Nomenclature for Alkenes

Higher ranked
substitutuents on the
same side



Z configuration

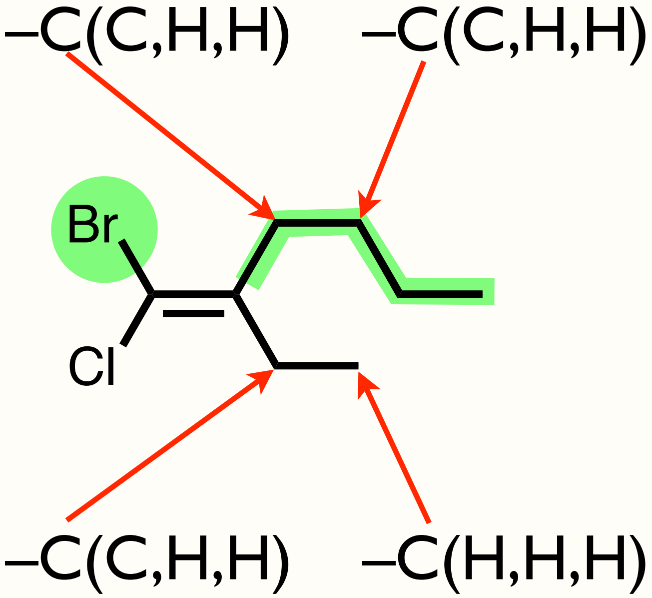
Higher ranked
substitutuents on the
opposite side



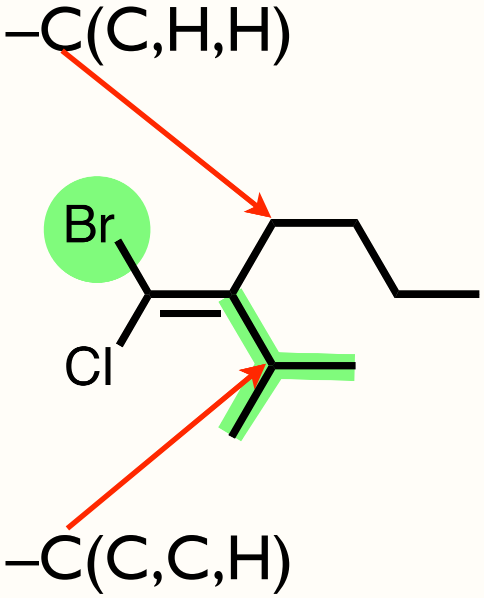
E configuration

- Groups are ranked according to atomic number
- Higher atomic number = higher rank
- *Z* (zusammen) = together; highest priority group on each alkene carbon on same side
- *E* (entgegen) = opposite; highest priority group on each alkene carbon on opposite sides

Cahn-Ingold-Prelog (CIP) Rules for Prioritizing



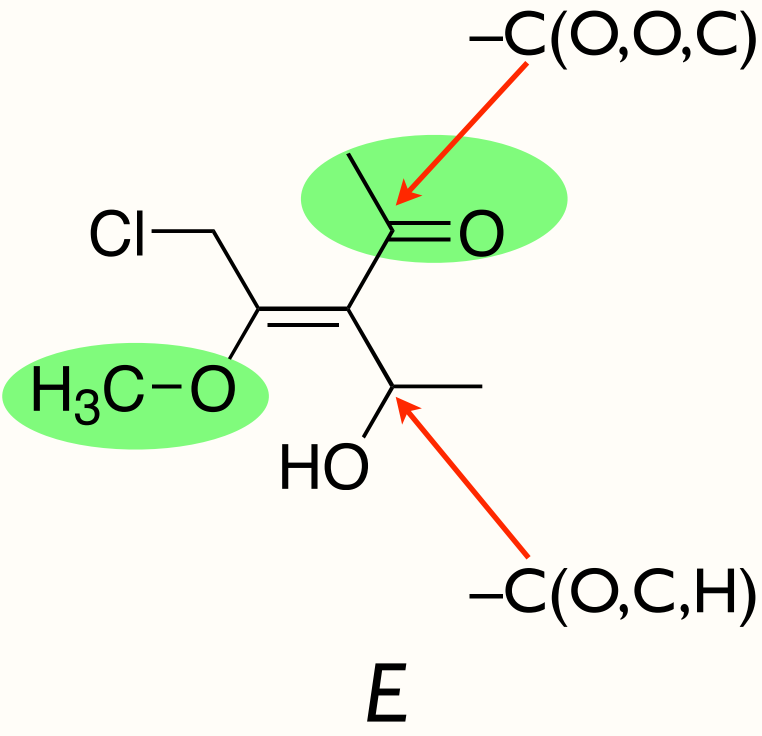
Z



E

- when geminal atoms are identical, compare "forward" atoms attached to these on the basis of atomic weight (list in decreasing order)
- work outward (one atom at a time) until point of difference is reached

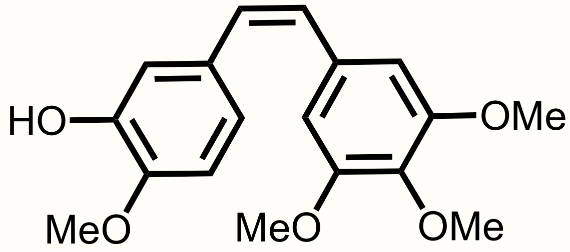
Cahn-Ingold-Prelog (CIP) Rules for Prioritizing



- an atom that is multiply bonded to another atom is listed as two separate atoms for nomenclature purposes
- remember to list attached atoms in decreasing order of atomic weight
- highest priority = highest atomic weight at first point of difference

Why Alkene Geometry Matters

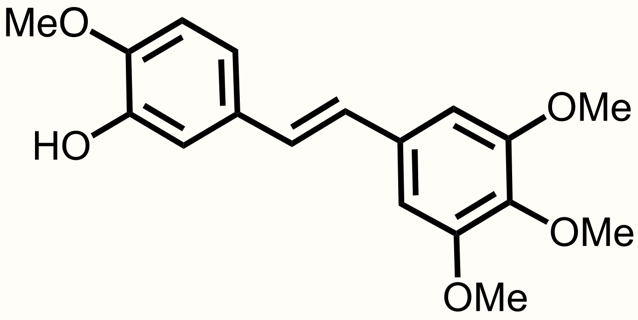
Geometry influences molecular shape and, in turn, physical, chemical & biological properties. . . .



Combretastatin A4 (CA-4)

Z Configuration

Vascular targeting agent



epi-Combretastatin A4 (CA-4)

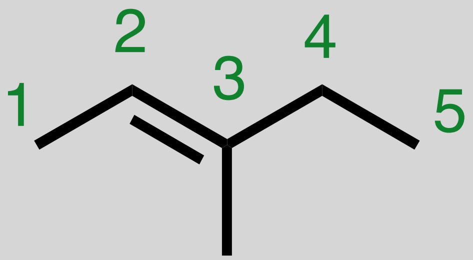
E Configuration

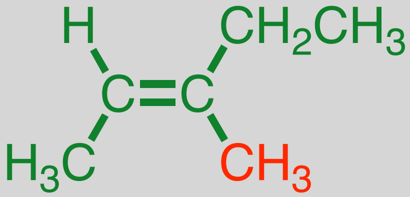
Biologically Inactive!

Combretum caffrum

S.A. bush willow tree

IUPAC: Stereoisomeric Alkenes





(E)-3-methyl-2-pentene or *(E)*-3-methylpent-2-ene

Steps:

1. Number the longest chain.
2. Replace -ane ending of parent alkane with -ene or -en, depending on priority.
3. In the name, list the locant of only the first alkene carbon.
4. Indicate geometrical isomers with (*Z*) or (*E*) at the beginning of the name.

Conventions/Rules:

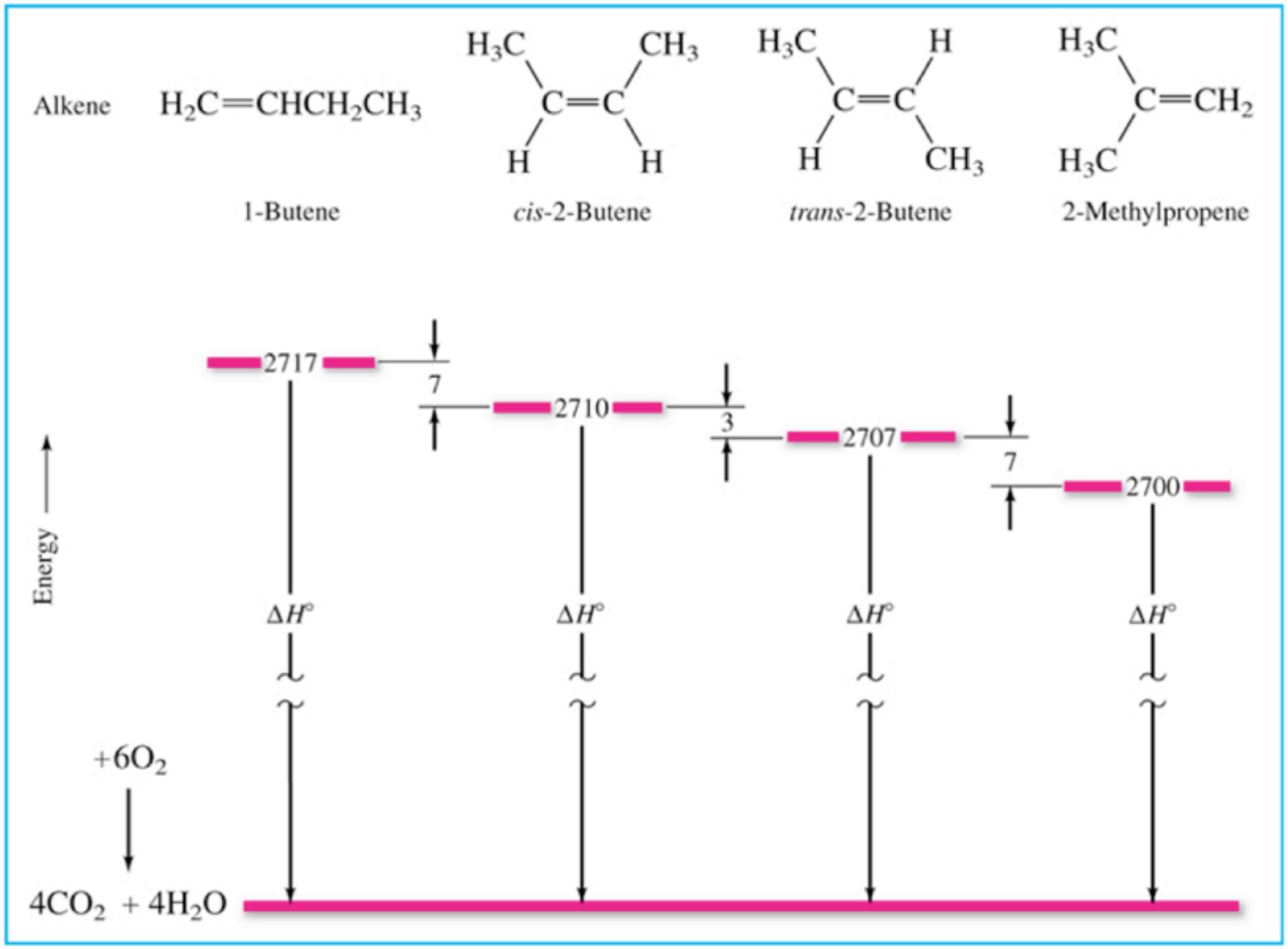
- *Z* and *E* are italicized
- *Z* and *E* are placed within parentheses at beginning of name: (*Z*) & (*E*).
- *cis* and *trans* may be substituted for E/Z when alkene is 1,2-disubstituted

"(*E*)" "(*Z*)" — **parent base** — **alkene locant** — **"ene"**

Relative Stabilities of Alkenes

Sections 5.5-5.6

Relative Stabilities of Alkenes



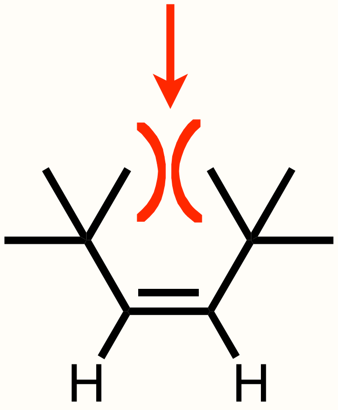
Observations:

- more stable = lower in energy = lower heat of combustion
- *cis* alkenes higher in energy than *trans* alkenes
- more alkyl group on alkene = more stable

Relative Stabilities of Alkenes

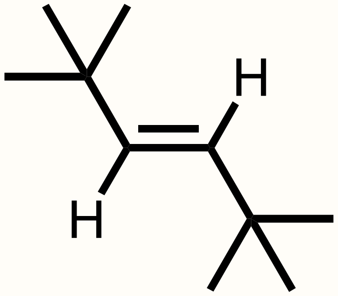
1. Steric Effects

van der Waals strain strain
between *cis* groups



(*Z*)-2,2,5,5-tetramethylhex-3-ene

(less stable)



(*E*)-2,2,5,5-tetramethylhex-3-ene

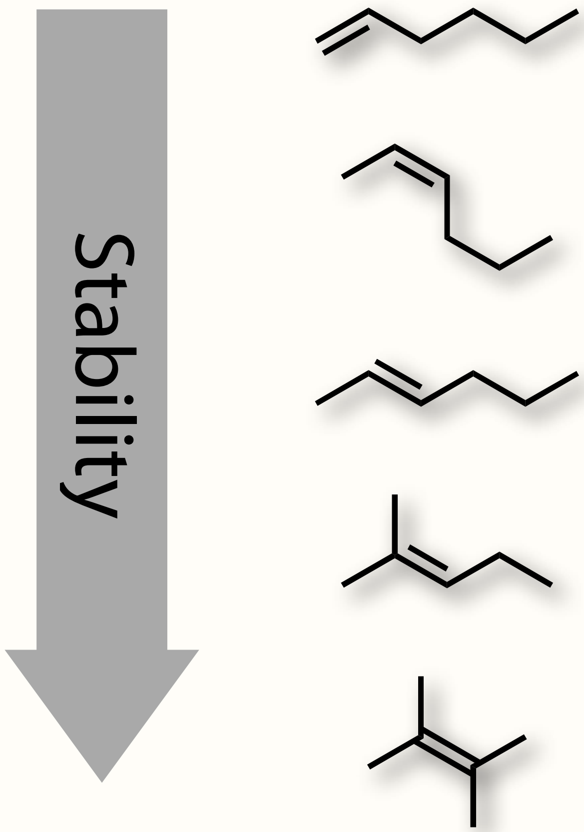
(more stable)

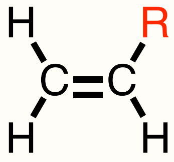
Energy Difference = 44 kJmol^{-1}

Relative Stabilities of Alkenes

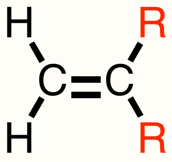
2. Substituent Effects

alkyl groups stabilize alkenes through donation (via induction and hyperconjugation) to the more electronegative sp^2-hybridized carbon atoms

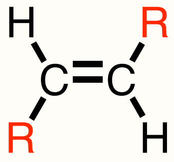




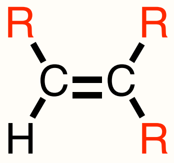
monosubstituted



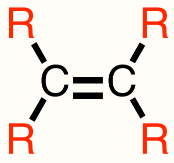
geminally disubstituted



vicinally disubstituted



trisubstituted



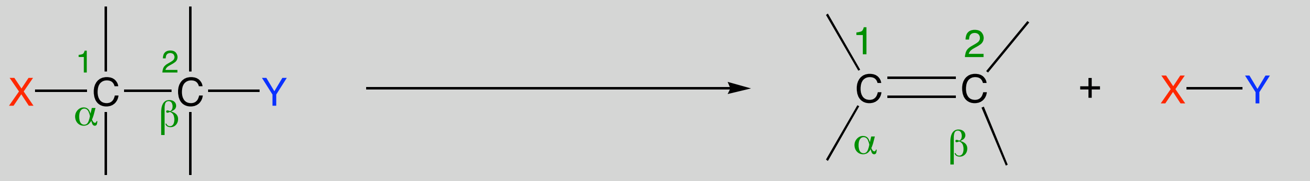
tetrasubstituted

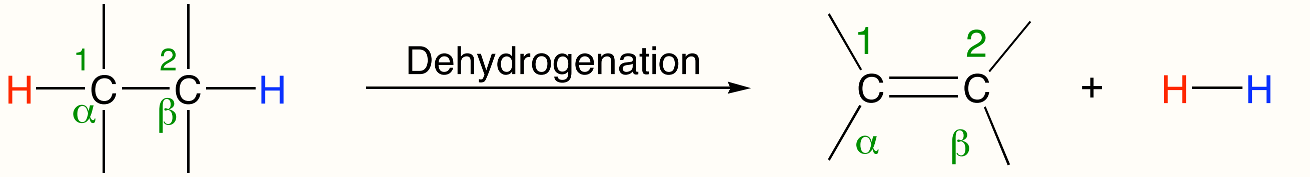
Preparation of Alkenes
Elimination

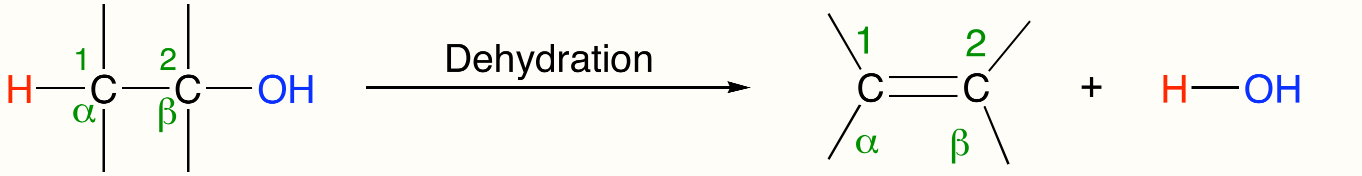
Sections: 5.8-5.11

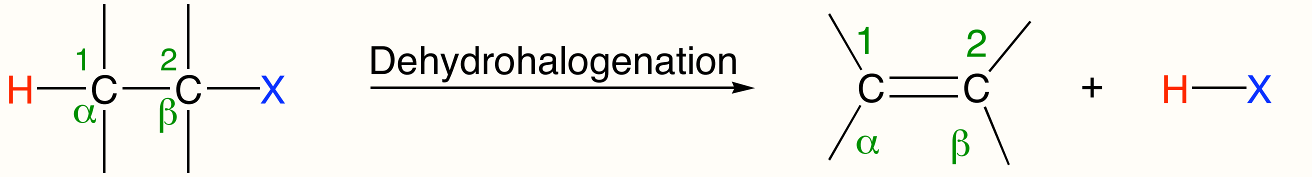
β-Elimination Reactions

Summary of β-Elimination (1,2-elimination) Reactions









Dehydrogenation

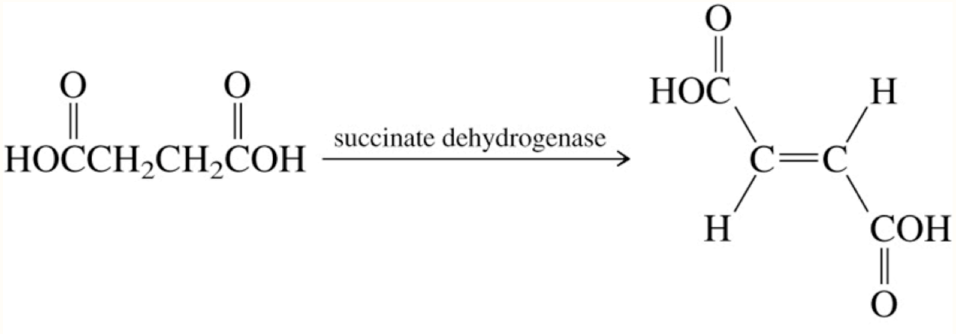
- limited to industrial synthesis of ethylene, propene, 1,3-butadiene and styrene
- important economically, but rarely used in laboratory-scale syntheses
- living systems utilize enzymes to catalyze this process

$$CH_3CH_3 \xrightarrow{750°C} H_2C{=}CH_2 + H_2$$

Ethane Ethylene Hydrogen

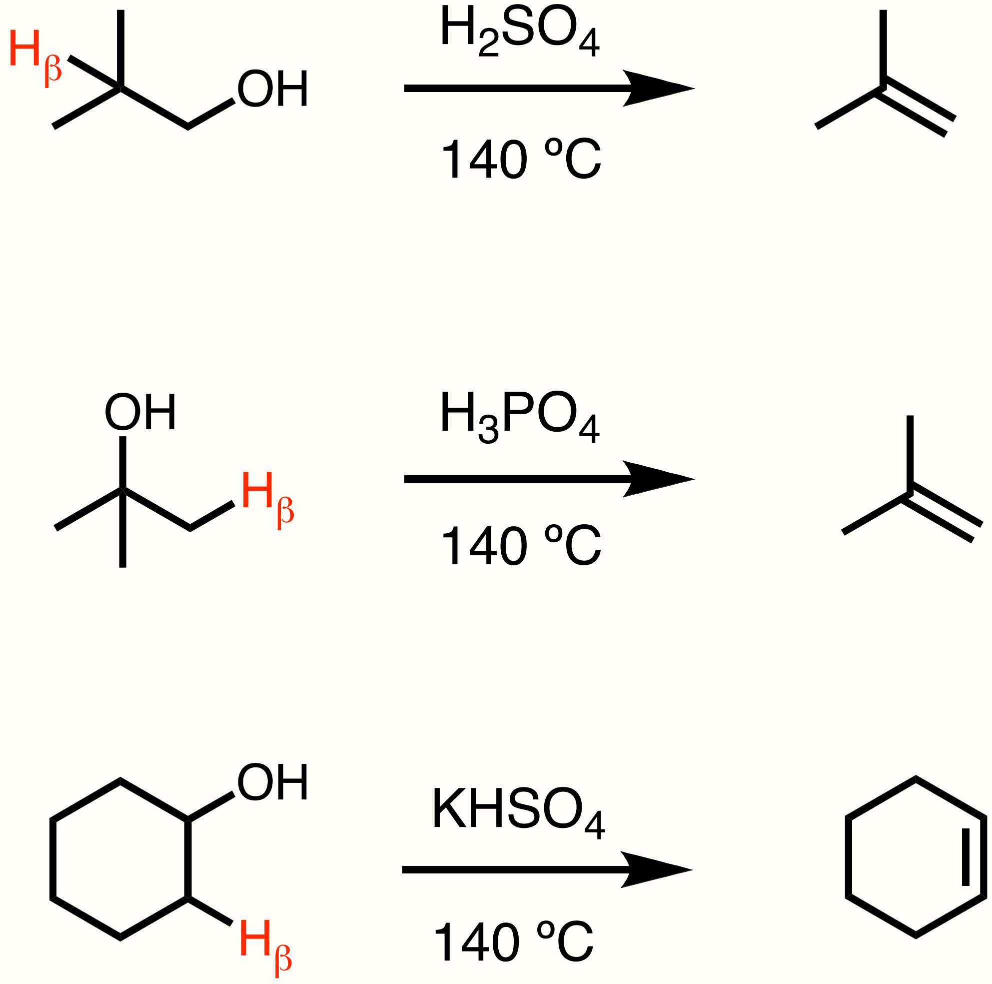
$$CH_3CH_2CH_3 \xrightarrow{750°C} CH_3CH{=}CH_2 + H_2$$

Propane Propene Hydrogen



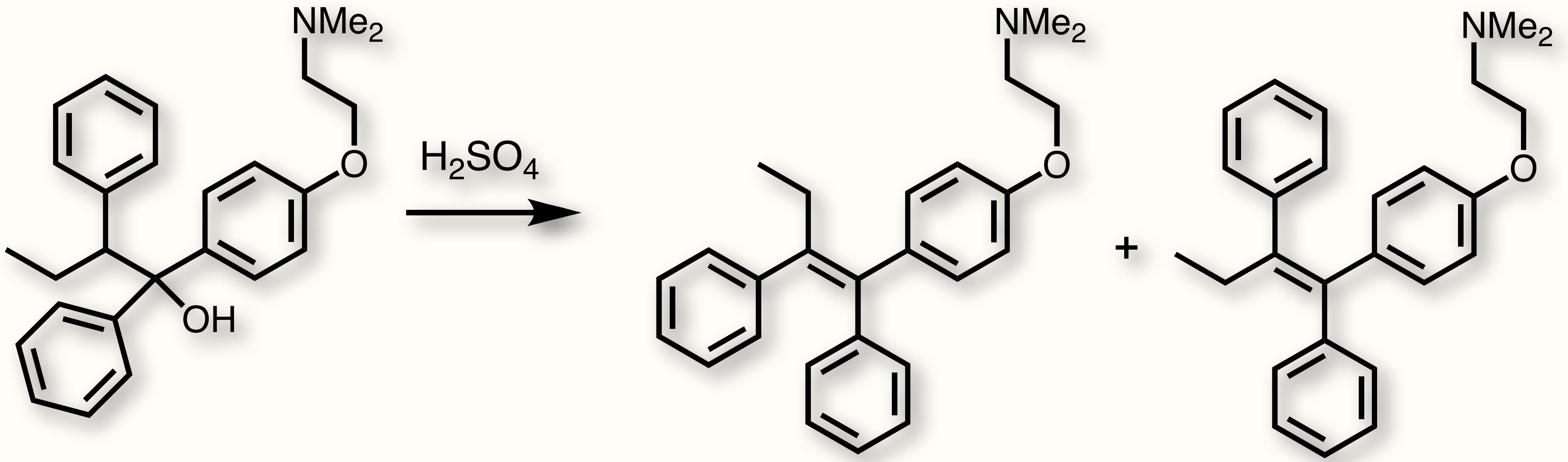
Succinic acid Fumaric acid

Strong Acids Catalyze the Dehydration of 2° & 3 ° Alcohols

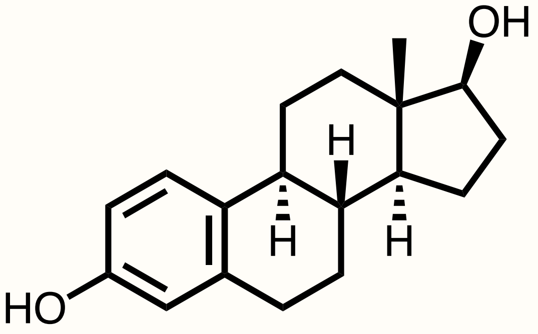


- H_2SO_4 and H_3PO_4 are most common acids used for dehydration: *protonation of OH group is first step*
- dehydration is reversible (hydration) in aqueous acid (Chapter 6)

Industrial Example of Dehydration



Tamoxifen (Nolvadex®)

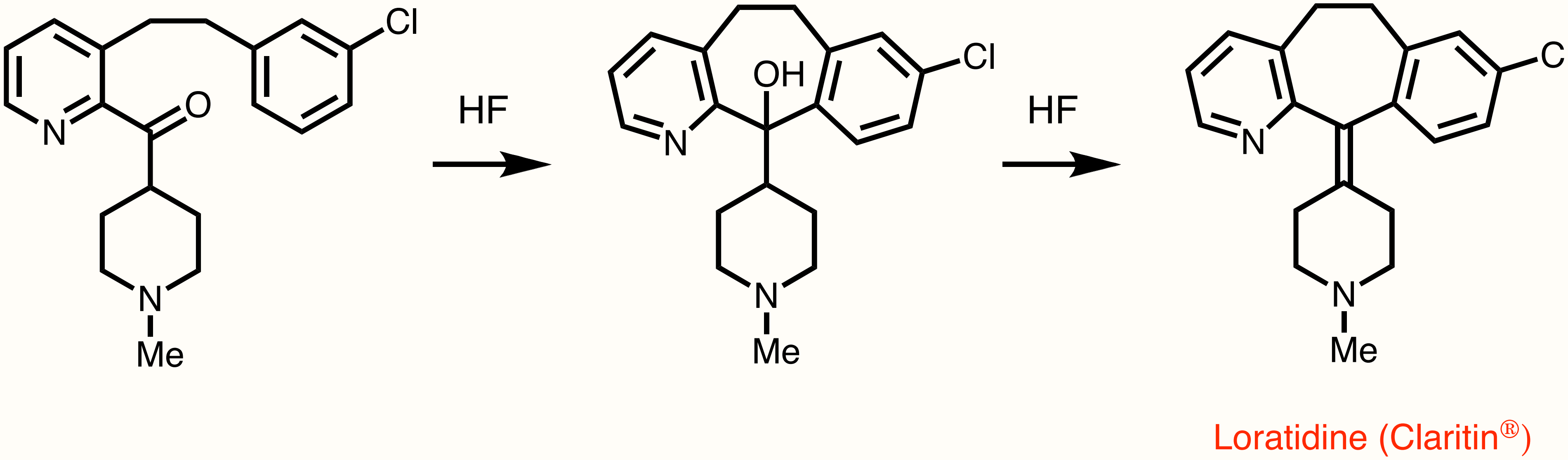


Estradiol

Tamoxifen mimics estrogens, such as estradiol, and inhibits their binding to the estrogen receptor in breast tissue

Tamoxifen blocks cancer cell growth

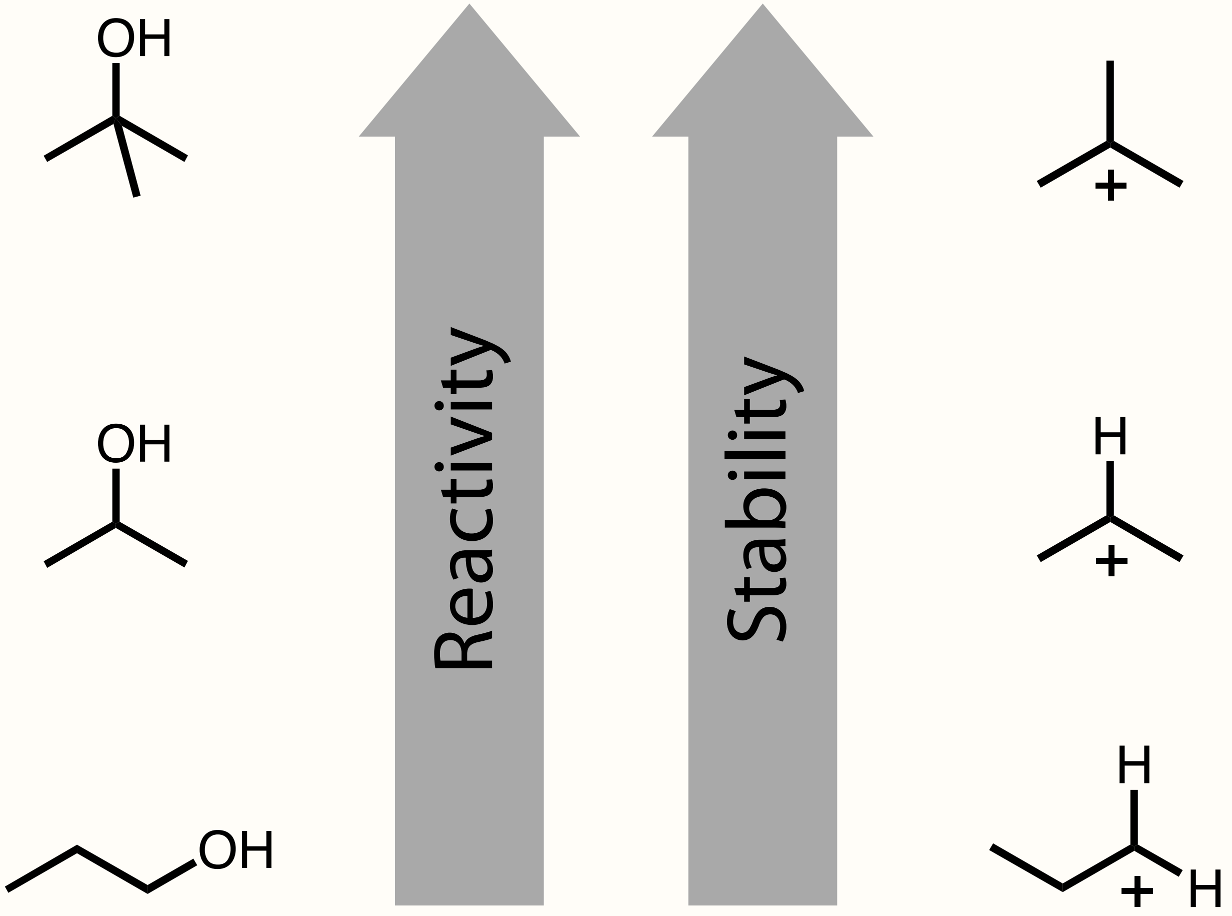
Dehydration can be "Coupled" with Other Chemical Transformation



Two-step, one-pot transformation involves a Friedel-Crafts reaction (see, Chapter 12) and dehydration of the resulting 3° alcohol

Rate of Alcohol Dehydration Mirrors Ease of Carbocation Formation

rate of dehydration = 3° > 2° > 1° alcohol



Reactivity

Stability

tertiary alcohol (3°)

secondary alcohol (2°)

primary alcohol (1°)

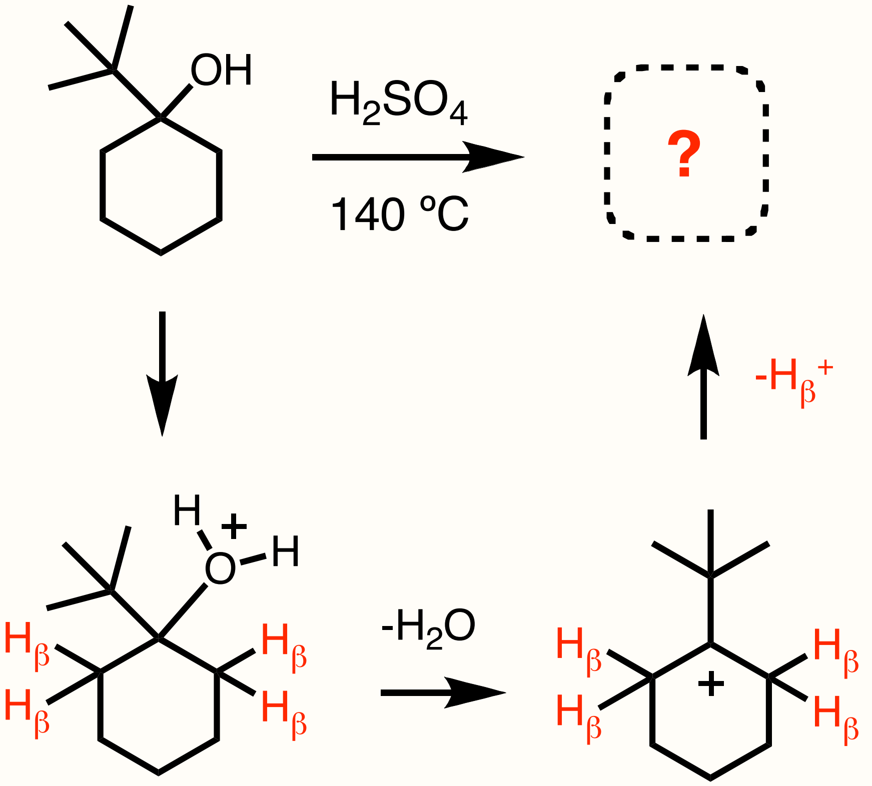
tertiary cation (3°)

secondary cation (2°)

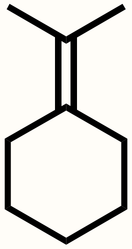
primary cation (1°)

Self Test Question

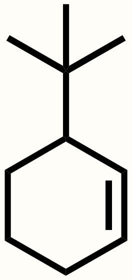
Predict the product for the following reaction scheme.



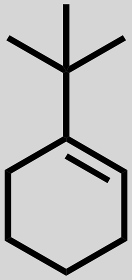
A.



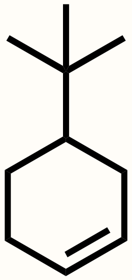
B.



C.



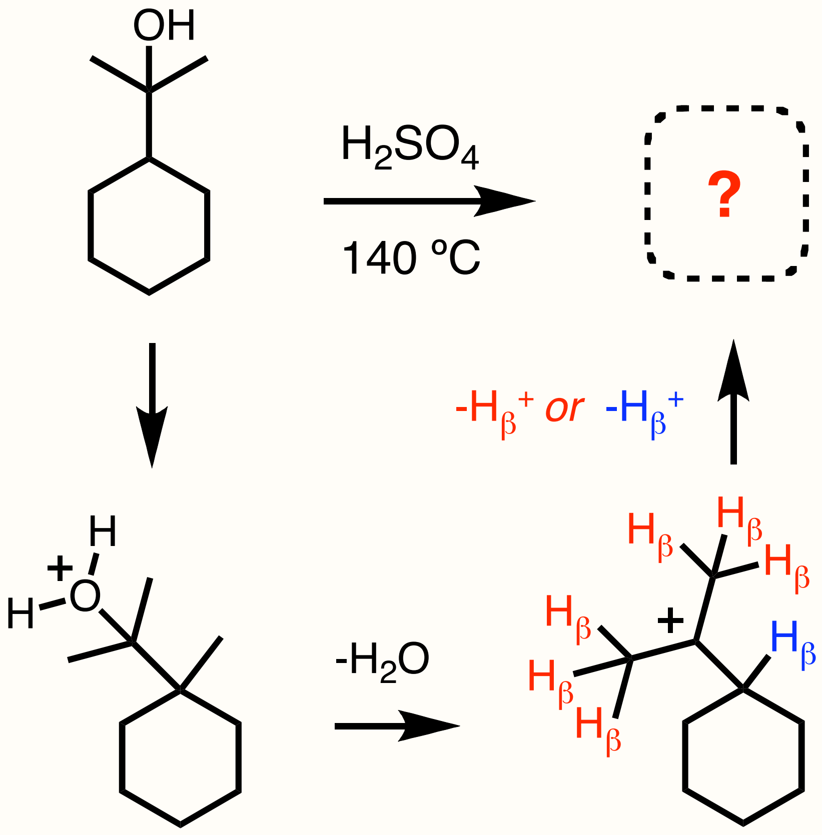
D.

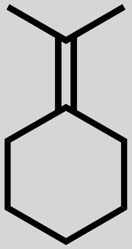


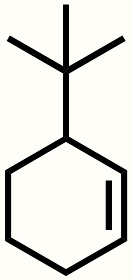
E. no reaction

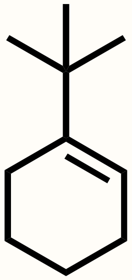
Self Test Question

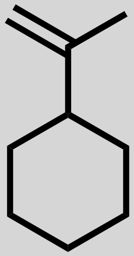
Predict the product for the following reaction scheme.



A.


B.


C.


D.


E. no reaction

Quiz This Week

- Topic = Chapter 4
- Bonding in Alcohols & Alkyl Halides
- Bonding of Alkyl Halides from Alcohols & HX
- The S_N1 & S_N2 Mechanisms
- Carbocations: Structure, Bonding & Stability
- Halogenation of Alkanes
- Radicals: Structure, Bonding & Stablity
- Mechanism of Alkane Halogenation

Next Lecture. . .

Chapter 5: Sections 5.12-5.18

Reminder - Bring ID to Exam!