

Stereoisomers as Reactants

- We are often interested in the differences in *reactivity* of various chemical compounds. Usually, we express the differences in reactivity in terms of the *rates* of the reactions. How is the rate of a reaction related to the energies of the reactant, the transition state, and the product?

- We can make several generalizations about rates of reactions involving various stereoisomers. Can you explain why each of these generalizations is true?

Compounds that are diastereomers may react at different rates with any reagents.

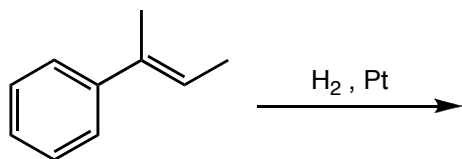
Compounds that are enantiomers must react at the same rate with *achiral* reagents.

Compounds that are enantiomers may react at different rates with *chiral* reagents.

Reading: Section 7.7

Stereoisomers as Products

- Determine the product of the following reaction:



- Is the product chiral or achiral? Are the reactants and reagents chiral or achiral?
- We can make several generalizations about reactions that form stereoisomeric products. Can you explain why each of these generalizations is true?

Achiral starting materials that give enantiomeric products will yield a racemic mixture.

Achiral starting materials that react in a *chiral* environment (e.g. a chiral catalyst or chiral solvent) may yield different amounts of each enantiomer.

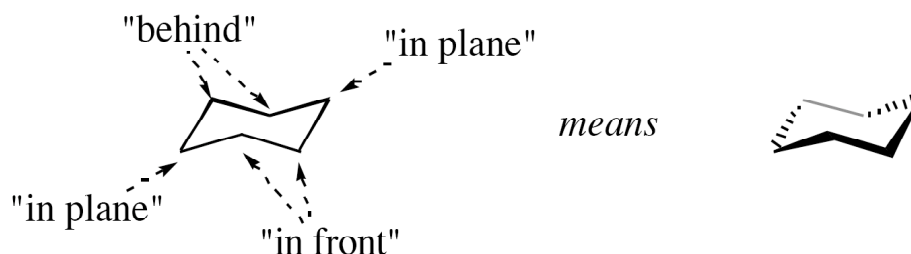
Achiral starting materials that give diastereomeric products may yield different amounts of each diastereomer.

Reading: Section 7.8

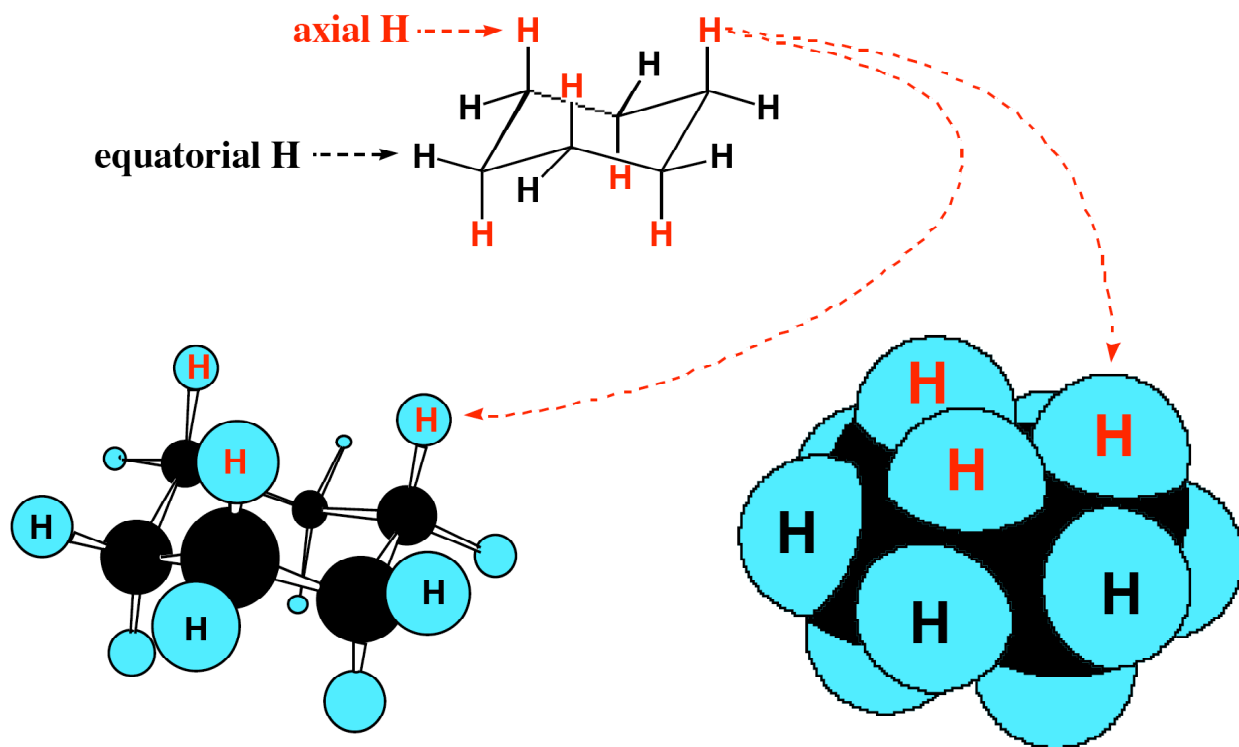
Introduction to Cyclic Compounds: Cyclohexanes

- The most common ring in natural compounds is a **6-membered ring**. Take out your model kits and make a model of cyclohexane:

cyclohexane - chair conformation is most stable...



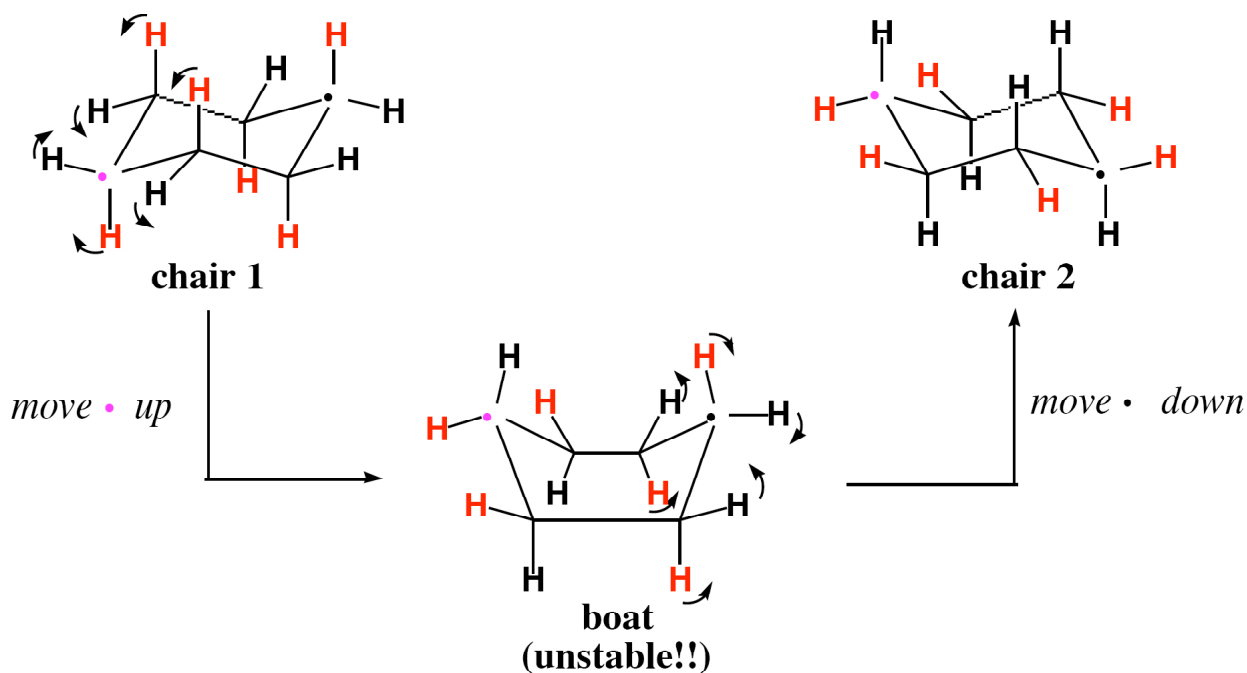
there are 2 "different types of H atoms"



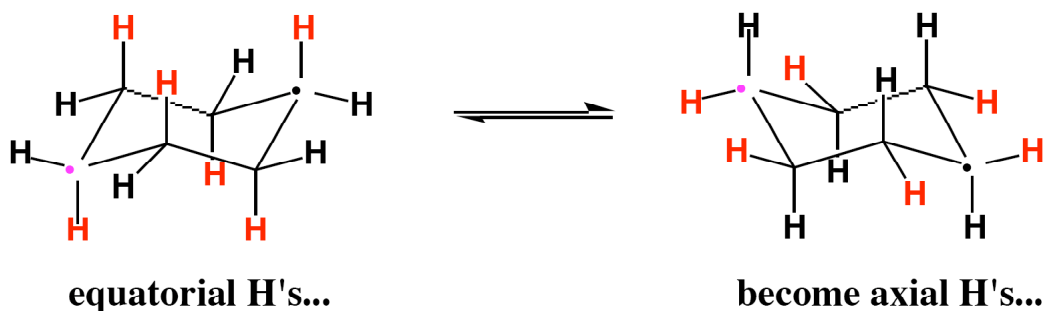
- How should you *draw* the chair conformation of cyclohexane?

Reading: Section 7.2

Cyclohexanes: Interconversion of Chair Conformations



Effectively the 2 chairs are in rapid equilibrium



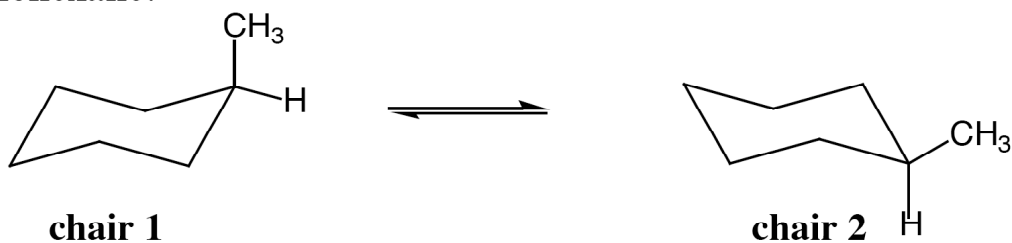
this equilibrium is very important for substituted cyclohexanes

- Can you accomplish this “ring flip” with your models?

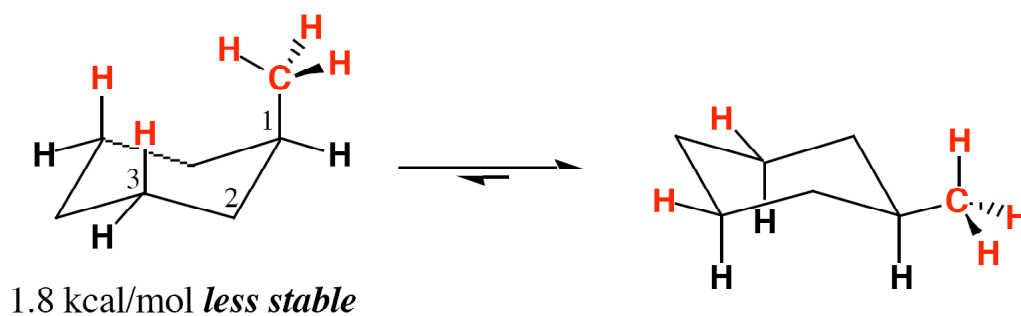
Reading: Section 7.2

Monosubstituted Cyclohexanes: Axial vs. Equatorial

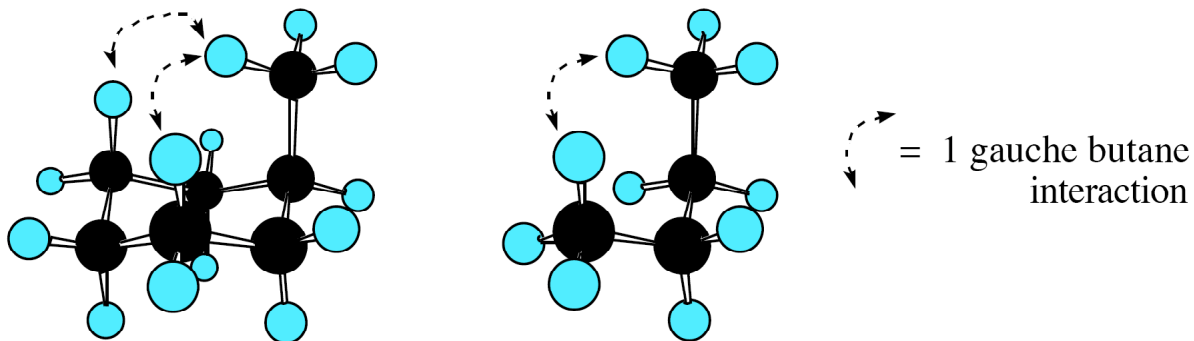
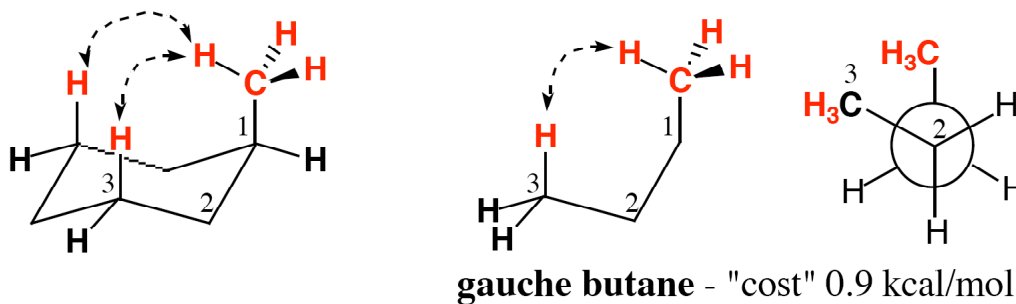
methylcyclohexane:



1,3-diaxial interactions (van der Waals repulsions)



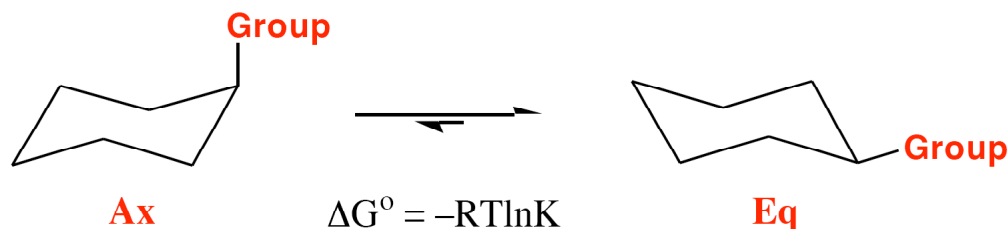
...which is 2 x the "cost" the CH₃ repulsion in gauche butane



Reading: Section 7.3

Energies of Axial vs. Equatorial Substitution

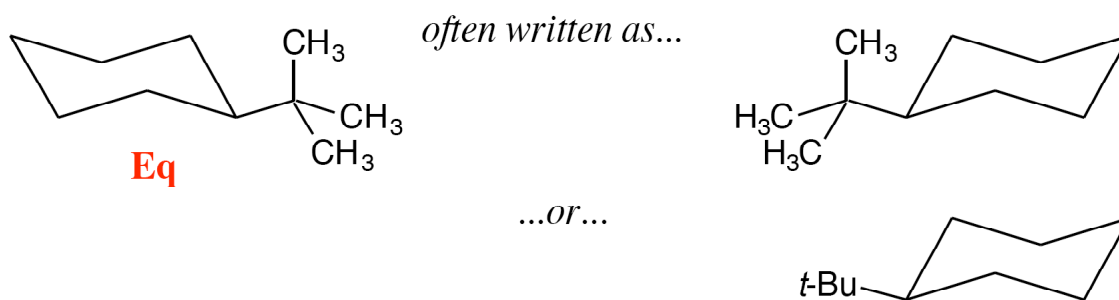
- The relative energy of axial vs. equatorial substitution is called the "*A value*" for that substituent. Generally, bulky substituents have larger A values:



"A Value" = $-\Delta G^\circ$

Group	A Value	K (25 °C)	% Eq
CH ₃	1.8 kcal/mol	21	95%
CH(CH ₃) ₂	2.2 kcal/mol	42	98%
C(CH ₃) ₃	4.8 kcal/mol	3316	99.9%
CH=CH ₂	1.6 kcal/mol	15	94
Cl	0.5 kcal/mol	2.3	70

Notice: A *tert*-butyl group effectively "locks" the chair conformation

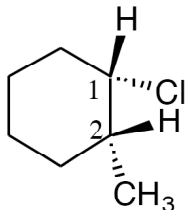


Reading: Section 7.3

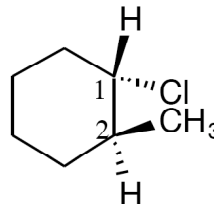
Disubstituted Cyclohexanes

Example: 1-chloro-2-methylcyclohexane

there are 2 possible diastereoisomers

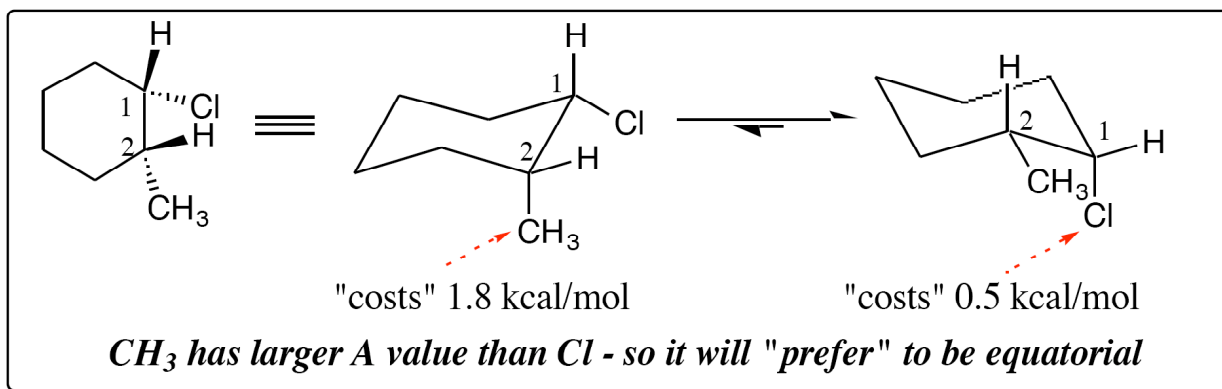
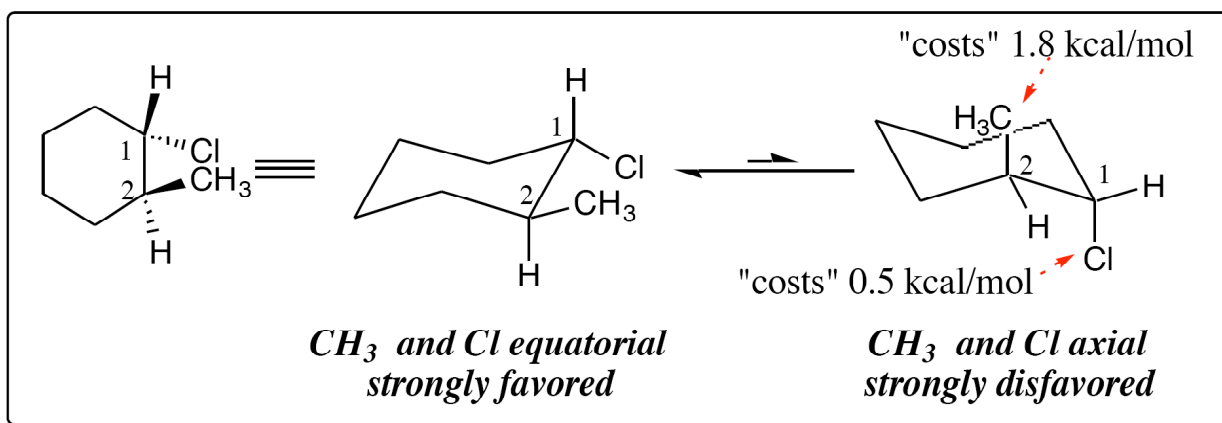


cis-1-chloro-2-methylcyclohexane



trans-1-chloro-2-methylcyclohexane

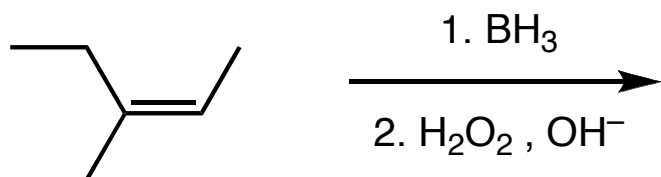
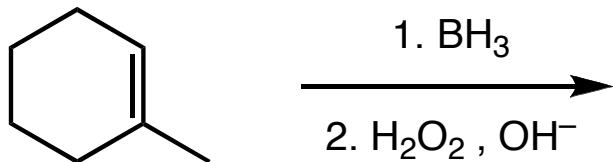
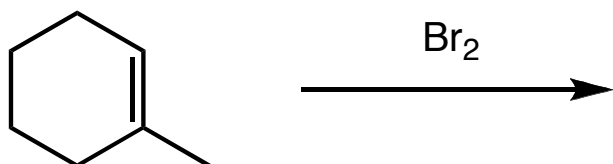
...so what about their conformations??



Reading: Section 7.4

Stereochemistry of Alkene Addition Reactions

- Predict the product(s) of each of the following reactions. Be sure to indicate stereochemistry when relevant!

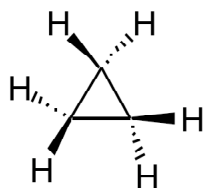


Reading: Section 7.9

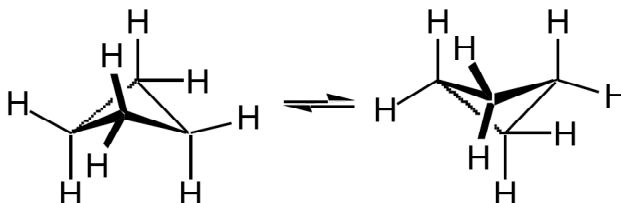
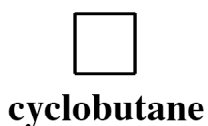
Other Cyclic and Bicyclic Compounds

Other Cyclic Compounds

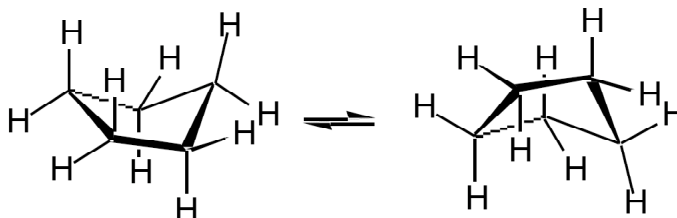
Examples:



planar ring
highly strained
v. reactive



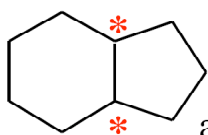
puckered ring
pretty strained
reactive



puckered ring
not strained

Bicyclic compounds

Examples:



bicyclo[4,3,0]nonane

a **fused bicyclic compound**: bridgehead atoms (*) adjacent



bicyclo[2,2,1]heptane

a **bridged bicyclic compound**: bridgehead atoms (*) not adjacent



spiro[4,4]nonane

a **spirocyclic compound**: one common atom (*)

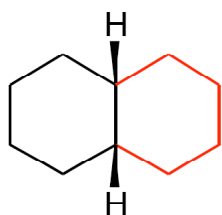
Reading: Sections 7.5 and 7.6

Bicyclic Compounds and Bredt's Rule

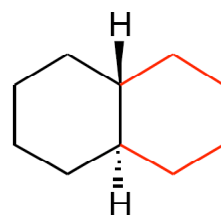
Decalins

Decalin... ..the common name for bicyclo[4,4,0]decane...

...exists as 2 diastereoisomers...

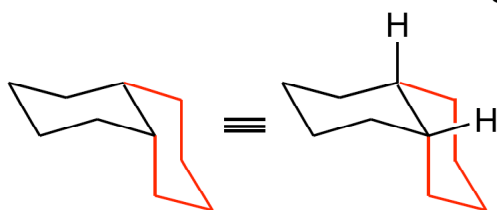


cis-decalin

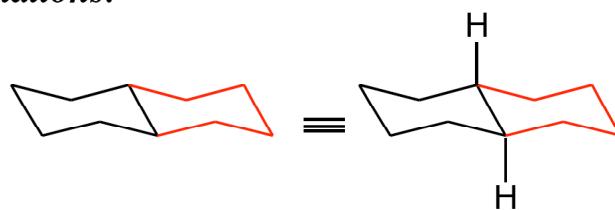


trans-decalin

conformations:



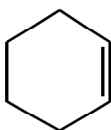
able to undergo ring flip



not able to undergo ring flip

...take out your models and prove this!!

...and while those models are out, prove that *trans*-cyclohexene is likely to be very unstable...



cis-cyclohexene



trans-cyclohexene

...as is a "bridgehead alkene" such as **bicyclo[2,2,1]hept -1(2) -ene** (Bredt's rule)

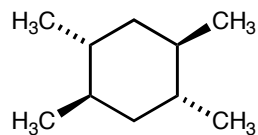
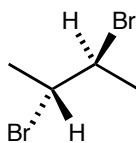
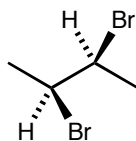
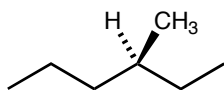


- Why is this "bridgehead alkene" so unstable?

Reading: Section 7.6

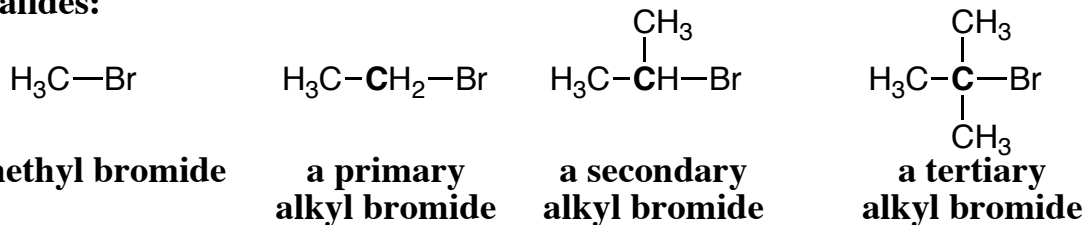
Test Yourself Now!

- For each of the following molecules, identify whether the molecule is chiral or achiral. For molecules that are chiral, assign *R* or *S* configurations to each stereocenter, and draw the enantiomer of the molecule.

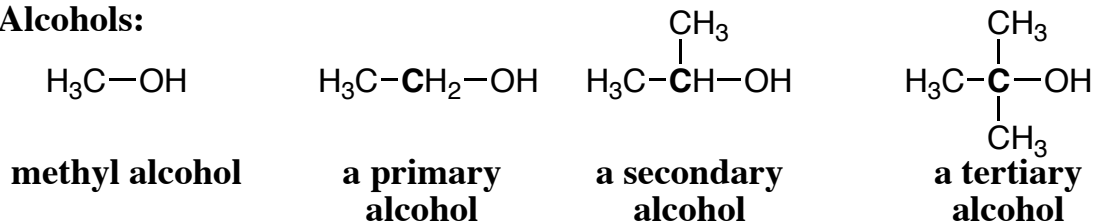


Alkyl Halides, Alcohols, Ethers, Thiols, and Sulfides

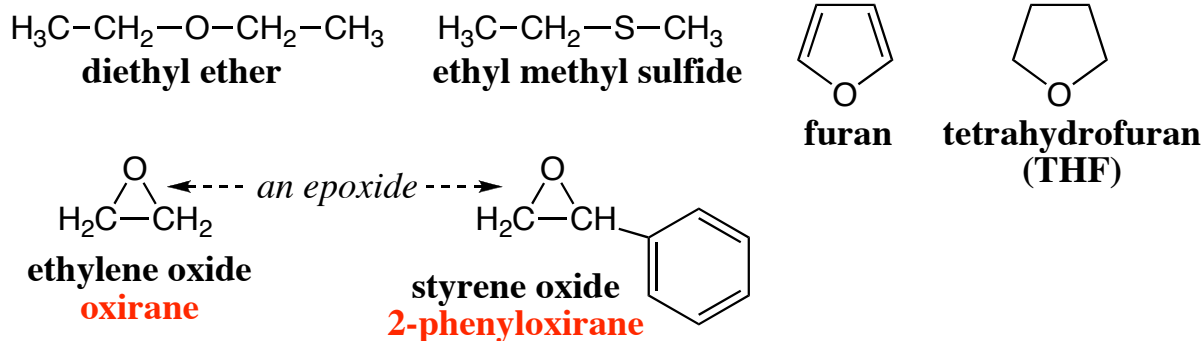
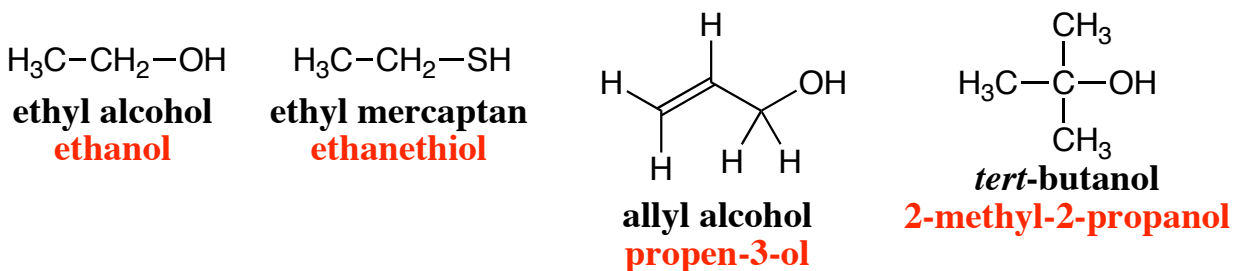
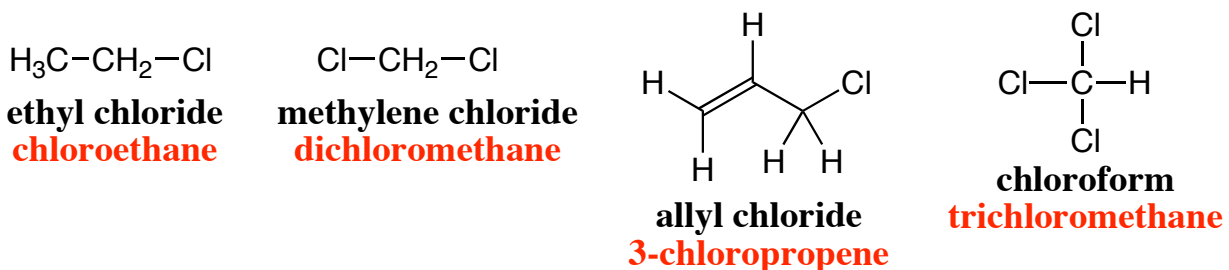
Alkyl halides:



Alcohols:



Common nomenclature & *substitutive* nomenclature:

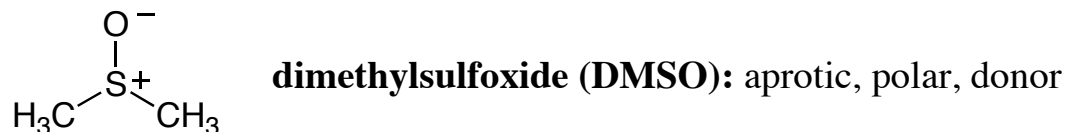
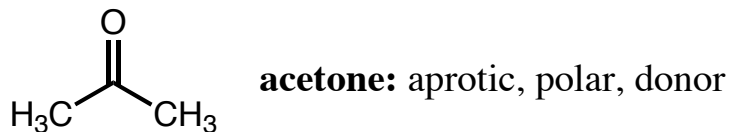


Reading: Section 8.1

Solvents in Organic Chemistry

- The vast majority of organic reactions are carried out in a **solvent**, a liquid that is used to dissolve the reactants, reagents, and products. Each solvent can be characterized based on three properties: whether it is **polar**, whether it is **protic**, and whether it is a **donor**:
- polar** or **nonpolar**:
 - polar** - dielectric constant greater than 15
 - nonpolar** - dielectric constant less than 15
- protic** or **aprotic**:
 - protic** - solvent acts as hydrogen bond donor
 - aprotic** - solvent cannot act as hydrogen bond donor
- donor** or **nondonor**:
 - donor** - solvent can share (donate) lone pair
 - nondonor** - solvent cannot share (donate) lone pair

a few examples:

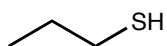
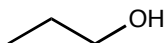


Reading: Sections 8.3 and 8.4

Acidity and Basicity of Alcohols and Thiols

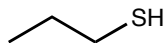
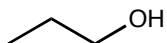
Alcohols and thiols are weakly acidic:

- What bases could you use to deprotonate the following compounds? Why?



Alcohols and thiols are also weakly basic (as are ethers and sulfides):

- What acids could you use to protonate the following compounds?



Reading: Sections 8.6 and 8.7

Making “Carbanion” Bases from Alkyl Halides: Grignard and Organolithium Reagents

- Do you recall what the pK_a of methane is?
- What is the conjugate base of methane? Why might we call this a “carbanion”?
- Carbanions are just about the strongest bases we know. Why might that make it difficult to form a carbanion?
- In that case, how can we form a “carbanion”?
- What are some uses for these “carbanions”?

Reading: Section 8.8