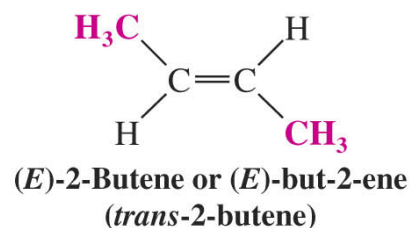
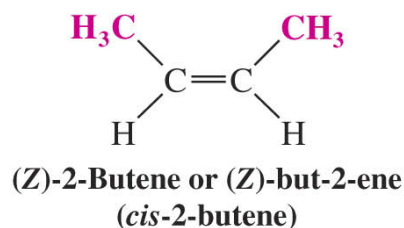
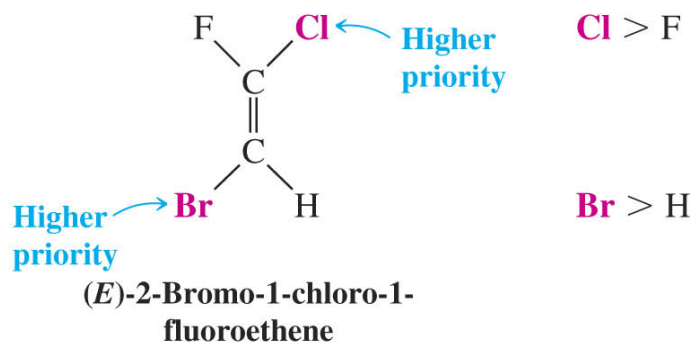
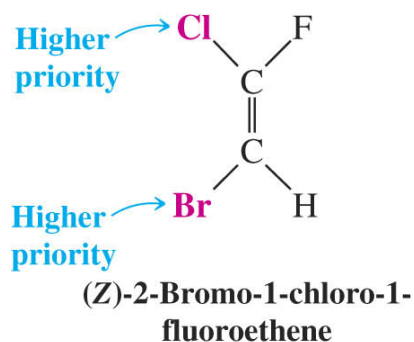


Chapter 7
Alkenes and Alkynes I:
Properties and Synthesis
Elimination Reactions of Alkyl Halides

The (*E*)-(*Z*) System for Designating Alkene Diastereomers

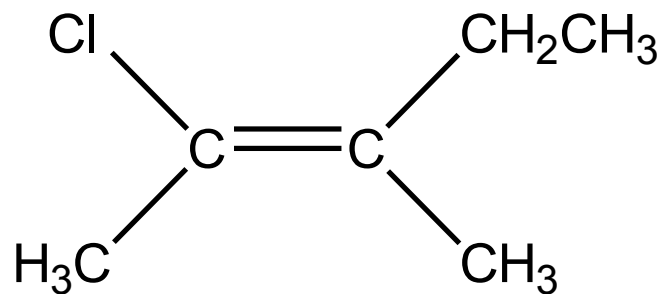
The Cahn-Ingold-Prelog convention is used to assign the groups of highest priority on each carbon

- ➔ If the group of highest priority on one carbon is on the same side as the group of highest priority on the other carbon the double bond is *Z* (zusammen)
- ➔ If the highest priority groups are on opposite sides the alkene is *E* (entgegen)



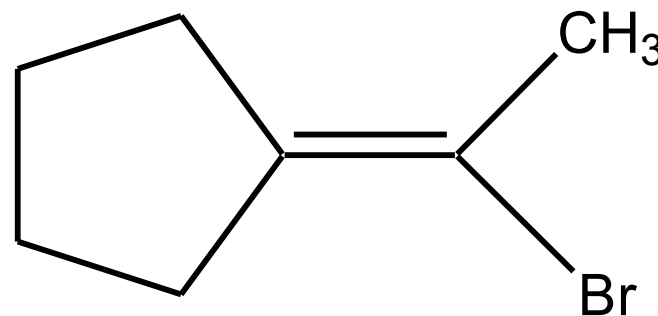
Name this compound

- A. E-2-chloro-3-methyl-2-pentene
- B. Z-2-chloro-3-methyl-2-pentene
- C. Z-2-chloro-3-ethyl-2-butene
- D. None of these



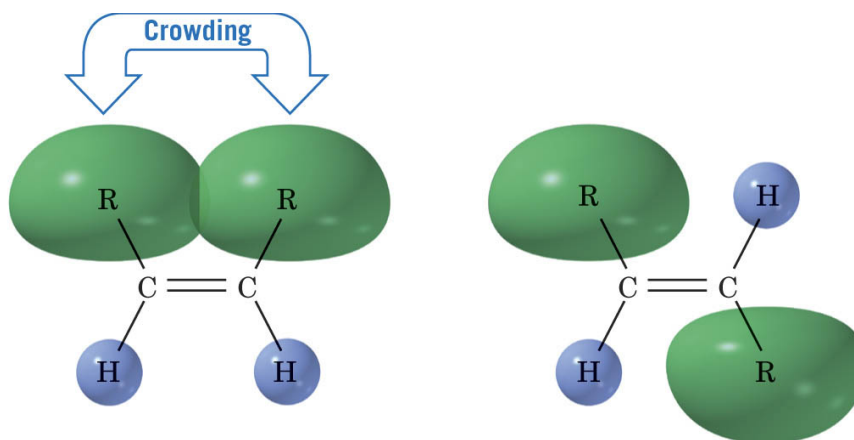
This compound is

- A. E diastereomer**
- B. Z diastereomer**
- C. Chiral**
- D. Neither E nor Z**



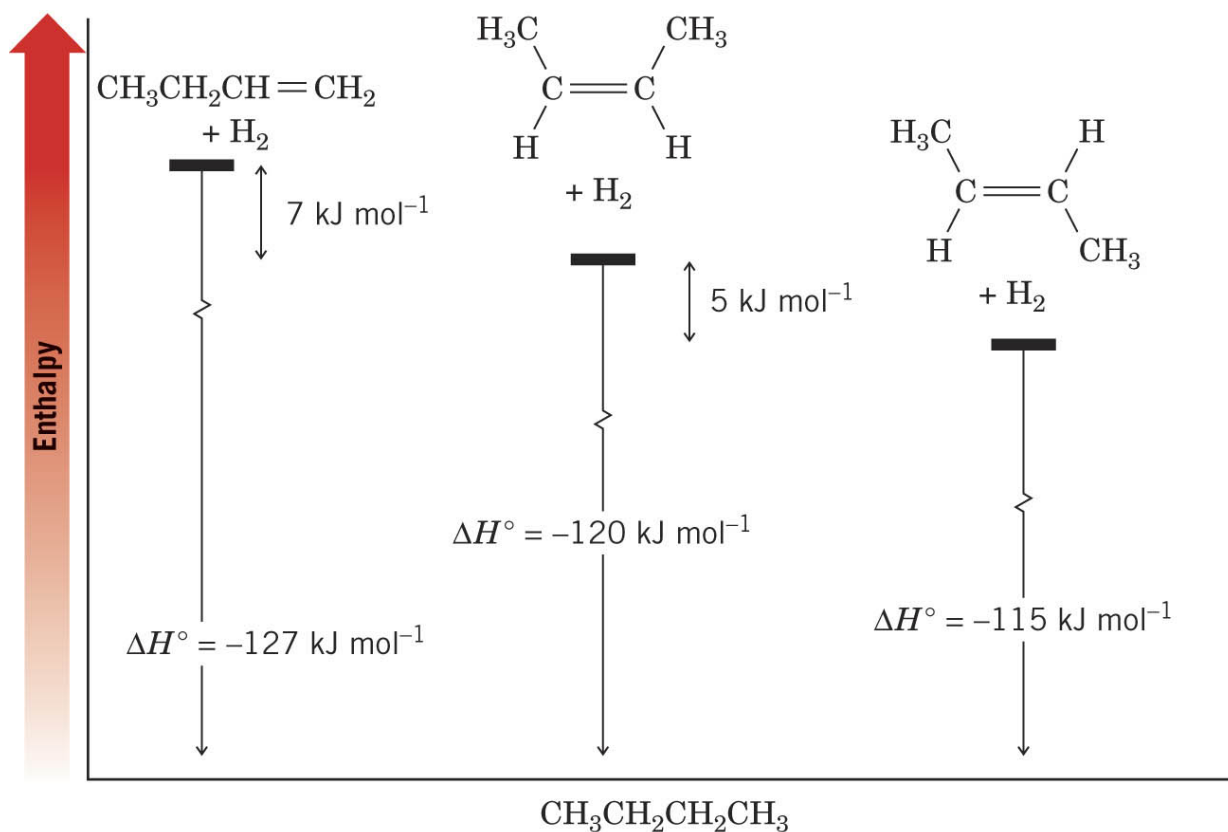
Relative Stabilities of Alkenes

- Generally cis alkenes are less stable than trans alkenes because of steric hinderance



- Heat of Hydrogenation
 - ➔ The relative stabilities of alkenes can be measured using the exothermic heats of hydrogenation

Heats of hydrogenation of three butene isomers

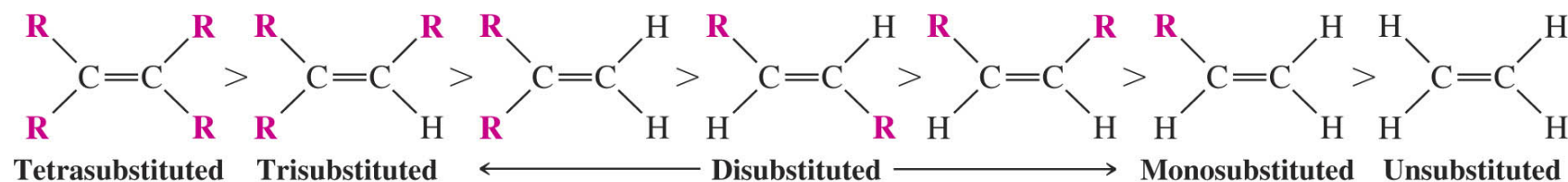


Since product is the same, the difference in ΔH are due to the alkene

Overall Relative Stability of Alkenes

The greater the number of attached alkyl groups (*i.e.* the more highly substituted the carbon atoms of the double bond), the greater the alkene's stability

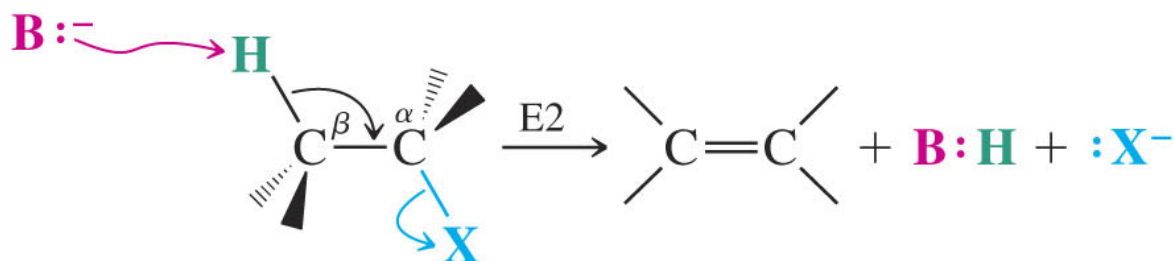
Relative Stabilities of Alkenes



Synthesis of Alkenes via Elimination Reactions

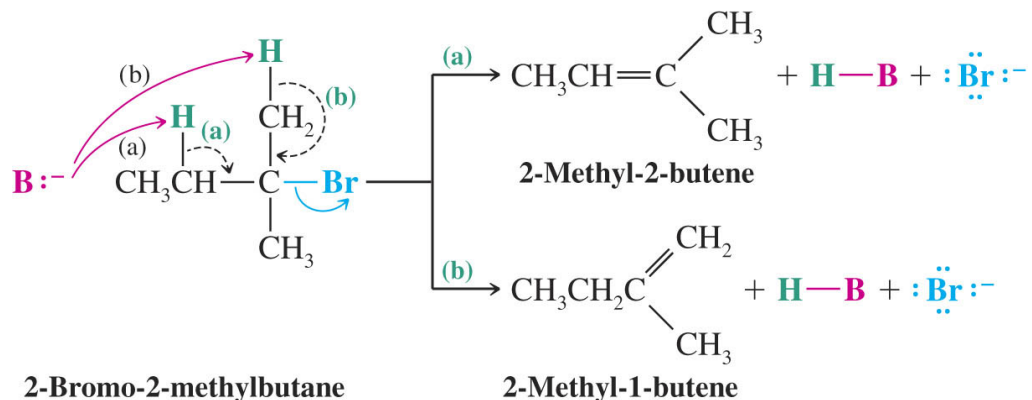
Dehydrohalogenation

- Reactions by an E2 mechanism are most useful
 - ➔ E1 reactions can be problematic (not easy to control)
- E2 reactions are favored by:
 - ➔ Secondary or tertiary alkyl halides
 - ➔ Alkoxide bases such as sodium ethoxide or potassium *tert*-butoxide
- Bulky bases such as potassium *tert*-butoxide should be used for E2 reactions of primary alkyl halides



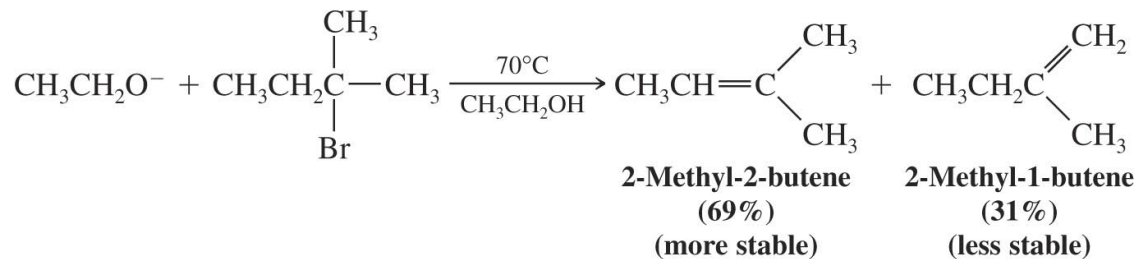
Zaitsev's Rule: Formation of the Most Substituted Alkene

Some hydrogen halides can eliminate to give two different alkenes



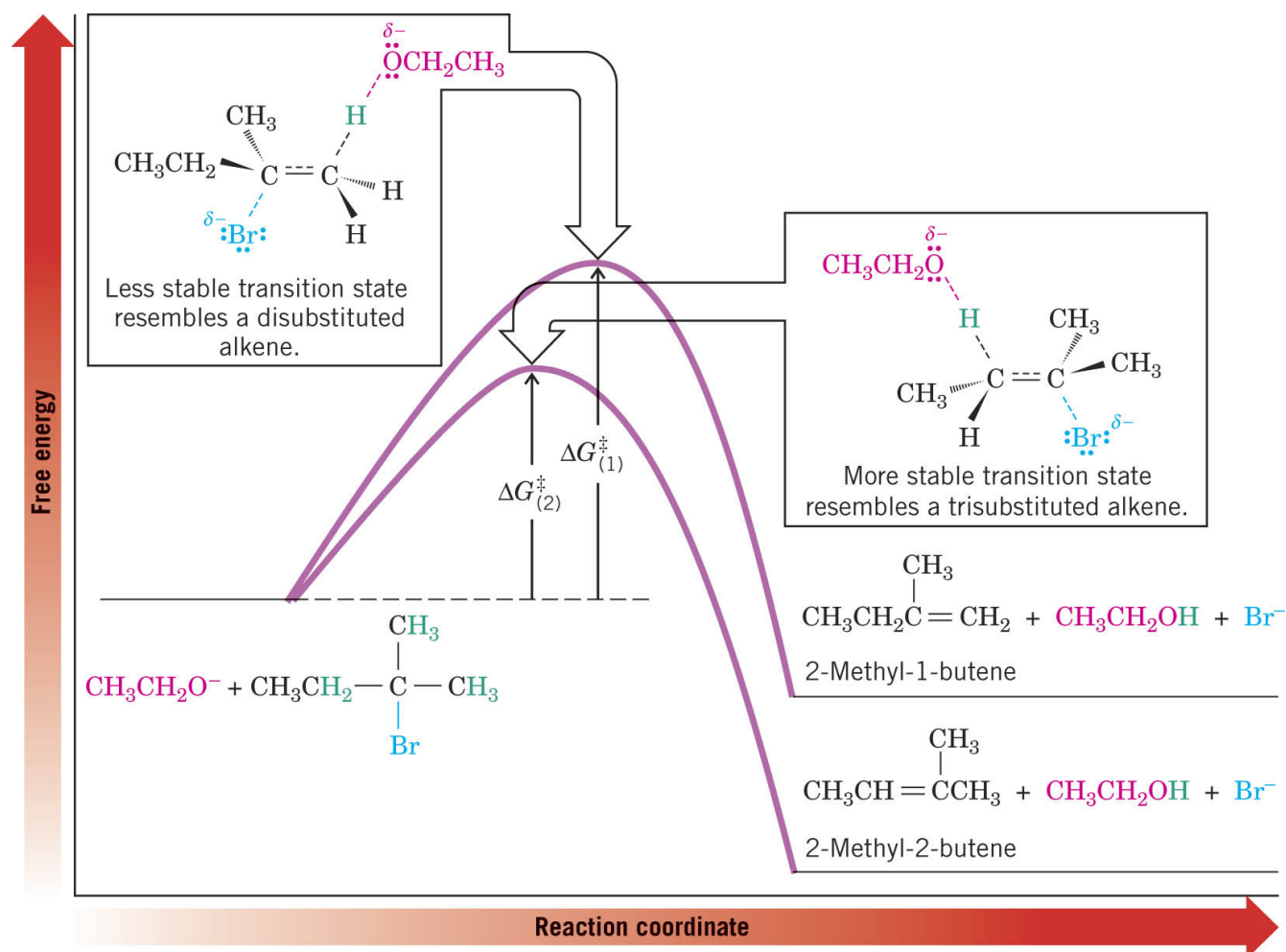
Zaitsev's Rule: when two different alkenes are possible in an elimination, the **most highly substituted alkene** will be the major product

➡ This is true only if a small base such as ethoxide is used



Basis of Zaitsev's Rule: Transition state has double bond character

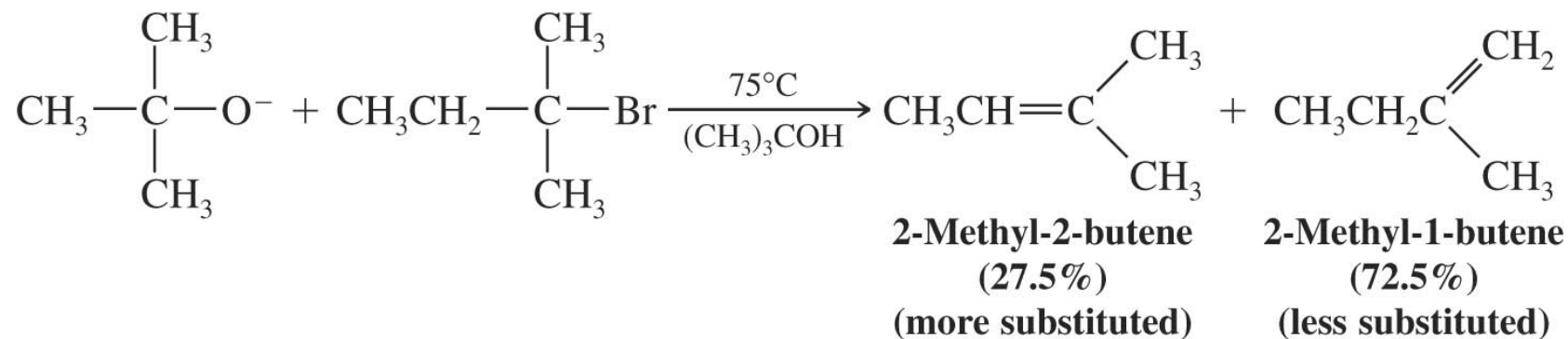
- ◆ T.S. reflects greater stability of the more substituted double bond
- ◆ An example of **Kinetic control**: When several products are possible, the one that is derived through the process having the lower activation energy is product that predominates.



Formation of the Least Substituted Alkene Using a Bulky Base

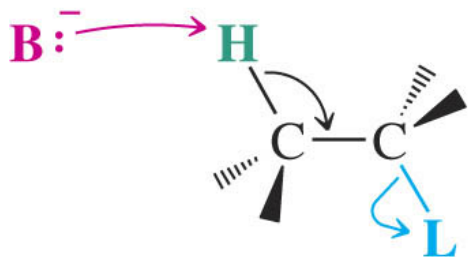
Bulky bases such as potassium *tert*-butoxide have difficulty removing sterically hindered hydrogens and generally **only react with more accessible hydrogens** (e.g. primary hydrogens).

This usually leads to the formation of the less substituted alkene.

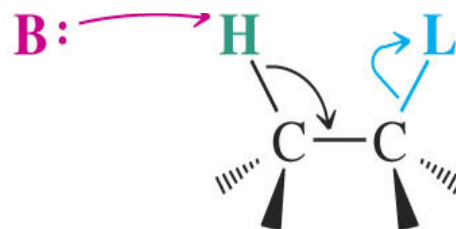


The Stereochemistry of E2 Reactions

All four atoms (H-C-C-L) must be in the same plane



» *Anti*-coplanar orientation

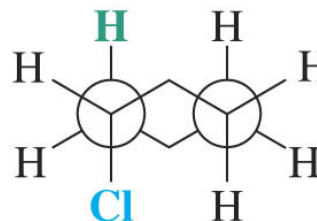
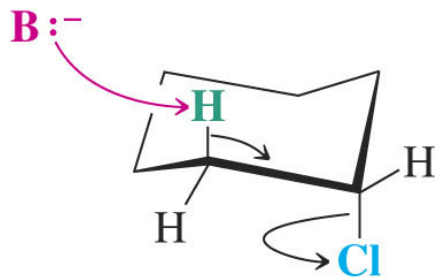


» *Syn*-coplanar orientation

NOTE:

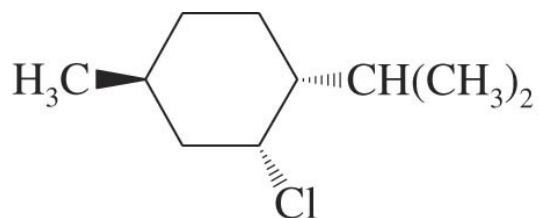
The *syn* co-planar orientation does occur in some rigid systems

- ◆ Anti coplanar orientation is preferred over *syn* coplanar orientation because all atoms are staggered in this conformation.
- ◆ In a cyclohexane ring the eliminating substituents must be diaxial to be anti coplanar

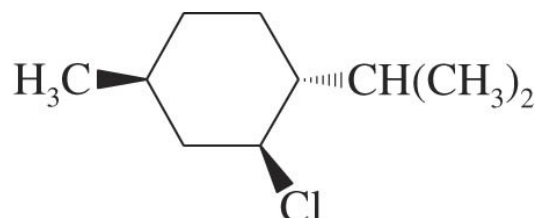


Example of stereochemical requirements

Neomenthyl chloride and menthyl chloride give different elimination products with sodium ethoxide



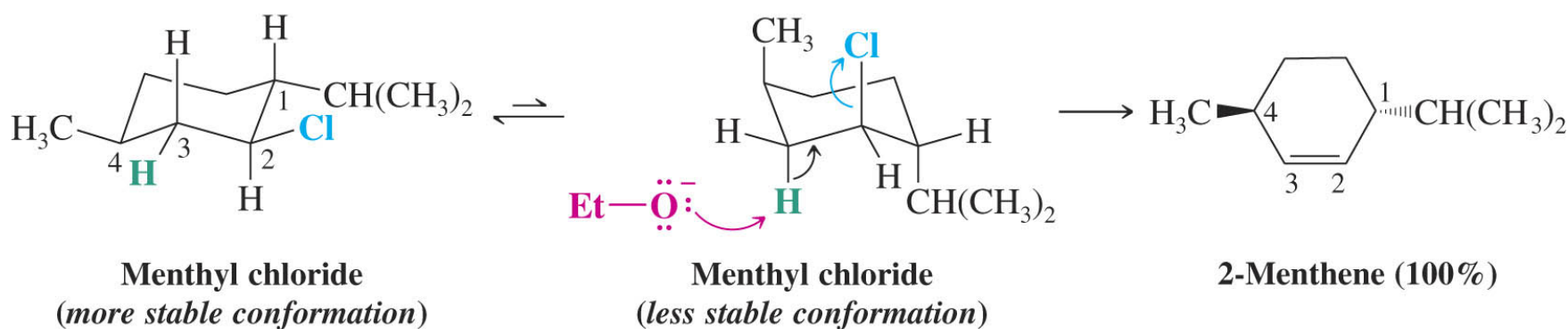
Neomenthyl chloride



Menthyl chloride

In menthyl chloride the molecule must first change to a less stable conformation to produce an axial chloride

- Elimination is slower
- Can yield only the less substituted (Hofmann) product from *anti* elimination

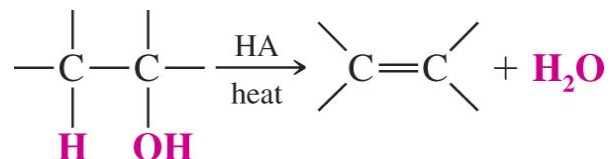


Anti elimination
is not possible

Only 1 H is *anti*
to the axial Cl

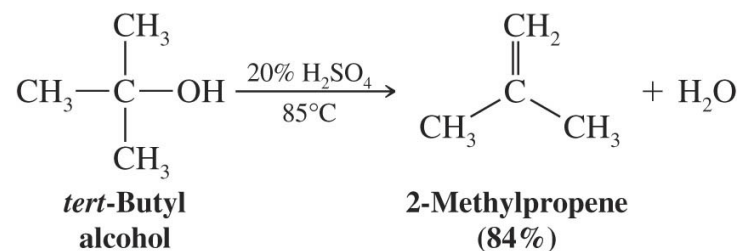
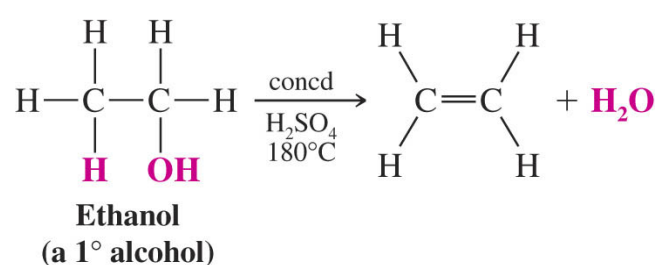
Acid Catalyzed Dehydration of Alcohols

Protonation by acids converts OH into a good leaving group $^+\text{OH}_2$



Typical acids used in dehydration are sulfuric acid and phosphoric acid (where the conjugate base is not a good nucleophile)

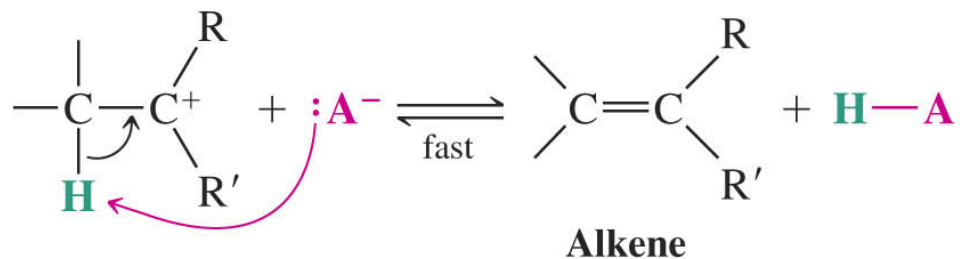
Primary alcohols are the most difficult to dehydrate; tertiary are the easiest.



Recall that elimination is favored over substitution at higher temperatures.

Caveat: Rearrangements of the carbon skeleton can occur

Step 3: carbocation loses a proton

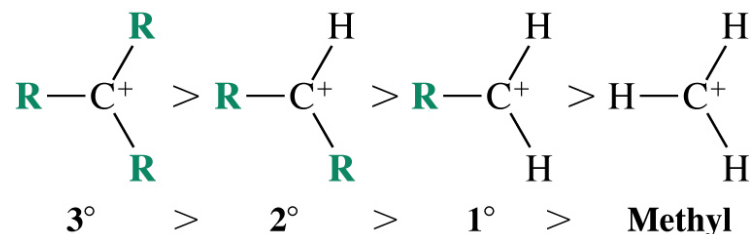


Another molecule of the alcohol, a water molecule, or the conjugate base of the acid may accept the proton.

Note that only a catalytic amount of acid is required since it is regenerated in the final step of the reaction.

Carbocation Stability and the Transition State

Recall the stability of carbocations is:



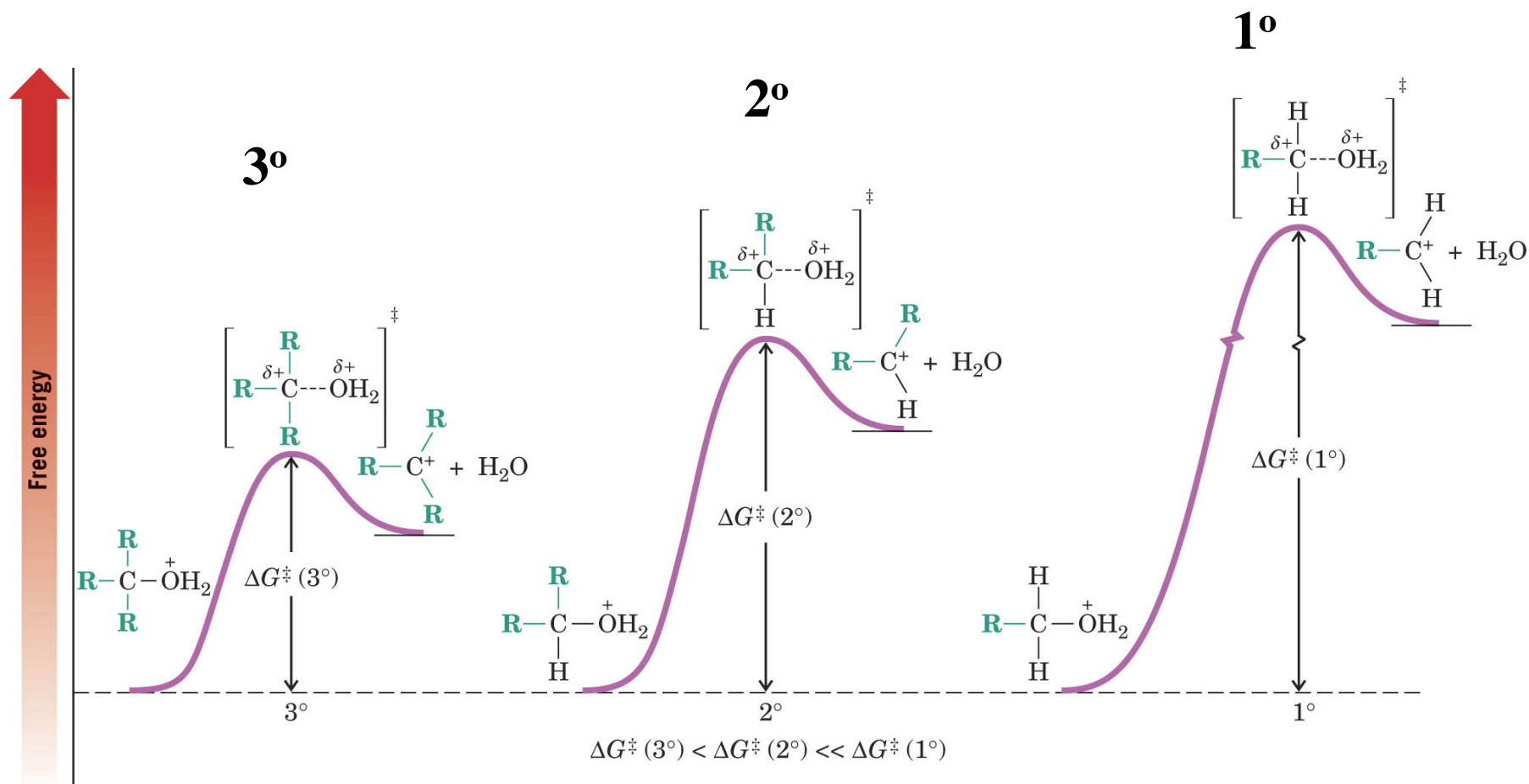
The second step in which the carbocation forms is rate determining.

The transition state for this reaction has carbocation character.

Tertiary alcohols react the fastest because they produce the most stable tertiary carbocation-like transition state in the second step.

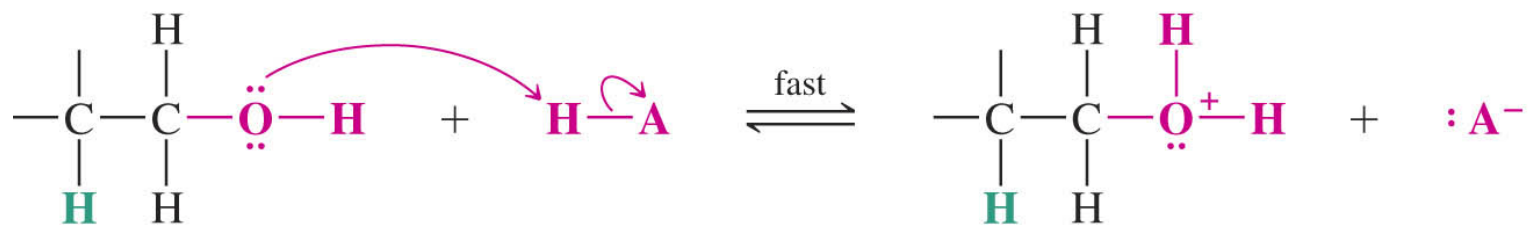
The relative heights of ΔG^\ddagger for the second step of E1 dehydration

Primary alcohols have a prohibitively large energy barrier

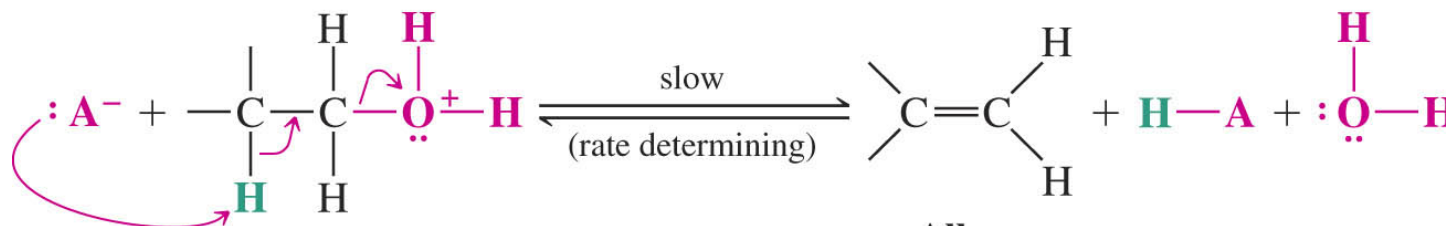


Mechanism for Dehydration of Primary Alcohols is E2

- ◆ Primary alcohols cannot undergo E1 dehydration because of the instability of the carbocation-like transition state.
- ◆ In the E2 dehydration the first step is the same: protonation of the hydroxyl group to yield the good leaving group, water.

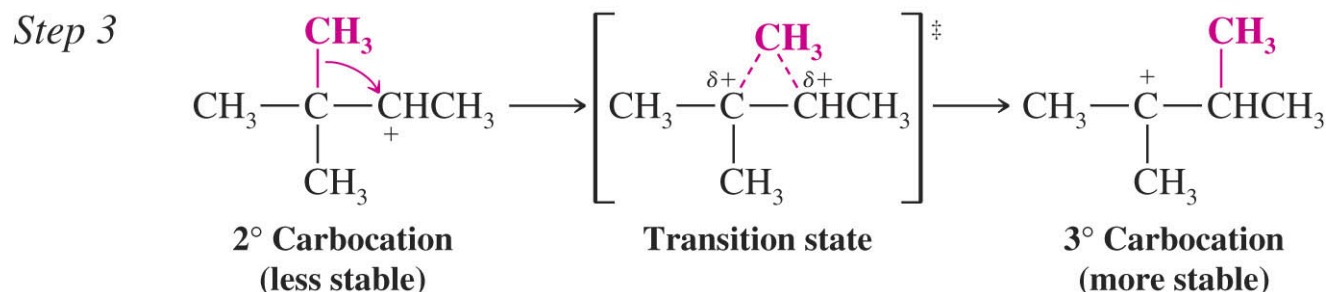


- ◆ Unable to form a carbocation, the protonated alcohol waits until some weak base assists in an E2 reaction

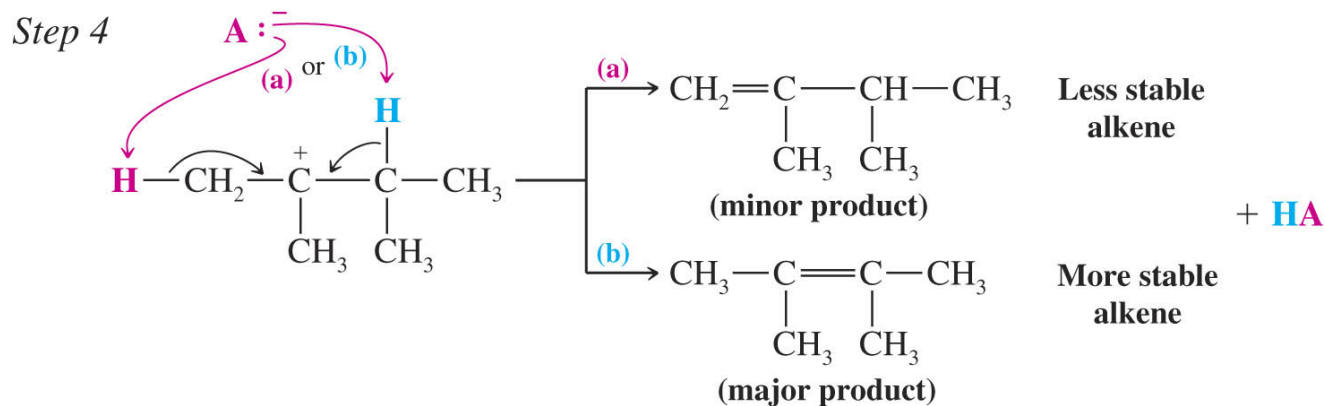


The less stable 2° carbocation rearranges by shift of a methyl group with its electrons to produce more stable 3° carbocation

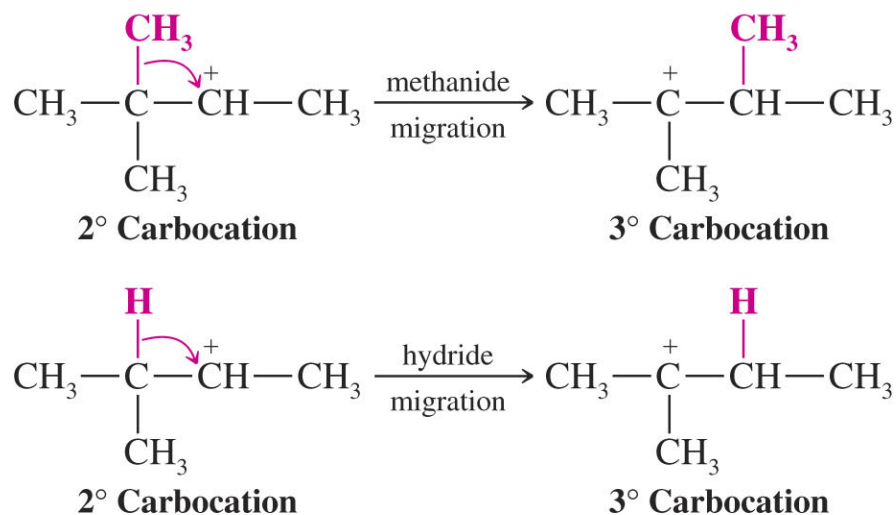
- This is called a **1,2 shift**



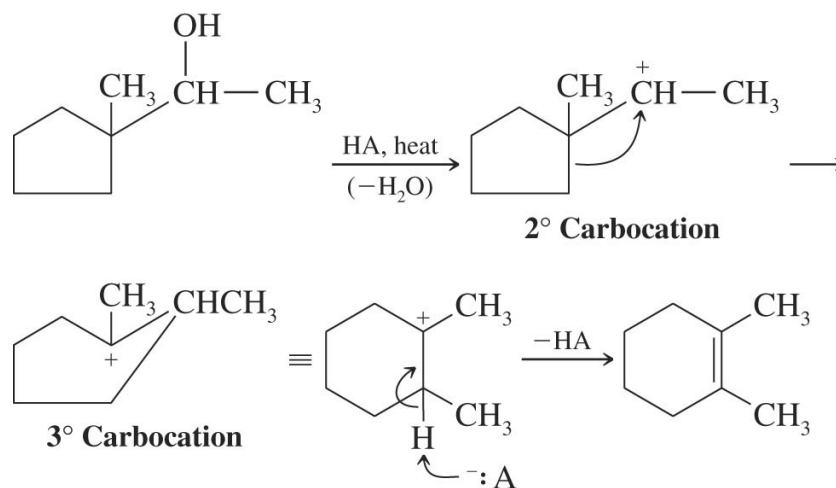
The removal of a proton to form the alkene occurs to give the Zaitzev (most substituted) product as the major one:



A hydride shift (migration of a hydrogen with its electrons) can also occur to yield the more stable carbocation:

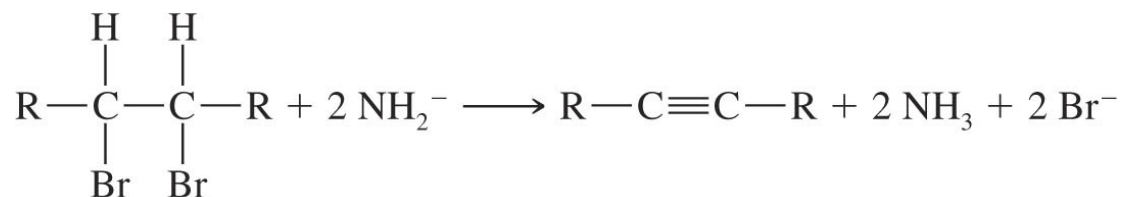


Carbocation rearrangements can lead to the expansion of rings:

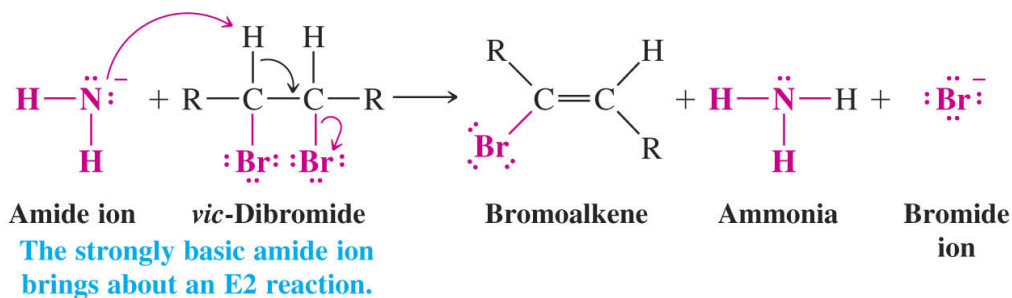


Synthesis of Alkynes by Elimination Reactions

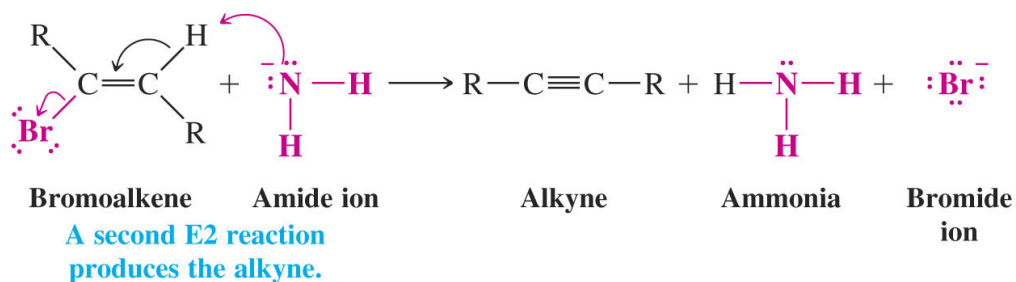
- ◆ Alkynes can be obtained by two consecutive dehydrohalogenation reactions of a vicinal dihalide



Step 1

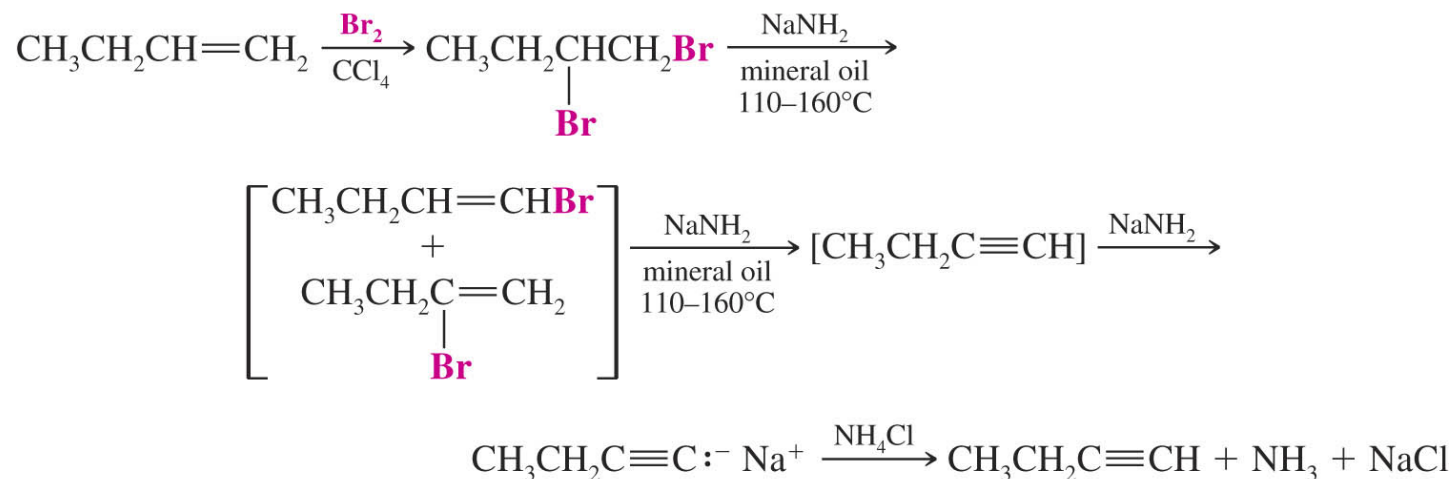


Step 2

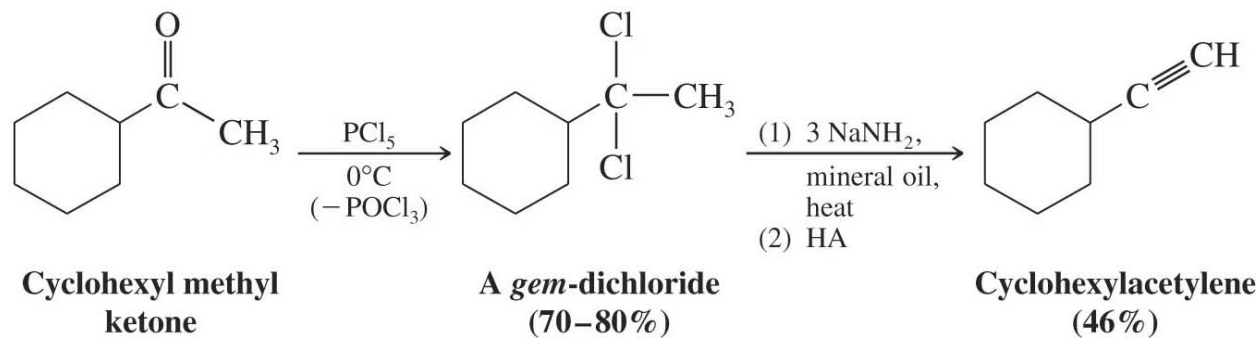


Alkenes can be converted to alkynes

1. By bromination and consecutive dehydrohalogenation reactions

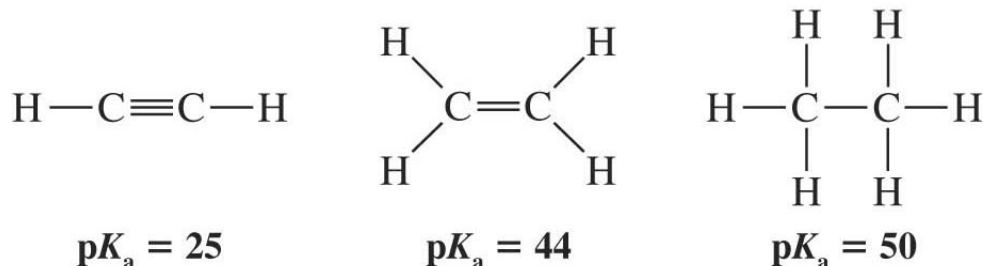


2. Geminal dihalides can also undergo consecutive dehydrohalogenation reactions to yield the alkyne

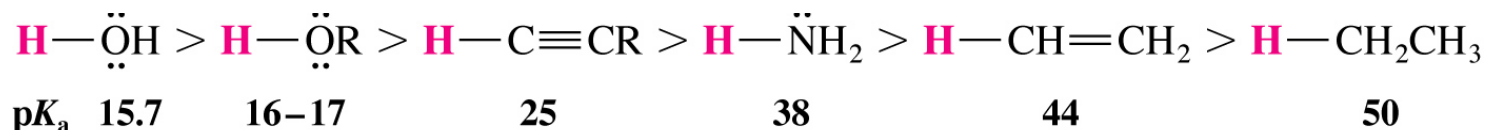


The Acidity of Terminal Alkynes

Recall that acetylenic hydrogens have a pK_a of about 25 and are much more acidic than most other C-H bonds.

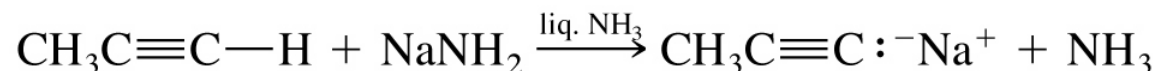
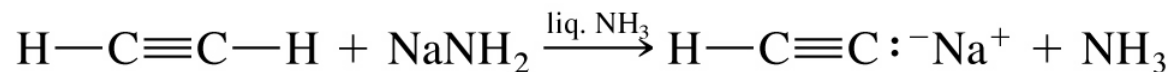


- The relative acidity of acetylenic hydrogens in solution is:



- Acetylenic hydrogens can be deprotonated with relatively strong bases (sodium amide is typical)

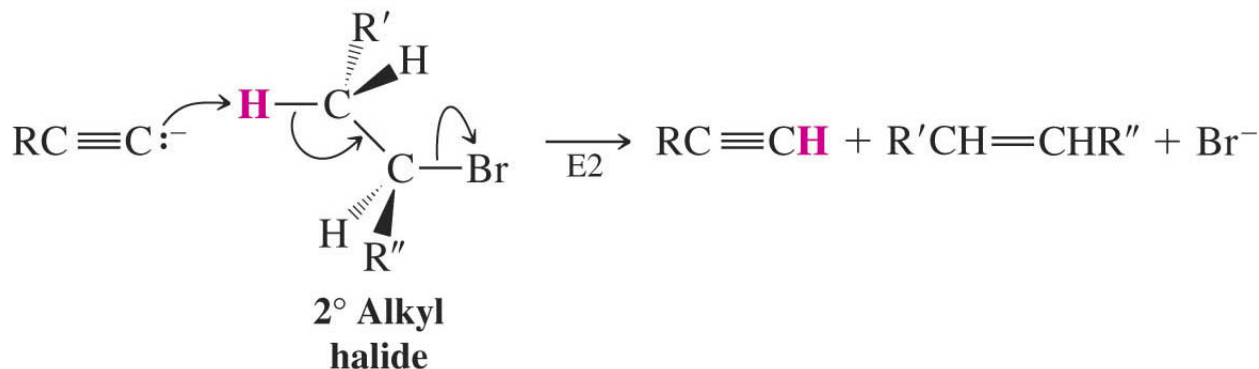
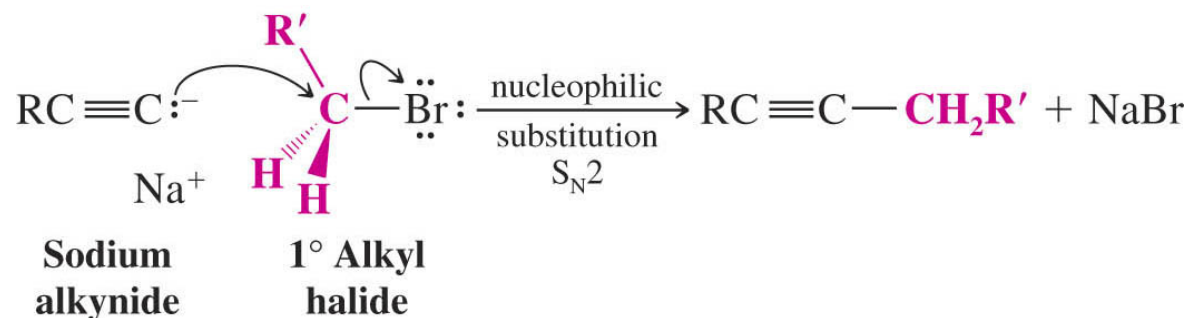
★ The products are called alkynides



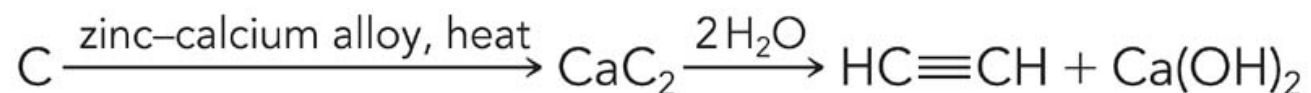
Substitutions on terminal alkynes

◆ Sodium alkynides can be used as nucleophiles in S_N2 reactions

- New carbon-carbon bonds are the result.
- Only primary alkyl halides can be used; otherwise, elimination reactions predominate



Generation of acetylene from carbon

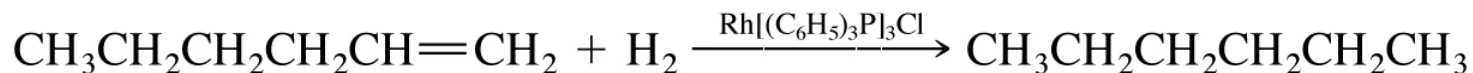
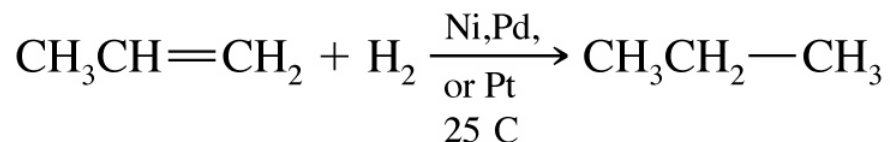
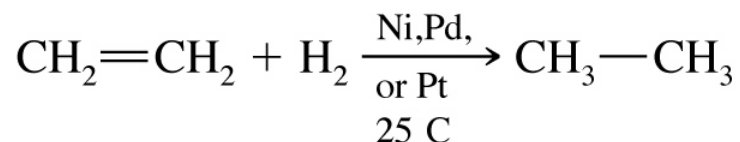


Big Bang cannons are fired by putting water in the barrel housing and then adding a measured amount of Bangsite (carbide powder). The powder dissolves in the water creating acetylene gas. The gas is then ignited by a spark....resulting in a safe and loud BOOM.

- ◆ **Big Bang® carbide cannons - at big savings!**
- ◆ **You probably remember these from days of your youth.**
- ◆ **Big Bang cannons have been in continuous production since 1912.**
- ◆ **We offer the most popular models at below factory prices!**
- ◆ **These are great gifts for the junior cannoneer (ages 10 to 100) fun for the whole family**

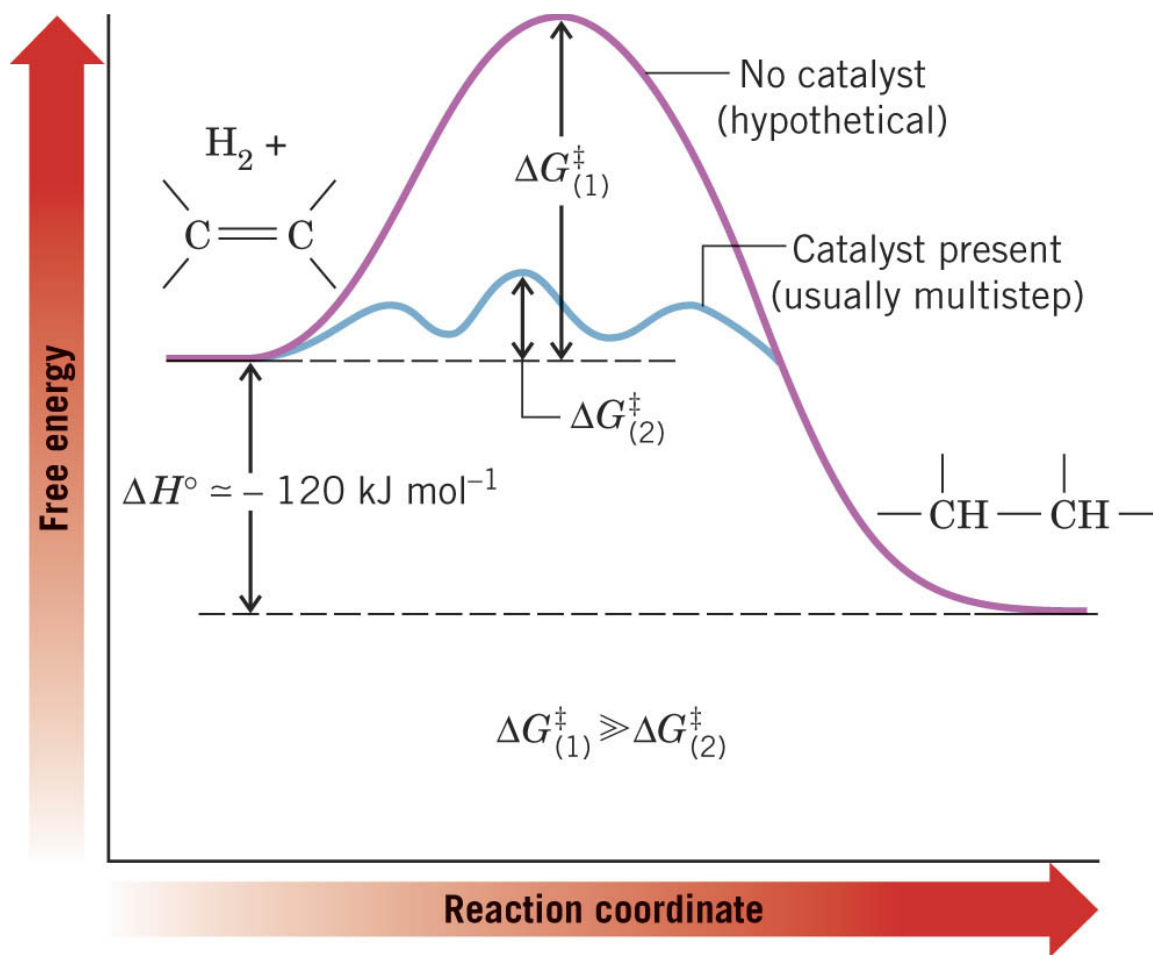
Hydrogenation of Alkenes

- ◆ Hydrogen adds to alkenes in the presence of noble metal catalysts.
- ◆ **Heterogeneous Catalysts:** finely divided insoluble platinum, palladium or nickel catalysts
- ◆ **Homogeneous Catalysts:** the catalyst (typically rhodium or ruthenium based) is soluble in the reaction medium.
 - For example, Wilkinson's catalyst is $\text{Rh}[(\text{C}_6\text{H}_5)_3\text{P}]_3\text{Cl}$
- ◆ This process is called a reduction or hydrogenation
 - An unsaturated compound becomes a saturated (with hydrogen) compound:

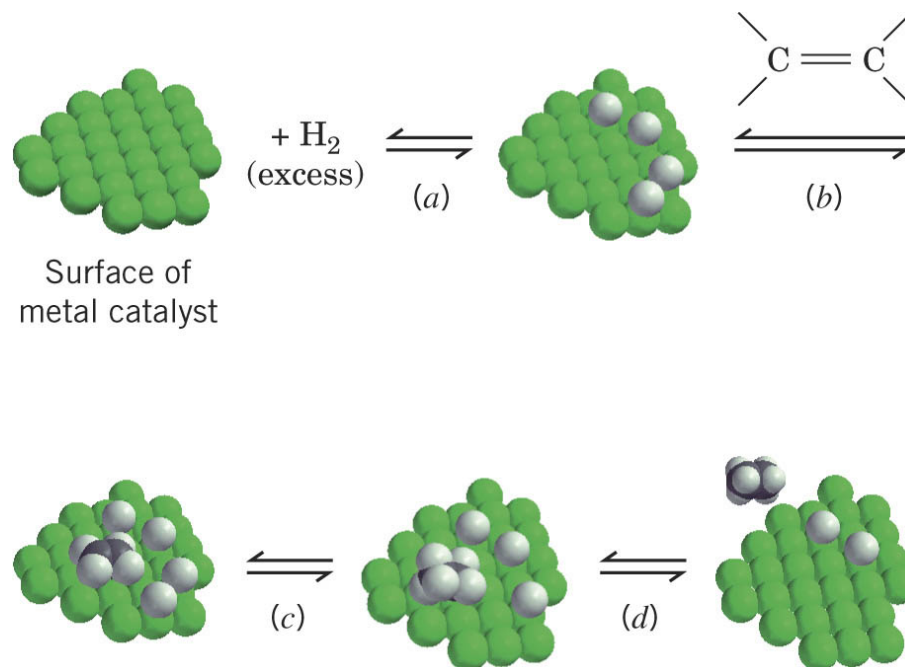


Hydrogenation: The Function of the Catalyst

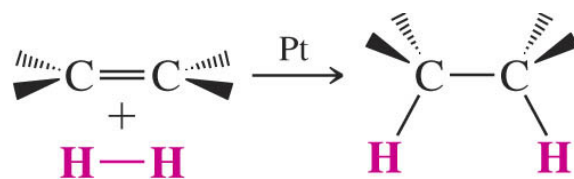
The catalyst provides a new reaction pathway with lower ΔG^\ddagger values



In heterogeneous catalysis the hydrogen and alkene adsorb onto the catalyst surface, and then a step-wise formation of C-H bonds occurs:



Both hydrogens add to the same face of the alkene (*i.e.*, a **syn addition**)

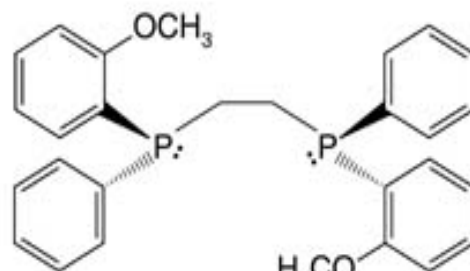
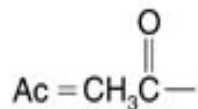
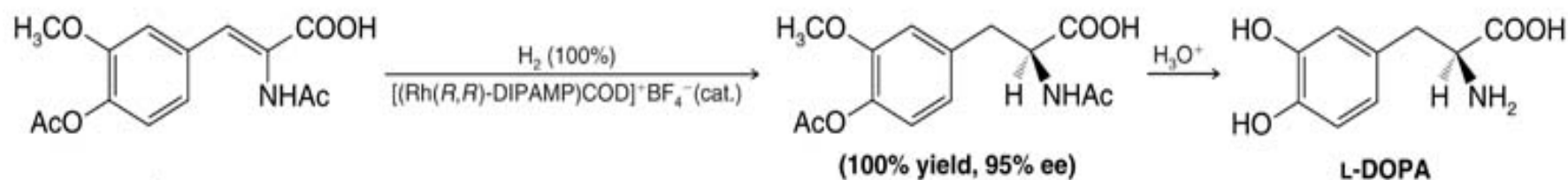


Catalytic hydrogenation is a syn addition.

Asymmetric Hydrogenation

Using chiral versions of Wilkinson's catalyst, one can get stereoselectivity

For example, the asymmetric synthesis of L-dopa, a drug for treating Parkinson's disease:



(*R,R*)-DIPAMP
(Chiral ligand for rhodium)

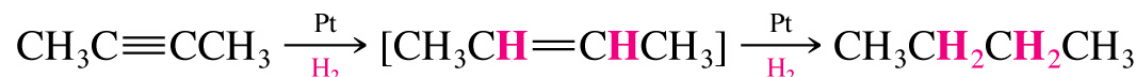


COD =
1,5-Cyclooctadiene

(continues on next p)

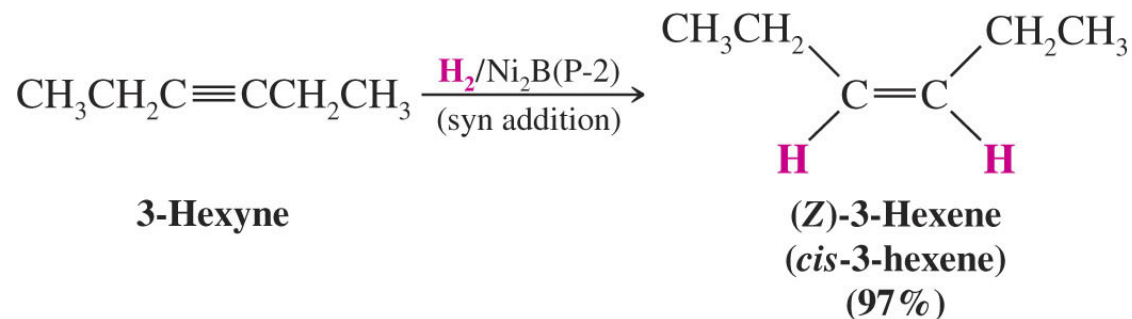
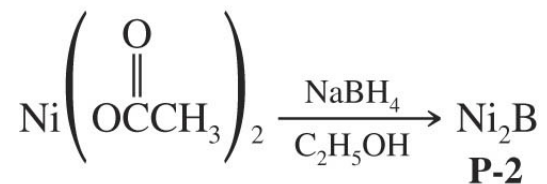
Hydrogenation of Alkynes

The reaction of hydrogen using regular metal catalysts results in formation of the alkane from an alkyne.

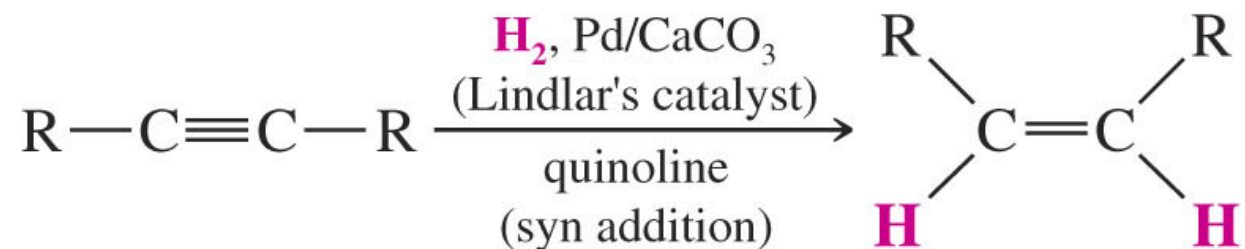


syn-Addition of Hydrogen: Synthesis of *cis*-Alkenes

- ➔ The **P-2 catalyst nickel boride** results in the syn addition of one equivalent of hydrogen to a triple bond.
- ➔ As a result, hydrogenation of an internal alkyne yields a *cis* alkene:



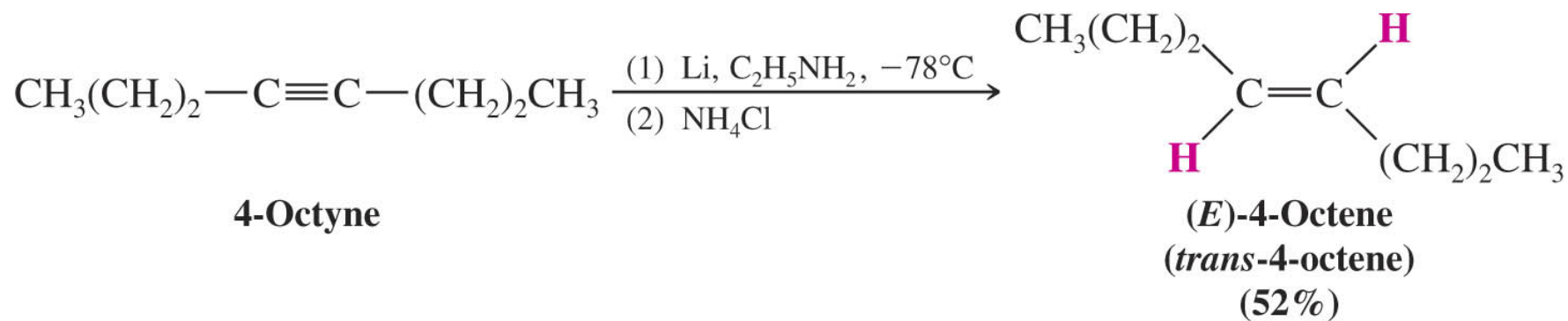
- **Lindlar's catalyst** also directs *syn* addition, stopping at the addition of only one molecule of hydrogen, thus producing *cis*-alkenes from alkynes



Anti Addition of Hydrogen: Synthesis of *trans*-Alkenes

A **dissolving metal reaction** which uses lithium or sodium metal at low temperature in ammonia or amine solvent **produces *trans*-alkenes**.

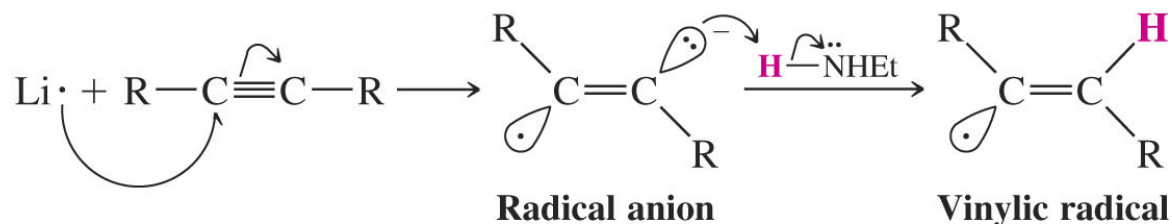
Net ***anti* addition** occurs by the formal addition of hydrogen to the opposite faces of the triple bond



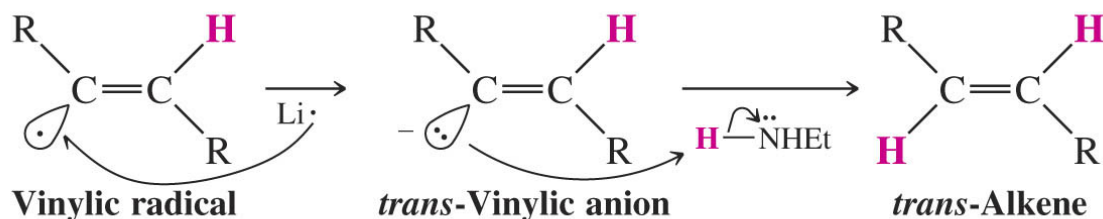
Mechanism involves two sequential electron transfers from the metal

Lithium donates an electron to the alkene (into its anti-bonding orbital!)

This produces a radical anion, which reacts as a base with the amine solvent:



Second electron converts the radical into an anion, which again acts as a base:



The vinylic anion prefers to be *trans* and this determines the *trans* stereochemistry of the product

Structural Information from Molecular Formulas

- ◆ Saturated alkane = molecular formula C_nH_{2n+2}
- ◆ Formula of C_nH_{2n} will have either a double bond or a ring



1-Hexene
(C_6H_{12})



Cyclohexane
(C_6H_{12})

- ◆ A compound with general formula C_nH_{2n-2} can have a triple bond, two double bonds, a double bond and a ring or two rings
- ◆ **Index of Hydrogen Deficiency:** the number of pairs of hydrogen atoms that must be subtracted from the molecular formula of the corresponding alkane to give the molecular formula of the compound under consideration.

Using the Index of Hydrogen Deficiency (IHD)

- ◆ **Example: A compound has the molecular formula C_6H_{12}**

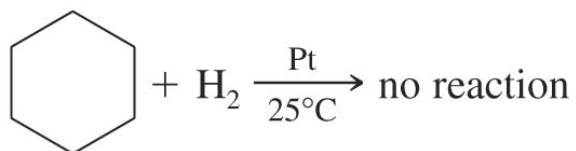
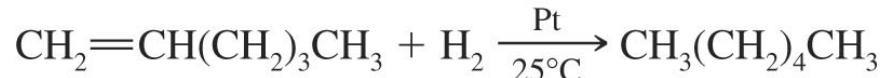
C_6H_{14} = formula of corresponding alkane (hexane)

C_6H_{12} = formula of compound (1-hexene or cyclohexane)

H_2 = difference = 1 pair of hydrogen atoms

Index of hydrogen deficiency = 1

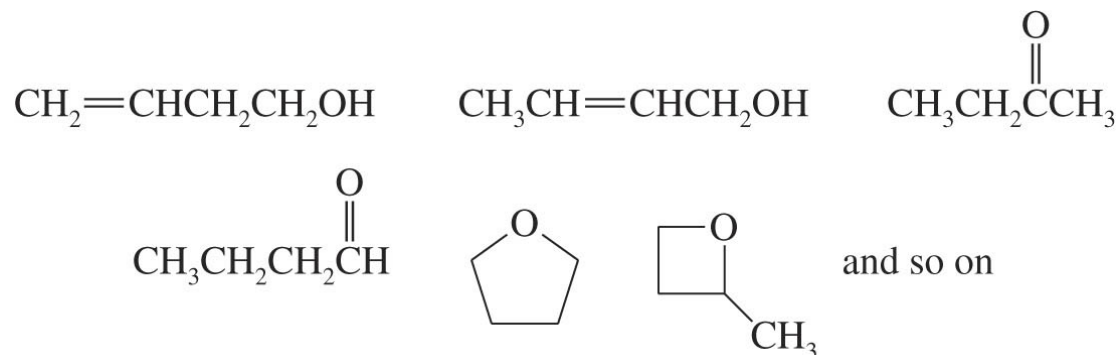
- ◆ **Hydrogenation allows one to distinguish a compound with a double bond from one with a ring**



- ◆ **Compounds Containing Halogens, Oxygen, or Nitrogen**
 - For compounds containing halogen atoms, the halogen atoms are counted as if they were hydrogen atoms.
 - **Example: A compound with formula $C_4H_6Cl_2$**
 - ➔ This is equivalent to molecular formula C_4H_8 which has IHD=1

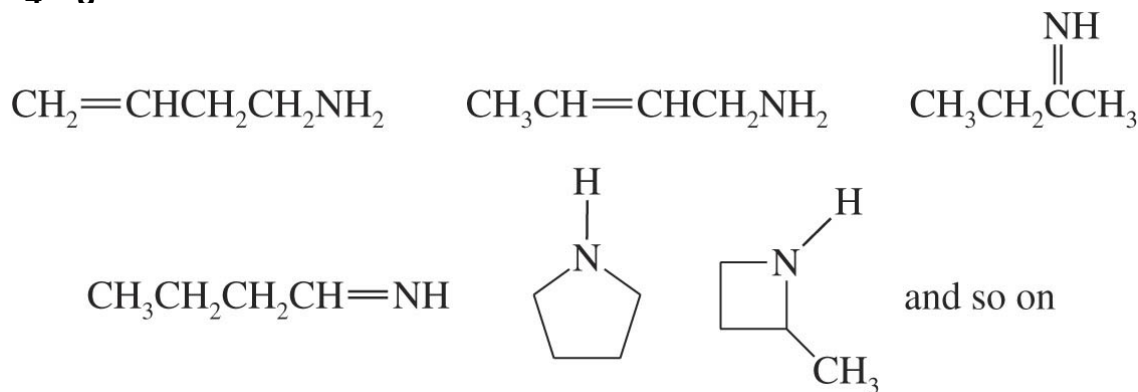
- ◆ **For compounds containing oxygen**, the oxygen is ignored and IHD is calculated based on the rest of the formula

- **Example: A compound with formula C_4H_8O has IHD = 1**



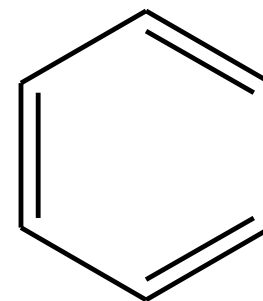
- ◆ **For compounds containing nitrogen**, one hydrogen is subtracted for each nitrogen and the nitrogen is ignored in the calculation

- **Example: A compound with formula C_4H_9N is treated as if it has formula C_4H_8 and has IHD = 1**



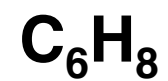
Benzene and Aromatic Rings

- ◆ Benzene has 3 double bonds and a ring
- ◆ IHD = 4
- ◆ Whenever IHD = 4 or more with a modest number of carbons, consider the possibility of an aromatic ring.



What is the IHD of

A) 1



B) 2

C) 3

D) 4

What is the IHD of

A) 1



B) 2

C) 3

D) 4

Retrosynthetic Analysis

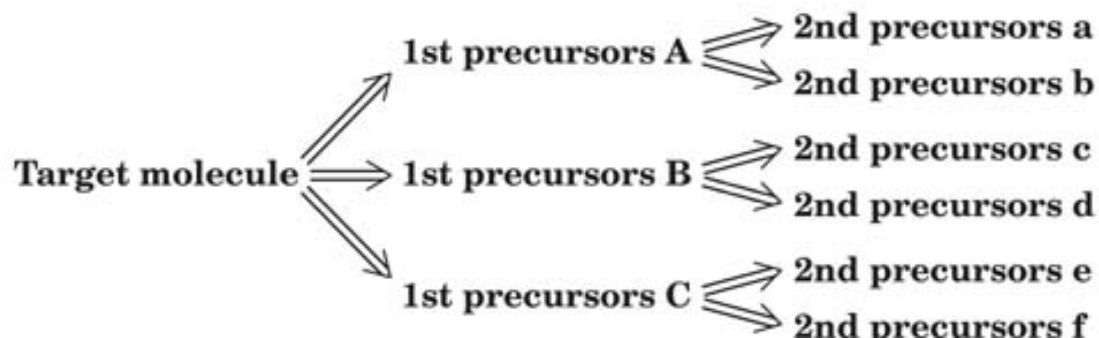
Organic synthesis is **making complex molecules from simpler ones**

Often we know where we want to finish (complex molecule) but not where to start so we work backwards

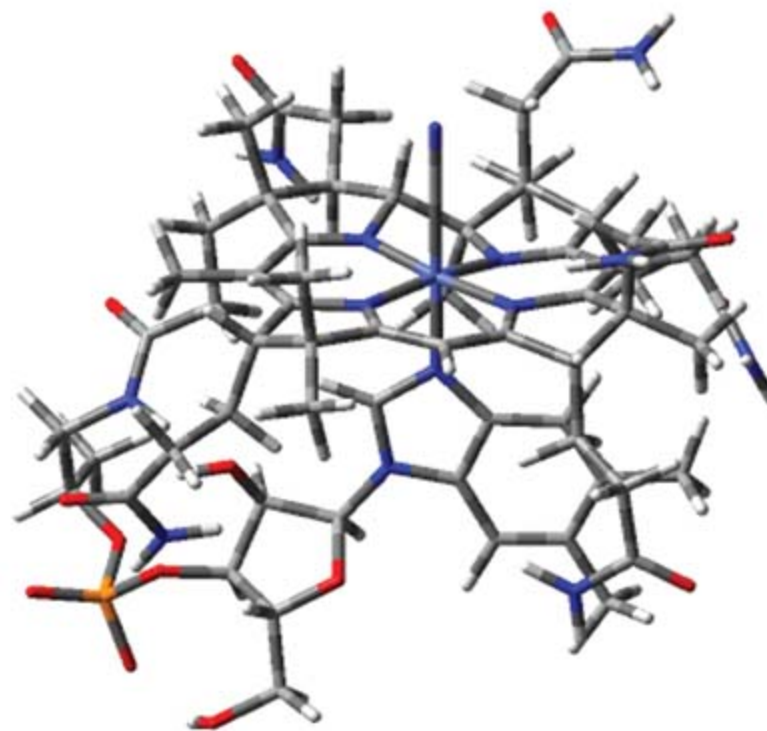
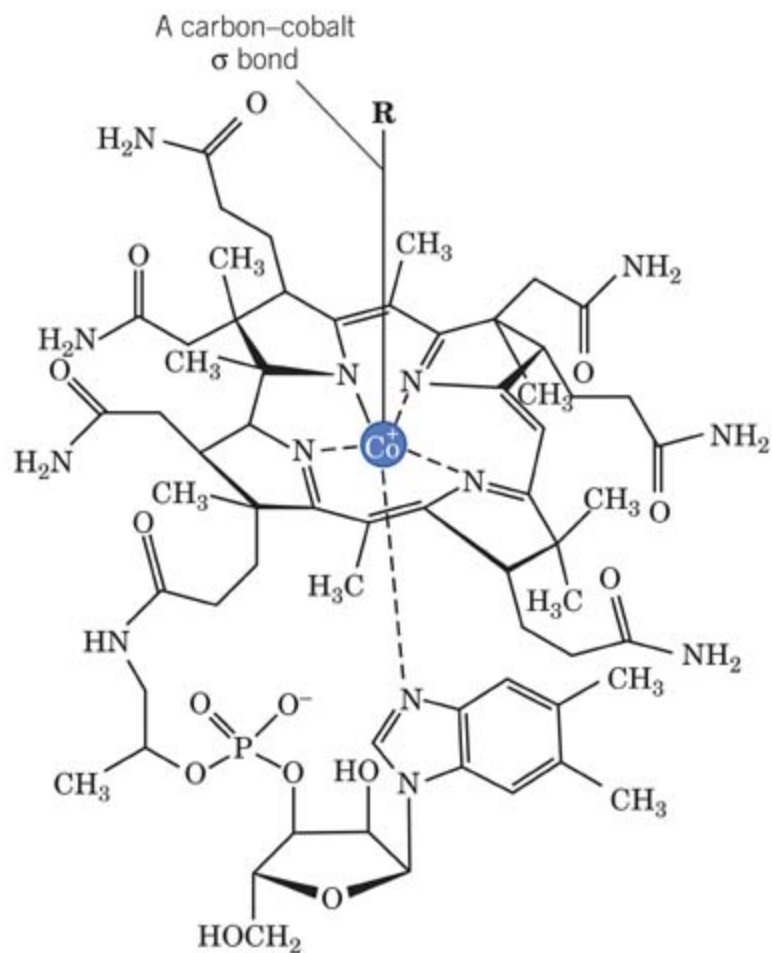
goal

Target molecule \implies 1st precursor \implies 2nd precursor $\implies \implies$ Starting compound

Usually need to consider several options so we can optimize



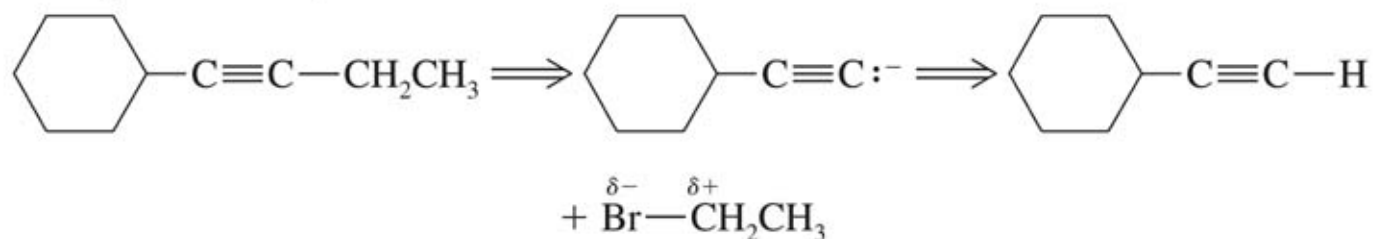
Synthesis target – Vitamin B₁₂



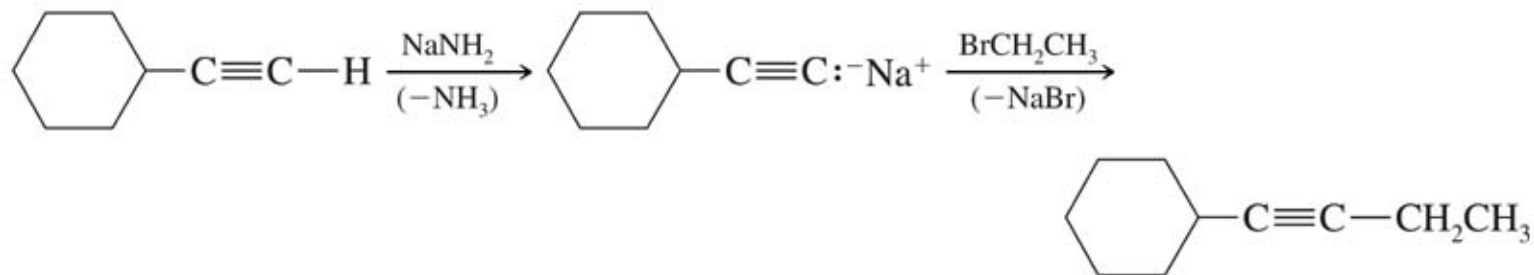
R. B. Woodward, 1972 – 90 steps, 11 years, 100 chemists

Example: synthesis of 1-cyclohexyl-1-butyne

Retrosynthetic Analysis



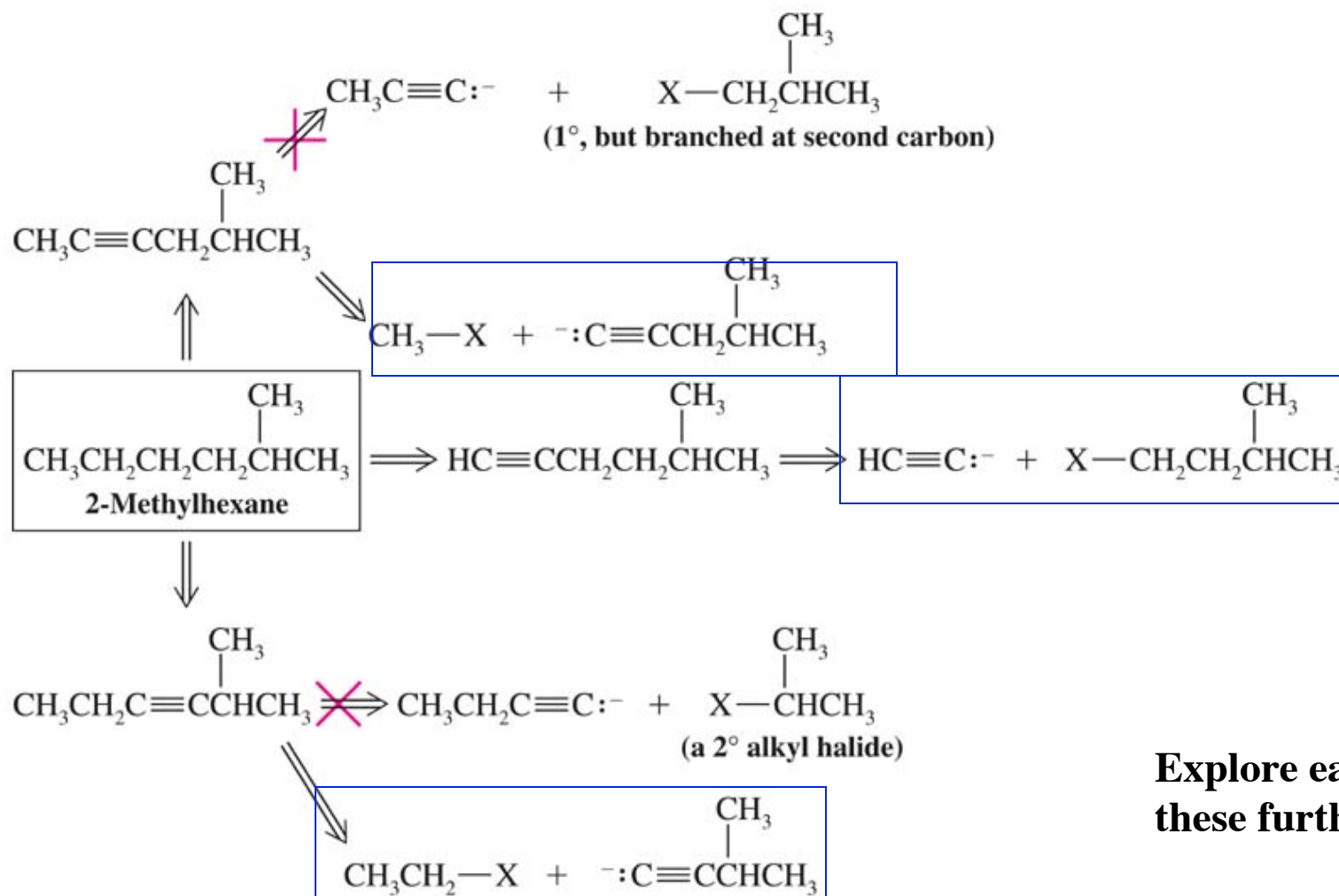
Synthesis



After doing retrosynthetic analysis, we write the normal synthetic sequence and check each step for feasibility

Options for preparing 2-methylhexane: from compounds with fewer carbons

Retrosynthetic Analysis



**Explore each of
these further**