

Show all reagents and intermediates for the multi-step synthesis below. You may use **any** organic or inorganic reagents in your synthesis, but you must begin with the indicated starting material. You do not need to show any mechanisms. The correct answer will require fewer than 5 steps.

Starting Material: HC#CH

Reaction 1: HC#CH $\xrightarrow[NH_3]{NaNH_2}$ HC#C:[-]

Reaction 2: HC#C:[-] $\xrightarrow{CH_3CH_2Br}$ HC#CC[CH2CH3]^-

Reaction 3: HC#CC[CH2CH3]^- $\xrightarrow{H^+ \text{ workup}}$ HC#CC[CH2CH3]OH

Reaction 4: HC#CC[CH2CH3]OH $\xrightarrow{H_2, Pd/C}$ CH_3CH_2CH_2CH_2OH

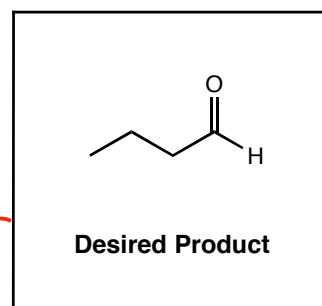
Reaction 5: CH_3CH_2CH_2CH_2OH $\xrightarrow{CrO_3 \cdot Py}$ CH_3CH_2CH_2CHO

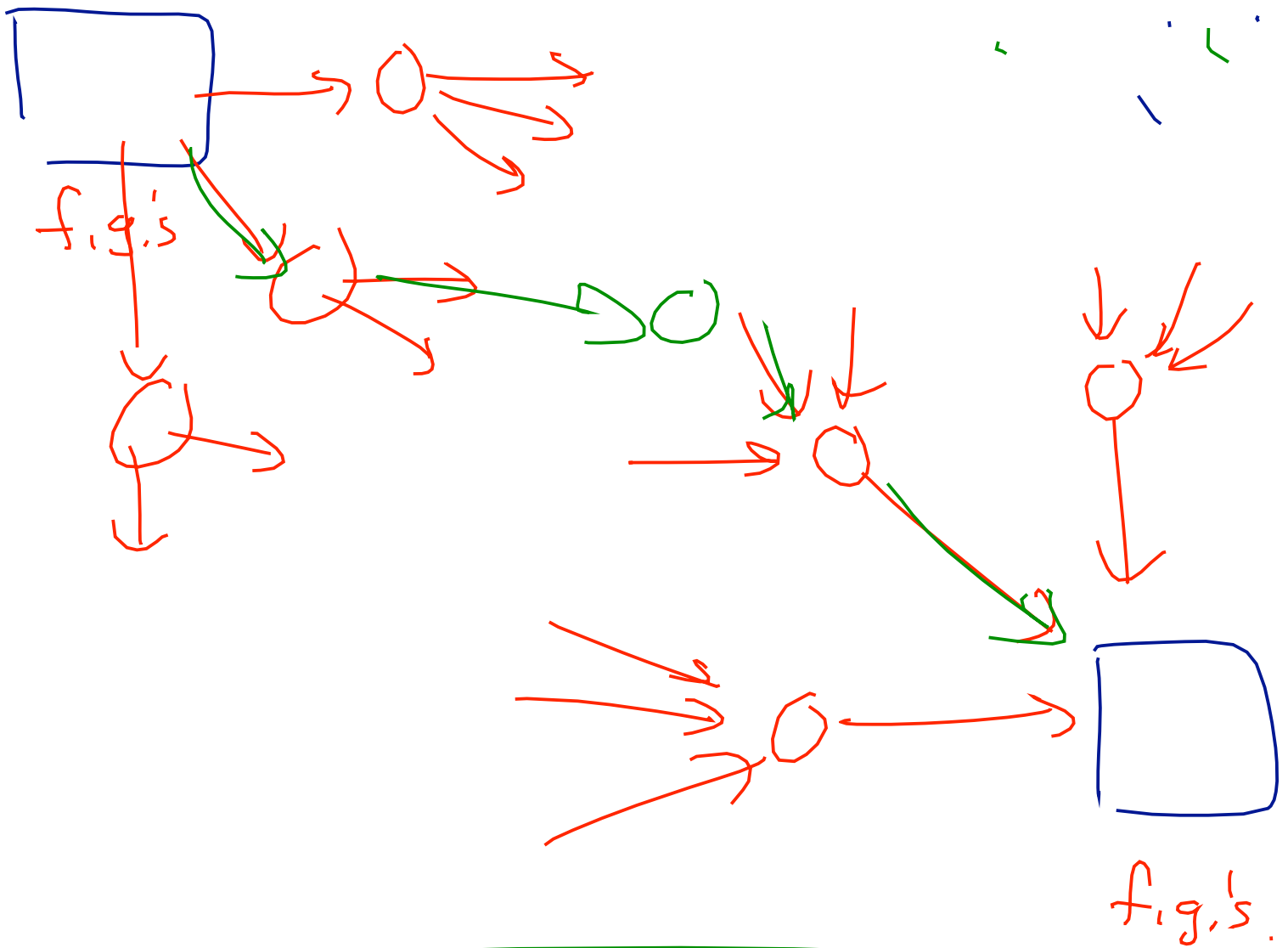
Reaction 6: HC#CC[CH2CH3]^- $\xrightarrow{H_2, Lindlar}$ CH_3CH=CHCH_3

Reaction 7: CH_3CH=CHCH_3 $\xrightarrow[2. (CH_3)_2S]{1. O_3}$ CH_3CH_2CH_2CHO

Reaction 8: CH_3CH=CHCH_3 $\xrightarrow[2. HIO_4]{1. OsO_4, H_2O}$ CH_3CH_2CH_2CHO

Desired Product: CH_3CH_2CH_2CHO

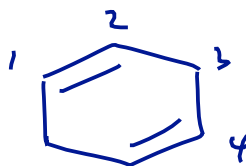




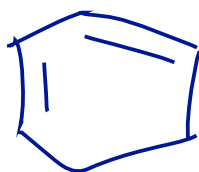
More than One Alkene In a Molecule

- Molecules with 2 C=C bonds are dienes. Draw the structures of the following dienes:

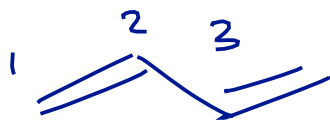
1,4-cyclohexadiene



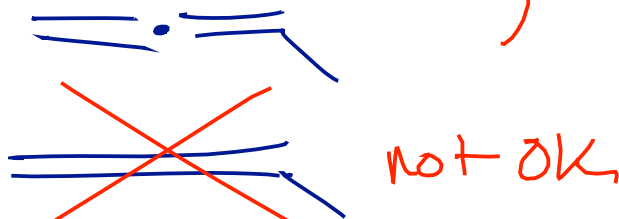
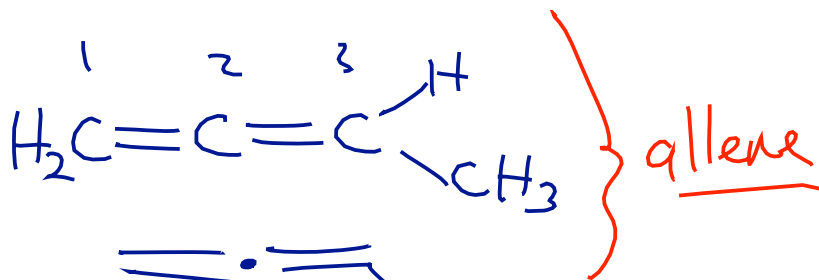
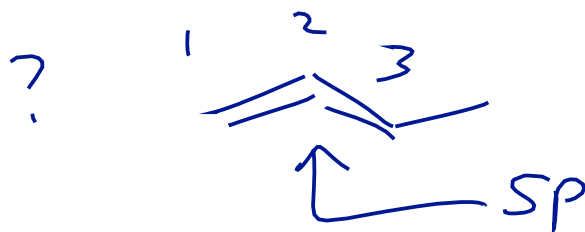
1,3-cyclohexadiene



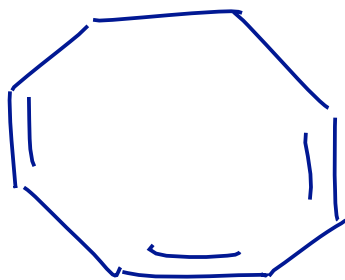
1,3-butadiene



1,2-butadiene



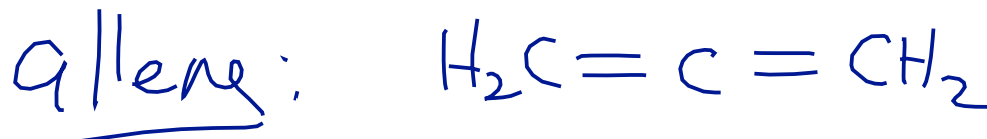
- Molecules with 3 C=C bonds are **trienes**. Draw the structure of 1,3,5-cyclooctatriene.



Reading: Chapter 15 (introduction)

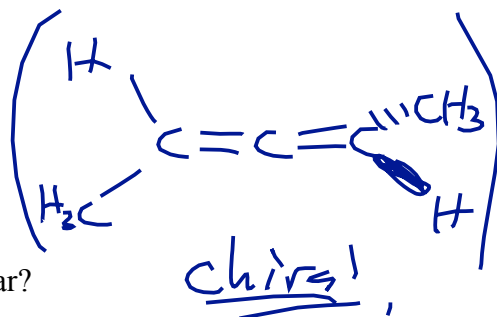
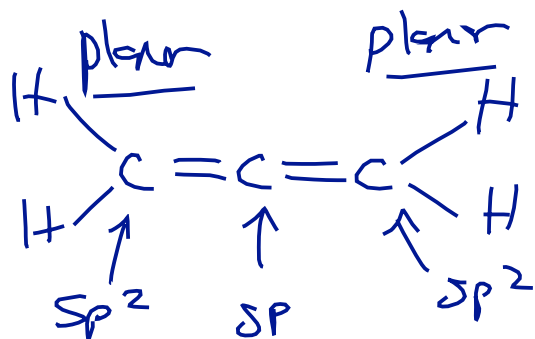
Cumulated π -Bonds: Allenes

- How close together can two C=C double bonds be in a single molecule?

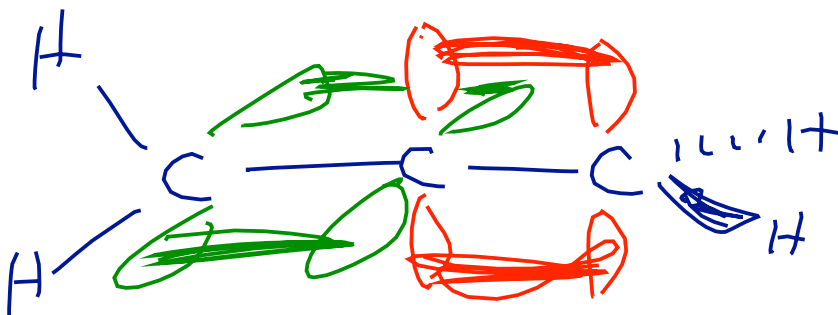


general:
cumulenes.

- When two C=C bonds share a single carbon atom, they are called cumulated double bonds. The simplest compound that contains cumulated double bonds is allene, C_3H_4 . Draw the structure of allene and determine the geometry and hybridization of each atom.

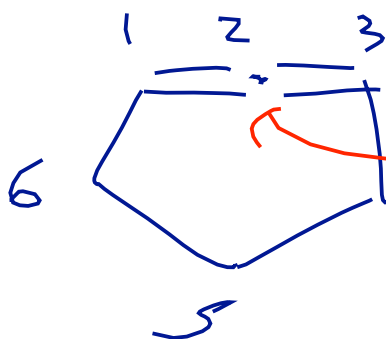


- Show the σ - and π -orbitals of allene. Is the entire molecule planar?



'ends' of
allene
in different planes,

- Draw the structure of 1,2-cyclohexadiene. This molecule can **not** be prepared as a stable compound. Can you explain why?



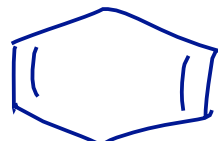
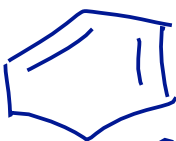
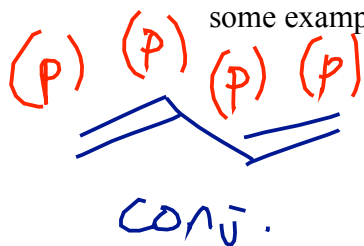
wants to be
sp - linear.

highly strained.

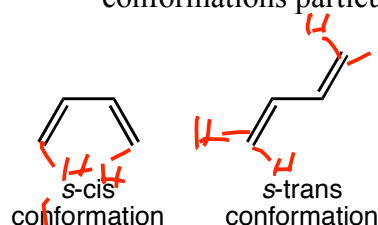
Reading: Section 15.1

Conjugated π -Bonds: 1,3-Dienes

- When two double bonds are on *adjacent* carbons they are said to be **conjugated**. Draw some examples of conjugated dienes. Why are these compounds often called 1,3-dienes?



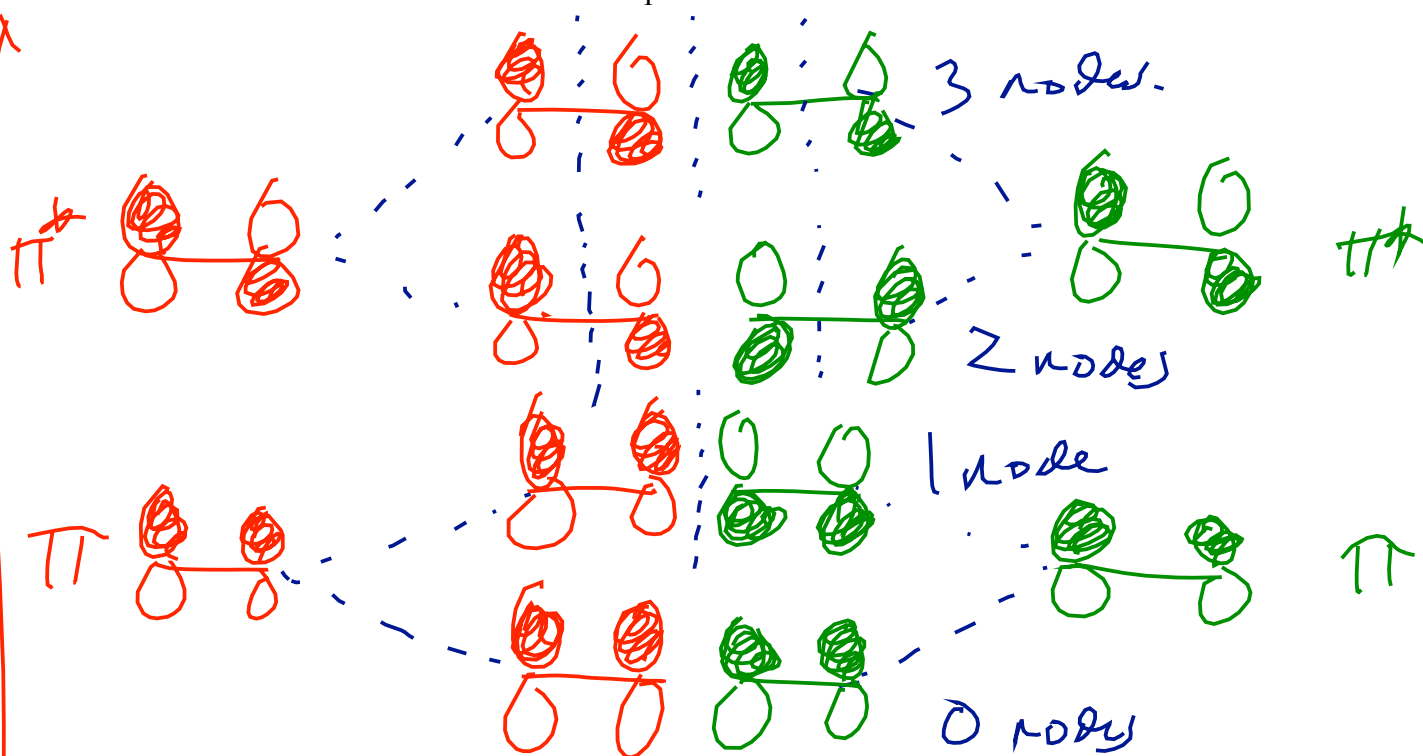
- Conformational analysis of rotation around the *single* bond in 1,3-butadiene shows that it has *two* stable conformations, both of which are (nearly) *planar*. Why are these conformations particularly stable? Which one is more stable, and why?



(s- means around single bond)

→ steric clash of H's.

- Draw the π -molecular orbitals (MOs) for 1,3-butadiene. Can you explain why the *planar* conformations of butadiene are preferred?



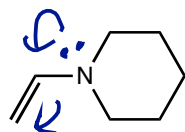
Reading: Section 15.1

Overlap of p/ π orbitals on adjacent atoms.

Find conjugation!

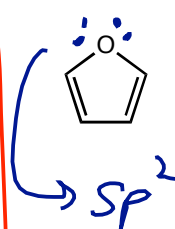
Multiple Conjugated p -Orbitals

- When a lone pair, vacant p -orbital, or radical (unpaired electron) is *adjacent* to a π -bond, the orbital in question can become *conjugated* with the π -bond. For each of the following structures, count *how many p -orbitals* are conjugated together, and count the total *number of π -electrons* in the conjugated system. Be sure to consider the appropriate hybridization for each atom in the conjugated system!



p -orb.
3

e^-
4



p -orb.
5

e^-
6



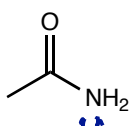
3

4



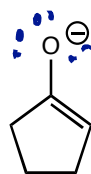
3

2



3

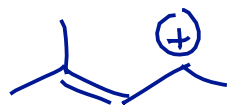
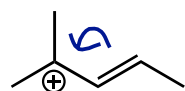
2



3

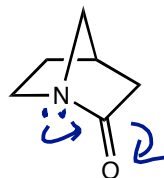
4

enolate



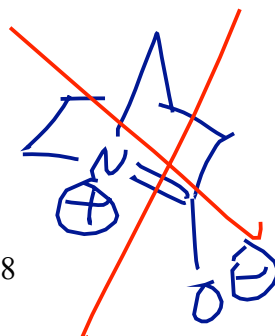
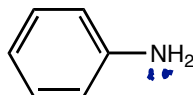
7

8



2

2



violates

Reading: Section 15.6

Bredt's rule.

increased stability

Conj. π -bands

- In general: Overlap of molecular orbitals (moderate effect)

more
stable

Conj.



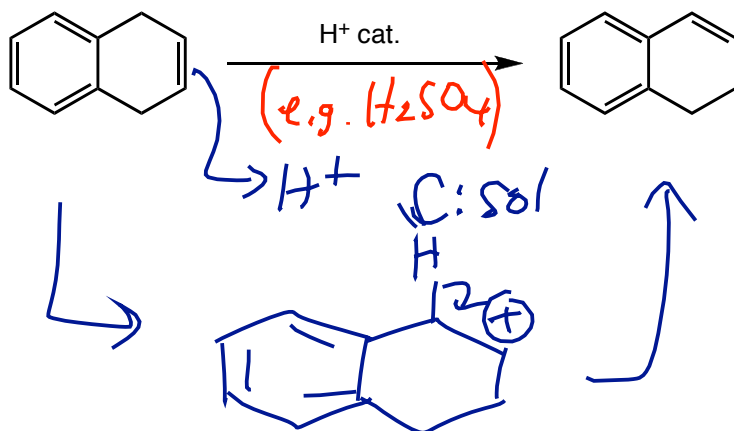
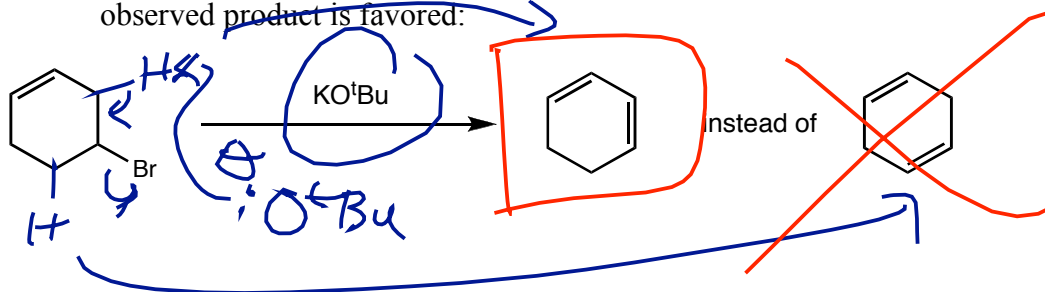
- For charged species: Delocalization of charge (large effect)

Example: allyl cation



much more stable

- Provide curved-arrow mechanisms for the following reactions and explain why the observed product is favored:



isomerize
alkene
to
most stable

Reading: Section 15.6

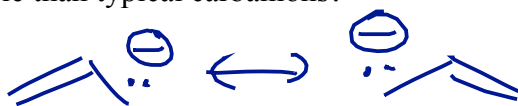
isomer.

Allylic and Benzylic Carbanions:

C-H Acidity and Allylic Grignard Rearrangements

Draw the structure of the *allyl anion* and the *benzyl anion*. What makes these carbanions more stable than typical carbanions?

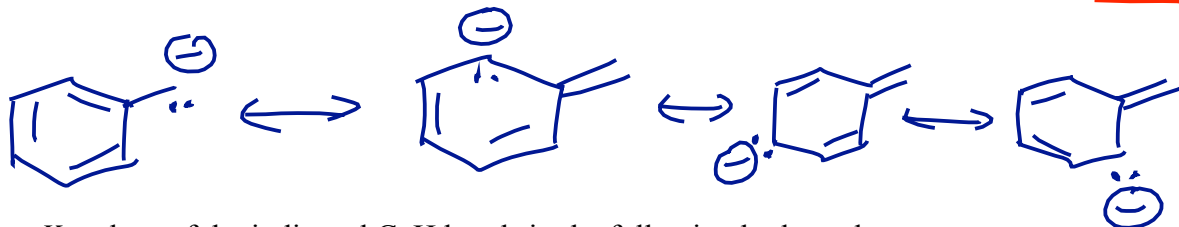
Allyl anion



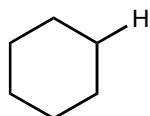
delocalize
⊖ charge

adjacent to
benzene
ring

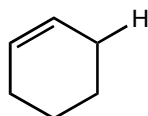
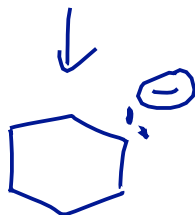
Benzylic anion



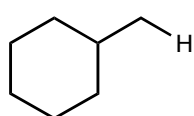
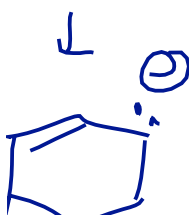
- Explain the pK_a values of the indicated C-H bonds in the following hydrocarbons:



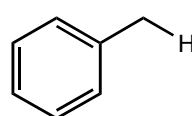
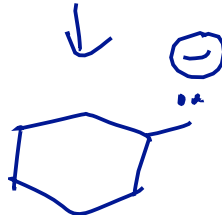
$pK_a \approx 55$



$pK_a \approx 43$



$pK_a \approx 55$

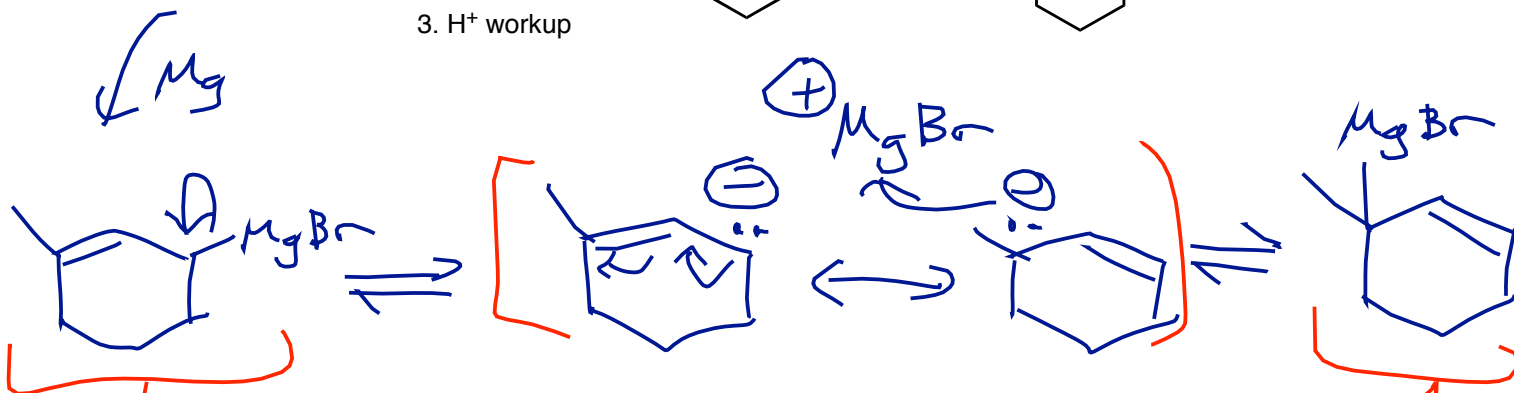
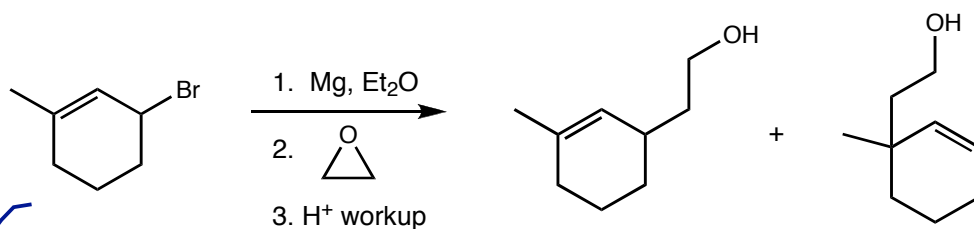


$pK_a \approx 41$



resonance
stabilized
carb-
anions

- Explain why *two* products are observed from the following reaction sequence:



What can we say about allylic and benzylic reactivity?

Reading: Section 17.3

allyl anion

equilibrium

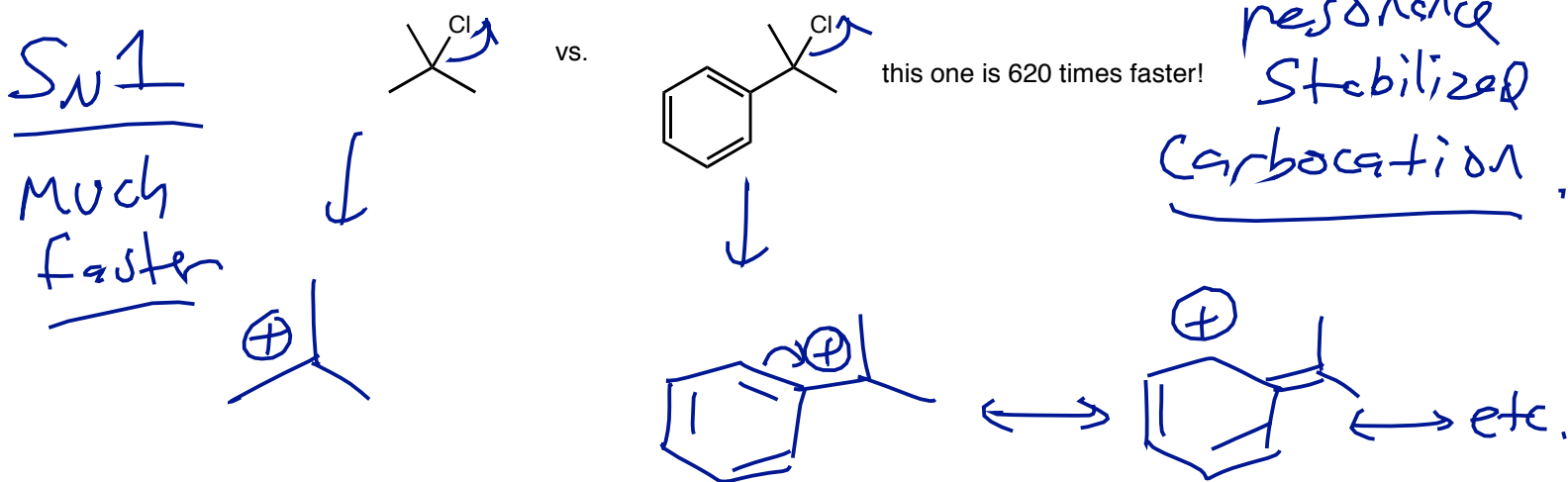
Conjugation

much more
stable

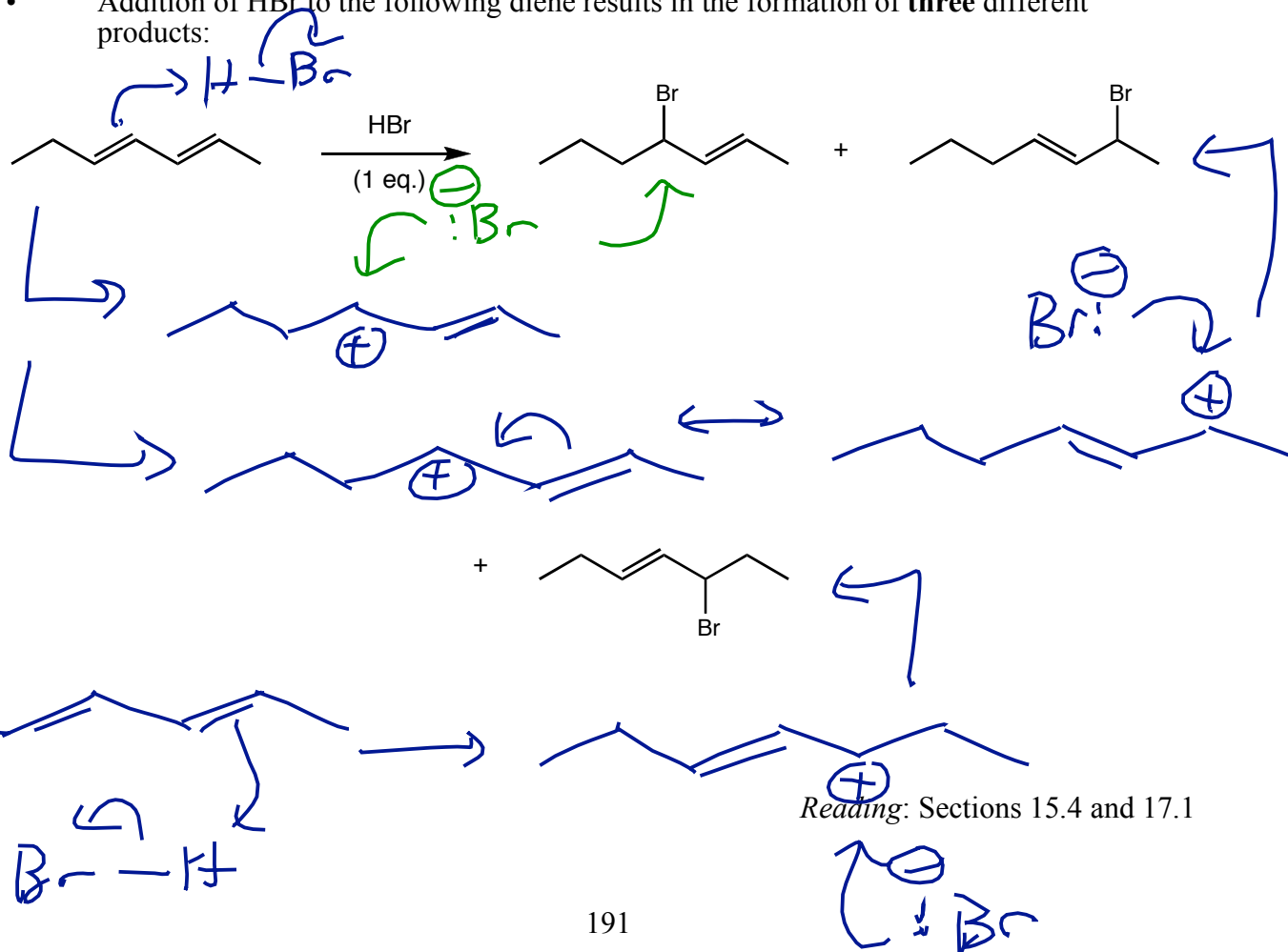
Allylic and Benzylic Carbocations: S_N1 Reactions and HX Addition

Explain the following observations:

- Replacing a methyl group in *t*-butyl chloride with a phenyl group increases the rate of S_N1 substitution by a factor of 620:

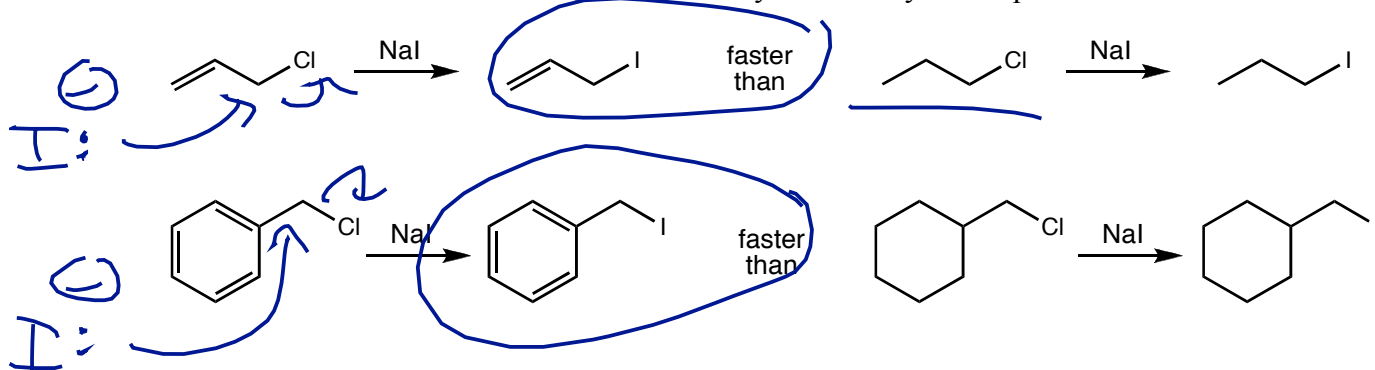


- Addition of HBr to the following diene results in the formation of **three** different products:

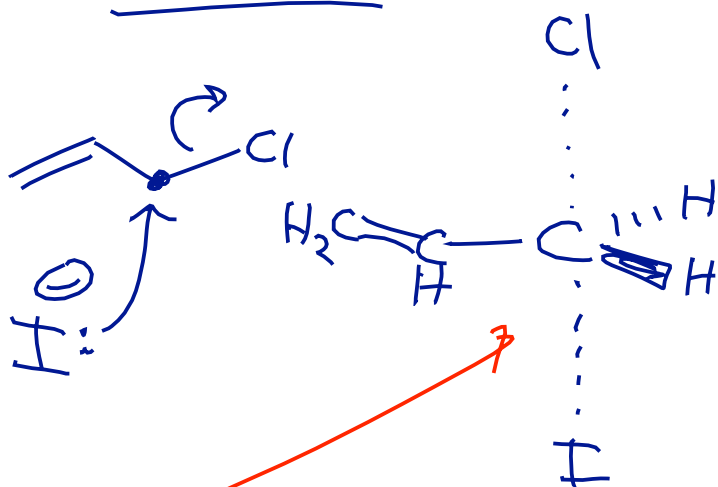


Allylic and Benzylic Alkyl Halides: S_N2 Reactions

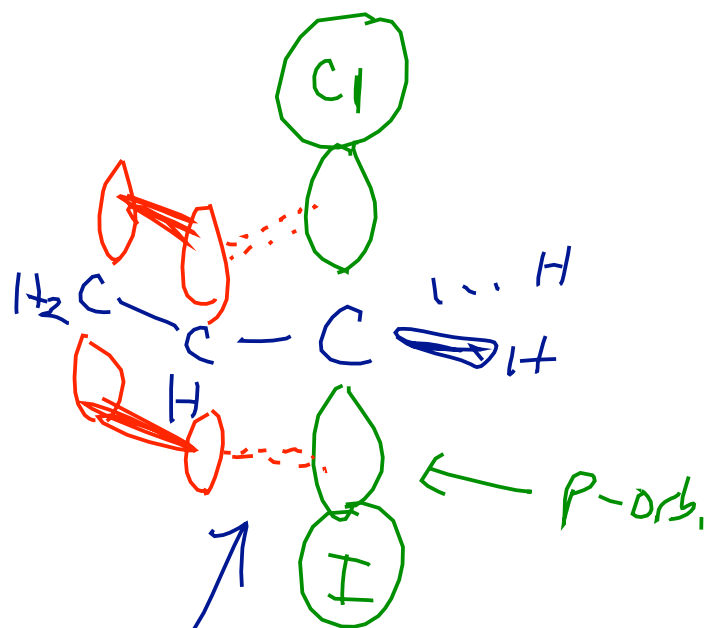
- The following reactions are S_N2 reactions—there's no free carbocation—yet the reactions are accelerated if the alkyl halide is allylic or benzylic. Explain.



Trans. state S_N2

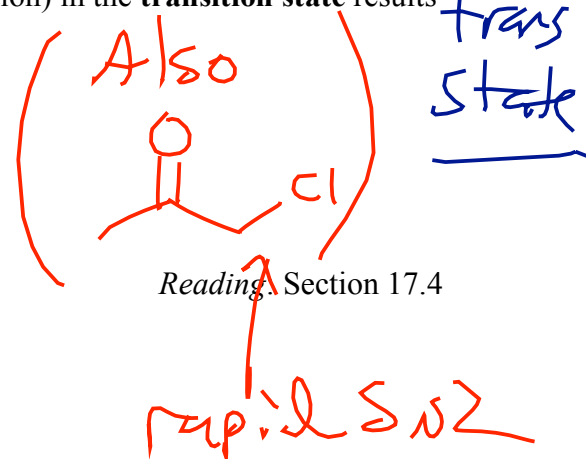
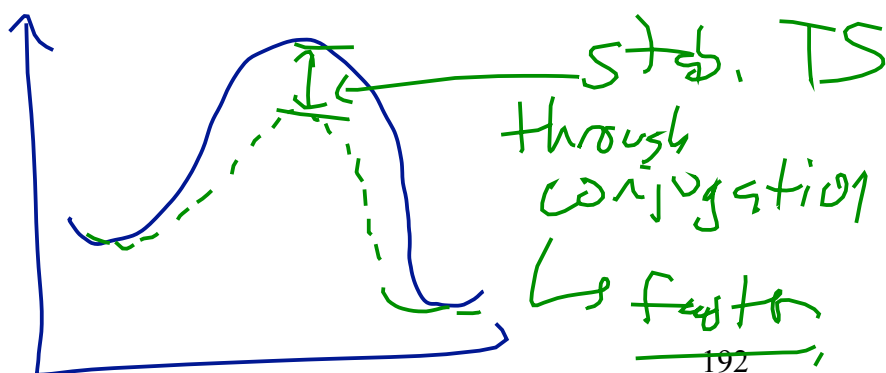


sp^2 hybrid TS.



Overlap $\pi_{C=C}$ with p-orb.

- This is a classic example of how conjugation (stabilization) in the **transition state** results in a faster reaction.

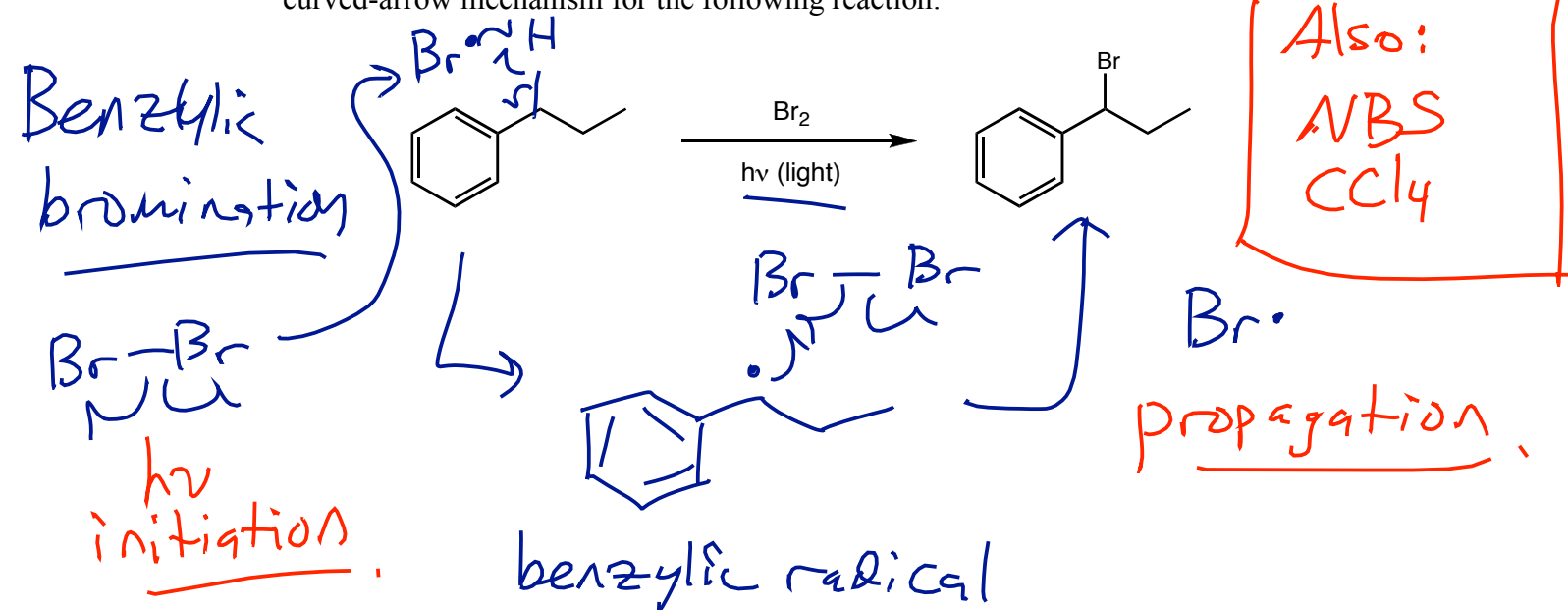


Benzylic C-H Bonds: Bromination and Oxidation

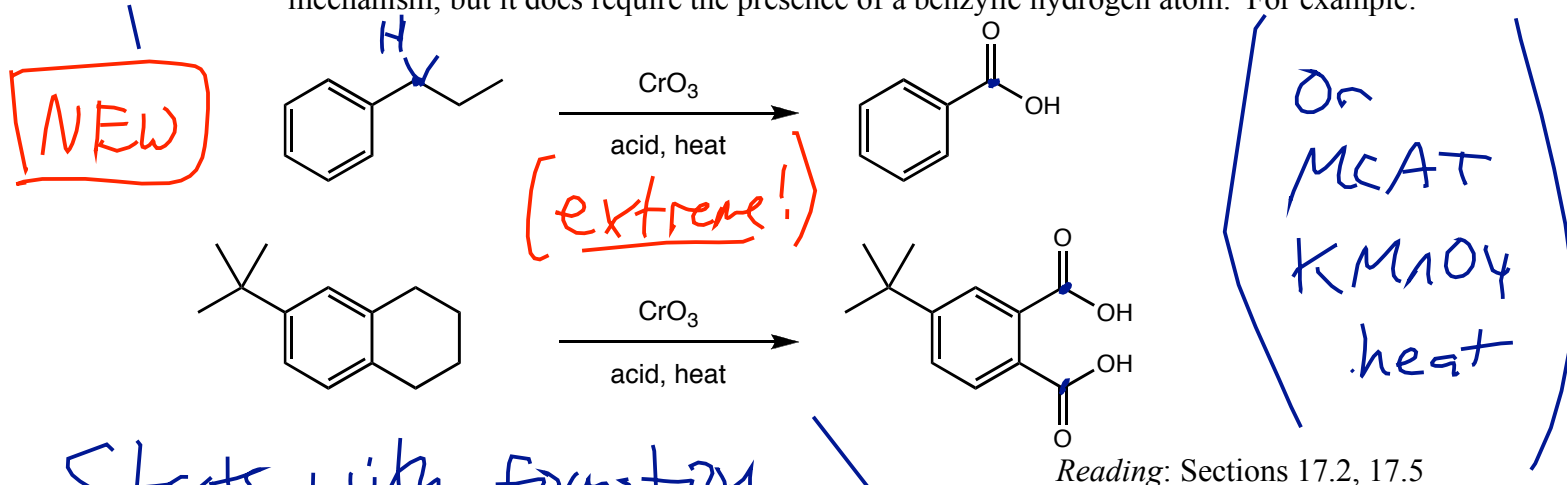
- The C-H bonds at a *benzylic* carbon are especially susceptible to radical (homolytic) dissociation. Why?



- Thus, one can carry out radical substitution *selectively* at the benzylic carbon. Propose a curved-arrow mechanism for the following reaction:



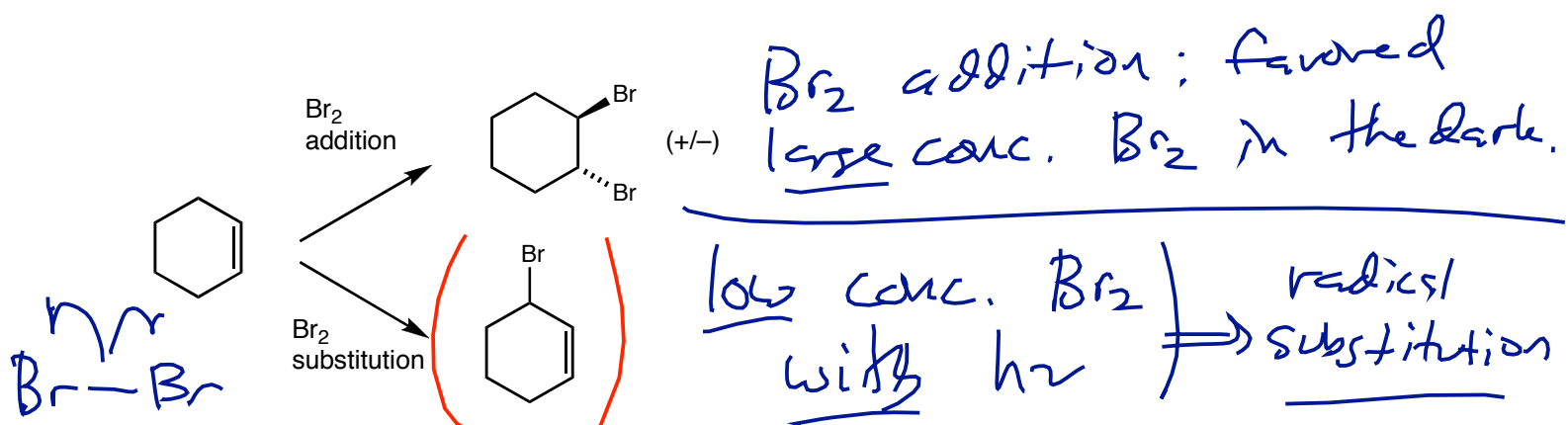
- In addition, strong oxidizing agents can **completely oxidize** any hydrocarbon sidechain of an aromatic ring to carboxylic acid (-COOH) groups. You need not worry about the mechanism, but it does require the presence of a benzylic hydrogen atom. For example:



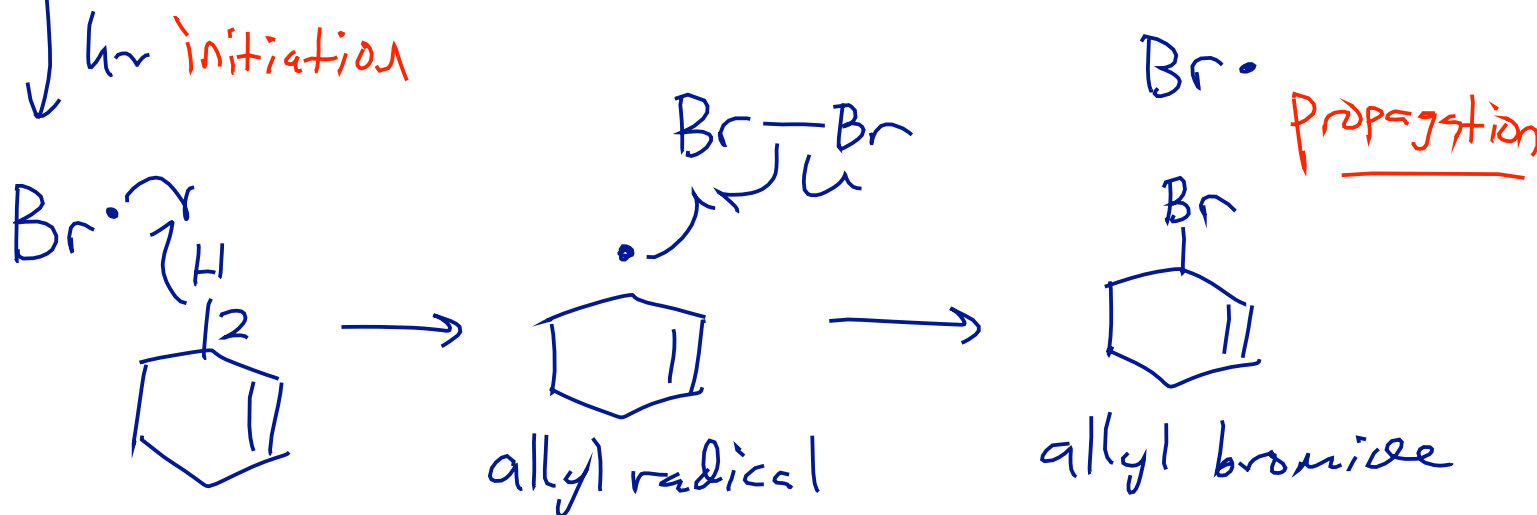
Starts with formation of benzylic radical \Rightarrow need C-H

important and useful!**Allylic C-H Bonds: Bromine Addition vs. Substitution**

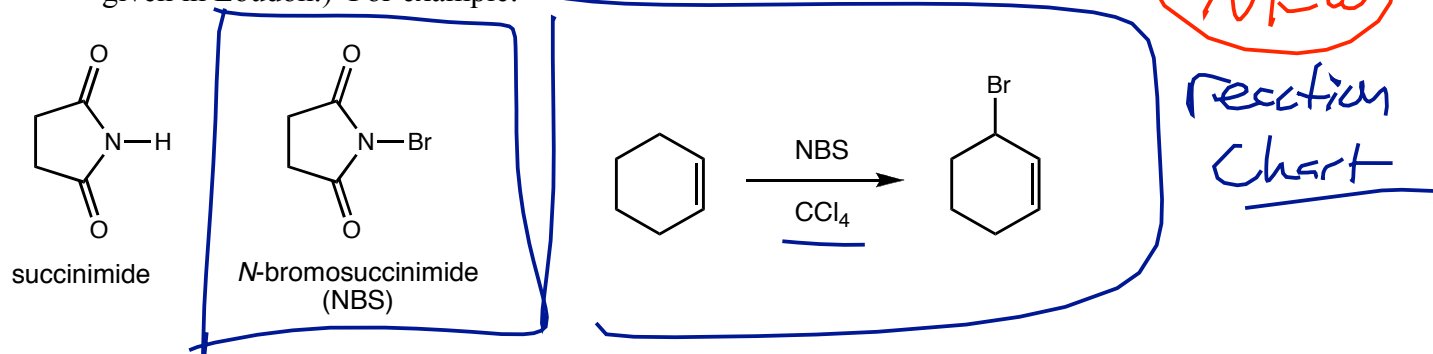
- Allylic C-H bonds are similarly susceptible to radical cleavage. However, in the case of allylic compounds there are two possible reactions that can take place. Under what conditions would each of the following reactions be favored?



- Draw a curved-arrow mechanism for allylic bromination of cyclohexene.



- Allylic bromination can be carried out selectively using the brominating agent *N*-bromosuccinimide (NBS) in carbon tetrachloride solvent (CCl₄). (The mechanism is given in Loudon.) For example:



used instead of
Br₂, hν

Reading: Section 17.2

Allylic bromination