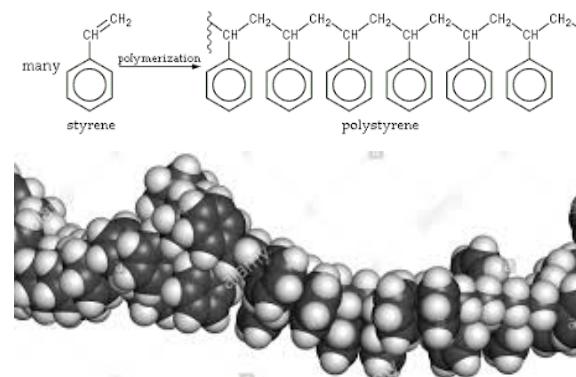
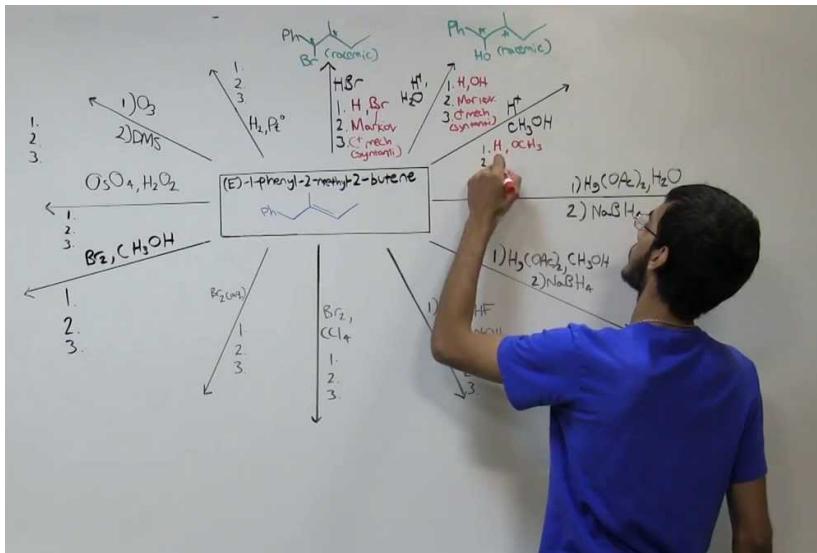
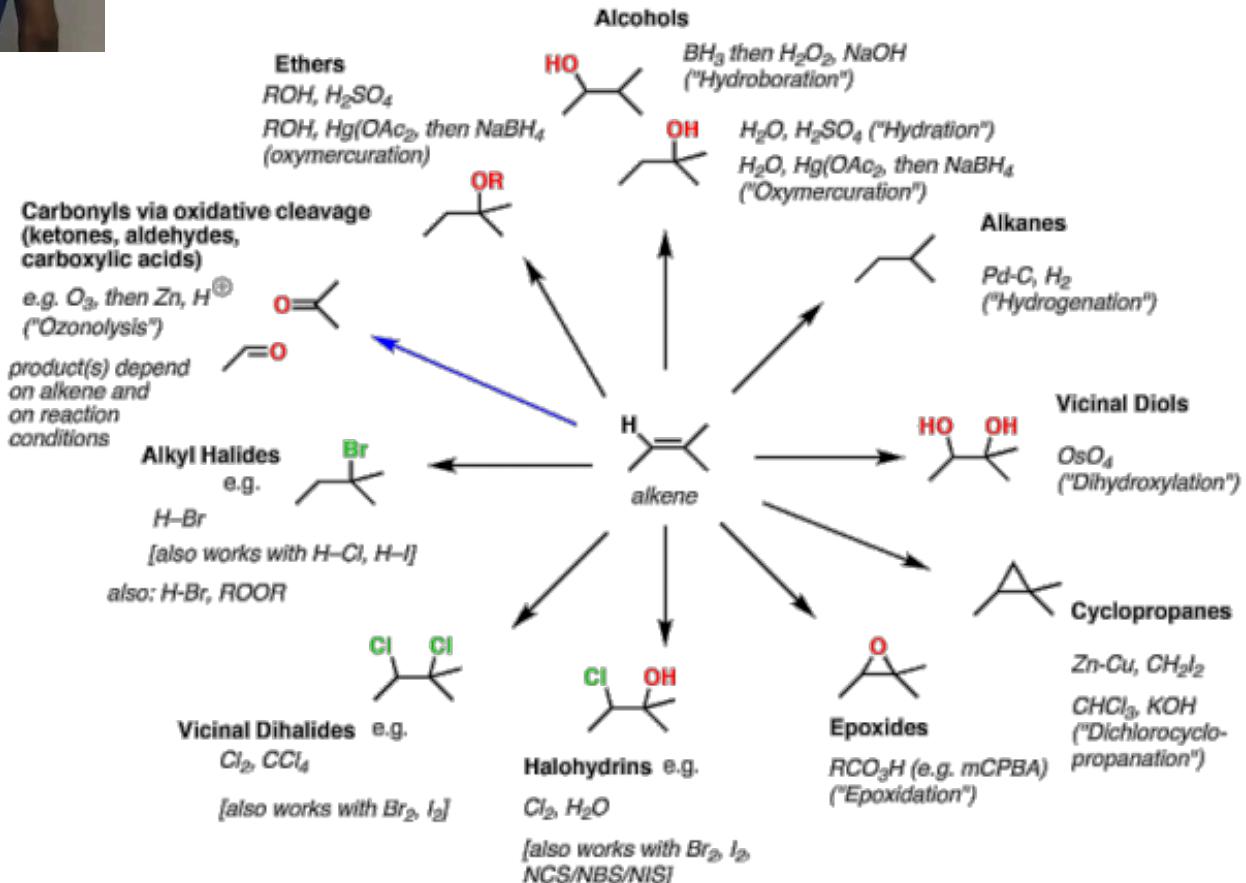
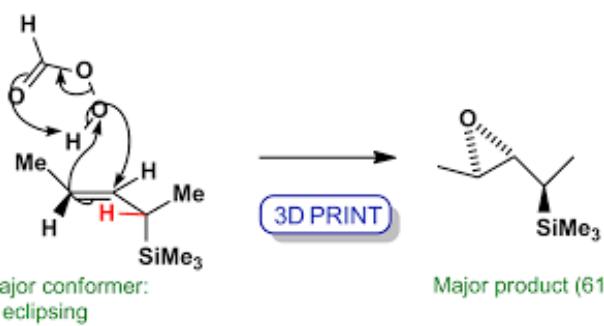


Chapter 8: Reactions of Alkenes

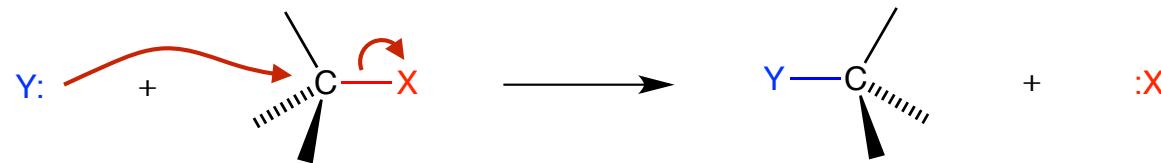


Addition and Oxidative Cleavage Reactions of Alkenes



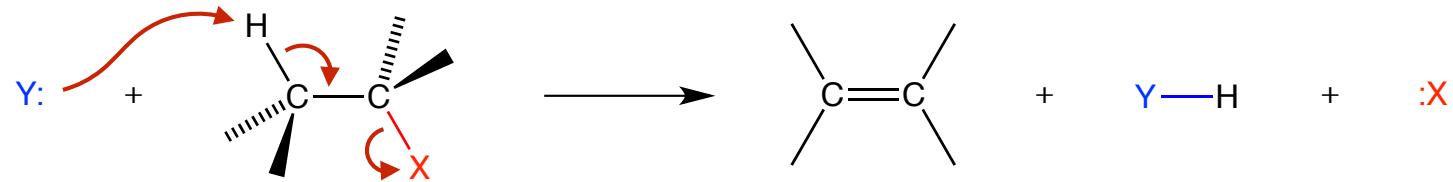
Three Major Types of Reactions

Substitution

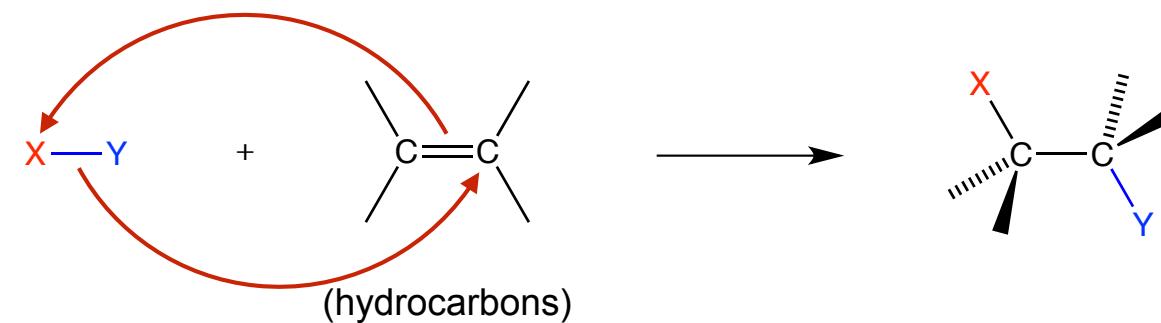


(alkyl halides & alcohols)

Elimination



Addition

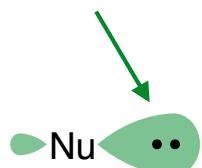


Q: What do these reactions share in common?

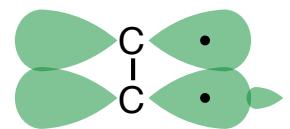
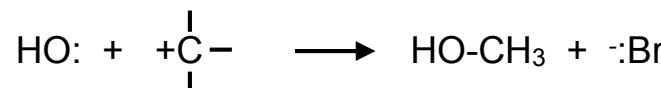
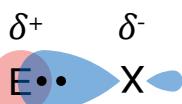
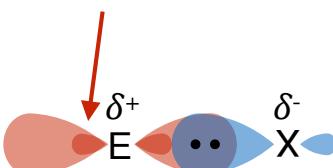
Q: What species usually are involved in formation and breaking of bonds?

Heterolytic Bond Formation

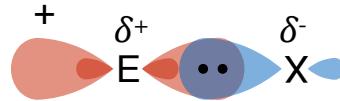
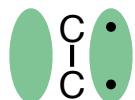
electron-rich orbital



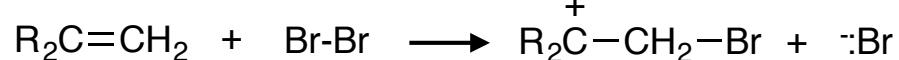
electron-deficient orbital



II

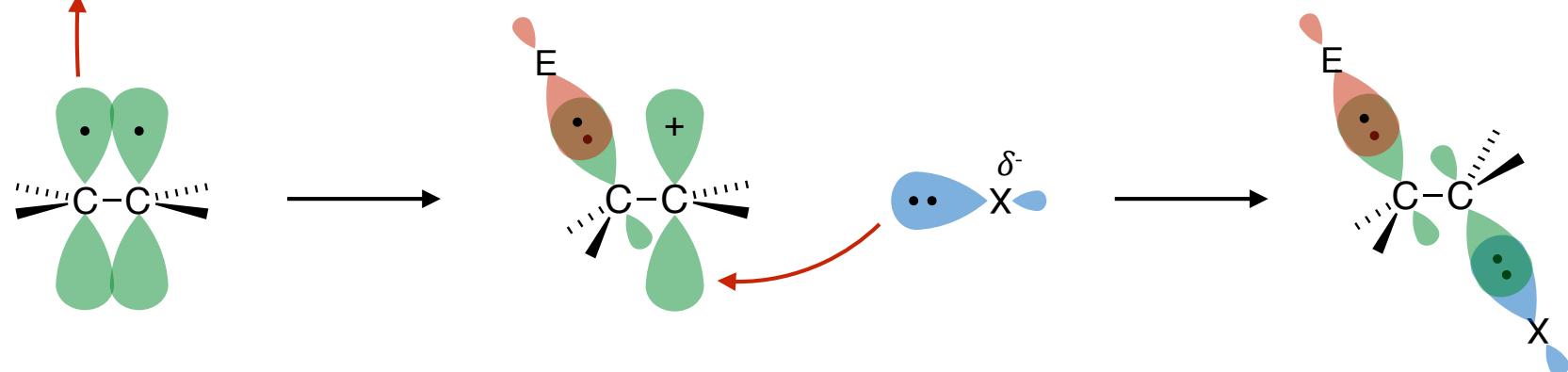
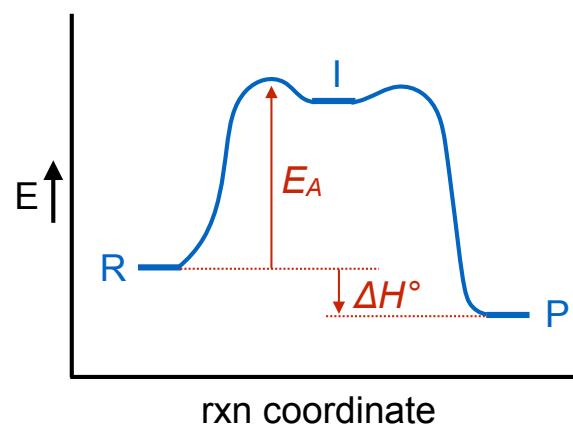
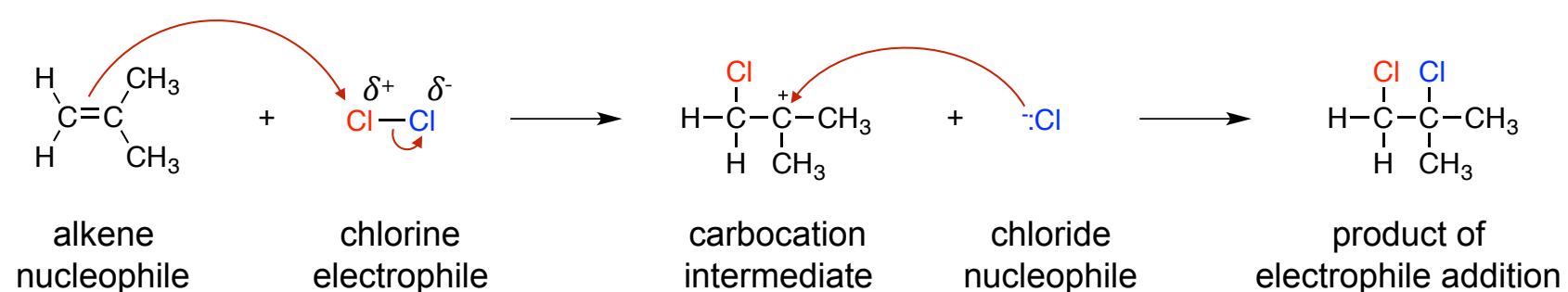


e^- -rich π cloud
(a nucleophile!)



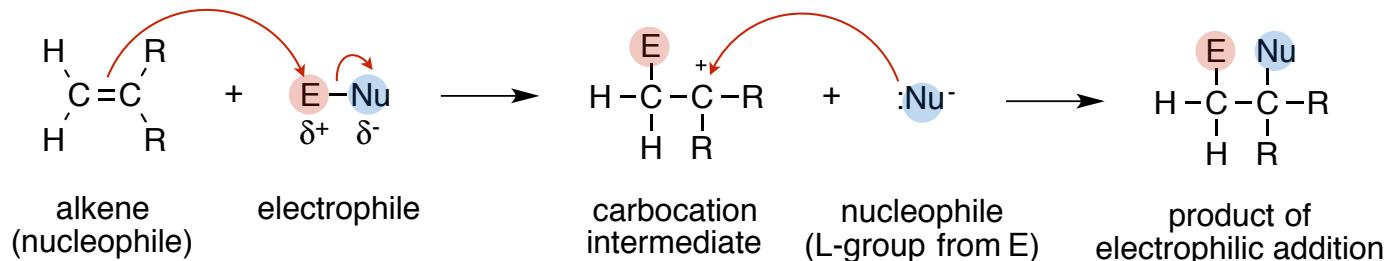
Electrophilic addition!

Ex: Electrophilic addition of chlorine to isobutylene

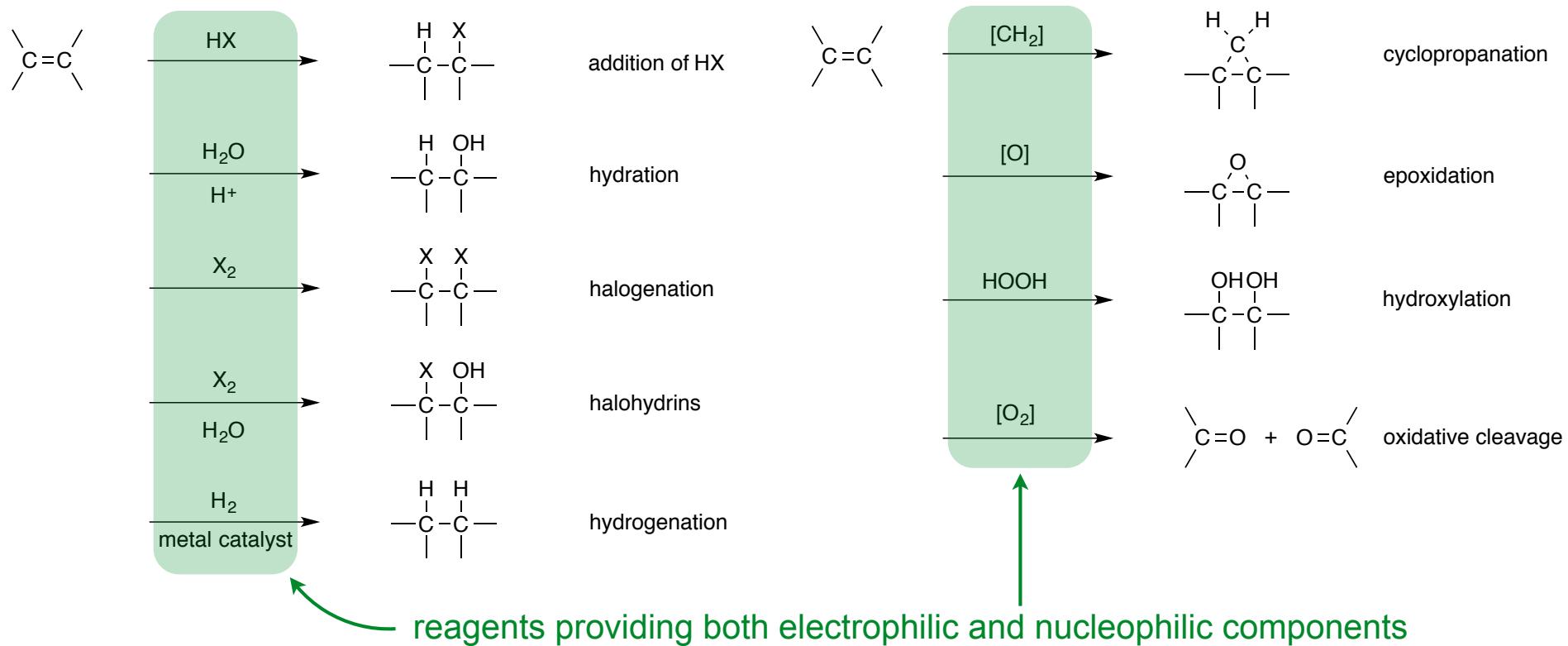


Electrophilic Addition to Alkenes (8-2)

General Rxn:

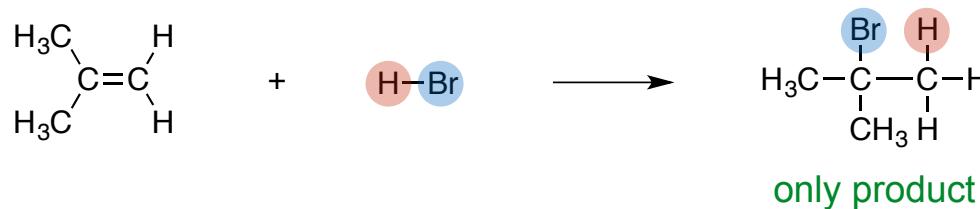


Addition reactions we'll examine



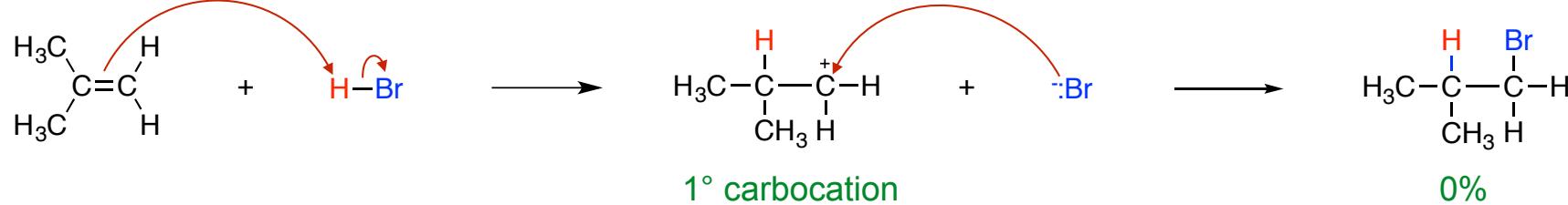
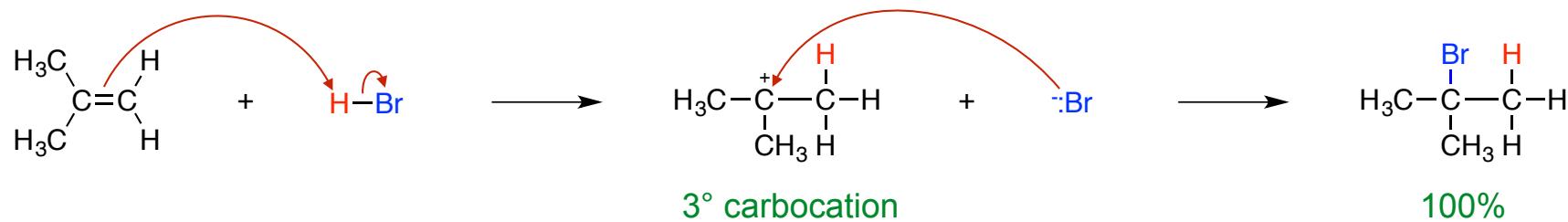
Addition of Hydrogen Halides to Alkenes (8-3A)

Ex:



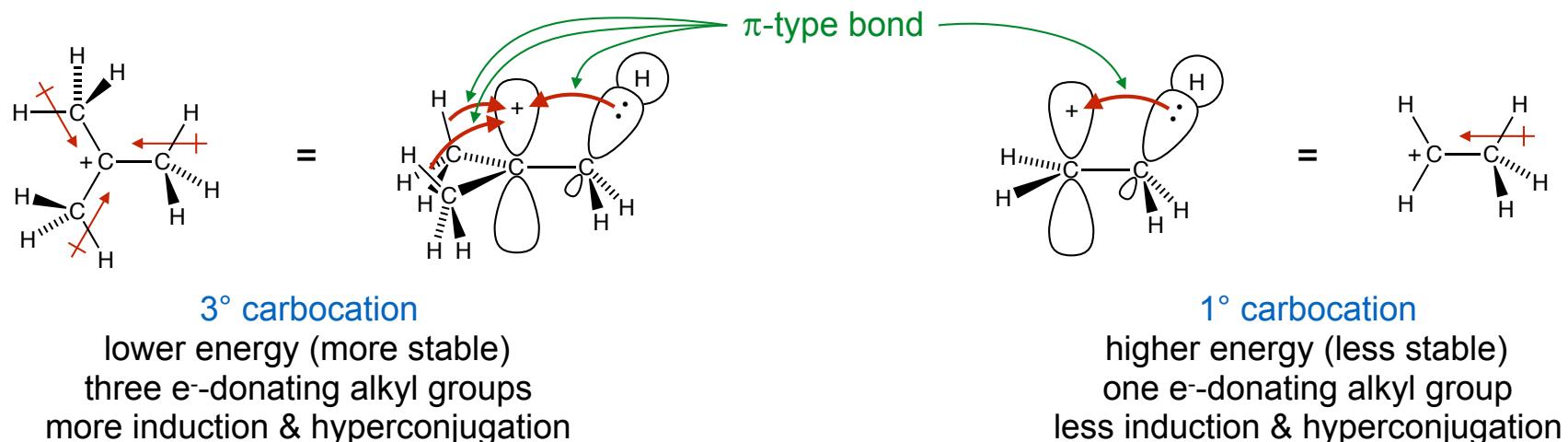
Q: Why just one product? Possible ways that HBr can add to the C=C bond?

Consider addition both ways



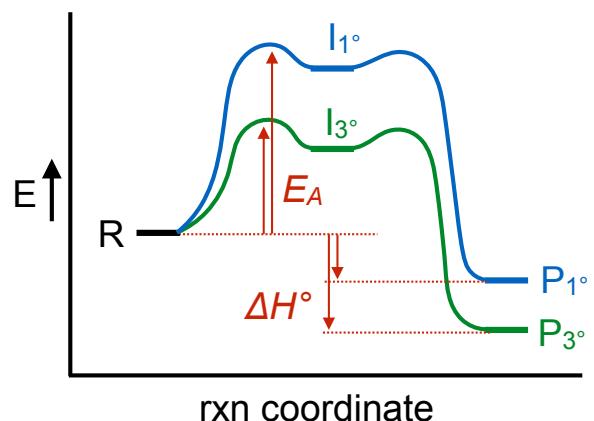
Q: Why is one pathway favored?

Consider the 1° and 3° carbocation intermediates



Induction - donation of electron density through σ bonds

Hyperconjugation - donation of electron density to an empty p orbital via weak π -type bonds



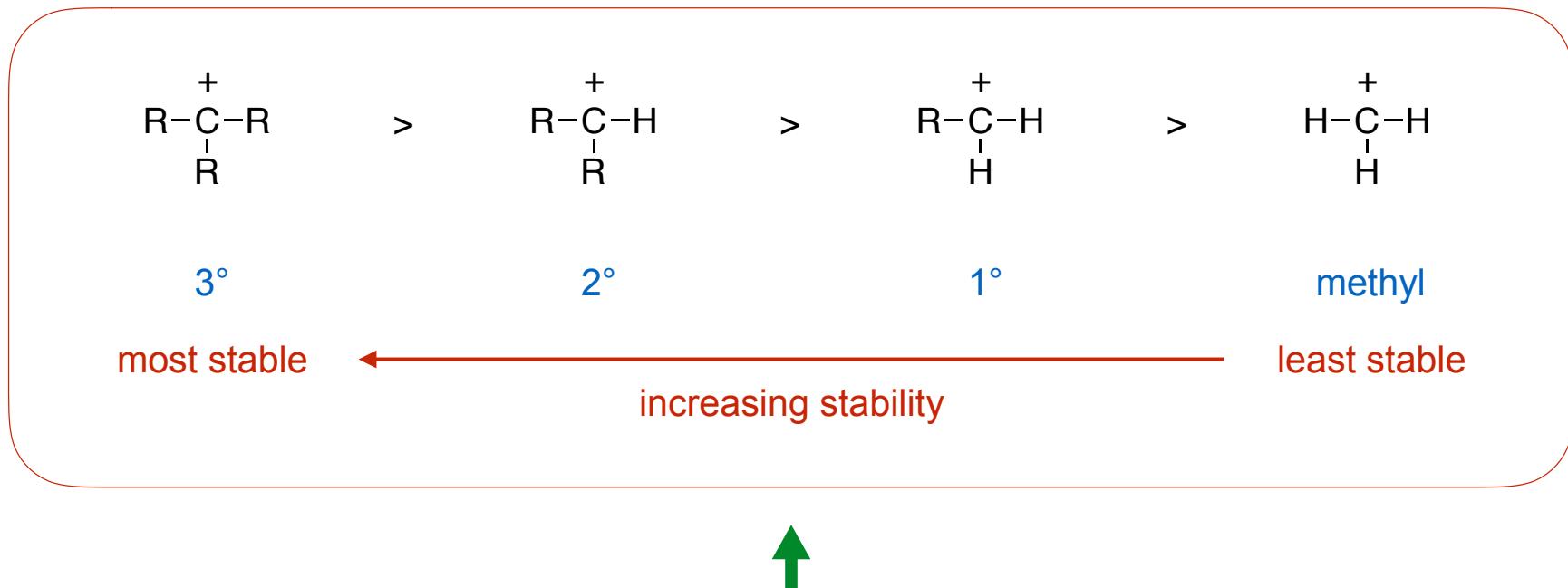
Q: Which carbocation forms fastest?

Q: Which product forms fastest?

Q: Which product is most stable?

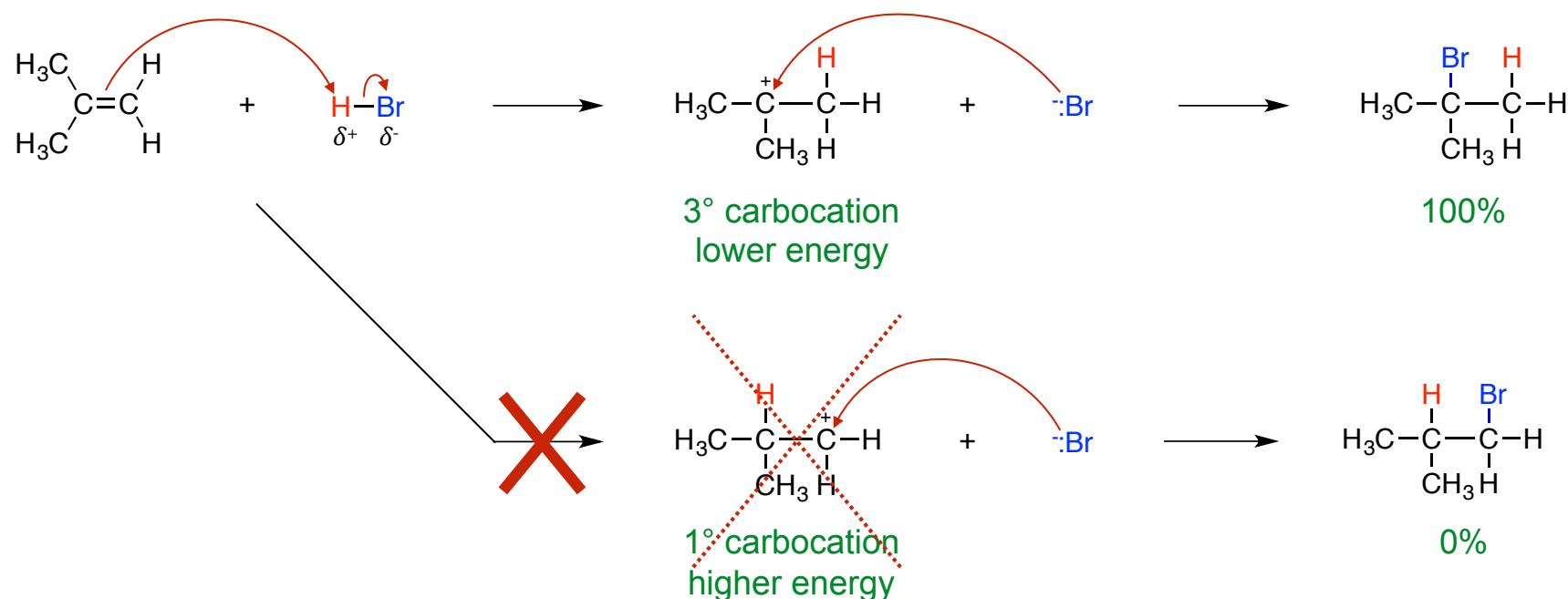
Q: Does the rate at which intermediates or products form have anything to do with the distribution of final products?

Order of Stability of Carbocations



Allows you to predict where the electrophile & nucleophile end up in electrophilic addition reactions

Back to the reaction

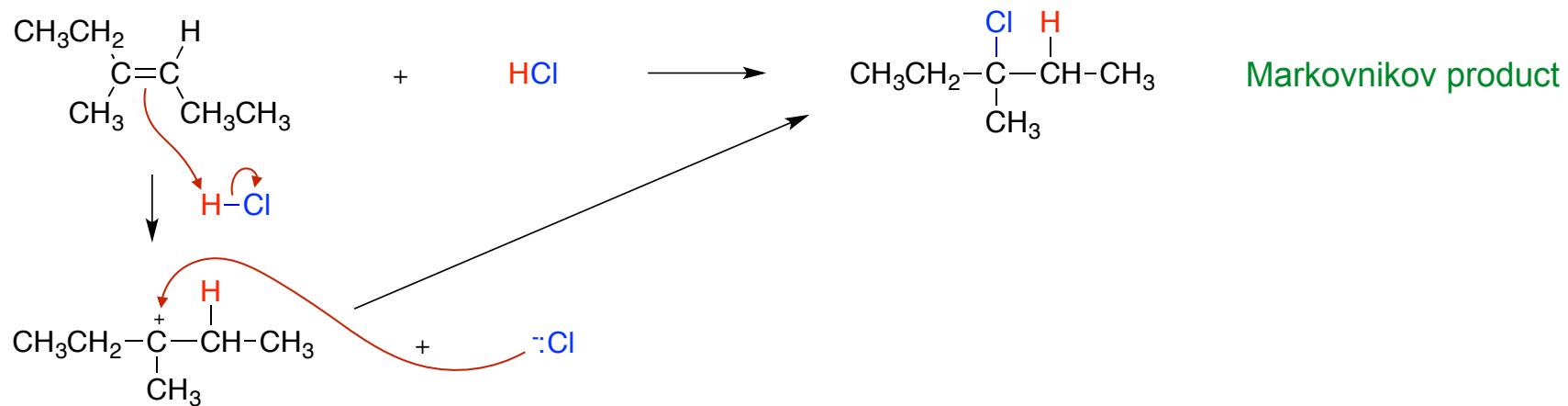


Markovnikov's Rule

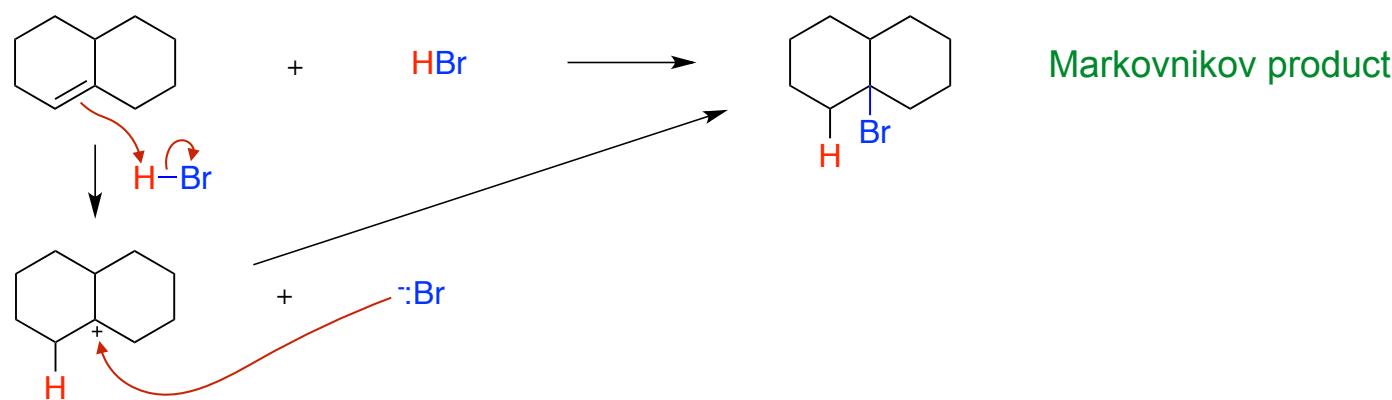
- An electrophile adds to form the most stable (lowest-energy) carbocation intermediate
- An electrophile adds to the less-substituted carbon atom in a C=C bond

→ Applies to all electrophilic addition reactions!

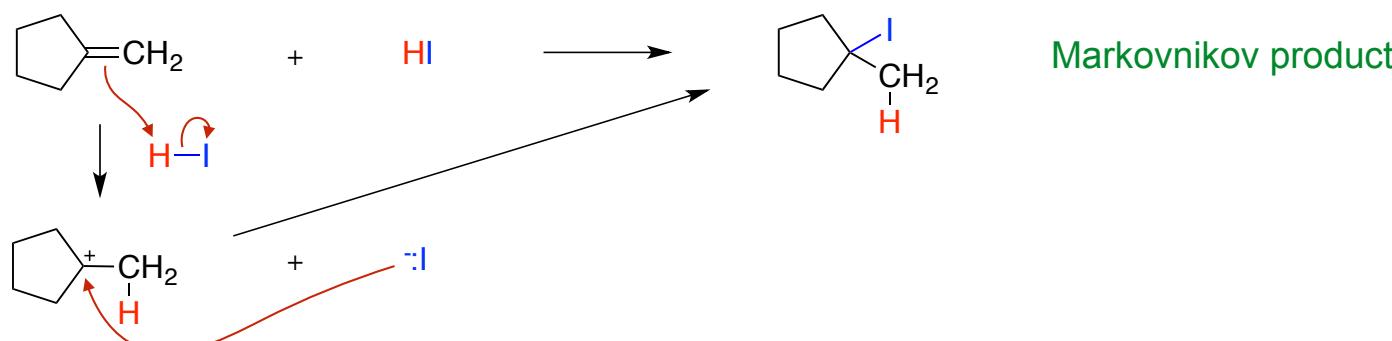
Ex:



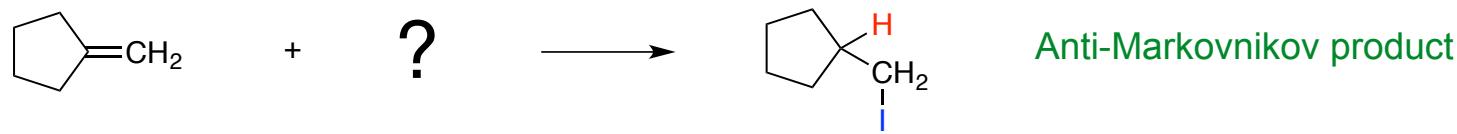
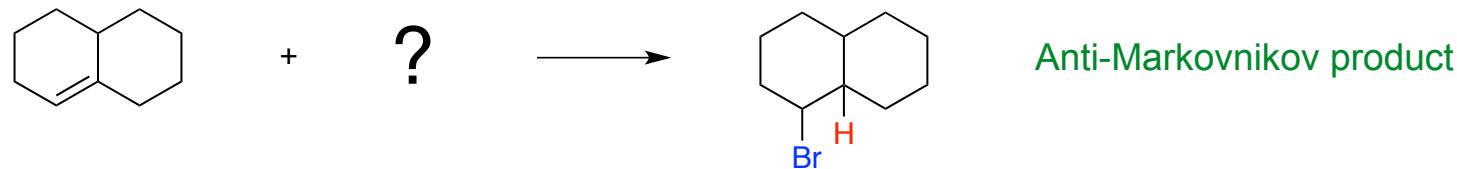
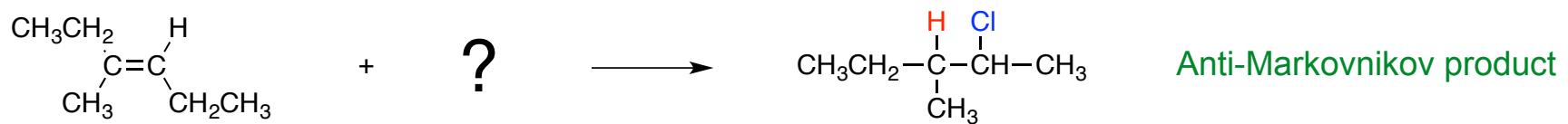
Ex:



Ex:



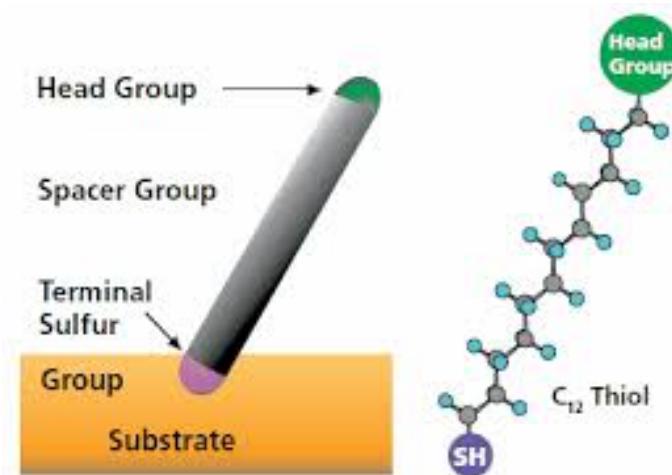
Q: What if you need these compounds?



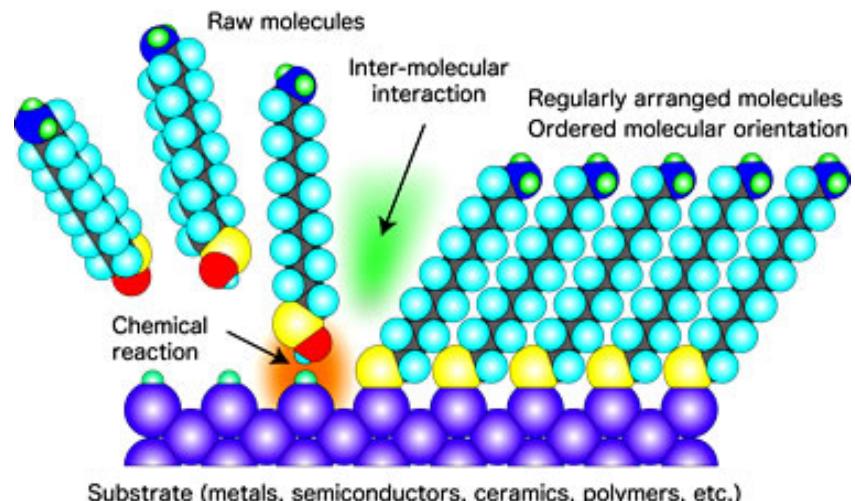
Q: Can addition be controlled to form these anti-Markovnikov products?

Q: Why is it important to be able to control the regioselectivity of addition reactions?

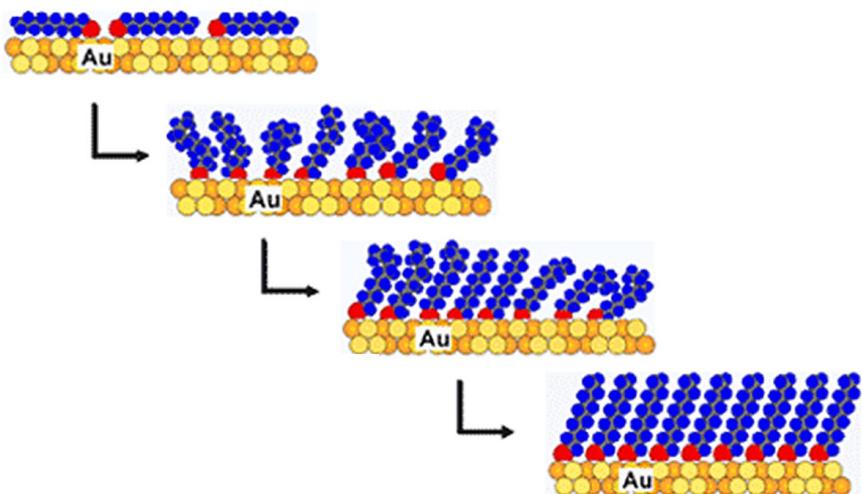
Surface Modification Using Self-Assembled Monolayers (SAMs)



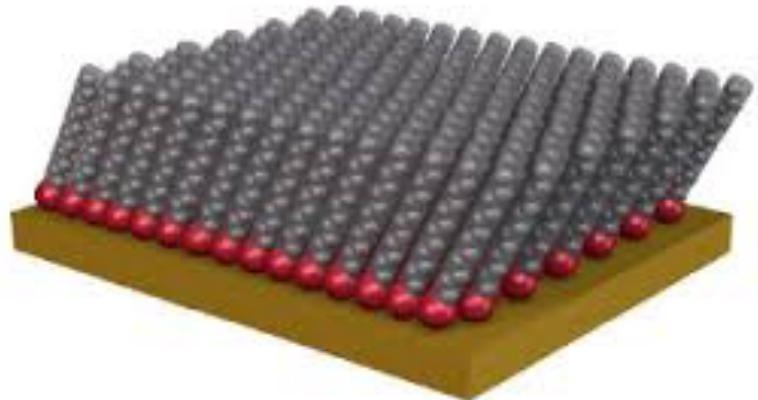
thiols bind to gold



spontaneous self-assembly forms a molecular monolayer

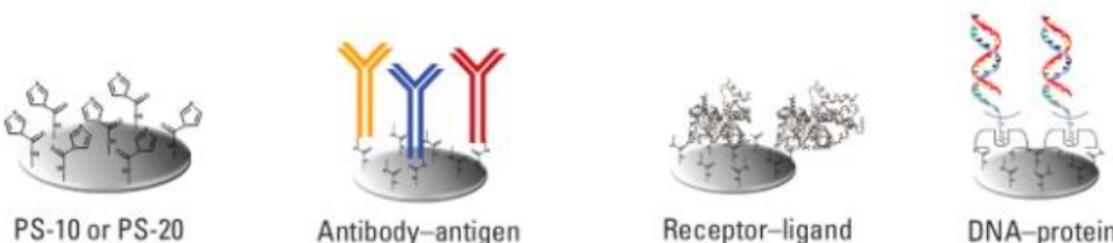


steps leading to formation of a self-assembled monolayer

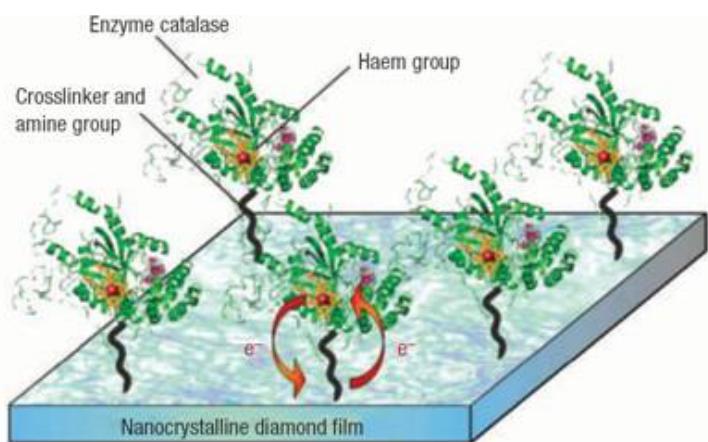


ordered self-assembled monolayer (SAM)

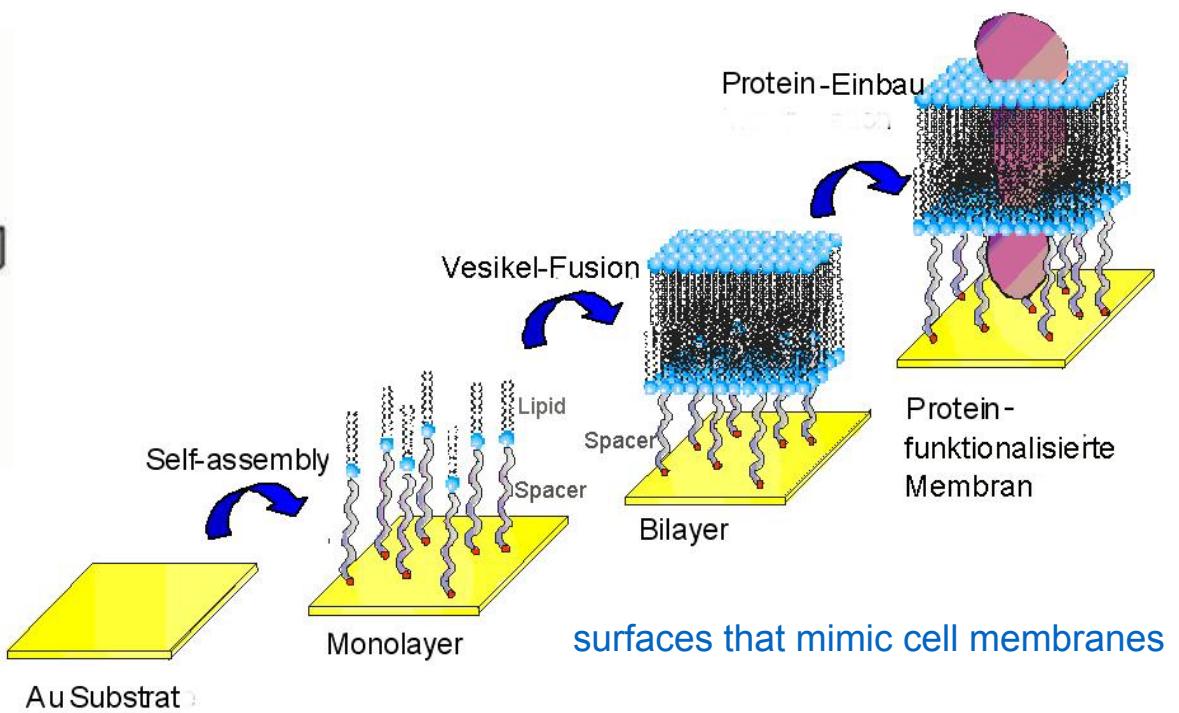
Function & Materials Derived From SAMs



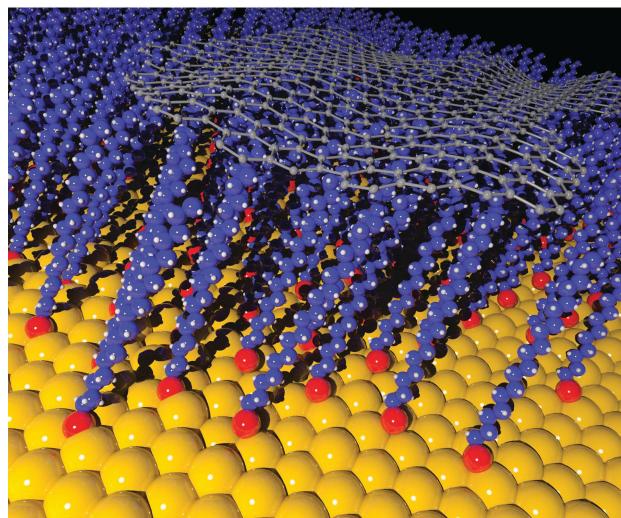
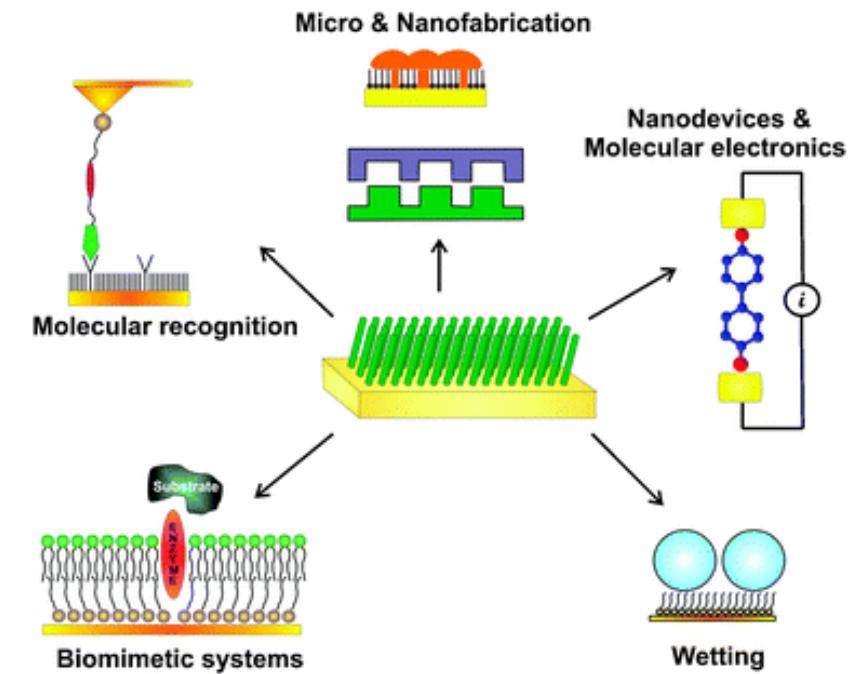
functional surfaces



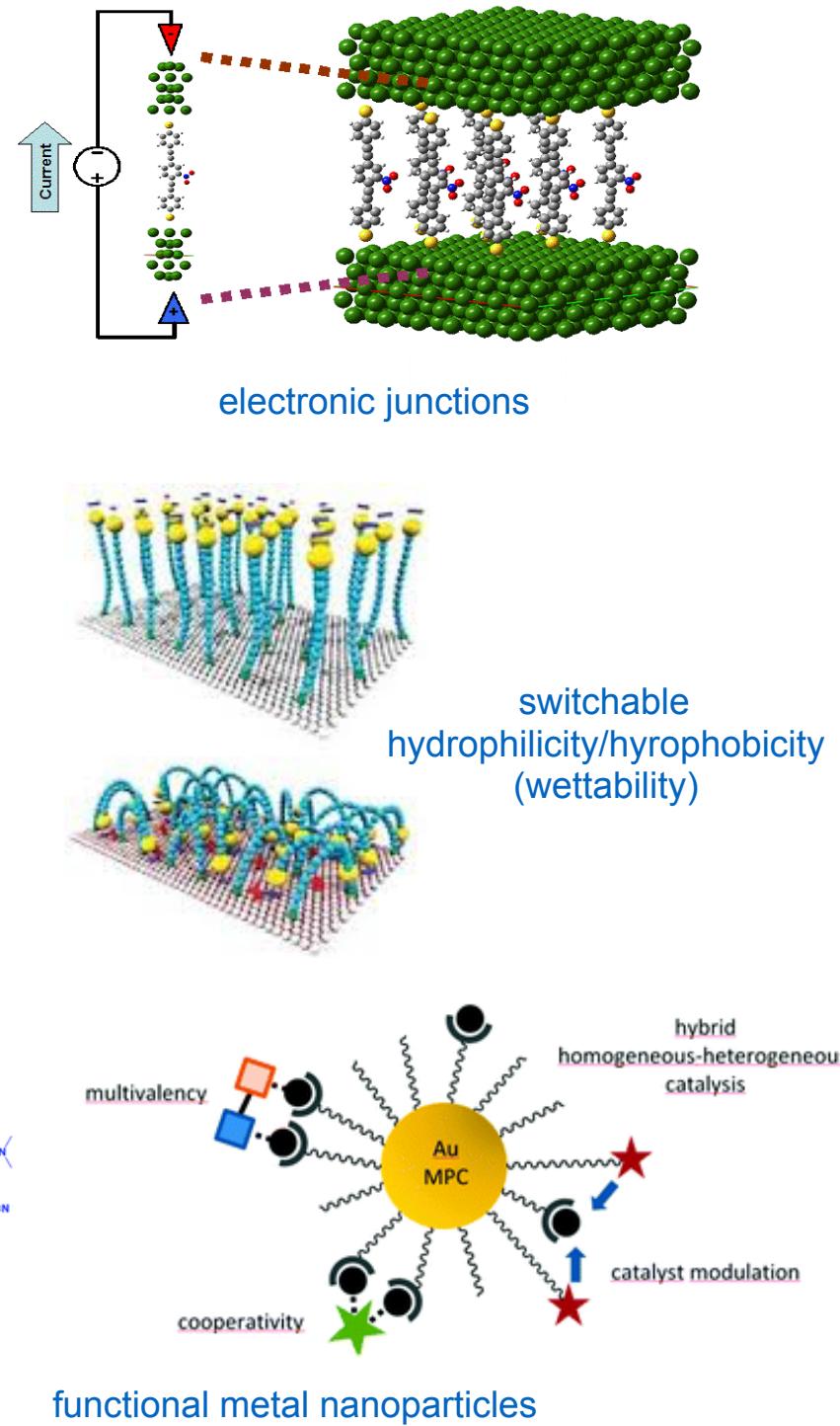
surfaces that catalyze reactions



Function & Materials Derived From SAMs



novel optical materials
(graphene)



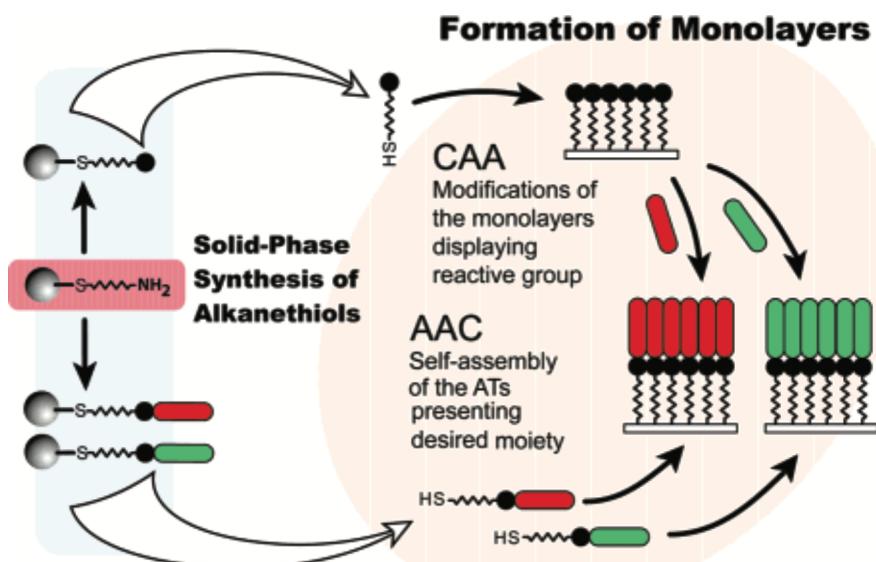
Solid-Phase Synthesis of Alkanethiols for the Preparation of Self-Assembled Monolayers

Ratmir Derda,[†] Daniel J. Wherritt,[§] and Laura L. Kiessling*,^{†,‡}

Departments of Chemistry and Biochemistry, University of Wisconsin, Madison, Wisconsin 53706

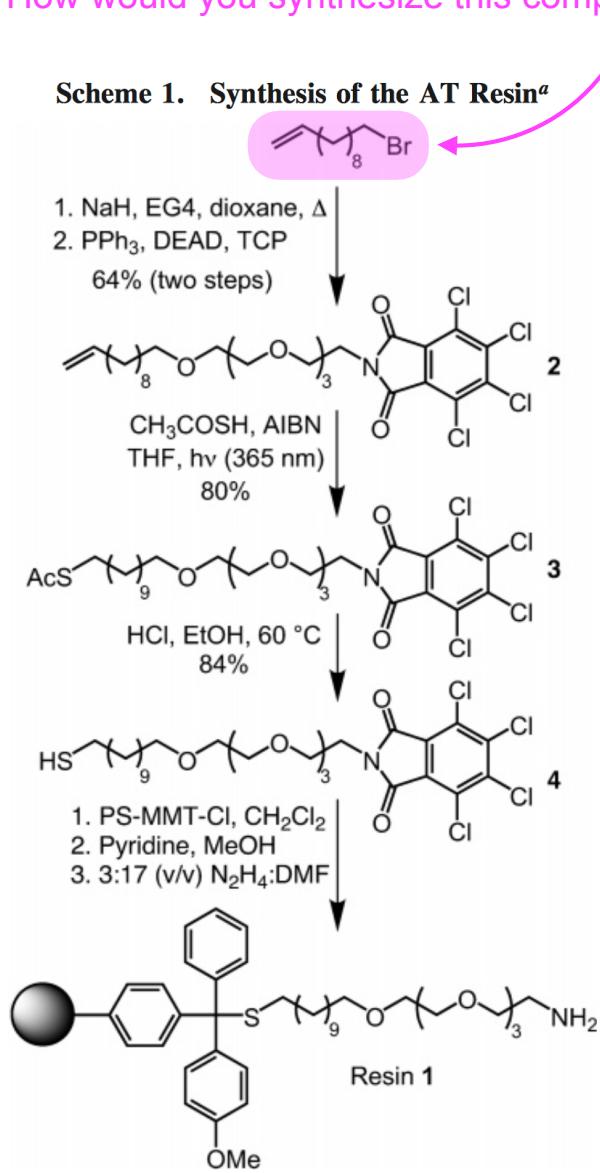
Received May 13, 2007

The spontaneous assembly of long-chain alkanethiols (ATs) on gold provides a powerful yet simple means of controlling surface properties at the molecular level.^{1,2} The molecular structure and physical properties of the resultant self-assembled monolayers (SAMs) are dictated by the chemical structure of the precursor ATs. Accordingly, the fabrication of monolayers with tailored properties hinges on access to chemically diverse ATs.^{3–6} We present a general synthetic approach to ATs to streamline access to structurally diverse SAMs.



Q: How would you synthesize this compound?

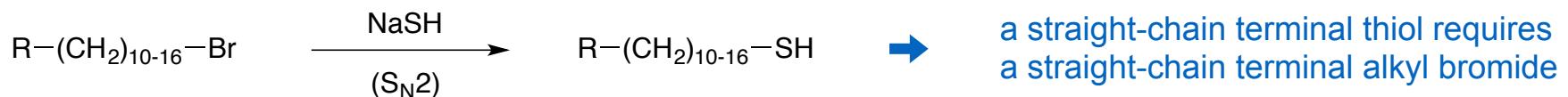
Scheme 1. Synthesis of the AT Resin^a



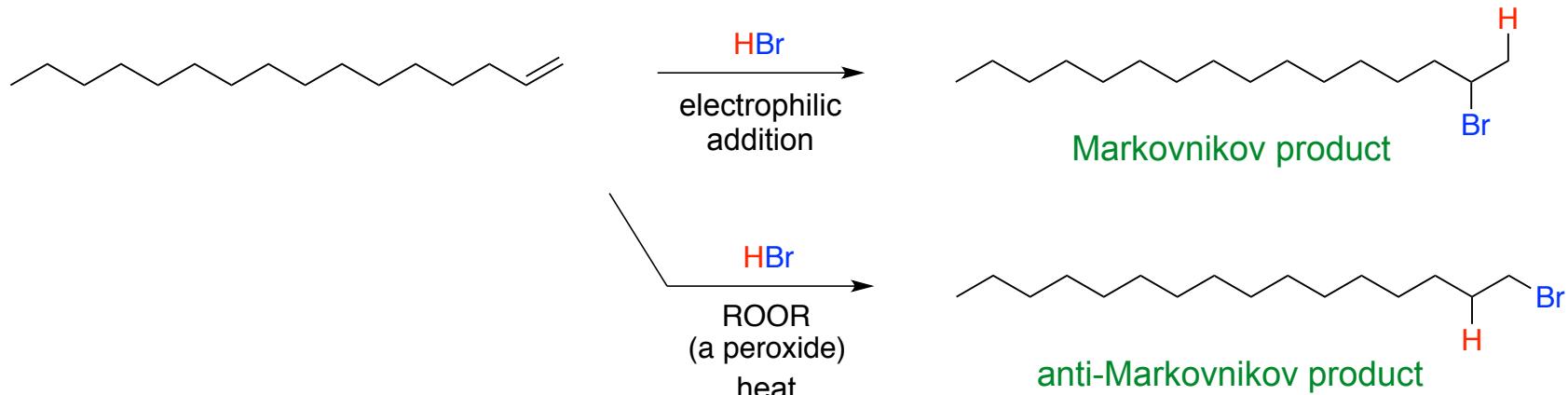
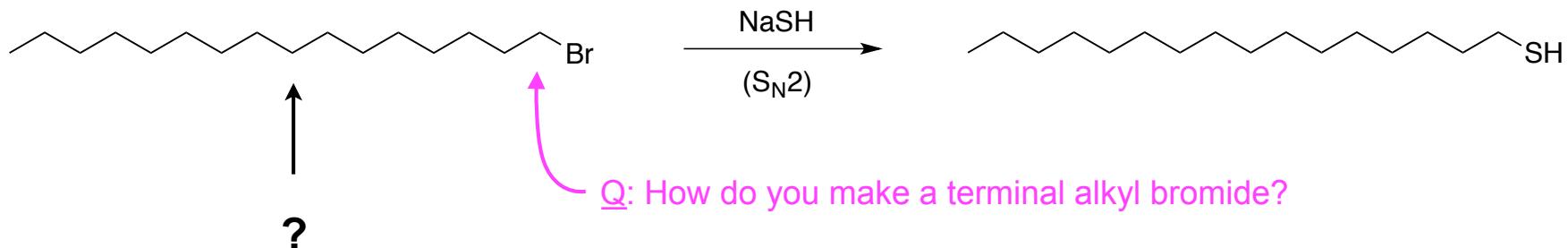
^a Abbreviations used: EG4 – tetra(ethylene glycol); DEAD – diethyl azodicarboxylate; TCP – tetrachlorophthalimide; AIBN – azobisisobutyronitrile; THF – tetrahydrofuran; EtOH – ethanol; Ac – acetyl; PS-MMT-Cl – polystyrene-bound monomethoxytrityl chloride; MeOH – methanol; and DMF – N,N-dimethylformamide.

Q: How are straight-chain terminal thiols prepared for generating SAMs (or for any other purpose)?

General Method to Prepare Thiols



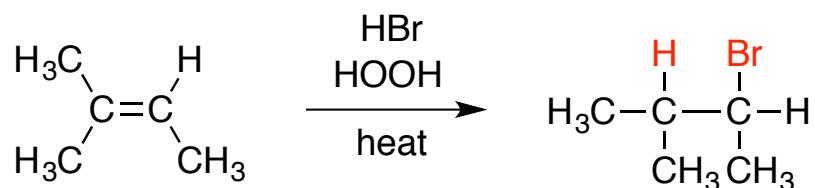
Ex:



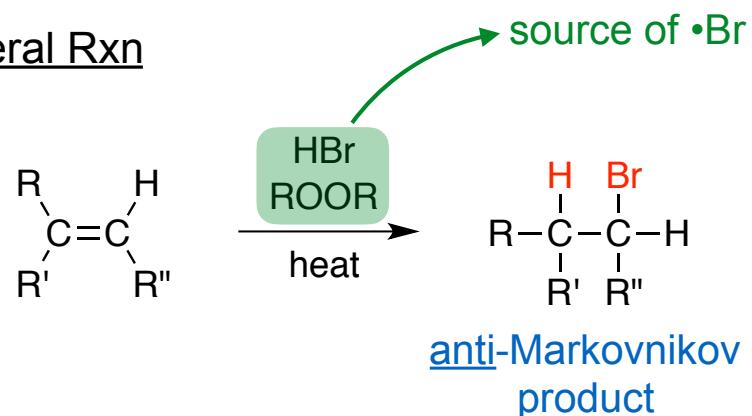
Free-Radical Addition of HBr to Alkenes (8-3B)

- Gives anti-Markovnikov addition of HBr to alkenes

Ex:



General Rxn



source of $\cdot\text{Br}$

ROOR = a peroxide	
\downarrow	
$\text{H}-\text{O}-\text{O}-\text{H}$	hydrogen peroxide
$\text{CH}_3-\text{O}-\text{O}-\text{CH}_3$	methyl peroxide
$\text{CH}_3\text{CH}_2-\text{O}-\text{O}-\text{CH}_2\text{CH}_3$	ethyl peroxide

Q: What does formation of anti-Markovnikov products indicate about the mechanism of these rxns?

Q: Mechanism?

Q: What does ROOR (a peroxide) do?

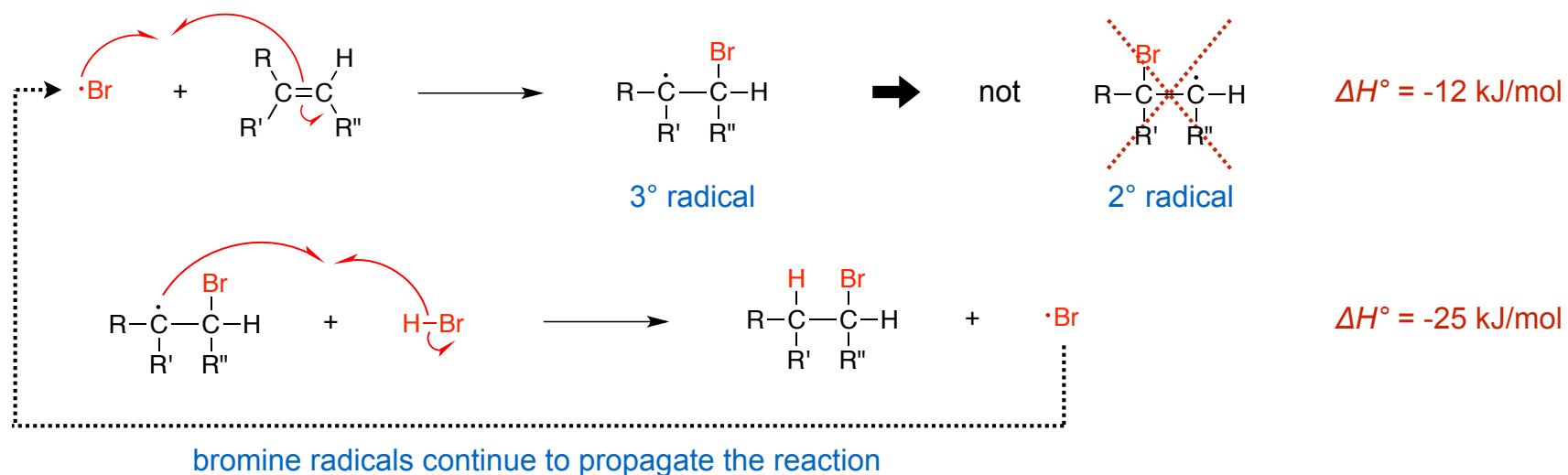
Mechanism for Free-Radical Addition of HBr to Alkenes

- Free-radical addition involves three distinct steps

1. Initiation



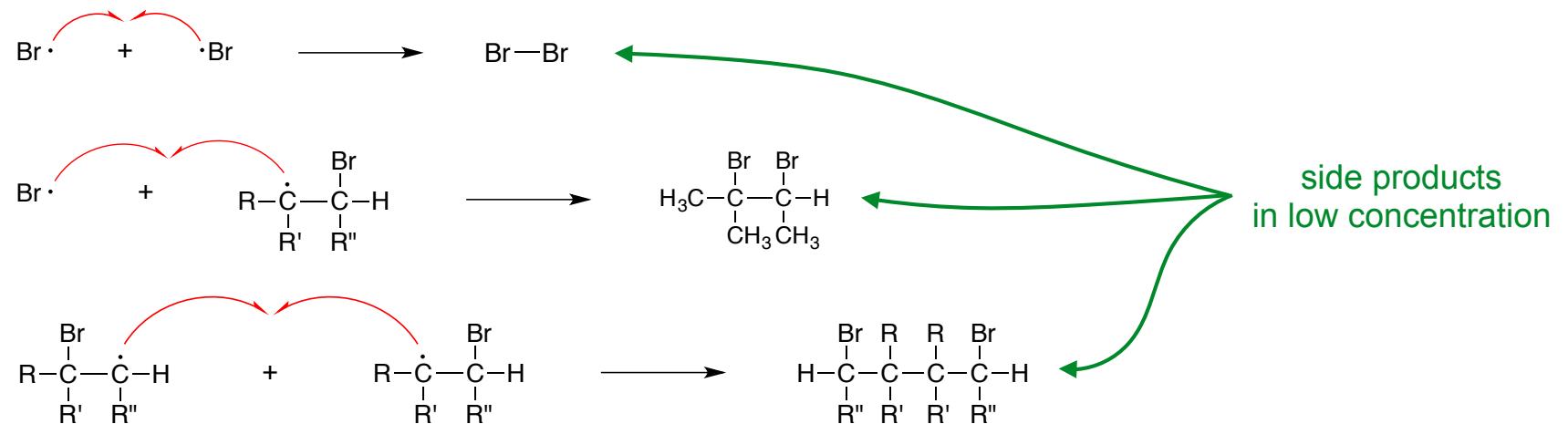
2. Propagation



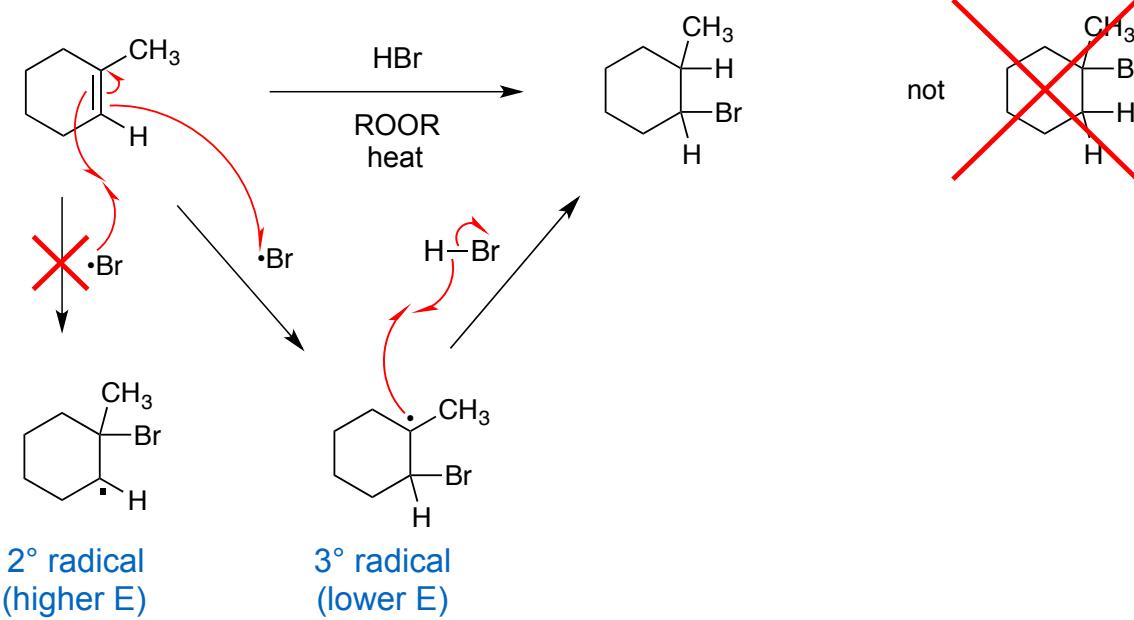
Q: How does free-radical addition differ from electrophilic addition?

Q: Why does a free-radical mechanism lead to the anti-Markovnikov product?

3. Termination



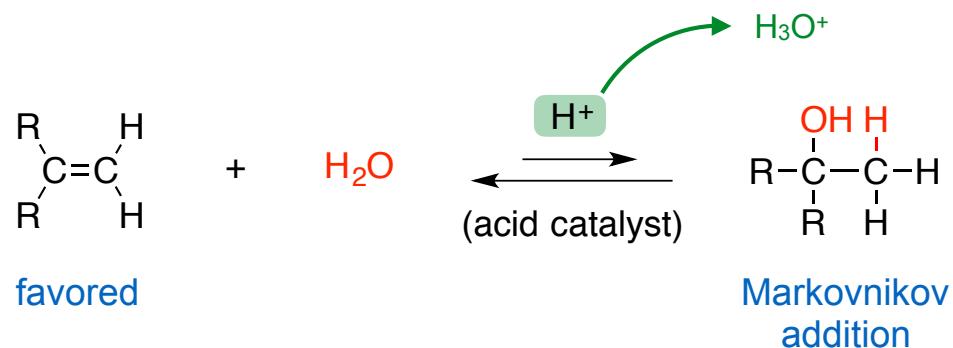
Ex:



Addition of Water: Hydration of Alkenes (8-4)

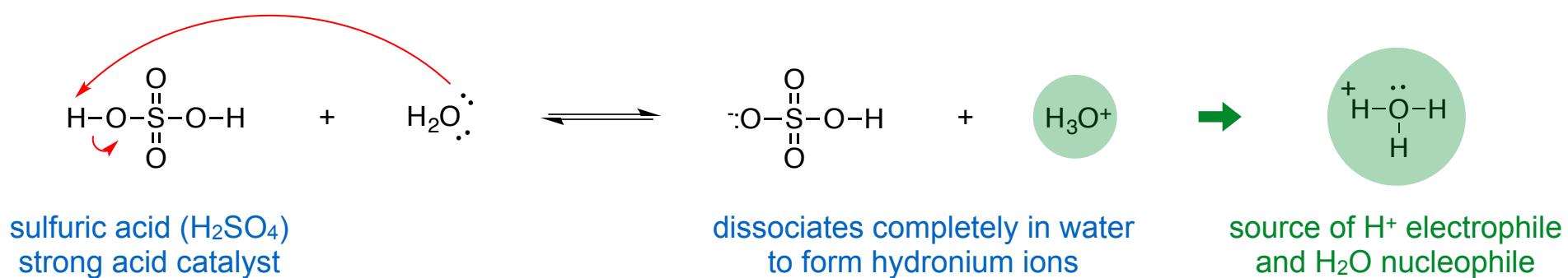
- Generally a poor method to prepare alcohols because the alkene is favored under equilibrium
- Many alkenes do not undergo hydration in aqueous acid
- Formation of a carbocation intermediate can lead to rearrangement and other side products

General Reaction

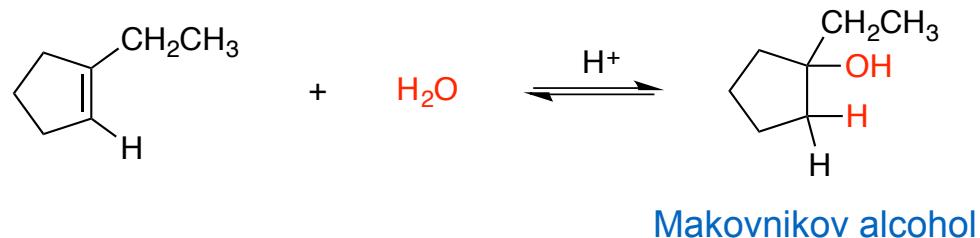


Q: What role does the acid catalyst play?

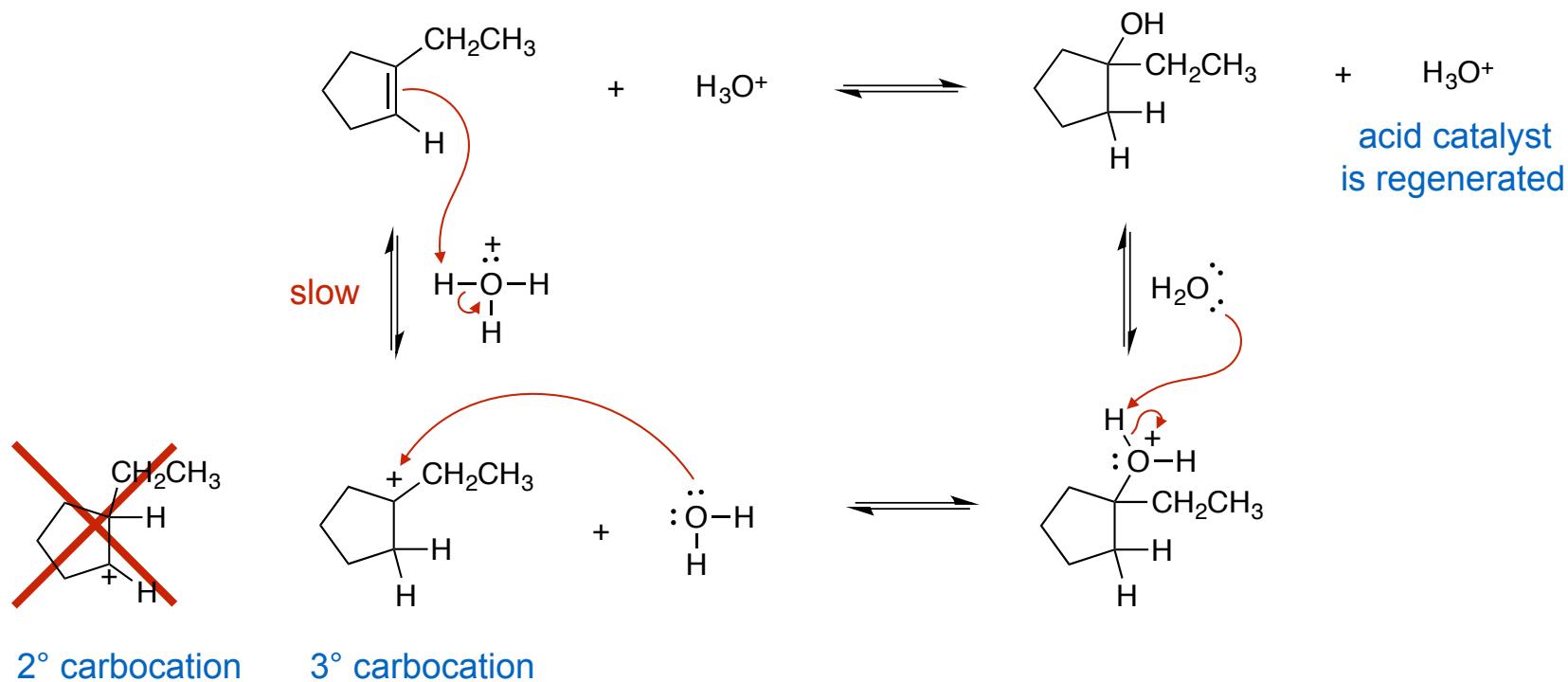
Q: Where does H^+ reside in the reaction solution when an acid catalyst is added?



Ex:



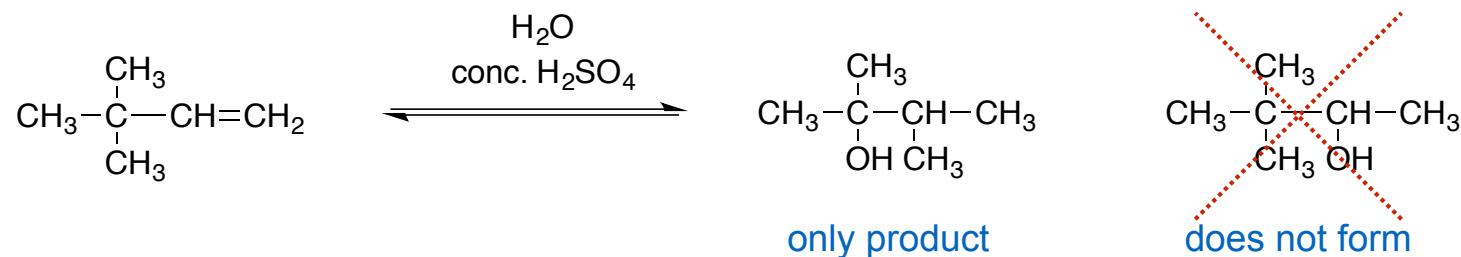
Mechanism of hydration



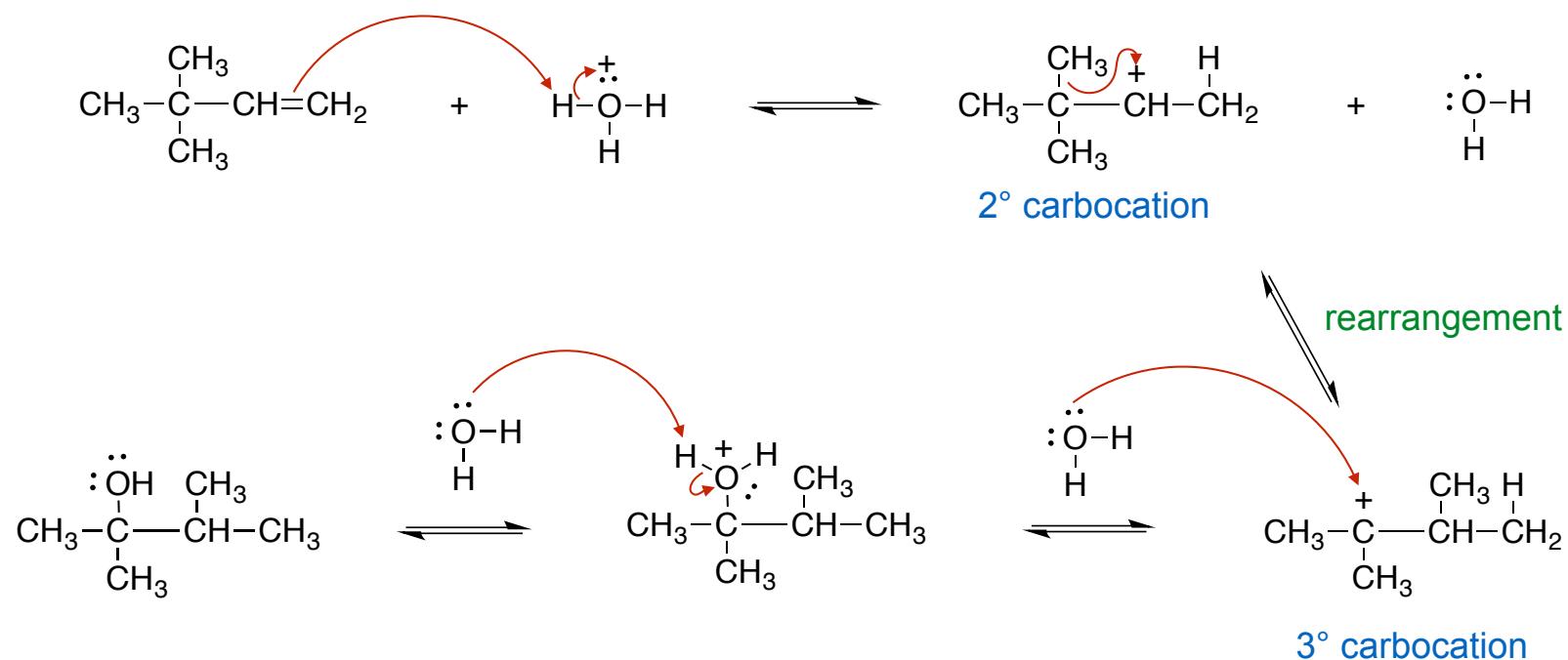
Note: Many alkenes do not undergo hydration in aqueous acid, or are insoluble, or undergo side reactions such as rearrangement or decomposition under acidic conditions

→ Need a more reliable method to carry out hydration that favors formation of the alcohol

Ex:



Q: How can the observed product be explained?



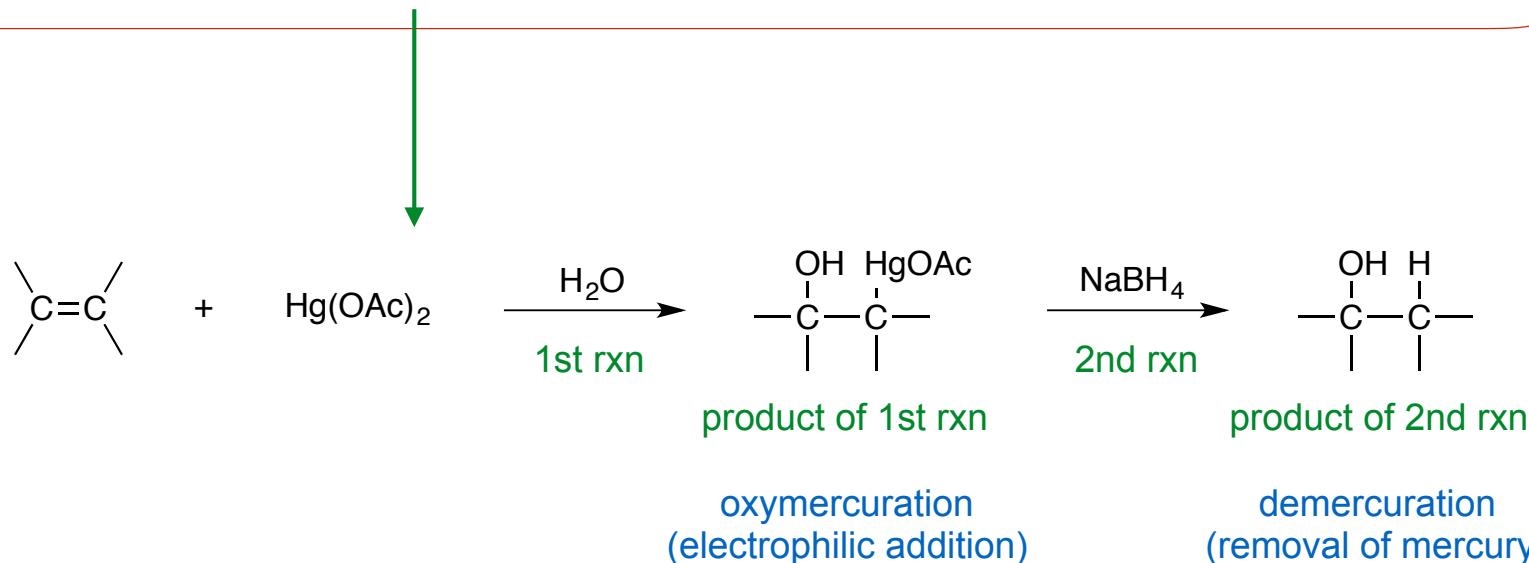
Q: Is there a better way to carry out hydration of alkenes to form alcohols that avoids rearrangement?

Hydration of Alkenes by Oxymercuration-Demercuration (8-5)

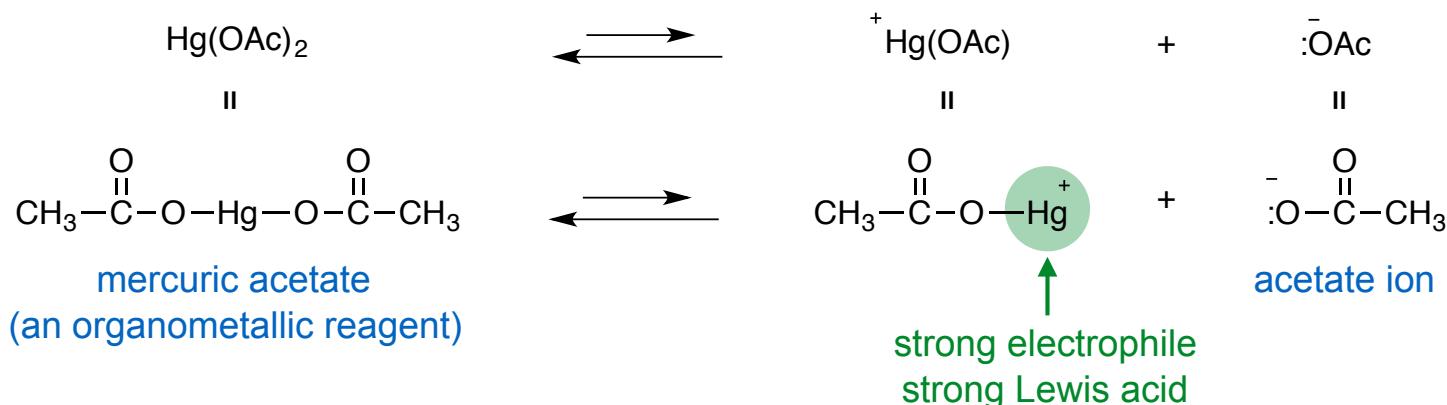
- An excellent, high-yield method to convert alkenes into Markovnikov alcohols
- Works with many alkenes that do not undergo acid-catalyzed hydration
- Occurs under milder conditions
- Does not form a classic carbocation → no rearrangement or side reactions

PERIODIC TABLE OF THE ELEMENTS																	
H	Li	Be	B	C	N	O	F	Ne									
	Na	Mg	Al	Si	P	S	Cl	Ar									
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
Cs	Ba		Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
Fr	Ra		Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	In	Uut	Fl	Uup	Lv	Uus	Uuo
	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu		
	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr		

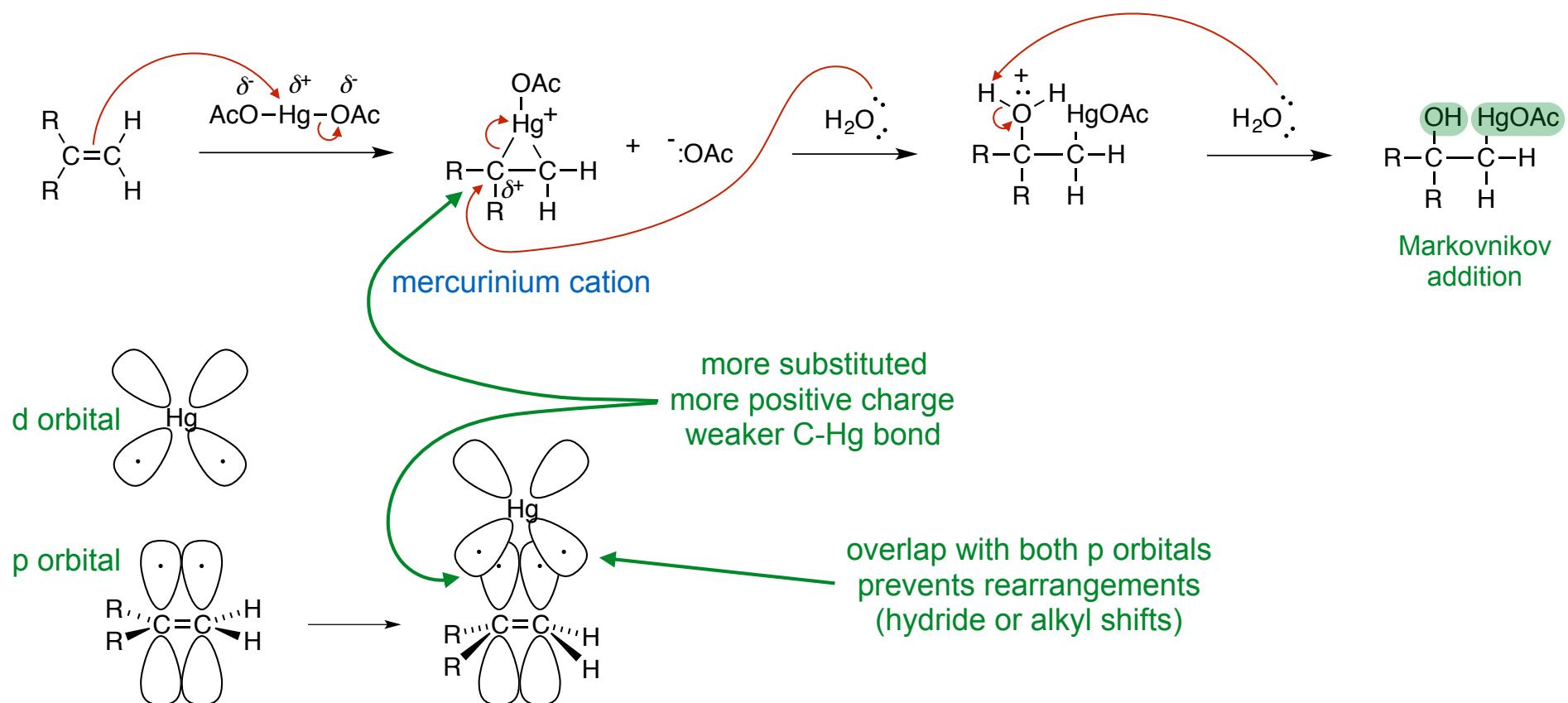
General Reaction



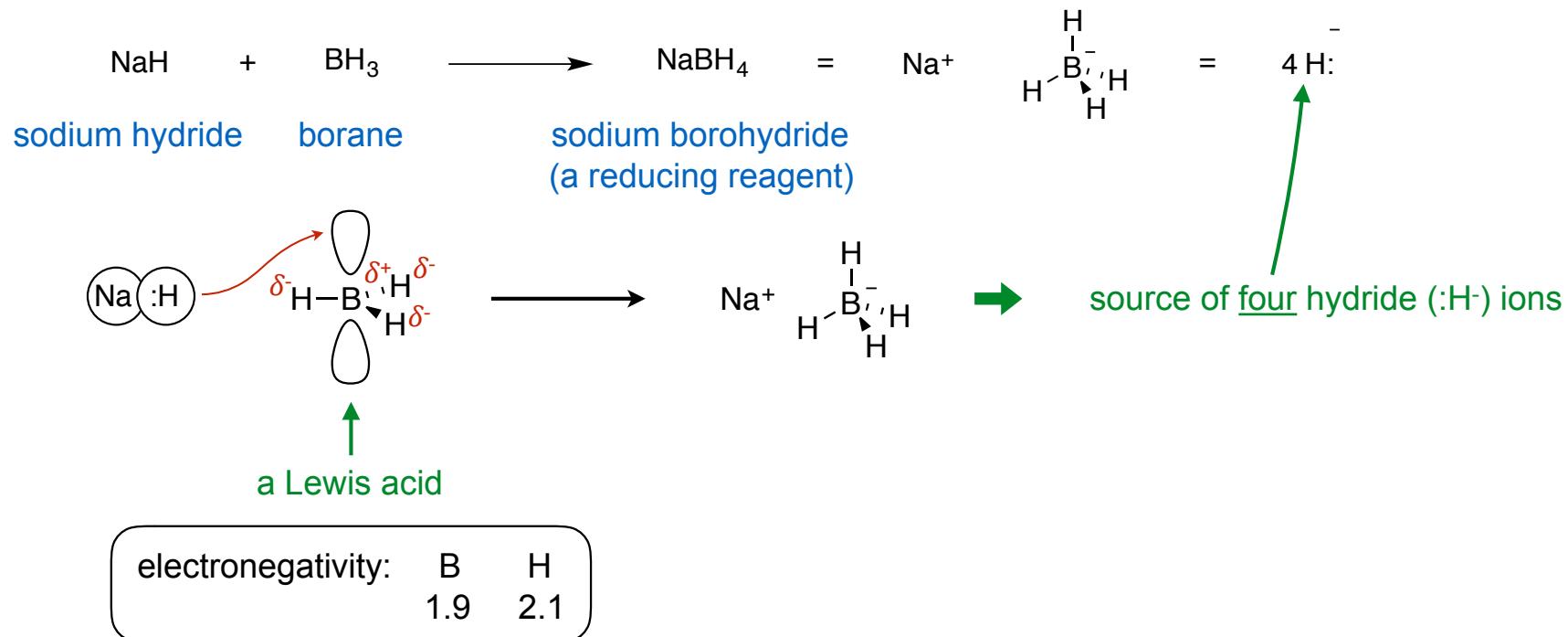
Q: What is mercuric acetate, Hg(OAc)_2 , and what role does it play?



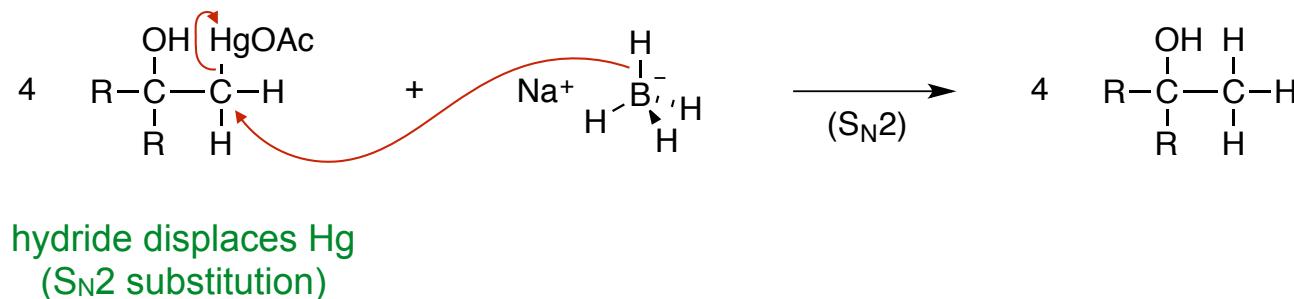
Mechanism of Oxymercuration



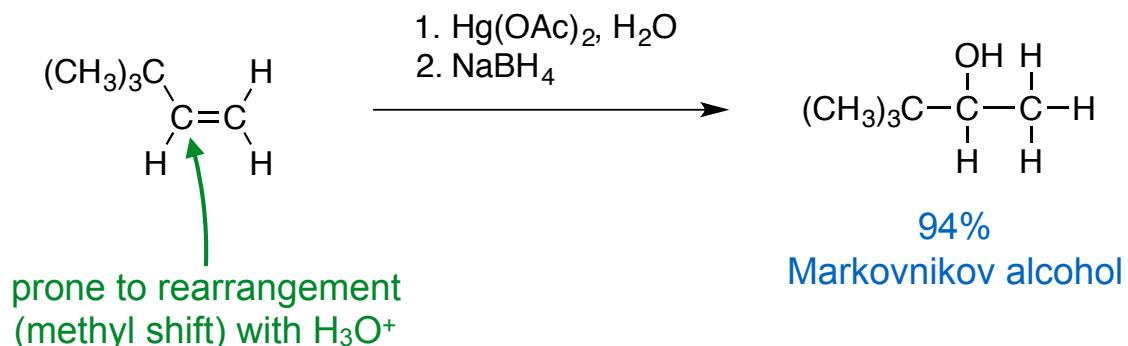
Q: What is sodium borohydride NaBH_4 , and what role does it play?



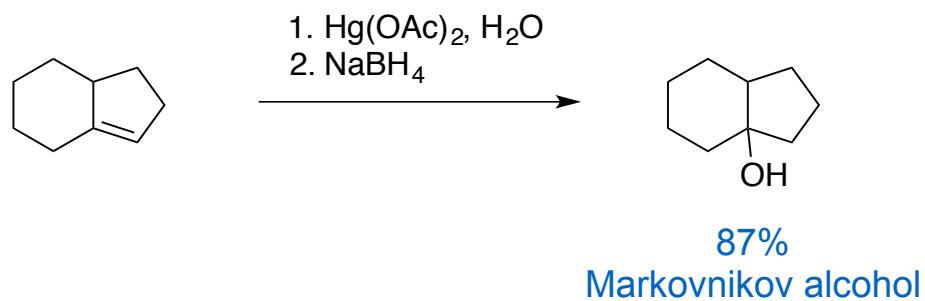
Mechanism of Demercuration



Ex:



Ex:



Highly Efficient and Diastereoselective Synthesis of (+)-Lineatin

Ramon Alibés,* Pedro de March, Marta Figueredo, Josep Font,*
Marta Racamonde, and Teodor Parella†

Departament de Química and Servei de Ressonància Magnètica Nuclear,
Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain

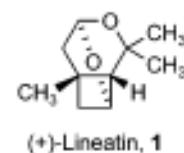
josep.font@uab.es

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Vol. 6, No. 9
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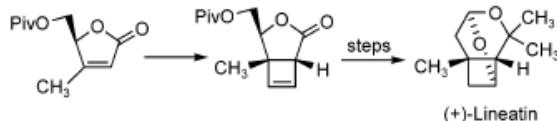
(+)-Lineatin, **1**, is the most important constituent of the aggregation pheromone isolated from the frass of the female ambrosia beetle *Trypodendron lineatum* Olivier, which is a deleterious pest to coniferous forests in Europe and North America (Figure 1).¹



(+)-Lineatin, **1**

Figure 1.

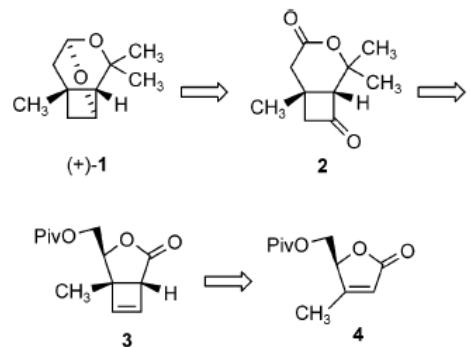
ABSTRACT



A linear sequence was used to synthesize (+)-lineatin in 14 steps and 14% overall yield from a homochiral 2(5*H*)-furanone. Key steps of this synthetic approach feature the diastereoselective construction of a cyclobutene through a photochemical [2 + 2] cycloaddition and a regiocontrolled oxymercuration reaction.

In the past two decades, this cyclobutane monoterpene has attracted the attention of many synthetic chemists.^{2,3} Among the large number of syntheses of lineatin published to date, only a few were devised to provide the pure (+)-enantiomer³ and, with a unique exception,^{3d} they all required resolution steps. Furthermore, the yields achieved in these syntheses were very low (0.2–4%).

Scheme 1. Retrosynthetic Analysis



At this juncture, we intended to introduce the O-functionality at C-2' through an oxymercuration–demercuration process. Our expectation was that either the hydroxyl group and/or the closer oxygen atom of the dioxolane in 8 would coordinate to and guide the Hg^{2+} to the *endo* face of the olefin. A subsequent trans addition of water should then occur at C-2' due to the steric hindrance exerted by the methyl group attached to the cyclobutane (Figure 2).¹⁰

Scheme 3

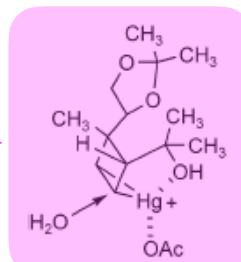
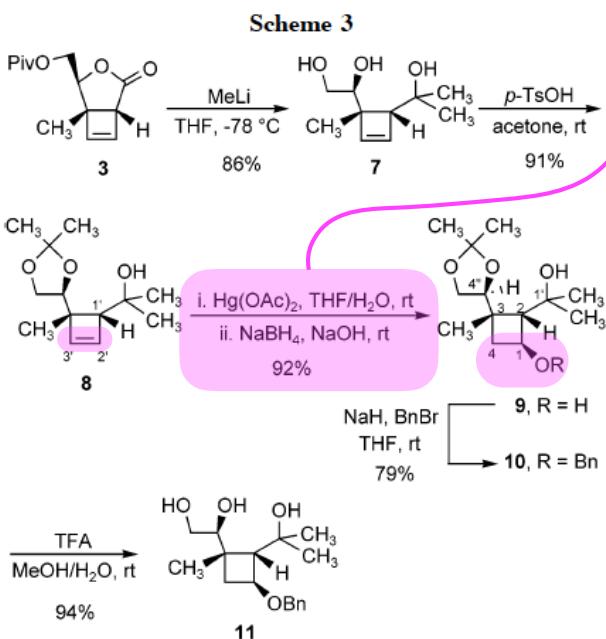
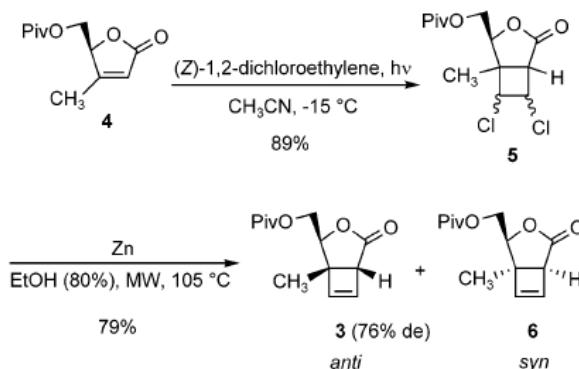


Figure 2. Mercurinium complex.

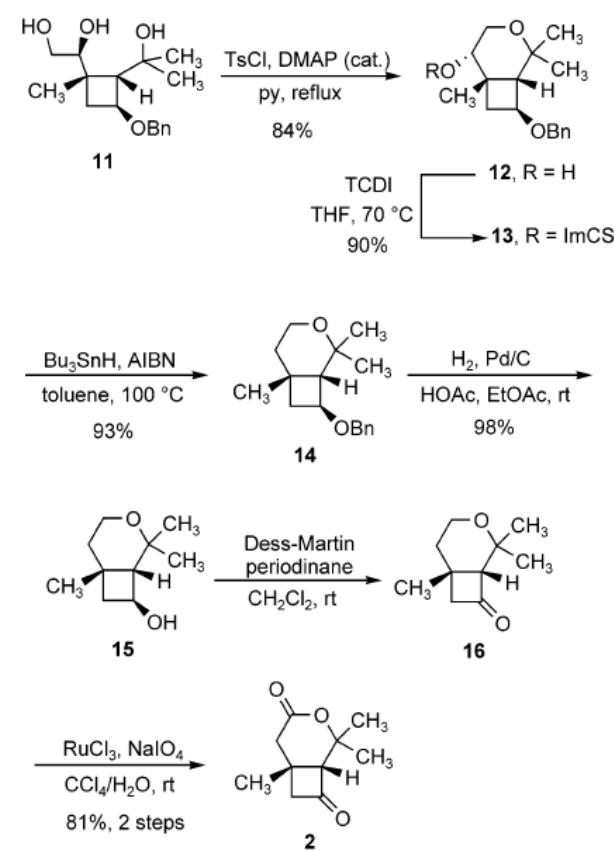
Although the configuration of the new stereogenic center would be opposite to that in the target pheromone, it was envisaged that an inversion could be performed at a later stage of the synthesis through an oxidation–reduction sequence.

To our great satisfaction, when 8 was treated with mercuric acetate in THF/water at room temperature for 2.5 h and demercuration was effected with alkaline sodium borohydride, the alcohol 9 was obtained as a single isomer in 92% yield. The structure and relative stereochemistry of 9

Scheme 2

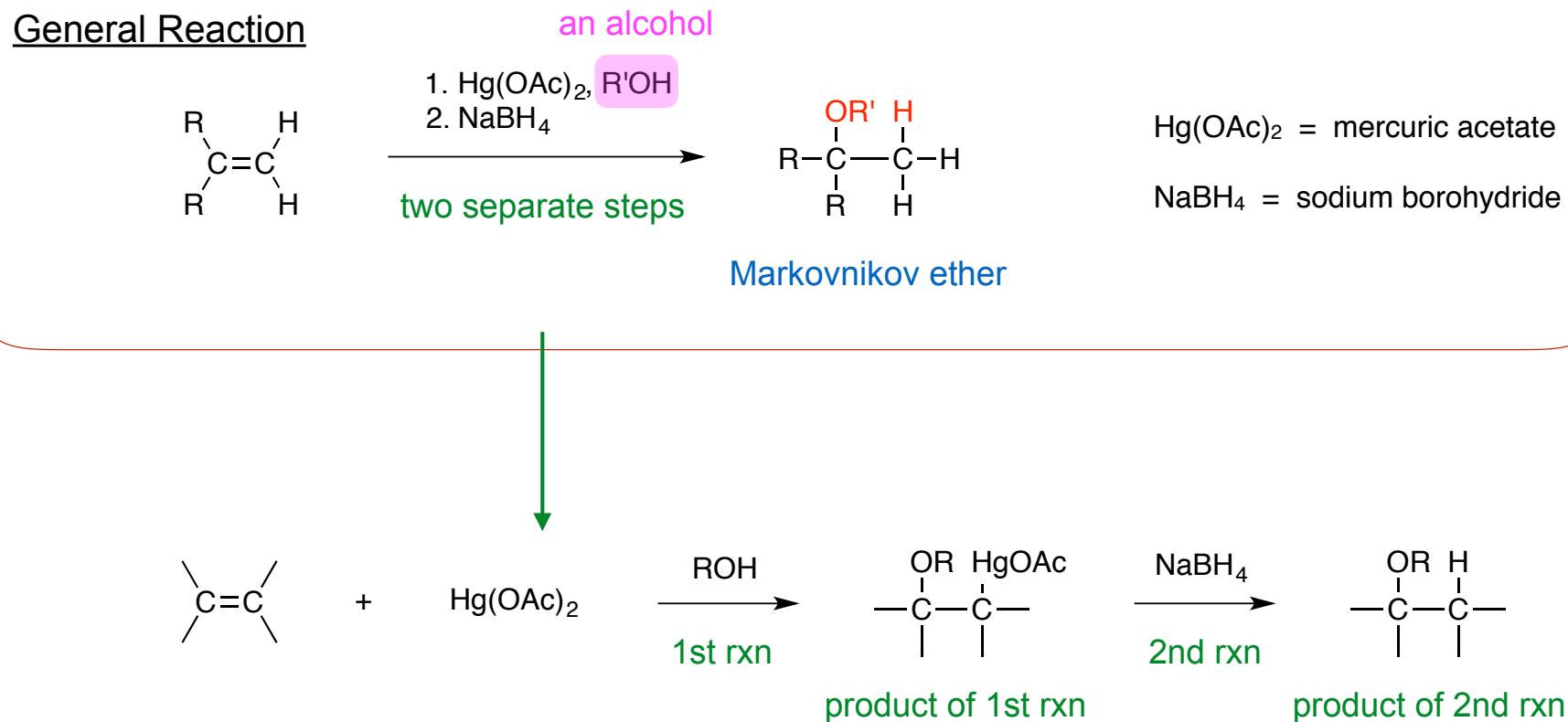


Scheme 4

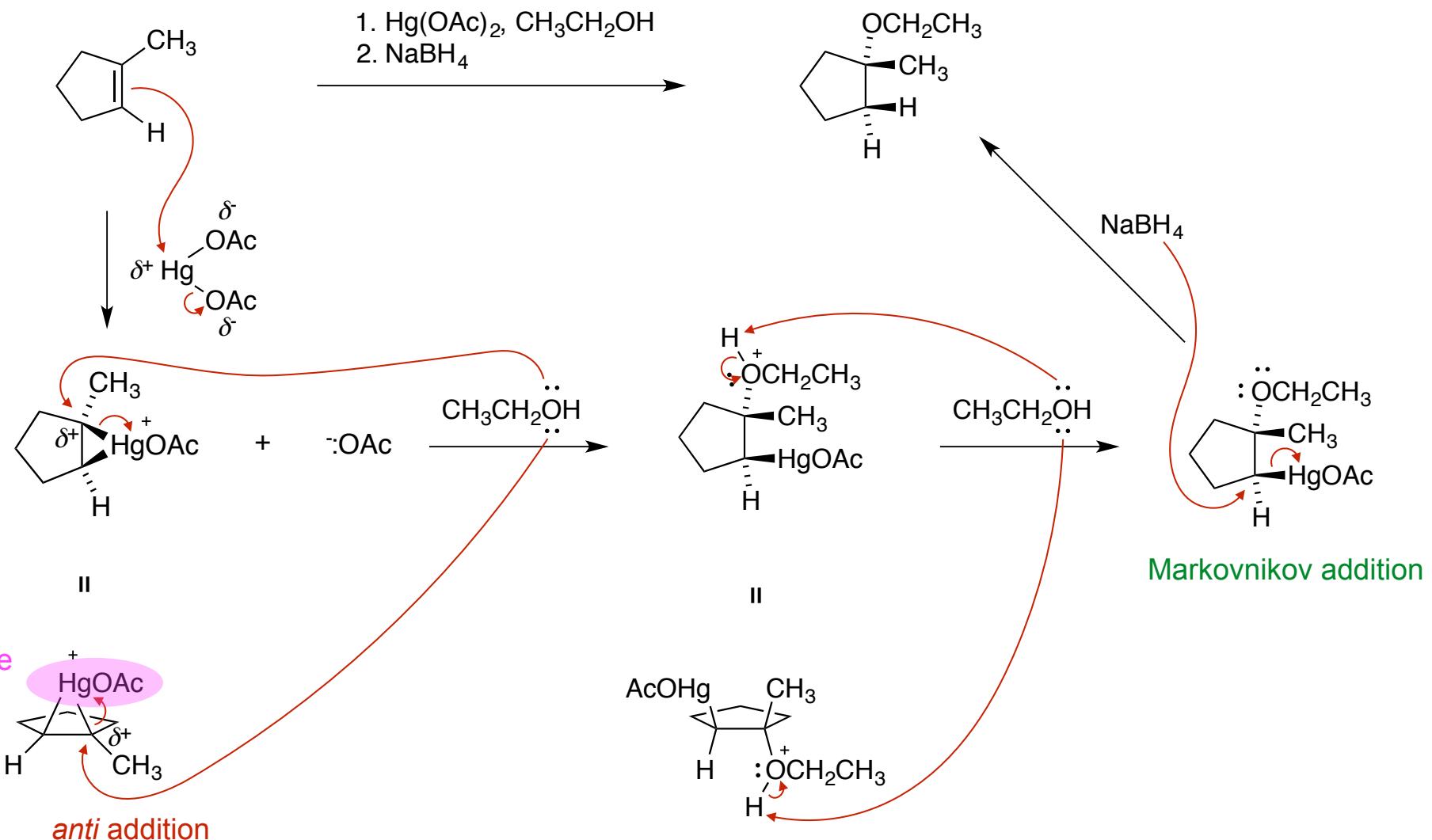


Alkoxymercuration-Demercuration (8-6)

- An excellent, high-yield method to convert alkenes into Markovnikov ethers (R-O-R')
 - Use an alcohol instead of water
 - Similar mechanism to oxymercuration-demercuration
 - Does not form a classic carbocation → no rearrangement or side reactions



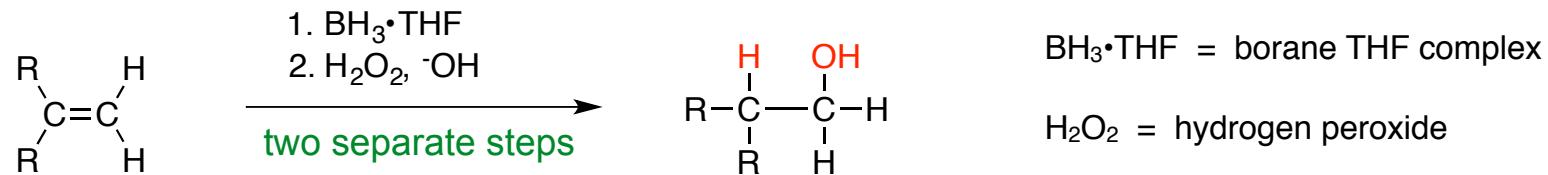
Ex:



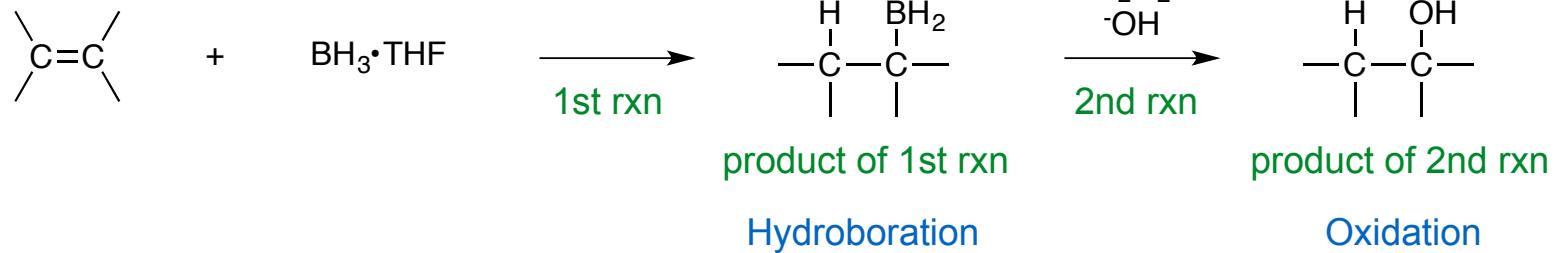
Hydroboration of Alkenes (8-7)

- Excellent method to prepare anti-Markovnikov alcohols

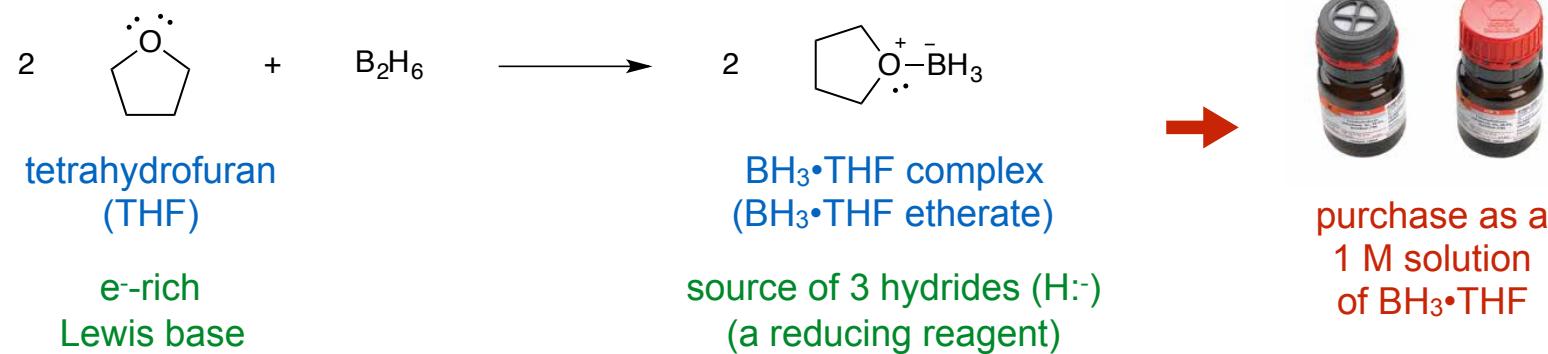
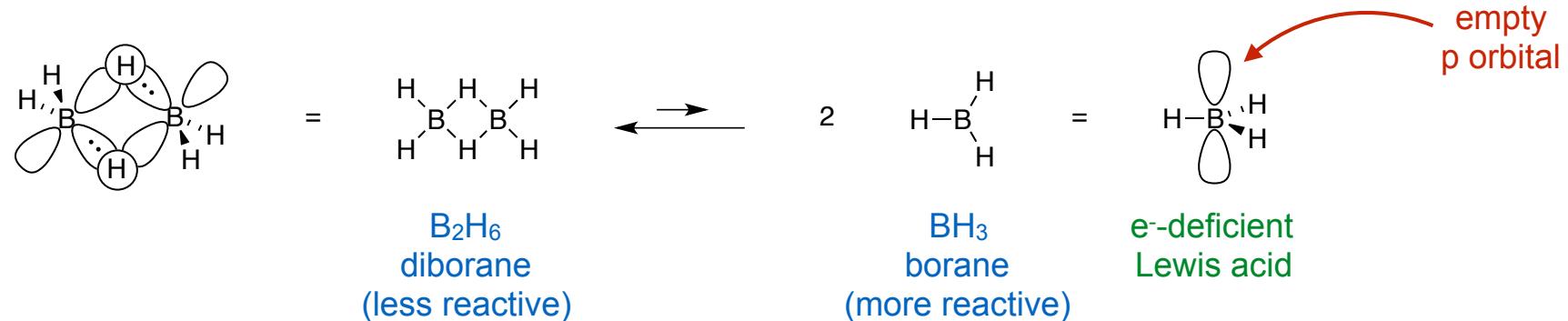
General Reaction



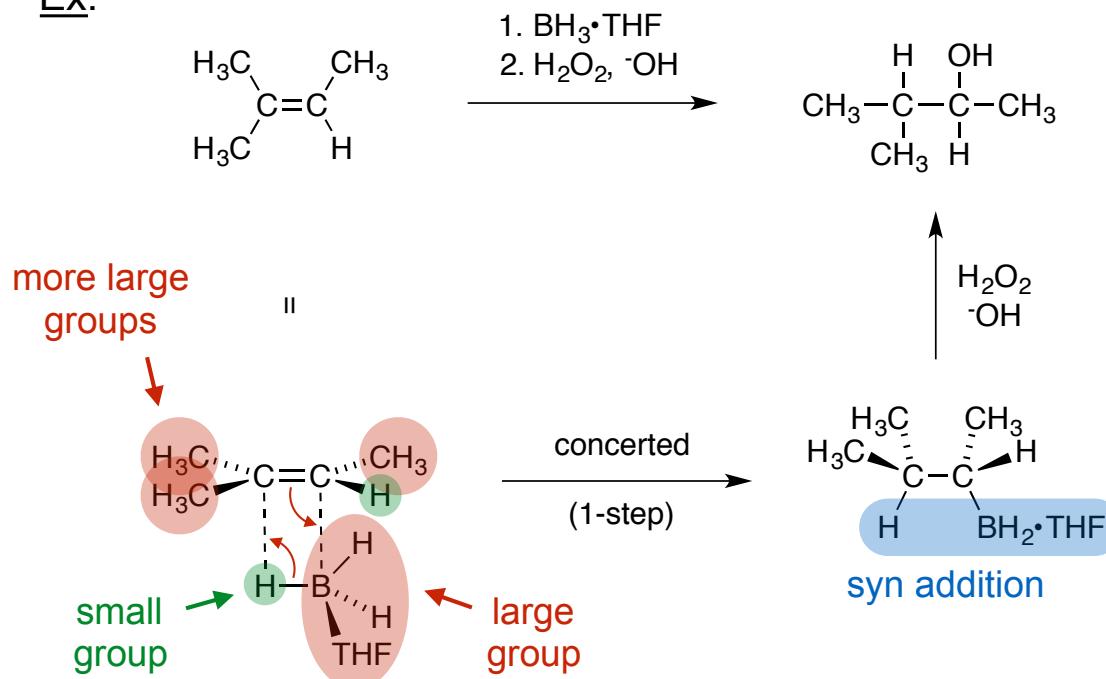
anti-Markovnikov alcohol



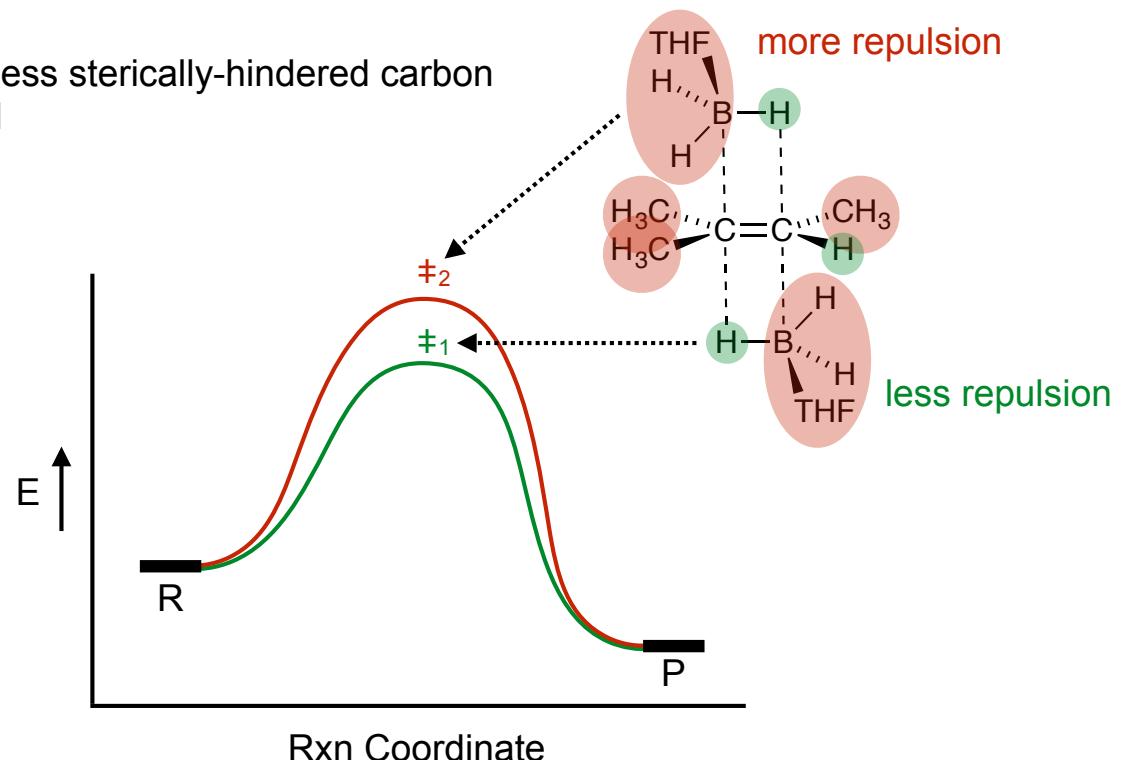
Structure of Borane



Ex:



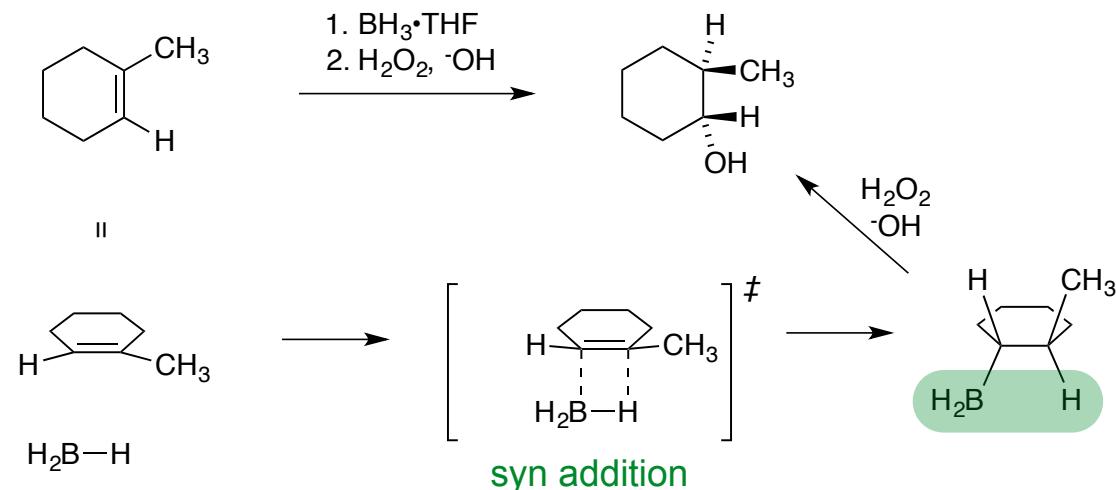
- Boron (electrophile) aligns under the less sterically-hindered carbon
- Regiochemistry is under steric control



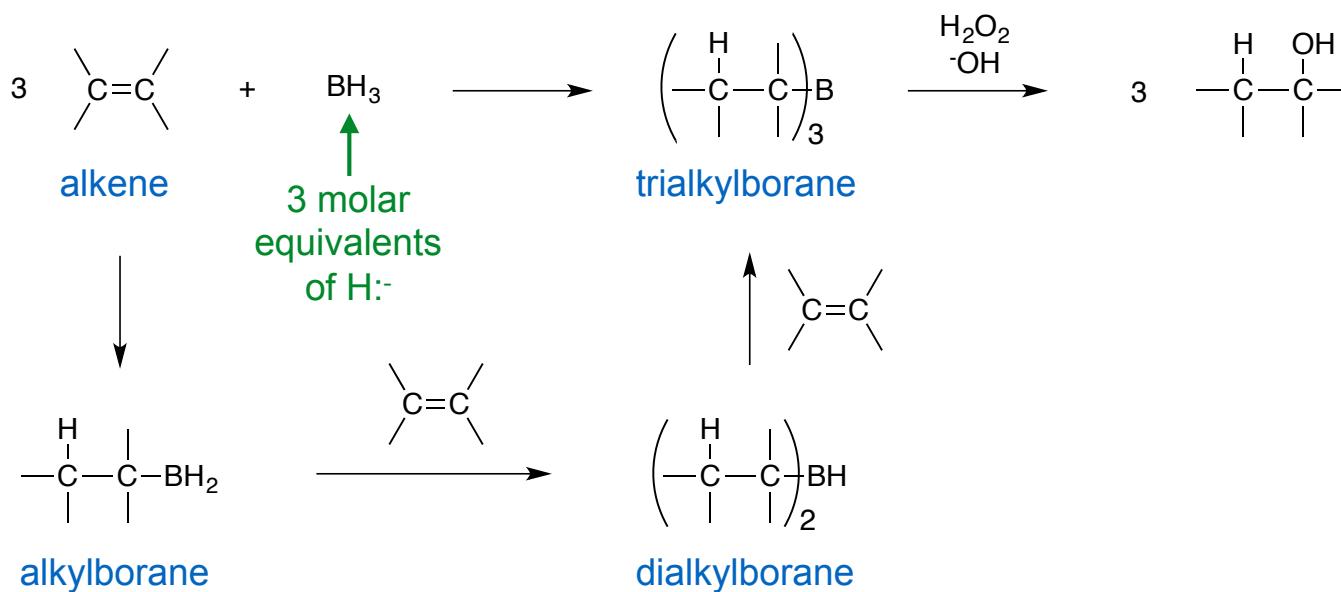
Stereochemistry of Hydroboration

- BH_3 adds to (collides with) one side of an alkene leading to **syn addition** of H and $\text{BH}_2(\text{OH})$

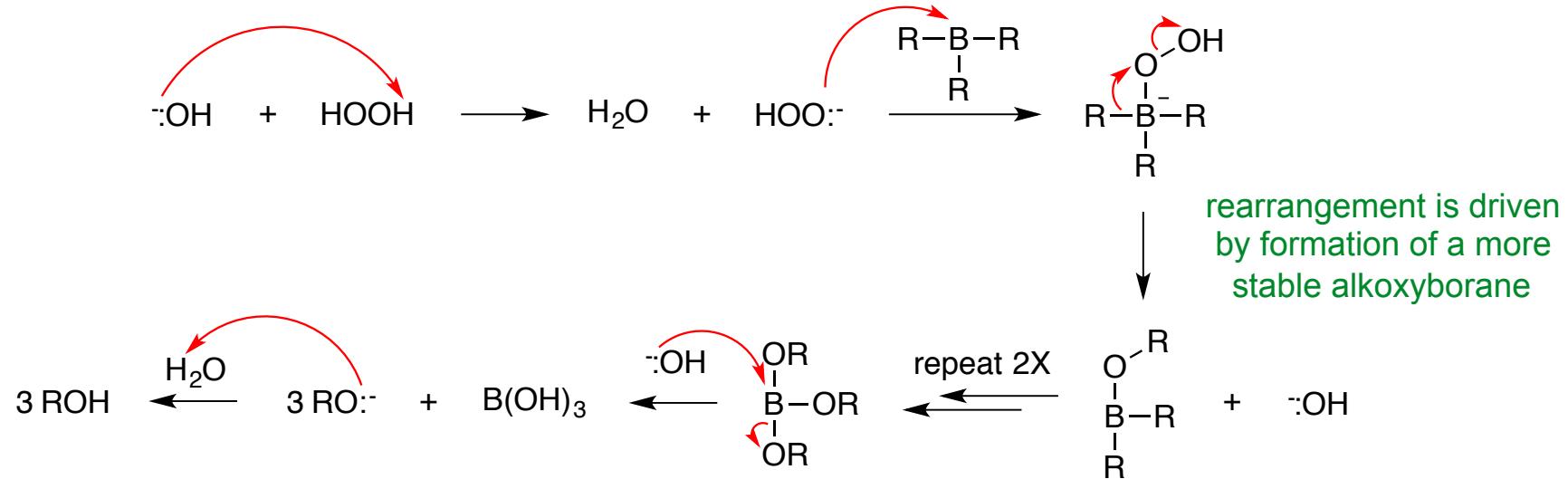
Ex:



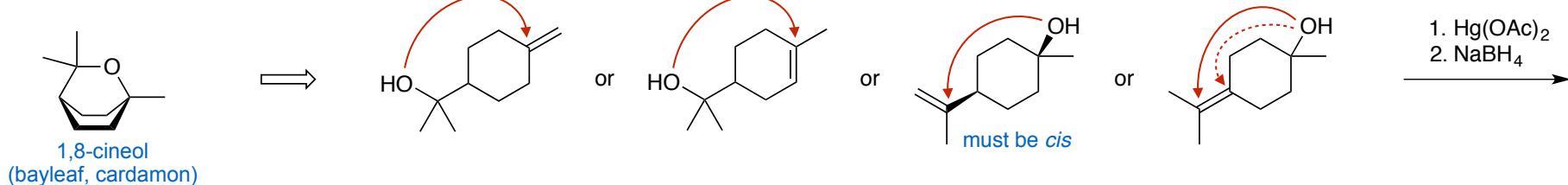
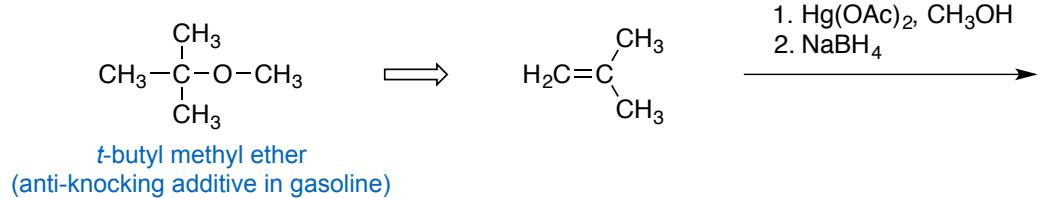
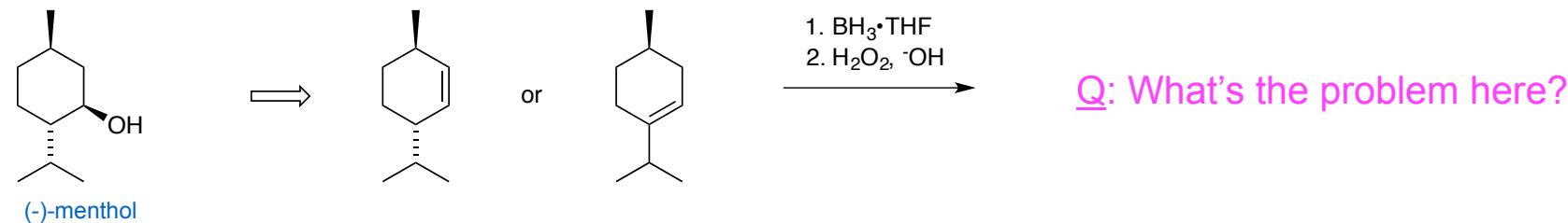
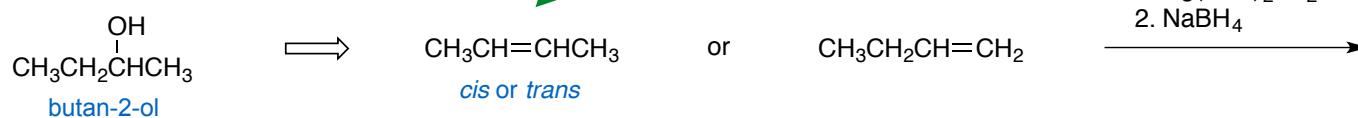
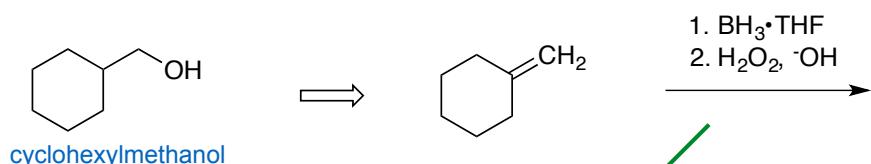
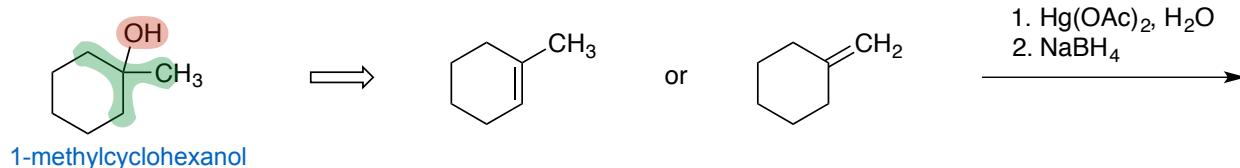
Stoichiometry of Hydroboration



Q: Mechanism for oxidation of trialkylboranes?



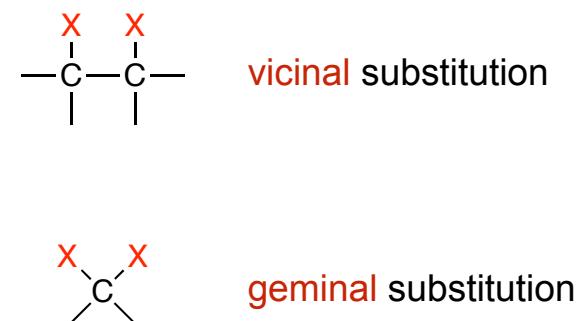
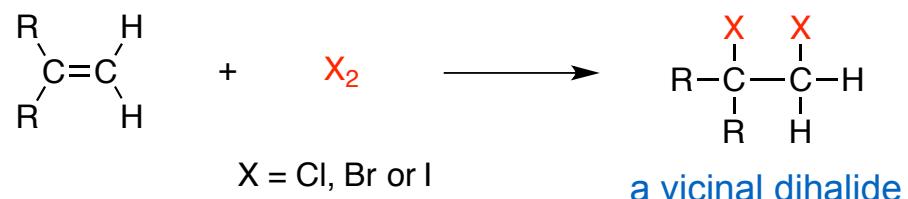
Q: How would you synthesize these alcohols/ethers from alkenes? Which alkenes would you use?



Addition of Halogens to Alkenes (8-8)

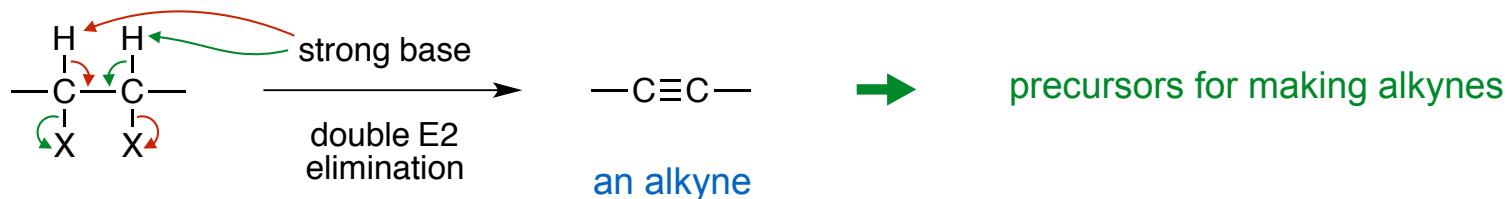
- Addition of halogens (X_2) to alkenes generates vicinal dihalides via **anti addition**
- Vicinal dihalides are used as precursors for synthesizing alkynes

General Reaction

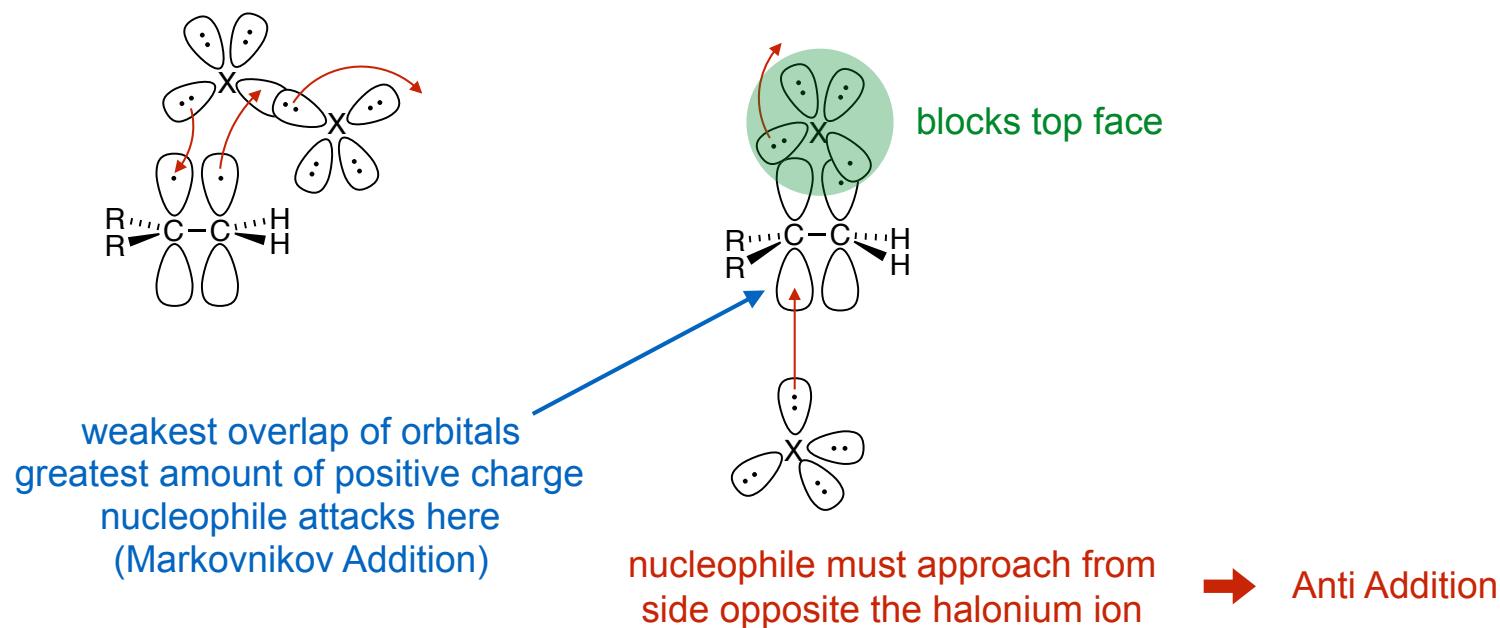
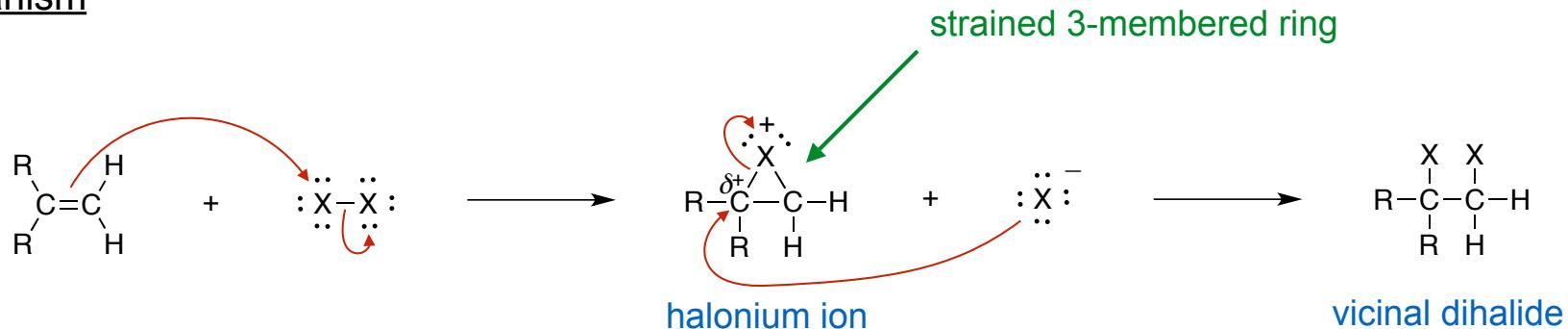


Q: What are vicinal dihalides used for?

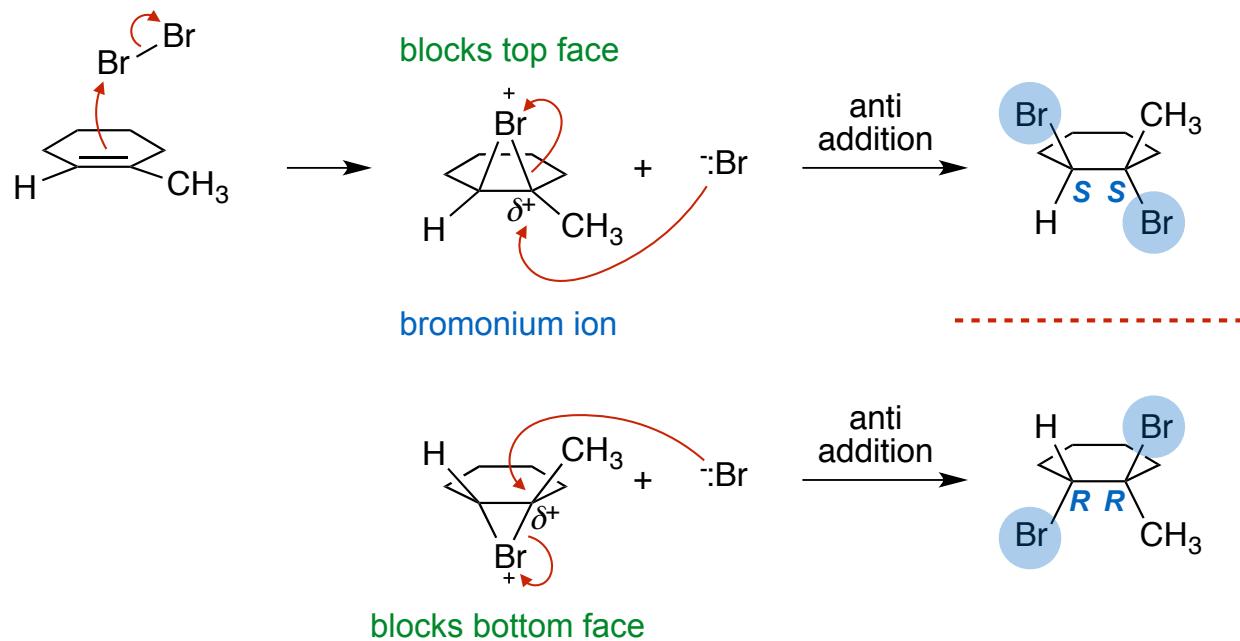
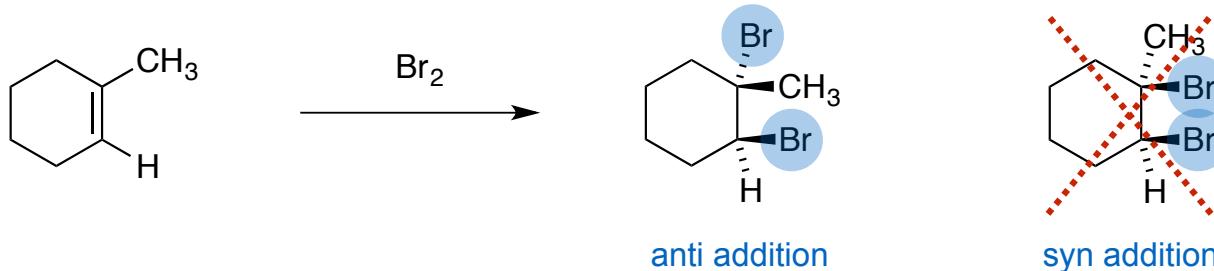
Preview from Ch. 9:



Mechanism



Ex:

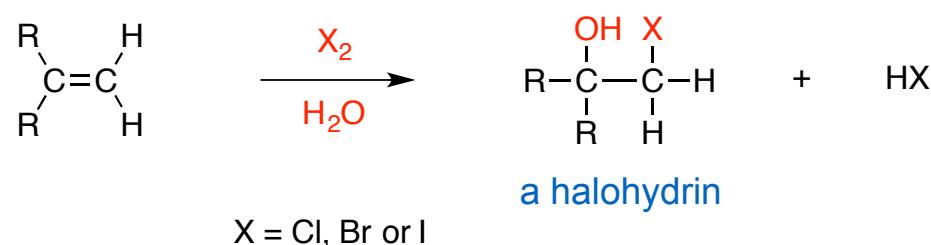


Note: Halogenation via electrophilic addition to cycloalkenes always generates products where the halogen atoms are *trans* due to **anti addition** resulting from a halonium ion blocking one face

Formation of Halohydrins (8-9)

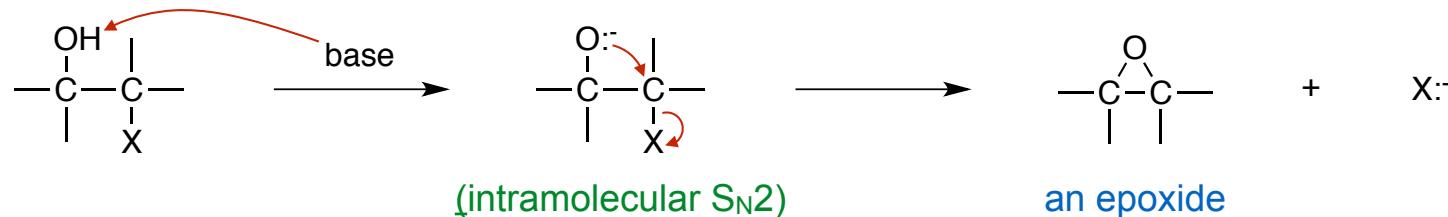
- Halohydrins contain a halogen and an alcohol group on adjacent carbons
- Halohydrins form when halogenation is carried out in the presence of an excess of water, which competes with X^- as the nucleophile
- Halohydrins are used as precursors to synthesize epoxides (Ch. 14)

General Reaction

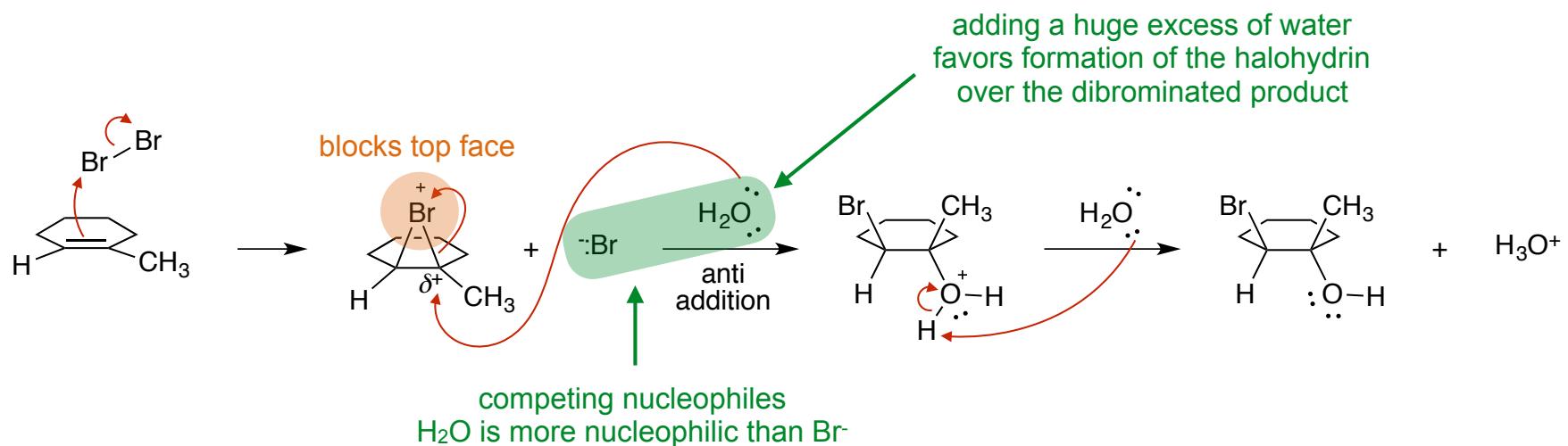
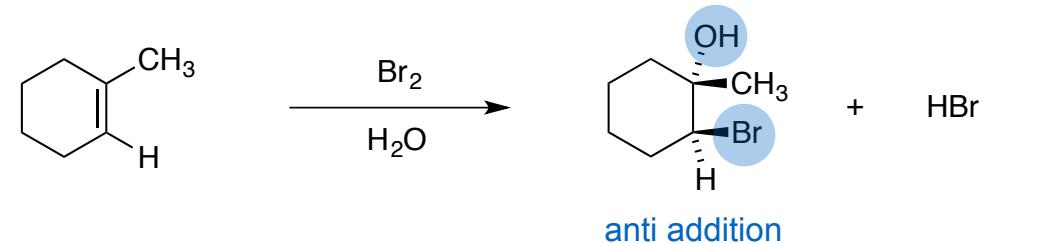


Q: What are halohydrins used for?

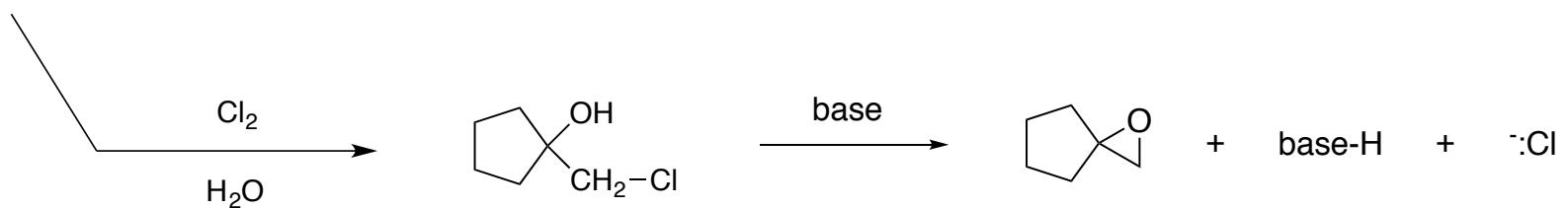
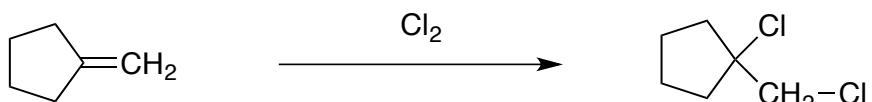
Preview from Ch. 14:



Ex:



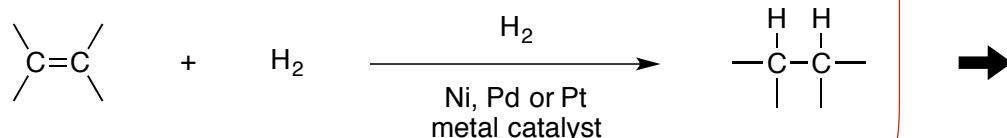
Ex:



Catalytic Hydrogenation of Alkenes (8-10)

- Alkenes can be converted to alkanes in high yield by adding H₂ across the C=C bond
- A transition metal catalyst such as Ni, Pd or Pt is required to activate H₂

General Rxn



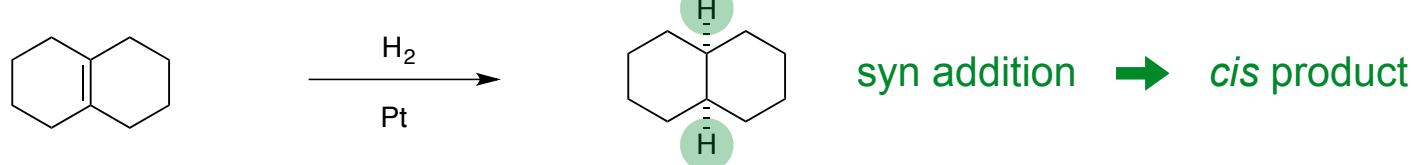
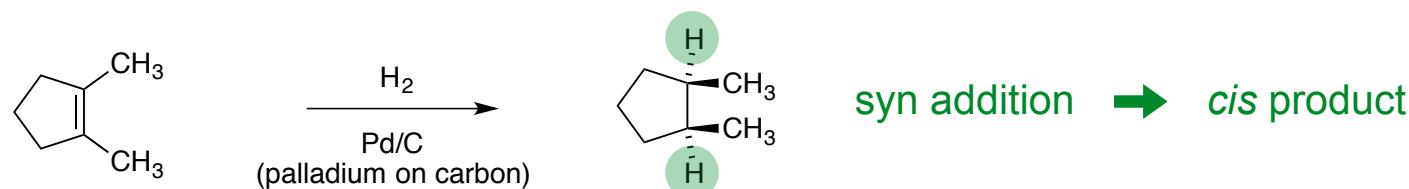
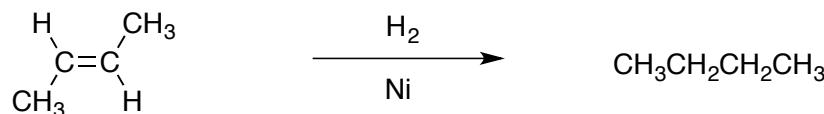
$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

$\Delta H^\circ = -(80-120) \text{ kJ/mol}$ (favorable)

$\Delta S^\circ = -125 \text{ J/K-mol}$ (disfavored)

Hydrogenation rxns are exothermic and favored at RT

Ex:

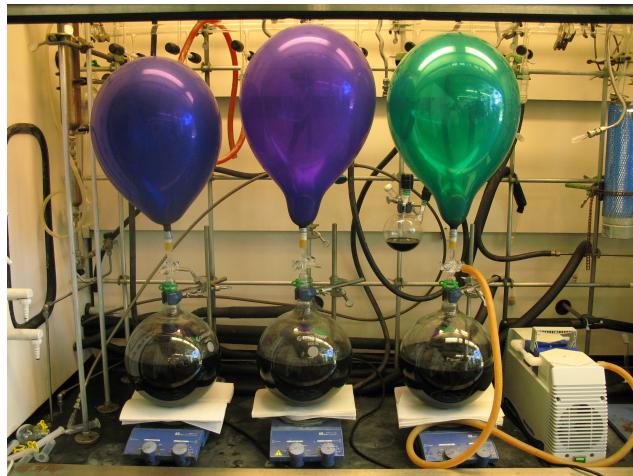


Q: What does the stereochemistry of the last two products indicate about the mechanism?

Setups Used to Carry Out Catalytic Hydrogenation



5% Pd metal dispersed
on particles of carbon
(Pd/C)

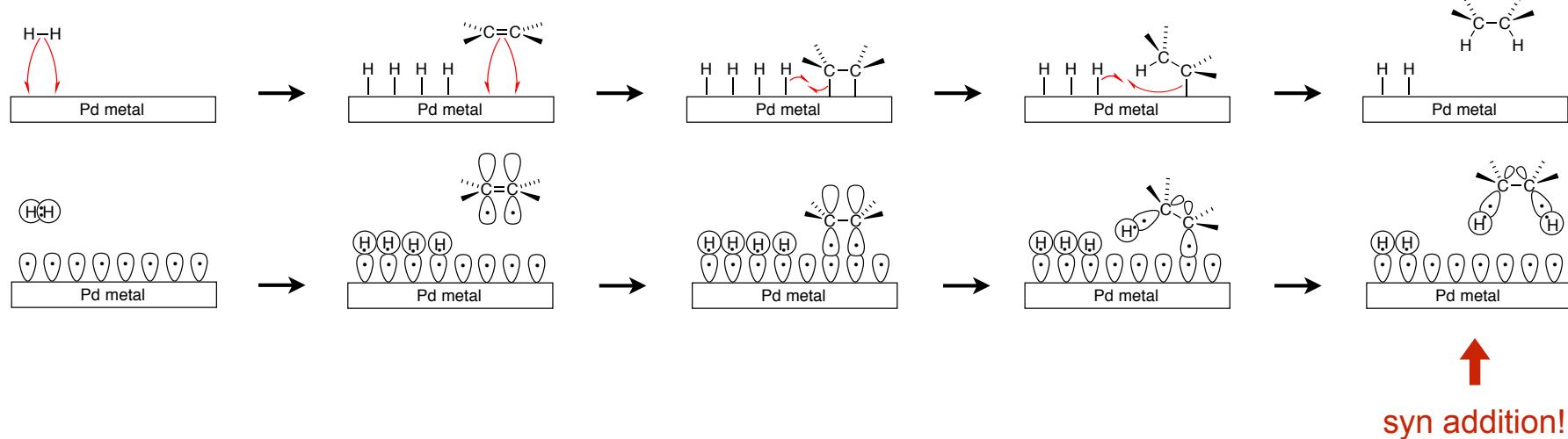


low-pressure hydrogenation in a flask

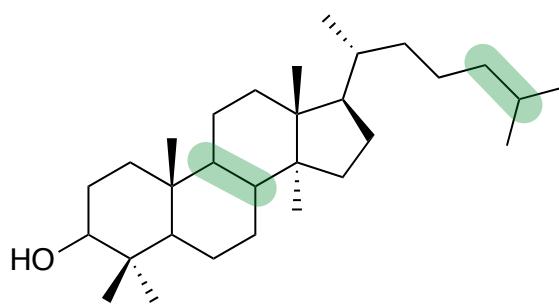
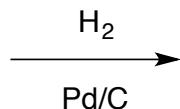
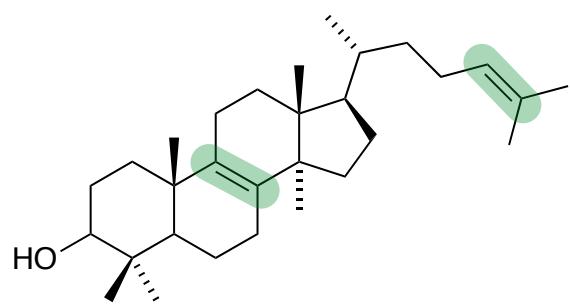
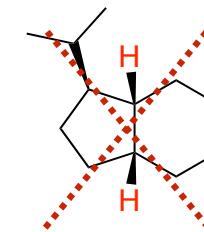
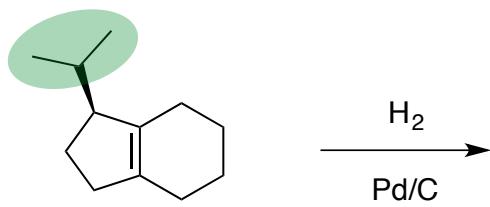
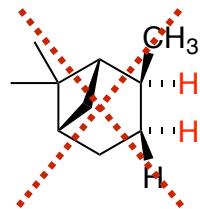
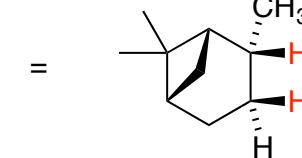
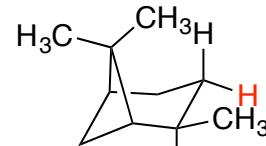
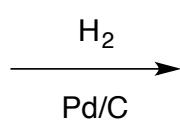
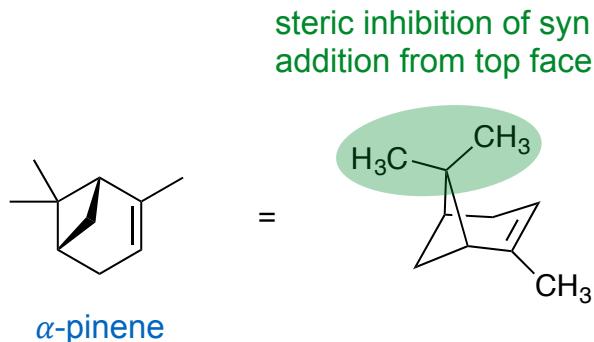


high-pressure hydrogenation
(Parr shaker)

Mechanism of Hydrogenation



Q: Major products of the following catalytic hydrogenation reactions?



difficult to control regioselectivity and stoichiometry
when multiple C=C bonds are present
(hydrogenation occurs at all C=C bonds)



TRANS FAT



Nutrition Facts	Amount/Serving	%DV*	Amount/Serving	%DV*
Serv. Size 4 cookies (32g)	Total Fat 7g	11%	Total Carb. 20g	7%
Servings 9	Sat. Fat 4.5g	23%	Dietary Fiber 1g	4%
Calories 150	Trans Fat 0g		Sugars 10g	
Calories from fat 60	Cholest. 0mg	0%	Protein 2g	
	Sodium 115mg	5%		
	Vitamin A 0% • Vitamin C 0% • Calcium 0% • Iron 4%			

INGREDIENTS: Enriched flour, riboflavin, sugar, partially hydrogenated vegetable oil, cocoa, cornstarch, hydrogenated oils, soy lecithin, salt, caramel color, artificial flavors.

6 Worst Trans Fat Foods

Breakfast Pastries



Processed pastries that are typically eaten in the morning. Examples include donuts, cinnamon buns, and coffee cakes.

Fried Foods



Almost any food that is battered and fried. Examples include French fries, onion rings, chicken wings, and fried chicken.

Salty Snacks



Salty and bite-sized foods that are typically quick to make or packaged ready-to-eat. Examples include crackers, popcorn, and beef jerky.

Pastas



Processed pastas that are boxed or come frozen. Examples include ravioli, macaroni and cheese, and lasagna.

Desserts



Ready-to-eat treats that often come individually packaged or frozen. Examples include snack cakes, cake and brownie mixes, and ice cream bars.

Breads



Processed breads that come frozen or can be bought packaged and pre-cut. Examples include garlic bread, Texas toast, and breadsticks.



GOOD FATS vs. BAD FATS



GROW ROCHESTER

PARTIALLY HYDROGENATED VEGETABLE OIL

A SEMI-SOLID FAT CREATED WHEN FOOD PROCESSORS FORCE HYDROGEN INTO UNSATURATED FATTY ACIDS.

PARTIALLY HYDROGENATED FATS ARE THE PRINCIPAL SOURCES OF TRANS FAT IN THE AMERICAN DIET. AND A HARVARD STUDY ESTIMATED THAT TRANS FAT CAUSES 10,000 HEART ATTACKS EVERY YEAR. A LOHOLE IN THE FDA'S LABELING REQUIREMENTS ALLOWS PROCESSORS TO ADD AS MUCH AS 0.49 GRAMS PER SERVING AND STILL CLAIM ZERO IN THEIR NUTRITION FACTS.

10 SCARY FOOD FACTS

SOURCE: MEN'S HEALTH

FDA U.S. Food and Drug Administration
Protecting and Promoting Your Health

The FDA recently took steps to eliminate Partially Hydrogenated Oils from the American diet.

Bunge Oils has helped our customers reduce the amount of trans fat in food products by more than 70% over the last decade.

Unsaturated, Partially Unsaturated/Hydrogenated, and Saturated fats



unsaturated fats
liquids at RT

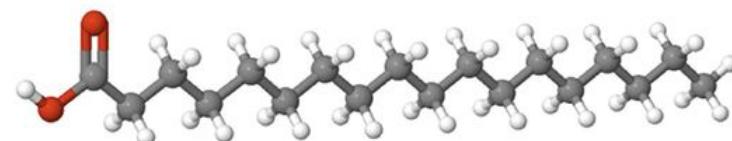


saturated fats
solids at RT

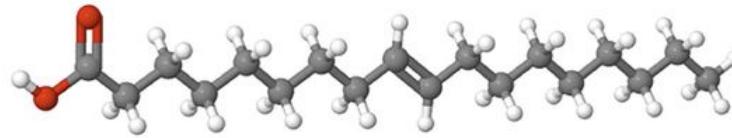


partially hydrogenated fats
solids at RT

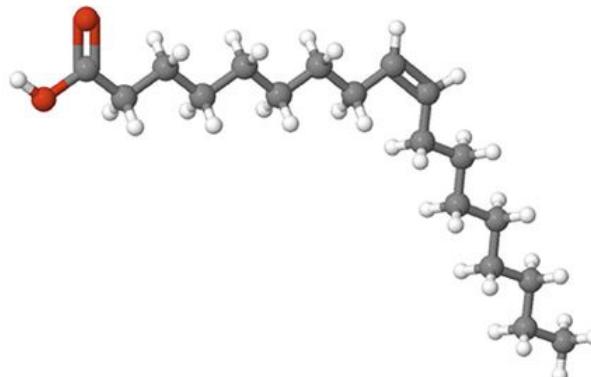
Stearic acid
(saturated)



Elaidic acid
(trans-unsaturated)



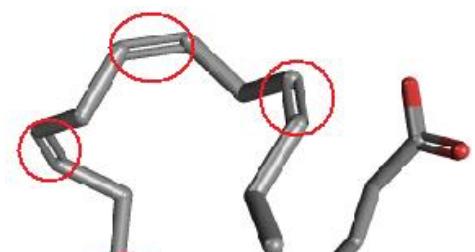
Oleic acid
(cis-unsaturated)



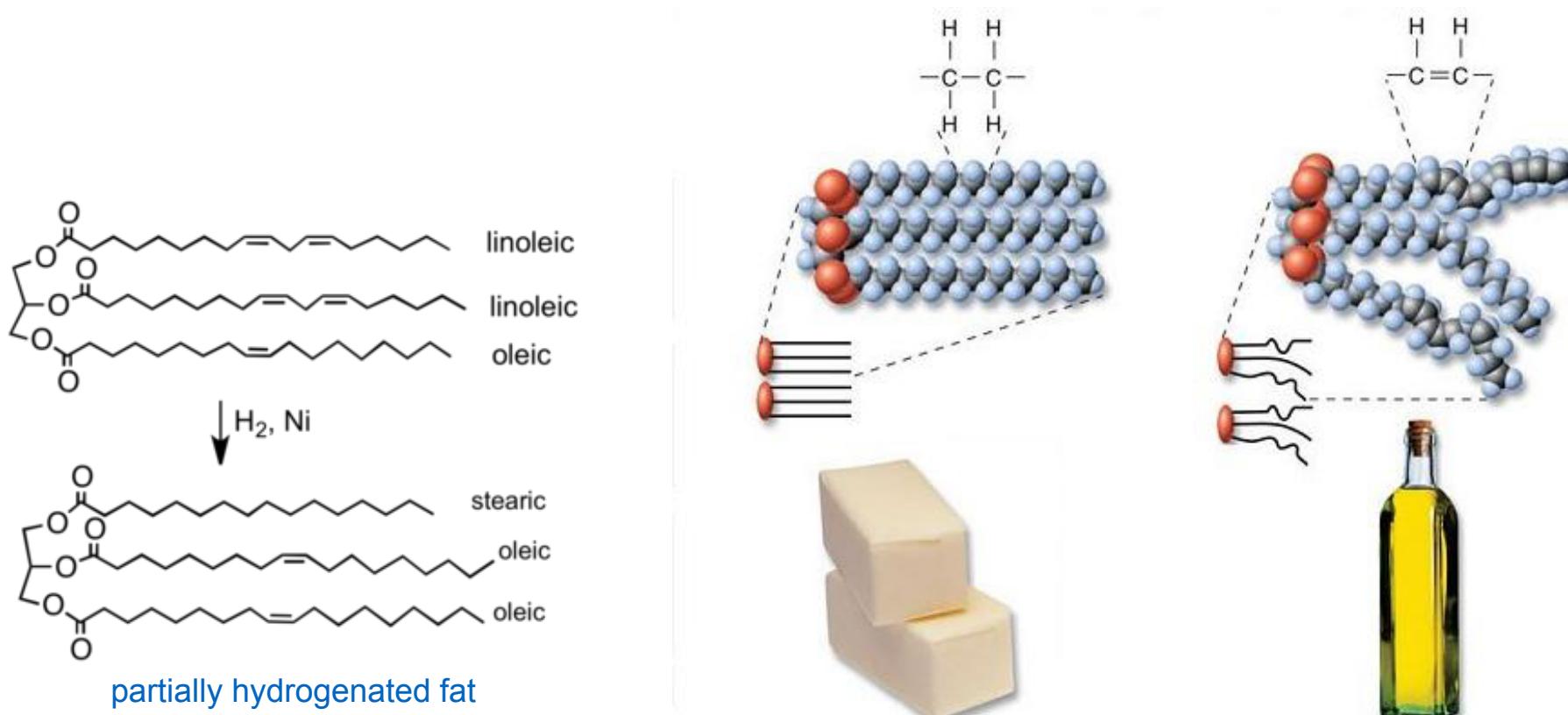
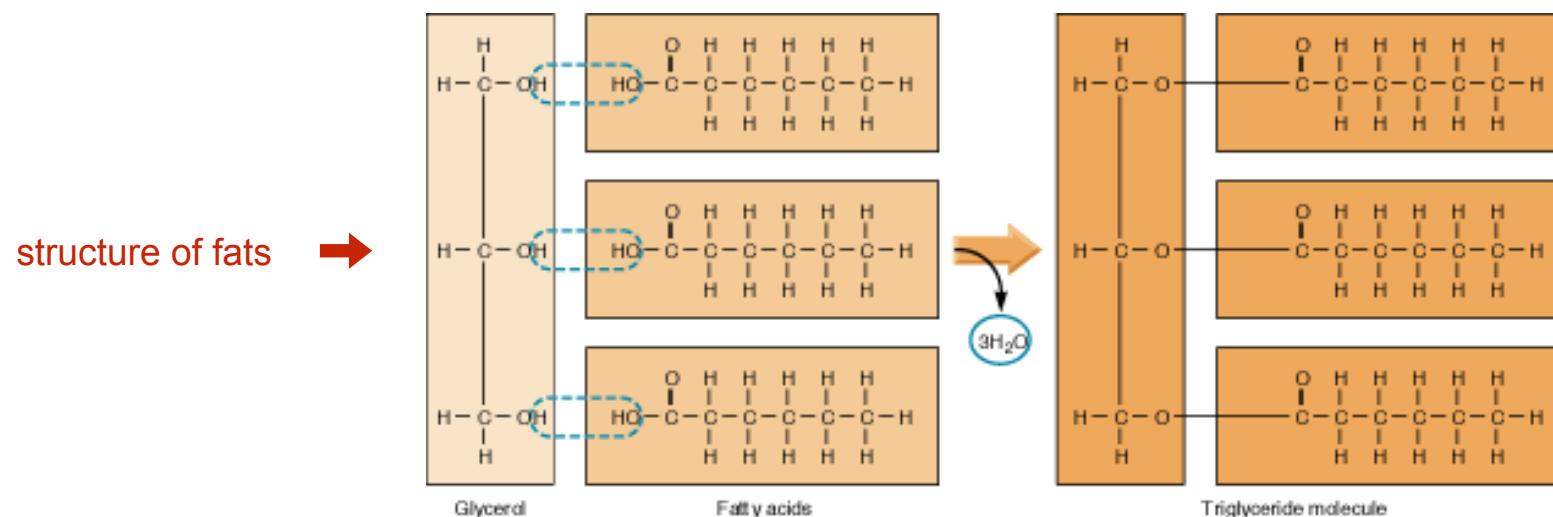
Lauric Acid (Coconut Oil)
Saturated (no double bonds)



Oleic Acid (from Olive Oil)
Monounsaturated (one double bond)

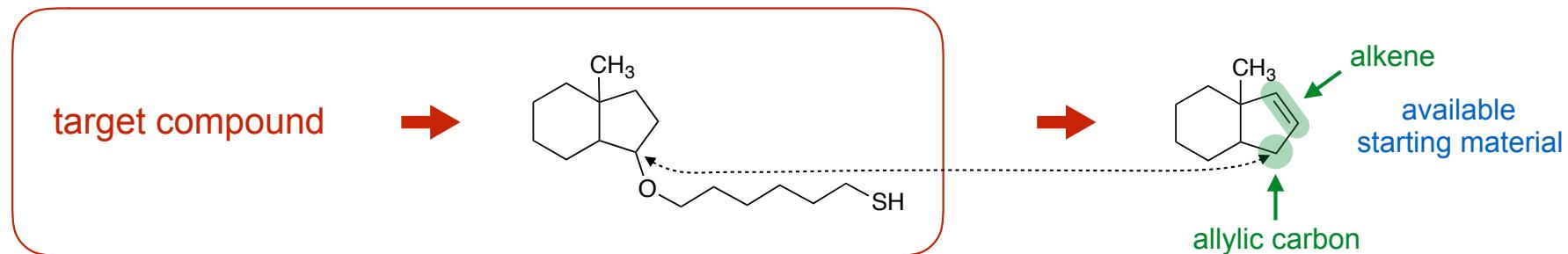


Eicosapentaenoic Acid (Fish Oil)
Polyunsaturated Omega-3 Fat

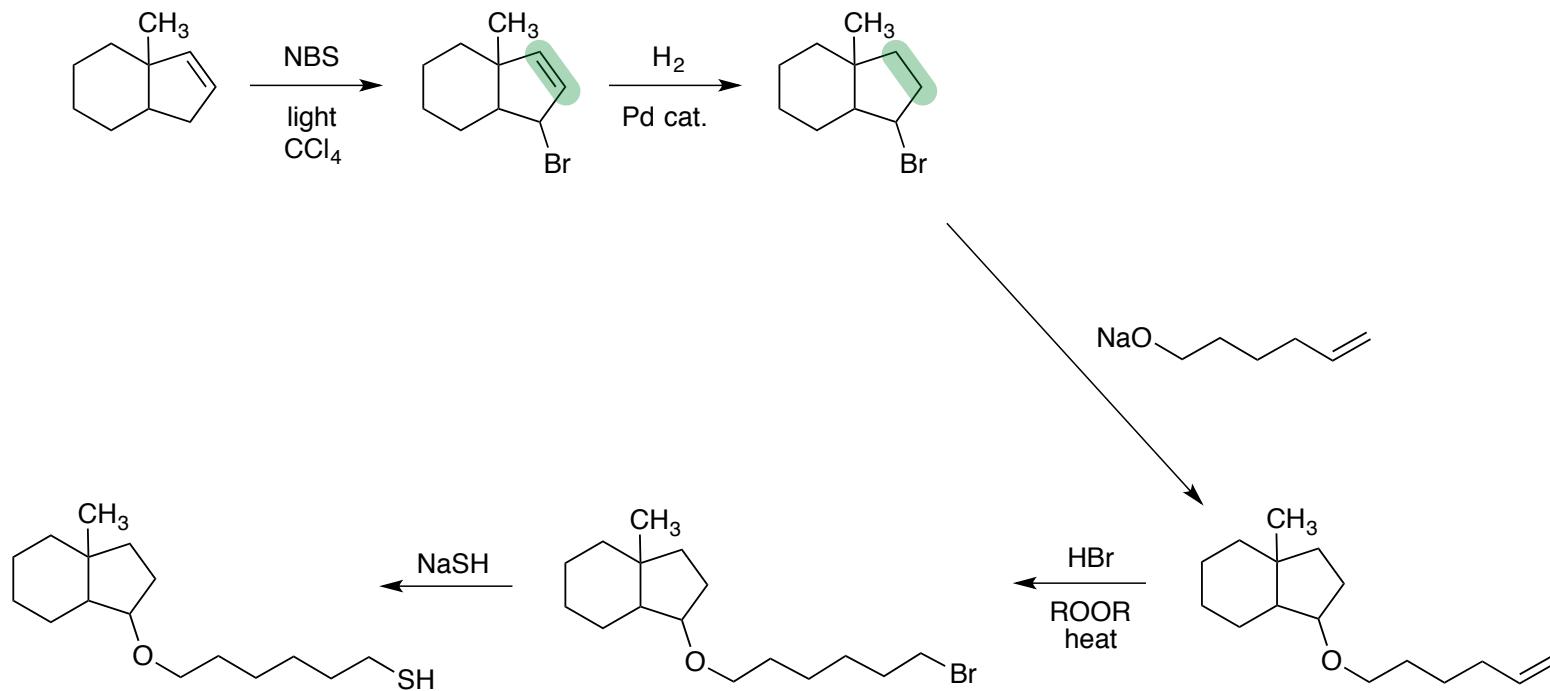


Q: How are hydrogenation reactions useful in organic synthesis?

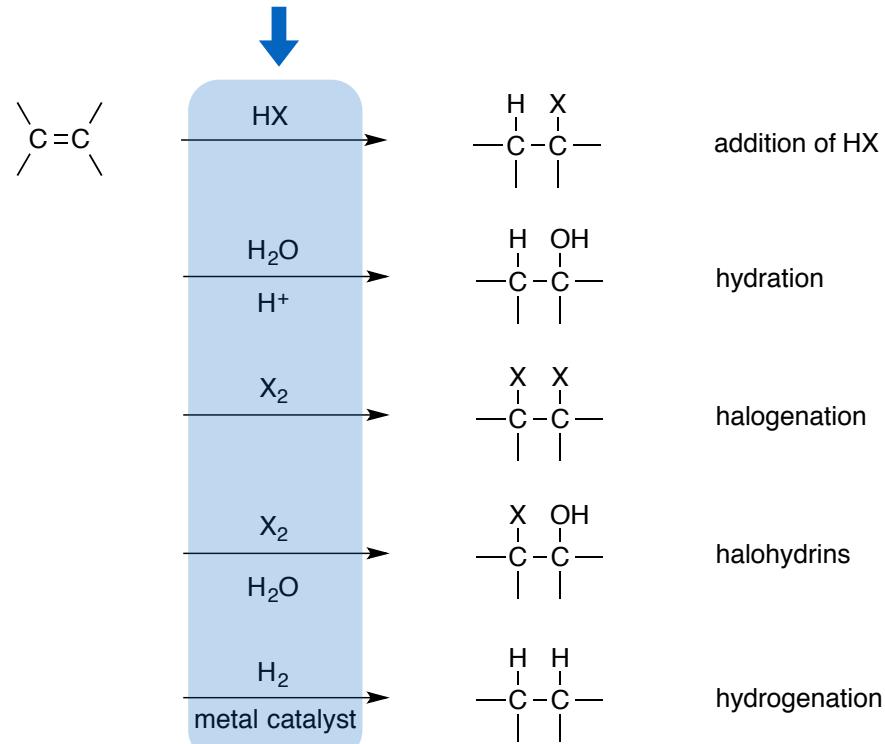
Ex: Using an alkene to control regiochemistry during synthesis & then removing it



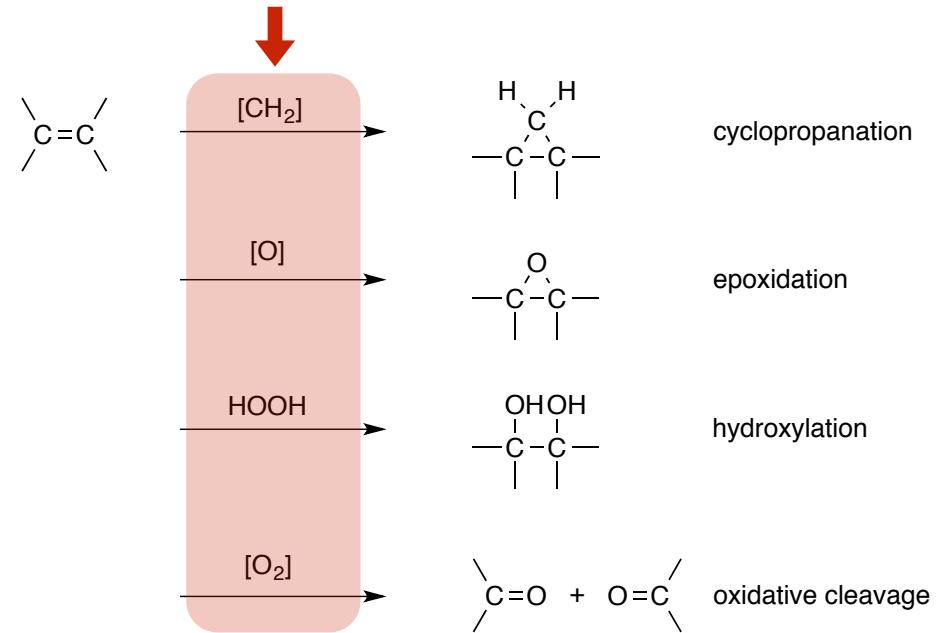
Proposed Synthesis



Addition reactions covered so far



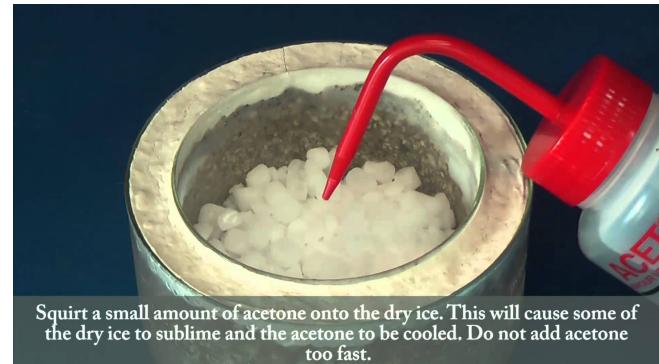
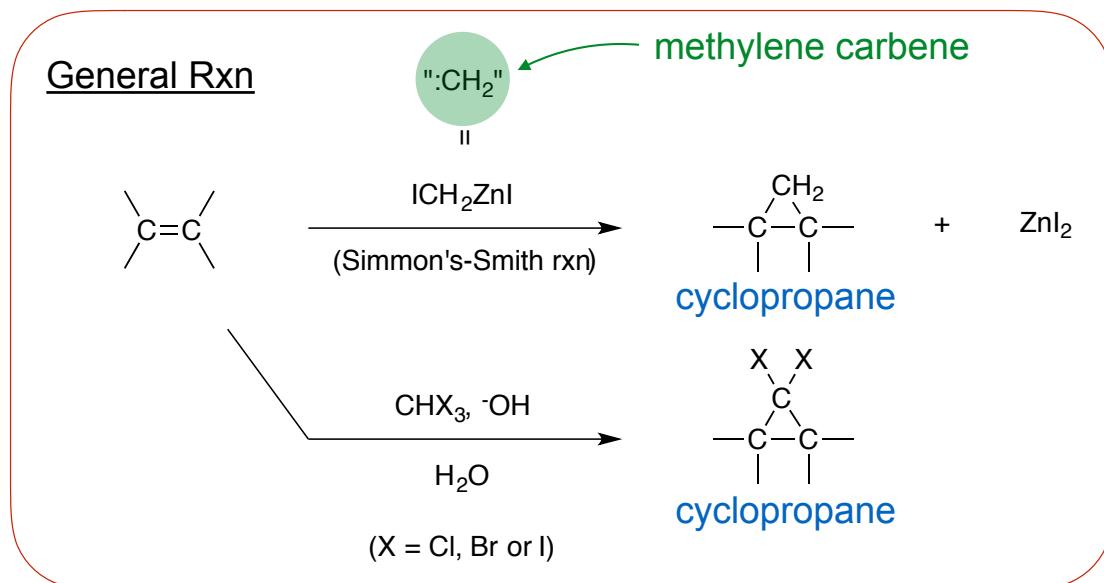
Addition reactions remaining to cover



reagents providing both electrophilic and nucleophilic components

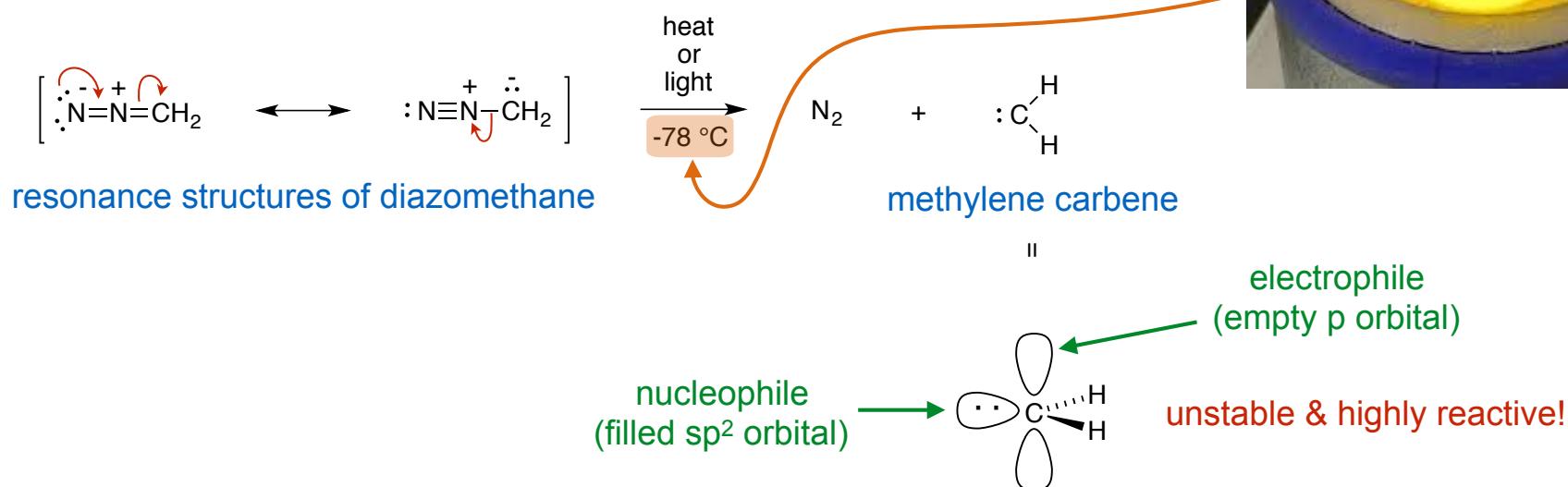
Addition of Carbenes to Alkenes (8-11)

- Method to prepare cyclopropane rings from alkenes
- Requires a carbon atom that is both an electrophile and a nucleophile → a carbene!

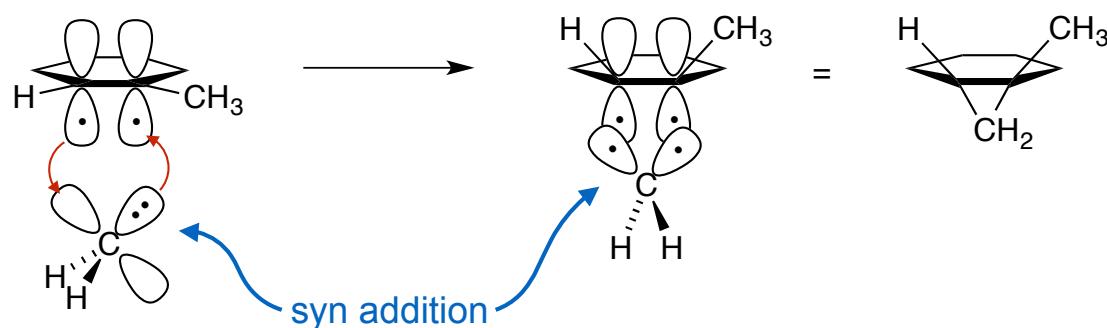
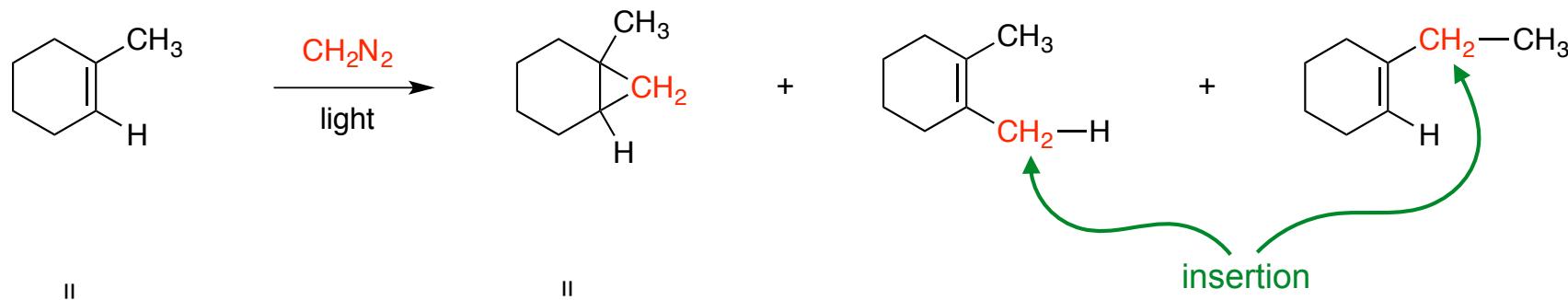


Q: What is a carbene? How do you prepare a carbene?

Ex: diazomethane (CH_2N_2)—first reliable precursor for generating methylene carbene



Ex: Reaction of diazomethane (CH_2N_2) with an alkene

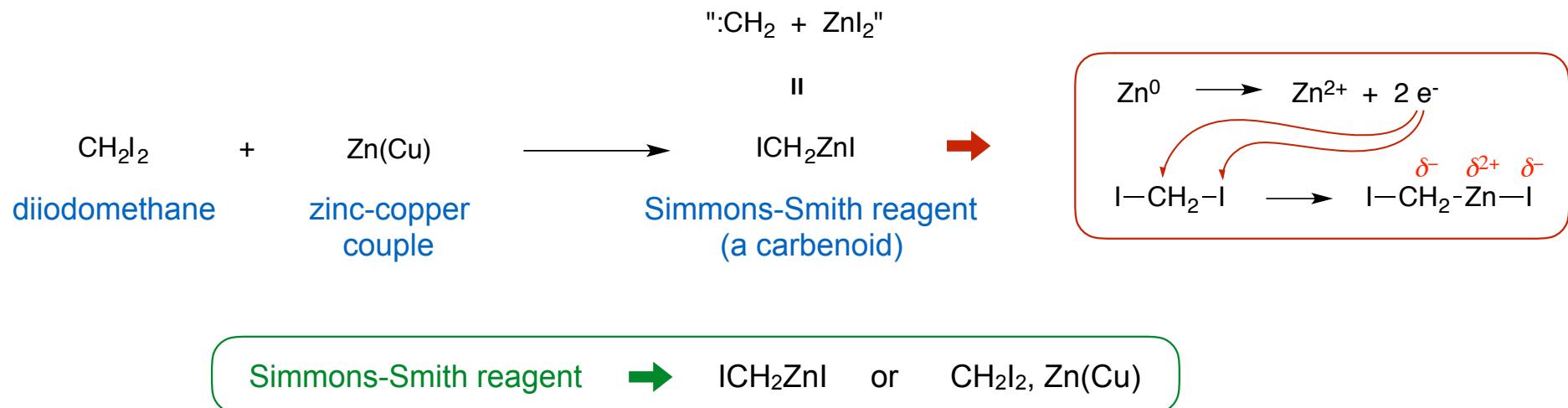


Problem: diazomethane (CH_2N_2) is too reactive and inserts between C-H and C-C bonds leading to unwanted side products in addition to cyclopropanation

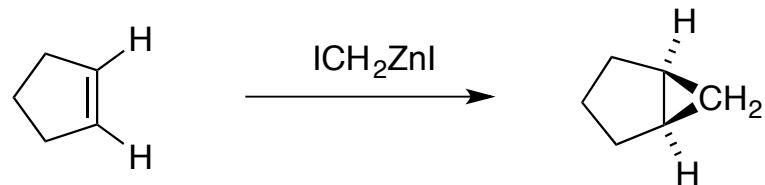
→ need a more selective, less reactive reagent for cyclopropanation

Simmons-Smith Reaction (8-11A)

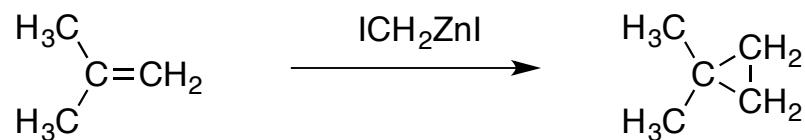
- Method to prepare unsubstituted cyclopropane rings from alkenes
- ICH_2ZnI (Simmons-Smith reagent) is more stable and more selective than CH_2N_2 (diazomethane)



Ex:



Ex:



A New and Efficient Total Synthesis of (\pm)-Longifolene

Wolfgang Oppolzer, Thierry Godel
J. Am. Chem. Soc., 1978, 100, 2583-2584

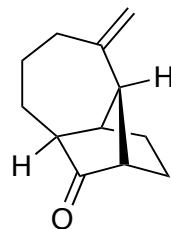


(+)-longifolene
constituent of pine resin

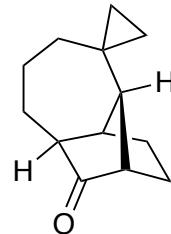


lapsang souchong tea (正山小种)
smoked tea (熏茶)

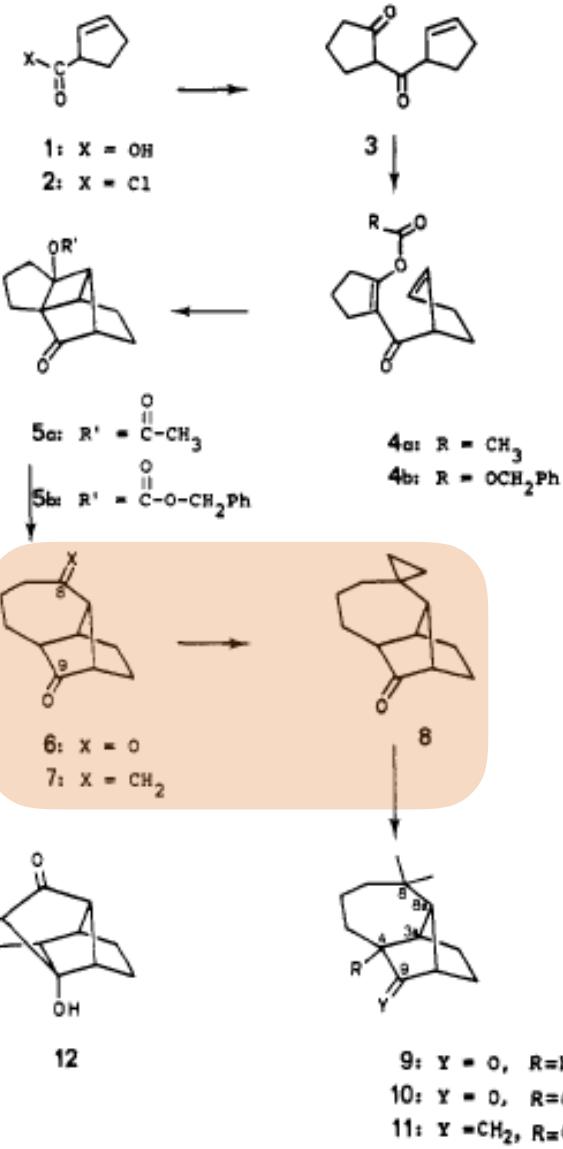
longifolene is an aroma constituent
from smoking the tea over pine fires



Zn(Cu), CH_2I_2
toluene
reflux 60 h
78%

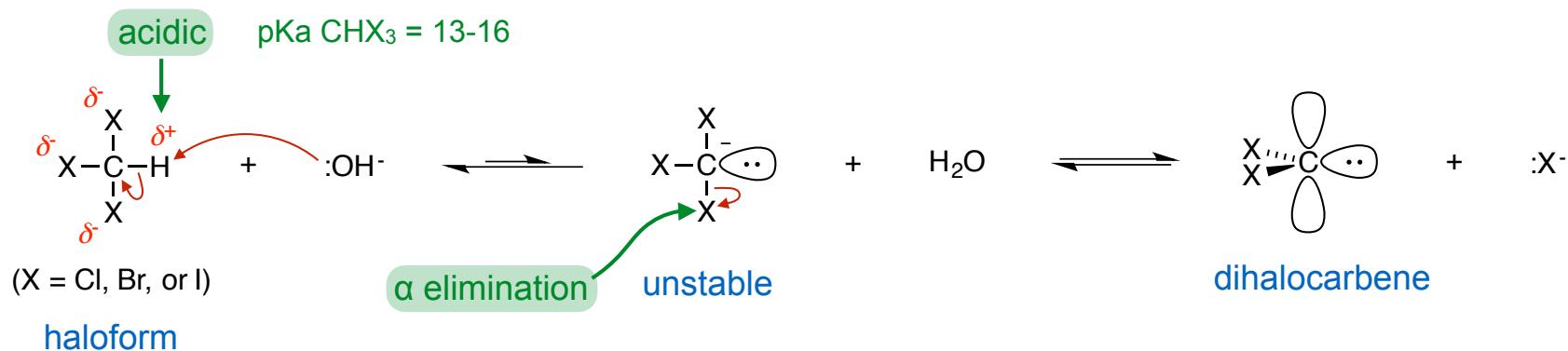


Scheme II



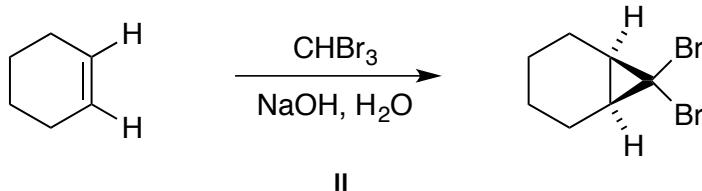
Formation of Carbenes by Alpha Elimination (8-11B)

- Method to prepare halogenated cyclopropane rings from alkenes



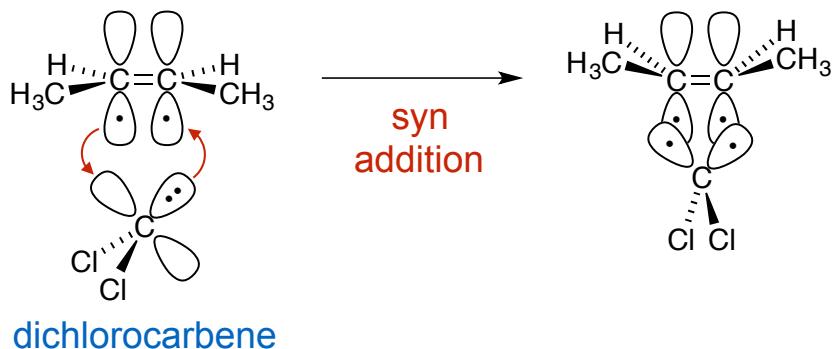
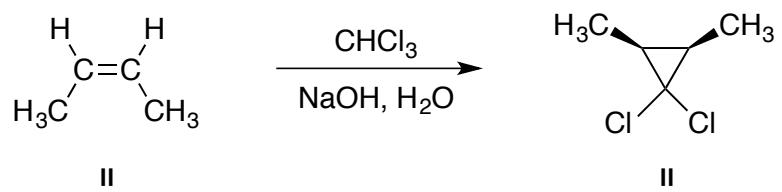
alpha (α) elimination → H^+ and Br^- are lost from the same carbon atom
beta (β) elimination → H^+ and Br^- are lost from adjacent carbon atoms

Ex:



$:\text{CBr}_2$
dibromocarbene

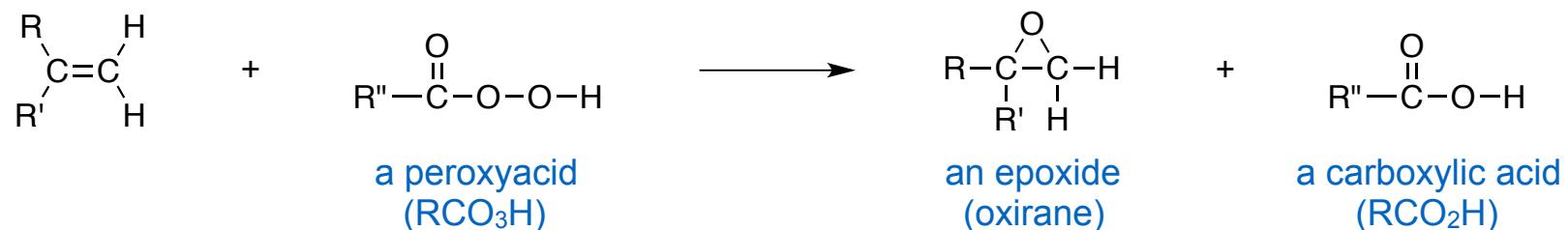
Ex:



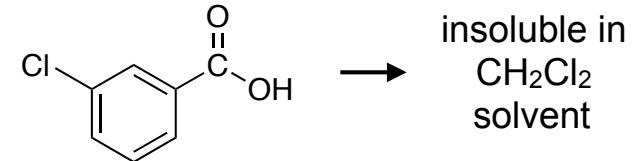
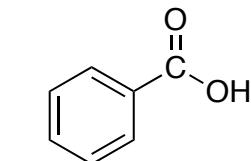
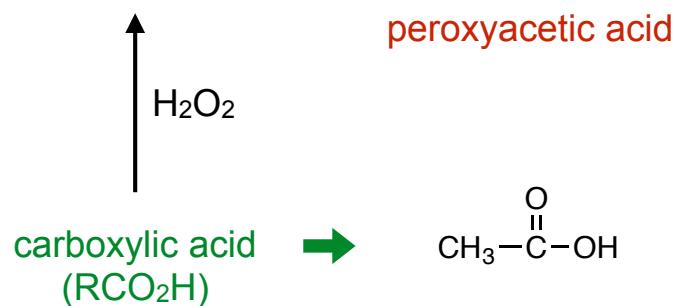
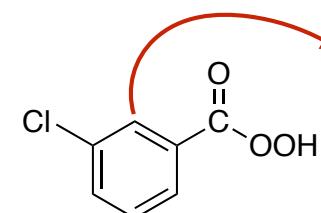
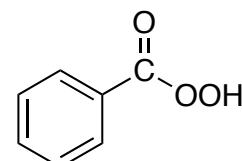
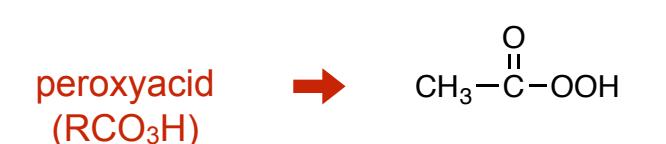
Epoxidation of Alkenes (8-12)

- best method to prepare epoxides (oxiranes)
 - epoxides are used to convert alkenes into a variety of other functional groups (e.g., alcohols)

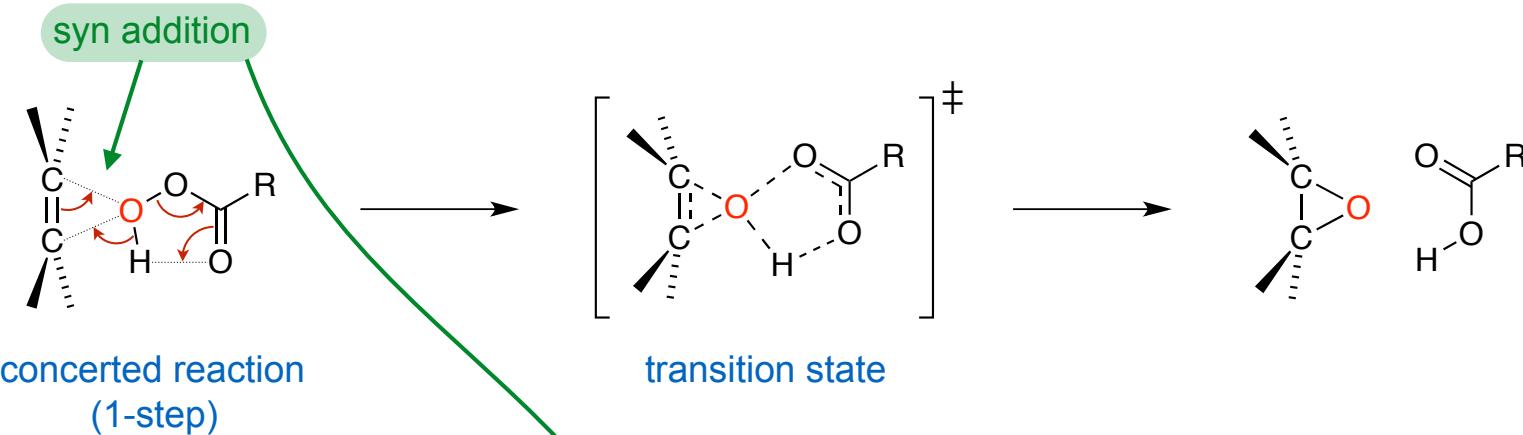
General Reaction



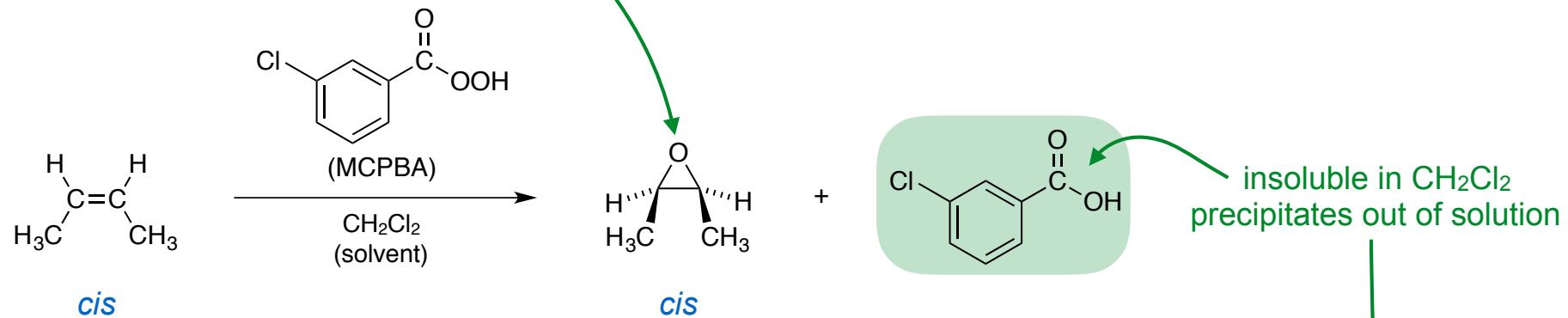
Commonly used peroxyacids



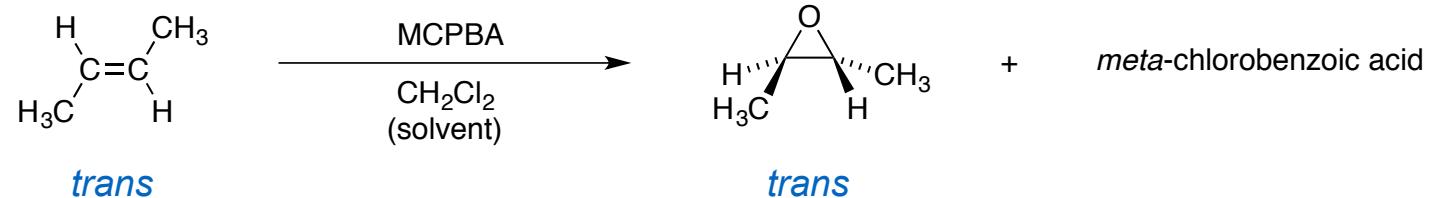
Mechanism of epoxidation



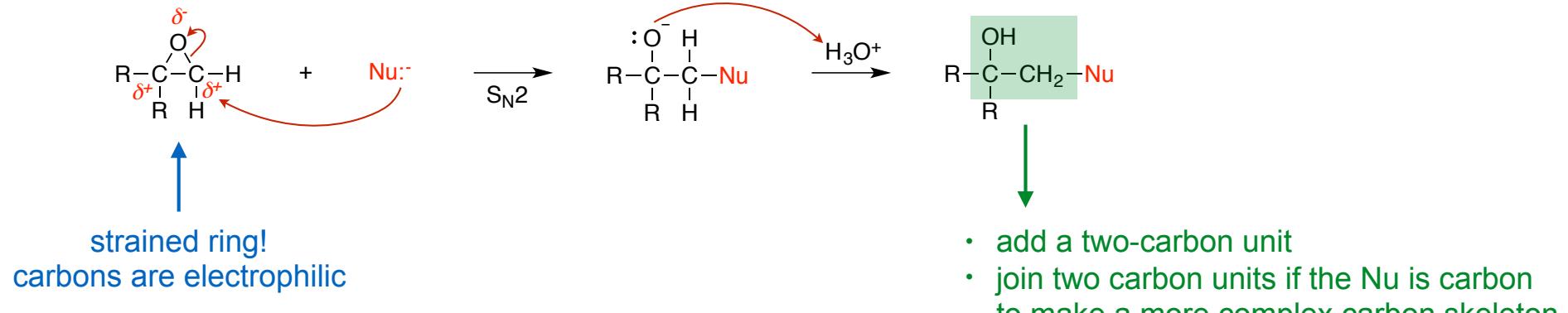
Ex:



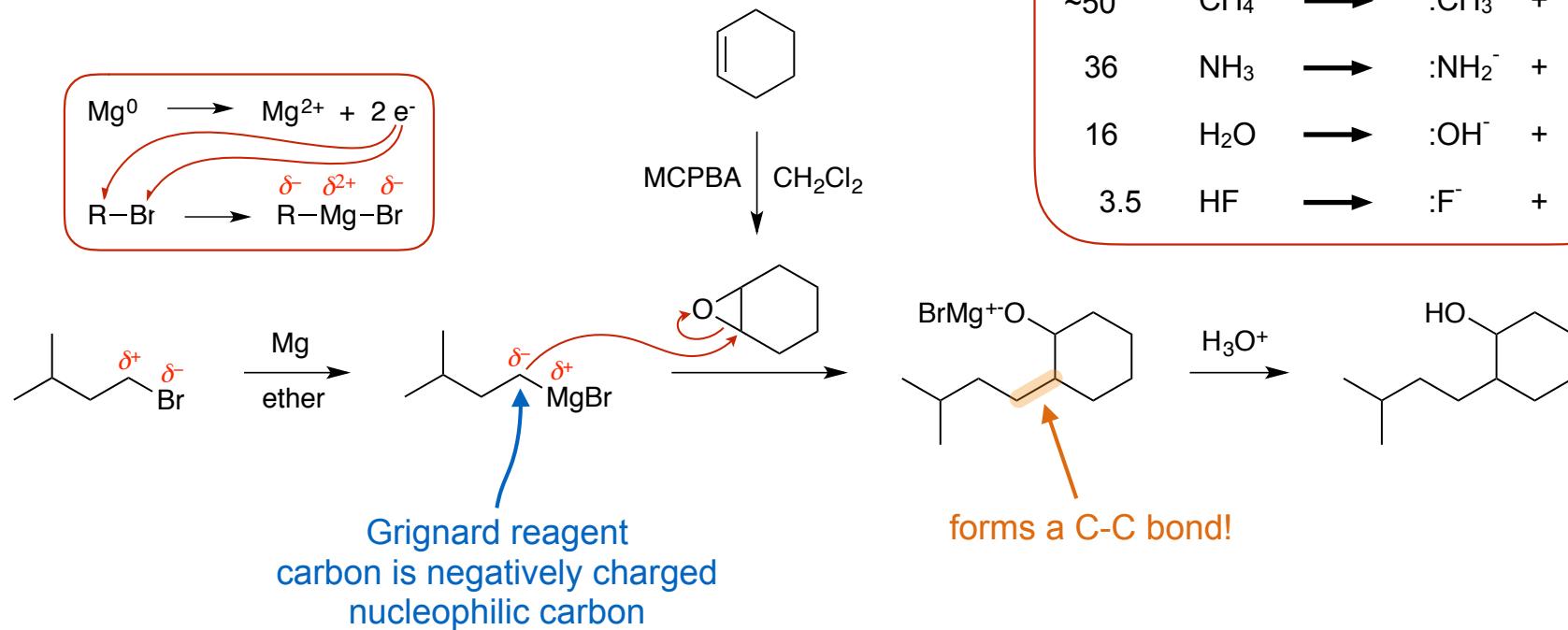
Ex:



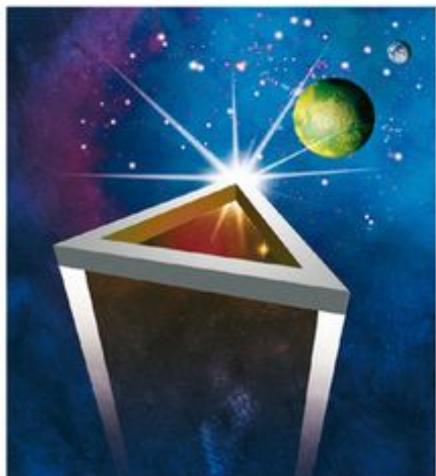
Q: Why are epoxides useful?



Ex: Preview of Chapter 10 - Synthesis of Alcohols



Aziridines and Epoxides in Organic Synthesis



Description

Aziridines and epoxides are among the most widely used intermediates in organic synthesis, acting as precursors to complex molecules due to the strains incorporated in their skeletons. Besides their importance as reactive intermediates, many biologically active compounds also contain these three-membered rings.

Filling a gap in the literature, this clearly structured book presents the much needed information in a compact and concise way. The renowned editor has succeeded in gathering together excellent authors to cover synthesis, applications, and the biological aspects in equal depth.

Divided roughly equally between aziridines and epoxides, the twelve chapters discuss:

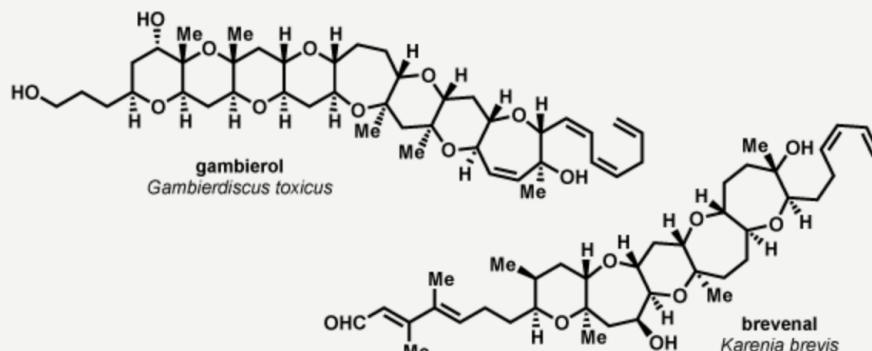
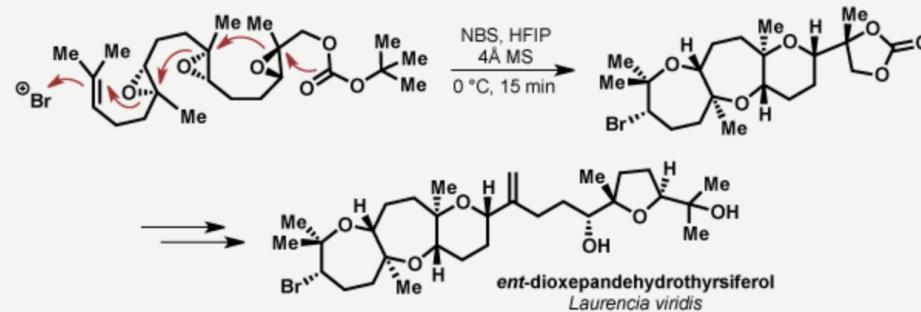
- * Synthesis of aziridines
- * Nucleophilic ring-opening of aziridines and epoxides
- * Organic synthesis with aziridine building blocks
- * Vinyl aziridines in organic synthesis
- * Diastereoselective aziridination reagents
- * Synthetic aspects of aziridinomitocene chemistry
- * Biosynthesis of biologically important aziridines
- * Organic catalysis of epoxide and aziridine ring formation
- * Metal-mediated synthesis of epoxides
- * Asymmetric epoxide ring opening chemistry
- * **Epoxides in complex molecule synthesis**
- * Biological activity of epoxide-containing molecules

[Overview](#)[Epoxide-Opening Cascades](#)[Ni-Cat C – C Bond Formation](#)[Target-Oriented Synthesis](#)[Continuous-Flow Chemistry](#)

Target-Oriented Synthesis

Natural product synthesis in the Jamison laboratory is closely linked to the development of new transformations and the elucidation of reaction mechanism. Methods developed in the group are used to gain rapid access to the core structures of targets bearing unique structural features and interesting biological activity.

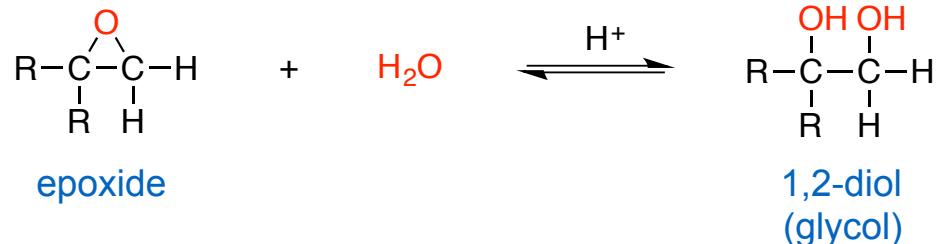
Regioselective epoxide-opening cascades, for example, have emerged as a powerful method to construct complex fused ring systems in a single step from an appropriate polyepoxide precursor. The Jamison group has completed the total synthesis of terpenoid polyether dioxepandehydrothrysiferol utilizing an epoxide-opening cascade and similar efforts are underway to prepare marine ladder polyether natural products (e.g., gambierol, brevenal, etc.).



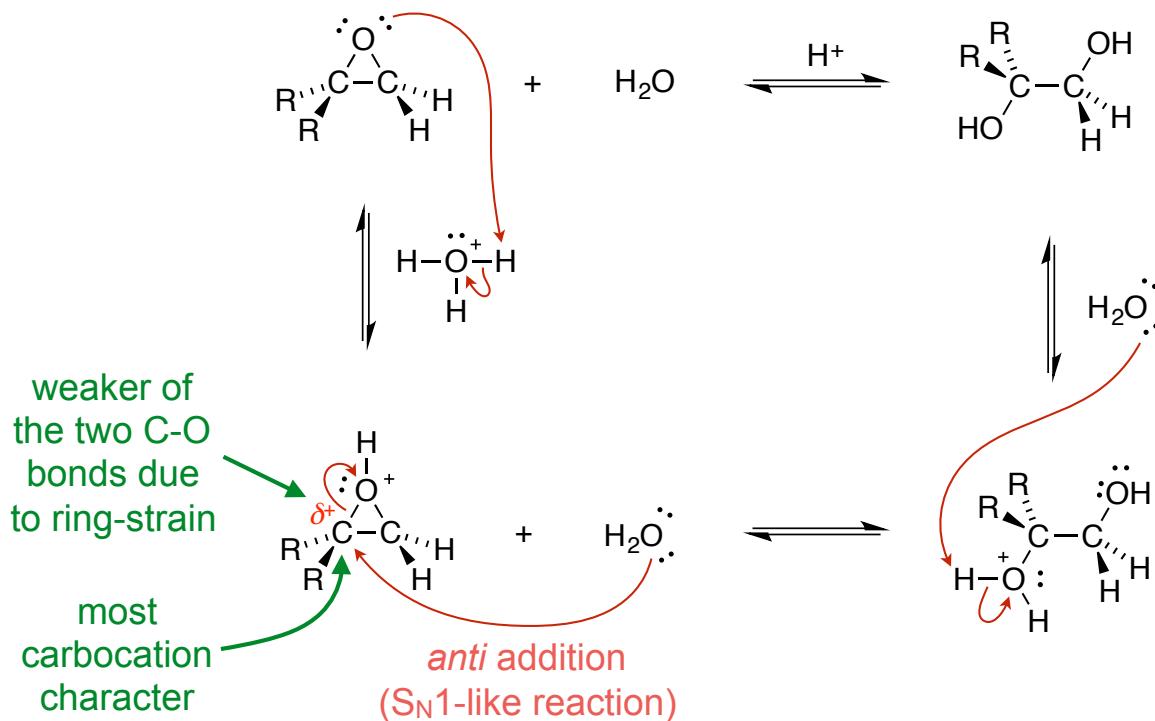
Acid-Catalyzed Ring-Opening of Epoxides (8-13)

- good method to prepare 1,2-diols (glycols)
- generates *trans*-1,2-diols on rings via *anti* addition

General Reaction

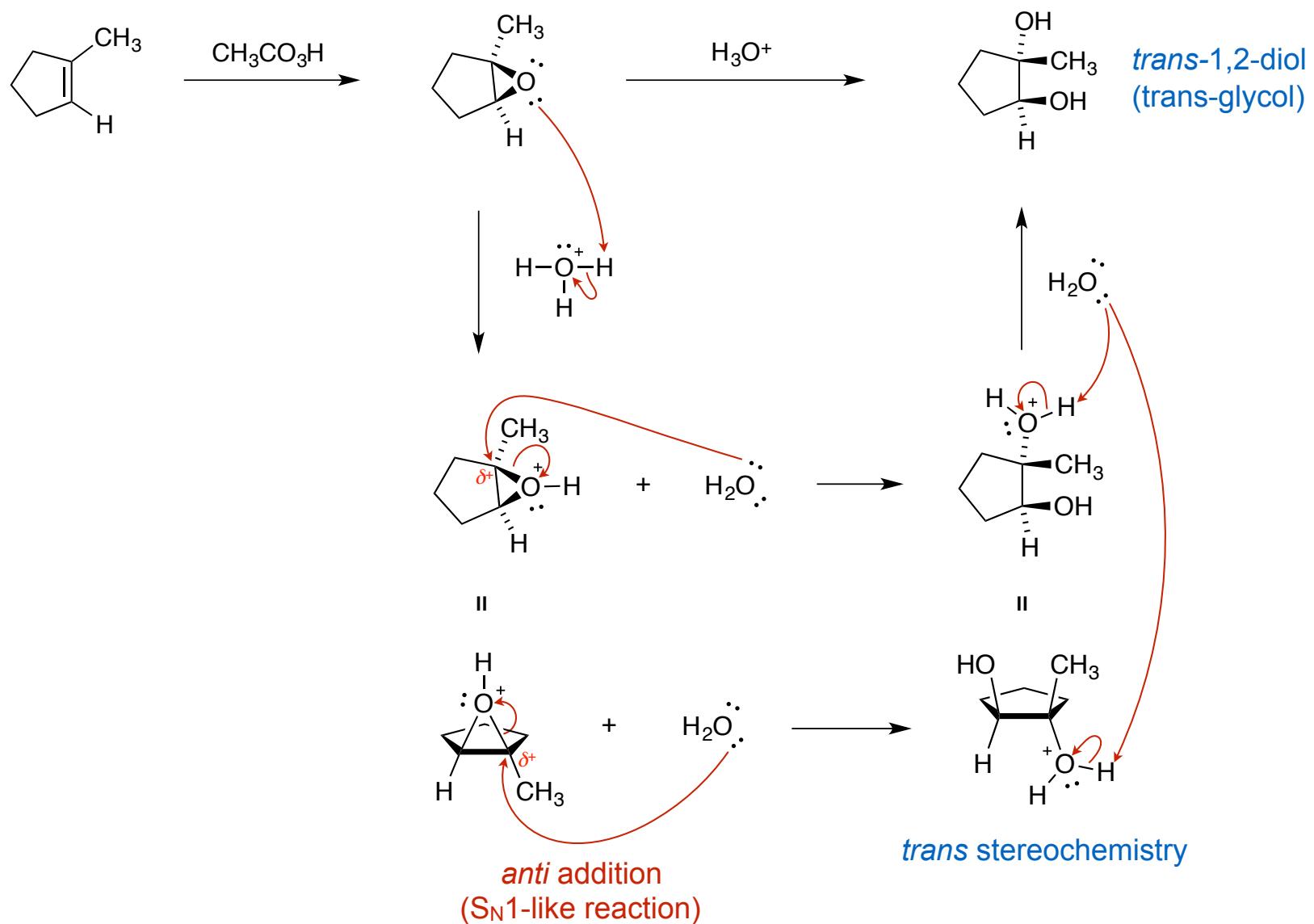


Mechanism



- protonation does not cause ring-opening to form a classical carbocation but epoxides behave as if they do
- water attacks at the more-substituted carbon via *anti* addition due to greater carbocation character (stability)

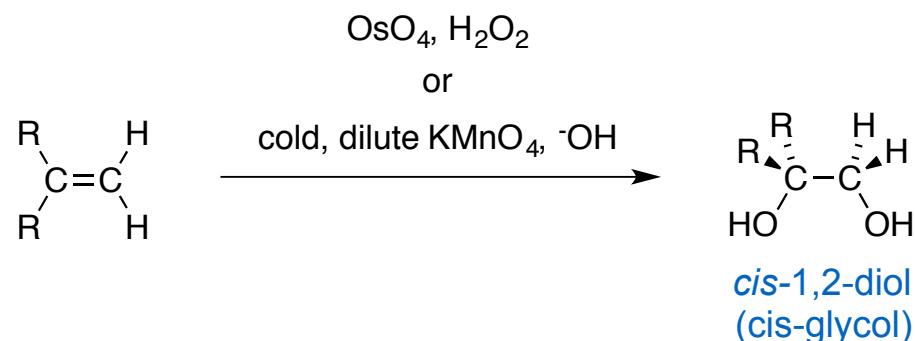
Ex:



Syn Hydroxylation of Alkenes (8-14)

- method to prepare *cis*-1,2-diols (*cis*-glycols)
- OsO_4 — catalytic, high yield, expensive, extremely toxic to humans
- cold, dilute KMnO_4 — stoichiometric (non-catalytic), lower yield, inexpensive
- both reagents cleave the π bond of alkenes

General Reaction

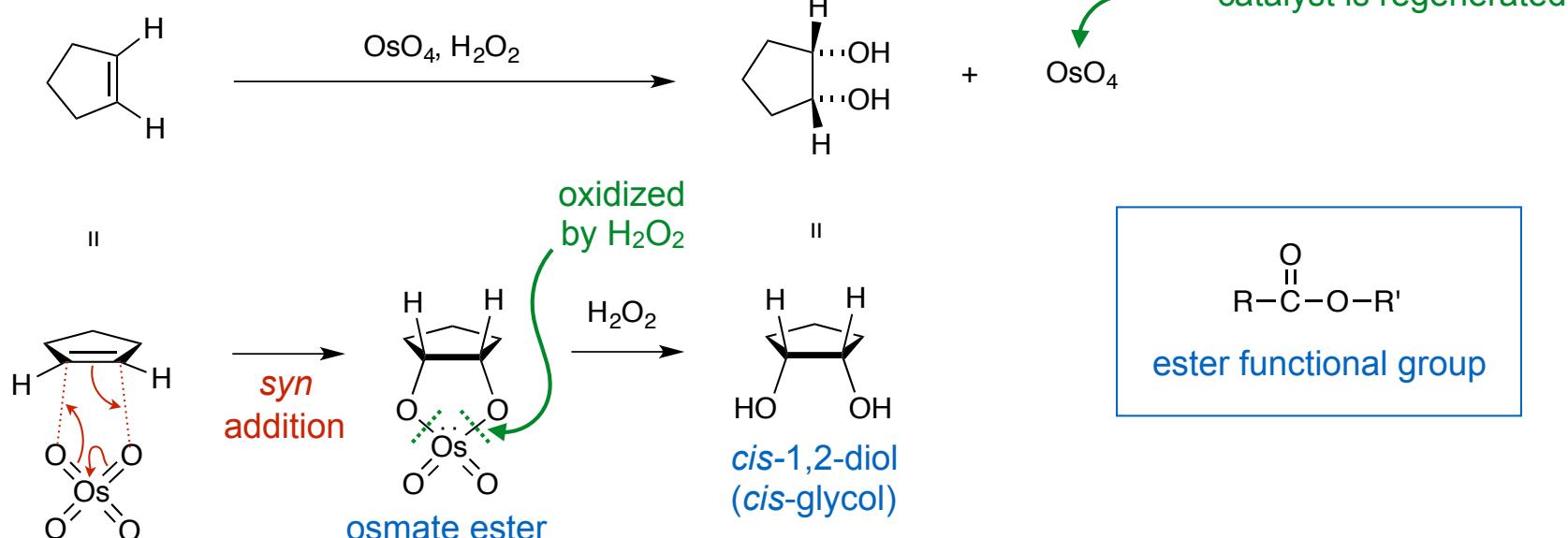


Oxidizing Reagents

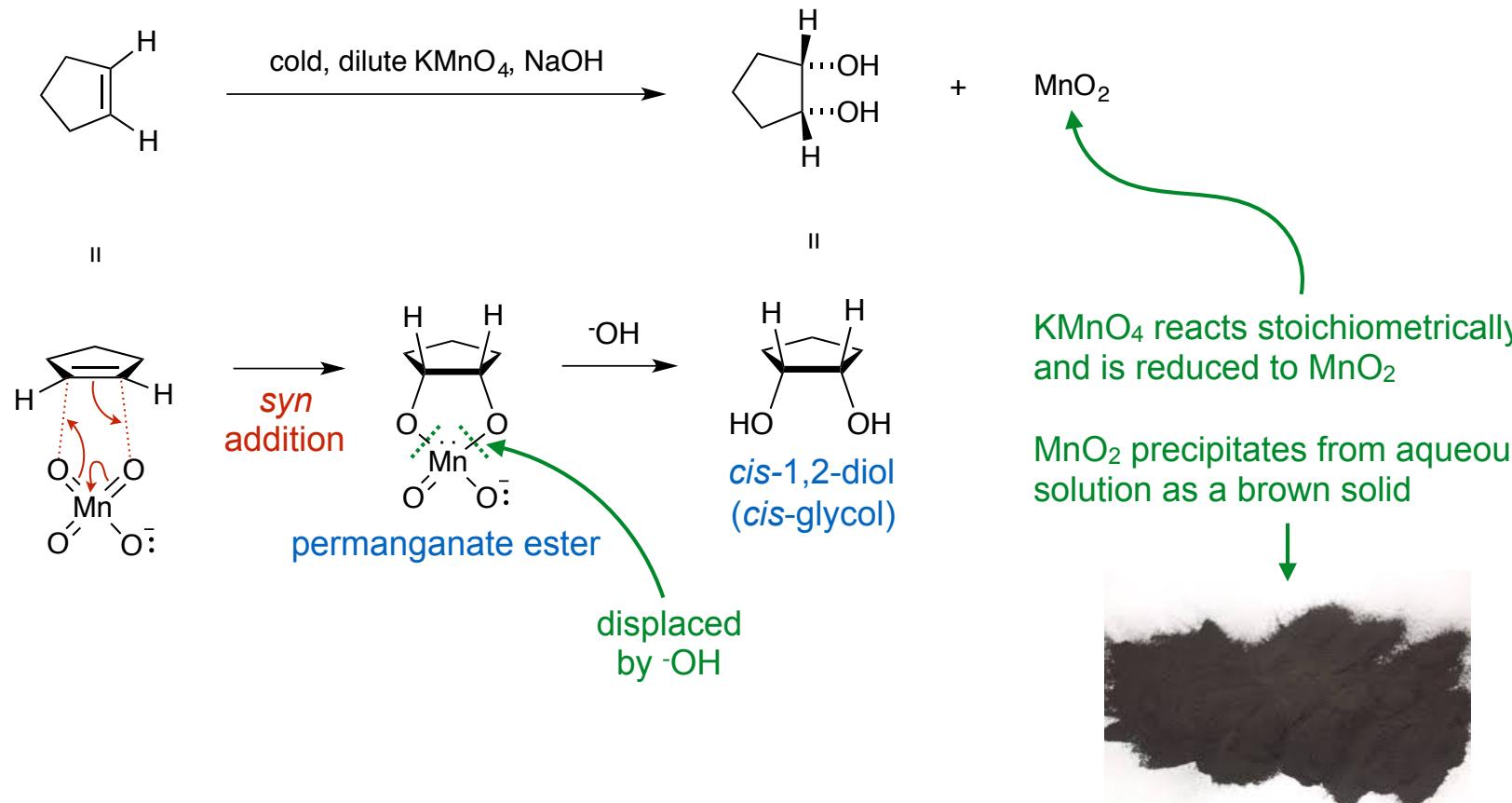
OsO_4 - osmium tetroxide

KMnO_4 - potassium permanganate

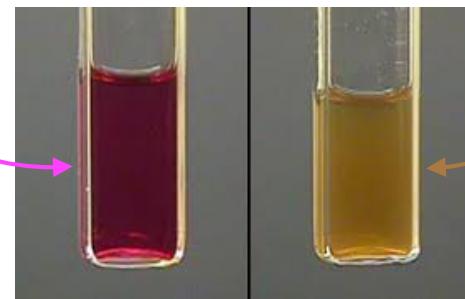
Ex:



Ex:



Baeyer Test for Alkenes

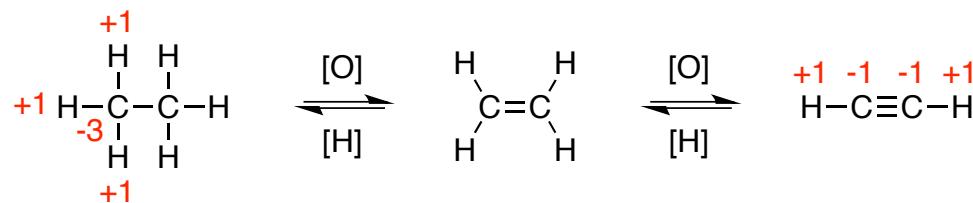
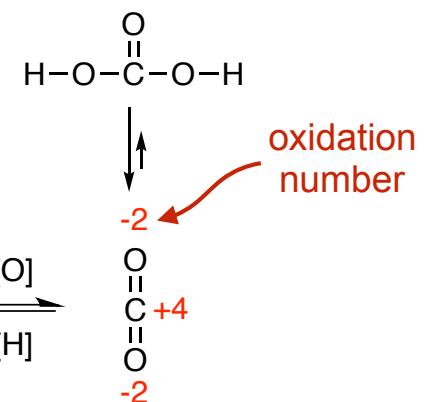
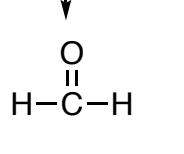
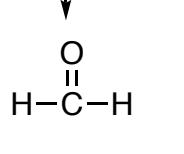
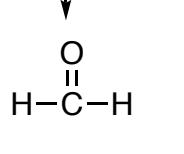
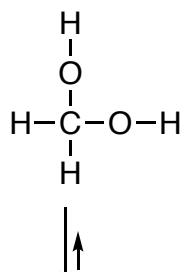
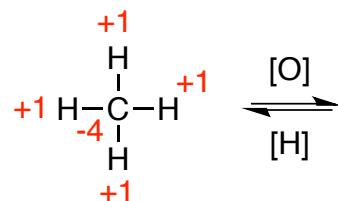


Oxidative Cleavage of Alkenes (8-15)

- Alkenes can be oxidized to form carbonyl (C=O) compounds by breaking both the C=C sigma and pi bonds
- Method to prepare aldehydes, ketones and carboxylic acids

Q: What is oxidation?

Reminder: oxidation vs. reduction



Element:	H	C	O
Electronegativity:	2.1	2.5	3.5

Oxidation:

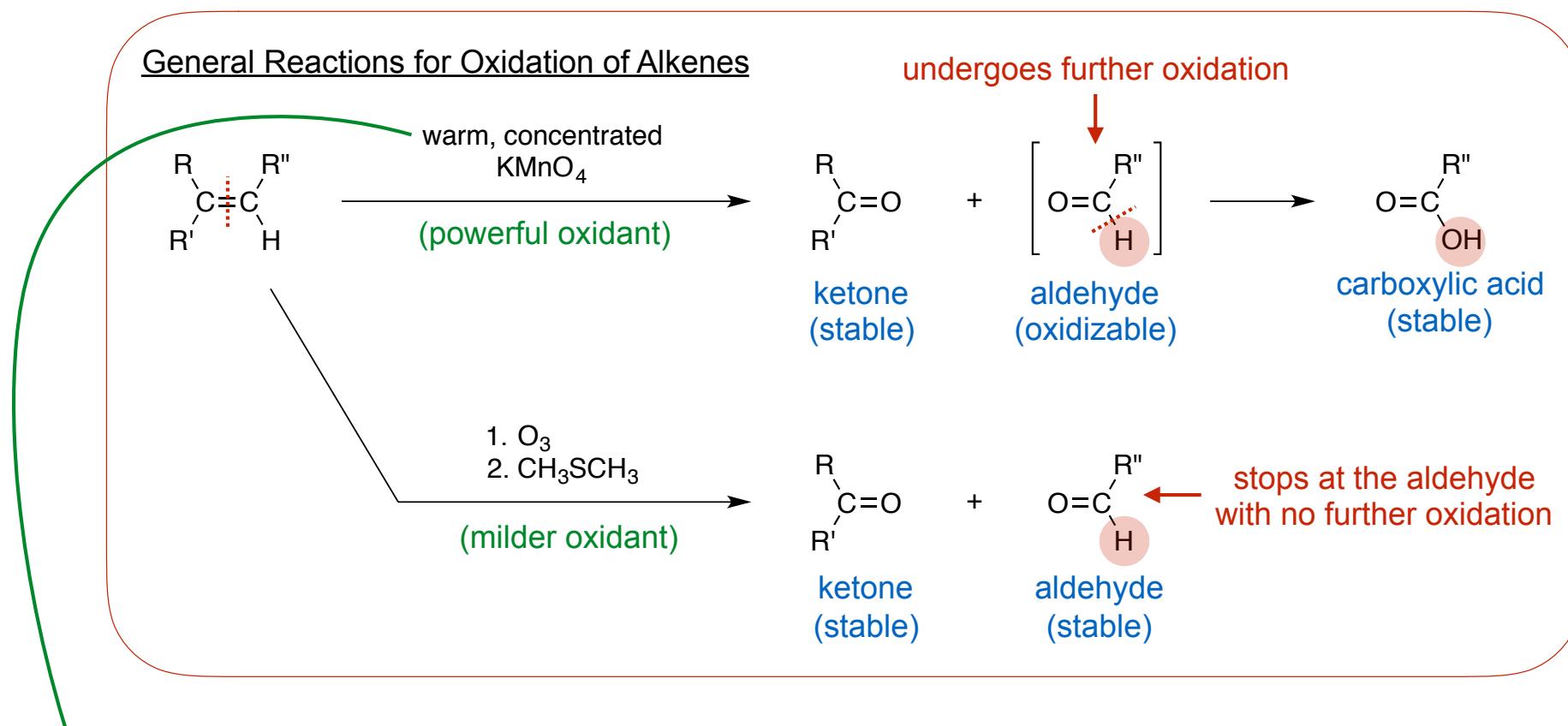
- Breaking a bond between C and H
- Forming a bond between C and O

Reduction:

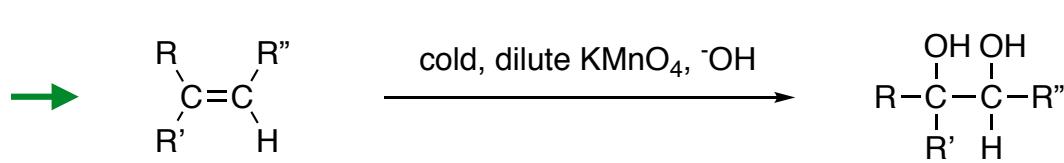
- Forming a bond between C and H
- Breaking a bond between C and O

Oxidative Cleavage of Alkenes (8-15)

- Warm, concentrated permanganate (MnO_4^-) is a strong oxidizing reagent that cleaves the π and σ bonds of alkenes to form carbonyl (C=O) compounds
- Warm, concentrated permanganate cleaves any C-H bonds on alkenes to form carboxylic acids
- Ozone (O_3) cleaves C=C π and σ bonds but not C-H bonds on alkenes

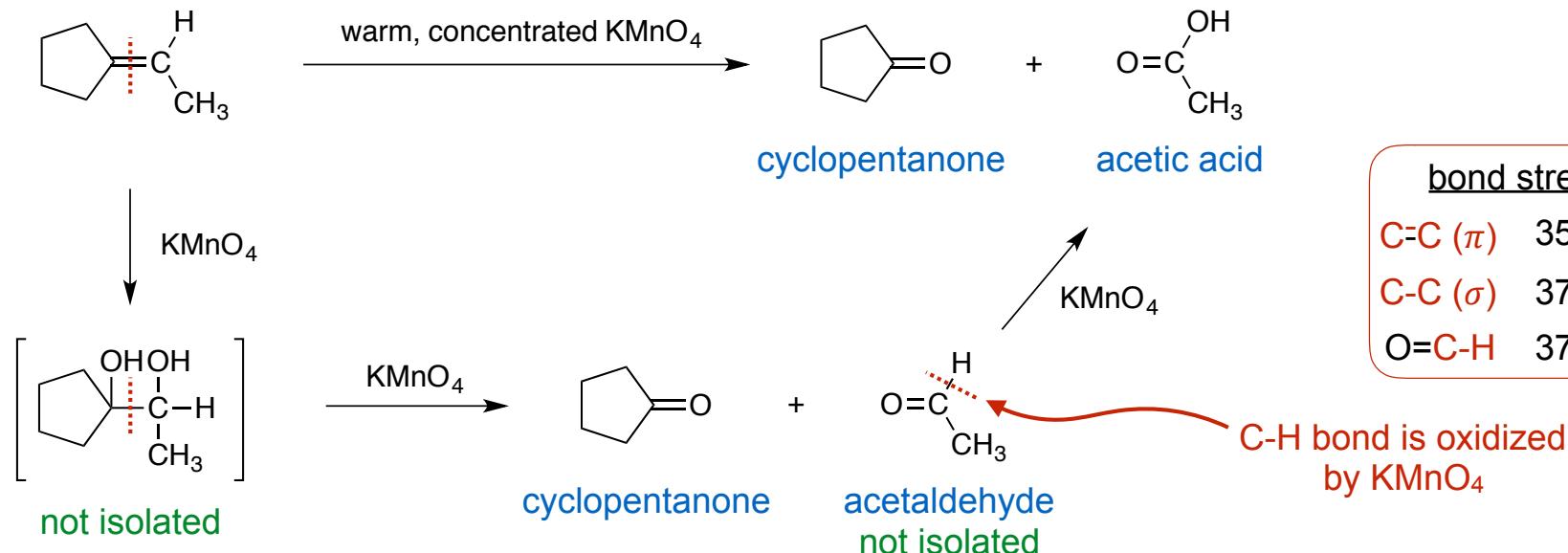


Note: KMnO_4 can be used to cleave only the C=C π bond (i.e., cold, dilute) or both the π and σ bonds (i.e., warm concentrated) depending on the conditions used



Oxidative Cleavage of Alkenes By Permanganate (8-15A)

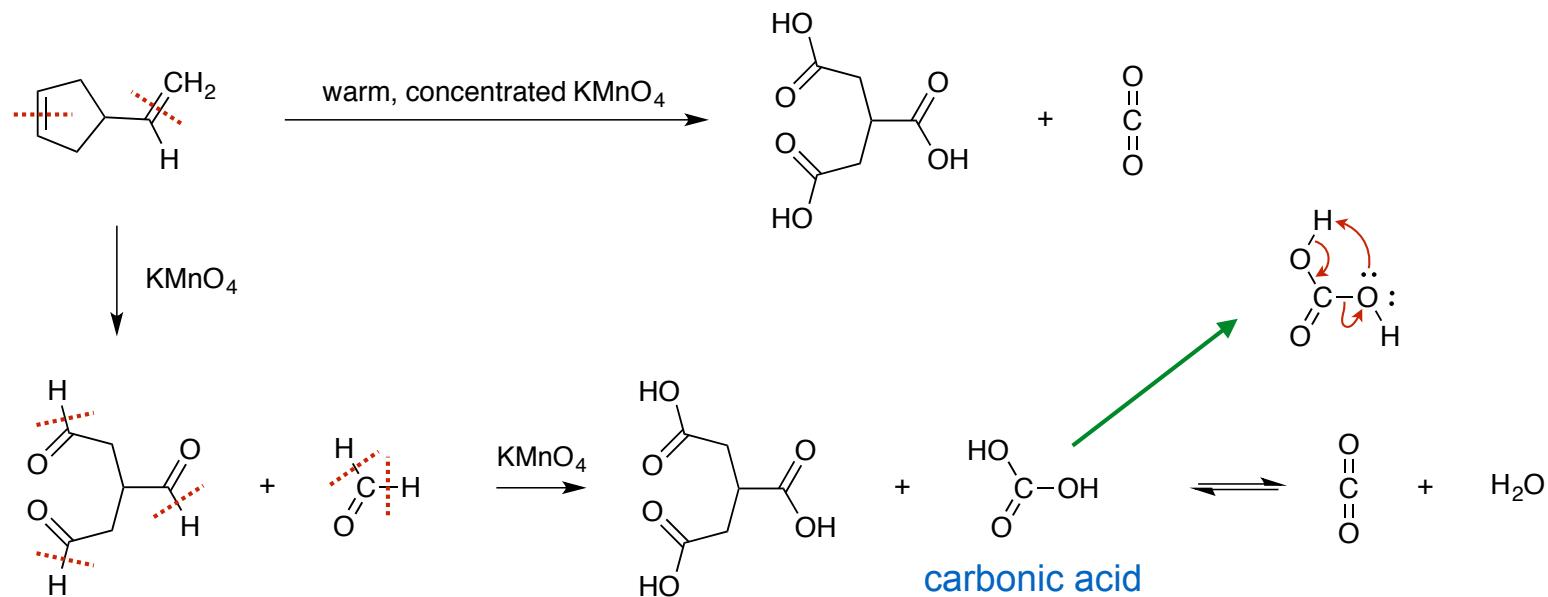
Ex:



bond strengths

$\text{C}=\text{C}$ (π)	350 kJ/mol
$\text{C}-\text{C}$ (σ)	370 kJ/mol
$\text{O}=\text{C}-\text{H}$	375 kJ/mol

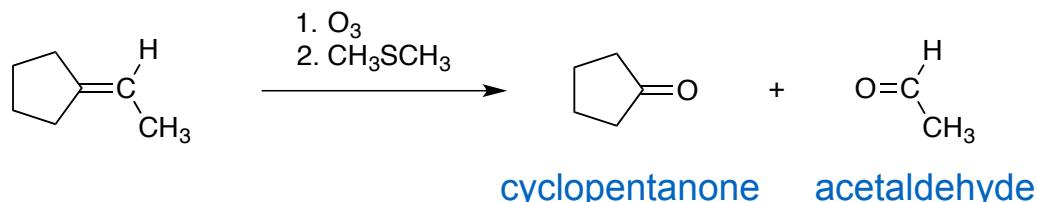
Ex:



Ozonolysis of Alkenes (8-15B)

- Ozone (O_3) is a milder oxidant that cleaves the π and σ bonds of alkenes to form carbonyl ($C=O$) compounds
- Ozone does not cleave C-H bonds, making ozonolysis a good method to prepare aldehydes from alkenes

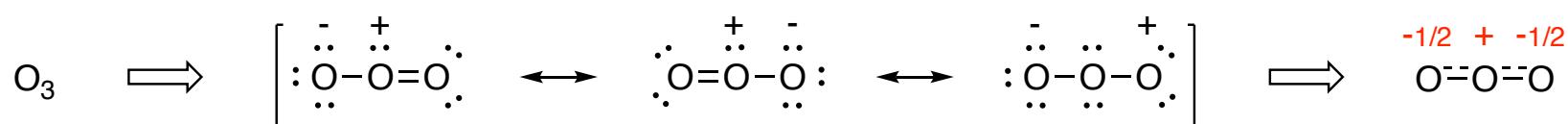
Ex:



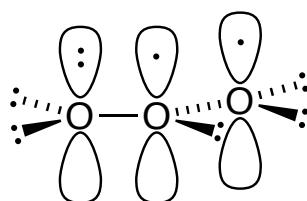
Q: What is ozone and how is it produced?



Q: Structure of ozone?

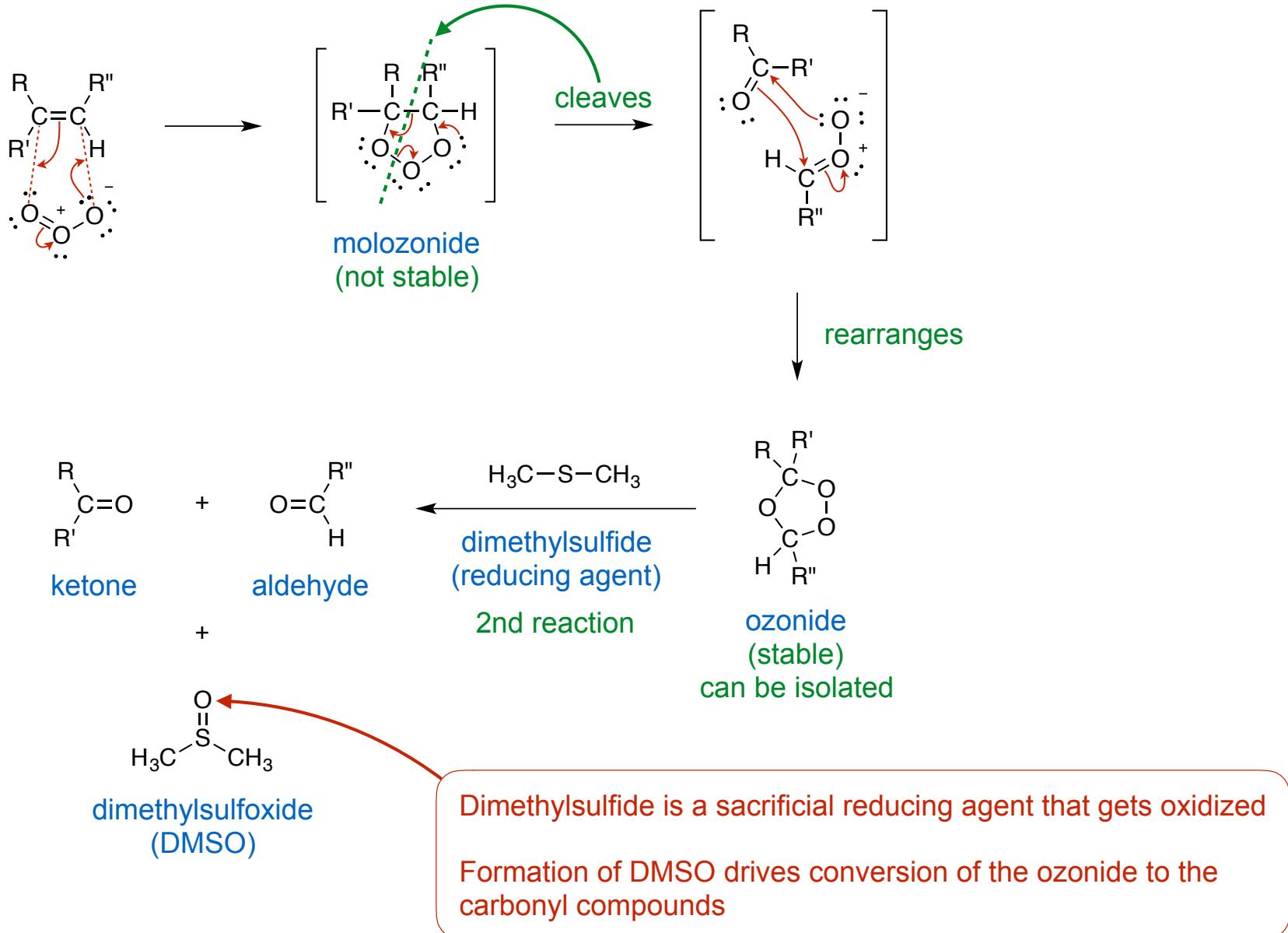


Q: How many p orbitals & π electrons?

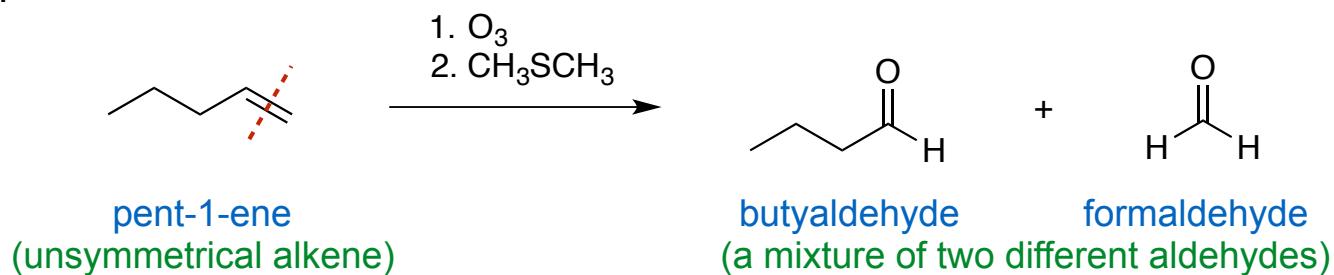


continuous π system
3 p orbitals, 4 π e⁻s

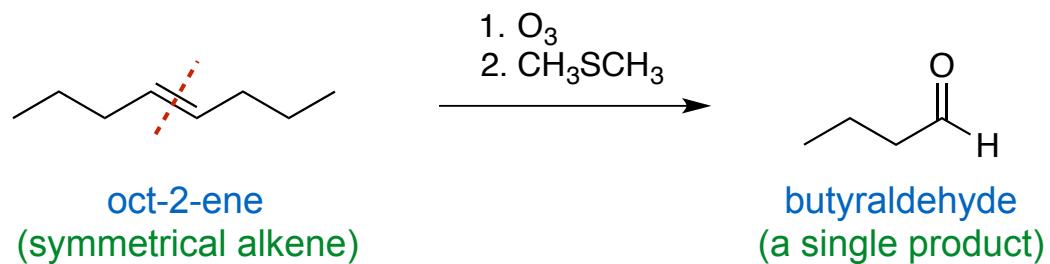
Mechanism of Ozonolysis



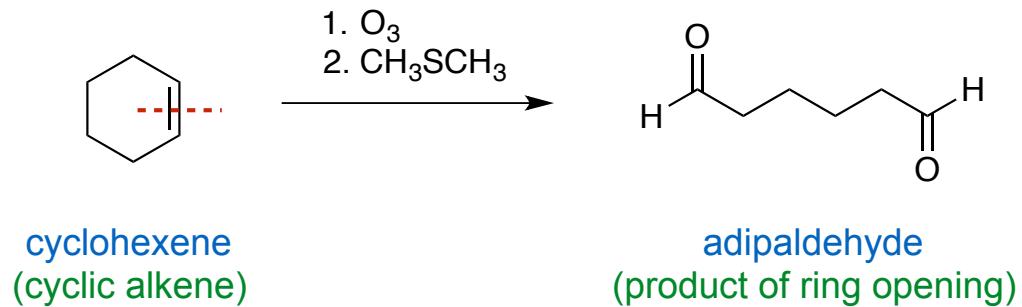
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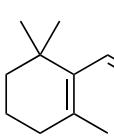
Ex:



Ex:

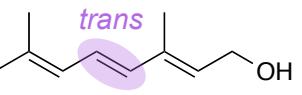
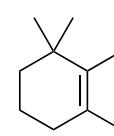


Ex: How humans detect light



β -carotene

oxidation by
enzyme in liver



vitamin A

Top Sources of Beta-Carotene
PLANT-BASED VITAMIN A



CARROTS KALE SPINACH
CANTALOUPE MANGOES

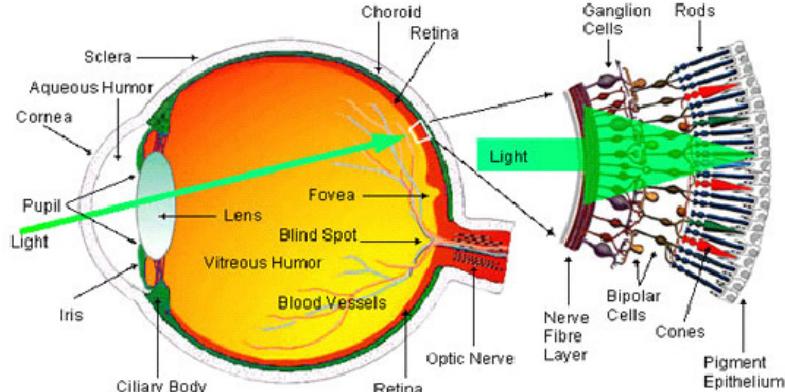
APRICOTS PEACHES

BROCCOLI PUMPKIN ASPARAGUS

PEACHES

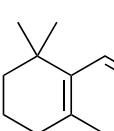


EYE



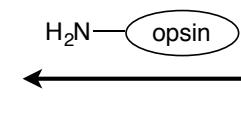
Adapted from WEBVISION <http://webvision.med.utah.edu/>

RETINA



11-cis-retinal

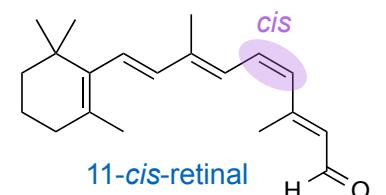
rhodopsin



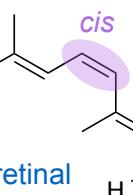
$H_2N - \text{opsin}$

$H - \text{N} = \text{C} - \text{opsin}$

oxidation



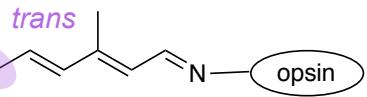
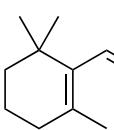
11-cis-retinal



$H - \text{C} = \text{O}$

rod cells in eyes

photon of light
causes cis-trans
isomerization

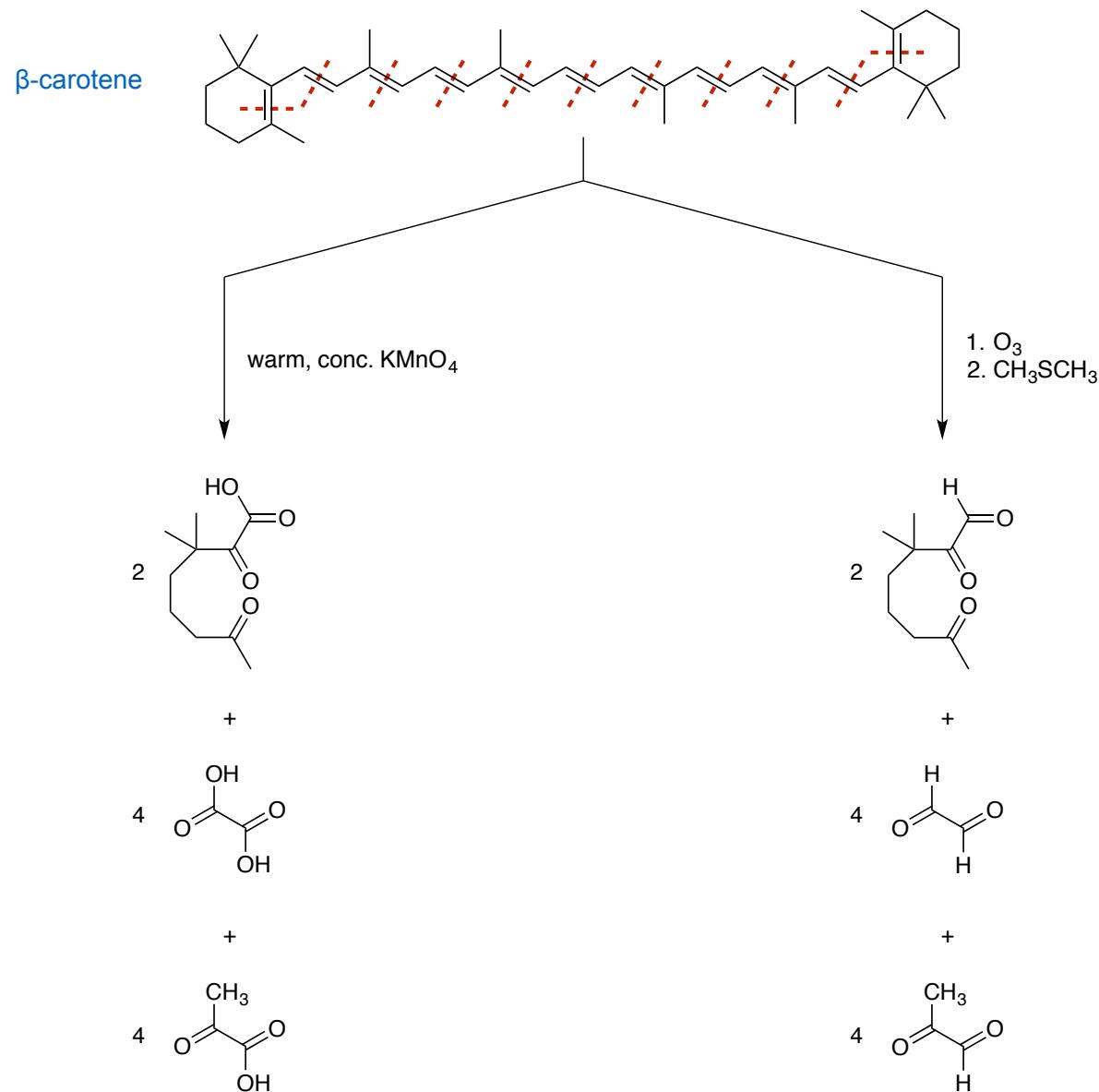


opsin



signal to brain

Q: What products would oxidative cleavage of β -carotene generate?



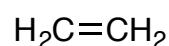
Polymerization of Alkenes (8-16)

Polymer — a large molecule composed of many smaller repeat units (monomers) bonded together

Polymerization — serial addition of monomers to a growing polymer one molecule at a time

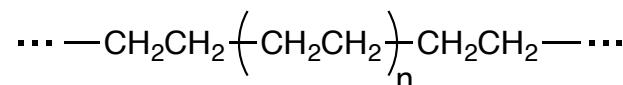
Examples of Common Polymers

monomer

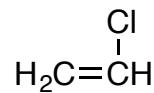


ethylene

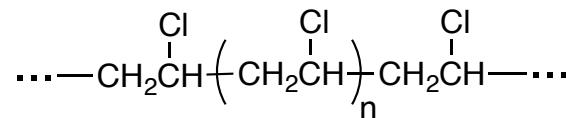
polymer



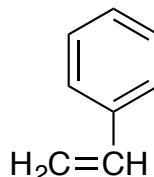
polyethylene



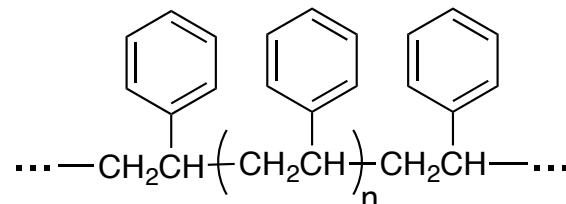
vinyl chloride



polyvinyl chloride (PVC)

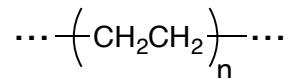


styrene

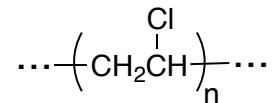
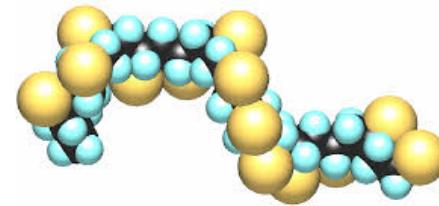


polystyrene

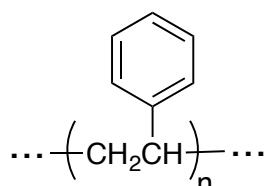
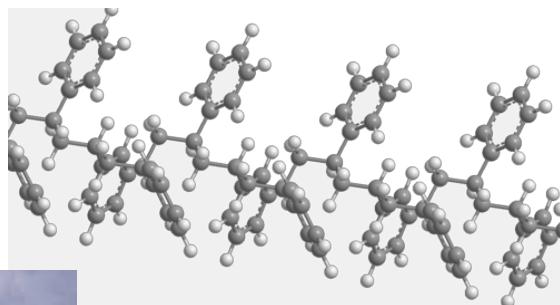
Q: What are polymers used for?



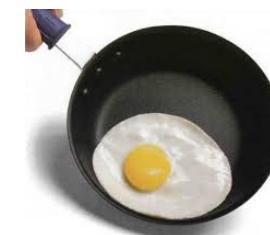
polyethylene



polyvinyl chloride
(PVC)



polystyrene
Styrofoam

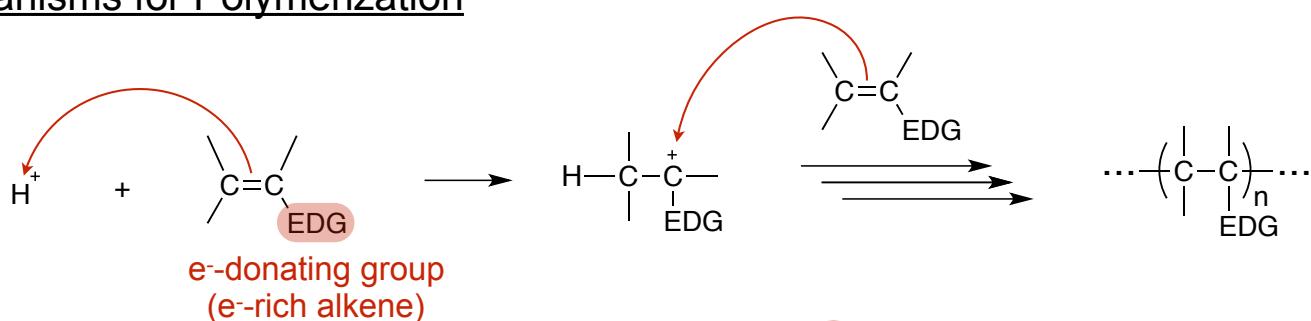


polytetrafluoroethylene
Teflon

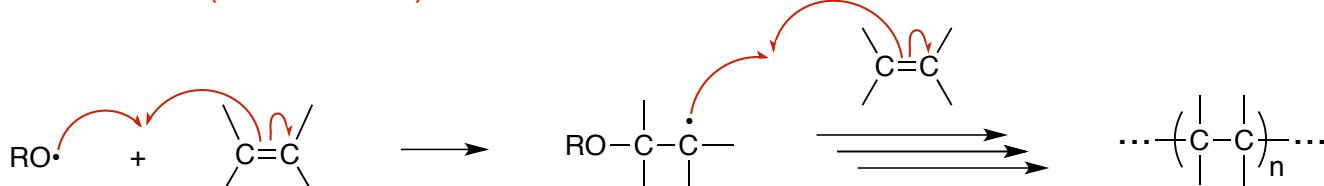


Consider 3 Different Mechanisms for Polymerization

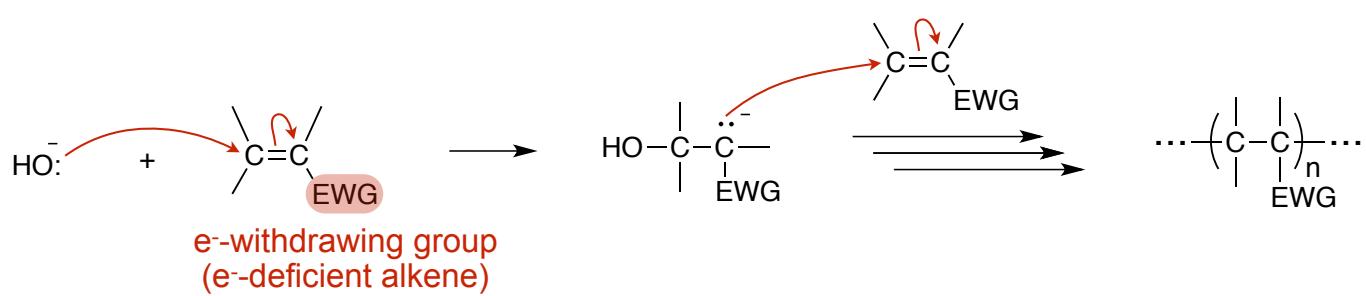
Cationic polymerization



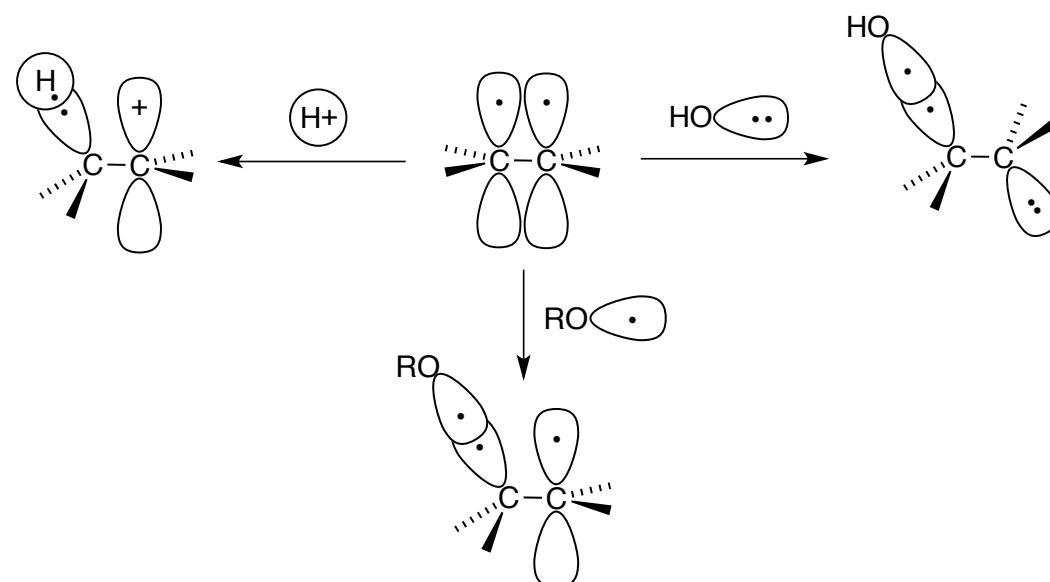
Free-radical polymerization



Anionic polymerization



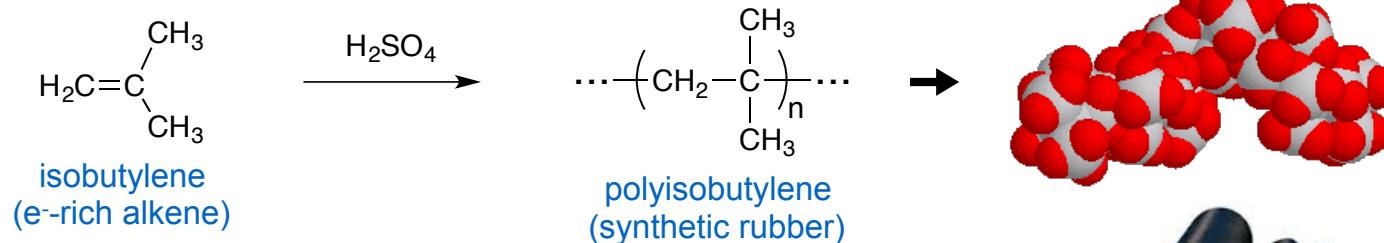
initiation
of
polymerization



Cationic Polymerization (8-16A)

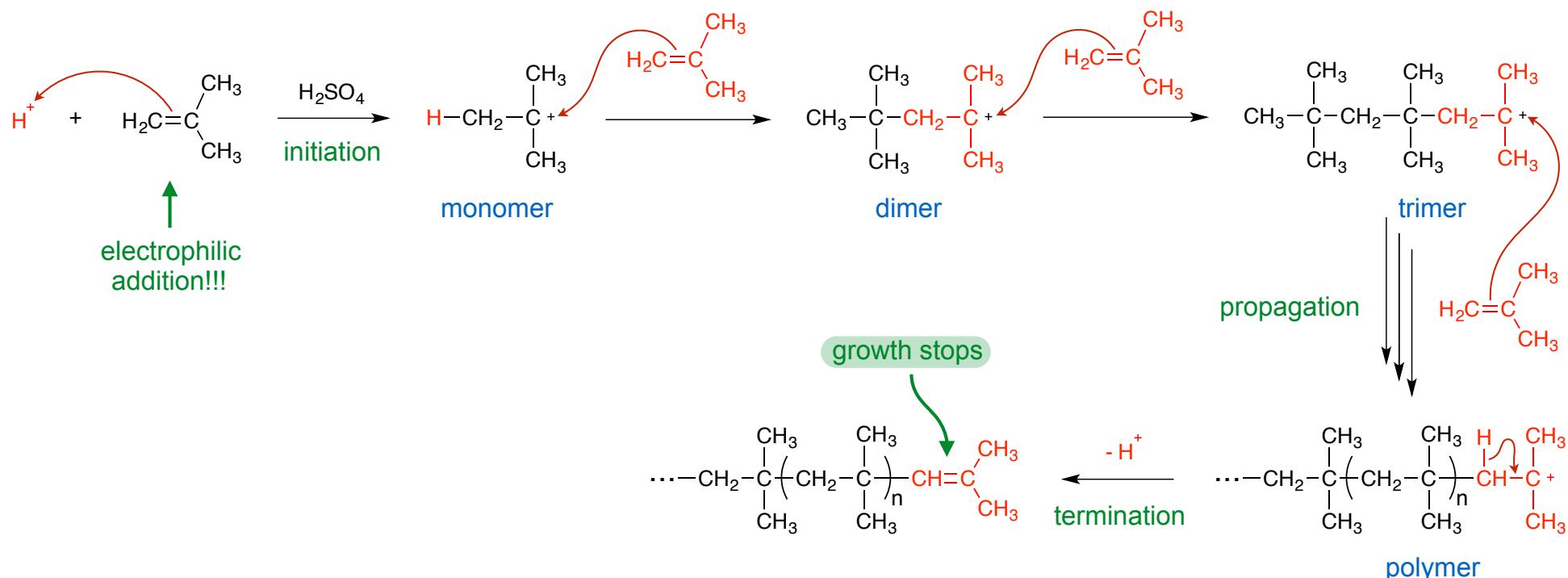
- e⁻-rich alkenes that easily form cations generally undergo cationic polymerization
- e⁻-donating alkyl groups push electron density into the π bond

Ex:



Mechanism

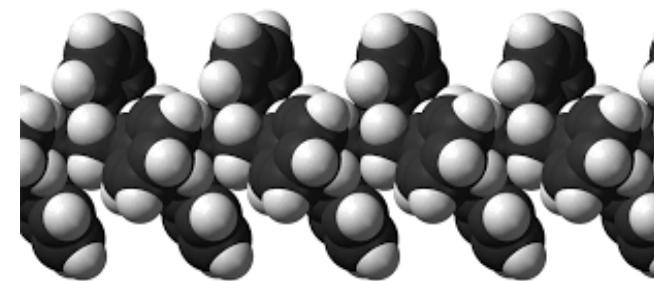
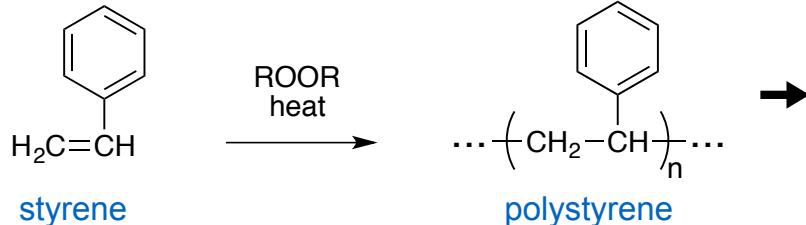
- 3 steps →
1. Initiation — start polymerization reaction
 2. Propagation — growth of polymer chain
 3. Termination — stop growth



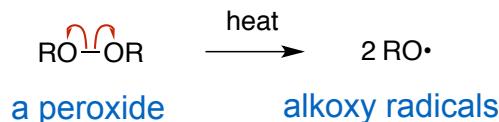
Free-Radical Polymerization (8-16B)

- Most alkenes undergo free-radical polymerization when heated with radical initiators such as peroxides (ROOR)
- Substituents that stabilize radicals promote free-radical polymerization

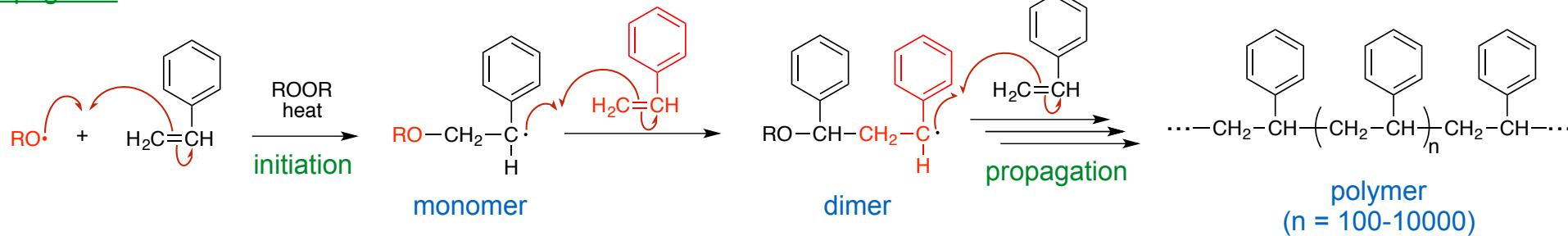
Ex:



Initiation

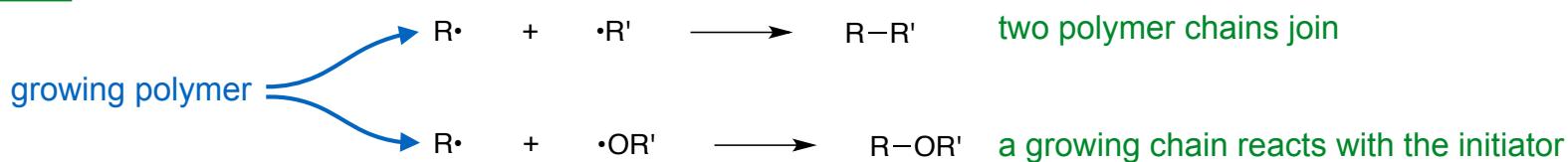


Propagation



Q: How does termination occur to stop growth?

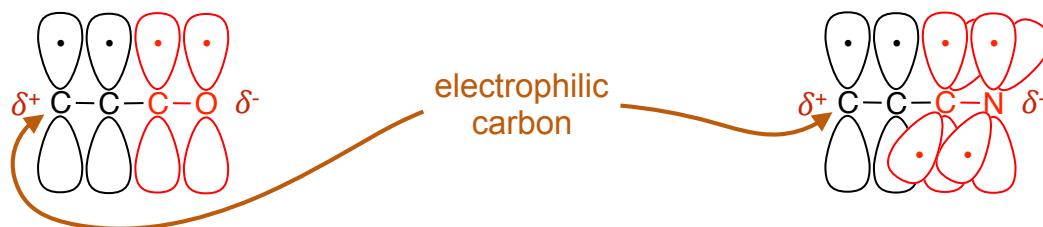
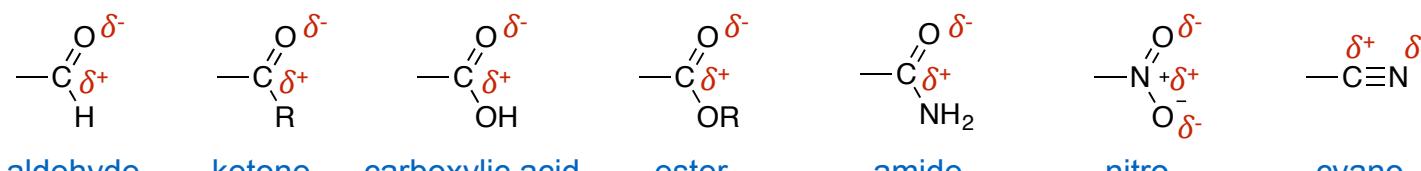
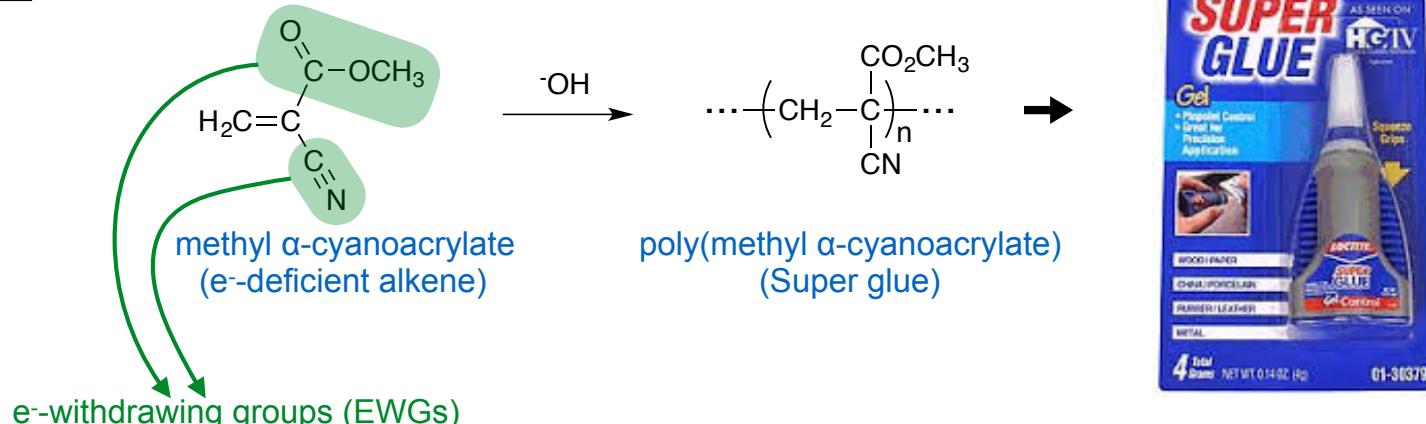
Termination



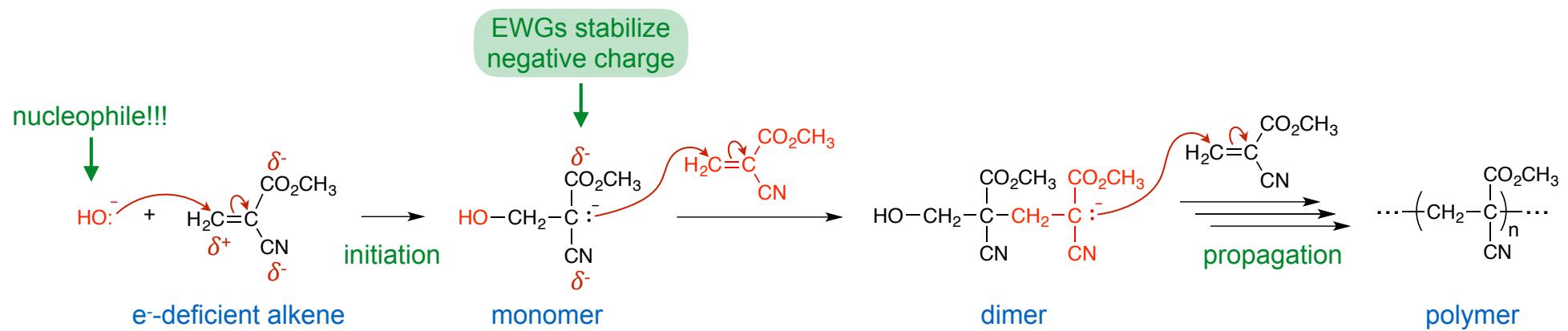
Anionic Polymerization (8-16C)

- Strongly e^- -withdrawing substituents such as carbonyl ($\text{C}=\text{O}$), cyano (CN), and nitro (NO_2) groups pull electron density out of π bonds
- e^- -deficient alkenes that can form stable anions undergo anionic polymerization via nucleophilic addition

Ex:



Q: What affect does pulling electron density out of an alkene have on reactivity?



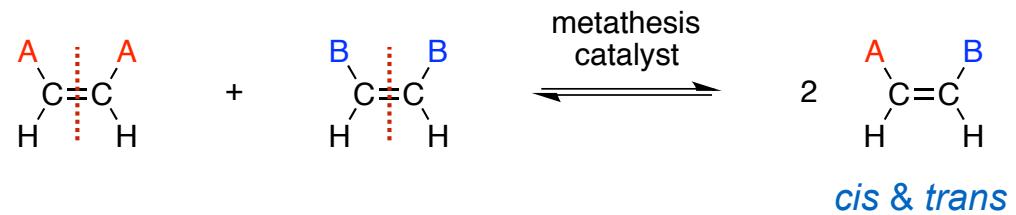
Olefin Metathesis (8-17)

- Good method to prepare new alkenes from existing alkenes by exchanging **alkylidene groups (=CHR)**
- Nobel Prize in chemistry awarded to Chauvin, Grubbs & Schrock in 2005 for developing alkene metathesis

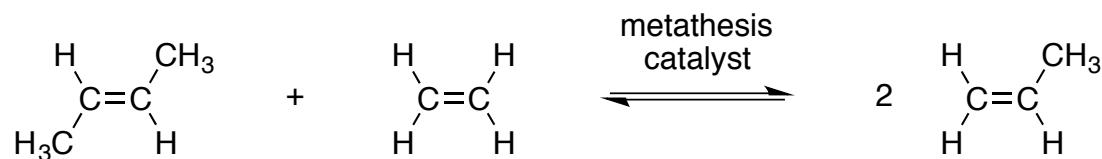


“change position”

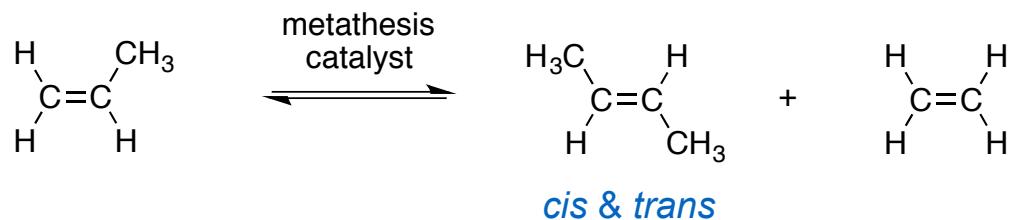
General Reaction



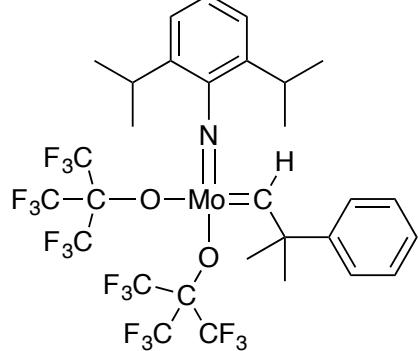
Ex:



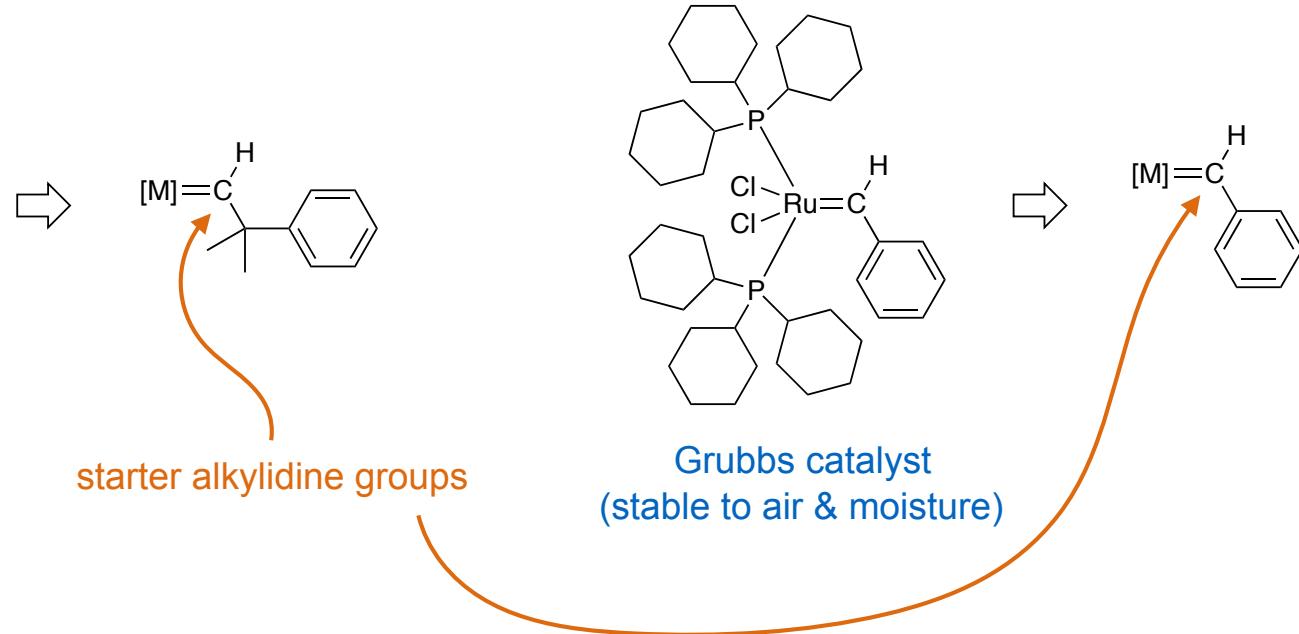
Ex:



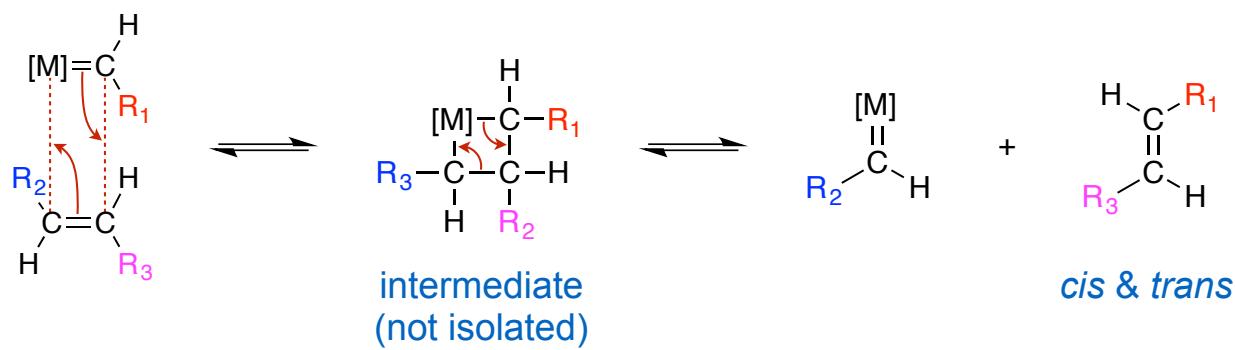
Metathesis Catalysts



Shrock catalyst
(air & moisture sensitive)



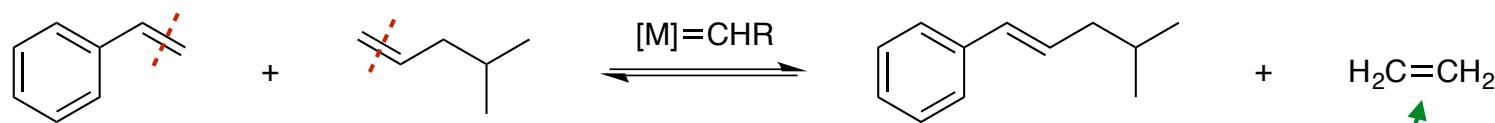
Mechanism of Olefin Metathesis



The catalyst, $[M]=CHR$, scrambles all alkylidene groups in all possible combinations under equilibrium

Useful Metathesis Reactions

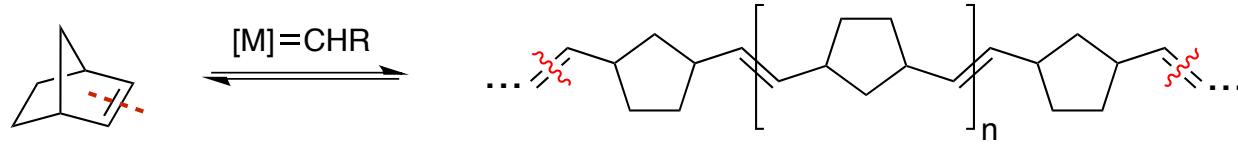
Ex: Cross metathesis



Ex: Ring-closing metathesis



Ex: Ring-opening polymerization



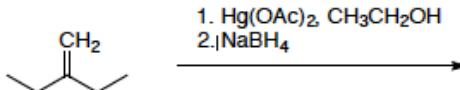
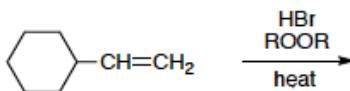
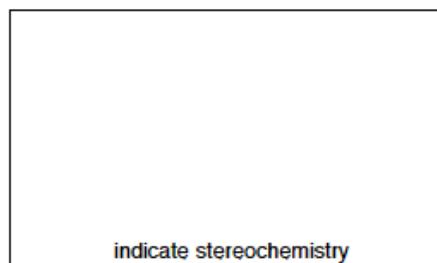
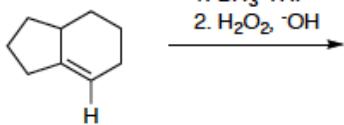
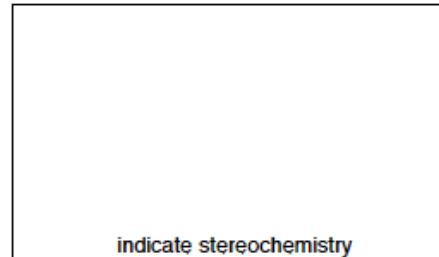
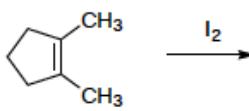
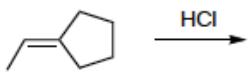
norbornene

Exam 3

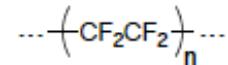
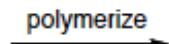
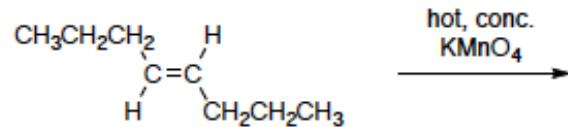
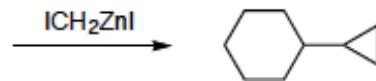
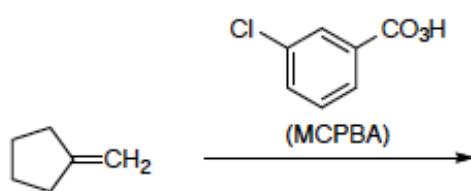
Exam 3 on the last day of class will cover:

- All material in Chapter 7
- All material in Chapter 8

4. Draw the major product for the reactions below in the boxes provided. Be sure to indicate the correct stereochemistry where indicated using dashed lines and wedges. Draw just one enantiomer if a racemic pair forms. [20 pts; 4 pts each]



11. Draw the missing starting material or major product for each of reaction below. [24 pts; 4 pts each]

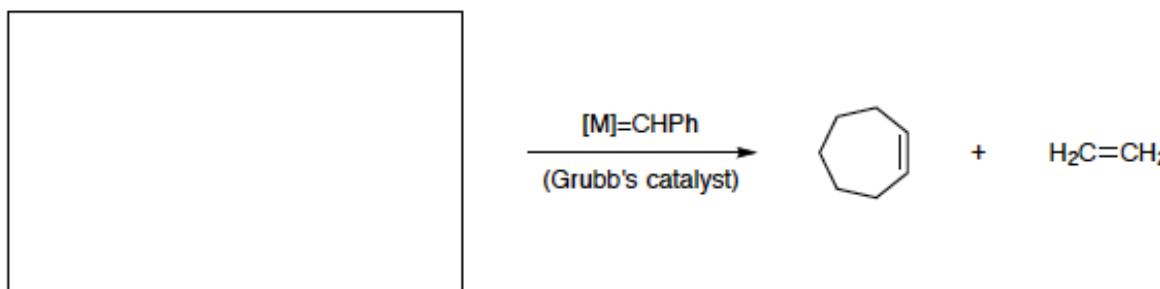


polymer used to make
Teflon & Gore-tex

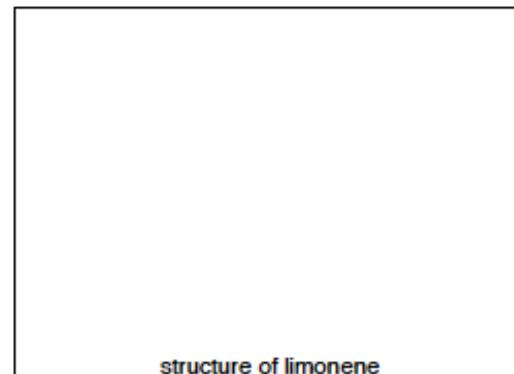
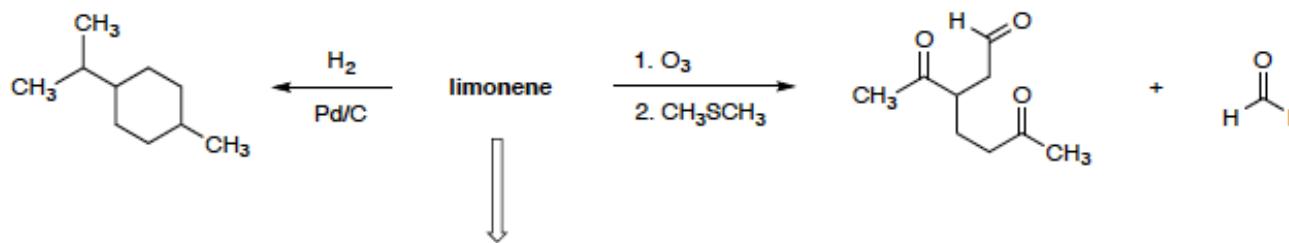
12. The two-step syntheses below each require sequential addition of two different reagents to convert the starting material into the product. Provide the necessary reagents in the correct order by writing the first reagent above and the second reagent below the reaction arrow. [8 pts; 4 pts each]



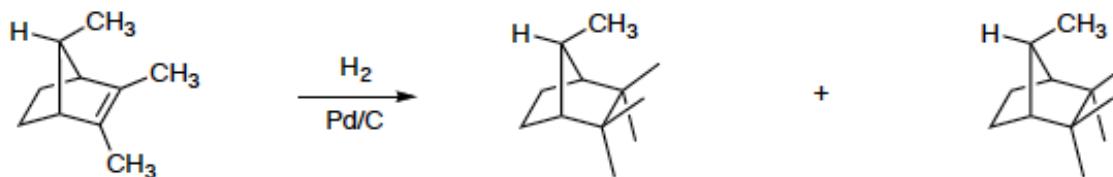
13. Cycloheptene can be synthesized readily via olefin metathesis by reacting an acyclic diene with Grubbs's catalyst as shown. The reaction also forms ethylene gas, which bubbles out of the reaction as it forms. Draw the structure of the diene required to form cycloheptene. [4 pts]



14. Limonene is a hydrocarbon diene ($C_{10}H_{16}$) found in citrus fruit. In the presence of a palladium metal catalyst, limonene reacts with two molar equivalents of H_2 to form 1-isopropyl-4-methylcyclohexane as shown. Ozonolysis of limonene gives the two carbonyl compounds shown. Draw the structure of limonene in the box provided. [4 pts]



6. a. Catalytic hydrogenation of the bicyclic alkene below with hydrogen and palladium on carbon (Pd/C) yields a mixture of two products in a 40:1 ratio. Draw the two products using templates provided. [6 pts; 3 pts each]

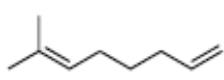
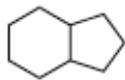
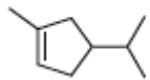


- b. Circle the major product of the reaction in part (a) above. [3 pts]

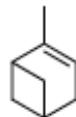
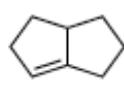
10. a. You find an unlabeled bottle containing an unknown reagent in the lab. Elemental analysis shows the compound is a hydrocarbon with the formula C_9H_{16} . Indicate the number of elements of unsaturation (also called degrees of unsaturation) in the box provided. [3 pts]

number of elements/degrees of unsaturation =

- b. In the presence of excess H_2 gas and a Pd metal catalyst, one mole of the compound in part (a) reacts with one mole of H_2 gas. Which one of the following molecules could be the unknown compound? Circle your answer. [3 pts]



11. Circle the bicyclic compound below that violates Bredt's Rule. [3 pts]



12. Circle the reagent or set of reagents that will react with an alkene via a mechanism that does not involve a cation intermediate. [3 pts]

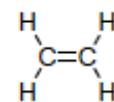
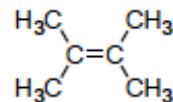
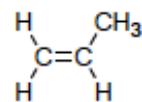
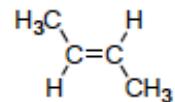
HBr, ROOR

Cl₂

I₂, H₂O

HCl

13. Circle the alkene that will be least reactive in the presence of a hydrogen halide acid such as HBr—that is, the alkene that will undergo electrophilic addition at the slowest rate. [3 pts]



14. Circle the cycloalkene that can form stable *cis* and *trans* isomers. [3 pts]

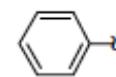
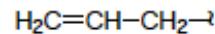
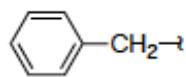
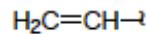
cyclohexene

cyclobutene

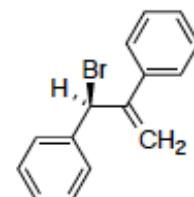
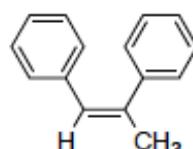
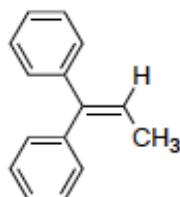
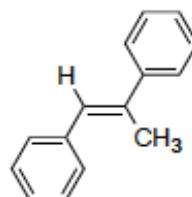
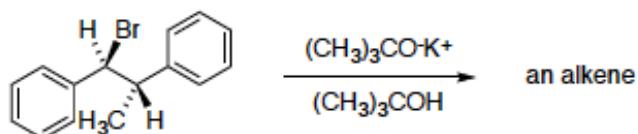
cyclodecene

cycloheptene

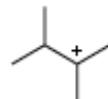
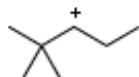
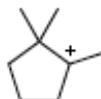
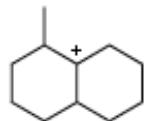
15. Circle the substituent that is an allyl group. [3 pts]



7. In the E2 reaction below, elimination of HBr by potassium *tert*-butoxide occurs predominantly from the anti periplanar conformation of the alkyl halide. Circle the structure of the alkene that forms as the major product. [3 pts]



12. Circle the carbocation that is most likely to undergo rearrangement via a methyl (:CH_3) shift. [3 pts]



19. Circle the alkene that will release the *greatest* amount of heat per mole when subjected to catalytic hydrogenation (i.e., H_2 , Pd metal catalyst) to form isopropylcyclohexane. [3 pts]

