**CHEM 221 section 01**

**LECTURE #14** Thurs., Oct.20, 2005

**Midterm exam: Tues.Oct.25 during class**
**Ch.1, 7.2-7.5, 7.10, 2, 3.1-3.5**

# ASSIGNED READINGS:

**TODAY'S CLASS:** Sections 4.7-4.10

**NEXT LECTURE:** finish Ch.4, start Ch.5

http://artsandscience.concordia.ca/facstaff/P-R/rogers

## 4.7 Addition of halogens: "halogenation"

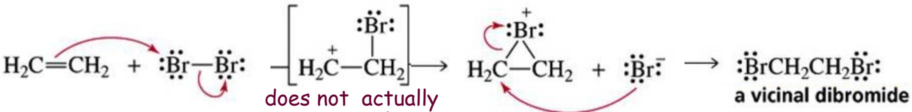
NET RESULT: Add X-X across the C=C bond ⇨ vicinal dihalide product

MECHANISM: polarizable X–X acts as $\delta^+$X–X$\delta^-$

1.) C=C bond attacks "X+" ⇨ cyclic *halonium ion* intermediate

2.) nucleophile ($X^-$) attacks halonium ion

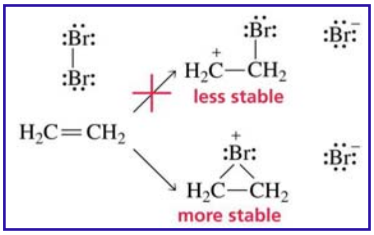
⇨ X ends up bonded to the more highly substituted C



does not actually exist ⇨ Br shares lone pair with C

Bromonium ion reacts with first Nu it encounters

"vicinal"= on adjacent C's



- Imagine it as if C+ forms 1st *(but not true!)* & then C+ shares adjacent X's lone pair

⇨ Result: no atoms have open valence! much more stable than a C+!

Thus: NO carbocation intermediate
∴ rearrangements do NOT occur.

## Some details about halogenation of alkenes

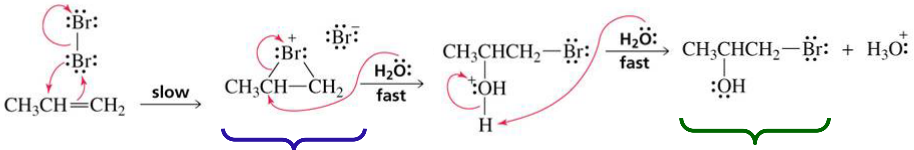
- **Can we use all the halogens to prepare vicinal dihalides from alkenes?**
  **NO:** $Cl_2$ & $Br_2$ are the only synthetically useful halogens
  $F_2$ is too reactive (explosive reaction → too dangerous)
  $I_2$ rxn thermo. unfavourable (diiodide products unstable)

- **Halonium ions are reactive intermediates** (even though more stable than C+)
  react with whichever Nu they encounter first
  THUS: be sure Nu of interest is most concentrated Nu present

THIS AFFECTS OUR CHOICE OF SOLVENT:

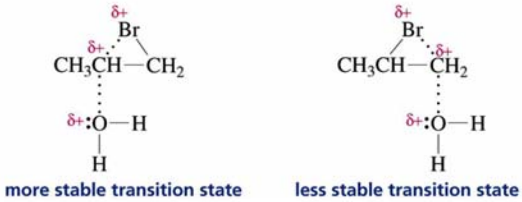
- **If want a vicinal dihalide:** use non-nucleophilic solvent *e.g.,* $CH_2Cl_2$
  only Nu the halonium ion sees is the $X^-$ anion
- **If we use a nucleophilic solvent:** *e.g.,* water
  solvent will be the nucleophile present in highest concentration!
  → solvent reacts with the halonium ion intermediate
  → **useful route to vicinally heterodisubstituted compounds**,
  such as "halohydrins" (next slide)

## Addition of Halogens in the Presence of Water: "Halohydrin" formation (cmpd with vicinal X & OH)



**Why does the Nu attack the more substituted C?**

**Regiochemistry:**
**the OH ends up on the more highly substituted C**
(as usual: electrophile bonds to the C with more H's on it)

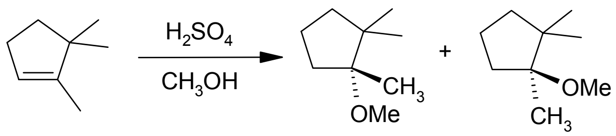


Resembles the more stable carbocation
*(but true C+ isn't formed...)*

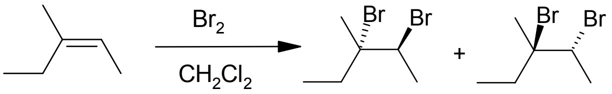
## What products would these reaction conditions yield?

**Ask yourself:**

1) **What is the electrophile?** → *π-bond attacks E's δ⁺ atom… …& E ends up on least substituted C*
2) **Does a carbocation result?** → *If yes: form most stable cation possible*
   - *1st: via regiochemistry of E addition*
   - *2nd: via rearrangement(s)*
3) **What is the nucleophile?** → *Nu reacts with electrophilic carbon*
   (of highest concentration) *(be sure to check if solvent is nucleophilic!)*



- E = ? $H^+$ from $H_2SO_4$
- C+ ? yes
  on 3° $sp^2$ C
  (no rearrangement)
- Nu = ? $CH_3OH$



- E = ? "$Br^{+}$" from $Br_2$
- C+ ? No
  bromonium ion
  (anti addition!)
- Nu = ? $Br^-$
  ($CH_2Cl_2$ not a Nu)

---

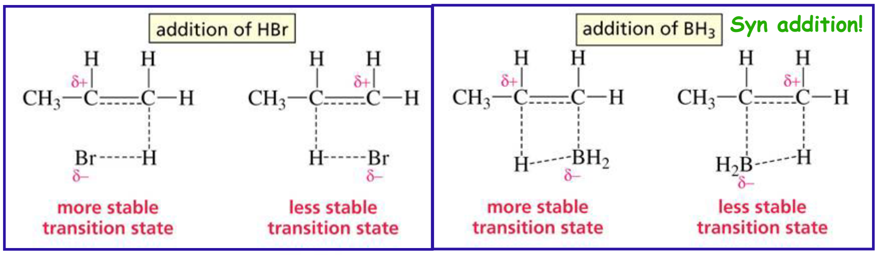
## 4.9 Addition of borane: "hydroboration-oxidation"
### anti-Markovnikov addition of water

**NET RESULT:** Add H-OH across the C=C bond ⇨ anti-Markovnikov!
Follows a different mechanism: different electrophile!

$$CH_3CH{=}CH_2 \xrightarrow[2.\ HO^-,\ H_2O_2,\ H_2O]{1.\ BH_3\ /\ THF} CH_3CH_2CH_2OH$$

propene — 1-propanol

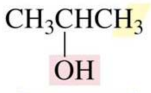
**Anti-Markovnikov addition**



**Syn addition!**

$$CH_3CH{=}CH_2 \xrightarrow[H_2O]{H_2SO_4}$$

propene



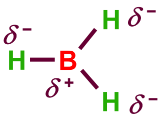
$CH_3CH(OH)CH_3$

2-propanol

**Markovnikov addition:**
H goes where more H's are

## Mechanism of hydroboration: *B is the electrophile*

Boron has lower electronegativity than hydrogen…BUT more importantly: in trivalent boron compounds: B has open valence shell!

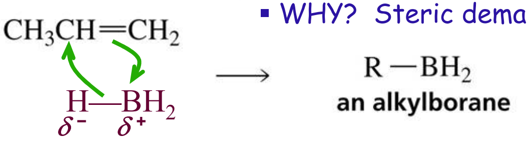


THUS: the BORON is the electrophilic part of $BH_3$
*highly reactive towards lone pairs & π-electrons!!*

**MECHANISM OF HYDROBORATION:**

1.) C=C bond attacks boron (δ⁺) at same time as δ⁻ H attacks $sp^2$ C
- a concerted (1-step) process
- thus: H & B on same side of C=C ⇨ syn addition

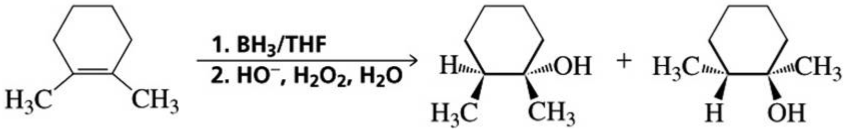
Follows usual rule: electrophile adds to the less highly-sub'd C
- WHY? Steric demand of borane group!



2.) & subsequent steps: oxidation by $H_2O_2$, $OH^-$, $H_2O$
removes boron group & replaces with OH
(you are not responsible for the details here)

## Stereochemistry of Hydroboration–Oxidation

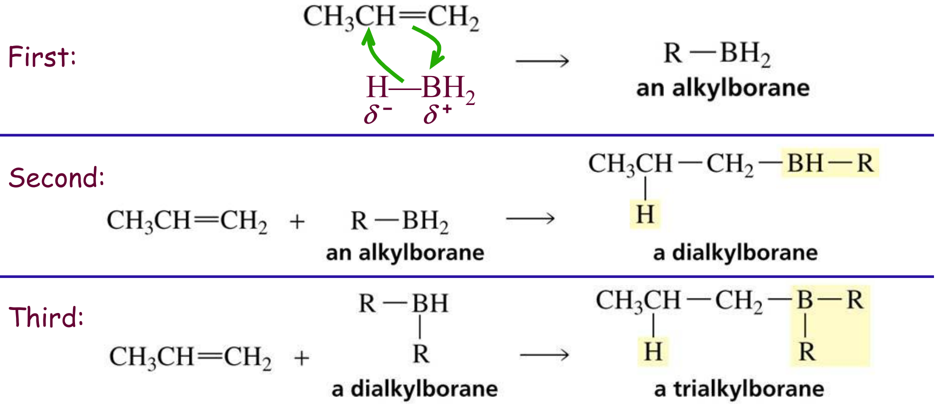
*i.e., relative* orientation of groups in the products (see more in Ch.5)



- Always syn addition
- In 1st step: H-B can add to either side of C=C initially, so get both possible syn products
- subsequent steps: do not change the orientation of the groups thus: stereochemistry dictated by 1st step

# MORE DETAILS ABOUT THE MECHANISM:
## 1st steps: formation of alkyl boranes

In hydroboration: 1 $BH_3$ actually reacts with 3 alkene molecules



First: $CH_3CH{=}CH_2$ + $\overset{\delta^-}{H}{-}\overset{\delta^+}{BH_2}$ $\longrightarrow$ $R{-}BH_2$ **an alkylborane**

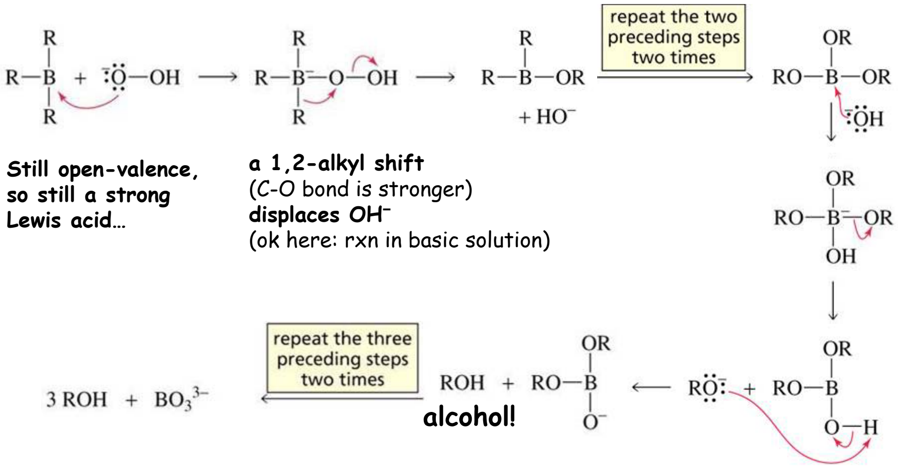
Second: $CH_3CH{=}CH_2$ + $R{-}BH_2$ (**an alkylborane**) $\longrightarrow$ $CH_3CH(H){-}CH_2{-}BH{-}R$ **a dialkylborane**

Third: $CH_3CH{=}CH_2$ + $R{-}BH{-}R$ (**a dialkylborane**) $\longrightarrow$ $CH_3CH(H){-}CH_2{-}B(R){-}R$ **a trialkylborane**

You are not responsible for reproducing this…
…but seeing the full mechanism will help you understand the reaction

# & then: subsequent oxidation steps (↑ bonds to O):
## OH replaces boron to yield alcohol

**You are not responsible for reproducing this…**
**…but it might help you understand how we end up with an alcohol!**



$R_3B$ + $\ddot{O}H{-}OH$ $\longrightarrow$ $R_3B^{-}{-}O{-}OH$ $\longrightarrow$ $R_2B{-}OR$ + $HO^-$ $\xrightarrow{\text{repeat the two preceding steps two times}}$ $(RO)_3B$ + $:\ddot{O}H$ $\longrightarrow$ $(RO)_3B^{-}{-}OH$ $\longrightarrow$ $R\ddot{O}:^-$ + $(RO)_2B{-}O{-}H$ $\longrightarrow$ ROH + $(RO)_2B{-}O^-$ $\xrightarrow{\text{repeat the three preceding steps two times}}$ 3 ROH + $BO_3^{3-}$

**Still open-valence, so still a strong Lewis acid…**

**a 1,2-alkyl shift**
(C-O bond is stronger)
**displaces OH⁻**
(ok here: rxn in basic solution)

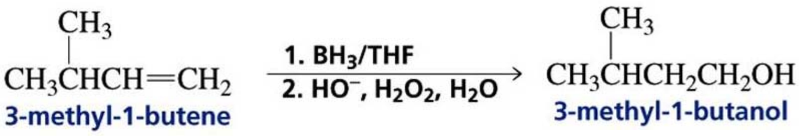
**alcohol!**

## Key synthetically useful features of hydroboration:

1.) adds H-OH with anti-Markovnikov regiochemistry

2.) avoids rearrangements of molecule (no carbocation int.)

→ predictable, clean regiochemistry (good product control!)



$$CH_3\overset{\overset{CH_3}{|}}{C}HCH{=}CH_2 \xrightarrow[\text{2. }HO^-,\ H_2O_2,\ H_2O]{\text{1. }BH_3/THF} CH_3\overset{\overset{CH_3}{|}}{C}HCH_2CH_2OH$$

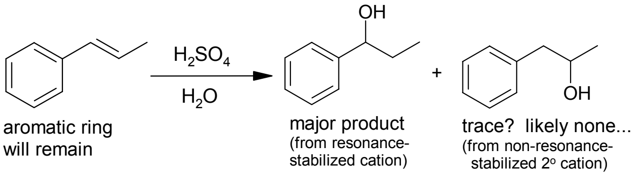
**3-methyl-1-butene** → **3-methyl-1-butanol**

Acid-catalyzed hydration
would involve 2° carbocation
⇨ would rearrange

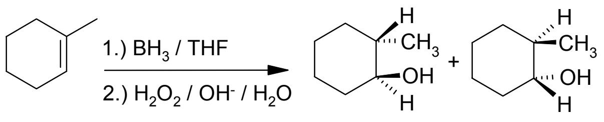
THUS:
major product would be
2-methyl-2-butanol
…3-methyl-2-butanol
as a minor product

Hydroboration product
⇨ no rearrangement
⇨ anti-Markovnikov
⇨ syn addition of H & OH
*(syn not noticeable here since rxn did not generate stereochemistry)*

## What products would these reaction conditions yield?

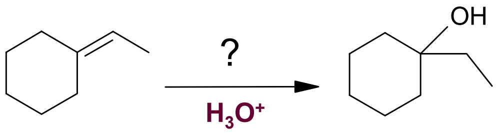


- E = ? $H^+$ from $H_2SO_4$
- C+ ? yes
  on 2° $sp^2$ C
  (benzylic preferred!)
- Nu = ? $H_2O$



- E = ? B from $BH_3$
- C+ ? No - hydroboration
  syn addition of $H_2O$
  anti-Markovnikov
- Nu = ? In 1st step: $H^-$

## What conditions would we use to prepare this compound?



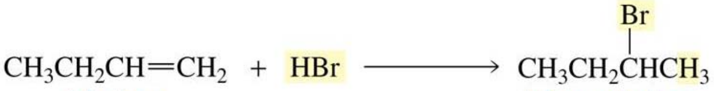
Specific conditions?
*e.g.,* $H_2SO_4$ / $H_2O$

- no rearrangement
(1st C+ already 3°)

- Addition of... ?
  H-OH (hydration)
- Regiochemistry?
  Markovnikov
- Conditions?
  Acid-catalyzed...

## 4.10 Addition of Radicals to Alkenes: Anti-Markovnikov addition of H-Br

So far: Hydrohalogenation = route to alkyl halides



$$CH_3CH_2CH{=}CH_2 + HBr \longrightarrow CH_3CH_2\overset{\displaystyle Br}{\overset{|}{C}}HCH_3$$

**1-butene** **2-bromobutane**

Markovnikov addition product

**RADICAL HYDROBROMINATION: opposite regiochemistry**

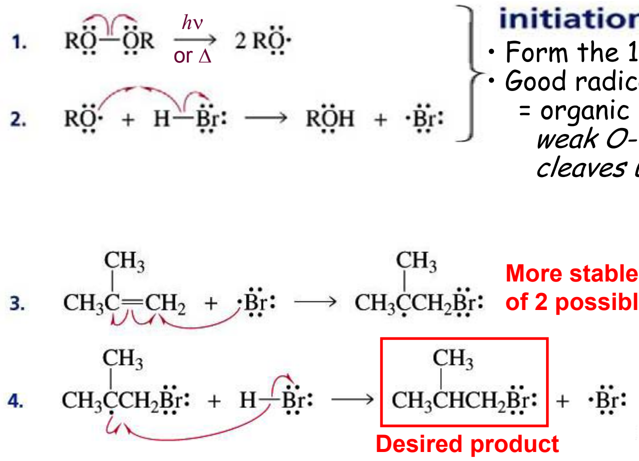
$$CH_3CH_2CH{=}CH_2 + HBr \xrightarrow[h\nu \text{ or } \Delta]{\text{peroxide}} CH_3CH_2CH_2CH_2Br$$

**1-butene** **1-bromobutane**

Anti-Markovnikov addition!

Choose reaction conditions that yield desired regiochemistry !
a) HBr at RT in the dark ⇨ Markovnikov addition
b) HBr with heat *or* light ⇨ anti-Markovnikov addition
(+peroxide)

# Mechanism: Addition of Radicals to Alkenes



**initiation steps**

- Form the 1st reactant radicals
- Good radical initiators
  = organic peroxides (ROOR)
  *weak O-O bond homolytically cleaves under heat or light*

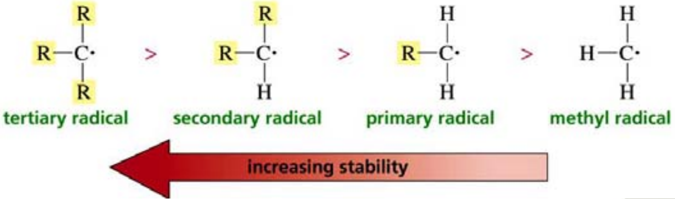
**More stable of 2 possible**

**Desired product**

**propagation steps**

Form radical intermediates that propagate radical chain rxn

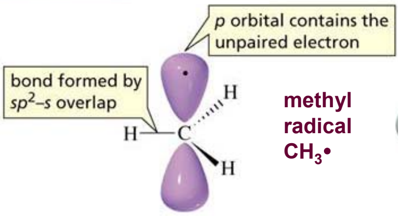
## Relative Stabilities of Alkyl Radicals:
## similar trend as for carbocations, for same reason



## Hydrobromination with peroxide:

<u>via a radical intermediate!</u>

- stability: 3° > 2° > 1° >> methyl
- C• centre is $sp^2$-hybridized (like C+)

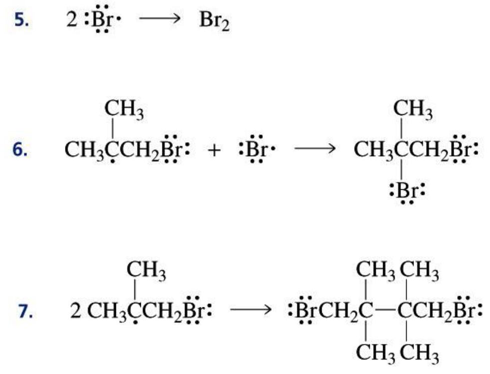


**methyl radical $CH_3$•**

<u>IMPLICATIONS:</u>

1. regiochemistry:
   radical centre (& then H) will be on the more substituted C
2. stereochemistry: racemization (if chiral) → *see this in Ch.5*

## …Mechanism: Addition of Radicals to Alkenes



5. $2\,:\ddot{\mathrm{Br}}\cdot \longrightarrow \mathrm{Br_2}$

6. $\mathrm{CH_3\overset{CH_3}{C}CH_2\ddot{Br}:} + :\ddot{\mathrm{Br}}\cdot \longrightarrow \mathrm{CH_3\underset{:Br:}{\overset{CH_3}{C}}CH_2\ddot{Br}:}$

7. $2\,\mathrm{CH_3\overset{CH_3}{C}CH_2\ddot{Br}:} \longrightarrow \mathrm{:\ddot{Br}CH_2\underset{CH_3}{\overset{CH_3}{C}}-\underset{CH_3}{\overset{CH_3}{C}}CH_2\ddot{Br}:}$

**Side product: dihalide**

**Side product: dimer** (*i.e.*, 2 units coupled)

**termination steps**

Radical-coupling rxns
→ do not generate
new radicals

### Summary: Radical hydrobromination

- **anti-Markovnikov HBr addition** (via more stable radical intermediate)
- **use dilute solution** (to minimize dimerization of radical intermediates)
- **use an inert solvent** (usually $CCl_4$ or benzene; never a protic solvent!)

And after Ch.5 (ignore for now), you'll see…

- **racemized alkyl halide product** (if chiral centre created…)

### Use of peroxide only changes the regiochemistry of HBr addition, *not* HCl or HI addition

A radical process will occur instead of the non-radical mechanism ONLY if *both* of the propagation steps are exothermic:

- propagation steps: (a) are sometimes exothermic, but not always
  (b) use radicals AND produce radicals
- termination steps (consuming only radicals) are always exothermic & fast
  - ⇨ they compete with desired propagation steps & can use up the radicals before endothermic propagation occurs

$\mathrm{Cl}\cdot + \mathrm{CH_2{=}CH_2} \longrightarrow \mathrm{ClCH_2\dot{C}H_2}$ $\Delta H^\circ = 63 - 82 = -19$ kcal/mol (or $-79$ kJ/mol) ←

$\mathrm{ClCH_2\dot{C}H_2} + \mathrm{HCl} \longrightarrow \mathrm{ClCH_2CH_3} + \mathrm{Cl}\cdot$ $\Delta H^\circ = 103 - 101 = +2$ kcal/mol (or $+8$ kJ/mol)

$\mathrm{Br}\cdot + \mathrm{CH_2{=}CH_2} \longrightarrow \mathrm{BrCH_2\dot{C}H_2}$ $\Delta H^\circ = 63 - 69 = -6$ kcal/mol (or $-25$ kJ/mol) ←

$\mathrm{BrCH_2\dot{C}H_2} + \mathrm{HBr} \longrightarrow \mathrm{BrCH_2CH_3} + \mathrm{Br}\cdot$ $\Delta H^\circ = 87 - 101 = -14$ kcal/mol (or $-59$ kJ/mol) ←

$\mathrm{I}\cdot + \mathrm{CH_2{=}CH_2} \longrightarrow \mathrm{ICH_2\dot{C}H_2}$ $\Delta H^\circ = 63 - 55 = +8$ kcal/mol (or $+33$ kJ/mol)

$\mathrm{ICH_2\dot{C}H_2} + \mathrm{HI} \longrightarrow \mathrm{ICH_2CH_3} + \mathrm{I}\cdot$ $\Delta H^\circ = 71 - 101 = -30$ kcal/mol (or $-126$ kJ/mol) ←

# ASSIGNED READINGS

## BEFORE NEXT LECTURE:

| | |
|---|---|
| **Read:** | rest of Ch.4 |
| **Practice:** | writing mechanisms & predicting products |