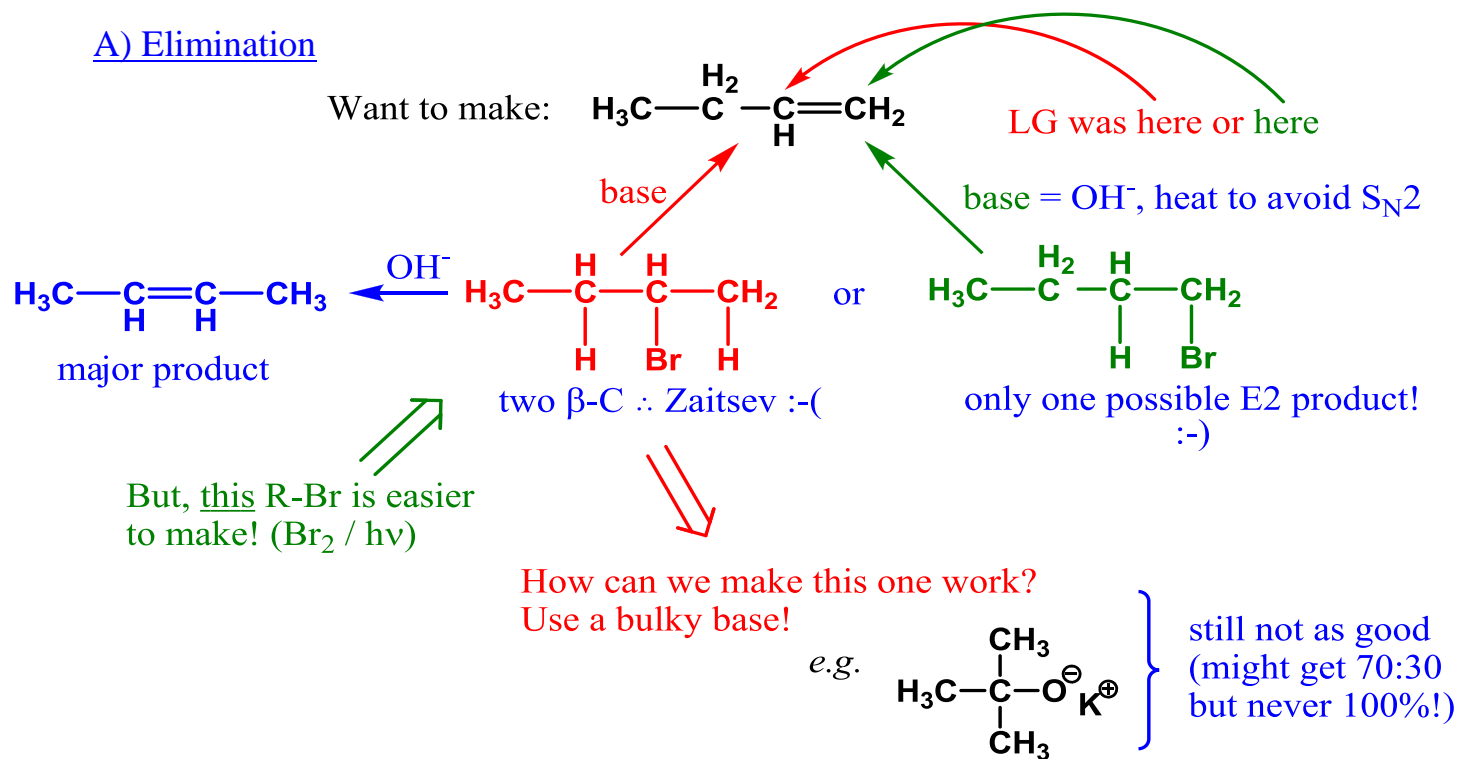Overheads: - Outline   Handout: Sub/Elim

Feedback Quiz #2
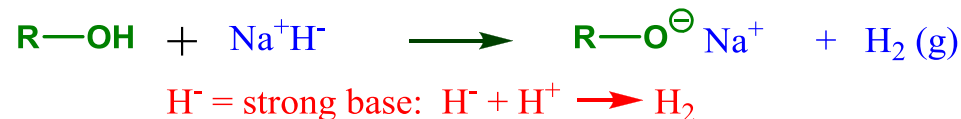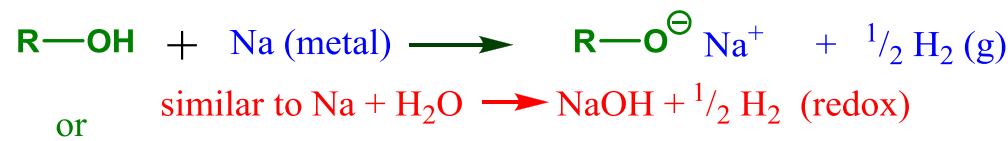
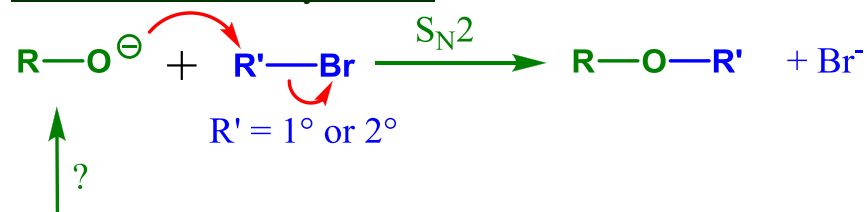Recap Wednesday:

Competition Between the 4 Reactions:

1) Is a C^+ likely formed?
- 1° R-LG ⇨ NO
- 3° ⇨ YES (except strong base = E2)
- 2° / allylic ⇨   strong base/Nu⁻, aprotic = NO
            weak base/Nu⁻, protic = YES

2) Substitution or Elimination? (Elim needs β-H)
    a)   If C+ S_N1 & E1 compete
    b)   If no C^+ S_N2 & E2 compete
       - E2 needs strong base (OH⁻ or better)

Also consider sterics:

$CH_3O^{\ominus}$ *vs*
E2 or S_N2

E2 only: bulky bases
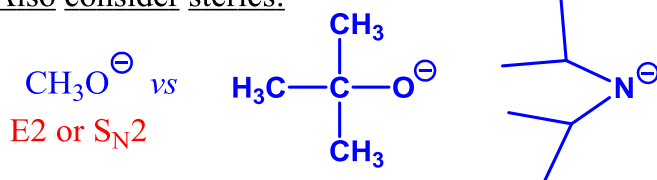
Last deciding factor: Temperature! (consider LAST)
⇨ increasing temperature increases rate of all reactions,
but rate of elimination increases more!
(effect of entropy: $\Delta G° = \Delta H° - T\Delta S°$)
- elimination gives more molecules ∴ more S

∴ E1 / E2 favored if HOT
(lab 2 *vs* lab 3!)

Substitution and Elimination Reactions in Synthesis

Synthesis: - always want desired product to be major (even better, only!) product
    Must consider: - competing reactions (sub *vs* elim etc)
                        - regiochemistry
                        - stereochemistry

A) Elimination

Want to make: $H_3C-\overset{H_2}{C}-\overset{}{\underset{H}{C}}=CH_2$ LG was here or here

base

base = OH^-, heat to avoid S_N2

$H_3C-\overset{H}{\underset{H}{C}}=\overset{H}{\underset{H}{C}}-CH_3$ $\xleftarrow{OH^-}$ $H_3C-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{Br}{C}}-\overset{H}{\underset{H}{C}}H_2$ or $H_3C-\overset{H_2}{C}-\overset{H}{\underset{H}{C}}-\overset{}{\underset{Br}{C}}H_2$

major product

two β-C ∴ Zaitsev :-(

only one possible E2 product!
:-)

But, <u>this</u> R-Br is easier to make! (Br_2 / hν)

How can we make this one work?
Use a bulky base!

e.g. $H_3C-\overset{CH_3}{\underset{CH_3}{\overset{|}{\underset{|}{C}}}}-O^{\ominus}K^{\oplus}$

still not as good (might get 70:30 but never 100%!)

B) Substitution: important application: R-O-H → R-O-R' (alcohol → ether)

Williamson Ether Synthesis:

$R-O^{\ominus}$ + $R'-Br$ $\xrightarrow{S_N2}$ $R-O-R'$ + Br^-

R' = 1° or 2°

?

$R-OH$ + Na (metal) $\longrightarrow$ $R-O^{\ominus} Na^+$ + $^1/_2 H_2$ (g)

similar to $Na + H_2O \longrightarrow NaOH + ^1/_2 H_2$ (redox)

or

$R-OH$ + Na^+H^- $\longrightarrow$ $R-O^{\ominus} Na^+$ + H_2 (g)

H^- = strong base: $H^- + H^+ \longrightarrow H_2$

⇨ need to consider competition from E2 (RO^- = strong base)

e.g.   Want to make:

$$H_3C - \overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}} - O - CH_3$$

- one R = ROH
- other R = R'-Br

1) NaH
2) CH_3Br

1) NaH
2) $(CH_3)_2CHBr$

$$H_3C - \overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}} - OH$$
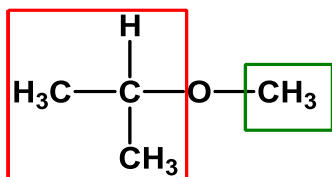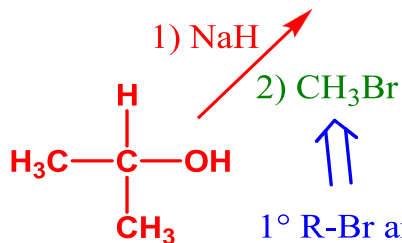
Which is best?

1° R-Br and no β-H, so S_N2 only possible reaction!   :-)

$HO - CH_3$

CH_3O^-

$$H_3C - \overset{\overset{\displaystyle H}{|}}{C} = CH_2$$

:-(

E2 competes
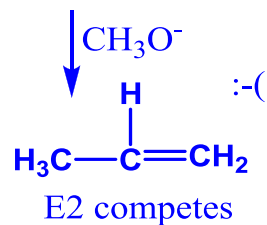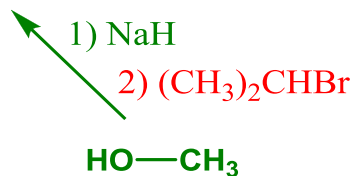
Reactions of Alcohols R-O-H

<u>Seen:</u> - can turn into strong Nu⁻ (alkoxide)

$$R-O-H \xrightarrow[\text{or NaH}]{\text{Na}} R-O^{\ominus}$$
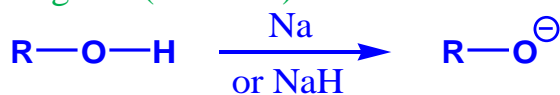
- can turn into good LG by protonation

$$R - \overset{..}{\underset{..}{O}} - H \xrightarrow{H^+} R - \overset{\oplus}{\underset{\underset{\displaystyle H}{|}}{\overset{..}{O}}} - H \longrightarrow R^{\oplus} + H_2O$$

- lab 2: S_N1
- lab 3: E1
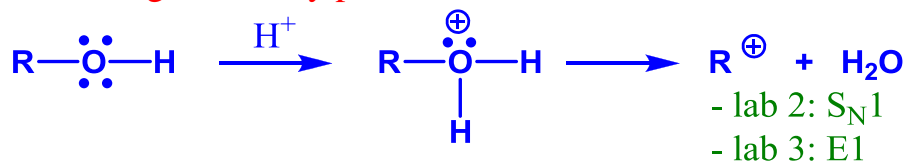
Substitution Reactions of Alcohols

$$-\overset{|}{\underset{|}{C}} - \overset{..}{\underset{..}{O}} - H \xrightarrow{H - Br} -\overset{|}{\underset{|}{C}} - \overset{\oplus}{\underset{\underset{\displaystyle H}{|}}{O}} - H + Br^{\ominus} \xrightarrow[\text{if } 3°/2°]{S_N1} -\overset{|}{\underset{|}{C}}^{\oplus} + H_2O \xrightarrow{Br^{\ominus}} -\overset{|}{\underset{|}{C}} - Br$$
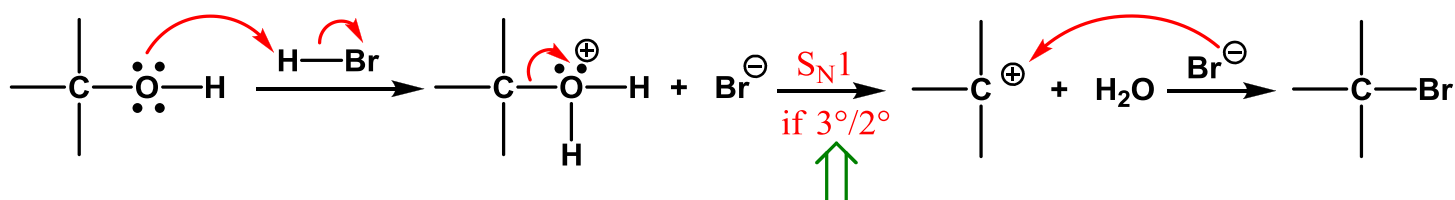
recall HBr is in H_2O ∴ protic

If 1° must be S_N2:

$$H_3C - \overset{\overset{\displaystyle H_2}{}}{C} - \overset{..}{\underset{..}{O}} - H \xrightarrow{H - Cl} H_3C - \overset{\overset{\displaystyle H_2}{}}{C} - \overset{\oplus}{\underset{\underset{\displaystyle H}{|}}{O}} - H + Cl^{\ominus} \longrightarrow H_3C - \overset{\overset{\displaystyle H_2}{}}{C} - Cl + H_2O$$
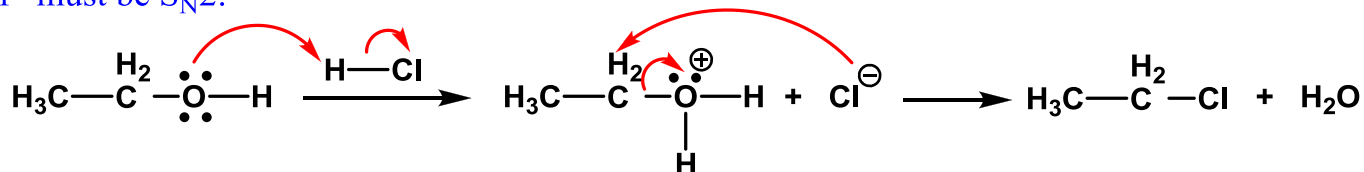
⟹ If HX has X⁻ that is <u>not</u> a good Nu⁻, can get <u>ethers</u> as products:

e.g.

∴ acid is a catalyst
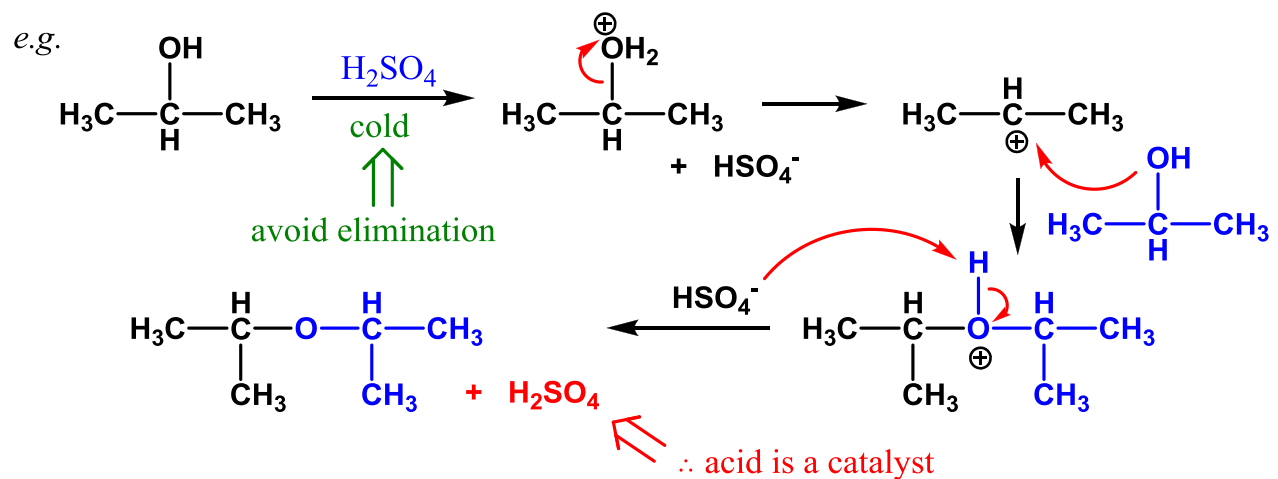
⟹ good way to make symmetrical ethers!   2 ROH $\xrightarrow{H^+}$ R-O-R