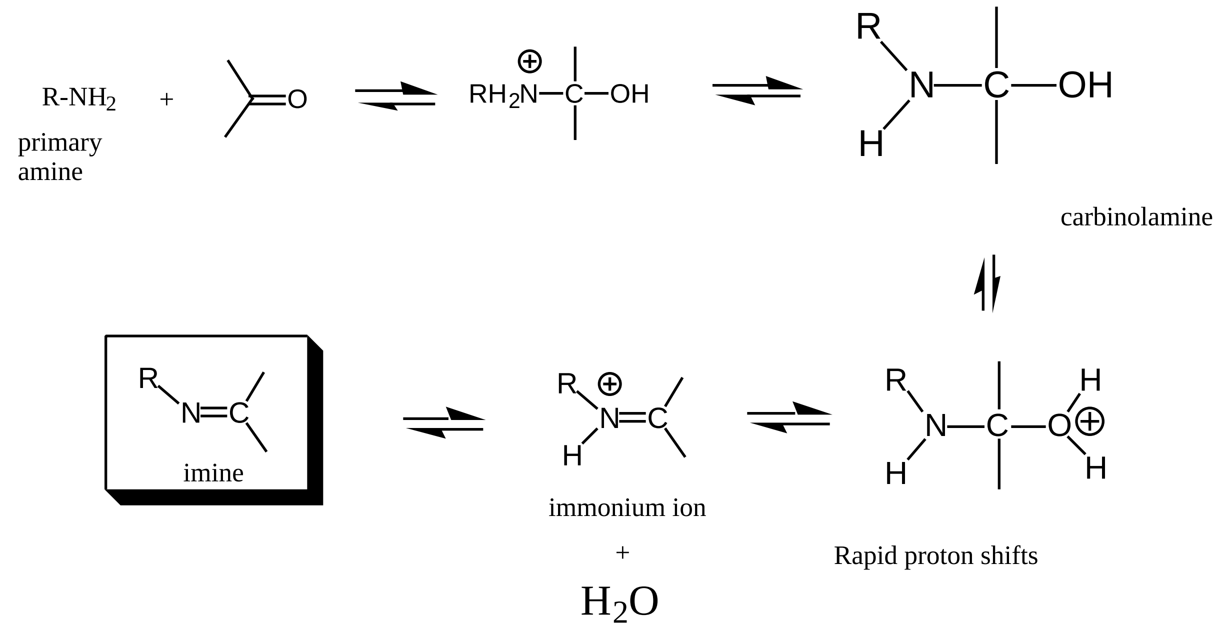
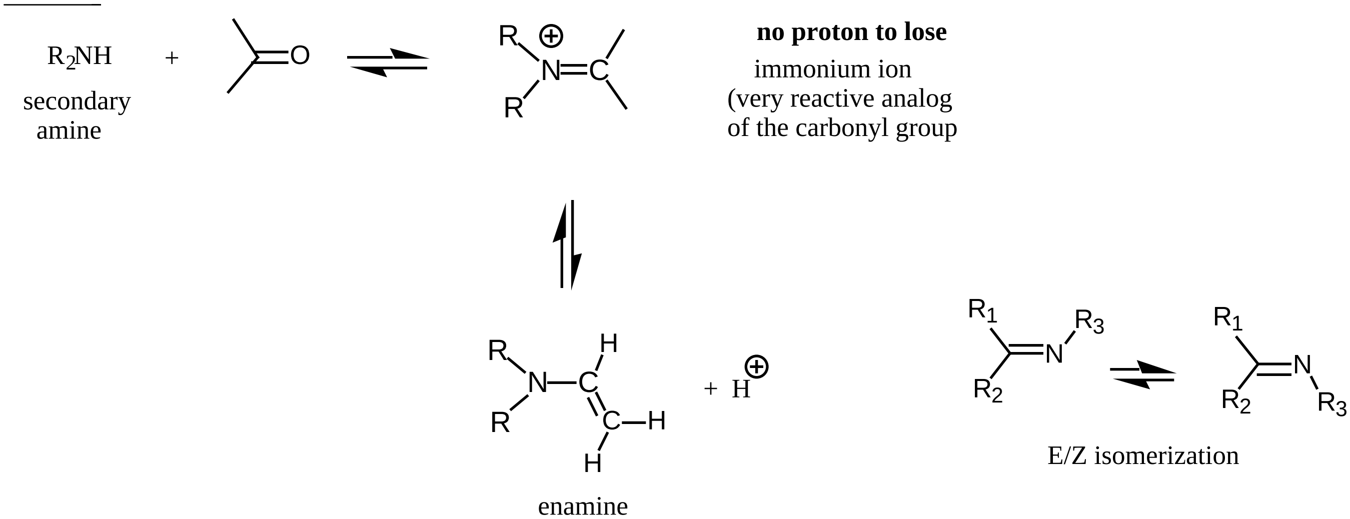
Chemistry 304B, Spring 1999 **Lecture Notes 16**

Reminder: turn in exam regrading request by Monday noon, in my mailbox.

From last time:





NOW: Carbon Nucleophiles. How to make a carbon electron-rich?

$H_3C—X$ $\qquad$ $H_3C—M$

a. Proton abstraction? $\quad CH_4 + \text{base} \longrightarrow {}^{\ominus}CH_3 + \text{H-base}^{\oplus}$

b. halide insertion (not F) $\quad H_3C—X + 2Li \longrightarrow H_3C—Li + LiX$

X = Cl, Br, I

c. halogen-metal exchange $H_3C{-}X$ + RLi $\rightleftharpoons$ $H_3C{-}Li$ + RX

X = Cl, Br, I

Equilibrium depends on relative stability of components, primarily depends on R-Li vs Me-Li:carbanion stability

d. metal-metal exchange $H_3C{-}M$ + M'-X $\rightleftharpoons$ $H_3C{-}M'$ + R-M

X = Cl, Br, I

Equilibrium depends on relative stability of components, more electropositive M prefers X

Eg,

$H_3C{-}Li$ + ZnX_2 $\rightleftharpoons$ $H_3C{-}Zn{-}X$ + Li-X

Very common case: the Grignard reagent

halide insertion (not F) $H_3C{-}X$ + Mg $\longrightarrow$ $H_3C{-}Mg{-}X$

X = Cl, Br, I

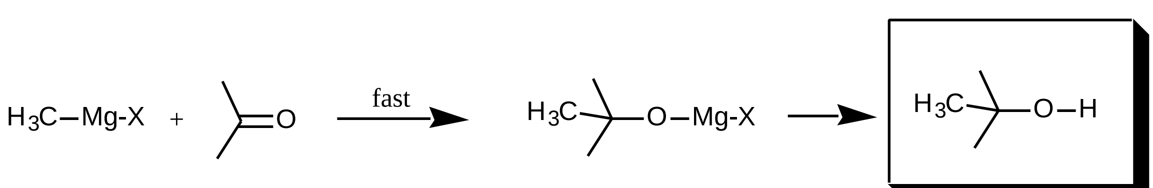
What about Na and K?

Wurtz reaction...

Relative reactivity of R-M correlates roughly with electropositive value for M:

more electropositive M
more (-) on CH_3
more reactive nucleophile

ADDITION TO KETONES AND ALDEHYDES:

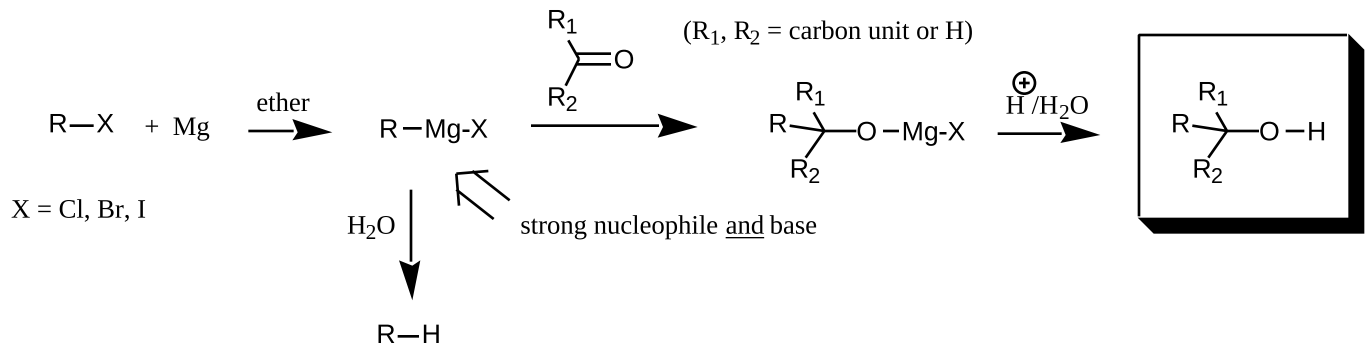


Alcohol synthesis

Essentially irreversible (CH_3^- is a lousy leaving group)

In general:

General alcohol synthesis from ketones and aldehydes:

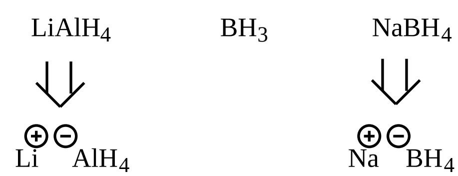


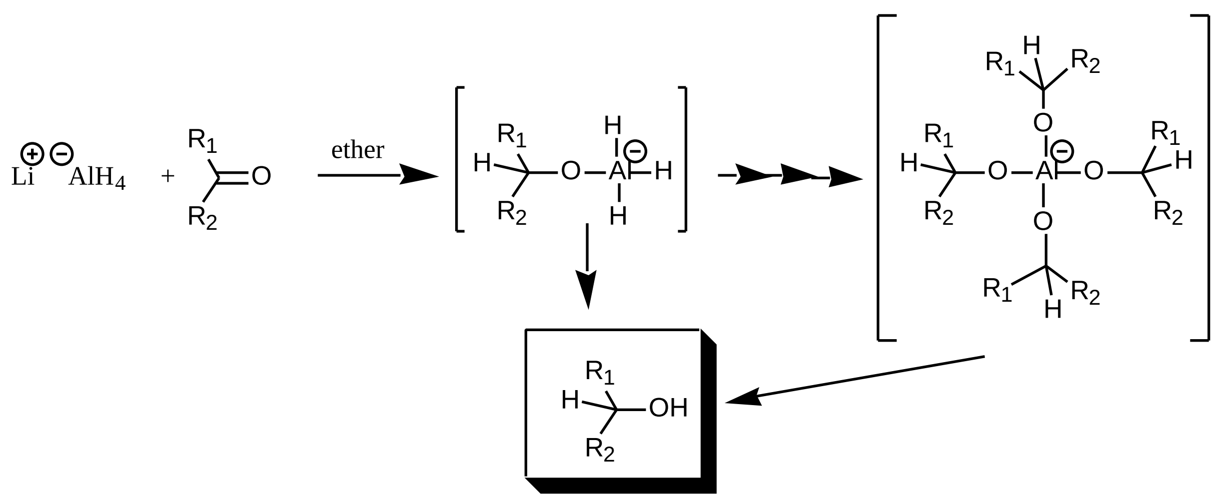
Hydrogen as a nucleophile:

$H^{\ominus}$

LiH
NaH
KH

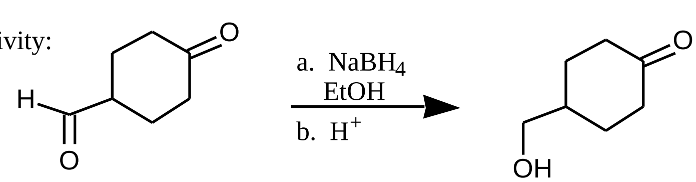
Extremely insoluble;
good base, zero nucleophile





Many variations on the theme: differing in reactivity by electronic and steric parameters.
$LiAlH_4$ reacts with all types of carbonyl groups: ketones, aldehydes, etc. and imines, nitriles
$NaBH_4$: Less reactive--can react selectively with aldehydes. Not at all with other carbonyl derivatives, including esters, amides, etc.

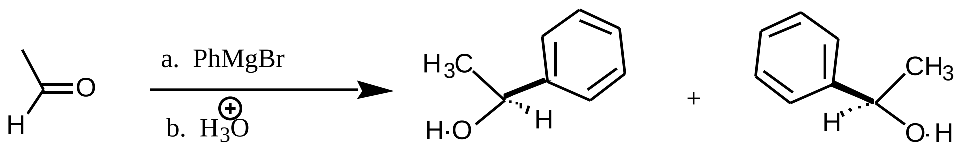
Selectivity:



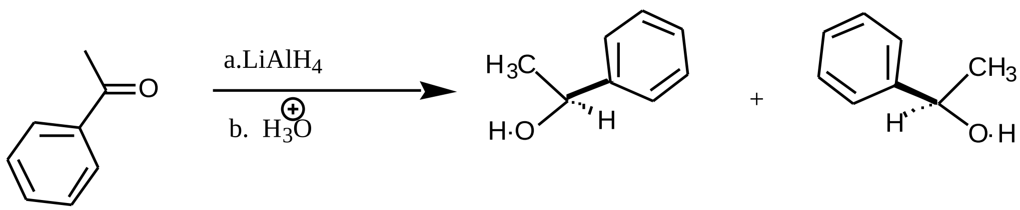
Note stereochemical issues:

A. Enantiomers

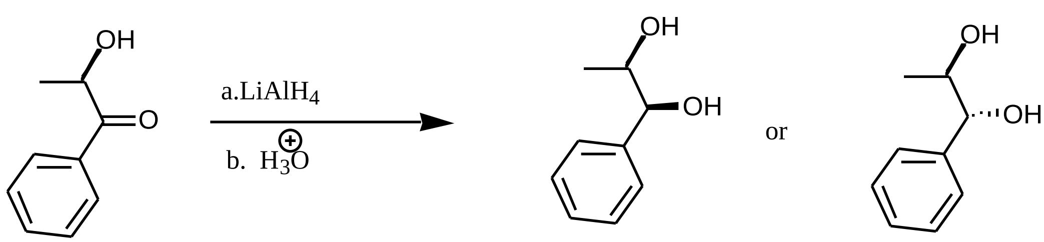
Addition of organometallic reagents to ketones and aldehydes



Addition of hydride reagents to ketones:



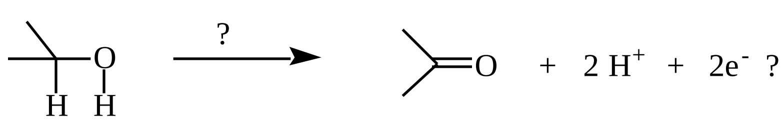
B. Diastereomers:



Should not be 1:1 (unless accidentally equal energy TS)

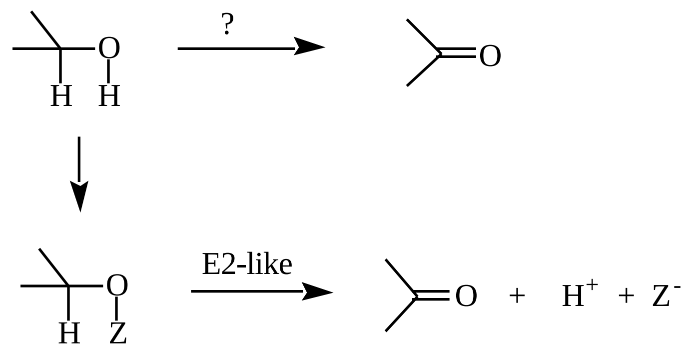
Reverse of Hydride Reduction: **Oxidation of Alcohols to Ketones**
Special case of elimination: Oxidation of alcohols

Elimination to form C=O



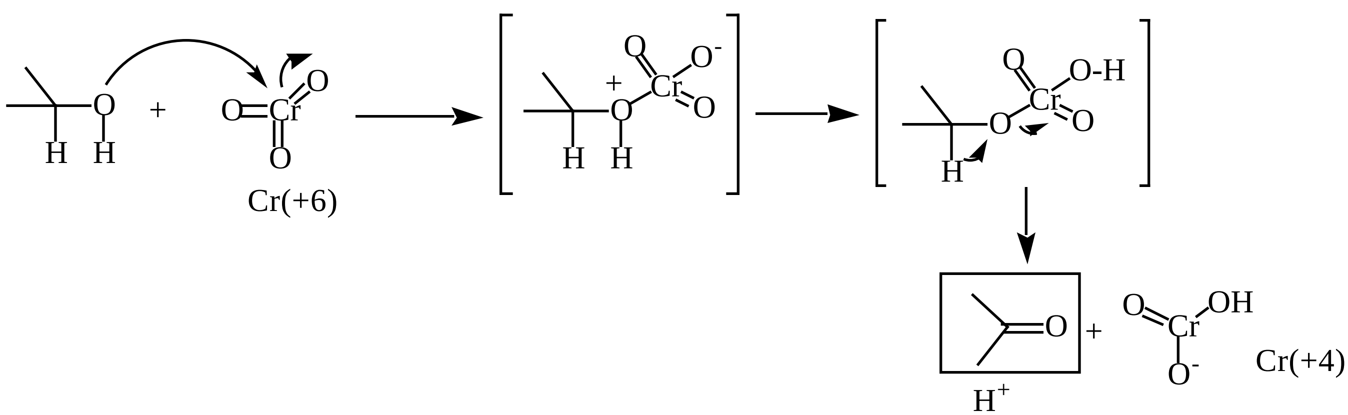
Is this an oxidation? Reduction/oxidation in organic chemistry a little fuzzy

How arrange the lowest energy **pathway** for oxidation of an alcohol to a ketone??

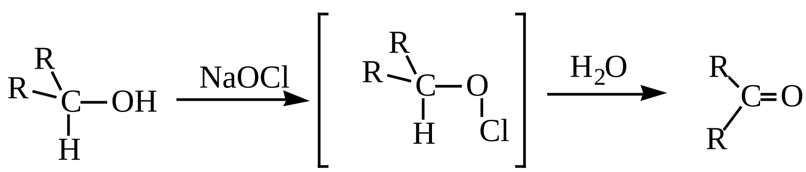


Z = good electron acceptor

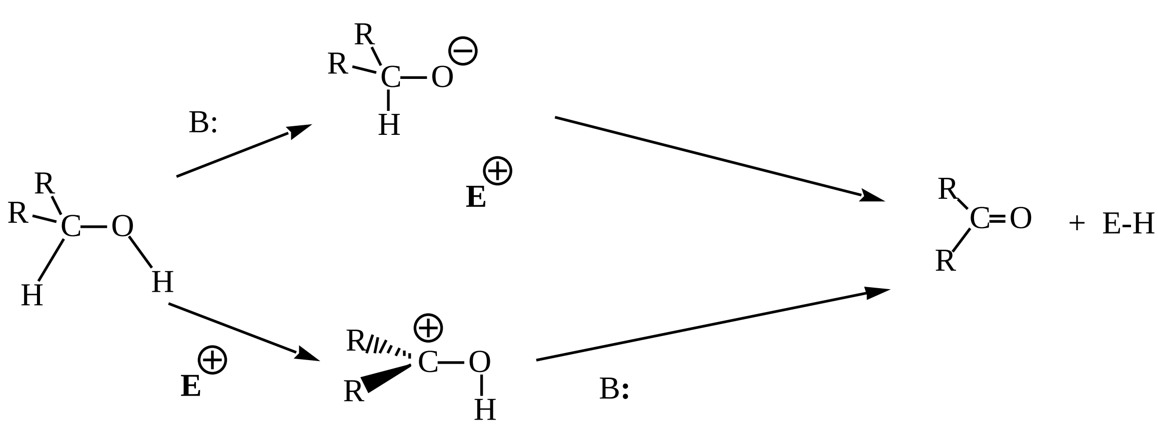
How arrange Z group efficiently? CrO_3 is one example



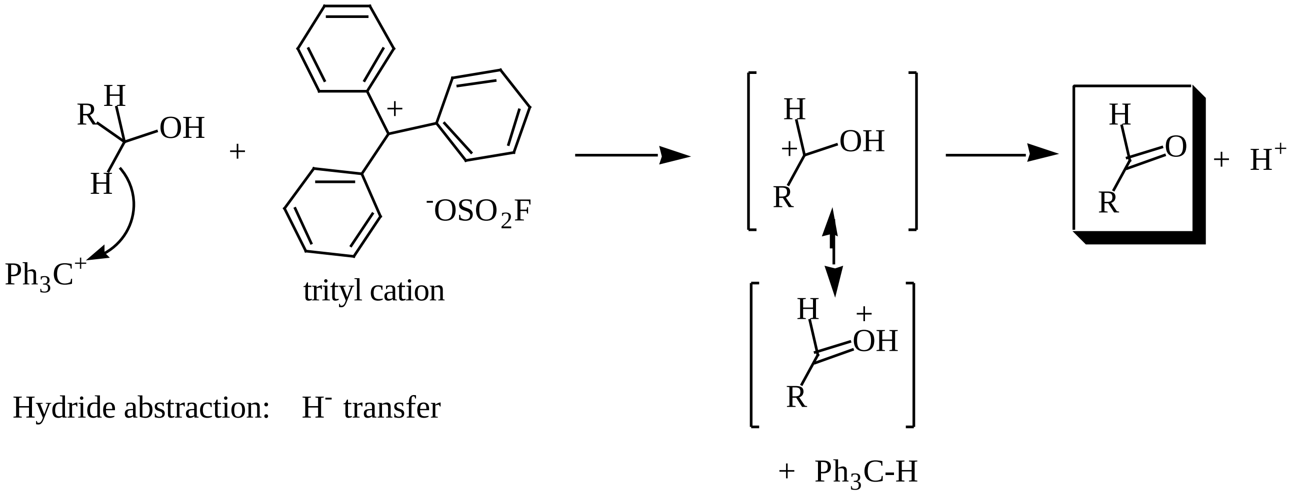
Clorox oxidation:



Consider Alternate Activation: Hydride Transfer



E⁺ could be a carbocation is stabilized by three phenyl groups $Ph_3C^+ X^-$



Hydride abstraction: H^- transfer