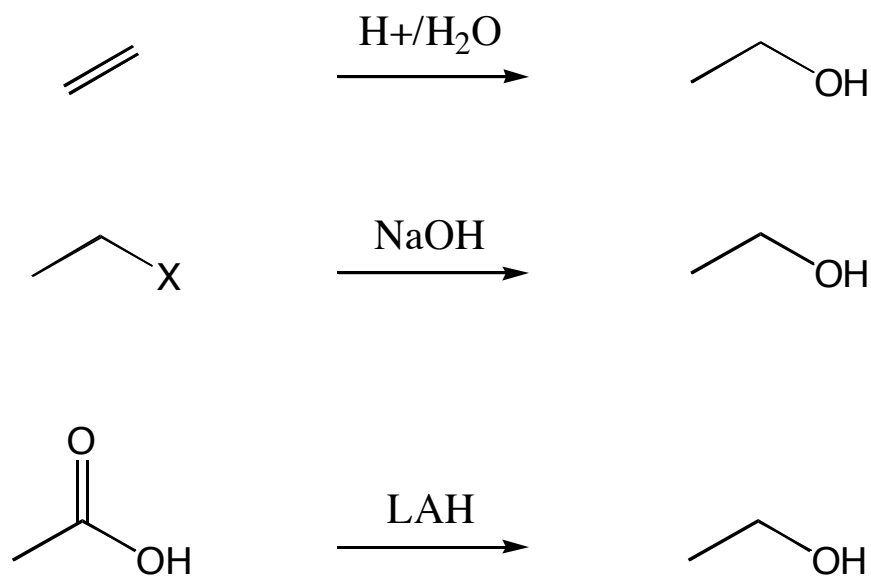


Alcohols

have seen many reactions to synthesize alcohols:



in this chapter we will study reactions of the alcohols

Oxidation

Need to understand the nomenclature of organic reduction/oxidation

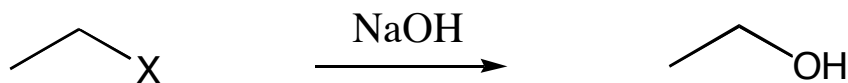
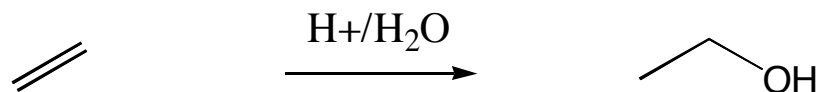
In general chemistry learn that reduction is gain of electrons
and oxidation is loss of electrons

this works well with transition metals, but it is hard to distinguish RED/OX reactions in
organic reactions by this definition

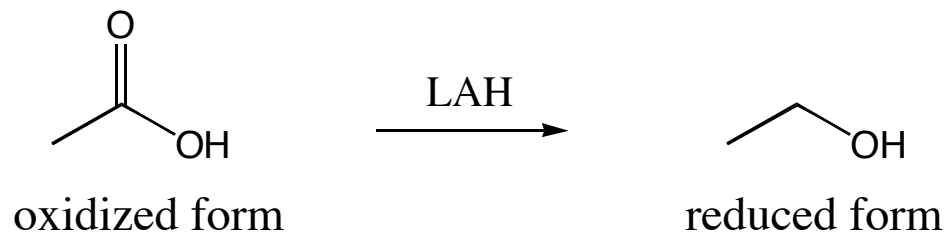
It is very important that one recognizes whether two compounds are of the same
oxidation level or whether one is "oxidized" relative to the other

Anytime two compounds can be converted with only water, basic water (NaOH), or acidic water (H+) then the two compounds are at the same oxidation level

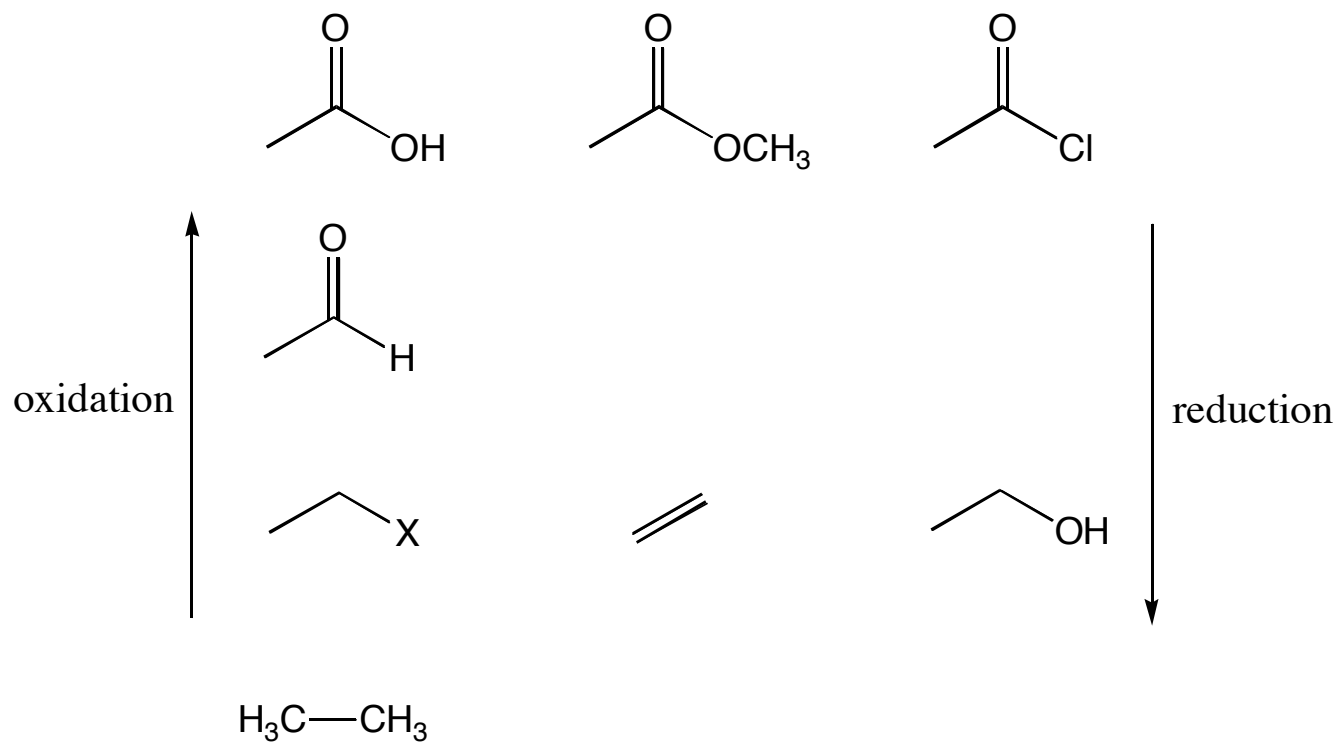
For example:



all compound are same oxidation level



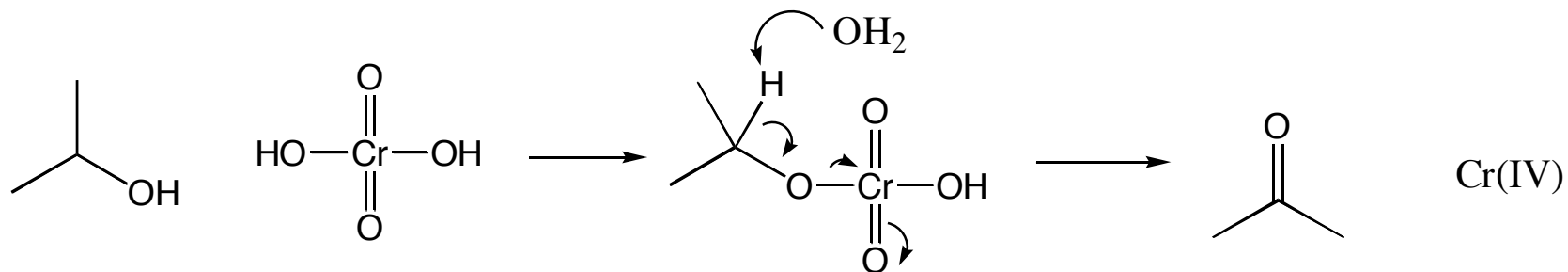
Comparison of Oxidation States



Oxidation of Alcohols

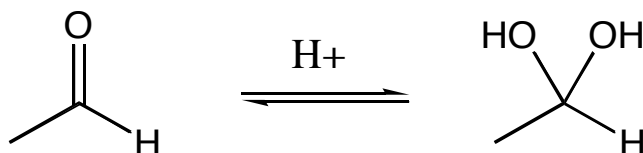
Typical procedure to oxidize an alcohol is to use a chromium (VI) reagent

e.g. CrO_3 , $\text{H}_2\text{Cr}_2\text{O}_7$, H_2CrO_4



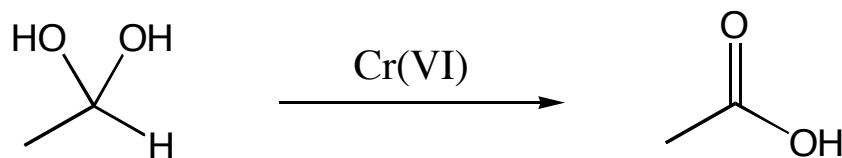
the alcohol reacts with Cr(VI) to form a chromate ester

With 1° alcohols the initially formed aldehyde reacts further



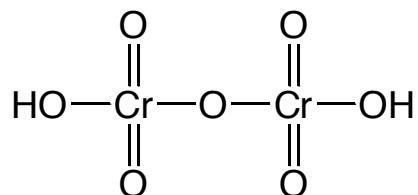
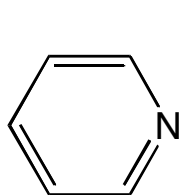
the aldehyde equilibrates to the geminal diol form, called acetal
(which is further promoted in acidic conditions)

this acetal can behave like an alcohol observed before to oxidize in a second step

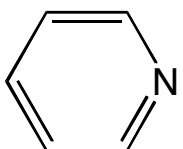


1° alcohols therefore give almost exclusively carboxylic acids
(especially in acidic conditions)

One way to avoid this overoxidation is to use a Cr(VI) reagent in nonacidic conditions



Pyridinium dichromate (PDC)



HCl

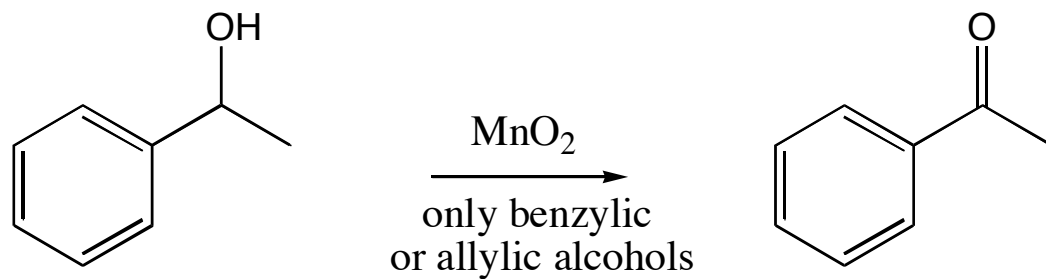
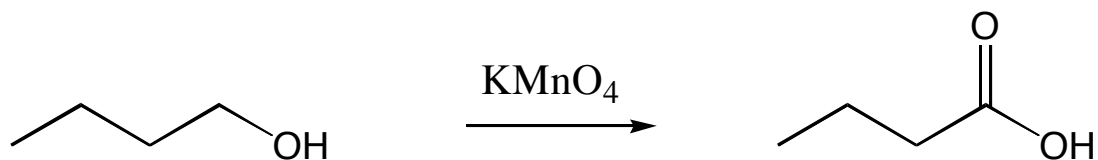
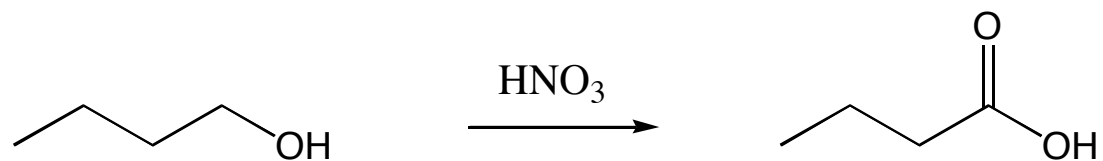
CrO₃

Pyridinium chlorochromate (PCC)

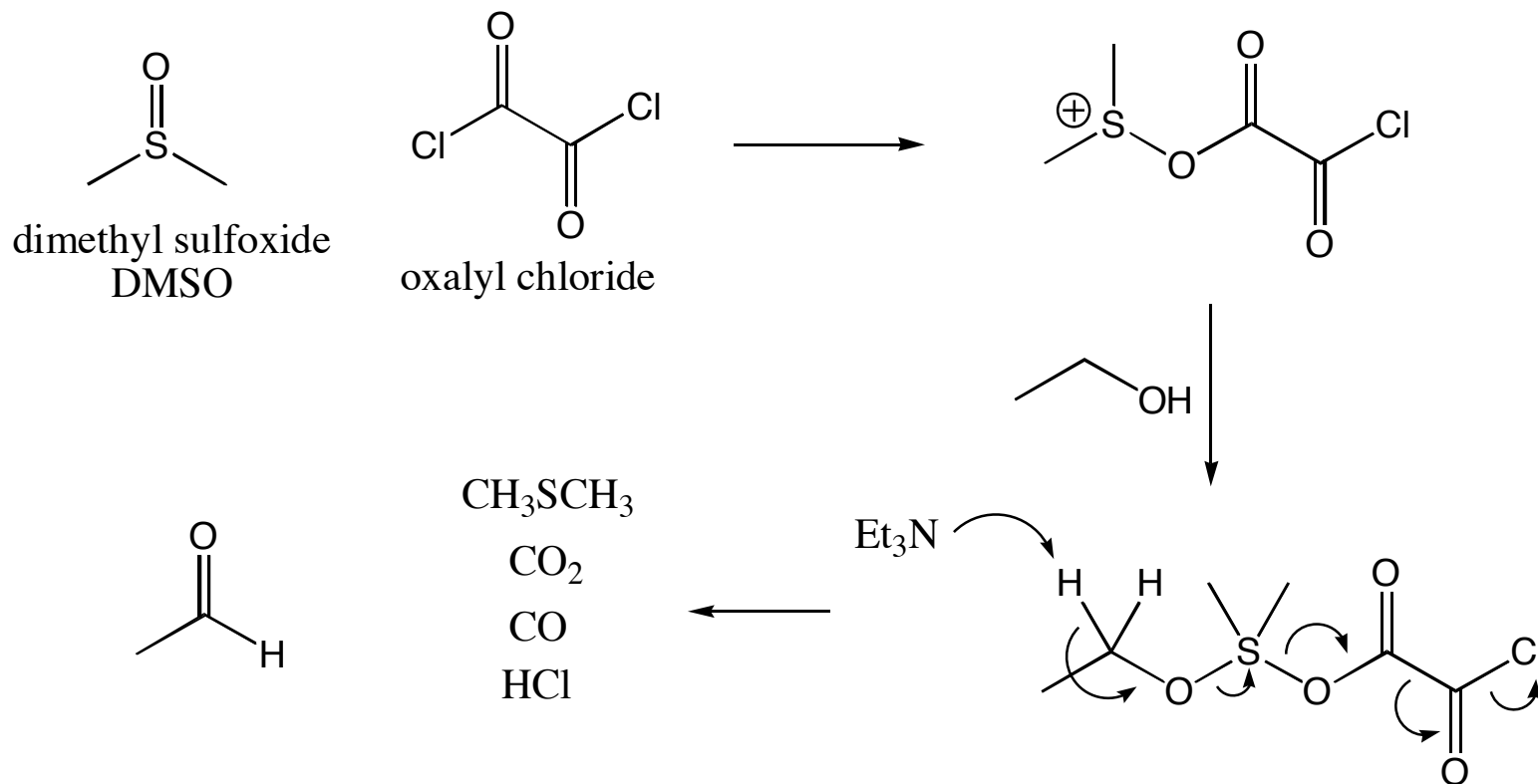
the pyridine acts as a base and therefore there is less acetal formation and hence oxidation of 1° alcohols stop at the aldehyde stage

Other Oxidants

Cr(VI) is not the only oxidant for alcohol oxidations



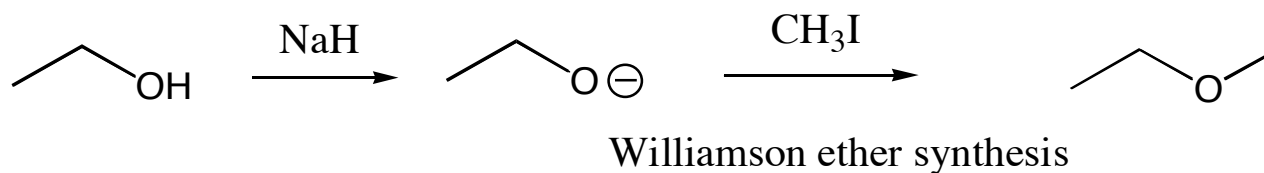
Swern Oxidation



advantages: mild method, easy to separate and purify products,
1° alcohol stops at aldehyde

In addition to oxidation, can also react alcohols as either nucleophiles or electrophiles

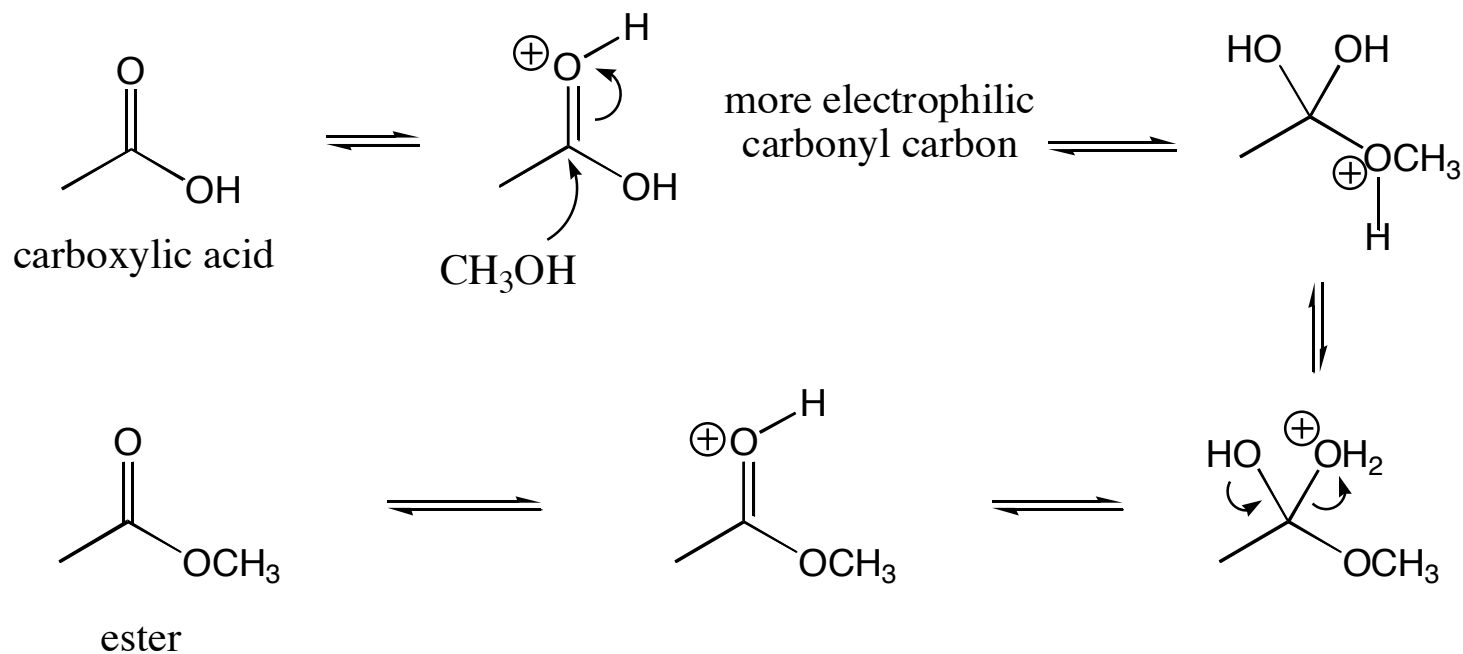
To make alcohol more nucleophilic need to abstract the acidic hydrogen (KNOW pKa's!)



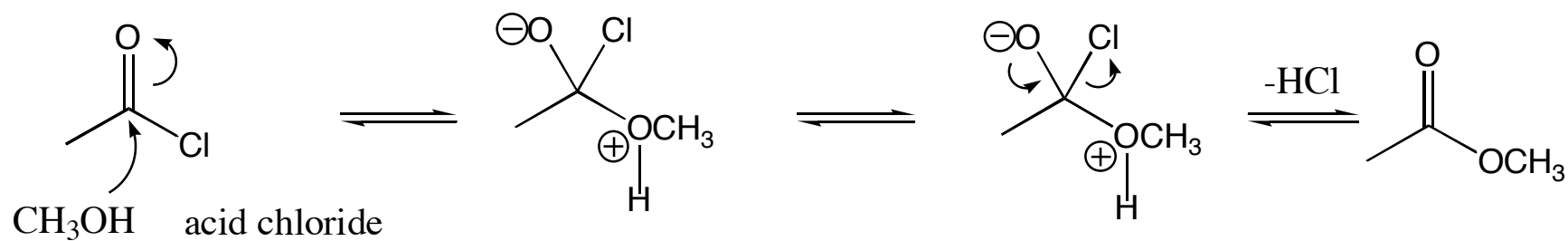
in this manner can make nucleophilic oxygen that can react
through any S_N2 type reaction already studied

Esterification

To form esters the alcohol can react as a nucleophile without forming the alkoxide
-generally need to activate the carbonyl first to make it more electrophilic



Esters can also be formed with alcohols with more reactive carbonyl groups

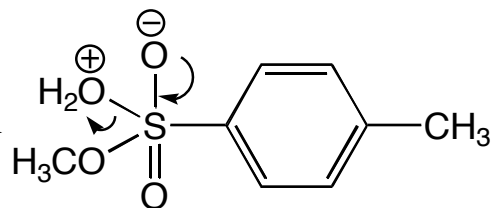
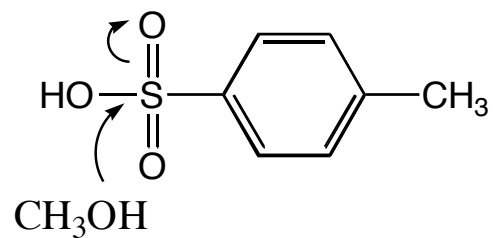


the better leaving group (chloride) allows the alcohol to react at the carbonyl without need for initial protonation

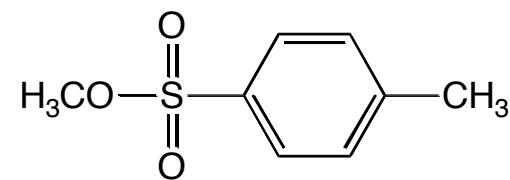
Formation of Inorganic Esters

- same type of mechanisms already observed

para-toluenesulfonic acid (TsOH)

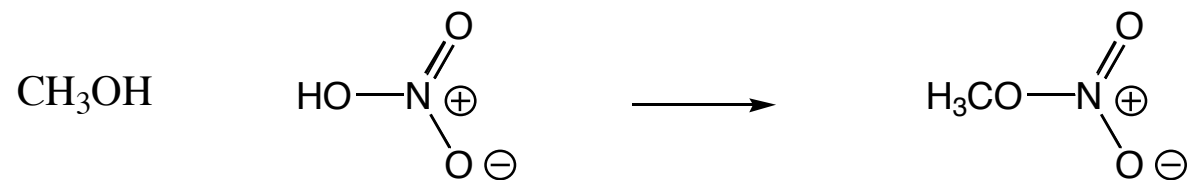


tosylate ester (ROTs)

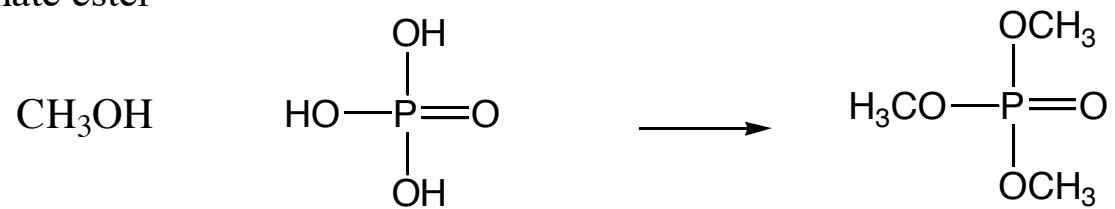


Other Common Ester Types

Nitrate ester



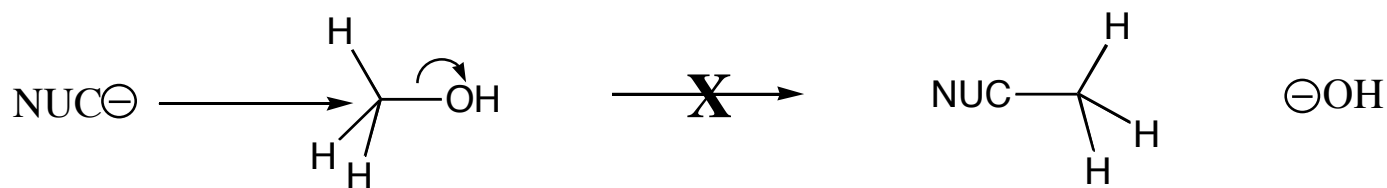
Phosphate ester



phosphoric acid (H_3PO_4)

Alcohol Functionalities Reacting as Electrophilic Sites

In these reactions the alcohol leaves in the reaction
(the C-O bond is broken during the reaction)

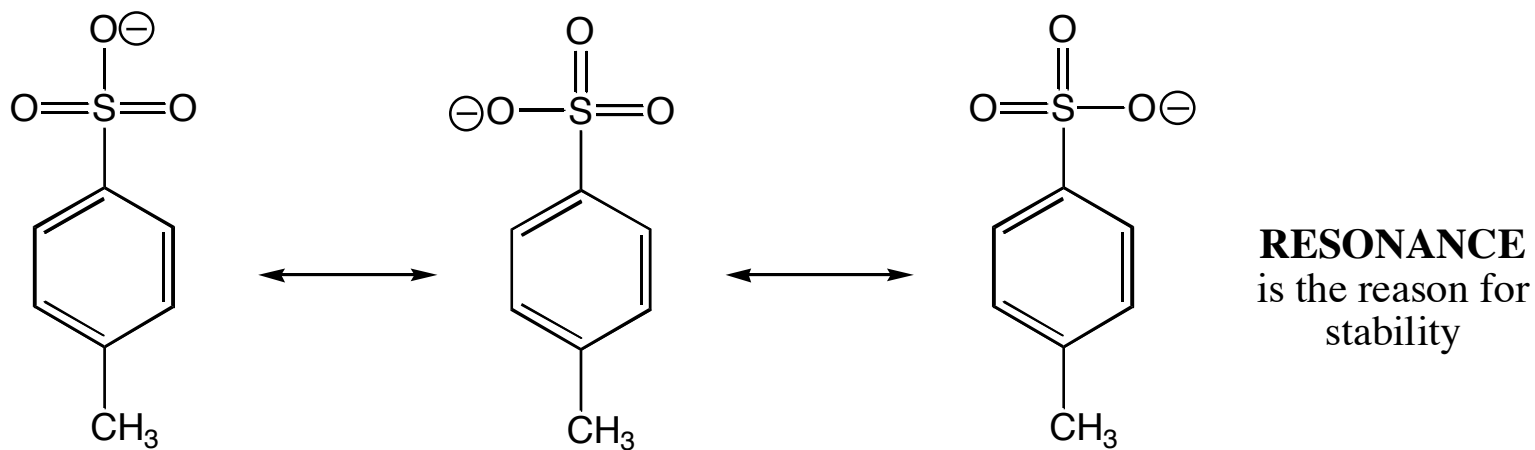
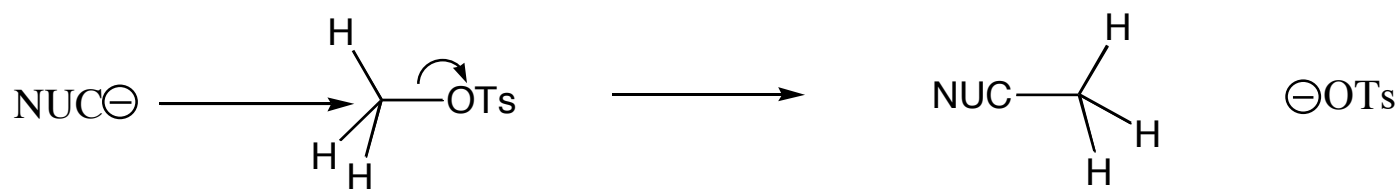


usually the hydroxide, or alkoxide, is a BAD leaving group

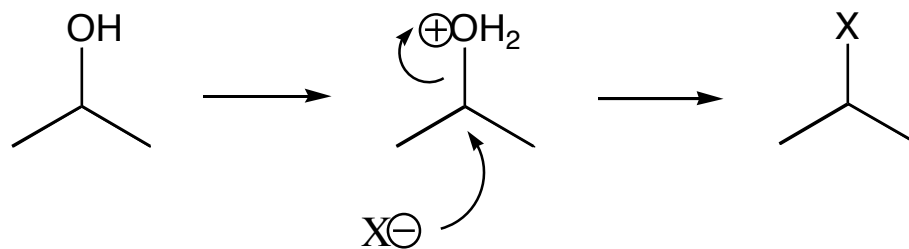
therefore we need a way to convert the alcohol into a GOOD leaving group

One Method is Tosylate Formation

The tosylate, which was seen earlier, is commonly used as a way to make the alcoholic oxygen a good leaving group



Another method we have already observed is protonation
to form water as the leaving group



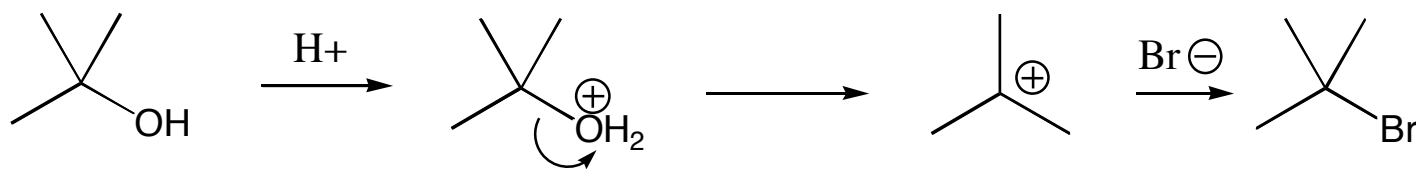
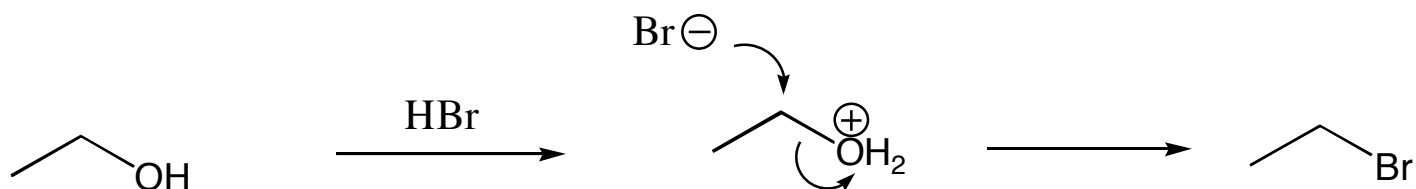
With either an $\text{S}_{\text{N}}1$ or $\text{S}_{\text{N}}2$ reaction the alcohol would need to be protonated first in order
to make a better leaving group

For alcohol reactions what type of reaction will occur (S_N1 or S_N2)
depends upon the order of the attached carbon

3° alcohols must be S_N1 (cannot undergo S_N2)

2° alcohols mainly S_N1

1° alcohols S_N2 (1° carbocations are high in energy)

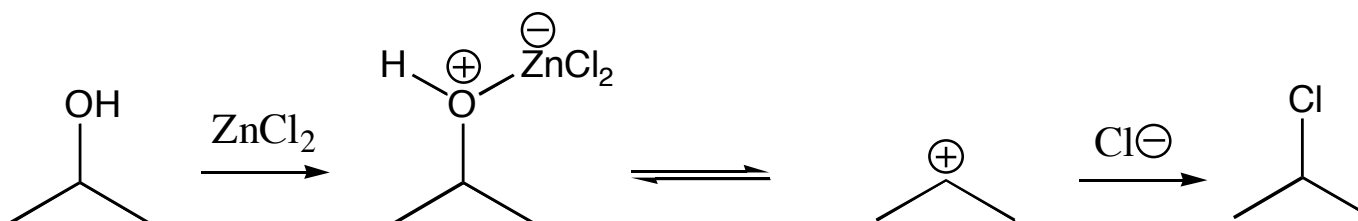


Lucas Reagent

Chloride reacts slower than bromide

Therefore often need to add an additional Lewis acid
to convert an alcohol to alkyl chloride

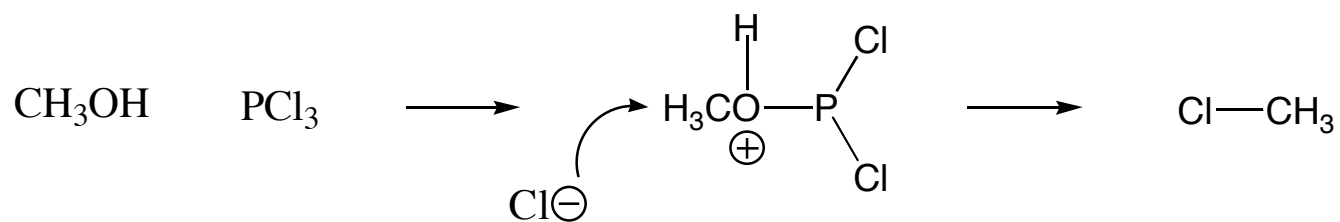
-with Lucas reagent need to add ZnCl_2 to affect reaction



While it is relatively easy to react alcohols with hydrobromic or hydrochloric acid, both hydrofluoric and hydroiodic acid are difficult to react in this manner

need different routes to these compounds

alkyl iodides can be prepared with phosphorous halides

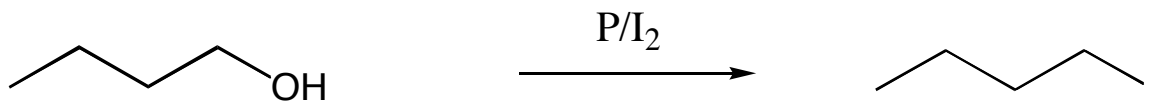


$\text{S}_{\text{N}}2$ reaction - works well for 1° and 2° alcohols, poor for 3° alcohols

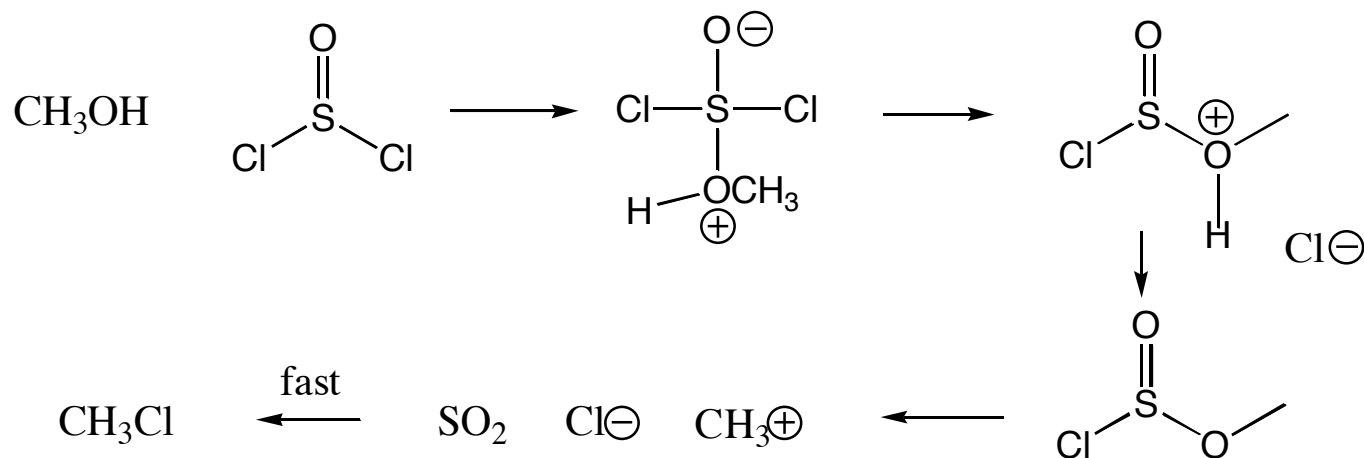
Method of Choice for Iodides

PI_3 can be used

Often in practice PI_3 is generated *in situ* from P/I_2



Another method for conversion of alcohols to alkyl halides is thionyl chloride

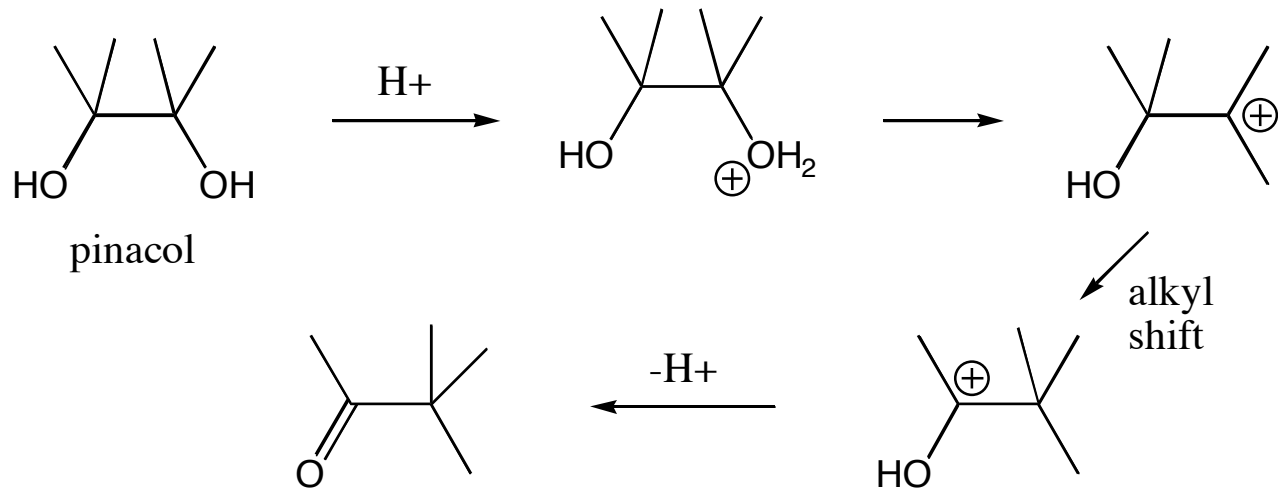


due to the rapidity of the last step, there is a retention of stereochemistry

Diol Reactions

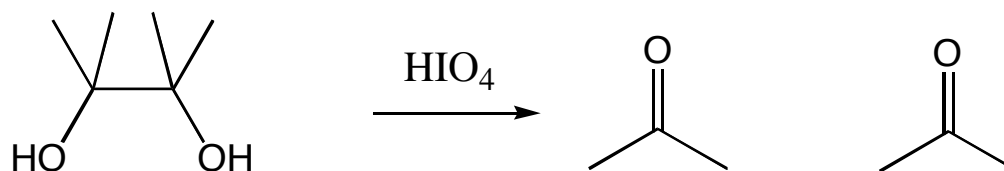
Some reactions are unique to vicinal diols (glycols)

Pinacol rearrangement:

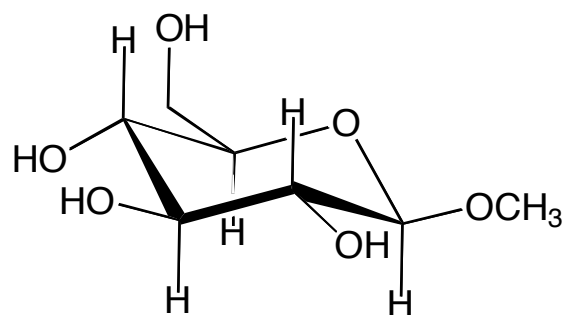


Periodic Cleavage of Glycols

HIO_4 will react with glycols



very important reaction to determine sugar structures



methyl- β -D-
glucopyranoside