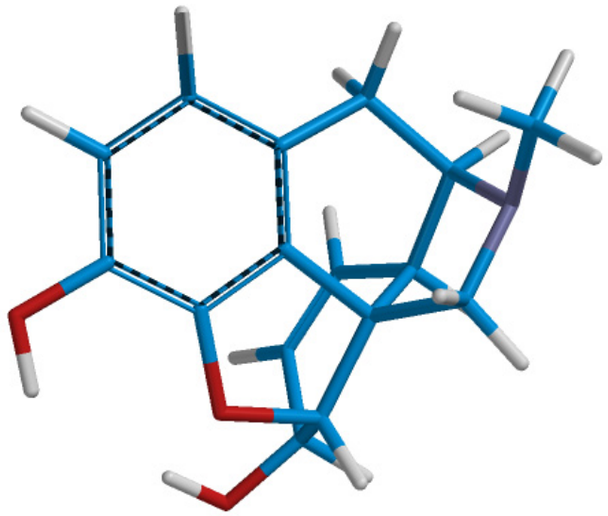
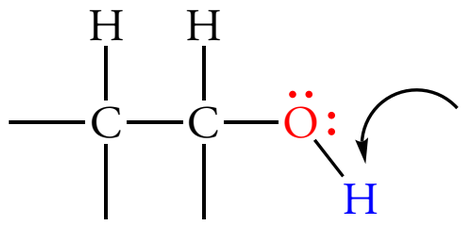
15

Alcohols: Reactions and Synthesis

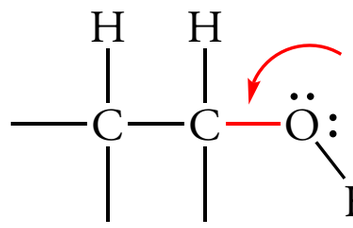


Azidothymidine (AZT)

15.1 OVERVIEW OF ALCOHOL REACTIONS

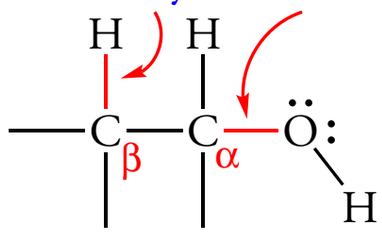


Replacing the alcohol hydrogen with an alkyl group gives an ether.
Replacing it with a carbonyl carbon atom yields an ester.

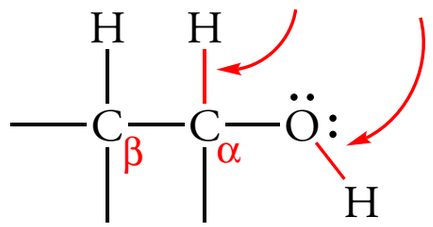


The carbon-oyxgen bond breaks in a nucleophilic substitution reaction, which is often acid-cartalyzed.

The carbon-oyxgen and carbon-hydrogen bonds break in a dehydration reaction, often acid-catalyzed.

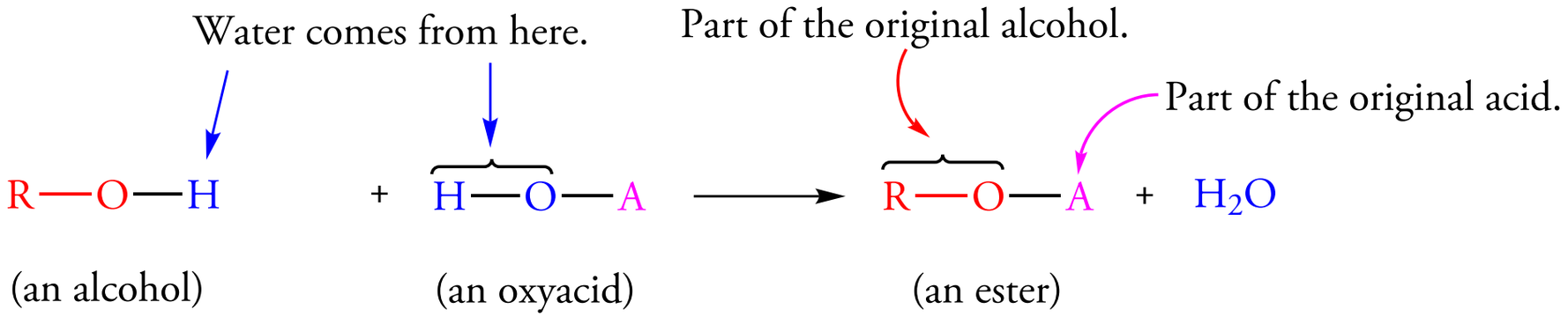


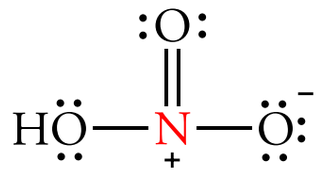
The oxygen-hydrogen and carbon-hydrogen bonds break in an oxidation reaction, an α-elimination,



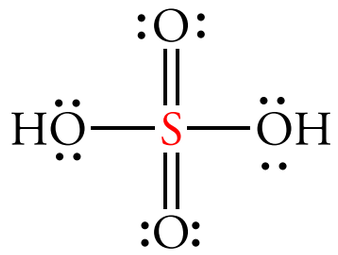
15.2 CONVERTING ALCOHOLS INTO ESTERS

Esters of Nitric, Sulfuric, and Phosphoric Acid

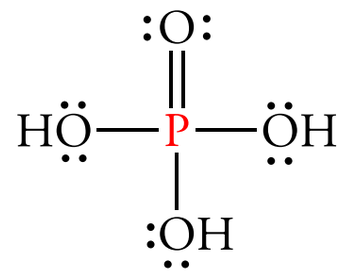




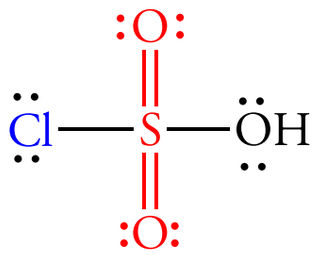
nitric acid



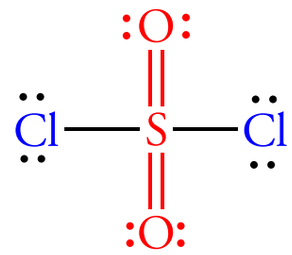
sulfuric acid



phosphoric acid



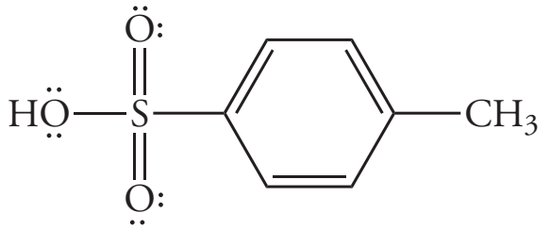
chlorosulfuric acid



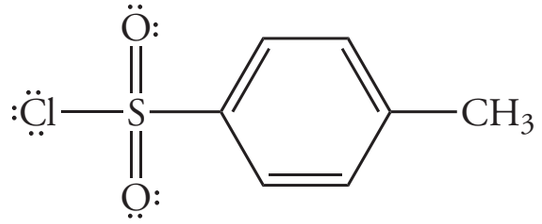
sulfuryl chloride

15.2 CONVERTING ALCOHOLS INTO ESTERS

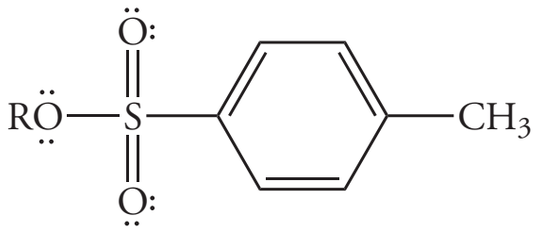
Reactions of Tosylate Esters



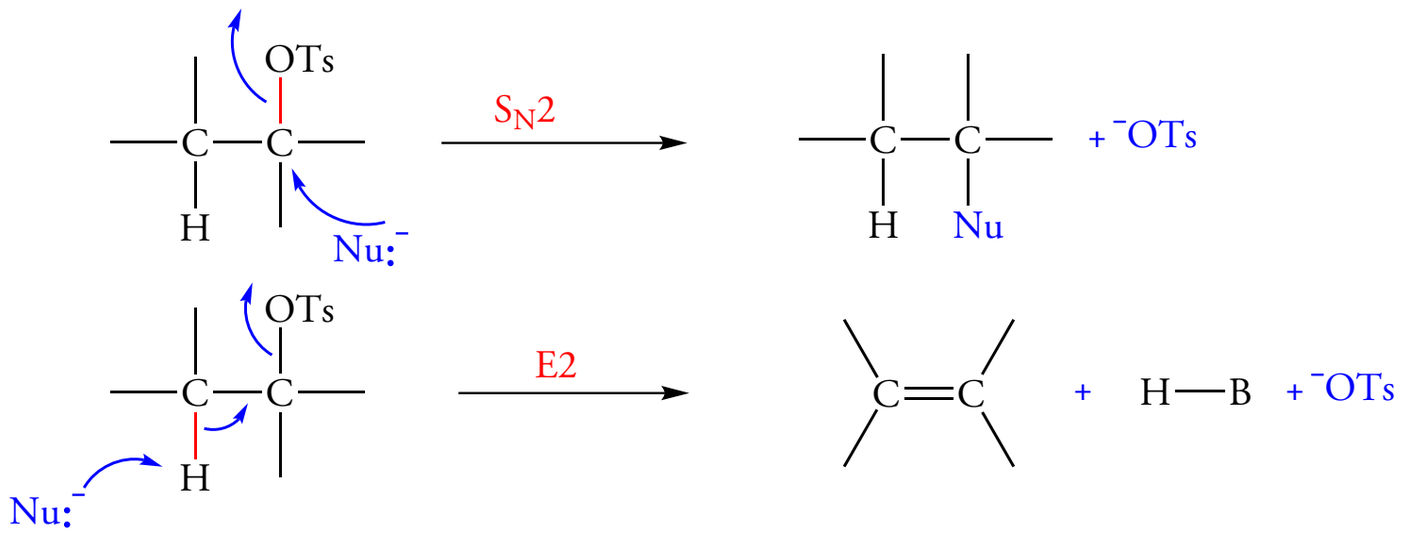
p-toluenesulfonic acid



p-toluenesulfonyl chloride
(tosyl chloride)

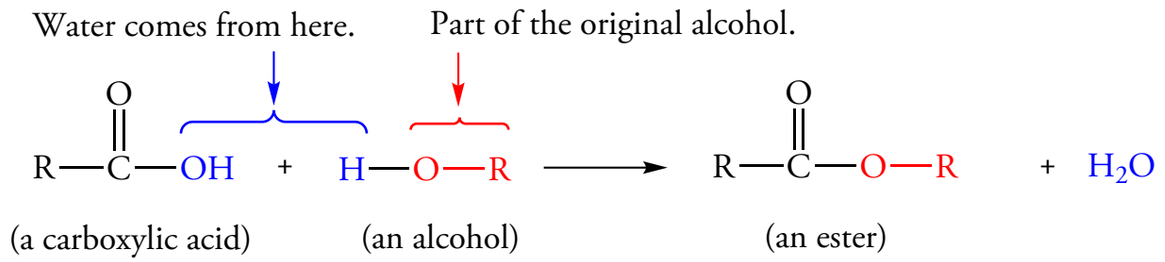


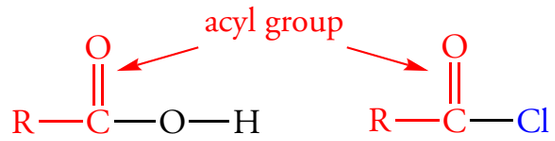
alkyl p-toluenesulfonate
(alkyl tosylate)

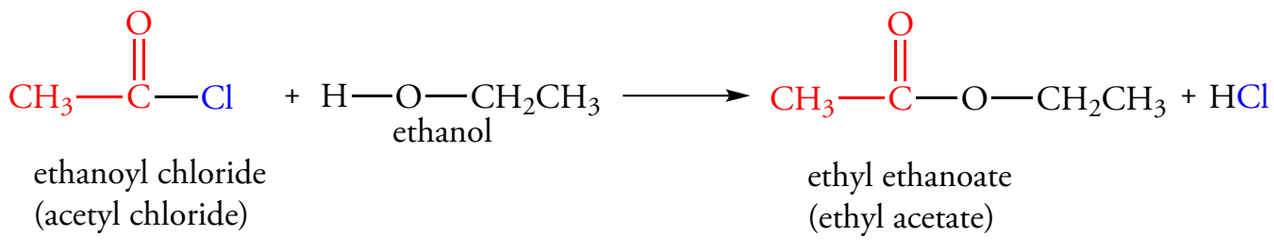


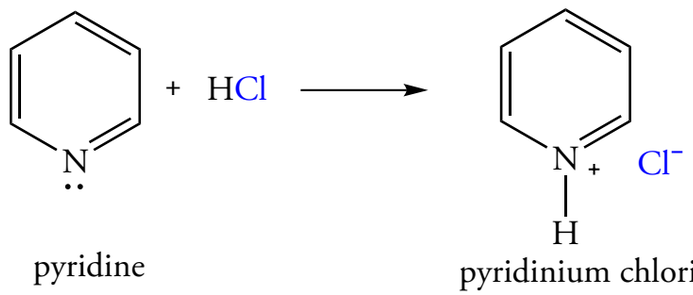
15.2 CONVERTING ALCOHOLS INTO ESTERS

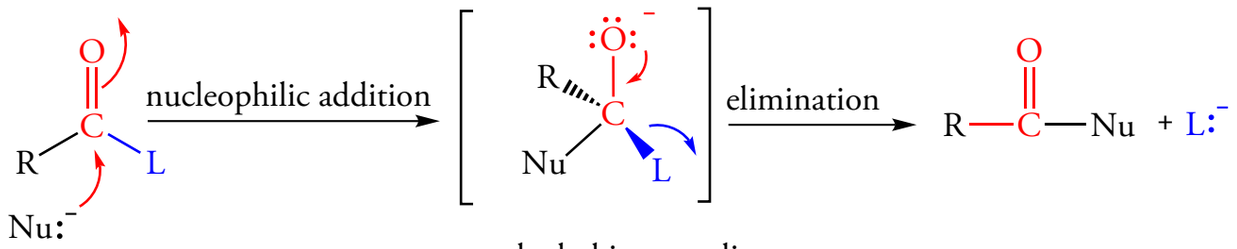
Esters of Carboxylic Acids





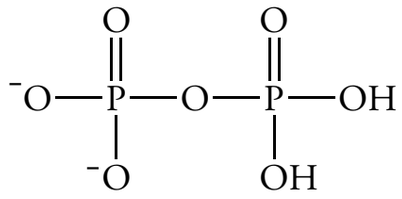




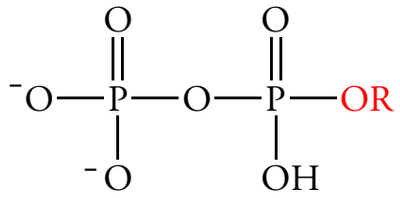


15.2 CONVERTING ALCOHOLS INTO ESTERS

Phosphate and Pyrophosphate Esters

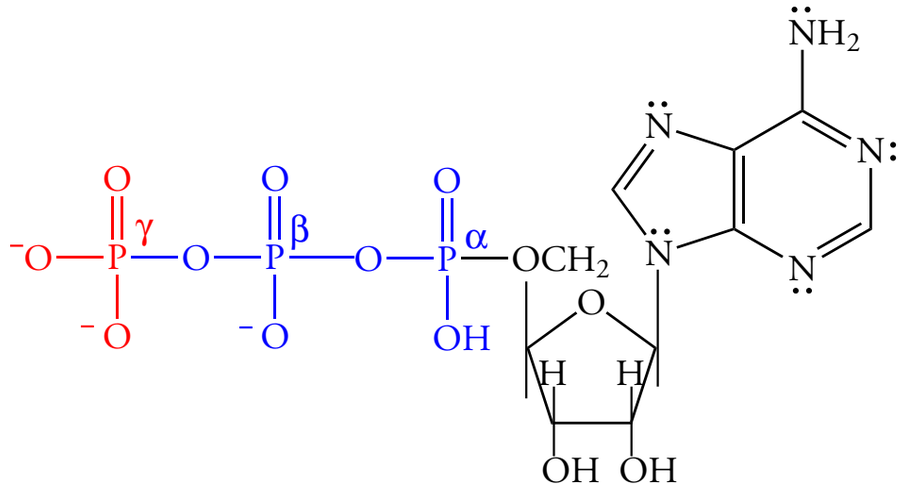


dihydrogen pyrophosphate

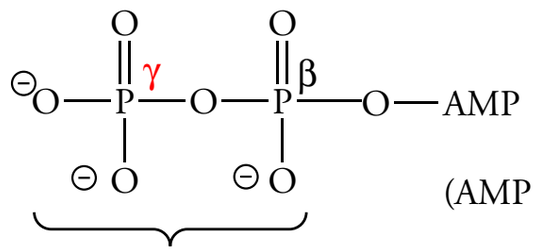


monohydrogen pyrophosphate ester

PO_3^{2-} is a *phosphoryl group*



Adenosine-5'-phosphate (ATP^{3-})

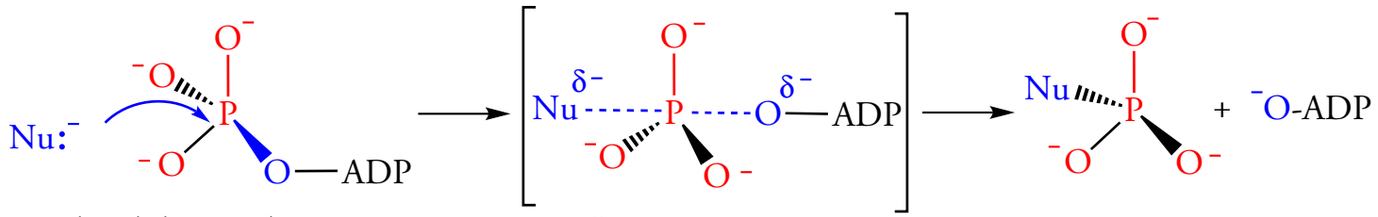


Pyrophosohoryl group
of ATP

(AMP is adenosine monophosphate.)

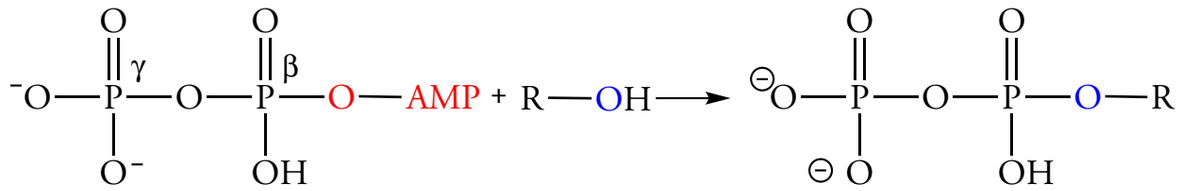
15.2 CONVERTING ALCOHOLS INTO ESTERS

Reactions Phosphate and Pyrophosphate Esters



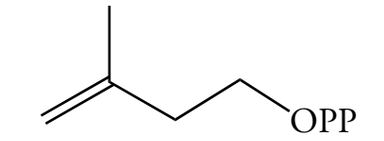
nucleophilic attack on tetrahedral phosphorus

S_N2 transition state

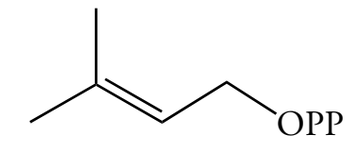


ATP^{2-}

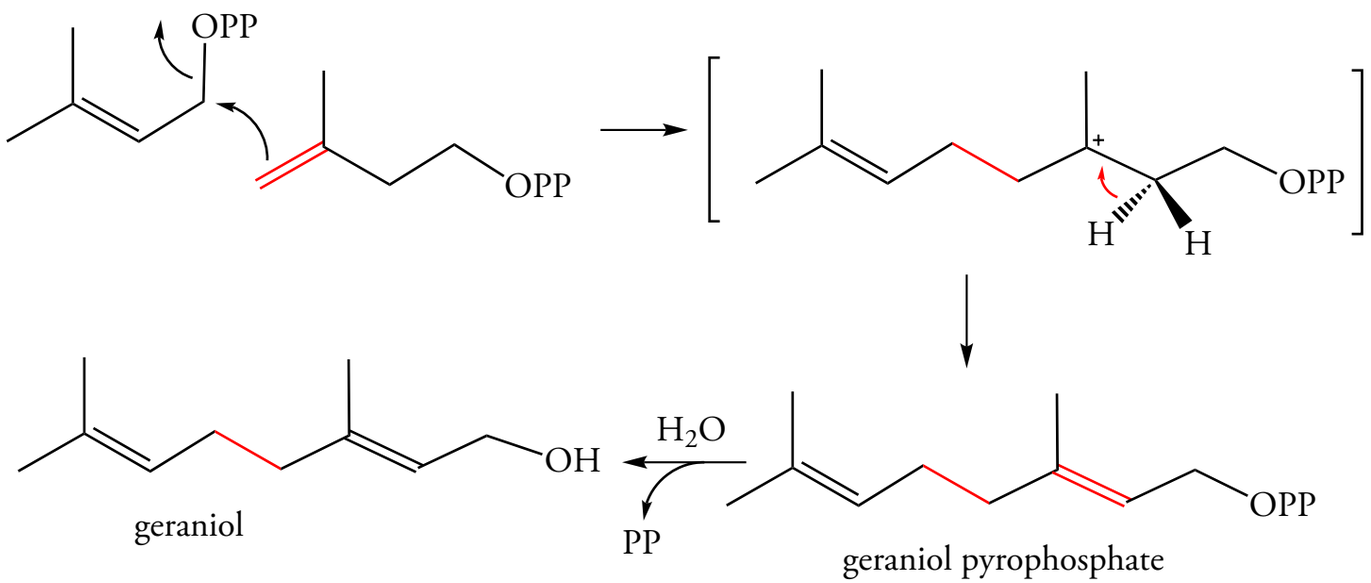
pyrophosphate ester



isopentenyl pyrophosphate



dimethylallyl pyrophosphate

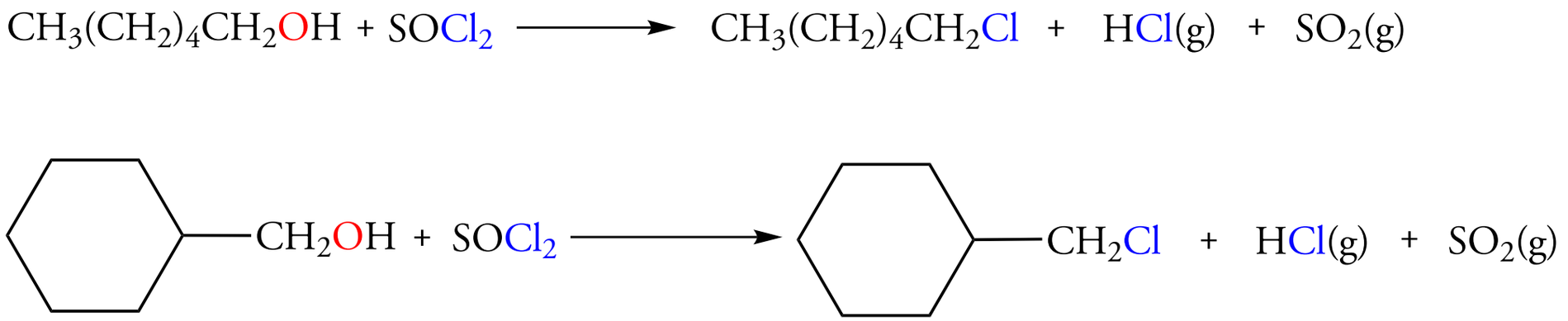


geraniol

geraniol pyrophosphate

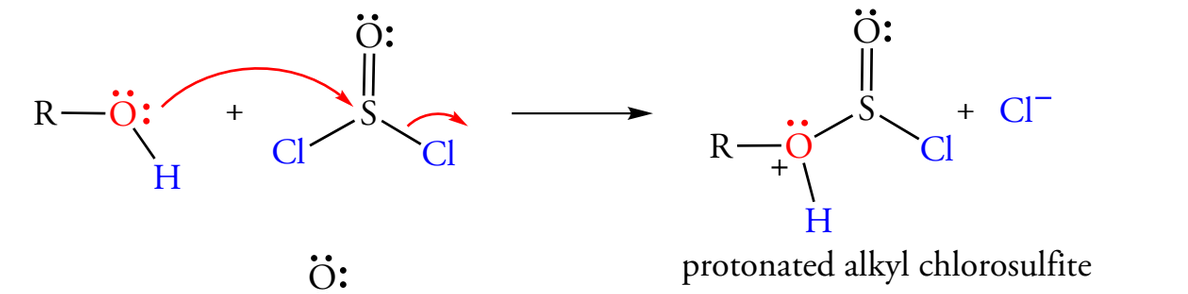
15.3 CONVERSION OF ALCOHOLS TO HALOALKANES

Reaction of Alcohols with Thionyl Chloride

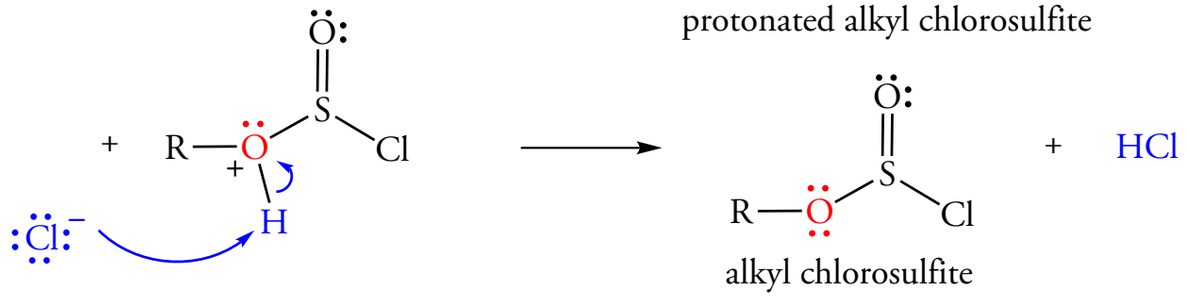


15.3 CONVERSION OF ALCOHOLS TO HALOALKANES

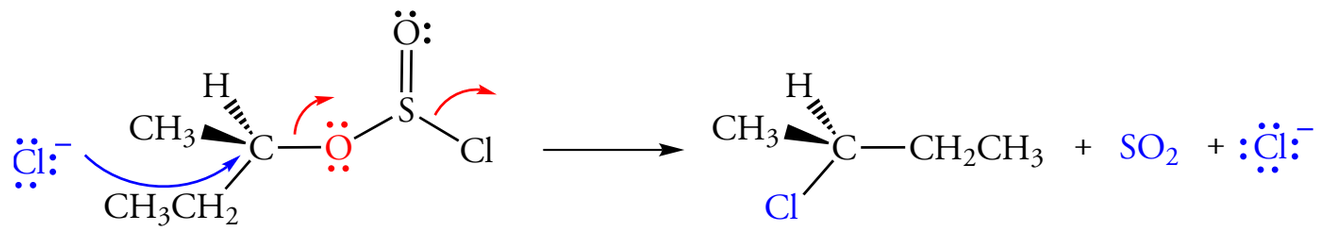
Mechanism of the Reaction of Alcohols with Thionyl Chloride

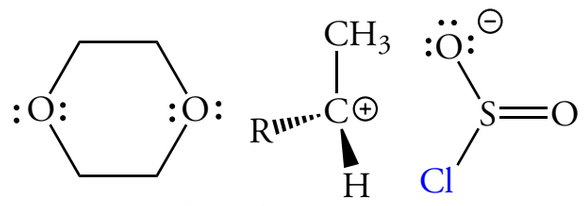


protonated alkyl chlorosulfite

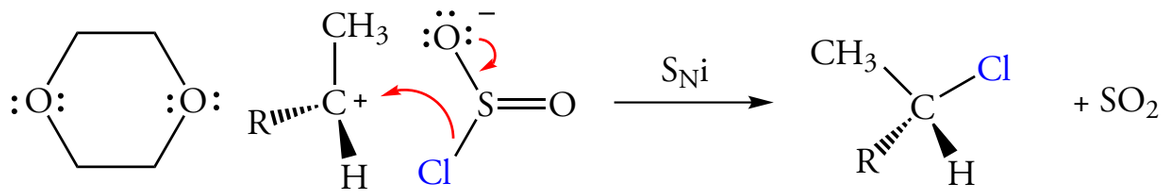


alkyl chlorosulfite





Solvated ion pair

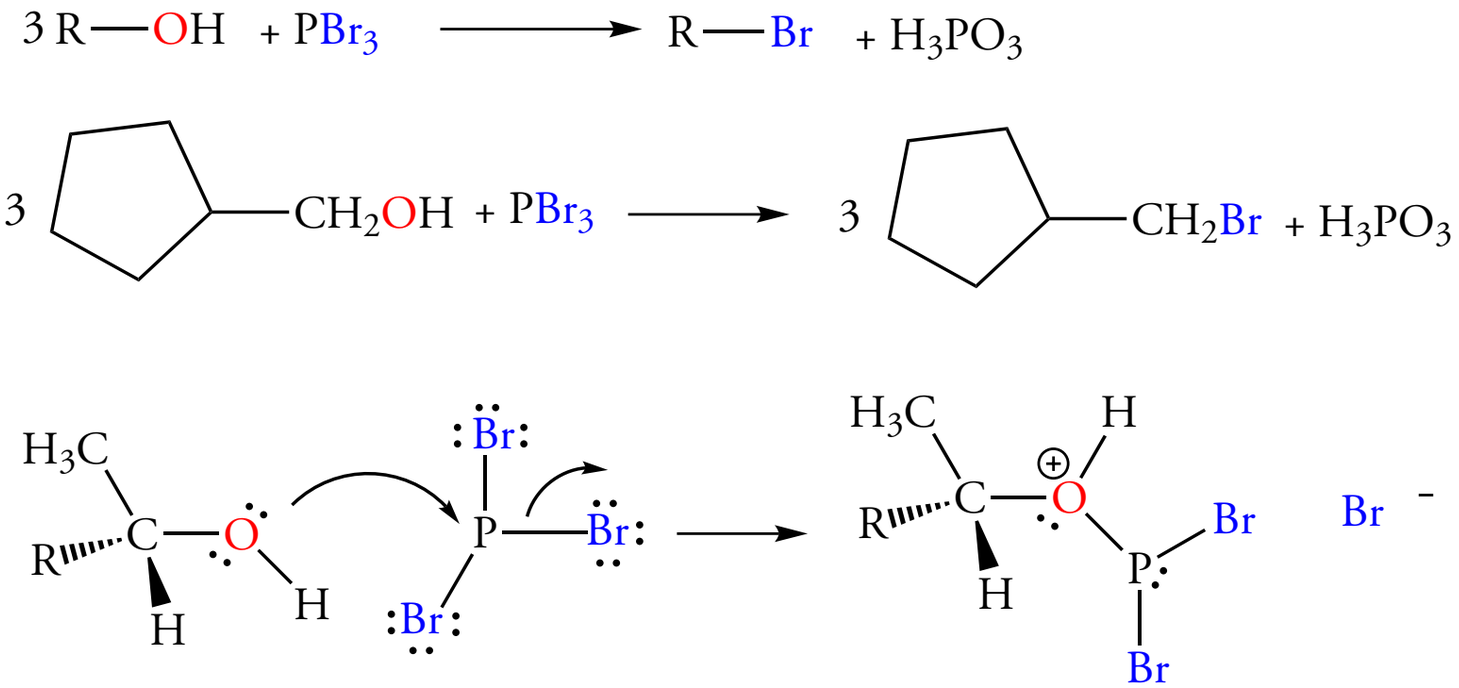


Solvated ion pair

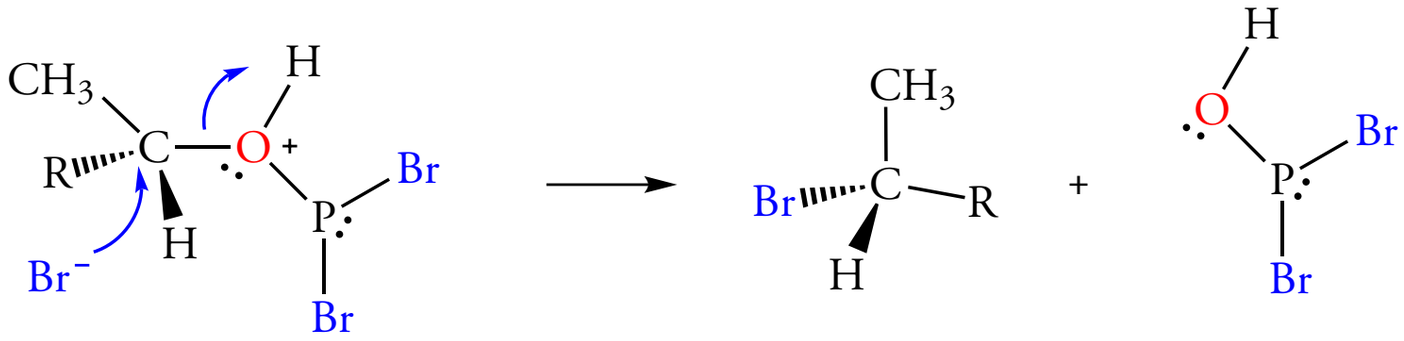
Retention of configuration

15.3 CONVERSION OF ALCOHOLS TO HALOALKANES

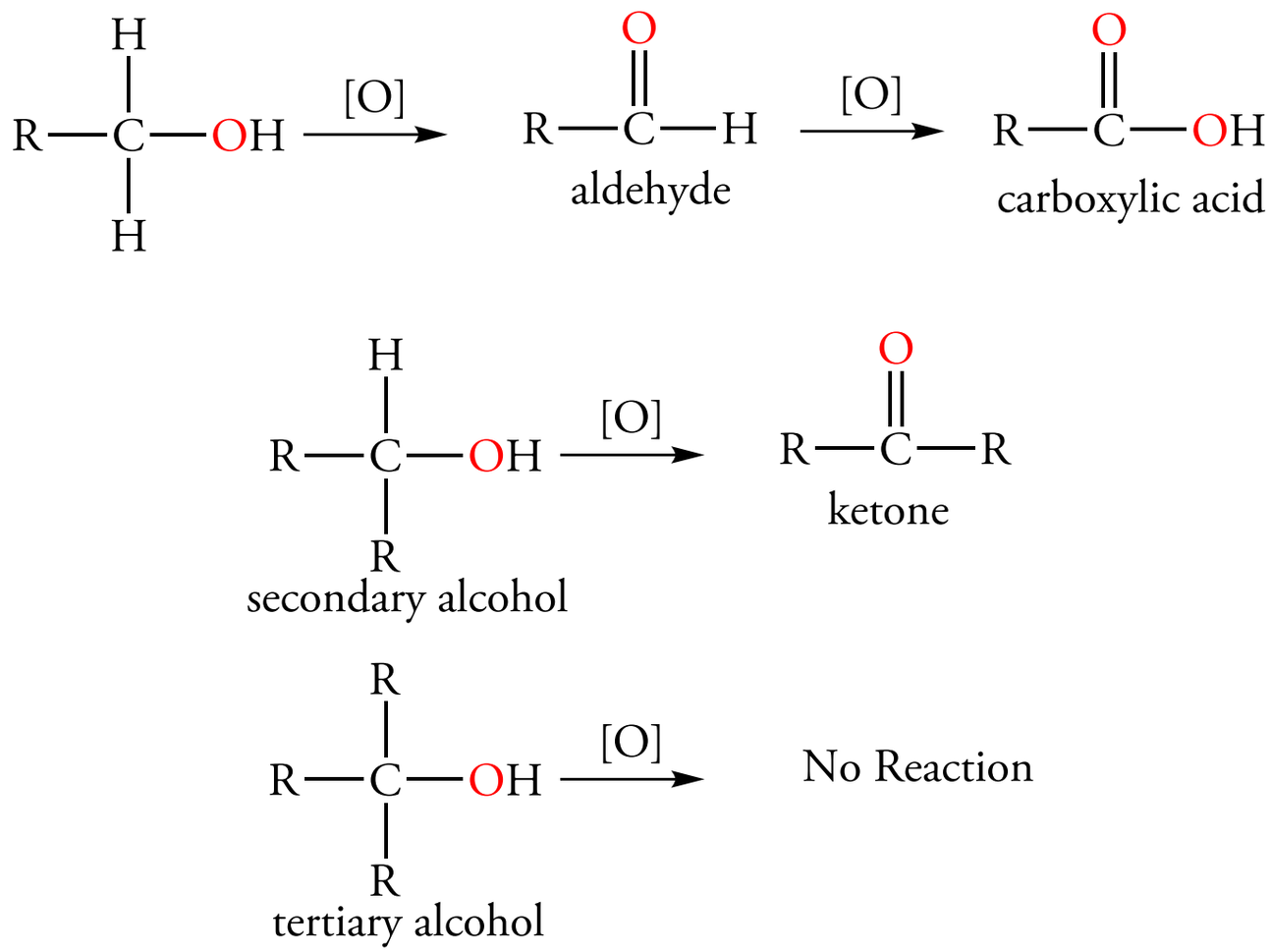
Reaction of Alcohols with Phosphorus Tribromide



protonated phosphite ester

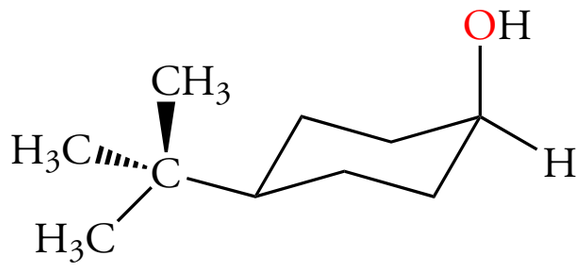


15.4 OXIDATION OF ALCOHOLS

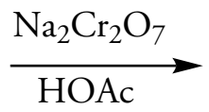


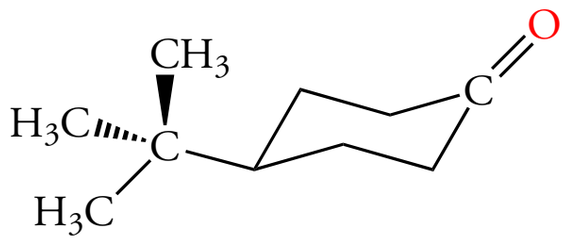
15.4 OXIDATION OF ALCOHOLS

Oxidizing Agents for Alcohols

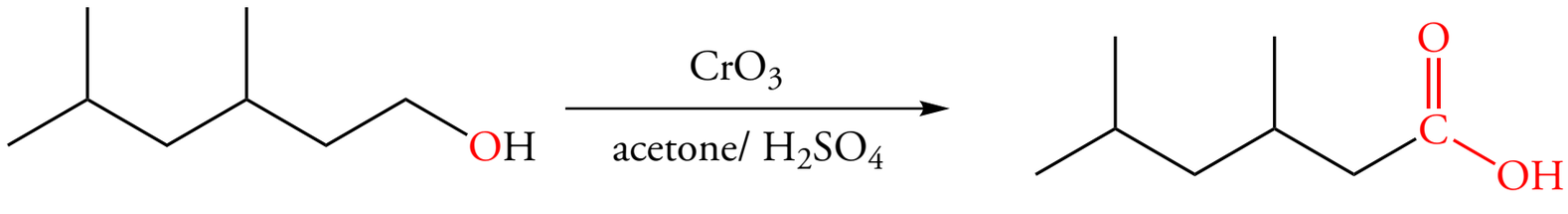


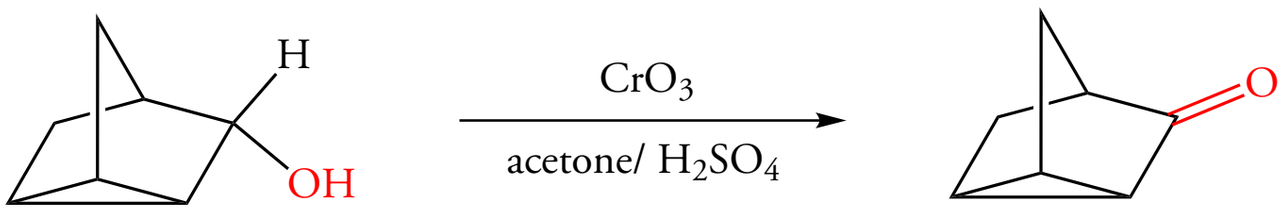
cis-4-tert-butylcyclohexanol

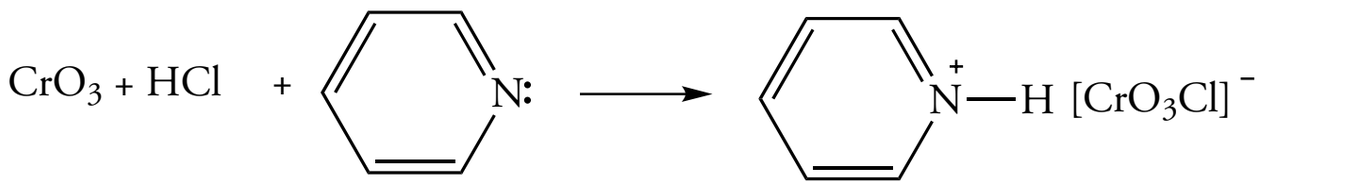




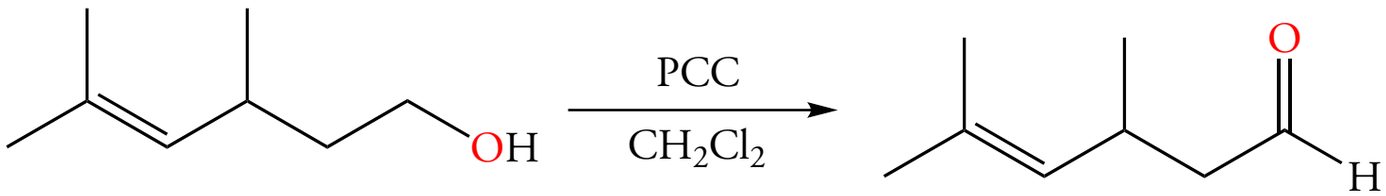
4-tert-butylcyclohexanone





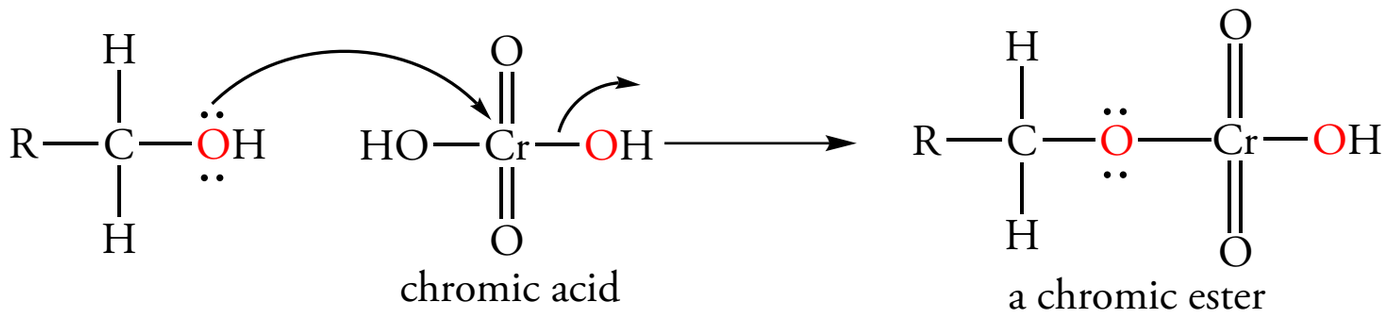


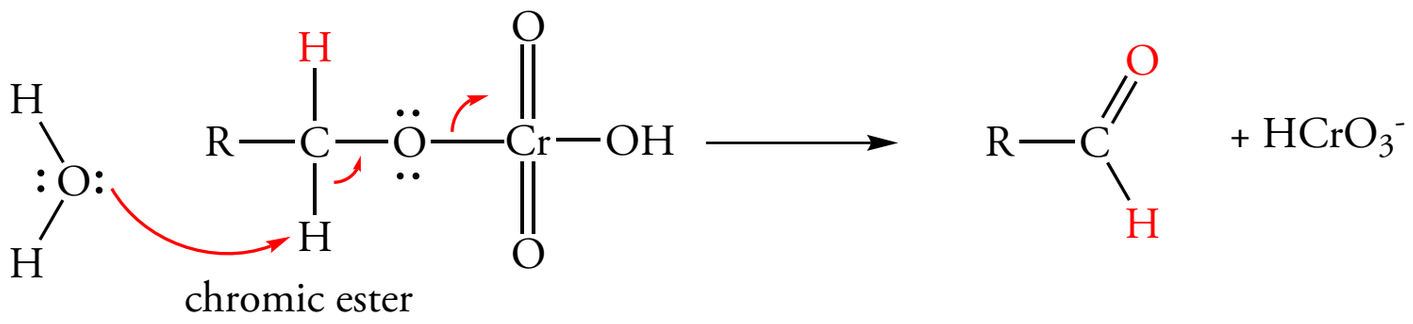
pyridinium chlorochromate (PCC)

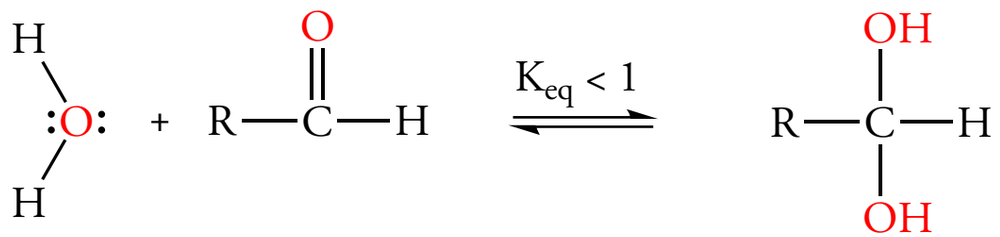


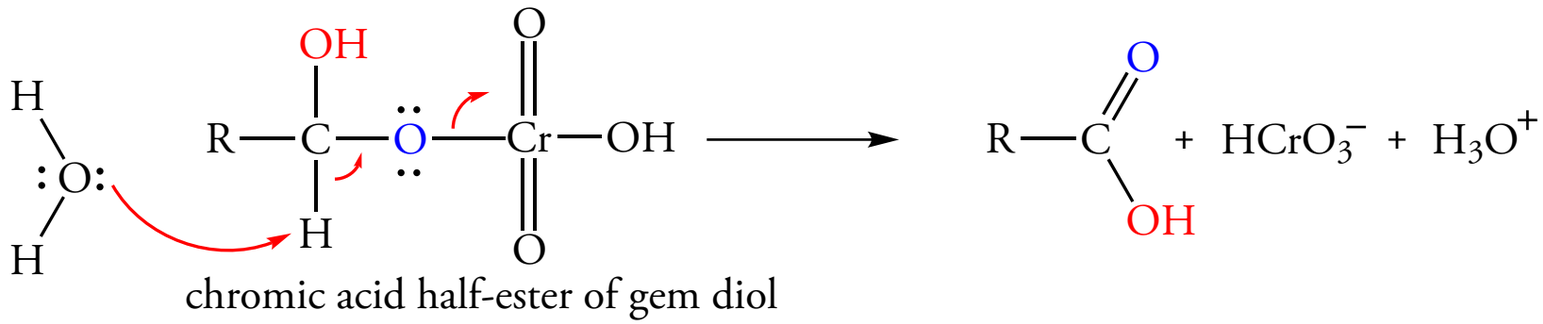
15.4 OXIDATION OF ALCOHOLS

Mechanism of Oxidation by Chromium(VI)

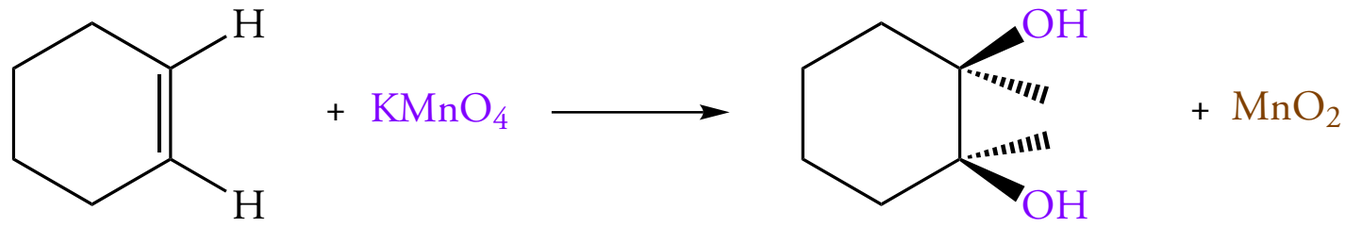


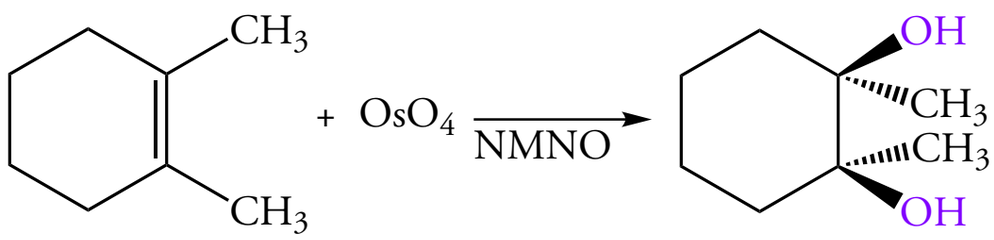


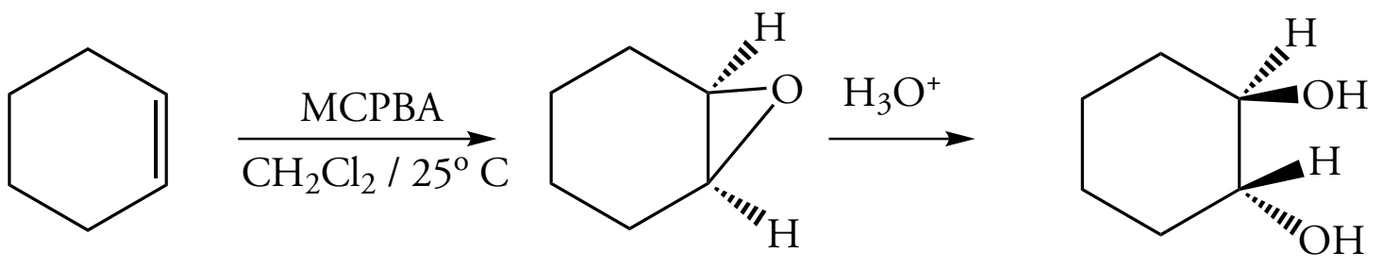




15.5 REACTIONS OF VICINAL DIOLS

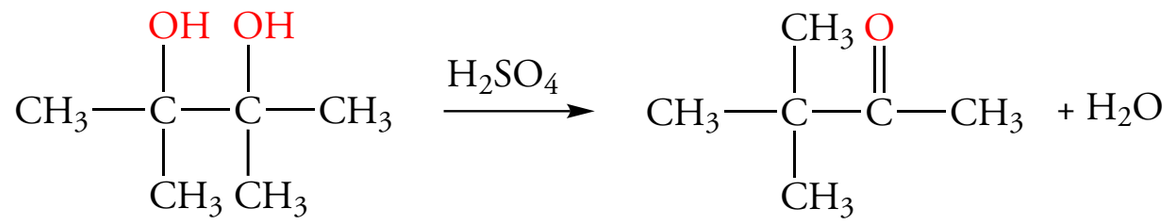




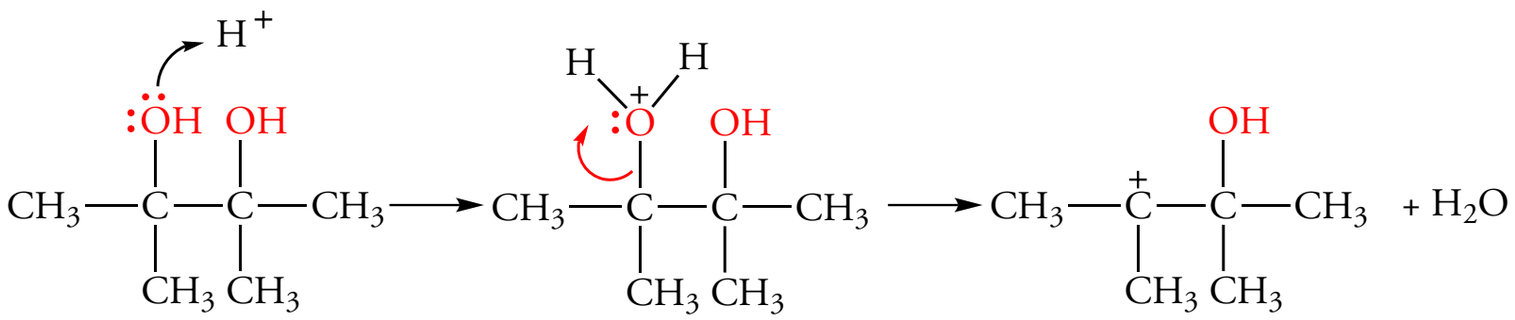


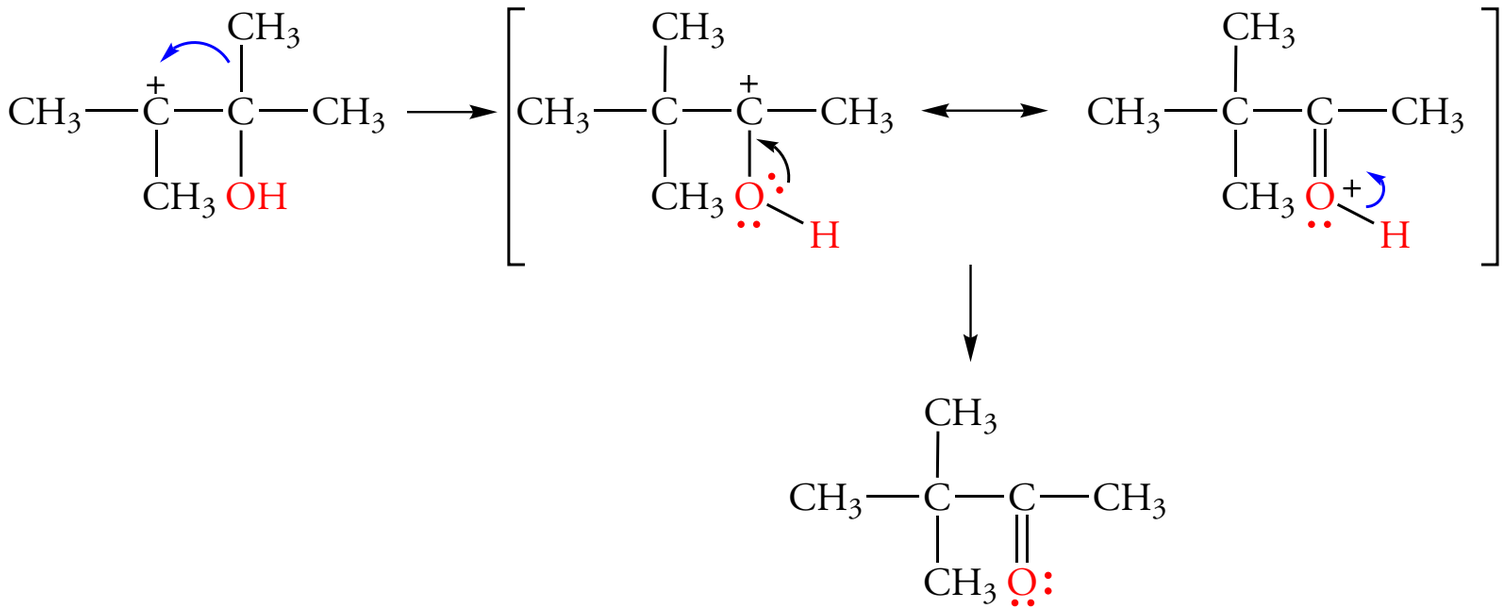
15.5 REACTIONS OF VICINAL DIOLS

The Pinacol Rearrangement



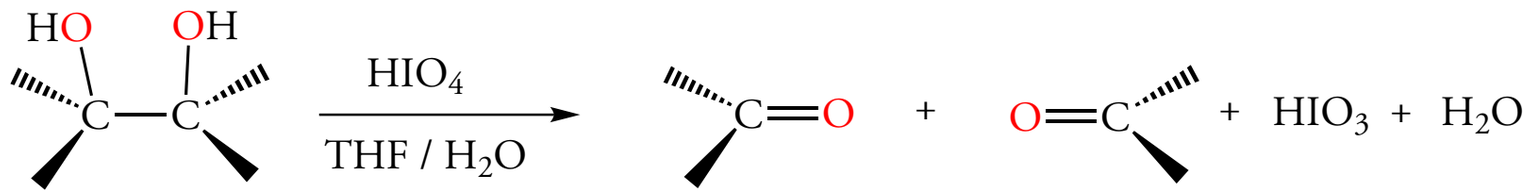
2,3-dimethyl-2,3-butanediol
(pinnacol)



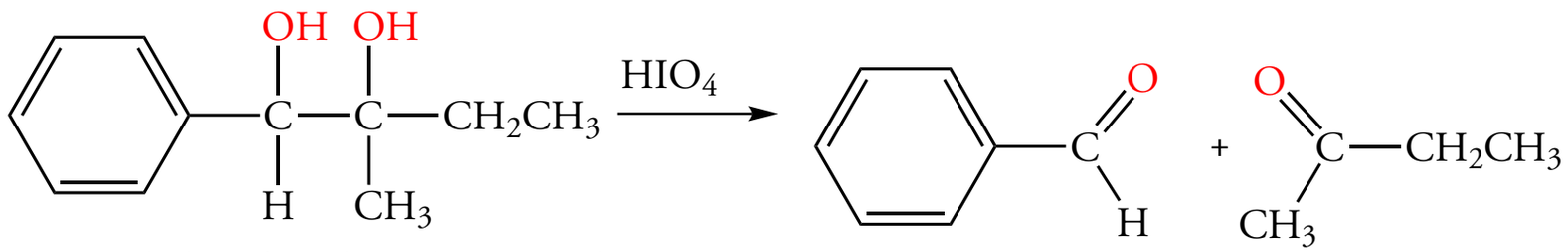


15.5 REACTIONS OF VICINAL DIOLS

Oxidative Cleavage of Vicinal Diols



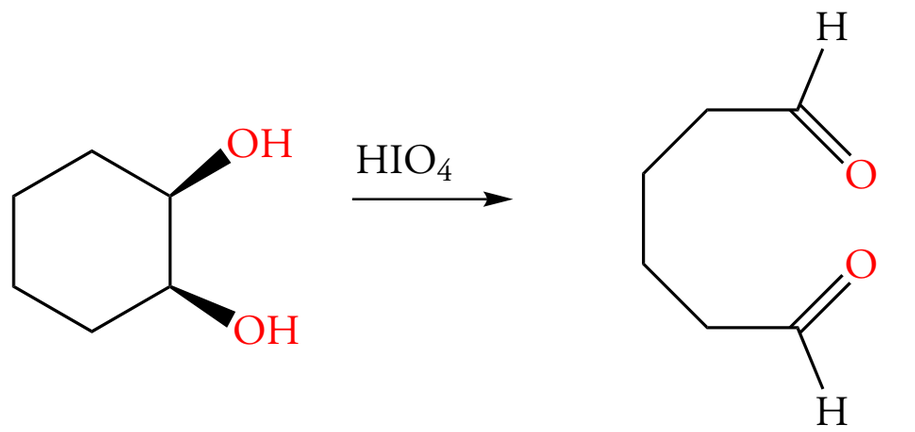
vicinal diol



2-methyl-1-phenyl-1,2-butanediol

benzaldehyde

2-butanone

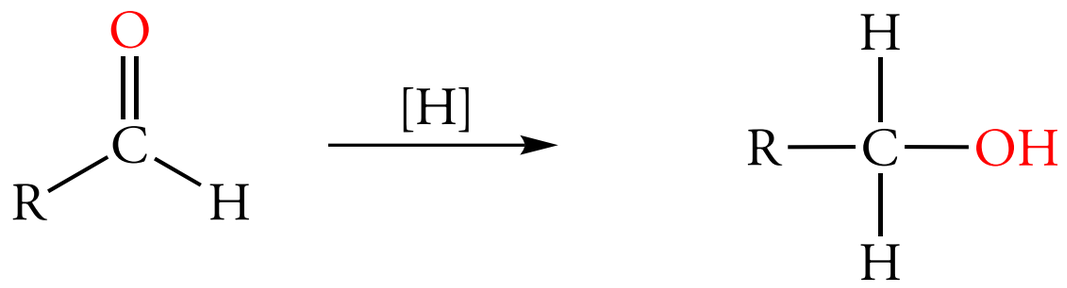


cis-1,2-cyclohexanediol

6-oxohexanal

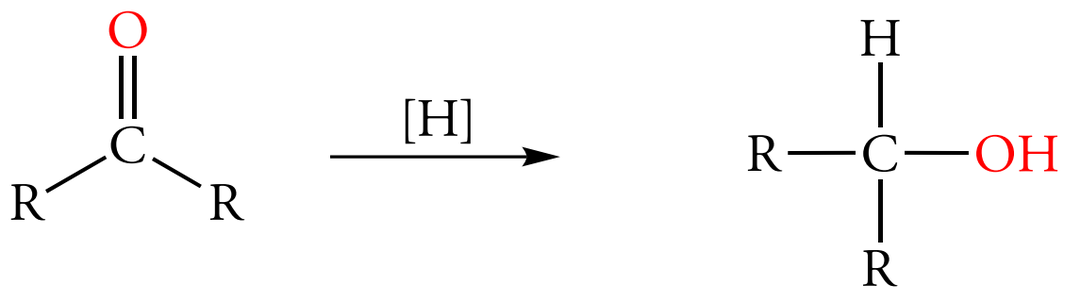
15.6 SYNTHESIS OF ALCOHOLS

Reductive Synthetic Methods



aldehyde

primary alcohol

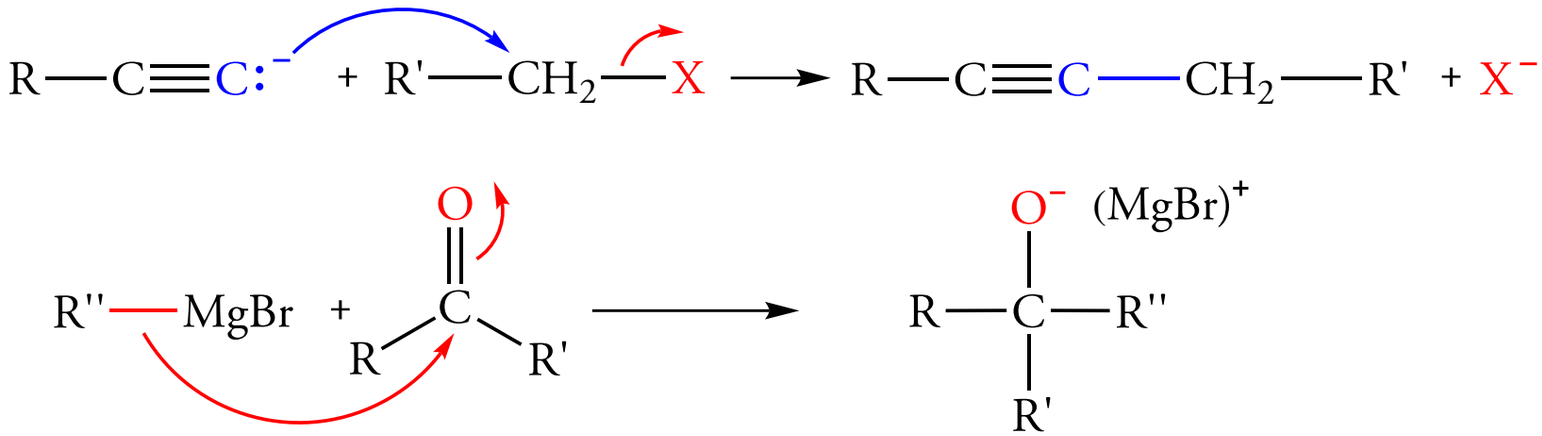


ketone

secondary alcohol

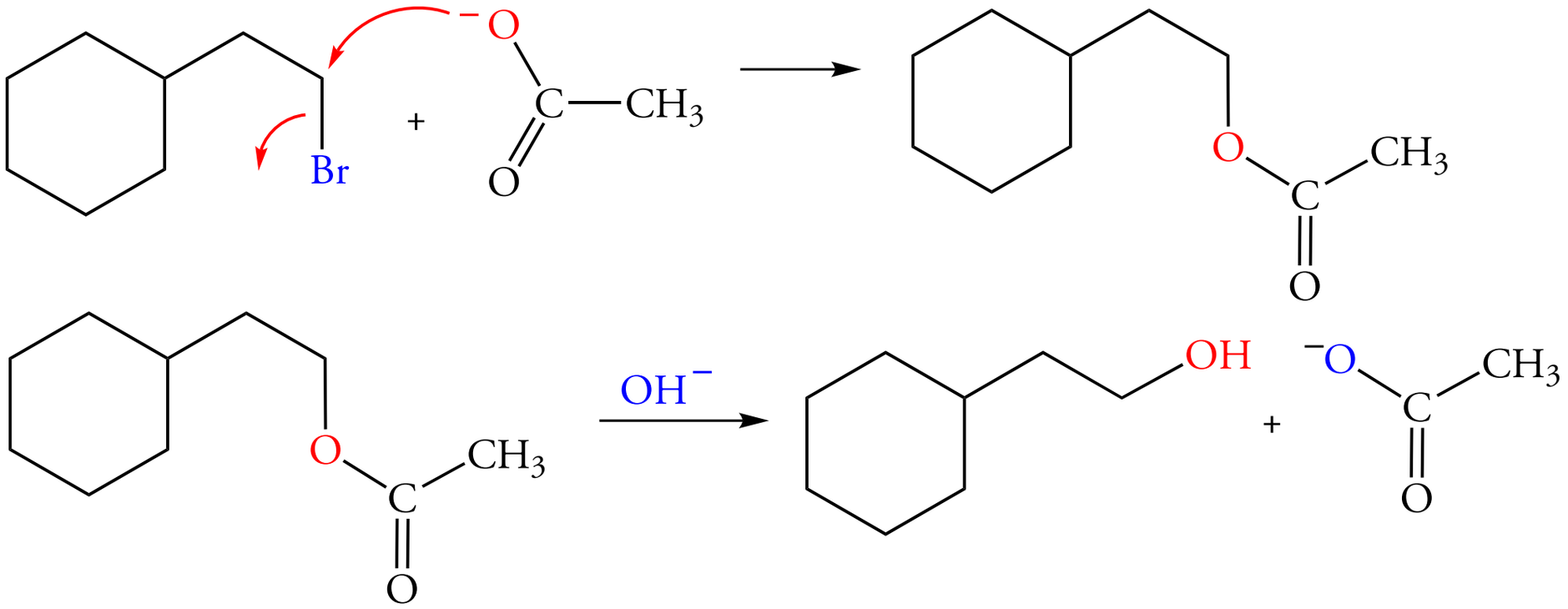
15.6 SYNTHESIS OF ALCOHOLS

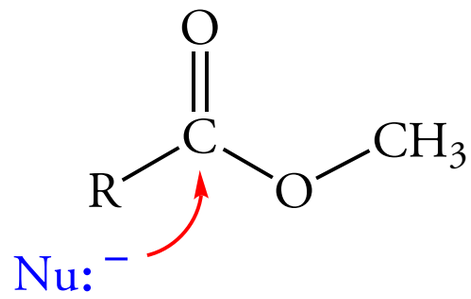
Alkylation Synthetic Methods



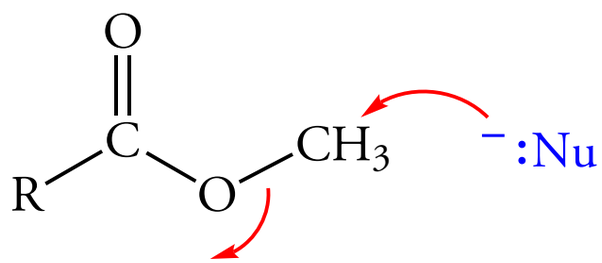
alkoxide ion,
(salt is neutralized to give alcohol)

15.7 SYNTHESIS OF ALCOHOLS FROM HALOALKANES





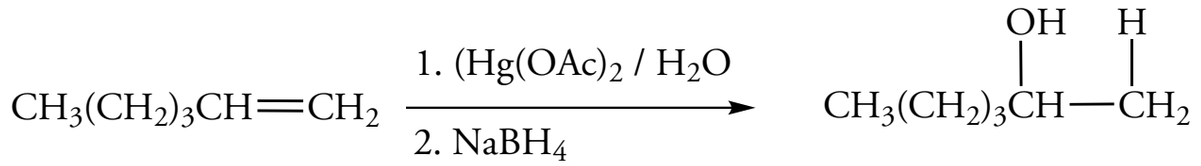
favored mode of attack

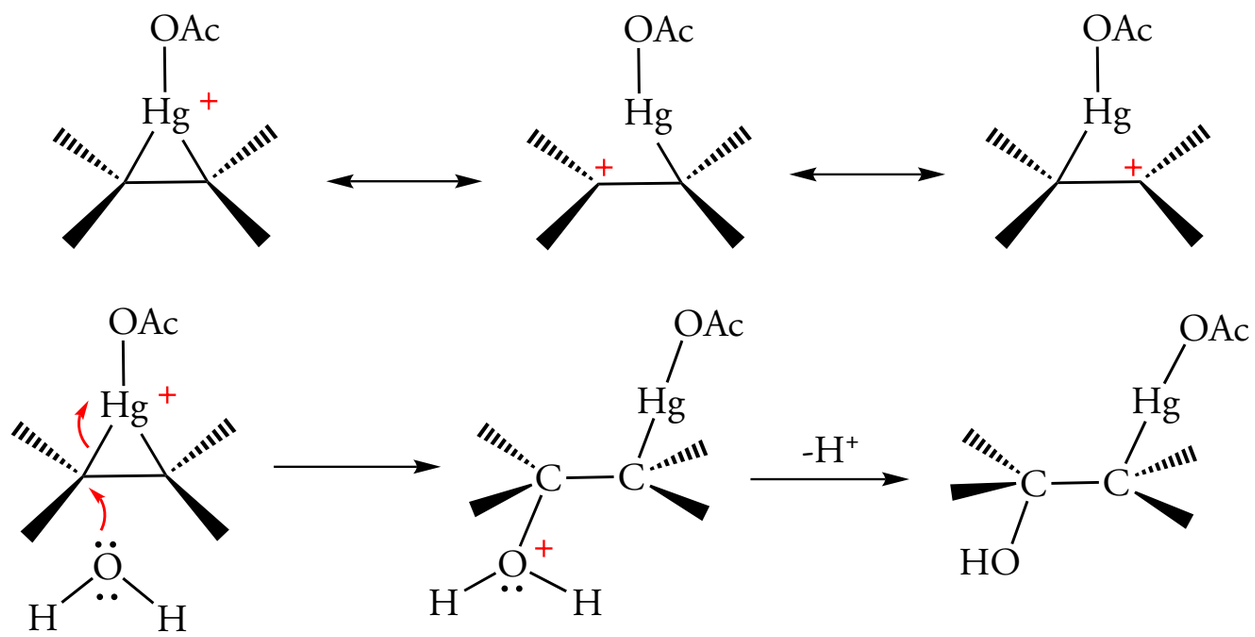


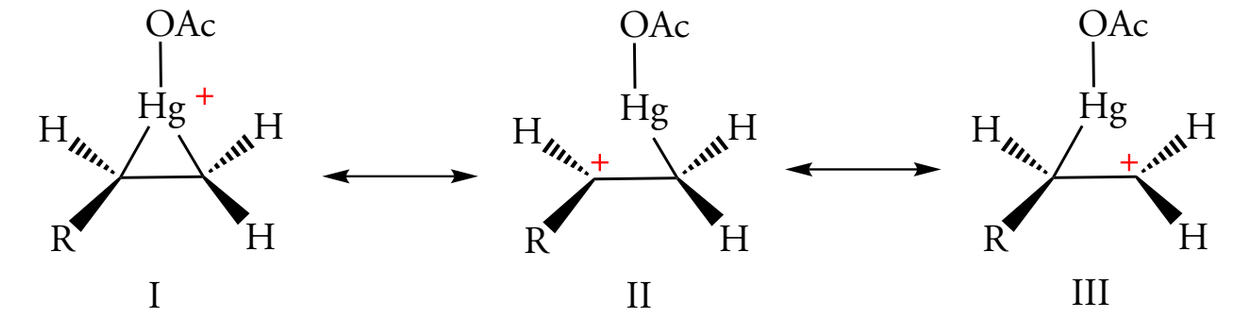
less favored mode of attack

15.8 INDIRECT HYDRATION METHODS

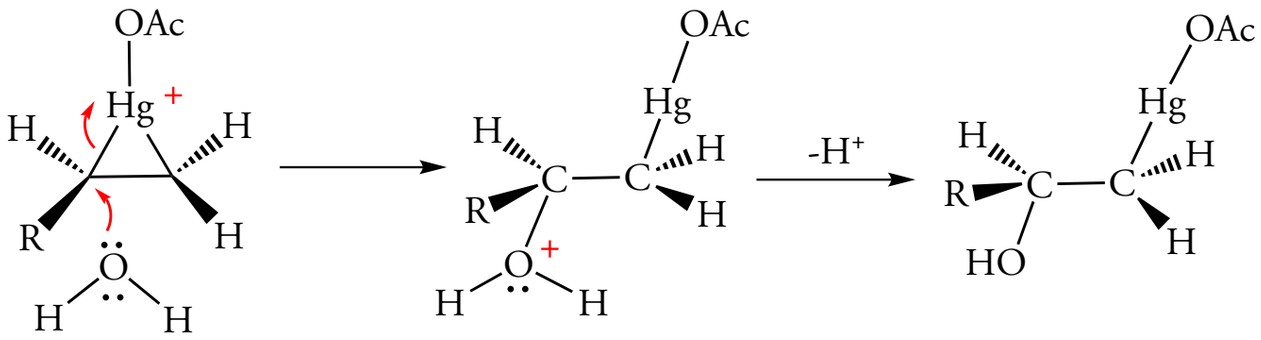
Oxymercuration-Demercuration





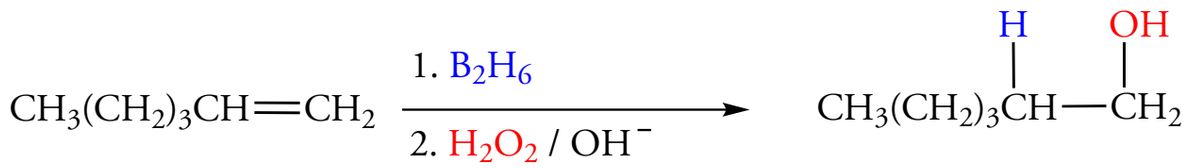


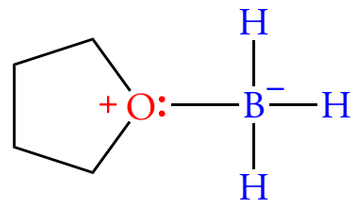
mercurinium ion of a terminal, monosubstituted alkene



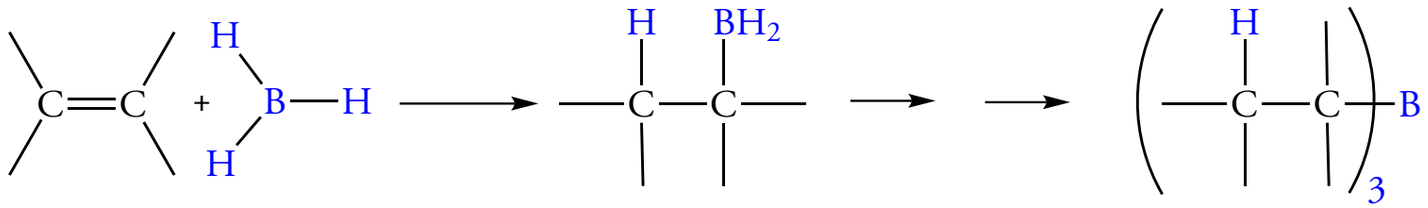
15.8 INDIRECT HYDRATION METHODS

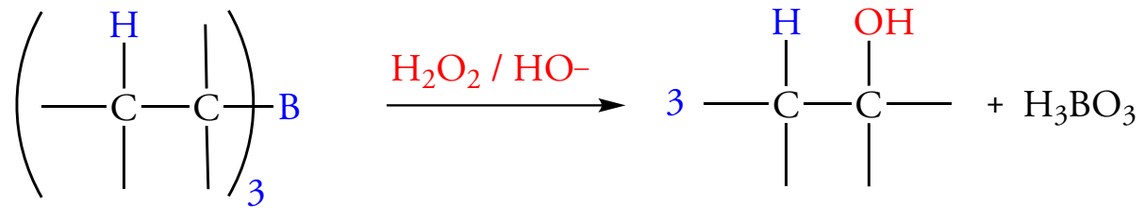
Hydroboration-Oxidation



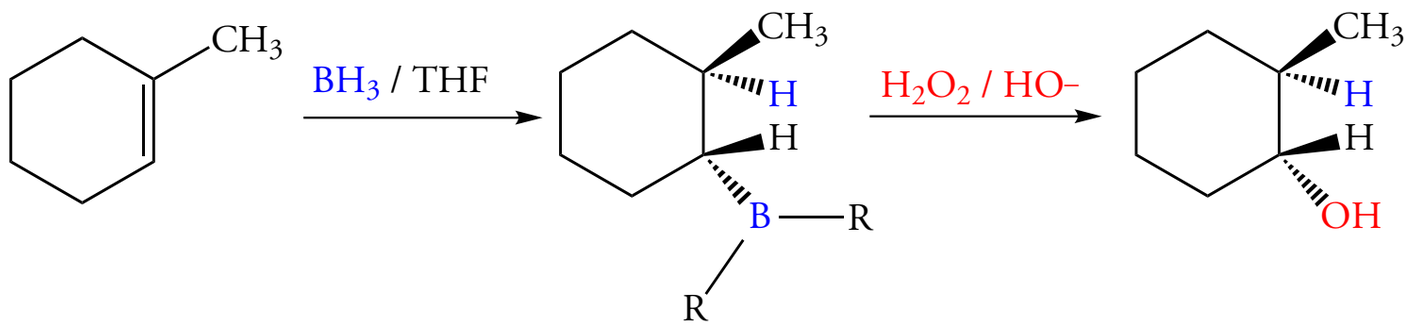


BH_3-tetrahydrofuran complex





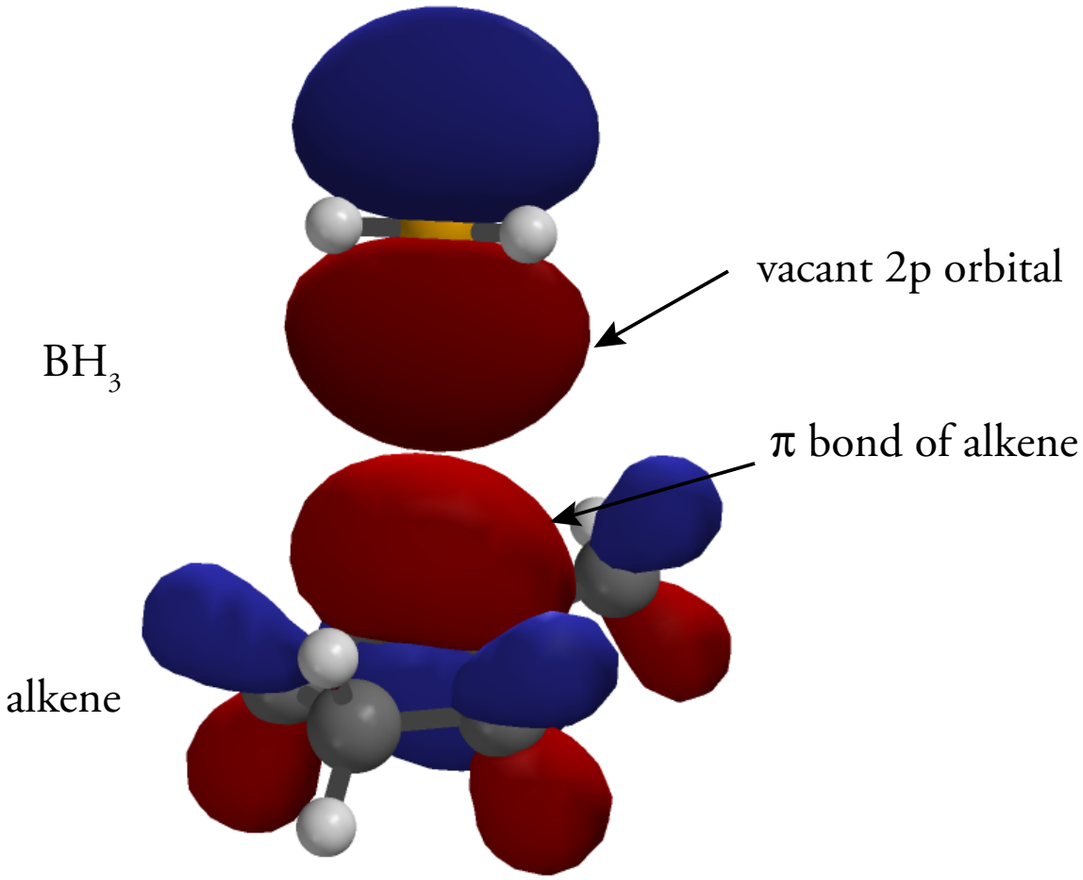
trialkylborane



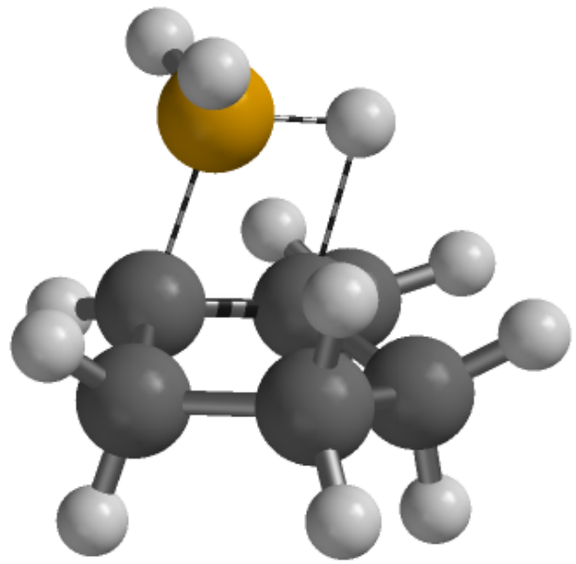
trialkylborane

syn addition

Figure 15.1 Transition State Structure for Hydroboration

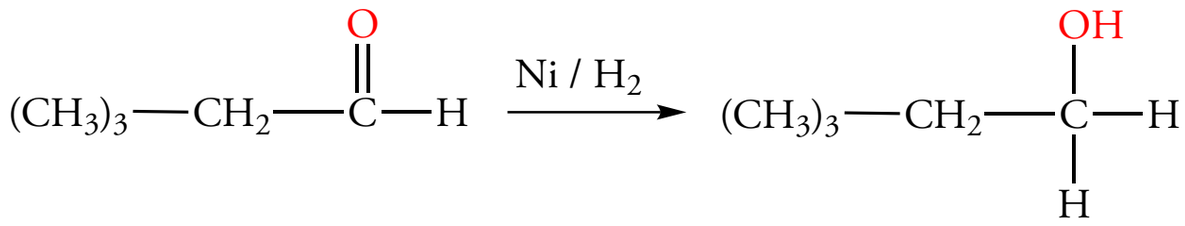


(a) Orbital interaction in the transition state of alkene hydroboration



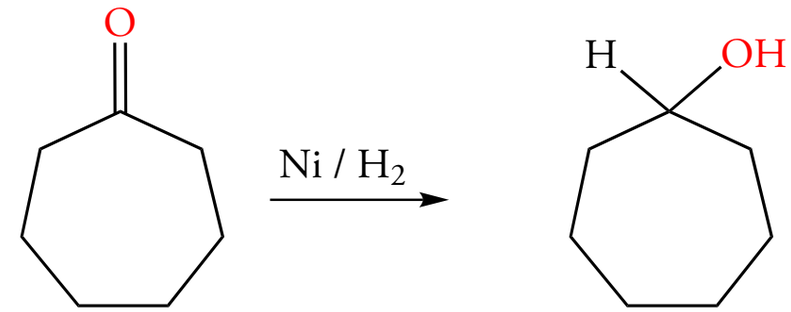
(b) Ball-and-stick-model of the transition state of alkene hydroboration

15.9 REDUCTION OF CARBONYL COMPOUNDS



3,3-dimethylbutanal

3,3-dimethylbutanol

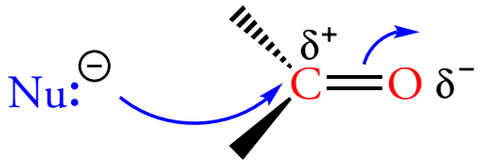


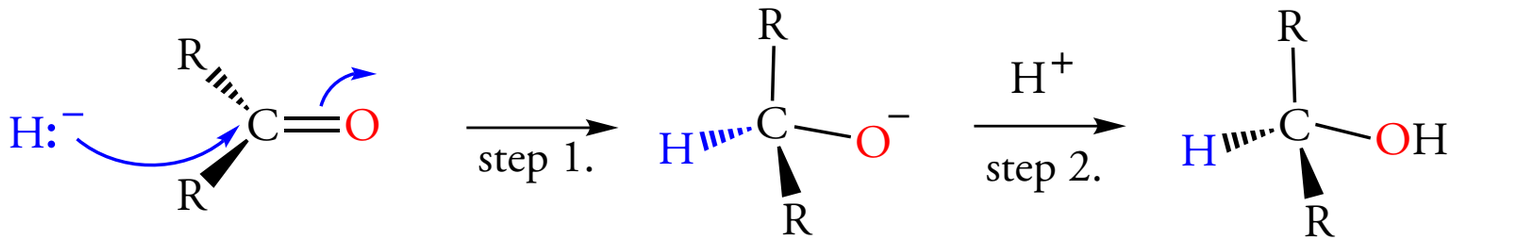
cycloheptanone

cycloheptanol

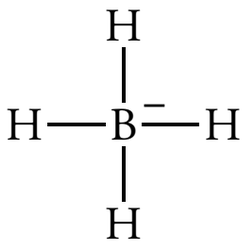
15.9 REDUCTION OF CARBONYL COMPOUNDS

Reduction by Metal Hydrides

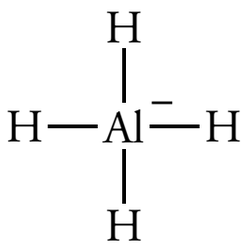




ketone alkoxide ion secondary alcohol



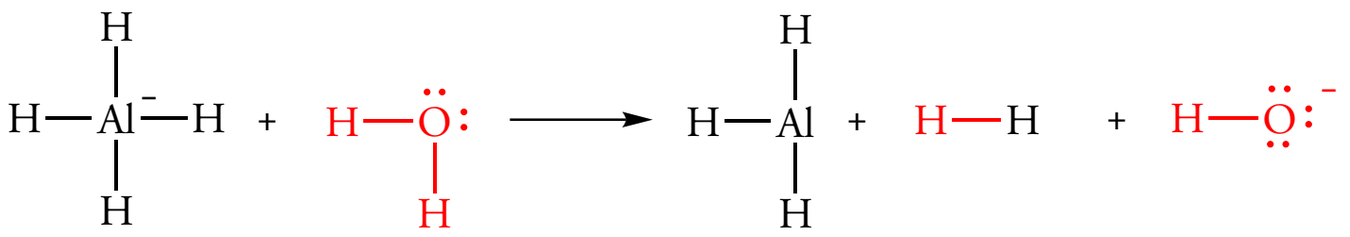
borohydride anion



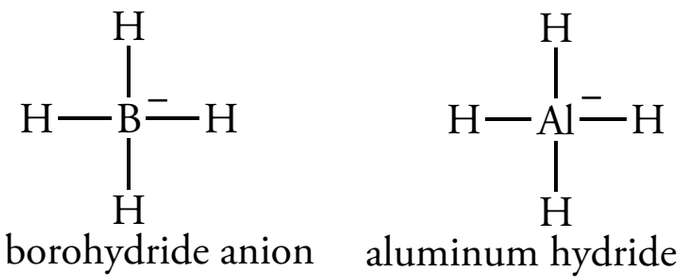
aluminum hydride anion

15.9 REDUCTION OF CARBONYL COMPOUNDS

Solvents for Lithium Aluminum Hydride and Sodium Borohydride



$$AlH_4^- + 4\ H_2O \longrightarrow [Al(OH_4)]^- + 4\ H_2$$



borohydride anion

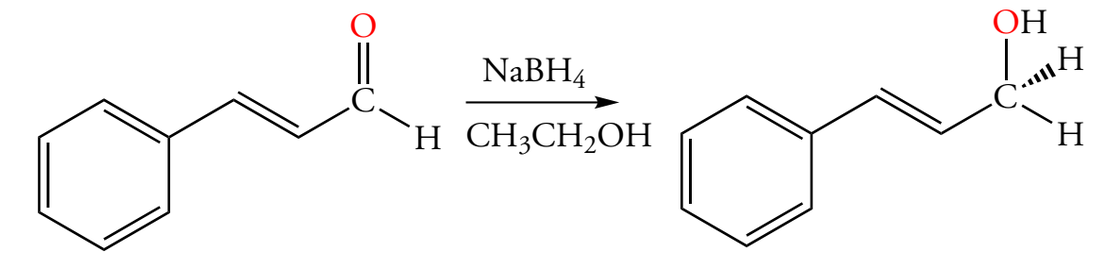
aluminum hydride anion

$$NaBH_4 + 4\ CH_3CH_2OH \xrightarrow{\text{slow}} Na^+ [B(OCH_2CH_3)_4]^- + 4\ H_2$$

$$LiAlH_4 + 4\ CH_3CH_2OH \xrightarrow{\text{fast}} Li^+ [B(OCH_2CH_3)_4]^- + 4\ H_2$$

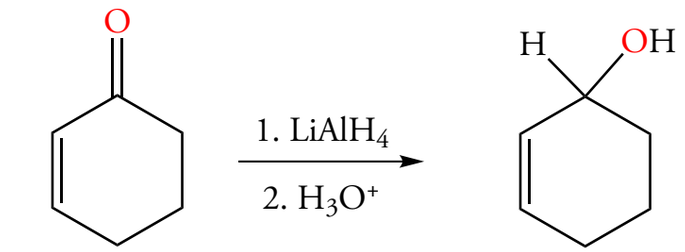
15.9 REDUCTION OF CARBONYL COMPOUNDS

Regioselectivity of Hydride Reduction



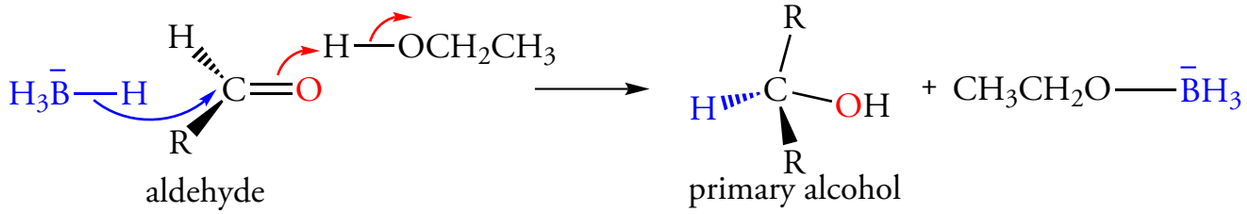
(E)-3-phenyl-2-propenal

(E)-3-phenyl-2-propen-1ol



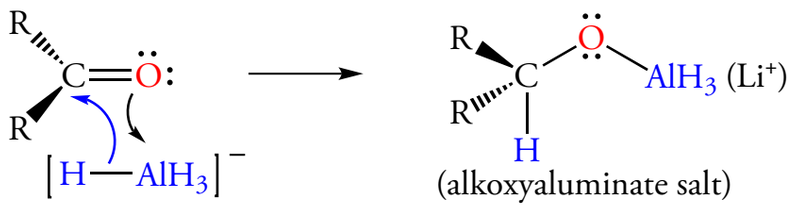
3-cyclohexenone

3-cyclohexenol

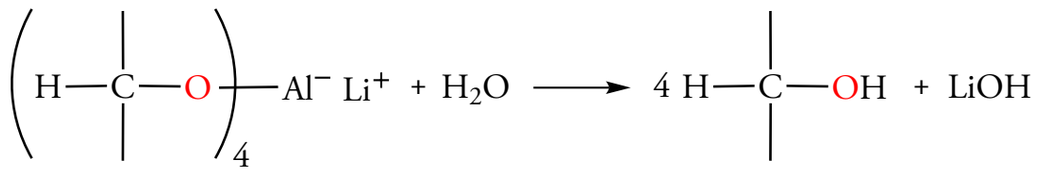


aldehyde

primary alcohol



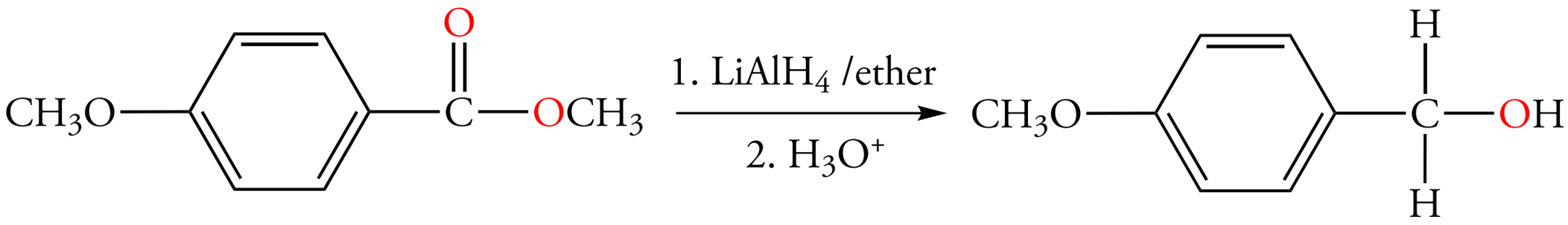
(alkoxyaluminate salt)



(alkoxyaluminate salt)

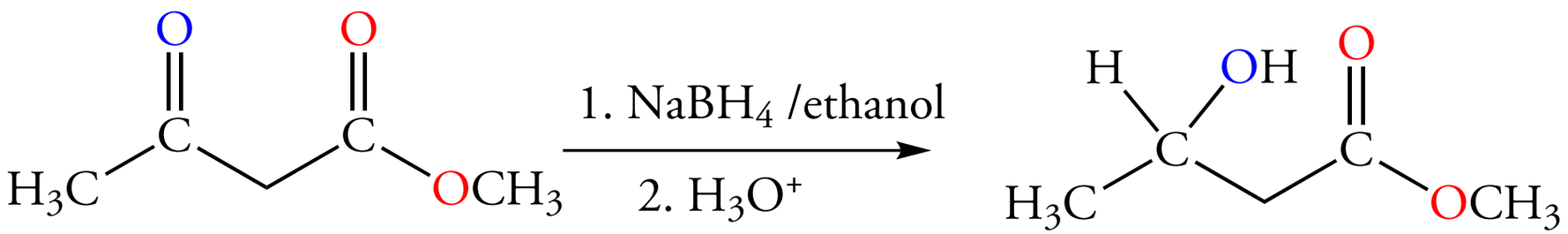
15.9 REDUCTION OF CARBONYL COMPOUNDS

Reduction of Other Carbonyl Compounds



methyl p-methoxybenzoate

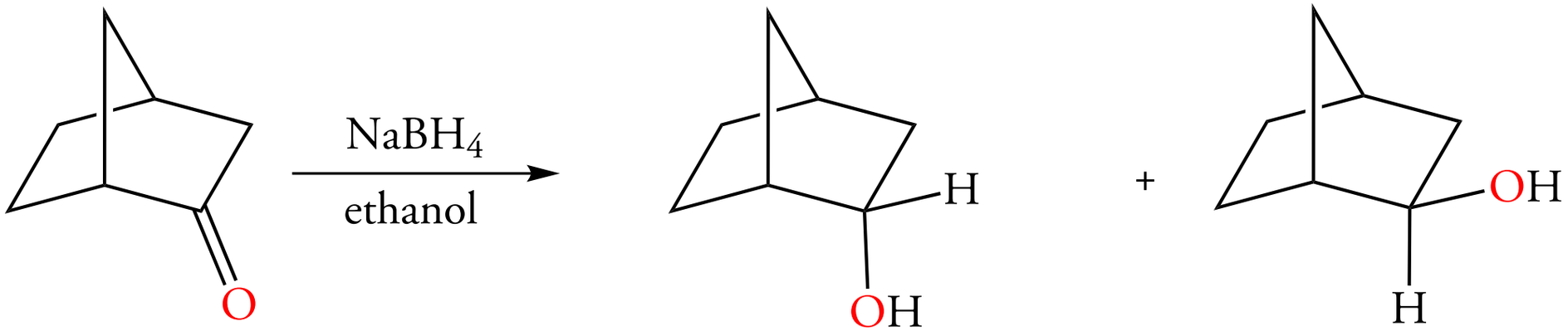
p-methoxybenzyl alcohol



Only the ketone is reduced.

15.9 REDUCTION OF CARBONYL COMPOUNDS

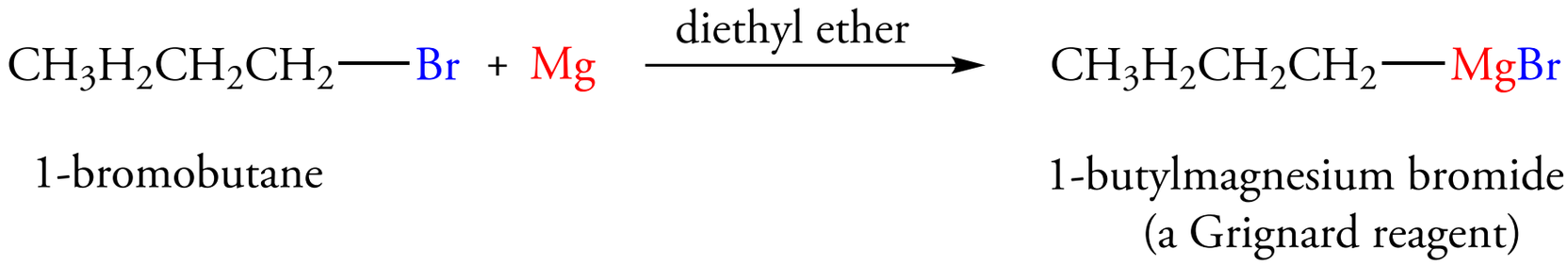
Stereoselectivity of Metal Hydride Reduction

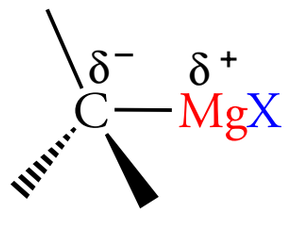


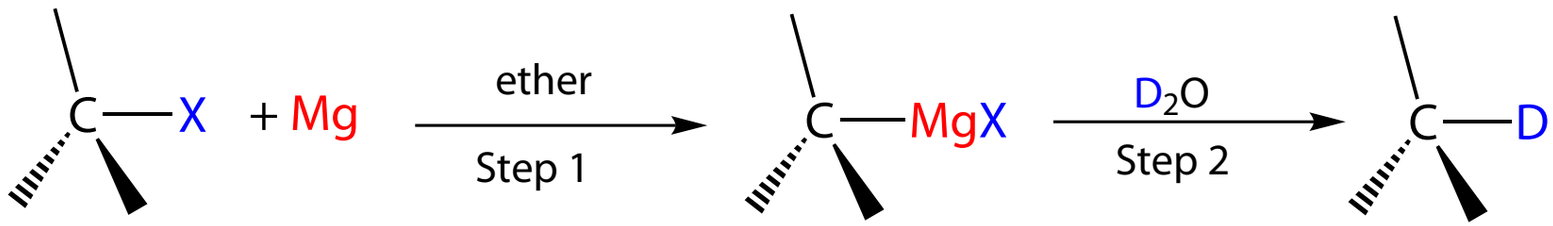
endo 86%
bicyclo[2.2.1]heptan-2-ol

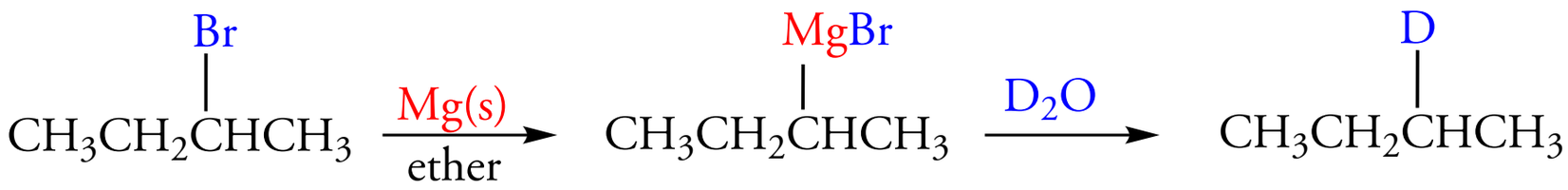
exo (14%)
bicyclo[2.2.1]heptan-2-ol

15.10 ALCOHOL SYNTHESIS USING GRIGNARD REAGENTS



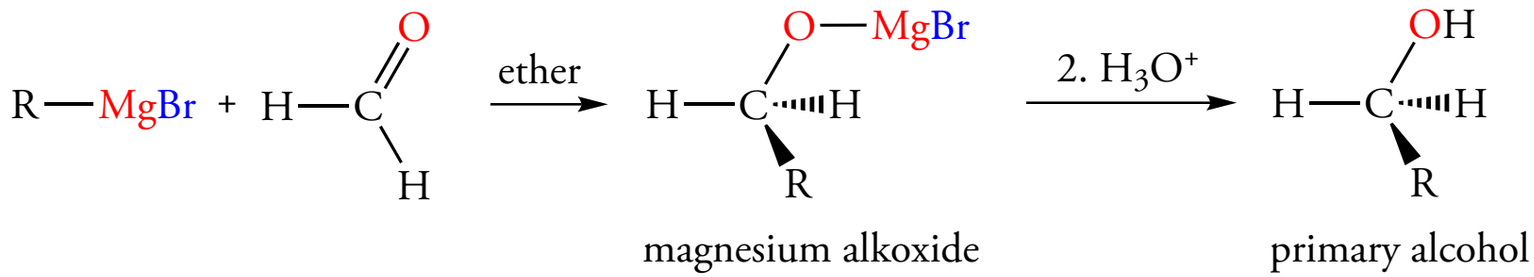






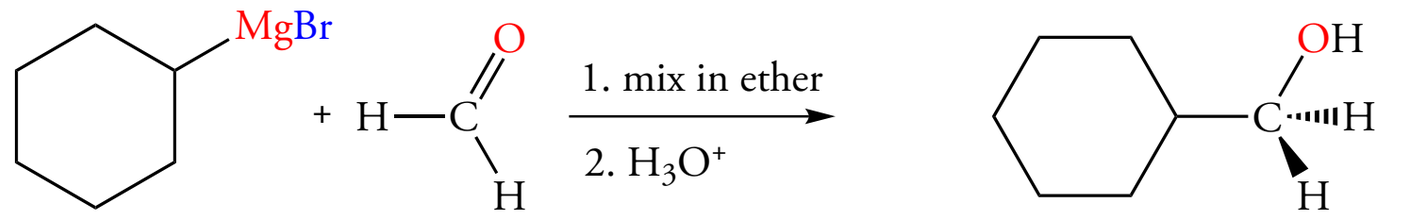
15.10 ALCOHOL SYNTHESIS USING GRIGNARD REAGENTS

Synthesis of Alcohols Using Grignard Reagents

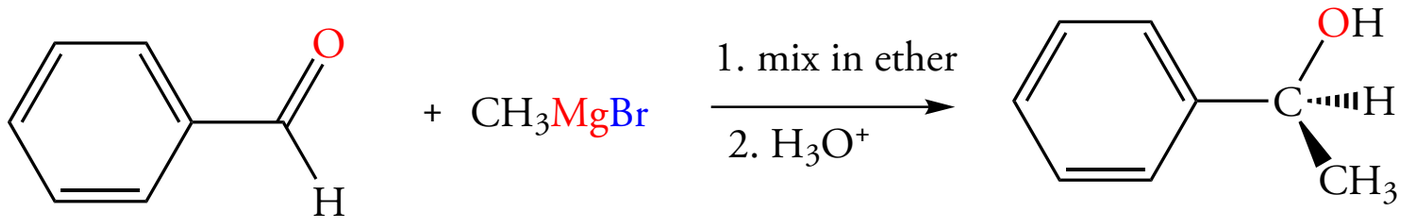


magnesium alkoxide

primary alcohol

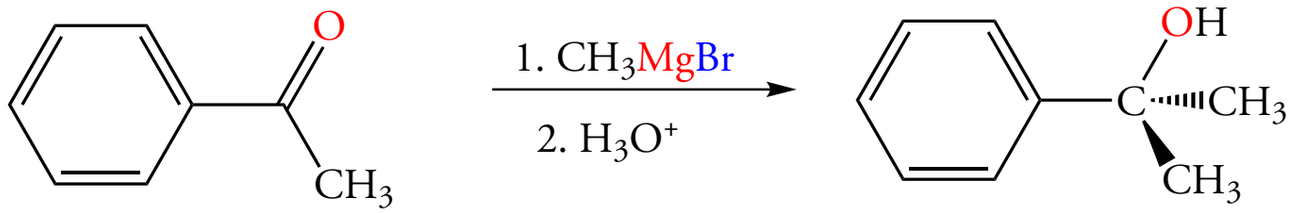


primary alcohol



aldehyde

secondary alcohol

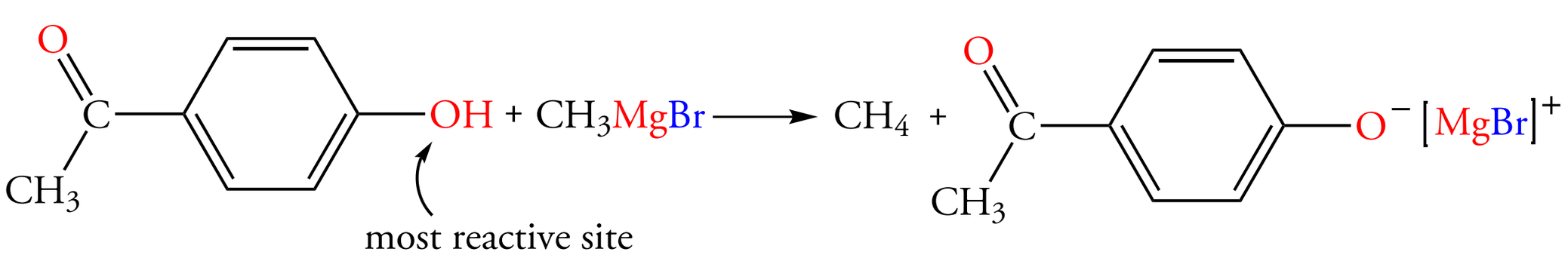


ketone

tertiary alcohol

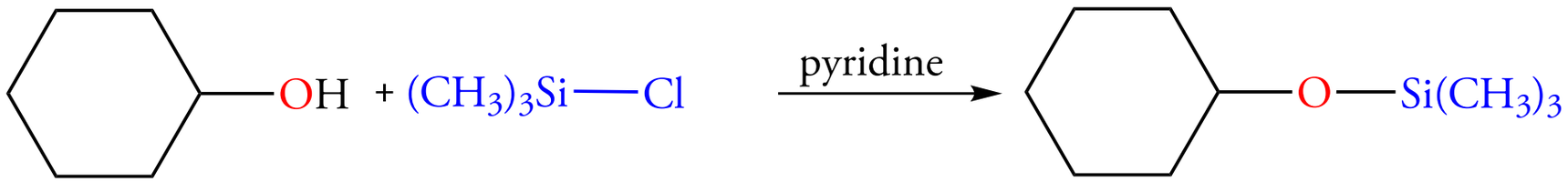
15.10 ALCOHOL SYNTHESIS USING GRIGNARD REAGENTS

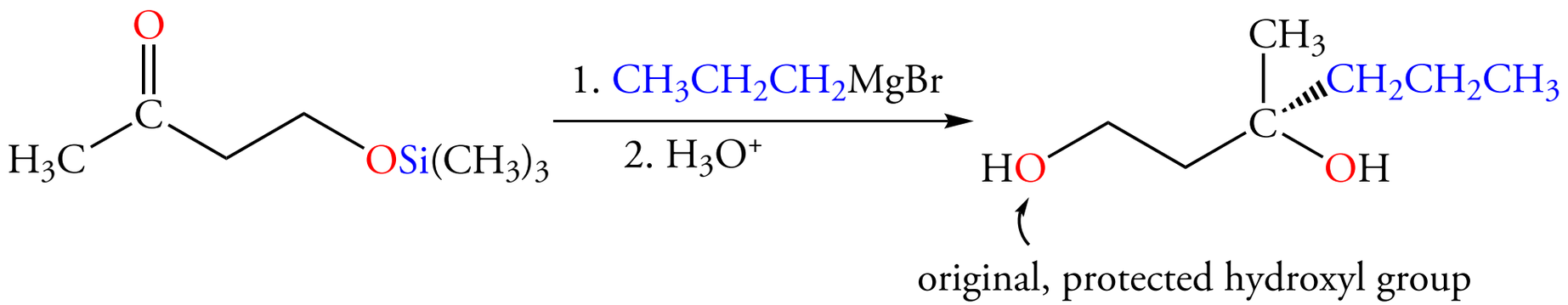
Limitations of the Grignard Reaction



15.10 ALCOHOL SYNTHESIS USING GRIGNARD REAGENTS

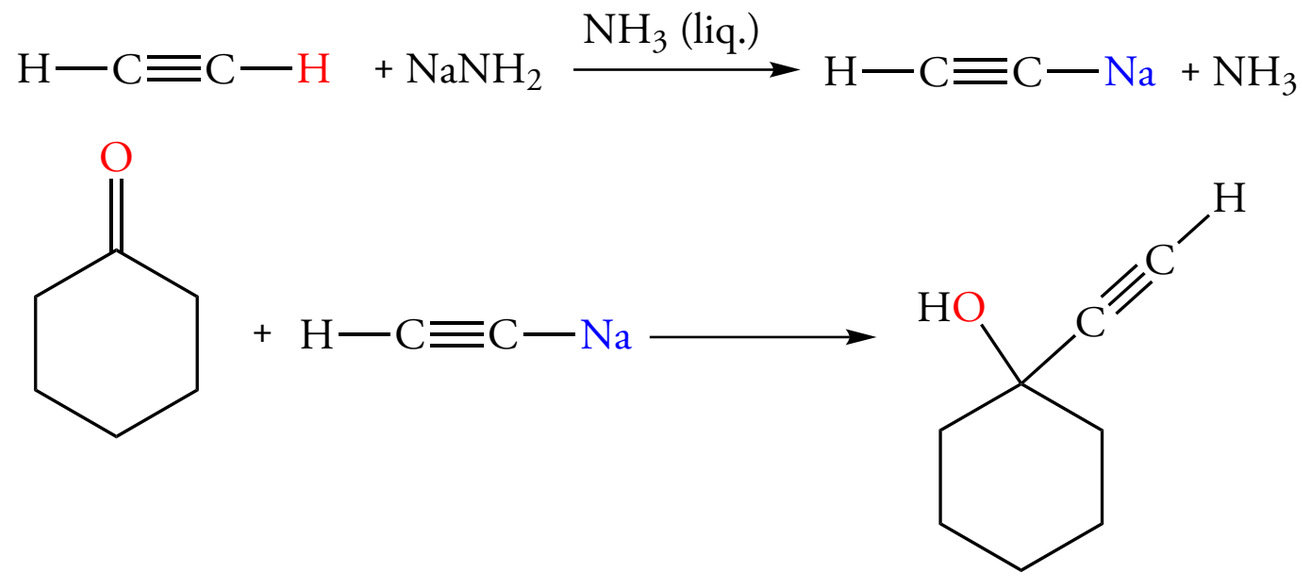
Alcohol Protecting Groups





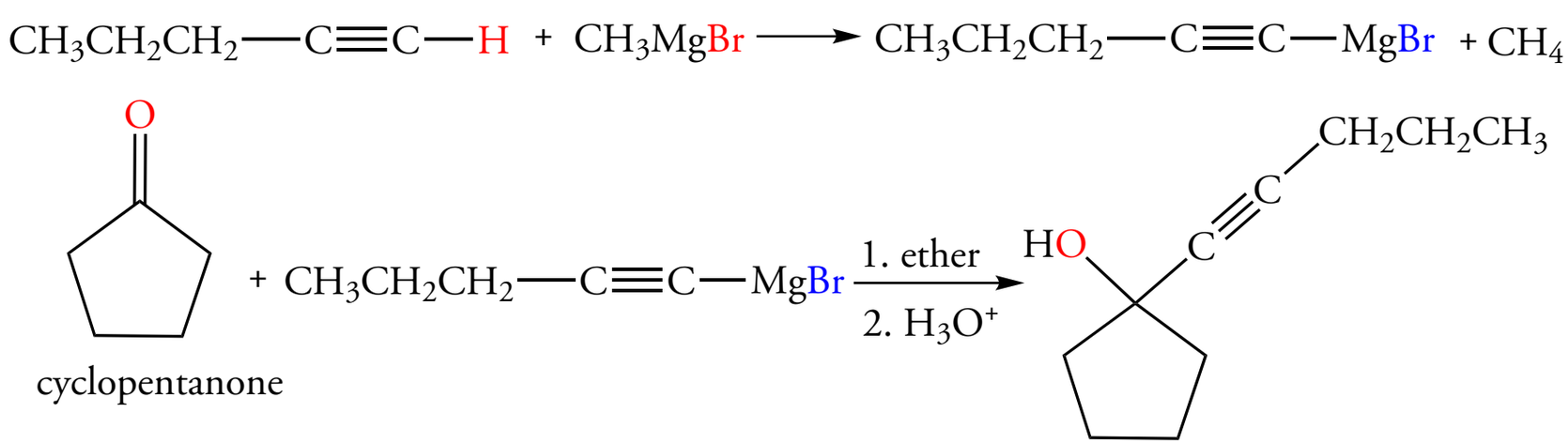
15.10 ALCOHOL SYNTHESIS USING GRIGNARD REAGENTS

Acetylenic Alcohols



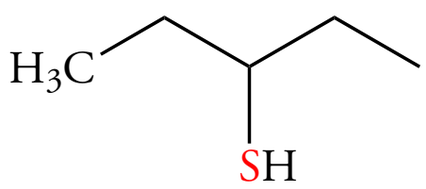
cyclohexanone

1-ethynylcyclohexanol

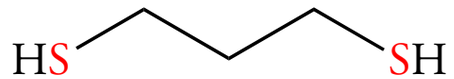


cyclopentanone

15.11 THIOLS AND THIOETHERS

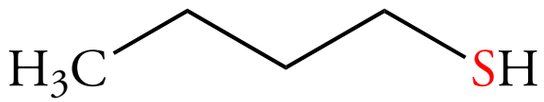


3-pentanethiol

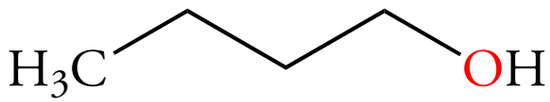


1,3-propanedithiol

Physical Properties of Thiols



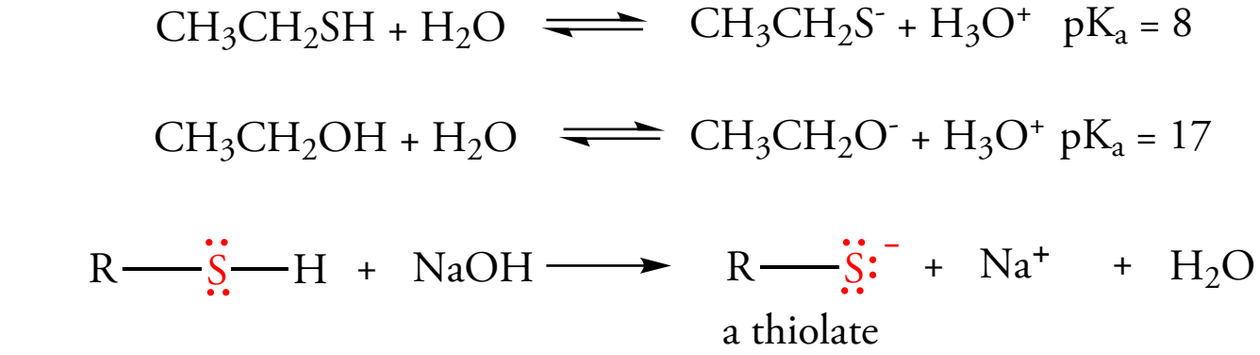
1-butanethiol (bp 98 °C)

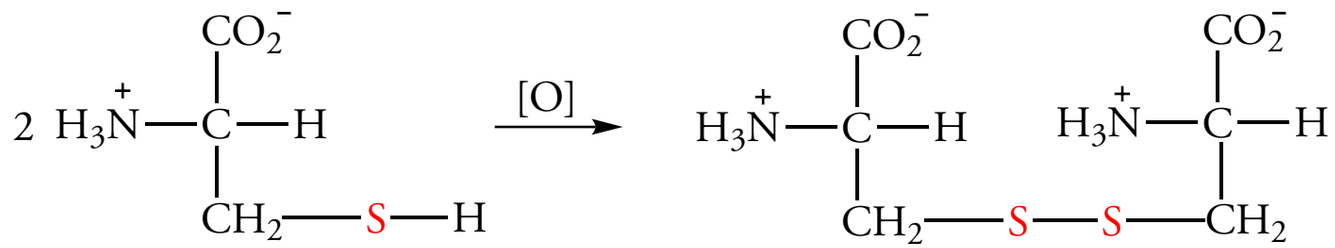


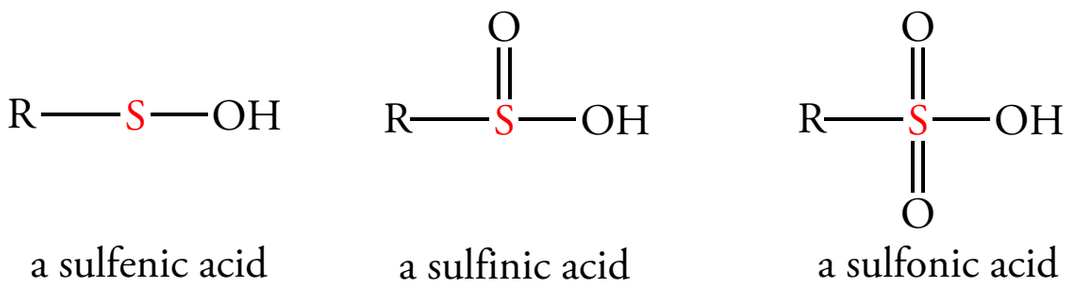
1-butanol (bp 117 °C)

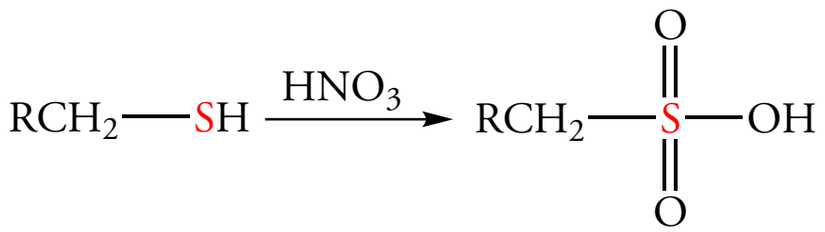
15.11 THIOLS AND THIOETHERS

Reactions of Thiols



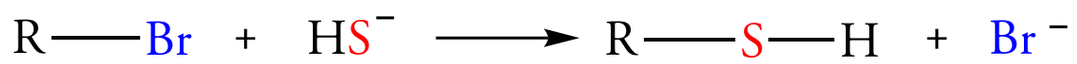


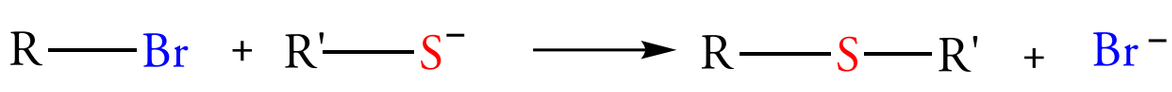




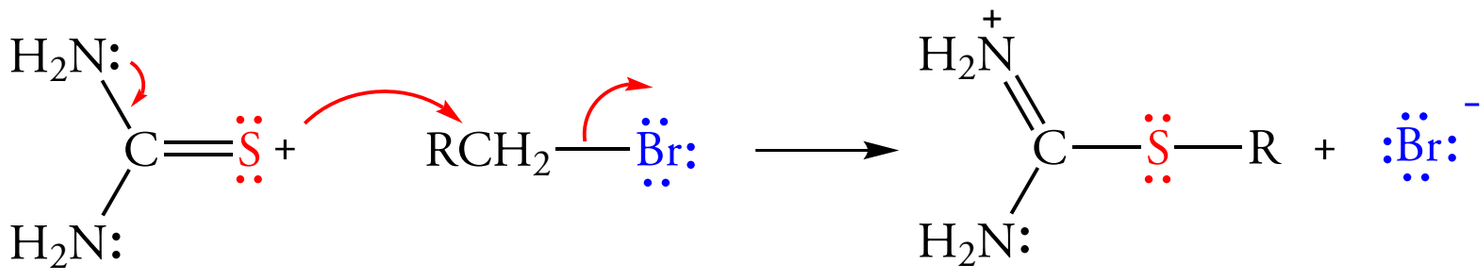
15.11 THIOLS AND THIOETHERS

Synthesis of Thiols



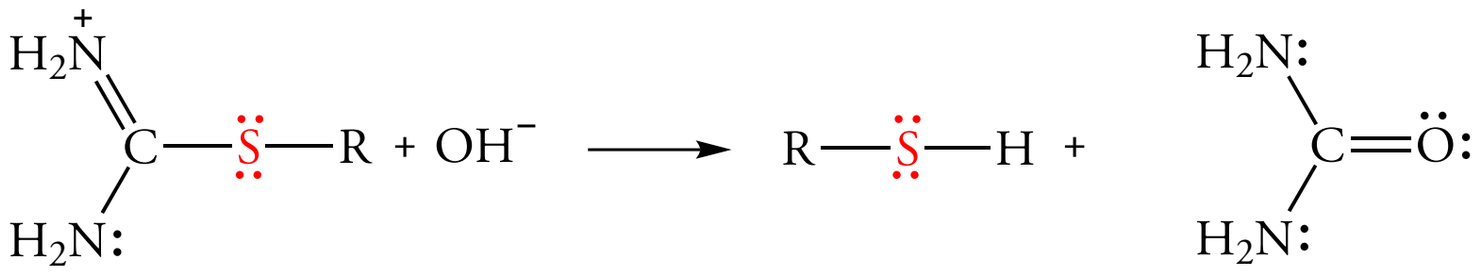


a thioether



thiourea

isothiouronium ion



urea