CHEM1201: Section 1

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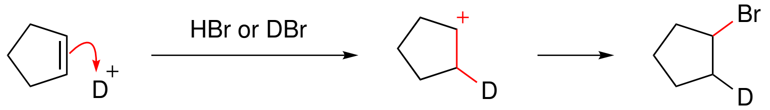
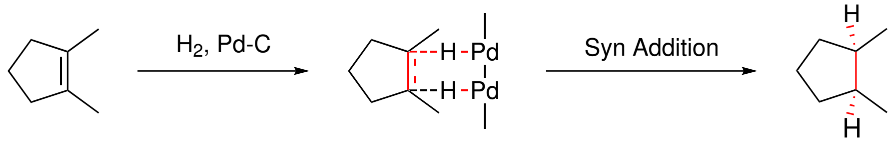
December 23, 2012

1 Alkenes

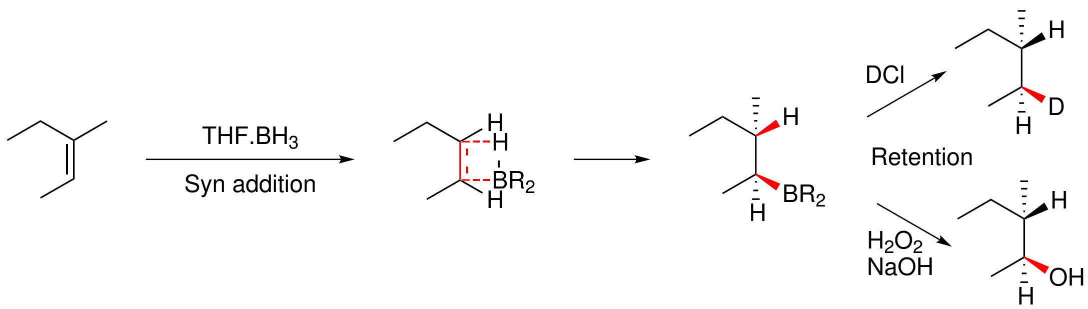
1.1 General



Carbocation mechanisms rarely permit stereocontrol.



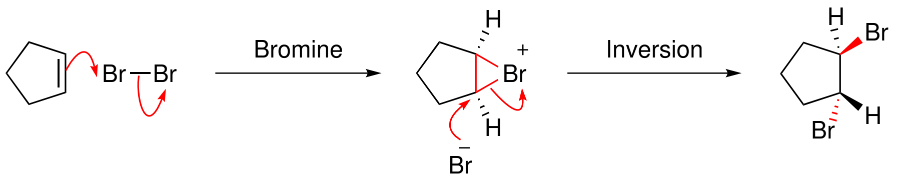
Carbocation mechanisms rarely permit stereocontrol.



1.2 Oxidations

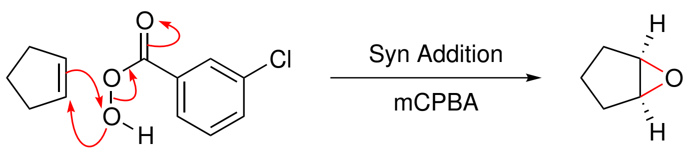
For each reaction, the first step involves synchronous bond formation.

1. Bromination

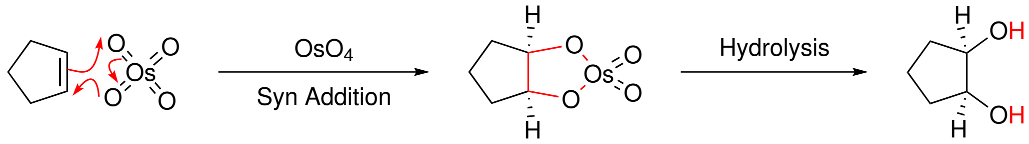


Overall an addition.

2. Epoxidation with mCPBA

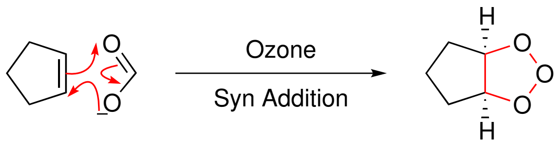


3. Formation of 1,2 Diols:



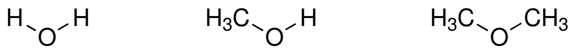
Proceeds with syn addition of osmium tetroxide.

4. Ozonolysis



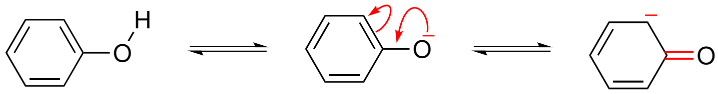
2 Alcohols

2.1 General



Water Alcohol Ether

Owing to conjugation of O via the sp^2 carbon, phenols and enols behave differently and neither is referred to as an alcohol.



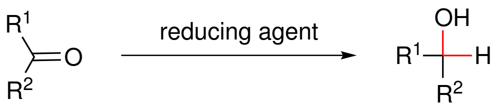
CH_3CH_2OH cannot be oxidized as there is no α–H

2.1.1 Physical Properties

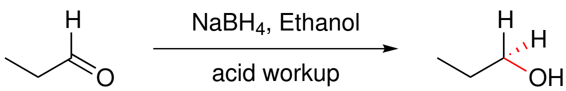
The electro-negativity of O means that alcohols are feebly acidic unlike amines that are only ever feebly basic. Alcohols are also feebly basic (O is less nucleophilic than N). They are also extensively hydrogen bonded which gives them much higher boiling points than alkyl halides.

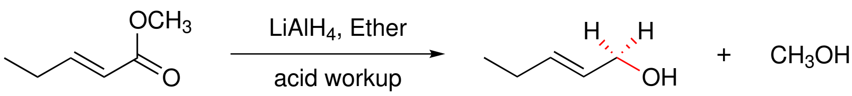
2.2 Preparation of Alcohols

1. Reduction of C=C compounds.



Examples:

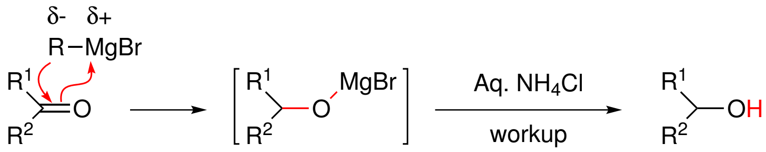




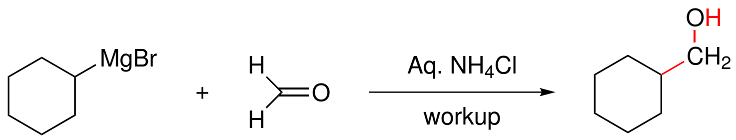
Note the double bond is unaltered.

2. Addition of grignard (RMgX) to a carbonyl compound.

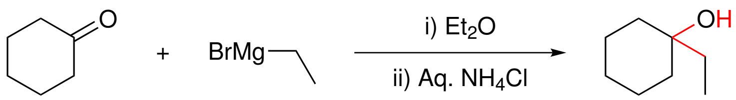
Mechanism



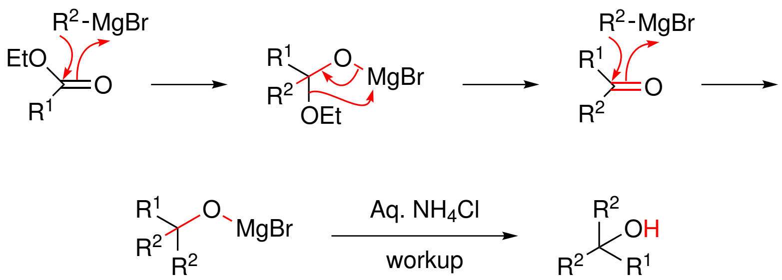
Example 1. Alcohols from aldehyde's.



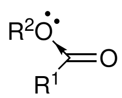
Example 2. Alcohols from ketone's.



Example 3. Alcohols from esters.

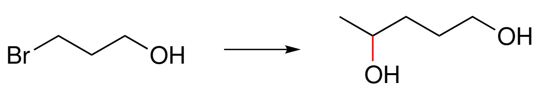
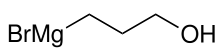


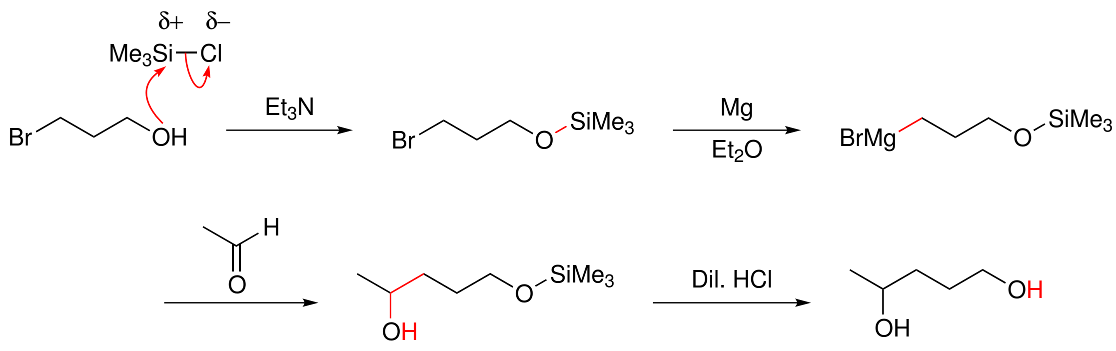
Esters only give alcohols with grignard reagents because the inductive effect increases reactivity but mesomeric effects are greater therefore the ketone's C=O is more reactive than an ester C=O.



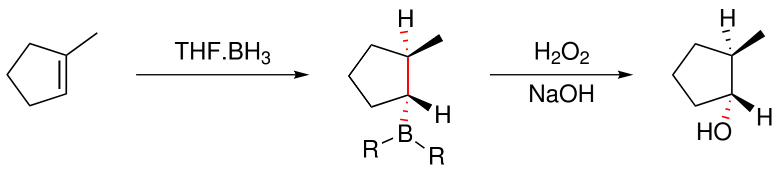
Grignard reagents are destroyed by groups with an exchangeable H e.g. OH, SH, NHR, COOH and thus require protective groups, e.g. silicon for an alcohol.

For example:

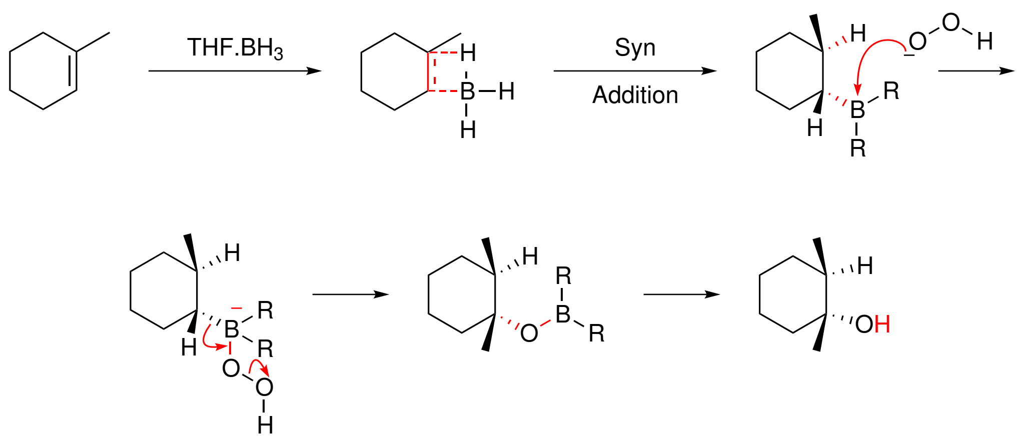
 cannot go via the intermediate 
as the OH would destroy the grignard reagent formed. Therefore instead, silicon is used as a protective group.



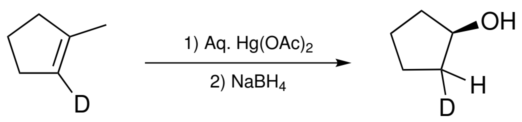
3. Hydroboration of alkenes (delivers OH to the less substituted C).



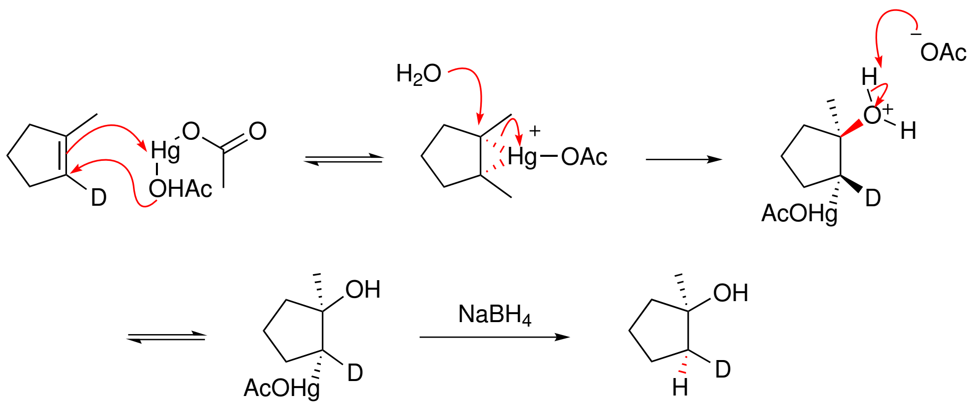
Mechanism



4. Oxymercuration of alkenes (delivering of OH to the more substituted C)



Mechanism



2.3 Reactions of Alcohols

2.3.1 Reaction at the alcohol oxygen atom.

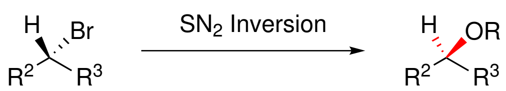
a) Formation of the alkoxide (Na, NaH)

With a strong base, the acidic H is lost and the alkoxide is formed. Grignard reagents must also be protected from this e.g.

$$\mathrm{ROH} + \mathrm{Na} \longrightarrow \mathrm{RO^{-}Na^{+}} + \tfrac{1}{2}\,\mathrm{H_2}$$
$$\mathrm{ROH} + \mathrm{Na^{+}H^{-}} \longrightarrow \mathrm{RO^{-}Na^{+}} + \mathrm{H_2}$$

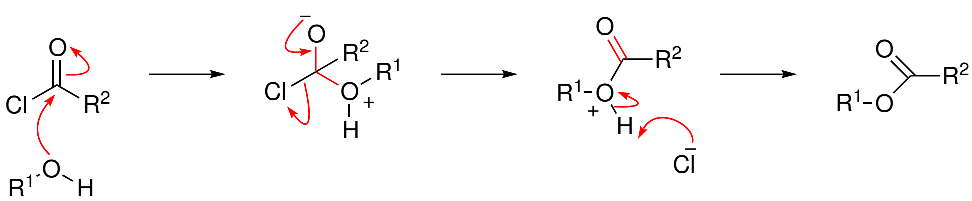
Alkoxides are good bases and good nucleophiles except tBuOH and 3° alcohols, which are good bases but non-nucleophilic due to their steric hindrance. NaH acts only as a base and is not a reducing agent.

b) O-Alkylation (alkoxide + alkyl halide)

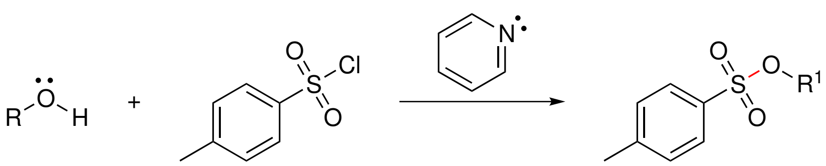


Williamson ether synthesis

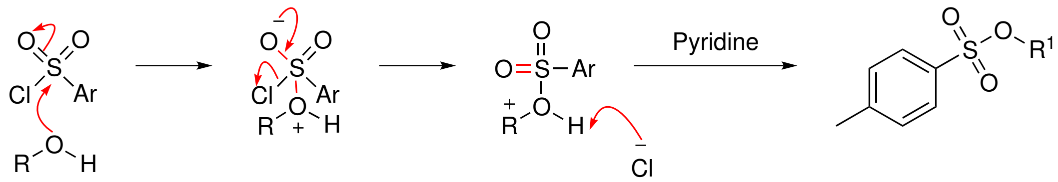
c) O-Acylation (alcohol + acid chloride)



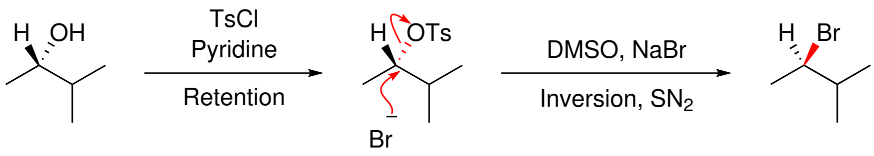
d) O-sylfonylation (p-TsCl + Pyridine)



Mechanism



Tosylate is a very good leaving group and can be displaced by many nucleophiles including all halides.

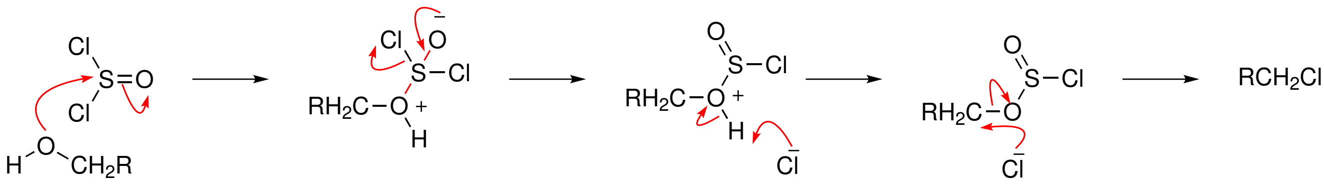


DMSO is $Me_2S{=}O$, a very popular solvent that gives fast rates of reaction.

2.3.2 Displacement at the alcohol carbon atom

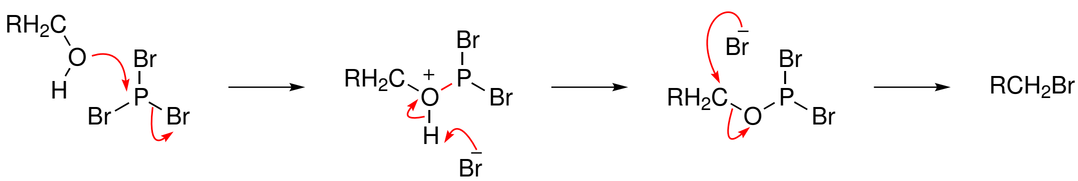
Activation of the OH group is the first step, in all cases a good leaving group (HOX) is generated.

a) Conversion of ROH into RCl (alkyl chloride)



The first transition state formed contains an O−S bond. This is followed by elimination of chlorine and loss of a proton. Then SN_2 displacement of the activated carbon atom occurs.

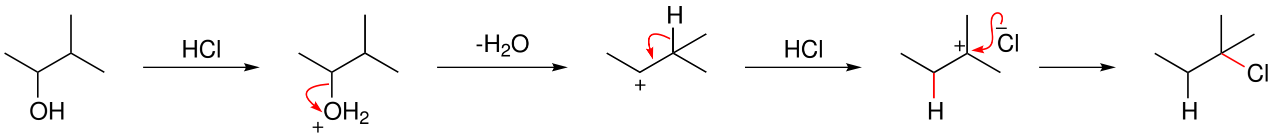
b) Conversion of ROH into RBr (alkyl bromide)



The limitations of using HCl/HBr to prepare alkyl halides are:

- 2° and 1° alcohols require forcing conditions (100 -120 °C)
- incompatibility of any unsaturated sites, which will react.
- Likely to undergo rearrangement

c) Rearrangment using HCl/HBr 2° carbocation



Mechanism results in the formation of a 3° carbocation

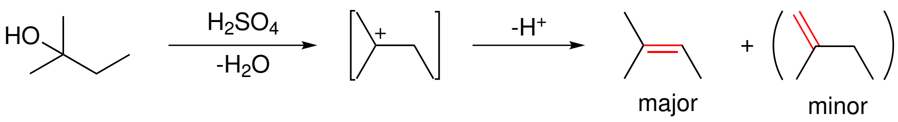
1,2 Hydride shifts are common where the resulting carbocation is more stable than the initial one.

2.3.3 Eliminations of Alcohols: Formal loss of water

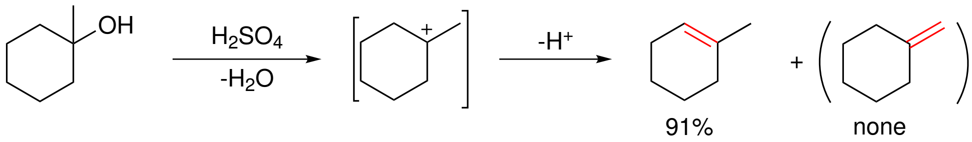
a) Where a carbocation is not trapped by a nucleophile (and does not rearrange) an elimination can occur. tBuOH reacts with H_2SO_4 to give a 3° carbocation, which then deprotonates to give 2-methylbutane. The conditions favour the most substituted alkene.

E.g.

i)



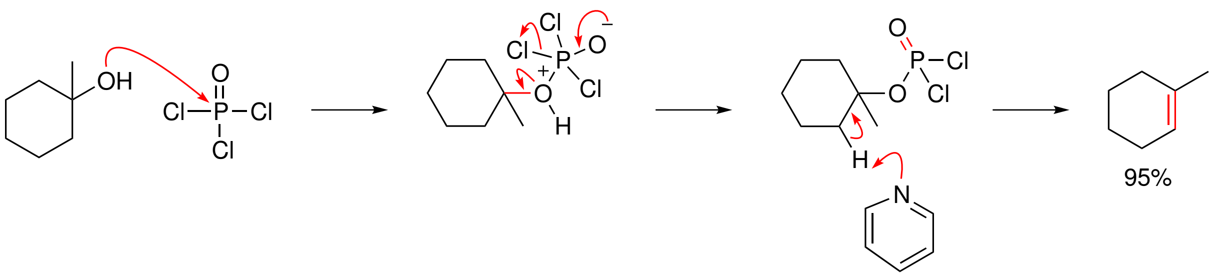
ii)



Limitations are that 2° and 1° alcohols require heating that may promote side reactions including rearrangements.

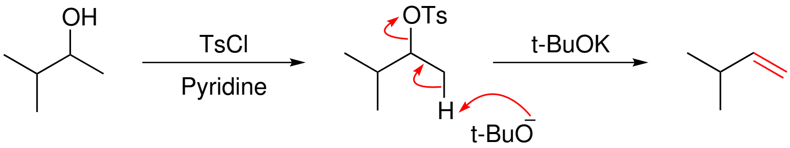
Alternatives are elimination using $POCl_3$ and pyridine and conversion of the alcohol into the tosylate followed by elimination with tBuOK.

b) E_2 elimination using $POCl_3$ and Pyridine (at O °C)



c) E_2 elimination of the tosylate using tBuOK

This is especially useful when the compound is sensitive to acidic reagents including ($POCl_3$)

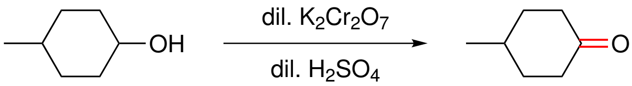


2.3.4 1,2 Elimination across the C−O: Oxidation of Alcohols

Oxidation can be loss of H, loss of e^- or gain of O.

a) Chromium (VI) reagents

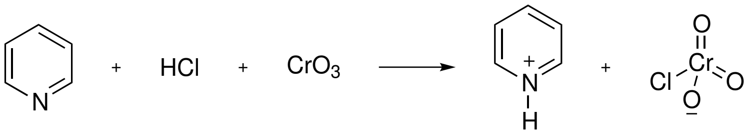
i) Dilute dichromate with dilute H_2SO_4



Over oxidation of 1° alcohols to RCOOH occurs. Any Cr(VI) reagent is good for 2° alcohols.

ii) Pyridinium Chlorochromate (PCC)

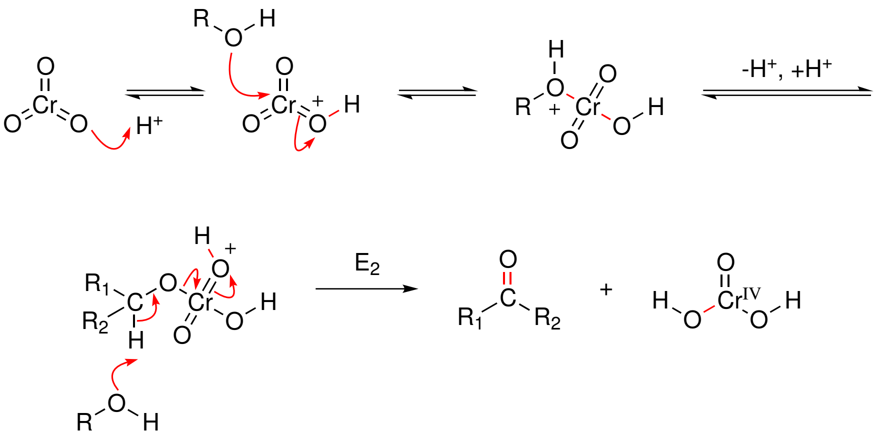
Good for converting 1° alcohols to aldehydes and 2° to ketones, with little over oxidation.



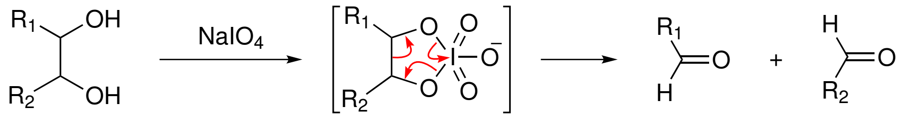
Formation of PCC

iii) CrO_3 in aqueous H_2SO_4: Jones reagent.

Oxidises 2° alcohols to the ketone and 1° to the acid. The mechanism of Cr(VI) oxidations all involve formation of a chromate ester that undergoes E_2 elimination.



b) Cleavage of 1,2-diols by sodium periodate, $NaIO_4$

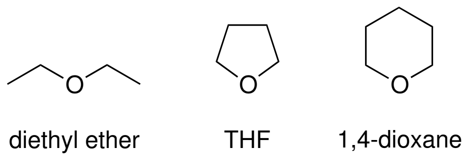


A central C−C bond is broken as part of the oxidation process

3 Ethers and Epoxides

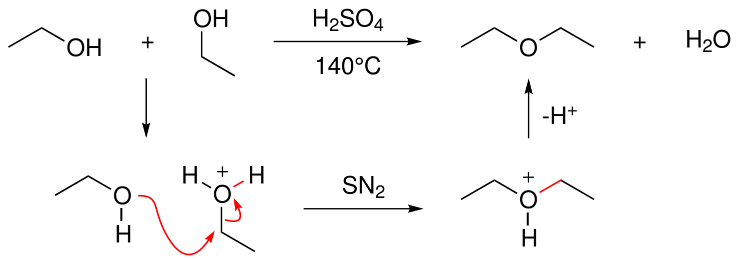
3.1 Ethers

Ethers are good solvents as they are chemically inert but slightly polar. Old bottles become oxidised by the air to give explosive peroxides.
Examples of ethers are:

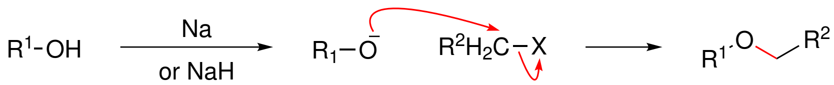


3.1.1 Preparation of ethers

a) For symmetrical ethers



b) Williamson ether synthesis; the most general route

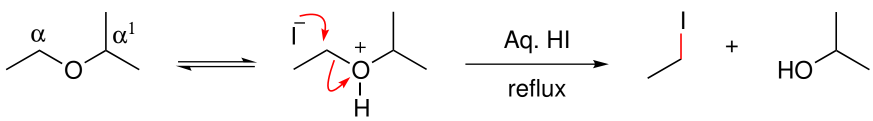


X= Br, I and OTs as long as there is not too much steric hindrance

R–O⁻ is a very powerful nucleophile.

3.1.2 Reactions of Ethers: Cleavage by HI

I⁻ attacks the less substituted (less sterically hindered) $\alpha - C$

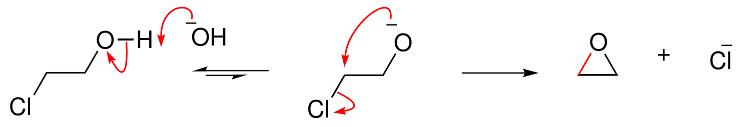


3.2 Epoxides

Epoxides are strained and highly reactive 3-membered ring ethers.

3.2.1 Synthesis of Epoxides

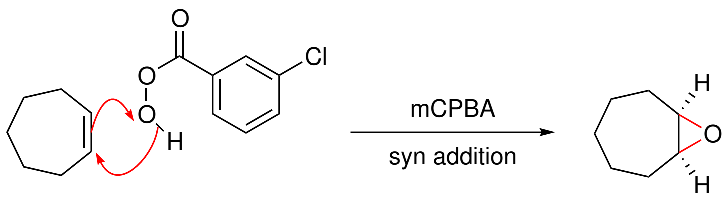
a) Cyclisation of halohydrins: Intramolecular Williamson ether synthesis



There is ring strain as the angles are normally 109° and in epoxides they are 60°.

b) Epoxidation of alkenes

The configoration of the alkene is retained in the epoxide.



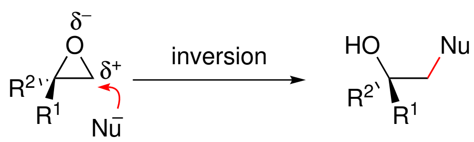
Does not work on many alkenes

3 membered rings are favoured as 4 membered rings have a lower entropy factor and therefore there is less chance of ring closure.

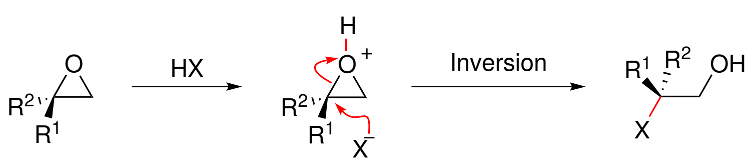
3.2.2 Reactions of Epoxides

3.2.3 Patterns of reactivity

i) All reagents except acid



ii) Acid attack by HX

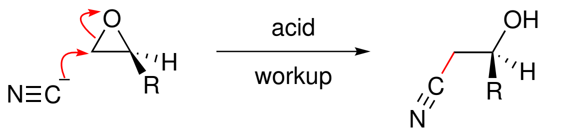


3.2.4 Nucleophilic attack of epoxides

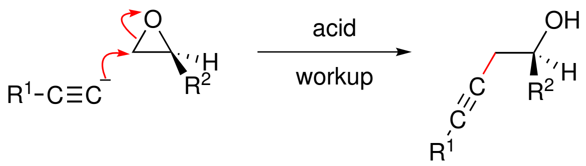
i) Attack by C–Nucleophiles

Powerful in synthesis as a new C–C bond is generated.

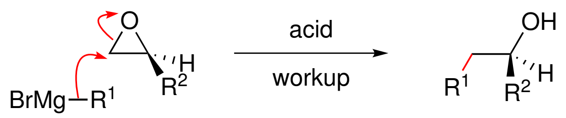
Example 1. Cyanide



Example 2. Alkynyl anions



Example 3. Grignard reagents



ii) Attack by Hydroxide, O$-$S$^-$ and N$^-$ nucleophiles.

These all react according to the first pattern of reactions.