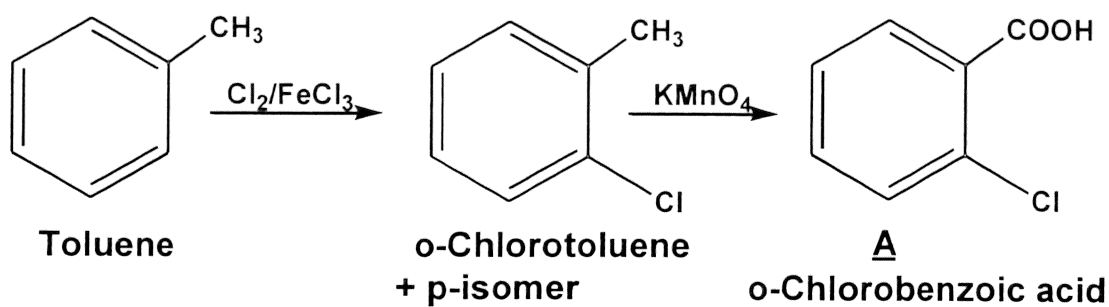


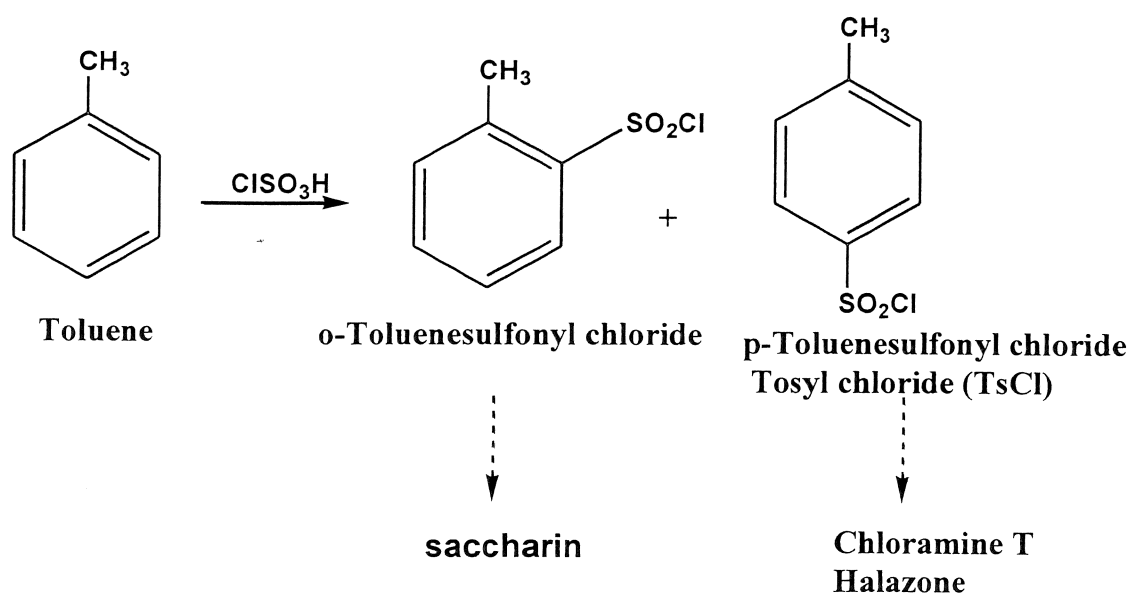
## Worked problem

Preparation of o-chlorobenzoic acid ( starting material for Diclofenac

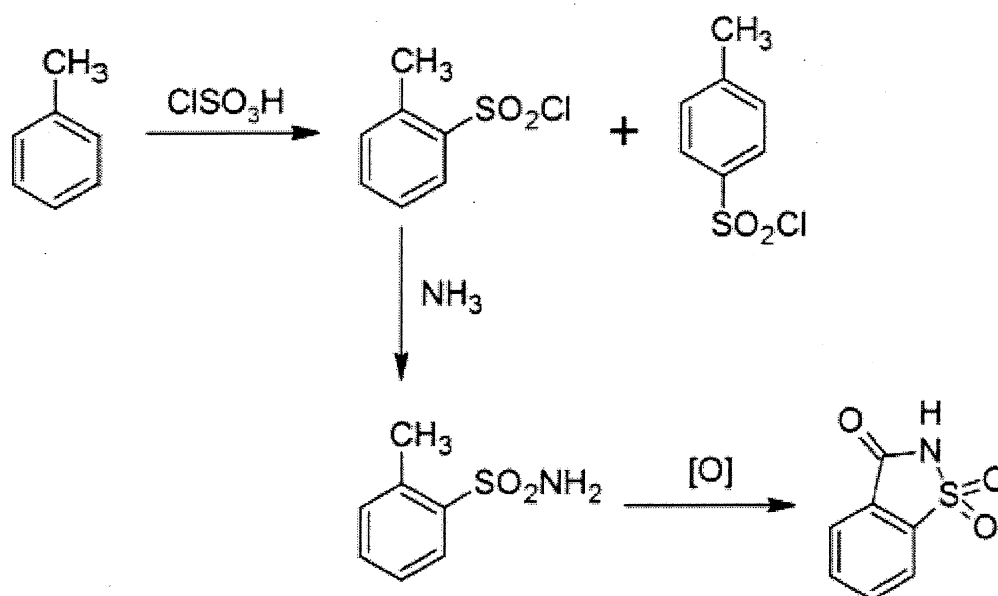


## Chlorosulfonation reaction

. ClSO<sub>3</sub>H : Chlorosulfonic acid ( caution)

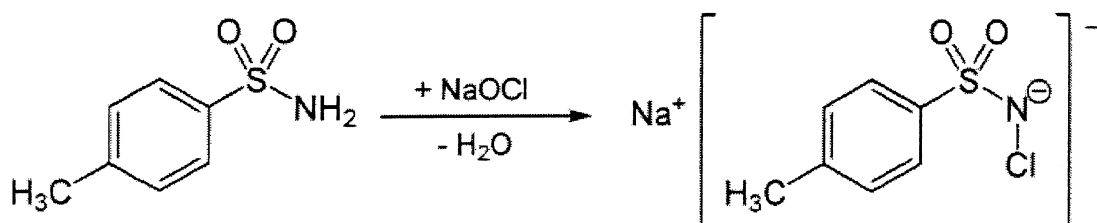


## Saccharin Synthesis



Sodium Saccharin (benzoic sulfimide) is an artificial sweetener

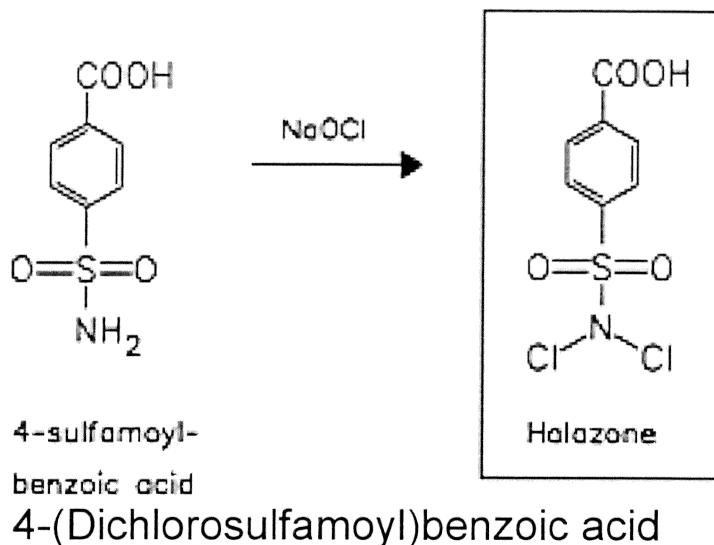
## Chloramine-T Synthesis



*N*-Chloro 4-methylbenzenesulfonamide, sodium salt

- Tosylchloramide or *N*-chloro tosylamide, sodium salt, sold as chloramine-T
- It is used as a biocide and a mild disinfectant.
- It is a white powder that gives unstable solutions with water.
- Chloramine-T is available in tablet or powder form and has to be dissolved before use.
- Trade names of chloramine-T products include Chloraseptin, Chlorazol, Clorina, among others.

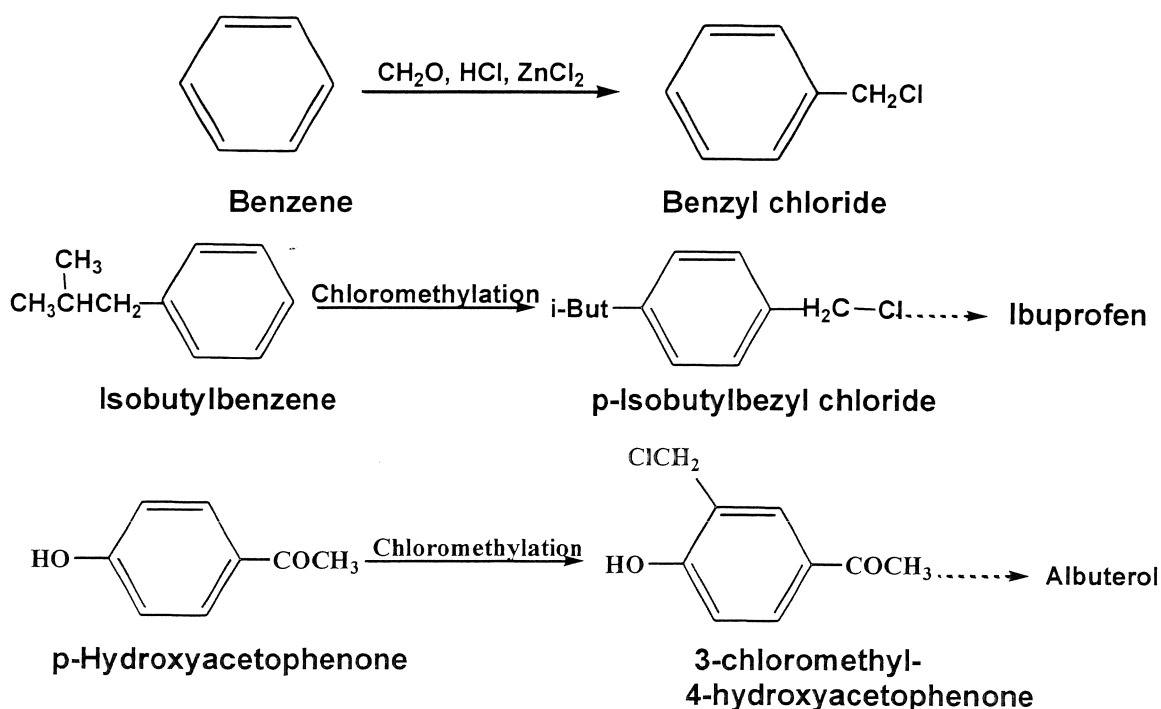
## Halazone Synthesis



- Other method: Oxidation of Dichloramine-T with  $\text{KMnO}_4$  in mild alkaline medium affords Halazone in high yield with 18–20% chlorine cont.
- It is used as disinfectant

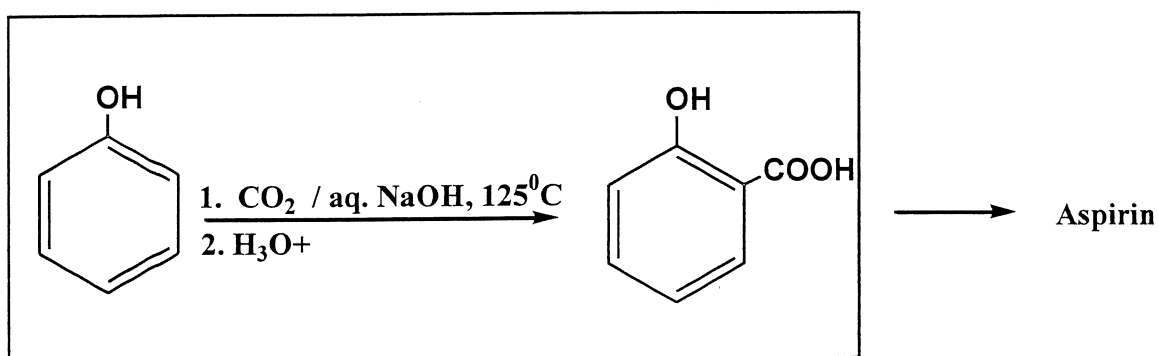
## Chloromethylation reaction

- . Unlike alkylation reaction, chloromethylation could be done on deactivated ring.
- . Solid paraformaldehyde is used as generator of  $\text{CH}_2\text{O}$  gas



## Kolbe-Schmidt reaction ( synthesis of salicylic acid from phenol)

- This reaction takes place on phenol (activated ring)
- Benzene doesn't give this reaction



# Drug Synthesis

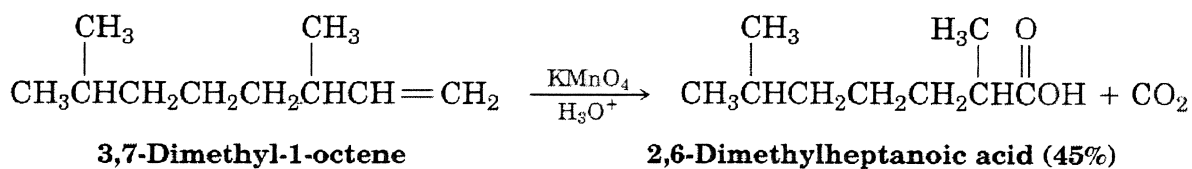
## الاصطناع (التخليق) الدوائي

### Some types of reactions used in drug synthesis

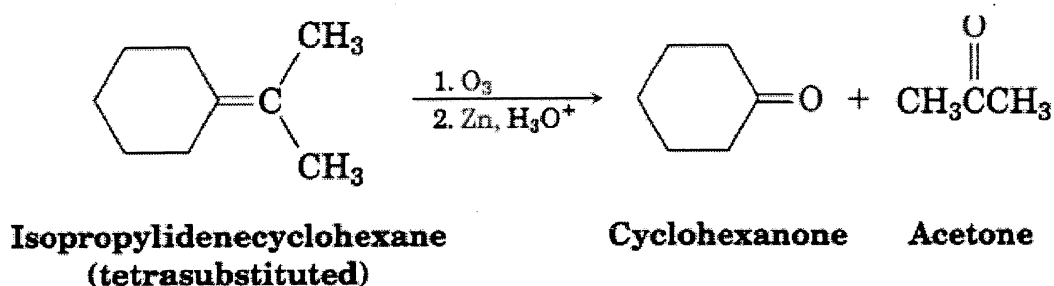
#### 4.Oxidation reactions

#### Oxidative clivage of alkenes by strong oxidizing agents

. Cleavage of alkenes is performed by strong oxidizing agents  $\text{KMnO}_4$ ,  $\text{CrO}_3$

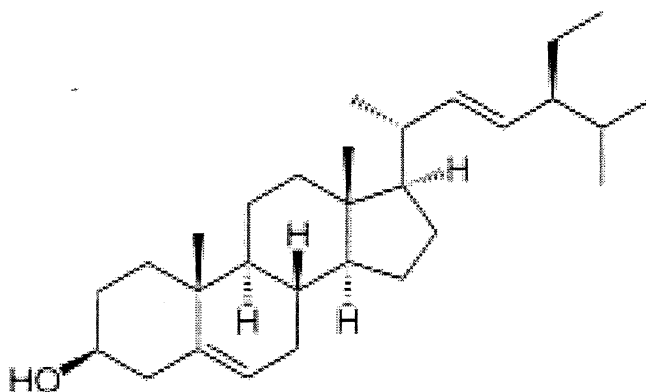


## Oxidative cleavage of alkenes by $O_3$ (ozonolysis)



## Stigmasterol (semi-synthesis of steroidal hormones)

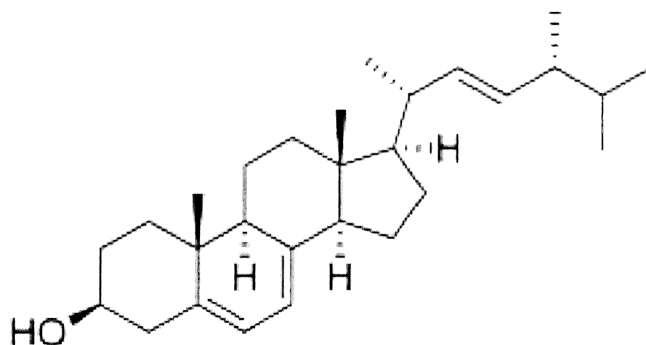
- Oxidative Cleavage of alkenes are used to shorten the side chain of the natural steroidal structures such as stigmasterol (occurs in soybean oil...), and ergosterol during the semi-synthesis of steroids



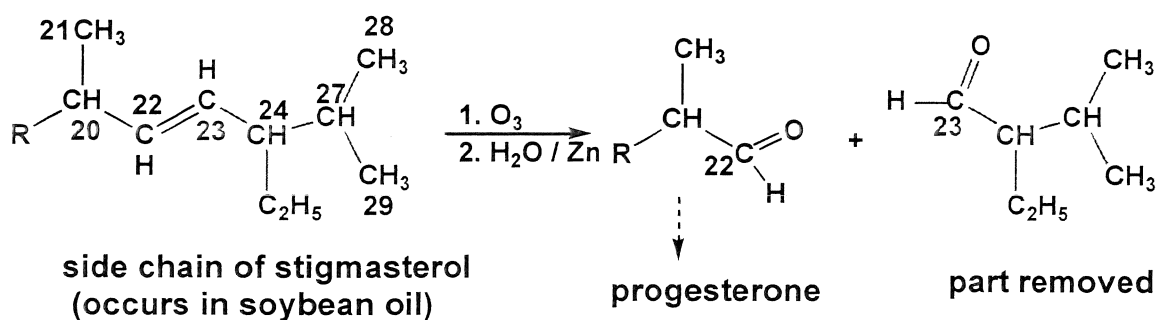
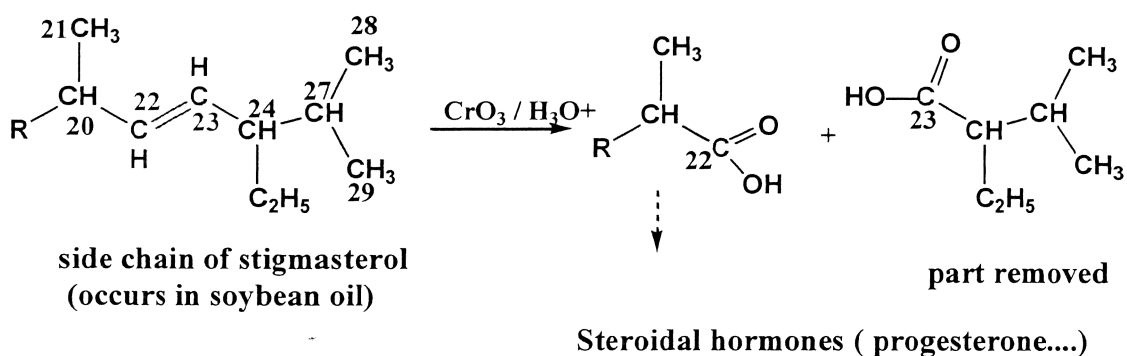
**Stigmasterol**

## Ergosterol (semi-synthesis of steroidal hormones)

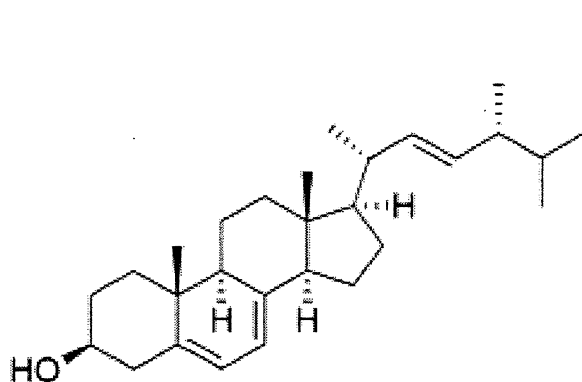
- **Ergosterol** occurs in yeast, fungi and protozoa.



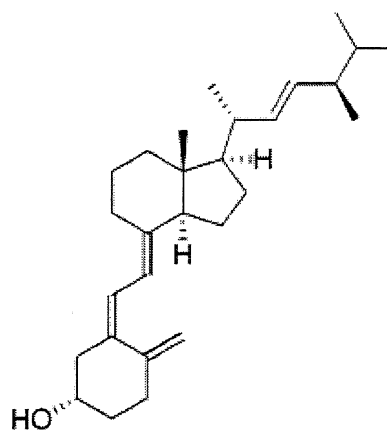
## Clivage of stigmasterol side chain (semi-synthesis of steroidal hormones)



## Ergosterol (semi-synthesis of Vitamin D<sub>2</sub>)



Ergosterol

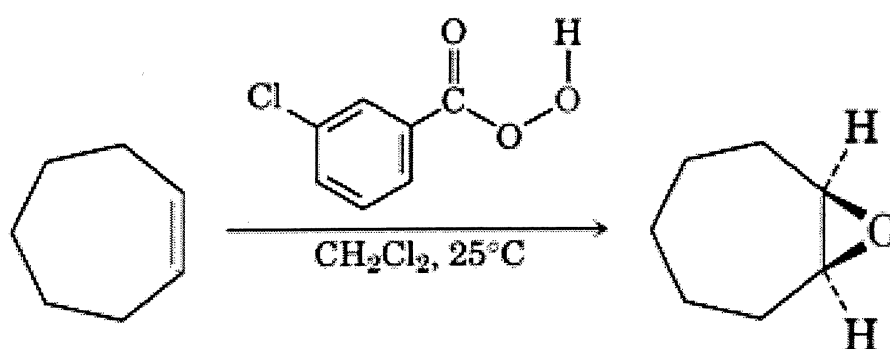


Ergocalciferol, vitamin D<sub>2</sub>.

- **Ergosterol** is a provitamin form of vitamin D<sub>2</sub>;
- Exposure to ultraviolet (UV) light causes a chemical reaction that produces vitamin D<sub>2</sub>.

## Epoxidation of Alkenes

- Reaction of an alkene with m-chloroperoxybenzoic acid or hydrogen peroxide produces an epoxide.



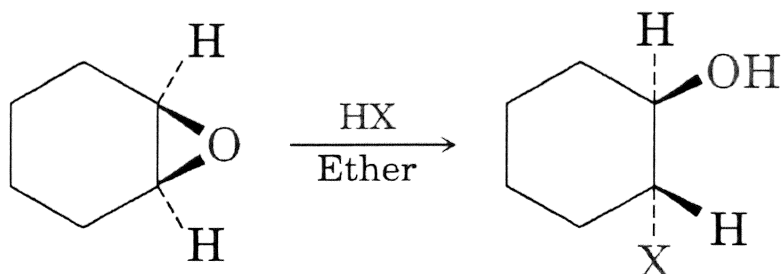
Cycloheptene

1,2-Epoxycycloheptane  
(78%)



## Ring Opening of Epoxides

- The action of acid halide on epoxides gives halohydrine (anti-addition).

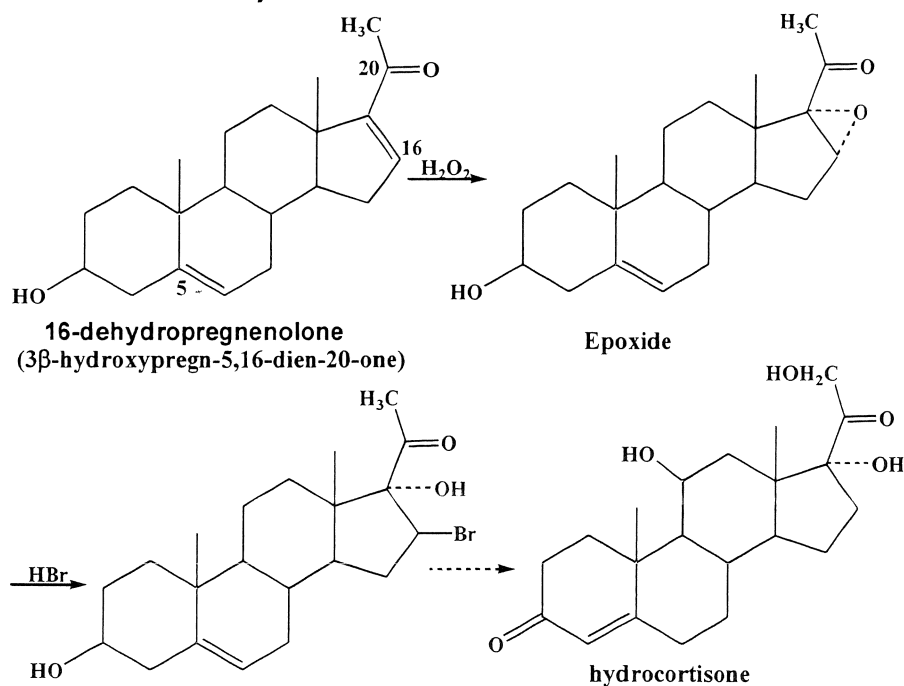


**A trans 2-halocyclohexanol**

where  $X = F, Br, Cl, \text{ or } I$

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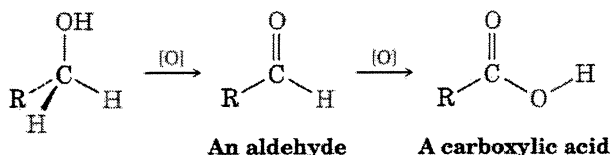
## The formation of 17-alpha hydroxy steroids by Epoxide formation - ring opening (synthesis of hydrocortisone)



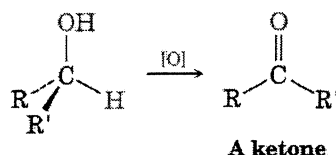
## Oxidation of Alcohols

- The oxidation of a primary or secondary alcohol can be accomplished by any of a large number of reagents, including  $\text{KMnO}_4$ ,  $\text{CrO}_3$ , and  $\text{Na}_2\text{Cr}_2\text{O}_7$ .
- Which reagent is used in a specific case depends on such factors as cost, convenience, reaction yield, and alcohol sensitivity.

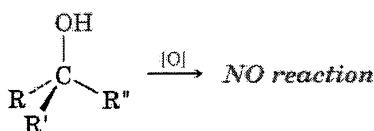
**Primary alcohol**



**Secondary alcohol**



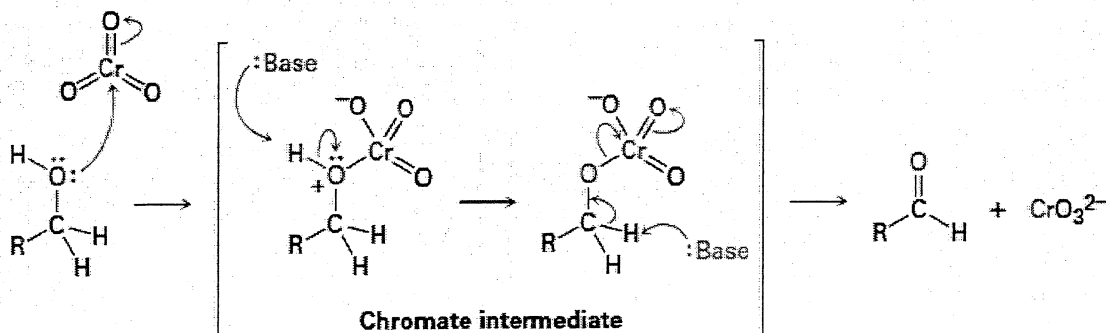
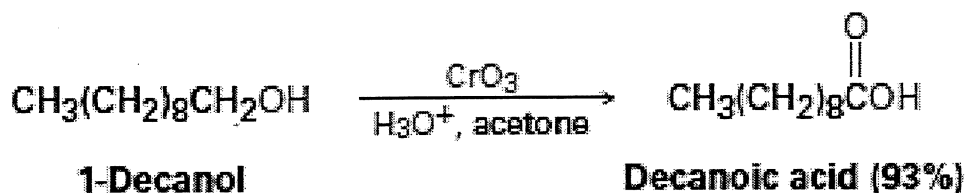
**Tertiary alcohol**



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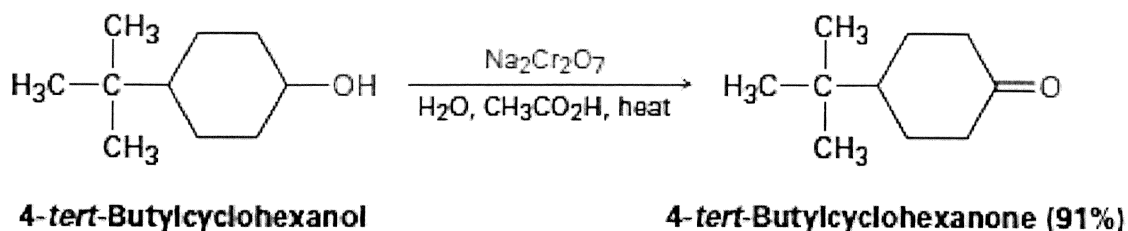
## Oxidation of Primary Alcohols

- Chromium trioxide,  $\text{CrO}_3$  in aqueous acid, oxidize primary alcohols to carboxylic acids through an aldehyde intermediate. The aldehyde is not usually isolated because it is further oxidized too rapidly)



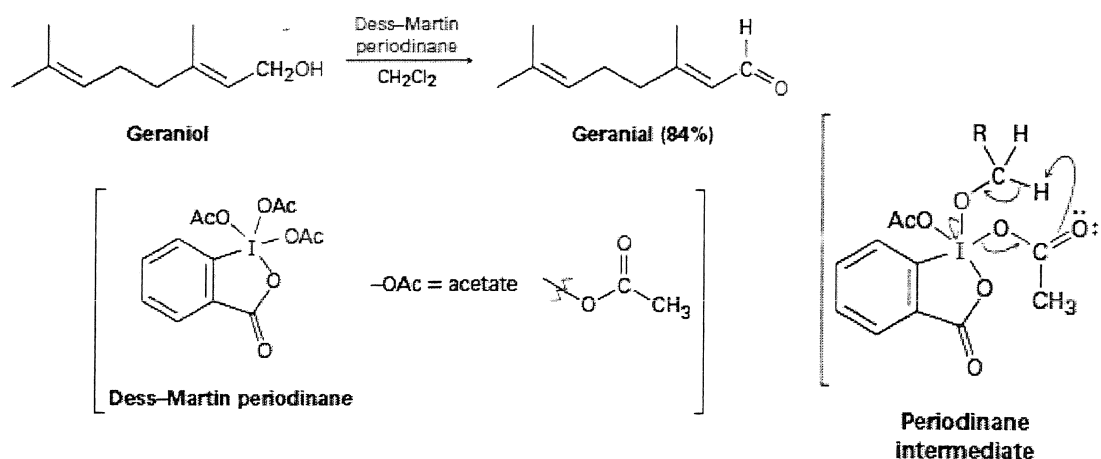
## Oxidation of Secondary Alcohols

- They are easily oxidized by  $\text{Na}_2\text{Cr}_2\text{O}_7$  in aqueous acetic acid to give ketones (industrial method: large scale process).



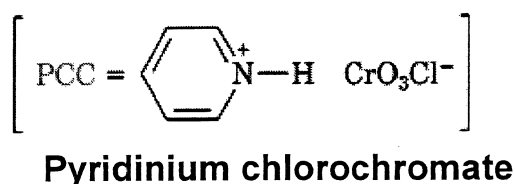
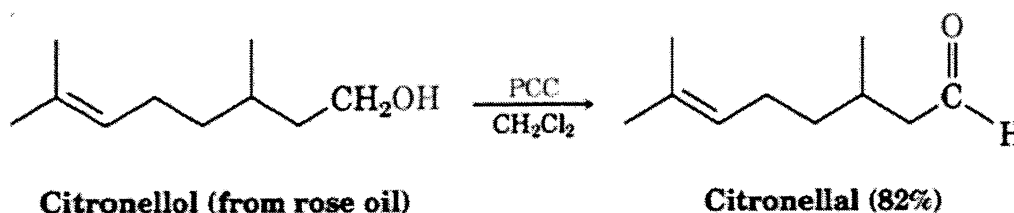
## Oxidation of primary alcohols to aldehydes by Dess–Martin periodinane

- The reaction is nonacidic and occurs at lower temperatures.
- Method is used for a sensitive or costly alcohol
- The reaction involves E2 elimination mechanism performed on the periodinane intermediate.



## Oxidation of primary alcohols to aldehydes by PCC

- Pyridinium chlorochromate (PCC) oxidizes primary alcohols to aldehydes.
- PCC is an expensive reagent



## Oxidation of 11 $\alpha$ -hydroxyprogesterone to 11-ketoprogesterone in the synthesis of cortisone

Steroid structure is fragile structures: sensitive to oxidation

