Reagents in Organic Synthesis
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Oxidation Mediated by Mn and Ag
Lecture 05

Keywords: MnO_2 and Fetizon's reagent

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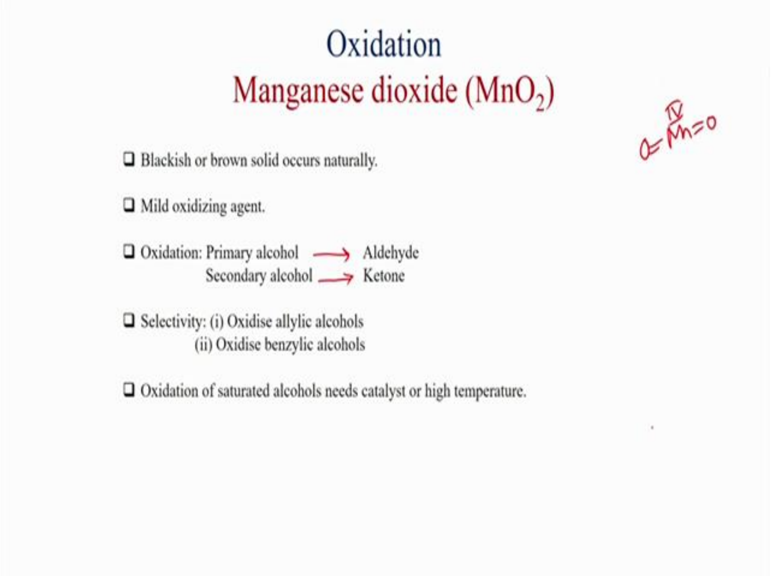

Oxidation

Manganese dioxide (MnO_2)

$O=\overset{IV}{Mn}=O$

- ❑ Blackish or brown solid occurs naturally.
- ❑ Mild oxidizing agent.
- ❑ Oxidation: Primary alcohol $\longrightarrow$ Aldehyde
  Secondary alcohol $\longrightarrow$ Ketone
- ❑ Selectivity: (i) Oxidise allylic alcohols
  (ii) Oxidise benzylic alcohols
- ❑ Oxidation of saturated alcohols needs catalyst or high temperature.

Welcome again, today we will discuss two more oxidizing agent. First one is manganese dioxide and second one silver carbonate on celite. So manganese dioxide is blackish or brown solid which occurs naturally. And if you see manganese dioxide structure, it is two oxygen is there and its oxidation state is plus 4. It is mild oxidizing agent. It is oxidized primary alcohol to aldehyde and secondary alcohol to ketone. Also it selectively oxidizes allylic alcohols and benzylic alcohols that is its main application. Also oxidation of saturated alcohols can be possible but it need catalyst or high temperature.

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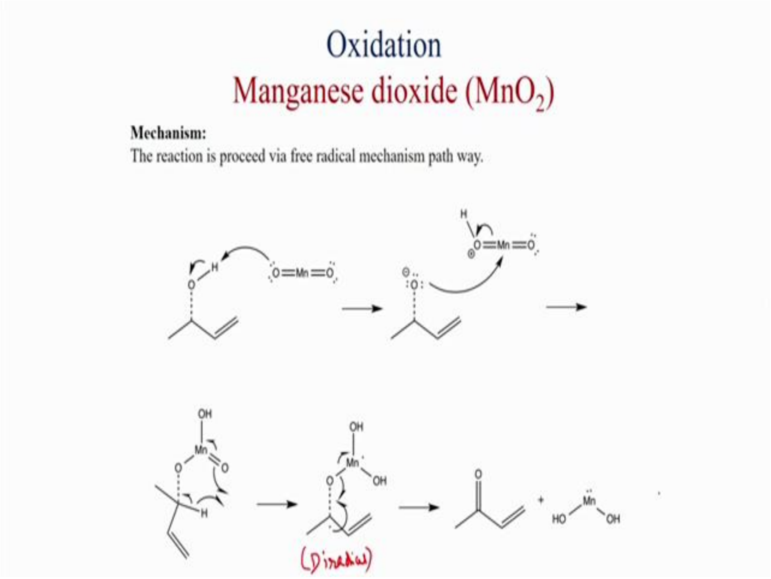

Oxidation

Manganese dioxide (MnO_2)

Mechanism:

The reaction is proceed via free radical mechanism path way.

And the mechanism of this oxidation follows a free radical pathway. So if you see the mechanism, first the oxygen of a manganese dioxide takes a proton from the OH and it is becomes the oxonium ion. And then the O minus attacks to the manganese, activated manganese and this species is formed. Now there will be a, if you see the arrow this is single electron arrow. So, now the single electron will circulate if you see that the oxygen reacts with a H dot and OH is formed here.

And one radical is formed here and another radical is formed on the manganese. So this is a diradical. And this diradical then fragments, if one electrons comes from here and another electron goes to the manganese. So manganese become manganese hydroxide.

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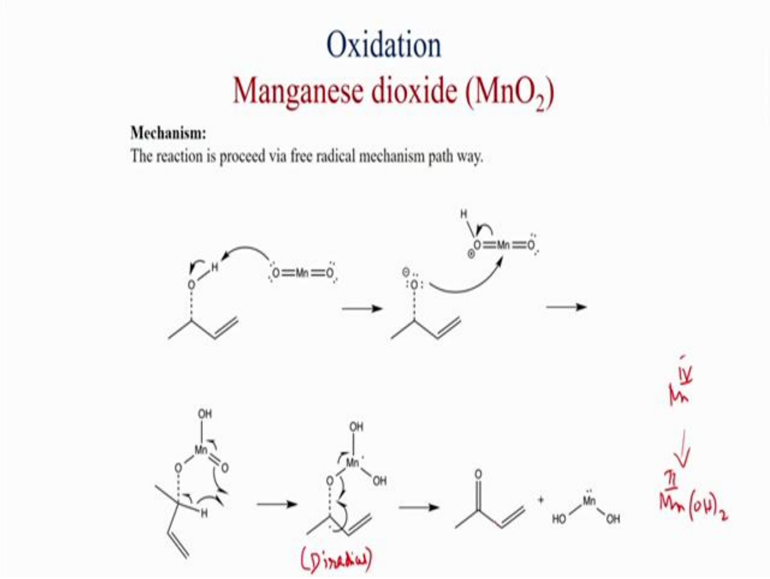

Oxidation

Manganese dioxide (MnO_2)

Mechanism:

The reaction is proceed via free radical mechanism path way.

So it becomes manganese hydroxide which is plus 2. So manganese 4 becomes manganese 2. So this is the, reduction is happening and here alcohol is becoming carbonyl compound. So the oxidation is happening.

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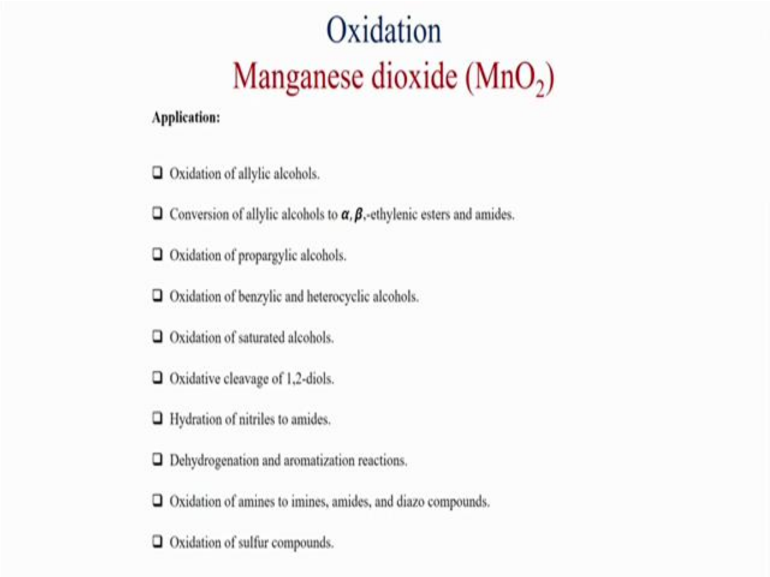

Oxidation

Manganese dioxide (MnO_2)

Application:

- ☐ Oxidation of allylic alcohols.
- ☐ Conversion of allylic alcohols to $\boldsymbol{\alpha}, \boldsymbol{\beta}$,-ethylenic esters and amides.
- ☐ Oxidation of propargylic alcohols.
- ☐ Oxidation of benzylic and heterocyclic alcohols.
- ☐ Oxidation of saturated alcohols.
- ☐ Oxidative cleavage of 1,2-diols.
- ☐ Hydration of nitriles to amides.
- ☐ Dehydrogenation and aromatization reactions.
- ☐ Oxidation of amines to imines, amides, and diazo compounds.
- ☐ Oxidation of sulfur compounds.

Its application, it is mainly applied oxidation of allylic alcohols. Conversion of allylic alcohols to alpha beta ethylenic esters and amides which is called Corey-Gilman-Ganem oxidation. This is also applied for the oxidation of propargylic alcohols. Oxidation of benzylic and heterocyclic alcohols and oxidation of saturated alcohols is possible. And for that you need catalyst or high temperature. Cleavage of 1,2-diols is also possible. Hydration of nitriles to amides. Dehydrogenation, aromatization reaction which we have seen with DDQ.

Manganese dioxide also can perform this reactions. And oxidation of amines to imines, amides, and diazo-compounds. Also oxidation of sulfur compounds to di-sulfides or sulfoxide that we will see in details.

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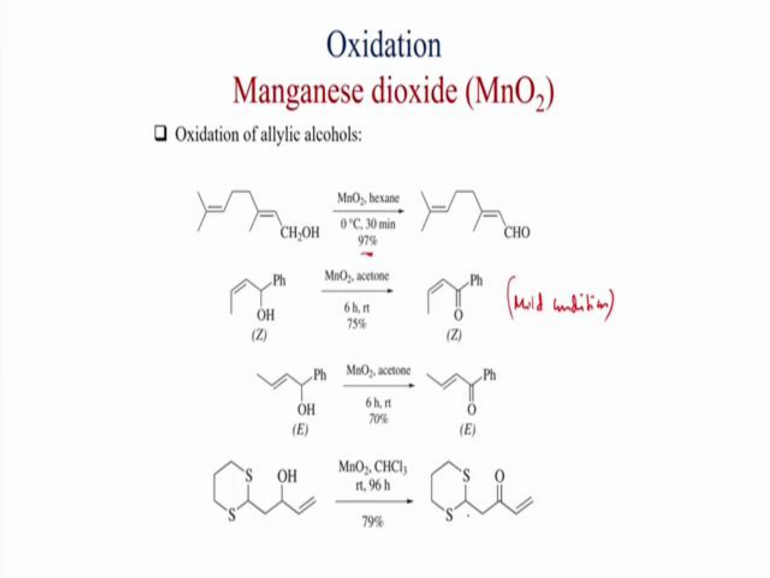

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidation of allylic alcohols:

So first we will discuss oxidation of allylic alcohols. So various kind of allylic alcohol can be oxidized to the alpha beta unsaturated aldehyde. Here you can see this geranyl alcohol oxidize under manganese dioxide hexane 0°C 30 minutes it gives this aldehyde in 97 percent yield. Also this Z allylic alcohol where it oxidized to this Z enone. And this is very selective that Z it does not isomerize to the E enone, so this is very mild condition.

Also this E allylic alcohol, this is an E allylic secondary alcohol which is also converting to E enone selectively. And here the yield also 70%. Also there is diethyne motive is there and secondary allylic alcohol. So MnO_2 chloroform room temperature 96 hours, it gives selectively this product diethyne does not get disturbed under this condition.

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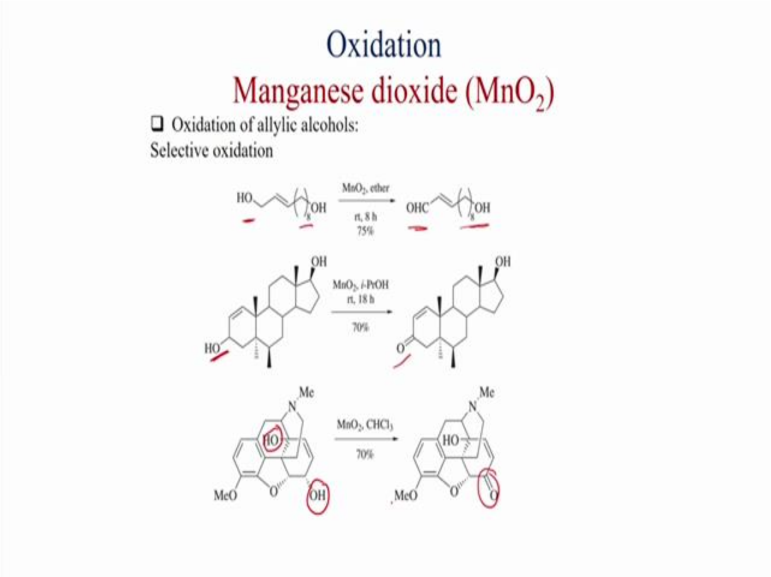

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidation of allylic alcohols:

Selective oxidation

Here selective oxidation of also allylic alcohol in presence of other saturated alcohol is possible. Like here a linear diol where allylic alcohol is there. This is allylic alcohol and this is saturated alcohol. So when MnO_2 is treated with this alcohol in ether solvent and room temperature only the allylic alcohol gets to aldehyde and the saturated alcohol remains unreactive. Also a steroid molecule here a secondary allylic alcohol and a saturated alcohol is present under this condition only. The secondary allylic alcohol gets oxidized to the alpha beta unsaturated enone and the saturated alcohol does not react.

Also a complex heterocyclic molecule here you can see the two OH are there both are allylic but one is secondary another is tertiary and tertiary does not do any rearrangement like we have seen in PCC cases. But here selectively the secondary allylic alcohol getting converted to the enone with MnO_2.

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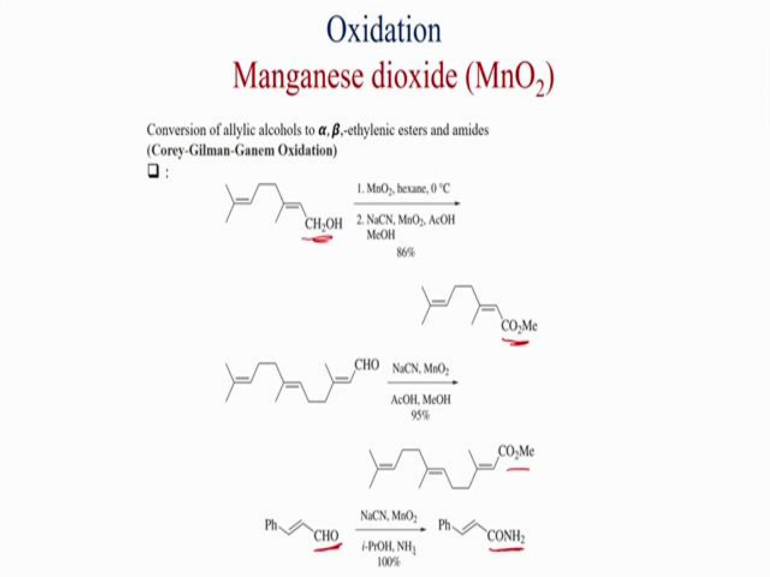

Oxidation

Manganese dioxide (MnO_2)

Conversion of allylic alcohols to **α**,**β**,-ethylenic esters and amides

(Corey-Gilman-Ganem Oxidation)

❑ :

Also conversion of allylic alcohols to alpha beta ethylenic esters and amides is possible which is called Corey-Gillman-Ganem oxidation. So here this geranyl alcohol first treated with MnO_2 in hexane at 0°C, it goes to the aldehyde and that aldehyde can react with sodium cyanide and again get oxidized with MnO_2 and acetic acid in methanol condition it gives the ester. So it is a possible to convert alpha beta unsaturated or allylic alcohol to the allylic ester.

Also this farnesyl aldehyde when is treated with sodium cyanide and MnO_2 acetic acid methanol it going to the ester. So this means that the aldehyde alcohol first goes to aldehyde and aldehyde reacted with sodium cyanide to make a compound and then it is going to be oxidize again with MnO_2 and then in methanol condition it gives the ester. The detail mechanism we will see later.

Here an alpha beta unsaturated aldehyde was treated with sodium cyanide and MnO_2 isopropanol and ammonia, under this condition the amide is formed from the aldehyde. So here also the mechanism is same but instead of methanol, ammonia is the nucleophile here and that is why you get the primary amide.

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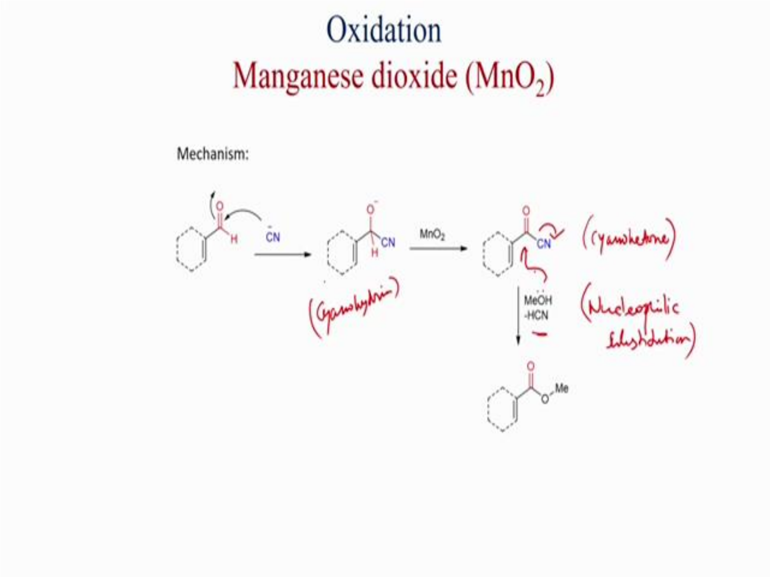

Oxidation

Manganese dioxide (MnO_2)

Mechanism:

This is the mechanism, so the OH, aldehyde first reaction cyanide to give this compound and then MnO_2 oxidizes this one. So MnO_2 oxidizes this compound which goes to the cyano ketone. And this cyano ketone then does a nucleophilic reaction, nucleophilic substitution reaction. And here the methanol is the nucleophile here and you get cyanide, ultimately HCN will be liberated and you get the alpha beta unsaturated ester.

So this is a three step process, first cyanide will react then this is cyanohydrin. So cyanide will react first aldehyde to make the cyanohydrin and cyanohydrin with MnO_2 oxidized to ketonitrile and then a nucleophilic substitution reaction will happen to get the ester and in presence of amide the ammonia acts as a nucleophile and here methanol acting as a nucleophile.

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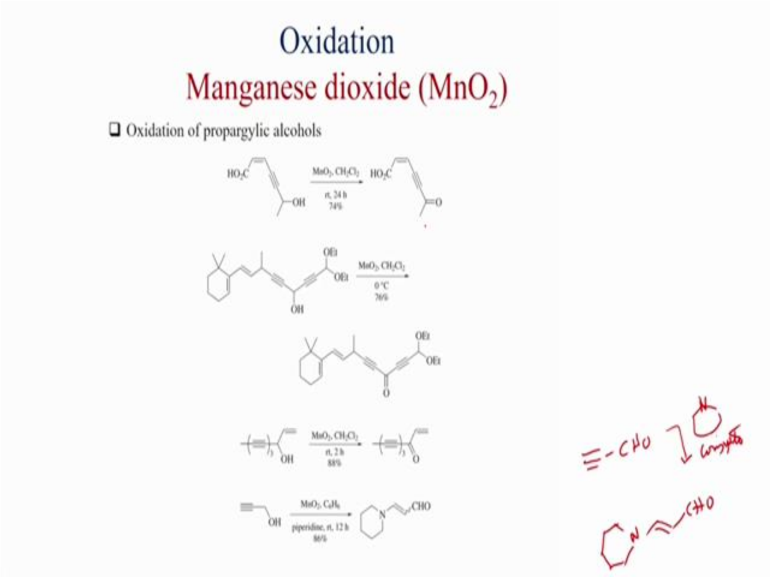

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidation of propargylic alcohols

Also oxidation of propargylic alcohol is possible, like this secondary propargylic alcohol under MnO_2 chloroform room temperature condition it gives the ketone in 74% yield. Also di propargylic secondary alcohol also with MnO_2 gives the ketone in good yield. Here this alcohol, secondary alcohol is both allylic as well as propargylic and with MnO_2 it gives the ketone in very high yield.

Also propargylic alcohol here we have seen that here propargylic alcohol can oxidize fast to propionaldehyde. So first, propionaldehyde is forming and when piperidine is reacted with this one then a conjugate addition is happening, so you get an alpha beta unsaturated aldehyde with piperidine motif. So this is a conjugate addition of the insitu generated propargylaldehyde.

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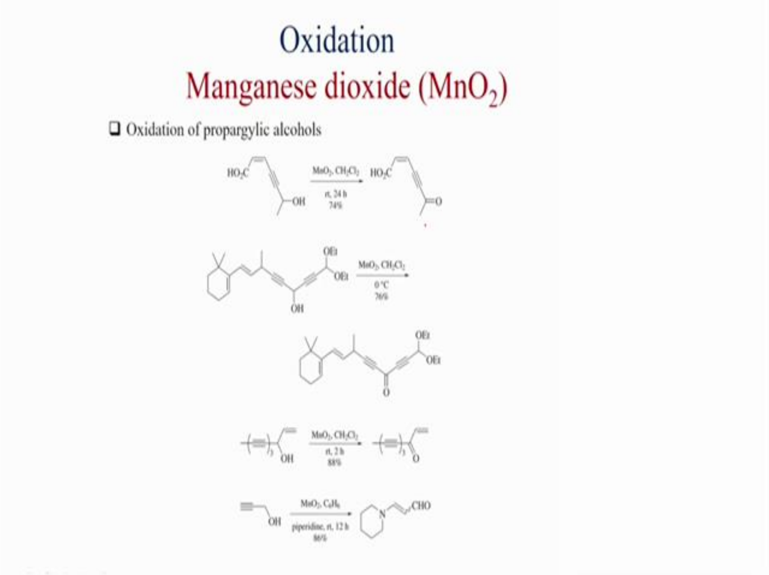

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidation of propargylic alcohols

Oxidation of benzylic and heterocycle alcohols is possible.

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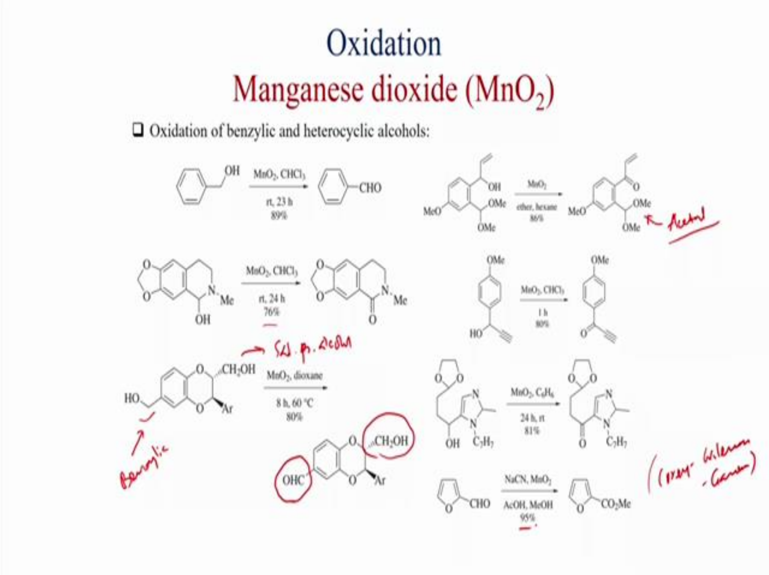

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidation of benzylic and heterocyclic alcohols:

Like here benzyl alcohol is converted to benzaldehyde with MnO_2 chloroform room temperature condition, this is very mild condition. Also a heterocyclic here secondary alcohol goes to the carbonyl in MnO_2 condition is very good a yield 76%. And here you can see there is a benzylic alcohol this is benzylic and this is simple saturated alcohol, saturated primary alcohol. So what is happening under this condition?

Only this benzylic alcohol is selectively oxidized to the benzaldehyde. So this is also a selective oxidation of benzylic alcohol over saturated primary alcohol. Here you can see there is an acetal motif and allylic alcohol is there. So acetal is not touched in this reaction condition. Only the allylic alcohol is selectively oxidize. Here also propargylic alcohol is selectively as well as benzylic is oxidized to the ketone without disturbing the methoxy group.

Here a ketal group is present and under this condition the ketal group does not react and only the secondary alcohol allylic will oxidize to the carbonyl compound. And here furfural is used as the starting material and under the Corey-Gilman-Ganem reaction, sodium cyanide MnO_2 acetic acid methanol it gives the furan ester in very high yield, 95 percent yield.

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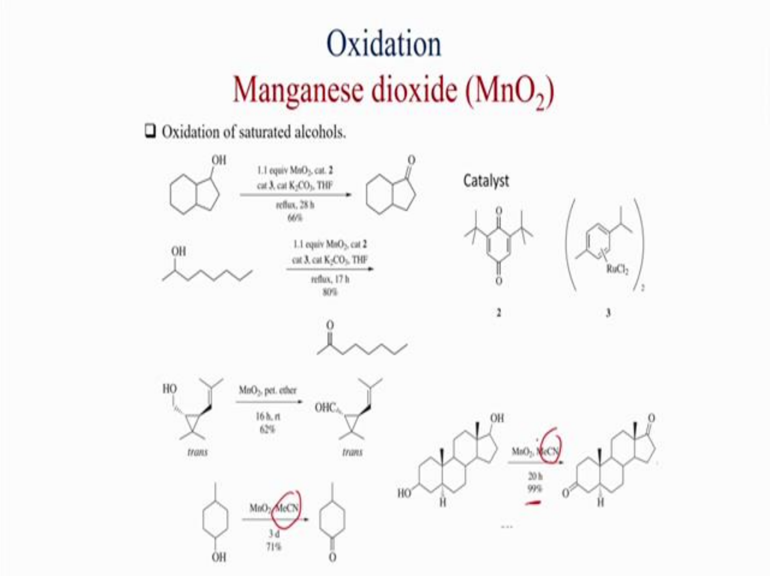

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidation of saturated alcohols.

So oxidation of saturated alcohols with MnO_2 also is possible only we need some catalyst a high temperature. Suppose here this two catalysts are used for oxidizing this saturated alcohol to the carbonyl, 1.1 equivalent manganese dioxide and catalyst 2 as well as catalyst 3 which is in the para benzoquinone and this is ruthenium complex it gives in 28 hours reflux condition 66 percent yield of the product.

Similarly this normal chain secondary alcohol also under this condition 70 hours reflux, it gives 80 percent of this ketone. It has been found that cyclopropyl alcohol CH_2OH also gives oxidation with MnO_2 pet ether this is very mild condition and under this condition this cycloproyl CH_2OH group oxidizes to the aldehyde and here is cyclohexanol 4 methyl cyclohexanol getting oxidized to the 4 methyl cyclohexanone under MnO_2 mild condition 3 days and it gives 71 percent yield.

Also here it has been found the acetonitrile solvent is good when saturated alcohols are present and here both saturated alcohols in this steroids getting oxidized to the carbonyl compound in very high yield. So what has been found? The acetonitrile solvent is good when you want to oxidize saturated secondary alcohol.

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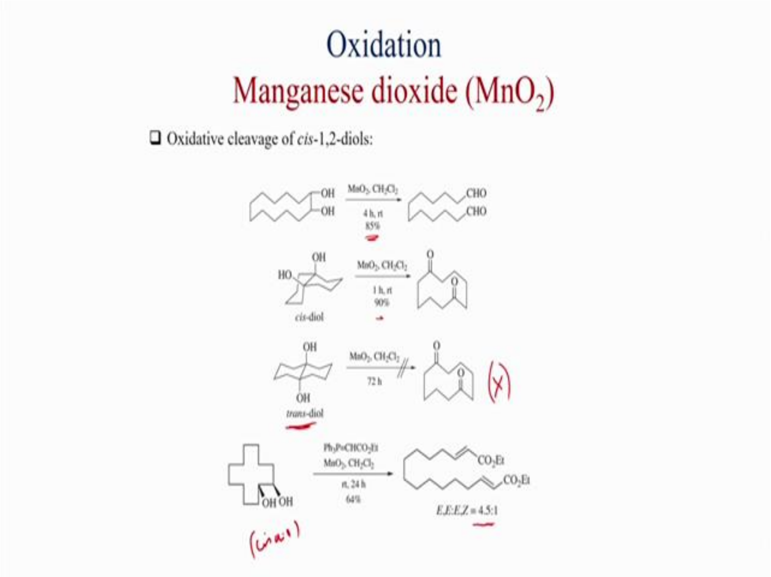

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidative cleavage of *cis*-1,2-diols:

Oxidative cleavage of cis 1, 2-diols: manganese dioxide can also perform cleavage like sodium periodate and here it has been found the various cis diols can be cleaved to di-aldehyde with MnO_2. Like MnO_2 dichloromethane 4 hours room temperature condition this diol gives the dialdehyde 85 percent yield. Here also cis diol decalin system it also oxidized to the di carbonyl compound.

Because secondary alcohol it gives to the diketone and very high yield of the product is obtained. However when the OH groups are trans to each other like this trans diol. Here MnO2 does not work, so this means that only cis diols can be oxidized with MnO_2. Here we can see that the dialdehyde here the cis diol and this cis diol first goes to the di-aldehyde and then Wittig-Horner olefination reaction was carried out to get the product where the selectivity is 4.5 is to 1.

So all EE versus EZ that ratio is 4.5 is to 1, so this reaction is very good when the aldehydes are difficult to separate, so under that condition you can treat the MnO_2 product that is the aldehyde product directly with Horner-Wittig olefination condition so that you can get the alpha beta unsaturated ester.

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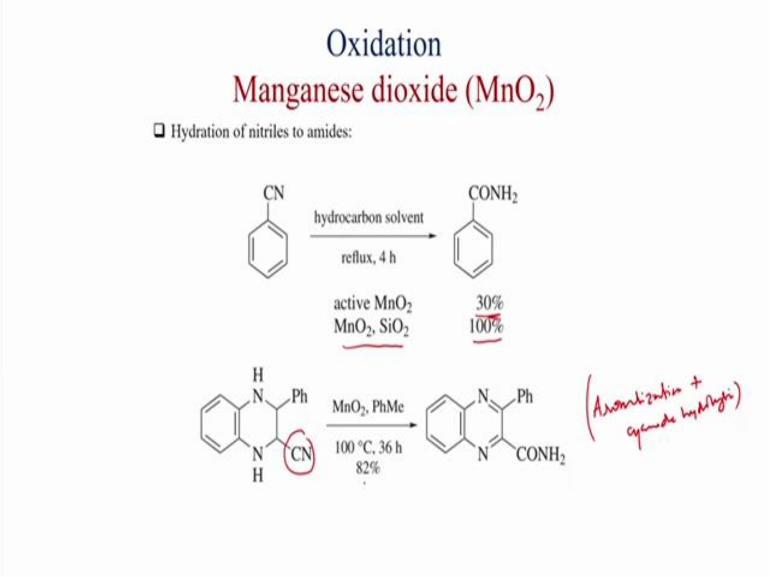

Oxidation

Manganese dioxide (MnO_2)

❑ Hydration of nitriles to amides:

Also hydration of nitriles to amides is possible with MnO_2, we know that potassium hydroxide or strong bases are good for cyanide hydrolysis but here manganese dioxide can also do this reaction and in hydrocarbon solvent active MnO_2 gives only 30 percent yield of this benzamide but when silica is present then the yield got enhanced to 100 percent so that means under this condition the yield is very good for the benzamide product.

Here an heterocyclic motif is present with the nitrile group and with MnO_2 condition these groups are undisturbed but aromatization along with a hydrolysis. So aromatization plus cyanide hydrolysis is happening. So this is dehydrogenation and aromatization that also we will discuss later. So manganese dioxide toluene 100 degrees centigrade, it gives this product in very good 82 percent yield and we get this product.

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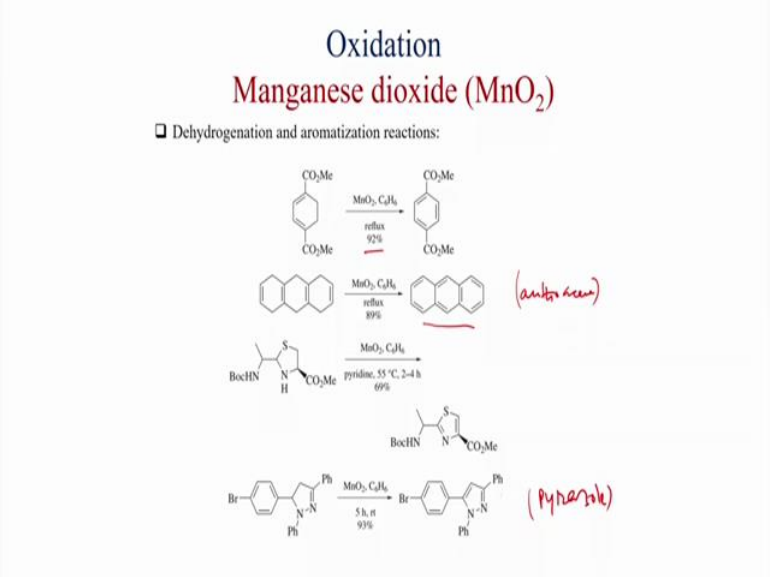

Oxidation

Manganese dioxide (MnO_2)

❑ Dehydrogenation and aromatization reactions:

So the dehydrogenation and aromatization reaction previously we have seen DDQ is mainly used for dehydrogenation and aromatization reaction but manganese dioxide also can do this kind of reactions like this compound diester when treated with manganese dioxide in benzene reflux condition, it gives this benzene derivative in 92 percent yield. Similarly when this unsaturated compound is treated with manganese dioxide benzene reflux condition it gives anthracene in 89 percent yield.

So, that means the aromatization is possible when manganese dioxide is used. Here a heterocycle saturated, heterocycle motif is used for this reaction with manganese dioxide, benzene and pyridine was used as an added base in 55 degrees centigrade, it gives this heterocycle in 69 percent yield. Also when this cyclic hydrazine was treated with manganese dioxide, benzene room temperature condition in for 5 hours it gives this pyrazole product in 93 percent yield.

So different benzene and heterocycle motif can be obtained by aromatization with manganese dioxide.

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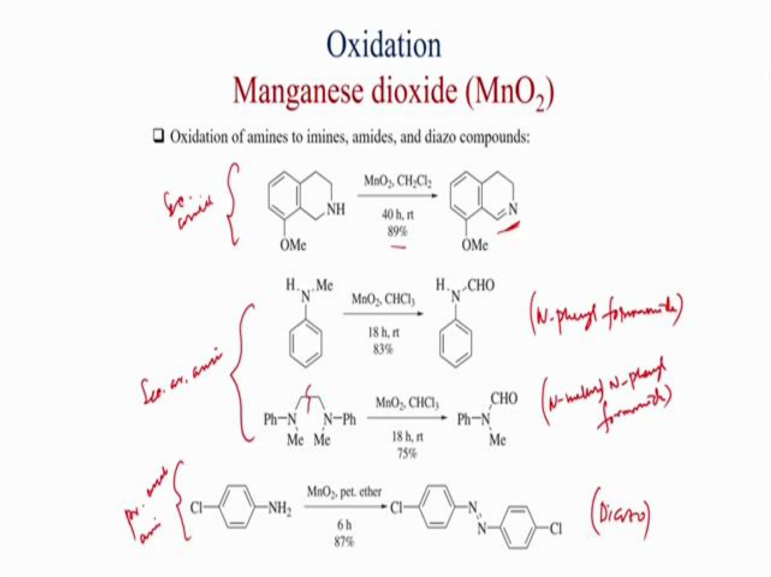

Oxidation

Manganese dioxide (MnO_2)

- ☐ Oxidation of amines to imines, amides, and diazo compounds:

Oxidation of amines to imines, amides and diazo compounds is also possible like here saturated tetrahydroisoquinoline was treated with manganese dioxide and dichloromethane it gives the imine, so here the aromatization does not happen when you treat manganese dioxide dichloromethane and room temperature which you get 89 percent yield of this imine, selectively.

And when an aromatic secondary amine was used like N-methylaniline with manganese dioxide chloroform for 84 hours you get N-phenyl formamide. So N-phenyl formamide is formed when N-methylaniline is treated with manganese dioxide and when a tertiary diamine is present with manganese dioxide than the cleavage of this bond, C-C bond happens along with an oxidation to aldehyde, so you get N-methyl, N-phenyl formamide. So this is N-methyl, N-phenyl formamide.

So that means when an amine, a secondary amine is used with MnO_2 then the formamide motif is formed. On the other hand when primary aromatic amine like 4 chloroaniline is used with manganese dioxide in pet ether solvent and 6 hours condition it gives 87 percent yield of this diazo compound. So primary amine gives diazo compound, secondary aromatic amine gives the formamide derivative and this is secondary amine, this is primary aromatic amine.

So since this secondary amine can gives imine but when N-phenyl or secondary aromatic amine is there then the formamide motif will form.

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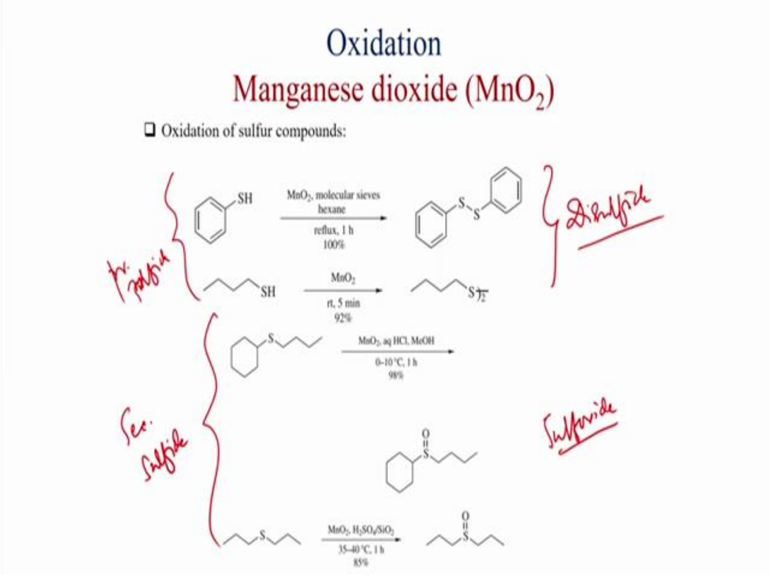

Oxidation

Manganese dioxide (MnO_2)

❑ Oxidation of sulfur compounds:

Oxidation of sulfur compounds here also when primary thiol or primary sulfide is present then it gives the disulfide. So primary sulfides give disulfide, so this is very useful reaction, a manganese dioxide convert this thiophenol with molecular sieves condition and reflux 100 percent yield, close to 100 percent yield of this disulfide is formed. Also in an aliphatic thiol like butane thiol is treated with manganese dioxide you get this disulfide in 92 percent yield.

On the other hand this is secondary sulfide. Secondary sulfide under this condition generates sulfoxide. So this is very important, primary sulfide will gives the disulfide. However, secondary sulfide with MnO_2 aqueous methanol, so you need some acid also as well as MnO_2 and then sulfoxide is formed in 98 percent yield. Also this aliphatic secondary sulfide was converted to the sulfoxide with manganese dioxide, H_2SO_4 silica condition 35 to 40 degree centigrade you get 85 percent yield of this product.

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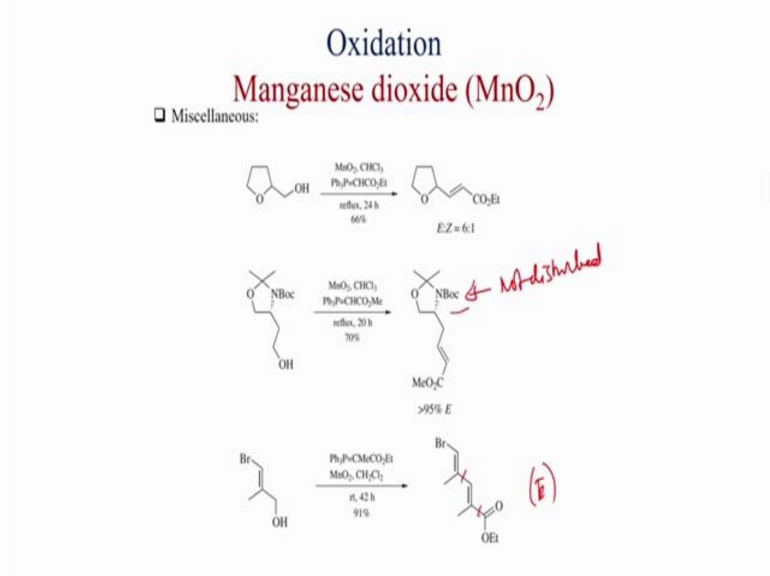

Oxidation

Manganese dioxide (MnO_2)

❑ Miscellaneous:

Here, miscellaneous example, so here this tetrahydrofuran alcohol, primary alcohol is oxidized to the aldehyde by manganese dioxide and then treated with Horner-Wittig ylide this is stabilized ylide and you get the alpha beta unsaturated ester in 6 is to 1 diastereoselctivities. Also a N-Boc derivative is oxidized with MnO_2 then the N-Boc group, this is not disturbed. So N-Boc group is not cleaved under this condition manganese dioxide and selectively the alcohol is getting to the aldehyde and then treated with this Horner-Wittig ylide to get the alpha beta unsaturated ester in 95 percent yield.

So this is very good method for converting alcohol to the alpha beta unsaturated ester and particularly when the aldehydes are unstable then you in situ, you can oxidize with MnO_2 and then treated with the Horner-Wittig ylide to get the alpha beta unsaturated ester. And this condition also very mild like N-Boc group will not be disturbed. Here a bromo containing allylic alcohol was treated with this similar condition manganese dioxide and Horner-Wittig ylide with methyl group present here you get this diene.

So first the alpha beta unsaturated aldehyde is form and then the Wittig Olefination is carried out and here selectively you can see, these 2 groups are trans to each other. So the major product is the E isomer here, so major product is E, so because stabilized ylide generally makes the E geometry.

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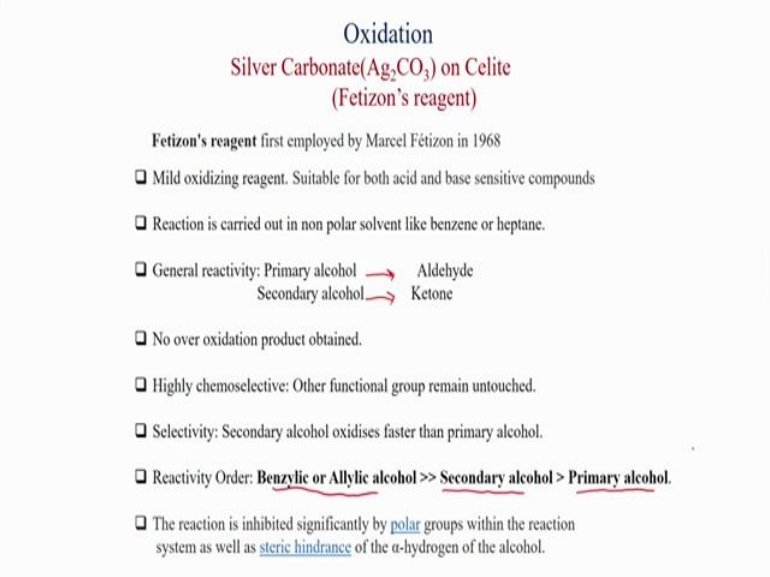

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite
(Fetizon's reagent)

Fetizon's reagent first employed by Marcel Fétizon in 1968

- Mild oxidizing reagent. Suitable for both acid and base sensitive compounds
- Reaction is carried out in non polar solvent like benzene or heptane.
- General reactivity: Primary alcohol → Aldehyde
  Secondary alcohol → Ketone
- No over oxidation product obtained.
- Highly chemoselective: Other functional group remain untouched.
- Selectivity: Secondary alcohol oxidises faster than primary alcohol.
- Reactivity Order: **Benzylic or Allylic alcohol** >> **Secondary alcohol** > **Primary alcohol**.
- The reaction is inhibited significantly by polar groups within the reaction system as well as steric hindrance of the α-hydrogen of the alcohol.

So now we will discuss silver carbonate on celite which is called Fetizon's reagent because the scientist Marcel Fetizon discovered this reagent in 1968. This is also mild oxidizing agent generally suitable for both acid and base sensitive compounds. Reaction is carried out in non-polar solvent like benzene or heptane. General reactivity primary alcohol will gives aldehyde and secondary alcohol gives ketone.

Now over oxidation product obtained. Highly chemoselective generally other functional group remain untouched. Selectivity, secondary alcohol oxidizes faster than primary alcohol, so this is also special of Fetizon reagent. And the reactivity order is benzylic or allylic alcohol reacts must faster than secondary alcohol and secondary alcohol reacts faster than primary alcohol.

Also the reaction is inhibited significantly by polar groups within the reaction system as well as steric hindrance of the alpha hydrogen of the alcohol.

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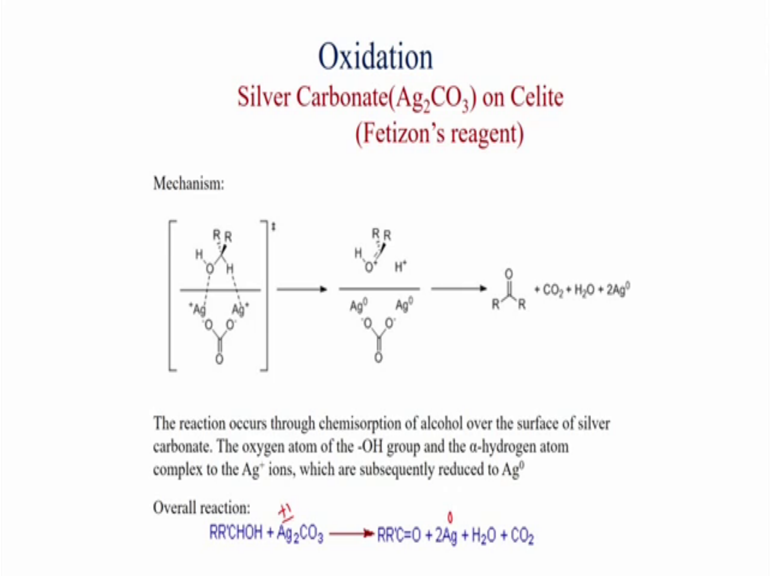

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

Mechanism:

The reaction occurs through chemisorption of alcohol over the surface of silver carbonate. The oxygen atom of the -OH group and the α-hydrogen atom complex to the Ag^+ ions, which are subsequently reduced to Ag^0

Overall reaction:

$$RR'CHOH + \overset{+1}{Ag}_2CO_3 \longrightarrow RR'C{=}O + 2\overset{0}{Ag} + H_2O + CO_2$$

So what is the mechanism of this reaction? The mechanism is that the chemisorption of the alcohol over the surface of silver happensand then the alcohol oxygen as well as the alpha hydrogen binds with silver and ultimately the silver 1 goes to silver 0 and here H plus is formed as well as oxonium ion and this oxonium ion finally gives the carbonyl compound, so what is the overall reaction?

The overall reaction is the alcohol plus Ag_2CO_3 you get carbonyl compound, 2Ag, water and one molecule of carbon dioxide. So Ag plus 1 to it is going to a silver which is 0 that is why it is getting reduced and the alcohol is getting oxidized.

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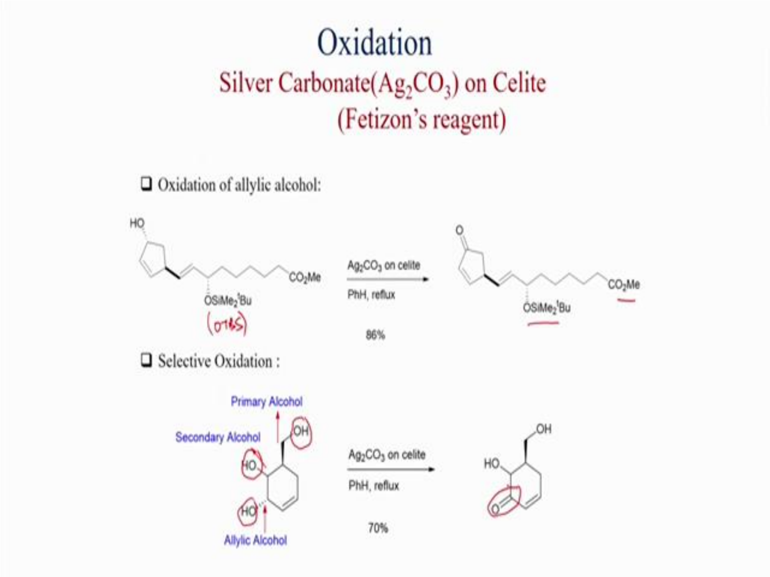

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

- ☐ Oxidation of allylic alcohol:

- ☐ Selective Oxidation :

It is useful for the oxidation of allylic alcohol like MnO_2. Here a TBS group is there and a ester group is present and selectively with silver carbonate or celite in benzene reflux conditions, allylic alcohol is getting oxidized and this group are untouched, a TBS group as well as ester group. Also selective oxidation of a primary or secondary allylic alcohol is possible over other alcohols.

So like in this triol here this is the allylic alcohol and this is a secondary saturated alcohol, this is primary saturated alcohol and when you treat this compound with silver carbonate on celite in benzene reflux condition you get only selectively this allylic alcohol is getting oxidized to the carbonyl compound and you get 70 percent yield of this product.

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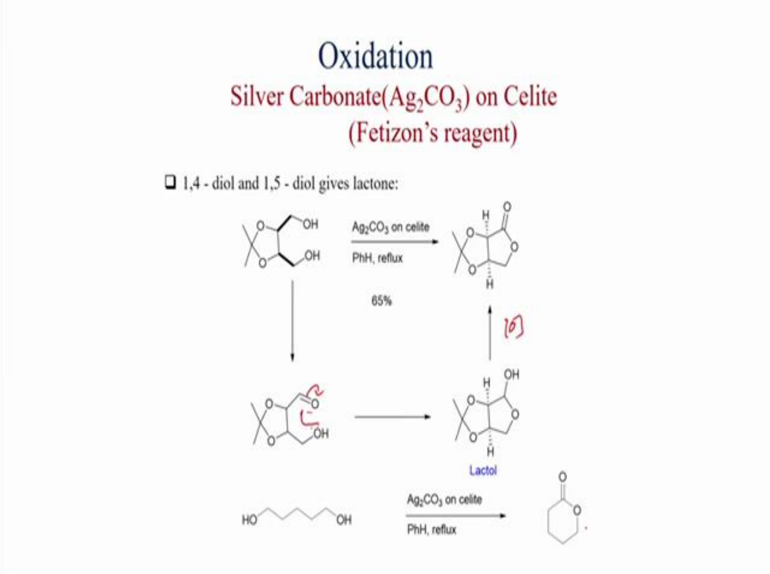

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

❑ 1,4 - diol and 1,5 - diol gives lactone:

1,4 diol and 1,5 diol gives lactone like this diol when was treated with silver carbonate it gives first the aldehyde, one alcohol oxidized to the aldehyde and then its gives the lactol, so lactol is formed. And this lactol then oxidation gives the lactone. Also when pentanediol is used with silver carbonate and celite benzene reflux condition you get this lactone is good yield.

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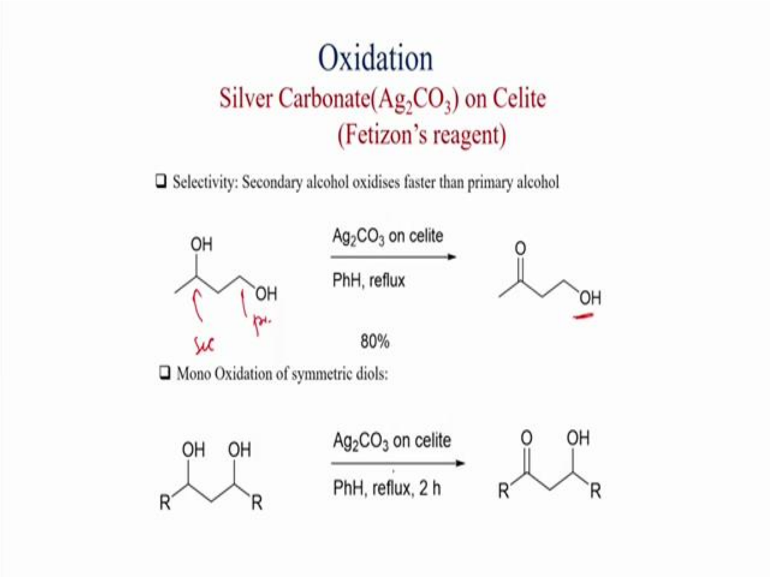

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

❑ Selectivity: Secondary alcohol oxidises faster than primary alcohol

❑ Mono Oxidation of symmetric diols:

Selectivity secondary alcohol oxidizes faster than primary alcohol like this diol is there, this is primary alcohol and this is secondary alcohol, so with silver carbonate on celite benzene reflux condition only the secondary alcohol getting oxidize and primary alcohol untouched does not react in this condition. Also when a symmetric diol is used like both are secondary, here one alcohol can be oxidized and you can get the beta hydroxy carbonyl compound in good yield.

Here silver carbonate benzene reflux condition is used.

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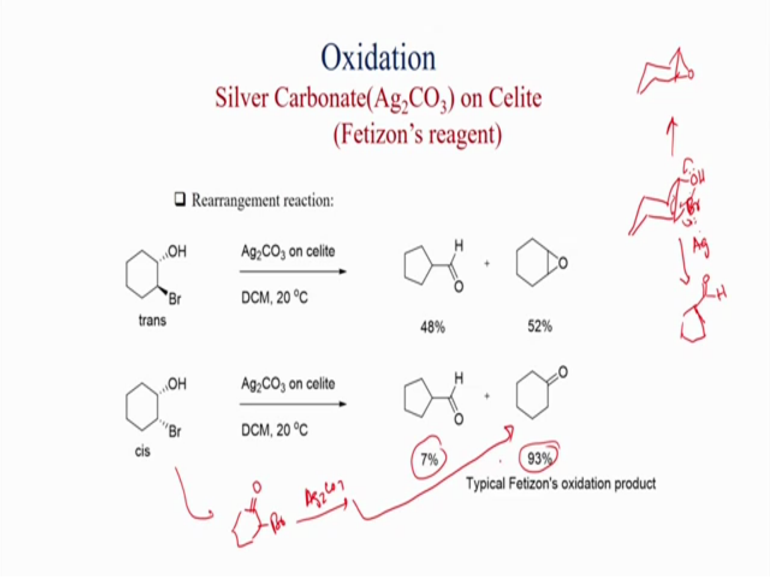

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

❑ Rearrangement reaction:

Typical Fetizon's oxidation product

Also silver carbonate is used for rearrangement reaction like this trans bromo compound. Trans bromo alcohol when treated with silver carbonate celite you get almost 1:1 mixture of cyclopentanecarbaldehyde plus epoxide. On the other hand when cis compound was treated with silver carbonate Celite condition you get cyclohexanone as the major product and this product is minor.

So this is typical Fetizon oxidation product, so what would be the mechanism? So generally bromo compound is bind to the silver and what happens? This bromo compound is getting activated and then a rearrangement will happen and you get this compound cyclopentanecarbaldehyde and also there is a possibility of the epoxide because they are trans, so you can get also epoxide.

On the other hand when cis is used that time because they are cis to each other, so they cannot rearrange on from the epoxide, so that is why rearrangement product is very less, only the cyclohexanone is formed, so most likely first is getting oxidized to the 2 bromo cyclohexanone and then silver carbonate converts this to cyclohexanone.

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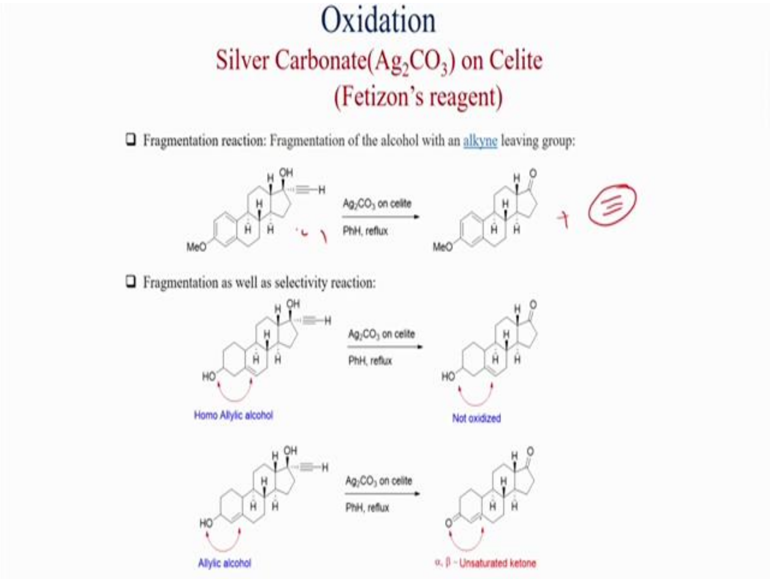

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

❑ Fragmentation reaction: Fragmentation of the alcohol with an alkyne leaving group:

❑ Fragmentation as well as selectivity reaction:

Fragmentation reaction. fragmentation reaction of the alcohol with the alkyne as a leaving group is possible with this reagent and generally this propargylic secondary alcohol with silver carbonate on celite in benzene reflux condition, it gives the ketone and alkyne as a living group. So this alkyne is getting eliminated or fragmented under this condition.

Also fragmentation as well as selectivity is possible like this steroid molecule. Here you can see there is a propargylic alcohol as well as a another secondary alcohol which is homoallylic and when silver carbonate on celite in benzene reflux used only this propargylic alcohol is getting fragmented and converting to the ketone and this homoallylic alcohol not oxidized under this condition.

On the other hand this substrate whereas a both allylic alcohol as well as propargylic alcohol is present and with silver carbonate on celite benzene reflux condition it cannot distinguish between these two groups and both gets oxidized. So here a saturated ketone is formed and here an unsaturated ketone is formed generally in good yield.

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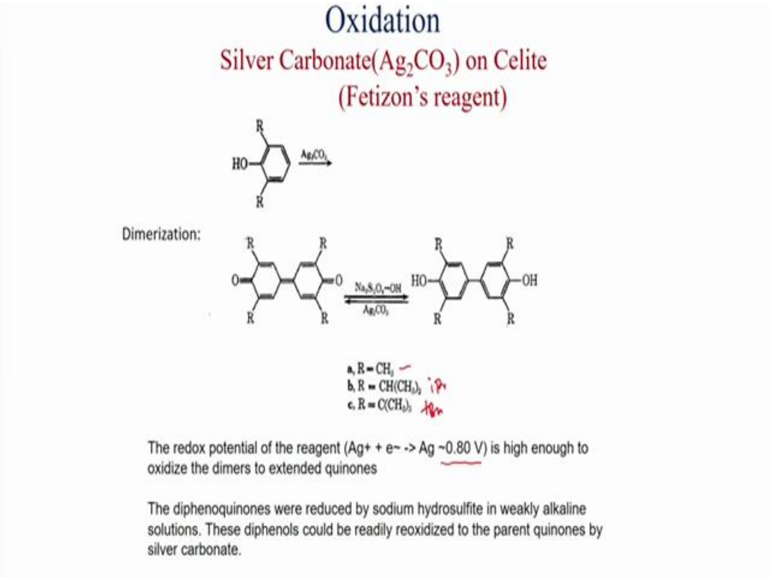

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

Dimerization:

a, R = CH_3

b, R = $CH(CH_3)_2$ iPr

c, R = $C(CH_3)_3$ tBu

The redox potential of the reagent (Ag+ + e- -> Ag ~0.80 V) is high enough to oxidize the dimers to extended quinones

The diphenoquinones were reduced by sodium hydrosulfite in weakly alkaline solutions. These diphenols could be readily reoxidized to the parent quinones by silver carbonate.

Also Fetizon reagent has been used for dimerization reaction of phenol derivatives, here 2, 6 disubstituted phenol and when R is equal to CH_3, R is equal to $CH(CH_3)_2$ which is isopropyl and tertiary butyl, so when 2, 6 disubstituted phenol is treated with silver carbonate then this quinone compound is formed and quinone compound is formed generally first this quinol will form and which also oxidizes with silver carbonate to get this quinone.

Here the redox potential of the reagents silver plus to plus electron to silver is 0.80 volt is high enough to oxidize the dimer to extended quinones, and this diphenoquinones are reduced by sodium hydrosulfite in weakly alkaline solution. So sodium hydrosulfite converts this diquinone to the quinol and then this diphenols could be readily oxidized to the parent quinones by silver carbonate.

So this means that this first getting to the dimer product, dimer diphenol product and then it is going oxidized with silver carbonate to the diphenoquinone. Also if you want to get back this then we can treat with sodium hydrosulfide to get this phenol diphenol compound.

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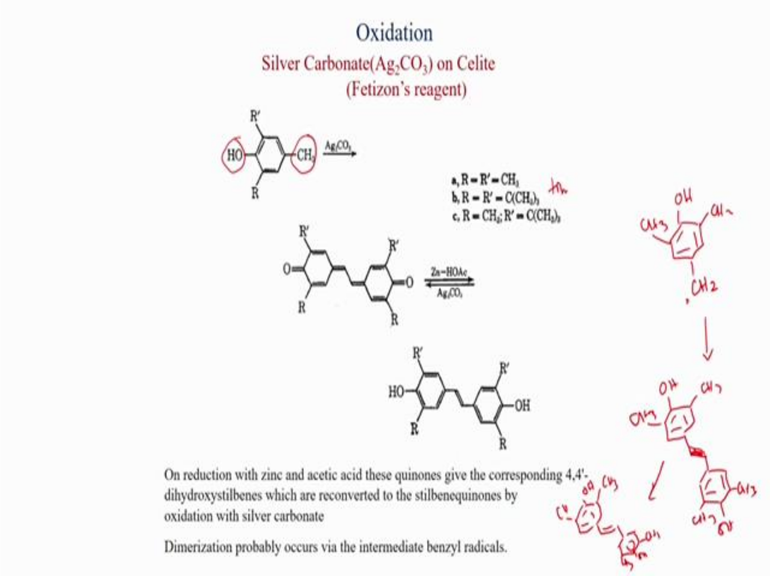

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

a, $R = R' = CH_3$

b, $R = R' = C(CH_3)_3$

c, $R = CH_3$; $R' = C(CH_3)_3$

On reduction with zinc and acetic acid these quinones give the corresponding 4,4'-dihydroxystilbenes which are reconverted to the stilbenequinones by oxidation with silver carbonate

Dimerization probably occurs via the intermediate benzyl radicals.

And it has been found that when a methyl group is present para to the OH group then this conjugated dione system is formed. Here also we can use different substitution like both methyl and both tertiary butyl and one methyl and another tertiary butyl, but para position will be CH_3 group then you get this quinone system and then with treatment with the zinc acetic acid you can get this conjugated bisphenol system which on oxidation with silver carbonate gives this quinone, conjugated quinone motif.

So on reduction with zinc acetic acid this quinone give the 4, 4 dihydroxystilbenes which are reconverted to the stilbenequinones by oxidation with silver carbonate. And the dimerization probably occurs via the intermediate benzylic radicals. So, most likely when CH_3 group present to the para to the OH group and if there is substitution is there like methyl then this benzylic radical is formed and this benzylic radical first goes to stilbene phenol.

First maybe the saturated compound, first maybe saturated, and then the unsaturation, so when a methyl group is present then this a conjugated enone system will form.

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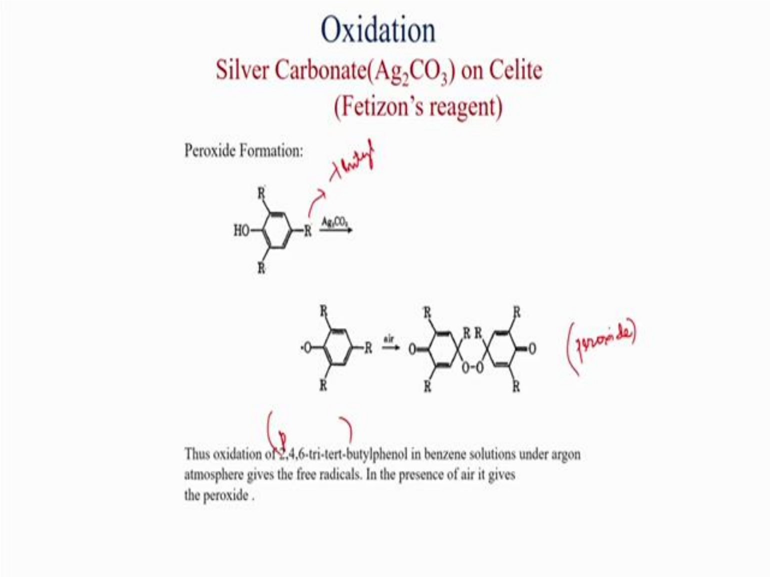

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

Peroxide Formation:

Thus oxidation of 2,4,6-tri-tert-butylphenol in benzene solutions under argon atmosphere gives the free radicals. In the presence of air it gives the peroxide .

And now when this para position instead of methyl group if tertiary butyl group is there, suppose R- here tertiary butyl group, then it has been found that this peroxide is formed because now there is no possibility of the benzylic radical, so only now phenoxy radical will form. Phenoxy radical is formed which dimerize under this condition, oxidative dimerization and it gives this peroxide compound.

Oxidation of 2, 4, 6 tri tert butylphenol in benzyl solution under atmosphere gives the free radicals. In the presence of air it gives the peroxide. So when there is a methyl group then the benzylic radical is possible.

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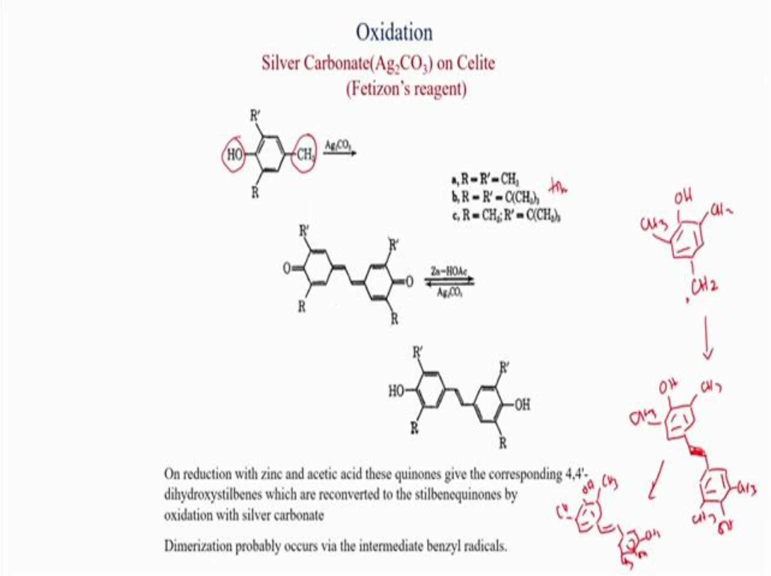

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

a, $R = R' = CH_3$

b, $R = R' = C(CH_3)_3$

c, $R = CH_3; R' = C(CH_3)_3$

On reduction with zinc and acetic acid these quinones give the corresponding 4,4'-dihydroxystilbenes which are reconverted to the stilbenequinones by oxidation with silver carbonate

Dimerization probably occurs via the intermediate benzyl radicals.

And that case you can get this kind of system and dienone with a quinone motif.

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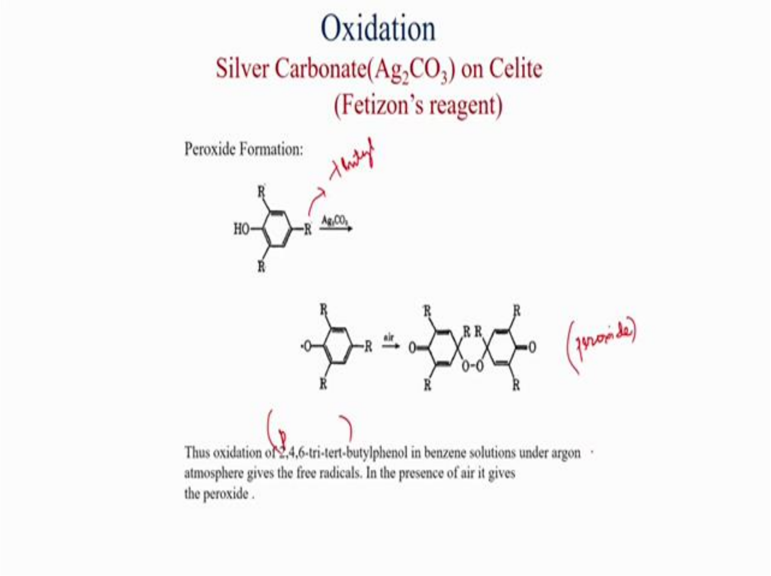

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

Peroxide Formation:

Thus oxidation of 2,4,6-tri-tert-butylphenol in benzene solutions under argon atmosphere gives the free radicals. In the presence of air it gives the peroxide .

And when there is a tertiary butyl group than the phenoxy radical will form and then the peroxide will form.

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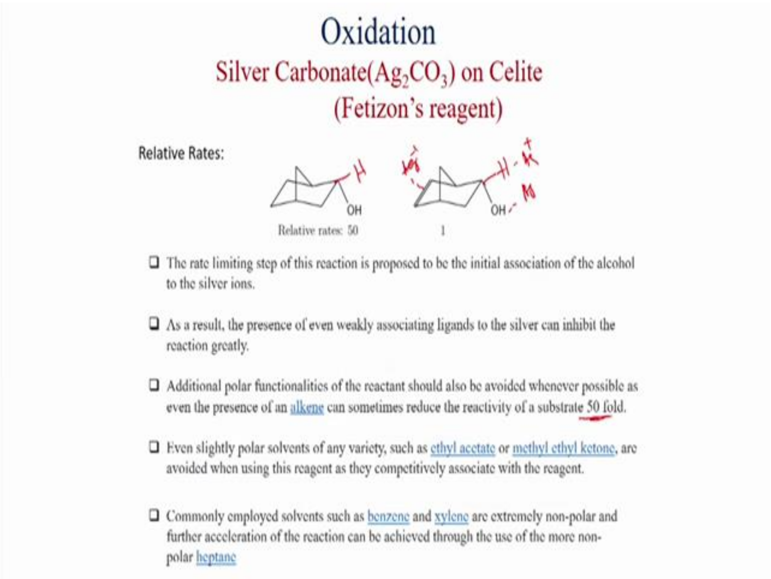

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite

(Fetizon's reagent)

Relative Rates:

Relative rates: 50 1

- ❑ The rate limiting step of this reaction is proposed to be the initial association of the alcohol to the silver ions.
- ❑ As a result, the presence of even weakly associating ligands to the silver can inhibit the reaction greatly.
- ❑ Additional polar functionalities of the reactant should also be avoided whenever possible as even the presence of an alkene can sometimes reduce the reactivity of a substrate 50 fold.
- ❑ Even slightly polar solvents of any variety, such as ethyl acetate or methyl ethyl ketone, are avoided when using this reagent as they competitively associate with the reagent.
- ❑ Commonly employed solvents such as benzene and xylene are extremely non-polar and further acceleration of the reaction can be achieved through the use of the more non-polar heptane

Now relative rate also has been found with silver carbonate reaction, so when there is a group which can bind to silver then the rate of the oxidation will get reduce. So like this bridge system here no olefin is present but here there is olefin and if these two alcohols both are secondary alcohols are treated with MnO_2 then the relative rates have been found 50 is to 1. So without double bond that substrate reacts 50 times faster than this compound.

The rate limiting step of this reaction is proposed to be the initial association of the alcohol to the silver ions. We have seen that alcohol binds to the silver as well as the alpha hydrogen, so this binding is very important. As a result, the presence of even weakly associating ligands to the silver can inhibit the reaction greatly. So if there are ligands on silver then the reaction can decrease.

The rate of the reaction can decrease significantly. Additional polar functionalities of the reactor should also be avoided whenever possible as even in the presence of an alkene can sometimes reduce the reactivity of a substrate 50 fold. So that is what we have seen here, so that means the double bond is binding with silver here. So there is a competing reaction is happening with the silver double bond as well as the OH and alpha hydrogen.

Even slightly polar solvents of any variety such as ethyl acetate or methyl ethyl ketone are avoided when using this reagent, as they competitively associate with the reagent. So ethyl acid polar solvents should be avoided. Commonly employed solvent such as benzene and xylene are extremely non-polar and further acceleration of the reaction can be achieved through the use of more non-polar heptane.

So choice of solvent is very important in silver carbonate or Fetizon reagent oxidation we have to use very non-polar solvent like benzene, xylene and sometimes you can add also non-polar heptane. So in today's class we have seen the manganese dioxide oxidation and silver carbonate which is Fetizon reagent, so manganese dioxide does many reactions and like it is major application is oxidation of allylic as well as benzylic alcohol.

It can selectively oxidize benzylic alcohol or allylic alcohol in the presence of other saturated alcohols and oxidation of saturated alcohols is also possible but we have to use high temperature or other catalyst. Also cleavage of diols cis 1,2 diols we have seen this is also a reaction which is generally carried out sodium periodate but here manganese dioxide under very mild condition can cleave cis 1,2 diols.

Also if this dialdehydes can be treated insitu with Horner-Wittig reagent to get the alpha beta unsaturated esters in good stereo selectivities. Also Corey-Ganem they have reported a insitu reaction with sodium cyanide, the aldehyde with sodium cyanide MnO_2 and acetic acid condition to give the alpha beta unsaturated ester by methanol used also alpha beta unsaturated amides $CONH_2$ when ammonia gas is used.

Also MnO_2 has been found for different dehydrogenation and aromatization reaction which you have seen with DDQ, so manganese dioxide also can perform different aromatization as well as dehydrogenation reaction, so different saturated heterocycles as well as benzene derivatives can be converted to unsaturated heterocycles. So heterocycles or aromatic heterocycles and aromatic benzene compounds in very good yields.

Also sulfide compounds, if we have primary sulfide then we get disulfide and if there is a secondary sulfide then we get sulfoxide. Also amine compounds can also be converted into imines when there is a saturated secondary amine that can be converted to the imine and even there is an N-phenyl or aromatic amine is present then you will get the formamide derivative. Also if the aromatic amine is present then we get the diazo compound.

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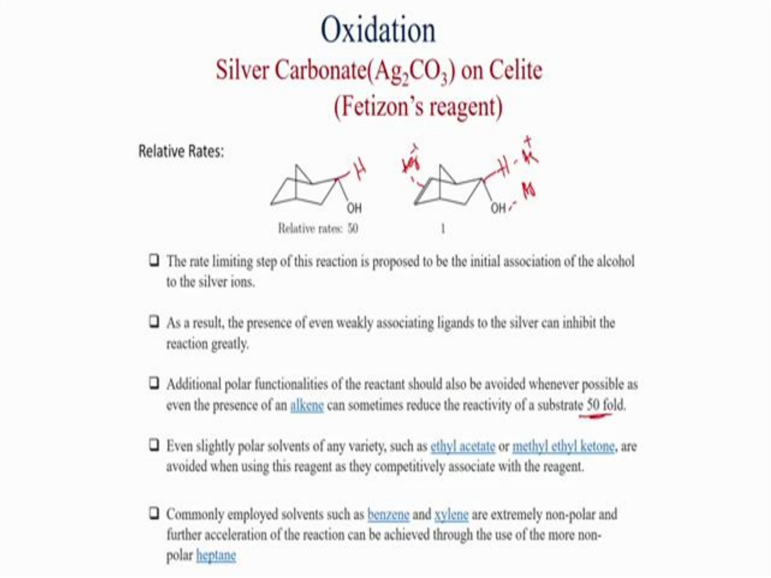

Oxidation

Silver Carbonate(Ag_2CO_3) on Celite
(Fetizon's reagent)

Relative Rates:

Relative rates: 50 1

- ☐ The rate limiting step of this reaction is proposed to be the initial association of the alcohol to the silver ions.
- ☐ As a result, the presence of even weakly associating ligands to the silver can inhibit the reaction greatly.
- ☐ Additional polar functionalities of the reactant should also be avoided whenever possible as even the presence of an alkene can sometimes reduce the reactivity of a substrate 50 fold.
- ☐ Even slightly polar solvents of any variety, such as ethyl acetate or methyl ethyl ketone, are avoided when using this reagent as they competitively associate with the reagent.
- ☐ Commonly employed solvents such as benzene and xylene are extremely non-polar and further acceleration of the reaction can be achieved through the use of the more non-polar heptane

Now with silver carbonate or Fetizon reagent we have seen that this is very useful for oxidizing benzylic, allylic alcohols also its reactivity is more than primary alcohol. So secondary alcohol much more reactive than primary alcohol and also it has been found that in the diol where primary and secondary alcohol is present, secondary alcohol is getting selectively oxidized to the ketone and the primary alcohol is getting untouched.

Also different fragmentation reactions like propargylic alcohol can be fragmented with silver carbonate with liberation of acetylene you can get the carbonyl compound and this reaction also is much faster compared to other saturated secondary alcohol. Also you have seen that rearrangement reaction like when trans bromo derivatives are there, trans bromo cyclohexanol is used then cyclopentanecarbaldehyde is formed whereas the cis compound there is no such rearrangement and simple cyclohexanone is formed.

And lastly, we have seen the substrate when there is an internal double bond is present, so that substrate is much less reactive compared to the substrate where no double bond is there that means there is a competition for the binding to the silver, the double bond can also bind and that is why the reactivity or the rate of this reaction is significantly decreased. And also in this silver carbonate reaction you have to use non-polar solvent like benzene, toluene also you can use heptane but polar solvent like ethyl acetate or ketone compounds should not be used.

I hope you have enjoyed thank you.