CH 2123 - Principles of Organic Chemistry

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PRINCIPLES OF ORGANIC CHEMISTRY II

CH 2123 (E) - Semester 3

31/8

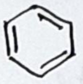
Lecture 1.1

Benzene and Aromaticity

To understand aromaticity from a structural standpoint:

sp^3 C − C 1.47 Å

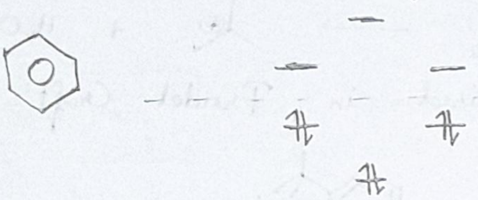
sp^2 C = C 1.33 Å



Bond length of benzene − 1.39 Å

[In between single & double bonds]

Structure of Benzene from an orbital perspective −



3 Antibonding

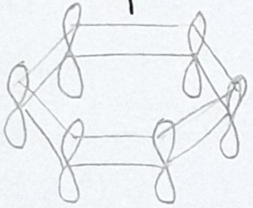
P orbitals out of phase

6 electrons present in the 3 bonding orbitals

3 Bonding

P orbitals of adjacent C-atoms are in phase ⇒ contribute to bonding

Since all 6 π electrons are in the Bonding MO of benzene, they give an exceptional stability to the molecule.



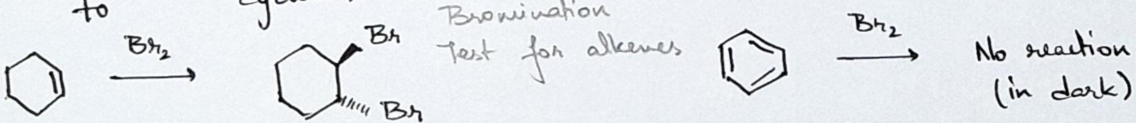
All 6 P orbitals are conjugated Make it very stable.

Revise Hybridis (!!)
sp^2 hybridised C atom has 1 unhybridised p-orbital which forms the π bond

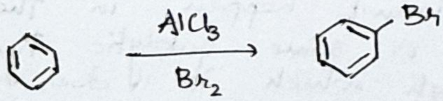
Reactivity of Benzene

To study its reactivity, we compare its reactions to cyclohexene.

→



But benzene in presence of a Lewis acid − Substitution reaction:

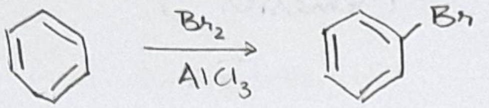


⇒
- Olefins are more reactive than benzene
- Nature of the reaction (addition v/s substitution) is very different.

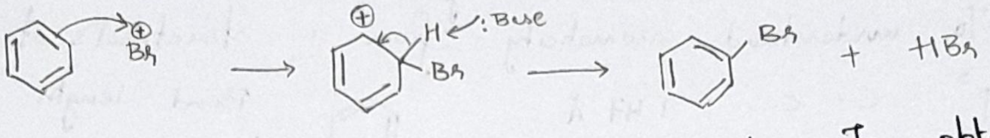
Lecture 1.2

Electrophilic Aromatic Substitution

Mechanism —

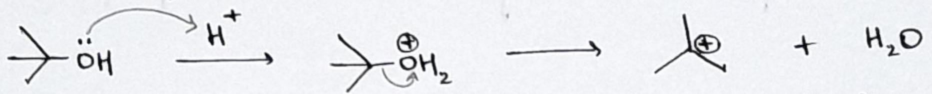


$Br-\ddot{Br}: \rightarrow AlCl_3 \longrightarrow Br^{\oplus} + Br-\overset{\ominus}{AlCl_3}$

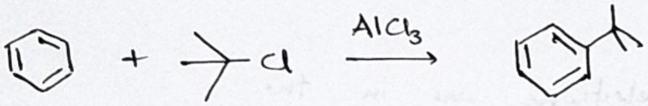


Electrophiles can be of different kinds. To obtain carbon based electrophiles —

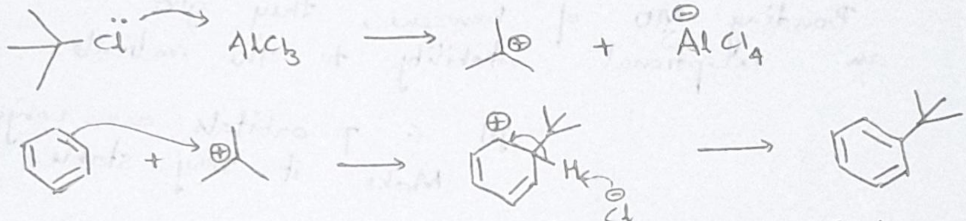
S_N1 or E1 reactions —



This is what is desired in Freidel Craft's Alkylation —

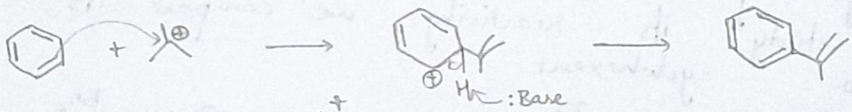


Mech :

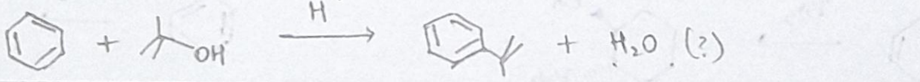


Q Mechanism of generating C-based E⊕ through S_N1 and using it in F-C Alkylation Reaction.

S_N1 : As shown above



So,



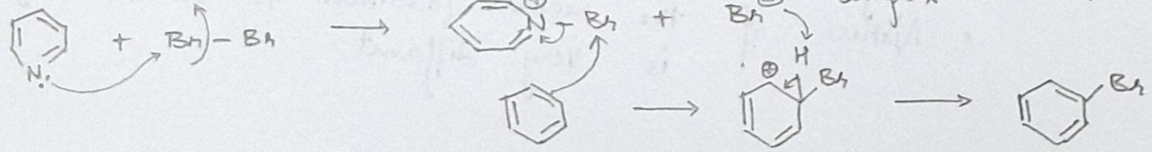
Lecture 1.3

P. Bromination of benzene doesn't happen in the dark — it needs a Lewis acid or some catalytic Pyridine. Write the mechanism through which it does.

Pyridine.

$Br^{\oplus}$ has to be generated

The pyridine – Br complex is unstable



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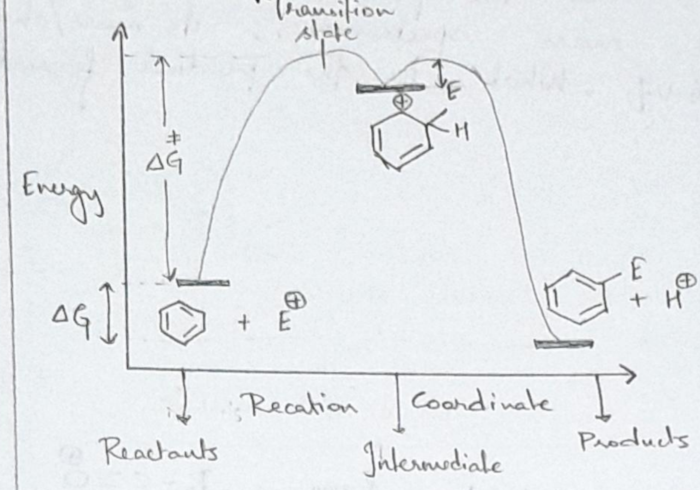
Energy Profile of Electrophilic Aromatic Substitution



- The intermediate has higher energy because aromaticity is * broken
- Most EAS reactions are exothermic, so energy of products is lower than that of reactants (i.e. more stable).

*EAS can be exothermic or endothermic based on the bonds that are broken.

Hammond Postulate : From this, in a highly endothermic reaction, the transition state resembles the product

- As a corollary, we can say that in highly exothermic reactions, the ~~intermediate~~ transition state resembles the reactant. This is true for EAS as well.
- $\Delta G^{\ddagger}$: Activation energy

$\Delta G / \Delta H$ (?) : Energy of Reaction

- In most cases, the intermediate collapses and gives rise to the product fairly quickly.

The formation of the intermediate is the Rate Determining Step

- Energy profiles can help us understand the stability issues and the selectivity (ortho, meta, para) in a reaction

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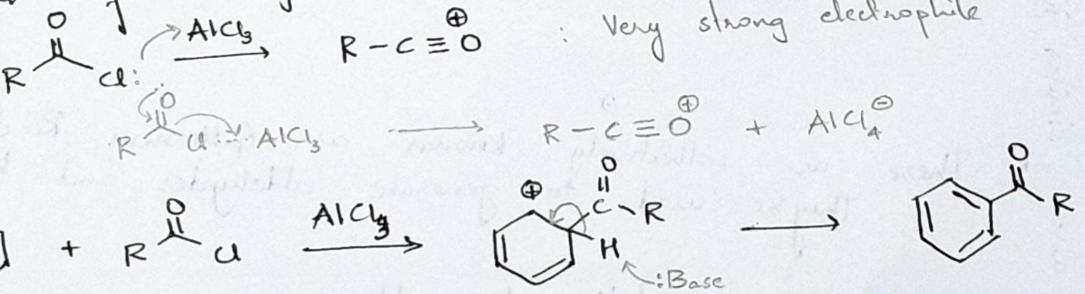
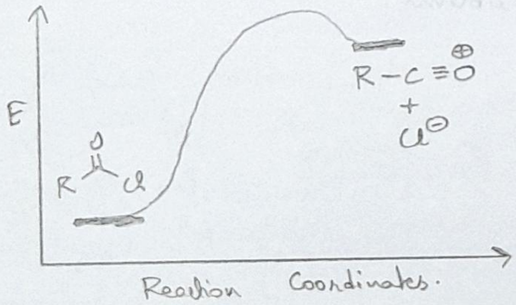
Lecture 1.4

Freidel Craft's Acylation.



: Very strong electrophile

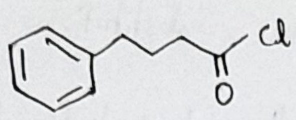


Energy Profile

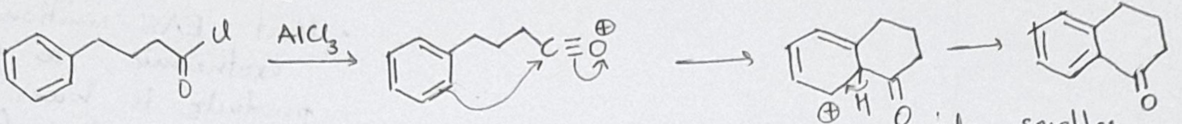
The energy profile of the whole reaction is similar to that of Freidel Craft's alkylation

FC Alkylation gives multiple products So its better to use acylation & the reduce using Zn-Hg | HCl

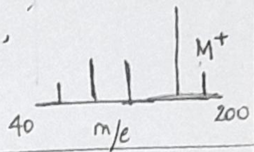
P.



When Lewis acid $AlCl_3$ is added to this and the product is analysed under mass spectrometer, its mass/charge value is : $\frac{m}{z} = 146.07$. What is the product formed?



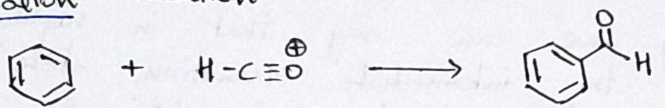
A mass spectrometer essentially fragments a molecule into smaller peices and its detected; and in the Mass Spectrum, m/e of each of the fragments is shown. The maximum mass - fragment gives us the molecular weight of the molecule



The $E^{\oplus}$ generated is of the form : $R-C\equiv\overset{\oplus}{O}$

R can be anything. If R- is H- we get -

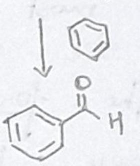
Formylation Reaction



: Benzaldehyde

→ To generate $H-C\equiv\overset{\oplus}{O}$, we need certain conditions -

$$* \; HCl + C\equiv O + AlCl_3 \underset{}{\overset{CuCl_2}{\rightleftharpoons}} H-C\equiv\overset{\oplus}{O} + AlCl_4^{\ominus} \; *$$



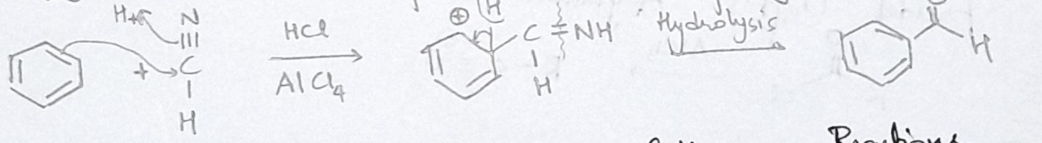
→ This is Gatterman - Koch Reaction

Its a modification of FC Acylation that allows us to make aromatic aldehyde

→ If we use HCN instead of CO

H - C ≡ N is isoelectronic to $H-C\equiv\overset{\oplus}{O}$

So we can use it for the same formylation reaction



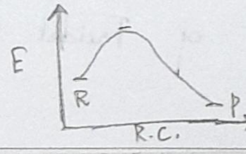
→ These are collectively known as Gatterman Reactions. They're used to generate aldehydes and ketones.

Lecture 1.5 - solution to problems.

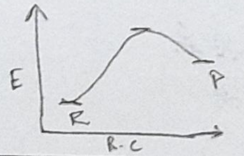
Hammond's Postulate - States that transition state of a reaction resembles either reactants or products, to whichever it is closer in energy

Structures close in energy that transform into each other directly are also similar in structure

* Exothermic Rxn
Closer to Reactant



* Endothermic Rxn
Closer to Product



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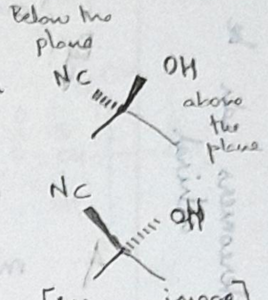
Lecture 02 (2.1)

Stereochemistry

Its very important because all proteins and biomolecules are stereospecific.

Chirality

This chiral molecule can't be superimposed on its mirror image.

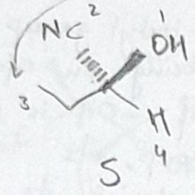


[Mirror image]

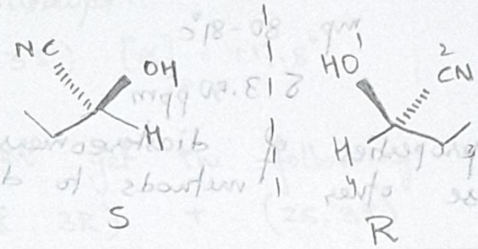
Achiral molecu

It requires an element of asymmetry — the four groups on sp^3 hybridised carbon have to be different.

Eg:



By Cahn - Ingold - Perlog nomenclature, assigning priorities to various groups, see if they're in clockwise (R) or anticlockwise direction (S)



In Fischer Projection —
- * Least priority group has to be on the vertical plane (below, ref)
- * If you've to turn 90°/180° to get it there —
  - → Even changes (180°) : Same configuration
  - → Odd changes (90°) : other enantiomer

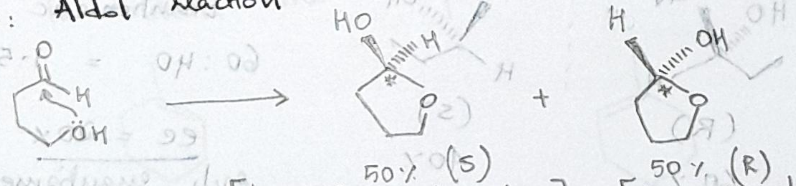
Lecture 2.2

Stereogenic center

Its a chiral carbon atom, which has 4 different substituent groups.

These sterogenic centers can be produced in a reaction.

Example: Aldol reaction



[Attack from below plane] [Above the plane]

The oxygen can attack the carboxylic carbon atom from below the plane or above plane. And based on this, the new -OH group is formed above/below.

Since there is no other factor, we get an equal mixture of both enantiomers — A Racemic Mixture

Diastereomers can be chiral or achiral

Diastereomers

They are non-mirror image, non-identical stereoisomers.

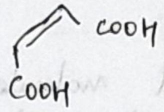
They can have different physical properties [while enantiomers only differ in their optical activity]

Eg:

(trans)

Fumaric acid

mp. ~ 300°C



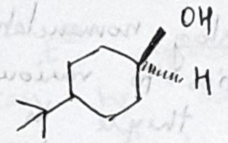
(cis)

Maleic acid

mp. ~ 140°C

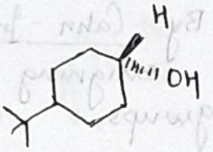
A mixture of diastereomers is easier to seperate

Eg:



(cis)

mp. 82°-83°C



(trans)

mp. 80-81°C

t-butyl group prefers being on equatorial plane So if -OH is on axial group, its cis & if on equatorial, its trans (on C_4)

^{1}HNMR : δ 4.02 ppm   δ 3.50 ppm

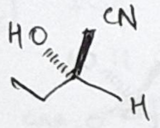
So if physical properties of diastereomers are close, one can use other methods to distinguish them.

Lecture 2.3

Enantiomeric Excess

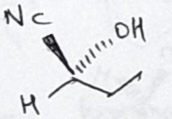
Its a measure of how much one enantiomer is produced more in relation to the other (relative excess)

Consider this example —



(R)

60 %



(S)

40 %

Enantiomeric Ratio :-

60 : 40 = 1.5 : 1

ee = 20% ∵ 40% of each enantiomer would cancel out the other's optical activity

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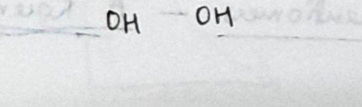
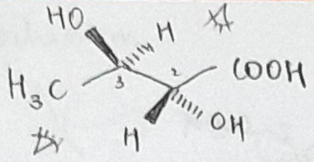
Lecture 2.4

Two chiral centres

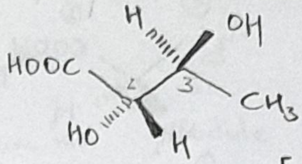
Example :



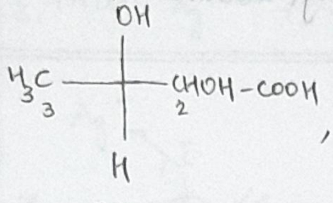
$\overset{4}{CH_3}-\underset{OH}{\overset{3}{C^*H}}-\underset{OH}{\overset{2}{C^*H}}-\overset{1}{COOH}$



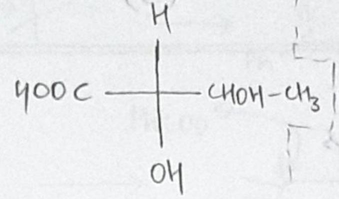
3R , 2R → $[\alpha] = -9.5°$



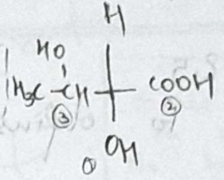
2S, 3S → $[\alpha] = +9.5°$



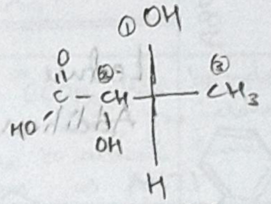
3R



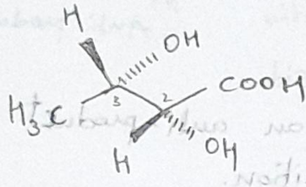
2R



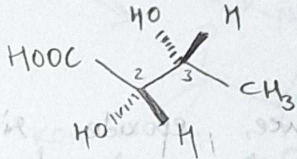
2S



3S



Just flip the 3R to get 3S



(2R , 3S) $[\alpha]_D = +17.8°$

(2S , 3R) $[\alpha]_D = -17.8°$

Eg: If we get the following as products —
(2R , 3R) + (2S, 3R)
95% 5%

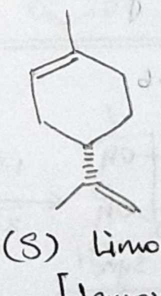
Diastereomeric ratio = 95 : 5
= 19 : 1
Diastereomeric excess = 90%

Chirality in Nature

All kinds of biomolecules (sugars, proteins, nucleic acid) are chiral in nature and found naturally. They're called the chiral pool because they can be extracted and used to obtain the compounds we want.

Eg:

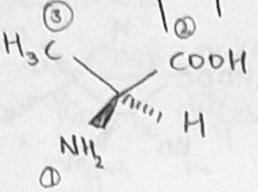
(R) Limonene
[oranges]



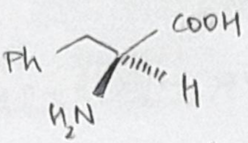
(S) Limonene
[lemons]

They can be used as starting materials for synthesis

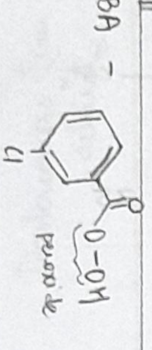
In case of proteins —



(S) + Alanine

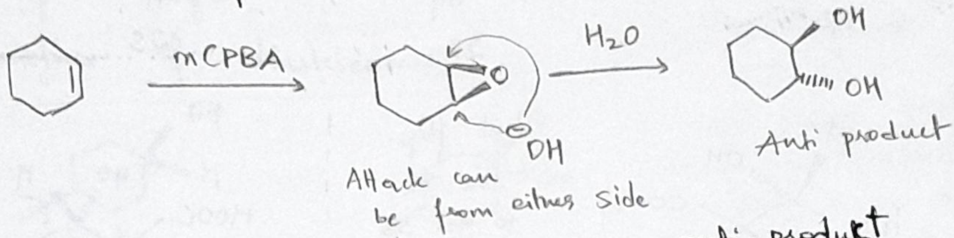


(S) - Phenyl alanine

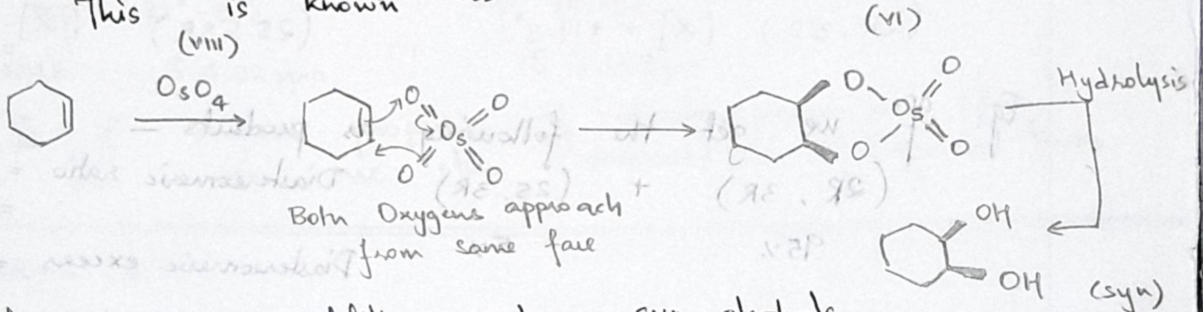


Lecture 2.5

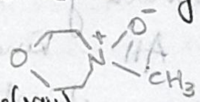
Addition to olefins



Hence, epoxide ring opening causes an anti-product
This is known as anti-addition.

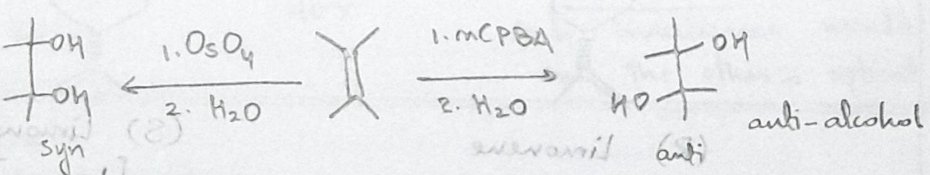


This is syn addition: produces syn alcohols.
But osmium is toxic. So, ~~an alternate~~ a solution is using —
NMO : N-metyl morpholine oxide :



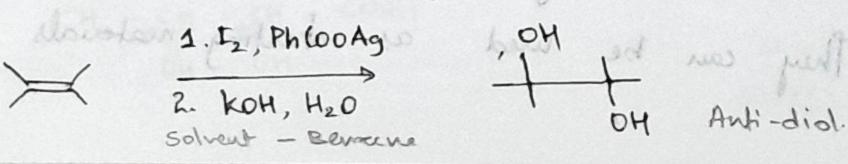
to re-oxidize osmium from Os(VI) — Os(VIII).
Catalytic NMO to reoxidize this & OsO_4 can be used to generate syn alcohols.

Lecture 2.6

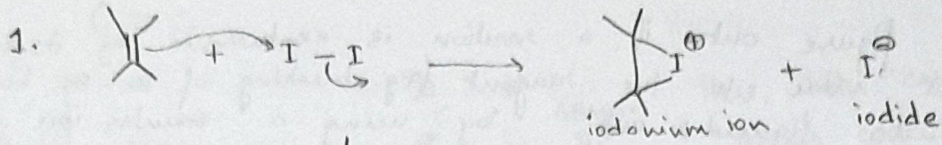


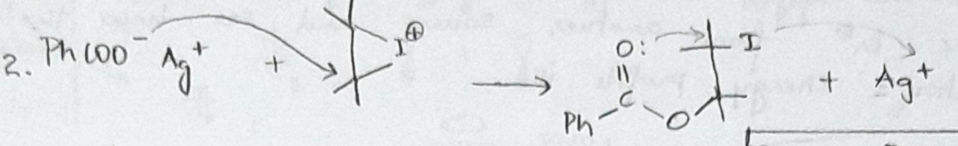
Some other methods of getting alcohols are —

Prévost Reaction :

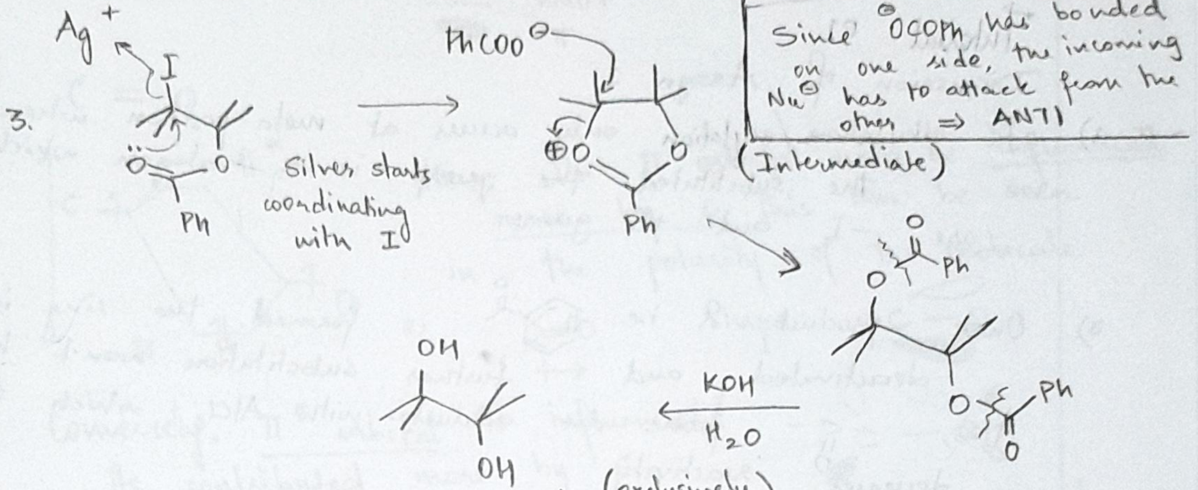


Mechanism





Since ⊖OCOPh has bonded on one side, the incoming Nu⊖ has to attack from the other ⇒ ANTI

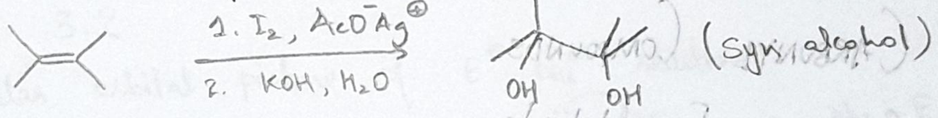


Anti-product (exclusively)

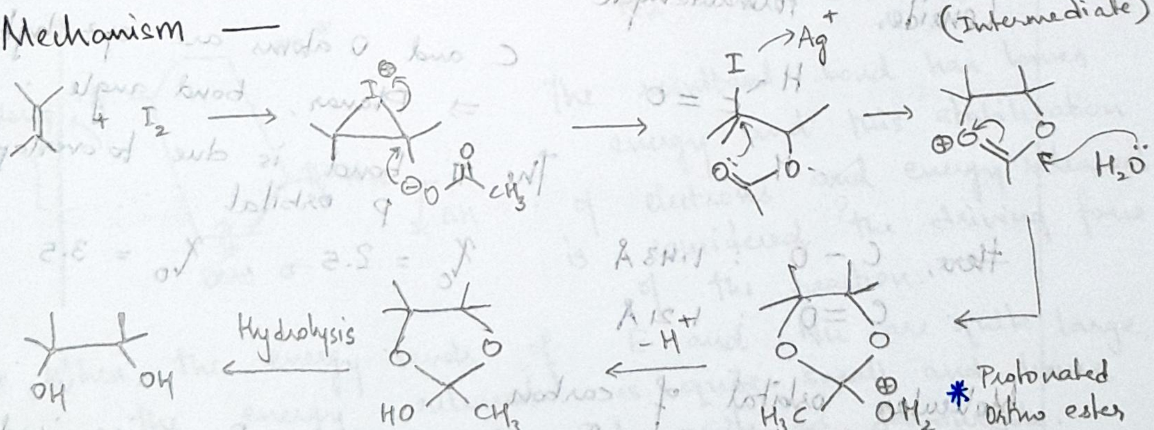
Lecture 2.7

Woodward's Reaction

Its a modification of Prévost Reaction

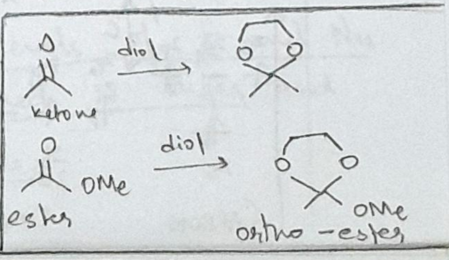


Mechanism —



Syn diol

Ortho ester ~ carboxylic acid equivalent



Discussion 01

To figure out if a reaction is exothermic by itself or due to the reagent (Eg. breaking of Br – Br bond) can be figured out by using a counter ion – we $Br^{\oplus}$ from another source and see how the reaction's energy profile is.

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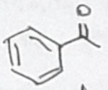
Tutorial 01

Discussion of Assgn 1

★ 2) FC alkylation / acylation only occurs at meta-position when the substituted the group is a halogen which are –I and +R groups.

3) Once product X i.e.  is formed, the ring is deactivated and further substitution won't happen. Also, $-\underset{\underset{O}{\|}}{C}-$ forms an adduct with $AlCl_3$ which further decreases reactivity

★ 1) Aniline's ring is not deactivated – it just forms an adduct with $AlCl_3$

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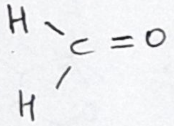
Lecture 3.1

CARBONYL COMPOUNDS

Consider Formaldehyde



C and O atoms are sp^2 hybridised

⇒ Planar, bond angle : 120°.

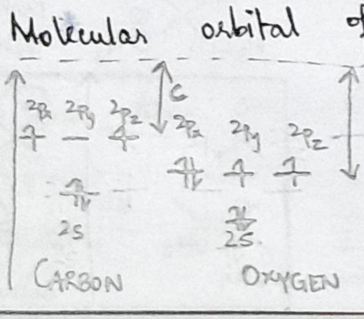
The π bond is due to overlap of parallel p orbital

Here, C – O : 1.43 Å

C = O : 1.21 Å

$\chi_C = 2.5$, $\chi_O = 3.5$

Molecular orbital of carbon

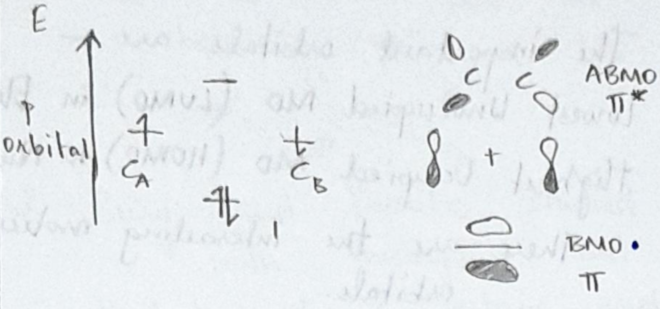


Ionization energy : Energy required to eject the electron from the atom

It gives a measure of how close the electron is to the nucleus and about the atom's electronegativity.

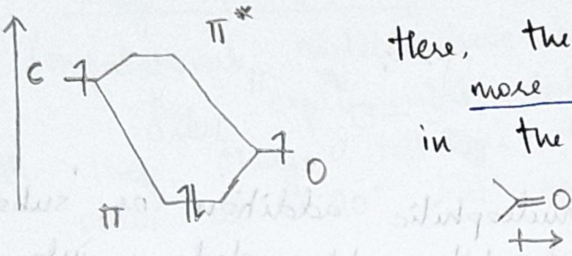
Molecular orbital picture of π bond.

C = C



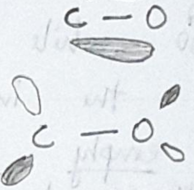
Here, both carbon * atoms contribute equally.

C = O



Here, the π orbital will be influenced more by O. This can be seen in the polarity of the molecule

Shape:



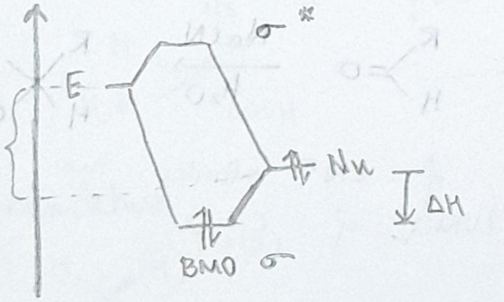
Conversely, π* orbital is influenced/ its contributed more by C.

So, when trying to break the C=O bond, we should put electrons into π* ABMO i.e. affect / target the carbon atom.

Lecture 3.2

Molecular orbital picture of E$^{\oplus}$. Nu$^{\ominus}$ reaction.

$\ddot{Nu} + E \rightarrow Nu - E$

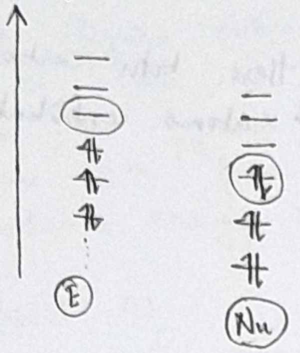


The resultant bond has lower energy and this stabilisation of electrons and energy released is considered the driving force of the reaction.

* When the energy levels of E and Nu are quite large, the energy released is quite small and hence, the bond formation is not quite as favourable.

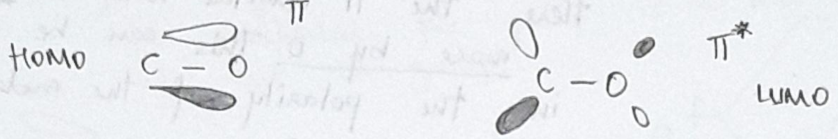
* On the other hand, when energy levels of E and Nu are similar, the stability gained is larger and hence bond formation is favourable.

In general,



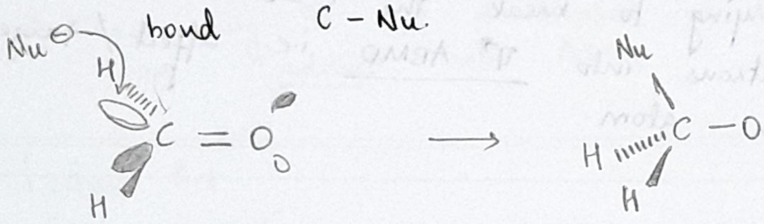
- The important orbitals are -
- Lowest Unoccupied MO (LUMO) in Electrophile
- Highest Occupied MO (HOMO) in Nucleophile
- These are the interacting molecular orbitals.

In carbonyls,



So while studying nucleophilic addition or substitution, the incoming nucleophile adds electrons into the empty LUMO i.e. π* orbital.

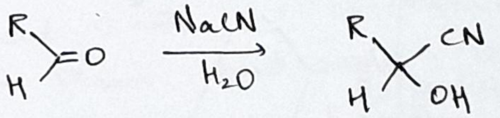
This breaks the C–O π bond and forms a new bond C – Nu.

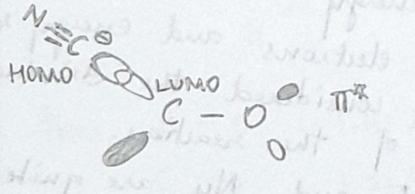


Lecture 3.3

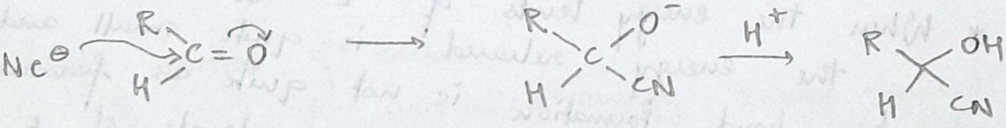
Nucleophilic Addition.

Formation of Cyanohydrin :

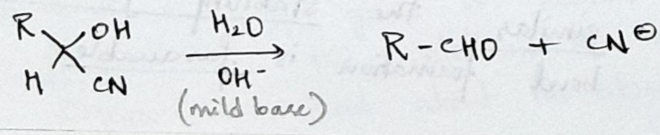




HOMO of CN⊖ attacks the LUMO of C=O.

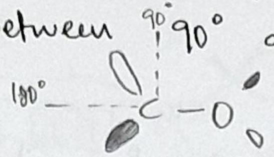


Note : This is a reversible reaction -



To understand the geometry of nucleophilic attack -

1. ~~Wht~~ We know that the π^* LUMO is at angle between 90° and 180° and that's where $Nu^{\ominus}$ attacks.



2. Bürgi and Dunitz studied the carbonyl crystals with nucleophile and found that the $Nu^{\ominus}$ attacked at a certain angle, now named the Bürgi - Dunitz angle ~ 105°.

3. Computational models have been developed that support the experimental data.

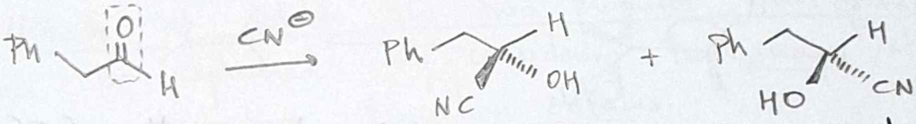
All these things tell us that the $Nu^{\ominus}$ attack doesn't occur at 90° but rather ~105°.

Lecture 3.4

Prochirality

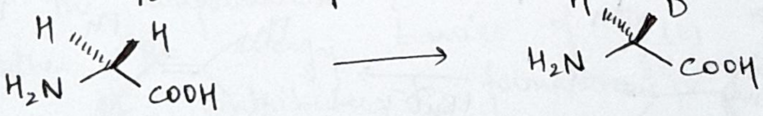
It's a (carbon) center that can become chiral.

Eg: 1)

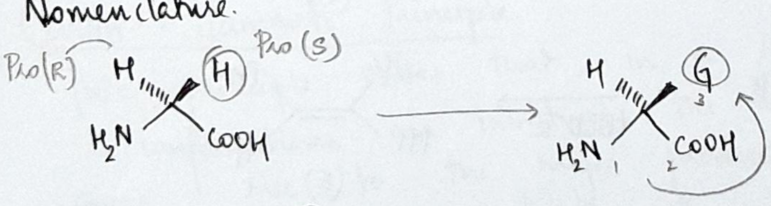


This carbonyl carbon is called the Prochiral center

2) Replacing -H of glycine gives us a chiral molecule, so its a prochiral center.

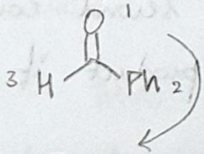


Nomenclature.

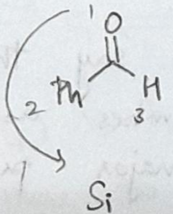


In case of tetrahedral compounds, replace -H with deuterium and name them as Pro(S) or Pro(R)

Enantiotopic Faces



Re



Si

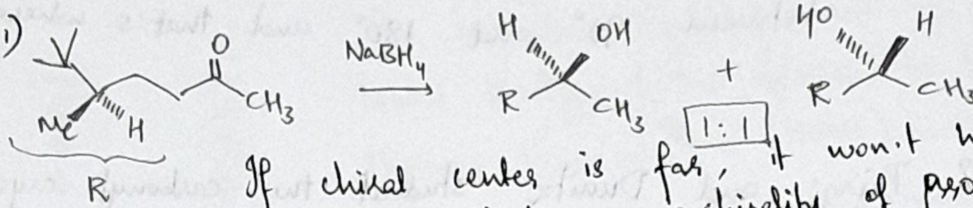
For sp^2 hybridised, planar molecules.

There is no connection b/w Re and Si & R & S of product

Lecture 3.5

If addition reaction happens, we get diastereomers

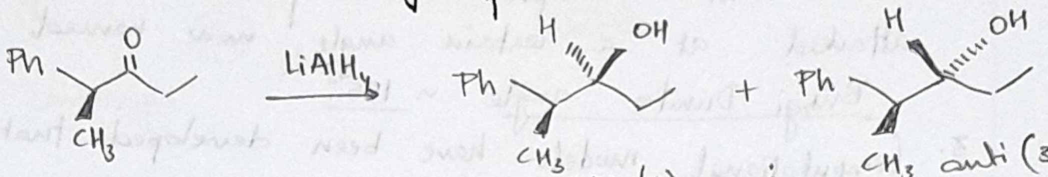
Eg: 1)



$\boxed{1:1}$

If chiral center is far, it won't have any affect on • chirality of product.

2)



syn (1) ; anti (3)

Counterintuitively, here, the products are formed in ratio syn : anti = 1 : 3. – WHY? Explored in next lectures

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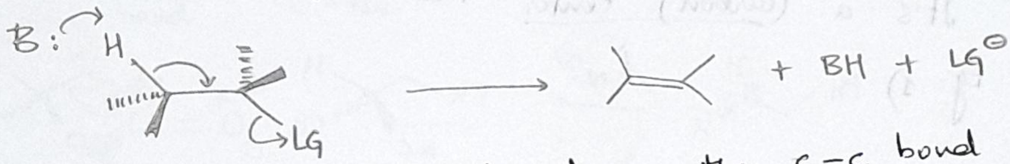
Lecture 4.1

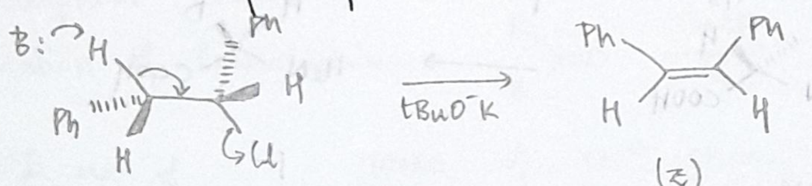
Recall : In elimination reaction (E2), we observe an anti-periplanar transition state.



Here, the abstracted H atom, the C–C bond and the leaving group are all on the same plane.

Eg: Formation of styrene –

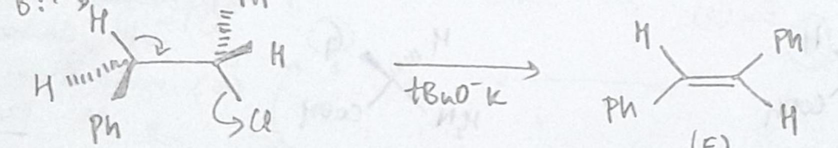
(A)



(Z)

Both –Ph are on the same plane

(B)

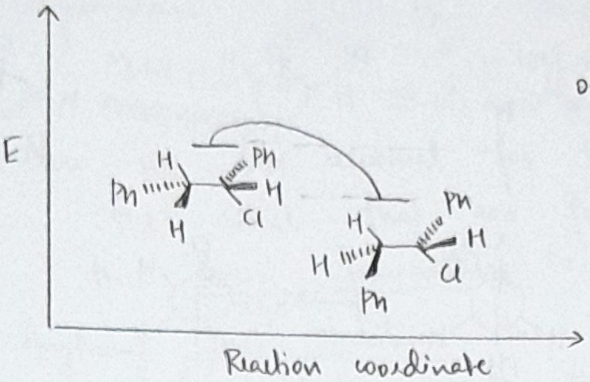


(E)

It's tempting to say that the second conformer is greater in numbers as the product it forms (E) is the major product.

But the barrier for C–C bond rotation is very low – keeps happening at room T.

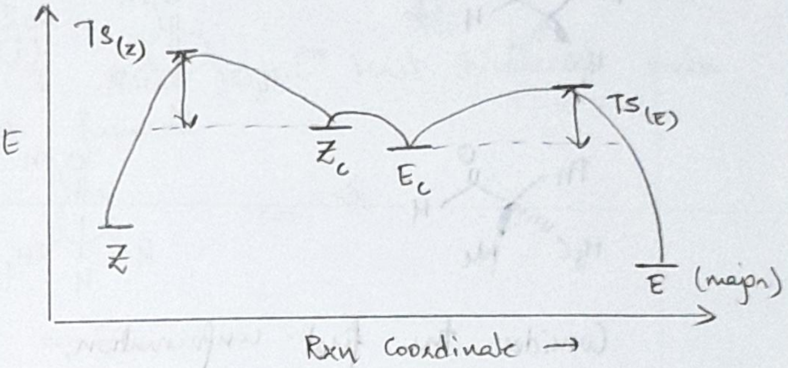
Energy Profile of the Reaction.



The energy barrier for rotation of C–C single bond is quite low, so the conformers keep interconverting rapidly. So its wrong to assume that the E conformer is greater in number.

E : Trans
Z : Cis

E is the major product as its more stable. WKT E configuration is more stable than Z by measuring the heat of hydrogenation.



The difference in product distribution is a reflection of the rate at which the two products are formed. This can be explained by considering the energy/stability of their respective transition states.

We see that the energy barrier of $TS_{(Z)}$ is substantially higher than the barrier of $TS_{(E)}$.

Hence, the conformation E_c is not in greater number, but rather the energy barrier of $TS_{(E)}$ is lesser.

Hence, ΔE_a contributes to formation of products.

Curtin - Hammett Principle.

This principle states that, in a reaction where multiple conformations are involved, the most reactive conformation gives rise to the major product.

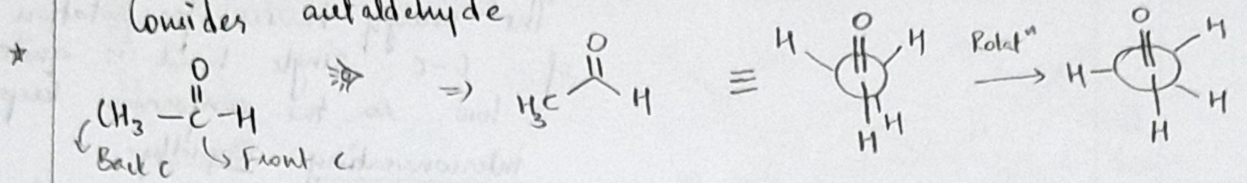
In general, $\text{minor} \xleftarrow{k_{min}} C_1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C_2 \xrightarrow{k_{maj}} \text{major}$

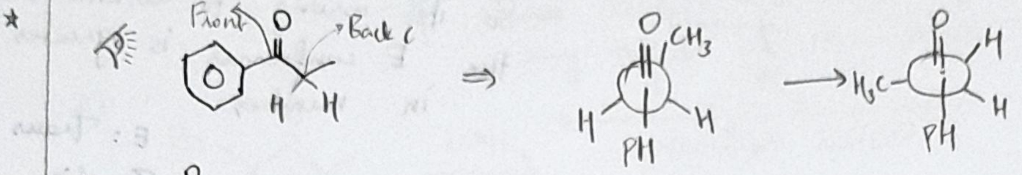
Here, $(k_1 \,\&\, k_{-1}) \gg k_{maj}$ or k_{min} ⇒ Conformation interconversion is rapid.

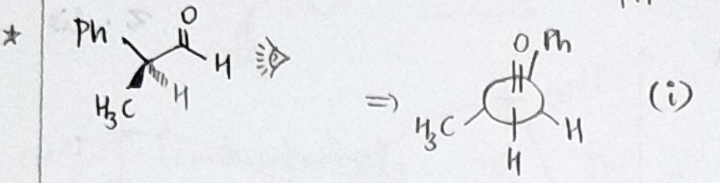
Hence, greater the k_{maj}, more the major product is formed.

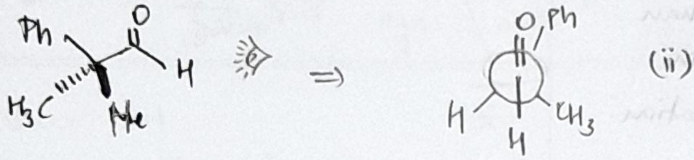
Lecture 4.2.

Consider acetaldehyde

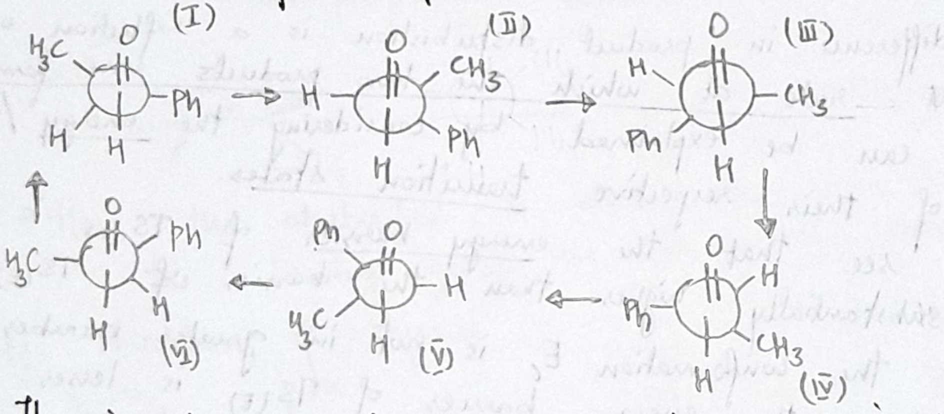








Consider the first conformation,



Largest group is further from O

The important conformations are the ones in which the largest group is perpendicular to the carbonyl O.

They're important / considered in the model we construct.
Conformations (I) and (IV)

Because eclipsing interaction are going to be minimal in this conformation.

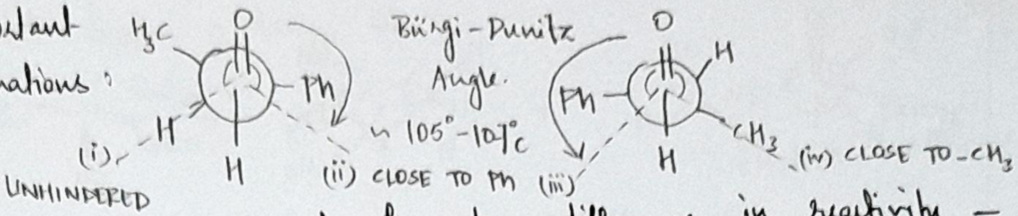
Lecture 4.3

We're trying to develop a model to explain the ~~Stereochem~~ stereoselectivity of syn : anti = 1 : 3. [Page 14]

We know that conformations where the largest group is ⊥ʳ to the carbonyl O are relevant.

(17)

Important Conformations:



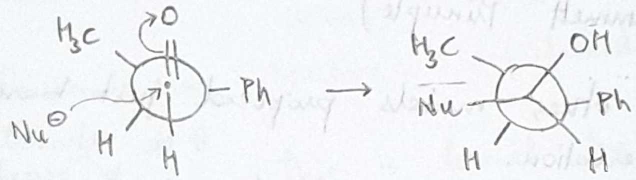
Now we can account for the difference in reactivity – the attack that has the least hindered approach is the most favourable i.e least energetic.

(*) Anything that stabilises the Transition State or removes the hinderance to the reaction center increases the rate of reaction.

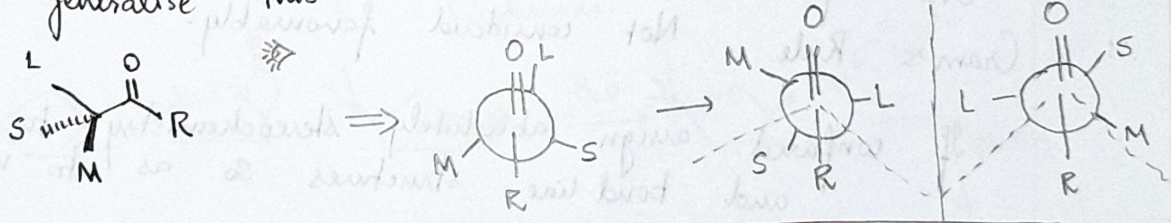
Only in conformation I, there is a least hindered path that is most favored.

Lecture 4.4

Consider the important conformation –



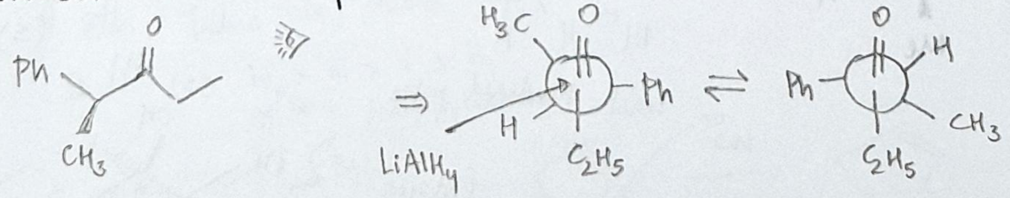
To generalise this –

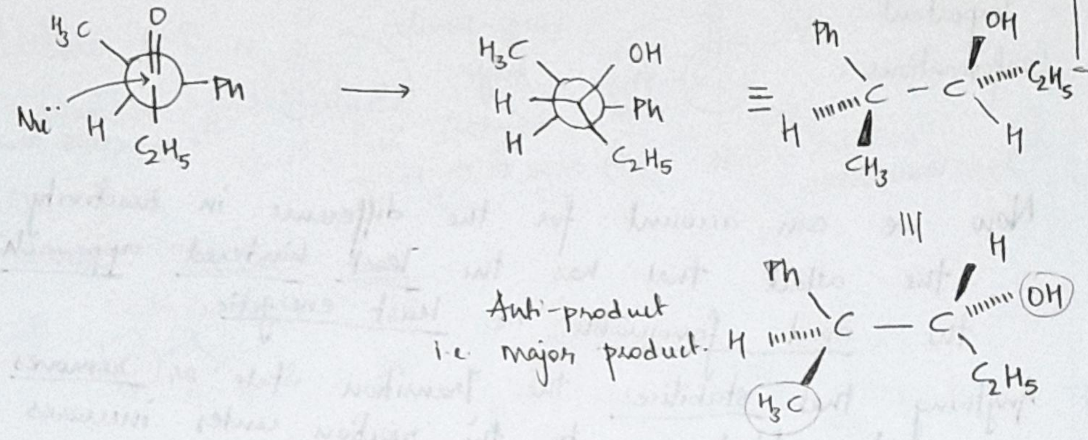


Felkin-Ahn Model

To predict the major product we've to see which of the two conformations is more reactive.

Consider the example we'd taken –





Lecture 4.5

Charecteristics of Felkin-Ahn Model —

1. Largest group is perpendicular to the carbonyl O
2. There are two possible conformations for this.

Due to the Bürgi-Dunitz angle, the $Nu^{\ominus}$ gets one path of attack that is least hindered.

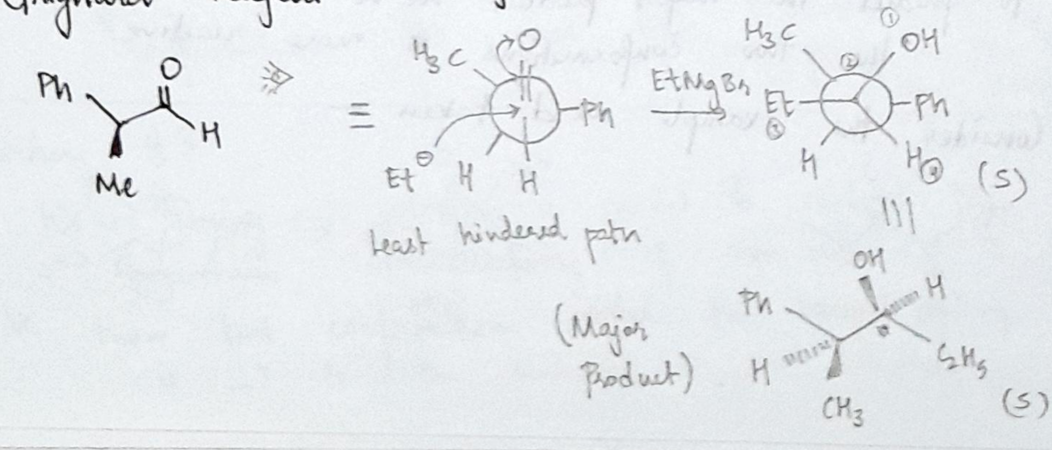
This gives us the major product (based on the Curtin-Hemmett Principle).

There have been other models proposed just based on the observation. # No rational reason to accept this.

One of the earliest proposed rule/model — Cram's Rule : Not considered favourably.

If confused, assign absolute stereochemistry to Newman and bond-line structures so as to not go wrong.

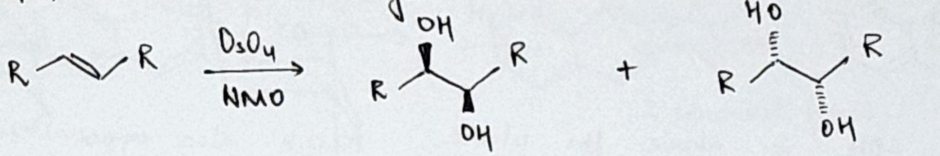
Grignard Reagent : RMgX



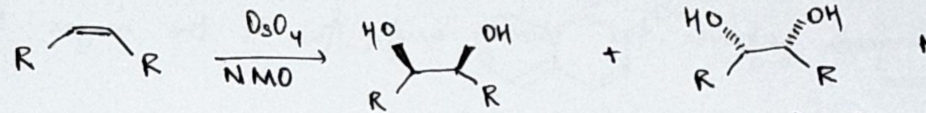
Tutorial Session - Assgn 02

23/9

1.



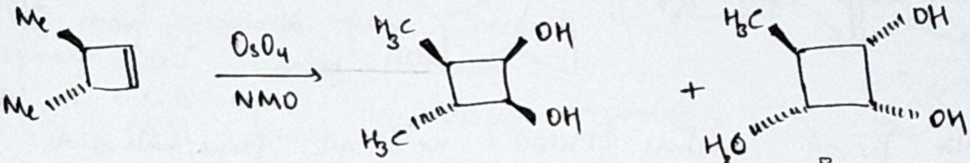
Racemic mixture



Meso compound

So, the products are ultimately optically inactive

3.

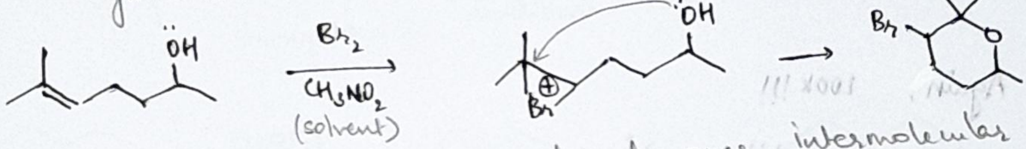


A B

We get the same product ~~at~~ by turning them upside-down

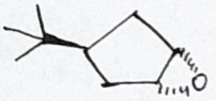
5. Do assignments with pen and papers !!

6.

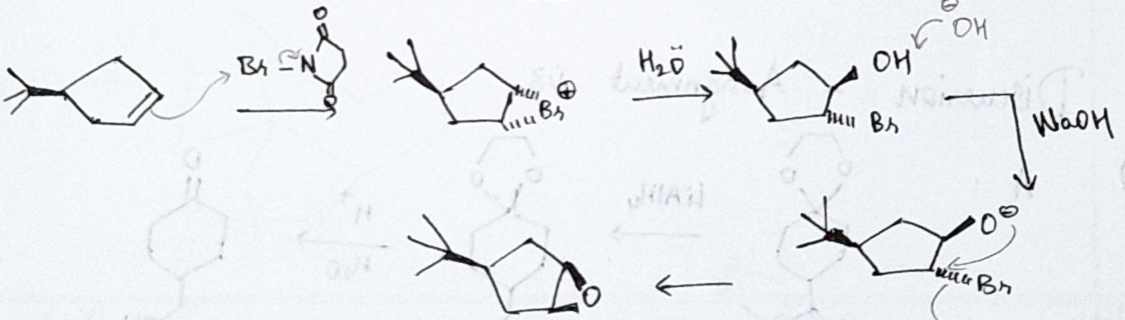


Intramolecular reaction is preferred over intermolecular

7.



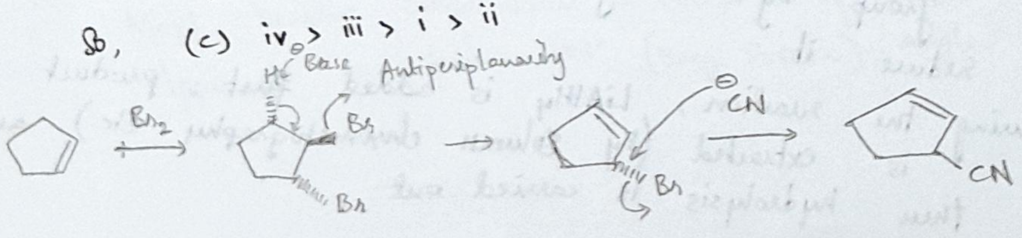
: This is formed by m-CPBA which comes from below the plane to avoid steric hinderance.

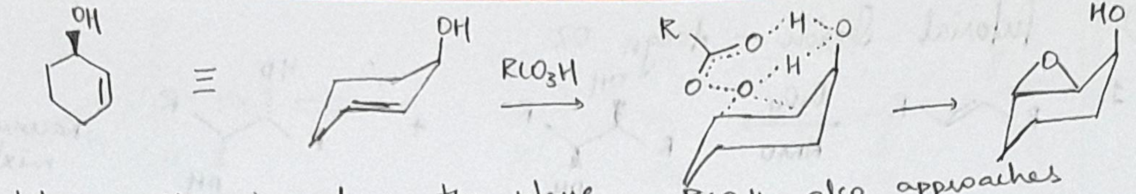


8. Trans-alkene is more stable than cis-alkene
⇒ Trans is more reactive

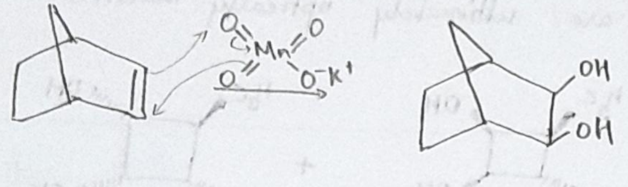
So, (c) iv > iii > i > ii

10.



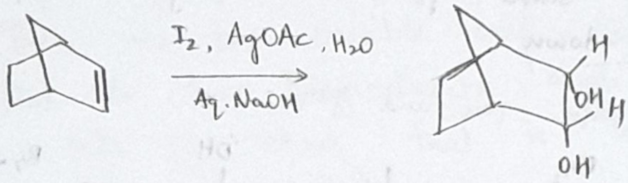
11) 

When -OH is above the plane, RCO$_3$H also approaches from above the plane and this is the major product.

12) a) 

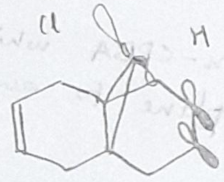
KMnO$_4$ (like OsO$_4$) prefers attacking from above because -OH groups are more stable in equatorial position

b) With Prevost reaction (PhCOO$^-$) we'd get trans/anti diols.
With Woodward reaction we get cis-diol.



15) Again, LOOK!!!

19) Molecular orbital picture —

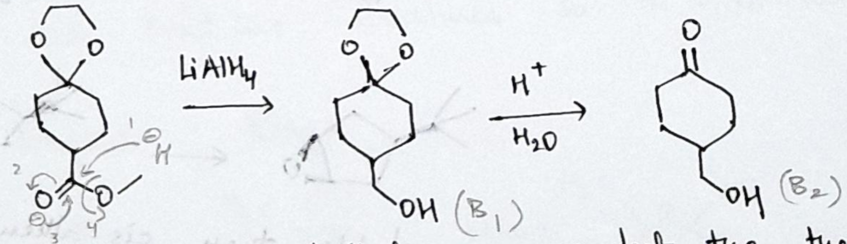


So, the left double bond is open to epoxidation, not the right one.

30/9

Discussion - Assignment 03

2) A :

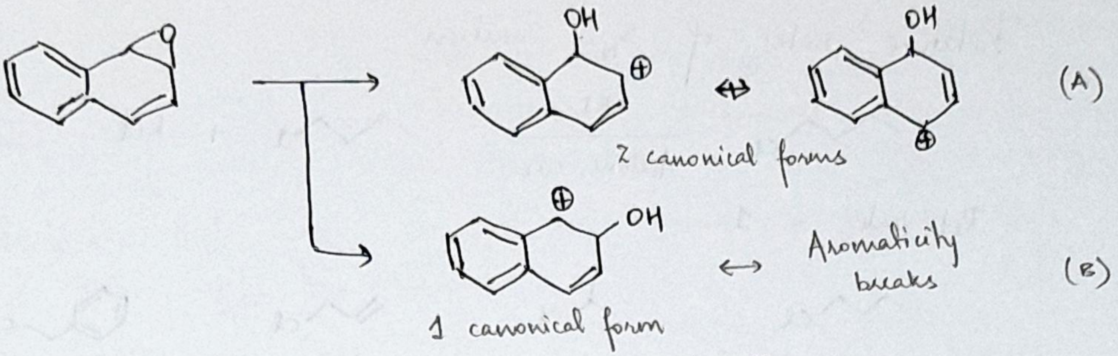


To reduce the ester selectively, we protect the the keto group by making it into a ketal and then reduce it

During the reaction, LiAlH$_4$ is added first, product B$_1$ is extracted (by column chromatography etc) and then hydrolysis is carried out.

(21) 3)

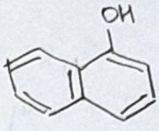
Wrong solⁿ in Assgn



(A) has 2 canonical forms - allyl carbocation

(B) has only 1 form because if it had more, aromaticity would break.

So, (A) forms the major compound —

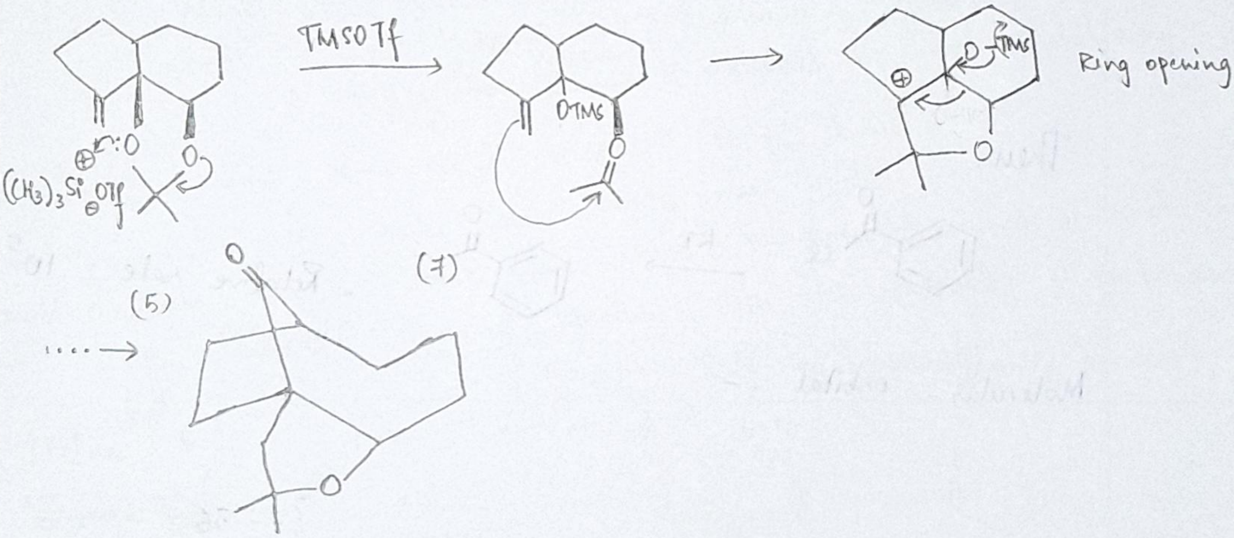


E_1 elimination

4) Retrosynthesis analysis.

7) Prins - Pinacol Rearrangement - Another way of dissociation of acetal

TMSOTf : Lewis acid, additive, used to protect groups from ? strong acidic conditions. Acts like H^+



14/10/20

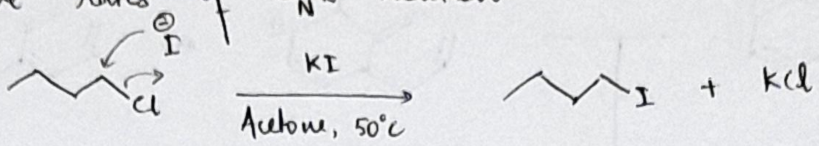
Lecture 5.1

Recall : Felkin- Anh Model

Most reactive conformation - dictated by sterics.

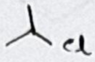
Approach is from 105° (Burgi Dunitz) angle.

Relative rates of S_N2 reaction



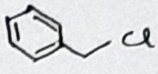
Rel. rate = 1.

1



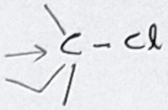
0.02

79



200

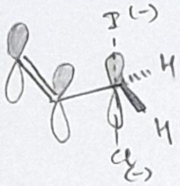
In S_N2, I attacks from behind :



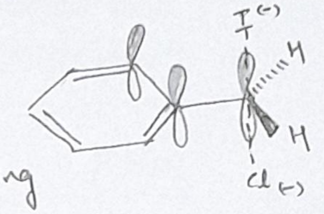
So, any substituents on C hinders the attack of I^-.

Then why is the rate increased in allyl & benzyl groups?

Ans: Molecular interaction – this stabilizes the transition state & hence increases the rate of reaction.

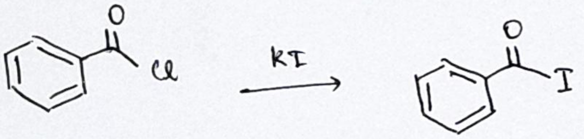


stabilisation of transition state by conjugation with π bond / benzene ring



$79 \xrightarrow[\text{2 fold increase}]{} 200$

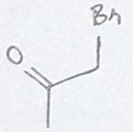
Then,



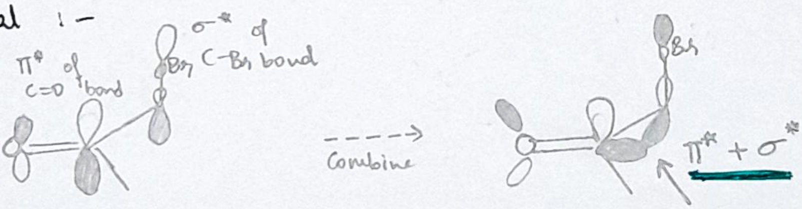
Relative rate : 10^5 !

Increases a 1000 times

Molecular orbital :–



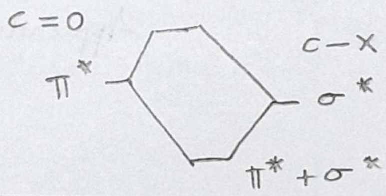
:



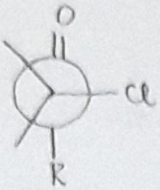
Two LUMOs, antibonding orbitals combine and the nucleophilic attack occurs easily here.

∴ Carbonyl compound with adjacent electronegative atom is very reactive because of the combined LUMOs.

Energy of LUMO decreases – its stabilised by combination of AB MOs & hence increase reactivity.



More Reactive



The rate of rxn of this conformation is significantly higher than others.

∴ C=O & C−X need to be perpendicular to the orbitals align correctly

Consider that −X is not a leaving group. How does this affect the reaction?

Ans: attack on this orbital will result in addition to the carbonyl group, because the new LUMO is substantially lower in energy & it can also activate the carbonyl carbon.

The Felkin-Anh model says the largest group should be perpendicular to the carbonyl group.

BUT when there's an electronegative atom on the adjacent carbon, this −X is perpendicular so as to increase the interaction of orbitals and make the molecule reactive.

Carey & Sundberg PART A Pg. 180

Ceiplak Model - emphasizes on interaction between C−X bond and antibonding orbital to nucleophile. should be most stabilizing.

A better ~~bo.~~ donor X should be most stabilizing.

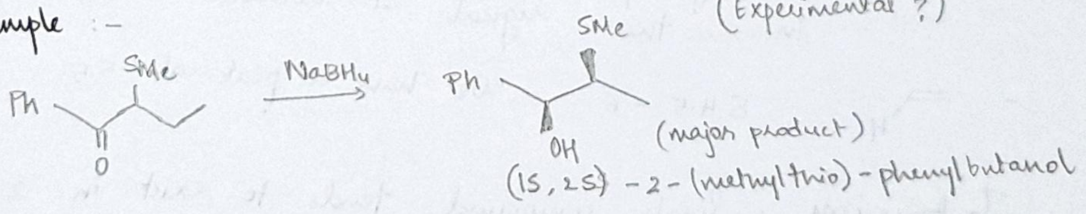
Clarify : Just C−X bond or σ* of the bond? make the LUMO more stable

Say, π* + σ* make the 'more stable' LUMO increase the rate of reaction?

How does a 'more stable' LUMO with less reactivity — for bonds we associate increased stability of transition state ⇒ thermodynamic product?

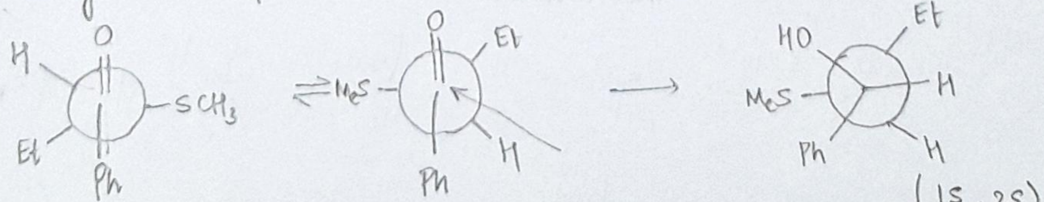
Lecture 5.2

Example :- (Experimental ?)



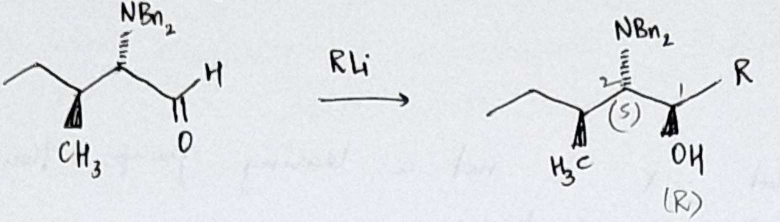
(1S, 2S) - 2 - (methylthio) - phenylbutanol

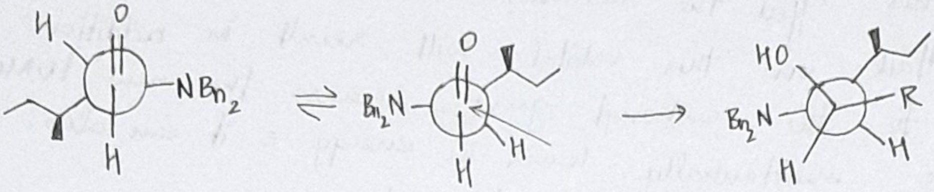
According to Ceiplak / model / Th



(1S, 2S)

Another example -





1R, 2S

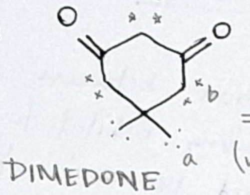
14/10/20

Lecture 6.1

Enols and Enolates

NMR Spectrum : No. of distinct protons in a molecule

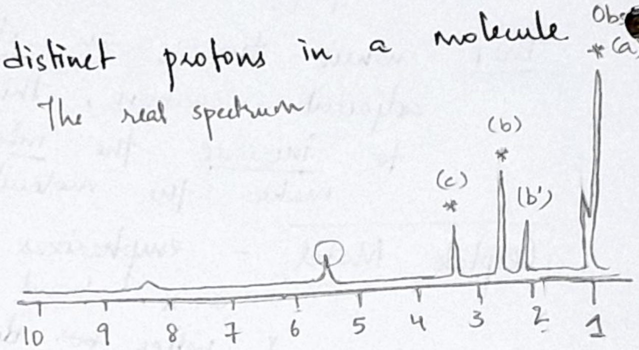
Eg:



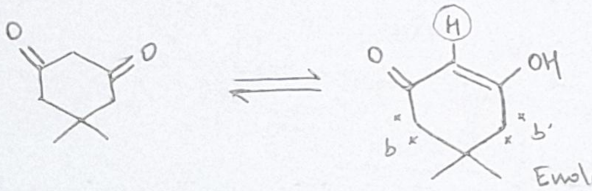
DIMEDONE

3 kinds of H-atoms
⇒ 3 signals (with no split)

The real spectrum



Enolisation :



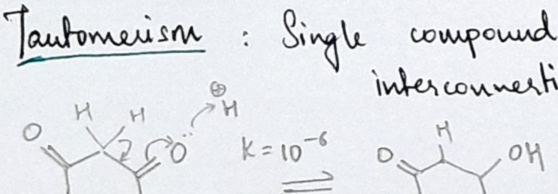
Enolate.

In the enolate :

- Since $-CH_3$ groups are far away, we only see a small shift in the signal at around ~1 (a).

- $=\!\!\diagdown_H$: δ 4.5 - 6 : We have a peak at 5.5

Tautomerism : Single compound tends to exist in 2 or more interconvertible structures



: Transfer of H⁺
No change in pH of medium

Keto Enol

Empirically, NMR Spectrum of ketone / aldehyde almost never records the enolate form.

This is because of bond strength

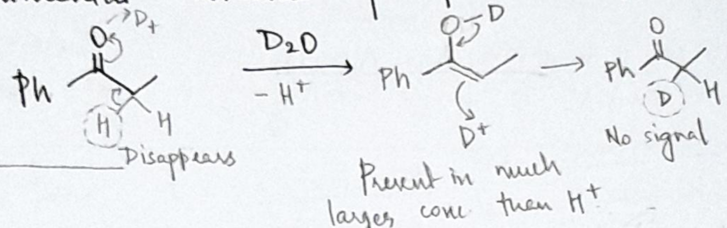
	X – H	π-bond	Total
Keto	440 (C – H)	720 (C = O)	1160 kJ mol⁻¹
Enol	500 (O – H)	620 (C = C)	1120 kJ mol⁻¹

⇒ Enol form is less stable by ~40 kJ mol⁻¹

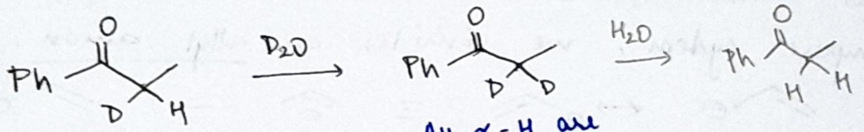
So, equilibrium constant : $K = 10^{-6}$

Experimental evidence for formation of enol :-

How do we know? Does the length of signal vary wrt no. of H?



D₂O is NMR silent
⇒ it doesn't give a signal
⇒ Makes it a great solvent



All α - H are replaced by D

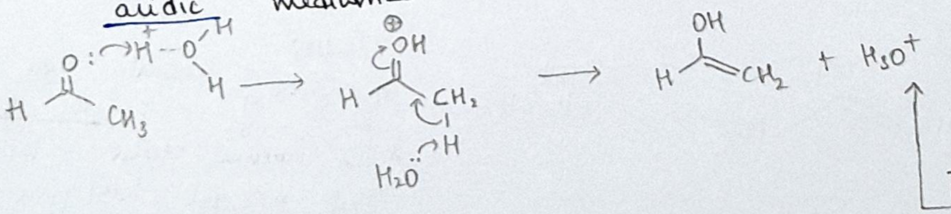
This tells us that :
- Enols are being produced even if we can't detect it in the H-NMR.
- Its a reversible reaction

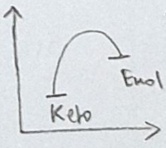
Lecture 6.2

Catalysing enolisation

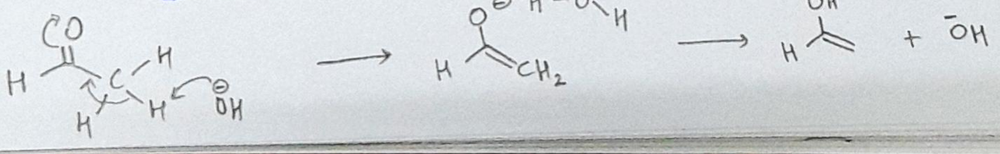
It can be catalysed by acids of bases

- We can assume that protonation of carbonyl occurs in acidic medium —

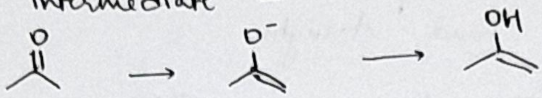




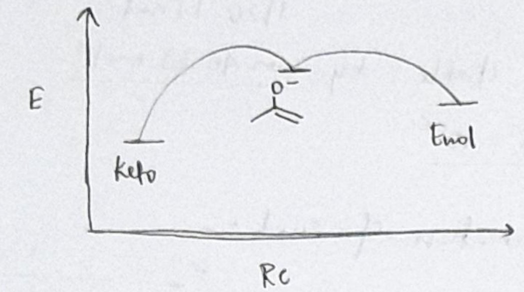
- With a base —



Both keto and Enol forms go through the enolate intermediate –

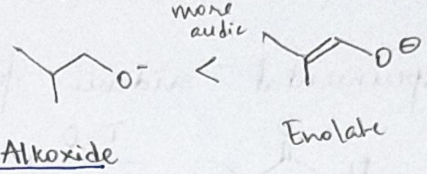


Which is more acidic?



Enol is more acidic.

Next, we compare the acidic nature of enolate with other functional groups.

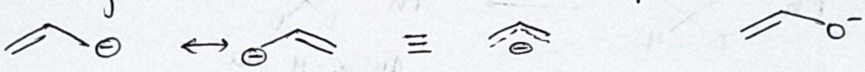


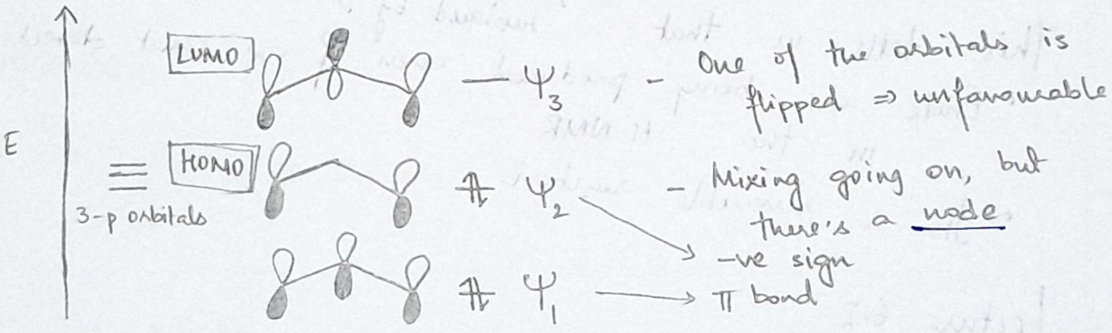
Since the -ve charge is in conjugation with π bond, enolate is more acidic.

Lecture 6.3

Molecular Orbital Picture

To compare system, we consider an allyl anion:





ψ_3 – One of the orbitals is flipped ⇒ unfavourable

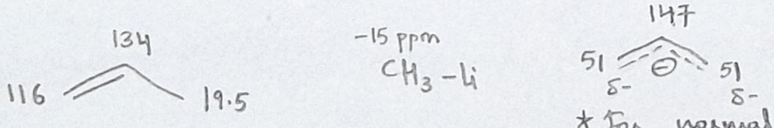
ψ_2 – Mixing going on, but there's a node → -ve sign

ψ_1 → π bond

According to this, maximum $e^{\ominus}$ density is at terminal C.

Experimental evidence :-

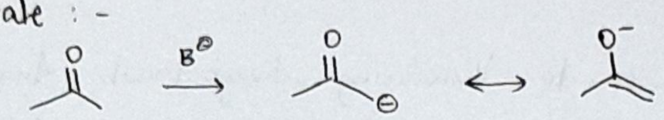
C^{13}-NMR shows us –

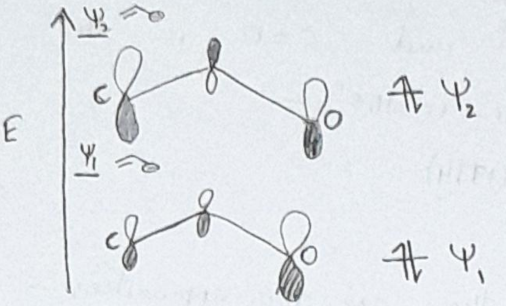


* Only two signals ∵ delocalised charge

* For normal olefin ~120 ppm But we get ~51 ppm because of association with Li

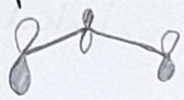
Enolate :-





- Since oxygen is very electronegative, it distorts the shape of orbital
- And, it decreases the total energy of ψ_1 & ψ_2 as compared to allyl carbanion

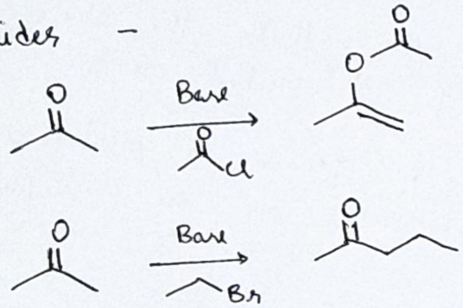
- The electron distribution is across all three atoms & lobe of oxygen is bigger in ψ_1
- In ψ_2 -



- ψ_2 : HOMO

Here, the lobe on the terminal carbon is large and it determines how reactions actually happen.

- So C and O are the two reactive centres
- Consider -



Reactions dominated by orbital interactions react with Carbon centre because it has the biggest lobe in HOMO. *

* When the reactions are dominated by charges & electrostatic interaction, occur at the oxygen centre (more electronegative) is more reactant.

20/10/20

Live Class

Computational Approach to Visualising Burgi-Dunitz Angle.

Hans Bürgi & Jack Dunitz hypothesized that the trajectory of approach b/w $Nu^{\ominus}$ and C=O is 105°

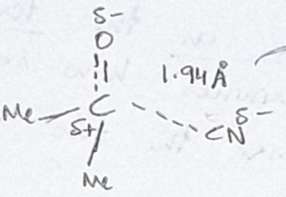
To undestand why the angle is 105° –

- Crystal structure mining (1974)
- Computational chemistry

In computational chemistry, there are two approaches –

1. Solve Schrodinger eq^n : Too expensive to solve exactly for anything but one or two electrons.
2. Electron density : Considering this instead of wavefunction.

Transition state :
Cannot be isolated

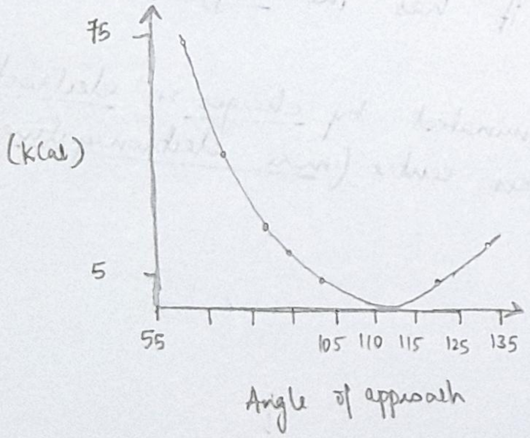


Forms a bond at this distance

The electron density of CN^- attacks the electrophilic center and this e^- density gets pushed on the oxygen.

What happens if the angle of approach is constrained to 90° ?
The e^- density gets distorted on the nucleophile.

Energetics



Increase in energy ⇒ disfavor in occurance of reaction.

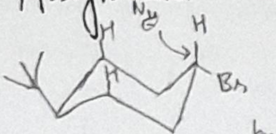
* B-D trajectory maximises the overlap of HOMO of nucleophile with LUMO of ketone

* Forcing nucleophile to approach from a different angle will incur a very steep penalty.

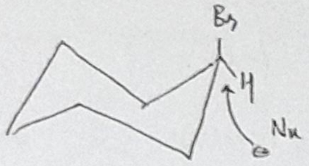
Assignment 04 Discussion (6/10)

21/10

2)



sterically hindered by axial hydrogen clash

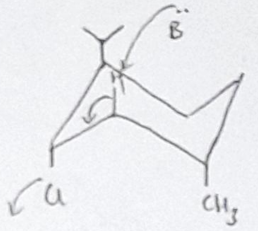


No clash

I got confused watching some Youtube video about periplanar effect.

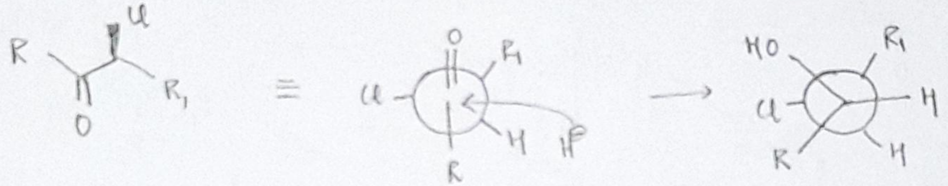
4)

No anti-periplanarity



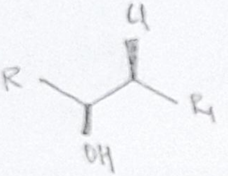
Antiperiplanarity exists
⇒ E_2 elimination occurs faster

5)



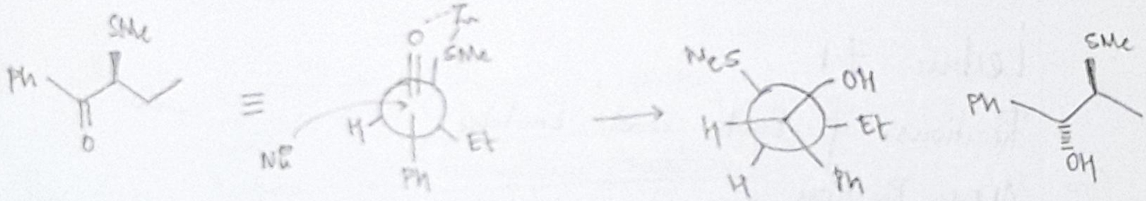
S_{Cl}, S_O – Got this right

⇒ Product:



– went wrong while choosing structure

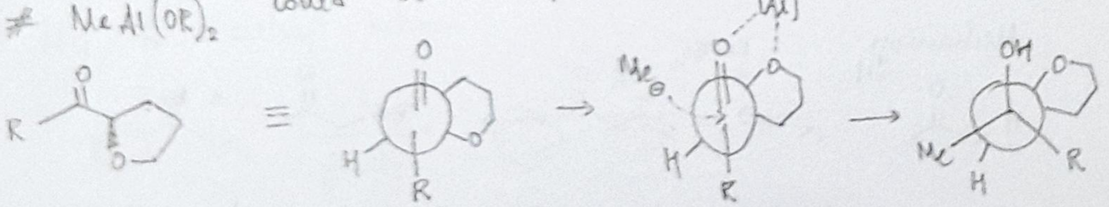
6)



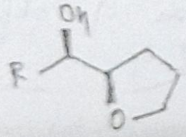
Zn chelates with =O and –SMe, constricting the conformation

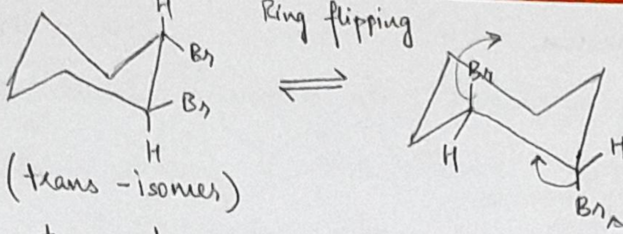
stabilizes the TS

8) Here too, Al chelates with carbonyl O and ethoxy O. MeLi generates nucleophile
≠ MeAl(OR)$_2$ could be catalytic while



Product :

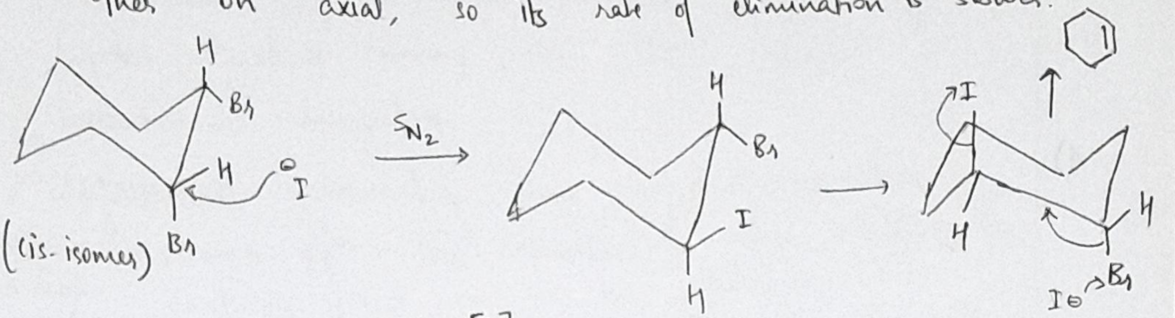




→ Undergoes E_2 elimination very fast

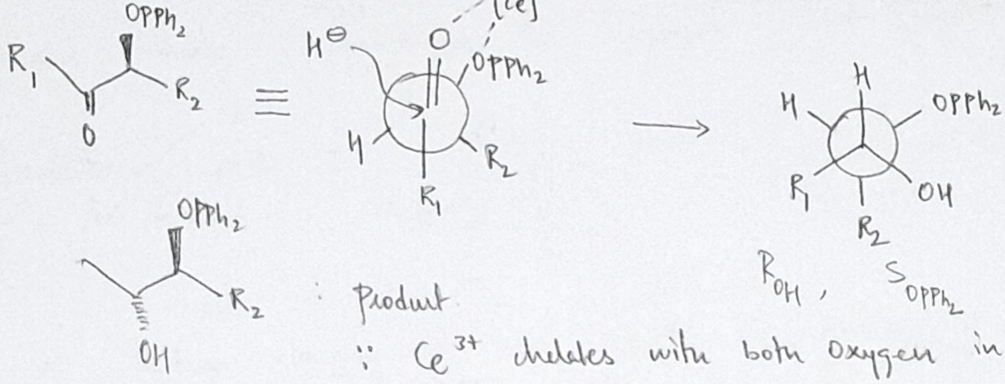
(trans-isomer)

In the other compound, one -Br is always on axial & the other on axial, so its rate of elimination is slower.



(cis-isomer)

10)



: Product

R_{OH}, S_{OPPh_2}

∵ Ce^{3+} chelates with both Oxygen in TS.

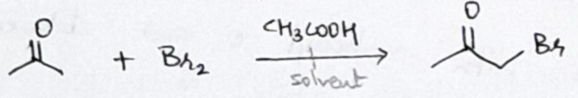
3/11

Lecture 7.1

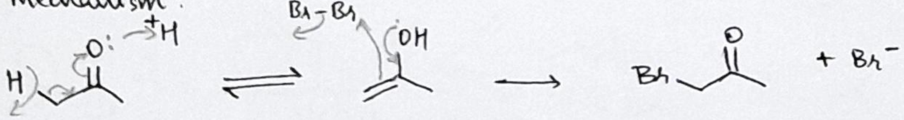
Reactions of Enols and Enolates

Aldol Reaction

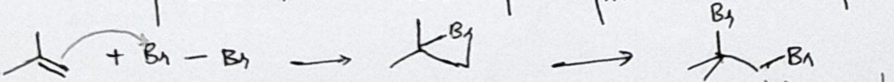
→ Reaction with Halogen

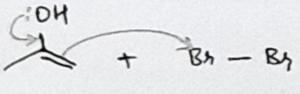


Mechanism:



This is comparable to reaction of olefin with halogen

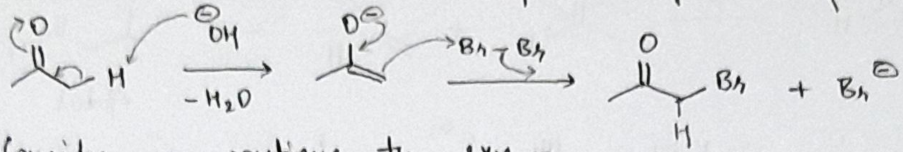




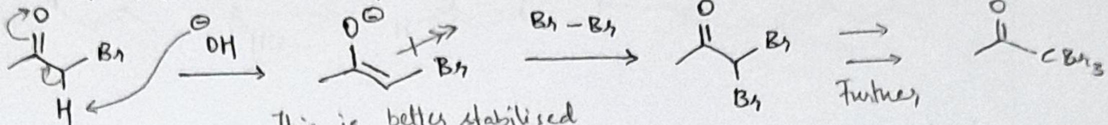
Here, the reaction is driven by lp of oxygen so reaction of enol is faster

∴ Enols are more reactive than olefins.

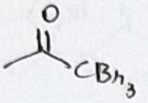
Reaction with Br_2 can also happen in presence of a base –

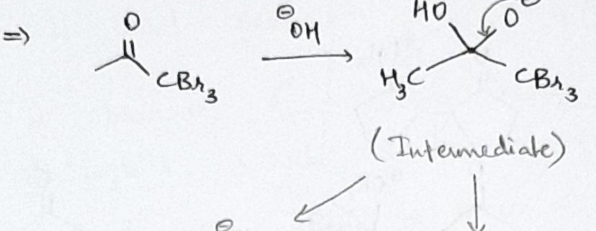


Consider we continue the rxn –



This is better stabilised ∵ of χ of Br

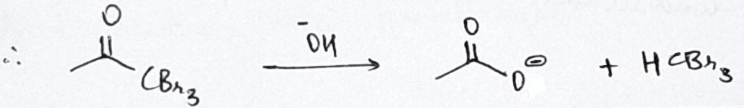
In , the carbonyl group is very reactive –



When lp of oxygen moves back, either –OH can get kicked out or $-CBr_3$

	$^{\ominus}OH$ ↓ H_2O	$^{\ominus}CBr_3$ ↓ $CHBr_3$	$^{\ominus}CH_3$ ↓ CH_4
pKa	14	9	~40

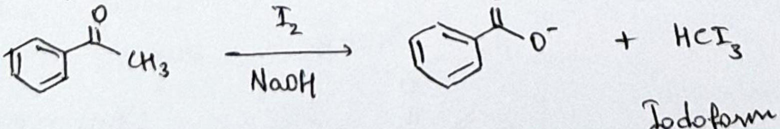
∴ $^{\ominus}CBr_3$ is the most feasible leaving group.



This is known as **Bromoform reaction**

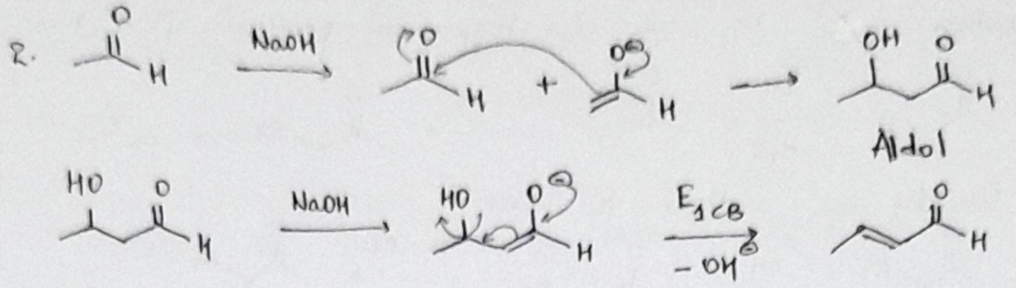
Hence, the reaction of ketones with halogen is carried out in acidic conditions because in presence of a base, it'll form bromoform.

⇒ Test for methyl ketones

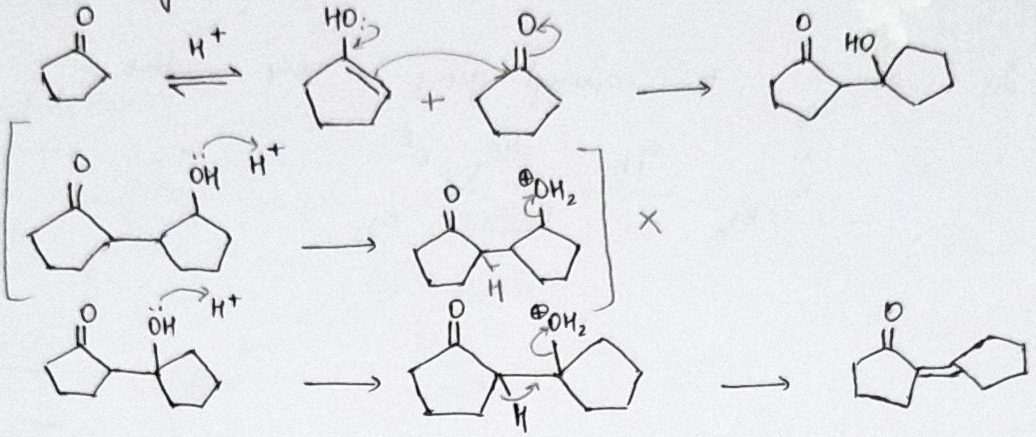


Iodoform
(YELLOW).

- Aldol reaction



- Acid catalysed aldol reaction



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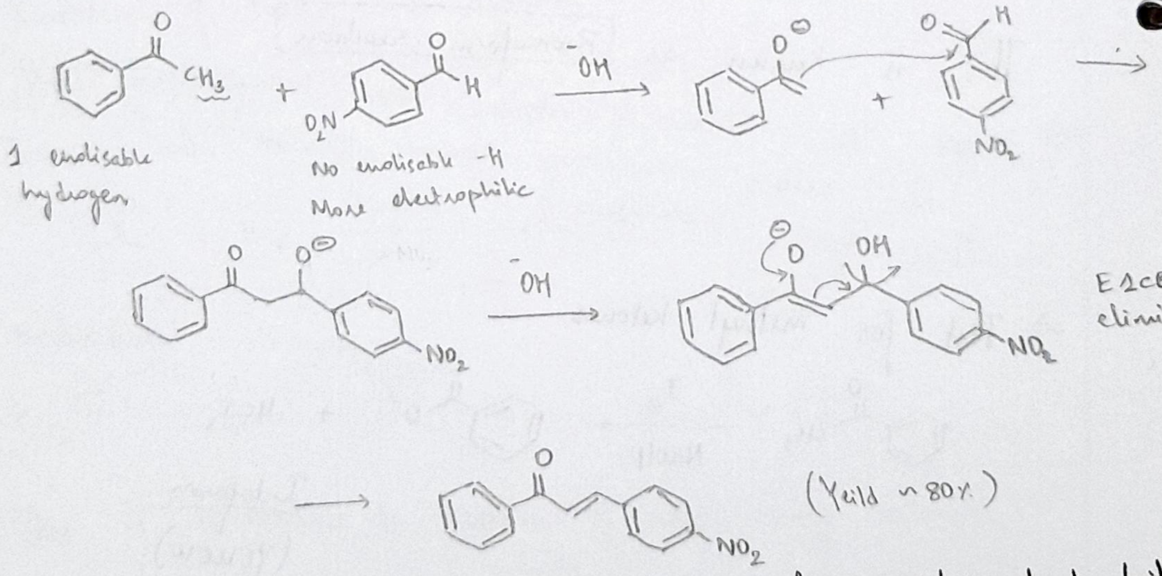
Lecture 7.2

Cross aldol reaction.

Also called cross-condensation reactions where there at 2 reactants,

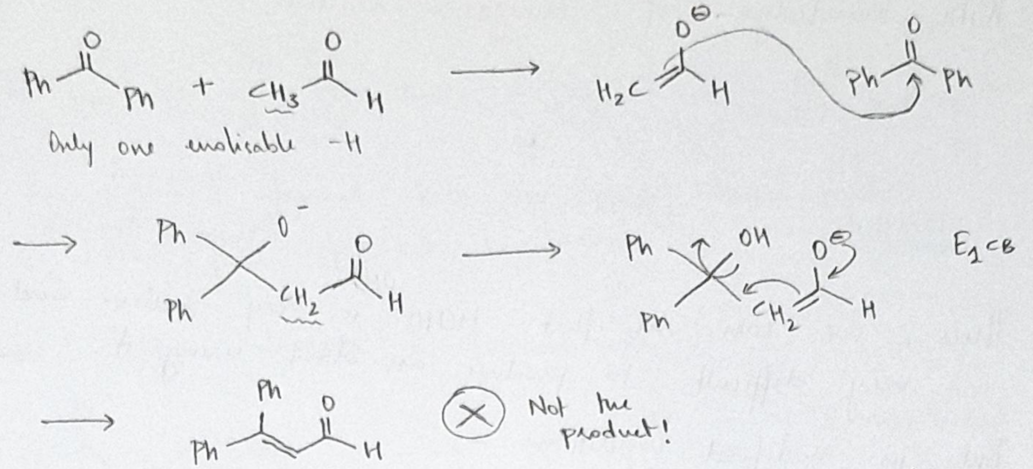
Examples :-

1)



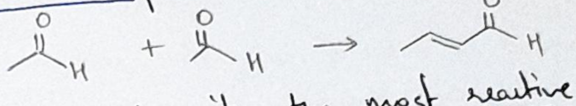
Also, the ketone can react with itself and form a byproduct, but since we've chosen a more reactive, electrophilic aldehyde, we get a cross-condensation product

2)



Only one enolisable -H

Here, acetaldehyde reacts with itself and we get the self aldol product :



This is because, the enolate reacts with the most reactive electrophile, which is the aldehyde in this case.

In order for cross aldol to occur - favourably -

1. Only one partner should enolize
2. The other partner is more reactive

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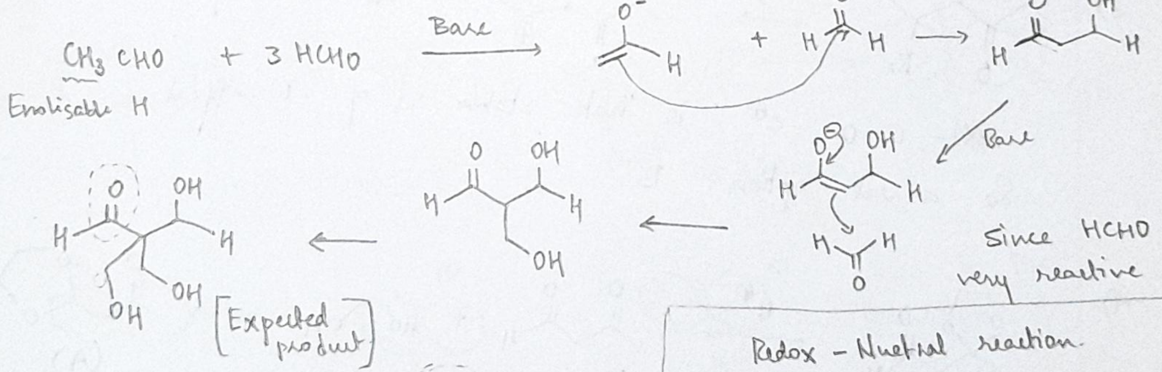
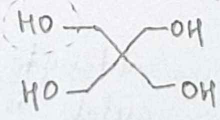
Lecture 7.3

Aldol reaction with Formaldehyde

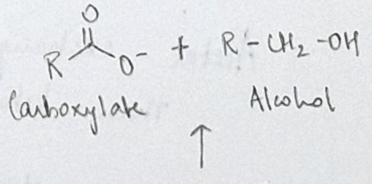


Since HCHO is very reactive

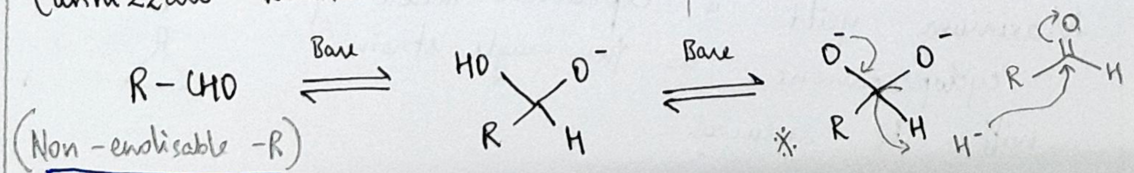
Isolated product : in 80-90% yeild



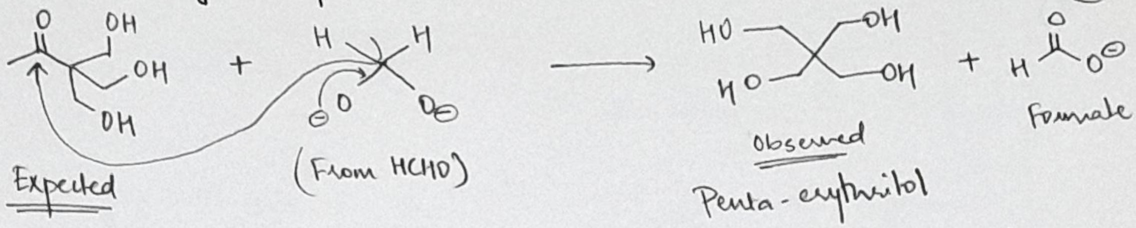
Redox - Neutral reaction.



Cannizzaro Reaction.

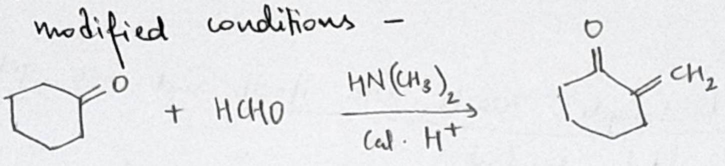


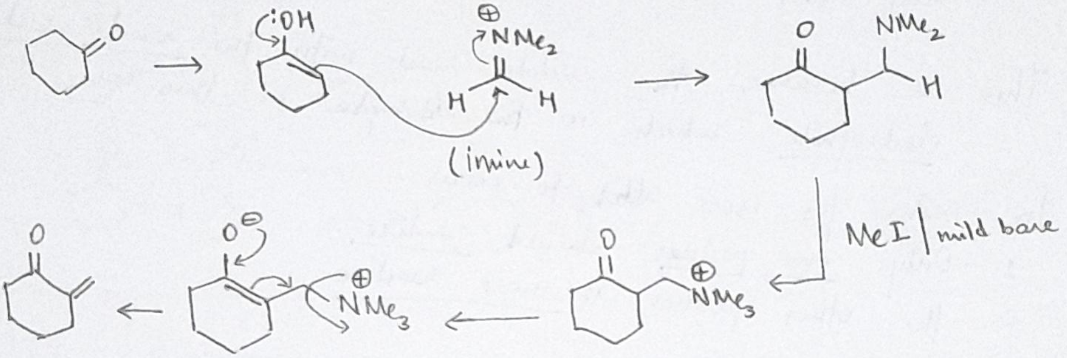
With knowledge of Cannizzaro reaction,



Thus, we can see that HCHO is very reactive and its very difficult to produce an aldol using it.

But in modified conditions -





Assignment 05

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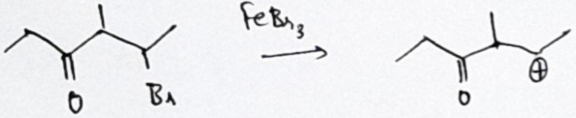
3)

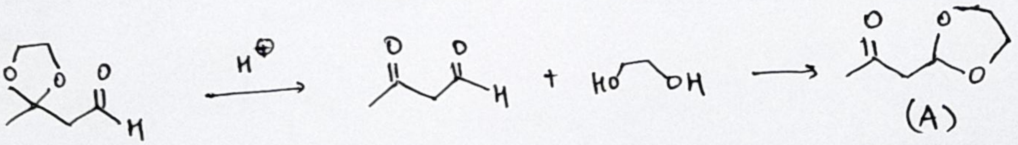


No rearrangement !

α - C=O C⊕ is not stable ∵ of -I effect.

So correct option : B.

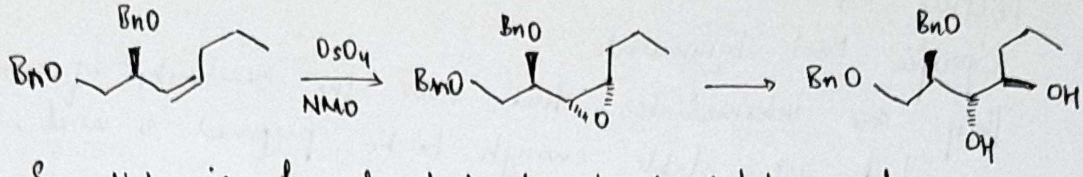
4)



Acetal exchange : Since, aldehyde is more reactive than ketone, this acetal is formed in acidic condition.

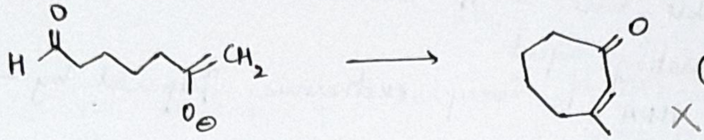
5) Maximum yeild is expectated incase of cyclopropanone, as the angle strain will be reduced

6) MAJOR PRODUCT !!



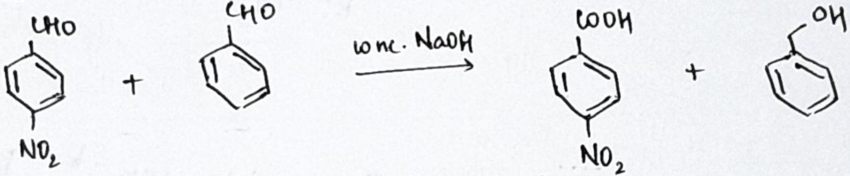
Syn-diol is formed but the bond rotates and the final product is trans.

? 7) More stable carbanion is formed ⇒



(D) ✓5 membered ring

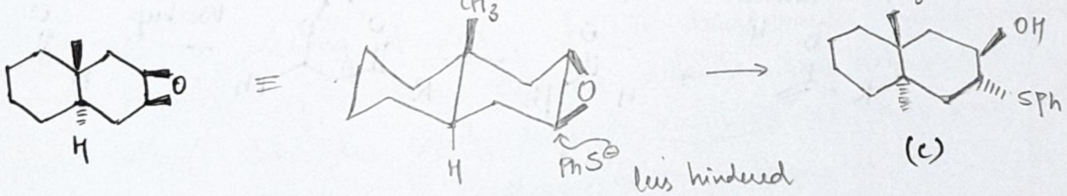
8) With respect to Cannizzaro reaction, in the p-nitro ~~of~~ benzaldehyd the e⊖ density around -CHO is reduced ⇒ the -OH attacks there -



Cross- Cannizzaro reaction (oxidised)

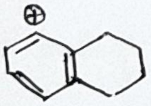
9) Will be discussed later. - concept not covered.

12)

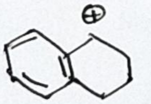


less hindered (C)

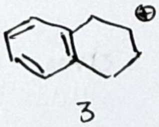
13)



1



2



3

RDS is the formation of C⊕.

Elimination occurs based on stability of C⊕

⇒ 2 > 3 > 1 (B)

14) C-numbers!! (A)

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Lecture 8.1

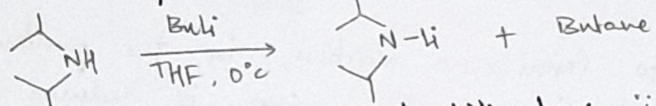
Specific Enol Equivalents

They are intermediates that have the reactivity of enolates but are stable enough to be prepared & used, so they give a good yeild.

* Lithium enolate.

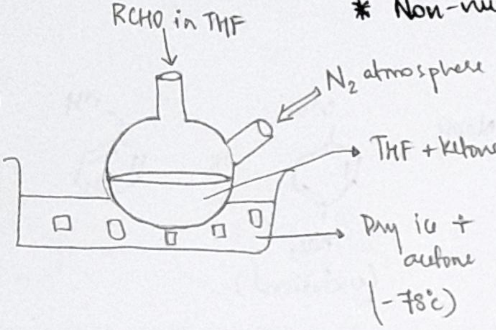
LDA: Lithium di-isopropyl Amine. Its a stable base - it can be stored. Used as a deprotonating agent.

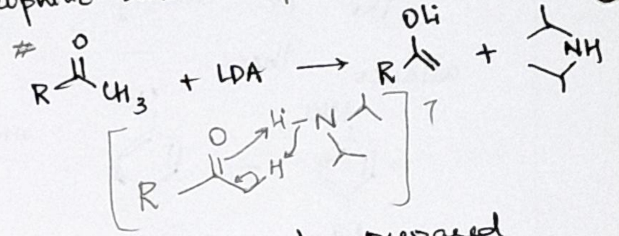
Protonation of LDA is very exothermic. Prepared by -



* Non-nucleophilic base ∵ of isopropyl groups

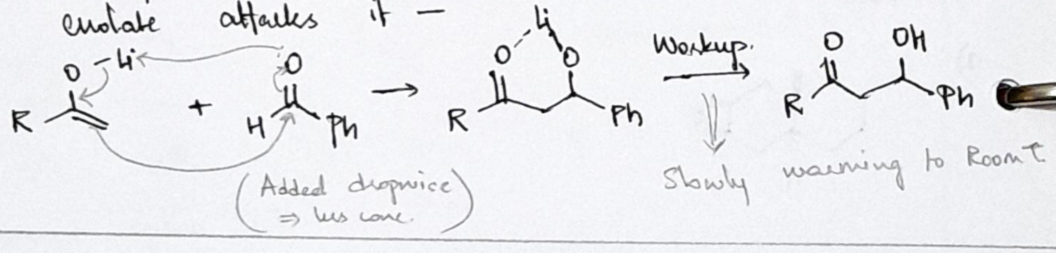
#irreversible





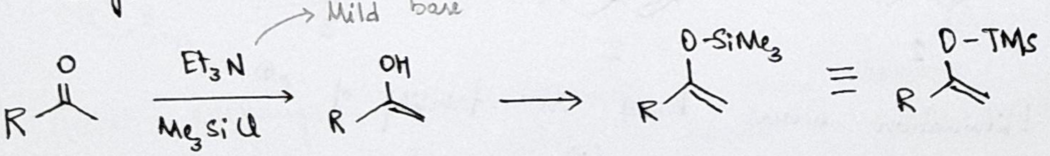
The enolate can be prepared in ~20-30 mins

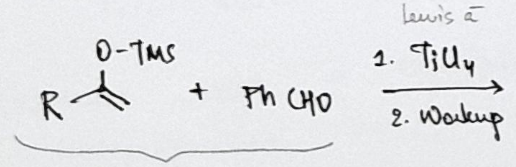
When aldehyde is added to the reaction mixture, the enolate attacks it -



Lecture 8.2

Silyl enol ethers.



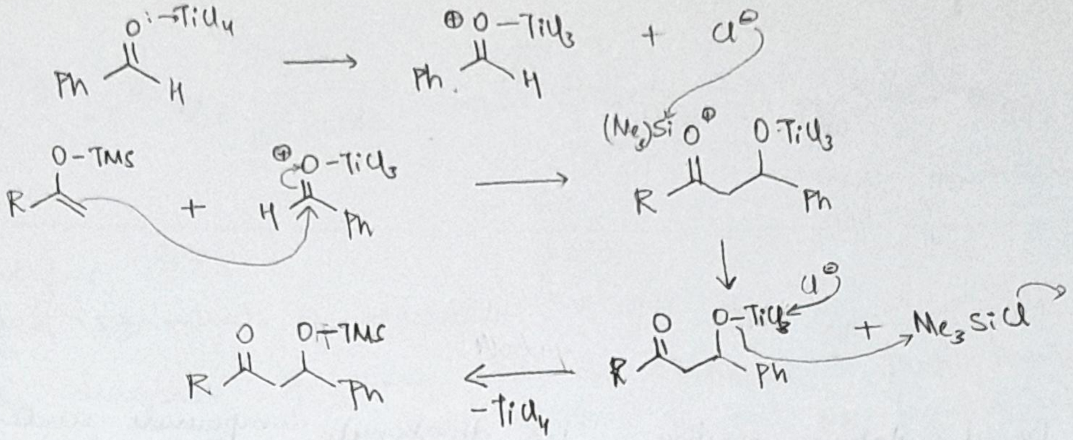


Mukaiyama Aldol Reaction.

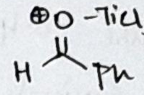
No reaction WITHOUT Lewis acid

(37)

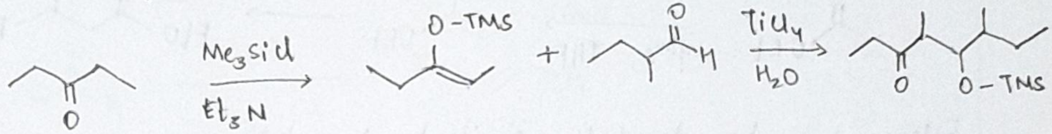
Mechanism –



★ There's no reaction if Lewis acid is not added ∴ enol is quite stable & aldehyde is not very reactive

★ Attack of silyl enol ether on electrophile  is the crucial step.

★ Eg:



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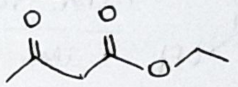
Lecture 8.3

1,3 - Dicarbonyl compounds

\# We're discussing how to control aldol reaction

Enol equivalent :1) Ethyl aceto-acetate

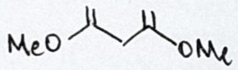


It has a strong tendency for it to remain in enol form because of two electron withdrawing groups.

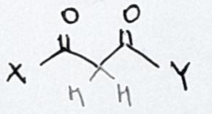
Any other aldehyde can't enolise as well as this one.

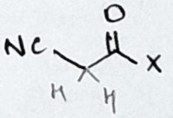
pKa = 12 – 14 Aldehyde ~ 18 Ketone ~ 20

2) Di-methyl malonate :



Molecules of form :



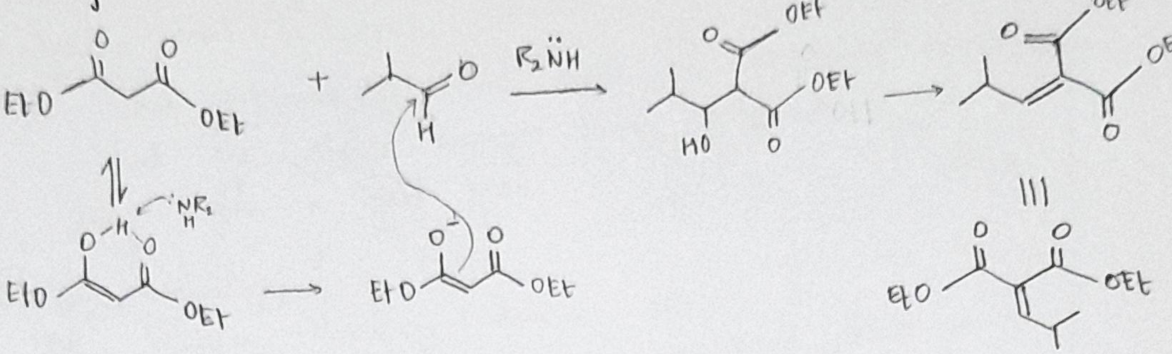


where X, Y are –R or –OR

act as very good enol equivalents.

\# Both ① and ② are very cheap, so they are good starting products to make anything.

Example —

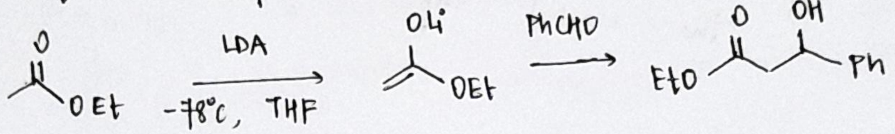


Decarboxylation reaction : 1,3 dicarbonyl compounds undergo this reaction easily.

Lecture 8.4

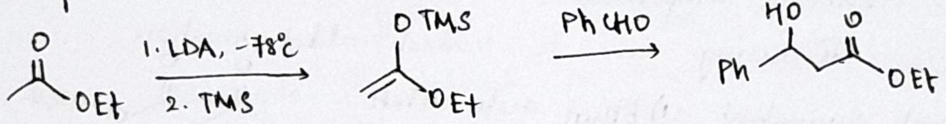
Enol equivalents of esters

★



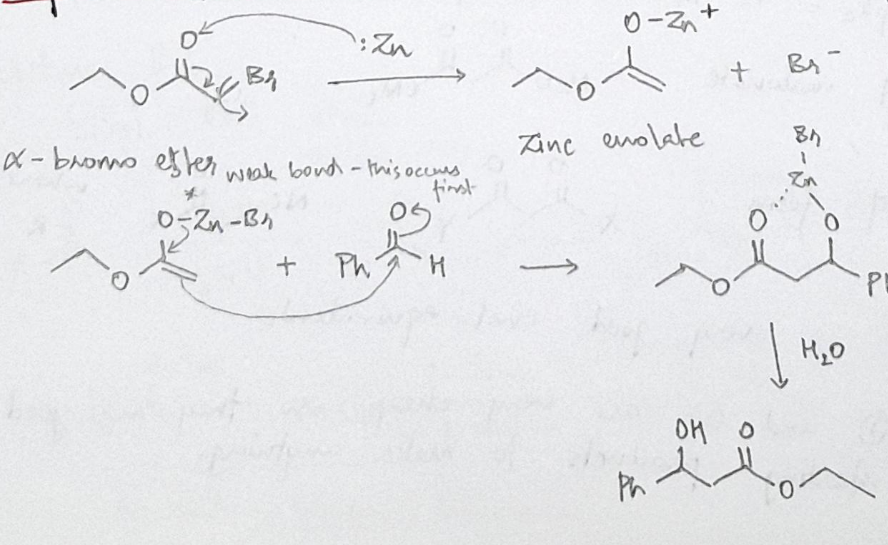
Esters can be treated similarly to ketones.

★ Silyl enol ether (needs a stronger base)



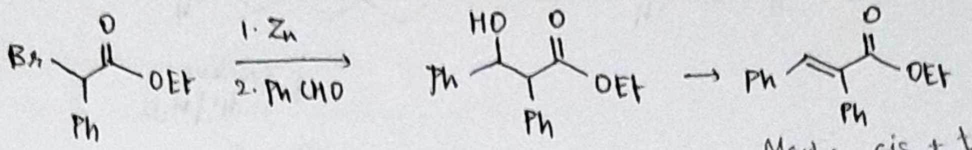
With esters, there's a powerful yet mild method that can be used to produce enol-eq

Reformatsky Reaction



This can be produced easily and cheaply.

Example –



Maybe cis + trans

Lecture 8.5

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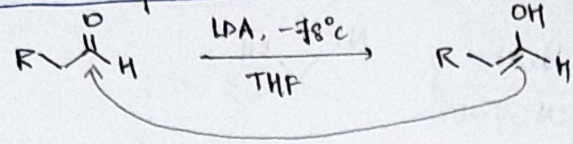
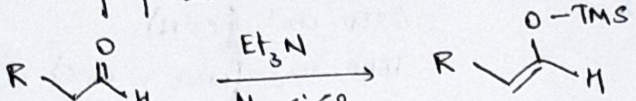
Enol equivalents of aldehydes

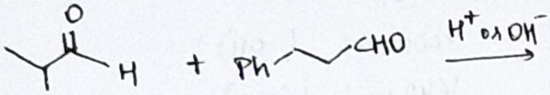
The drawback of using LDA on aldehydes is that they're i.e. enols are very reactive & end up forming self-condensed products.



So, the preferred method is to use TMS

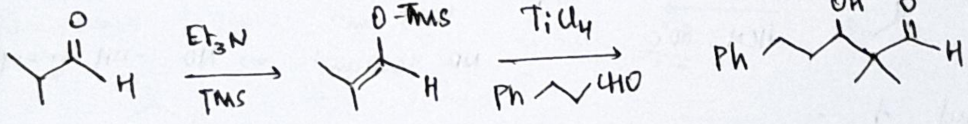


Example of cross condensation reactions –

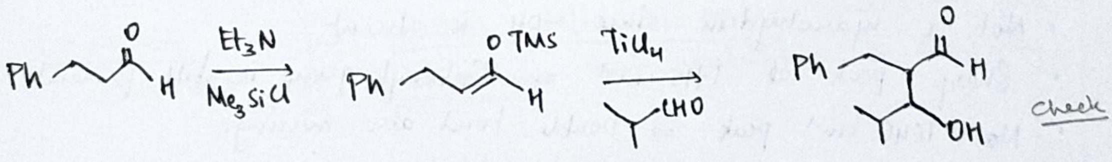


self + cross condensatⁿ products.

If we want to control the product formed, we use an enol equivalent –

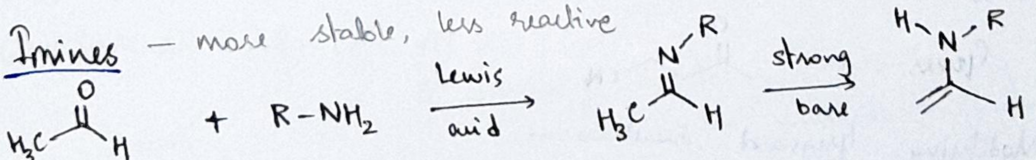


95% Yeild.



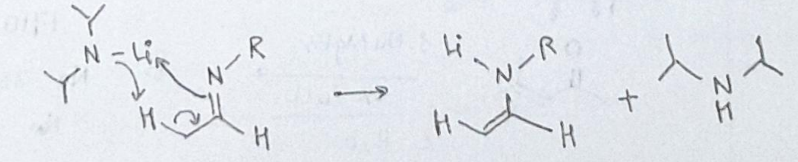
Check

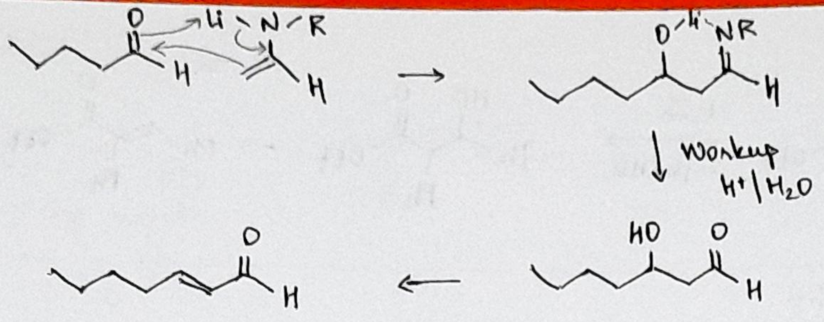
Imines – more stable, less reactive



Eza -enolate?

Mechanism – with LDA



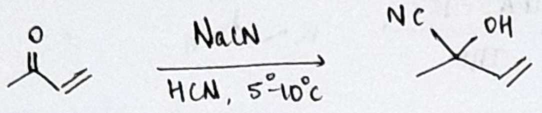


Lecture 9.1

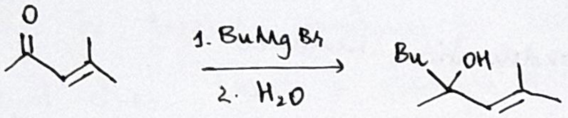
7/12/20

Conjugate Addition

Consider –



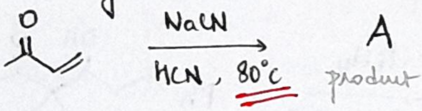
IR
1700 cm⁻¹ (C=O)
3600 cm⁻¹ (-OH broad)
2250 cm⁻¹ (C≡N)
1640 cm⁻¹ (weak - C=C)



1700 cm⁻¹ (C=O)
3600 cm⁻¹ (-OH) broad
1640 cm⁻¹ (C=C)

If we change the conditions a little –

⇒

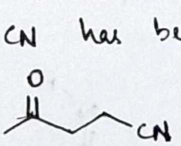


2250 cm⁻¹
1715 cm⁻¹ – sharp
NO 3600 cm⁻¹ ⇒ NO –OH group.

Product A –

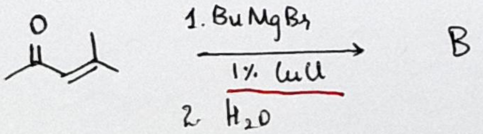
- Not a cyanohydrin since –OH is absent
- Sharp peak at 1715 cm⁻¹ ⇒ Carbonyl group is still present
- No 1640 cm⁻¹ peak ⇒ Double bond also missing.
- 2250 cm⁻¹ ⇒ –CN has been added

Guess :



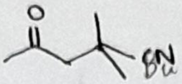
: Fits the given IR spectrum

⇒ Modifying Grignard reaction –



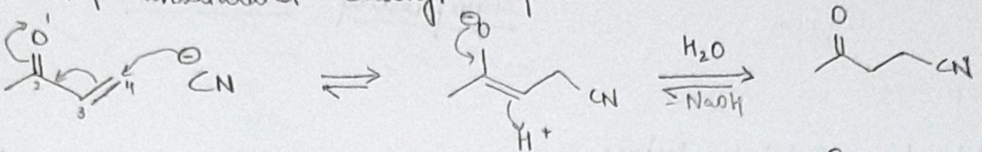
1710 cm⁻¹
No 3600 cm⁻¹ ⇒ no –OH
No double bond either.

Guess - B :

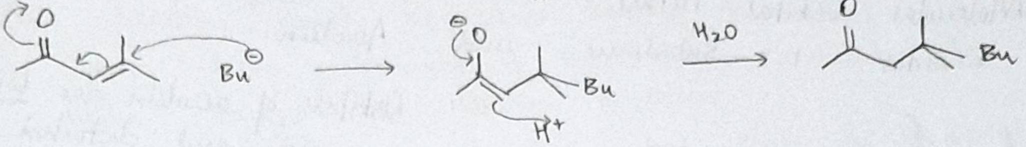


Arrow pushing mechanism -

α-β unsaturated carbonyl compound -

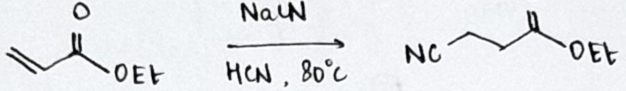


Do it yourself.

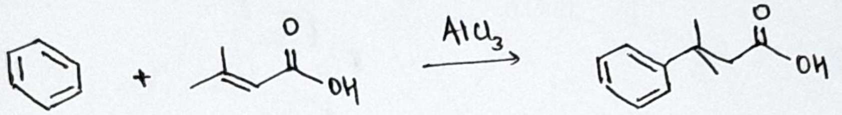


Examples -

1.

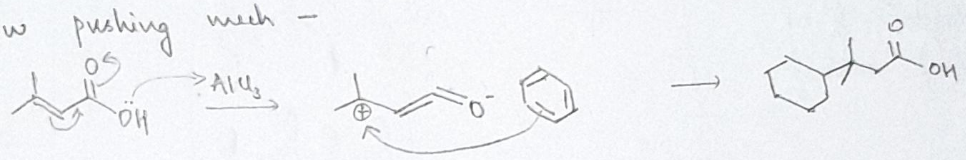


2.



Arrow pushing mech -

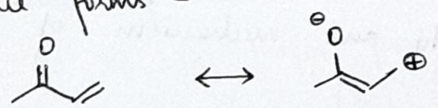
?



Lecture 9.2

Reactivity of α-β unsaturated carbonyls -

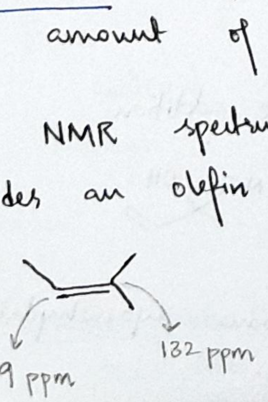
Resonance forms -



β - carbon is the electron deficient centre. There's a fair amount of polarisation that contributes to reactivity.

^{13}C NMR spectrum

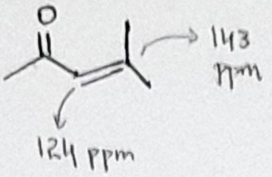
Consider an olefin -



Generally, as the strength / no. of EWG increases, the chemical shift value of that C-atom also increases, because the electron cloud around it decreases.

Higher value ⇒ 'De-sheilded' atom.

Consider -

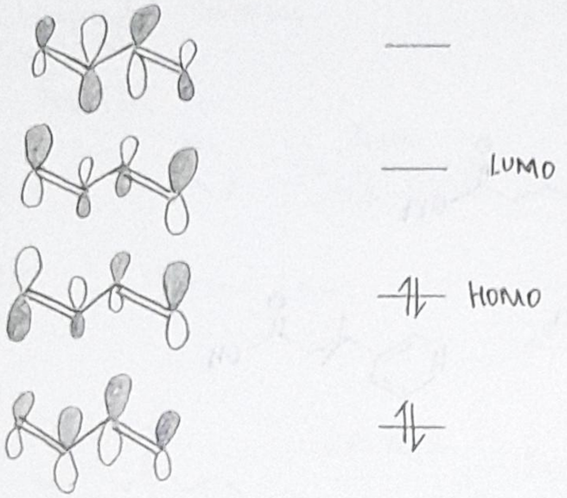


When there's a -C=O group instead of $-CH_3$, the C atoms are significantly deshielded.

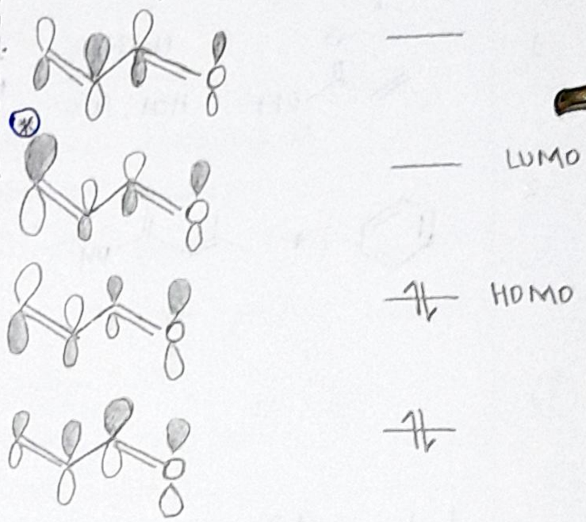
Chap 22 in Clayden

Molecular Orbital Picture

Consider 1,3- Butadiene and Acrolein



Orbitals of acrolein are lower in energy and distorted because of O atom

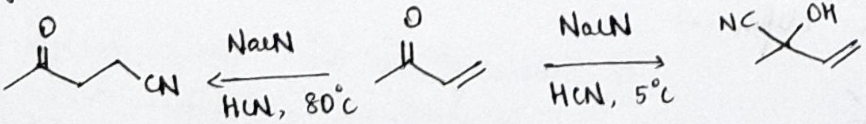


In the LUMO of acrolein, the β-C atom has the largest coefficient. This molecular orbital picture helps in explaining the reactivity and mechanism of conjugate addition.

Lecture 9.3

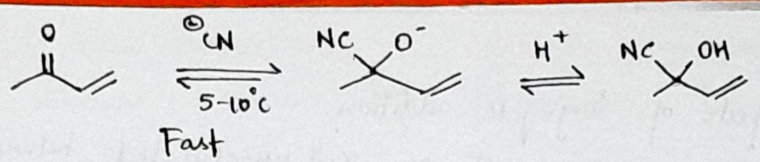
7/12/20

Difference between 1-2 addition & conjugate addition

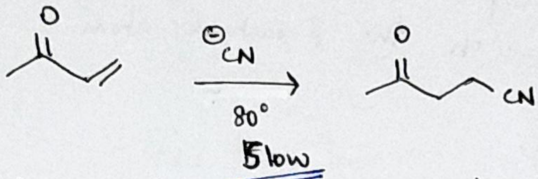


At 5°-10°C, we know that compound forms cyanohydrin and its a reversible reaction.

①



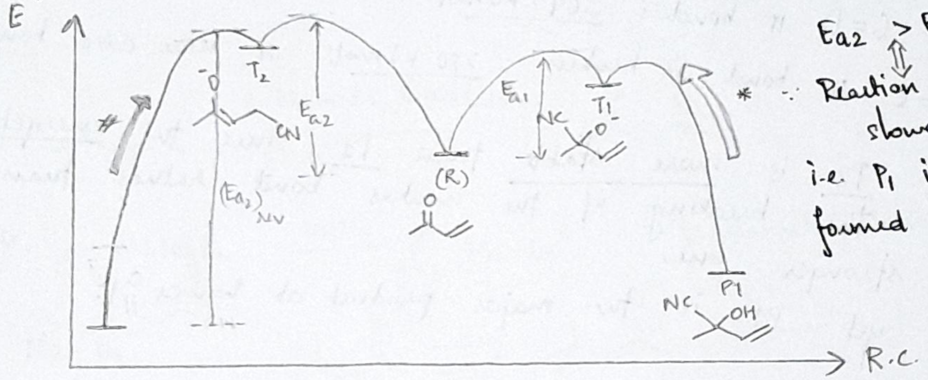
②



This reaction must be slow because it doesn't occur at lower temp. because it needs more molecules at higher energy for reaction to occur.

Reaction ① also occurs at 80°C, but since its reversible, the product formed is lesser in conc.

Energy profile



$E_{a2} > E_{a1}$

⇕

* ∴ Reaction ② is slower than ①

i.e. P_1 is always formed faster than P_2

* If a reaction is reversible, then the energy barrier for it would be accessible at that temperature. i.e 5-10°C

For P_2 to be the major product at 80°C, we've to invoke the concept that $(E_{a2})_{rev}$ ‡ is inaccessible at that Temperature

⇒ Even if P_1 is formed at 80°C, it gives back the starting material since its a reversible reaction, which goes through reaction 2, which is irreversible

Consider — $P2 \xleftarrow{k_2} R \overset{k_1}{\rightleftharpoons} P1$ Rate of formation of P1 >> P2

$k_1 > k_2$

P1: Kinetic Product — outcome of the reaction is dictated by the rate of reaction, P1 is the major product (at all temperatures)

BUT — If Reaction ① is reversible, P2 is formed.

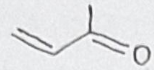
P2: Thermodynamic product — its more stable than P1

8/12/20

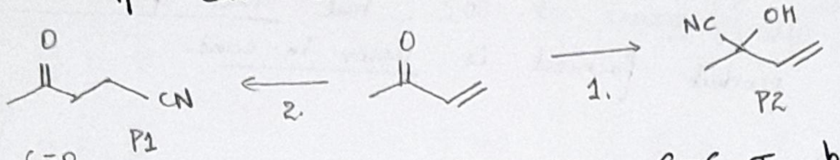
Lecture 9.4

Structural aspects of conjugate addition.

We know that the LUMO of an α-β unsaturated ketone has the largest coefficient on the β-carbon atom.



The Nu⊖ will most likely attack at β-C (from MO perspective), it can also attack the carbonyl carbon.



C=O

1. π bond is broken and a new C–C σ bond is formed

   C=O π bond : 369 $kJ\,mol^{-1}$

2. C=C π bond is broken : 280 $kJ\,mol^{-1}$ & new C–C bond is formed.

So, P2 is more stable than P1, since the energetics favor the breaking of the weaker bond rather than the stronger one.

And yet P1 is the major product at lower T.

Nucleophilicity

A nucleophile is a species that has a -ve charge or an electron pair, through which they attack and form a new bond

Hard	Soft
• Small in size very electronegative	• They're comparitively large
• Highly charged i.e localised	• Diffused charge
Eg: ^-OH, RO^-, F^-, $R^-\overset{+}{Mg}Br$, Cl^- RLi etc	Eg: RSH, RSe^-, S^{2-}, I^-, PPh_3 Aromatic ring, olefins

RNH_2, ^-CN, Br^- are nucleophiles of intermediate strength

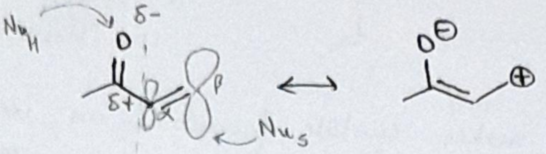
Premis : Hard bases interact well with hard acids. Similarly, hard compounds' interaction with other hard compounds is favored.

Eg: R-Cl and RLi

Same is true for soft – soft.

With hard interactions, the charges dominate i.e δ^+, δ^-
✳ * whereas with soft interactions, the orbitals dominate *

Now,



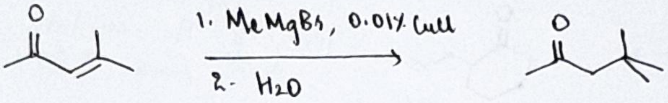
More stable form

Ketone is the more stable form & here the Hard nucleophiles prefer to attack the carbonyl atom (charges dominate) whereas with soft Nu, they prefer β-C atom (orbitals).

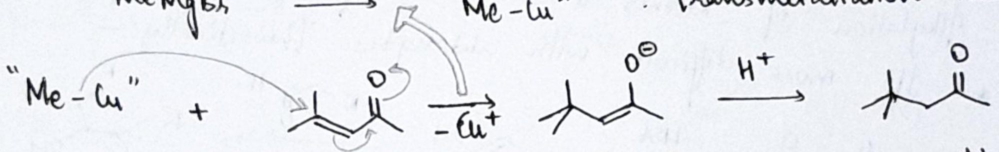
^-CN is an intermediate Nu but it seems to prefer to attack as a Hard nucleophile, attacking the C=O.

Lecture 9.5

Going back,



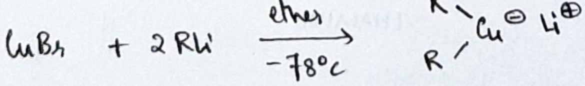
Here, MeMgBr $\xrightarrow{CuI}$ "Me-Cu" : Transmetallation reaction.



Since Cu is recycled & used in transmetallation reaction, a very small amount is required for this reaction

MeMgBr is a hard nucleophile which we're converting into an organometallic compound, which is a Soft Nu. This changes the outcome of the reaction.

Alternatively, we could directly use the organometallic compound –



$$CuBr + 2RLi \xrightarrow[-78°C]{ether} R_2Cu^{\ominus}Li^{\oplus}$$

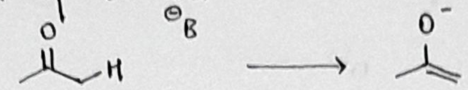
Li-Cuprate Reagents

Li Cuprate reagents can be formed and isolated, but they're unstable, so they've to be used quickly.

They give the conjugate addition product.

Lecture 9.6

Alkylation of Enolates

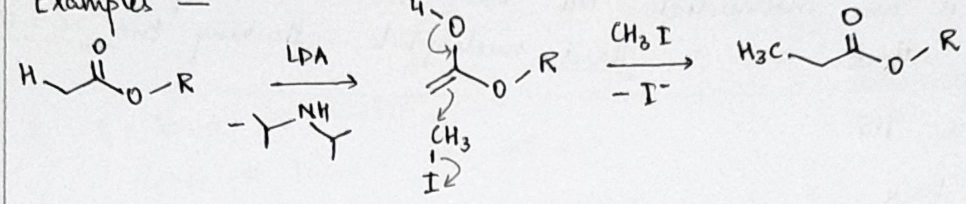


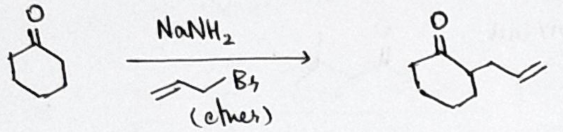
B : Strong base like LDA, $NaNH_2$

Using strong bases makes enolate formation an irreversible process. At low temp, the enolate can go to a strong population level.

Using a weak base makes the process reversible — incomplete enolate formation.

Examples —

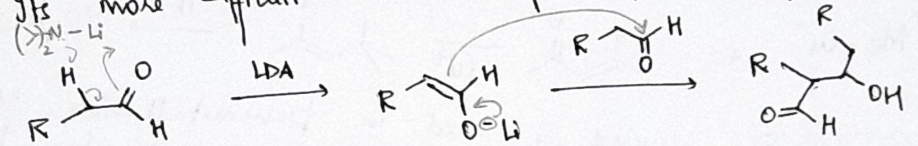
1. 

2. 

Forms a Na-enolate

Alkylation of ketones & esters is fairly straightforward

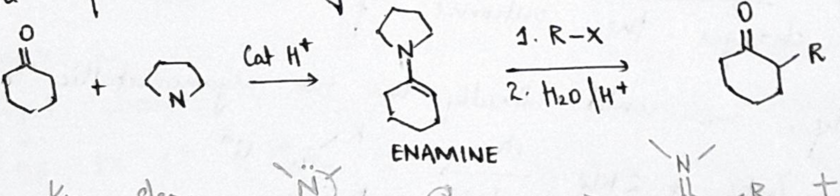
⇒ * Its more difficult with aldehydes. Theoretically —



Aldol reaction competes with alkylation even at -78°C.

So, LDA is not used with aldehydes.

* One of the strategies is to use specific enol equivalents,



Key step:

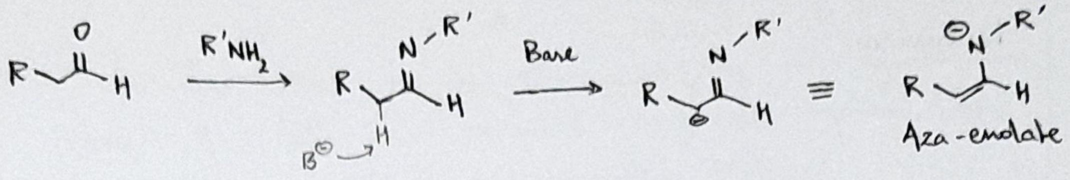
This is an S_N2 reaction.

The advantage of using Enamines for the alkylation reaction is that → there's no risk of self-condensation reaction because they're not very reactive.

→ Its a mild reaction that's compatible with many functional groups

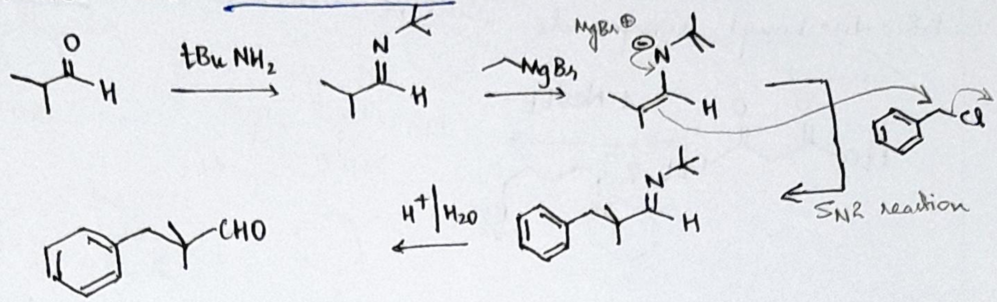
Other electrophiles are also compatible i.e enamines can be used to generate α-bromine products

★ Aza-enolates



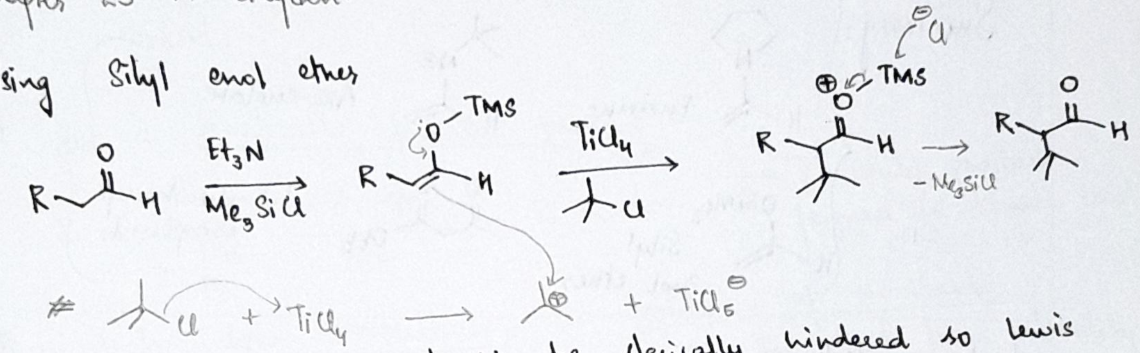
Aza-enolates are more reactive than enamines - better nucleophiles

Eg:



Chapter 23 in Clayden.

★ Using Silyl enol ethers

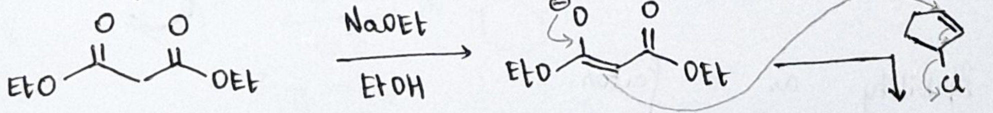


The electrophile used should be sterically hindered so lewis acid (like TiCl₄) can be used i.e capable of forming a carbocation.

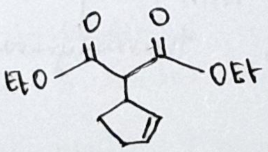
This reaction works well with electrophiles that can react through S_N1.

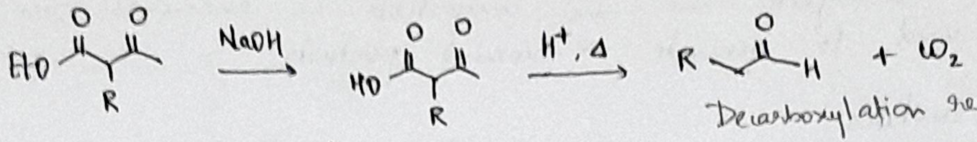
(1,3)

★ β-dicarbonyl compounds.



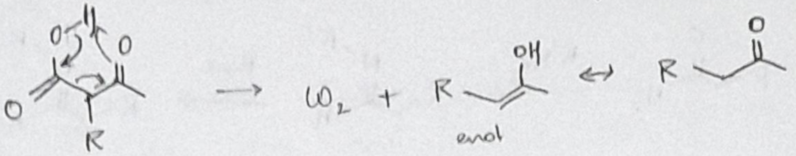
This 1,3-dicarbonyl compound can be converted to a mono-carbonyl compound as outlined in the next page





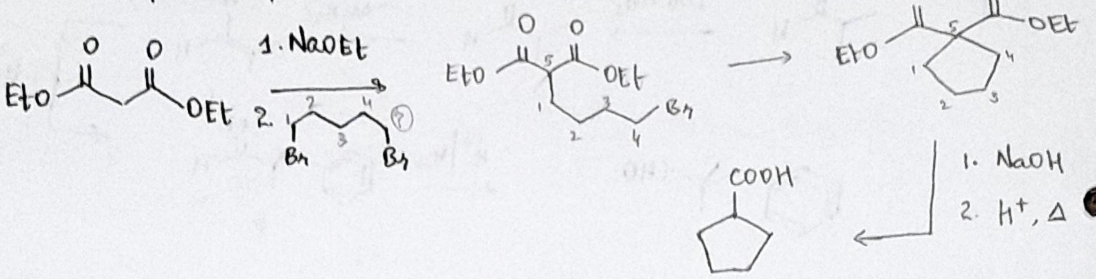
Decarboxylation reaction

Mechanism:

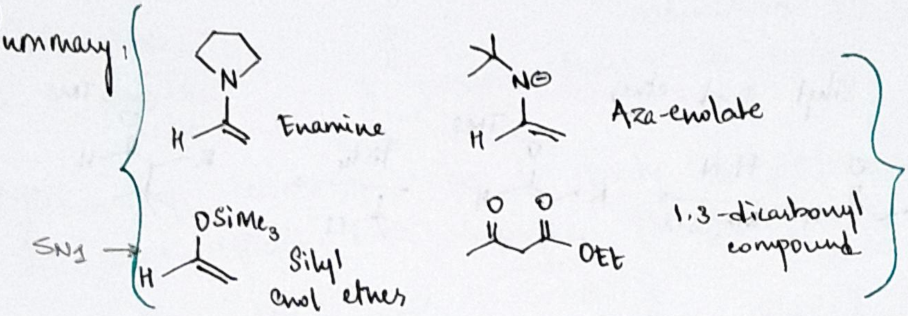


(?) This reaction requires S_N2 conditions.

1,3-dicarbonyl compounds can be used to make cyclic compounds -



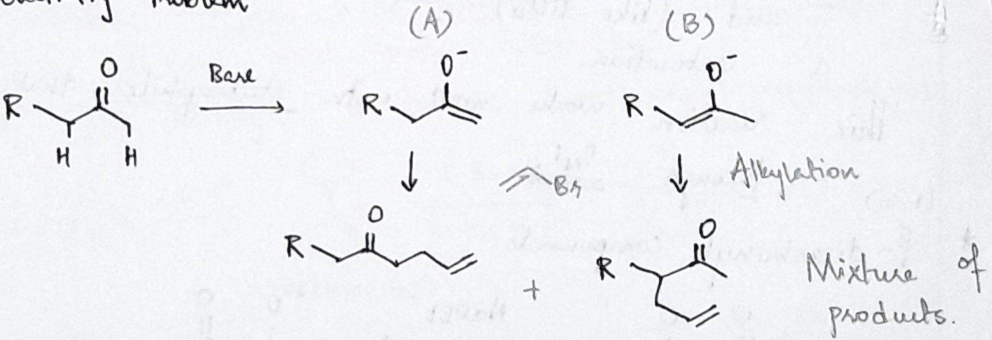
Summary:



Lecture 9.7.

9/12/2020

Regioselectivity Problem



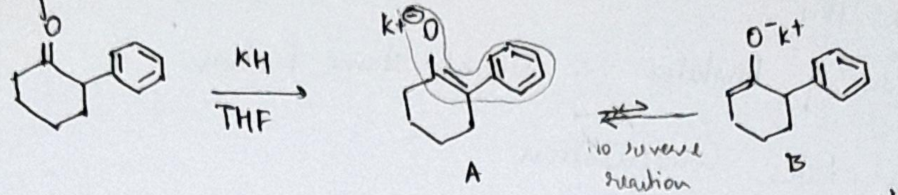
Mixture of products.

Stability as a factor.

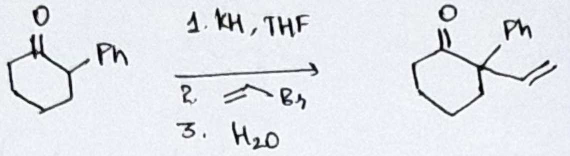
As with olefins, the more substituted enolate is more stable.
So, thermodynamically, enolate B is preferred over A.

Example -

★

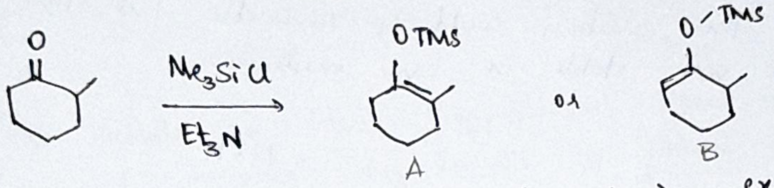


We'd assume that A & B would be in equilibrium, but since A has an extended conjugate system, its more stable ⇒ thermodynamically prefered.



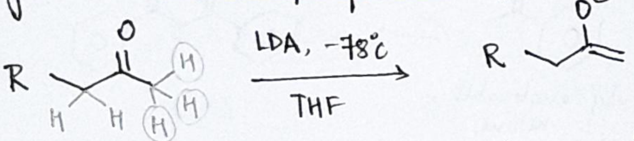
Thermodynamic product is favored.

★



A is almost exclusively formed i.e excellent thermodynamic control.

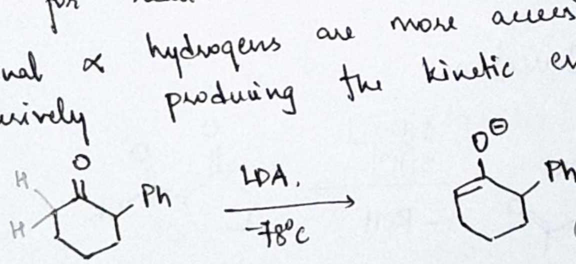
To get a kinetically favored product -



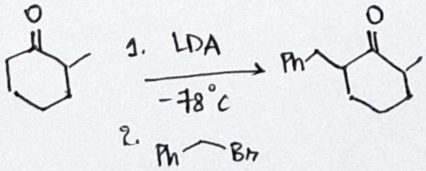
→ The only product formed is kinetic enolate

At such low temperatures, the population of available atoms for reaction becomes more important than stability. The terminal α hydrogens are more accessible to LDA, thus exclusively producing the kinetic enolate.

Similarly.



(exclusive)



When there's competition between 2 kinds of enolates,

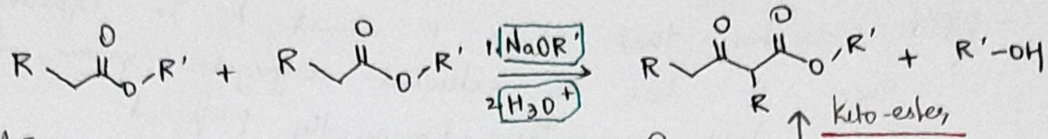
Thermodynamic - more stable ∵ more ~~str~~ substituted - reacted at room temperature or higher & reacted for long so it can equilibriate

Kinetic - less substituted & stable - short reaction time and low temperatures are used for this.

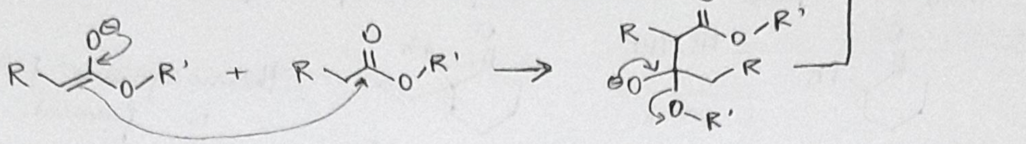
Lecture 10.1

Acylation of Enolates & Related Name Reactions

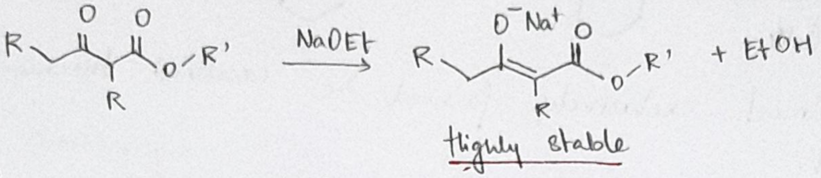
1. Claisen - Ester Condensation



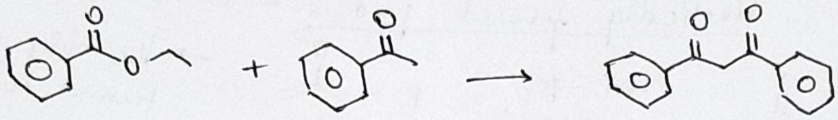
Mech -



In principle this reaction could be reversible, but the product is very stable in basic medium -



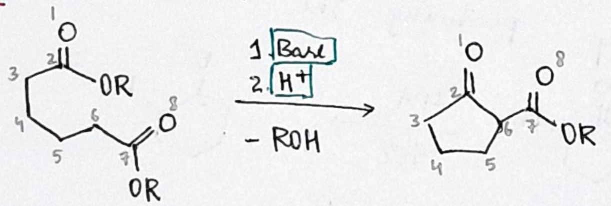
→ Crossed-Claisen condensation.



only enolisable ketone.

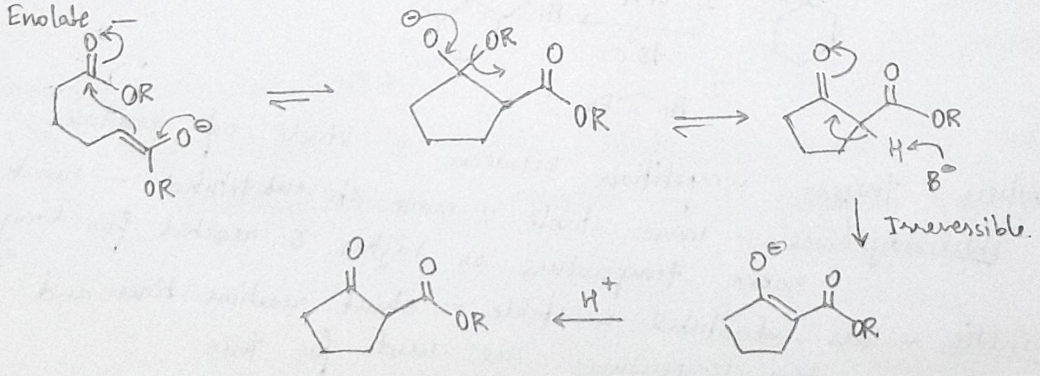
Mechanism - similar as above.

2. Dieckmann Condensation

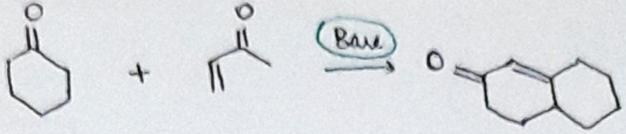


Intramolecular Claisen condensation

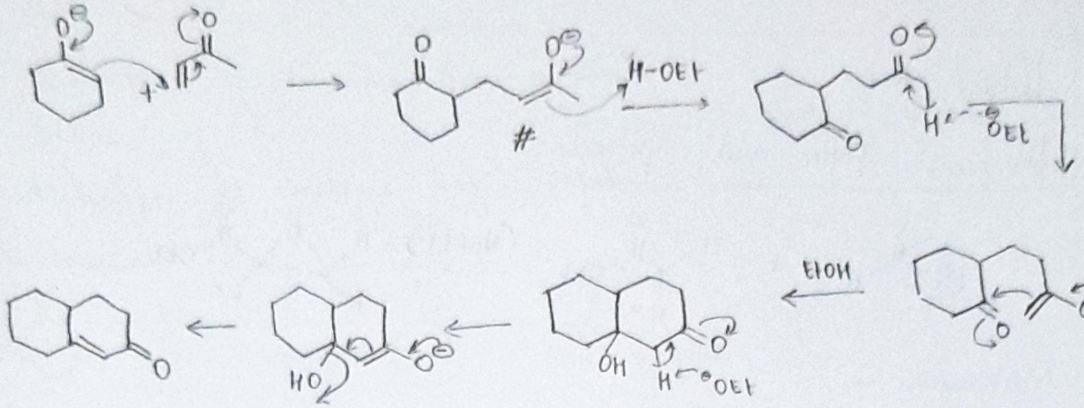
Mechanism -



(51) 3. Robinson Annulation

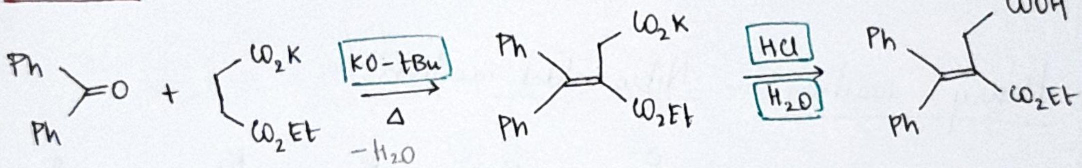


Mech –

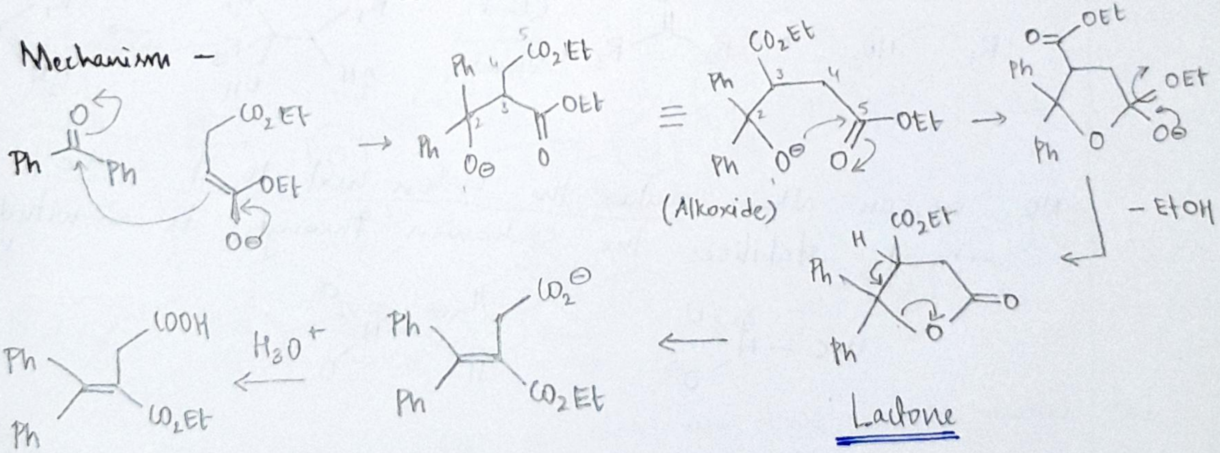


\# The enolate in that step doesn't react directly because a 4 membered ring would be formed, which is not very stable

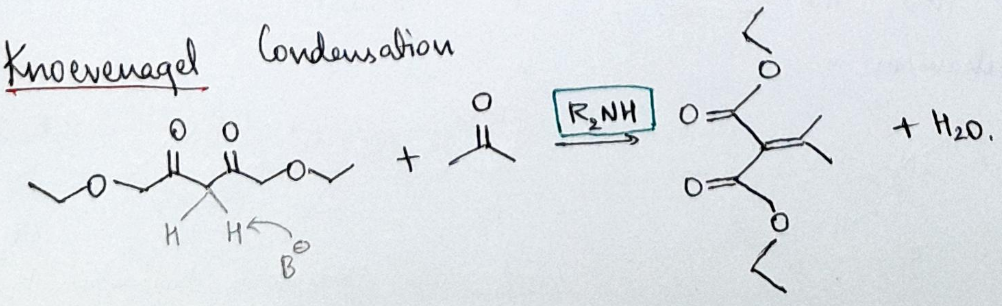
4. Stobbe Condensation.

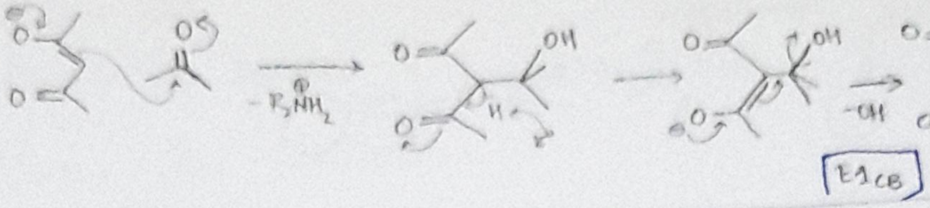


Mechanism –



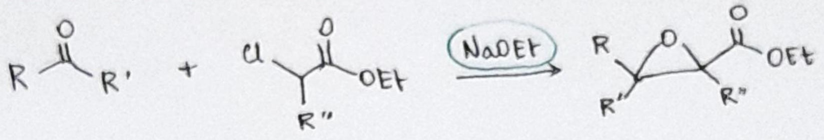
5. Knoevenagel Condensation





Lecture 10.2.

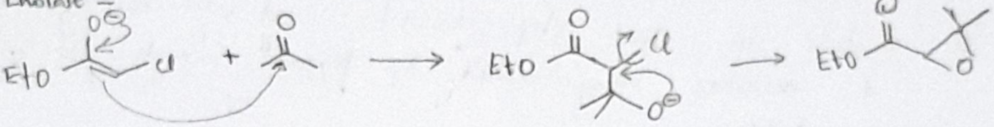
6. Darzen's Glycic acid synthesis



easily synthesized ?

Mechanism –

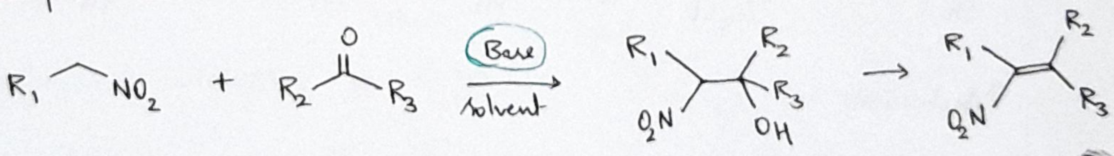
Enolate –



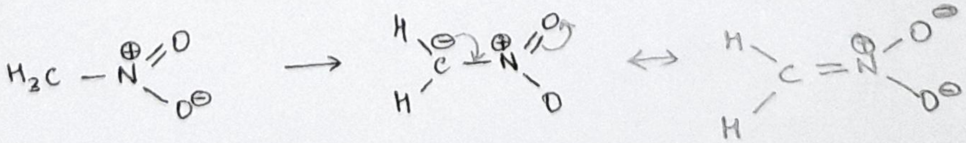
\# One of the methods of synthesis of epoxide

Note: no olefin is formed

7. Henry reaction – Nitro-aldol reaction

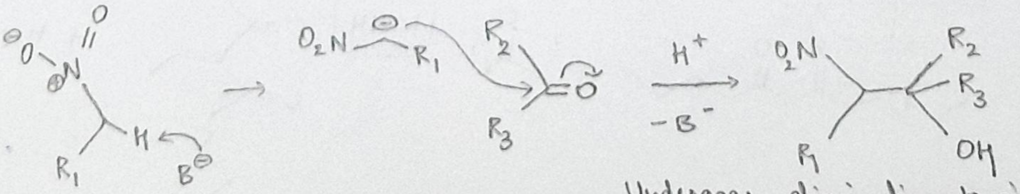


NO_2 on an alkane makes the carbon next to it acidic ∵ it stabilises the carbanion through its $e^{\ominus}$-withdrawing nature



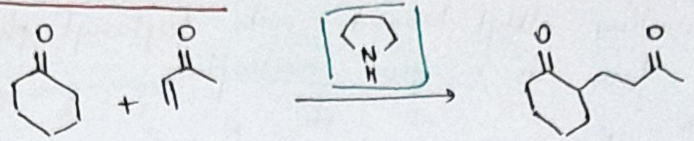
⇒ Here, the "enolate" is produced by the nitro group.

Mechanism –



Undergoes elimination to give product

8. Stark enamine reaction



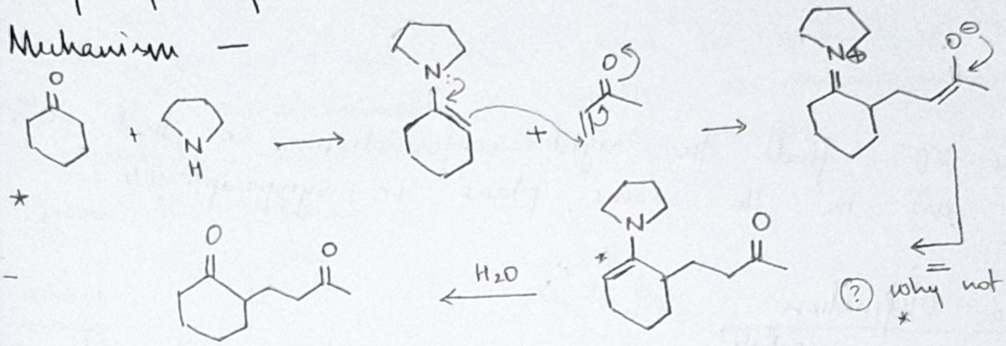
Same reactants as Robbinson annulation

Steps –

- Formation of enamine from a ketone
- Addition of enamine to α, β- unsaturated aldehyde / ketone
- Hydrolysis of enamine back to ketone

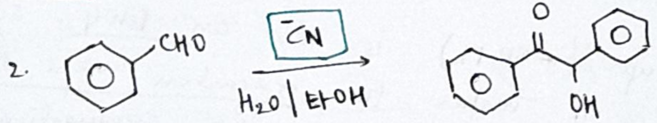
Mechanism –

For mech formatn of enamine – Pg. 39-40 *

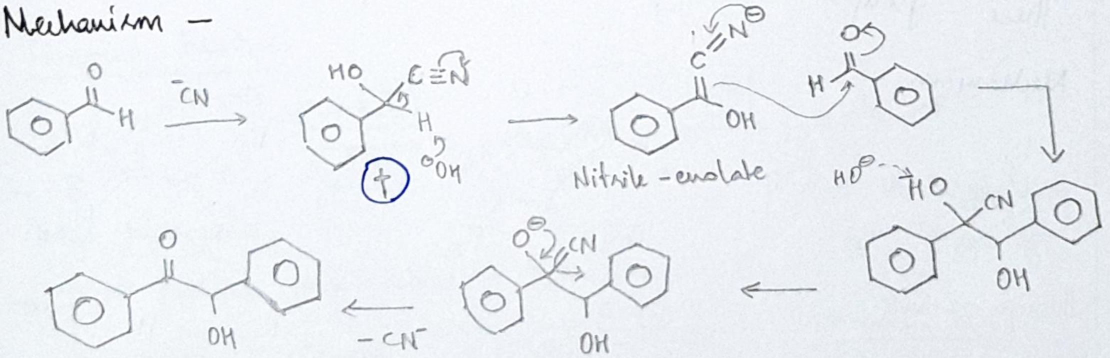


? why not towards 3° C? *

9. Benzoin condensation

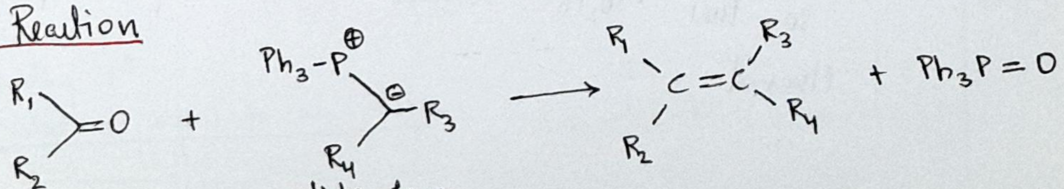


Mechanism –



(†) Just like $-NO_2$, $-CN$ is also an EWG, which makes the α carbon acidic

10. Wittig Reaction



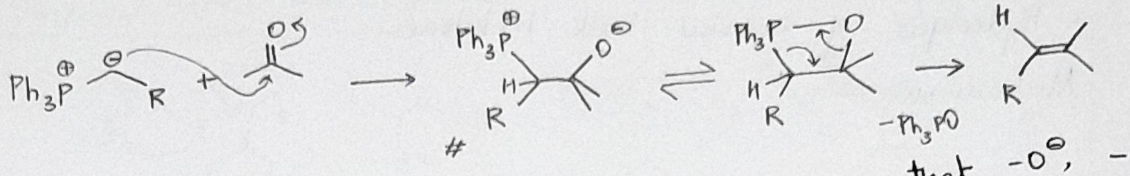
ylide form.

Ylide / Phosphorane form

Its produced by reacting alkyl bromide with triphenyl phosphine (PPh_3)

This ylide form is a good nucleophile

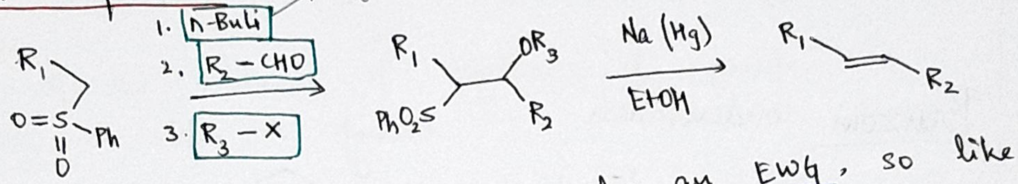
Mechanism –



The $-O^-$ finds the right conformation so that $-O^\ominus$, $-P^\oplus$ are in the same plane i.e synperiplanar

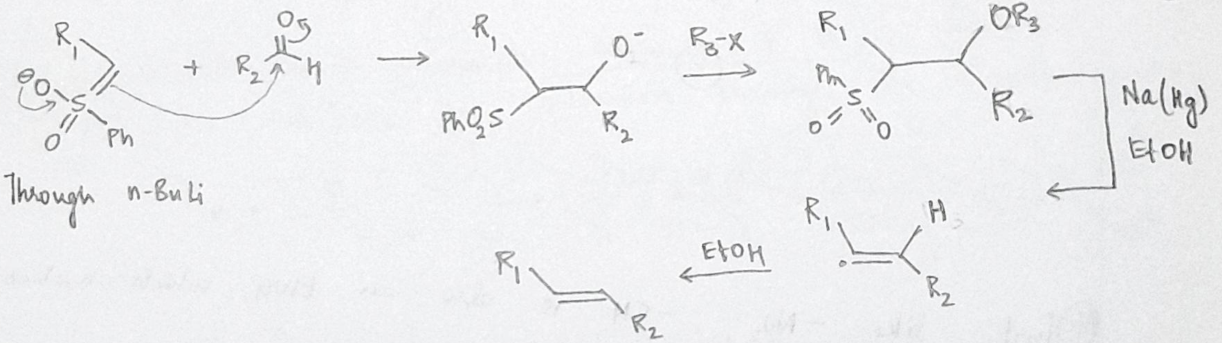
11. Julia Olefination

Just to create an enol



The sulphone group ($-SO_2Ph$) is also an EWG, so like $-NO_2$ & $-CN$, it makes the α-carbon more acidic. These groups stabilise the anion through conjugation

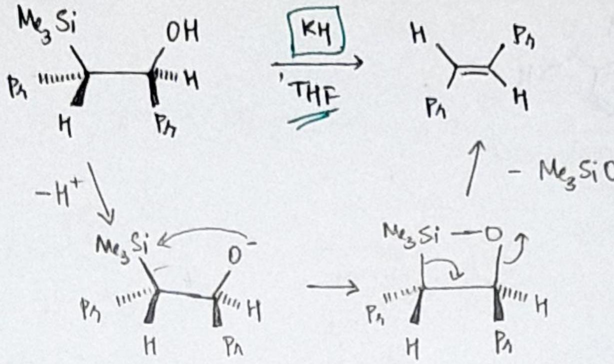
Mechanism →



Through n-BuLi

Na (Hg) is a source of electrons – it cleaves the C – S bond so that $\cdot SO_2Ph$ leaves and C$\cdot$ picks up an $\cdot H$ from ethanol.

12. Peterson Reaction

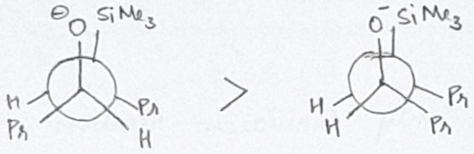


like Wittig

Since the $-O^{\ominus}$ and Me_3Si- react, the geometry of the product is pre-determined ie. we get an overwhelmingly major product, without a mixture of products

Trans is preferred

Lower energy barrier



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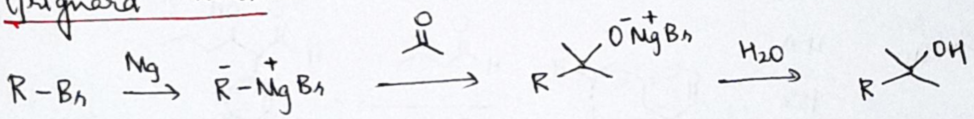
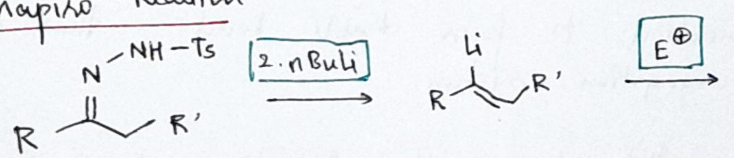
13. Grignard Reaction



14. Shapiro Reaction

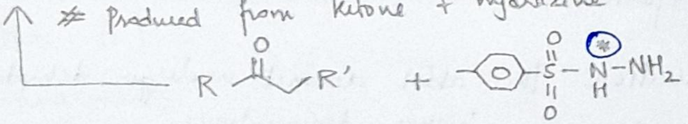


Tosyl hydrazone

E : Electrophile

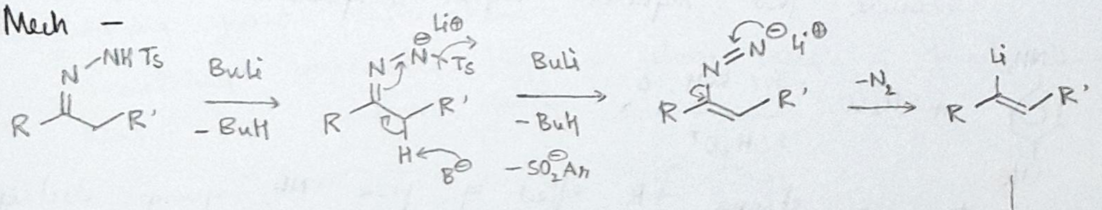
H^+, R''CHO etc.

Produced from ketone + hydrazine



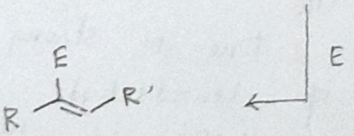
* Acidic N

Mech –

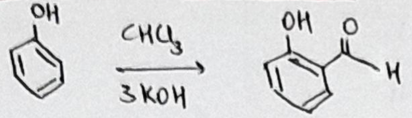


Before adding E⊕

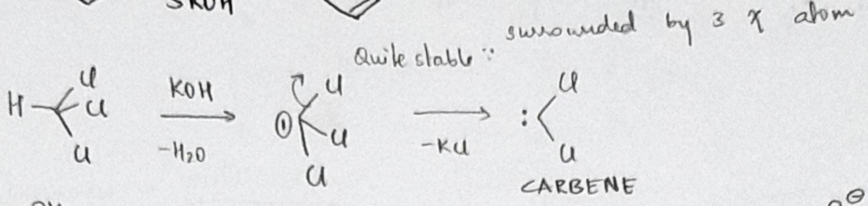
we converted a ketone to an olefin with Li !!



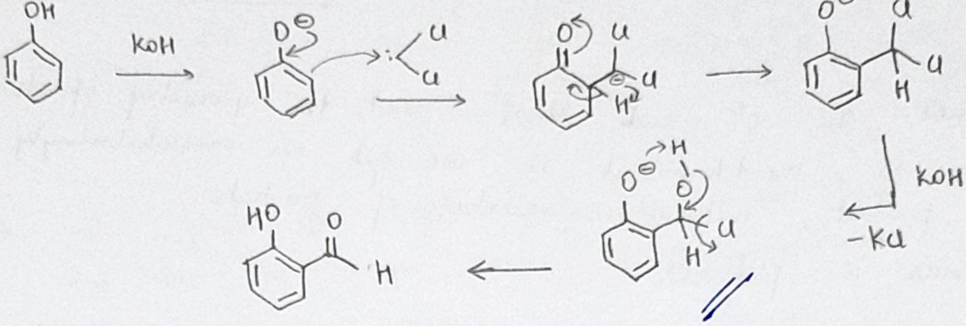
15. Reimer - Tiemann Reaction (carbene intermediate)



a)



b)



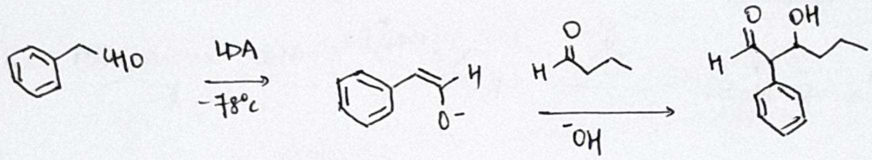
Assignment 6

16/12/20

2. No enolizable hydrogen - only Cannizzaro reaction is possible

3. LDA is a bulky base, so it will grab a proton from less hindered site.

5.

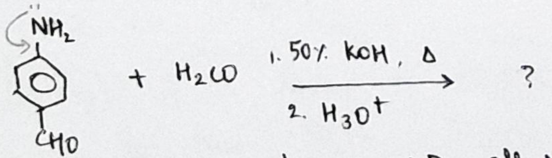


6. Spontaneous elimination to form double bond ∵ that creates an extended conjugation system.

7. Both kinetically & thermodynamically, formation of 5-membered ring is formed

8. Called nitro-aldol reaction. The aldol doesn't undergo dehydration because that requires higher temperatures.

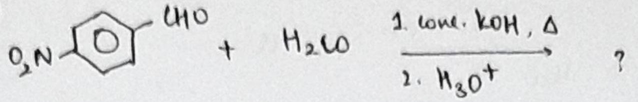
11)

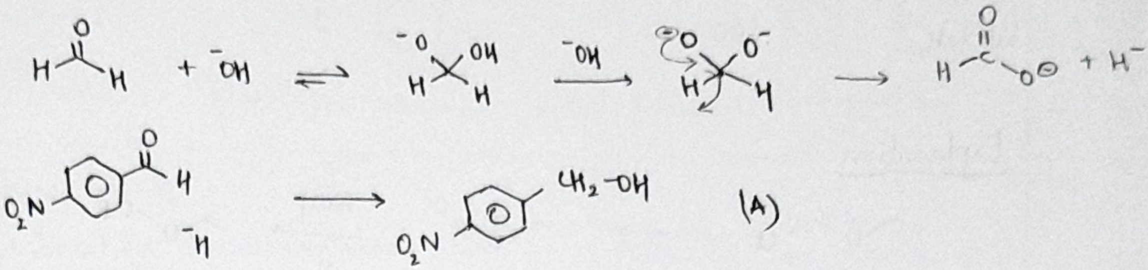


Due to strong +R effect of para $-NH_2$ group, electrophilicity of benzaldehyde is very low ⇒ it won't accept H^- from H_2CO i.e. no reaction (D)

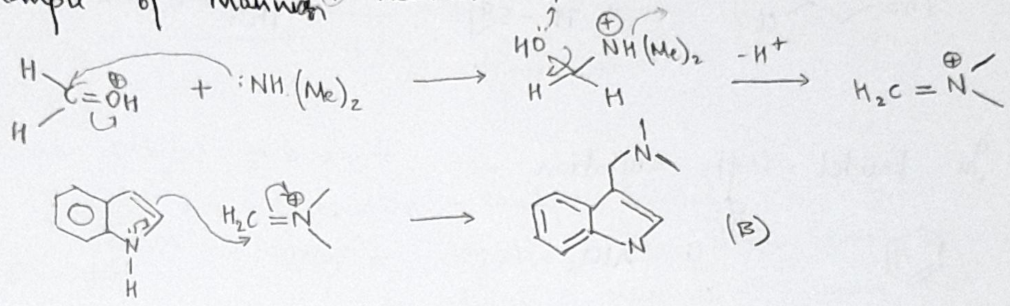
$2\,HCHO \xrightarrow{^-OH} HCOOH + CH_2OH$: will occur.

12)

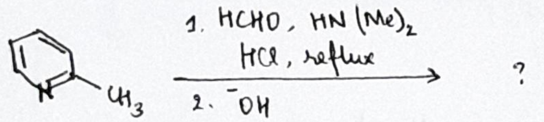




13) Example of Mannich (?) Reaction

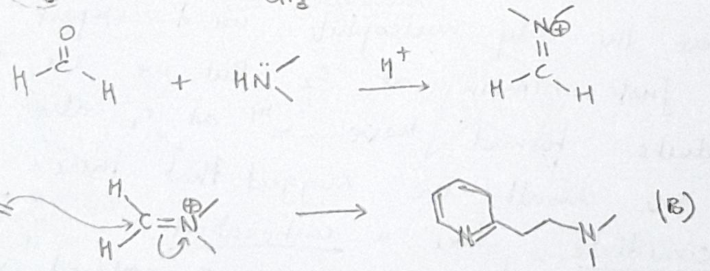


15)



Eq of
<u>Mannich</u> Reaction

⇒ Protons of −CH₃ are enolisable

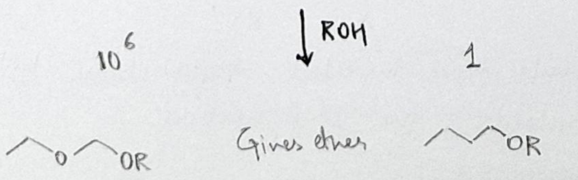


Lecture 11.1 Ch 36 – Clayden 23/12

Rearrangements

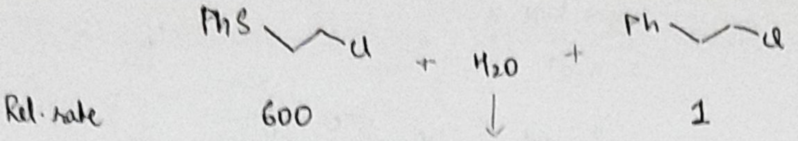
Neighbouring group participation

Something unexpected happens when there's a functional group near the reactive group

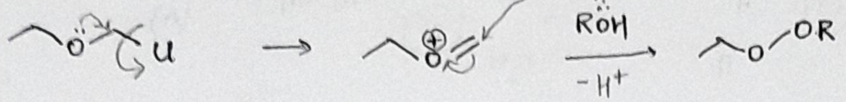


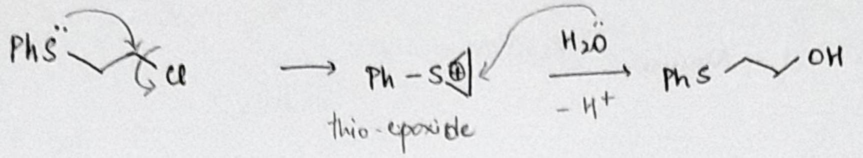
Relative rate

Million-fold increase S_{N2} sub



Explanation -



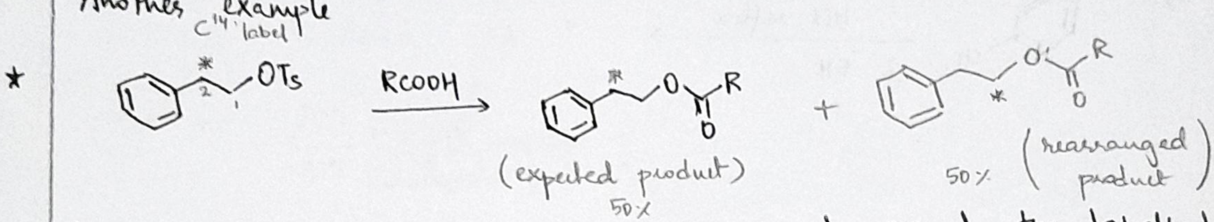


can attack either carbon.

In Freidel - Crafts acylation -

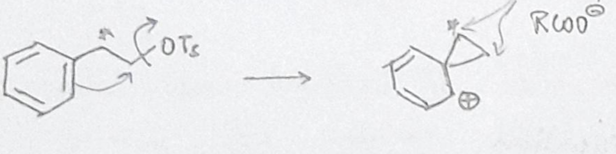
This increases rate of reaction

Another example



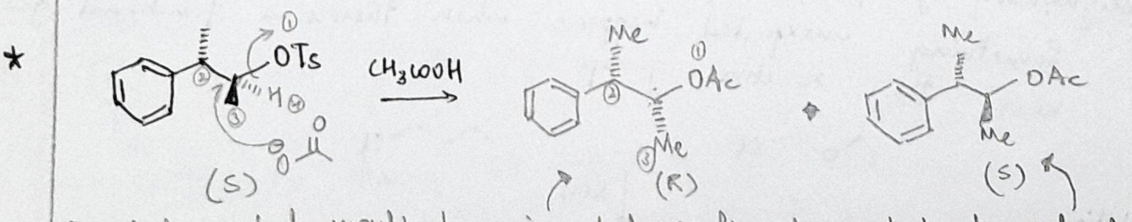
If $RCOO^-$ were the only nucleophile, we'd expect the labelled C^{14} to just remain at C_2. But we see that the products formed have C^{14} at C_1 also.

To explain the result, we suggest that there's a symmetrical intermediate, like a carbocation.



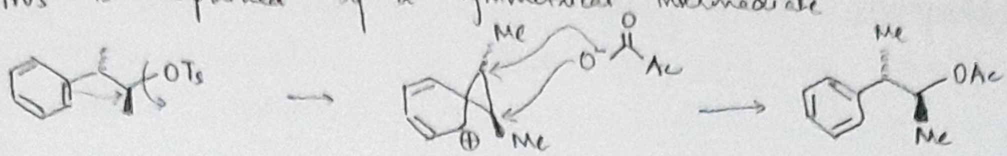
or 3-membered ring

Equally probable attack on either carbon
⇒ 2 products



Expected product would have inverted configuration. but the actual product retains the configuration.

This is explained by a symmetrical intermediate

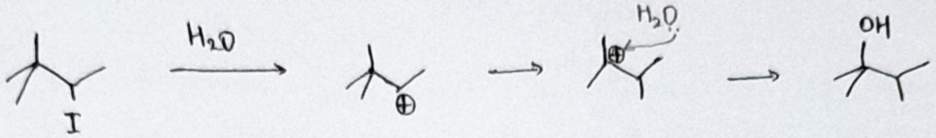


Both attacks give the product with retained configuration

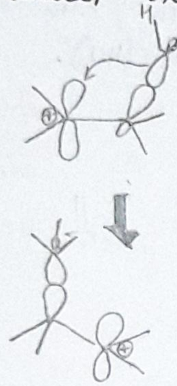
Lecture 11.2 24/12

→ ① Carbocation rearrangement

Consider —



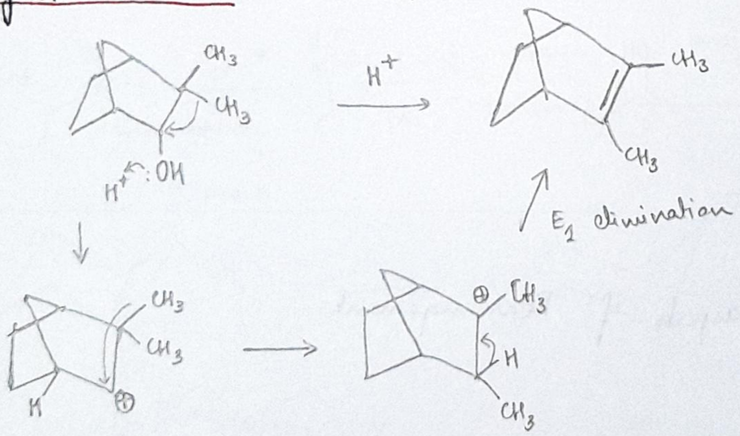
Molecular orbital picture —



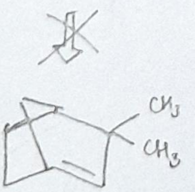
Carbocation - empty p-orbital

HOMO σ migrates to the LUMO (empty p orbital) to form a new C—C bond and an empty p-orbital

② ⇒ Wagner - Meerwin Rearrangement.



Norborane



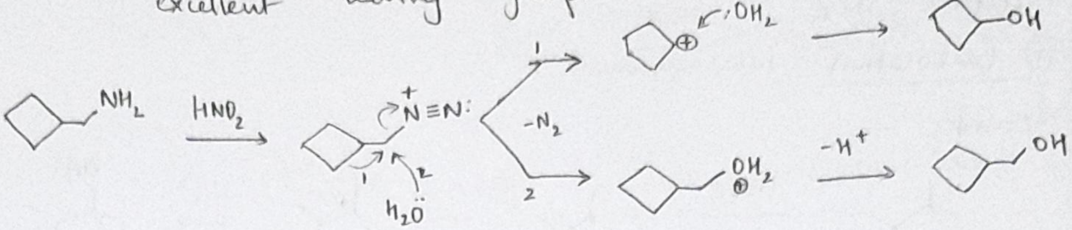
This is another example of C⊕ rearrangement.

Not favored — double bond at the bridgehead

Bredt's Rule

→ ③ Demjanov rearrangement

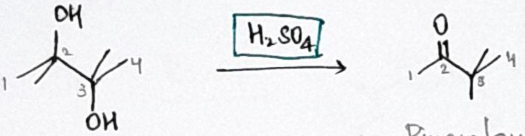
\# HNO_2 forms a diazonium salt, where N_2 is an excellent leaving group.



In first case, there's ring expansion.

\# HNO_2 is very toxic, so it's produced in situ by reacting $NaNO_2$ with mineral acid (HCl).

→ ④ Pinacol rearrangement.



Pinacol

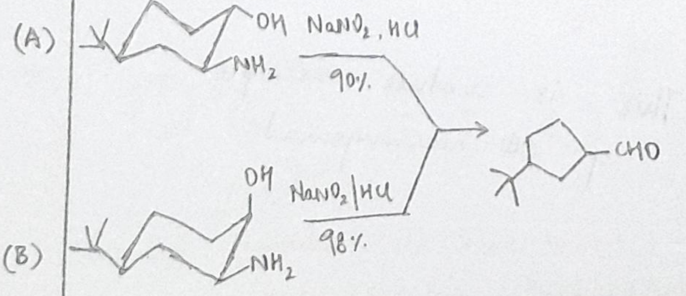
Pinacolone (70%)

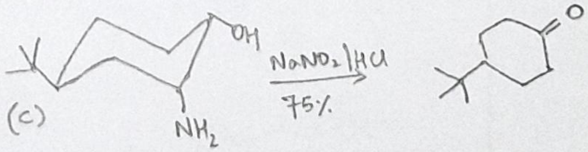
Mechanism

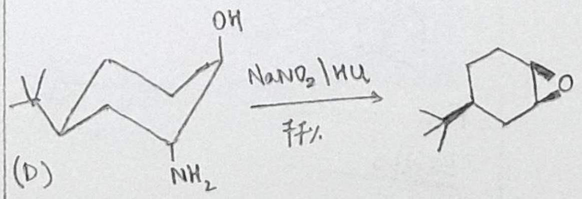
Lecture 11.3

24/11/20

Stereochemical aspects of Rearrangement.



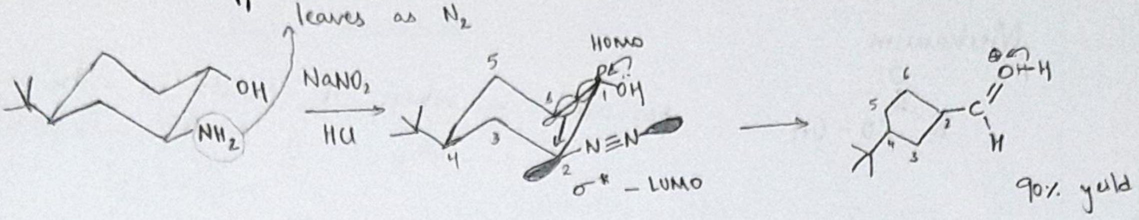




All the conformers have tButyl group, which pushes the equilibrium so that the conformer where -tBu occupies equatorial position.

Diazotization reaction is carried out with $-NH_2$ and $-OH$ at different positions —

(A)



90% yield

Here, the diazonium salt part is linear i.e. sp hybridised

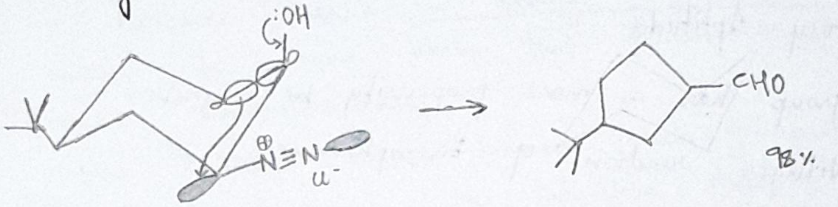
The the ABMO of C–N bond is the LUMO.

The sp^3 hybridised orbitals of C–C bond is the HOMO.

It is conveniently situated so that it can interact with the LUMO & form a new bond as the N_2 leaves.

The C⊕ is balanced by lp. e⊖s on oxygen.

(B) Similarly —

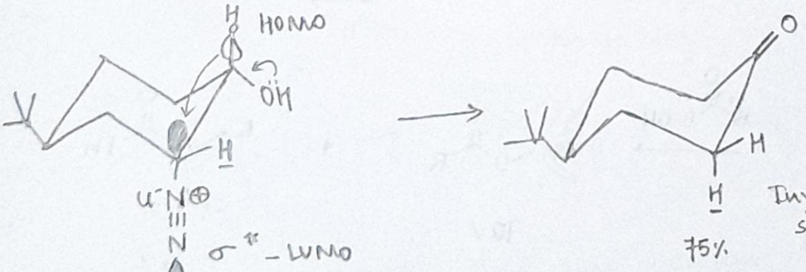


98%

Why more? Axial -OH?

Here too, $\underline{\sigma^*}$ of $\underline{C-N}$ plays a major role in determining the outcome.

(C)

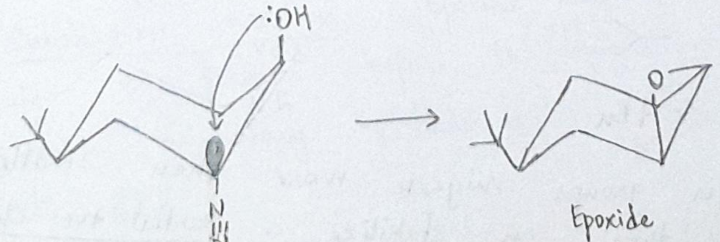


75%

This product is consistent with our hypothesis.

Inversion of stereochemistry

(D)

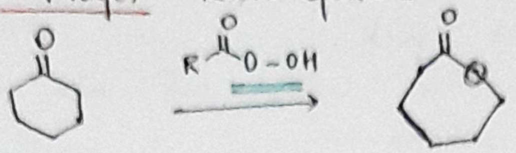


Epoxide

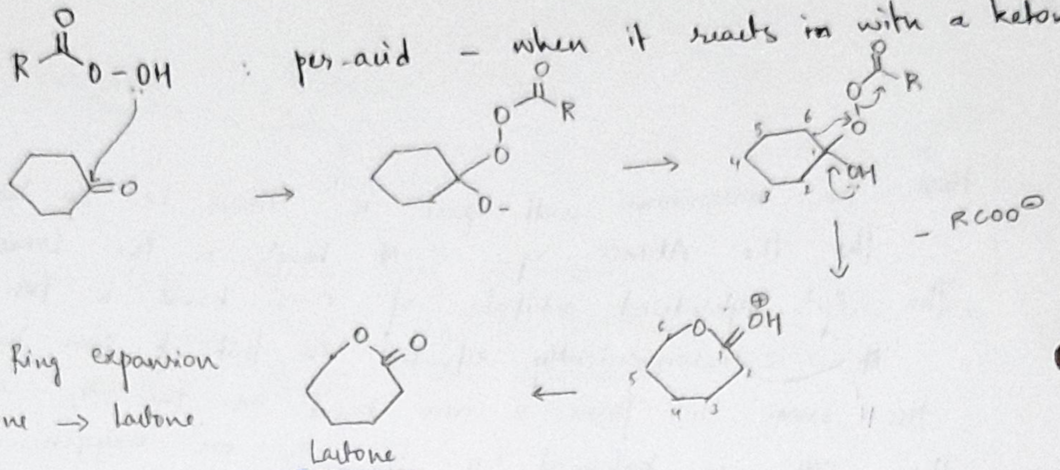
77%

Lecture 11.4 24/12

⑤ Baeyer - Villiger Rearrangement



Mechanism.



: per-acid - when it reacts in with a ketone -

* Ring expansion

Ketone → lactone

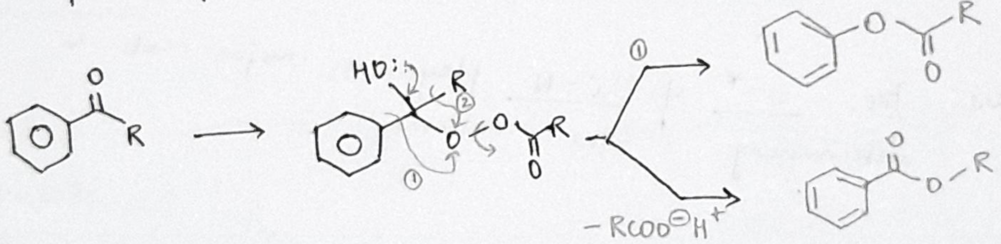
Lactone

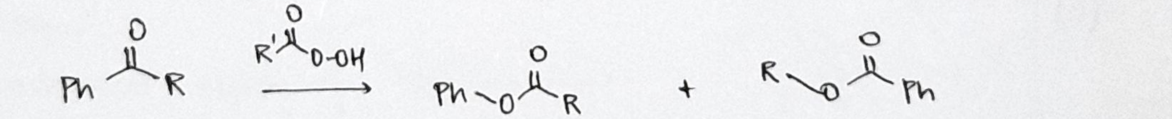
Lecture 11.5 26/12

Migratory Aptitude

Which group has a more propensity to migrate?

Baeyer-Villiger reaction of benzophenone -



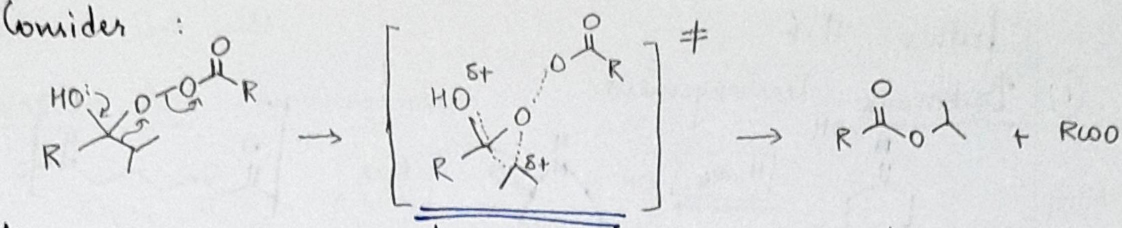
⇒ 

$$\mathrm{PhC(O)R} \xrightarrow{\mathrm{R'C(O)O{-}OH}} \mathrm{Ph{-}O{-}C(O)R} + \mathrm{R{-}O{-}C(O)Ph}$$

R =	- CH_3	90%	0%
	- C_2H_5	87%	6%
	(iPr)	33%	67%
	- tBu	2%	77%

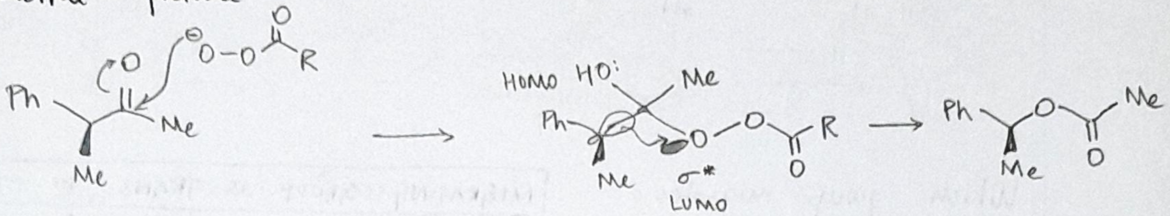
⇒ Bigger groups migrate more than smaller ones because they can stabilize a partial +ve charge much better.

Consider :



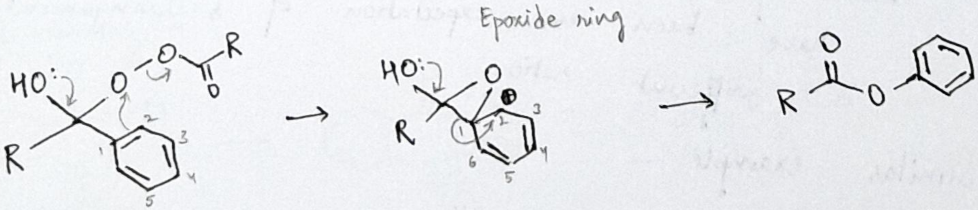
The $\delta+$ is better stabilised by a group with more alkyl branches.

→ Orbital picture

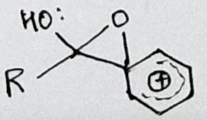


- The HOMO (σ orbital of C–C bond) is oriented so as to attack the LUMO (σ^* of O atom). The group migrates so that its stereochemistry is retained
- ⇒ There's no intermediate (like carbocation intermediate) formed because there's no change in stereochemistry. Which means its more likely that bonds are broken and formed simultaneously
- So –tBu migrates better because such groups can stabilise the $\delta+$ charge in the transition state

→ Phenyl Ring

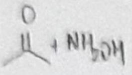


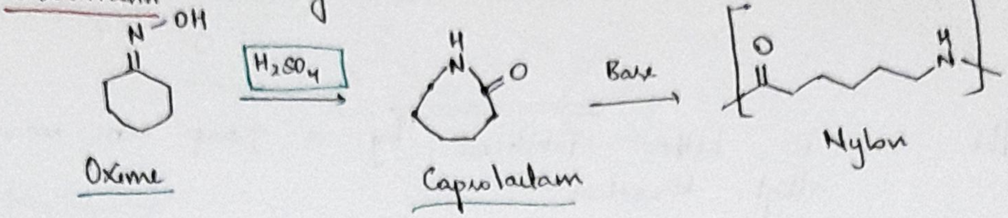
The migration of benzene ring occurs like an electrophilic substitution reaction. Epoxide ring & carbocation intermediate is formed before the migration completes.



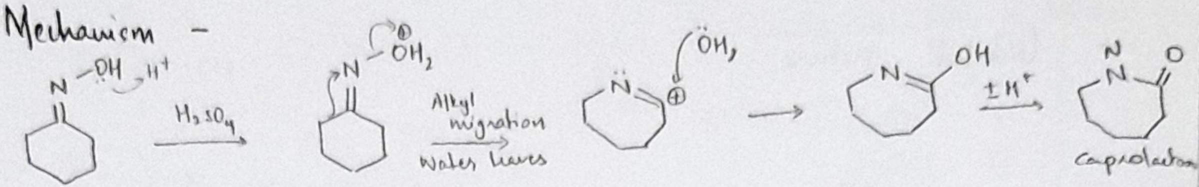
Phenyl group's migratory aptitude is quite good.

⑥ Beckmann Rearrangement



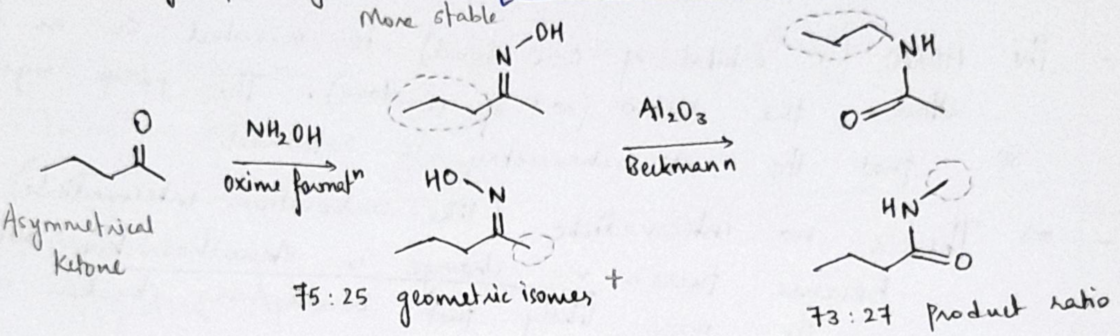


Mechanism -



Which group migrates? **MIGRATING GROUP IS TRANS TO -OH**

+ Refers Lecture 4i Pg 16-17

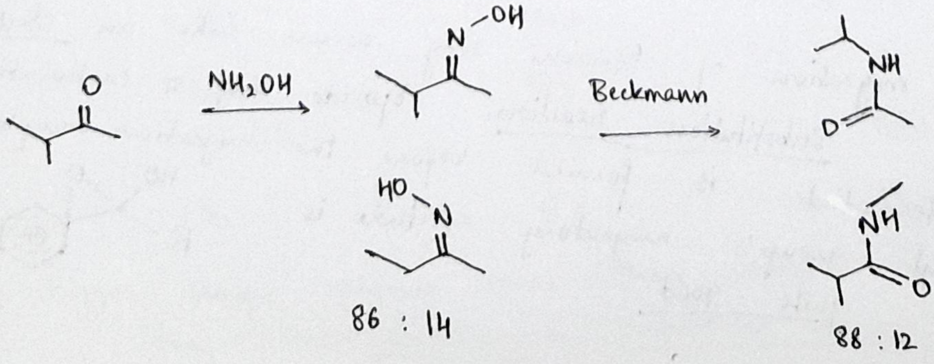


Because the oxime ratio is maintained in the products, we can say that $\overset{\oplus}{-OH_2}$ leaves simultaneously as the -R group migrates.

Here, the -R group that's trans to -OH migrates despite its nature. (~~-Me~~, -Et)

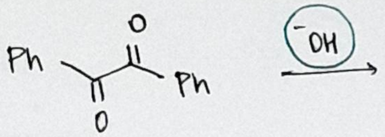
Also, if there were a C⊕ intermediate, there would have been an expectation of rearrangement and a different ratio.

Similar example -

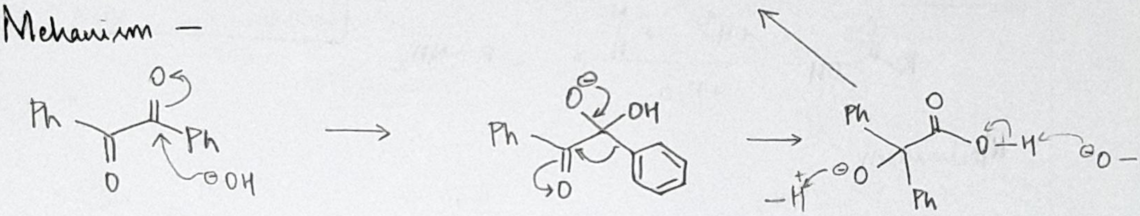


Lecture 11.6 contd.

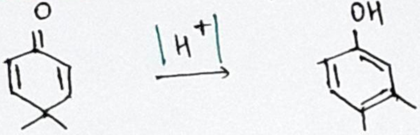
⑦ Benzillic Acid Rearrangement



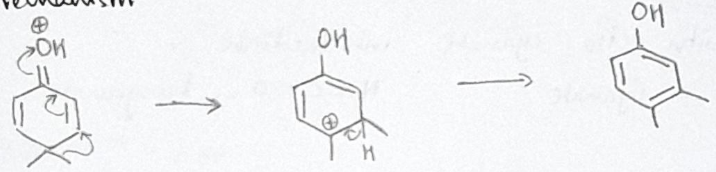
Mechanism –



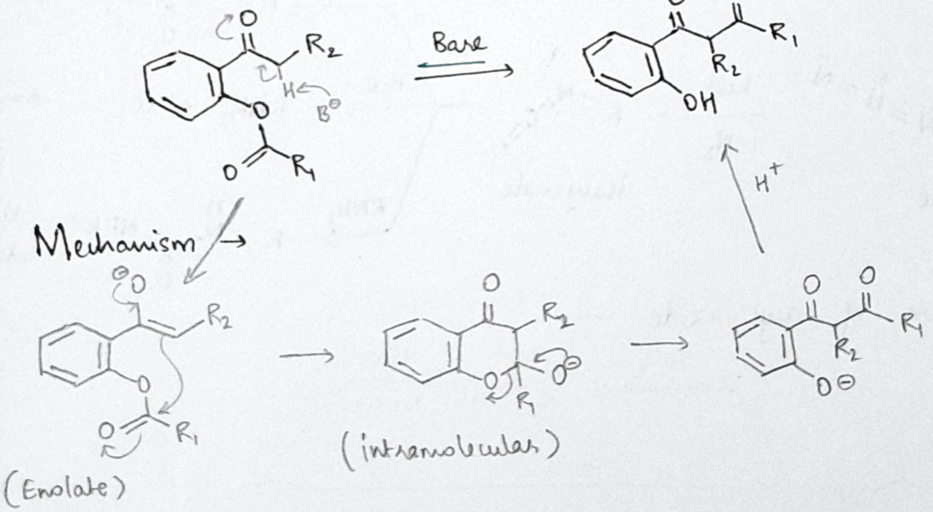
⑧ Dienone - Phenol Rearrangement



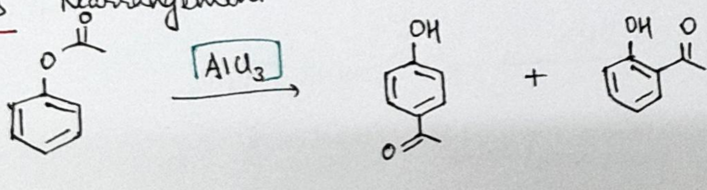
Mechanism



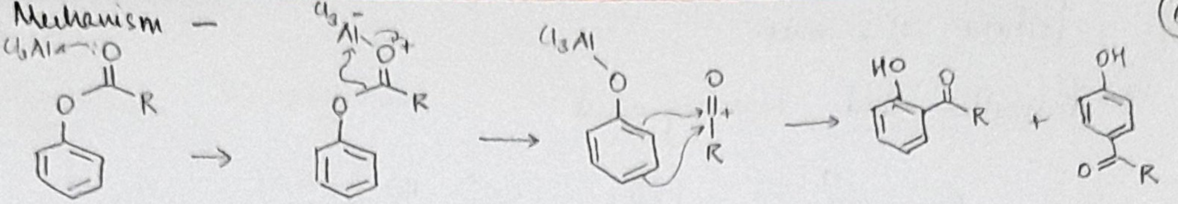
⑨ Baker - Venkataraman Rearrangement



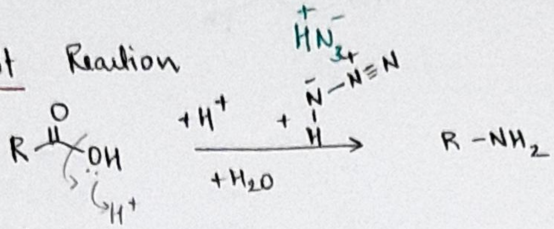
⑩ Fries Rearrangement



Mechanism —

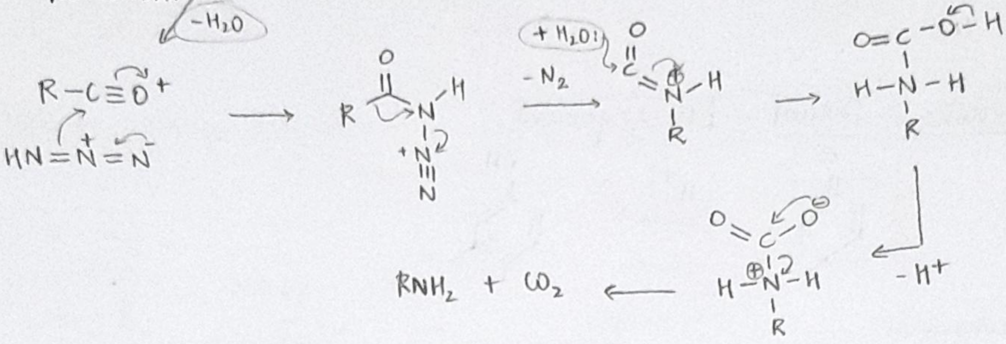


⑪ Schmidt Reaction



Converting –COOH to NH2

Mechanism

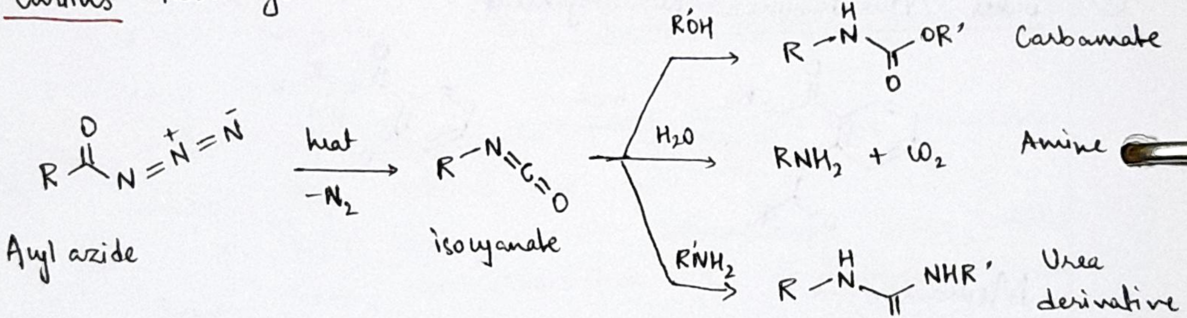


⑫ Rearrangements with iso-cyanate intermediate

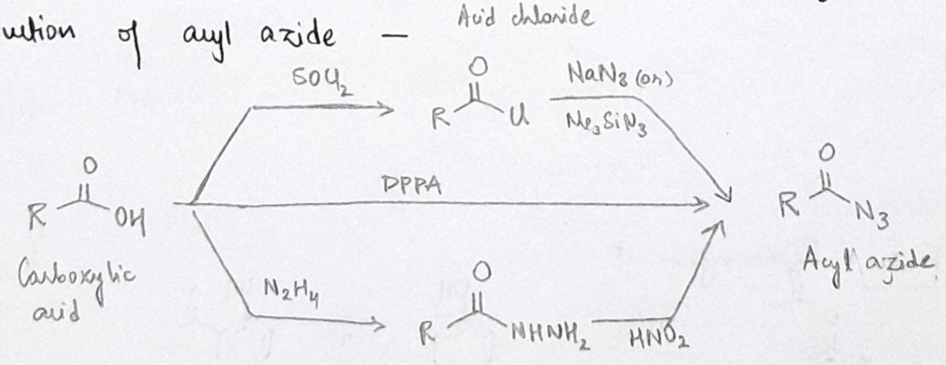
$C=N=O$: Cyanate

$N=C=O$: Isocyanate

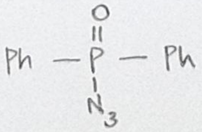
⑫ Curtius Rearrangement



Production of acyl azide —

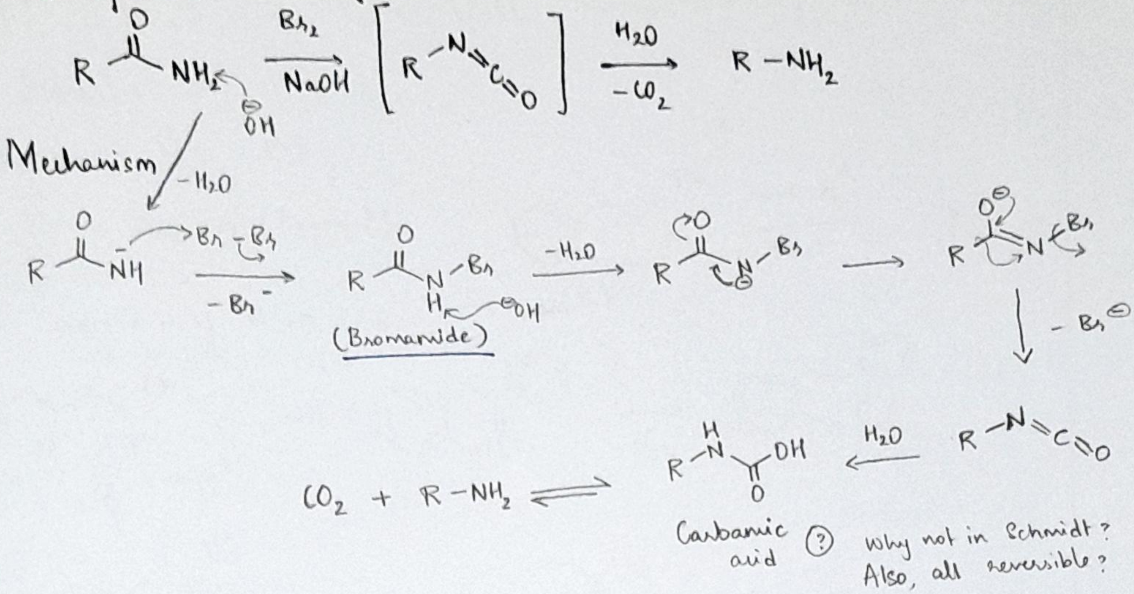


DPPA : Diphenyl phosphoryl azide



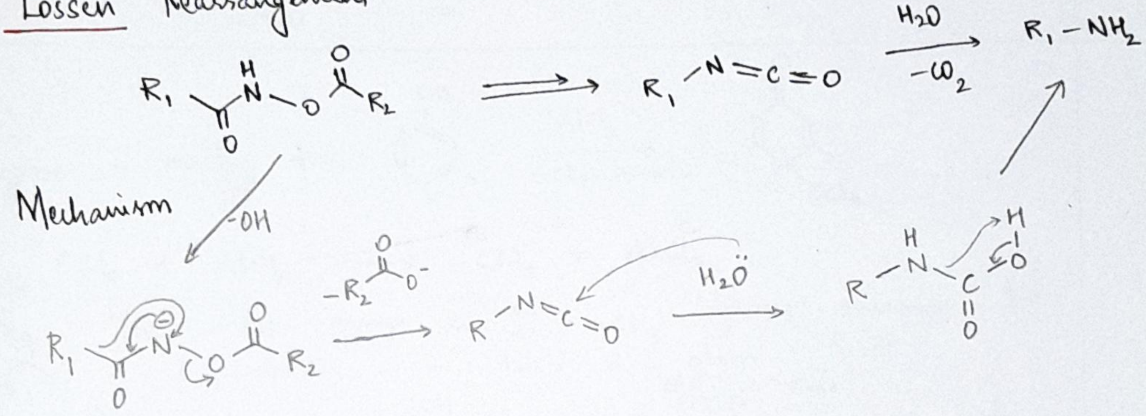
$Ph-\overset{\overset{O}{\|}}{\underset{\underset{N_3}{|}}{P}}-Ph$

⑬ Hofmann Rearrangement



? why not in Schmidt?
Also, all reversible?

⑭ Lossen Rearrangement

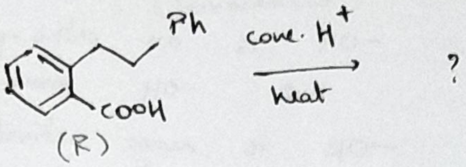


CH 2123 - ORGANIC CHEMISTRY II

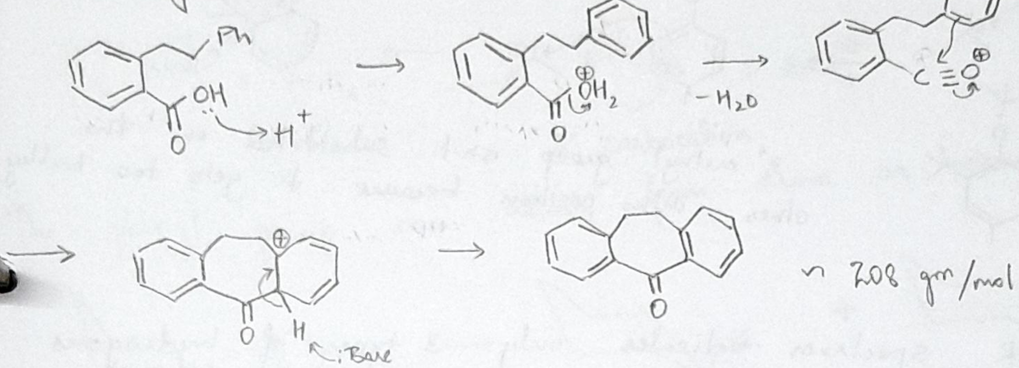
Semester 3

PROBLEM SET 01

1) $\frac{m}{z}$ = 208.09 (Product)



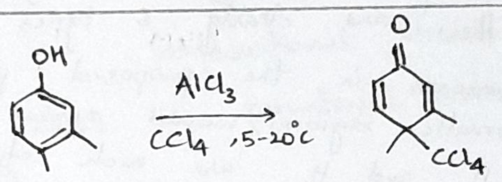
Mol. weight of R ~ 226



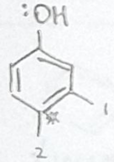
~ 208 gm/mol

---

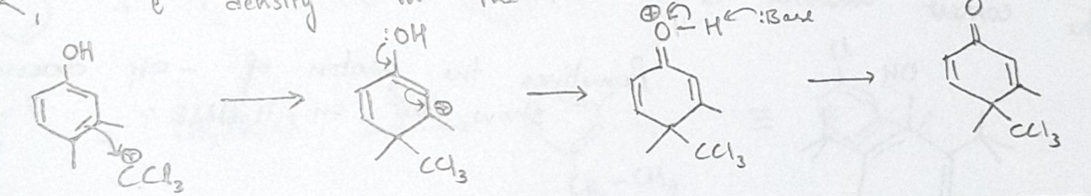
2) Propose a mech. for



$CCl_4 + AlCl_3 \longrightarrow \overset{\oplus}{C}Cl_3 + Al\overset{\ominus}{Cl_4}$



The -OH group & 1st -CH3 group increase the e⁻ density in the * C-atom. So —



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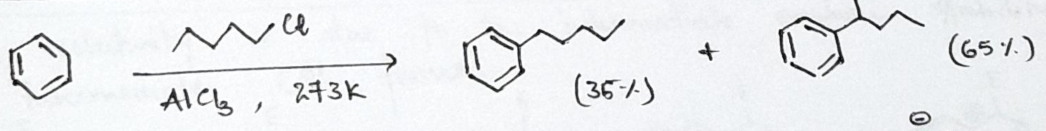
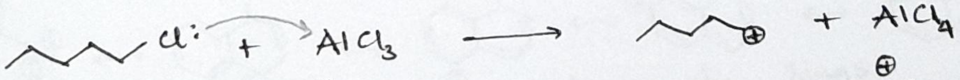
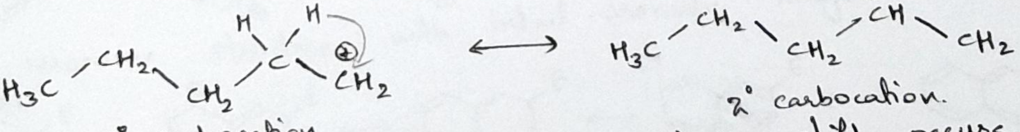
3)







1° carbocation

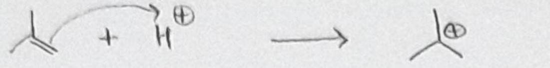
2° carbocation.

Secondary C⊕ is more stable. So, hydride shift occurs.

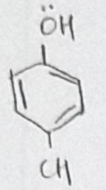
The E⊕ attack on benzene happens and we get the two products.

4) "Product doesnot dissolve in aq. KOH" ⇒ Non-polar product (?)

Mechanism for the proposed product :



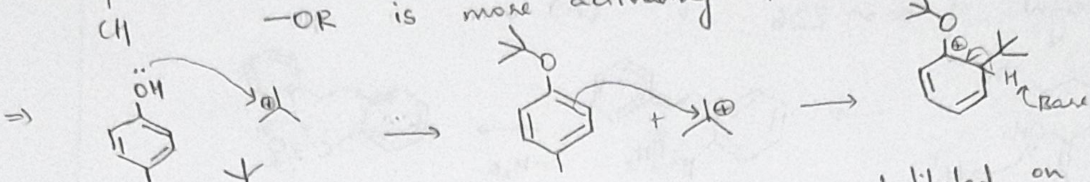
3° carbocation

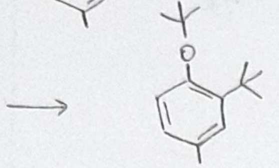


-OH is an ortho-para directing group. So is -CH$_3$.

but -OH more so.

-OR is more activating than -OH because of +I effect

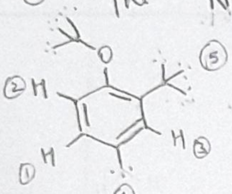




3° methyl group isn't substituted on the other ortho position because it gets too bulky (?)

---

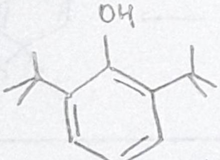
⑥ The NMR spectrum indicates only 3 types of hydrogens



There are clearly 6 types of Hydrogens. Moreover in the proposed product (among 3 spikes in aromatic region) 2 would appear as doublets because H_1 and H_2 are each other's neighbours (n+1 rule).

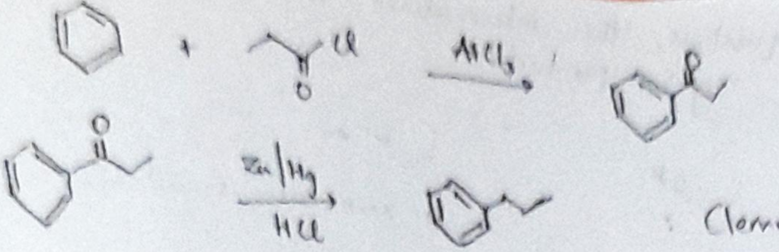
So the proposed product is not Product A ; it could one of the byproducts.

The correct answer is - BHT



Sometimes the proton of -OH doesn't show up on H-NMR ?

5)



: FC Acylation

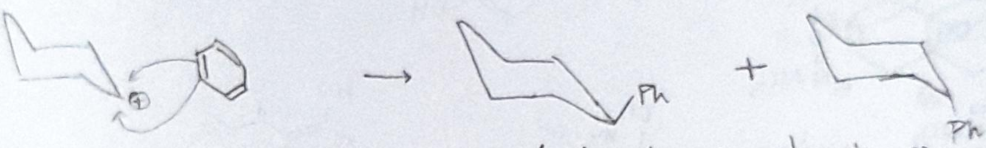
: Clemmensen's reduction.

---

6)

2° carbocation

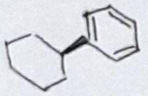
The phenyl group can attack from above or below



Conformational stereoisomers.

Bulky groups are more stable in equatorial position (>99% in equilibrium)

∴ Product –



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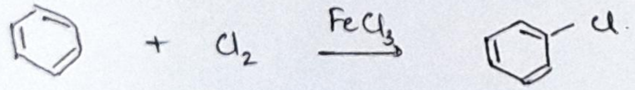
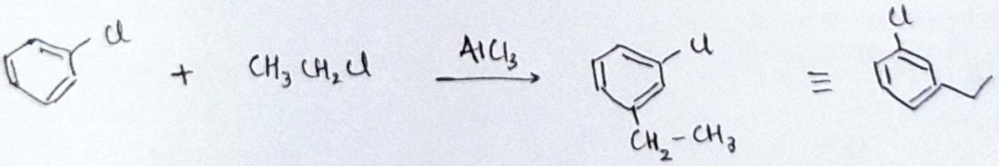
7)



– Cl is a meta-directing deactivator.



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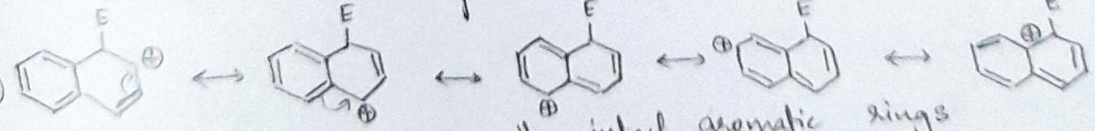
8) The selectivity is due to the intermediate ~~carbon~~ stability of intermediate C⊕ formed.

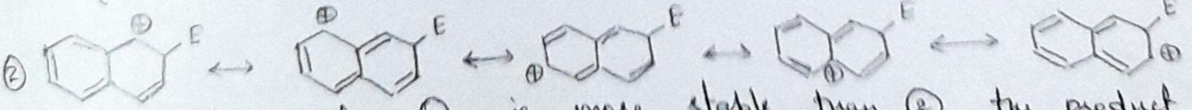
E: electrophile

①

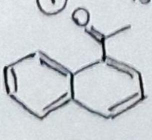


2 resonance structures with intact aromatic rings

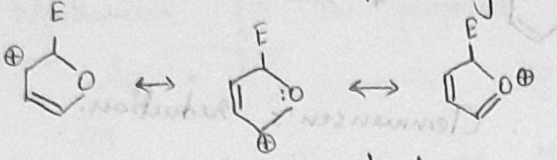
②

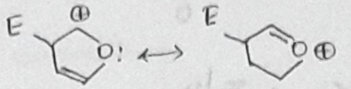


As intermediate for ① is more stable than ②, the product formed is :



9) Similar to last question, the intermediate with more stable C⊕ will be the major product.



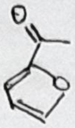


2 Resonance structures

3 Resonance structures

⇒ more stable

Hence, the product is



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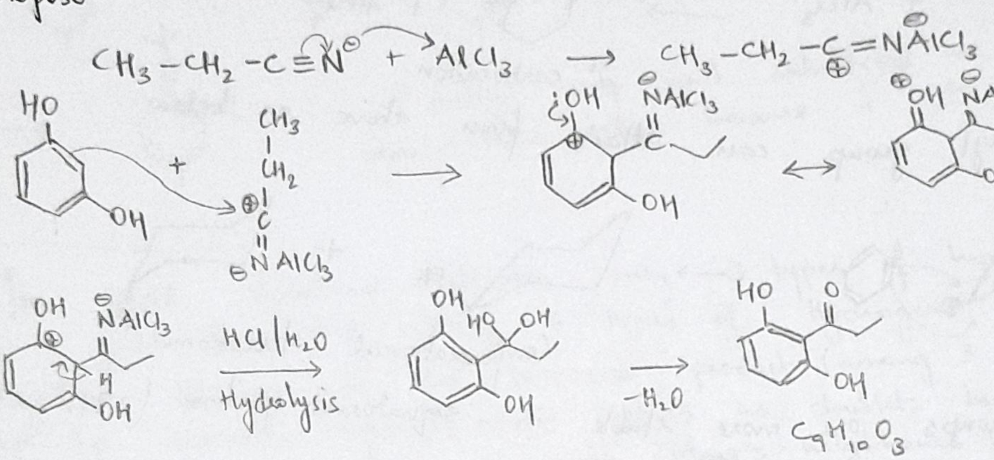
10) Propose a mechanism –



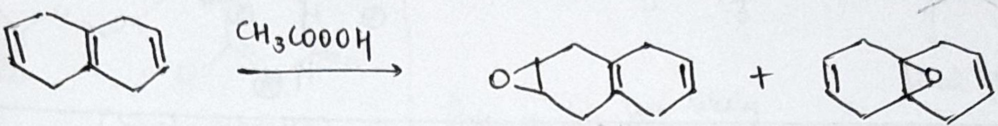
IR Spectrum : 1710 cm⁻¹ – Ketones.

CH2123 - Problem Set 02.

1. Yes. When the intermediate is cyclic bromonium ion, only anti-product is formed as $Br^{\ominus}$ approaches from the other plane.

---

2. * More substituted alkenes are more stable. Moreover, their double-bond is also more nucleophilic due to positive inductive (+I) effect of multiple alkyl groups. Hence, rate of epoxidation is higher for more substituted alkenes.

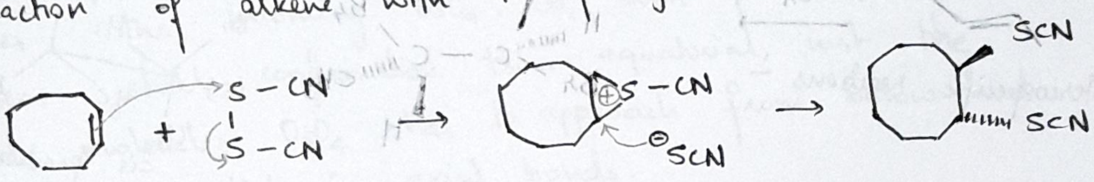


A B

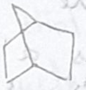
B is the major product (79%) for above reason.

---

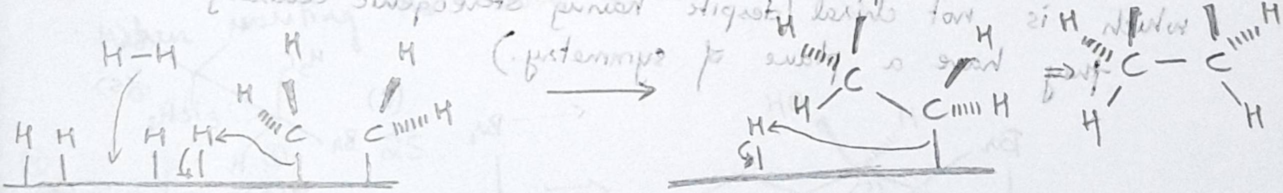
4. Reaction of alkene with thiocyanogen -



Norbornane, - 2 fused 5 member rings

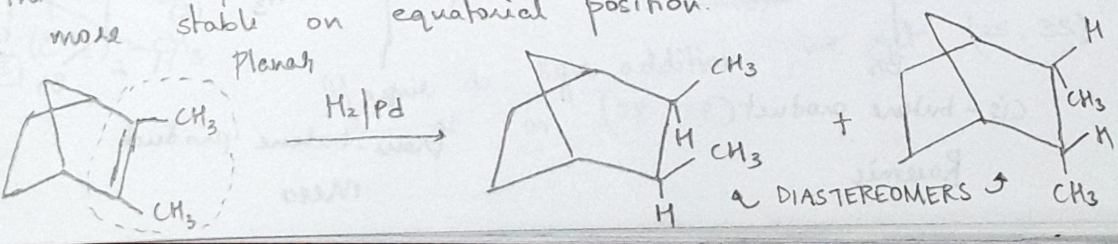


5. Mechanism of H_2 | Pd -



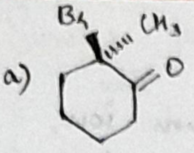
Catalytic surface

For the given reactant, H can add as 'equatorial' or 'axial' because $-CH_3$
The axial product will be predominant
are more stable on equatorial position.

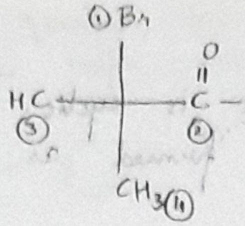


6)

a)

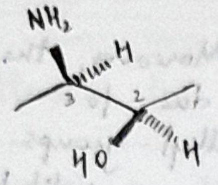


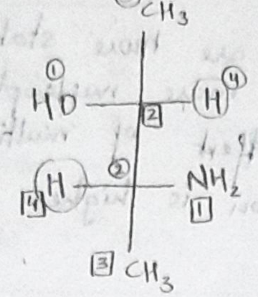
:



R

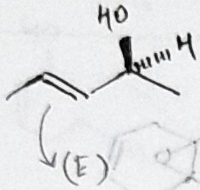
b)

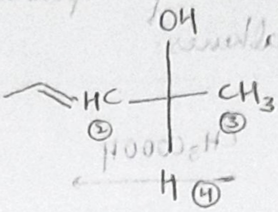




2R , 3R

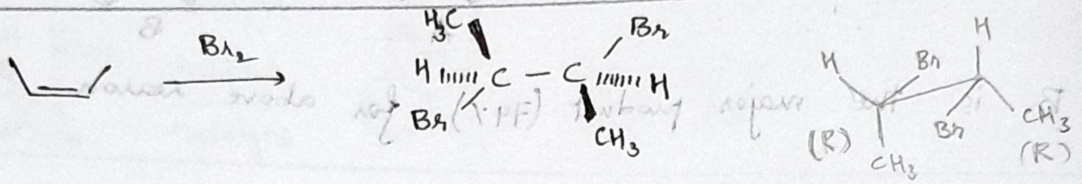
c)





R

7)



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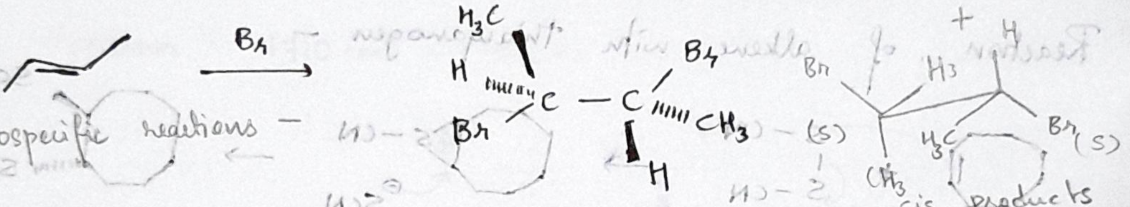
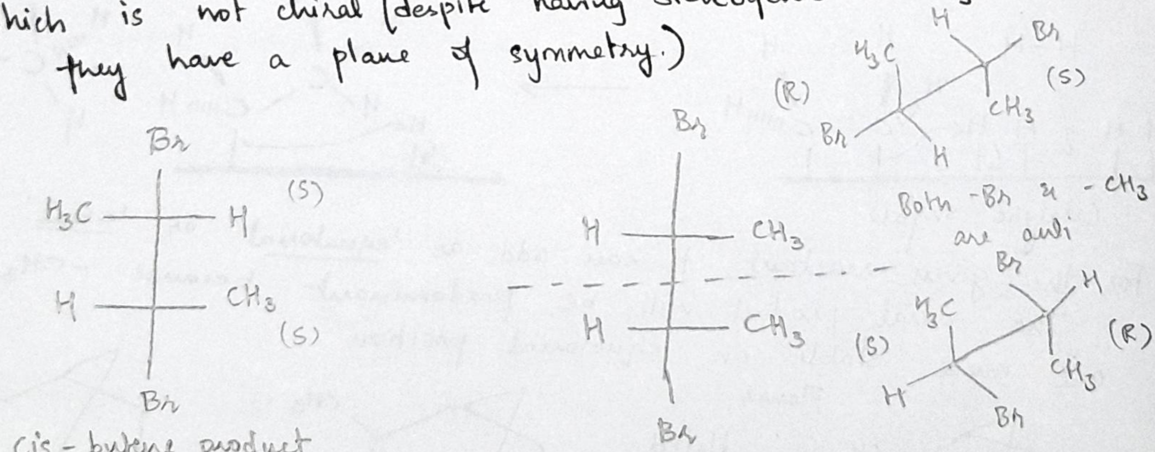


Stereospecific reactions ←

cis products

In both products, addition of bromine gives an anti product. But while cis-but-2-ene gives a racemic mixture, trans-bute-2-ene gives a mesocompound; (stereoisomer which is not chiral [despite having stereogenic centres] because they have a plane of symmetry.)



Both -Br & -CH3 are anti

Cis - butene product

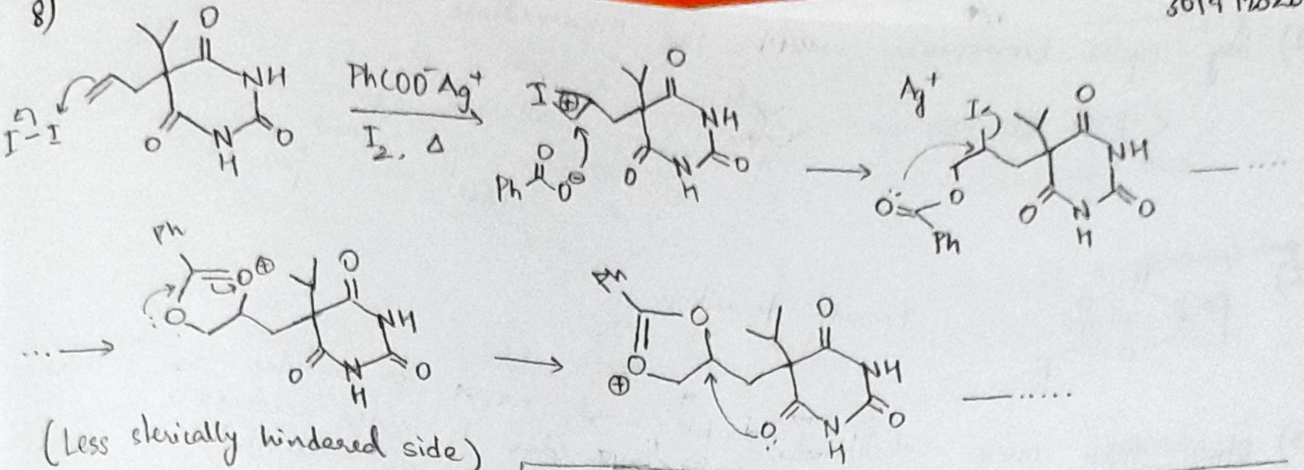
Racemic

Trans - butene product

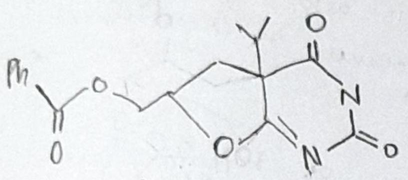
Meso

30/9/2020

8)

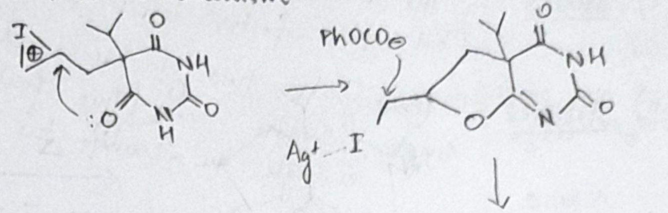


(Less sterically hindered side)



(Final product)

Another mechanism



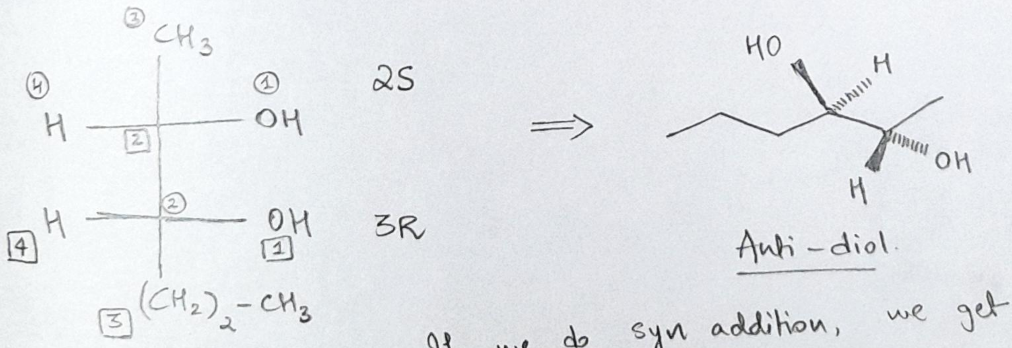
Final product

This is the less likely mechanism

9) OsO_4 is a fairly bulky molecule that approaches the double bond in a plane. In the second molecule, the tip has two alkyl groups which might sterically hinder the incoming OsO_4. So, even if axial bonds are less stable conformation than equatorial, wrt the second molecule, OsO_4 has to approach from below and form a diol in axial bonds.

10) Products : (2S, 3R) - 2,3 - hexane diol , (2R, 3S) - 2,3 - hexane diol.

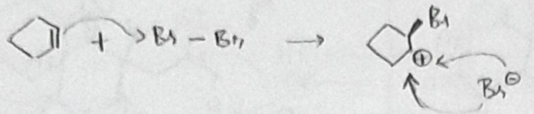
When writing the above structure, weget -



Anti-diol.

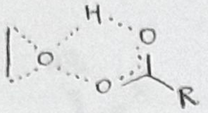
If we do syn addition, we get (2S, 3S) or (2R, 3R).

1) Say cyclic bromonium wasn't the intermediate, then –



As C⊕ is planar, Br⊖ could have attacked from top or bottom
⇒ Both syn & anti product should have been formed

2)



: Epoxide transition state.

3) Other than more substituted double bond, we've to consider two factors –

i) Sterics – the double bond at the edge is more accessible (but this factor isn't as important as reactivity)

ii) Statistics – There are two double bonds at edge as compared to a single middle one. (This factor is also not important enough to trump the difference in reactivity.

4) OsO_4 can either approach from top face or bottom face.

★ From first case, we can see that there's a preference to attack from the top (EXO) face if there are no substituent groups on the bridgehead carbon.

★ When there are substituents, OsO_4 attacks from ENDO (bottom) face because there's sterical hinderance from methyl groups.

CH 2123 - Problem Set 03 30/9/2020

1) The conc of carbonyl compound and its hydrated form can be experimentally determined by measuring the absorbance of the solution –

$$K_{hydr} = \frac{[\text{Hydrate}]}{[\text{carbonyl compd}][\text{water}]}$$

Total conc (hydrate + carbonyl compd) is assumed to be 1 M

[water] = 55.5 M

Let [Hydrate] = x $\Rightarrow K = \frac{x}{(1-x)\,55.5}$ $\Rightarrow x = \frac{55.5K}{1+55.5K}$

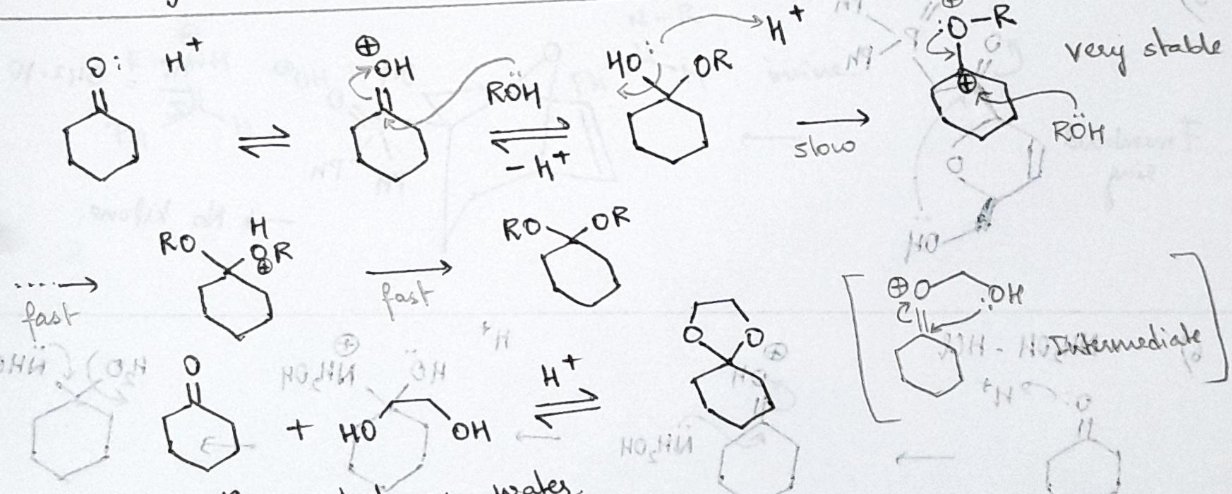
% conversion = $\frac{x}{1} \times 100$

$\longrightarrow$ Increasing stability

HCHO	CH_3CHO	$(CH_3)_3CHO$	CH_3COCH_3
99.96%	50%	19%	0.14%

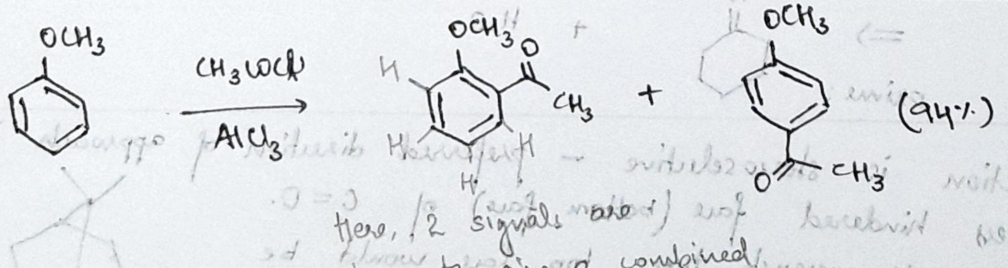
The substituents on carbonyl carbon affect its stability (due to steric & electronic environment) and factors that increase stability decrease the equilibrium constant.

2)



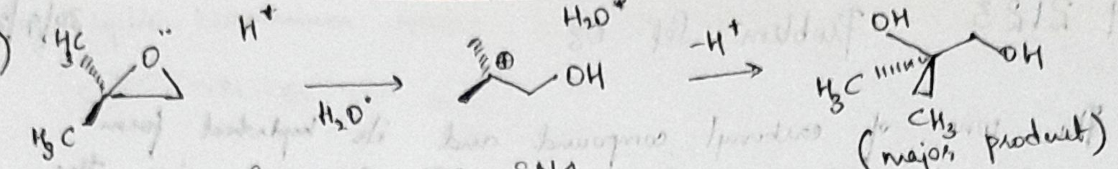
Labelled O^{18} is lost as water

3)

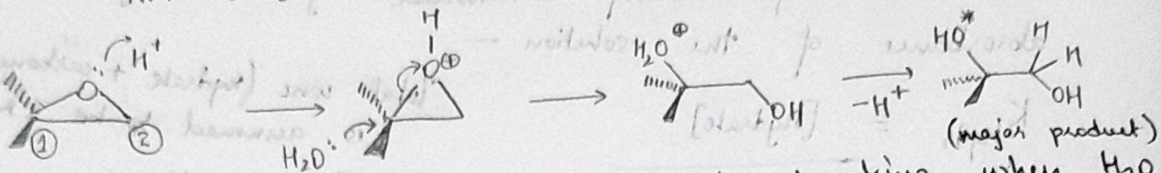


Here, 2 signals are merging to give a combined signal.

4)



NOT SURE IF ITS SN1

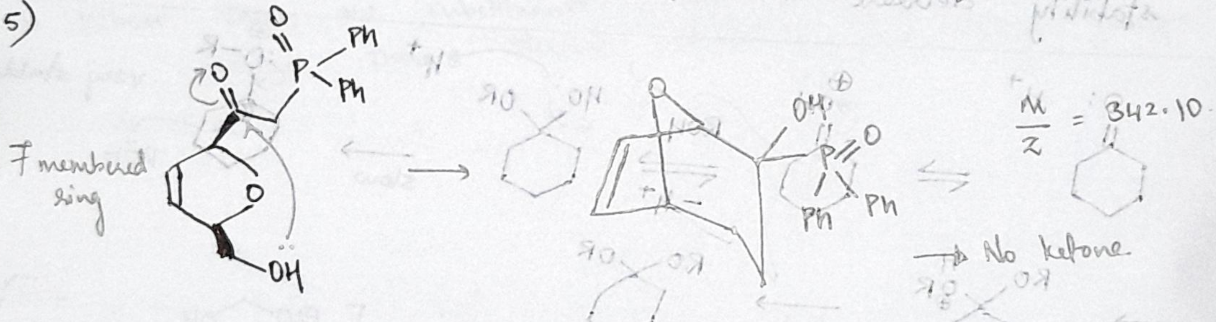


It seems like C① – O bond is already breaking, when H2O attacks – this is became more substituted C atom can accommodate δ+ charge better.

- No exchange of labelled water with epoxide oxygen ⇒ opening of epoxide ring is irreversible
- Very high regioselectivity – more substituted C atom is preferred site of attack ⇒ Epoxide ring opens partially and partial +ve charge can be accommodated better.

---

5)



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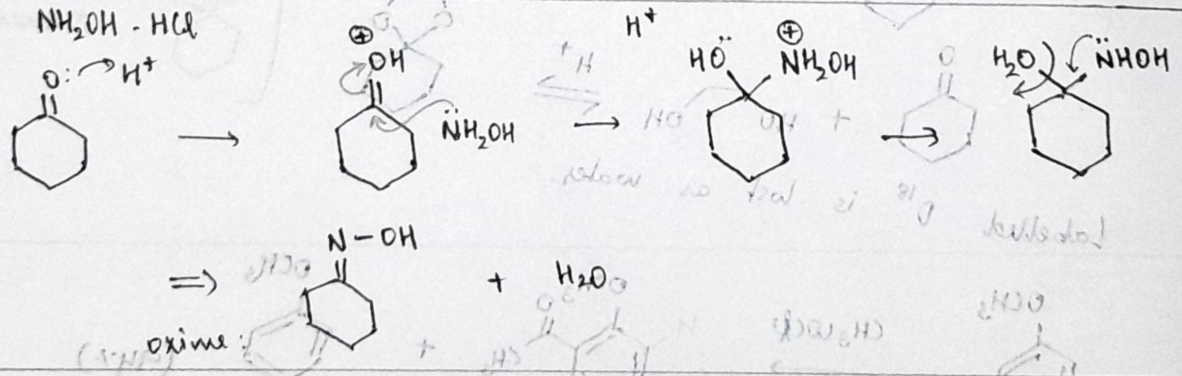
6)



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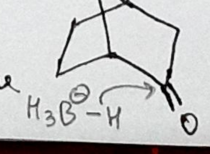
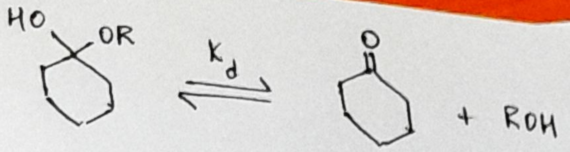
7) Reduction is stereoselective – preferred direction of approach is less hindered face (bottom face) of C = O.

If top –CH3 weren't there, top face would be preferred, because, equatorial bond more stable



11/19

8)

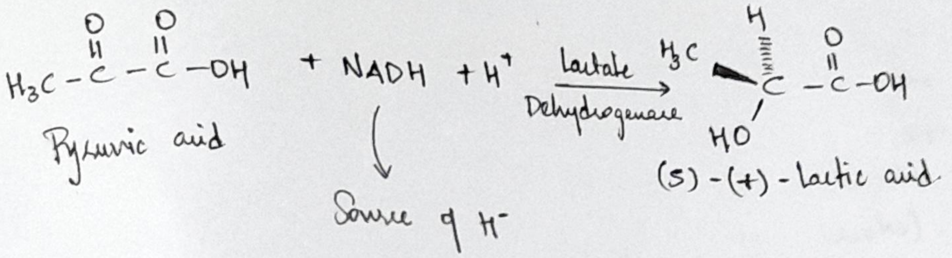


	K_d
$-CH_3$	2.16
$-C_2H_5$	237

Inference : Larger the -R group (alcohol), the equilibrium is pushed more towards right.

---

9) Pyruvic acid to (s)-lactic acid



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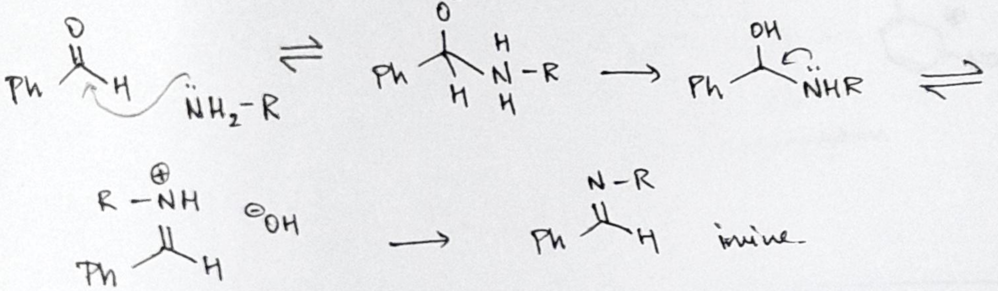
10) Benzaldehyde + ethylamine

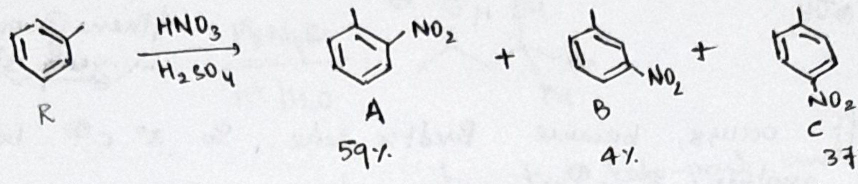


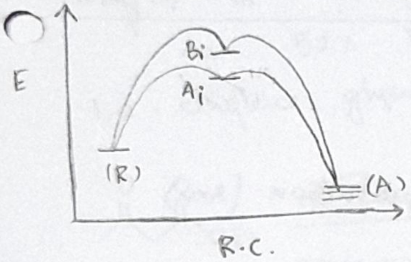
CH 2123 - Problem Set 04

11/10 (officially)

01) Nitration of Toluene : $E^\oplus$ substitution (aromatic)

- When multiple products are formed, the yeild of a product is proportional to the rate of formation of that product.
- This is an irreversible product.

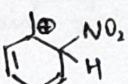




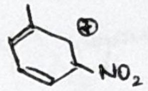
Hammonds Postulate : In a highly endothermic reaction (∵ aromaticity breaks), the transition state resembles the product.

The diff. in energy of products doesn't matter

A_i :



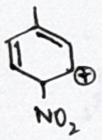
B_i :



So this is less stable

C⊕ can interact with $-CH_3$ by hyperconjugation

C_i :



ortho substituent is more stable

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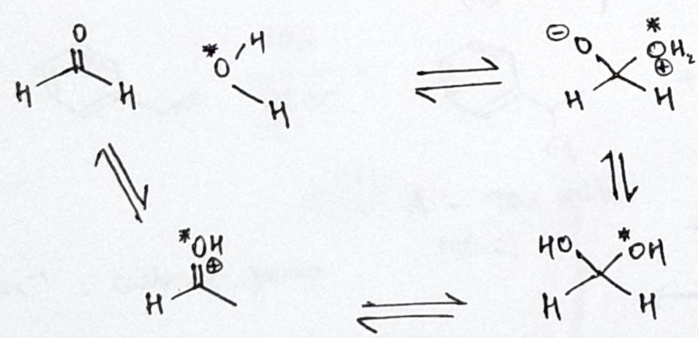
02)



LOSS OF IDENTITY

i.e. any -OH can be kicked out.

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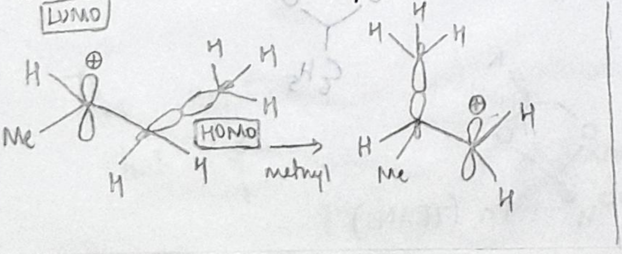
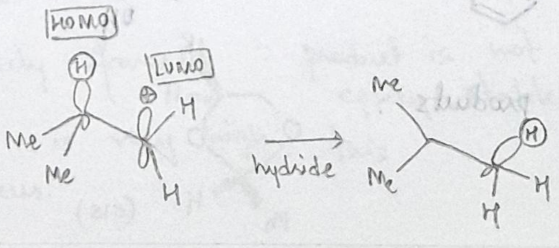
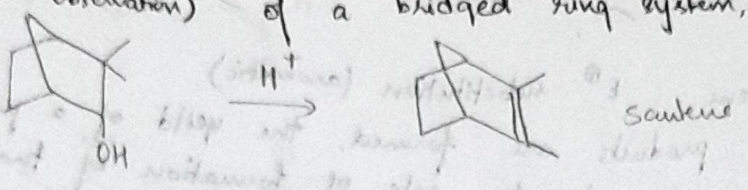
03) Orbital view of hydride / methyl shifts

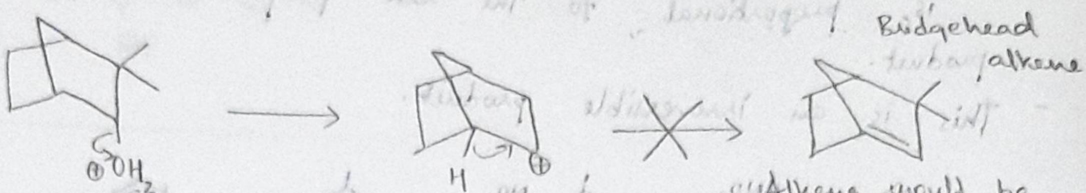




Bredt's Rule - Double bond cannot be placed at bridgehead of a bridged ring system, unless ring is large enough
(empirical observation)

Camphenilol





Alkene would be very strained.

Methyl shift occurs, because Bredt's rule. So 3° C⊕ becomes another 3° C⊕

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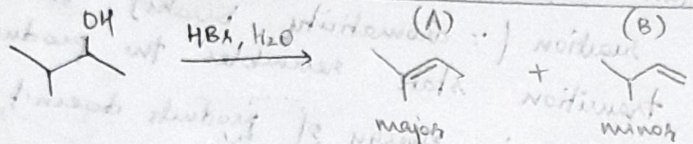
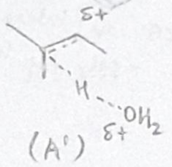
04)

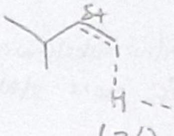


The major product has a higher rate of production (rxn).

Transition state :



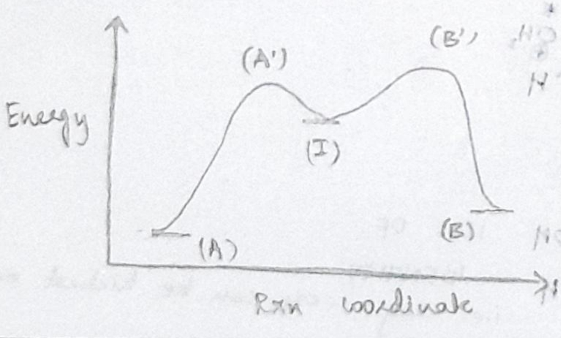
(A')



(B')

Intermediate state :

(I)



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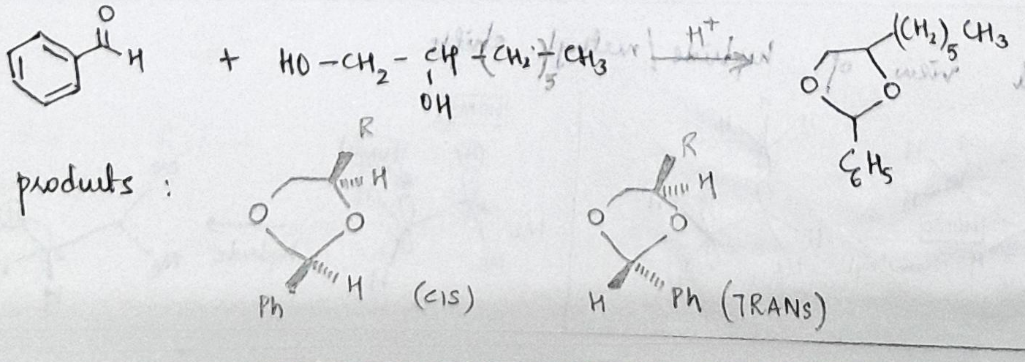
05)

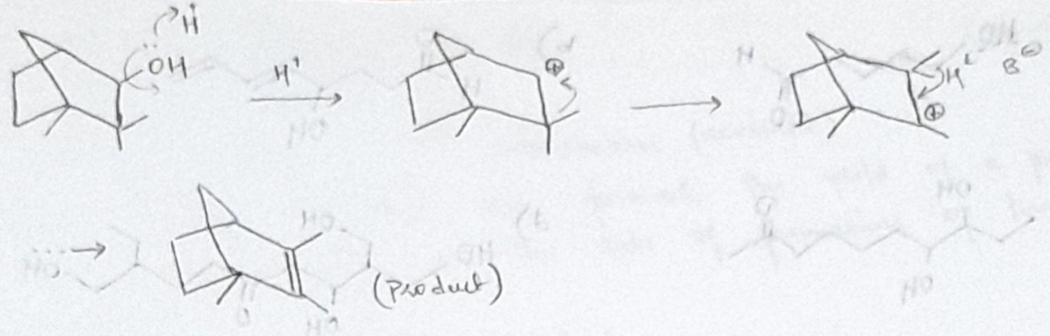


Two products :

(CIS)

(TRANS)

06)



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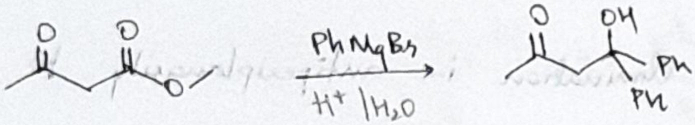
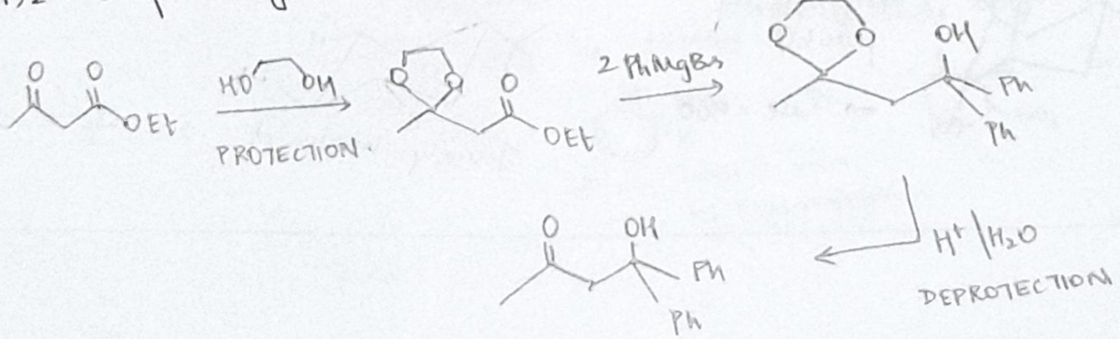
07)



PhMgBr in reality, reacts with the keto-part and gives a 52% yeild. To protect the ketone, we use 1,2-ethylene glycol, which reacts with ketone & not the ester.



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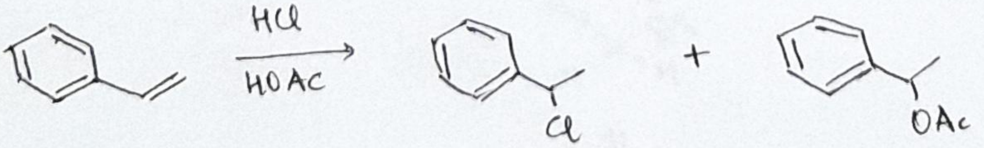
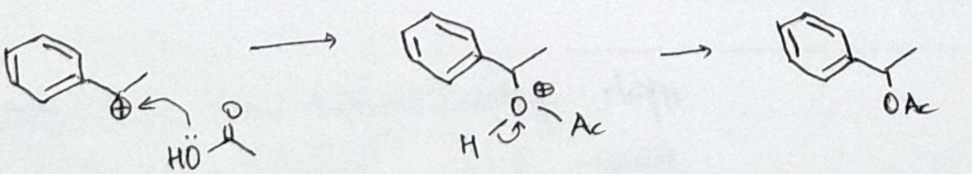
08)



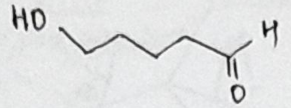
A - 92% yeild

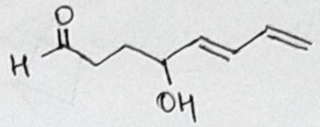
140.61

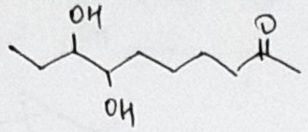
1740 cm⁻¹ : carbonyl group

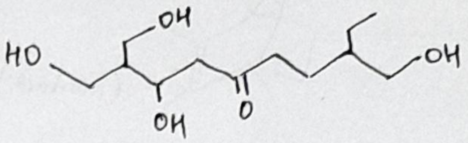


This reaction is not particularly favored ∵ product is not epidy stable, but if conc. of CH_3COOH is very high, this product can occur.

09) a) 

b) 

c) 

d) 

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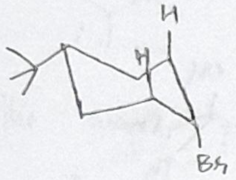
10) This requires an E_2 elimination i.e antiperiplanarity to form the alkene.

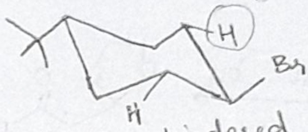
The tBu group on hexane ring should always be at equatorial position ∵ its very bulky.



Antiperiplanity possible

⇒ rate = 500

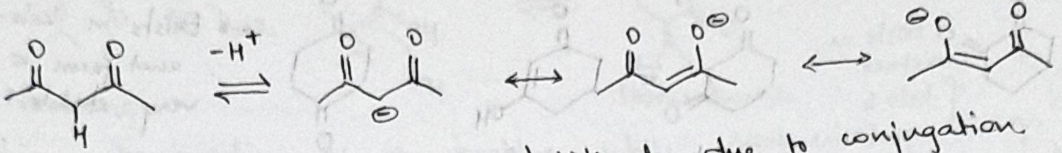
Doesn't work



Sterically hindered ⇒ rate = 1

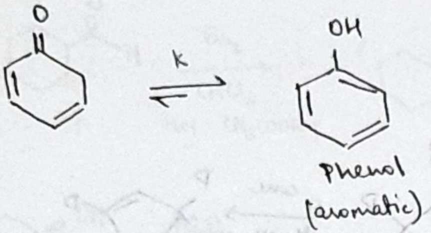
Problem Set 05, 06

01)



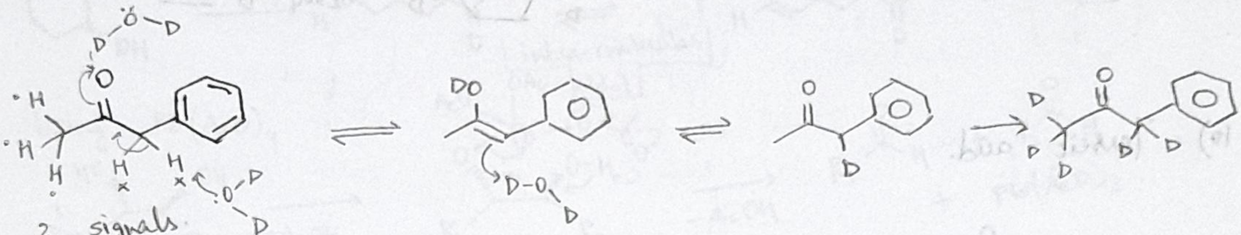
The conj. base is highly stabilised due to conjugation

02)



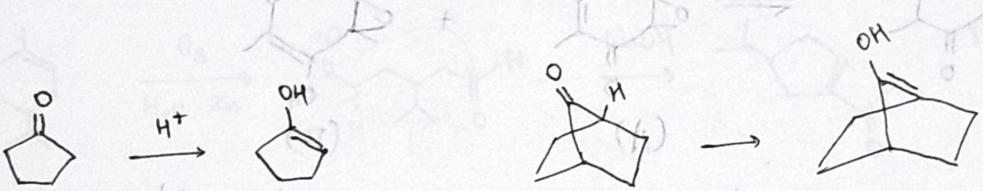
K is too large to measure.
Keto form exists in v. low conc

03)



Aromatic H can't be substituted.

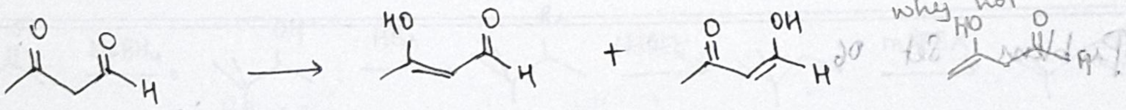
04)



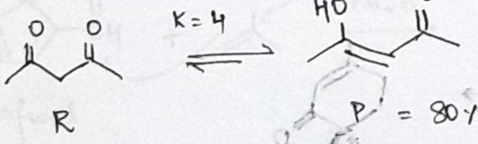
Not favoured.

∵ Bredt's rule

05)



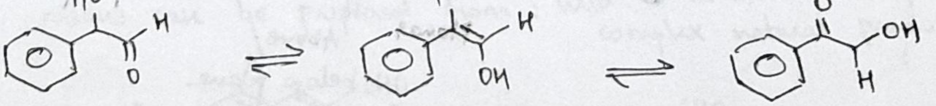
06)



$K = \frac{[P]}{[R]} = 4 \Rightarrow [P] = 4[R]$

P = 80%

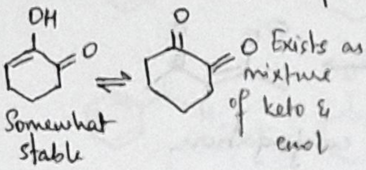
07) $\frac{m}{z} = 136.05$



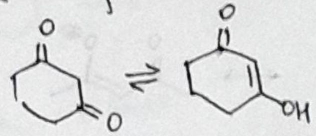
Keto-form more stable ∵ its in conjugation with ⌬

08) Cyclohexane ring   IR signal : 1700 cm^{-1} $C_6H_8O_2$

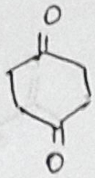
The possible compounds are –



ΔG° = 1 kcal mol^{-1}



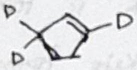
Exists in enol form
pKa = 5.24 ⇒ litmus ?

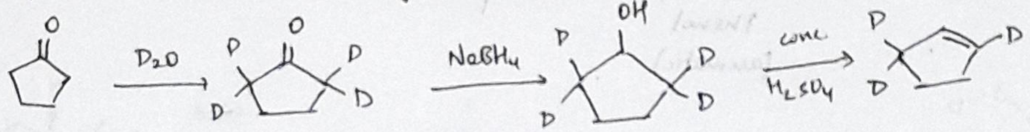


→ Exists in keto-form ∵ enol form is not very stable.

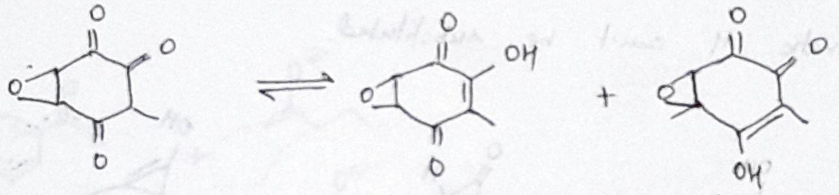
HPLC or TLC analysis can be used to distinguish them

09) Propose a synthesis for





10) Terreic acid.

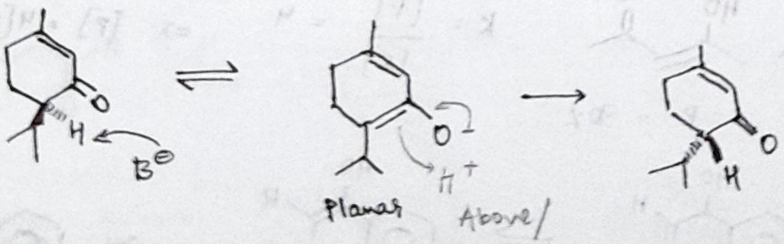


(A)   (B)

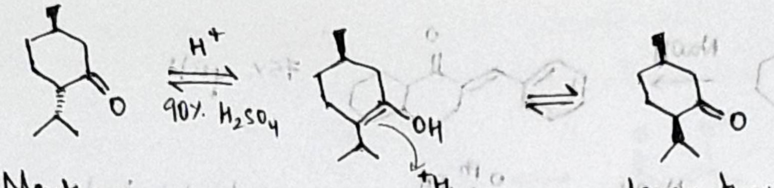
Enol A is more stable than B. because it exists in conjugation with two carbonyl groups.

Problem Set 06.

01. a) Piperitone in $CH_3CH_2O^-Na$ | CH_3CH_2OH becomes racemic



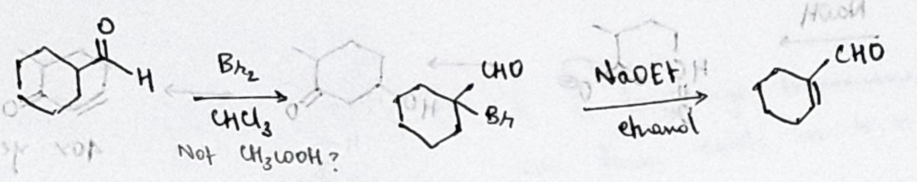
b)



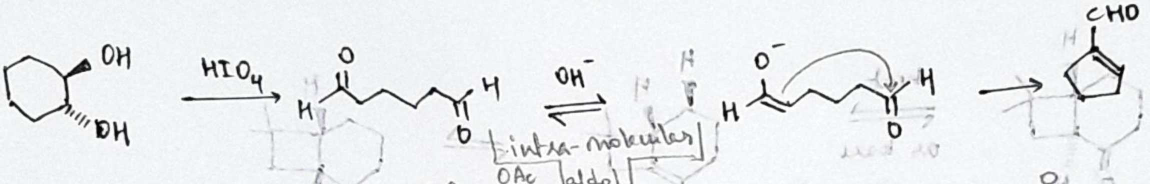
Menthone Isomenthone

This racemisation is a problem while synthesizing drugs because during metabolysis, they're in acidic/basic mediums So both isomers of such drugs are tested

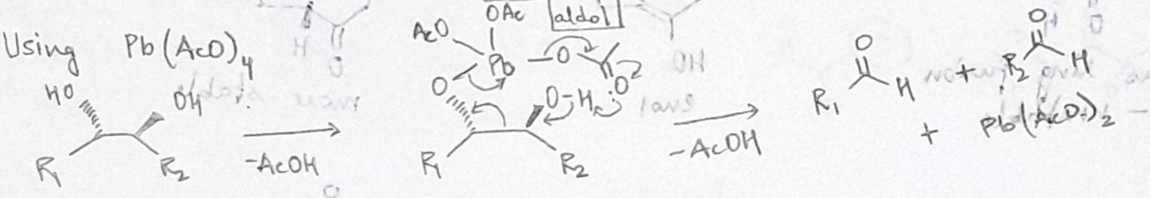
2. a)



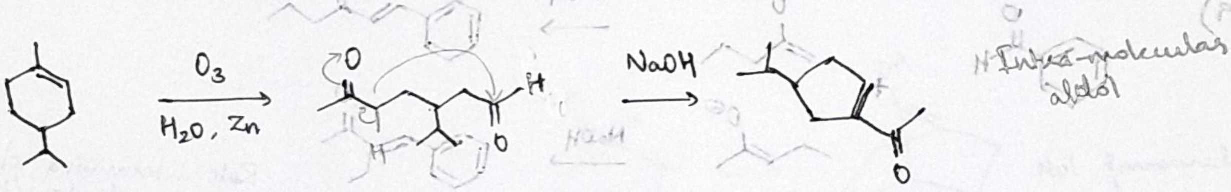
b)



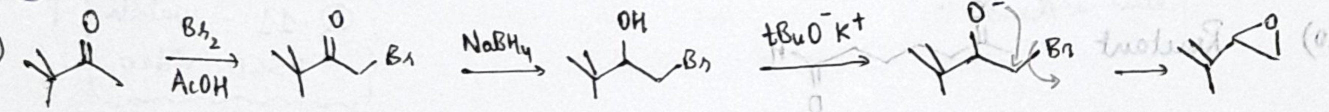
Using $Pb(AcO)_4$



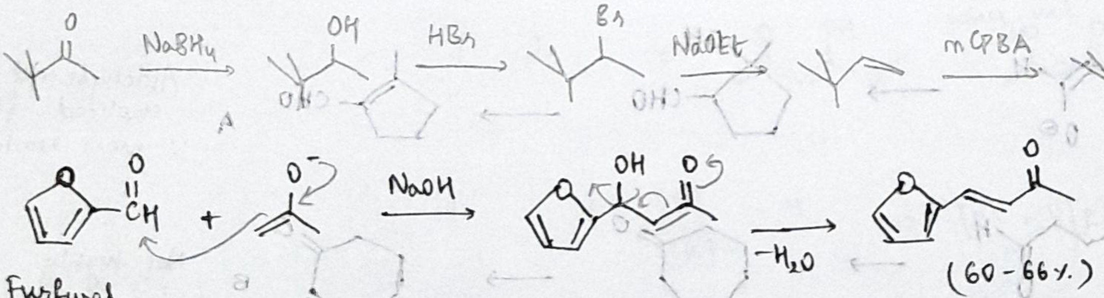
c)



3)



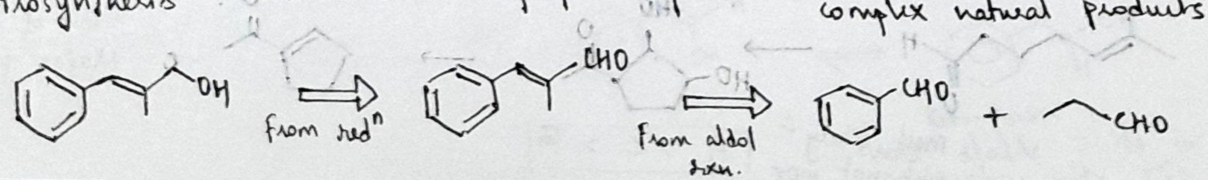
4)



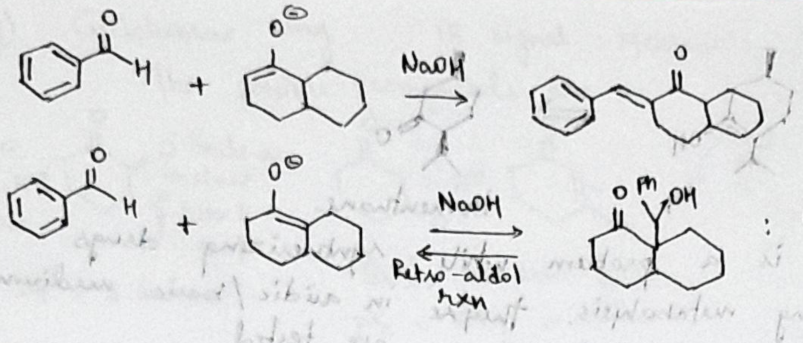
Furfural

(60-66%)

5) Retrosynthesis : means can be prepared from : used in construction of complex natural products



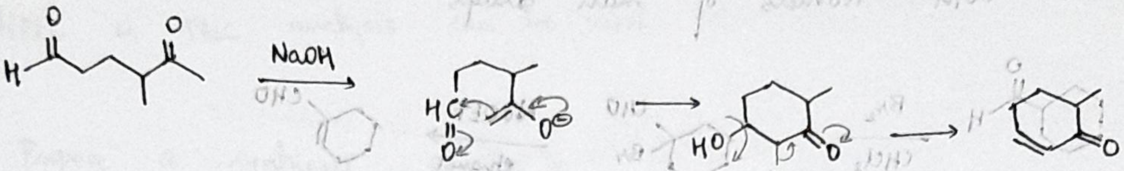
6)



75% yeild

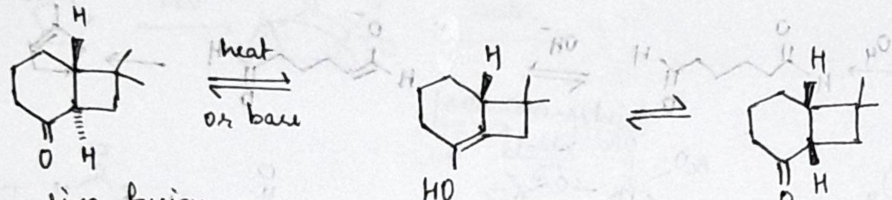
: Cannot dehydrate ⇒ reverts to starting material

7)



40% yeild

8)

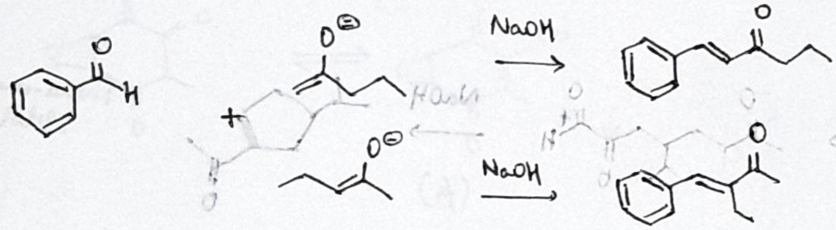


Trans ring fusion - unstable

enol

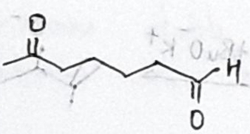
more stable

9)

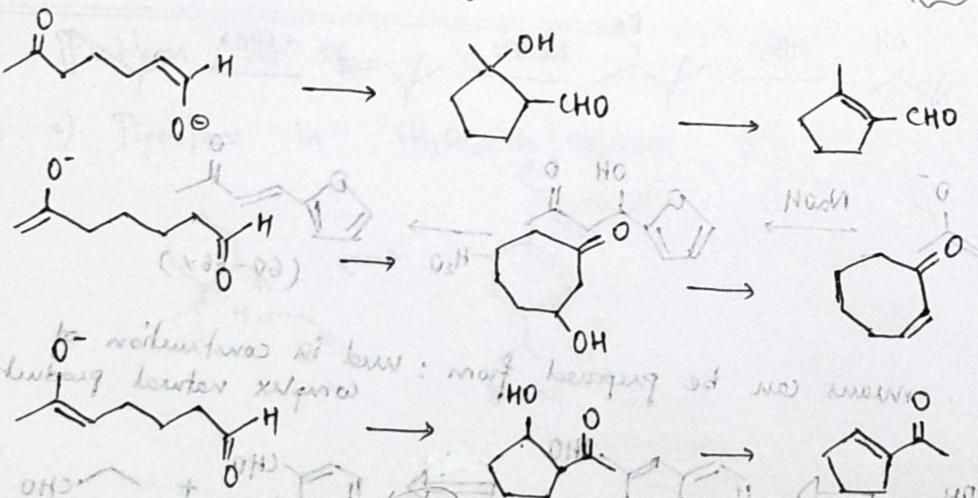


Rate-determining step changes at low/high conc of ue

10) Reactant



Q. 11 - watch PS6D video



Aldehyde get enolised faster ∵ more reactive

Not highly favoured

one of Major product

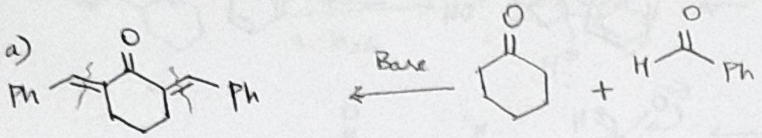
most likely but not 100%

A > C > B

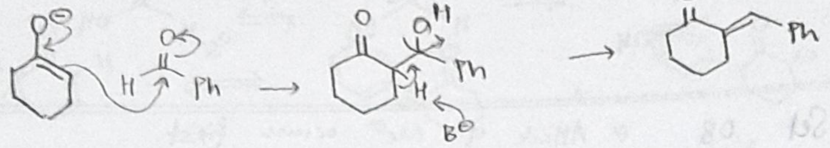
15/12/20

Problem Set 07, 08, 09

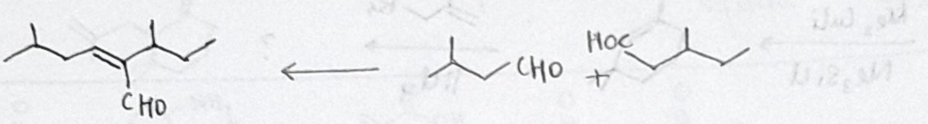
1. a)

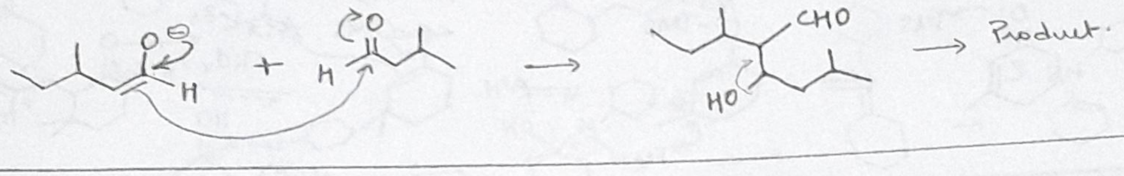


Mech –



b)

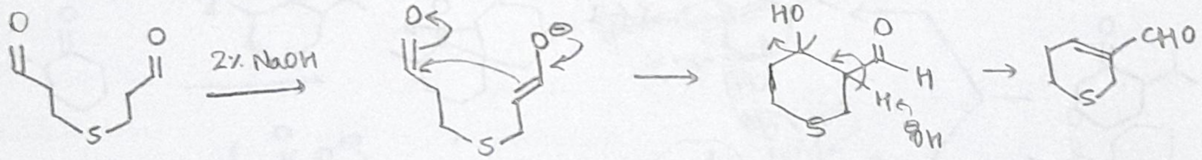




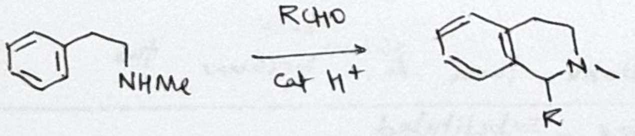
2) D-fructose 6-phosphate is converted to its corresponding 1,6-phosphate diester which is cleaved to two 3-C fragments under the influence of aldolase

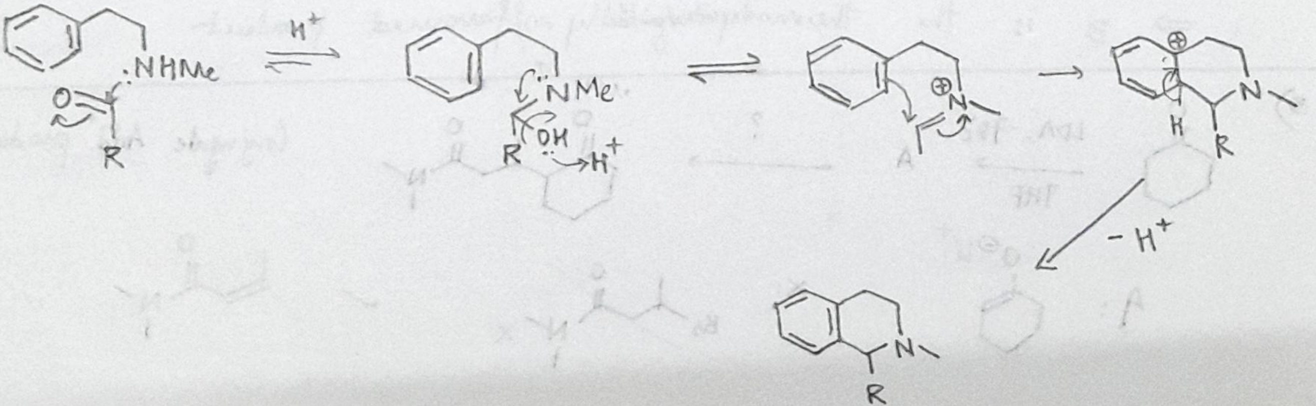
(?)

3)

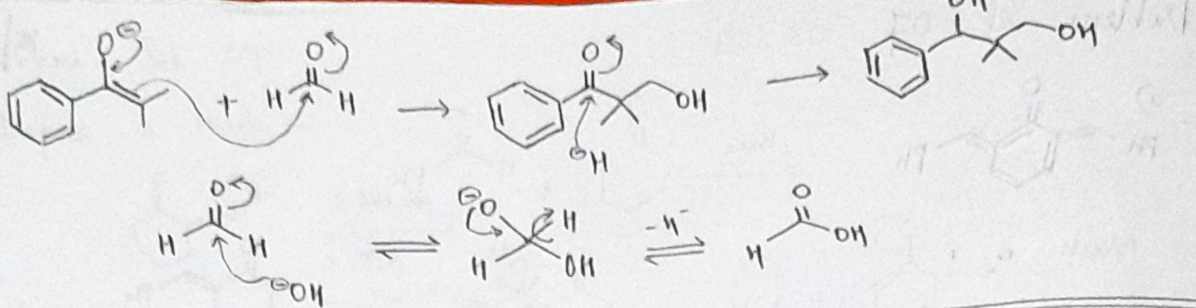


4)





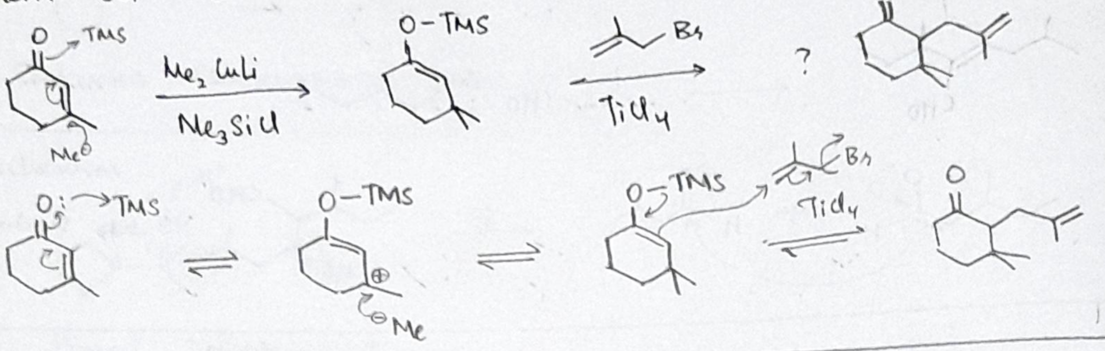
5)



Problem Set 08

Attack of Me⊖ occurs first

1)



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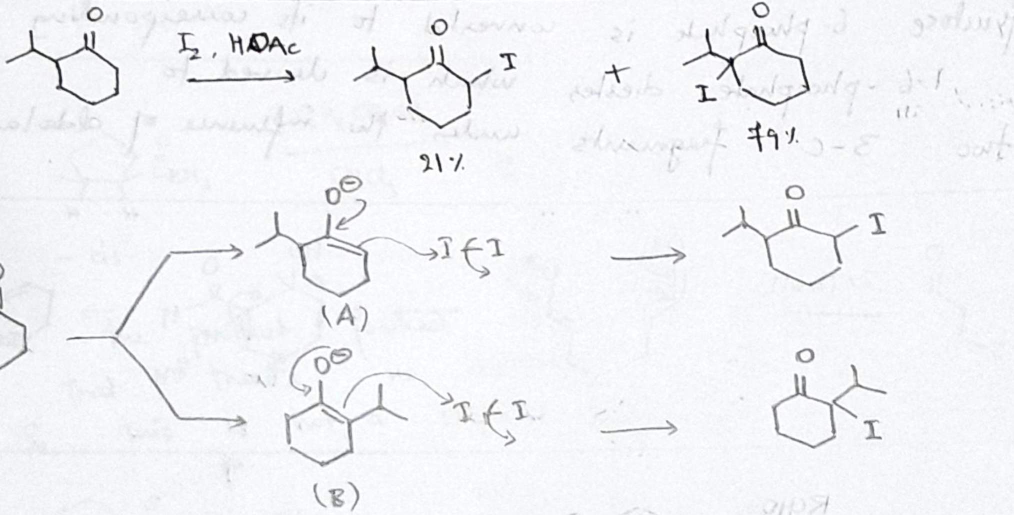
2)

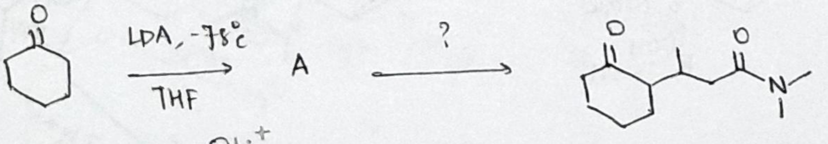


Intermediate B is more stable than A, because the double bond is more substituted

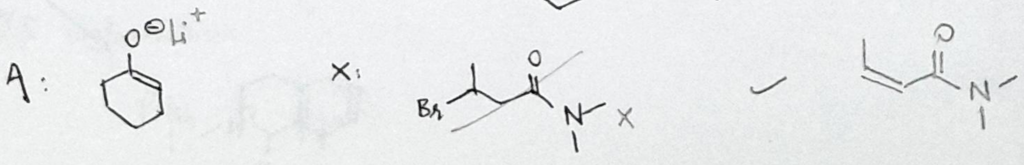
⇒ B is the thermodynamically favoured product.

---

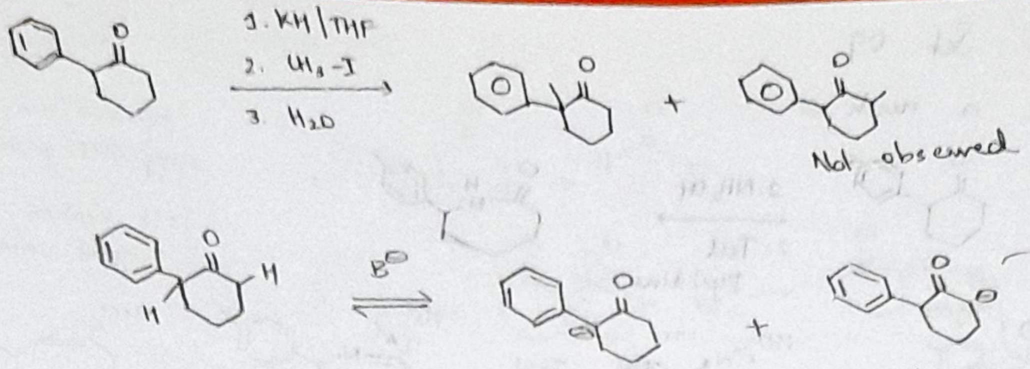
3)



Conjugate Add^n product



4)



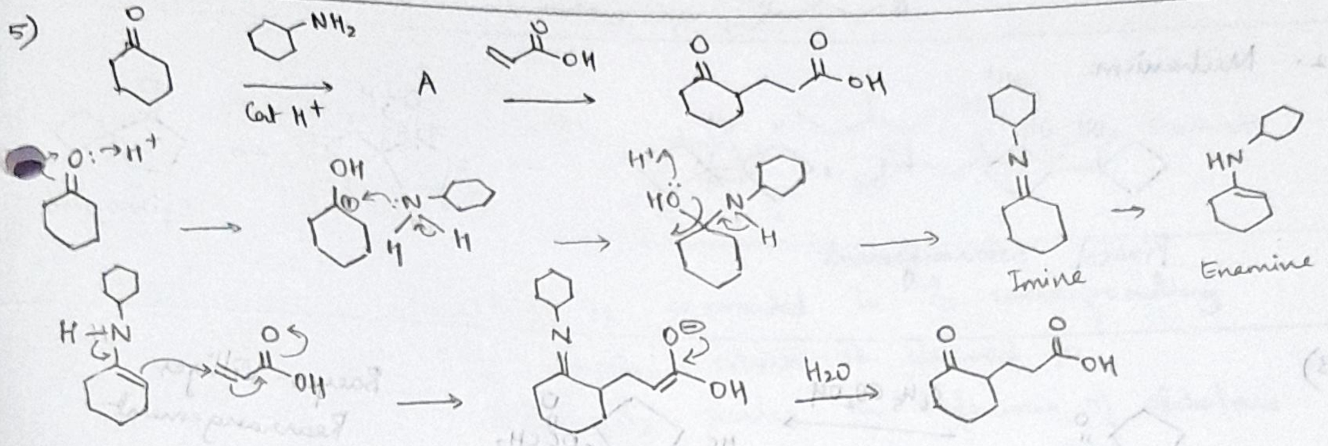
Not observed

→ Not stable enough

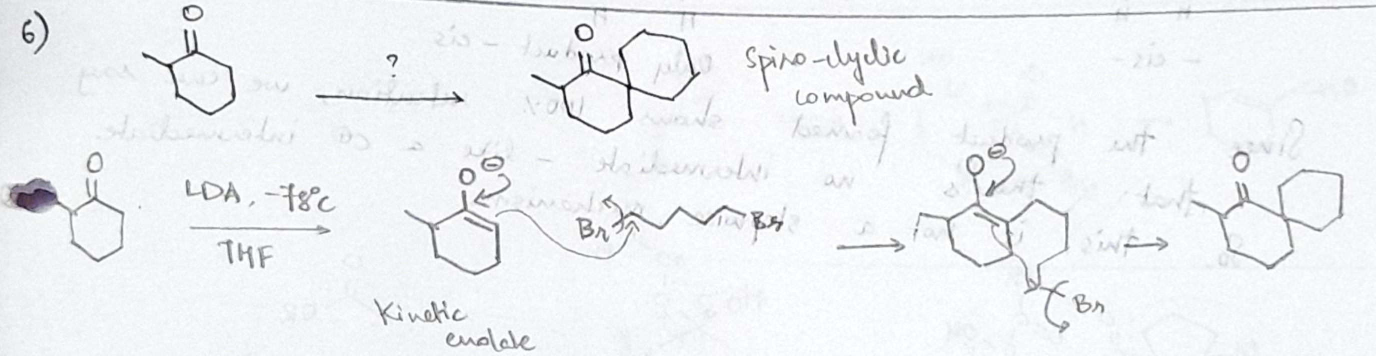
Very stable ∴ extended conjugate system

Must be: Thermodynamically controlled system

5)



6)



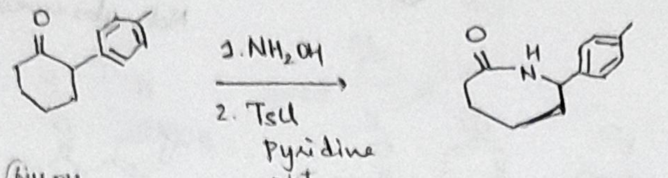
Spiro-cyclic compound

Kinetic enolate

(?) Where to use -Br and where to use olefins for alkylation.

Problem Set 09

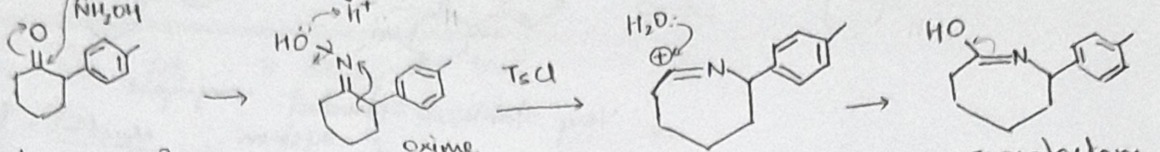
1. Propose a mech –



Pyridine mops up any HCl produced

TsCl makes –OH a good leaving group

Mech :

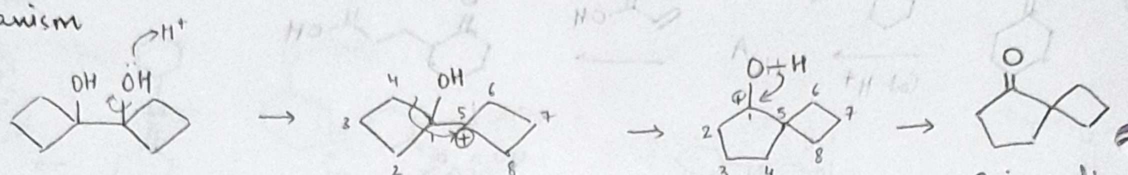


Beckmann Rearrangement (oxime – trans – only/major product)

caprolactam

---

2. Mechanism

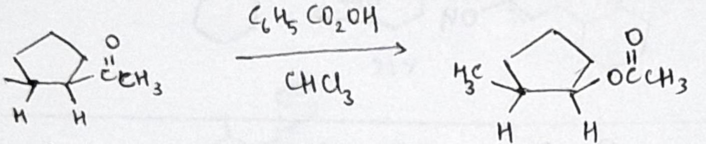


Pinacol rearrangement

Spirocyclic

---

3)

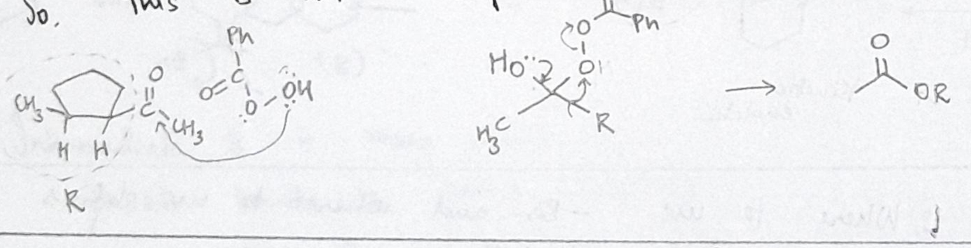


Baeyer-Villiger Rearrangement

– cis –

Only product – cis

Since the product formed shows 100% retention, we can say that there's no intermediate – like a C⊕ intermediate So, this is not a stepwise mechanism.



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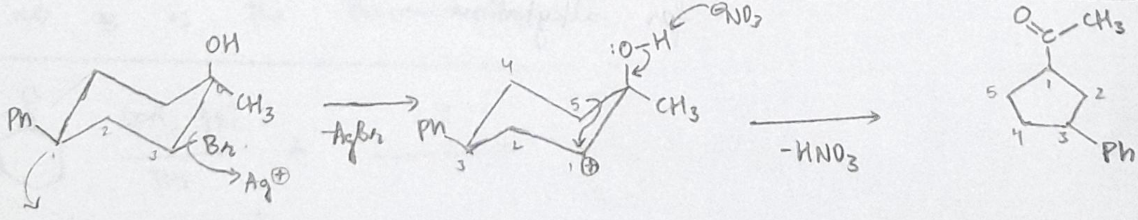
4)



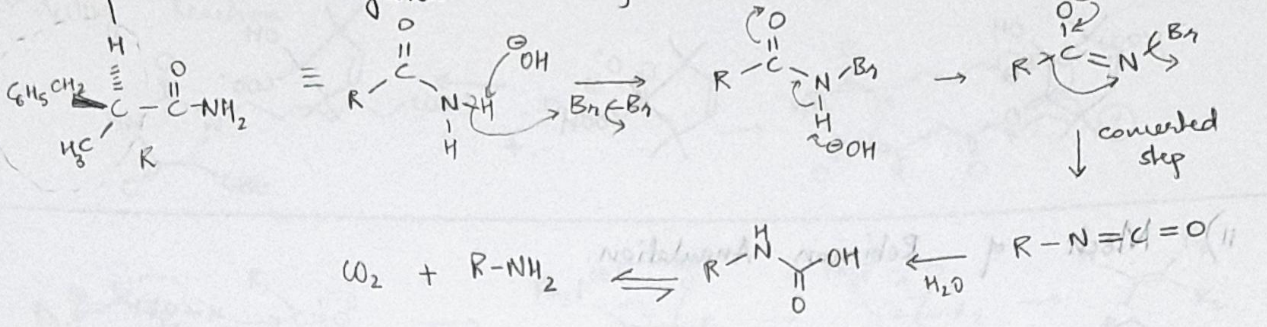
Locked conformation

Refer to pg. 60

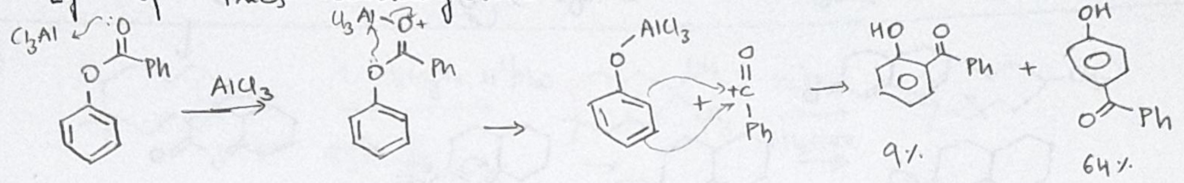
Problem Set 09 (contd)

5) 100% retention in stereochemistry ⇒ the reaction occurs in a single step without a planar intermediate stage. – concerted reaction

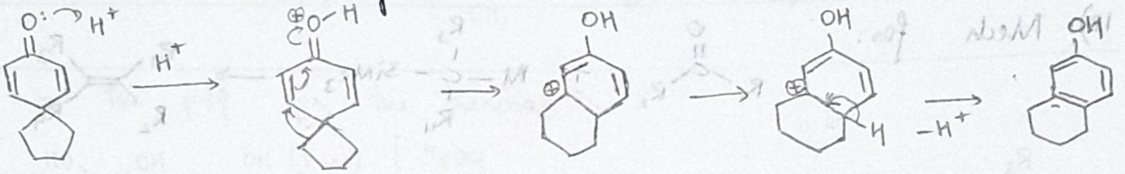
Hofmann rearrangement – isocyanate intermediate.



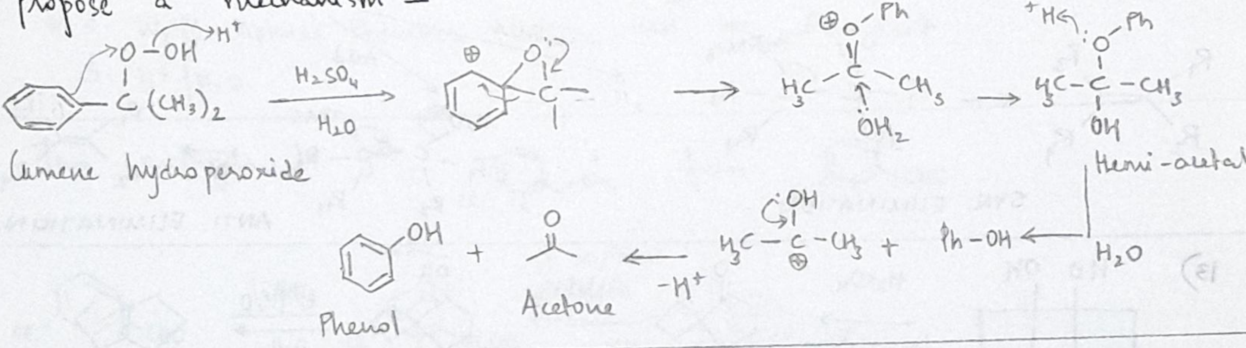
6) Eg. of Fries rearrangement –



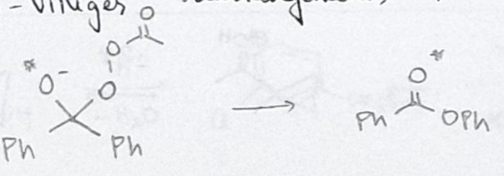
7) Di-enone – Phenol Rearrangement.



8) Propose a mechanism –

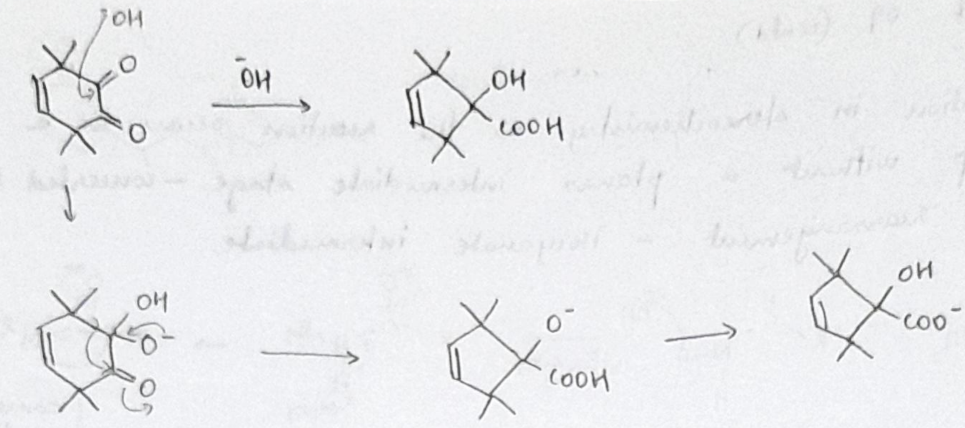


9) In Baeyer-Villiger rearrangement, the labelled O* is retained

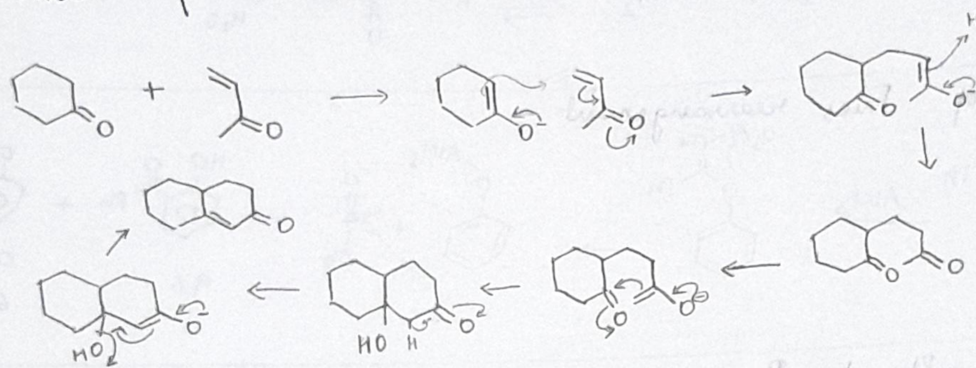


This tells us that the reaction occurs in a concerted step, where there's no possibility of scrambling

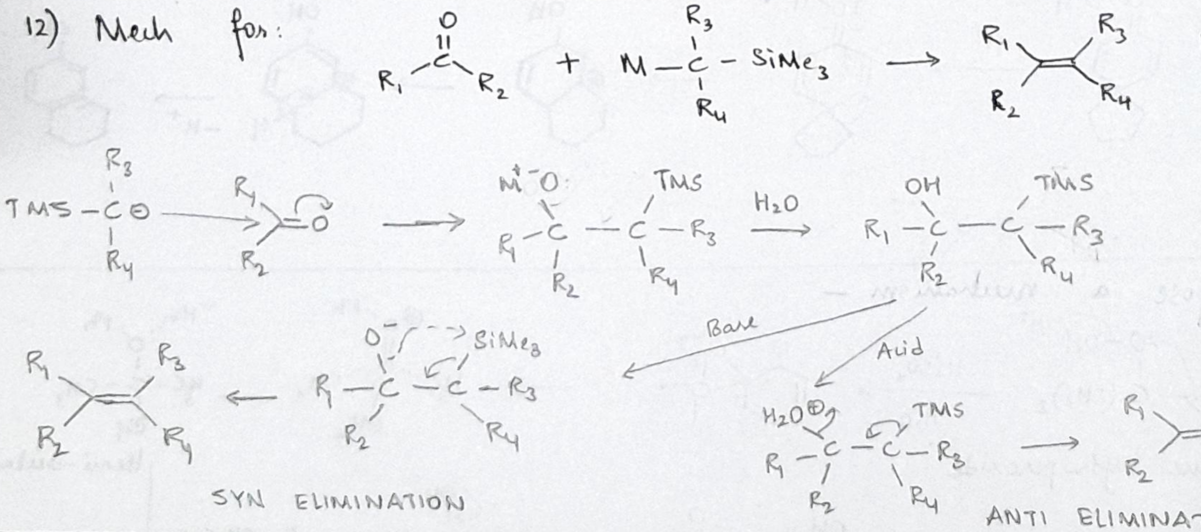
10)



11) Mech of Robinson Annulation.

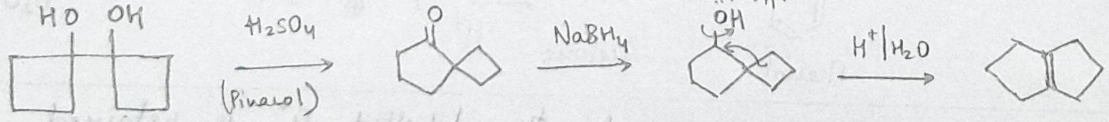


12) Mech for:

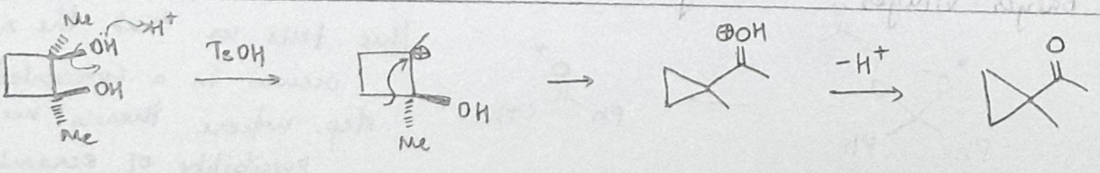


M = Li
or
MgBr

13)

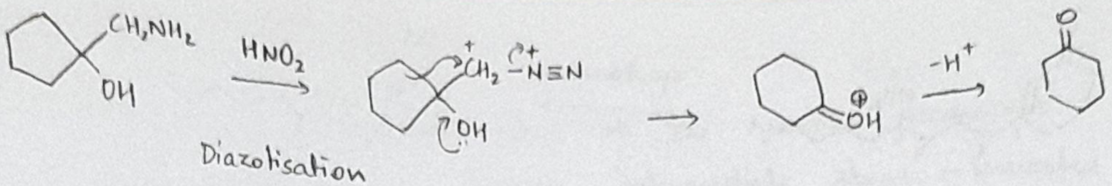


14)



~ Pinacol rearrangement

15)



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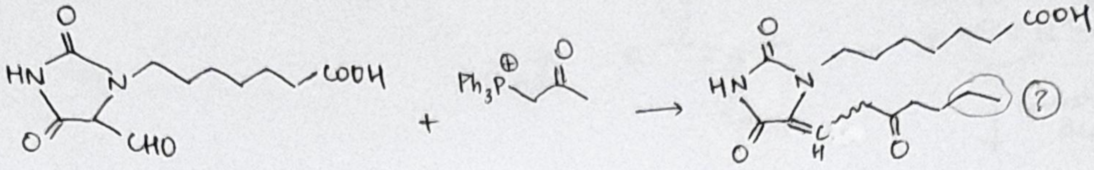
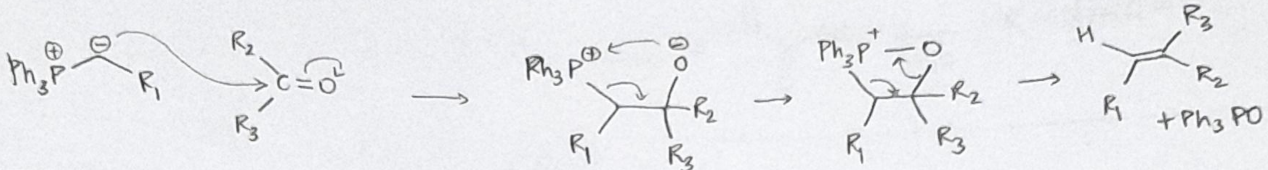
16) – Witting Reaction





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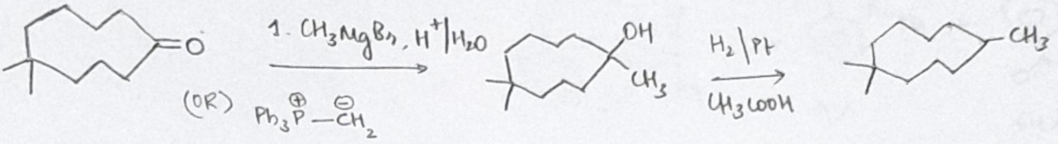
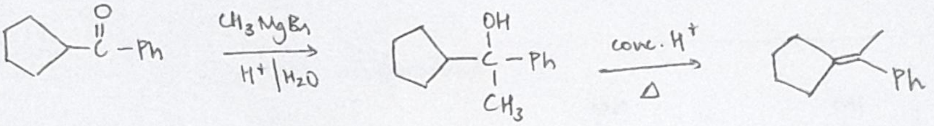
17) a)



b)



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18) Refer to the pdf for the reaction

1. HO⌣⌣OH , ⁻OH (base) | TsOH
2. LiAlH$_4$, THF
3. Pyridinium chlorochromate (mild oxidising agent) Cl – Cr
* 4. Wolff - Kishner Reduction – N$_2$H$_4$, KOH, HO⌣⌣OH, heat
5. H$^+$ | H$_2$O

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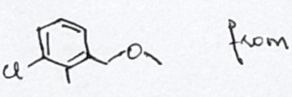
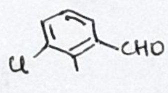
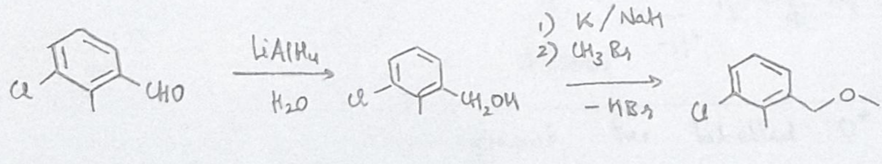
19) Two methods to get



from



i)



ii)