31/03/2026 Prof. Olomola's part

Organic Reactions & Synthesis

Introduction

Organic synthesis is the process of building organic molecule from simple precursors. It typically involves;

(i) Carrying out a reaction following an exact or slight modified procedure from a scientific paper. This usually involves stirring, addition of reagent and in some cases, temperature control.

ii) Work up procedure such as, quenching, solvent extraction, adsorption of impurities, neutralization, removal of solvents and so on

iii) Purification using techniques such as recrystalization, preparative thin layer chromatography column chromatography, radial chromatography, high performance liquid chromatography etc

iv) Identification using chemical test and more conveniently instrumentation techniques such as IR, UV, NMR, MS and X-ray crystallography

The overriding concern in a synthesis is the yield, including the inherent concept of simplicity (fewest possible steps) and selectivity (chemoselectivity, regioselectivity

diastereoselectivity and enantioselectivity)
Furthermore, the experimental ease of a transformation an whether they are environmentally acceptable must be considered

01/04/26

Retrosynthetic Analysis

The synthesis of any molecule involves careful planning and strategy. E.J. Corey the winner of the 1990 nobel price in chemistry introduced and promoted the concept of retrosynthetic analysis whereby a molecule is disconnected leading to logical precursors.

Today retrosynthetic analysis plays an integral and indispensable role in research

Synthetic planning starts with the product which is fixed and unchangeable (called the target molecule) and Walks backwards towards the starting material

This process is called retrosynthesis (backward synthesis) and the art of planning the synthesis of target molecule is called retrosynthetic analysis.

Definitions

(1.) Target molecule (TM): It is the molecule to be synthesized

(2) Arrow:

(a) simple reaction arrow (⟶): It means "react to give"

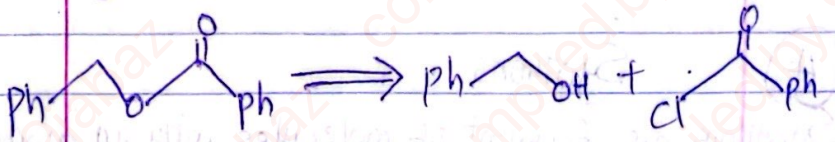
(b) delocalization arrow (⟷) means that the two different structures are the same or there are two different ways to draw a delocalized structures

(c.) Equilibrium arrow (⇌): Meaning the two structures are interconverting

(d) retrosynthesis arrow (⟹): It means "could be made from". E.g

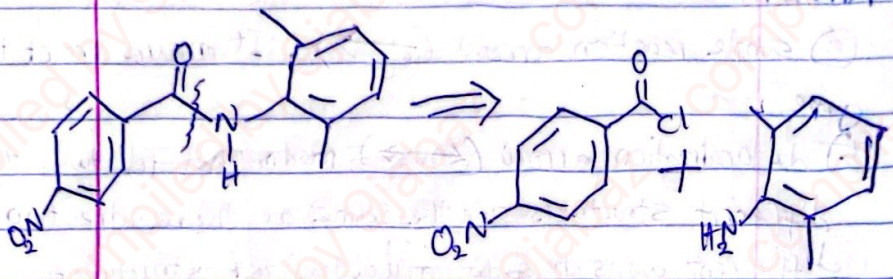
$$Z \Longrightarrow x + y$$

It means that target molecule Z could be made by reacting x and y under specific reaction condition

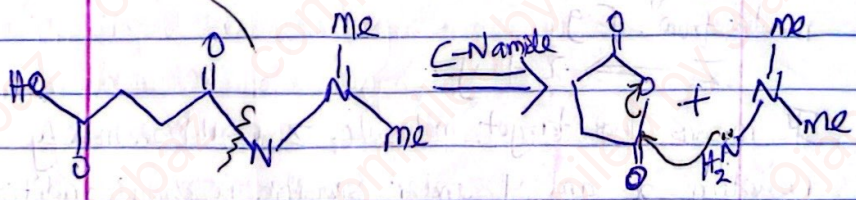


(3.) Disconnection: Mentally breaking a molecule into its component parts is known as disconnection and it is normal to indicate the site of the disconnection

with a wiggly line. Disconnection is an imaginary bond cleavage corresponding to the reverse of a real reaction.



Note: Disconnection must correspond to known reliable reaction



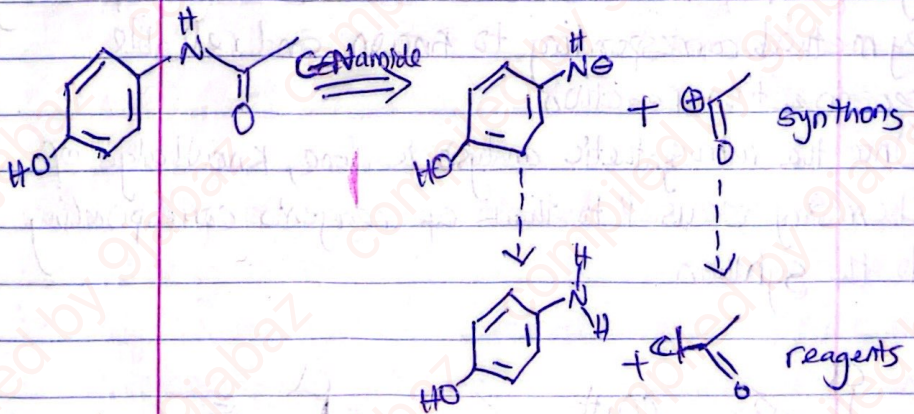
(4) Synthons

Synthons are fragment of molecules with an associated polarity (represented by a + or −) which stands for reagent used in the forward sythesis. They are not themselves reagent, though they made occasionally turn out to be intermediate along the reaction pathway.

By disconnecting bonds to synthons rather than actual reagent, the polarity of the bond forming reaction can be indicated without having to specify details of the reagent.

Simply put – synthons are idealized fragment resulting from a disconnection. Synthons need to be replaced by reagent in a suggested synthesis.

TM ⟹ Synthons ·····> Synthetic equivalent or reagents



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(5) Synthetic Design

It involves two distinct steps;

(I) retrosynthetic anaylsis

(II) Subsequent translation of the analysis into a forward reaction synthesis

retrosynthetic analysis;

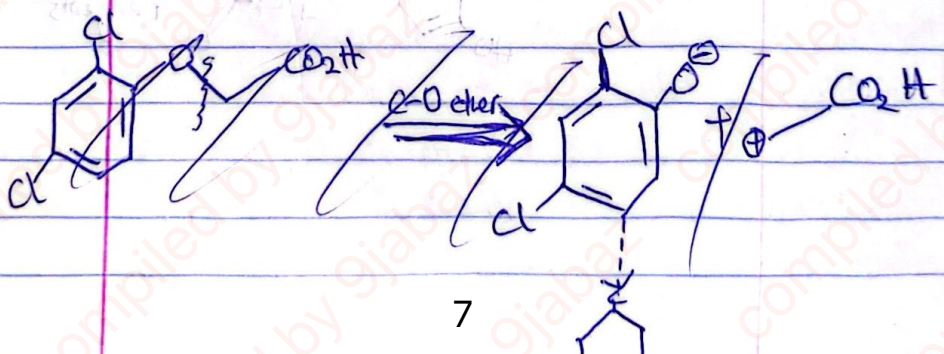
$TM \Rightarrow A + B \Rightarrow C$

forward sythesis

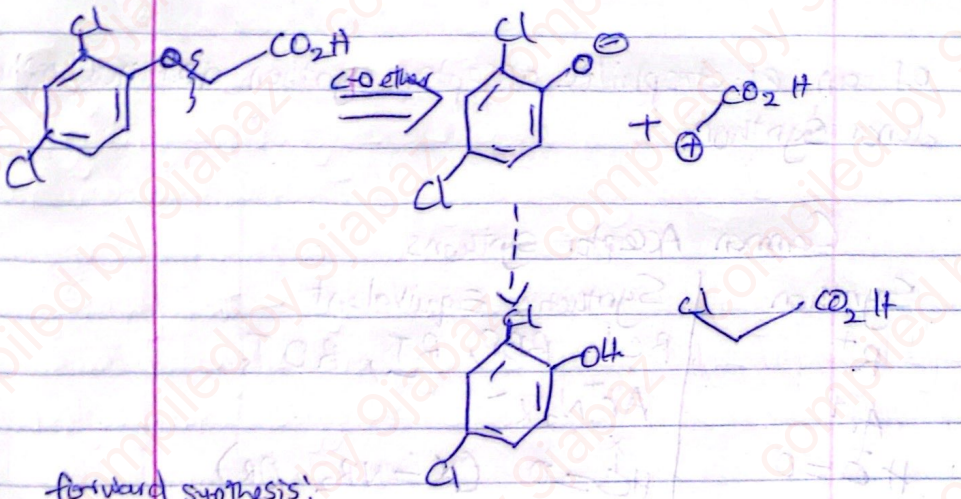
$C \longrightarrow A + B \longrightarrow TM$

In the analysis, the chemist recognizes the functional groups in a molecule and disconnects them proximally by methods corresponding to known and reliable reconnection reaction.

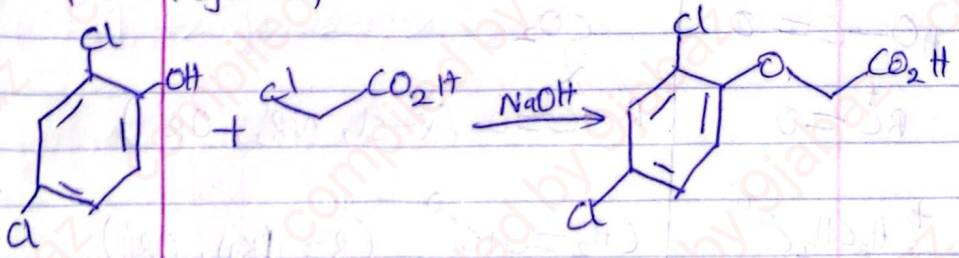
Once the retrosynthetic analysis is done, knowledge of chemistry is used to think of reagents corresponding to the synthon



retrosynthetic analysis;



forward synthesis;

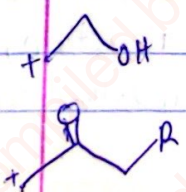
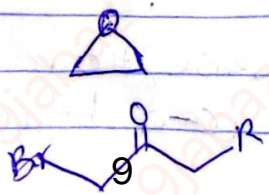


Chemical bonds can be cleaved heterolytically, homolytically or through concerted transformation Heterolytic retrosynthetic disconnection of a C–C bond in a molecule breaks the target molecule into an acceptor synthon (a carbocation) and a donor synthon (carbonanion).

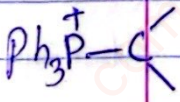
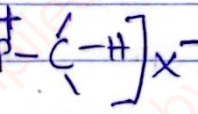
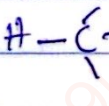
In a formal sense, the reverse reaction, i.e the formation of a C–C bond, then involves the union

of an electrophilic acceptor synthon and nucleophilic donor synthon

Common Acceptor synthons

Synthon	Synthetic Equivalent
R^+	RCl, RBr, RI, ROTs
Ar^+	ArN_2X^-
$HC^+=O$	$HC(X)=O$ (X = NR_2, OR)
$HO-C^+=O$	CO_2
$RC^+=O$	$R-C(X)=O$ (X = Cl, NR'_2, OR')
$^+CH_2CH_2C(=O)R$	$CH_2=CHC(=O)R$ (R = alkyl, OR')
$^+CH_2-CH_2C\equiv N$	$CH_2=CHC\equiv N$
$^+CH_2OH$	HCHO
R_2C^+-OH	$R_2C=O$
	

Common Donor Synthons

Synthon	Derived reagent	Synthetic Equivalent
R^-	$RMgX$, RLi, R_2CuLi	RX
^-CN	$NaC\equiv N$	HCN
$RC\equiv C^-$	$RC\equiv CMgX$, $RC\equiv CLi$	$RC\equiv CH$
		
		

Choosing a Disconnection

The hardest ~~task~~ part in designing a retrosynthetic analysis is spotting where to make the disconnection(s). The overall aim of retrosynthetic analysis is to get back to starting materials that are available from chemical suppliers and to do this as efficiently as possible, Below are summarized important guidelines for choosing disconnections of bond.

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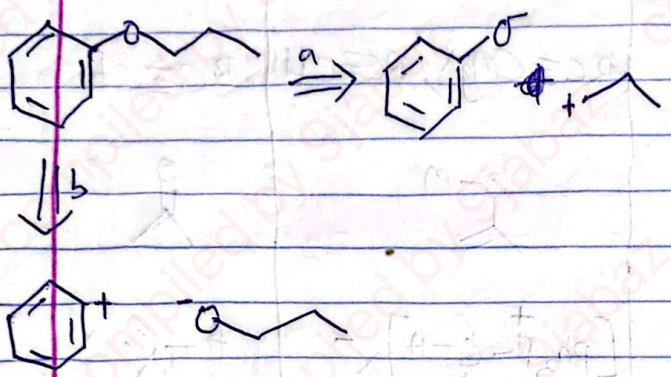
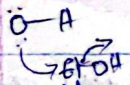
1) Disconnection of bond should be carried out only if the resultant disconnected fragment can be reconnected by known and reliable reaction.



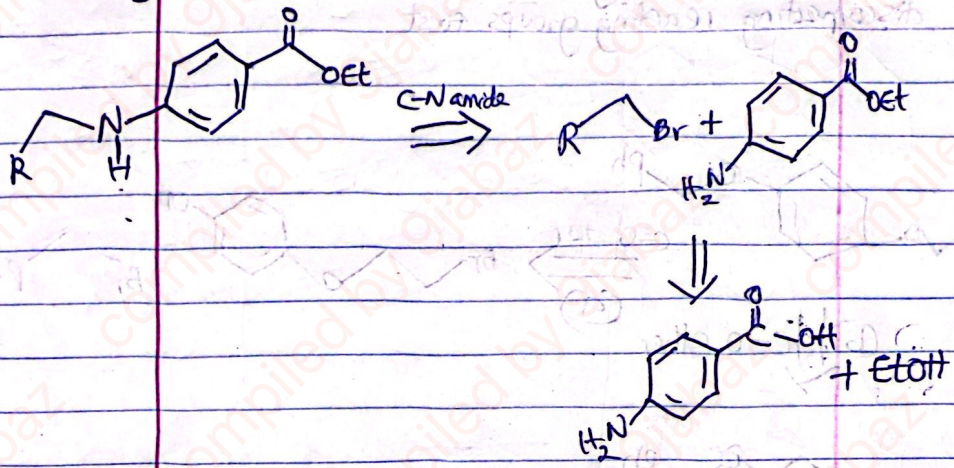
Disconnection of the acyl side of the oxygen atom is a bad choice because there is no reliable reaction corresponding to nucleophilic attack of an alcohol on an unactivated aromatic ring.

(2) Aim for the fewest number of disconnection. Adding large fragment in a single reaction is more productive than adding several small fragments sequentially

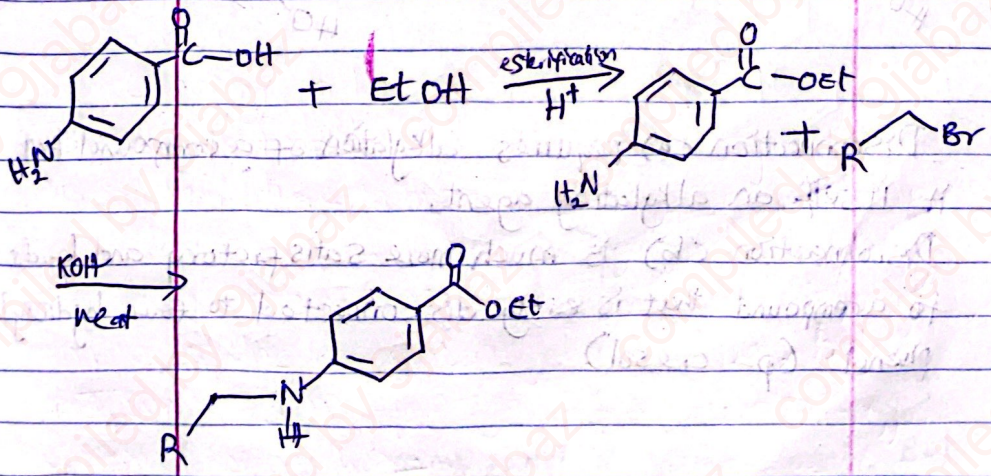
(3) For compounds consisting of two parts joined by a hetero atom disconnects next to the hetero atom. This guideline works for esters, amides, ethers, amines,



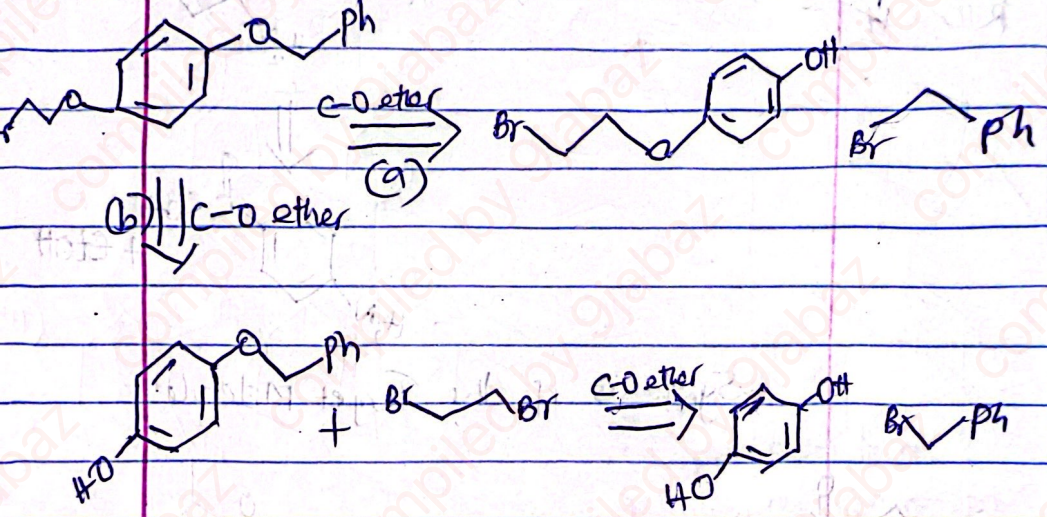
acetals and sulphides, because this compounds are often made by a substitution reaction.



Synthesis of the Target Molecule



(4) Consider alternative disconnection and choose route that avoid chemoselectivity problems. This often means disconnecting reacting groups first



Disconnection (a) requires alkylation of a compound that is itself an alkylating agent.

Disconnection (b) is much more satisfactory and leads to a compound that is easily disconnected to four hydroxyl phenol (p-cresol)

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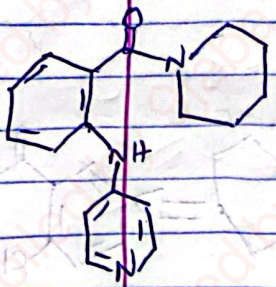
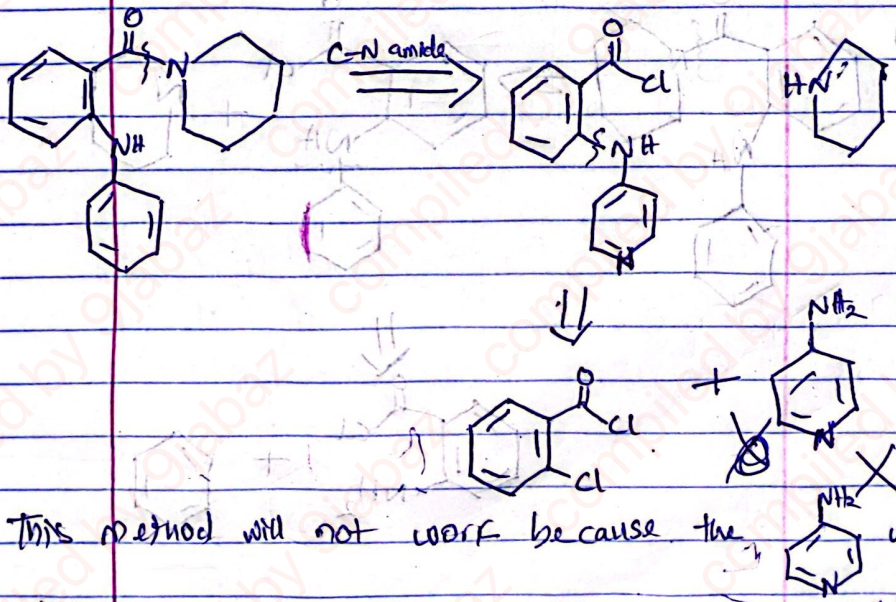
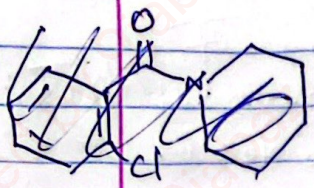


Using the disconnection approach, outline a synthesis for the target molecule above;

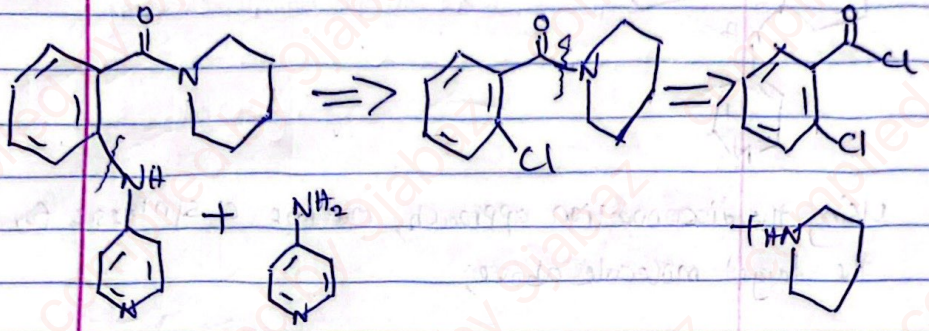


This method will not work because the will attack the carbonyl group, not the second C–Cl. But if OH is used (for the second C–Cl) instead of Cl, it would have worked

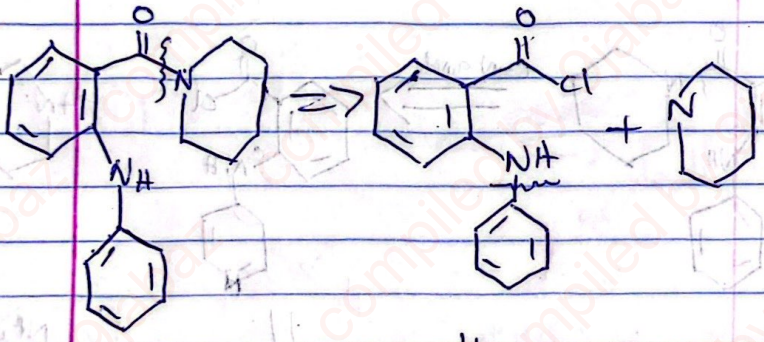
c)

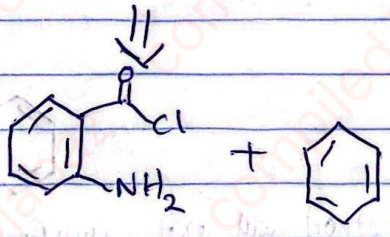


(i)



(ii)





Write the Synthesis

R–X

Functional Group Interconversion

(i) haloalkane → alcohol
haloalkane → nitrile

synthesis involve either formation of new bond or functional group interconversion (no. of C-atom doesn't change).

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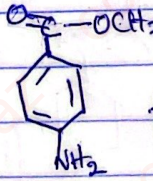
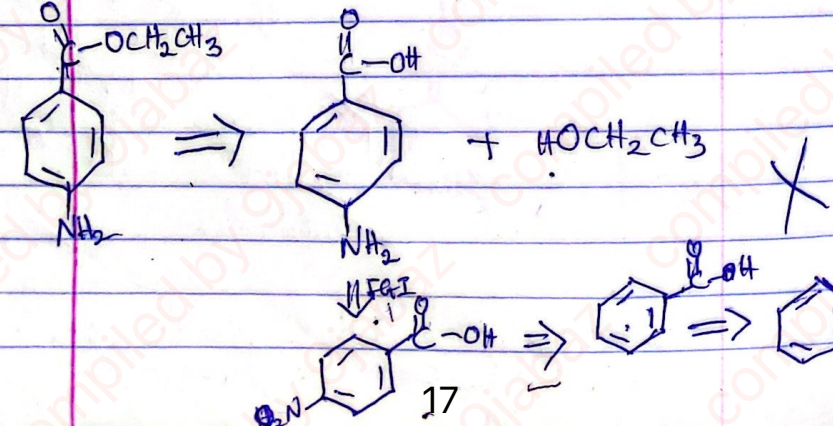
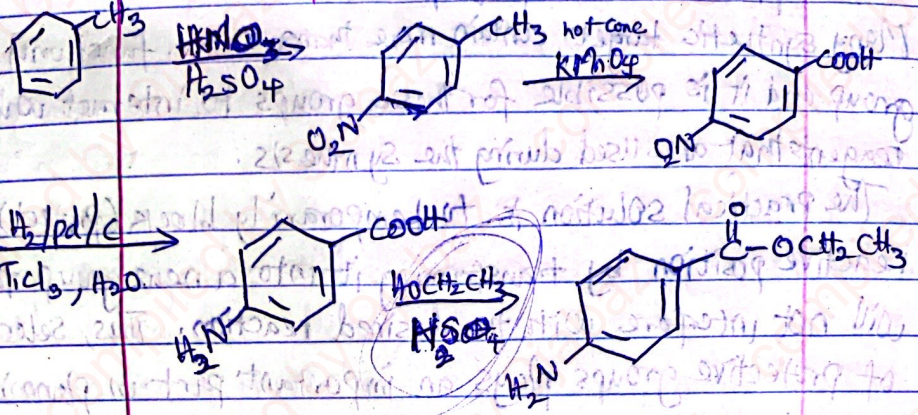
Using the disconnection approach, write the synthesis for the compound below



from toluene



Synthesis



Retrosynthesis

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① $CH_2=CH_2 \xrightarrow{??} CH_3CH_2CONH_2$

② $CH_2=CH_2 \xrightarrow{??} CH_3CH_2NH_2$

③ $H_2C=CH_2 + HBr \longrightarrow H_3C-CH_2-Br \xrightarrow{NH_3} H_3C-CH_2-NH_2 + HBr$

④ $H_2C=CH_2 + HBr \longrightarrow CH_3-CH_2Br + NaCN \longrightarrow CH_3-CH_2CN$

$CH_3CH_2CONH_2 \xleftarrow{NH_3} CH_3CH_2COCl \xleftarrow{SOCl_2} CH_3CH_2COOH \xleftarrow{H_3O^+} CH_3CH_2CN$

26/05/26

Protection and Deprotection

Many synthetic target contain more than one functional group and it is possible for these groups to interact with reagents that are used during the synthesis.

The practical solution is to temporarily block (protect) one reactive position by transforming it into a new group that will not interfere with the desired reaction. Thus, selection of protective groups plays an important part in planning a synthesis

A protective group must fulfill a number of requirements

(1) The protective group reagent must react selectively in good yield to give a desired protected substrate that is stable to the projected reactions

(2) The protective group must be selectively removed in good yield by readily available reagents

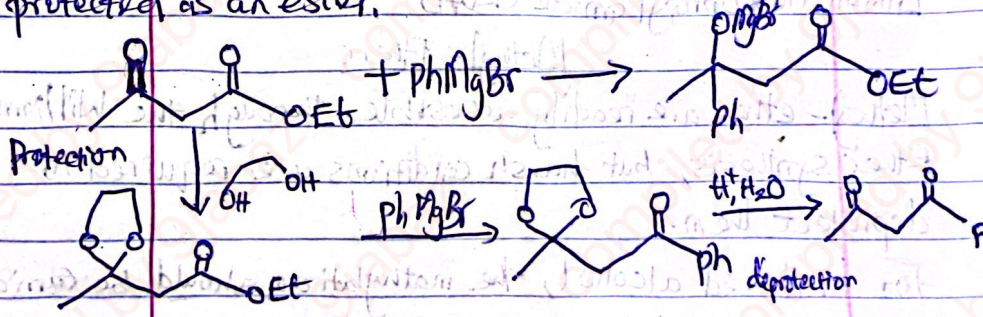
(3) The protective group should not add additional functionality that might provide other side reactions

Example

* There are some reagent that could affect both the double bond

and the –OH functional group. For this not to happen, we could decide to protect one of the groups. This is not a desired step because when we protect, we still have to deprotected

Introduction of a protecting group adds at least two additional steps to a synthetic scheme with possible effect of reduced yield and extra cost. Hence, all efforts should be made to keep the use of protecting group to a minimum. Effectively planning the order for insertion of each functional group can actually minimize the use of protecting groups and ; where possible this option should be used.
Most important functional groups which cause reactivity problems are alcohols, ketones, aldehyde and amines. Carboxylic acid group can give some concern as this is often protected as an ester.



Alcohol Protection

The interfering part of the alcohol group is always the acidic proton. The most important protective group for alcohol are ethers and mixed acetals. The proper choice of protecting group is critical if chemoselectivity is desired. Reactivity of alcohol is $1^{\circ} > 2^{\circ} > 3^{\circ}$

The stability of ethers and mixed acetals as protecting groups for alcohol varies from very stable methyl-ether to the highly acid labiles. However, all ethers are stable to basic reaction conditions. Hence, ether mixed acetal protecting group, specifically tetorate grignard reagent ($RMgX$), RLi, nucleophilic reducing reagent such as $LiAlH_4$, $NaBH_4$, oxidizing agents such as PCC (pyridium chlorochromate), MnO_2 (mganes (IV) oxide), wittig reagent and strong bases such as Lithiumdiisopropyl amide (LDA)

Methyl-Ethers

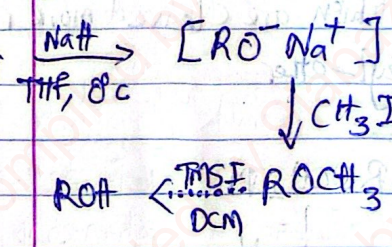
Methyl-ether are readily accessible through the Williamson-ether synthesis, but harsh conditions are required to deprotect them.

For hindered alcohol, the methylation should be carried out in the presence of KOH and DMSO (dimethylsulphoxide)

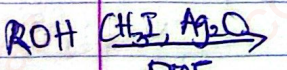
The reagent for clearing methyl-ethers include;

(i) Conc HI (ii) Me_3SiI (Trimethylsilaneiodide) in DCM
(iii) BBr_3 in DCM

BBr_3 is especially effective for cleaving $PhOCH_3$ i.e phenolmethyl ether



Methylation of 2°-OH groups in sugars with methyl iodide and silver oxide (Ag_2O) is often the method of choice.

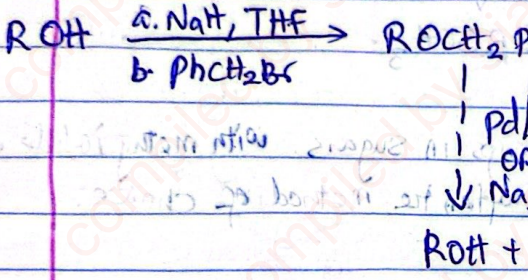


Benzyl – Ethers

Benzyl ethers are quite stable under both acidic and basic conditions and towards a wide range of oxidizing and reducing reagent. Hence, they are frequently used in organic Synthesis as protecting groups.

Note: n-BuLi may deprotect a benzylic hydrogen especially in the presence of tetramethylethylene diamine (TMEDA)

Catalytic hydrogenolysis offers the mildest method for deprotecting benzyl-ether. Hydrogenolysis of 2° and 3° benzyl ethers may be sluggish. Protection of alcohols using benzyl(oxy) methyl chloride produces the corresponding benzyloxymethyl-ether which are cleaved more readily than the corresponding benzyl-ether



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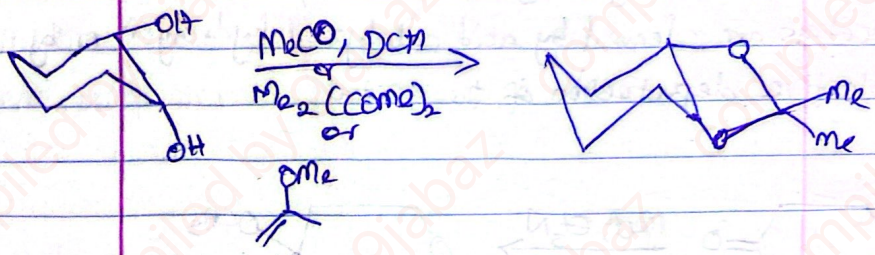
Only vicinal cis-OH group of cyclic 1,2-diol readily form acetal



Aqueous HCl, acetic acid or para-toluene sulfonic acid can be used to cleave the Acetal

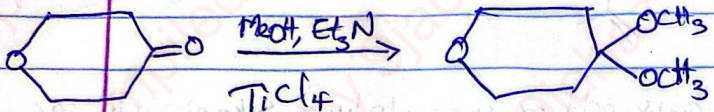
Aldehyde and ketone protection

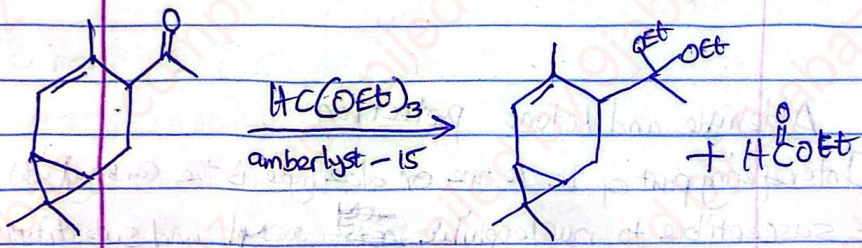
Interfering part of the ketone or aldehyde is the carbonyl which is susceptible to nucleophilic acyl and substitution reaction. To prevent these reactions, the electrophilic carbon and the π-bond of the carbonyl must be removed and this is accomplished by converting the carbonyl to cyclic or acyclic ketal or acetal using alcohol or diol reactants. Acetals are stable to strong aqueous bases nucleophilic reducing agent, organometallic reagents, oxidations under non acidic conditions and sodium or Lithium / Ammonia reduction.

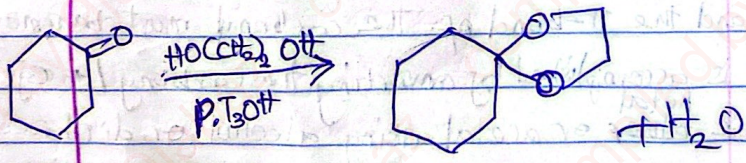
The acetal protective group is introduced by treating the

Carbonyl compound with an alcohol or orthoester in the presence of a lewis acid catalyst, dry HCl or H_2SO_4.

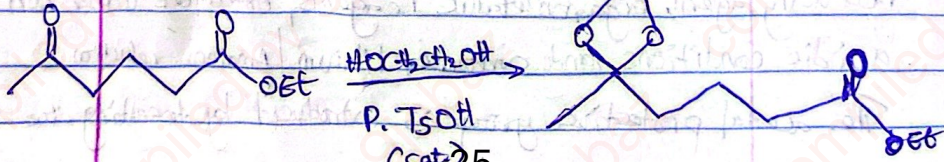
Acetals are cleaved by acid catalyzed hydrolysis or by a selective deprotection of the acetal







1, 3-dioxolane

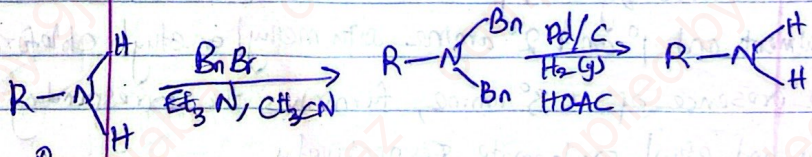


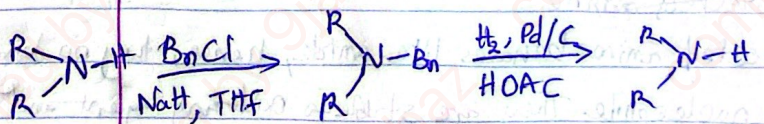
Amine Protection

The interfering portion of amine is the basic and nucleophilic lone pair of electron on nitrogen which is susceptible to alkylation basicity and oxidation reaction. The common method of amine group protection involves conversion of primary and secondary amine to a 3° amine (usually benzyl or trialkylsilyl) Conversion to an amide (or a carbamate) and conversion to a sulphonamide

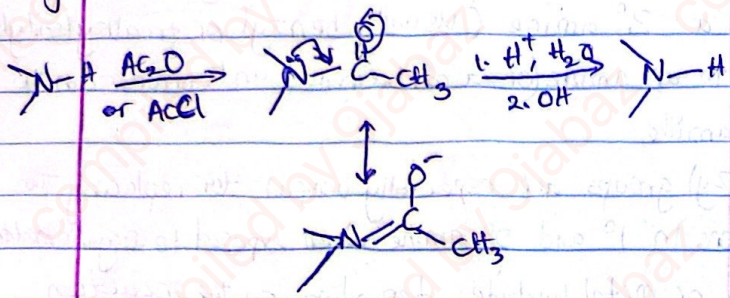
N-Benzyl groups are especially useful for replacing the NH protons in 1° and 2° amine when exposed to organometallic reagents or metal hydride depending on the reaction conditions, 1° can form mono and/or dibenzylated products. Hydrogenolysis of benzyl amine with pd catalyst in the presence of an acid regenerates the amine.

Note: benzyl amines are generally not cleaved by Lewis acid





Acylation of 1° and 2° amine with acetic anhydride or acid chlorides gives the corresponding amides in which the basicity of the nitrogen is reduced making them less susceptible to attack by electrophilic reagents



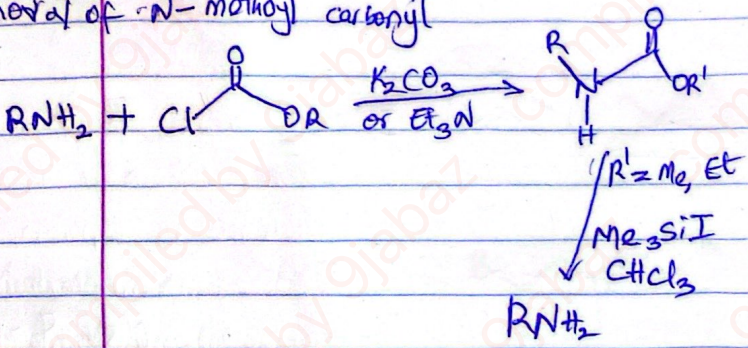
Benzamides are formed by the reaction of amines with benzoyl chloride in pyridine or trimethylamine, the group is stable from pH 1 to 14, nucleophile, organometallic, (except organolithium reagent), catalytic hydrogenation and oxidation. It is cleaved by strong acids such as 6N HCl or HBr

Treatment of 1° and 2° amine with methyl or ethyl chloroformate in the presence of a 3° amine, furnishes the corresponding methyl and ethyl carbamate respectively

~~Deprotected amine~~

The protected amine behaves like amide, hence, they no longer acts as nucleophile They are stable to oxidizing agent and aqueous bases, but will react with reducing agents

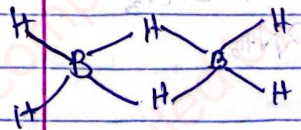
Trimethylsilyl iodide is often the reagent of choice for the removal of N-methoxyl carbonyl



Hydroboration

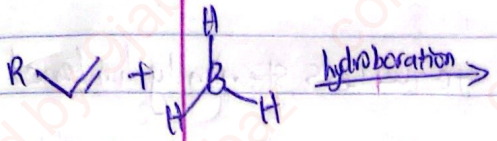
Boron has only nine electrons in the second shell, and so typically forms three conventional two centre two electron bonds with other atoms in a planar structure leaving a vacant 2p orbital.

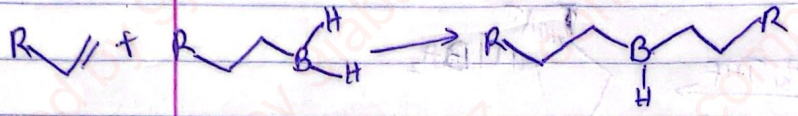
Borane exist as mixture of B_2H_6 (a dimer with hydrogen bridges) and the monomer BH_3

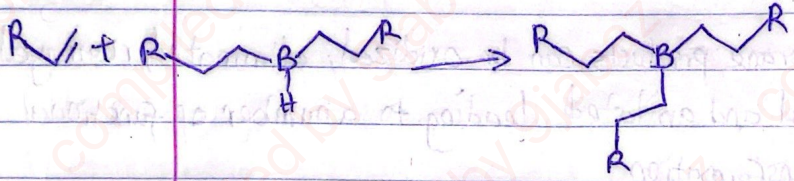


A vacant orbital is able to accept a lone pair of electron from a lewis base to give a neutral specie or can combine with a nucleophile to form a negatively charged tetrahedral anion.

Brown (Nobel price recipient 1979) discovered that diborane (B_2H_6) reacts with alkenes in ether solvent to form trialkyl borane. Alkene reaction with borane, described as hydroboration is an overall addition of borane across the double bond. Unlike most electrophilic additions to alkenes that occur in a stepwise manner via charged intermediates. These addition is concerted so that both new bonds are formed more or less at the same time, the result is an alkyle borane in which one of the hydrogen atoms has been replaced by an alkyl group.

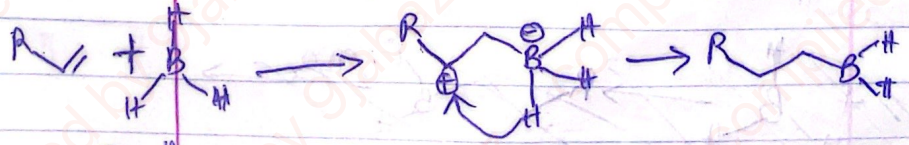


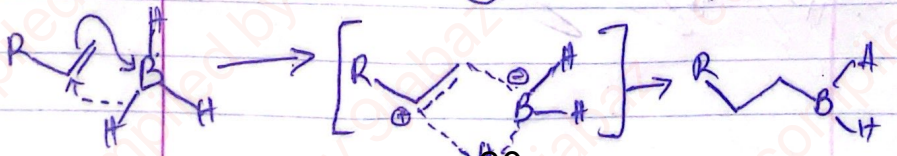




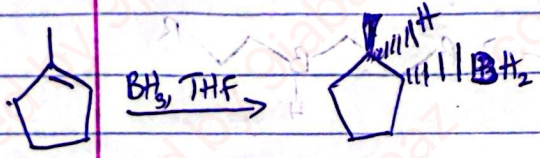
Hydroboration is a syn addition across the alkene. As the addition of the empty p-orbital to the less substituted alkene is occuring, a hydrogen atom from the boron adds with its pair of electrons to its carbon atom.

The two steps are concerted but the formation of the Carbon-Boron bond goes ahead of the carbon-Hydrogen bond so that boron and carbon are partially charged in the first centered transition state





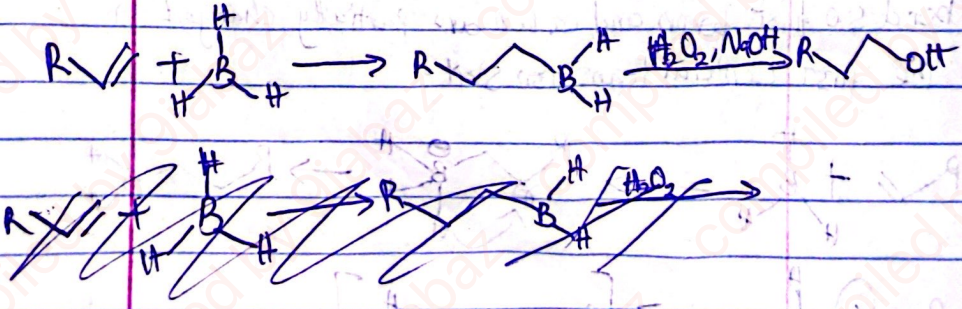
Boranes have regioselectively to the less sterically hindered position

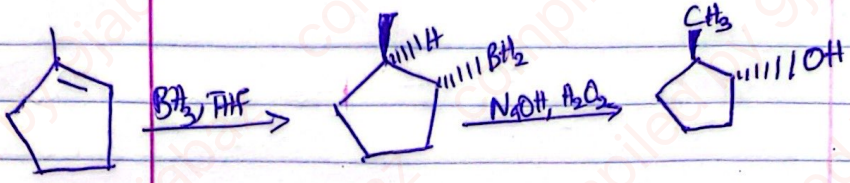


Organoborane products can be oxidized, eliminated, rearranged, protonated and anilated leading to a number of functional group transformation

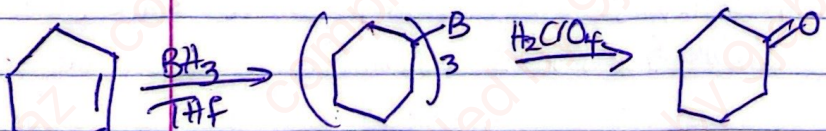
(1) Oxidation of Borane to Alcohol

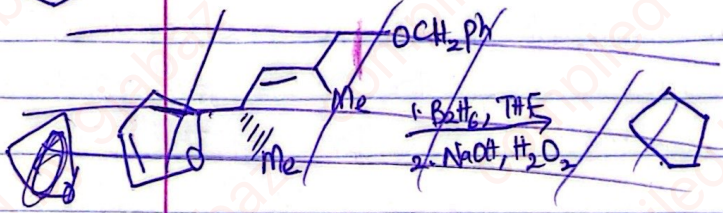
Perhaps, the most utilized transformation of hydroboration is the oxidation of alkyl borans to alcohol, accomplished by basic hydrogen peroxide

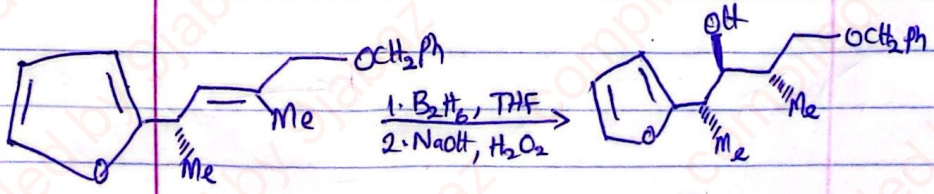




(2) Oxidation of Boranes to aldehydes and ketone while 1° or 2° alcohols produced from hydroboration followed by oxidation and the further oxidized to carbonyl compounds. The organoborane can be directly oxidized to corresponding carbonyl compounds by treatment with chromic acid







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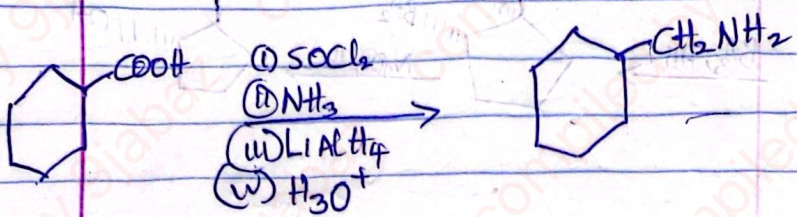
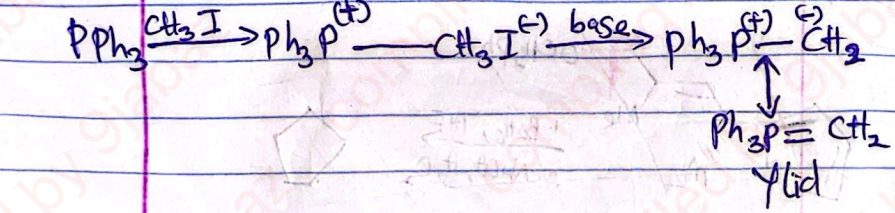
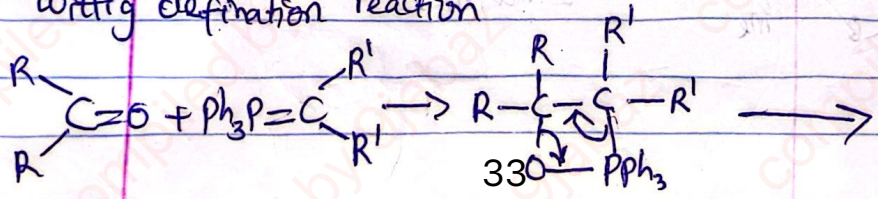


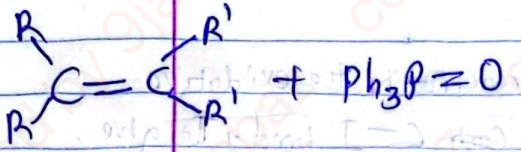
Wittig Reaction

Ylids are compound in which a carbonanionic carbon is adjacent to an atom bearing a five centre. The reactivity of phosphorus Ylid was first exploited by Wittig who found that phosphonium salts were generated by an SN2 reaction of a trialkyl-phosphene with an alkyl halide. The phosphonium salt reacts with a strong base such as N-butyllithium (N-BuLi)



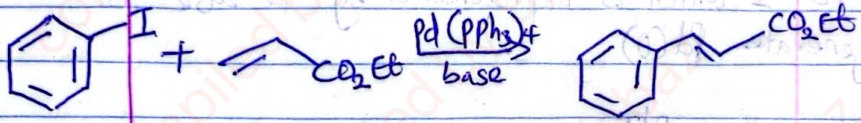
Wittig discovered that phosphorus Ylid reacts with aldehydes and ketones to form an alkene. This reaction is called Wittig defination reaction





Heck Reaction

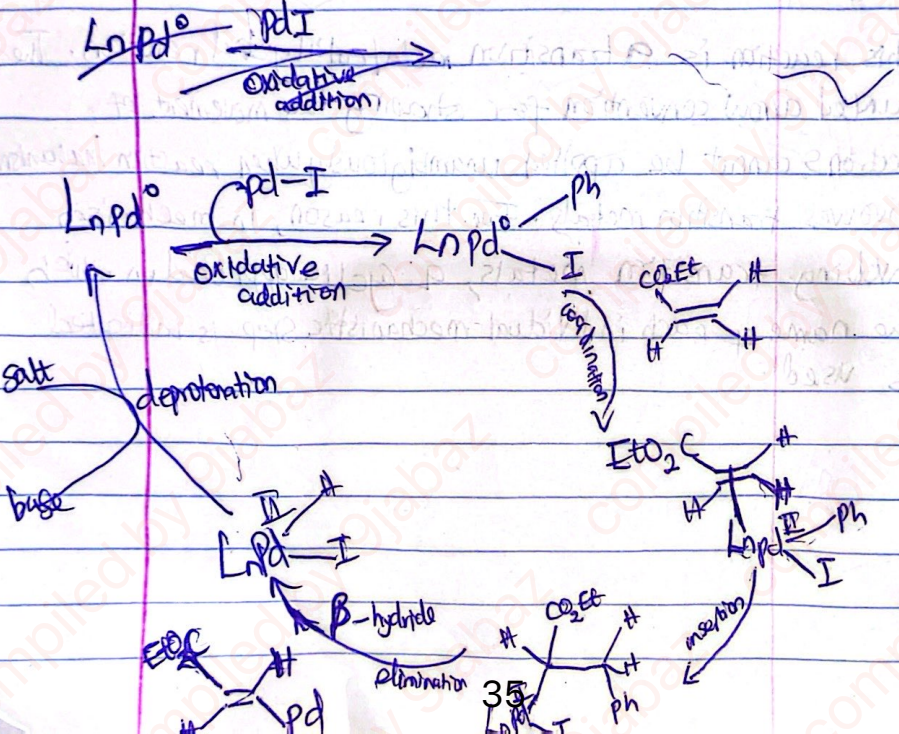
This is the chemical reaction of an unsaturated halides or triflate with an alkene in the presence of a base and a palladium catalyst to form a more substituted alkene. The heck reaction can be carried out intra or intermolecularly



This reaction is a transition metal catalysed reaction. The curved arrow convention for showing the movement of electrons cannot be applied unambiguously when reaction mechanism involves transition metals. For this reason, in mechanism involving transition metals, a cyclic approach in which the name of each individual mechanistic step is indicated is used.

The first step of the Heck reaction is the oxidative reaction of Pd(0) to the C—I bond, to give Pd(II)—Ph. The Pd(II)—Ph complex then coordinates to the alkene and this is followed by an insertion of the alkene into the Pd(II)—Ph bond giving a new C—C bond.

A β-hydride elimination then gives the product and H—Pd—I which is deprotonated by the base to regenerate Pd(0)



10/04/26 Prof. Adeogba's part

Transformations of Compounds/molecules into different forms occurs through chemical reactions. for examples

$$Na_2SO_4 + KNO_3 \longrightarrow K_2SO_4 + NaNO_3$$

$$2Na^+ SO_4^{2-} + K^+ NO_3^- \rightarrow 2K^+ SO_4^{2-} + Na^+ NO_3^-$$

Inorganic reactions are instantaneous, because they exists in ion

The reactions of inorganic compounds are reactions of ions usually such reactions are instantaneous because the ions are already present in the reaction medium

$$CH_3COOH + C_2H_2OH \rightleftharpoons CH_3COOC_2H_5 + H_2O$$

On the other hand, reactions of the organic compounds are molecular in nature, because the consitutent atoms of molecules of organic compounds are firmly bonded by covalent bonds. In this case, for a compound to undergo chemical reactions, it is essential that existing bonds must be broken and new bonds created.

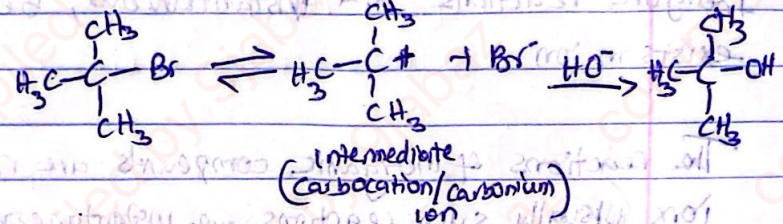
At times, Usually, the sequence and timing of the bond breaking and making processes are important

in the study of organic reactions.

Examples

(i) hydrolysis of tertiary halo alkane

SN1

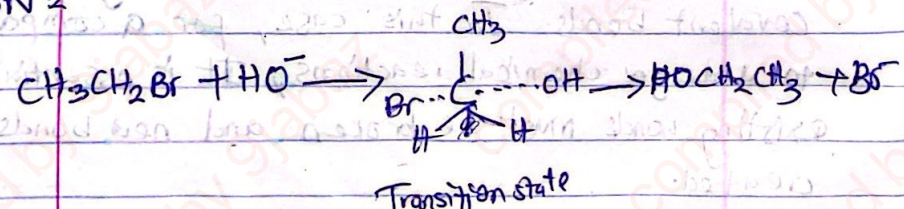


(intermediate carbocation/carbonium ion)

When we have a carboncation that is stable, that it can be isolated, we called it Isolable

Bond breaking may precede bond formation or vice versa resulting in a stepwise reaction and formation of compound known as intermediate which may or may not be isolable

(ii) SN2



Transition state

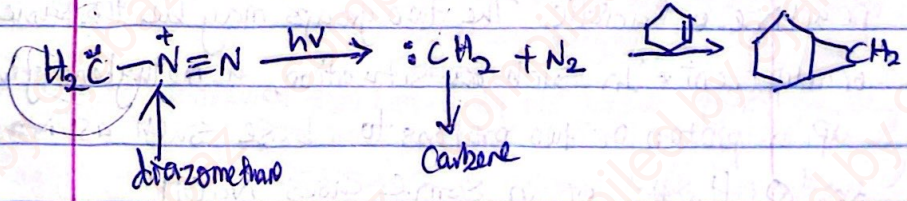
Alternatively, both processes may occur simultaneously giving synchronous or concerted step. This reaction results in the formation of transition state which may or may not be isolable.

Alkylation Reactions

It is the transfer of an alkyl group from one molecule to another. The alkyl group may be transferred as an alkyl carbocation, ~~The alkyl group may be transferred~~ a free radical, carbene or their equivalent

For example, termination reaction of halogenation of methane

$$^{\bullet}CH_3 + {}^{\bullet}CH_3 \longrightarrow CH_3CH_3$$



Carbenes are neutral compounds containing divalent carbon and are often formed from nitrogen containing molecules called diazo compounds.

This reaction forms new C–C bond (and the two reaction formed) are important in the synthesis of organic compound.

Without such reactions, we could not convert molecules with small carbon skeleton to larger ones. The product of the reaction will always have the same number of carbon as the starting material

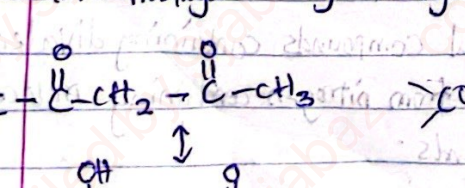
Specific Reactions

Reactive methylene Compounds. ($X_1 - \overset{\alpha\text{-hydrogen}}{\uparrow} CH_2 - X_2$)

When a methylene group is present between two strongly electron attracting group such as carbonyl, $-C\equiv N$, $-COOR'$, $-CHO$, $CONR'_2$, NO_2 etc.

The hydrogen atom for the methylene group becomes reactive or acidic. The two groups may be the same or different. In such situation, a methylene gives up a proton or two protons to a base such as $R_4N^+OCH_2CH_3$ or in some cases NaOH

Reactive methylene e.g acetylacetone

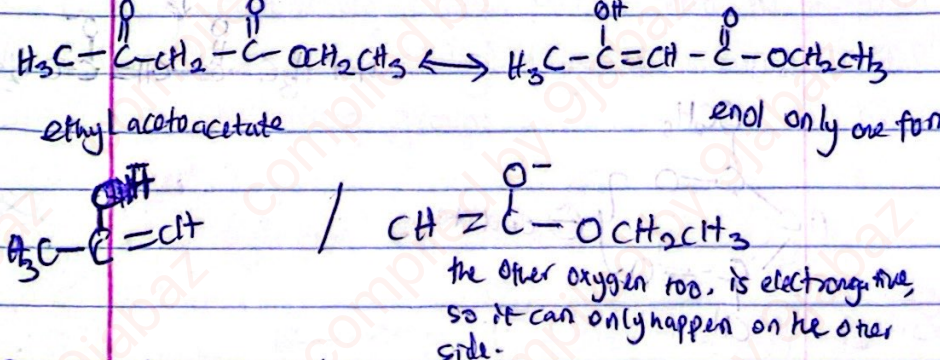


enol

on enol

If the reacting methylene compound is symmetrical, the hydrogen atom of the methylene group migrates to either of the ketone group

If the compound is unsymmetrical, only one form is present predominantly and the migration of H-atom depends upon the inductive effect of the alkyl group or other group present in either side of the $-CH_2-$



ethyl acetoacetate

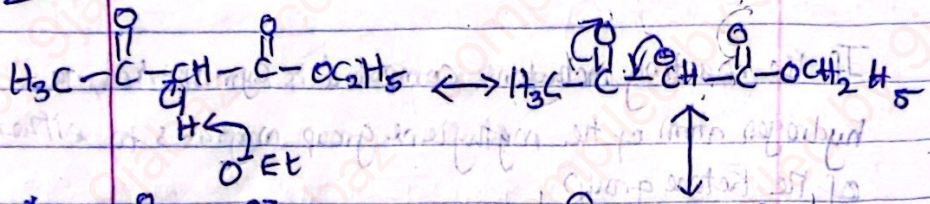
enol only one form

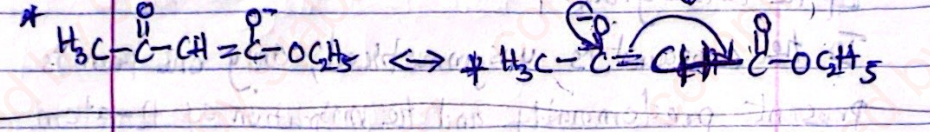
the other oxygen too, is electronegative, so it can only happen on the other side.

* Proton can be abstracted from both enol and ketone form, are the products obtained from both same or not?

When a molecule containing a active methylene group reacts with a strong base, the proton removal of (abstraction of proton) may take place from both keton and enol form. The resultant enolate form (a carbanion stabilized by an adjacent carbonyl group) obtained by resonance stabilization is the same in both cases.

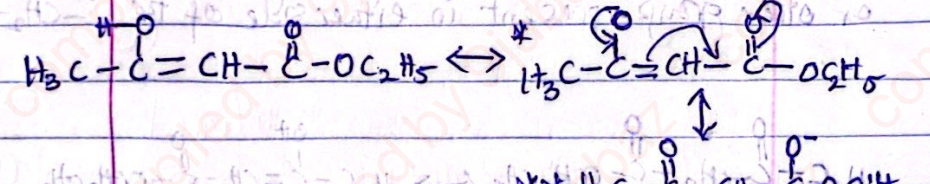
Ketone

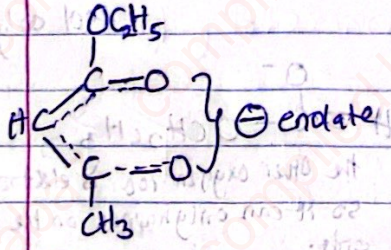




$EtONa \rightarrow EtO^- + Na^+$

Enol





18th April, 2026

Some other examples with reactive methylene groups

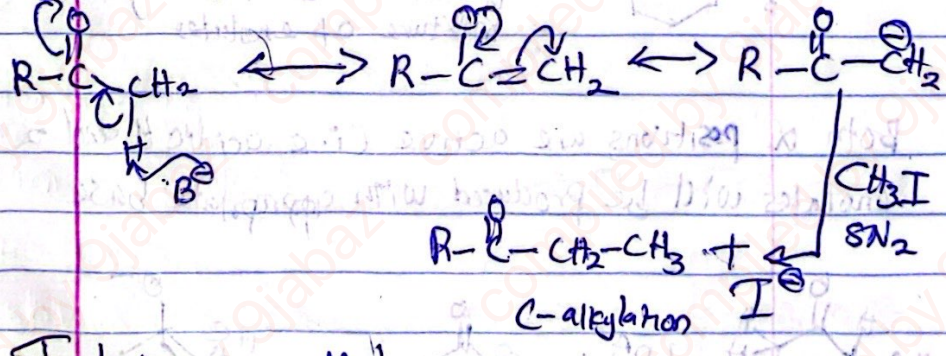
① $C_2H_5O-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OC_2H_5$ diethyl malonate

② $C_2H_5O-\overset{O}{\overset{\|}{C}}-CH_2-C\equiv N$ ethyl cyanoacetate

③ $C_2H_5O-\overset{O}{\overset{\|}{C}}-CH_2-N^{+}(=O)(-O^{-})$ ethyl nitroacetate

$NaNH_2$ been a stronger base can be used to perform reaction with reactive methylene groups with just one electron withdrawing groups

Alkylation of Enolate



In the presence of alkyl

$R-C(=O^{-})=CH_2 \xrightarrow{R'-X} R-C(-O-R')=CH_2$ O-alkylation

The enolate acts as a nucleophile. The resonance formulation of enolate anions shows that the negative charge is shared between an oxygen and a carbon atom. ①

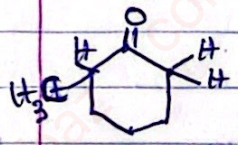
At which atom would the alkylation be faster?

It turns out that most enolates are better nucleophile at carbon. So, alkylation takes place faster at carbon than oxygen.

Limitation

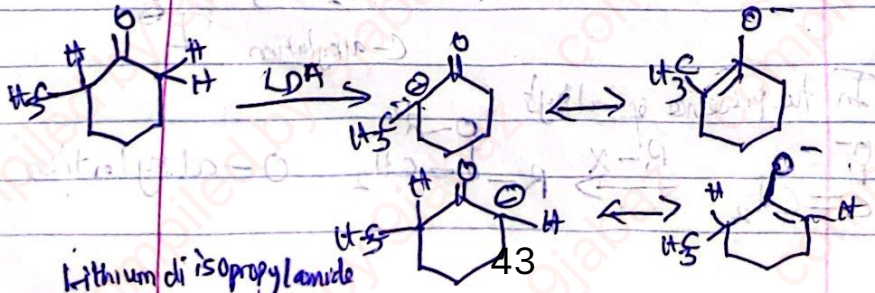
① We cannot a 3° alkyl halide due to steric hindrance

② 2-methyl cyclohexanone



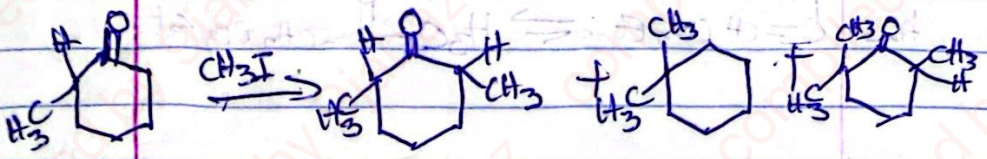
This compound has its α- and α'-H active. It thereby leads to mixture of enolates

Both α positions are active (i.e acidic H and 2 enolates will be produced with appropriate base



Lithium diisopropylamide

For many ketones, there are at least two (2) possible enolate as a result, mixtures are obtained in the alkylation



Important Examples

(1) Application in the synthesis of ethylacetoacetate

$CH_3-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OC_2H_5$

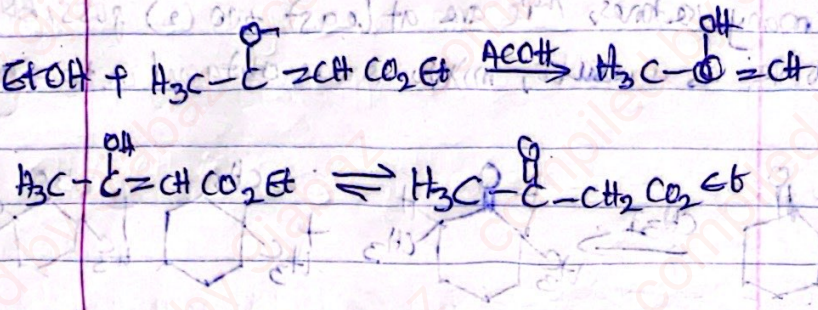
Ethylacetoacetate is the ethylesters of acetoacetic acid $CH_3\overset{O}{\overset{\|}{C}}-CH_2-COOH$. It is prepared by condensation of 2 molecules ethyl acetate in the presence of a base NaOEt. This is an example of Claisen condensation reaction

$$EtONa \longrightarrow EtO^- \; Na^+$$

$$EtO^- + H-CH_2CO_2C_2H_5 \rightleftharpoons EtOH + {}^-CH_2CO_2C_2H_5$$

$$H_3C-\overset{O}{\overset{\|}{C}}-OEt + {}^-CH_2CO_2C_2H_5 \rightleftharpoons H_3C-\overset{O^-}{\overset{|}{C}}(OEt)-CH_2CO_2Et$$

$$\rightleftharpoons H_3C-\overset{O}{\overset{\|}{C}}-\overset{H}{\overset{|}{C}}HCO_2Et + EtO^-$$



Properties of Ethyl acetoacetate (physical)

Properties of Ethyl Acetoacetate — P

It is a colourless, pleasant smelling liquid, with boiling Point 181°C and the reagent is sparingly soluble in water but readily soluble in alcohol (i.e ethanol) and ether. It is neutral to

Chem

(i) It behaves as a ketone and as an alcohol, (because of the presence of OH) — because it exhibit keto-enol tautomerism

The equilibrium mixture contains both forms but the percentage of the enolic form, 7.5% to show that the equilibrium contains both specie.

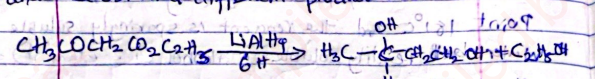
Reduction

In the presence Sodium amalgam ($NaHg$) and alcohol or hydrogen in lithium aluminium hydride ($LiAlH_4$) in the presence of hydrogen and pyridine.

The ketonic form forms β-hydroxybutyric ester and the equations of the reaction,

$$CH_3COCH_2CO_2C_2H_5 + 2H \rightarrow CH_3CHOHCH_2CO_2C_2H_5$$

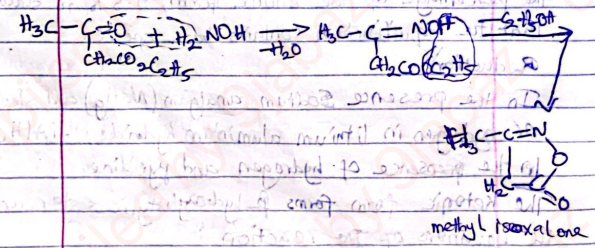
We can also carry this reaction in the absence of pyridine, and we obtain a different product



① Common reaction: Test for carbonyl

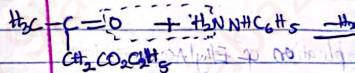
② Reaction with hydroxyamine

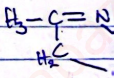
② Ketonic form forms an oxime which immediately uses a molecule of alcohol (ethanol) and forms methyl isoxazolone.



③ Reaction with phenyl hydrazine

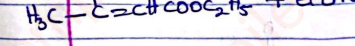
If forms phenyl hydrazone which us... ethanol and forms 3-methyl-1-phenyl...





Reactions Involving the Enol...

① Reaction with Na, or NaOEt ... of the reagent

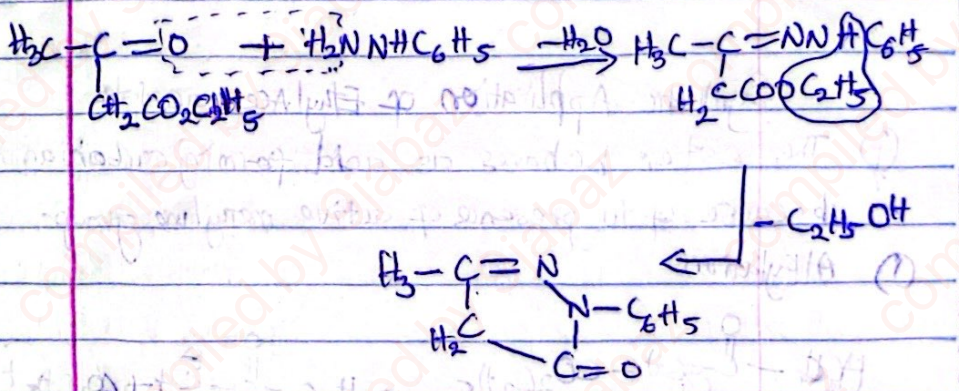


② Acetylation reaction

If happens in the presence

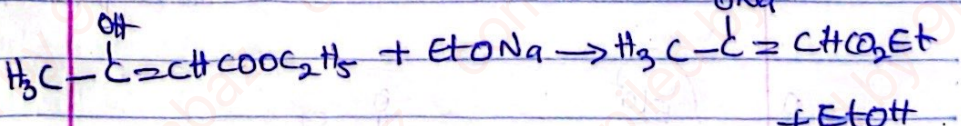
(b) Reaction with phenyl hydrazine

It forms phenyl hydrazone which uses a molecule of ethanol and forms 3-methyl-1-phenyl pyrazolone



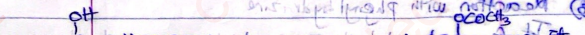
Reactions Involving the Enolate form

(1) Reaction with Na, or NaOEt to form sodio derivative of the reagent



(2) Acetylation reaction

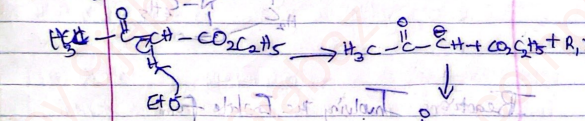
It happens in the presence of acetyl chloride

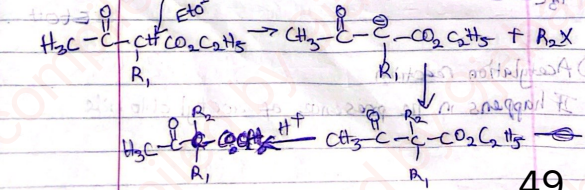


Synthetic Application of Ethyl Aceto acetate

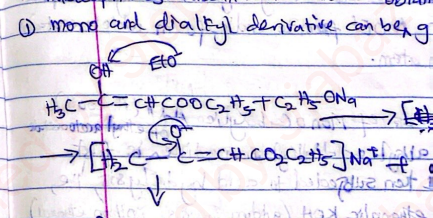
(1) The ester behaves as acid forming carbanion because of the presence of active methylene group.

(2) Alkylation

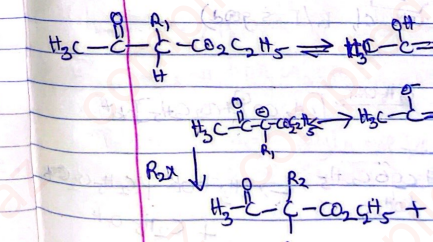




The carbanion is resonance stabilized and co
nucleophilic substitution reaction. obtain
(1) mono and dialkyl derivative can be g

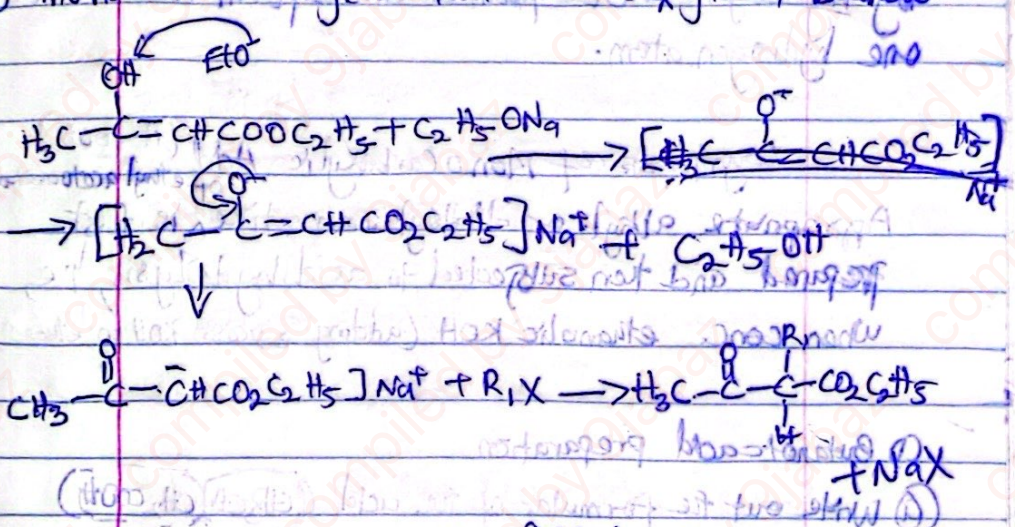


For the reaction to proceed, the form
the mono alkyl derivative must be
enol form.

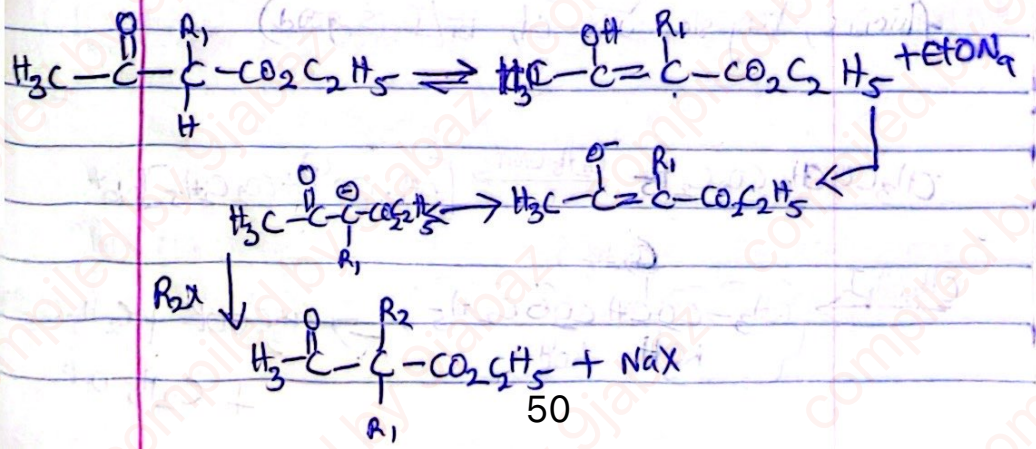


The carbanion is resonance stabilized and can undergo nucleophilic substitution reaction. obtained as

① mono and dialkyl derivative can be given



For the reaction to proceed, to form dialkyl derivative; the monoalkyl derivative must be converted to the enol form.



Both alkyl group cannot be simultaneously introduced in one single step because the hydrogen can only be displaced by hydrogen NaOEt from to enolic form which contains one hydrogen atom.

Synthesis of Monocarboxylic Acid ($R-COOH$)

Appropriate alkyl or dialkyl derivative of ethyl acetoacetate is first prepared and then subjected to acid hydrolysis, i.e, when conc. ethanolic KOH (adding excess KOH in ethanol)

(A) Butanoic acid preparation

(a) Write out the formular of the acid ($CH_3CH_2CH_2COOH$)

(b) Identify acetic acid nucleus

(c) The alkyl group attached to the acetic acid nucleus is introduced CH_3CH_2 CH_2COOH (almost impossible with fluorine, very slow with Cl, Br/I is good)

$CH_3COCH_2CO_2C_2H_5 \xrightarrow{C_2H_5ONa} [CH_3CO\overset{\ominus}{C}HCO_2C_2H_5]Na^+$

$\xrightarrow{CH_3CH_2I}$ $CH_3-CO-\underset{C_2H_5}{CH}-CO-C_2H_5 \xrightarrow[KOH]{KOH} CH_3COOK + C_2H_5-\underset{C_2H_5}{CH}-COOK$

$+ C_2H_5$

$C_2H_5CH_2COOH \xrightarrow{H^+}$ $CH_3CH_2CH_2CO$

24 Oct 26

2-ethylpentanoic acid Synthesis

Ethyl propyl acetic acid

$CH_3CH_2CH_2\underset{CH_2CH_3}{CH}COOH$

Synthesis

$CH_3COCH_2CO_2C_2H_5 \xrightarrow{EtONa} [CH_3C\overset{\ominus}{C}HCO_2$

$\xrightarrow{CH_3CH_2CH_2Br} CH_3COCH(C_3H_7)CO_2C_2H_5 \xrightarrow{Et}$

$CH_3CO\overset{\ominus}{C}(C_3H_7)CO_2C_2H_5 \xrightarrow{CH_3CH_2I} CH_3CO$

$\xrightarrow{KOH} CH_3COOK + CH_3CH_2CH_2$

$\xrightarrow{H^+} CH_3COOH + CH_3CH_2CH_2-\underset{C_2H_5}{\overset{H}{C}}-COOH$

Introduce the larger alkyl group before

$C_2H_5CH_2COOH \xrightarrow{H^+} CH_3CH_2CH_2COOH$

24/04/26

2-ethylpentanoic acid Synthesis

Ethyl propyl acetic acid

$CH_3CH_2CH_2\underset{\underset{CH_2CH_3}{|}}{CH}COOH$

Synthesis

$CH_3COCH_2CO_2C_2H_5 \xrightarrow{EtONa} [CH_3C\overset{\ominus}{O}CHCO_2C_2H_5]$

$\xrightarrow{CH_3CH_2CH_2Br} CH_3COCH(C_3H_7)CO_2C_2H_5 \xrightarrow{EtONa}$

$CH_3C(\overset{\ominus}{O})C(C_3H_7)CO_2C_2H_5 \xrightarrow{CH_3CH_2I} CH_3C(O)C(C_2H_5)(C_3H_7)CO(OC_2H_5)$

$\xrightarrow{KOH} CH_3COOK + CH_3CH_2CH_2-\underset{\underset{CH_2H_5}{|}}{C}HCOOK + CH_3CH_2OH$

$\xrightarrow{H^+} CH_3COOH + CH_3CH_2CH_2-\underset{\underset{C_2H_5}{|}}{\overset{H}{C}}-COOH$

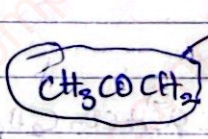
Introduce the larger alkyl group before the smaller one in dialkyl addition (because of steric hinderance)

Synthesis of Ketone

Ketone can be synthesized via ethyl acetoacetate provided it contains the group, CH_3CO-

Steps

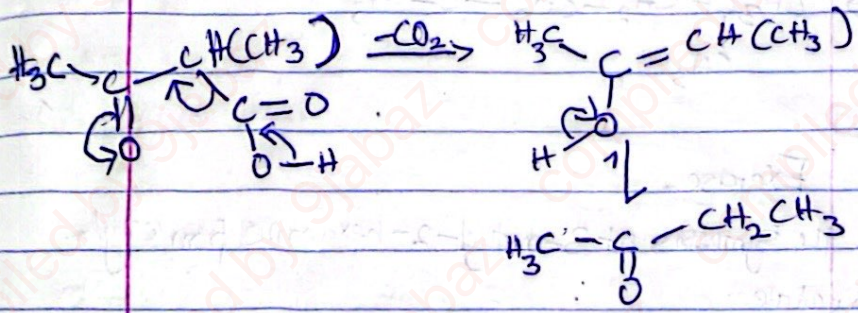
(1) Write out the formula of the ketone
(2) Within the formula of the ketone, identify the acetone nucleus.
(3) Alkyl group attached to the nucleus (acetone needed) is/are introduced to the ester one at a time
(4) Carry out Kenoic hydrolysis using aqueous or dilute KOH



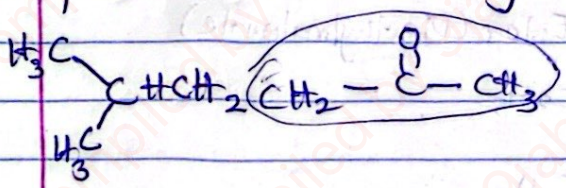
Preparation of $CH_3COCH_2CH_3$

$$CH_3COCH_2CO_2C_2H_5 \xrightarrow{EtONa} CH_3CO\overset{(-)}{C}HCO_2C_2H_5 \xrightarrow{CH_3Br} CH_3COCH(CH_3)CO_2C_2H_5 \xrightarrow{dil.\ KOH} CH_3COCH(CH_3)COOK \xrightarrow{H^+} CH_3COCH(CH_3)COOH \xrightarrow{-CO_2} CH_3COCH_2CH_3$$

Mechanism of Decarboxylation

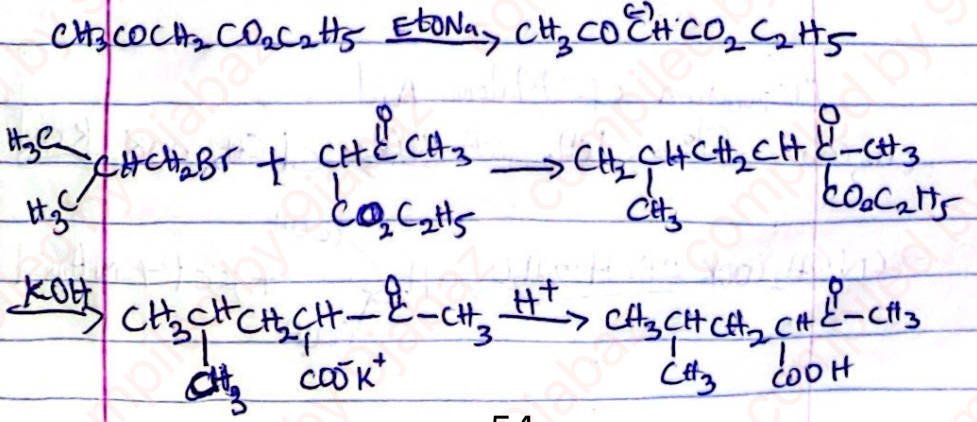


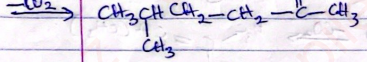
Preparation of 5-methyl-2-hexenone



$CH_3COCH_2CO_2C_2H_5$

In order to prepare the ketone above by ethylacetate synthesis, isobutylbromide must be made use of

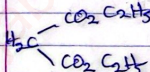




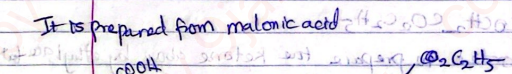
Exercise

Outline the synthesis of 3-methyl-2-hexanone from ethyle acetoacetate

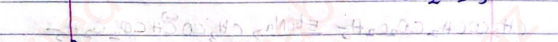
Malonic Ester (Dimethylmalonate)

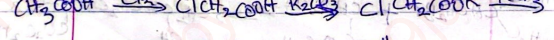


It is prepared from malonic acid

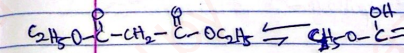


Preparation of Malonic Acid

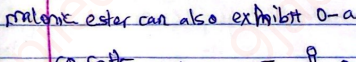


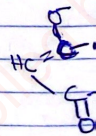


In presence of 2 carbonyl groups, on side of methylene group except neg effect. The effect added to the form stabilized anion and makes the H o acidic. The compound exists in the follow but contains a minute quantity of enol mixture



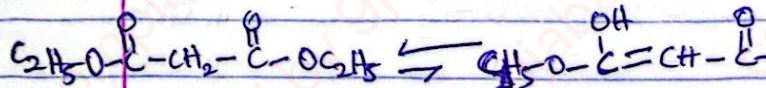
malonic ester can also exhibit O-a



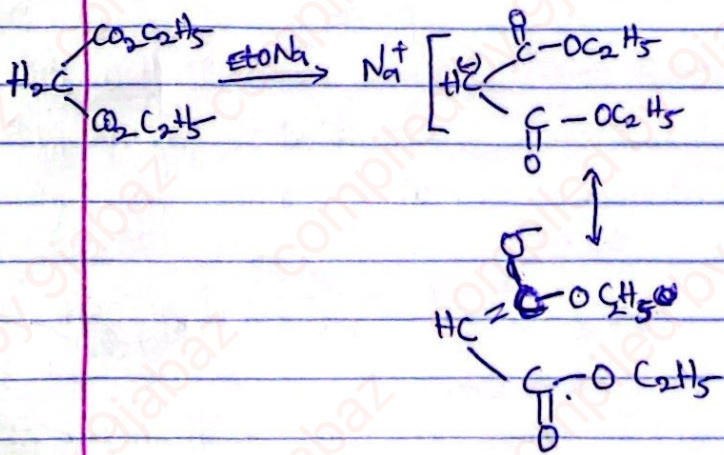


The anion acts as a nucleophil nucleophilic substitution reacti

In presence of 2 carbonyl groups, one each on either side of methylene group exert -ve inductive effect. The effect added to the formation of resonance stabilized anion and makes the H of the methylene group acidic. The compound exists in the following keto-enol form but contains a minute quantity of enol form in the equilibrium mixture



malonic ester can also exhibit O-alkylation & C-alkylation



The anion acts as a nucleophile and can participate in nucleophilic substitution reaction

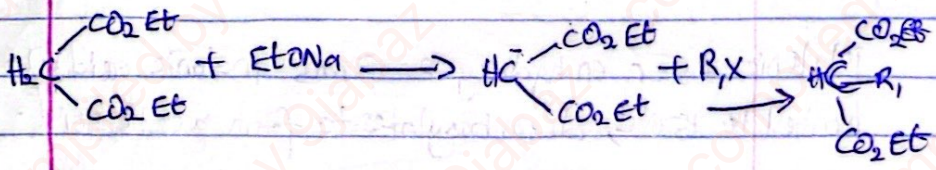
25th April, 2026

KOH in ethanol attack carbonyl

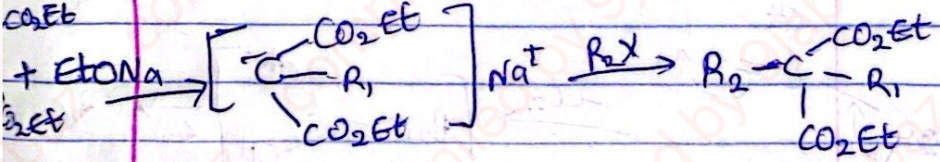
KOH dilute attack carbonyl ester

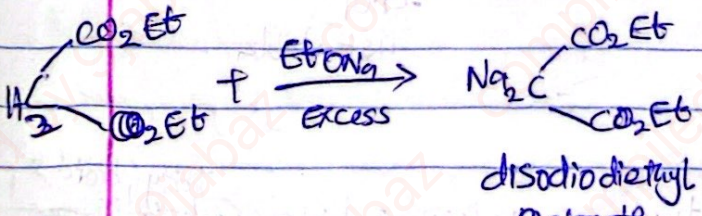
Example of nucleophilic substitution reaction

(i) Reaction with alkyl halide (alkylation)



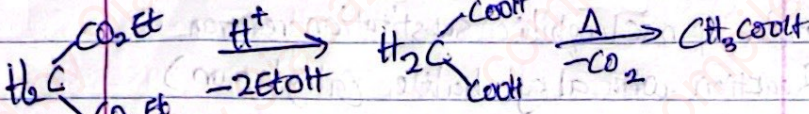
Mono alkyl ester contains an active hydrogen and can undergo further nucleophilic substitution forming dialkyl ester.





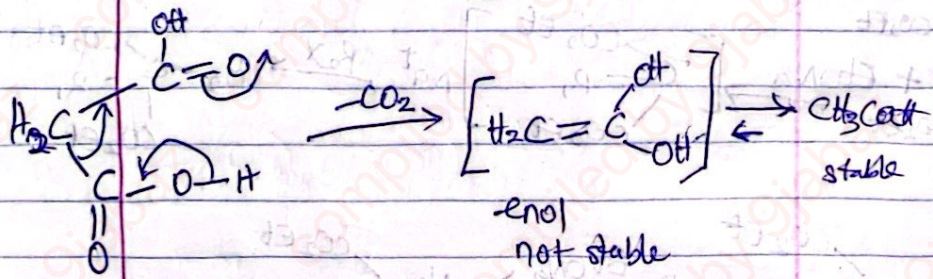
Synthetic Application

Synthesis of Monocarboxylic acid



Malonic ester on hydrolysis forms malonic acid which heated to 150°C, decarboxylates to form acetic acid.

Mechanism of Decarboxylation

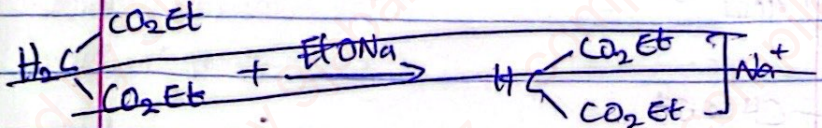


Using this method, we can prepare higher ~~Carboxylic acid~~ fatty acids as follows;

(i) Write out the structural formulae of the acid required

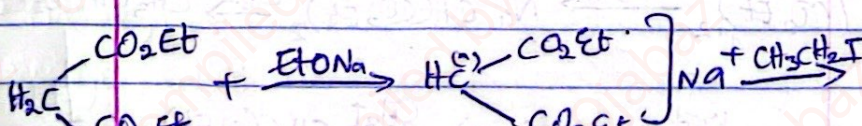
(ii) Identify acetic acid nucleus from the structural formula of the acid required.

1) Prepare Sodio malonic, and treate it with an approxiate alkyl halide followed by ~~acid~~ acid hydrolysis.



Synthesis of Butanic Acid

(1) $CH_3CH_2CH_2COOH$



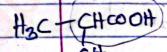
$$C_2H_5CH(CO_2Et)_2 \xrightarrow[-2EtOH]{KOH} C_2H_5CH(COOK)_2$$

Ethyl malonic ester

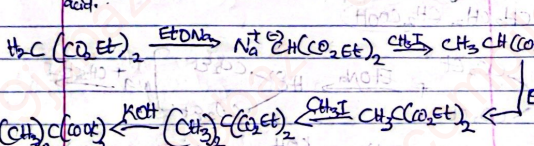
$$\xrightarrow{H^+} C_2H_5CH(COOH)_2 \xrightarrow[-CO_2]{\Delta,\ 150-200^\circ C} C_2H_5CH_2COOH$$

2) Synthesis of α-branched substituted fatty acids can be prepared by first converting monoalkyl malonic ester to dialkyl malonic acid by treatment with NaOEt, then alkyl halide. Dialkyl ester form obtained when ~~you~~ refluxed with

KOH and acidified HCl to form dialkyl malonic acid which decarboxylate on heating and form dialkyl acid



dimethyl acetic acid.

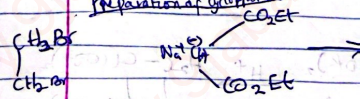


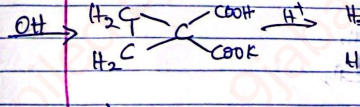
This reaction indicates where two alkyl groups are the same, the dialkyl derivatives is obtained in one operation by taking 2 moles of NaOEt ~~and~~ per mole of diethylmalonate and ~~heating in dioxane~~ treat the mixture with excess alkyl halide

(3) Synthesis of Cyclic Compounds

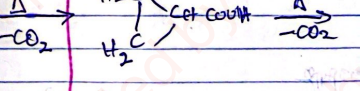
Alicyclic compounds may be prepared between certain dihalogen derivatives and Sodium malonic ester

Preparation of cyclopropane





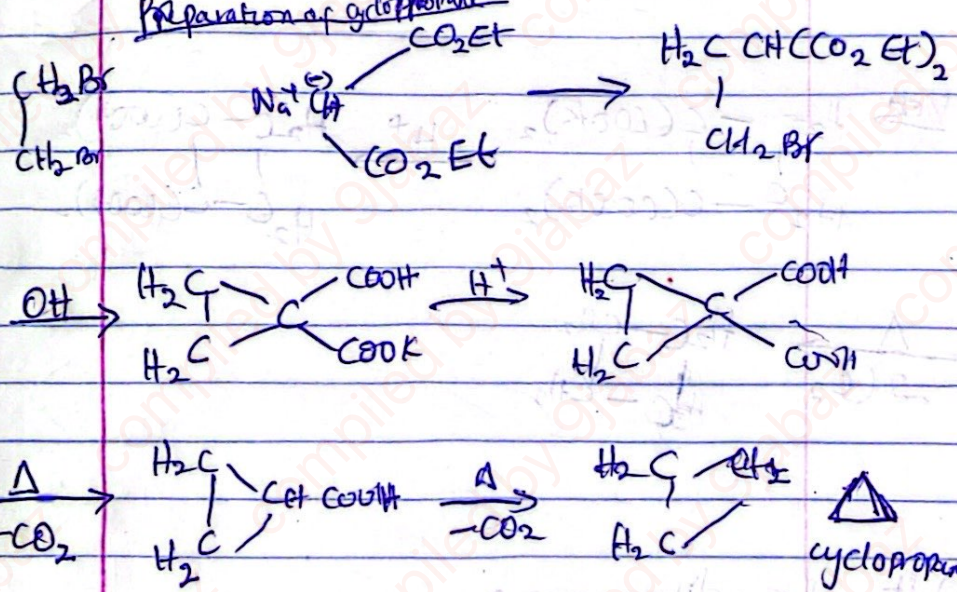
Preparation of cyclobutane



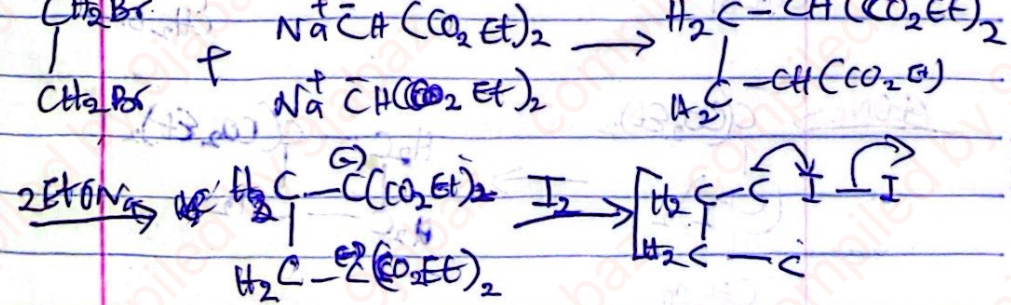
(5) Synthesis of Cyclic Compounds

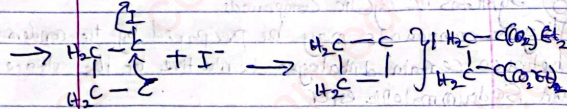
Alicyclic compounds may be prepared by the condensation between certain dihalogen derivative of the alkane and Sodium malonic ester

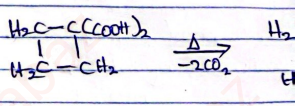
Preparation of cyclopropane

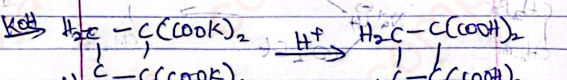


Preparation of cyclobutane

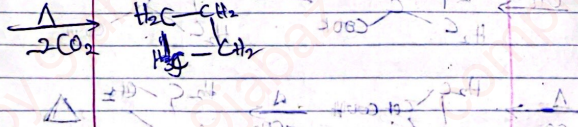




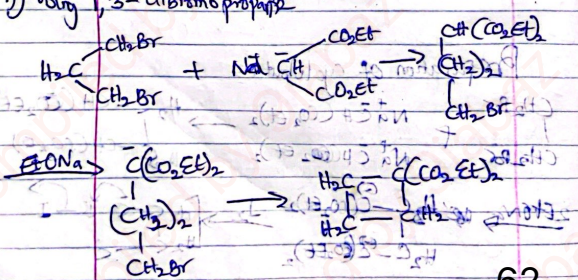


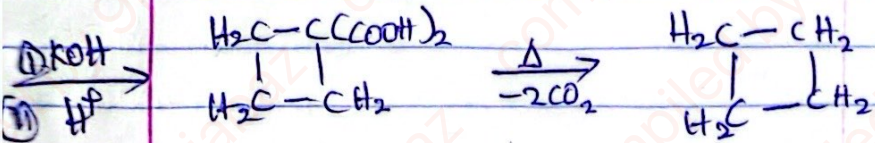


By using appropriate dihalogen derivati... undergo suitable conditions, it is possible ... containing 3–7 carbon atoms.



b) Using 1,3-dibromopropane





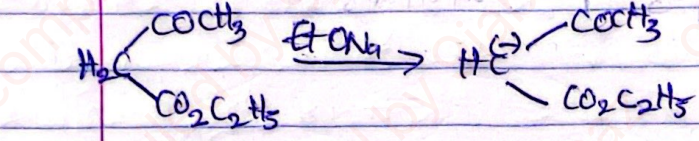
By using appropriate dihalogen derivative of the alkane undergo suitable conditions, it is possible to prepare rings containing 3–7 carbon atoms.

Alicyclic compounds

Preparation of Cyclohexane (from ethylacetoacetate)

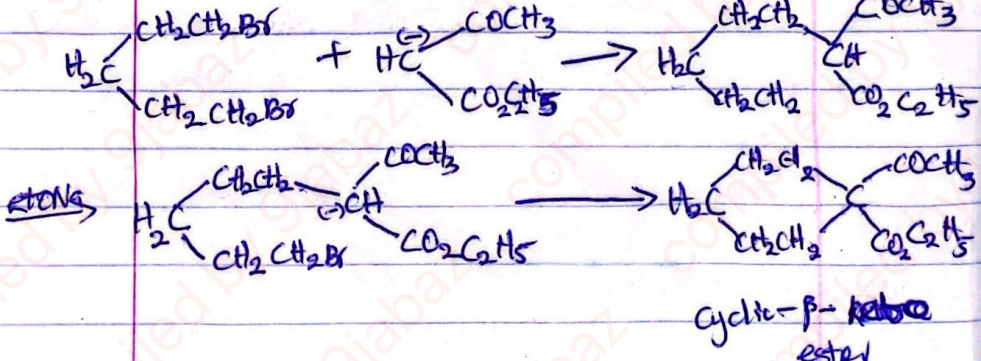
① formation of enolate ion

Ethylacetoacetate reacts with a strong base, i.e $Na^+OCH_2CH_3$ in ethanol. The base selectively deprotonates the acidic methylene to form a stable enolate ion



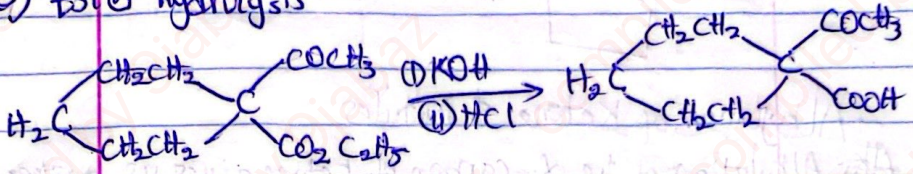
② Dialkylation

Treat the enolate ion with 1,5-dibromopentane or 1,5-dibromoalkane in this case. Intramolecular displacement of the bromides results in the formation of the cyclic-β-keto ester



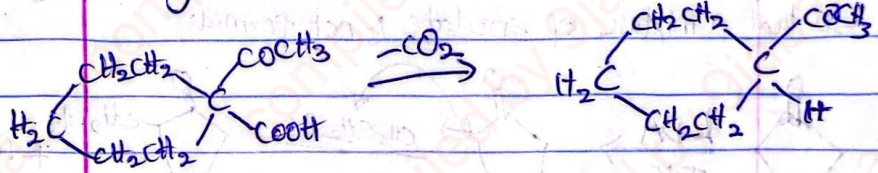
~~Treat the~~

③ Ester hydrolysis



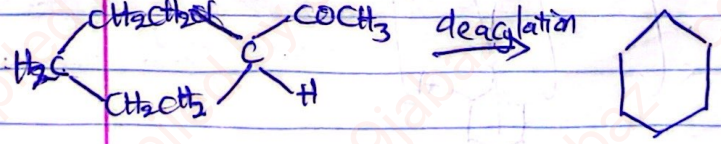
Reflux the cyclic ester with dilute acid, this hydrolyses the ester group to carboxylic group creating a cyclic β-ketoacid

④ Decarboxylation



~~Heat~~ the resulting β-keto acid, this promotes loss of CO_2 leaving behind an alicyclic methyl ketone

Acetoacetic acid or ethyl acetoacetate method can Prepare 3, 5, 6 & 7 Carbon ring, except 4, because 4 will lead to formation of tetrahydropyran

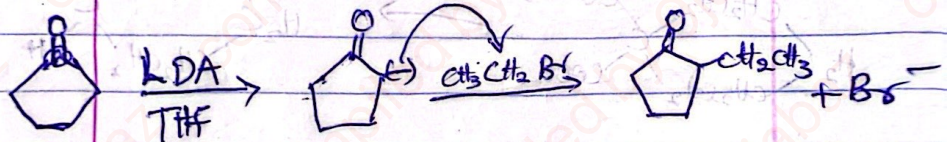


4-C-atom rings will lead to tetrahydrofuran

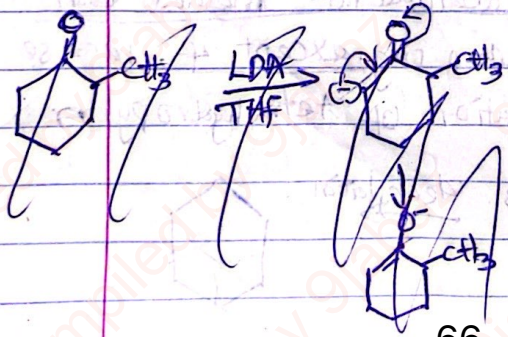
Alkylation of Ketone & Nitriles

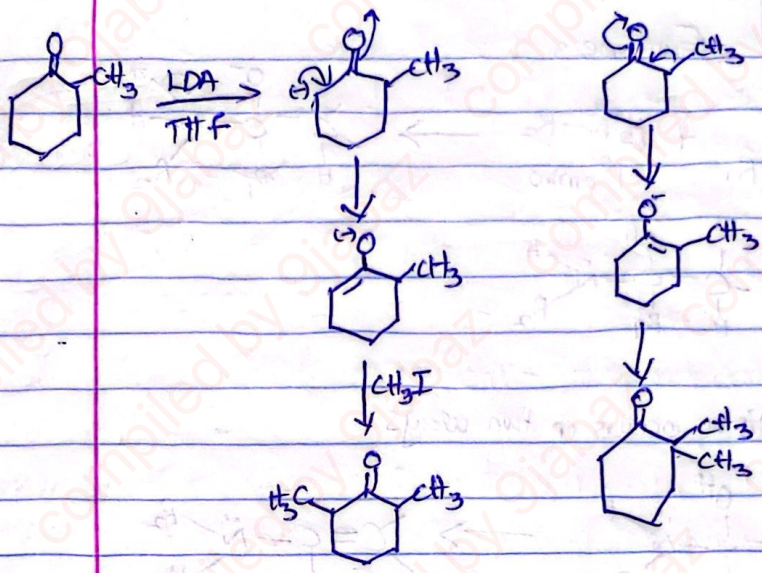
Alkylation of the α-carbon of ketone gives us another way to form a new C–C bond. The alkylation is carried out by removing a carbon from the α-carbon with a strong base such as LDA (lithium diisopropyl amide) $LiN[CH(CH_3)_2]_2$ or $NaNH_2$ (sodium amide)

This procedure works best with ketone that are symmetrical so that a mixture of enolate is not formed.



But if the ketone is unsymmetrical



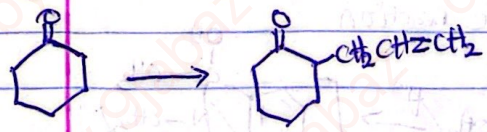


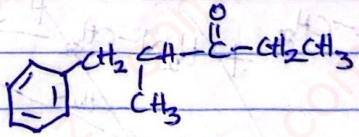
$CH_3CH_2CH_2C{\equiv}N \xrightarrow[THF]{LDA} CH_3CH_2\underset{\underset{CH_2CH_3}{|}}{CH}C{\equiv}N$

CH_3CH_2I

Exercise

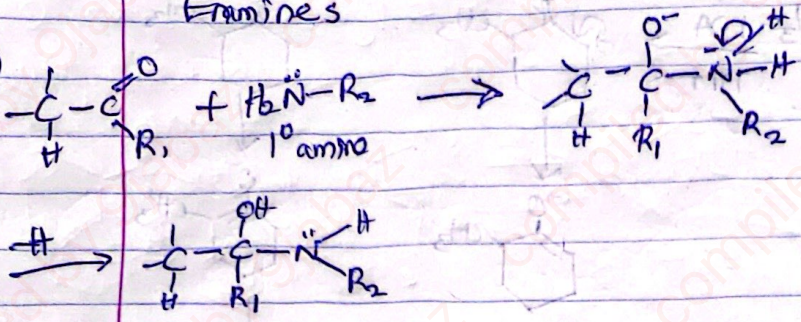
How could each of the following compound be prepared from the given starting material.

(i) 

(ii) $CH_3CH_2\overset{O}{\overset{\|}{C}}-CH_2CH_3$ 

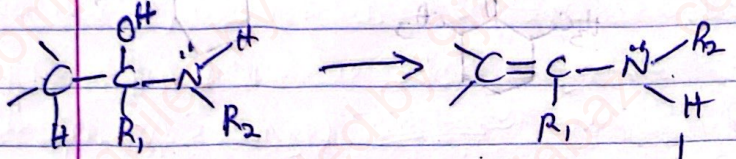
Eramines

(I)



Dehydration occurs in two ways

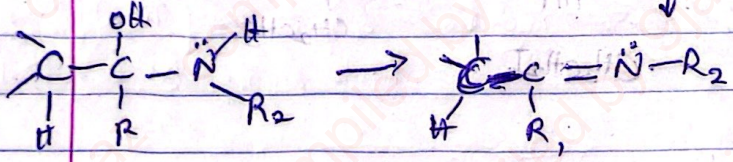
(II)



Enamine ↑

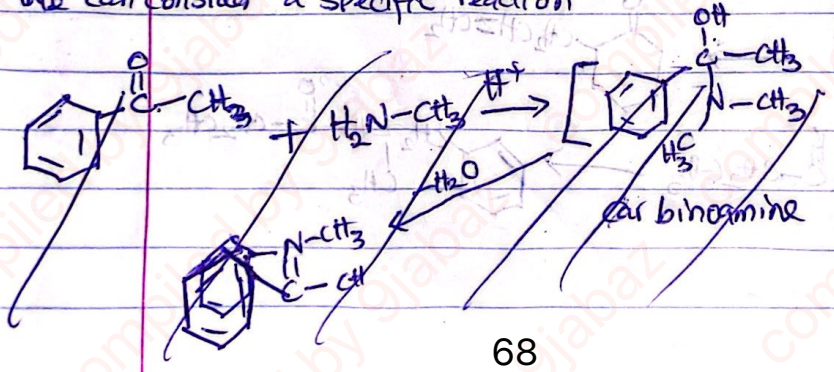
enamine ⟷ imi
tautomerism

(II)

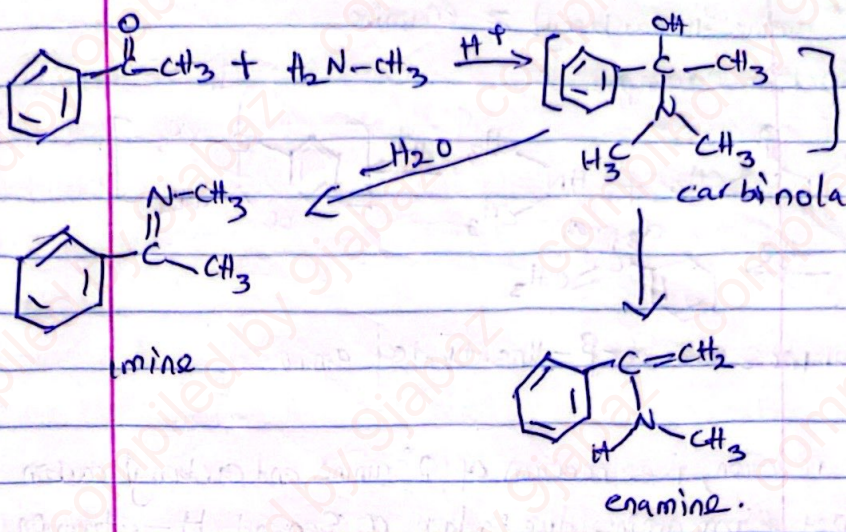


imine

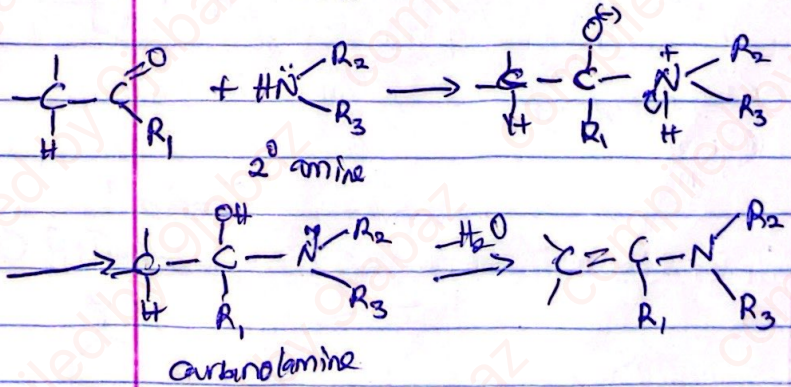
We can consider a specific reaction



carbinoamine

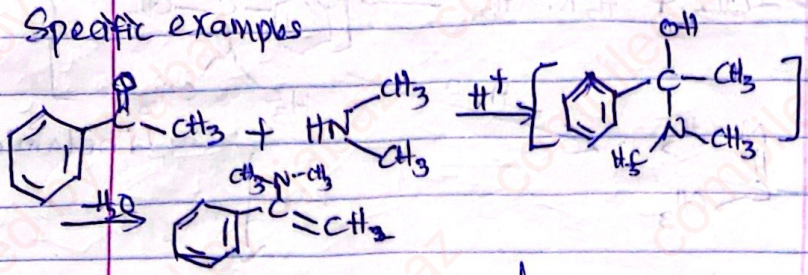


In ~~long~~ case, the reaction of 1° amine, carbonyl compound, ketone and aldehyde, enamine-ketone tautomerism is possible and the equilibrium lies on the imine side, because C=N bond is most stable than the C=C bond.



2° amine + carbonyl = enamine

Specific examples



Examples are α-β-Unsaturated amine

* The reaction, i.e. reaction of 2° amine and carbonyl carbon cannot form amine due to lack of second H-atom on Nitrogen on 2° amine, ~~This is~~ So we have an alkene, this special alkene is called enamine. The word is derived from ~~the~~ -ene used from the suffix alkene and the word amine from amine

alkene + amine

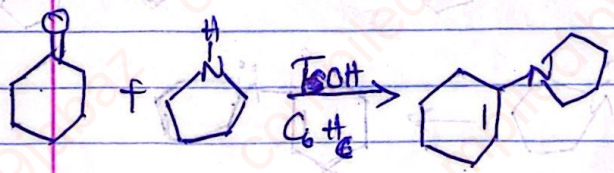
Enamine are reffered to α–β– unsaturated amine and their most common methods of Preparation is their reaction between a carbonyl compound with contains at least one α–H and 2° amine

Note

(1) Enamine derived/obtained from ketones are more stable than those obtained from aldehyde.

(2) Enamine derived from acyclic 2° amine are less stable than those from cyclic 2° amines. Example of cyclic 2° amines are pyrollidine and piperidine.

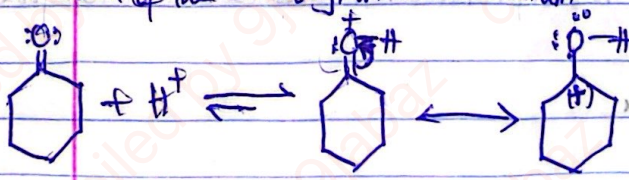
Reaction between cyclohexanone and pyrollidine



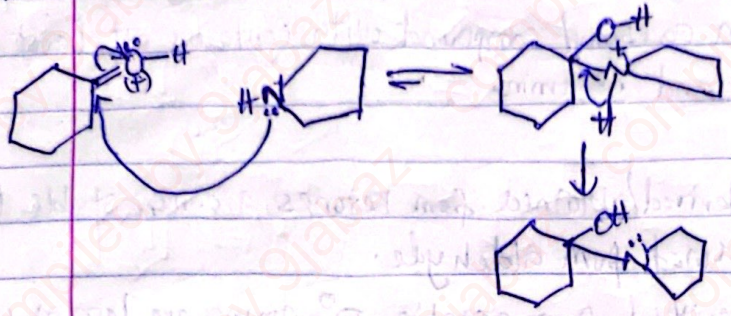
N–cyclohexenopyrollidine

Mechanism (Cyclohexanone)

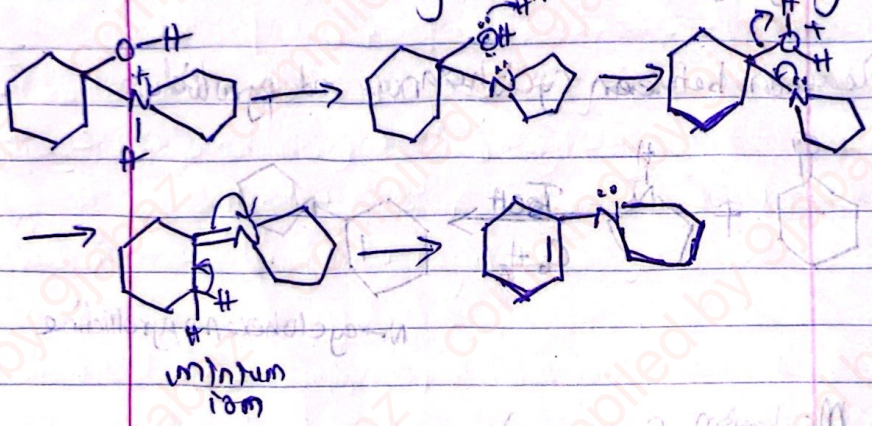
(1) Protonation of the Carbonyl in acidic medium



(2) Pyrrolidine undergoes nucleophilic addition to carbonyl to give a carbinoamine

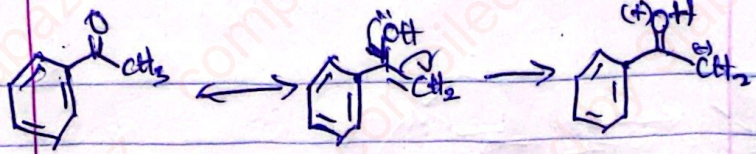


(3) The carbinoamine dissociates by loss of water. This dissociation is assisted by lone pair donation of Nitrogen.

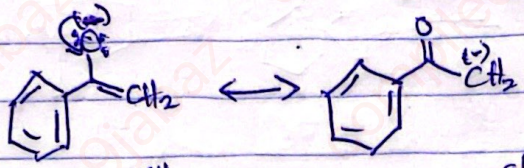


* The iminium ion is deprotonated in the direction to give a C=C

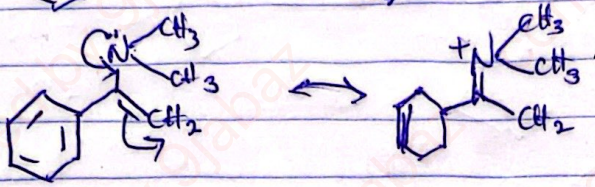
Enol



Enolate ion.



Enamine



Enamines are closely related to enols and enolate ion, Ketone exists in solution in equilibrium with the enol tautomerism

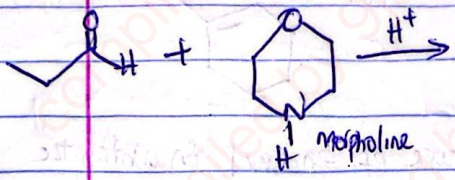
* Enolate ion exists as a resonance hybrid in which the -ve charge resides primarily on the carbonyl oxygen of α-C.
* Charged delocalization occurs in enamine in which the α-Carbon bears the formal negative charge

* In all of these compounds, a lone pair of electrons is conjugated in π-systems of the C=C bond. These interactions leads nucleophilic character to the α-carbon atom in each case.
However, there are significant difference between these types of nucleophilic reagents

(1) N is a better electron pair donor than oxygen, as a result, an enamine is more nucleophilic than phenol.

(2) Enamines being a neutral molecules are however less nucleophilic than enolates which are amines

Exercise: Draw the structure of the enamine that can be formed in these reactions.



(2) Write the structure of the carbinoamine intermediate and the enamine product formed in the reaction of each of the following

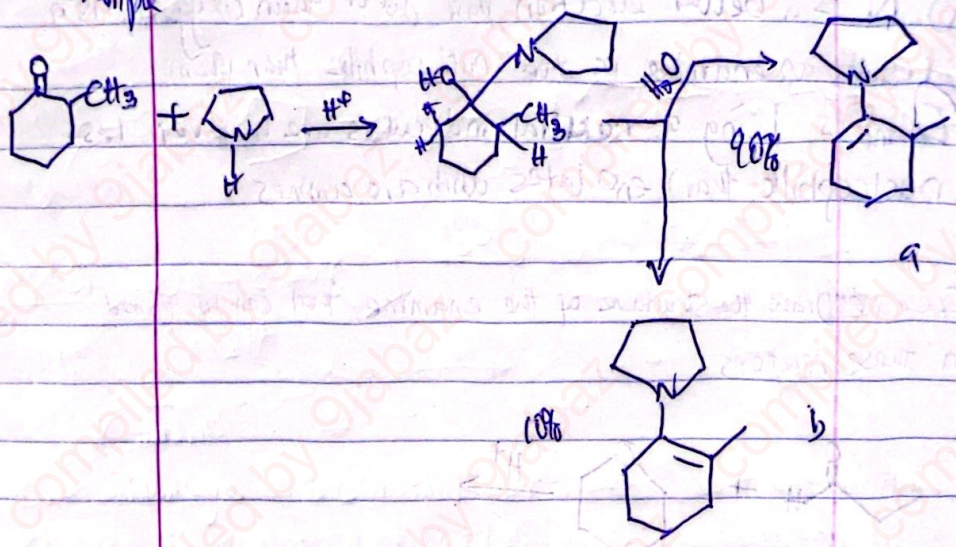
(a) propanal + diethylamine

(b) acetone + piperidine

Two enamine can be formed in an unsymmetrical ketone which can react two side from the carbonyl

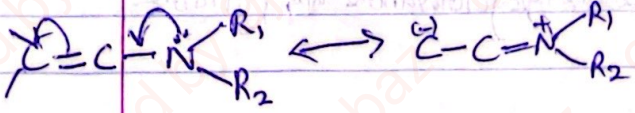
Eg Reaction of 2-methylcyclohexanone and pyridine

Example



The reaction produces a mixture of enamel in which the less substituted isomer will dominate, this is because an enamine is stabilized by the interaction of the alkene π-system, steric interaction of the methyl group of the cyclohexyl group and the methylene group of pyrrolidine ring reduces the extent of the conjugation in ~~most~~ the more substituted case.

Alkylation of Enamine



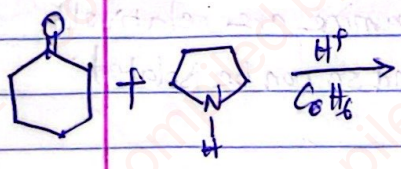
The enamine can be alkylated at the nucleophilic carbon

ly reactive alkyl halides. The product of alkylation is an iminium ion which is readily hydrolyzed to regenerate the carbonyl group.

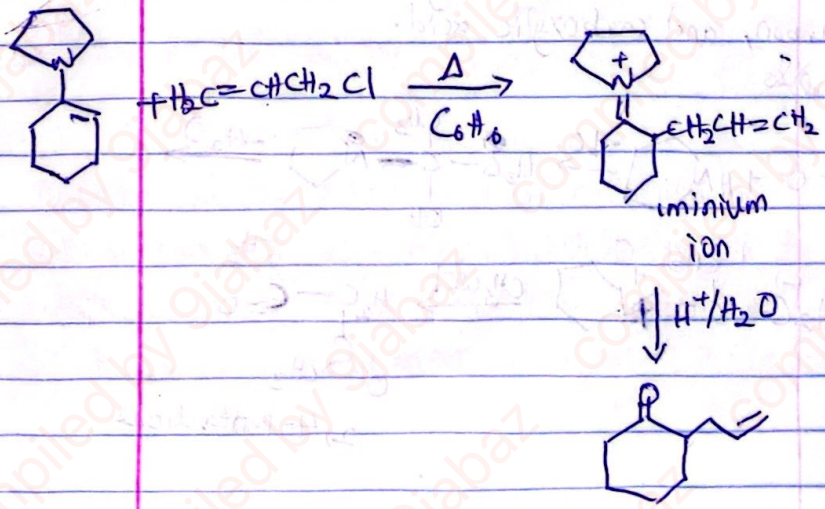
The following are examples of reactive alkyl halides;

1° allylic and benzylic halide, α-halo ether and α-halo nitrile, acyl chloride, α-β-unsaturated nitriles

Best yield are obtained with reactive halides like benzyl and allyl halides to halo ester and halo ketone



N-cyclohexenopyrollidine



2-allylcyclohexanone

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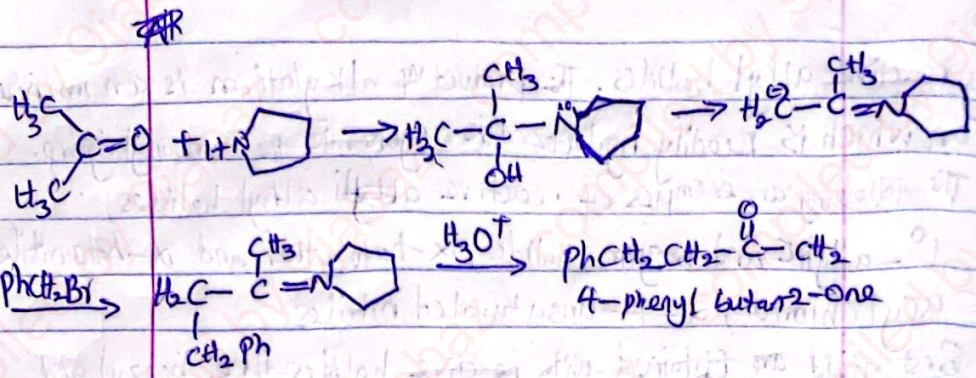


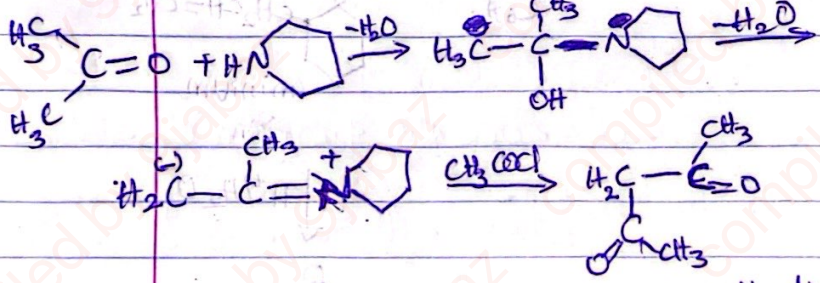
Comment:

One advantage of this method over that of direct action the ketone is that mono substituted enamine are relatively difficult to alkylate further and so can be isolated

Acetylation Of Enamines

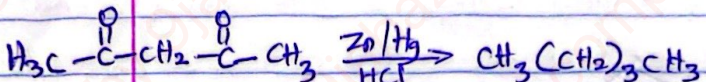
This particular reaction can give substituted ketone, hydrocarbon, and carboxylic acid.

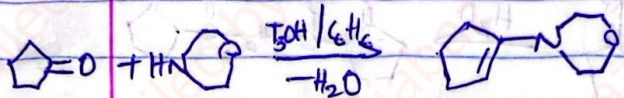
Examples

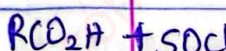


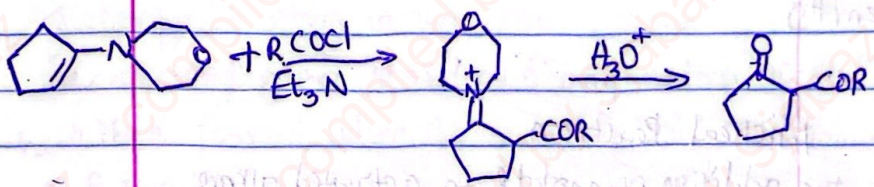
2, 4-pentadione

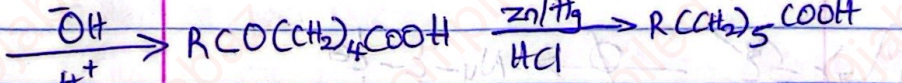
Penta-2, 4-dione can be reduced with Zn amalgam Zn/Hg and HCl to get the hydrocarbon



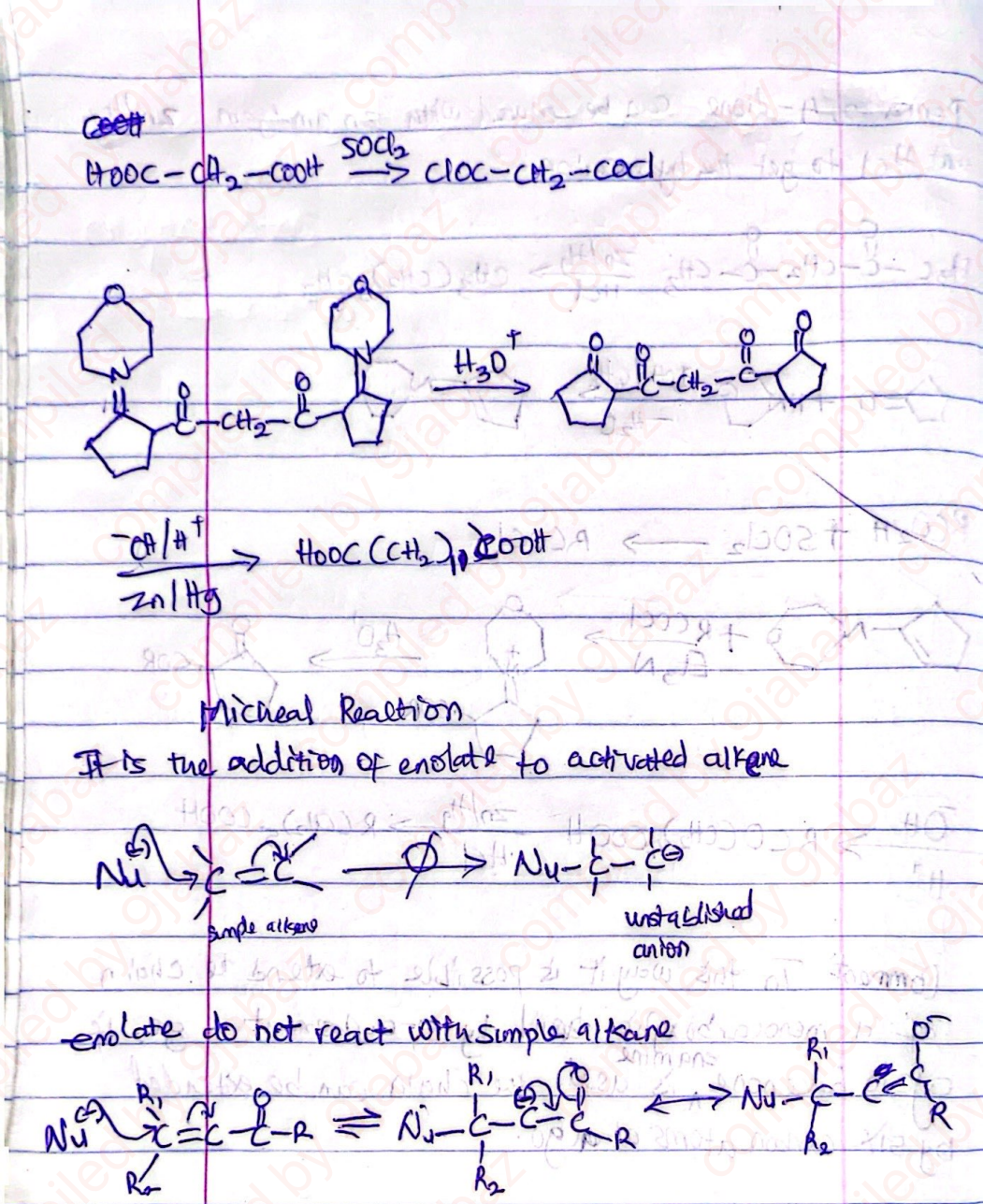








Comment: In this way it is possible to extend the chain of a monocarboxylic acid by 5-carbon at a go, if cyclohexenone, enamine is used, the chain can be extended by six carbon atoms at a go.

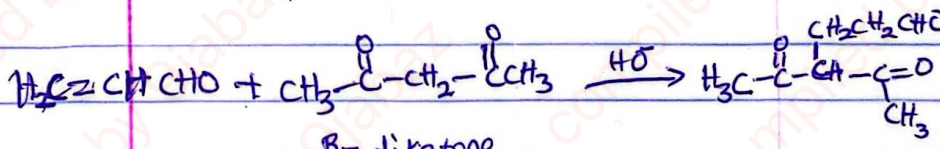

HOOC-CH2-COOH
SOCl2
ClOC-CH2-COCl
H3O+
-CH/H+
Zn/Hg
HOOC(CH2)10COOH
Micheal Reaction
It is the addition of enolate to activated alkene
Nu
simple alkene
Nu-
unstabilised anion
enolate do not react with simple alkene
R1
R2
R

Enolate will not react with simple alkene they only do so if the C=C is conjugated to an electron withdrawing group (i) C=C are unreactive towards nucleophile (enamine) because the addition require formation of an unstabilized anion

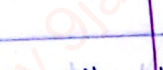
(ii) The enolate and many nucleophiles reacts or add easily to the C=C of α,β unsaturated carbonyl compounds In this case, the addition will form an ion that is stabilized and delocalization of the charge unto the electronegative atom in this case, oxygen.

The carbonyl group stabilizes any anion no matter how it is formed, when the specie adding to the α,β unsaturated compound is an enolate, the rxn is called micheal reaction

The enolate that works best in micheal reaction are β-diketone, β-diesters, β-ketoesters and β-ketonitriles,



β-diketone



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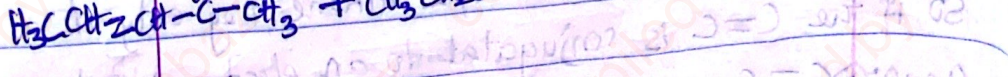
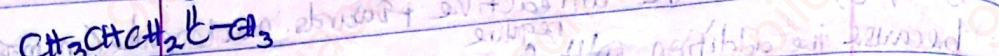


β-Ketonitrile

A wide variety of α-β-unsaturated carbonyl compounds undergo Micheal reactions All these reactions take place by the same mechanism

Malonic ester & mesityl oxide →

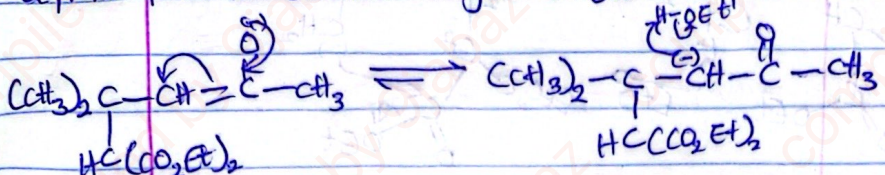


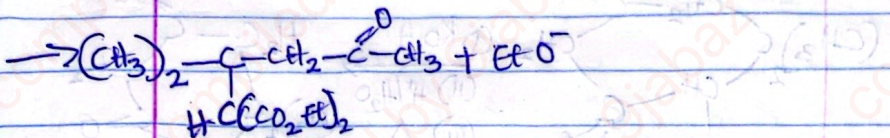
Mechanism

(1) A base removes a proton of α-carbon from the nucleophile

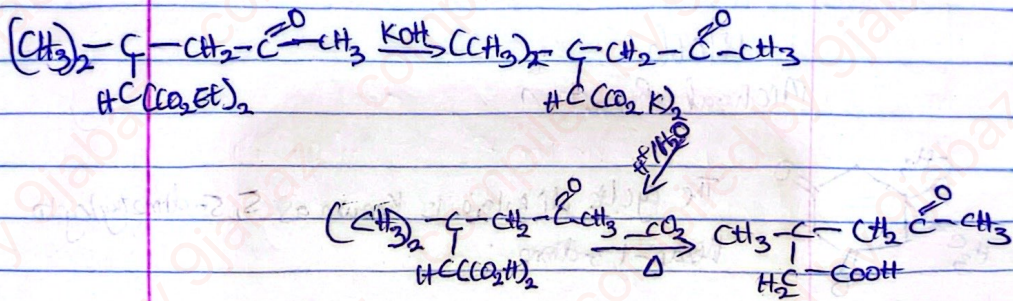
(2) The enolate adds to the β-carbon of an α,β-unsaturated carbonyl compounds

(3) The intermediate formed in the nucleophilic addition step abstracts a proton from the solvent (ethanol) to give the observed product

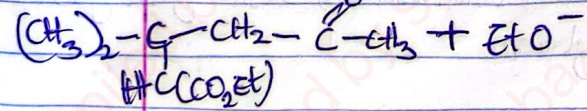


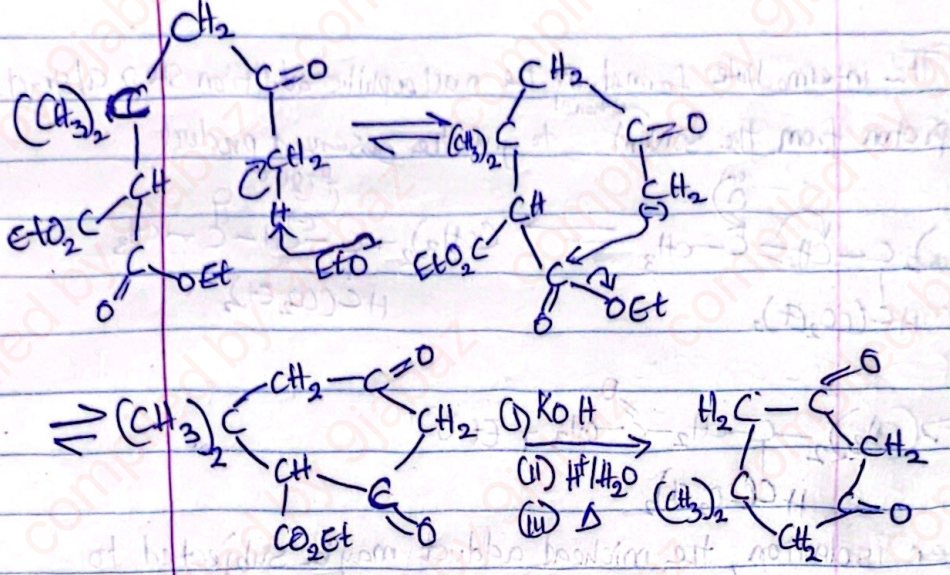


After isolation, the micheal adduct may be subjected to ester hydrolysis and decarboxylation to give 5-ketone acid



The complication is the formation of side reactions and formation of by-product knew as Dimedon





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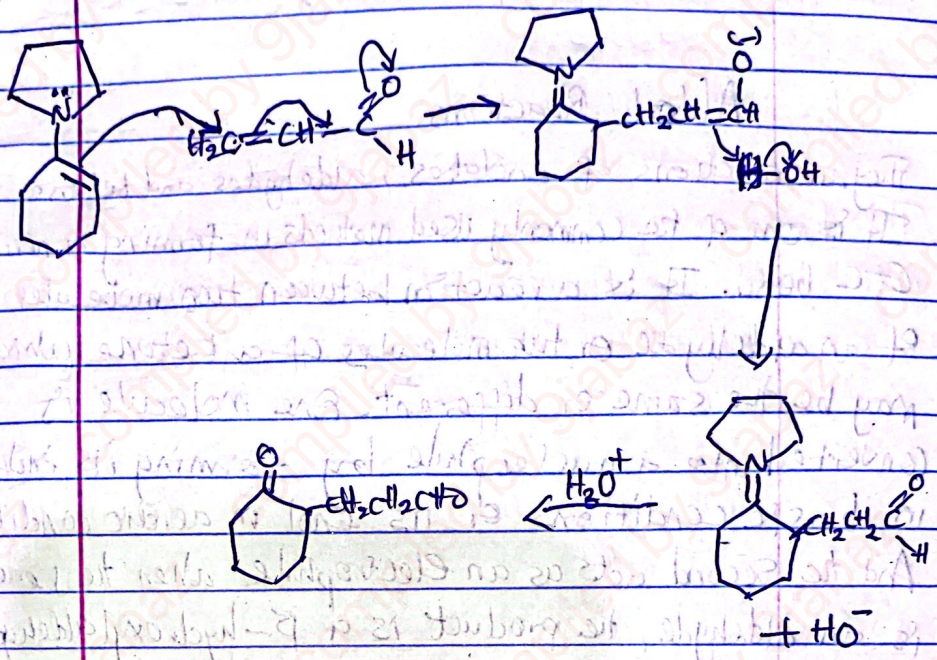
Micheal Reaction

The cyclic diketone is known as 5, 5-dimethylcyclohexan-1,3-dione.

The molecule is formed as a by product reaction of diethyl malonate and mesityl oxide through a micheal addition reaction followed by intramolecular Claisen condensation, basic hydrolysis and finally decarboxylation.

Stork – Enamine Reaction

Enamine can be used in placed of enolate in michael reaction, when an enamine is used as a nucleophile, the reaction is called a stork-enamine reaction

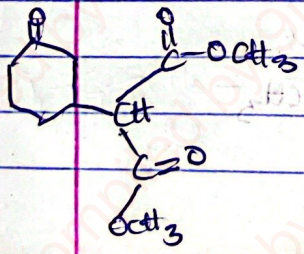


Exercise

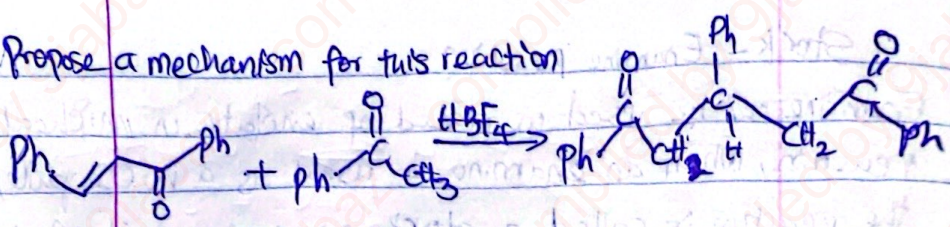
What reagent would you use to prepare the following compounds:

(1) $CH_3C(=O)CH_2CH_2CH(COOCH_2CH_3)_2$

(2)



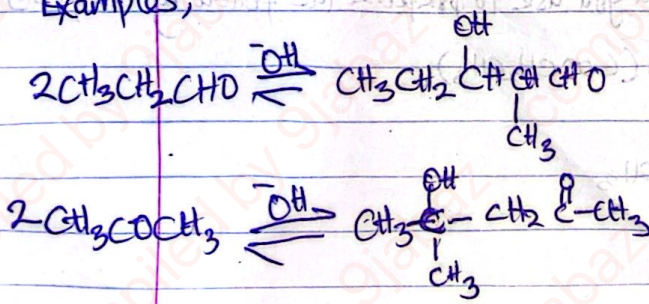
Propose a mechanism for this reaction



Aldol Reactions

They are reactions of enolates, aldehydes and ketone. It is one of the commonly used methods in forming a new C-C bond. It is a reaction between two molecules of an aldehyde or two molecules of a ketone which may be the same or different. One molecule is converted into a nucleophile by forming its enolate in basic conditions or its enol in acidic conditions. And the second acts as an electrophile when the reactant is an aldehyde, the product is a β-hydroxylaldehyde, ketone gives β-hydroxyl ketone

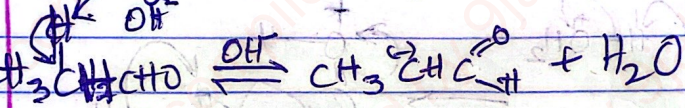
Examples;



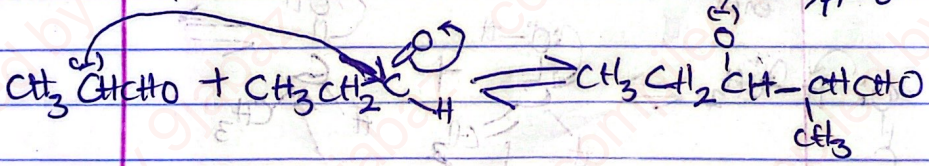
The resulting equilibrium lies to the right for many aldehydes and to the left for most ketone.
β-hydroxyl aldehyde is called an aldol because it contains both an aldehyde and alcohol function.
-al from aldehyde, -ol from alcohol. This C–C bond forming reaction is called aldo addition.

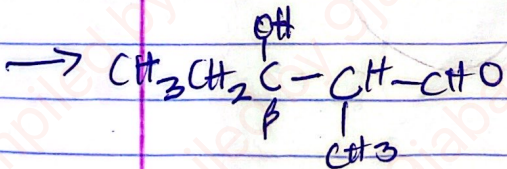
Mechanism of the Reaction

(1) Enolate is formed by deprotonation of α-carbon (either aldehyde or ketone).

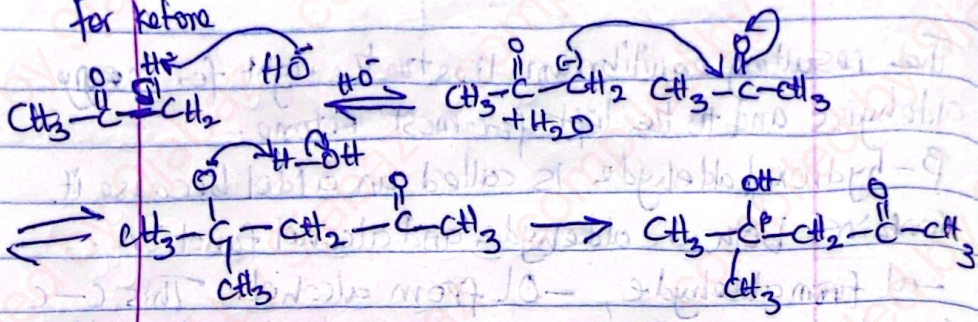


(2) Nucleophilic addition of the enolate to the carbonyl group. This forms the new C–C bond to give alkoxide ion

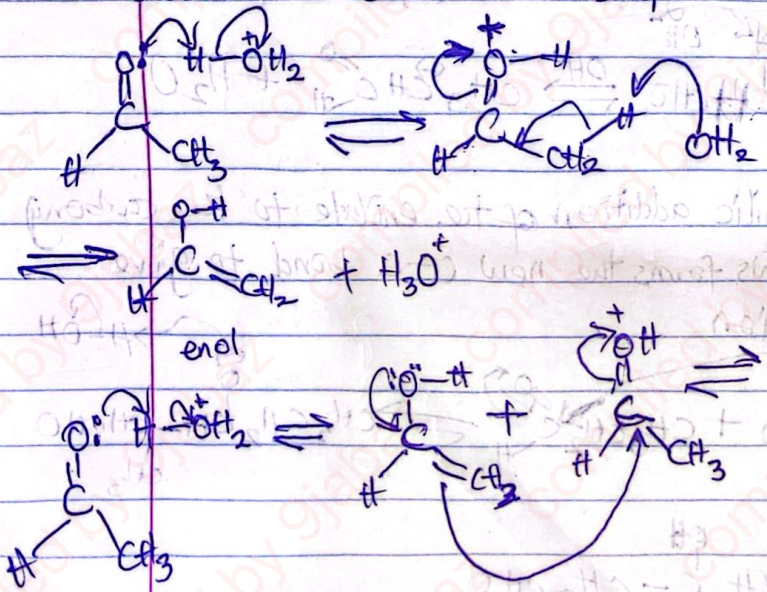


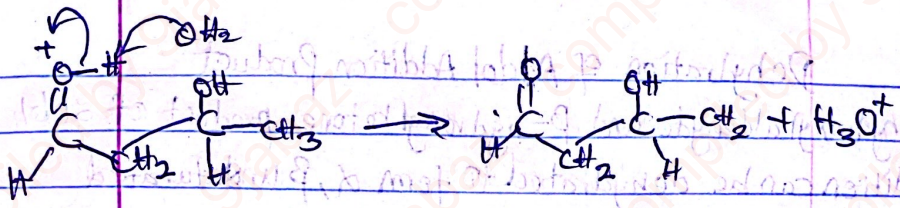


For ketone



This base catalyzed reaction has a acid catalyzed counterpart, the catalyst is H_3O^+ and the active ingredient is not enolate ion but the enol itself.





The acid and base catalyzed aldol reaction gives the same product. Aldol contains functional groups capable of further transformation. They provide access to a host of useful material

$CH_3CH_2CH_2CHO \xrightarrow[\text{addition}]{\text{aldol}} CH_3CH_2CH_2\underset{\underset{CH_2CH_3}{|}}{\overset{OH}{\overset{|}{C}}}-CHCHO \xrightarrow{H_2/Ni}$

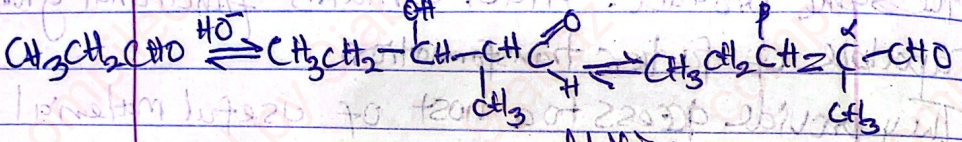
$CH_3CH_2CH_2\underset{\underset{CH_2CH_3}{|}}{\overset{OH}{\overset{|}{C}}}H-CHCH_2CH_2OH$ 2-ethyl-1,3-hexanediol

The molecule is an insect repellent

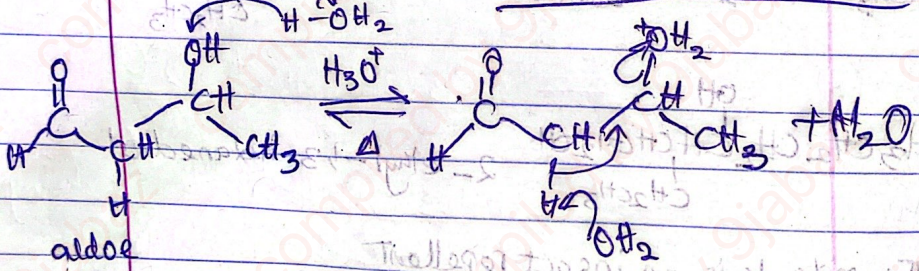
Dehydration of Aldol Addition Product

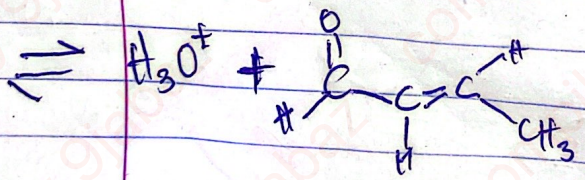
β-hydroxyl aldehyde and β-hydroxyl ketone product of aldol addition can be dehydrated to form α, β unsaturated aldehyde and ketone

Conjugation of the double bond formed with a carbonyl group increases the stability of the product.



If the product of an aldol addition reaction is dehydrated, the overall reaction is called an aldol condensation.

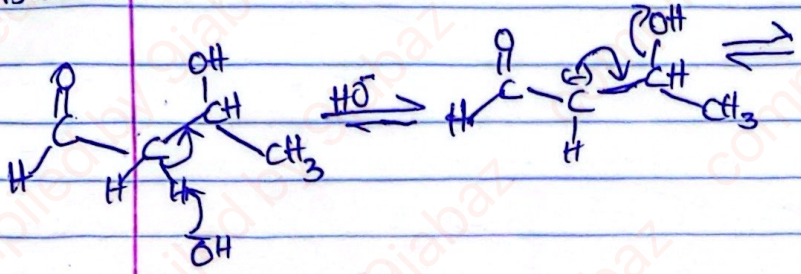


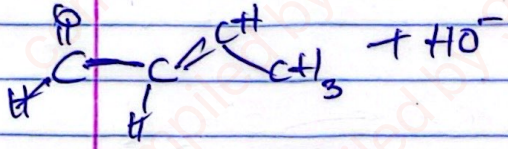


Comment

β-hydroxyl aldehyde and β-hydroxyl ketone can also be dehydrated under basic condition. Under basic condition, dehydration is difficult because OH^- is a poor leaving

group, as a result β-hydroxyl compound can also be isolated.





Excercise

What are the products of aldol condensation of the compounds;

(i)

(ii)