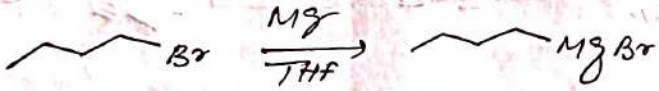
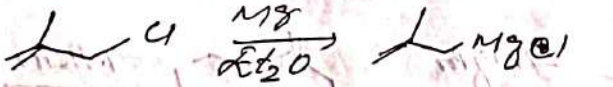
Organometallic reagents

The polarity of a covalent bond between two different elements is determined by electronegativity. The more electronegative an element is, the more it attracts the electron density in the bond. So the greater the difference between the electronegativity, the greater the difference between the attraction for the bonding electrons and the more polarized the bond becomes. Organometallic reagent is an example of polarized 'C' bond.

Making of organometallics:

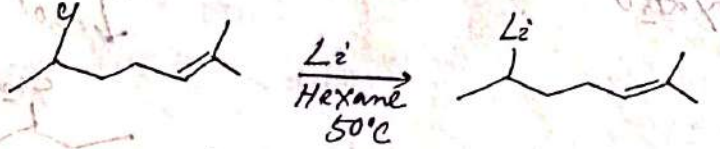
Grignard reagents are made by reacting magnesium turnings with alkyl halides in ether solvents to form solution of alkylmagnesium bromide. Iodides, bromides, and chlorides can be used, as can both aryl and alkyl halides.





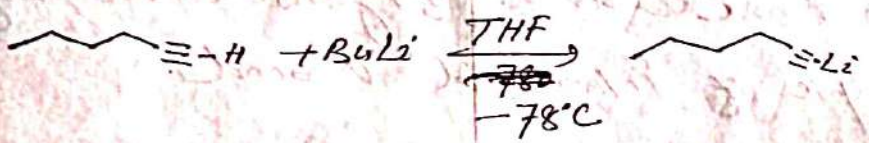
The solvents are all ethers either Et_2O or THF. Other solvents that are sometime used are dioxane and DME (dimethoxy ethane)

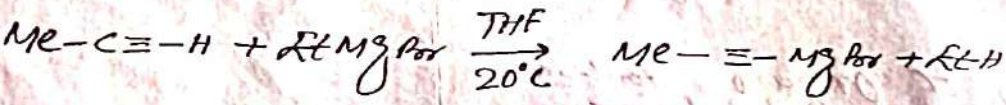
Organo lithium compounds may be made by a similar oxidative insertion reaction from lithium metal and alkyl halides. Each inserting reaction requires two atoms of lithium and generates one equivalent of lithium halide salt.

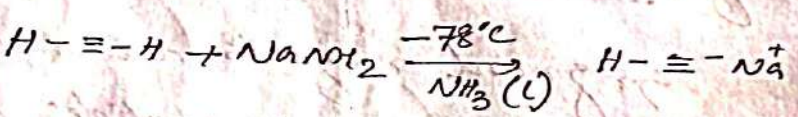


Making organometallics by deprotonating alkynes:

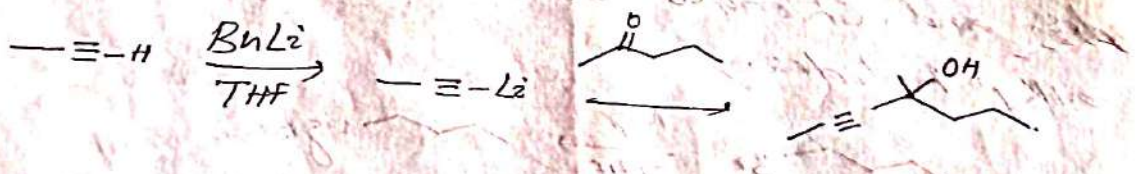
Alkynes can be deprotonated by more basic organometallics such as butyllithium or ethylmagnesium bromide. Alkynes are sufficiently acidic to be deprotonated even by nitrogen bases like $NaNH_2$ in liq NH_3.

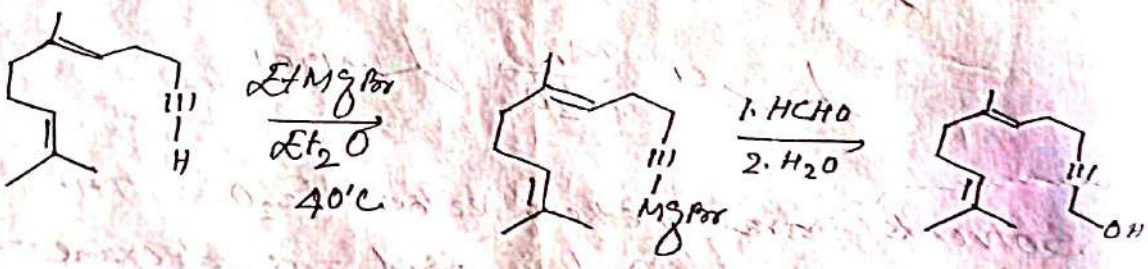






Reaction





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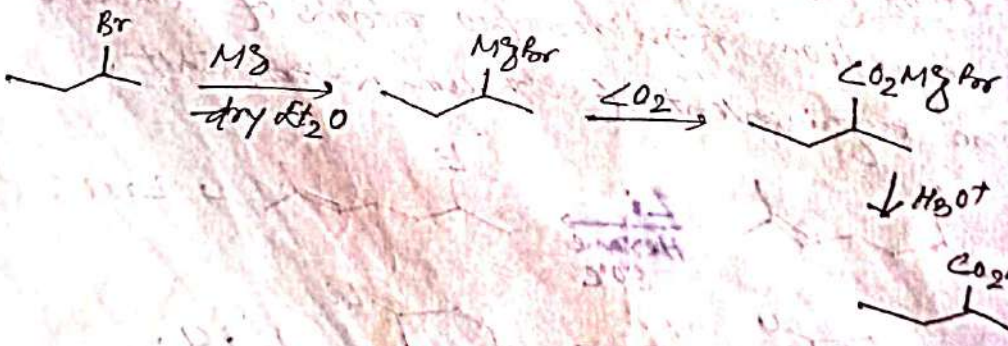

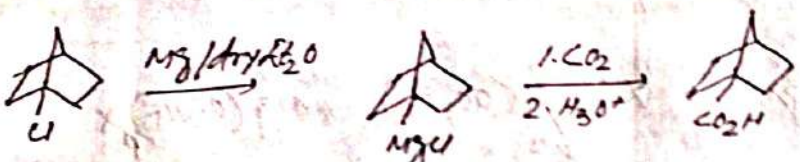

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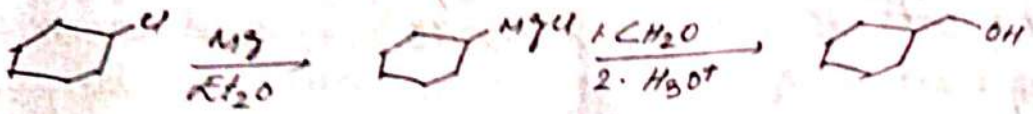

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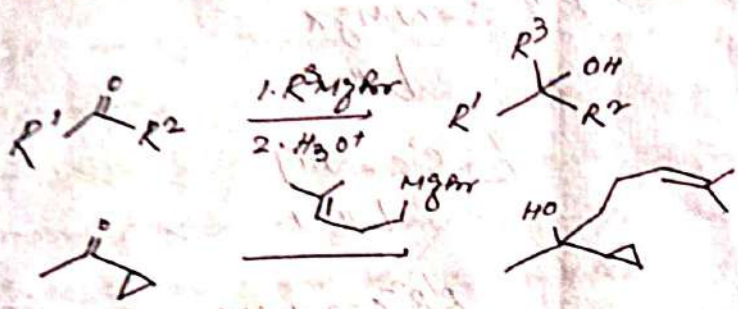

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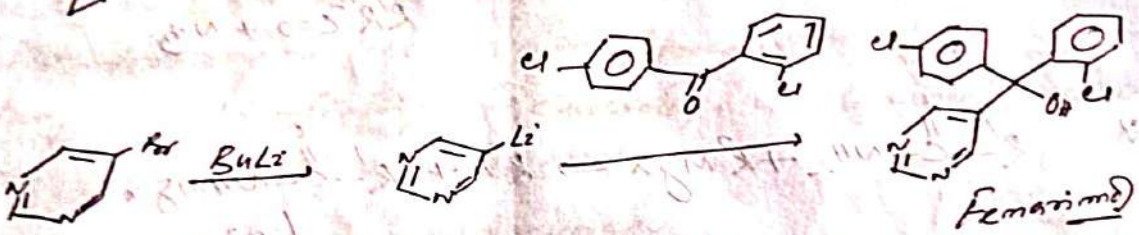


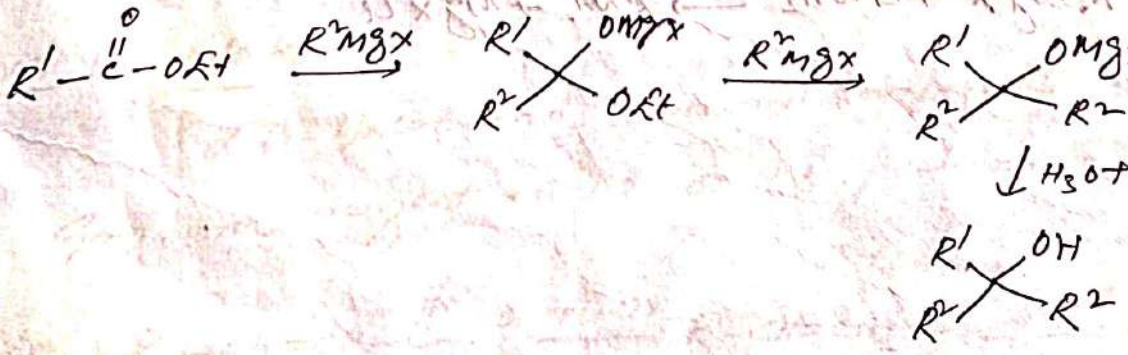
Fenarimol

* When grignard reagent is treated with any compound containing active hydrogen, a hydrocarbon is produced; in practice, water or dilute acid is used:

$$RMgBr + H_2O \xrightarrow{H^+} RH + Mg(OH)Br.$$

* $RMgX \xrightarrow{O_2} RO_2MgX \xrightarrow{RMgX} 2ROMgX \xrightarrow{H_3O^+} 2ROH$

*



*

$$R^1-C(OC_2H_5)_3 + R^2MgX \longrightarrow R^1-\underset{R^2}{C}(OC_2H_5)_2 + Mg(OC_2H_5)X$$

$$\downarrow H_3O^+$$

$$R^1-\underset{R^2}{C}=O$$

*

$$R^1CN + R^2MgX \longrightarrow R^1R^2C=NMgX$$

$$\downarrow H_3O^+$$

$$[R^1R^2C=NH]$$

$$\downarrow H_3O^+$$

$$R^1R^2C=O + NH_3$$

*

$$R^1-\overset{O}{\overset{\|}{C}}-NH_2 + R^2MgX \longrightarrow R^2H + R^1-\overset{O}{\overset{\|}{C}}-NHMgX$$

$$\downarrow R^2MgX$$

$$R^1-\underset{R^2}{\overset{NHMgX}{\overset{|}{C}}}-OMgX$$

$$\downarrow H_3O^+$$

$$R^1-\underset{R^2}{C}=O$$

Formamide give rise to formation of an aldehyde.

*

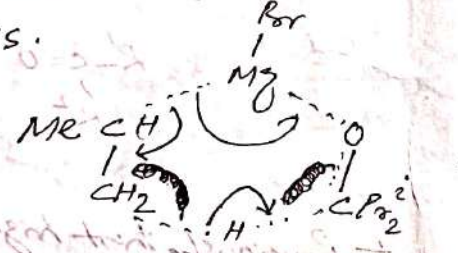
$$RMgX + ClNH_2 \longrightarrow RNH_2 + MgXCl.$$

Abnormal Behaviour of Grignard reagents:

In certain cases a Grignard reagent does not react with compound containing a functional group which is normally capable of reaction. Generally, branching of the carbon chain near the functional group prevents reaction; the cause is probably the steric effect, e.g. methyl magnesium bromide or iodide does not react with $Me_3C{-}CO{-}CMe_3$. It is also been found that if the Grignard reagent contains large alkyl groups, reaction may be prevented; e.g. iso-propyl methyl ketone reacts with methyl magnesium iodide but not with t-butyl magnesium chloride. In other cases, abnormal reaction may take place e.g. when isopropyl magnesium bromide is added to di-isopropyl ketone, the expected tertiary alcohol is not formed; instead, the secondary alcohol, di-isopropyl carbinol, is obtained, resulting from the reduction of the ketone.

$$Me_2CHCOCHMe_2 \xrightarrow{MgBr} Me_2CHOHCHMe_2 + MeCH{=}CH_2$$

This abnormal reaction may be explained by the transfer of a hydride ion from the Grignard reagent via a cyclic T.S.



$\rightarrow MeCH{=}CH_2 + {}^{i}Pr_2CH{-}OMgBr$

Hydride-Shift

1,2 vs 1,4-Addition:

α,β-Unsaturated carbonyl compounds react with a Grignard reagent in 1,2- or 1,4-positions:

1,2-addition: $R^1{-}CH{=}CH{-}\underset{\displaystyle O}{\overset{\displaystyle \|}{C}}{-}R^2 \xrightarrow{R^3MgX} R^1{-}CH{=}CH{-}\underset{R^2}{\overset{OMgX}{\overset{|}{\underset{|}{C}}}}{-}R^3 \xrightarrow{H_3O^+} R^1{-}CH{=}CH{-}\underset{R^2}{\overset{OH}{\overset{|}{\underset{|}{C}}}}{-}R^3$

1,4-addition:

$$R^1{-}CH{=}CH{-}\underset{\displaystyle O}{\overset{\displaystyle \|}{C}}{-}R^2 \xrightarrow{R^3MgX} R^1{-}\underset{R^3}{\overset{|}{CH}}{-}CH{=}\underset{\displaystyle OMgX}{\overset{|}{C}}{-}R^2 \xrightarrow{H_3O^+} R^1{-}CH{-}CH{=}\underset{R^2}{\overset{OH}{\overset{|}{C}}}{-}R^2 \text{ (enol)}$$

$$R^1{-}CH{-}CH_2{-}\underset{\displaystyle O}{\overset{\displaystyle \|}{C}}{-}R^2 \leftarrow$$

The predominant factor in deciding the course of addition is steric hindrance, and when both R^1 and R^2 are large, R^2 has greater influence than R^1. On the other hand 1,4-addition can be made to predominate by carrying out the reaction of e.g. cuprous chloride, cuprous acetate, etc.

* Reaction of organo lithium:

$$RLi + CO_2 \longrightarrow R-C(=O)-OLi \xrightarrow{RLi} R-C(OLi)(R)-OLi \xrightarrow{H_2O} R-C(=O)-R$$

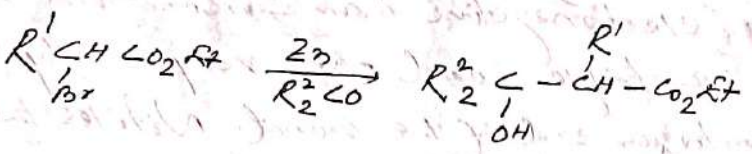
* $$R^1-C(=O)-OH \xrightarrow{R^2Li} R^1-C(=O)-OLi \xrightarrow{R^2Li} R^1-C(OLi)(R^2)-OLi \xrightarrow{H_2O} R^1-C(=O)-R^2$$

* It has been pointed out previously that highly sterically hindered 3-alcohols cannot be prepared by the Grignard reaction. On the other hand, many of these alcohols can be prepared by means of lithium alkyls, e.g.

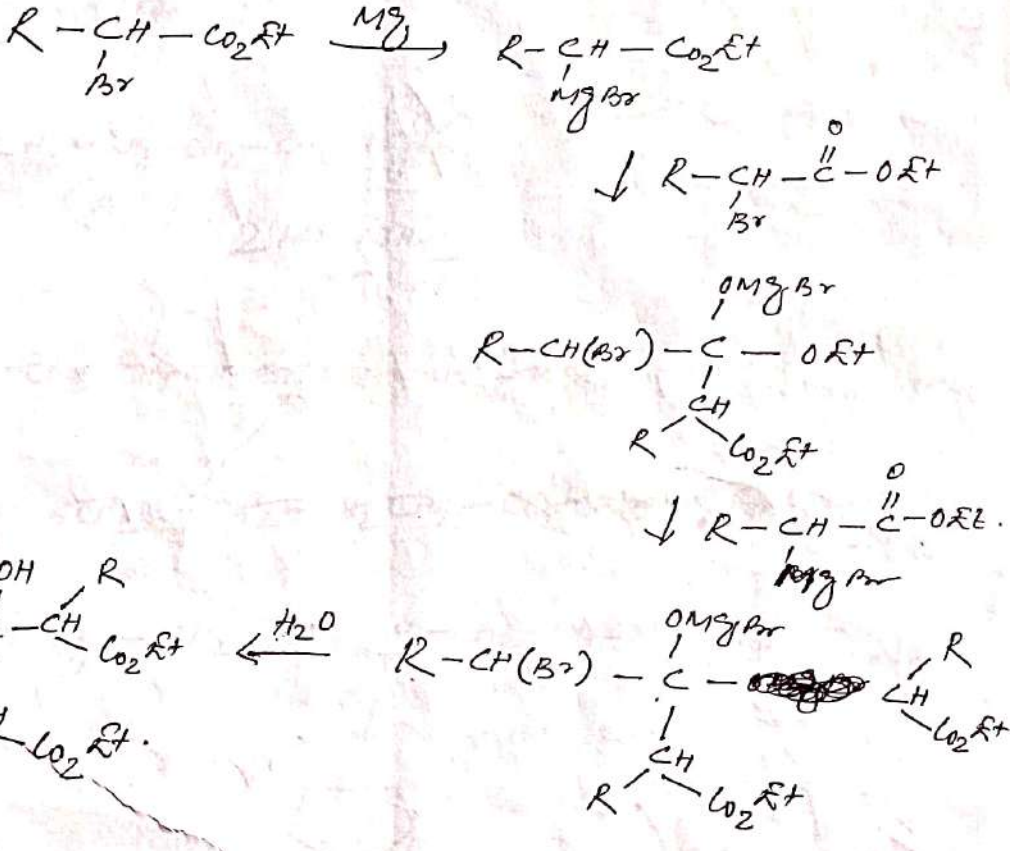
$$(Me_2CH)_2CO + Me_2CHLi \longrightarrow (Me_2CH)_3COLi \xrightarrow{H_3O^+} (Me_2CH)_3COH$$

*

Organo Zinc / The Reformatsky reaction:



The use of Zinc instead of magnesium in the Reformatsky reaction is based on the fact that the Grignard reagent formed immediately attacks the ~~Grignard reagent~~ ester group of a second molecule.



* Organocadmium compounds:

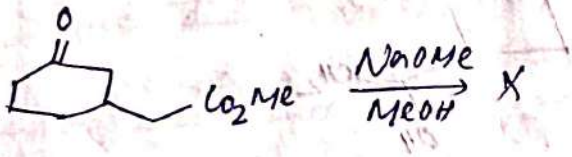
Cadmium dialkyls are readily prepared as follows:

$$2RMgX + CdCl_2 \rightarrow R_2Cd + 2MgClX$$

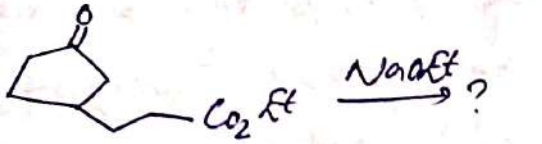
Dialkylcadmium compounds are used to prepare ketones from acid chlorides; they are prepared in situ:

$$2R'COCl + R_2^2Cd \rightarrow 2R'COR^2 + CdCl_2$$

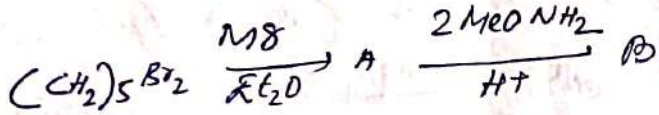
i

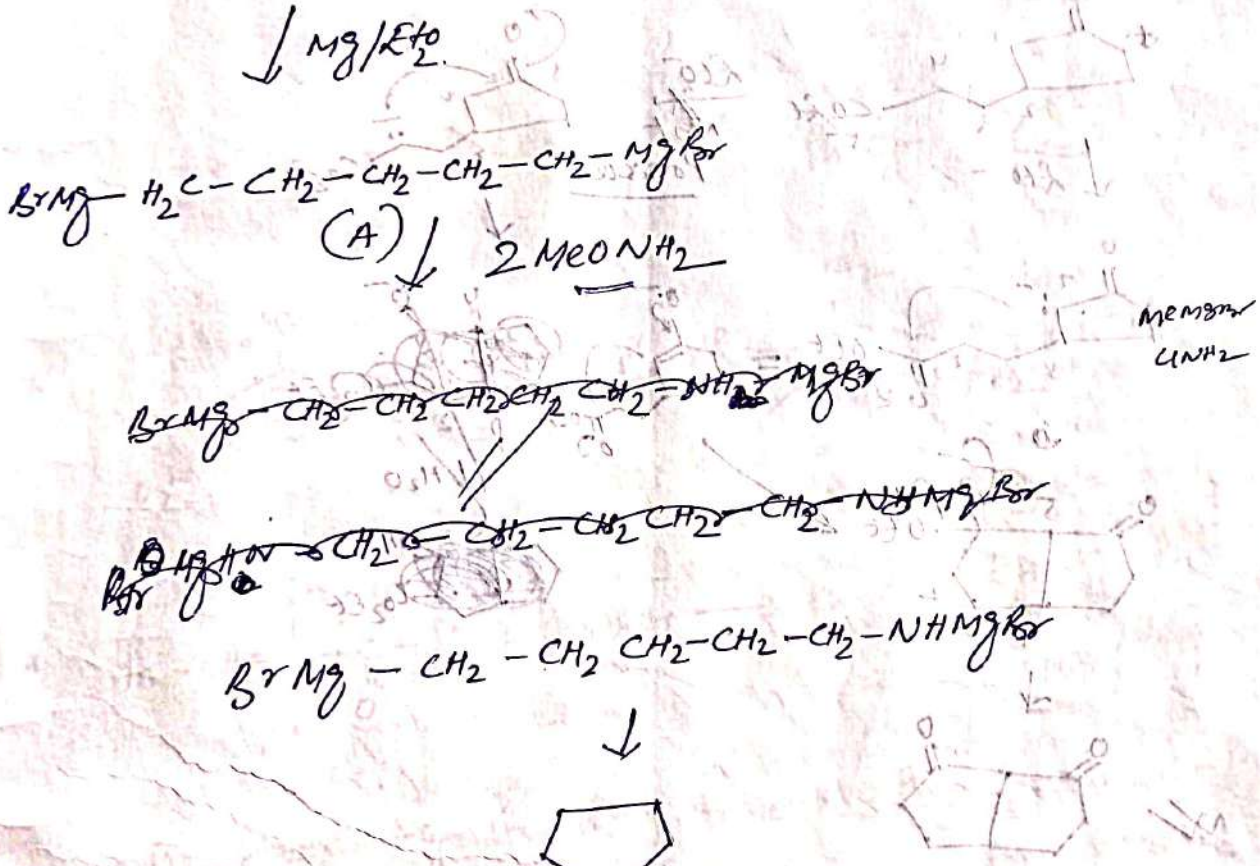

CO2Me
NaOMe
MeOH
X

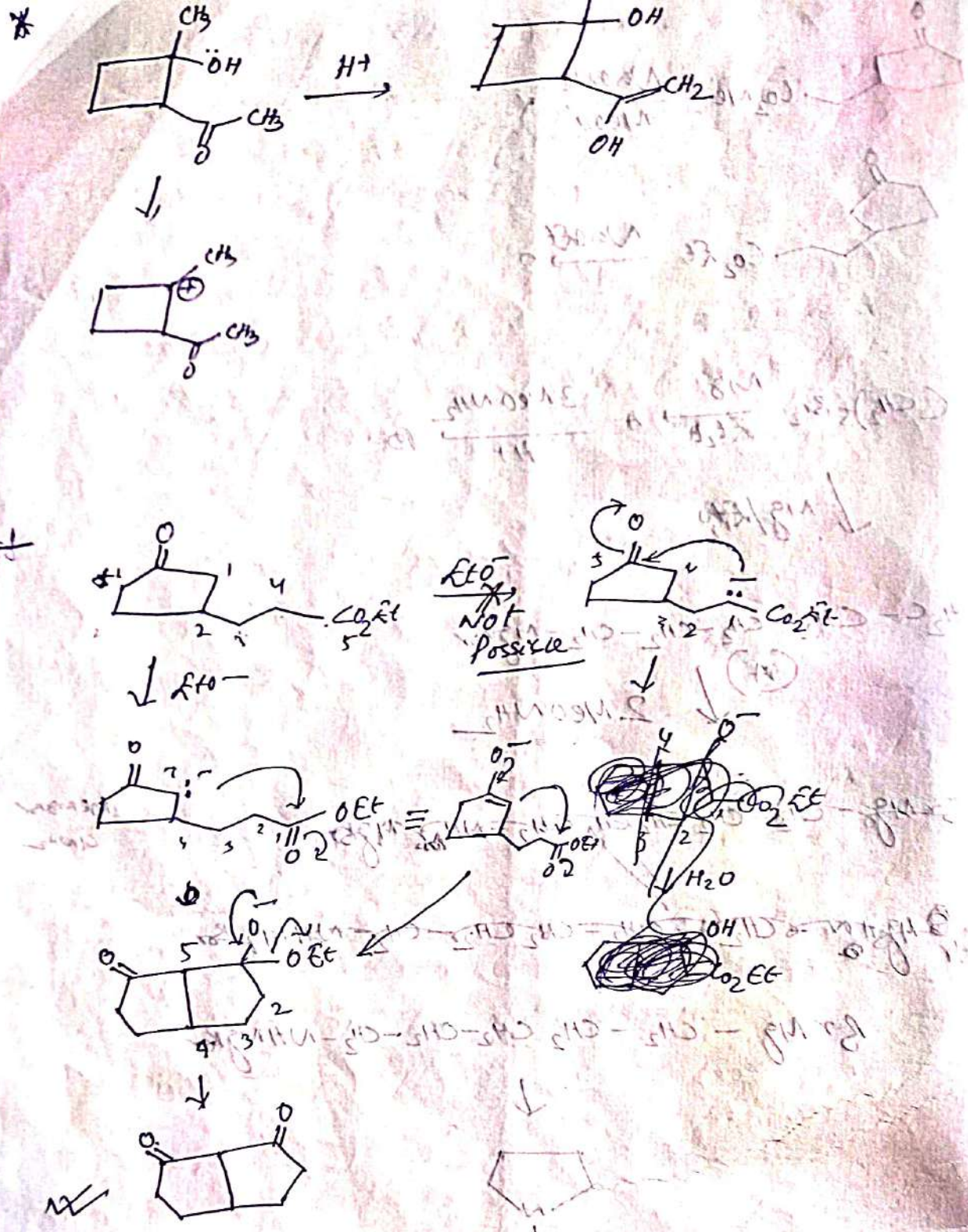
ii


CO2Et
NaOEt
?

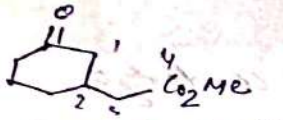
iii


(CH2)5Br2
Mg
Et2O
A
2 MeO NH2
H+
B

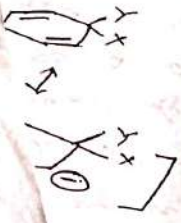

Mg/Et2O
BrMg – H2C – CH2 – CH2 – CH2 – CH2 – MgBr
(A)
2 MeO NH2
BrMg – CH2 – CH2 CH2 – CH2 – CH2 – NHMgBr
(D)



We could form enolate on the other side of the ketone at the star mark site and attack the ester in the same way. The product would be a bridged bicyclic diketone and is not formed. The third possible enolate site (next to ester) could give an aldol reaction but the product would again be a bridged bicyclic compound and is not formed.



Would
Cyclization ~~will~~ result a six membered ring fused with a four membered ring which is very difficult to form and other possibility would result in Bridged cyclic system which is highly unfavorable :



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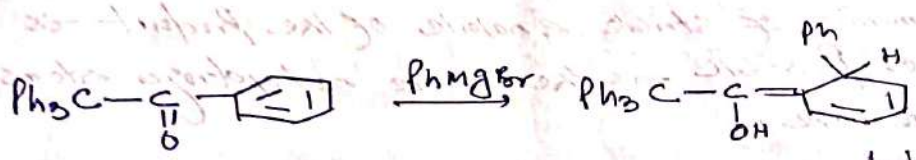

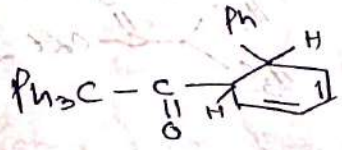

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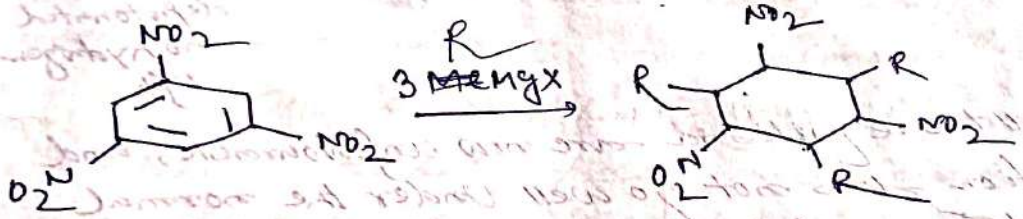

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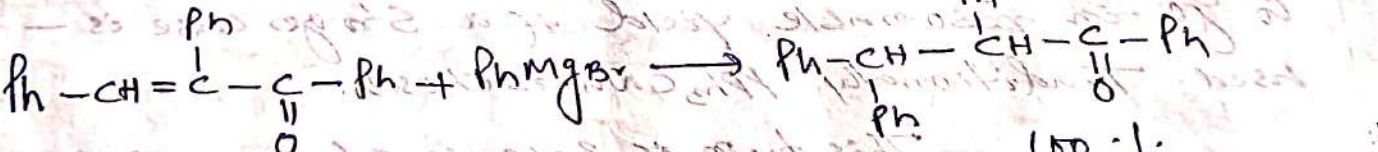

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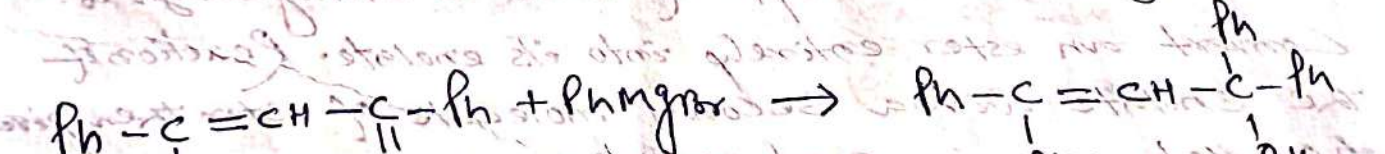

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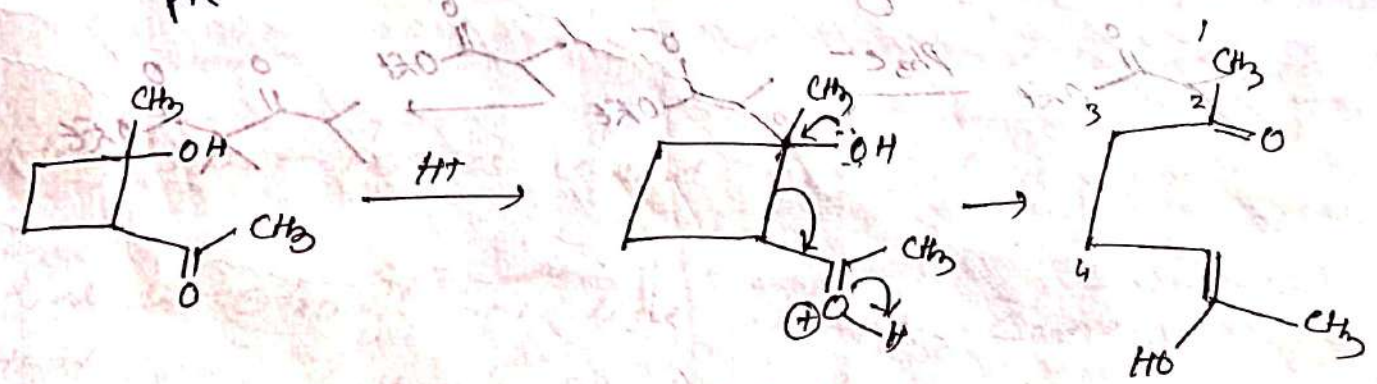
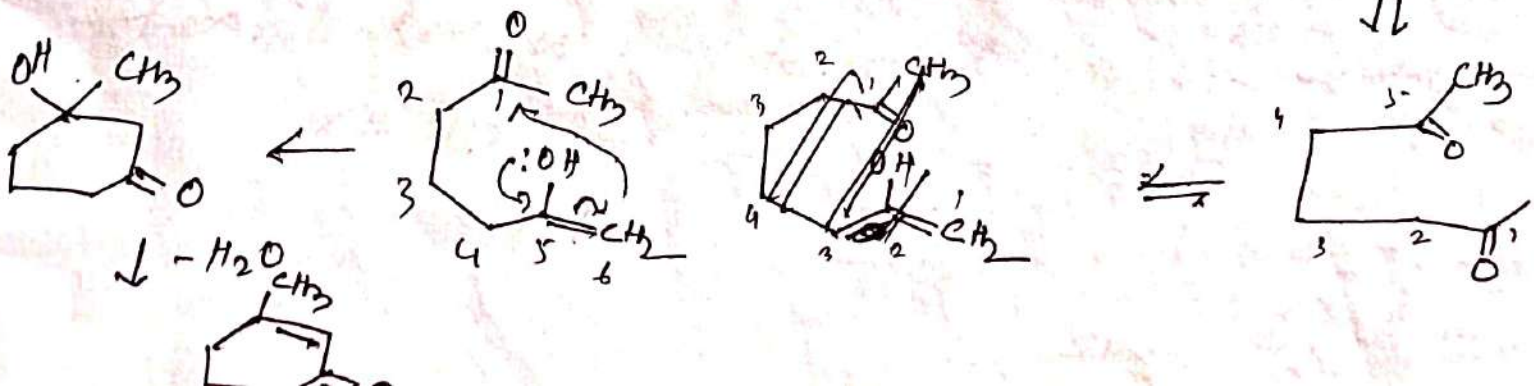


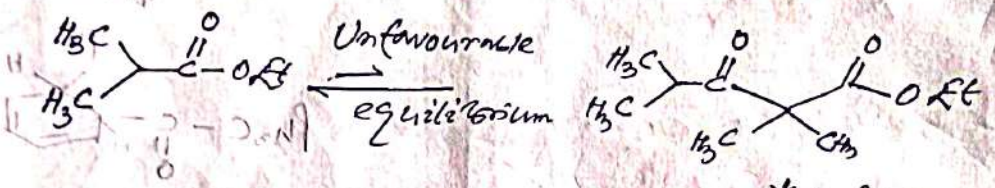


*

Explain why ethyl isobutyrate fails to undergo Claisen condensation in the presence of NaOEt but will in the presence of very strong base like NaH / $NaNH_2$ / $Ph_3C^-Na^+$ / LDA etc.

Ans:

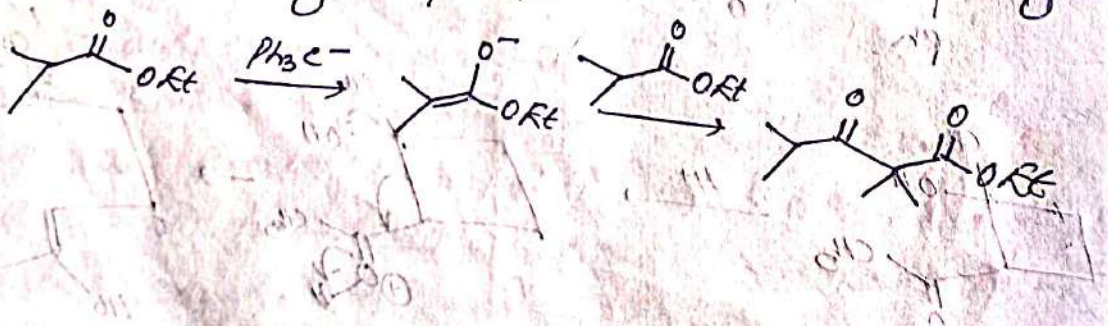
Isobutyrate has two substituents on the α carbon, the formation of stable enolate of the product is no longer possible as there is/are no hydrogen atoms left to remove.



* Can't be deprotonated no hydrogen left

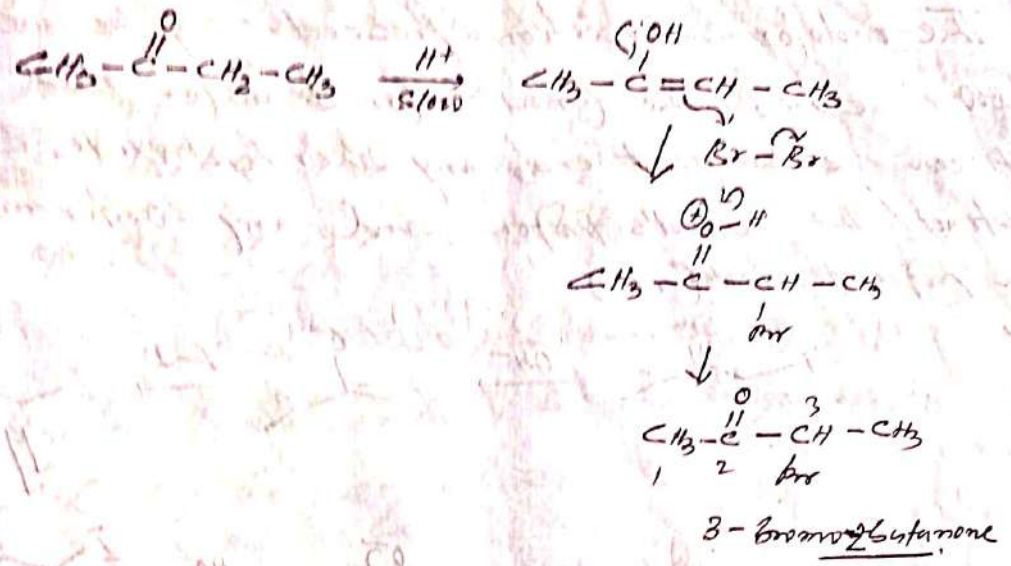
Since all the equilibria are now unfavourable, and this reaction does not go well under the normal equilibrating conditions (EtO⁻ in EtOH). It can be made to go in reasonable yield if a stronger base is used. Traditionally $Ph_3C^-Na^+$ is chosen.

This type of base is strong enough to convert an ester entirely into its enolate. Reaction of the enolate with a second molecule of ester then gives the keto-ester in good yields.



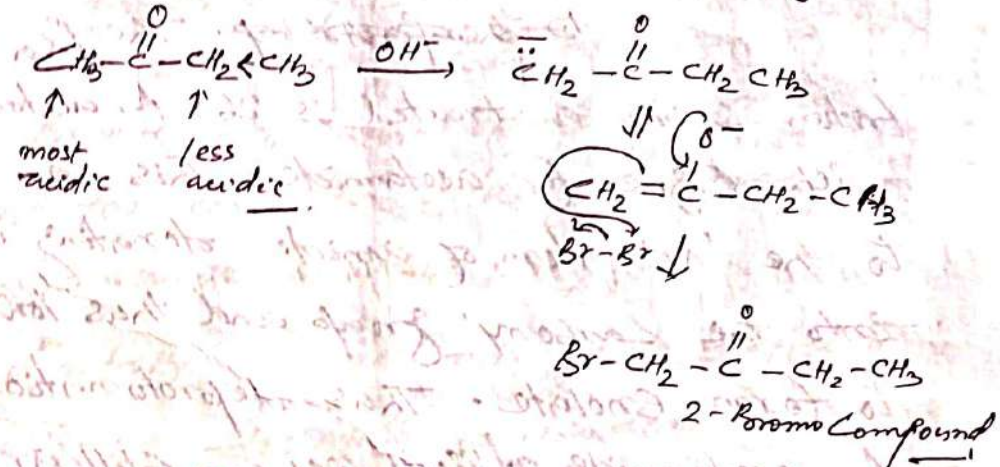
3-bromo compound whereas base catalyzed bromination gives 1-bromo compound. — Explain.

Ans



In the absence of base reaction proceeds through the formation of most stable (thermodynamic control) intermediate and leads to the formation of 3-bromo-compound.

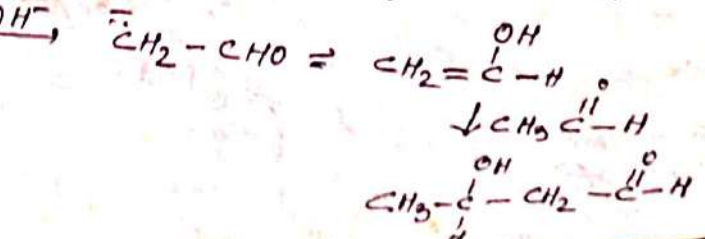
On the other hand in the presence of base, proton abstraction ~~of proton take place from the~~ of most acidic proton take place which leads to the formation of 2-bromo compound.



* Aldehyds that possess α-H do not undergo Cannizzaro rex^n?

Ans. *

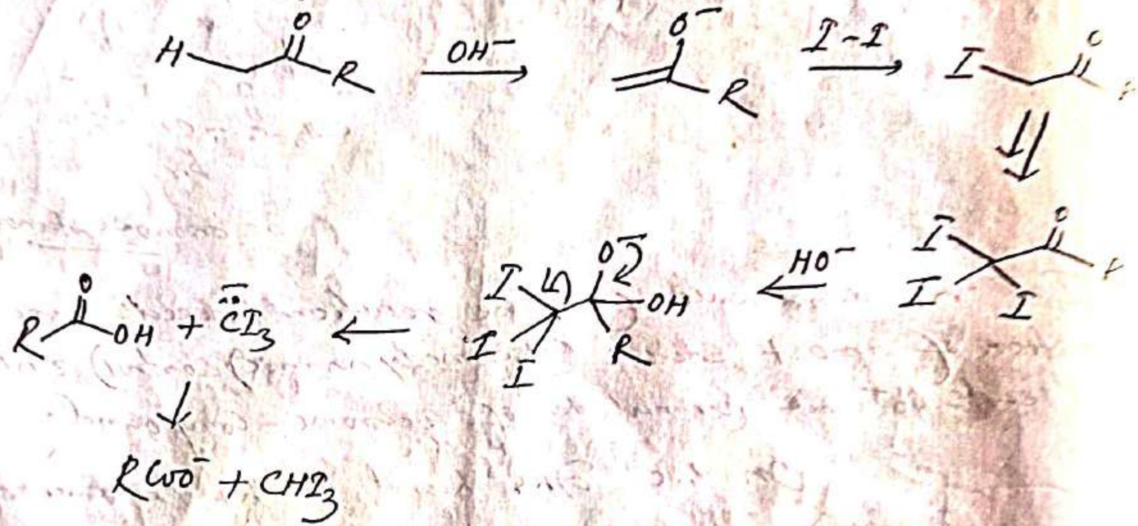
Due to strongly alkaline reaction conditions, aldehyd that have α-H atom(s) instead undergo deprotonation there, leading to enolates and possible aldol reaction



* Acetamide does not response to Iodoform test though it contains a keto-methyl group.

Ans

The iodoform reaction proceeds by the mech... shown below. (The final proton transfer need ... between the two partners, any other hydroxide could abstract the acid's proton and any water molec... can protonate iodoform).



~~This can fail for acetamide in two ways:~~

~~1) The first step.~~ The pKa value of the proton being abstracted is 26.5 for acetone and it is much higher for acetamide. This can be attributed to the 'N' atom of amide donating electron-densi... into the carbonyl group and thus lowering the tend... to form enolate. Thus deprotonation is quite di... for acetamide and ~~if~~ we can still argue that ~~a~~ acetamide will be deprotonated to ~~into~~ iodination to take place hence iodination can't take pl...

~~B.~~