

CSIR-JRF (NET), GATE DRDO, BARC, IISC.....

LONG COURSE For CSIR-NET (JRF)-June-2017

CHEMISTRY BY H. GAUR

ORGANIC CHEMISTRY

NAMED REACTIONS

SHEET-2

ACHARYA INSTITUTE

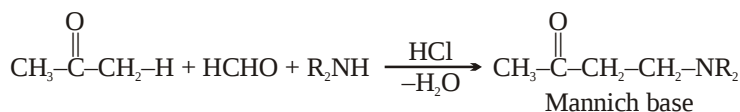
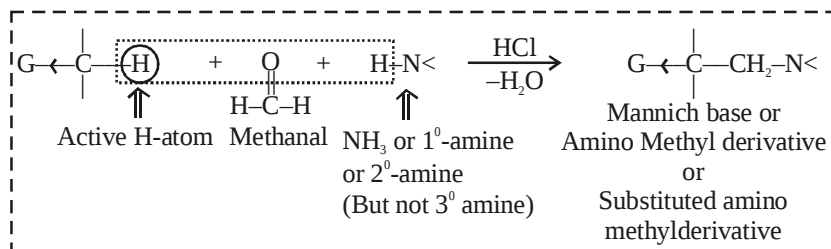
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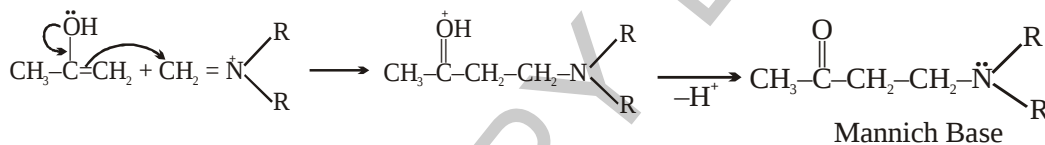
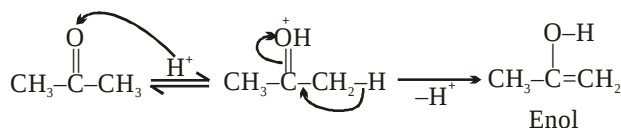
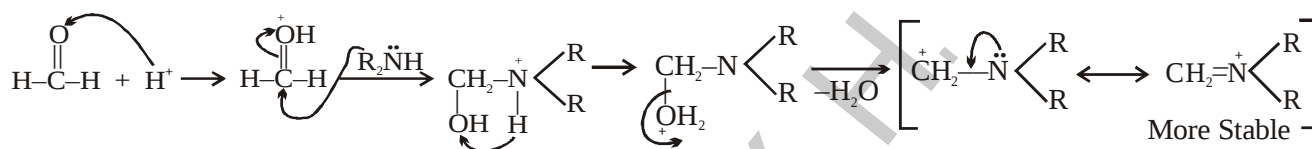
MANNICH REACTION:

* It involves the condensation of a compound having an active methylene group (active H-atom) with formaldehyde & $\text{H}-\text{N}<$ ($\text{H}-\text{N}< \rightleftharpoons \text{NH}_3$ or NH_2R or NHR_2 , but not used NR_3) in the presence of acid and forms an amino methyl derivative or substituted amino methyl derivative (**Mannich base**) is called **Mannich Reaction**.

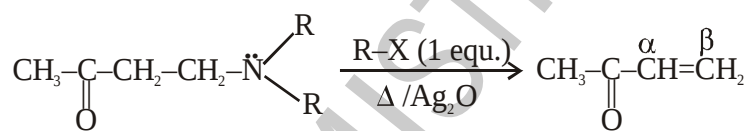


Mechanism:

* It is acid catalysed as well as base catalysed.



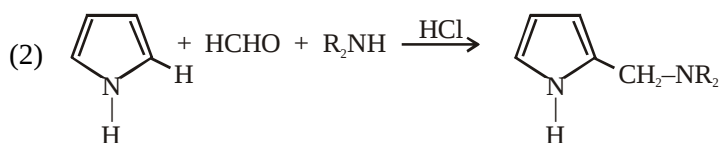
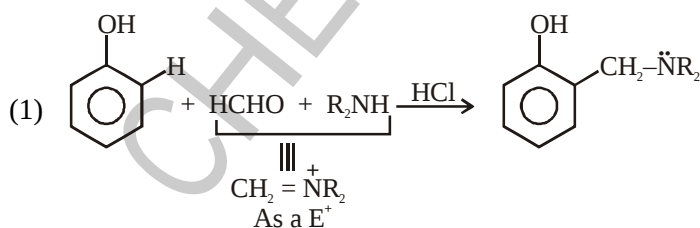
Generally, mannich base, used for the synthesis of α, β - unsaturated carbonyls.

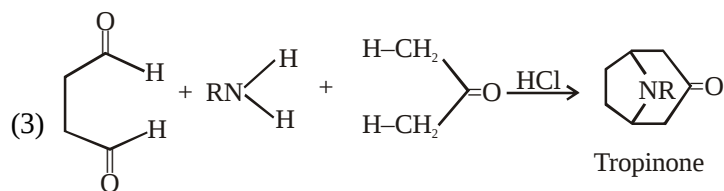


α, β -Unsaturated carbonyl

* It is substrate of Michael addition

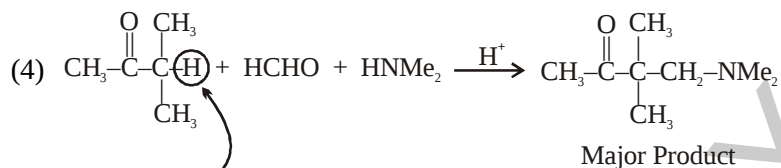
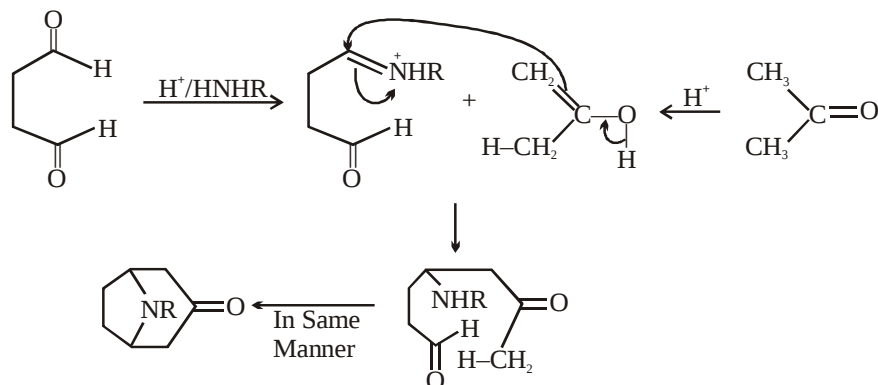
Examples of Mannich Reactants:



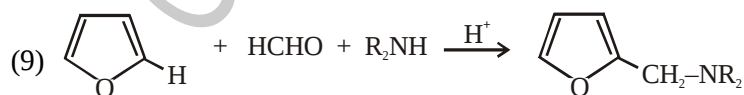
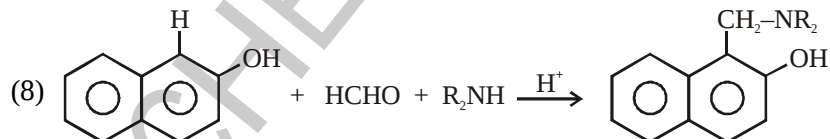
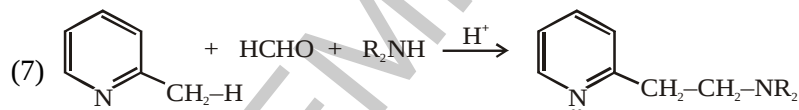
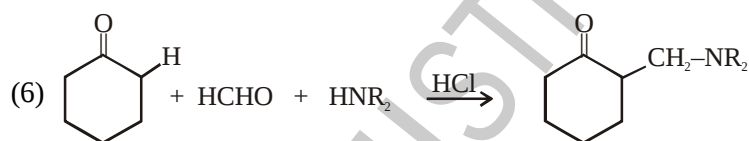
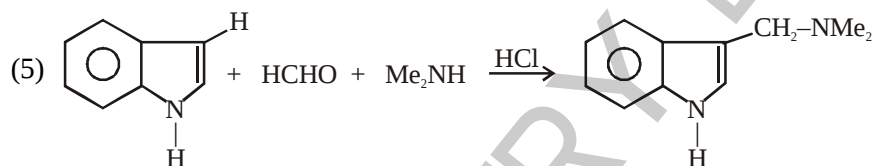


* It is example of double **mannich base reaction**.

* This reaction takes place as;



This H-atom involve in enol formation B'coz of in acidic medium more substituted enol is the formed.



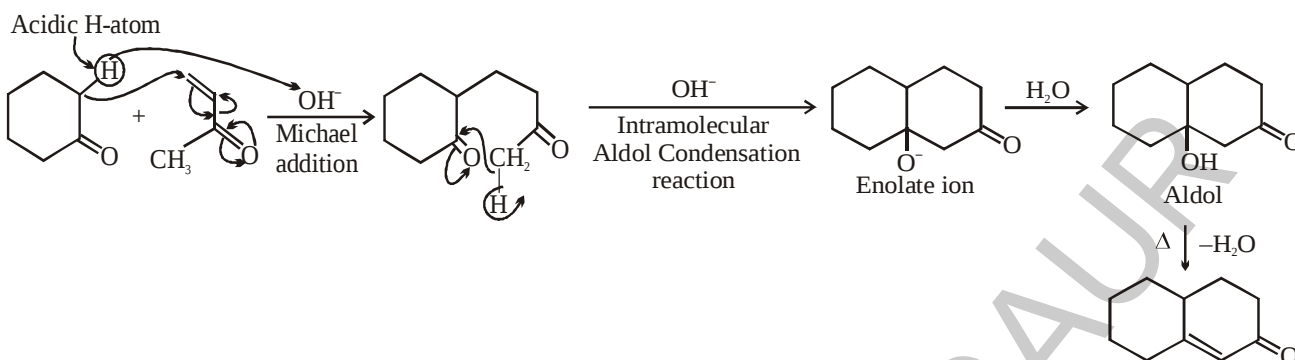
ROBINSON ANNELENATION REACTION:

* It involve two reaction in following order.

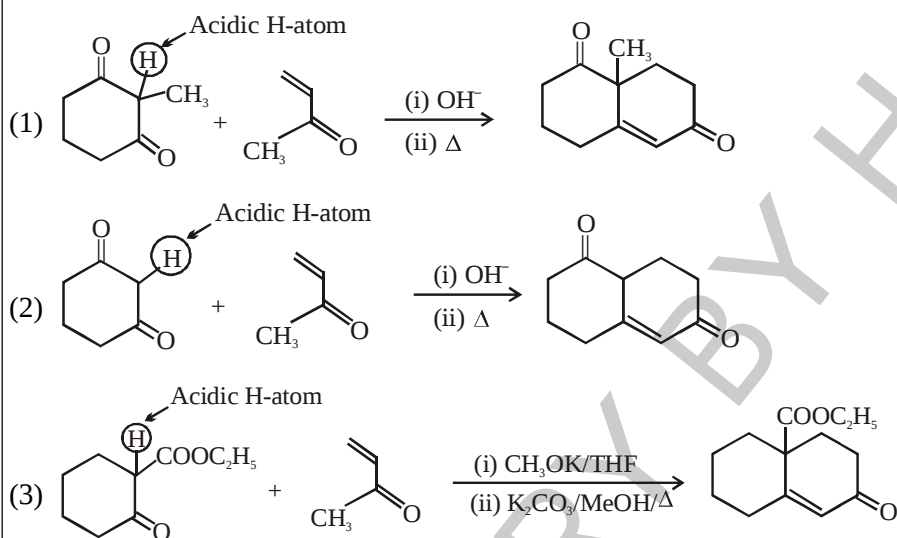
(A) Michael Addition followed by

(B) Intramolecular aldol condensation reaction.

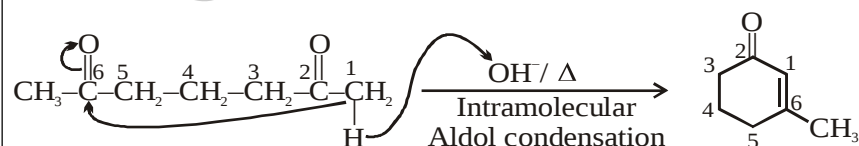
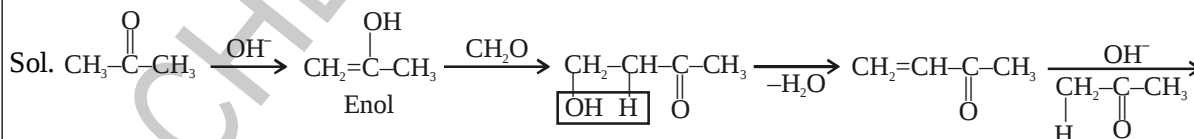
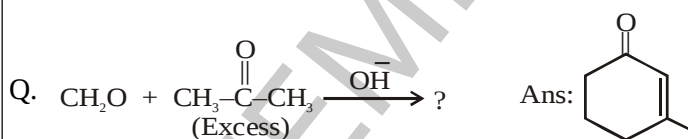
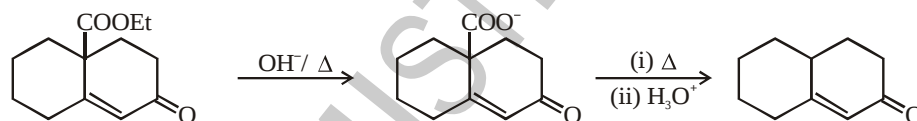
* This reaction can be very usefull in the synthesis of polycyclic molecules due to this reason this reaction is also called **Robinson ring forming reaction**.



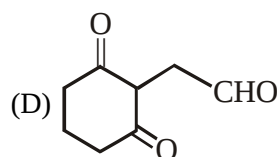
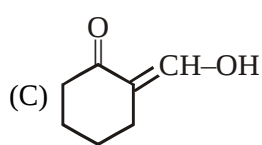
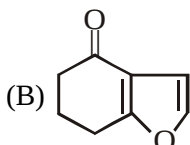
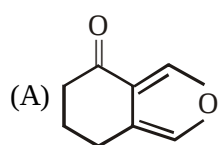
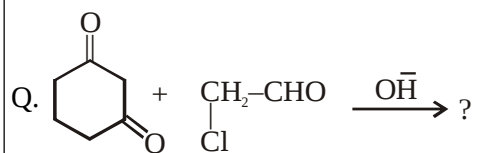
Examples of Robinson Annulation Reaction:



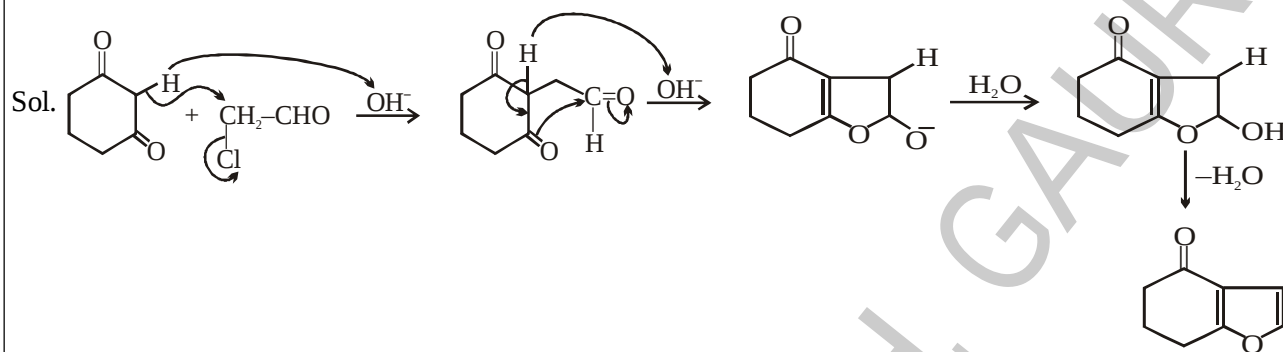
* In this reaction, the ester group can be removed by Hydrolysis followed by decarboxylation



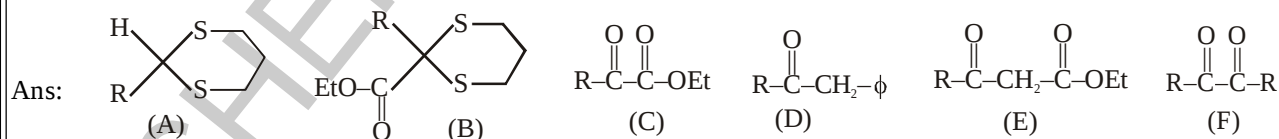
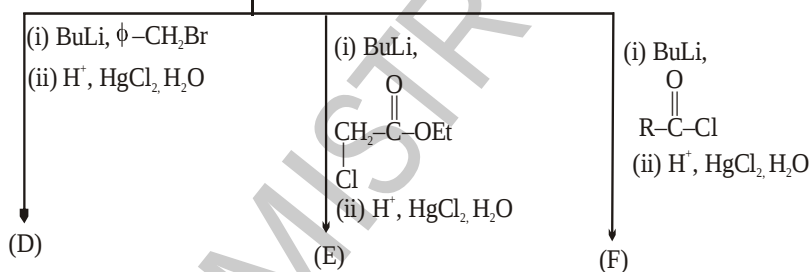
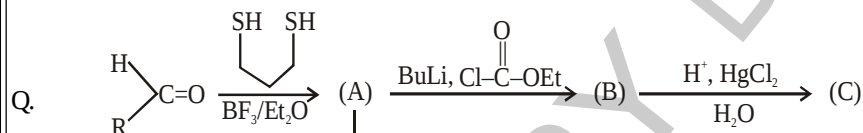
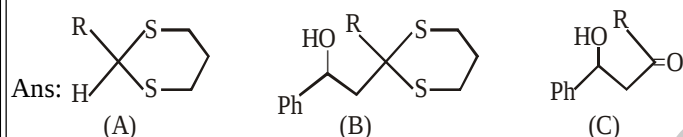
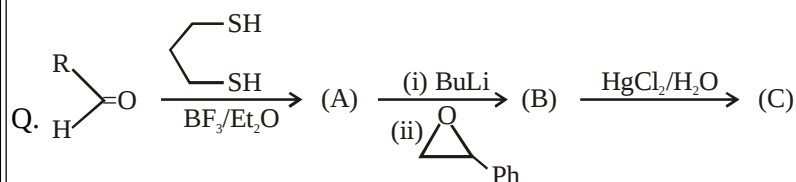
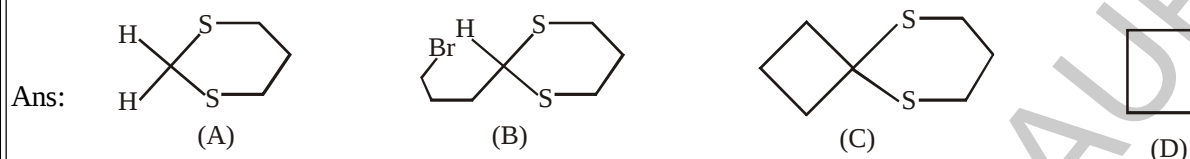
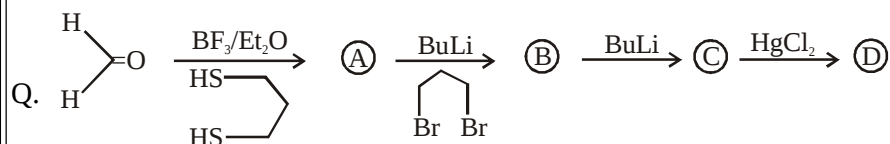
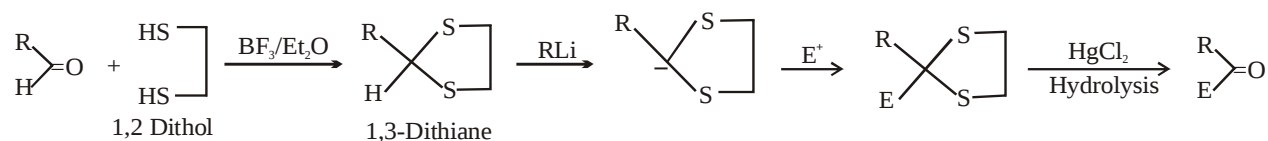
it is also substrate for Michael addition



Ans: (B)

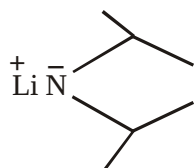


1,3-DITHIANES:

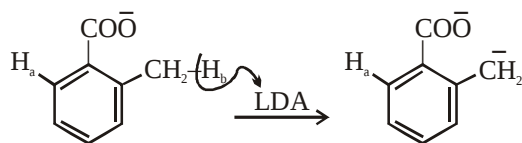
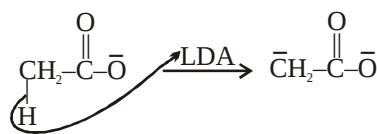
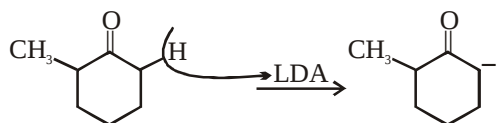
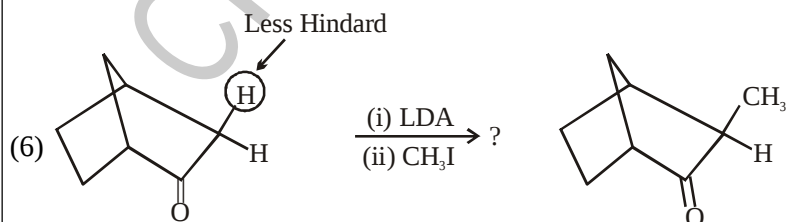
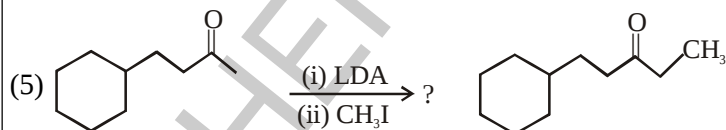
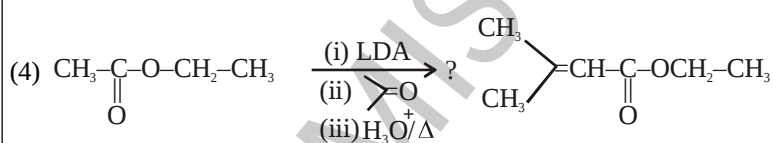
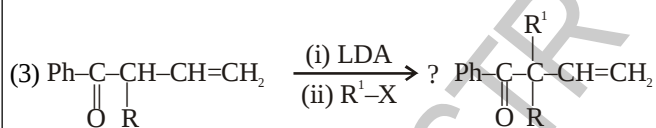
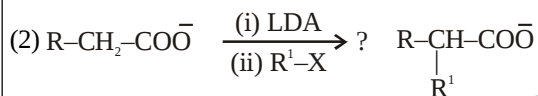
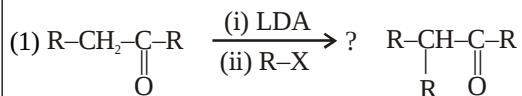


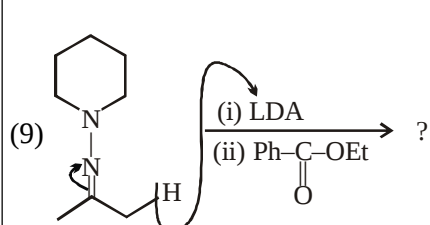
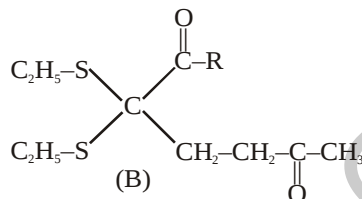
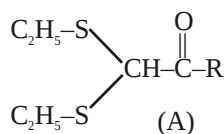
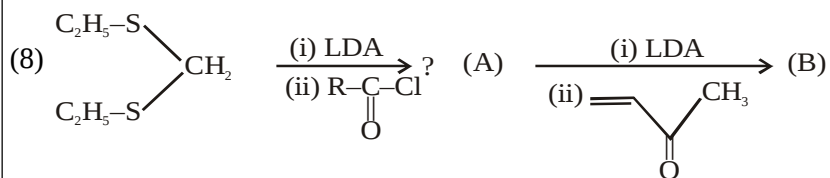
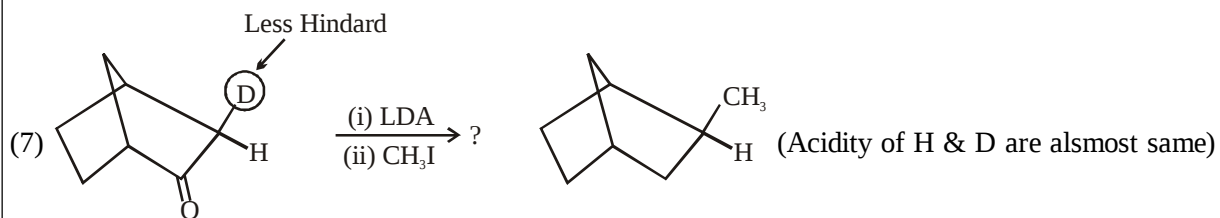
LDA (LITHIUM DIISOPROPYLAMIDE):

- * It is strong base but weak nucleophile.
- * It is Bulky base
- * Abstract less sterically hindered acidic H-atom
- * Since, it is a strong base so it can also abstract very less acidic H-atom.

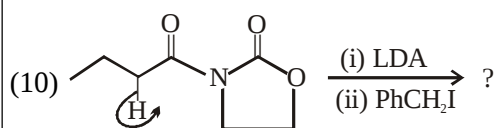
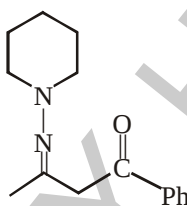


LDA (Lithium Diisopropyl Amide)

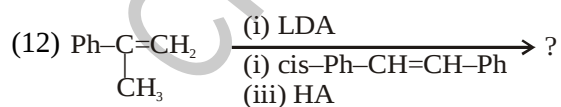
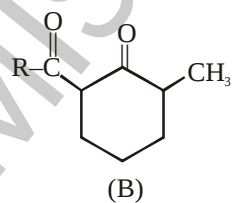
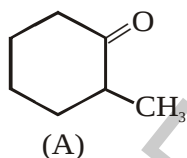
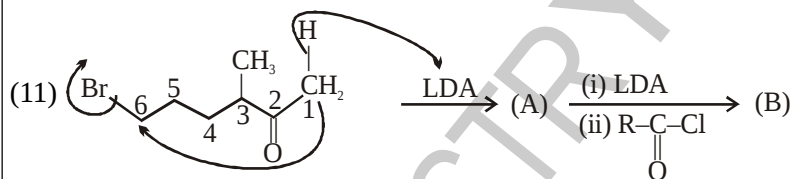
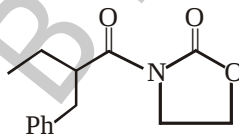
**Important Questions:**



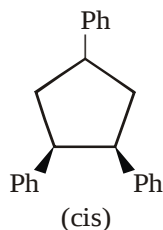
Ans:



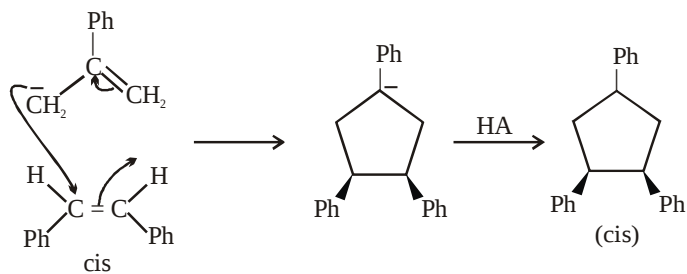
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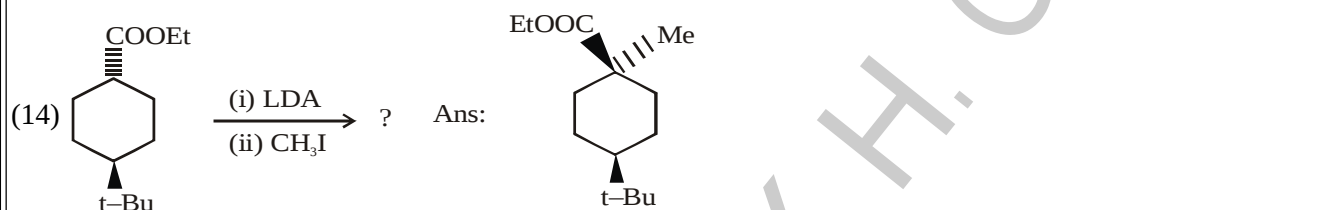
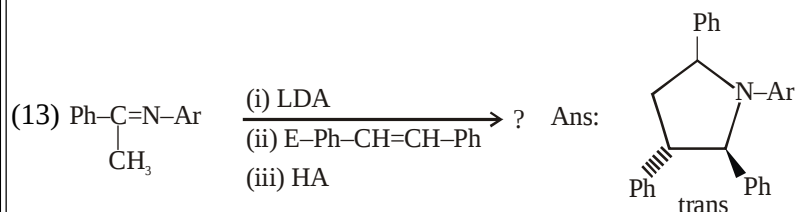
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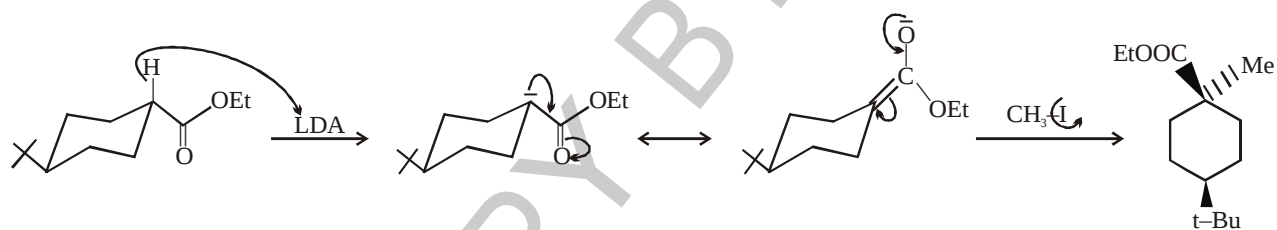
Solution:



This reaction takes place by the concerted mechanism so that symmetry of reactant maintain in the product (i.e., cis $\longrightarrow$ cis & trans $\longrightarrow$ trans)

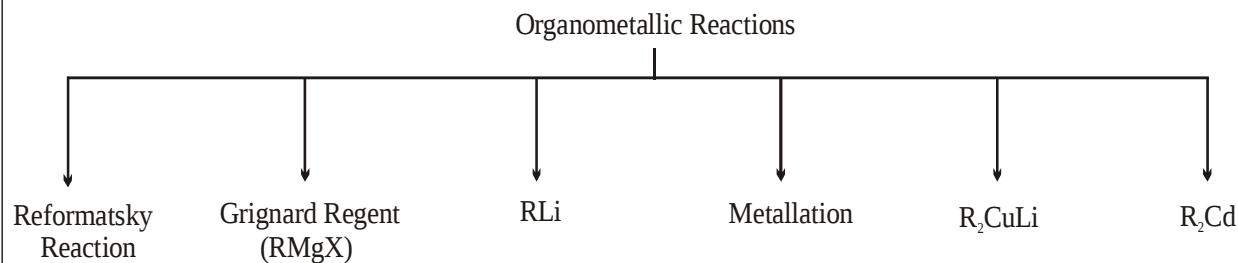


Solution:



$\text{CH}_3\text{-I} \Rightarrow$ Bulky Base, so equatorial attack takes place

ORGANOMETALLIC REACTION:

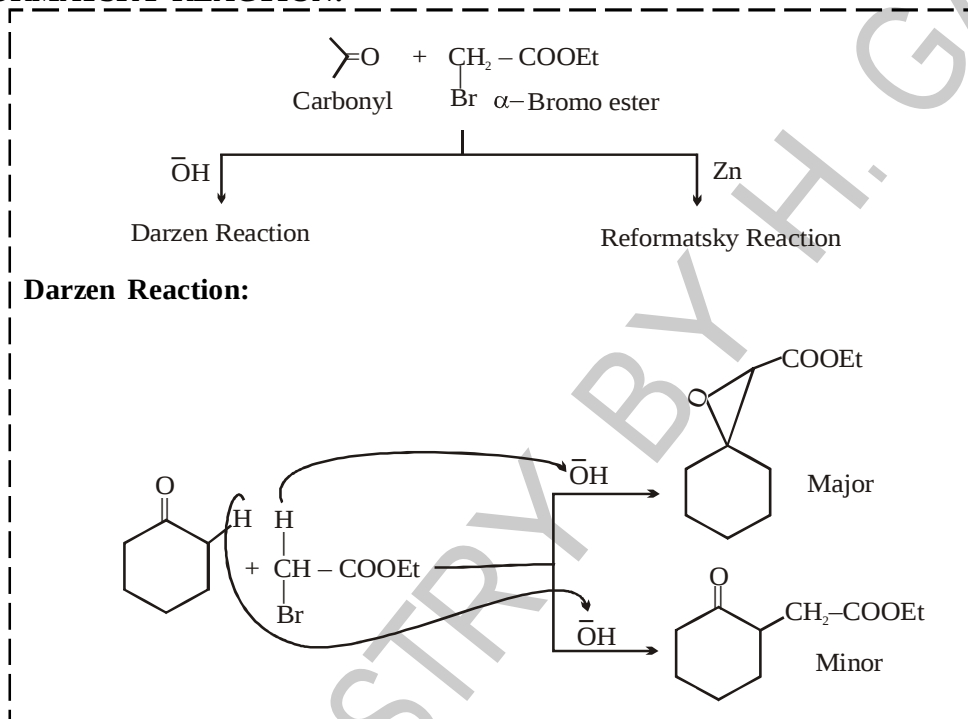


* Organometallic reactions takes place in following order always

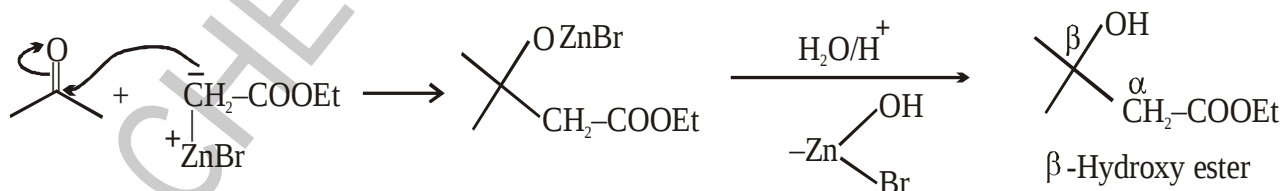
1. Acid-base Reaction
2. Addition Reaction
3. Substitution Reaction
4. Elimination Reaction

[AASE]

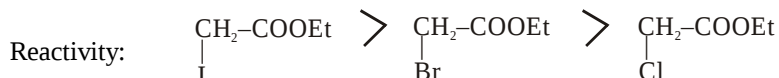
REFORMATSKY REACTION:



* Reformatsky Reaction take place with organozinc ester



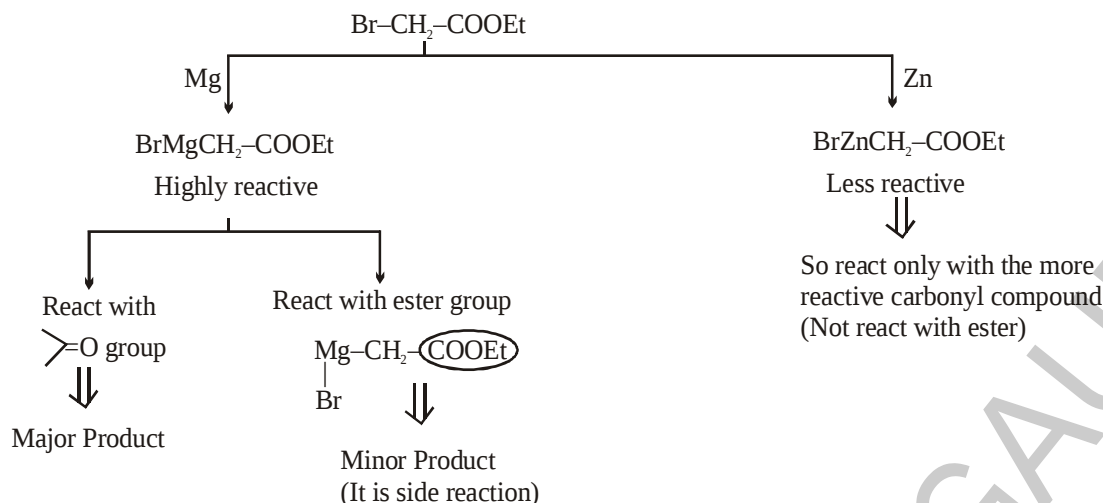
Reactivity w.r.t. Reformatsky reaction.



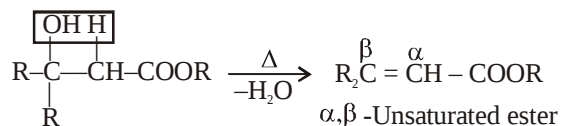
* **RMgX** have nucleophilic as well as basic character so it react with acidic-H-atom & give acid-base reaction.

*** Advantage of Zn:**

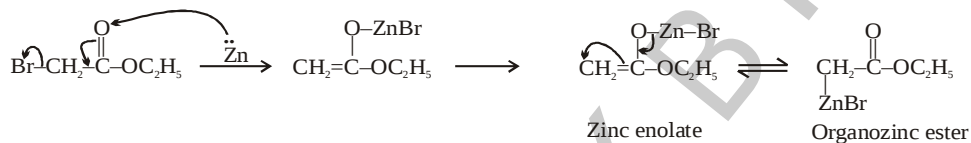
Zn is in place of Mg because organozinc compounds are less reactive than the organomagnesium compound of α -bromo ester. So it does not react with other ester molecules.



* On heating, β -hydroxy ester gives α, β -unsaturated ester

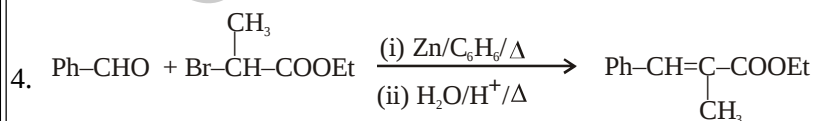
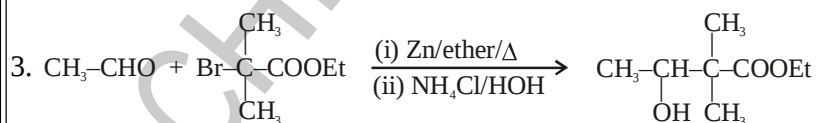
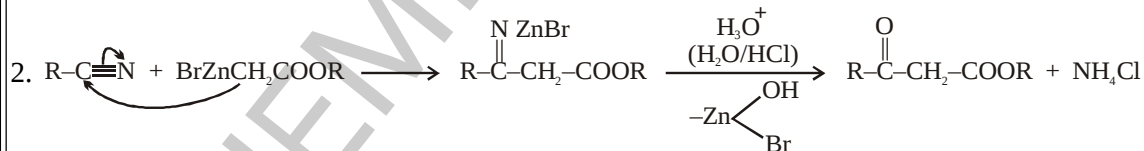
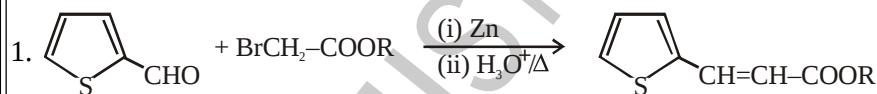


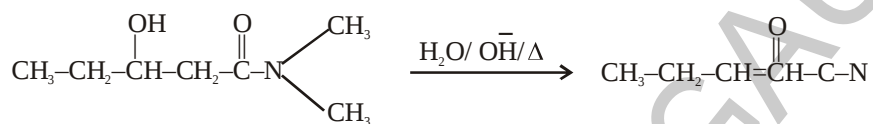
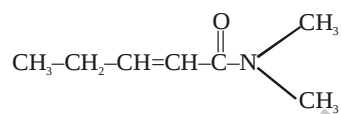
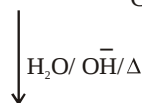
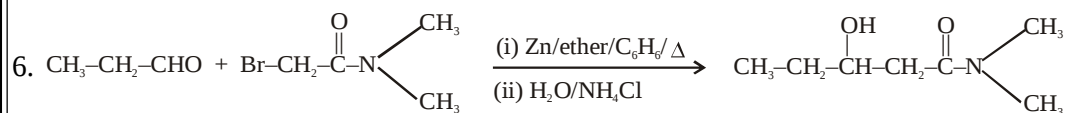
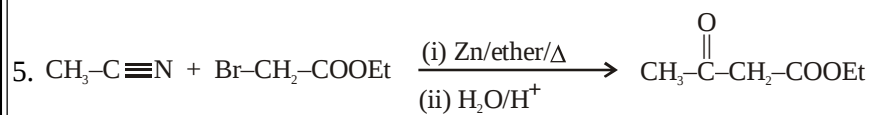
* During the Reformatsky reaction, zinc enolate formed as a **Reformatsky reagent**.



* During the Reformatsky reaction, zinc (Zn) behaves as a two-electron donor

Example of Reformatsky reaction:

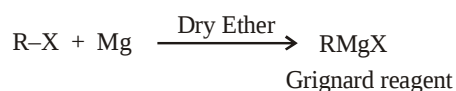




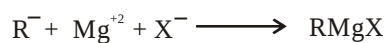
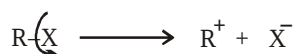
GRIGNARD REAGENTS:

- * It is very strong base
- * It gives following reactions.
 1. Acid-base reaction
 2. Addition reaction
 3. Substitution reaction
 4. Elimination reaction
- * It is an organometallic compound which has a polar C-Mg bond.

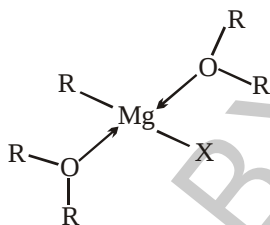
Preparation:



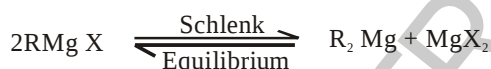
Mechanism:



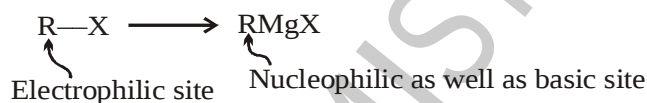
- * Etheral solution of Grignard Reagent is used for the synthetic application because of it is highly reactive.



- * Solvated form of RMgX is stable. It cannot be isolated in individual form (i.e., pure form)
- * In the Grignard Reagent, the following equilibrium also exists. (Schlenk equilibrium)



- * Grignard Reagent is an **umpolung reagent**

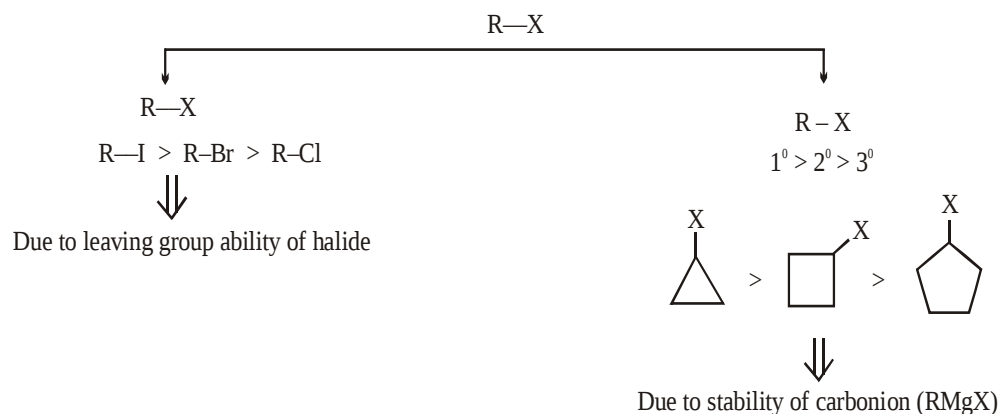


- * There is a polar covalent bond between C-Mg in Grignard Reagent

	Hard	
C-Na		
C-Li		
C-Mg		Above this hard
C-Al		
C-Zn		Below this soft
C-Pb		
C-Cd		
C-Sn		
C-Cu		
C-Hg		
	Soft	

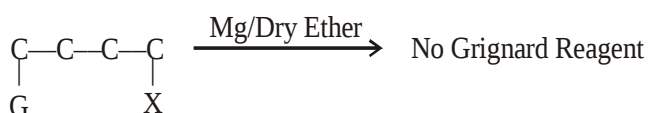
* Ionic bond in C-Na & C-Li
* In all other, polar covalent bond

*** Reactivity Order w.r.t. Preparation of Grignard Reagent:**



Points about the preparation of Grignard Reagent:

1. Compounds having acidic H-atom can not be used in preparation of Grignard Reagent.



G = Functional groups having active H-atom like: $-\text{NH}_2$, $-\text{OH}$, $-\text{SH}$, $-\text{COOH}$ etc.

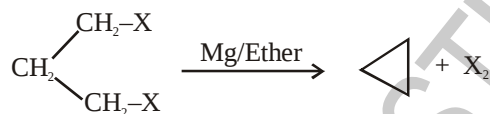
2. 1,2-dihaloalkanes (Vicinal) are not used for the preparation of Grignard Reagent.



3. $\begin{array}{c} \text{C} - \text{C} \\ | \quad | \\ \text{X} \quad \text{L} \end{array} \xrightarrow{\text{Mg/Ether}} \text{No Grignard Reagent but formed } \text{C} = \text{C}$

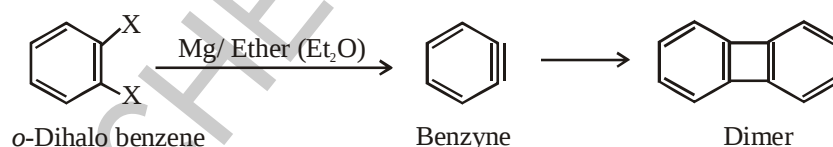
* L = OTs, OBs, OAc, etc.

4. 1,3- Dihaloalkanes not used for the preparation of Grignard Reagent



5. 1,4- & higher dihalides may be used for the preparation of Grignard Reagent

6. m- & p- may be used for the preparation of Grignard Reagent but O-form is not used because of,



7. Generally allylic & benzylic halides are not used for the preparation of Grignard Reagent. (Also rarely used so answer give according to option)

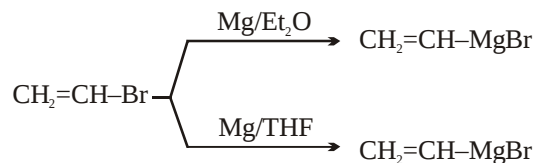
8. $\text{CH}_2 = \text{CH} - \text{Cl} \xrightarrow{\text{Mg/Et}_2\text{O}} \text{No Grignard reagent}$

In the reaction Grignard reagent is not formed, because of, during the reaction high temperature is required which is greater than boiling point of Et_2O but if THF is used then.



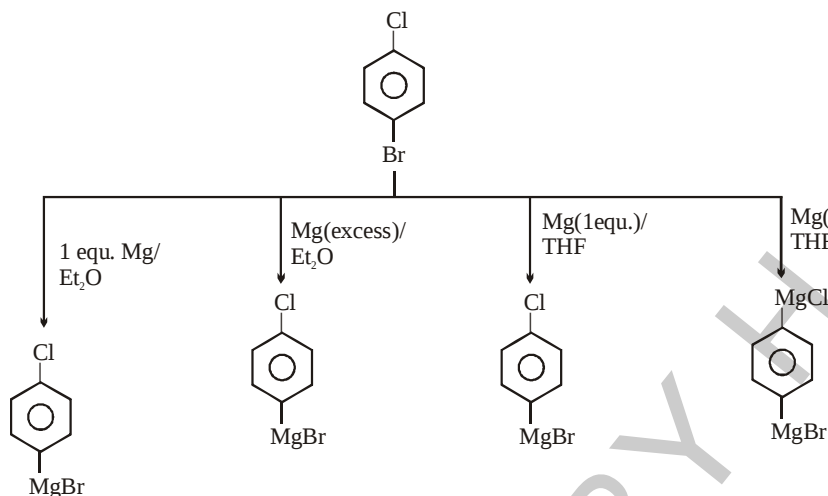
Due to high boiling point of THF

But

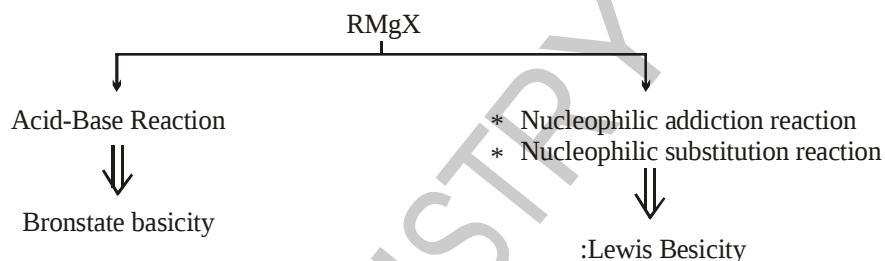


Because of less double bond character in C-Br bond of $\text{CH}_2=\text{CH}-\text{Br}$

similarly:



Chemical Properties of the Grignard reagent:



Acid-Base Reaction:

It is required less amount of energy (activation energy) so allowed always first.

So that, Always first check acid-base reaction with RMgX. before the other reactions.

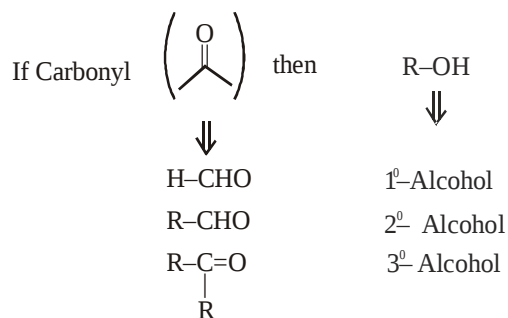


High Electronegative atom. Like
O, N, F, S or sp-hybrid-carbon

Above reaction takes place in

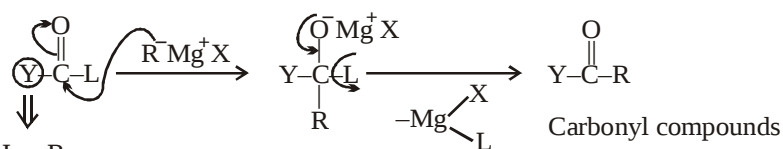


* During the acid base reaction Grignard reagent behave as the Bronstate base.



* Formation of MeOH is not possible

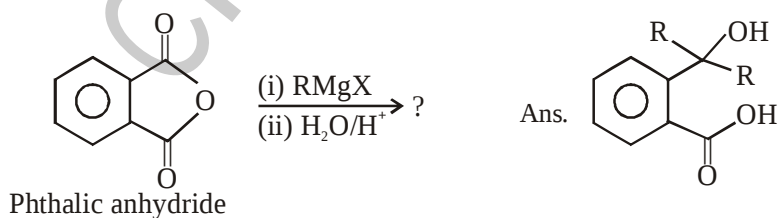
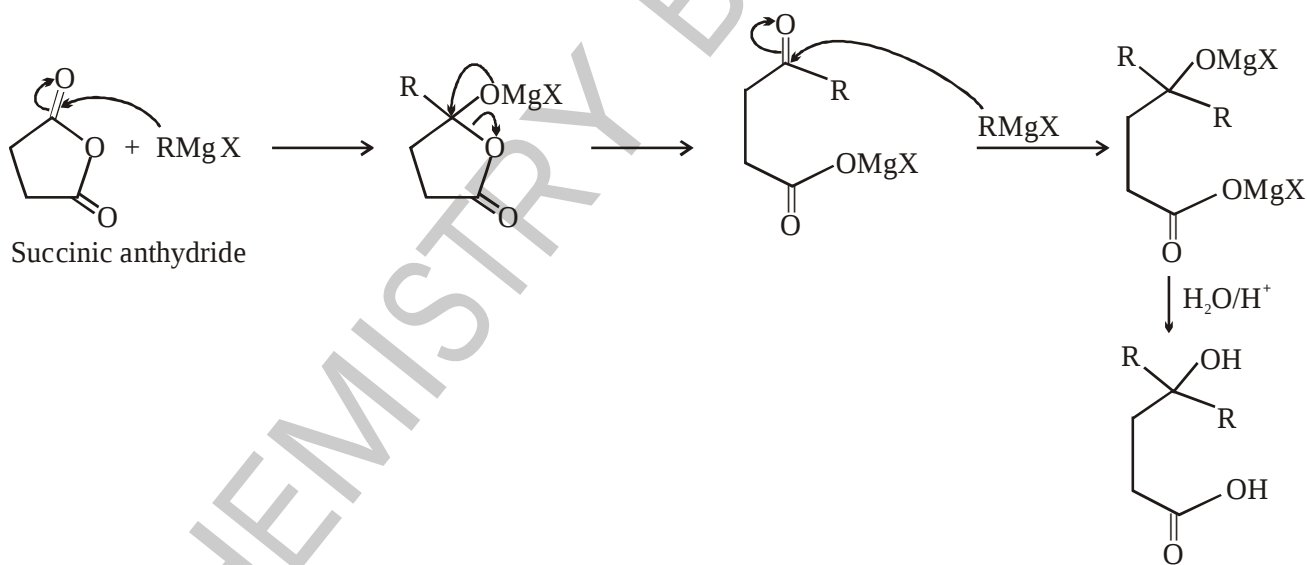
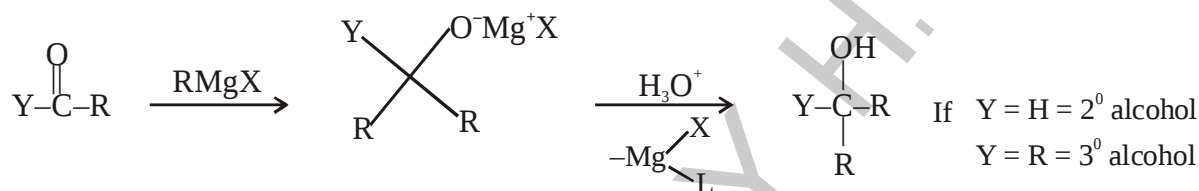
Reaction with Acid Derivation:

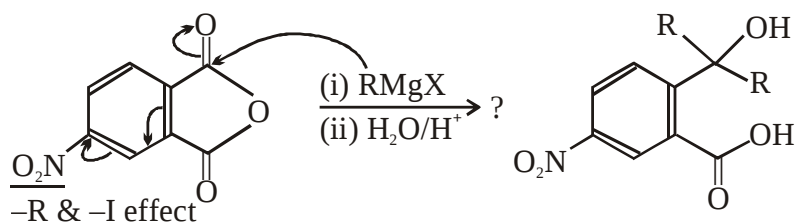


* H or R

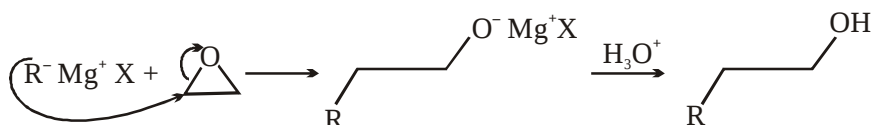
* Acid halide,
Ester or Anhydride

* MeOH & 1° alcohol can not be formed by this reaction

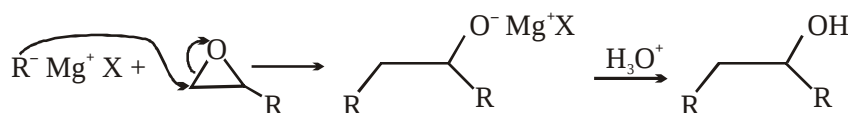




Reaction with Epoxide Ring:



If Grignard reagent react with the unsymmetrical epoxide ring, then ring opening takes place from the less hindered site.



* **Here:** o-atom can be replaced by the other hetero atom like S, N etc.

* Prepared alcohol have two C-atom more than the R of Grignard reagent

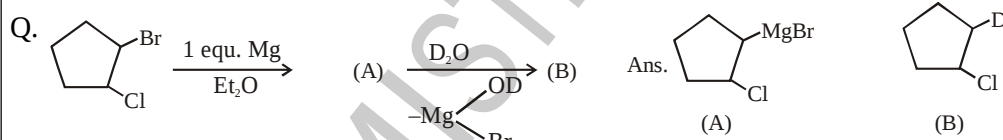
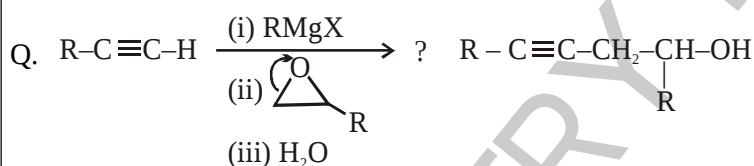
But in case of carbonyl only one C-atom more than the R of G.R.

if the case of

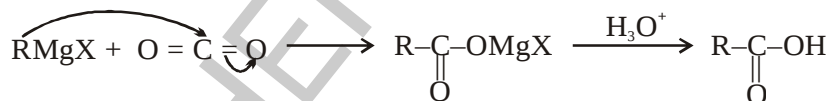
(i) O_2 with $\text{RMgX} = \text{ROH}$ of same C

(ii) >C=O with $\text{RMgX} = \text{ROH}$ of more than one C.

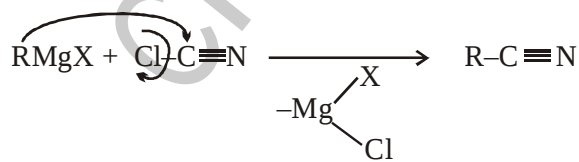
(iii) with $\text{RMgX} = \text{ROH}$ of more than two C.



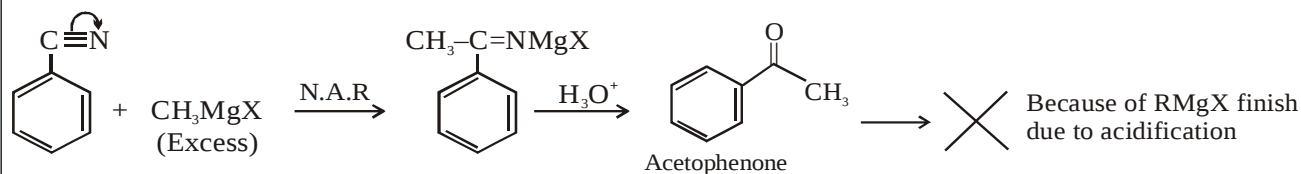
* Preparation of Acid:



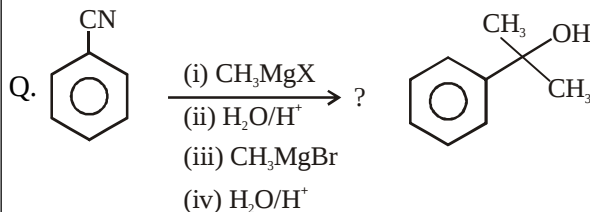
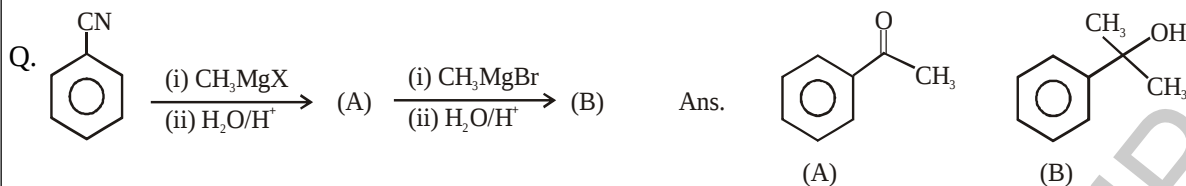
* Preparation of Cyanide:



*** Reaction with benzene carbonitrile:**

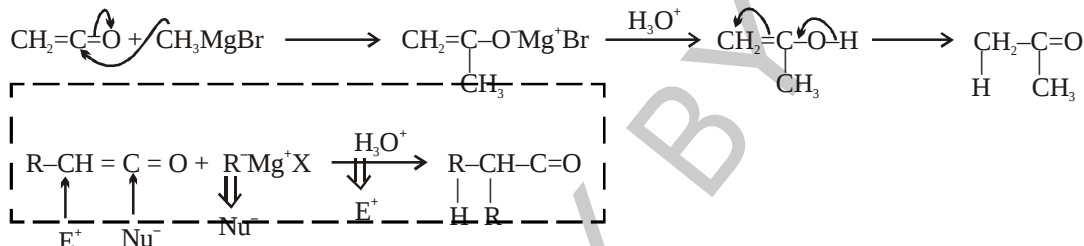


* If is best method for preparation of acetophenone

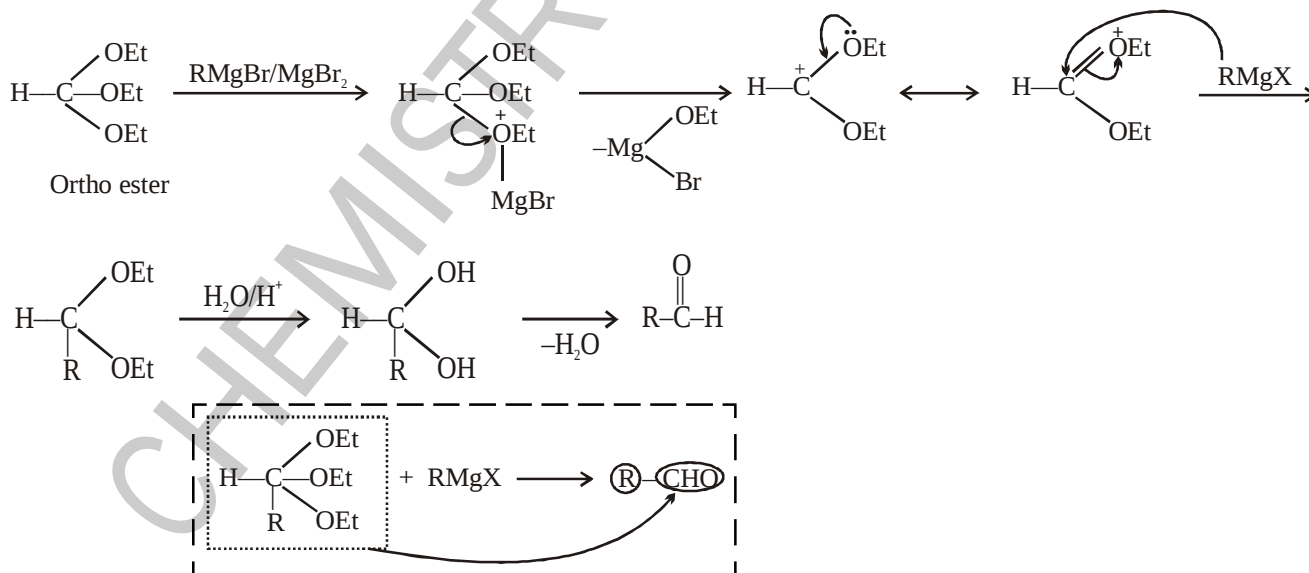


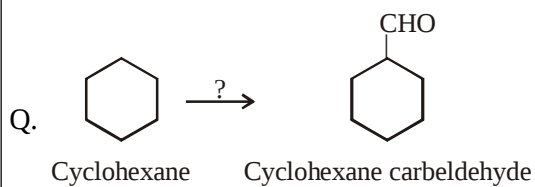
RMgX
* or RMgX(excess) $\Rightarrow$ Assuming both condition as excess

*** Reaction with ketene:**

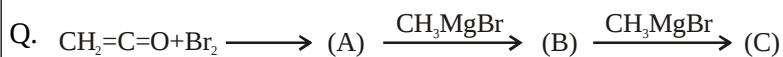
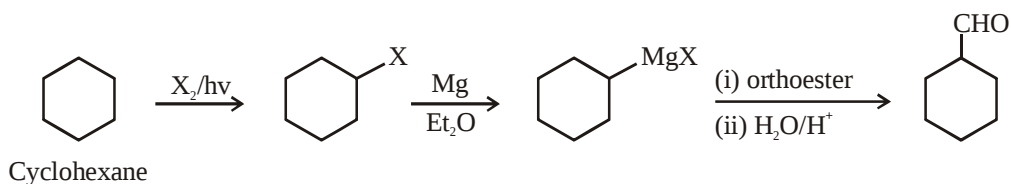


*** Reaction with Ortho Ester:**

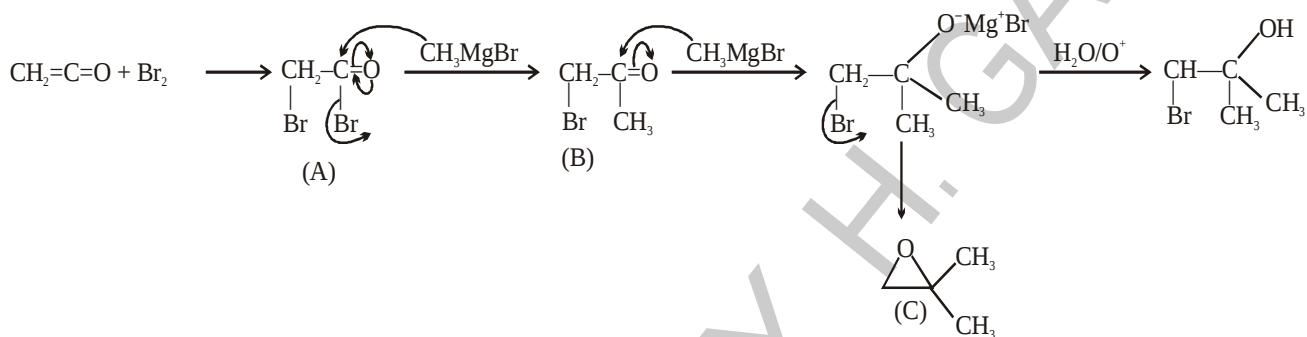




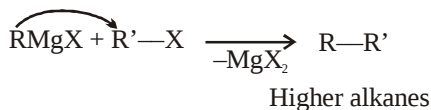
Solution:



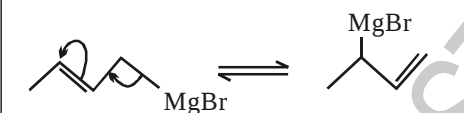
Solution:



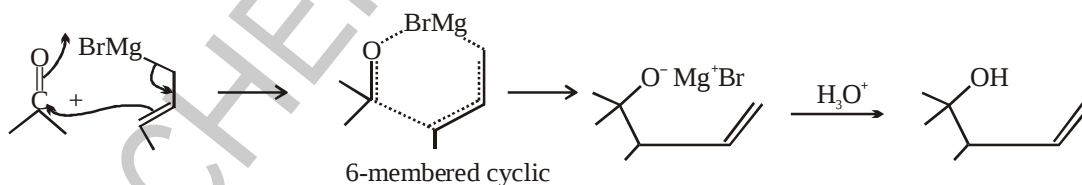
* Reaction With Alkylhalide:



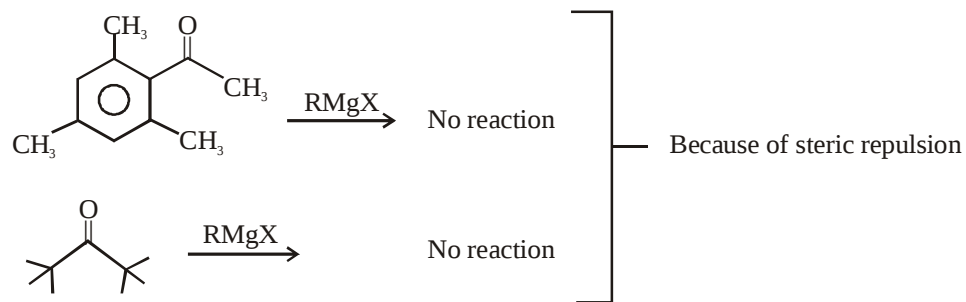
Abnormal Behaviour of Grignard reagent:



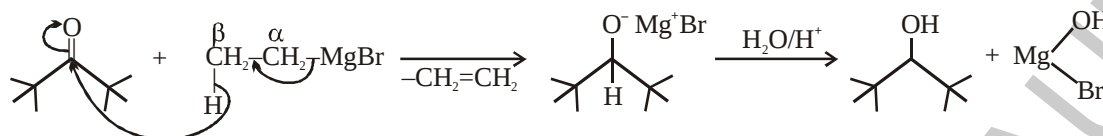
Solution:



* Allylic Grignard reagent react with the allylic shift.

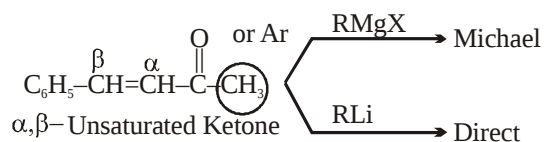


* If the Grignard reagent has β -H-atom then following reaction takes place.

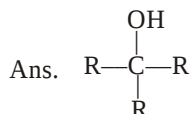
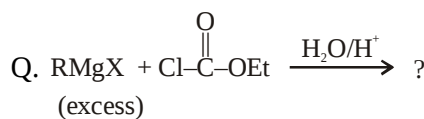
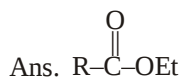
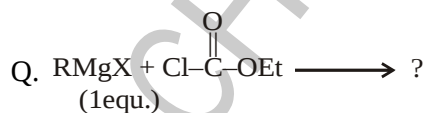
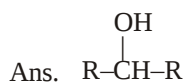
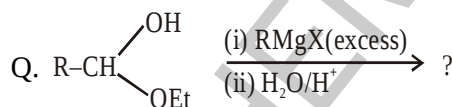
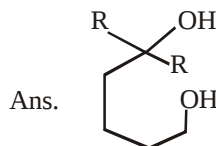
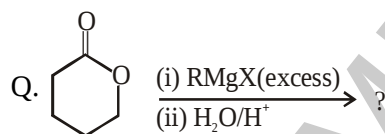
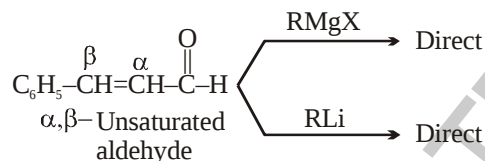
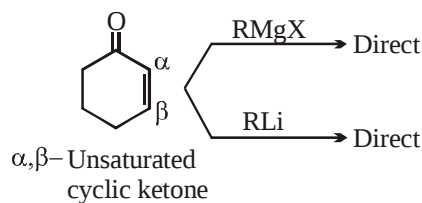


G.R. & Michael Addition:

Michael addition takes place only in acyclic α, β unsaturated ketones with G.R. (in carbonyl compounds)



But in

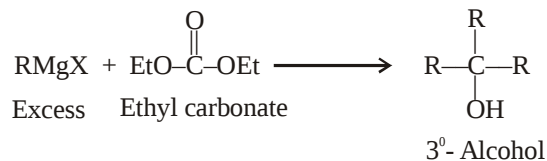


Q. $\text{HO}-\text{CH}_2-\text{CH}_2-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-\text{CH}_2-\text{CH}_2-\overset{\text{O}}{\text{C}}-\text{OEt} \longrightarrow$ How many equivalents of RMgX will be used

Ans. 4-equivalent of RMgX is used.

Q. $\text{RMgX} + \text{Ethylcarbonate} \xrightarrow{\text{H}_2\text{O}/\text{H}^+} ?$ Ans. $\text{R}-\overset{\text{R}}{\underset{\text{OH}}{\text{C}}}-\text{R}$
(excess)

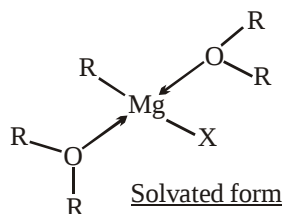
Solution:



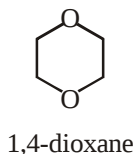
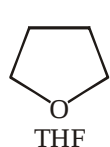
* **Best Grignard reagent** $\Rightarrow \text{CH}_3\text{MgI}$

* In Grignard reagent $\text{R} \Rightarrow$ Alkyl group, phenyl group, allylic group but **not vinyl group**.

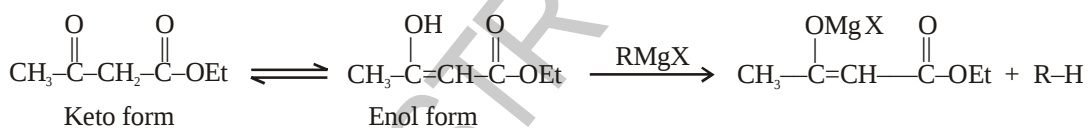
* Solvated form of RMgX is stable. It can not be isolated in individual (pure) form.



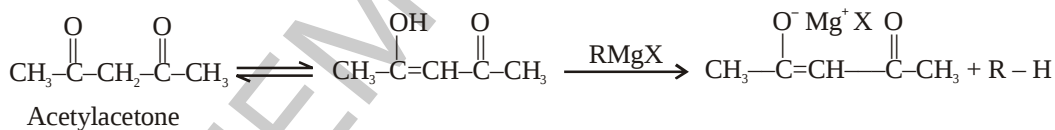
* Solvents for $\text{RMgX} \Rightarrow$ Saturated ethers



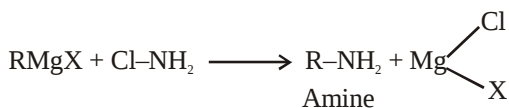
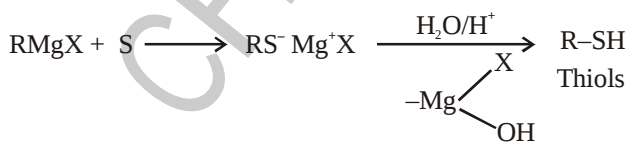
* **Reaction with AAE:**

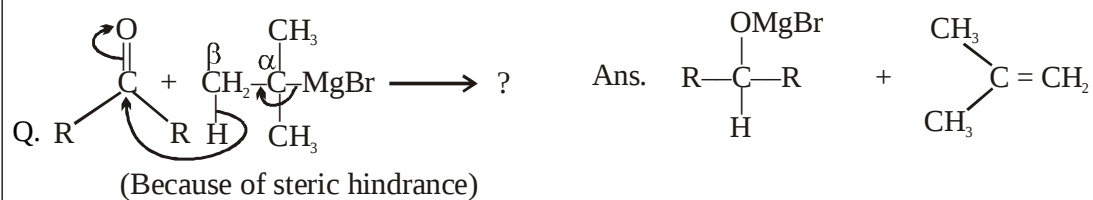
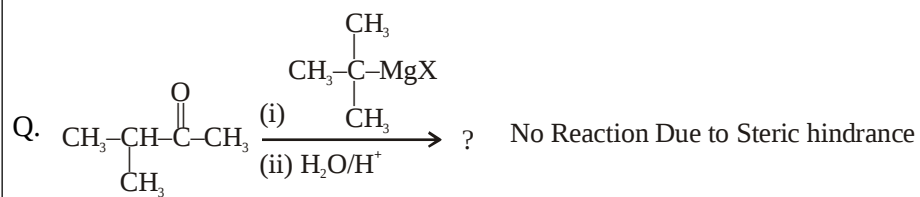


Similarly:



* **Preparation of thiols, amines & ethers:**





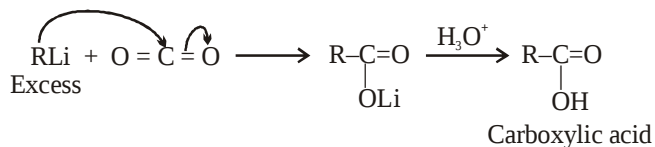
ORGANOLITHIUM COMPOUNDS:

* ionic bond in between C-Li so hard species than RMgX

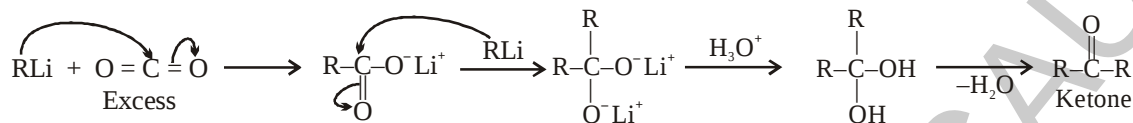


* Reaction with CO₂:

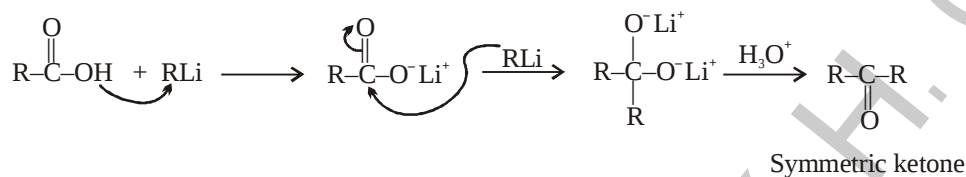
When CO₂ in excess:



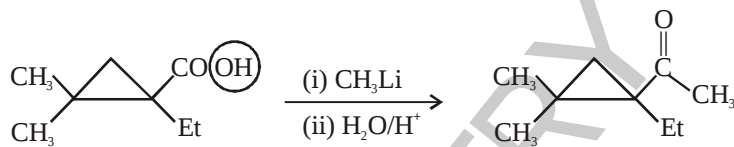
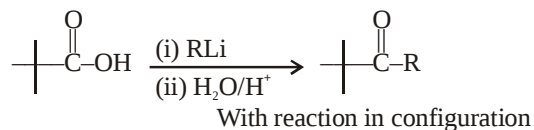
* When RLi in excess:



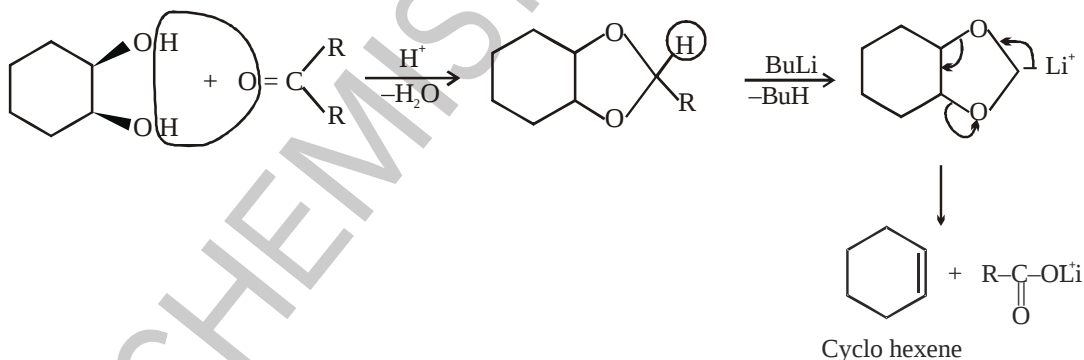
* Reaction with Carboxylic Acid:



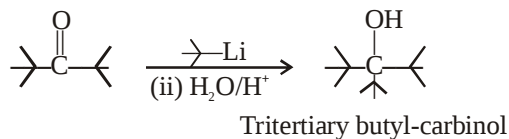
* Similarly:



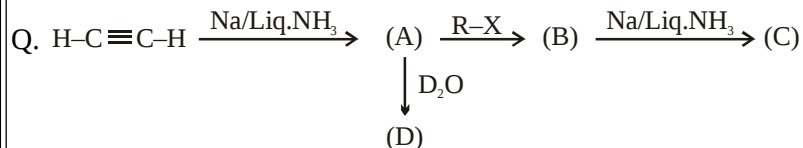
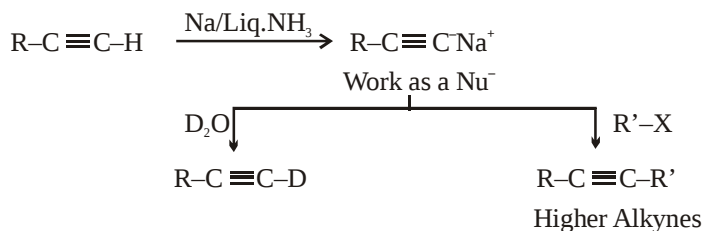
* Reaction with Acetal:



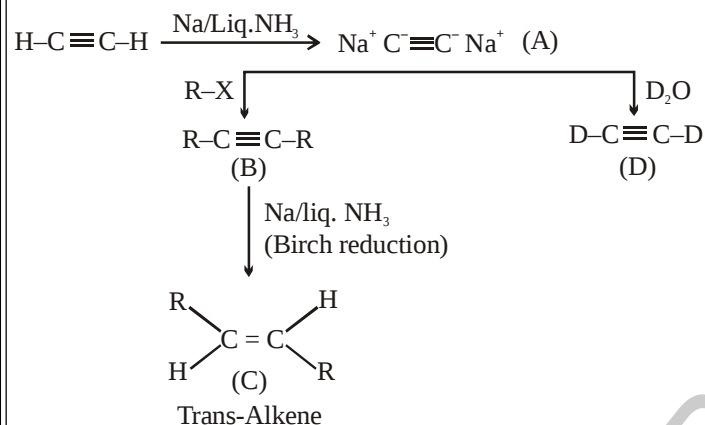
* RLi has advantage over Grignard reaction when the Grignard reaction is fail to react with highly hindard carbonyl group, the oganolithium react with such compound to give normal product.



METALLATION REACTIONS:



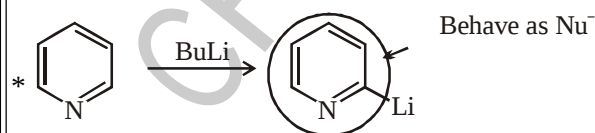
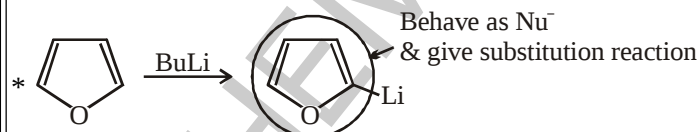
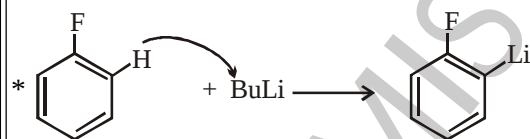
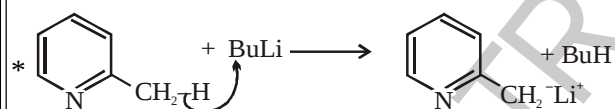
Solution:



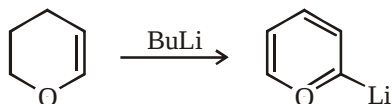
Lithation Reaction:

* It is addition of Lithium

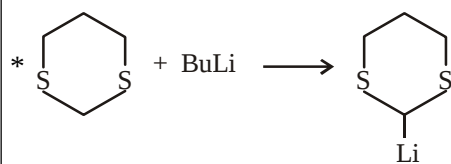
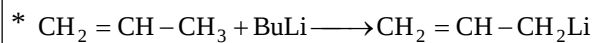
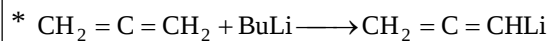
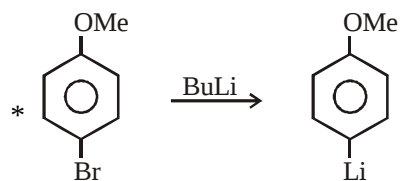
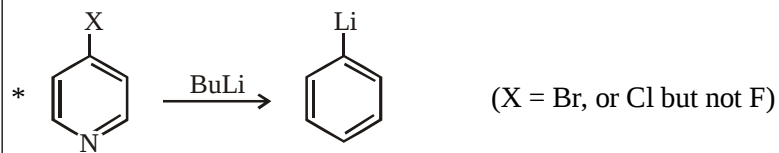
* Takes place of active H-atom



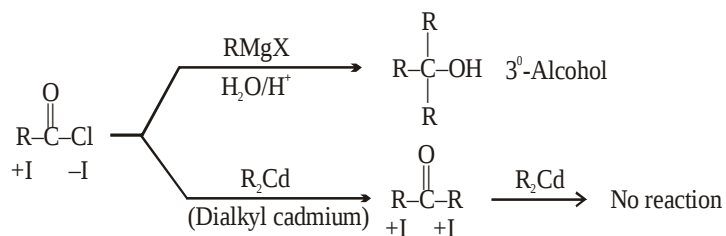
* For Pyridine, first priority lithation (acid-base reaction) after then chichibabine reaction (second priority)



*** Lithiation reaction by Halogen Exchange:**



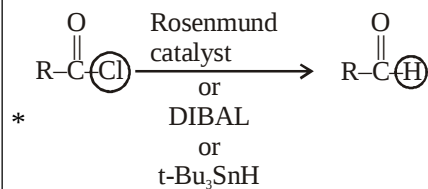
DIALKYL CADMIUM:



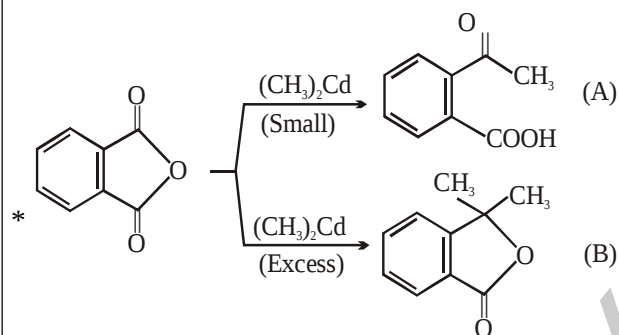
Reactivity towards the nucleophilic addition reaction.

Acid halide > Carbonyl

$\text{RMgX} > \text{R}_2\text{Cd}$

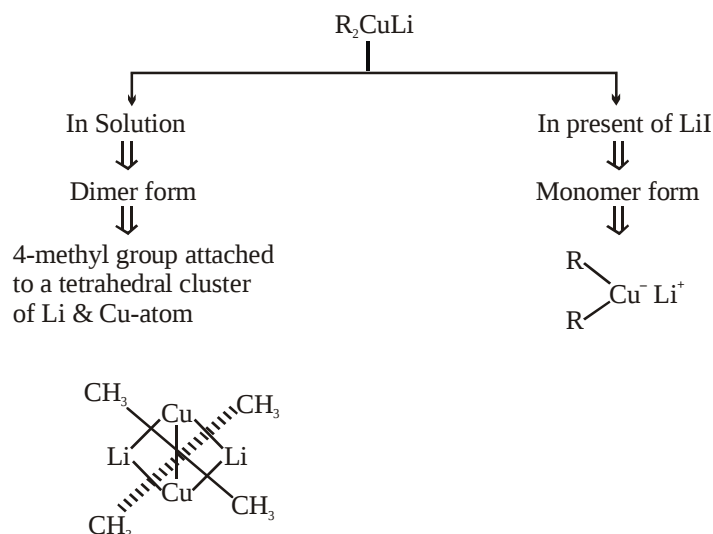


Reaction with Acid Anhydride:

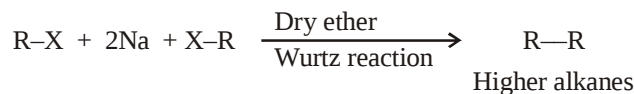


* But the above reaction in acyclic anhydrides is not particularly useful.

GILMAN REAGENTS:

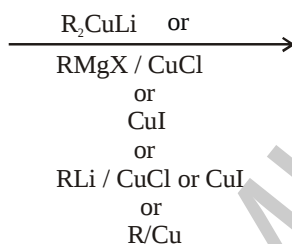


- * It is soft organocupper reagent.
- * It is source of carbanions.
- * It is a umpolung reagent.
- * It is very weak base so in the presence of Gilman reagent present, halides does not give elimination reactions.
- * It is replacement method of the wurtz reaction.



- * & by using this method we can also prepared alkanes having odd number of C-atom (**corey-house method**)

Reagents:



- * Gilman reagents give following type of reactions.

- (i) S_N -reaction (Nucleophilic substitution reactions)
- (ii) Nucleophilic addition reactions.
- (iii) Michael addition.
- (iv) Intramolecular cyclisation reactions.

Nucleophilic Substitution Reactions:

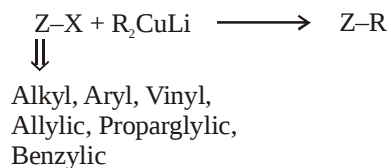
- (i) In alkyl halides $\Rightarrow R-X$ (But 3° alkyl halides are not used because of eliminated product will be formed)
- (ii) In Aryl halides $\Rightarrow Ar-X$
- (iii) In Vinyl halides $\Rightarrow >C=X$

(iv) In Allyl halides $\Rightarrow >C=C-C-X$

(v) In Propargylic halides $\Rightarrow -C\equiv C-C-X$

(vi) In Benzyl halides $\Rightarrow Ar-C-X$

* Above all substrates give coupling reaction with R_2CuLi

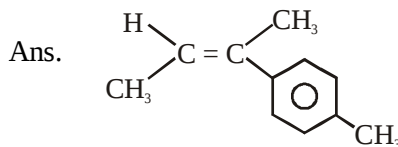
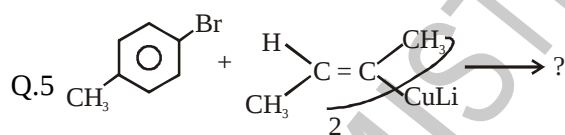
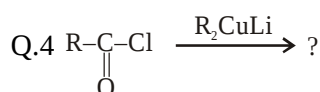
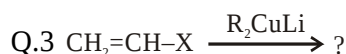
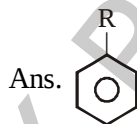
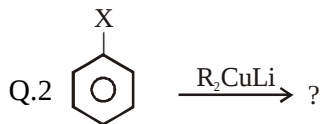
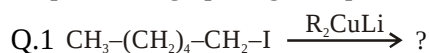


* In the case of Allylic & propargyl substrates, allylic shift will be takes place (Migration of π -bond or $SN^{2'}$ mechanism) always.

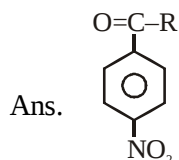
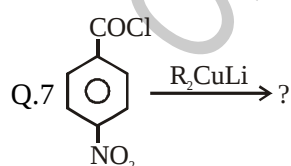
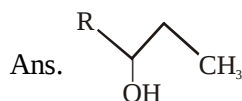
* Epoxides ring opening takes place from less hindard side (if possible allylic shift or $SN^{2'}$ - mechanism takes place.)

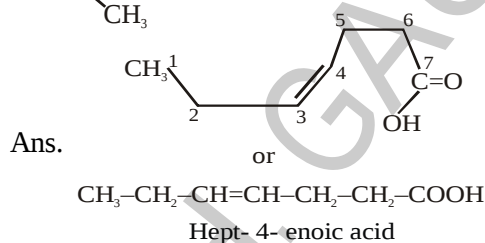
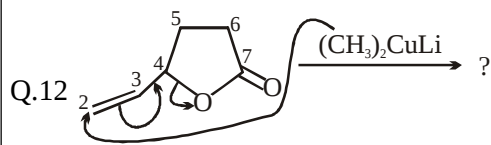
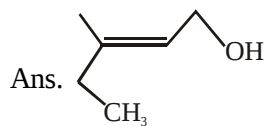
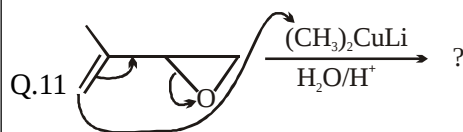
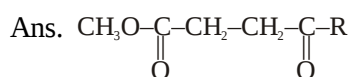
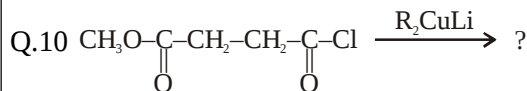
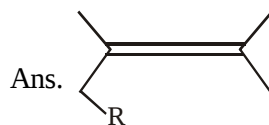
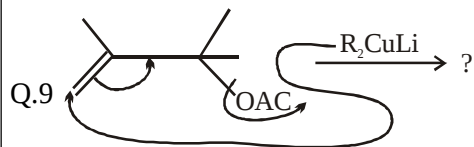
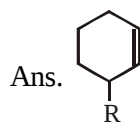


* Epoxide ring opening take place always anti periplaner manner.

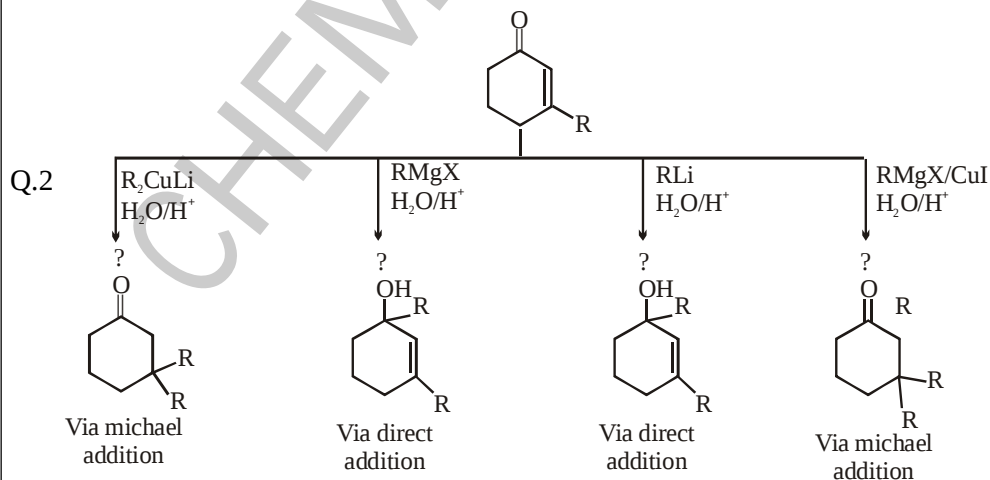
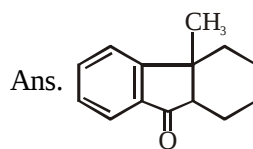
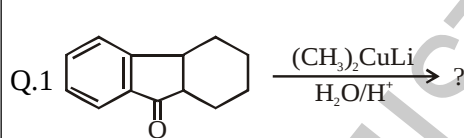
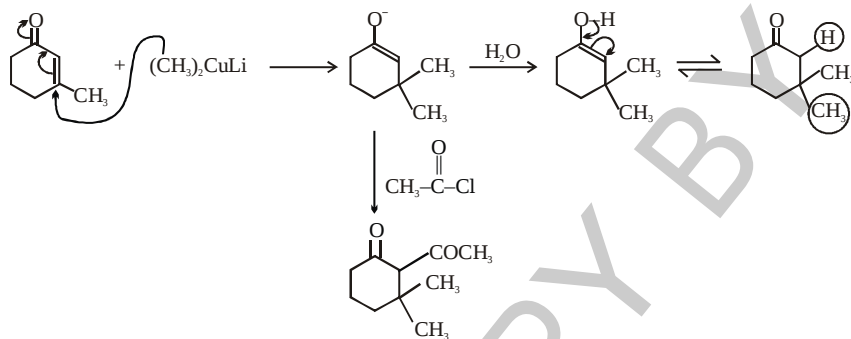


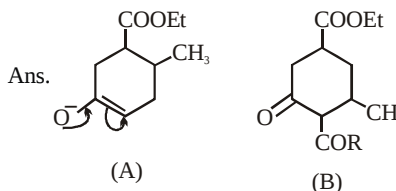
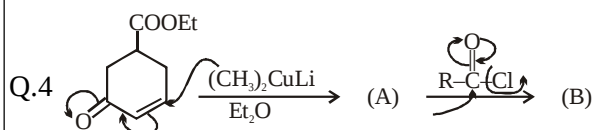
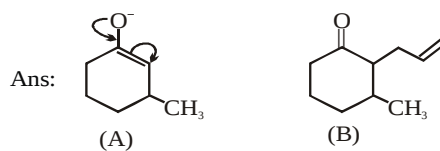
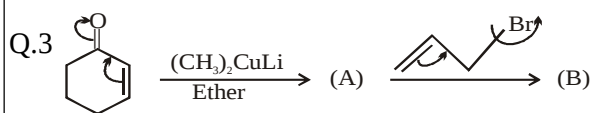
Here stereo-chemistry will be maintain i.e., Retention in configure.



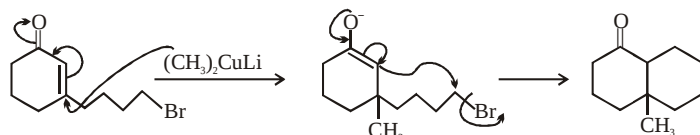


Michael Addition:

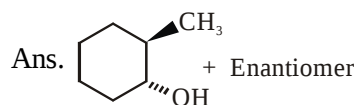
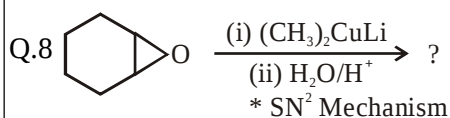
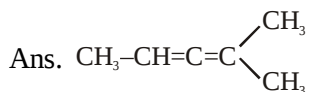
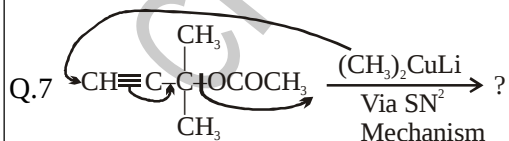
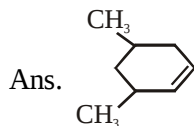
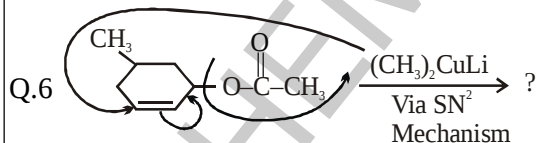
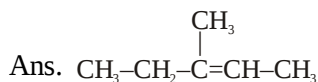
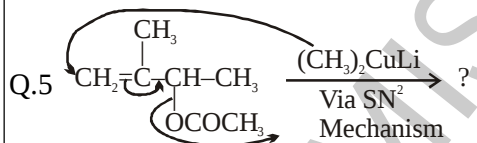
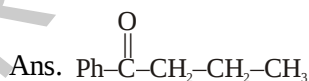
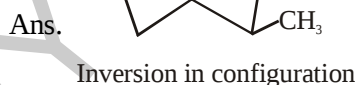
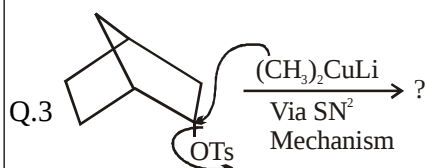
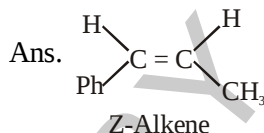
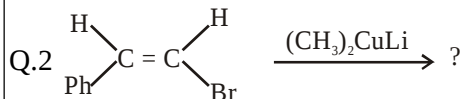
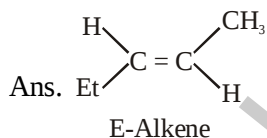
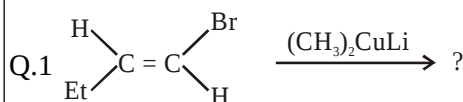


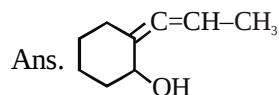
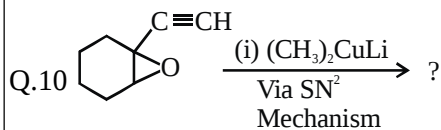
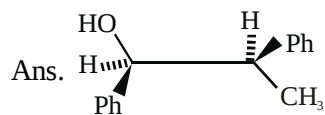
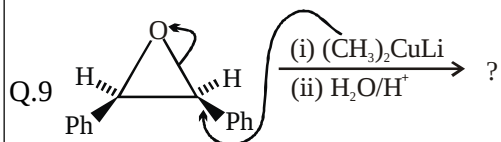


Cyclisation Reaction:



Questions:





* Michael addition takes place at less substituted C–C double bond.

* In bicyclic α, β – unsaturated ketones always only cis product will be formed.

* In chiral centre containing α, β – unsaturated ketones, give two diastereomeric product.

