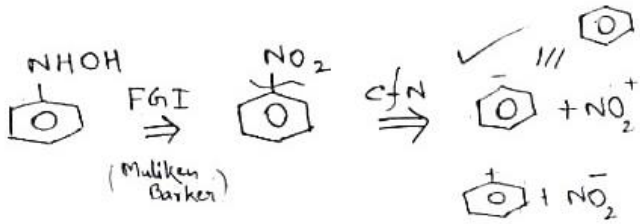
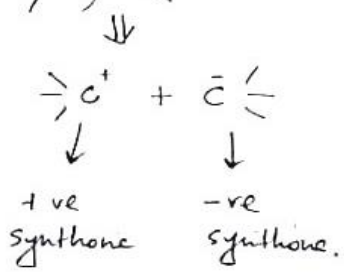
RETROSYNTHETIC ANALYSIS- 1

: Planning of Synthesis :

In this chapter we synthesis different types of compounds. To synthesise all these compounds appropriate starting meterial are to be chosen. The starting molecule is to be converted to the required pdt molecule, called target molecule (TM), through roots which will give the optimum yield of the target molecule with minimum trable and time. These roots involve the formation of several types of bonds like - C–C, C–N, C–O etc, ring closer rxns, and introduction of functional groups and their interconversions. In this chapter our intension is to find out the starting molecules and the roots through which target molecules can be synthesized. To do this we want to work backword and the process may be called synthetic analysis.





c. H_2SO_4 + c. HNO_3 → NO_2^+ (+ ve synthone)

$NO_2^+ BF_4^-$, $NO_2^+ ClO_4^-$, HNO_3/AcOH.

Q:) What is retrosynthetic analysis?

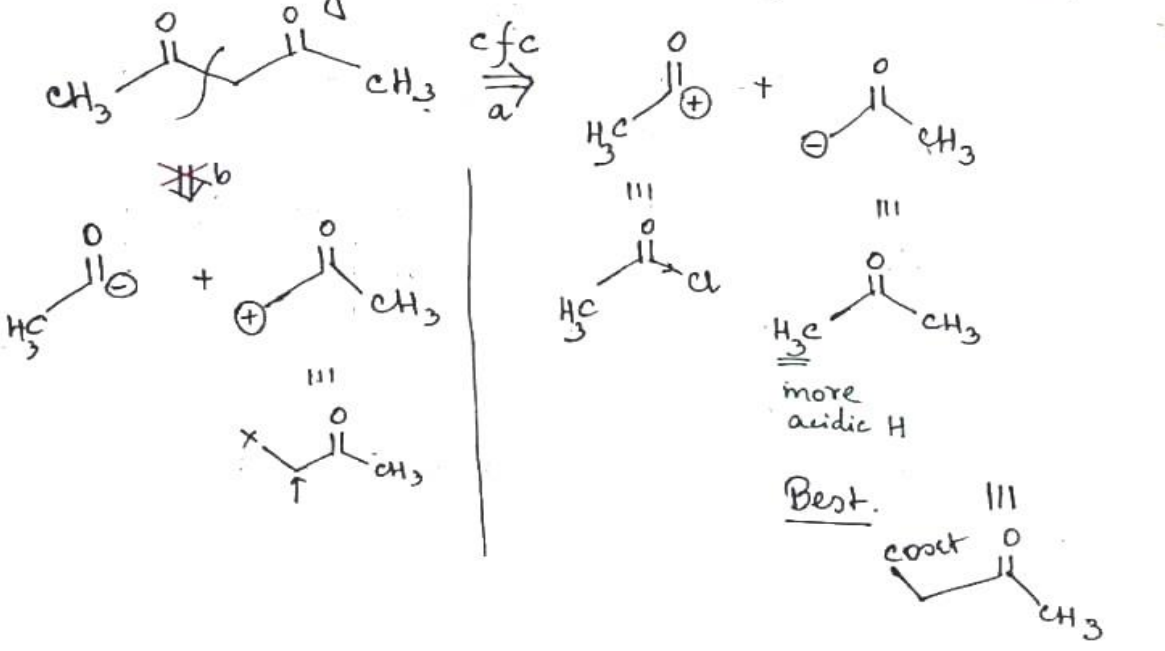
⇒ A problem solving technique for transforming the structure of a target molecule to a sequence of progressively simpler structure along a pathway which ultimately needs to simple or commercially available starting meterials for a chemical synthesis. Before synthesis we have to plan i.e. opposite synthesis. This is analysis not rxn.

Eg: 

Q:) What is disconnection?

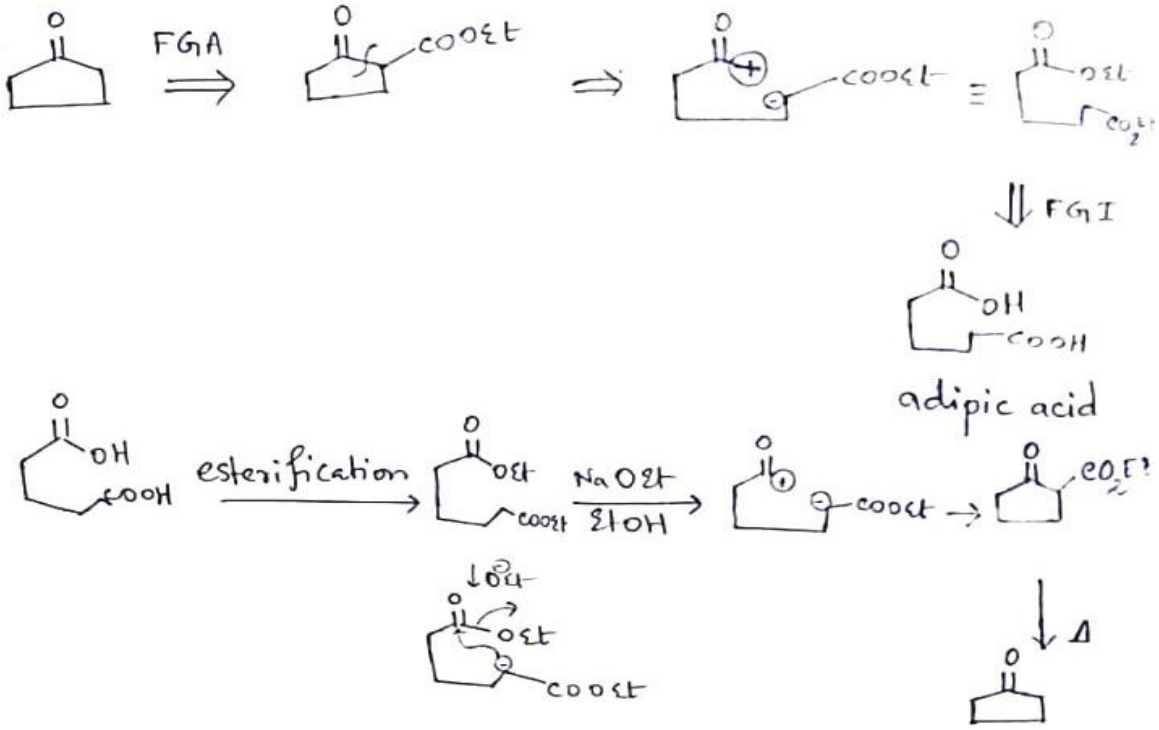
⇒ An analytical approach which breaks a bond and converts a molecule into possible starting meterials.

Symbol of disconnection '⇒' and "S", curve line drawn through the bond broken are used.



Functional group addition: (FGA)

⇒ It is the addition of a functional group to facilated disconnection.



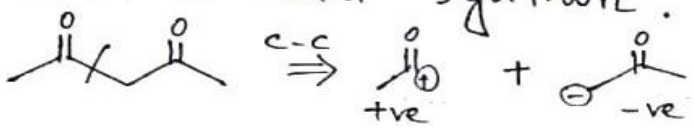
Functional gr. interchange :- (FGI)

⇒ By definition, the replacement of a functional gr. by another functional group show that disconnection become possible.

$$R-CH_2-CH_2-Br \xrightarrow[PBr_3]{} R-CH_2-CH_2-OH$$

Synthon :-

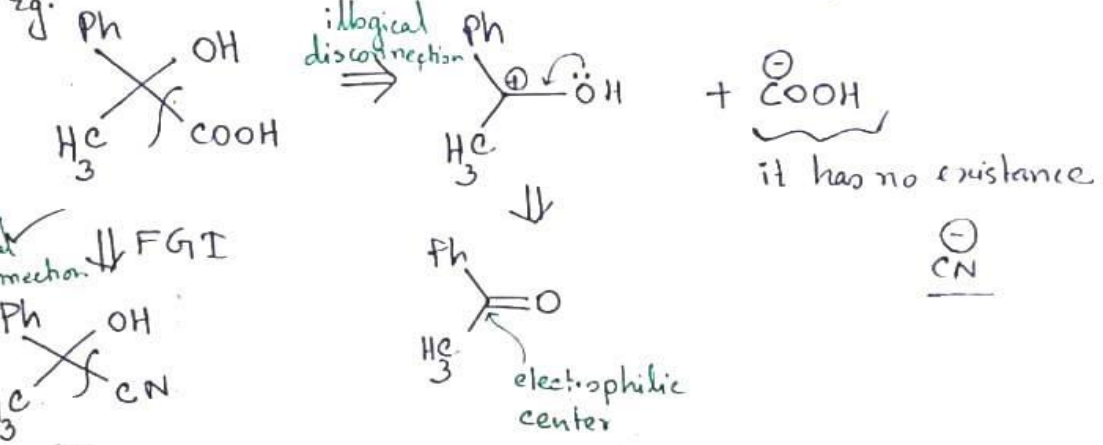
⇒ Idealised fragments resulting from a disconn-ection is called synthon.



Absent synthon :

⇒ The synthon which has no existance of the synthesis is called absent synthon.

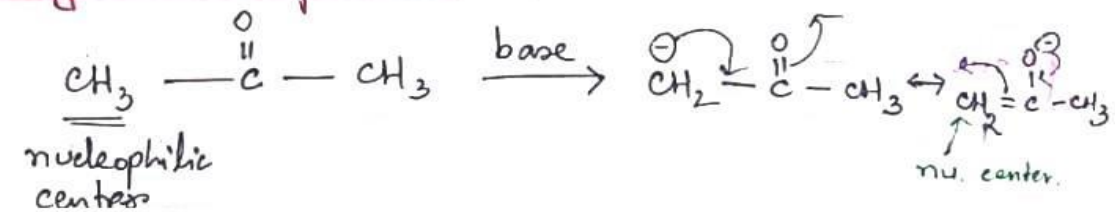
Eg:



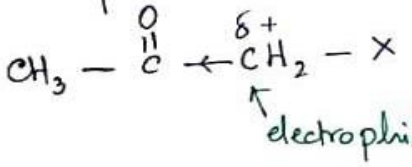
Illogical disconnection :

It is a disconnection when an absent synthon is produced after disconnection.

Illogical electrophile :

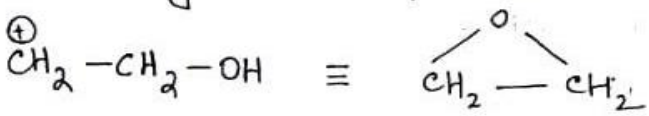


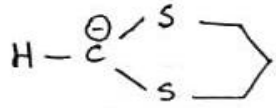
Generally C atom next to C=O gr. acts as a nucleophilic center but when C atom next to C=O gr. is electrophilic in nature, it is a case of illogical electrophile.

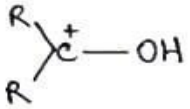
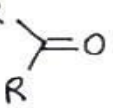


Synthetic equivalent :

⇒ A reagent carrying out a function of a synthon is called synthetic equivalent.

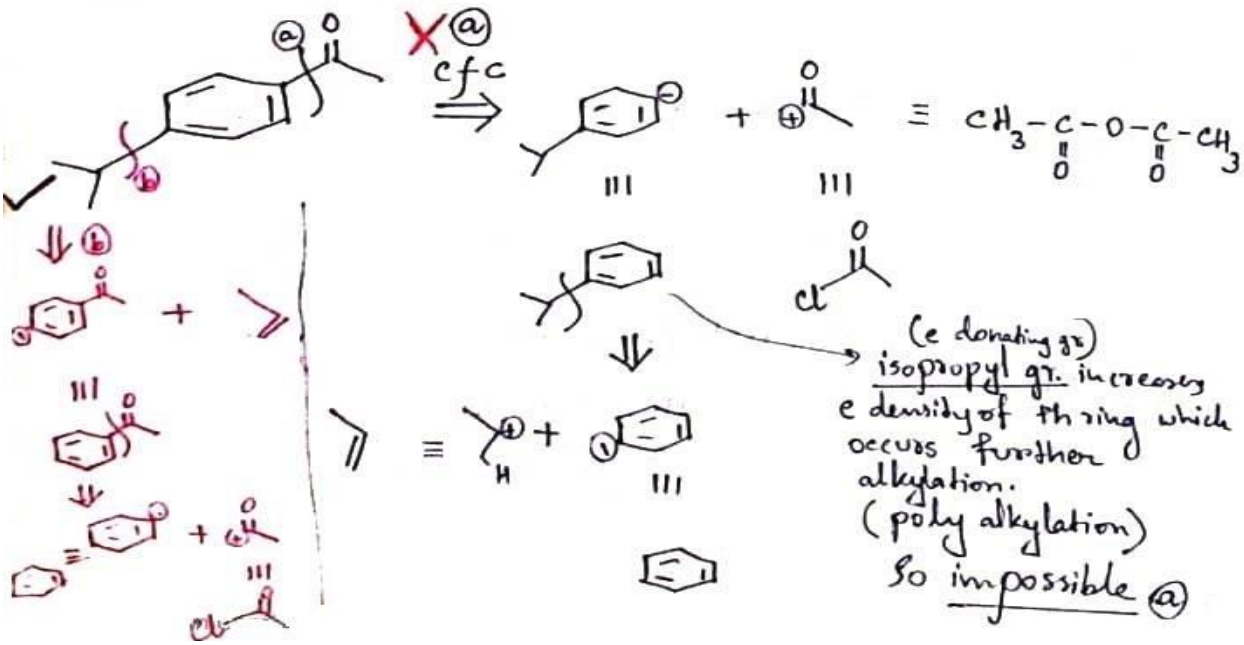


Synthons	Synthetic equivalent.
1. R^-	1. RLi , $RMgX$, R_2Cd , R_2CuLi
2. $R-C\equiv C^-$	2. $R-C\equiv C^-Na^+$, $R-C\equiv C-MgX$
3. $CH_2(COOH)_2$	3. $CH_2(COOR)_2$, $CN-CH_2-COOR$
4. $\bar{C}H_2-C(=O)-R$	4. CH_3COR , $R-C(=O)-CH_2-CO_2R$
5. $\bar{C}(R)(R')$	5. $Ph_3P=C(R)(R')$
6. $H-\overset{\ominus}{C}=O$	6. 
7. R^+	7. RCl, RBr, RI, ROH , alkene
8. $R-CH=\overset{+}{C}H_2$	8. $R-CH=CH-Br$
9. $R-\overset{+}{C}=O$	9. $R-C(=O)-Cl$, $(RCO)_2O$
10. $O=\overset{+}{C}-OH$	10. CO_2

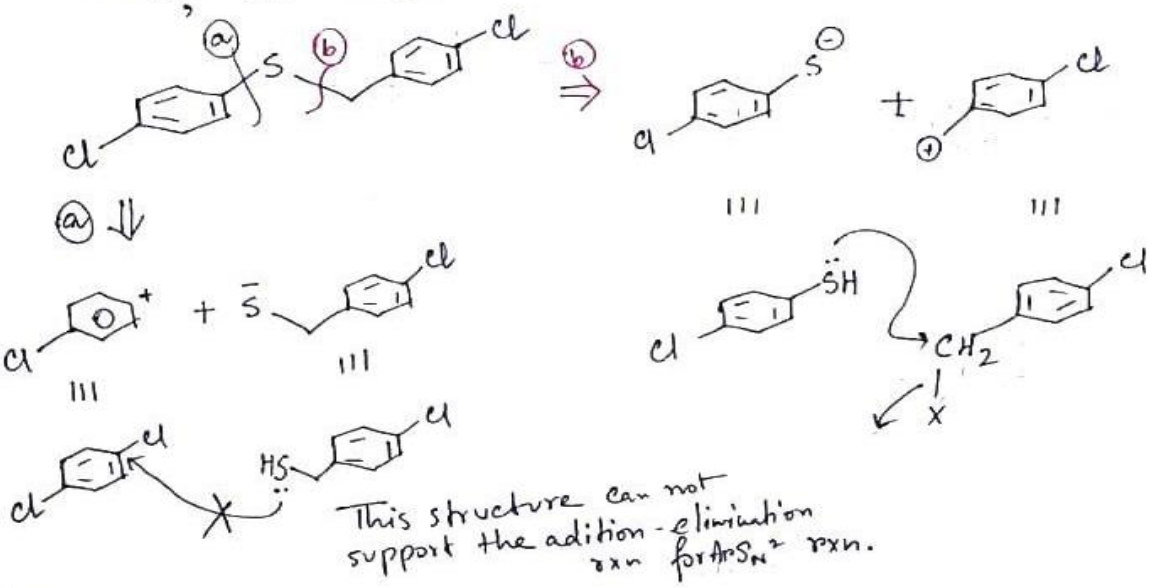
Synthons	Synthetic equivalent
11. $^{+}CH_2OH$	11. HCHO
12. $R-\overset{+}{C}H-OH$	12. R-CHO
13. 	13. 
14. $\overset{+}{C}H_2-CH_2-\ddot{O}H$	14. 
15. $\overset{+}{C}H_2-CH_2-CHO$	15. $CH_2=CH-CHO$
16. $\overset{+}{N}O_2$	16. $c.H_2SO_4/c.HNO_3$
17. $\overset{+}{Cl}$	17. Fe/Cl_2
18. $\overset{+}{N}O$	18. HNO_2
19. $\bar{N}H_2$	19. KNH_2
20. $\bar{C}N$	20. KCN

-: Guide line for disconnection :-

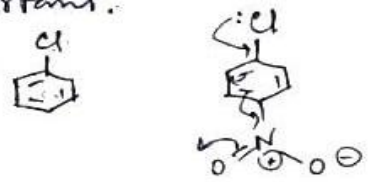
1) Disconnection must correspond to known reliable rxns.



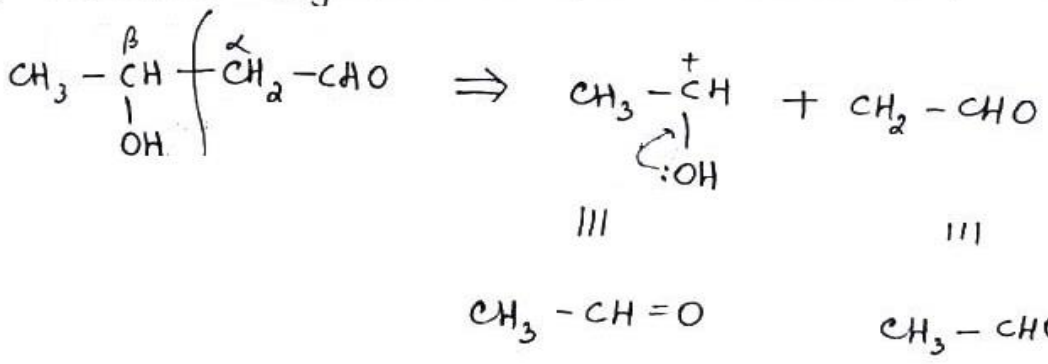
2) For compounds containing two parts joined by hetero atom, disconnect next to the hetero atom.



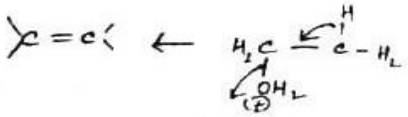
[Electron substitution rxn → electron delocalisation ↓ important.

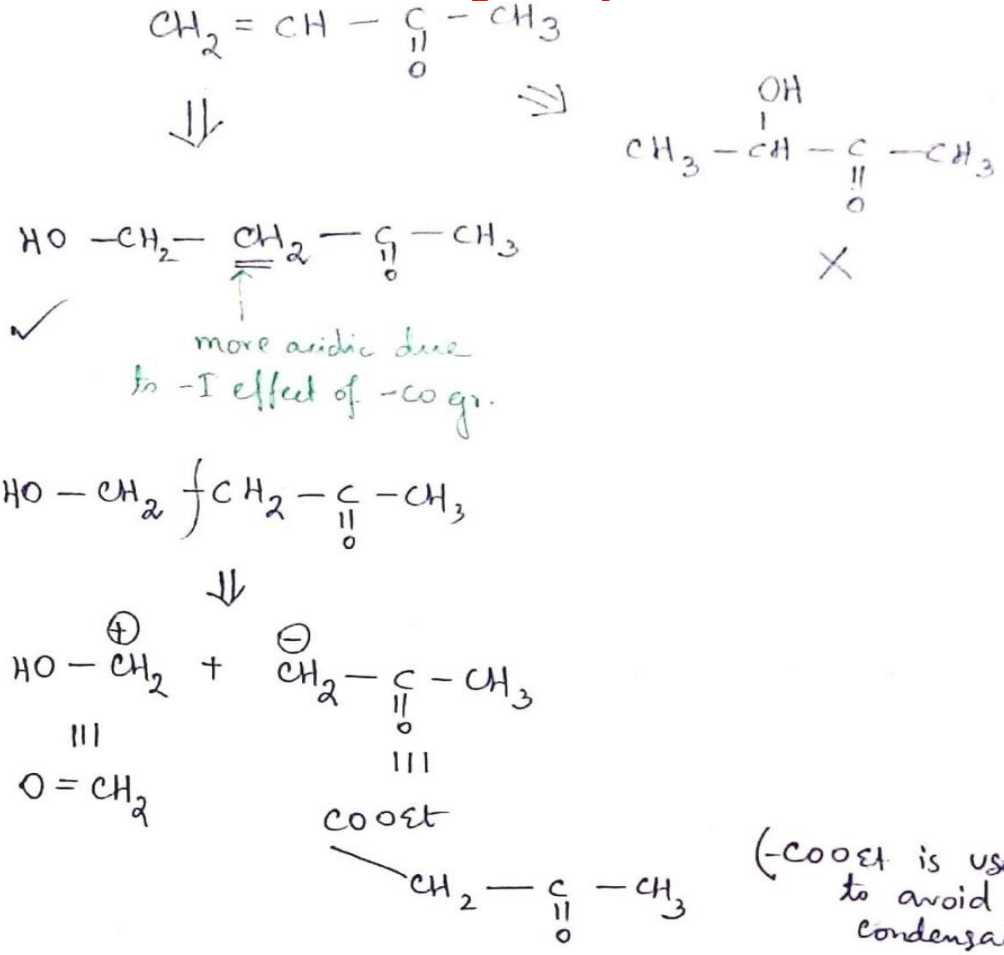


3) Disconnect adjousend to the -OH and -co, -CHO, gr.

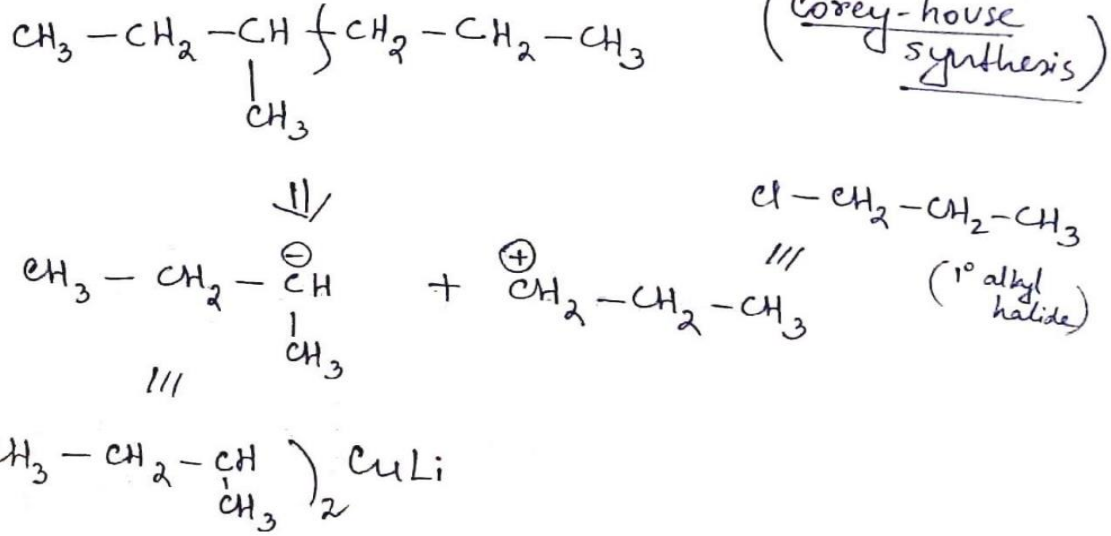


4) C = C may be converted to $-CH(OH)-\underset{H}{CH}-$

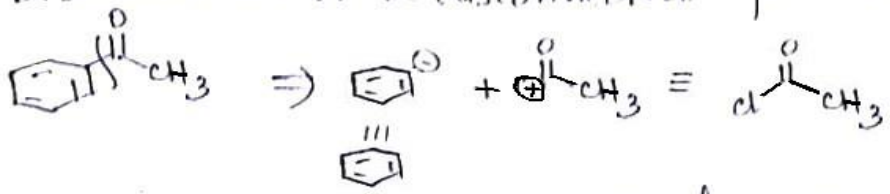




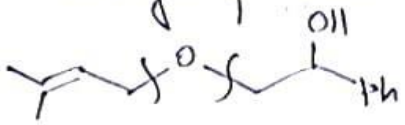
5) The branched point is to be disconnected to get unbranched carbon system which are more likely to be available.



6) Branches must be disconnected from the ring.

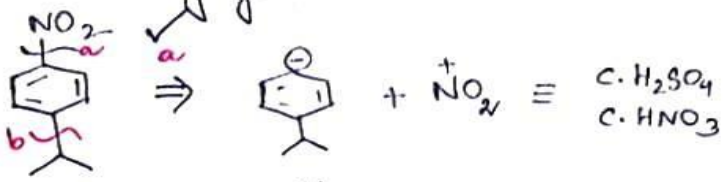


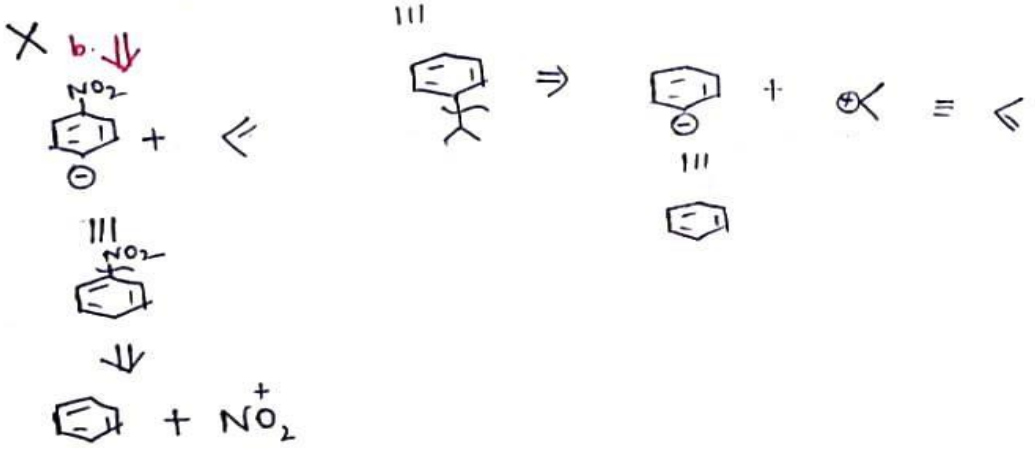
7) Use two group disconnections where ever possible.



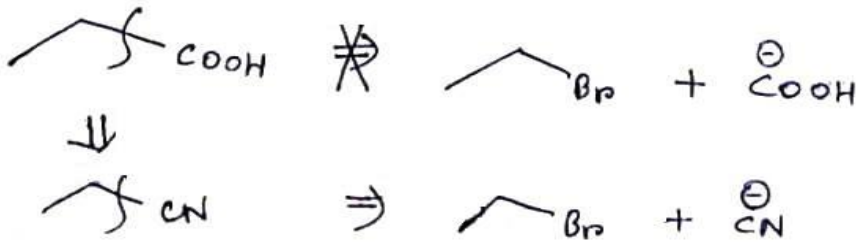
(disconnection & synthesis)

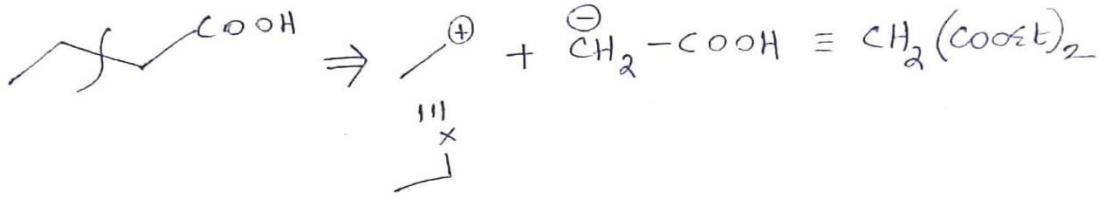
8) If there is a choice disconnect fast the most electron withdrawing gr.

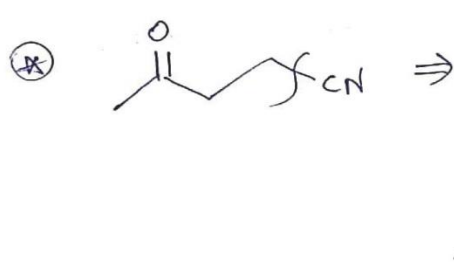




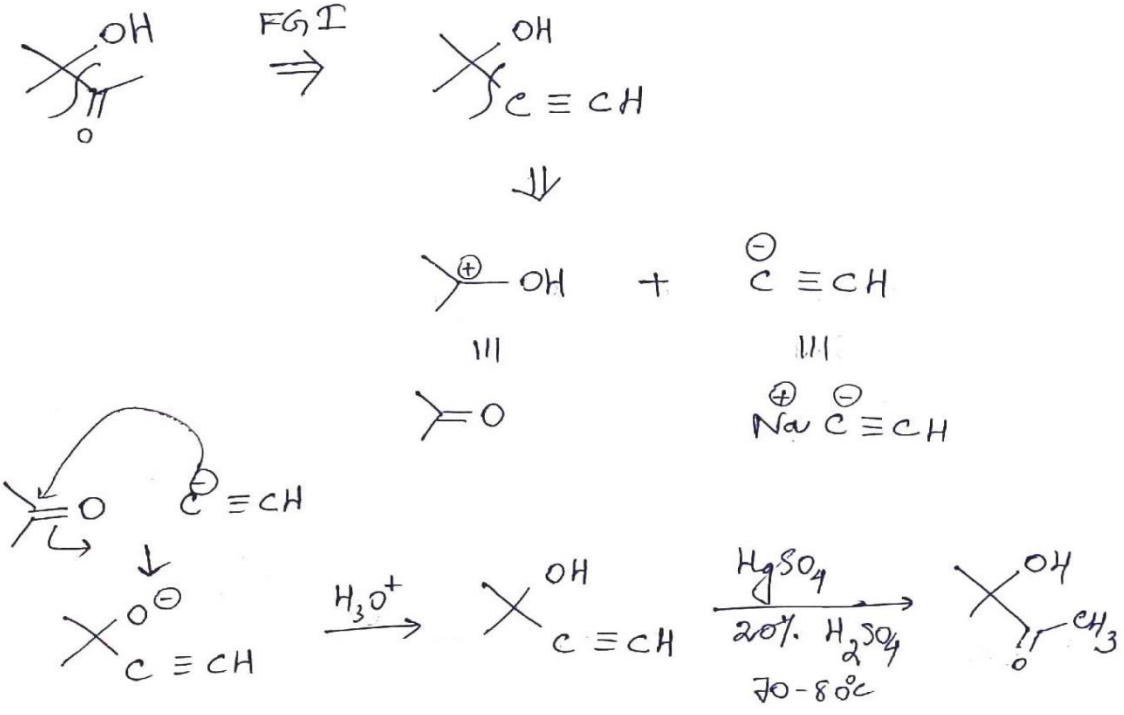
9) If the target molecule contains only C–C bond disconnection should be as follows.







10) Always try to disconnect in between functional group for a poly functional target molecule.



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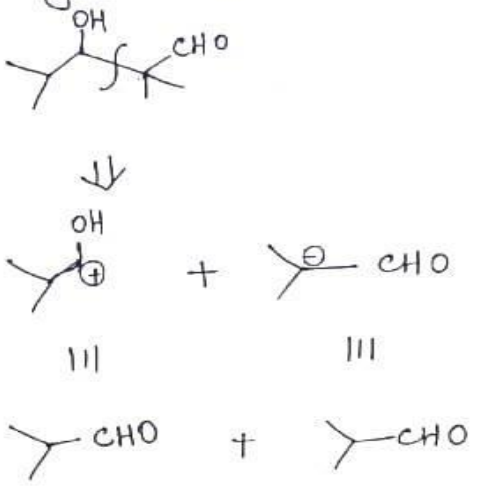
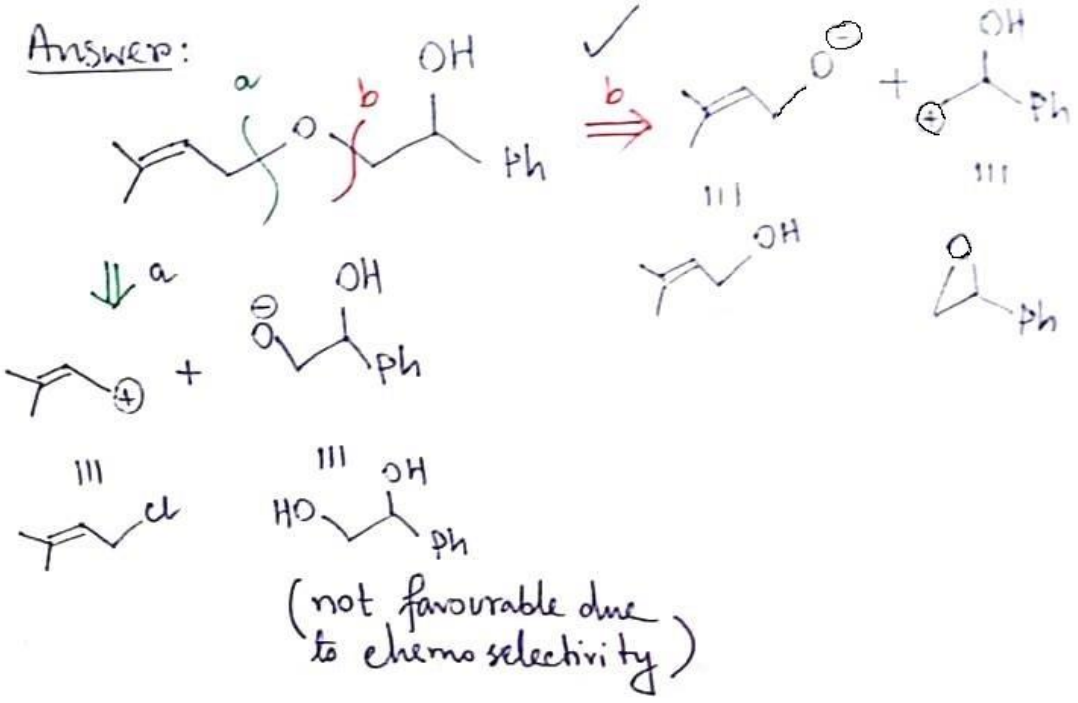
11) Symmetrical disconnection should be done if possible.

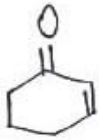


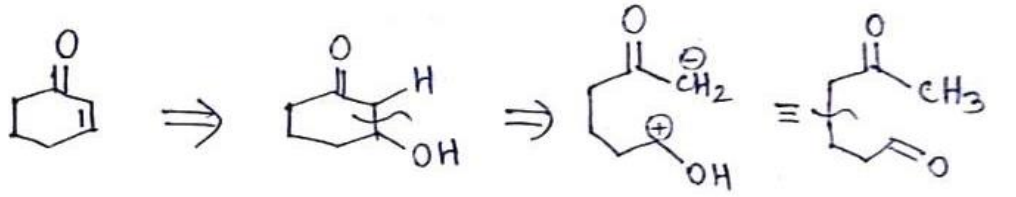
Answer:

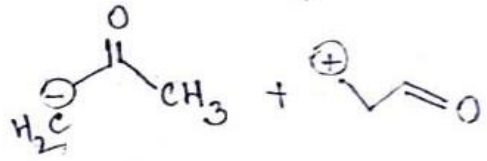


(not favourable due to chemoselectivity)

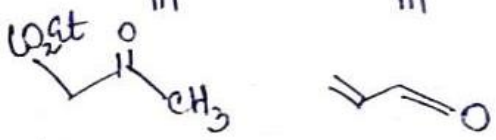
12) Six membered ring and α,β unsaturated carbonyl compound → try Birch reduction followed by hydrolysis



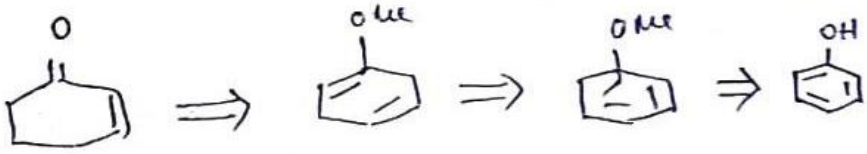


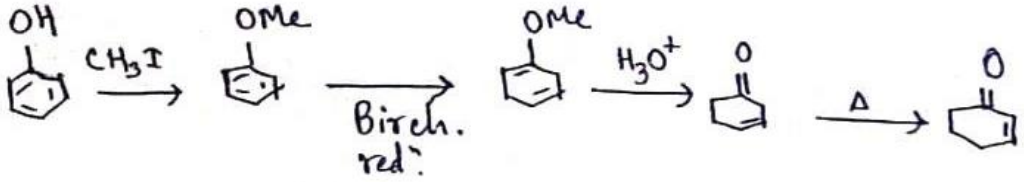


III III

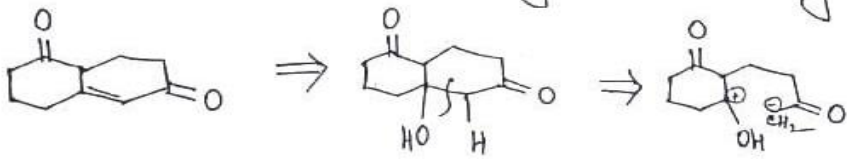


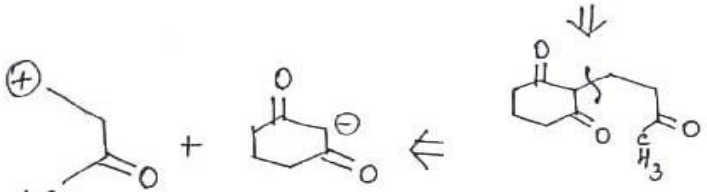
Using Birch red^{n}:





13) If target molecule is bicyclic ring having α,β-unsaturated ketone → try Robinson ring annulation.





III III