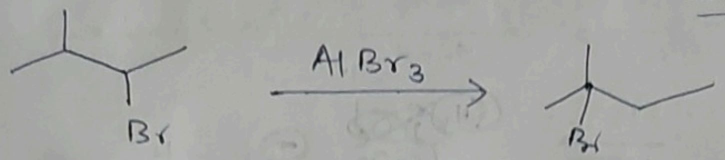
The wagner- Meerwein rearrangement

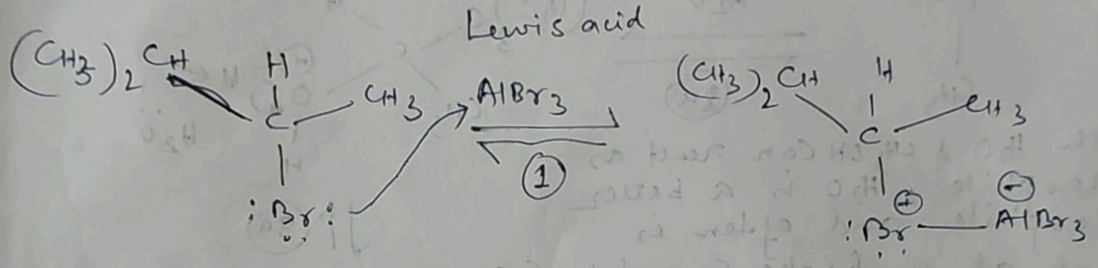
- The migration of an alkyl group to a cationic centre is known as wagner- Meerwein rearrangement.



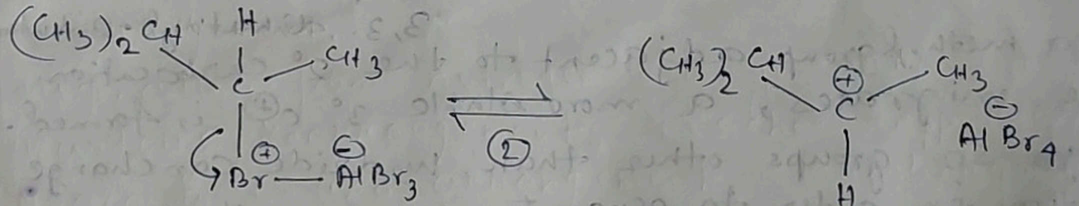
2-bromo-3-methyl butane

2-bromo-2-methyl butane

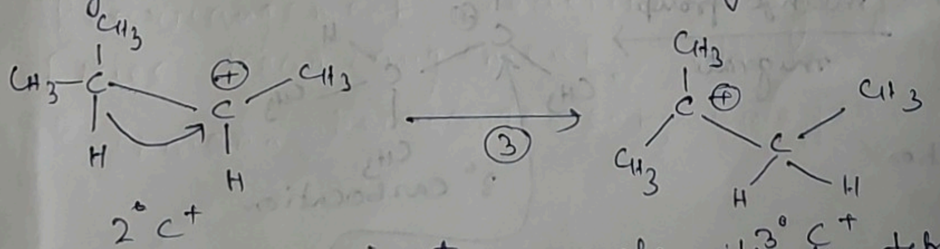
Mechanism



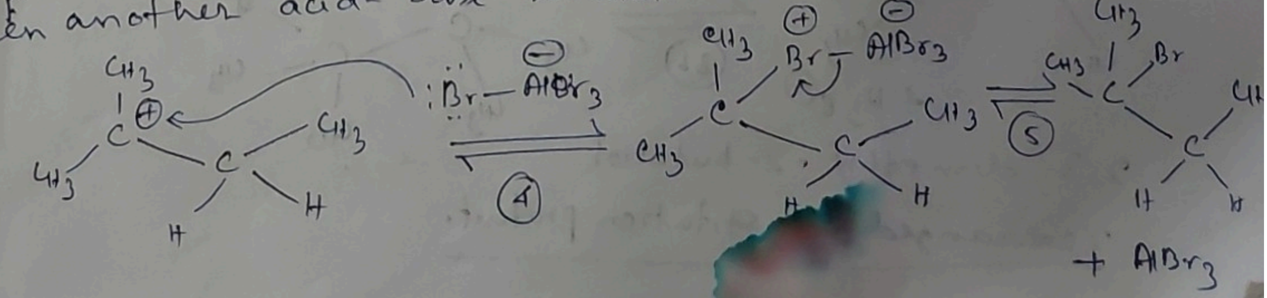
The species can ionize in one of two ways. The first is simply a reverse of the initial step; the 2nd possibility involves loss of the tetrabromo-aluminate ion to form a secondary carbocation.



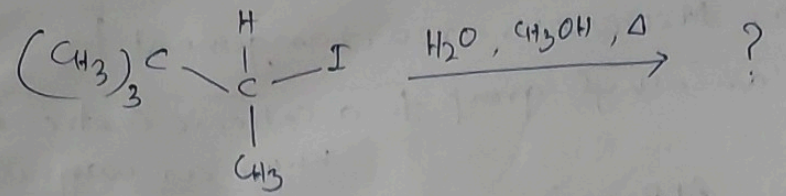
A hydrogen atom with its pair of electrons - a hydride ion - subsequently migrates from the neighbouring carbon atom to generate more stable tertiary carbocation.



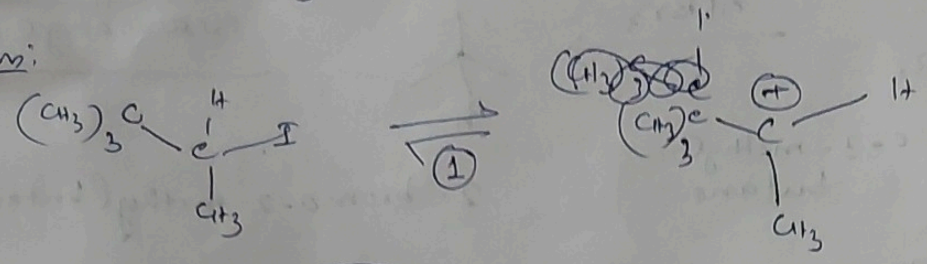
This carbocation in turn reacts with the tetrabromoaluminate ion, which is a nucleophile, to yield the rearranged product after dissociation of aluminium tribromide in another acid- base reaction.

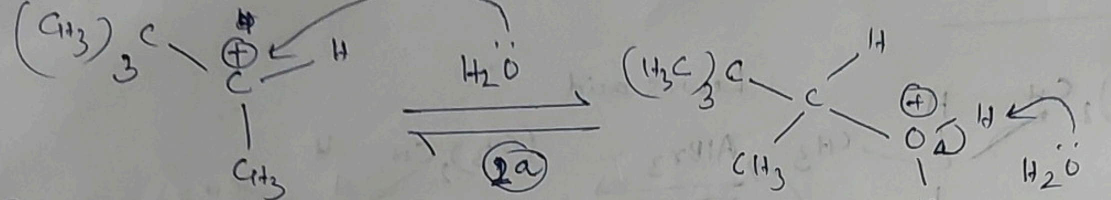


Q

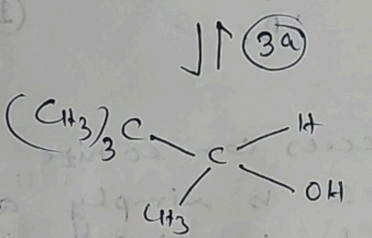


Ans:





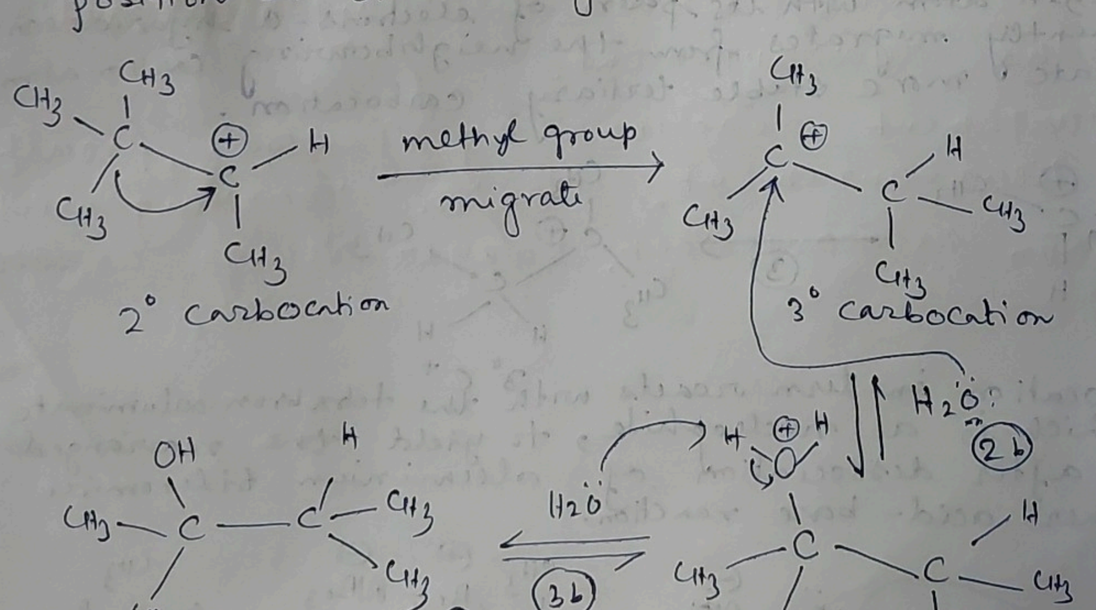
both H_2O & CH_3OH can react as nucleophile, H_2O is a better nucleophile and often is present at a higher concentration than methanol, so it react preferentially.



direct substitution product.

3,3-dimethyl-2-butanol.

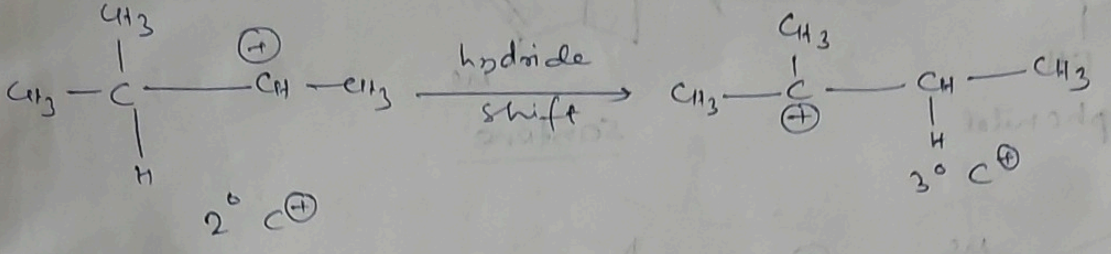
If a methylgroup adjacent to the 2° carbocation centre migrates, a more stable 3° $C^{\oplus}$ is formed. so groups other than hydride can change position in order to generate a more stable carbocation.

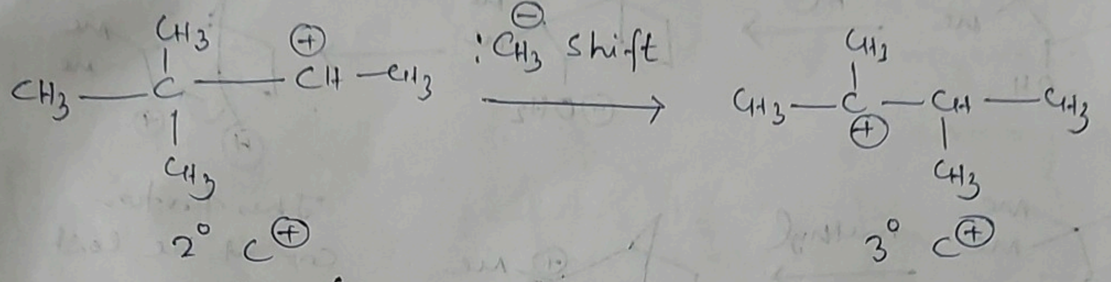


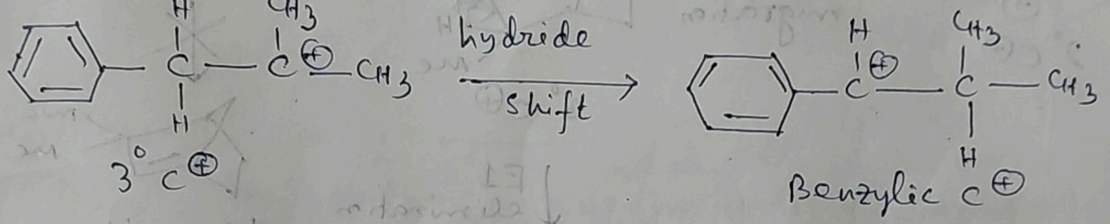
2,3-dimethyl-2-butanol

rearranged substitution product.

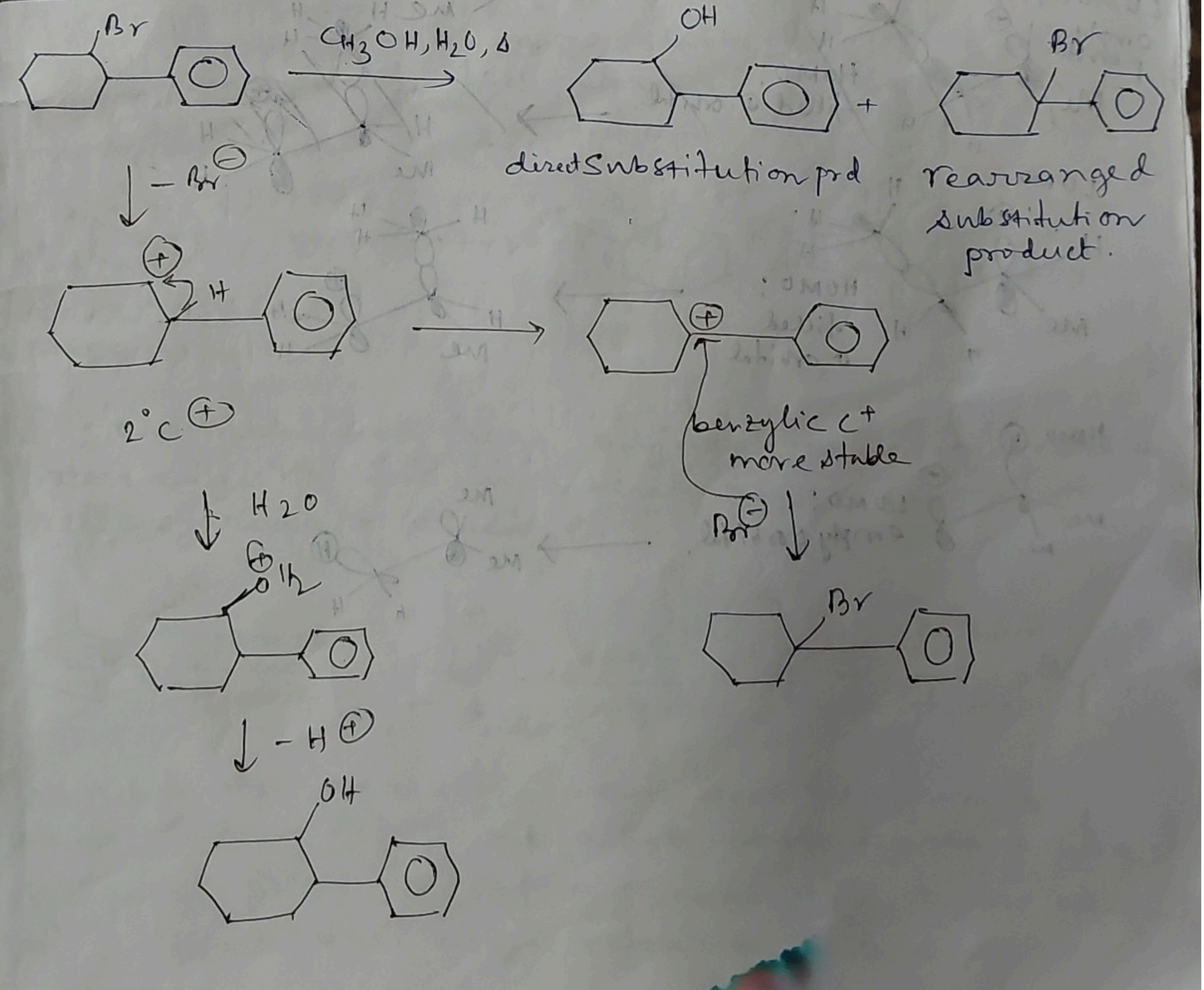
Common instances are 2° → 3°, 2° → benzylic,
3° → benzylic.

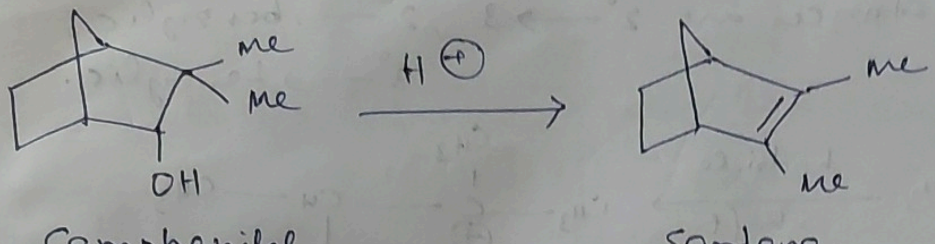






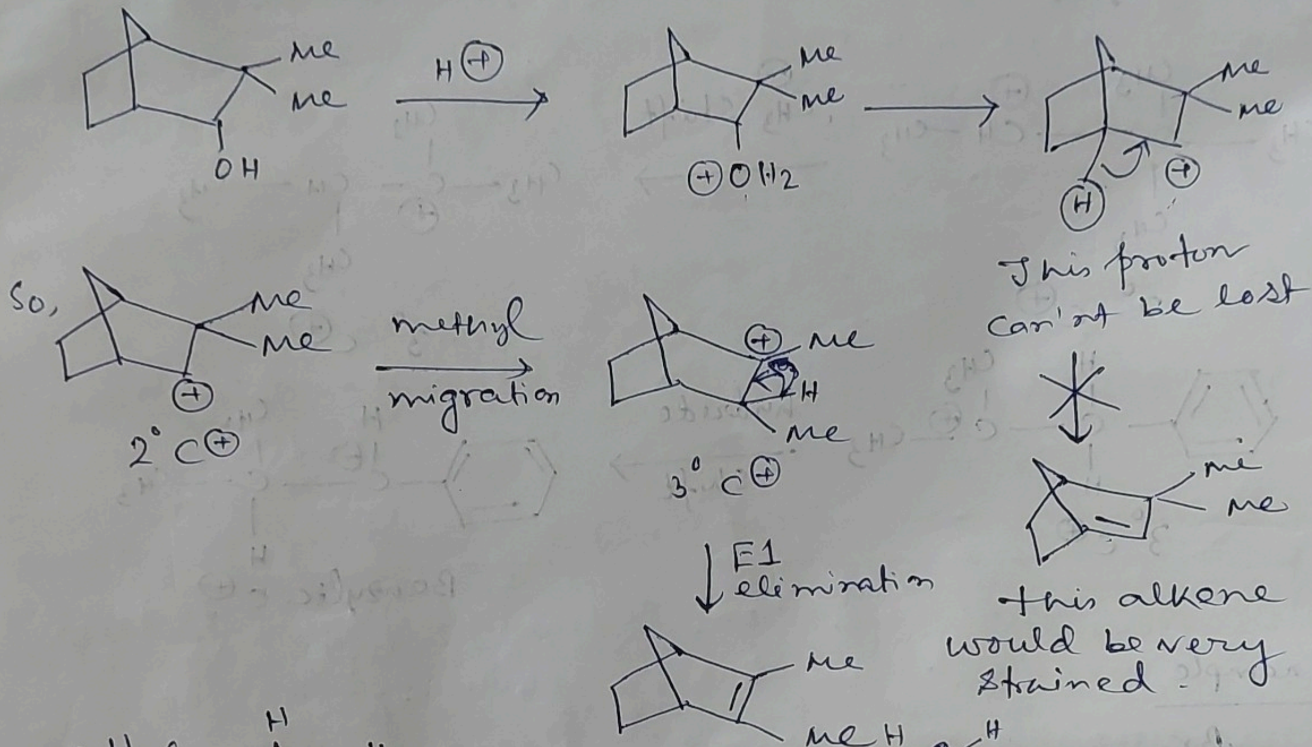
Example





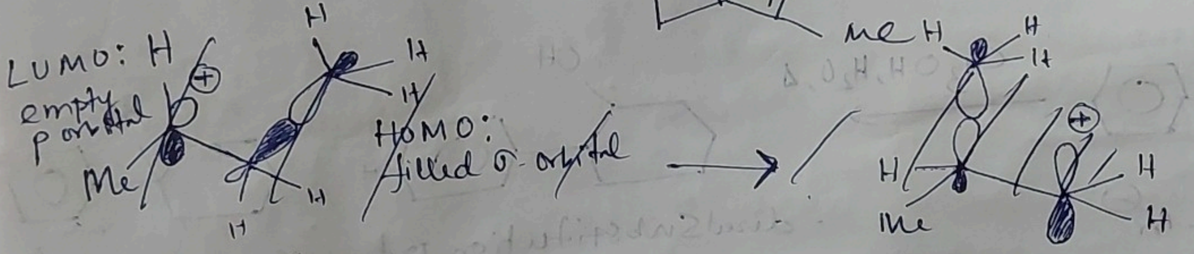
Camphenilol

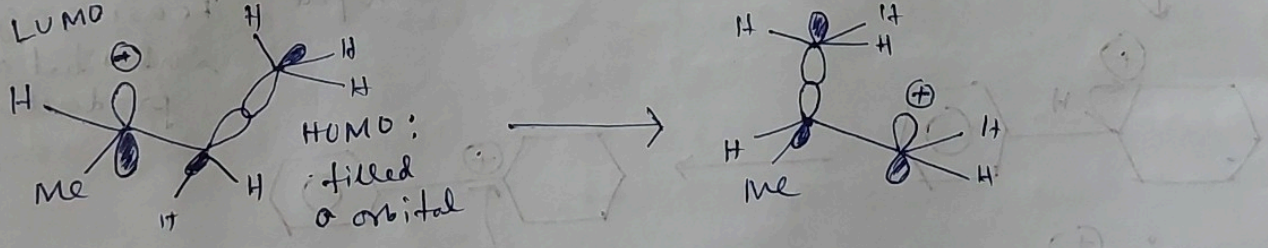
Santene.

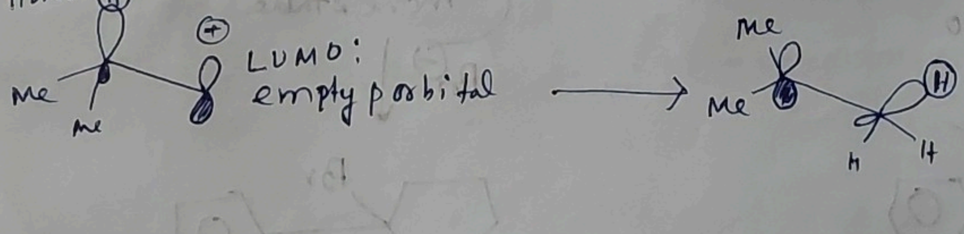


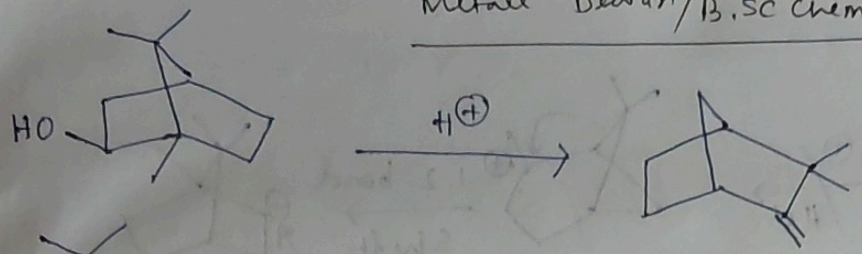
This proton can't be lost

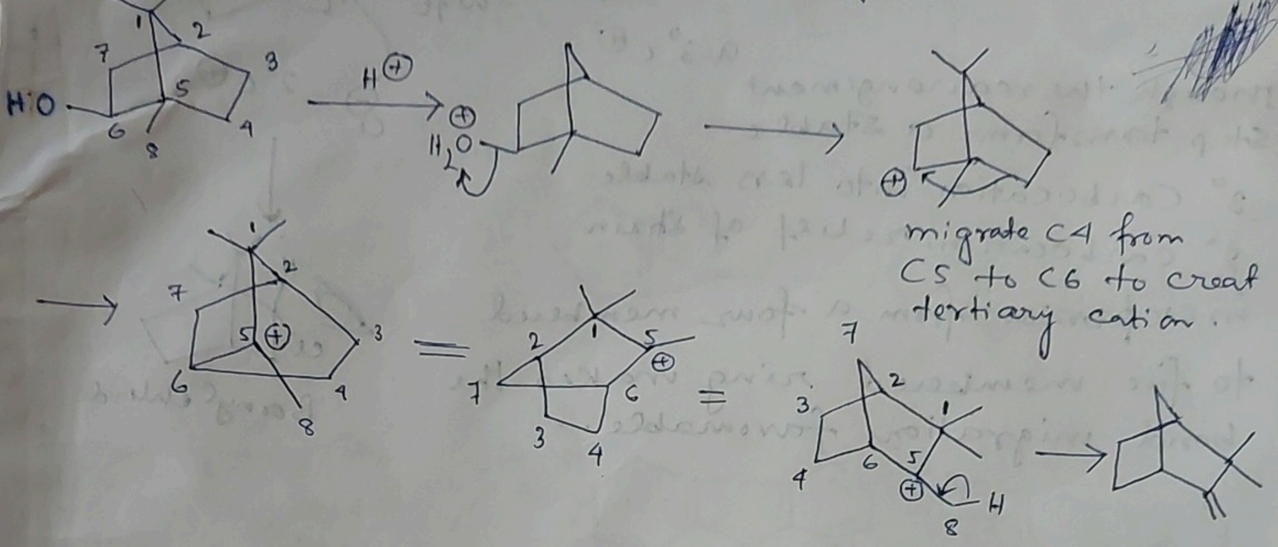
this alkene would be very strained.







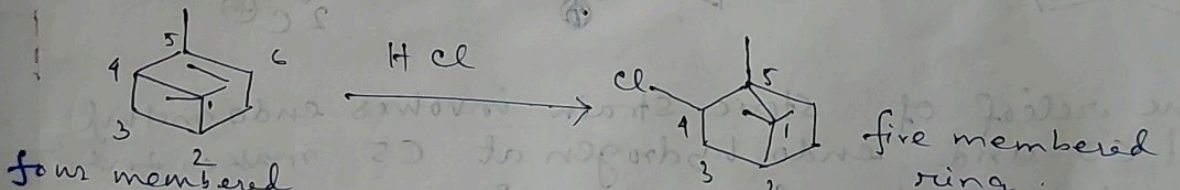




migrate C4 from C5 to C6 to creat tertiary cation.

* Alkyl migration occur in order to make a Carbocation more stable.

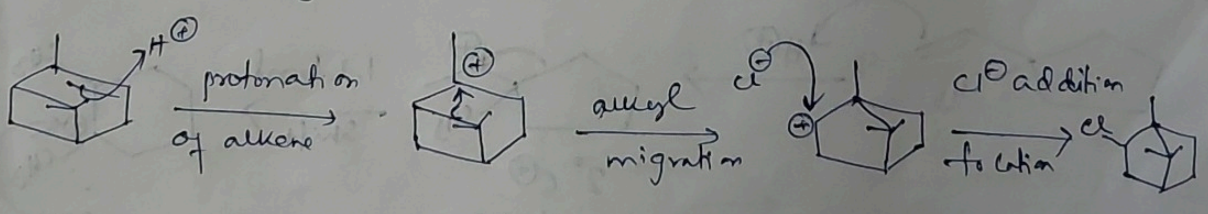
" More stable' usually means " more substituted " but cations can be more stable if they become ~~less~~ ~~hindered~~ less strained.



four membered ring

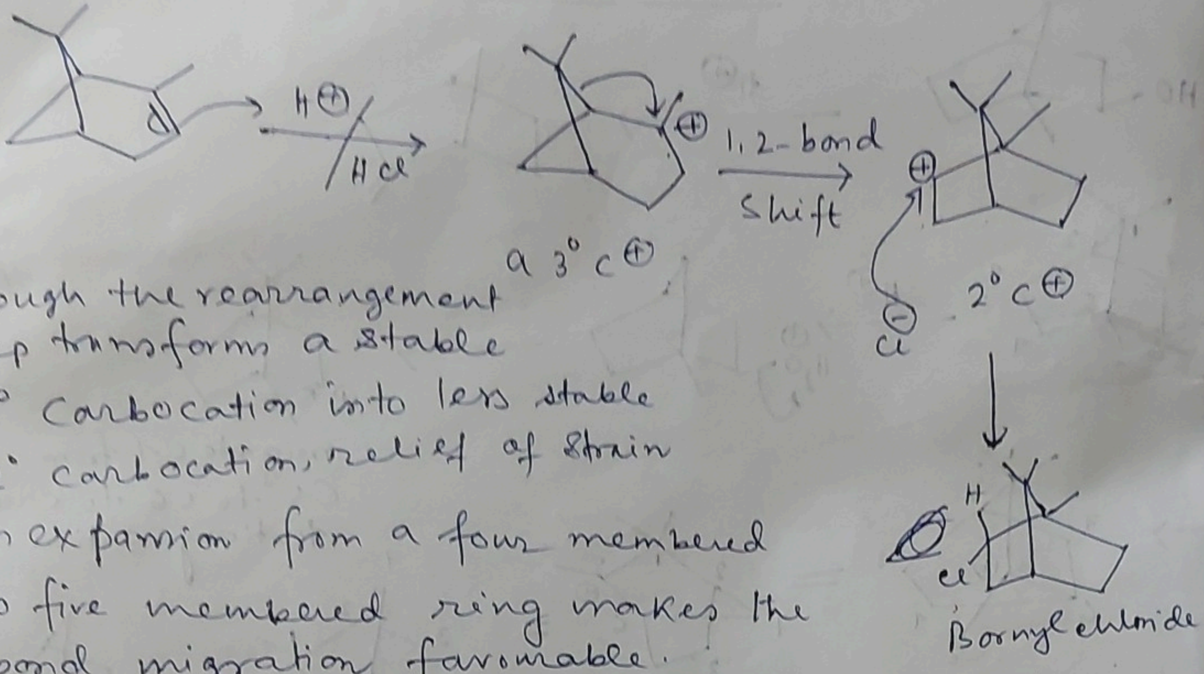
five membered ring

⊛ four membered ring adjacent to cations readily rearrange to five membered rings in order to releeve ring ~~s~~ strain.



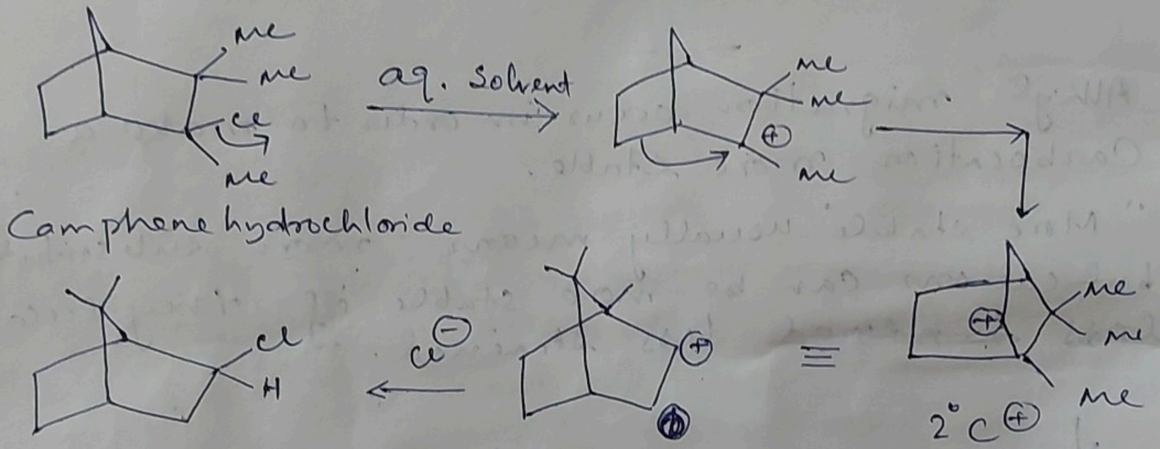
although the rearrangement steps transform a stable tertiary cation into a less stable secondary cation, relief of strain in expansion from four to five membered ring make the alkyl migration favourable.

*



Though the rearrangement step transforms a stable 3° Carbocation into less stable 2° carbocation, relief of strain in expansion from a four membered to five membered ring makes the bond migration favourable.

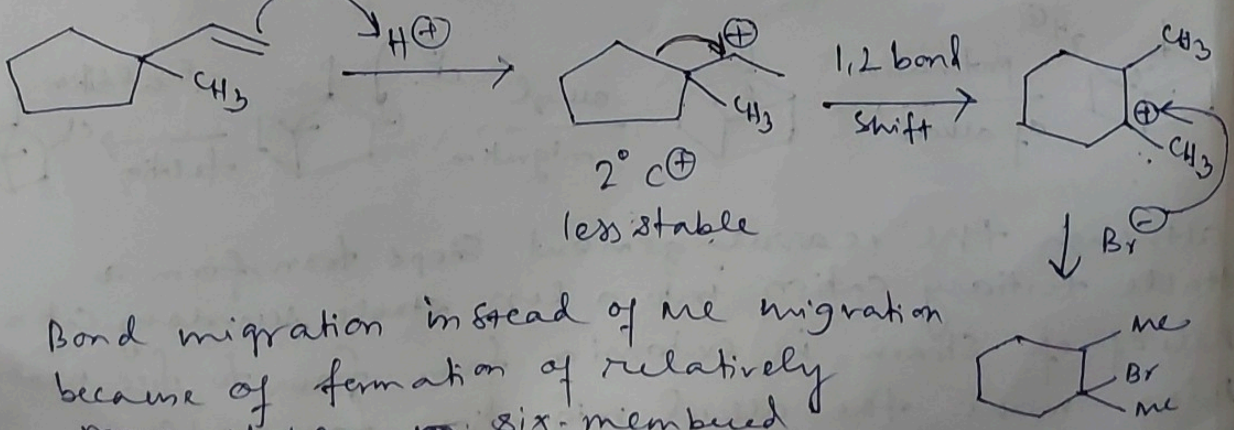
*



Camphene hydrochloride

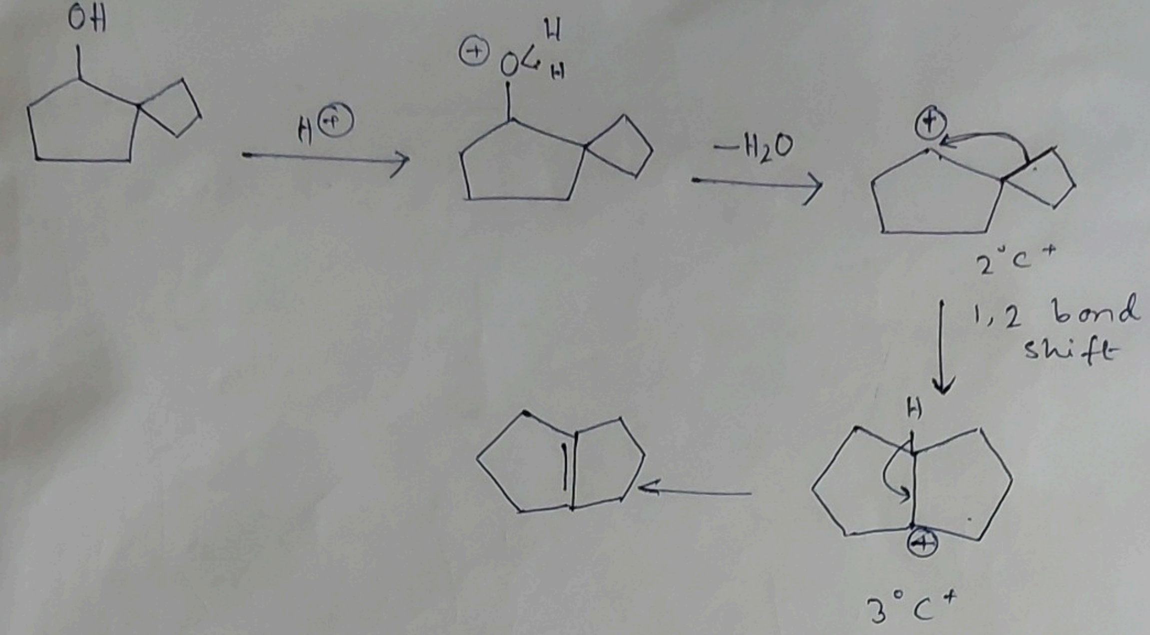
here relief of steric strain involves endo methyl at C3 and endo hydrogen at C5 makes the bond migration favourable. In the final step, the carbocation combines with a chloride ion to yield isobornyl chloride, in which chlorine is exo, due to the same steric reason.

*



Bond migration instead of Me migration because of formation of relatively more stable six-membered ring.

*



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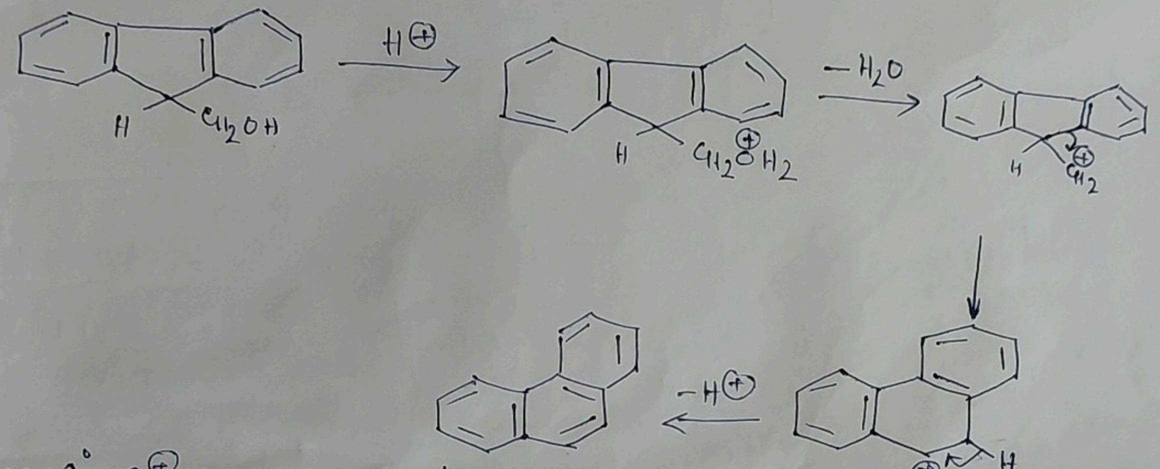
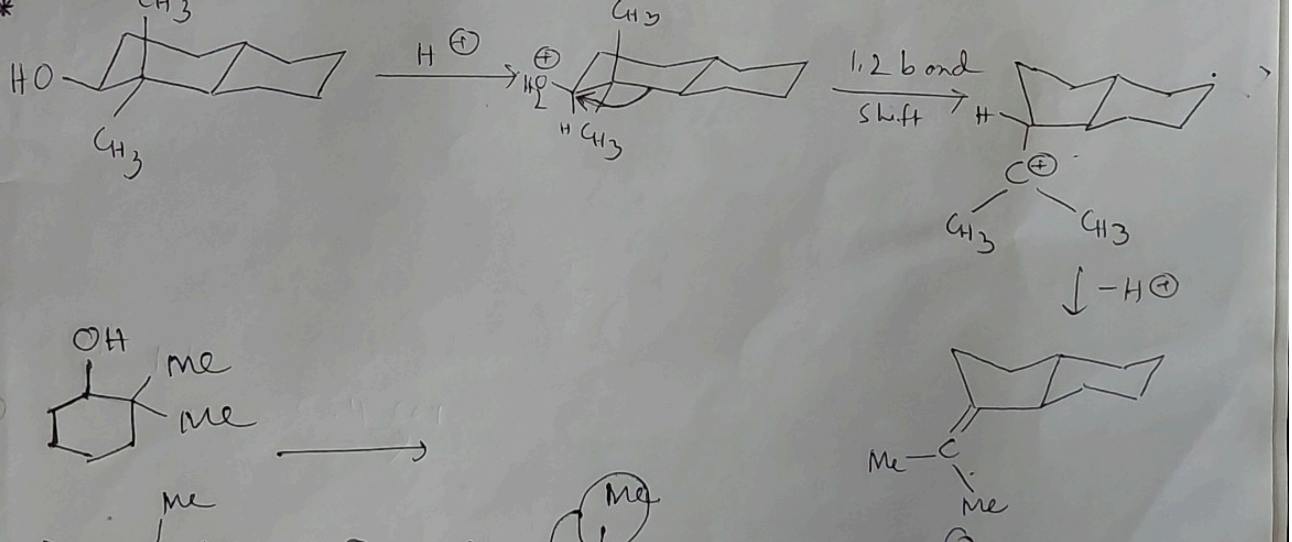
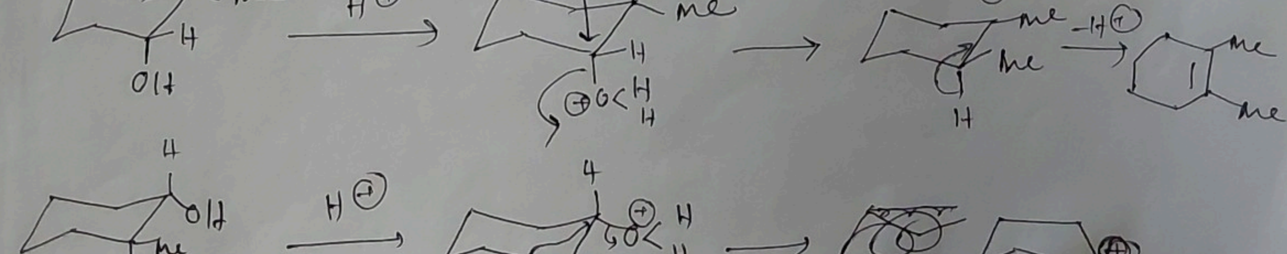
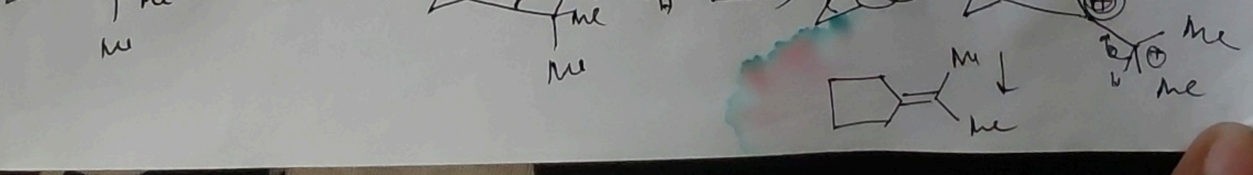


Here 1° C⊕ rearrange to more stable benzylic C⊕

*



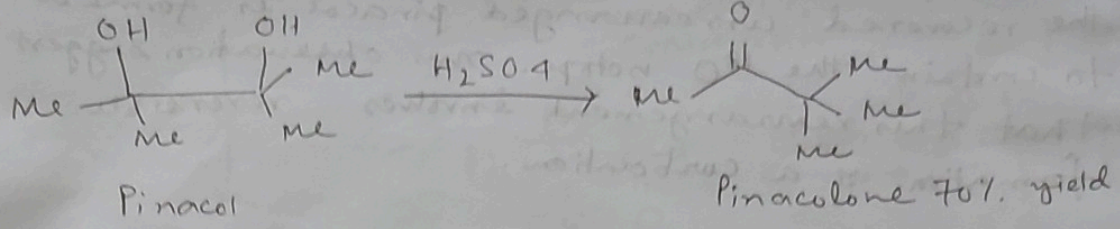


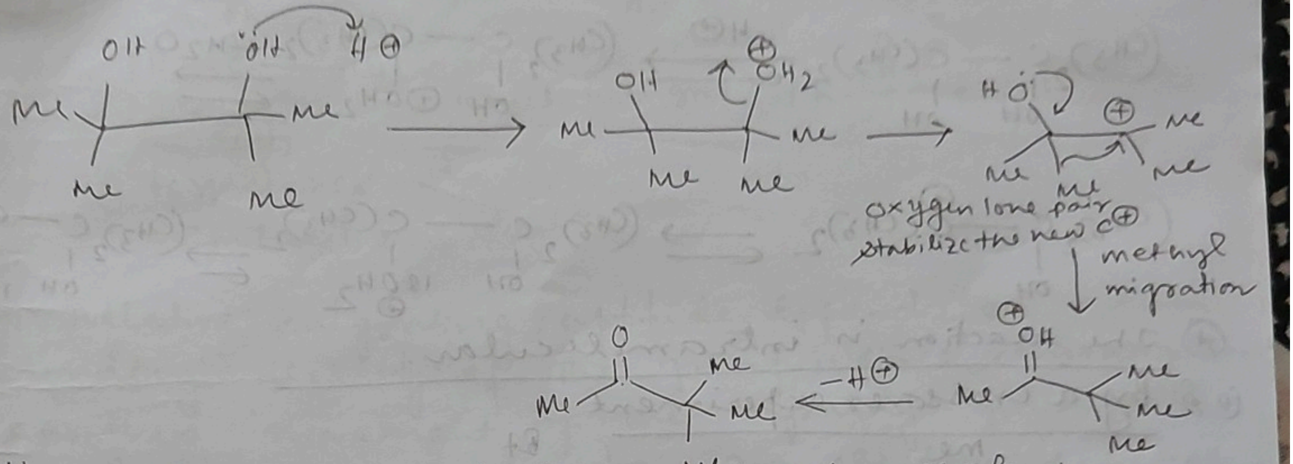


The Pinacol Rearrangement

Mitali Dewan/B.Sc Chem(H)/SEM-4
/CC-10

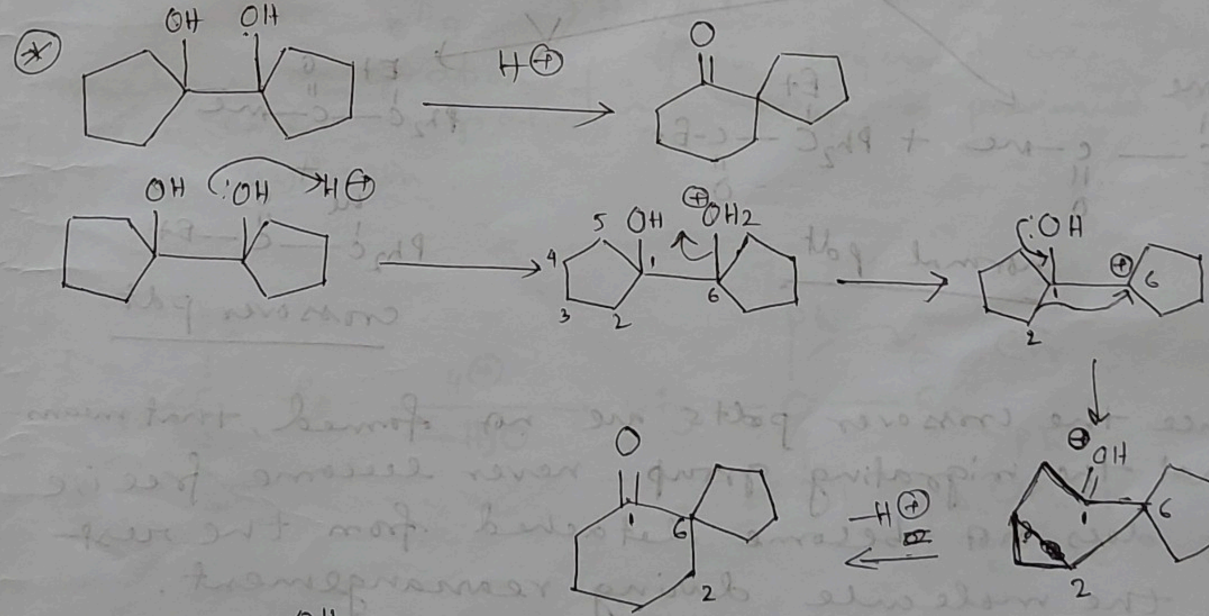
When the 1,2-diol pinacol is treated with acid, a rearrangement take place.





Here rearrangement take place to shift the positive charge into a position where the oxygen can stabilize it, and loss of a proton from oxygen gives a stable ketone.

*



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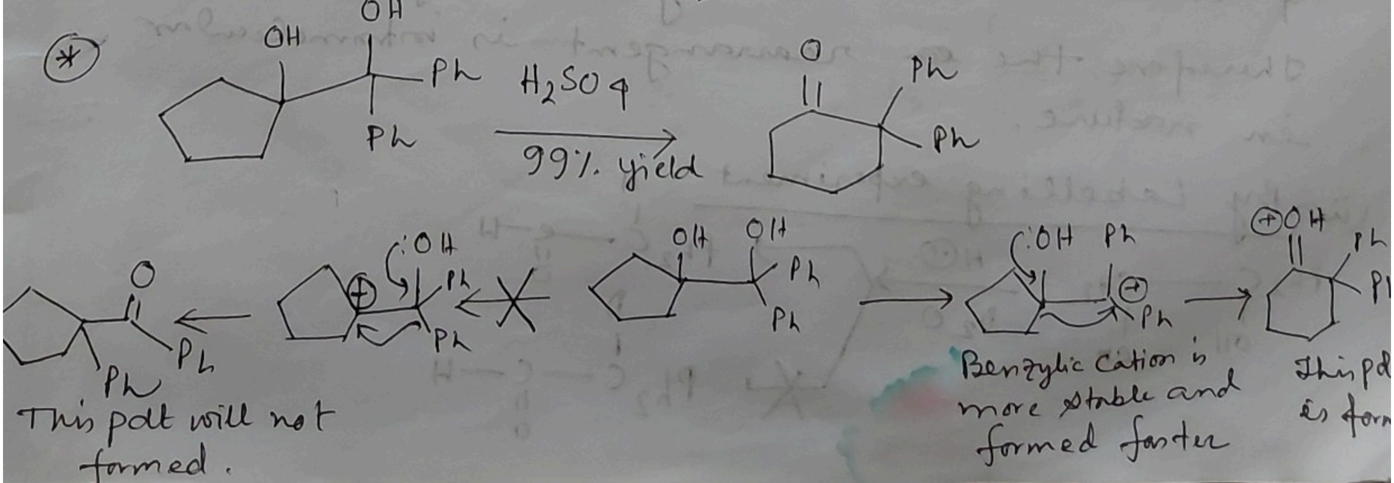


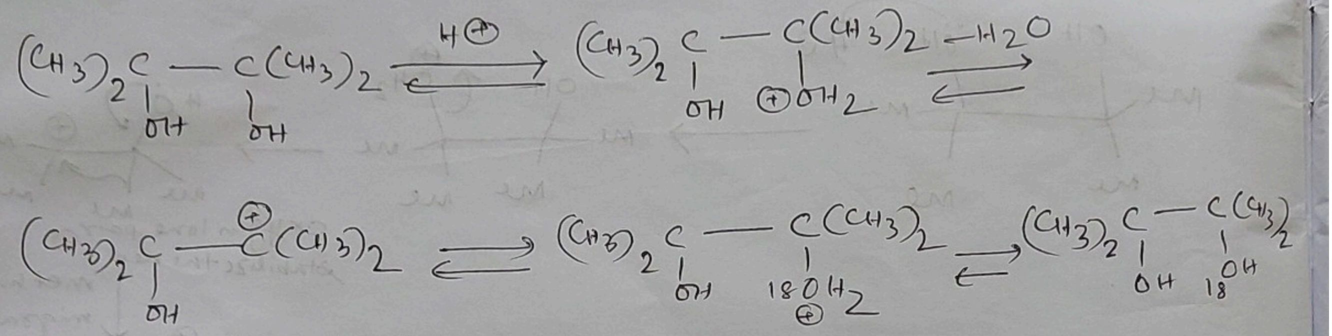
This pdt will not formed.

Benzylic Cation is more stable and formed faster

This pd is form

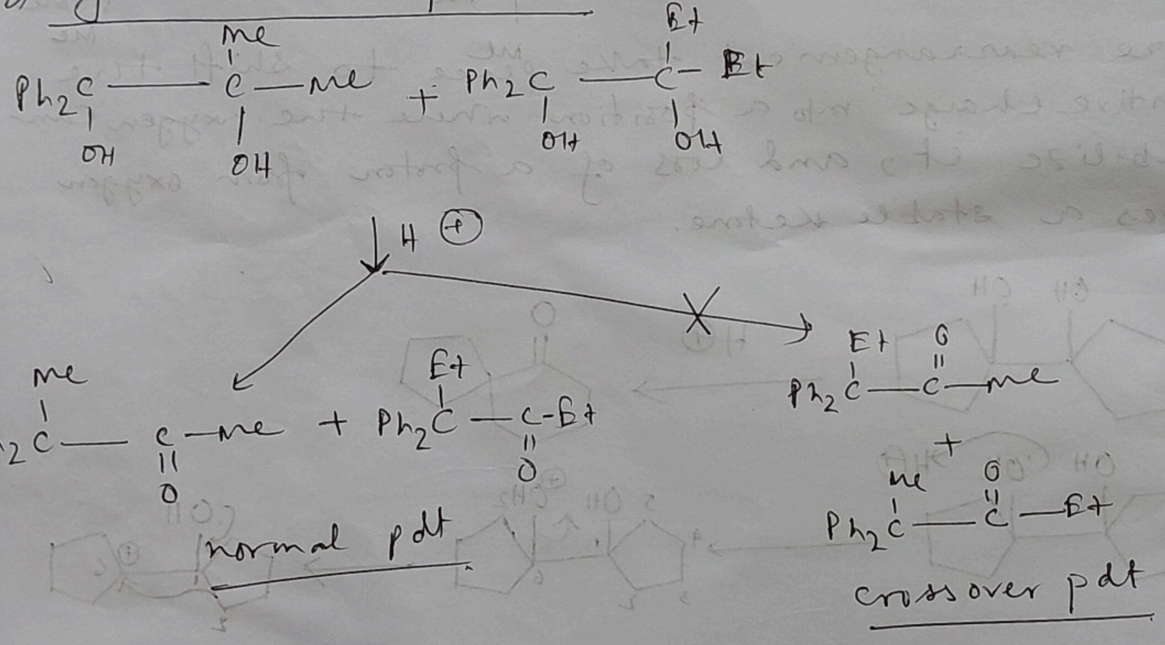
* The evidence for the intermediacy of a carbocation

1) When pinacol is treated with acid in $H_2^{18}O$ solution, the recovered unrearranged pinacol is formed to contain the ^{18}O isotope. This observation suggest that this rearrangement involves reversible formation of a carbocation.



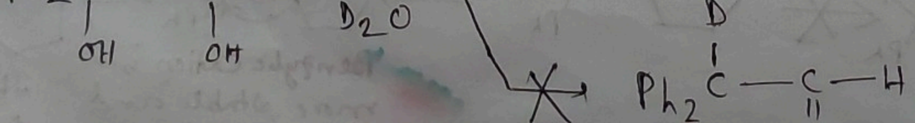
⊛ The reaction is intramolecular.

(i) ~~2)~~ By a crossover experiment

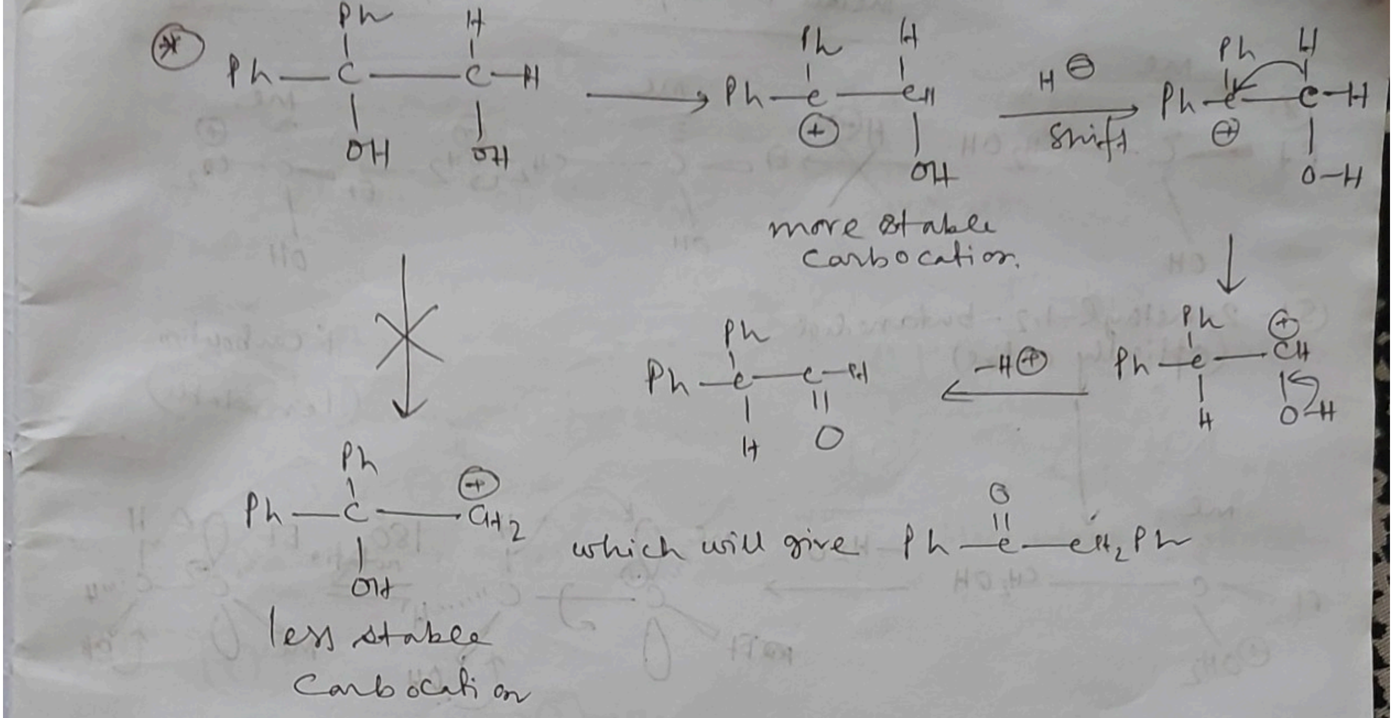


Since the crossover pdts are not formed, that means that the migrating group never become free i.e it does not become detached from the rest of the molecule during rearrangement. Therefore the ~~ex~~ rearrangent is intramolecular in nature.

(ii) By Labelling experiment



⊛



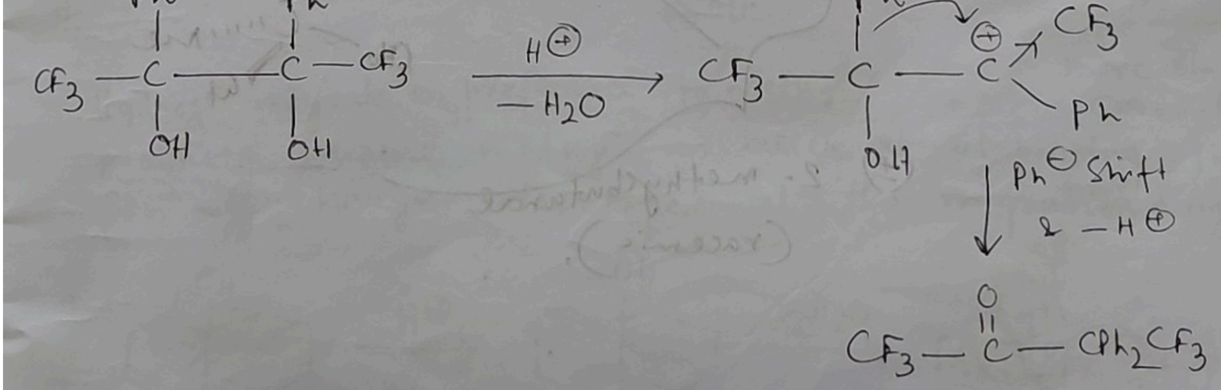
⊛ The relative migrating aptitude depends on electron-donating ability of the group, since rearrangement involves movement of the migrating group with its bonding electron to an electron deficient centre. The relative ease of migration is

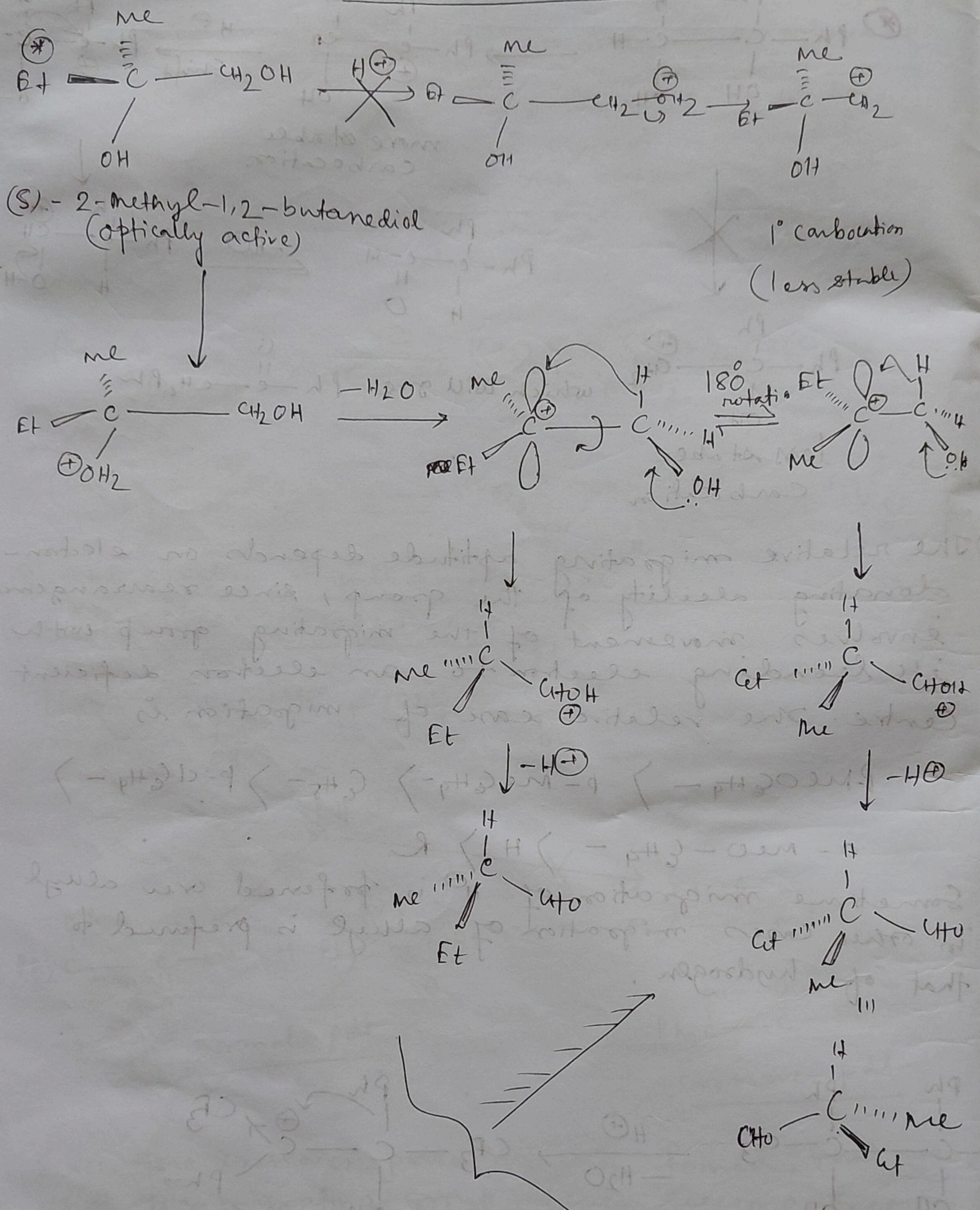
$p\text{-}MeOC_6H_4- > p\text{-}MeC_6H_4- > C_6H_5- > p\text{-}ClC_6H_4- >$

$o\text{-}MeO\text{-}C_6H_4- > H > R$

Sometime migration of $H^{\ominus}$ is prefered over alkyl in other cases migration of alkyl is prefered to that of hydrogen.

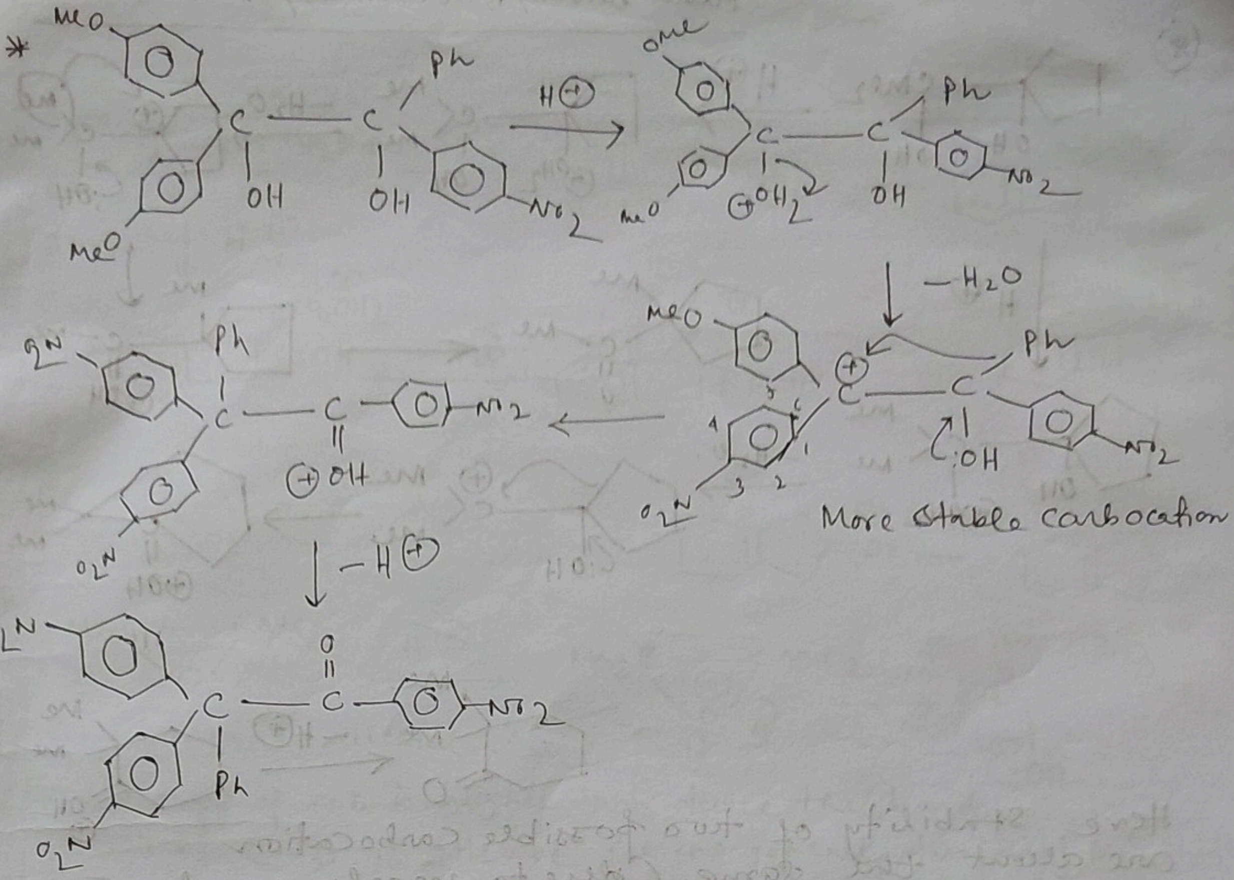
*



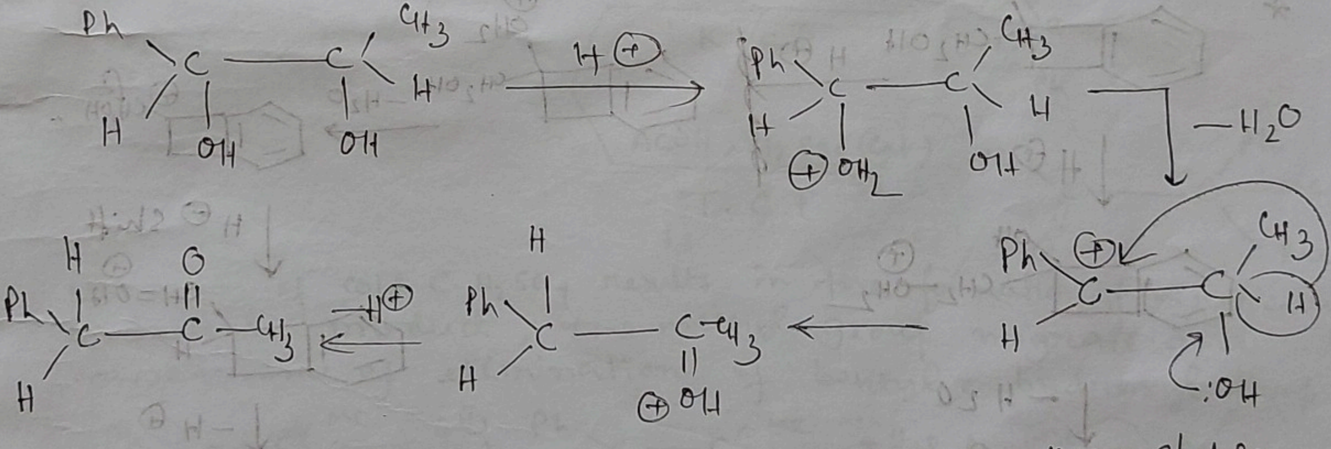


(±) 2-methylbutanal
(racemic).

*



* $PhCHOHCHOHCH_3 \xrightarrow{H^{\oplus}} ?$



Hydrogen migrate in preference to methyl probably because methyl is better at stabilizing the positively charge developed at the migration origin.

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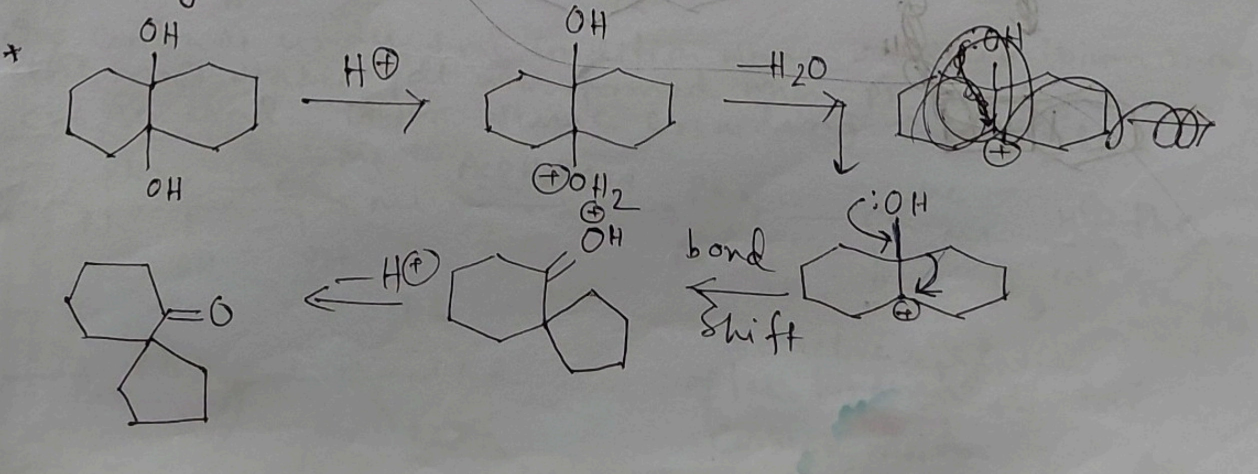

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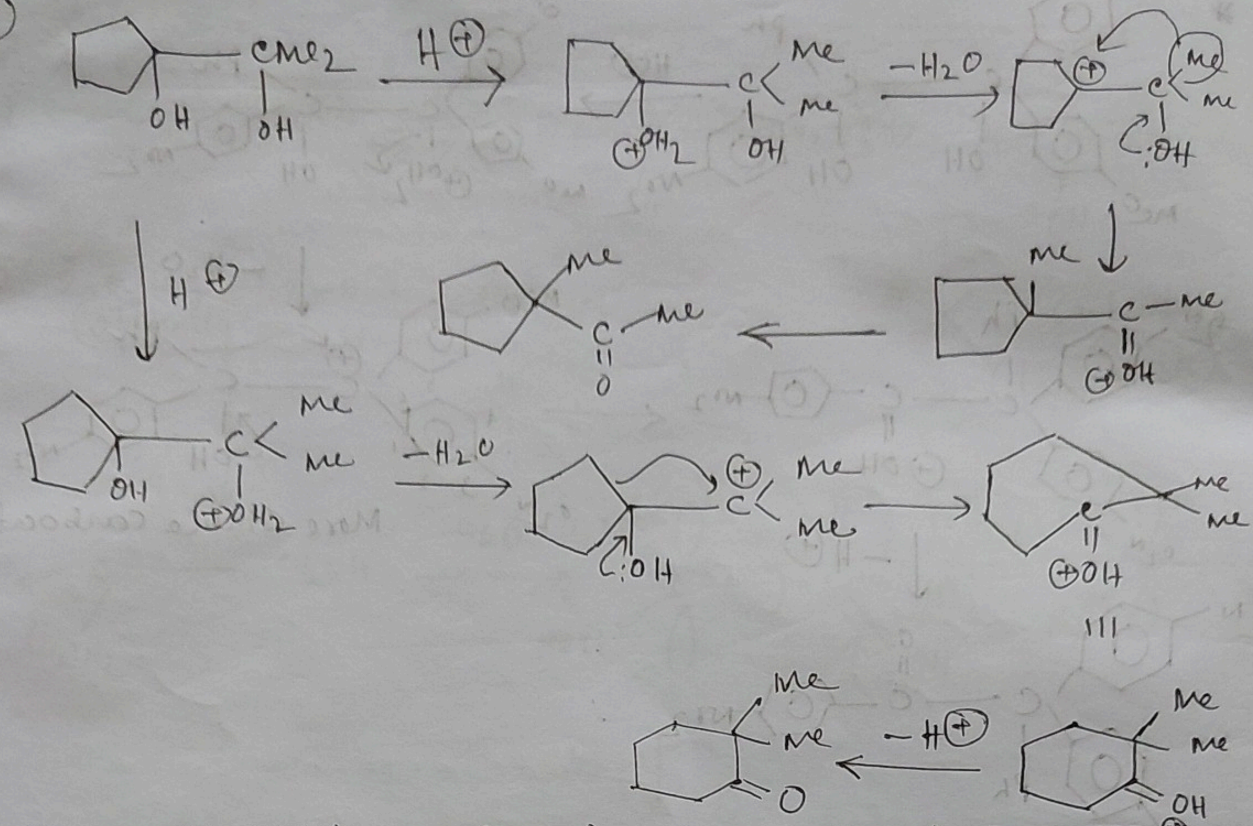

Here stability of two possible carbocation are about the same (due to nearly equal +I and hyperconjugative effect of alkyl and cyclo alkyl group) two rearrangement product are obtained.

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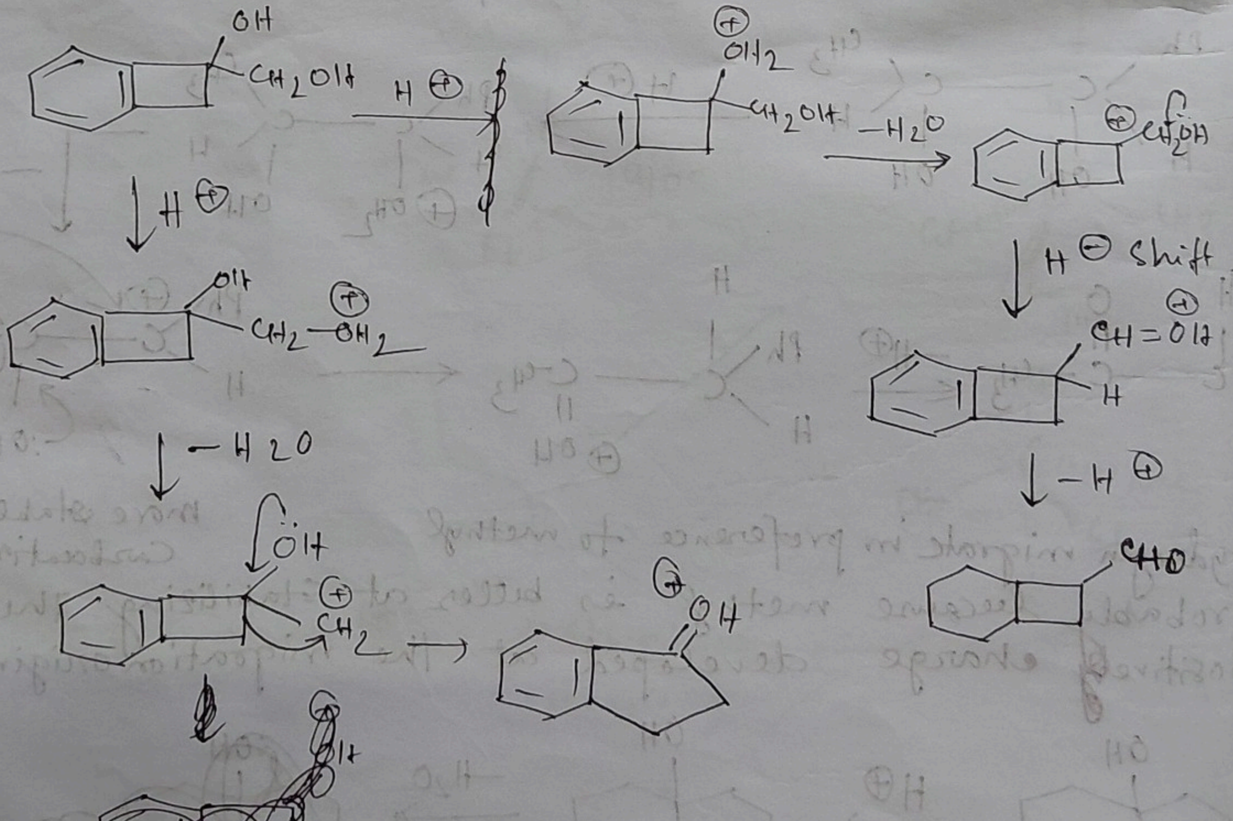

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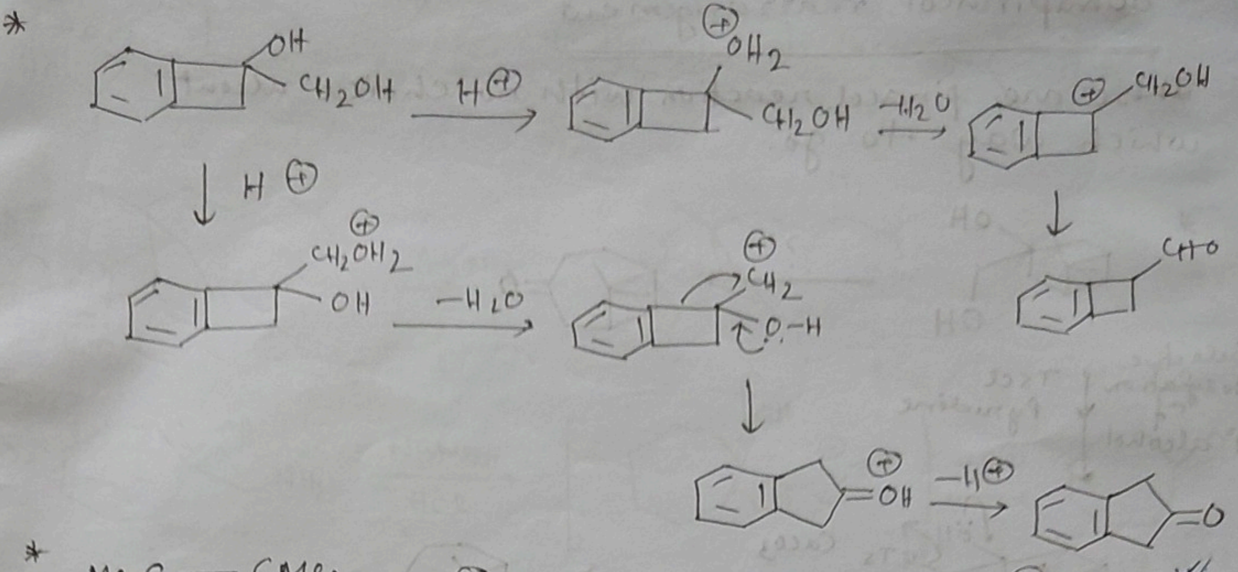

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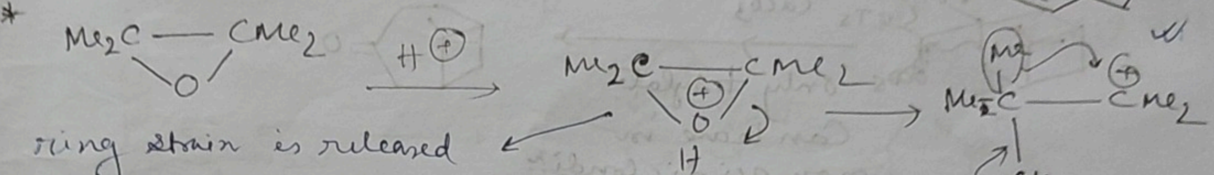
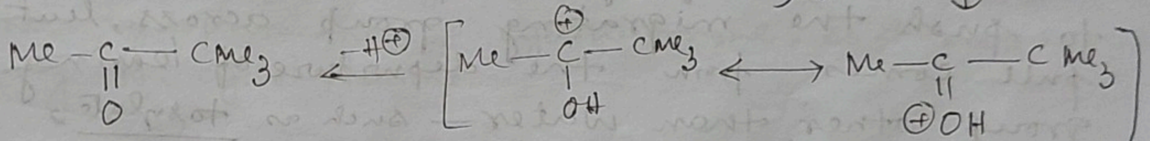
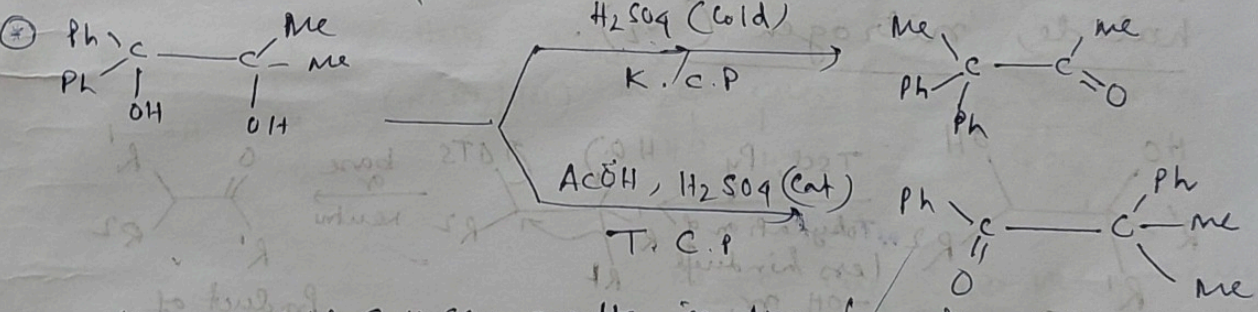


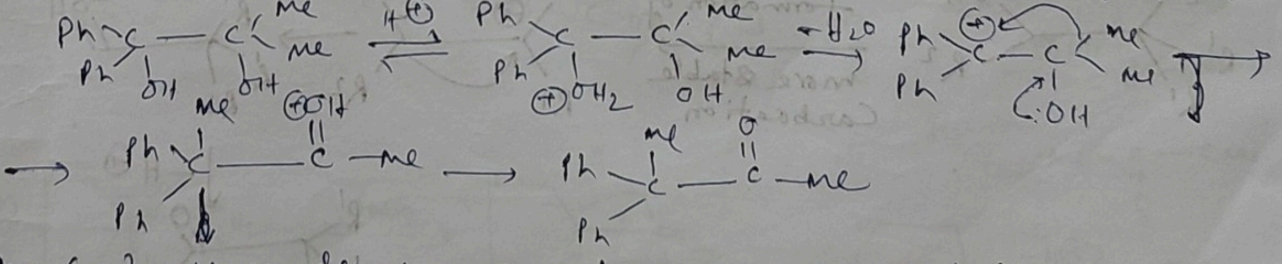
ring strain is released

Bond energy of $C=O$ is higher than twice the bond energy of $C-O$. ∴ $\Delta H = -ve$ i.e energetically favourable] $Me^{\ominus}$ Shift

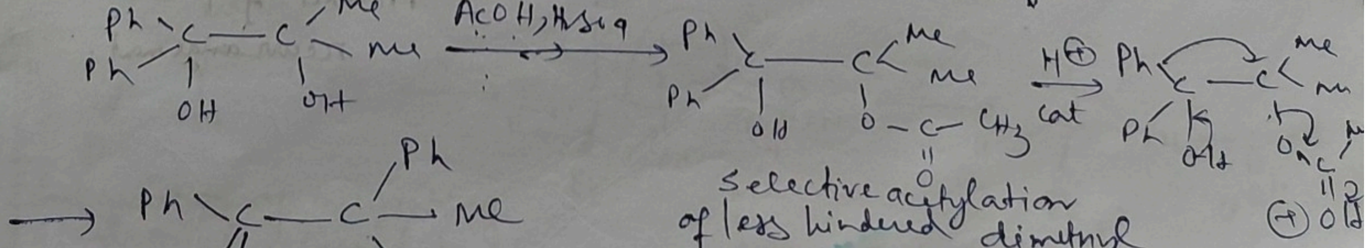




The action of cold C. H_2SO_4 results in the formation of kinetically controlled product, the methyl group migrate as a consequence of elimination of benzylic hydroxyl group



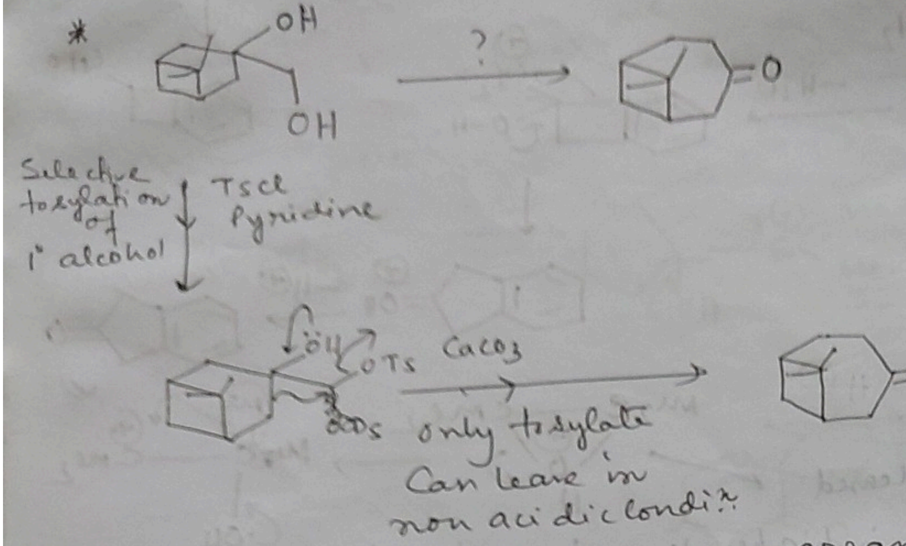
In contrast under the condition where equillibribium may occur, the most stable pdt will formed when Ph is conjugation with $C=O$ gr. and lower steric crowding in the pdt.



Selective acetylation of less hindered dimethyl carbinol moiety.

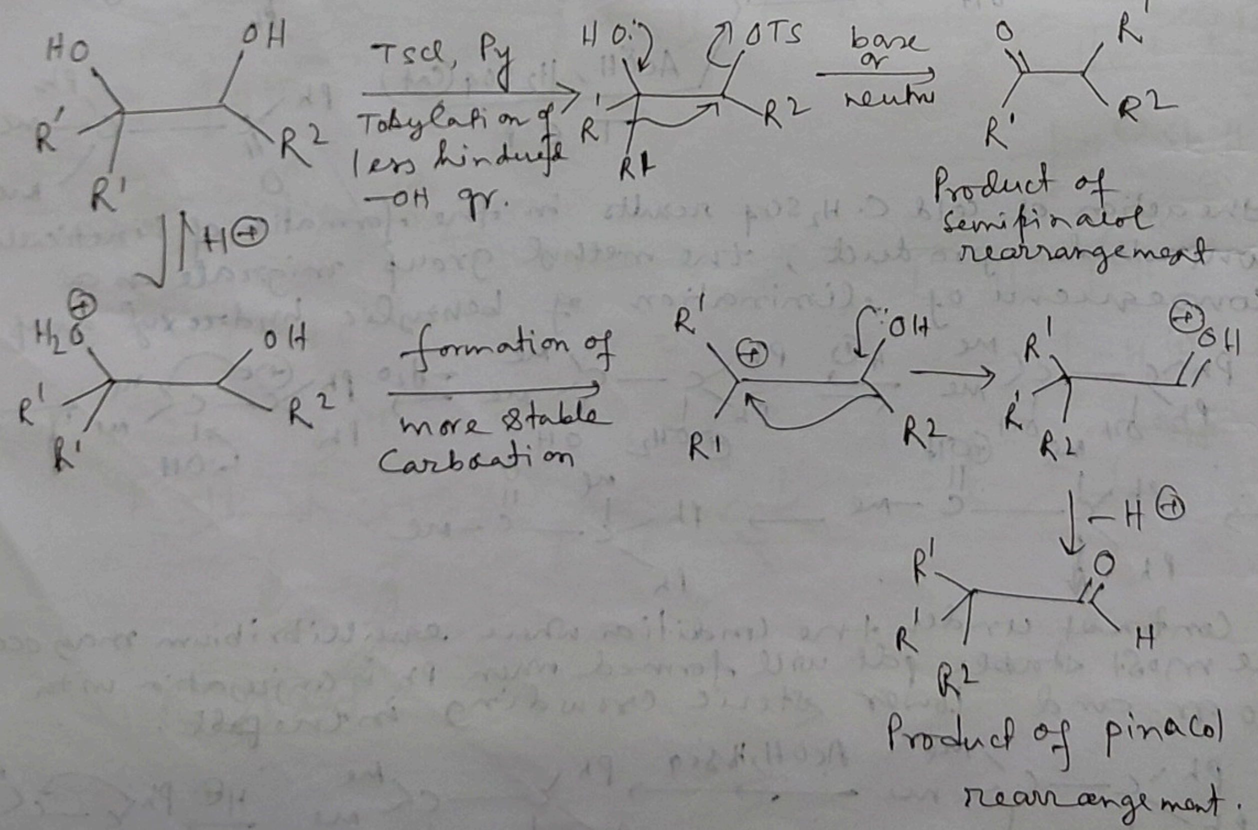
Semipinacol rearrangement

These are pinacol reaction with no choice about which way to go.

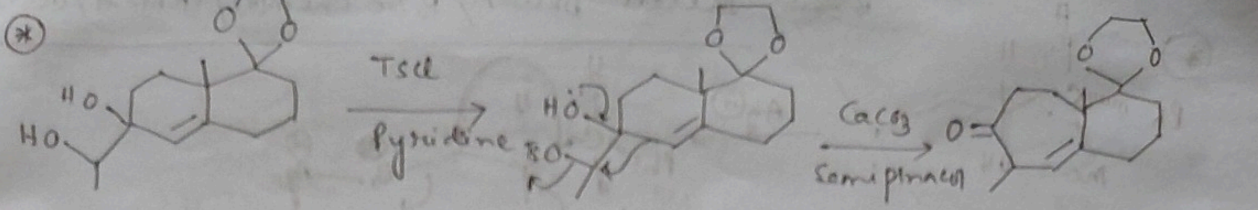


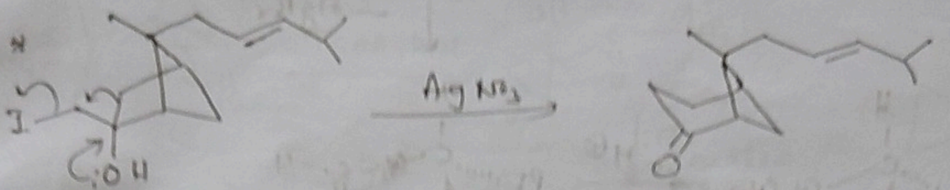
only tosylate Can leave in non acidic condiⁿ

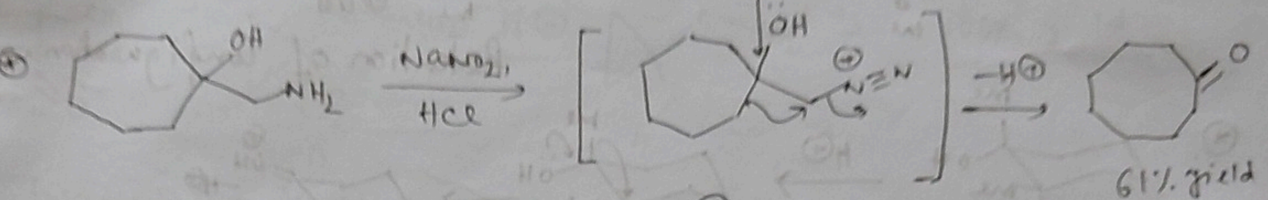
Semipinacol rearrangement are rearrangements in which a hydroxyl group provide the electron to push the migrating group across, but pull comes from the depurture of leaving group other than water — such as <u>tosylate</u>, <u>halide</u>, <u>nitrogen</u> (N_2).

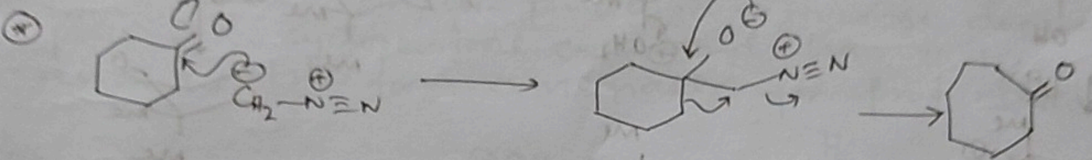


㊀

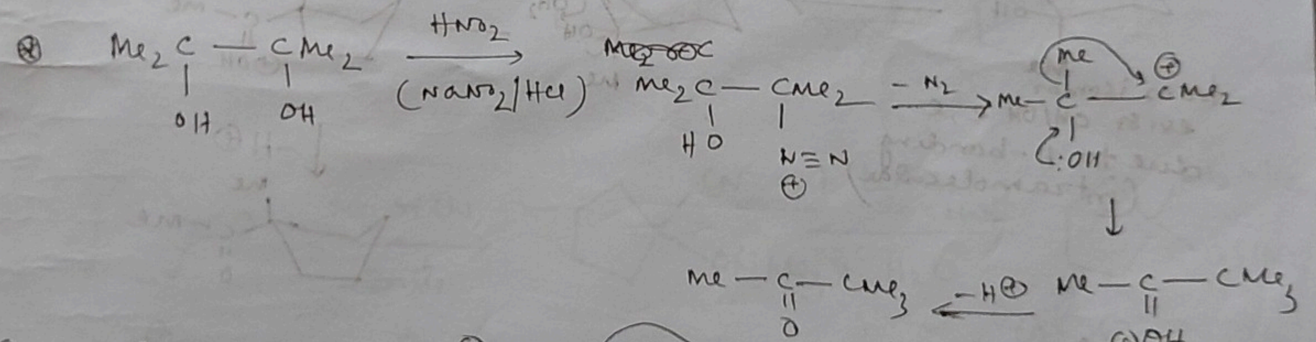


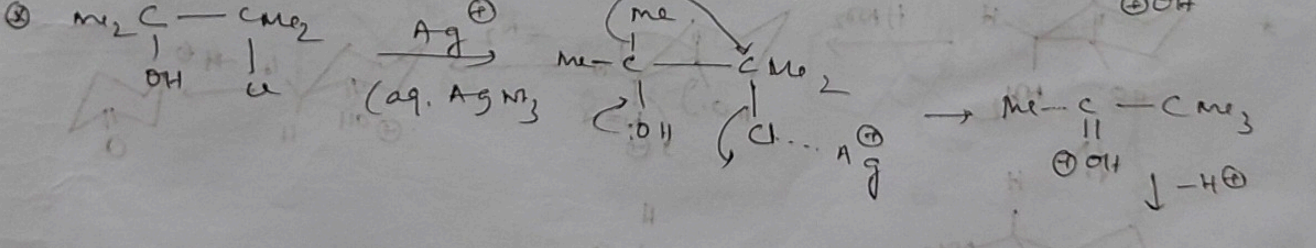


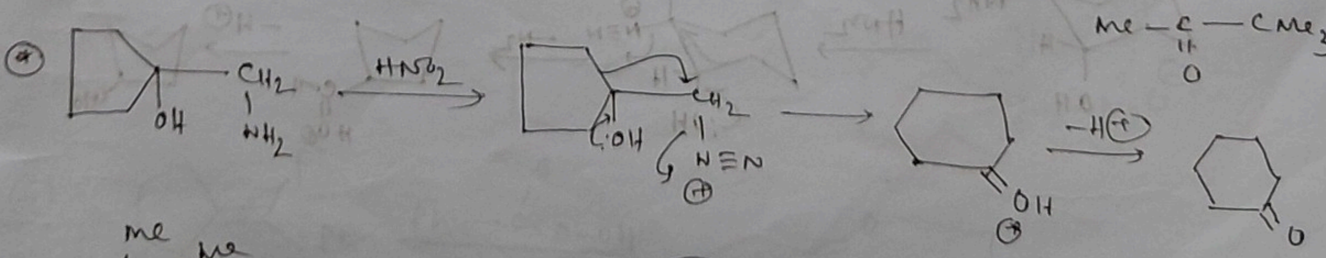


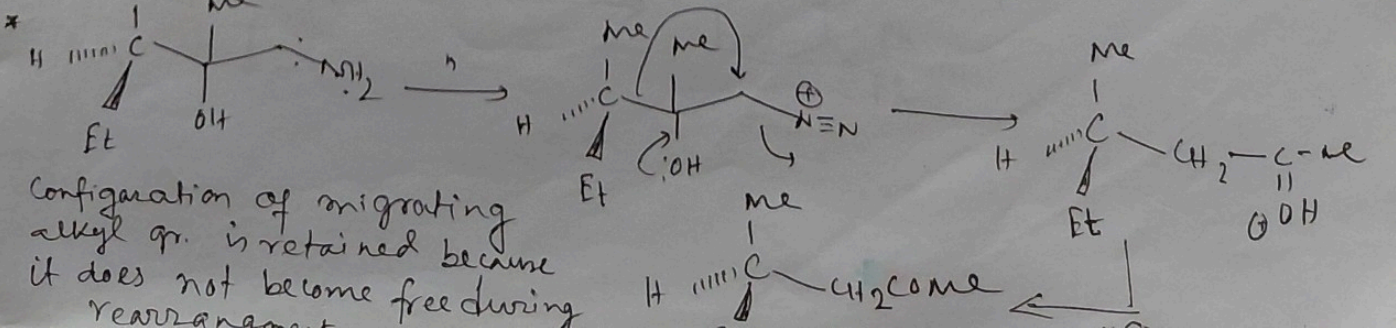


㊀ cyclohexanone is more reactive as an electrophile than either cyclopentanone or cycloheptanone, so it ring expands cleanly to cycloheptanone.



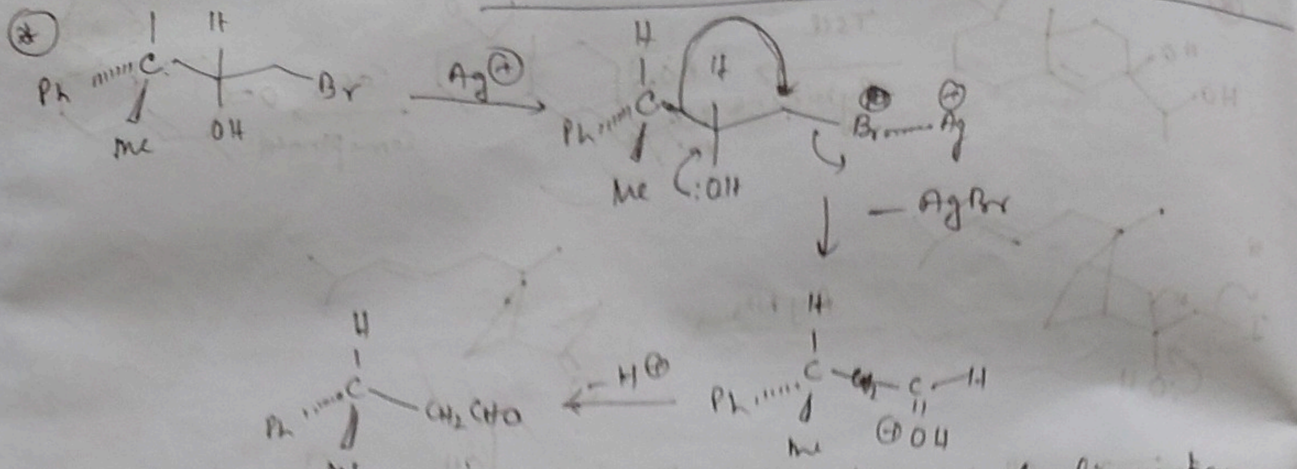






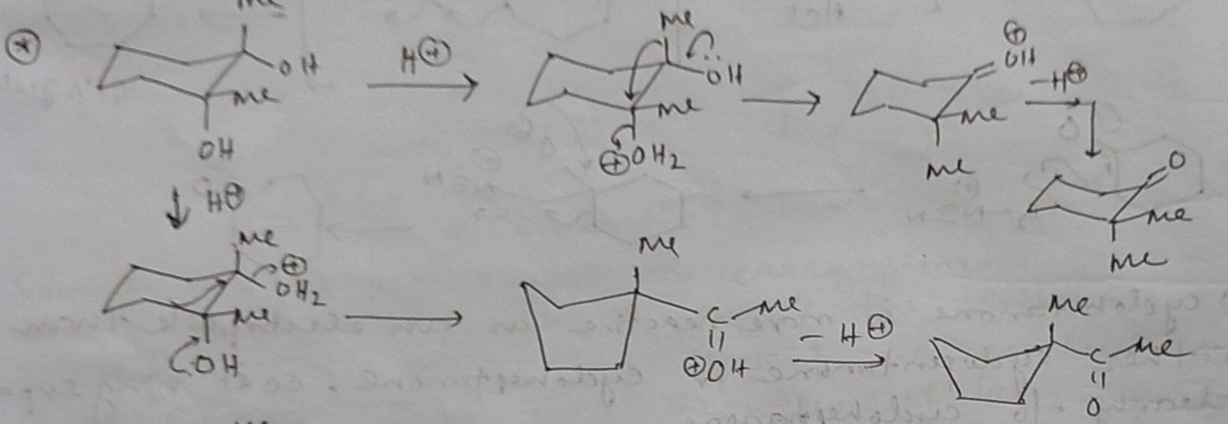
Configuration of migrating alkyl gr. is retained because it does not become free during rearrangement

*



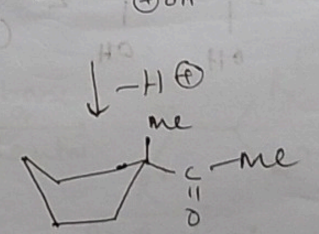
Retention of Configuration.

*



*

from isomer exist OH/OH e,e due to H-bonding (intramolecular)



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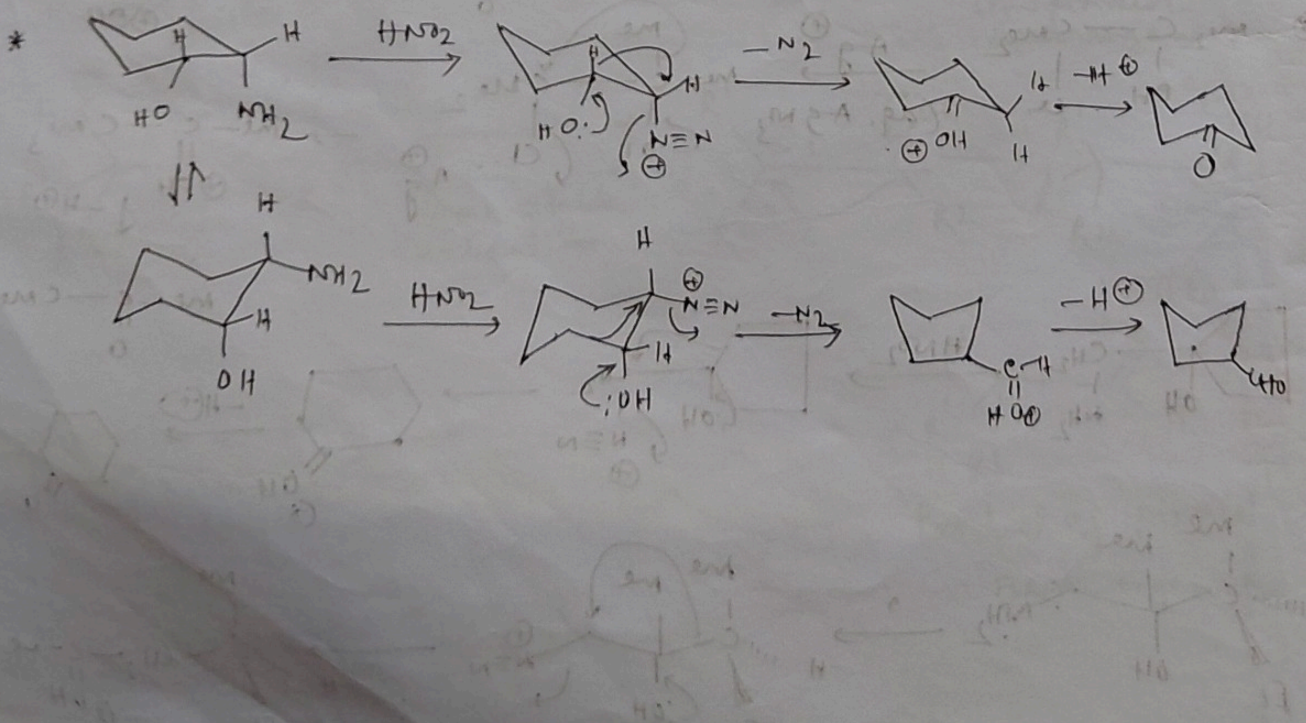
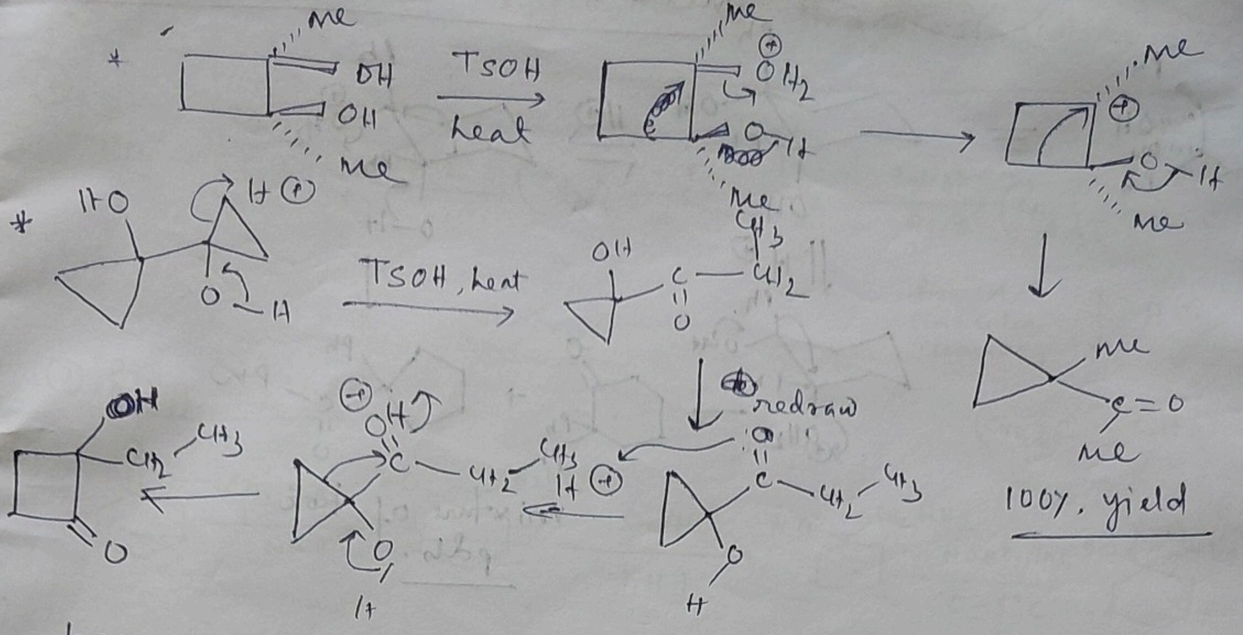
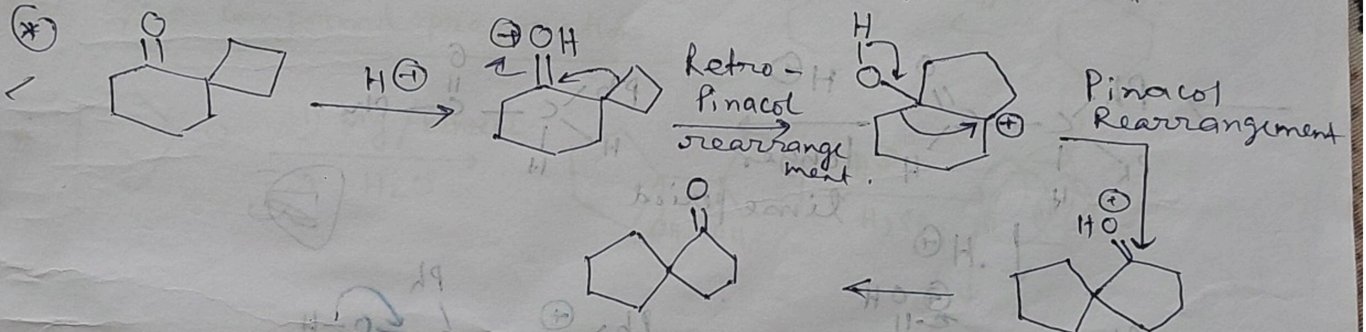
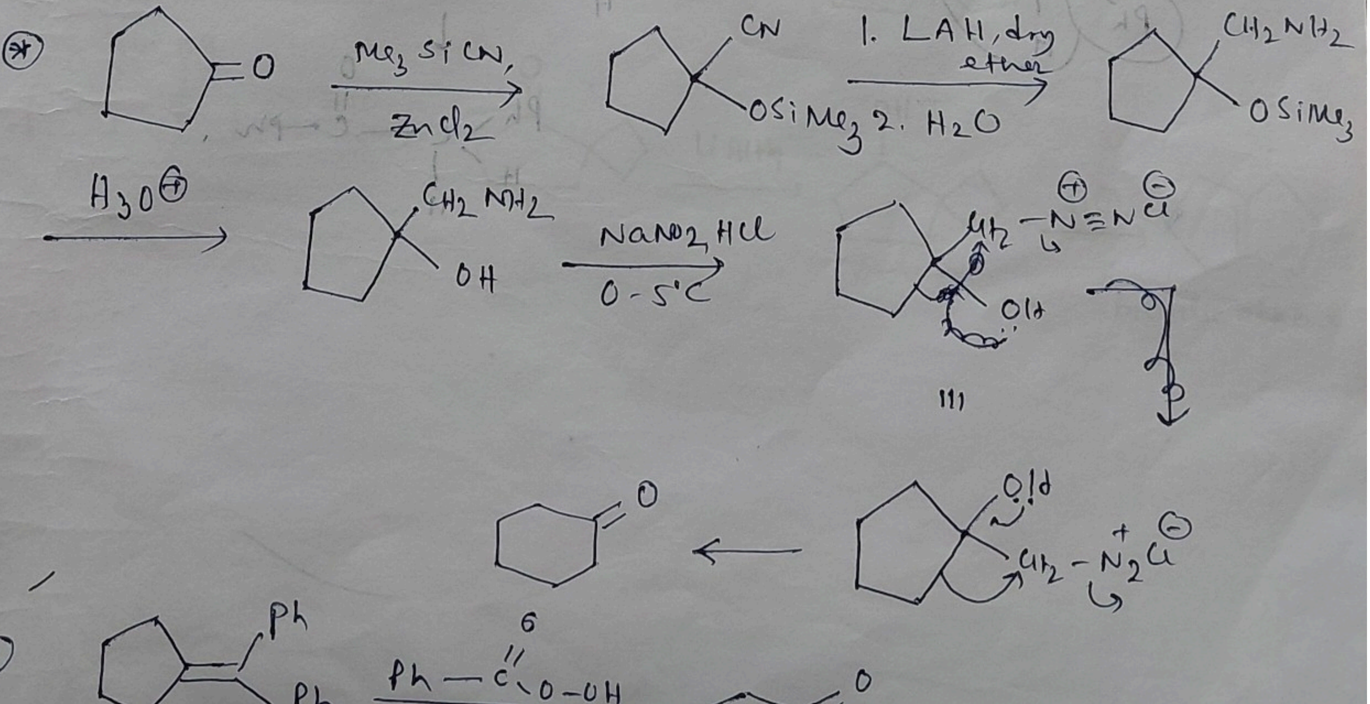
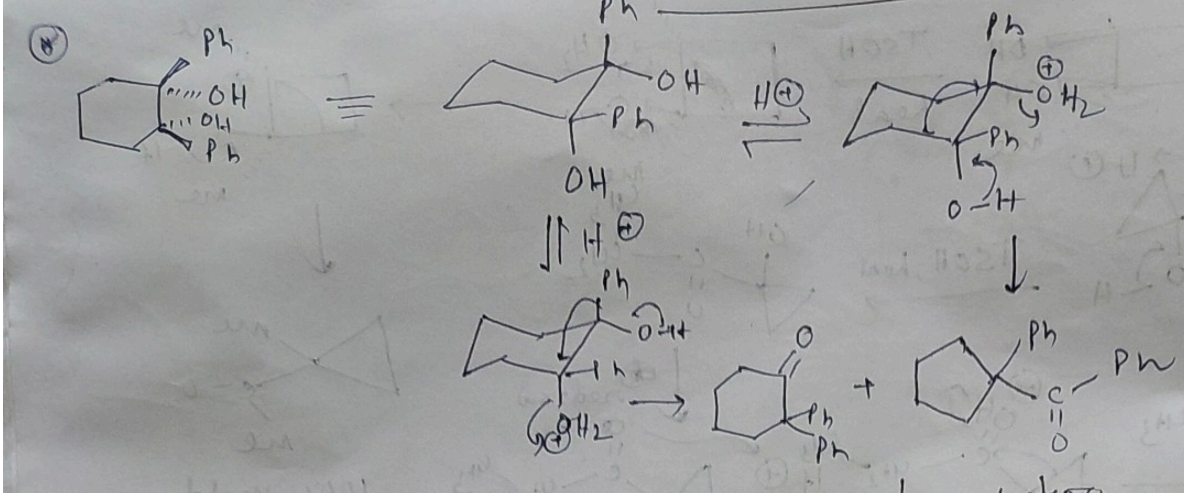


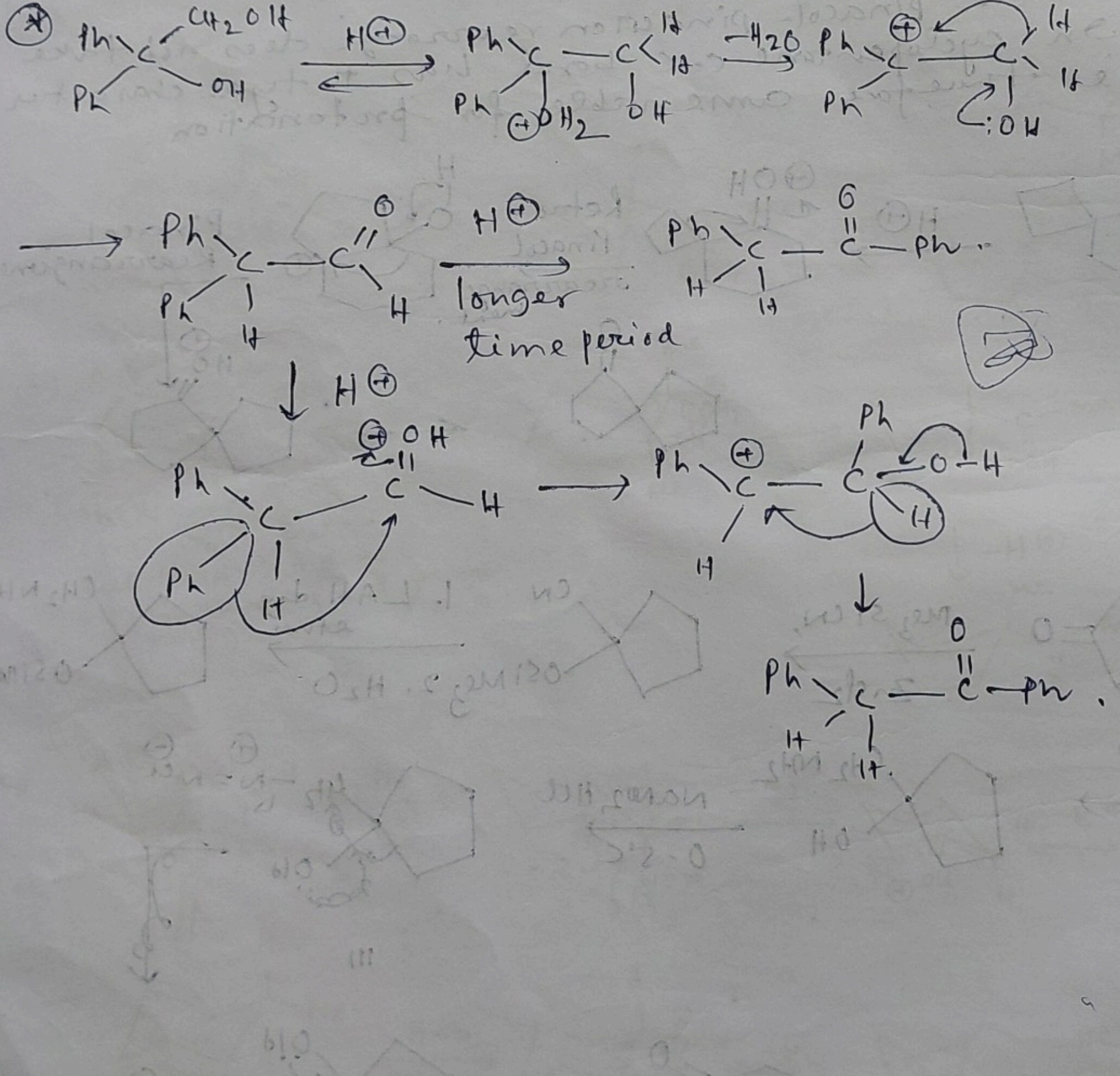


here normal pinacol- pinacolon rearrange does not take place. In cyclopentane c-C bond has π type character and is therefore amenable for protonation



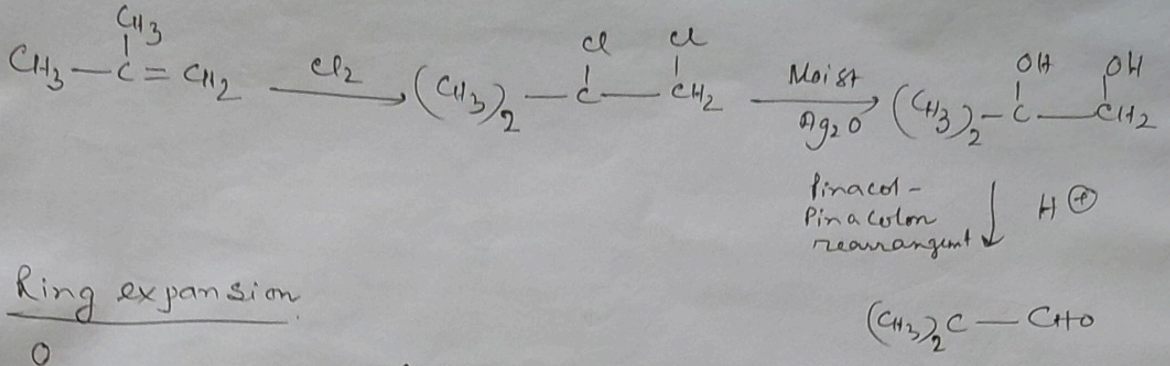



Ph
OH
OH
Ph
H⊕
OH₂
O–H
H⊕
mixture of two pdts.

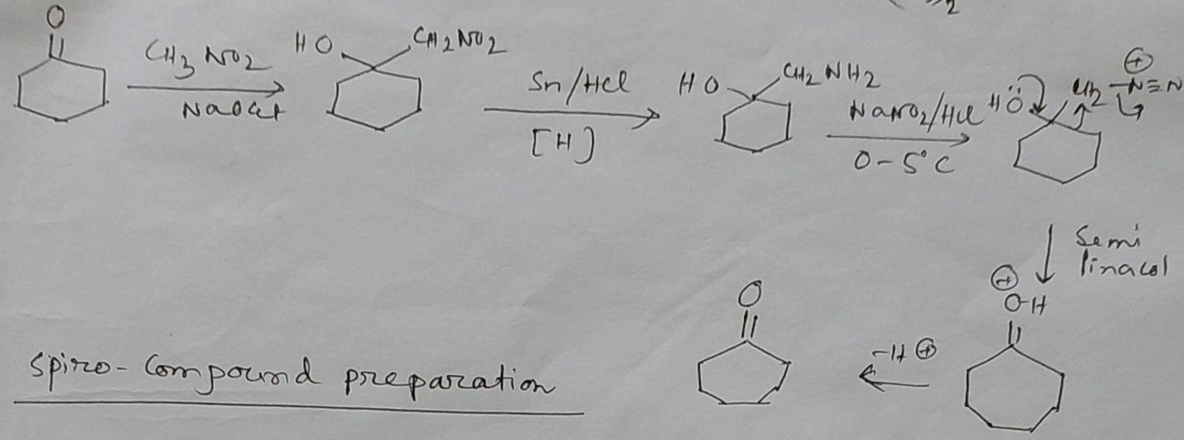

CH₂OH
Ph
OH
H⊕
–H₂O
:OH
longer time period
H⊕
Ph
H

Some important application of Pinacol-Pinacolone rearrangment

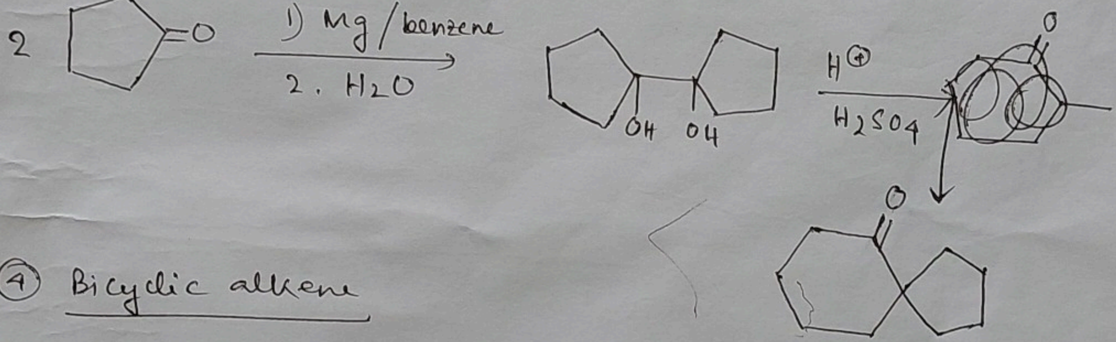
①



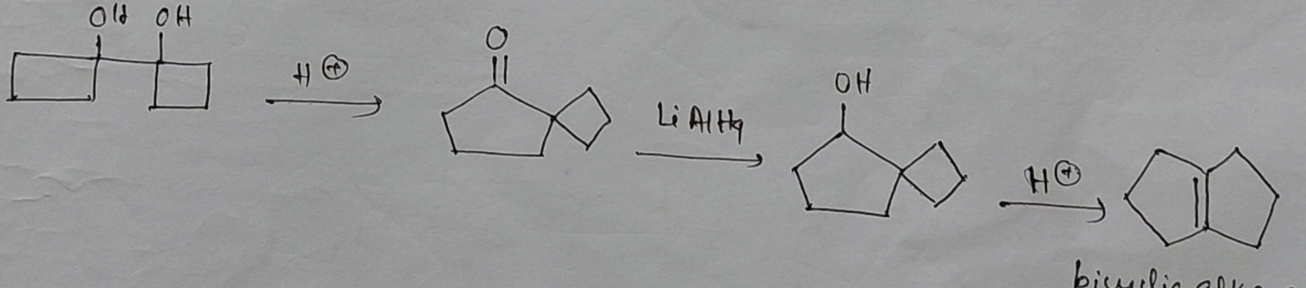
② Ring expansion



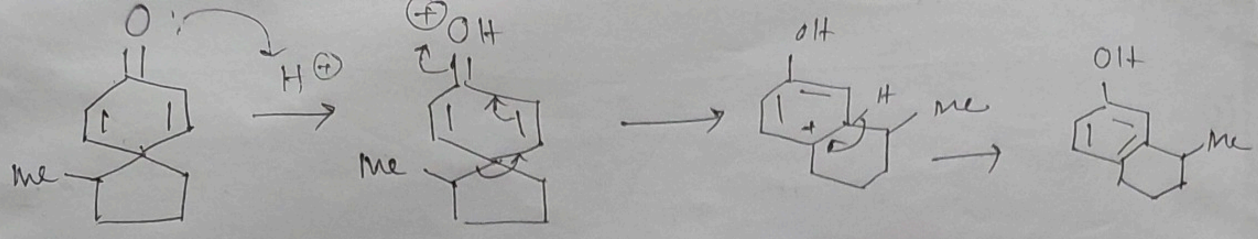
③ Spiro-compound preparation

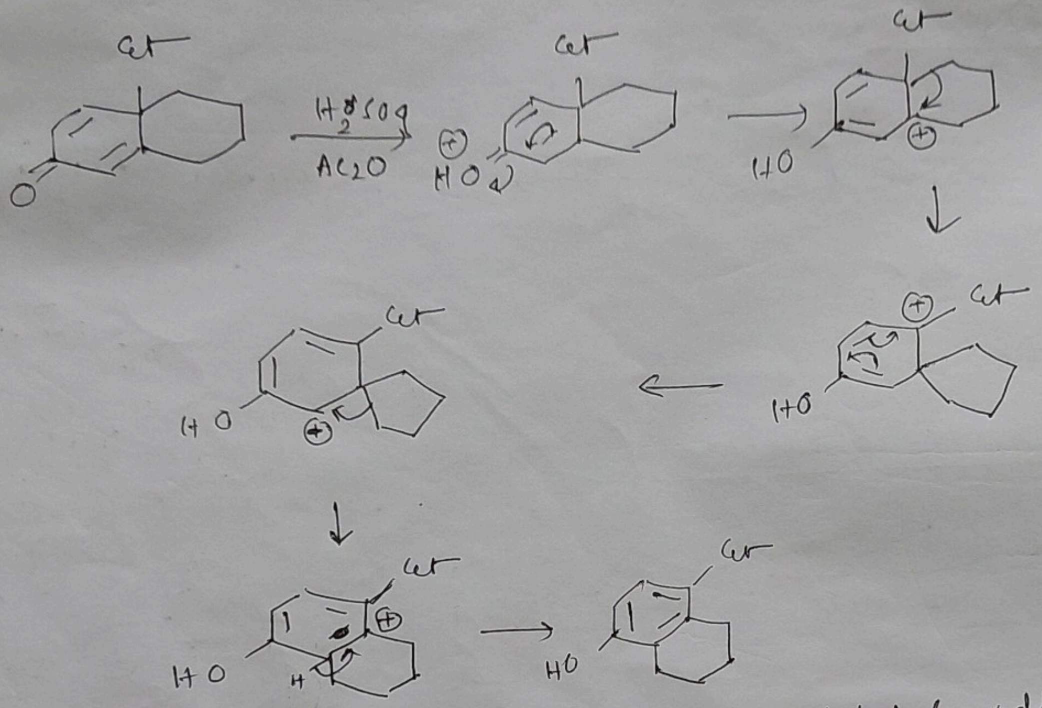


④ Bicyclic alkene



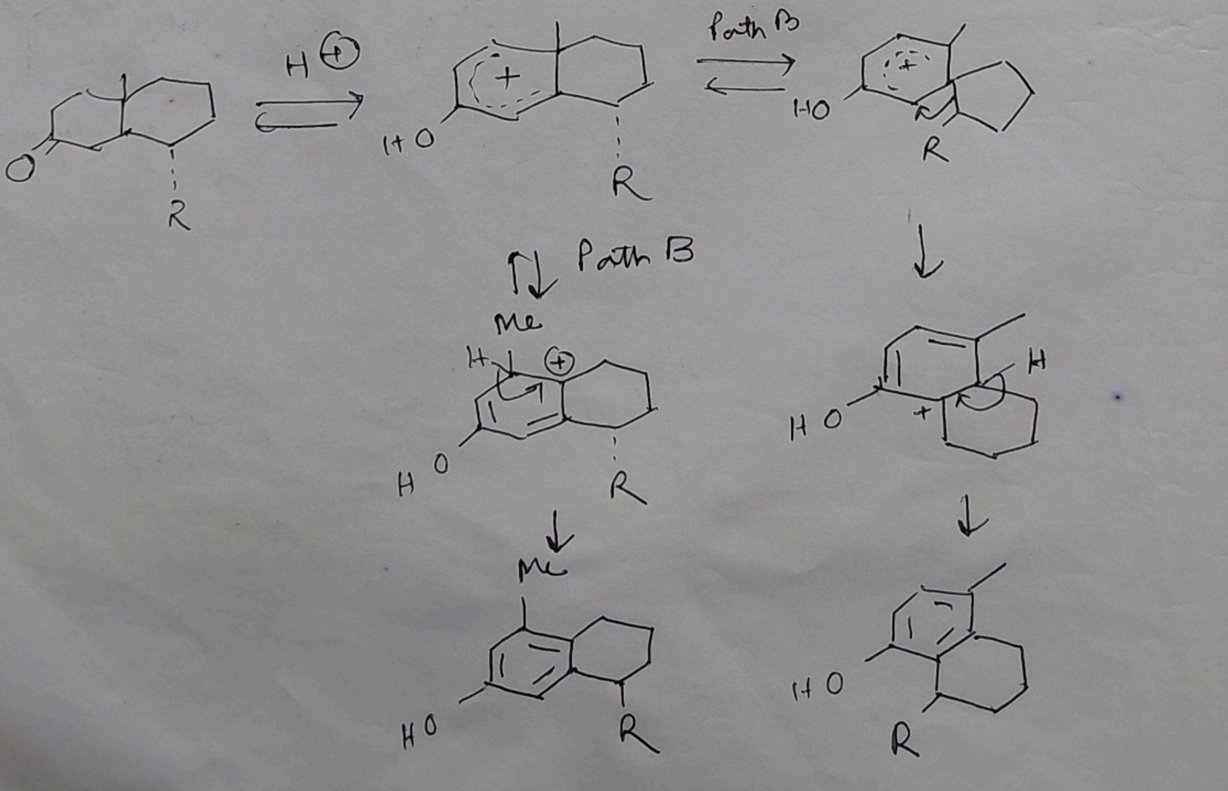
bicyclic alkene





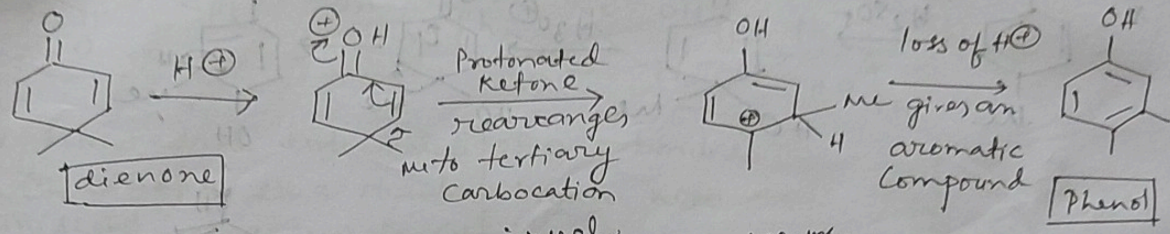
Para substituted pdt.

In aq. condition 1,2 migration of but (Path A) is favoured but in anhydrous condition C–C bond of ring migrate (Path B) preferrably.



Dienone-phenol Rearrangement

In this rearrangement a protonated carbonyl compound rearranges to a tertiary carbocation. The reaction is driven from dienone to phenol because the product cation can rapidly undergo elemination of H⊕ to become aromatic.



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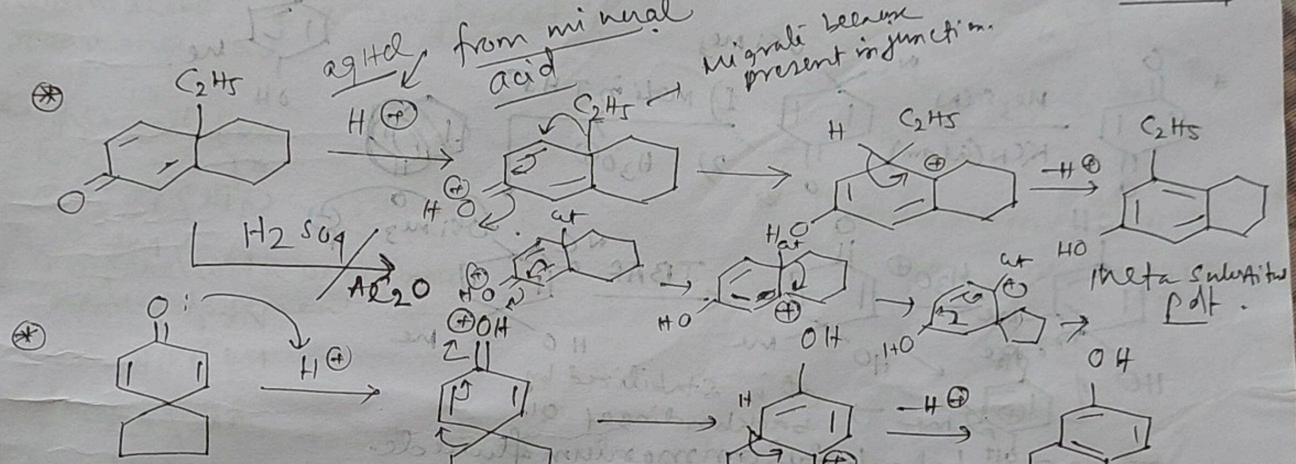

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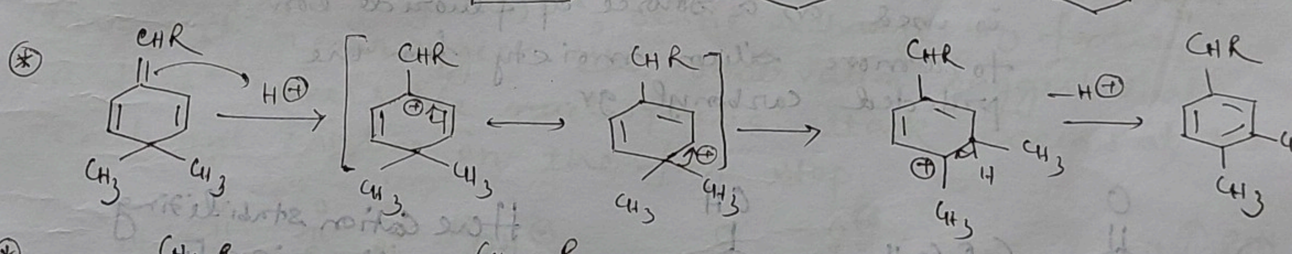

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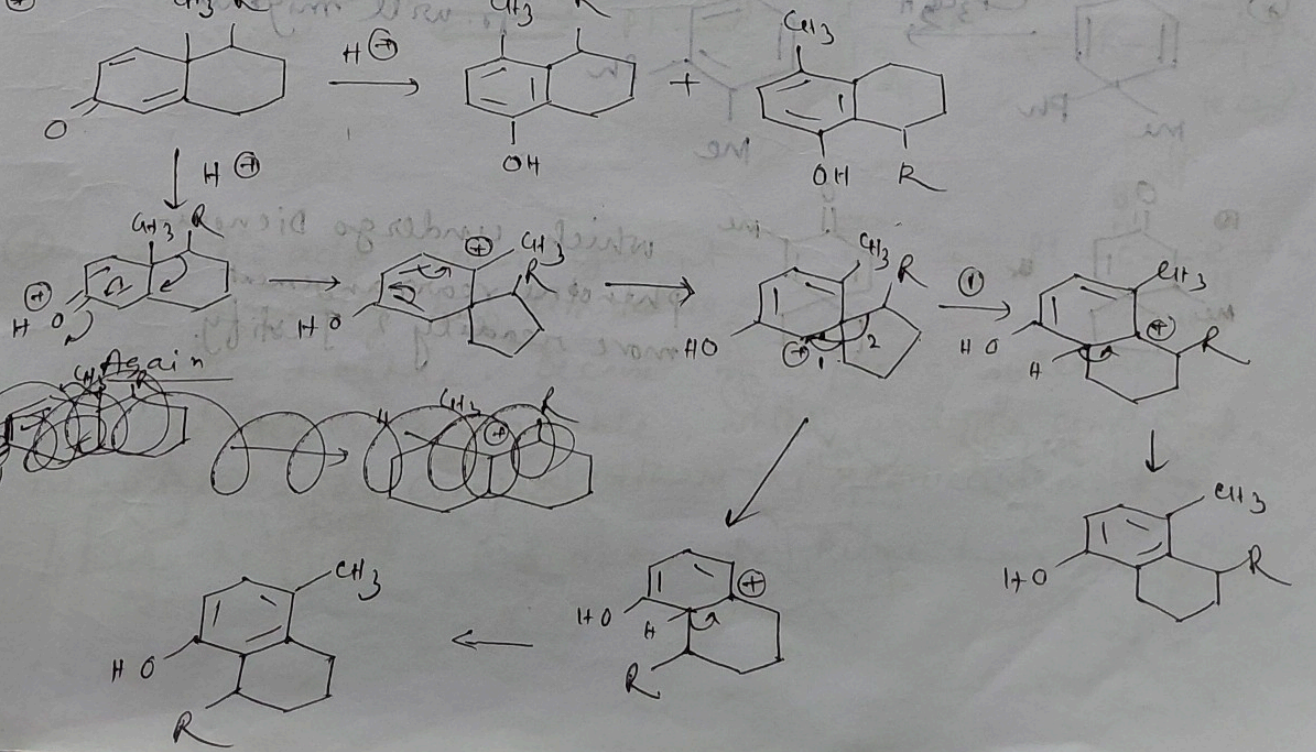

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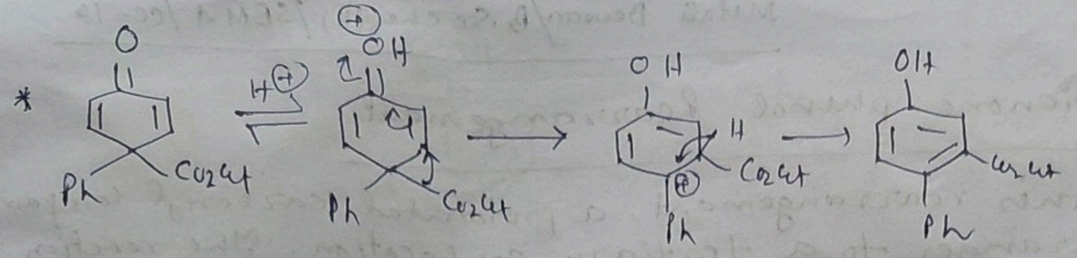
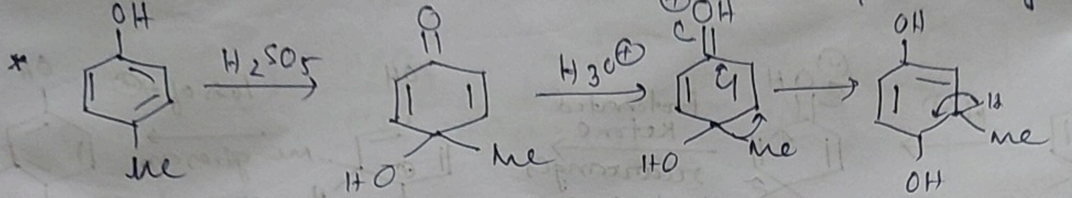


Benzylic as well as allylic C⊕

Here Co2Et migrate because intermediate benzylic C⊕ is highly stable. and Co2Et is so cationic destabilizing that it prefer to migrate.

*



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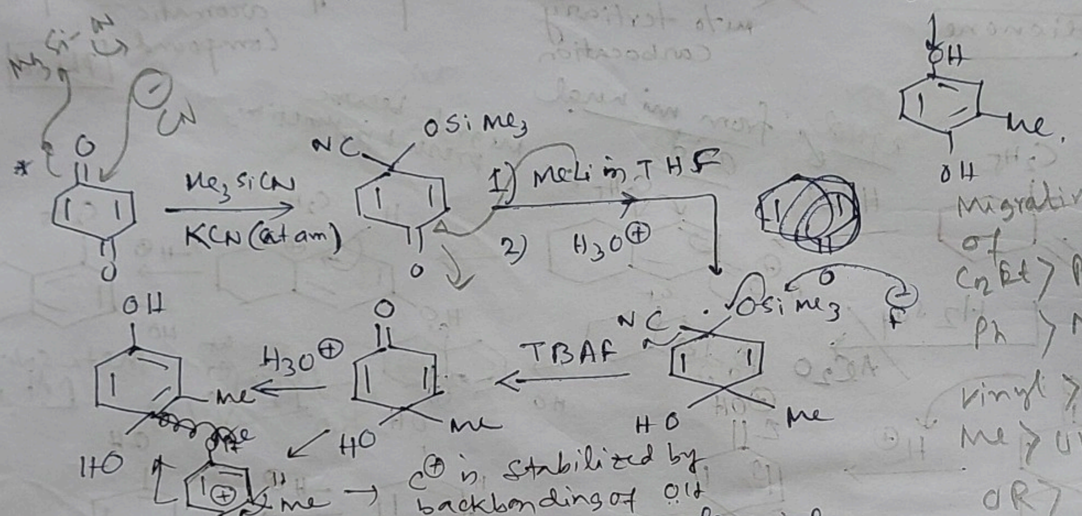
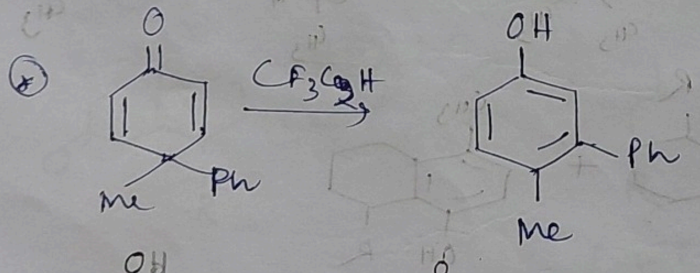


C⊕ is stabilized by backbonding of OH

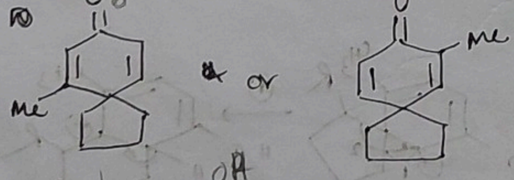
Migrating aptitude of
$CO_2Et > Ph$,
$Ph > Me$
vinyl > Me
Me > OR
OR > Ph

TBAF = tetra butyl ammonium fluoride. is used as a source of fluoride ion to remove silicon moiety from the protected carbonyl gr.

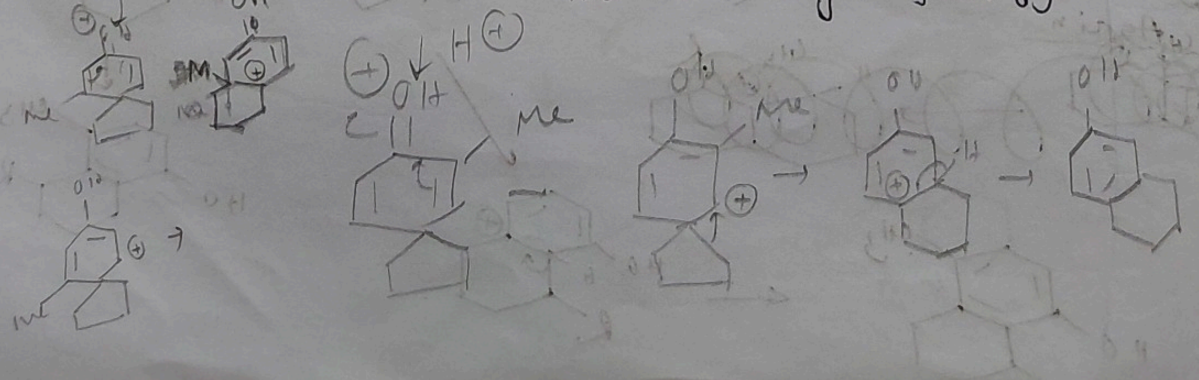
*



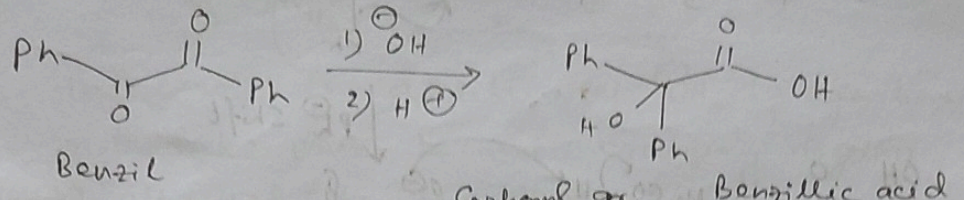
Here cation stabilizing gr. will migrate.

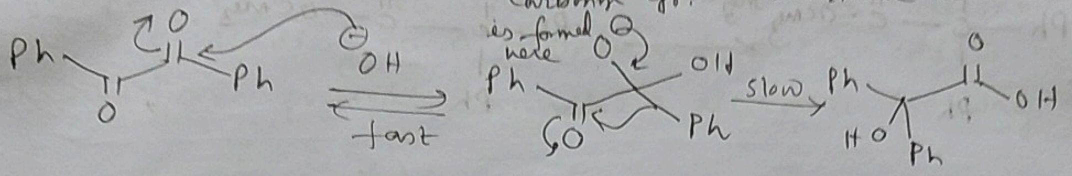


which undergo Dienone-phenone rearrangement more readily? Justify.



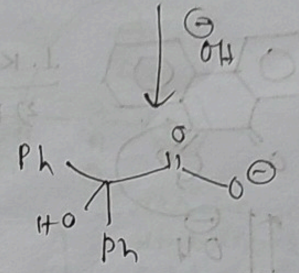
Benzil - Benzillic acid rearrangement



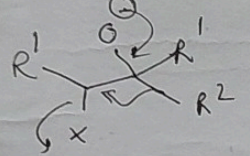


The tetrahedral intermediate can ~~coa~~ collapse in a reaction reminiscent of a semipinacol rearrangement.

C=O π bond is broken here

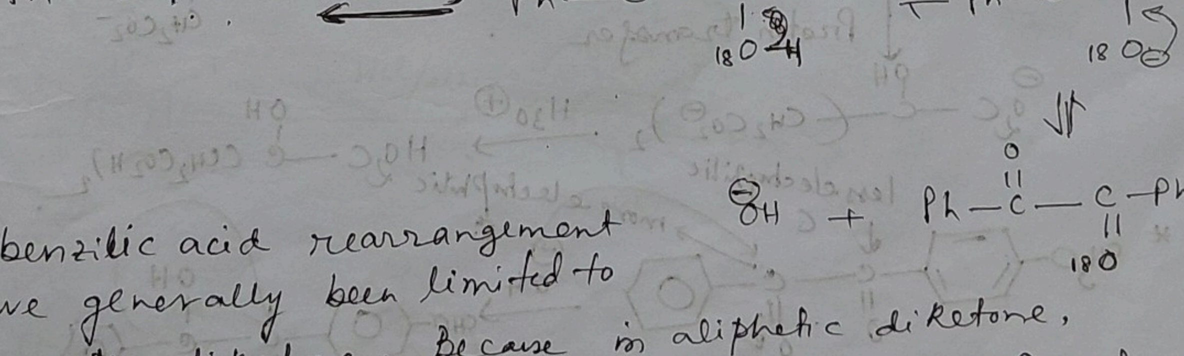


Deprotonation makes the reaction irreversible.

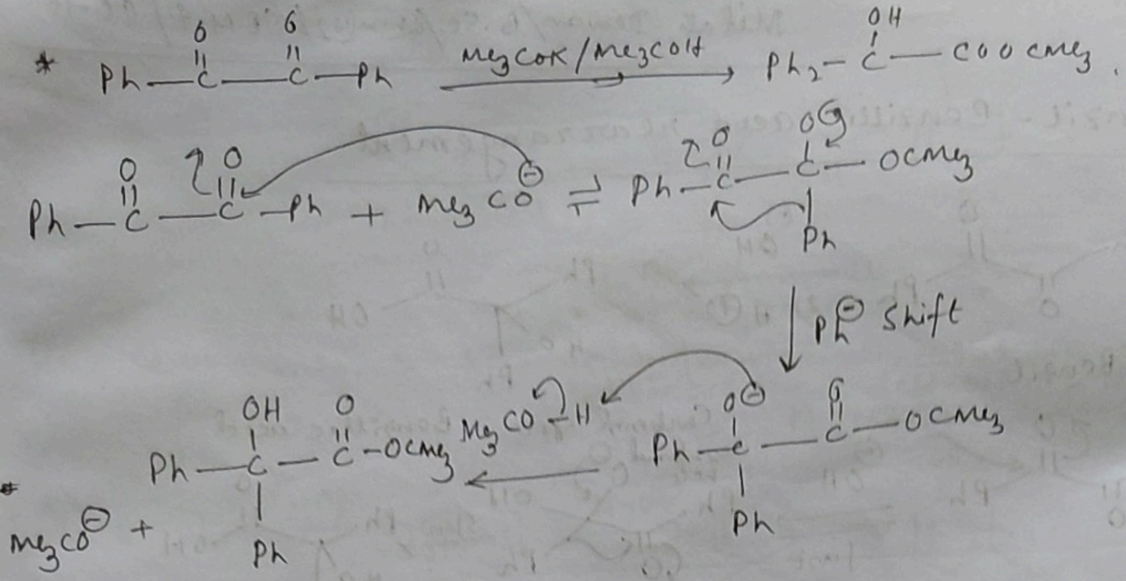


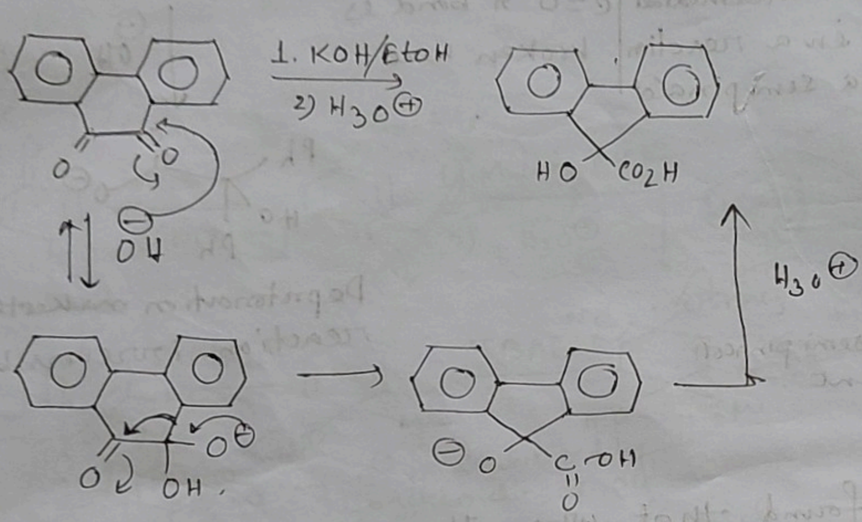
Compare with semi pinacol rearrangement.

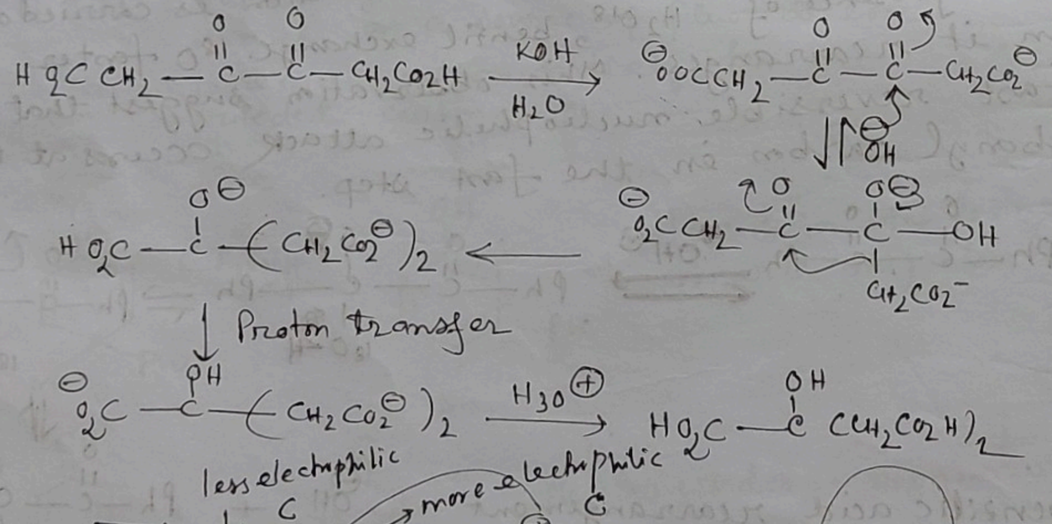
It has been found that when the reaction is carried out in the presence of H_2O^{18}, benzil exchange ^{18}O faster than it rearranges. This observation suggest that a fast reversible nucleophilic attack occurs at the carbonyl carbon in the fast step.

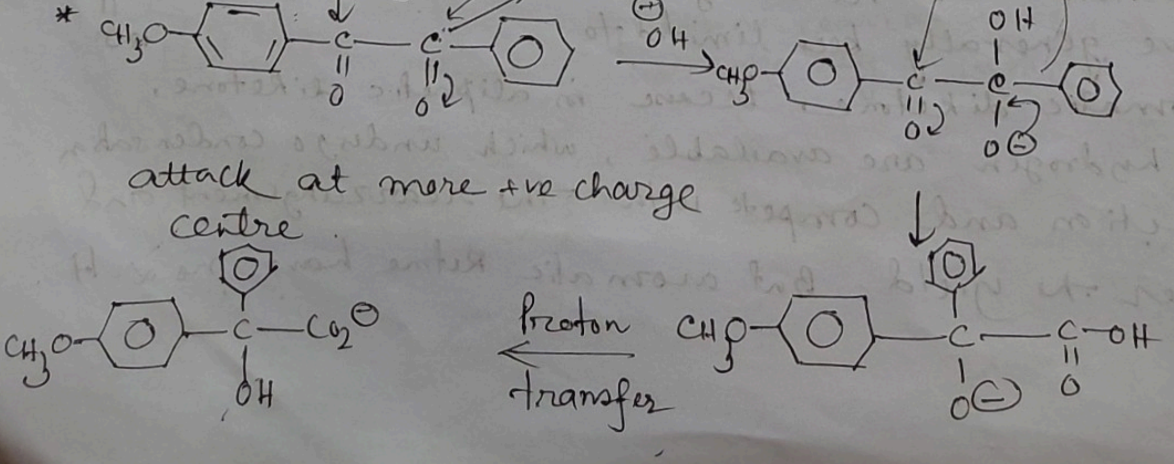


(*) benzilic acid rearrangement have generally been limited to aromatic diketone. Because in aliphatic diketone, α-hydrogen are available, which undergo condensation reaction and compete with the rearrangement and lower the yield. But aromatic Ketone have no α-H.

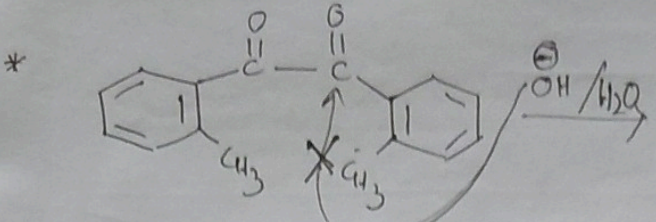
*

Me3COK / Me3COH
Ph⊖ shift

*

1. KOH/EtOH
2) H3O⊕
H3O⊕

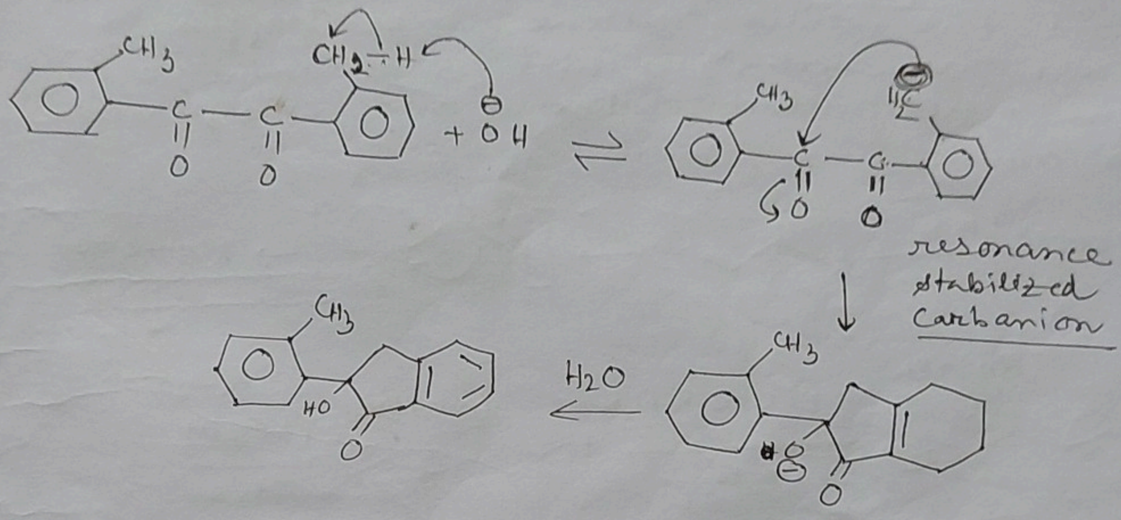
*

KOH
H2O
Proton transfer
H3O⊕

*

less electrophilic C
more electrophilic C
⊖OH
attack at more +ve charge centre
Proton transfer

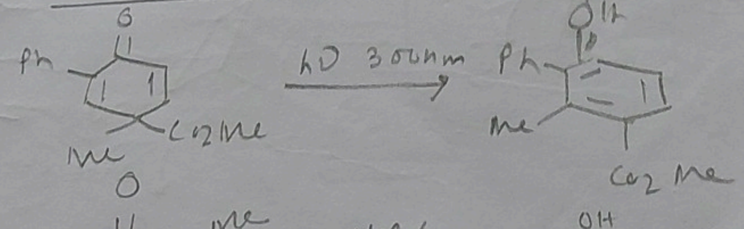
*

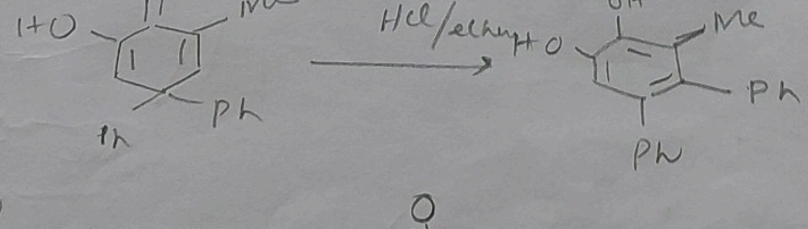


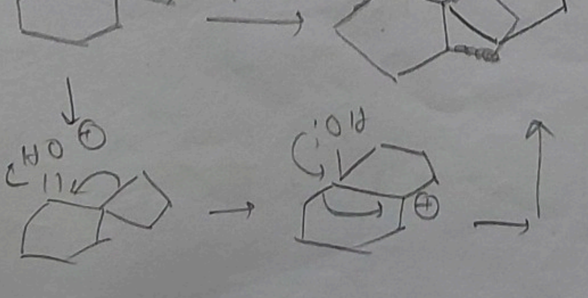
In this case, the addition of $\ominus OH$ to a carbonyl carbon does not take place because crowding together of the groups attached to the carbonyl carbon destabilizes the T.S leading to a tetrahedral intermediate. Actually, the reaction proceeds through a alternate pathway.



Dienone - phenol Rearrangement



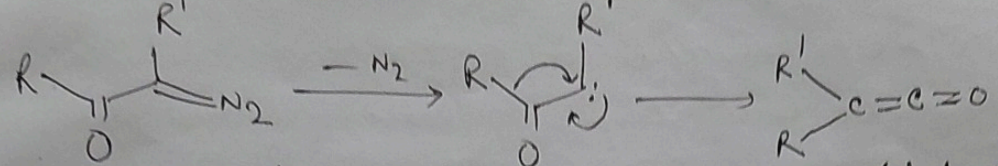




Mitali Devram/B.Sc Chem(H)/SEM-4/CC-10

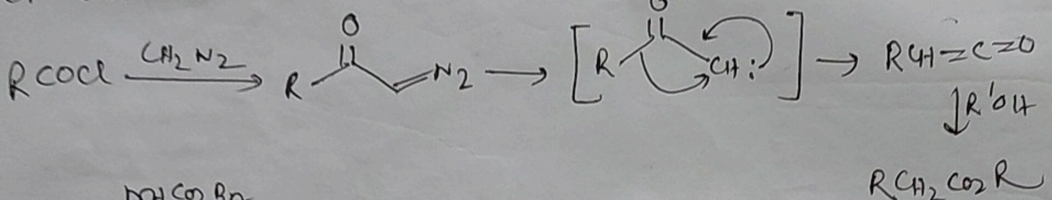
wolf Rearrangement

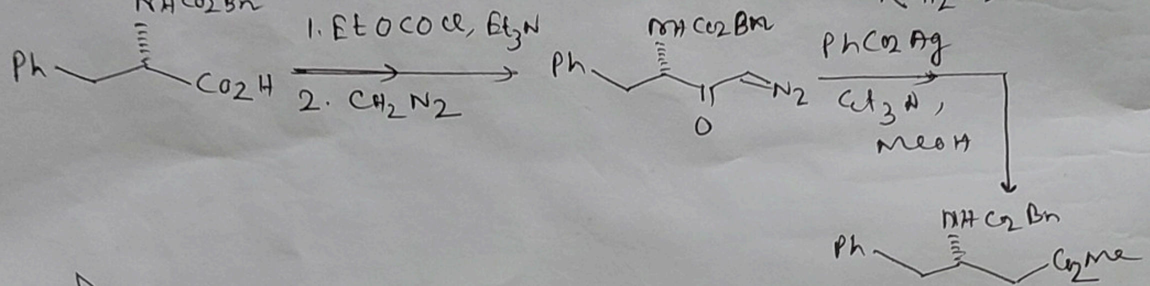
wolf Rearrangement is rearrangement reaction, in which a diazo Ketone is converted to ketene.

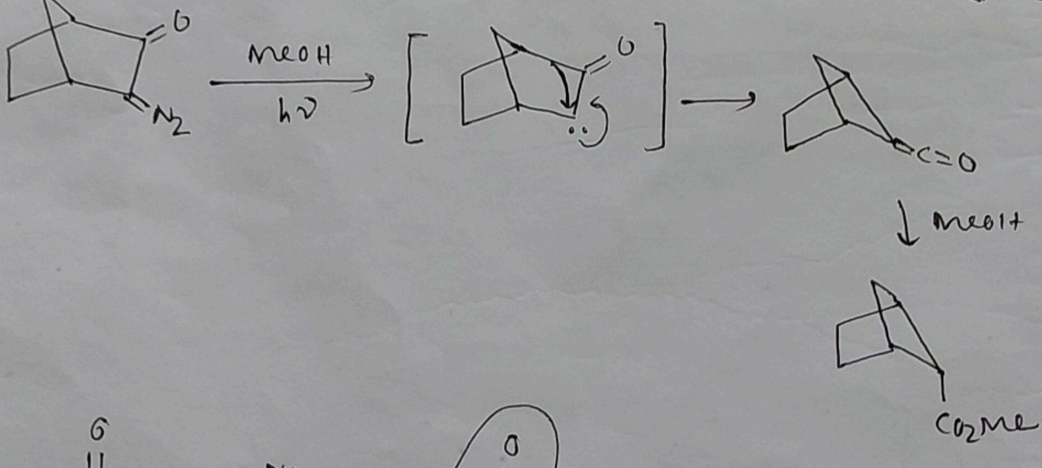


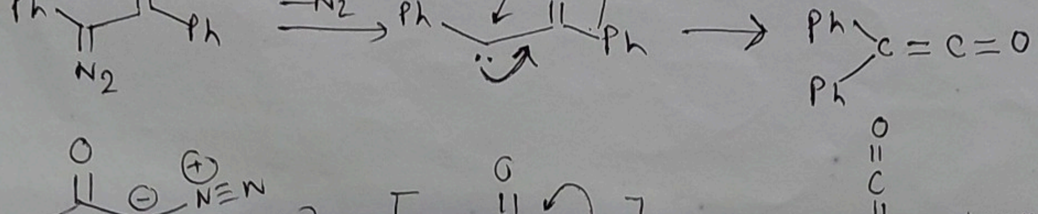
The reaction takes place in presence of light, heat or transition metal catalyst such as Ag_2O.

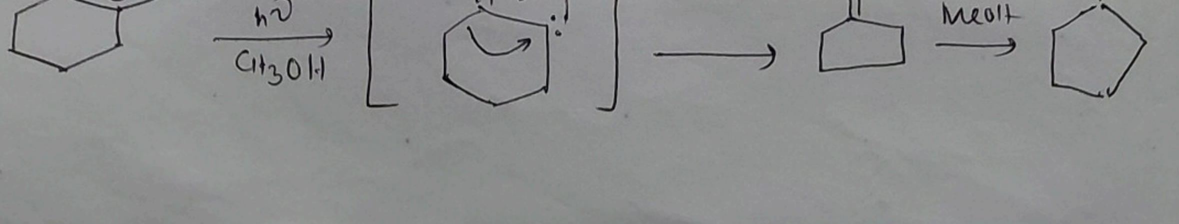
The R group migrates with retention of configuration and the resulting ketene can be trapped by water, an alcohol, a thiol or an amine to give the product carboxylic acid, ester, thioester or amide.

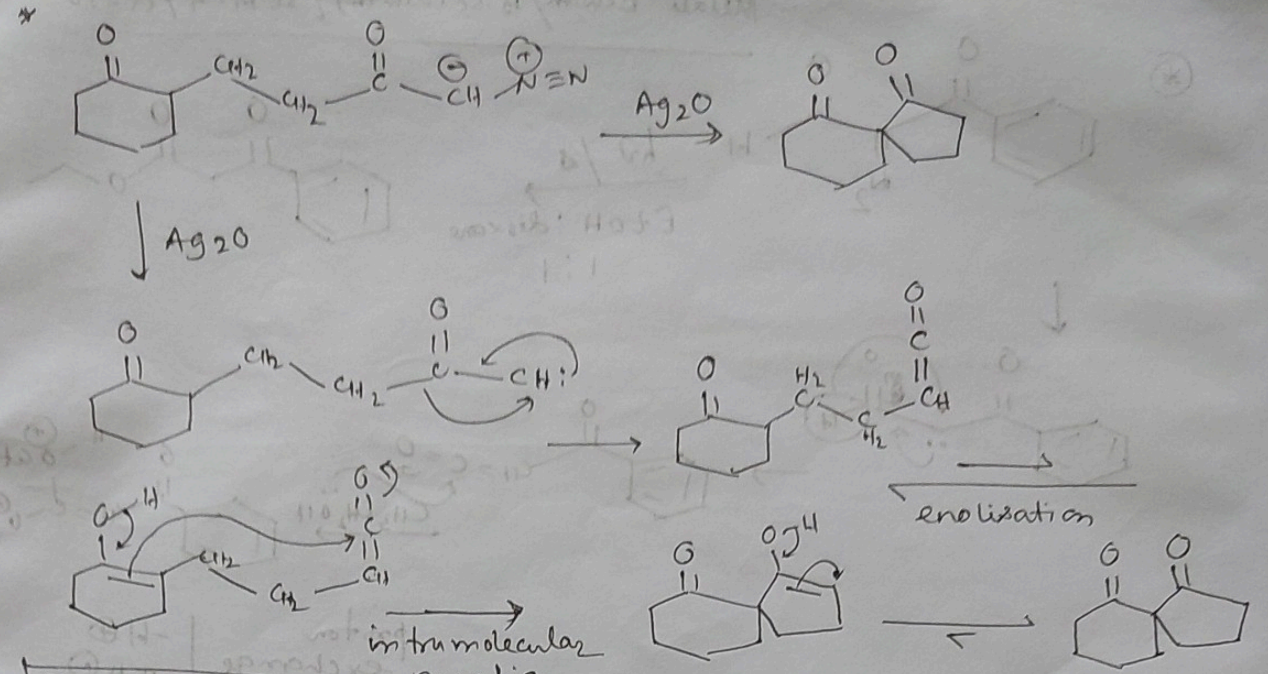




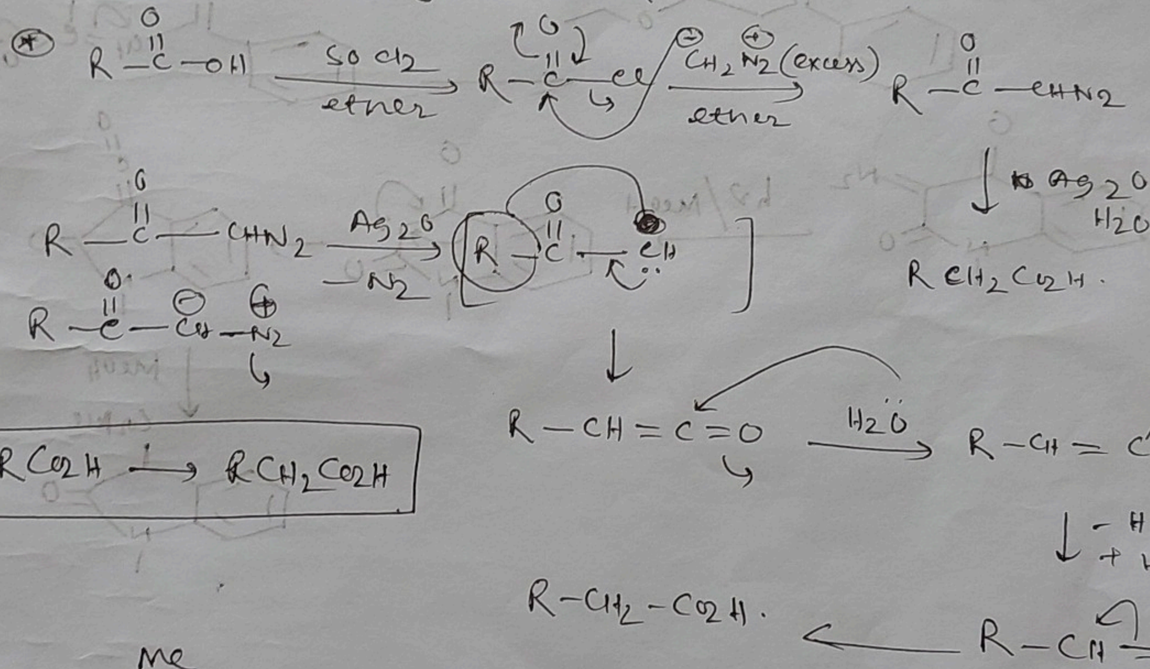




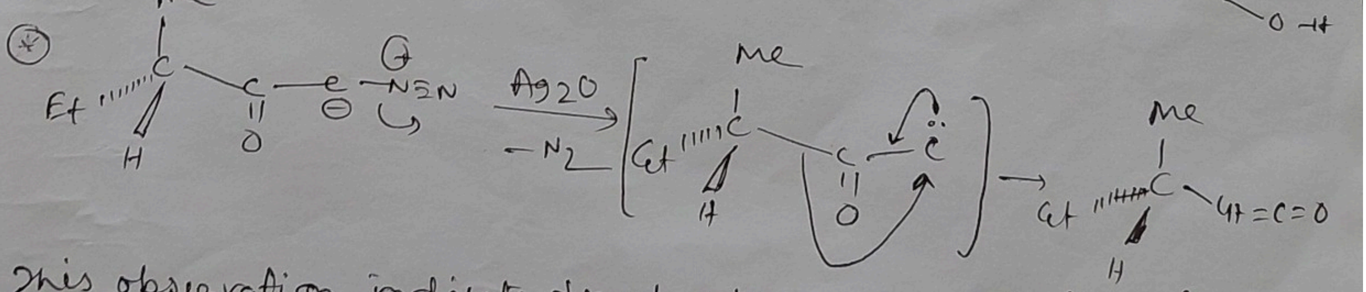




Earndt - Ester Synthesis

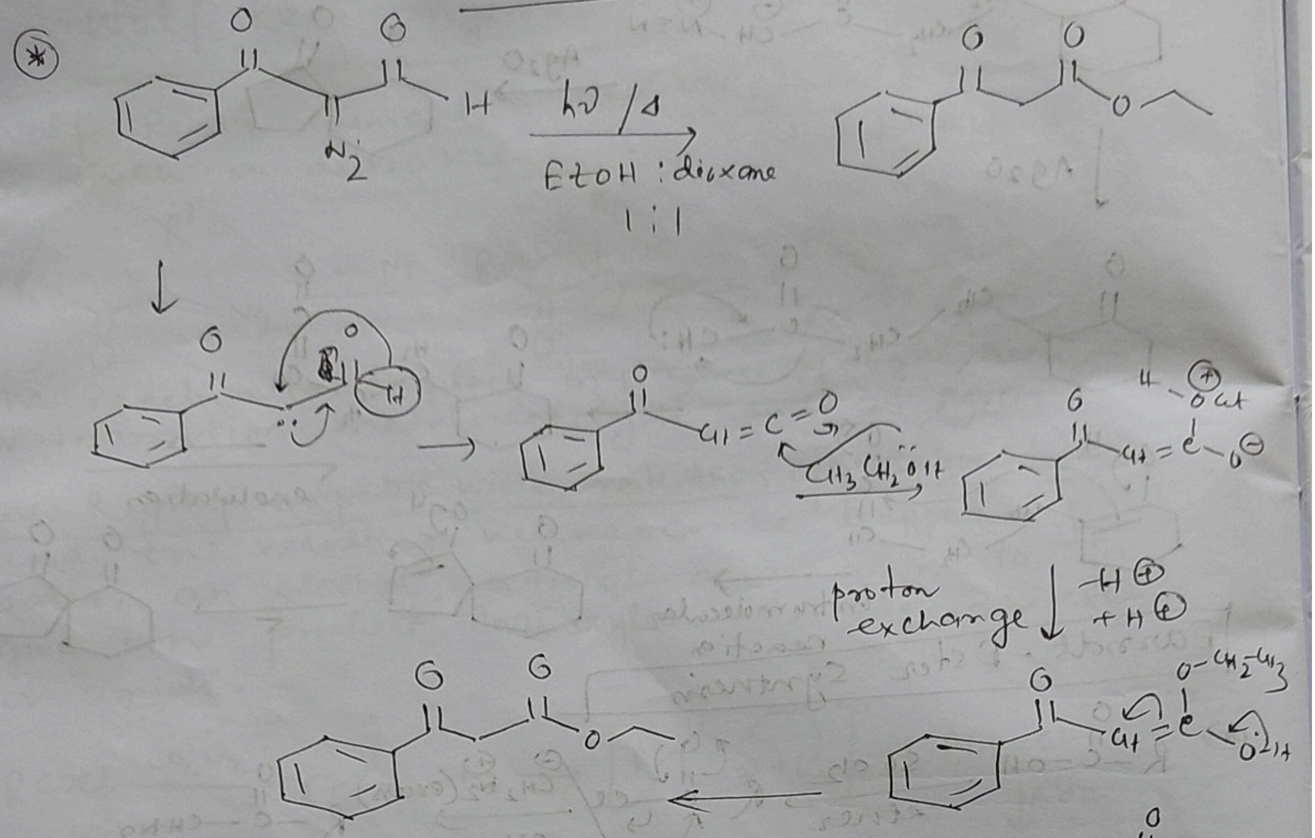


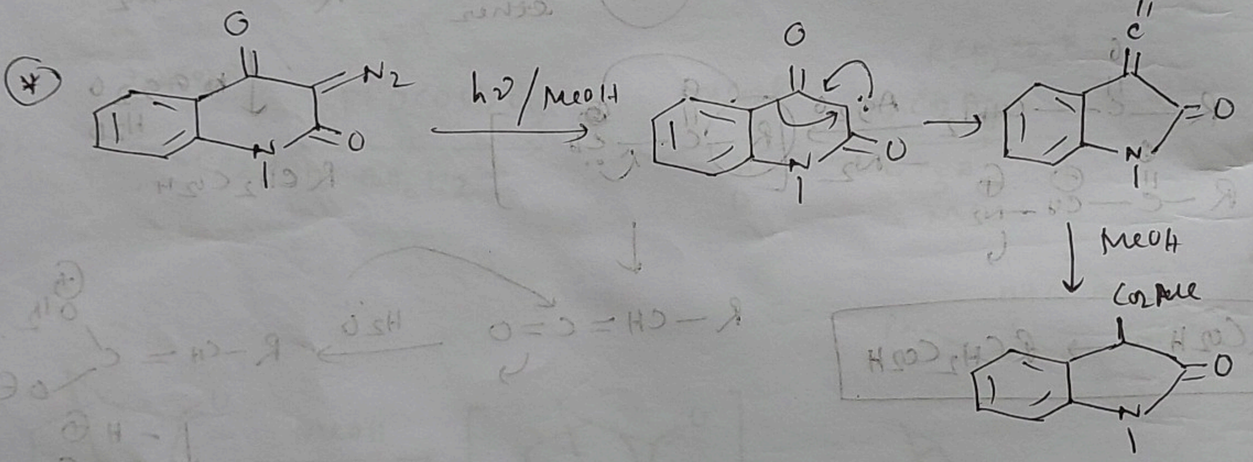
$$\boxed{RCO_2H \longrightarrow RCH_2CO_2H}$$



Configuration retained.

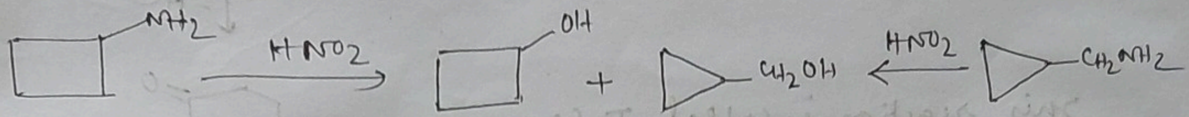
This observation indicate that the group R does not migrate as free carbanion (i.e, the rearrangement is intramolecular in nature).


hν / Δ
EtOH : dioxane
1:1
CH_3CH_2OH
proton exchange
$-H^⊕$
$+H^⊕$
$O-CH_2-CH_3$

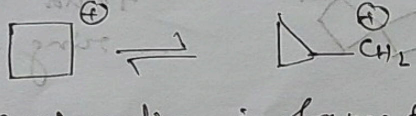

N_2
hν/MeOH
MeOH
CO_2Me

Demjanov - Rearrangement

Expansion and contraction of ring

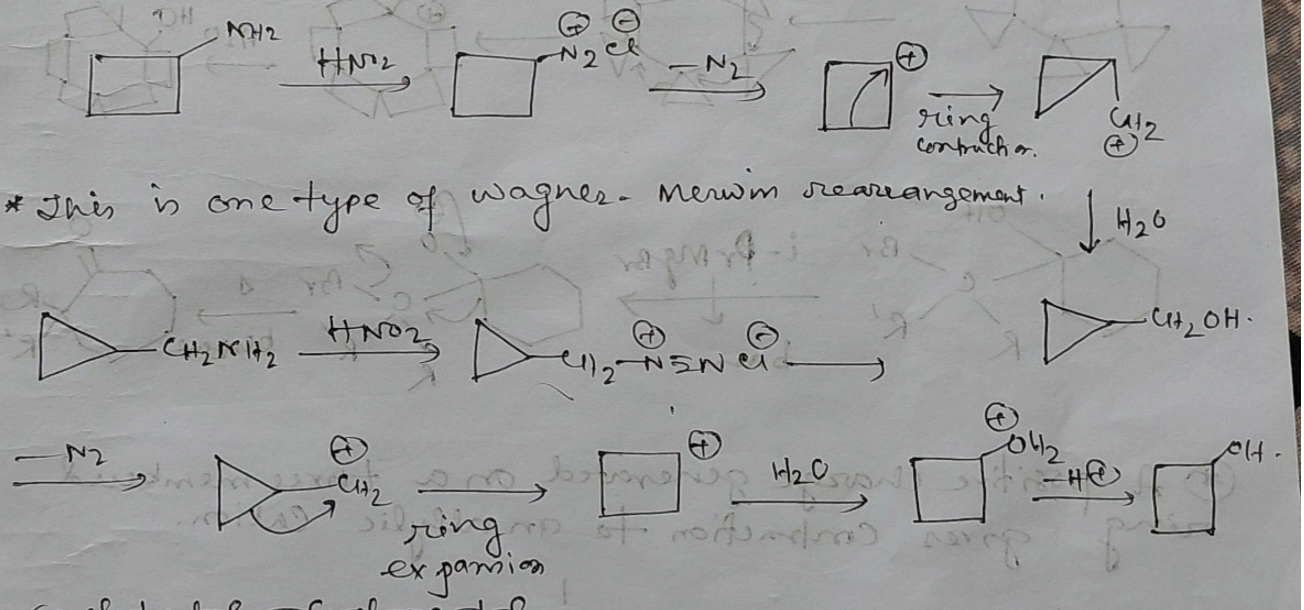


when a positive charge is formed on an alicyclic carbon, migration of an alkyl group can take place to give ring contraction, producing a ring that is one carbon smaller than the original.



when the carbocation is formed by diazotization of an amine, the reaction is called the Demyanov rearrangement.

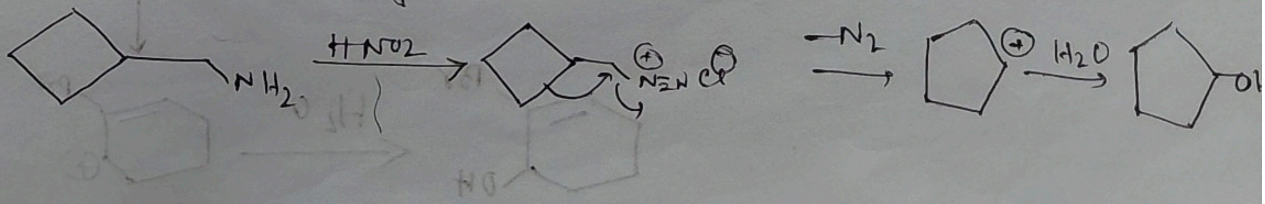
* This is one type of wagner- Merwin rearrangement.



~~cyclobutyl - Sycloopentyl~~

cyclobutyl - cyclopropylmethyl interconversion is feasible became additional strain is not involved.

But contraction of cyclopentyl cation to cyclobutyl methyl system is generally not feasible because of the additional strain involved.



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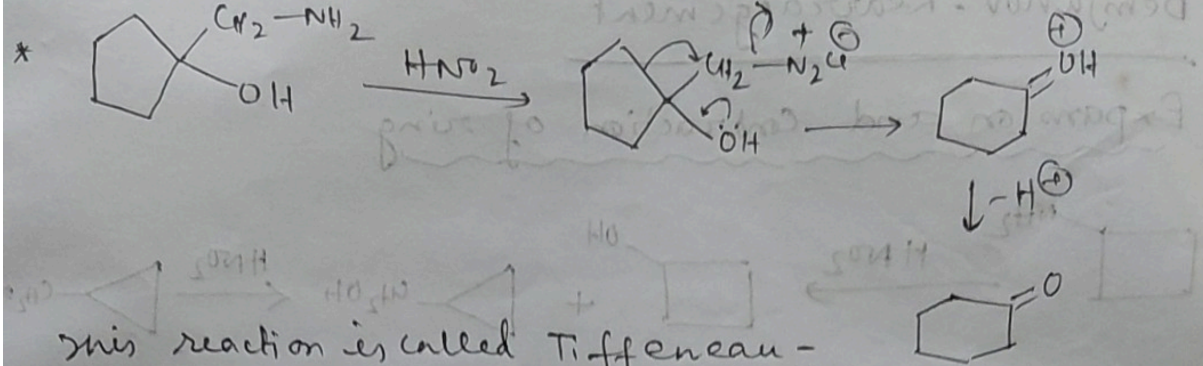
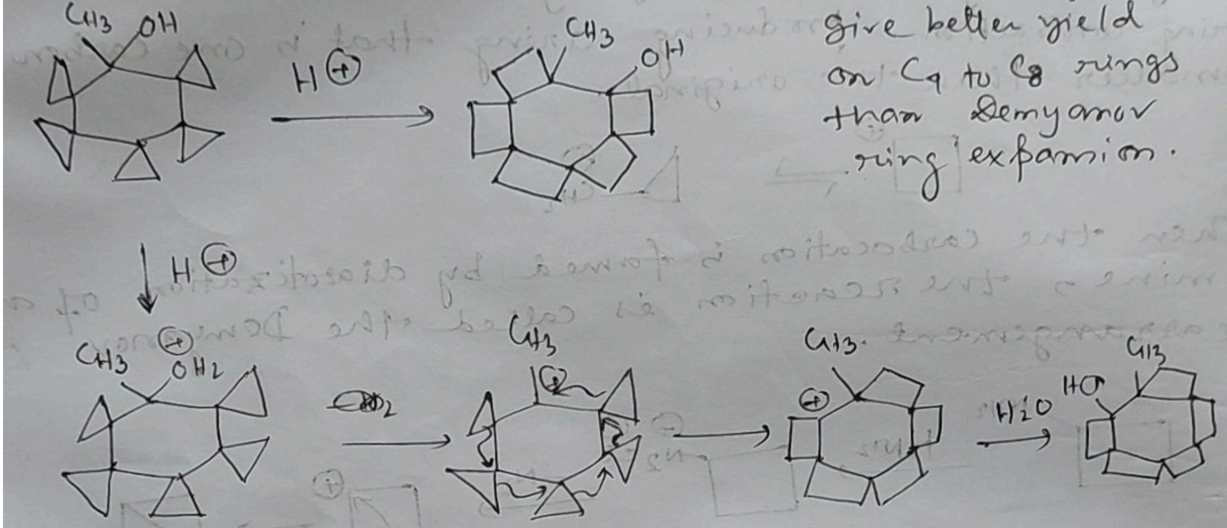
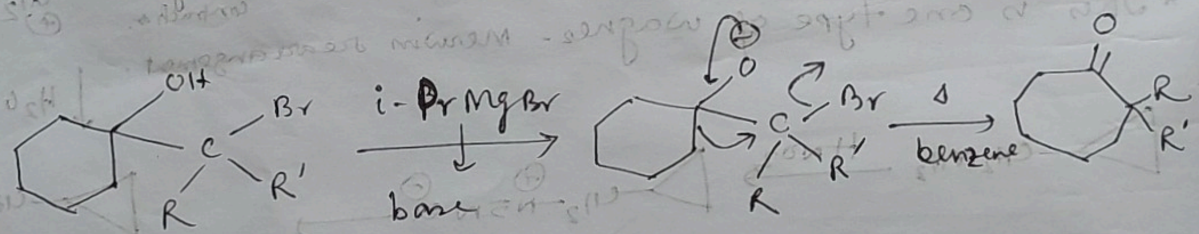


This reaction is called Tiffeneau-Demjanov rearrangement.

- This rearrangement give better yield on C_4 to C_8 rings than Demjanov ring expansion.





A positive charge generated on a three membered ring gives contraction to an allylic cation.