

Organic chemistry

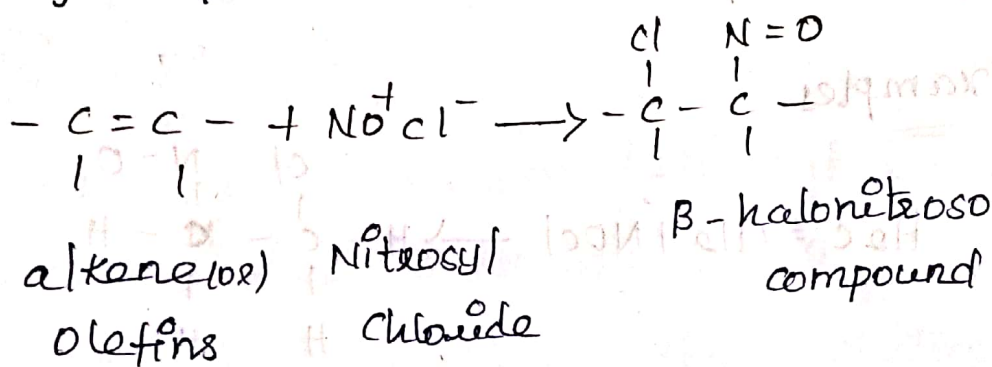
Unit - I

Addition to carbon-carbon Hetero atom multiple bonds.

1. Addition of Nitrosyl chloride to olefins:

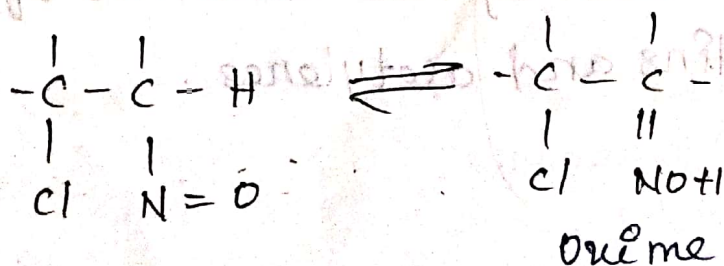
Reaction

Addition of nitrosyl chloride to olefins to give β -halo nitroso compound.



There are three possible products when NOCl added to olefins. The initial product is always the β -halo nitroso compound, but these are stable only if the carbon bearing nitrogen has no hydrogen.

If it has, the nitroso compound tautomerizes to the oxime.

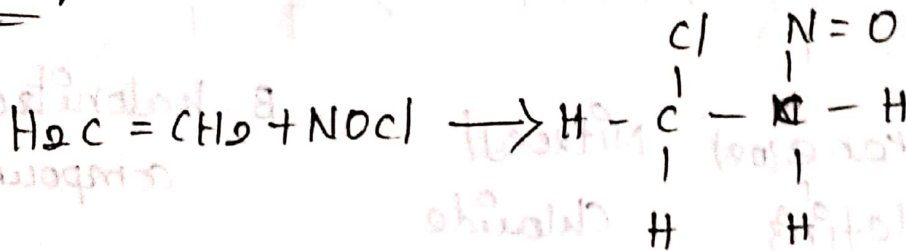


with some olefins, the initial β -halo nitroso compound is overclised by the NOCl to a β -halo nitro compound. many functional groups can be present without interference.

E.g

$\text{COOH, COOR, CN, OR}$. The mechanism in most cases is probable simple electrophilic addition is usually anti, though syn addition has been reported in some cases.

Examples

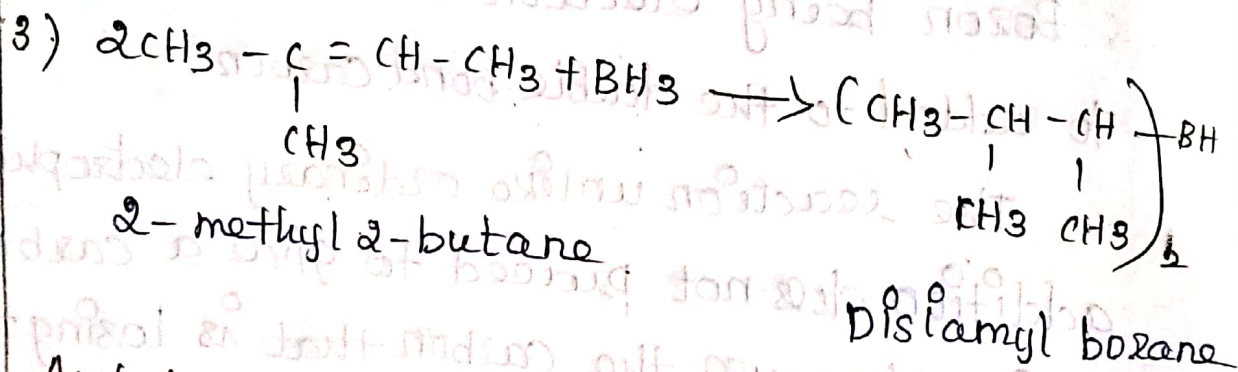
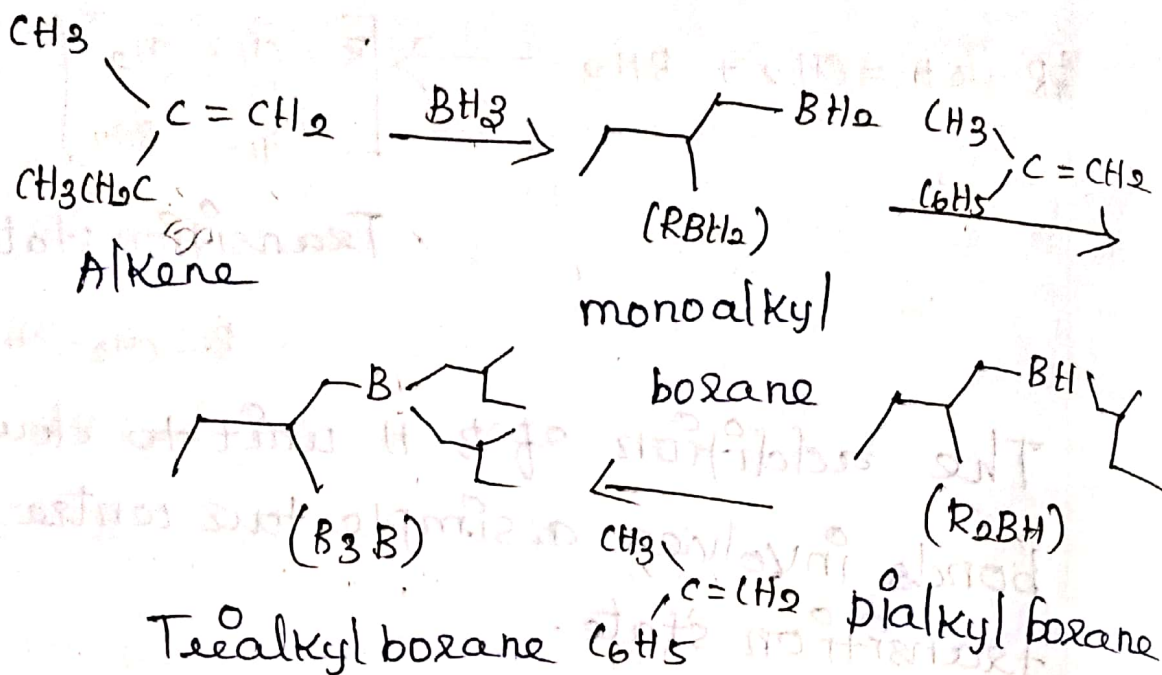
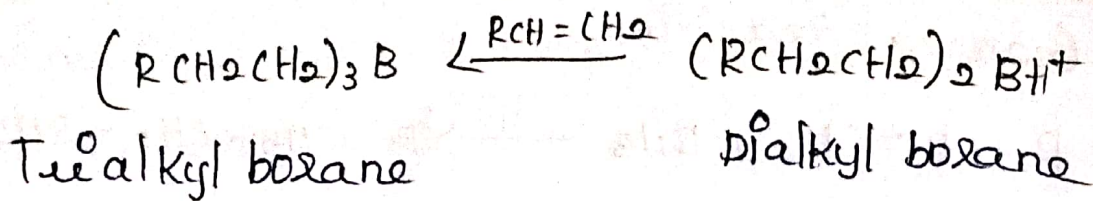


1 chloro, 2-nitroso ethane.

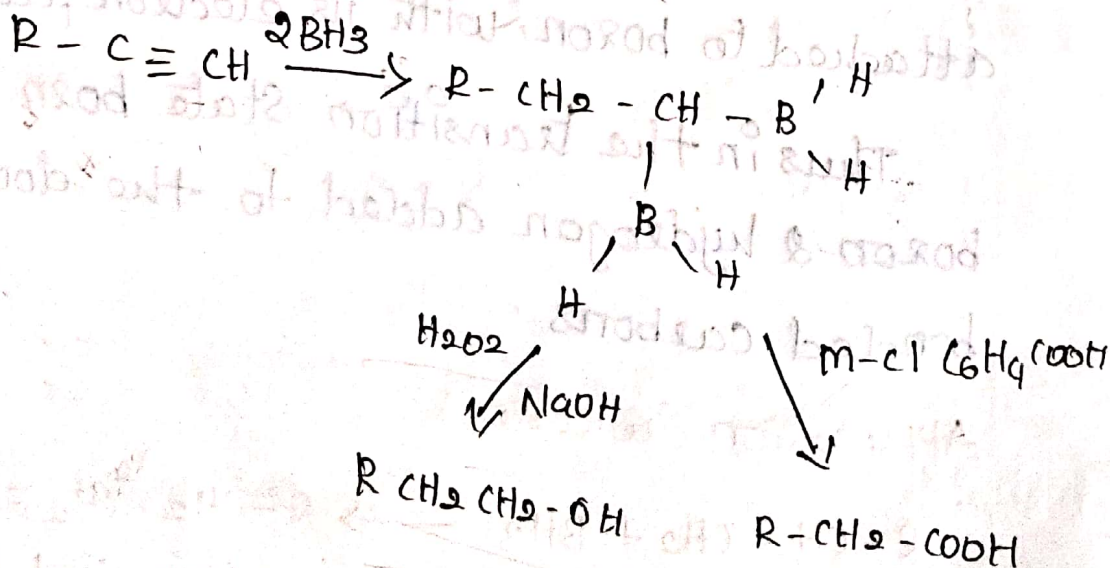
2) Hydroboration of olefins and Alkynes

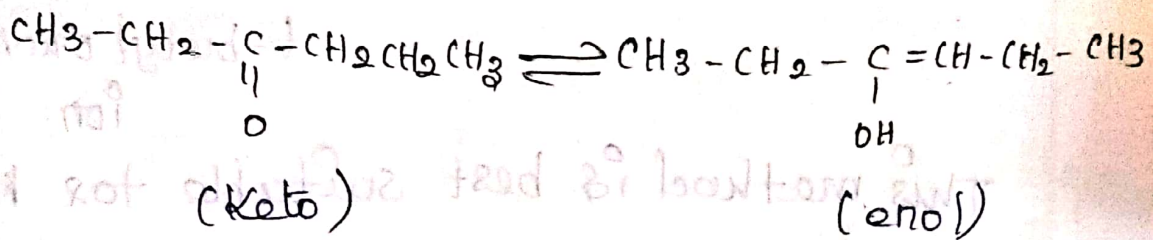
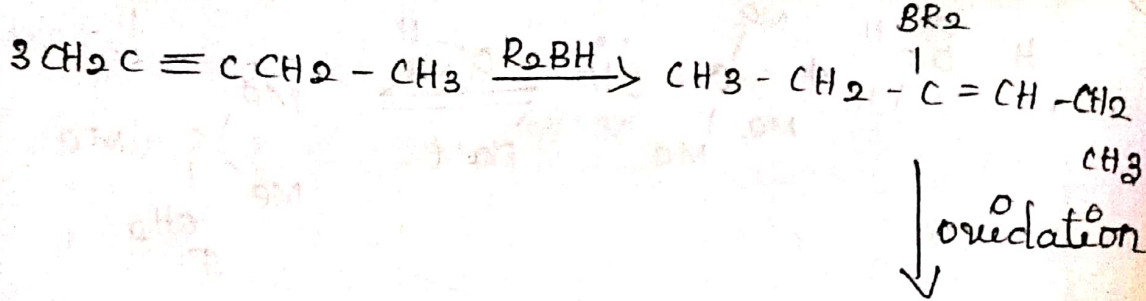
Definition

Hydroboration is the process in which alkyl and alkynyl boranes are prepared by the addition of borane to olefins and alkynes.



Acetylene





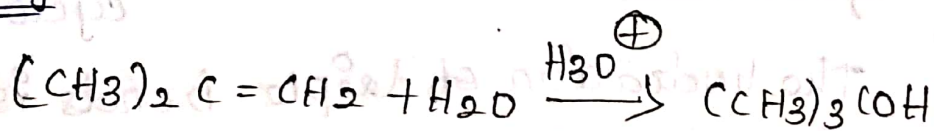
3) Hydration of olefins and acetylenes

Hydration of olefins

Many of alkenes are known to added elements of water in presence of acid to yield alcohols. This addition also follows markownikoff's Rule.

Reaction

E.g

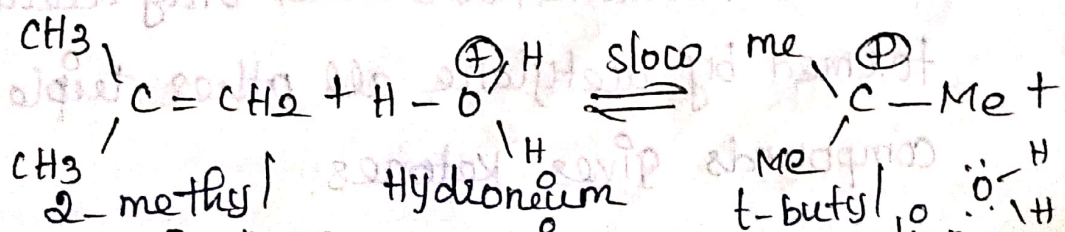


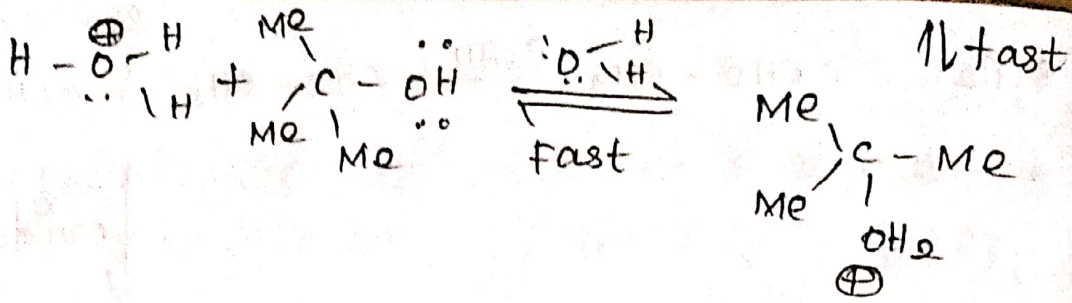
2-methyl

t-butyl alcohol

propene

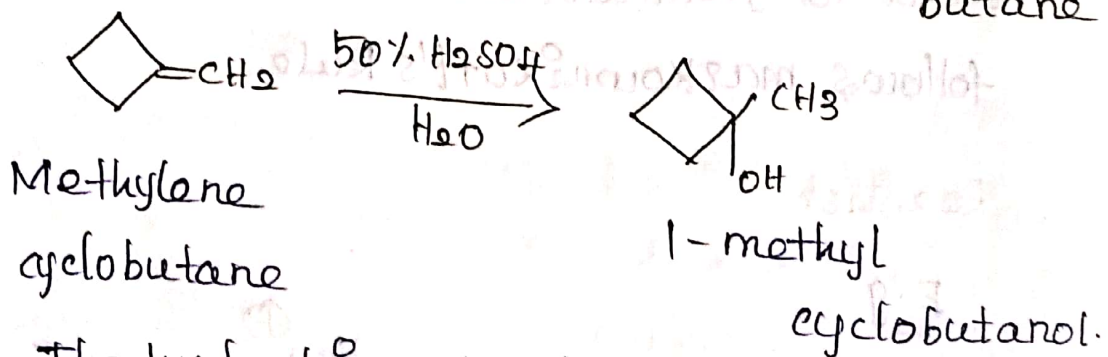
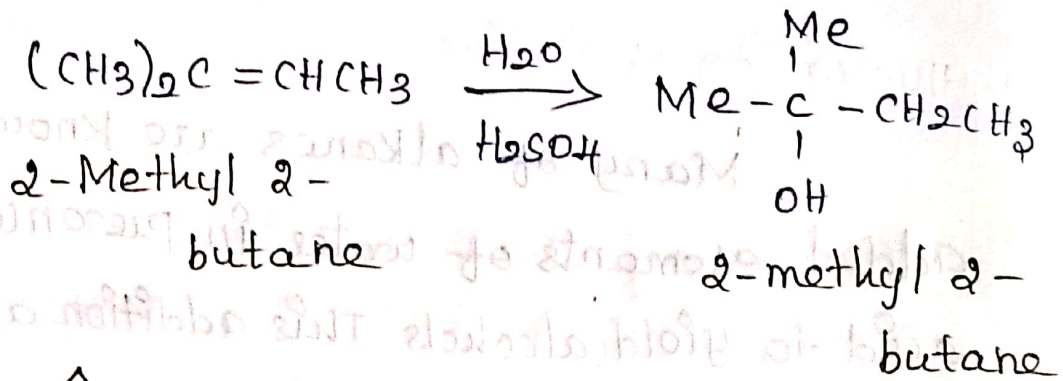
Mechanism





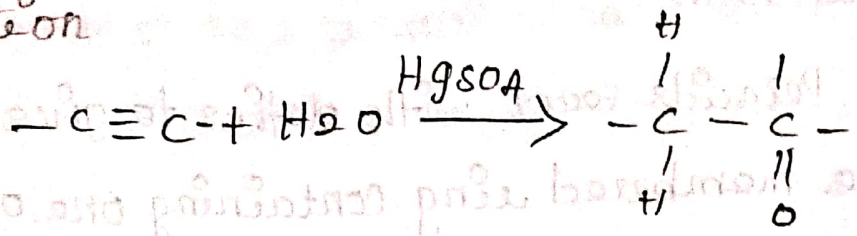
This method is best suitable for the preparation of 3° alcohol.

Examples

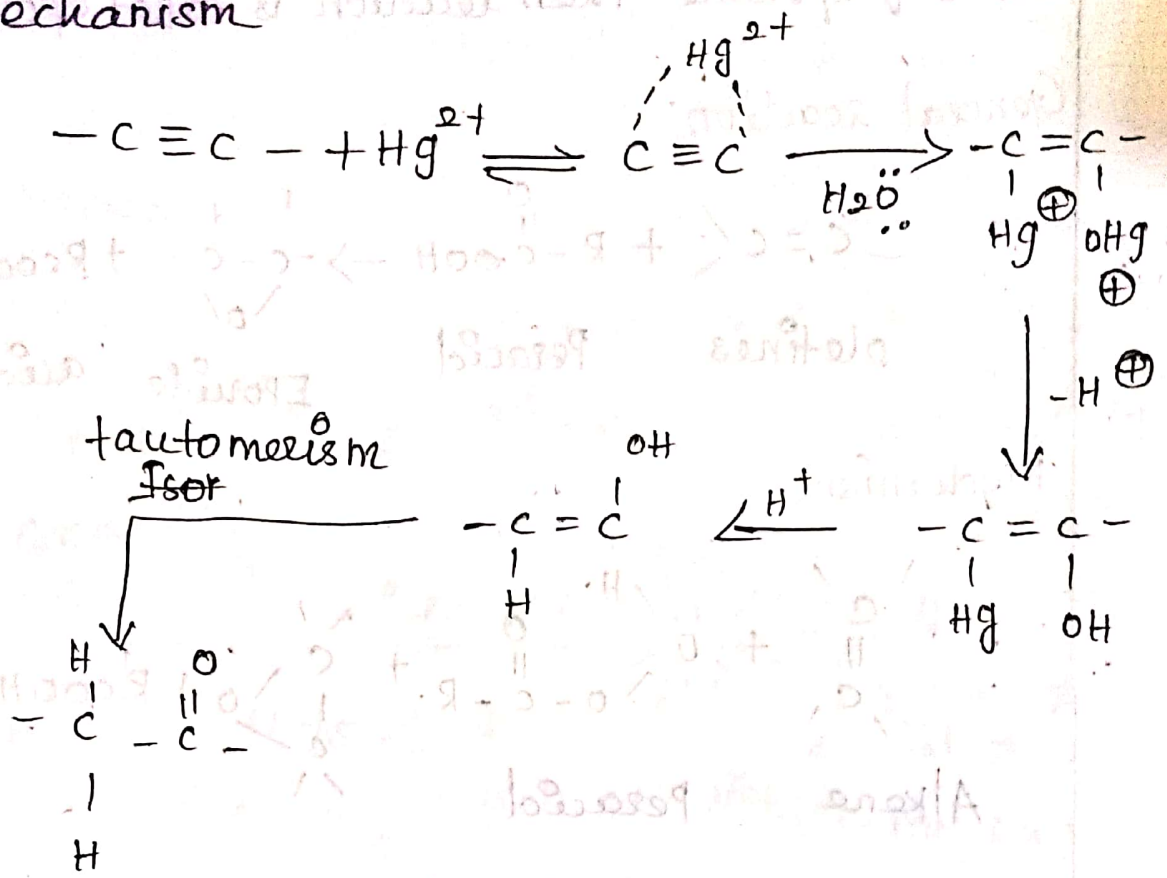


The hydration of triple bonds is generally carried out with mercuric ion salts (sulfate or acetate) as cations mercuric oxide in presence of an acid also a known common reagent. Since, the addition follows Markovnikov's rule, only acetaldehyde formed by acetylene all other triple-bond compounds gives ketones.

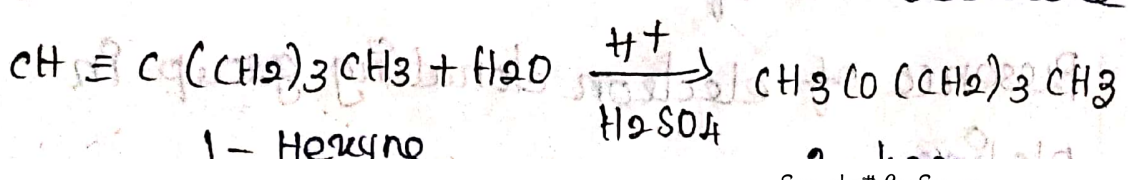
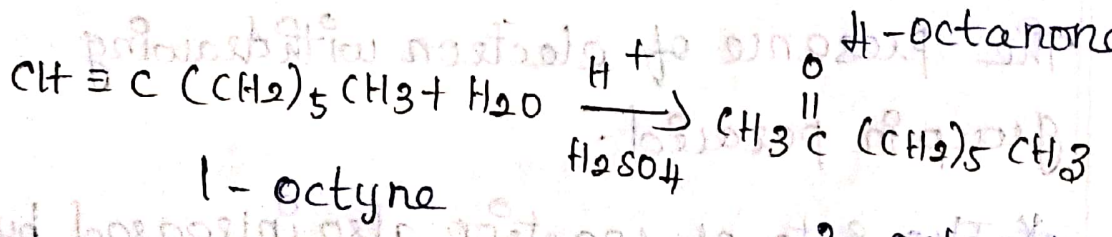
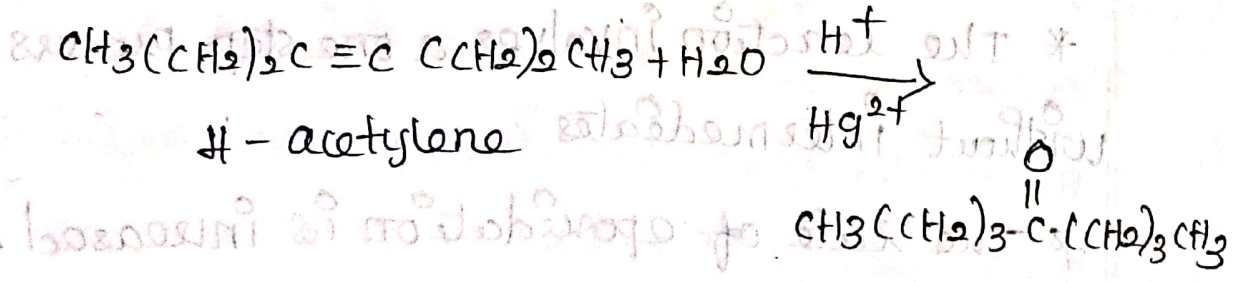
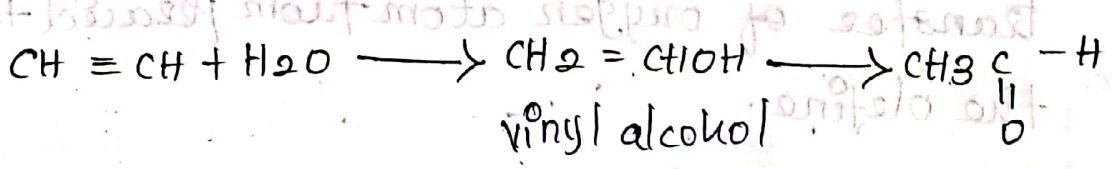
Reaction



Mechanism



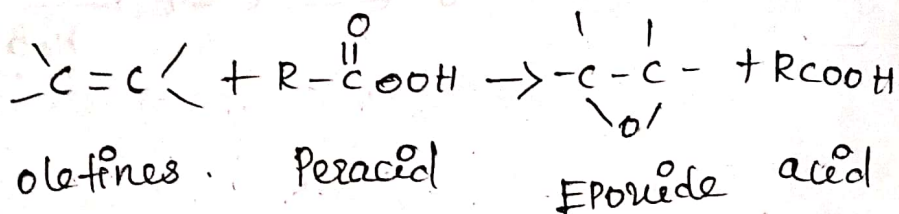
Example



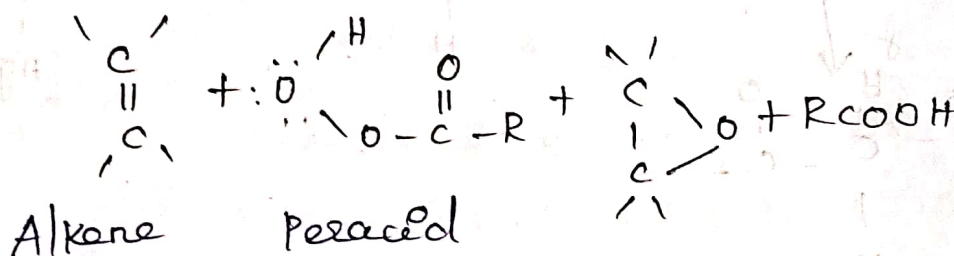
4) Epoxidation

Peroxy acids react with olefins to give stable three membered ring containing one oxygen atom of epoxide. This reaction is called epoxidation.

General reaction



Mechanism



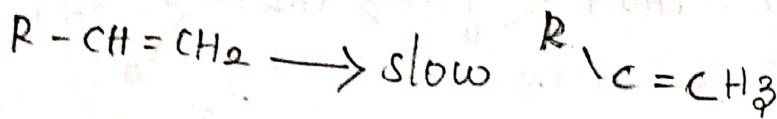
* The rxn is believed to take place by transfer of oxygen atom from peroxy acid to the olefine.

* The reaction involves a one step process without intermediates.

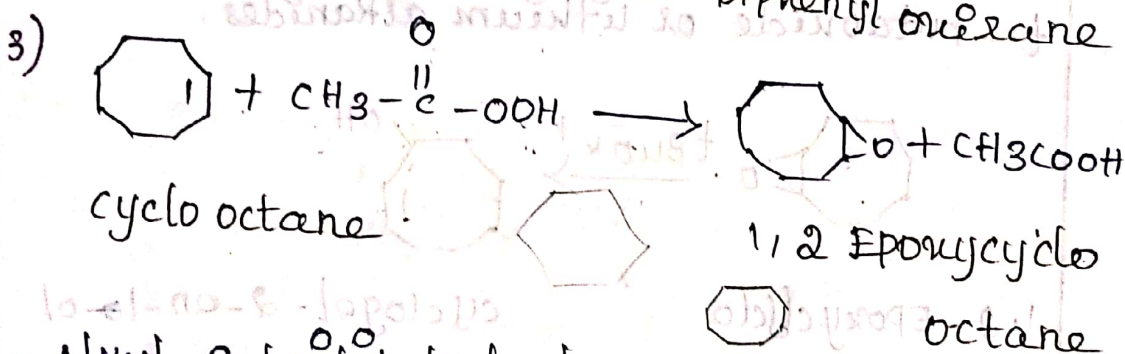
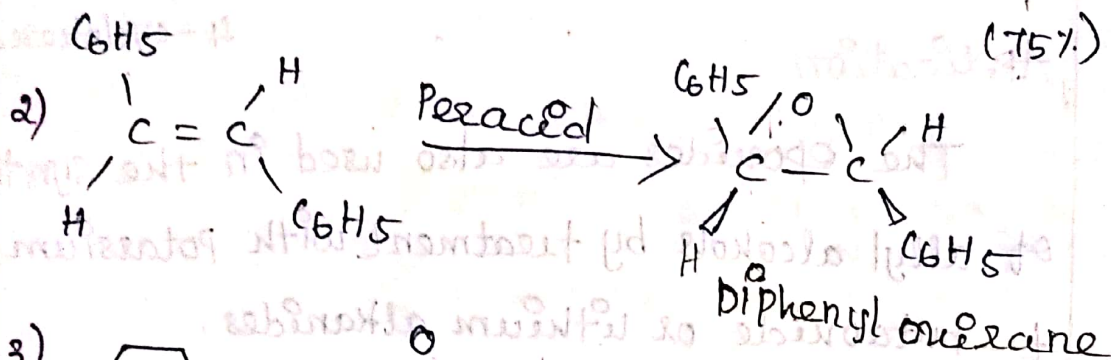
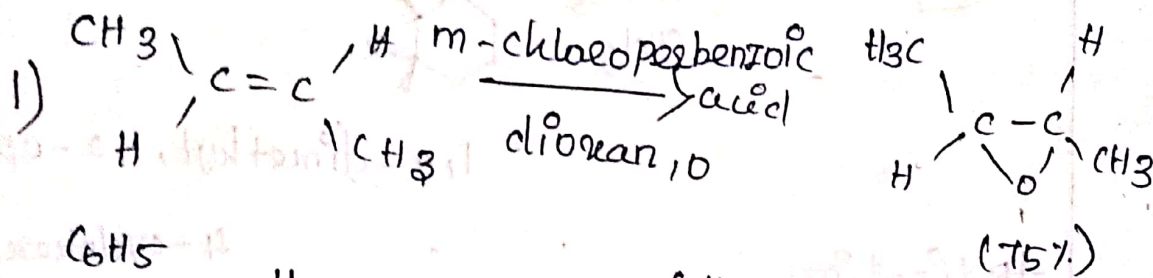
* The rate of epoxidation is increased by the presence of electron withdrawing group in peroxy acid.

* The rate of reaction also increased by the presence of electron donating group in olefins.

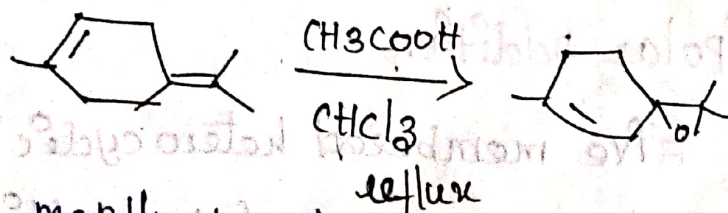
* Terminal and olefins slowly react with peracids compared to alkyl substituted alkenes.



Examples

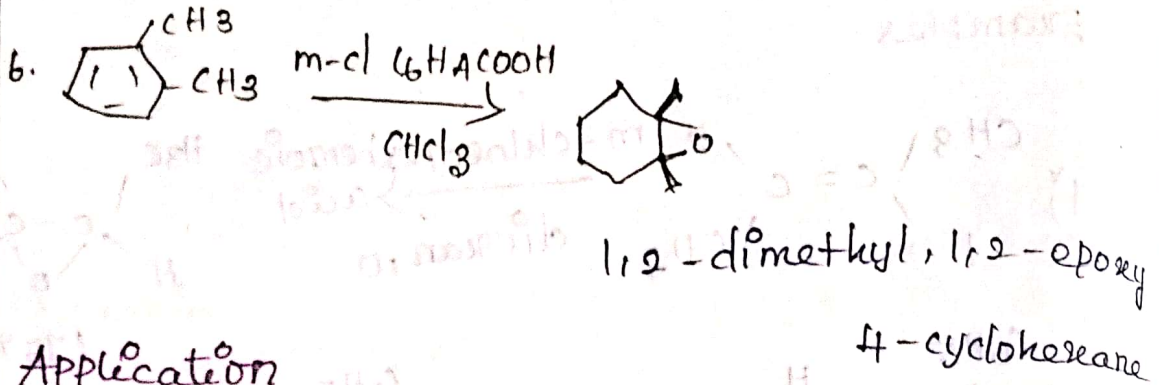
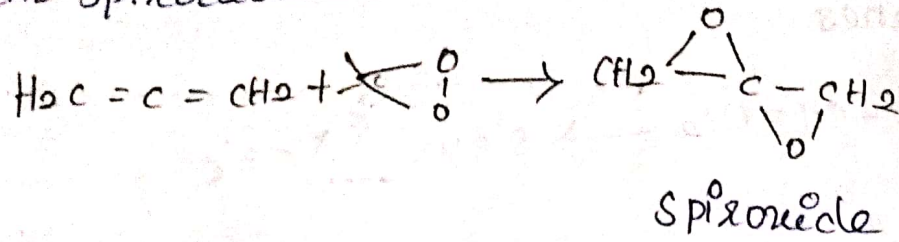


Alkyl substituted alkenes faster than terminal alkene. This has been use of in the preferential epoxidation of the substrate having two double bonds (dienes).



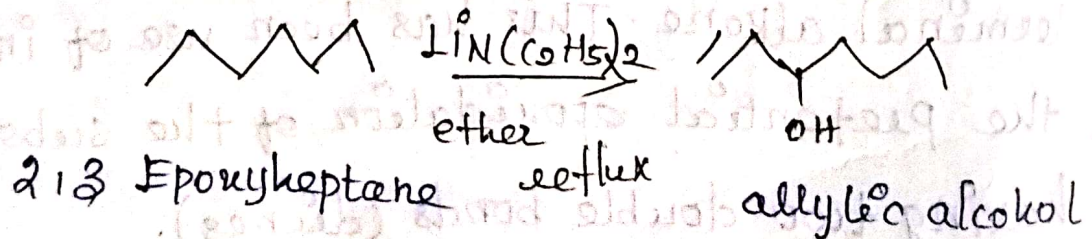
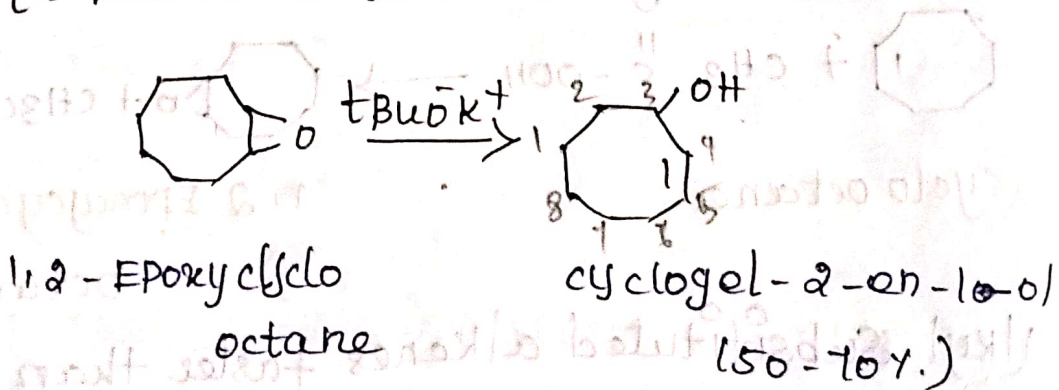
p-mentha-1,4 (8)
diene

Allenes react with dimethyl dioxide to form spirocyclic.



Application

The epoxides are also used in the synthesis of allyl alcohols by treatment with potassium *t*-butoxide or lithium alkoxides.

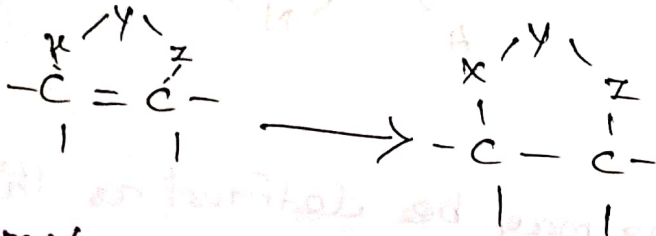


5) 1,3 Dipolar Addition

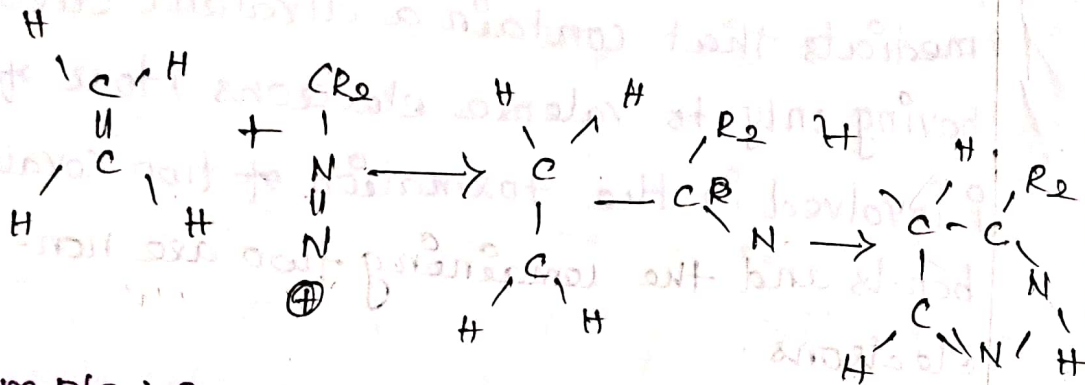
Five membered heterocyclic compounds are prepared by addition of

1.3 dipolar compounds to double bond.

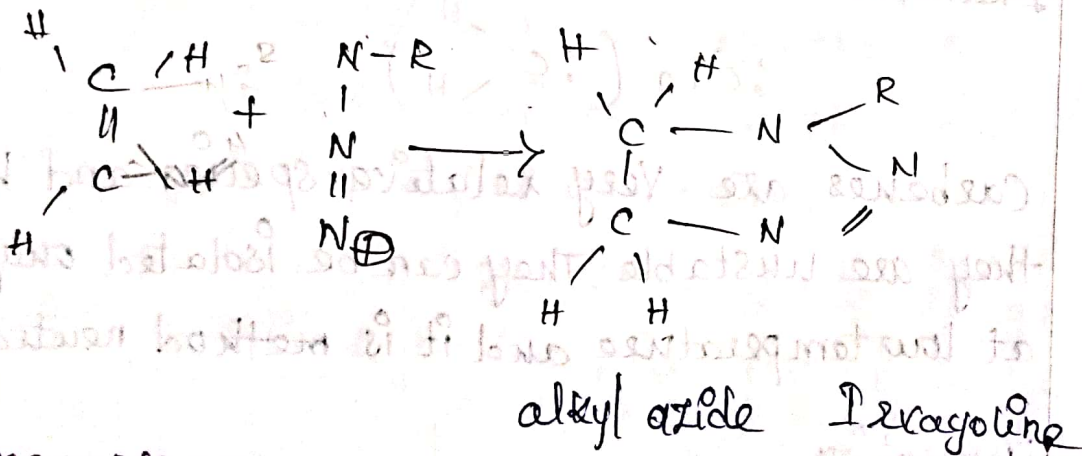
These are compounds that have a sequence of three atoms x-y-z with x has a octat with atleast one unshared pair. The reaction can be formulated as



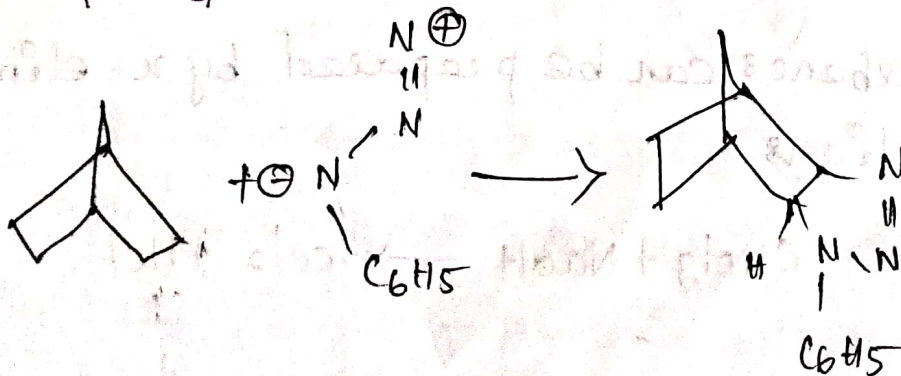
Example



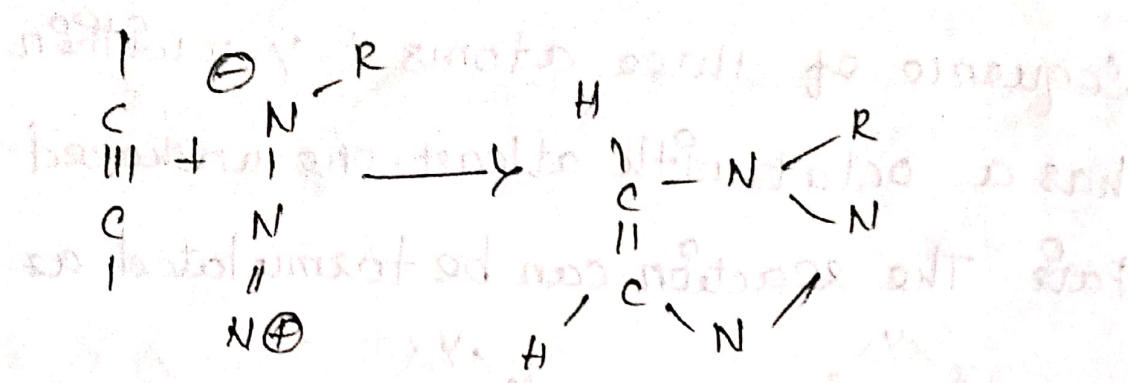
Example: 2



Example: 3



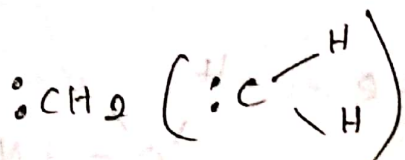
Carbon carbon triple bonds also undergo 3 dipolar addition. For example acids gives



b) Carbenes

Carbenes may be defined as the intermediates that contain a divalent carbon atom having only two valence electrons, two of which are involved in the formation of two covalent bonds and the remaining two are non-bonding electrons.

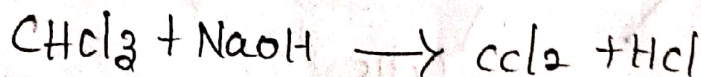
Examples :



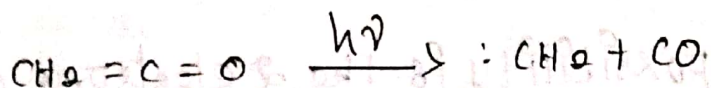
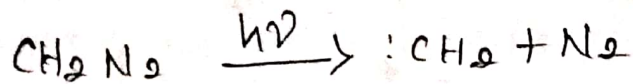
Carbenes are very reactive species and hence they are unstable. They can be isolated only at low temperature and it is method neutral.

Preparation

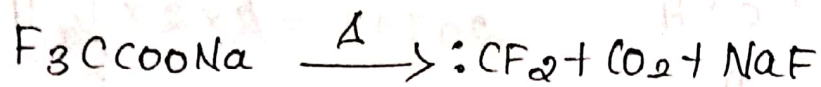
1. Carbenes can be prepared by α -elimination reactions.



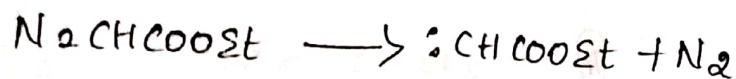
2. Photolysis of diazomethane (or) ketone



3. By heating sodium salt of trifluoro acetic acid give difluoro carbene.



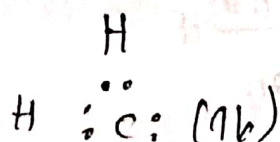
4. From diazo ethyl ketone.



Structure of carbenes

Carbenes has four available atomic orbitals capable of containing electrons. Since, carbenes only two bonding molecular orbitals. The two non-bonding electrons occupy the remaining two atomic orbitals. The two possibilities are singlet and triplet.

The two electrons in the same orbital with opposite spins ($\uparrow\downarrow$) gives rise to singlet state.

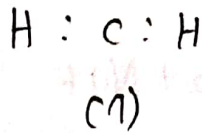


The resistance of singlet carbene can also be explained by E.S.R spectra. In E.S.R spectrum the no. of peaks is $2nI+1$

$$2nI+1 = 2 \times 0 \times \frac{1}{2} + 1$$

$$= 1$$

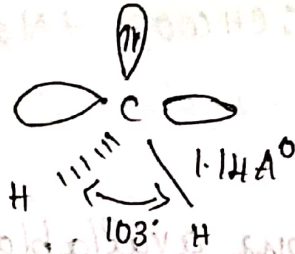
The second possibility is the 2 electrons can occupy in the different orbital having parallel spins (1).



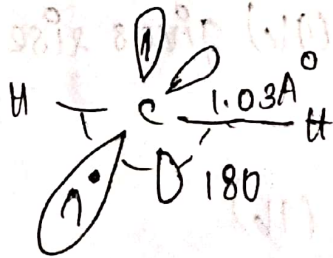
$$2nI+1 = 2 \times 2 \times \frac{1}{2} + 1$$

$$= 3$$

Structure of singlet carbene



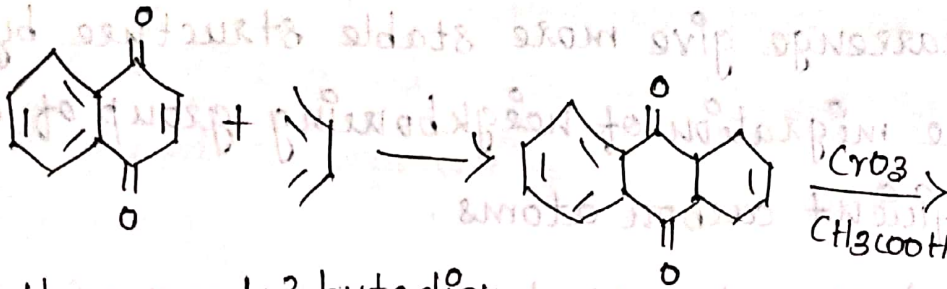
In the singlet state the carbon atom sp^2 hybridised. Two sp^2 hybrid orbitals are involved in the formation of 2 covalent bonds whereas the third sp^2 hybrid orbital contains unshared pair of electrons with the opposite spins. So the geometry of singlet carbenes bent structure.



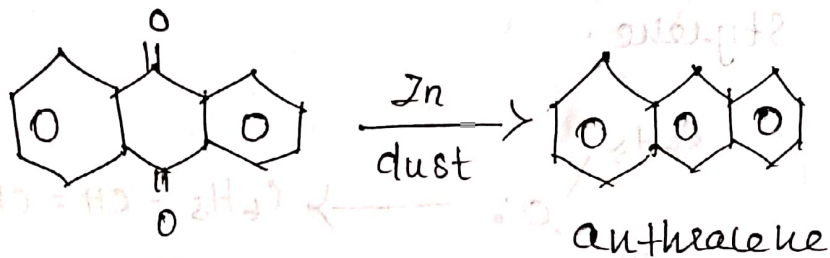
In this structure the carbon atom is sp hybridised. The two sp hybrid orbitals are involved in the bond formation with the

two groups [2 CH bond] and the remaining 2 electrons are placed perpendicular to each other and these electrons have parallel spins. so the geometry of triplet carbene is linear and it behaves as a diradical.

Synthesis of Anthraene



Naphthoquinone + 1,3 butadiene



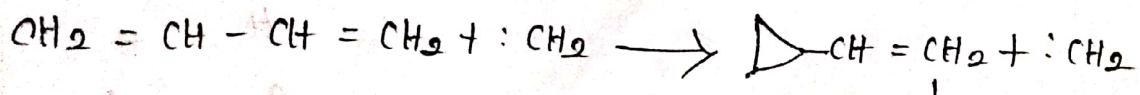
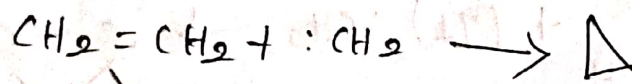
Reaction of carbene

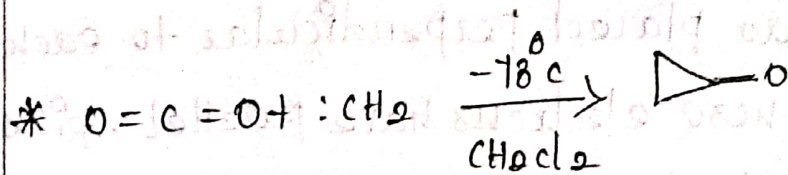
Carbenes undergo variety of reaction such addition rearrangement etc.

Addition Reaction

Carbenes react on the double bond to form cyclopropane derivative.

Simmons-Smith cyclopropanation

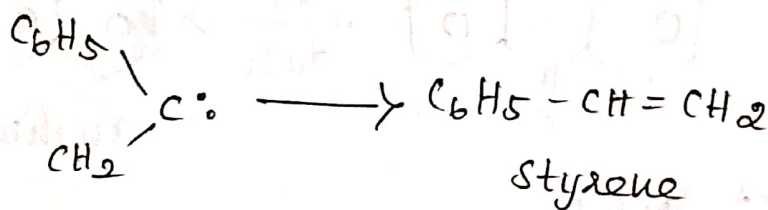




Rearrangement Reaction

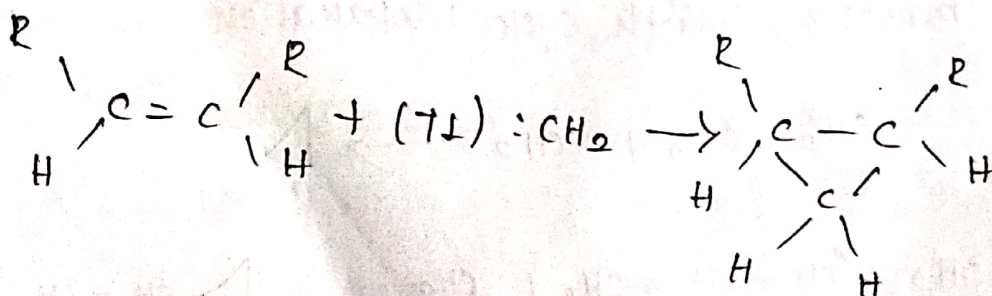
Many carbenes like carbocation ion rearrange give more stable structure by which the migration of neighbouring group of electron deficient carbon atoms.

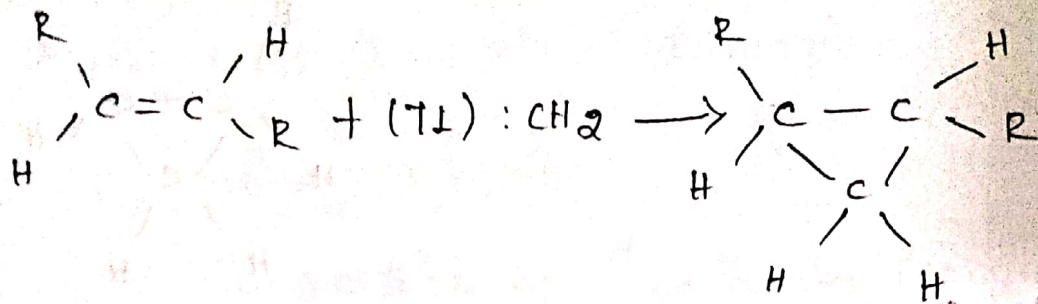
(Eg) Phenyl methyl carbenes rearrange to give styrene.



Stereochemistry of carbenes

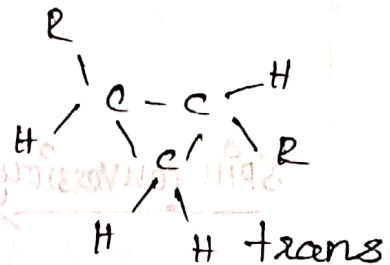
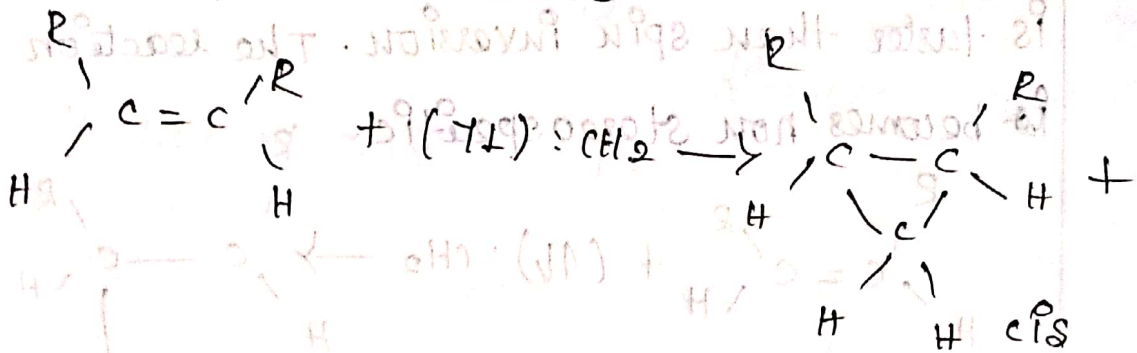
i) singlet carbenes add to alkenes in a stereospecific manner. It is a concerted due to addition of singlet carbene to cis 2 butene to give cis cyclo propane and trans 2 butene to give trans cyclo propane.





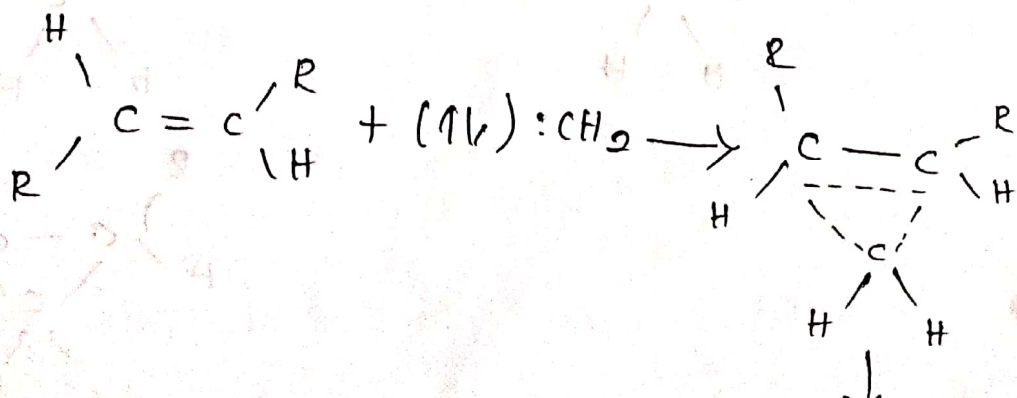
Trans - cyclo propane

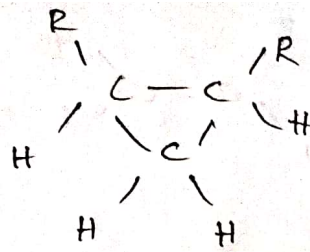
ii) triplet carbenes add to alkene non stereo specifically via triplet carbene add to cis or trans 2 butene give a mixture of cis and trans cyclo propane derivative.



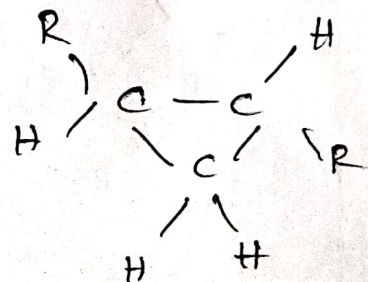
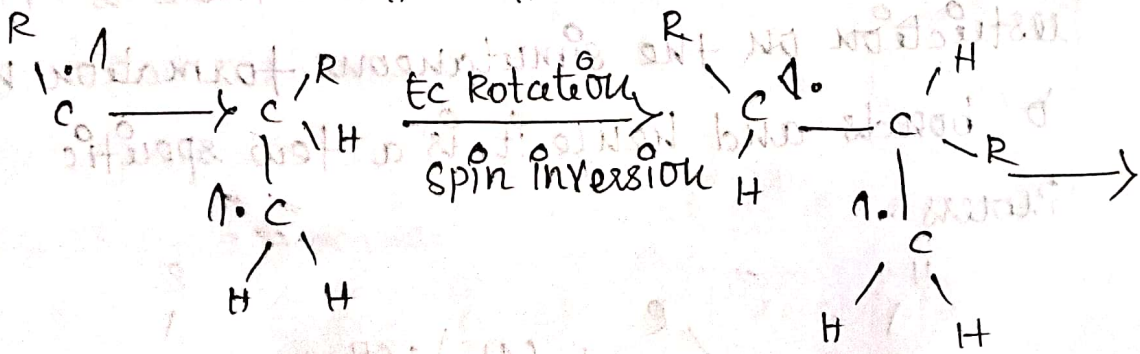
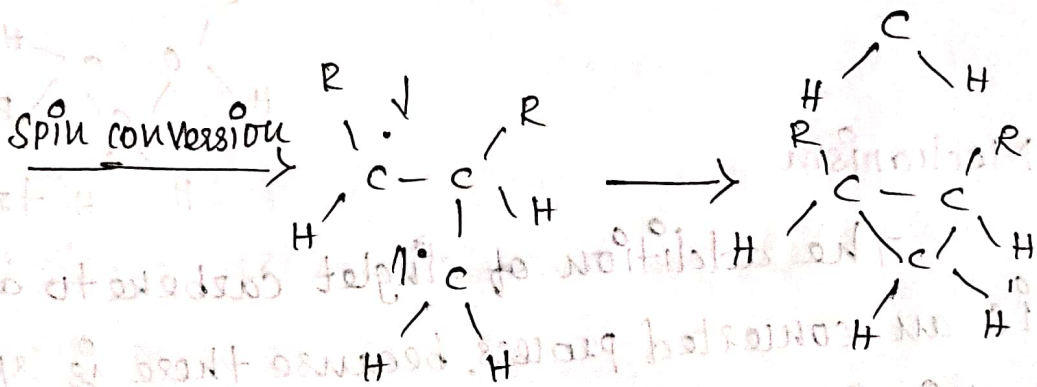
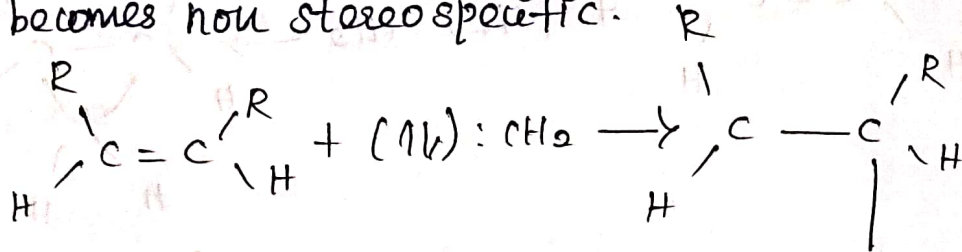
Mechanism

The addition of singlet carbene to an alkene is an concerted process because there is spin restriction on the simultaneous formation new C-C bonds and hence it is a few specific process.





The process of 1st step leads to the formation of "triplet biradical" which will have to undergoes spin inversion before it collapse to form a cyclopropane derivative. Since the biradical has a C-C single bond C-C single bond. This reaction is faster than spin inversion. The reaction becomes non stereospecific.



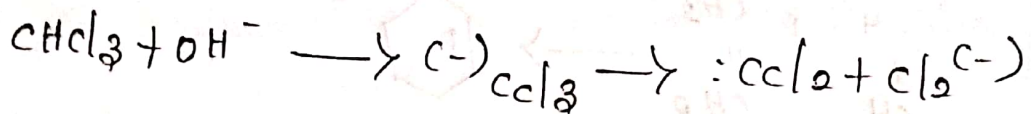
Carbenes As Reaction Intermediate

carbylamine reaction.

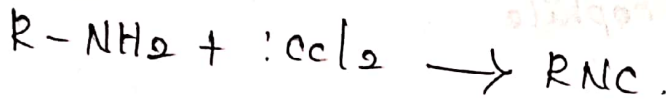
Conversion of 1° amine to isocyanide by means of alkaline chloroform.



Mechanism



dichloro carbene



The same cases the choice may be named as



[K-O=C-N] shows sp hybrid orbitals

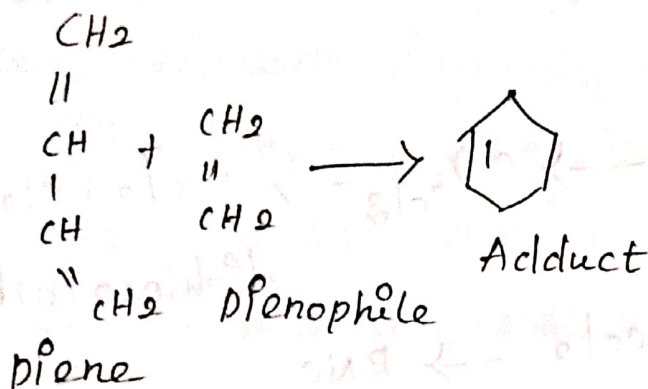
as to sp [K-O=C-N]



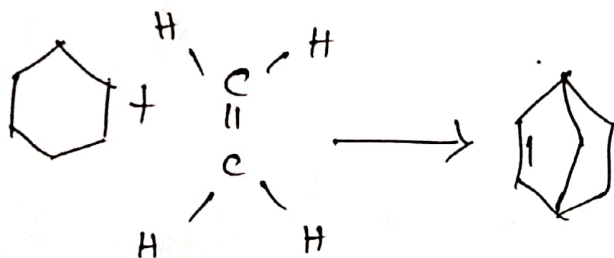
carbenes are not involved in the

4. Diels - Alder Reaction

Most of the dienophiles are of the form $-C=C-Z$ (or) $Z-C=C-Z'$ where Z and Z' are $CHO, COR, COOR, COOH, COCl, COAr, NO_2, CN, Ar, CH_2OH, CH_2Cl, CH_2NH_2, CH_2CN, CH_2COOH,$ halogen (or) $C=C$.



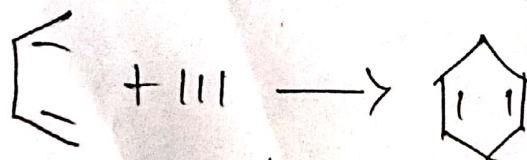
See



In some cases the dienes may be named as dienophiles.

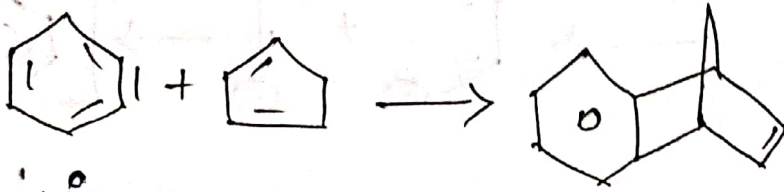


Triple bonded compounds $[-C\equiv C-Z]$ (or) $Z-C\equiv C-Z'$ may act as dienophile.

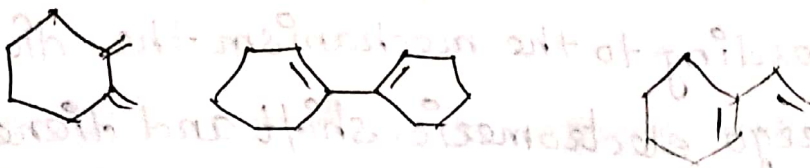


Ketones however do not undergo acid alder reaction (It reacts with conjugation diene)

to give 1,2 addition] [5 Benzyne although not insoluble but as dienophile and can be trapped with dienes.



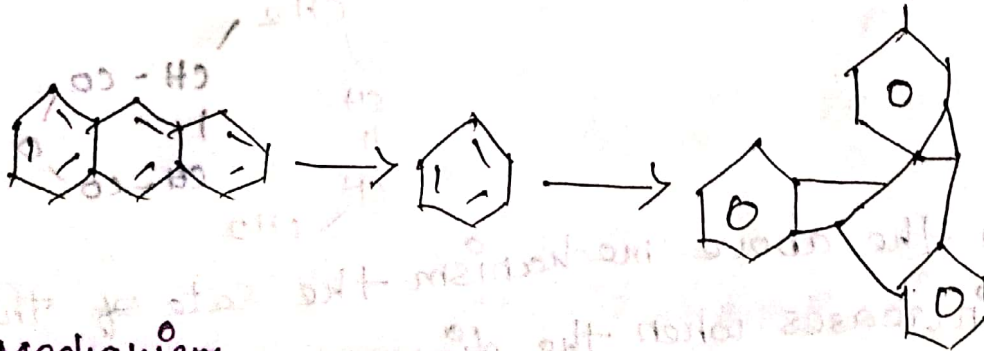
dienes can be open-chain - inner ring, outer ring across (or) inner - outer except that they may not be broken into a transoid conformation.



outer ring A-cross ring inner-outer ring

Aromatic compounds also behave as dienes enzyme as unreactive towards dienophile, very few dienophiles like naphthalene and phenanthrene gives diels alder addition at high-temp.

However anthracene and other compounds with atleast three linear benzene rings give diels alder reaction readily. Triptylene can be prepared by diels alder rxn b/w benzene and anthracene.

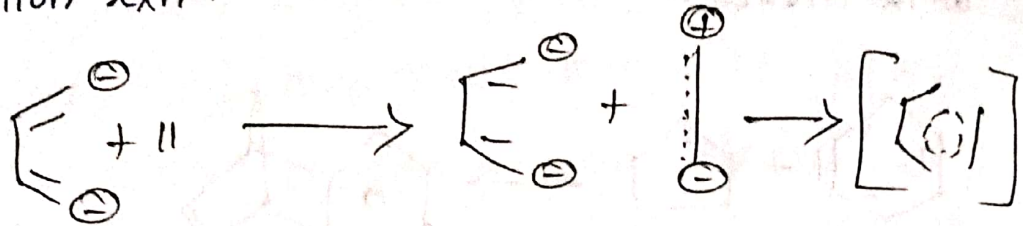


Mechanism

Three mechanism are possible for the react.

1) one step concerted.

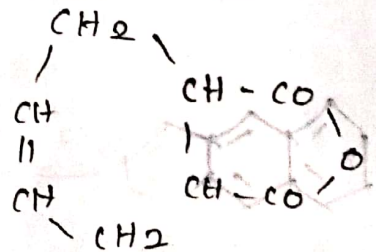
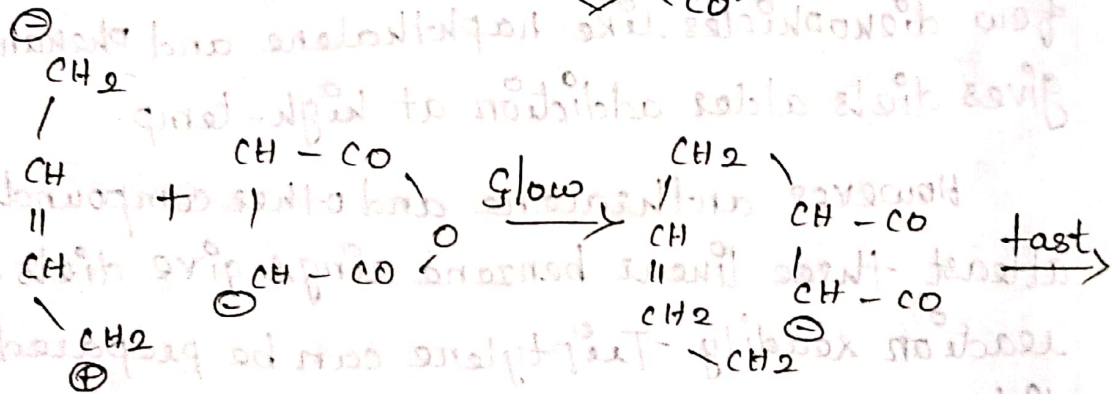
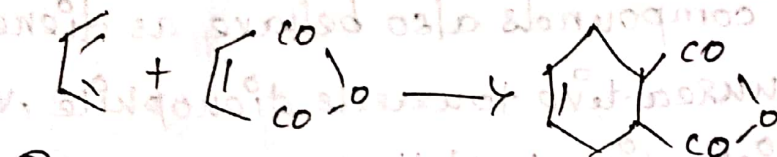
The mechanism involve the formation of cyclic central transition state and it an ex of polar addition rxn.



2) Heterolytic mechanism (or) Formation of ions mechanism.



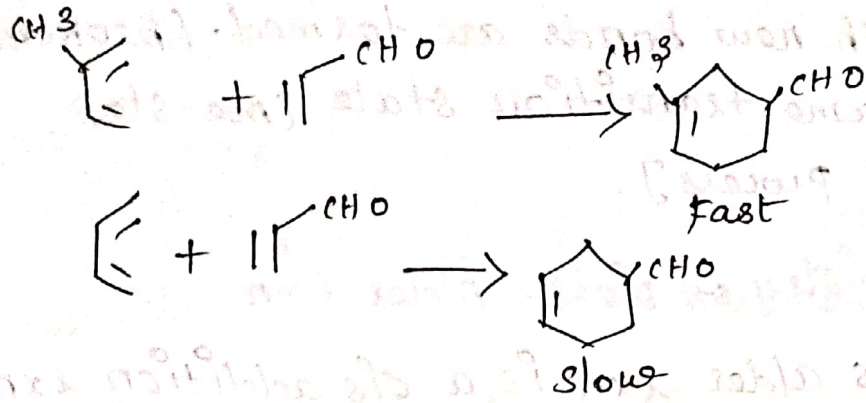
According to the mechanism the dienophile may undergo electromeric shift and dienes formed will condense to produce the adduct.



In the above mechanism the rate of the rxn increases when the diene contains electron repelling group.

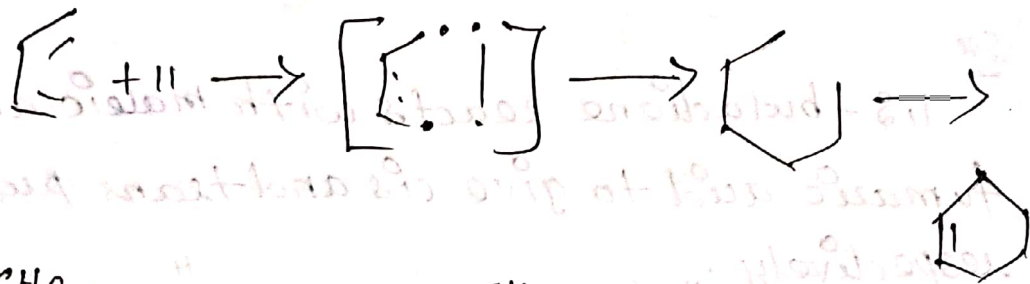
The rate of the rxn b/w isoprene and acrylic aldehyde is further fast than that of...

the rxn b/w butadiene and acrylic aldehyde.

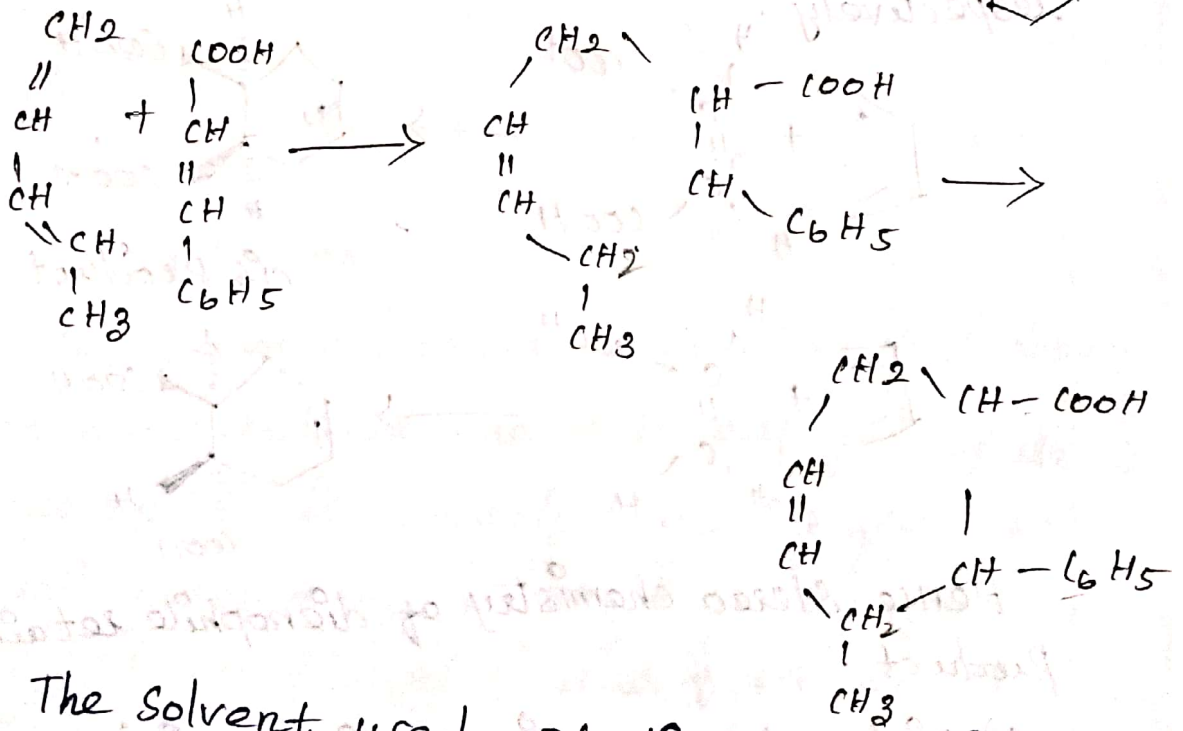


Homolytic mechanism (or) diradical mechanism

one end of the diene is attached to dienophile to give diradical and in the second step the two ends get attached. It involves the formation of diradical intermediate.



Ex



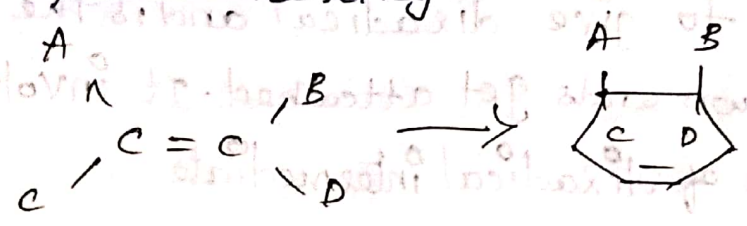
The solvent used. If diene intermediate is formed the rate of the reaction increases when polar solvents are used.

3) The stereochemistry of dienophile is retained

in the product. This stereospecificity indicates that both new bonds are formed (broken in the same transition state [one step concerted process]).

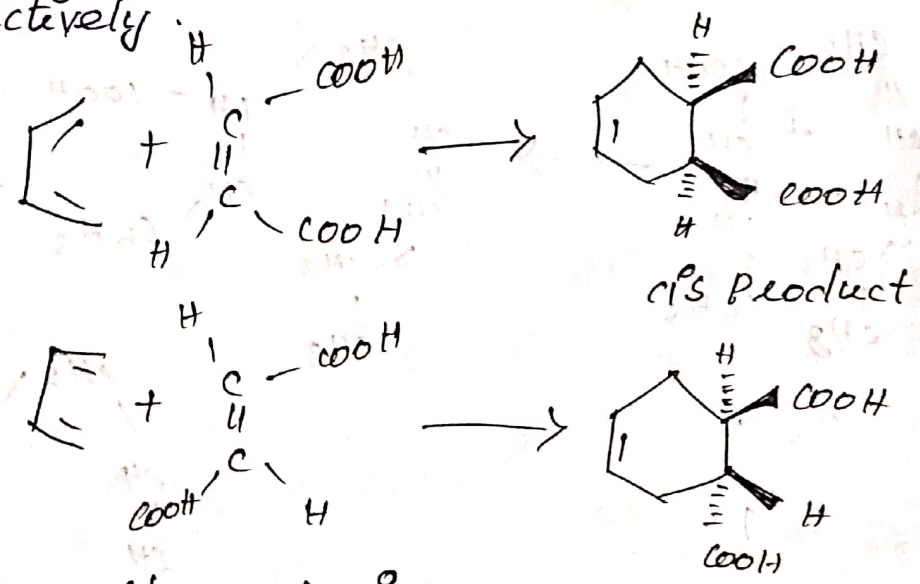
Stereochemistry of Diels-Alder Rxn

Diels Alder rxn is a cis addition rxn with respect to the dienophile. It means that the groups are cis to the olefine will be cis to the cyclohexane ring.



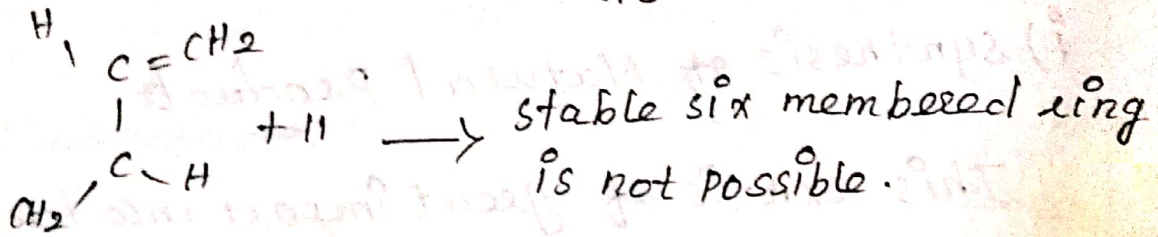
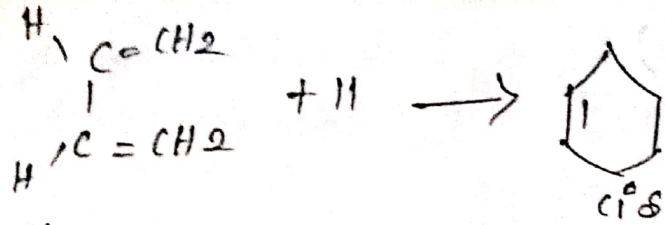
Ex

1,3-butadiene reacts with maleic acid and fumaric acid to give cis and trans products respectively

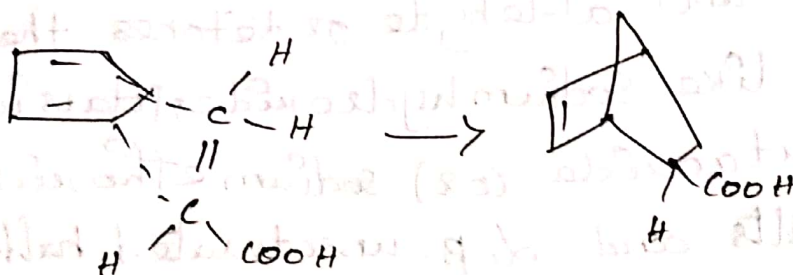
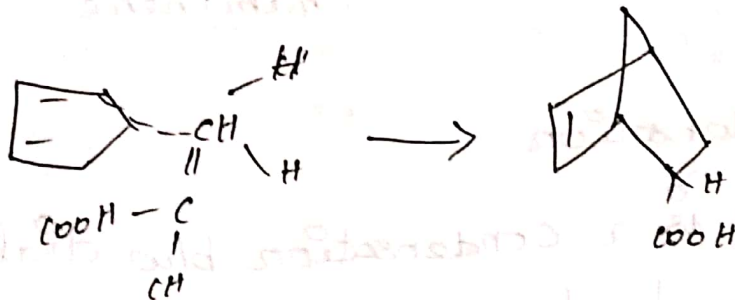


Hence stereochemistry of dienophile retains the product.

2) Diels Alder rxn is the cis addition reaction with respect to diene hence diene always reacts in its cis form and not in trans form.



3) when the diene in cyclic addition occurs in two possible ways if the dienophile is not symmetrical the larger side of the dienophile may be under the ring or it may be the smaller side (exo addition).



In most of the cases the addition is predominantly endo the bulkier side of the dienophile is under the ring and their probably trace for open-chain diene also. However there are exceptions and in many cases mixture of exo and endo addition products are formed.

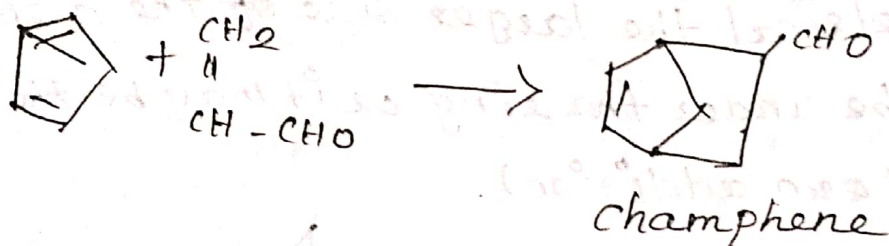
The exo isomer is more stable than the endo isomer (there is less steric concentration)

in two product).

Applications

i) Synthesis of Natural Products

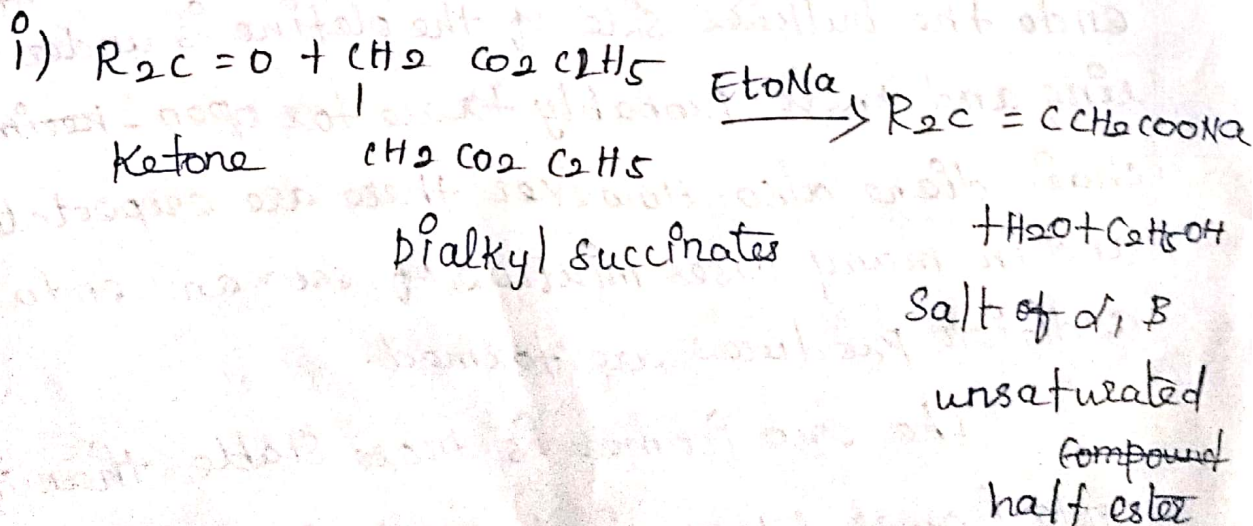
This rxn is of great importance for the synthesis of polycyclic hydrocarbons and terpenes champhene reserpene etc...

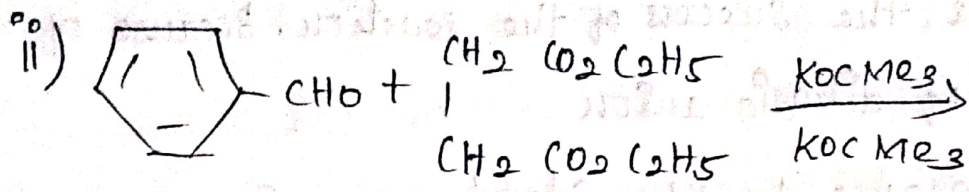


8. Stobbe Condensation

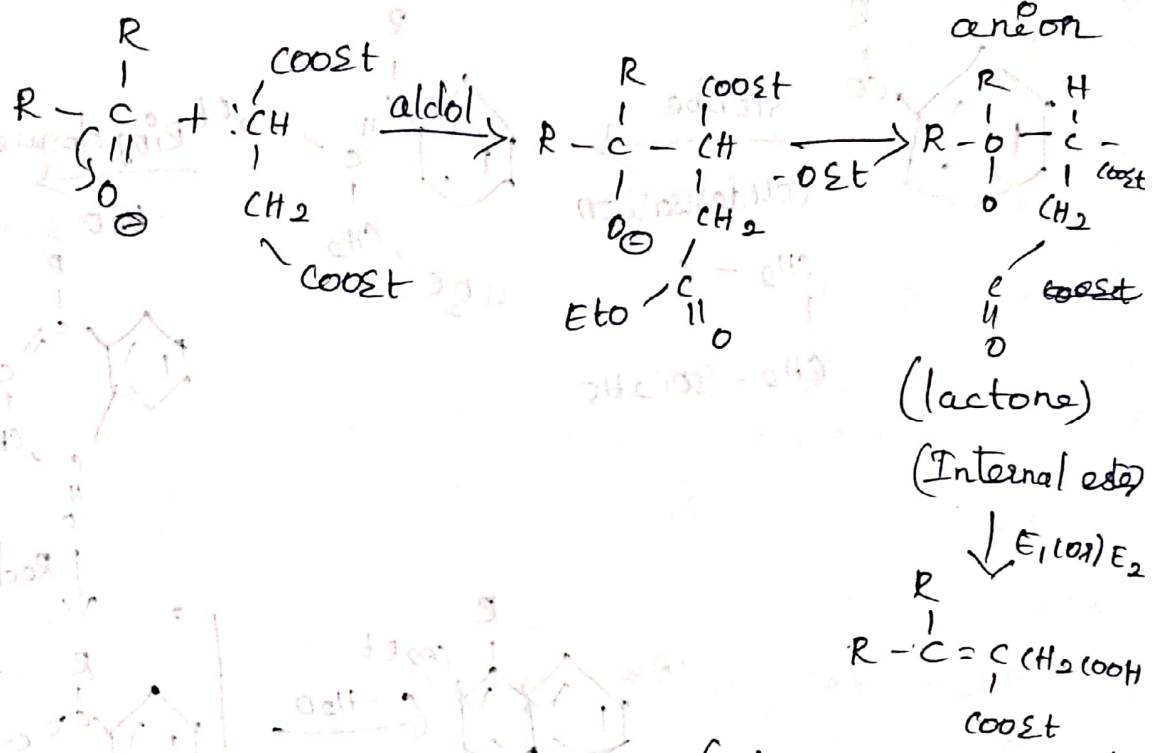
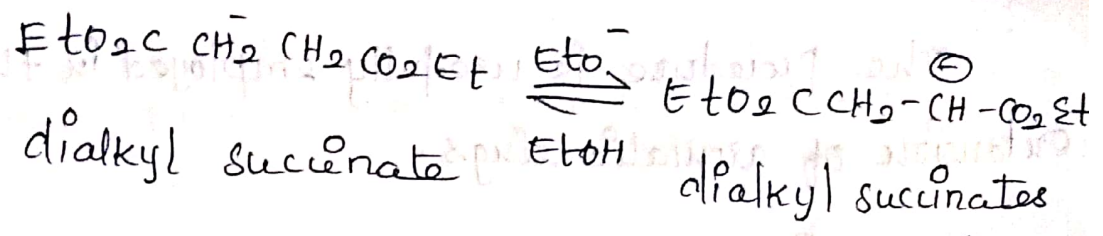
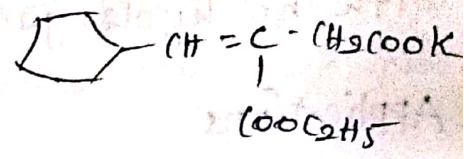
This is a condensation b/w dialkyl succinates and aldehyde or ketones the presence of base like sodium hydroxide, potassium tert-butoxide (or) sodium ethoxide to form salts and α, β -unsaturated half esters.

Reaction





Mechanism



* The enolate form of diethyl succinate (half ester) attacks the carbonyl group, followed by the cyclization to give lactone intermediate.

* Lactone then undergoes base catalysed ring opening to give salt of unsaturated half ester.

* One of the ether group is hydrolyzed in the course of reaction (The rxn is limited to those diesters which do not undergo Dieckmann condensation).

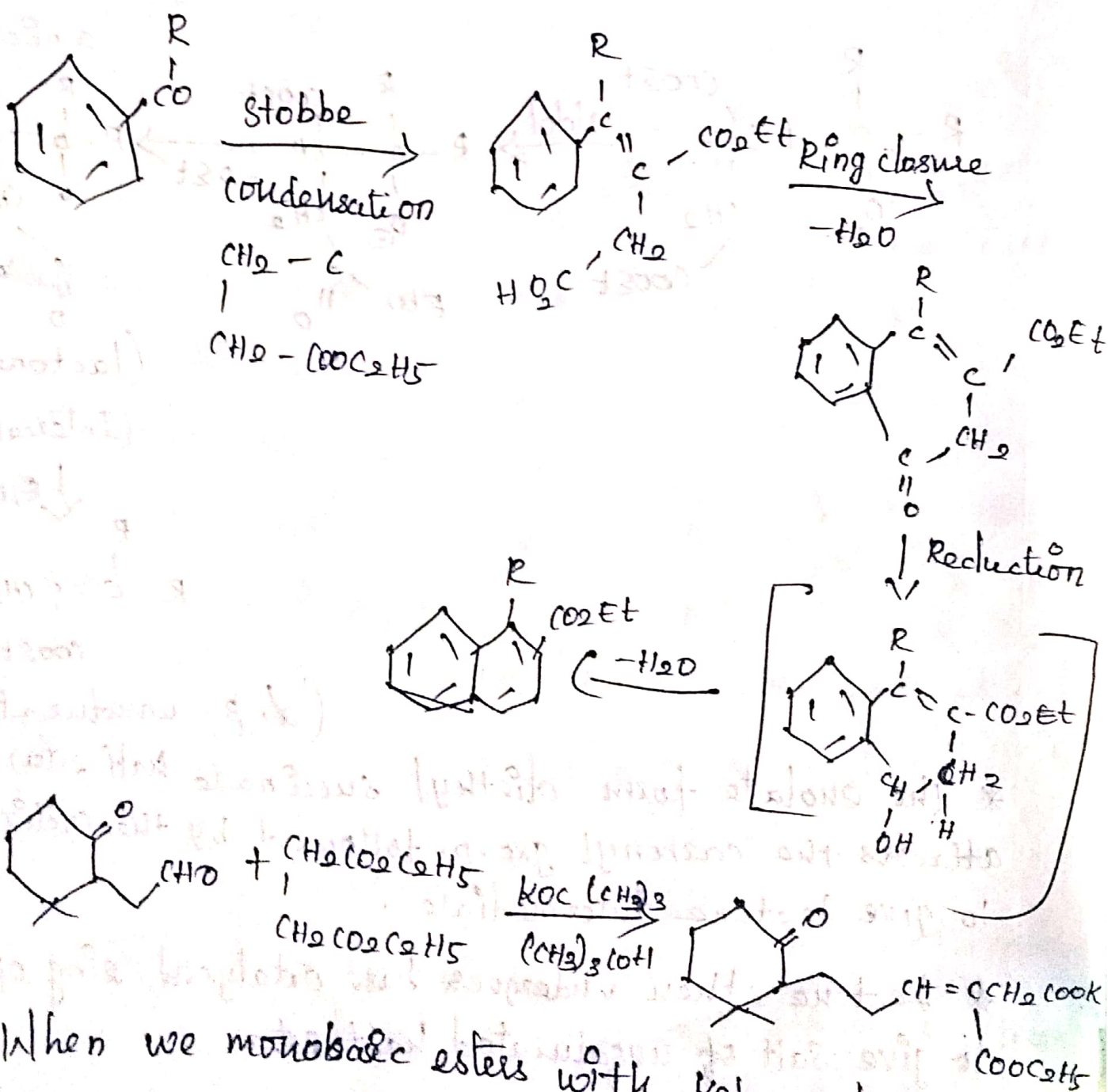
* The stability of the carboxylate anion is the

basis for the success of the reaction. Because of the presence of dibasic anion

Reference to the Stobbe reaction, but those with no hydrogen (Eg: Benzaldehyde).

Applications

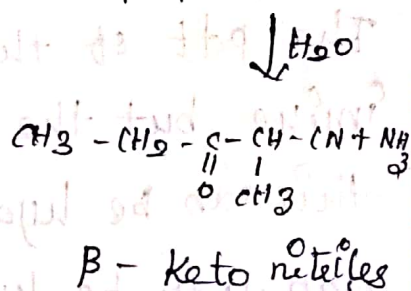
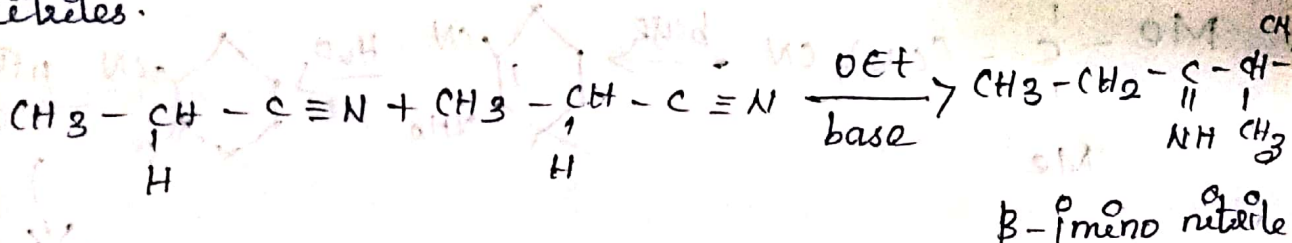
The procedure is usefully employed in the extension of aromatic rings.



* When we monobasic esters with ketone claisen condensation product occur

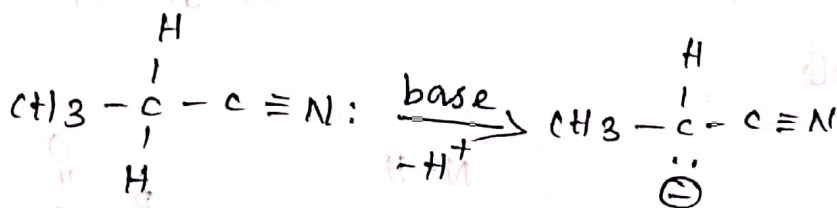
4. Thorpe Reaction

In the Thorpe reaction, the α -carbon of one nitrile molecule (carbonium source) adds to the β -carbon (acceptor site) of the other molecule. The $C=NH$ bond that results can be hydrolysed to get β -keto nitriles.

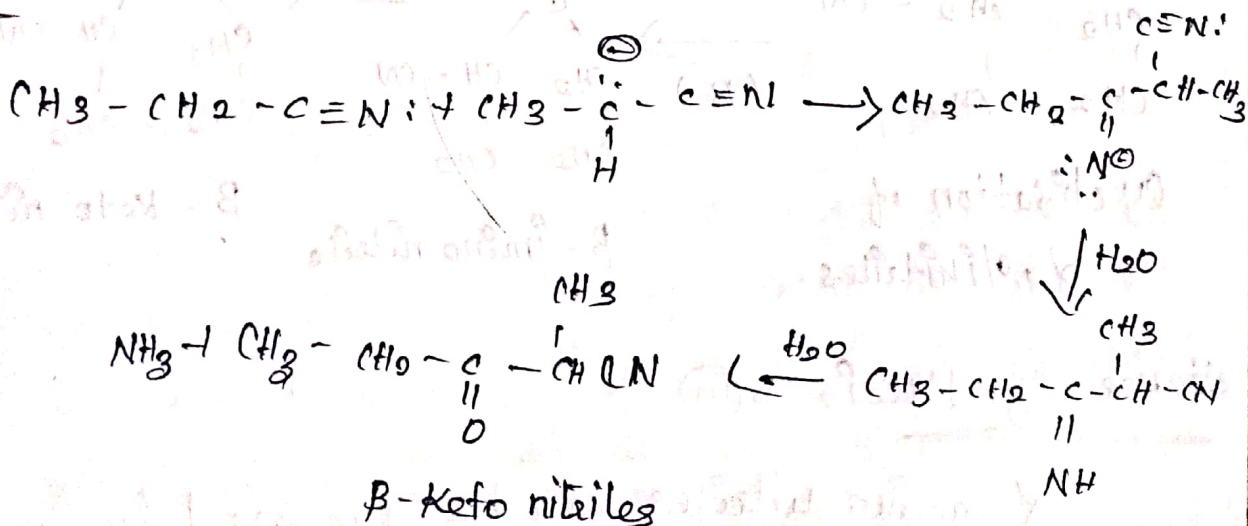


Mechanism

Step: 1



Step: 2

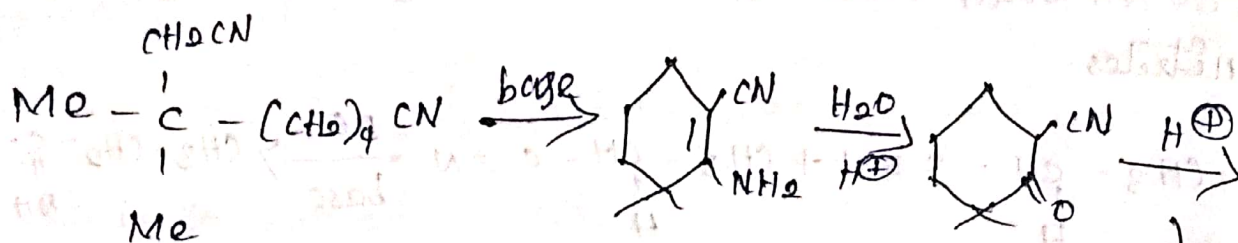


The Thorpe rxn can be done internally in which base it is called the Thorpe-Ziegler rxn.

Appln

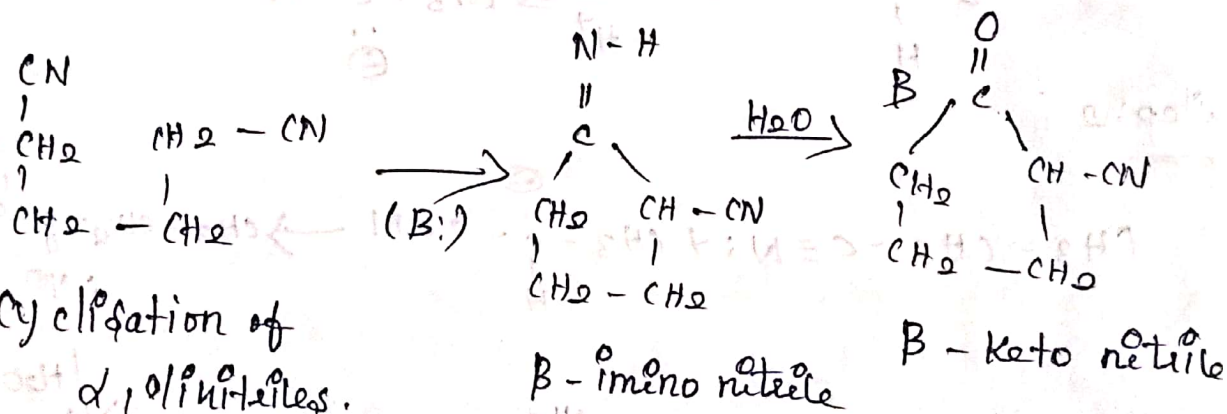
> This is useful method for closing large rings which are 10 to 12 to eight membered.

rings 8.5%. falls off to about zero for rings of nine to thirteen members, but are high again for fourteen membered and larger rings if high dilution techniques are employed.



The prod of the thorp zigler rxn is not the imine but the tautomeric enamine, if desired this can be hydrolysed to an α -cyano ketone, which can then be hydrolyzed and decarboxylated.

Other example

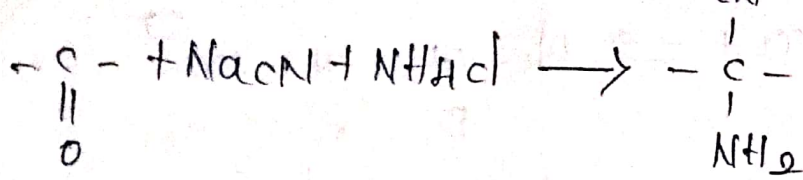


Cyclisation of α, ω -nitriles.

Stecker synthesis \rightarrow (10)

α -amino nitriles can be prepared in one step by the treatment of an aldehyde (or) ketone with NaCN and NH_4Cl . This is called the Stecker synthesis.

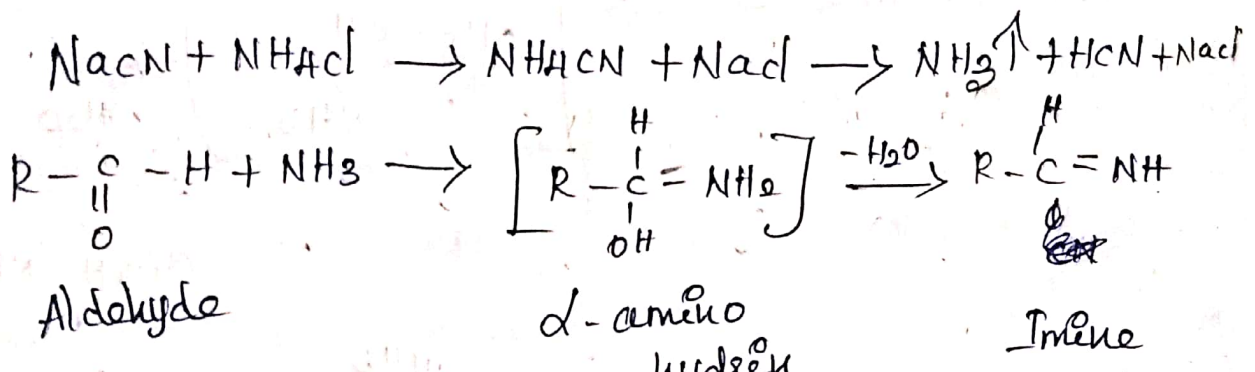
General Reaction.



α -amino nitrile

* since the CN is easily hydrolysed to the acid this is a convenient method for the preparation of α -amino acids.

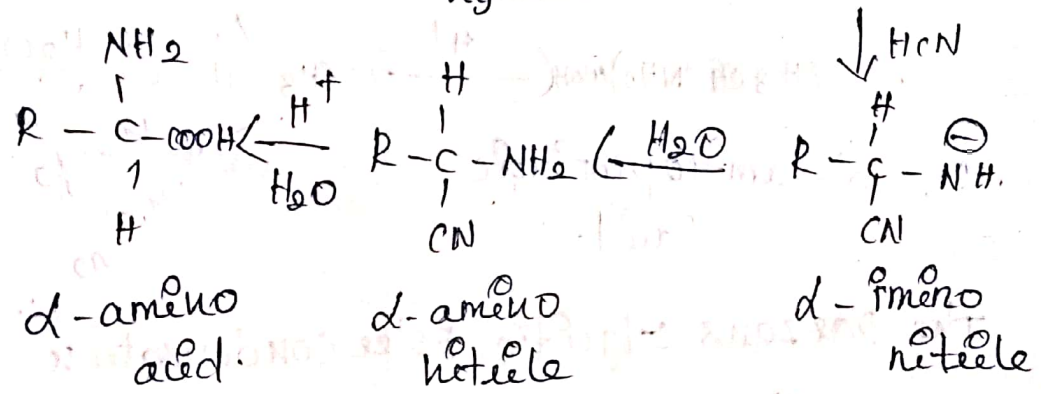
Mechanism



Aldehyde

α -amino hydrate

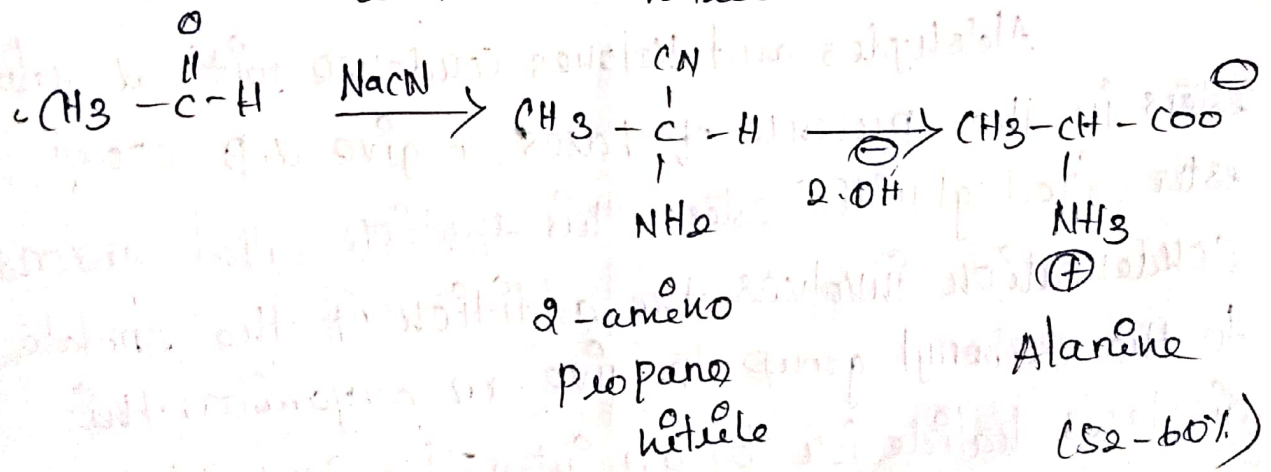
Imine



α -amino acid

α -amino nitrile

α -imino nitrile

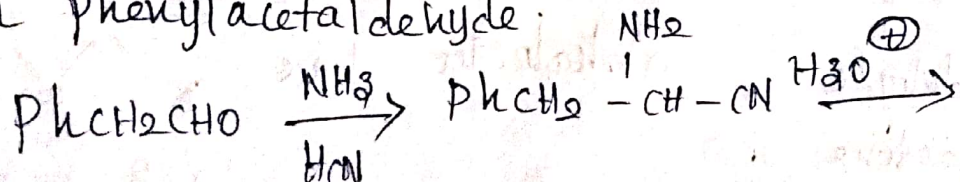


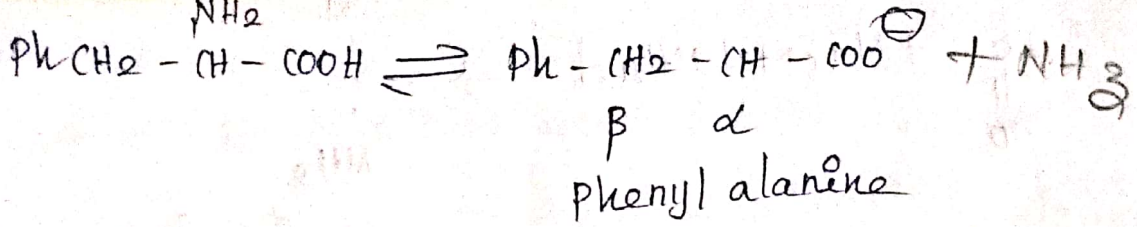
α -amino propano nitrile

Alanine

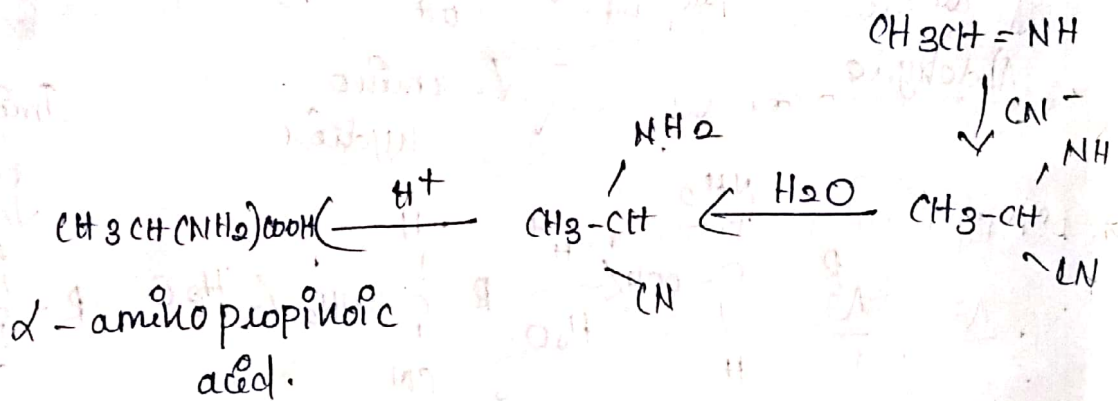
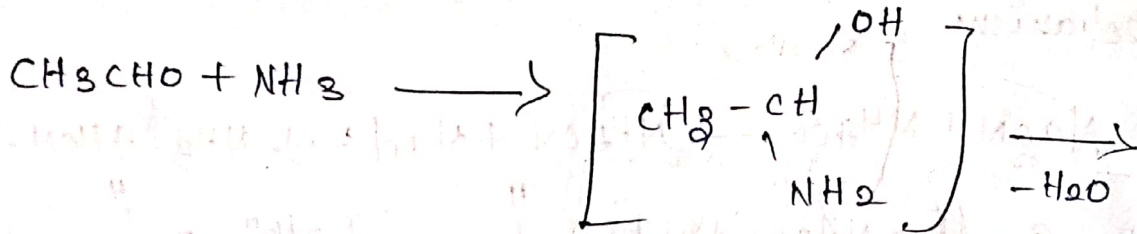
(52-60%)

2. A simple example is the synthesis of phenylalanine from phenylacetaldehyde:



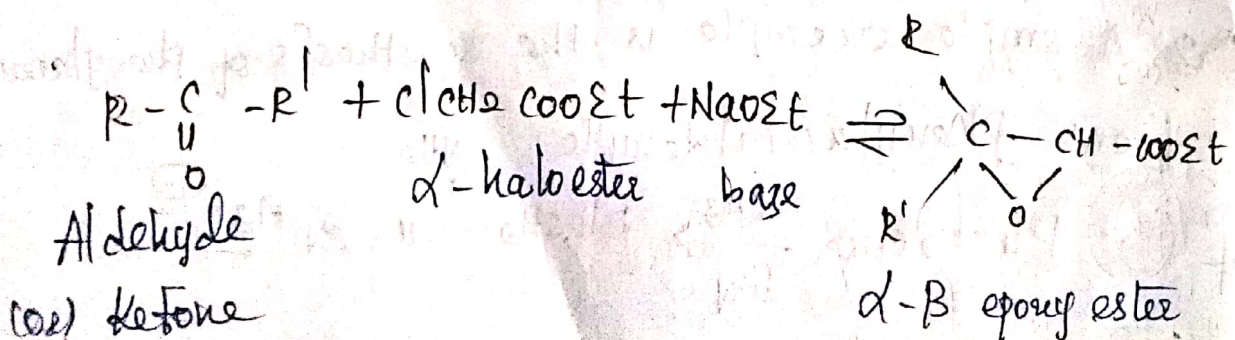


3. This method is useful for preparing the following amino acid, glycine, serine, alanine, valine, methionine, glutamic acid, leucine and phenyl alanine.

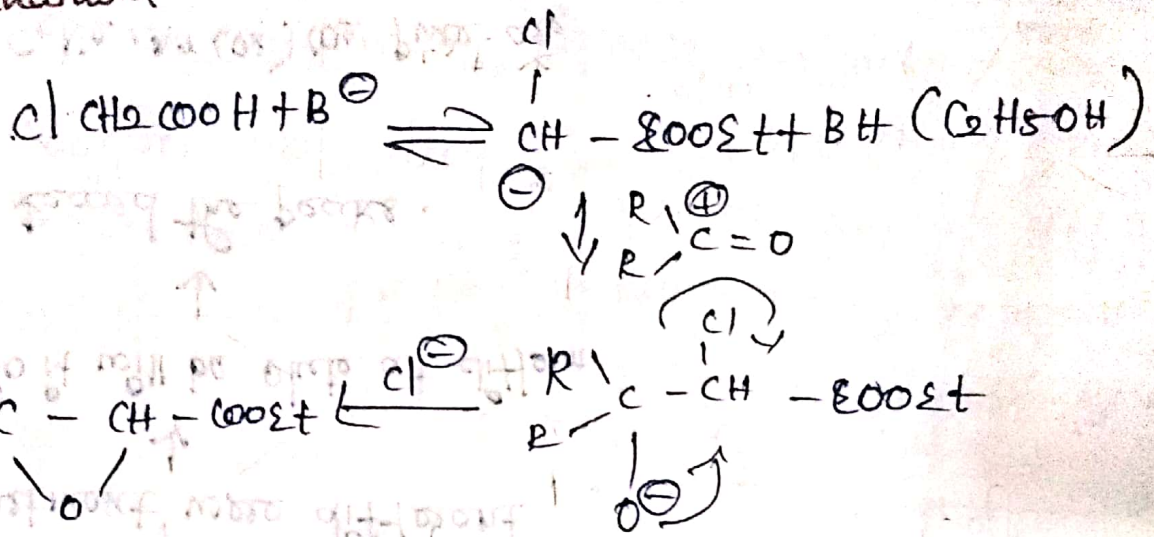


The Darzens glycidic Ester condensation → (ii)

Aldehydes and ketones condense with α-halo esters in the presence of bases to give α,β-epoxy ester called glycidic ester. This reaction called Darzens condensation involves the addition of the enolate to the carbonyl group to give an oxyanion this displaces halide ion by an internal S_N² reaction.



Mechanism



The oxyanion is formed by the addition of the carbanion to the carbonyl group preferentially displaces halide ion.

The intramolecular nucleophilic substitution whereas in the later oxyanion removes a proton from the solvent.

The glycidic acids obtained by base catalysed hydrolysis the ester readily undergo a decarboxylative reaction