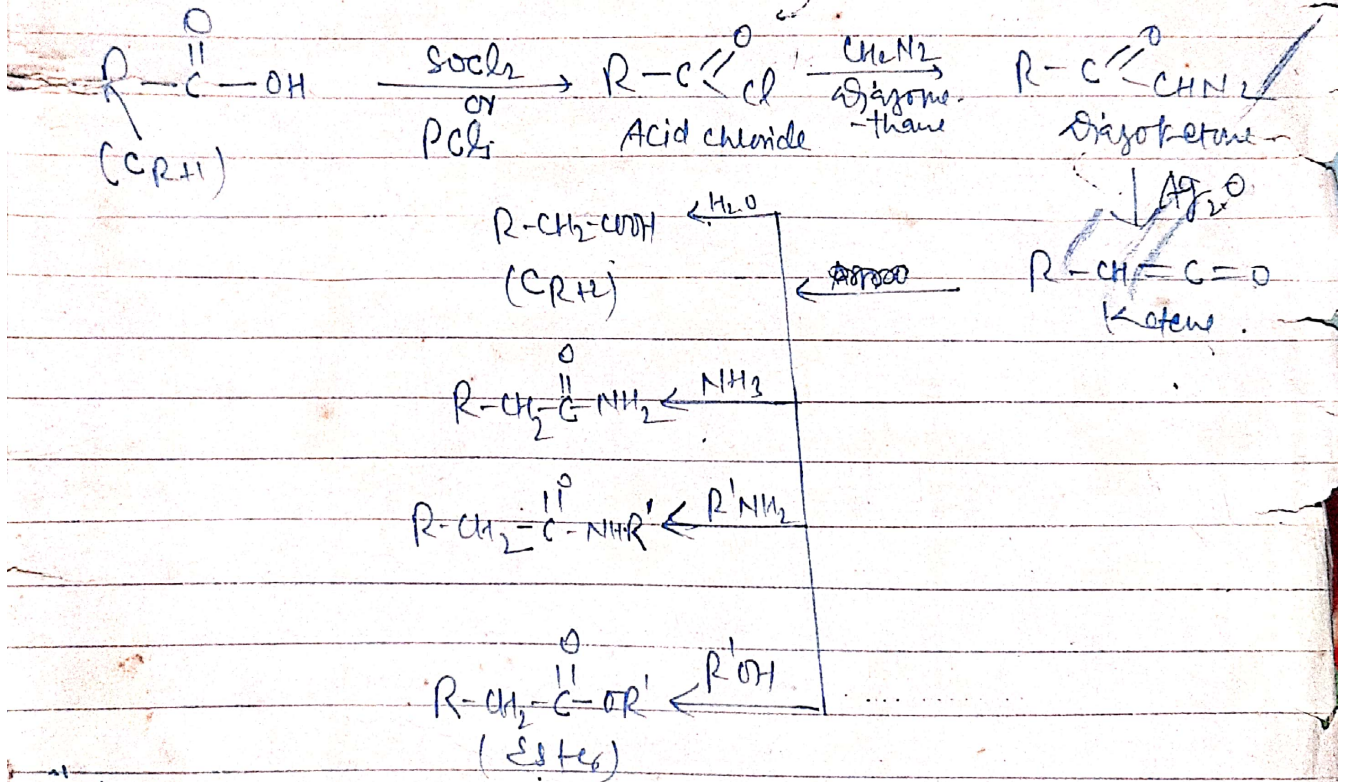


ARNOLD EISTERT SYNTHESIS

WOLF REARRANGEMENT → Conversion of a Carboxylic acid into its next higher homologue or its derivative i.e. known as Arnold Eistert synthesis, i.e. in this synthesis chain is lengthened by one carbon atom.

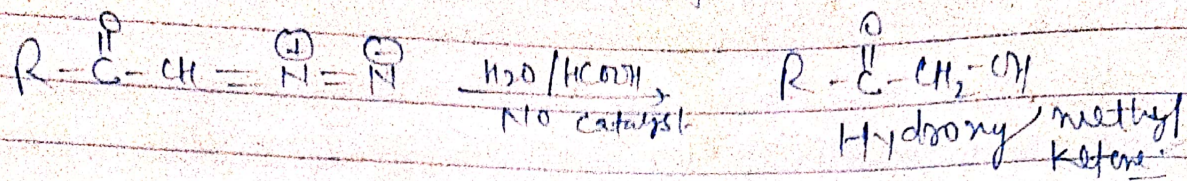
The acid is first converted into its chloride which on further treatment with diazomethane, gives diazoketone. The diazoketone after treatment with silver oxide (Ag₂O) in presence of water gives the homologous acid. This reaction is of wide scope. In presence of other reagents such as alcohols, ammonia, amine, in stead of water, corresponding acid derivatives of higher homologue i.e. esters, amides, substituted amides, are obtained.



This as well as the general* conversion of diazoketone to higher homologues of acid and acid derivative via the ketone intermediate is known as Wolf Rearrangement.

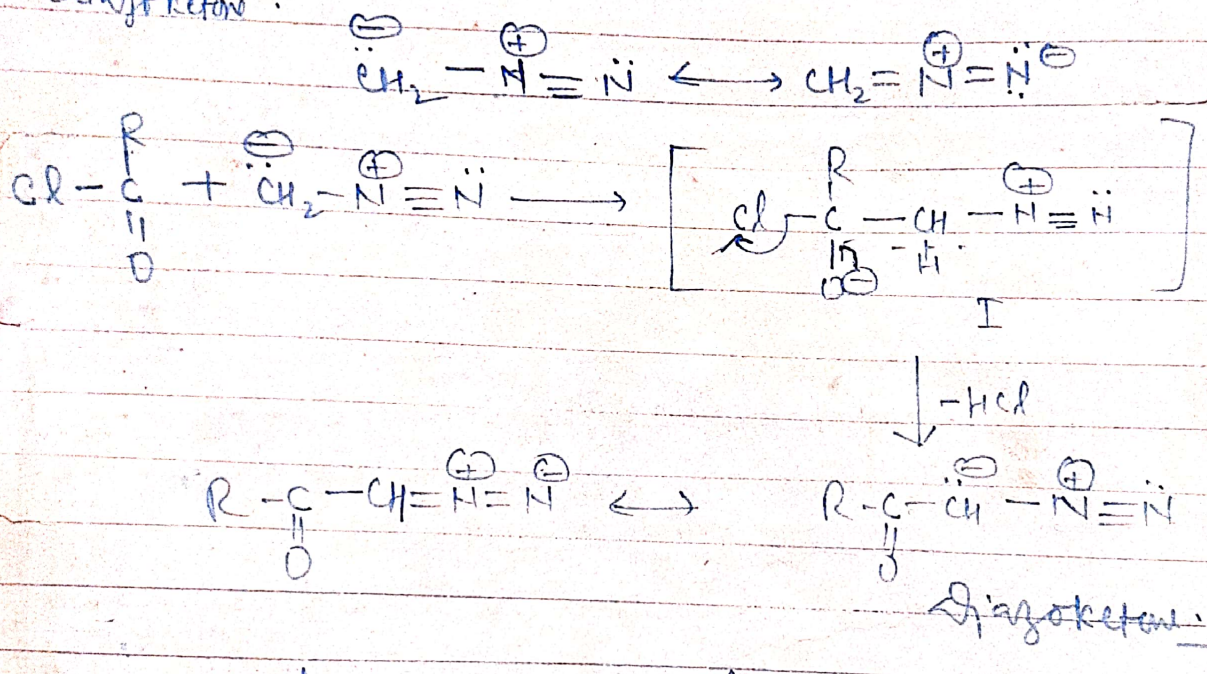
* It means that, of course, diazoketones prepared in any other way also give the rearrangement. R may be alkyl or aryl and may contain many functional groups including unsaturation, but not including groups acidic enough to react with CH₂N₂ or diazoketones. Besides Ag₂O, colloidal platinum etc. are used as catalyst.

In absence of Ag₂O catalyst simple addition of water to the diazoketone occurs in presence of HCOOH acid & hydroxymethyl ketones are formed. (C₁N₂Rⁿ)

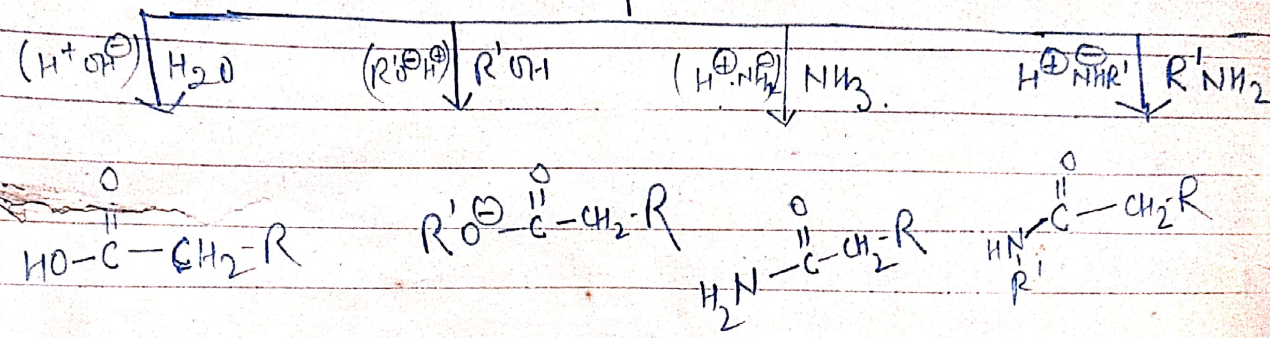
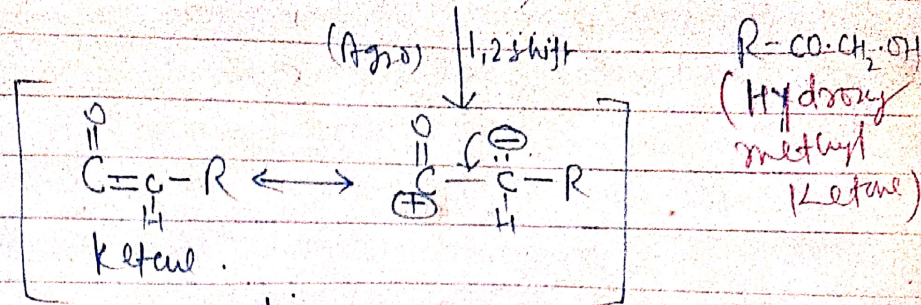
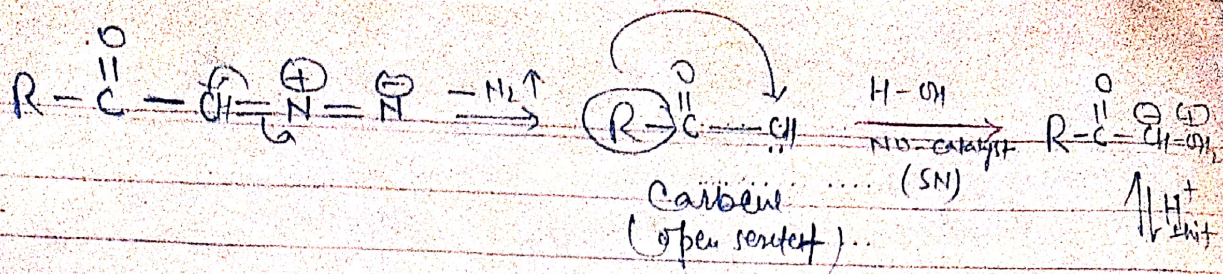


Mechanism: →

I. Formation of Diazoketone: → It is assumed that the diazomethane attacks on carbon of carbonyl group of acid chloride (nucleophilic attack) to form an intermediate (I) which loses a molecule of HCl and gives the diazoketone.



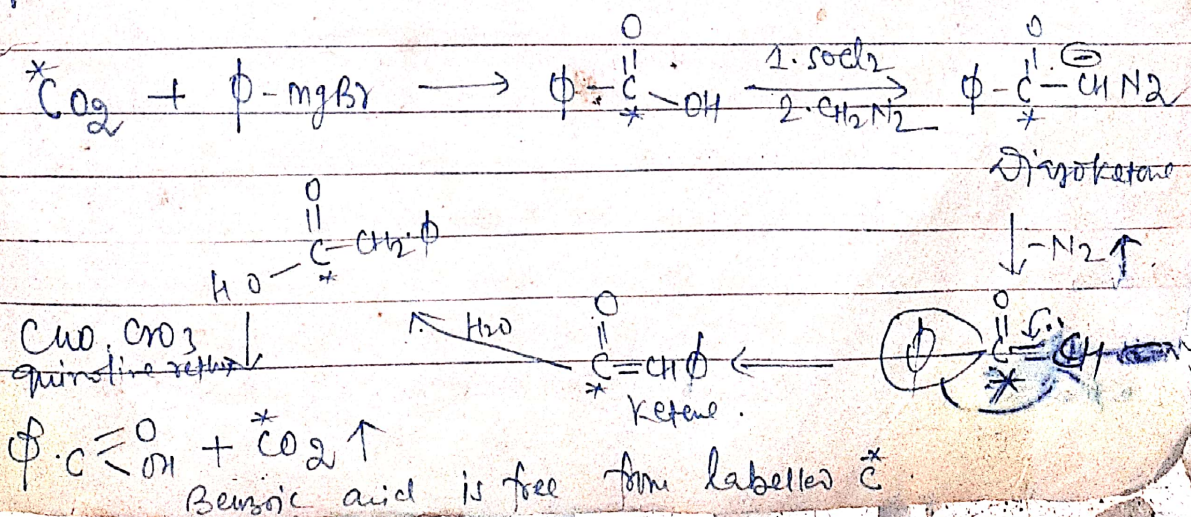
The diazoketone, so formed evolves a molecule of Nitrogen & a carbene is formed, which has the open sextet. Thus the electron-deficient carbon is carbene here instead of a carbenium ion. In presence of Ag₂O or by irradiation with light it (carbene) rearranges to the highly reactive ketene ^{by the migration of R.} The ketene formed then adds on the solvent molecule to yield higher homologues of acid or acid derivative. (In the silver catalyst react loss of nitrogen and migration R is simultaneous.)



The formation of hydroxy methyl ketone involves the addition of atoms with a filled valence electron shell, essentially an SN-reaction.

The mechanism cited above is confirmed by the fact that ketene formed has been isolated in a number of cases.

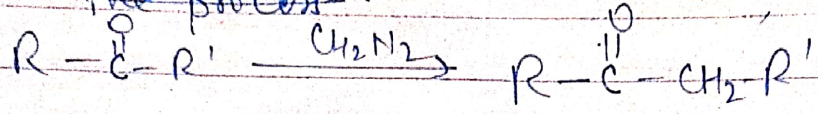
The fact that >C=O group of the diago ketene changes into the -COOH group of the higher homologues acid is established by the following C¹⁴ tracer application:-



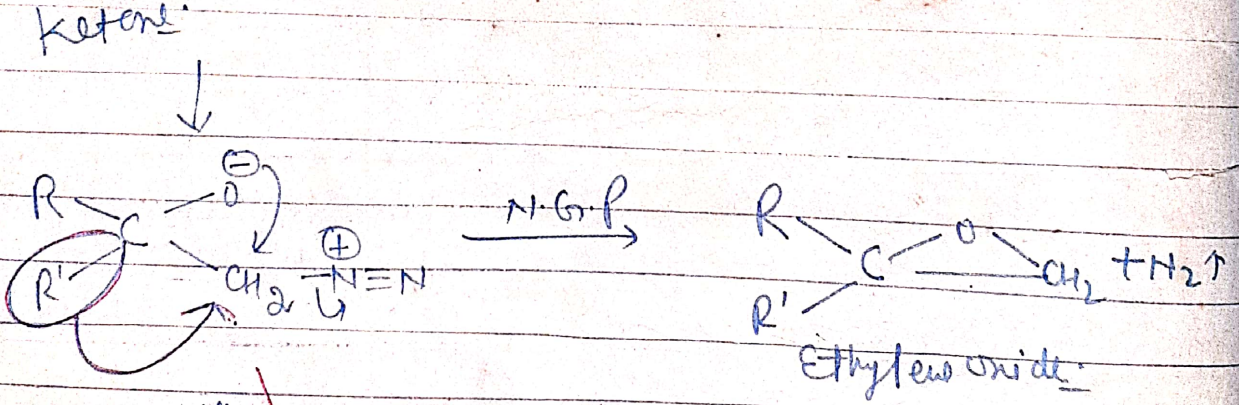
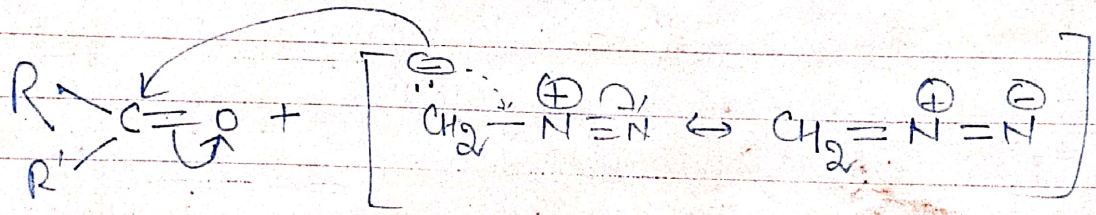
[Note: If the tertiary Radical linked with the carbonyl group of the diketones contains an asymmetric carbon atom (e.g. C_6H_5 , $C(Me)Ph$) then (Wolf, Hoffmann, Losseu, Schmidt also) proceeds with retention of configuration.

If the asymmetric atom is secondary instead of tertiary, the rearrangement proceeds with complete racemisation.]

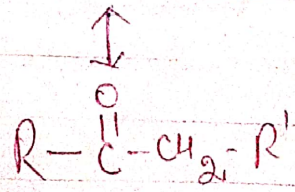
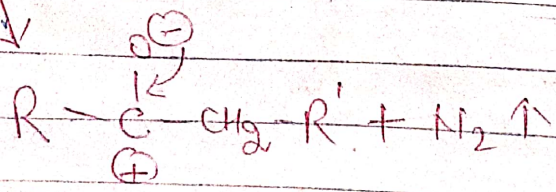
Diagonmethane is also used in an analogous reaction that converts ketones to their homologous ketones. The process:



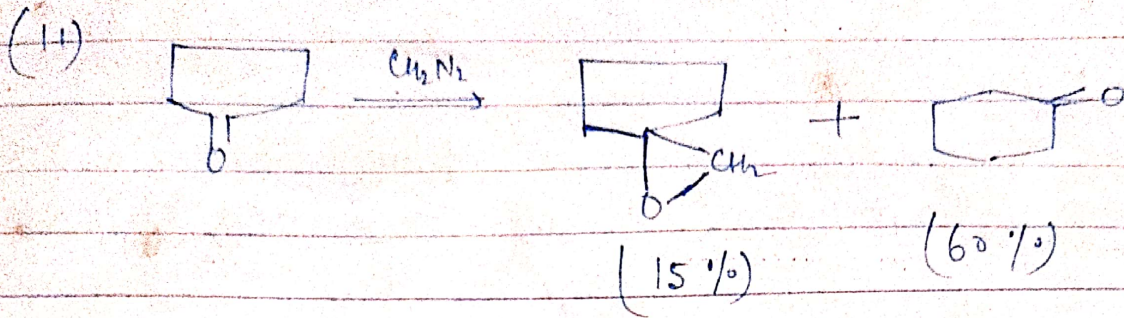
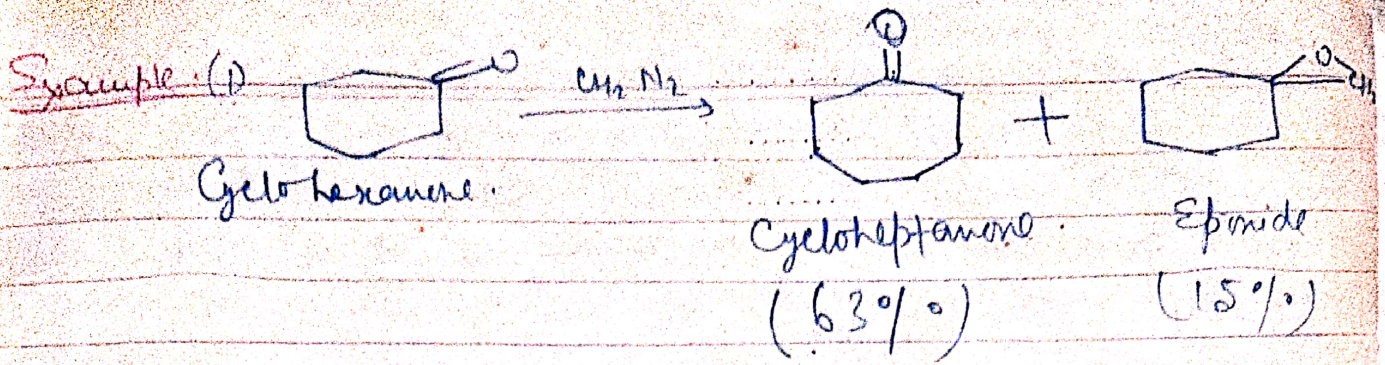
The process has been used to expand cycloalkanone rings. A ring closure to form ethylene oxide competes with rearrangement step and often becomes the principal reaction.



Where R or R' will migrate depends on their migratory aptitude etc.



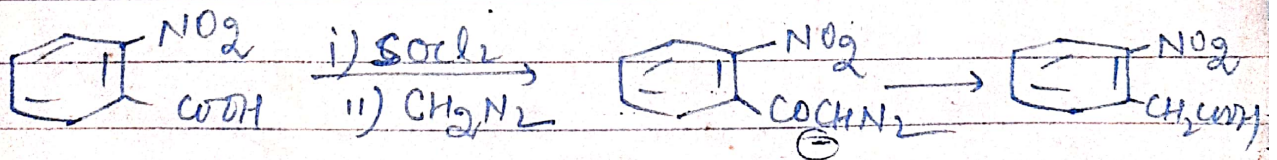
(Higher homologue of the ketone)



Synthetic Importance of (A & E synthesis) \rightarrow (Synthesis of acids & their derivatives) \rightarrow Arndt-Eistert method

~~is used~~ ^{hence wolf rearrangement} for the synthesis of higher acids from lower ones. Arndt-Eistert synthesis ^{of acids} has an important advantage over other methods, which is that this method does not require reduction & hence it is extremely useful for the compounds containing reducible groups; viz Nitro, cyano, keto, lactone, ester etc.

e.g., Conversion of o-nitrobenzoic acid into o-nitrophenyl acetic acid.



(ii) It is also used for the synthesis of various natural products viz - testosterone, corticoids. It is also used for the synthesis of Papaverine.