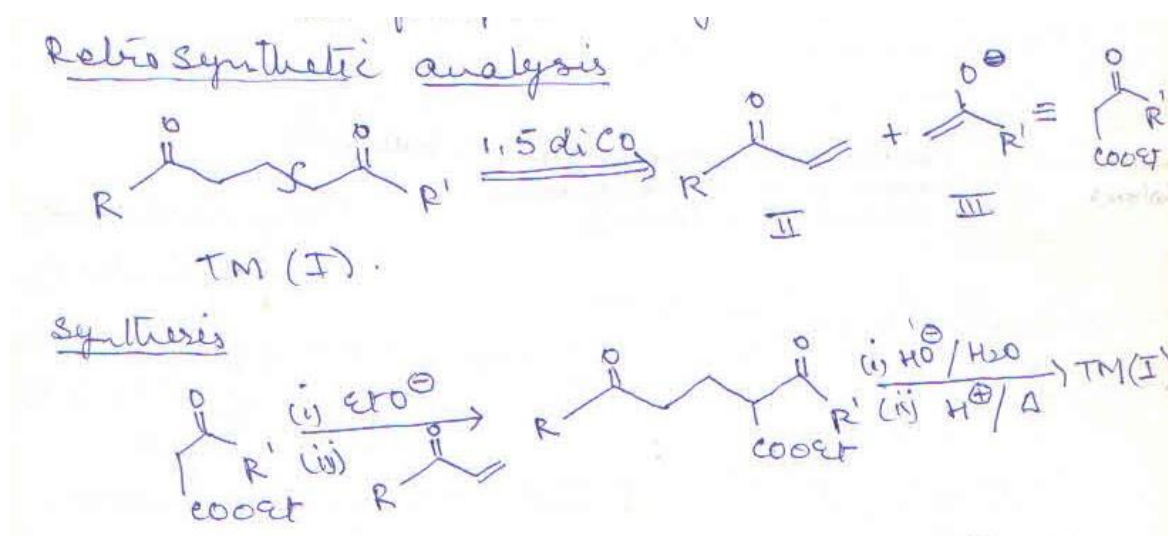
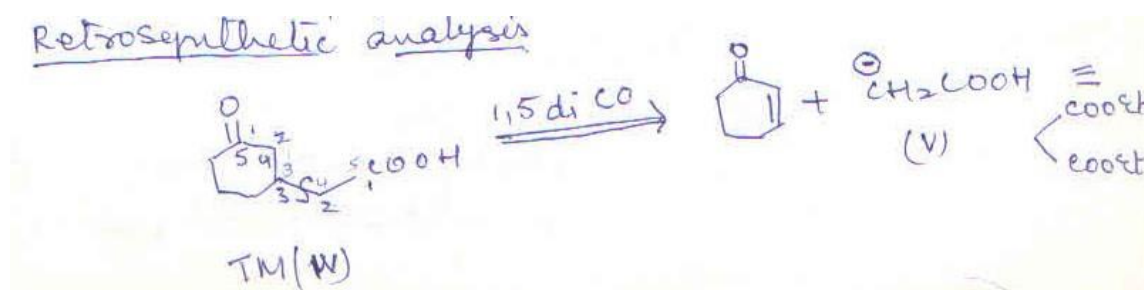


Two Group C-C Disconnection : 1,5 Difunctionalised compounds, Michael Addition and Robinson Annellation.

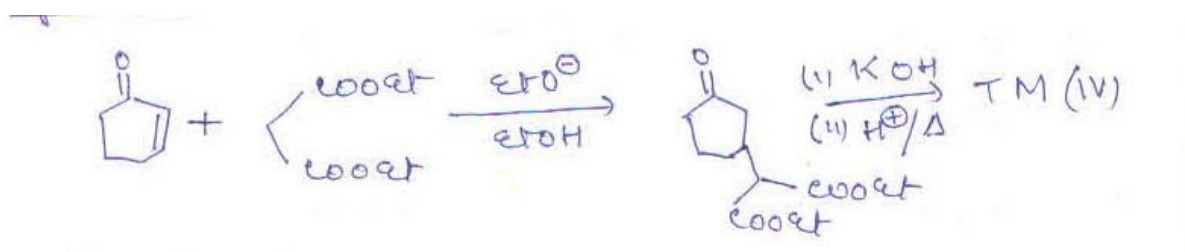
1,5 dicarbonyl compounds (I) can be disconnected at either α,β bond in a reverse Michael reaction. All the previous questions of control remain so, therefore there should be an activating group on enolate III to ensure both enolisation at this site and Michael rather than direct addition to II. The COOEt group serves the purpose very well.



The cyclic ketone (IV) is best disconnected where ring and chain meet and synthon (V) is best represented by malonate.



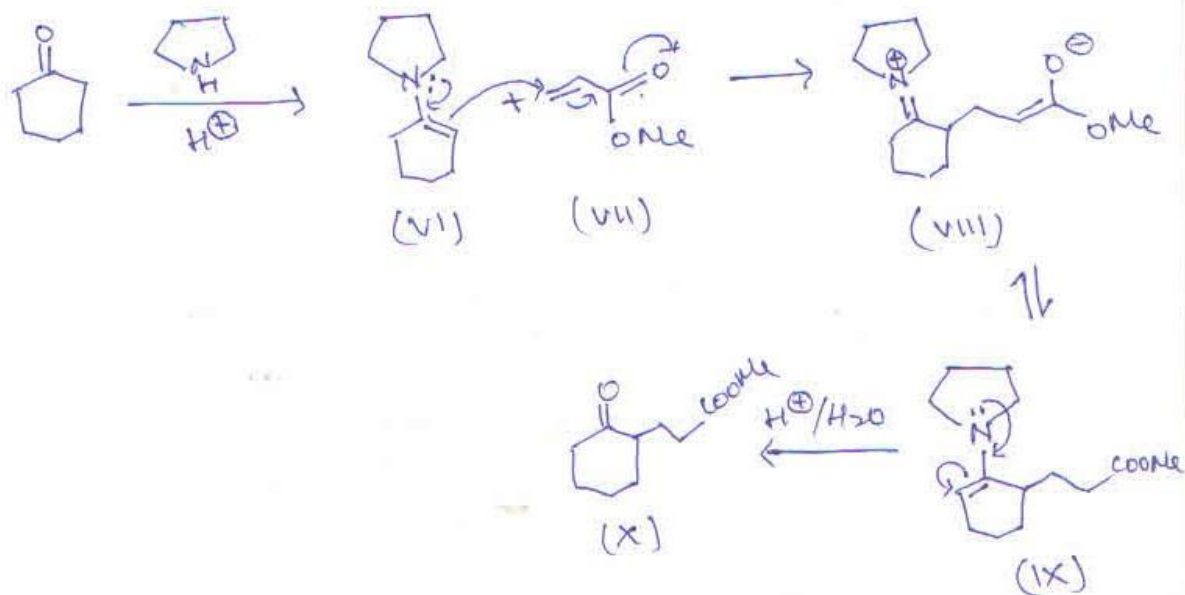
Synthesis



Activation by enamine formation

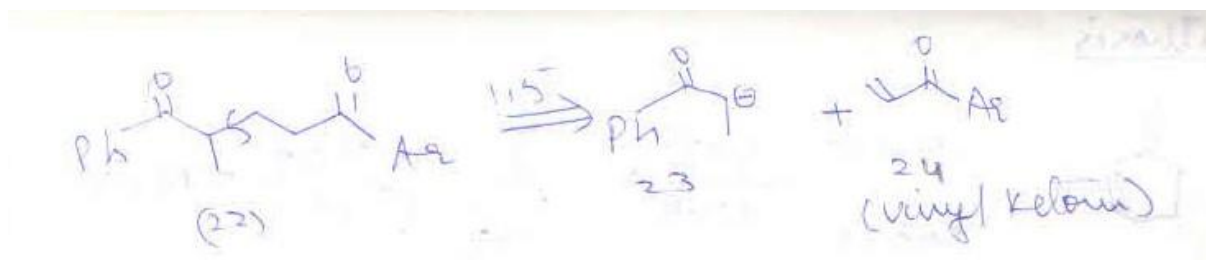
Use of enamine as specific enol equivalents

Enamines are equally useful in Michael reactions. Enamines (VI) adds cleanly to acrylic ester (VII) in Michael fashion and the first formed product (VIII) is in equilibrium with (IX). Hydrolysis of (IX) in aqueous acid releases 1,5 dicarbonyl product(X).

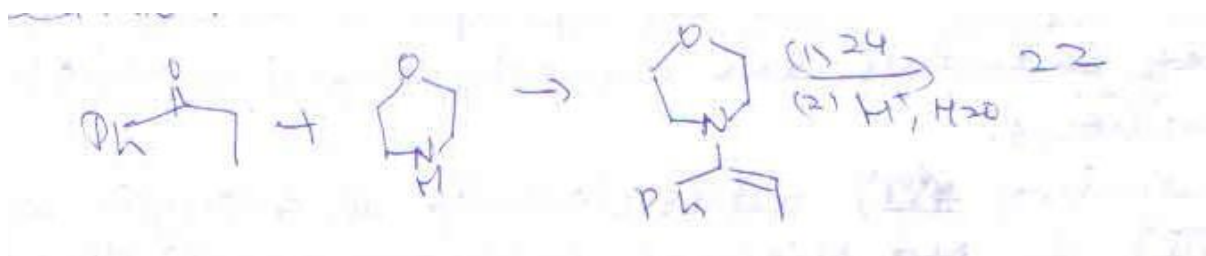


Michael acceptor by Mannich reaction

Vinyl ketones are very reactive and dimerise readily by Diels Alder reaction to give I. It is better not to make them until they are needed.

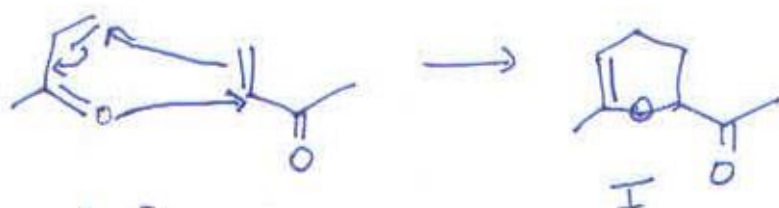


Synthon (23) was represented by an enamine and vinyl ketone (24) could be made by the Mannich reaction.

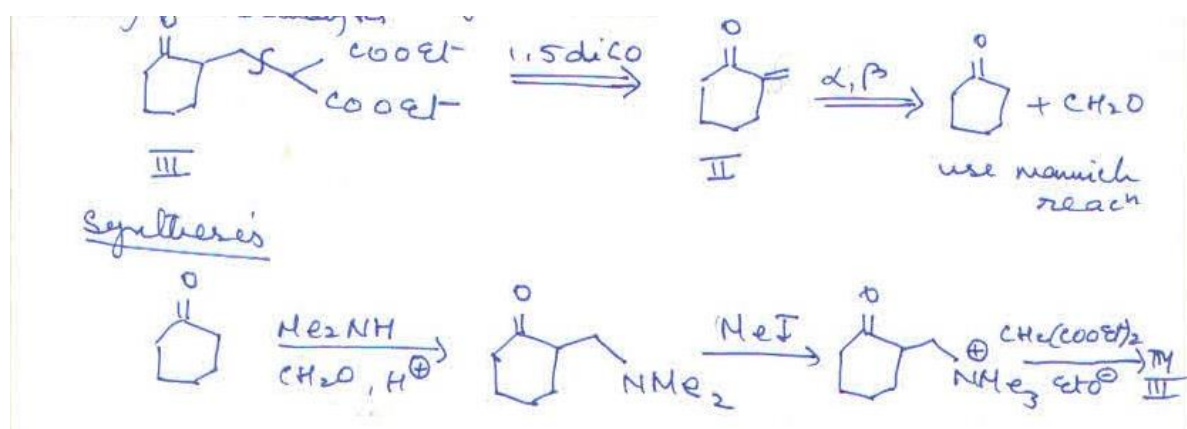


This can be done by using alkylated Mannich base instead of vinyl ketone which decomposes under the basic conditions used for Michael reaction to release the vinyl

ketone into the reaction mixture. Here the alkylated Mannich base acts as vinyl ketone equivalent.

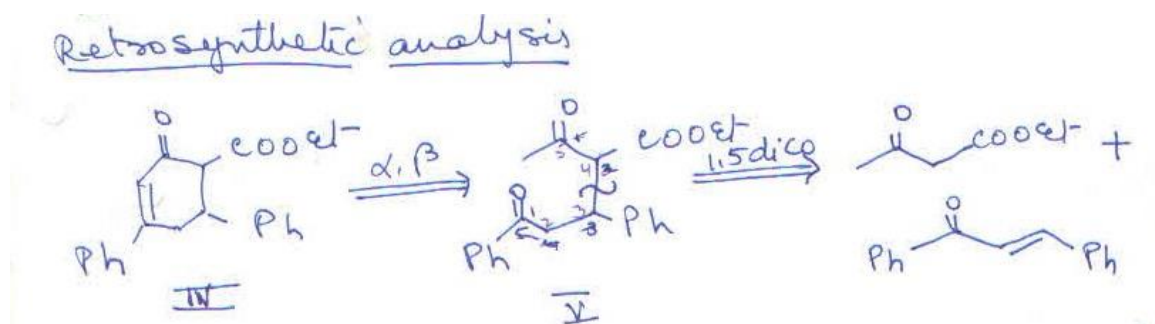


Cyclic ketone with exo-methylene group eg. II are usually protected in this way, as the exposed CH_2 group is very electrophilic. In the synthesis of III an alkylated Mannich base has been used in place of a vinyl ketone.

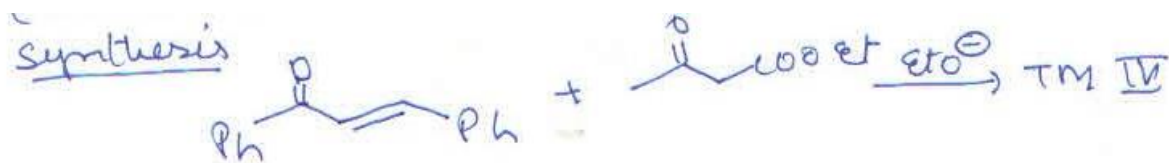


ROBINSON ANNELETION : A CYCLISATION REACTION OF PRODUCTS OF MICHAEL REACTION.

One extension of the Michael reaction is an important way to make six membered rings. At first glance one might think of a Diels Alder disconnection for IV as it is a cyclohexene with carbonyl groups, but the relationship is wrong. Disconnection of the α,β double bond, however reveals a simple 1,5 dicarbonyl disconnection.

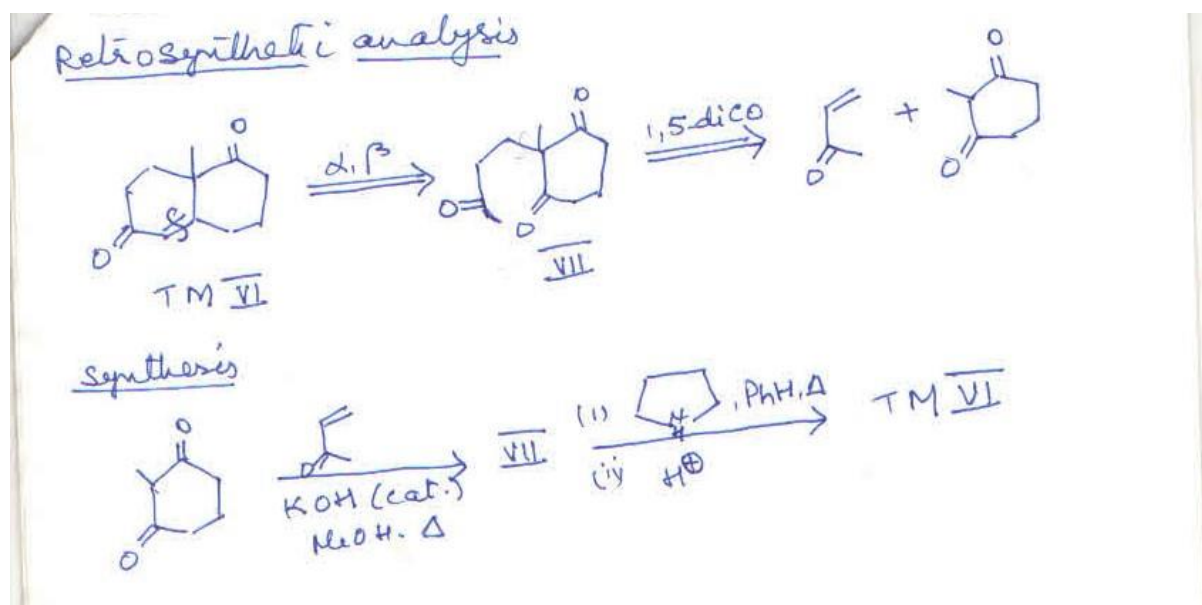


The second step of the synthesis, the cyclisation of V to IV often goes spontaneously and the whole process of addition and cyclisation (ring formation) is known as Robinson annelation (Robinson Annulation).



In Robinson annelation a cyclic ketone is converted into another cyclic ketone, with a fused pair of six membered rings containing a double bond, in essentially one step

EG. Synthesis of the bicyclic ketone VI which is an ideal intermediate in the synthesis of steroids.



X-----X-----X