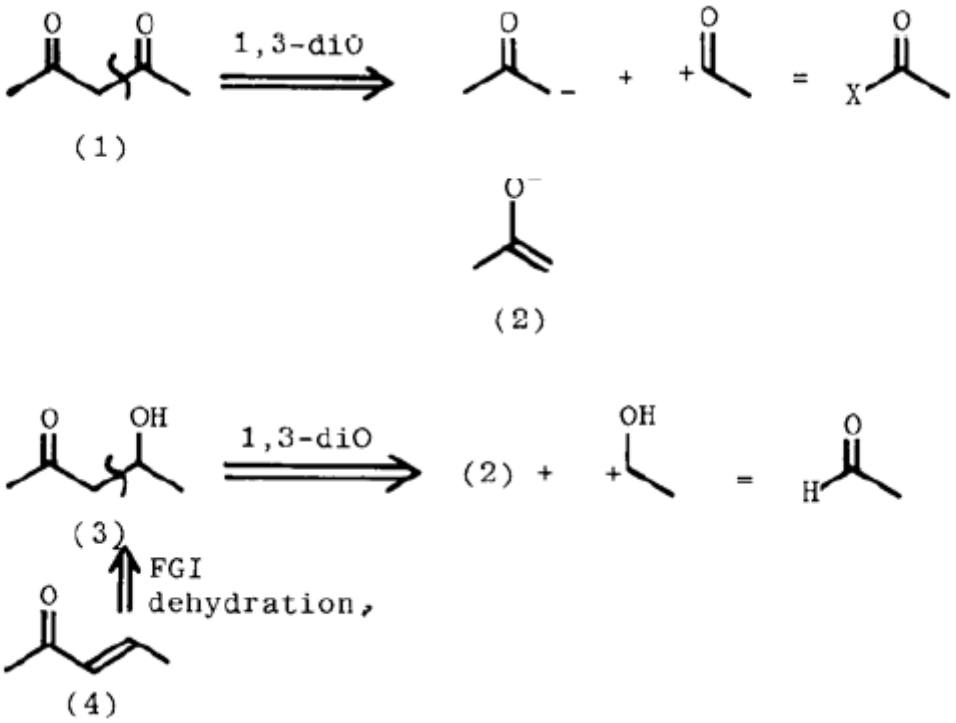
# Two group disconnections

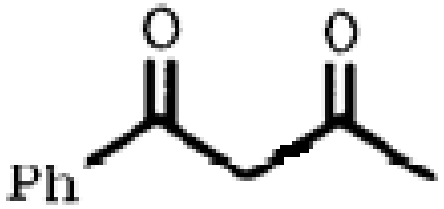
Direct disconnection of this group of compounds is possible at two oxidation levels-dicarbonyl (1) and beta- hydroxy carbonyl (3).
Enones (4) come into this category since they are usually made by dehydration of (3).




Disconnection (1) means we look for a reaction which is the acylation of enolate anion and it is possible with esters (X = OR) or acid chlorides

# 1,3-difunctionalized compounds: 1,3-Dicarbonyl compounds and β-hydroxyl carbonyl compounds

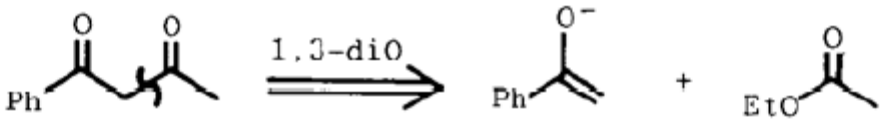
# 1,3-Dicarbonyl compounds




(5)

# Compound can be disconnected to enolate of ketone and ester

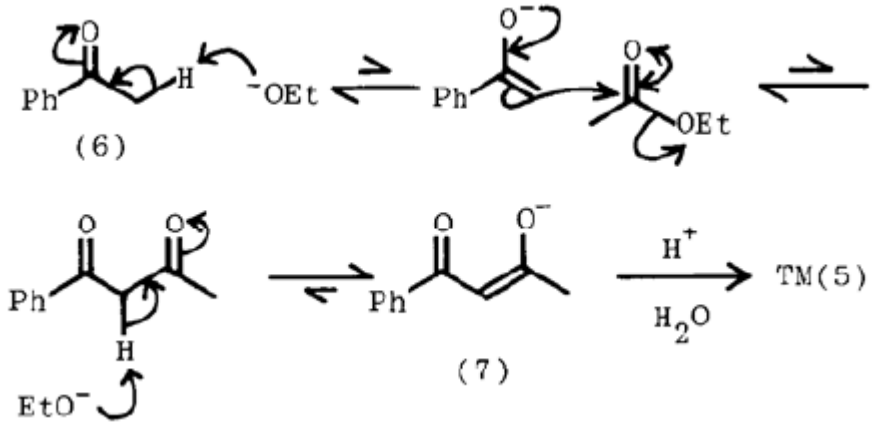
***Analysis***

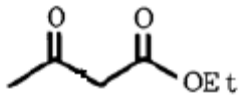



(5)

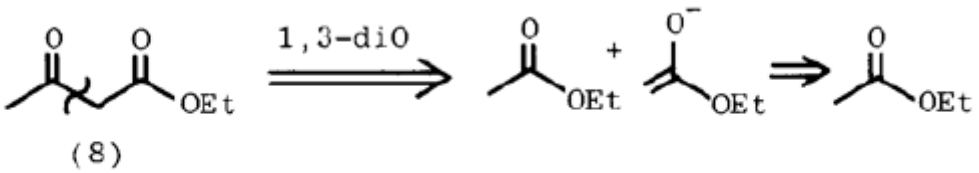
Rx can be carried out by combining ketone 6 with ester and a base strong enough to produce only a small concentration of the enolate. Rx is therefore an equilibrium and is driven over by formation of stable delocalized enolate 7 of the product. Acid work up releases TM

The reaction is known as Claisen condensation.



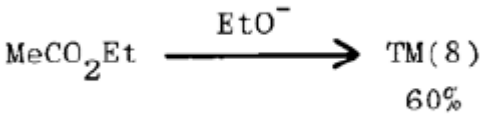


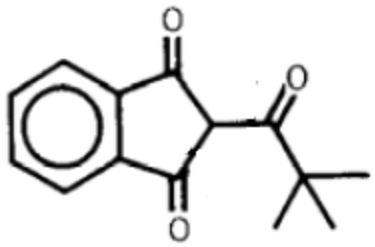

(8)



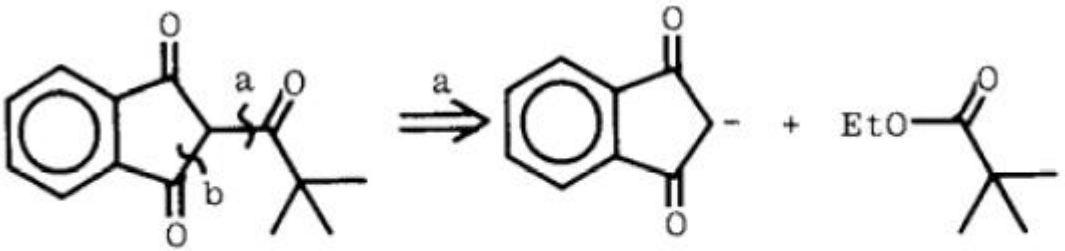

(8)

## Claisen ester condensation

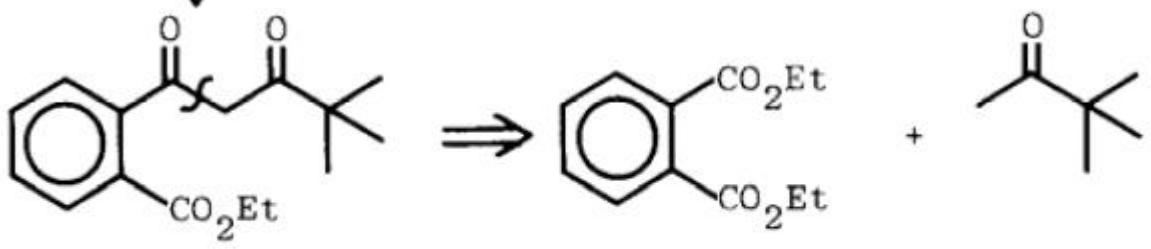




(9)

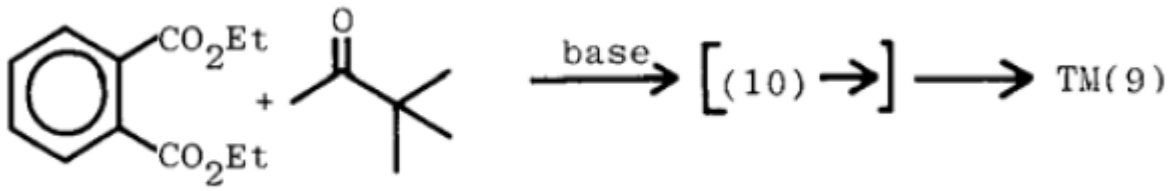



(9)

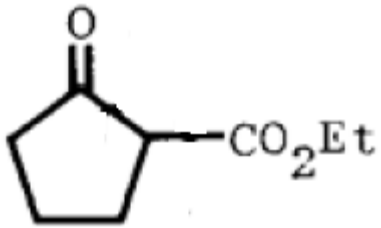



(10)

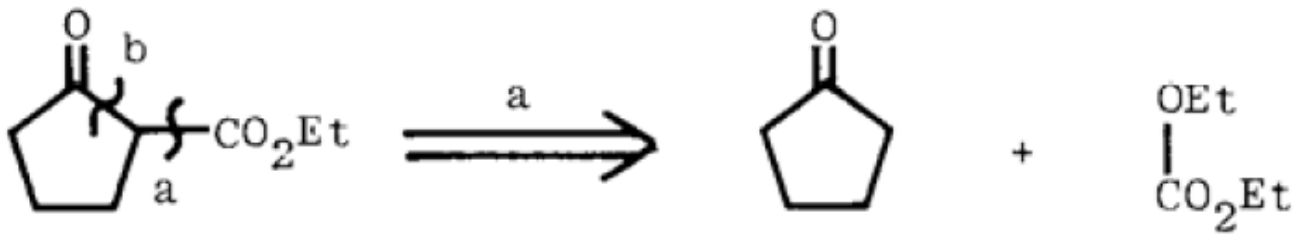
b route leads to available starting materials



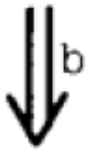

10 cyclizes to 9 under conditions of its formation

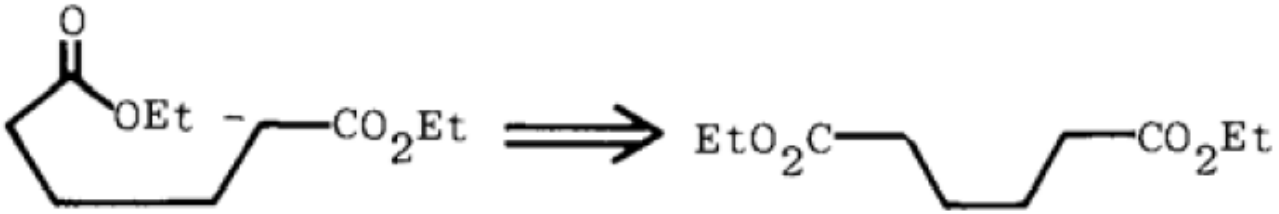



(11)

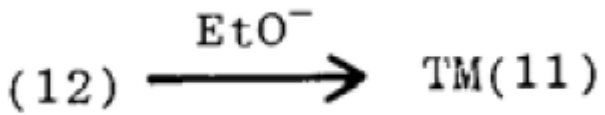



(11)



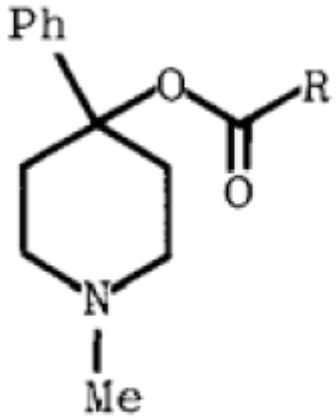




(12)




(a) Removes only one C atom, is a bad strategy

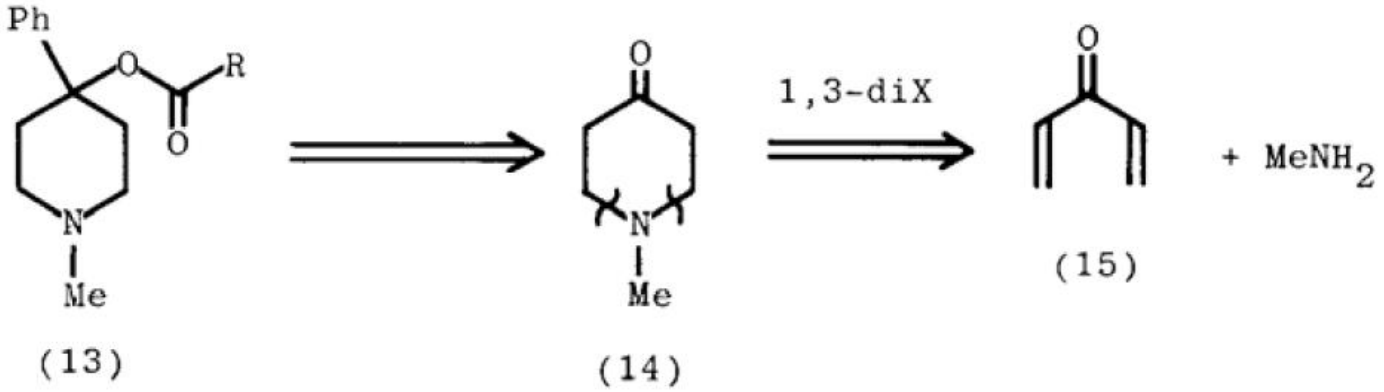
(b) gives symmetrical and readily available diester

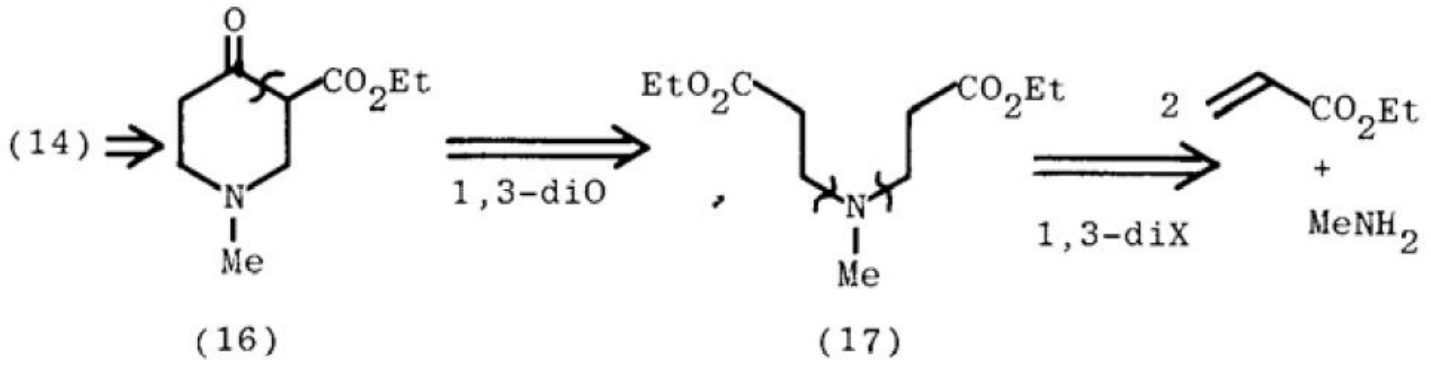


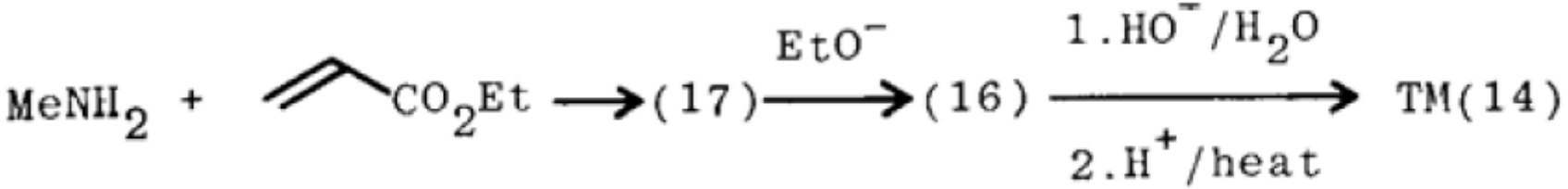

(13)

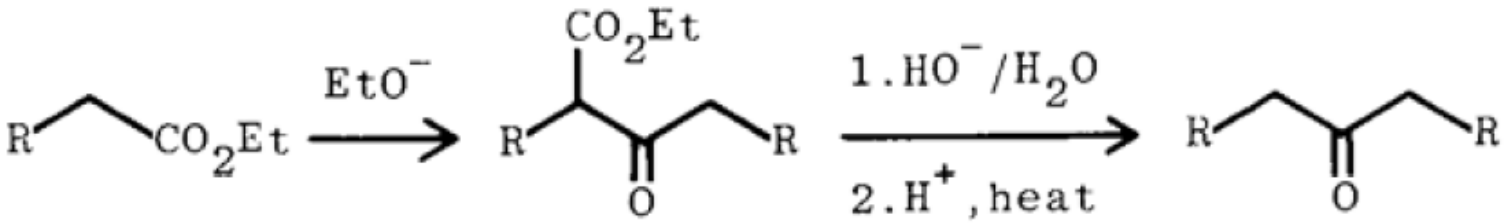
Disconnection of (14) by 1,3-diX requires unstable ketone as SM

Inserting $CO_2Et$ gp beta to ketone to get (16), 1,3-diX gives symmetrical diester (17) which undergoes two 1,3-diX



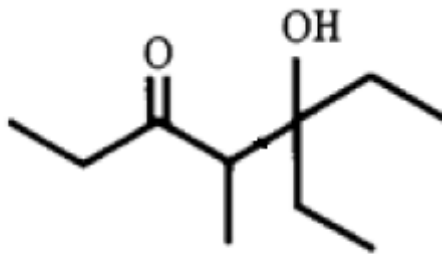





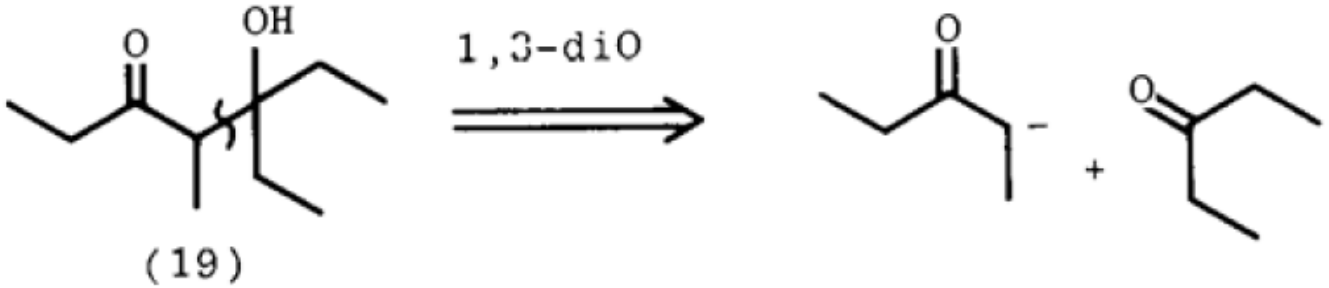

(18)

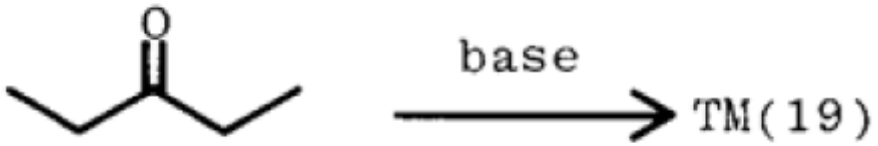
# β-Hydroxy carbonyl compounds

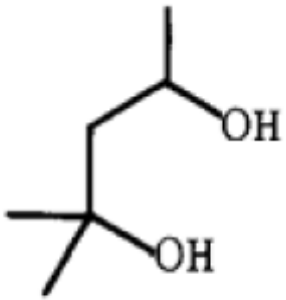
1,3-diO at lower oxidation level




(19)

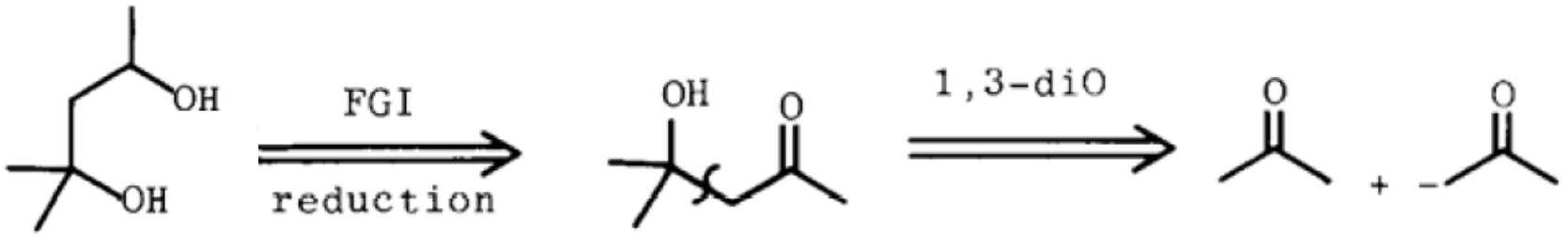

O
OH
1,3-diO
O
O
(19)


O
base
TM(19)

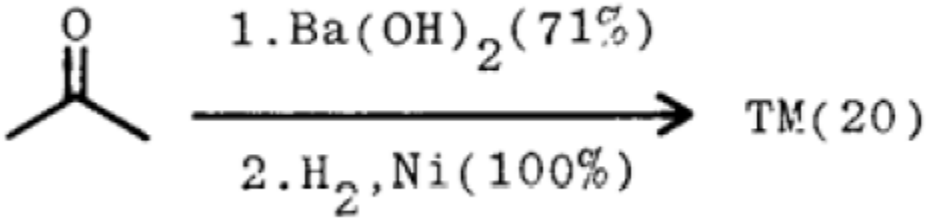


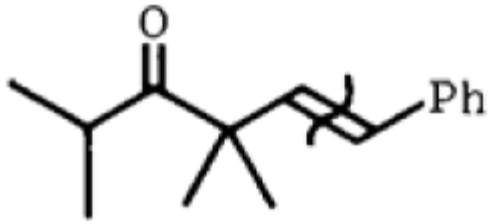

(20)

Compounds may need FGI before disconnection

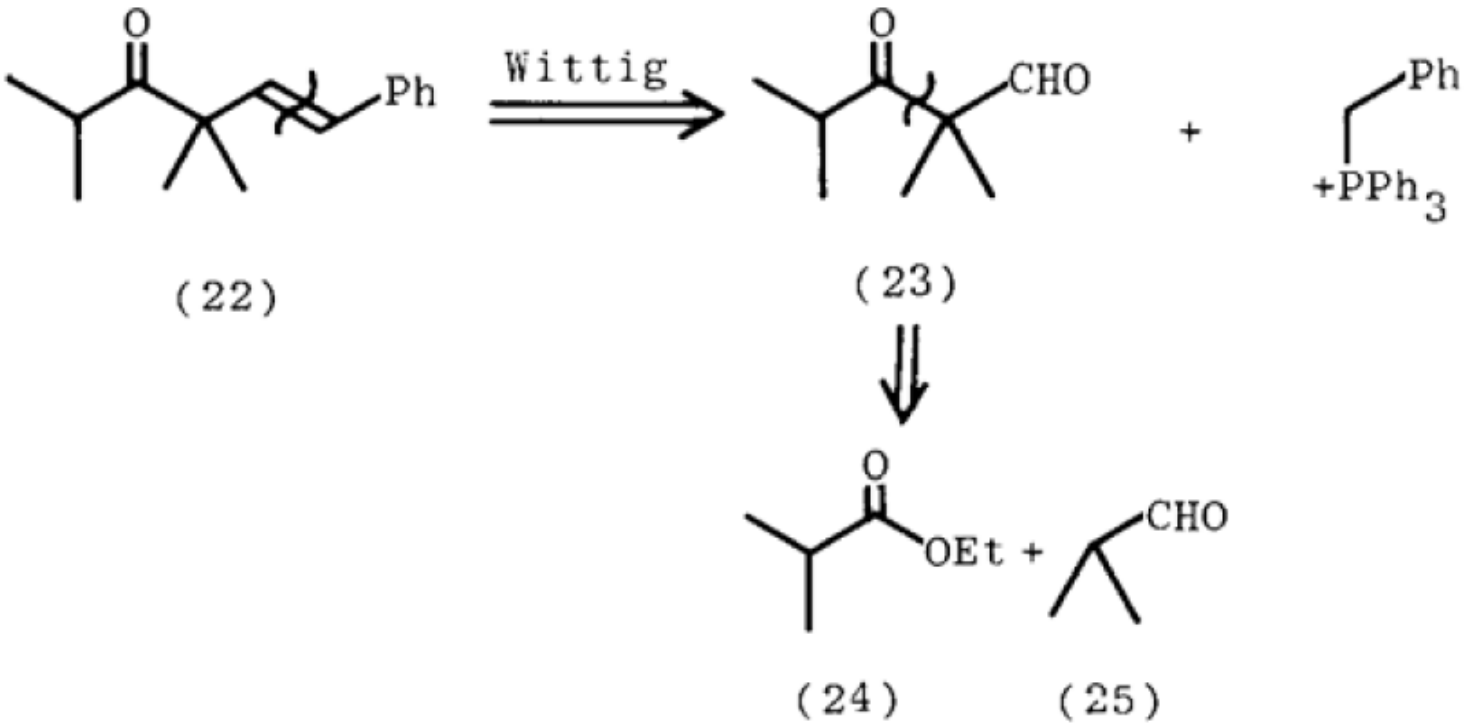


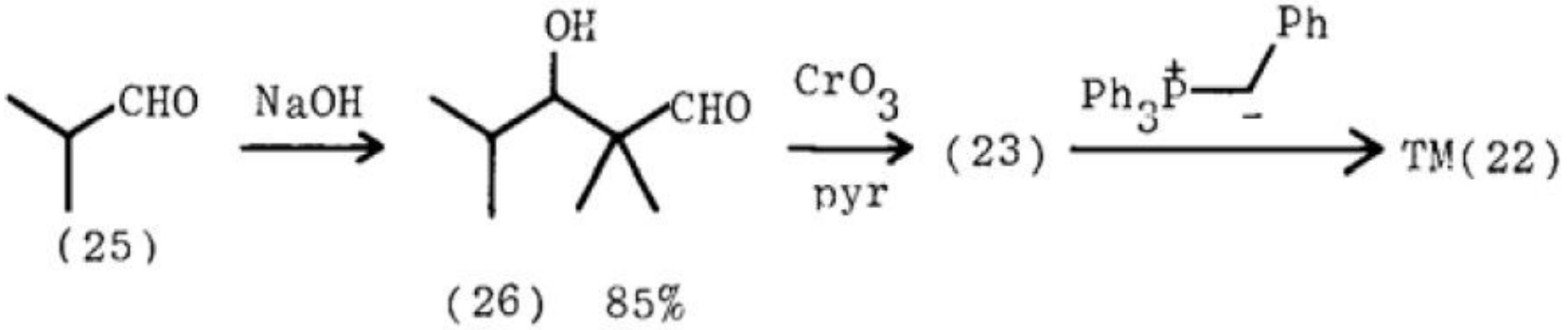

(20)





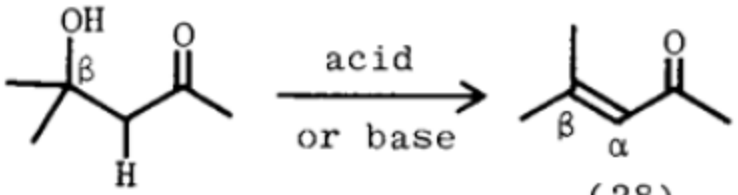

(22)


O
Ph
Wittig
O
CHO
+
Ph
+PPh3
(22)
(23)
O
OEt +
CHO
(24)
(25)


CHO
NaOH
OH
CHO
CrO3
pyr
(23)
Ph3P
Ph
TM(22)
(25)
(26) 85%

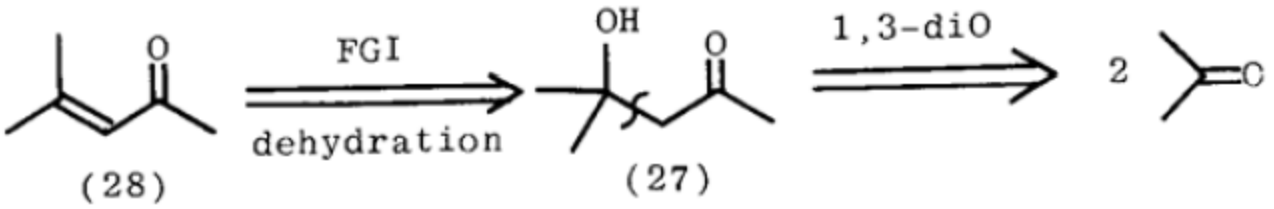
# α,β-Unsaturated Carbonyl Compounds

Dehydration of β-hydroxy carbonyl compounds is very easy because proton to be removed is enolic and product is conjugated.



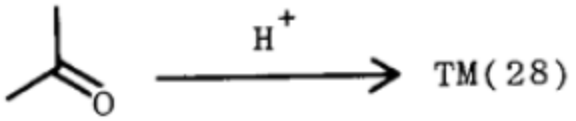

(27) (28)

*Analysis*



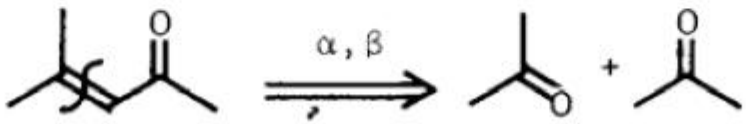

(28) (27)

*Synthesis*

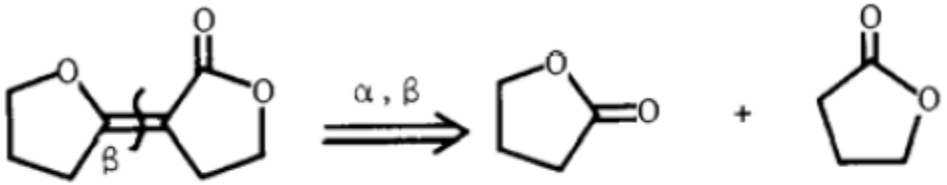



We therefore usually write a shorthand disconnection of the enone directly to the two carbonyl components:

*Analysis*

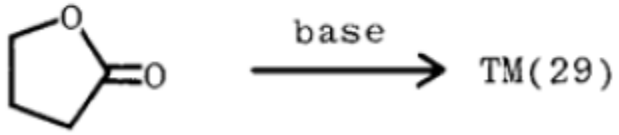


*Analysis*

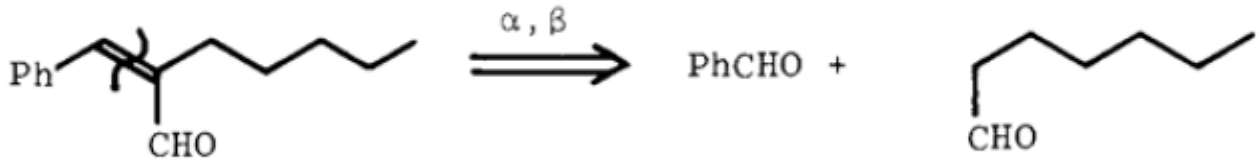



(29)

*Synthesis*



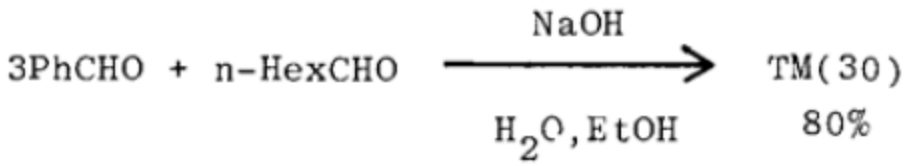
## Flosal: *Analysis*

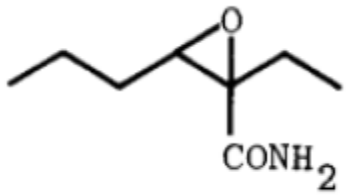



(30)

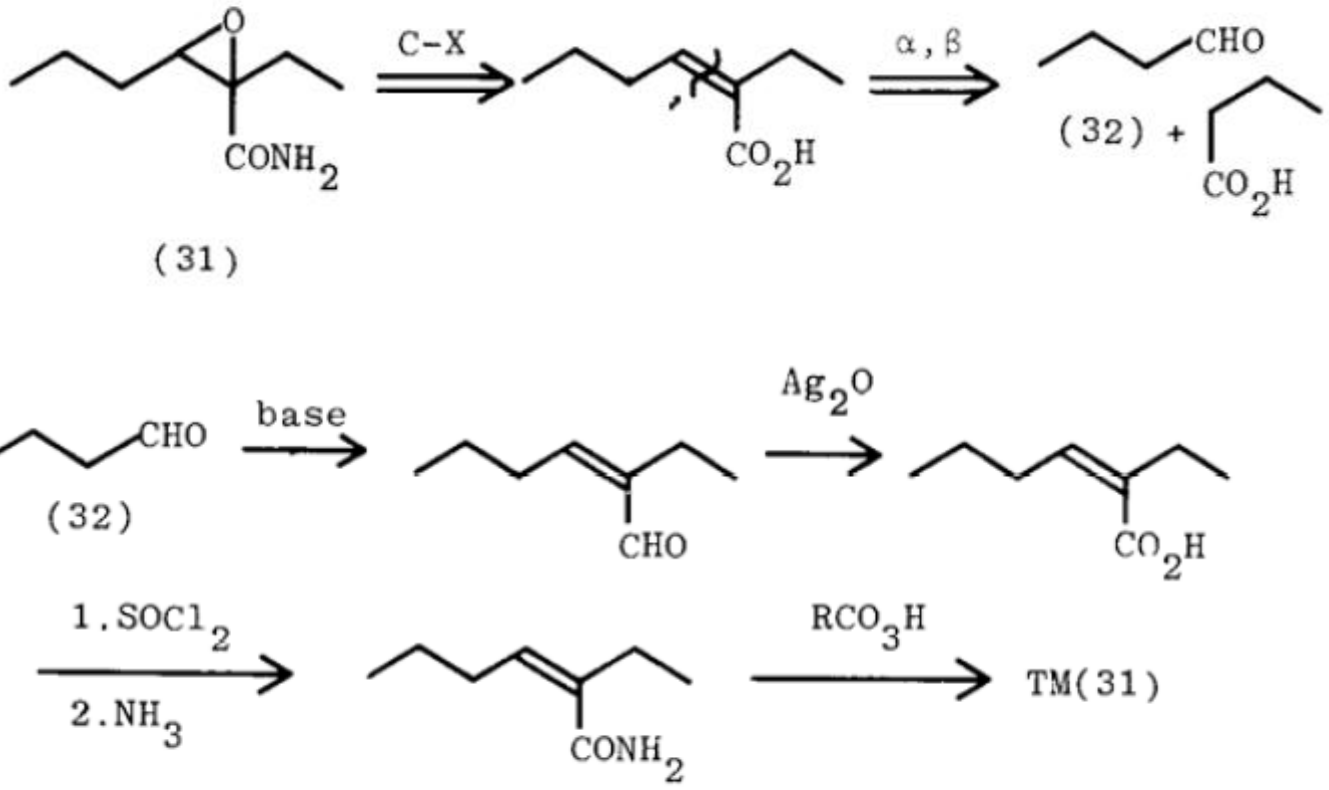
Synthesis is carried out with large excess of benzaldehyde to minimize self-condensation of the aliphatic aldehyde

## *Synthesis*




O
CONH2

## Oxanamide: *Analysis*

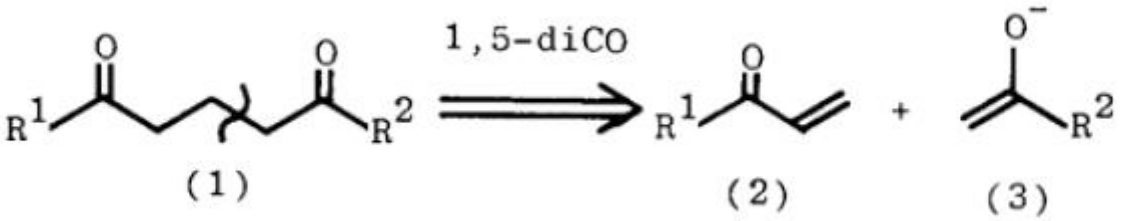



Trials revealed that it was best to put in amide before epoxide

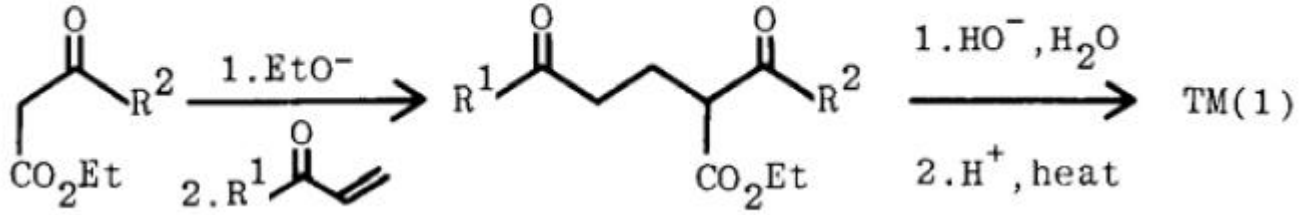
# 1,5-Difunctionalized compounds

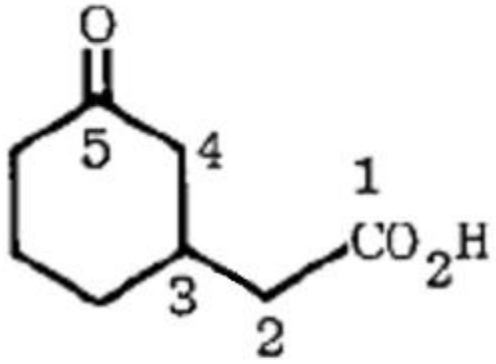
Can be disconnected at either α,β-bond

Have to add activating gp on enolate 3 to ensure both, enolization at this site and Michael rather than direct addition



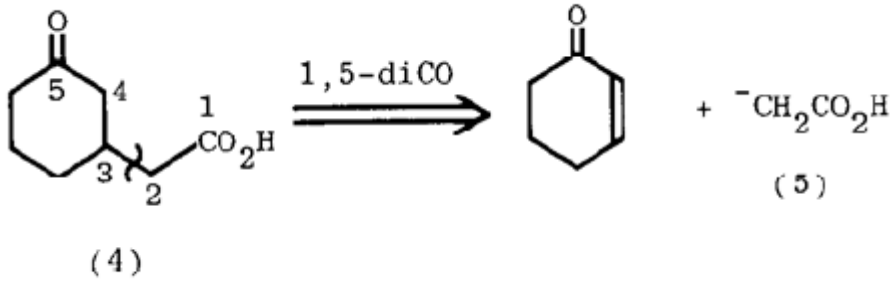

*Synthesis*



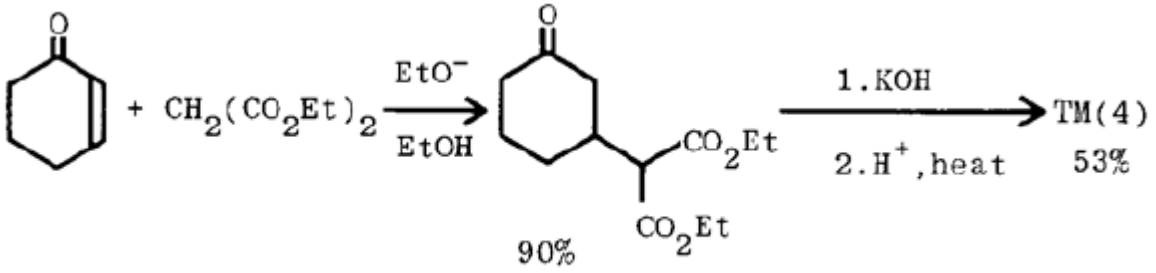



(4)

# Disconnected where ring and chain meet

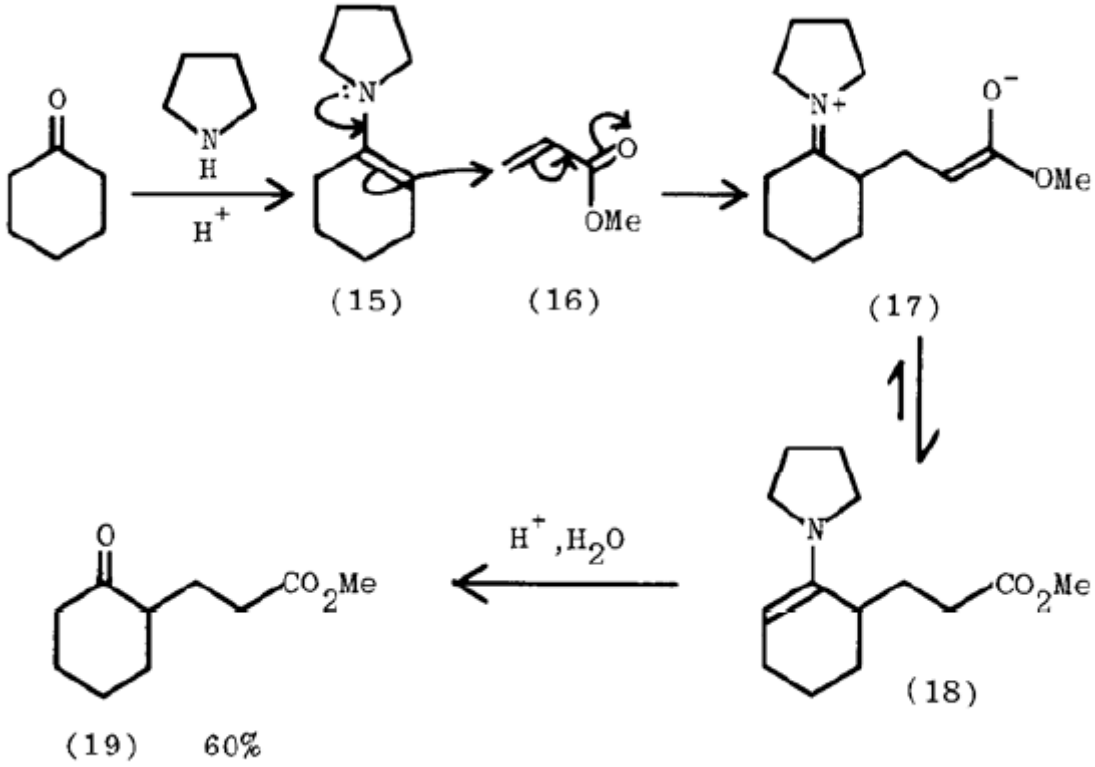


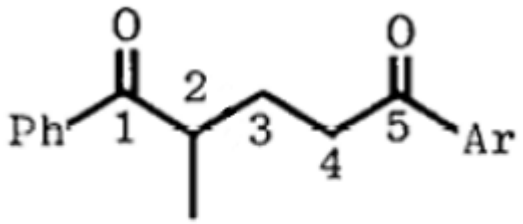

(4) (5)




90%

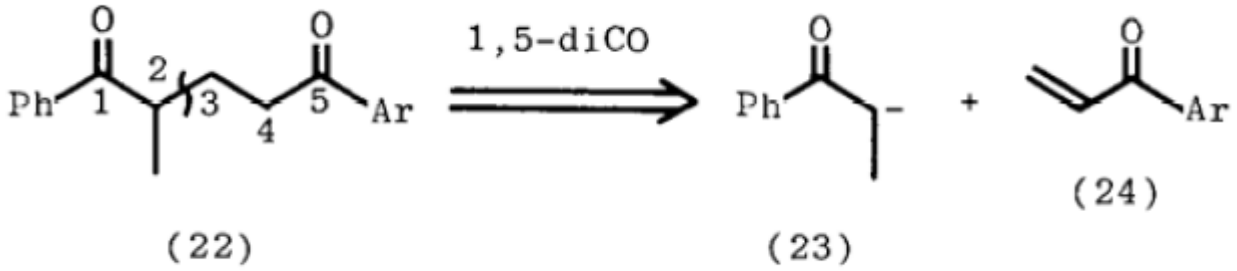
# Activation by enamine formation: enamines as enol equivalents

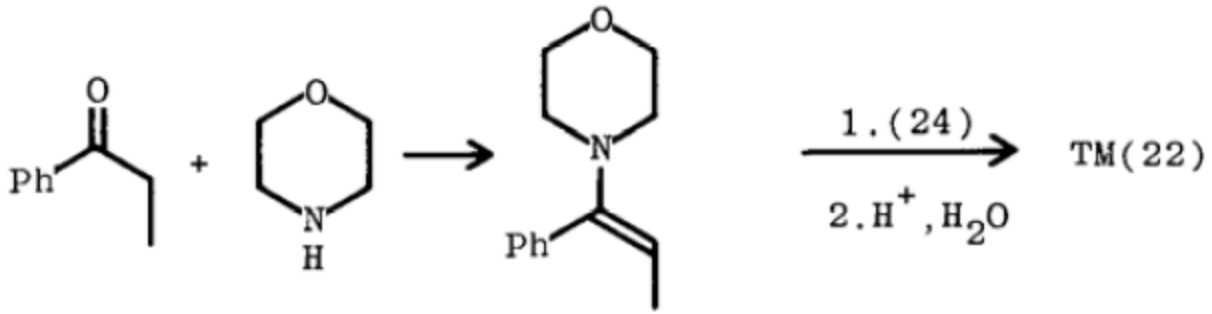




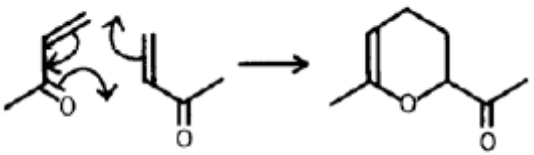

(22)

Disconnection at branch point
Synthon 23 presented by enamine and 24 could be made by mannich rx



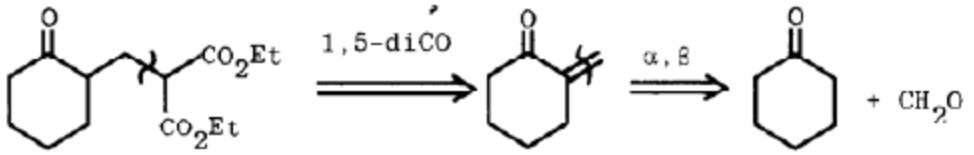



Michael acceptors by Mannich reaction: Vinyl ketones are reactive, an alkylated mannich base can be added



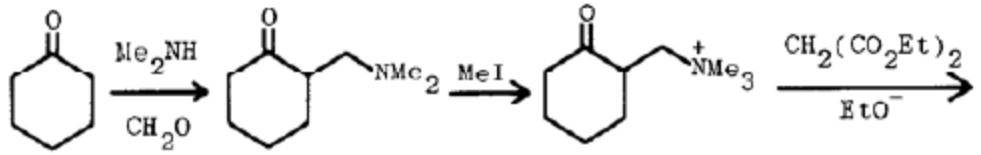
(25)

*Analysis*




(26) (27) use Mannich

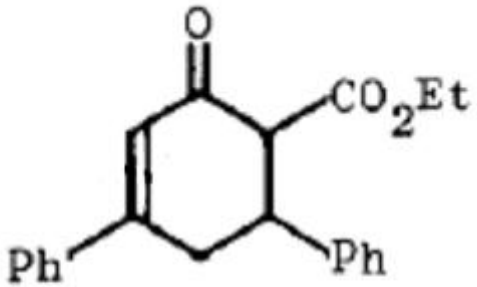
*Synthesis*




85%

TM(26)
66%

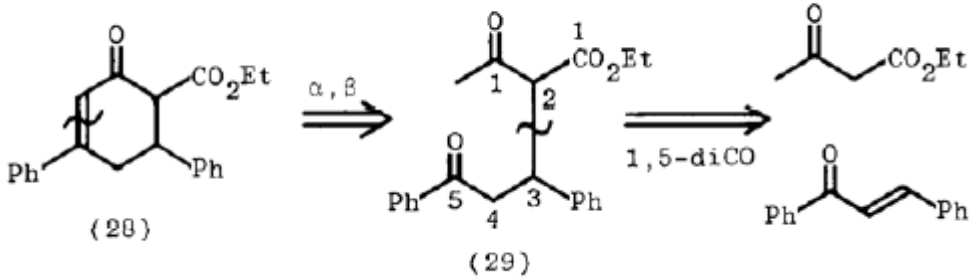
# Robinson Annelation




(28)

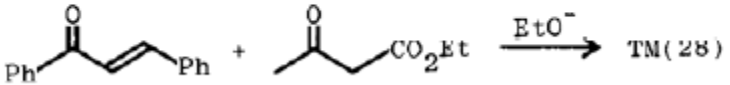
# Robinson Annelation

*Analysis*

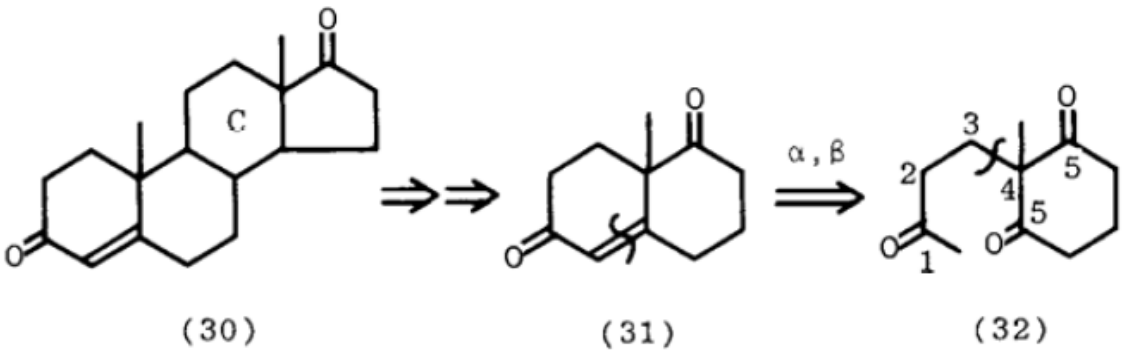



(28) (29)

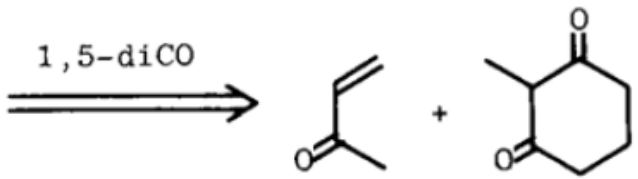
*Synthesis*



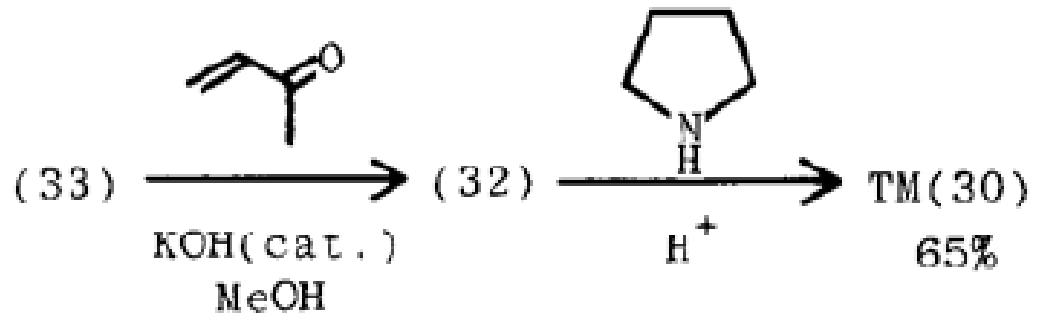
# Symmetrical diketone as reactant



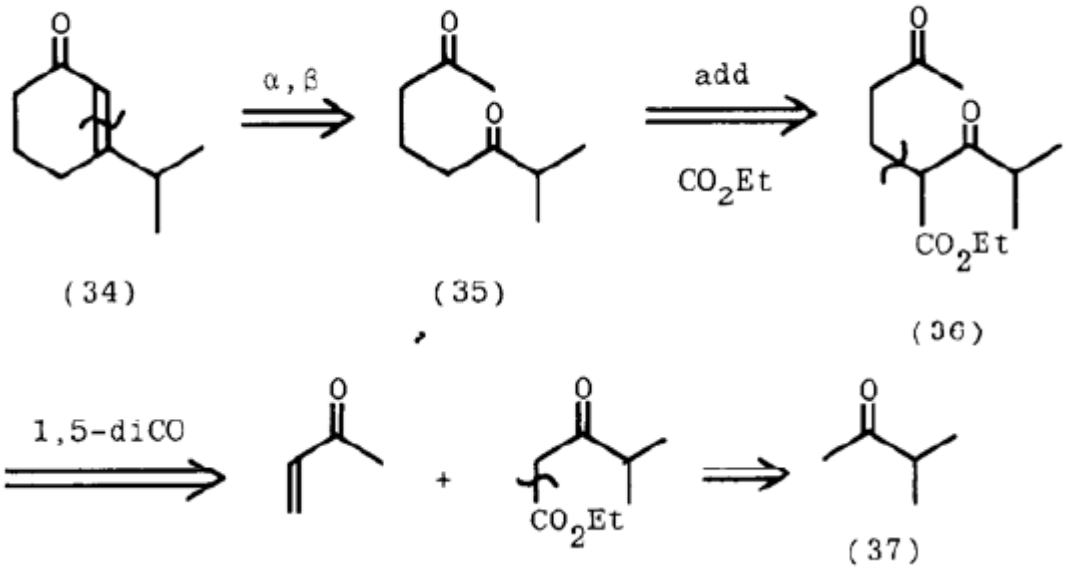

(30) (31) (32)

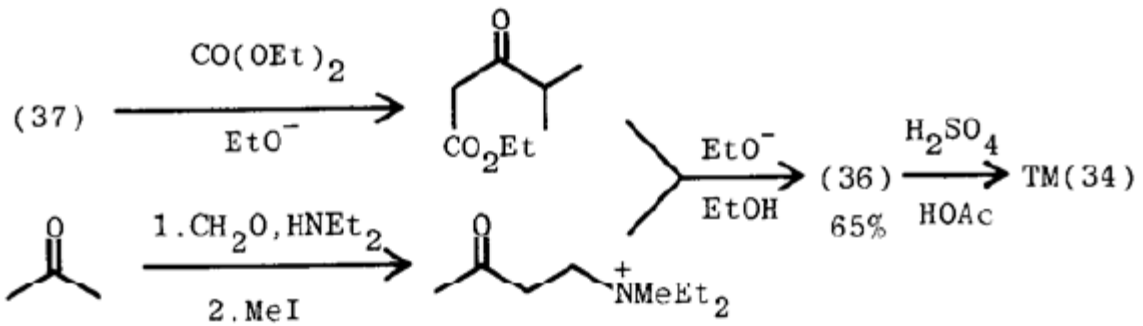



(33)



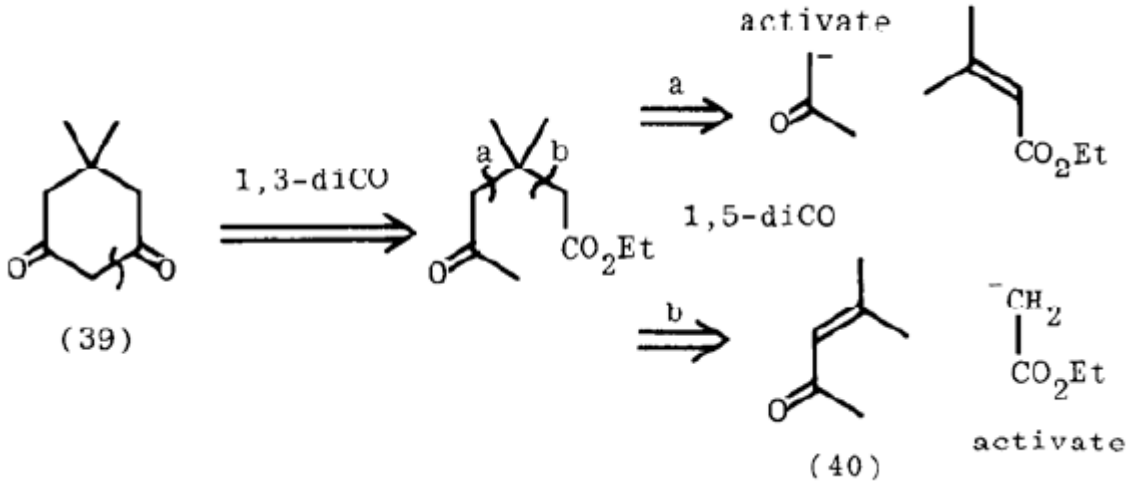
*Analysis*

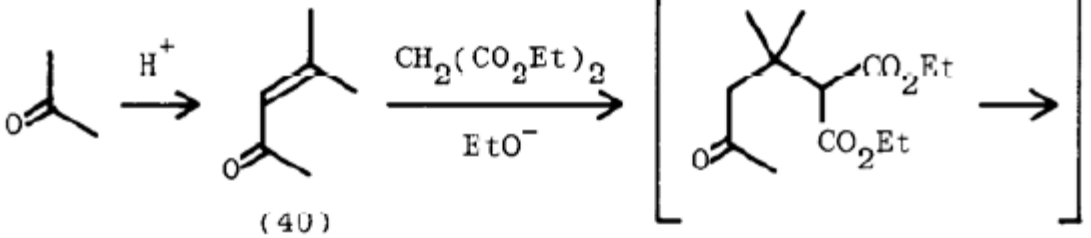

α,β
add
$CO_2Et$
(34)
(35)
(36)
1,5-diCO
+
$CO_2Et$
(37)

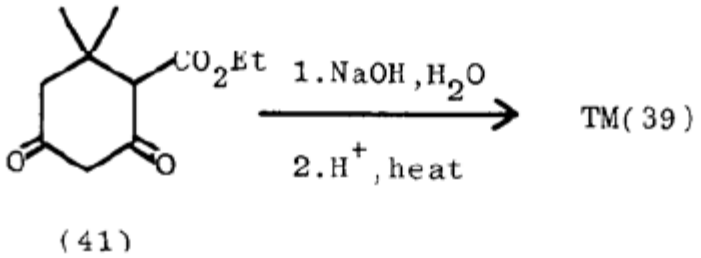

(37)
$CO(OEt)_2$
$EtO^-$
$CO_2Et$
$EtO^-$
EtOH
(36)
65%
$H_2SO_4$
HOAc
TM(34)
1.$CH_2O$,$HNEt_2$
2.MeI
$^+NMeEt_2$

# Cyclic 1,3-diketones

**Dimedone: *Analysis***




b route is used as both SM are available