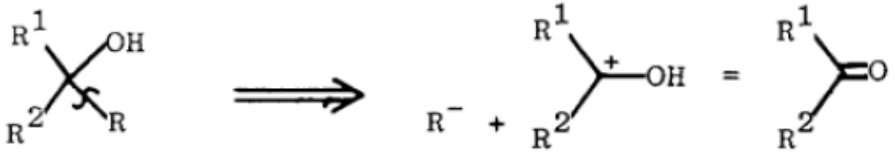
One group C-C Disconnections

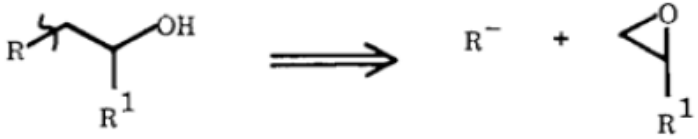


- Till now, we have studied the disconnections of bonds between carbon and other atoms
- Now, we will discuss more challenging C-C disconnections
- These are challenging because organic molecules contain many C-C bonds and must learn which to disconnect.
- In one way, they are easier than C-X disconnections. Reagents are available for both electrophilic (RBr) and nucleophilic (RMgBr) carbon whereas heteroatoms are almost always added as nucleophiles.

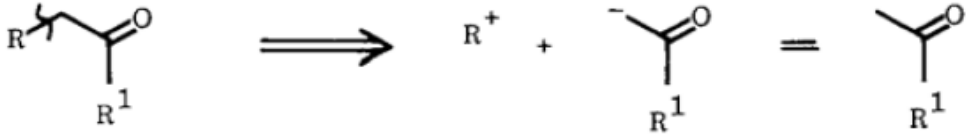
1.1 (a)



1.2 (b)

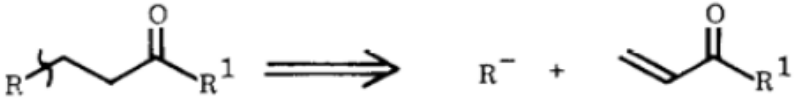


(c)



(1)

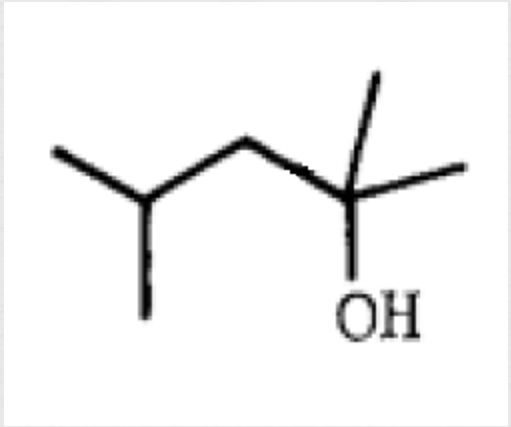
1.3 (d)



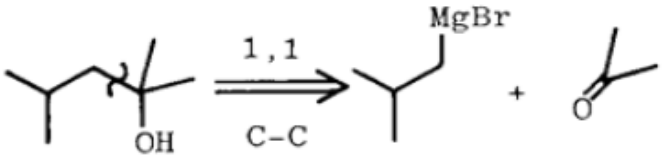
C-C disconnection of alcohols

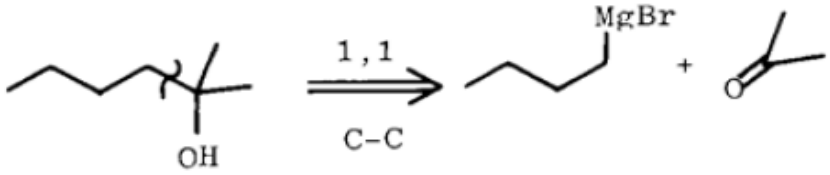


1,1 C-C disconnections

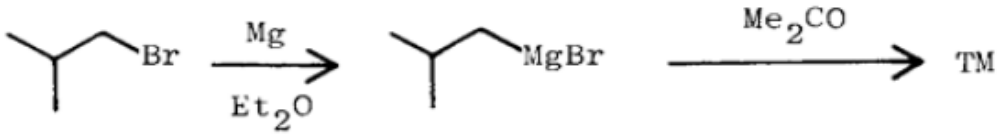


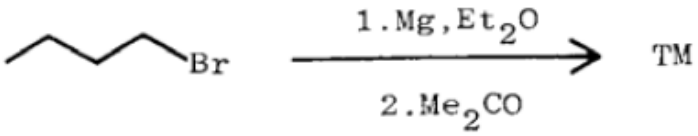
Analysis

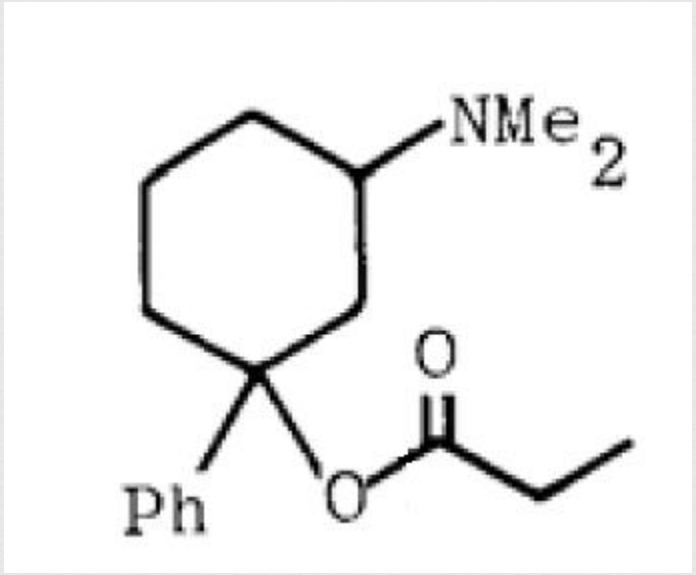


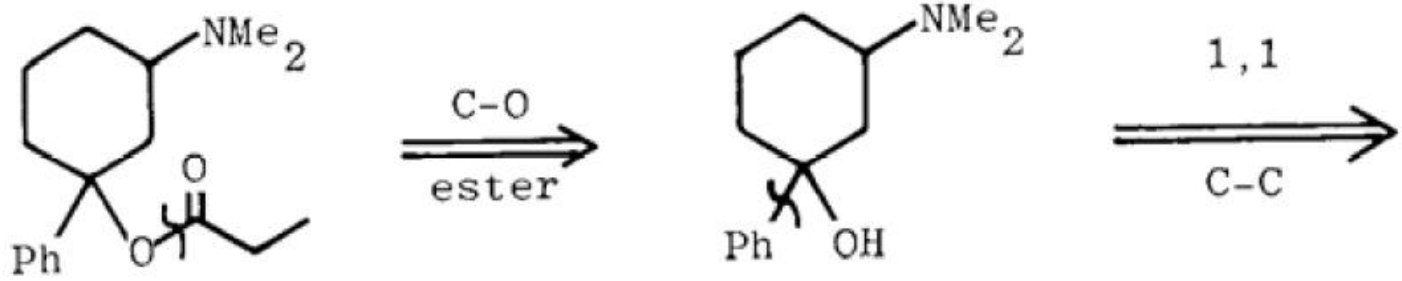


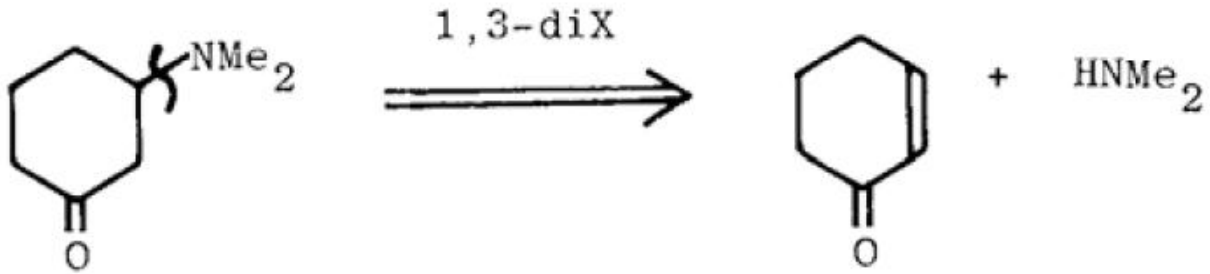
Synthesis



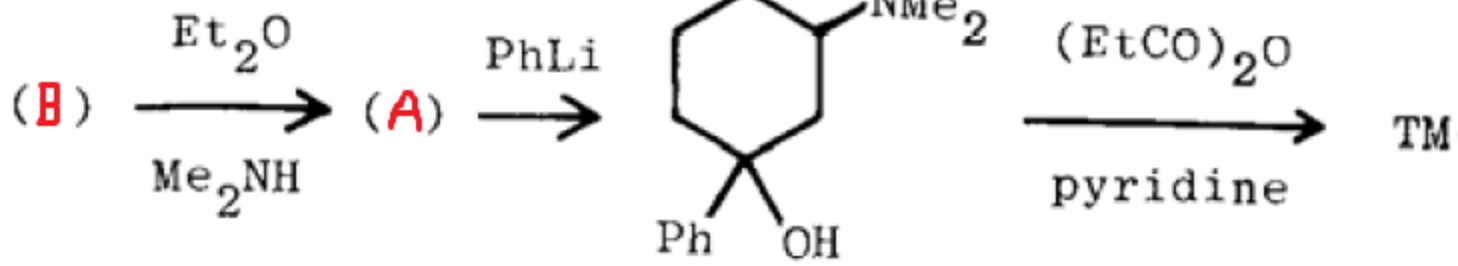


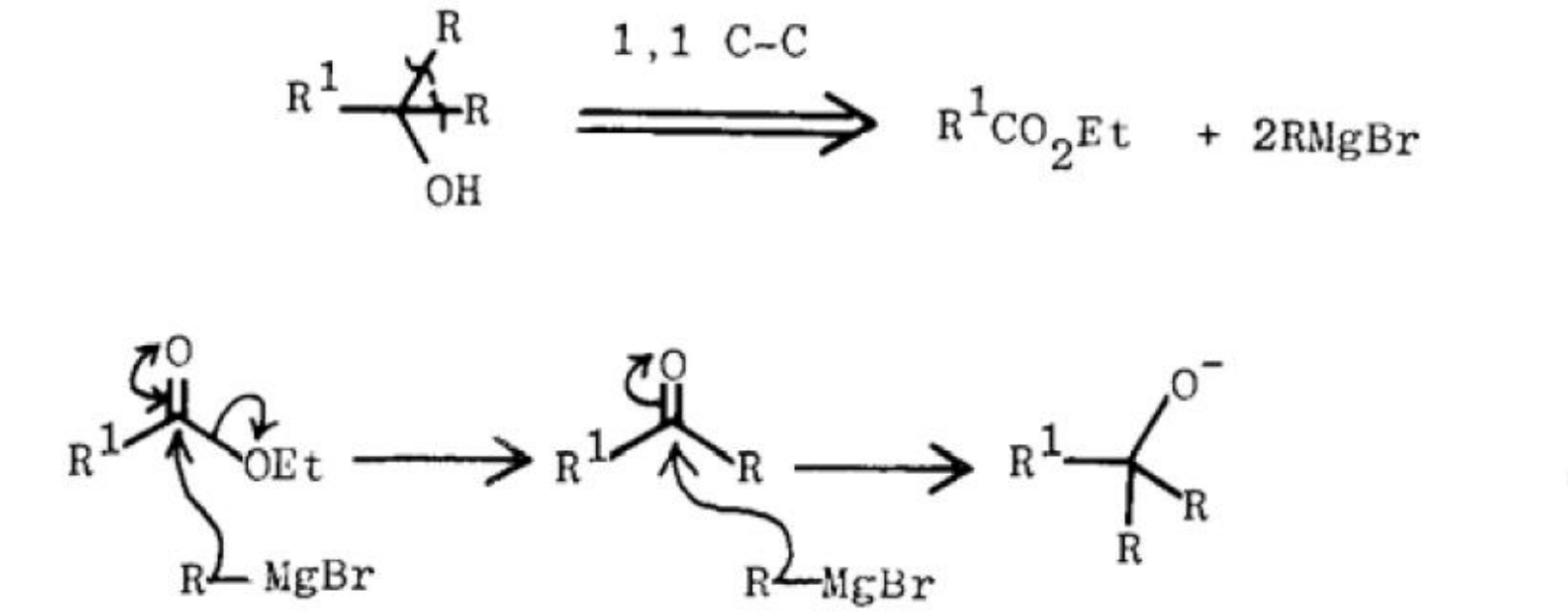

NMe2
O
Ph
O

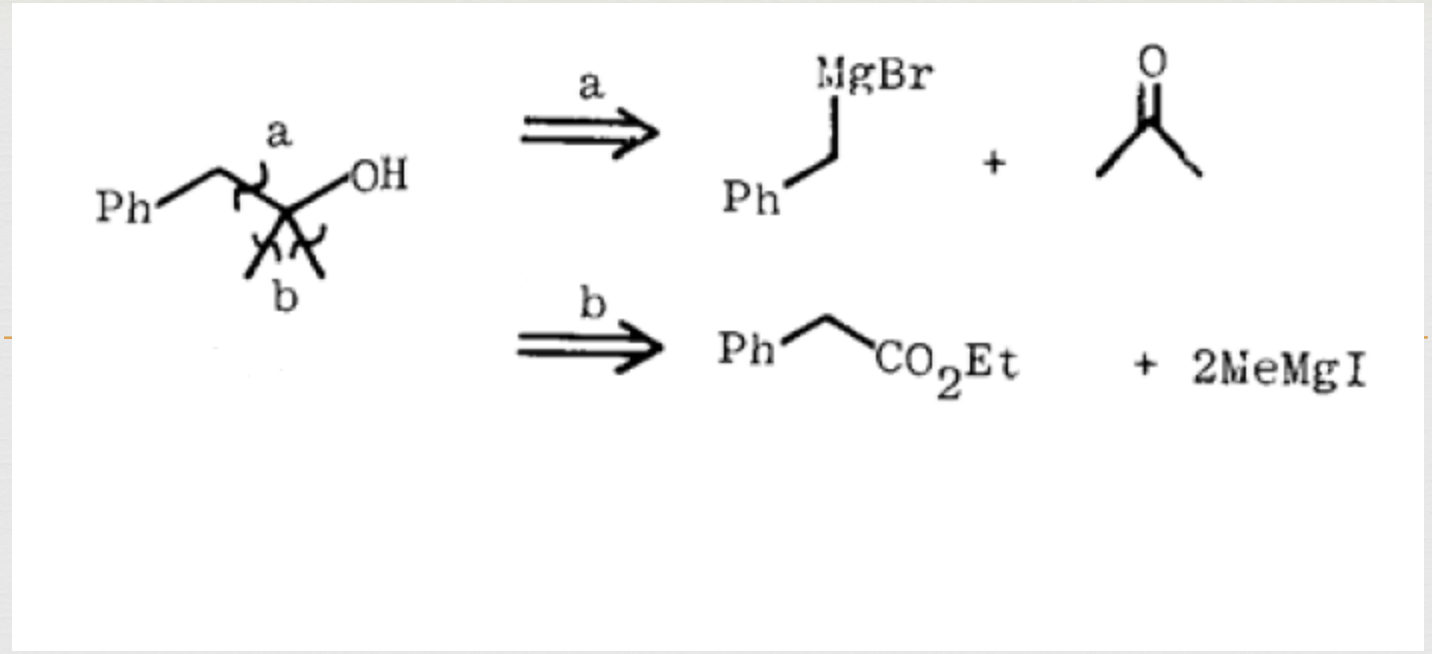

NMe2
O
Ph
O
C-O
ester
NMe2
Ph
OH
1,1
C-C

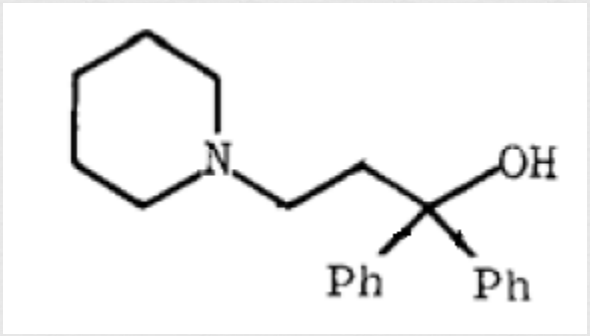

NMe2
O
1,3-diX
O
+
HNMe2

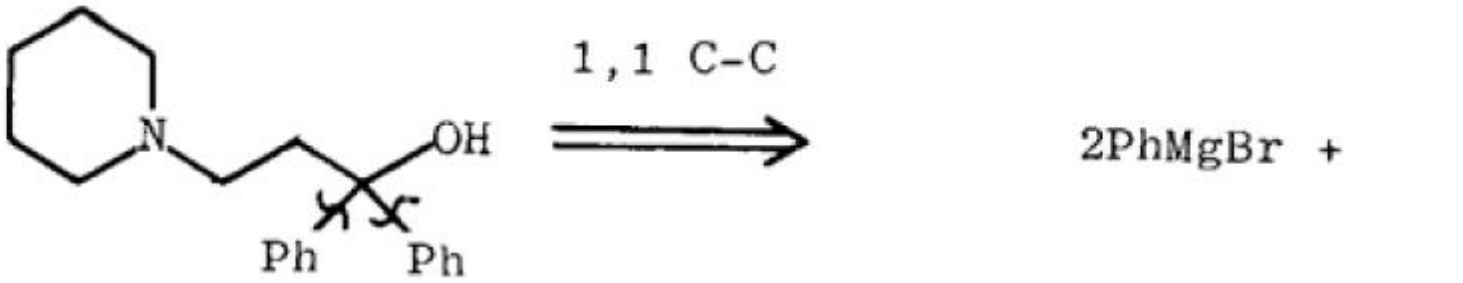
(A) (B)

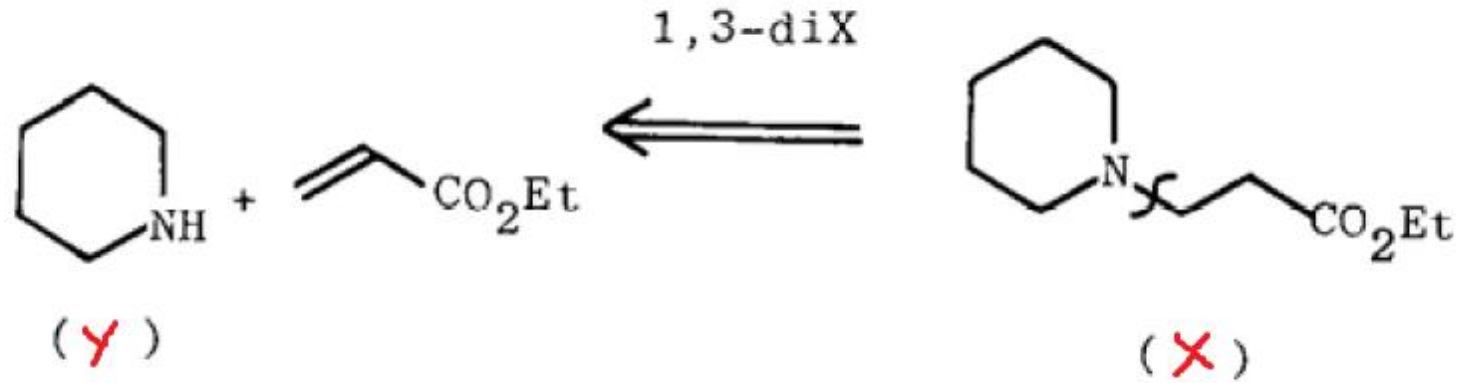

(B)
Et2O
Me2NH
(A)
PhLi
NMe2
Ph
OH
(EtCO)2O
pyridine
TM

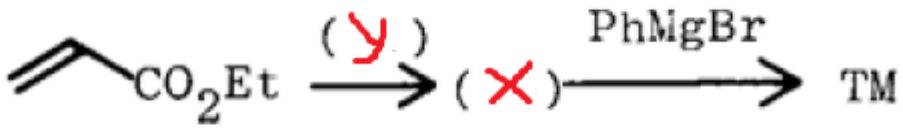

R
R1
R
OH
1,1 C-C
R1CO2Et + 2RMgBr
O
R1
OEt
R MgBr
O
R1
R
R MgBr
O−
R1
R
R


a
b
Ph
OH
a
MgBr
Ph
+
O
b
Ph
CO2Et
+ 2MeMgI


N
OH
Ph
Ph

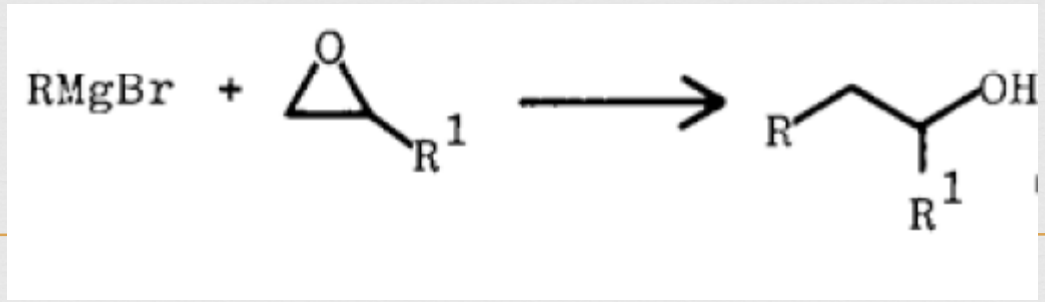

1,1 C-C
N
OH
Ph
Ph
2PhMgBr +

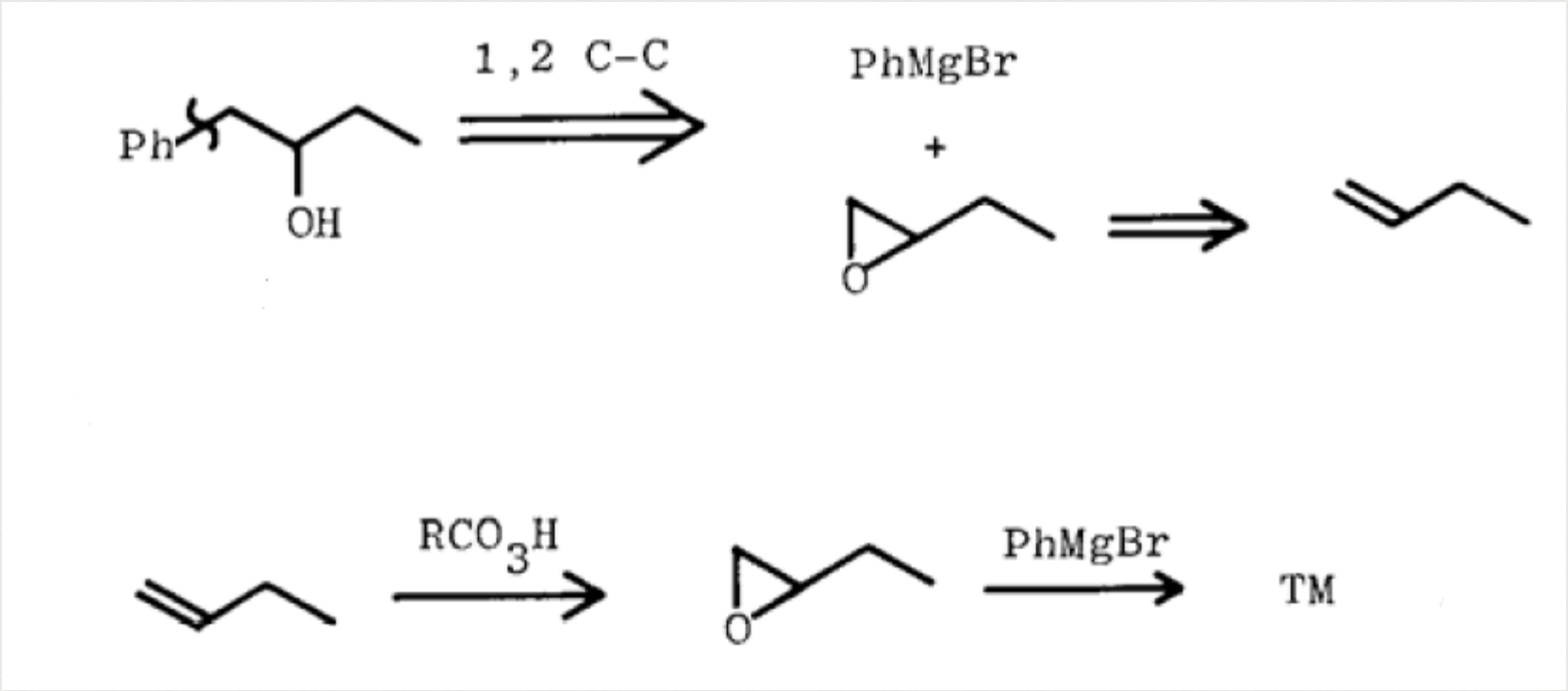

1,3-diX
NH
+
CO2Et
N
CO2Et
(Y)
(X)


CO2Et
(Y)
(X)
PhMgBr
TM

1,2 C-C disconnections



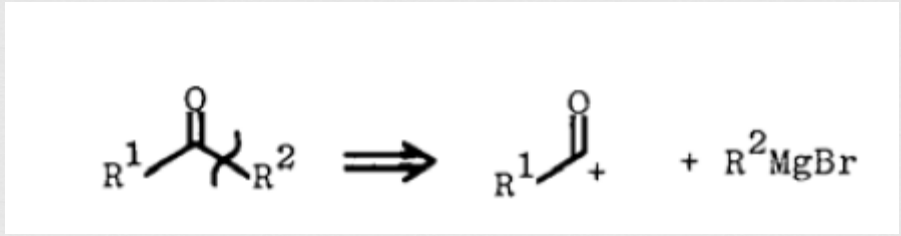

RMgBr
+
O
R1
OH
R
R1

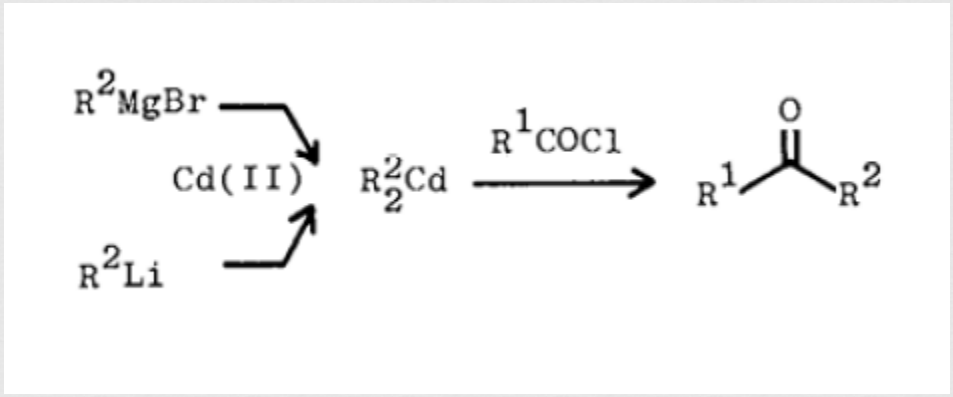

1,2 C-C
Ph
OH
PhMgBr
+
O
RCO3H
O
PhMgBr
TM

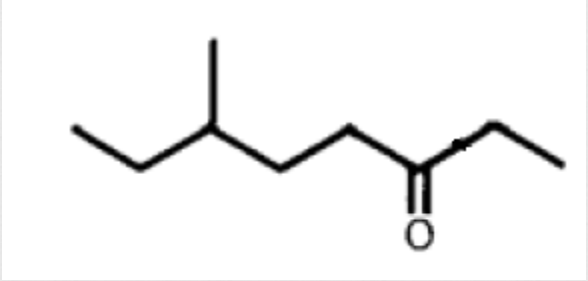
C-C disconnection of carbonyl compounds

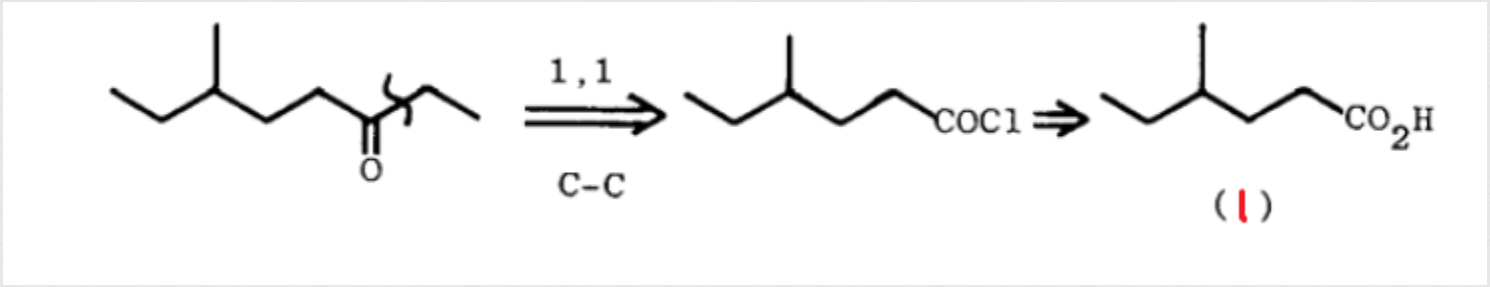


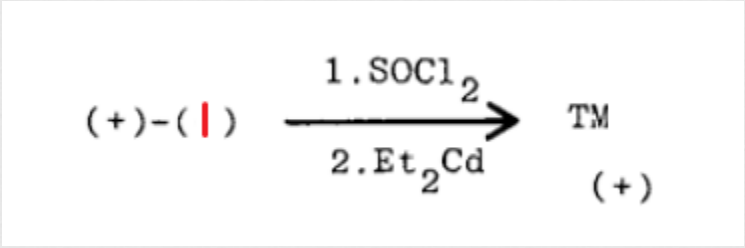
1,1 C-C disconnections

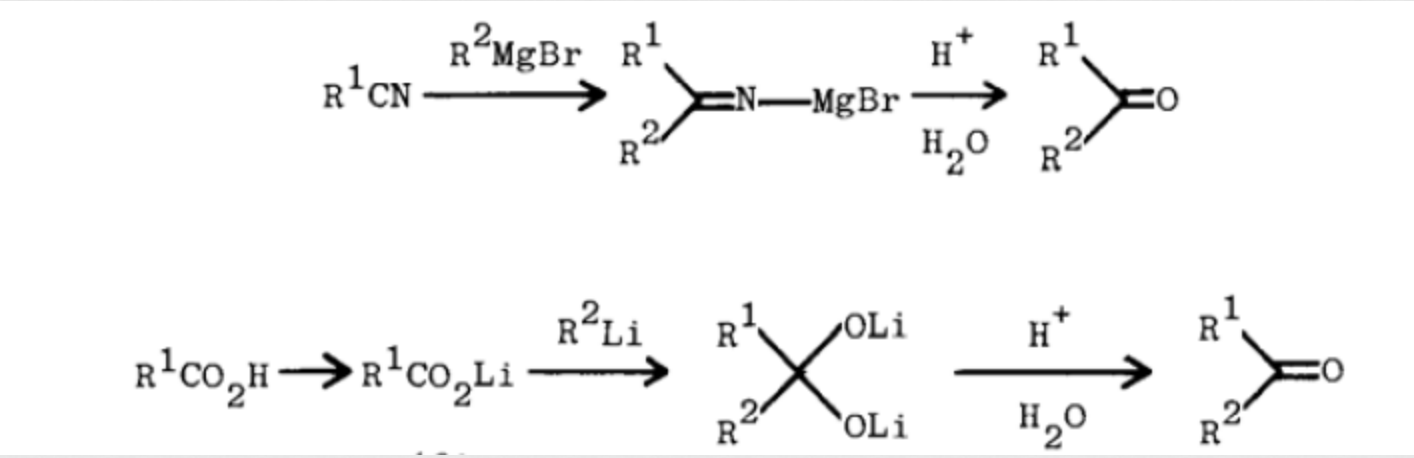





O

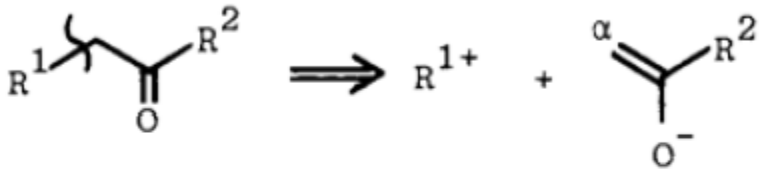

1,1
C-C
COCl
CO_2H
(|)


(+)-(|)
1. $SOCl_2$
2. Et_2Cd
TM
(+)

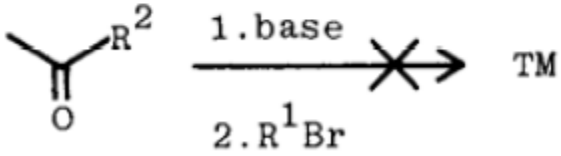

R1CN
R2MgBr
R1
R2
N—MgBr
H+
H2O
R1
R2
O
R1CO2H
R1CO2Li
R2Li
R1
R2
OLi
OLi
H+
H2O
R1
R2
O

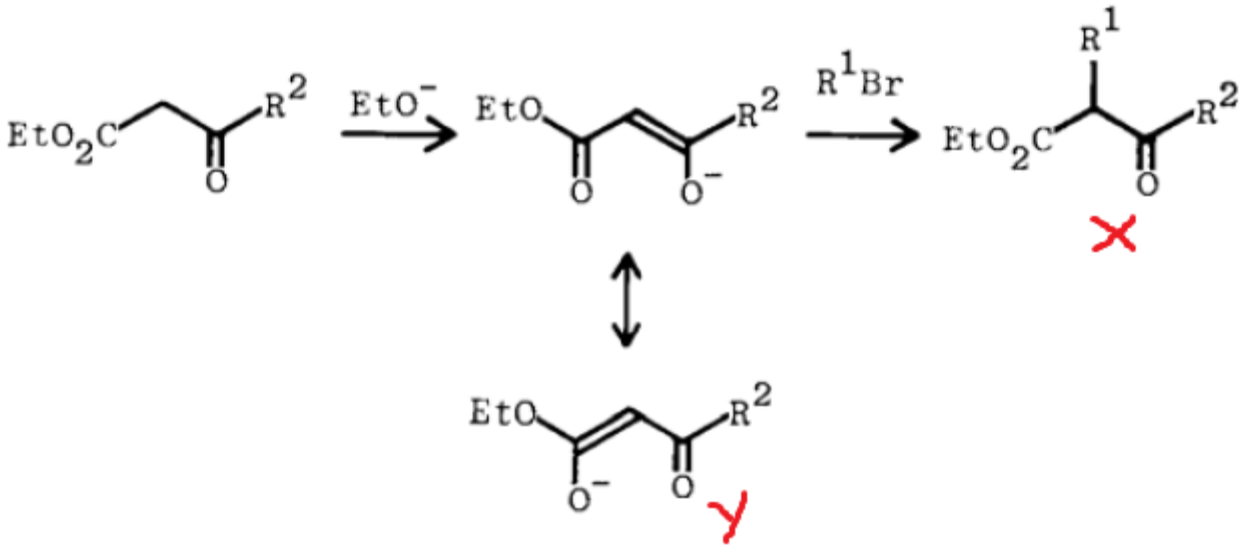
1,2 C-C disconnections: carbonyl compounds by alkylation of enols

Analysis

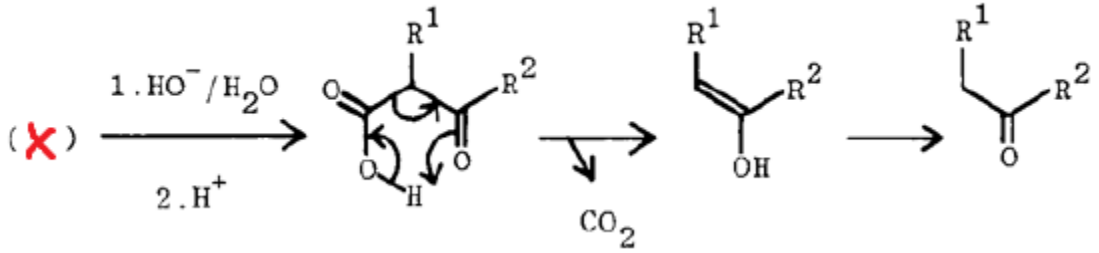


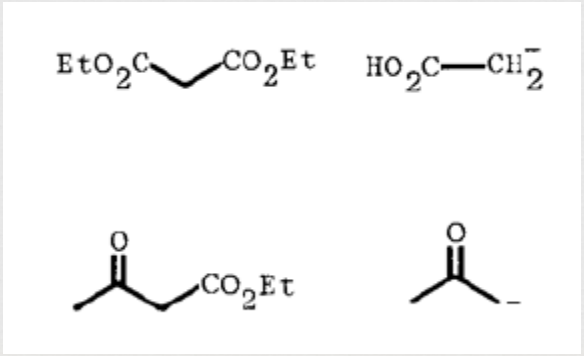
Synthesis (no good)



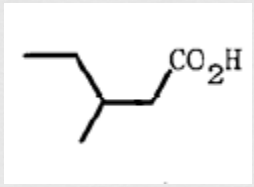


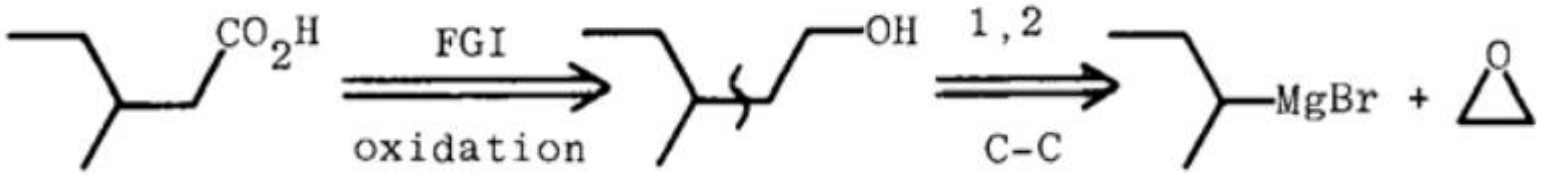
Activating group must be removed easily once the reaction is over. Hydrolysis of X gives acid which gives ketone after lossing CO2





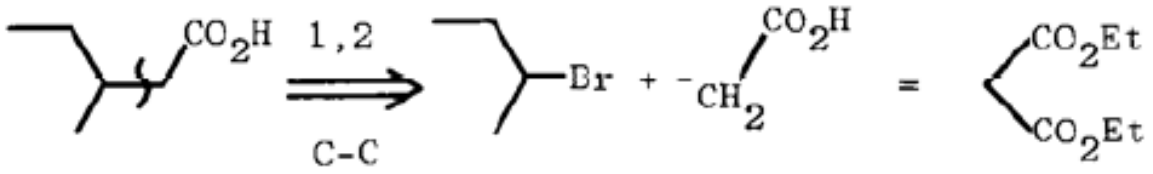
Malonate and acetoacetate esters are used as reagents for the synthons (activated versions of acetic acid and acetone).


CO2H

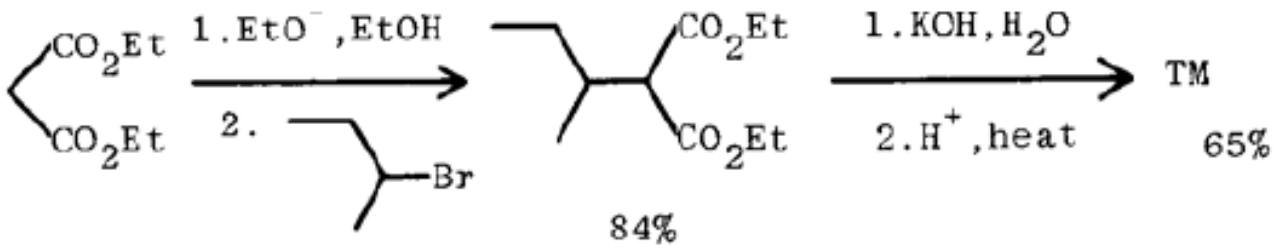


The acid can be synthesized by oxidation of alcohol.
Alternative is to disconnect at branch point and use malonic ester.

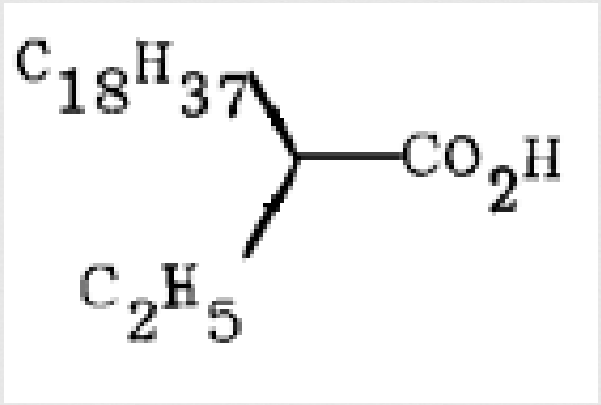
Analysis

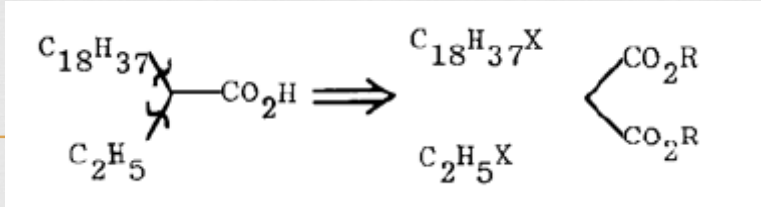


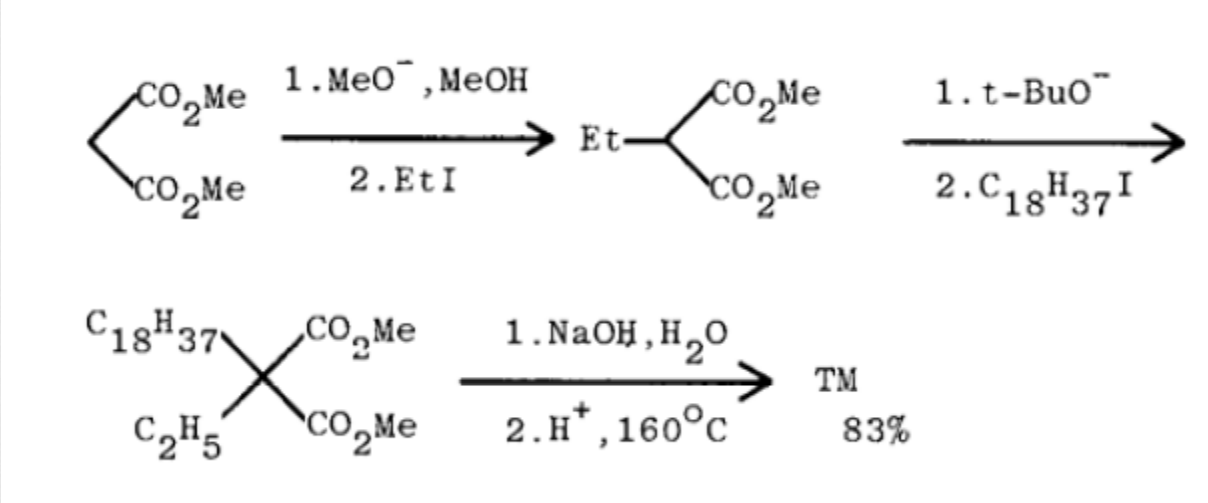
Synthesis

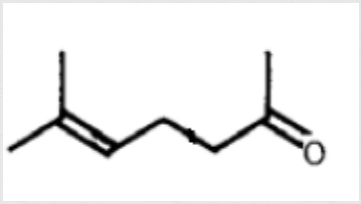


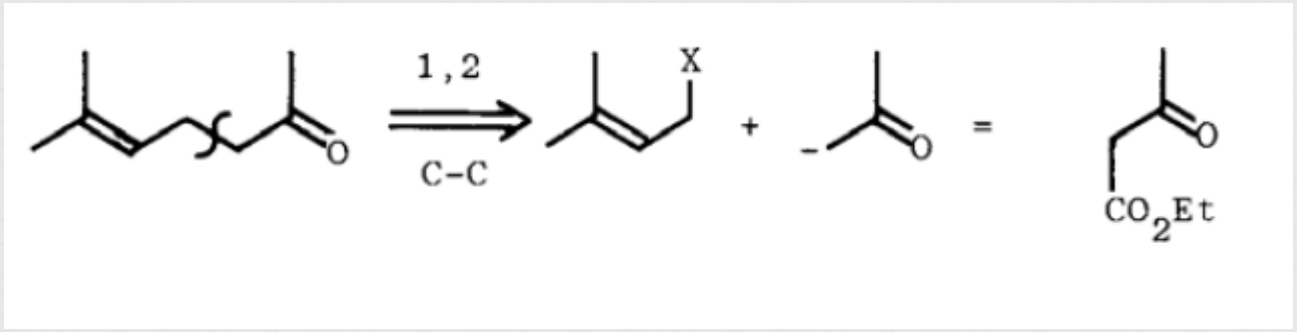
- The process can be repeated to make acids with branched chains at alpha atom
- Order of disconnection is not important
- Long chain fatty acids can be made by this method

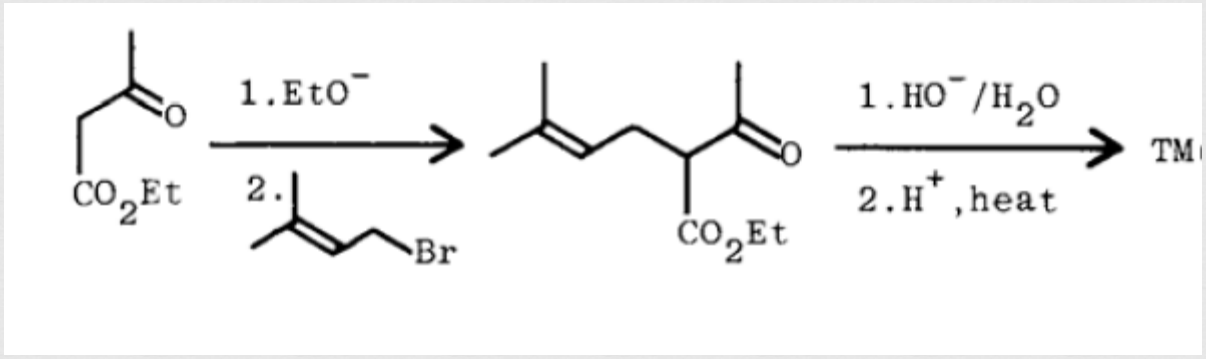



C18H37
CO2H
C2H5
C18H37X
C2H5X
CO2R
CO2R

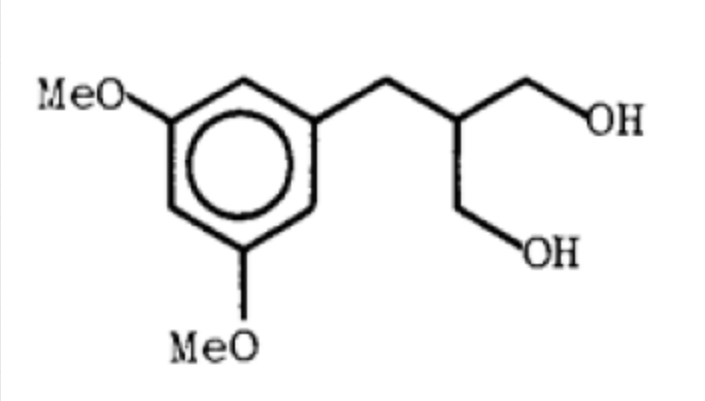

CO2Me
CO2Me
1. MeO⁻, MeOH
2. EtI
Et
CO2Me
CO2Me
1. t-BuO⁻
2. C18H37I
C18H37
C2H5
CO2Me
CO2Me
1. NaOH, H2O
2. H⁺, 160°C
TM
83%

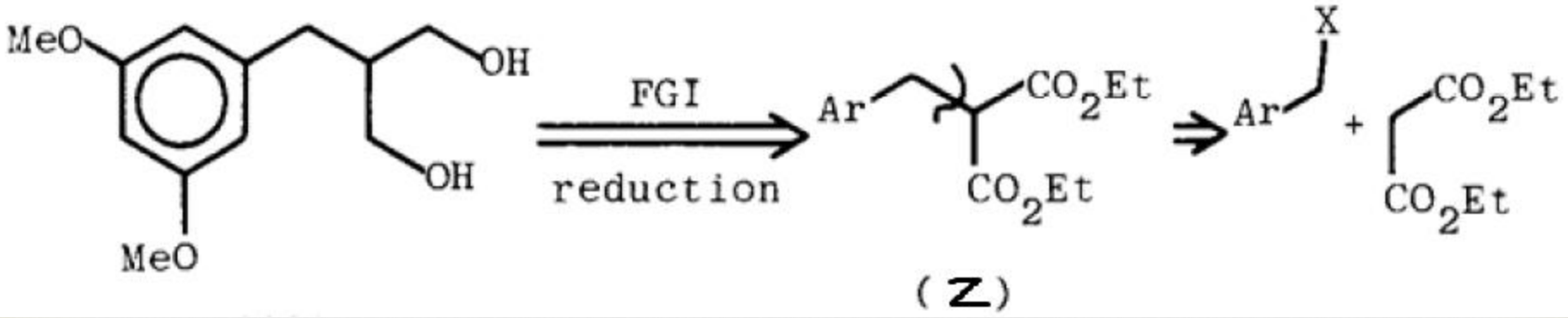

O


1,2
C-C
X
+
=
O
O
CO2Et

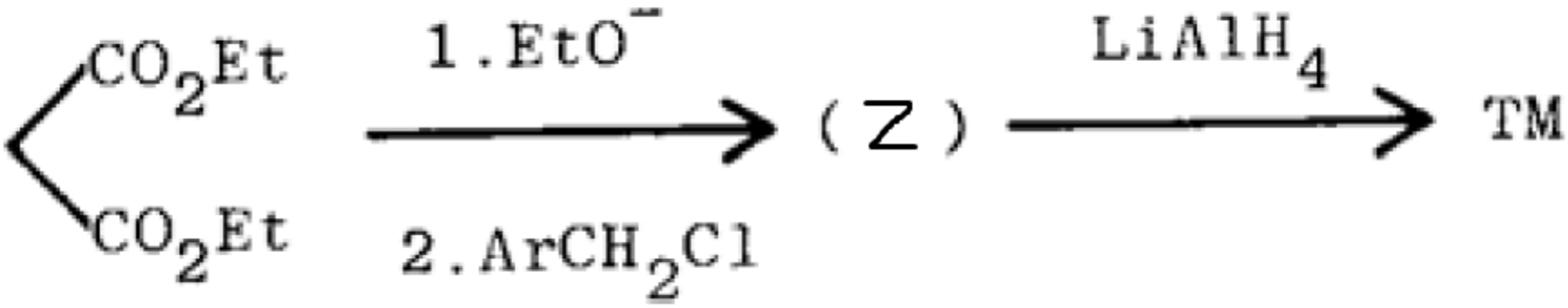

1.EtO⁻
2.
Br
O
CO2Et
1.HO⁻/H2O
2.H⁺,heat
TM

All usual FGIs can be carried out on these alkylated products
An important one is to reduce activating group instead of removing it

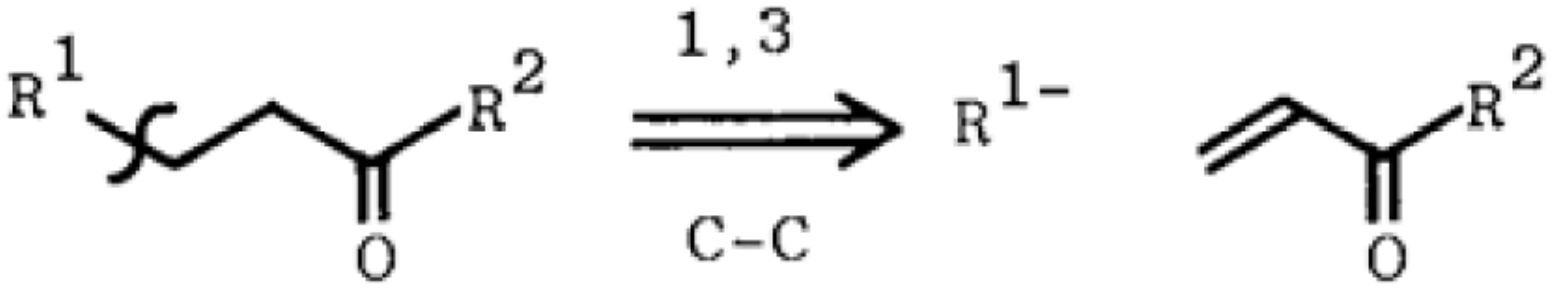


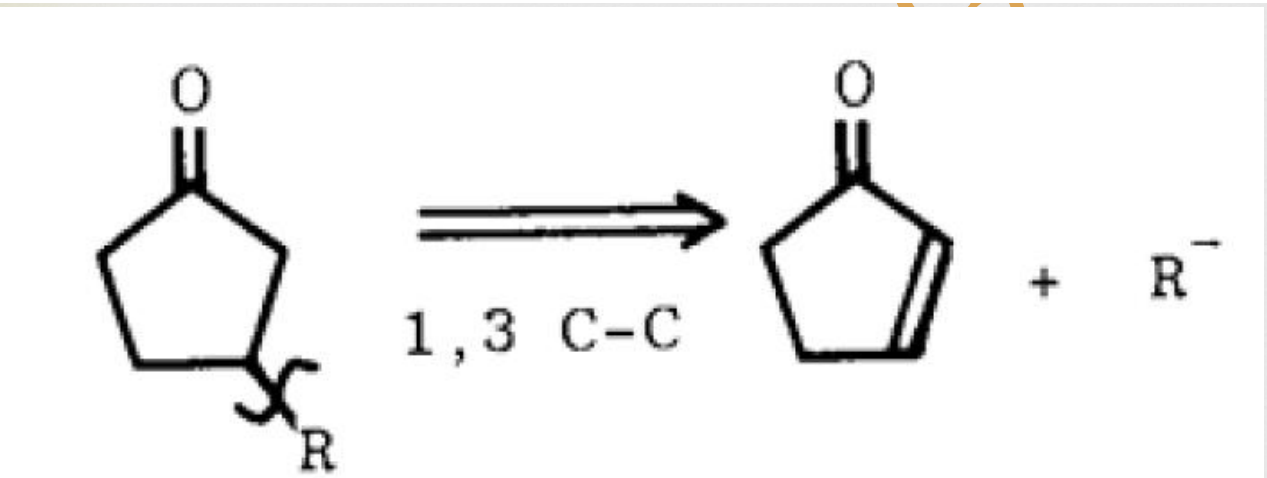

MeO
OH
OH
MeO
FGI
reduction
Ar
CO2Et
CO2Et
X
Ar
+
CO2Et
CO2Et

(Z)

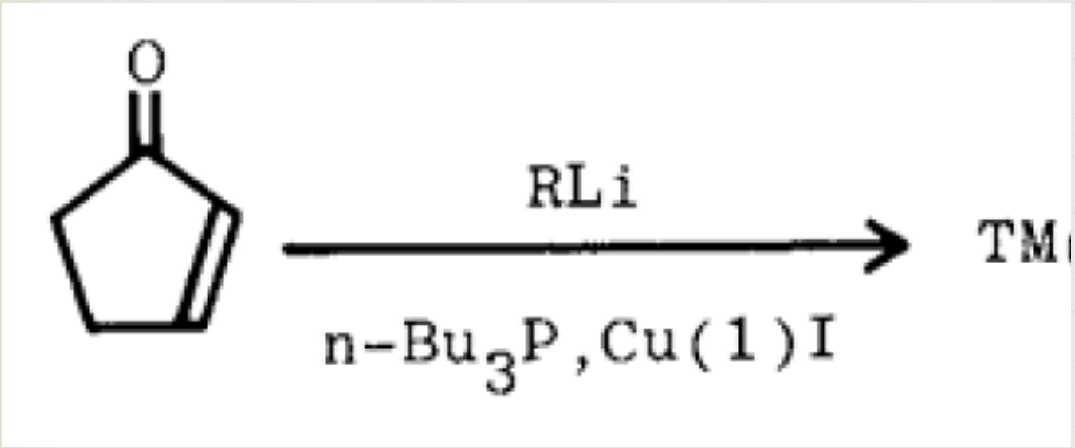

CO2Et
CO2Et
1. EtO⁻
2. ArCH2Cl
(Z)
LiAlH4
TM

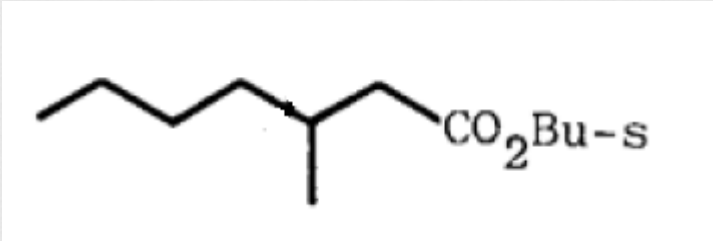
1,3 C-C disconnections: carbonyl compounds by Michael addition



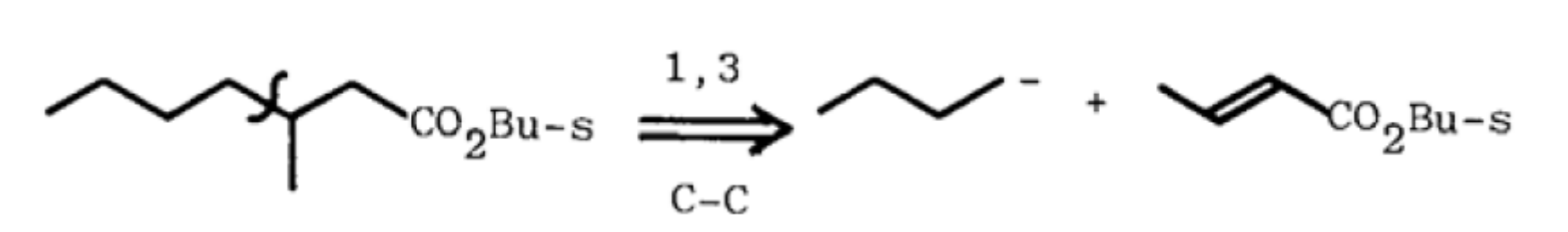


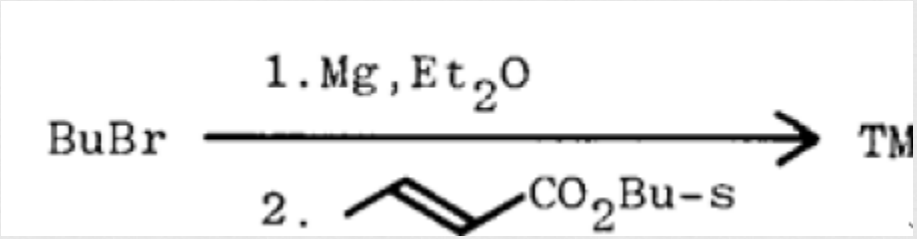
We can look for this disconnection when there is branch point at beta or gamma carbon and particulary when the bond to be disconnected joins a ring to the chain




CO2Bu-s

Where we have a choice, it is better to disconnect the longer chain to get back to simple starting materials





Aromatic compounds are good enough nucleophiles to add in this way under Friedel-Crafts conditions so that it is not necessary to make organometallic reagent in the synthesis

