Two-group C-X disconnections

1,1-difunctionalised compounds

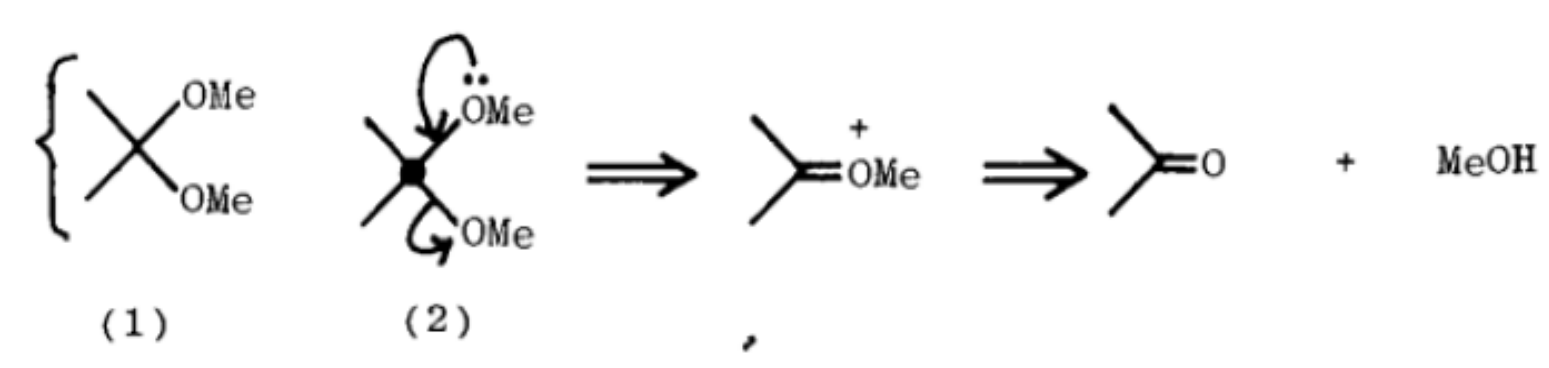
1,2-difunctionalised compounds

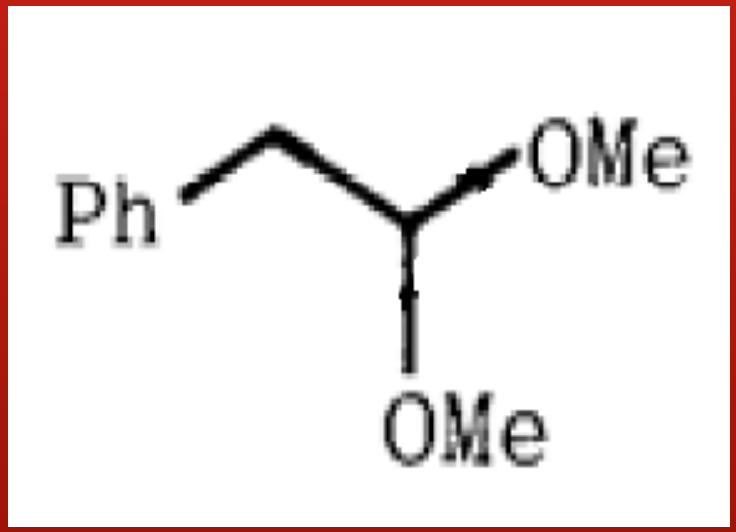
1,3-difunctionalised compounds

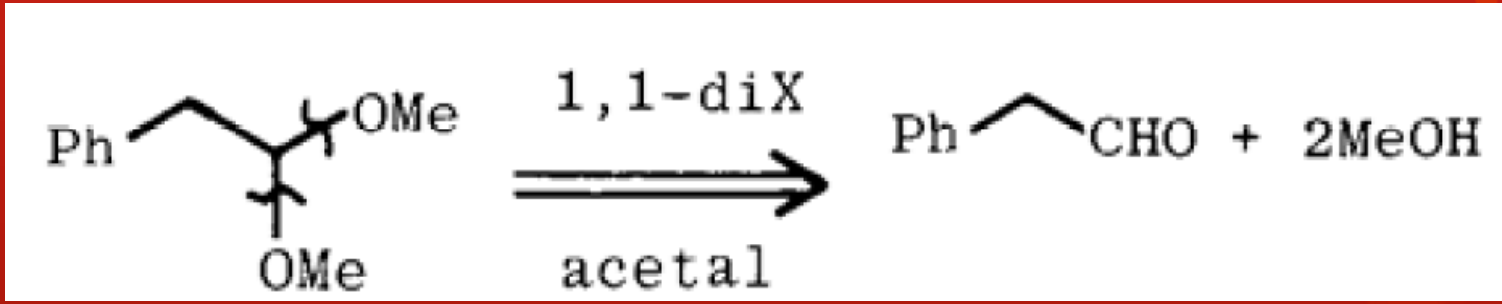
1,1-difunctionalised compounds

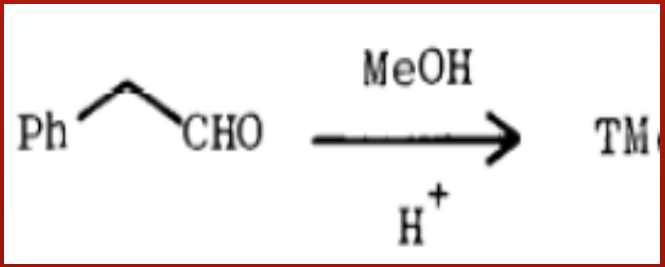
In one-group disconnection, we have to recognize a single functional group and the disconnection corresponded to a reliable reaction to make that functional group.

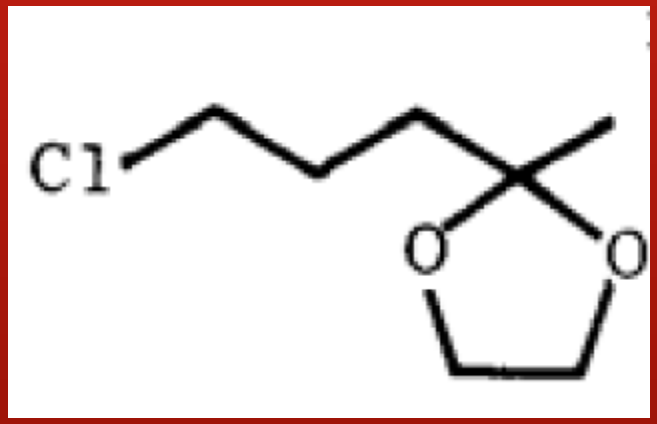
An important extension is to use a functional group to help disconnect another elsewhere in the molecule

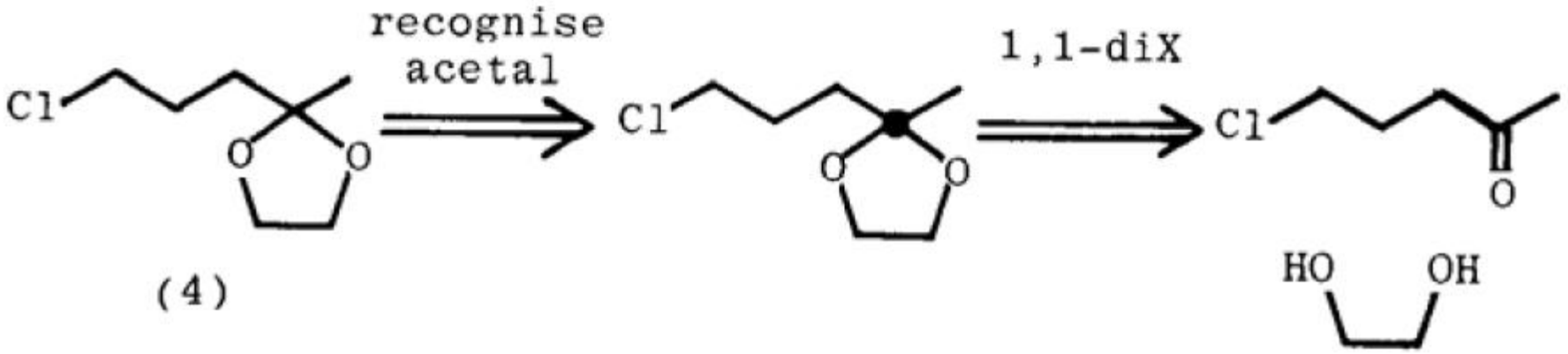



Ph
OMe
OMe

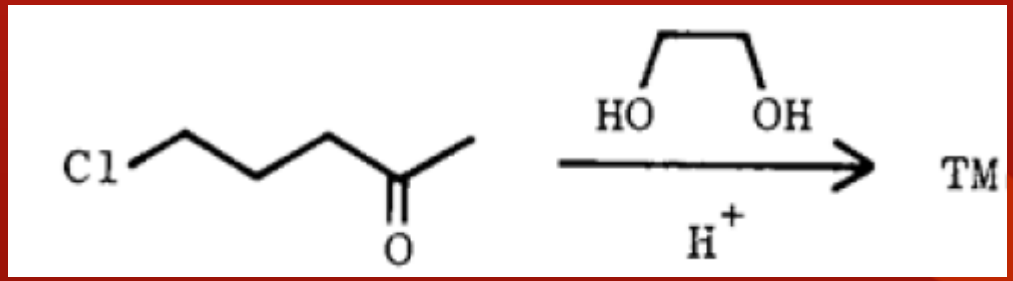

Ph
OMe
OMe
1,1-diX
acetal
Ph
CHO + 2MeOH

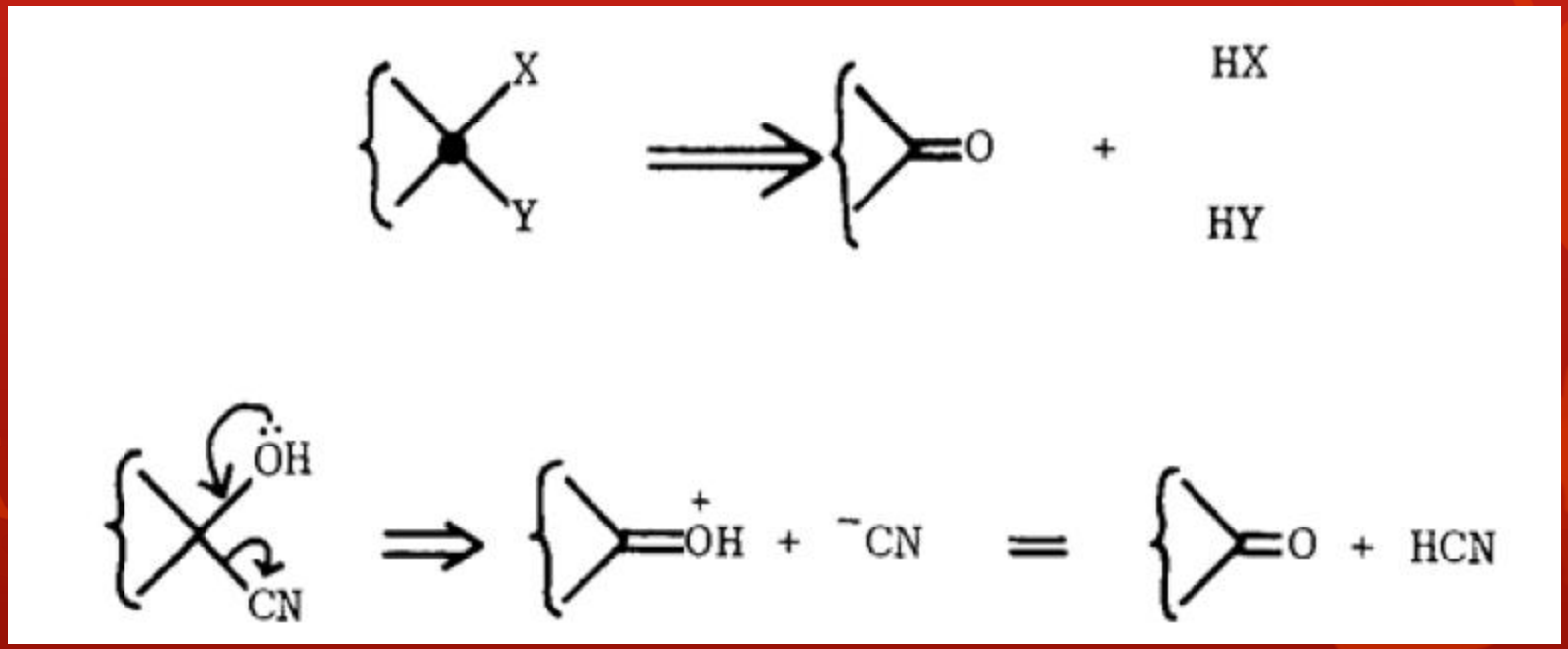

Ph
CHO
MeOH
H+
TM

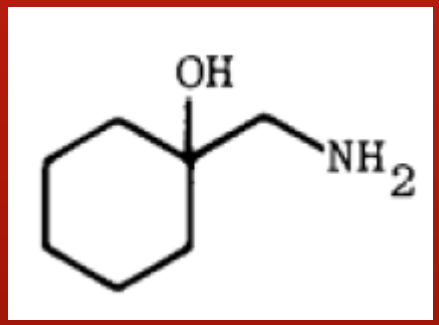

Cl
O
O

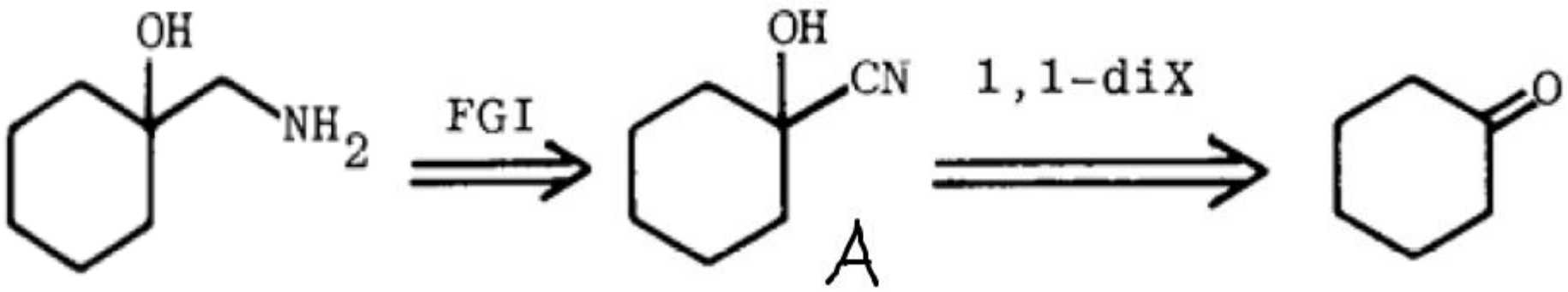


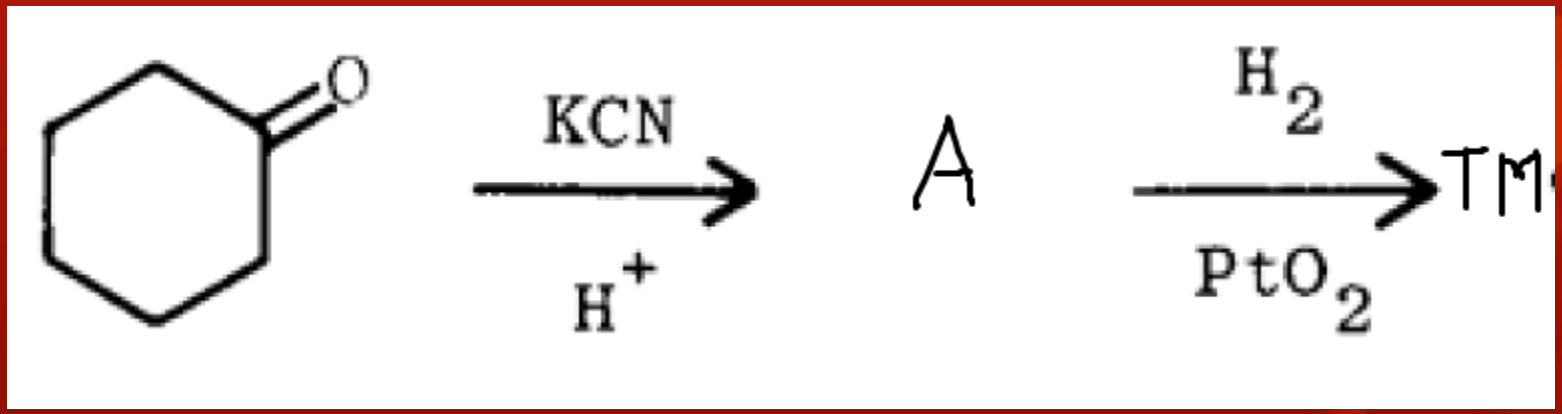
(4)

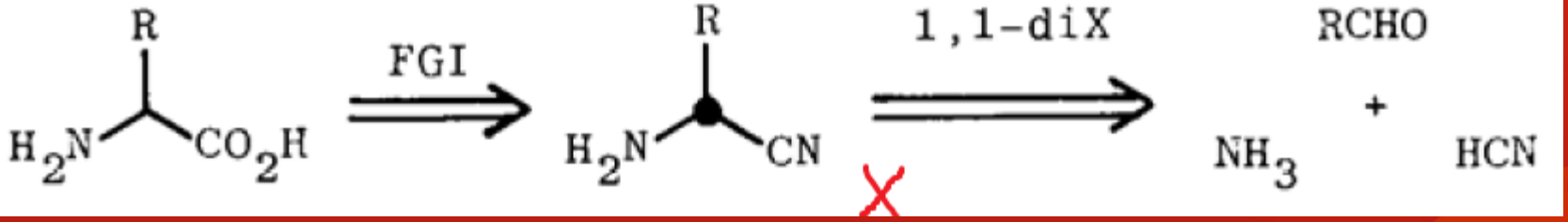


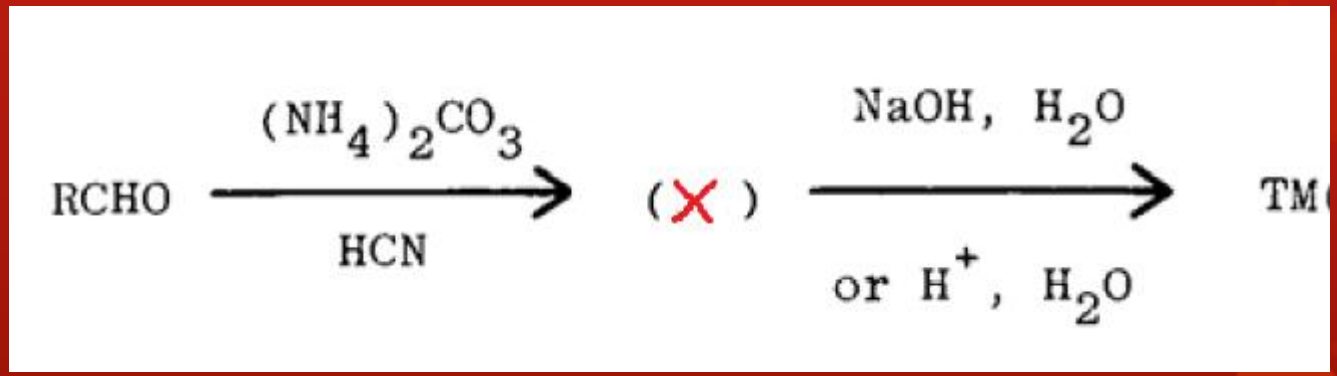

X
Y
O
+
HX
HY
ÖH
CN
+
OH
+
⁻CN
O
+
HCN

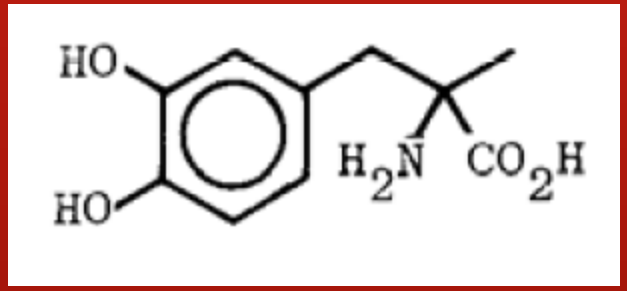

OH
NH2

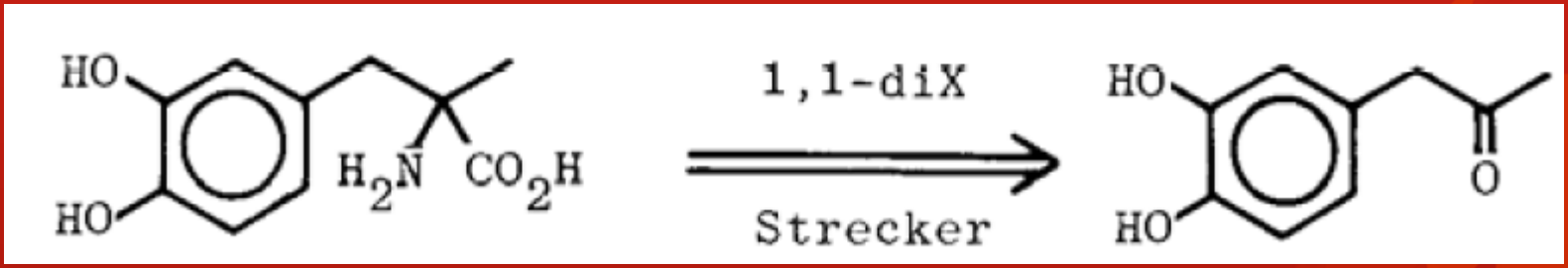

OH
NH2
FGI
OH
CN
A
1,1-diX
O

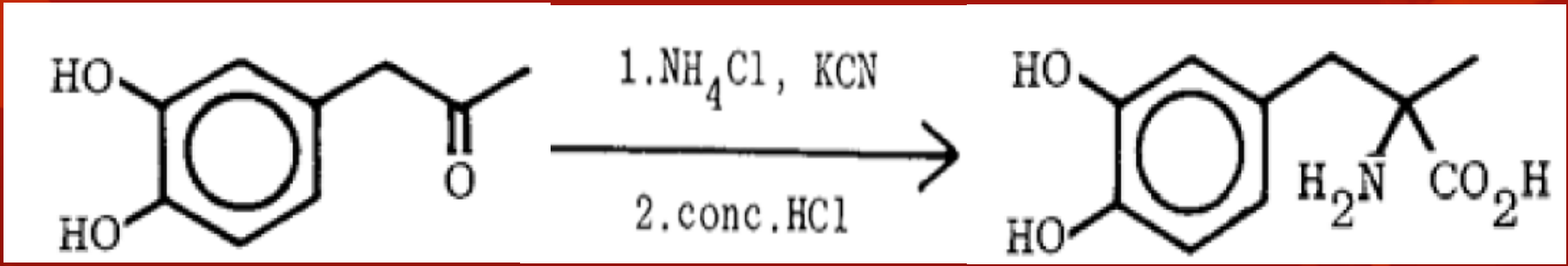

O
KCN
H+
A
H2
PtO2
TM


R
H2N
CO2H
FGI
R
H2N
CN
1,1-diX
RCHO
+
NH3
HCN

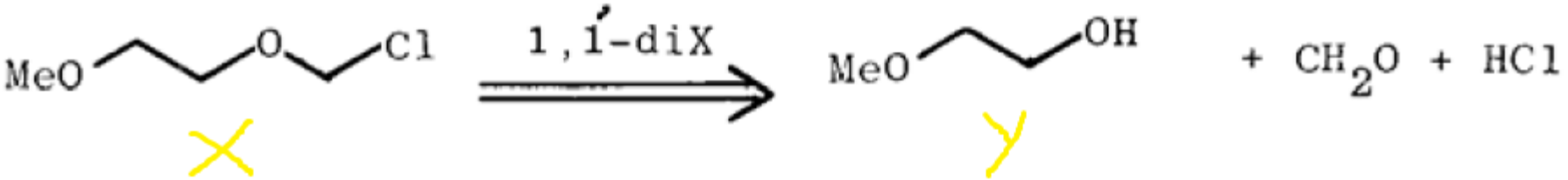

RCHO
(NH4)2CO3
HCN
NaOH, H2O
or H+, H2O
TM

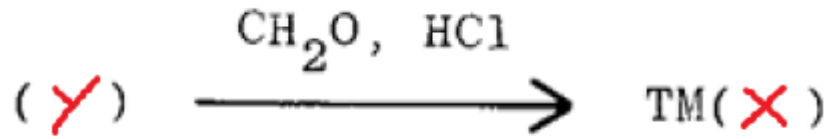

HO
HO
H2N
CO2H


HO
HO
H2N
CO2H
1,1-diX
Strecker
HO
HO
O

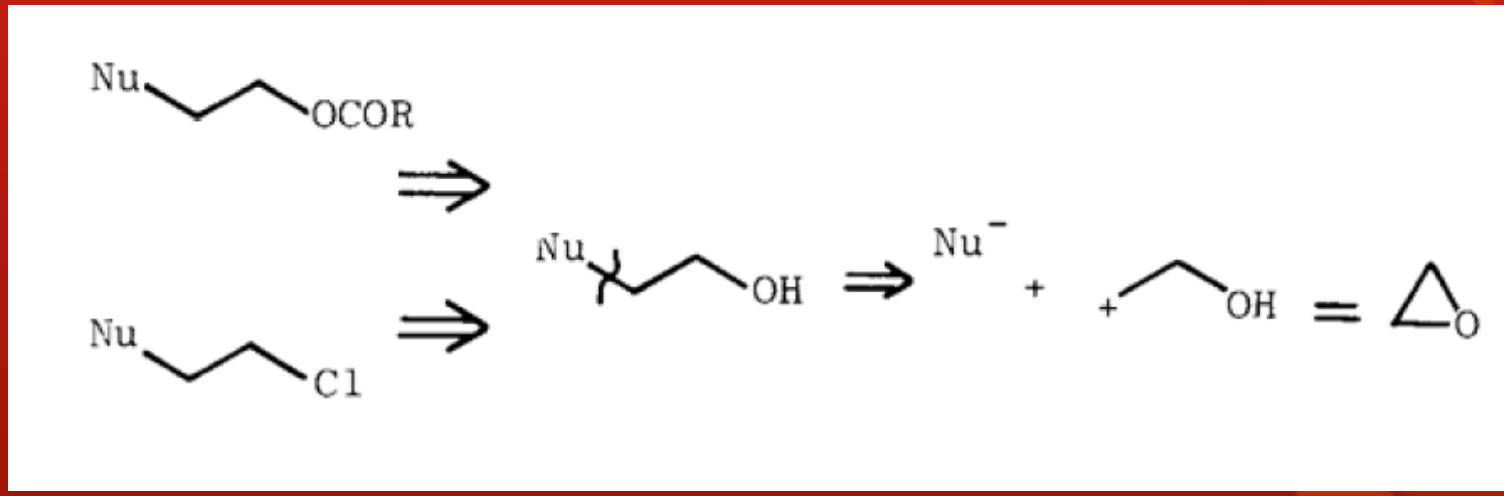

HO
HO
O
1.NH4Cl, KCN
2.conc.HCl
HO
HO
H2N
CO2H


RO
Cl
ROH
O
HCl

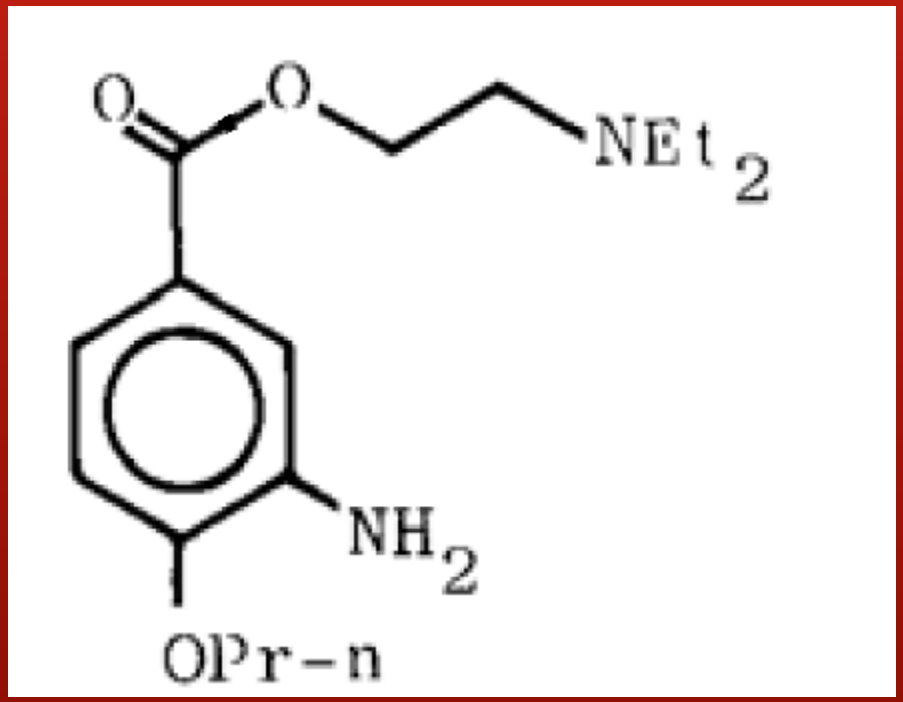

MeO
O
Cl
1,1'-diX
MeO
OH
+ CH2O + HCl


CH2O, HCl
(Y)
TM(X)

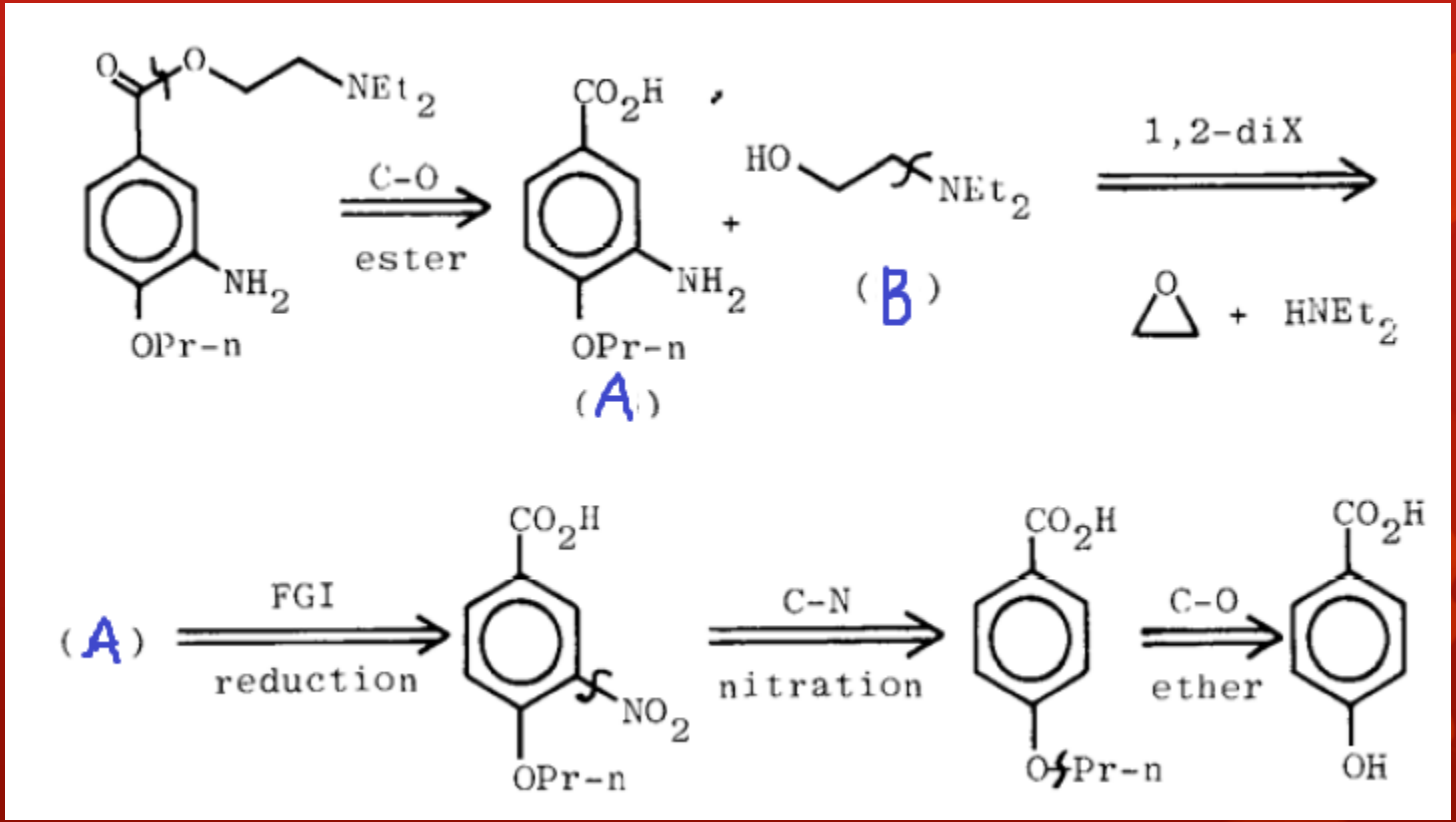
1,2-difunctionalised compounds


Nu
OCOR
Nu
Cl
Nu
OH
Nu⁻
+
+
OH
O

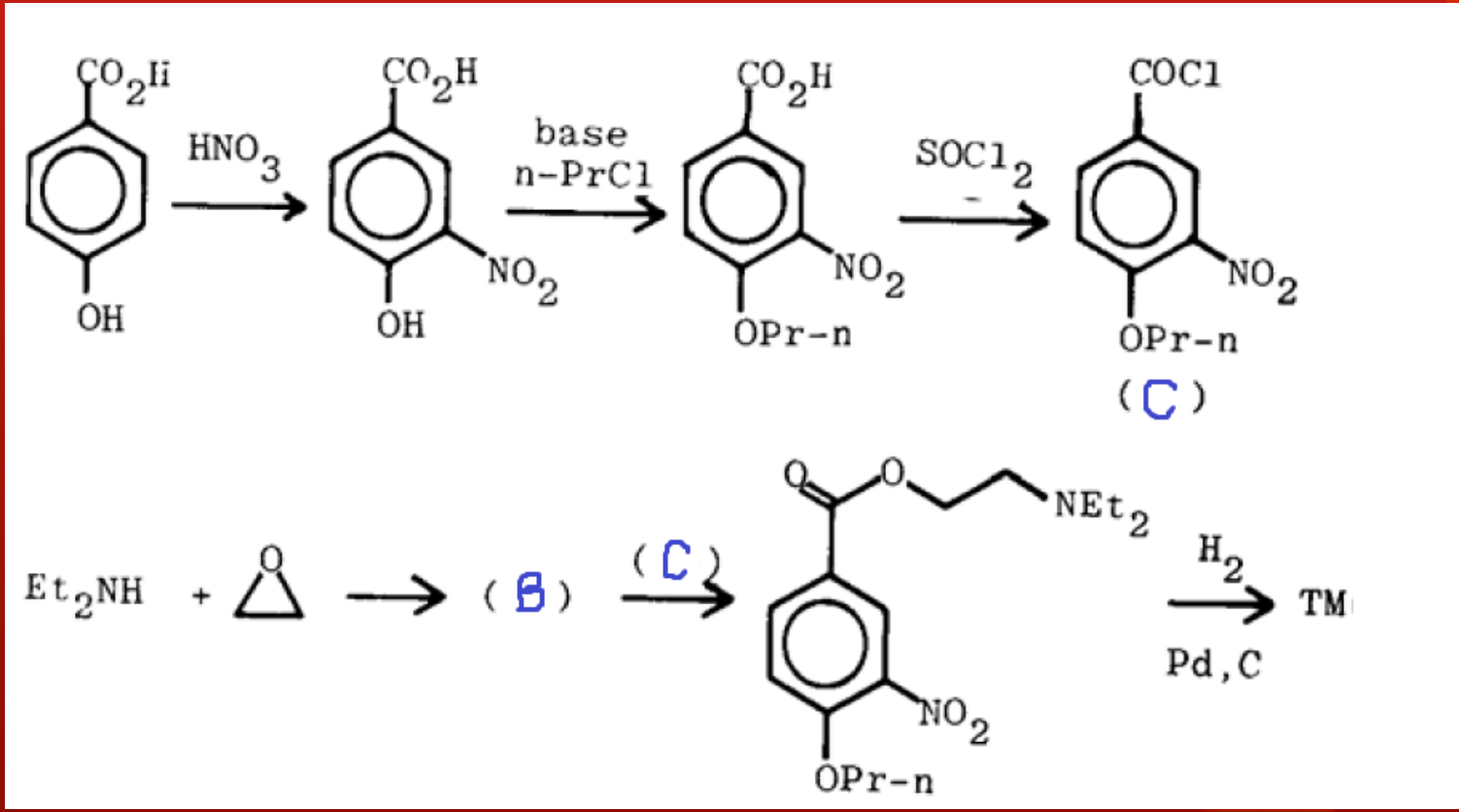
1,2-difunctionalised compounds

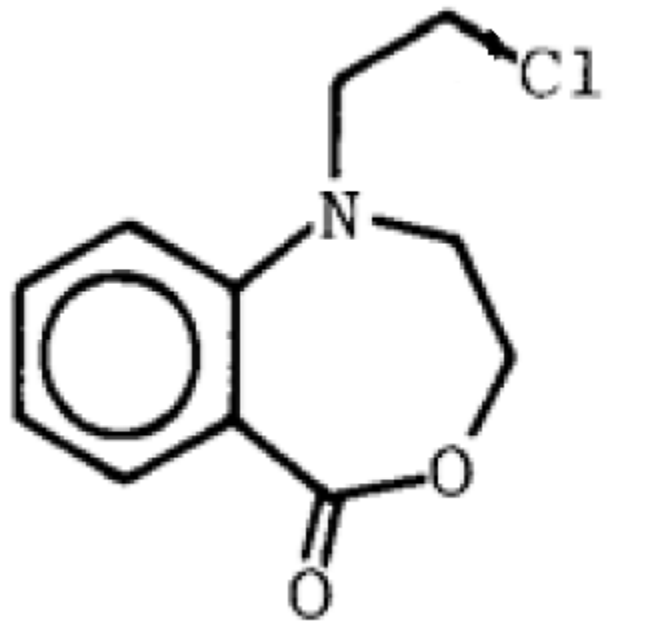


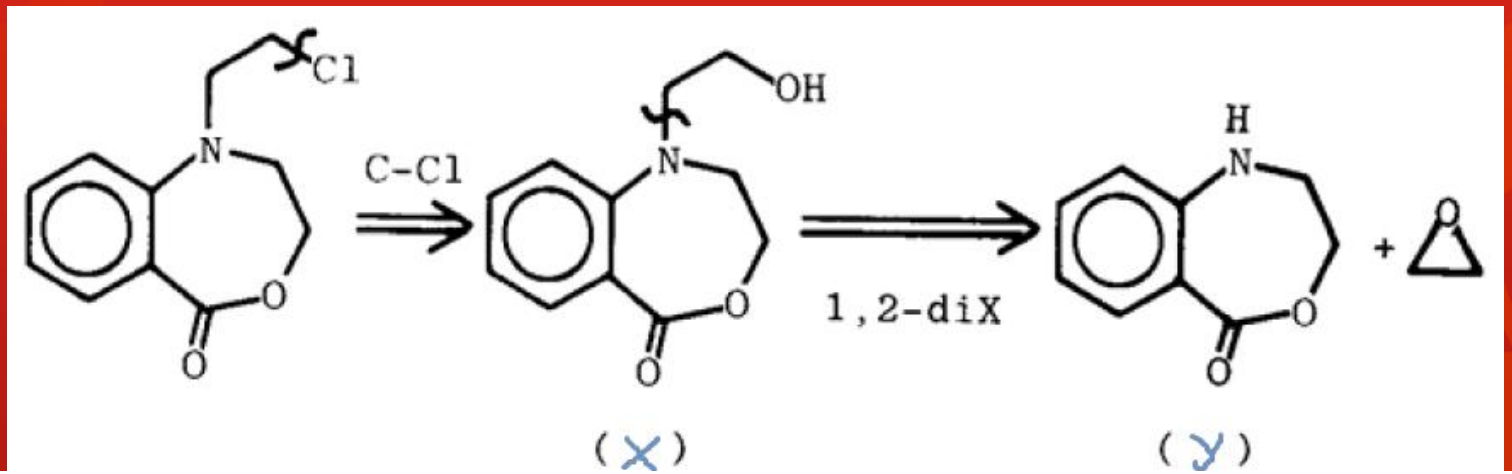
1,2-difunctionalised compounds: Proparacaine

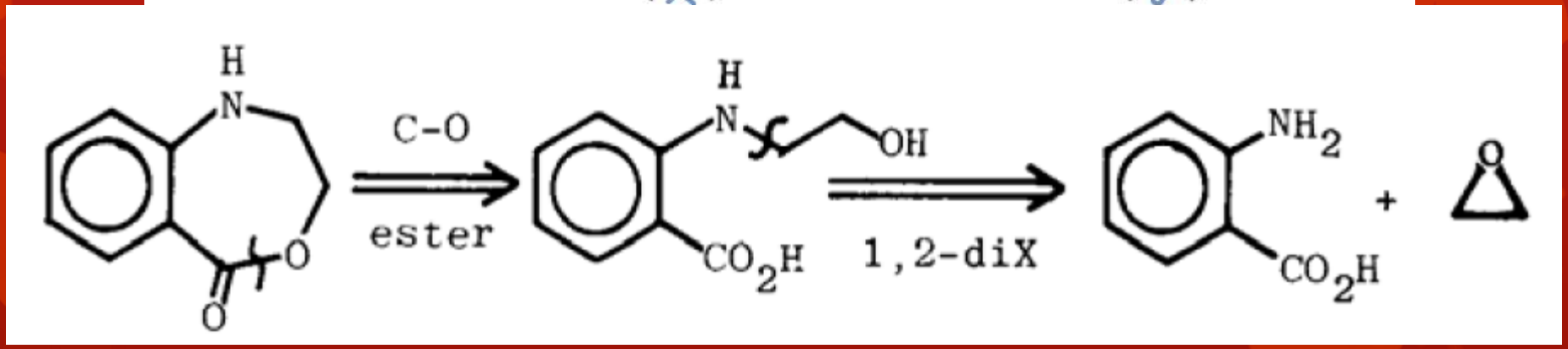


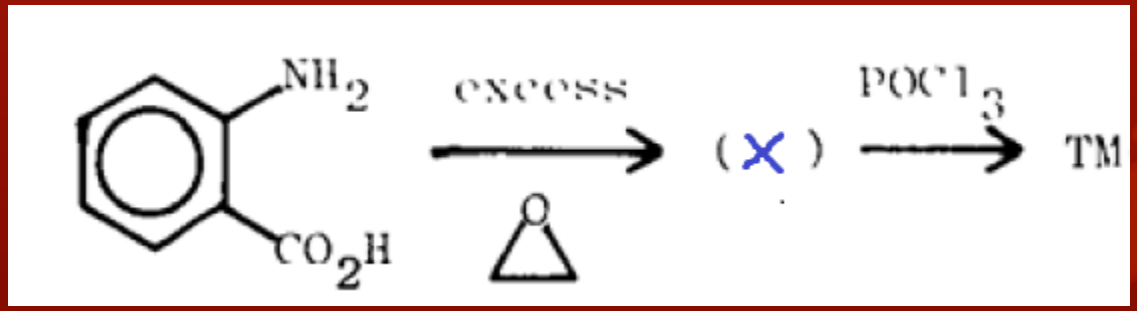
1,2-difunctionalised compounds: Proparacaine

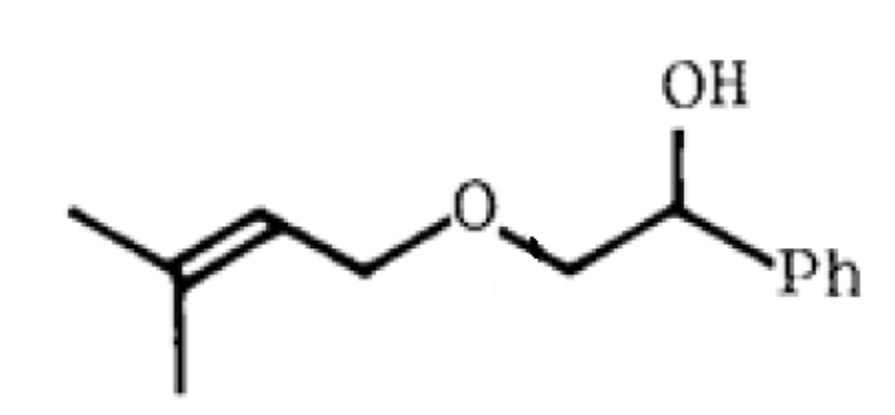


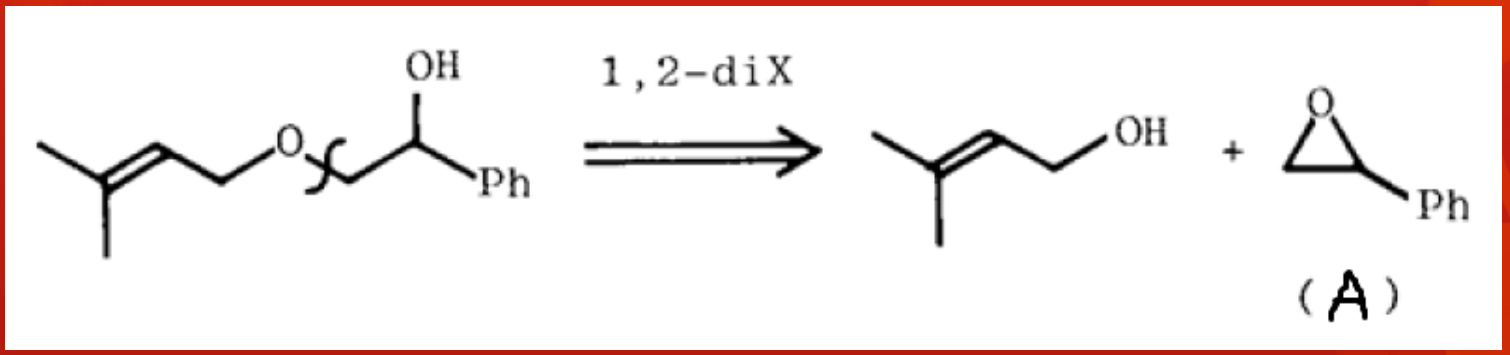

Cl
N
O
O

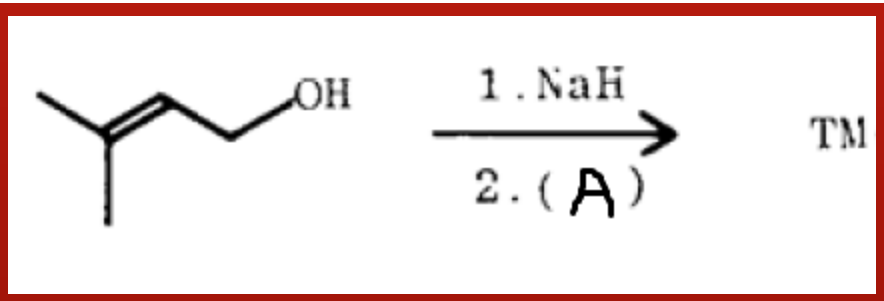

Cl
C-Cl
OH
1,2-diX
H
(X)
(Y)

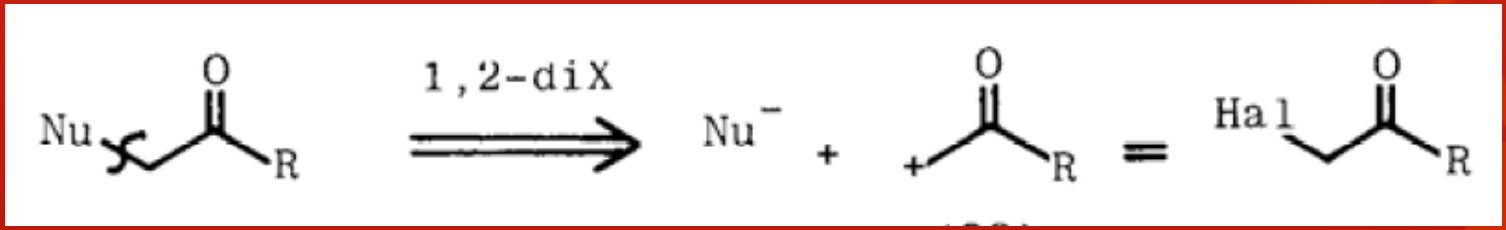

H
C-O
ester
OH
CO_2H
1,2-diX
NH_2
CO_2H

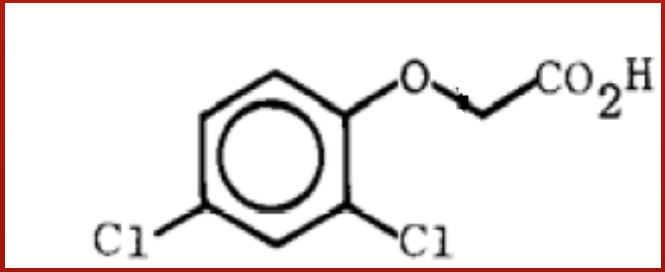

NH_2
CO_2H
excess
(X)
$POCl_3$
TM

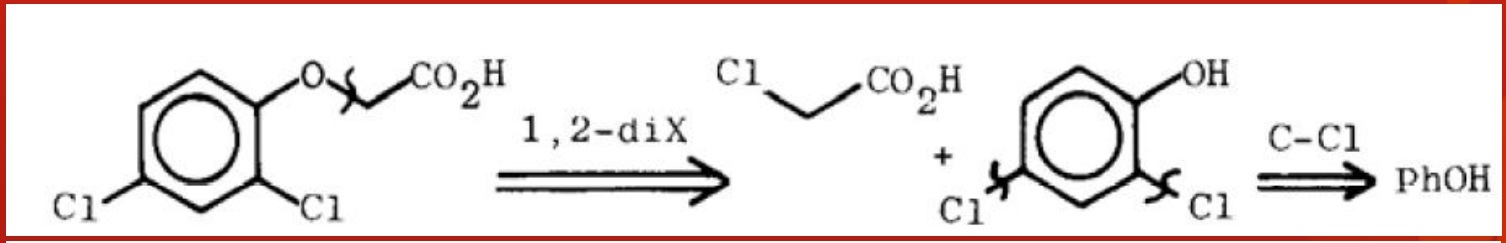

OH
O
Ph

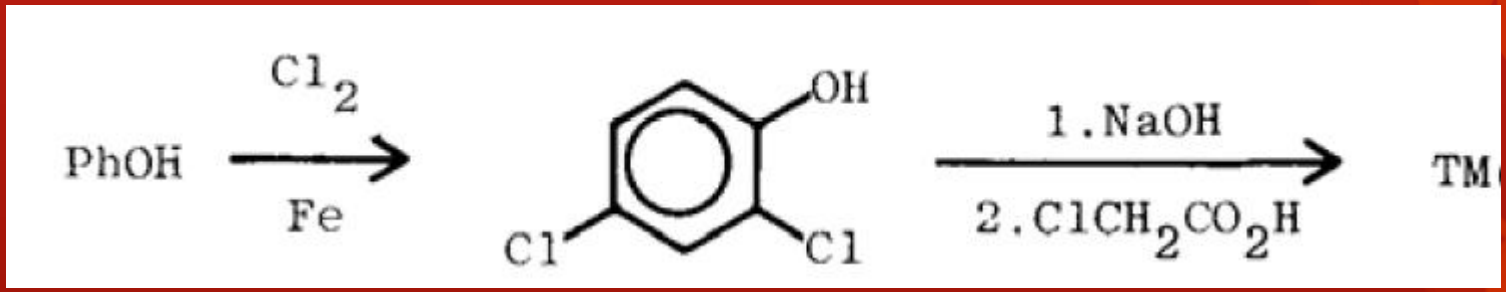

OH
O
Ph
1,2-diX
OH
O
Ph
(A)

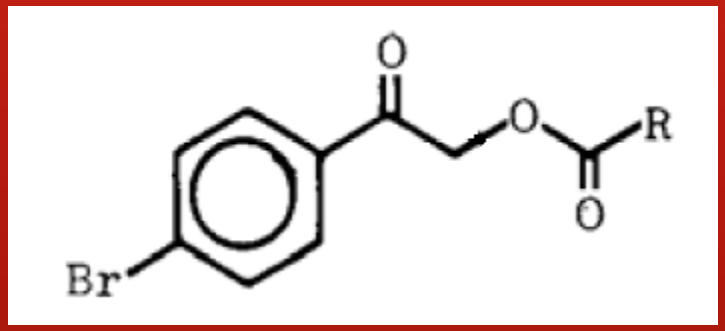

OH
1.NaH
2.(A)
TM

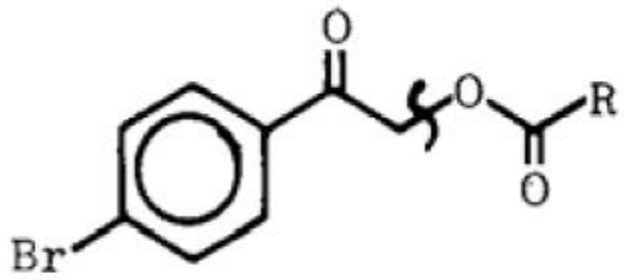

Nu
O
R
1,2-diX
Nu⁻
+
O
R
=
Hal
O
R


O
CO2H
Cl
Cl

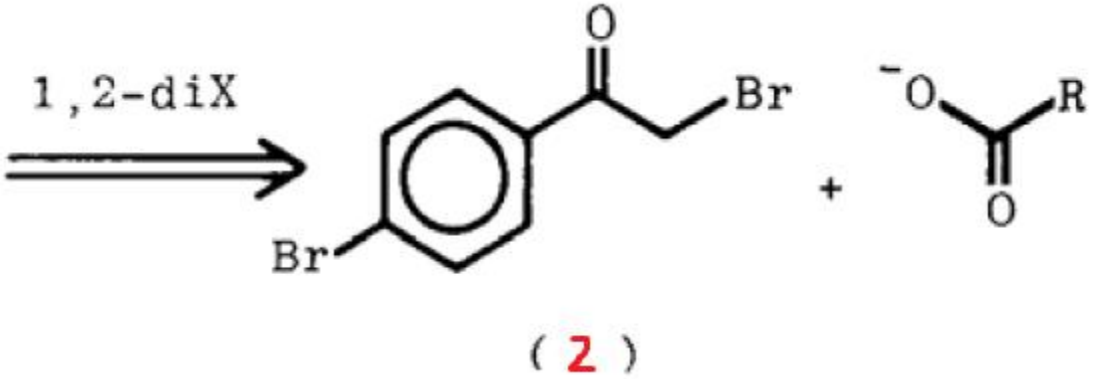

O
CO2H
Cl
Cl
1,2-diX
Cl
CO2H
+
OH
Cl
Cl
C-Cl
PhOH


PhOH
Cl2
Fe
OH
Cl
Cl
1.NaOH
2.ClCH2CO2H
TM

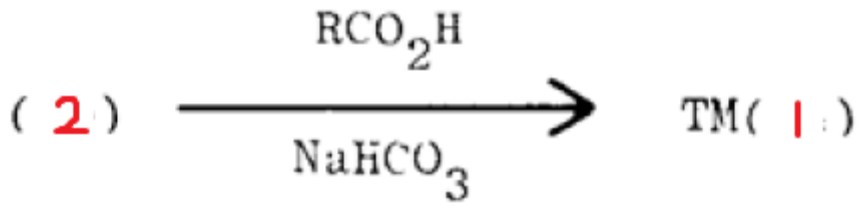

O
O
R
O
Br



(1)

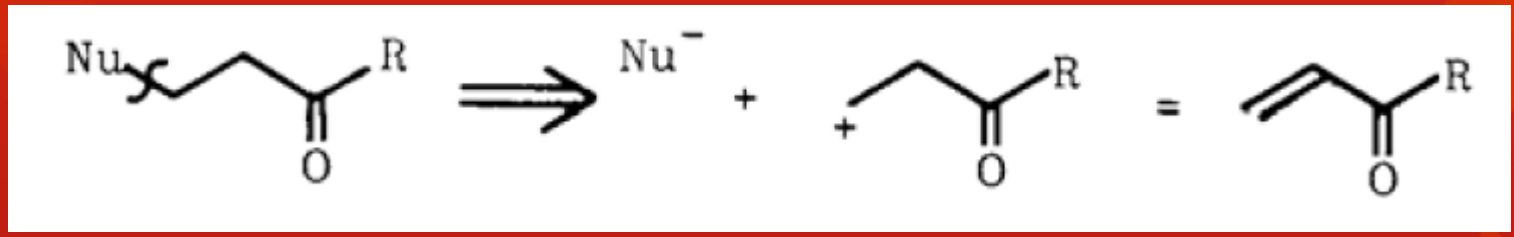


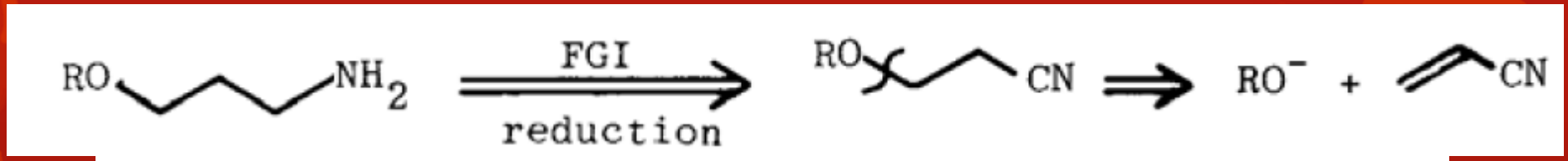
(2)

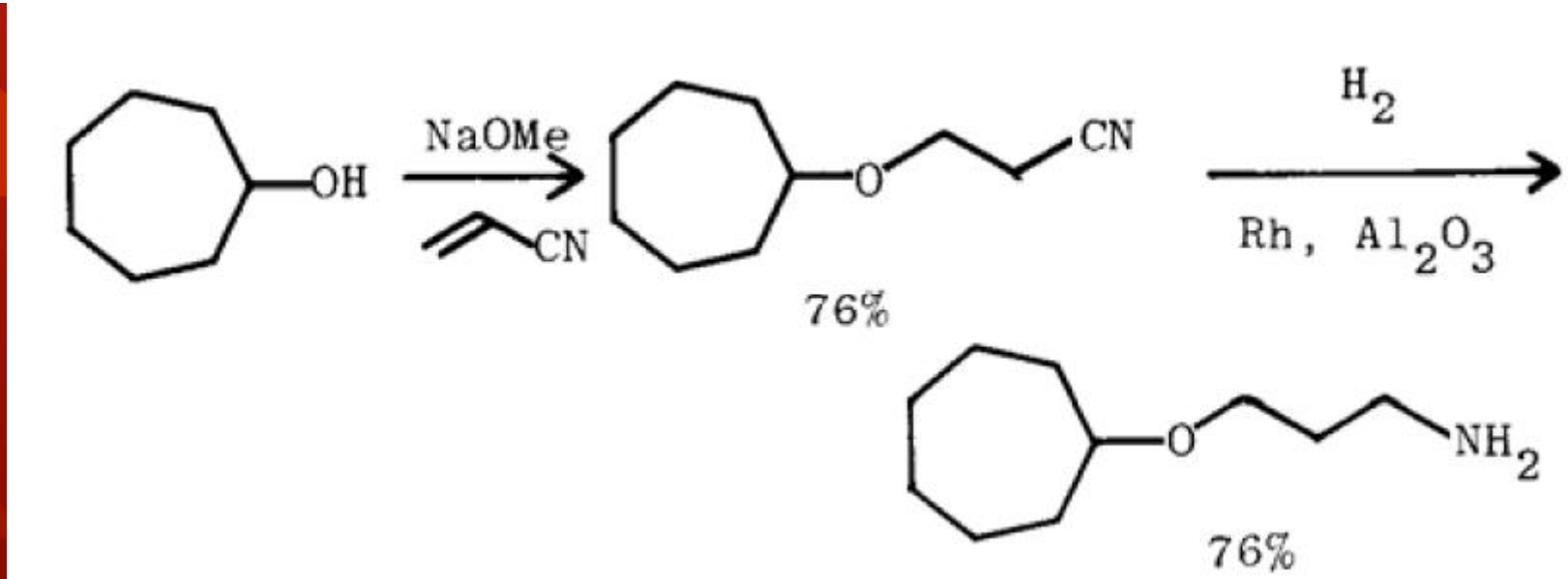


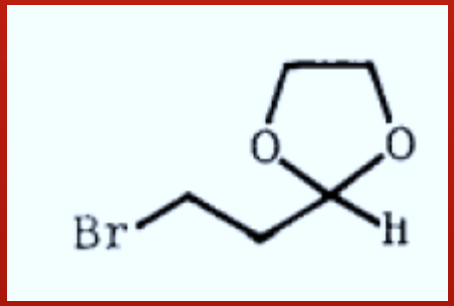
(2) TM(1)

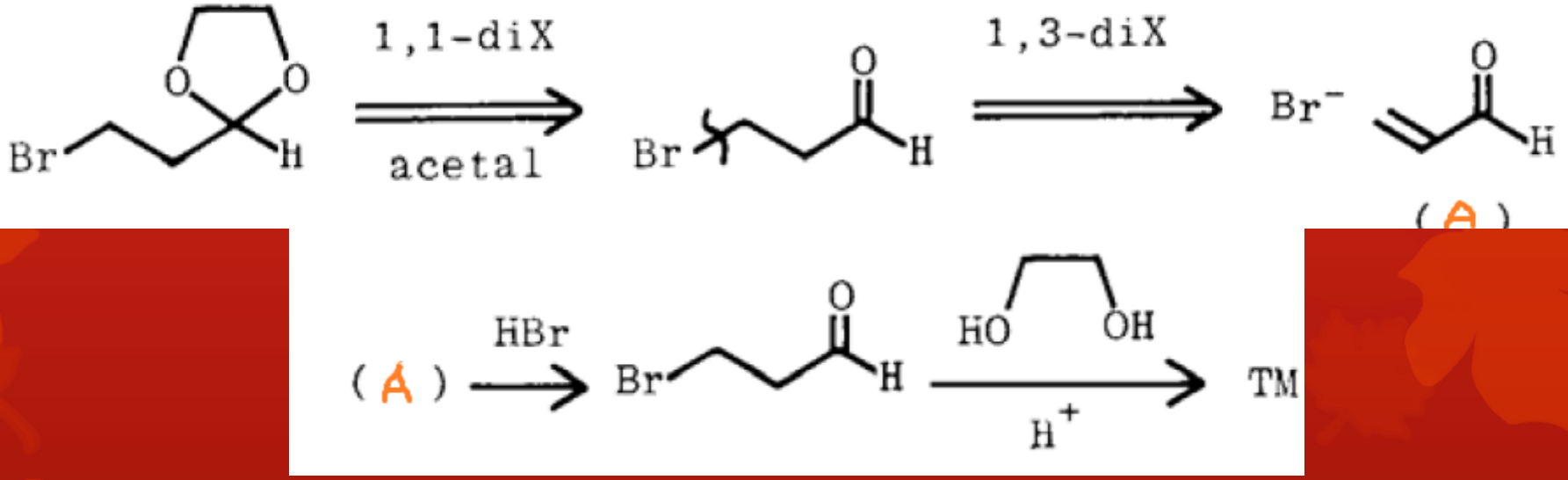
1,3-DIFUNCTIONALISED COMPOUNDS

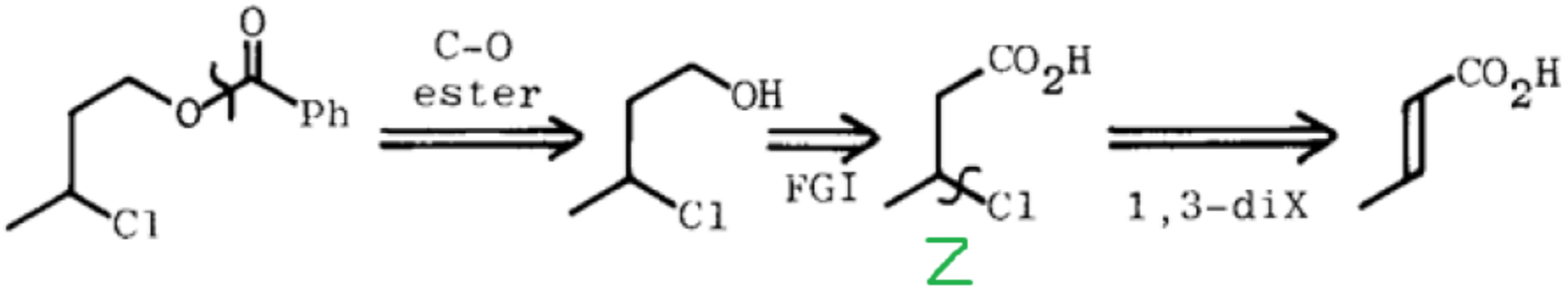

Nu
R
O
Nu⁻
+
R
O
=
R
O

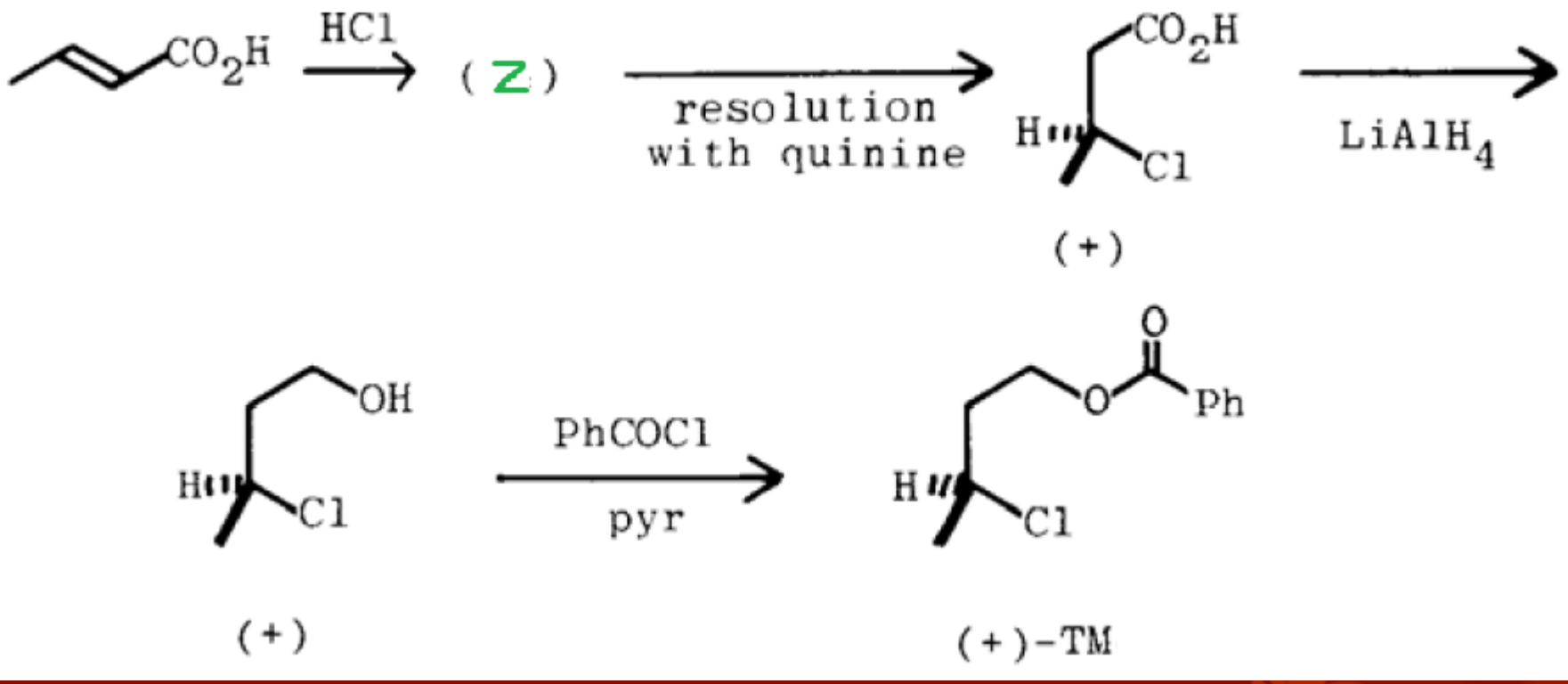

RO
NH2
FGI
reduction
RO
CN
RO⁻
+
CN


OH
NaOMe
CN
O
CN
76%
H2
Rh, Al2O3
O
NH2
76%


O
O
Br
H


1,1-diX
acetal
1,3-diX
Br⁻
(A)
HBr
(A)
HO
OH
H⁺
TM


O
O
Ph
Cl
C-O
ester
OH
Cl
FGI
CO2H
Cl
Z
1,3-diX
CO2H


CO2H
HCl
(Z)
resolution
with quinine
CO2H
H
Cl
(+)
LiAlH4
OH
H
Cl
(+)
PhCOCl
pyr
O
O
Ph
H
Cl
(+)-TM