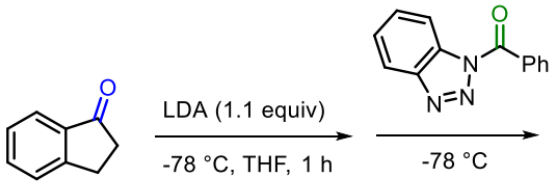
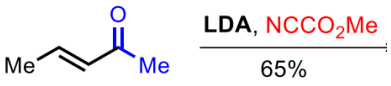
Chapter 4

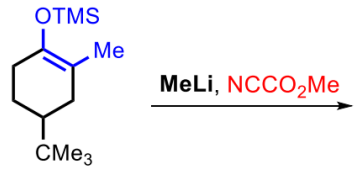
- ❑ **Synthesis of 1,3-Dicarbonyl Compounds:**
- ➢ Claisen and Dieckmann Condensation
- ➢ Acylation with Acid Chlorides, N-Acylbenztriazoles, Mander Reagents, etc.
- ➢ Blaise Reaction
- ➢ Michael Addition/α-Acylation Sequence
- ❑ **Synthesis of 1,4-Dicarbonyl Compounds :**
- ➢ Enolate Alkylation
- ➢ Michael Addition of 1,3-Dithianes, Hydrozones, Cyanides, and Cyanohydrins
- ➢ Stetter Reaction
- ➢ Addition of Zn-Homoenolate to Acid Chlorides
- ❑ **Synthesis of 1,5-Dicarbonyl Compounds :**
- ➢ Michael Addition to α,β-Unsaturated Carbonyl Compounds
- ❑ Synthesis of 1,6-Dicarbonyl Compounds :
- ➢ Michael Addition with Homoenolates
- ❑ **Synthesis of 1,2-Dicarbonyl Compounds :**
- ➢ Addition of 1,3-Dithianes to Acid Chlorides
- ❑ Synthesis of β-Hydroxyl Carbonyl Compounds:
- ➢ Aldol Reaction
- ➢ Reformatsky Reaction
- ➢ Ring Opening of Epoxides by 1,3-Dithianes
- ➢ Morita-Baylis-Hillman Reaction
- ❑ **Synthesis of β-Amino Carbonyl Compounds :**
- ➢ Mannich Reaction
- ➢ Aza-Reformatsky Reaction
- ➢ Ring Opening of Aziridines by 1,3-Dithianes
- ➢ Aza-Morita-Baylis-Hillman Reaction
- ➢ Aza-Michael Reaction
- ❑ **Synthesis of α-Hydroxyl Carbonyl Compounds :**
- ➢ Hydrolysis of Cyanohydrins
- ➢ Addition of 1,3-Dithianes to Carbonyl Compounds
- ➢ Benzoin Reaction
- ❑ **Synthesis of α-Amino Carbonyl Compounds:**
- ➢ Strecker Synthesis
- ➢ Addition of 1,3-Dithianes to Imines
- ➢ Aza-Benzoin Reaction
- ➢ Petasis Reaction
- ➢ Ugi Reaction
- ❑ **Synthesis of γ-Hydroxyl Carbonyl Compounds :**
- ➢ Ring Opening of Epoxides by Enolates
- ➢ Homo-Reformatsky Reaction
- ➢ Ketyl Olefin Coupling
- ❑ Synthesis of γ-Amino Carbonyl Compounds :
- ➢ Ring Opening of Aziridines by Enolates

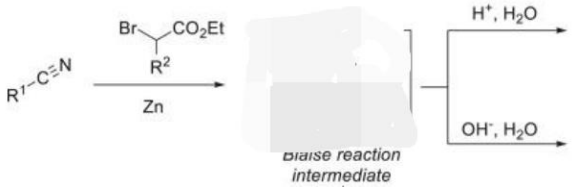
- ➢ Homo-Aza-Reformatsky Reaction
- ➢ Aza-Ketyl Olefin Coupling

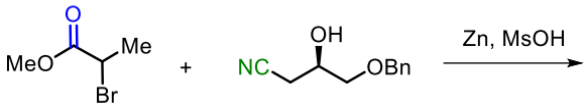
❑ **Synthesis of Vicinal Diols, Amino Alcohols, and Diamines**

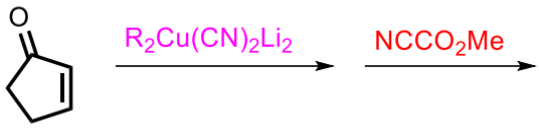

LDA (1.1 equiv)
-78 °C, THF, 1 h
-78 °C
Ph

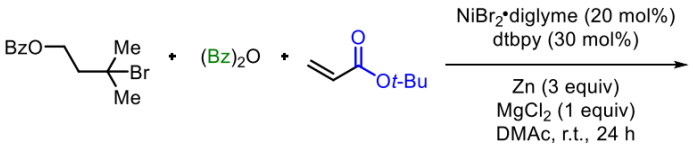

LDA, NCCO2Me
65%

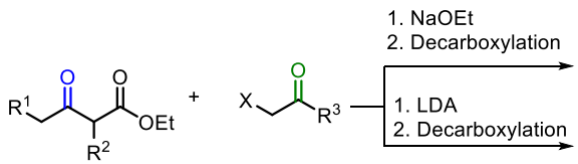

MeLi, NCCO2Me

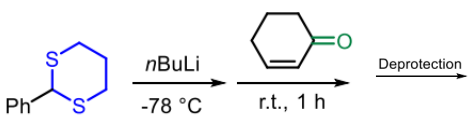

Zn
H+, H2O
OH-, H2O
Blaise reaction intermediate

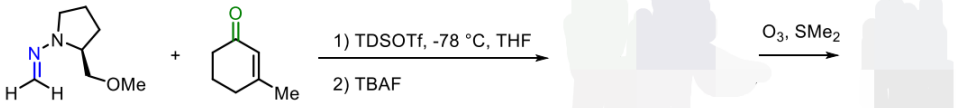

Zn, MsOH

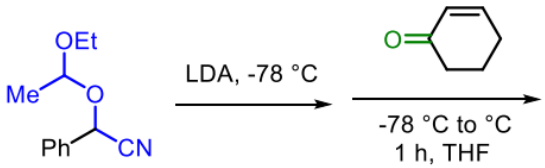

R2Cu(CN)2Li2
NCCO2Me

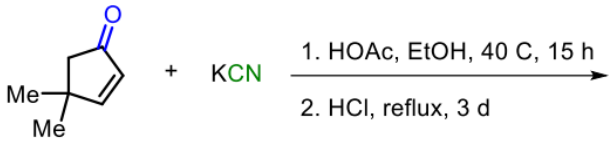

NiBr2•diglyme (20 mol%)
dtbpy (30 mol%)
Zn (3 equiv)
MgCl2 (1 equiv)
DMAc, r.t., 24 h

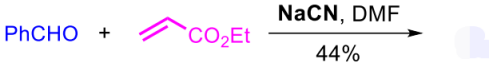

1. NaOEt
2. Decarboxylation
1. LDA
2. Decarboxylation

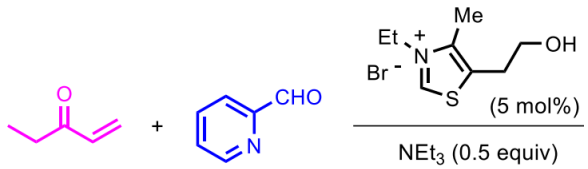

nBuLi
-78 °C
r.t., 1 h
Deprotection

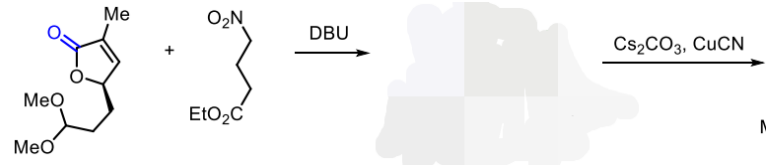

1) TDSOTf, -78 °C, THF
2) TBAF
O_3, SMe_2

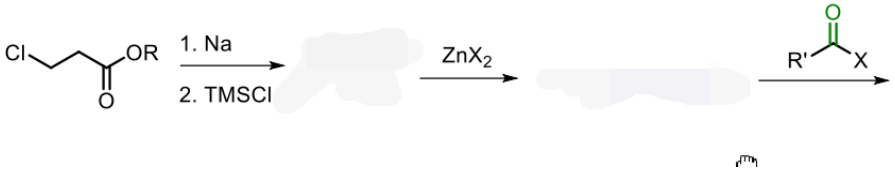

LDA, -78 °C
-78 °C to °C
1 h, THF

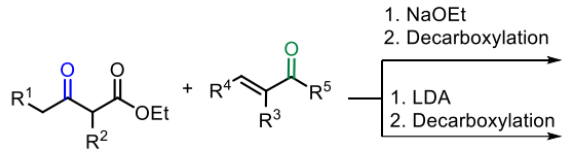

KCN
1. HOAc, EtOH, 40 C, 15 h
2. HCl, reflux, 3 d


PhCHO
NaCN, DMF
44%

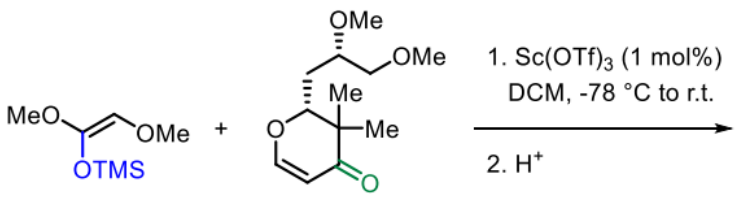

(5 mol%)
NEt_3 (0.5 equiv)

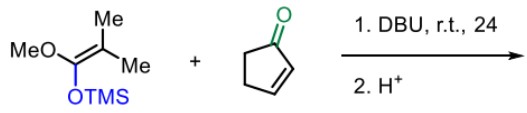

DBU
Cs_2CO_3, CuCN

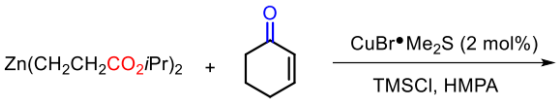

1. Na
2. TMSCl
ZnX_2

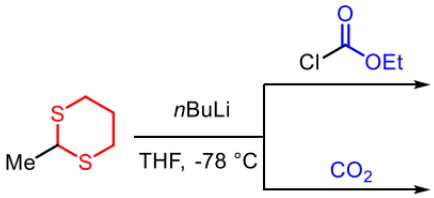

1. NaOEt
2. Decarboxylation
1. LDA
2. Decarboxylation

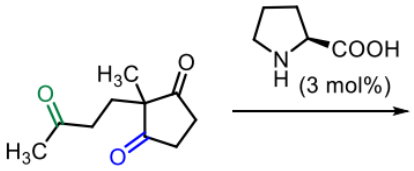
ample

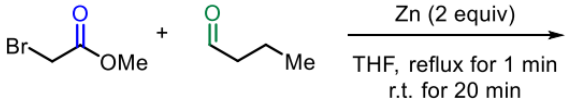

1. $Sc(OTf)_3$ (1 mol%)
DCM, -78 °C to r.t.
2. H^+

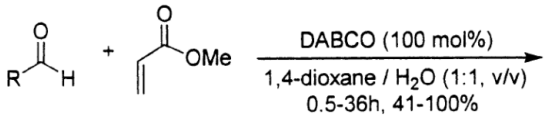

Me
MeO
Me
OTMS
O
1. DBU, r.t., 24
2. H+

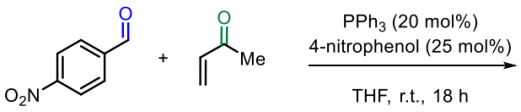

Zn(CH2CH2CO2iPr)2
O
CuBr•Me2S (2 mol%)
TMSCl, HMPA

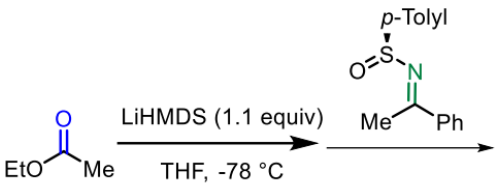

S
Me
S
nBuLi
THF, -78 °C
O
Cl
OEt
CO2

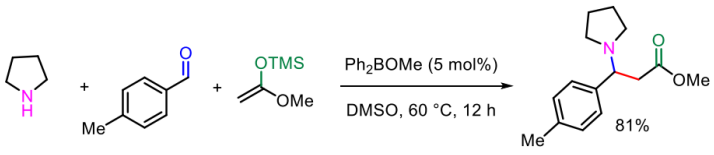

H3C
O
O
H3C
O
N
H
COOH
(3 mol%)


Br
O
OMe
+
O
Me
Zn (2 equiv)
THF, reflux for 1 min
r.t. for 20 min

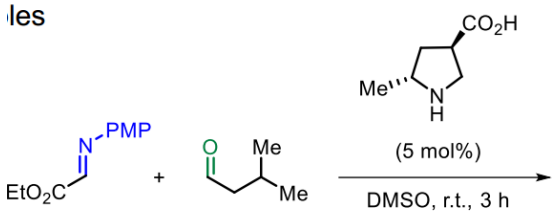

O
R
H
+
O
OMe
DABCO (100 mol%)
1,4-dioxane / H2O (1:1, v/v)
0.5-36h, 41-100%

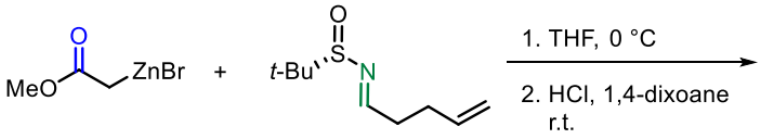

O
O2N
+
O
Me
PPh3 (20 mol%)
4-nitrophenol (25 mol%)
THF, r.t., 18 h

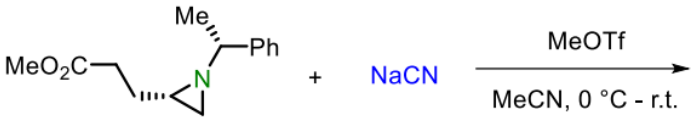

p-Tolyl
O
S
N
Me
Ph
O
EtO
Me
LiHMDS (1.1 equiv)
THF, -78 °C

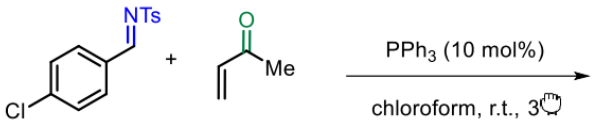

N
H
+
O
Me
+
OTMS
OMe
Ph2BOMe (5 mol%)
DMSO, 60 °C, 12 h
N
O
OMe
Me
81%

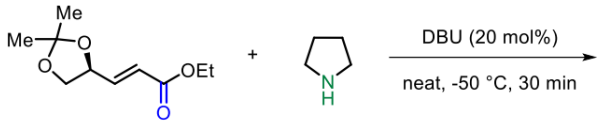
les

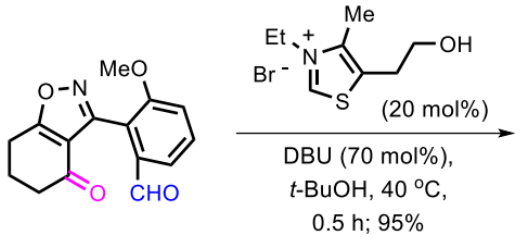

CO2H
Me
N
H
N-PMP
EtO2C
O
Me
Me
(5 mol%)
DMSO, r.t., 3 h


O
MeO
ZnBr
t-Bu
S
N
1. THF, 0 °C
2. HCl, 1,4-dixoane
r.t.

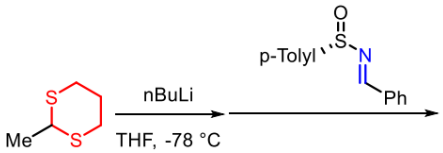

Me
MeO2C
Ph
N
NaCN
MeOTf
MeCN, 0 °C - r.t.

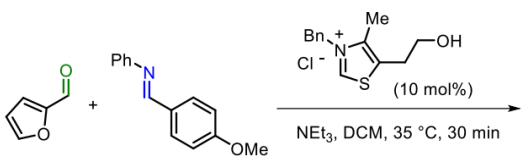

NTs
Cl
O
Me
PPh3 (10 mol%)
chloroform, r.t., 3

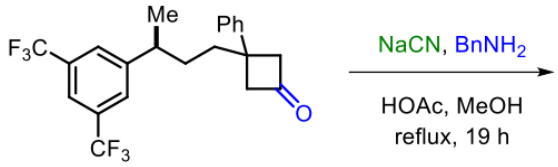

Me
Me
O
OEt
O
N
H
DBU (20 mol%)
neat, -50 °C, 30 min

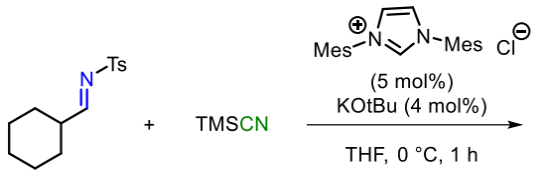

MeO
O-N
O
CHO
Et
N
Br -
Me
OH
S
(20 mol%)
DBU (70 mol%),
t-BuOH, 40 °C,
0.5 h; 95%

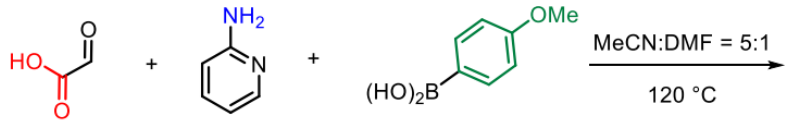

O
Me
MeO
TMSCN
NMO (0.3 equiv), DCM
r.t., 3 h

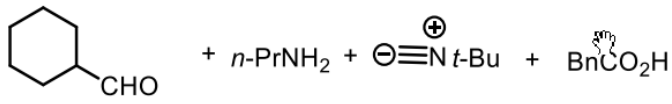

S
Me
S
nBuLi
THF, -78 °C
p-Tolyl
S
O
N
Ph

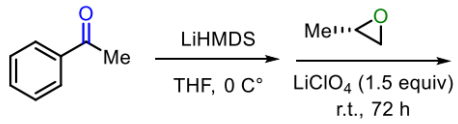

O
O
Ph
N
OMe
Bn
N
Cl -
Me
OH
S
(10 mol%)
NEt3, DCM, 35 °C, 30 min

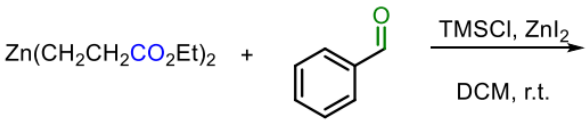

Me
Ph
F3C
CF3
O
NaCN, BnNH2
HOAc, MeOH
reflux, 19 h

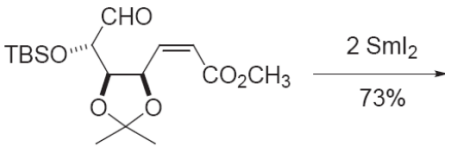

N
Ts
+
TMSCN
Mes
N
N
Mes
Cl
(5 mol%)
KOtBu (4 mol%)
THF, 0 °C, 1 h

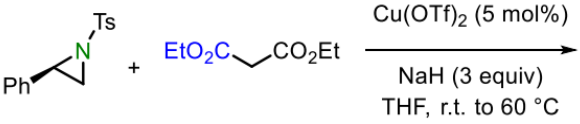

HO
O
O
+
NH2
N
+
OMe
(HO)2B
MeCN:DMF = 5:1
120 °C

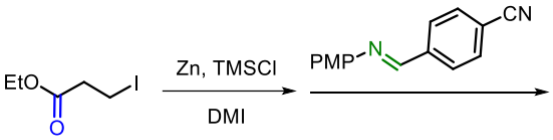

CHO
+ n-PrNH2 +
N t-Bu
+
BnCO2H

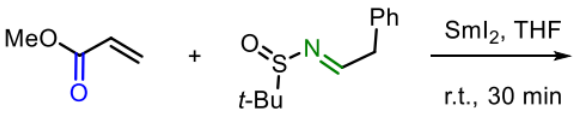

O
Me
LiHMDS
THF, 0 C°
Me
O
LiClO4 (1.5 equiv)
r.t., 72 h

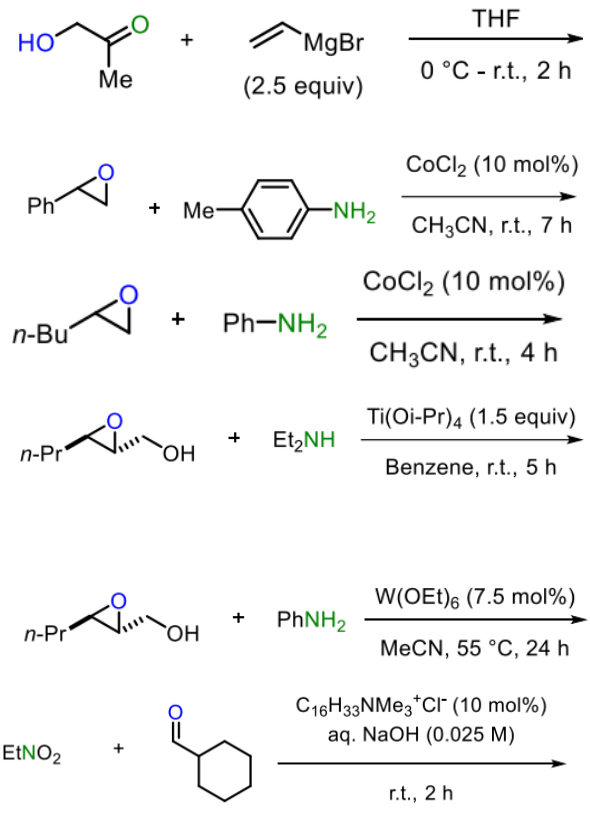

Zn(CH2CH2CO2Et)2
+
O
TMSCl, ZnI2
DCM, r.t.


CHO
TBSO
CO2CH3
O
O
2 SmI2
73%


Ts
N
Ph
+
EtO2C
CO2Et
Cu(OTf)2 (5 mol%)
NaH (3 equiv)
THF, r.t. to 60 °C


EtO
O
I
Zn, TMSCl
DMI
PMP
N
CN


MeO
O
+
O
S
N
Ph
t-Bu
SmI2, THF
r.t., 30 min


HO
O
Me
+
MgBr
(2.5 equiv)
THF
0 °C - r.t., 2 h
Ph
O
+
Me
NH2
CoCl2 (10 mol%)
CH3CN, r.t., 7 h
n-Bu
O
+
Ph—NH2
CoCl2 (10 mol%)
CH3CN, r.t., 4 h
n-Pr
O
OH
+
Et2NH
Ti(Oi-Pr)4 (1.5 equiv)
Benzene, r.t., 5 h
n-Pr
O
OH
+
PhNH2
W(OEt)6 (7.5 mol%)
MeCN, 55 °C, 24 h
EtNO2
+
O
C16H33NMe3+Cl- (10 mol%)
aq. NaOH (0.025 M)
r.t., 2 h