Asymmetric total syntheses of Communesin F and a putative member of Communesin Family

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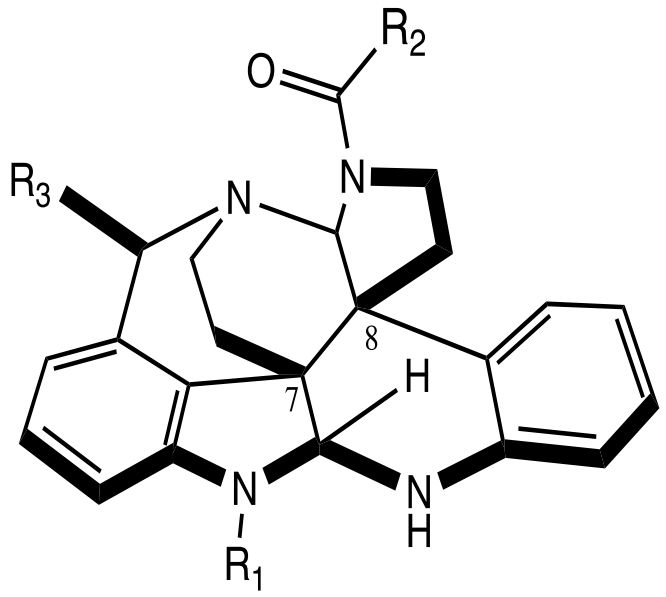


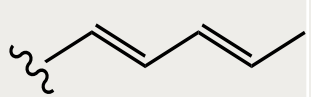
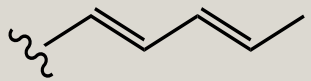
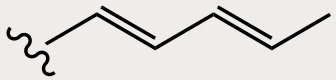
Communesin Family

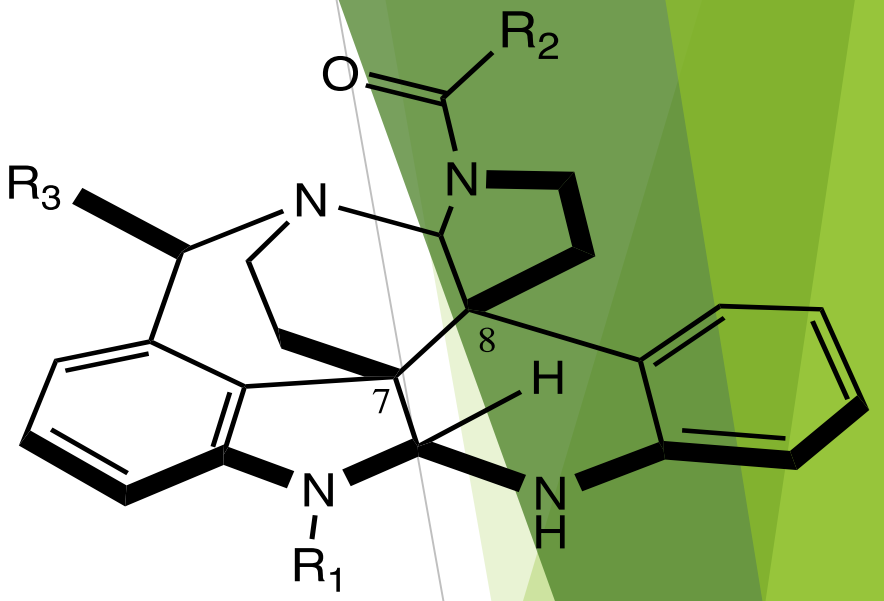
- Communesin A and B first identified by Numata in **1993** from a strain of Penicillium isolated from Marine Algae Entermorpha Intestinalis.

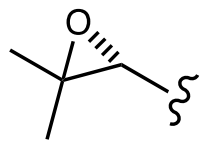
- The metabolite exhibited cytotoxic activity against lymphocytic leukemia cells.

A, Numata, C. Takahashi, Y. Ito, T. Takada, K. Kawai, Y. Usami, E. Matsumura, M.Imachi, *Tetrahedron Lett*. **1993**,34,2355

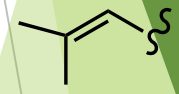
Penicillium

	R_1	R_2	R_3
Communesin A	Me	Me	diMe epoxide
Communesin B	Me		diMe epoxide
Communesin C	H		diMe epoxide
Communesin D	CHO		diMe epoxide
CommunesinE	H	Me	diMe epoxide
Communesin F	Me	Me	diMe vinyl
Communesin G	Me	Et	diMe epoxide
Communesin H	Me	nPr	diMe epoxide



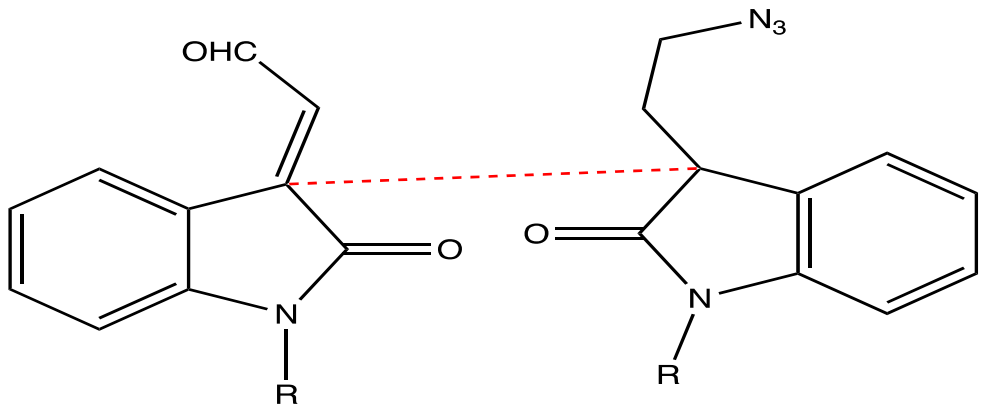


diMe epoxide



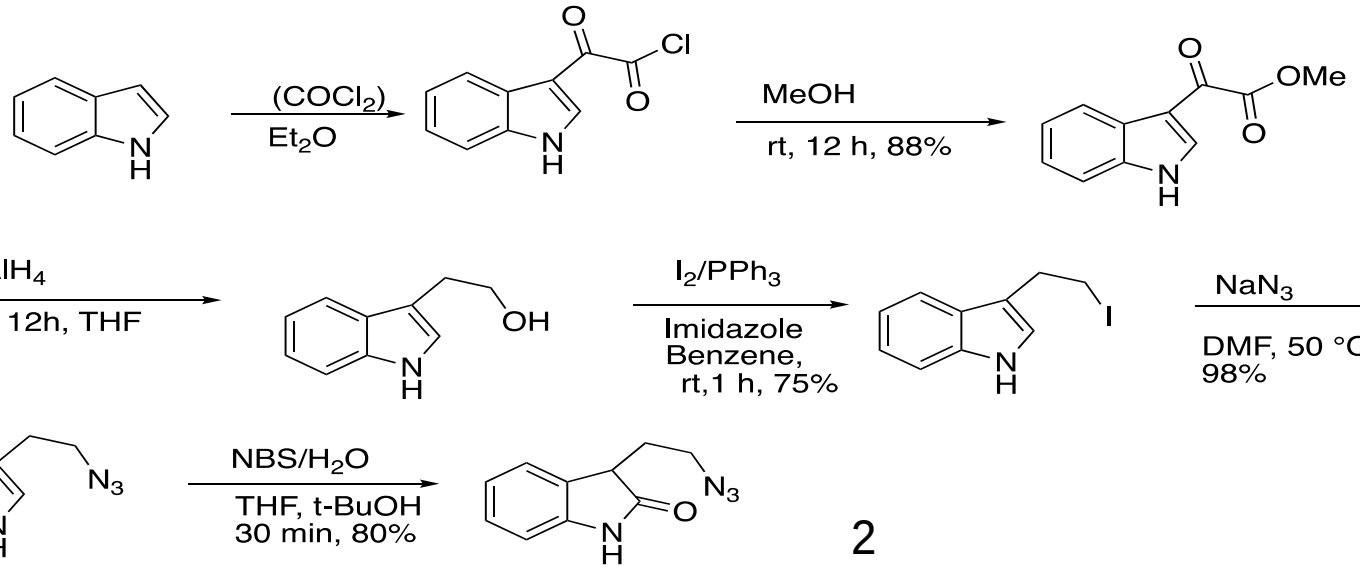
diMe vinyl

Retrosynthesis



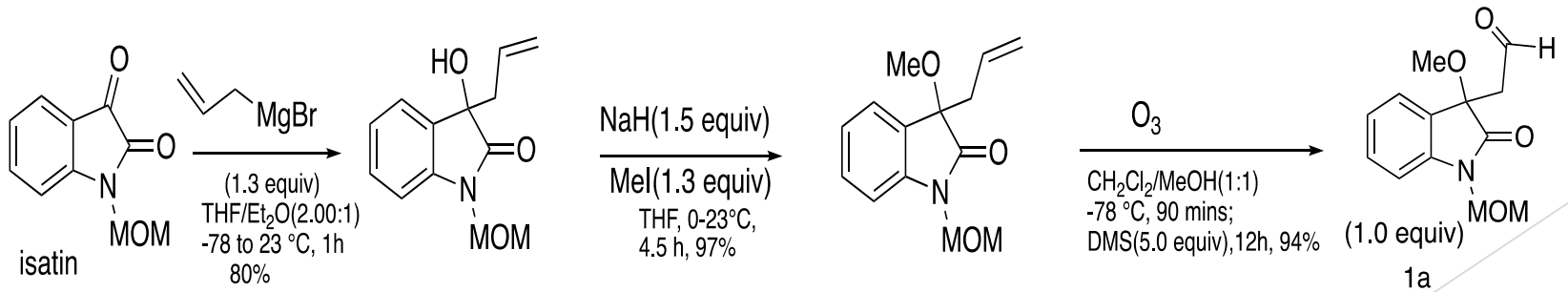
1a 2

Synthesis of Synthons

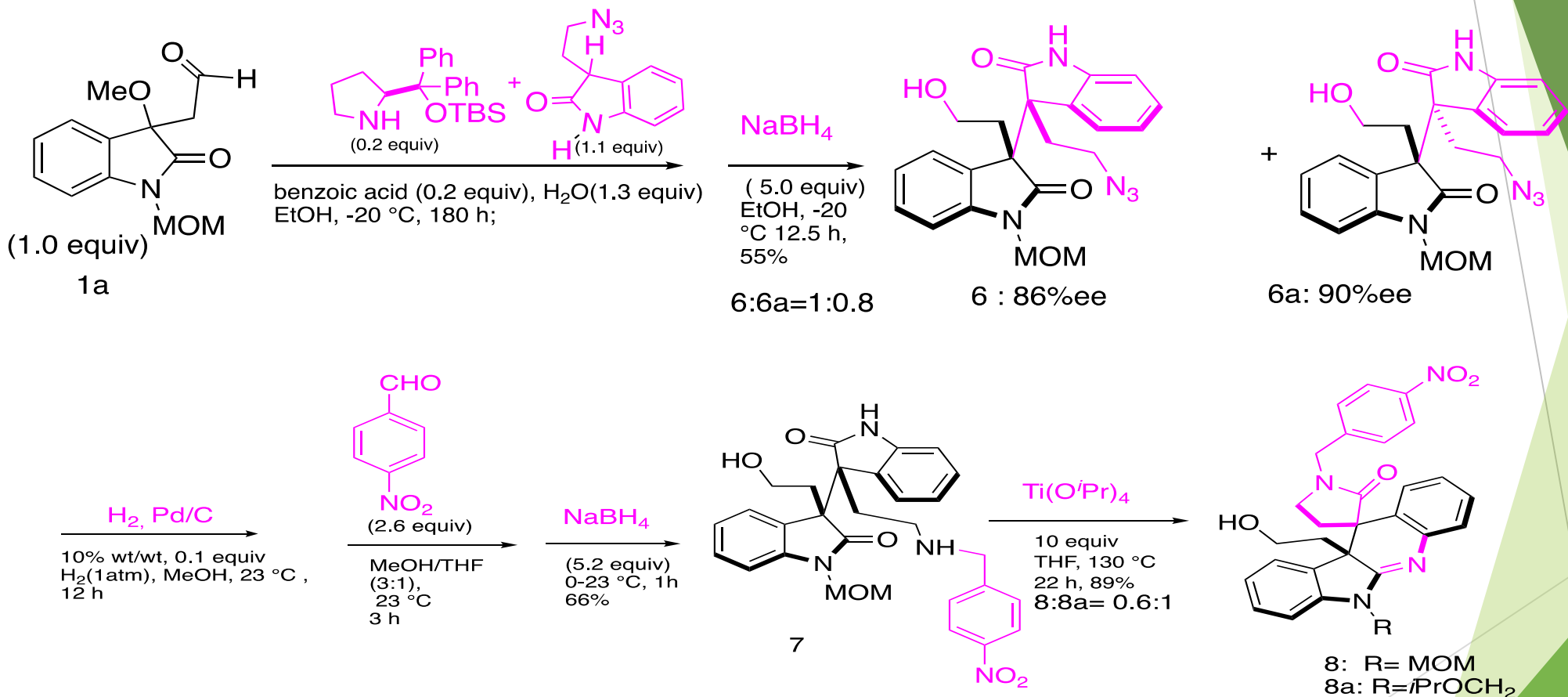
- 

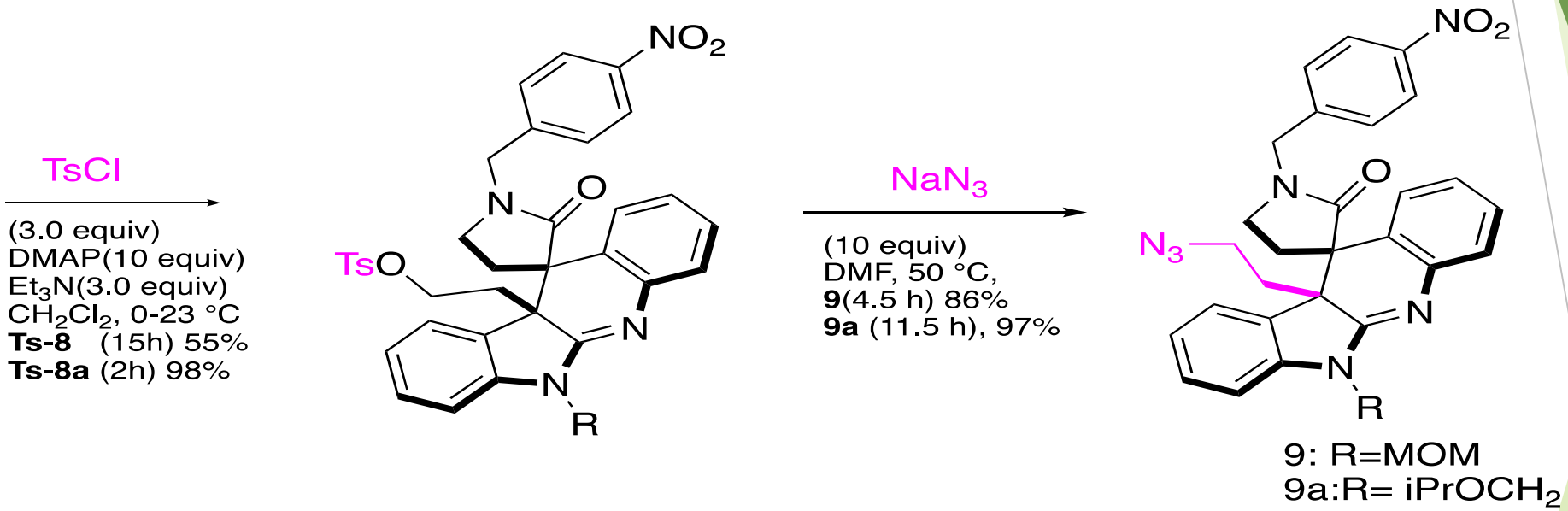
2

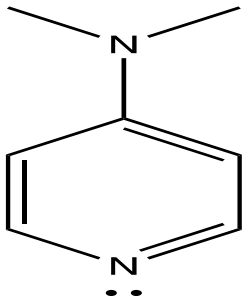
Reference: C. Menozzi, P.I. Dalko, J. Cossy, *Chem. Commun*. 2006, 4638.

- 

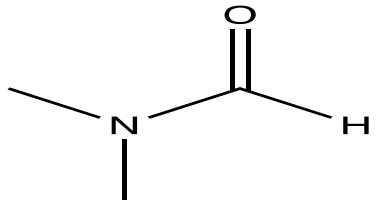
Scheme 1


(1.0 equiv)
1a
(0.2 equiv)
(1.1 equiv)
benzoic acid (0.2 equiv), H2O(1.3 equiv)
EtOH, -20 °C, 180 h;
NaBH4
(5.0 equiv)
EtOH, -20 °C 12.5 h,
55%
6:6a=1:0.8
6 : 86%ee
6a: 90%ee
H2, Pd/C
10% wt/wt, 0.1 equiv
H2(1atm), MeOH, 23 °C ,
12 h
(2.6 equiv)
MeOH/THF
(3:1),
23 °C
3 h
NaBH4
(5.2 equiv)
0-23 °C, 1h
66%
7
Ti(OiPr)4
10 equiv
THF, 130 °C
22 h, 89%
8:8a= 0.6:1
8: R= MOM
8a: R=iPrOCH2

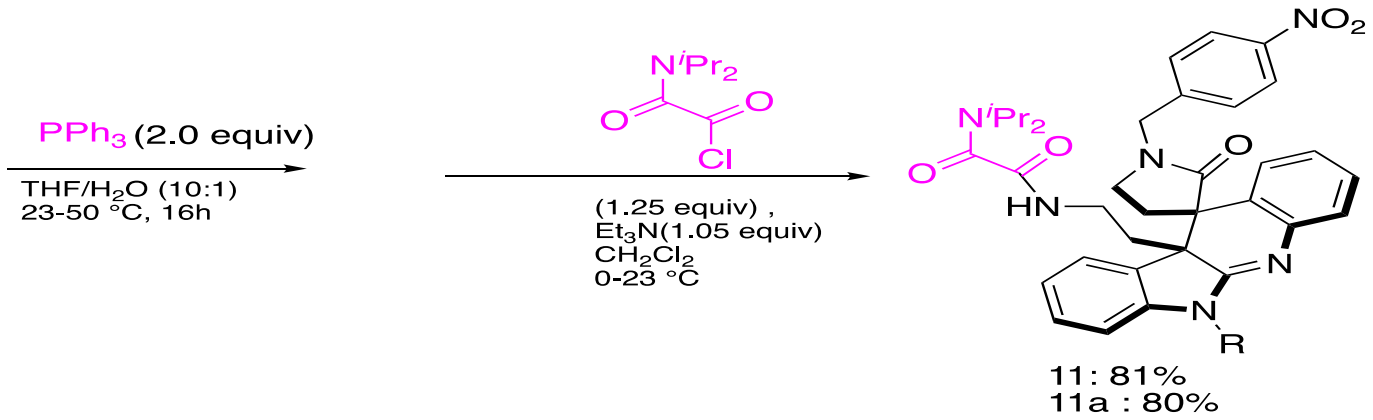

TsCl
(3.0 equiv)
DMAP(10 equiv)
Et3N(3.0 equiv)
CH2Cl2, 0-23 °C
Ts-8 (15h) 55%
Ts-8a (2h) 98%
NO2
TsO
N
O
N
N
R
NaN3
(10 equiv)
DMF, 50 °C,
9(4.5 h) 86%
9a (11.5 h), 97%
N3
9: R=MOM
9a:R= iPrOCH2


N
N

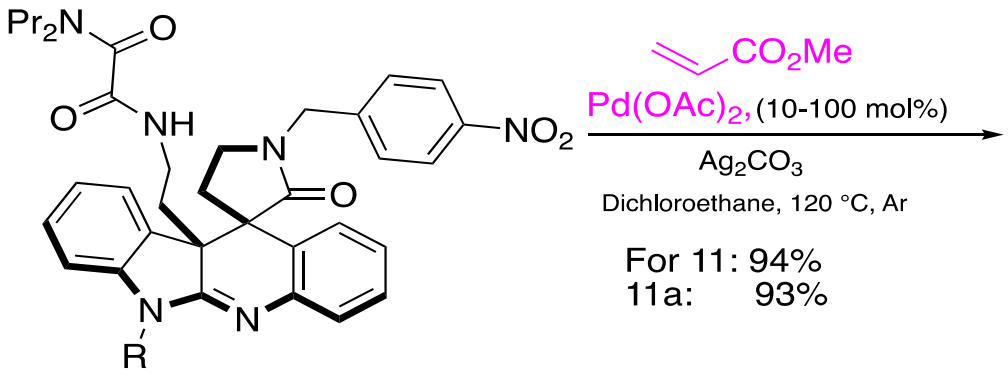
DMAP

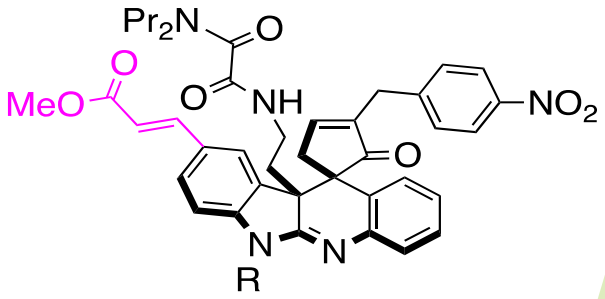

O
N
H

DMF



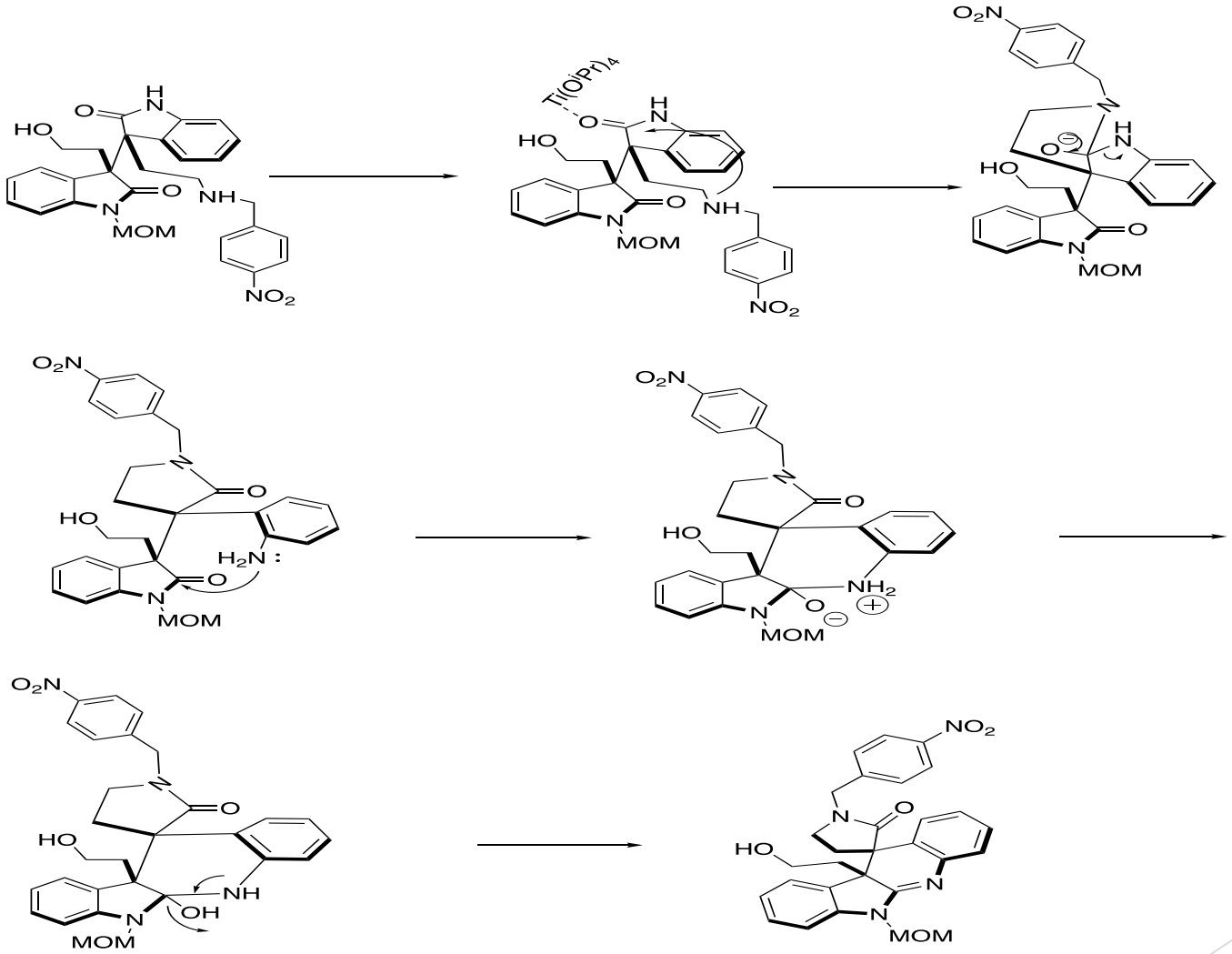
C-H Functionalization



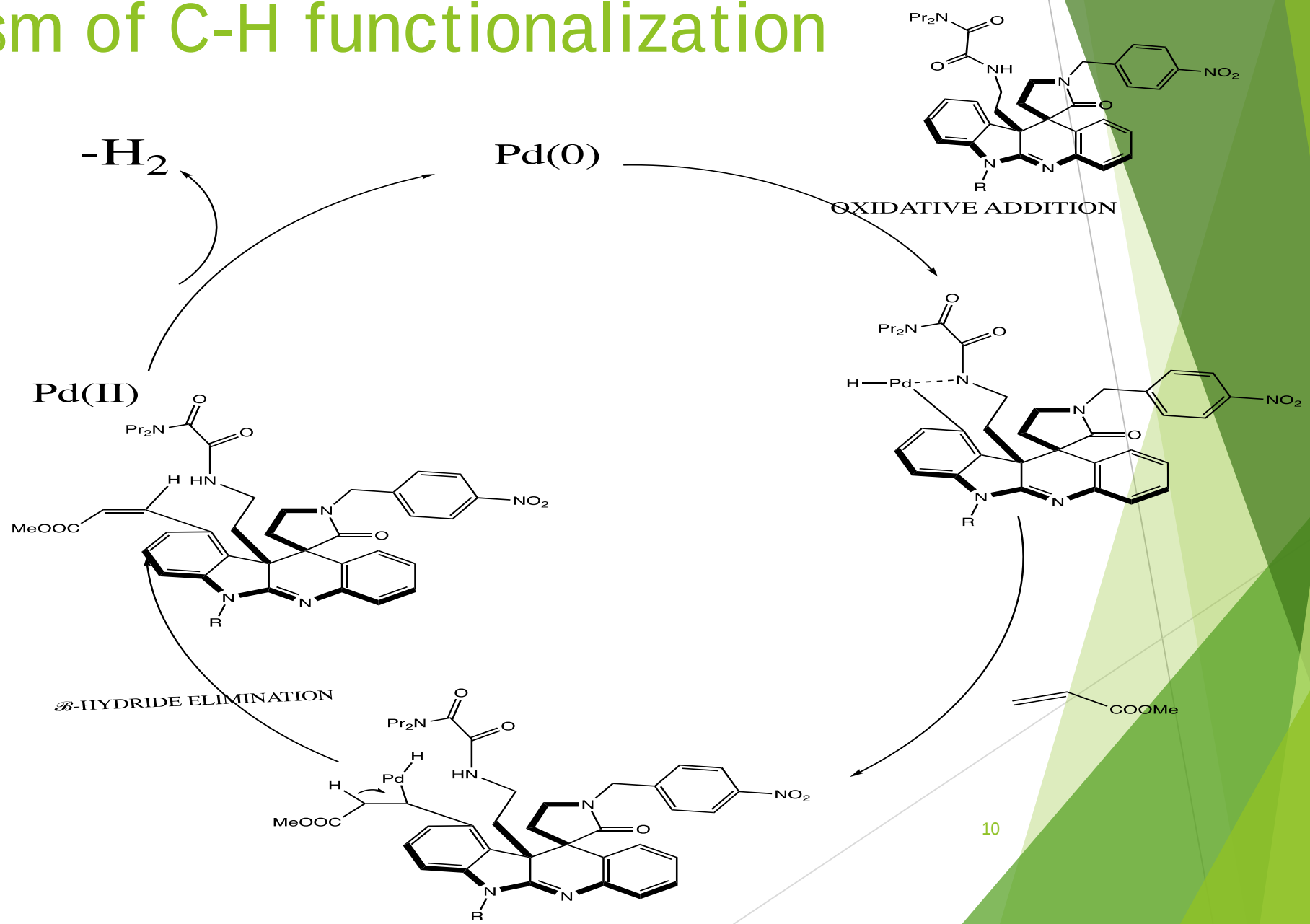


12: R= MOM
12a: R= ^{i}PrOCH$_2$

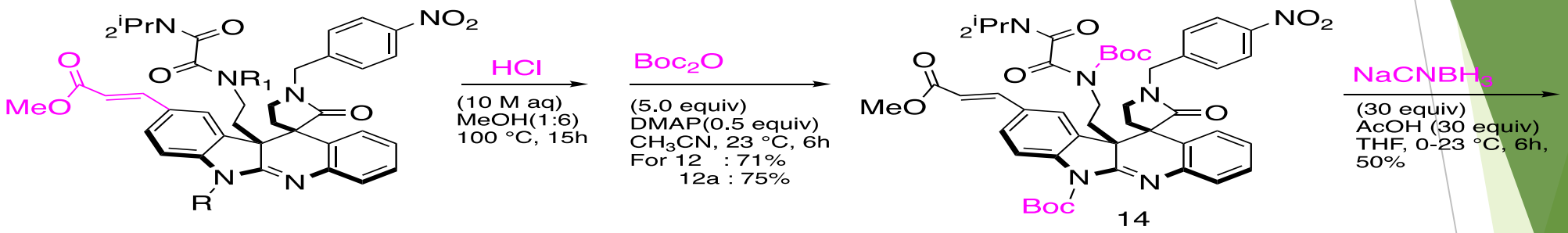
Rearrangement by $Ti(O^iPr)_4$



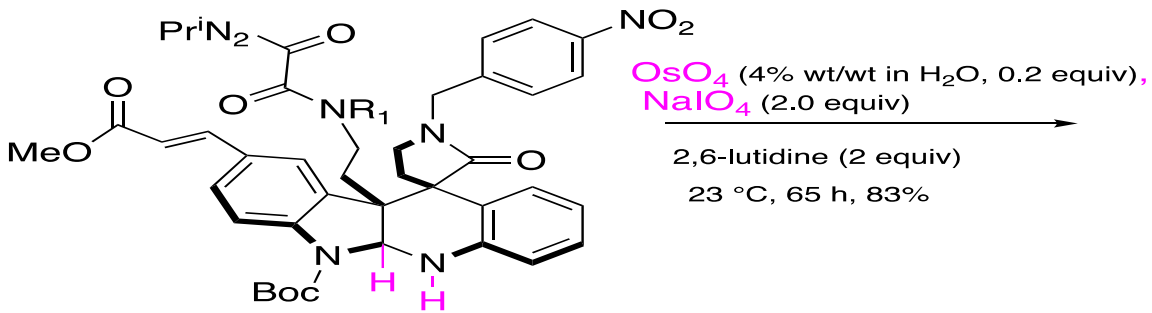
Mechanism of C-H functionalization



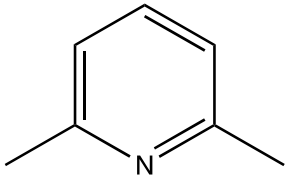
Scheme 2



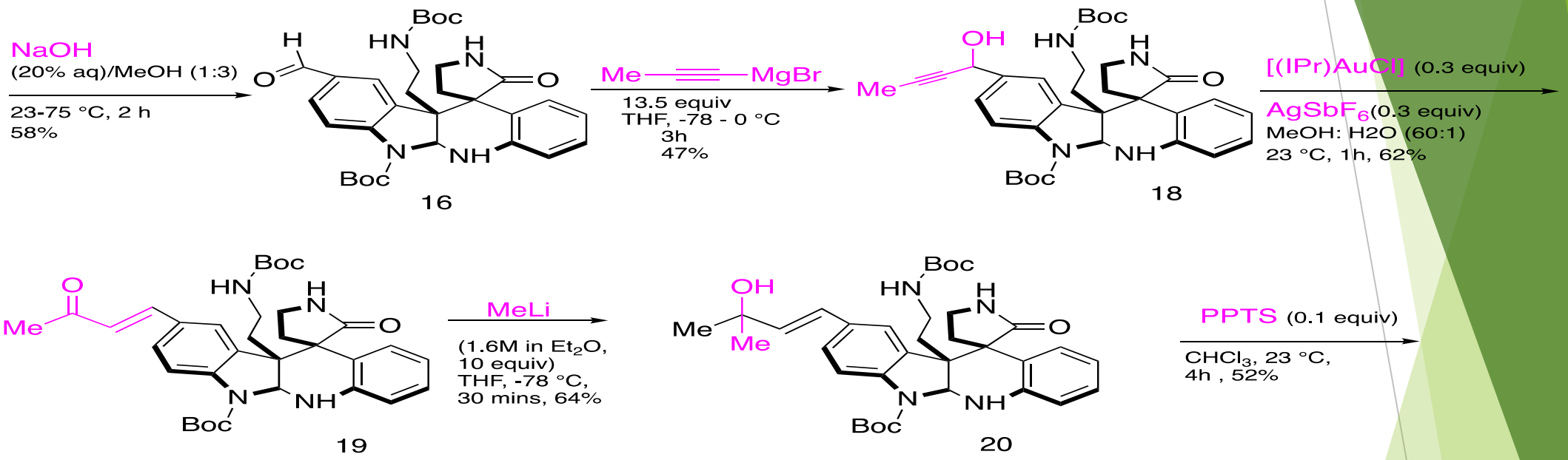
14

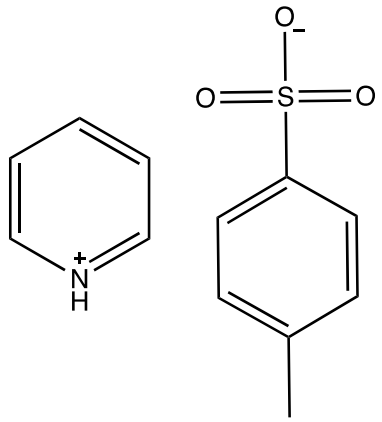


15



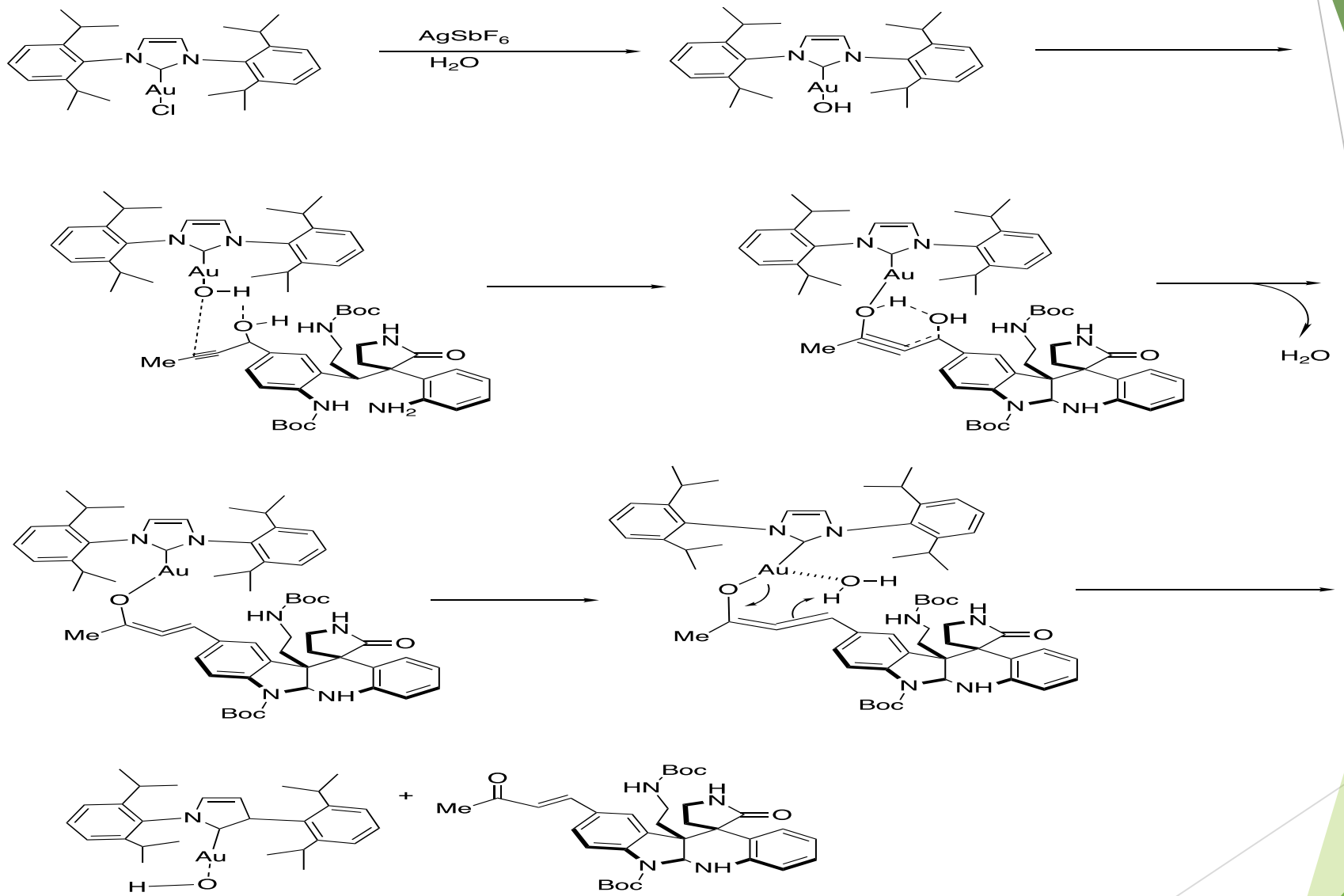
Lutidine



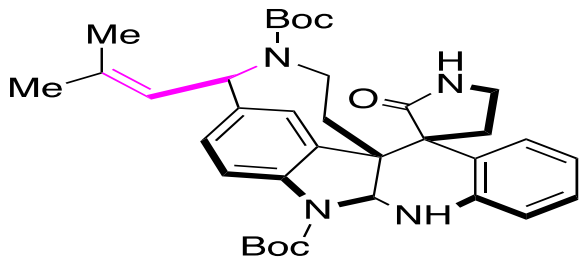


Pyridinium ptoluenesulfonate

Meyer Schuster Rearrangement



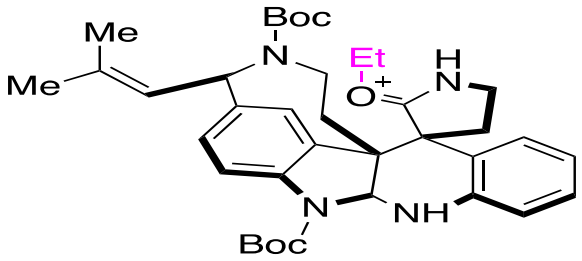
Reference: R.S. Ramòn, N. Marion, S.P. Nolan, *Tetrahedron* **2009,65,1767**



21

$BF_4.OEt_3$

(5 equiv),
iPrNEt(18.5 equiv),
CH_2Cl_2, 0°C, 45 min

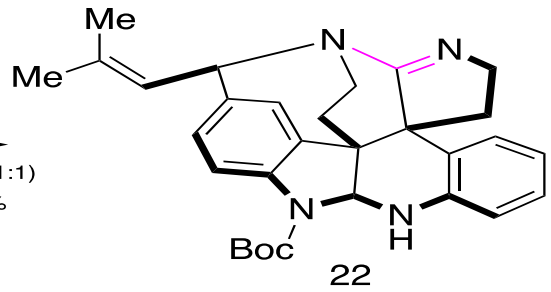


TFA

5 wt% in CH_2Cl_2,
23 °C, 2h

silica gel

$MeOH/CH_2Cl_2$(1:1)
50 °C, 18h, 31%



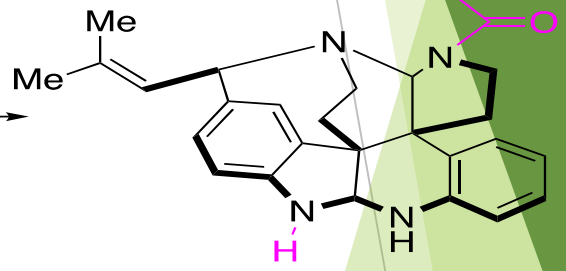
22

$AcOH, Ac_2O$ (1:1)

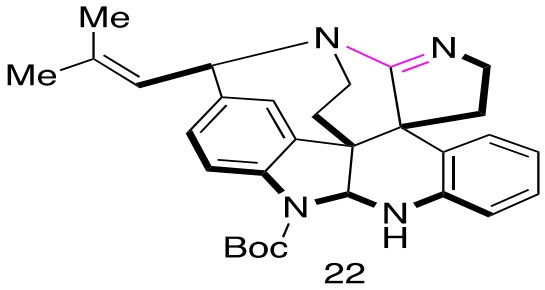
$NaBH_4$(excess)
0 °C, 10 mins

TFA/CH_2Cl_2 (1:2.5)

23 °C, 2h, 36%



23



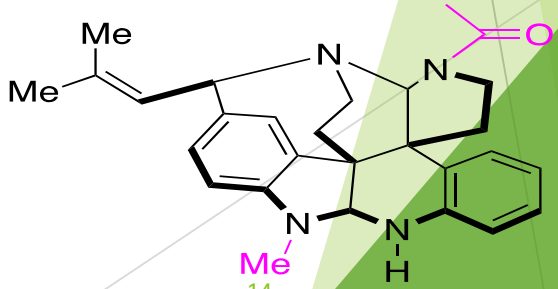
22

$NaBH_4$(excess),

AcOH, 0 °C, 25 mins
$LiAlH_4$, THF, 80 °C,2.5 h

$AcOH/AC_2O$ (1:1)

0 °C, 20 min, 43%



24

THANKYOU!