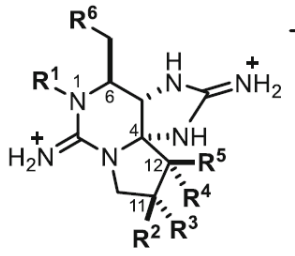
Synthesis of Shellfish Toxins:

Saxitoxins

Saxitoxins

- 石房蛤毒素（*Saxitoxin*，STX）是一种极强的神经毒素，是已知毒性最强的麻痹性贝类毒素（PST）。石房蛤毒素首次分离于帘蛤科的石房蛤体内，并由此得名。
- 石房蛤毒素实际上是一些藻类和蓝细菌所合成，通过食物链聚集到贝类体内。已知自然存在结构相似的神经毒素有超过50种，统称为石房蛤毒素类，除了石房蛤毒素本身外，还有新石房蛤毒素（NSTX）、脱氨甲酰基石房蛤毒素（dcSTX）等。
- 石房蛤毒素是一种选择性的细胞膜钠离子通道阻滞剂。它与神经元细胞膜上的钠离子通道结合，抑制钠离子通过细胞膜，从而阻止细胞电位的传导，最终导致瘫痪。小鼠的致死剂量与与给药途径有关为，静脉注射（LD50 = 3.4 μg/kg），口服（LD50 = 263 μg/kg）。人类经口服的LD50为5.7 μg/kg，注射的致死量约为0.6 μg/kg

Fig. 1 Structure of saxitoxin (STX; **1**)



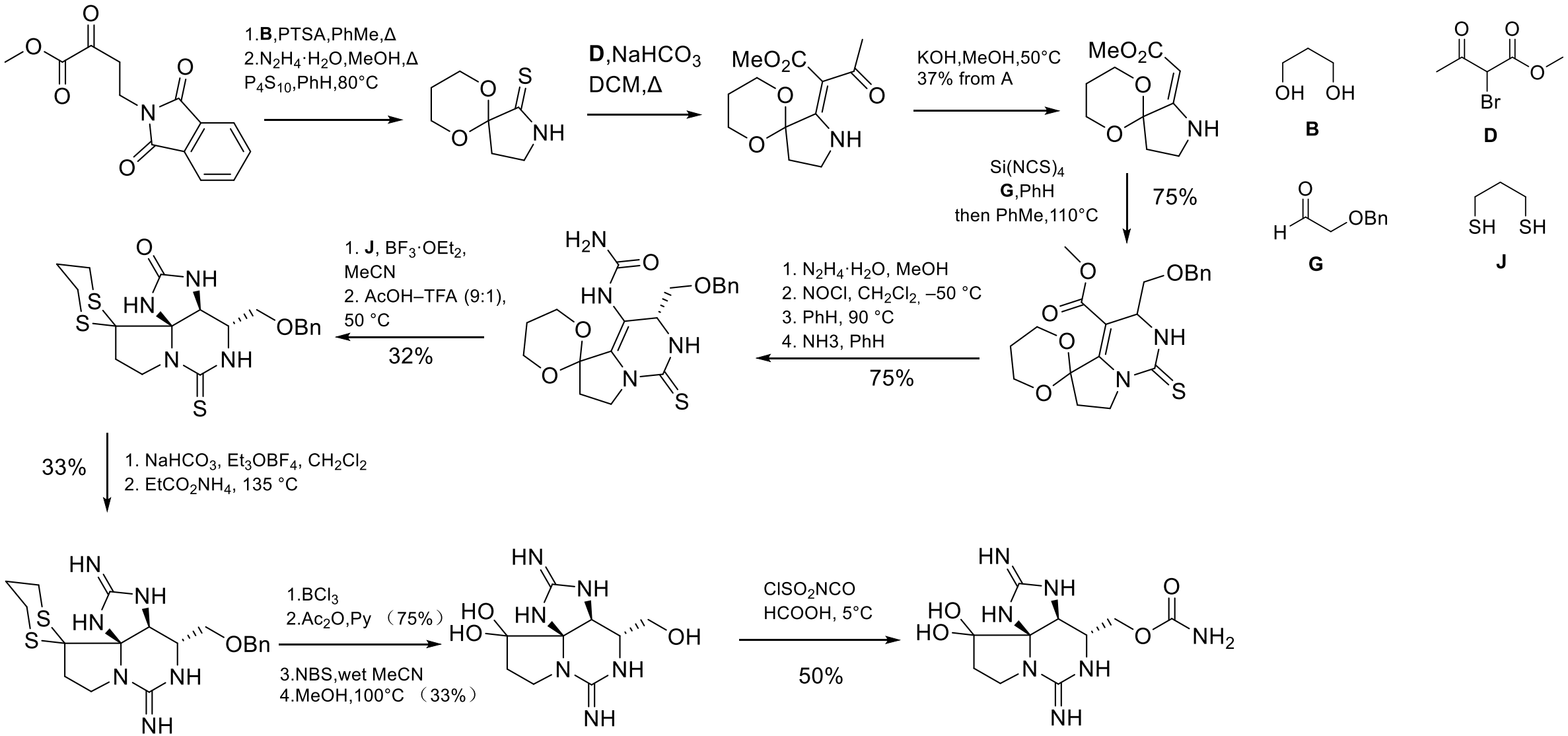
STX skelton

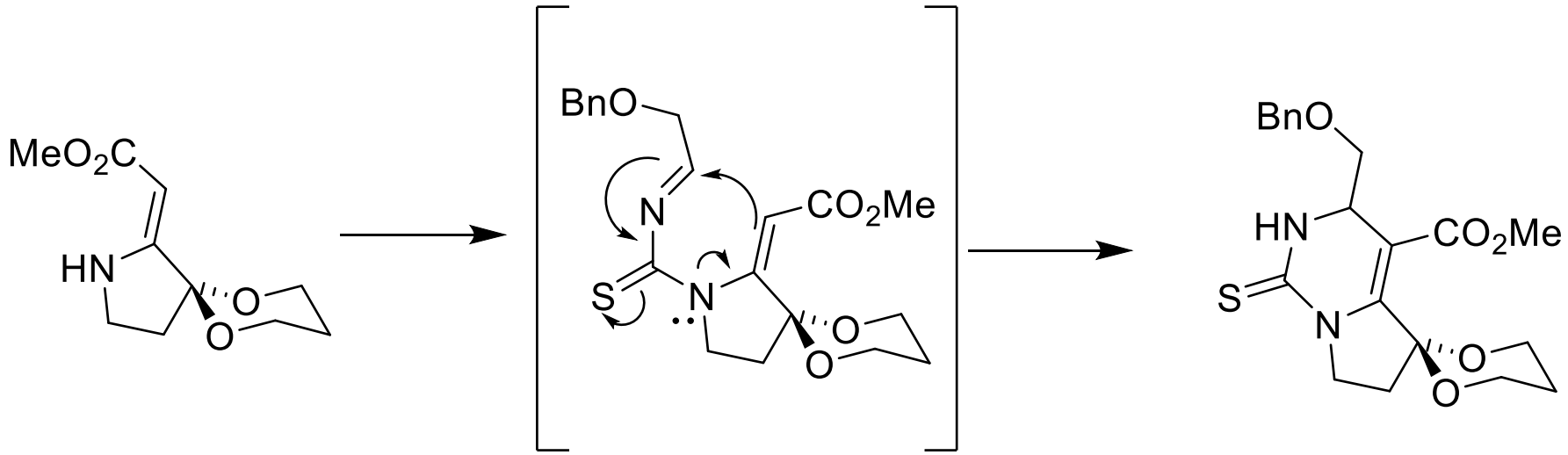
	R^1	R^2	R^3	R^4	R^5	R^6
STX (**1**)	H	H	H	OH	OH	$OCONH_2$
doSTX (**2**)	H	H	H	OH	OH	H
dcSTX (**3**)	H	H	H	OH	OH	OH
neoSTX (**4**)	OH	H	H	OH	OH	$OCONH_2$
GTX1 (**5**)	OH	H	OSO_3^-	OH	OH	$OCONH_2$
GTX2 (**6**)	H	H	OSO_3^-	OH	OH	$OCONH_2$
GTX3 (**7**)	H	OSO_3^-	H	OH	OH	$OCONH_2$
GTX4 (**8**)	OH	OSO_3^-	H	OH	OH	$OCONH_2$
β-STXol (**9**)	H	H	H	H	OH	$OCONH_2$
dc-α-STXol (**10**)	H	H	H	OH	H	OH

合成历史

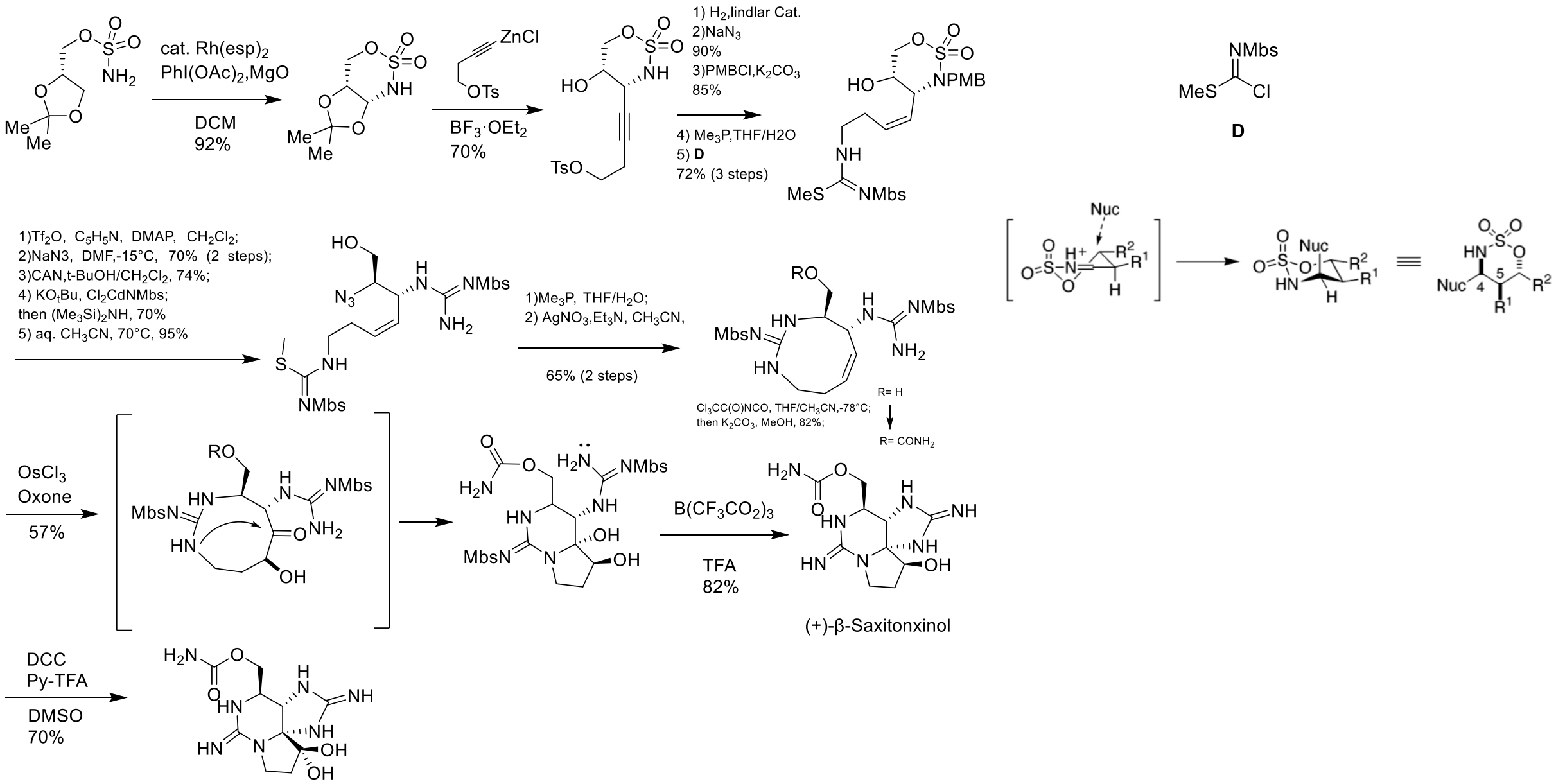
- Kishi Group 1977
- Du Bois Group 2006
- Nagasawa Group 2009
- Nishikawa Group 2011
- Okuyama Group 2020

Kishi's work

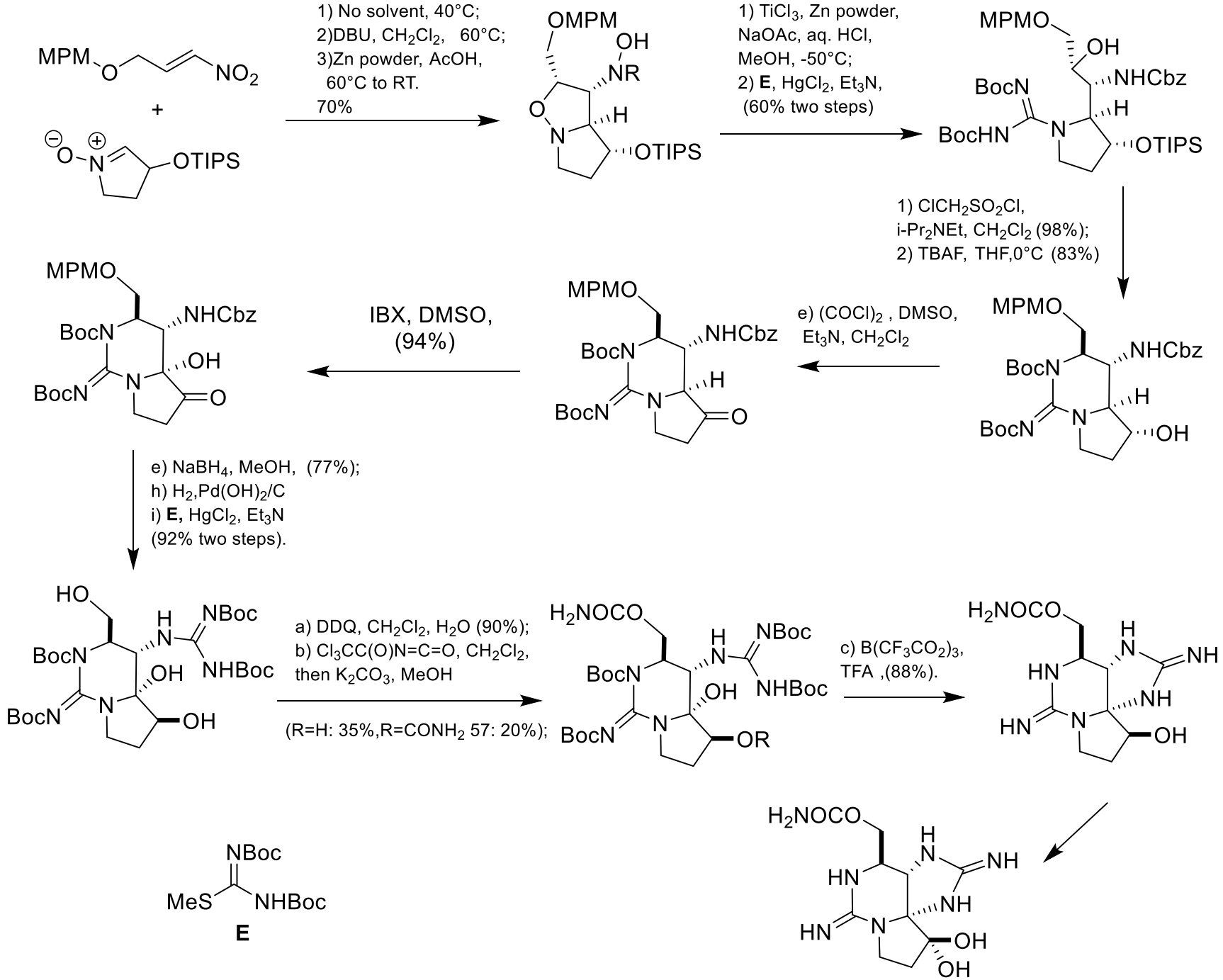

1.B,PTSA,PhMe,Δ
2.N2H4·H2O,MeOH,Δ
P4S10,PhH,80°C
D,NaHCO3
DCM,Δ
KOH,MeOH,50°C
37% from A
Si(NCS)4
G,PhH
then PhMe,110°C
75%
B
D
G
J
1. J, BF3·OEt2,
MeCN
2. AcOH–TFA (9:1),
50 °C
32%
1. N2H4·H2O, MeOH
2. NOCl, CH2Cl2, –50 °C
3. PhH, 90 °C
4. NH3, PhH
75%
33%
1. NaHCO3, Et3OBF4, CH2Cl2
2. EtCO2NH4, 135 °C
1.BCl3
2.Ac2O,Py （75%）
3.NBS,wet MeCN
4.MeOH,100°C （33%）
ClSO2NCO
HCOOH, 5°C
50%

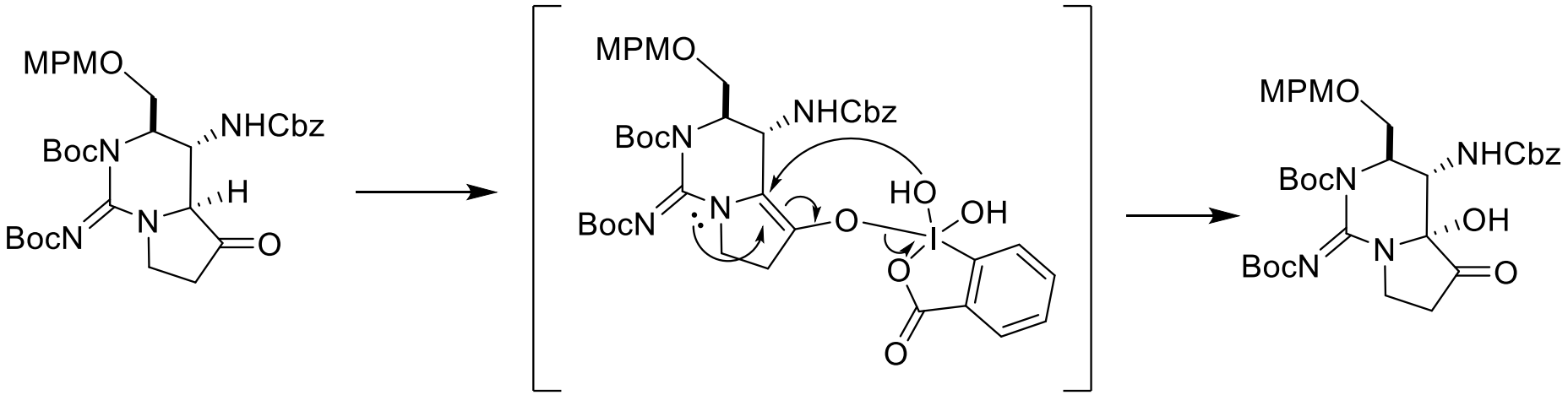

MeO2C
HN
O
O
BnO
N
CO2Me
S
N
O
O
BnO
HN
CO2Me
S
N
O
O

Du Bois's work

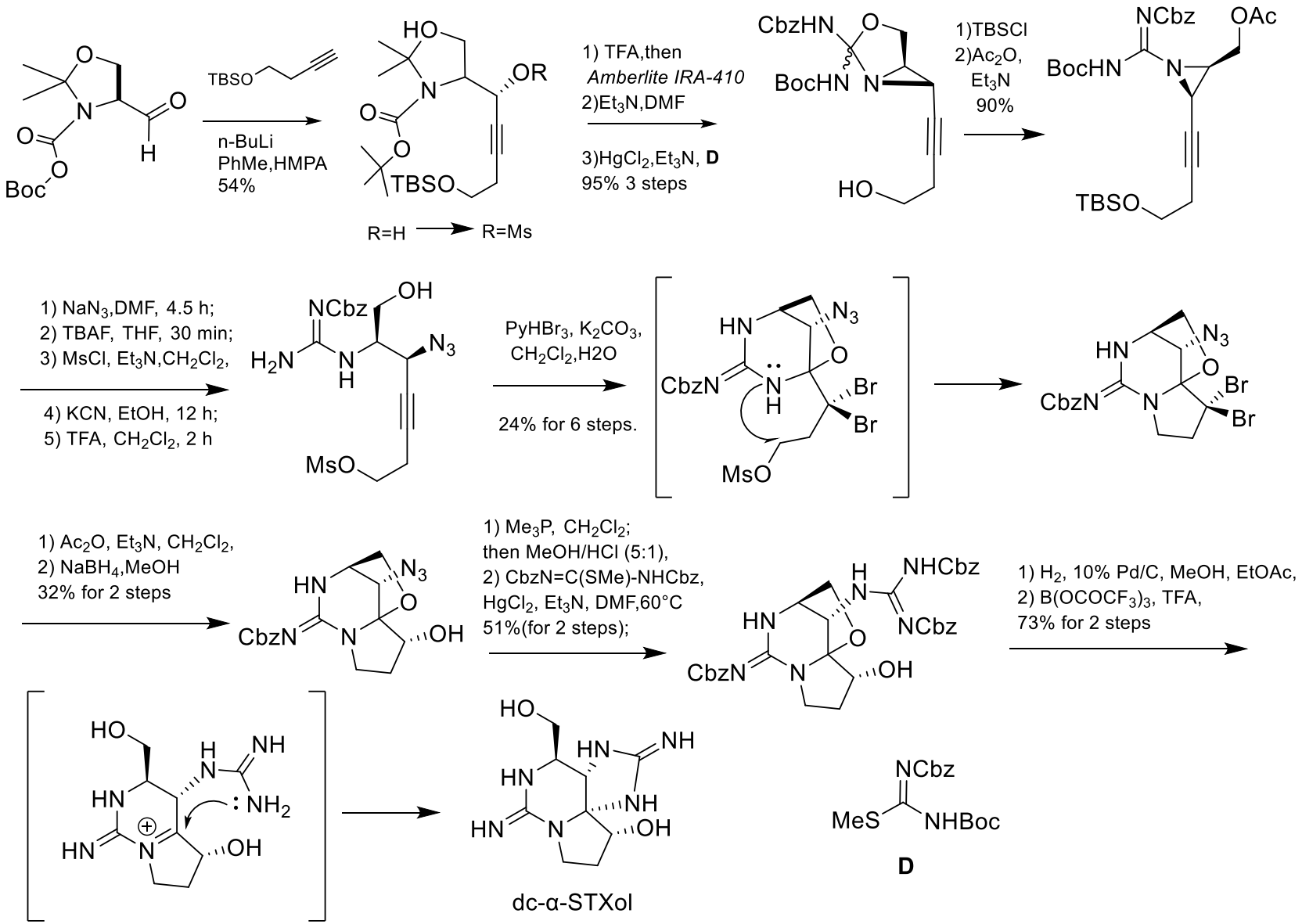


Nagasawa's work

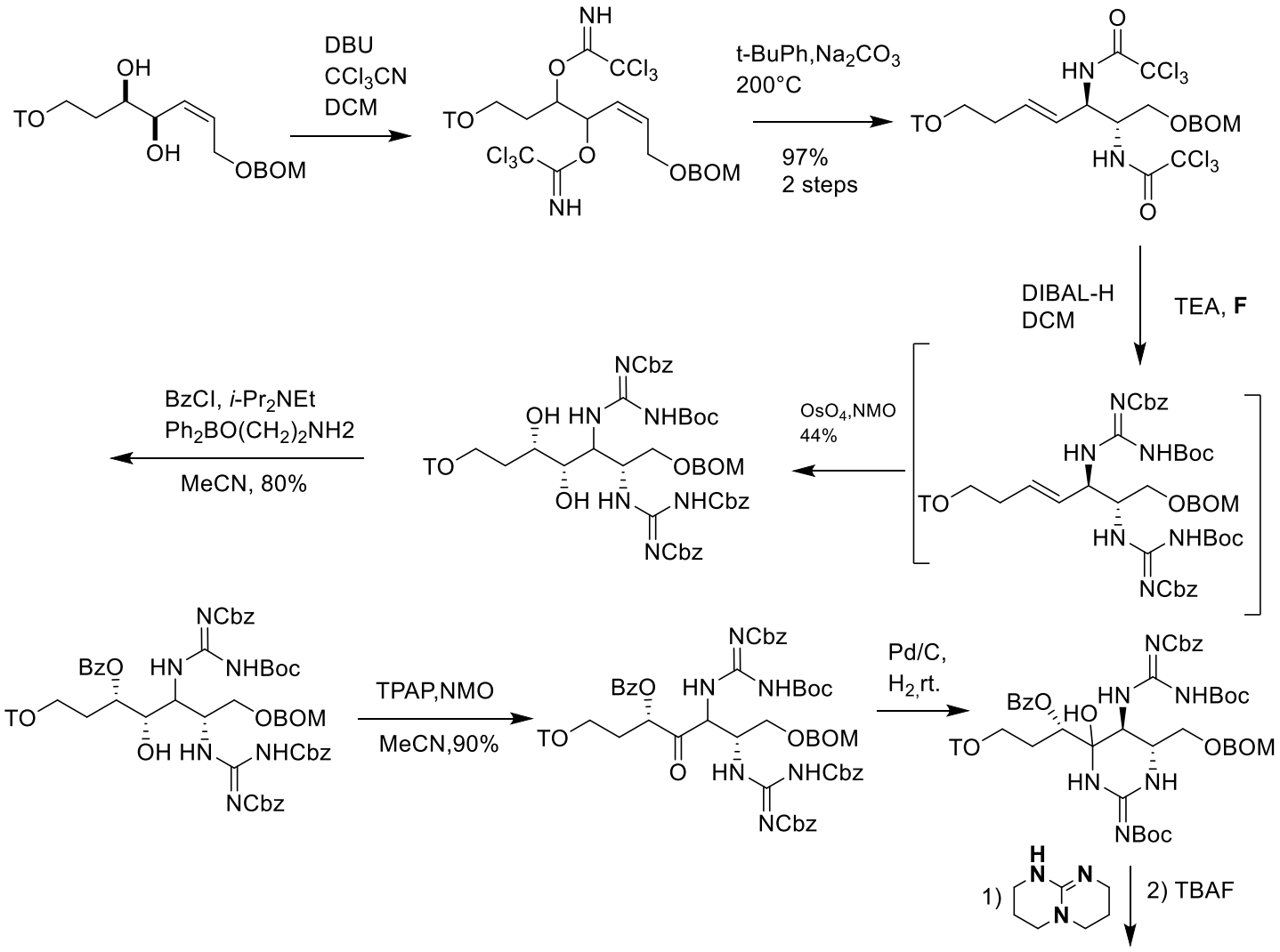


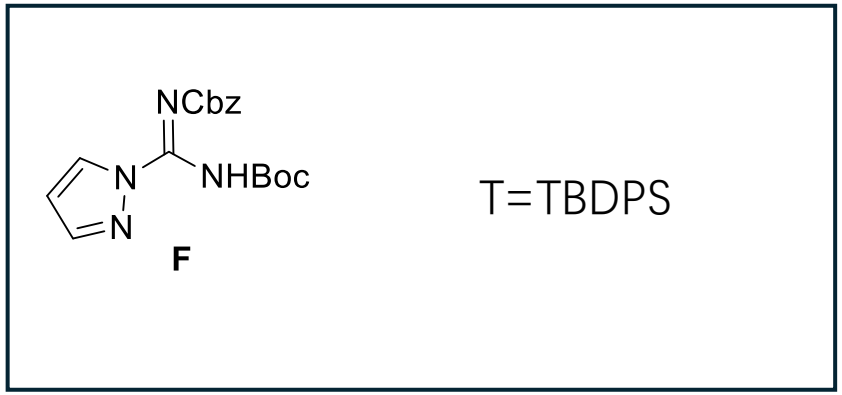

MPMO
NHCbz
BocN
H
BocN
N
O
MPMO
NHCbz
BocN
BocN
N
O
HO
OH
I
O
O
O
MPMO
NHCbz
BocN
OH
BocN
N
O

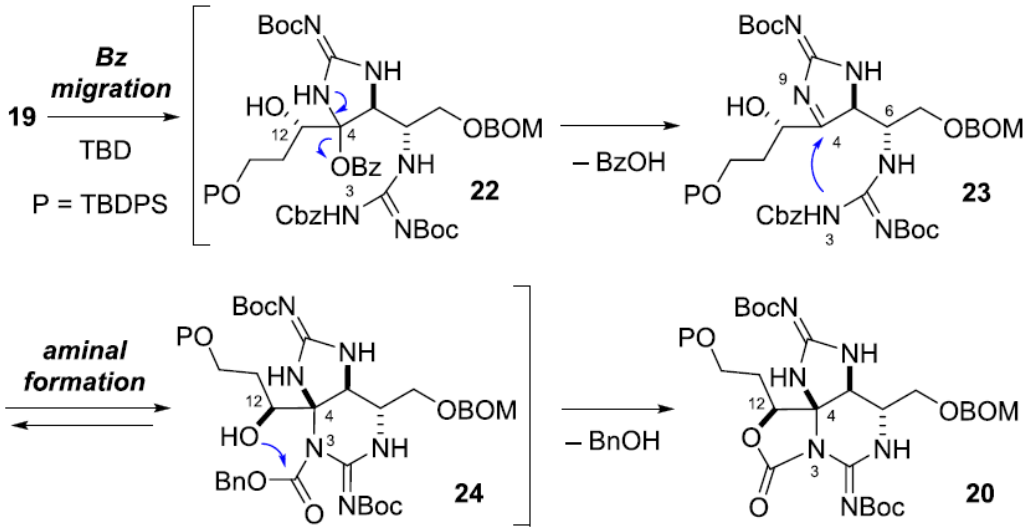
Nisikawa's work



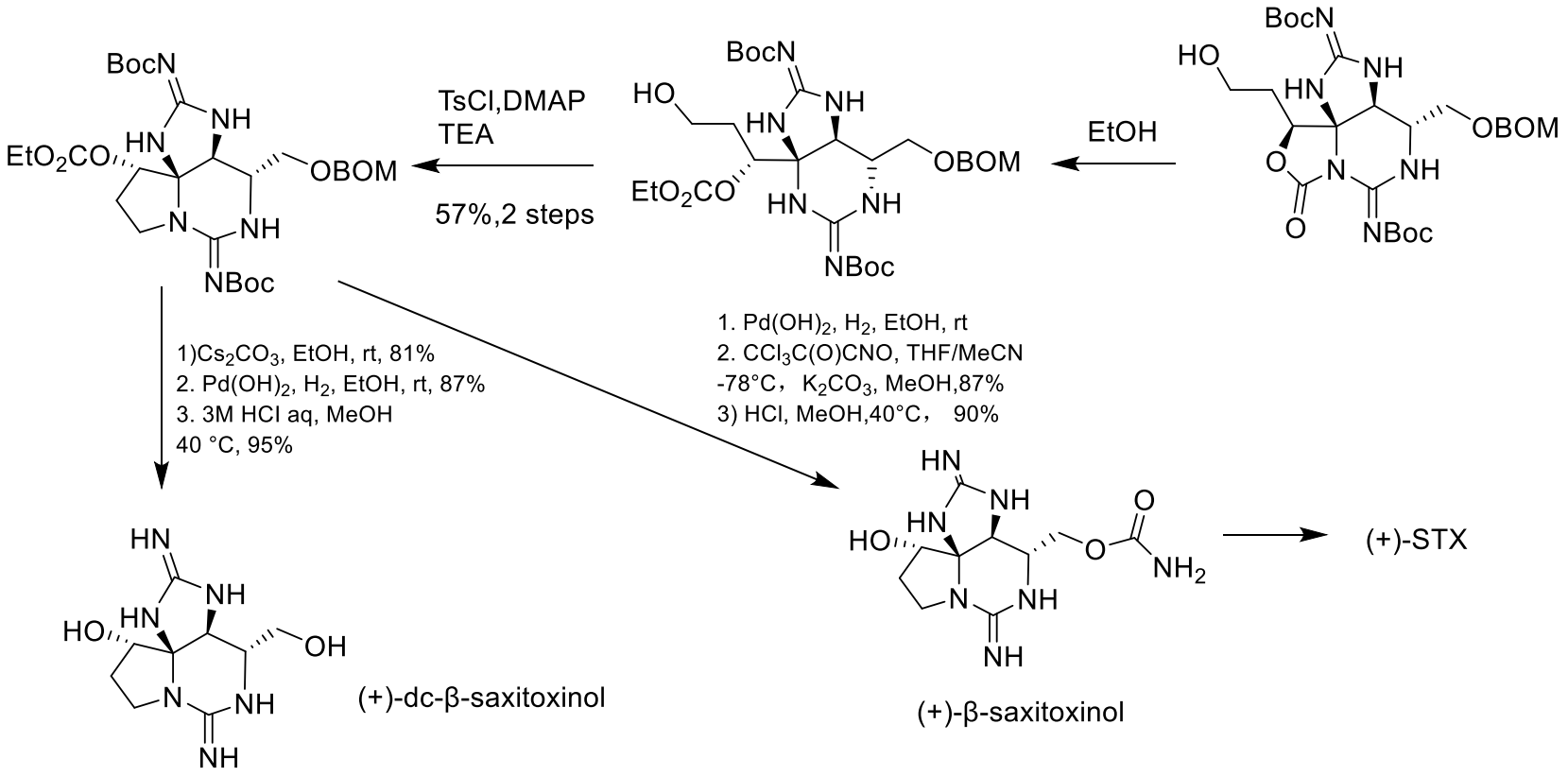
Okuyama's work







Okuyama’s work



Thanks !