

Total synthesis of Ecteinascidin-743 (ET-743)

Zhenyu Zhang

2024-11-27

Laboratory safety—Cannulas and Needles

ACS CHEMICAL HEALTH & SAFETY
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Safe Handling of Cannulas and Needles in Chemistry Laboratories

Tilak Chandra,* Jeffrey P. Zebrowski, and Lisa Y. Lenertz

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ABSTRACT: Cannulas and needles (sharps) are frequently used for chemical manipulations involving air- and moisture-sensitive chemicals. When using these devices, the presence of sharp tips poses a risk of puncture wounds and increases the likelihood of chemical exposure. While these devices are regularly used in chemistry, facts on their proper usage, as well as the prevention of injuries, are scarce in the literature. Needle injuries often reflect inadequate hands-on training in their use during chemical transfer procedures, incorrect recapping, and improper storage and disposal procedures. Preventing needle injuries in the lab requires having situational awareness which is achieved by using proper techniques and a proper reaction set up, performing a risk assessment, and having group discussions about the procedure. As in all chemical manipulations, it is critical to be familiar with the reaction setup, to receive the necessary training for the chemicals being used, and to have reviewed all associated standard operating procedures (SOPs). Thorough planning can reduce injuries and exposures incurred by students and other researchers. This paper will discuss safe techniques for the use of needles and cannulas in chemistry laboratories.

KEYWORDS: air-sensitive, cannula, complacency, hazard assessment, hazard analysis, hazard controls, high-hazard operations, needles, pyrophoric, risk assessment, risk analysis, safety education, Schlenk line techniques, standard operating procedures (SOPs), syringes, toxic, training, vacuum

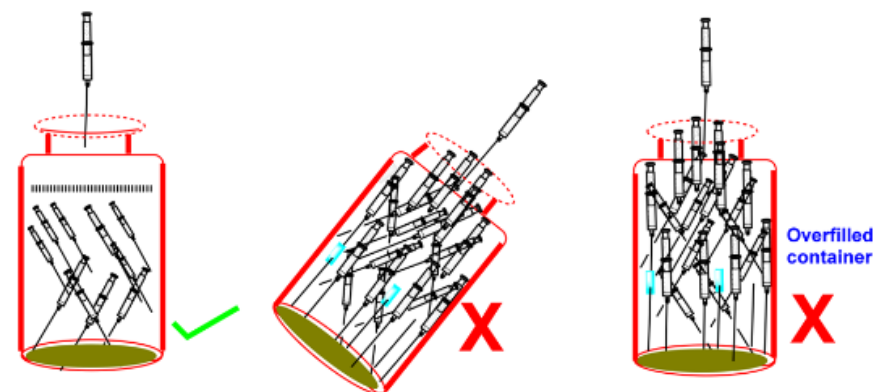
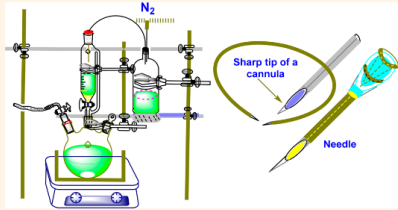
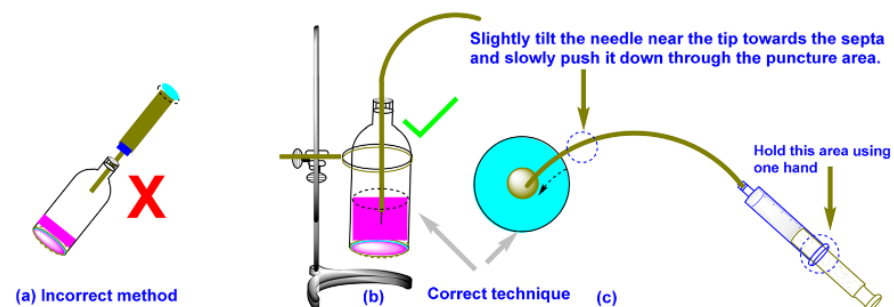


Figure 11. Correct use of sharp/needle containers for disposal.

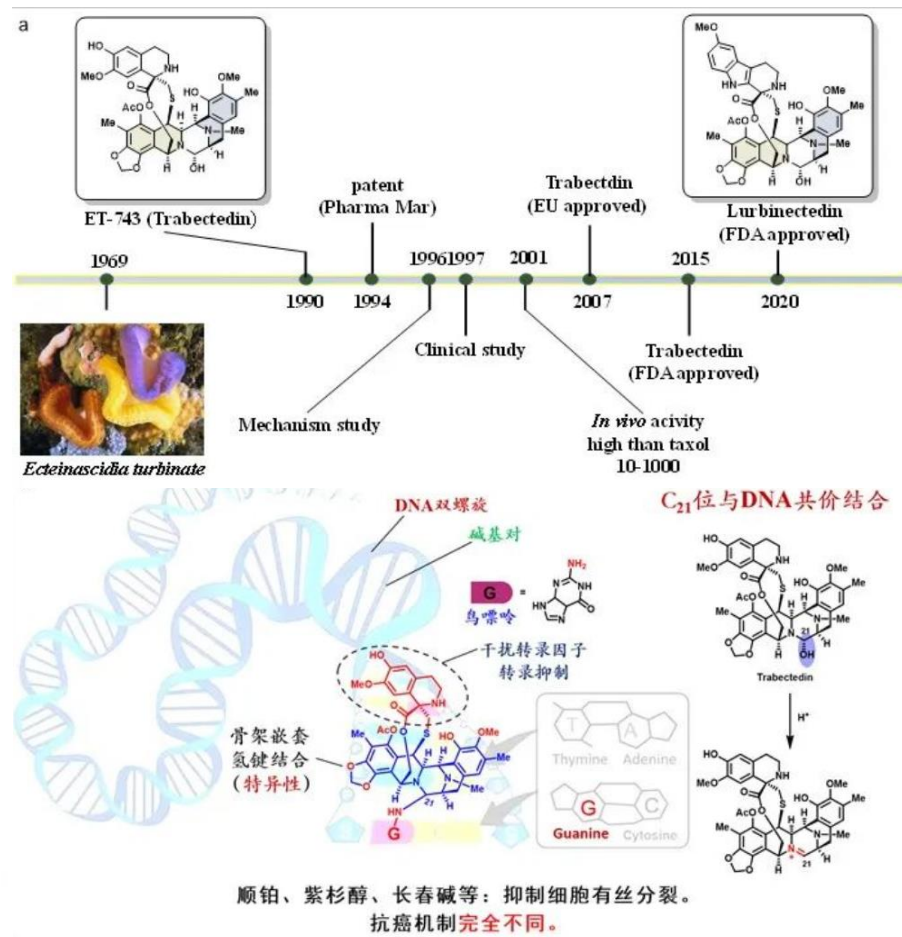


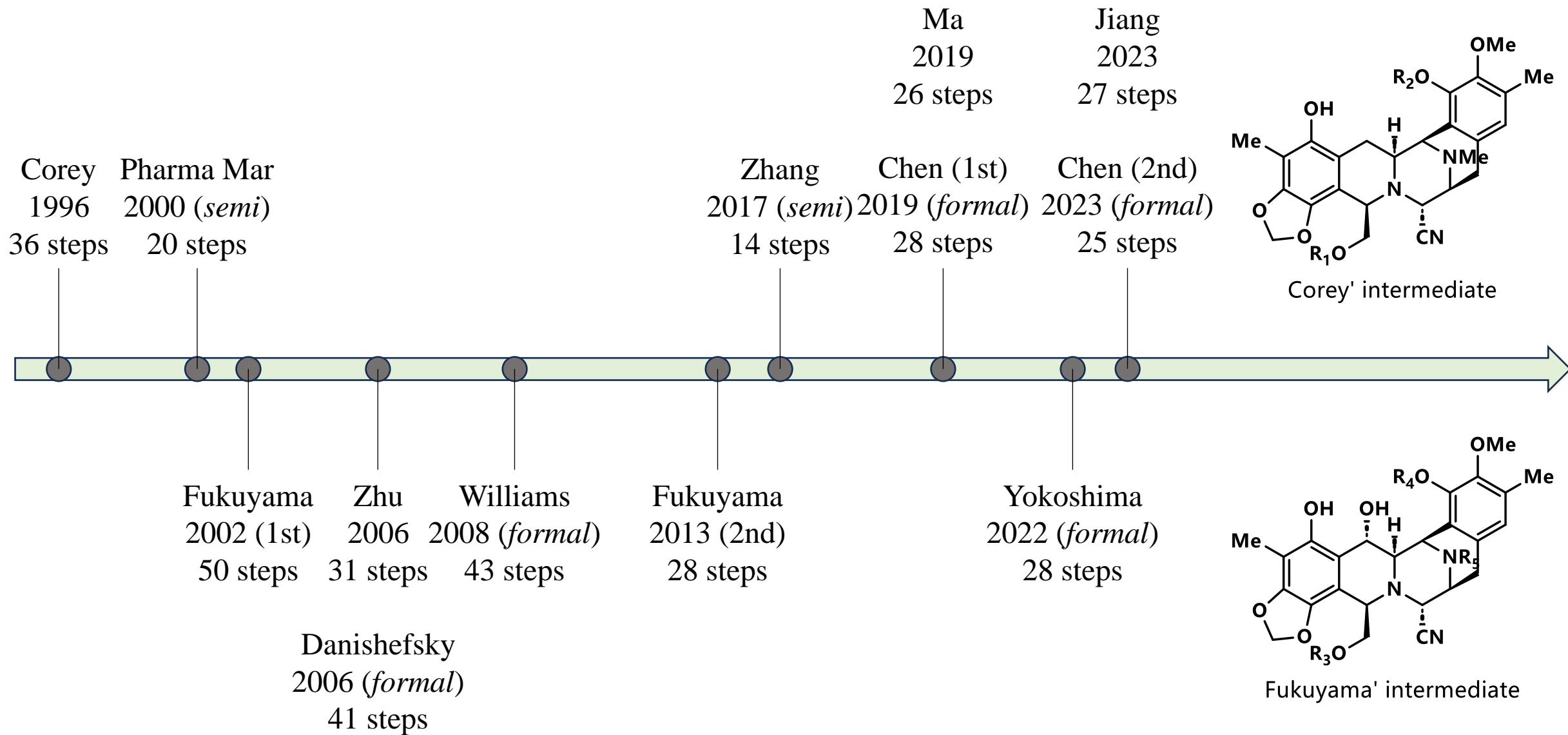
当不小心被针头扎伤时，一般应尽量促使伤口流血（可将伤口置于流水下），尽量排出进入创口的化学试剂。在确保排净化学试剂后，擦干伤口并用绷带包扎。

Ecteinascidin-743 (ET-743)

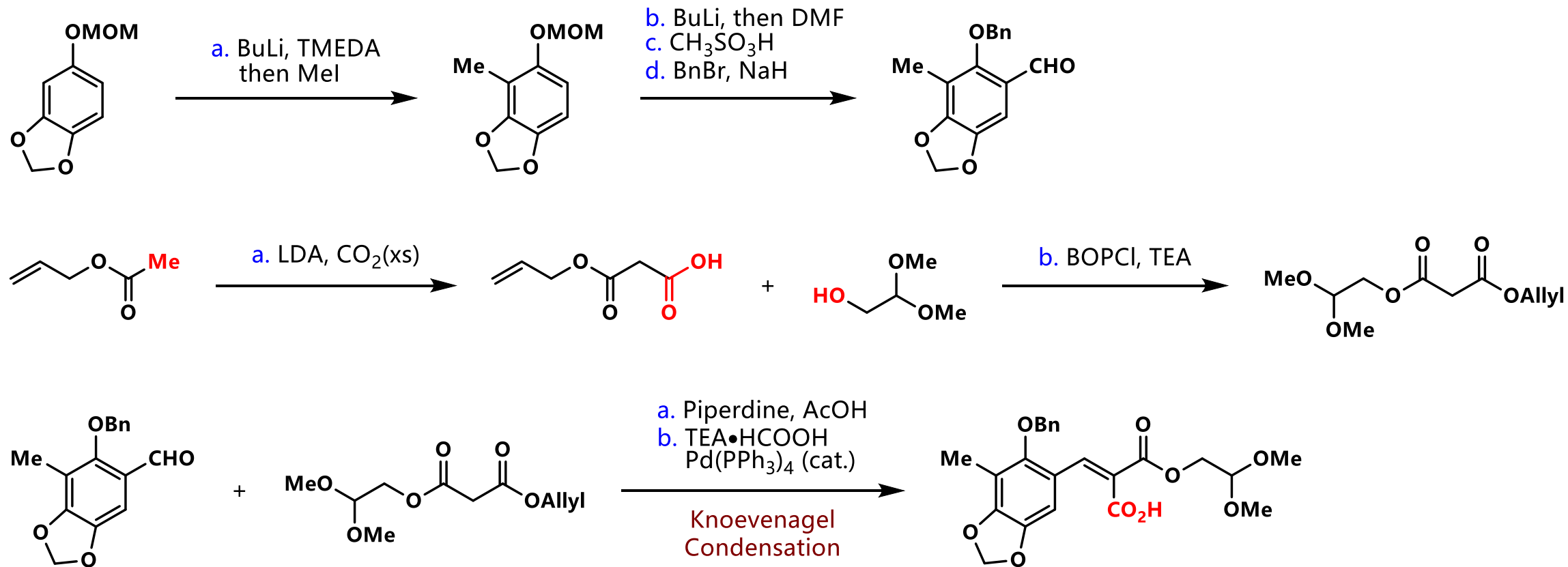
- Isolated from the Caribbean tunicate *Ecteinascidia turbinata* in 1986.
- Remarkable antitumor activity.
- Approved by FDA and used clinically as a drug.(Trabectedin/Yondelis)
- Tetrahydroisoquinoline alkaloids.
- Aza-bicyclo[3.3.1] system.
- A 10-member sulfurcontaining bridge ring,

J. Nat. Prod. **1990**, 53, 771
Nat. Med. **2001**, 7, 961



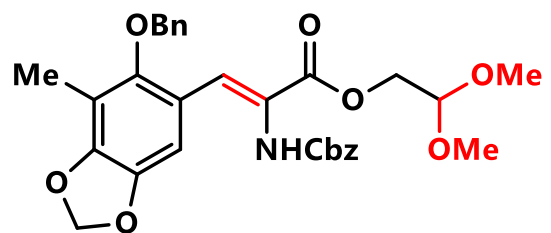


◆ E. J. Corey 课题组的工作 J. Am. Chem. Soc., 1996, 118, 9202

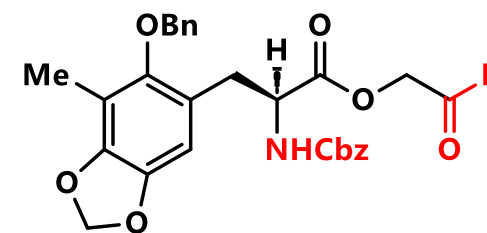


c. $(\text{PhO})_2\text{P}(\text{O})\text{N}_3$
TEA, BnOH

Curtius
Rearrangement

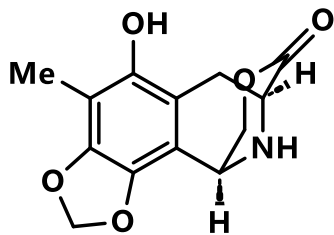


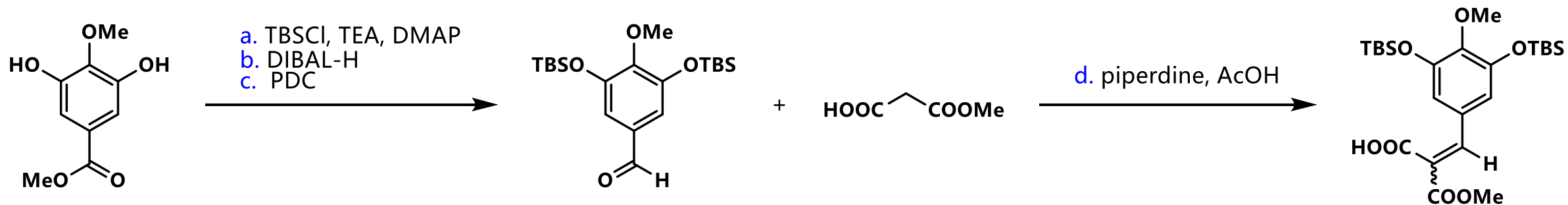
d. H_2 , $\text{Rh}[(\text{COD})R, R\text{-DIPAMP}]^+\text{BF}_4^-$ (cat.)
e. $\text{BF}_3 \cdot \text{OEt}_2$, H_2O



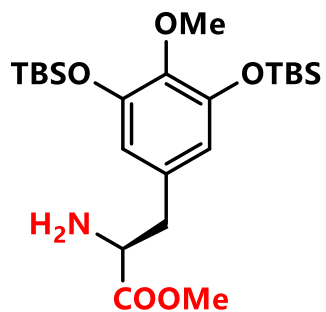
f. $\text{BF}_3 \cdot \text{OEt}_2$, 4 Å
g. H_2 , Pd/C

Pictet–Spengler
Reaction

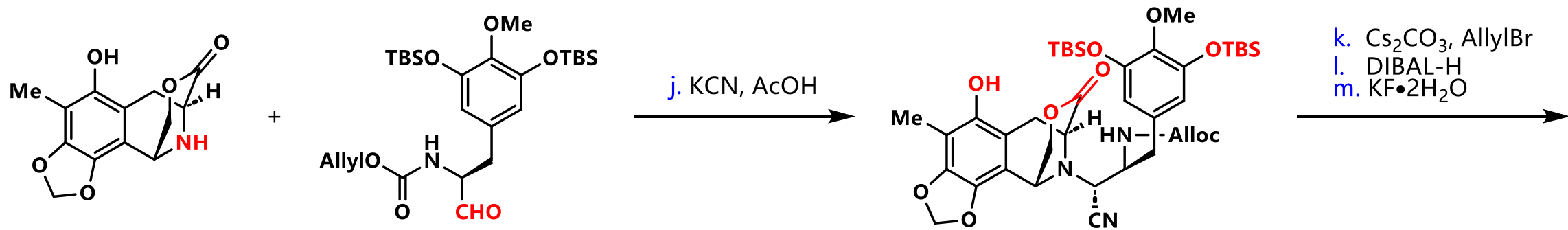
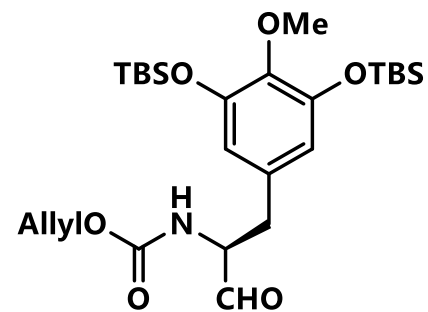


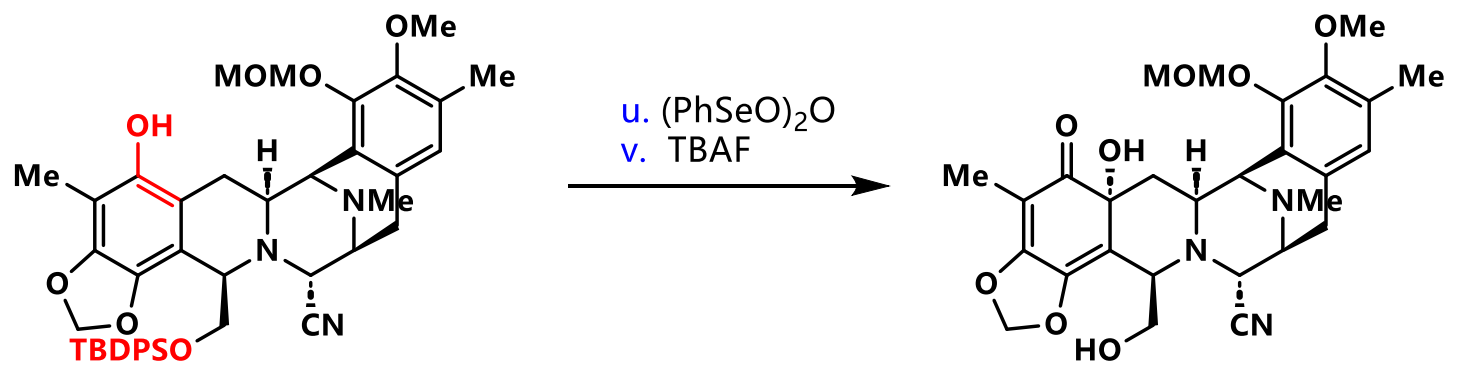
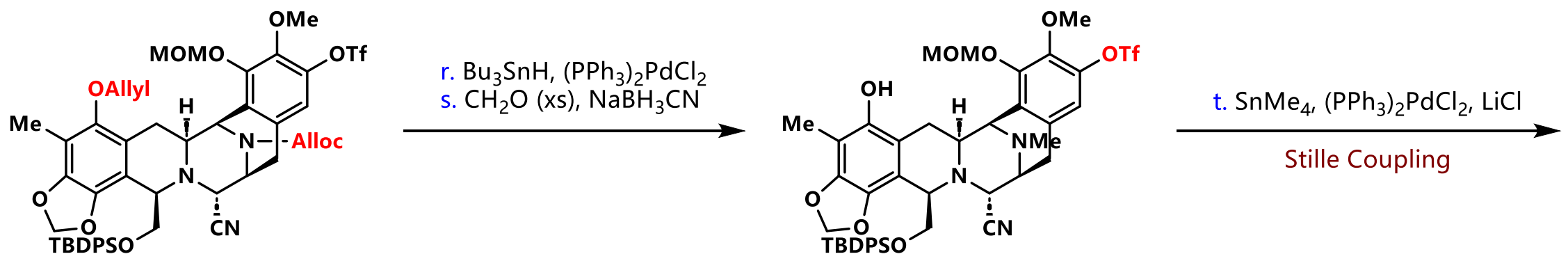
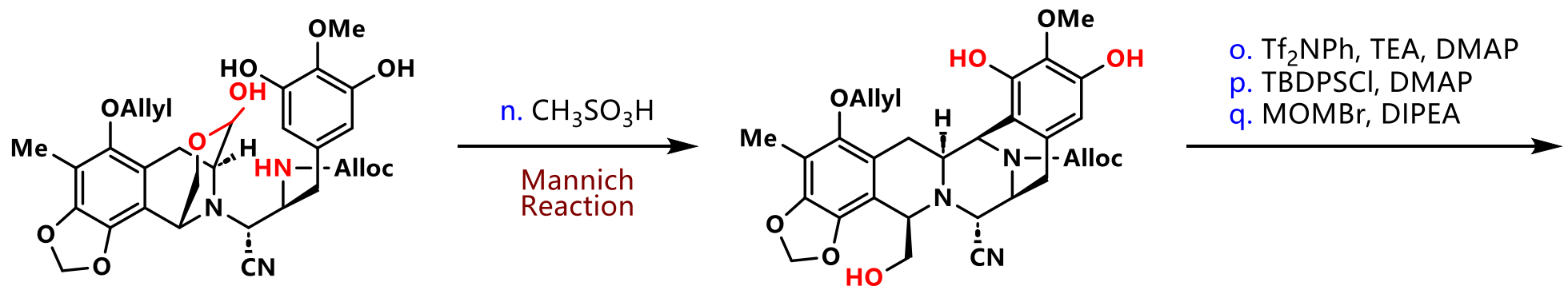


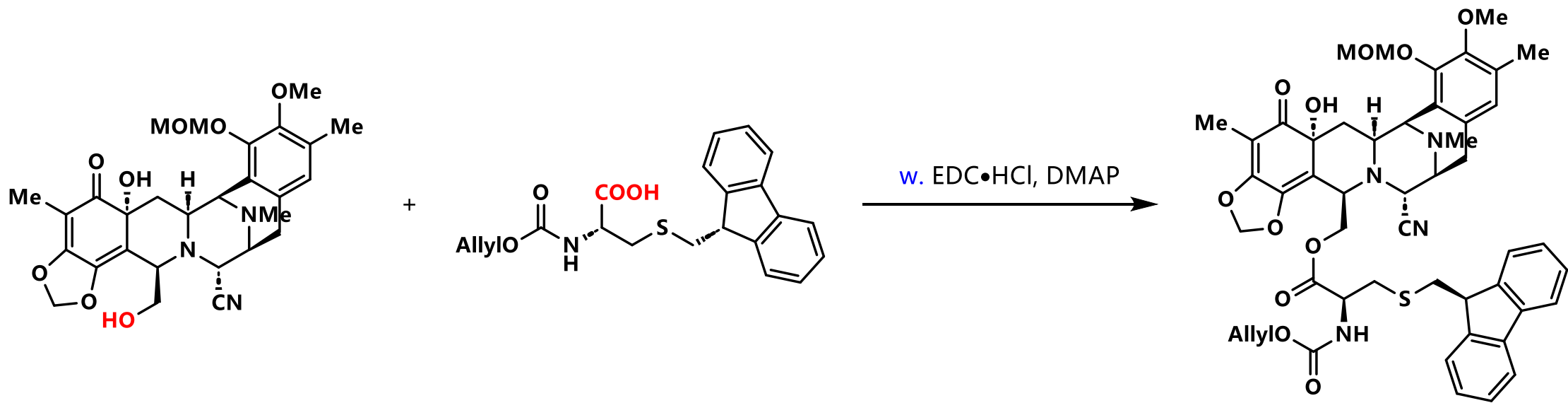
- e. $(\text{PhO})_2\text{P}(\text{O})\text{N}_3$, TEA, BnOH
 f. H_2 , $\text{Rh}[(\text{COD})R, R\text{-DIPAMP}]^+\text{BF}_4^-$ (cat.)
 g. H_2 , Pd/C



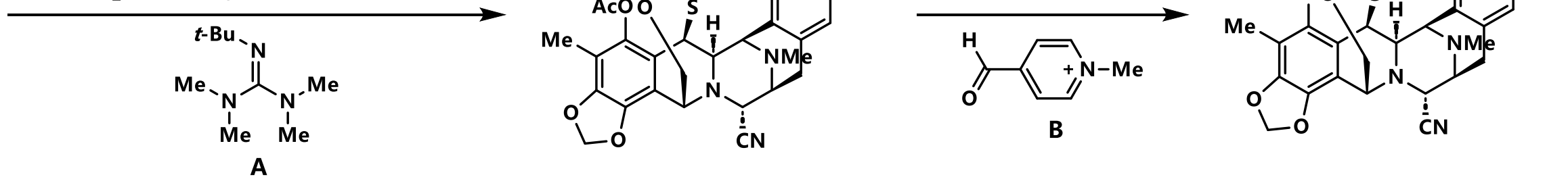
- h. AllylOCCl, pyr
 i. DIBAL-H



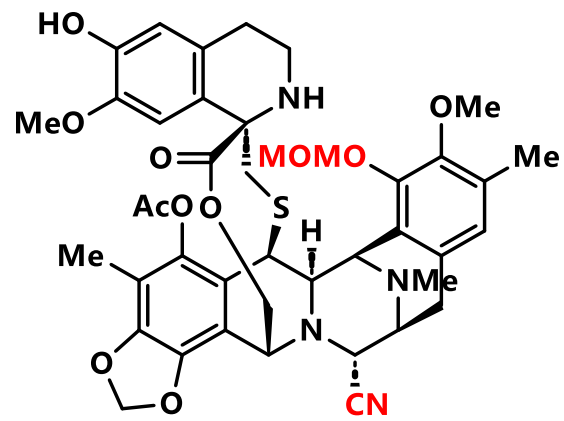
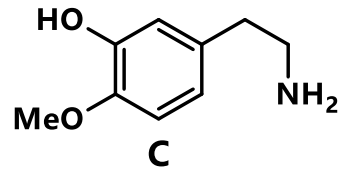




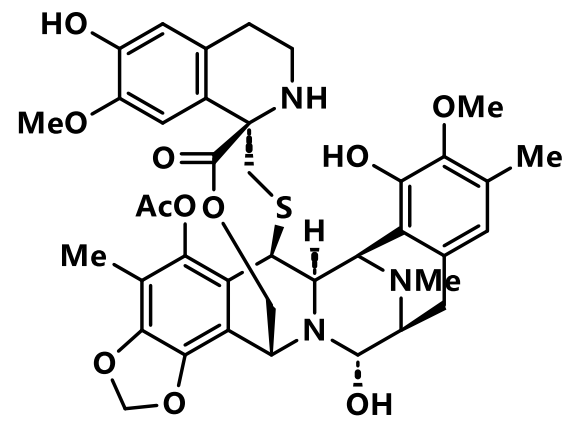
- x. Tf_2O (16 eq), DMSO (33 eq), $-40\text{ }^\circ\text{C}$
- y. DIPEA (100 eq), $0\text{ }^\circ\text{C}$
- z. *t*-BuOH (61 eq), $0\text{ }^\circ\text{C}$
- aa. **A**, $0\text{ }^\circ\text{C}$
- ab. Ac_2O (184 eq), $23\text{ }^\circ\text{C}$



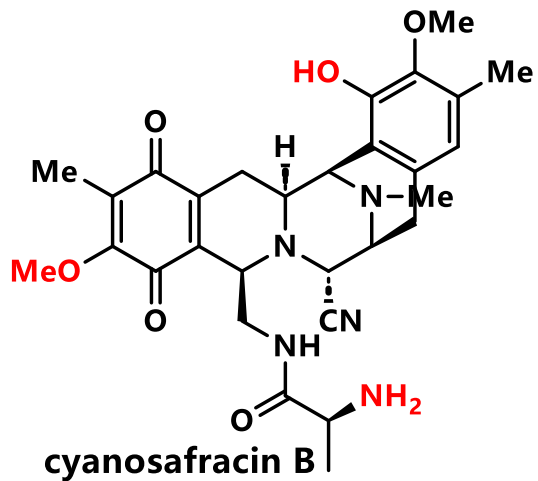
ae. C, silic gel, EtOH



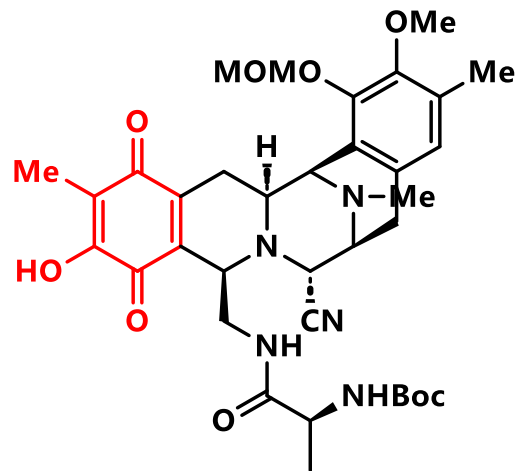
af. TFA
ag. AgNO₃, H₂O



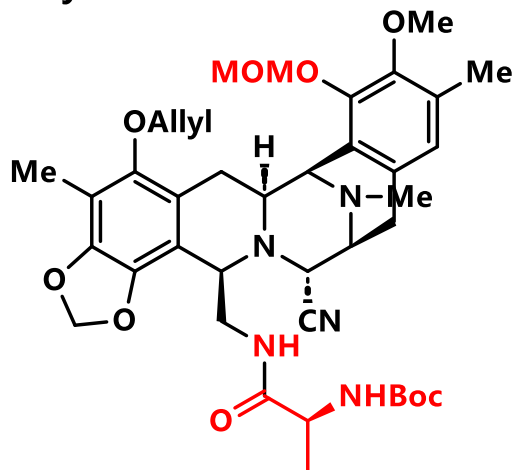
◆ Pharma Mar公司的工作 Org. Lett., 2000, 2, 2545



a. Boc_2O
b. MOMBr, DIPEA
c. NaOH 1 M, MeOH

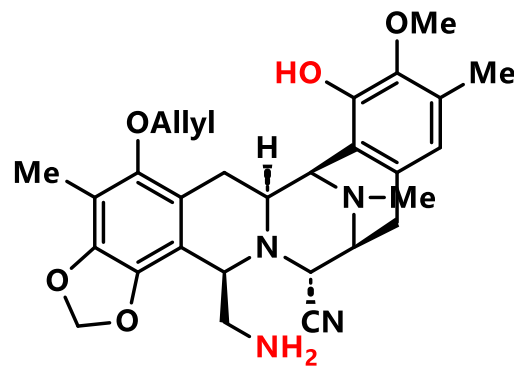
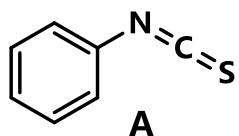


d. H_2 , Pd/C;
 ClBrCH_2 , Cs_2CO_3
e. AllylBr, Cs_2CO_3

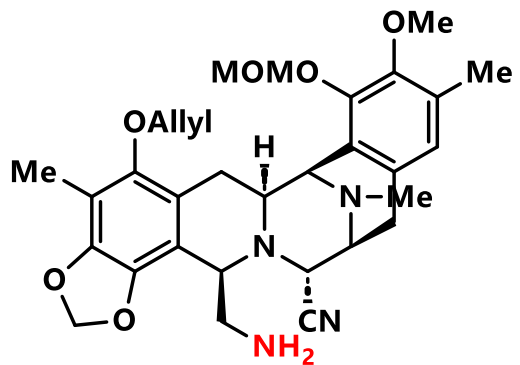


Edman degradation

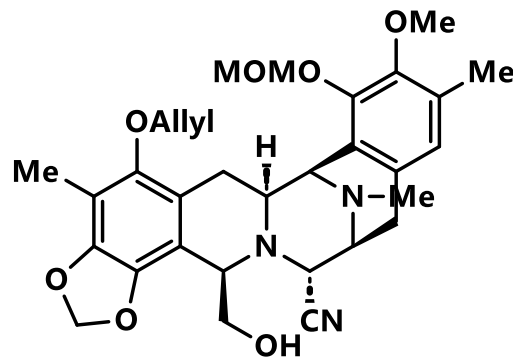
f. TFA
g. **A**
h. HCl/dioxane



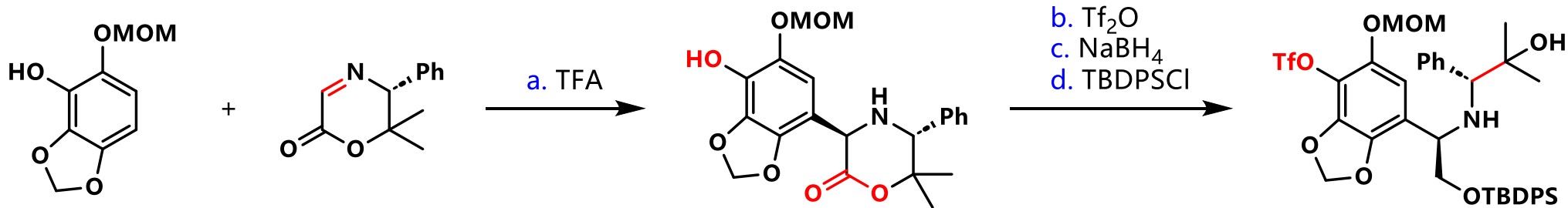
i. TrocCl, pyr
j. MOMBr, DIPEA
k. Zn, AcOH



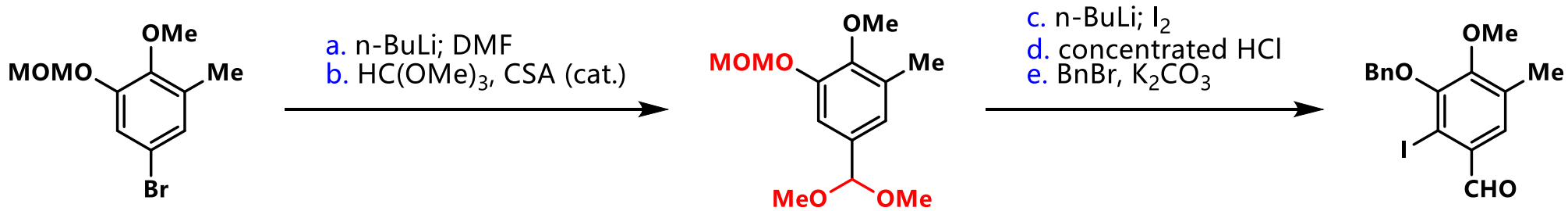
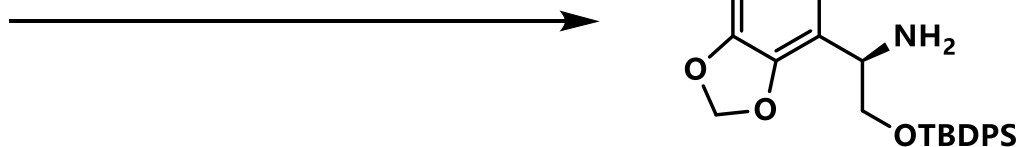
l. NaNO_2 , AcOH



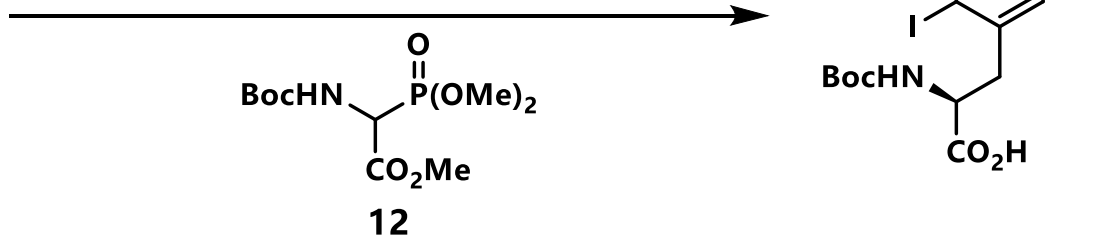
◆ T. Fukuyama 课题组的工作 J. Am. Chem. Soc., 2002, 124, 6552

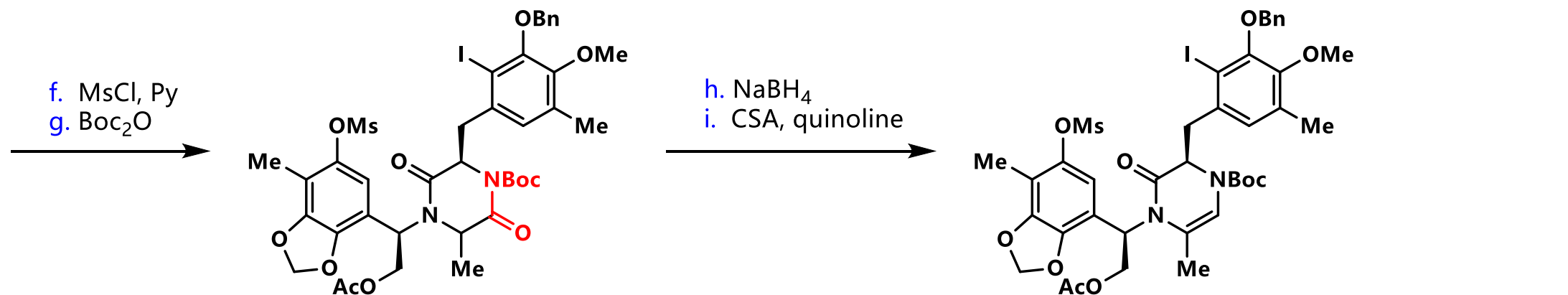
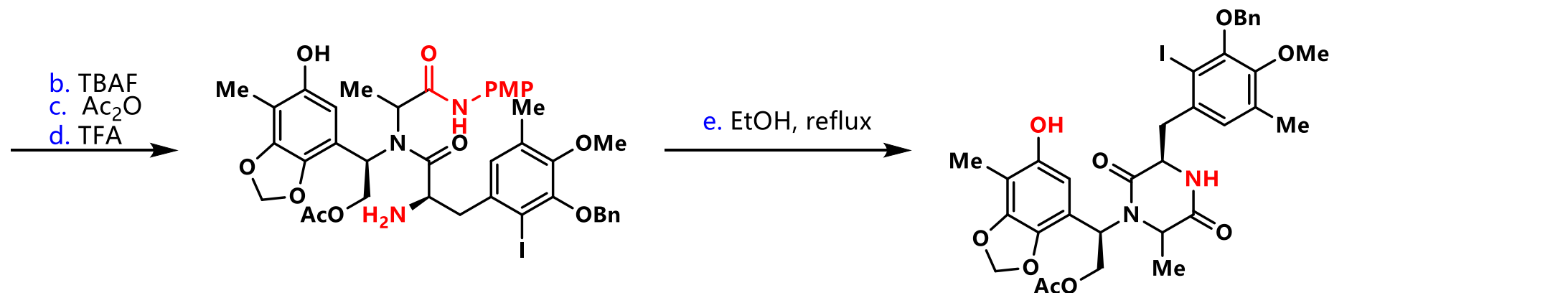
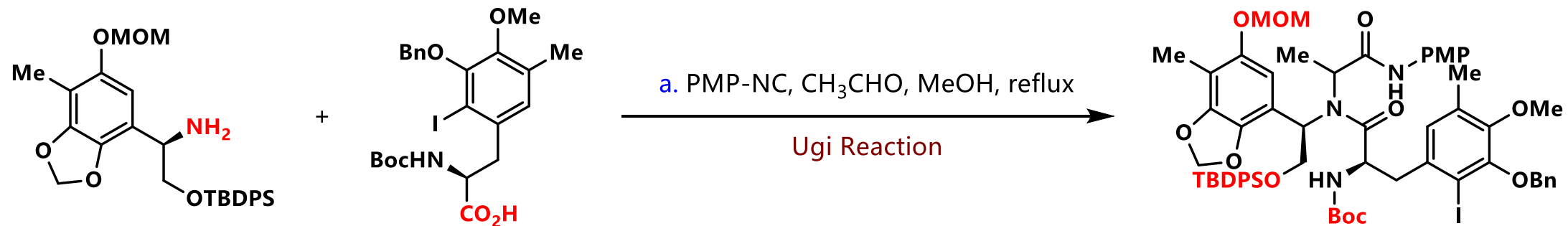


- e. MeZnCl , $\text{PdCl}_2(\text{dppf})$ (cat.)
f. $\text{Pb}(\text{OAc})_4$
g. $\text{NH}_2\text{OH}\cdot\text{HCl}$, NaOAc , EtOH

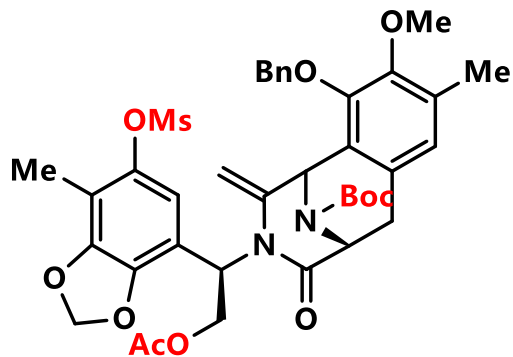


- f. **12**, TMG
g. H_2 , $\text{Rh}[(\text{COD})-(S,S)\text{-Et-DuPHOS}]^+\text{OTf}^-$
h. LiOH

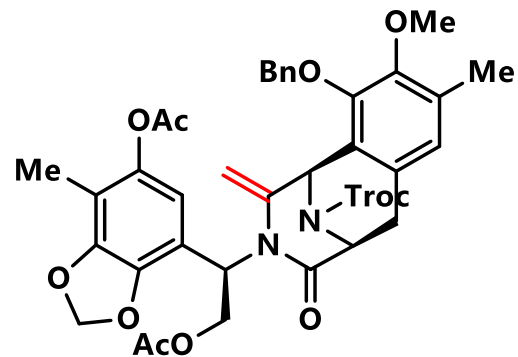




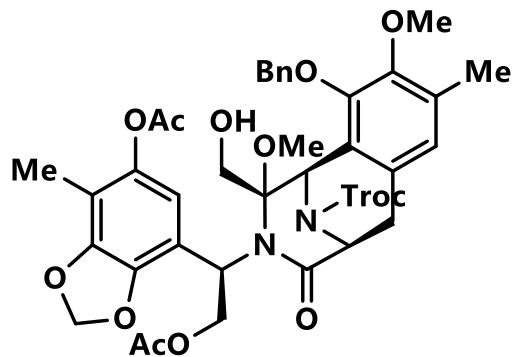
j. Pd₂(dba)₃ (5 mol %)
P(o-tol)₃ (20 mol %)
TEA, CH₃CN, reflux



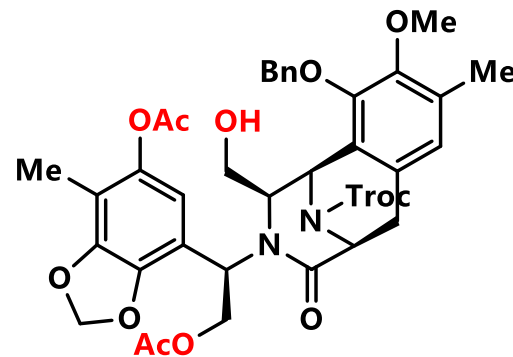
k. NaOH
l. Ac₂O
m. TFA
n. TrocCl



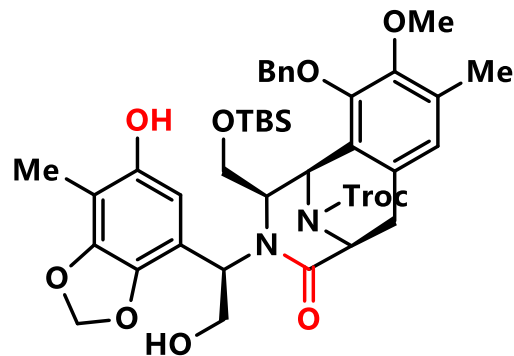
o. DMDO
MeOH-acetone;
CSA (cat.)



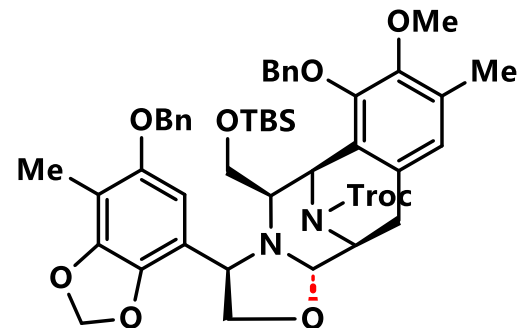
p. NaBH₃CN

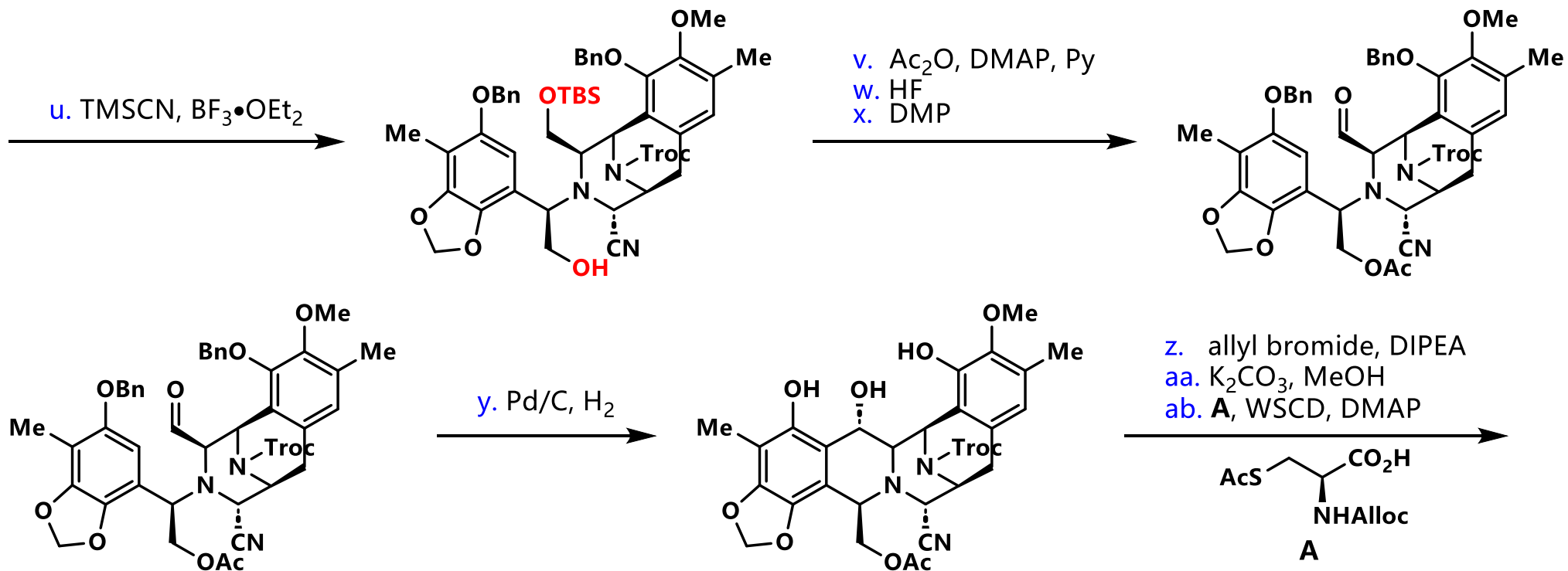


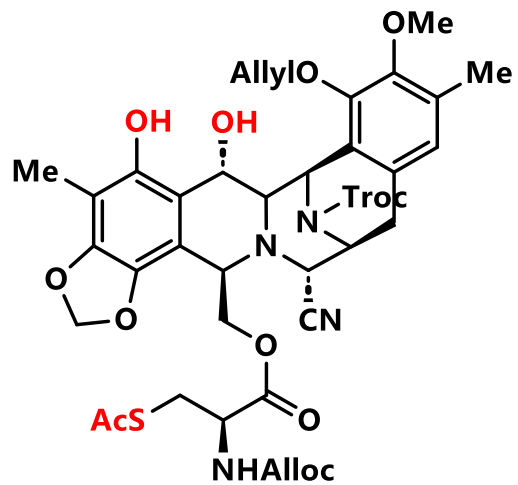
q. TBSCl, Imid
r. guanidinium nitrate
NaOMe, MeOH-DCM



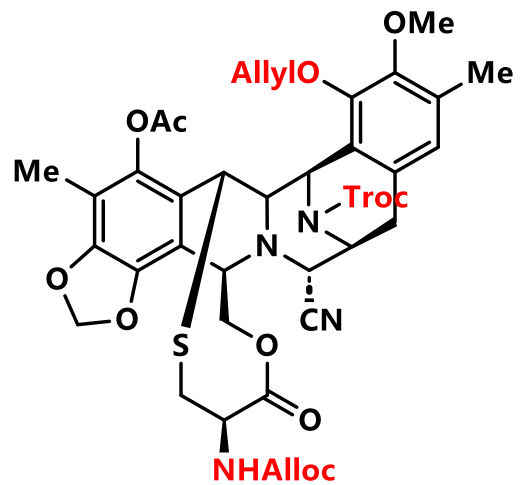
s. BnBr, K₂CO₃
t. Red-Al



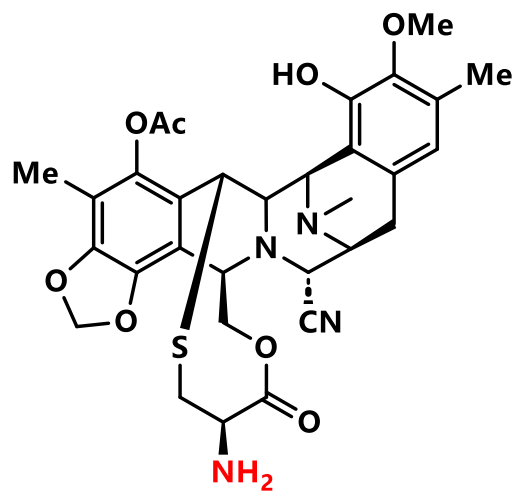




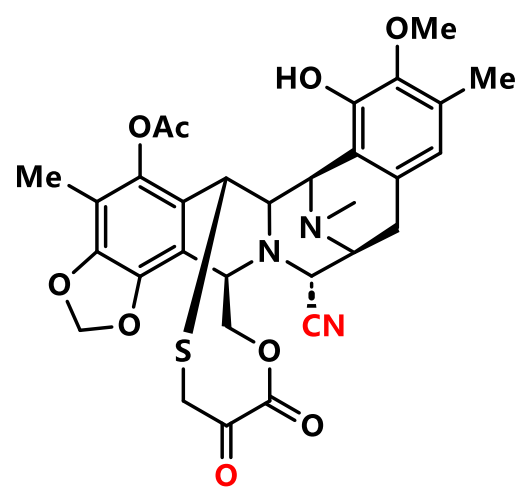
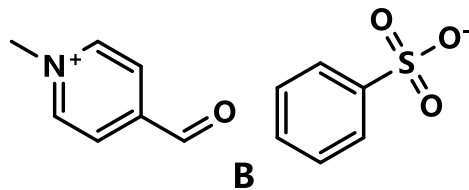
ac. NH_2NH_2
 ad. TFA
 ae. Ac_2O , Py, DMAP



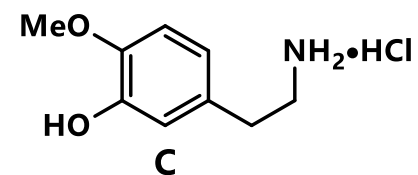
af. Zn, AcOH
 ag. HCHO, AcOH
 NaBH₃CN
 ah. $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$
 AcOH, Bu₃SnH



ai. **B**; DBU; citric acid

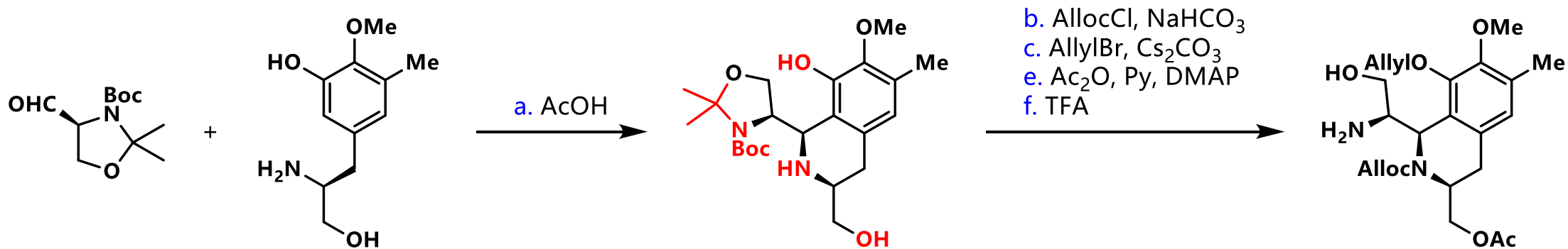
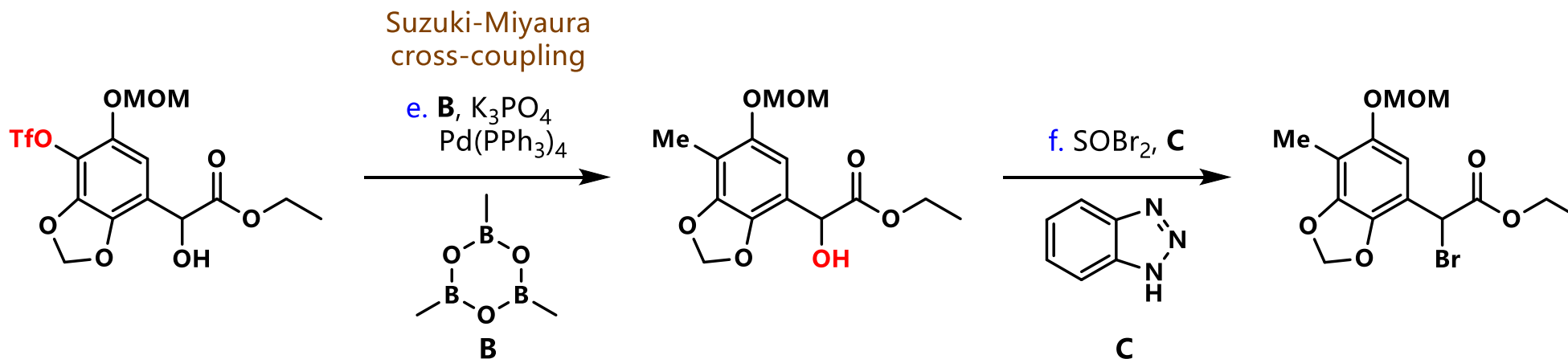
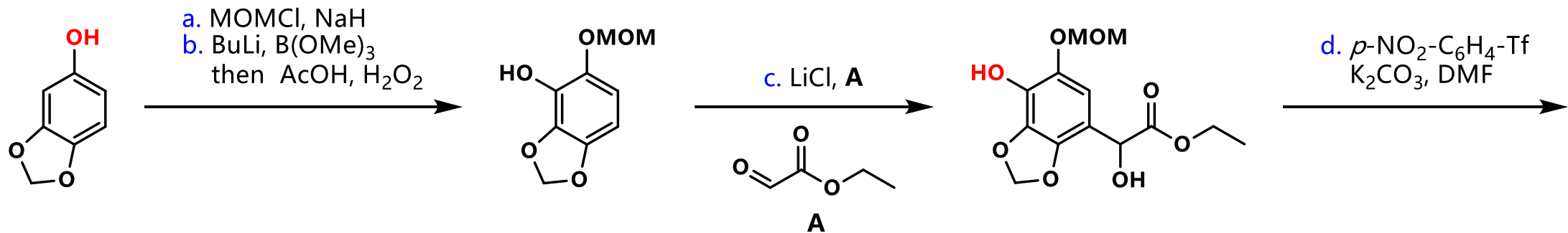


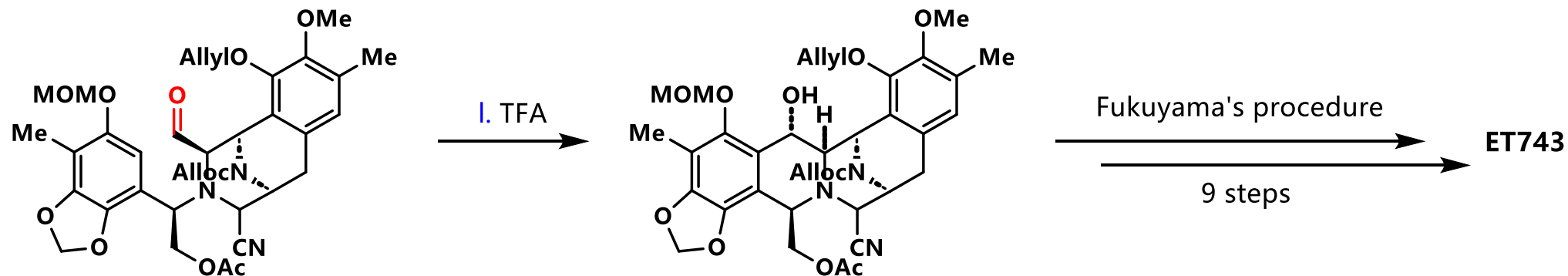
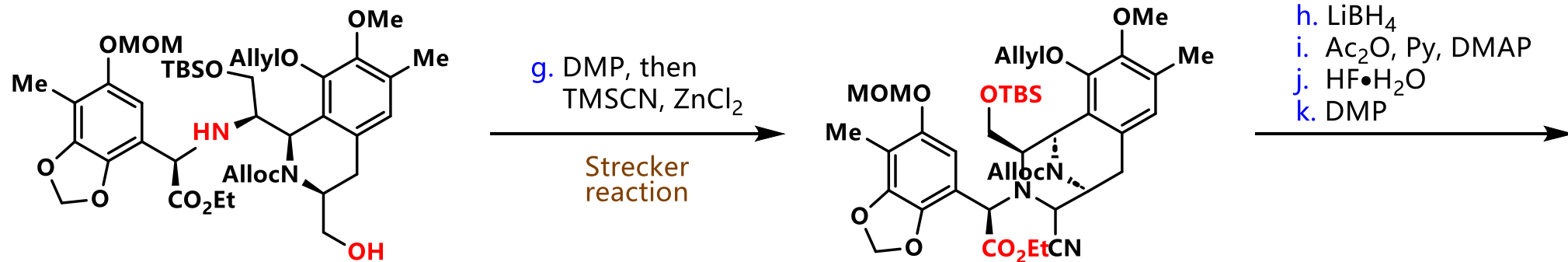
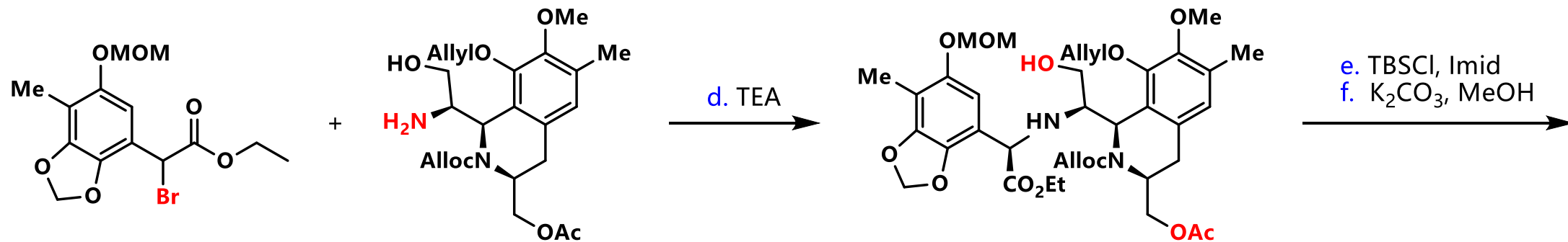
aj. **C**
 ak. AgCO_3



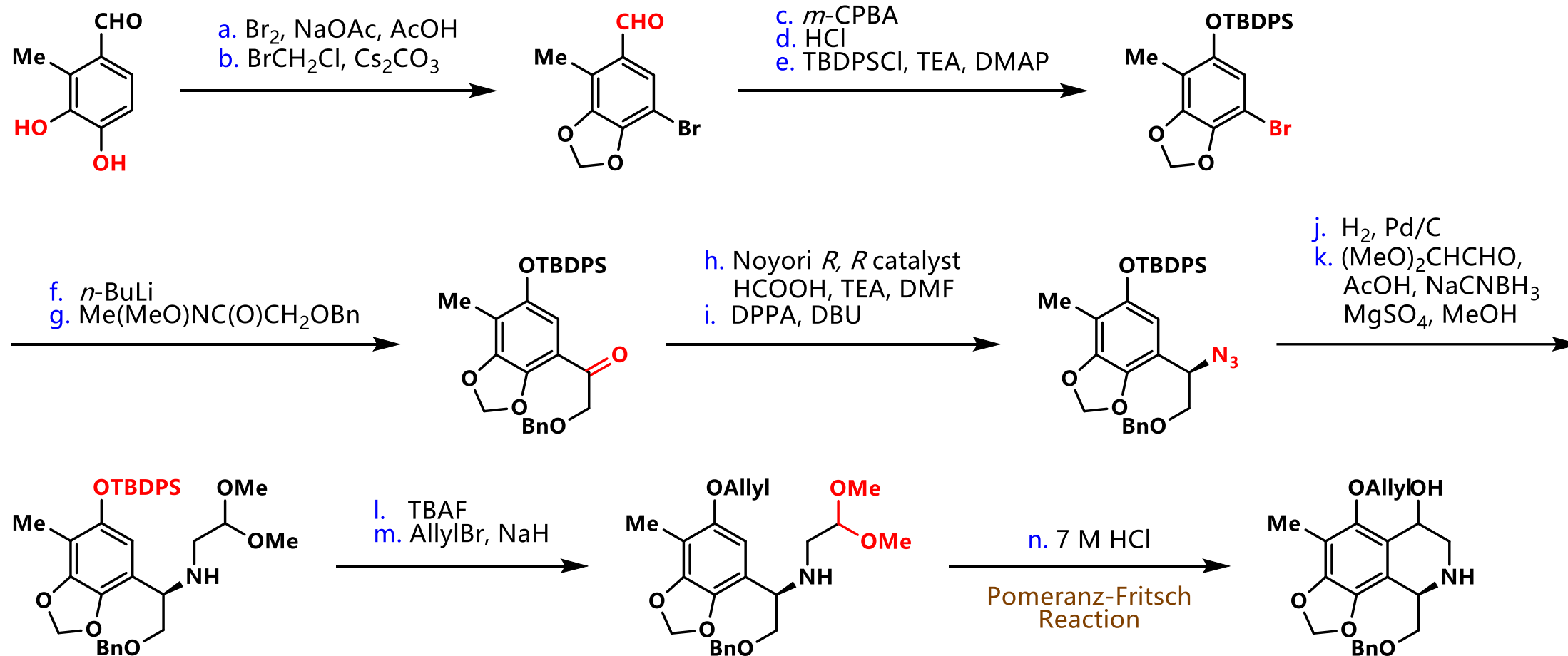
ET743

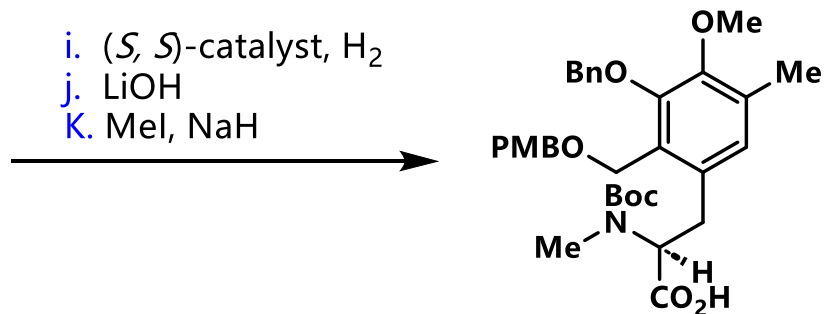
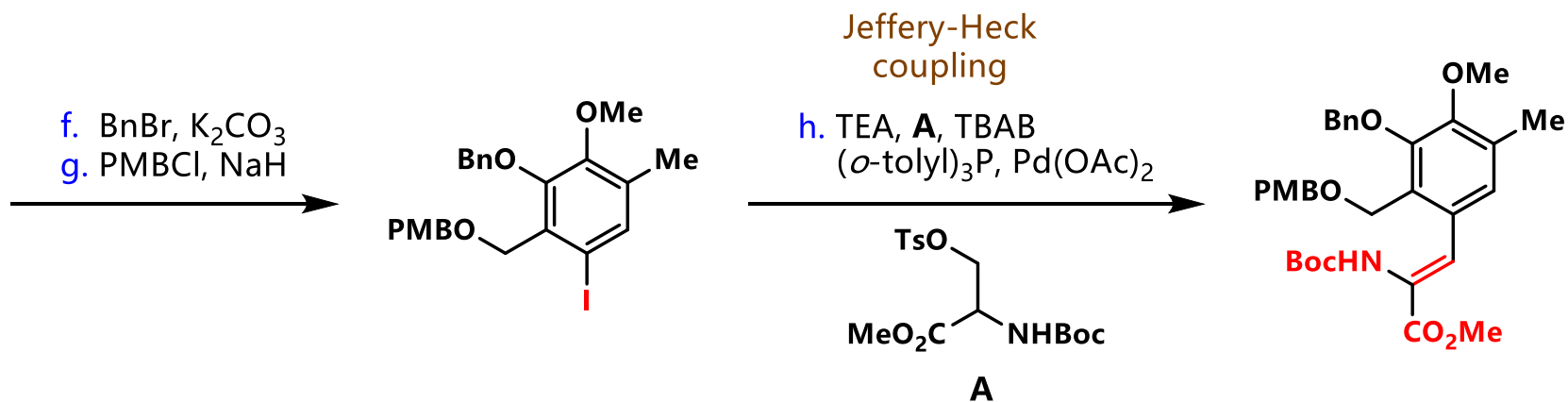
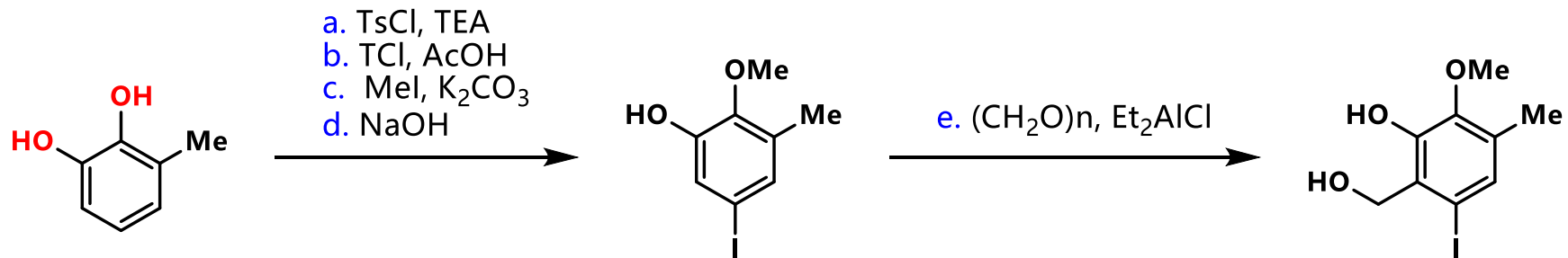
◆ J. P. Zhu 课题组的工作 J. Am. Chem. Soc., 2006, 128, 87

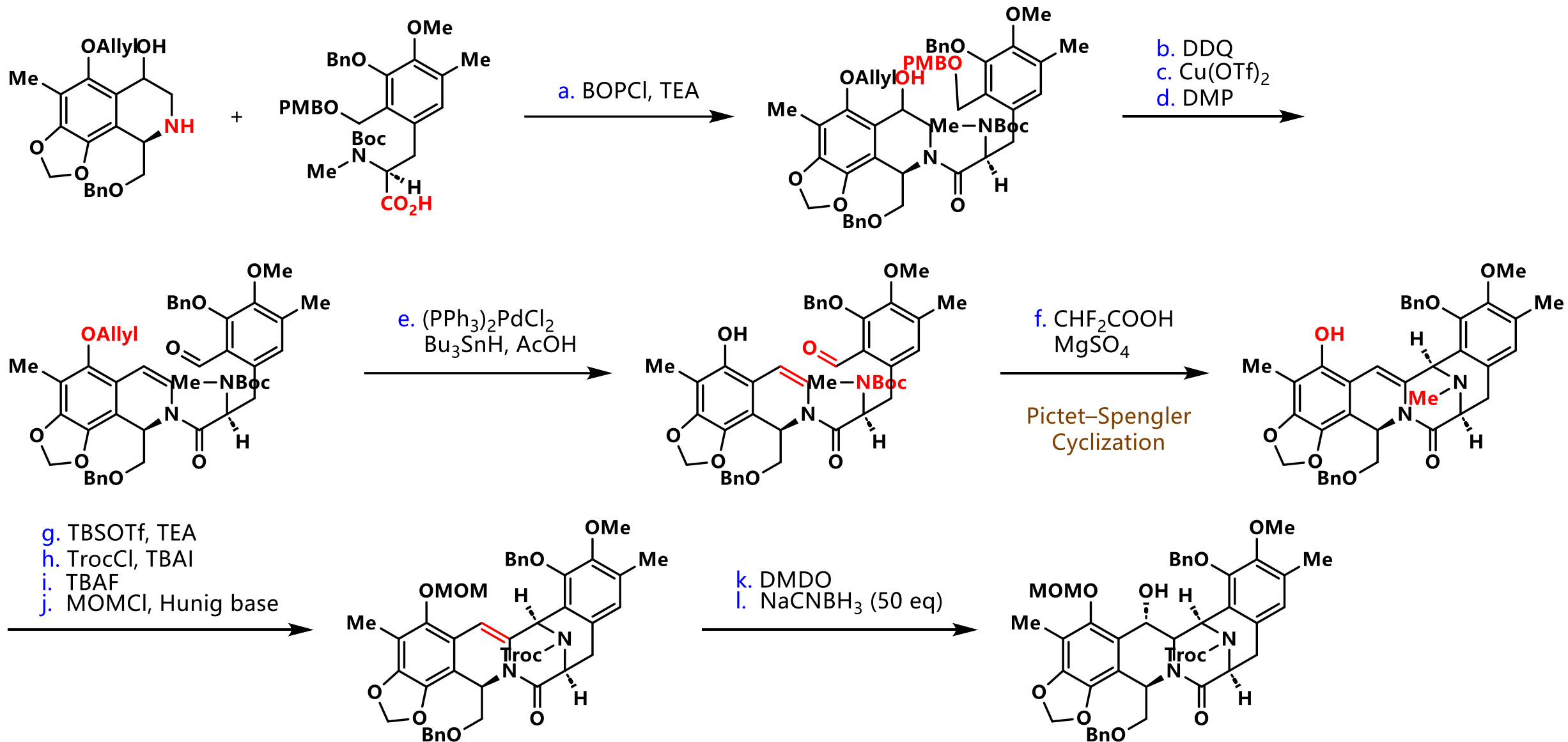


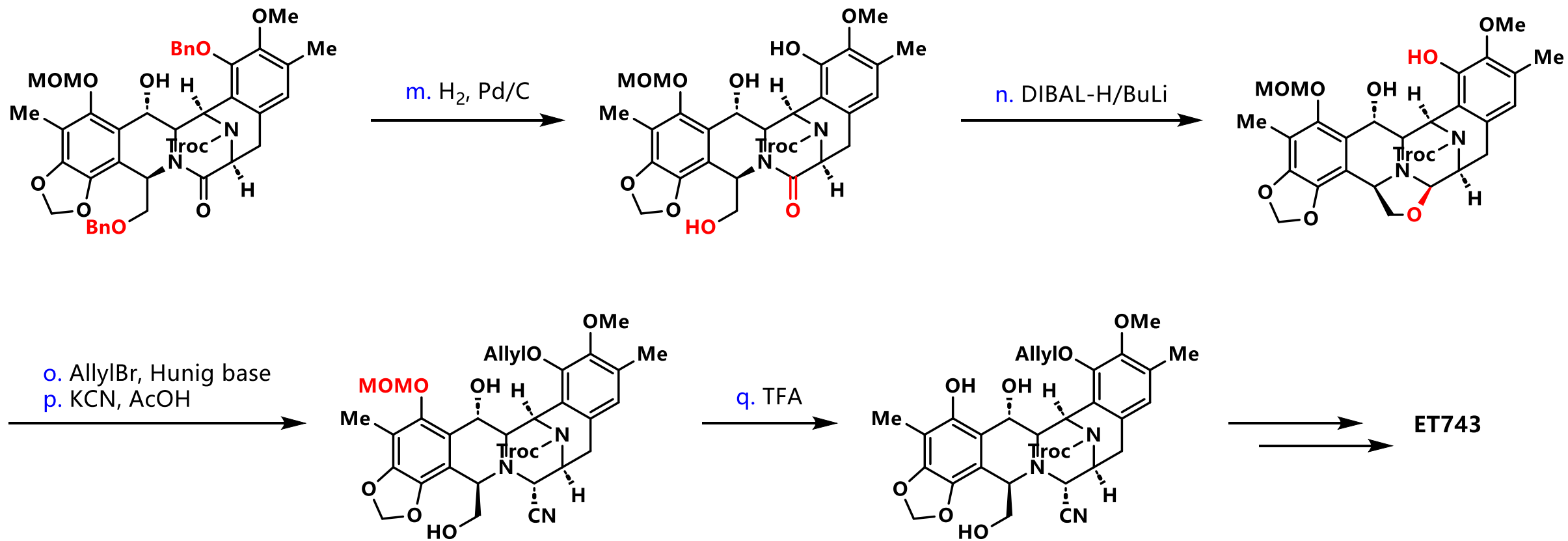


◆ S. J. Danishefsky 课题组的工作 *Angew. Chem. Int. Ed.*, 2006, 45, 1754

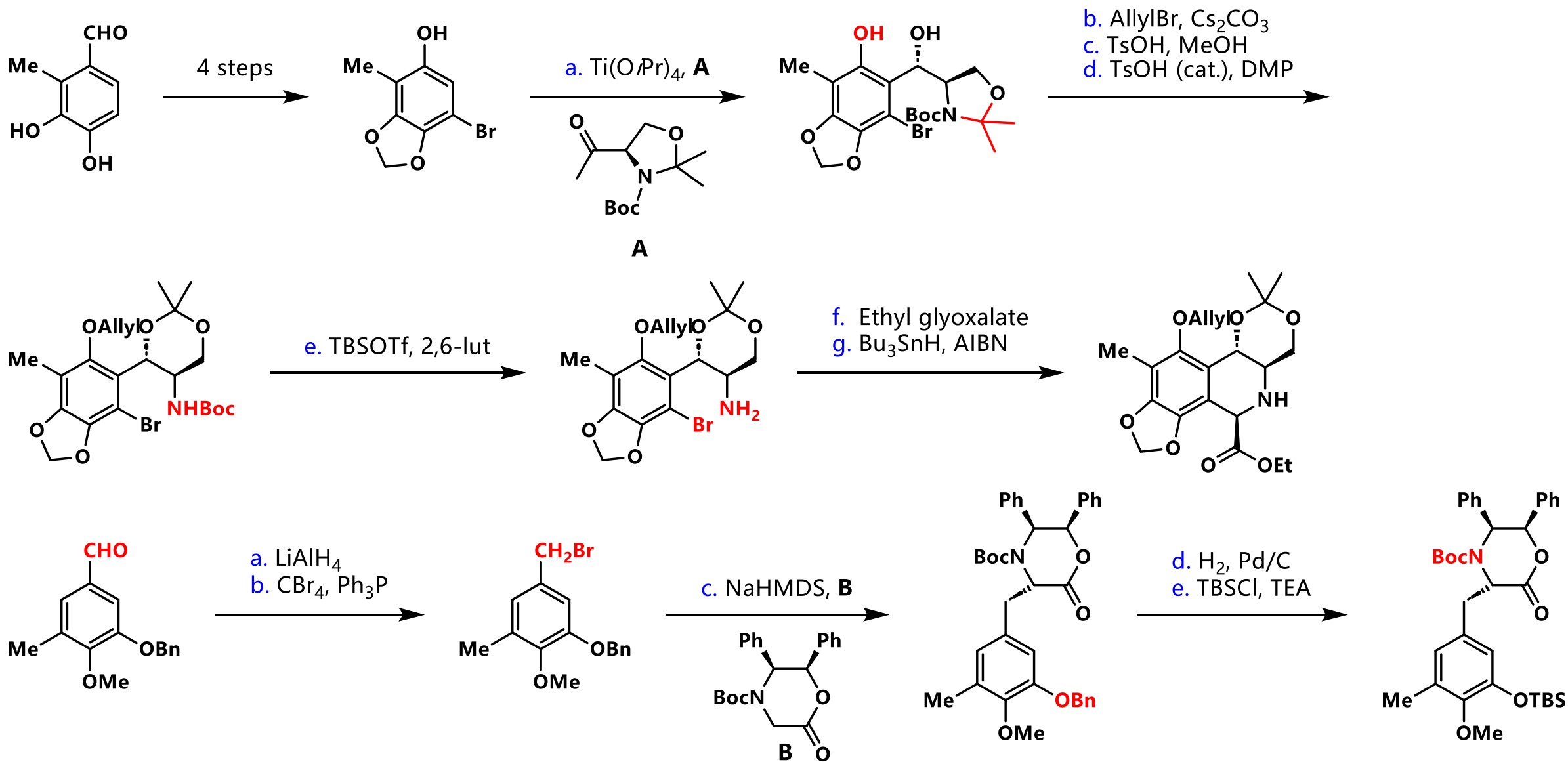


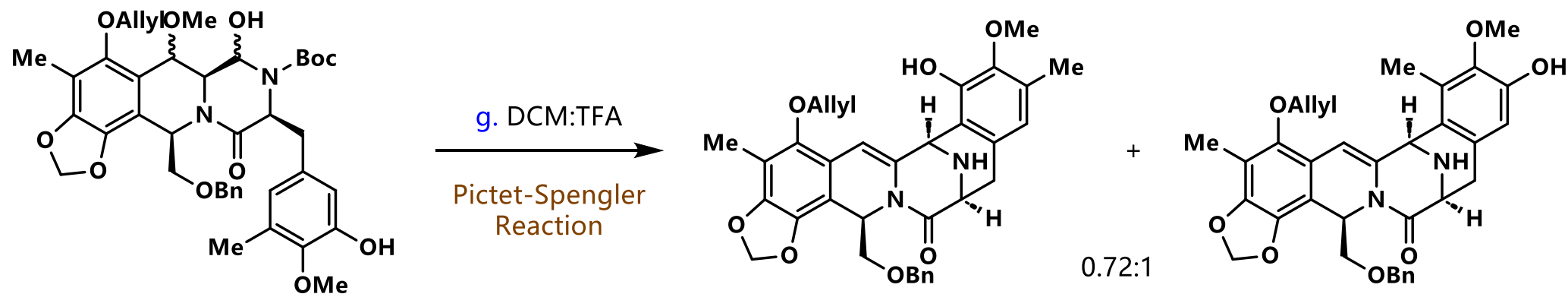
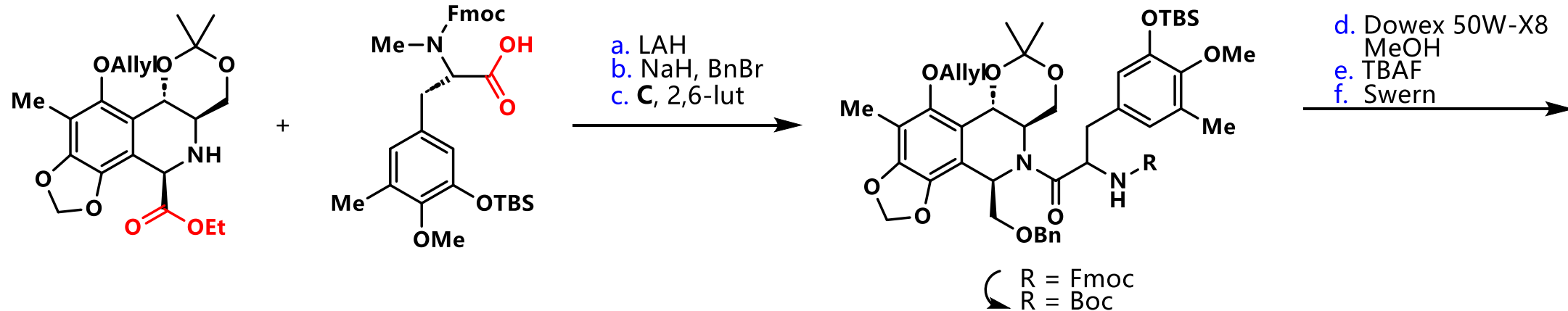
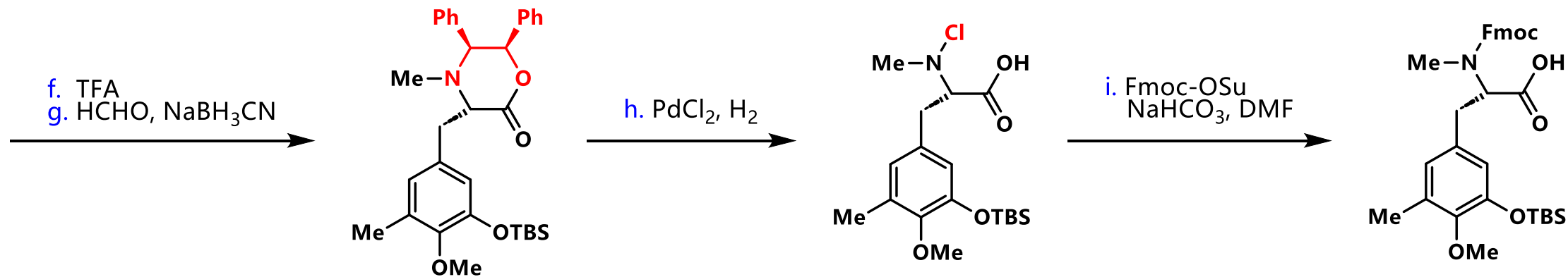


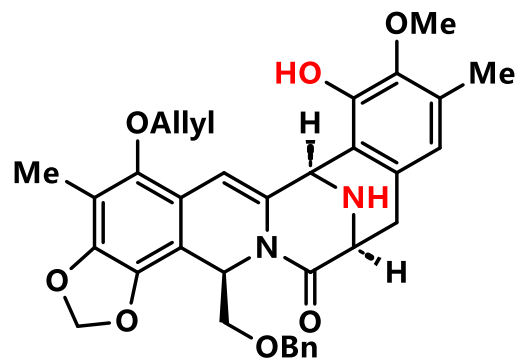




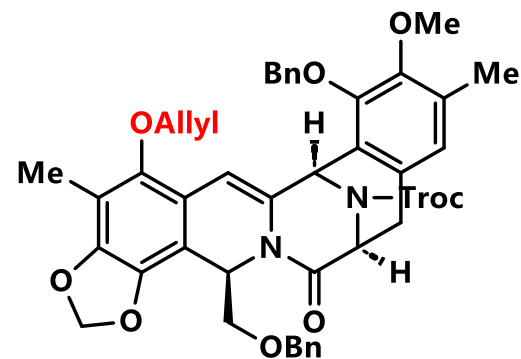
◆ R. M. Williams 课题组的工作 J. Org. Chem., 2008, 73, 9594



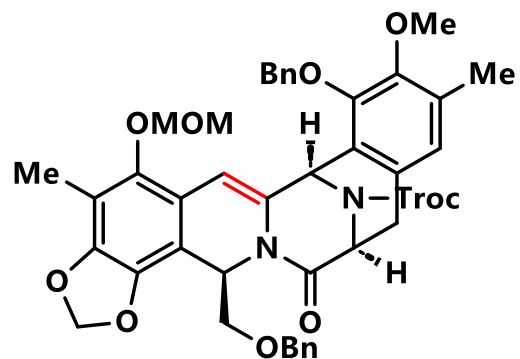




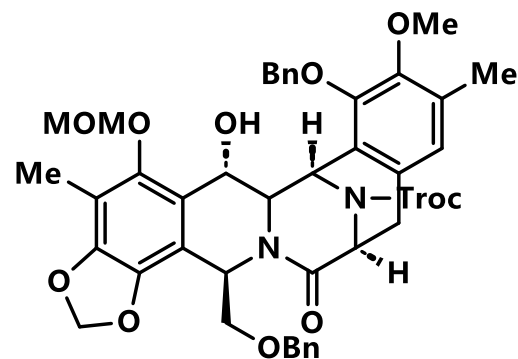
h. TrocCl, pyr
i. BnBr, K₂CO₃, TBAI



j. pyrrolidine, Pd(PPh₃)₄
k. MOMBr, DIPEA

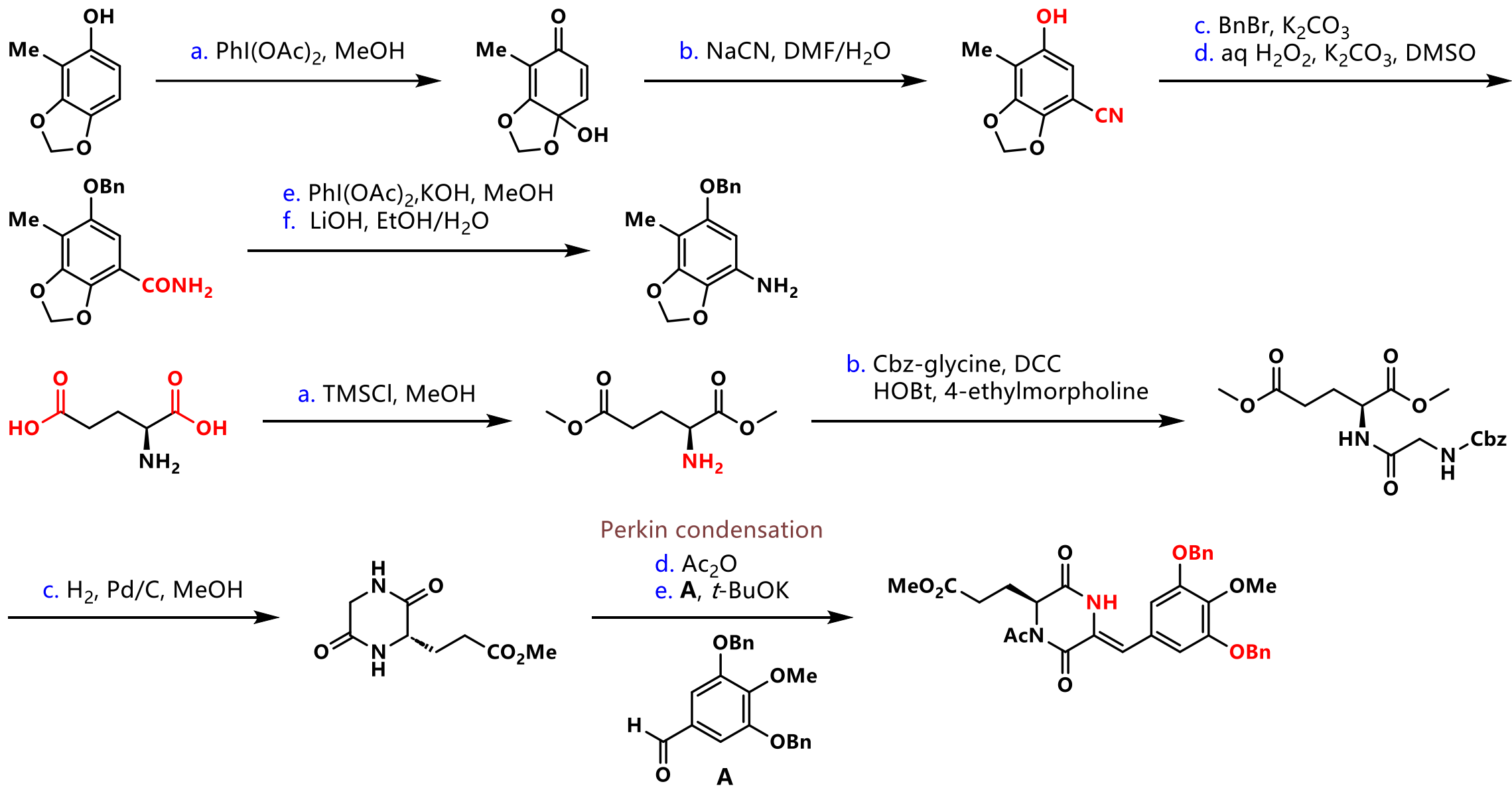


l. DMDO
m. NaCNBH₃

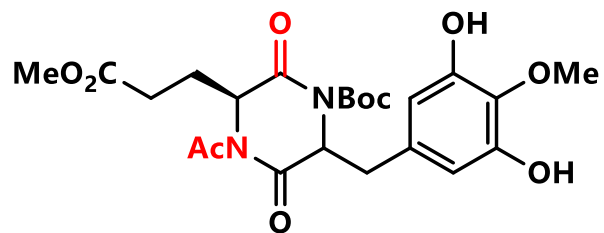


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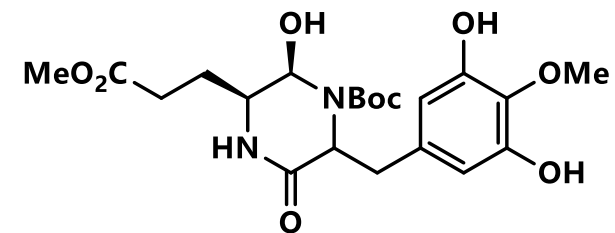
◆ T. Fukuyama 课题组的工作 J. Am. Chem. Soc., 2013, 135, 13684



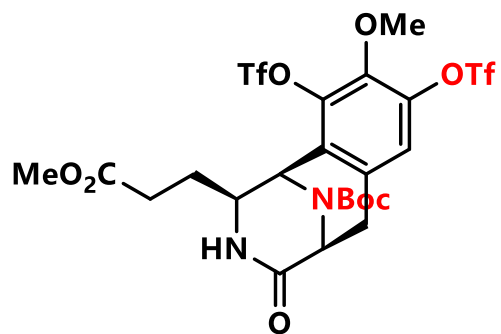
f. Boc_2O , DMAP
g. H_2 , Pd/C



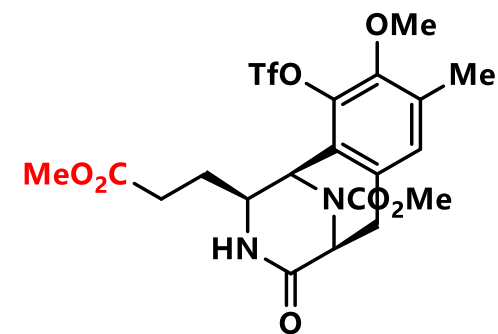
h. $\text{H}_2\text{NNH}_2 \cdot \text{H}_2\text{O}$;
 NABH_4 , MeOH



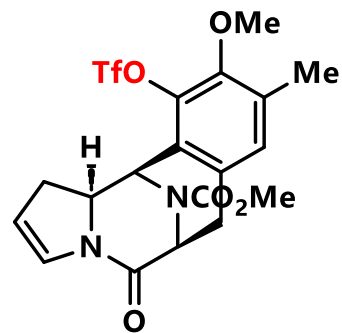
i. TFA, $\text{CF}_3\text{CH}_2\text{OH}$;
 PhNTf_2 , DMAP, Cs_2CO_3



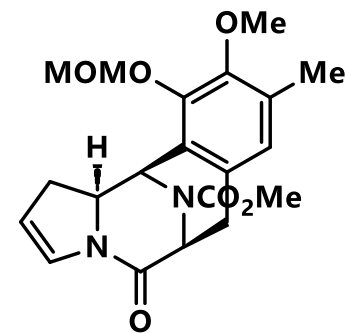
j. trimethylboroxine
 $\text{Pd}(\text{PPh}_3)_4$, K_3PO_4
k. HCl, EtOAc;
 ClCO_2Me , NaHCO_3

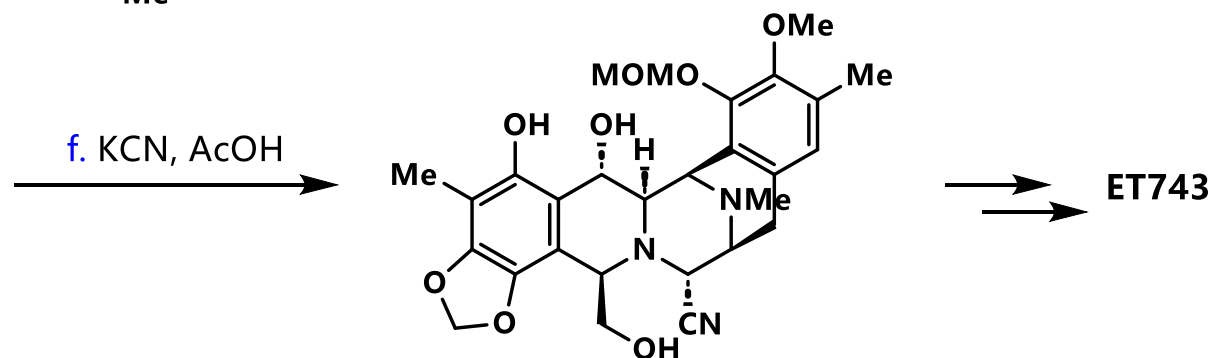
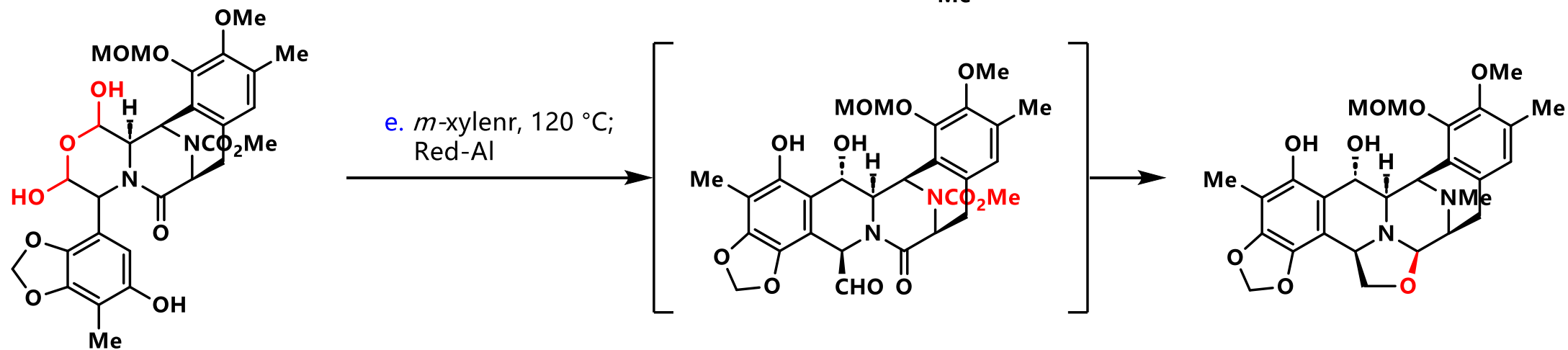
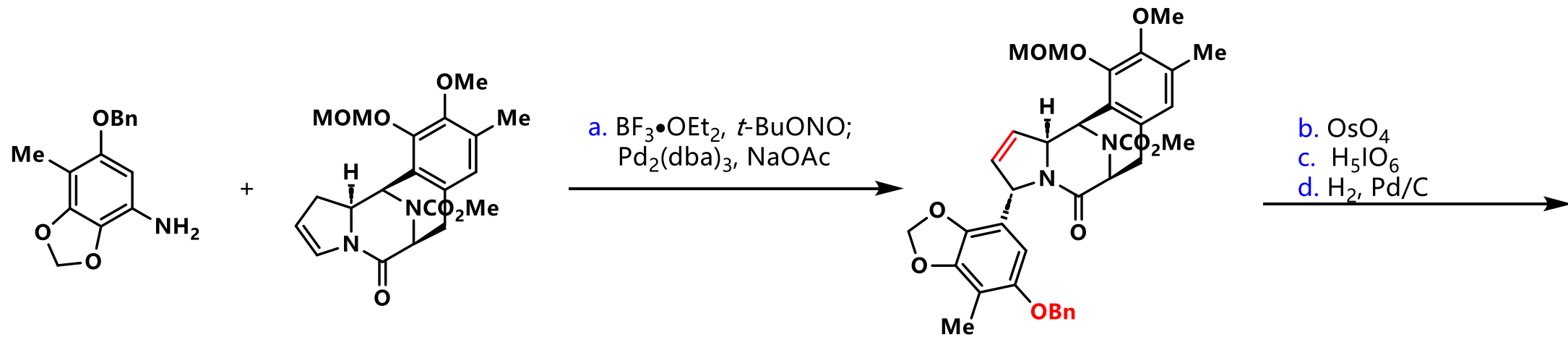


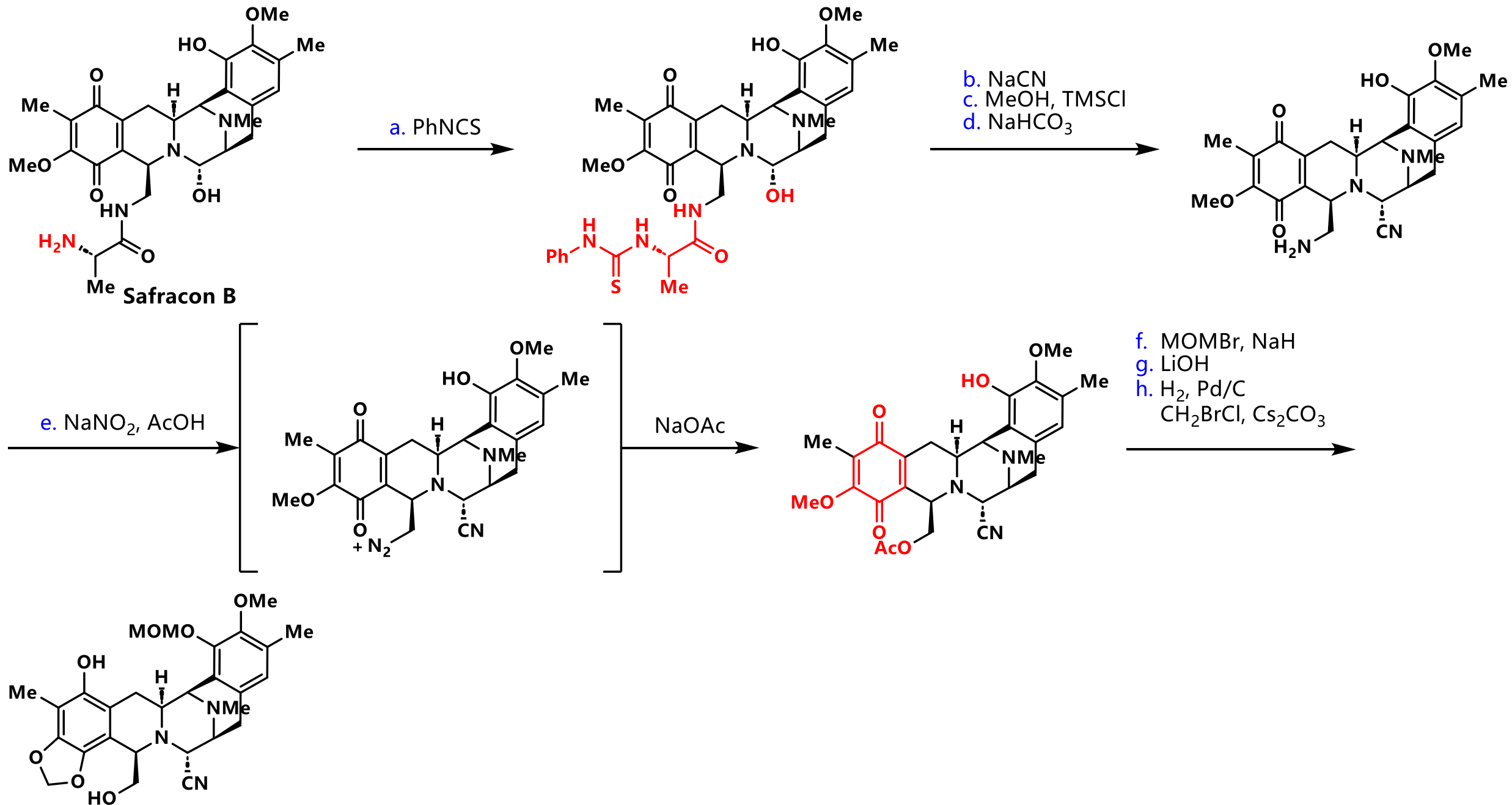
l. L-Selectride
m. CSA



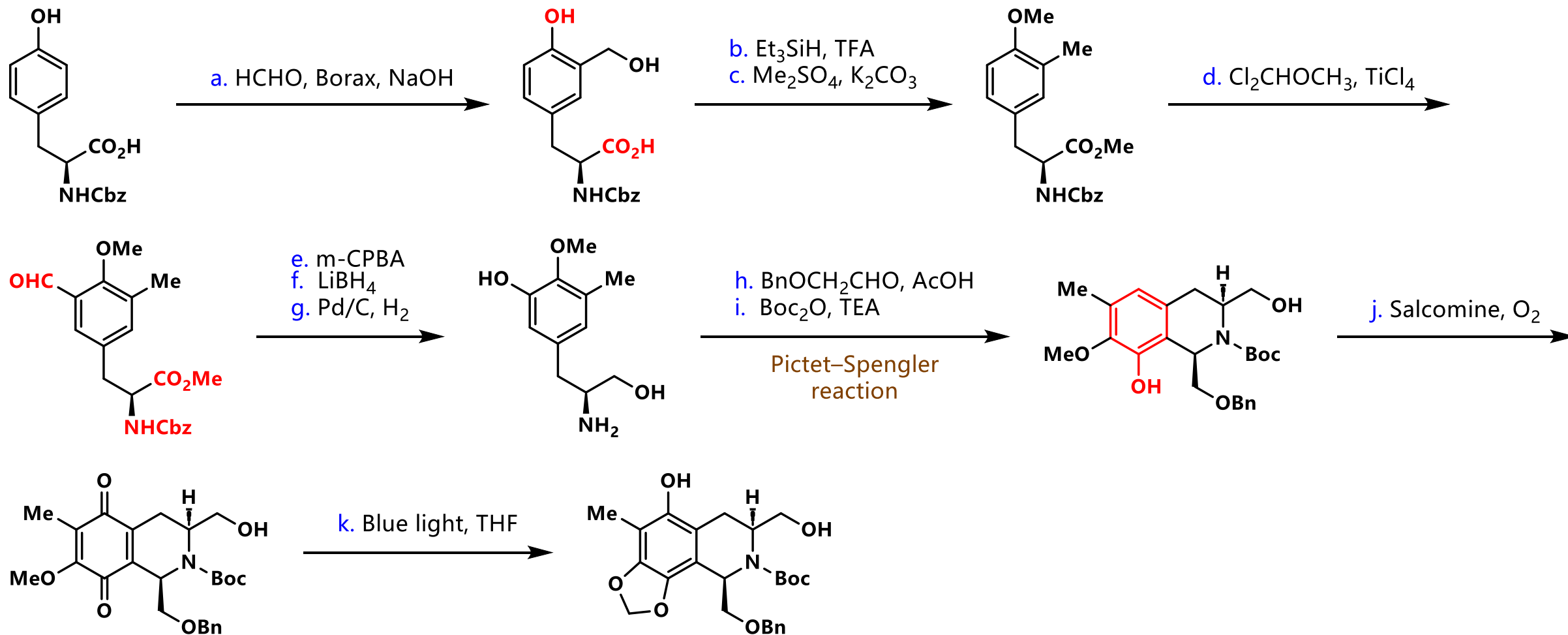
n. aq KOH; MOMCl

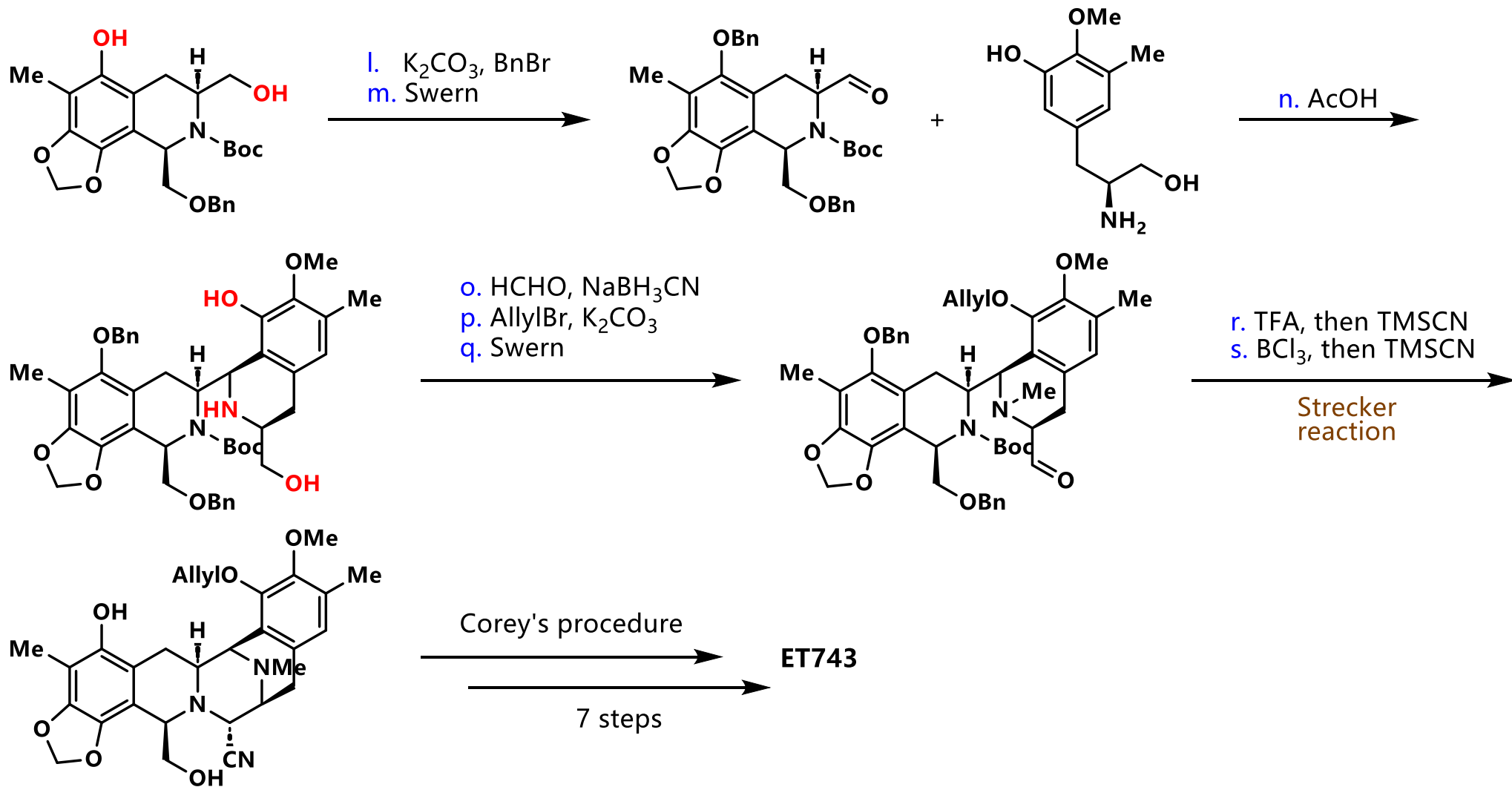




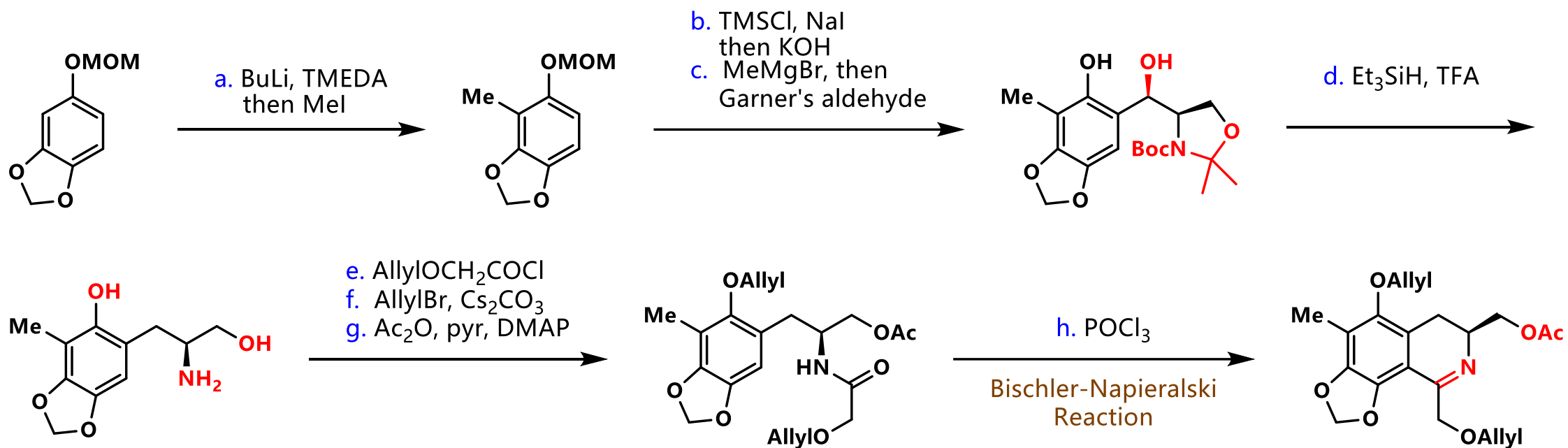


◆ D. W. Ma 课题组的工作 *Angew. Chem. Int. Ed.*, 2019, 58, 3972

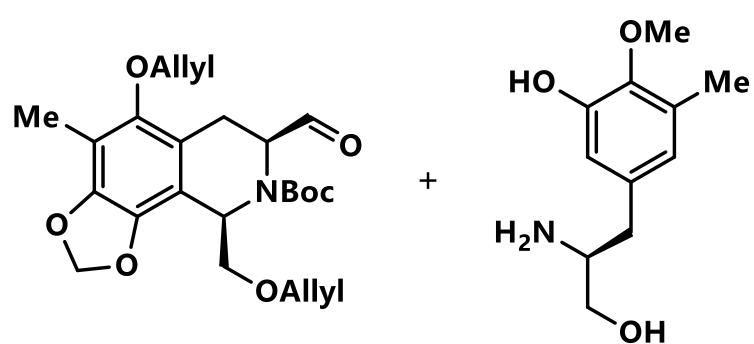




◆ X. C. Chen 课题组的工作 J. Org. Chem., 2019, 84, 13696

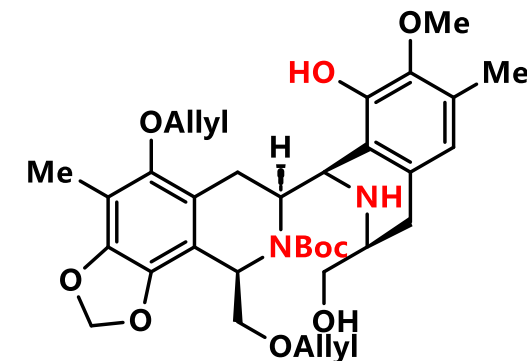


- i. NaBH_4
- j. Boc_2O , DIPEA
- k. Swern

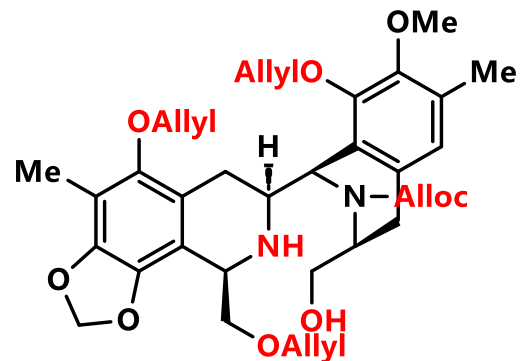


l. AcOH , $(\text{BnO})_2\text{P}(\text{O})\text{OH}$

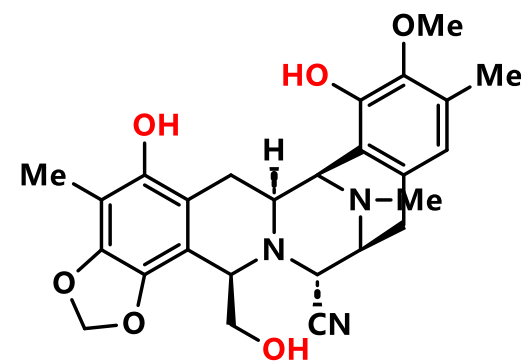
Pictet-Spengler
Reaction



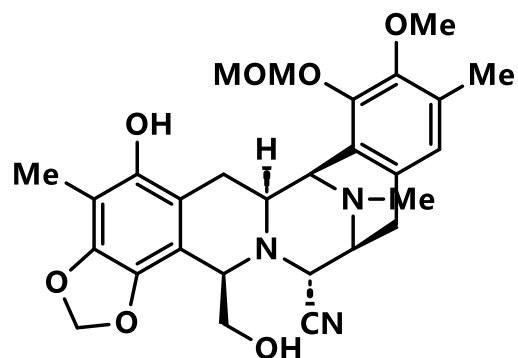
- m. AllocCl
- n. AllylBr , Cs_2CO_3
- o. HCl/MeOH



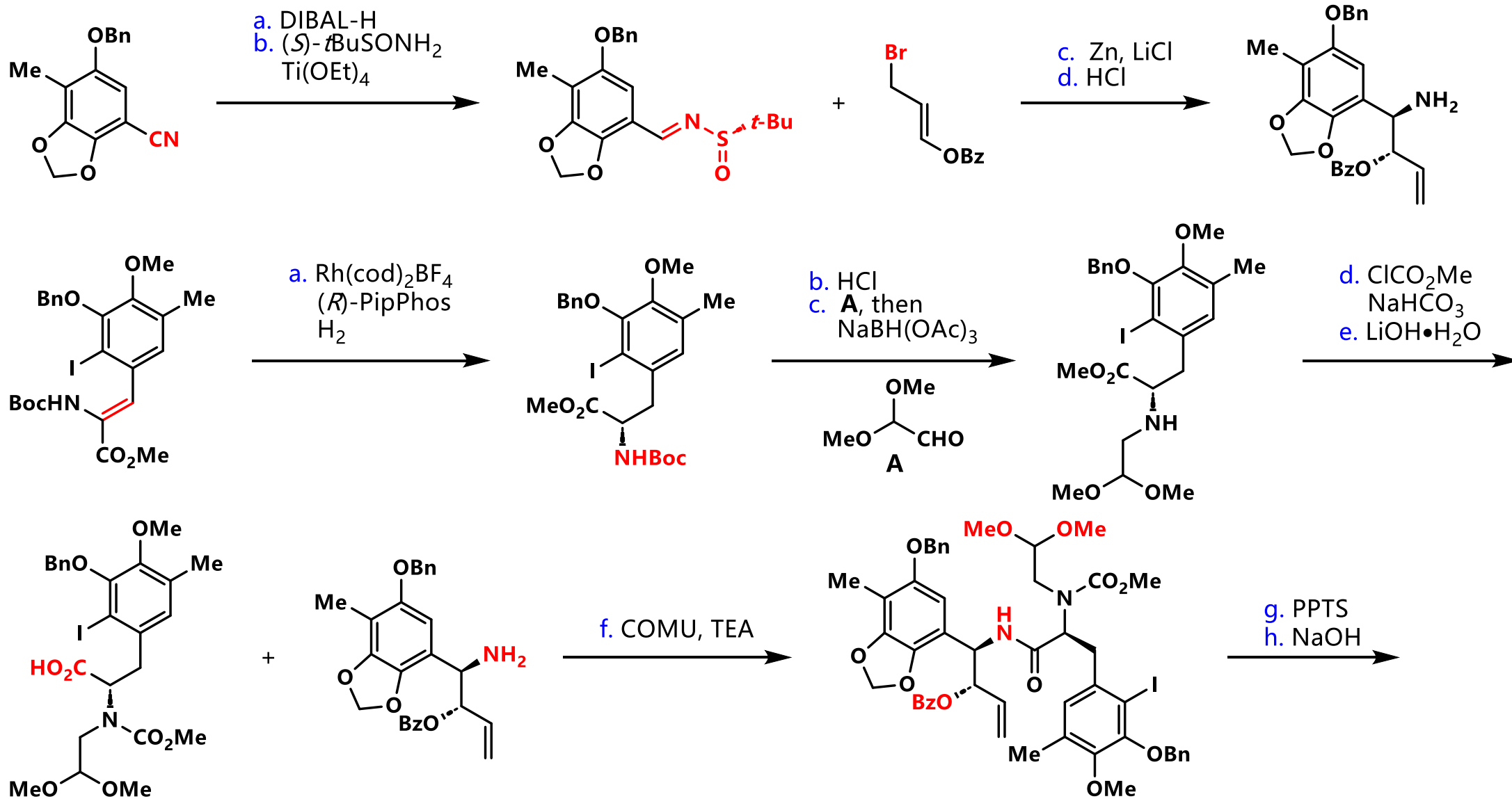
- p. Swern
- q. TMSCN , ZnCl_2
- r. $\text{Pd}(\text{PPh}_3)_4$, Bu_3SnH , AcOH
- s. HCHO , NaBH_3CN

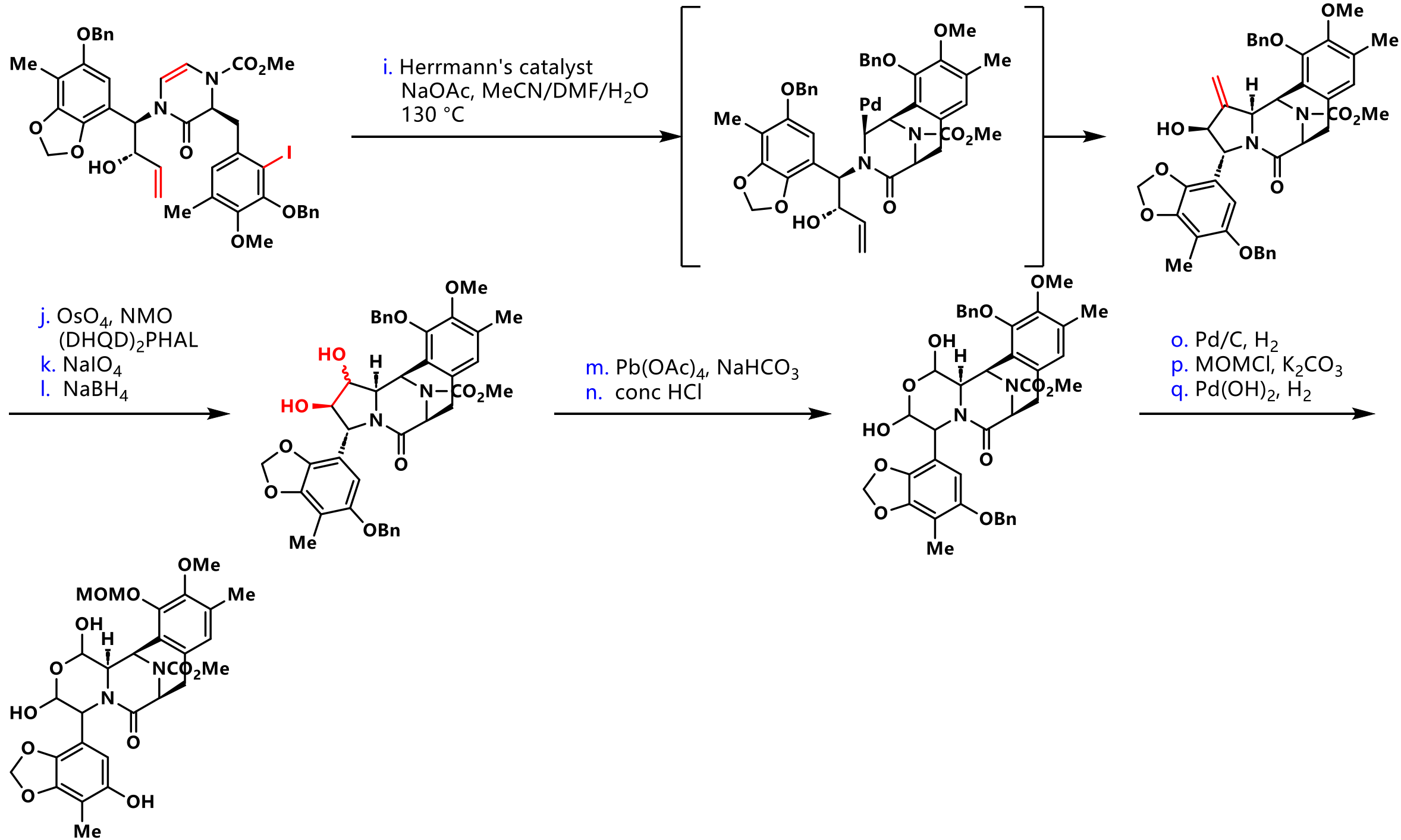


- t. TBSCl , Imid , DMAP
- u. MOMCl , NaH
- v. HF/pyr

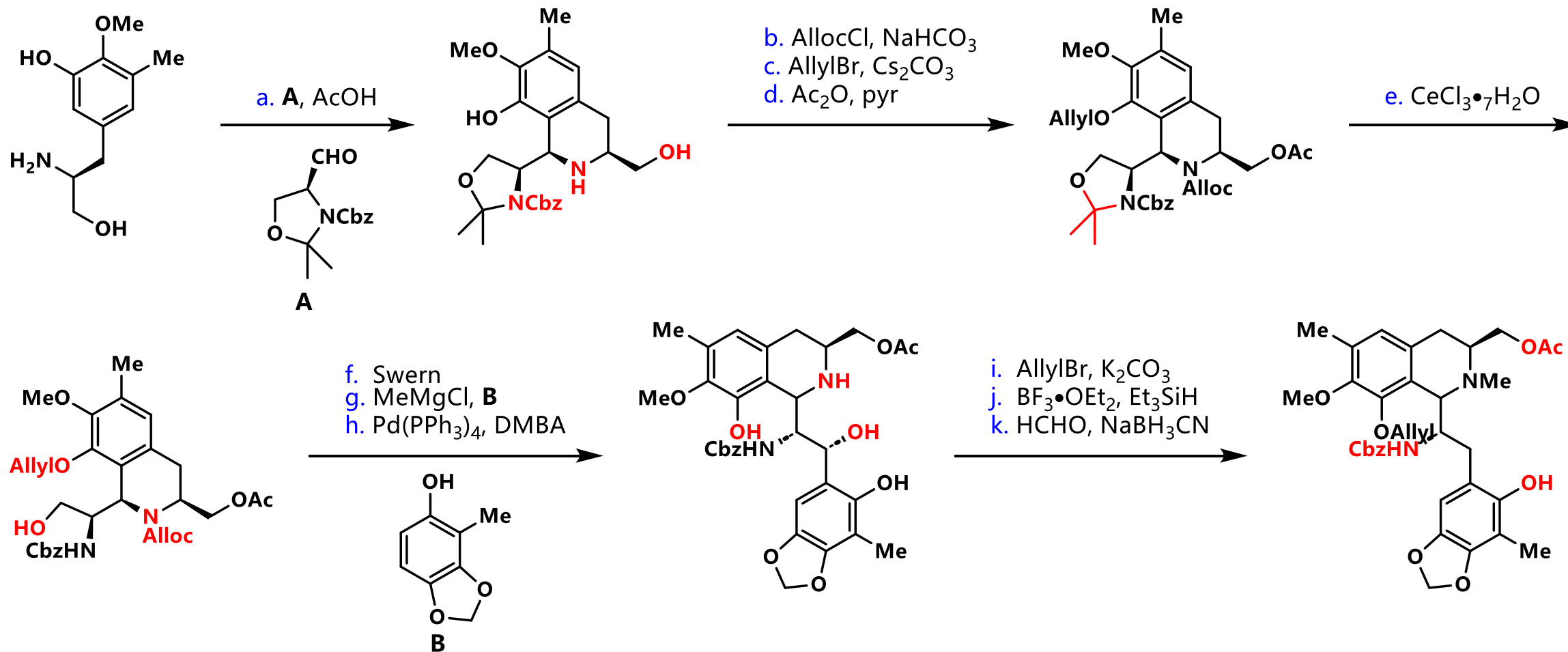


◆ S. Yokoshima课题组的工作 Org. Lett., 2022, 24, 8228

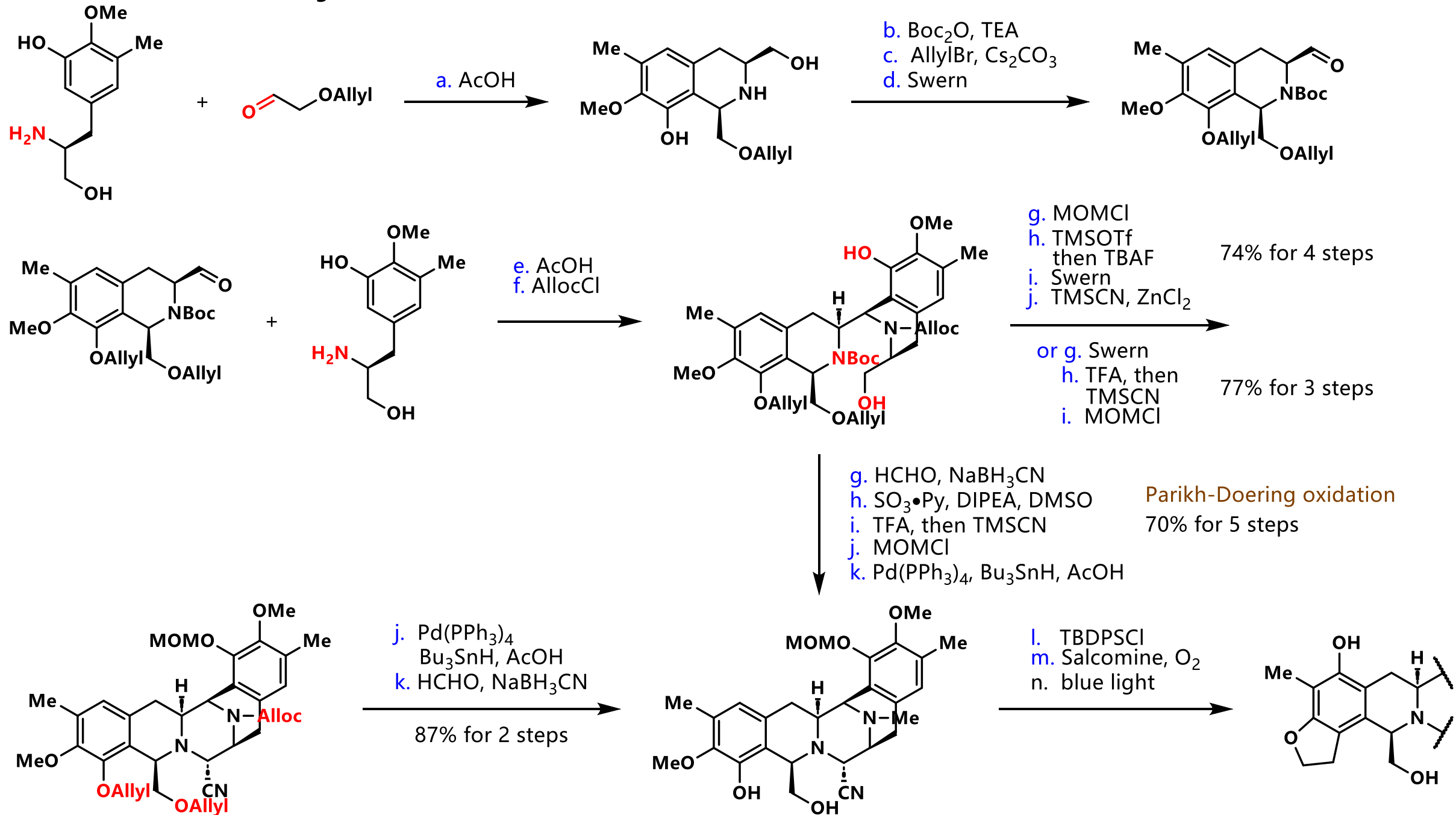




◆ X. F. Jiang课题组的工作 CCS Chem., 2023, 5, 2152



◆ X. C. Chen 课题组的工作 J. Org. Chem., 2023, 88, 10905



Group	B环	C环	D环	构环顺序
E. J. Corey (2006)	Pictet-Spengler	Mannich	Mannich	B→C.D
T. Fukuyama (2002)	Aldol	Ugi	Heck	C→B→D
J. P. Zhu (2006)	Aldol	Strecker	Pictet-Spengler	D→C→B
S. J. Danishefsky (2006)	Pomeranz-Fritsch	Pictet-Spengler	Pictet-Spengler	B→C.D
R. M. Williams (2008)	Radical Addition	Aldol	Friedel-Crafts	B→C→D
T. Fukuyama (2013)	Aldol	Amino Acid Condensation	Friedel-Crafts	C→D→B
D. W. Ma (2019)	Pictet-Spengler	Strecker	Pictet-Spengler	B→D→C
X. C. Chen (2019)	Bischler-Napieralski	Strecker	Pictet-Spengler	B→D→C
S. Yokoshima (2022)	Aldol	Amino Acid Condensation	Heck	C→D→B
X. F. Jiang (2023)	Pictet-Spengler	Strecker	Pictet-Spengler	D→B→C
X. C. Chen (2023)	Pictet-Spengler	Strecker	Pictet-Spengler	D→B→C

Thank You for Listening