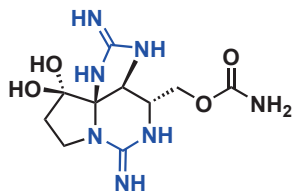


Saxitoxins

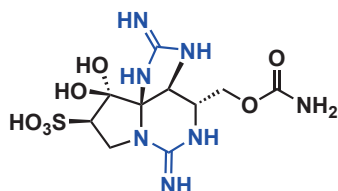


Saxitoxin (STX)

Separated from Shellfish
(*Saxidomus*, *Mytilus*...)
Produced by Dinoflagellate
(*Gonyaulax tamarensis*)

- Causing "shellfish paralysis"
- 540 μg is lethal to human
- LD₅₀ = 9.7 $\mu\text{g}/\text{kg}$
= 5150 Mouse Units/mg
- Regarded as a chemical weapon
(*CWC*, *United Nations*, 1992)

First Asymmetric Synthesis:
Y. Kishi (1992)

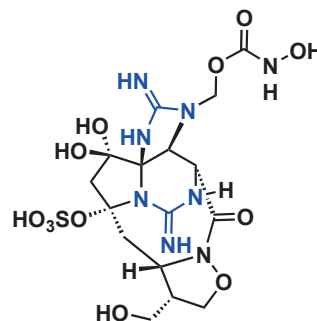


Gonyautoxin (show GTX-III)

Separated from Dinoflagellate
(*Gonyaulax Catenella*)

- Main toxin in red tide
- LD₅₀ = 10.4 $\mu\text{g}/\text{kg}$
= 4800 Mouse Units/mg
- All STX and GTX analogs could work
as selective Na⁺ channel blocker

First Asymmetric Synthesis (GTX-III):
K. Nagasawa (2007)



Zetekitoxin (ZTX)

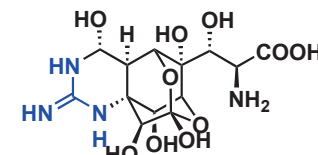
Separated from Frogs
(*Atelopus*, *Xenopus*...)

- IC₅₀ = 280 pM
(Human heart Na⁺ channel)
- IC₅₀ = 6.1 pM
(Mouse brain Na⁺ channel)
- 580 times stronger than STX

No Synthesis Finished (2024)

Tetrodotoxins

Separated from Puffer Fish



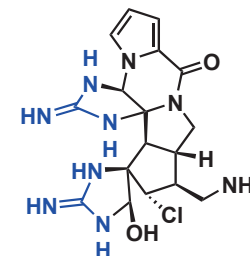
Chiriquitoxin

Produced by Endozoic
Bacteria (*Vibrio*, *Bacillus*...)

- High toxicity (most species)
- Efficient & selective Na⁺
channel blocker

Pyrrole-Imidazoles (Sceptrins)

Separated from Sponges
(*Agelasidae*, *Axinellidae*...)

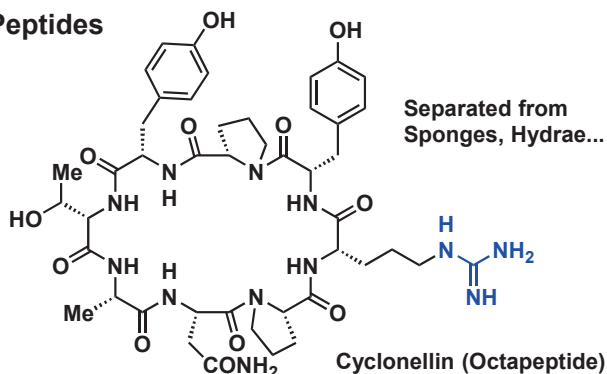


Palau'amine

- Low Human-toxicity
- Immunomodulating
- Cytotoxic
- Antibiotic
- Antifungal

Naturally Generated by
[2+2] Dimerization
Mutable & Fragile Structure

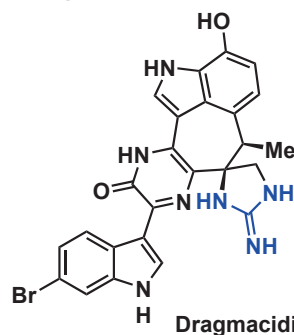
Peptides



Separated from
Sponges, Hydrae...

Cyclonellin (Octapeptide)

Dragmacidins



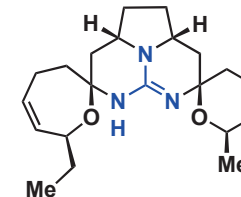
Dragmacidin E

Separated from Sponges
(*Dragmacidon*, a genus of
Axinellidae)

- Selective ST-PK (a protein
phosphatase) inhibitor
- NO inhibitor (modifying blood
pressure)
- Potential in treating neuro-
degenerations (AD, PD...)

Crambescins

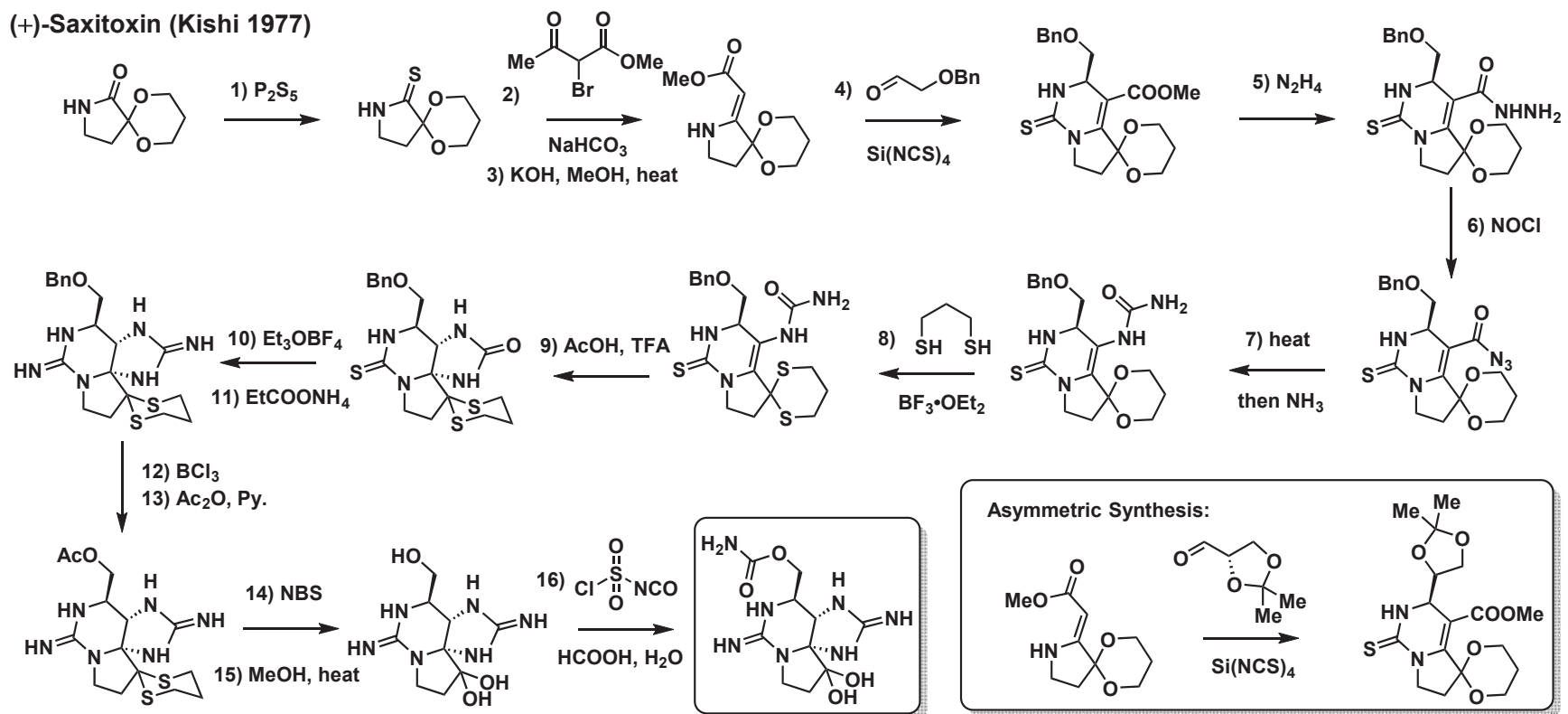
Separated from Sponges
(*Chondropsidae*...)



Crambescidin 359

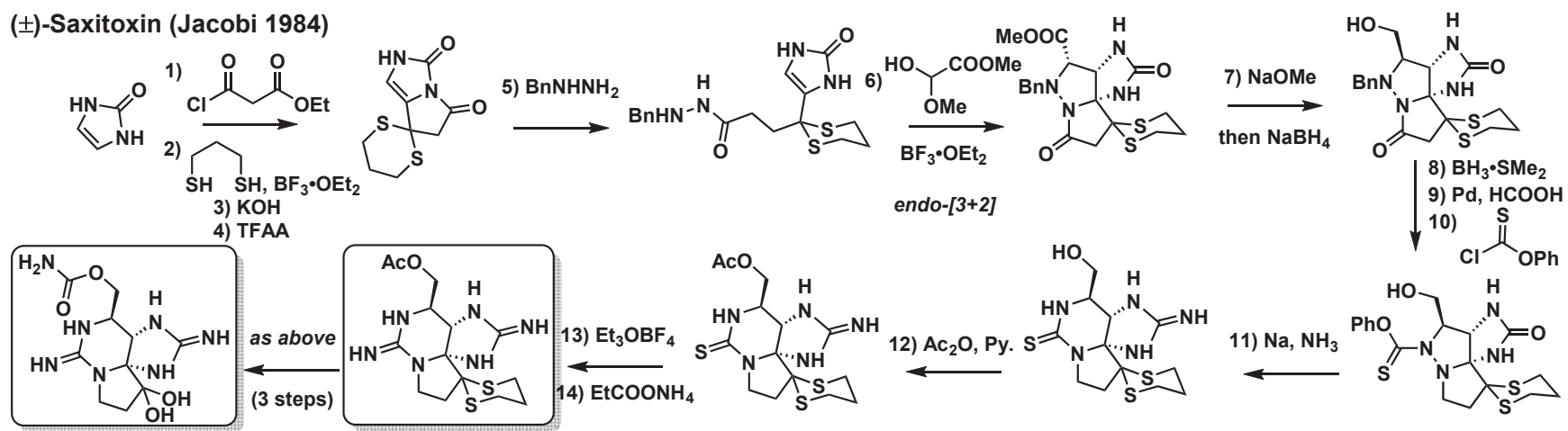
- Antivirus
- Cytotoxic (anti-Leukemia)
- Na⁺, K⁺ and Ca²⁺ channel
blocker

Relatively Stable Structure

(+)-Saxitoxin (Kishi 1977)

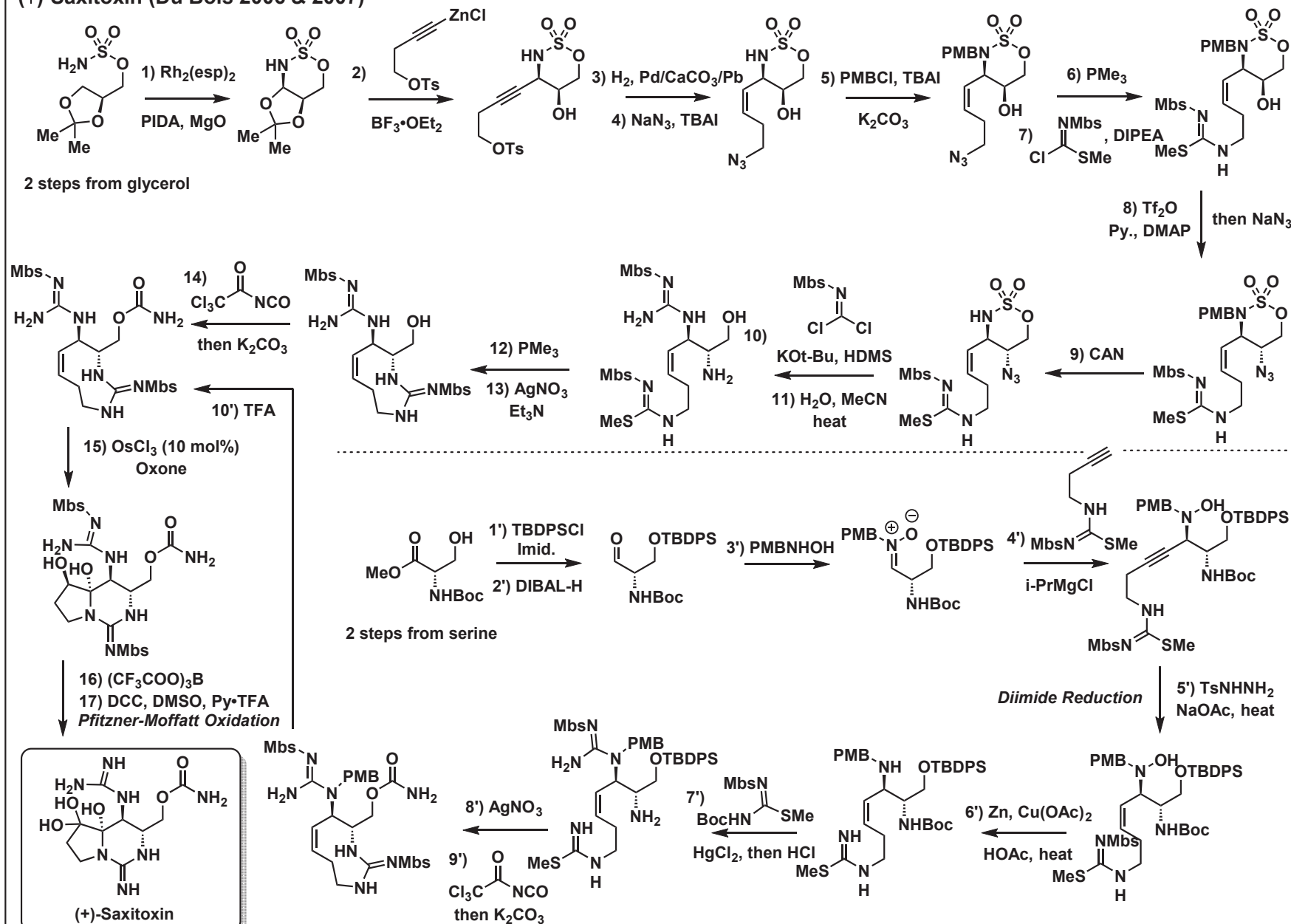
Prof. Yoshito Kishi
(1937 - 2023)
Harvard

JACS, 1977, 99, 2818
JOC, 1983, 48, 3833
JACS, 1992, 114, 7001

(±)-Saxitoxin (Jacobi 1984)

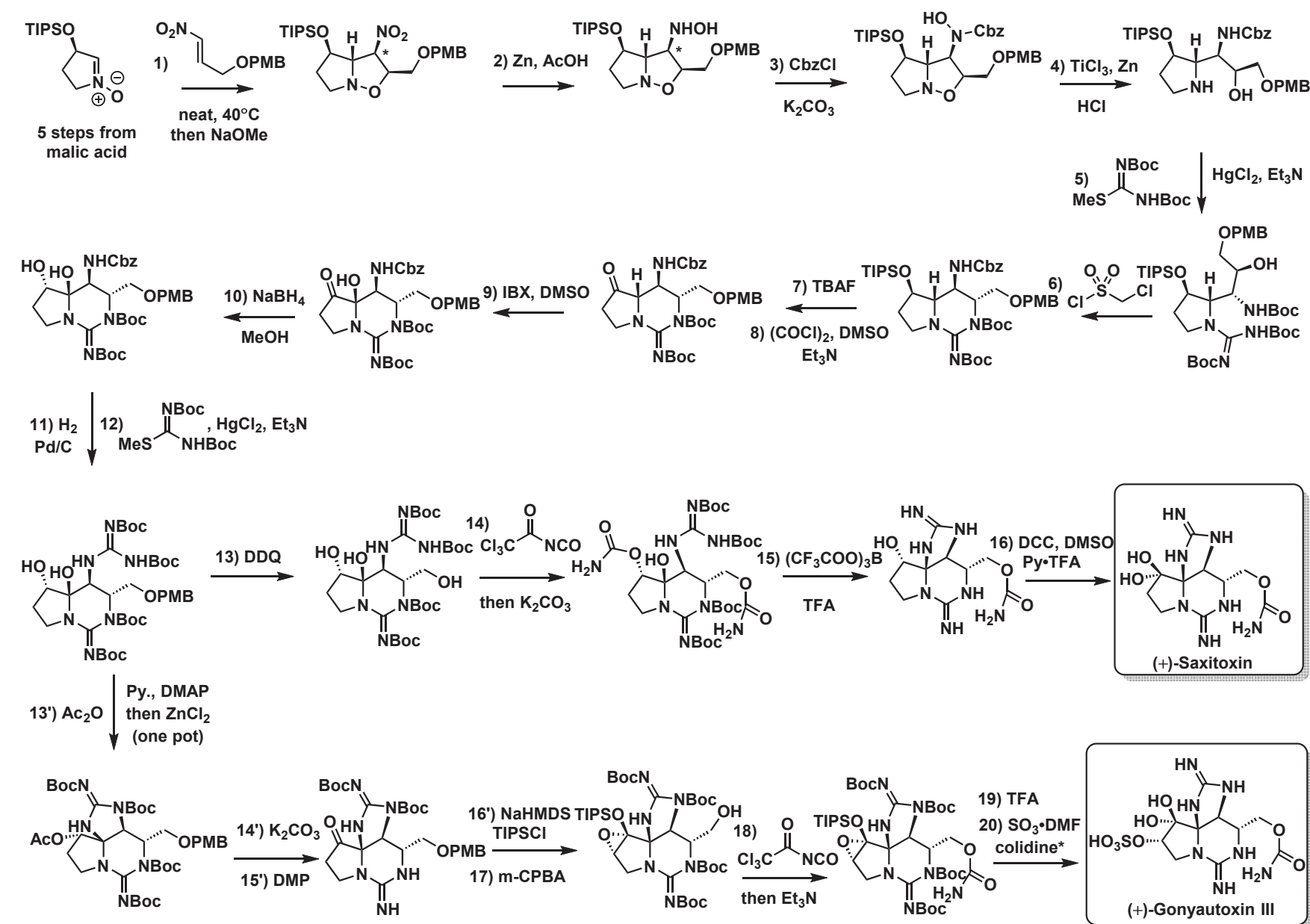
Prof. Peter A. Jacobi
(1945 -)
Dartmouth

JACS, 1981, 103, 239
JACS, 1984, 106, 5594

(+)-Saxitoxin (Du Bois 2006 & 2007)

Prof. Justin Du Bois
(1969 -)
duboislab.stanford.edu

JACS, 2006, 128, 3926
 JACS, 2007, 129, 9964

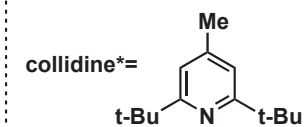
(+)-Saxitoxin & (+)-Gonyautoxin III (Nagasawa 2007, 2009 & 2011)

SM preparation:
TL, 1998, 39, 2765

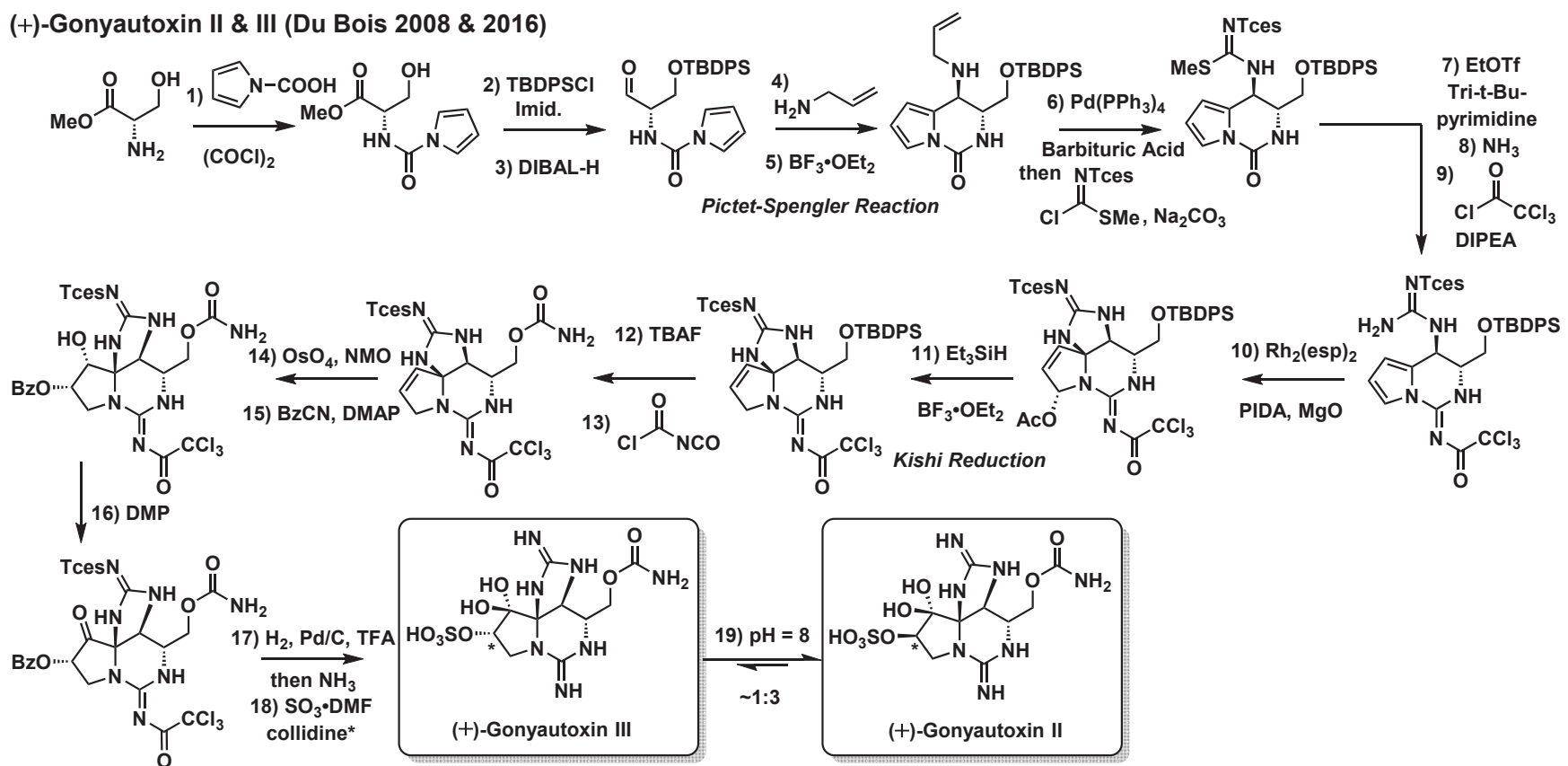


Prof. Kazuo Nagasawa
(1965 -)

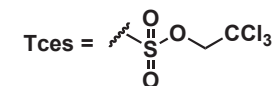
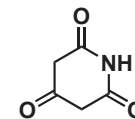
web.tuat.ac.jp/~nagasawa



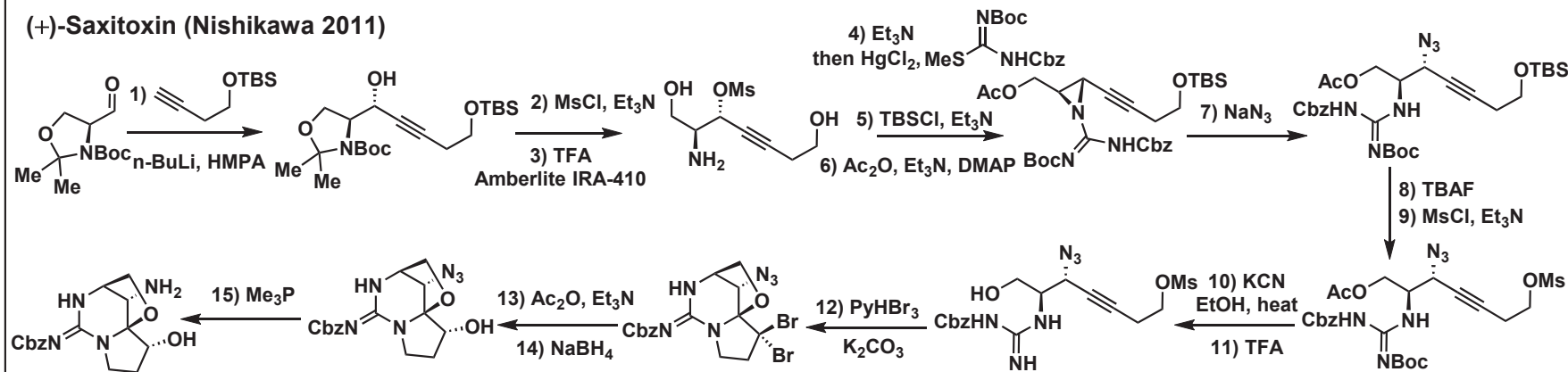
ACIE, 2007, 46, 8625
Chem Eur J, 2009, 4, 277
Chem Eur J, 2011, 17, 12144

(+)-Gonyautoxin II & III (Du Bois 2008 & 2016)

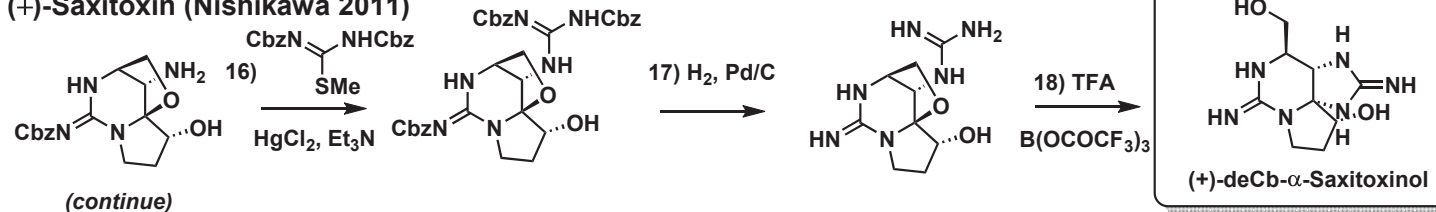
Barbituric Acid =



JACS, 2008, 130, 12630
JACS, 2016, 138, 5994

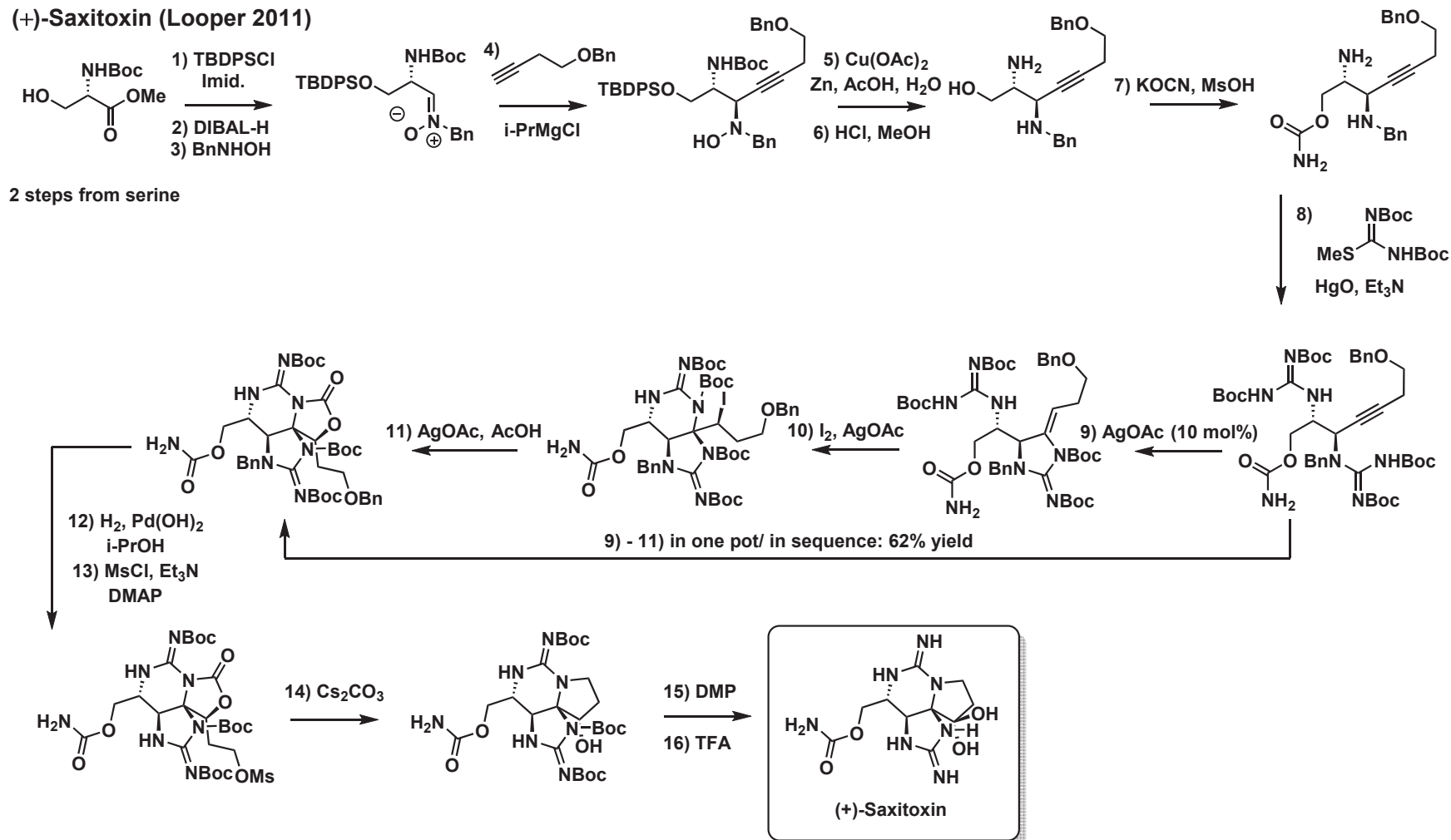
(+)-Saxitoxin (Nishikawa 2011)

Prof. Toshio Nishikawa
(1963 -)
www.agr.nagoya-u.ac.jp/~organic

(+)-Saxitoxin (Nishikawa 2011)

(continue)

ACIE, 2011, 50, 7176

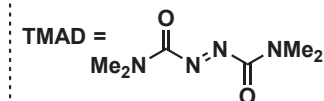
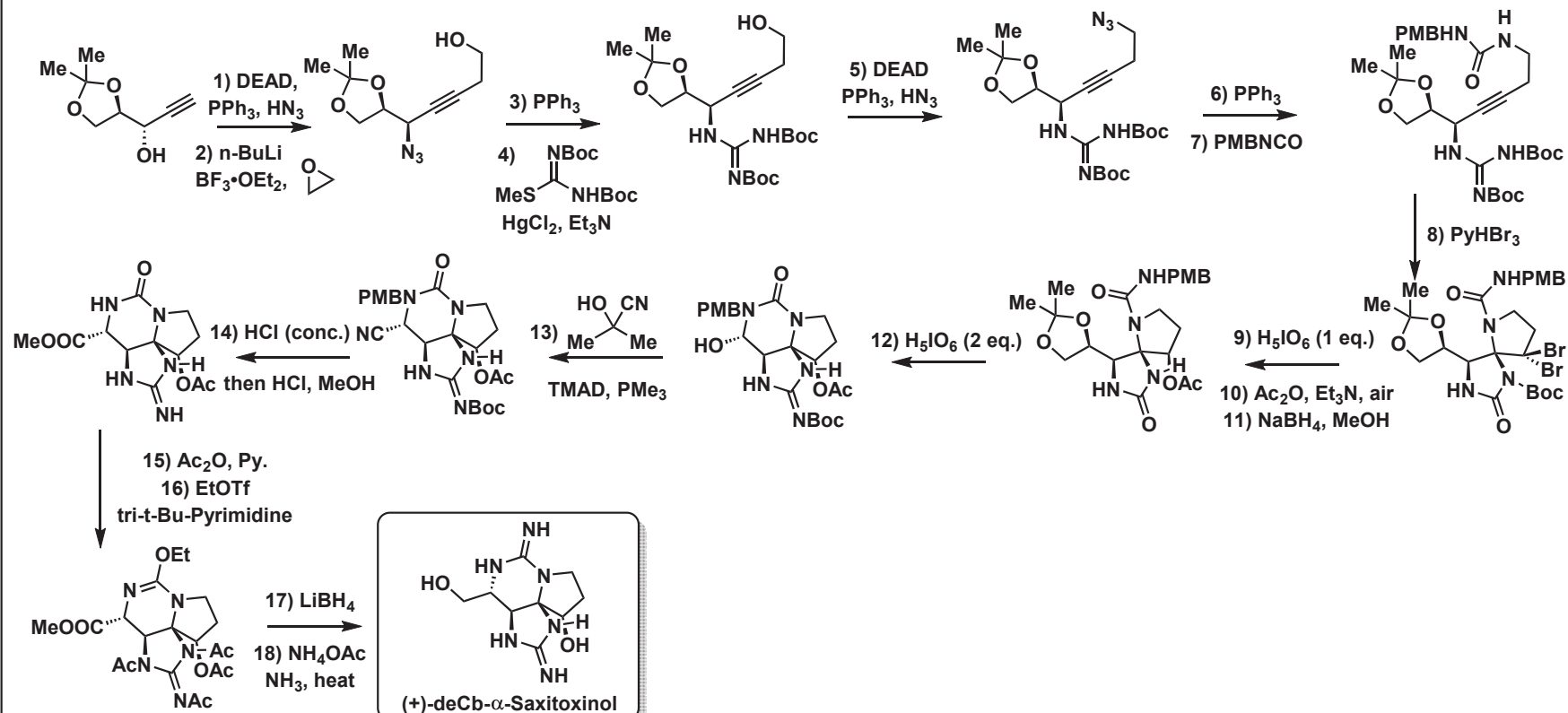
(+)-Saxitoxin (Looper 2011)

2 steps from serine

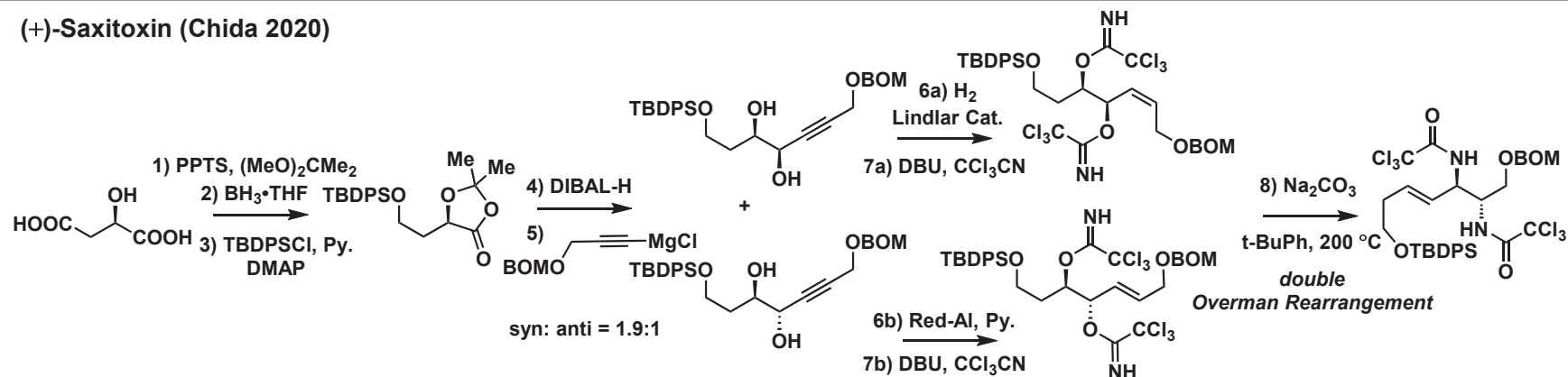


Prof. Ryan E. Looper
(1977 -)
chem.utah.edu/directory/looper

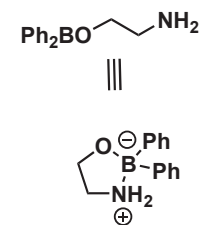
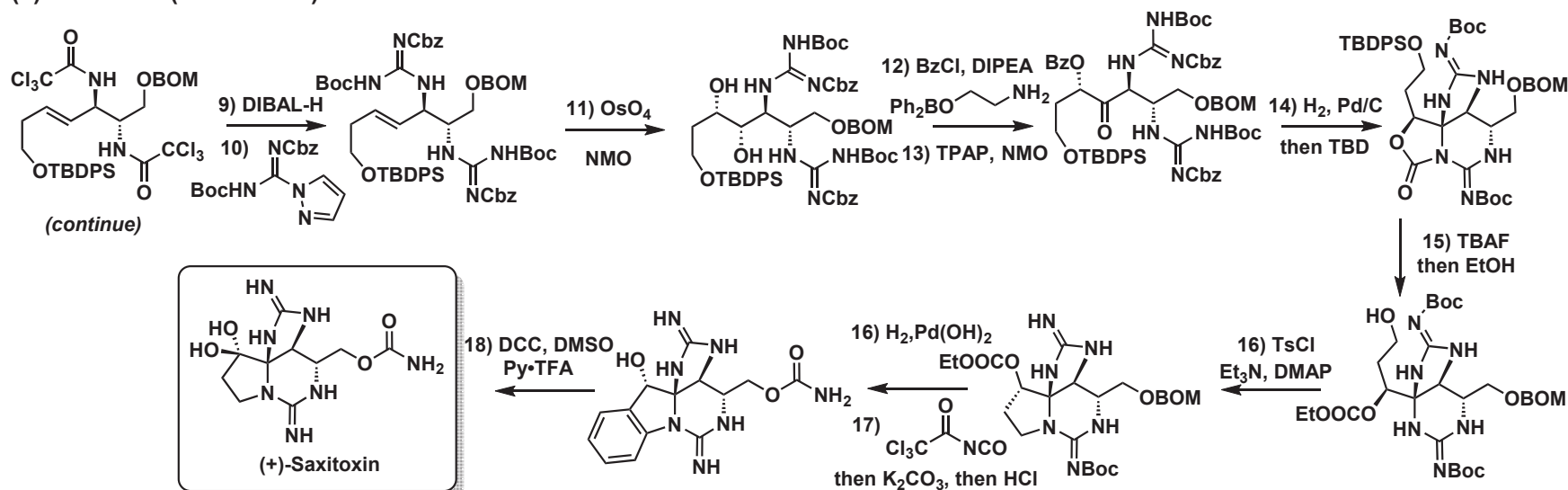
JACS, 2011, 133, 20172

(+)-Saxitoxin (Nishikawa 2016)

OL, 2016, 18, 6368

(+)-Saxitoxin (Chida 2020)

Prof. Noritaka Chida
(1967 -)
www.applc.keio.ac.jp/~takaakis

(+)-Saxitoxin (Chida 2020)

OL, 2020, 22, 8697