

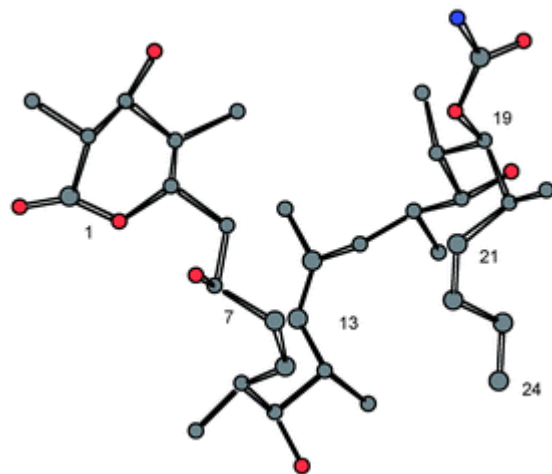
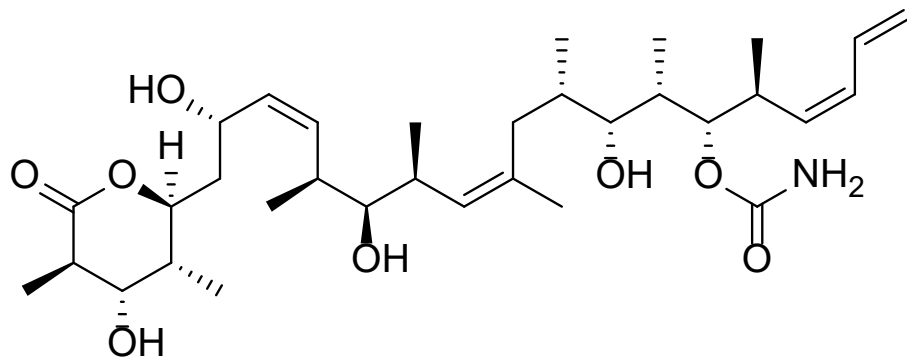
Total synthesis of Discodermolide

ORG. PROC. RES. DEV. 2004, 8, 92-130

PRODUCTION OF 60G OF DISCODERMOLIDE

NOVARTIS

Structure and properties



- Linear polypropionate containing 13 stereocenters
- Tetrasubstituted δ -lactone
- Alkenes of defined geometry
- U-shaped conformation

Natural source

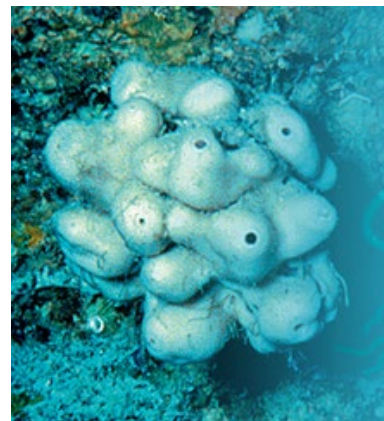
Caribbean deep-sea sponge

Isolated at the Harbor Branch Oceanographic Institution in 1990

0.002% w/w isolation yield from frozen sponge

Potent immunosuppressive agent

Potent cytotoxicity (microtubule stabilizing agent)



Historical overview

1990

Isolation / Harbor Branch Oceanographic Institution

J. Org. Chem. **1990**, *55*, 4912-4915

J. Org. Chem. **1991**, *56*, 1346 (correction)

1993

First Total Synthesis; S. Schreiber

J. Am. Chem. Soc. **1993**, *115*, 12621-12622

1999

First gram scale synthesis; A. B. Smith

Org. Lett. **1999**, *1*, 1823-1826

1998

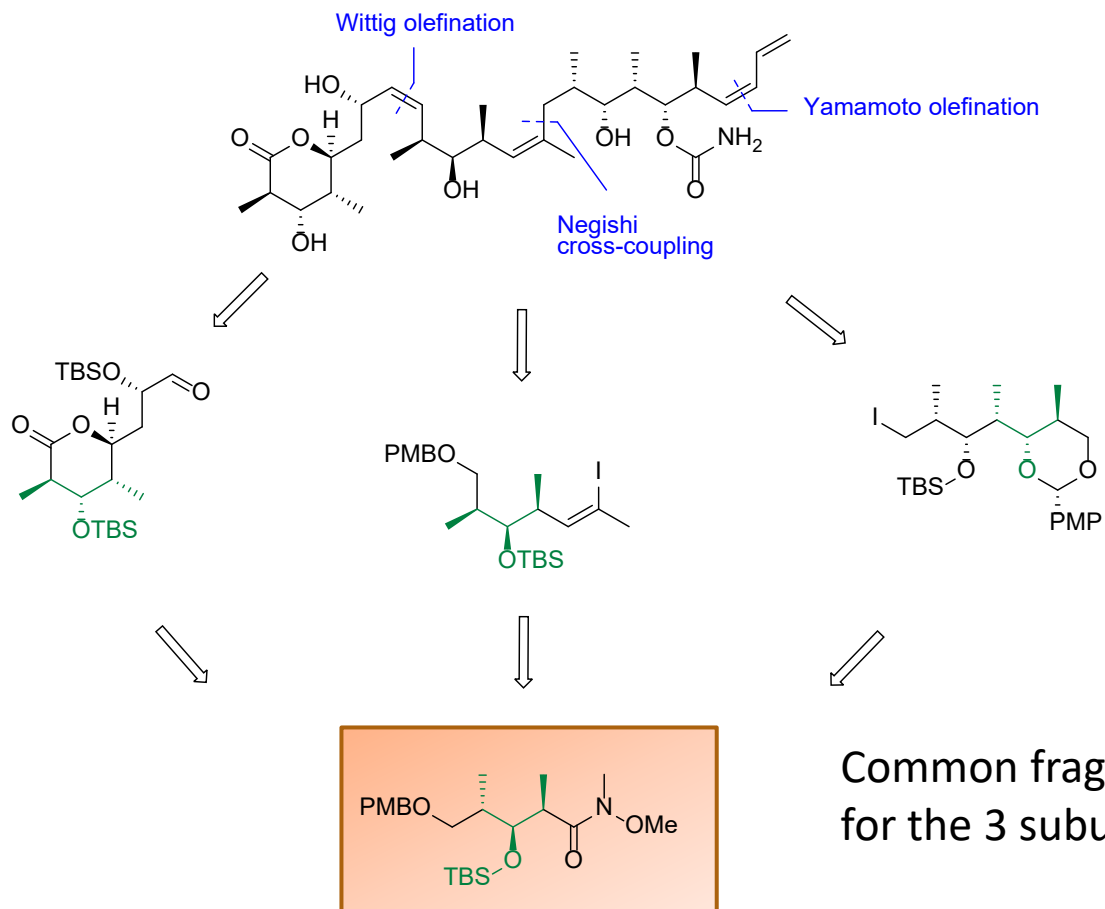
Licensed by Novartis for development as a new-generation anticancer drug

2004

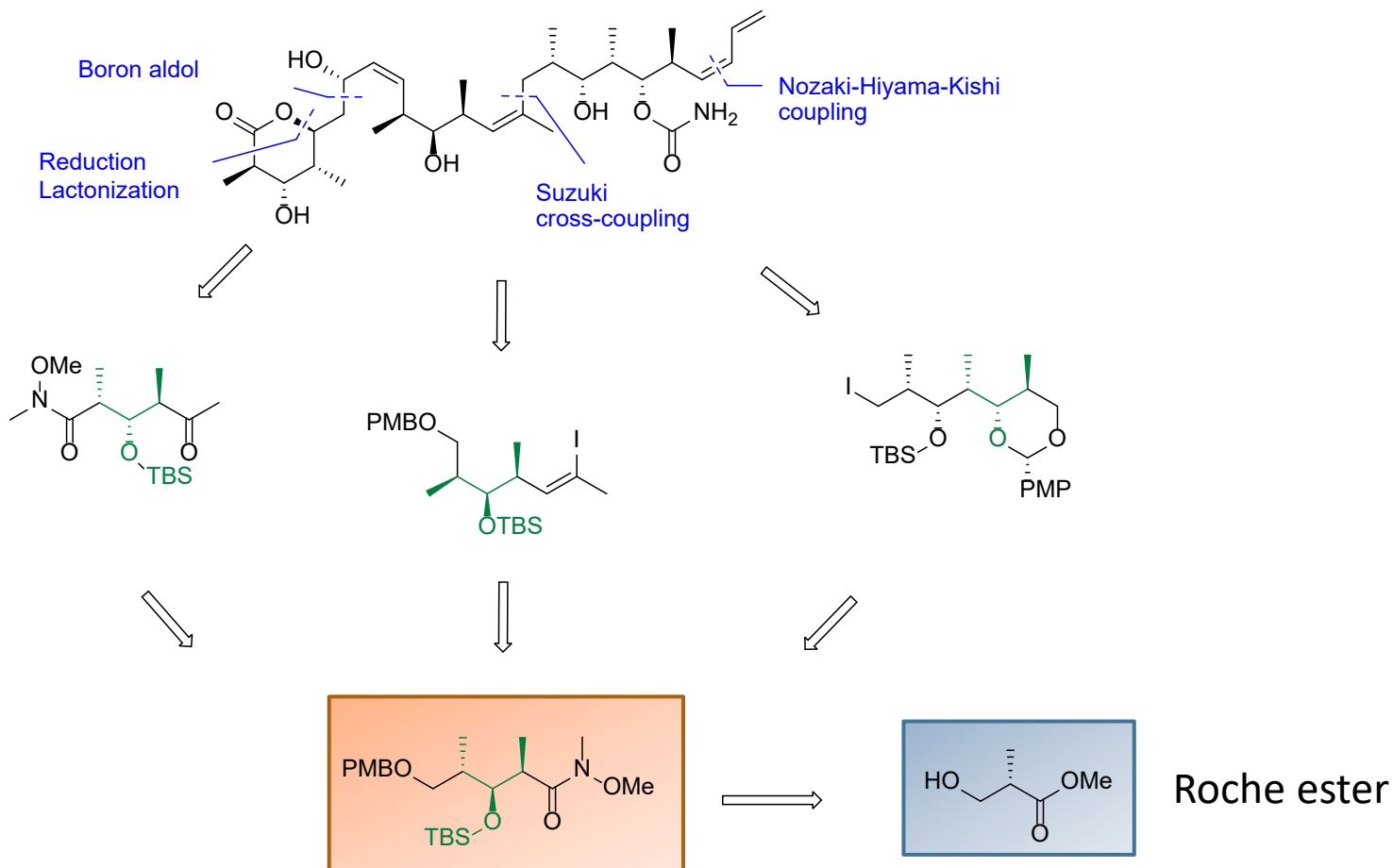
60 g scale synthesis; Novartis Process Group

Org. Res. Proc. Dev. **2004**, *8*, 92-130

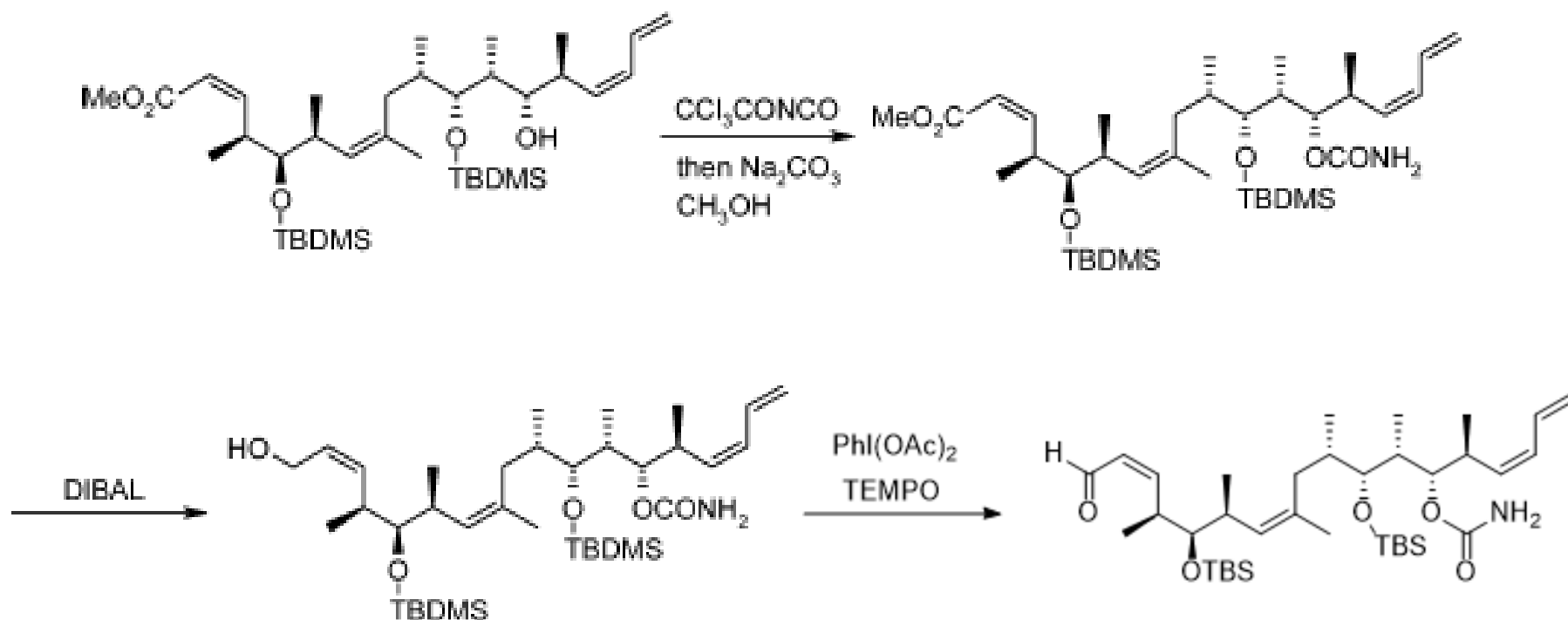
Strategy of A. B. Smith, III



Strategy by Novartis



Final assembly



Final assembly

60 g of final product

39 steps in total

