

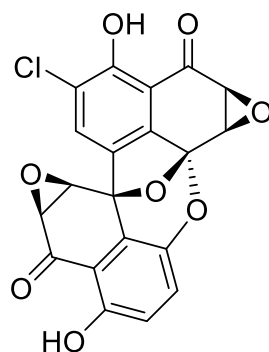
Stereochemical Dichotomy in Two Competing Cascade Processes: Total Syntheses of Both Enantiomers of Spiroxin A

Dr. Yoshio Ando, Daisuke Tanaka, Ryota Sasaki, Prof. Dr. Ken Ohmori, Prof. Dr. Keisuke Suzuki 

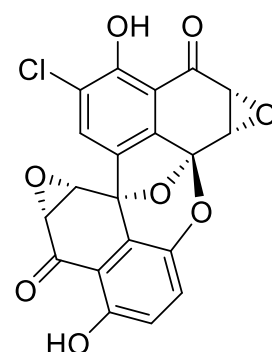
Sierra Bentley
Liu Research Group
September 26th, 2019

I. Introduction

- First total synthesis of both enantiomers of spiroxin A
- Spiroxin A is a marine antibiotic which has potential biological activity.
- Its structure contains a unique naphthoquinone dimer along with a highly complex architecture, strain from the distorted caged, various functional groups and multiple stereogenic centers.

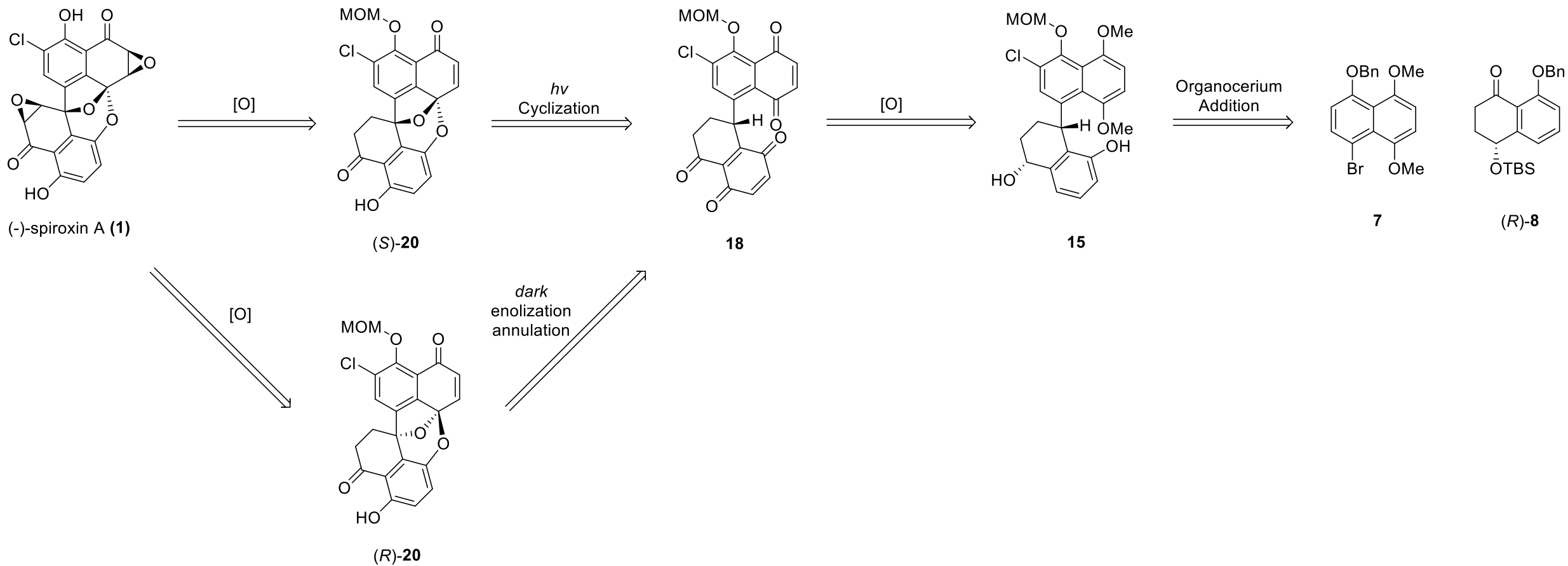


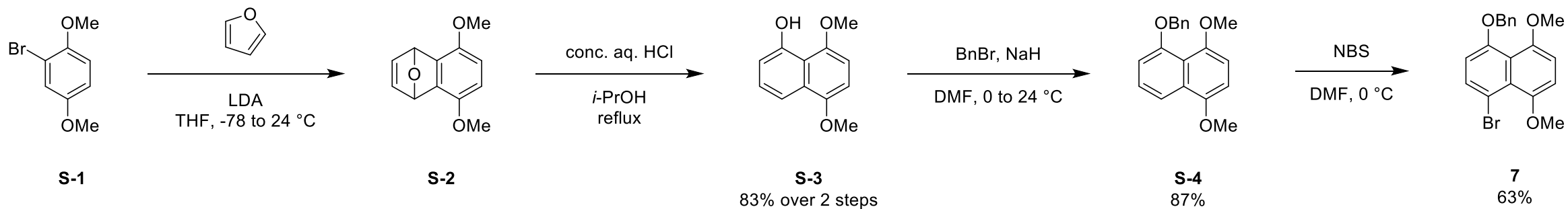
(-)-spiroxin A (**1**)



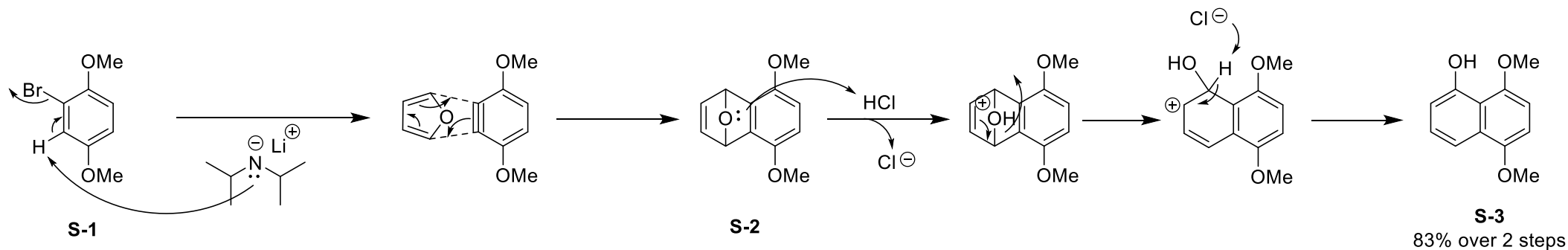
(+)-spiroxin A (*ent*-**1**)

II. Retrosynthesis

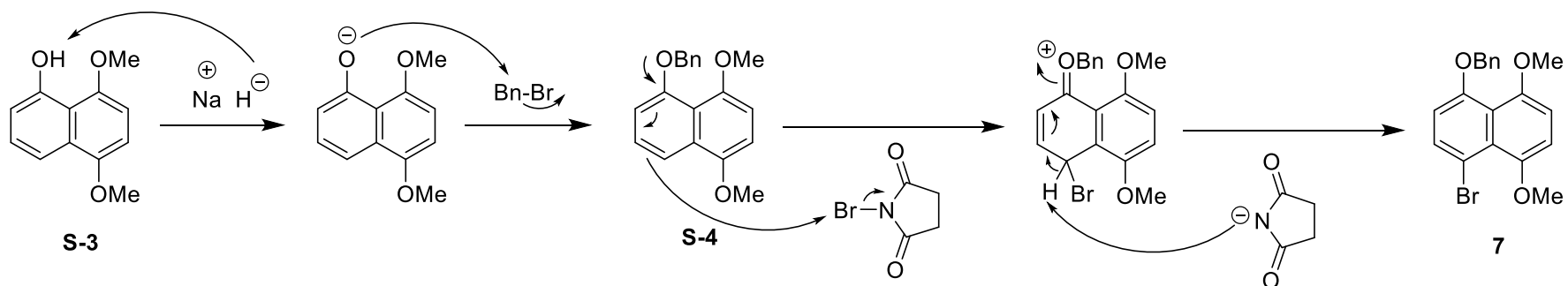


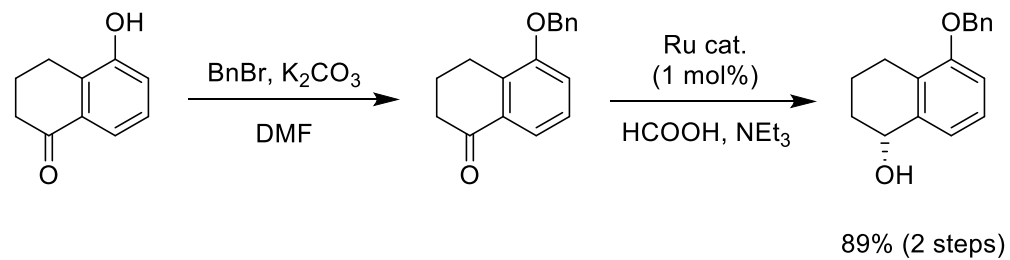


Diels-Alder followed by ring opening:

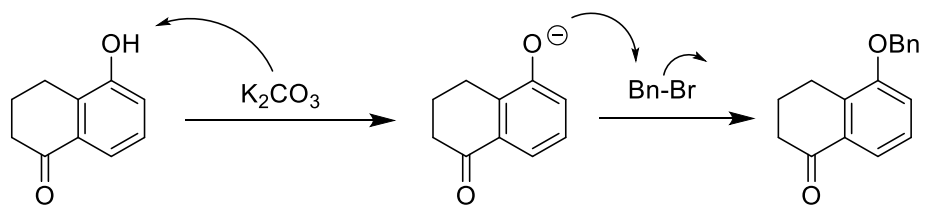


Benzyl Protection and NBS bromination:

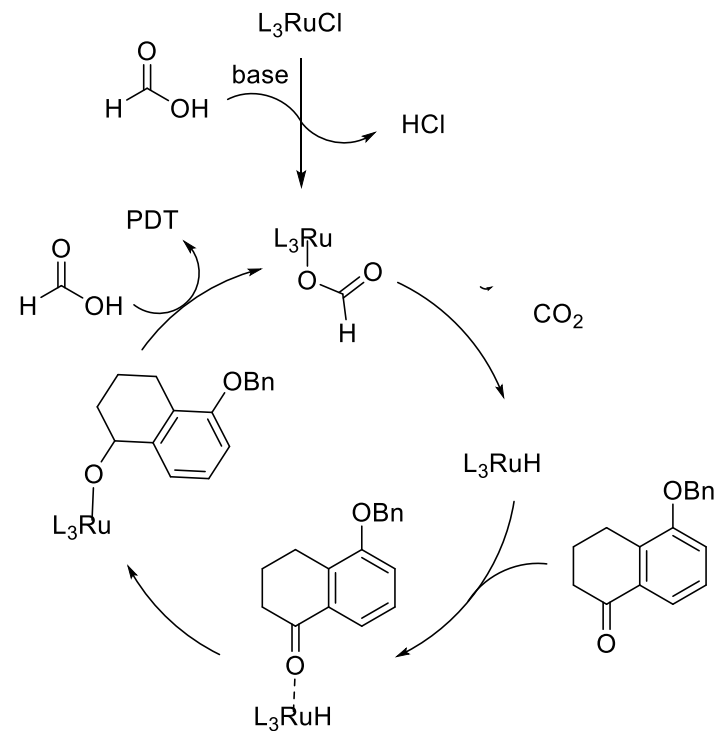




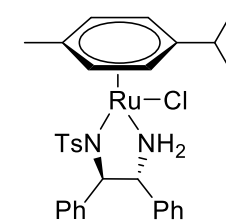
Benzyl Protection:

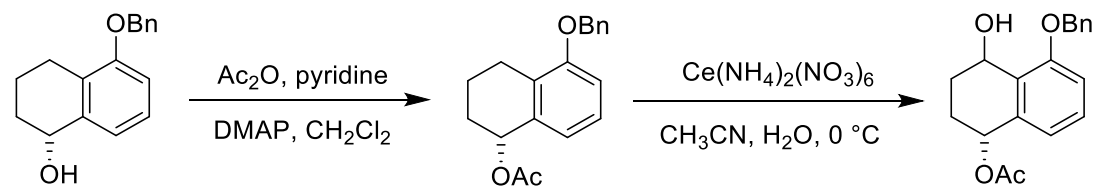


Reduction using Ruthenium Catalyst:

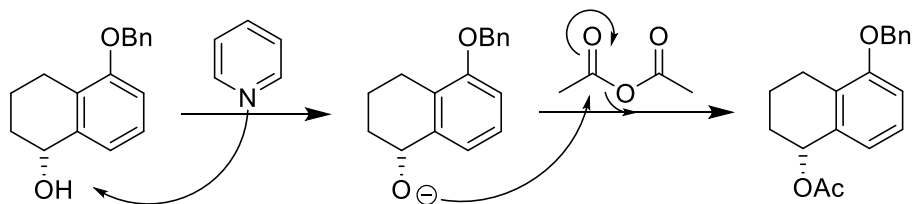


Ru cat.:

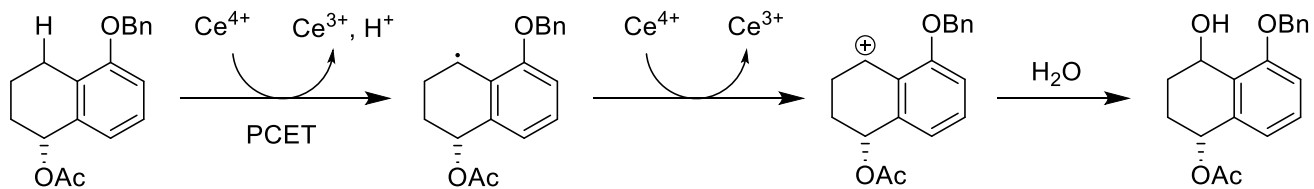


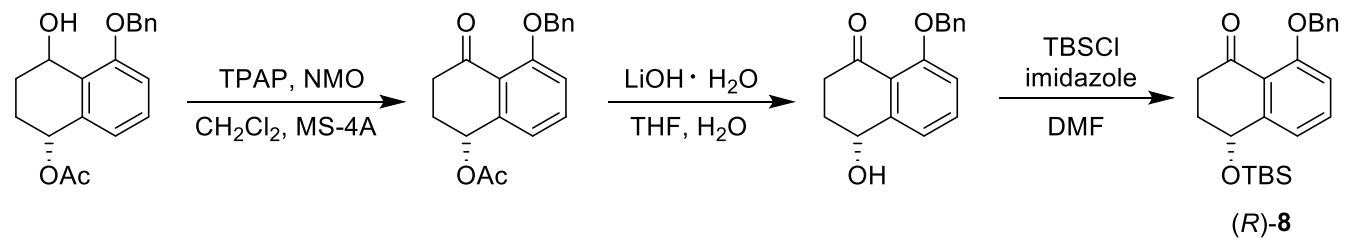


Protection of alcohol:



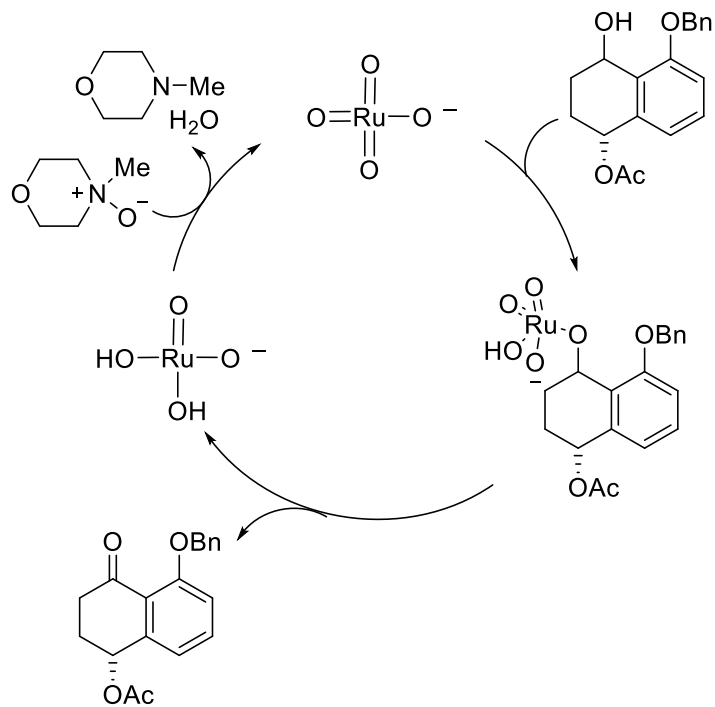
Oxidation using Ceric Ammonium Nitrate:



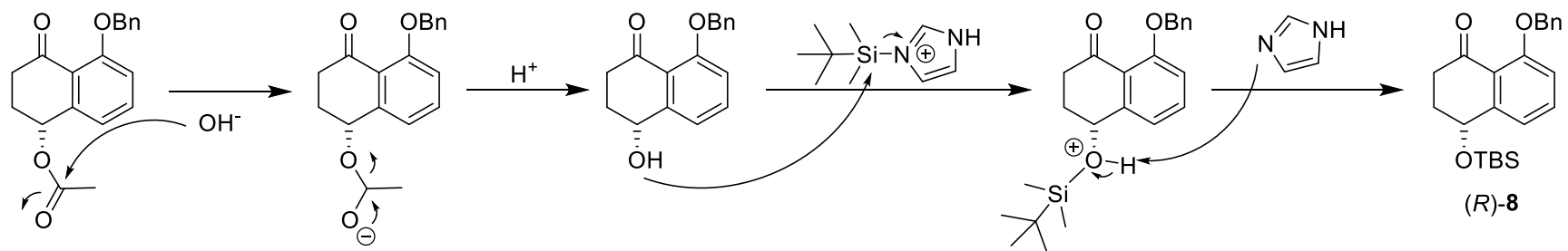


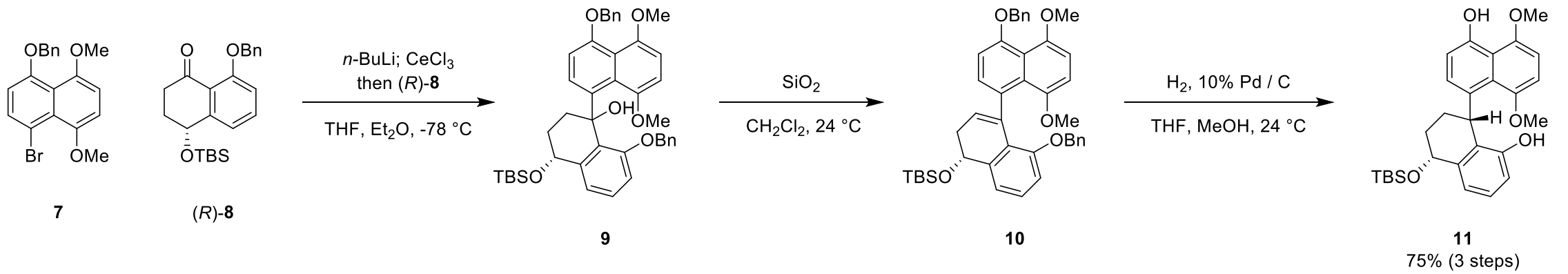
65% (5 steps)

TPAP Oxidation:

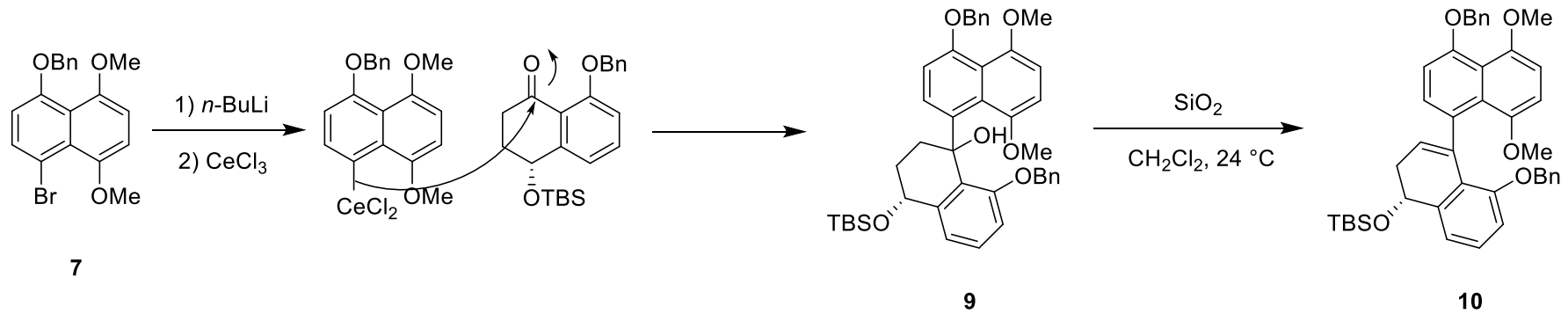


Deprotection and Reprotection of Alcohol:

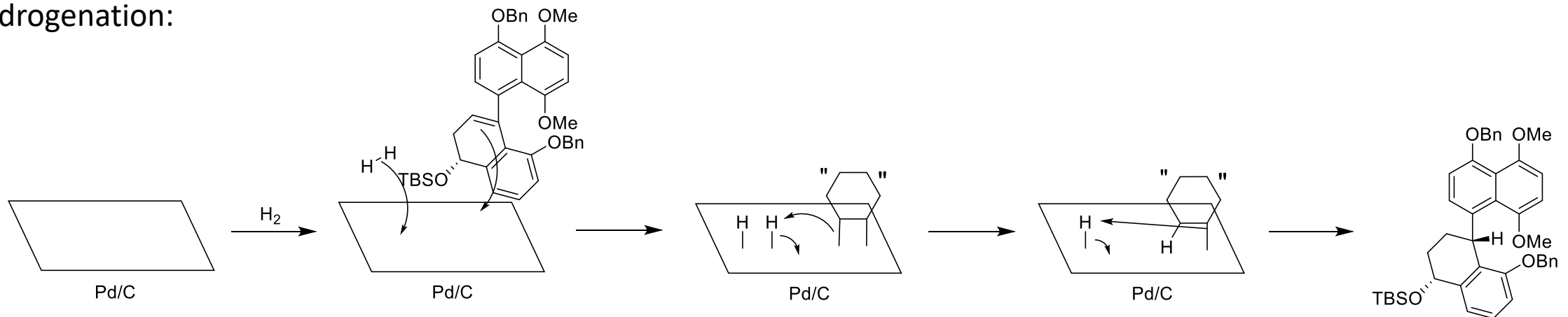


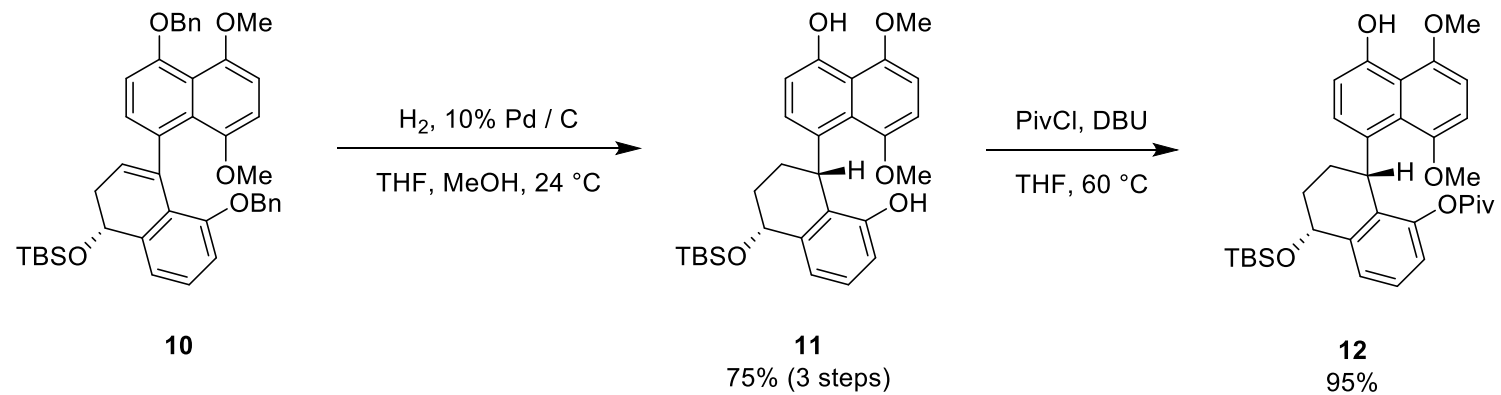


Lithium halogen exchange followed by addition to ketone and dehydration:

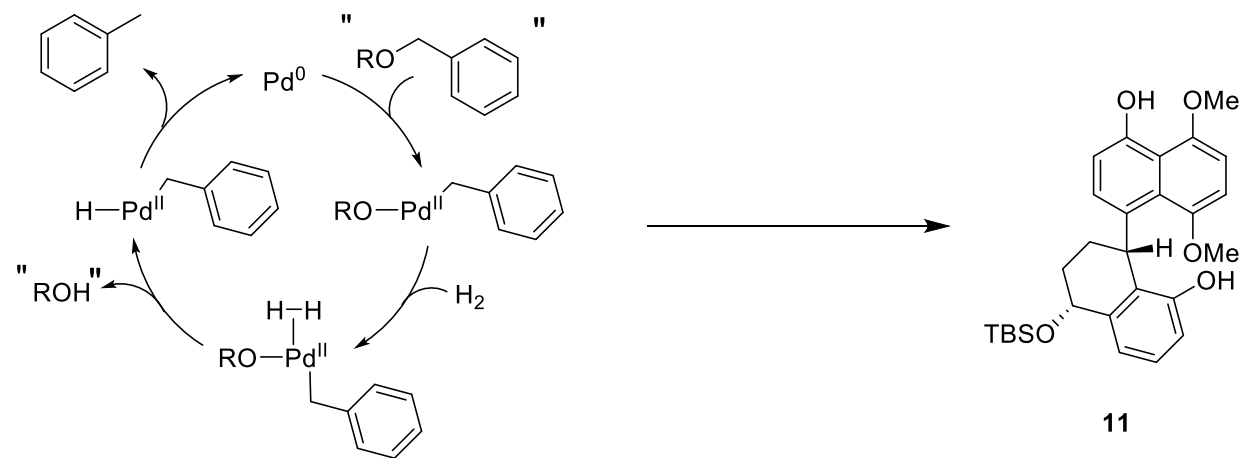


Hydrogenation:

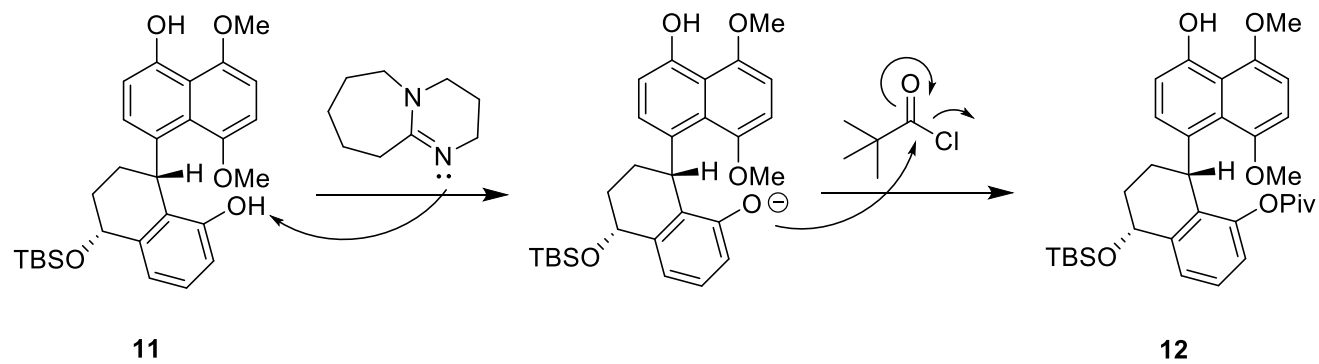


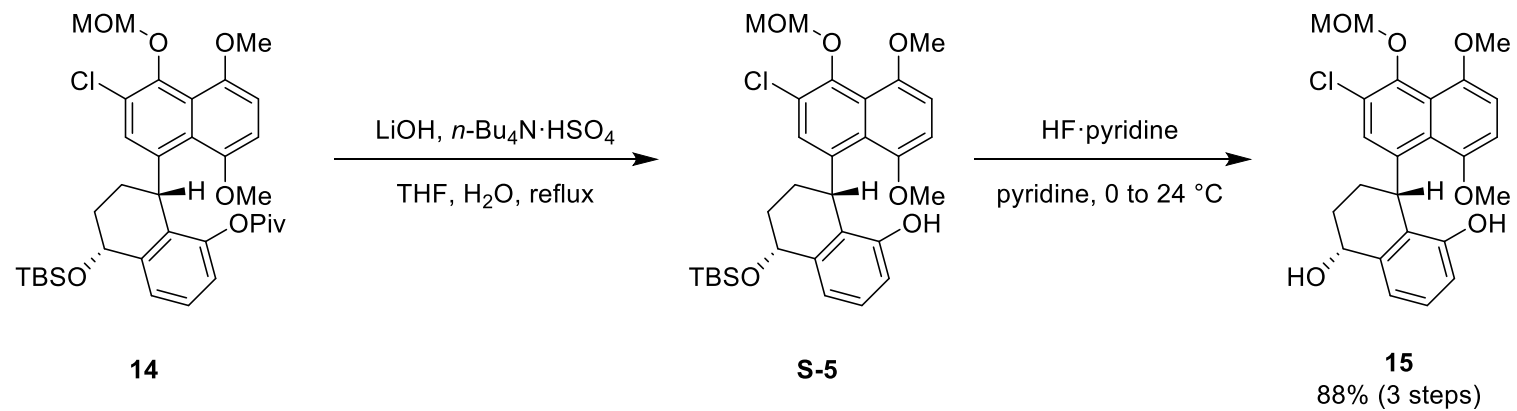


Benzyl Deprotections:

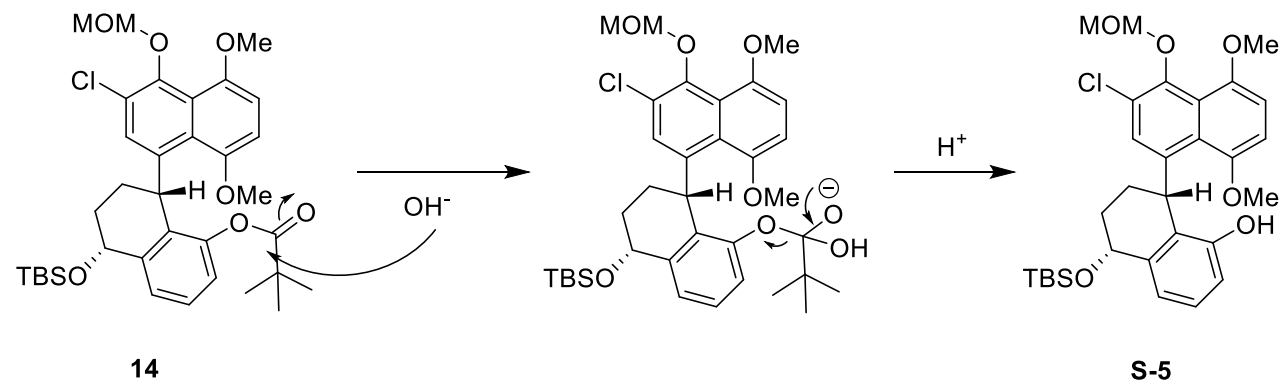


Pivaloyl Protection:

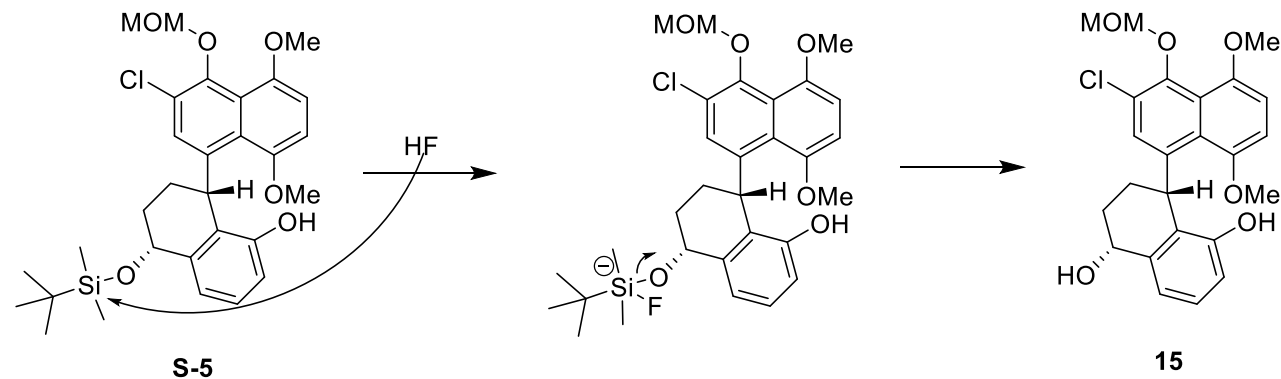


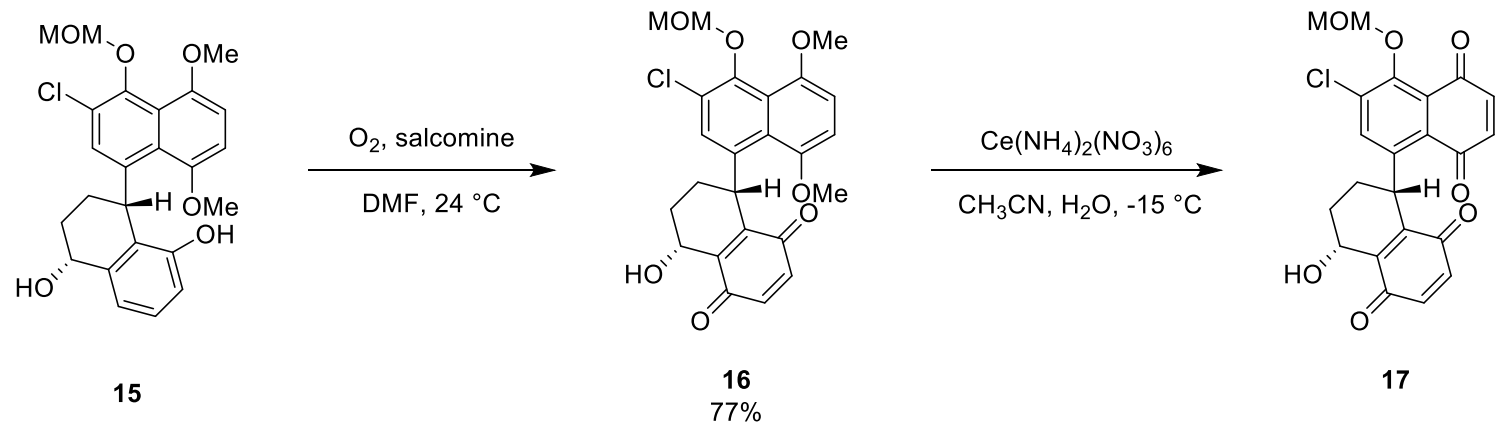


Deprotection of the Pivaloyl group:

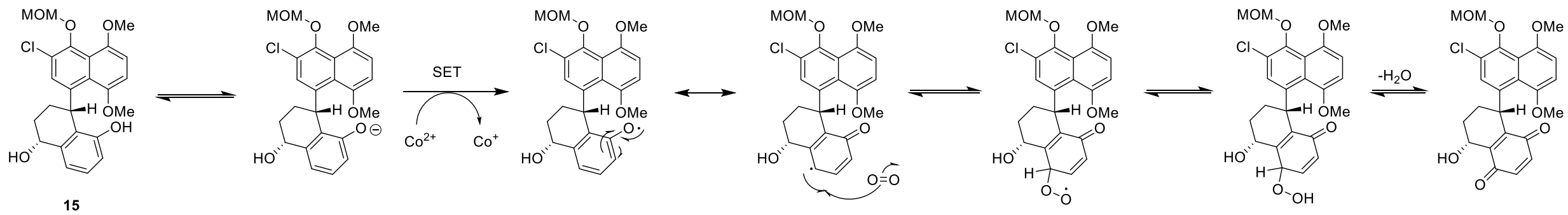


Deprotection of the TBS group:

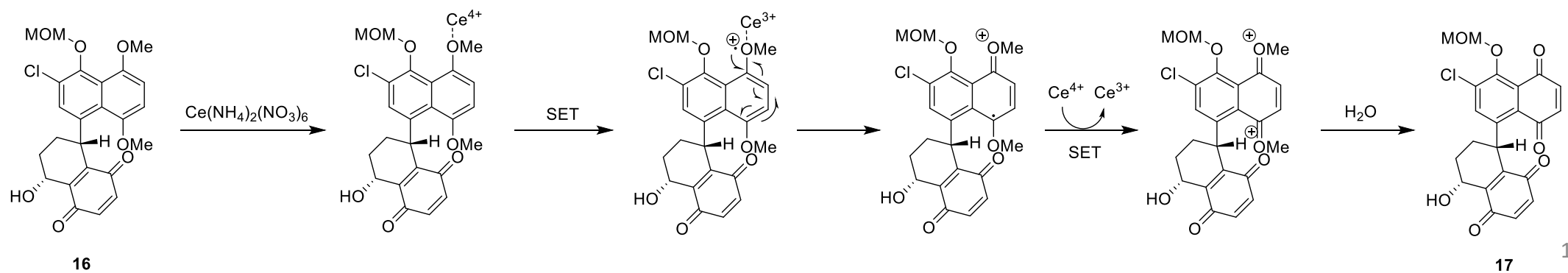


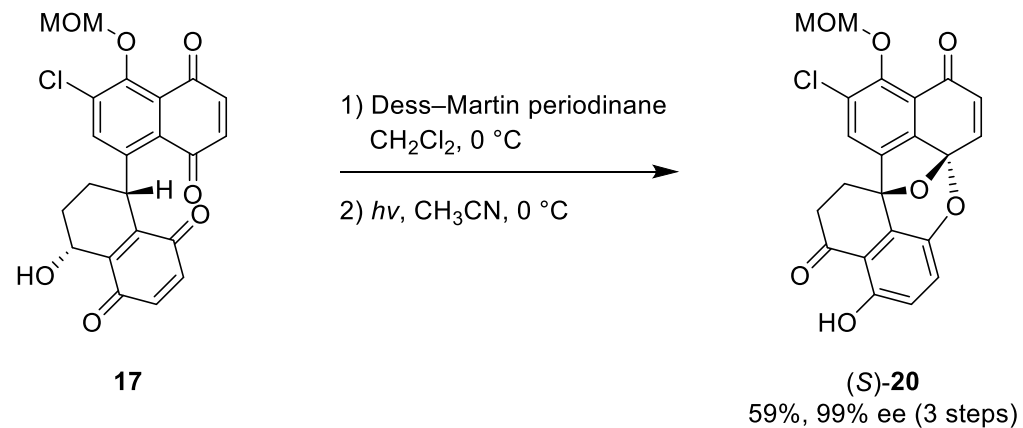


Quinone Oxidation of phenol:

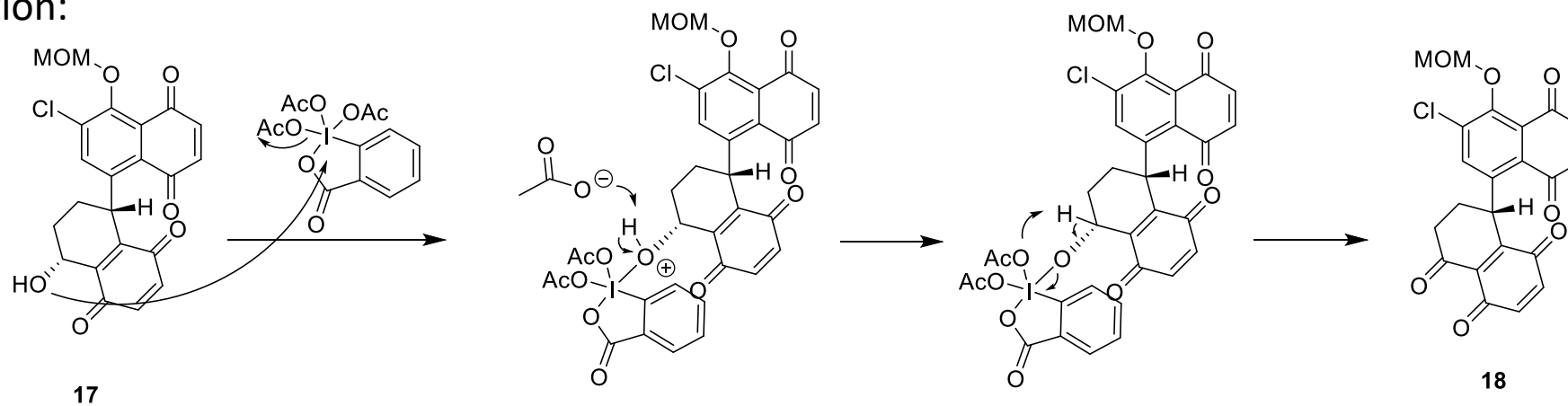


Quinone Oxidation using CAN:

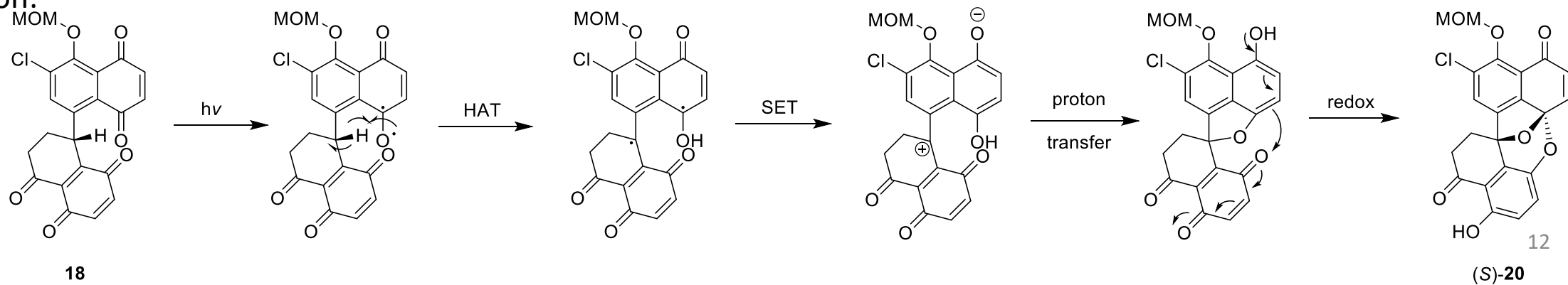


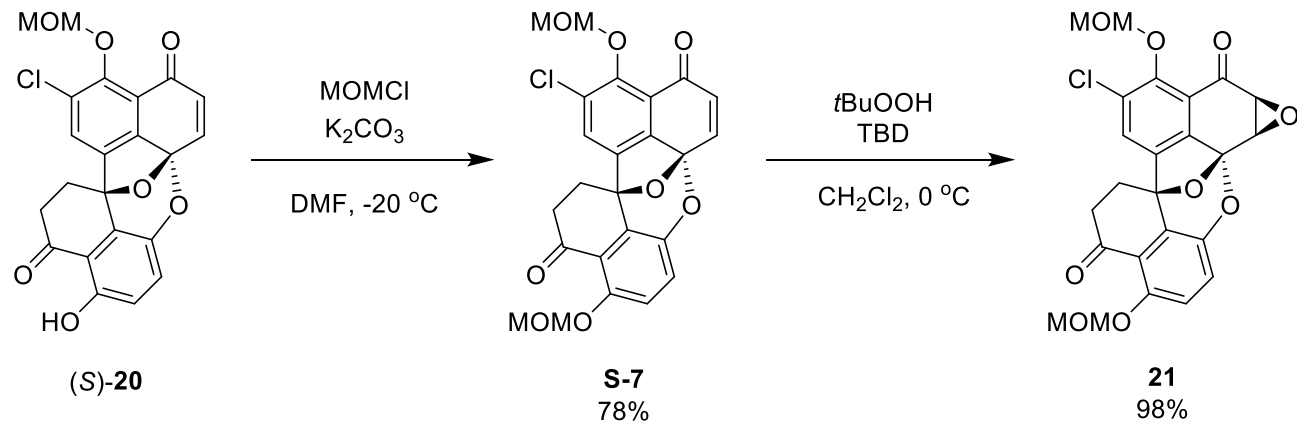


Dess-Martin Oxidation:

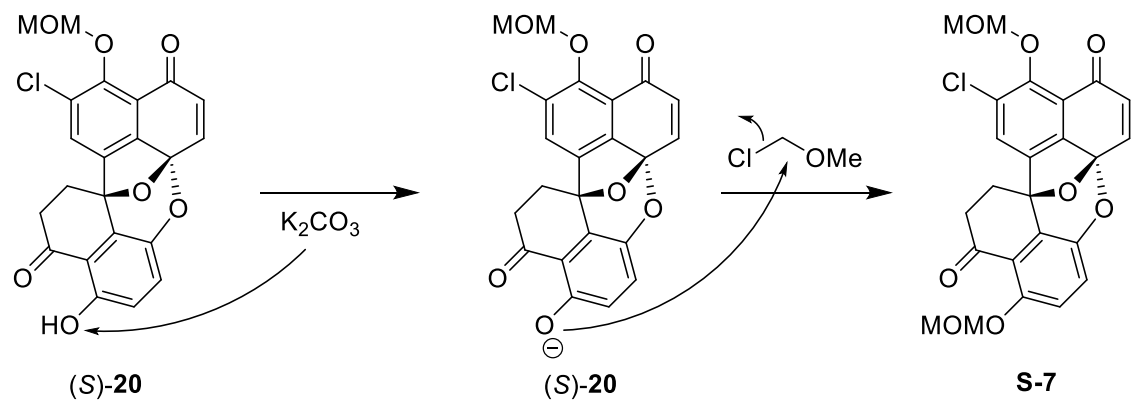


Cyclization:

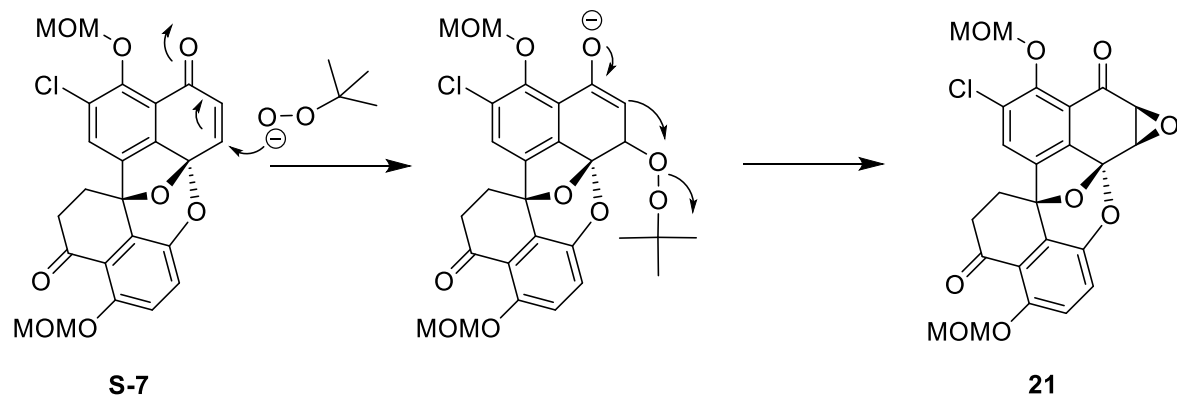


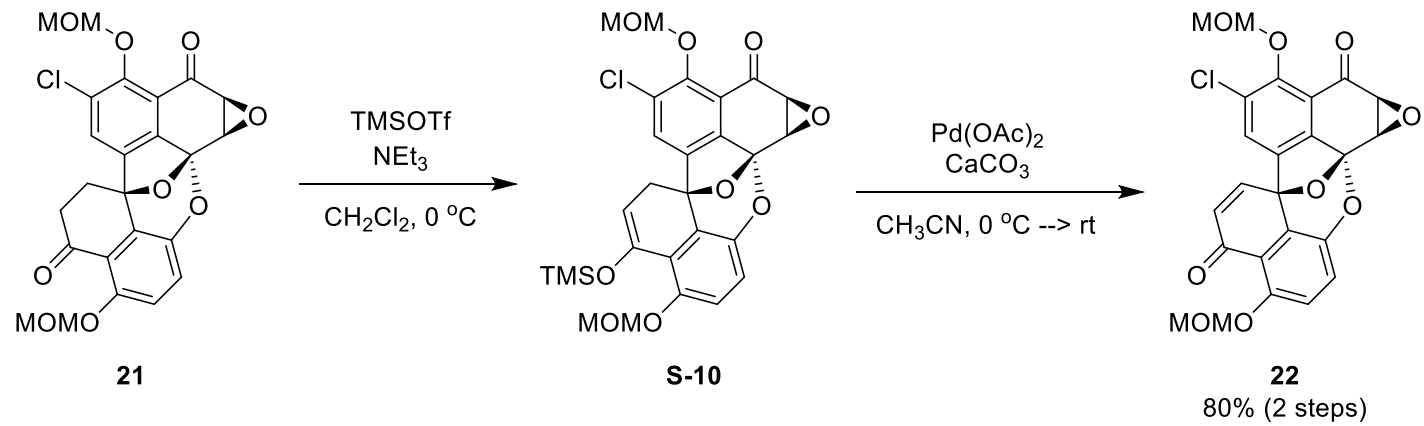


MOM Protection:

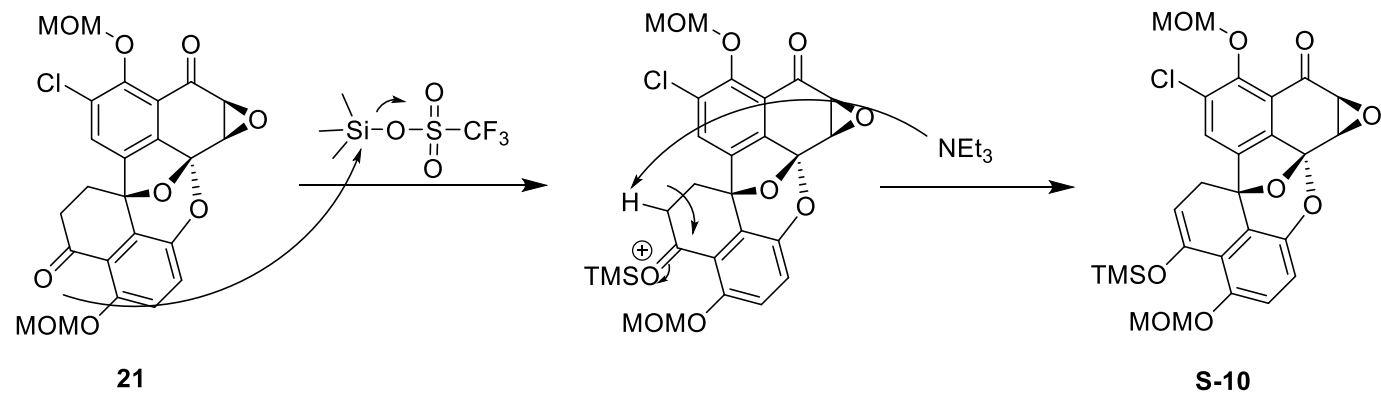


Nucleophilic Epoxidation:

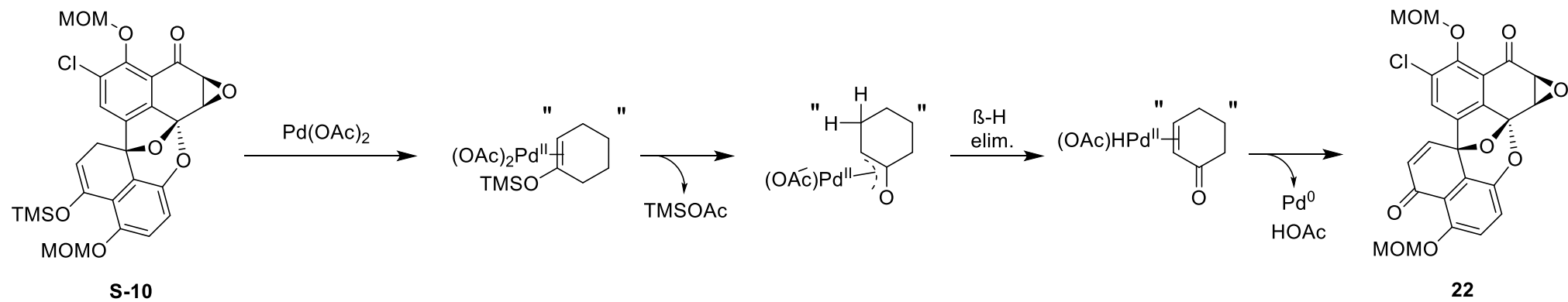


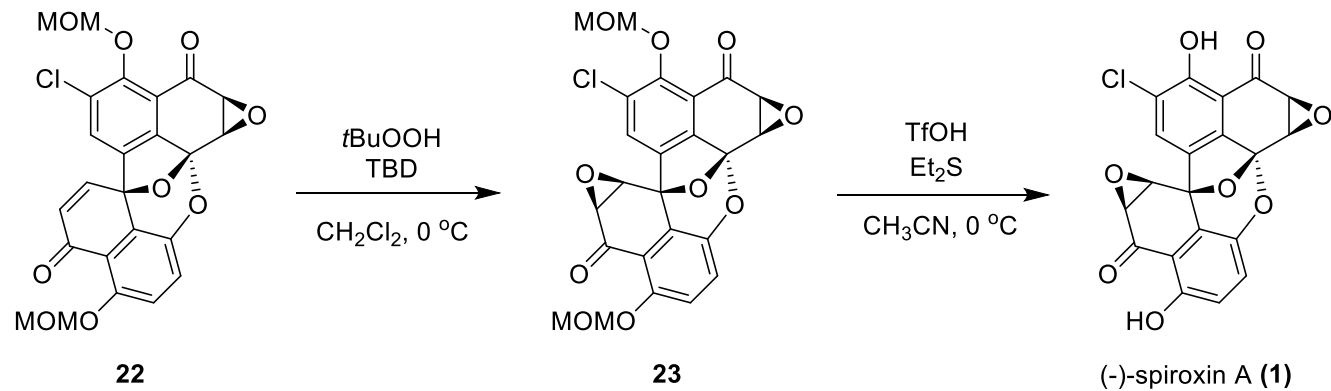


TMS Enolation:

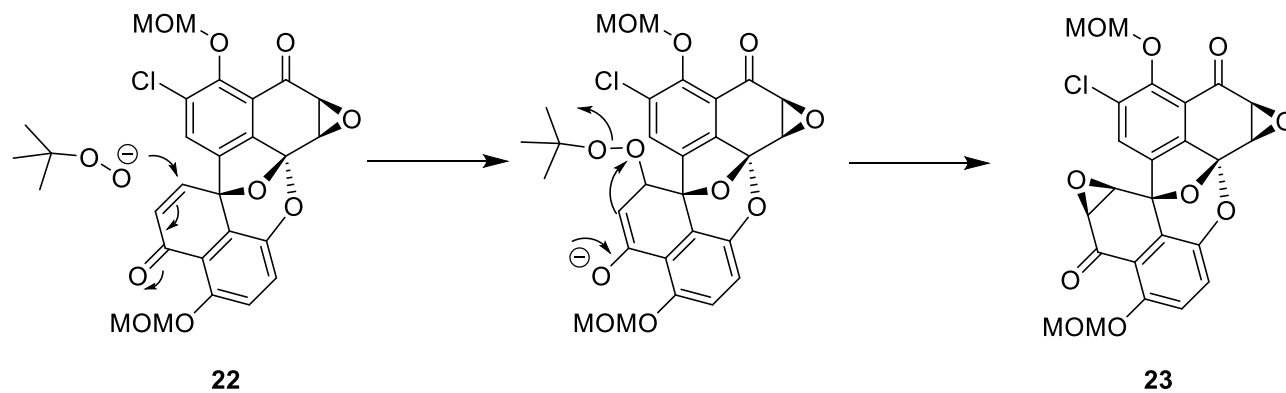


Ito-Saegusa Oxidation:

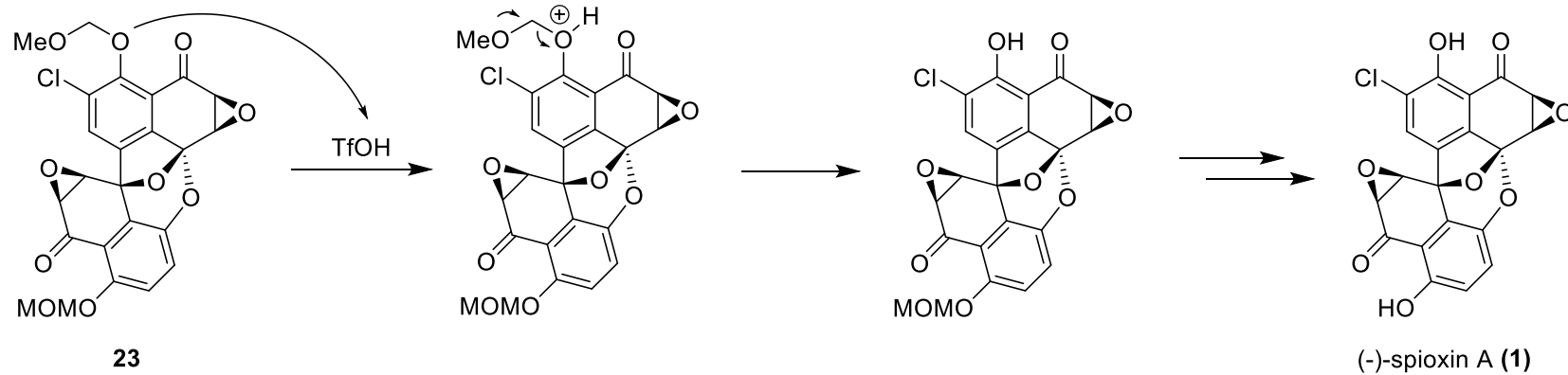




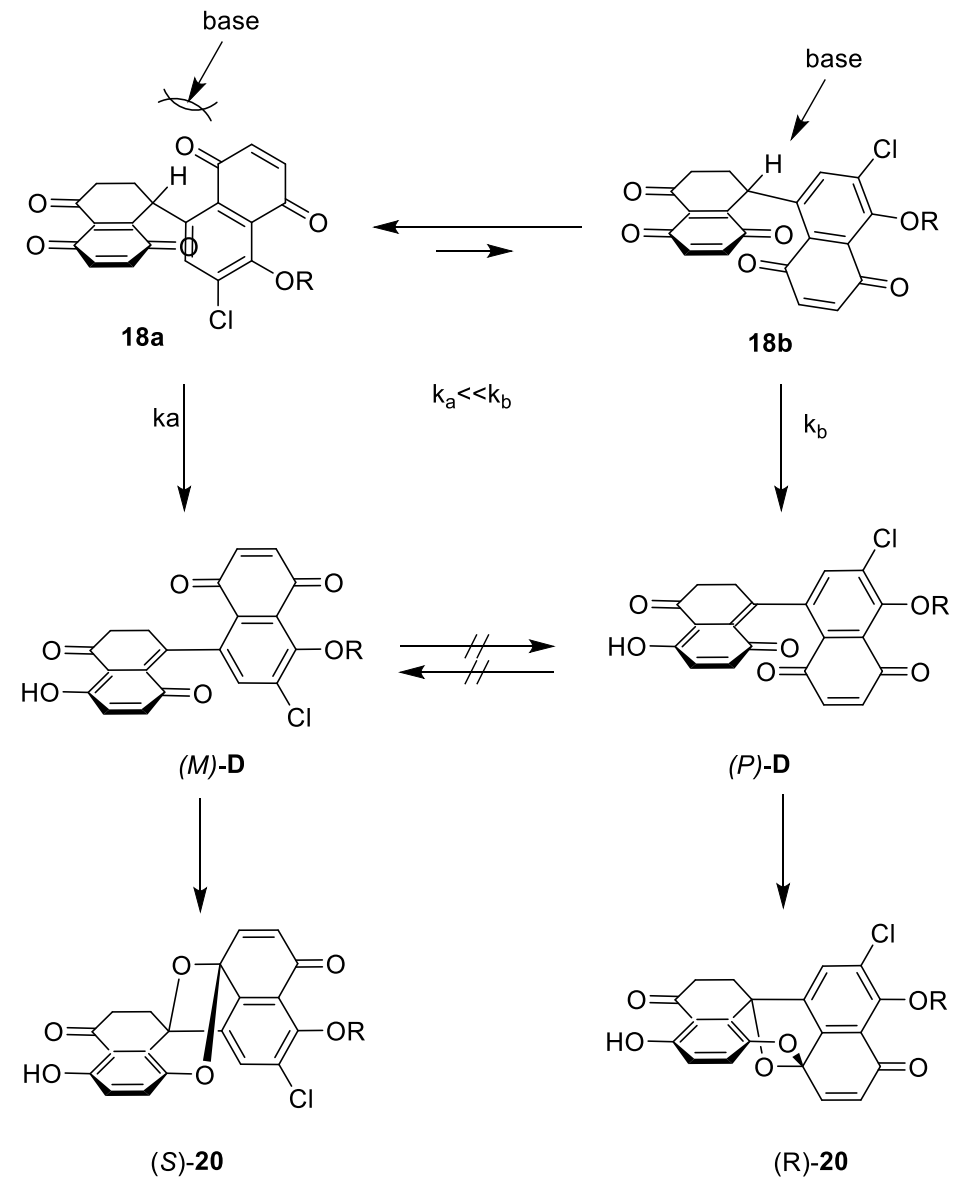
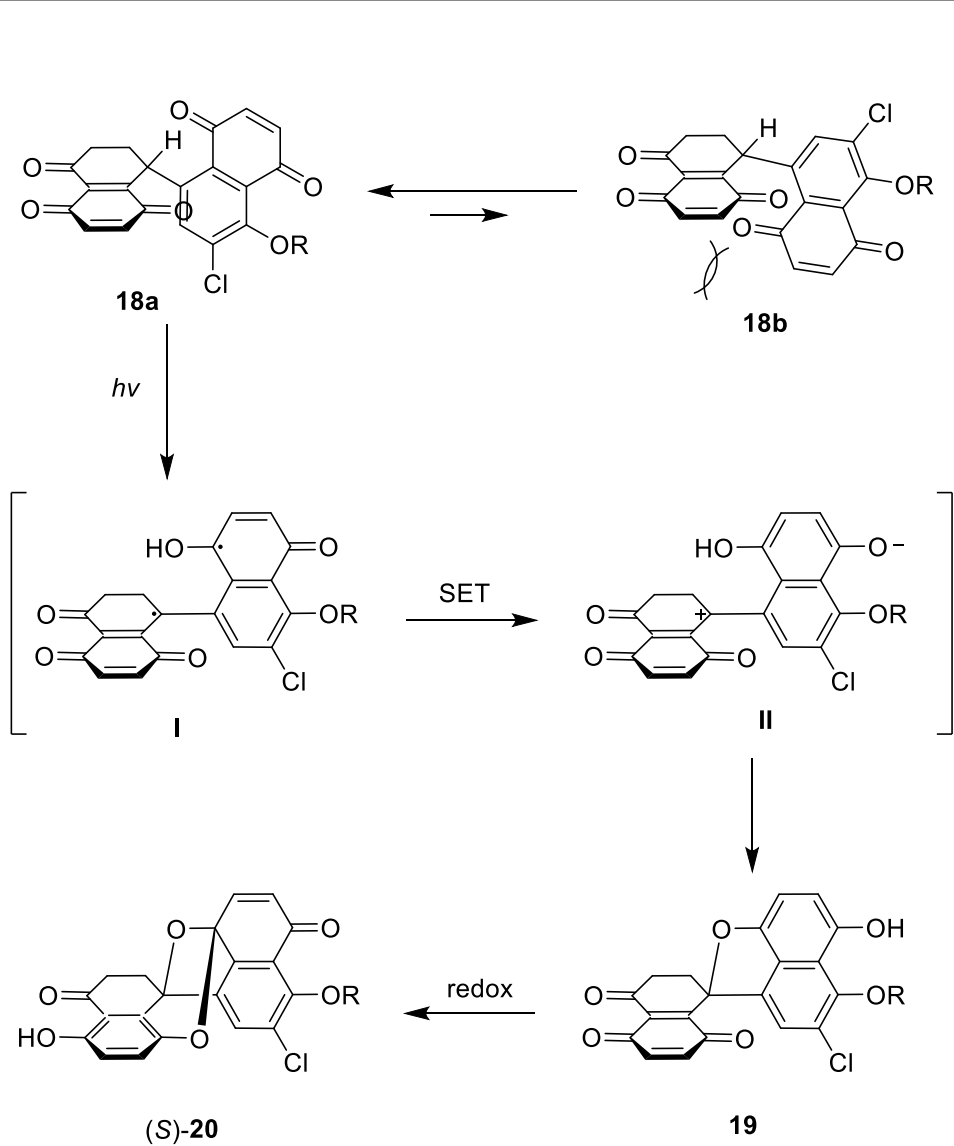
Nucleophilic Epoxidation:



MOM Deprotection:



Rationale for Dark Reaction



Synthetic Pathway for the (R) Enantiomer in the Dark

Enolization-annulation:

