

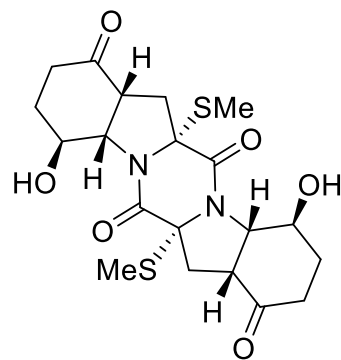
# Efficient and Divergent Total Synthesis of (–)-Epicoccin G and (–)-Rostratin A Enabled by Double C(sp<sup>3</sup>)–H Activation

Pierre Thesmar and Olivier Baudoin\*<sup>✉</sup>

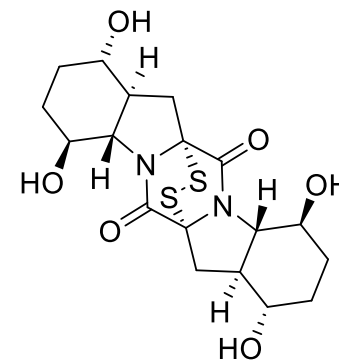
Sierra Bentley  
 Liu Research Group  
 January 16<sup>th</sup>, 2020

## Introduction

- Dithiodiketopiperazines are naturally occurring complex polycyclic molecules.
- (–)-epicoccin G is isolated from the fungus *Epicoccum nigrum* and has in vitro anti-HIV-1 and antiplasmodial activities
- (–)-rostratin A is isolated from the fungus *Exserohilum rostratum* and is cytotoxic against HCT-116 cancer cells
- First ever synthesis of (–)-rostratin A and second synthesis of (–)-epicoccin G

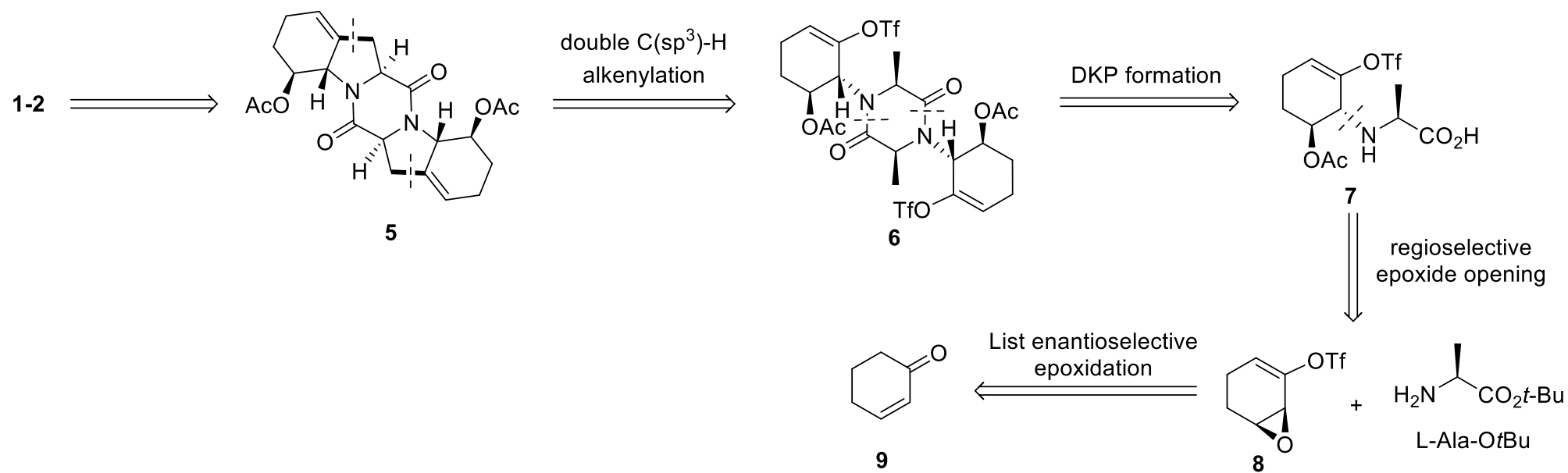


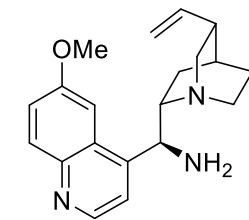
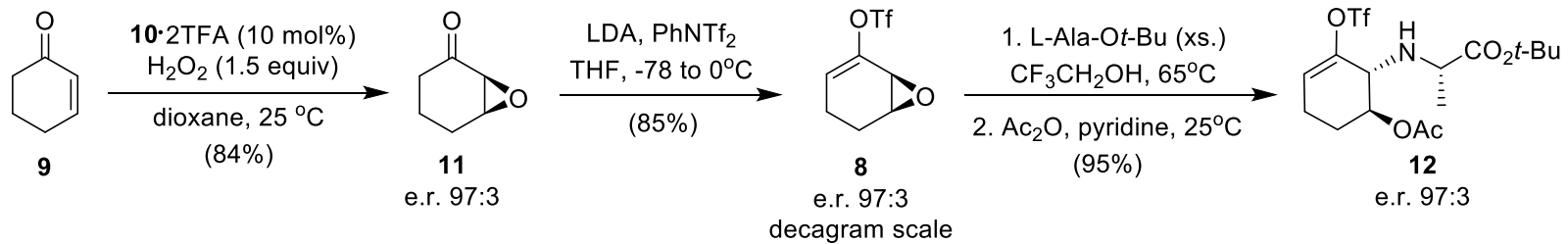
1: epicoccin G



2: rostratin A

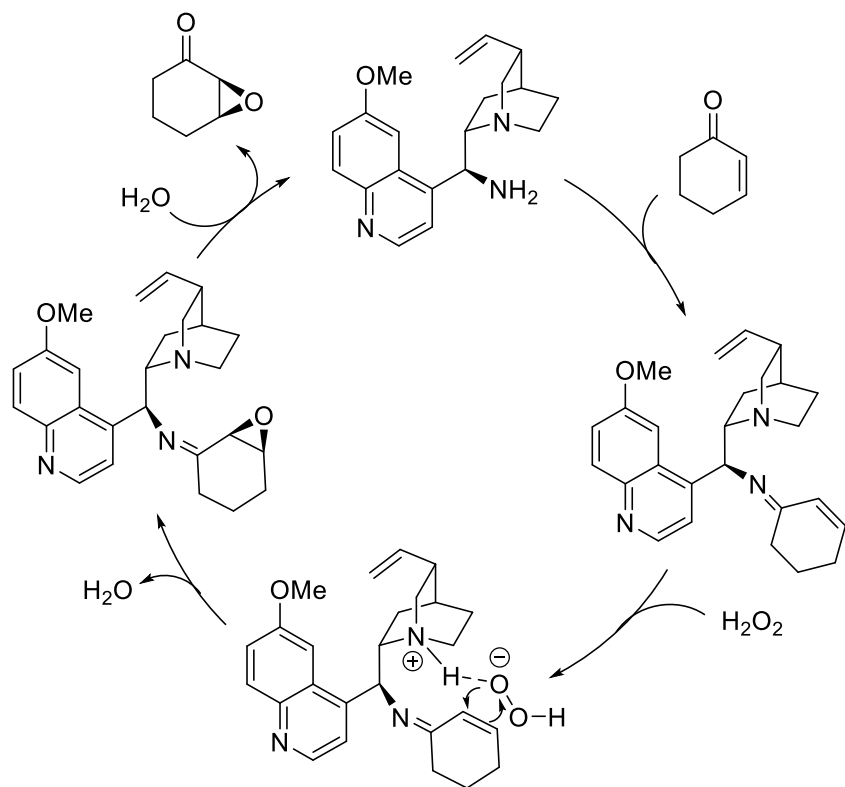
# Retrosynthesis



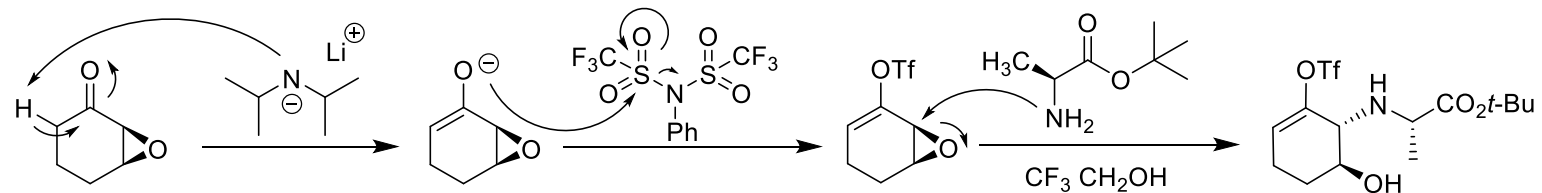


10

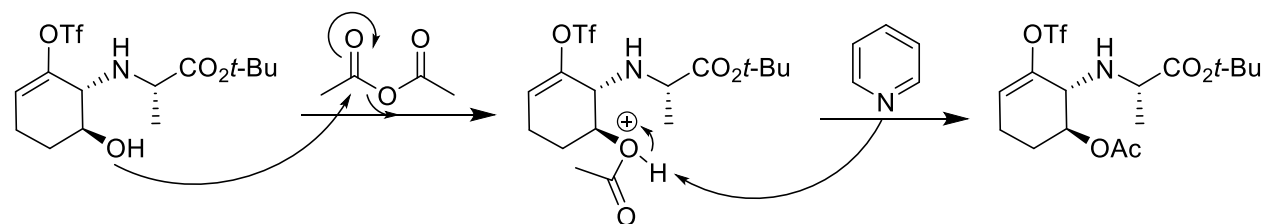
### Enantioselective epoxidation:

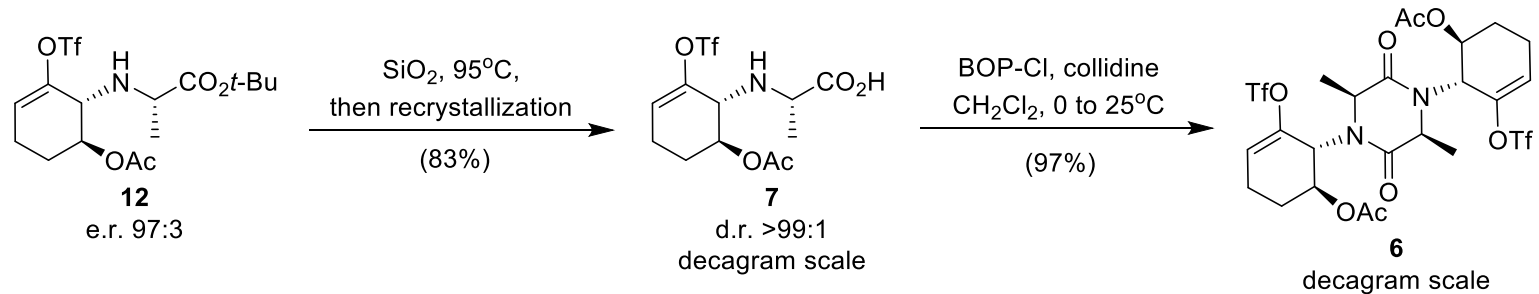


### Enolate formation followed by opening of the epoxide:

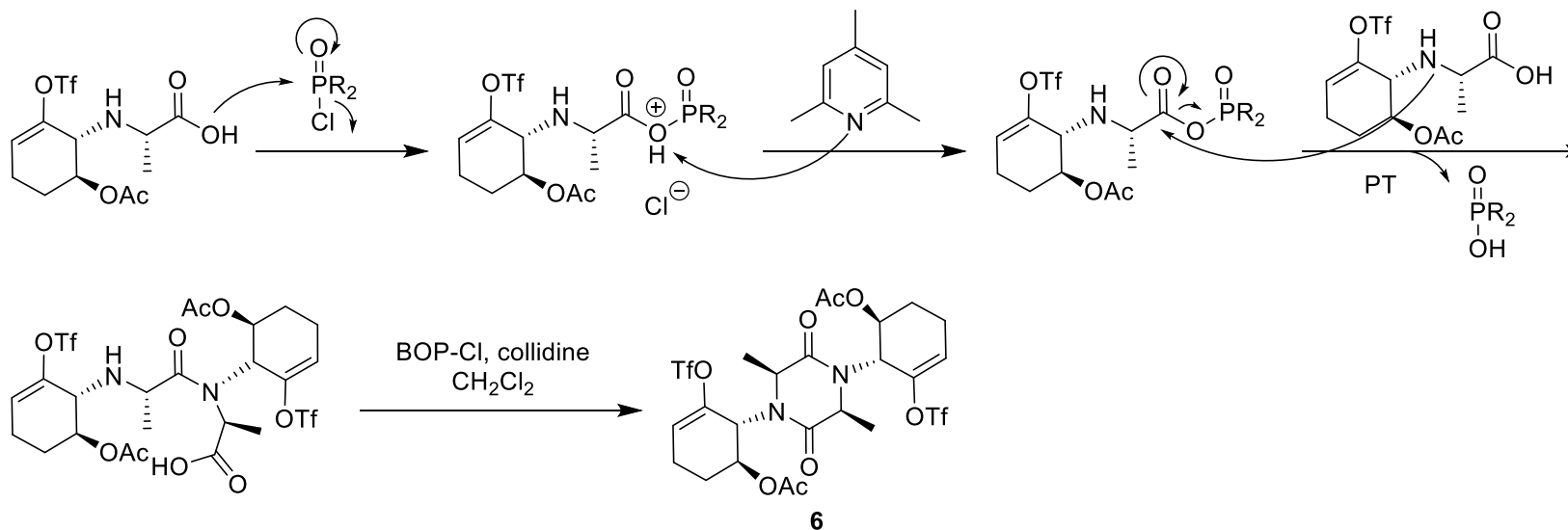
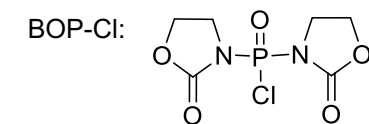


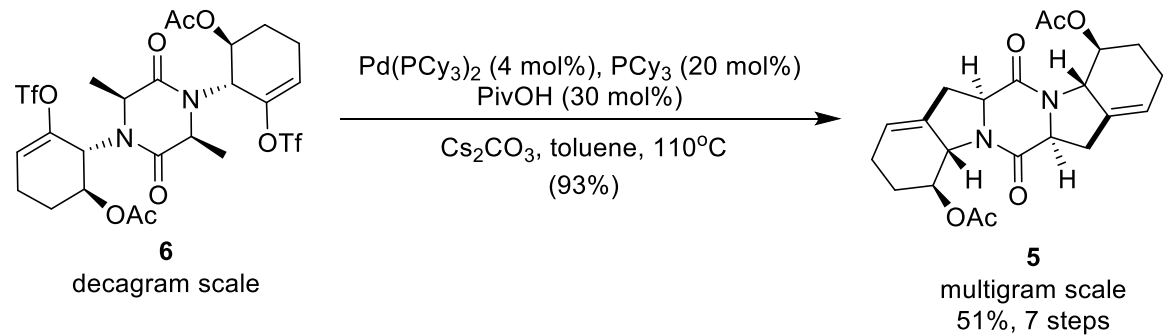
### Protection of alcohol:



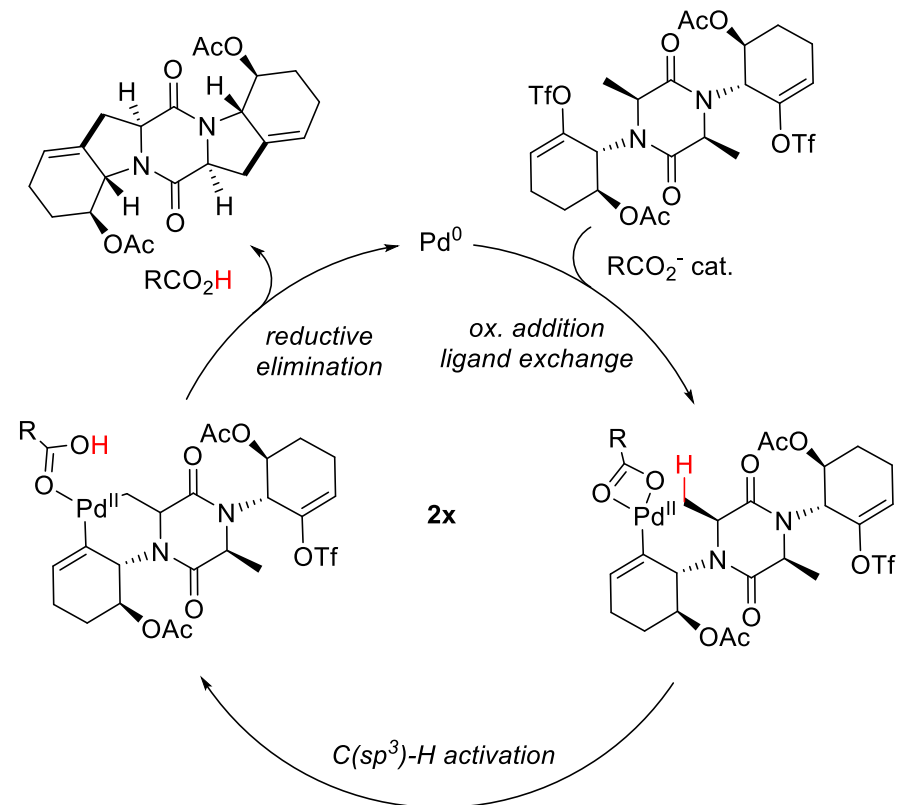


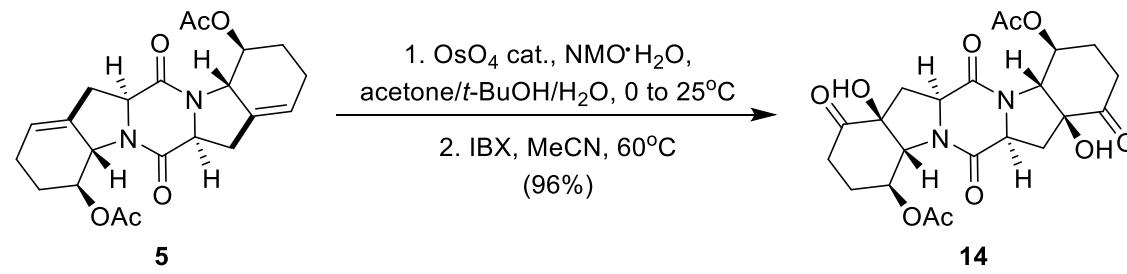
## Cyclodimerization mediated by BOP-Cl:



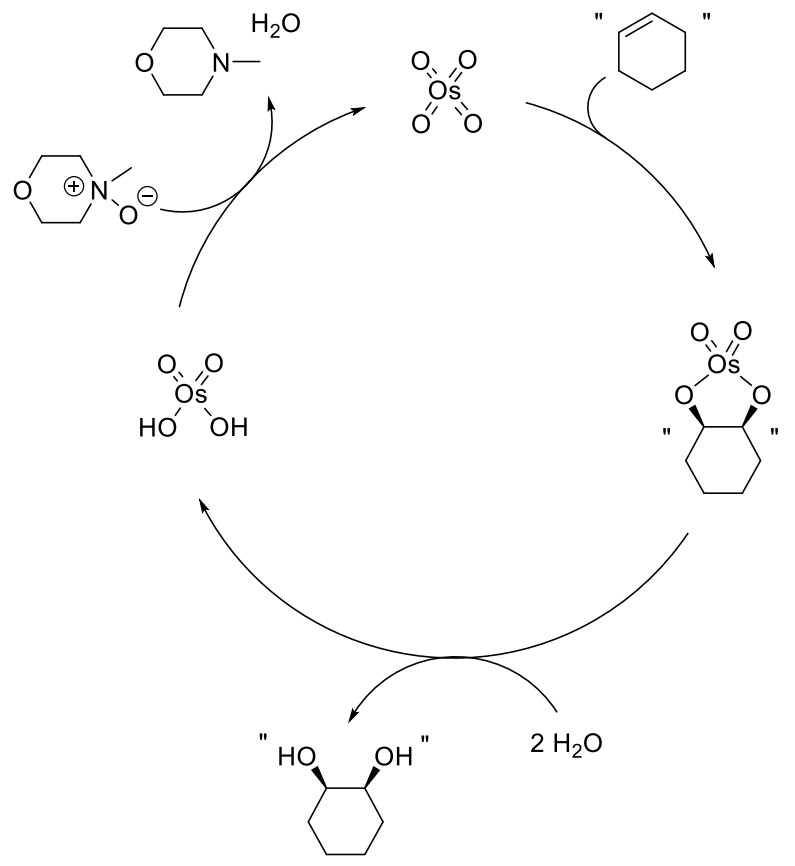


C(sp<sup>3</sup>)-H alkenylation:

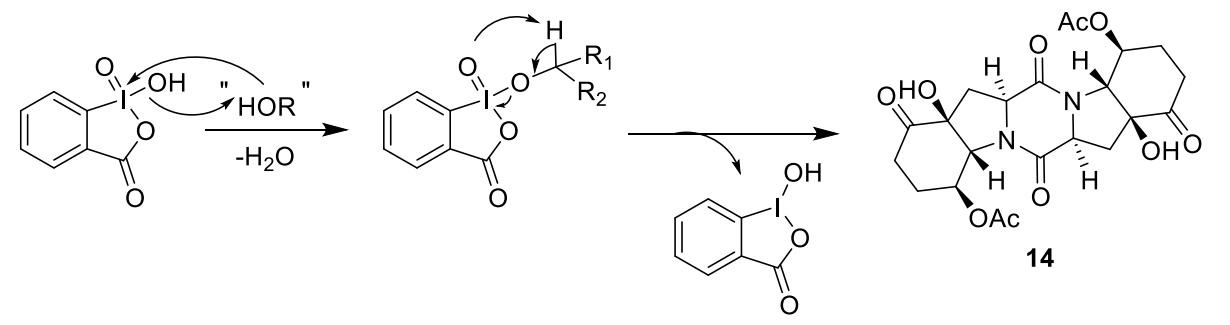


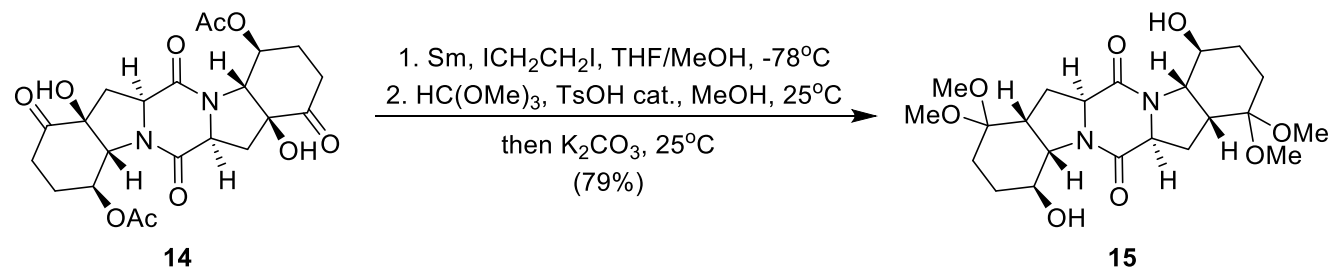


Upjohn dihydroxylation:

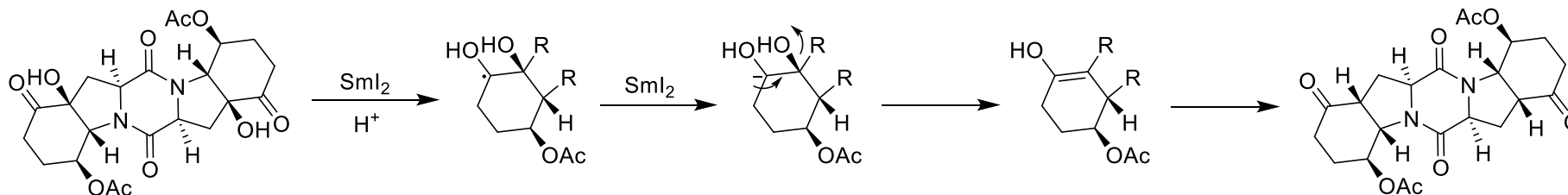


IBX Oxidation:

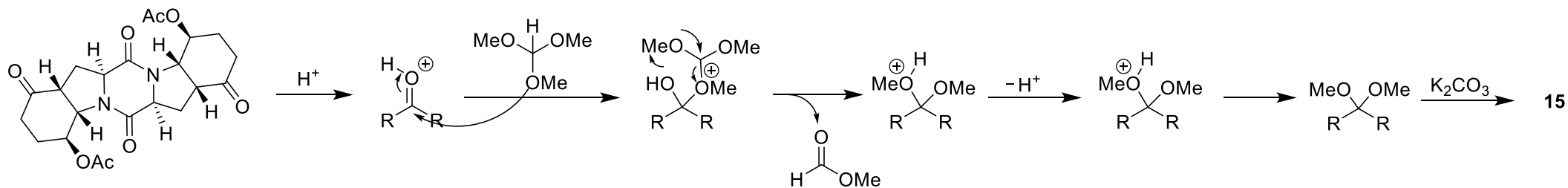


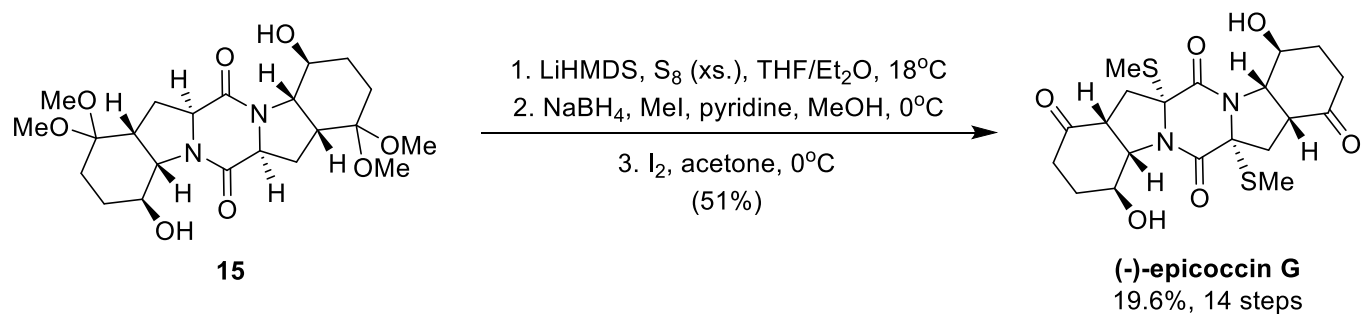


Samarium (II) iodide mediated reduction of hydroxyketones:

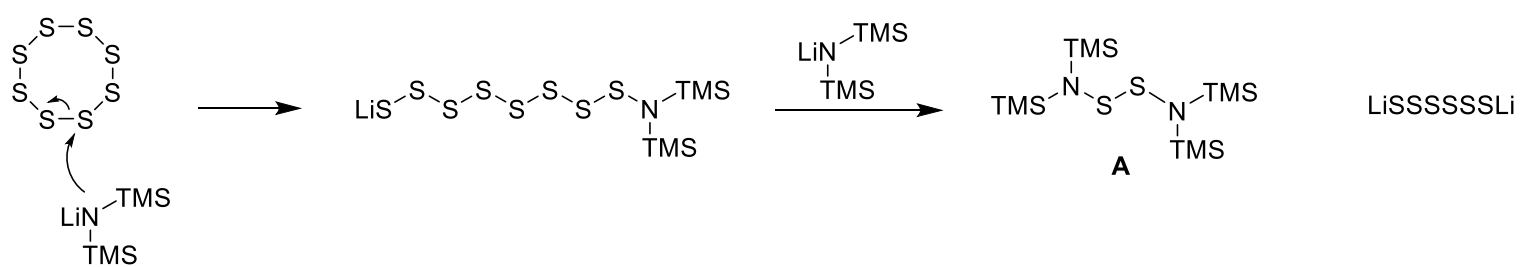


Dimethoxyketal protection and deacylation:

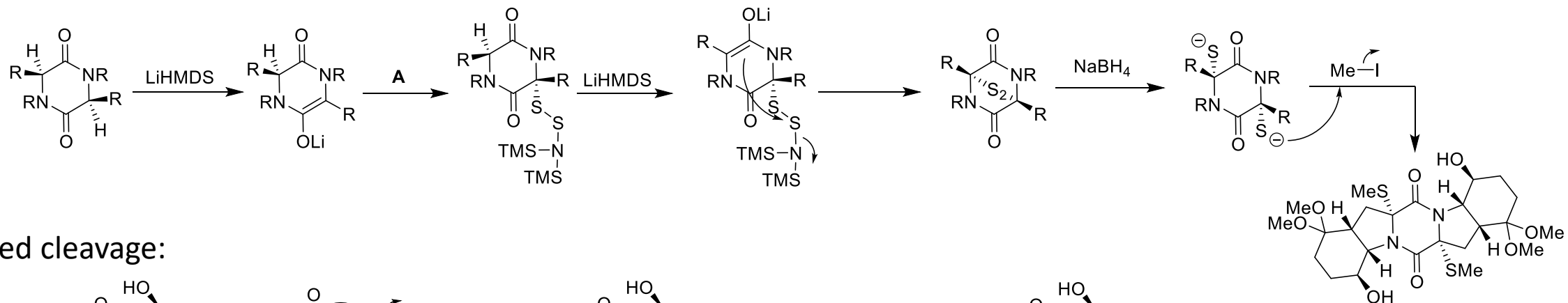




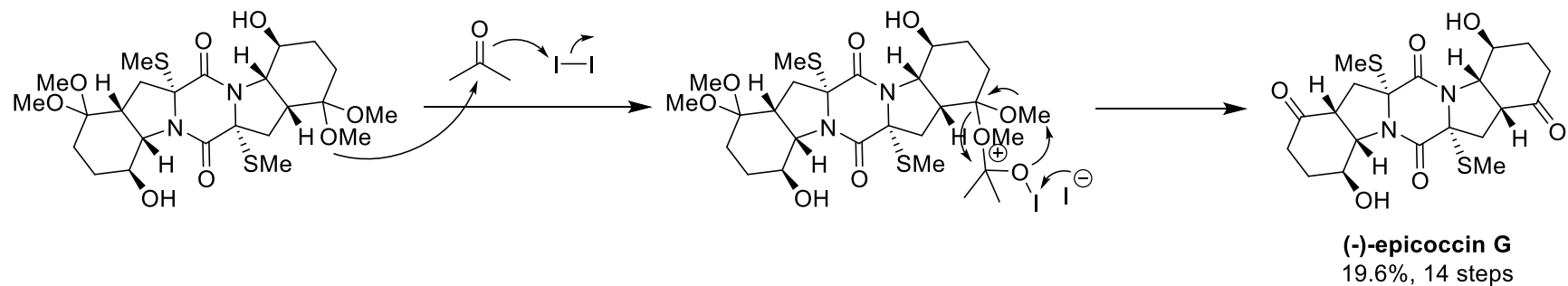
## Preparation of A:



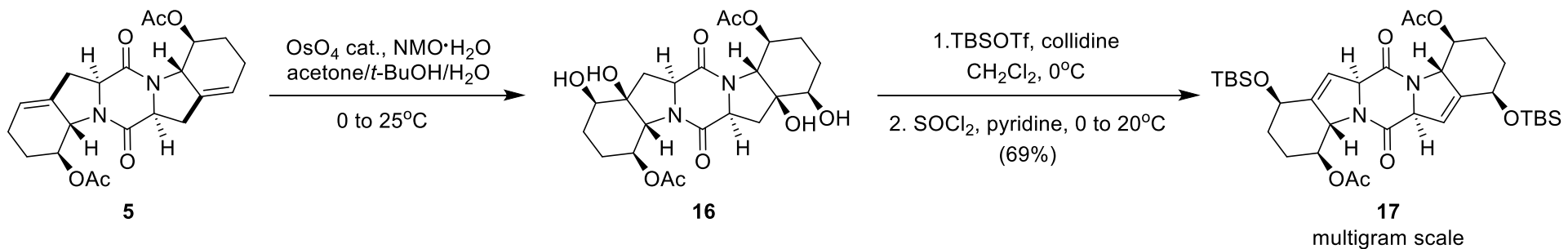
## Sulfuration:



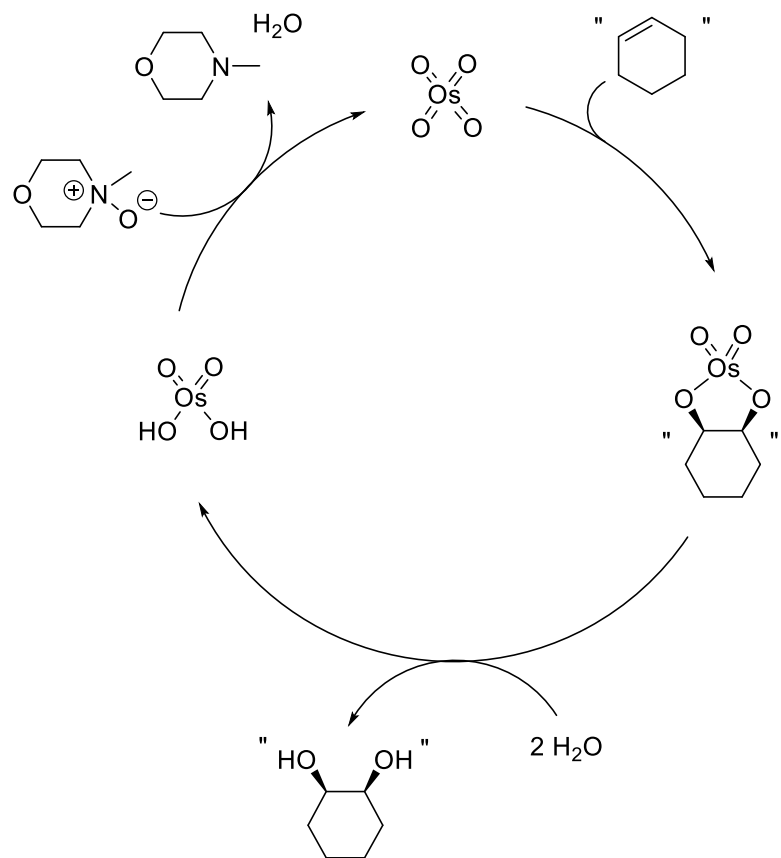
## Iodine mediated cleavage:



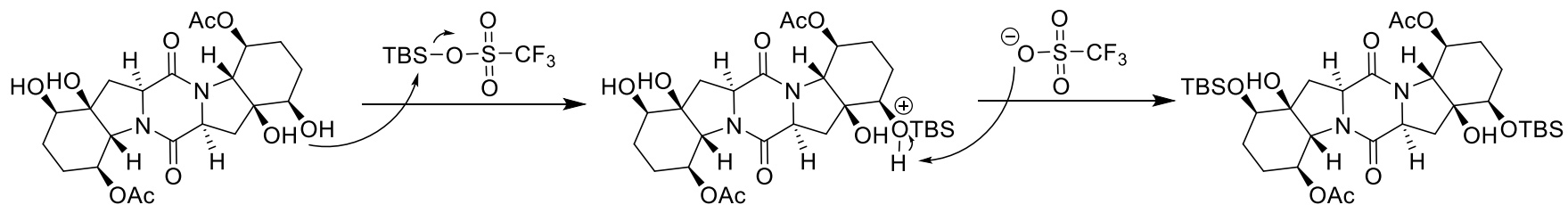




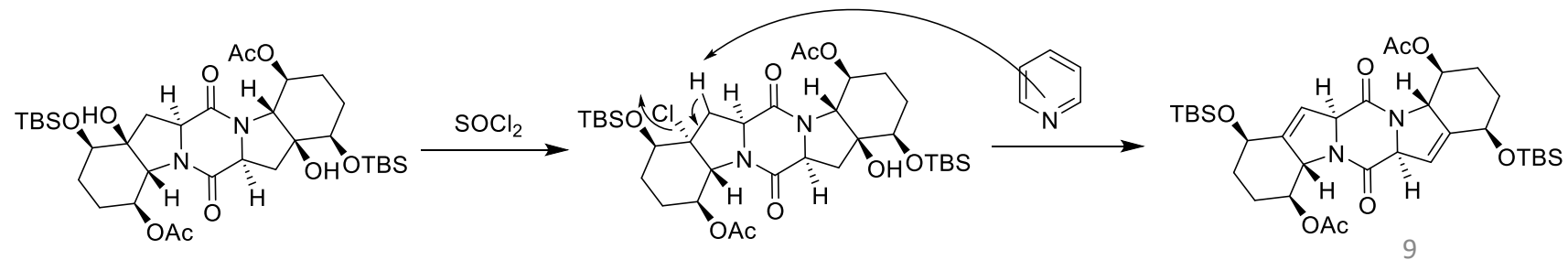
### Upjohn dihydroxylation:

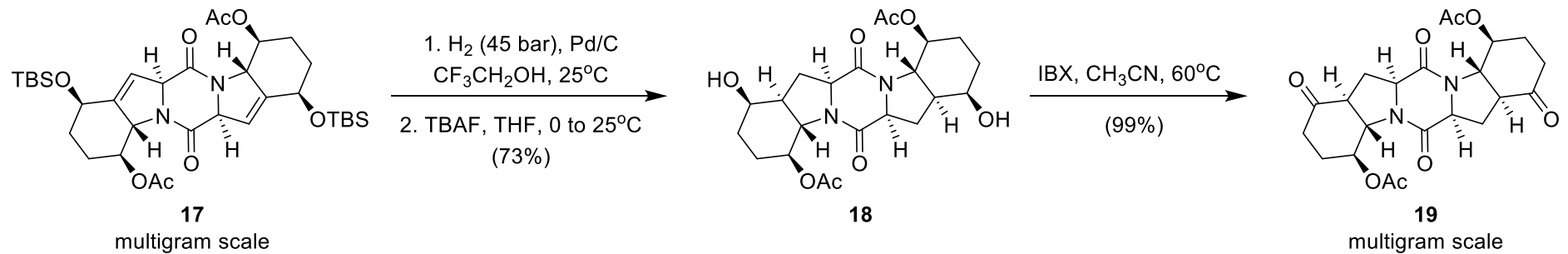


### TBS Protection:

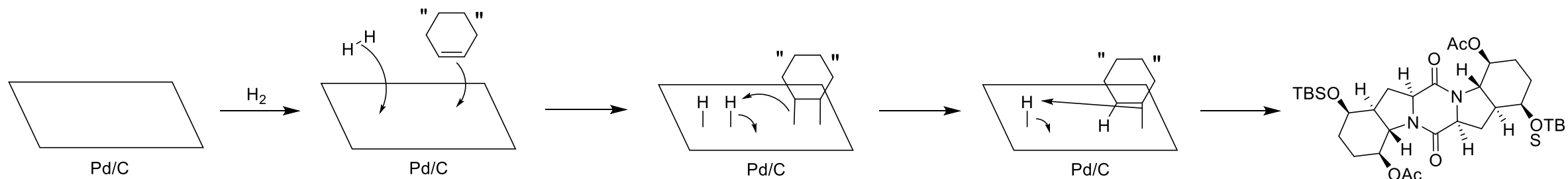


### Elimination:

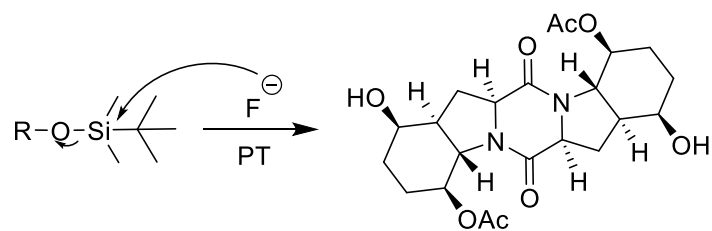




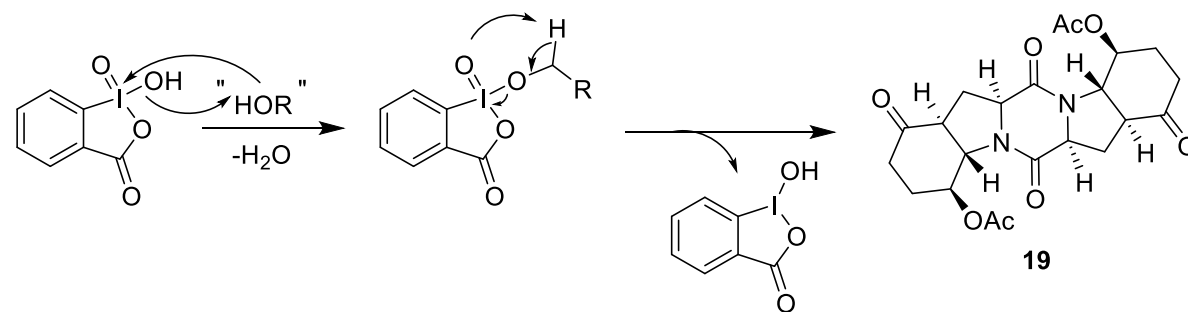
## Hydrogenation:

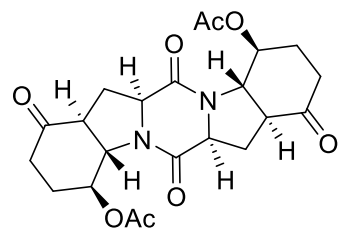


## Deprotection of the TBS group:

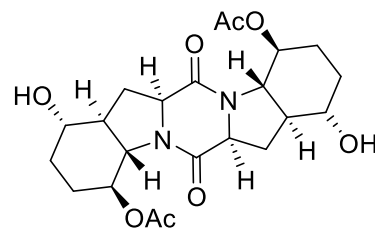
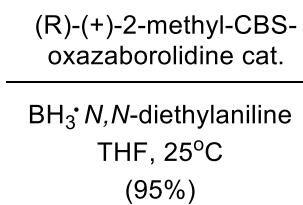


## IBX Oxidation:

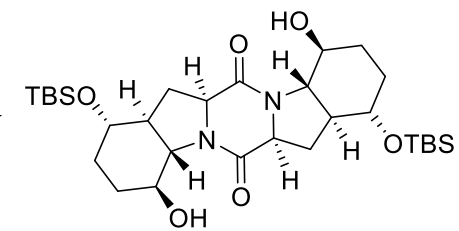
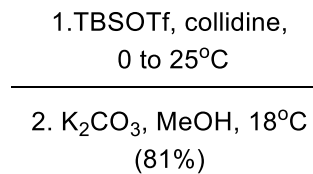




**19**  
multigram scale

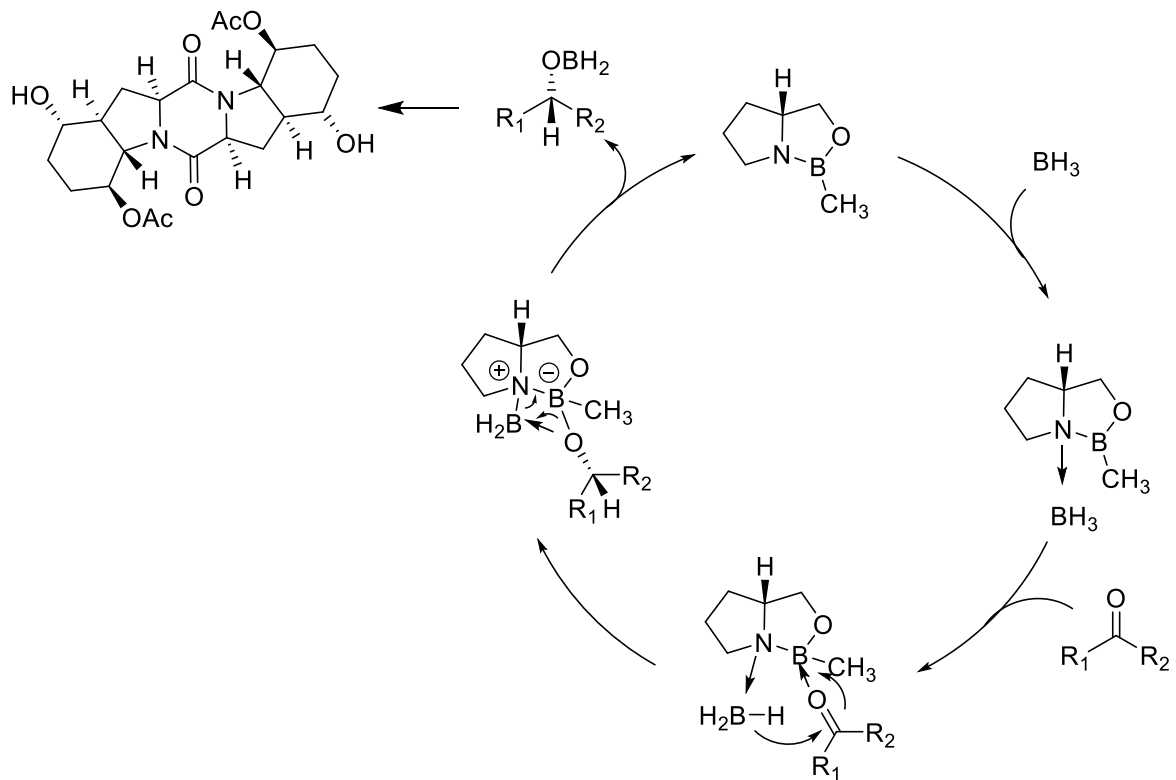


**21**

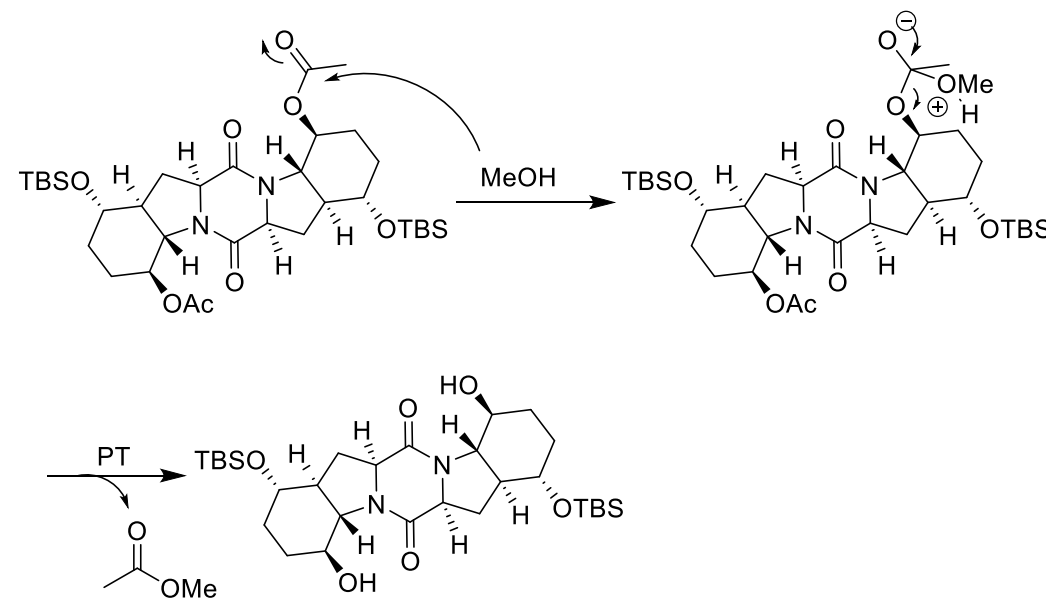


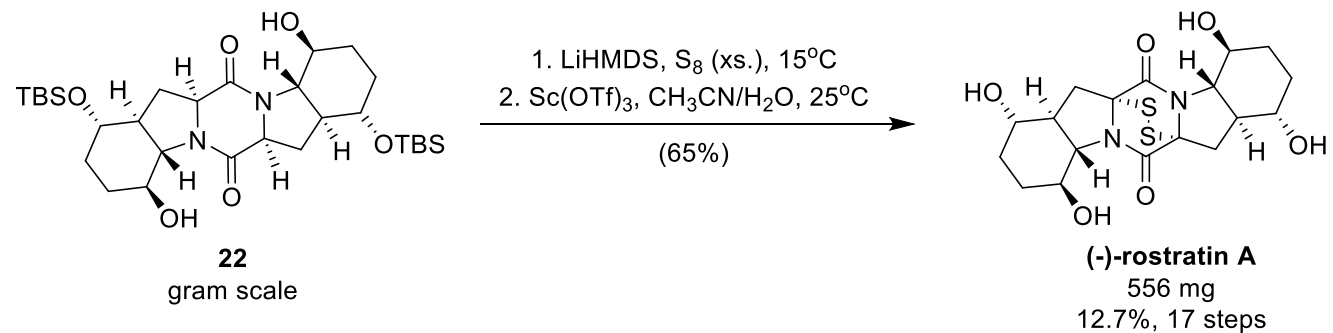
**22**  
gram scale

### CBS Reduction:

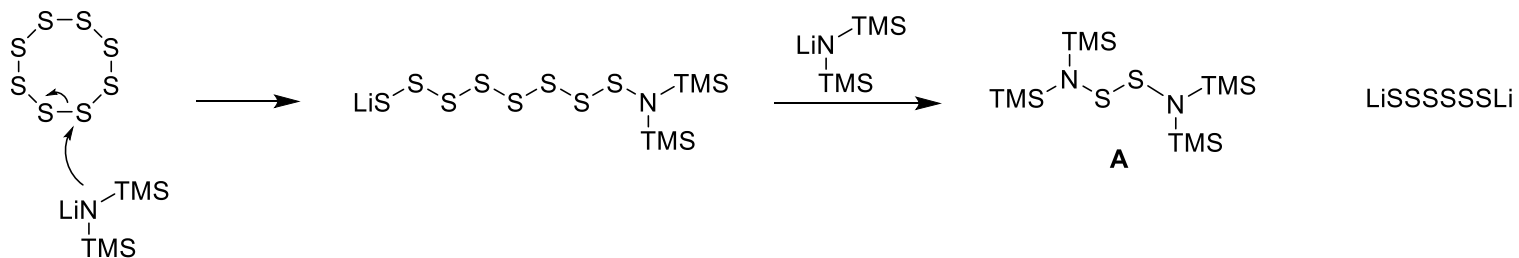


### Deacylation:

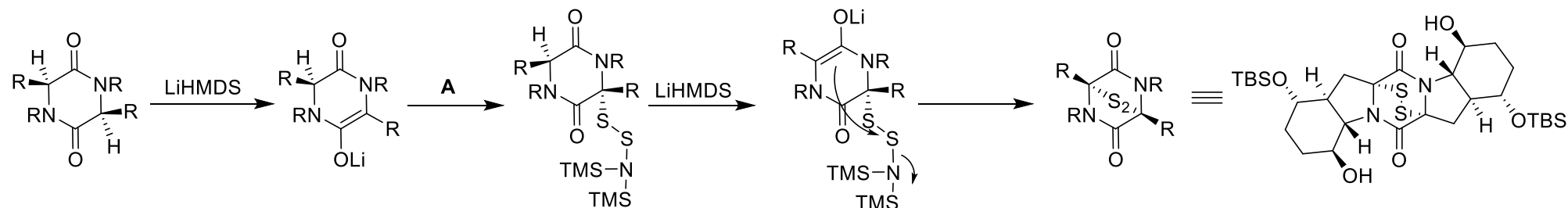




### Preparation of A:



### Sulfuration:



### Scandium triflate-mediated deprotection:

