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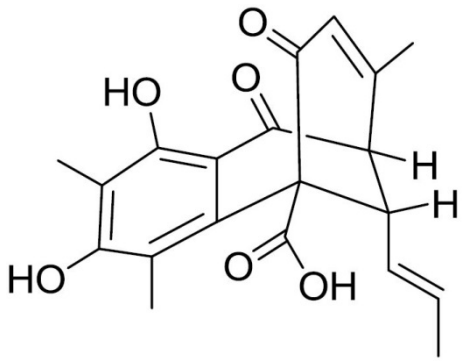


Total Synthesis and Stereochemical Assignment of (±)-Sorbiterrin A

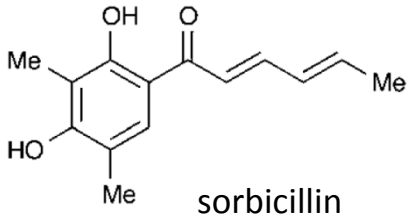
Qi, C; Qin, T; Suzuki, D; Porco Jr, J. A. *J. Am. Chem. Soc*. **2014**, ASAP

Nicolas Volkoff
06/03/13

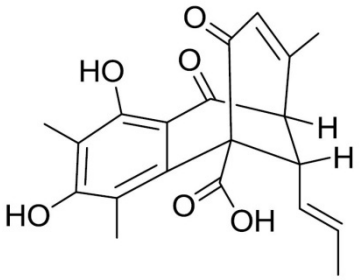
Introduction

Sorbiterrin A:

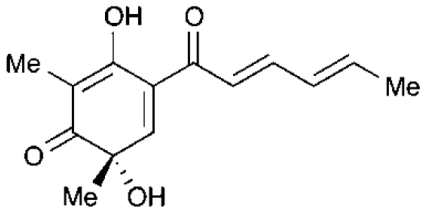
- Sorbicillinoid family
- Isolated in 2011
- Acetylcholinesterase inhibitory activity
- [3.3.1] ring system



sorbicillin



sorbiterrin A

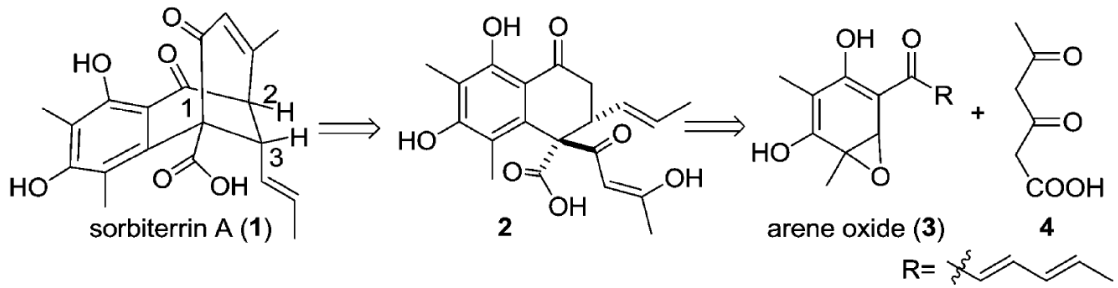


sorbicillinol

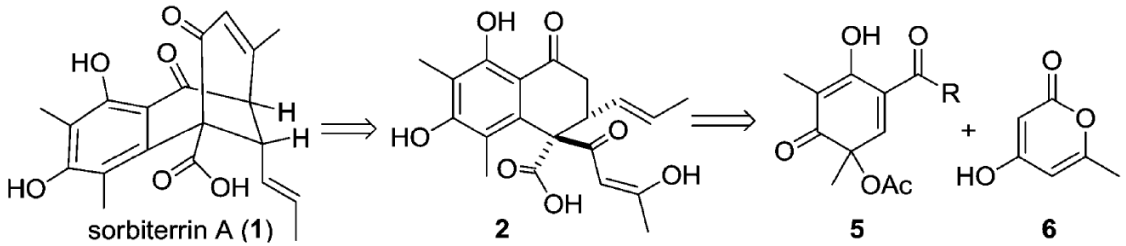
Harned, A. M.; Volp, K. A. *Natural Product Reports* **2011**, *28*, 1790.
Chen, L.; Zhu, T.; Ding, Y.; Khan, I. A.; Gu, Q.; Li, D. *Tetrahedron Lett.* **2012**, *53*, 325.

Introduction

- Biosynthetic pathway :



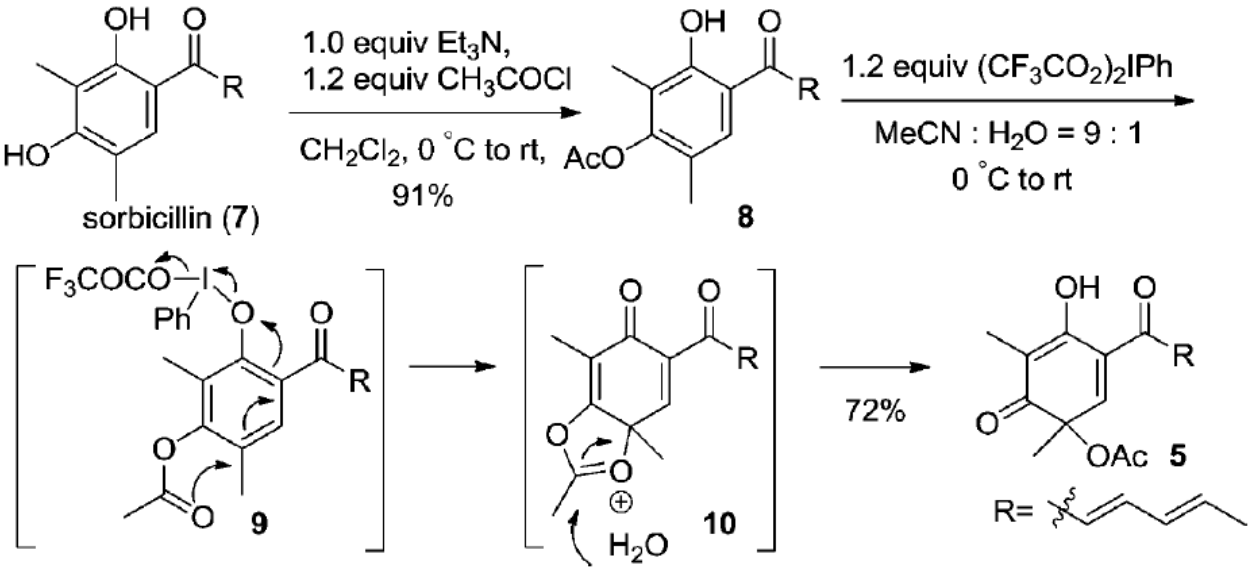
- Biomimetic synthesis



Chen, L.; Zhu, T.; Ding, Y.; Khan, I. A.; Gu, Q.; Li, D. *Tetrahedron Lett.* **2012**, *53*, 325.

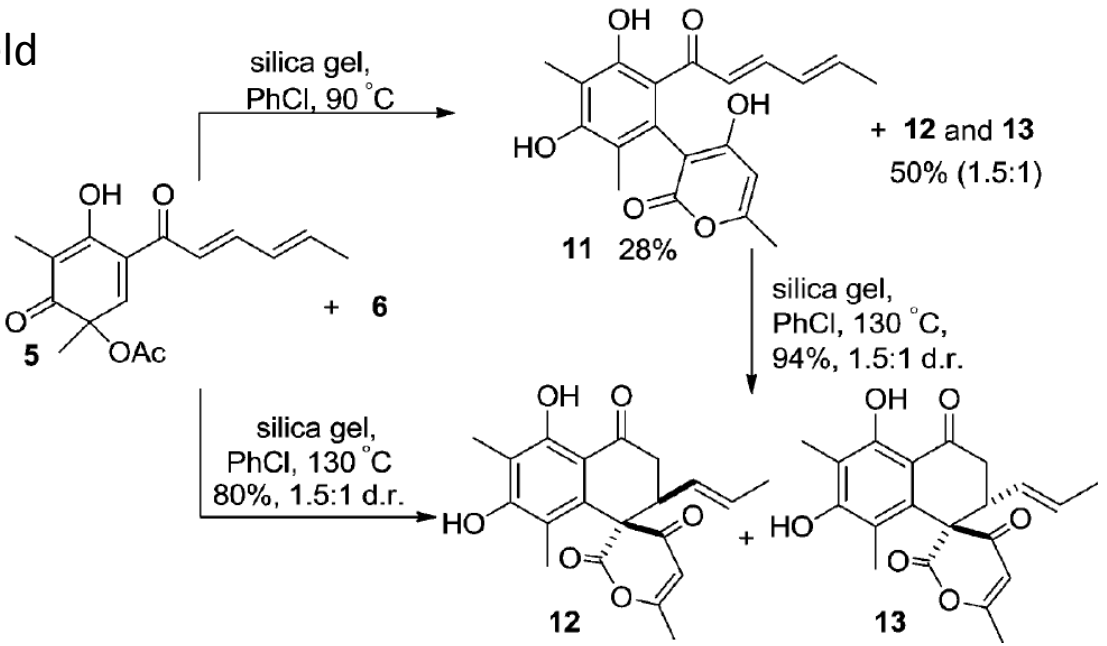
Biomimetic Synthesis

- Preparation of the acetoxy sorbicillinol **5** starting from sorbicillin **7**



Quaternary center's formation

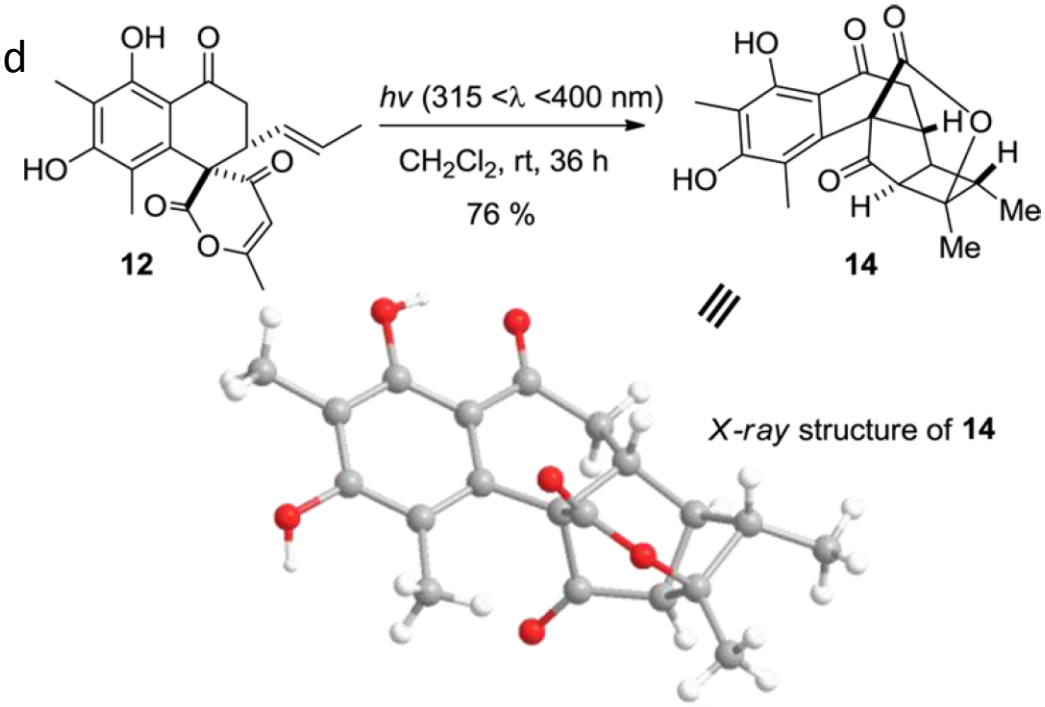
- Basic conditions : degradation
- Lewis acids : decomposition or traces amount of **11**
- Silica gel : 80% yield



Stereochimical assignment

[2 + 2] Photocycloaddition :

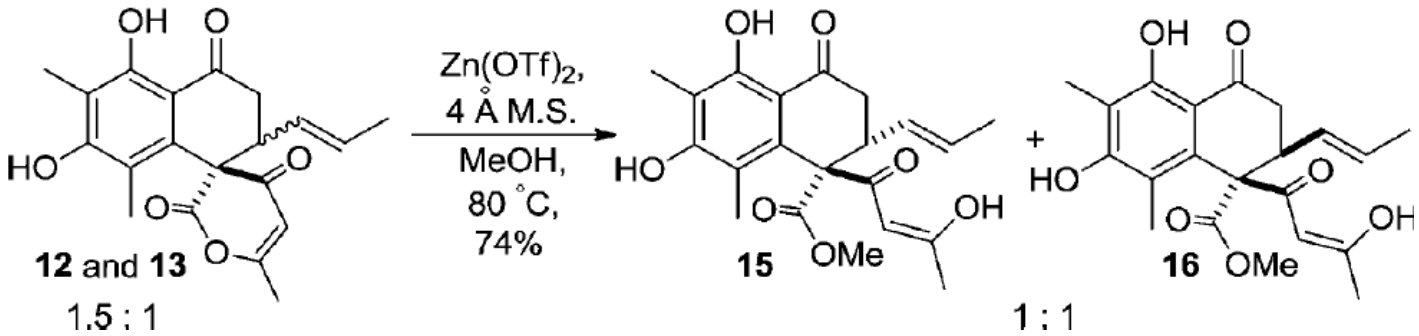
- Possible for **12** but not for **13** due to spatial arrangement
- One diastereoisomer converted



Transesterification

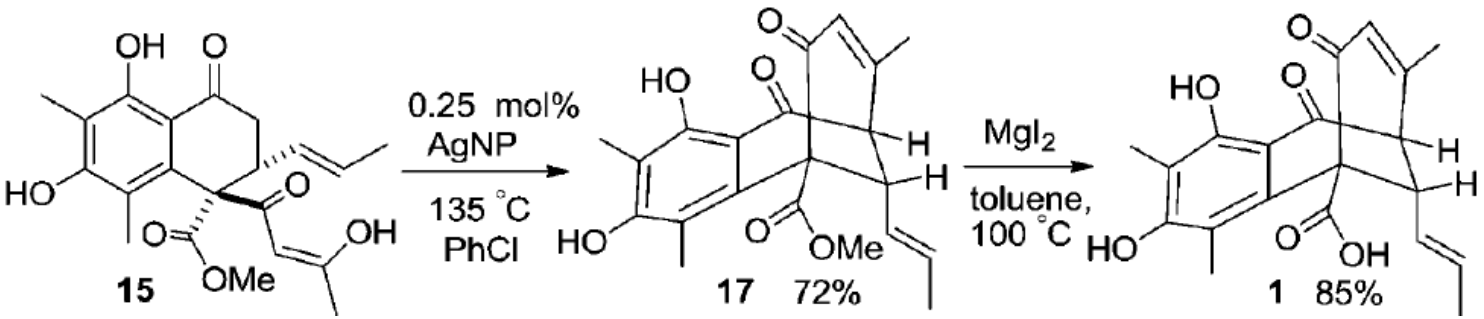
- Hydrolysis using acids or bases : degradation
- Transesterification using lewis acid in methanol : epimerization
  dichloroethane : no reaction

→ Reaction with the mixture of **12** and **13**



[3.3.1] ring system formation

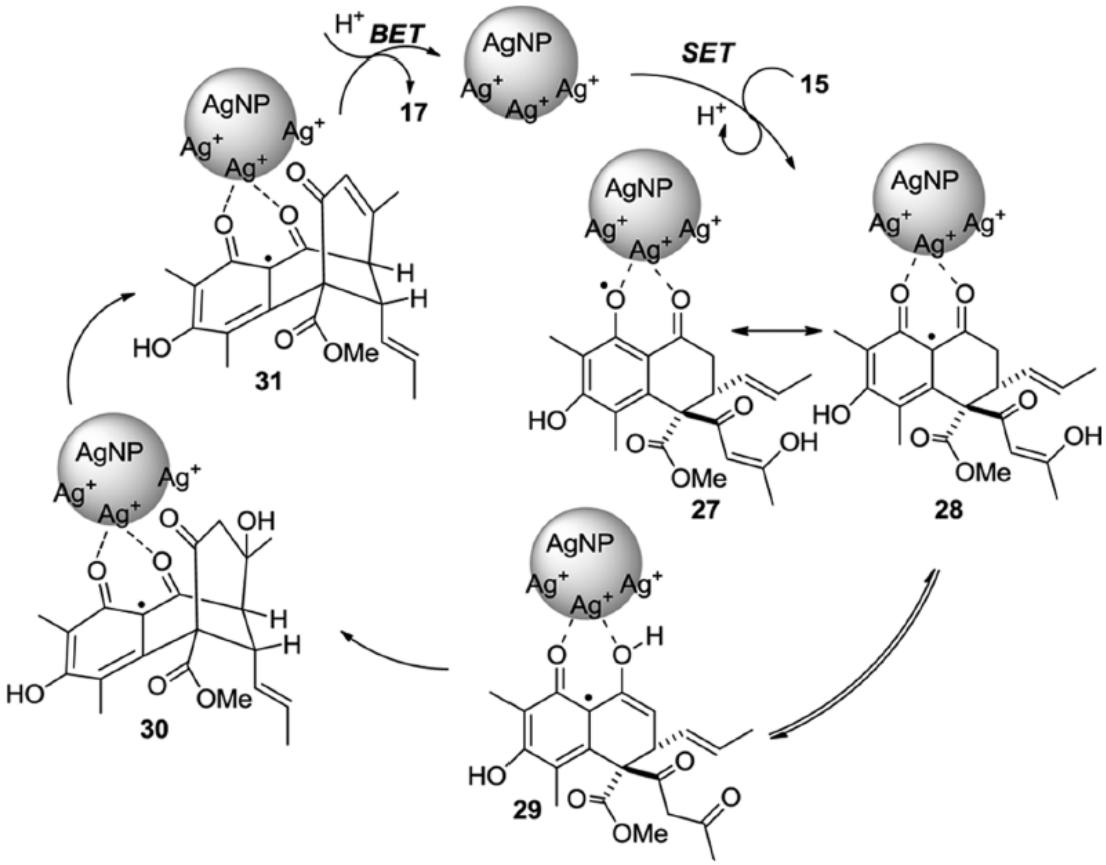
- Bronsted and Lewis acids : degradation or no reaction
- Silica-supported silver nanoparticles (AgNP's) : 72% yield



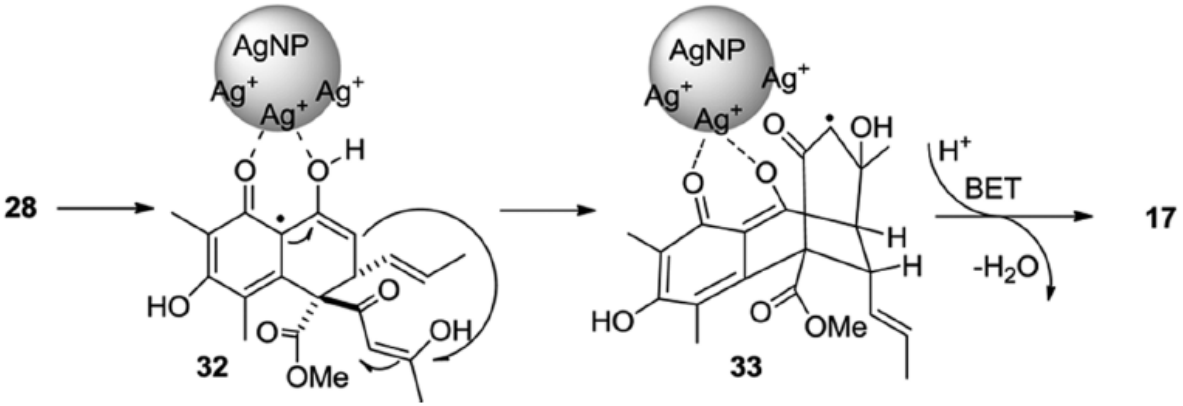
sorbiterrin A

Proposed mechanism

- Radical intermediate observed by EPR measurments

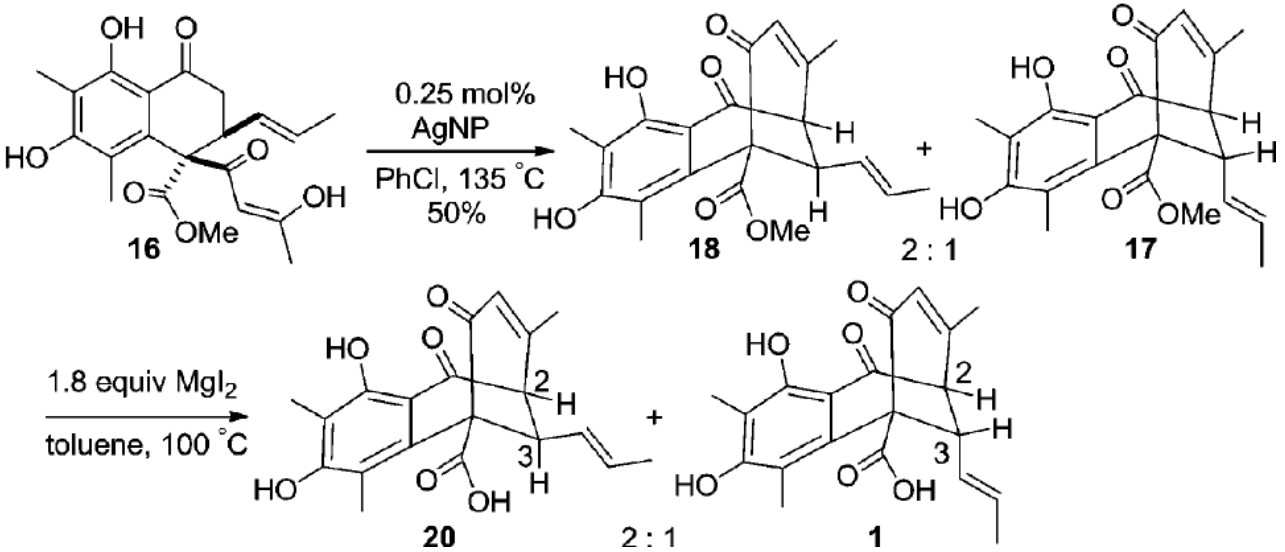


Proposed mechanism



[3.3.1] ring system formation

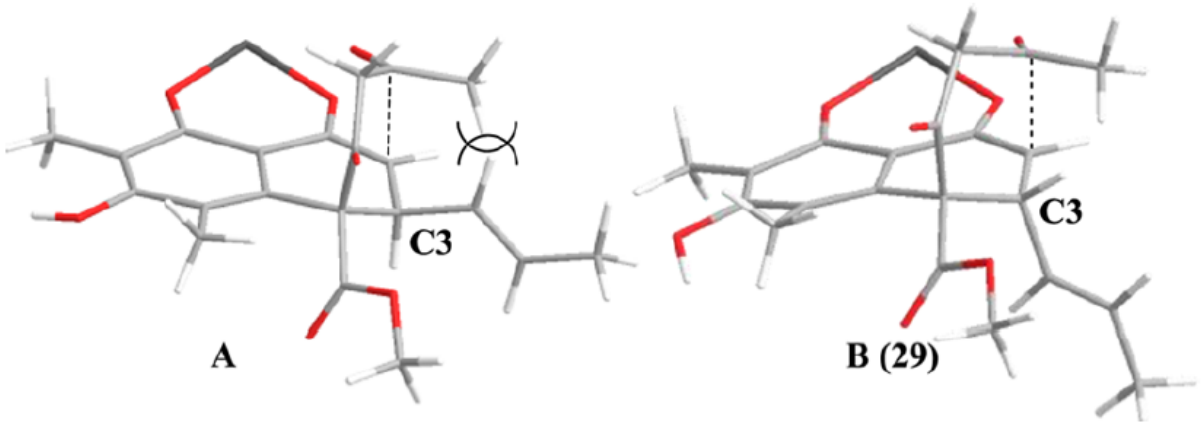
- Synthesis of 3-*epi*-Sorbiterrin A from the diastereoisomer **16**



3-*epi*-sorbiterrin A sorbiterrin A

C3 epimerization

- 1,3-diaxial interaction between the propenyl and the methyl ketone
- Epimerization may occur by retro-Michael/Michael addition



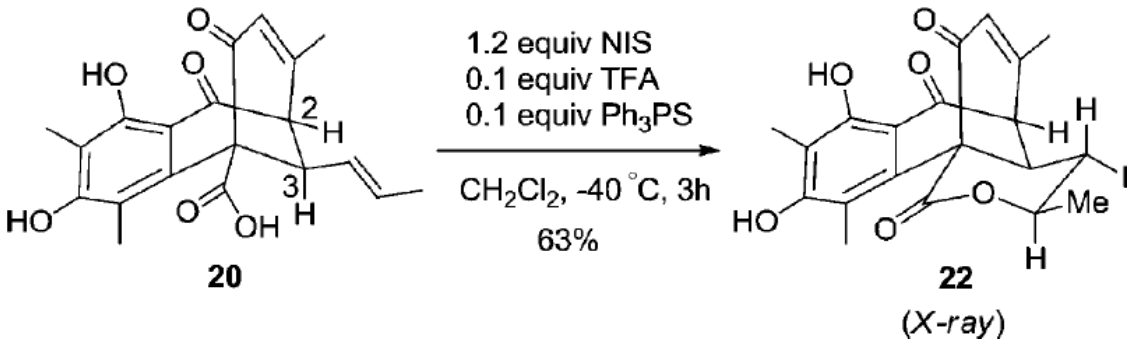
16 → 18

15 → 17

Stereochemical assignment

- Sorbiterrin A and 3-*epi*-sorbiterrin A form the corresponding Iodolactonization product

- Only **22** form a crystal



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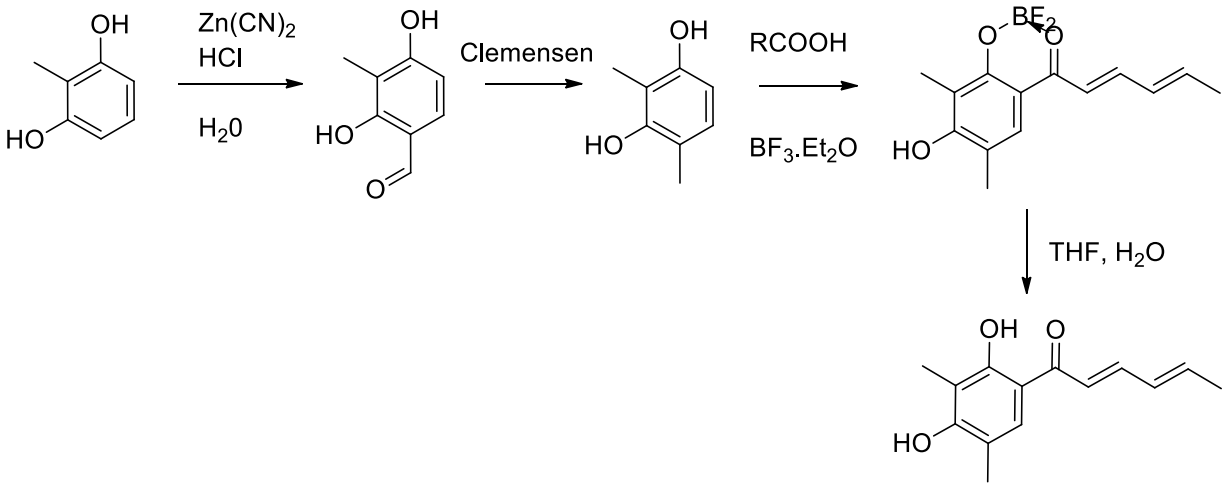
Conclusion

- Biomimetic synthesis of the bicyclo [3.3.1] natural product : Sorbiterrin A
- Quaternary carbon center formed by consecutive Michael additions
- Cyclisation using AgNP-catalyzed bridged aldol condensation
- Mechanistic studies by EPR to show the involvement of radical intermediates

Sorbicillin Synthesis



Michael additions mechanism