

# Synthesis of Fijiolide A via an Atropselective Paracyclophane Formation

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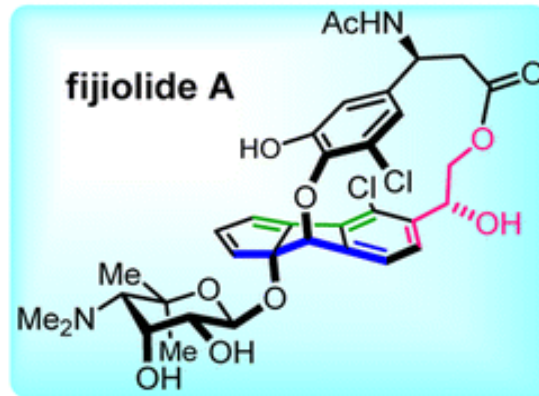
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Group Reanud Meeting-Journal Club-October 2015

Camilo Meléndez

# Fijiolide A

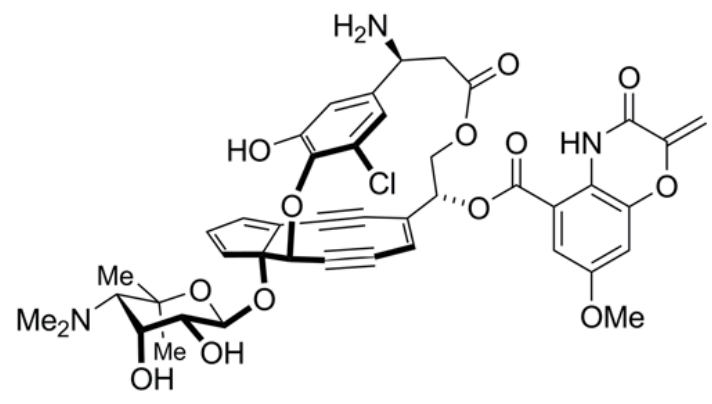


Isolated from marine bacterium of the genus *Nocardopsis*.

Potent inhibitor of NFκB factor activation

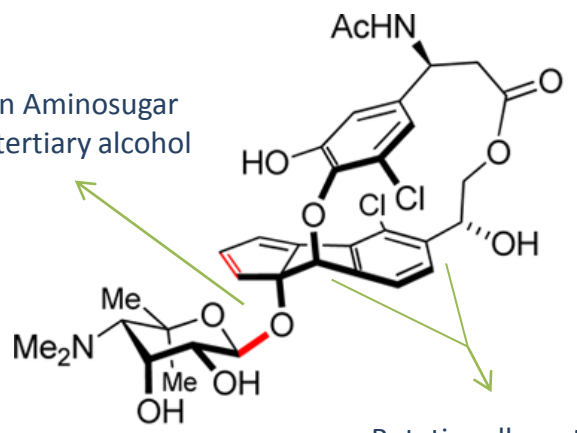
Among the new 2500 metabolites with antiproliferative activity

# Initial Considerations



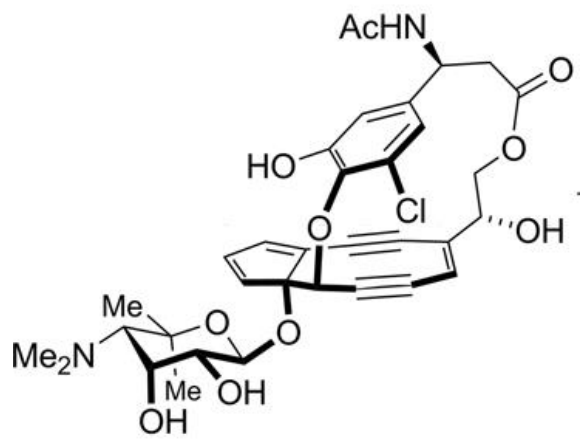
C-1027

Insertion of an Aminosugar  
At a hindered tertiary alcohol



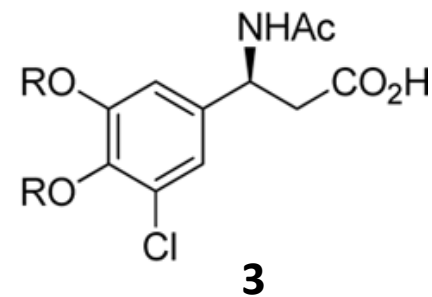
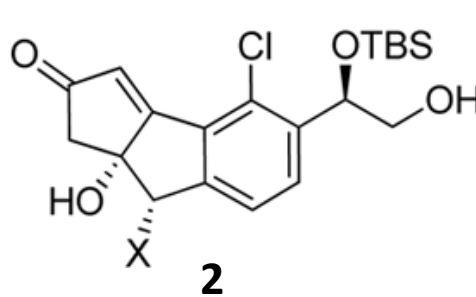
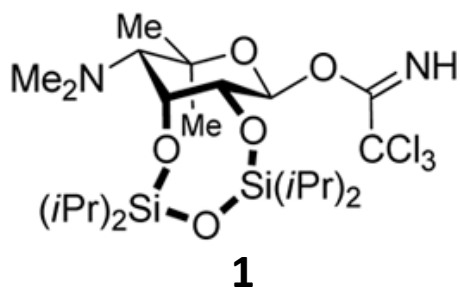
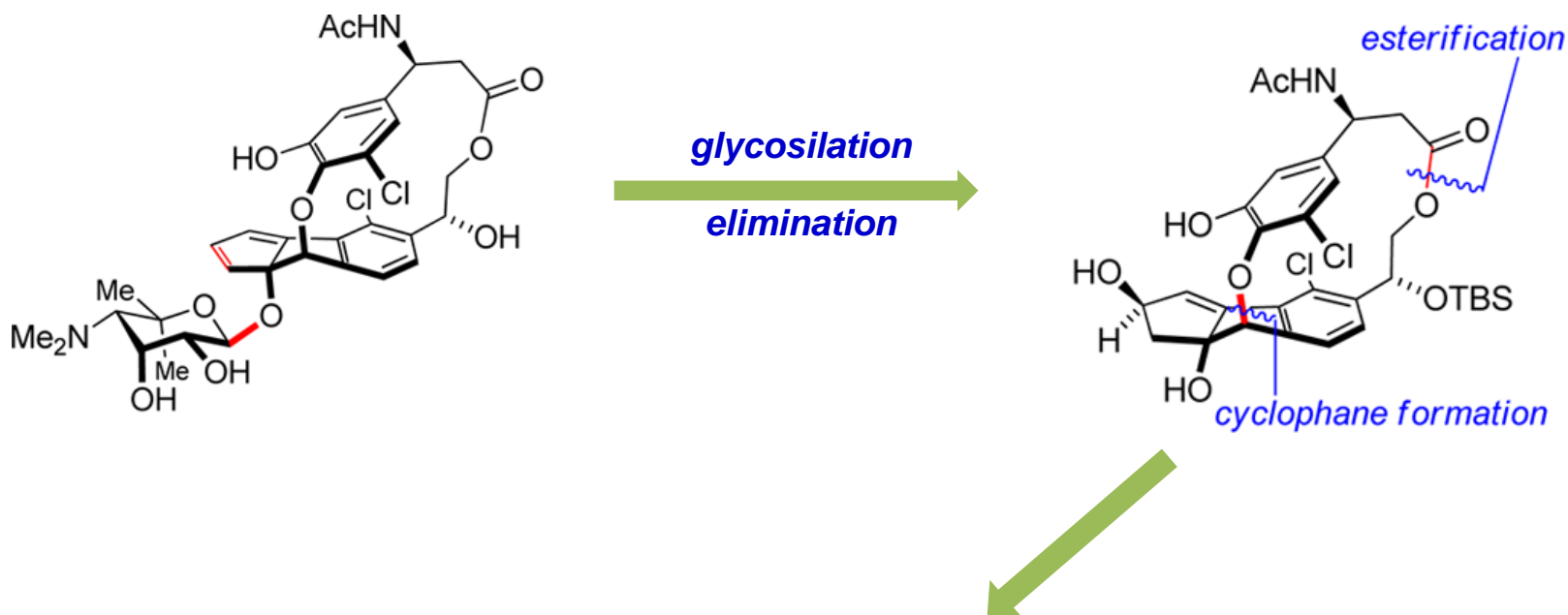
Rotationally restricted  
[2.6]paracyclophane

Common Biosynthetic Origin

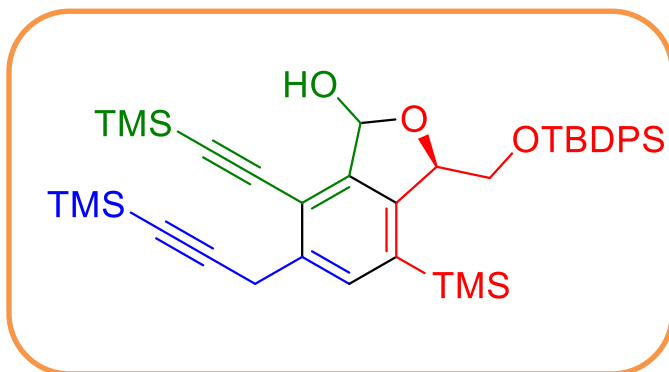
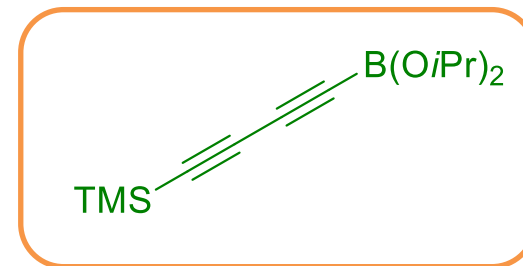
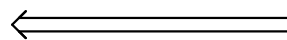
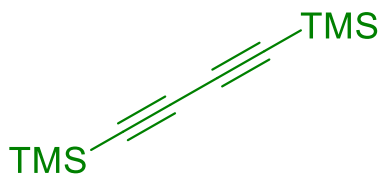


Bergman Cyclization

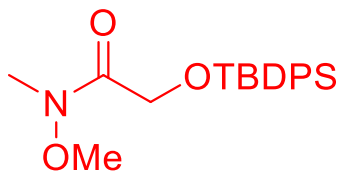
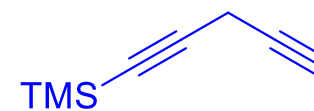
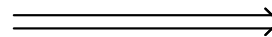
# Retrosynthetic Analysis



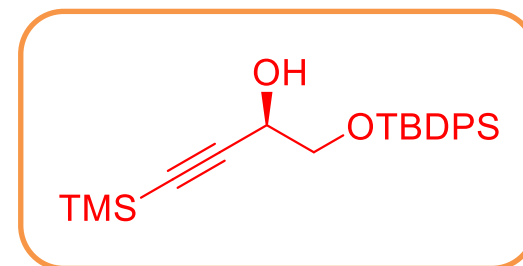
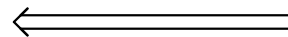
# Retrosynthetic Analysis - Fragment 2

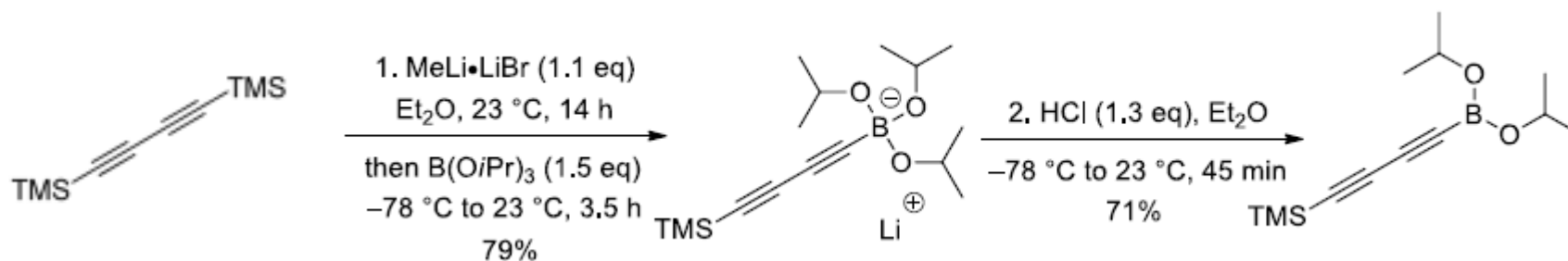
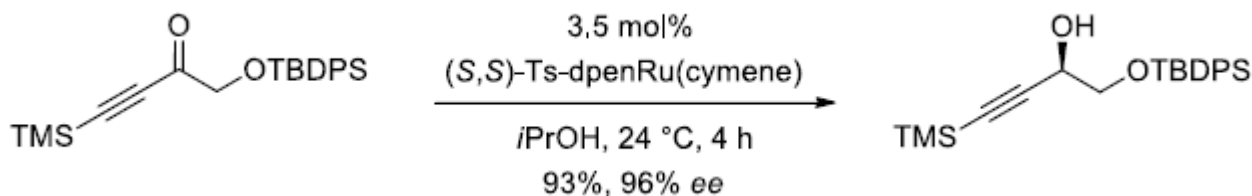
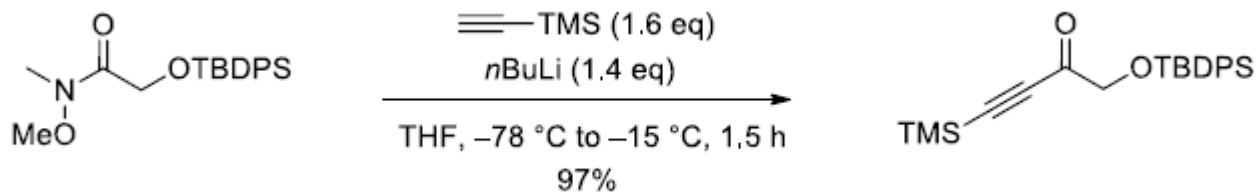


[2,2,2]-Cyclotrimerization

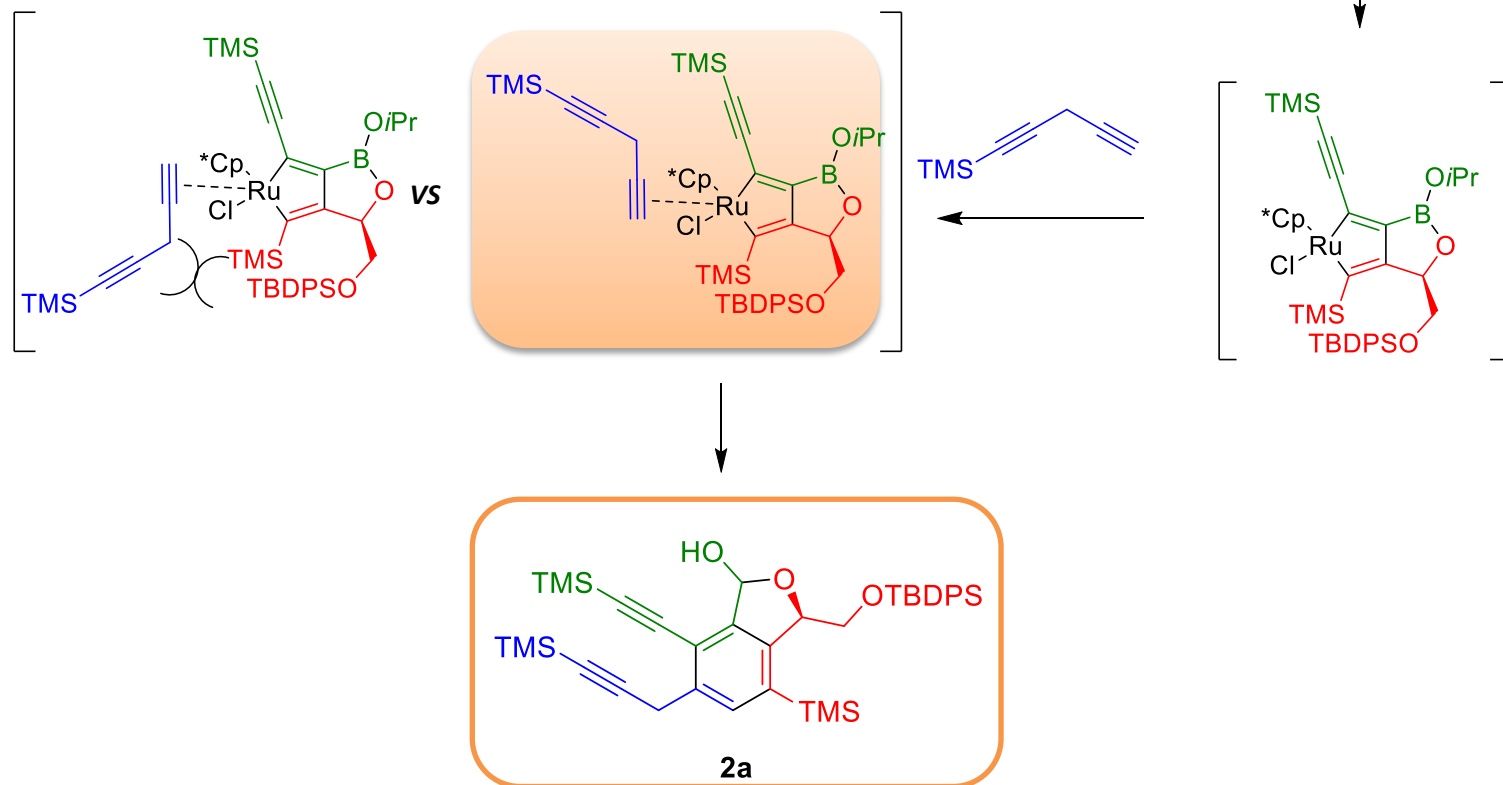
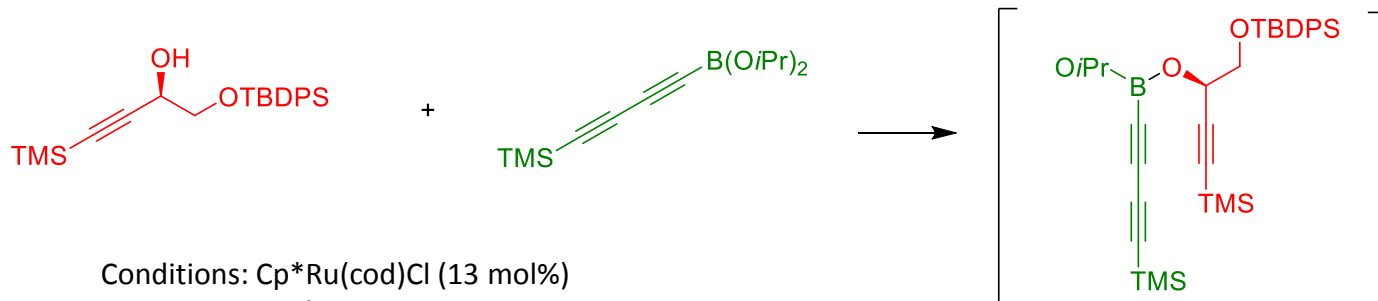


+

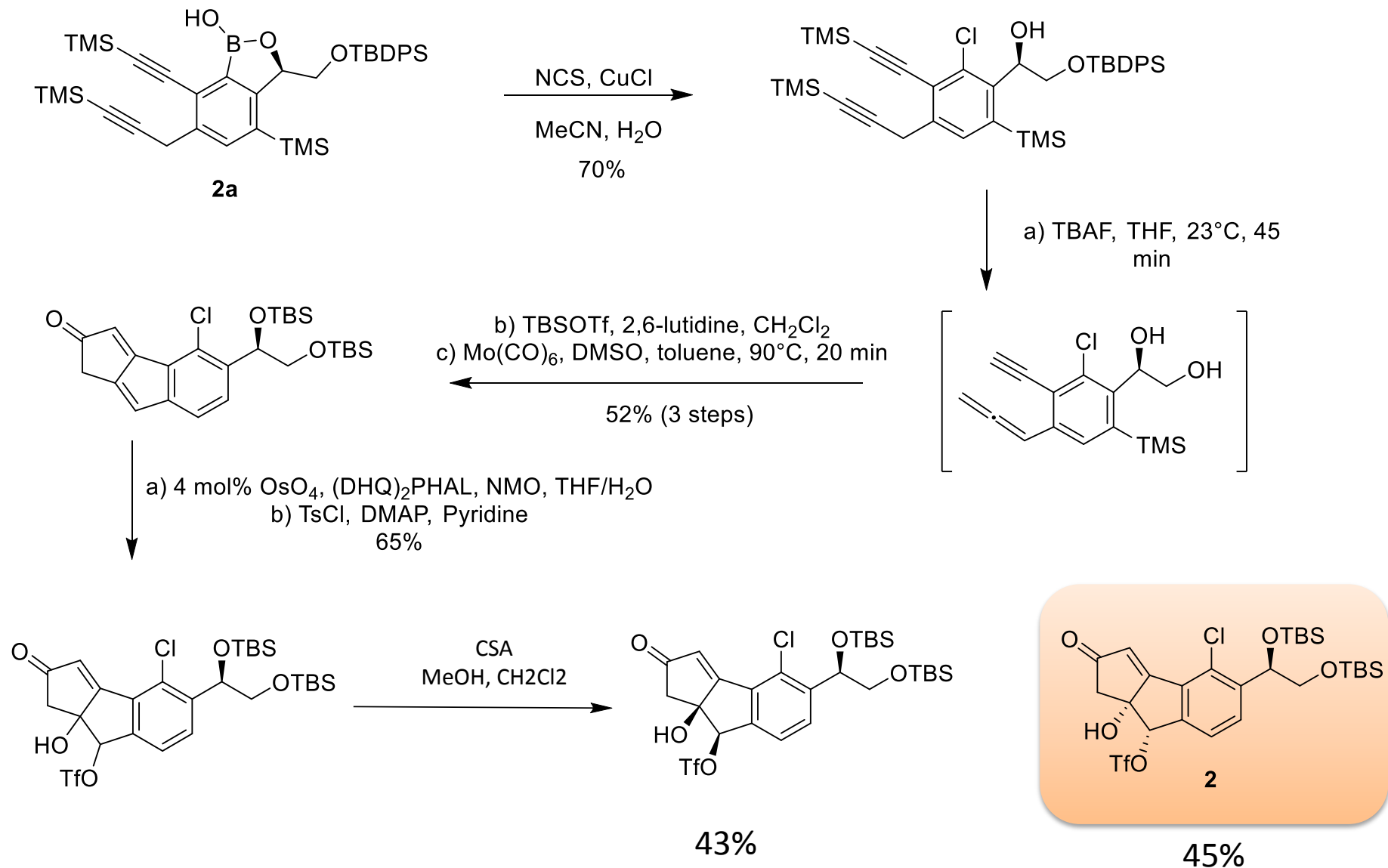




# Synthesis of fragment 2a

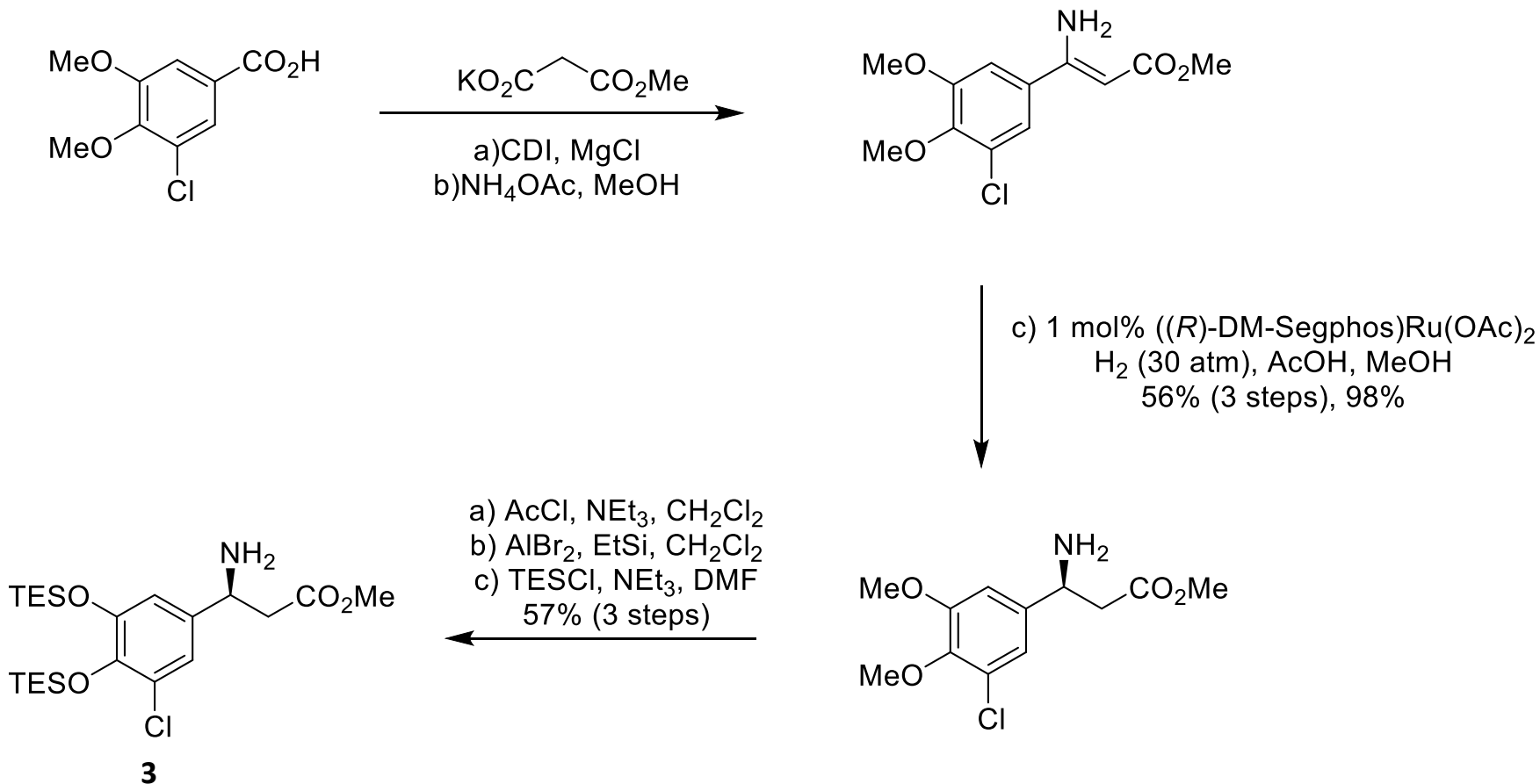


# Synthesis of fragment 2

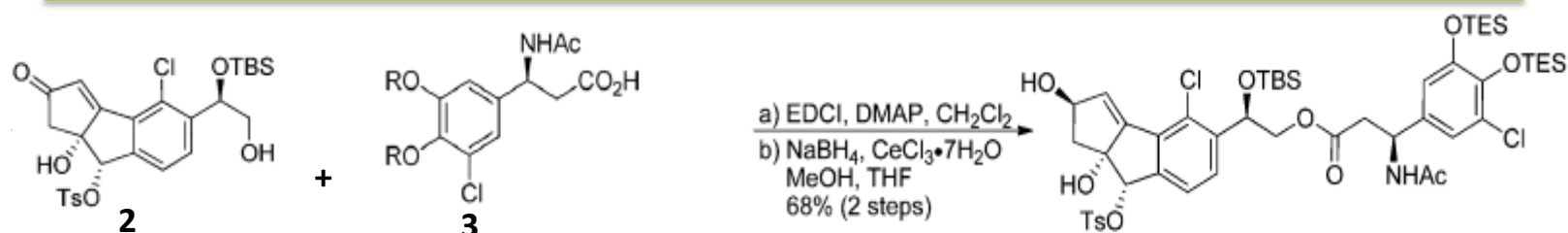




# Synthesis of fragment 3

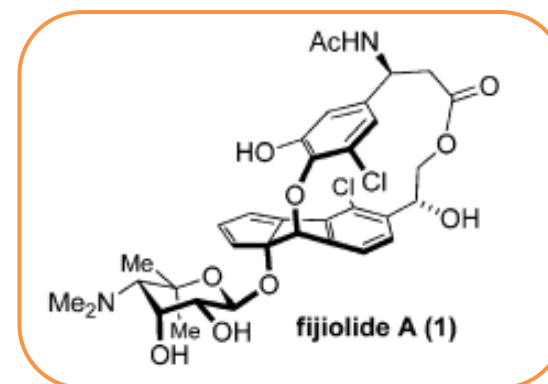
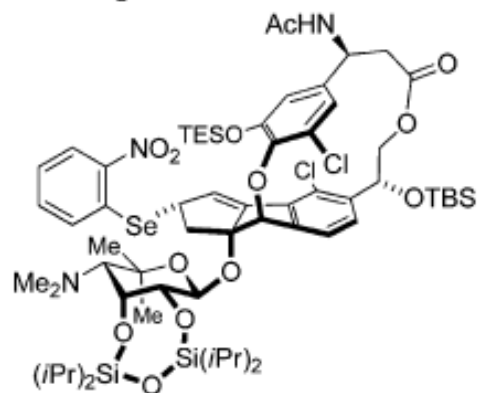
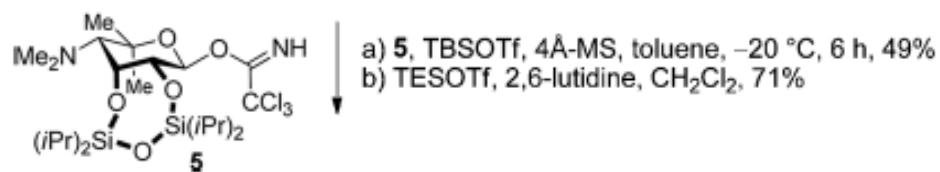


# Fragment Assembly and completion of the Synthesis



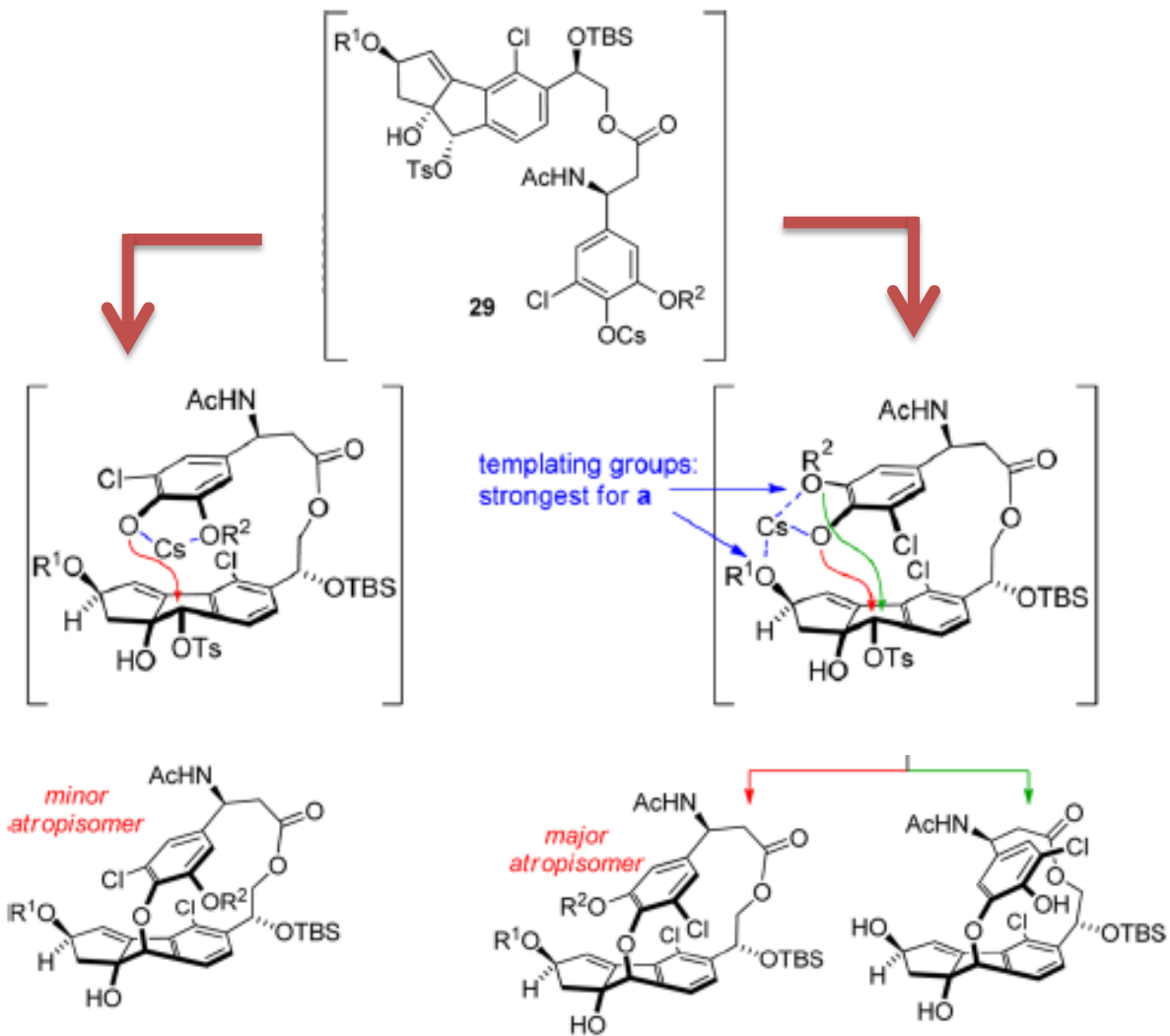
60%
   
 CsF, 4Å-MS
   
 DMF, 100 °C

$\xleftarrow[\text{PBU}_3, \text{THF}, -78^\circ\text{C}]{o\text{-NO}_2\text{PhSeCN}}$ 
  
 93%



# Atrop- and Regioselectivity

a ( $R^1 = H, R^2 = TES$ )  
b ( $R^1 = H, R^2 = Me$ )



# Conclusion

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- First enantioselective total synthesis reported
- 36 total steps (including 11 for the preparation of glycosyl donor)
  - 18 steps in the longest linear sequence
- Potential use of ruthenium-catalyzed cyclopolymerizations for the construction of heavily substituted arenes
  - Atroposelectivity in the construction of cyclophanes

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**THANK YOU**

