# Total Synthesis of (+)-Dendrowardol C

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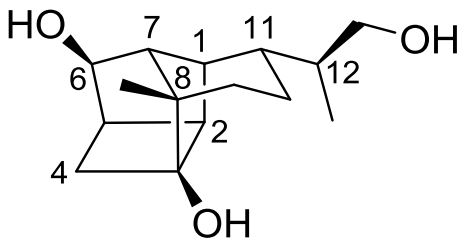
Current Literature 08/05/17
Wipf Group

# (+)-Dendrowardol C

- Isolated from *Dendrobium wardianum* Warner
  - An orchid endemic to southern China and Southeast Asia.
  - No cytotoxicity against human cancer cell lines HL-60, SMMC-7221, A-549, MCF-7, and SW480.

- Sesquiterpenoid with unprecedented tetracyclic caged system with 9 contiguous stereogenic centers.

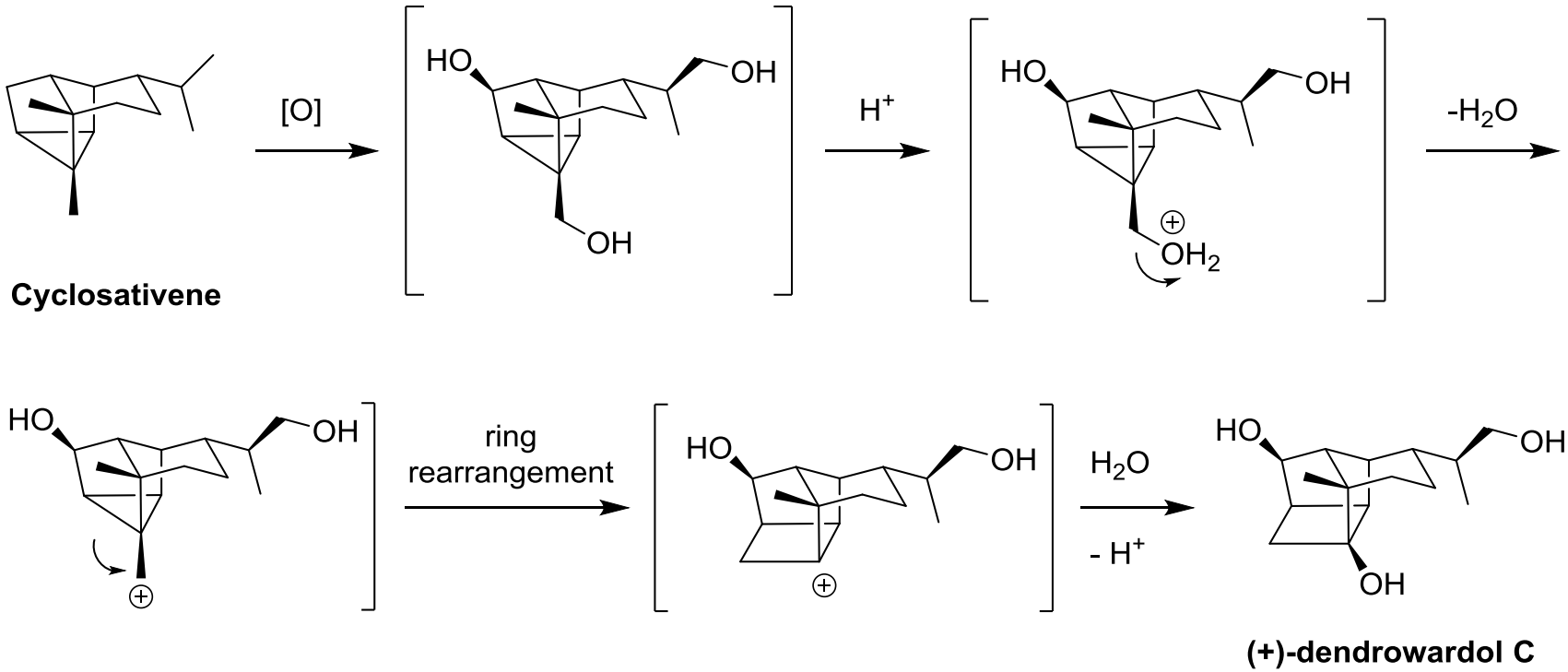



**(+)-dendrowardol C**

http://www.orchidspecies.com/denwardii.htm

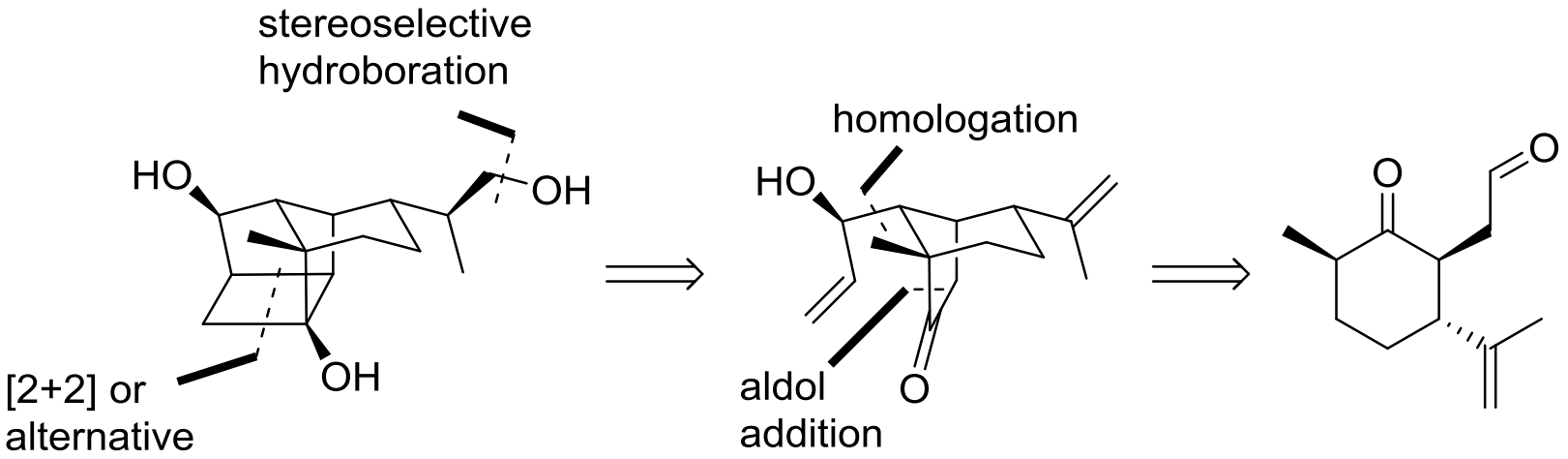
*Nat. Prod. Bioprospect.* **2013**, *3*, 89.
*Angew. Chem. Int. Ed.* **2017**, *56*, DOI: 10.1002/anie.201705809.

# Plausible Biogenetic pathway of (+)-Dendrowardol C




*Nat. Prod. Bioprospect.* **2013**, *3*, 89.

# Retrosynthetic Approach




**(+)-dendrowardol C**



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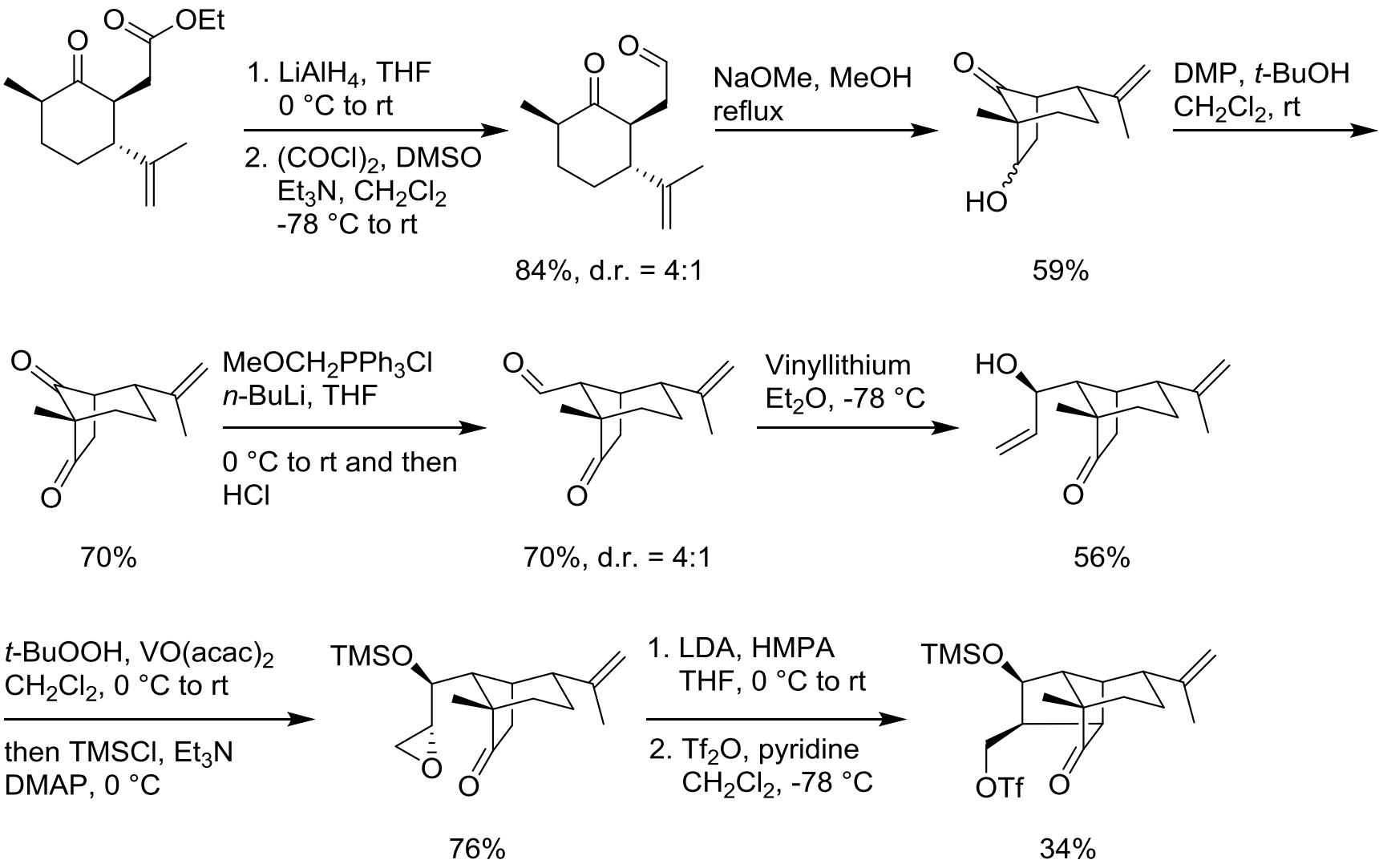
# Synthesis of (+)-Dendrowardol C

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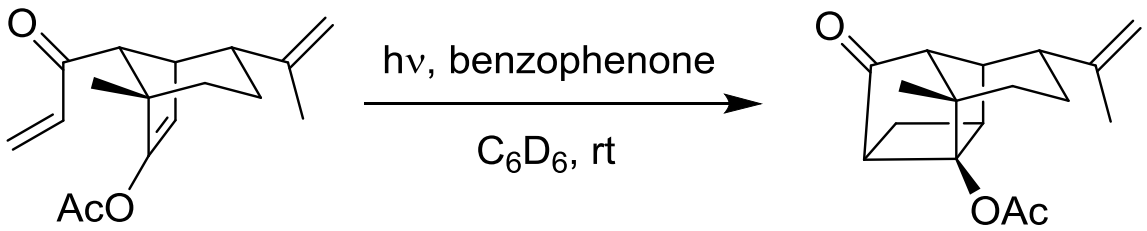
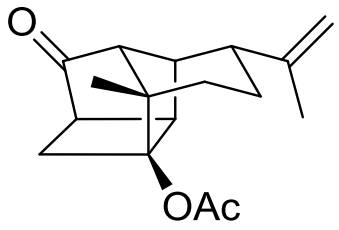
# [2+2] Gives Undesired Product




20%




desired product



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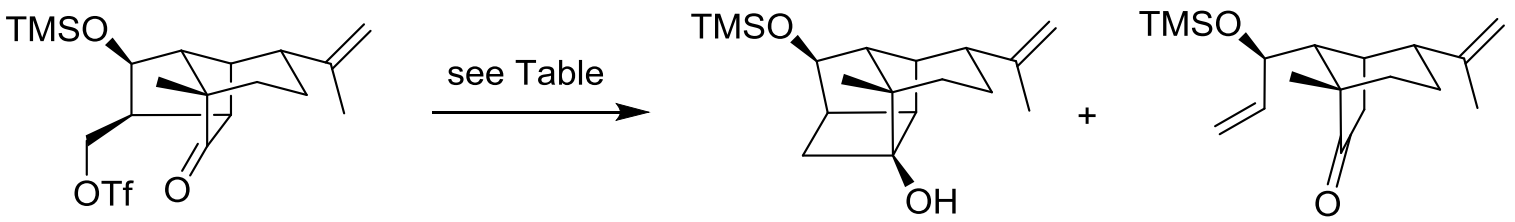
# Optimization of Ring Closure Reaction




**A** **B**

| entry | reductant | solvent | *T* [°C] | A/B | yield B |
|---|---|---|---|---|---|
| 1 | LiNp | THF | -78 | 37:63 | 16% |
| 2 | LiBp | THF | -78 | 19:81 | n.d. |
| 3 | NaNp | THF | -78 | **B** | n.d. |
| 4 | LiNp | THF/benzene (1:10) | 10 | 53:47 | 27% |
| 5 | LiNP | 2-MeTHF/benzene (1:10) | 10 | 46:54 | 40% |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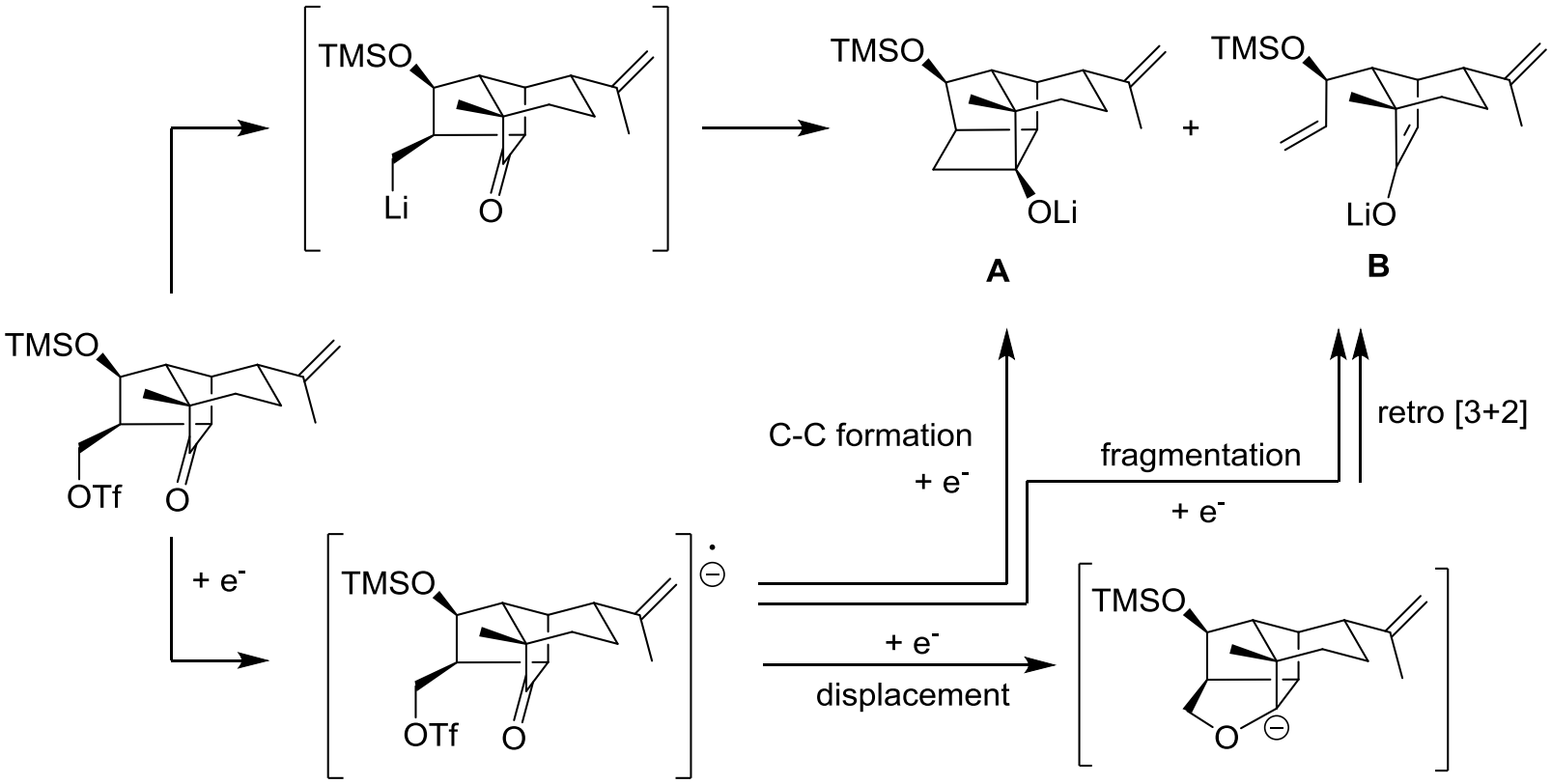
# Potential Pathways towards A and B



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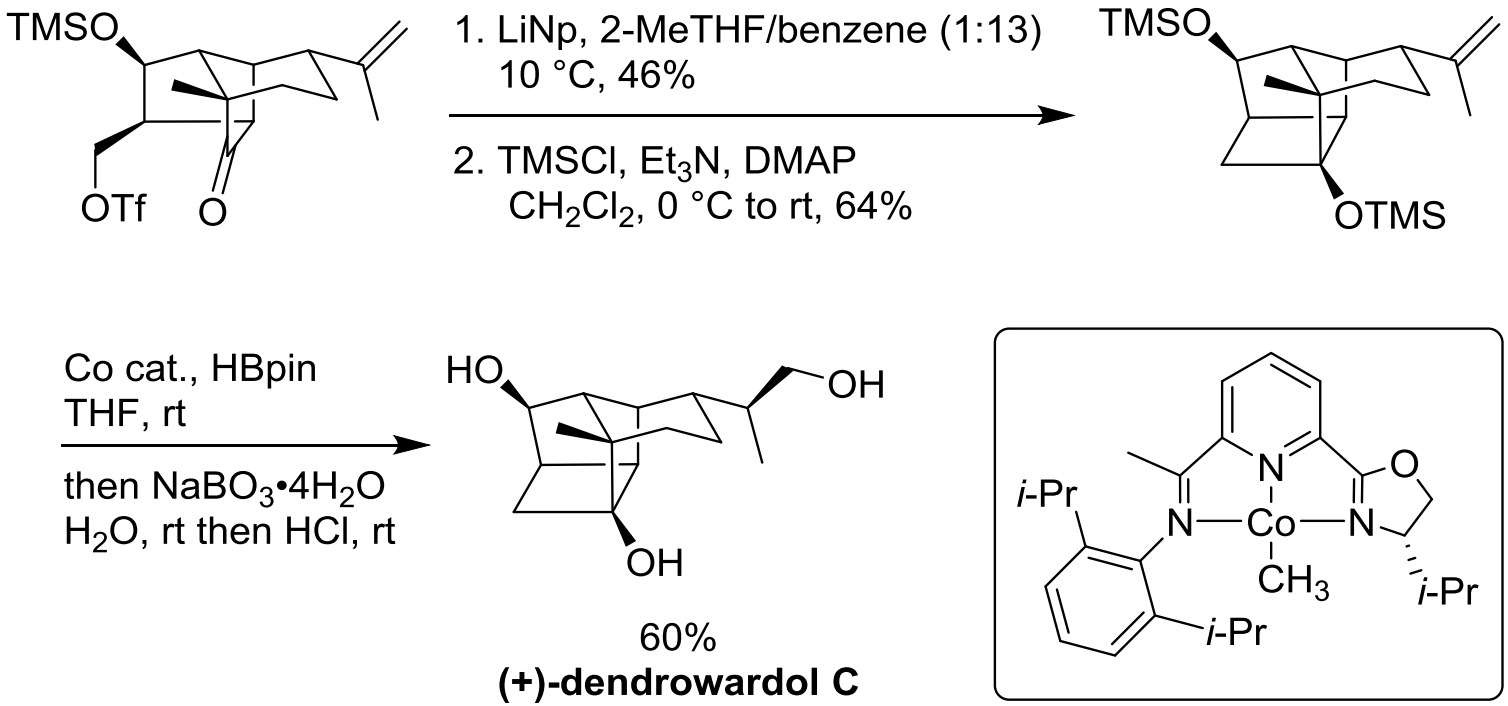
# Synthesis of (+)-Dendrowardol C cont'd





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# Conclusions

- A concise synthesis of (+)-Dendrowardol C
- Features a late-stage cyclobutane formation via a cyclization of a γ-triflyloxy ketone
- Diastereoselective hydroboration in the last step.

- Future Outlooks:
  - Many low yielding steps
    - The key cyclization generates more of the undesired product than the desired product.
  - Biological utility of this class of compounds remains unknown,