

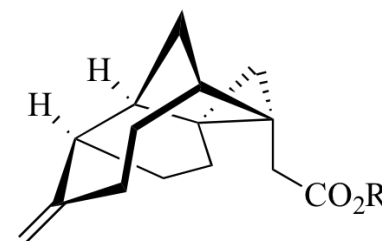
Total Synthesis of Echinopines A and B

K. C. Nicolaou, Hanfeng Ding, Jean-
Alexandre Richard, and David Y.-K. Chen
JACS, ASAP, DOI: [10.1021/ja9093988](https://doi.org/10.1021/ja9093988)

Gary Davis Current Literature 3-6-2010

Isolation

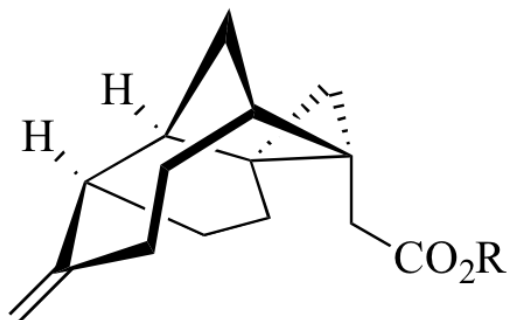
- Isolated from genus *Echinops* (Compositae) ~100 species worldwide.
- Used as medicinal herbs worldwide.
- Two novel sesquiterpenoids were isolated in 2008 from *E. spinosus*-Morocco.
- From 3 Kg of root: 2 mg of echinopine A, 1.6 mg of echinopine B.



R = H; echinopine A
R = Me; echinopine B

Dong, M.; Cong, B.; Yu, S.-H.; Sauriol, F.; Huo, C.-H.; Shi, Q.-W.; Gu, Y.-C.; Zamir, L.; Kiyota, H.
OL **2008**, 10, 701-704.

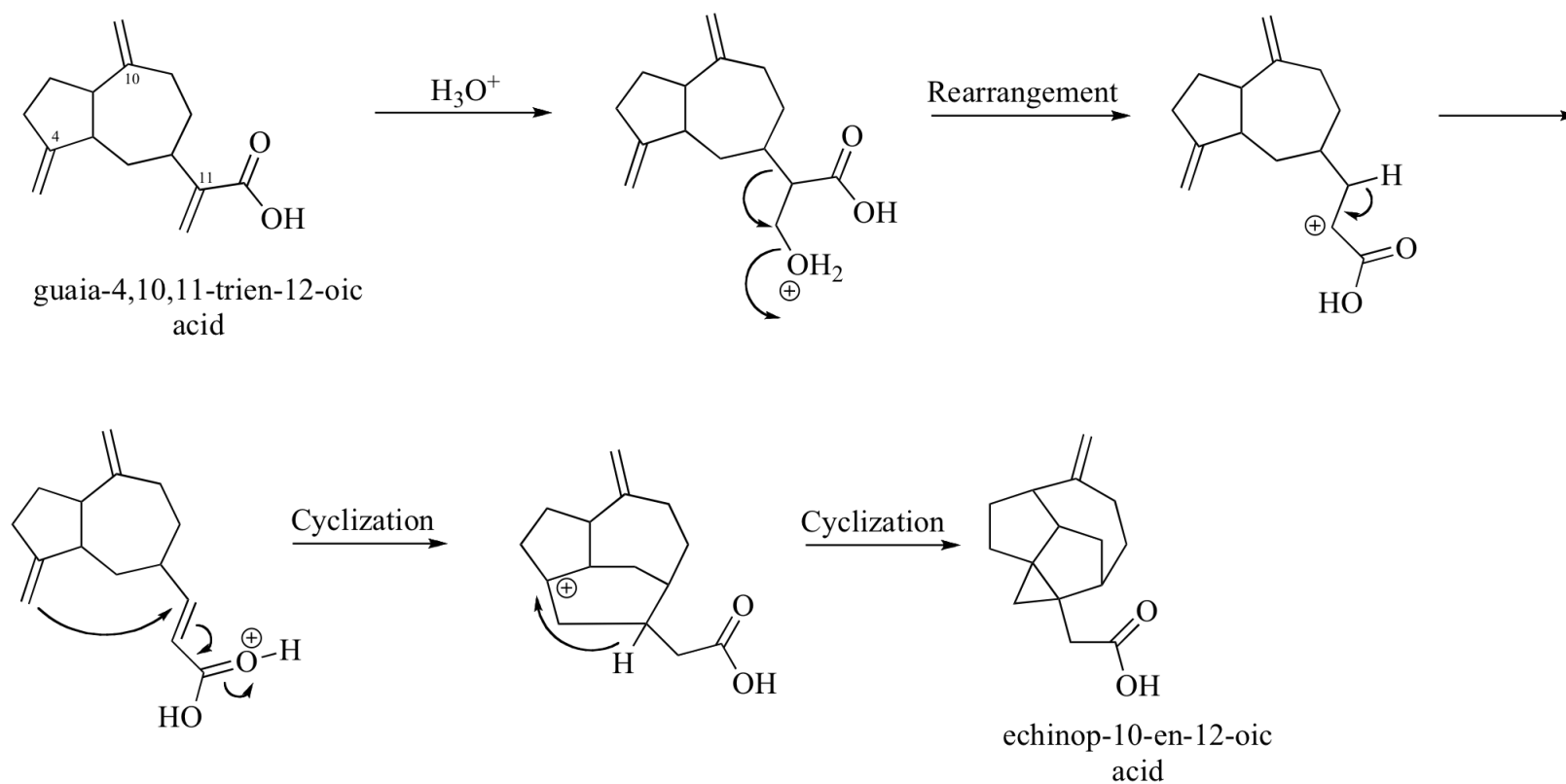
Structure Elucidation



R = H; echinopine A
R = Me; echinopine B

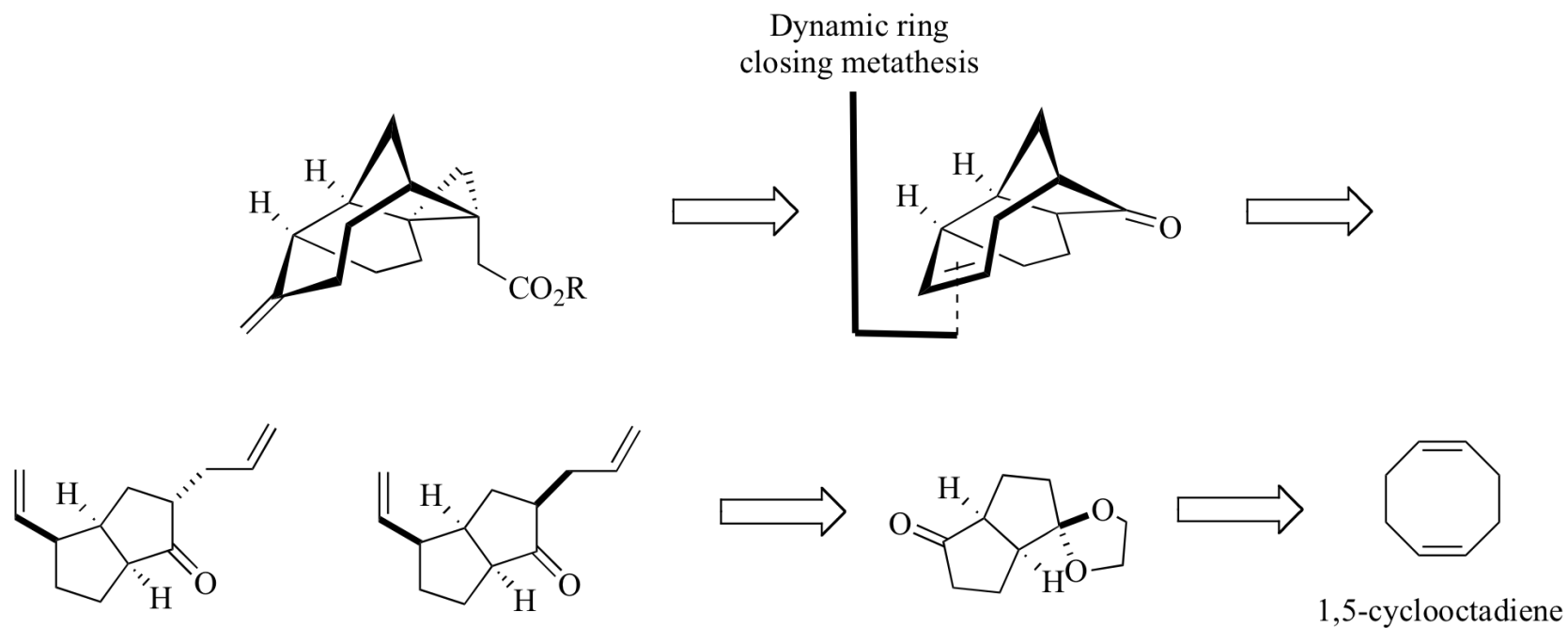
- Contains unprecedented [3.5.5.7]-membered ring carbon framework.
- Structure determined by 1D-, 2D-NMR, MS, no crystal structure from original isolation.
- No biological data obtained from limited sample collected.

Proposed Biosynthetic Pathway



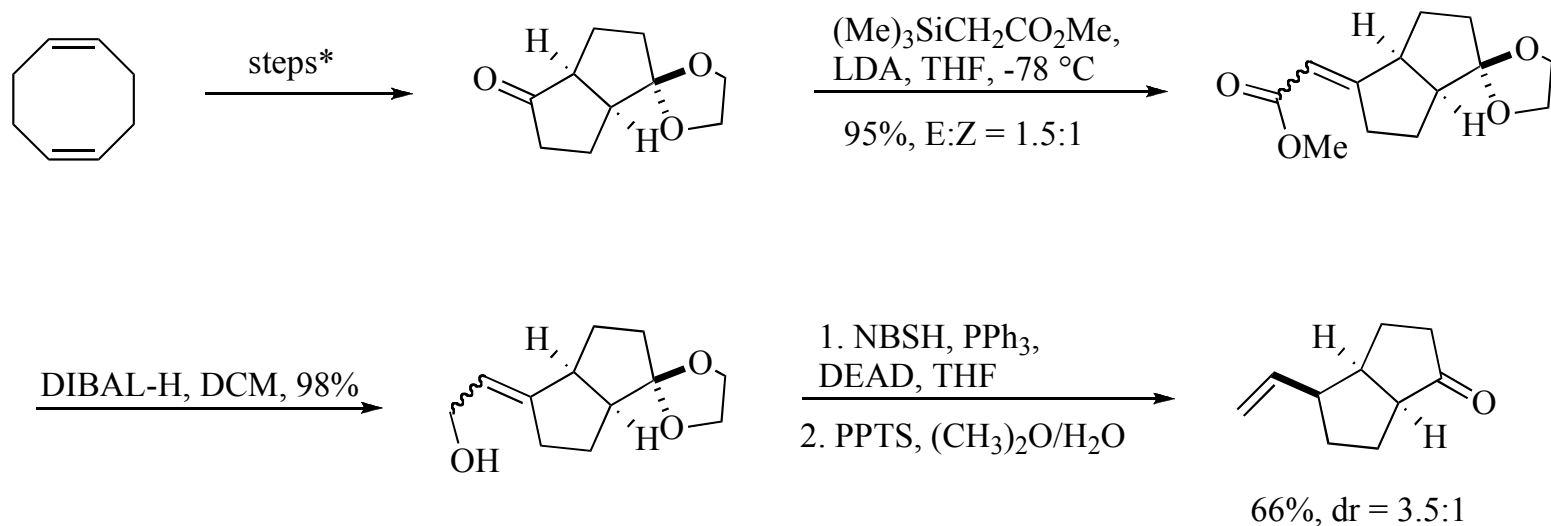
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Tiefenbacher Retrosynthesis

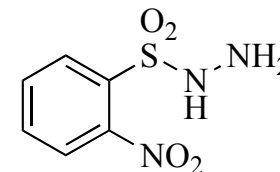


Magauer, T.; Mulzer, J.; Tiefenbacher, K. *OL* **2009**, *11*, 5306-5309.

Tiefenbacher Synthesis



NBSH
o-Nitrobenzenefulfonylhydrazide



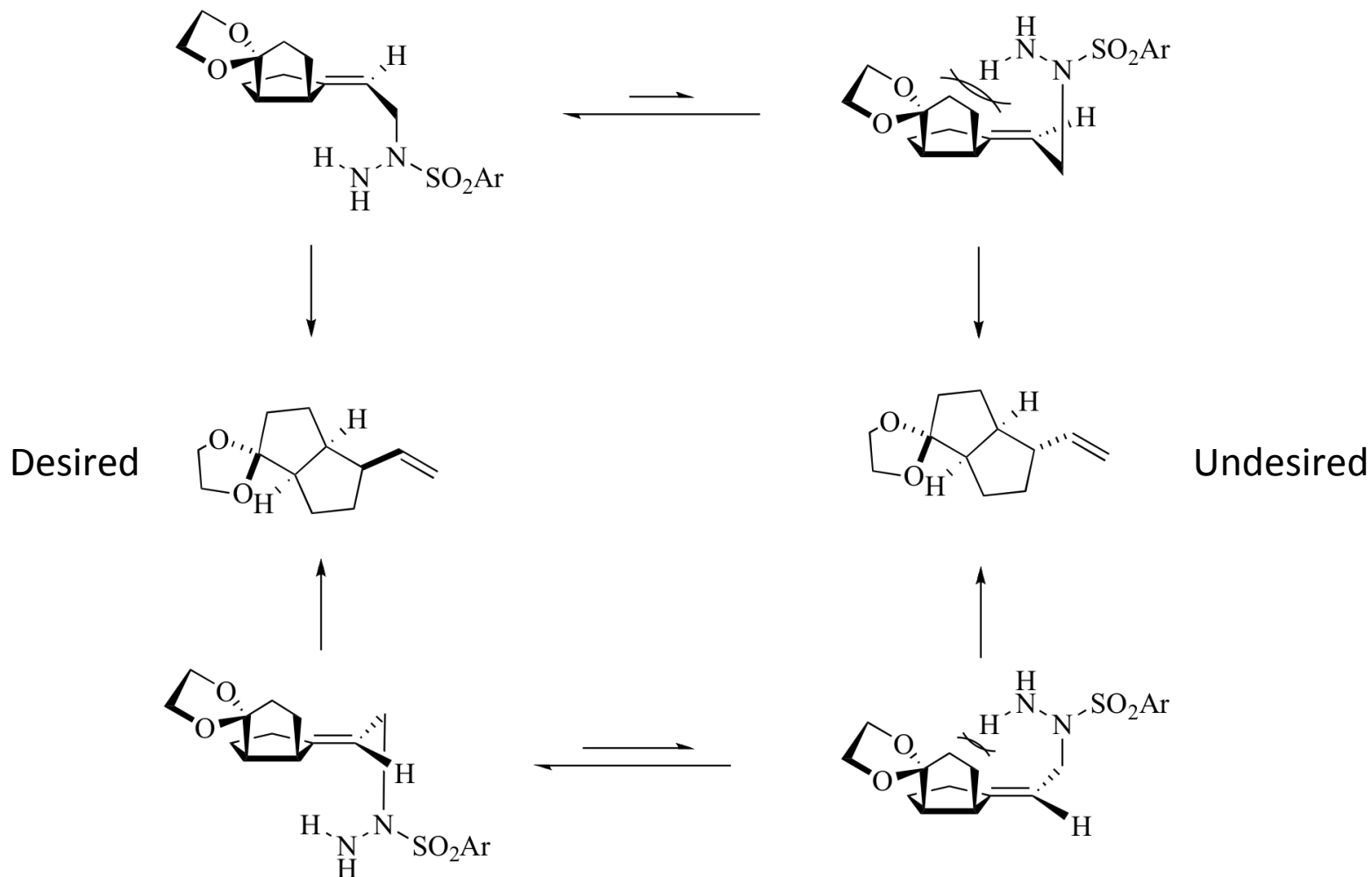
*Starting material synthesis:

Perard-Viret, J.; Rassat, A. *Tet. Asymm.* **1994**, *5*, 1-4.

Zhong, Y.-W.; Lei, X.-S.; Ling, G.-Q. *Tet. Asymm.* **2002**, *13*, 2251-2255.

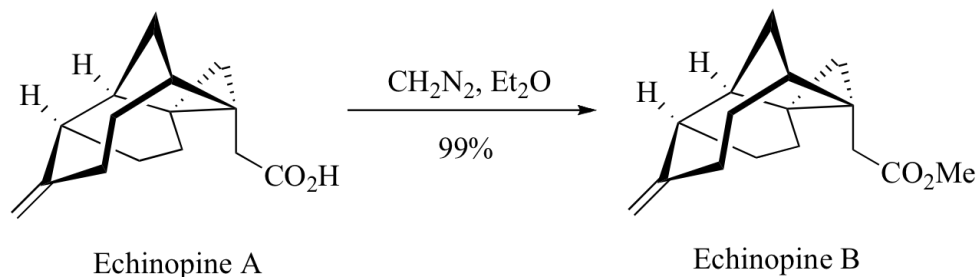
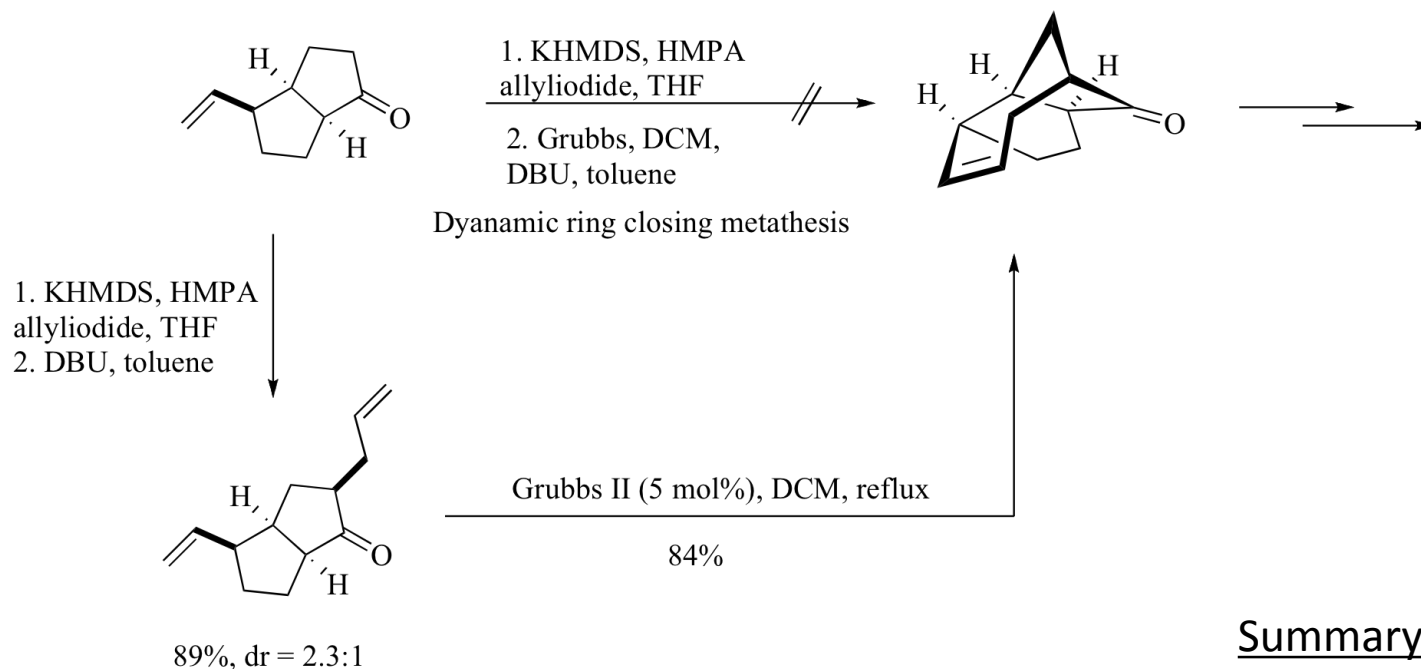
Lemke, K.; Ballschuh, S.; Kunath, A.; Theilm, F. *Tet. Asymm.* **1997**, *8*, 2051-2055.

Myers [3,3]-Sigmatropic Rearrangement



Meyers, A. G.; Zheng, B. *Tet. Lett.* **1996**, 37, 4841-4844.

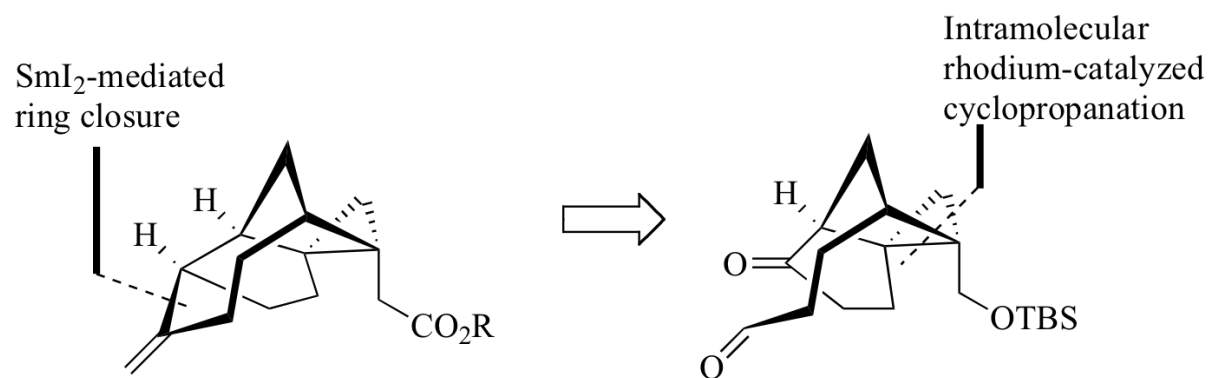
Tiefenbacher Synthesis



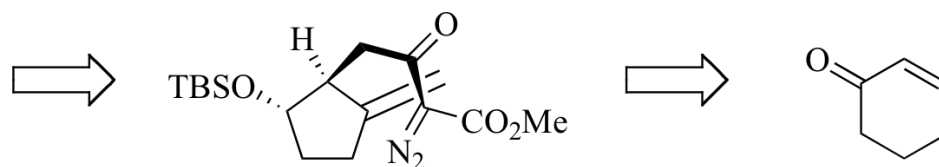
Summary:

- 15 steps from known ketone in 7% overall yield.
- Meyers [3,3]-sigmatropic rearrangement.
- X-ray crystal structure.
- No biological data reported.

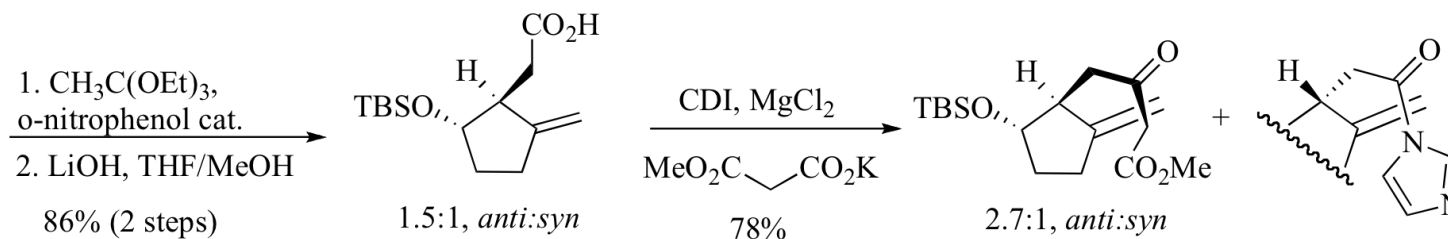
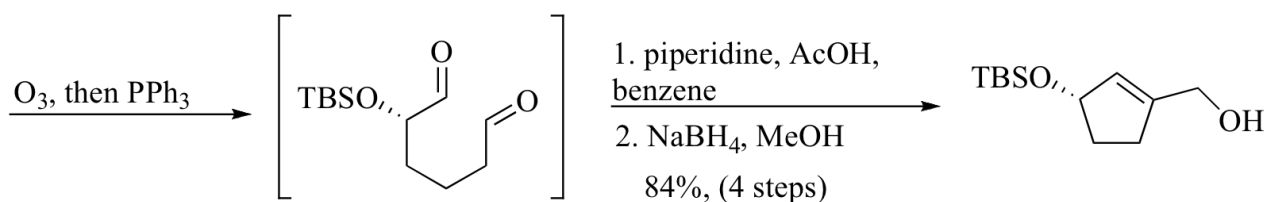
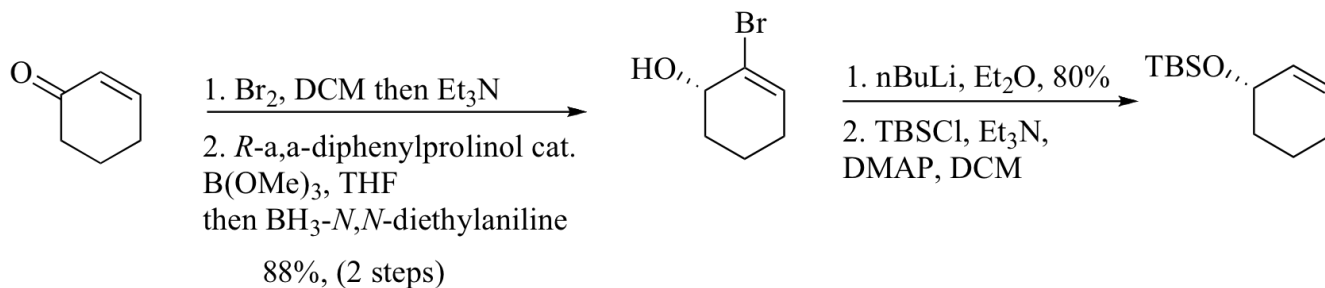
Title Paper-Retrosynthesis



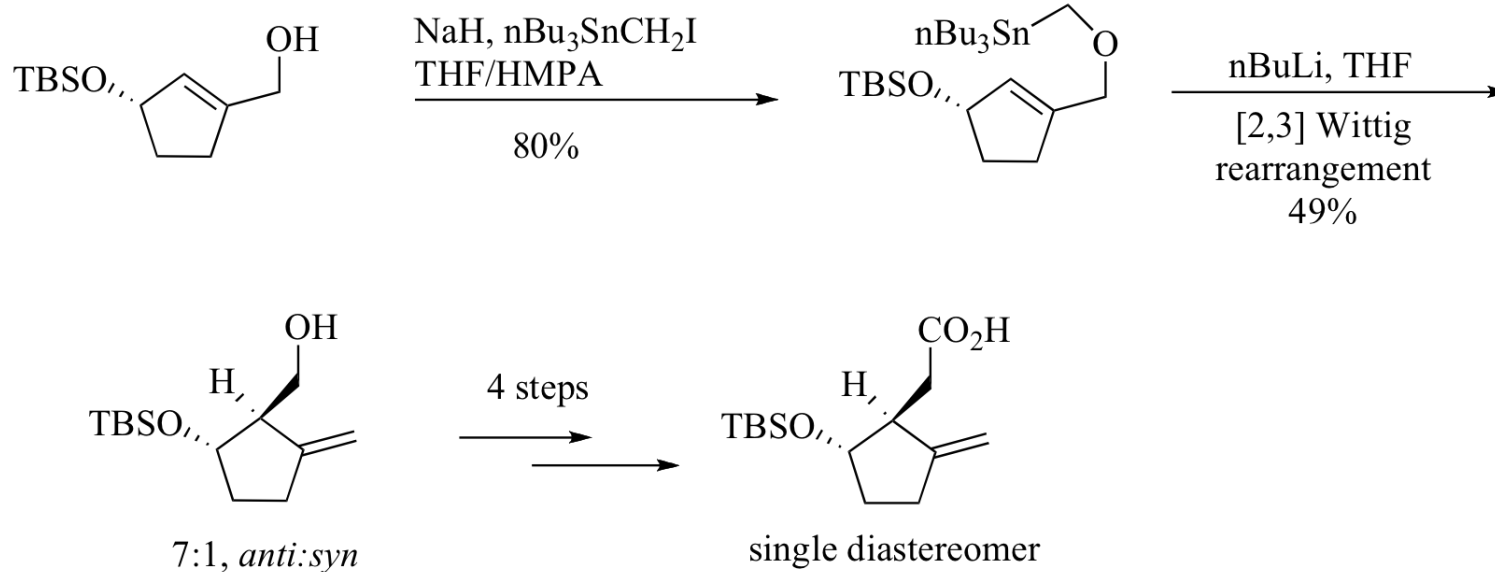
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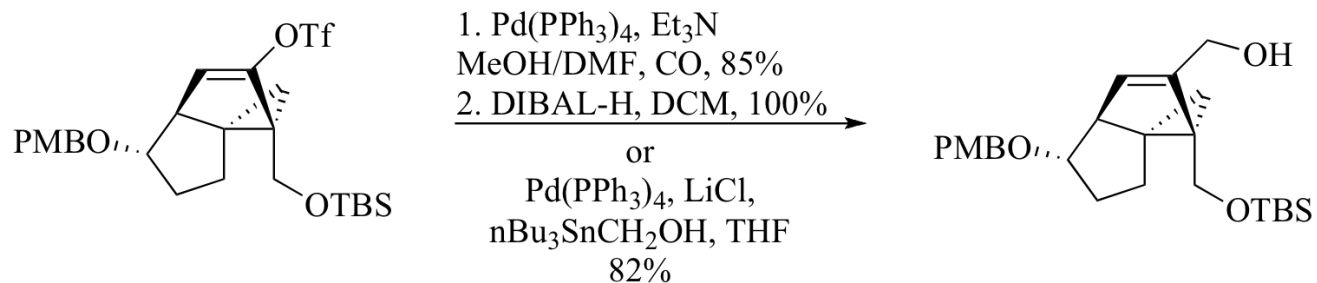
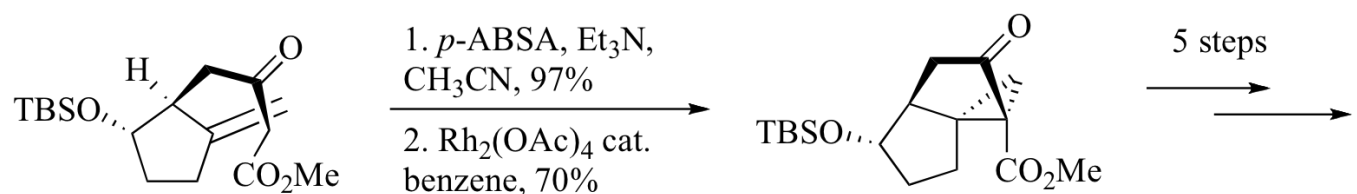
Title Paper Synthesis



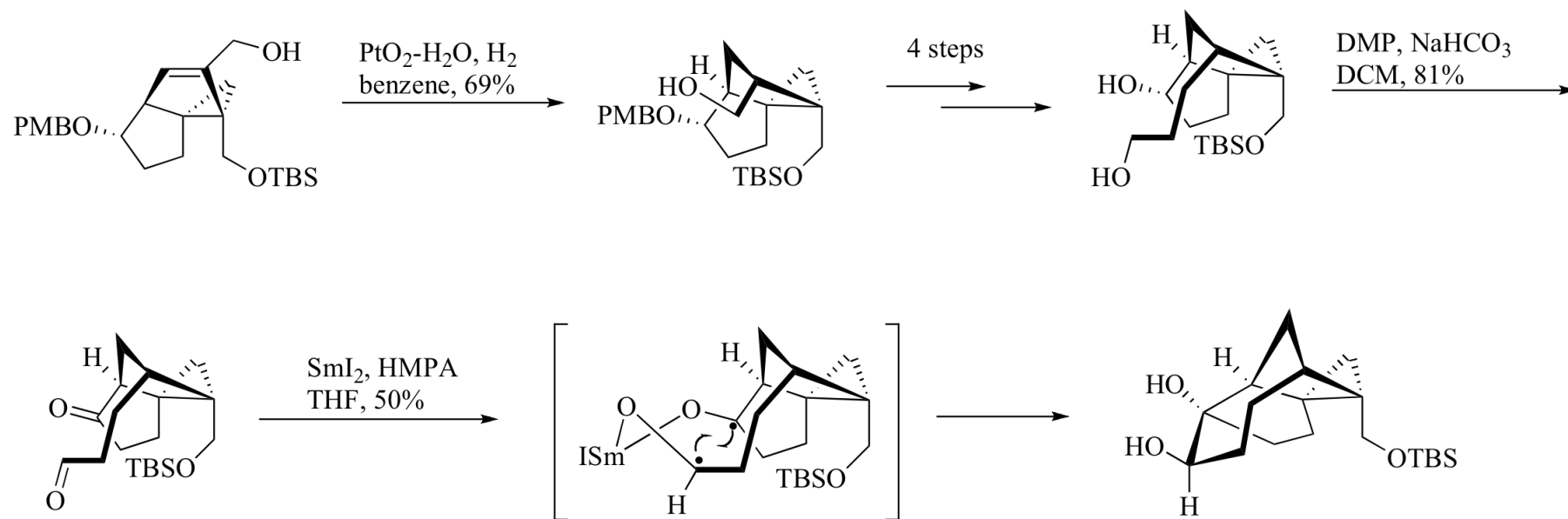
Alternative Synthesis of Acid



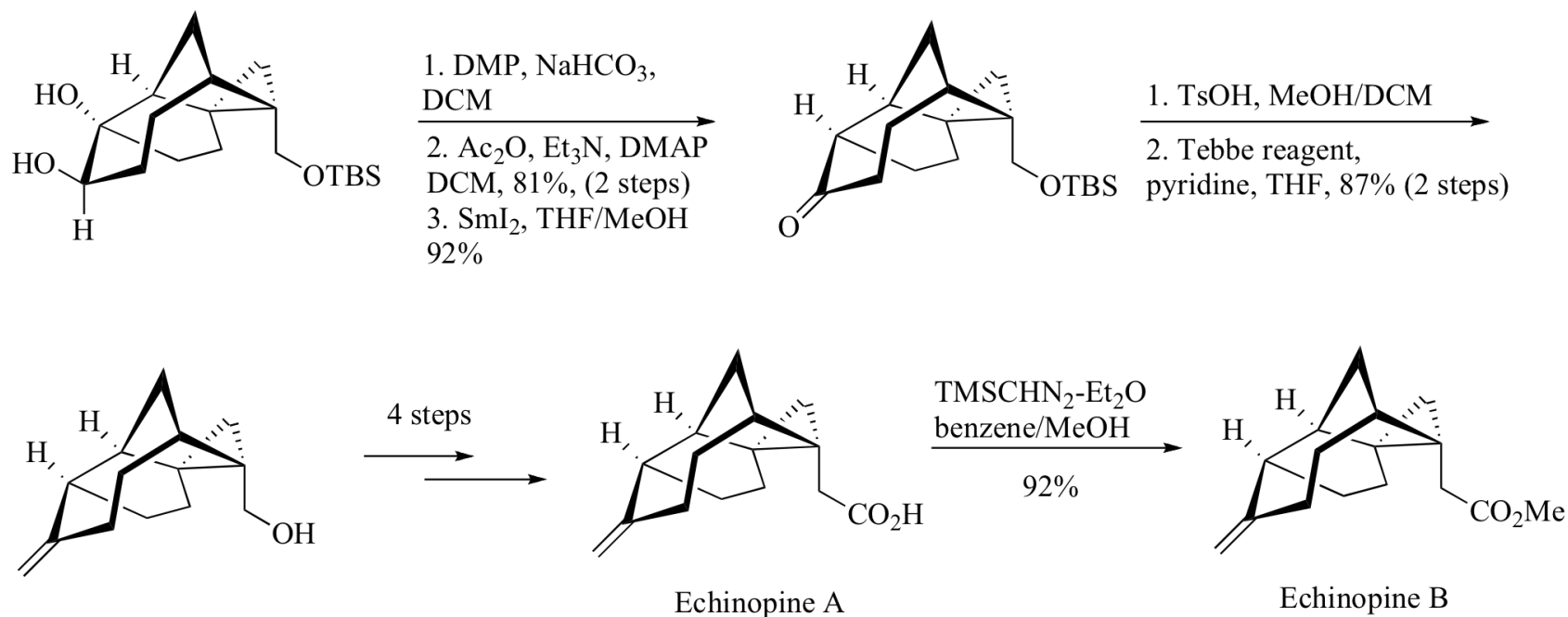
Synthesis of Tricyclic Allylic Alcohol



Synthesis of Tetracycle



Echinopine End Game



Summary

- Asymmetric total synthesis of unique [3.5.5.7] ring system.
- SmI_2 mediated pinacol coupling to form 7 membered ring.
- Intramolecular rhodium catalyzed cyclopropanation.
- No biological activity reported to date.