Formal Asymmetric Synthesis of Echinopine A and B

Natural Products

Formal Asymmetric Synthesis of Echinopine A and B

Philippe A. Peixoto, Rene Severin, Chih-Chung Tseng and David Y.-K. Chen

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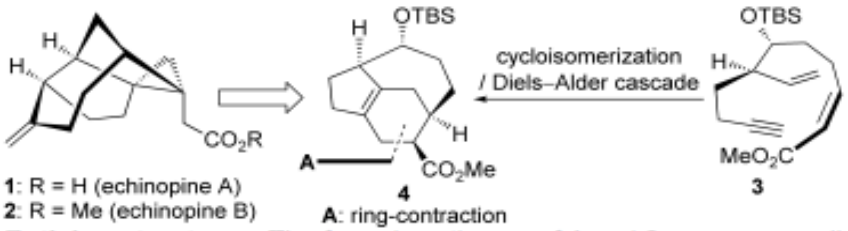


1: R = H (echinopine A)
2: R = Me (echinopine B)

4

A: ring-contraction

3

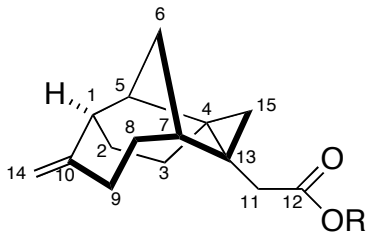
Enticing structures: The formal syntheses of **1** and **2** were accomplished by using a cascade strategy involving an enyne cycloisomerization reaction and an intramolecular Diels–Alder reaction starting from **3**. The resulting **4** underwent a late-stage ring contraction to enable the preparation of a reported advanced intermediate, thereby constituting a formal synthesis of the structurally intriguing title compounds.

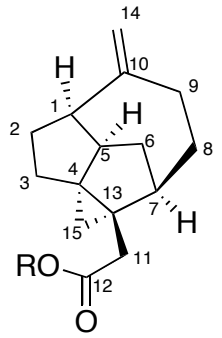
Abstract | **PDF(404K)** | **References** | **Supporting Information**

Peixoto, P. A.; Severin, R.; Tseng, C.-C.; Chen, D. Y. –K.
Angew. Chem. Int. Ed. **2011**, Early view.

Echinopines A and B: Sesquiterpenoids Possessing an Unprecedented Skeleton

Echinops spinosus





R = H, Echinopinoic acid = Echinopine A
R = CH_3, Echinopine B

- unique 3,5,5,7-framework
- structure elucidated by spectroscopic analysis
- 7-membered ring adopts a (flat) chair form

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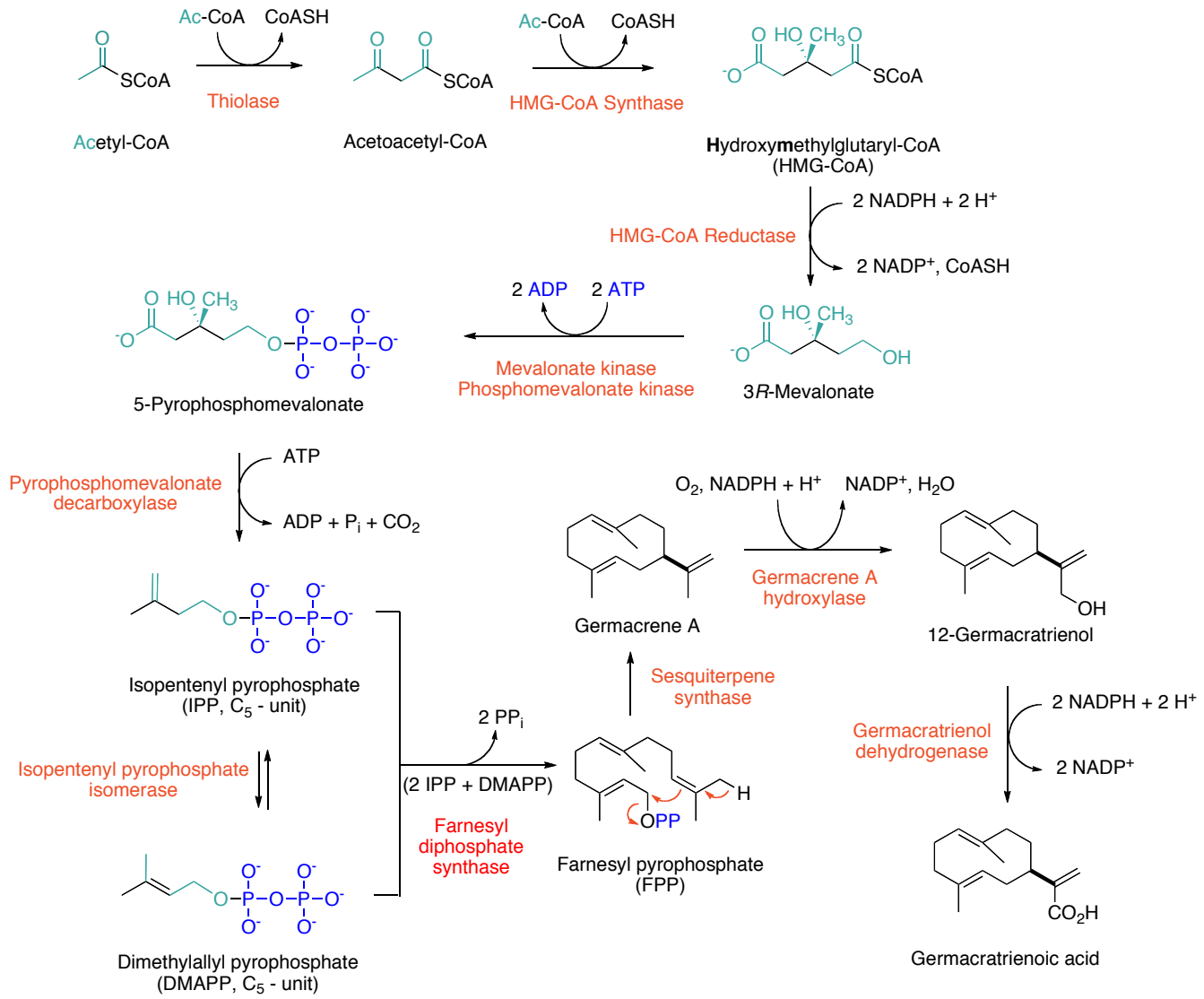
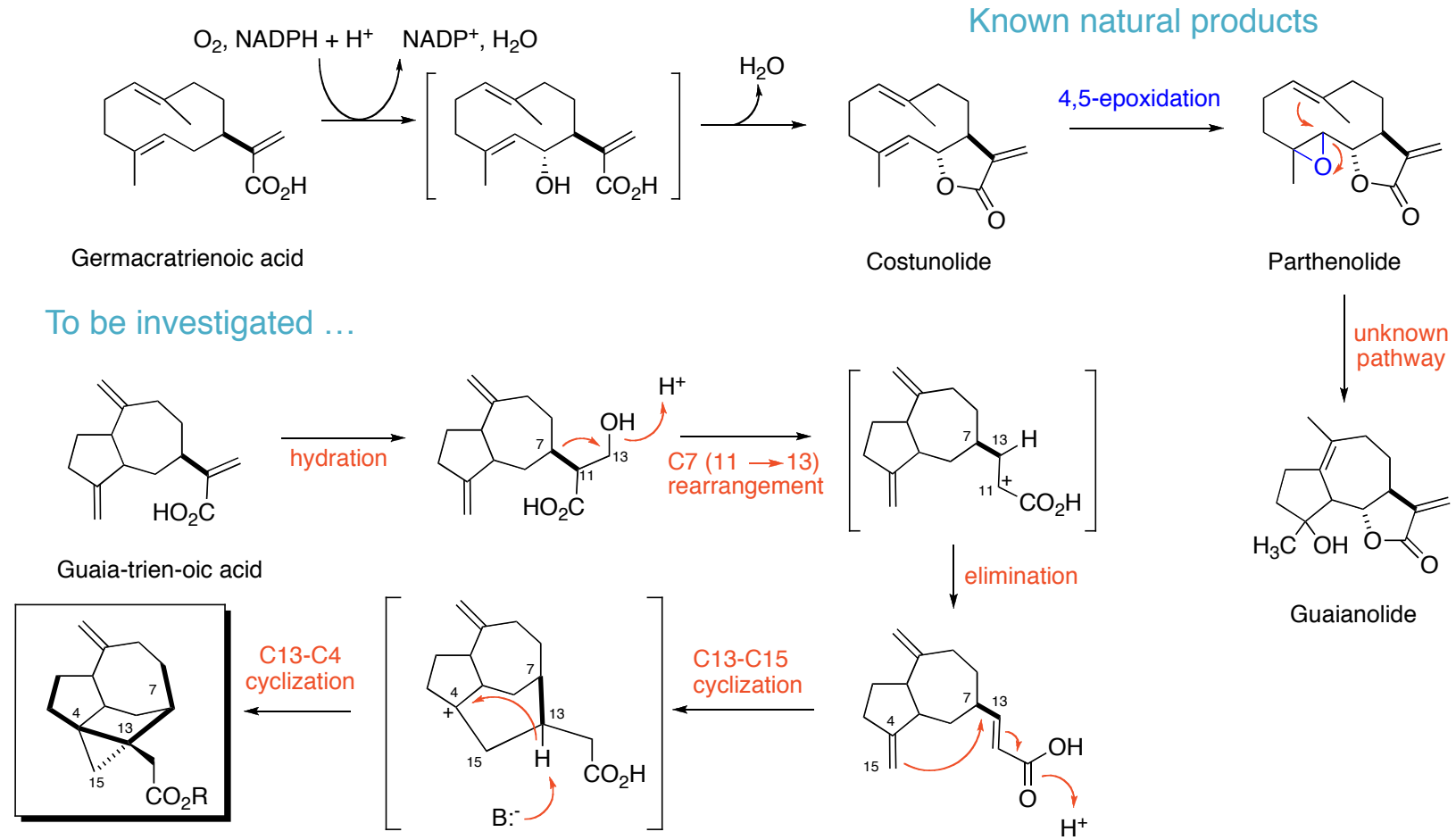
(b) http://www.metafro.be/prelude/view_plant?pi=05205.

Part 1: How Does Nature Make Echinopines A and B?



(a) A.A. Newman, Chemistry of Terpens and Terpenoids, Academic Press, London and New York, 1970. (b) Rohdich, F.; Kis, K.; Bacher, A.; Eisenreich, W. *Curr. Opin. Chem. Biol.* **2001**, *5*, 535. (c) Kraker, J.; Franssen, M.C.; Dalm, M. C.; Groot, A.; Bouwmeester, H.J. *Plant Physiol.* **2001**, *125*, 1930. (d) drew, D. P.; Krichau, N.; Reichwald, K.; Simonsen, H. T. *Phytochem Rev* **2009**, *8*, 581.

Part 2: How Does Nature Make Echinopines A and B?



(a) A.A. Newman, Chemistry of Terpens and Terpenoids, Academic Press, London and New York, 1970. (b) Rohdich, F.; Kis, K.; Bacher, A.; Eisenreich, W. *Curr. Opin. Chem. Biol.* **2001**, *5*, 535. (c) Kraker, J.; Franssen, M.C.; Dalm, M. C.; Groot, A.; Bouwmeester, H.J. *Plant Physiol.* **2001**, *125*, 1930. (d) drew, D. P.; Krichau, N.; Reichwald, K.; Simonsen, H. T. *Phytochem Rev* **2009**, *8*, 581.

Previous Work in the Field of Echinopines' Synthesis

Letter

Prev.

Total Syntheses of (+)-Echinopine A and B: Determination of Absolute Stereochemistry

Thomas Magauer*, Johann Mulzer and Konrad Tiefenbacher*
University of Vienna, Institute of Organic Chemistry, Währingerstrasse 38, 1090 Vienna, Austria

Org. Lett., **2009**, *11* (22), pp 5306-5309
DOI: 10.1021/ol902263k
Publication Date (Web): October 13, 2009

thomas.magauer@univie.ac.at; konrad.tiefenbacher@univie.ac.at

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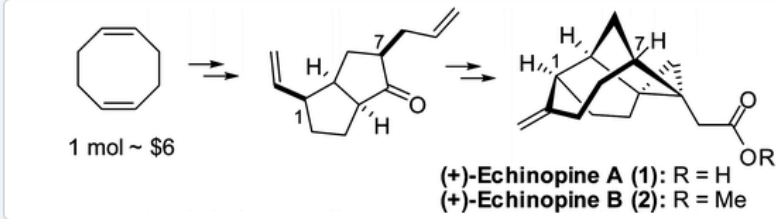
Abstract



The first total syntheses of the novel 3,5,5,7-sesquiterpenoids (+)-Echinopine A (**1**) and B (**2**) were achieved. Thereby the proposed structures were confirmed, and the absolute

Article

Prev

Total Synthesis of Echinopines A and B

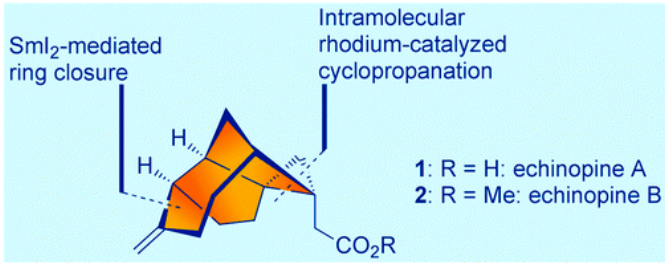
K. C. Nicolaou*, Hanfeng Ding, Jean-Alexandre Richard and David Y.-K. Chen*
Chemical Synthesis Laboratory@Biopolis, Institute of Chemical and Engineering Sciences (ICES), Agency for Science, Technology and Research (A*STAR), 11 Biopolis Way, The Helios Block, #03-08, Singapore 138667

J. Am. Chem. Soc., **2010**, *132* (11), pp 3815-3818
DOI: 10.1021/ja9093988
Publication Date (Web): February 25, 2010

kcn@scripps.edu; david_chen@ices.a-star.edu.sg

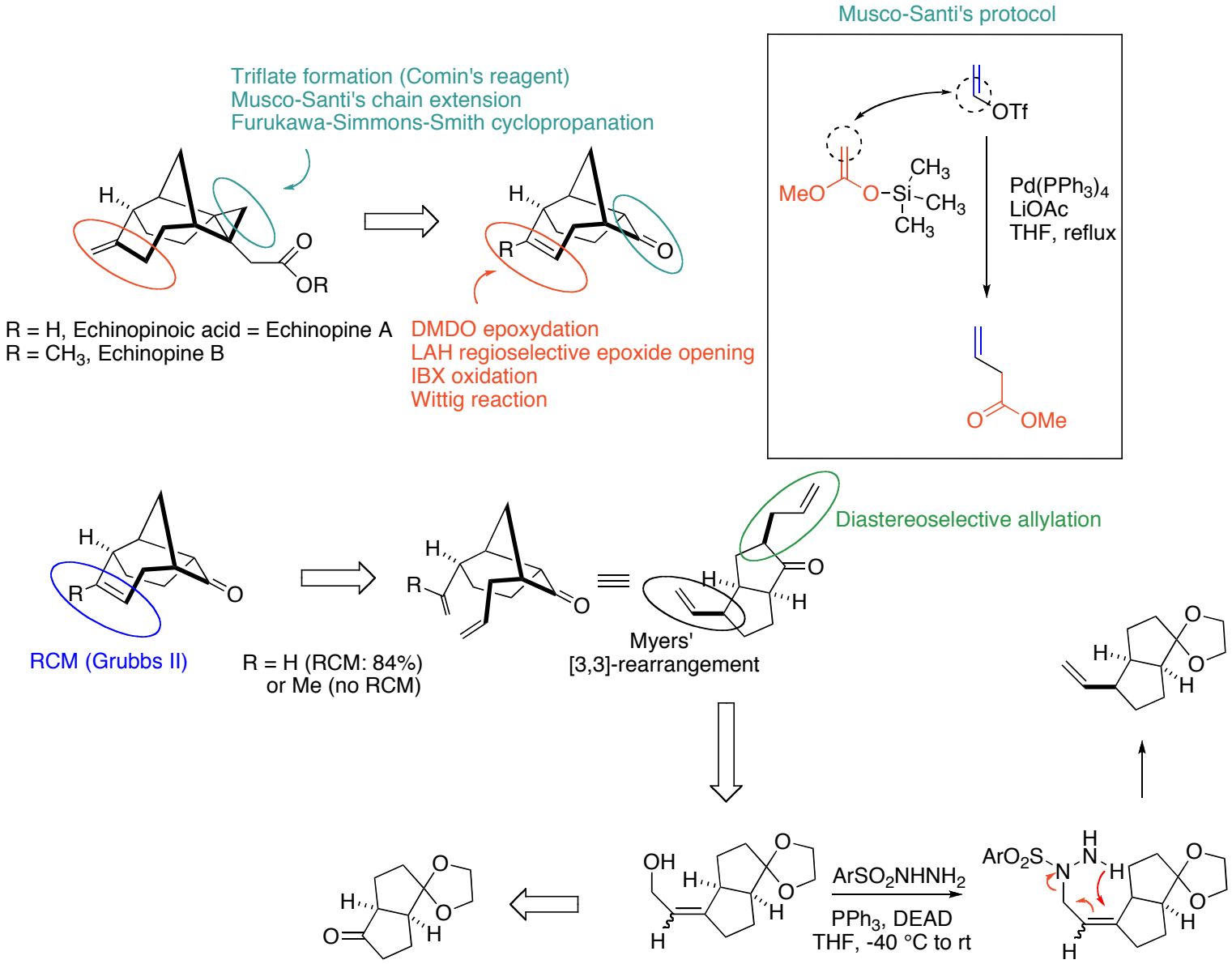
Abstract | Supporting Info | Full Text HTML | Figures | Hi-Res PDF [386 KB] | Citing Articles | PDF w/ Links [280 KB]

Abstract



Echinopines A and B [(+)-**1** and (+)-**2**], two naturally occurring compounds characterized with

The Magauer-Tiefenbacher Sytnhesis of (+)-Echinopine A and B



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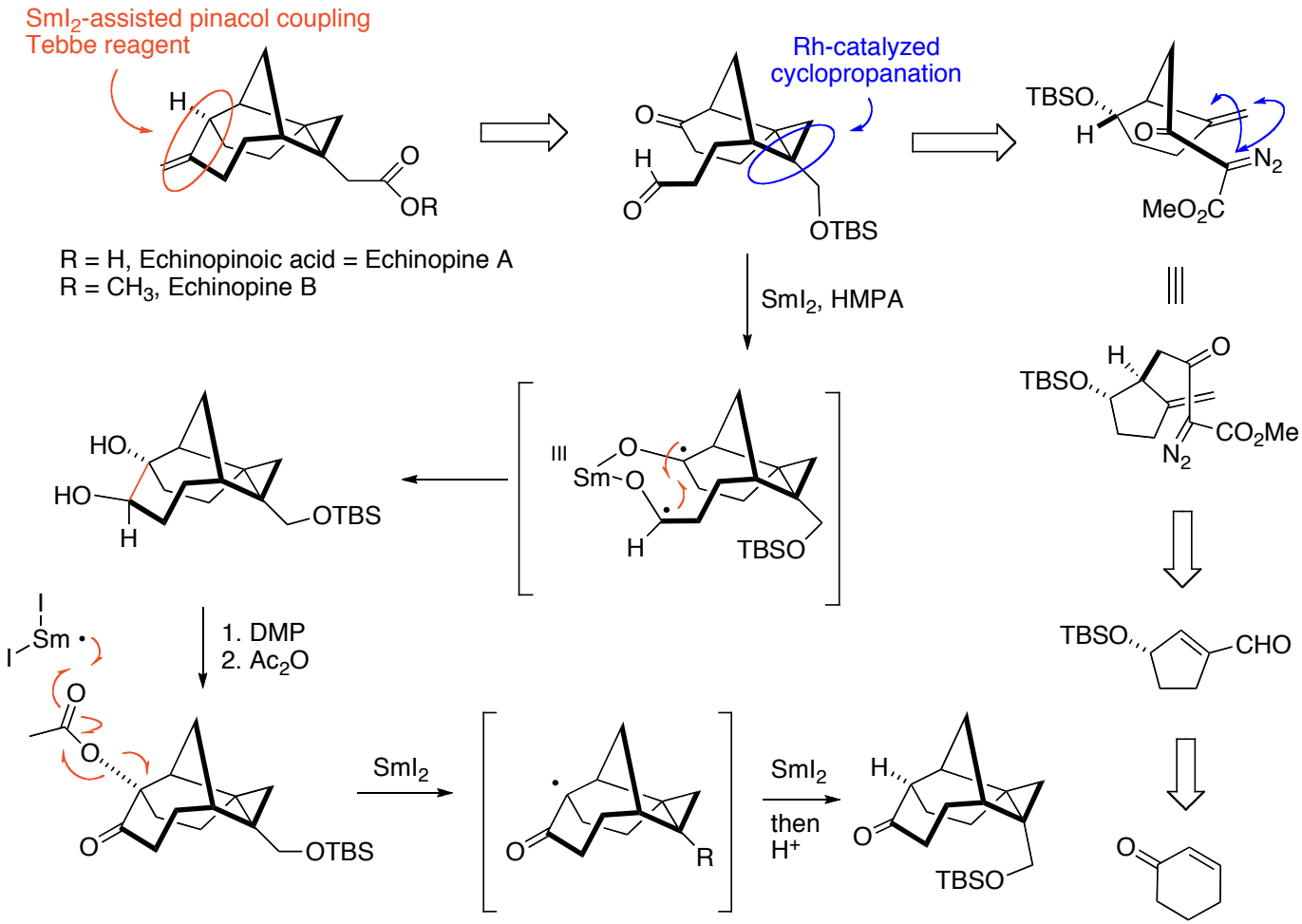
The Nicolaou-Chen Synthesis of Echinopines A and B



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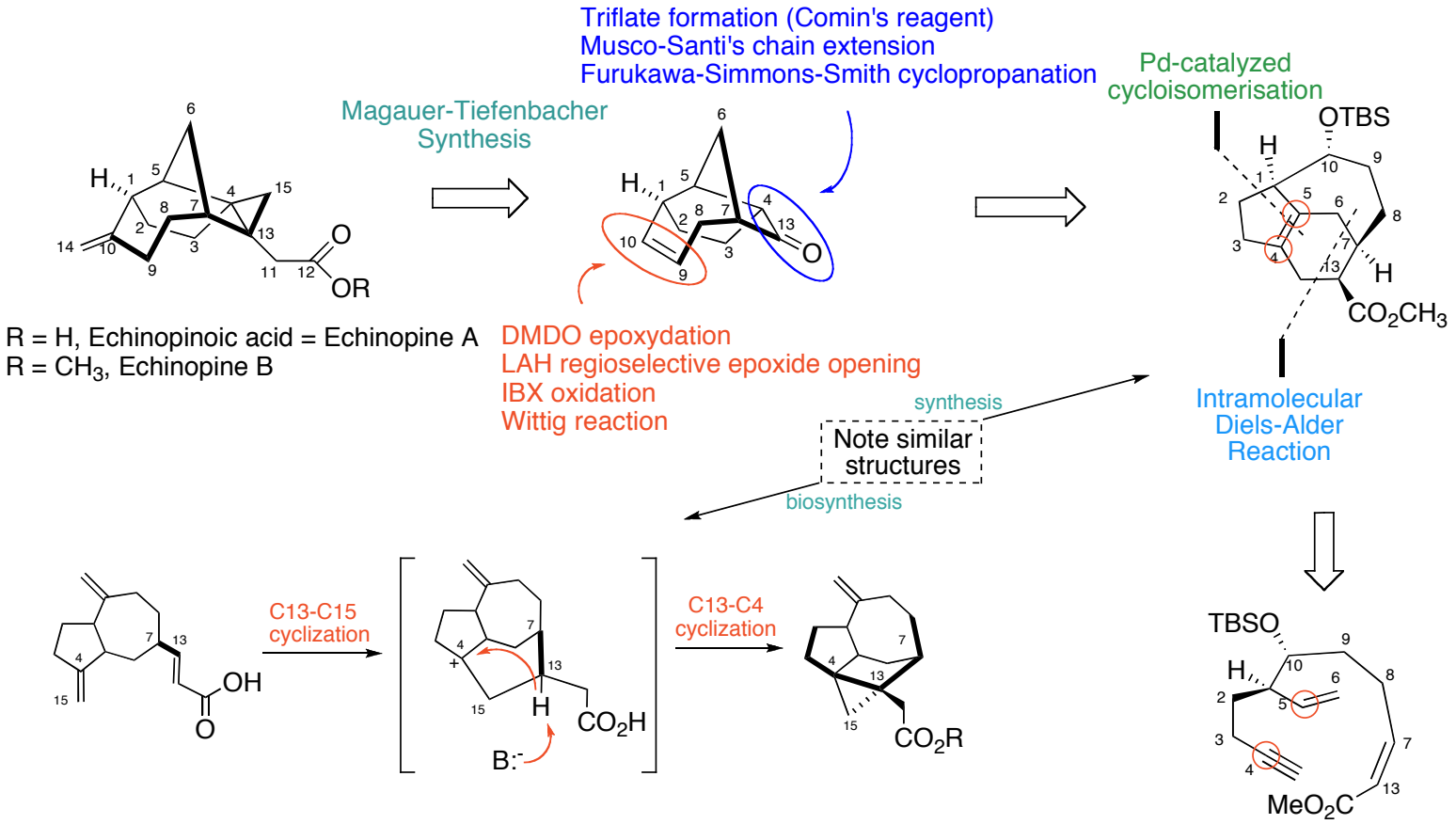
Chen's Formal Aymmetric Synthesis of Echinopine A and B: Retrosynthesis



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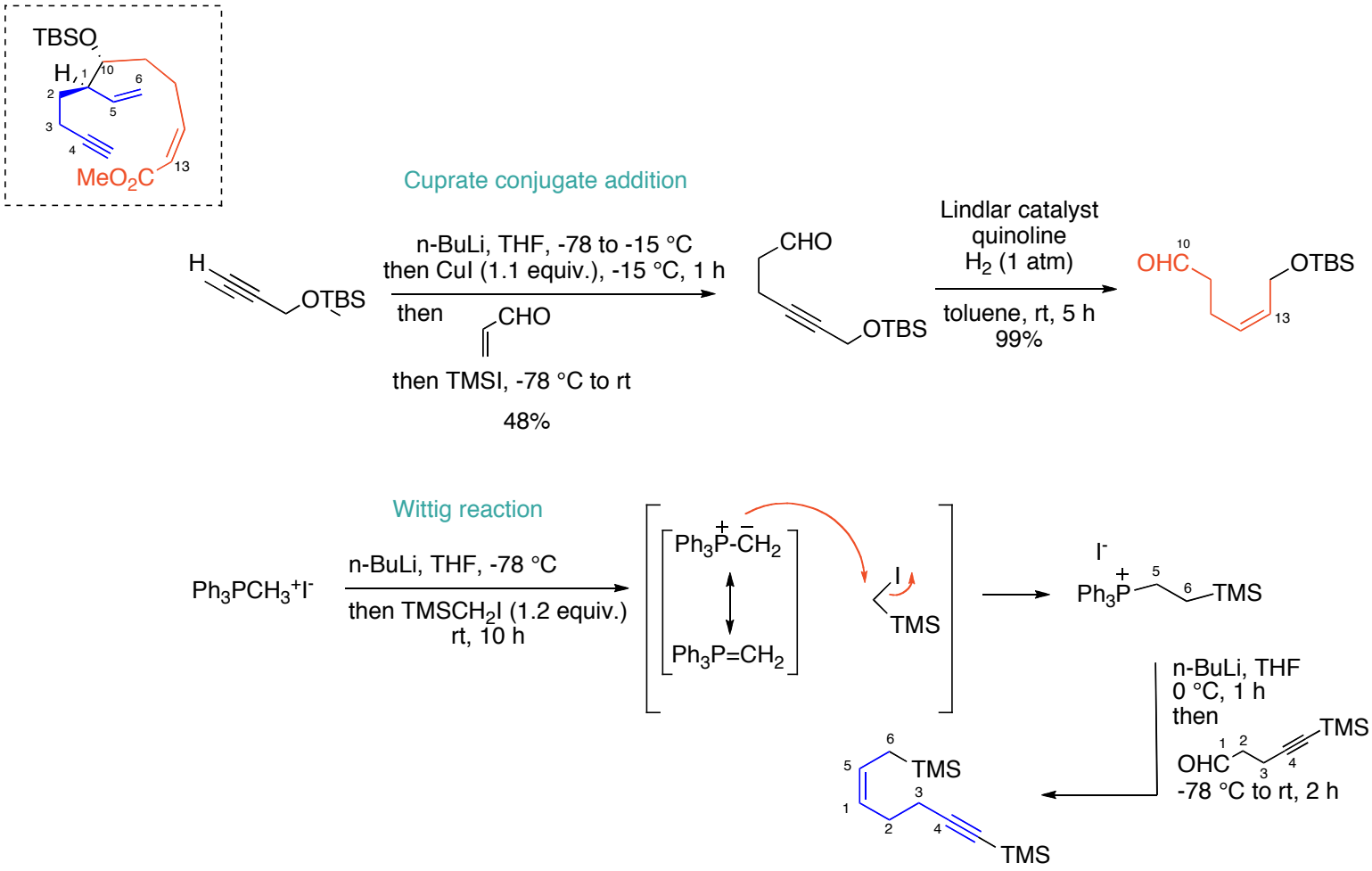
Chen's Synthesis of Echinopines: Construction of the Acyclic Cycloisomerisation/DA Cascade precursor



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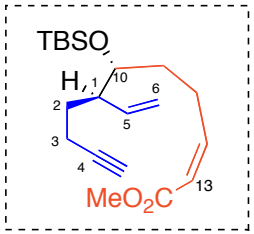
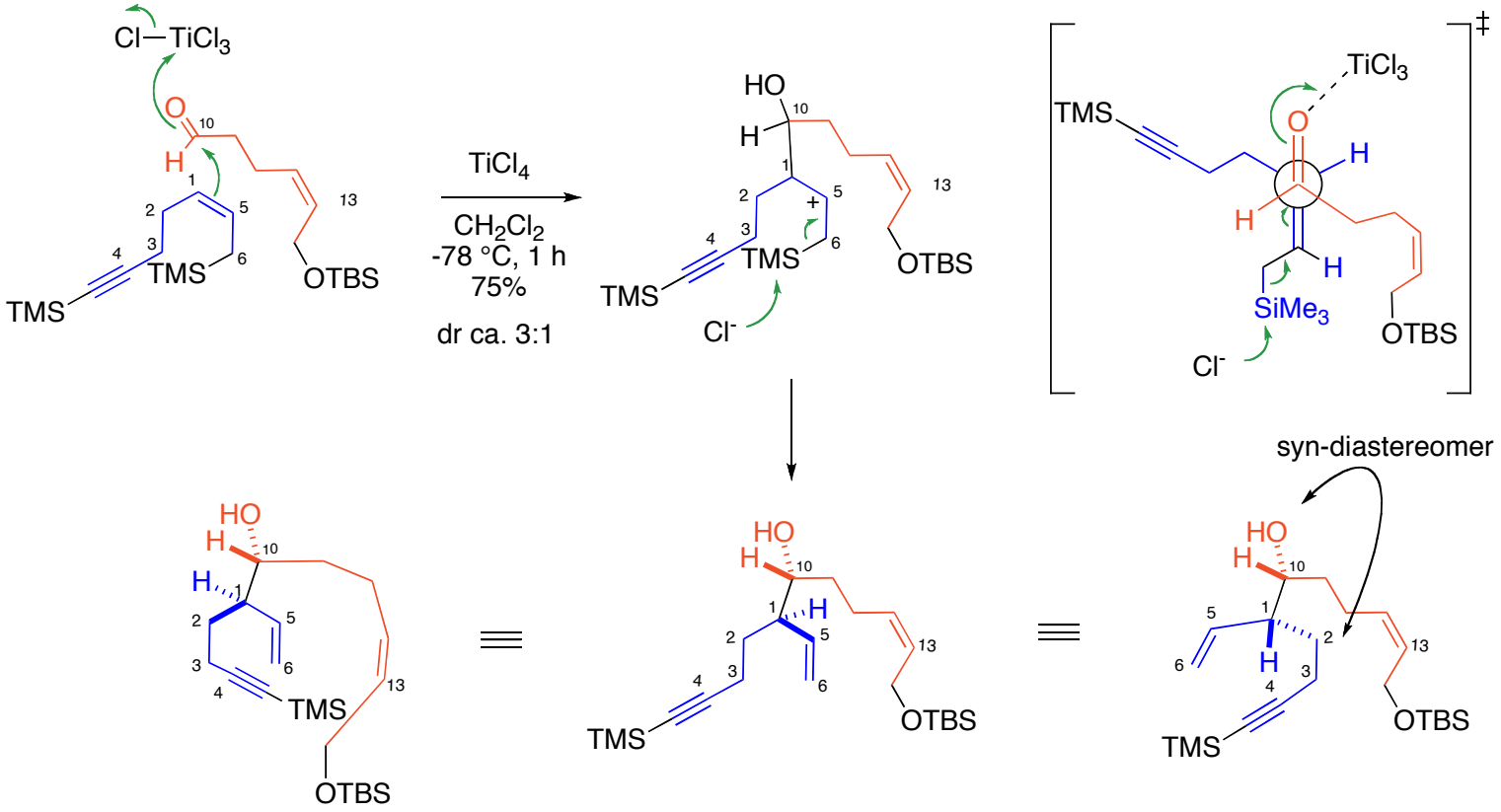


Coupling Red and Blue: Sakurai reaction



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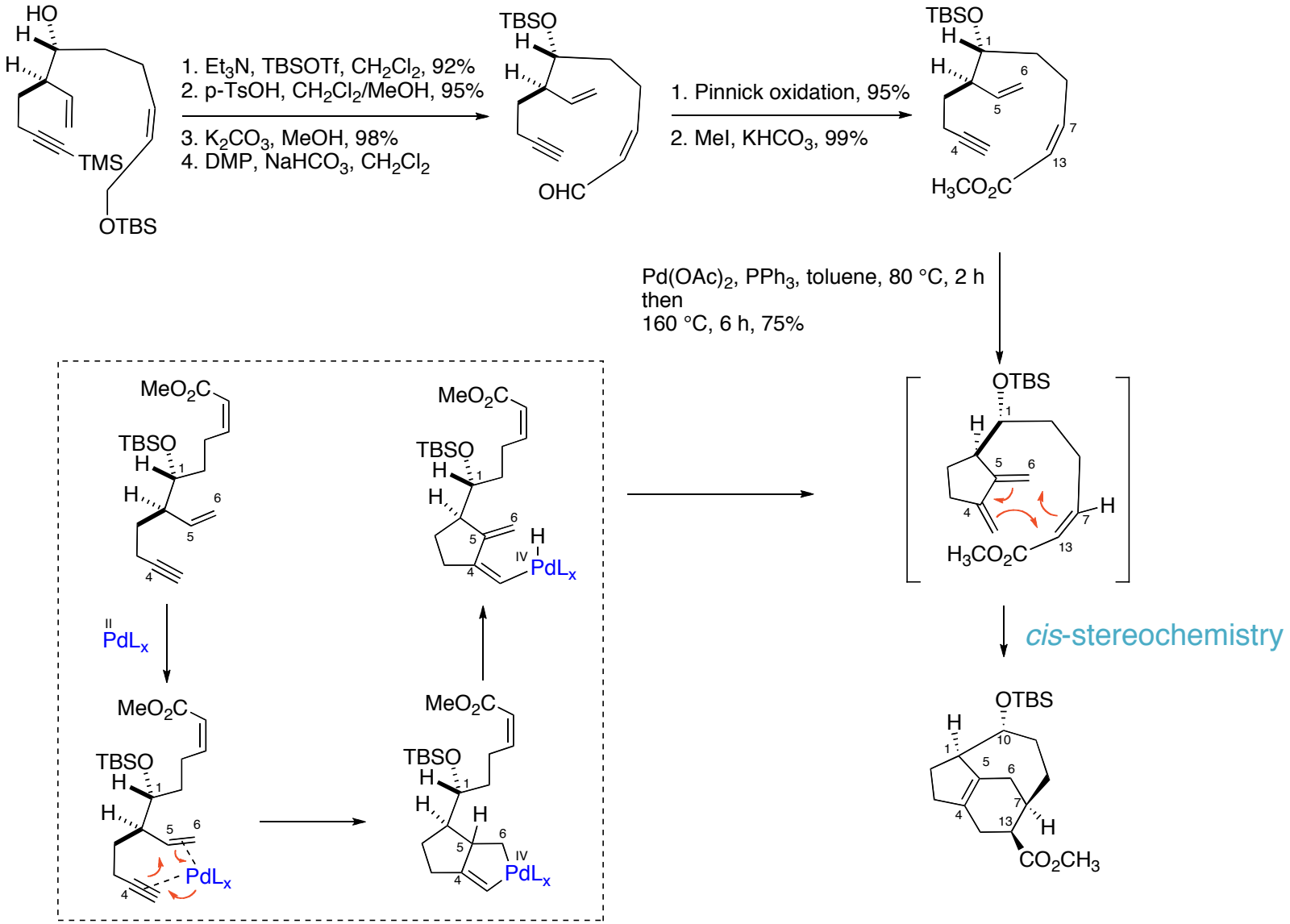
Cascade Cyclization/Intramolecular Diels-Alder Reaction



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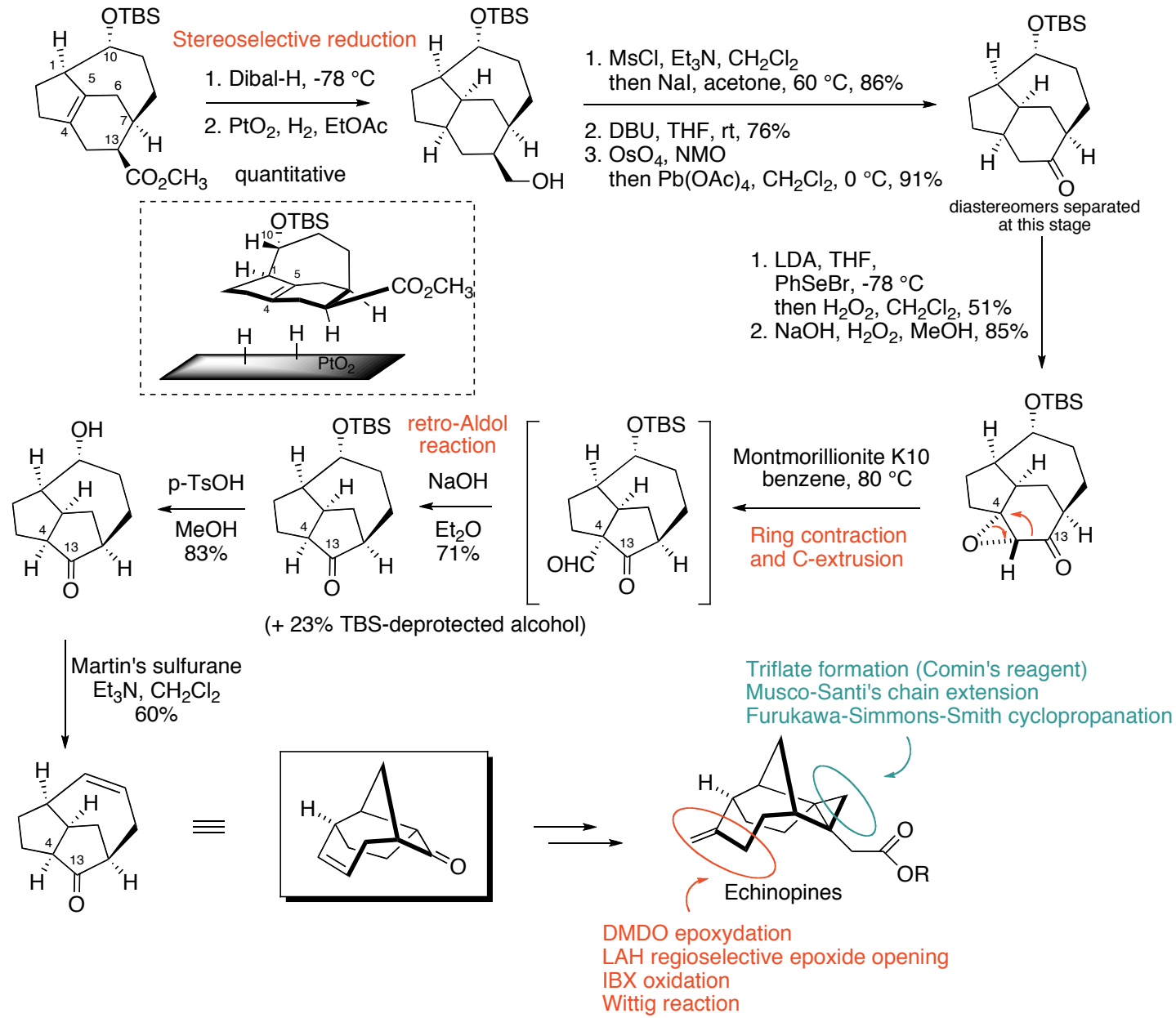
Finishing the Formal Synthesis of Echinopines



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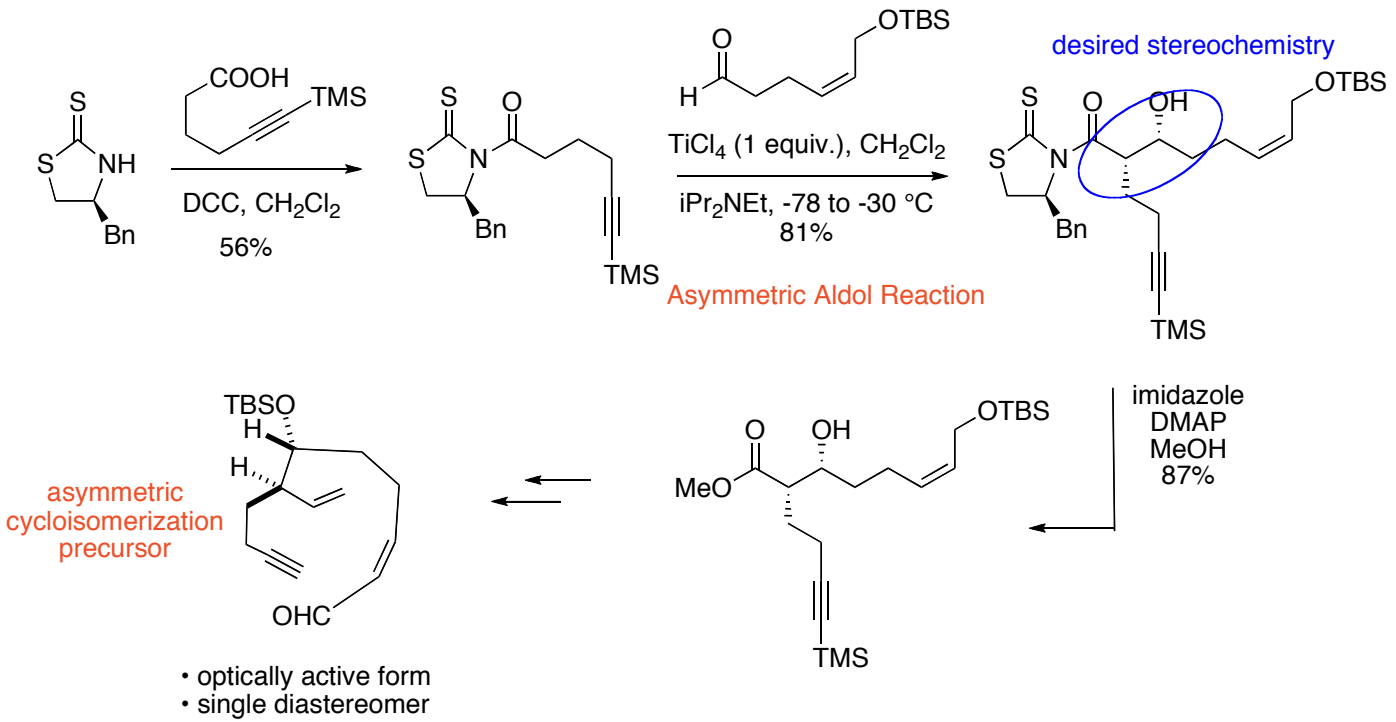
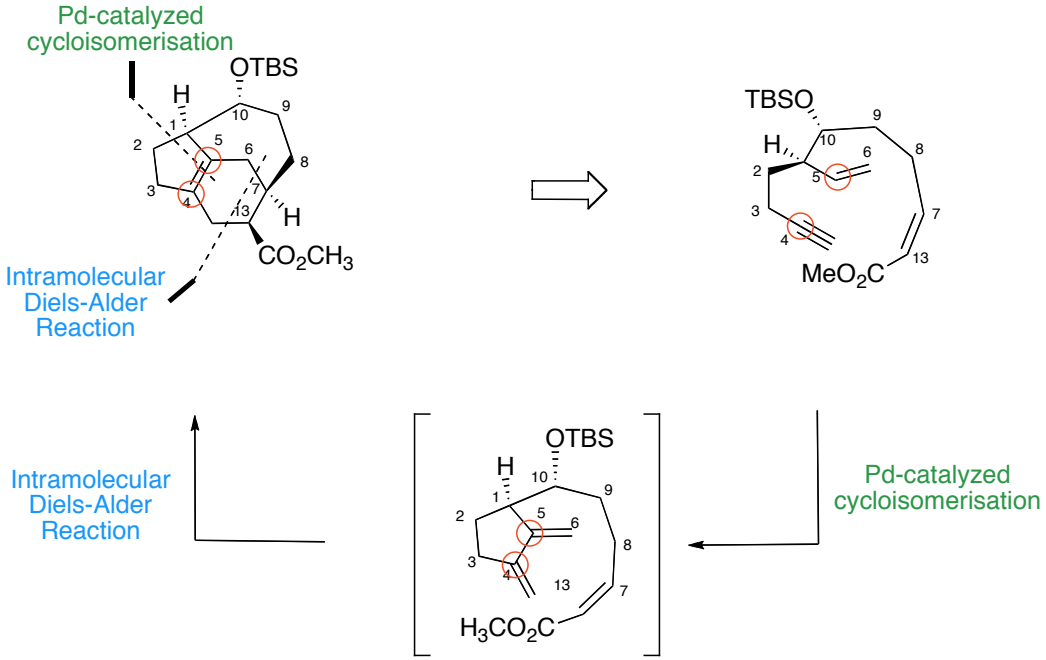
Echinopine A and B: An Asymmetric Approach by Aldol Chemistry



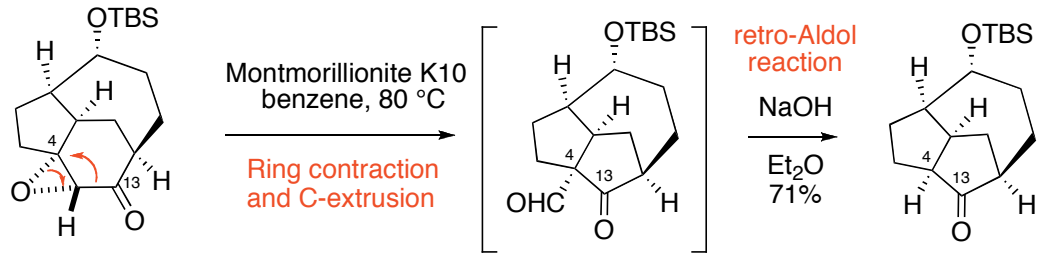
Peixoto, P.A.; Severin, R.; Tseng, C. –C., Chen, D.Y.-K. *Angew. Chem. Int. Ed.* **2011**, Early view

Conclusions

- Asymmetric formal synthesis of (+)-Echinopine A and B has been accomplished through cycloisomerization/intramolecular Diels-Alder reaction



- 5,5-system made by contraction of 5,6-system



- Asymmetric version through Aldol Chemistry has been demonstrated