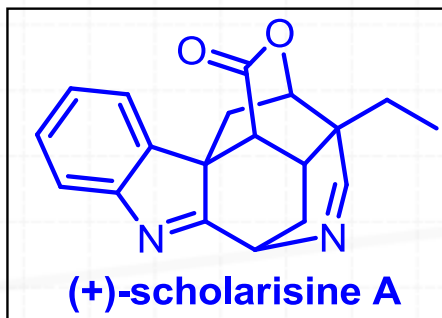


Total Synthesis of (+)-Scholarisine A



Smith, M. W.; **Snyder**, S. A. *J. Am. Chem. Soc.* **2013**, *135*, 12964.

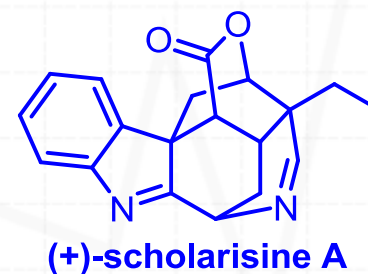
Adams, G. L.; Carroll, P. J.; **Smith, A. B., III.** *J. Am. Chem. Soc.* **2012**, *134*, 4037.



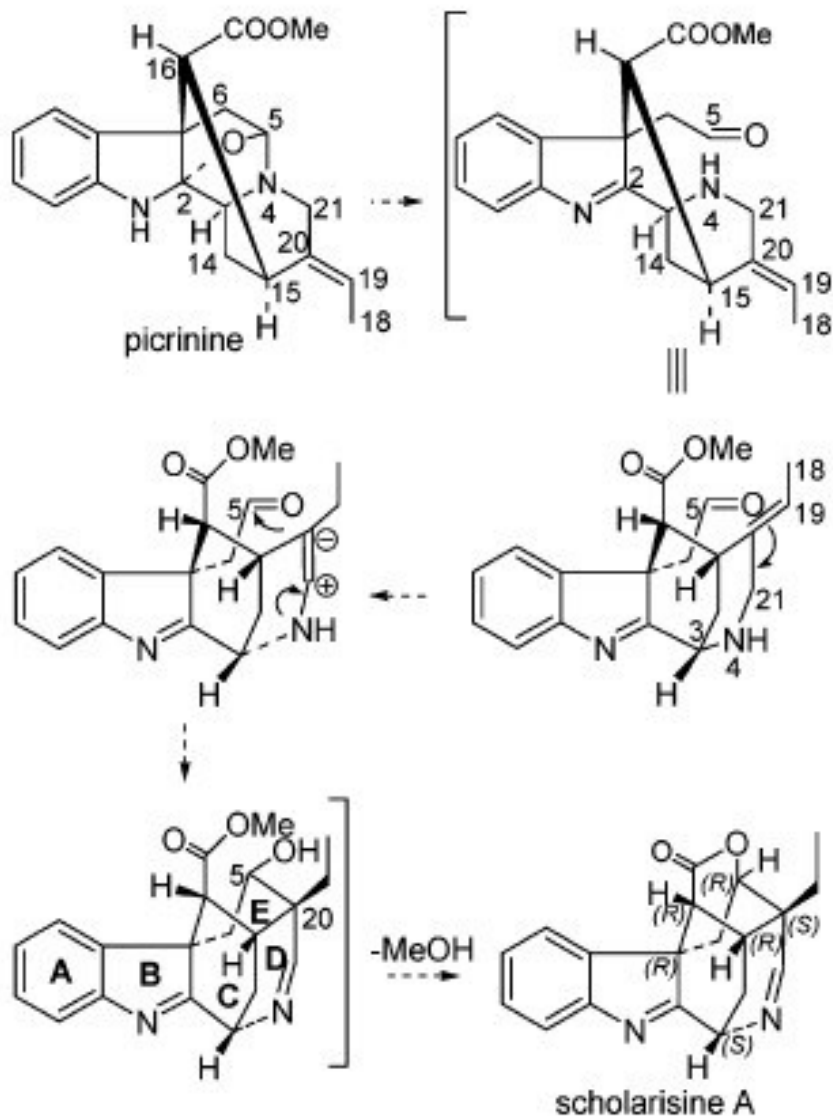
Current literature
Gong Xu
2013-11-07

About (+)-Scholarisine A

- **Monoterpenoid** indole alkaloid;
- Isolated from the leaves of *Alstonia scholaris* in 2008, a plant used in traditional Chinese medicine to treat various respiratory diseases;
- A dense, polycyclic compound:
 - an **indolenine** fused to a **strained carbocyclic cage**;
 - several tertiary and quaternary stereocenters;
 - potentially labile **imine** and **bridging lactone** functional groups.

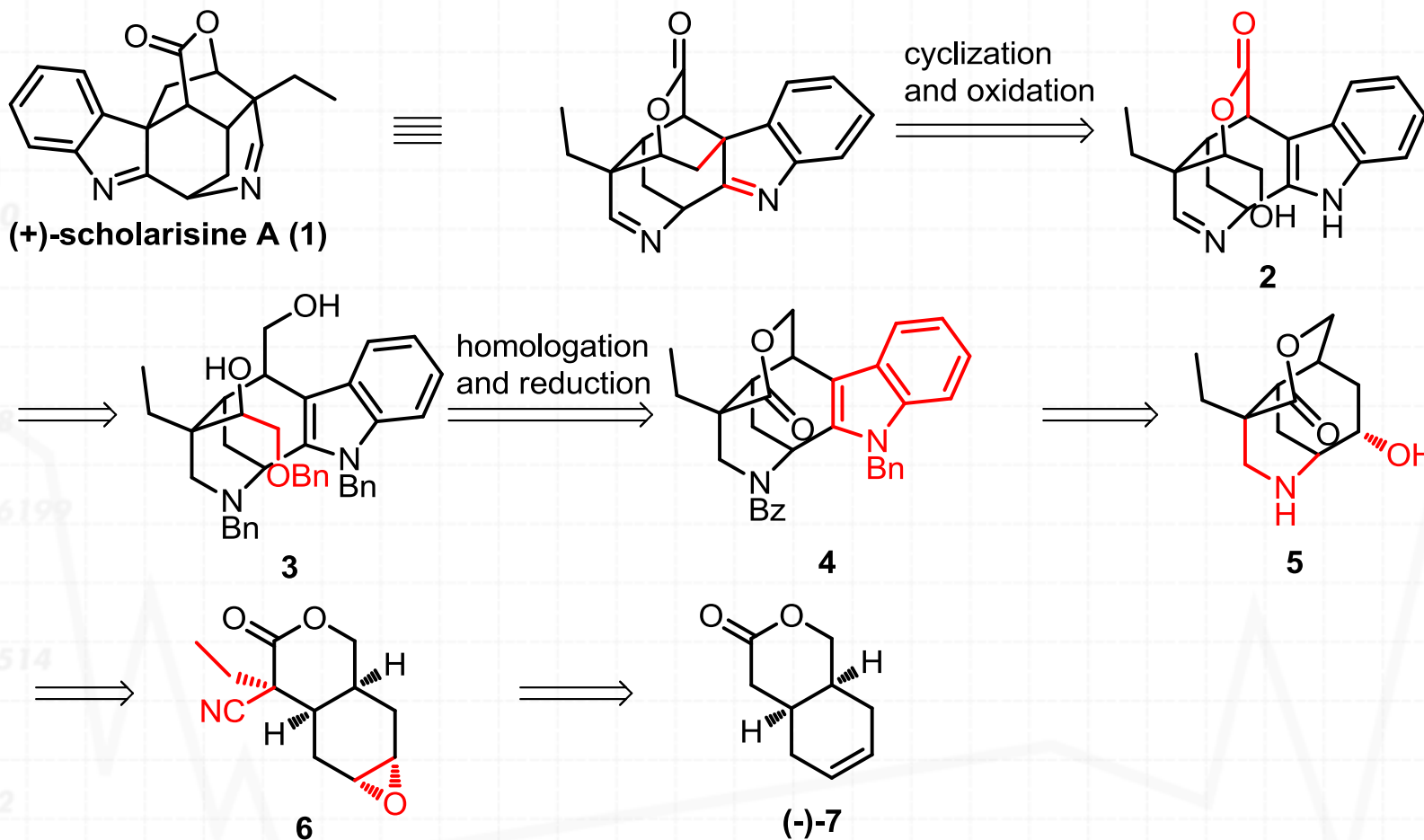


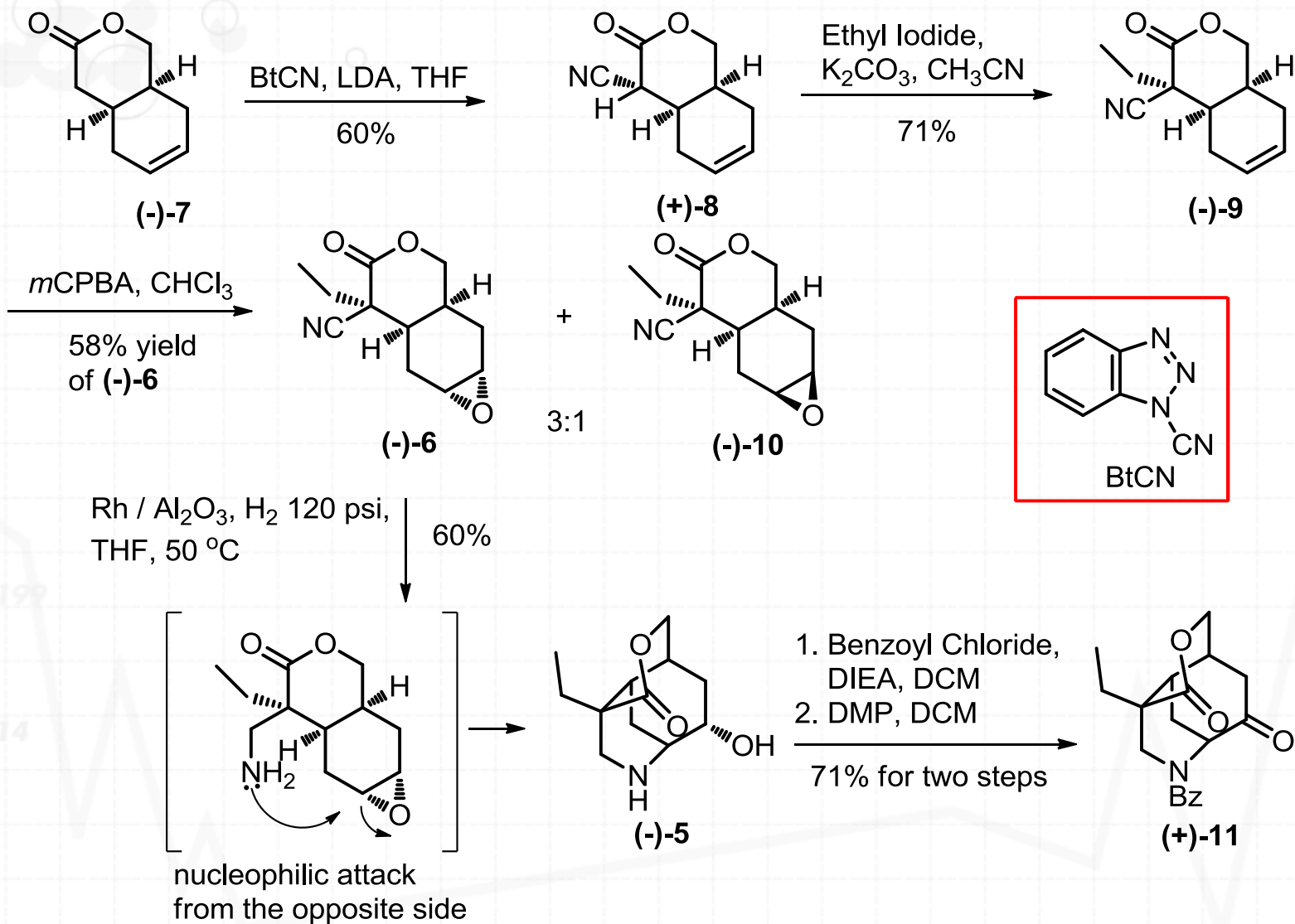
Proposed biosynthesis of Scholarisine A

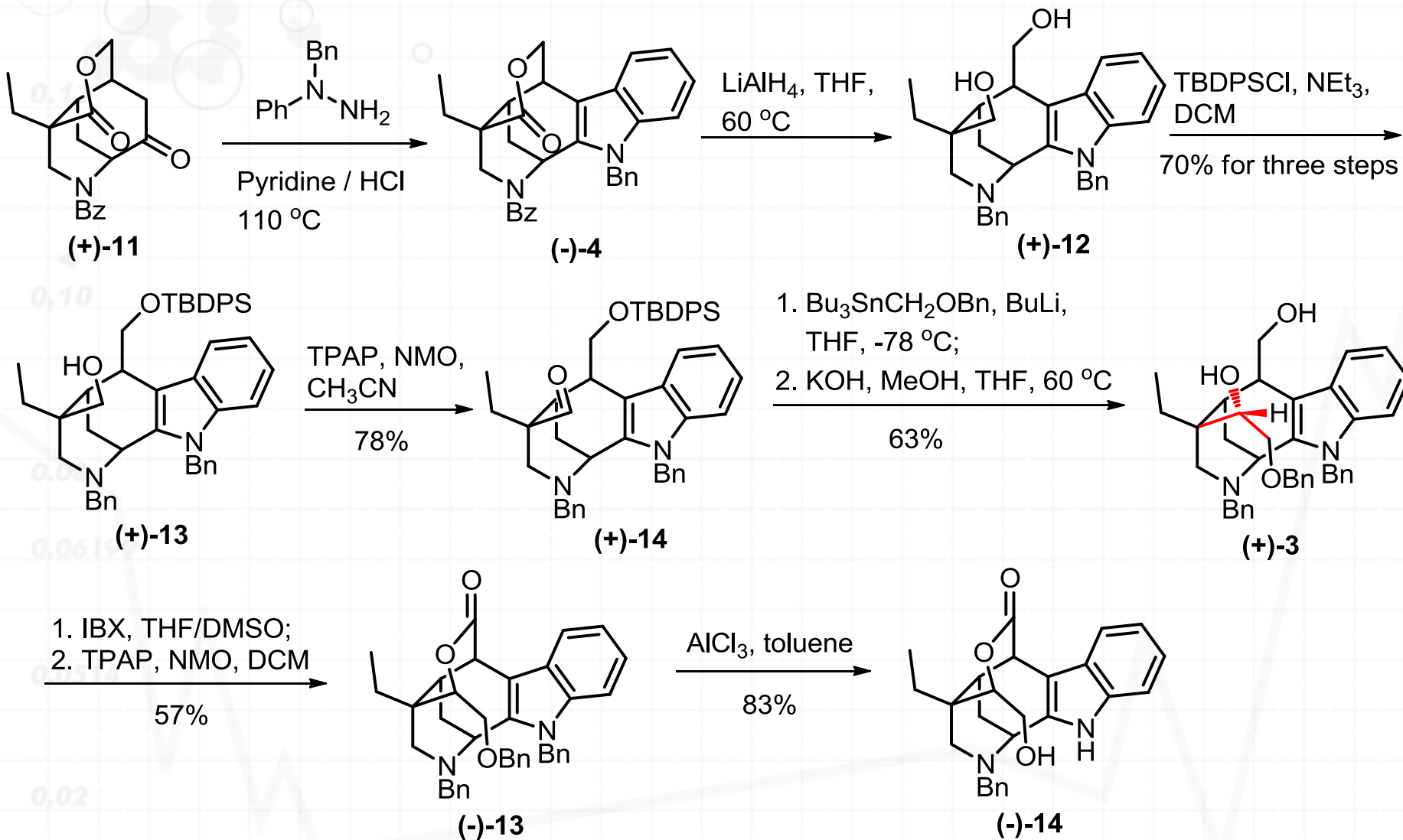


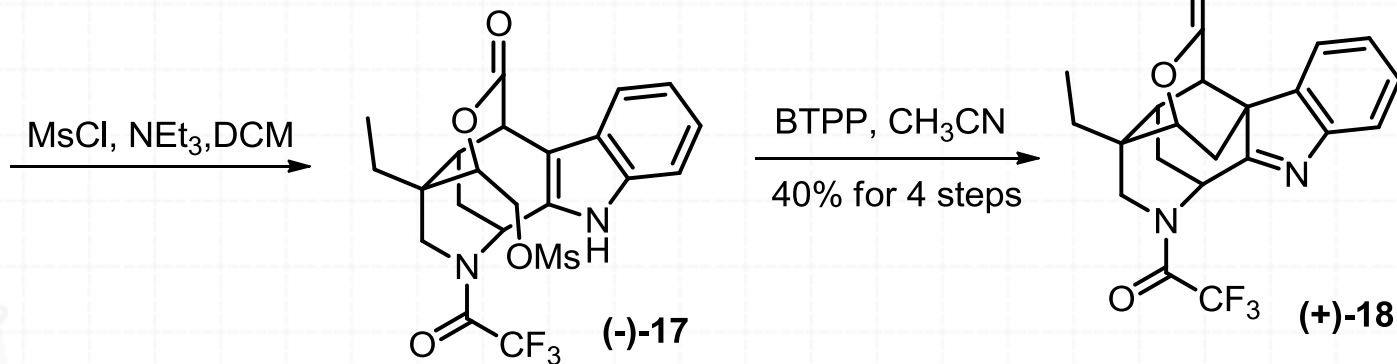
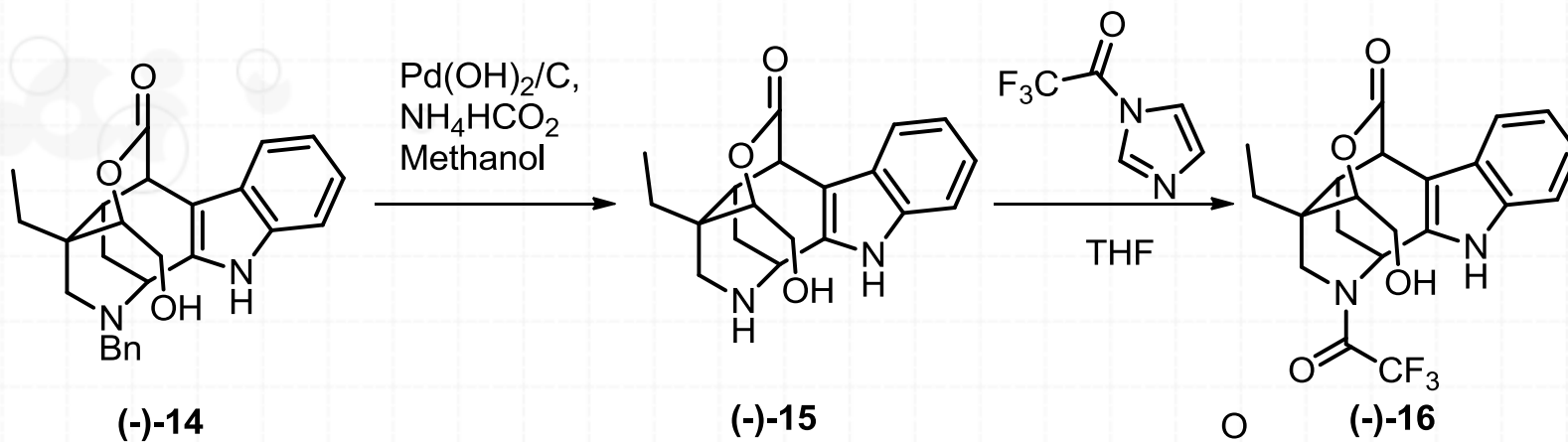
- Derived from picrinine.
- The oxygen bridge between C-2 and C-5 and the C5-N4 bond could be cleaved and formed an aldehyde carbon at C-5.
- An **enamine** among N-4, C-21, and 20 might be formed by double bond migration from C-19/20 to C-20/21 of the intermediate.
- Nucleophilic addition to form a new C-C bond between C20/5 and an **imine** at N4/C21.
- Formation of a **lactone bridge ring** through an intramolecular condensation reaction.

First total synthesis of (+)-Scholarisine A by Smith



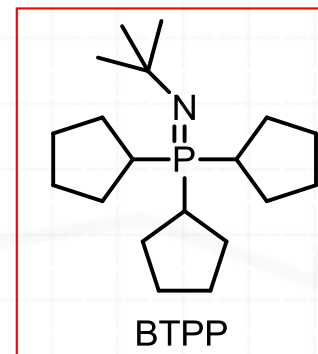
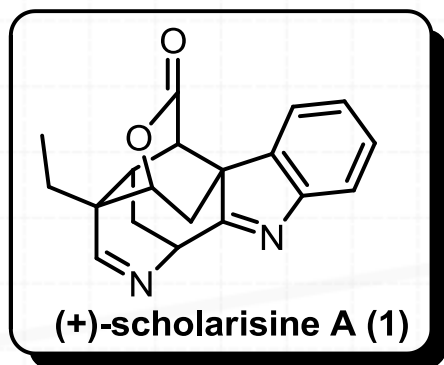




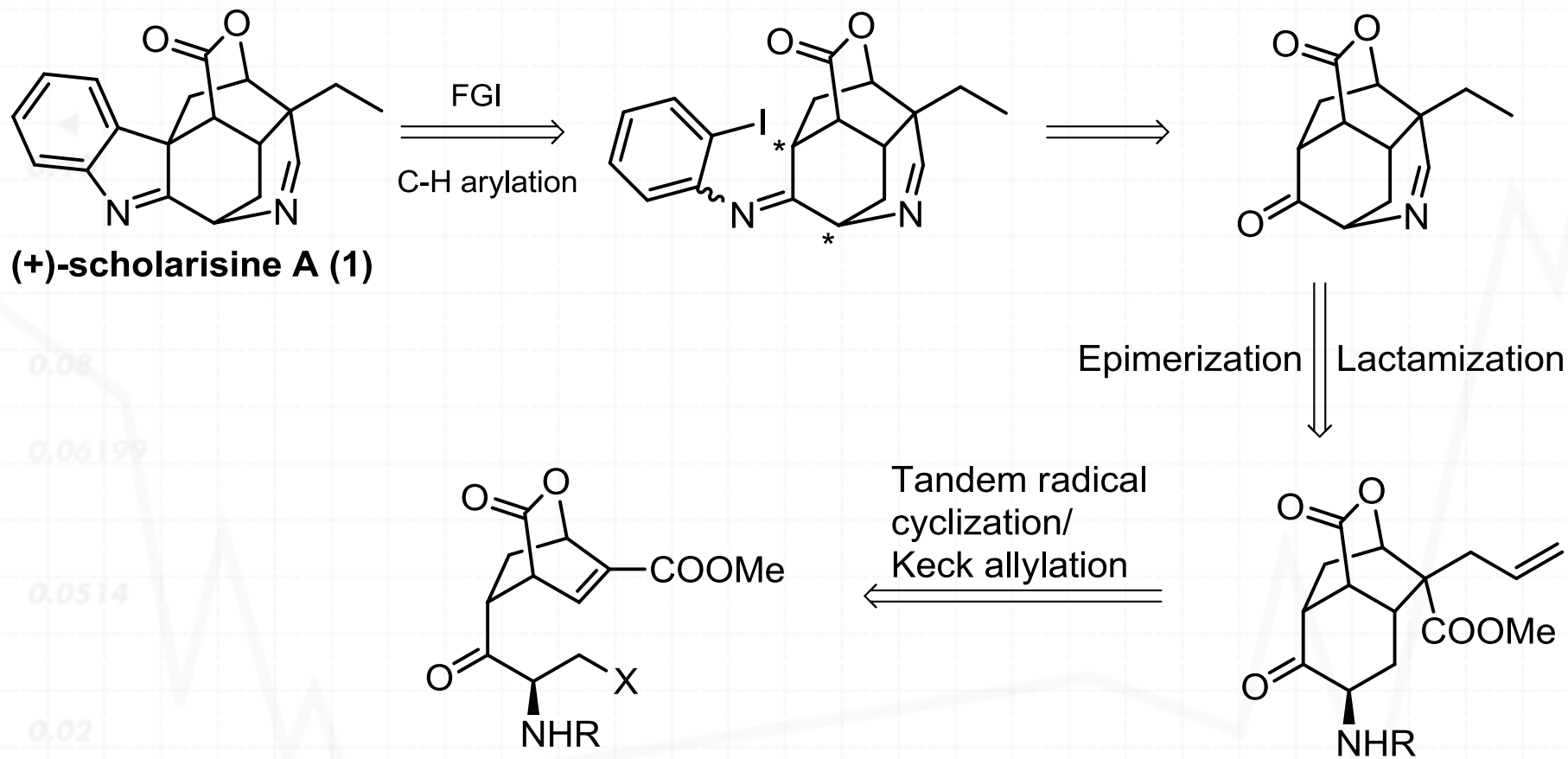


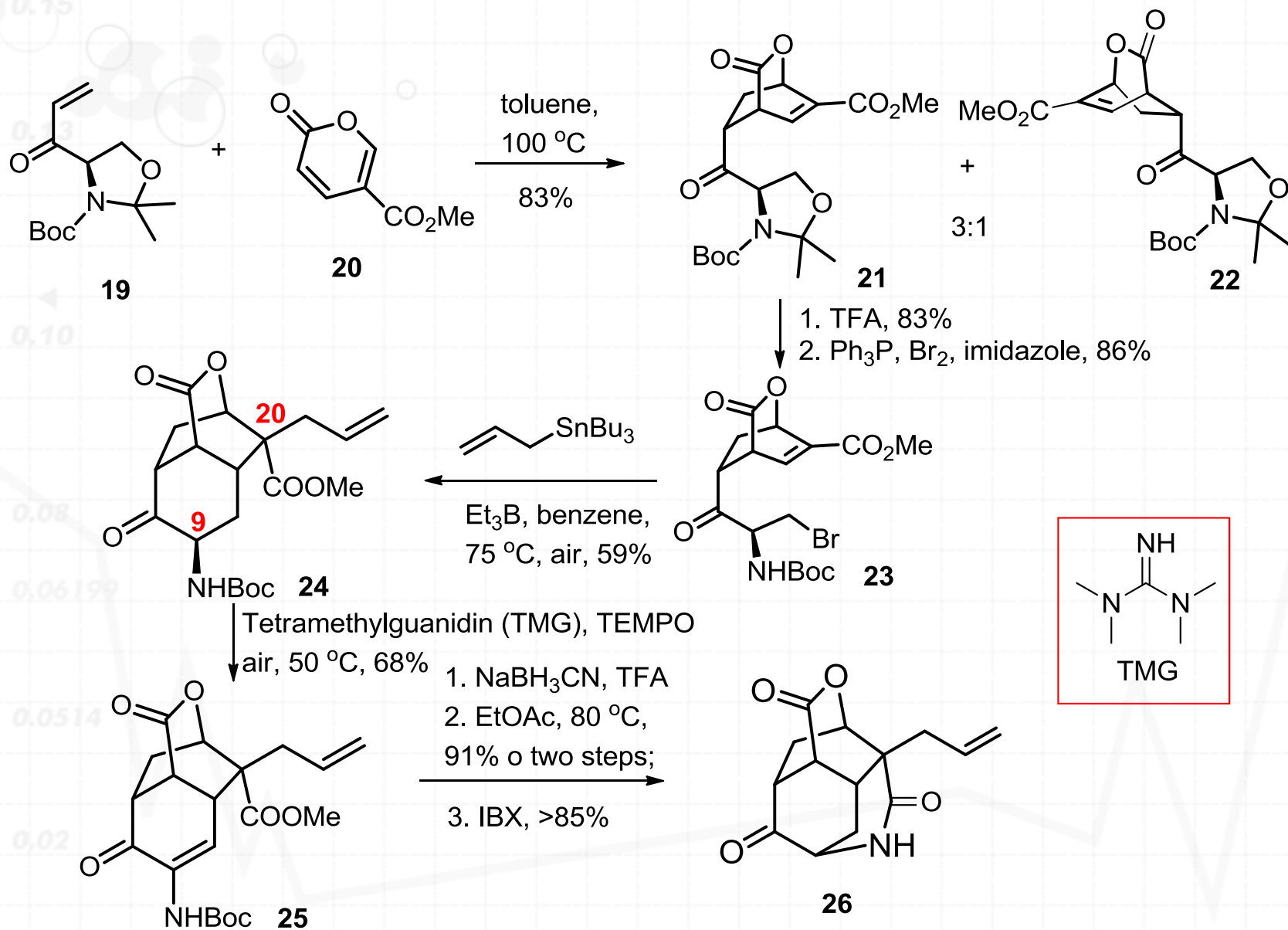
1. K_2CO_3 (aq),
Methanol
2. PhIO , DCM

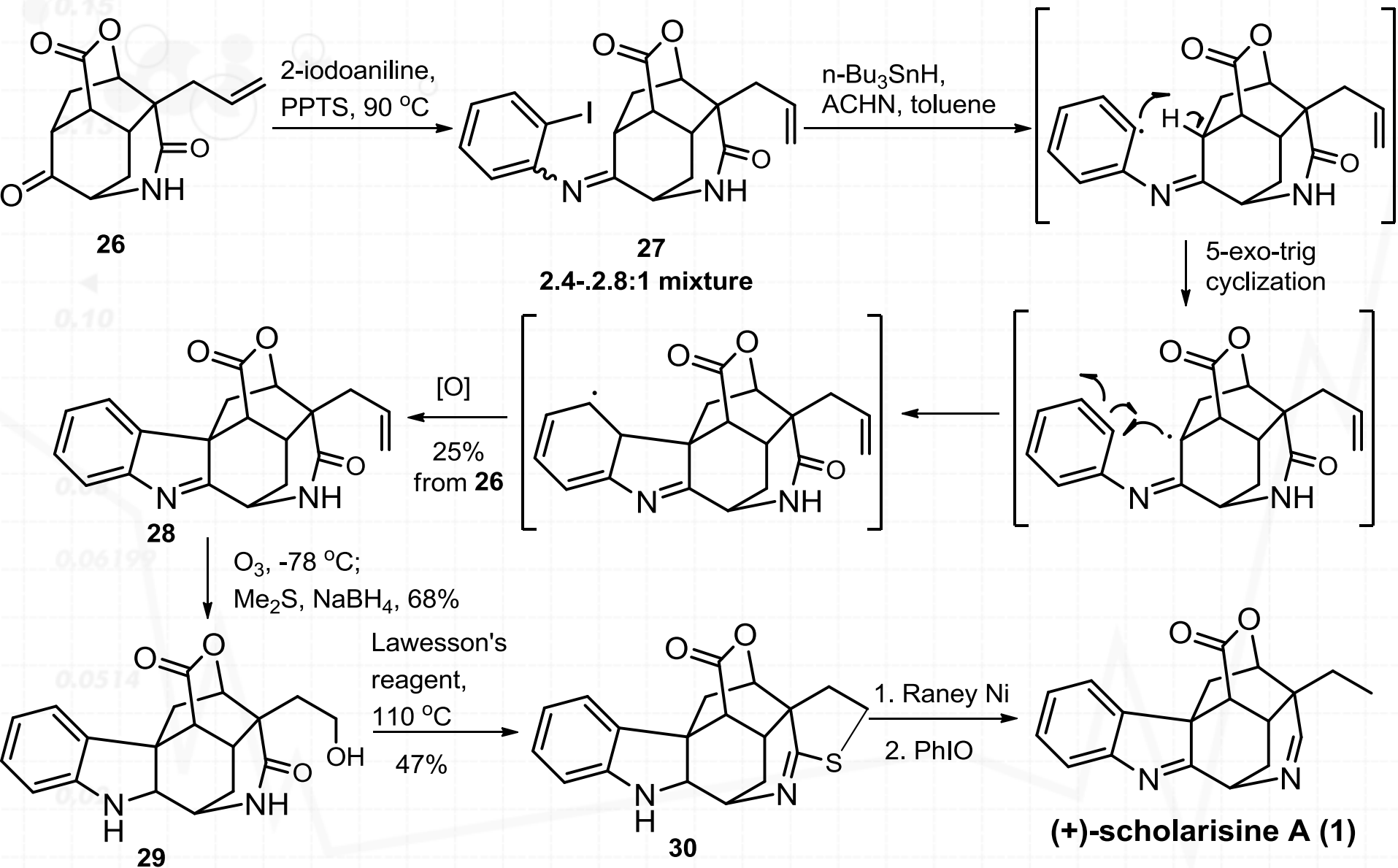
77%



Total synthesis of (+)-Scholarisine A by Snyder







Summary

- ❖ 14 steps from known enone **19** (**15 steps** from commercial materials).
- ❖ Key discoveries :
 - an efficient and diastereoselective pyrone **Diels–Alder reaction** to rapidly form the appropriately functionalized [2.2.2]-bicycle;
 - a **radical cyclization/Keck allylation** to concurrently forge the [3.3.1]-bicycle and C-20 quaternary center;
 - an indolenine annulation at a nonenolizable tertiary center via a novel late-stage radical **C–H arylation**;
 - the use of a pendant hydroxyl group to facilitate the chemoselective reduction of an extremely unreactive lactam.



The background features a light gray grid. A line graph is plotted, starting at approximately 0.08, dipping to 0.02, rising to 0.05, dipping to 0.01, and then rising to 0.10. There are several data points scattered across the grid, with labels 0.15, 0.13, 0.10, 0.08, 0.06199, 0.0514, and 0.02. A faint logo of three stylized figures is visible in the upper left quadrant.

Thank you!