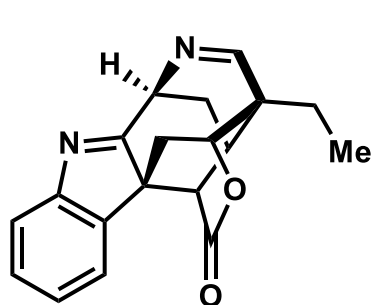


Total Synthesis of Scholarisines A, I, T, and W and Identification of Scholarisine I as a Lysosome Inhibitor

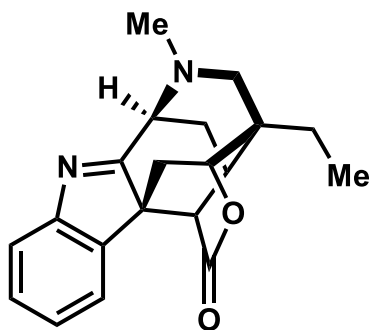
Abigail Halloran

10/01/26

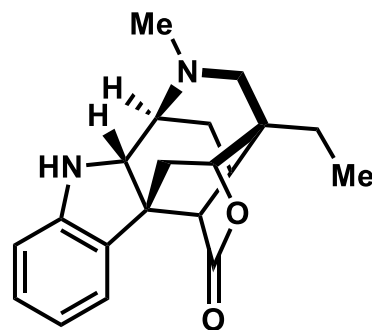
Group Meeting



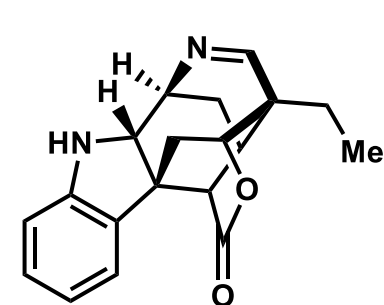
Scholarisine A



Scholarisine I



Scholarisine T



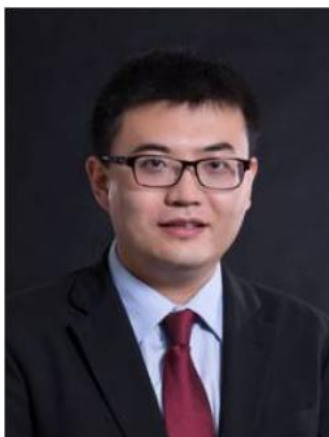
Scholarisine W

Total Synthesis of Scholarisines A, I, T, and W and Identification of Scholarisine I as a Lysosome Inhibitor

Rui Guo,[§] Fan Li,[§] Lin Wang,[§] Mengyu Ba, Zhicong Guo, Weiwei He,^{*} and Ang Li^{*}

 Cite This: *J. Am. Chem. Soc.* 2026, 148, 27023–27029

 Read Online



Ang Li

State Key Laboratory of Chemical Biology, Shanghai Institute of Organic Chemistry

Postdoc: Institute of Chemical and Engineering Sciences, Singapore

Advisor: Prof. K.C. Nicolaou

Ph.D.: Scripps Research Institute

Advisor: Prof. K.C. Nicolaou

B.Sc.: Peking University, Beijing, China
Advisor: Prof. Zhen Yang



Weiwei He

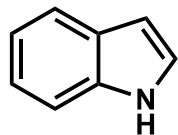
School of Pharmacy
East China University of Science and Technology
Shanghai, China

Postdoc: Scripps Research Institute

Ph.D.: Cell and Molecular Biology
The Scripps Research Institute

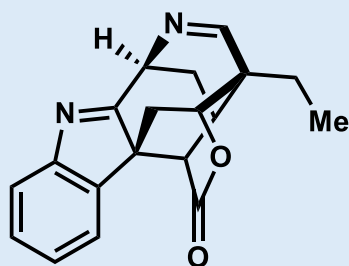
B.Sc.: Biology
Shantou University

Investigation of the scholarisine family as autophagy inhibitors



Indole alkaloids

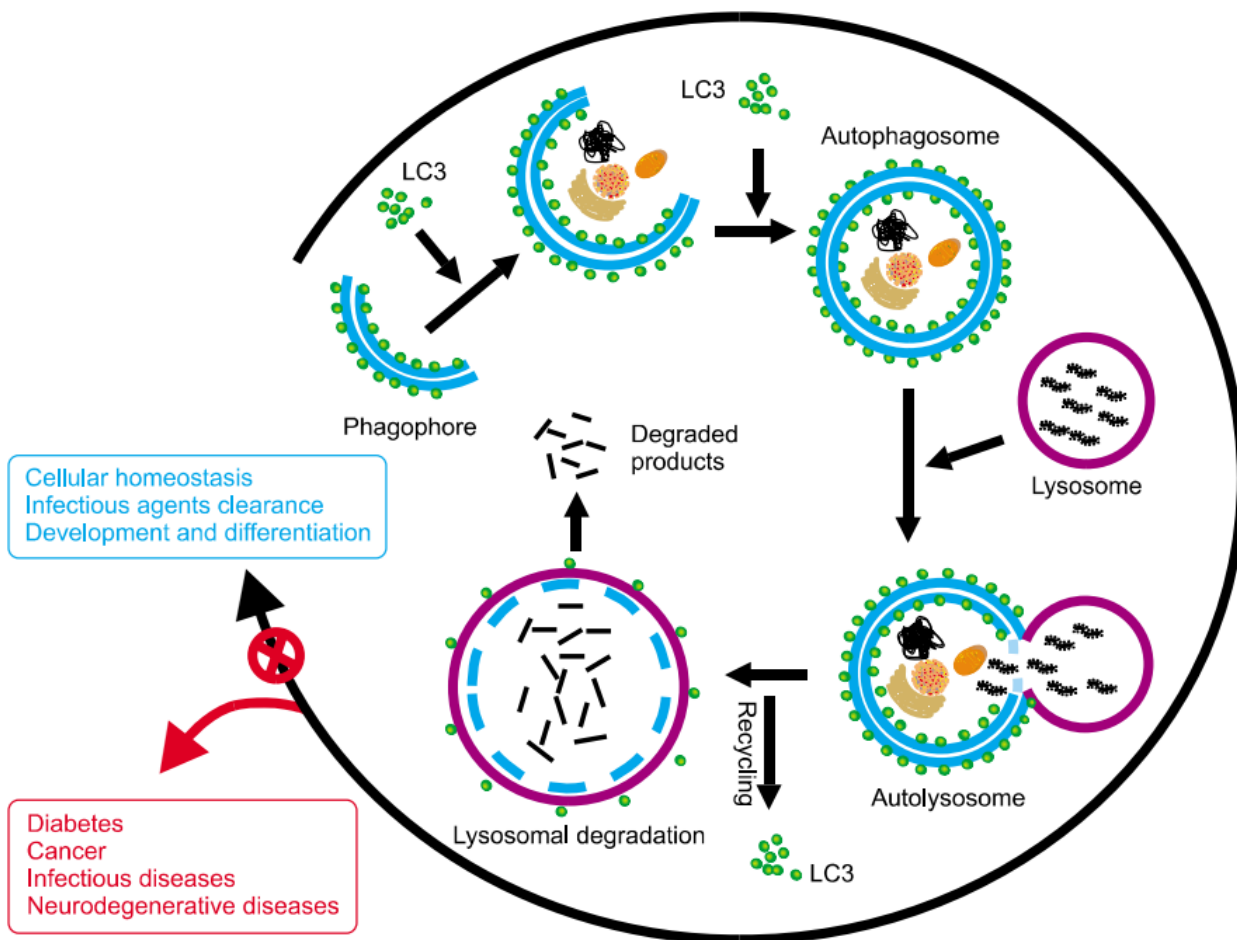
Very rich in
pharmacological activities



Scholarisine A

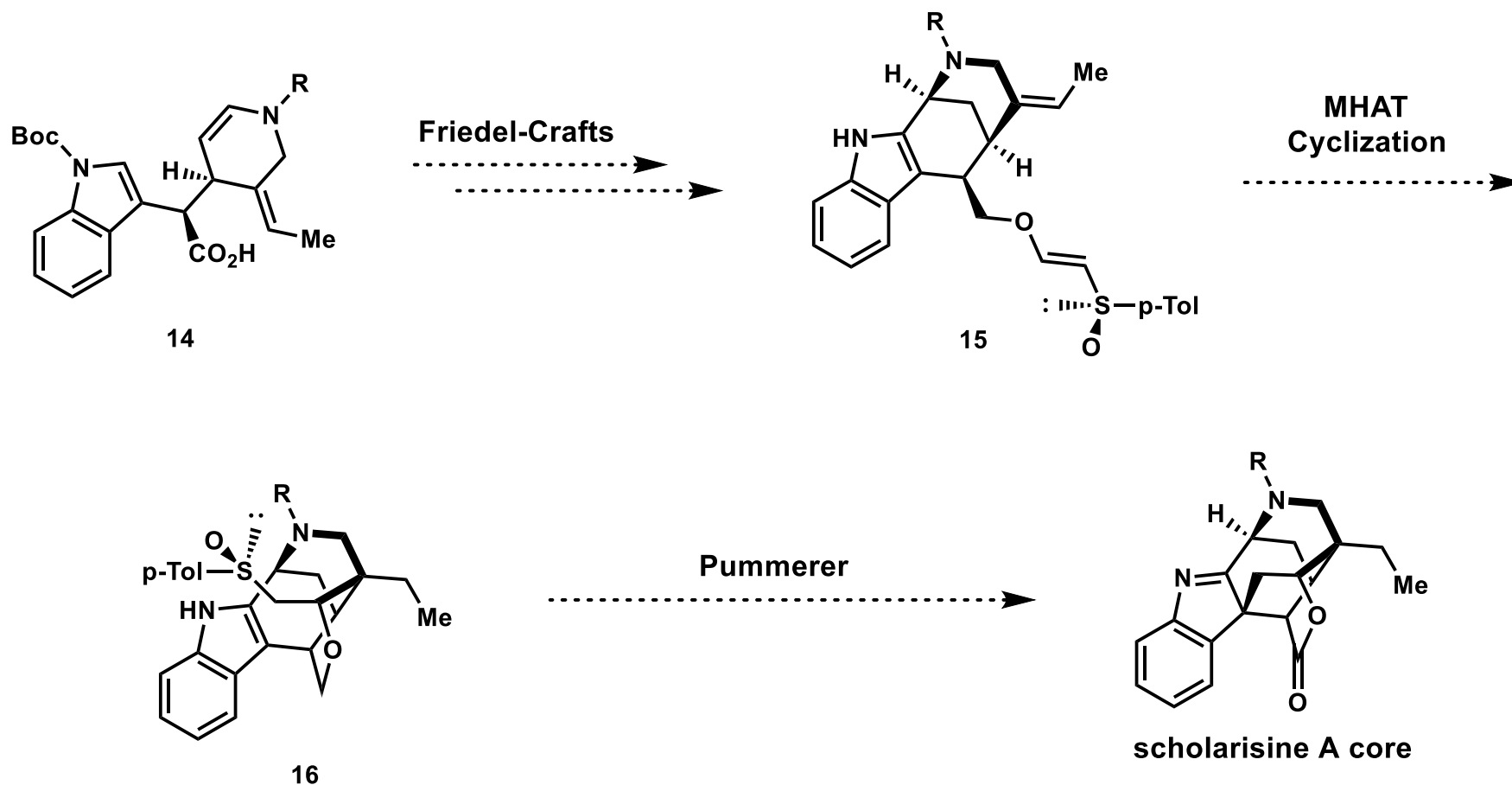
Isolated from *Alstonia scholaris* in 2008

Two reported syntheses from
A. B. Smith in 2012 and
Snyder in 2013

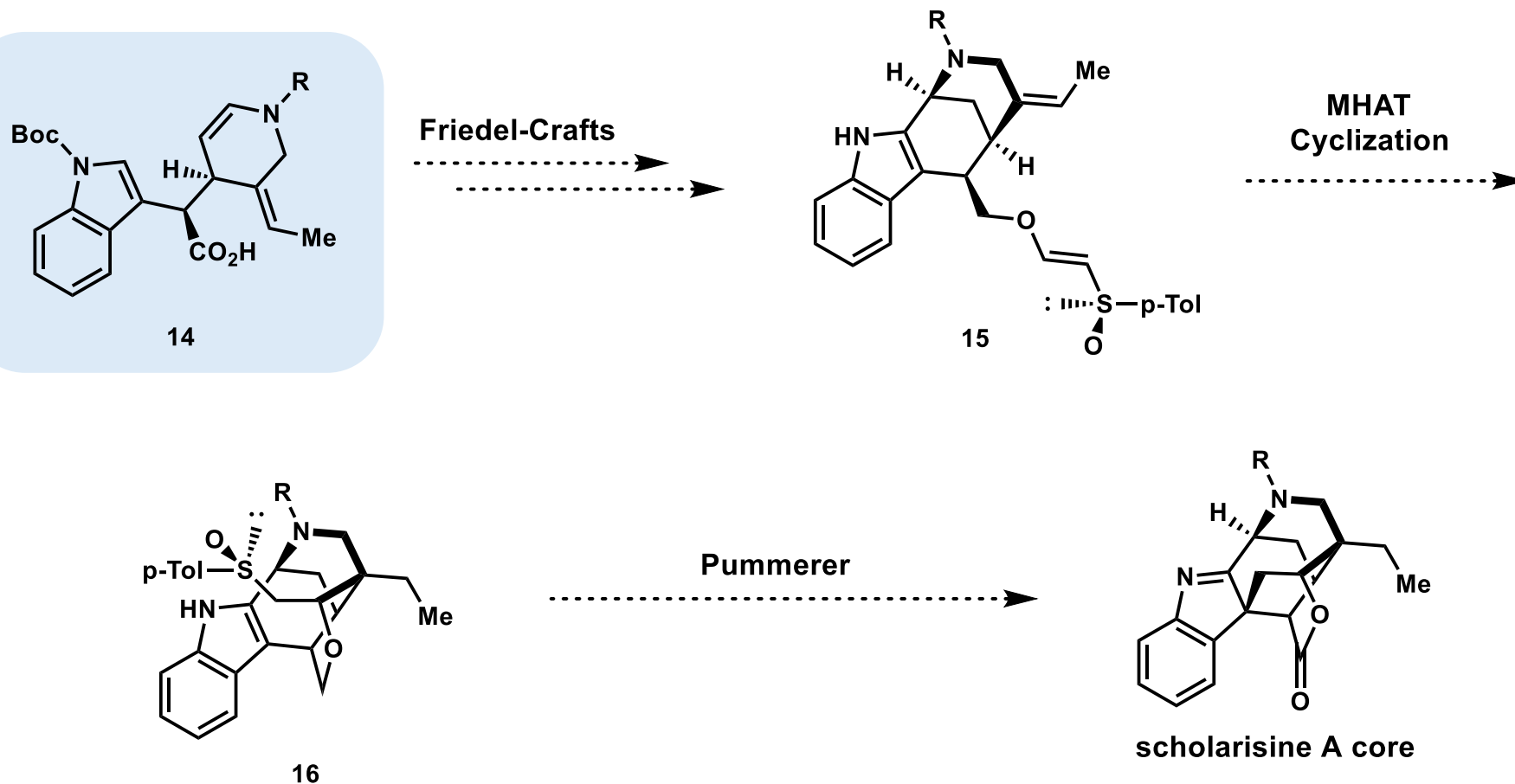


Report a 13 step and scalable strategy to the scholarisine A subfamily

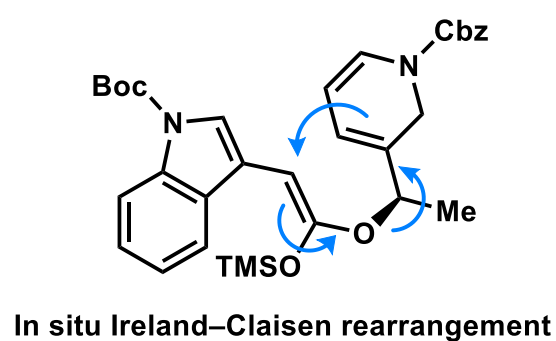
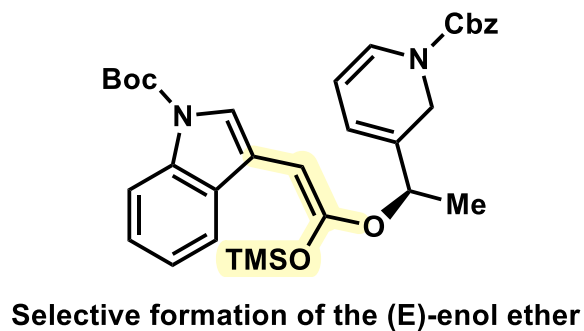
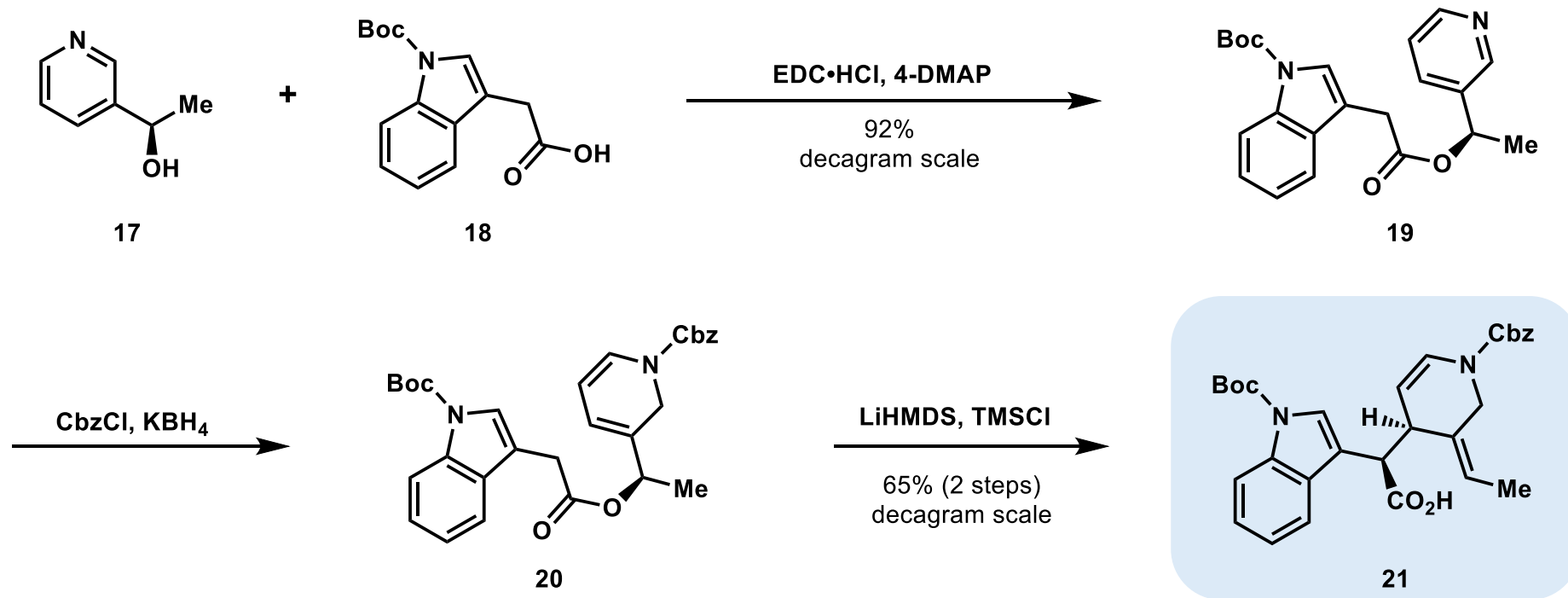
Devised route to the hexacyclic core of the scholarisine A subfamily



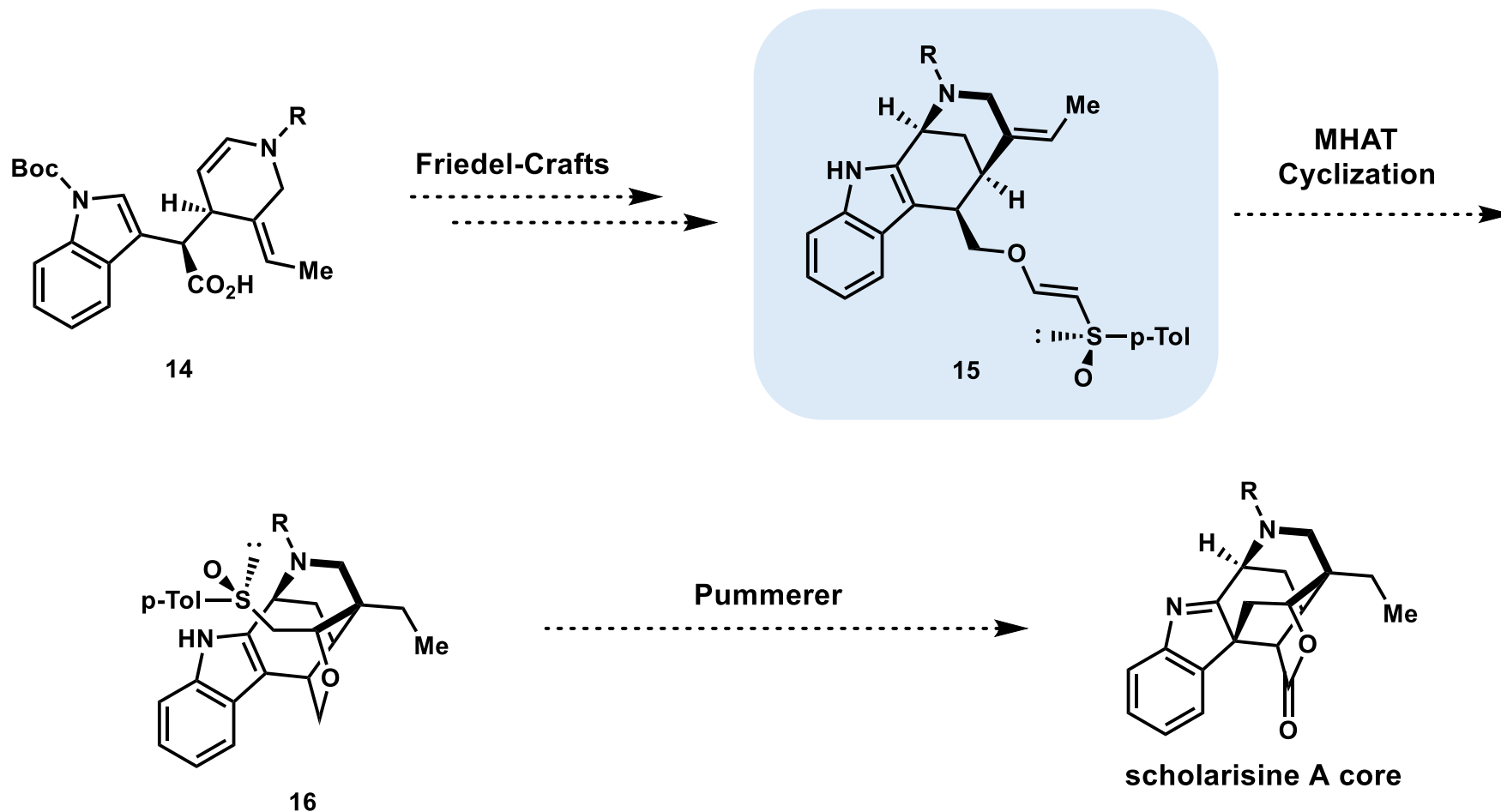
Devised route to the hexacyclic core of the scholarisine A subfamily



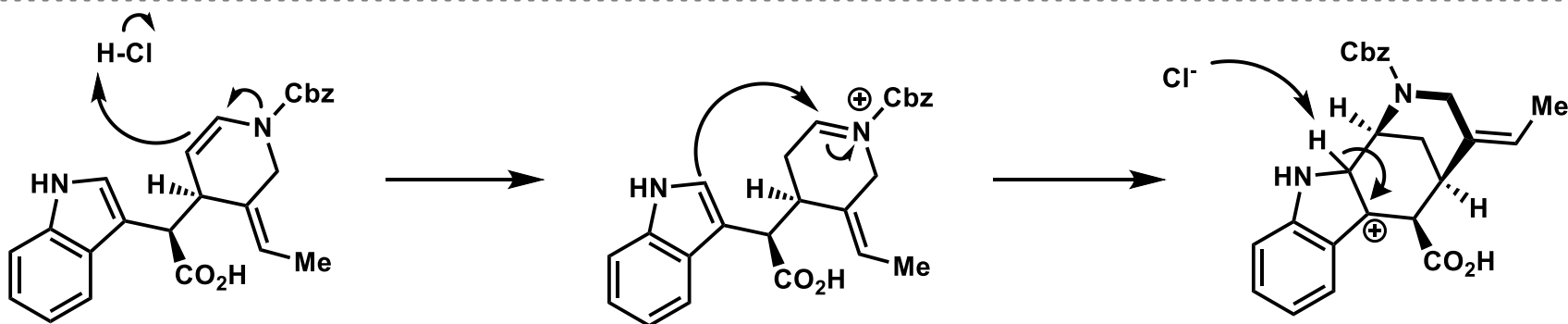
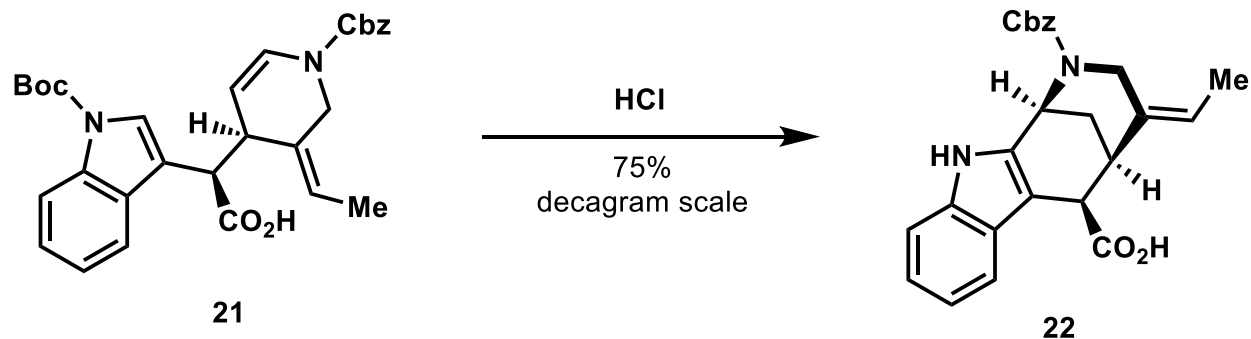
Pathway to Carboxylic Acid (21)



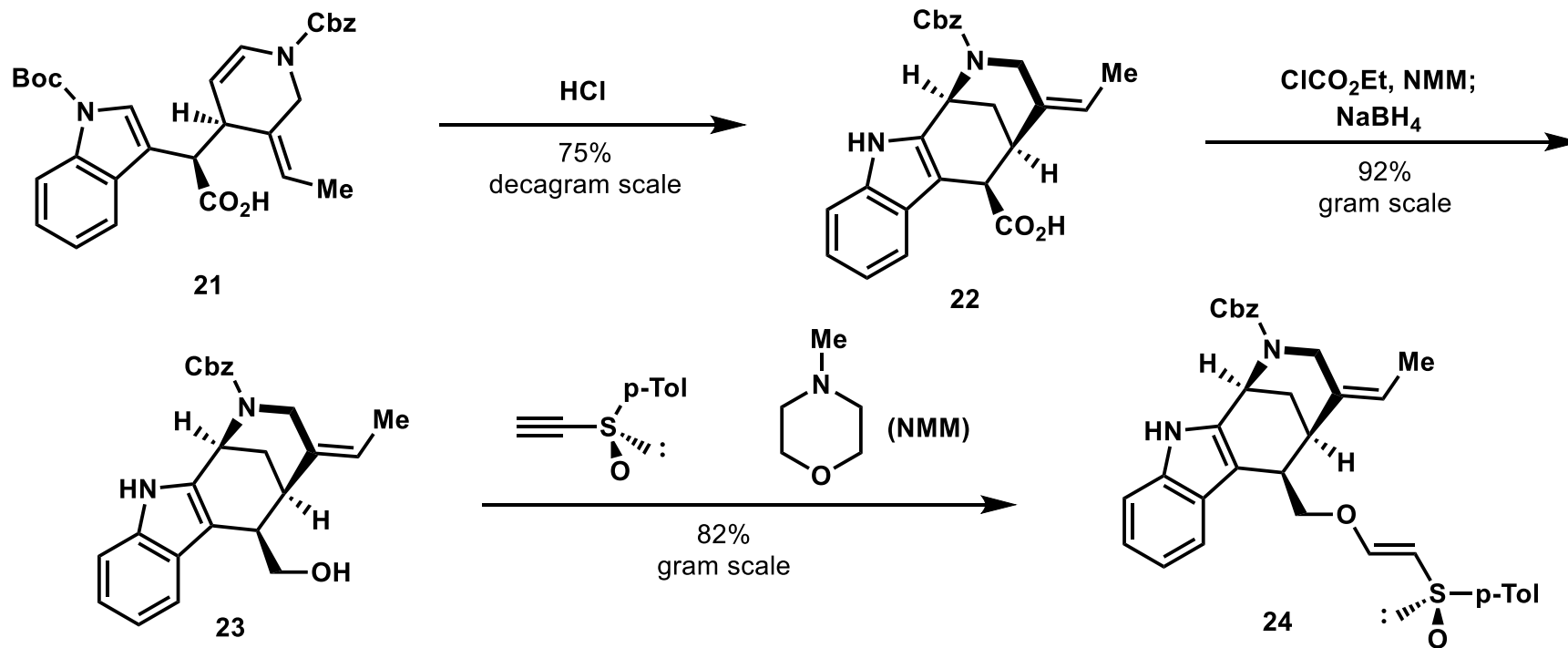
Devised route to the hexacyclic core of the scholarisine A subfamily



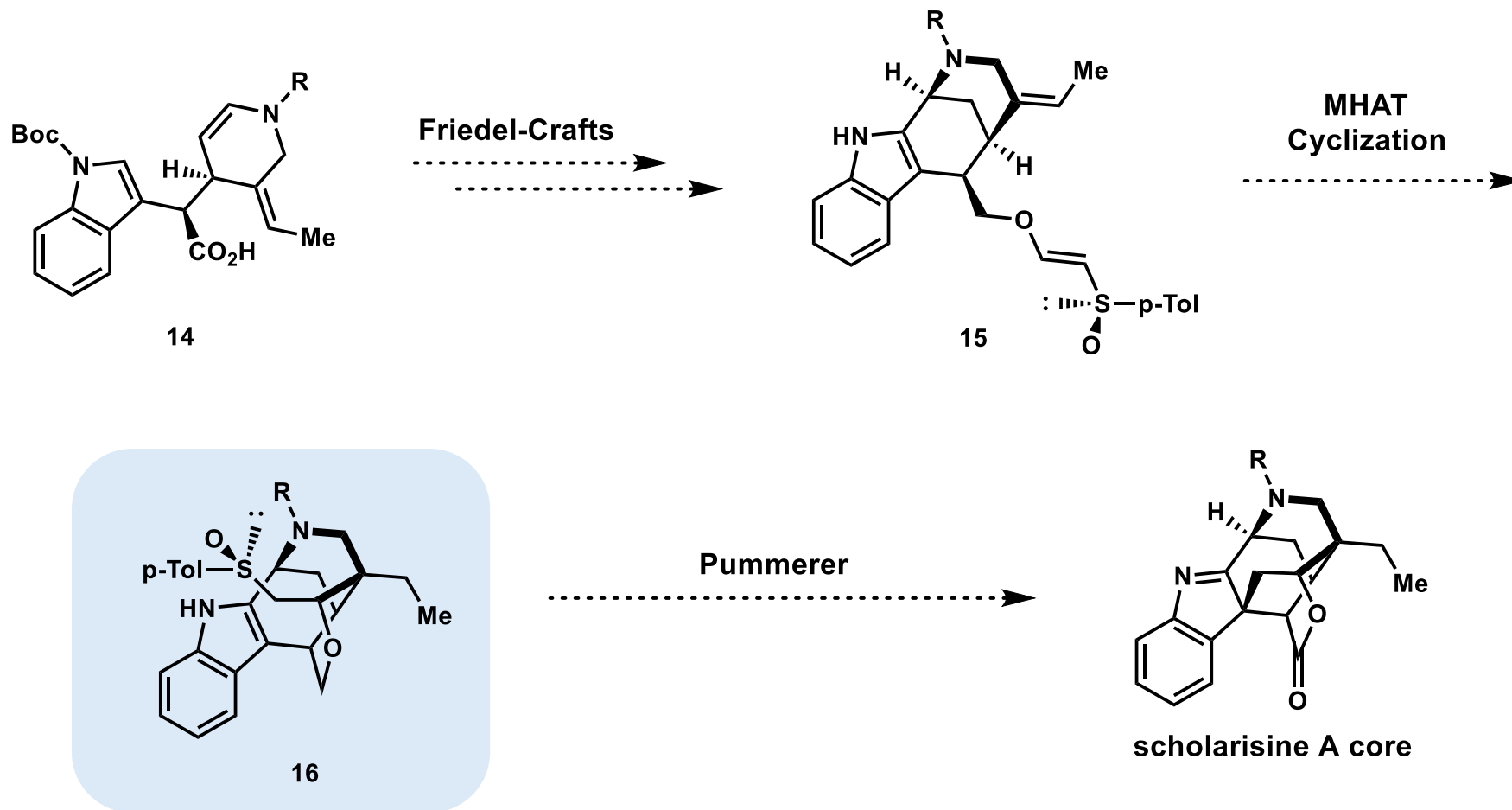
Pathway to compound 24 as a radical cyclization substrate



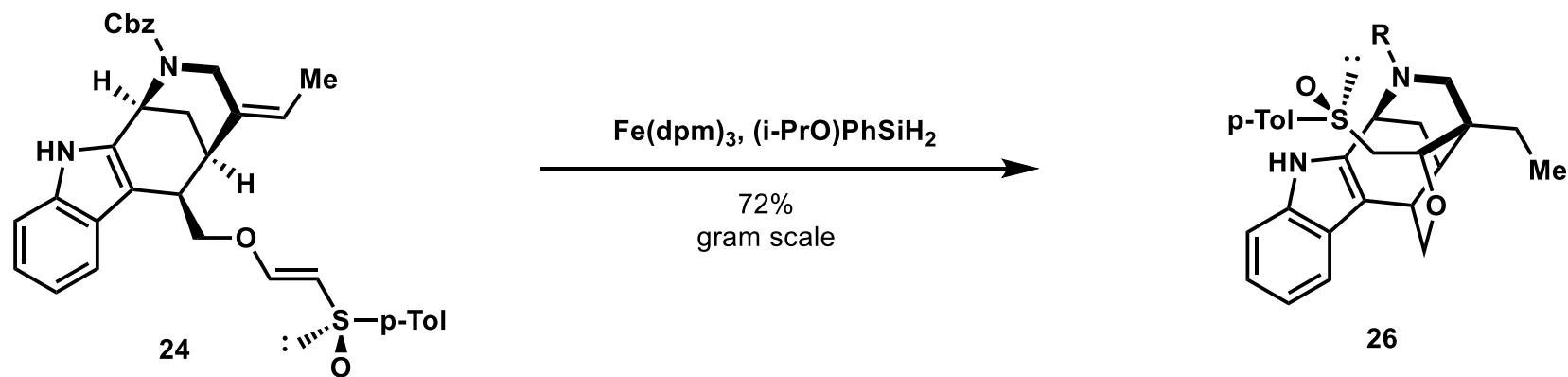
Pathway to compound 24 as a radical cyclization substrate



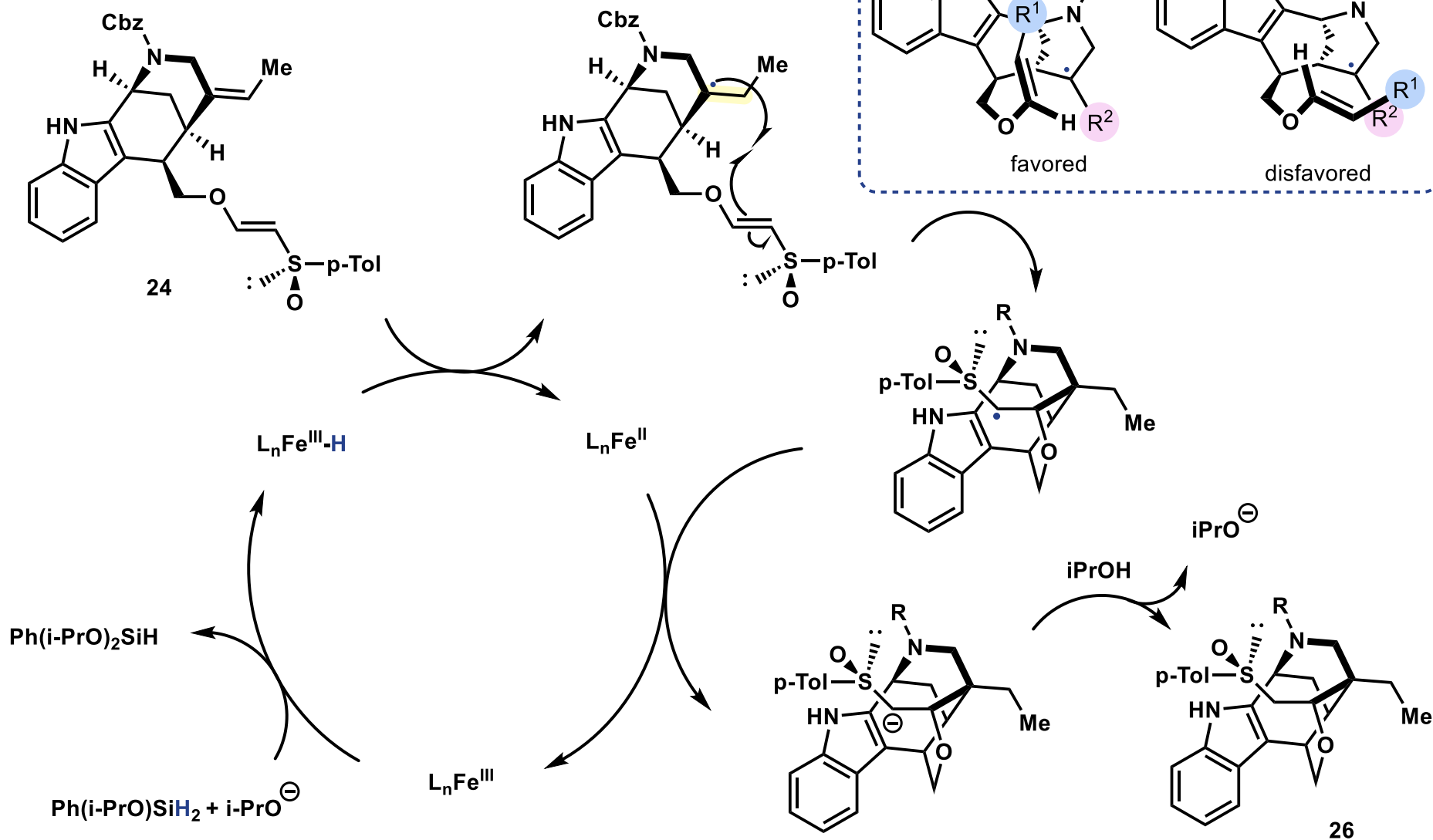
Devised route to the hexacyclic core of the scholarisine A subfamily



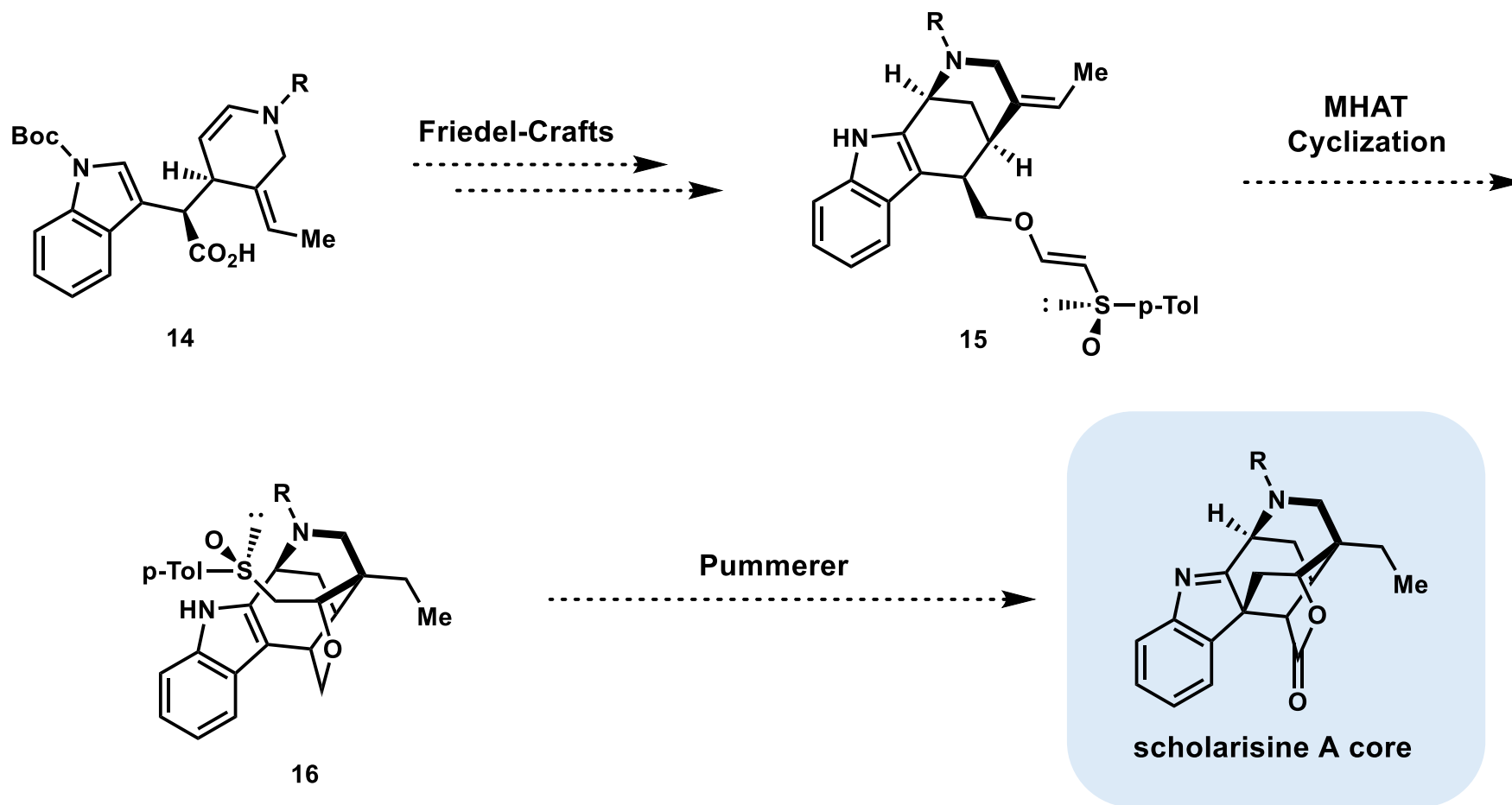
MHAT-Mediated Radical Cyclization of 24



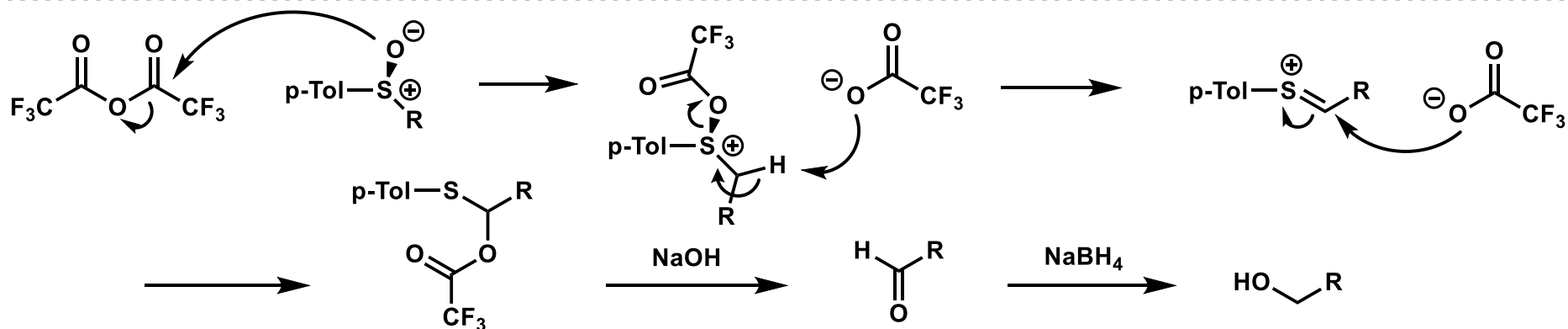
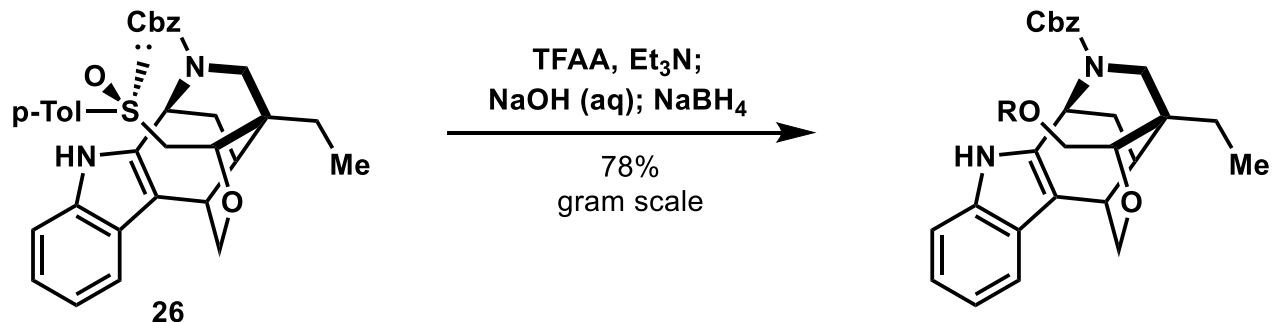
MHAT-Mediated Radical Cyclization of 24



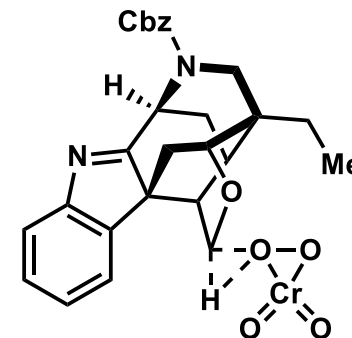
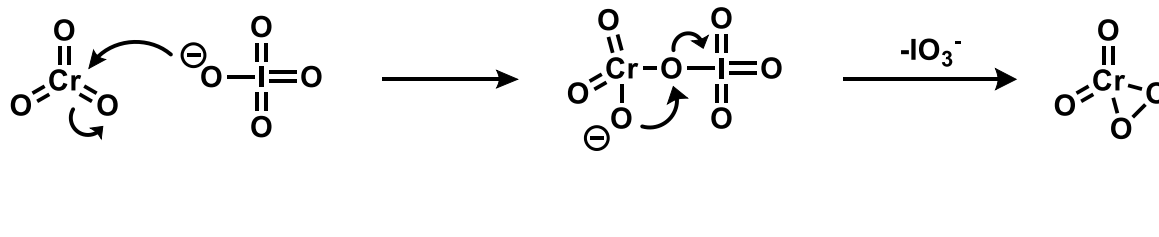
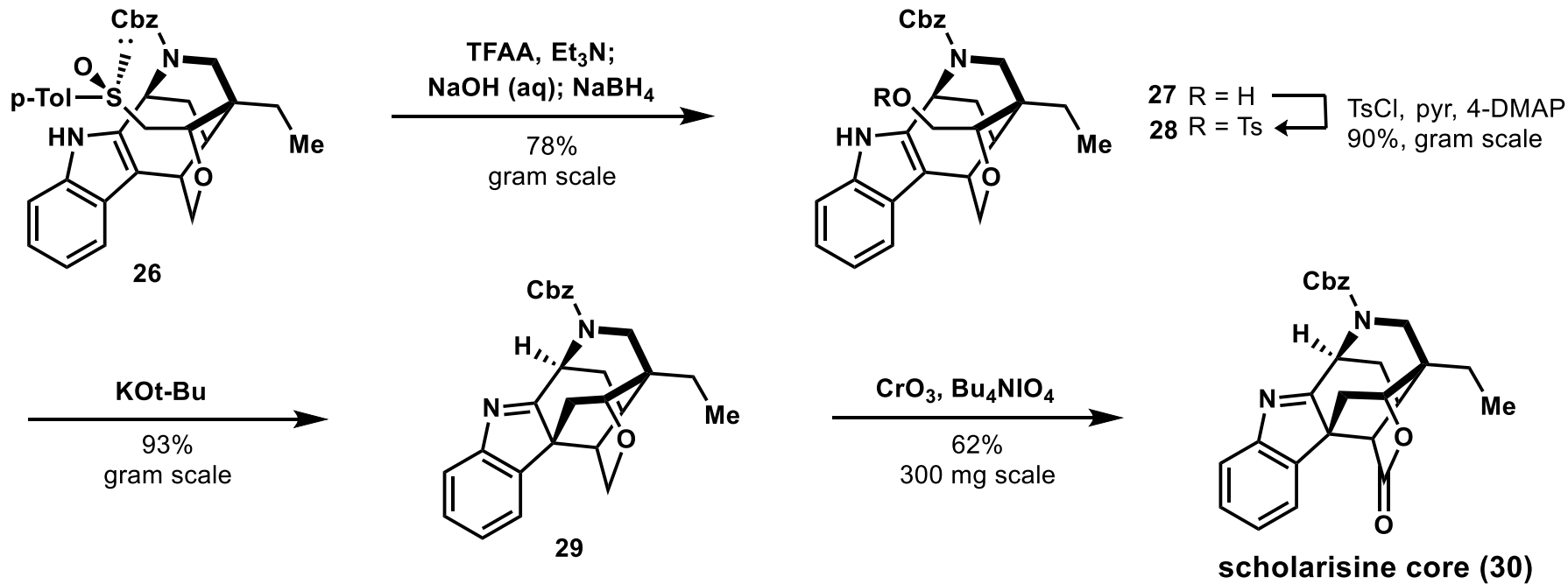
Devised route to the hexacyclic core of the scholarisine A subfamily



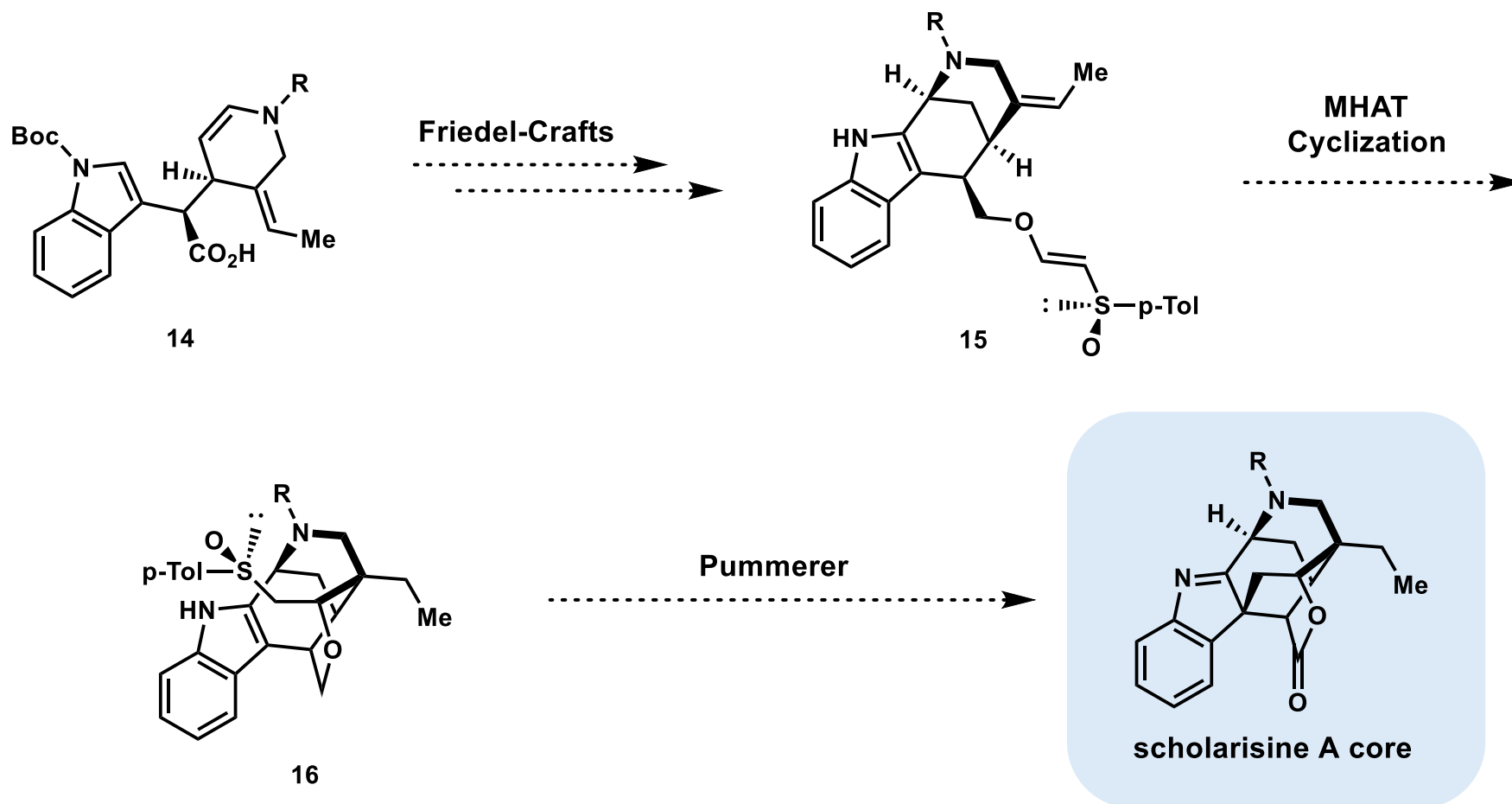
Pathway to scholarisine core



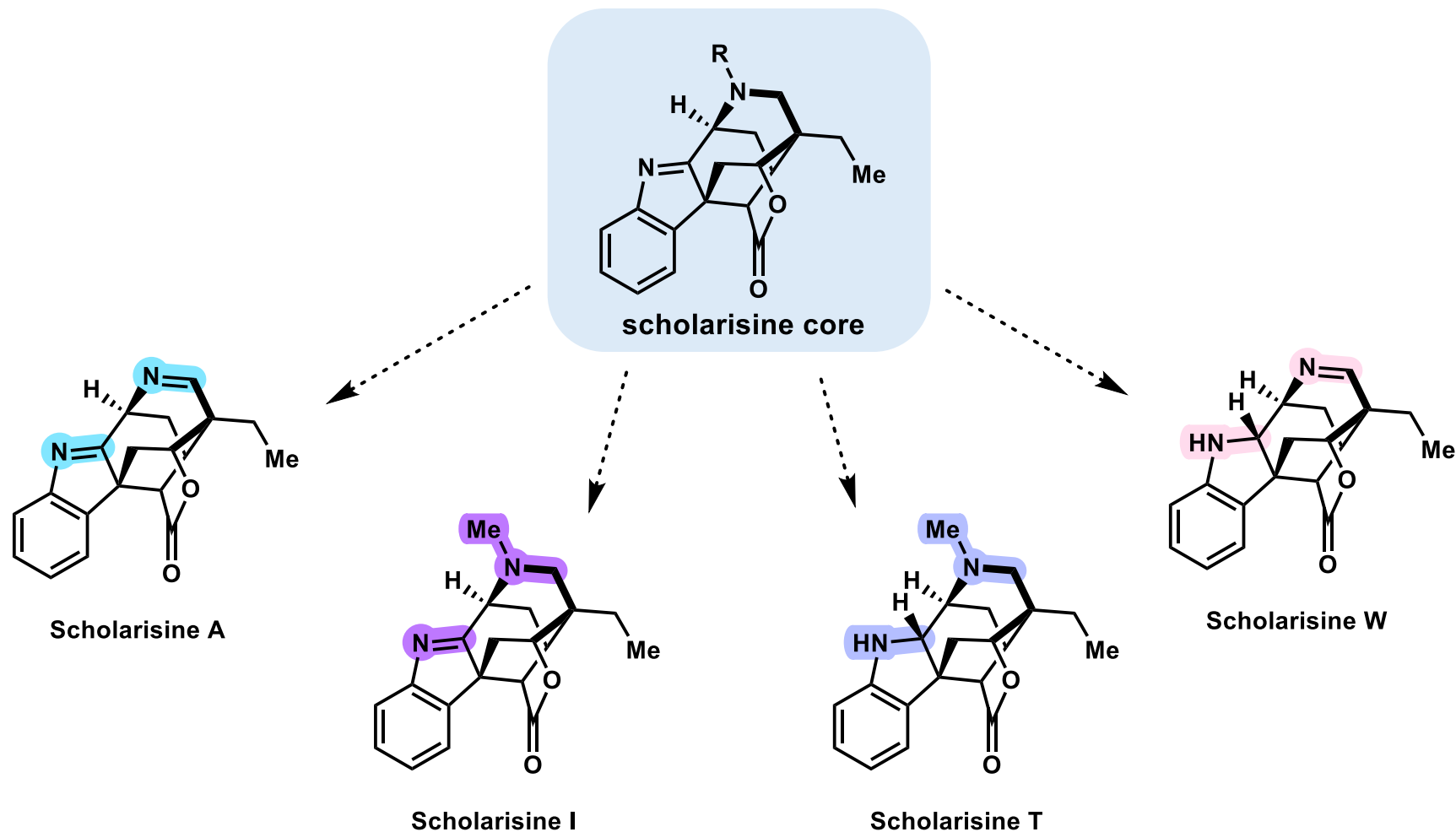
Pathway to scholarisine core



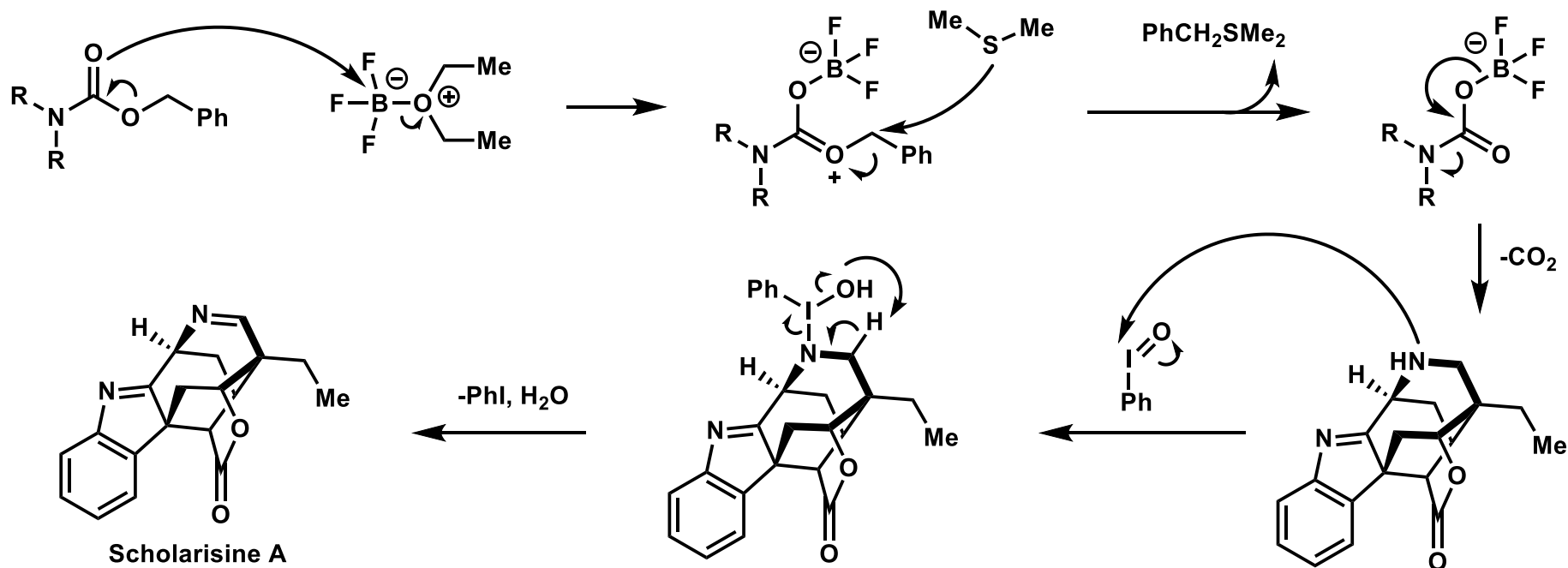
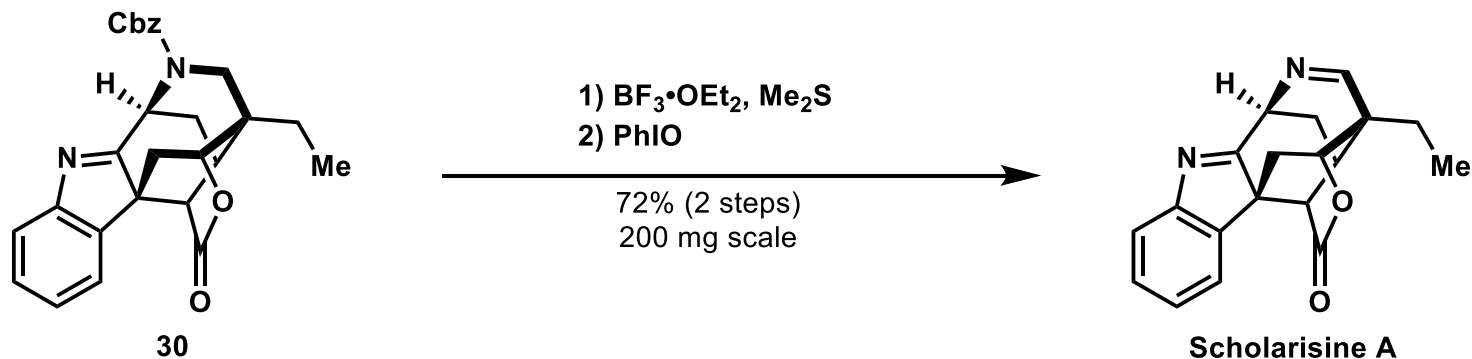
Devised route to the hexacyclic core of the scholarisine A subfamily



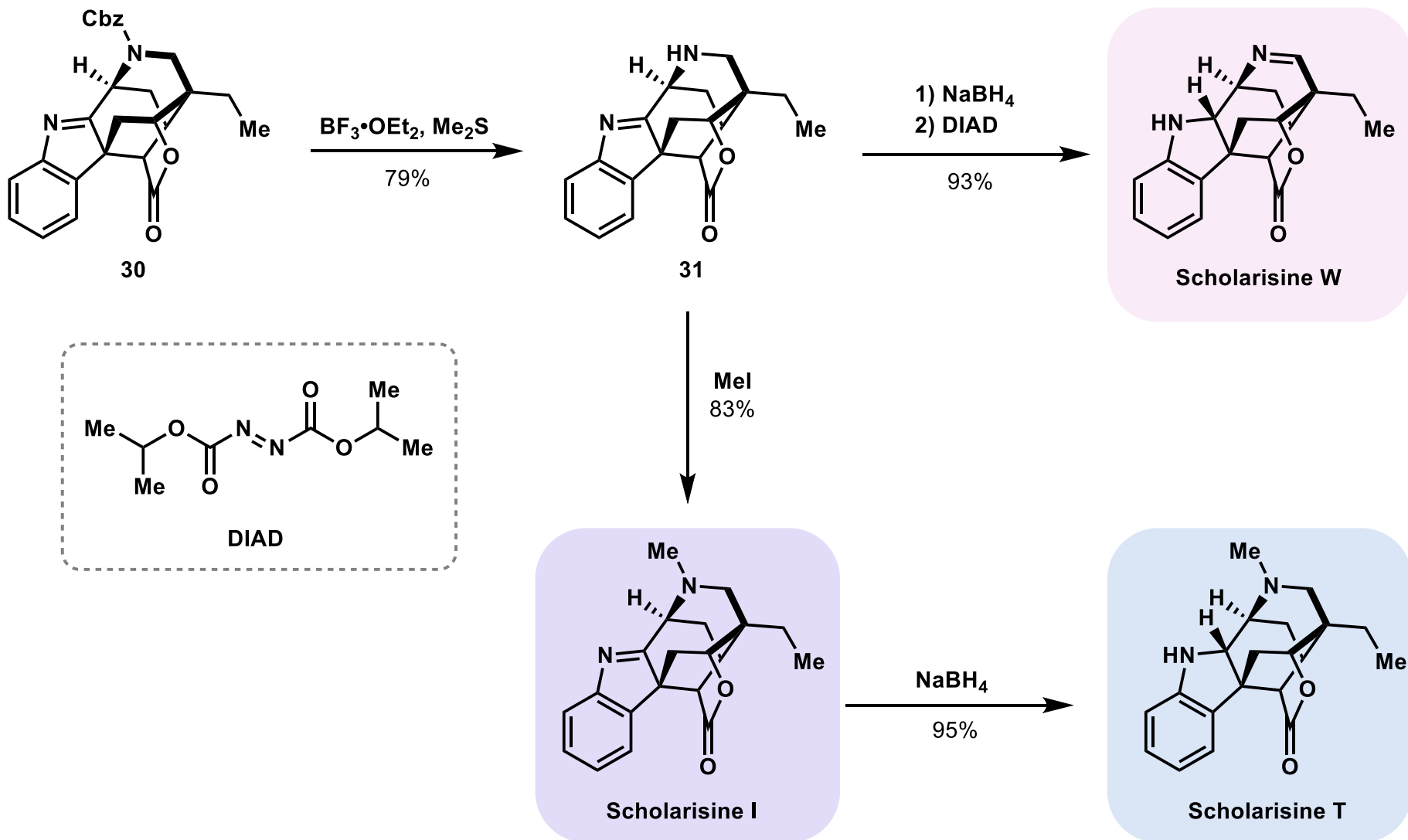
Devised route to scholarisine subfamily



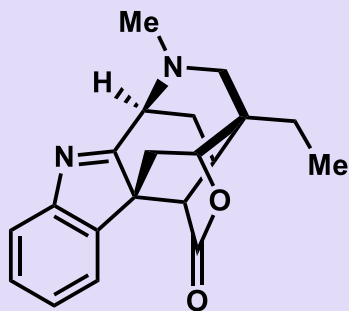
Pathway to scholarisine A



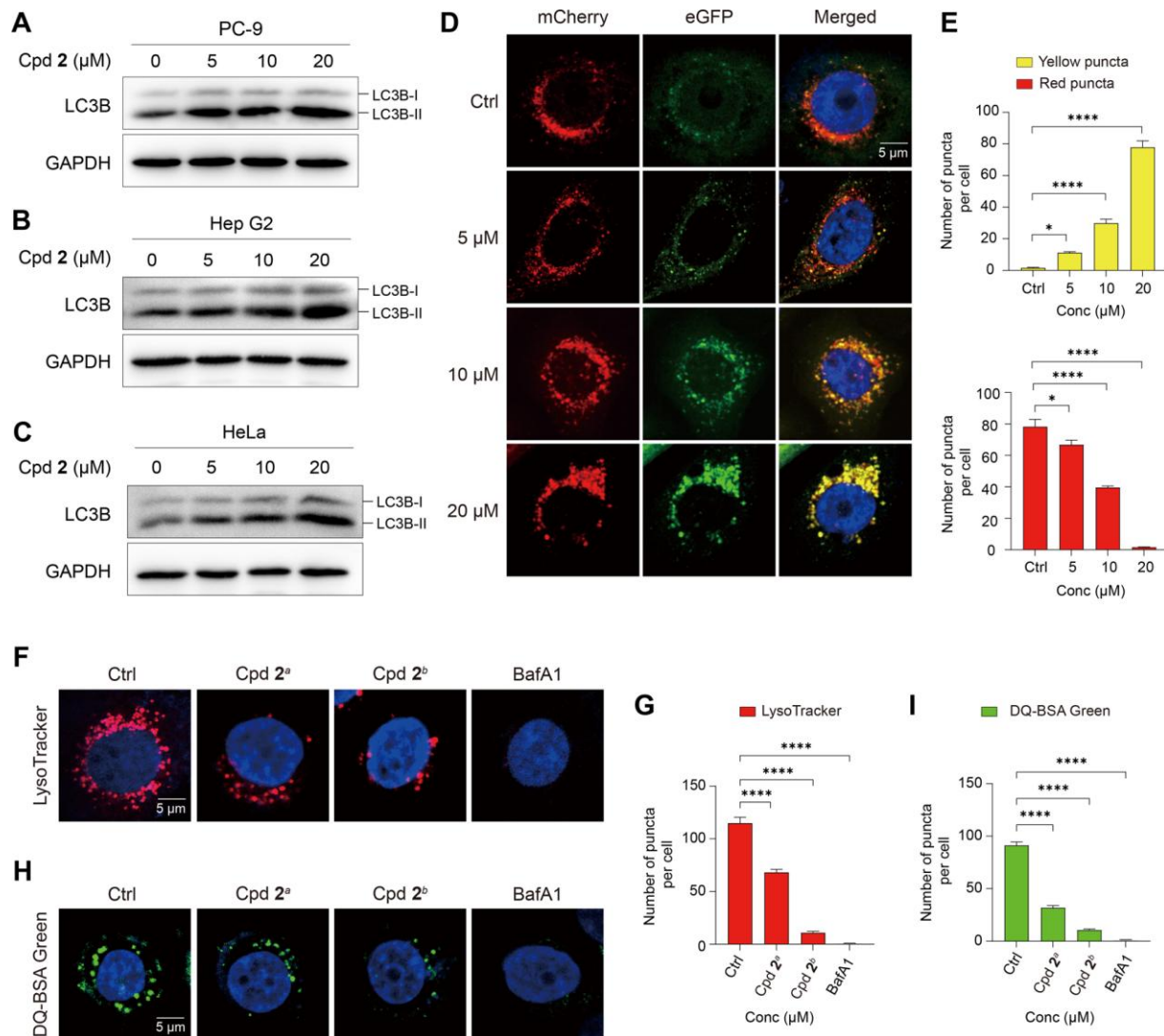
Pathway to scholarisine I, T, and W



Scholarisine I impairs lysosomal degradative capacity and thus inhibits autophagy at a late stage in cancer cells



Scholarisine I



Summary

