

Problem Session (9)

2023.9.2

Haruka Fujino

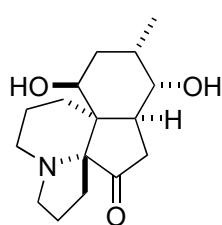
Propose a **reasonable** plan for the **asymmetric** synthesis of **(-)-serratinine** from **commercially-available compounds**.

Make maximum efforts to consider chemo- and regio-selectivities and functional group tolerance.

Cite proper references, if necessary.

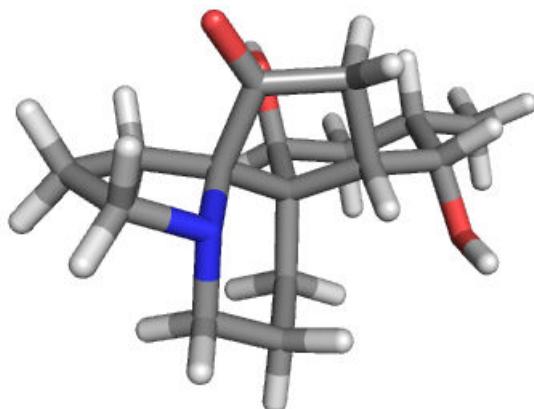
Submit your synthetic plan to hfujino@mol.f.u-tokyo.ac.jp as a ChemDraw file if you want to share and discuss it in the whole group seminar.

Submission due date: Aug 28 (Mon), 10 am

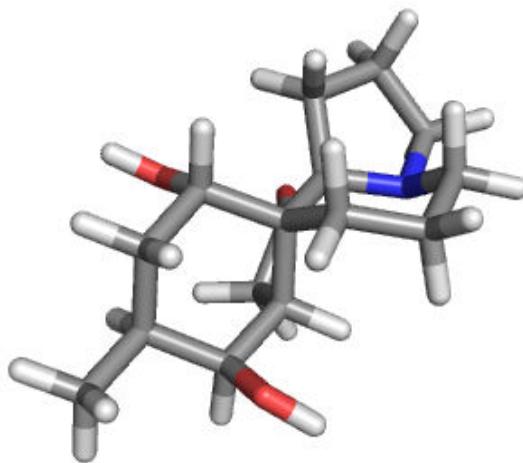


(-)-serratinine

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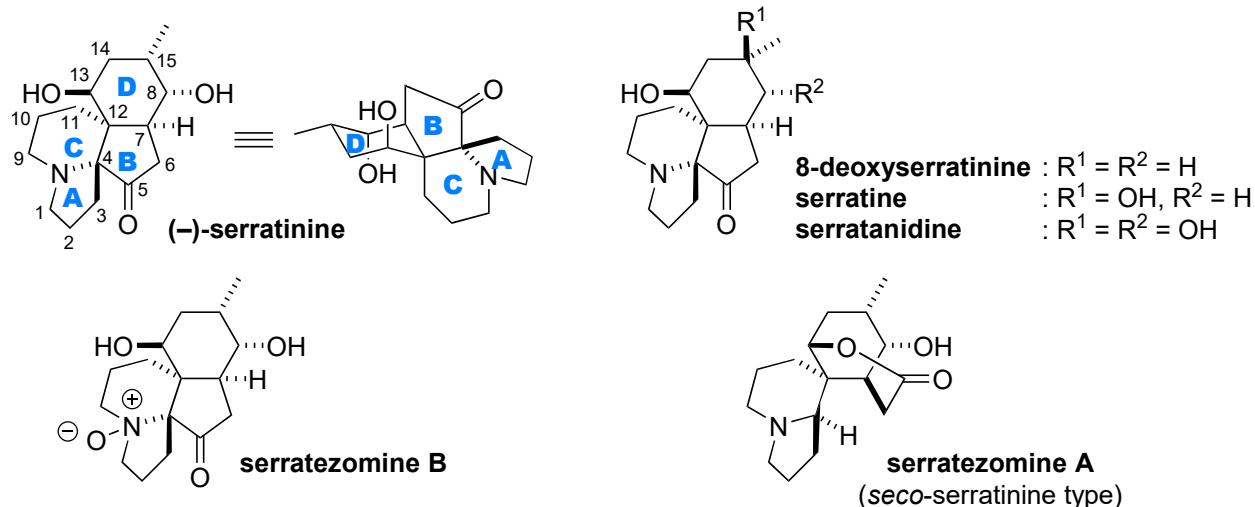
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Topic: Synthetic Plan of (-)-Serratinine Proposed by Inoue Lab Members and Synthia™

1. Introduction

1-1 Serratinine-type *Lycopodium* alkaloids



• **isolation of (-)-serratinine**

from *Lycopodium serratum*

Inubushi, Y.; Ishii, H.; Yasui, B.; Harayama, T.; Hosokawa, M.; Nishino, R.; Nakahara, Y. *Yakugaku Zasshi* 1967, **87**, 1394.

• **bioactivities of (-)-serratinine**

unexplored

(cf. Serratezomins B has cytotoxicity against murine lymphoma L1210 cells.

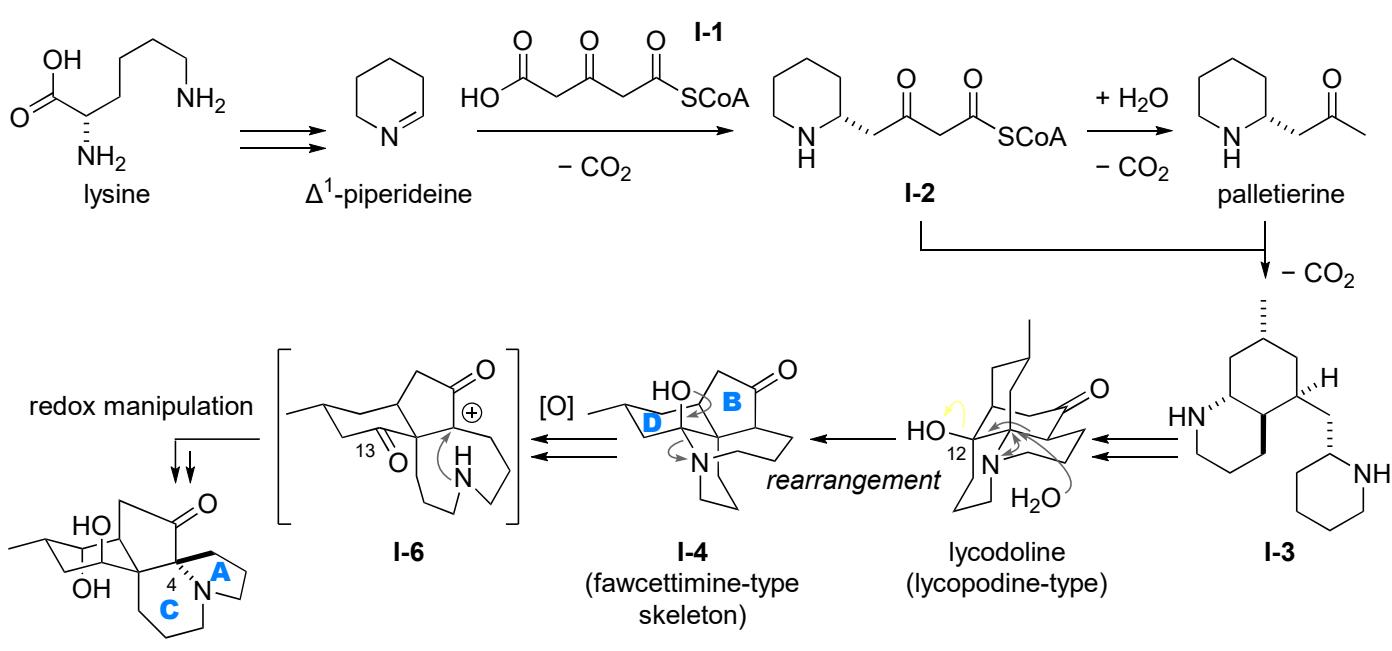
Morita, H.; Kobayashi, J. J. Org. Chem. 2002, **67**, 5378.)

• **structural features of (-)-serratinine**

a unique 6/5/6/5-taracyclic core

two contiguous tetra-substituted stereocenters

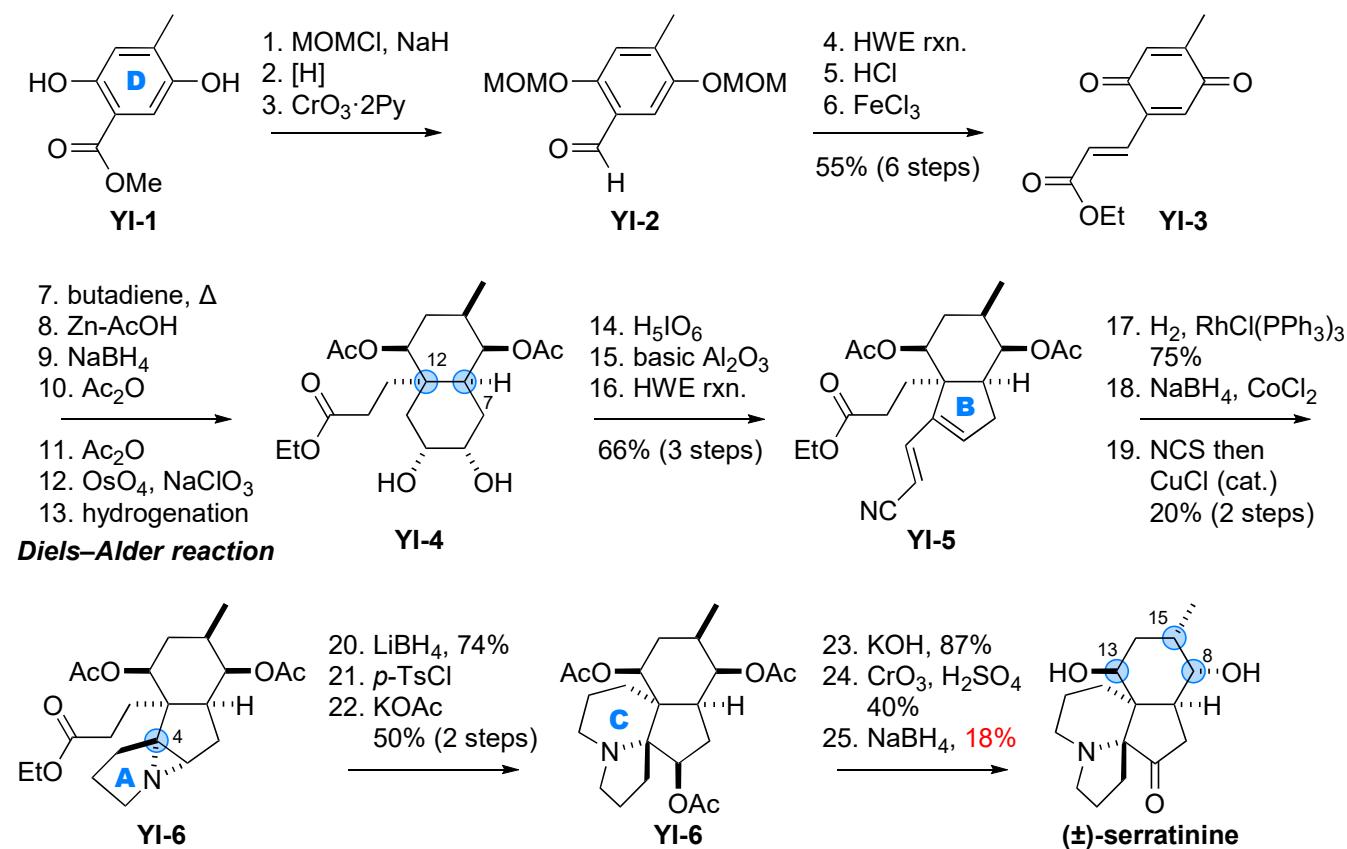
1-2 Proposed biogenesis of *Lycopodium* alkaloids



Inubushi, Y.; Ishii, H.; Yasui, B.; Harayama, T. *Tetrahedron Lett.* **1966**, *14*, 1551.
 Pati, S. P. *Future J. Pharm. Sci.* **2020**, *6*, 99.

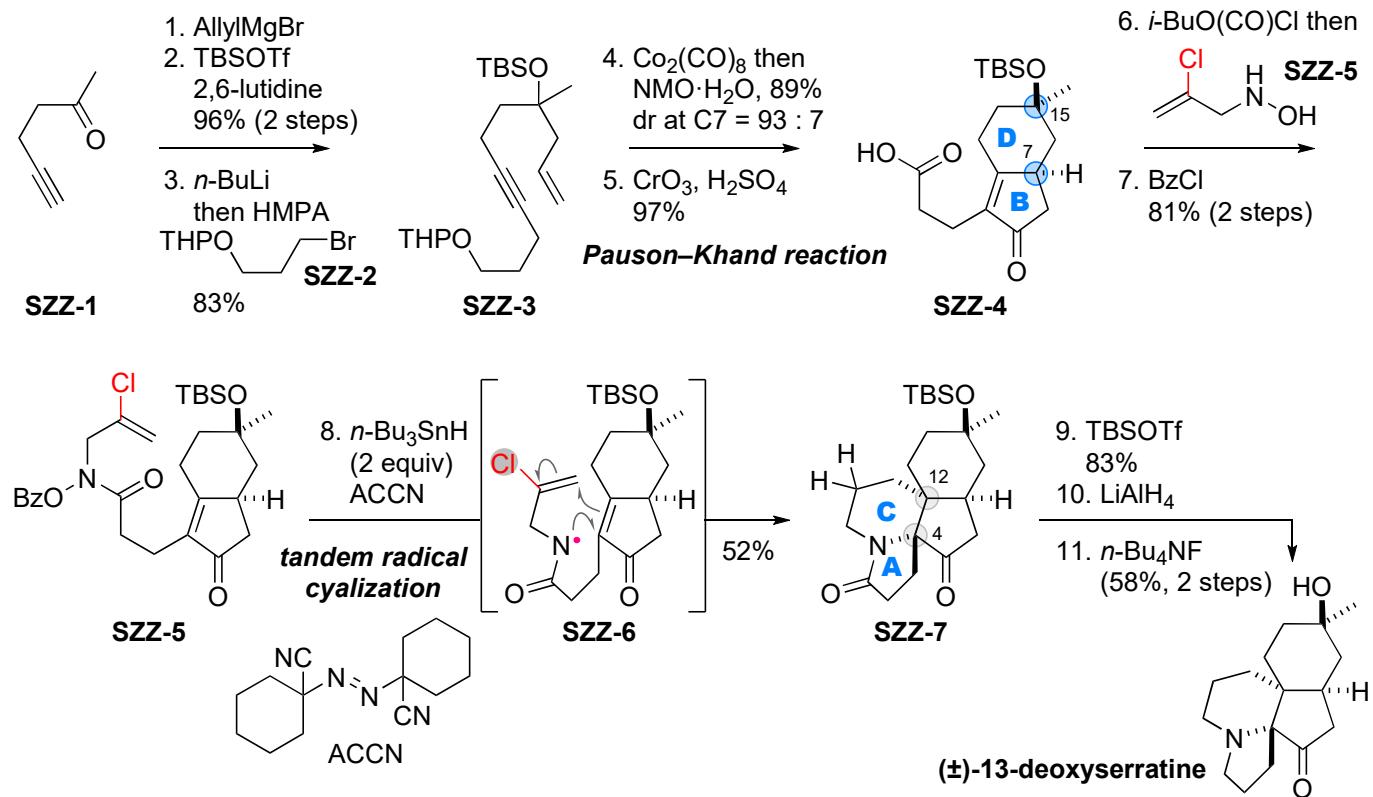
2. Past Total Syntheses of serratinine and related serratinine-type alkaloids

Inubushi Group (1974, (\pm)-serratinine)



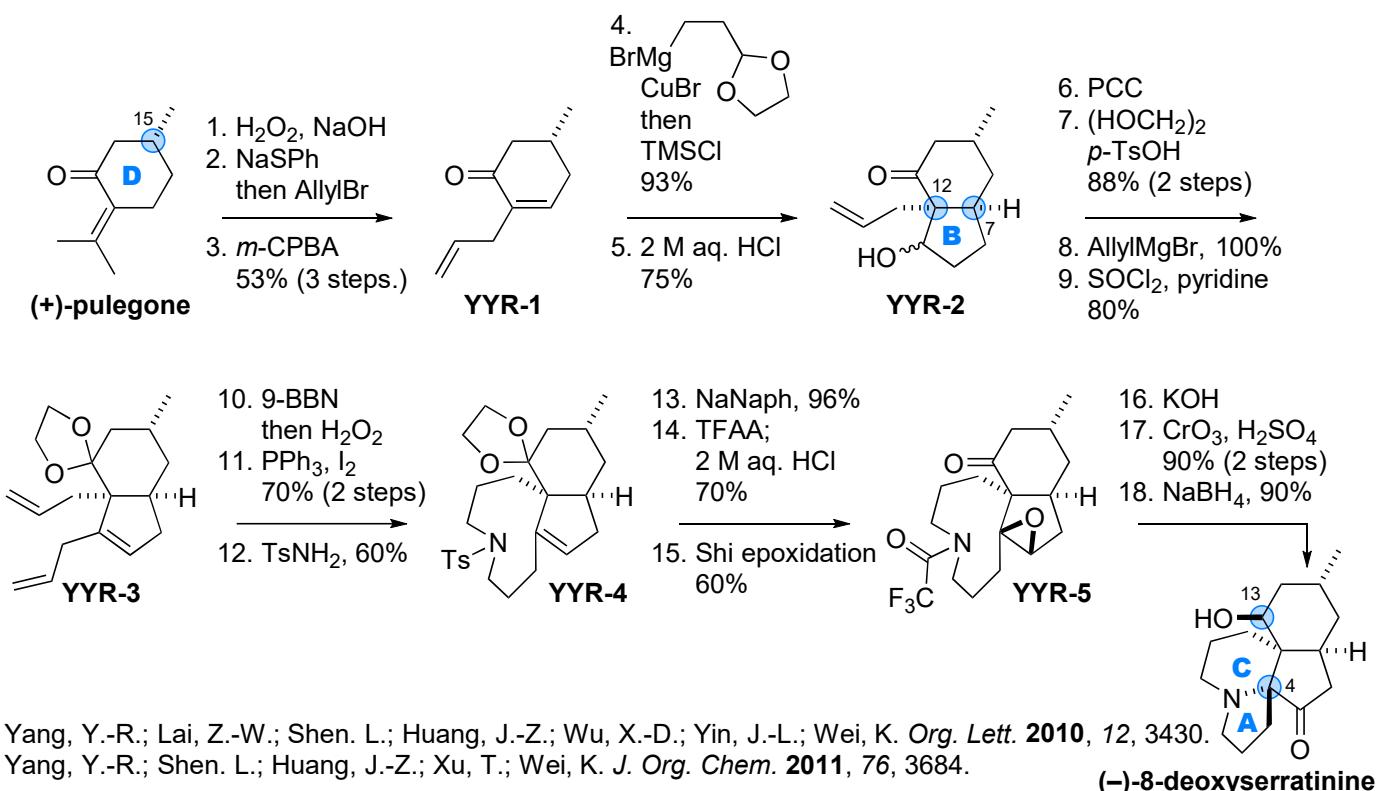
Harayama, T.; Ohtani, M.; Oki, M.; Inubushi, Y. *J. Chem. Soc., Chem. Commun.* **1974**, 827.
Harayama, T.; Ohtani, M.; Oki, M.; Inubushi, Y. *Chem. Pharm. Bull.* **1975**, 23, 1511.

Zard Group (2002, (\pm)-13-Deoxyserratinine)



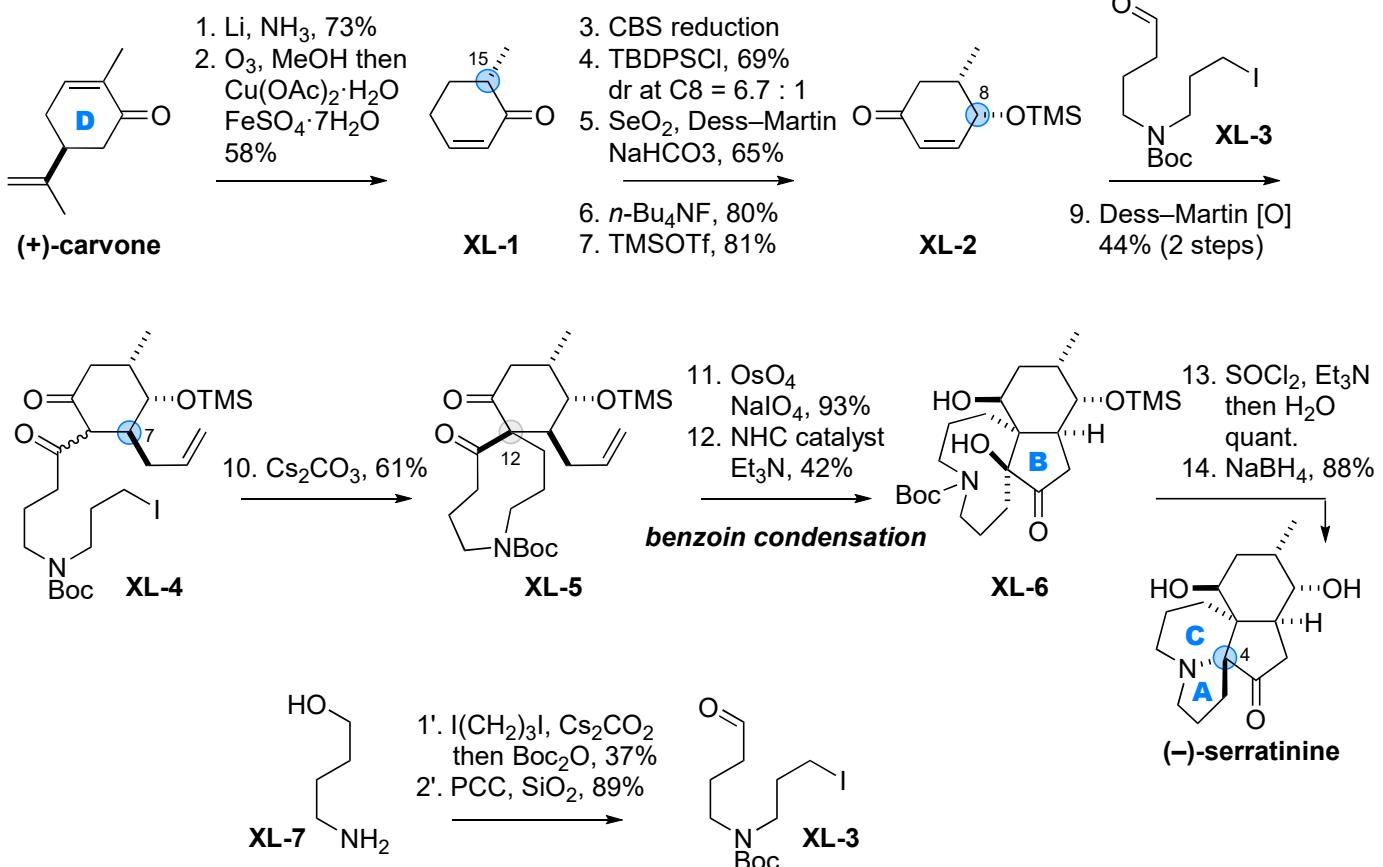
Cassayre, J.; Gagosz, F.; Zard, S. Z. *Angew. Chem. Int. Ed.* **2002**, 41, 1783.

Yang Group (2010, (-)-8-Deoxyserratinine)



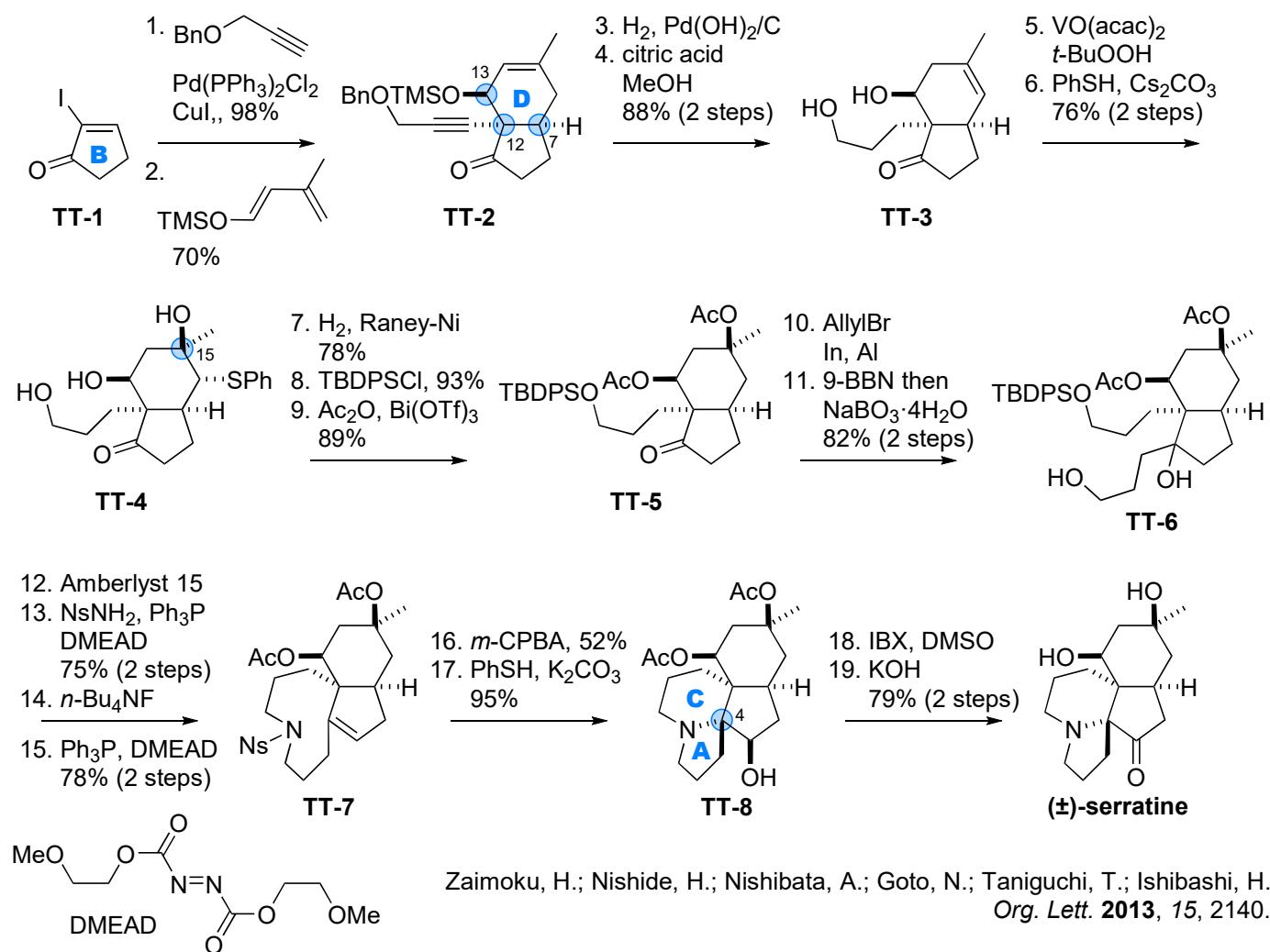
Yang, Y.-R.; Lai, Z.-W.; Shen, L.; Huang, J.-Z.; Wu, X.-D.; Yin, J.-L.; Wei, K. *Org. Lett.* **2010**, *12*, 3430.
Yang, Y.-R.; Shen, L.; Huang, J.-Z.; Xu, T.; Wei, K. *J. Org. Chem.* **2011**, *76*, 3684.

Lei Group (2012 and 2014, (-)-serratinine)



Li, H.; Wang, X.; Lei, X. *Angew. Chem. Int. Ed.* **2012**, *51*, 491.
Zhang, J.; Wu, J.; Hong, B.; Ai, W.; Wang, X.; Li, H.; Lei, X. *Nat. Chem.* **2014**, *5*, 4614.

Taniguchi Group (2013, (\pm) -serratinine)



Zaimoku, H.; Nishide, H.; Nishibata, A.; Goto, N.; Taniguchi, T.; Ishibashi, H.
Org. Lett. **2013**, *15*, 2140.

Our original synthetic plans are closed to the public.