Literature Report

Total Synthesis of Leuconoxine Melodinine E, and Mersicarpine through a Radical Translocation–Cyclization Cascade

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Checker: Xin-Wei Wang

October 28, 2019

Dalian Institute of Chemical Physics

Kim, R.; **Beaudry. C. M.** *et al. Angew. Chem. Int. Ed.* **2019**, *58,*12595.

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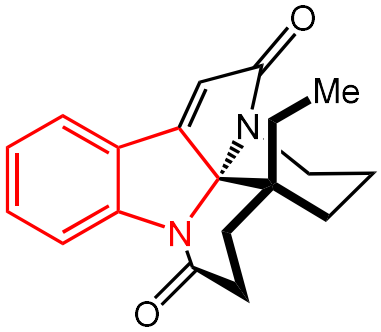
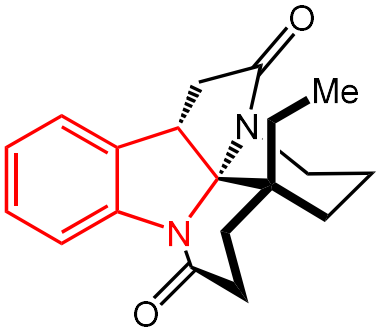
Introduction

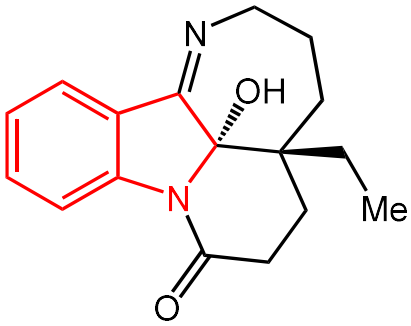
The Aspidosperma Alkaloids



Melodinine E



Leuconoxine

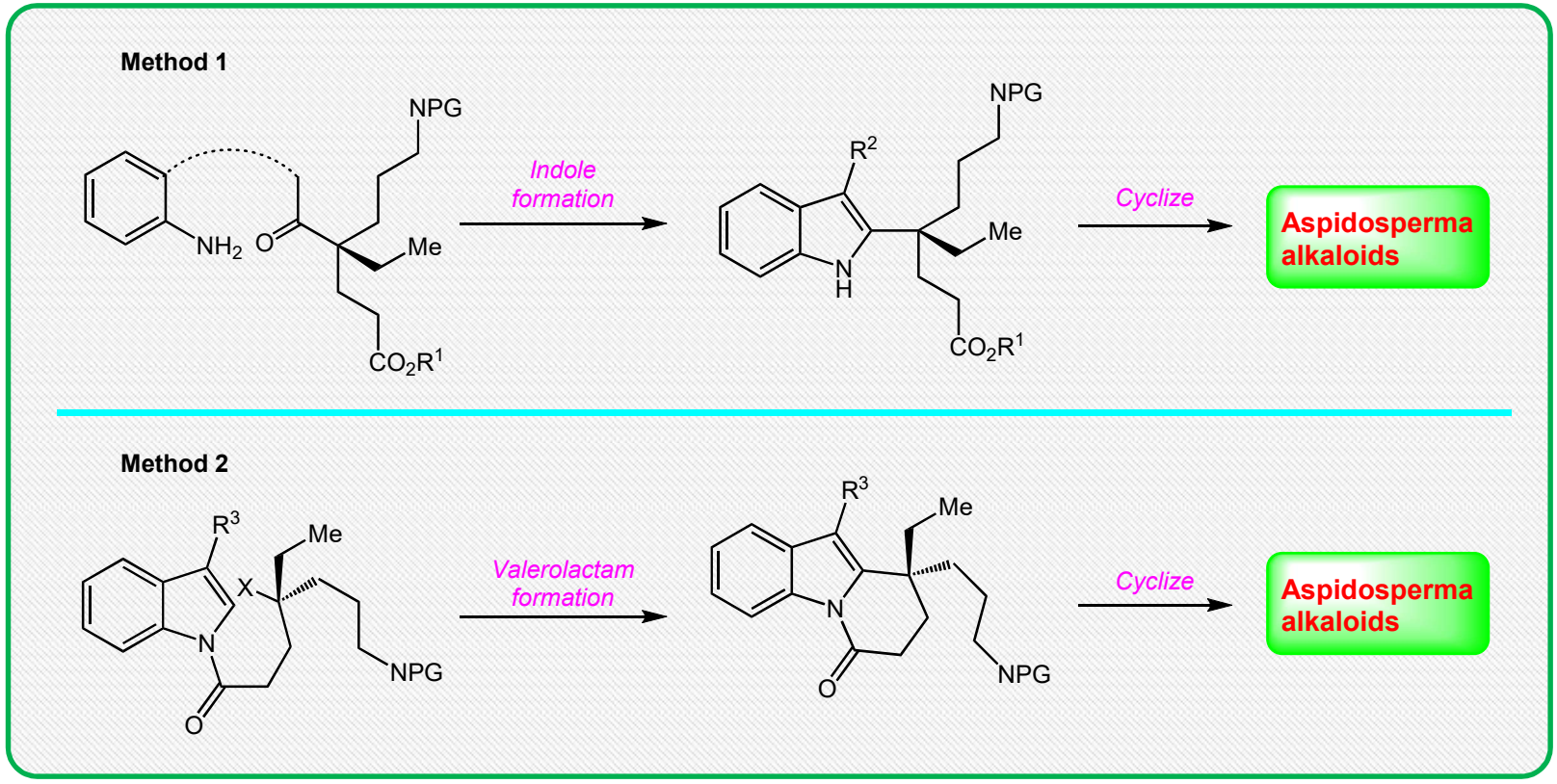


Mersicarpine

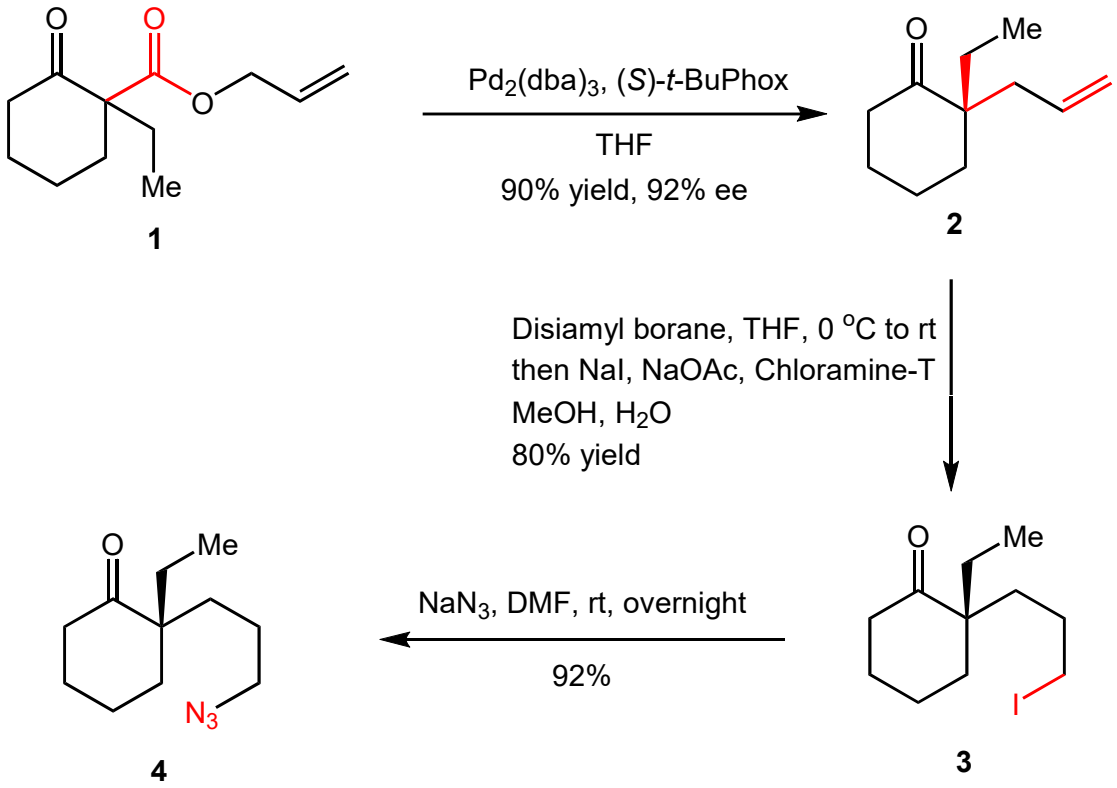
- Isolated from dogbane trees;
- Polycyclic structures;
- An indoline structural motif.

Bhadane, B. S. *et al*. *Phytother. Res*. **2018**, *32*, 1181.

Retrosynthetic Analysis

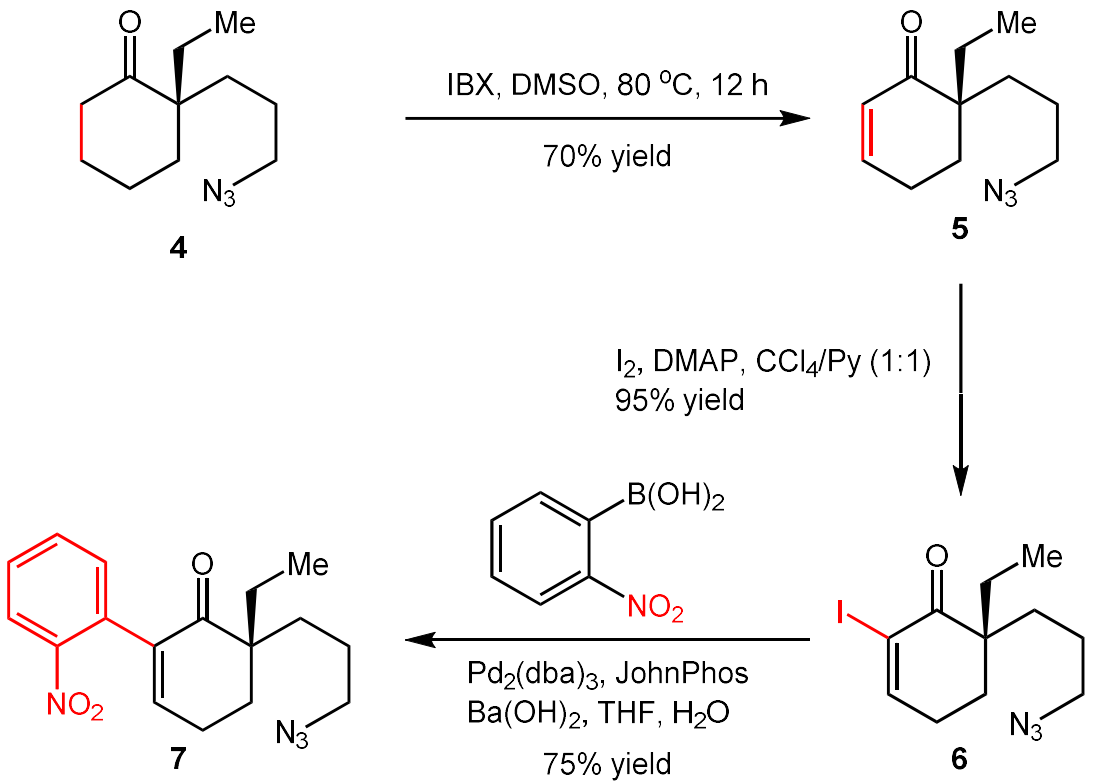


Synthesis of Intermediate 4



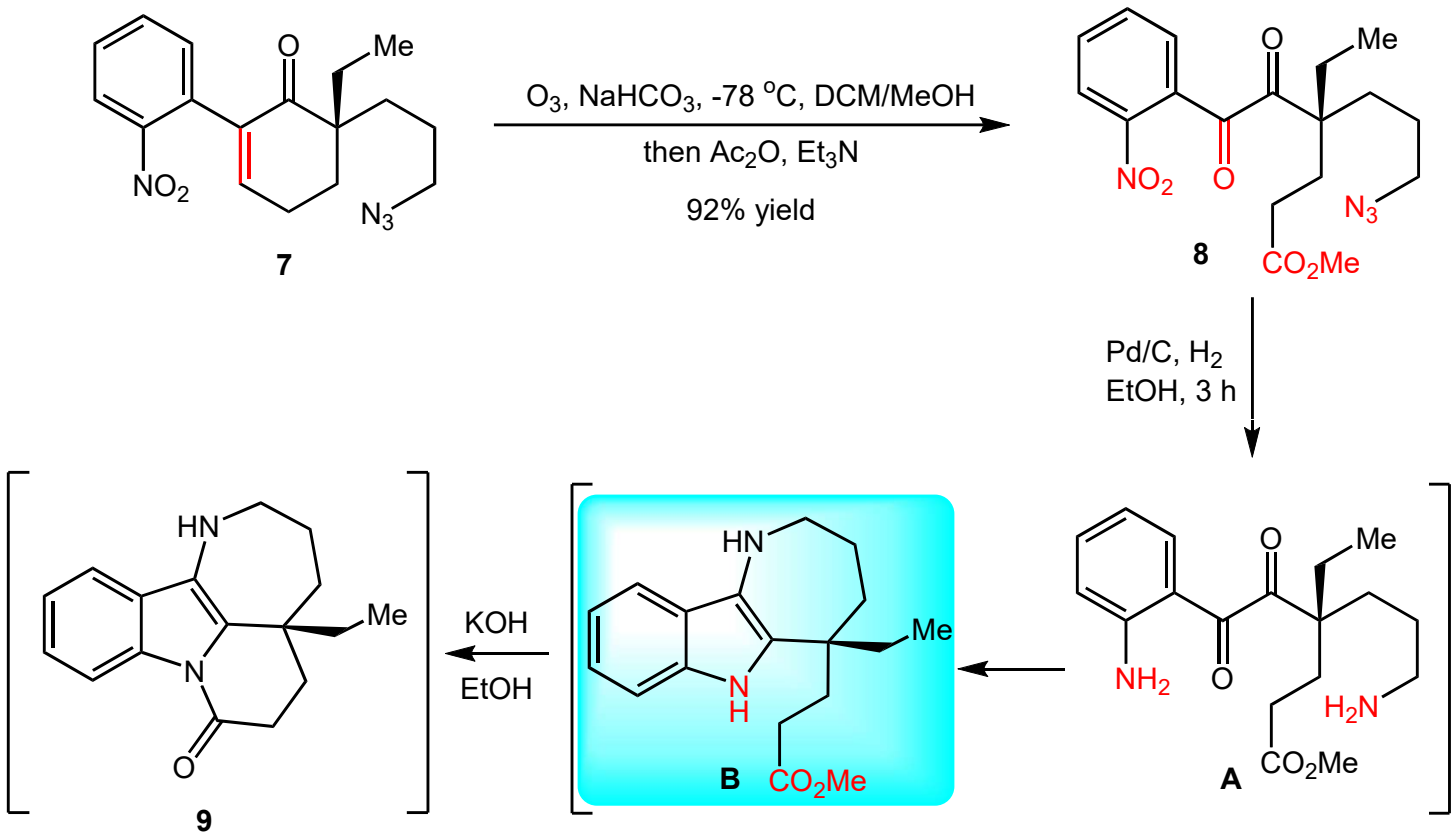
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 7



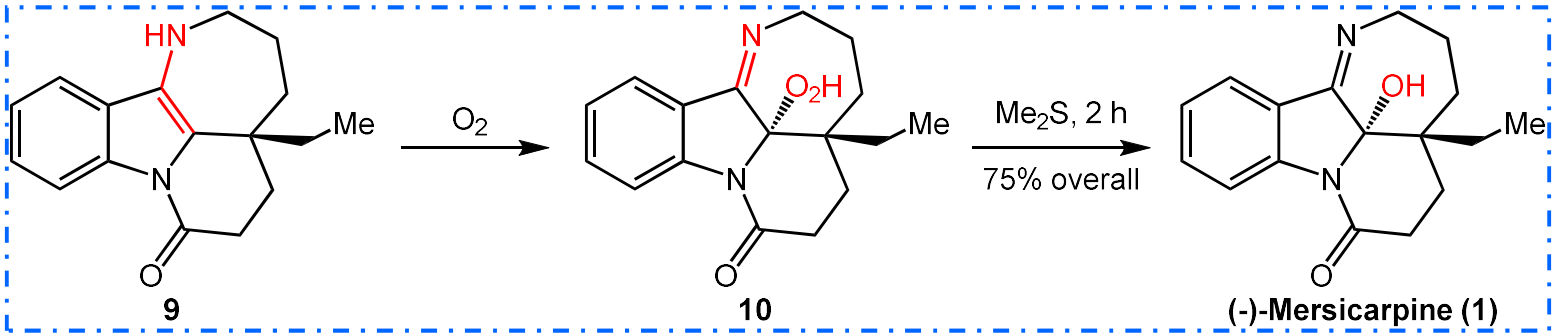
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 9



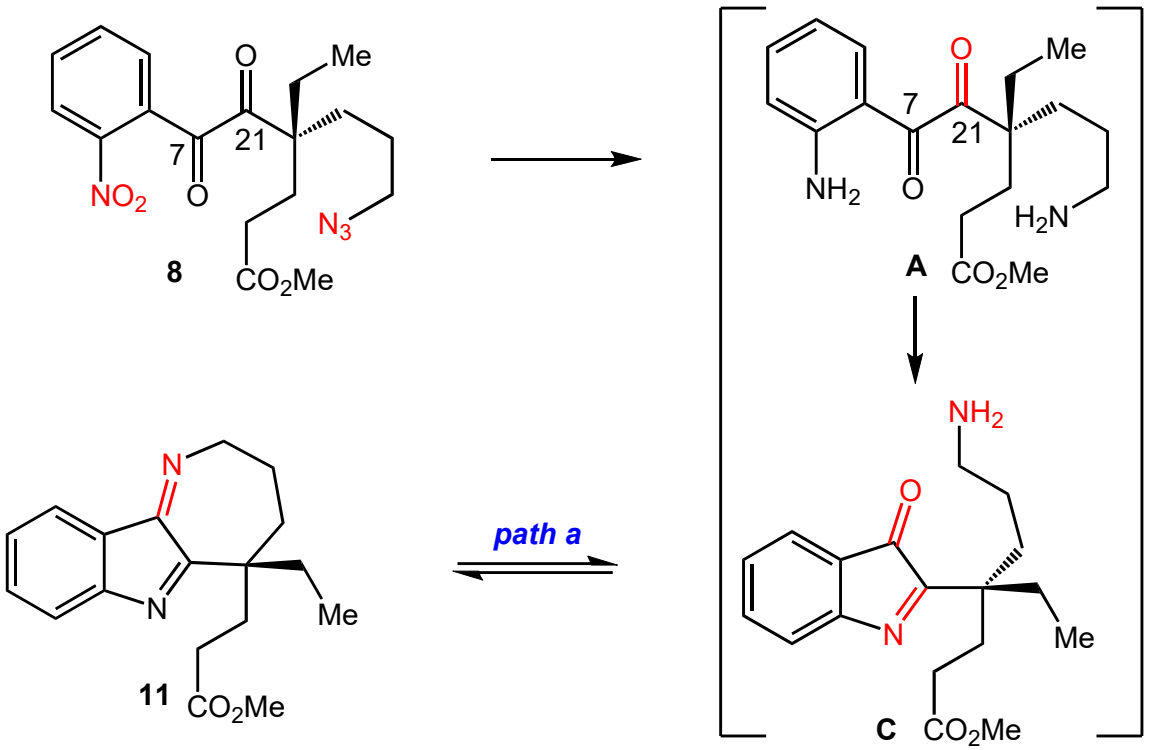
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 16



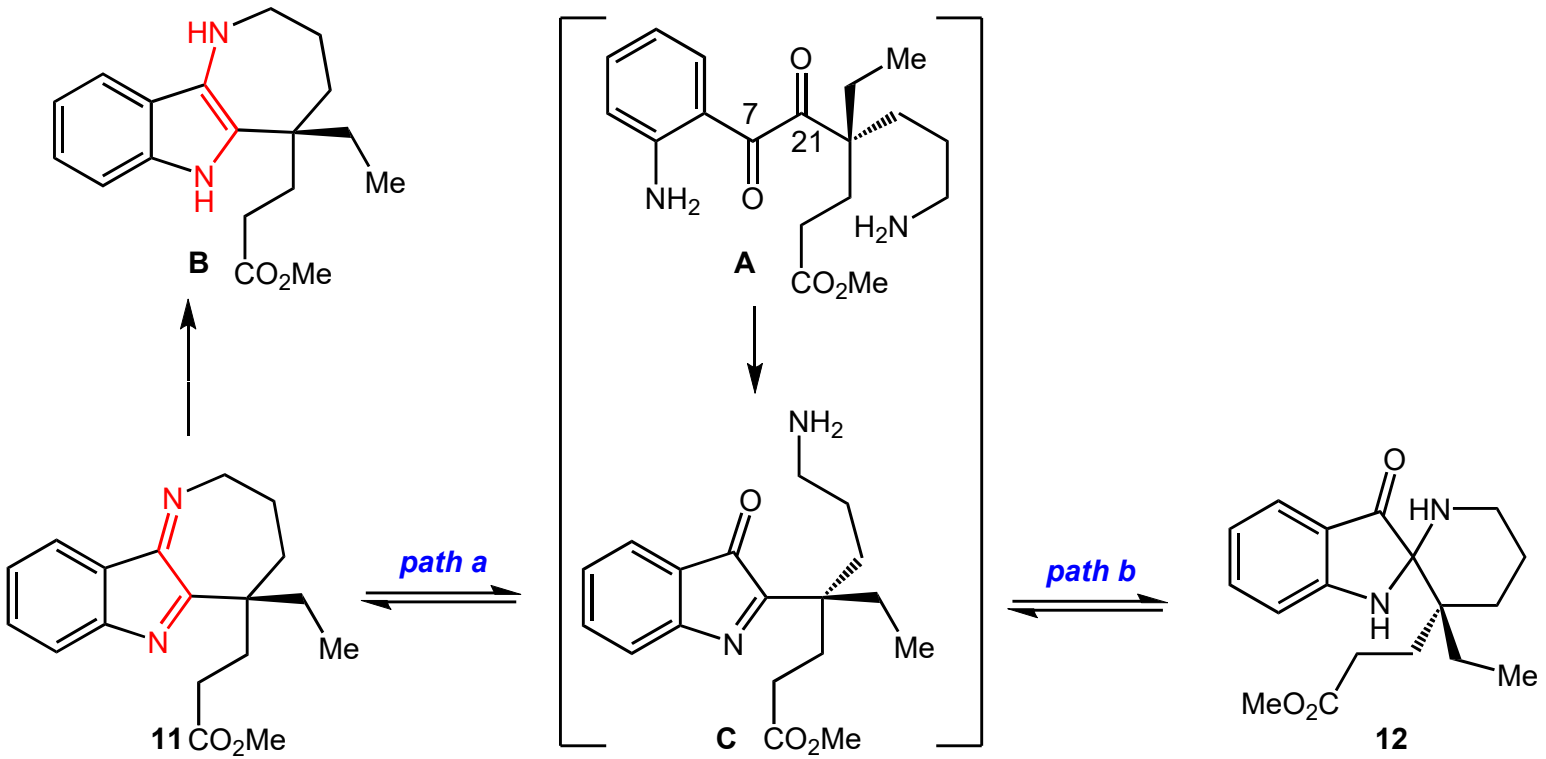
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 11



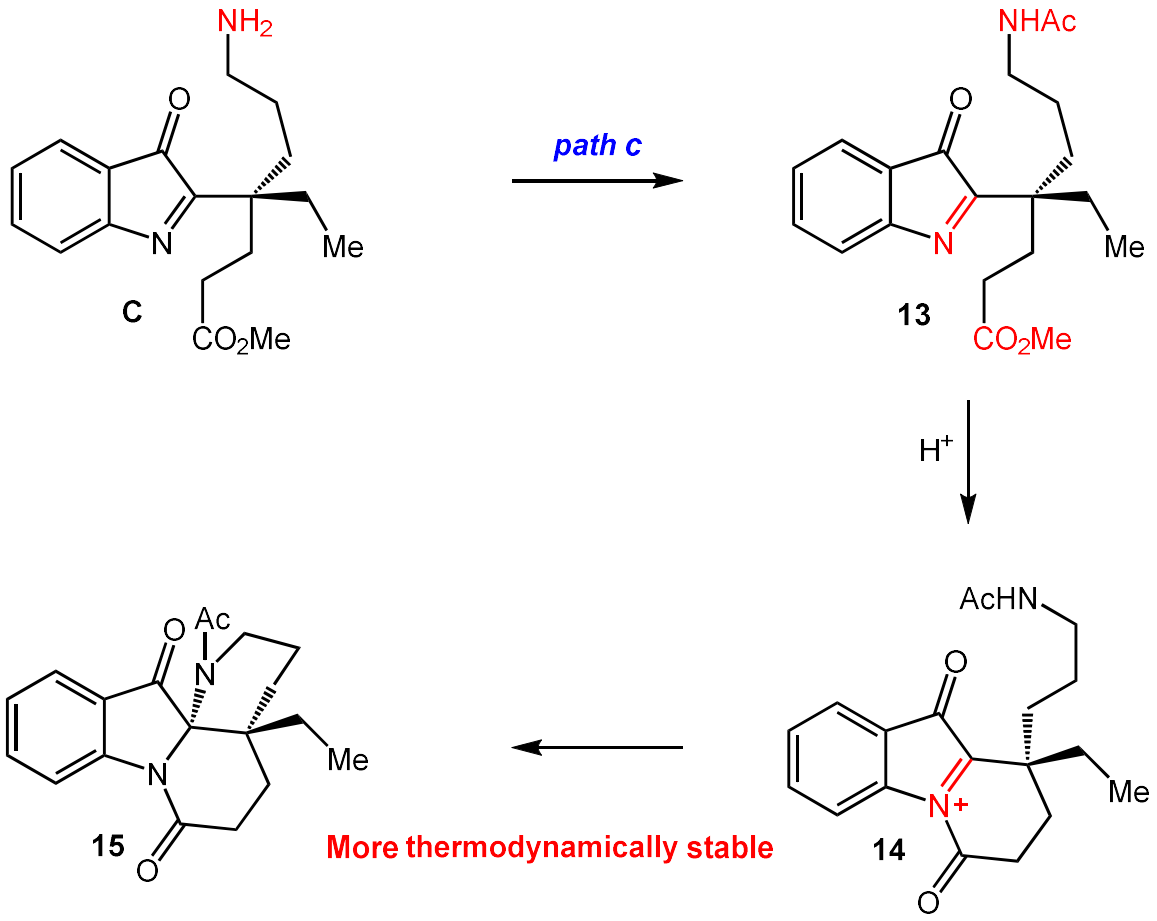
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 12



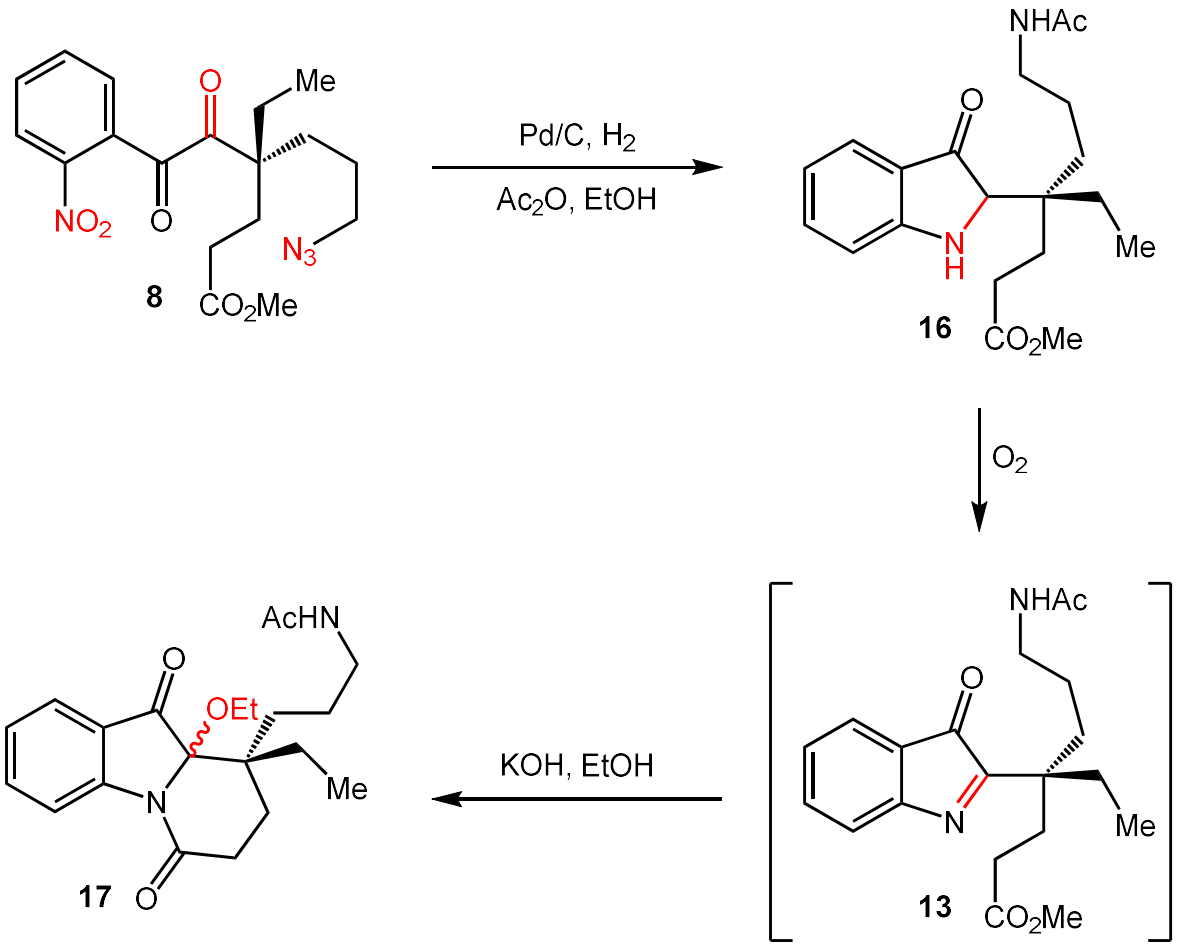
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 15



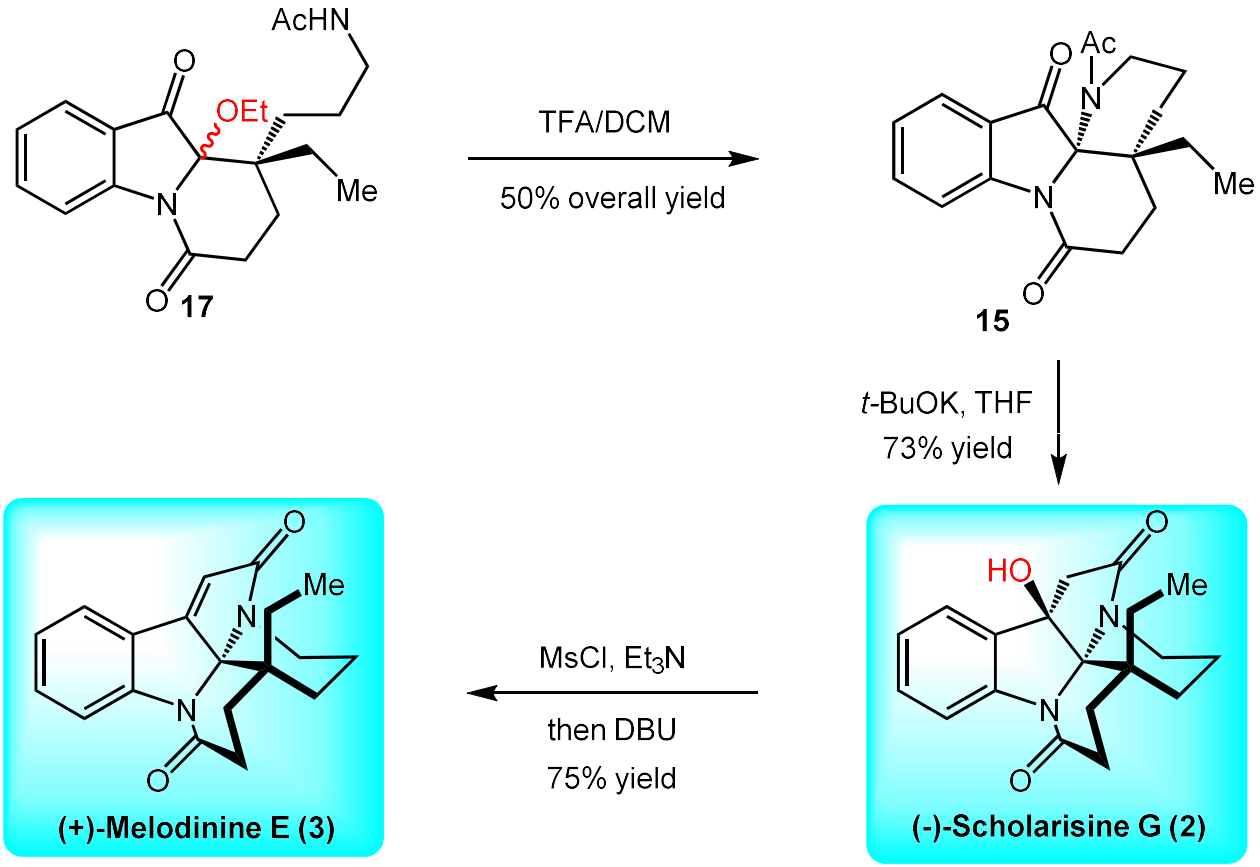
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 17



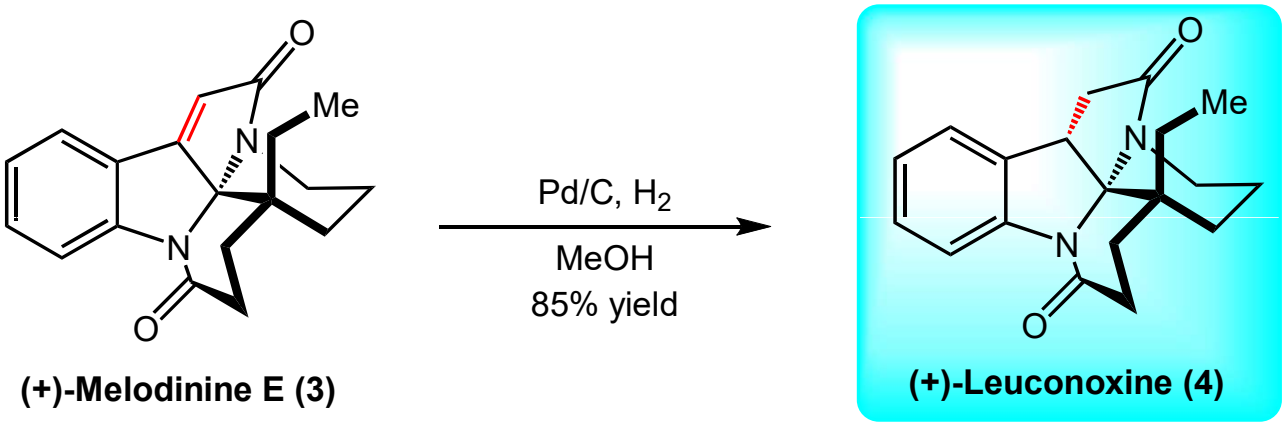
Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of (+)-Melodinine E, (-)-Scholarisine G



Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of (+)-Leuconoxine

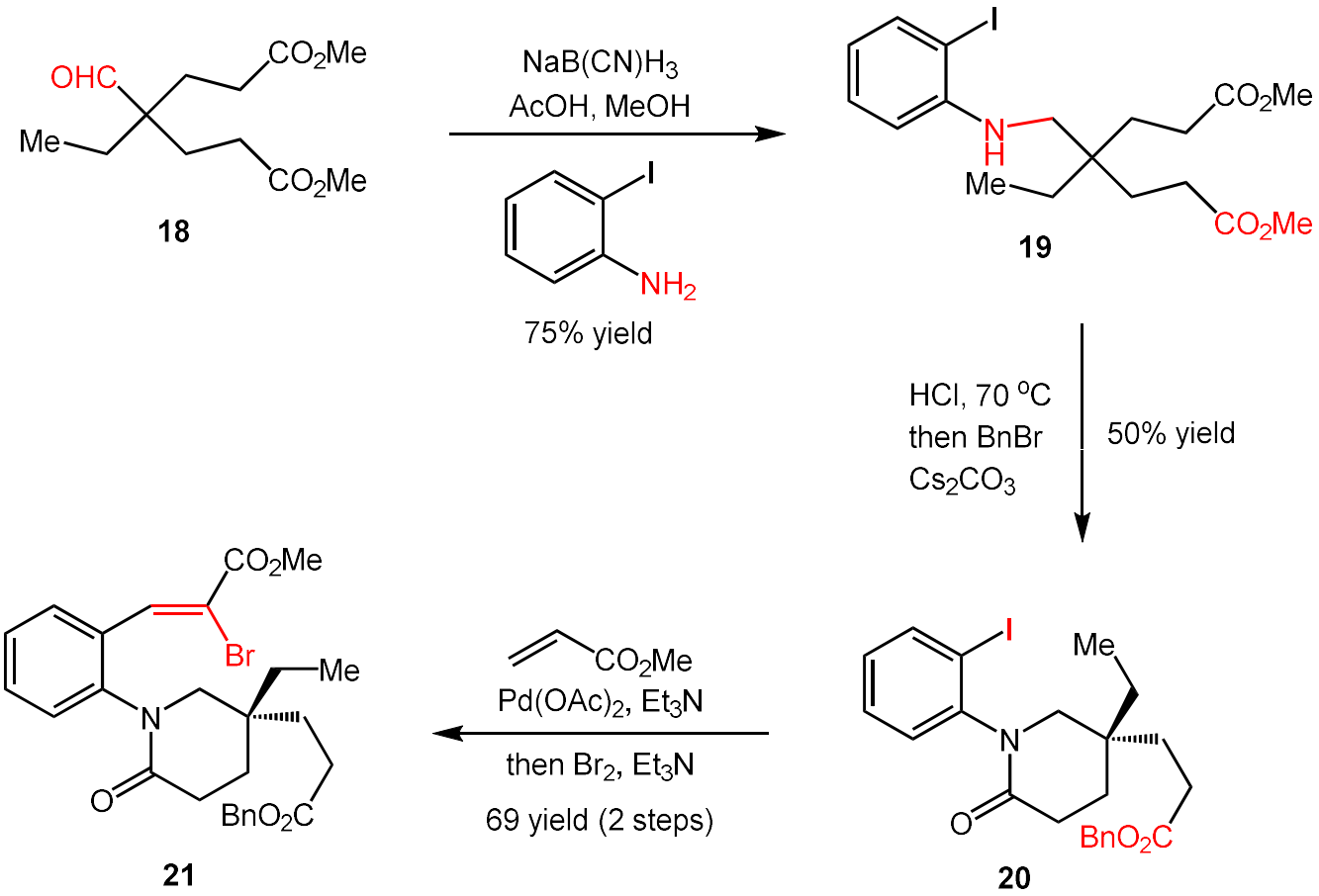


(+)-Melodinine E (3)

(+)-Leuconoxine (4)

Xu, Z.; **Zhu. J**. *et al. J. Am. Chem. Soc.* **2013**, *135,* 19127.

Synthesis of Intermediate 21



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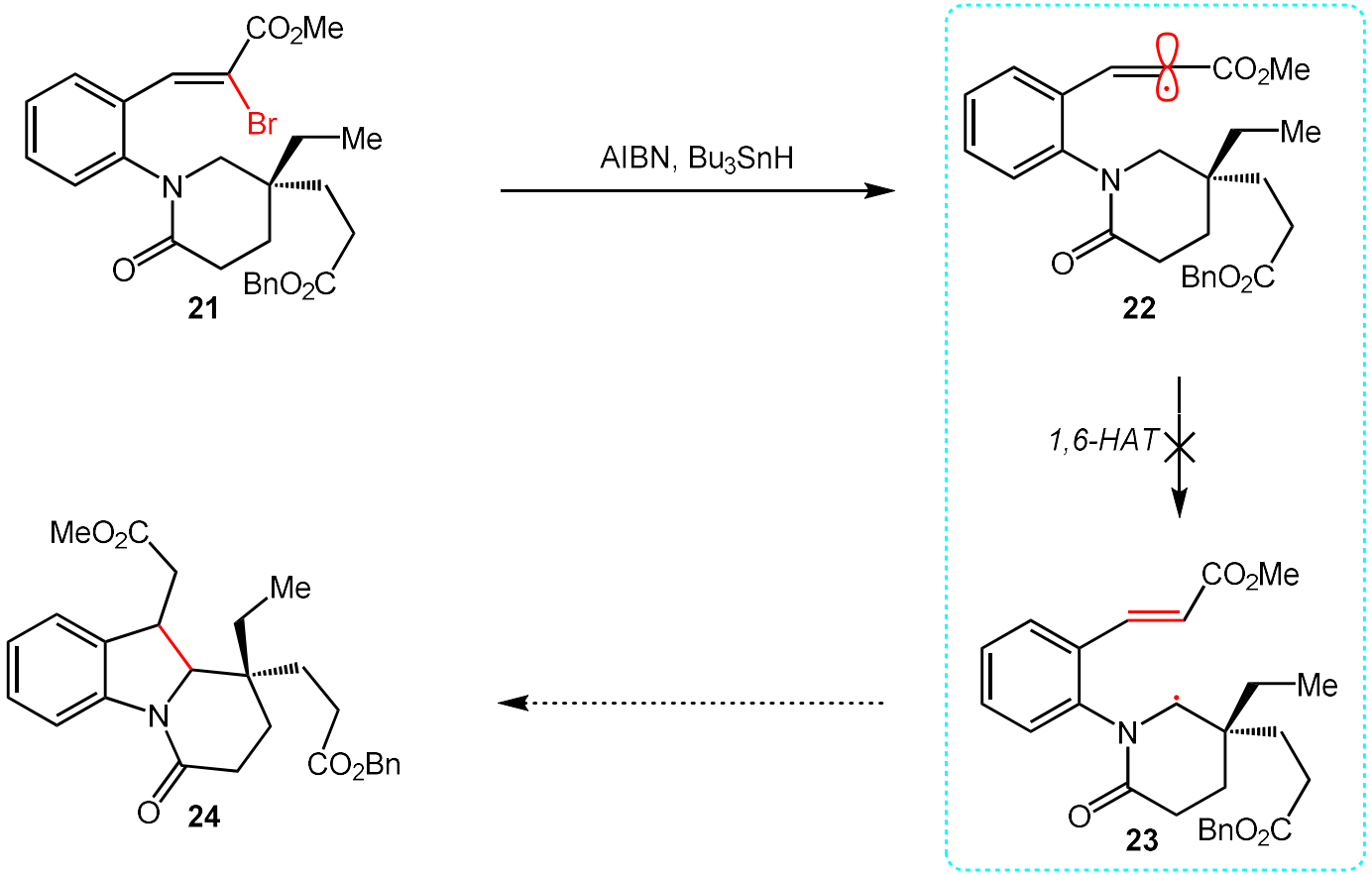
Synthesis of Intermediate 24



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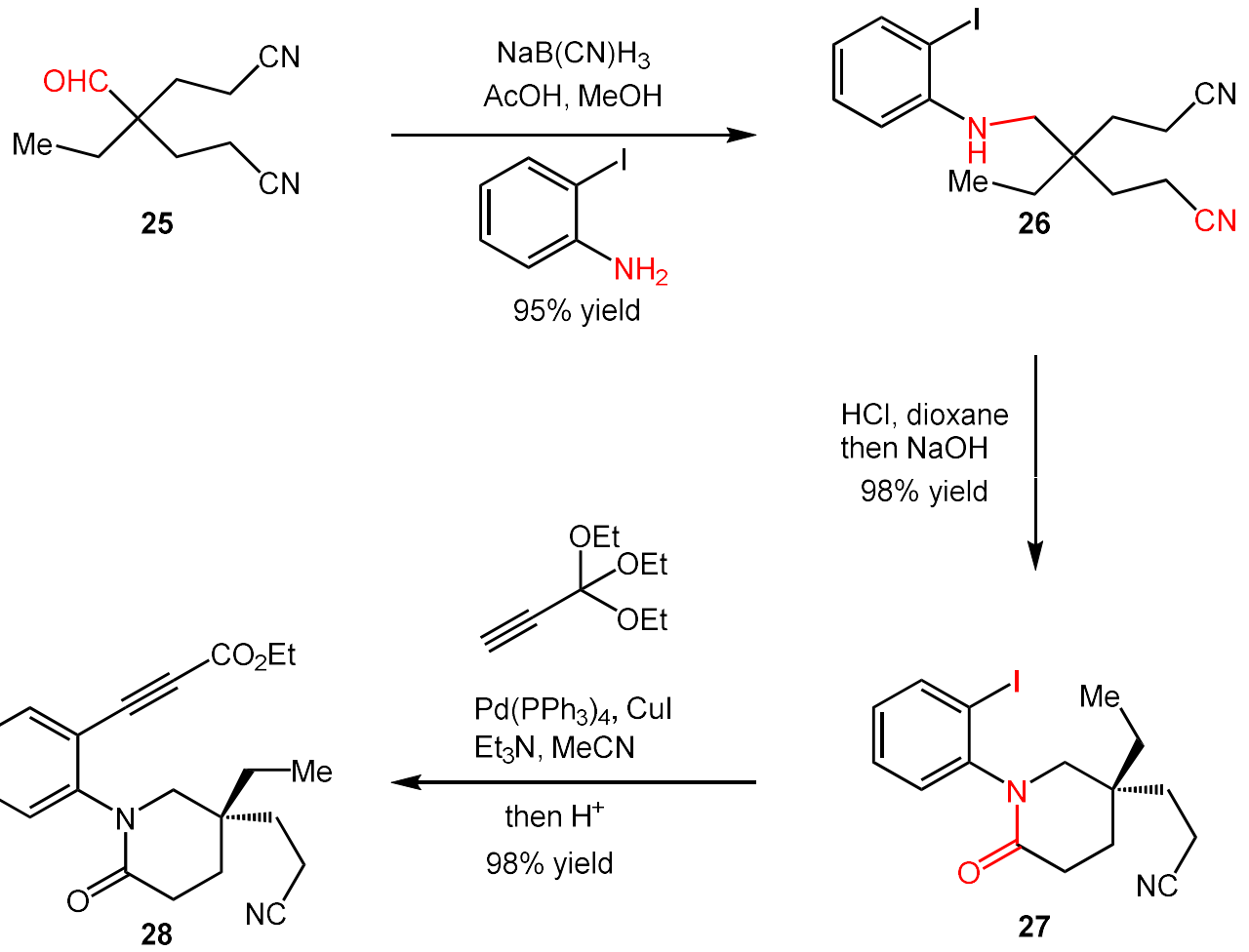
Synthesis of Intermediate 28



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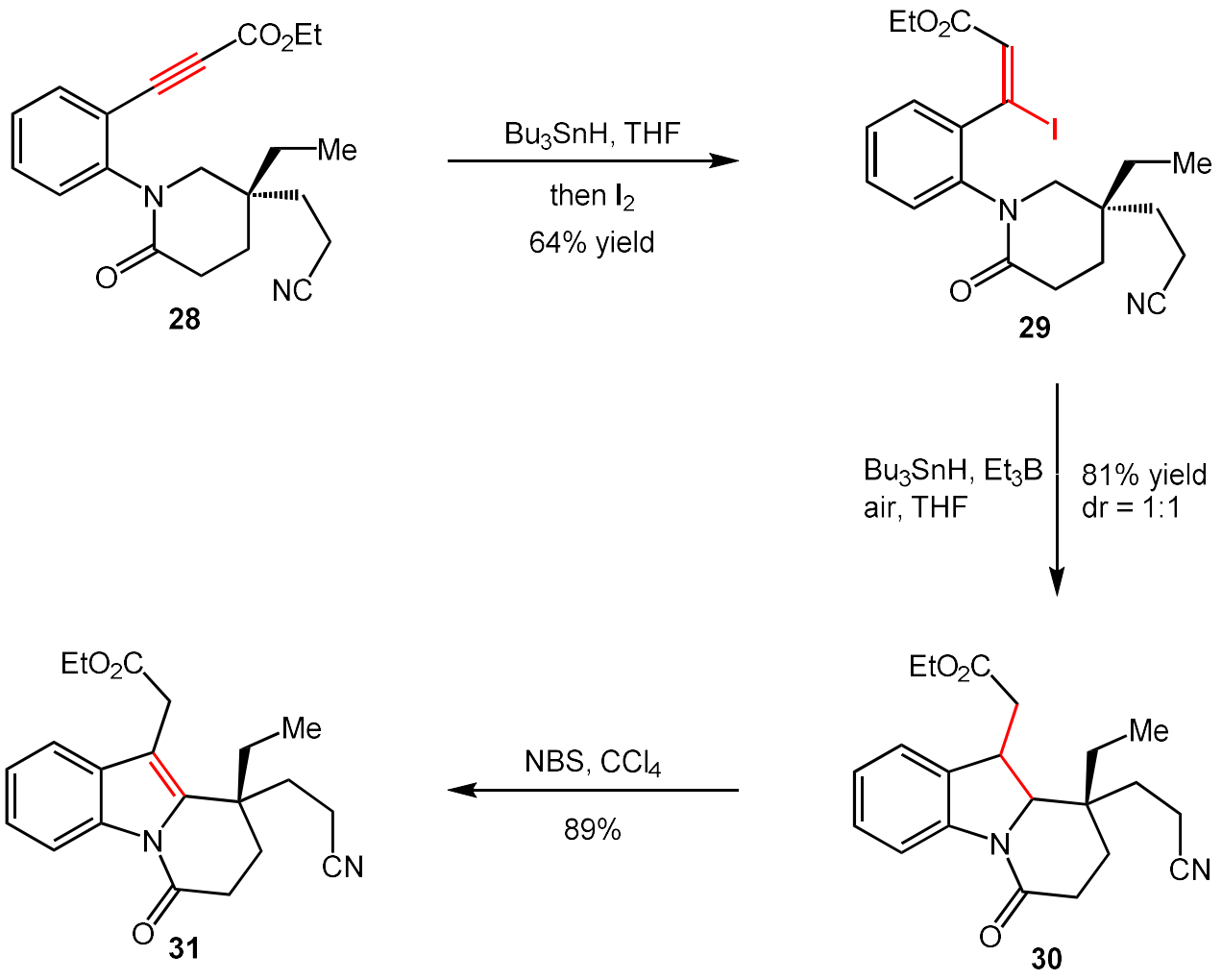
Synthesis of Intermediate 31



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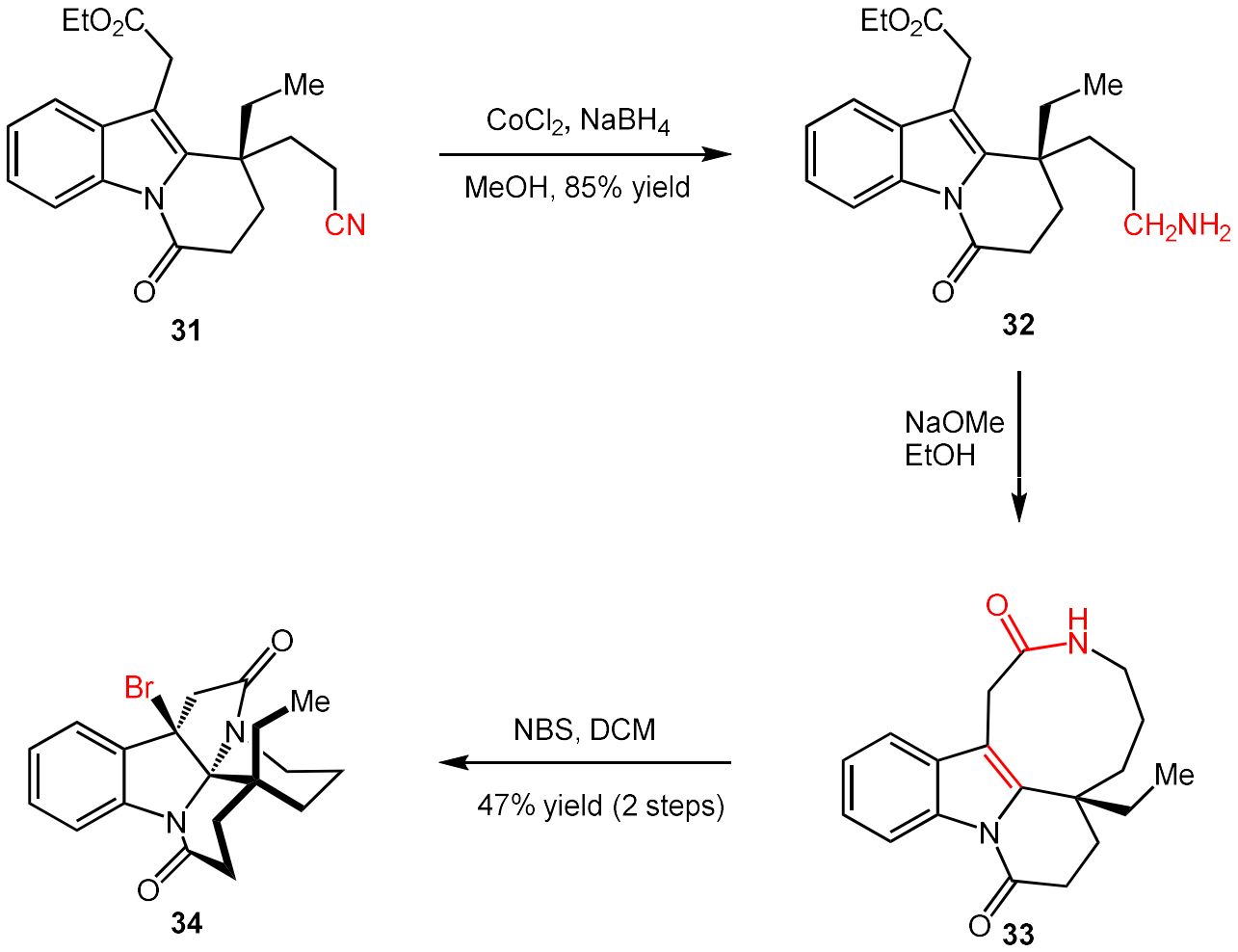
Synthesis of Intermediate 34



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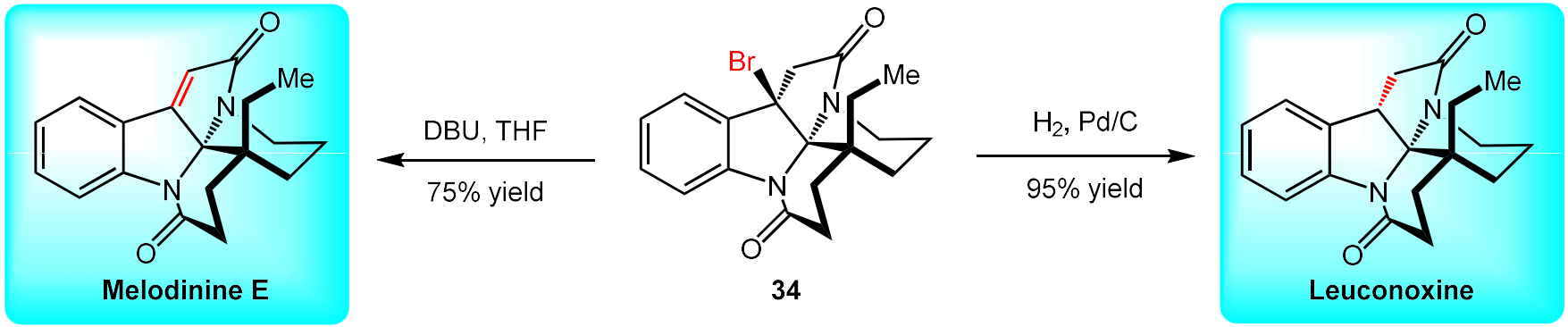
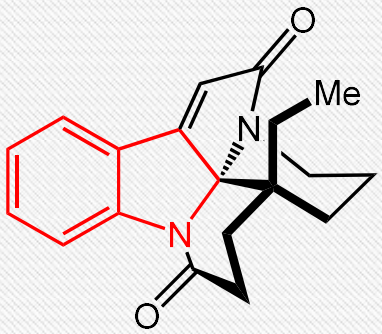
Synthesis of Melodinine E, Leuconoxine

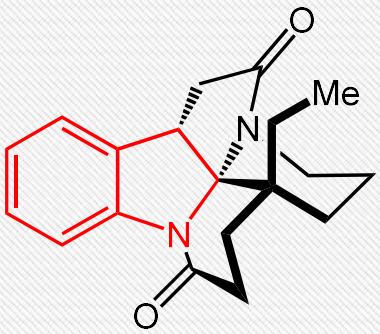


Kim, R.; **Beaudry. C. M.** *et al. Angew. Chem. Int. Ed.* **2019**, *58,* 12595.

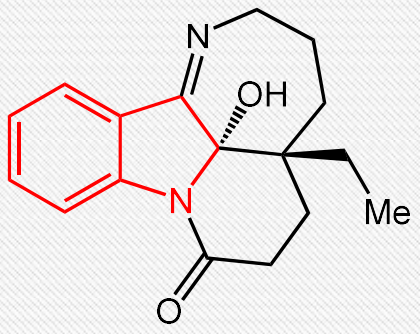
Summary



Melodinine E



Leuconoxine



Mersicarpine

Beaudry's work:

The Sonogashira reaction;

1,5-Hydrogen atom transfer.

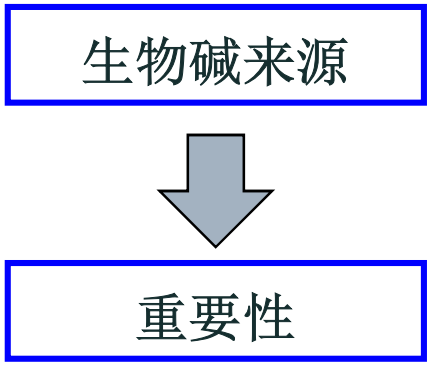
Zhu's work:

The Suzuki−Miyaura reaction;

Oxidation/reduction/cyclization processes.

The First Paragraph

写作思路：

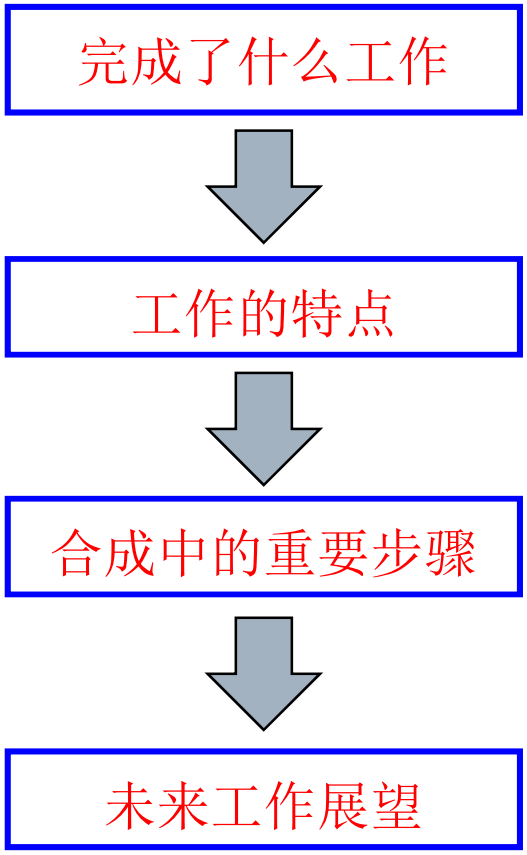


The First Paragraph

The Aspidosperma alkaloids are a large class of molecules isolated from dogbane trees native to Central and South America. These alkaloids have attracted considerable attention due to their polycyclic structures, biological activities, and interesting biosyntheses.

The Last Paragraph

写作思路：



The Last Paragraph

In summary, we have synthesized leuconoxine, melodinine E, and mersicarpine. Our synthesis features a 1,5-hydrogen atom transfer to give a substituted indoline product. The indoline intermediate was a common precursor to the three title natural products. Leuconoxine and melodinine E were accessed using a transannular bromo-lactamization. Efforts to apply the key radical reaction in other alkaloid architectures are currently underway in our laboratory.

Representative examples

These alkaloids **have attracted considerable attention due to** their polycyclic structures, biological activities, and interesting biosyntheses.

Our synthesis **features** a 1,5-hydrogen atom transfer to give a substituted indoline product.

However, no total synthesis of these natural products **has been reported until now**.

In the context of our continuous interest in the construction of indole rings at the late stage of total synthesis, **we devised a** unified strategy to reach different skeletons of aforementioned alkaloids from the same intermediate.

Efforts to apply the key radical reaction in other alkaloid architectures **are currently underway** in our laboratory.

Acknowledgement

Thanks

for your kind attention !