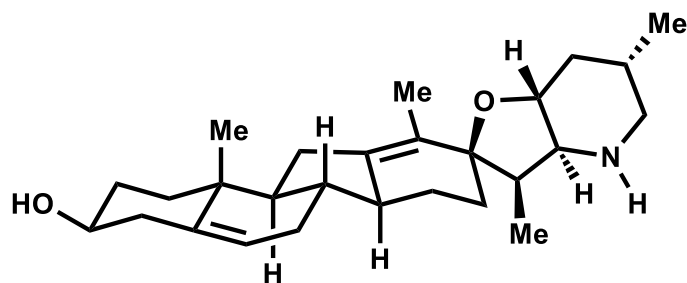
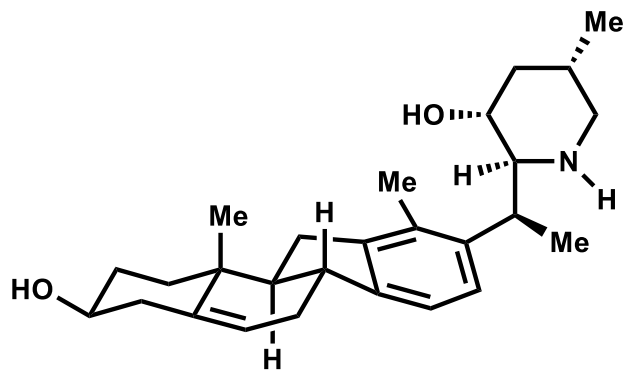


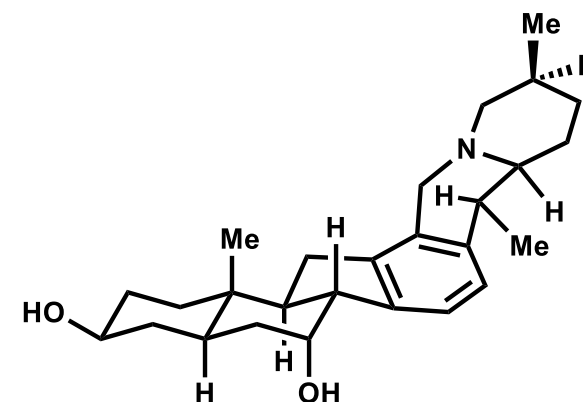
Total Syntheses of Isosteroidal Alkaloids: Cyclopamine, Veratramine and Heilonine



Cyclopamine



Veratramine



Heilonine

Reporter: Ruiyang Gao

Supervisor: Prof. Quan Cai

2025.10.24

Content

➤ Introduction

➤ Total Synthesis of Cyclopamine and Veratramine

- ✓ Athanassios Giannis (2009, **Cyclopamine**)
- ✓ Phil S. Baran (2023, **Cyclopamine**)
- ✓ 高栓虎 (2023, **Cyclopamine** and **Veratramine**)
- ✓ 秦勇 (2024, **Cyclopamine** and **Veratramine**)
- ✓ Dirk H. Trauner (2025, **Veratramine**)

➤ Total Synthesis of Heilonine

- ✓ Viresh H. Rawal (2021, **Heilonine**)
- ✓ 代明骥 (2024, **Heilonine**)

➤ Summary

Content

➤ Introduction

➤ Total Synthesis of Cyclopamine and Veratramine

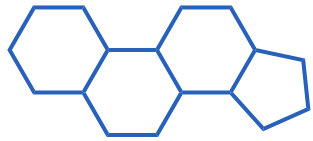
- ✓ Athanassios Giannis (2009, **Cyclopamine**)
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- ✓ Dirk H. Trauner (2025, **Veratramine**)

➤ Total Synthesis of Heilonine

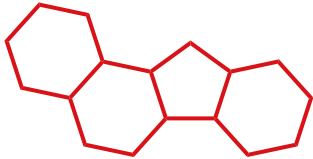
- ✓ Viresh H. Rawal (2021, **Heilonine**)
- ✓ 代明骥 (2024, **Heilonine**)

➤ Summary

Introduction

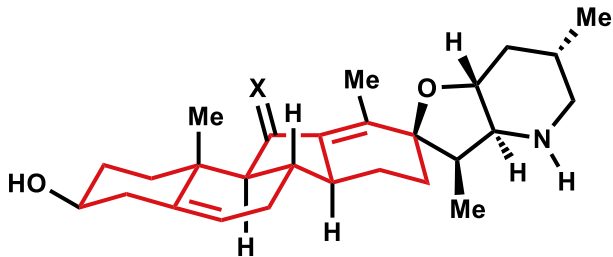


steroidal alkaloids skeleton



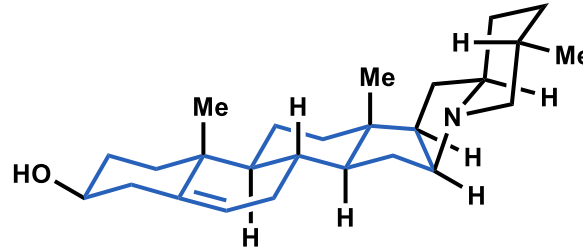
isosteroidal alkaloids skeleton

Cyclopamine type



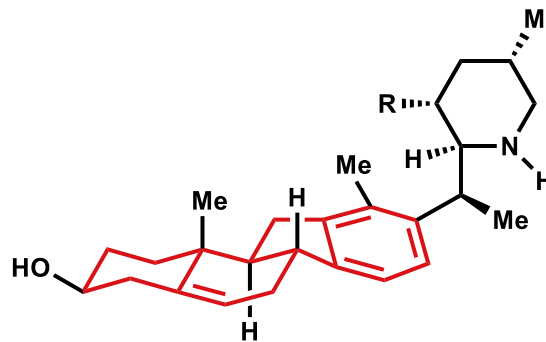
X = H, H, Cyclopamine
X = O, Jervine

Solanidine type



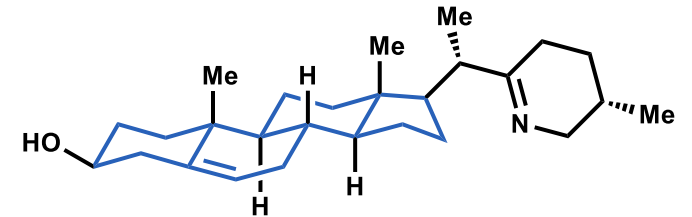
Solanidine

Veratramine type



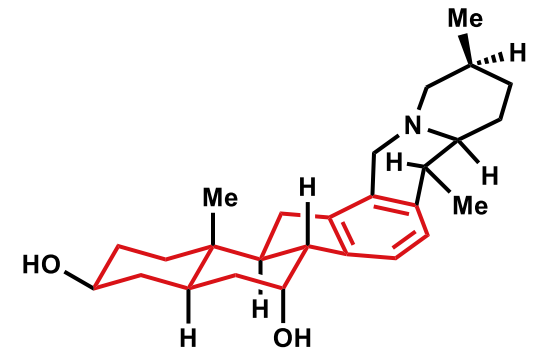
R = OH, Veratramine
R = H, Verarine

Verazine type



Verazine

Cevanine type



Heilonine

Content

➤ Introduction

➤ Total Synthesis of Cyclopamine and Veratramine

- ✓ Athanassios Giannis (2009, **Cyclopamine**)
- ✓ Phil S. Baran (2023, **Cyclopamine**)
- ✓ 高栓虎 (2023, **Cyclopamine** and **Veratramine**)
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➤ Total Synthesis of Heilonine

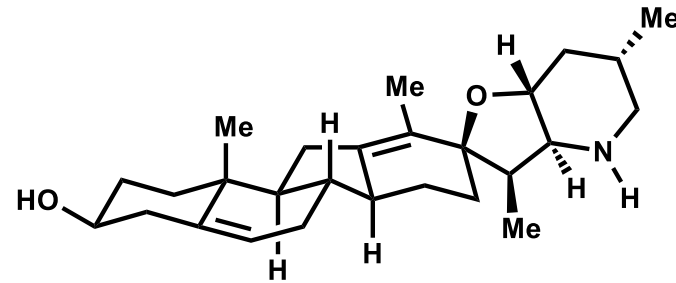
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➤ Summary

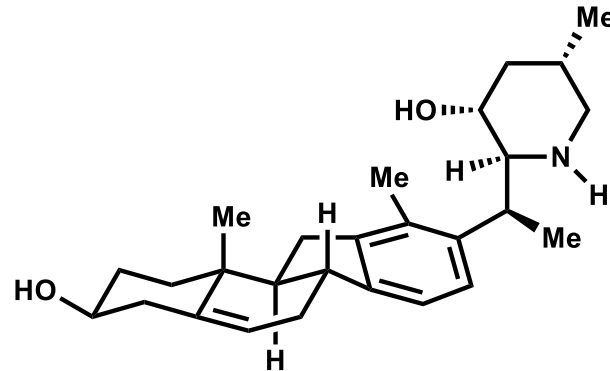
Cyclopamine and Veratramine



Veratrum Californicum



Cyclopamine



Veratramine

Bioactivity

- ✓ Inhibitor of hedgehog (Hh) pathway
- ✓ Teratogenic Activity
- ✓ Anticancer Properties
- ✓ Inhibitor of Viral Transcription

Bioactivity

- ✓ Anti-hypertension
- ✓ Serotonin (5-HT) Agonist Activity
- ✓ Anticancer Properties
- ✓ Antiplatelet

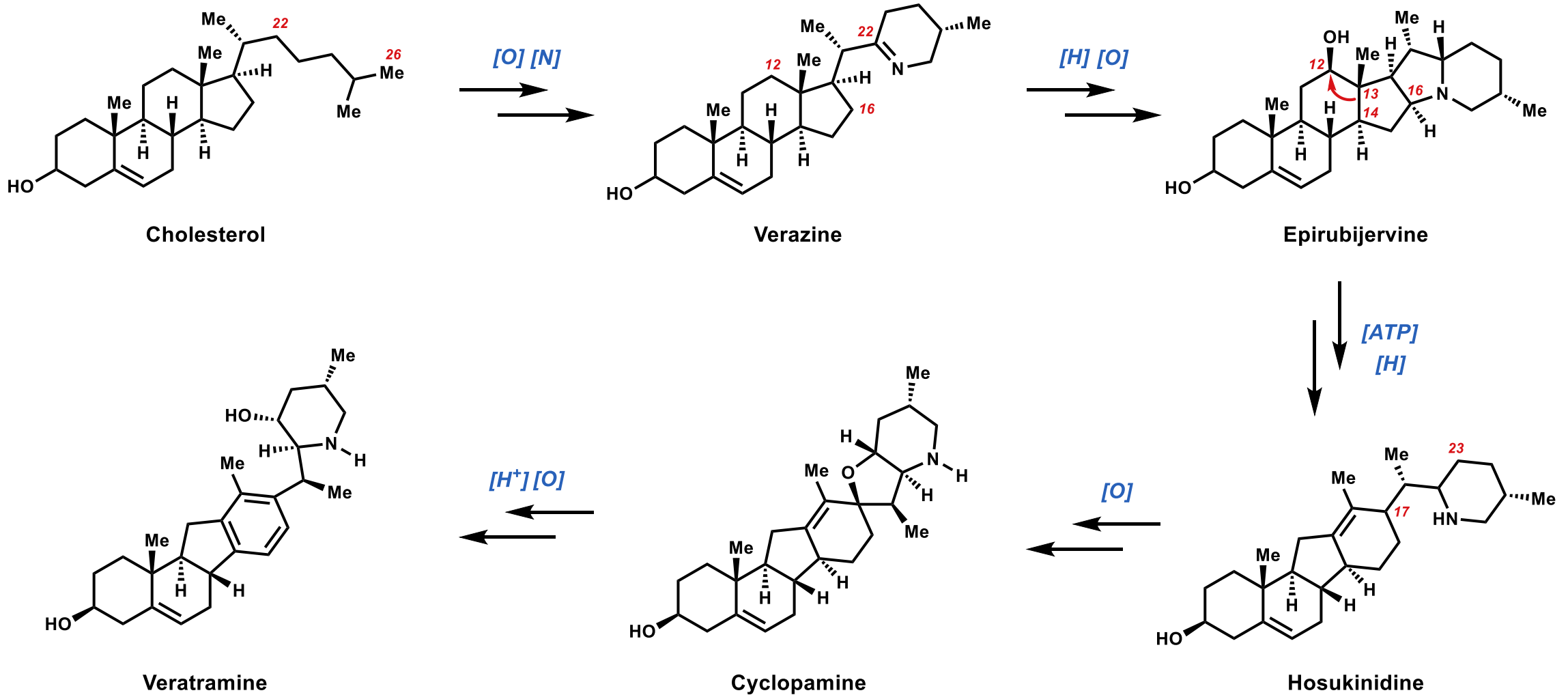
Keeler, R. F. *J. Agric. Food. Chem.* **1969**, 17, 473.

Heretsch, P.; Tzagkaroulaki, L.; Giannis, A. *Angew. Chem. Int. Ed.* **2010**, 49, 3418.

Cong, Y.; Zhang, J.-L.; Li, S.-S.; Shen, S.; Wang, J.-Y.; Cai, Z. *Biomed. Chromatogr.* **2016**, 30, 1515.

Cyclopamine and Veratramine

Simplified Biosynthetic Pathway

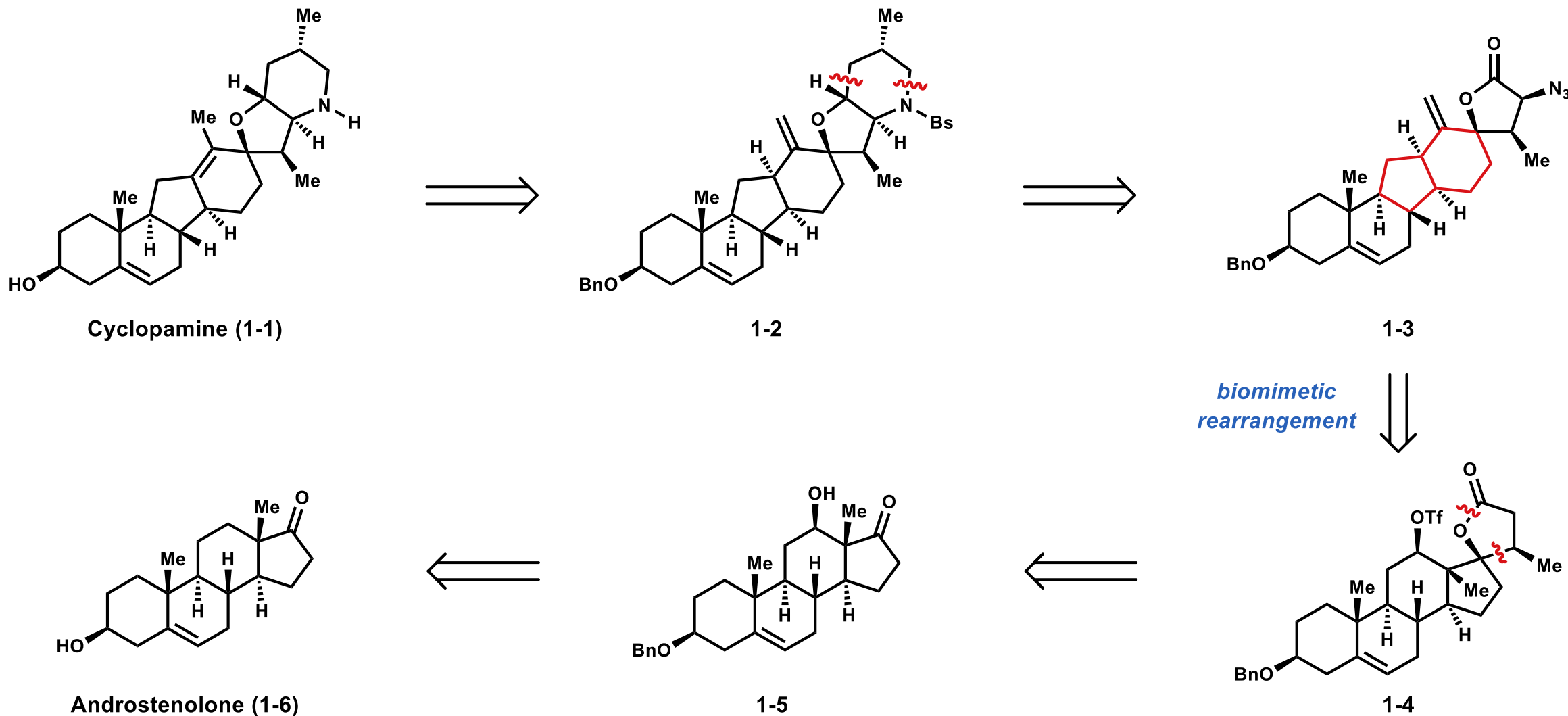


Kaneko, K.; Mitsuhashi, H.; Hirayama, K.; Ohmori, S. *Phytochemistry* **1970**, 9, 2497.

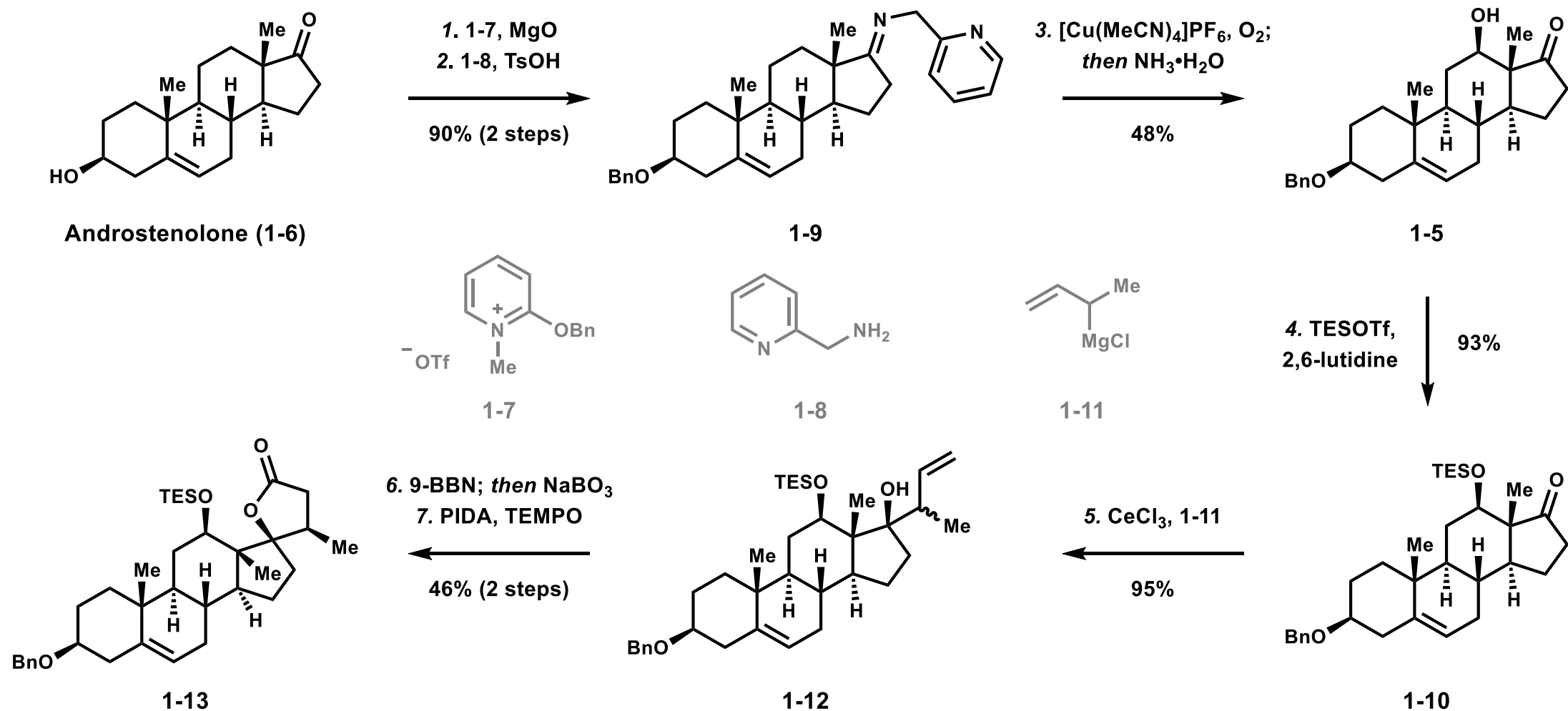
Heretsch, P.; Tzagkaroulaki, L.; Giannis, A. *Angew. Chem. Int. Ed.* **2010**, 49, 3418.

Total Synthesis of Cyclopamine — *Giannis* (2009)

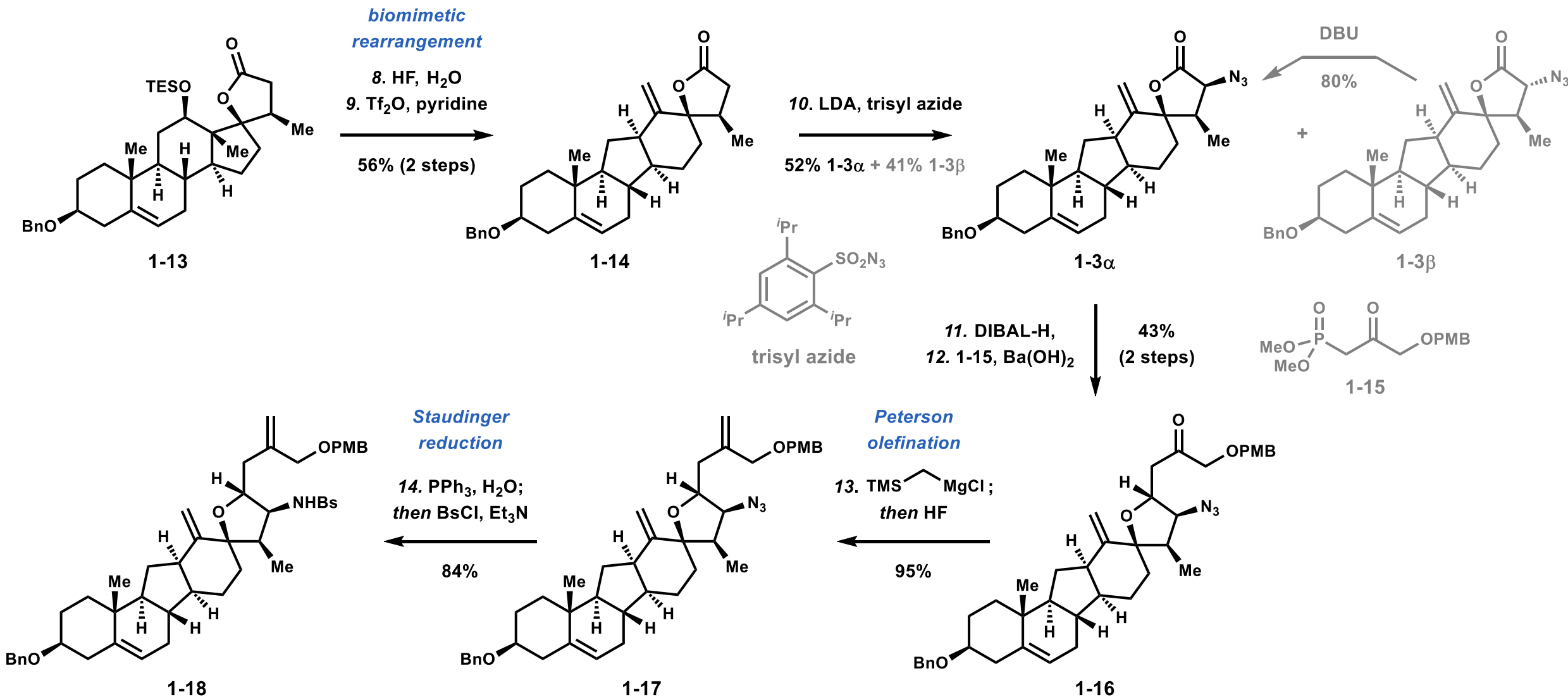
Retrosynthetic Analysis



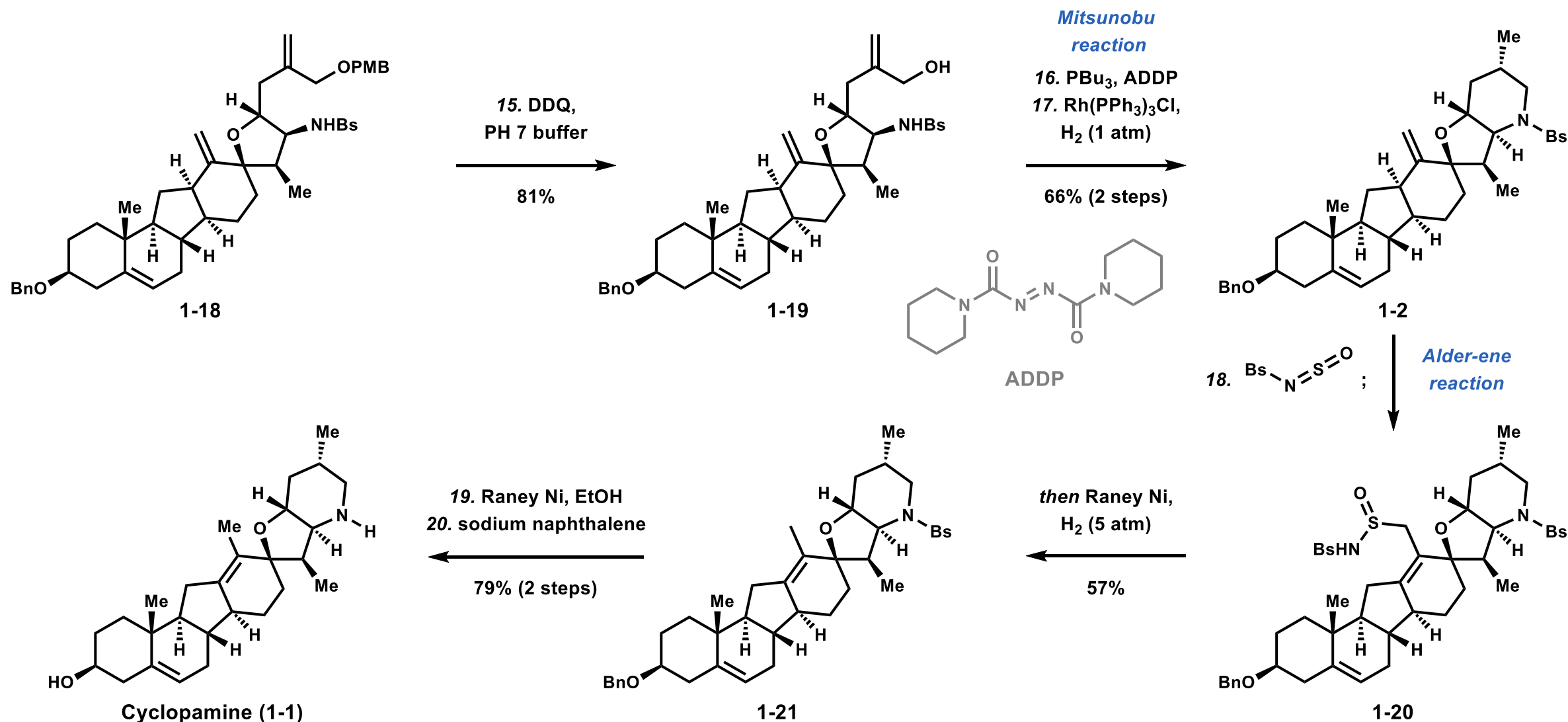
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Total Synthesis of Cyclopamine — *Giannis* (2009)

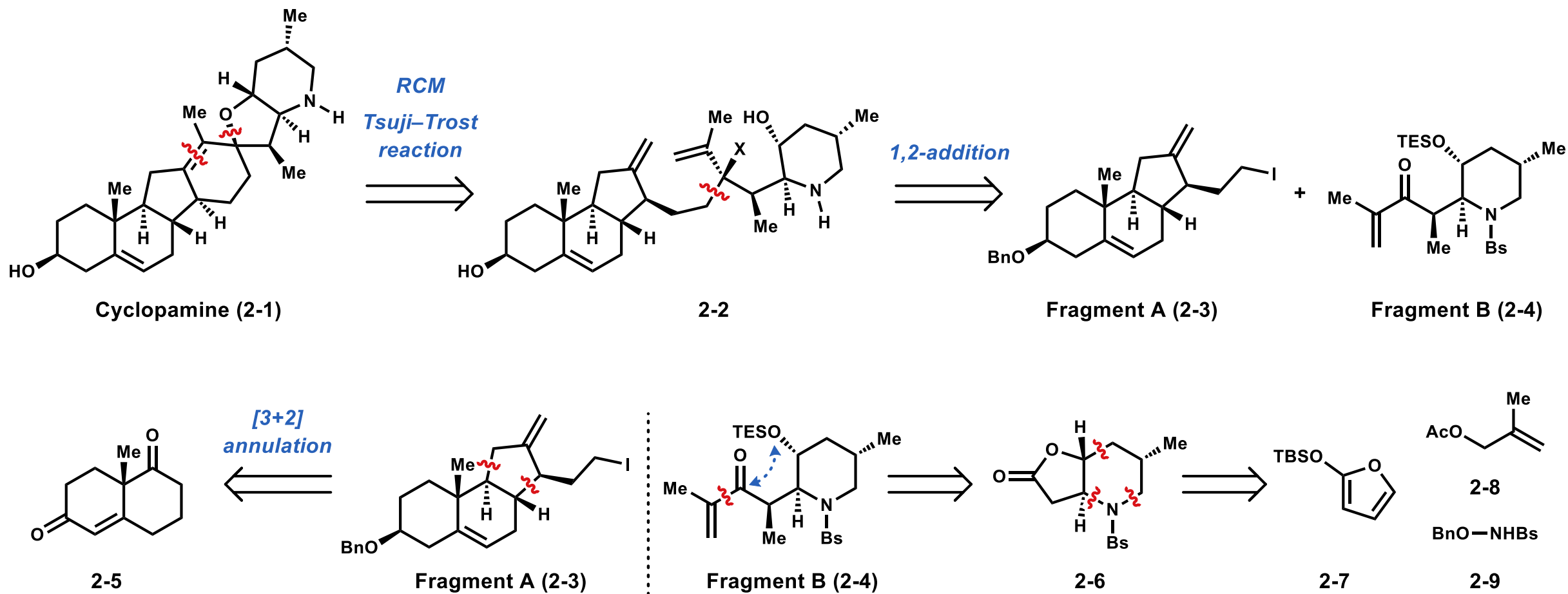


Total Synthesis of Cyclopamine — *Giannis* (2009)



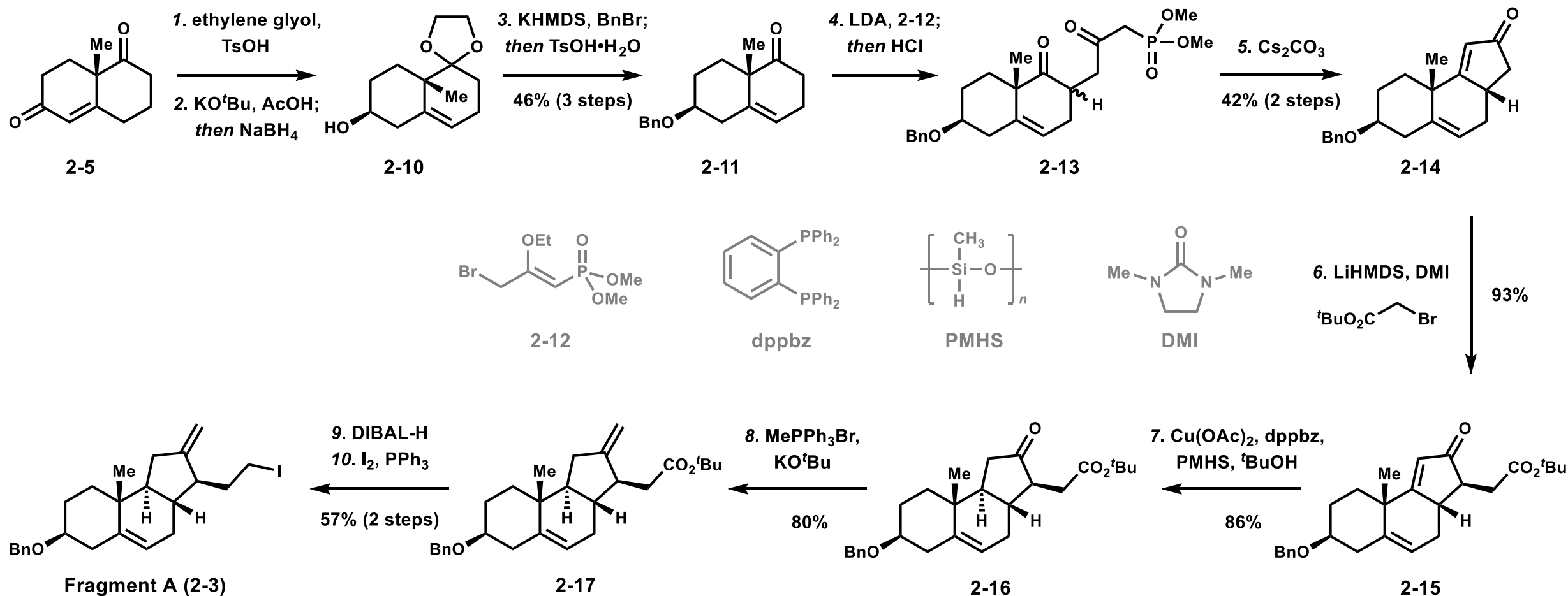
Total Synthesis of Cycloamine — Baran (2023)

Retrosynthetic Analysis



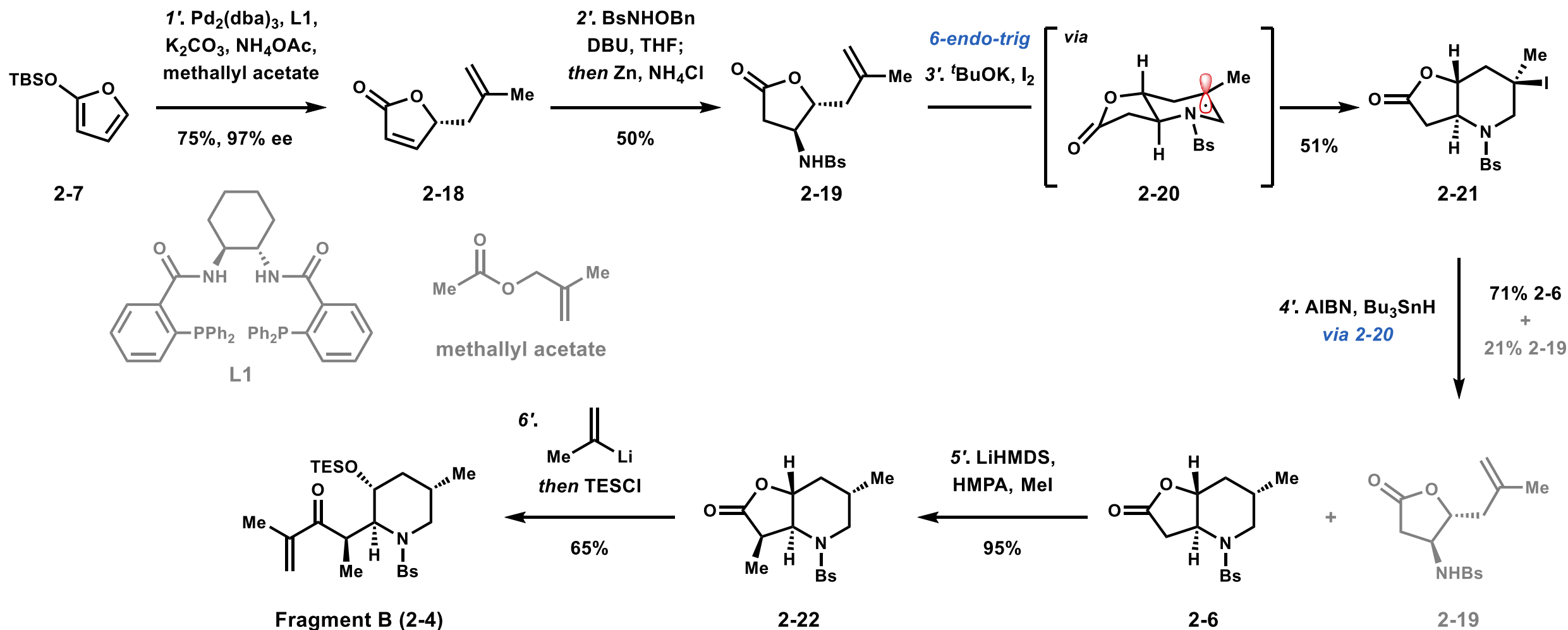
Total Synthesis of Cyclopamine — Baran (2023)

Synthesis of Fragment A



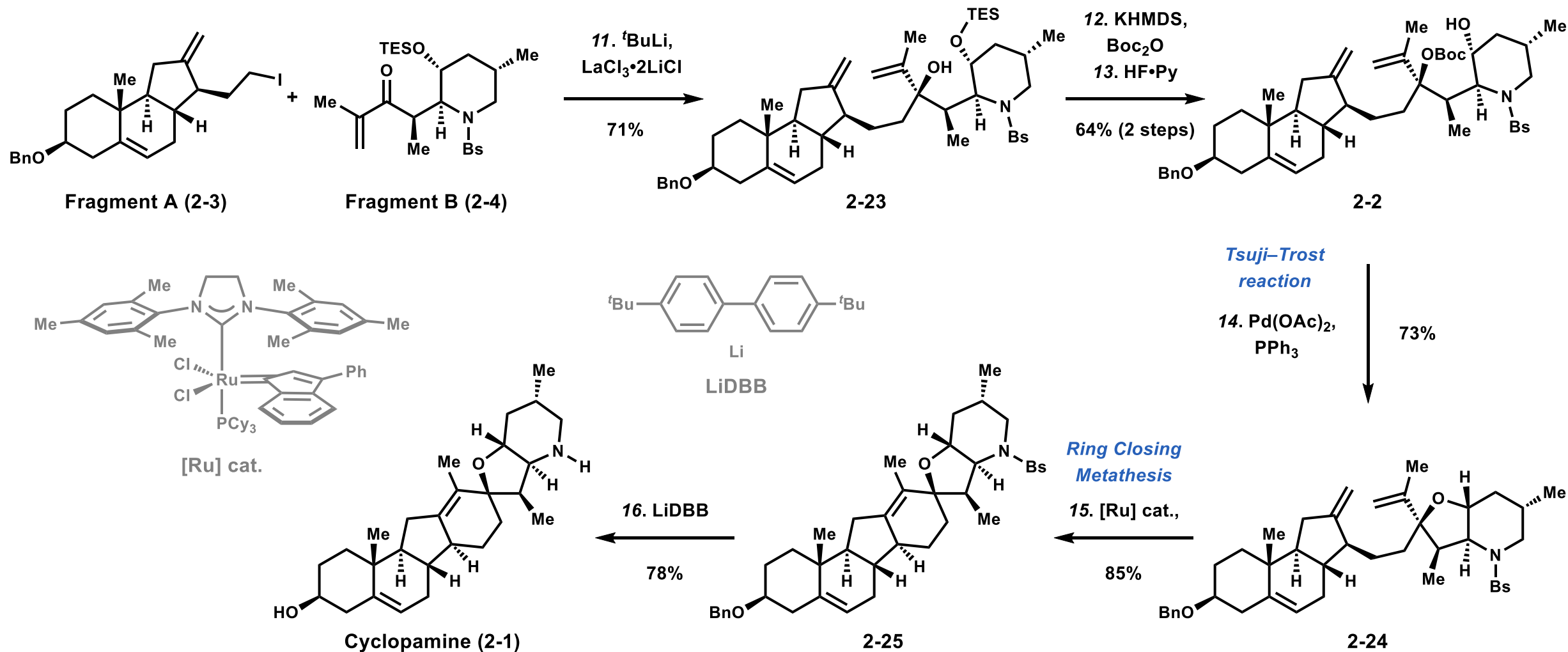
Total Synthesis of Cyclopamine — Baran (2023)

Synthesis of Fragment B



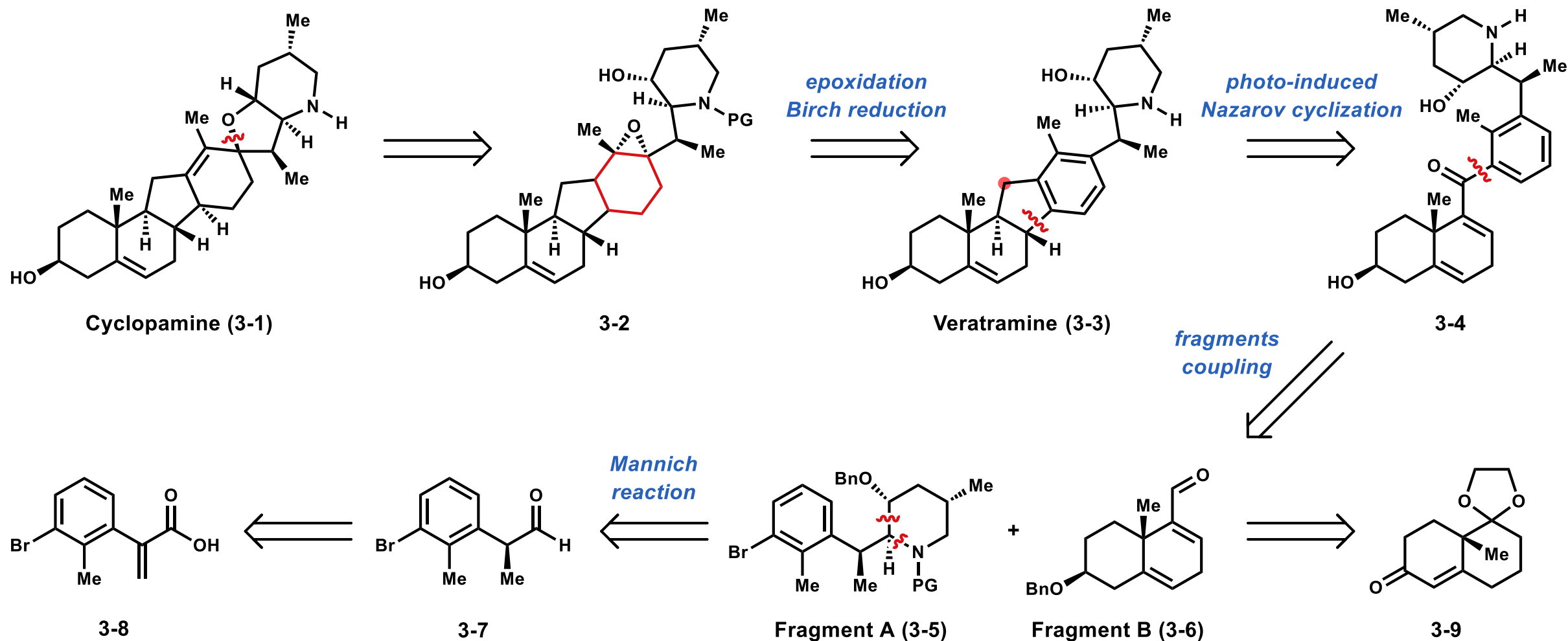
Total Synthesis of Cyclopamine — *Baran* (2023)

Synthesis of Cyclopamine



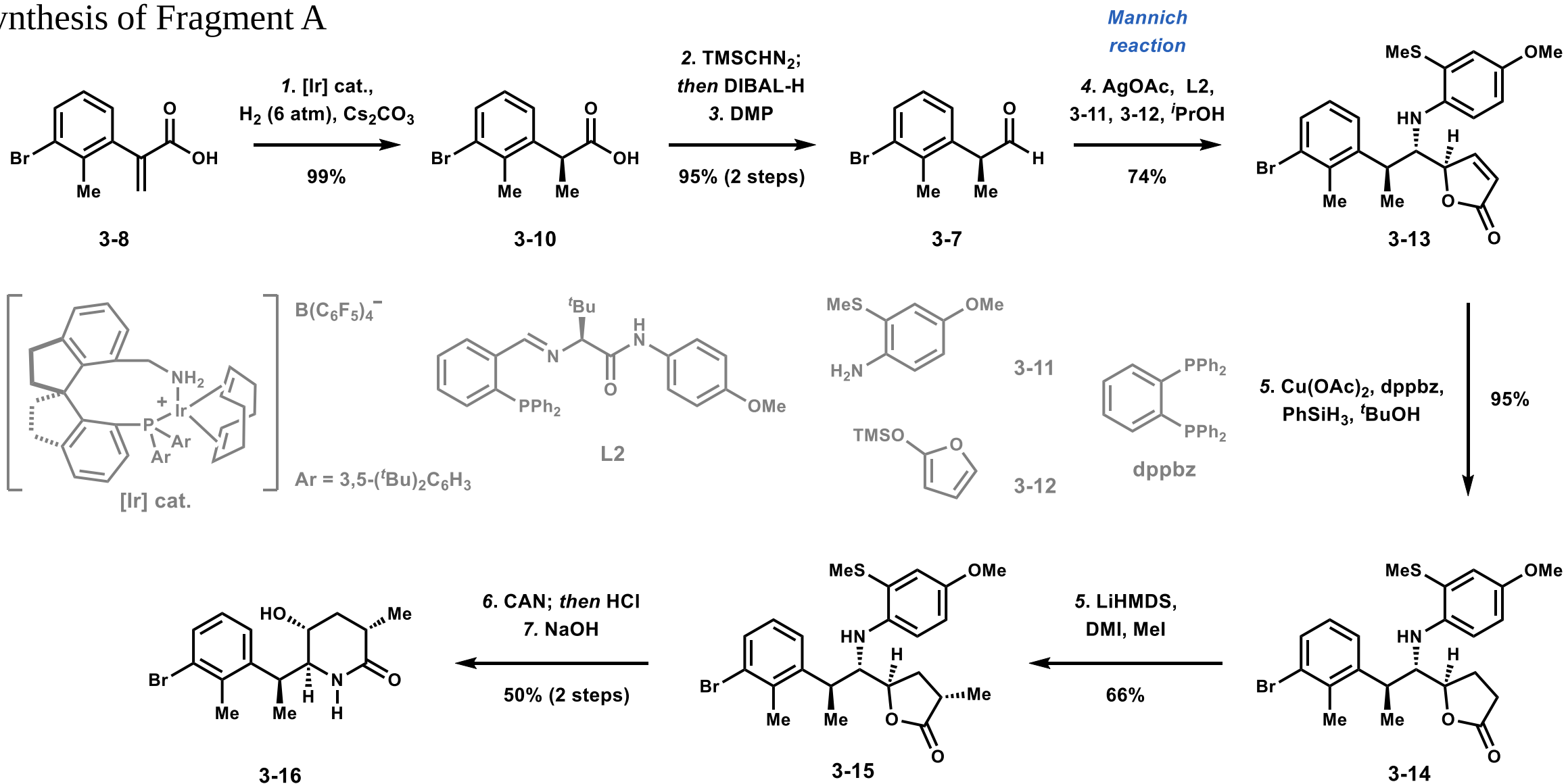
Total Synthesis of Cyclopamine and Veratramine — 高栓虎 (2023)

Retrosynthetic Analysis



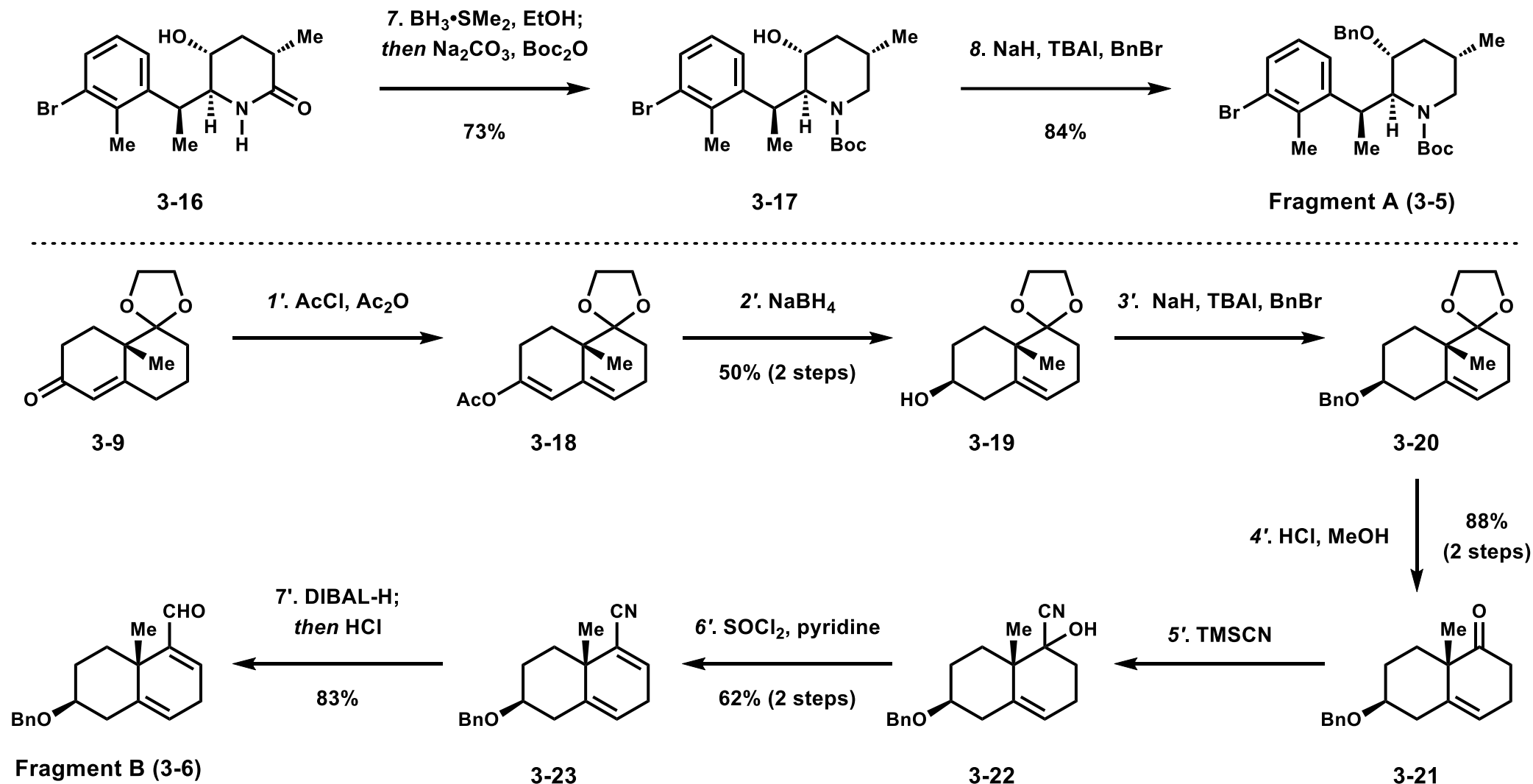
Total Synthesis of Cyclopamine and Veratramine — 高栓虎 (2023)

Synthesis of Fragment A



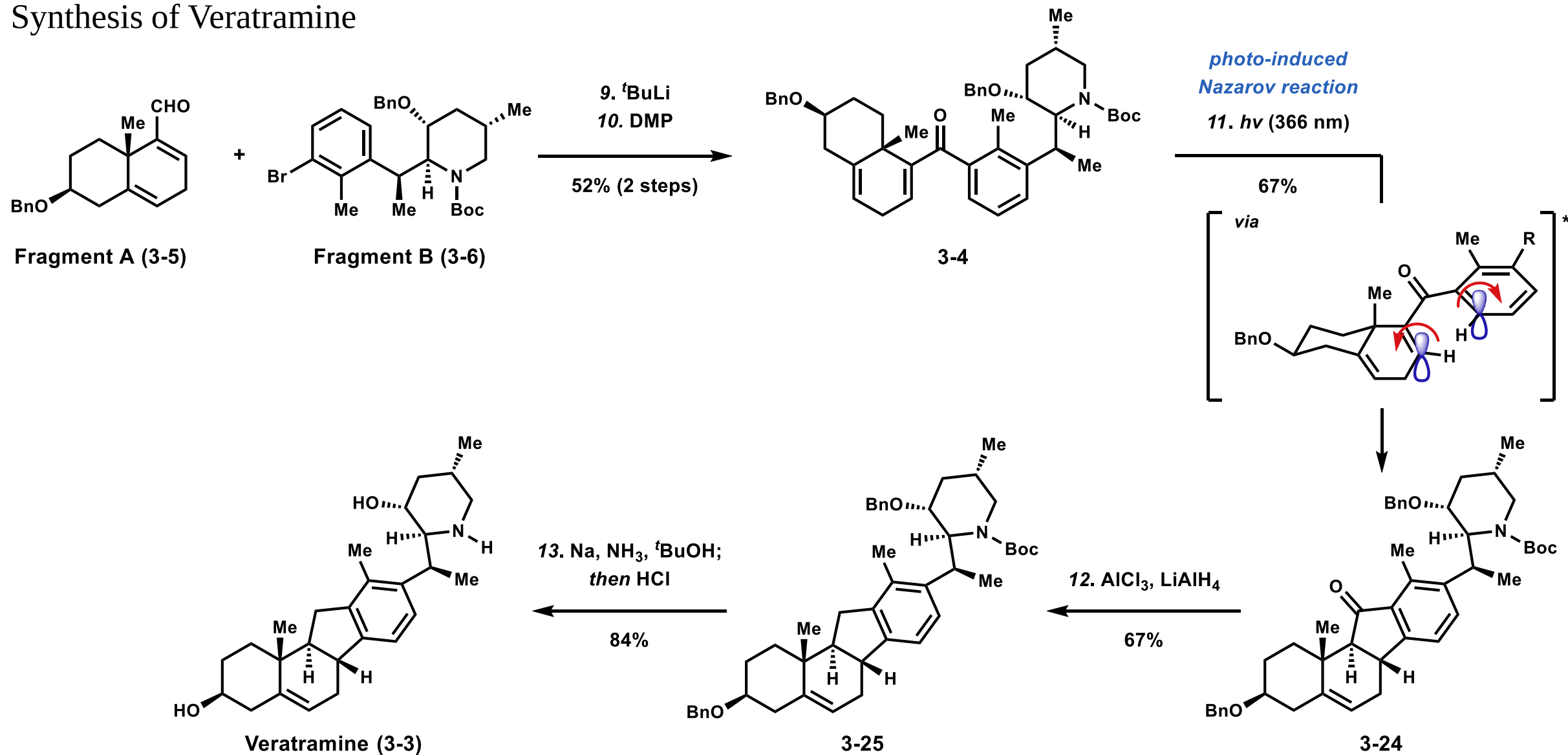
Total Synthesis of Cyclopamine and Veratramine — 高栓虎 (2023)

Synthesis of Fragment A and Fragment B



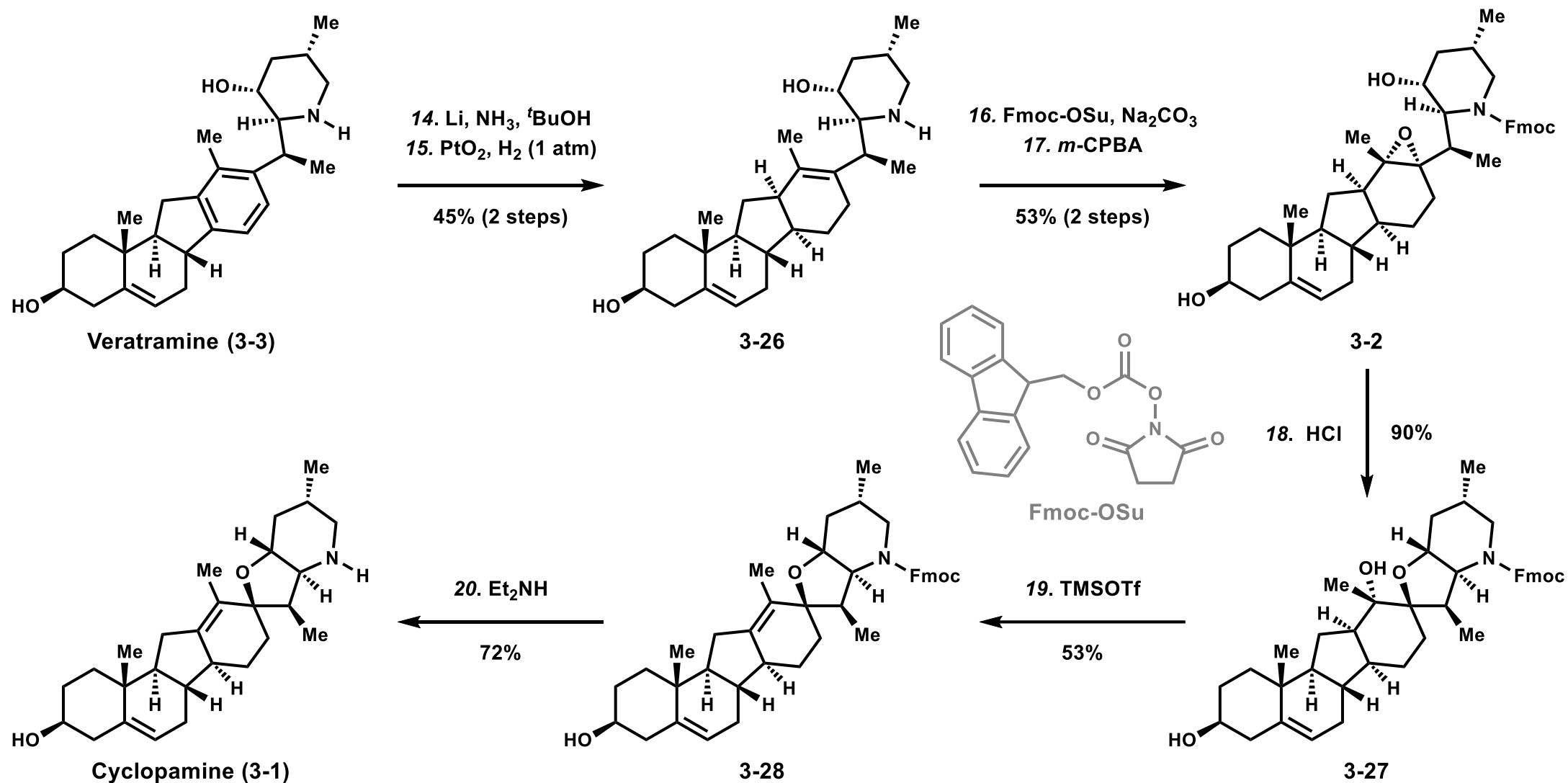
Total Synthesis of Cyclopamine and Veratramine — 高栓虎 (2023)

Synthesis of Veratramine



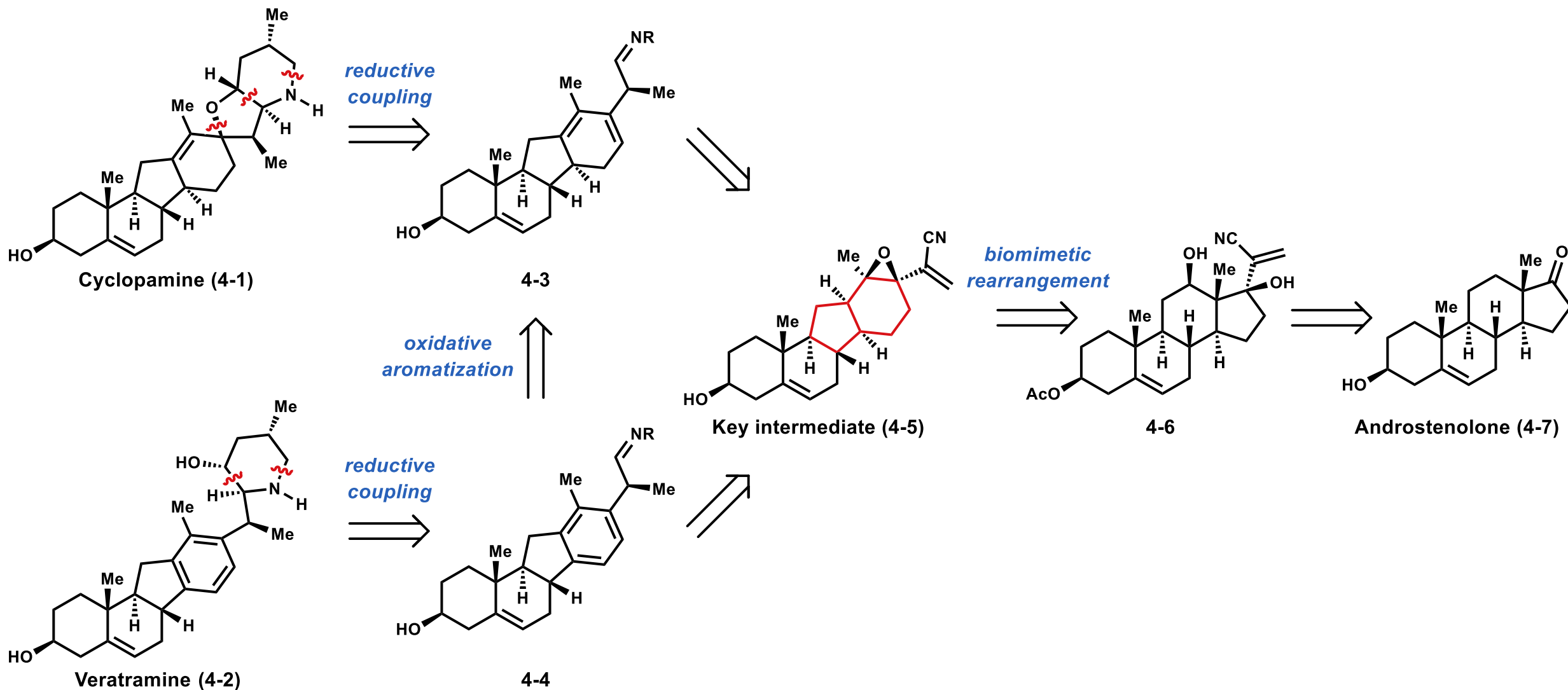
Total Synthesis of Cyclopamine and Veratramine — 高栓虎 (2023)

Synthesis of Cyclopamine



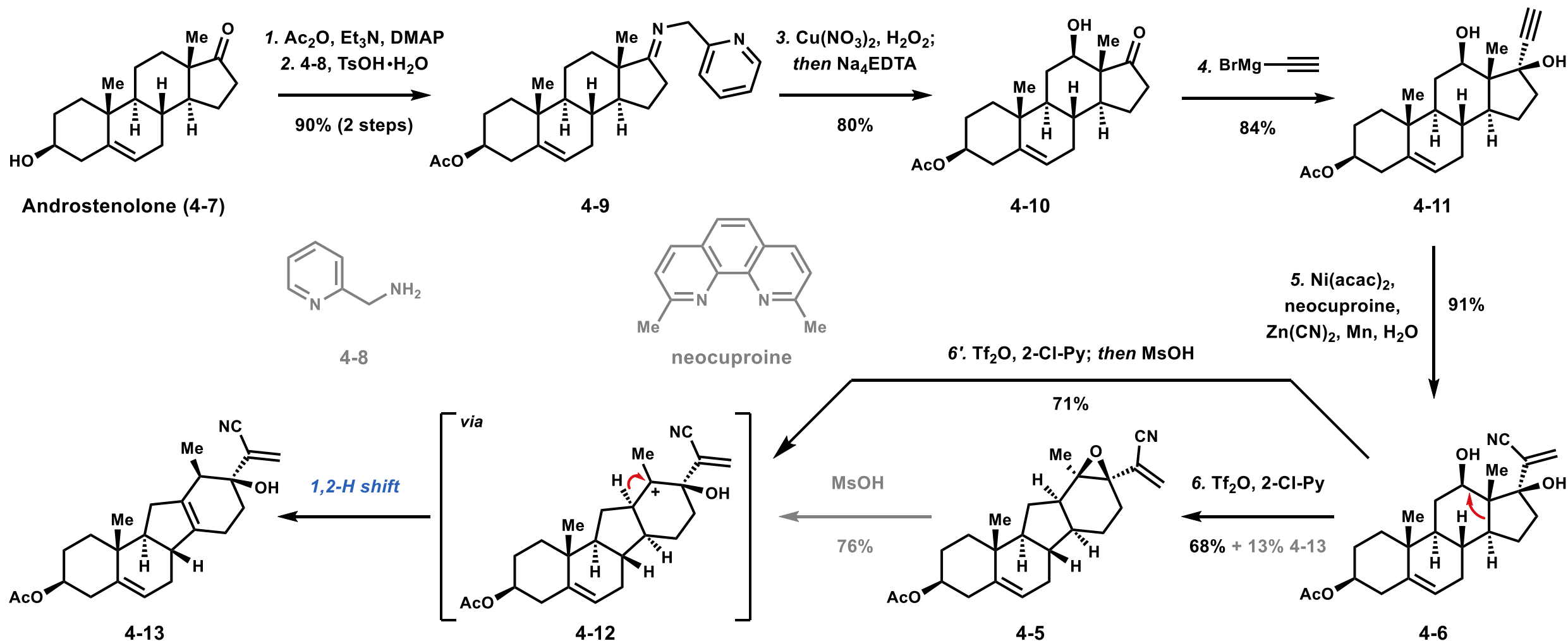
Total Synthesis of Cyclopamine and Veratramine — 秦勇 (2024)

Retrosynthetic Analysis



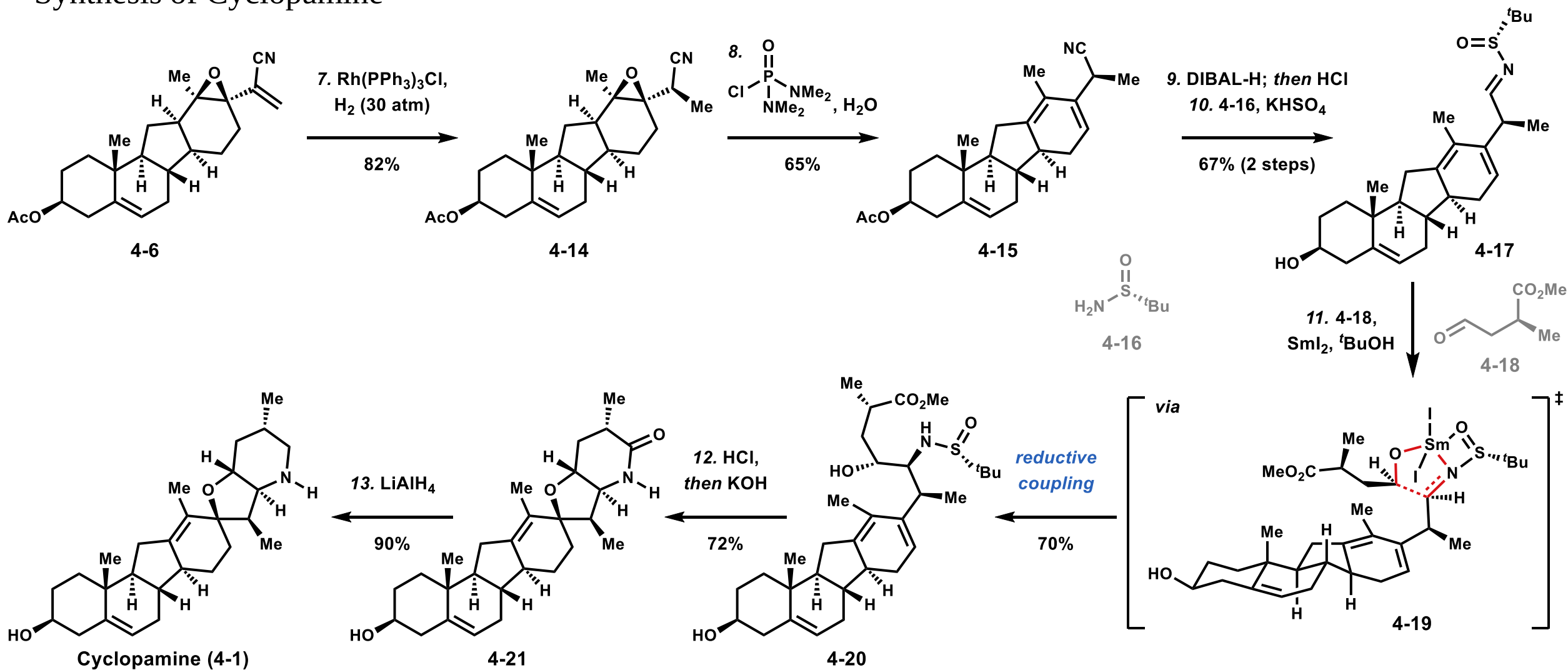
Total Synthesis of Cyclopamine and Veratramine — 秦勇 (2024)

Synthesis of Key Intermediate



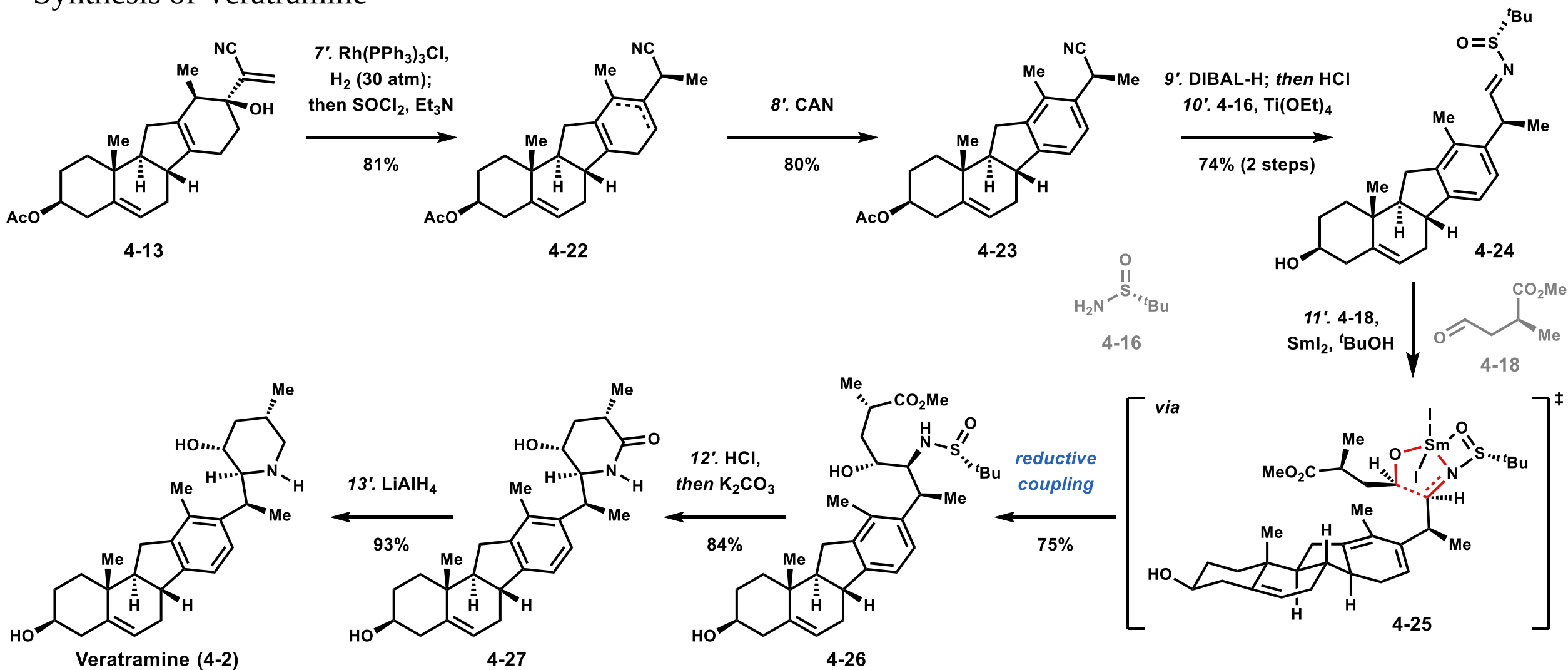
Total Synthesis of Cyclopamine and Veratramine — 秦勇 (2024)

Synthesis of Cyclopamine



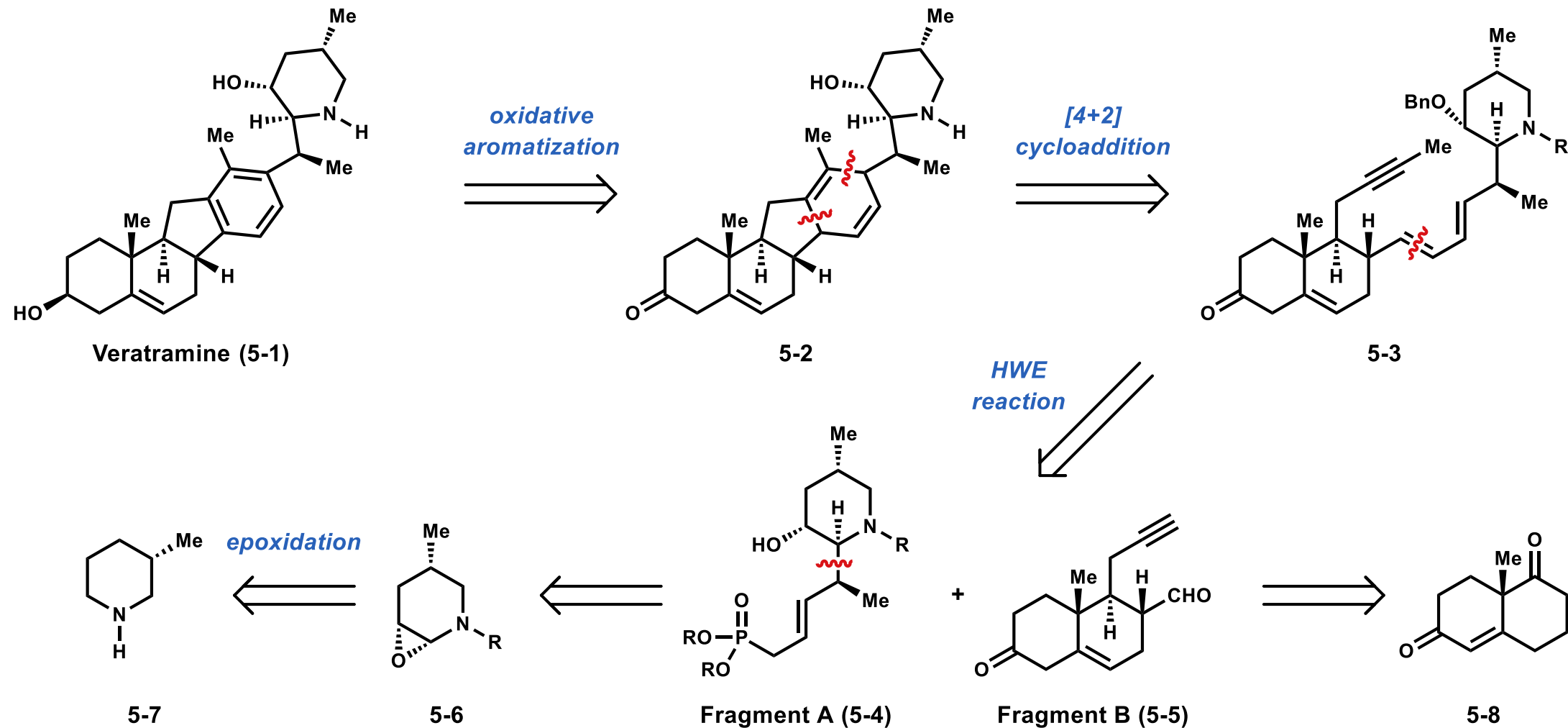
Total Synthesis of Cyclopamine and Veratramine — 秦勇 (2024)

Synthesis of Veratramine



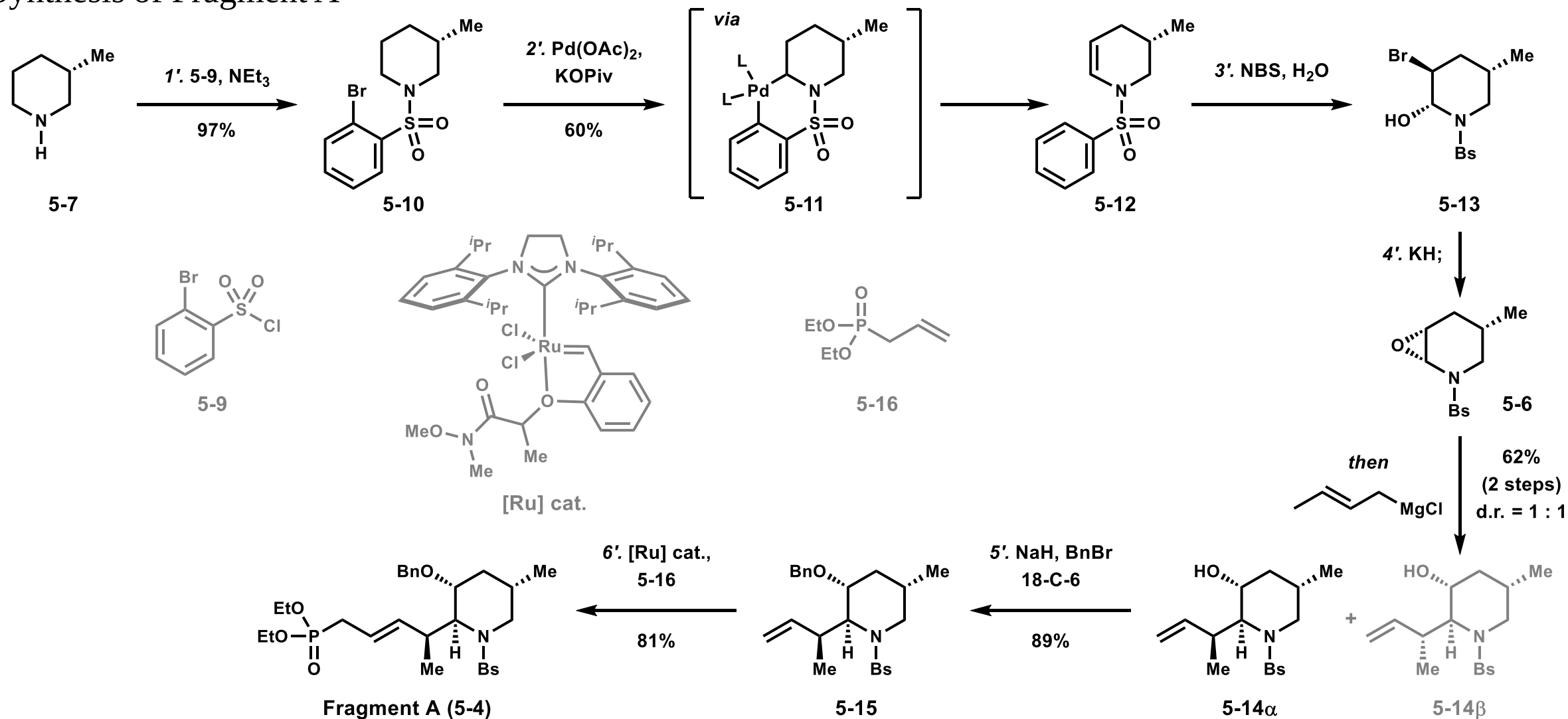
Total Synthesis of Veratramine — Trauner (2025)

Retrosynthetic Analysis



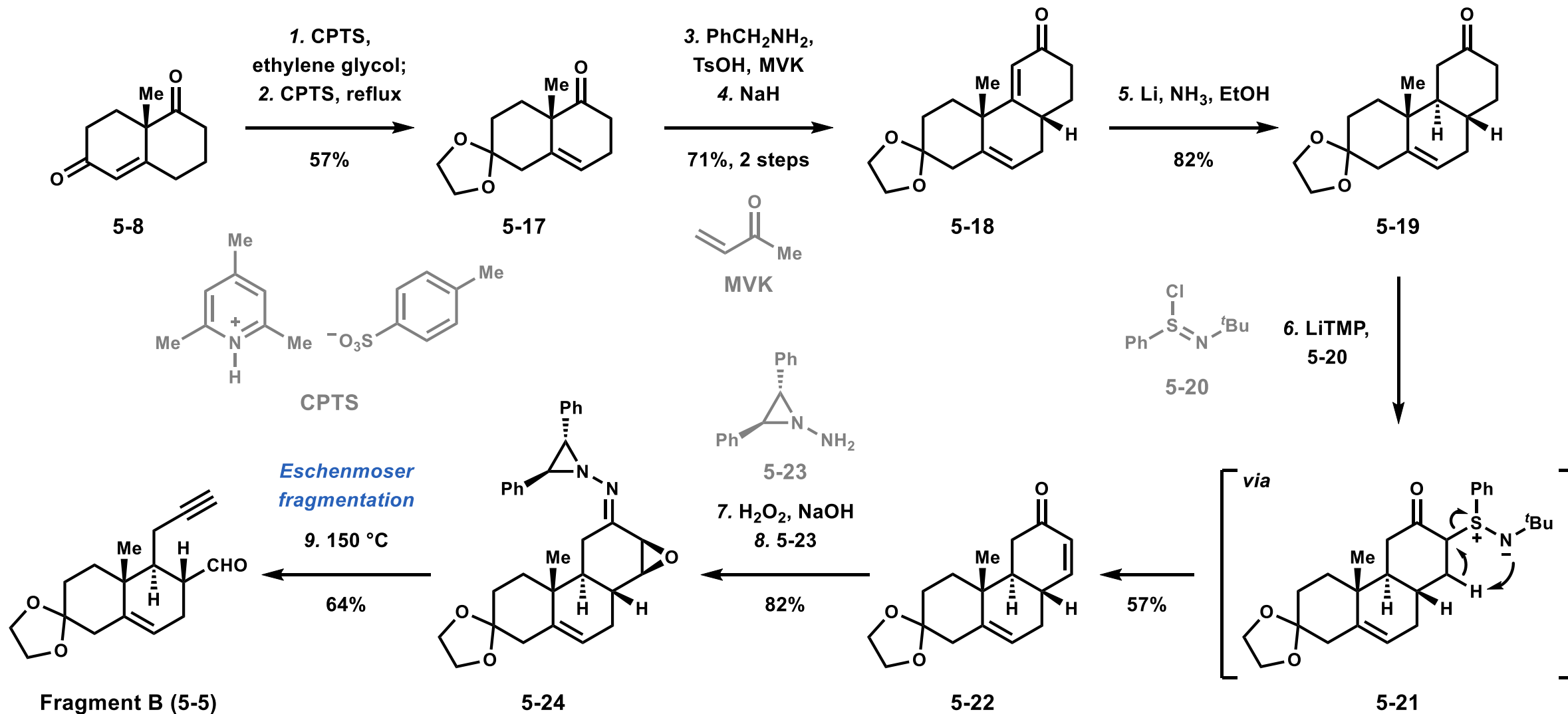
Total Synthesis of Veratramine — Trauner (2025)

Synthesis of Fragment A



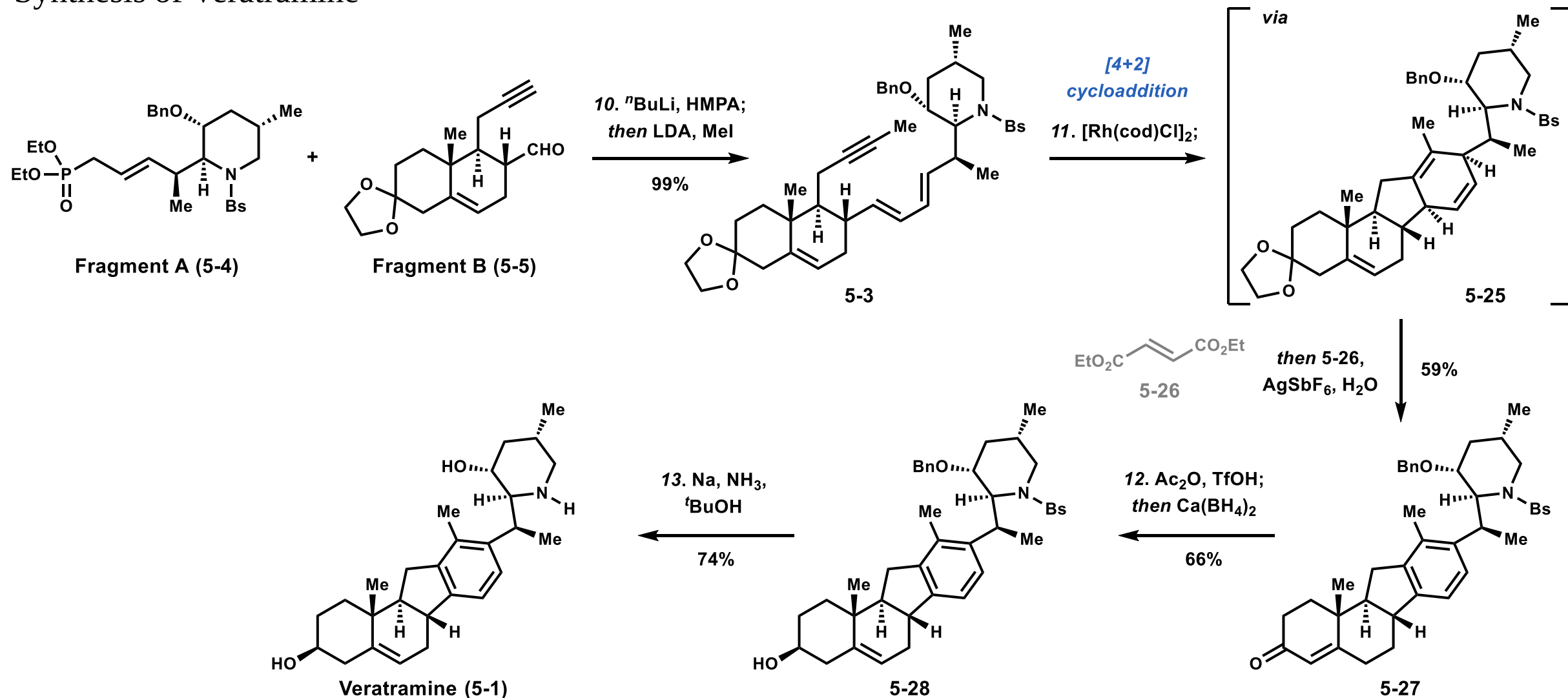
Total Synthesis of Veratramine — Trauner (2025)

Synthesis of Fragment B



Total Synthesis of Veratramine — Trauner (2025)

Synthesis of Veratramine



Content

➤ Introduction

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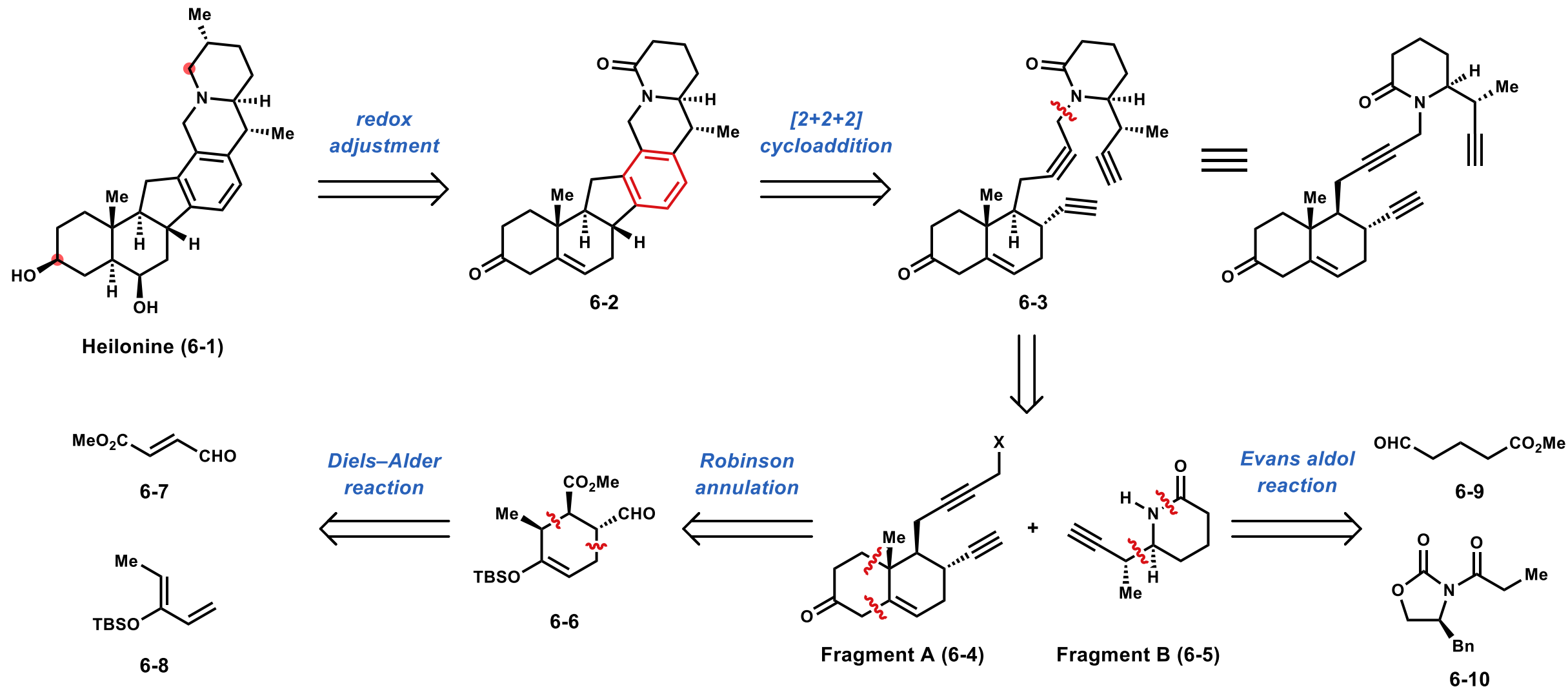
➤ Total Synthesis of Heilonine

- ✓ Viresh H. Rawal (2021, **Heilonine**)
- ✓ 代明骥 (2024, **Heilonine**)

➤ Summary

Total Synthesis of Heilonine — *Rawal* (2021)

Retrosynthetic Analysis

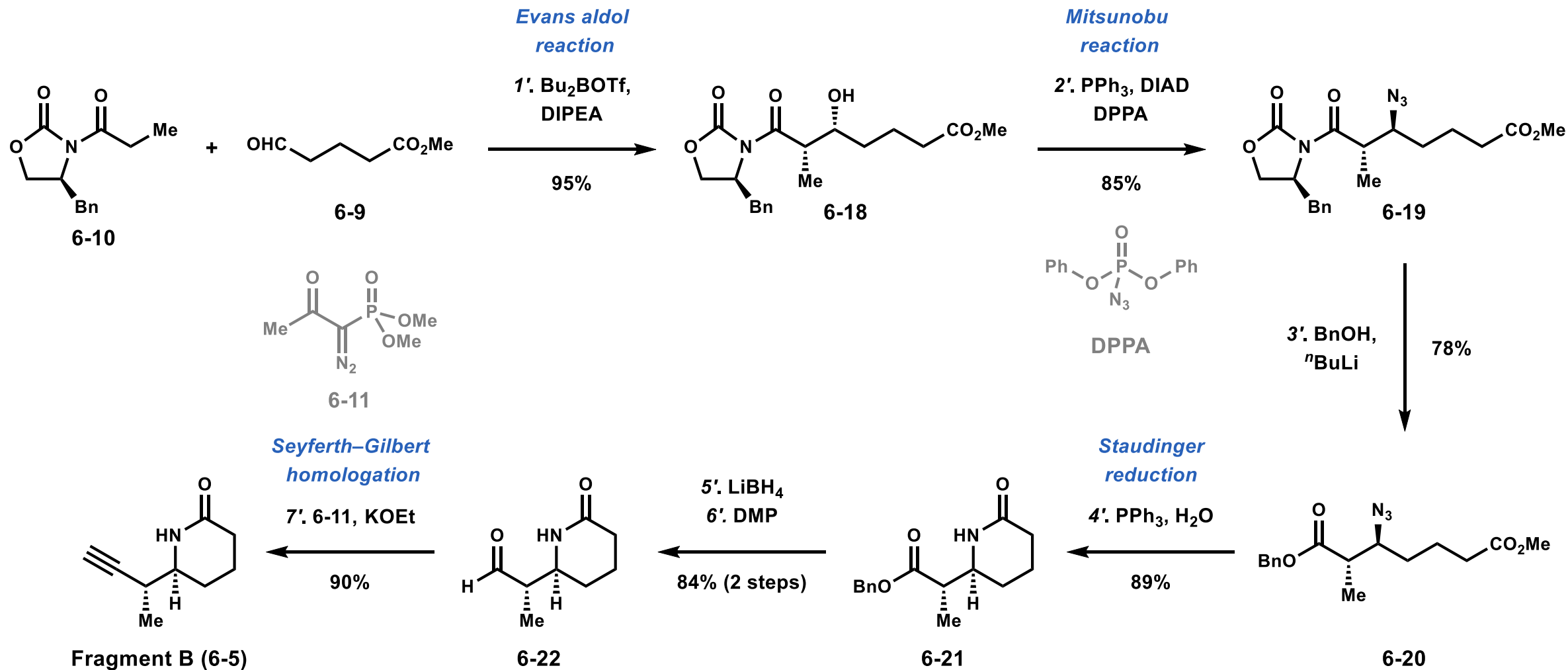


Synthesis of Fragment A



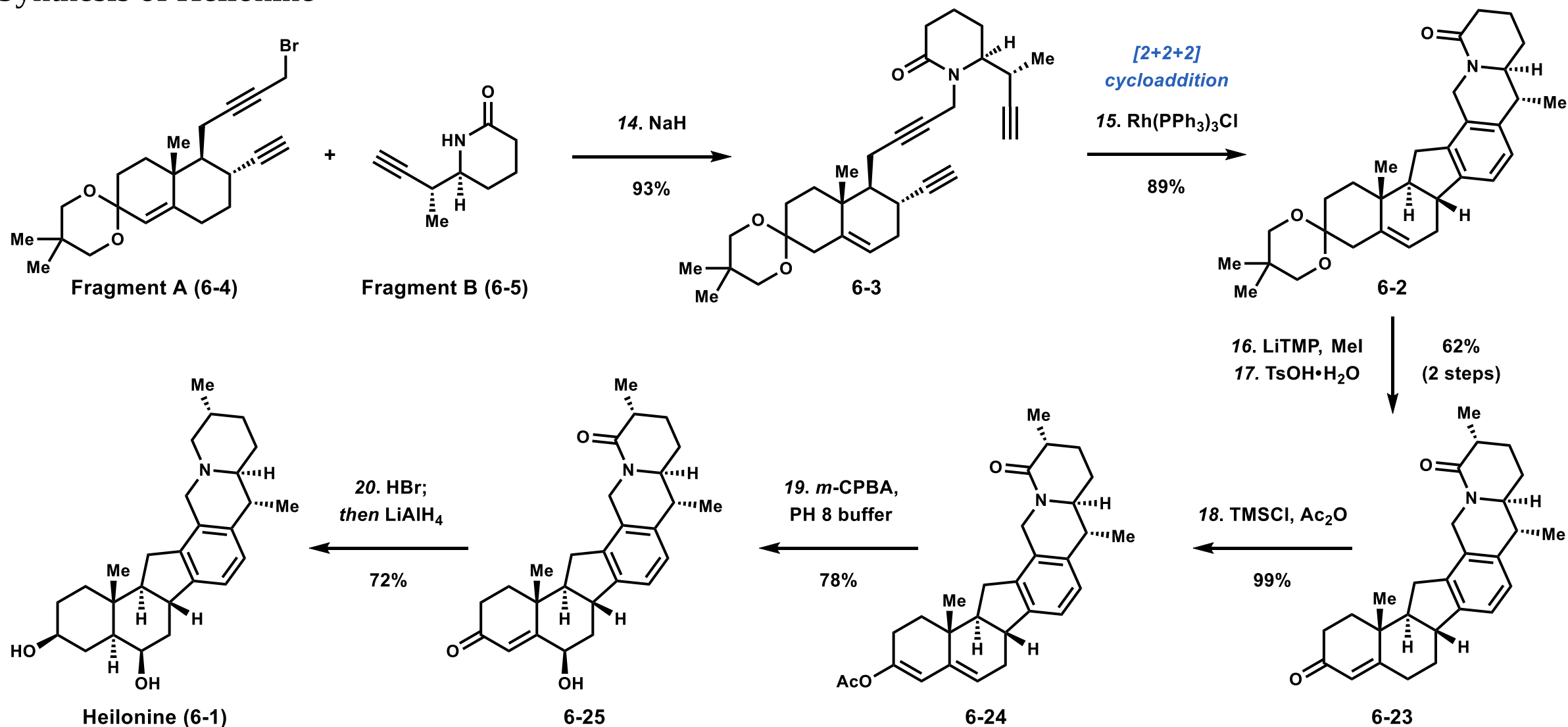
Total Synthesis of Heilonine — *Rawal* (2021)

Synthesis of Fragment B



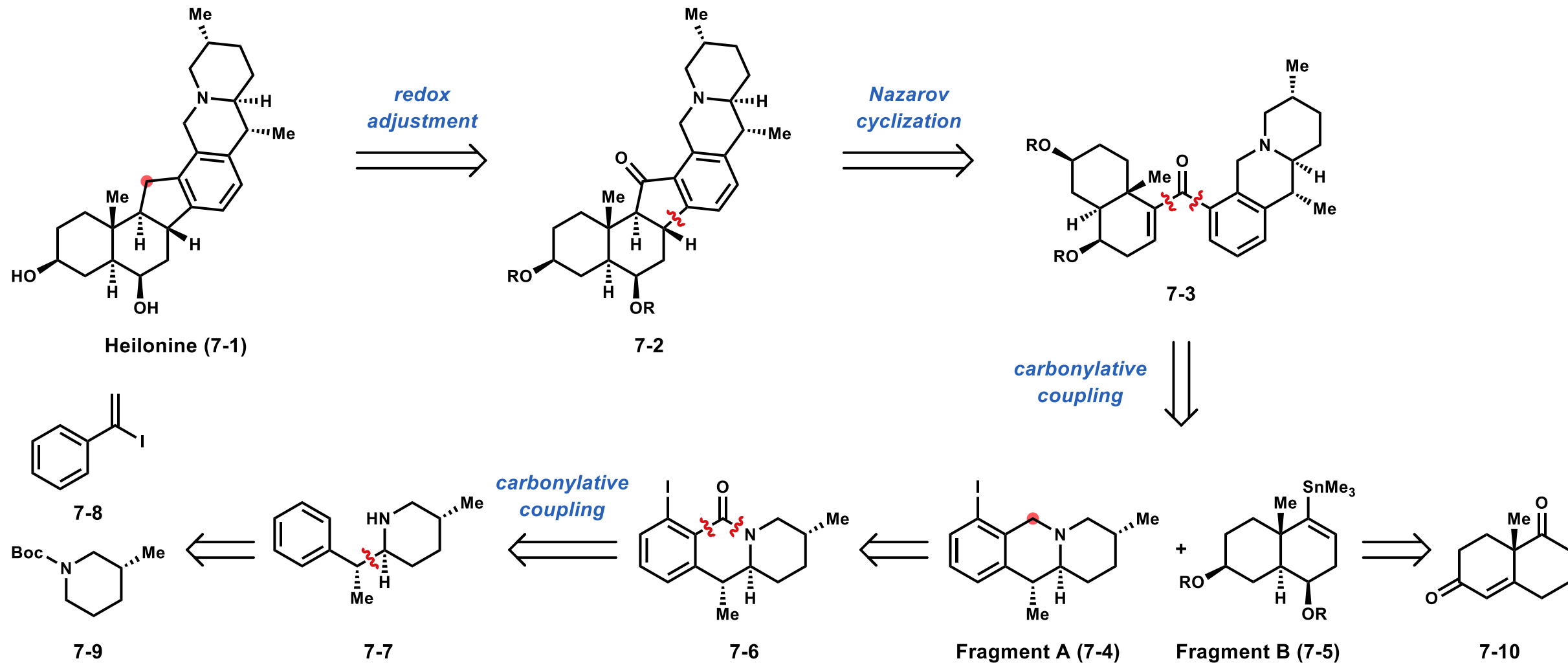
Total Synthesis of Heilonine — Rawal (2021)

Synthesis of Heilonine



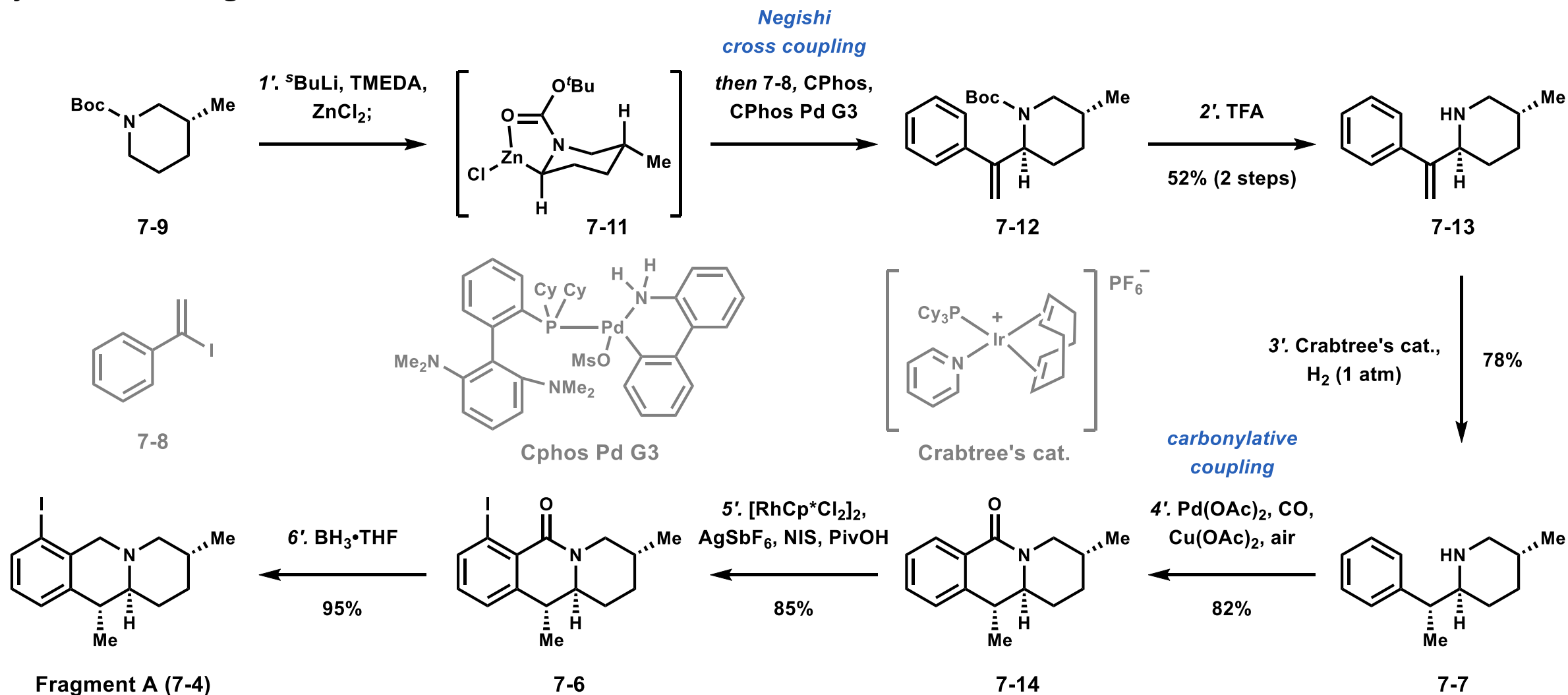
Total Synthesis of Heilonine — 代明驥 (2024)

Retrosynthetic Analysis



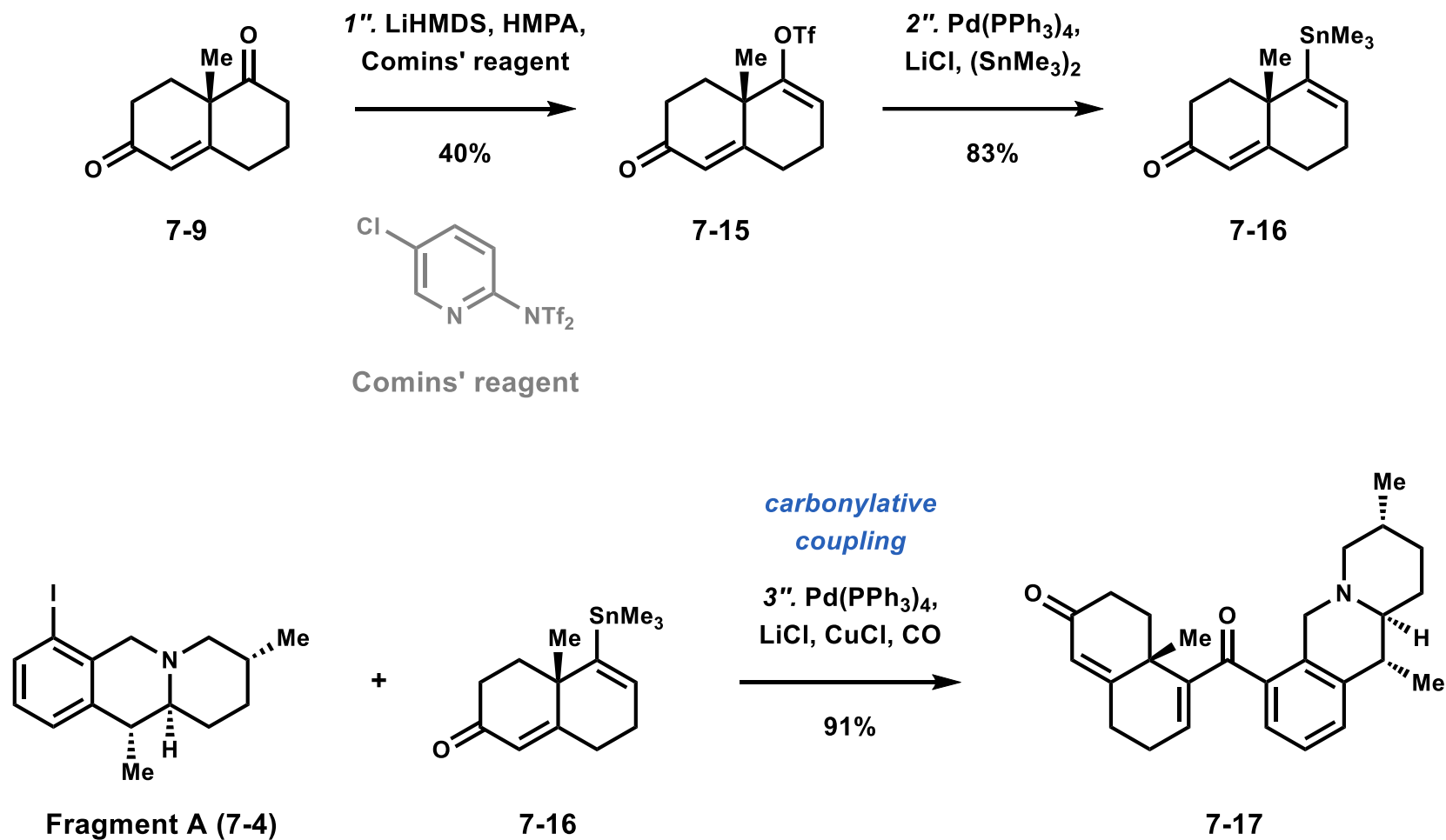
Total Synthesis of Heilonine — 代明驥 (2024)

Synthesis of Fragment A



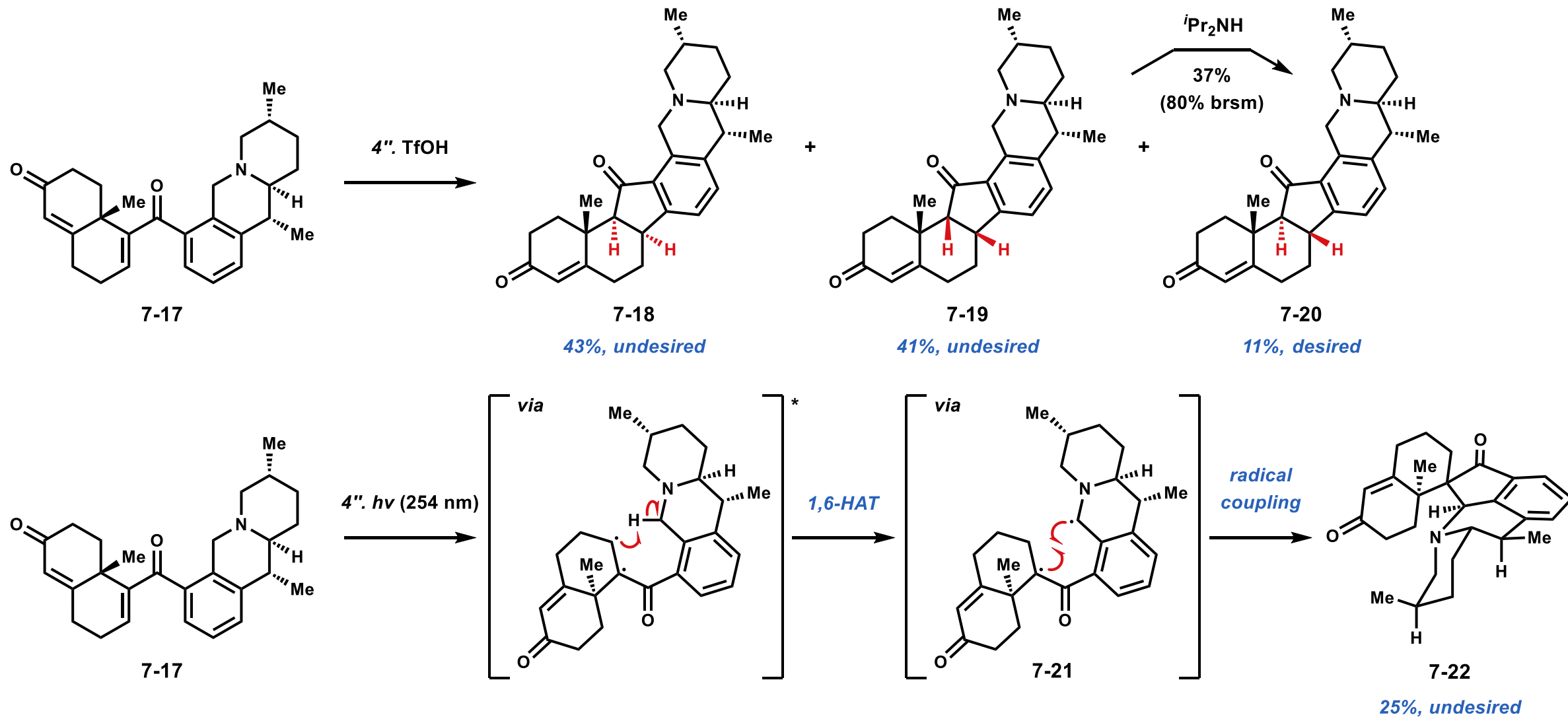
Total Synthesis of Heilonine — 代明驥 (2024)

Attempted Conditions for Nazarov Cyclization



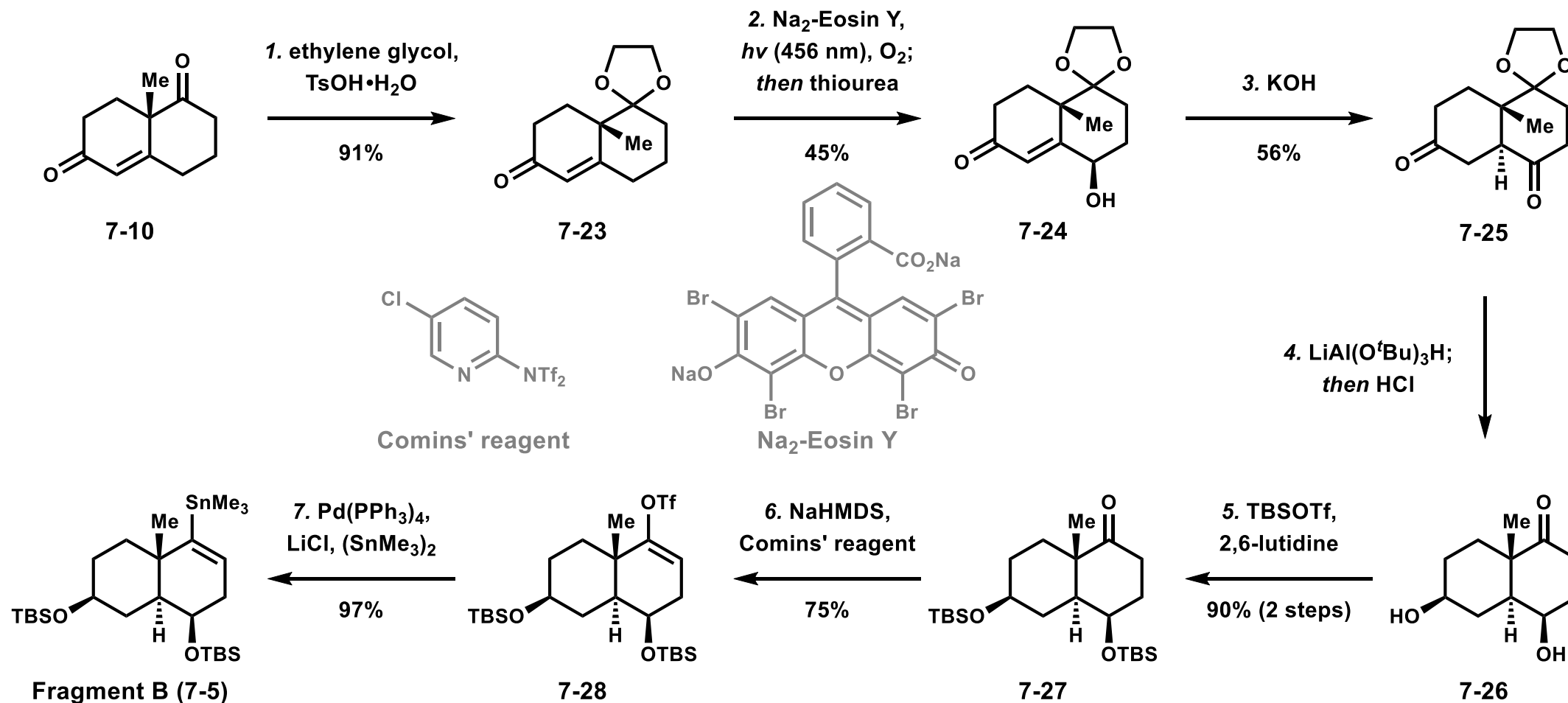
Total Synthesis of Heilonine — 代明驥 (2024)

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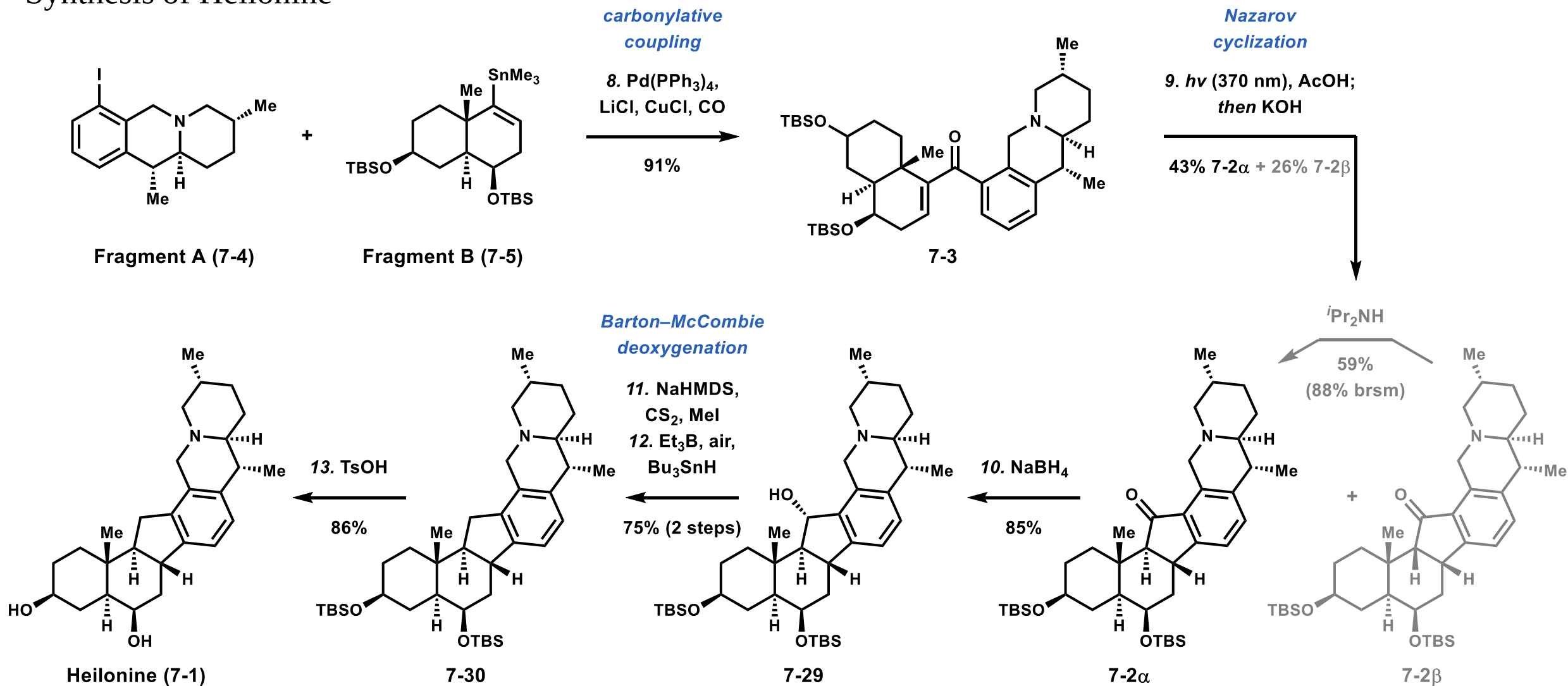
Total Synthesis of Heilonine — 代明驥 (2024)

Synthesis of Fragment B



Total Synthesis of Heilonine — 代明驥 (2024)

Synthesis of Heilonine



Content

➤ Introduction

➤ Total Synthesis of Cyclopamine and Veratramine

- ✓ Athanassios Giannis (2009, **Cyclopamine**)
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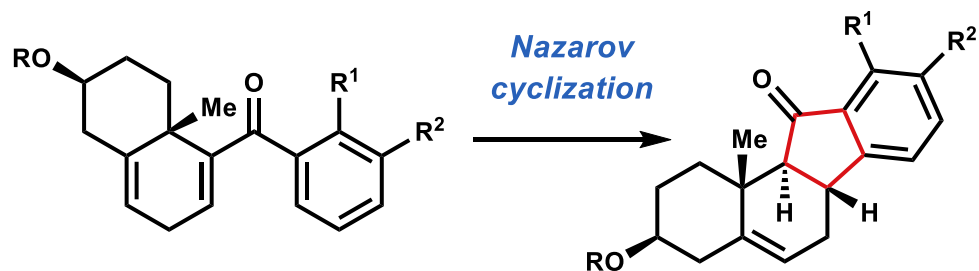
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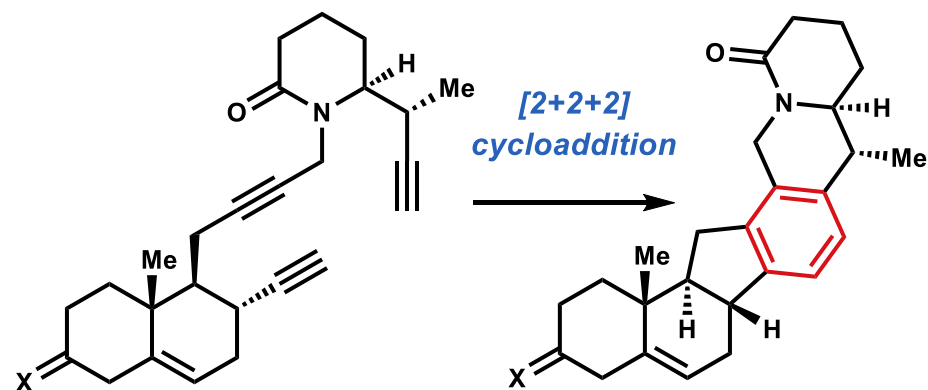
➤ Summary

Summary

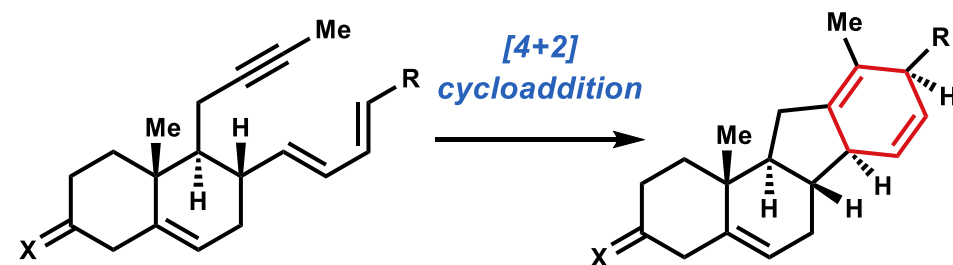
Gao (2023) & Dai (2024)



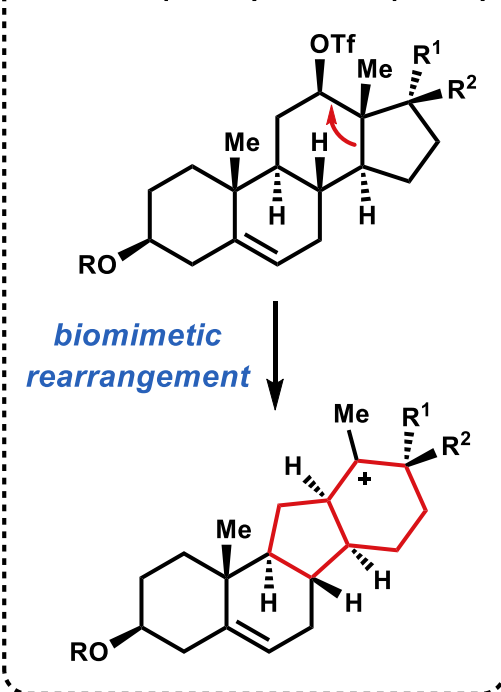
Rawal (2021)



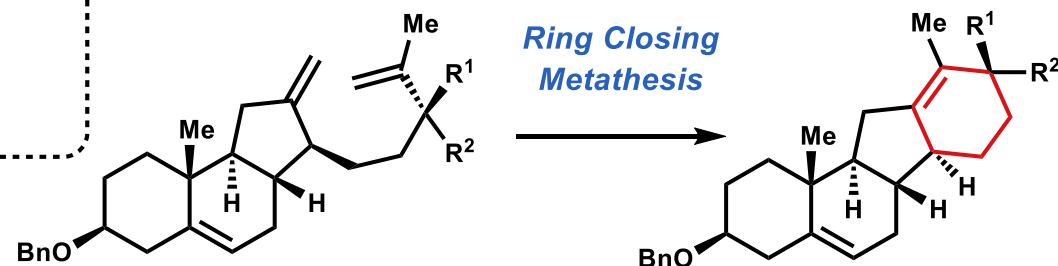
Trauner (2025)



Giannis (2009) & Qin (2024)



Baran (2023)



***Thanks for your
kind attention***