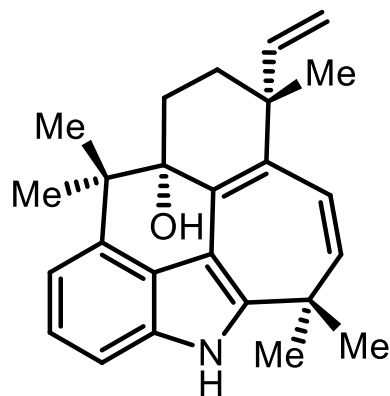
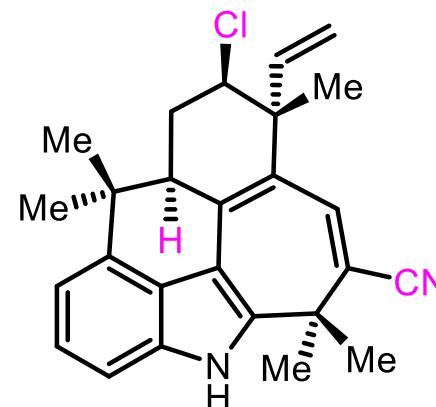


Total Syntheses of Ambiguine P and G



Ambiguine P



Ambiguine G

Reporter: Shixiong Feng

Supervisor: Prof. Quan Cai

2025.09.26

Content

1. Introduction

2. Total Synthesis of Ambiguine P and G

- ✓ Sarpong, R. (**Ambiguine P**, 2019)
- ✓ Rawal, V. H. (**Ambiguine P**, 2019)
- ✓ Rawal, V. H. (**Ambiguine G**, 2021)
- ✓ 李 昂 (**Ambiguine P**, 2025)

3. Summary

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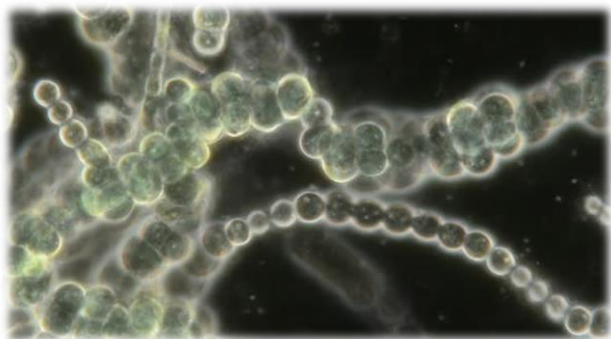
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3. Summary

Introduction——Isolation

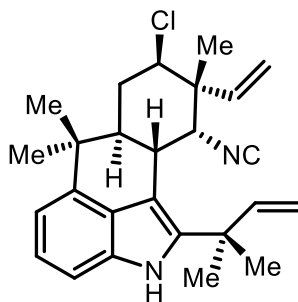


Fischerella ambigua

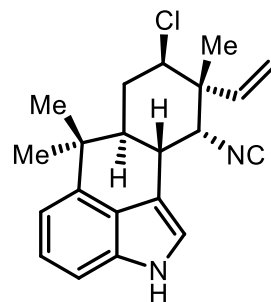
Bioactivity

- antibacterial
- antimycotic
- insecticidal
- anticancer ...

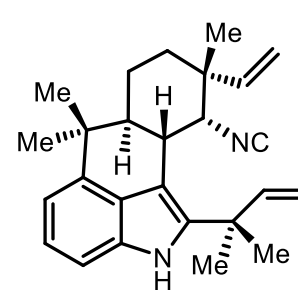
Tetracyclic hapalindole-type natural products



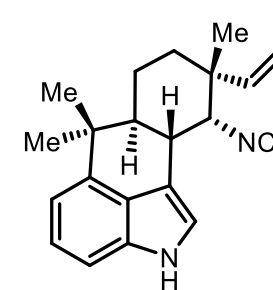
Ambiguine A



Hapalindole G

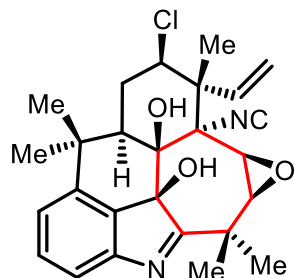


Ambiguine H

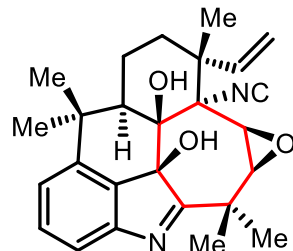


Hapalindole U

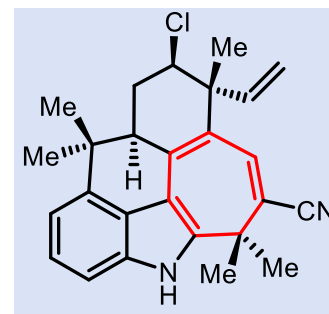
Representative pentacyclic hapalindole-type natural products



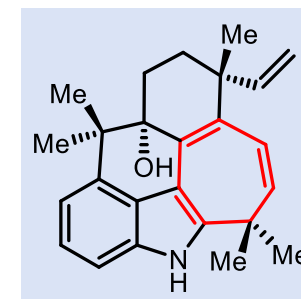
Ambiguine D



Ambiguine J



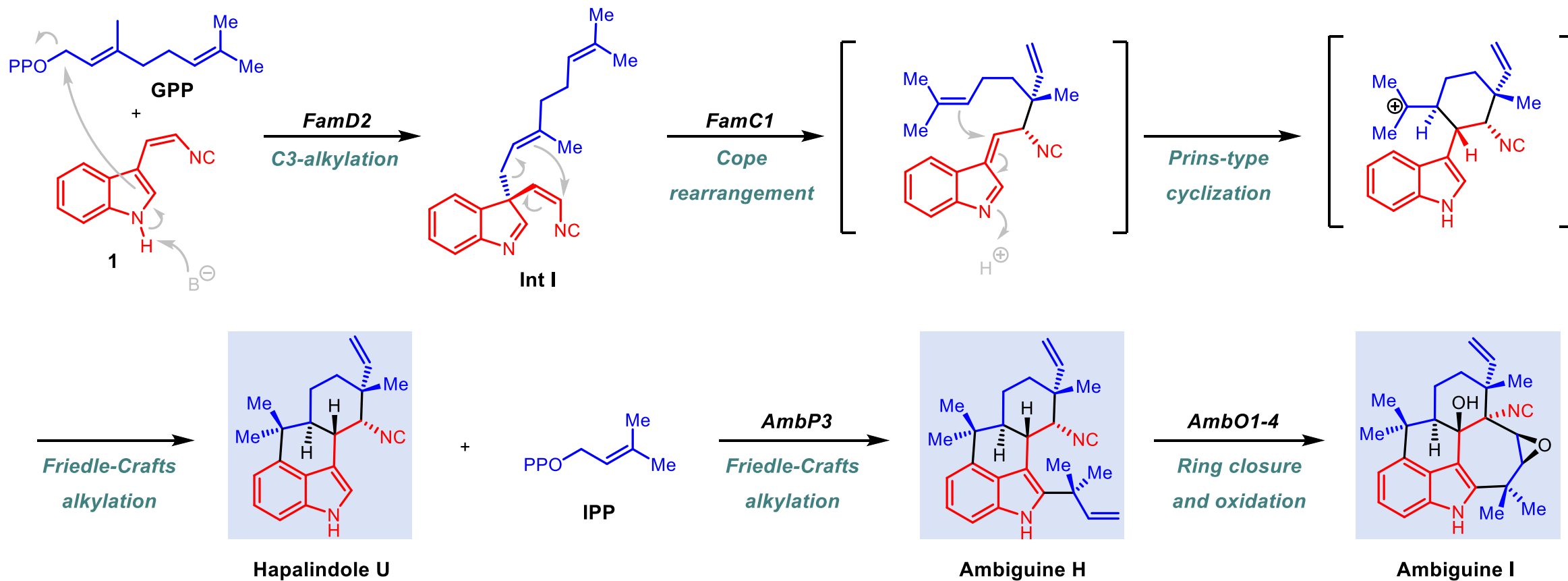
Ambiguine G



Ambiguine P

Smitka, T. A.; Bonjouklian, R.; Doolin, L.; Jones, N. D.; Deeter, J. B.; Yoshida, W. Y.; Prinsep, M. R.; Moore, R. E.; Patterson, G. M. L. *J. Org. Chem.* **1992**, 57, 857–861.

Introduction—Biosynthesis



(1) Li, S.; Lowell, A. N.; Yu, F.; Raveh, A.; Newmister, S. A.; Bair, N.; Schaub, J. M.; Williams, R. M.; Sherman, D. H. *J. Am. Chem. Soc.* **2015**, *137*, 15366–15369. (2) Hillwig, M. L.; Zhu, Q.; Liu, X. *ACS Chem. Biol.* **2014**, *9*, 372–377.

Content

1. Introduction

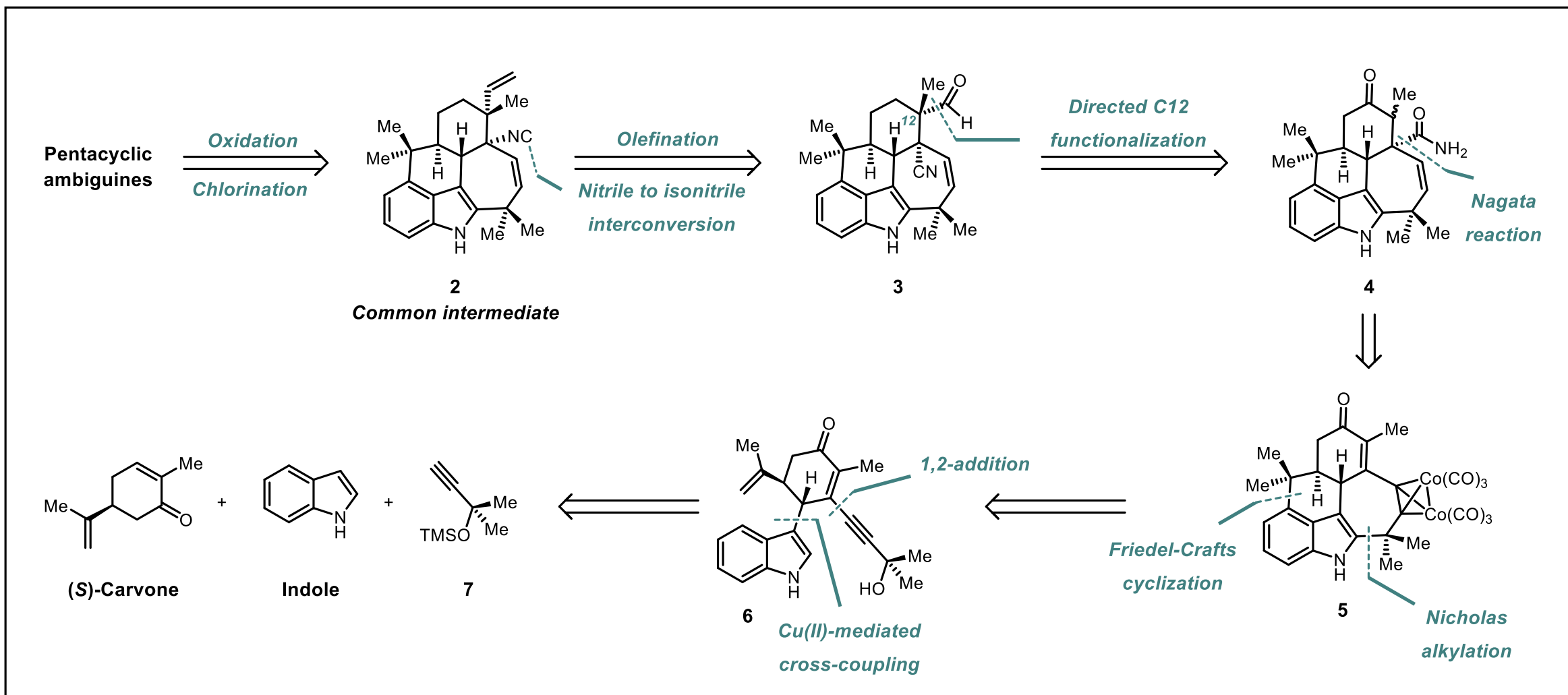
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3. Summary

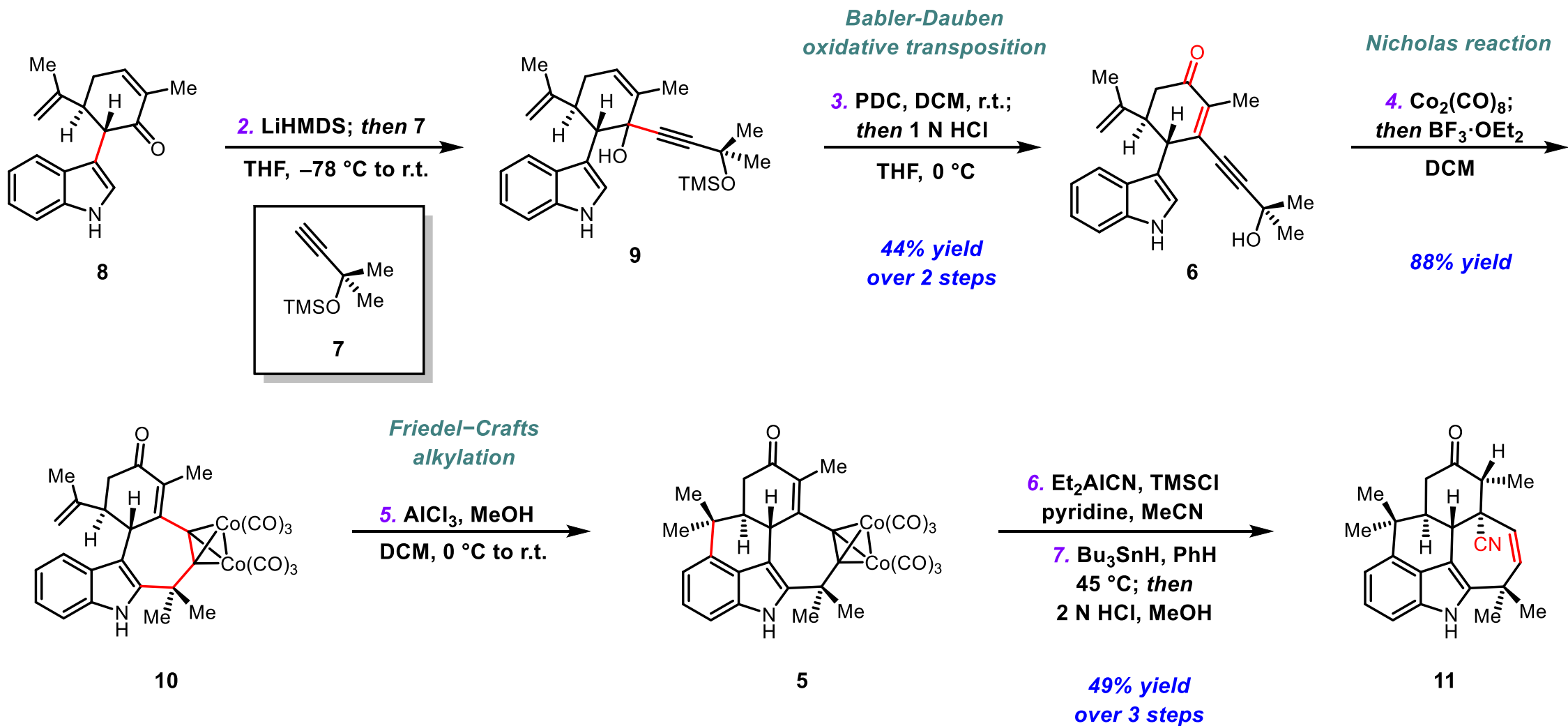
Total Synthesis of Ambiguine P——Sarpong (2019)

Retrosynthetic Analysis

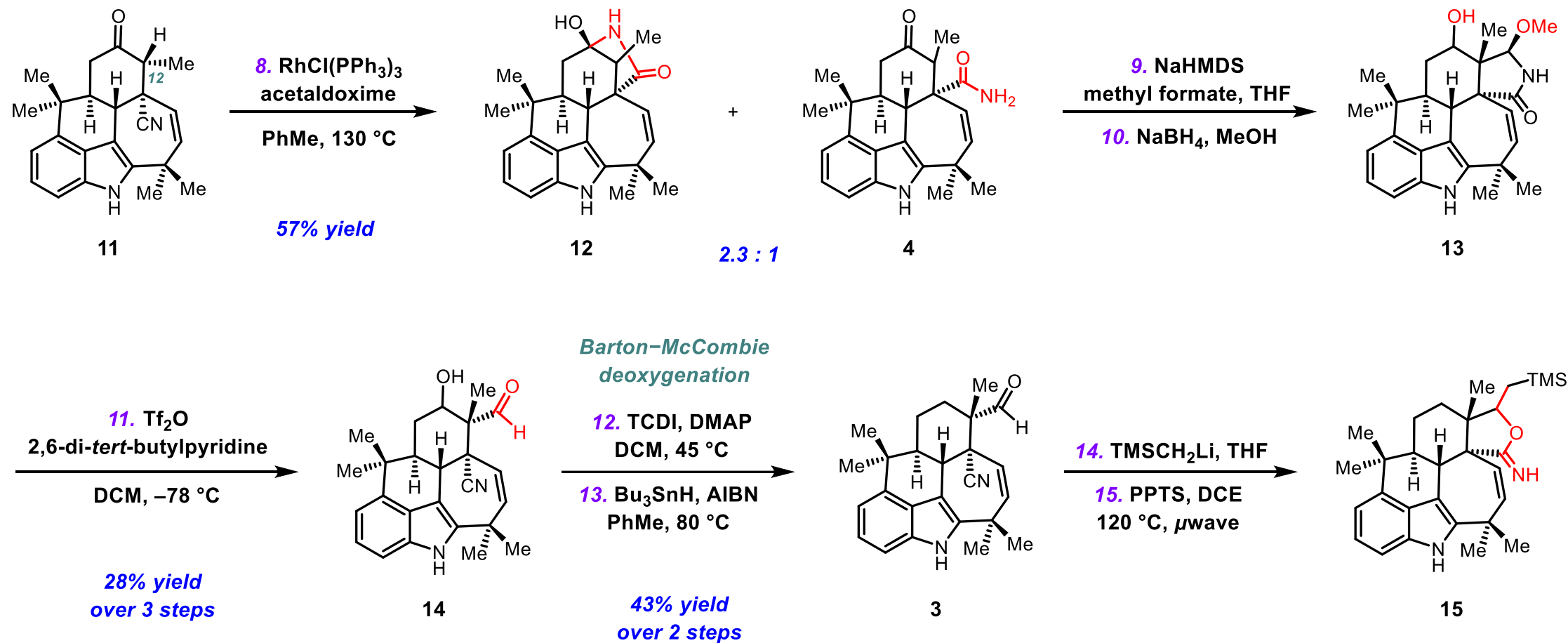


Total Synthesis of Ambiguine P——Sarpong (2019)

Construction of the pentacyclic core

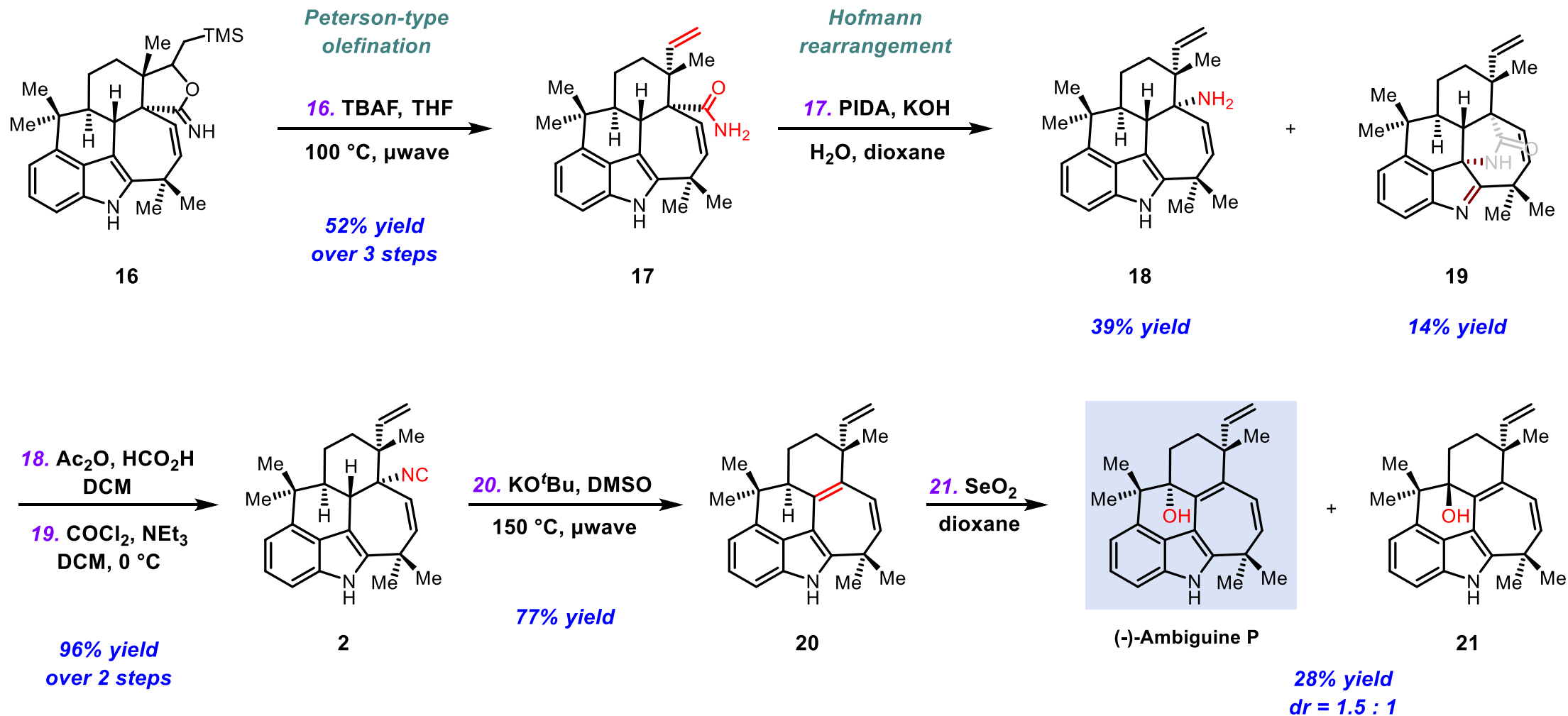


Total Synthesis of Ambiguine P——Sarpong (2019)



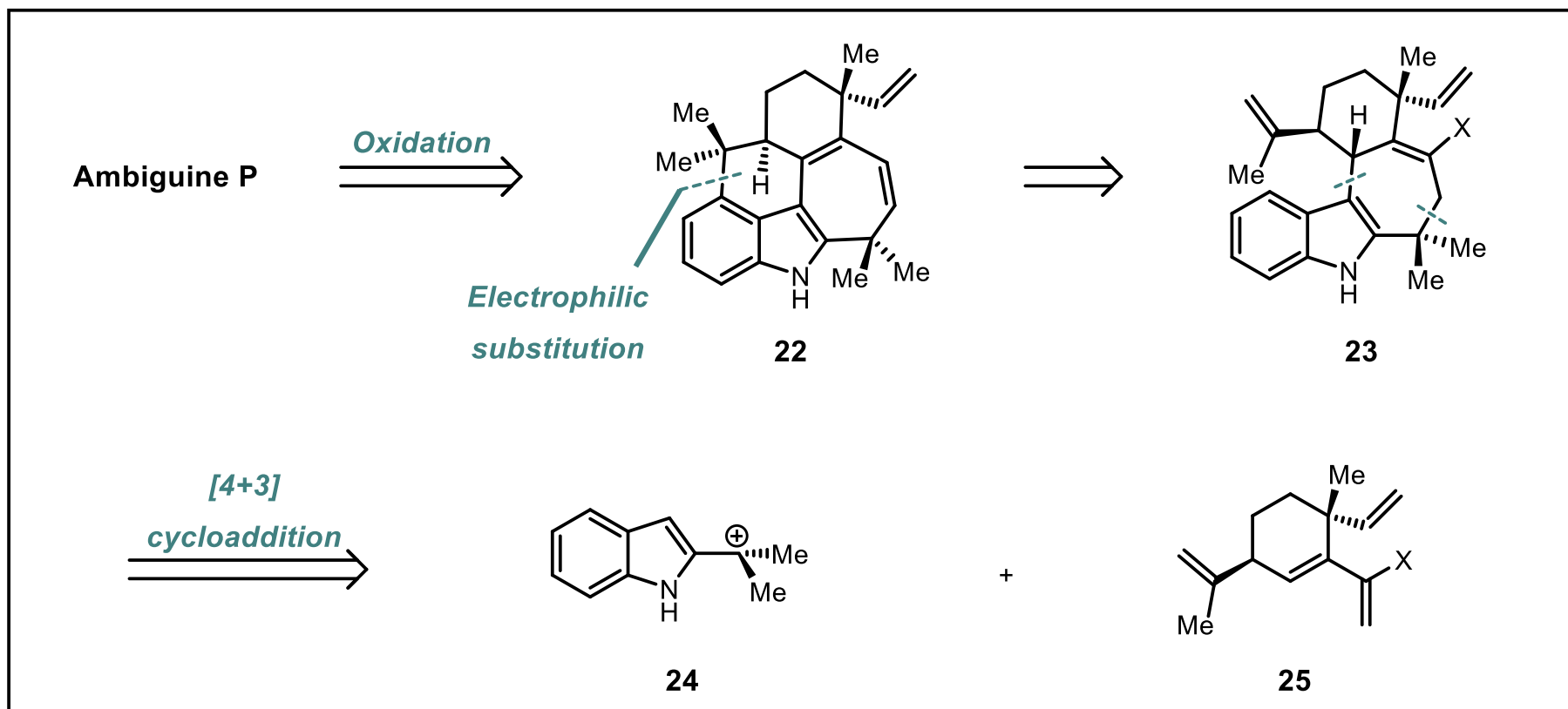
Total Synthesis of Ambiguine P——Sarpong (2019)

End game



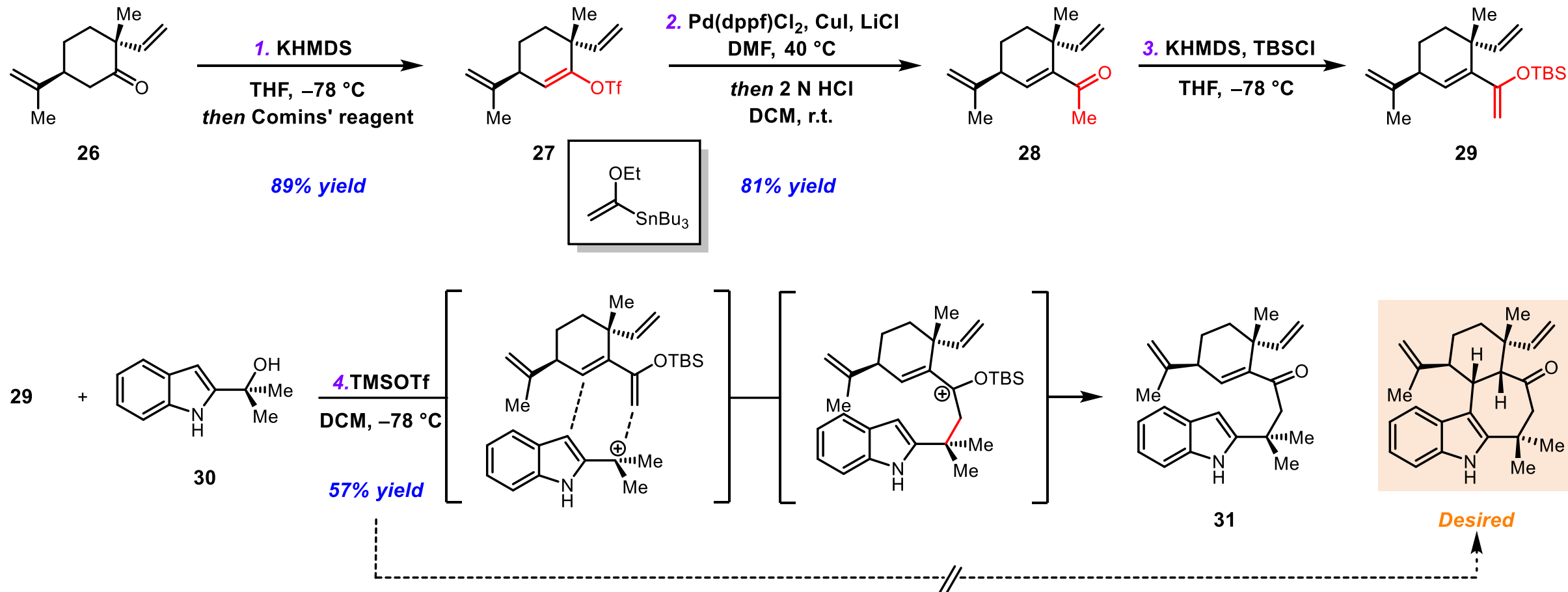
Total Synthesis of Ambiguine P——Rawal (2019)

Retrosynthetic Analysis



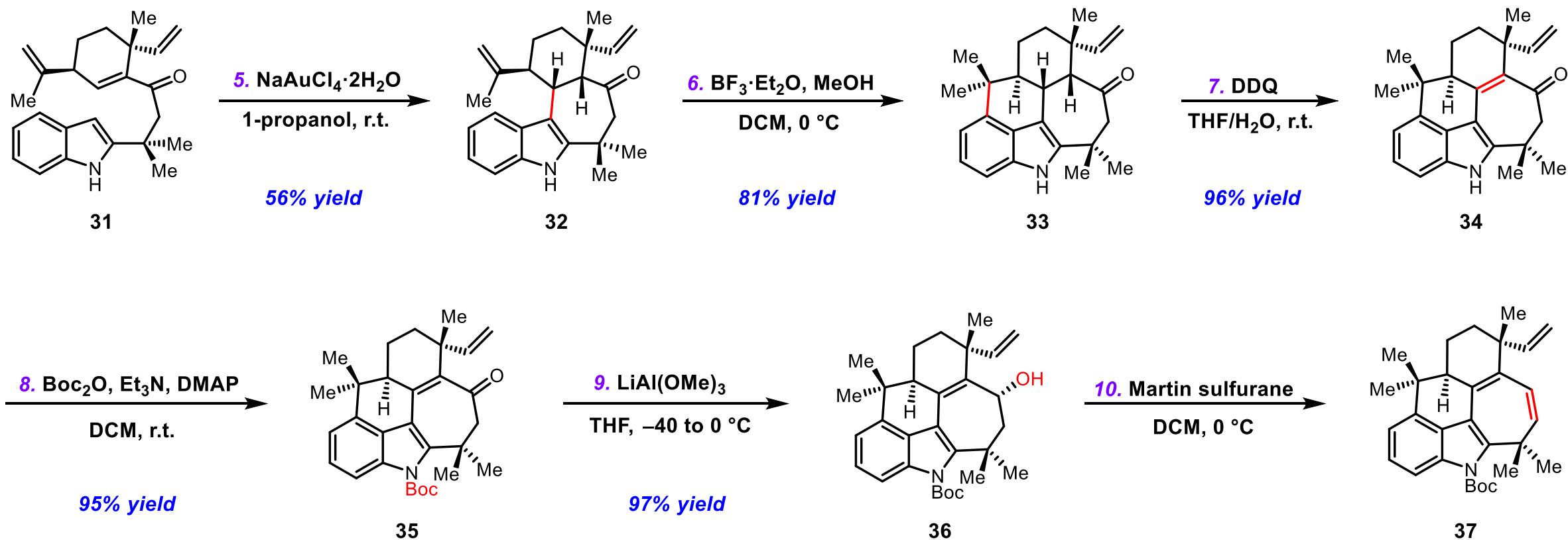
Total Synthesis of Ambiguine P——Rawal (2019)

Failed [4+3] cycloaddition



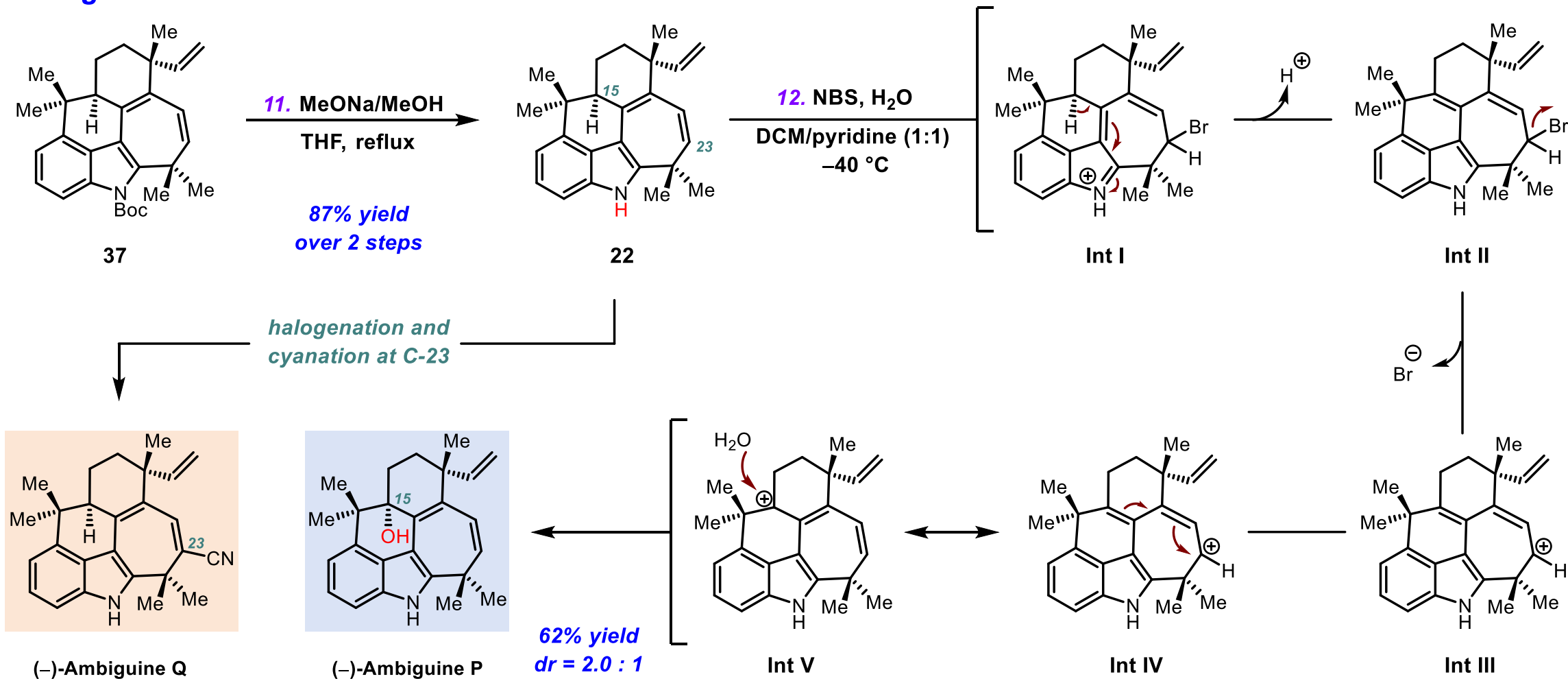
Total Synthesis of Ambiguine P——Rawal (2019)

Construction of the pentacyclic core



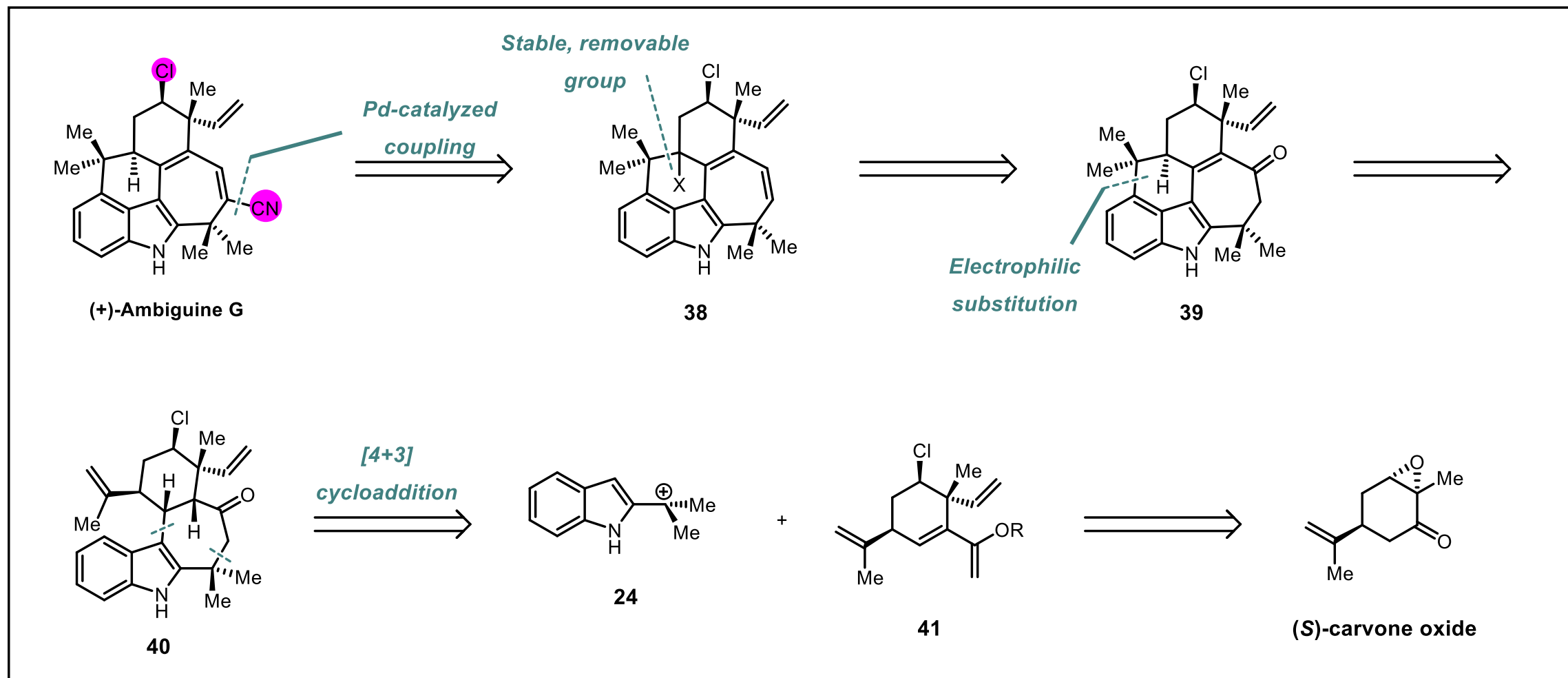
Total Synthesis of Ambiguine P——Rawal (2019)

End game



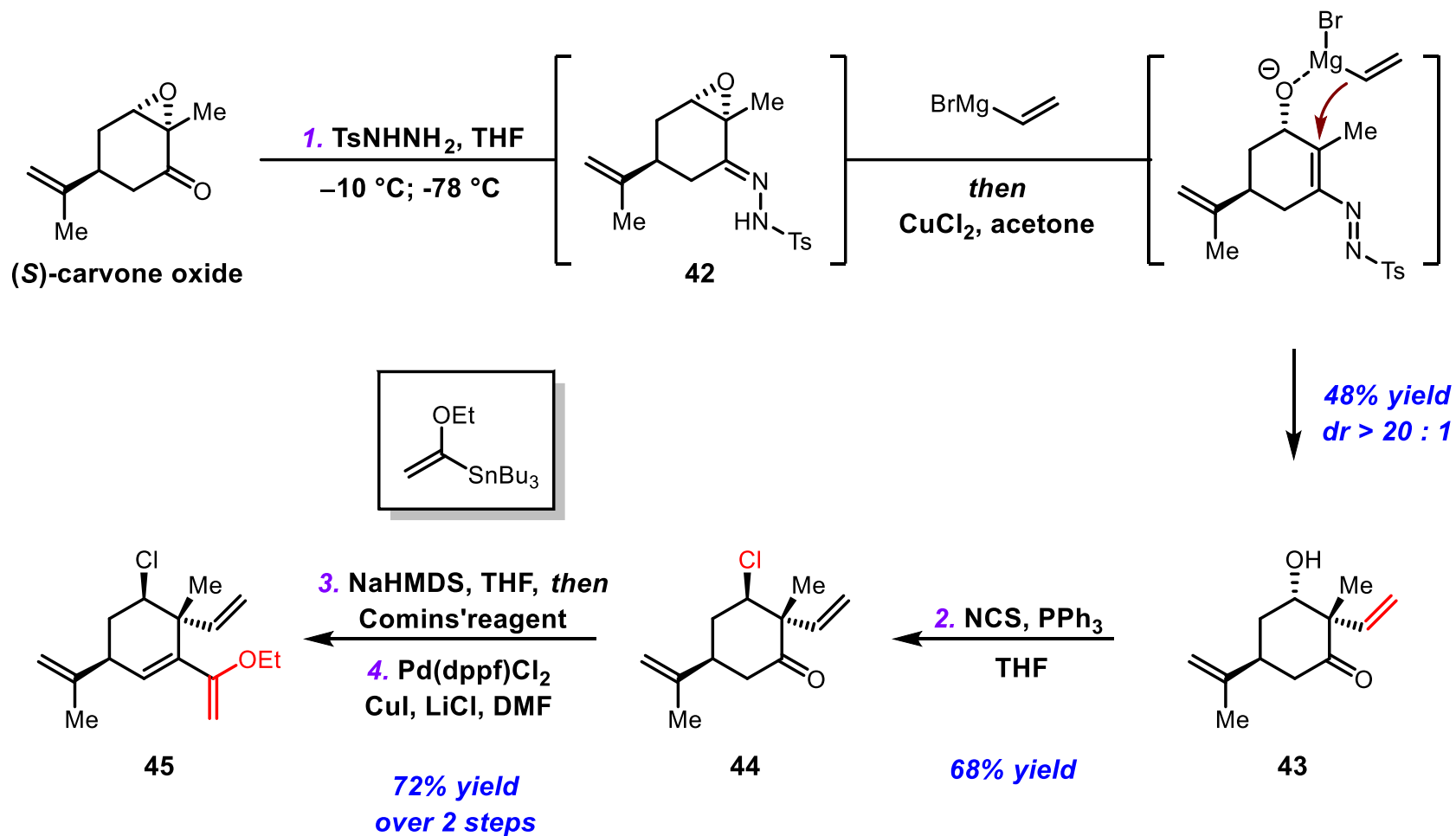
Total Synthesis of Ambiguine G — Rawal (2021)

Retrosynthetic Analysis

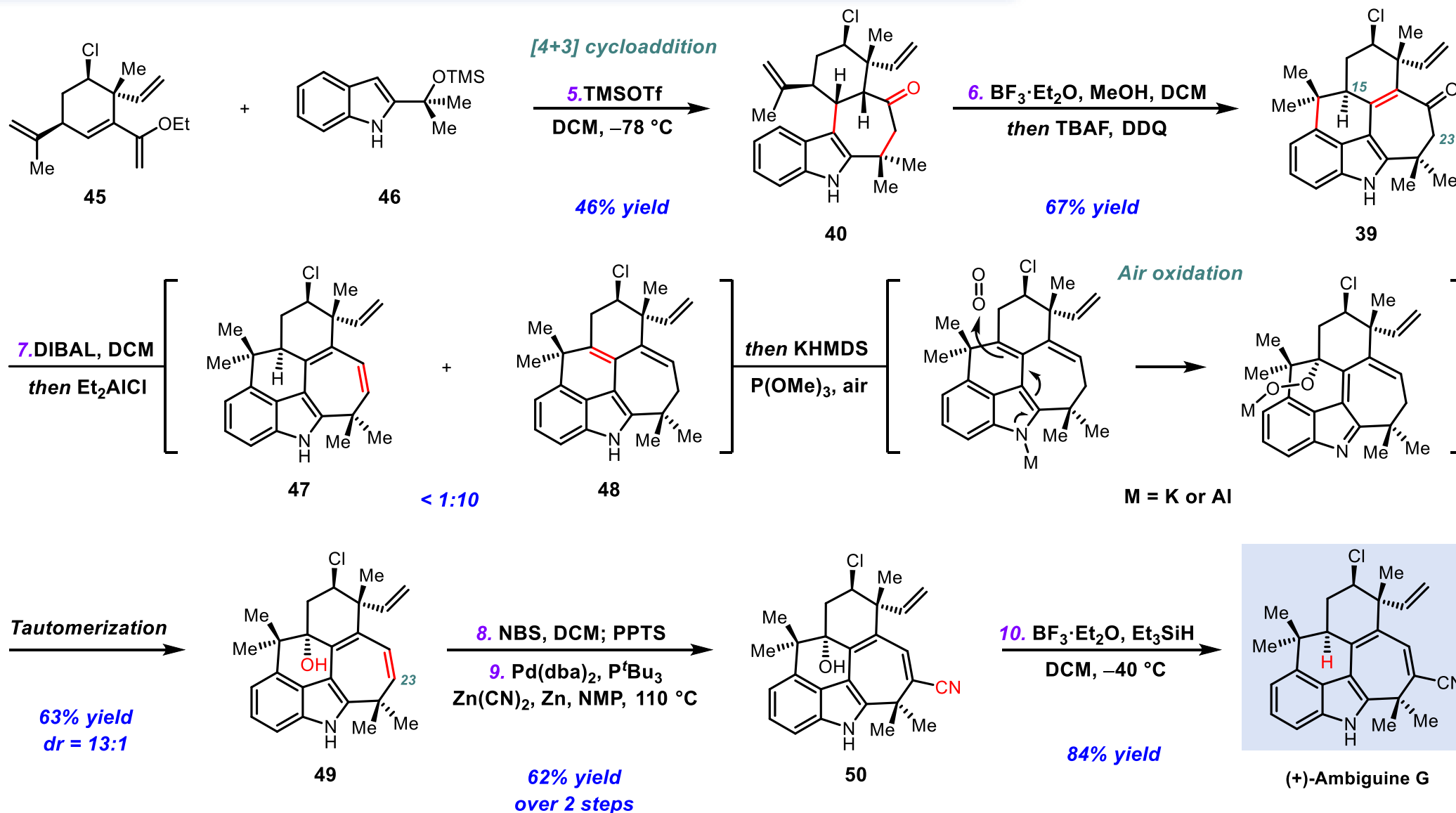


Total Synthesis of Ambiguine G—Rawal (2021)

Construction of the diene 45

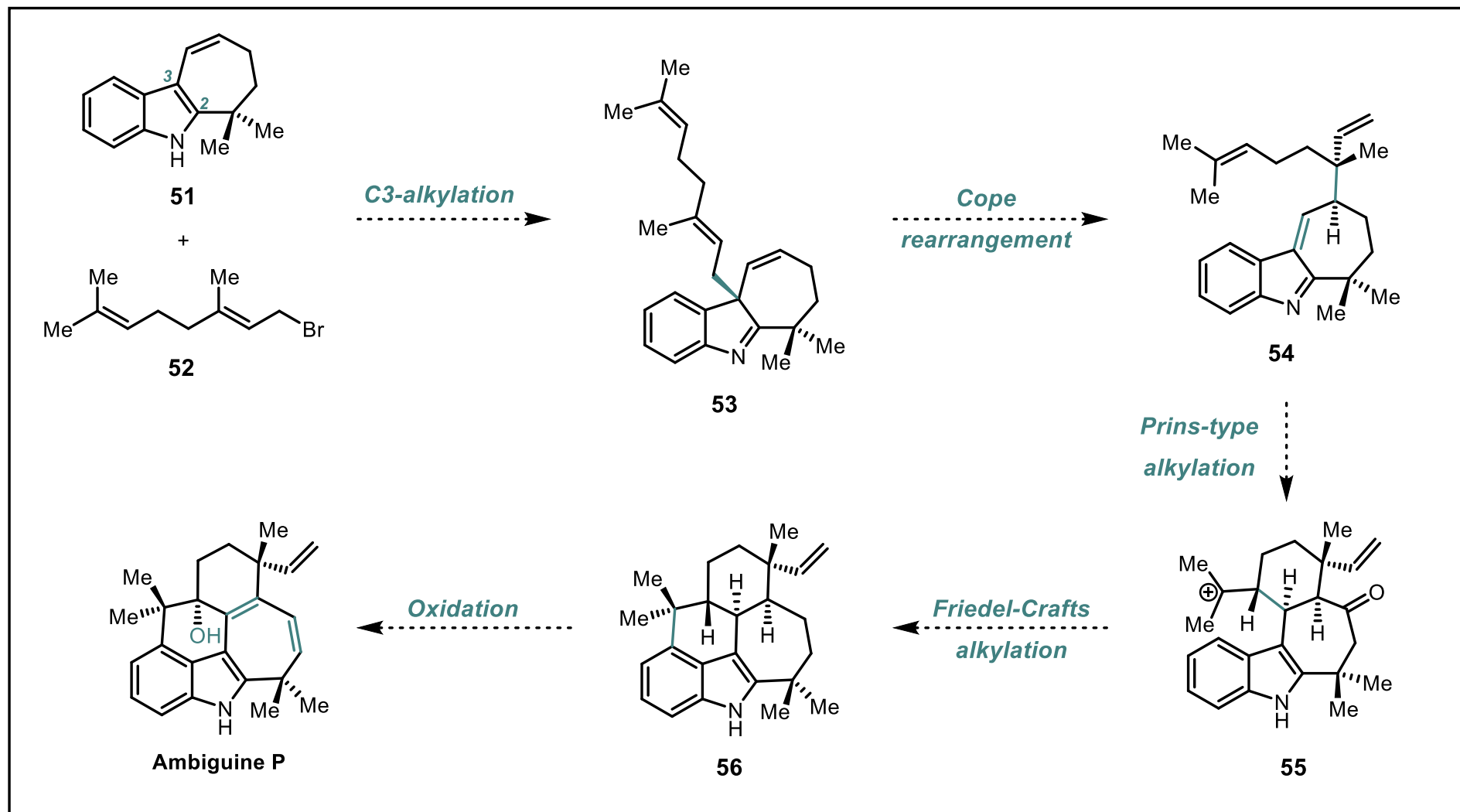


Total Synthesis of Ambiguine G——Rawal (2021)

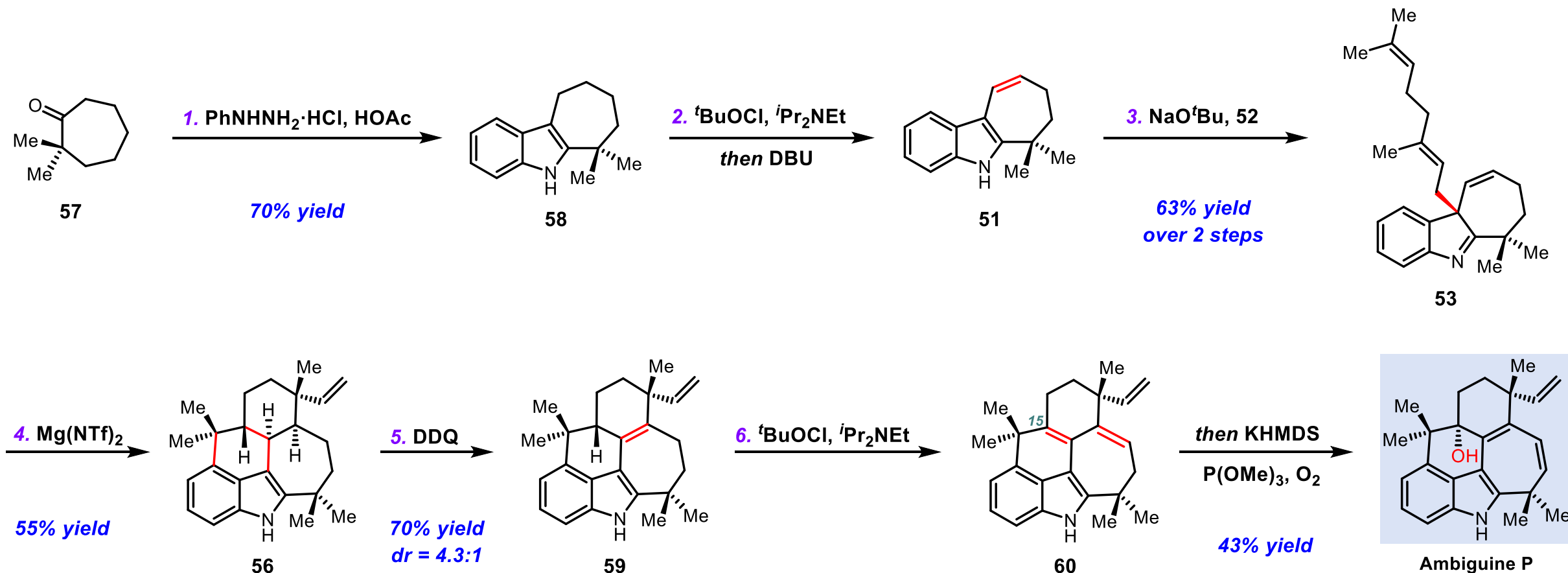


Total Synthesis of Ambiguine P——李 昂 (2025)

Devised synthetic route



Total Synthesis of Ambiguine P——李 昂 (2025)



Content

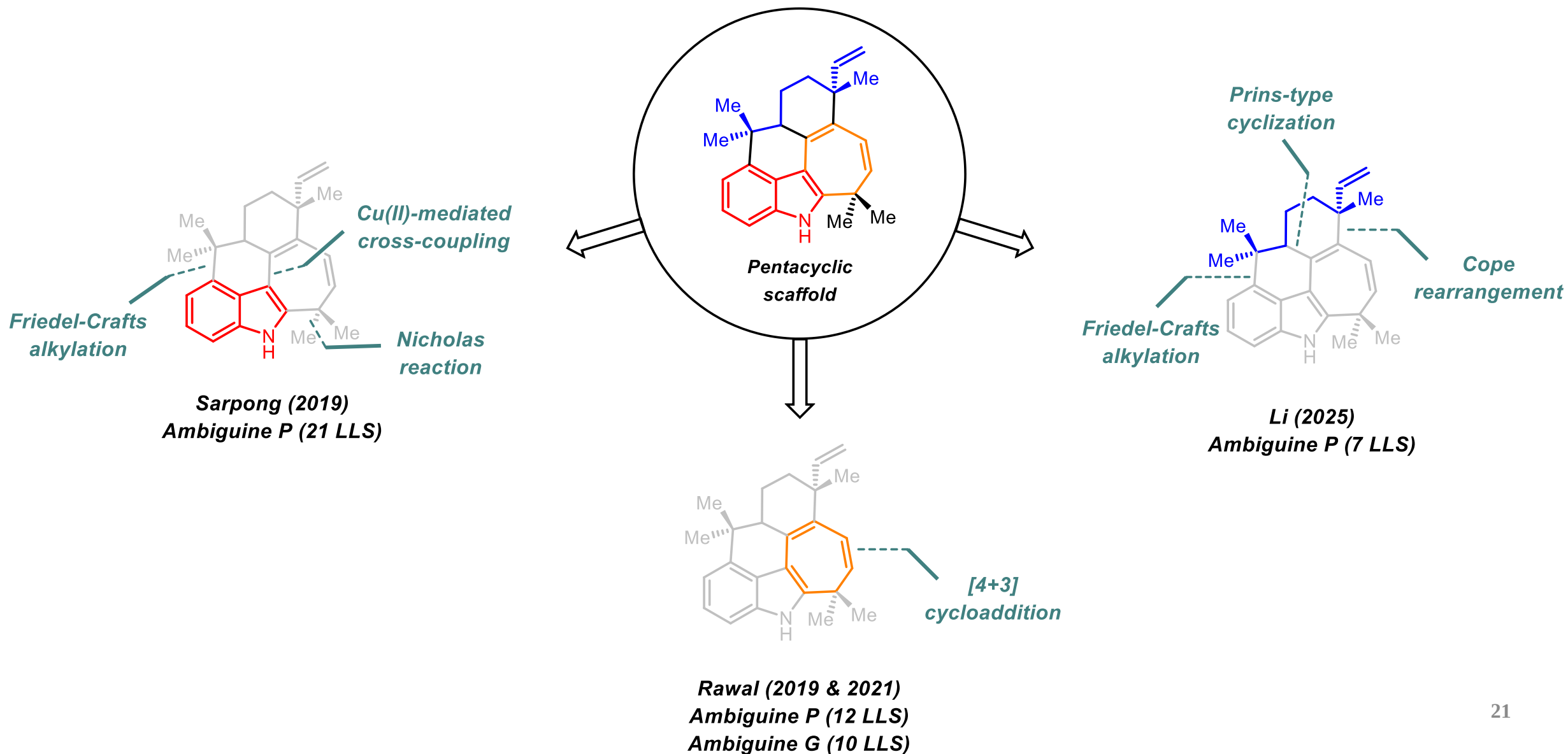
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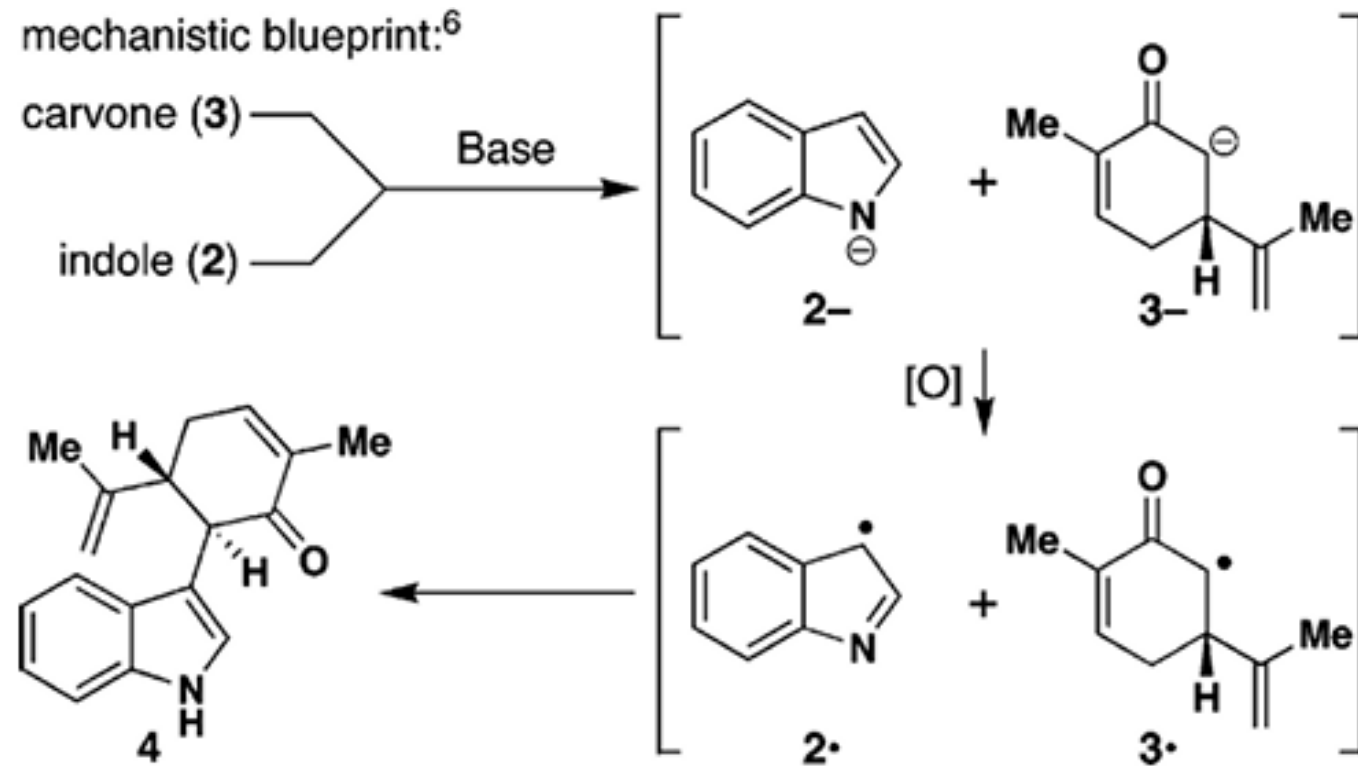
3. Summary

Summary

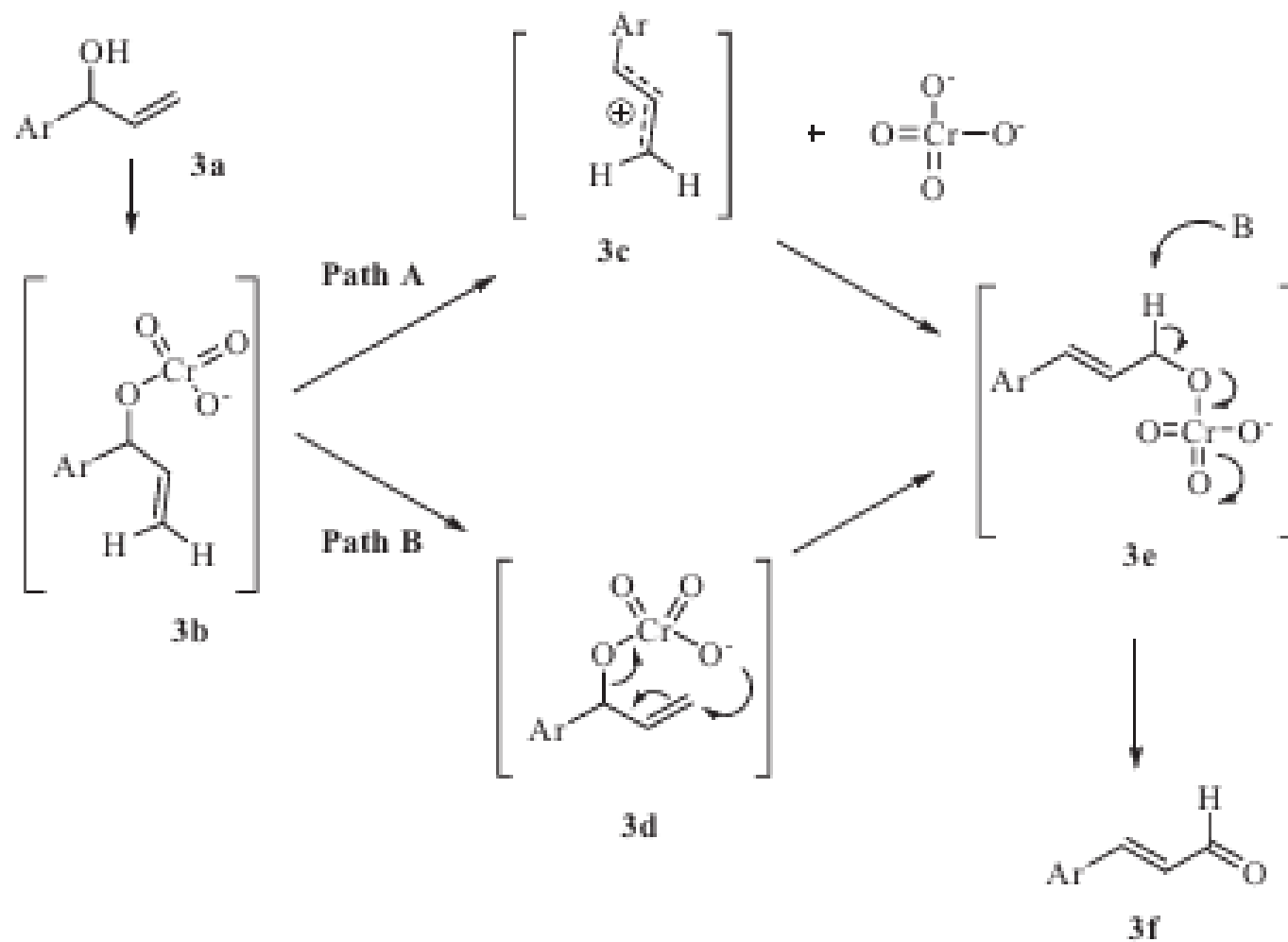


Thanks for your kind attention!

Cu(II)-mediated oxidative coupling of indole with (*S*)-carvone

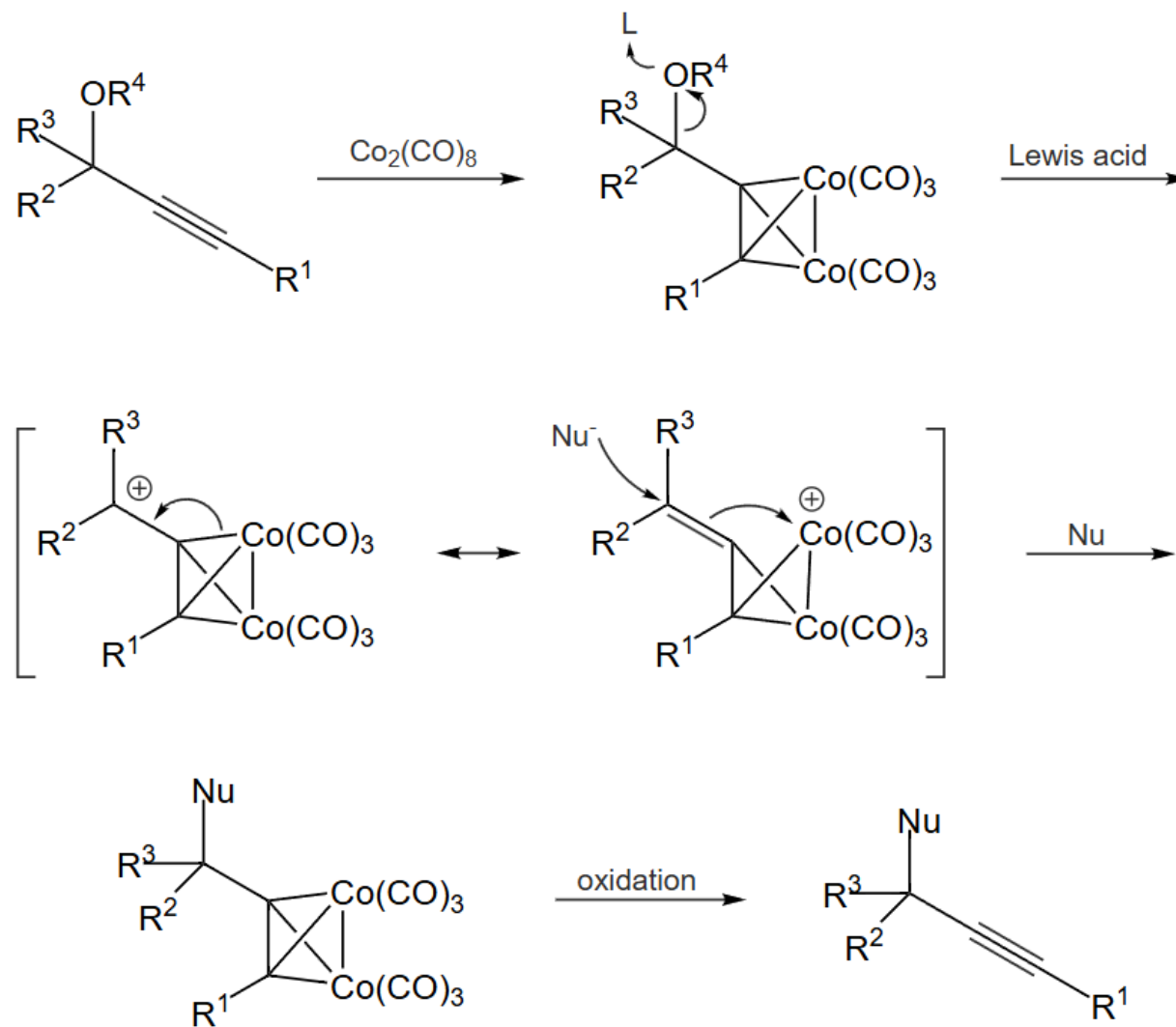


Babler–Dauben oxidative transposition

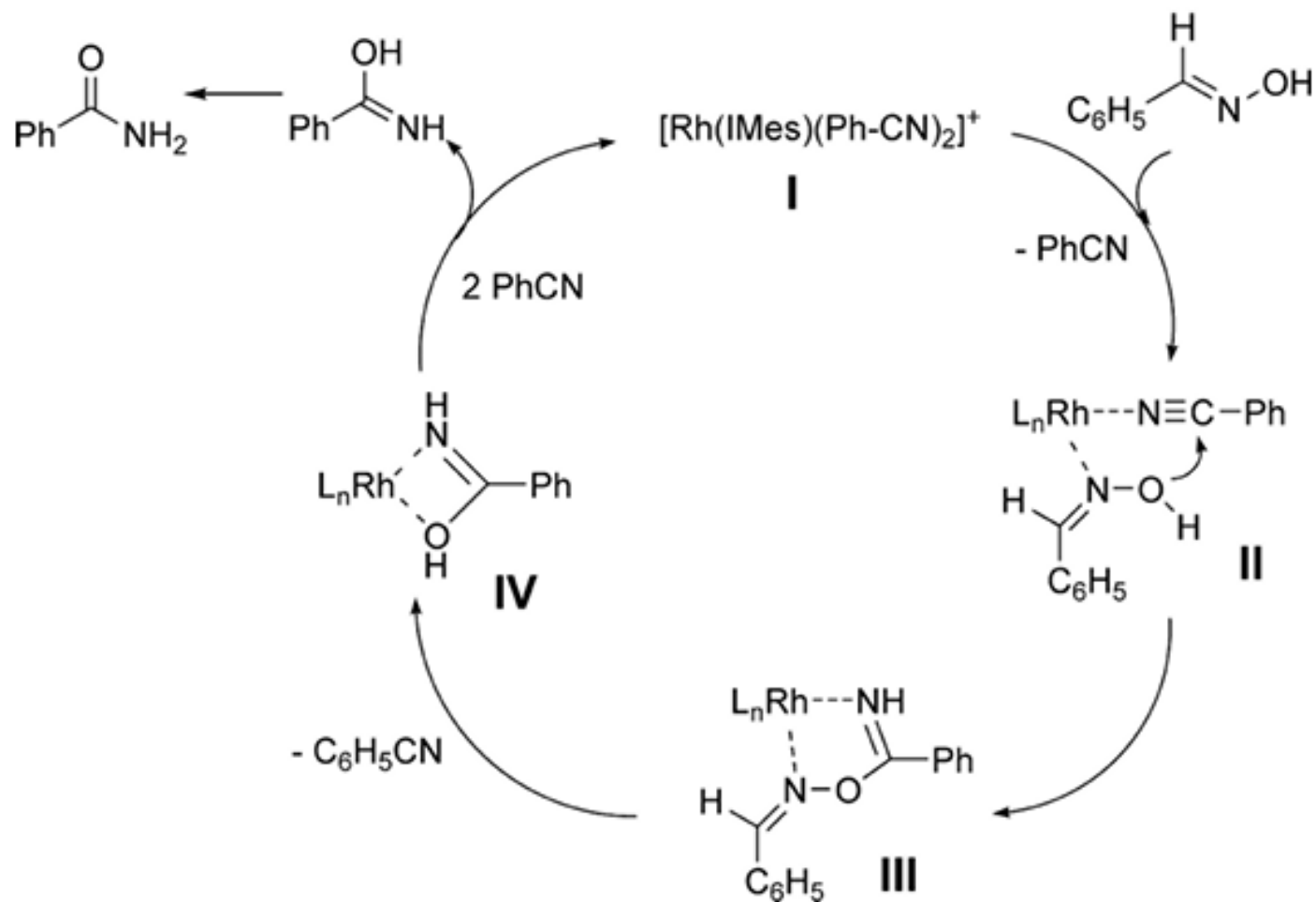


- (1) Babler, J. H.; Coghlan, M. J. *Synth. Commun.* **1976**, 6, 469–474.
 (2) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, 42, 682–685.

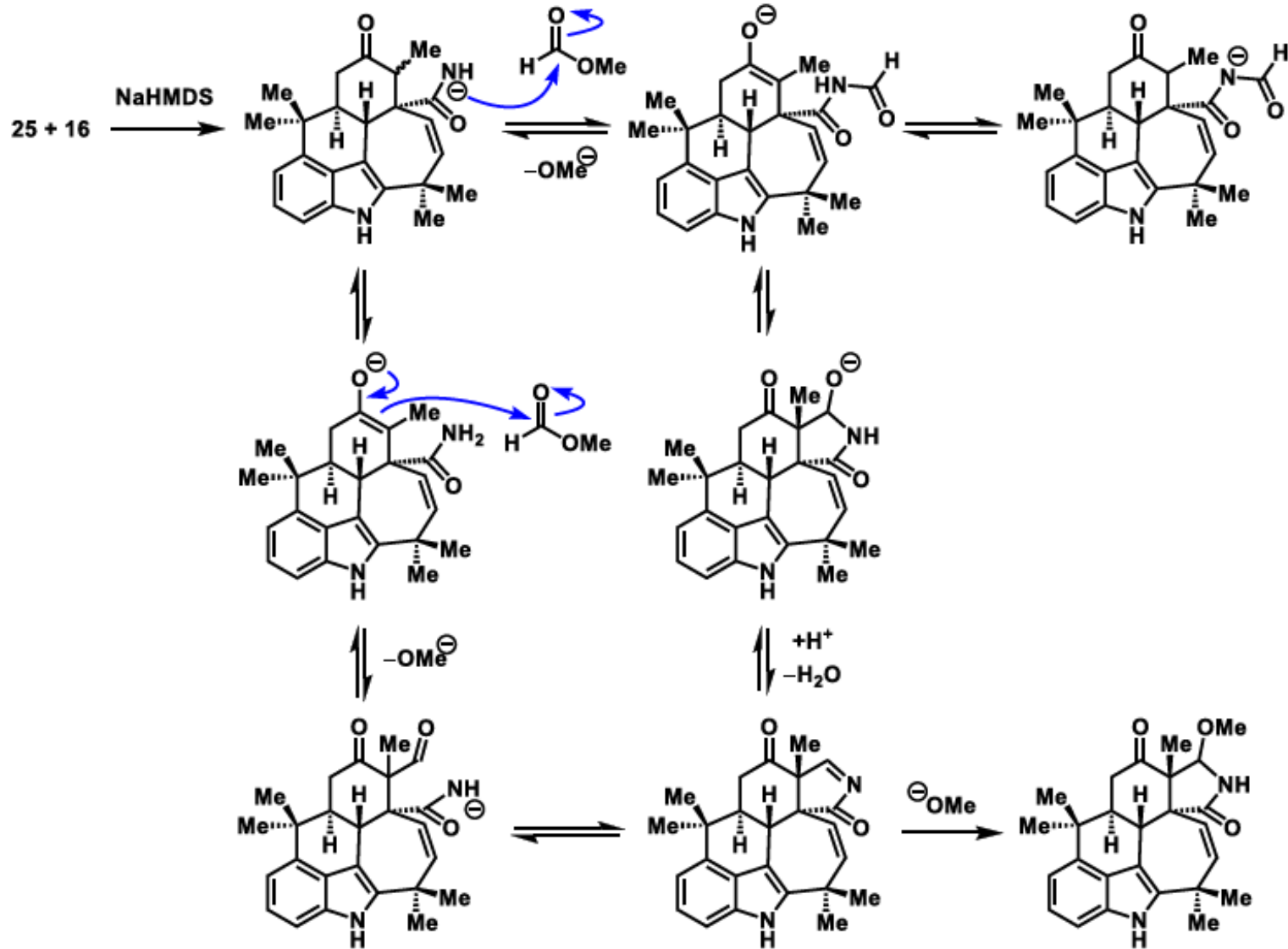
Nicholas reaction



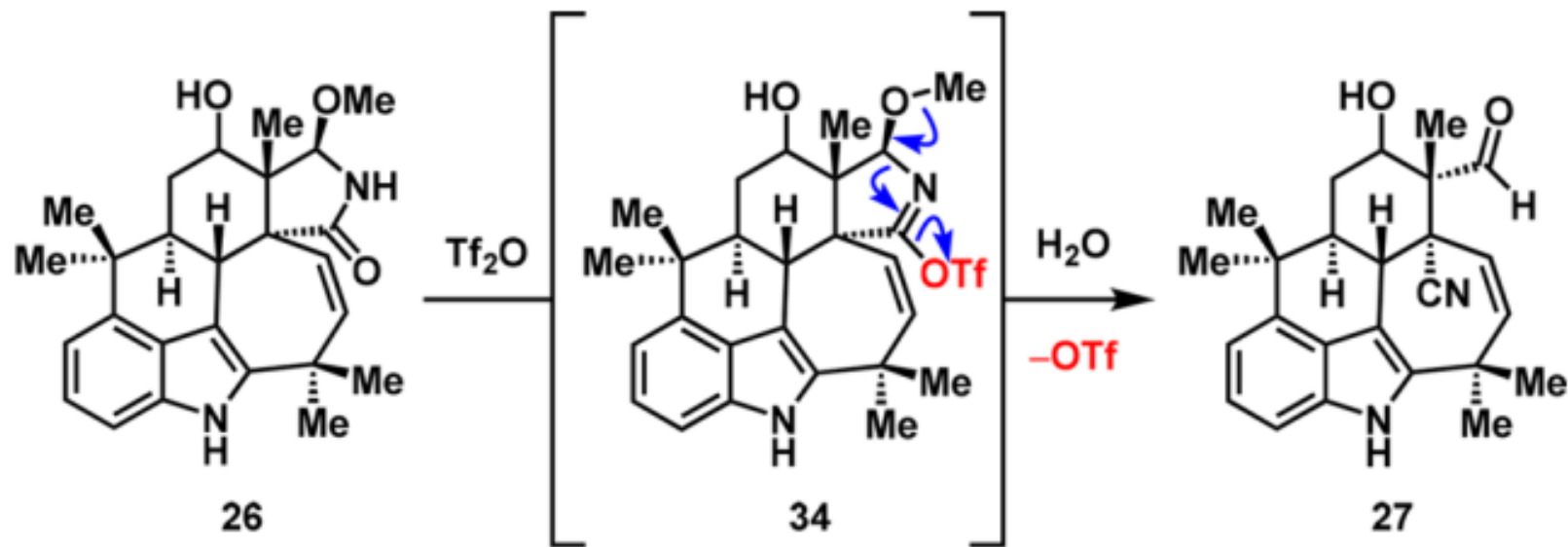
Rh(I)-catalyzed nitrile hydration



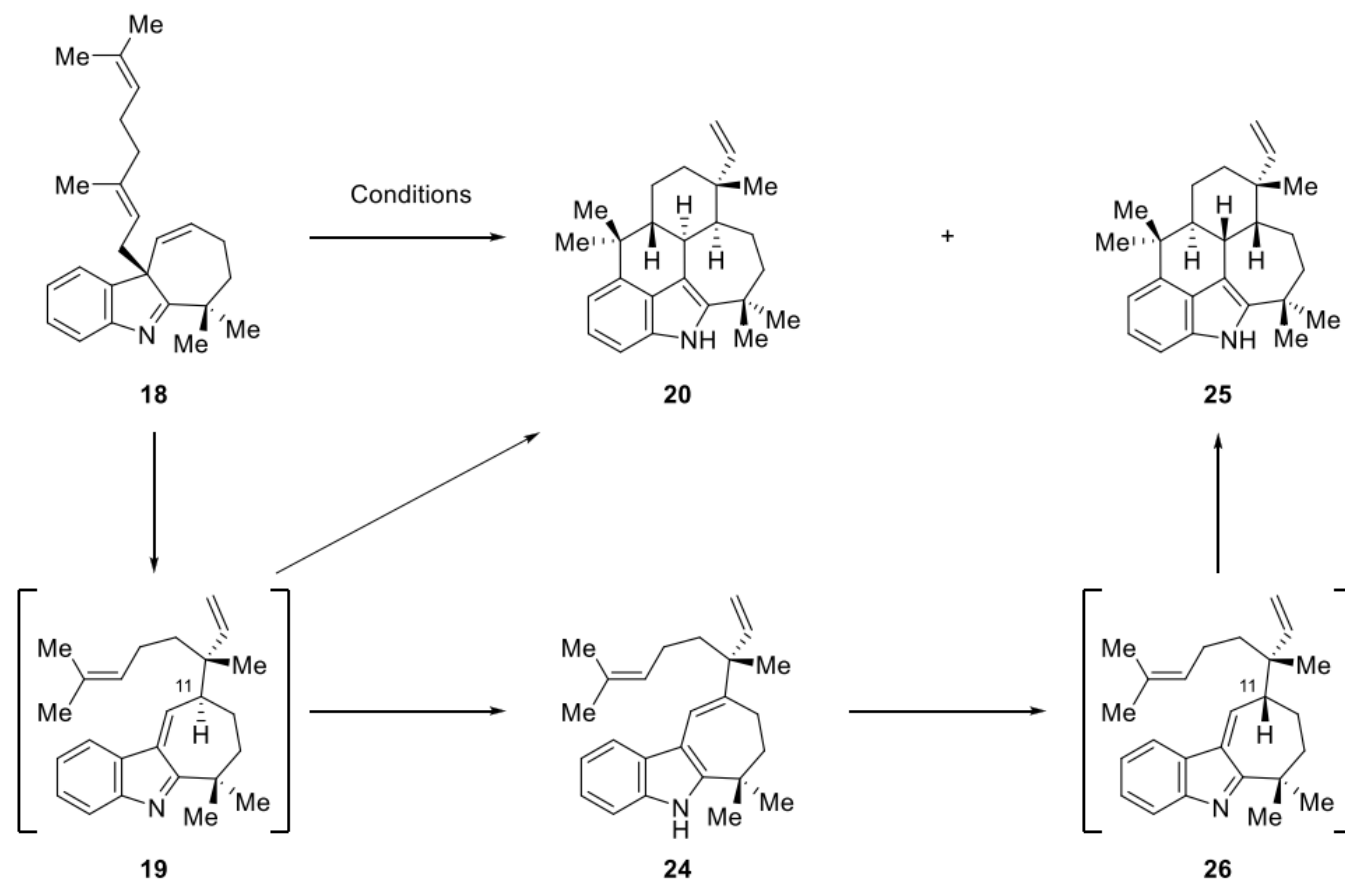
Possible mechanism for the amide-directed C12 functionalization



Possible mechanism for the ring opening of hemiaminal ether



Investigation of the Cope/Prins/Friedel–Crafts Cascade



Entry	Conditions	20 + 25 (%)	20:25
1 ^a	150 °C	0 ^b	—
2 ^c	Sc(OTf) ₃ , ^d 70 °C, 15 h	42	1.2:1
3 ^c	Bi(OTf) ₃ , ^d 70 °C, 15 h	36	1.3:1
4 ^c	Zn(OTf) ₂ , ^d 70 °C, 24 h	45	3:1
5 ^c	Zn(NTf ₂) ₂ , ^d 70 °C, 72 h	62	7:1
6 ^c	Ca(NTf ₂) ₂ , ^d 70 °C, 120 h	51	2:1
7 ^c	Mg(NTf ₂) ₂ , ^d 70 °C, 72 h	68	10:1
8 ^c	Mg(NTf ₂) ₂ , ^e 70 °C, 36 h	59	10:1
9 ^c	Mg(NTf ₂) ₂ , ^d 80 °C, 24 h	49	4:1

^aBHT (3.5 equiv) was added. *o*-DCB was used as a solvent. ^bCompound **24** was obtained in 52% yield. ^cDCE was used as a solvent. ^d20 mol %. ^e30 mol %.