



Skeletal Editing of Strained Rings

Reporter: Yu Haoting

Supervisors: Prof. Zhang Junliang

Dr. Zhang Zhanming

2026.04.10



Content

1. Introduction

2. Skeletal Editing of Strained Rings

2.1 Atom Insertion

2.2 Atom Transmutation and Translocation

2.3 Atom Deletion

3. Summary and Outlook



Content

1. Introduction

2. Skeletal Editing of Strained Rings

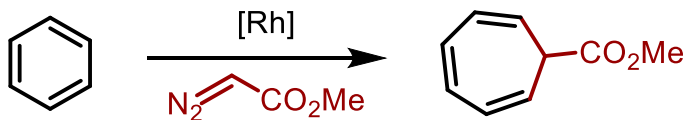
2.1 Atom Insertion

2.2 Atom Transmutation and Translocation

2.3 Atom Deletion

3. Summary and Outlook

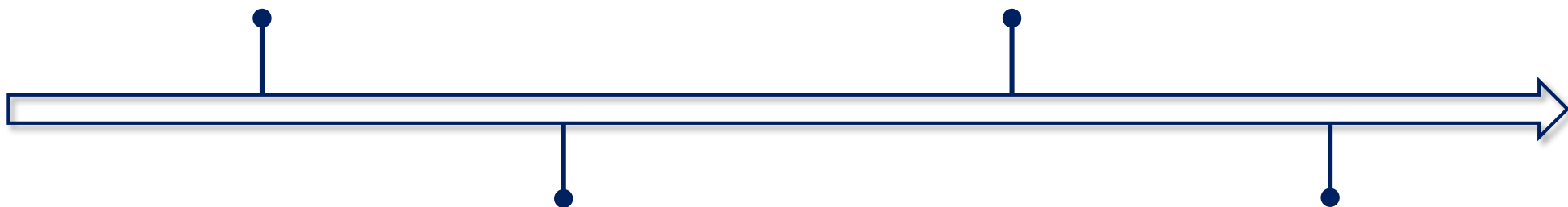
Introduction



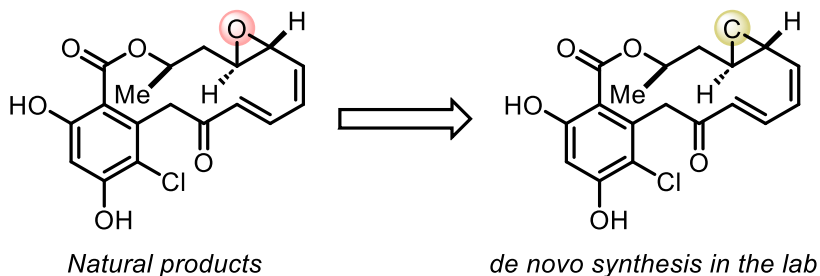
Since the 1880s
 Büchner ring expansion
 Beckmann rearrangement
 Favorskii rearrangement



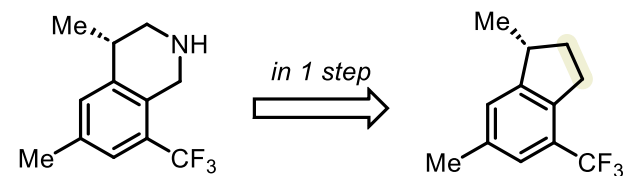
Early 2010s
 genome-editing technology
 sparked the concept



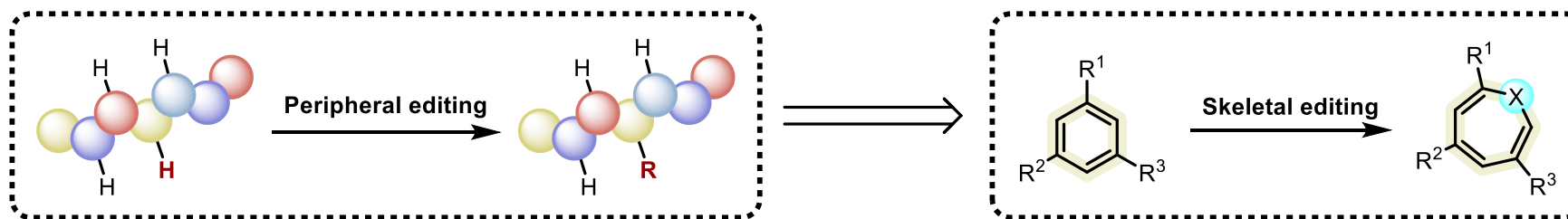
2006, Danishefsky
 “molecular editing”



2021, Levin & Sarpong
 coined the term
 “skeletal editing”

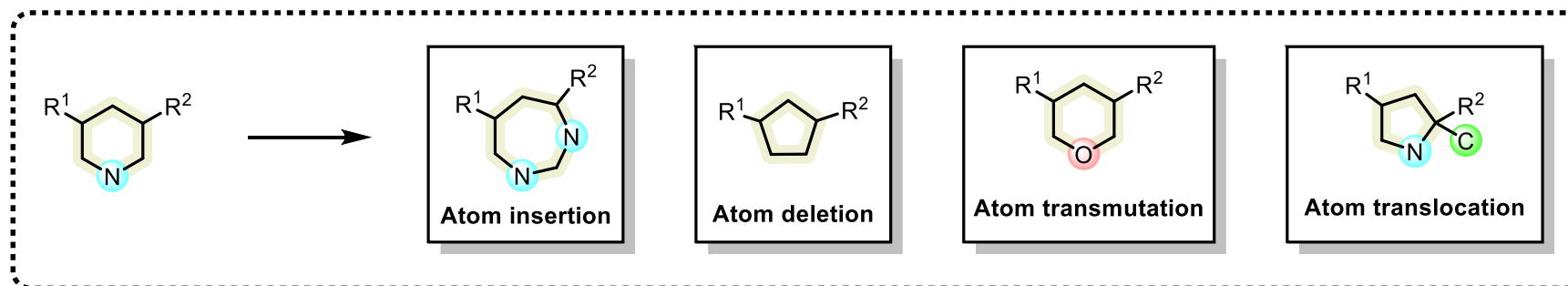


Introduction

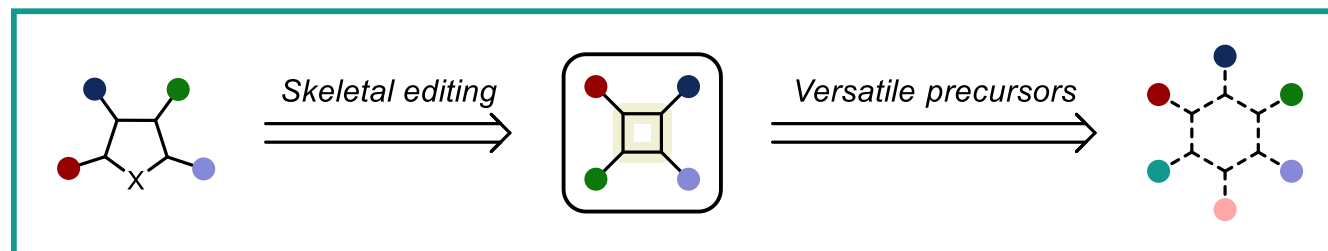
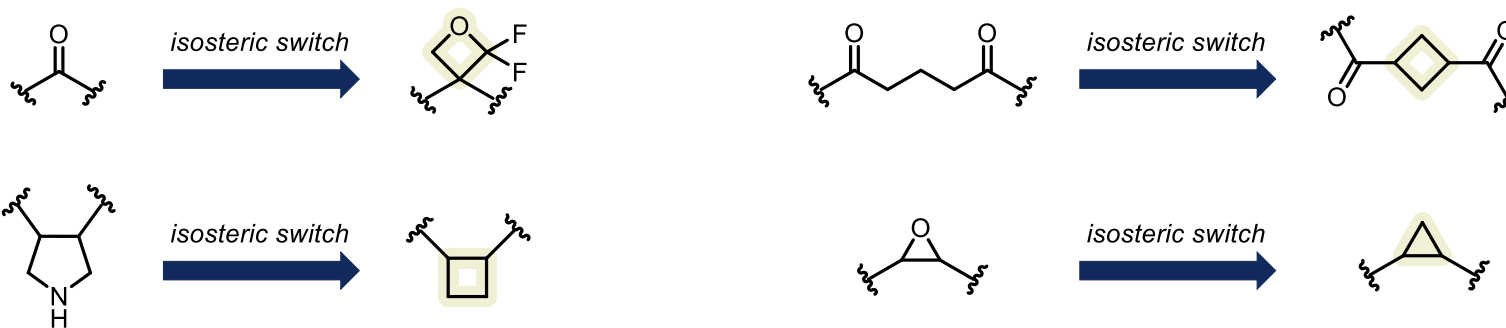
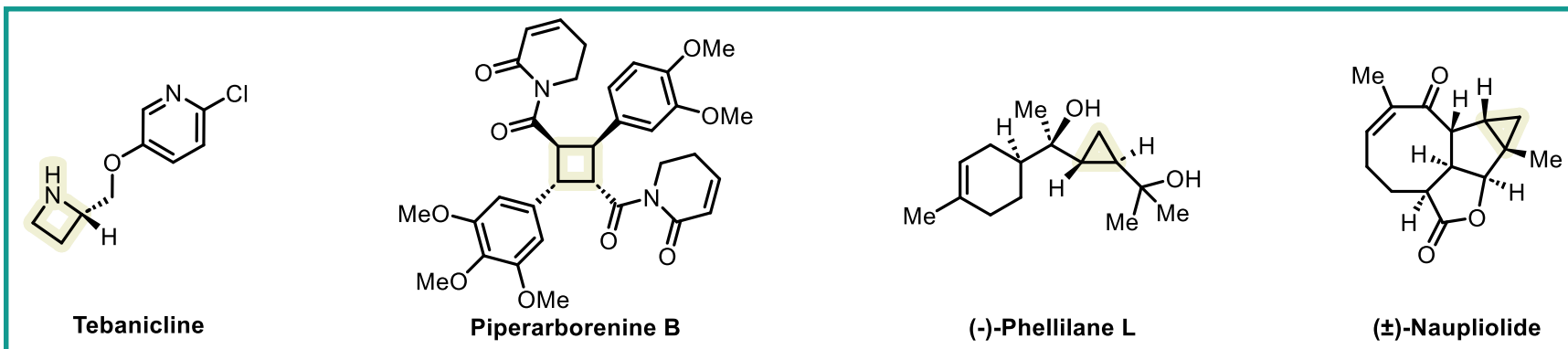


- ❑ One-pot procedure
- ❑ Well-developed
- ❑ Modify peripheral functional groups
- ❑ Core skeleton largely unaltered

- ❑ One-pot procedure
- ❑ Underdeveloped
- ❑ Modify core skeletons
- ❑ Precise and minimal modifications



Introduction





Content

1. Introduction

2. Skeletal Editing of Strained Rings

2.1 Atom Insertion

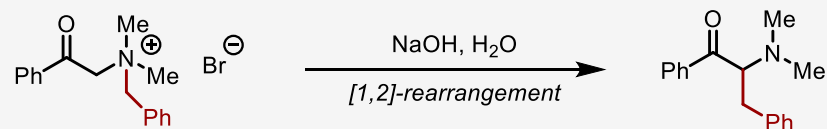
2.2 Atom Transmutation and Translocation

2.3 Atom Deletion

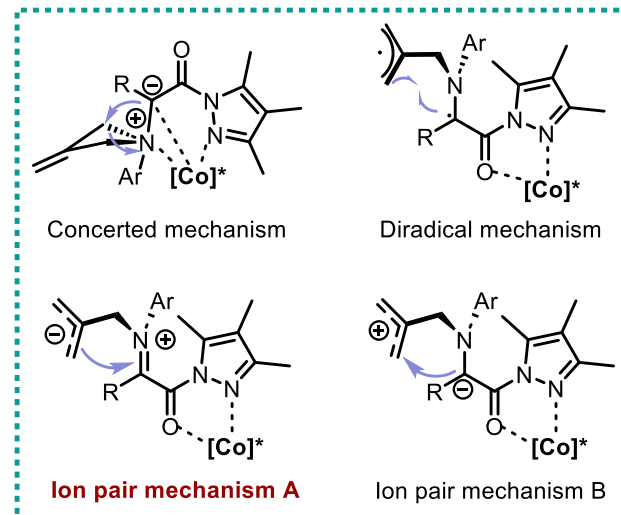
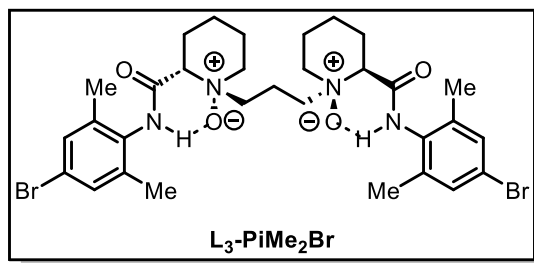
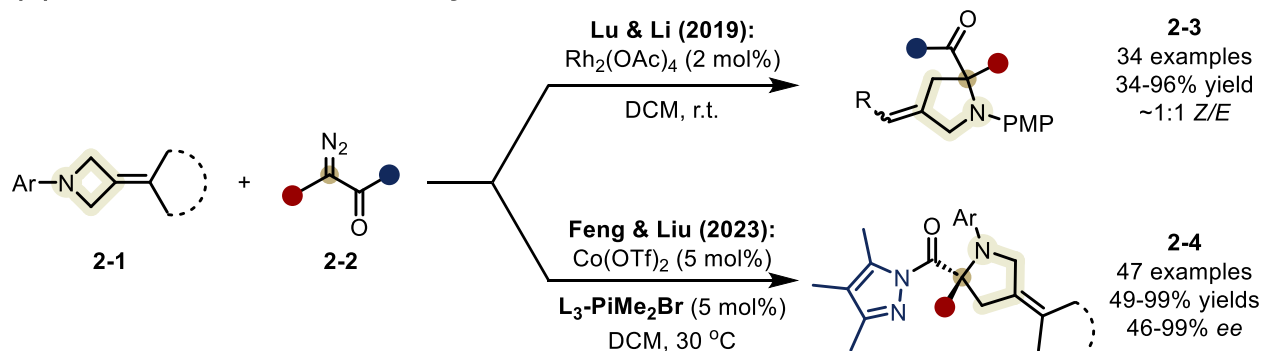
3. Summary and Outlook

Atom Insertion

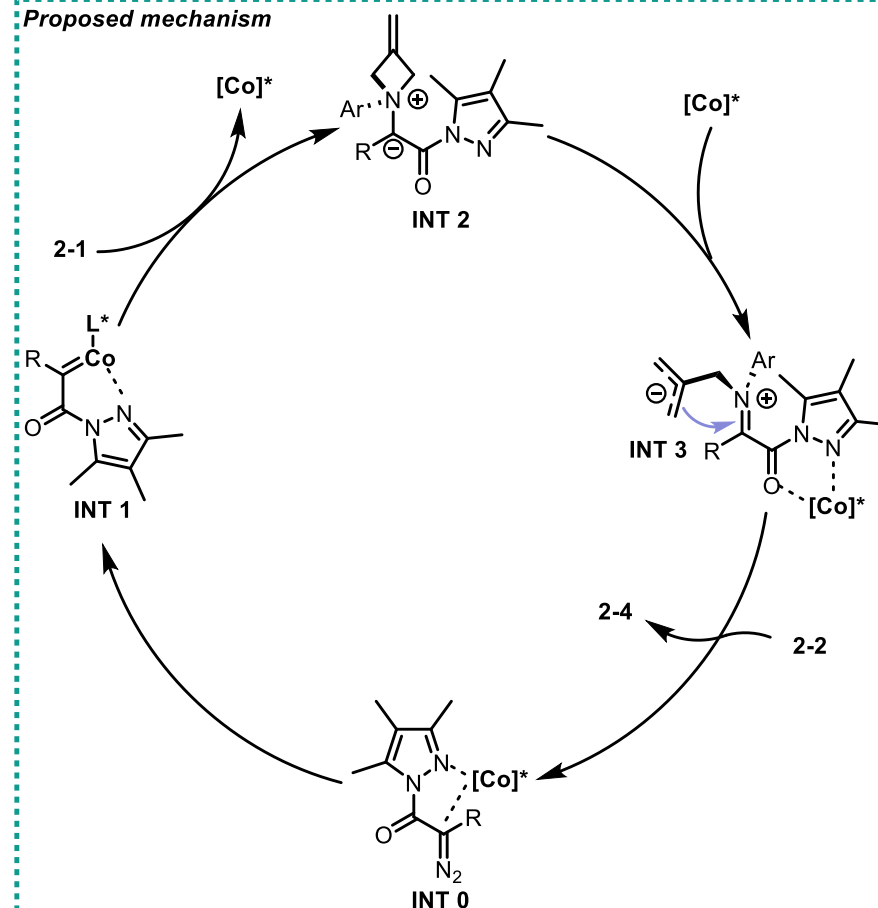
Stevens Rearrangement (1928):



(a) Atom insertions of methylene azetidines

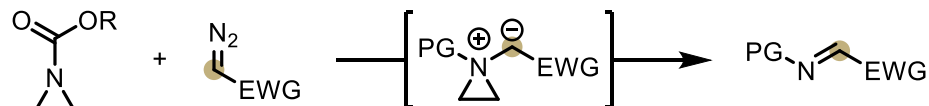


Proposed mechanism



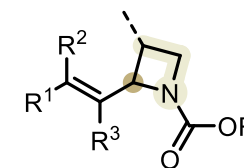
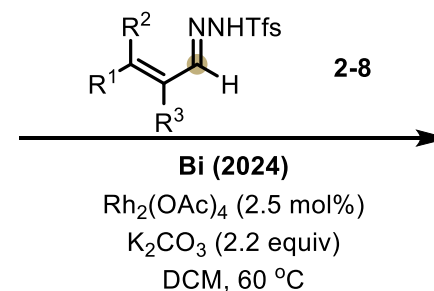
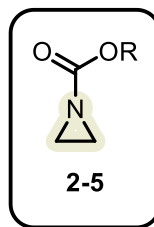
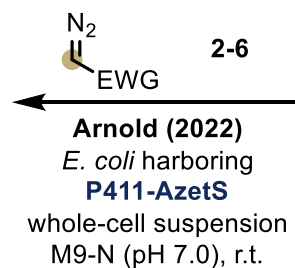
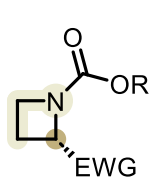
Atom Insertion

Possible *cheletropic extrusion* side reactions



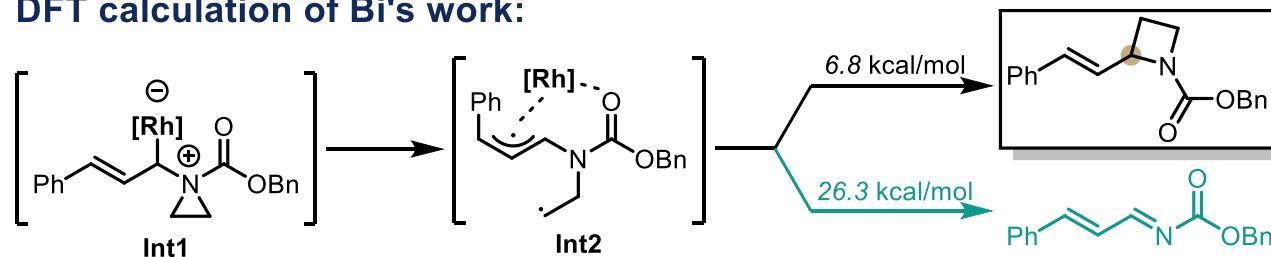
(b) Atom insertions of aziridines

2-7
8 examples
17-67% yields
62-98% ee



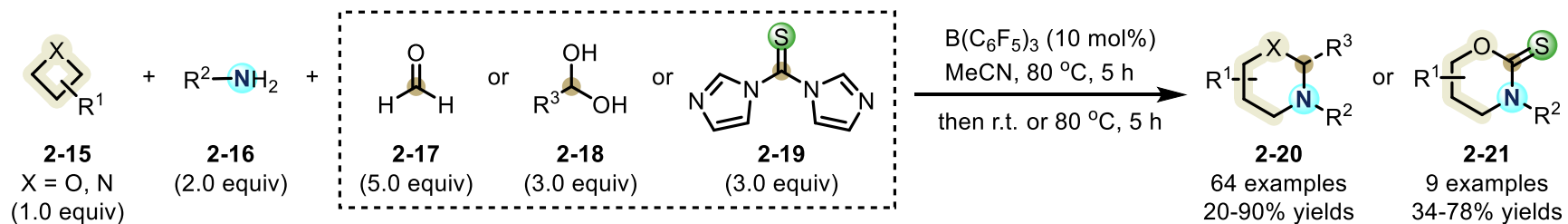
2-9
47 examples
62-95% yields

DFT calculation of Bi's work:

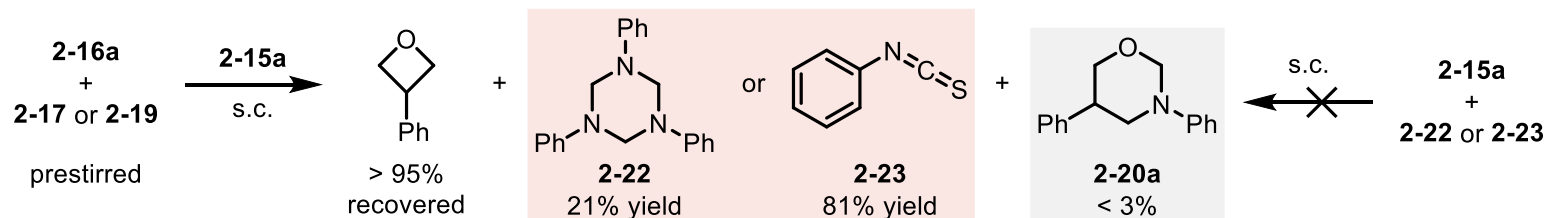


Atom Insertion

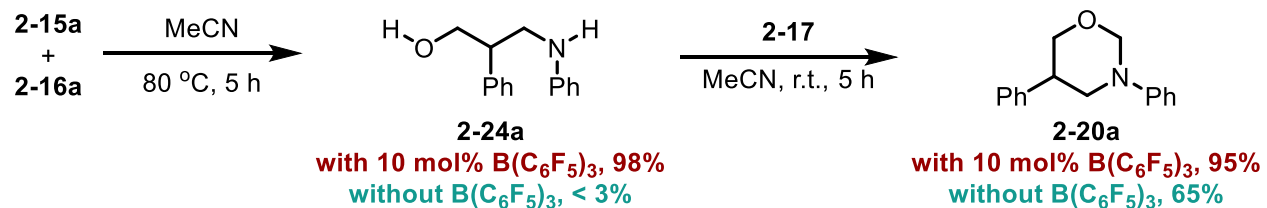
(d) Koh (2026):



Control experiments: reaction sequence

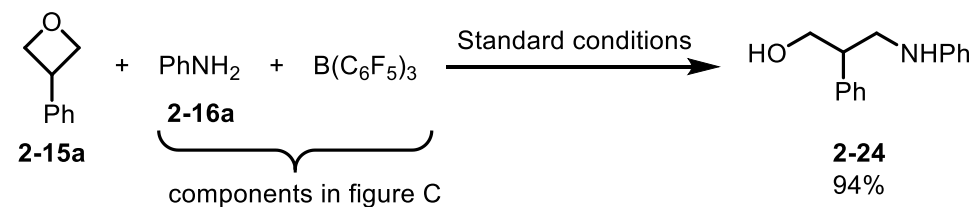
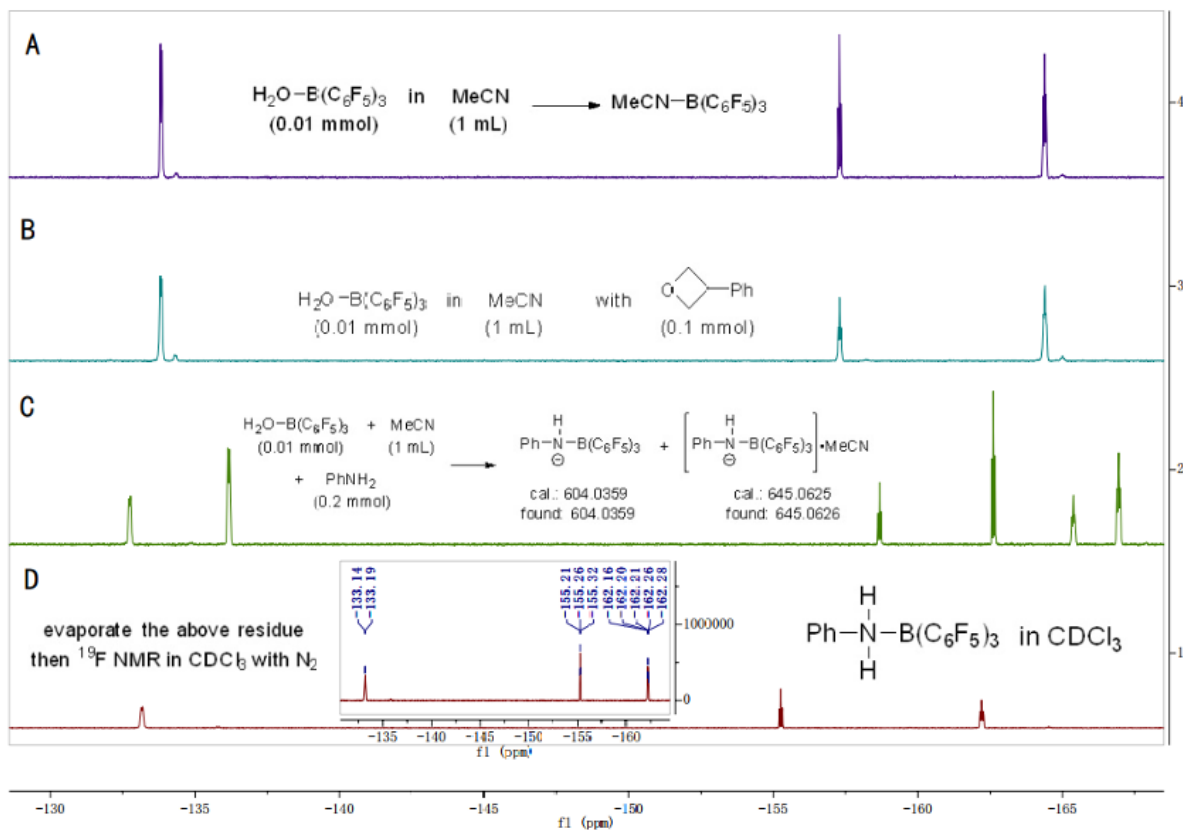


Control experiments: existence of amino alcohol intermediate

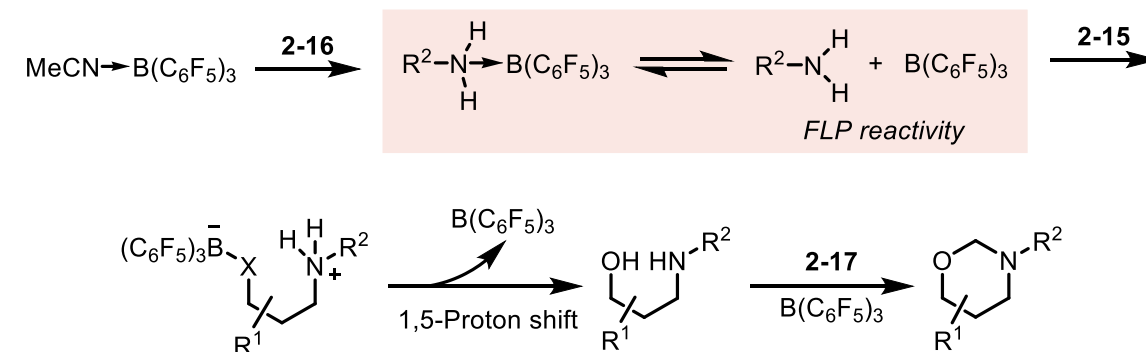


Atom Insertion

Analysis of $B(C_6F_5)_3$ - $PhNH_2$ adduct and its FLP reactivity

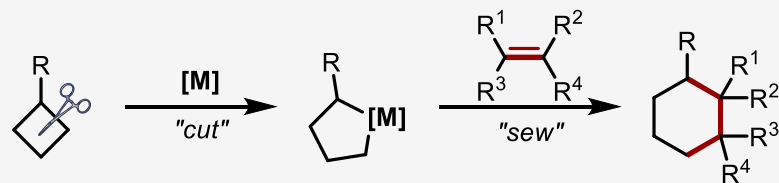


Proposed mechanism

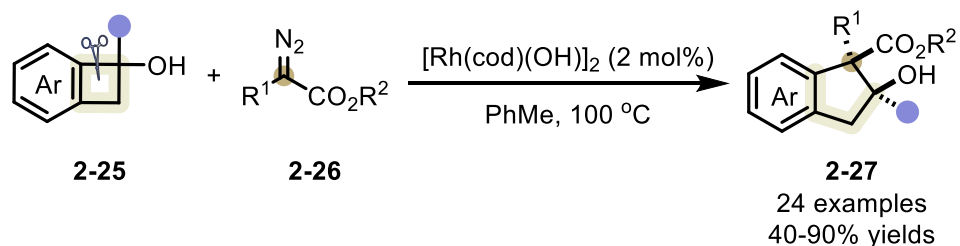


Atom Insertion

"Cut and sew" strategy (2012):

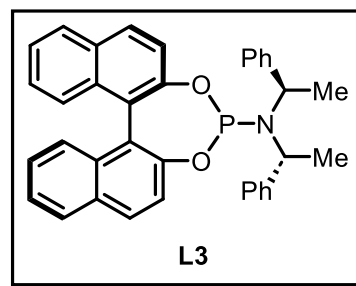
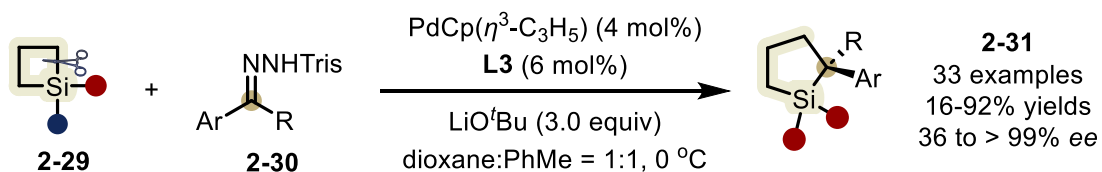


(a) Atom insertions of hydroxylcyclobutanes: Wang (2014)

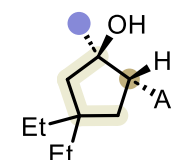


complete
regioselectivity
diastereoselectivity

(b) Atom insertions of siletanes: Wang (2021)

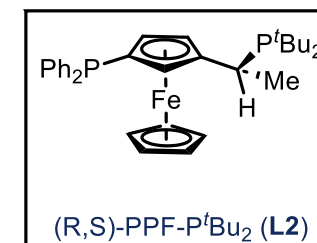
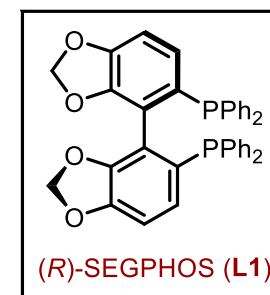


Murakami (2014):



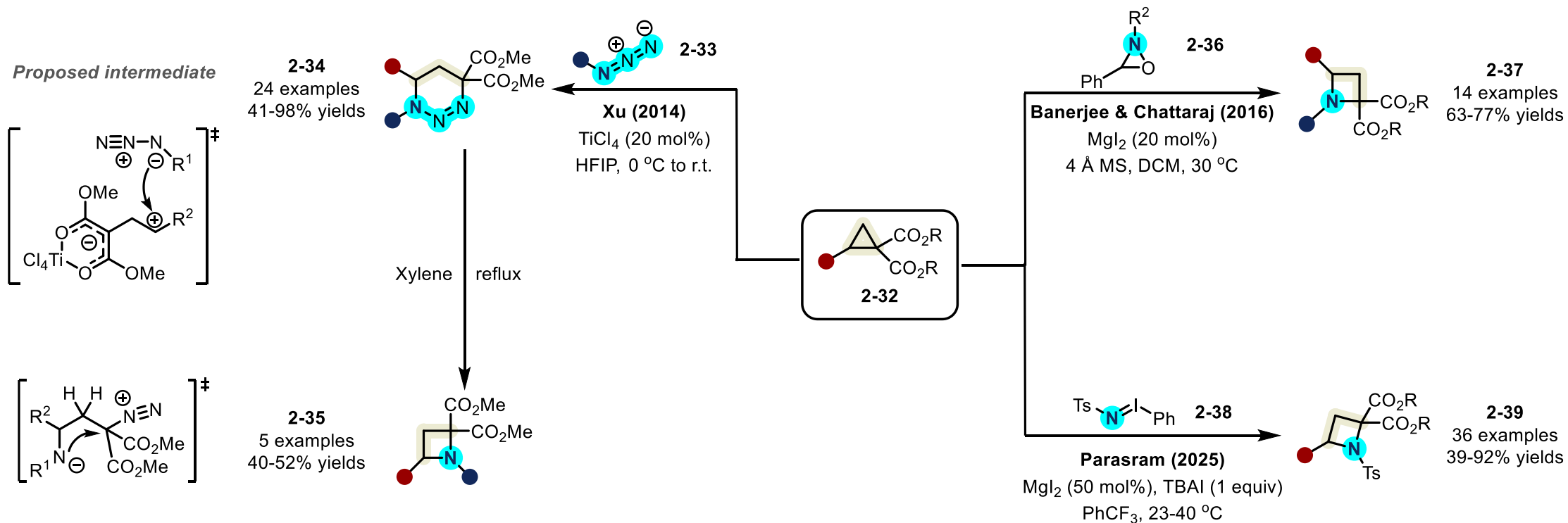
2-28 (L1)
9 examples
45-78% yields
> 90% ee
3.9:1 - 14:1 d.r.

epi-2-28 (L2)
9 examples
68-94% yields
> 90% ee
2.3:1 - 13:1 d.r.



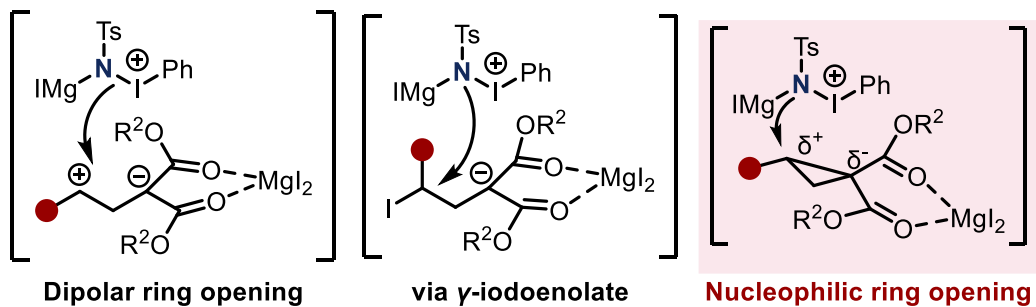
Atom Insertion

(c) Atom insertions of donor-acceptor cyclopropanes (DACs)

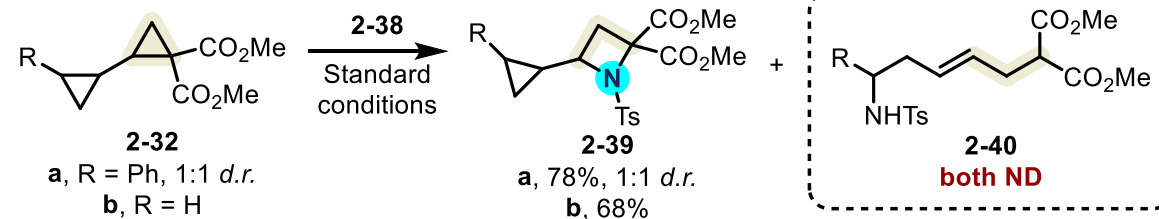


Atom Insertion

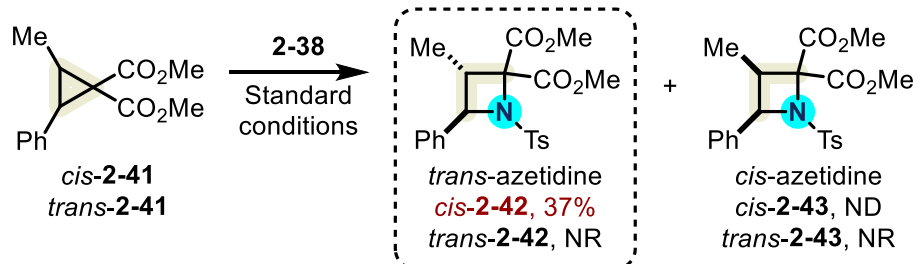
Possible mechanism



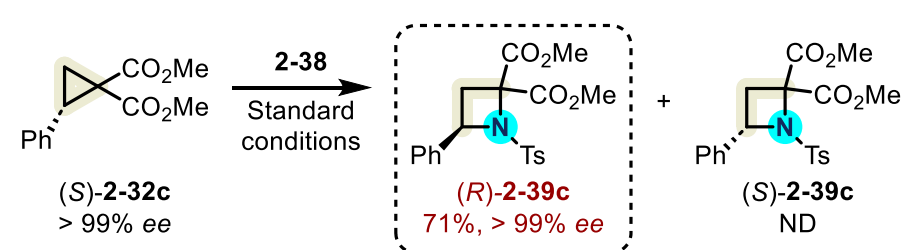
Cation probe



Nucleophilic ring-opening

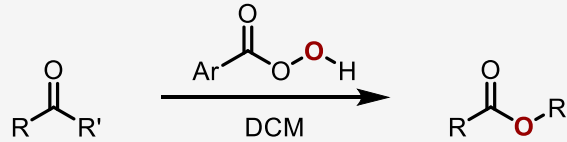


Chiral probe

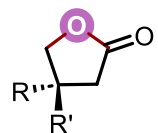


Atom Insertion

Baeyer-Villiger oxidation:

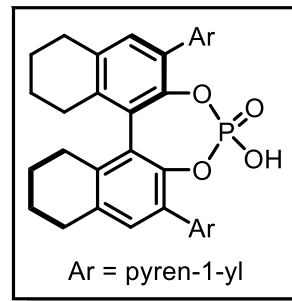


(a) Ding (2008)

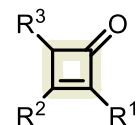


2-44

12 examples
91-99% yields
55-93% ee

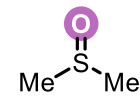


(b) Jiao (2023):



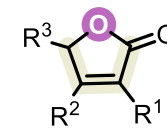
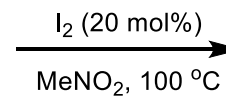
2-45

(1.0 equiv)



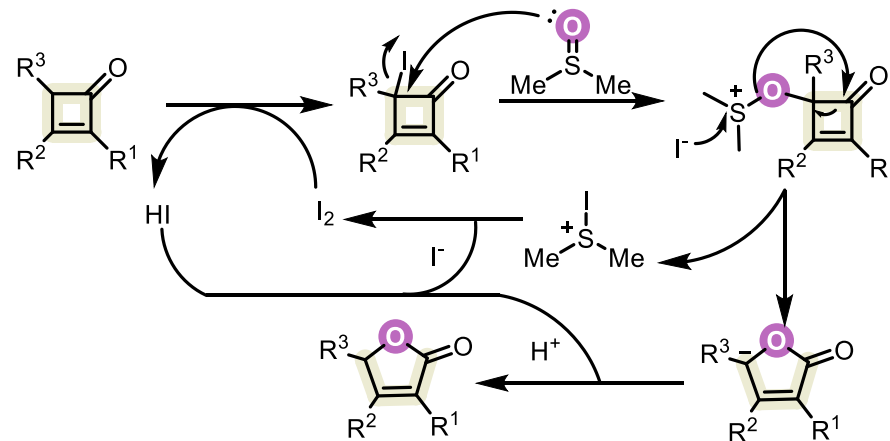
2-46

(5.0 equiv)



2-47

22 examples
41-94% yields





Content

1. Introduction

2. Skeletal Editing of Strained Rings

2.1 Atom Insertion

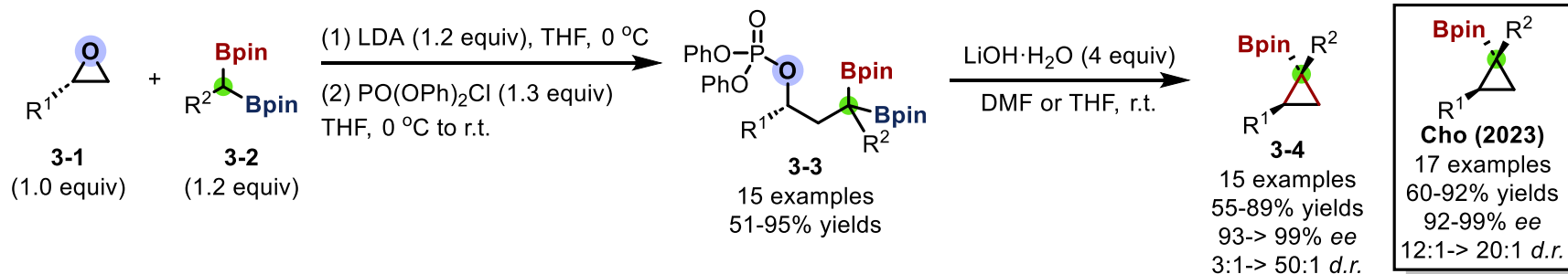
2.2 Atom Transmutation and Translocation

2.3 Atom Deletion

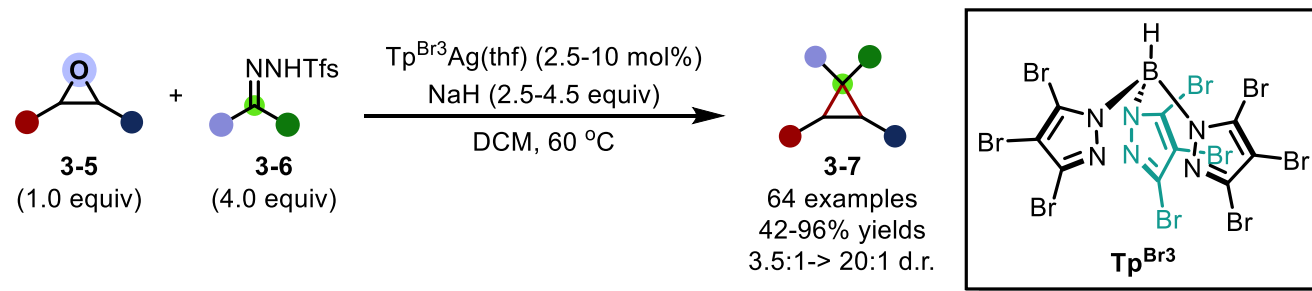
3. Summary and Outlook

Atom Transmutation

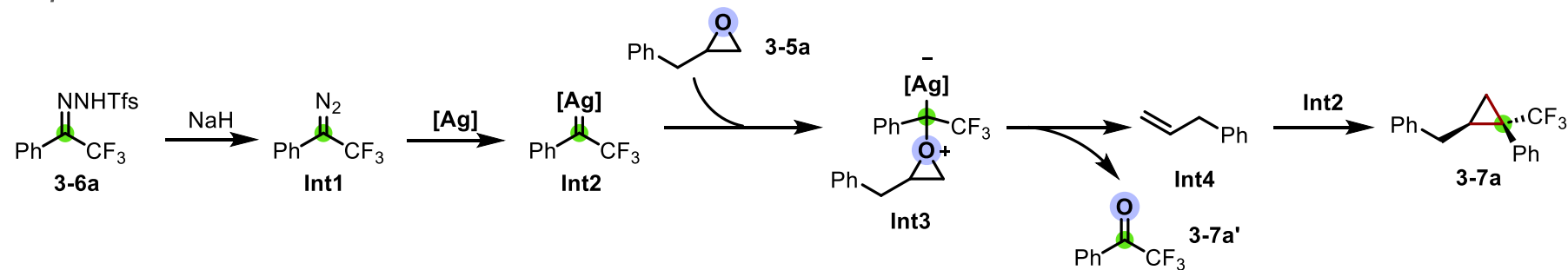
(a) Hong (2023):



(b) Bi (2024):

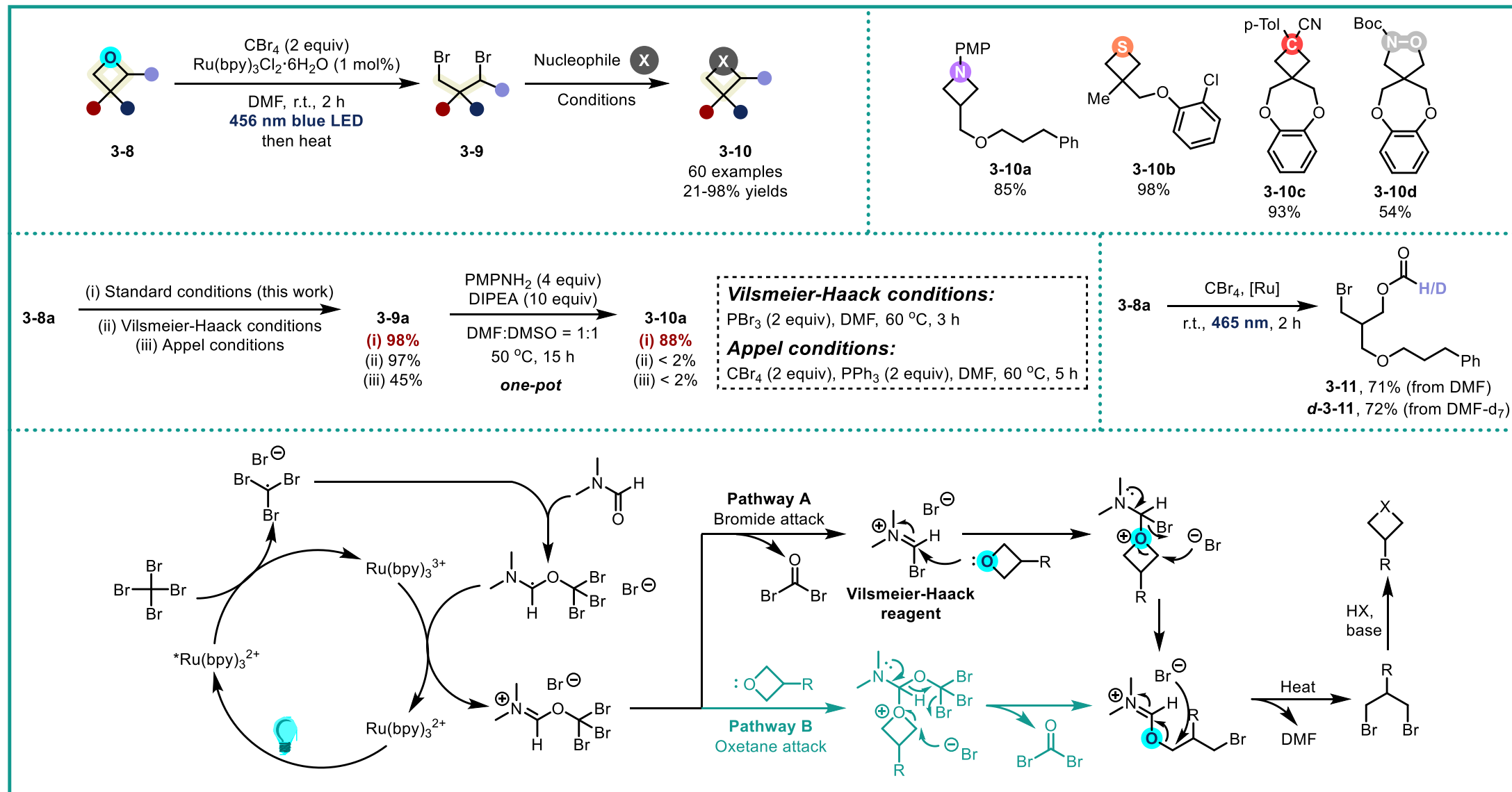


Proposed mechanism



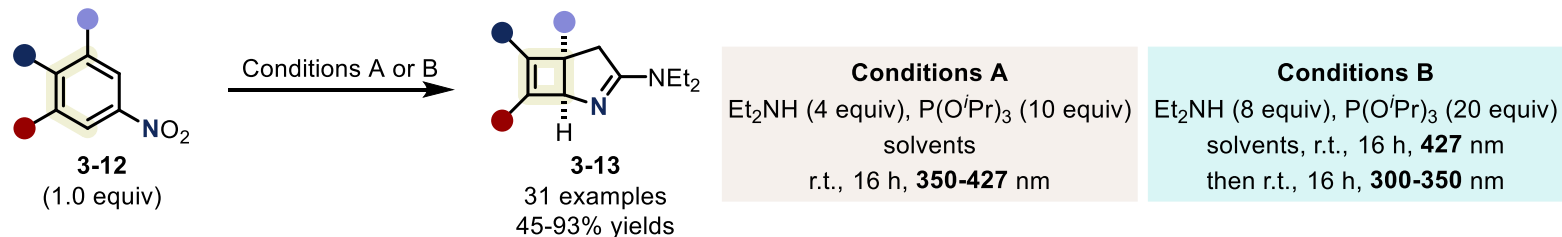
Atom Transmutation

(c) Koh & Zhang (2025):

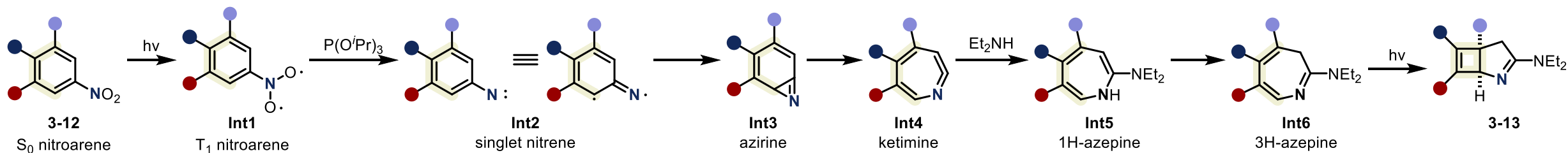


Atom Translocation

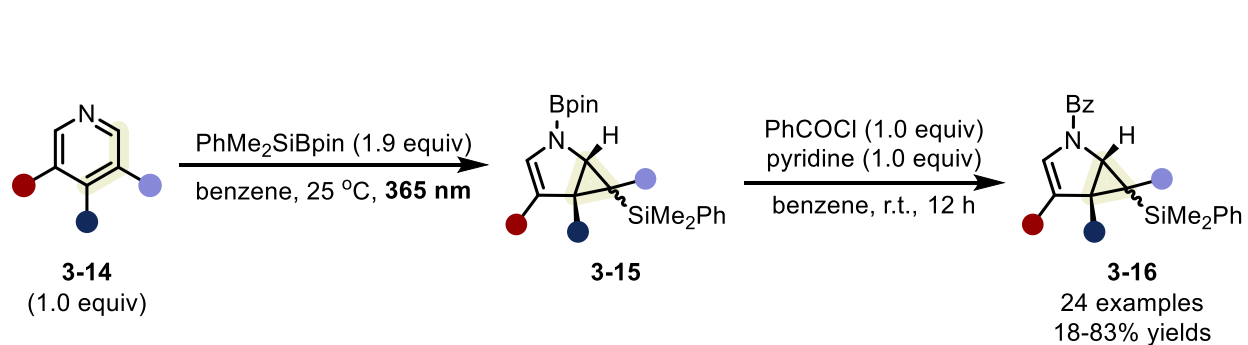
(a) Leonori & Ruffoni & Merino (2023):



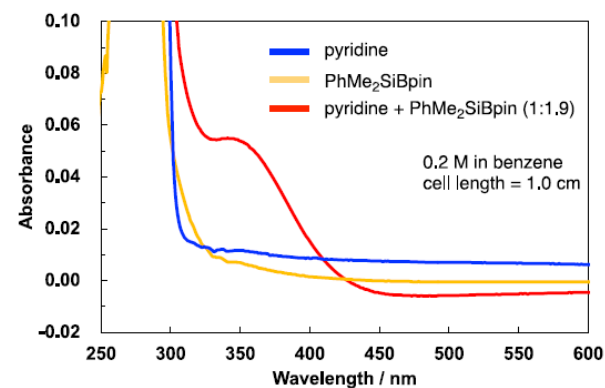
Proposed mechanism



(b) Takaya (2025):

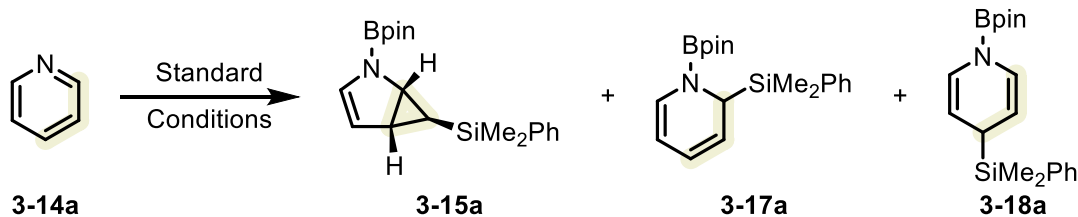


UV/Vis spectra



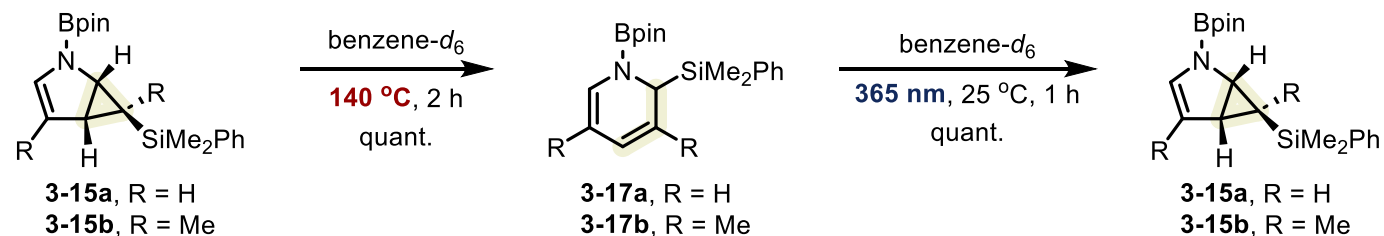
Atom Translocation

Time course analysis

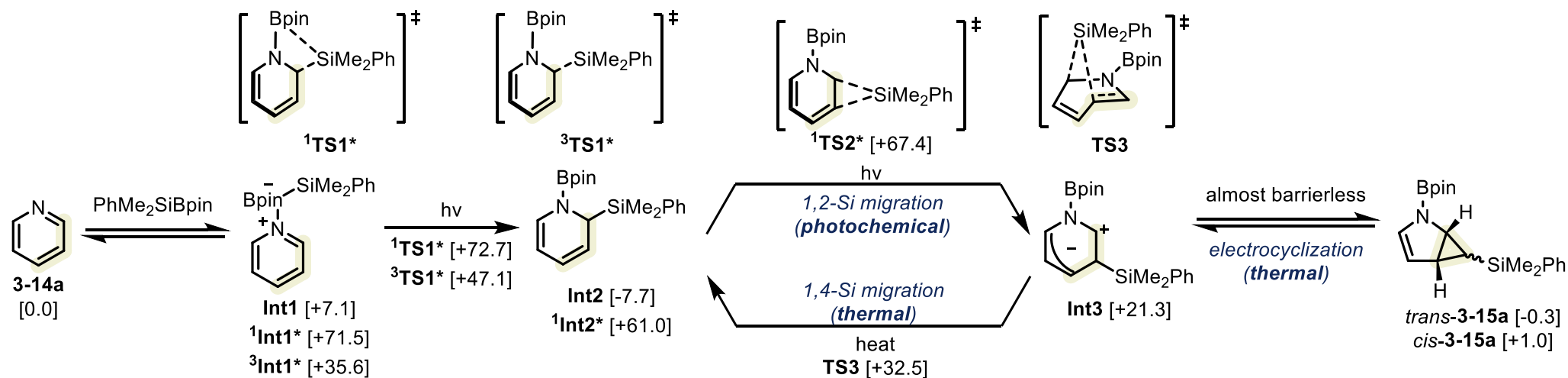


	3-15a	3-17a	3-18a
430 nm + 30 min	14%	1%	0%
430 nm + 2 h	48%	1%	2%
430 nm + 8.5 h	85%	0%	3%
365 nm + 2 h	quant.	0%	0%

Interconversion between 3-15 and 3-17

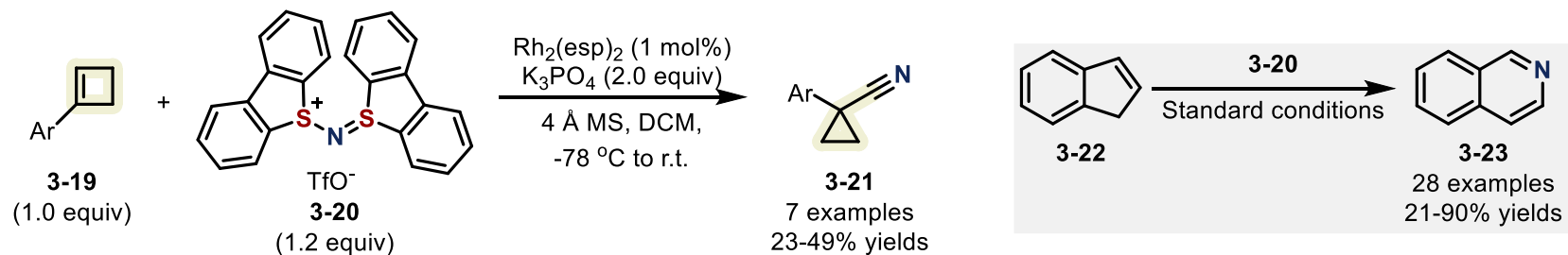


DFT calculations

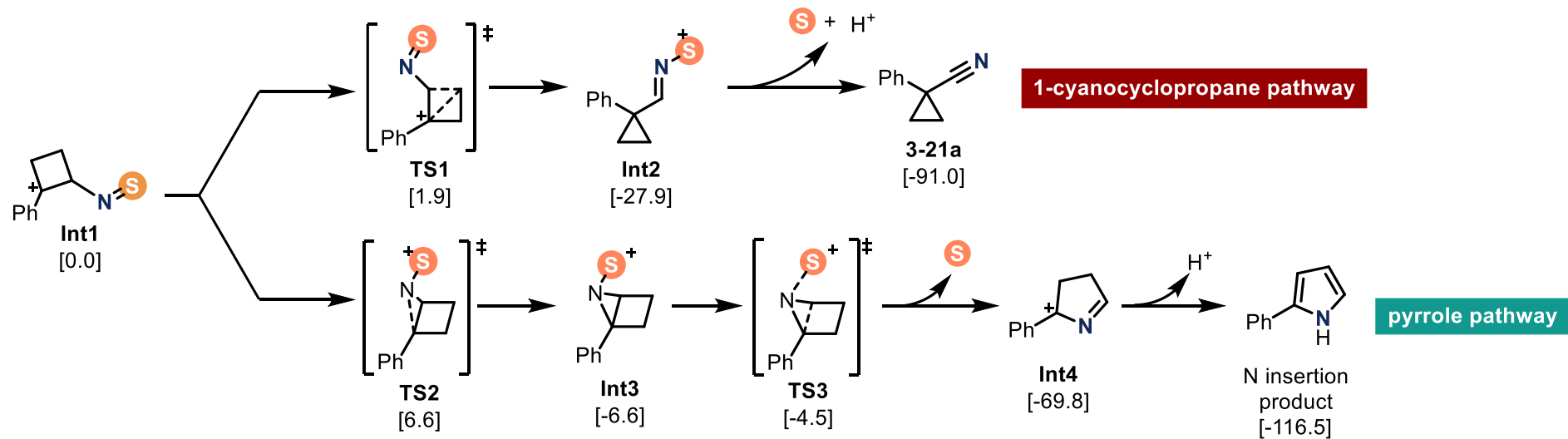


Atom Translocation

(c) Alcarazo (2024):

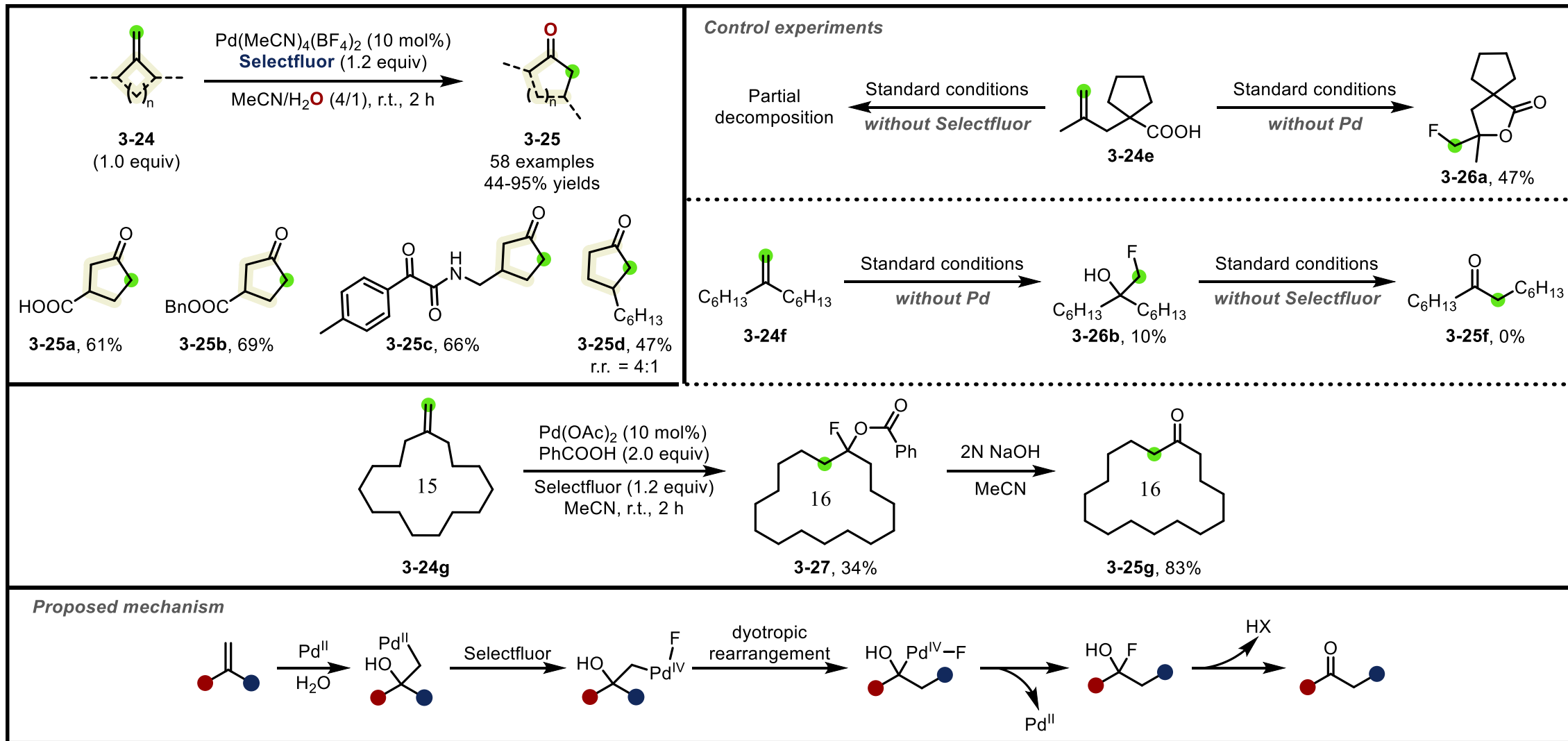


DFT calculation



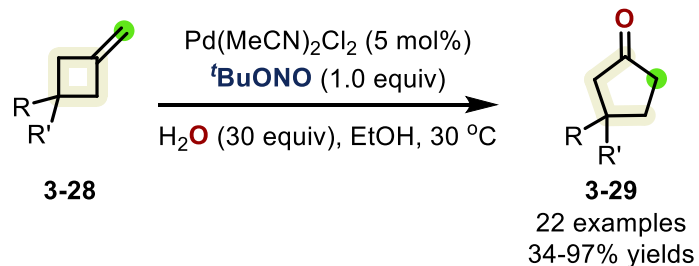
Atom Translocation

(a) Zhu (2023):

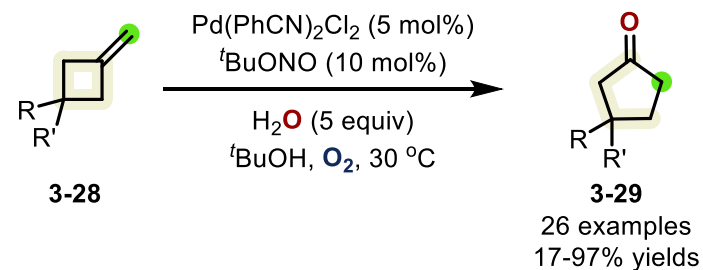


Atom Translocation

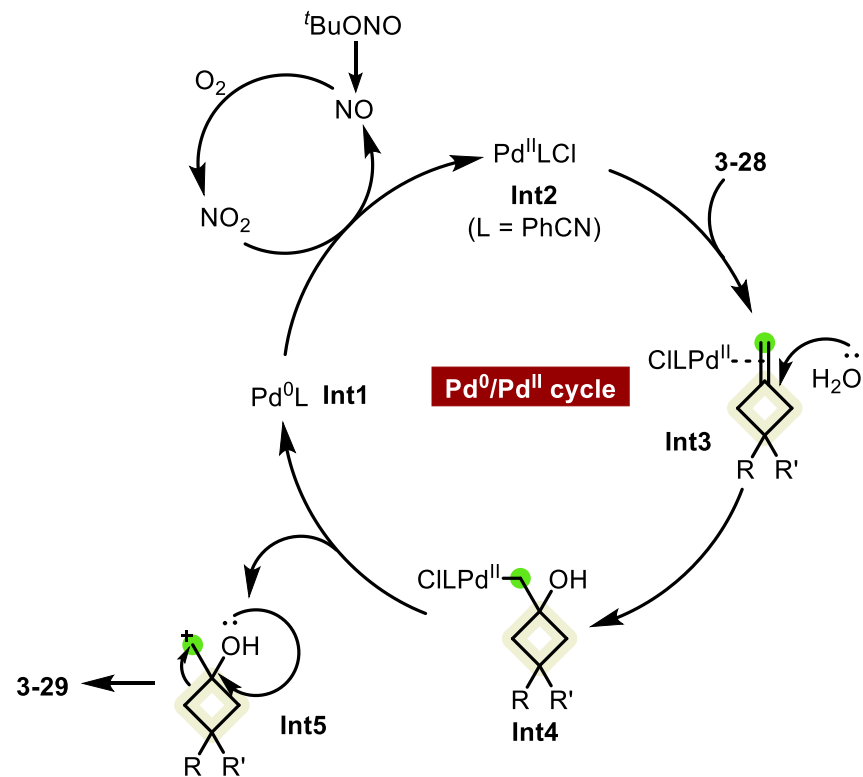
(b) Wahl (2023):



Kang & Qu (2024):



Proposed mechanism





Content

1. Introduction

2. Skeletal Editing of Strained Rings

2.1 Atom Insertion

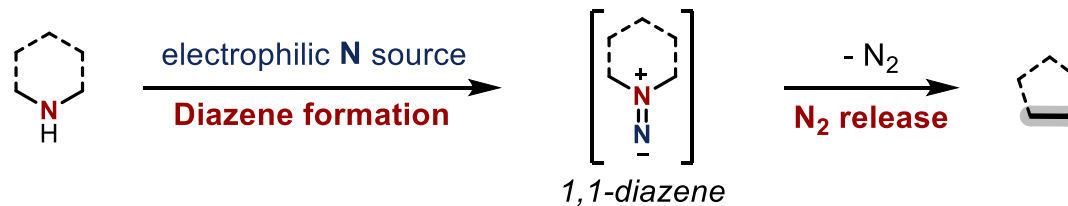
2.2 Atom Transmutation and Translocation

2.3 Atom Deletion

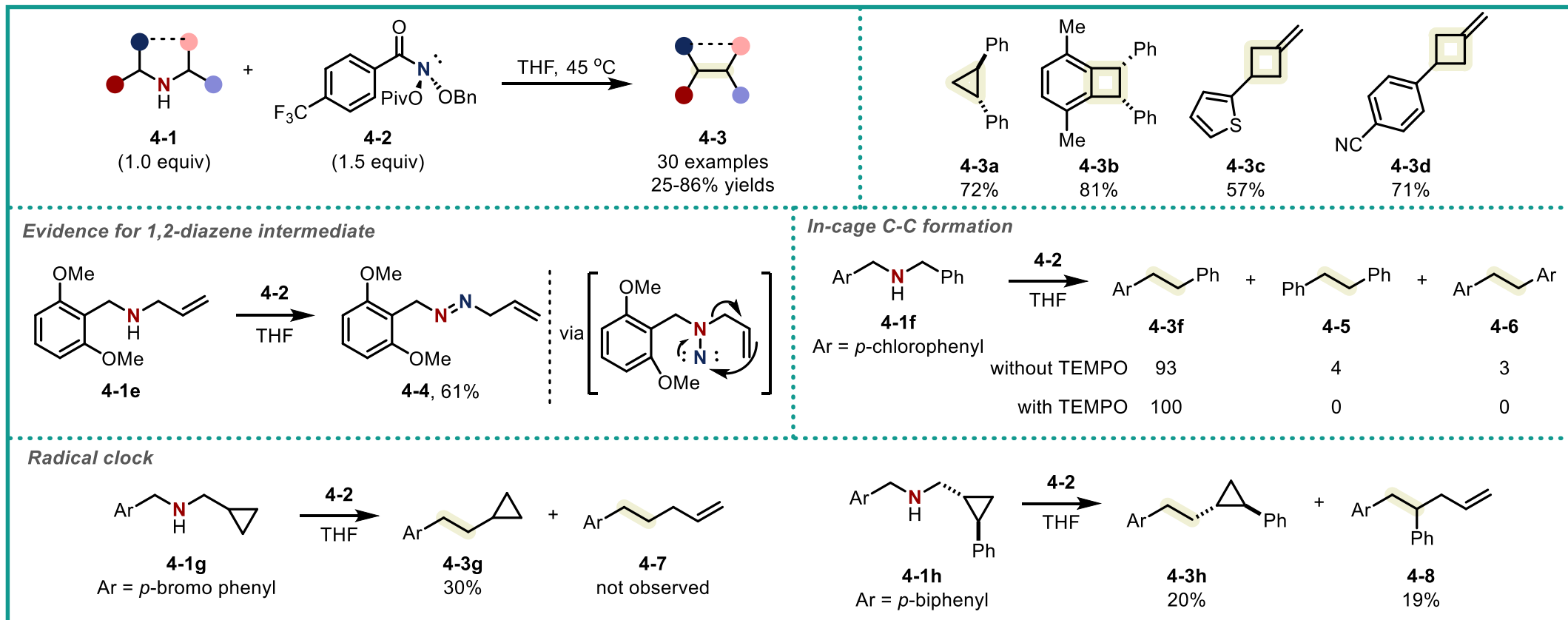
3. Summary and Outlook

Atom Deletion

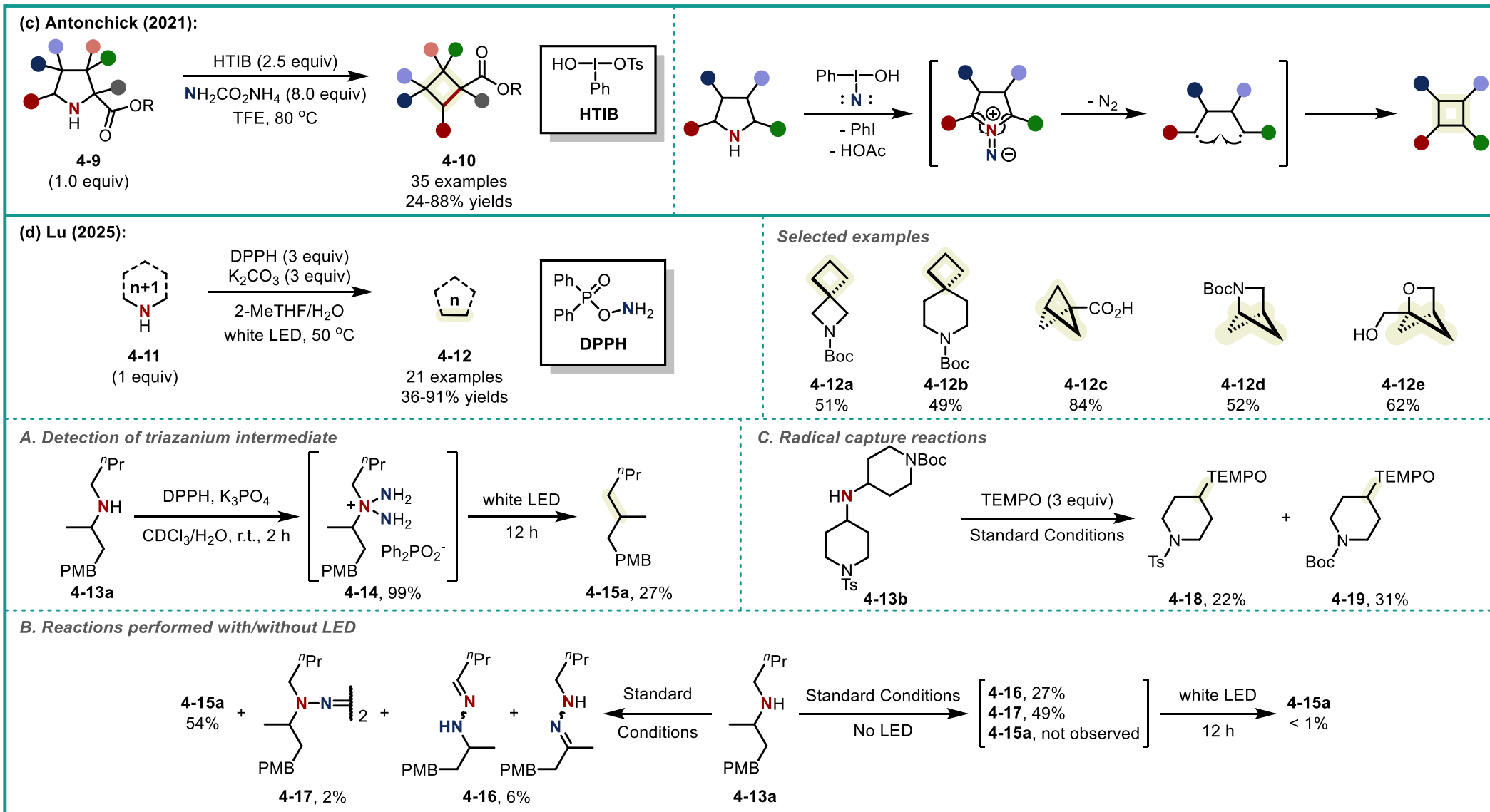
(a) Typical procedure for the N deletion reaction



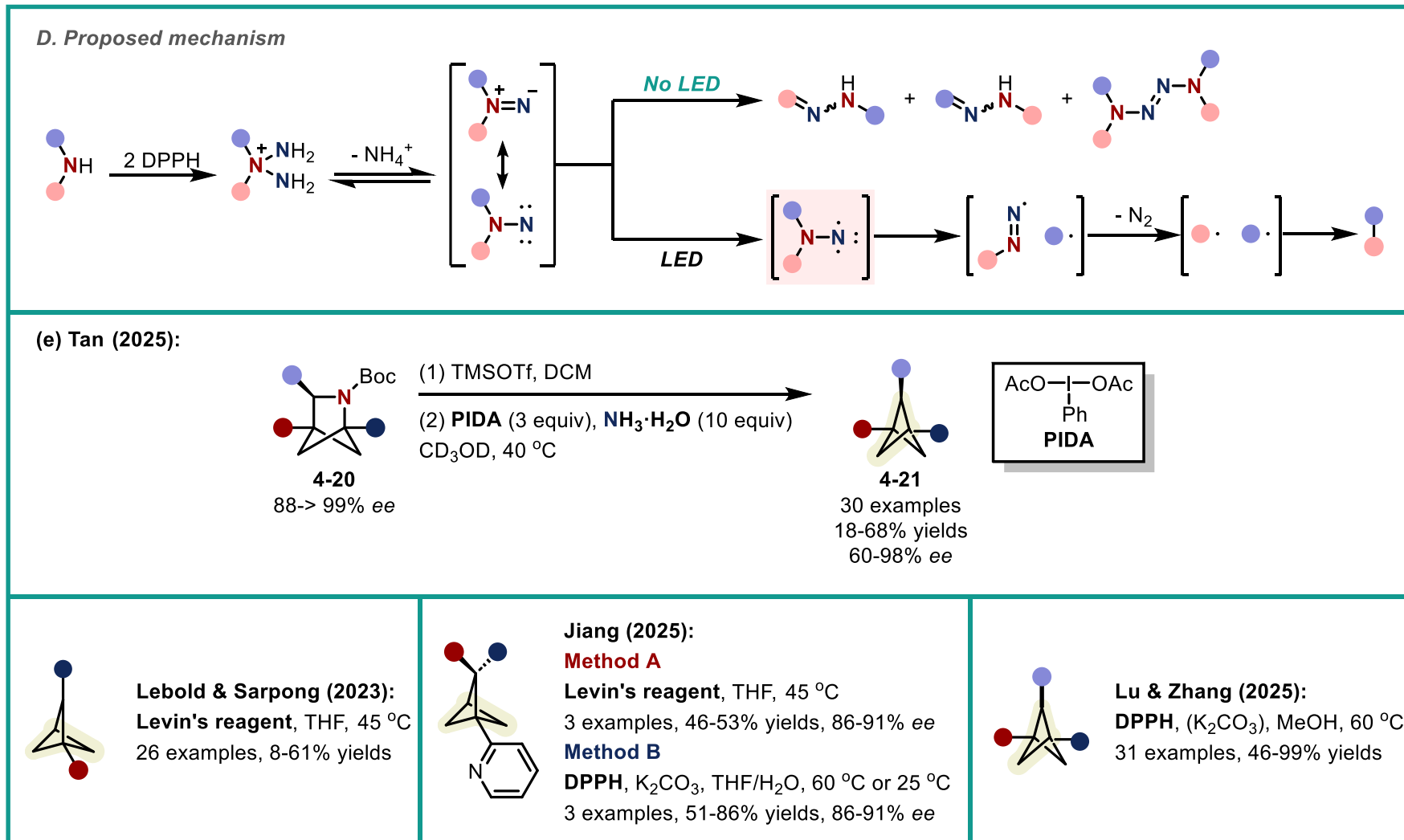
(b) Levin (2021):



Atom Deletion



Atom Deletion





Content

1. Introduction

2. Skeletal Editing of Strained Rings

2.1 Atom Insertion

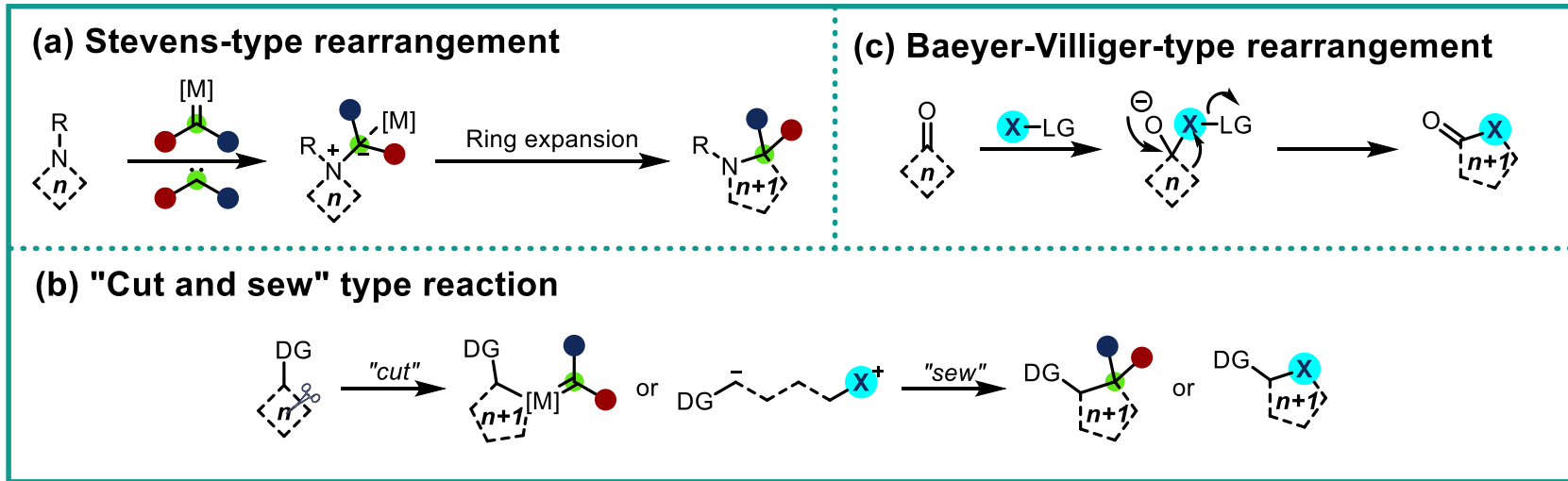
2.2 Atom Transmutation and Translocation

2.3 Atom Deletion

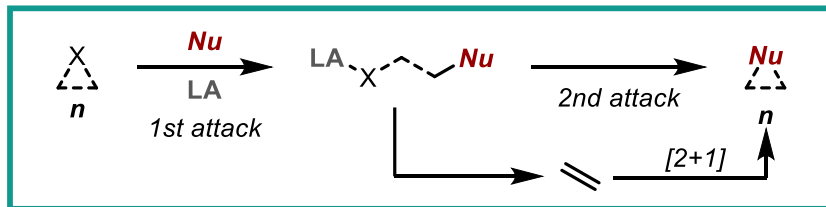
3. Summary and Outlook

Summary

➤ Atom **insertion** — *Many reports*



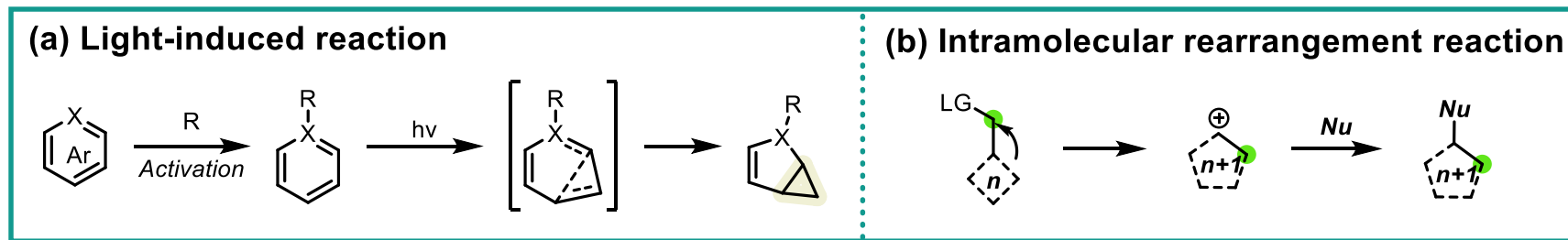
➤ Atom **transmutation** — *Few reports*



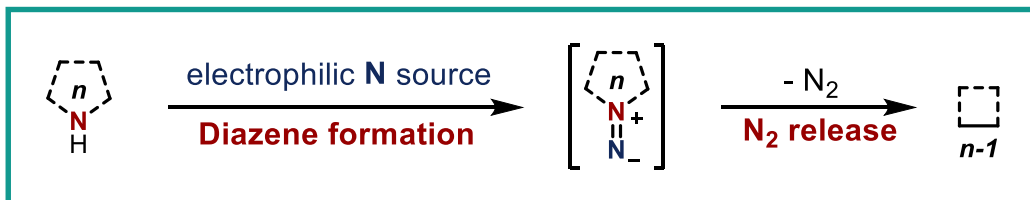
- Easy to open, hard to close
- High ring-strain energy
- Challenging C-C activation process
- Multiple side reactions

Summary

➤ **Atom translocation** — *Many reports*

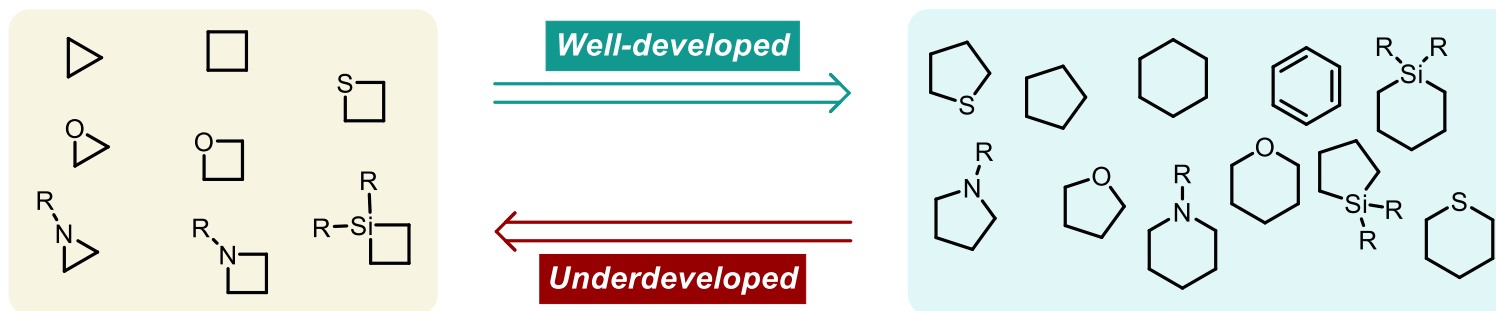


➤ **Atom deletion** — *Few reports*

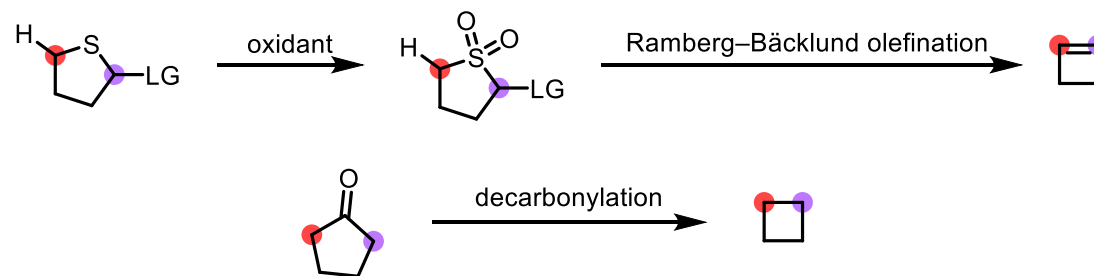


- Thermodynamically unfavorable
- Lack of appropriate leaving groups

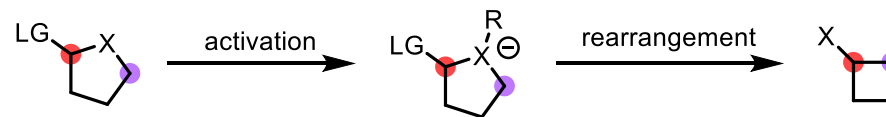
Outlook



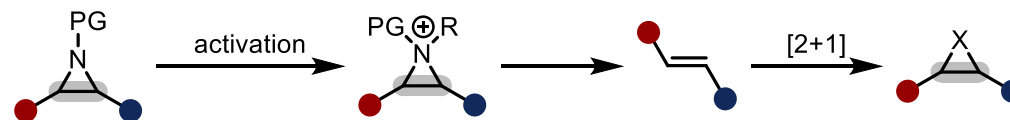
1. Through atom deletion



2. Through atom translocation



3. Through atom transmutation

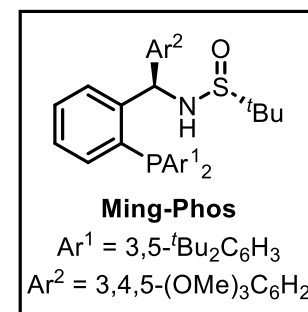
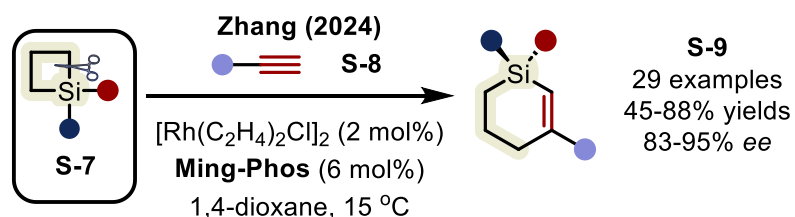
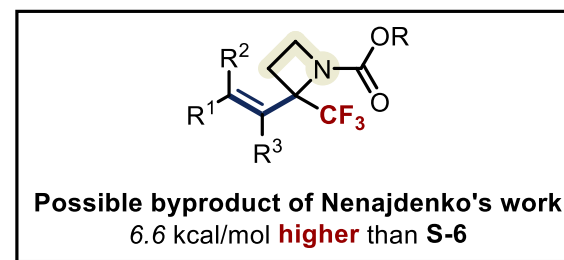
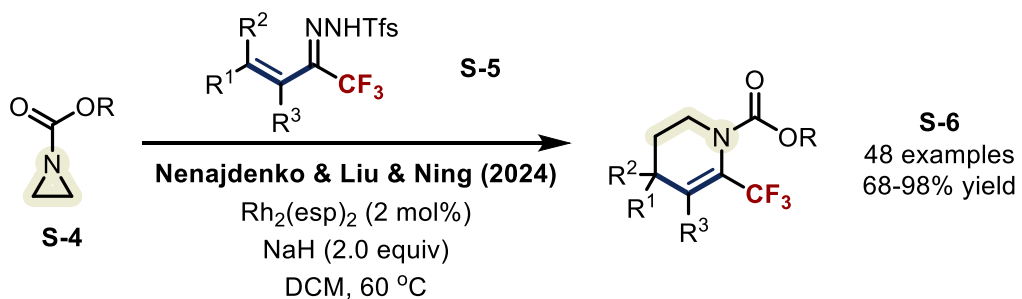
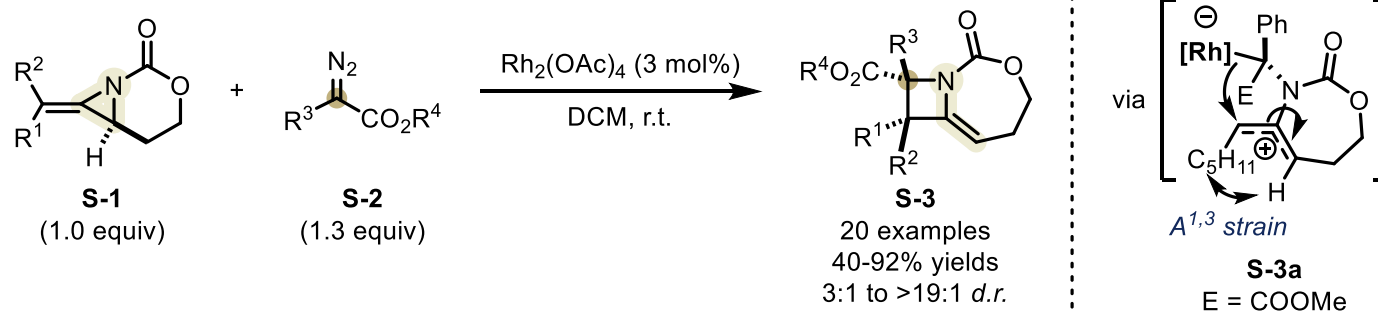




Thanks for Listening

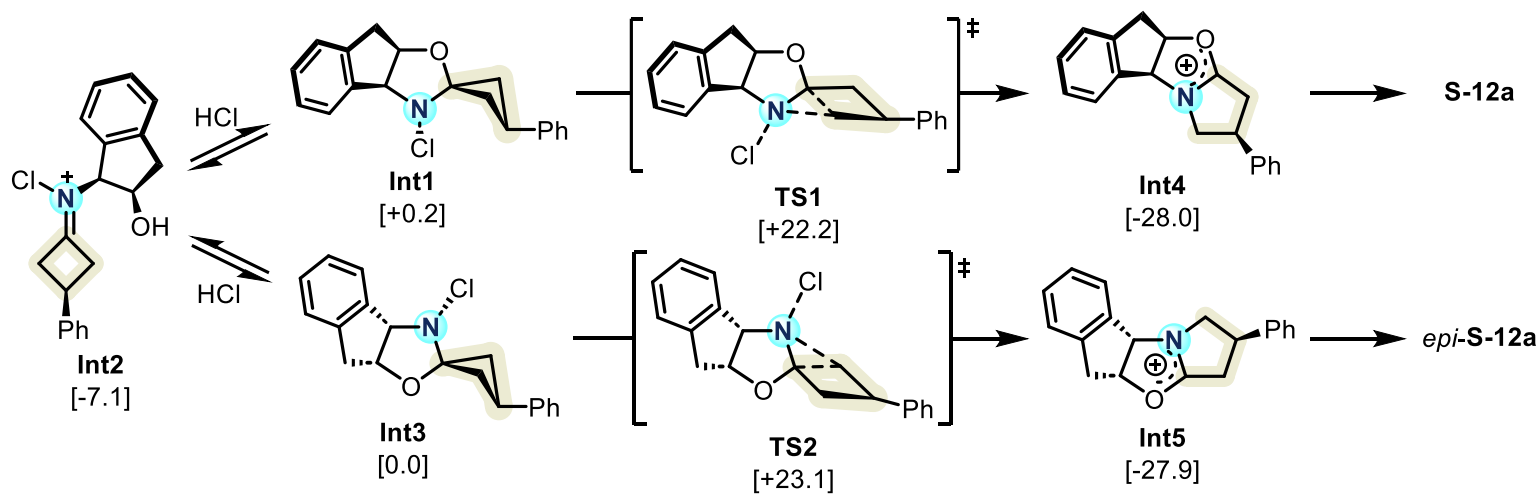
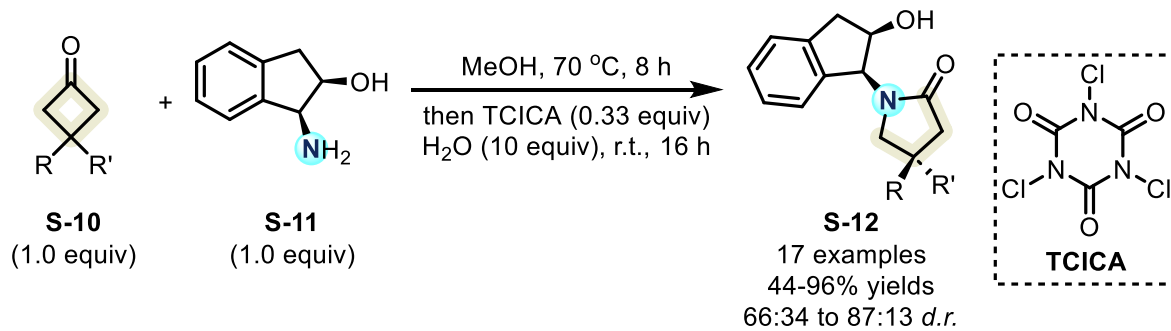
Supporting Information

Schomaker (2017):



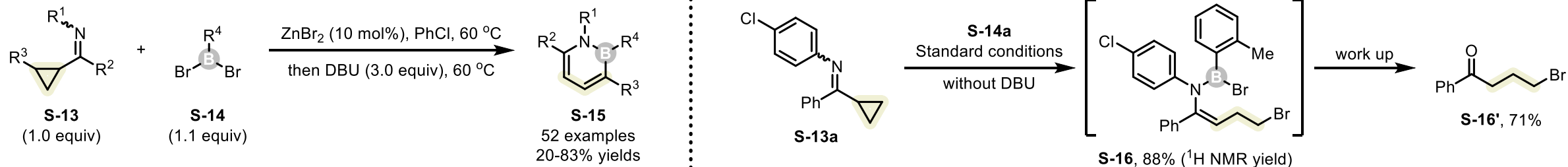
Supporting Information

Wahl (2021):

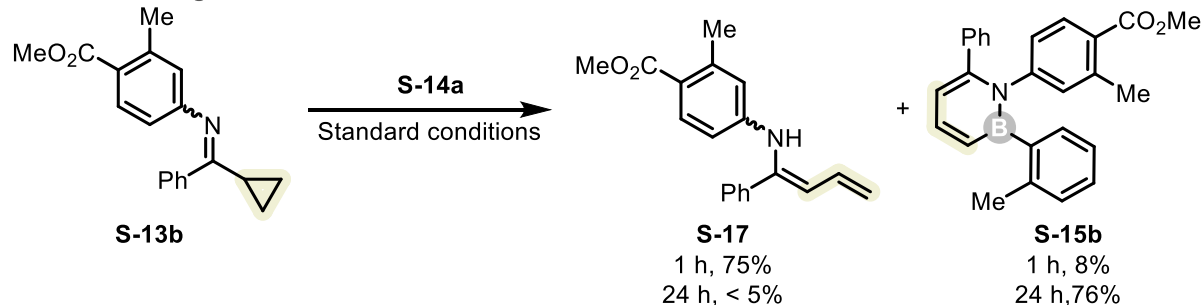


Supporting Information

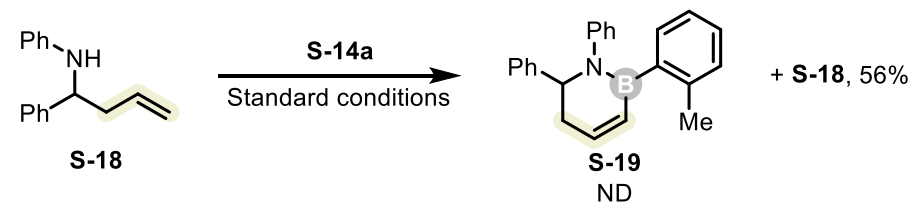
Dong & Liu & Houk(2023):



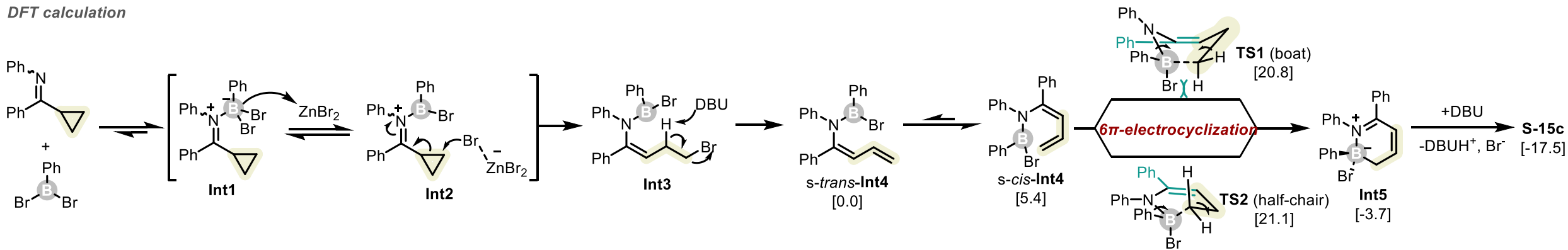
Intermediate catching



Active species identification

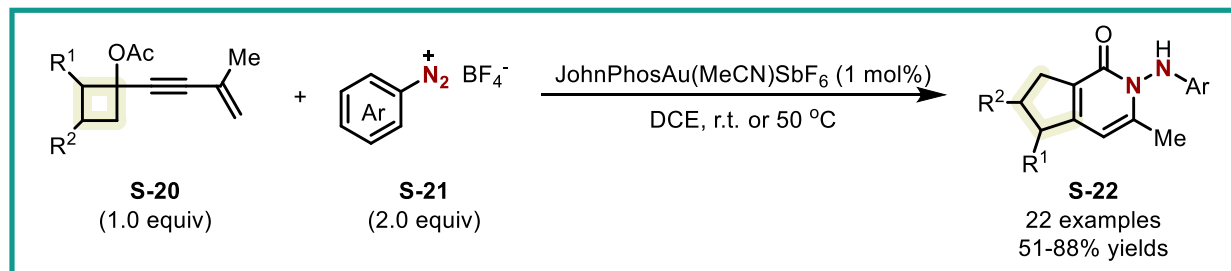


DFT calculation



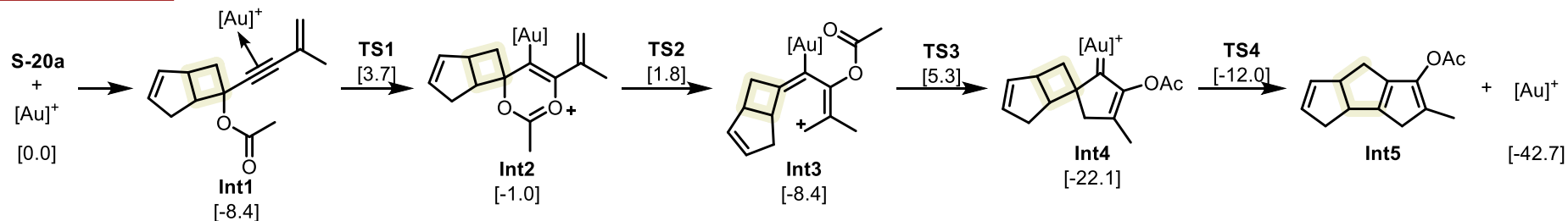
Supporting Information

Jiang & Lan & Hao (2022):

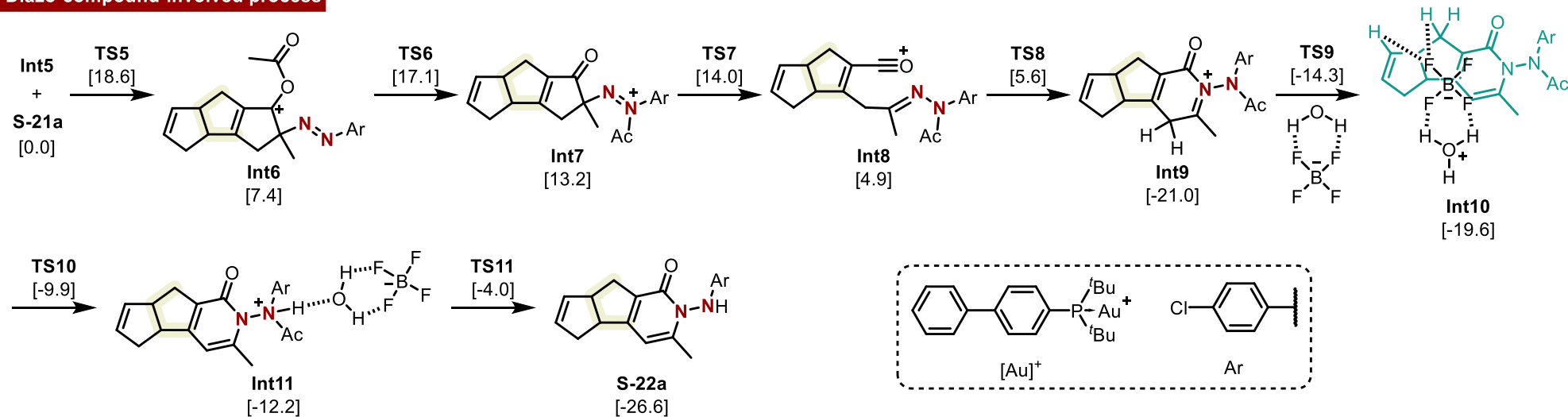


DFT calculation

Gold-involved process

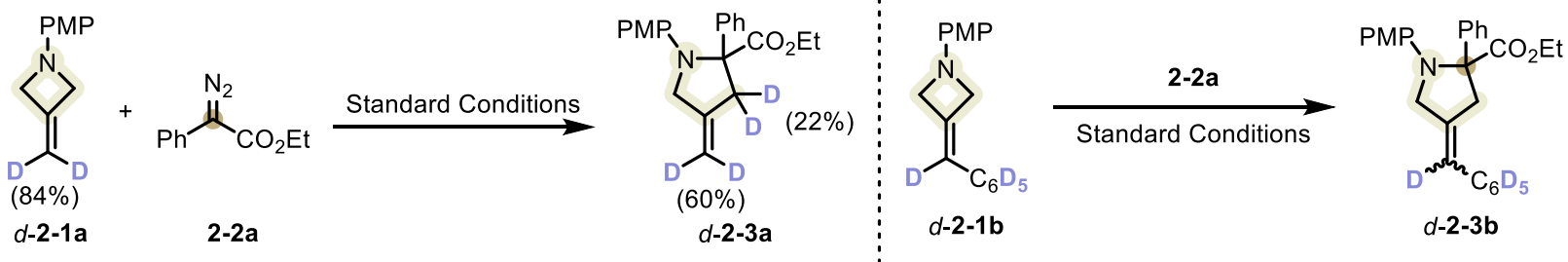


Diazo-compound-involved process

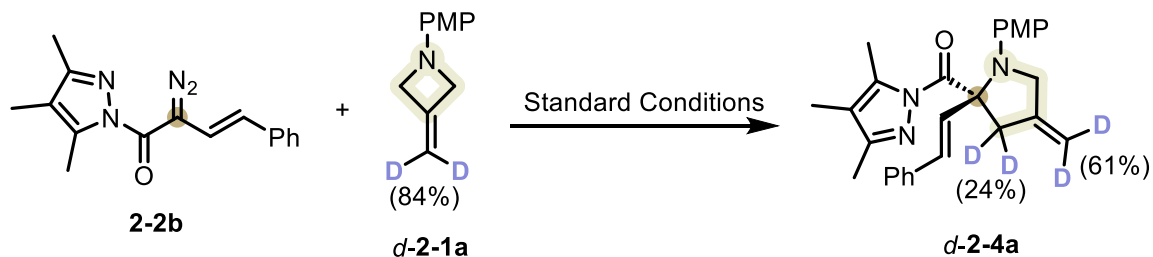


P8

Lu & Li (2019):

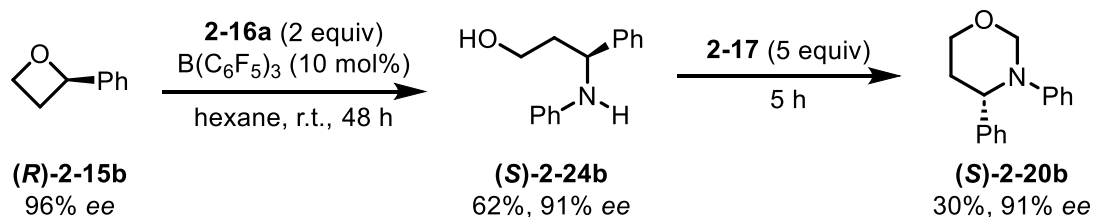


Feng & Liu (2023):



P11

Koh (2026): study of aminolysis step



Supporting Information

Equilibrium and reactivity experiments of $B(C_6F_5)_3-H_2O$ in acetonitrile solution

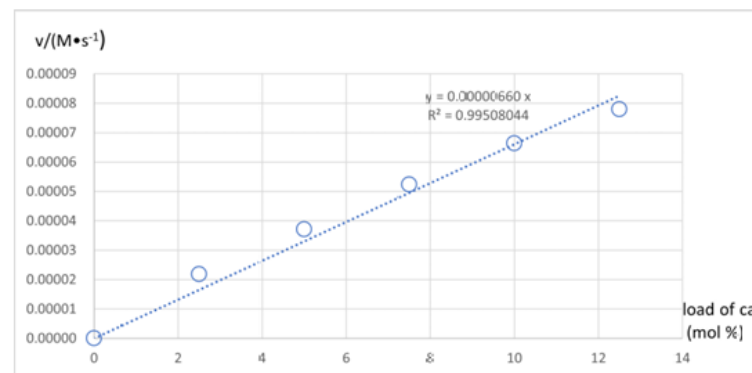
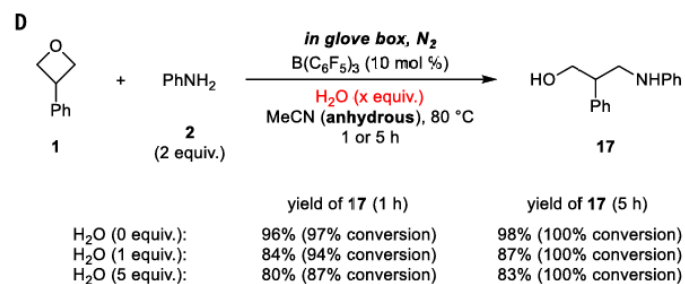
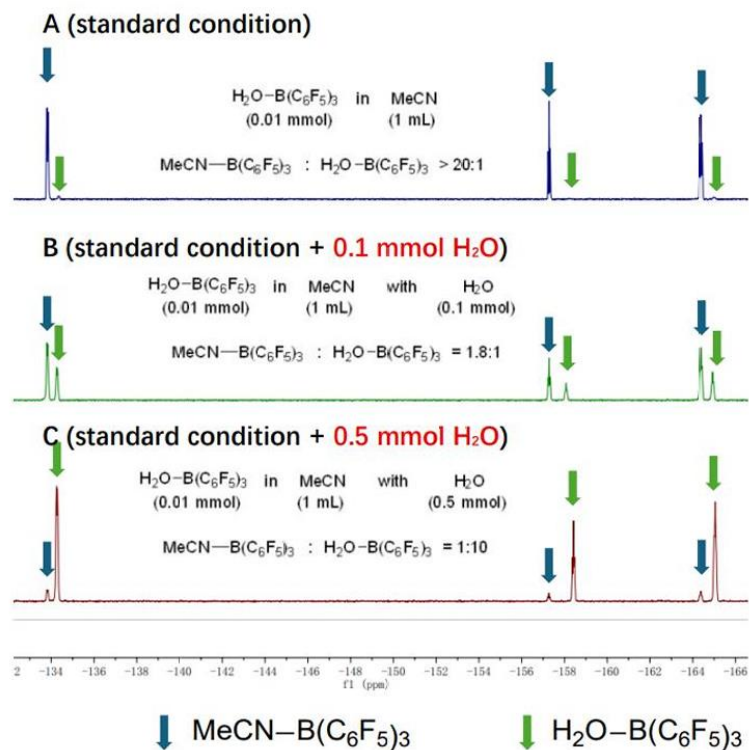


Fig. S6. Kinetic experiments with $B(C_6F_5)_3$.

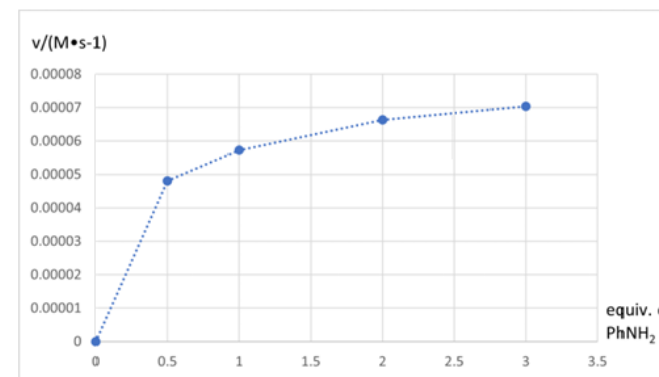


Fig. S7. Kinetic experiments with $PhNH_2$.

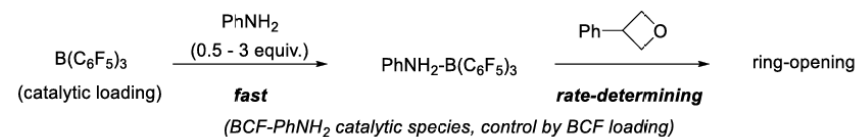
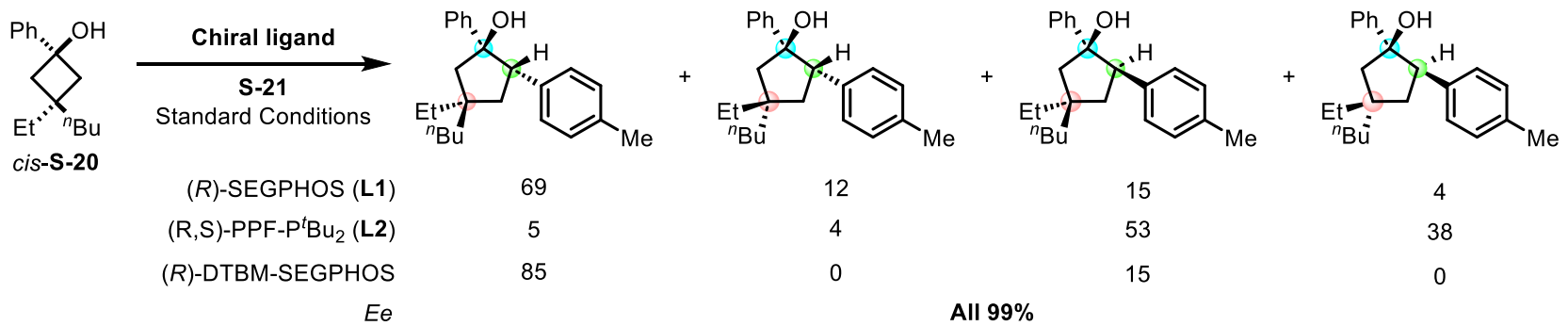


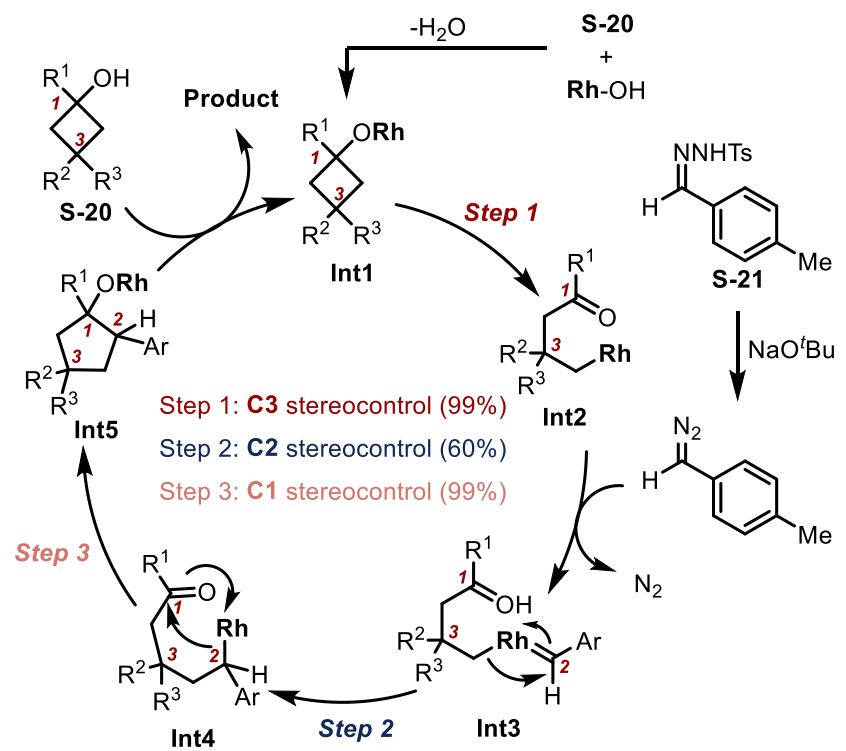
Fig. S8. Kinetic understanding of $B(C_6F_5)_3-PhNH_2$ formation and subsequent oxetane ring-opening.

Supporting Information

P13 Murakami (2014)

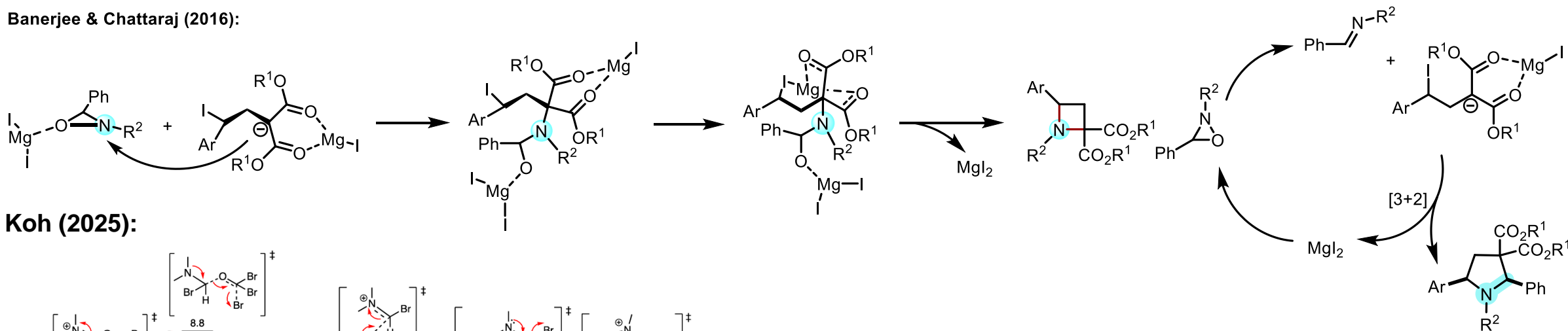


Possible mechanism

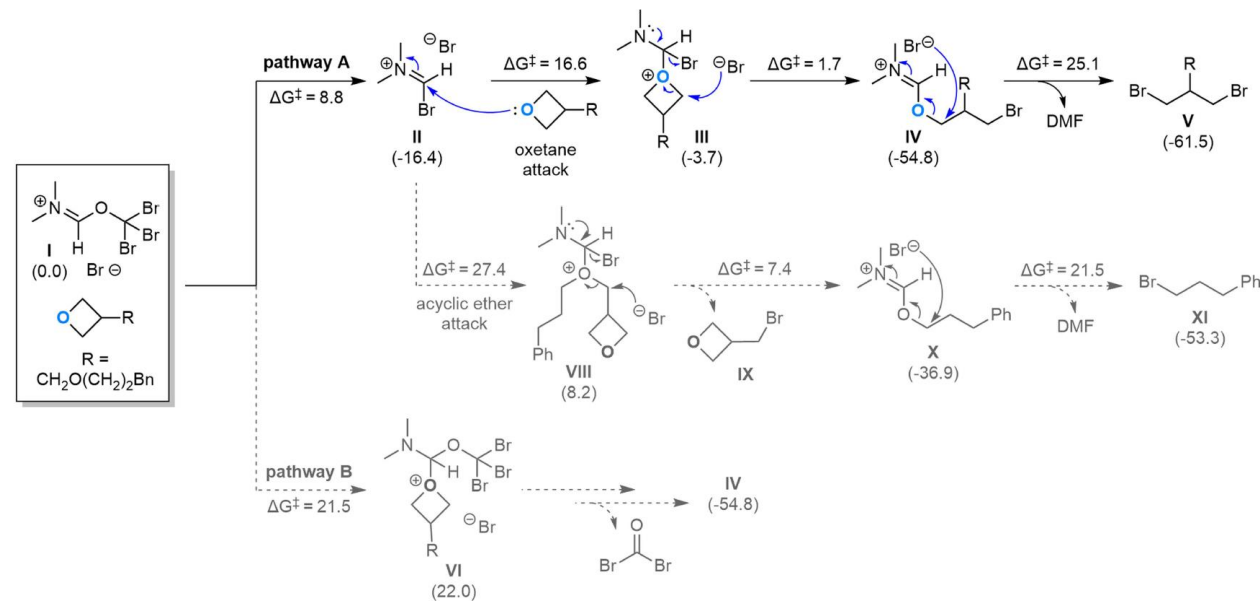
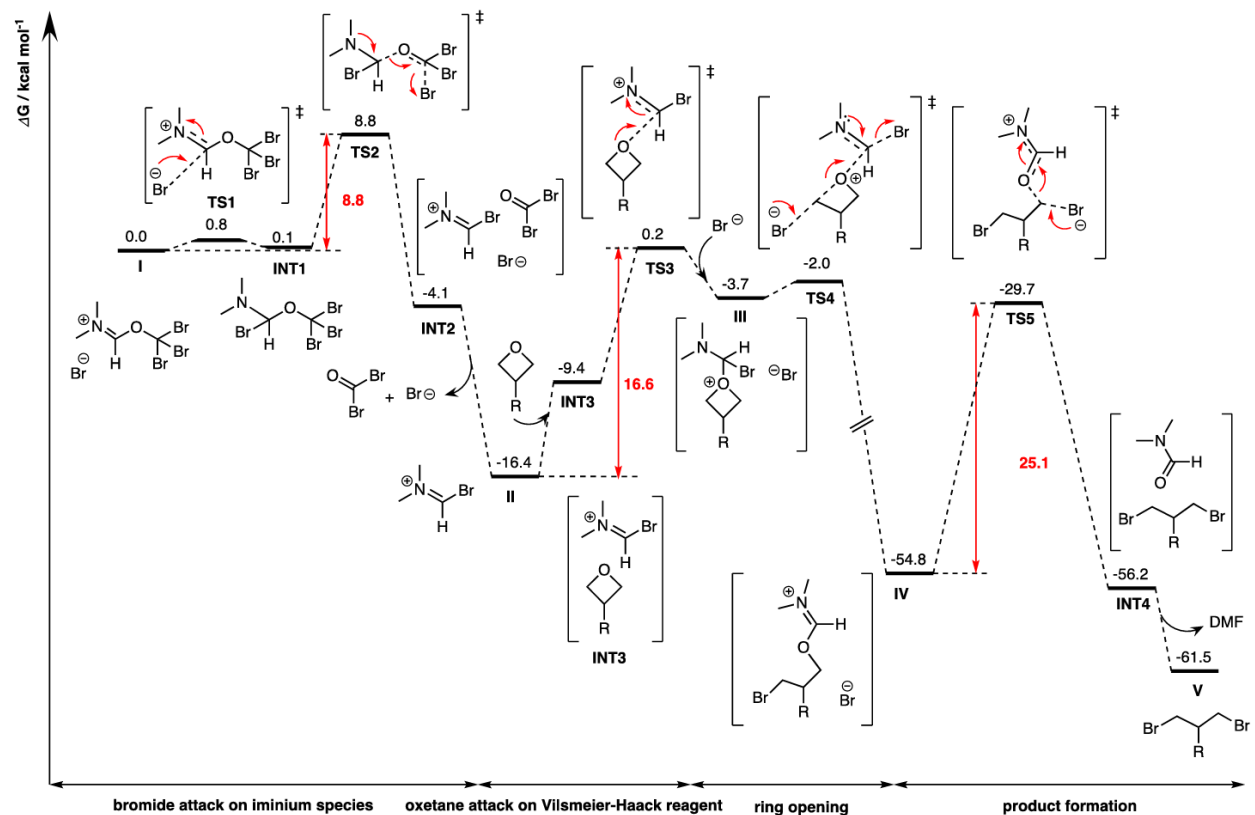


Supporting Information

P14 Banerjee & Chattaraj (2016):

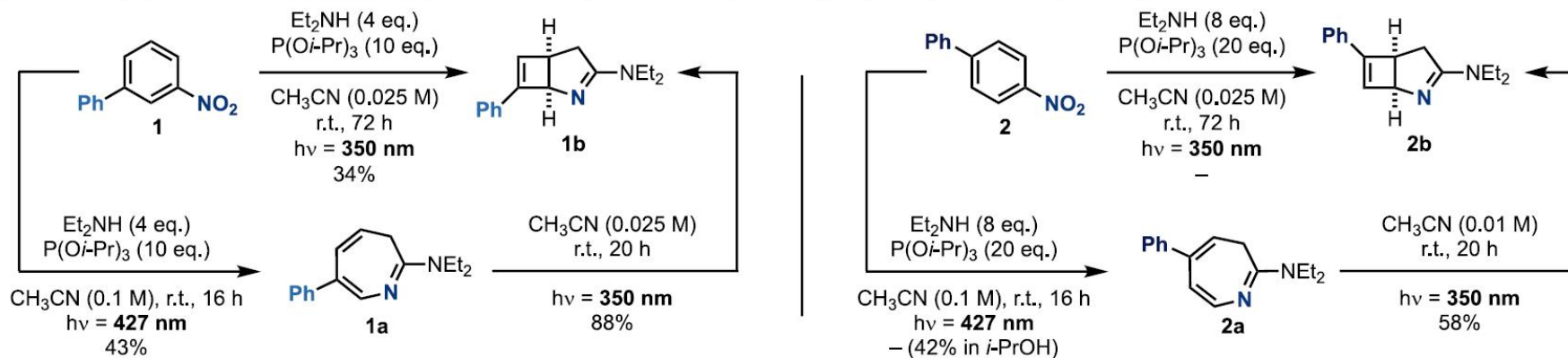


P19 Koh (2025):

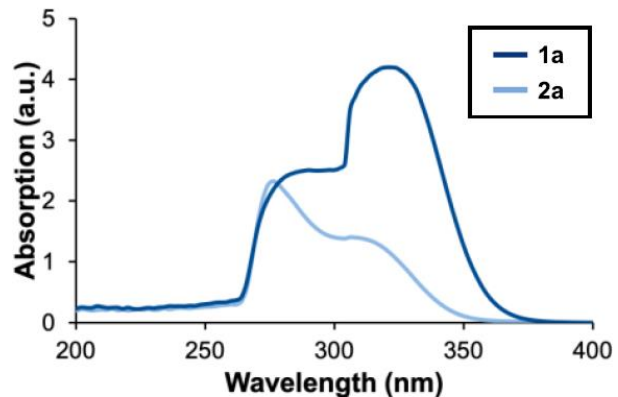


P20 (a) Leonori & Ruffoni & Merino (2023):

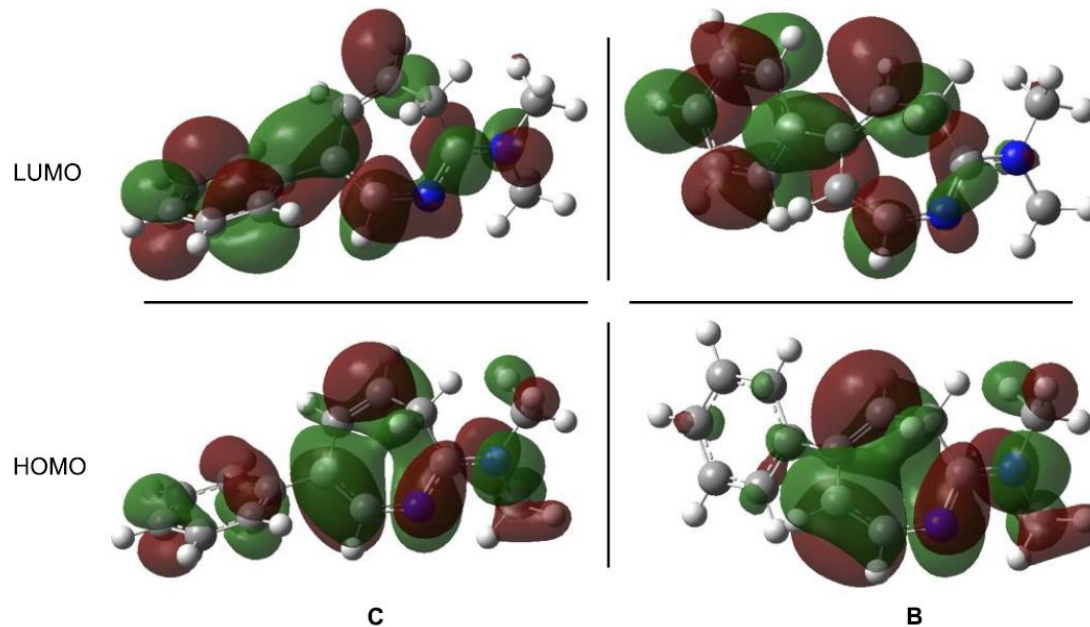
B) Different behaviour of *meta*-Ph and *para*-Ph substituted nitroarenes and their 3H-azepines in the photochemical strategy



C) UV/Vis absorption spectra



E) HOMO and LUMO analysis for C and B



D) S_1 excitation energies and oscillator strengths

Substrate	E_{ex} (eV)	f
A	3.80	0.3641
B	4.32	0.1350
C	4.15	0.4753
D	4.00	0.2846