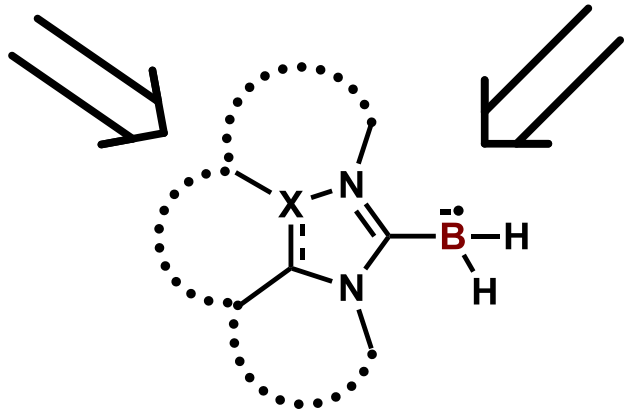
Boryl radical catalysis enables asymmetric radical cycloisomerization reactions

chiral NHC unit

boryl radcial



NHC-boryl radical catalysts

(*NHC-$\dot{B}H_2$)

Yao Fu & Yi-Feng Wang et al. *Science* **2023**, 382, 1056–1065

Biography

Yifeng Wang

2015.09- USTC, Professor

2011.03-2015.08 Nanyang Technological University, Postdoctoral fellow

2006.08-2011.03 Nanyang Technological University, PhD

2003.09-2006.06 Nankai University, Master

1999.09-2003.06 Huazhong Normal University, Bachelor

Current research direction: Organoboron Radical Chemistry

Yao Fu

2010.06- USTC, Professor and doctoral supervisor, the School of Chemistry and Materials Science, Hefei National Research Center for Microscale Physical Sciences.

2005.06-2010.06 USTC, Associate professor, the School of Chemistry and Materials Science

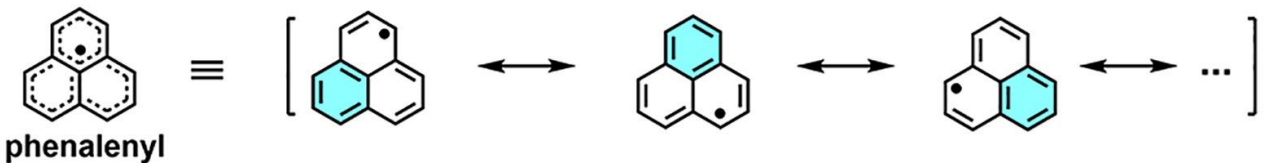
2005.06 USTC, Department of Chemistry, Doctorate of Science degree

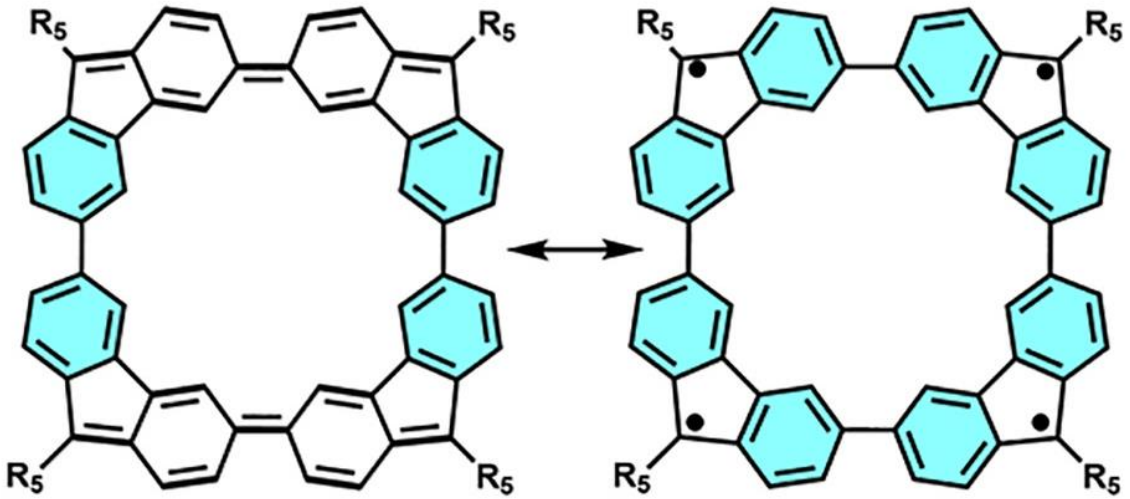
2000.06 USTC, Department of Polymer Science and Engineering, Bachelor's degree

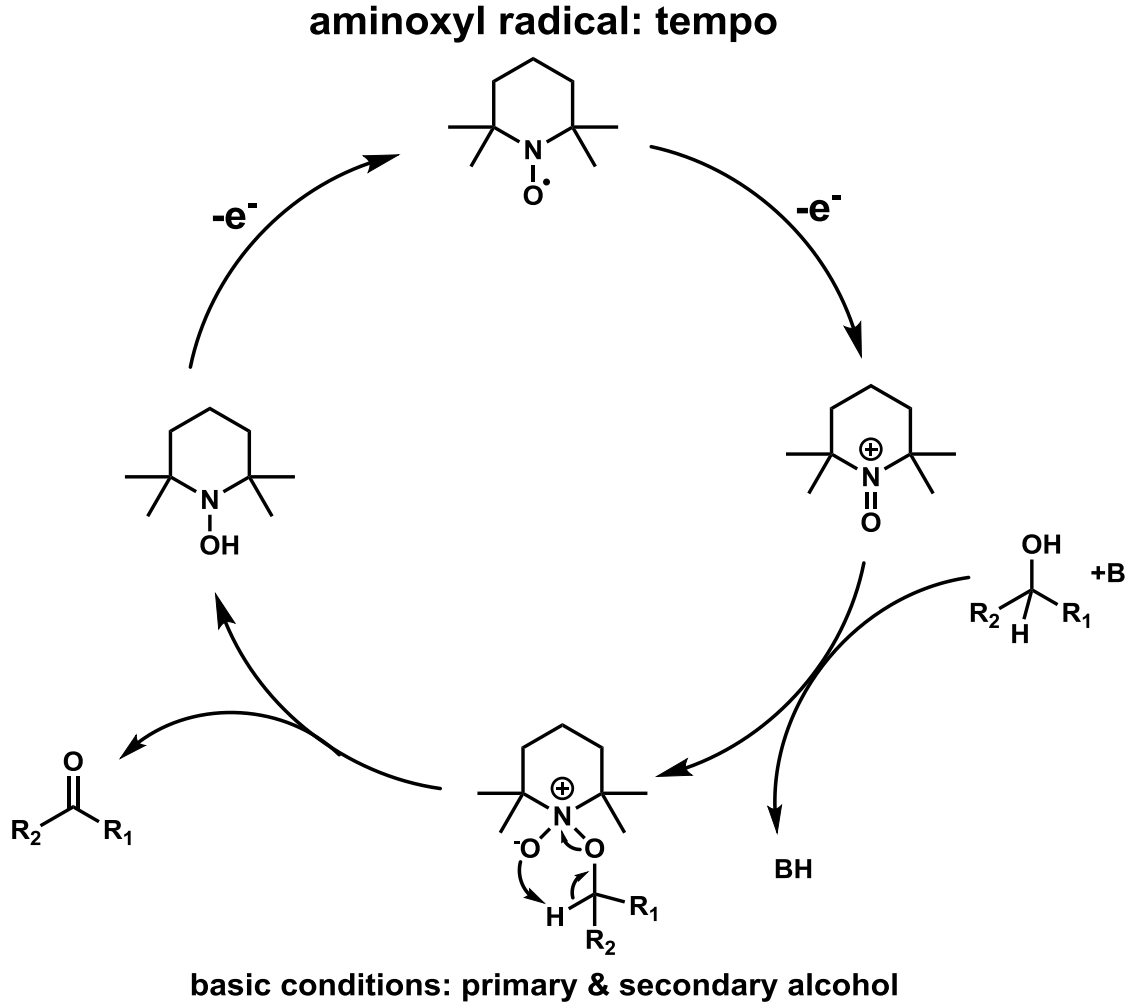
Current research direction: Develop new green organic chemistry reactions and catalytic systems and successfully apply them to high-value utilization of renewable resources

Background

Persistent and Stable Organic Radicals:

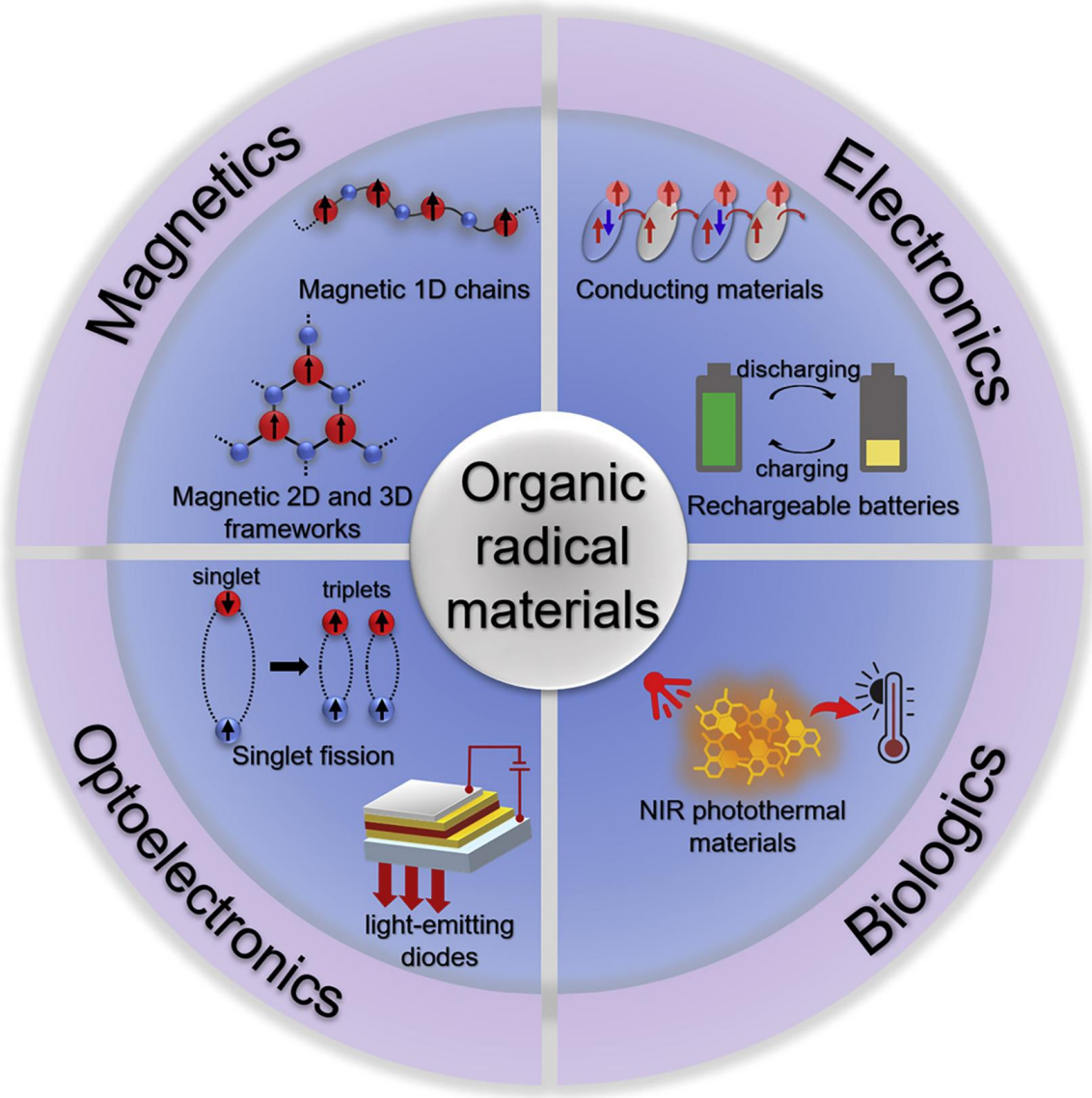




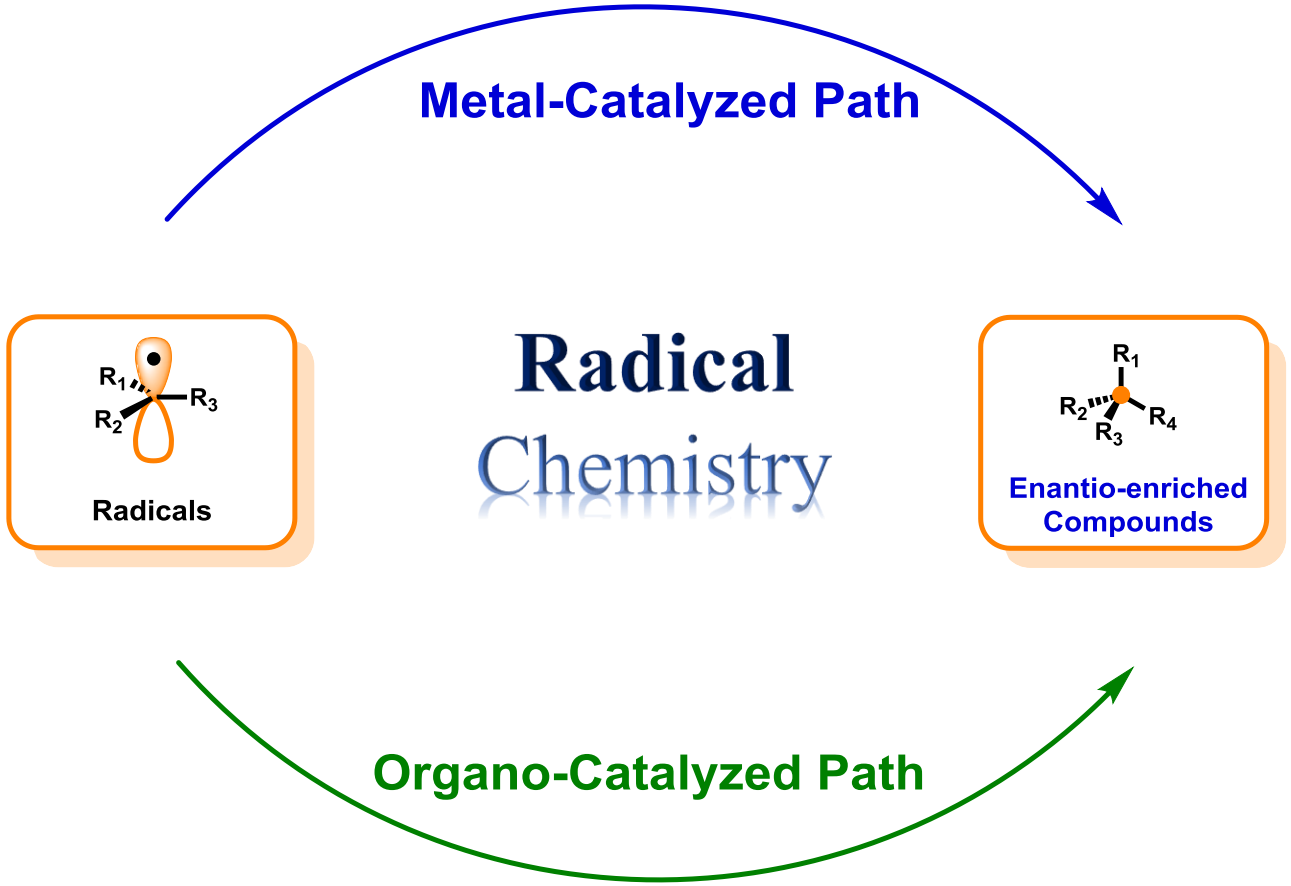


W. Zeng, J. Ding et al *J. Am. Chem. Soc.* **2017**, 139, 13173-13183

Background

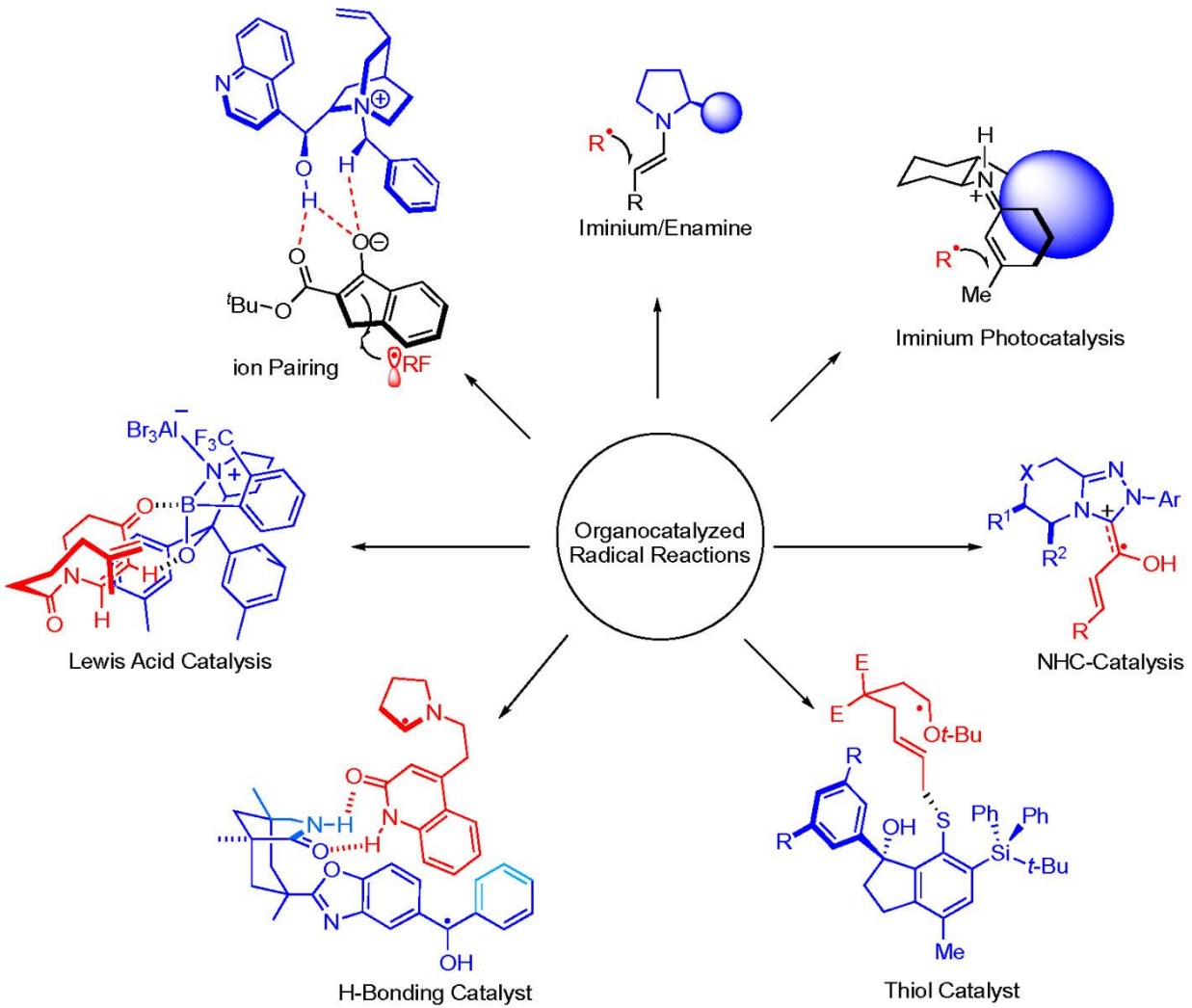


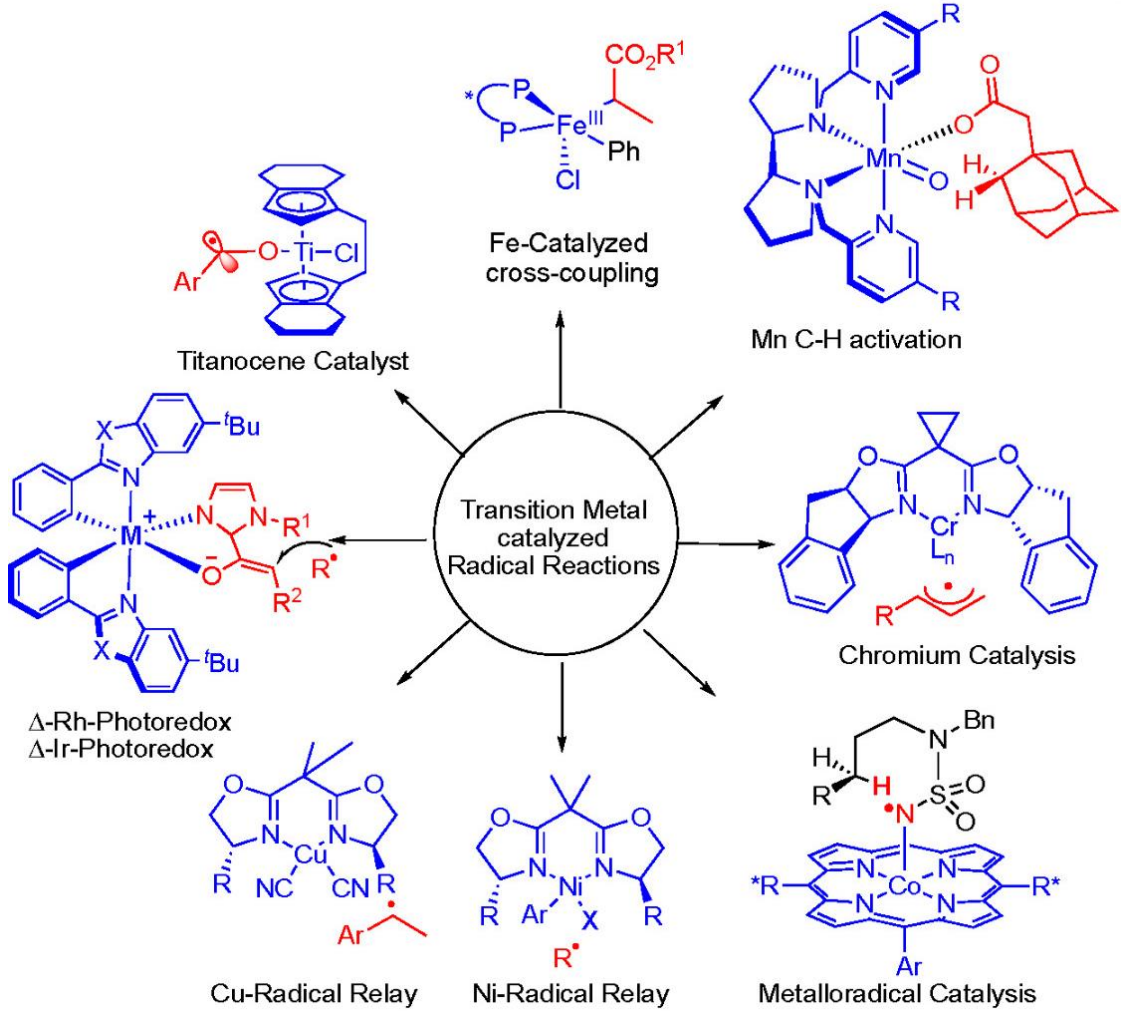
F. Huang et al. *Chem* **2021**, 7, 288–332



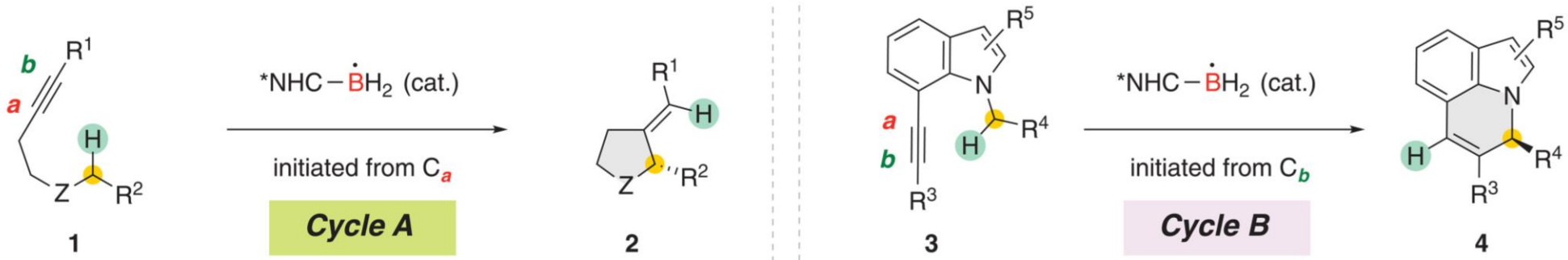
Malek Nechab et al. *Chem. Rev.* **2022**, 122, 5842–5976

Background


Organocatalyzed Radical Reactions
Iminium/Enamine
Iminium Photocatalysis
ion Pairing
Lewis Acid Catalysis
NHC-Catalysis
H-Bonding Catalyst
Thiol Catalyst

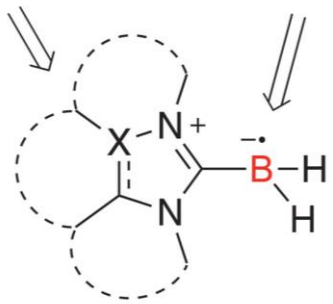

Transition Metal catalyzed Radical Reactions
Titanocene Catalyst
Fe-Catalyzed cross-coupling
Mn C-H activation
Δ-Rh-Photoredox
Δ-Ir-Photoredox
Chromium Catalysis
Cu-Radical Relay
Ni-Radical Relay
Metalloradical Catalysis

This work



Unexplored:

chiral NHC unit | ***boryl*** *radical*

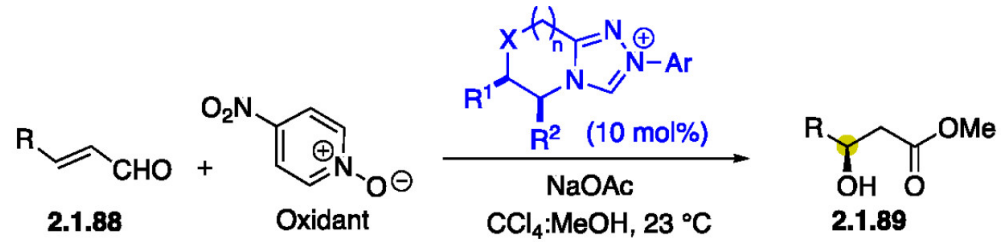


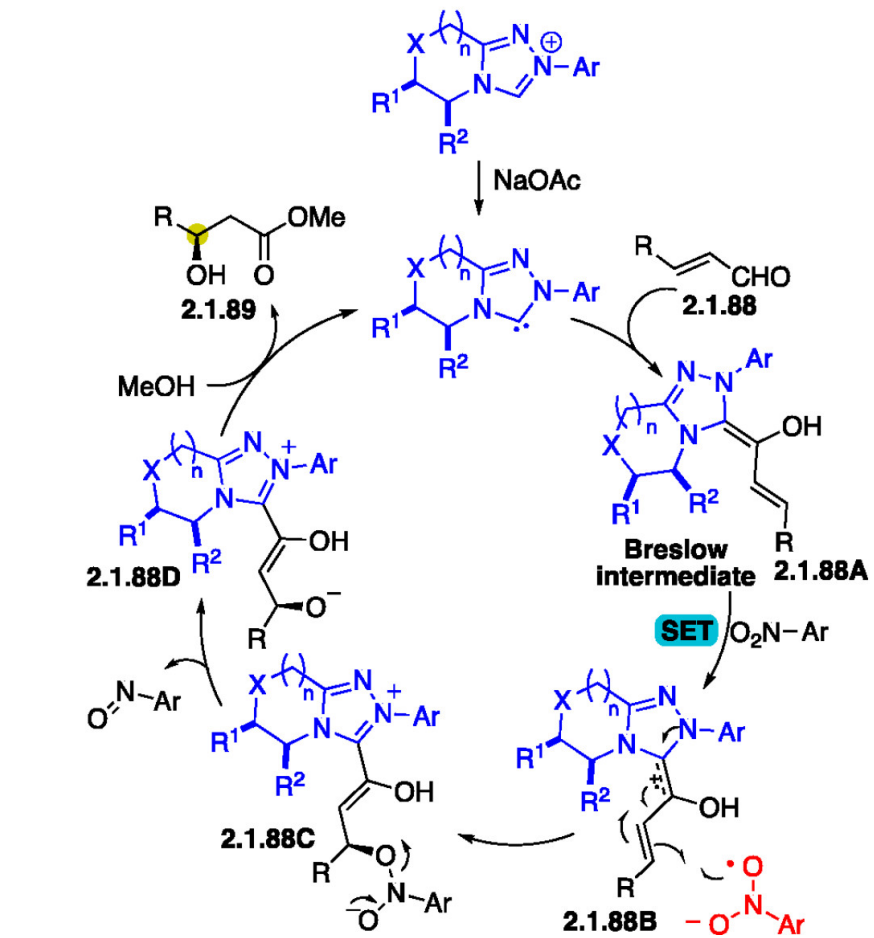
NHC-boryl radical catalysts

$(^*NHC-\dot{B}H_2)$

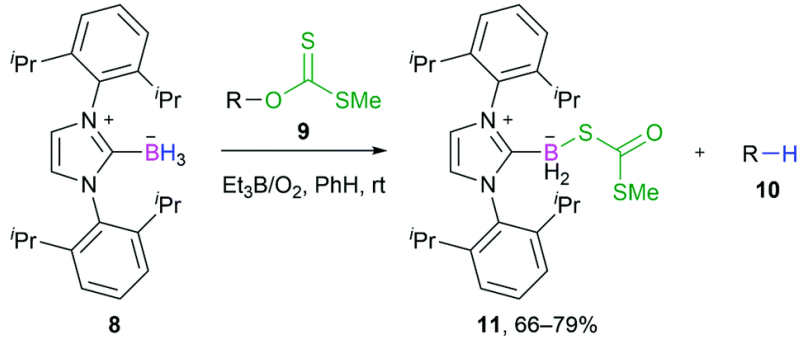
- Readily accessible
- Abundant chiral NHCs
- Unique reactivity of boryl radicals

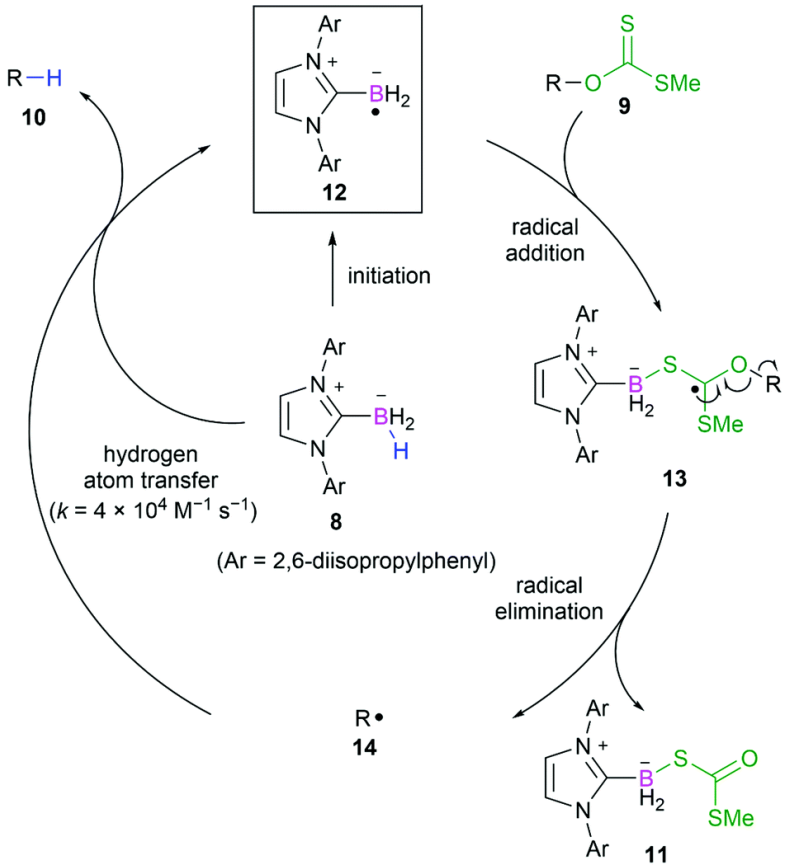
NHC-BH_3





Rovis, T et al. *J. Am. Chem. Soc.* **2014**, 136, 14674– 14677

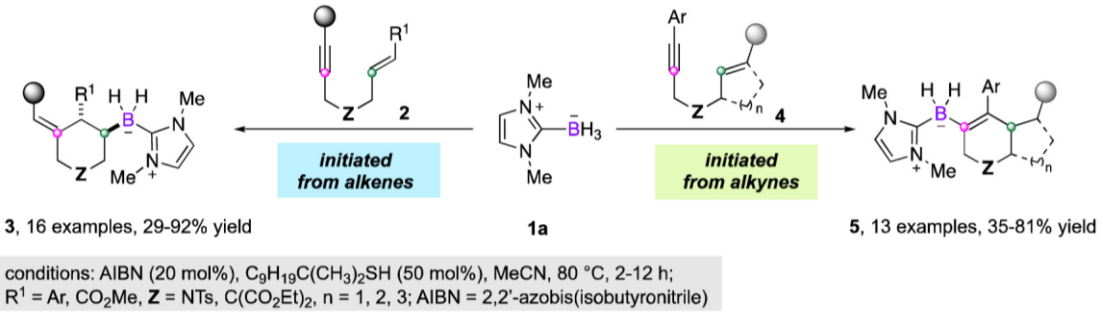


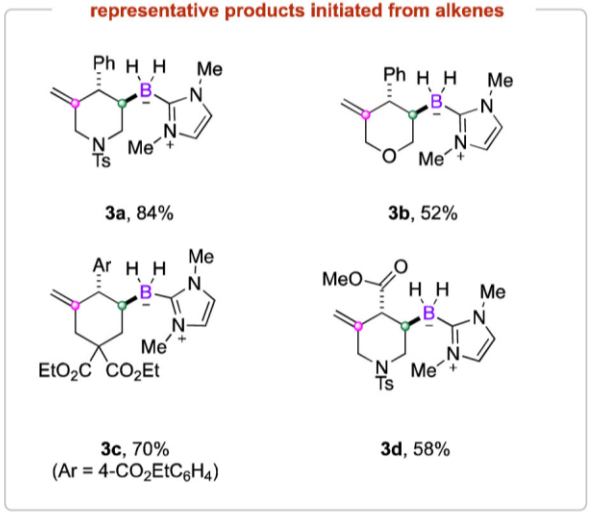


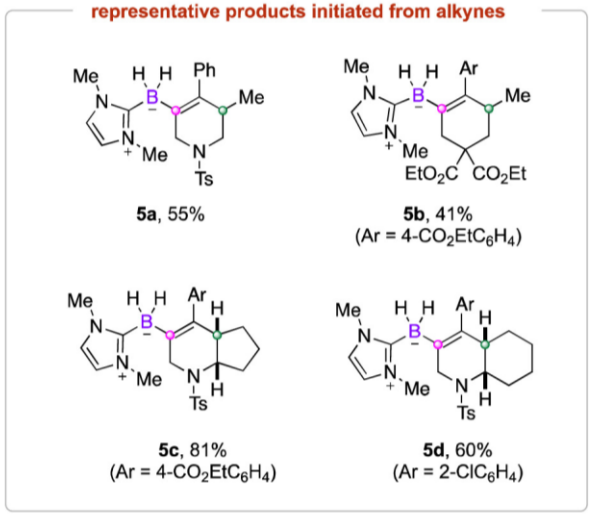
Curran, D. P. et al *J. Am. Chem. Soc.* **2008**, *130*, 10082– 10083

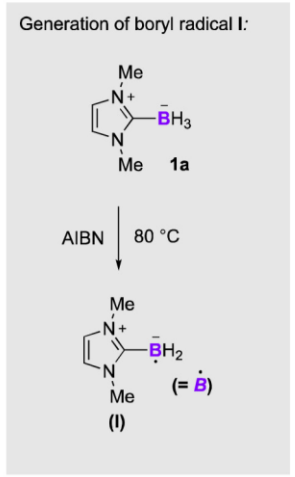
NHC-BH_3

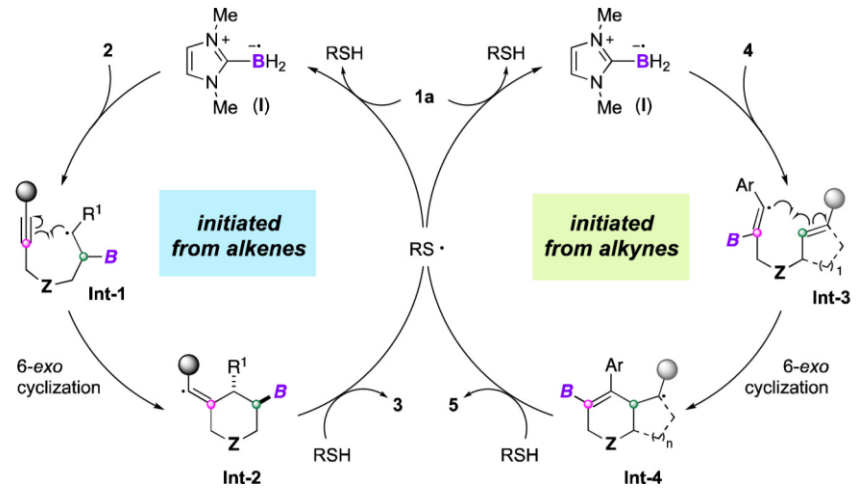
Borylation/Cyclization Cascades

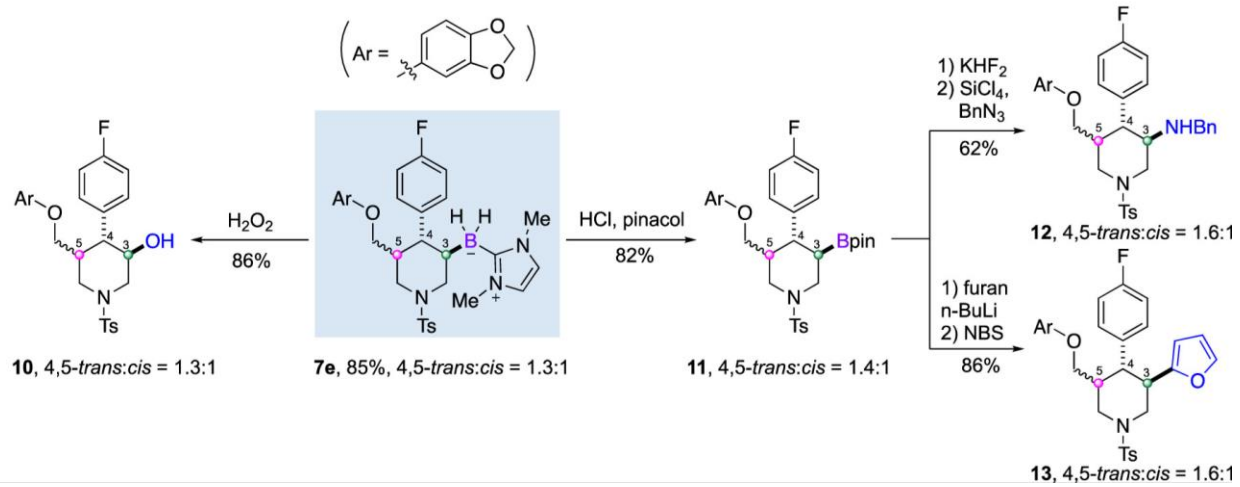








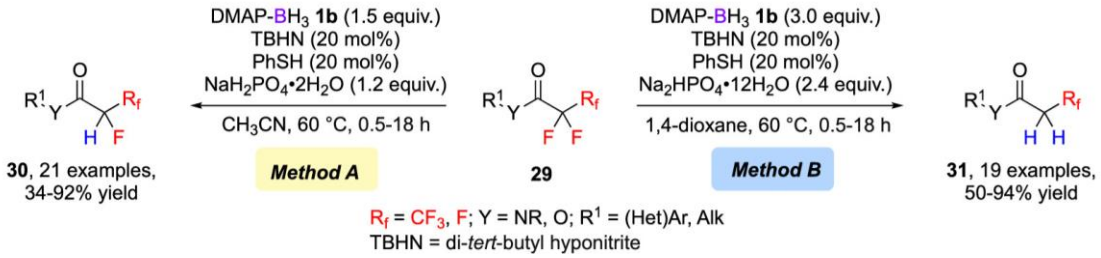




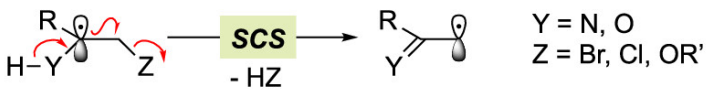
Wang, Y.-F. et al. *Org. Lett.* **2018**, 20, 2360– 2364

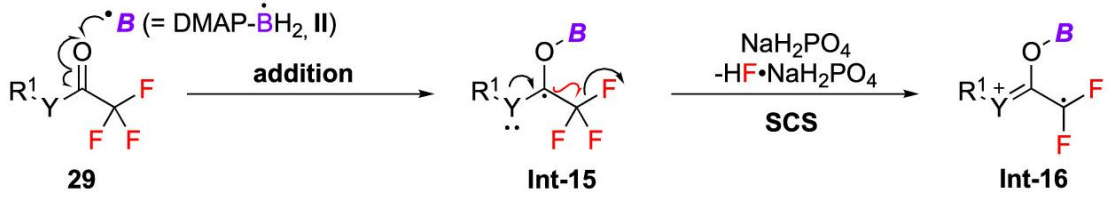
Lewis Base-BH_3

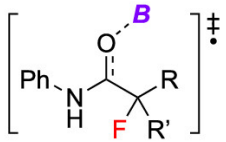
Cabon–Heteroatom Bond Activation



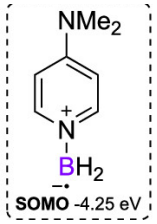
(a) Spin-Center Shift







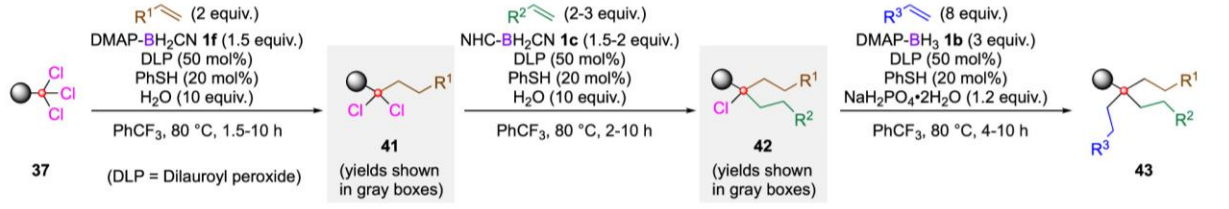
TS	ΔG‡
TS-6 (29a, CF_3)	7.9 kcal/mol
TS-7 (30a, CF_2H)	9.2 kcal/mol
TS-8 (31a, CFH_2)	11.1 kcal/mol



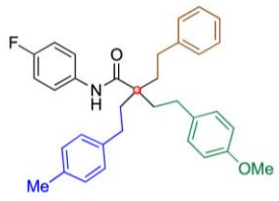
SOMO/LUMO gap	
DMAP-BH_2/29a	4.03 eV
DMAP-BH_2/30a	4.14 eV
DMAP-BH_2/31a	4.45 eV

Wang, Y.-F. et al. *Chin. Chem. Lett.* **2022**, 33, 1193– 1198

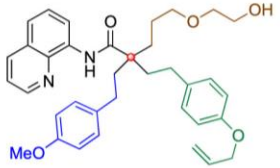
Construction of All-Carbon Quaternary



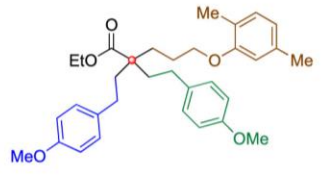
representative all-carbon quaternary centers tethering three alkyl chains



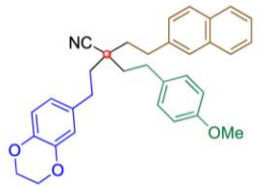
37a→41a : 76%
41a→42a : 85%
43a, 65%



37b→41b : 52%
41b→42b : 55%
43b, 40%

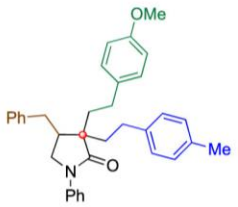


37c→41c : 60%
41c→42c : 72%
43c, 75%

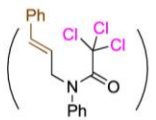


37d→41d : 60%
41d→42d : 48%
43d, 47%

other CCl_3 groups for two successive dechlorination

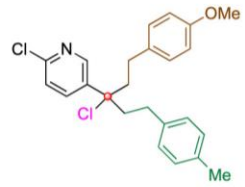


37e→41e : 75%
41e→42e : 67%
43e, 50%

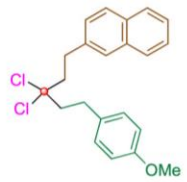


37e

42f
37f→41f : 85%
41f→42f : 43%



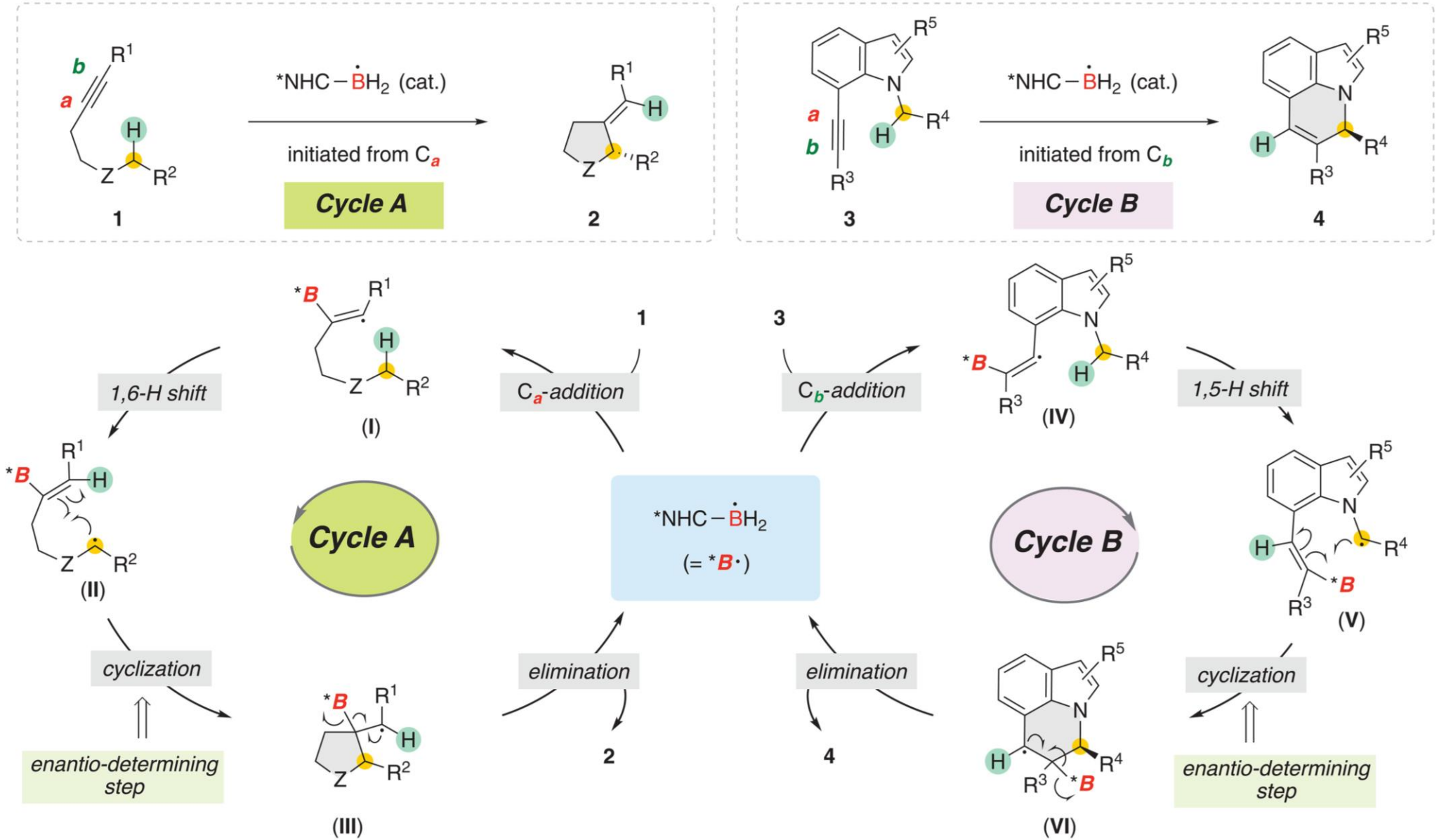
42g
37g→41g : 66%
41g→42g : 52%



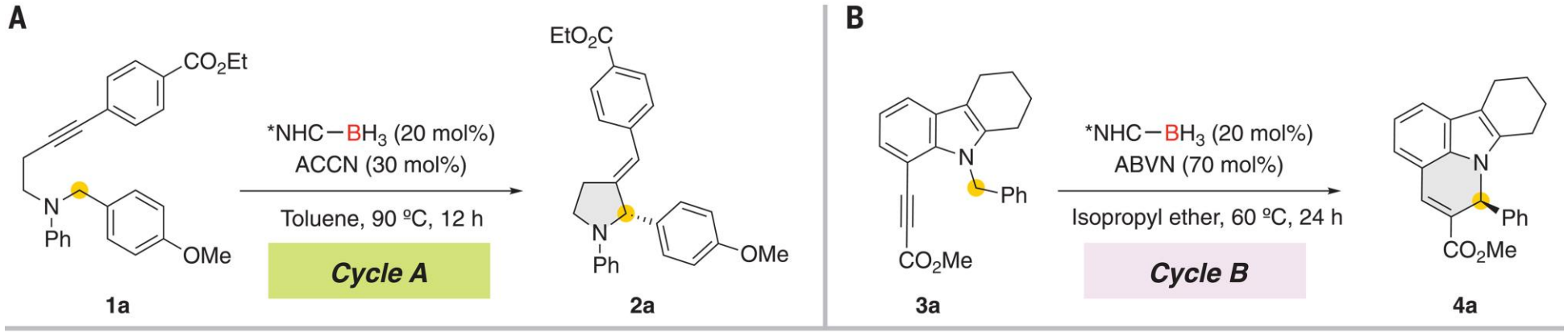
42h
37h→41h : 86%
41h→42h : 71%

Wu, J. et al. *J. Am. Chem. Soc.* **2022**, 144, 14288– 14296

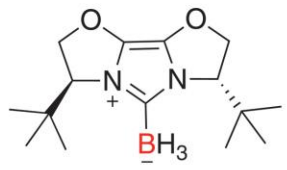
This Work


*NHC – $\dot{B}H_2$ (cat.)
initiated from C_a
Cycle A
*NHC – $\dot{B}H_2$ (cat.)
initiated from C_b
Cycle B
1
2
3
4
1,6-H shift
C_a-addition
C_b-addition
1,5-H shift
cyclization
elimination
elimination
cyclization
enantio-determining step
enantio-determining step
*NHC – $\dot{B}H_2$
(= *B·)
(I)
(II)
(III)
(IV)
(V)
(VI)

This Work

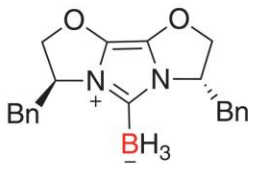


C



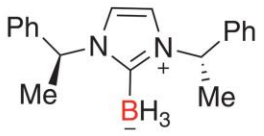
B-1

2a, 83%, *E*/*Z* > 95:5, 96:4 er
(gram-scale, 86%, *E*/*Z* > 95:5, 95:5 er)
4a, 36%, 88.5:11.5 er



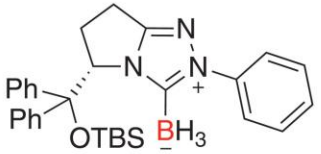
B-2

2a, 53%, *E*/*Z* > 95:5, 73:27 er
4a, 50%, 53:47 er



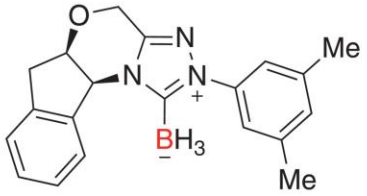
B-3

2a, 10%, *E*/*Z* = 86:14, 46:54 er
4a, 66%, 48:52 er



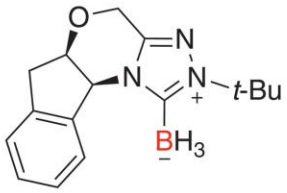
B-4

2a, 37%, *E*/*Z* = 91:9, 71.5:28.5 er
4a, 35%, 18:82 er



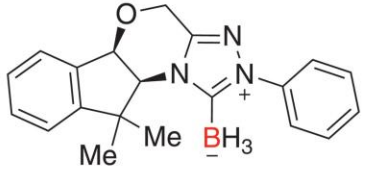
B-5

2a, 29%, *E*/*Z* = 89:11, 37:63 er
4a, 94%, 93.5:6.5 er
(gram-scale, 65%, 93.5:6.5 er)



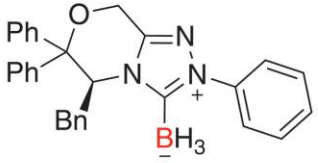
B-6

2a, 10%, *E*/*Z* = 80:20, 73:27 er
4a, 61%, 89.5:10.5 er



B-7

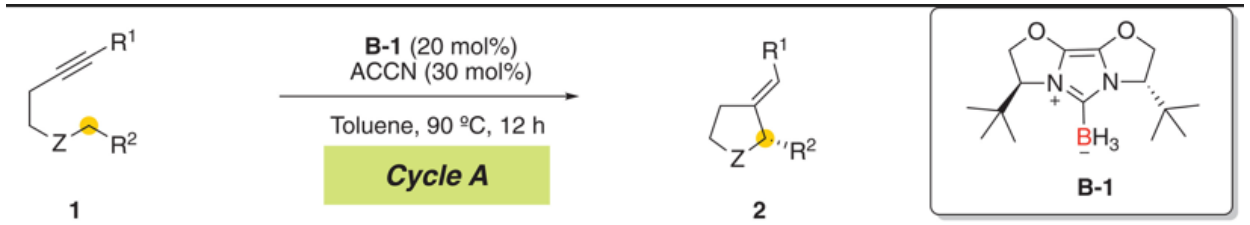
2a, 49%, *E*/*Z* = 94:6, 25:75 er
4a, 20%, 88:12 er

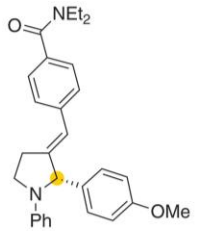


B-8

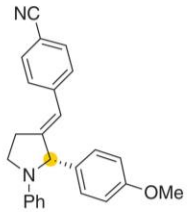
2a, 19%, *E*/*Z* = 88:12, 32:68 er
4a, 70%, 44:56 er

Substrate Scope

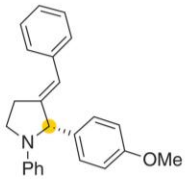




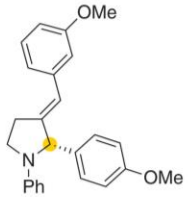
2b, 54%, *E*/*Z* > 95:5, 96.5:3.5 er



2c, 90%, *E*/*Z* > 95:5, 92.5:7.5 er

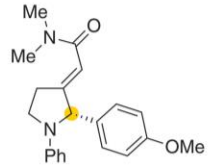


2d, 43%, *E*/*Z* > 95:5, 97:3 er

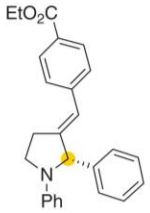


2e, 38%, *E*/*Z* > 95:5, 94.5:5.5 er

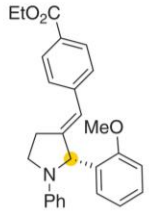
2f, 61%*, *E*/*Z* = 88:12, 94:6 er



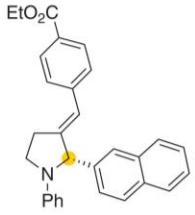
2g, 55%*, *E*/*Z* = 77:23, 93:7 er



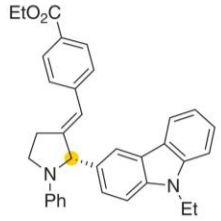
2h, 74%, *E*/*Z* > 95:5, 96:4 er



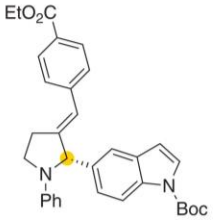
2i, 52%, *E*/*Z* > 95:5, 95.5:4.5 er



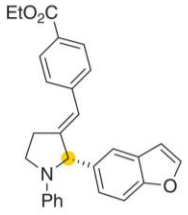
2j, 46%, *E*/*Z* > 95:5, 96:4 er



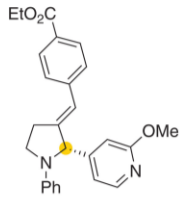
2k, 82%, *E*/*Z* = 95:5, 95.5:4.5 er



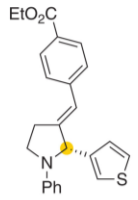
2l, 76%, *E*/*Z* > 95:5, 94.5:5.5 er



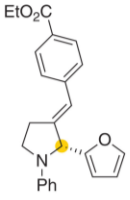
2m, 76%, *E*/*Z* > 95:5, 95.5:4.5 er



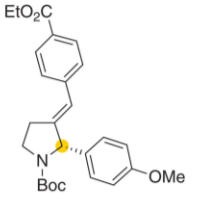
2n, 51%†, *E*/*Z* > 95:5, 95.5:4.5 er



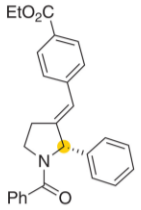
2o, 84%, *E*/*Z* = 91:9, 95:5 er



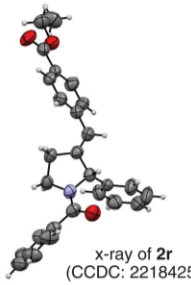
2p, 51%, *E*/*Z* = 83:17, 94.5:5.5 er



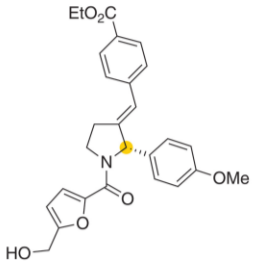
2q, 44%, *E*/*Z* > 95:5, 92.5:7.5 er



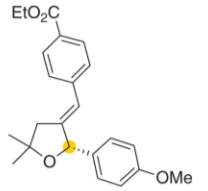
2r, 43%, *E*/*Z* > 95:5, 94.5:5.5 er



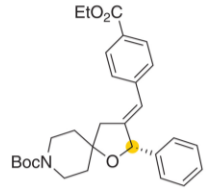
x-ray of **2r**
(CCDC: 2218425)



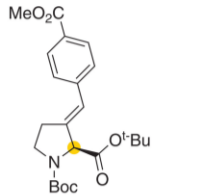
2s, 60%, *E*/*Z* = 92:8, 96:4 er



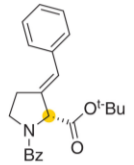
2t, 85%, *E*/*Z* > 95:5, 87:13 er



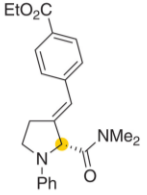
2u, 52%, *E*/*Z* > 95:5, 84:16 er



2v, 36%‡, *E*/*Z* > 95:5, 91.5:8.5 er

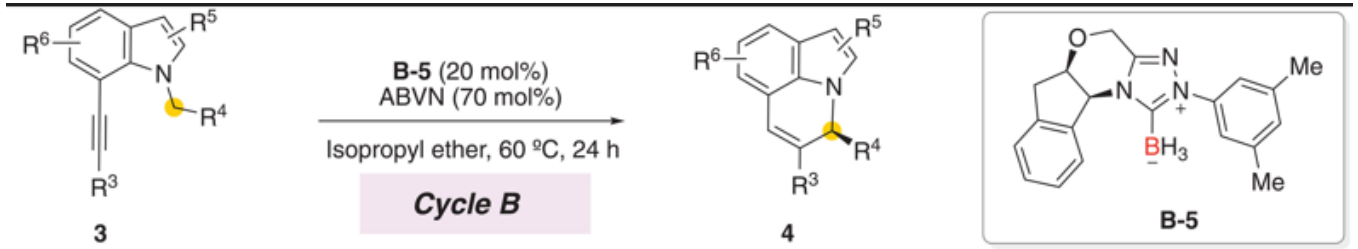


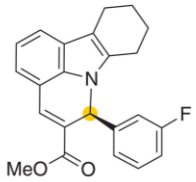
2w, 40%§, *E*/*Z* > 95:5, 94:6 er



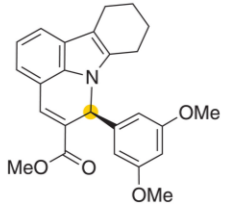
2x, 59%§, *E*/*Z* > 95:5, 85:15 er

Substrate Scope

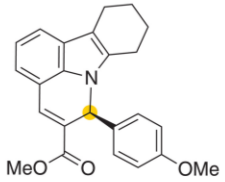




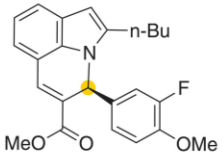
4b, 72%, 92:8 er



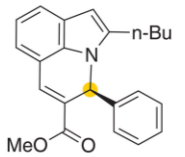
4c, 90%, 92:8 er



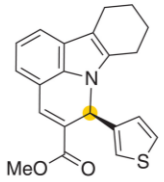
4d, 75%, 94:6 er



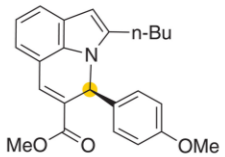
4e, 77%, 91:9 er



4f, 95%, 93.5:6.5 er

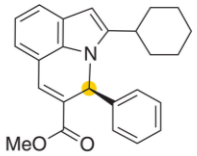


4g, 66%, 93:7 er

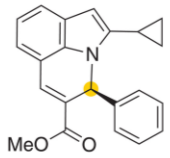


4h, 85%, 93.5:6.5 er

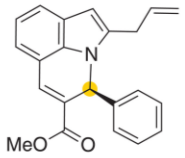
4i, 88%, 90:10 er



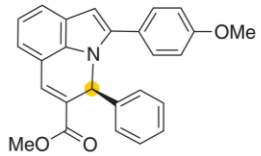
4j, 94%, 94:6 er



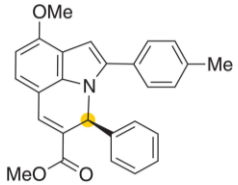
4k, 90%, 93:7 er



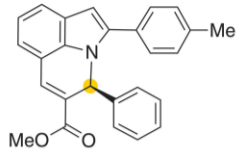
4l, 76%, 89.5:10.5 er



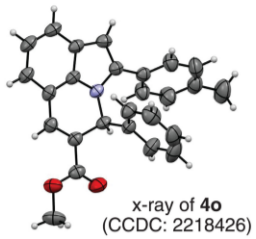
4m, 72%, 95.5:4.5 er



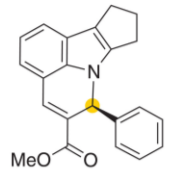
4n, 87%, 91:9 er



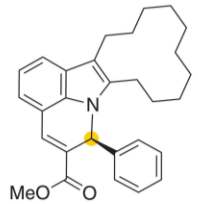
4o, 85%, 90.5:9.5 er



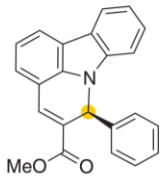
x-ray of **4o**
(CCDC: 2218426)



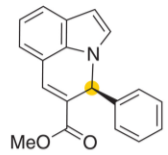
4p, 86%, 89:11 er



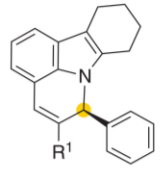
4q, 90%, 91:9 er



4r, 88%, 87.5:12.5 er

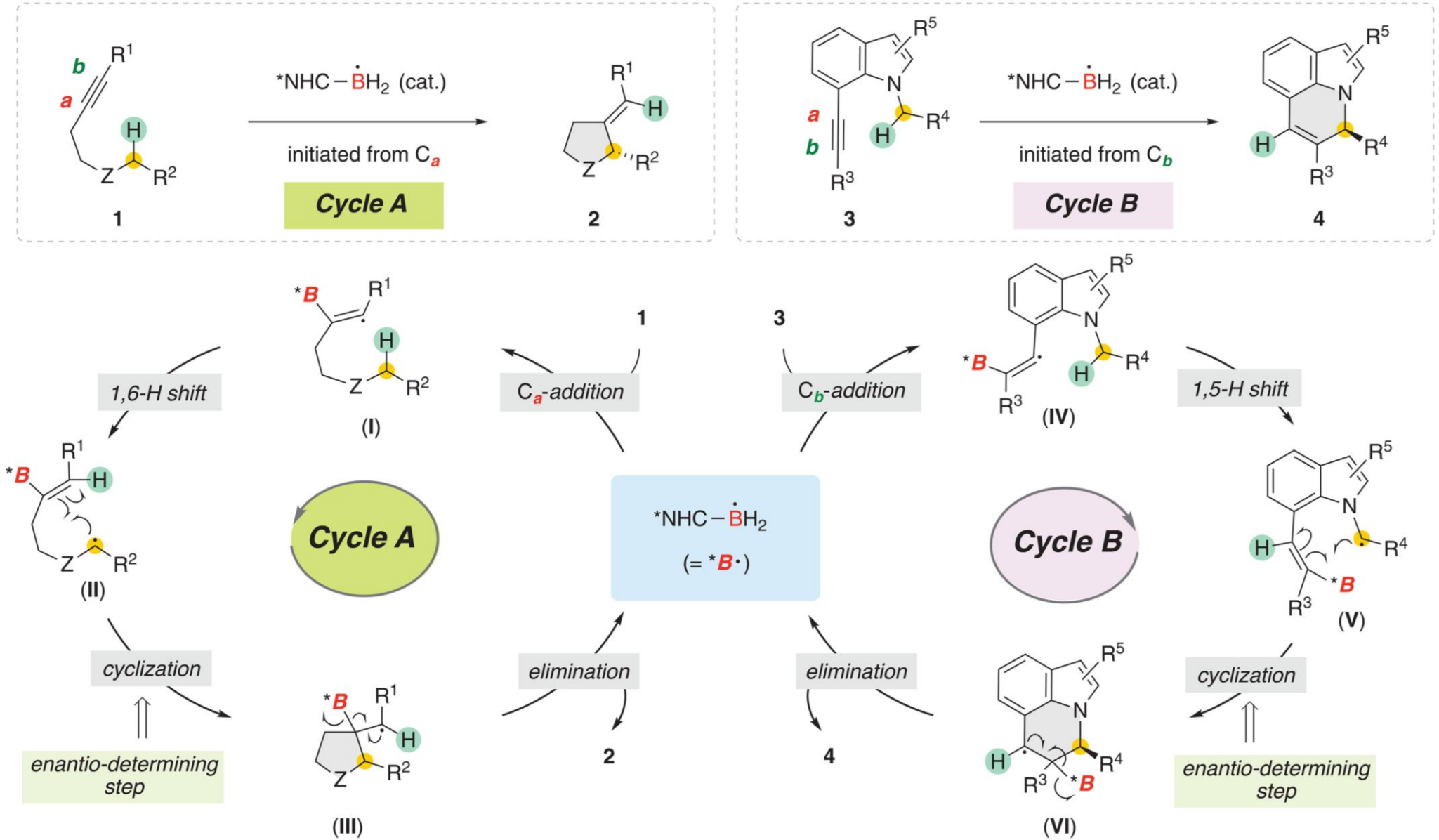


4s, 49%, 87.5:12.5 er



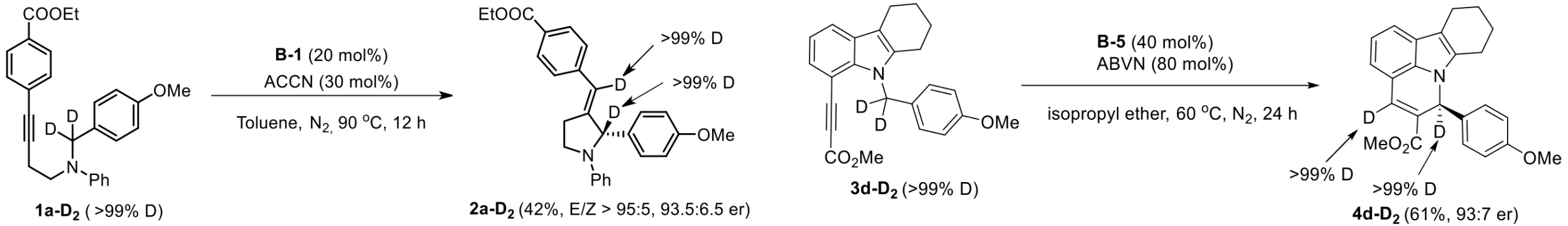
4t, R^1 = 4-$CO_2MeC_6H_4$, not formed
4u, R^1 = CF_3, not formed

This Work


*NHC – $\dot{B}H_2$ (cat.)
initiated from C_a
Cycle A
*NHC – $\dot{B}H_2$ (cat.)
initiated from C_b
Cycle B
1
2
3
4
1,6-H shift
C_a-addition
C_b-addition
1,5-H shift
cyclization
elimination
elimination
cyclization
enantio-determining step
enantio-determining step
*NHC – $\dot{B}H_2$
(= *B·)
(I)
(II)
(III)
(IV)
(V)
(VI)

Mechanistic Studies

Deuterium-labelled Experiemnt:



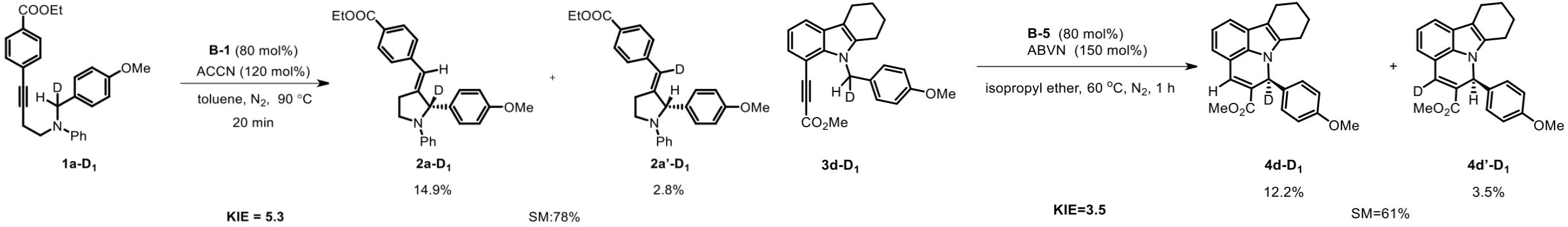
1a-D_2 (>99% D)

2a-D_2 (42%, E/Z > 95:5, 93.5:6.5 er)

3d-D_2 (>99% D)

4d-D_2 (61%, 93:7 er)

KIE Experiment:



1a-D_1

2a-D_1

14.9%

2a'-D_1

2.8%

SM:78%

3d-D_1

KIE = 5.3

KIE=3.5

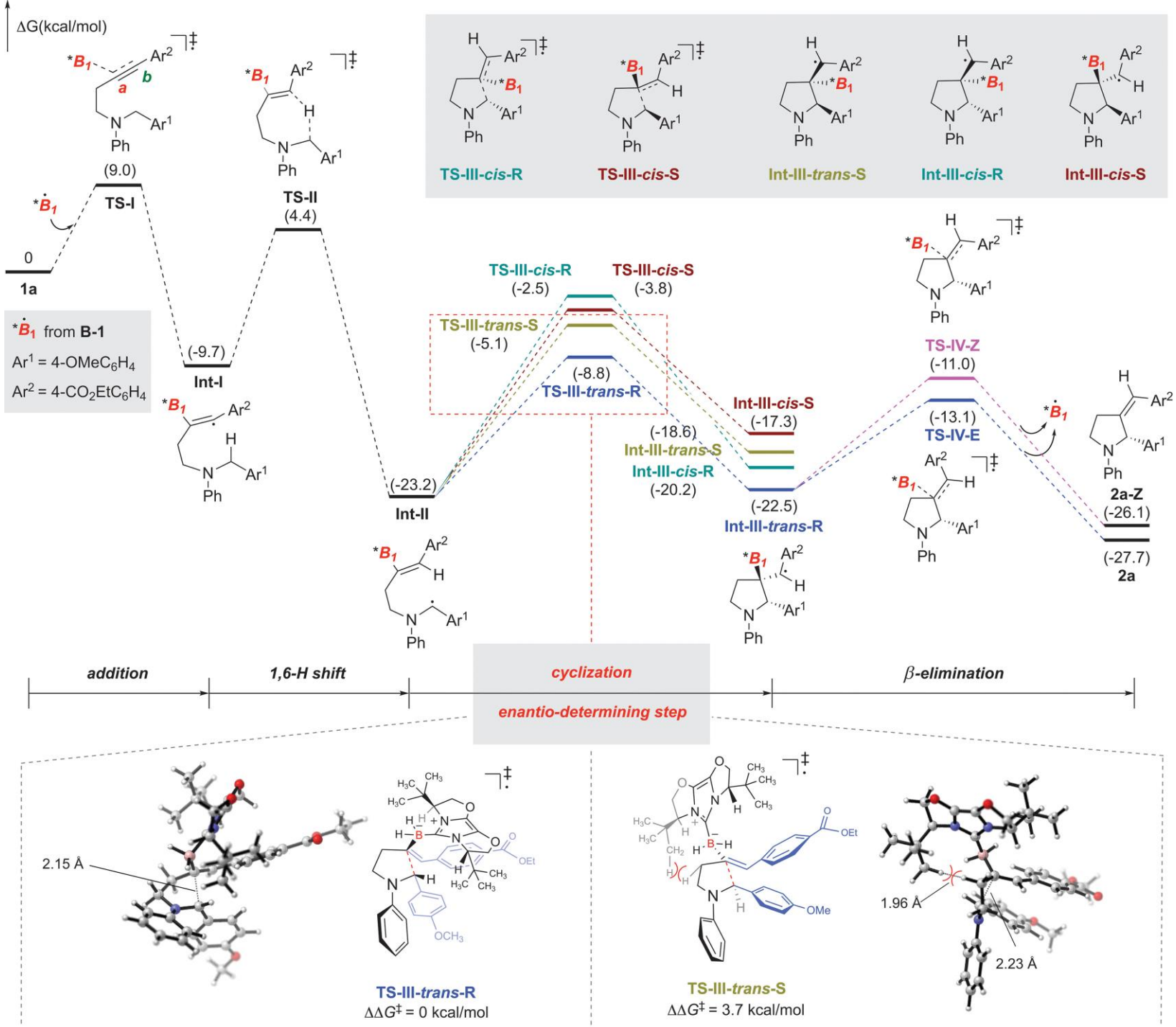
4d-D_1

12.2%

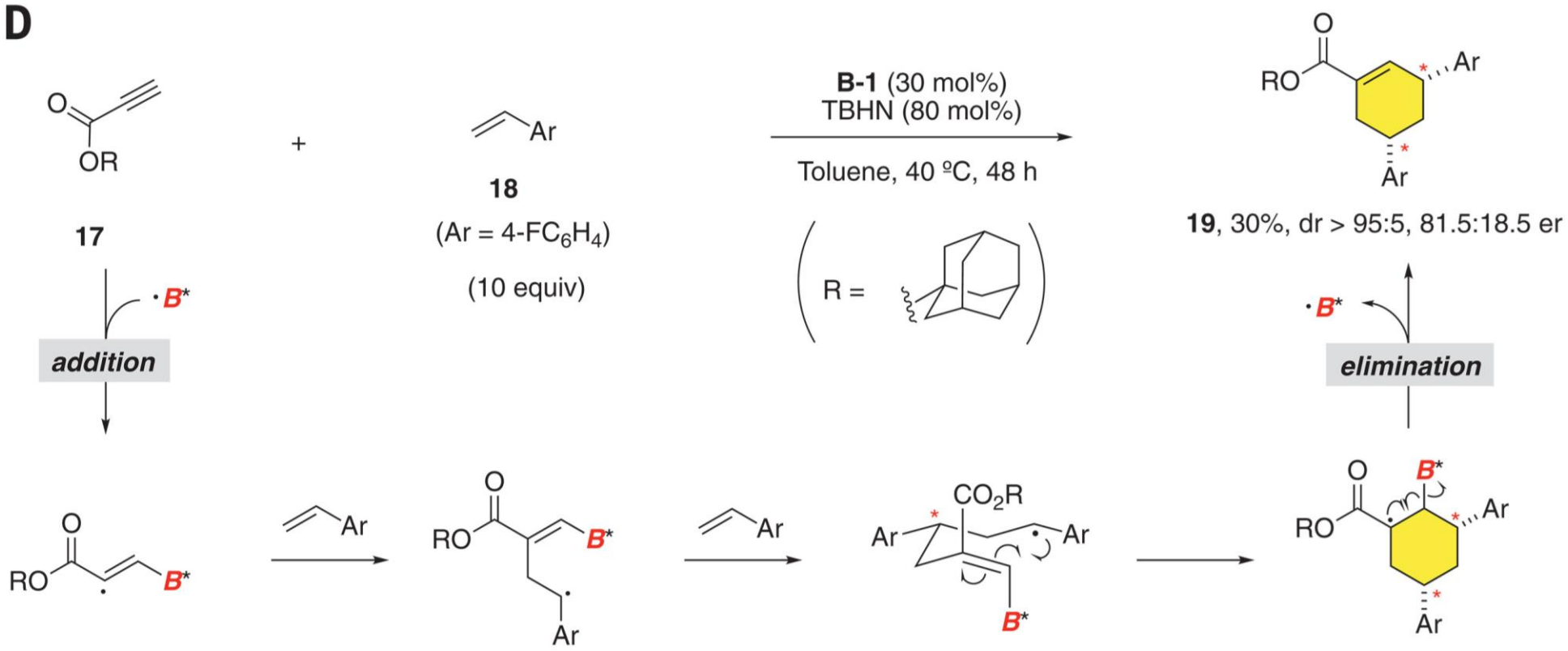
4d'-D_1

3.5%

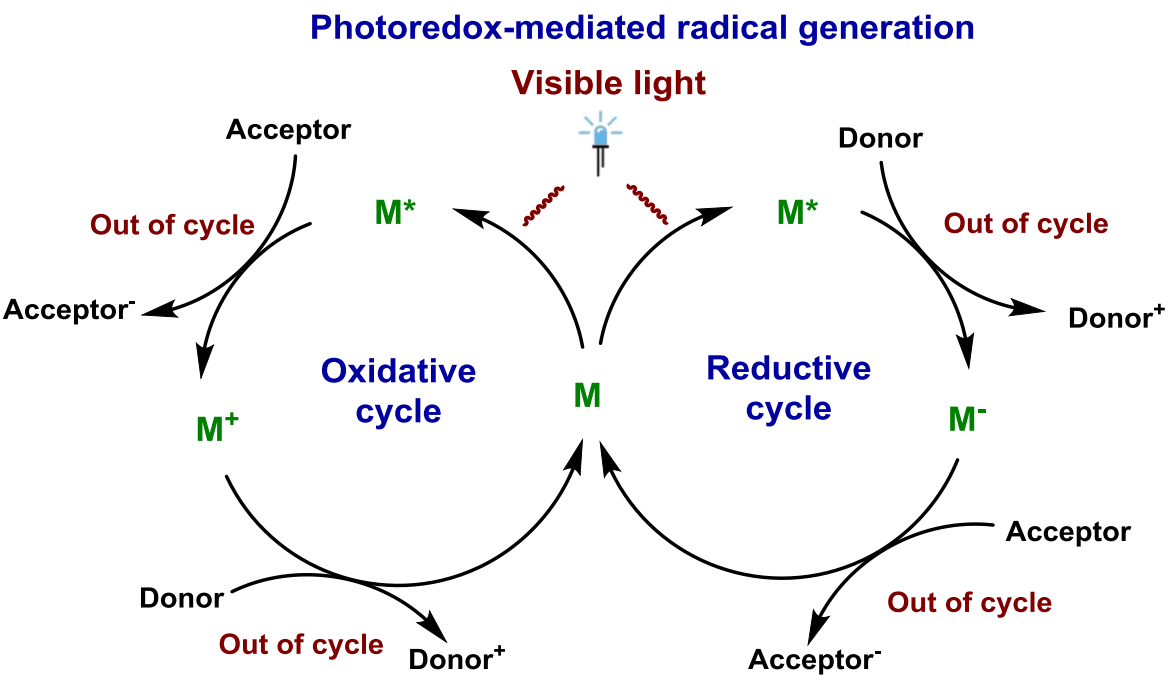
SM=61%

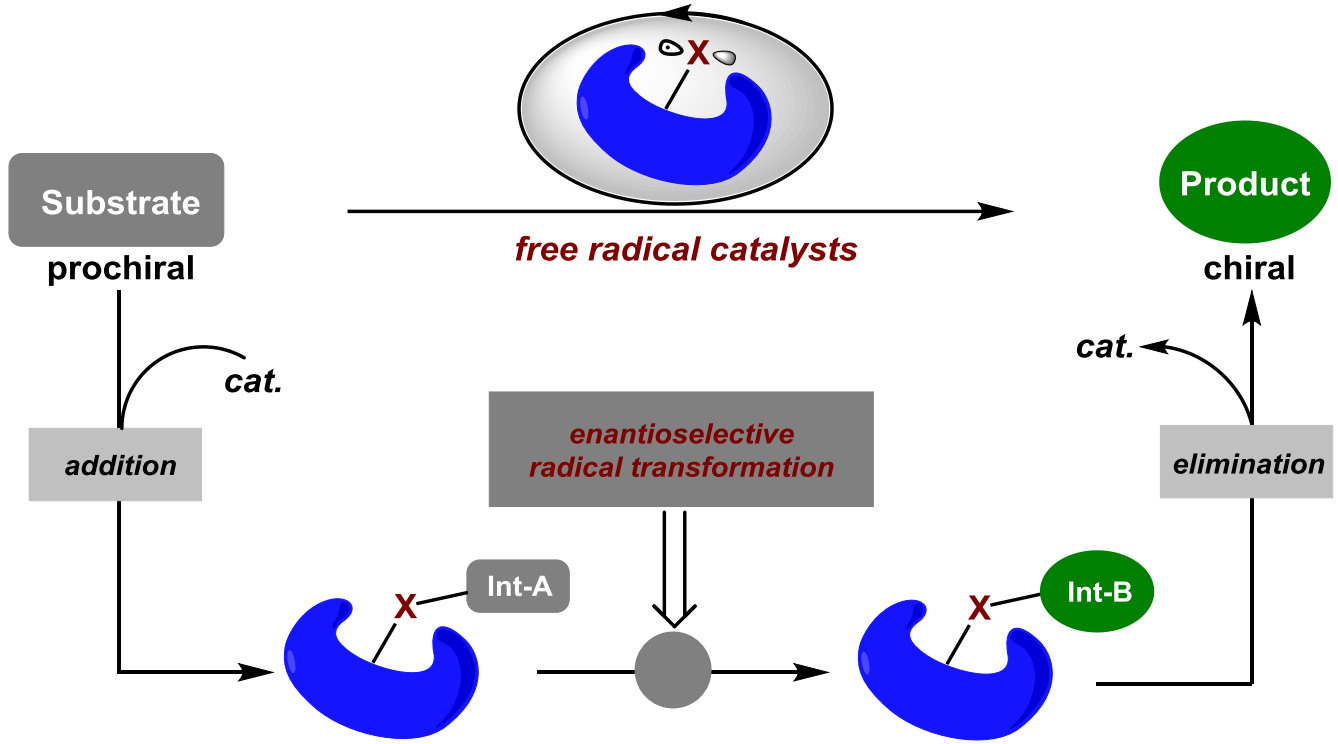

ΔG(kcal/mol)
TS-III-cis-R
TS-III-cis-S
Int-III-trans-S
Int-III-cis-R
Int-III-cis-S
(9.0)
TS-I
TS-II
(4.4)
0
1a
(-9.7)
Int-I
(-23.2)
Int-II
*B1 from B-1
Ar1 = 4-OMeC6H4
Ar2 = 4-CO2EtC6H4
(-2.5)
(-3.8)
(-5.1)
(-8.8)
TS-III-trans-R
(-18.6)
Int-III-trans-S
(-20.2)
Int-III-cis-R
Int-III-cis-S
(-17.3)
(-22.5)
Int-III-trans-R
TS-IV-Z
(-11.0)
(-13.1)
TS-IV-E
2a-Z
(-26.1)
(-27.7)
2a
addition
1,6-H shift
cyclization
enantio-determining step
β-elimination
2.15 Å
TS-III-trans-R
ΔΔG‡ = 0 kcal/mol
TS-III-trans-S
ΔΔG‡ = 3.7 kcal/mol
1.96 Å
2.23 Å

Synthetic Applications



Summary


Photoredox-mediated radical generation
Visible light
Acceptor
Out of cycle
Acceptor-
M*
M+
Oxidative cycle
M
Donor
Out of cycle
Donor+
M*
Donor
Out of cycle
Donor+
Reductive cycle
M-
Acceptor
Out of cycle
Acceptor-


X
Substrate
prochiral
cat.
addition
free radical catalysts
enantioselective radical transformation
X
Int-A
X
Int-B
Product
chiral
cat.
elimination

Thanks for Your Attention

Reporter: Han S.
Date: 2024.01.13