Seminar

Transition Metal Catalyzed Dyotropic Rearrangement Reaction

Speaker: Chenyu Ge

Supervisor: Prof. Junliang Zhang

2023.5.12

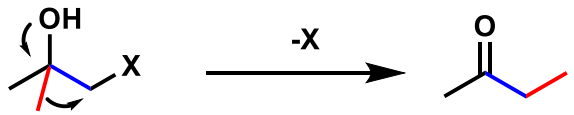
Content

Content

1.1 [1. 2]-Rearrangement Reaction

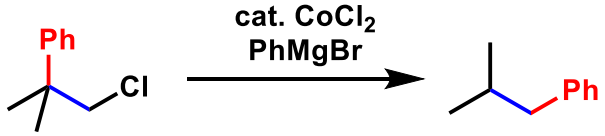
Carbocation Intermediate

Wagner-Meerwein Rearrangement



Radical Intermediate

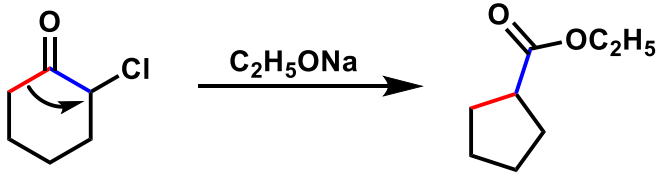
Neophyl Rearrangement



15% yield

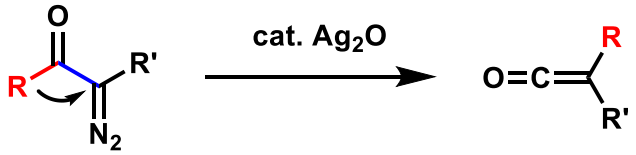
Carbanion Intermediate

Favorskii Rearrangement



Carbene Intermediate

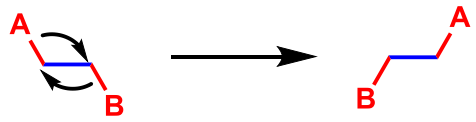
Wolff Rearrangement



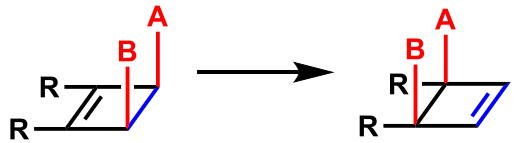
Single σ-bond Migrate.

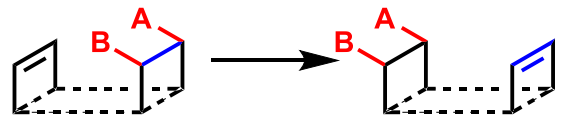
Two σ-bonds Migrate

Dyotropic *Rearrangement Type I*



Dyotropic *Rearrangement Type II*





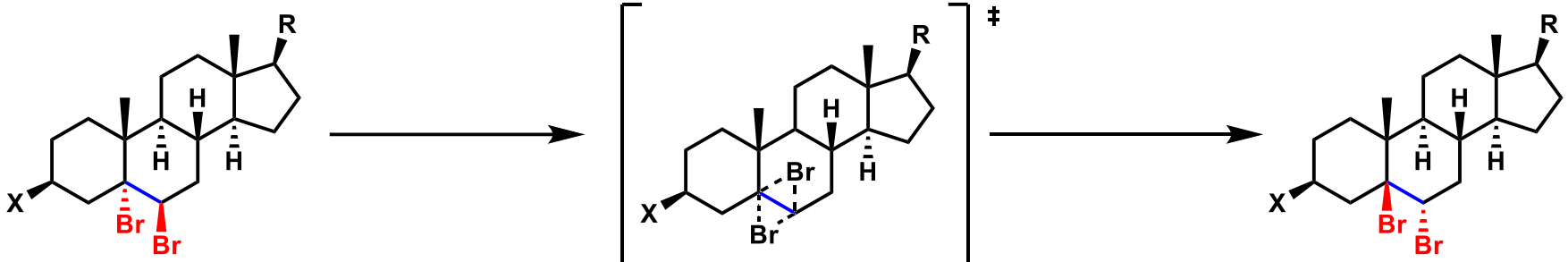
a) H. Meerwein, et al. *Liebigs. Ann. Chem.* **1914**, *405*, 129-175; b) M. Kharasch, et al. *J. Am. Chem. Soc.* **1944**, *66*, 1438; c) A. Favorskii, et al. *J. Russ. Phys. Chem. Soc.* **1905**, *37*, 643.d) L. Wolff, et al. *Liebigs. Ann. Chem.* **1902**, *325*, 129; e) M. Reetz, et al. *Angew. Chem. Int. Ed.* **1972**, *11*, 129-131.

1.2 Type I Dyotropic Rearrangement

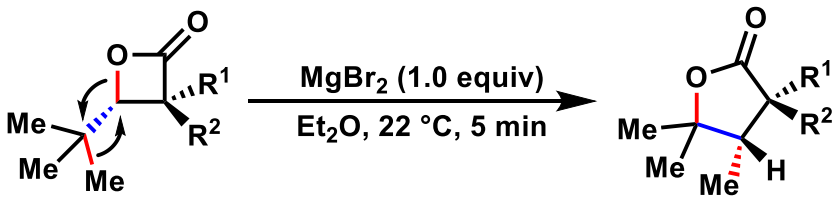
C-C Bond as Scaffold

1952

Winstein group (1952)

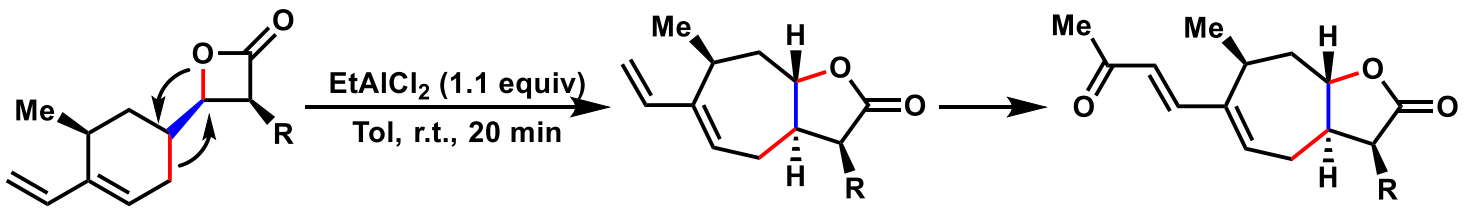


Mulzer group (1977)



98% yield

Tang group (2012 and 2021)



R = CH_3 or CH_2

83-99% yield

R = CH_3, *11a,13-dihydroxanthatin*
R = CH_2, *Xanthatin*

a) S. Winstein, et al. *Helv. Chim. Acta.* **1952,** *35*, 782; b) S. Mulzer, et al. *Angew. Chem. Int. Ed.* **1979**, *18*, 793; c) Y. Tang, et al. *Angew. Chem. Int. Ed.* **2021**, *60*, 4221-4230.

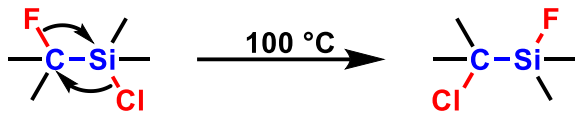
1.2 Type I Dyotropic Rearrangement

C-X Bond as Scaffold

1973

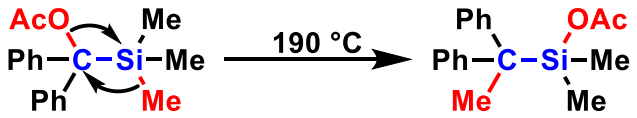
C-Si bond as Scaffold

Haszeldine group (1973)



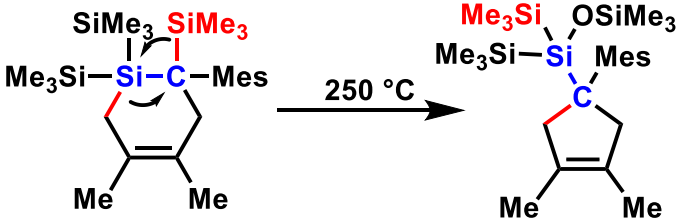
82% yield

Reetz group (1977)



75% yield

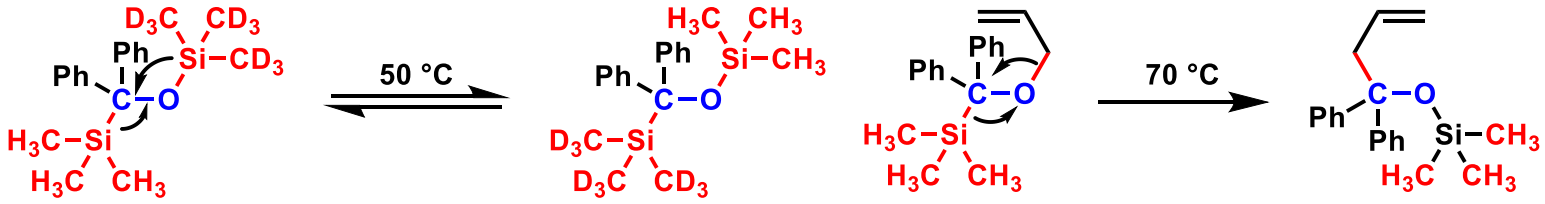
Ishikawa group (2008)



53% yield

C-O bond as Scaffold

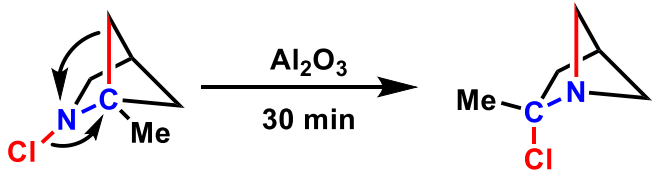
Reetz group (1977)



62% yield

C-N bond as Scaffold

Malpass group (1985)



70% yield

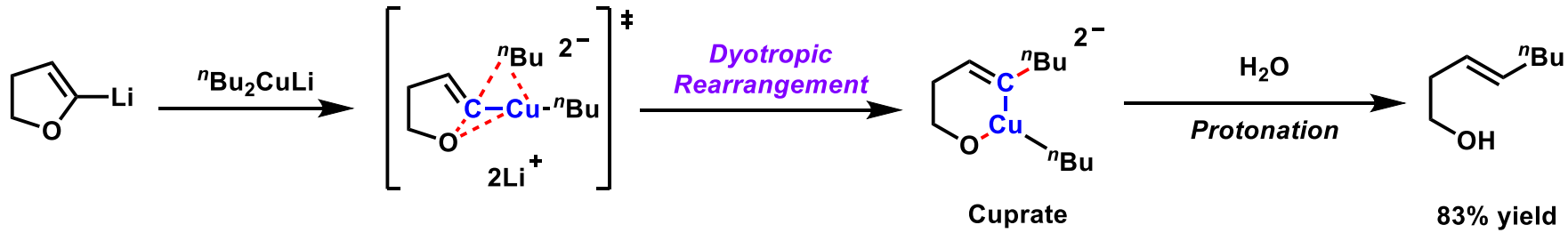
a) R. Haszeldine, et al. *J. Organomet. Chem.* **1973**, *47*, 53; b) M. Reetz, et al. *Angew. Chem. Int. Ed.* **1977**, *16*, 712; c) M. Ishikawa,et al. *Organometallics.* **2008**, *27*, 2922; d) M. Reetz, et al. *Adv. Organomet. Chem.* **1977**, *16*, 33; e) J. Malpass, et al. *Chem. Comm.* **1985**, 686.

1.2 Type I Dyotropic Rearrangement

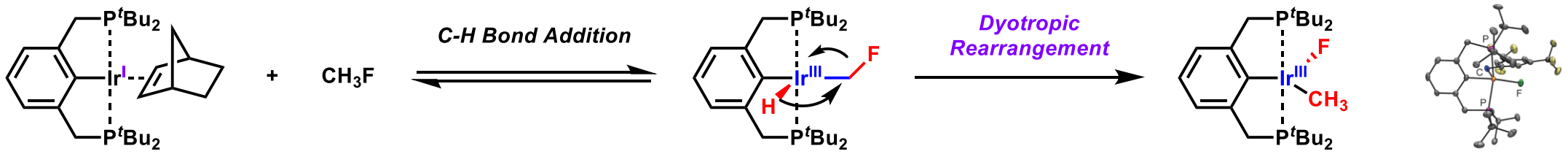
C-M Bond as Scaffold

1990

Barber group (1990)



Goldman group (2010)

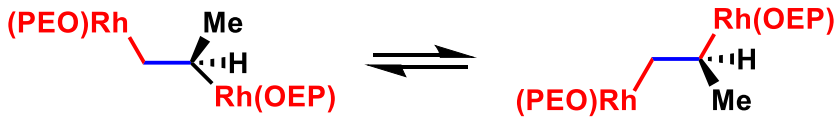


a) C. Barber, et al. *Pure Appl. Chem.* **1990**, *62*, 1933-1940. b) A. Goldman, et al. *Science.* **2011**, *332*, 1545-1548.

1.2 Type I Dyotropic Rearrangement

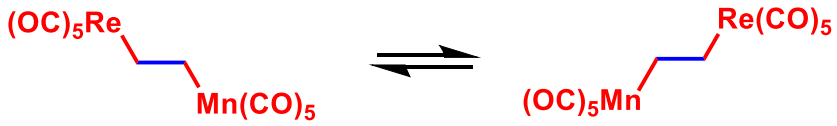
C-M Bond as Migration Group ?

Wayland group (1989)

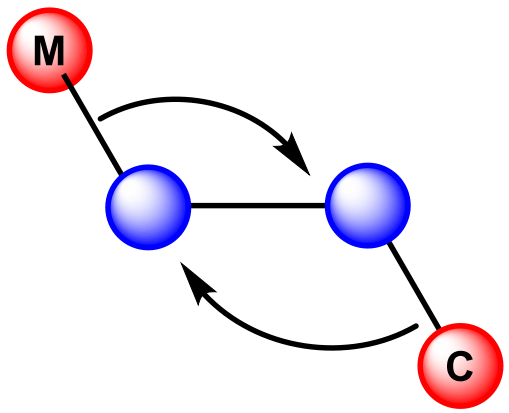


OEP = octaethylporphyrin

Beck group (1991)



Stoichiometric amount metals and synthetically useless



Advantage

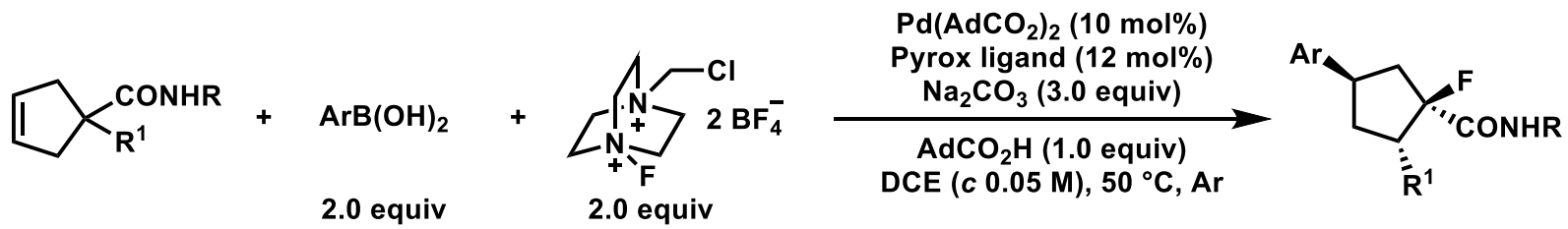
- Catalytic amount of metal.
- A new strategy for the C-C bond activation.
- A new C-C and C-M bond would be formed simultaneously.
- A new useful catalytic transformation.

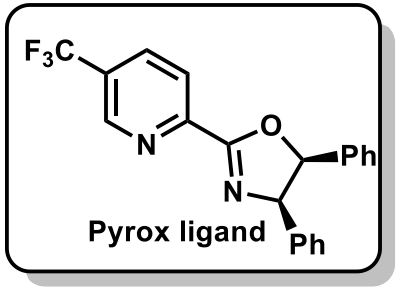
a) B. Wayland, et al. *Organometallics.* **1989**, *8*, 1438; b) W. Beck, et al. *Chem. Ber.* **1991**, *124*, 1059.

Content

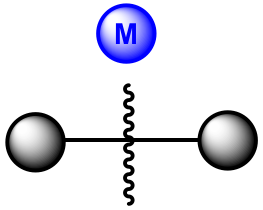
2.1 C-C Activation by Dyotropic Rearrangement

Zhu group (2021)





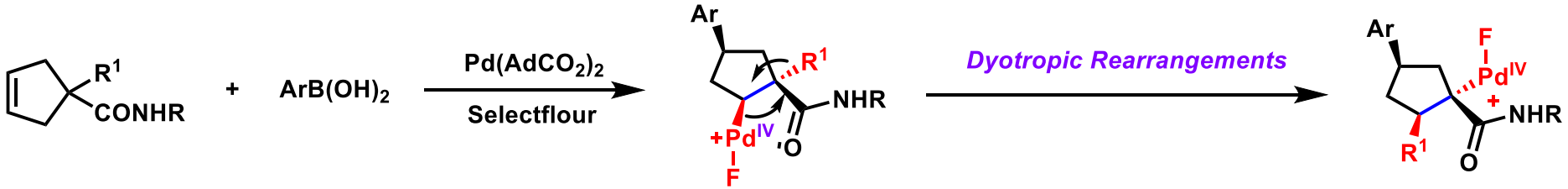
Carbon-Carbon Activation



Great Challenge

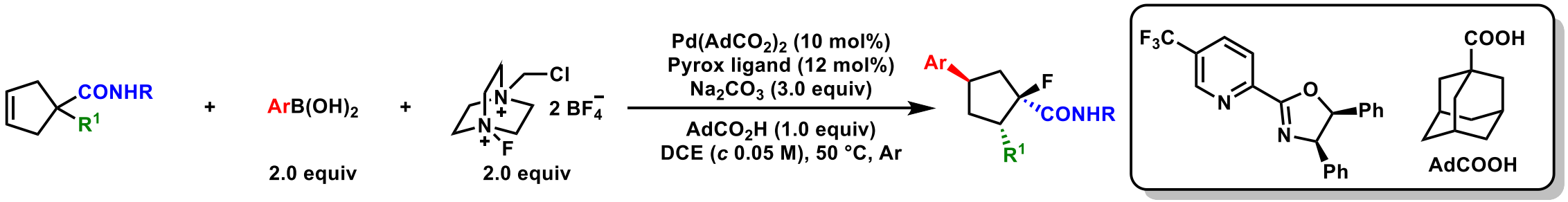
- **Thermodynamic Stability**
- **Kinetic Stability**

Reaction Design

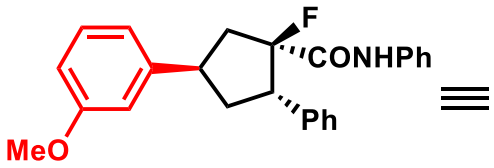


J. Zhu, et al. *Nat. Chem.* **2021**, *13*, 671-676.

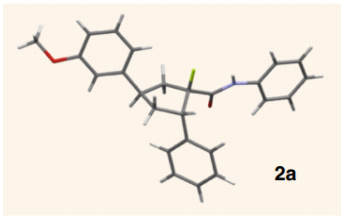
2.1 C-C Activation by Dyotropic Rearrangement

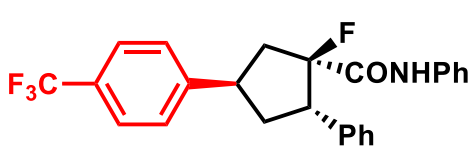


Scope of Aryl Boronic Acids

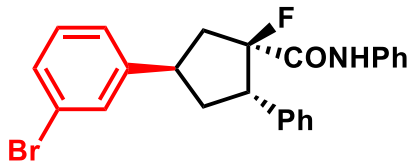


70% yield, 92% *ee*

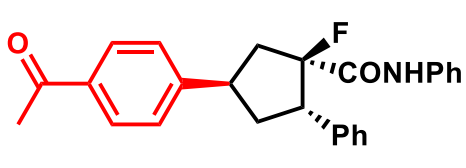




43% yield, 92% *ee*

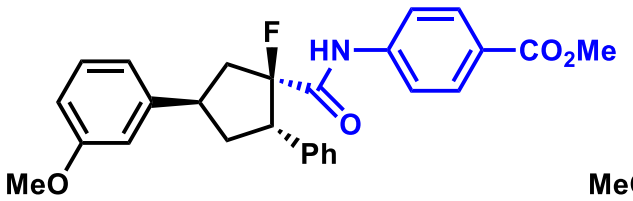


52% yield, 83% *ee*



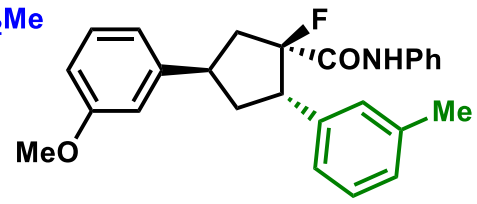
63% yield, 88% *ee*

Scope of Amides

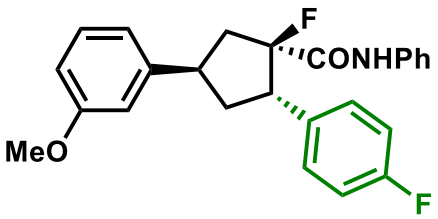


59% yield, 93% *ee*

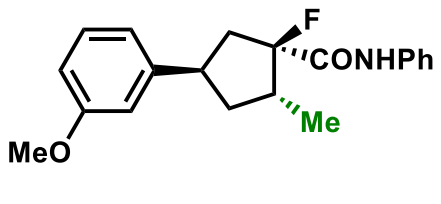
Scope of Migrating Groups



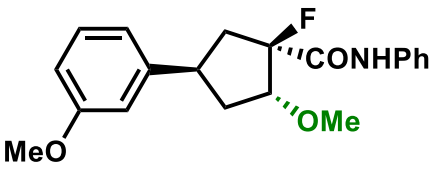
70% yield, 84% *ee*



38% yield, 91% *ee*



27% yield, 95% *ee*

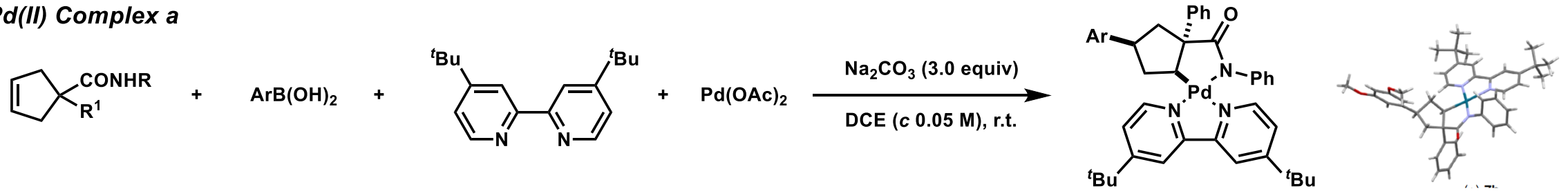


26% yield, 80% *ee*

J. Zhu, et al. *Nat. Chem.* **2021**, *13*, 671-676.

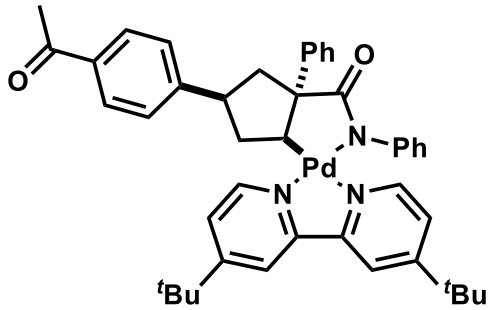
2.1 C-C Activation by Dyotropic Rearrangement

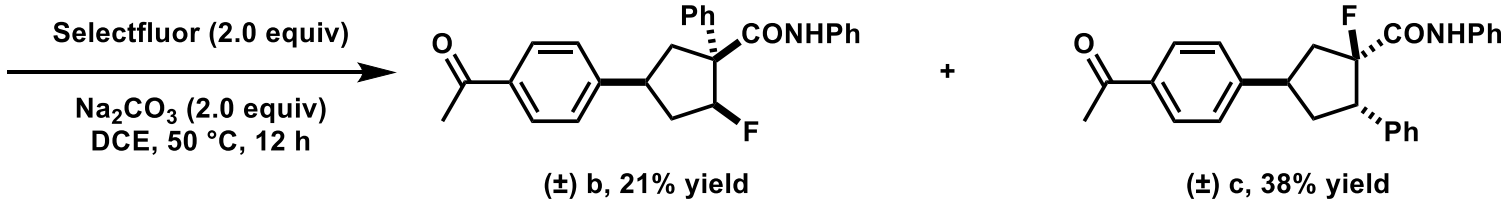
Pd(II) Complex a



Complex a 66% yield

Ar = 4-acetylphenyl

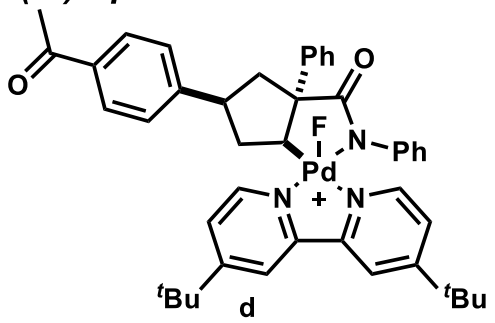




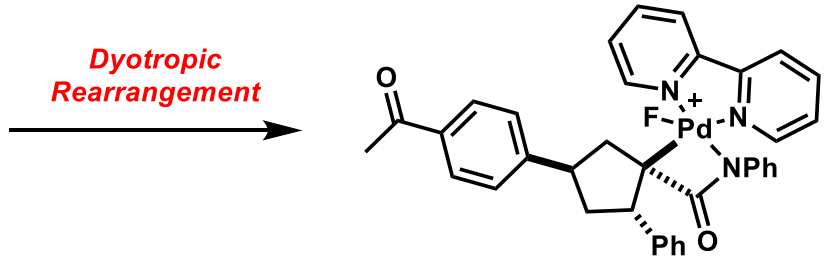
(±) b, 21% yield

(±) c, 38% yield

Pd(IV) Species



d



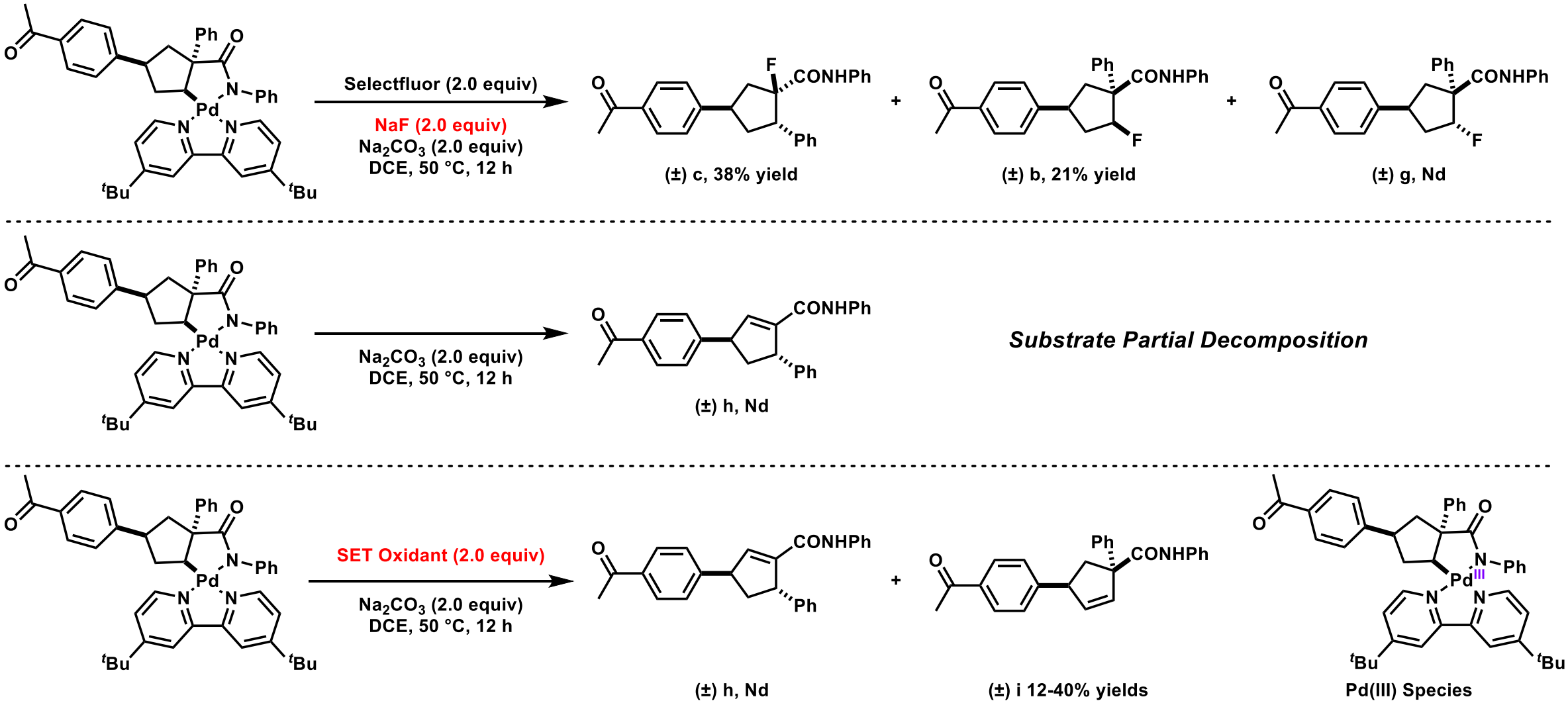
e

Failed to observe by ^{19}F NMR spectroscopy

Detected by HRMS

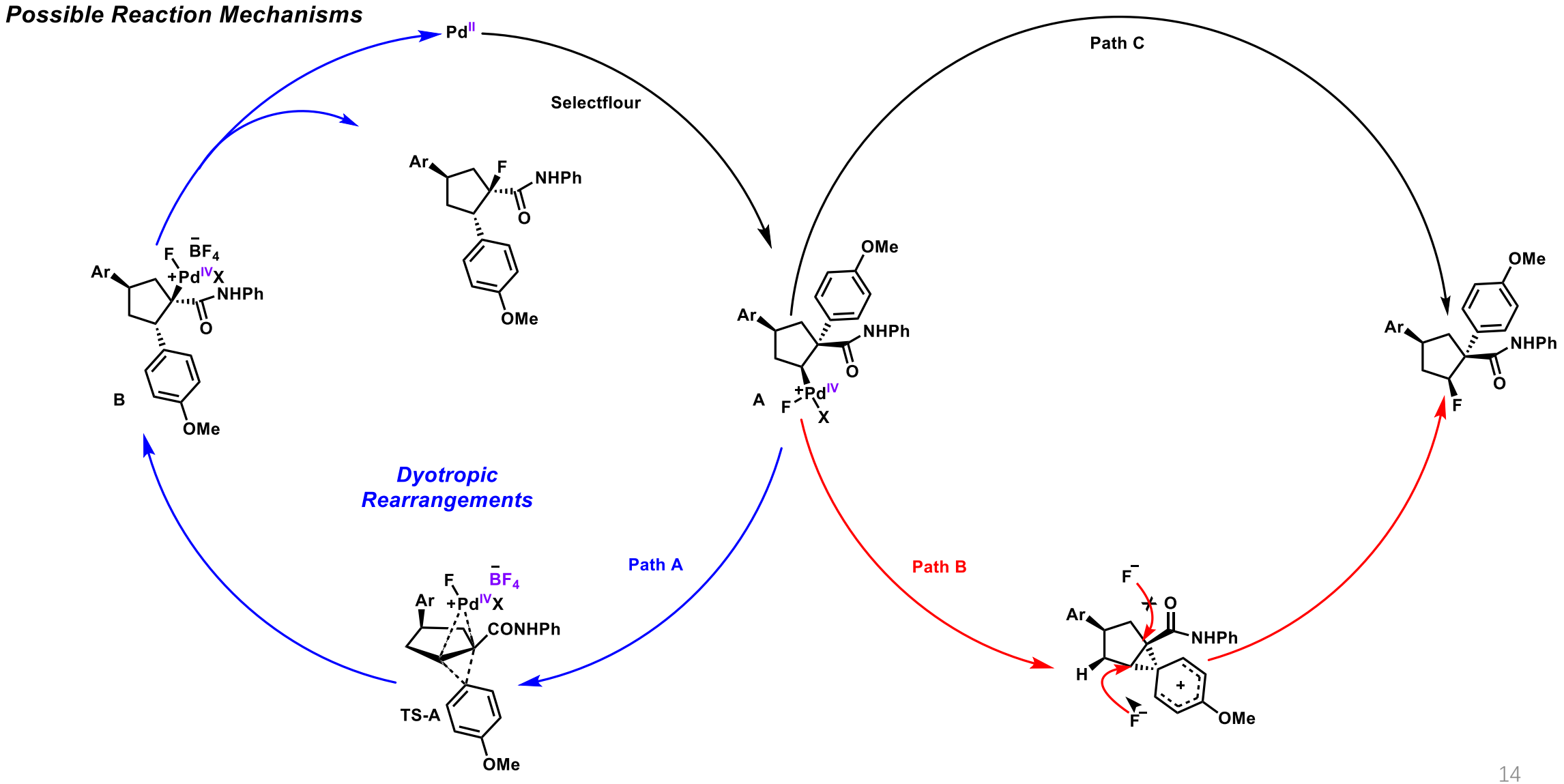
J. Zhu, et al. *Nat. Chem.* **2021**, *13*, 671-676.

2.1 C-C activation by Dyotropic Rearrangement



J. Zhu, et al. *Nat. Chem.* **2021**, *13*, 671-676.

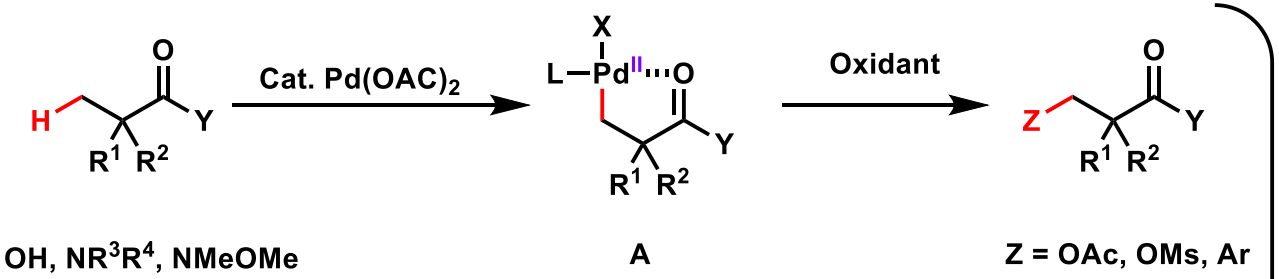
2.1 C-C activation by Dyotropic Rearrangement



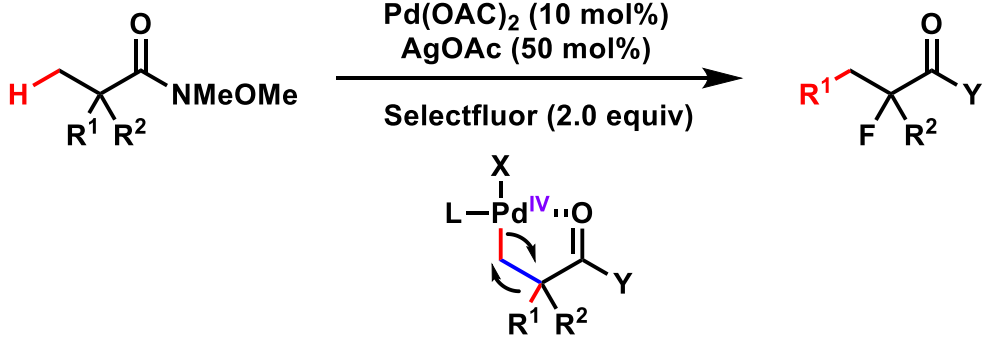
J. Zhu, et al. *Nat. Chem.* **2021**, *13*, 671-676.

2.2 α,β-Difunctionalization of Saturated Amide

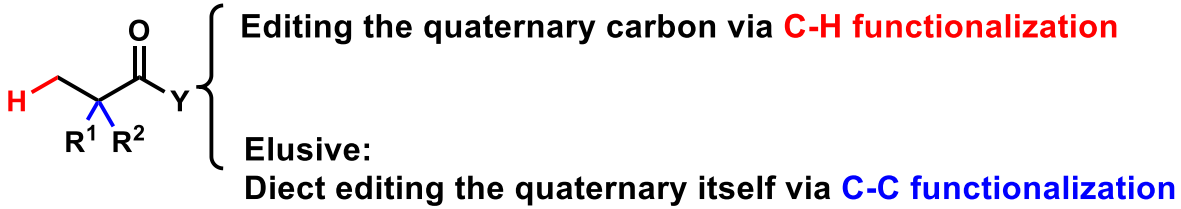
Transition Metal Catalyzed β-C-H Activation



This Work:

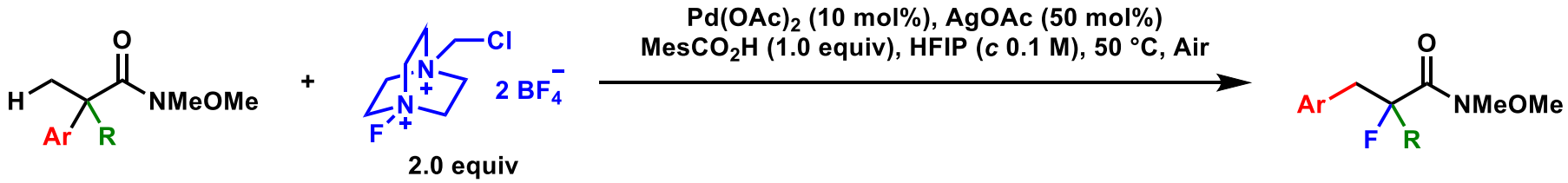


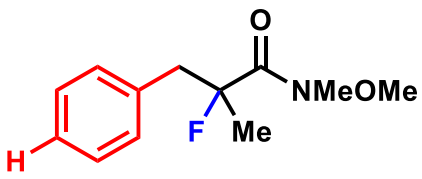
An Elegant Method for Editing a Quaternary Carbon



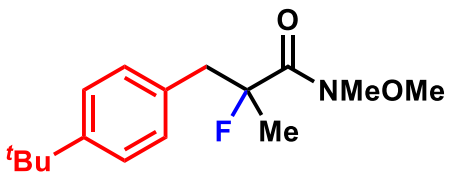
J. Zhu, et al. *J. Am. Chem. Soc.* **2022**, *144*, 14047-14052.

2.2 α,β-Difunctionalization of Saturated Amide

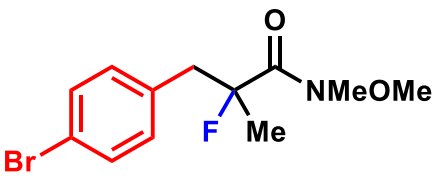




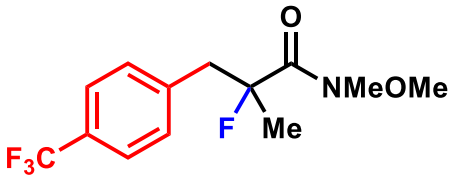
68% yield



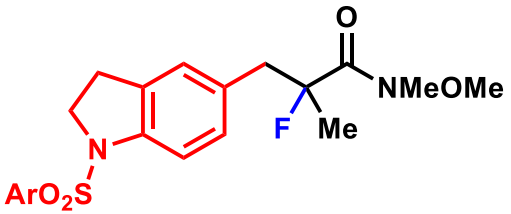
65% yield



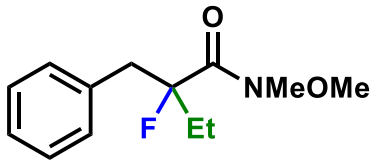
60% yield



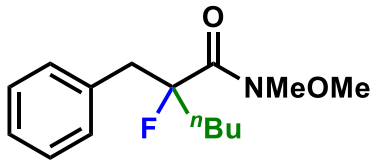
41% yield



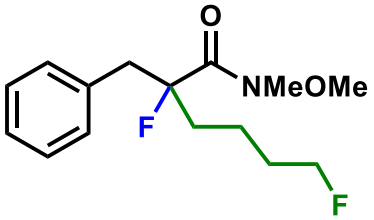
50% yield



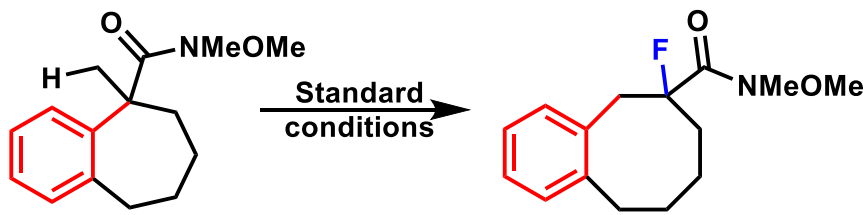
43% yield



44% yield



43% yield

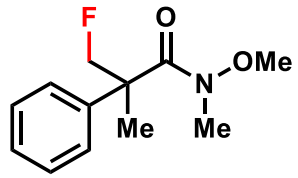


65% yield

J. Zhu, et al. *J. Am. Chem. Soc.* **2022**, *144*, 14047-14052.

2.2 α,β-Difunctionalization of Saturated Amide

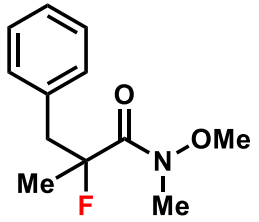
Control Experiment



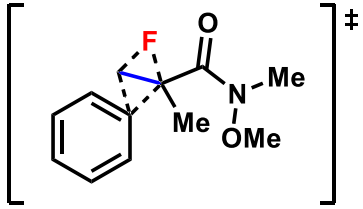
b

$Pd(OAc)_2$ (10 mol%), AgOAc (50 mol%)
$MesCO_2H$ (1.0 equiv), Selectfluor (1.7 equiv)

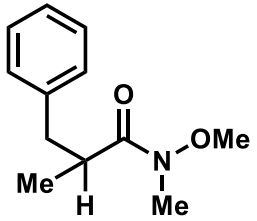
HFIP (1 mL), 50 °C, Air, 2 h



a Nd



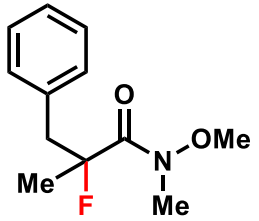
Dyotropic rearrangement transition state



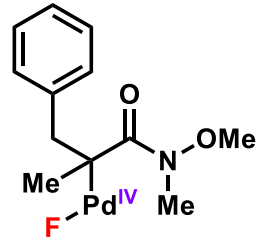
c

$Pd(OAc)_2$ (10 mol%), AgOAc (50 mol%)
$MesCO_2H$ (1.0 equiv), Selectfluor (1.7 equiv)

HFIP (1 mL), 50 °C, Air, 2 h

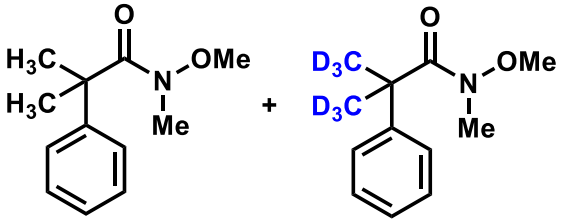


a Nd



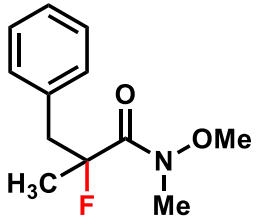
α-fluorination intermediate

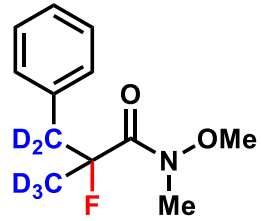
KIE Experiment



$Pd(OAc)_2$ (10 mol%), AgOAc (50 mol%)
$MesCO_2H$ (1.0 equiv), Selectfluor (1.7 equiv)

HFIP (1 mL), 50 °C, Air, 2 h

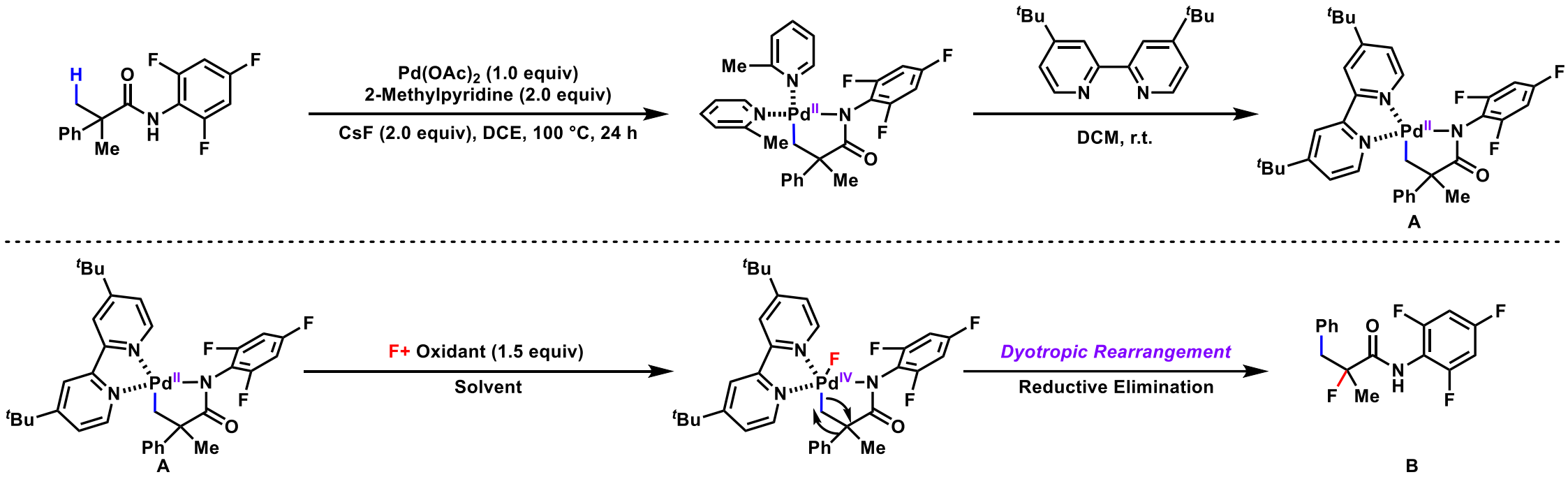




^{1}H NMR yield K_H/K_D = 5.7

J. Zhu, et al. *J. Am. Chem. Soc.* **2022**, *144*, 14047-14052.

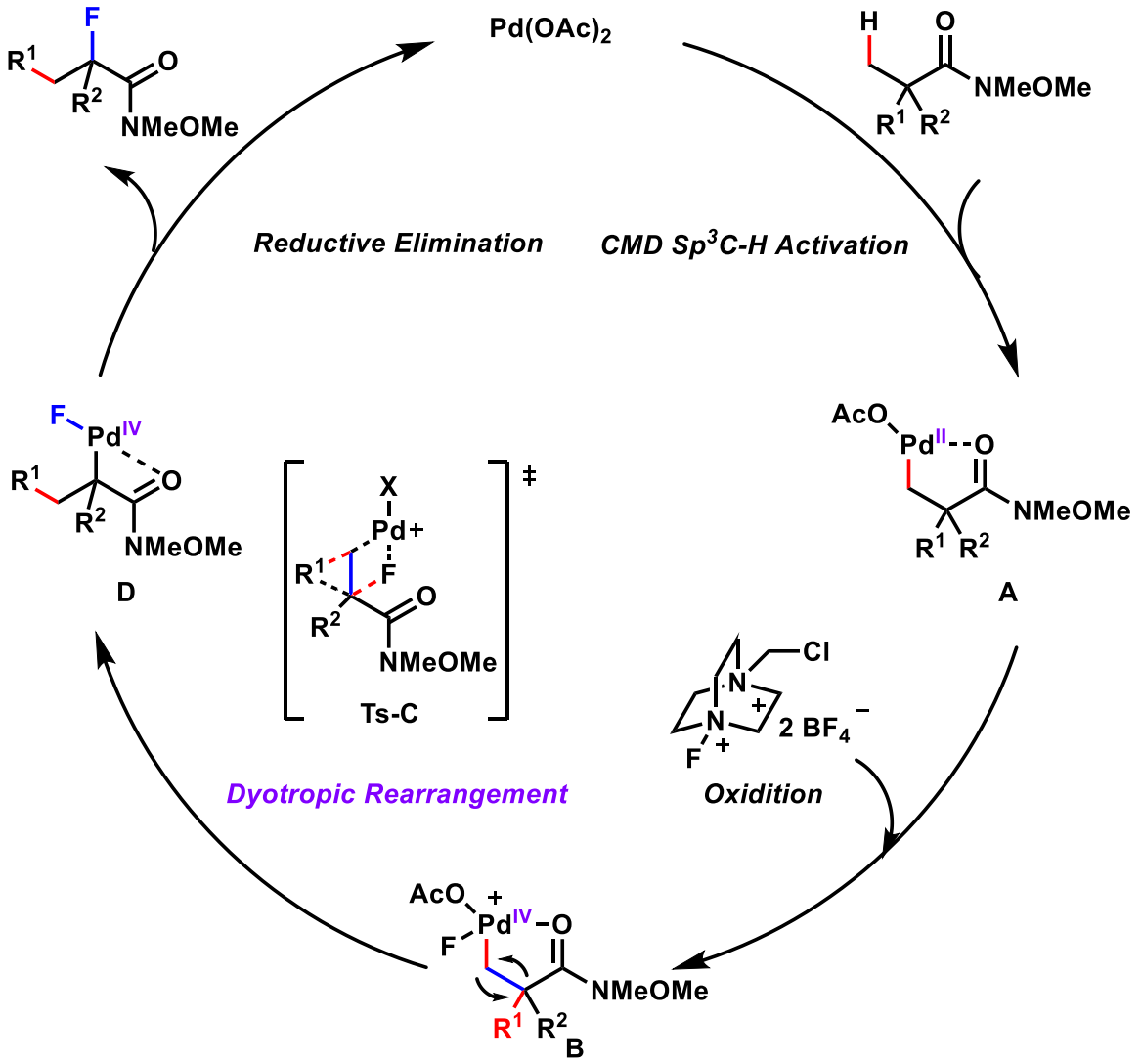
2.2 α,β-Difunctionalization of Saturated Amide



Entry	F^+ Oxidant	Solvent	Yield (%)
1	Selectfluor	HFIP	63
2	Selectfluor	MeCN	87
3	NFSI	HFIP	68
4	Pyridinium Salt	HFIP	50

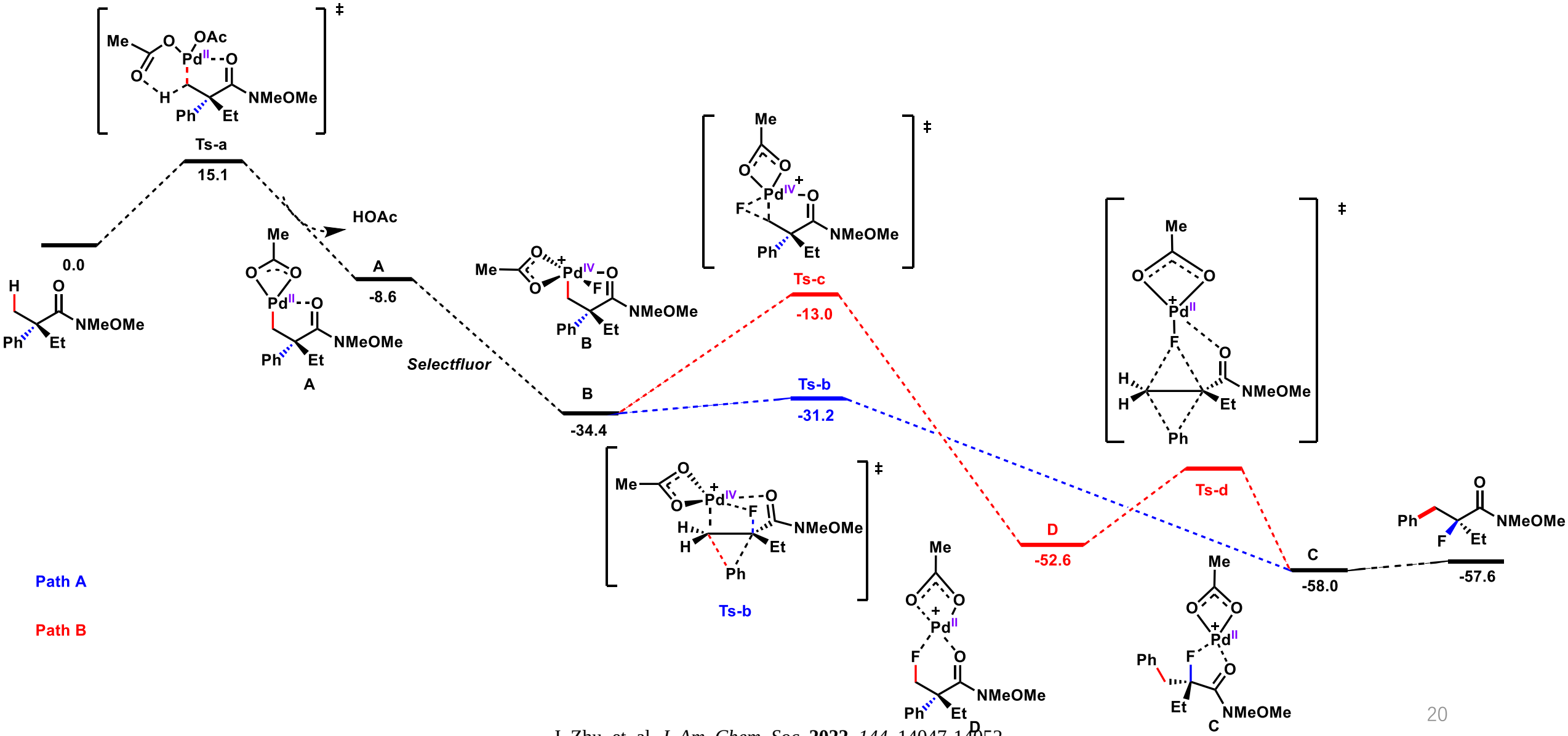
J. Zhu, et al. *J. Am. Chem. Soc.* **2022**, *144*, 14047-14052.

2.2 α,β-Difunctionalization of Saturated Amide



J. Zhu, et al. *J. Am. Chem. Soc.* **2022**, *144*, 14047-14052.

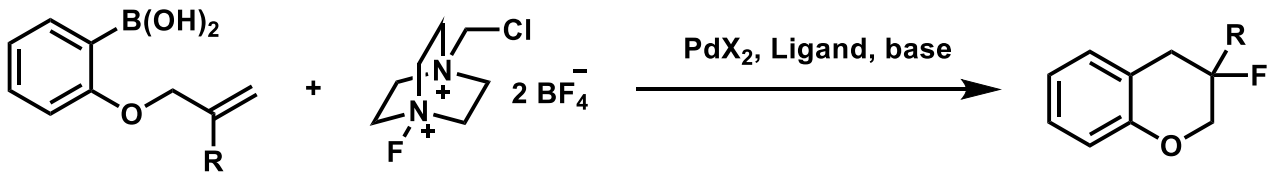
2.2 α,β-difunctionalization of Saturated Amide



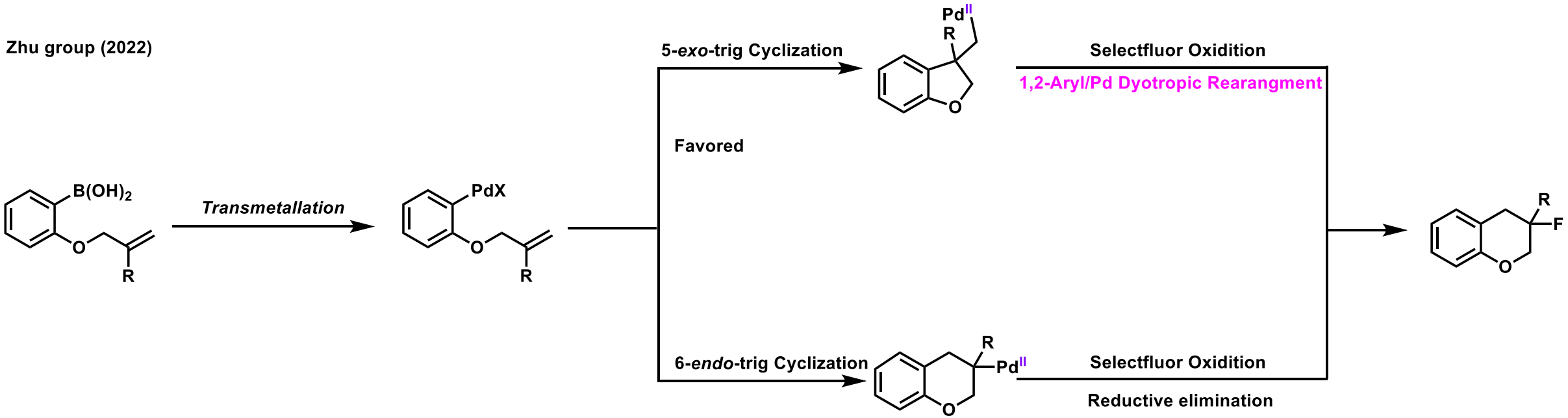
J. Zhu, et. al. *J. Am. Chem. Soc.* **2022**, *144*, 14047-14052.

2.3 6-endo-trig Cyclization Reaction

Intramolecular carbometallation initiated domino processes

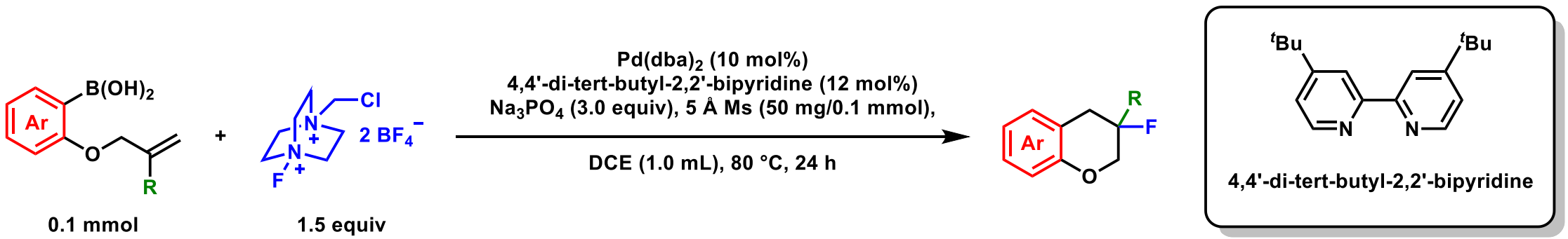


Zhu group (2022)



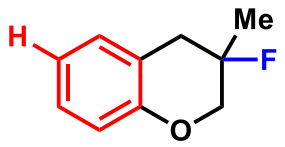
J. Zhu, et al. *Angew. Chem. Int. Ed.* **2022**, *61*, e202211470.

2.3 6-endo-trig Cyclization Reaction

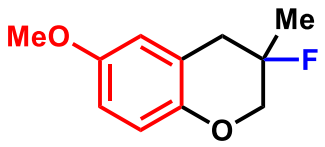


0.1 mmol

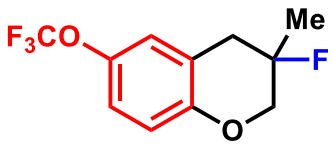
1.5 equiv



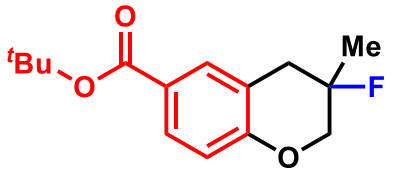
55% yield



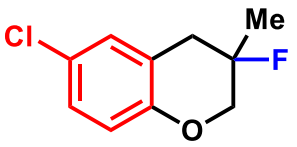
34% yield



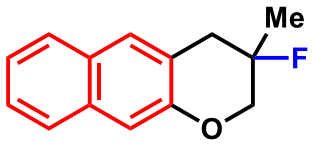
45% yield



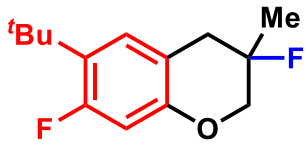
40% yield



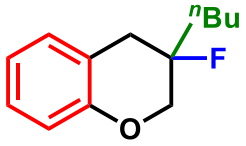
37% yield



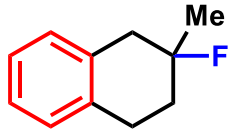
41% yield



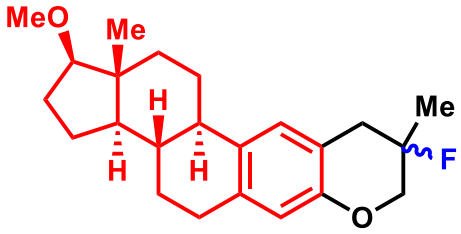
48% yield



38% yield



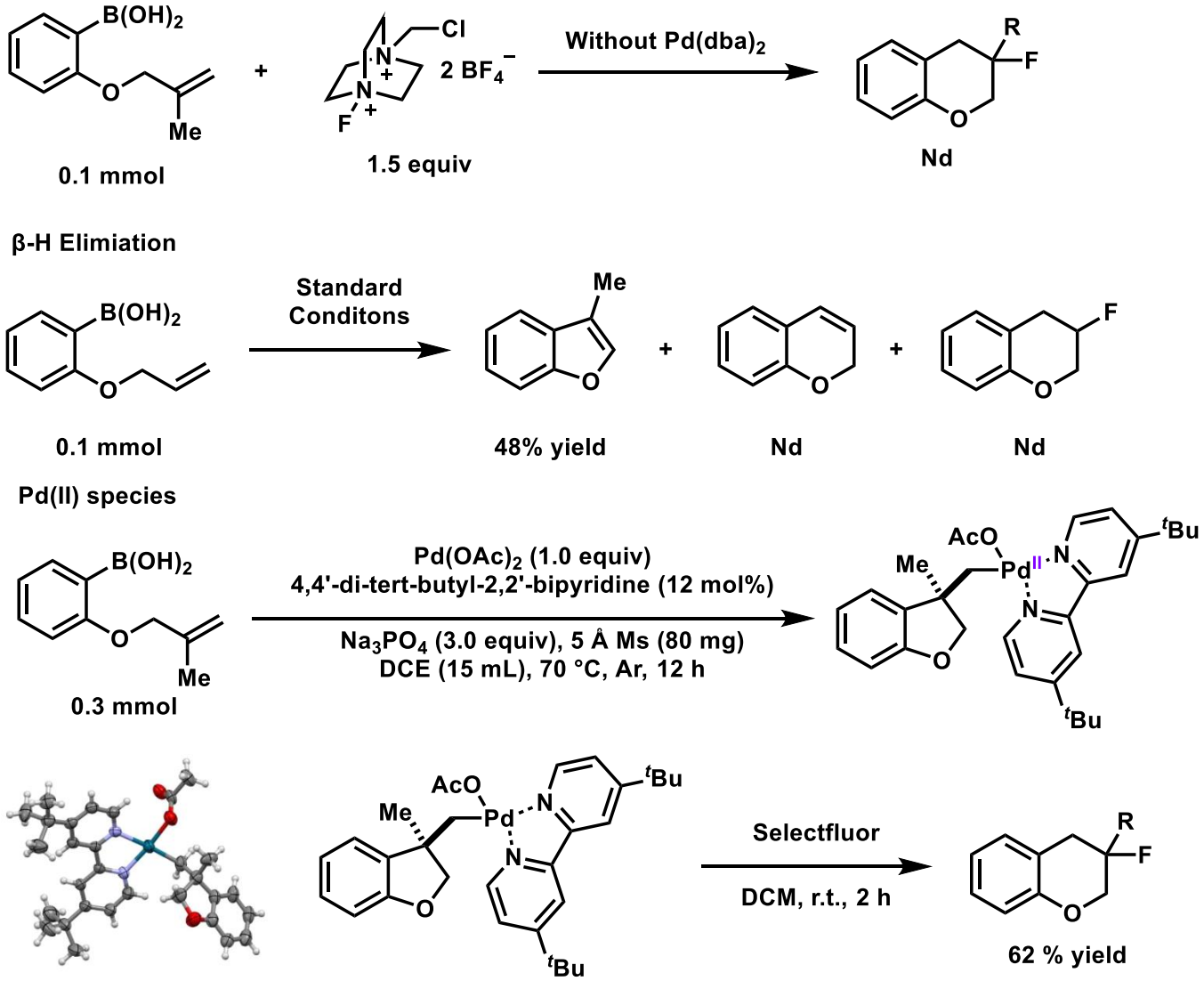
30% yield

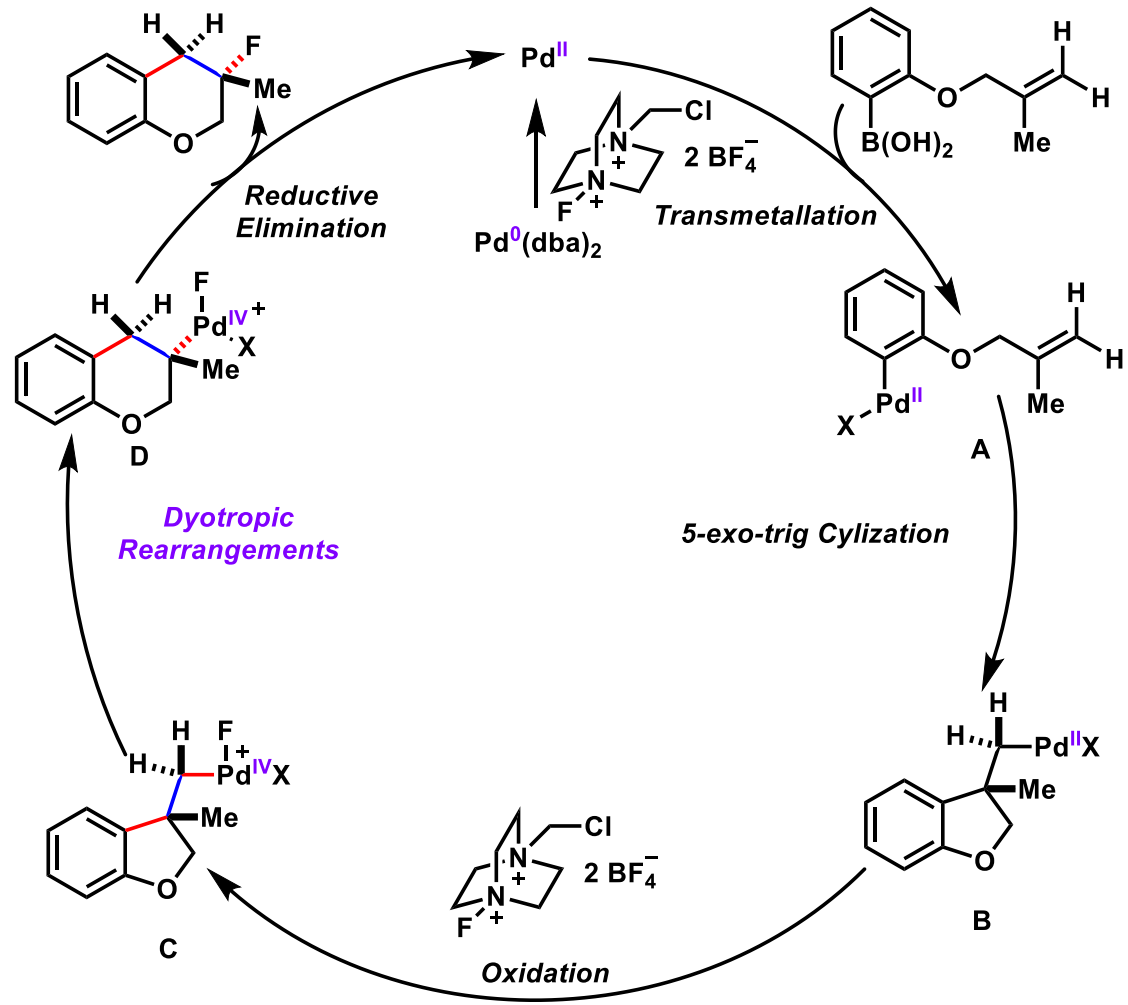


38% yield, d.r. 2.5 : 1

J. Zhu, et al. *Angew. Chem. Int. Ed.* **2022**, *61*, e202211470.

2.3 6-endo-trig Cyclization Reaction

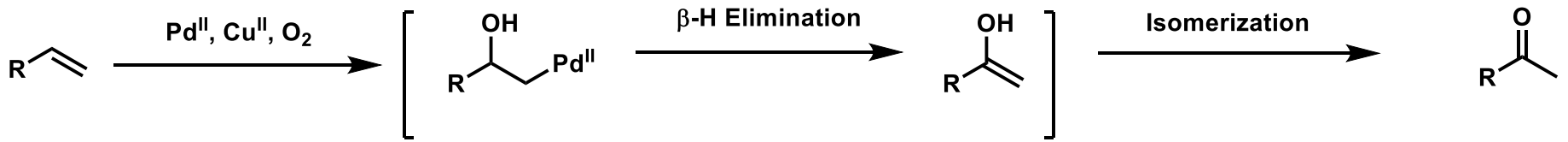




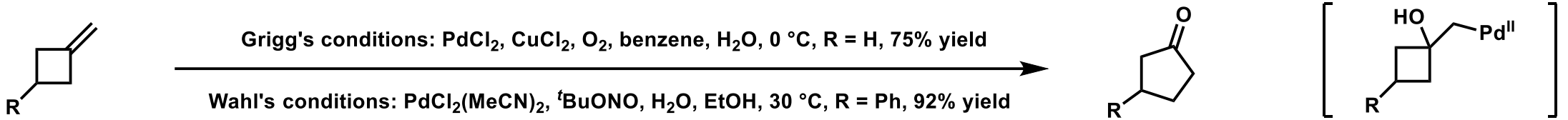
J. Zhu, et al. *Angew. Chem. Int. Ed.* **2022**, *61*, e202211470.

2.4 Dyotropic Rearrangement in Wacker Reaction

Wacker Reaction

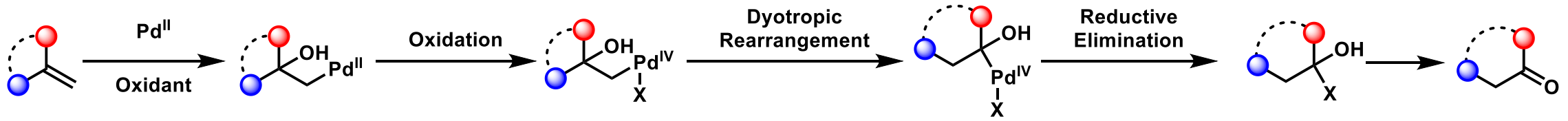


Semi-Pinacol Rearrangement Reaction



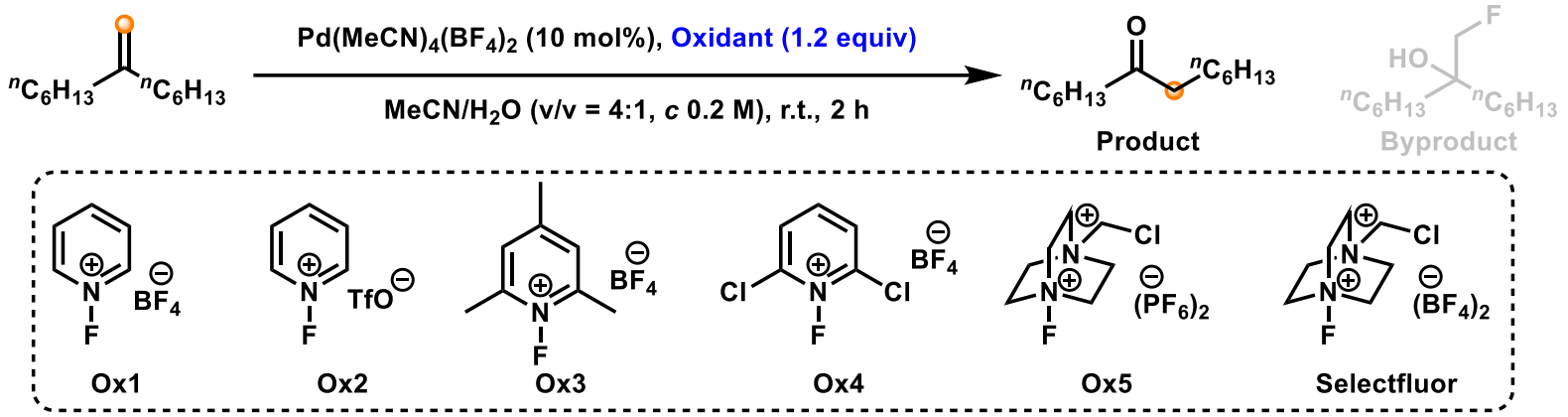
Tiffeneau-Demjanov Reaction

This Work: Dyotropic Rearrangement Reaction



J. Zhu, et al. *Science.* **2023**, *379*, 1363-1368.

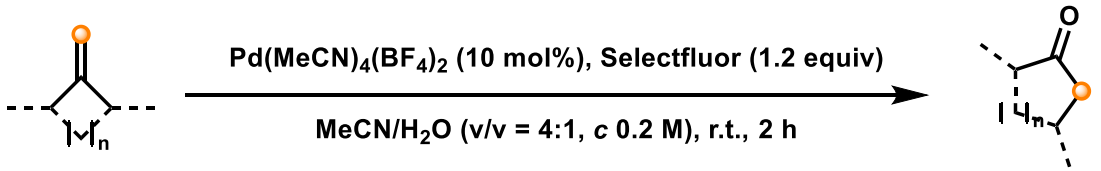
2.4 Dyotropic Rearrangement in Wacker Reaction



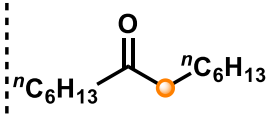
Entry	Oxidant	Con. (%)	Yield (%)
1	Ox1	<5	0
2	Ox2	32	0
3	Ox3	<5	0
4	Ox4	25	6
5	Ox5	>99	58
6	Selectfluor	>99	75
7	NFSI	<5	0
8	Oxone	88	8

J. Zhu, et. al. *Science.* **2023**, *379*, 1363-1368.

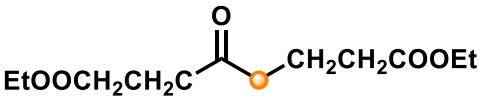
2.4 Dyotropic Rearrangement in Wacker Reaction



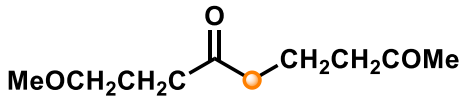
Symmetric linear Alkenes



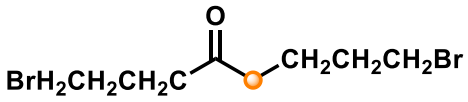
72% yield



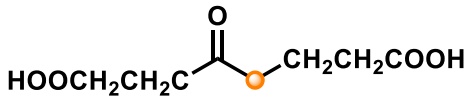
53% yield



68% yield

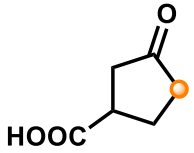


52% yield

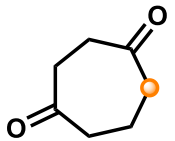


55% yield

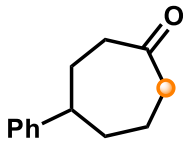
Symmetric Cyclic Alkenes



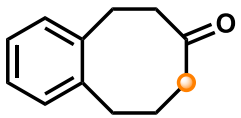
61% yield



63% yield

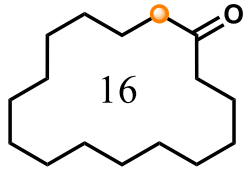


63% yield



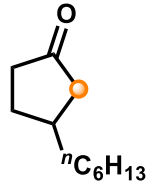
58% yield

Macrocycles

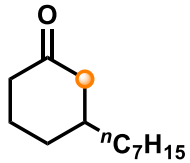


70% yield

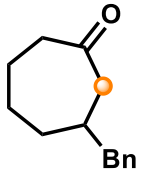
Unsymmetric Alkenes



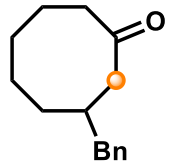
47% yield, r.r. = 4 : 1



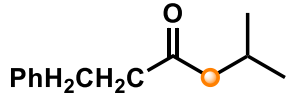
49% yield



63% yield, r.r. = 6.5 : 1



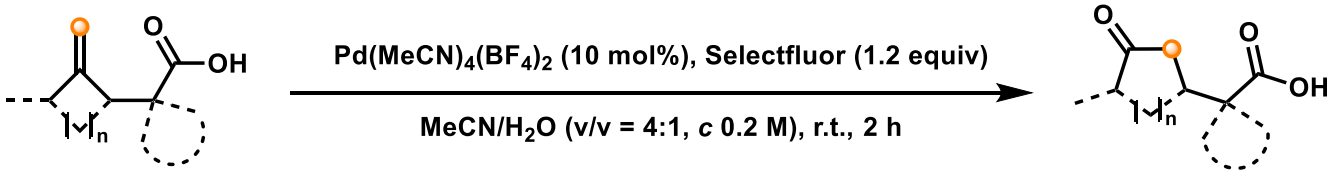
59% yield



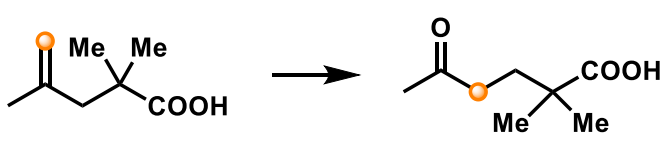
59% yield, r.r. = 1.4 : 1

J. Zhu, et al. *Science.* **2023**, *379*, 1363-1368.

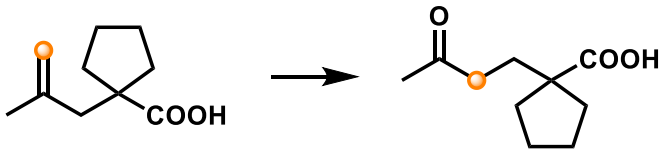
2.4 Dyotropic Rearrangement in Wacker Reaction



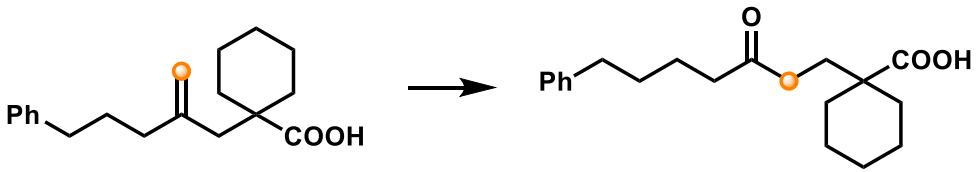
Linear Unsymmetric Alkenes



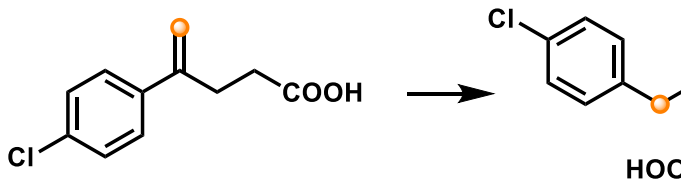
90% yield, r.r. = 10 : 1



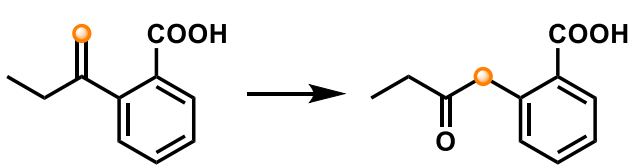
89% yield, r.r. = 13 : 1



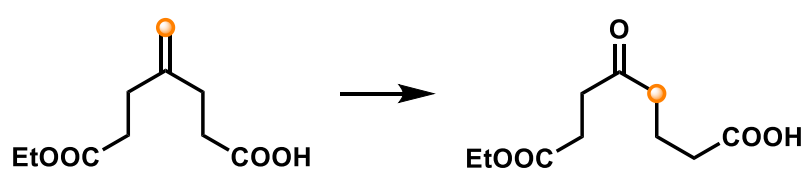
93% yield, r.r. = 11 : 1



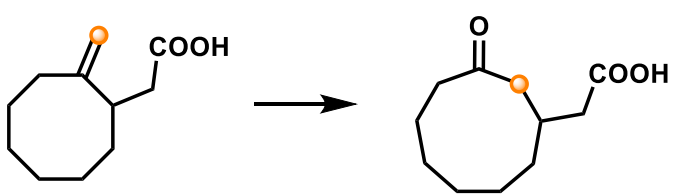
49% yield, r.r. = 1.7 : 1



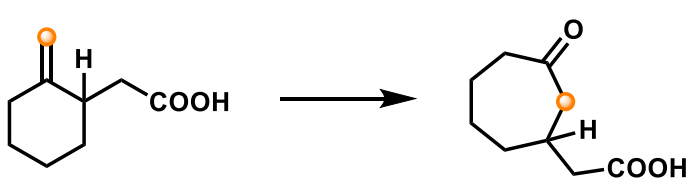
85% yield



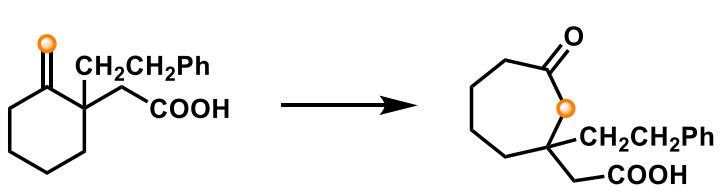
72% yield, r.r. = 7 : 1



69% yield



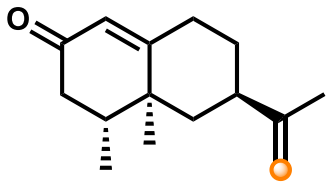
75% yield



61% yield, r.r. = 1.7 : 1

J. Zhu, et al. *Science.* **2023**, *379*, 1363-1368.

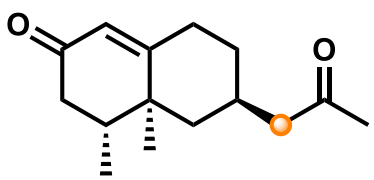
2.4 Dyotropic Rearrangement in Wacker Reaction



nootkatone

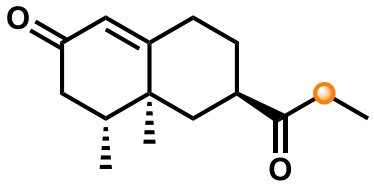
$Pd(MeCN)_4(BF_4)_2$ (10 mol%), Selectfluor (1.2 equiv)

$MeCN/H_2O$ (v/v = 4:1, *c* 0.2 M), r.t., 2 h



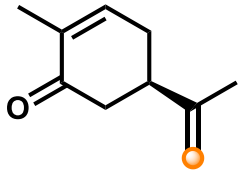
43% yield

\+



7% yield

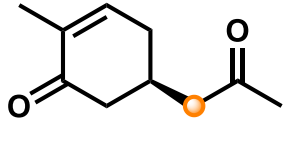
Regioselectivity 6:1



(*S*)-carvone

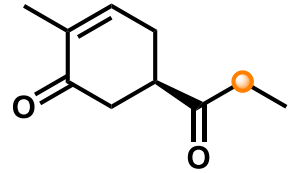
$Pd(MeCN)_4(BF_4)_2$ (10 mol%), Selectfluor (1.2 equiv)

$MeCN/H_2O$ (v/v = 4:1, *c* 0.2 M), r.t., 2 h



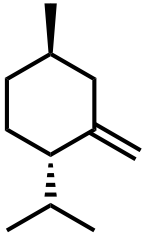
45% yield

\+



11% yield

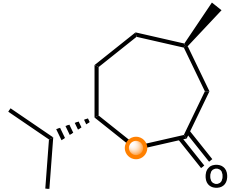
Regioselectivity 4:1



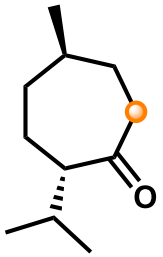
L-menthone derivative

$Pd(MeCN)_4(BF_4)_2$ (10 mol%), Selectfluor (1.2 equiv)

$MeCN/H_2O$ (v/v = 4:1, *c* 0.2 M), r.t., 2 h



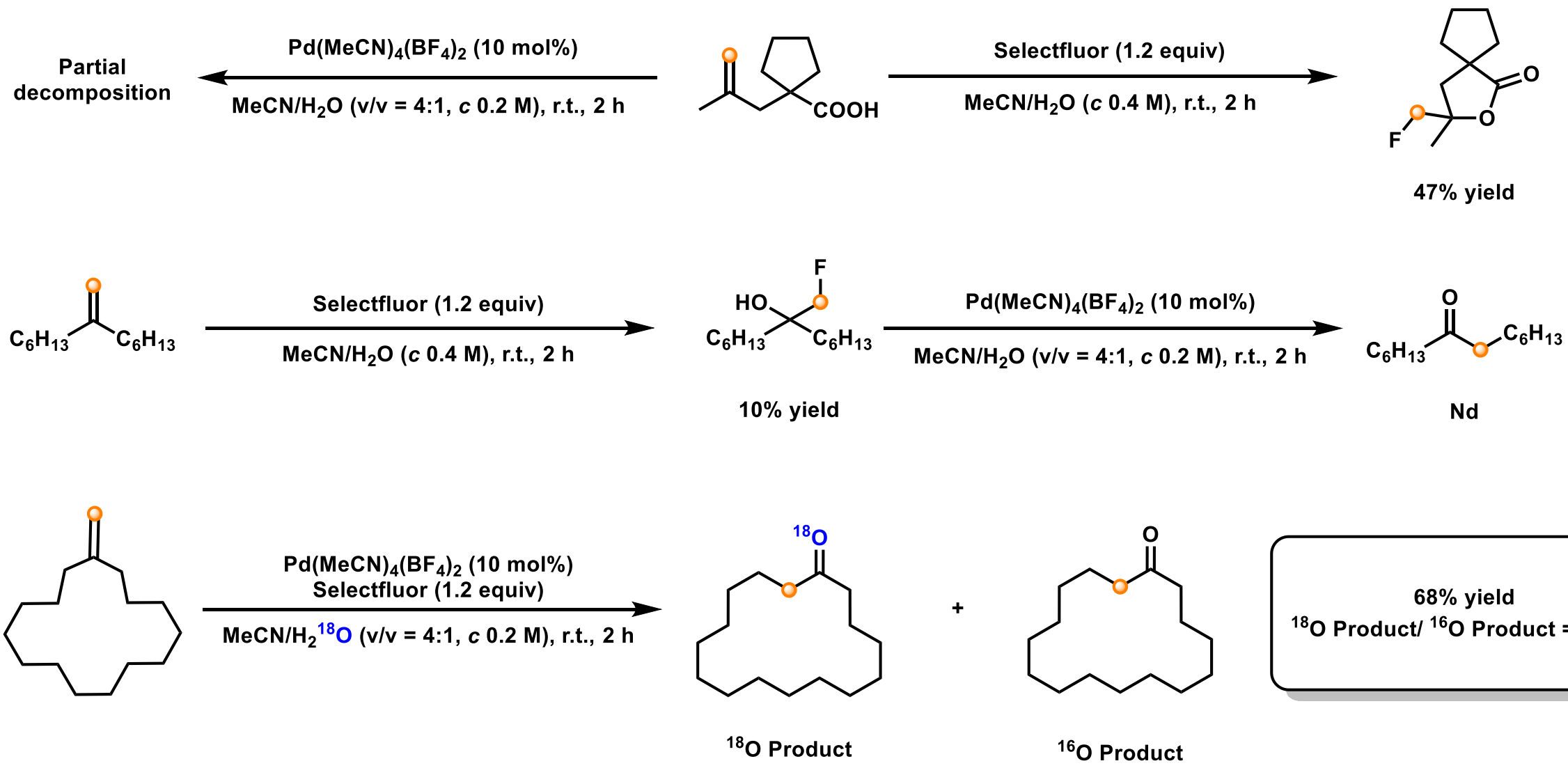
61% yield



Nd

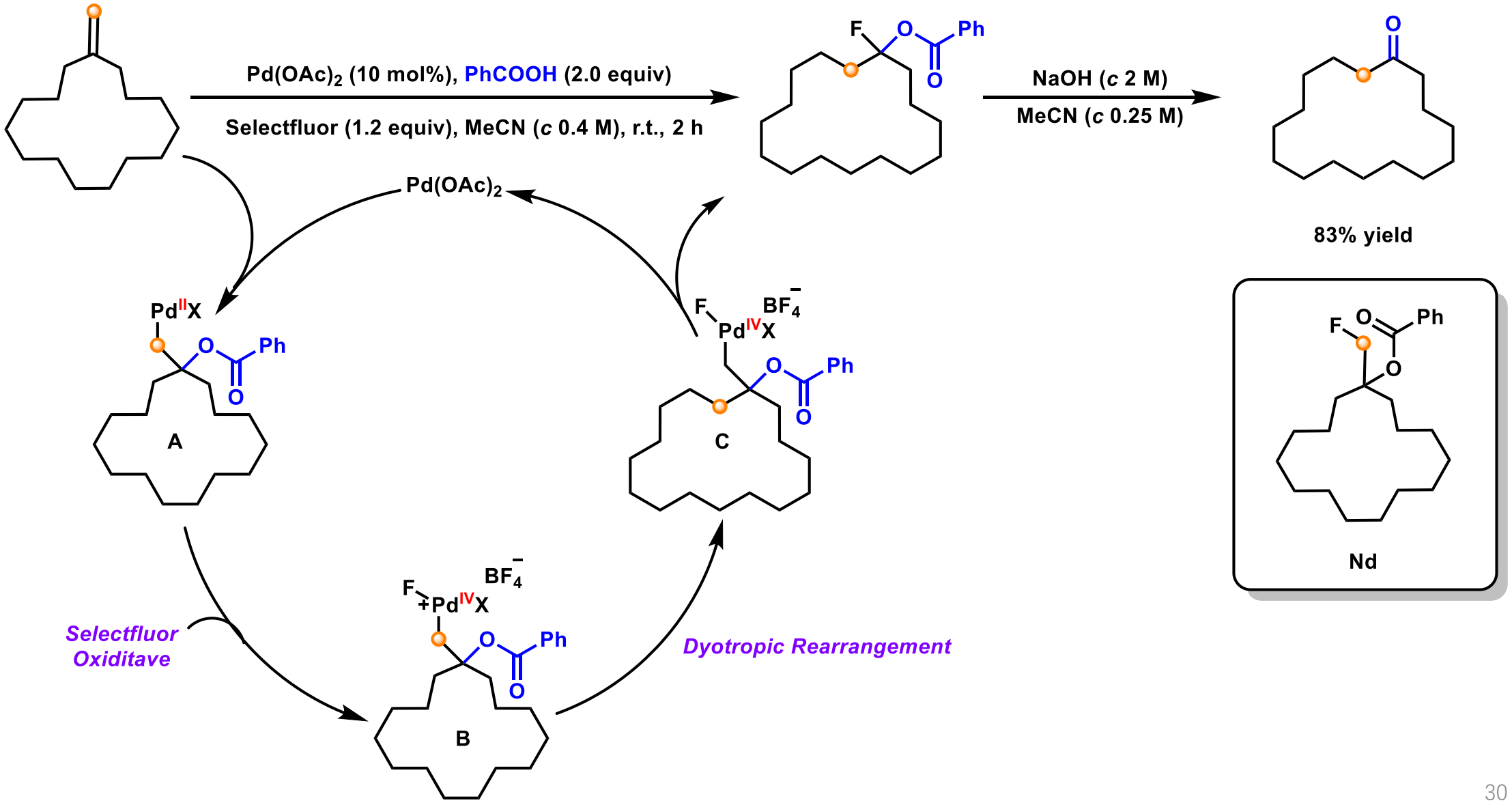
J. Zhu, et al. *Science.* **2023**, *379*, 1363-1368.

2.4 Dyotropic Rearrangement in Wacker Reaction



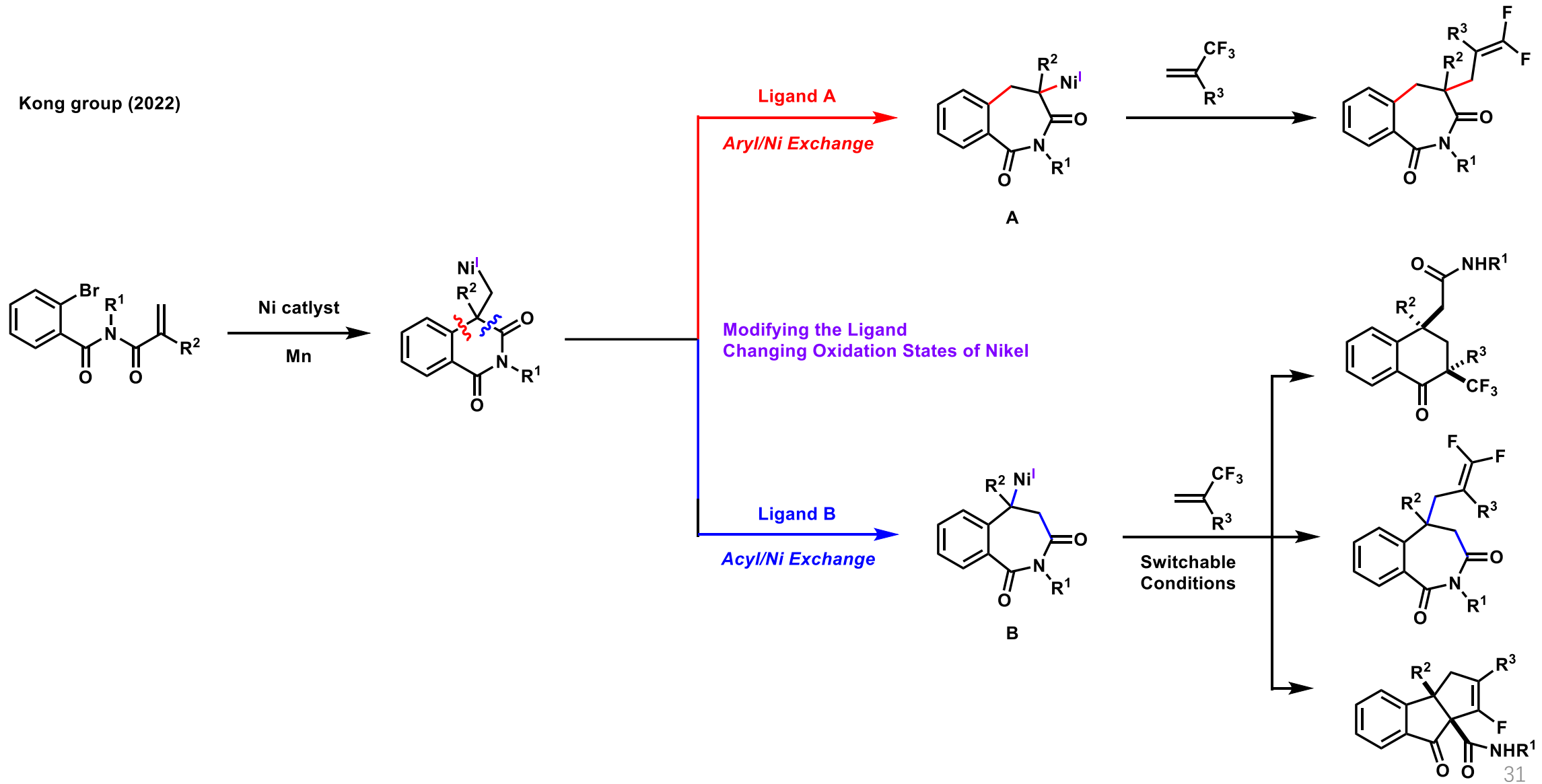
J. Zhu, et al. *Science.* **2023**, *379*, 1363-1368.

2.4 Dyotropic Rearrangement in Wacker Reaction



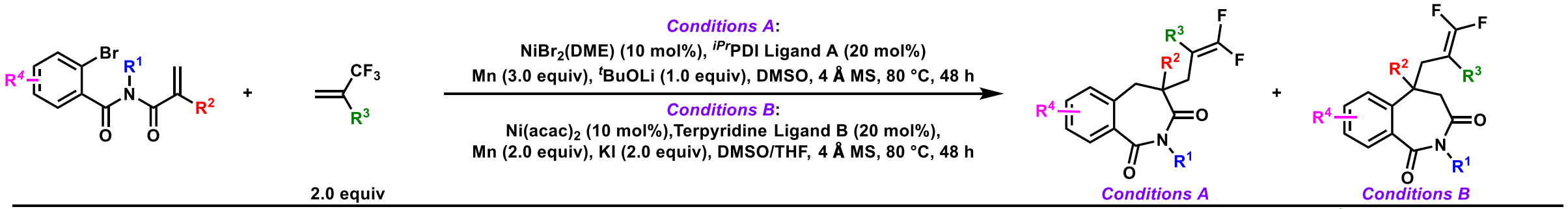
J. Zhu, et al. *Science.* **2023**, *379*, 1363-1368.

2.5 Switchable Dyotropic Rearrangement

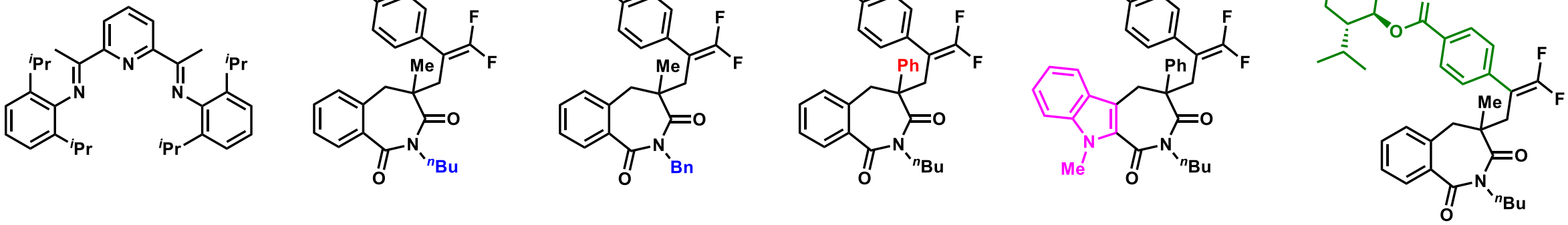


W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

2.5 Switchable Dyotropic Rearrangement

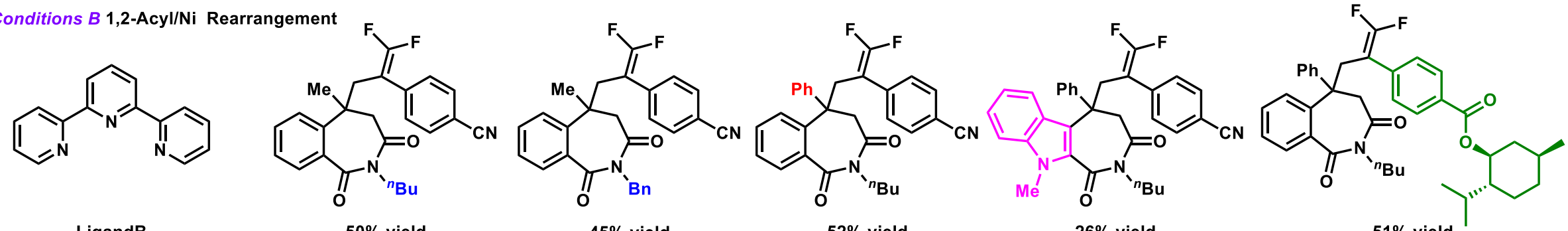


Conditions A 1,2-Aryl/Ni Rearrangement



Ligand A | 70% yield | 62% yield | 50% yield | 43% yield | 75% yield

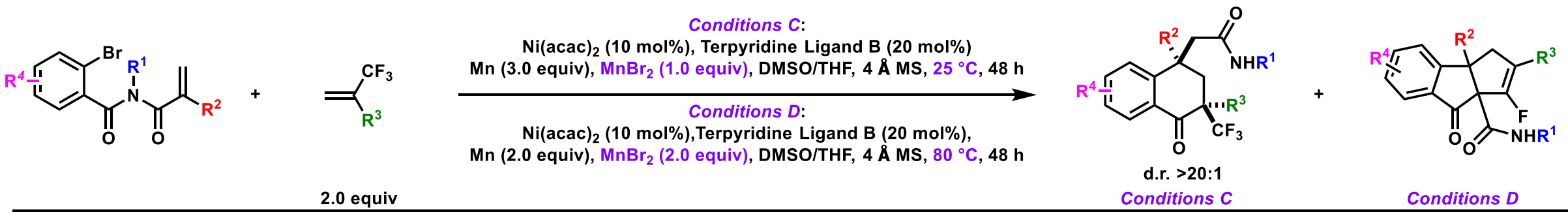
Conditions B 1,2-Acyl/Ni Rearrangement

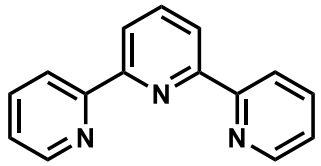


LigandB | 50% yield | 45% yield | 52% yield | 26% yield | 51% yield

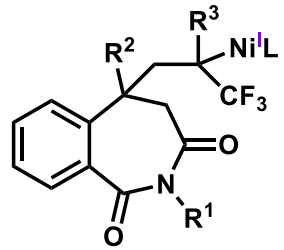
W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

2.5 Switchable Dyotropic Rearrangement



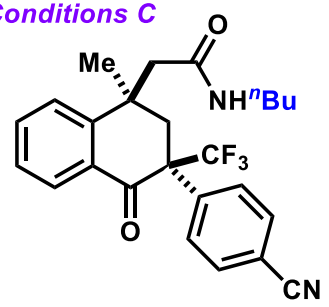


Terpyridine Ligand B

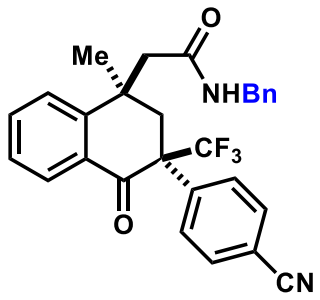


1,2-Acyl/Ni Rearrangment

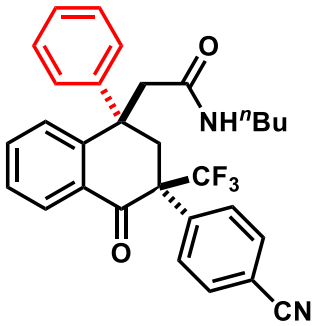
Conditions C



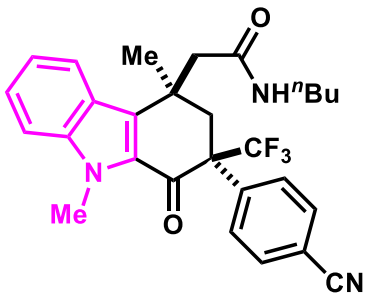
64% yield



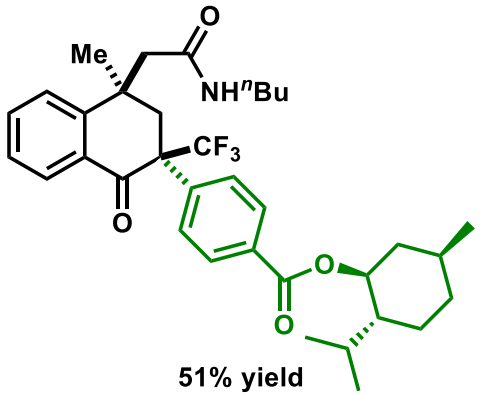
62% yield



35% yield

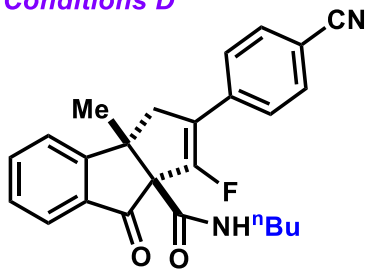


34% yield

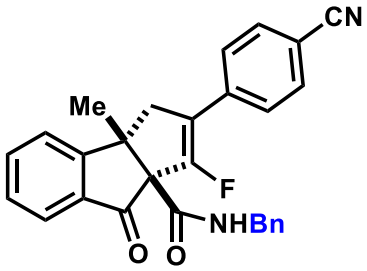


51% yield

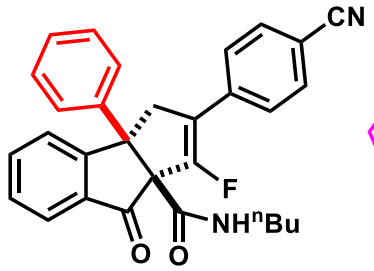
Conditions D



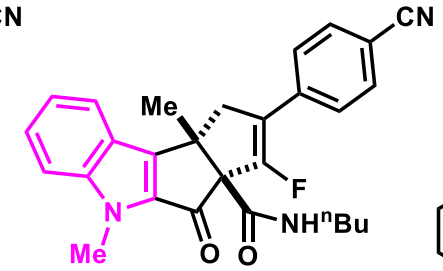
68% yield



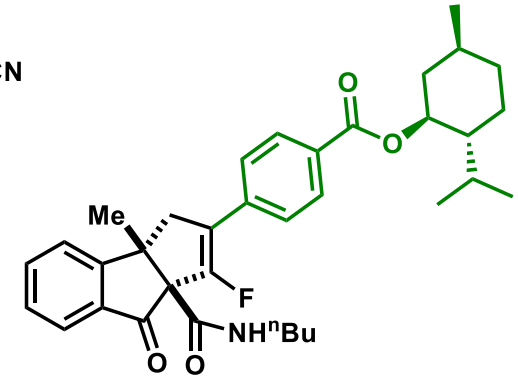
69% yield



39% yield



52% yiedl



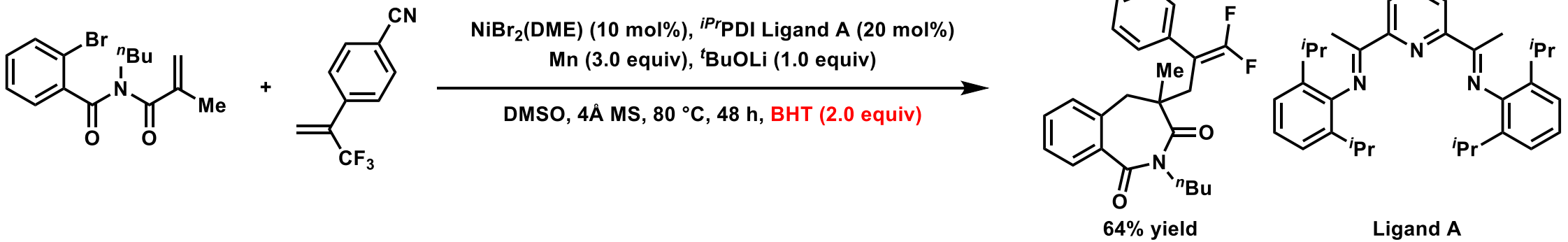
57% yield

W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

2.5 Switchable Dyotropic Rearrangement

Radical Trapping Experiments:

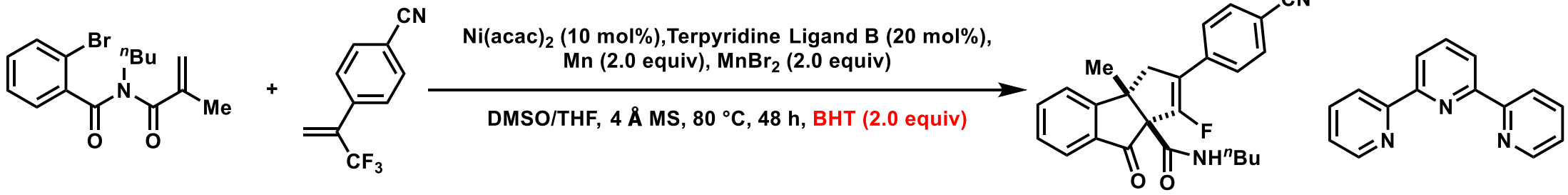
***1,2-Aryl/Ni* Rearrangement**



64% yield

Ligand A

***1,2-Acyl/Ni* Rearrangement**

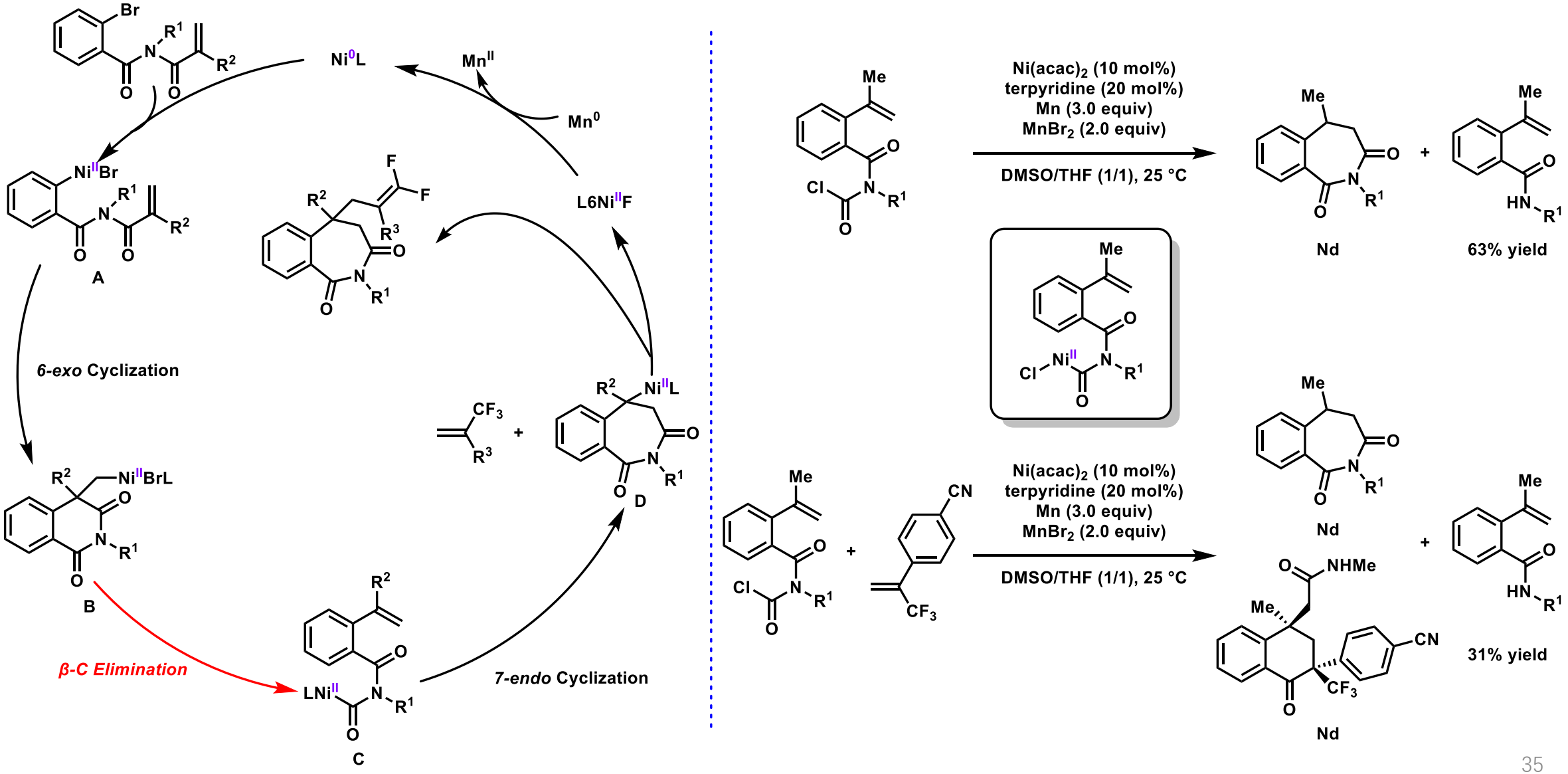


69% yield

Ligand B

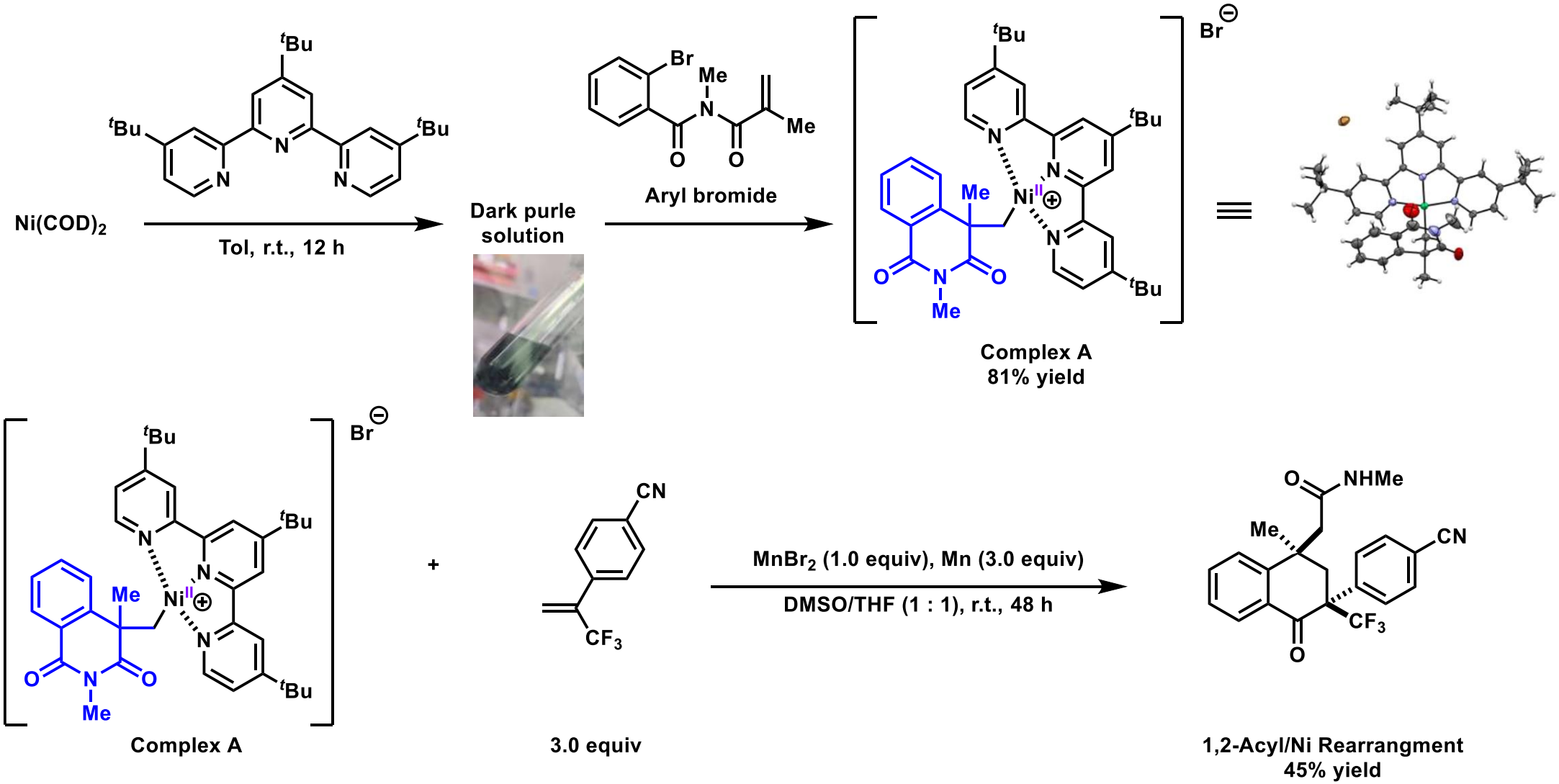
W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

2.5 Switchable Dyotropic Rearrangement



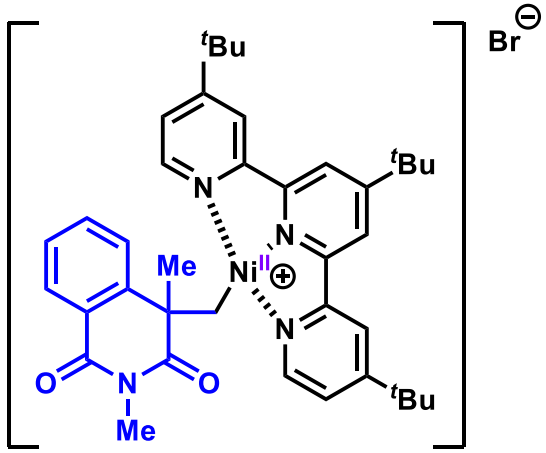
W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

2.5 Switchable Dyotropic Rearrangement



W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

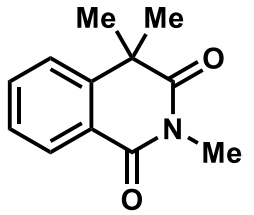
2.5 Switchable Dyotropic Rearrangement



Complex A

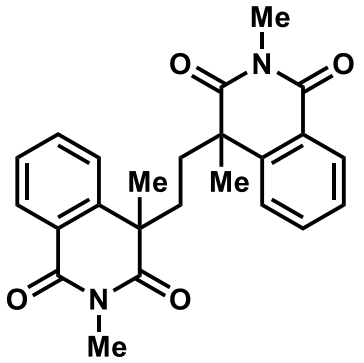
Without Mn^0

DMSO/THF (1 : 1), 30 °C, 18 h

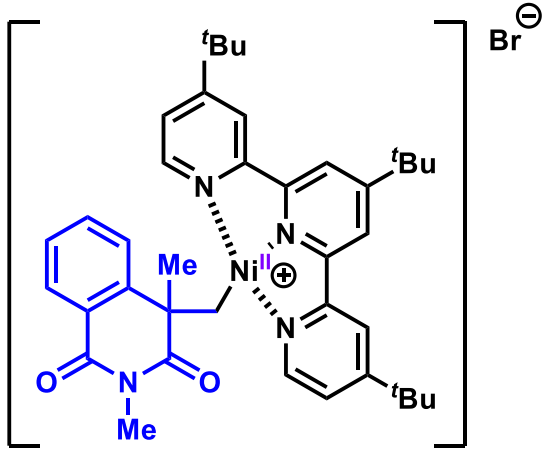


Protonolysis Product
30% yield

+



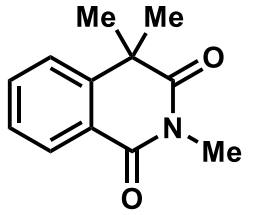
Dimerization Product
22%



Complex A

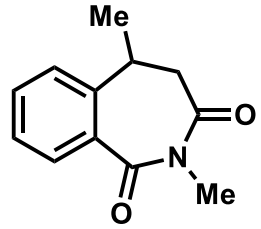
Mn^0 (3.0 equiv)

DMSO/THF (1 : 1), 80 °C, 18 h



Protonolysis Product
30% yield

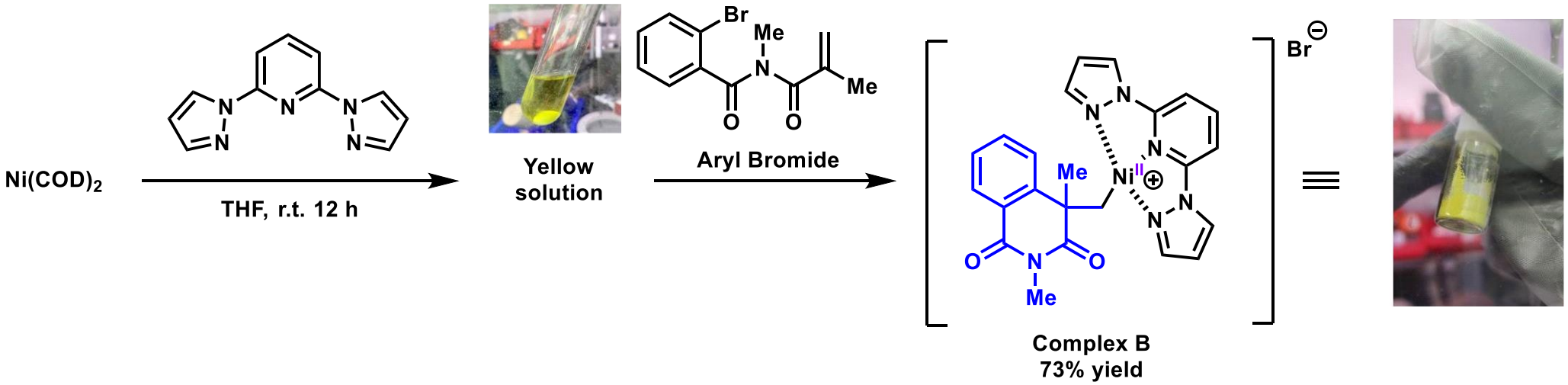
+

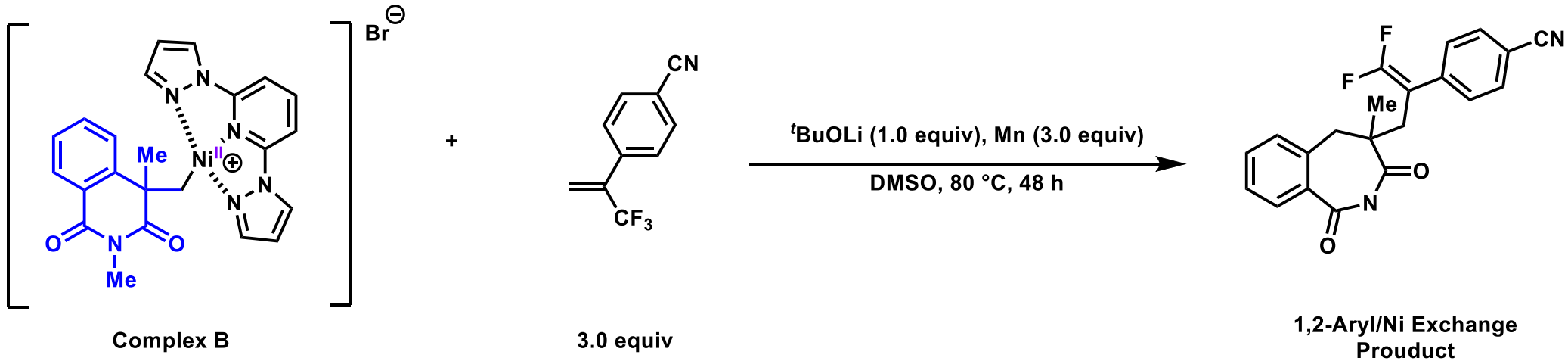


1,2-Acyl/Nikel
Rearrangement Product
40% yield

W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

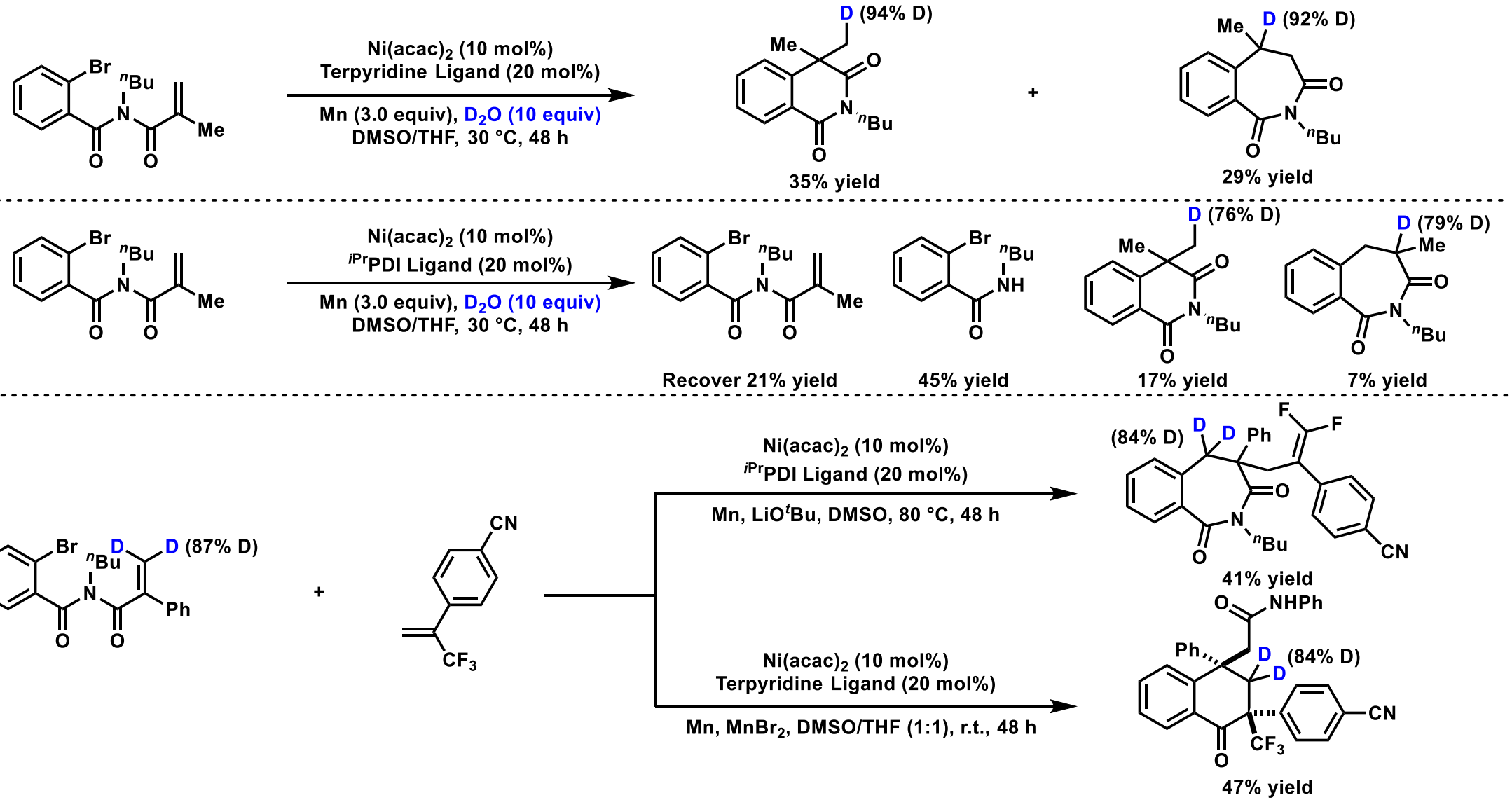
2.5 Switchable Dyotropic Rearrangement





W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

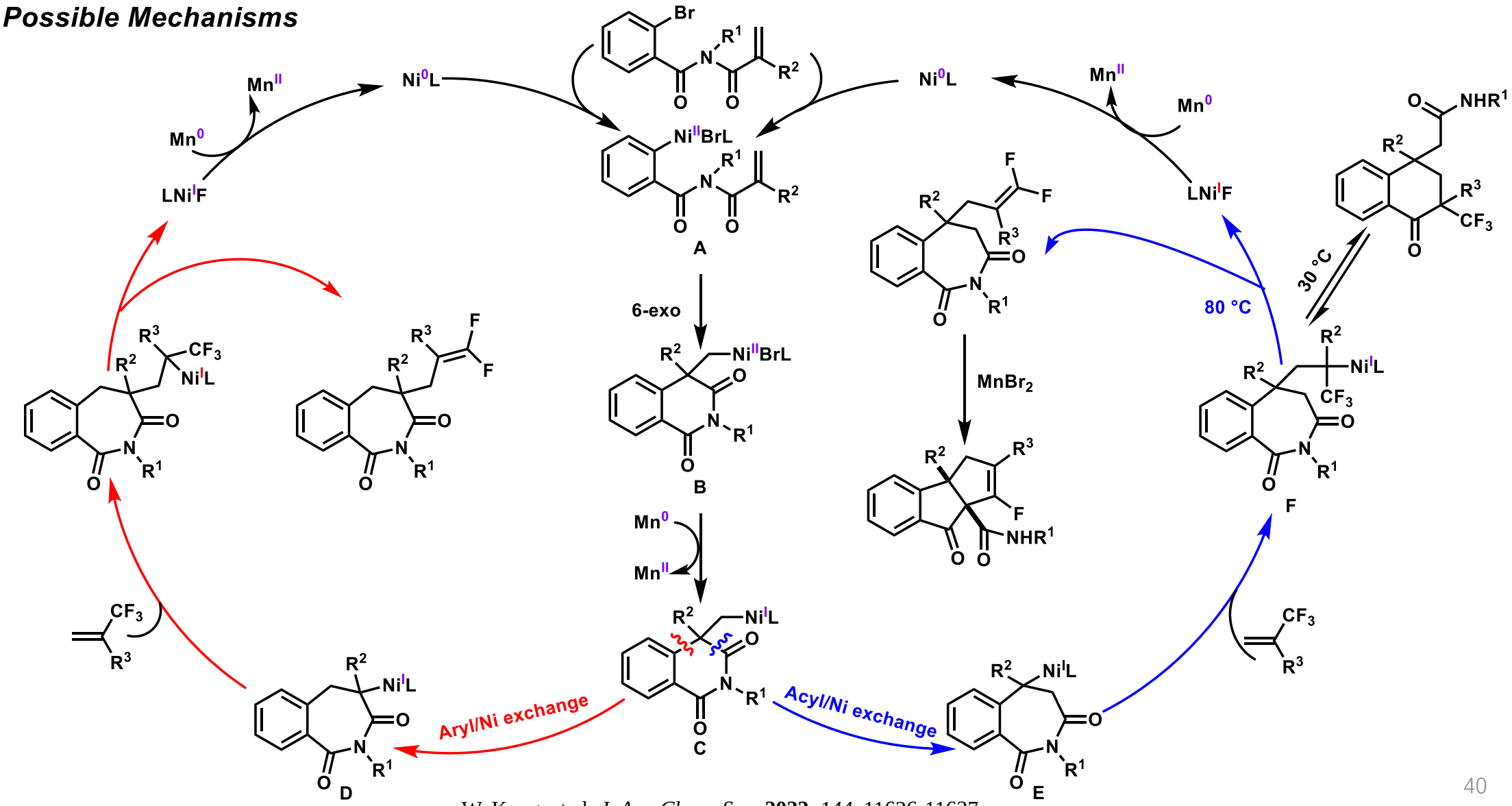
2.5 Switchable Dyotropic Rearrangement



W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

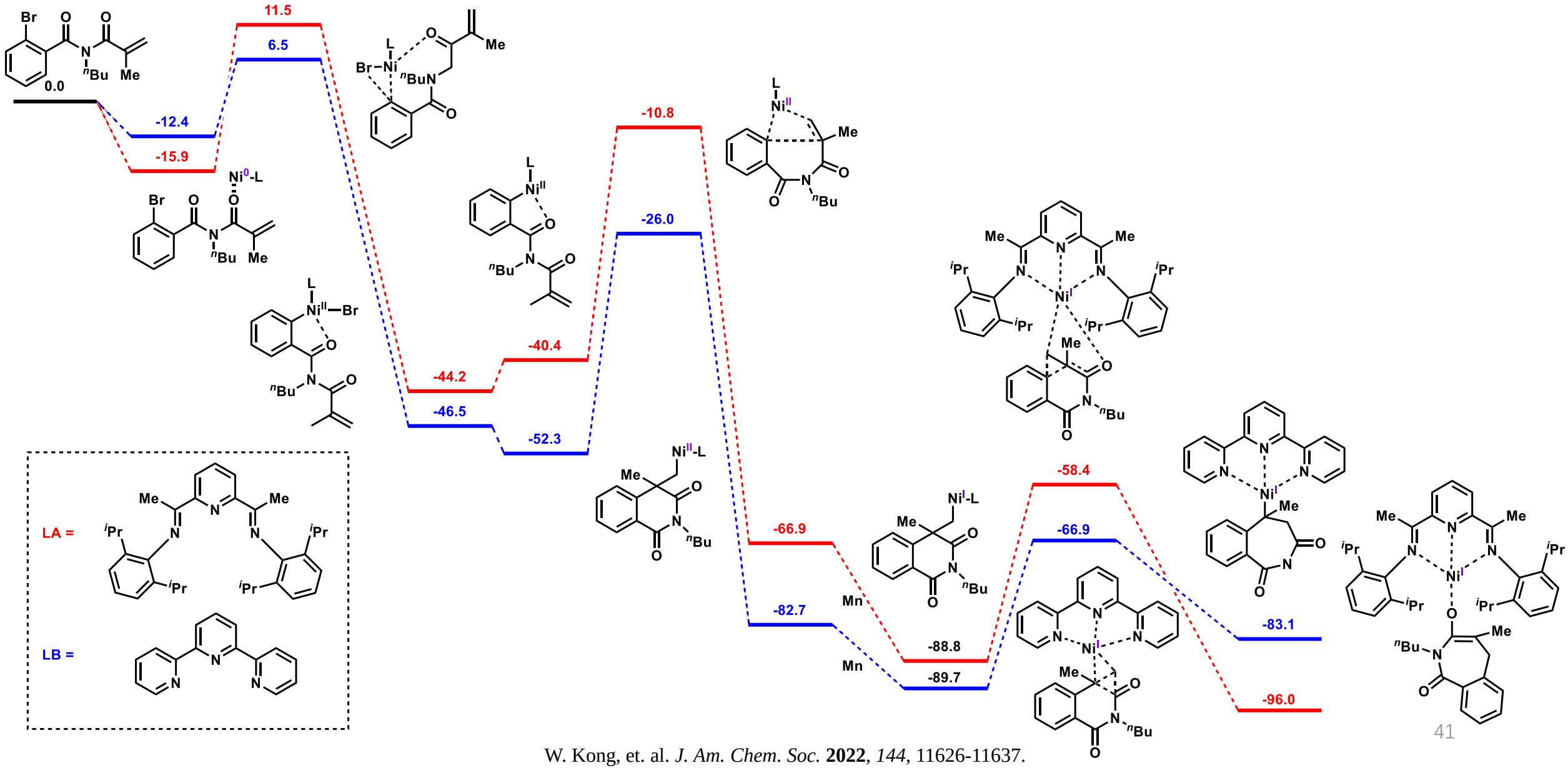
2.5 Switchable Dyotropic Rearrangement

Possible Mechanisms



W. Kong, et al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

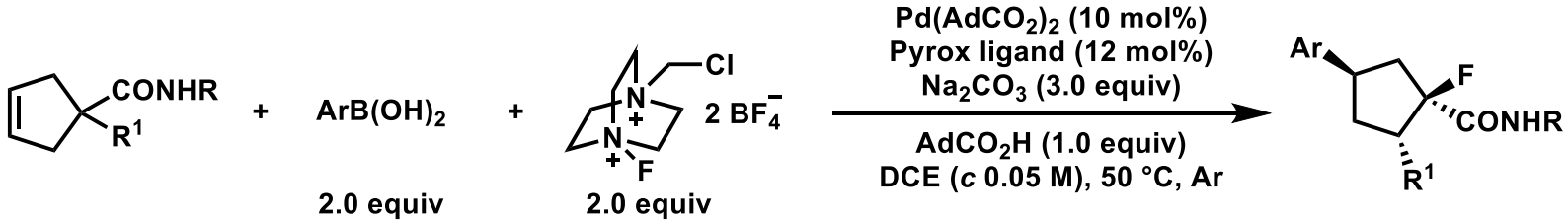
2.5 Switchable Dyotropic Rearrangement



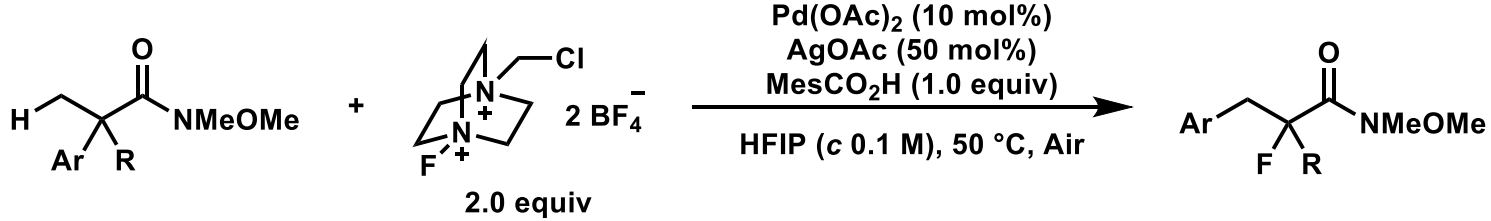
W. Kong, et. al. *J. Am. Chem. Soc.* **2022**, *144*, 11626-11637.

3. Summary and Outlook

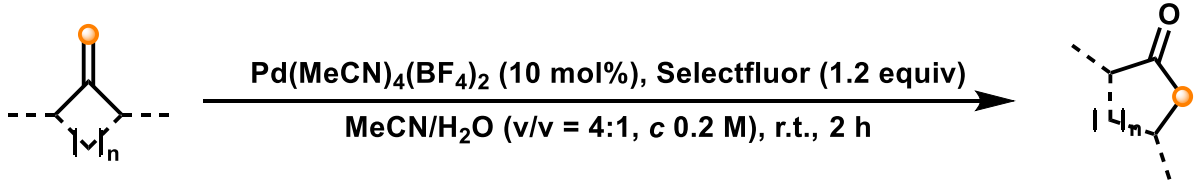
C–C Activation



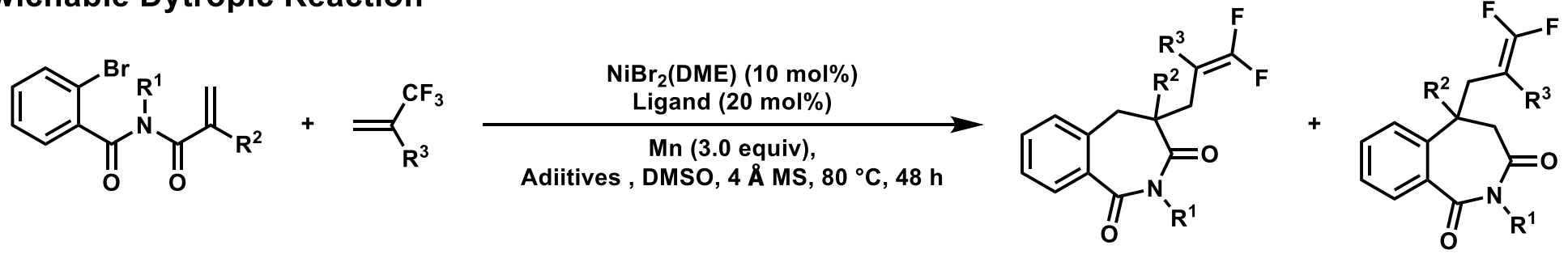
α,β-Difunctionalization



Wacker Reaction



Swichable Dytropic Reaction



3. Summary and Outlook

Transition Metal

- Try new transition metals and change the oxidation states of them to adjust the reactivity.

  Pd^{IV}, Ni^{I}, M^{n}?

  Development of new ligand to adjust the migratory aptitude of different group.

- Move from the Pd^{II}/Pd^{IV} catalytic cycle to Pd^{0}/ Pd^{II} catalytic cycle to avoid oxidants

Scaffold

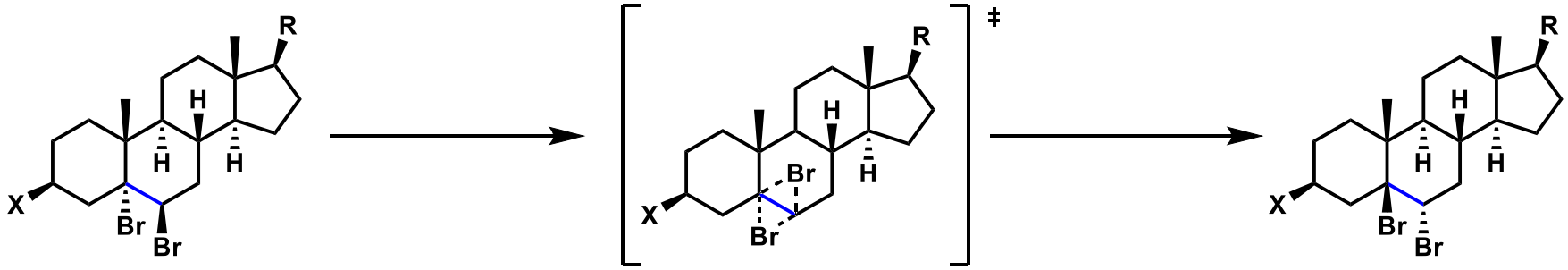
- Move from the C-C to C-X bond.

Thanks For Your Attention

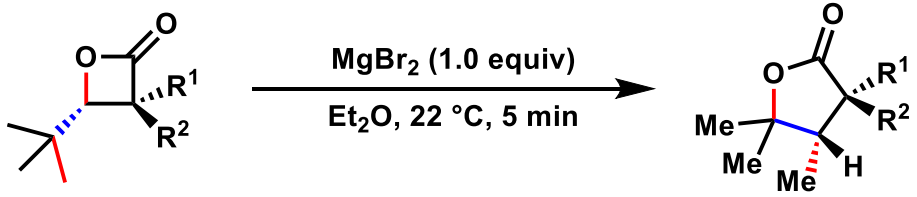
附录

Type I Dyotropic Rearrangements

S. Winstein group (1952) **Earliest examples of a dyotropic rearrangement**

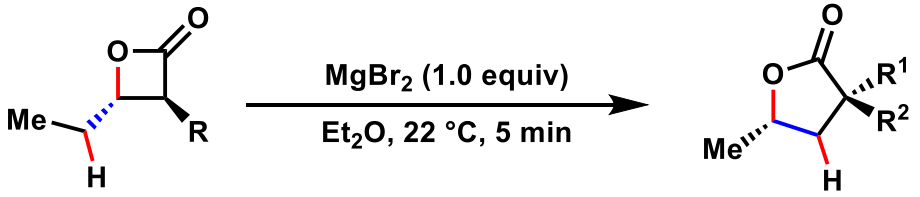


S. Mulzer group (1979)



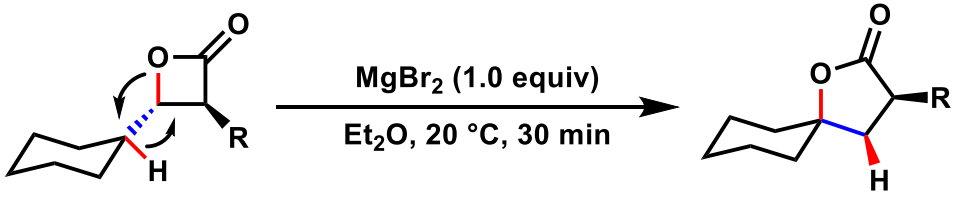
98% yield

H. Black group (1988)



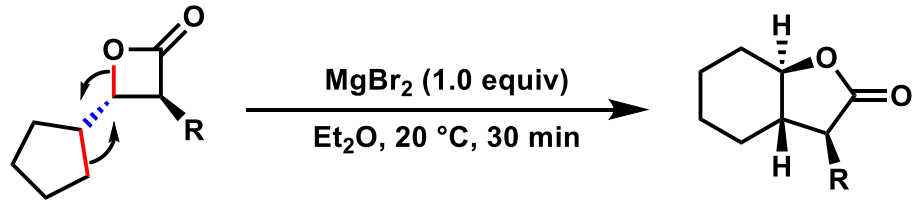
98% yield

H. Black group (1988)



42-86% yield

H. Black group (1988)



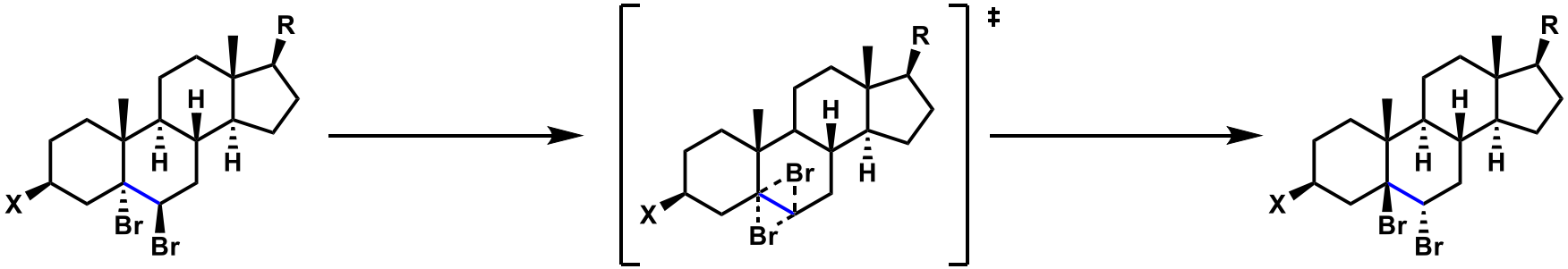
R = Ph, OPh, SPh

98% yield

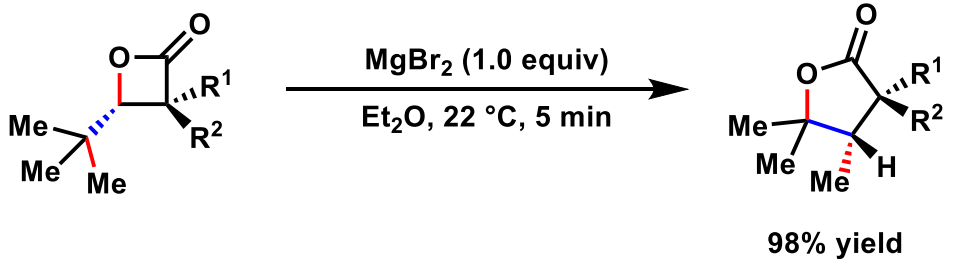
a) S. Winstein, et al. *Helv. Chim. Acta.* **1952,** *35*, 782; b) S. Mulzer, et al. *Angew. Chem. Int. Ed.* **1979**, *18*, 793-795; c) H. Black, et al. *Synth. Commun.* **1988**, *29*, 1747-1749. d) H. Black, et al. *Synth. Commun.* **1988**, *29*, 1747-1749.

1.2 Type I Dyotropic Rearrangement

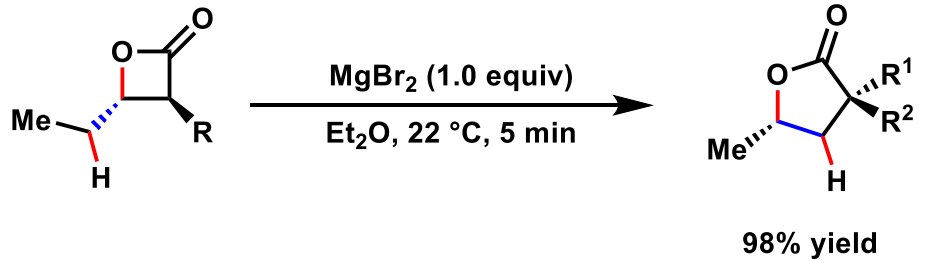
S. Winstein group (1952) **Earliest examples of a dyotropic rearrangement**



S. Mulzer group (1979)



H. Black group (1988)



H. Black group (1988)

a) S. Winstein, et al. *Helv. Chim. Acta.* **1952,** *35*, 782; b) S. Mulzer, et al. *Angew. Chem. Int. Ed.* **1979**, *18*, 793-795; c) H. Black, et al. *Synth. Commun.* **1988**, *29*, 1747-1749. d) H. Black, et al. *Synth. Commun.* **1988**, *29*, 1747-1749.