Topic

陈宜峰教授在有机不对称催化方面的研究

汇报人：张丹　　2025年1月10日

目 录

1. Author introduction

Yi-Feng Chen, Ph. D.

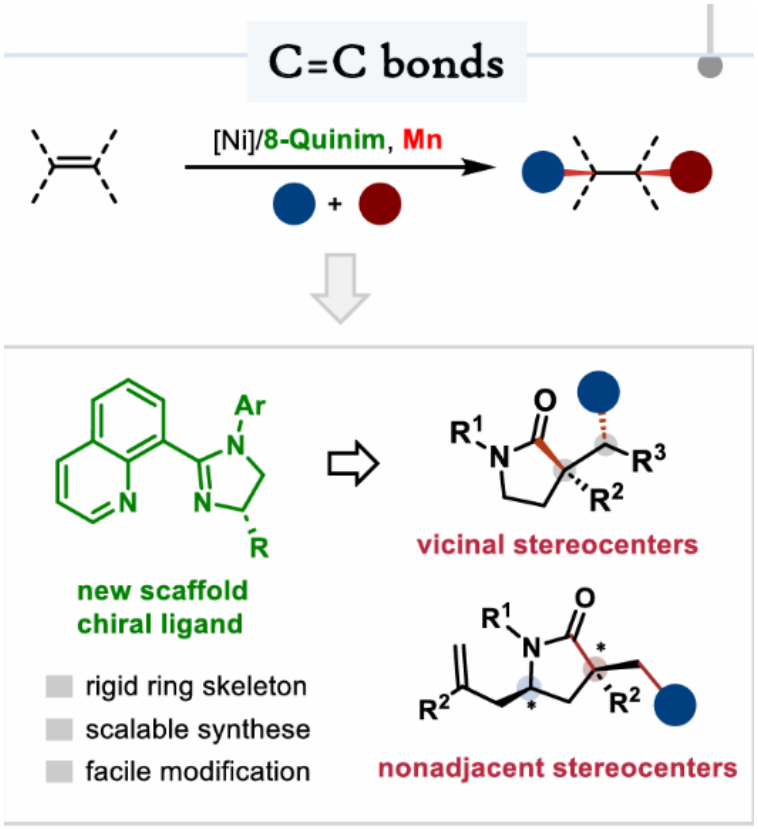
- **Education and research experience**

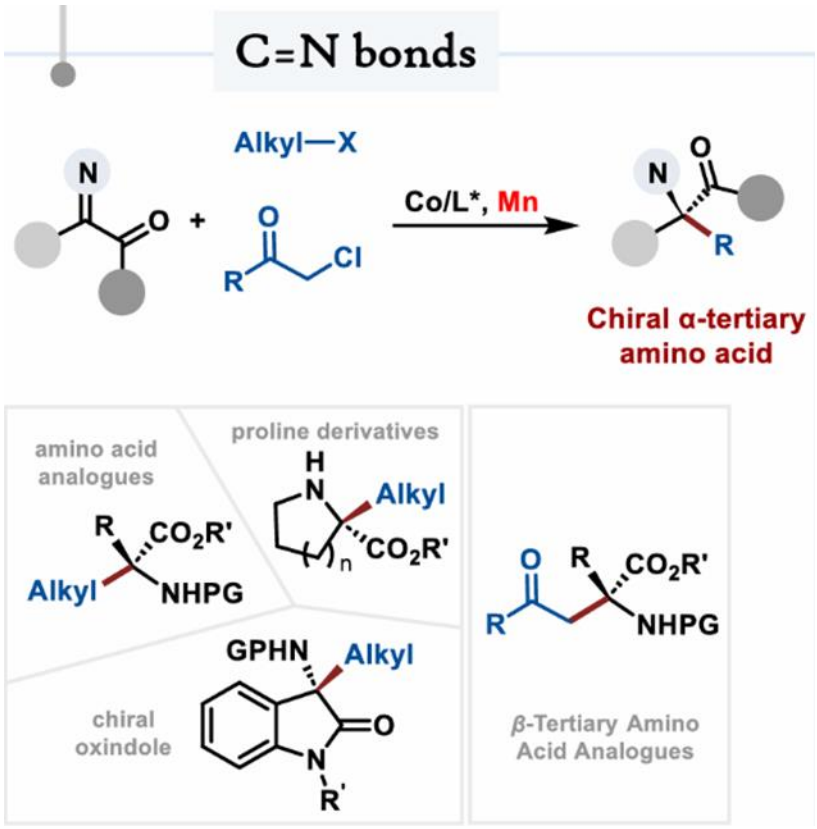
2003-2007	**B.S.** Soochow University. (Advisor: Jianping Zhou)
2007-2012	**Ph.D.** SIOC. (Advisor: Yuanhong Liu)
2012-2013	**Research Assistant.** SIOC. (Advisor: Yuanhong Liu)
2013-2014	**Postdoctoral Fellow.** MIT. (Advisor: Stephen L. Buchwald)
2014 – 2017	**Postdoctoral Fellow.** Yale University. (Advisor: Timothy R. Newhouse)
Present	**Professor.** ECUST.

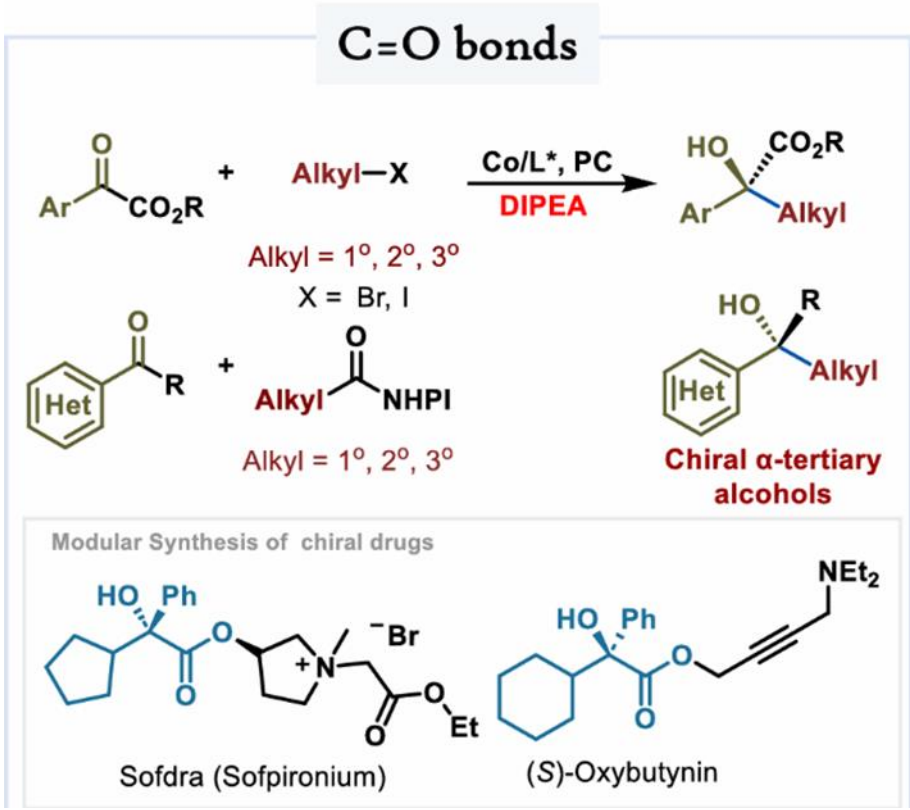
Research field

I.廉价金属催化的羰化反应研究；
II.通过手性配体的从头设计合成来发展不对称催化的新方法。

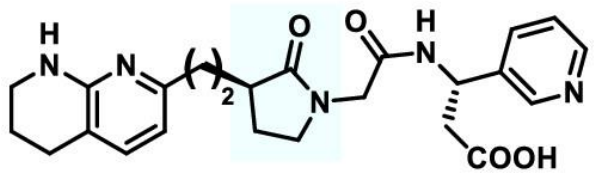
2. Catalytic Asymmetric Reductive Addition (CARA) Reaction



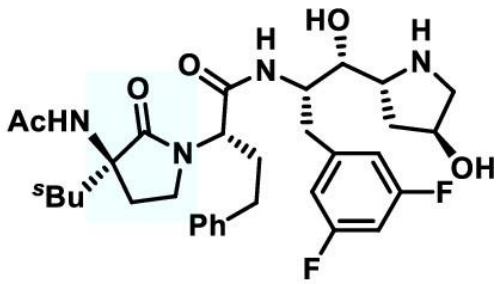




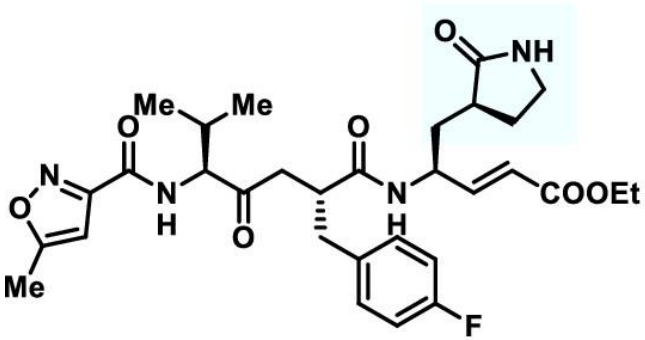
2.1 C=C bonds



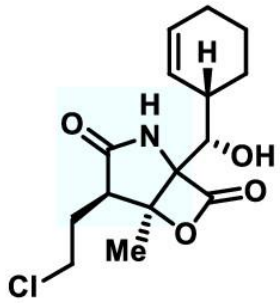
$\alpha_v\beta_3$ integrin antagonists



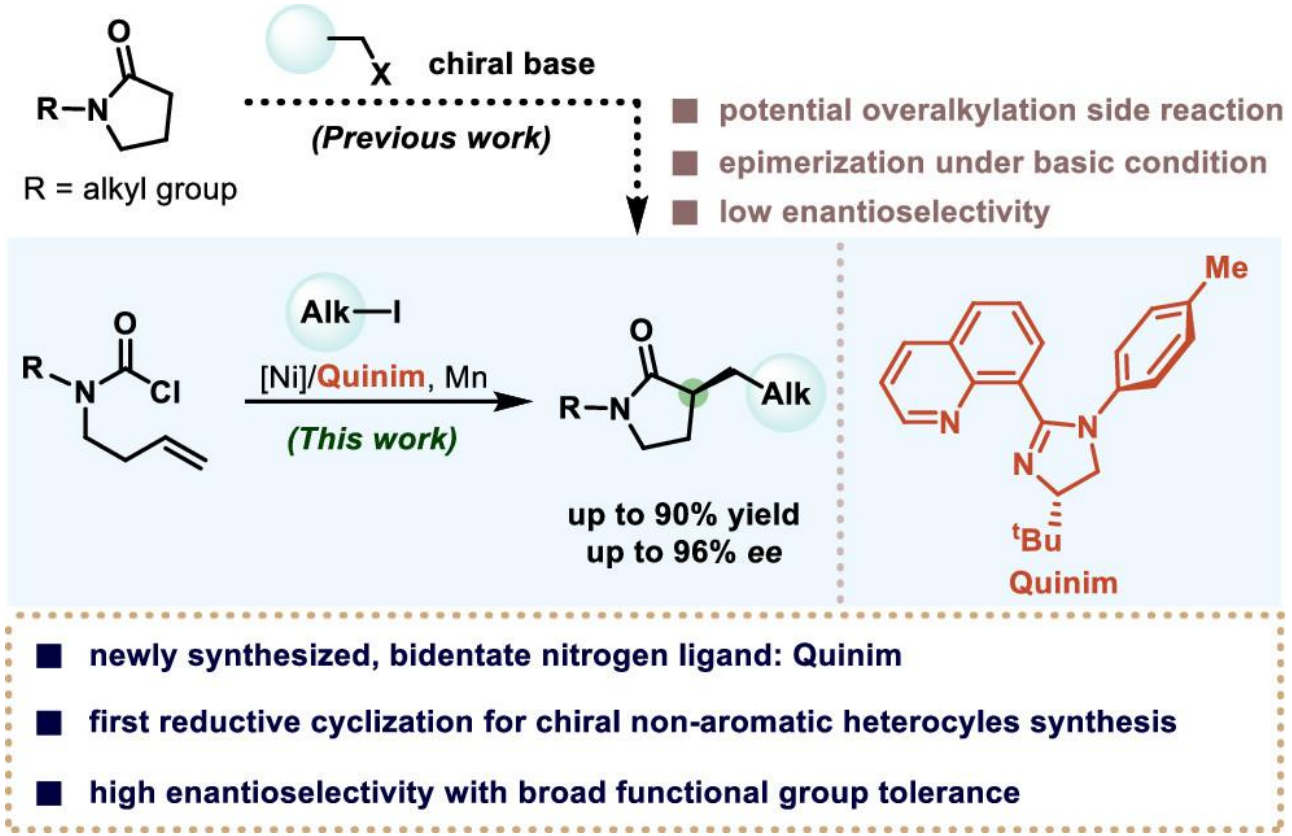
BACE-1 inhibitor



Rupintrivir



(-)-Salinosporamide A



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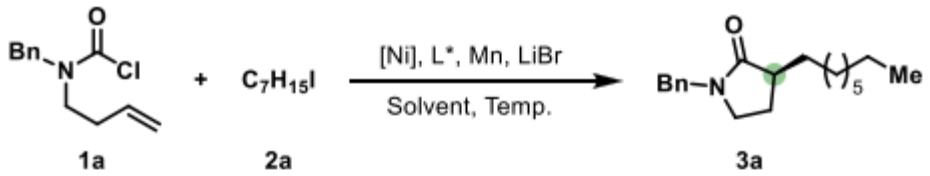
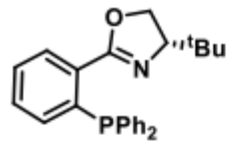
2.1 C=C bonds

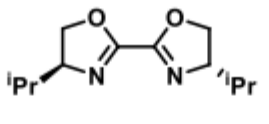


1a 2a 3a

Entry	Ligand	Catalyst	Solvent	Temp. (°C)	3a (%)[b]	e.r.[c]
1	L1	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	0	-
2	L2	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	12	56:44
3	L3	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	33	68:32
4	L4	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	54	85:15
5	L5	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	17	51:49
6	L6	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	0	-
7	L7	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	0	-
8	L8	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	30	30	92:8
9	L8	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	55	96:4
10	L9	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	39	95:5
11	L10	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	46	96:4
12	L11	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	21	84:16
13	L12	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	36	91:9
14	L13	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	39	84:16
15	L14	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	9	96:4
16	L15	$Ni(ClO_4)_2{\cdot}6H_2O$	NMP	0	12	70:30
17	L8	$Ni(ClO_4)_2{\cdot}6H_2O$	DMF	0	64	97:3
18[d]	**L8**	**$Ni(cod)_2$**	**DMF**	**0**	**92 (86)**	**97:3**
19[d,e]	L8	$Ni(cod)_2$	DMF	0	0	-
20[d,f]	L8	$Ni(cod)_2$	DMF	0	16	83.5:16.5



L1



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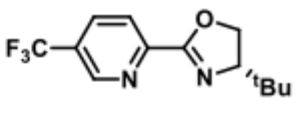

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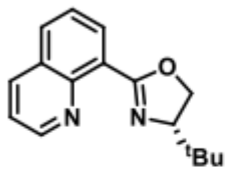

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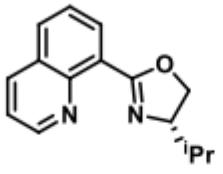

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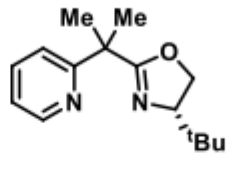

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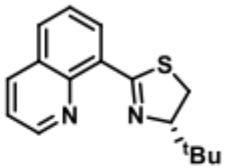

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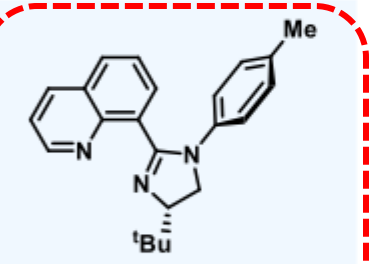
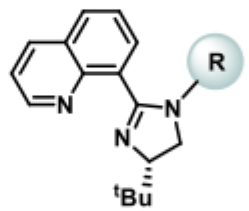


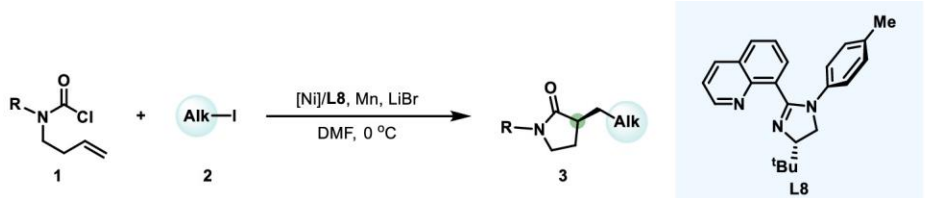
L8



L9, R = C_6H_5
L10, R = 4-^{t}Bu-C_6H_4
L11, R = 4-OMe-C_6H_4
L12, R = 4-CF_3-C_6H_4
L13, R = 3,5-$(CF_3)_2$-C_6H_3
L14, R = 2,4,6-$(CH_3)_3$-C_6H_2
L15, R = Cy

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (3.0 equiv., 0.6 mmol), [Ni] (15 mol%, 0.03 mmol), ligand (22 mol%, 0.044 mmol), Mn (4.0 equiv., 0.8 mmol), LiBr (1.0 equiv., 0.2 mmol), solvent (1 mL) under the indicated temperature for 48 h. [b]Corrected GC yield. [c]Determined by HPLC analysis. [d]$Ni(cod)_2$ (15 mol%, 0.03 mmol); **L8** (18 mol%, 0.036 mmol), 48 h, isolated yield in parentheses. [e] $^n C_7H_{15}Br$ (3.0 equiv) was used instead of **2a**. [f]Zn (4.0 equiv) was used instead of Mn.

2.1 C=C bonds



Variation of alkyl iodide

3a, 86%, 97:3 e.r.
3b, 86%, 97.5:2.5 e.r.
3c, 41%, 90.5:9.5 e.r.
3d, 85%, 94.5:5.5 e.r.
3e, 86%, 96.5:3.5 e.r.
3f, 81%, 96.5:3.5 e.r.
3g, 79%, 97:3 e.r.
3h, 87%, 95:5 e.r.
3i, 64%, 94:6 e.r.
3j, 35%, 91:9 e.r.[b]
3k, 62%, 90.5:9.5 d.r.
3l, 82%, 95:5 e.r.
3m, 55%, 95.5:4.5 e.r.
3n, 70%, 95.5:4.5 e.r.
3o, 87%, 95:5 e.r.
3p, 76%, 94.5:5.5 e.r.
3q, 63%, 97:3 e.r.
3r, 44%, 93.5:6.5 e.r.
3s, 90%, 97:3 e.r.

Variation of carbamoyl chloride

N-aryl substituted pyrrolidinone

3t, 53%, 94:6 e.r.
3u, 67%, 95:5 e.r.
3v, 66%, 92:8 e.r.
3w, 74%, 95.5:4.5 e.r.
3x, 40%, 93:7 e.r.

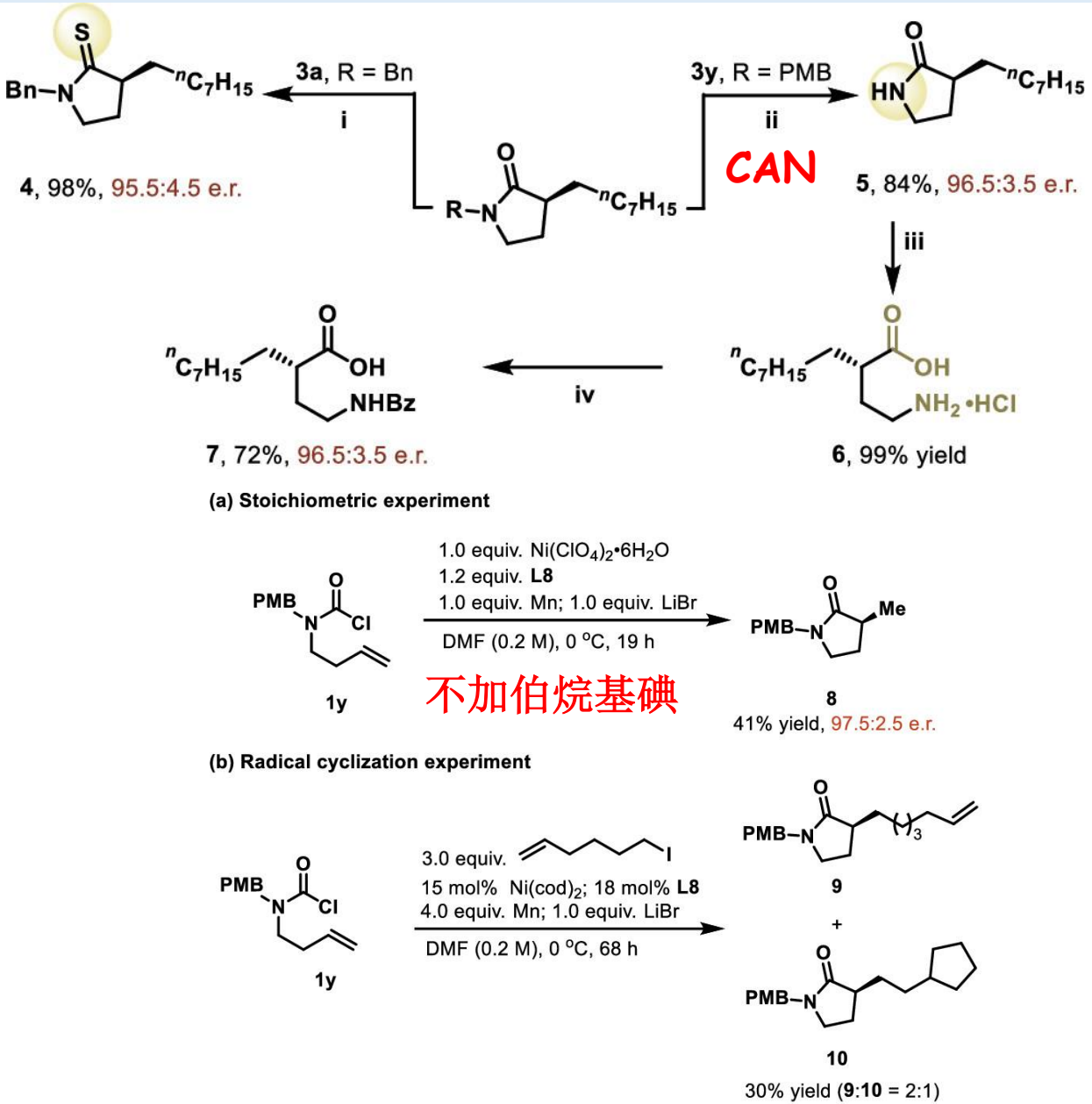
N-alkyl substituted pyrrolidinone

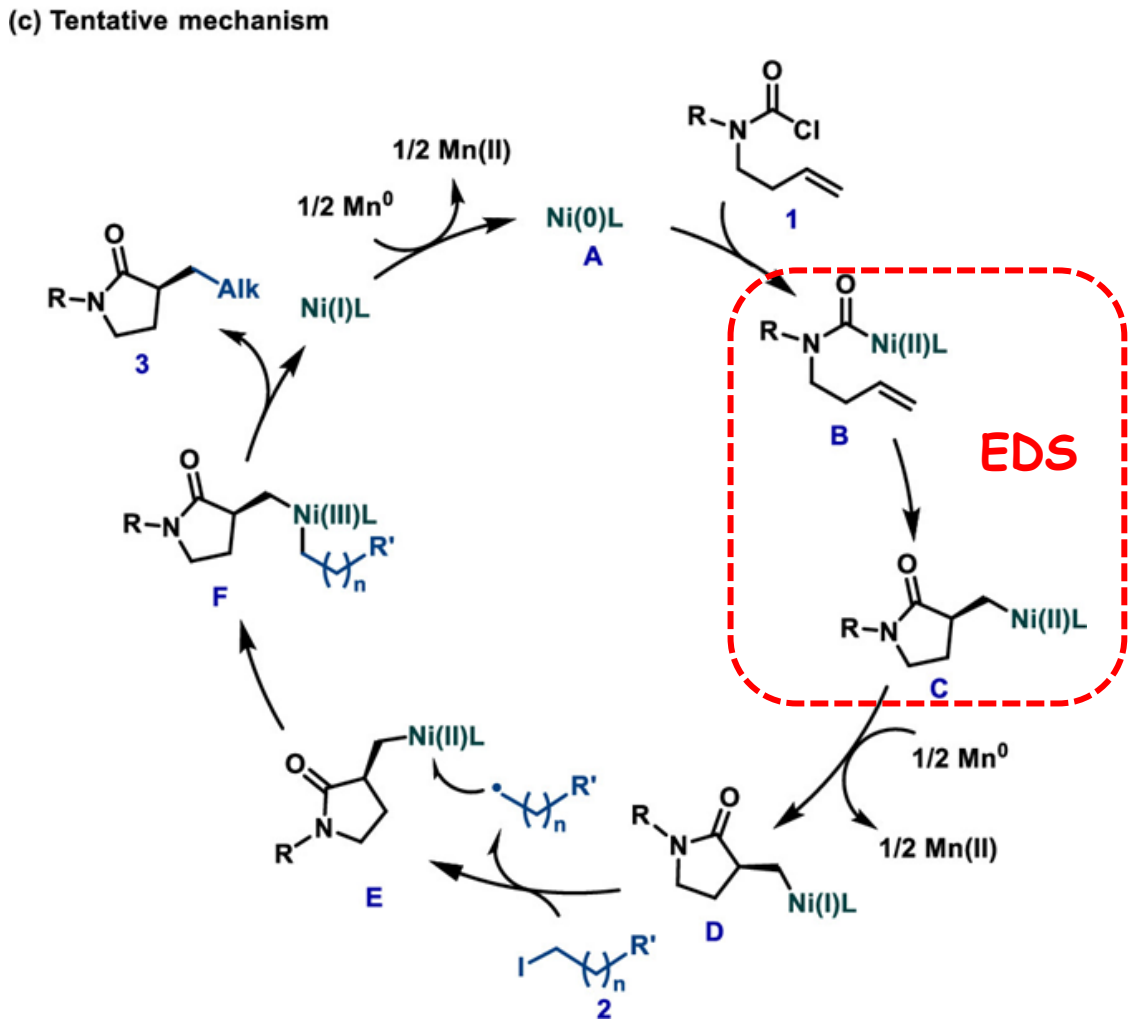
3y, 83%, 97:3 e.r.
3z, 82%, 96:4 e.r.
3aa, 88%, 94.5:5.5 e.r.
3ab, 84%, 94:6 e.r.
3ac, 80%, 95.5:4.5 e.r.
3ad, 84%, 96:4 e.r.
3ae, 62%, 94:6 e.r.
3af, 84%, 96.5:3.5 e.r.
3ag, 81%, 98:2 e.r.
3ah, 85%, 95:5 e.r.
3ai, 59%, 95.5:4.5 e.r.
3aj, 70%, 95.5:4.5 e.r.
3ak, 72%, 94.5:5.5 e.r.
3al, 73%, 95:5 e.r.
3am, 61%, 95.5:4.5 d.r.

Limitations

3an, low yield
3ao, low yield
3ap, low yield
3aq, no reaction

2.1 C=C bonds

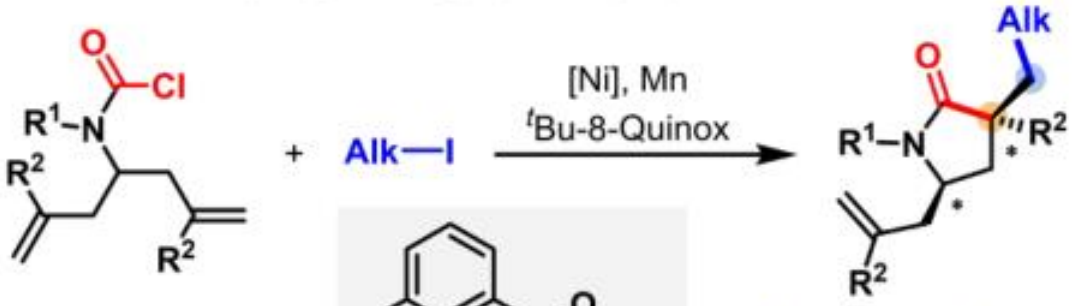

3a, R = Bn
i
3y, R = PMB
ii
CAN
4, 98%, 95.5:4.5 e.r.
5, 84%, 96.5:3.5 e.r.
iii
iv
7, 72%, 96.5:3.5 e.r.
6, 99% yield
(a) Stoichiometric experiment
1.0 equiv. Ni(ClO4)2•6H2O
1.2 equiv. L8
1.0 equiv. Mn; 1.0 equiv. LiBr
DMF (0.2 M), 0 °C, 19 h
1y
不加伯烷基碘
8
41% yield, 97.5:2.5 e.r.
(b) Radical cyclization experiment
3.0 equiv.
15 mol% Ni(cod)2; 18 mol% L8
4.0 equiv. Mn; 1.0 equiv. LiBr
DMF (0.2 M), 0 °C, 68 h
1y
9
+
10
30% yield (9:10 = 2:1)

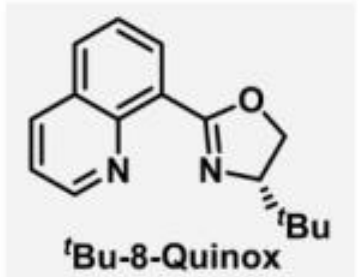

(c) Tentative mechanism
1/2 Mn(II)
1/2 Mn0
Ni(0)L
A
Ni(I)L
Alk
3
1
Ni(II)L
B
EDS
C
Ni(III)L
F
1/2 Mn0
1/2 Mn(II)
Ni(II)L
E
D
Ni(I)L
2

2.1 C=C bonds

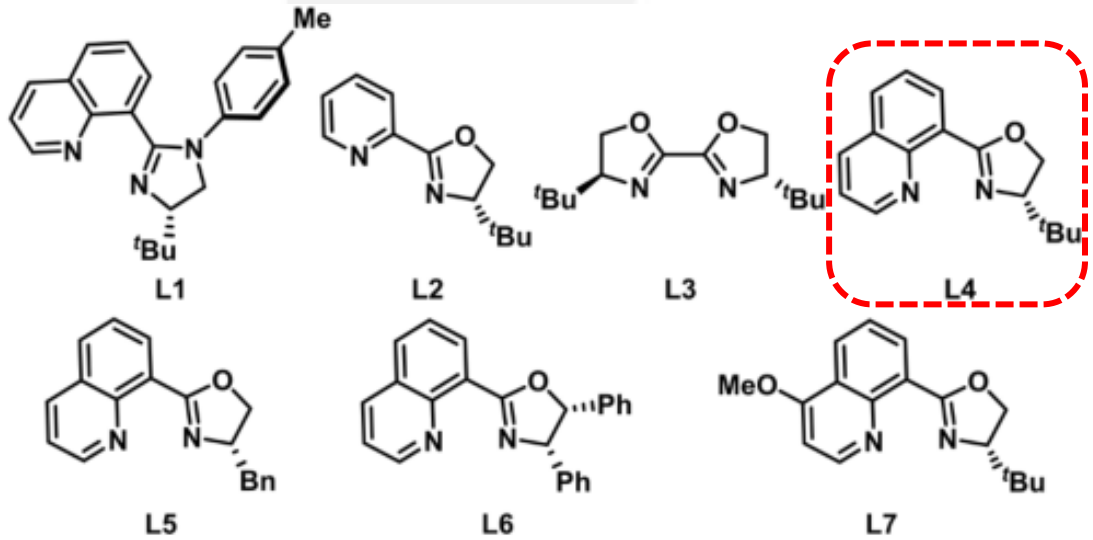
c) Desymmetric dicarbofunctionalization of unactivated alkene

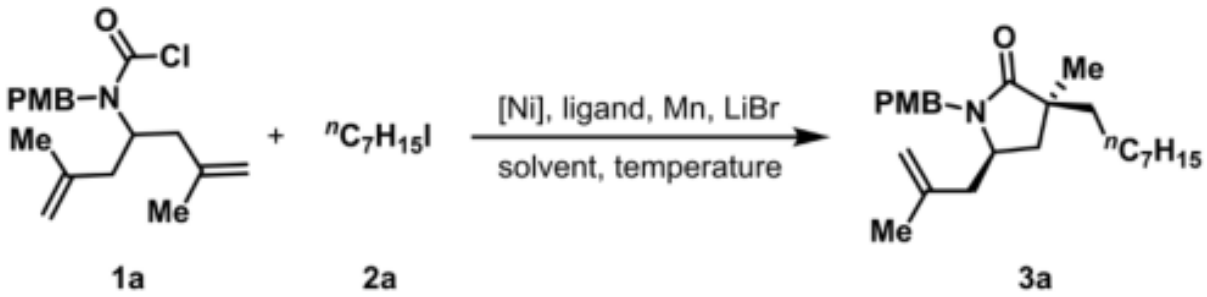
■ Cross-coupling strategy (this report)





2 stereogenic centers with high er and dr





1a 2a 3a

entry	ligand	catalyst	solvent	T (°C)	3a[b]	er[c]	dr[d]
1	L1	$NiBr_2$•DME	DMF (0.2 M)	10	27	90:10	>20:1
2	L2	$NiBr_2$•DME	DMF (0.2 M)	10	0	-	-
3	L3	$NiBr_2$•DME	DMF (0.2 M)	10	0	-	-
4	L4	$NiBr_2$•DME	DMF (0.2 M)	10	29	94:6	>20:1
5	L4	$NiBr_2$•DME	DMA (0.2 M)	10	34	94:6	>20:1
6	L4	$NiBr_2$•DME	DMA (0.2 M)	25	37	95:5	>20:1
7	L4	$NiBr_2$•DME	DMA (0.4 M)	25	53	96.5:3.5	>20:1
8	L4	$Ni(ClO_4)_2$•$6H_2O$	DMA (0.4 M)	25	92	98.5:1.5	>20:1
9	L5	$Ni(ClO_4)_2$•$6H_2O$	DMA (0.4 M)	25	78	75.5:24.5	17:1
10	L6	$Ni(ClO_4)_2$•$6H_2O$	DMA (0.4 M)	25	43	67:33	3:1
11	L7	$Ni(ClO_4)_2$•$6H_2O$	DMA (0.4 M)	25	92	98:2	>20:1

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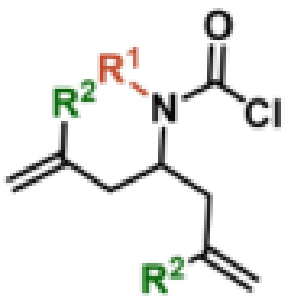
2.1 C=C bonds



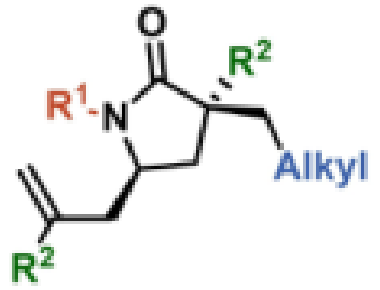
1

R^2=Me,Et

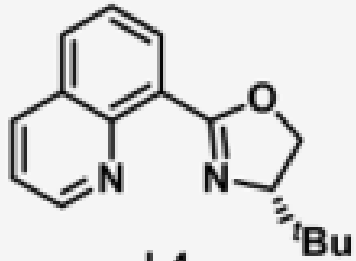
+ I—Alkyl (3.0 equiv)

2

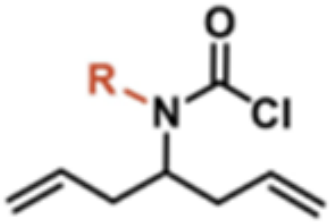
10 mol% $Ni(ClO_4)_2 \cdot 6H_2O$
12 mol% **L4**
3.0 equiv Mn; 1.0 equiv LiBr
DMA (0.4 M), 25 °C



3



L4

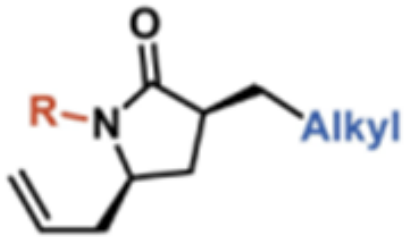


4

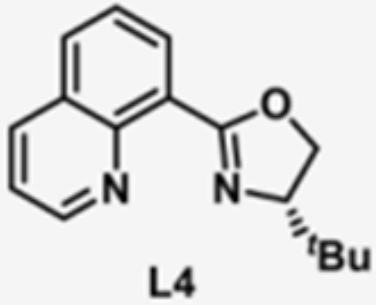
+ I—Alkyl (3.0 equiv)

2

10 mol% $Ni(ClO_4)_2 \cdot 6H_2O$
12 mol% **L4**
3.0 equiv Mn; 1.0 equiv LiBr
DMF (0.4 M), 10 °C

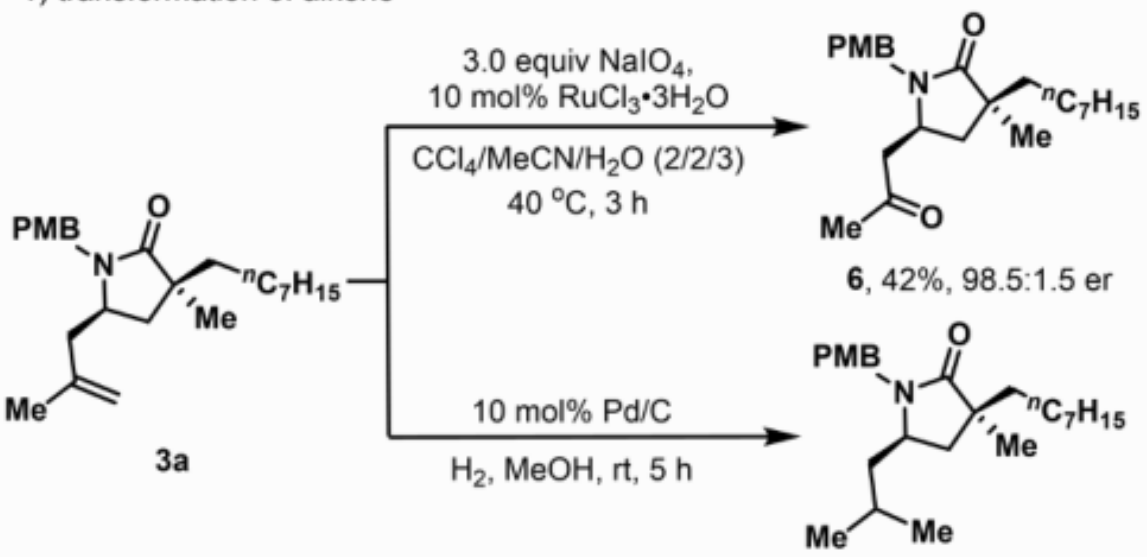


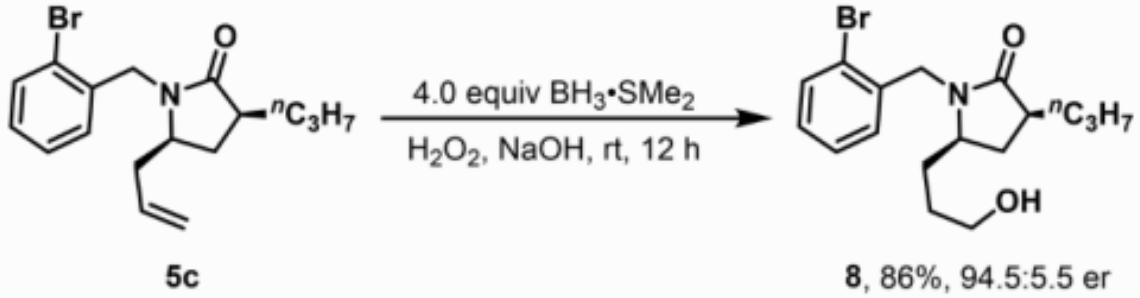
5



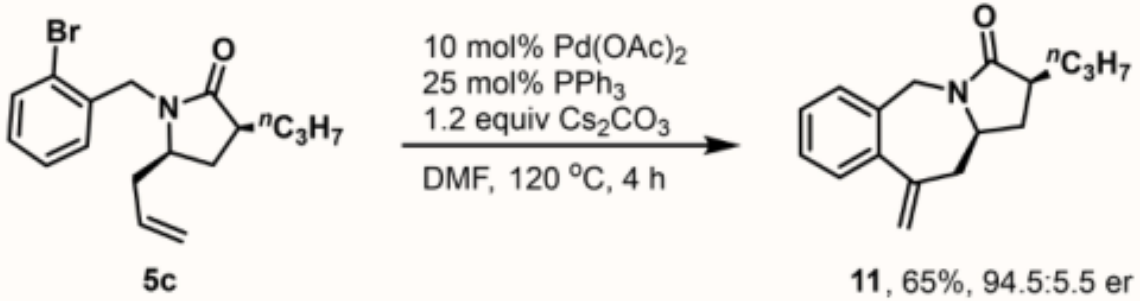
L4

1) transformation of alkene

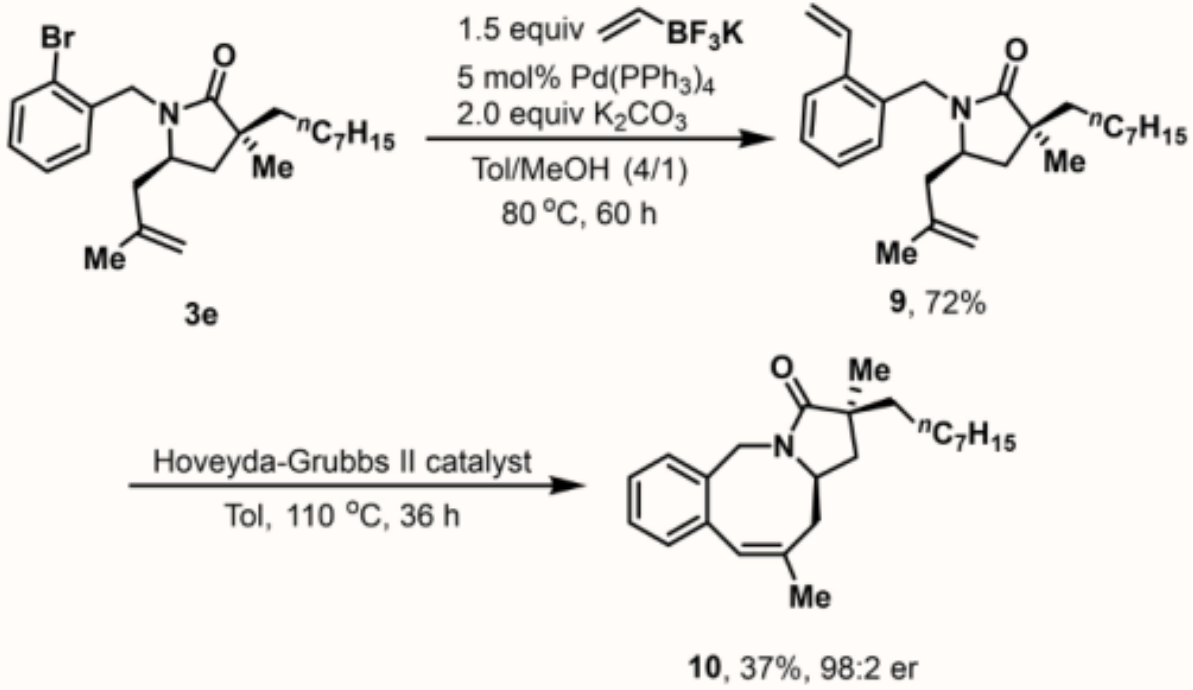




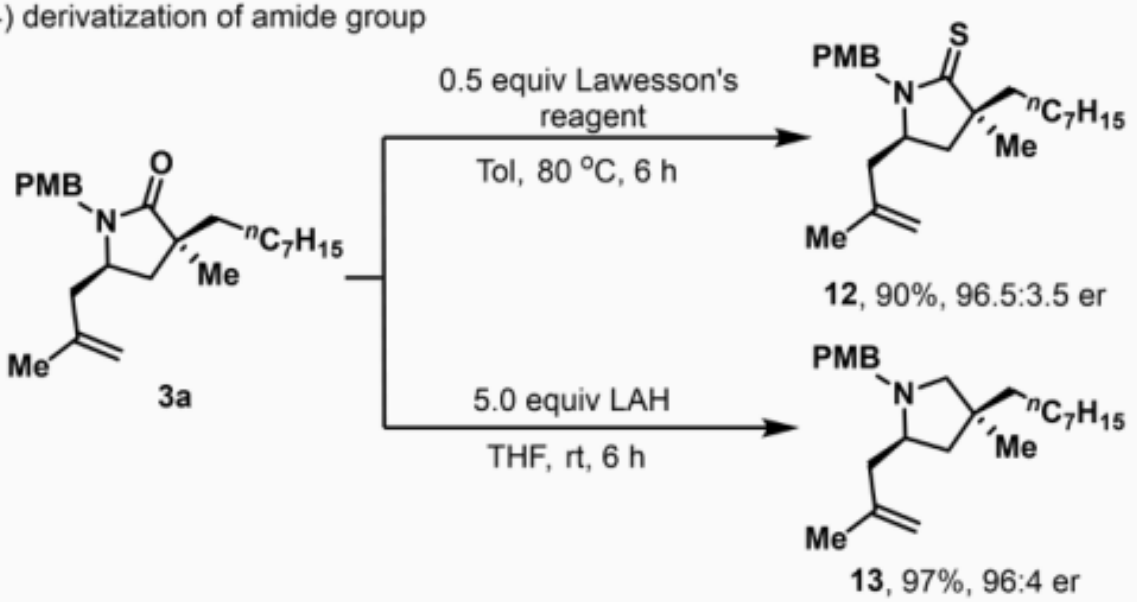
3) Heck reaction



2) RCM reaction

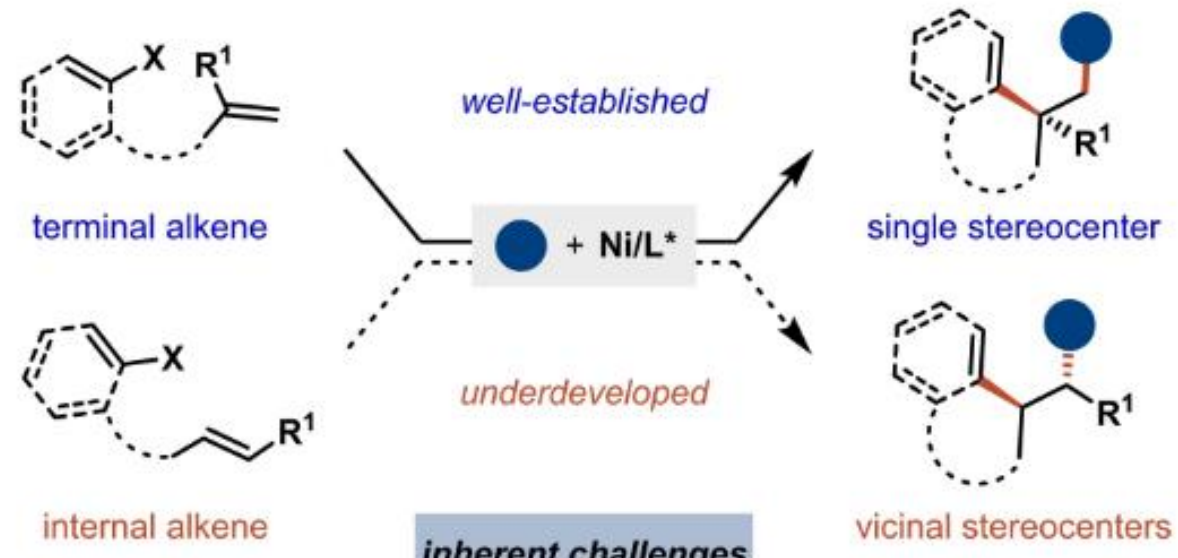


4) derivatization of amide group

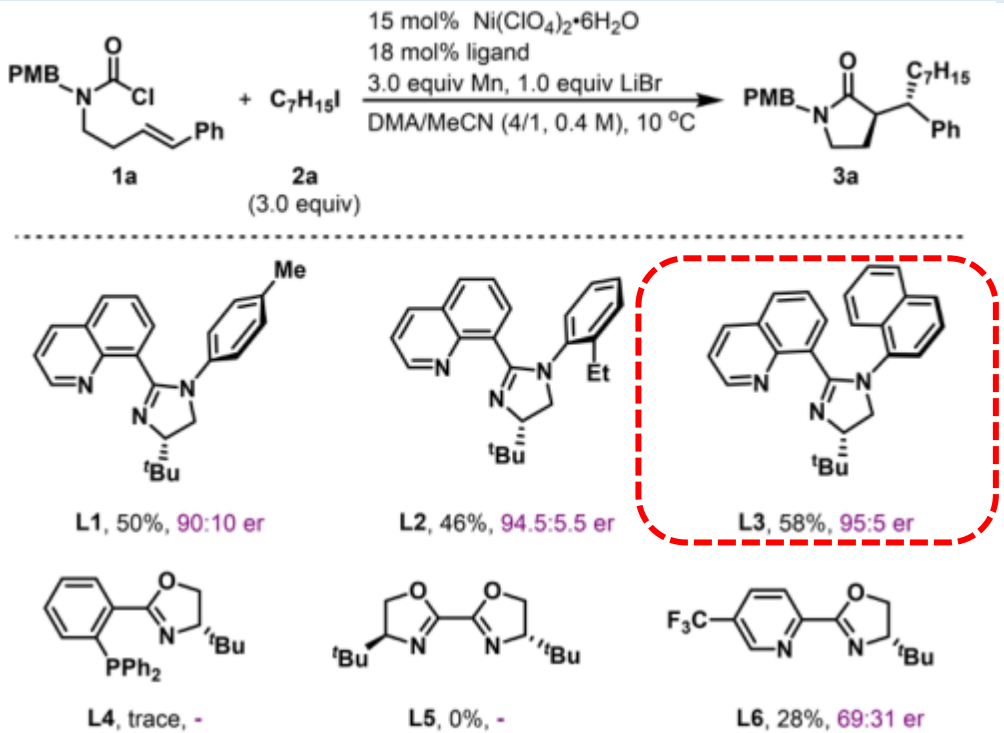


2.1 C=C bonds

a) Ni-catalyzed enantioselective difunctionalization of pendant alkenes



- low affinity of internal alkenes for migratory insertion
- diastereoselectivity issue for vicinal stereogenic centers
- potential Heck reaction through undesired β-H elimination

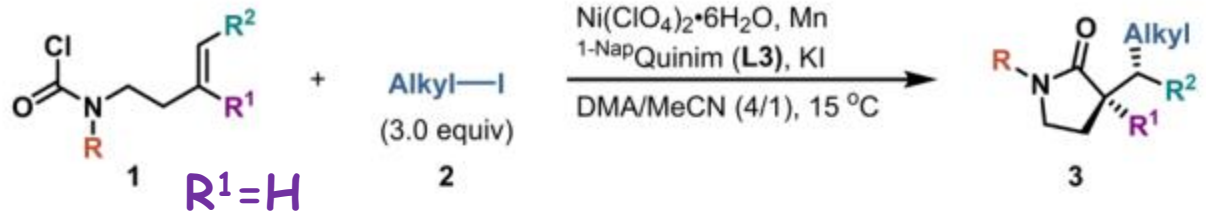


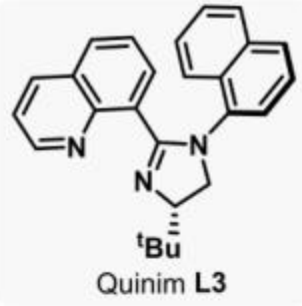
Entry	Deviation from standard condition	3a (%)[b]	e.r.[c]
1	none	58	95:5
2	DMA as solvent	51	89:11
3	MeCN as solvent	<5	-
4	$Ni(cod)_2$ instead of $Ni(ClO_4)_2$•$6H_2O$	30	85.5:14.5
5	$NiBr_2$•DME instead of $Ni(ClO_4)_2$•$6H_2O$	36	89:11
6	Zn instead of Mn	5	85.5:14.5
7	KI instead of LiBr	67	97:3
8[d]	15 °C	77 (69)	97:3

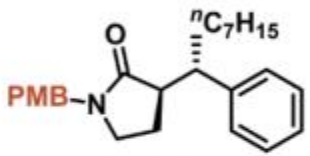
analysis. All the diastereoselectivities are >20:1. [d] $Ni(ClO_4)_2$•$6H_2O$ (20 mol%, 0.020 mmol), **L3** (24 mol%, 0.024 mmol) with 1.0 equiv KI (1.0 equiv, 0.1 mmol) as additive; isolated yield is reported in parentheses.

Angew. Chem. Int. Ed. **2022**, *61*, e202207536.

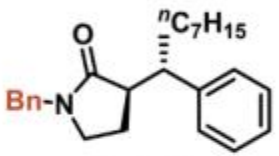
2.1 C=C bonds



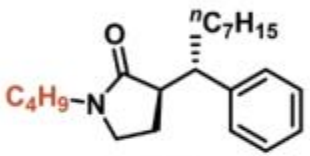




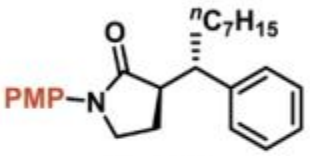
3a, 69%
97:3 er, 31:1 dr



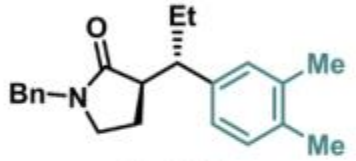
3b, 68%
95.5:4.5 er, >99:1 dr



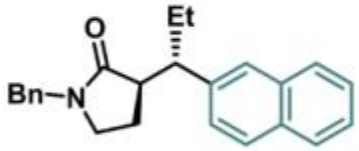
3c, 59%
96.5:3.5 er, >99:1 dr



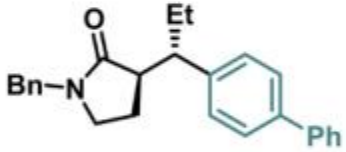
3d, 38%
96:4 er, >99:1 dr



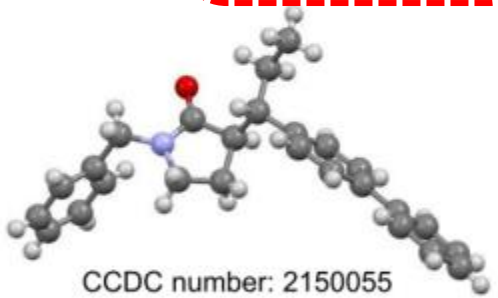
3e, 63%
98.5:1.5 er, >99:1 dr



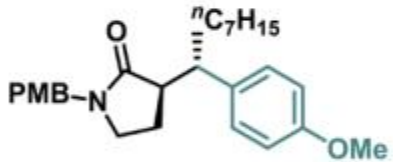
3f, 75%
97:3 er, >99:1 dr



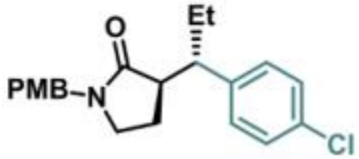
3g, 68%
95.5:4.5 er, >99:1 dr



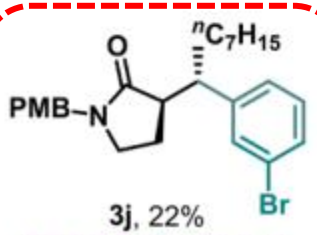
CCDC number: 2150055



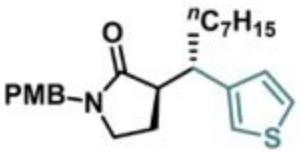
3h, 76%
97:3 er, 24:1 dr



3i, 50%
94.5:5.5 er, >99:1 dr

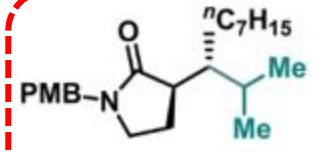


3j, 22%
90.5:9.5 er, >99:1 dr

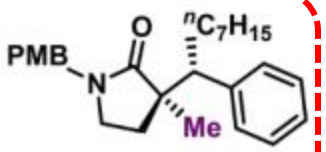


3k, 86%
97.5:2.5 er, 7:1 dr

乙烯基芳烃可能用于稳定Ni中间体



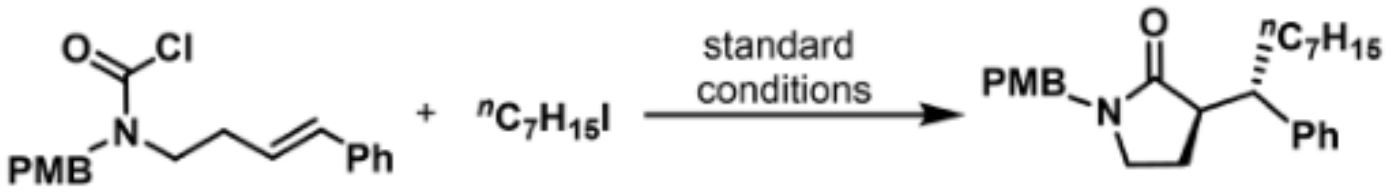
3l, low yield



3m, N.D.

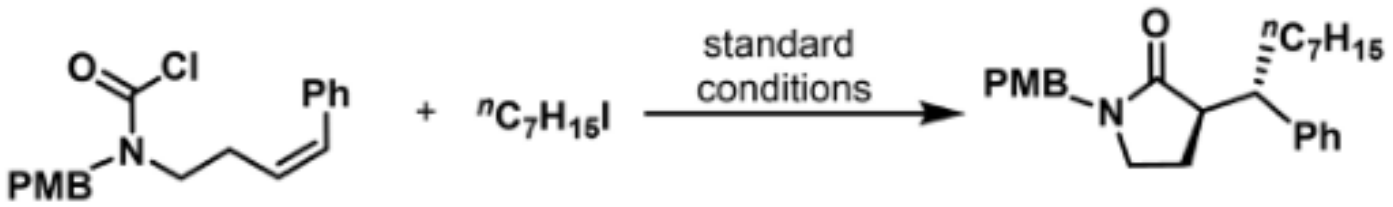
2.1 C=C bonds

(a) Ni-catalyzed enantioselective alkyl-carbamoylation of *trans*-alkenes



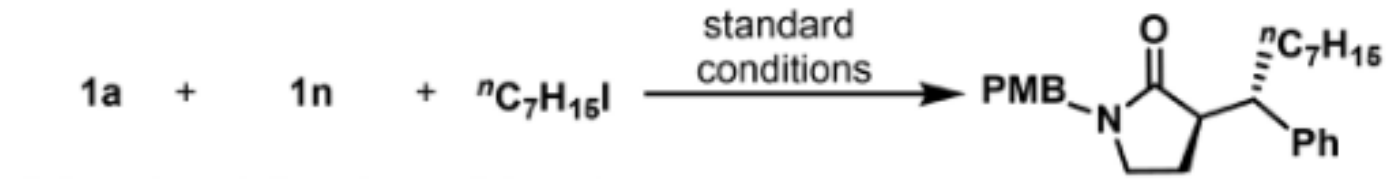
1a 3.0 equiv **3a**, 69%, 97:3 er, 31:1 dr

(b) Ni-catalyzed enantioselective alkyl-carbamoylation of *cis*-alkenes



1n 3.0 equiv **3a**, 62%, 98:2 er, 31:1 dr

(c) crossover experiments of *trans*- and *cis*-alkenes



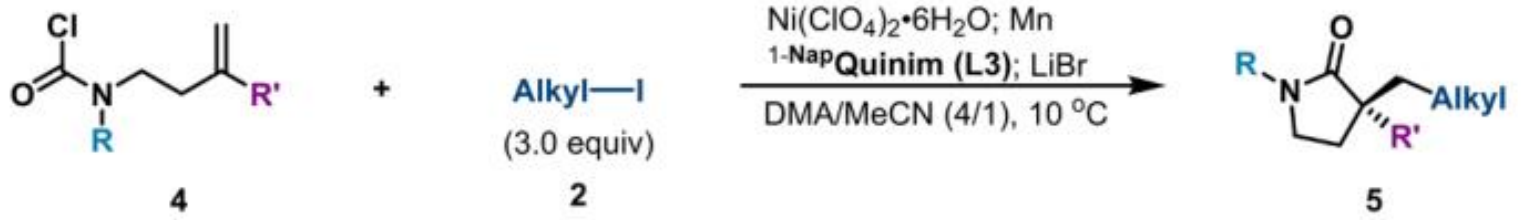
0.5 equiv 0.5 equiv 3.0 equiv **3a**, 55%, 97:3 er, 31:1 dr

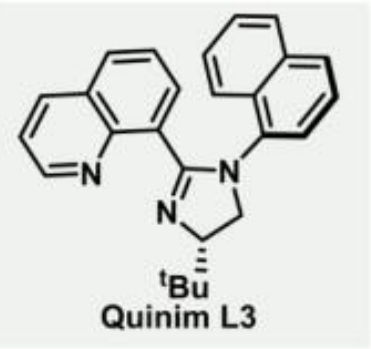
两种不同Z/E构型的烯烃底物

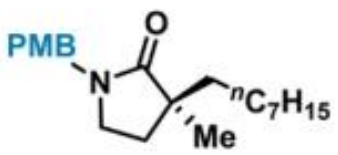
相同的主要非对映异构体

吡咯烷酮产物的立体化学与烯烃起始原料的构型无关

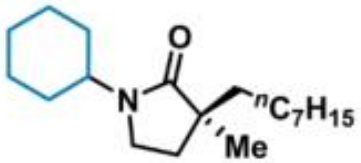
2.1 C=C bonds



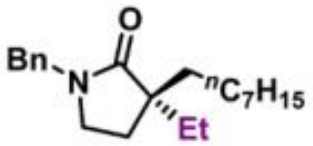




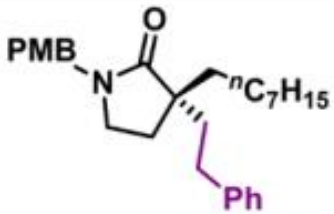
5a, 85%, 96.5:3.5 er
74%, 92:8 er[b]



5b, 88%, 96.5:3.5 er

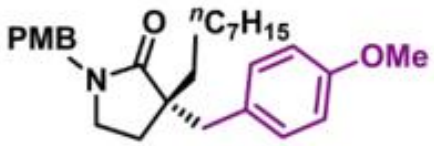


5c, 91%, 96.5:3.5 er

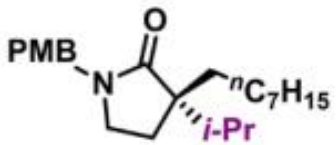


5d, 95%, 97.5:2.5 er

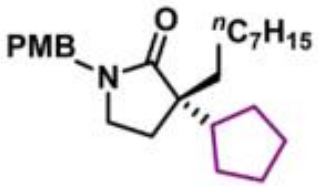
5e, 54%, 96:4 er



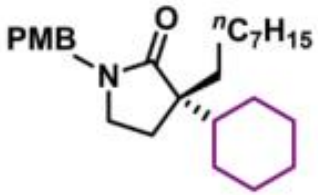
5f, 88%, 95.5:4.5 er



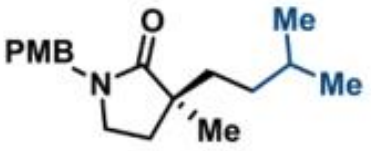
5g, 63%, 91.5:8.5 er



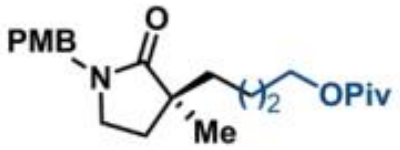
5h, 65%, 95.5:4.5 er



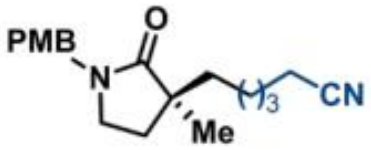
5i, 65%, 94.5:5.5 er



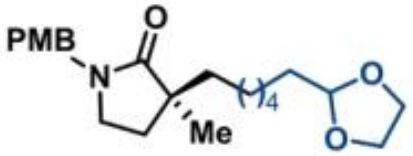
5j, 72%, 95.5:4.5 er



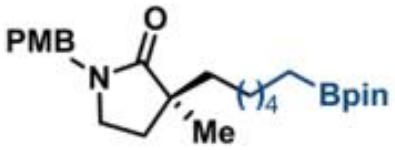
5k, 99%, 97:3 er



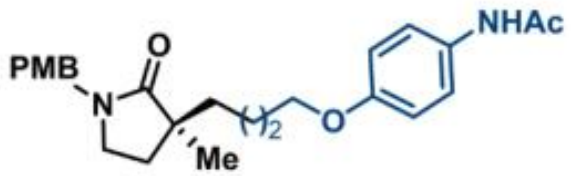
5l, 74%, 96:4 er



5m, 95%, 97:3 er



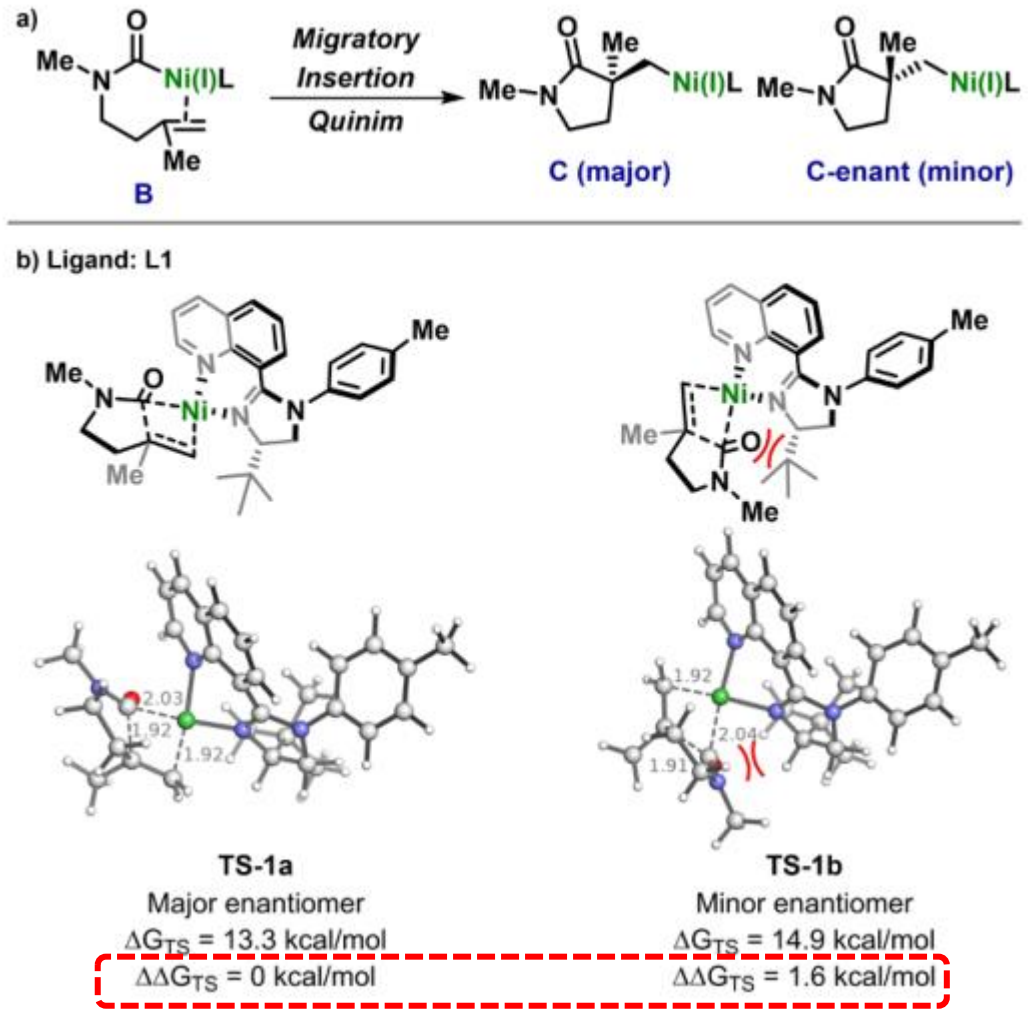
5n, 78%, 97.5:2.5 er



5o, 79%, 98.5:1.5 er

2.1 C=C bonds

对映选择性（EDS）：迁移插入



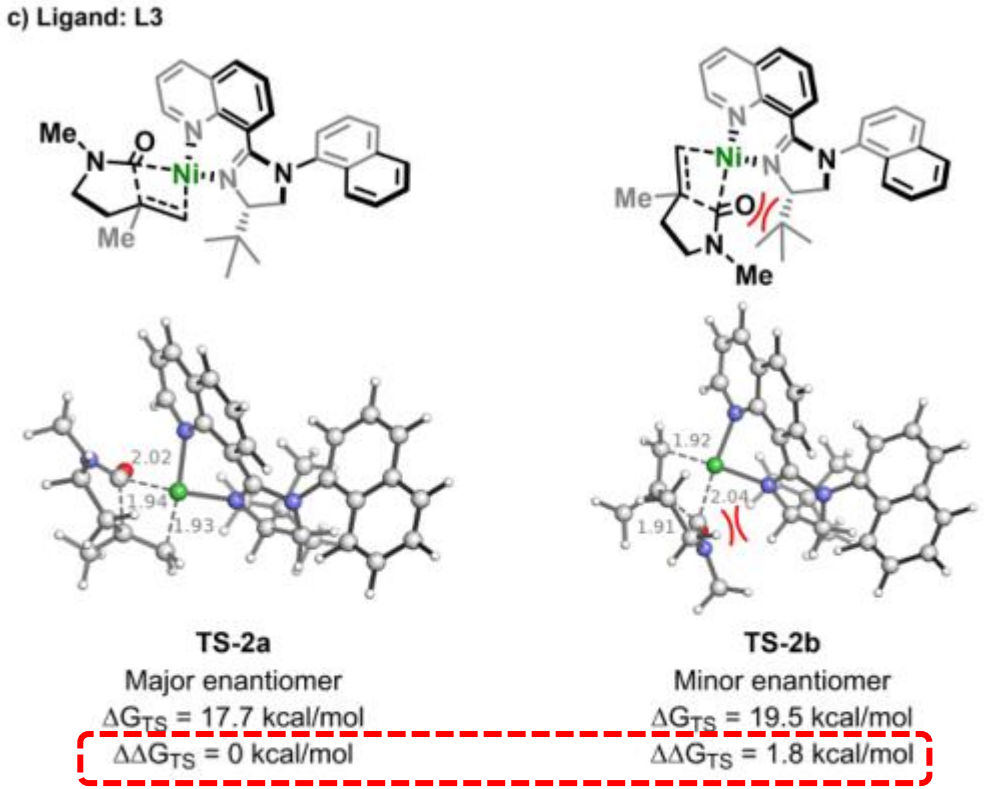


Figure 1. a) Migratory insertion step of model substrate B. b) Comparison of transition states for the formation of two enantiomers with ligand **L1**. c) Comparison of transition states for the formation of two enantiomers with ligand **L3**.

底物的取向方式：将羰基和N-取代基定位在配体的另一侧

修订反应机理

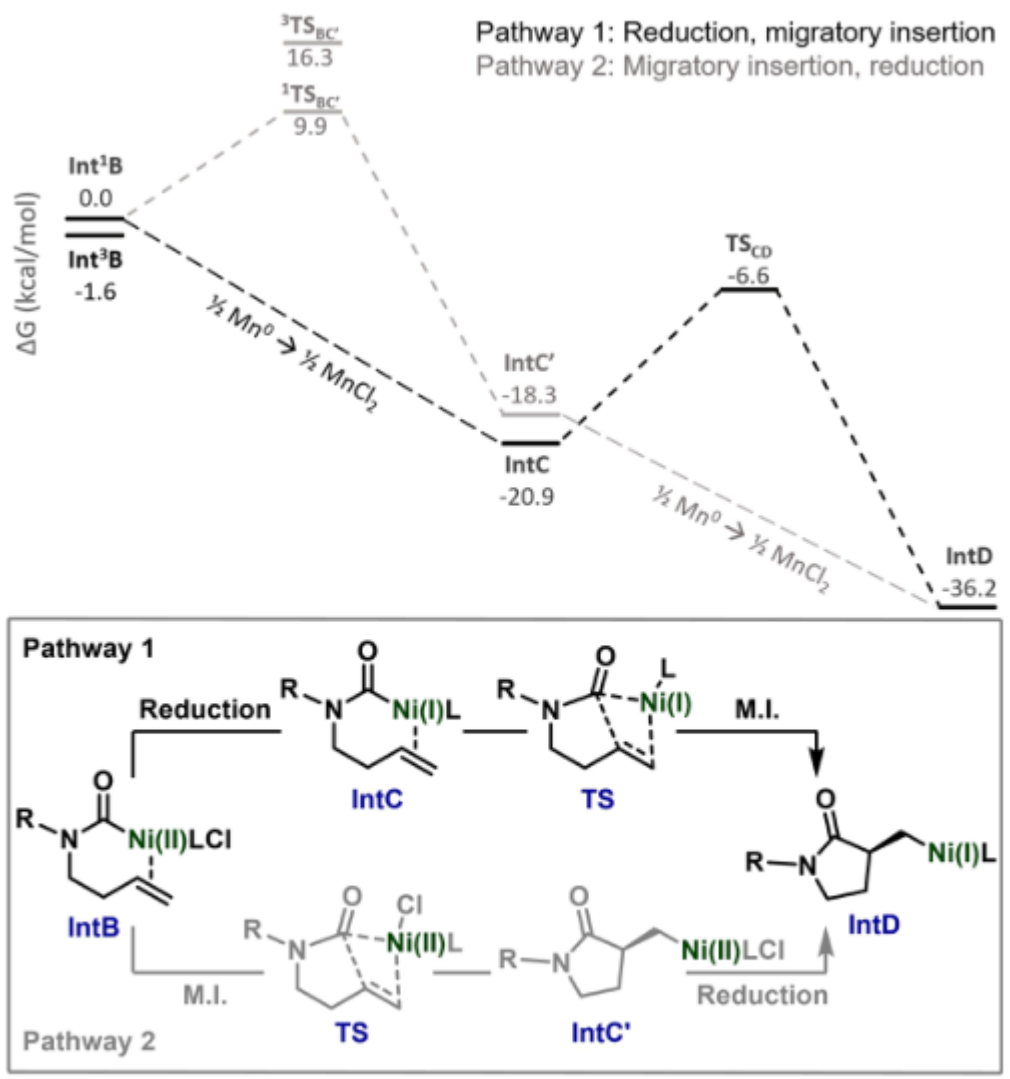


Figure 2. Gibbs free energy profile of two possible pathways for conversion of **IntB** to **IntD**. Energies in kcal mol^{-1}.

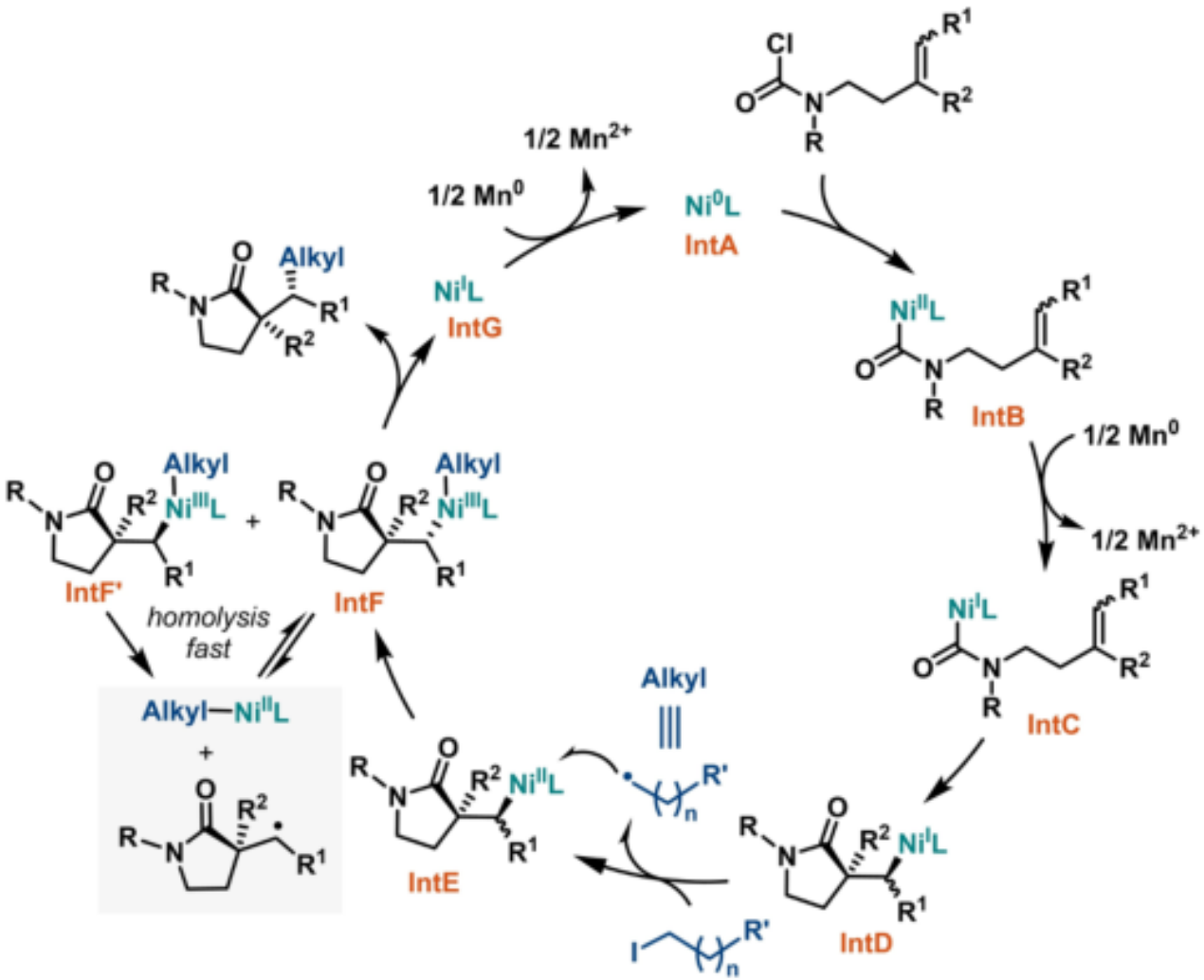
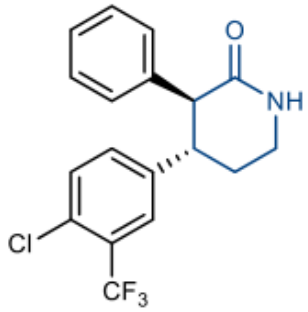


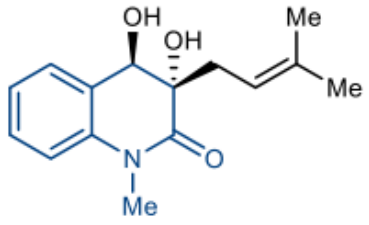
Figure 3. Proposed mechanistic cycle for reductive cyclization.

2.1 C=C bonds

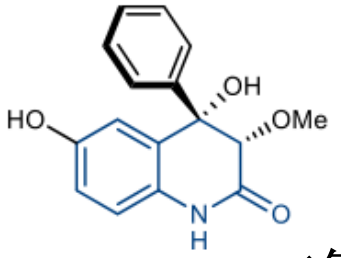
d) biologically active moleculars bearing six-membered lactam scaffold



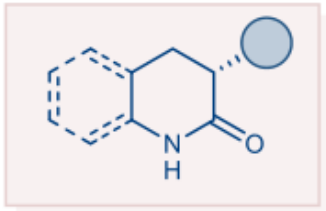
antihypertensive



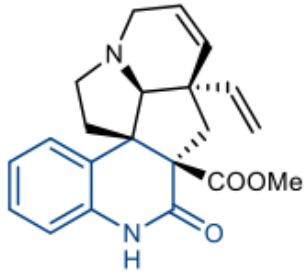
pinolinone



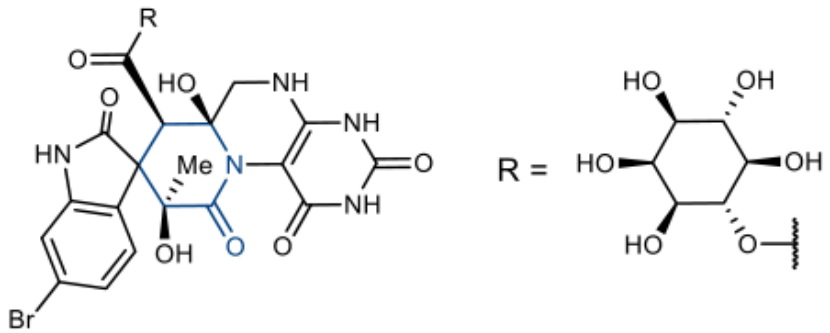
isoaflaquinolone E



二氢喹啉酮（δ内酰胺）

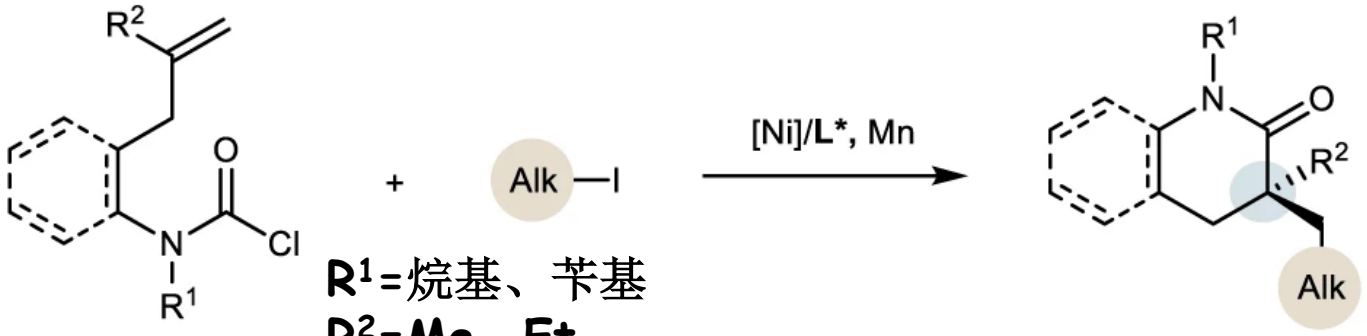


(+)-scandine



surugatoxin

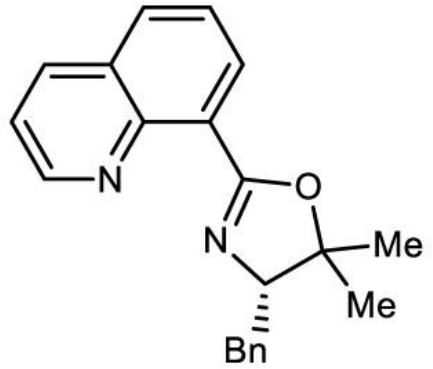
c) synthetic gap: asymmetric carbamoylation for six-membered lactam synthesis



R¹=烷基、苄基

R²=Me、Et

up to 98:2 er



Quinox **L8**, 39%, 93:7 er

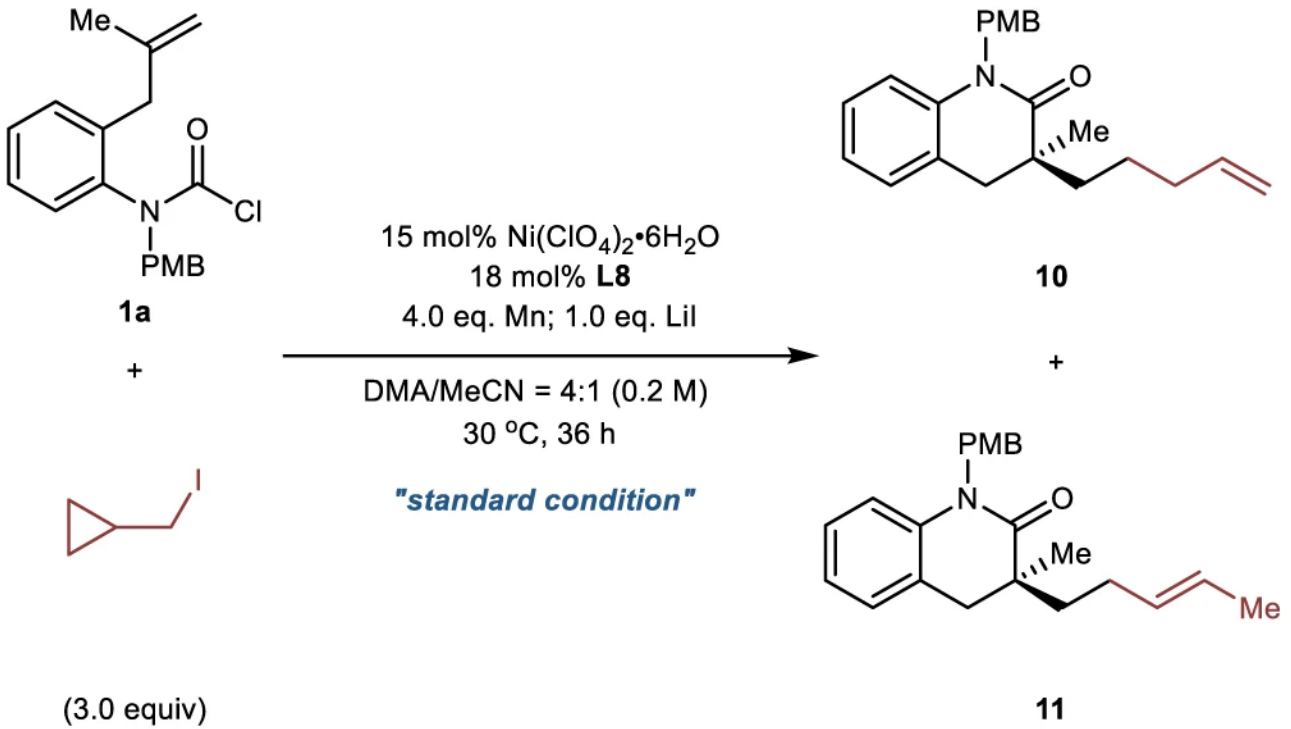
60%, 94:6 er[a]

89% (85%), 96.5:3.5 er[a,b]

Nat. Commun. **2022**, *13*, 5964.

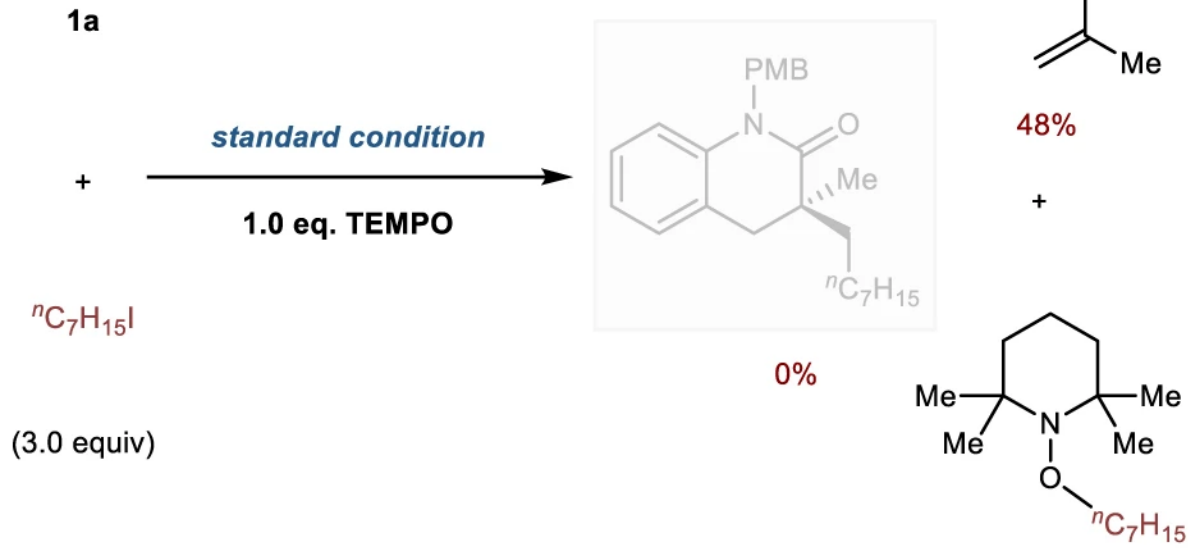
2.1 C=C bonds

a) Radical ring-opening experiment



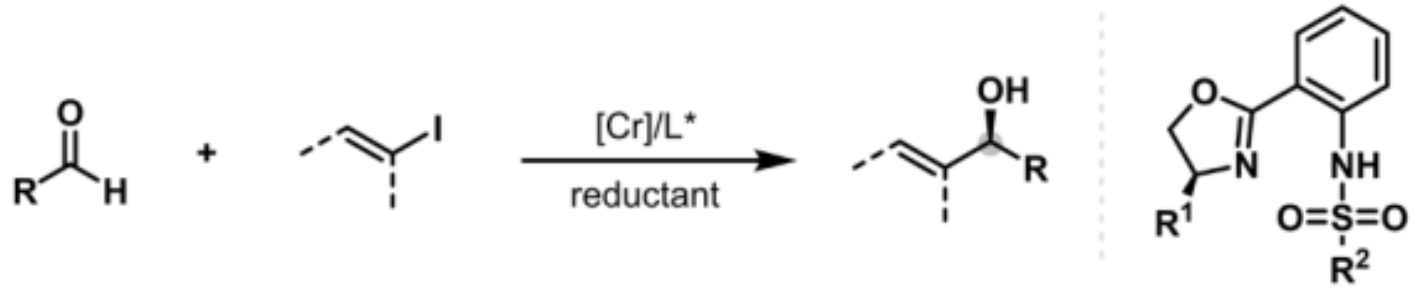
b) Radical trap reaction

TEMPO完全抑制还原交叉偶联

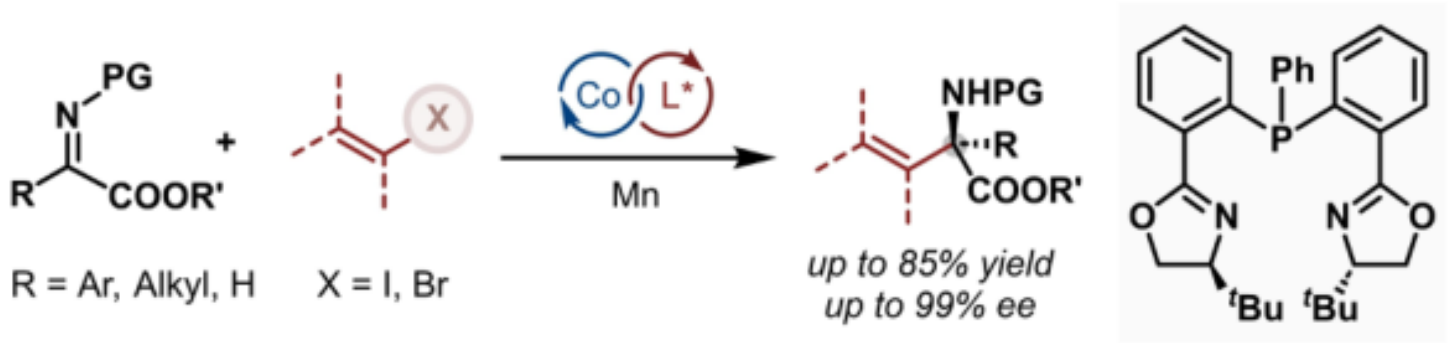


2.2 C=N bonds

(a) Asymmetric NHK (Nozaki–Hiyama–Kishi) reaction of aldehyde (Established protocol)



(b) Asymmetric aza-NHK reaction of α-imino ester with alkenyl halides (This work)



R = Ar, Alkyl, H X = I, Br

up to 85% yield
up to 99% ee

- expedient construction of chiral α-vinylic amino acid anologues
- asymmetric reductive addition reaction with alkenyl electrophiles
- excellent enantioselectivity with broad substrate scope

Scheme 1. The development of catalytic asymmetric aza-NHK reaction.

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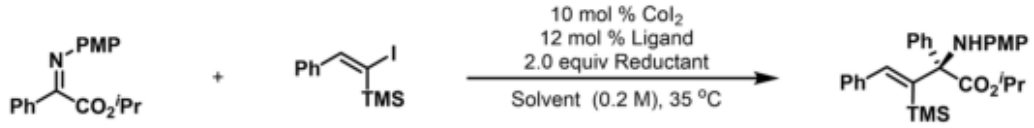
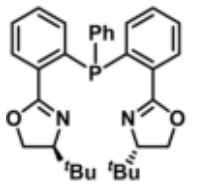
2.2 C=N bonds



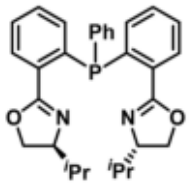
1a 2a 3a

Entry	Ligand	Reductant	Solvent	Alkenyl halide	3a (%)[b]	ee (%)[c]
1	**L1**	Mn	THF	**2a** (1.5 equiv)	59	72
2	**L1**	Mn	THF with 1.0 equiv ^{i}PrOH	**2a** (1.5 equiv)	49	>99
3	**L1**	Mn	THF/^{i}PrOH = 4/1	**2a** (1.5 equiv)	51	>99
4	**L2**	Mn	THF/^{i}PrOH = 4/1	**2a** (1.5 equiv)	20	90
5	**L3**	Mn	THF/^{i}PrOH = 4/1	**2a** (1.5 equiv)	21	77
6	**L4**	Mn	THF/^{i}PrOH = 4/1	**2a** (1.5 equiv)	36	99
7	**L5**	Mn	THF/^{i}PrOH = 4/1	**2a** (1.5 equiv)	16	-
8	**L1**	Zn	THF/^{i}PrOH = 4/1	**2a** (1.5 equiv)	44	>99
9	**L1**	Mn	DME/^{i}PrOH = 4/1	**2a** (1.5 equiv)	79	>99
10	**L1**	Mn	MeCN/^{i}PrOH = 4/1	**2a** (1.5 equiv)	80	>99
11	**L1**	Mn	MeCN/^{i}PrOH = 4/1	**2a** (2.0 equiv)	85 (84)[de]	>99
12	**L1**	Mn	MeCN/^{i}PrOH = 4/1	**2b** (2.0 equiv)	85[de]	>99

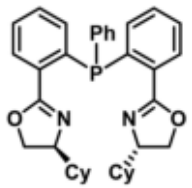
烯基溴化物有相似的效果



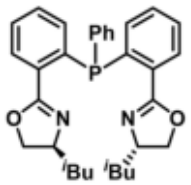
L1



L2

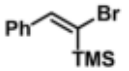


L3



L4

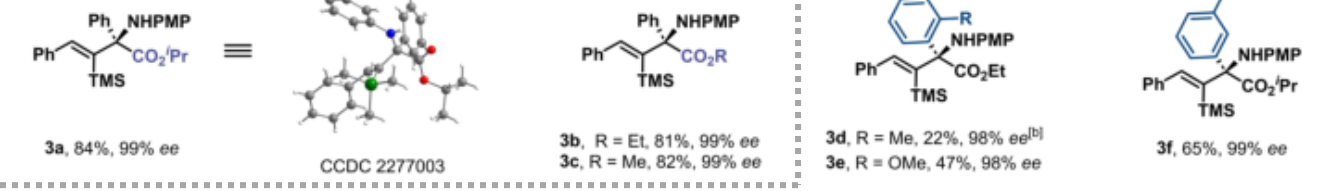
L5



2b

2.2 C=N bonds

α亚胺酯



3a, 84%, 99% *ee*

3b, R = Et, 81%, 99% *ee*
3c, R = Me, 82%, 99% *ee*

3d, R = Me, 22%, 98% *ee*[b]
3e, R = OMe, 47%, 98% *ee*

3f, 65%, 99% *ee*

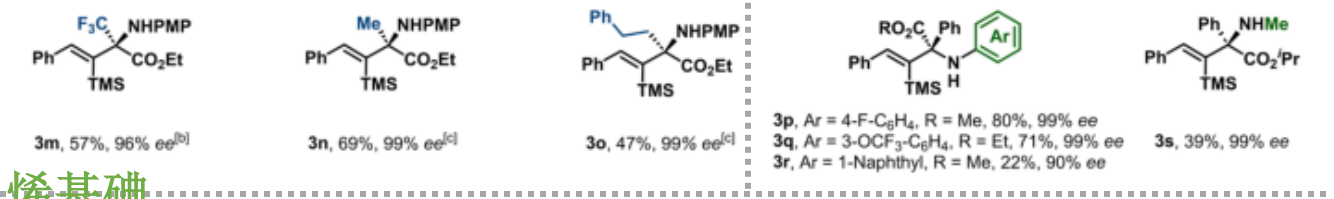
3g, R = OMe, 71%, 99% *ee*
3h, R = CF_3, 85%, 99% *ee*

3i, 59%, 99% *ee*

3j, 71%, 99% *ee*

3k, 55%, 99% *ee*

3l, 72%, 99% *ee*



3m, 57%, 96% *ee*[b]

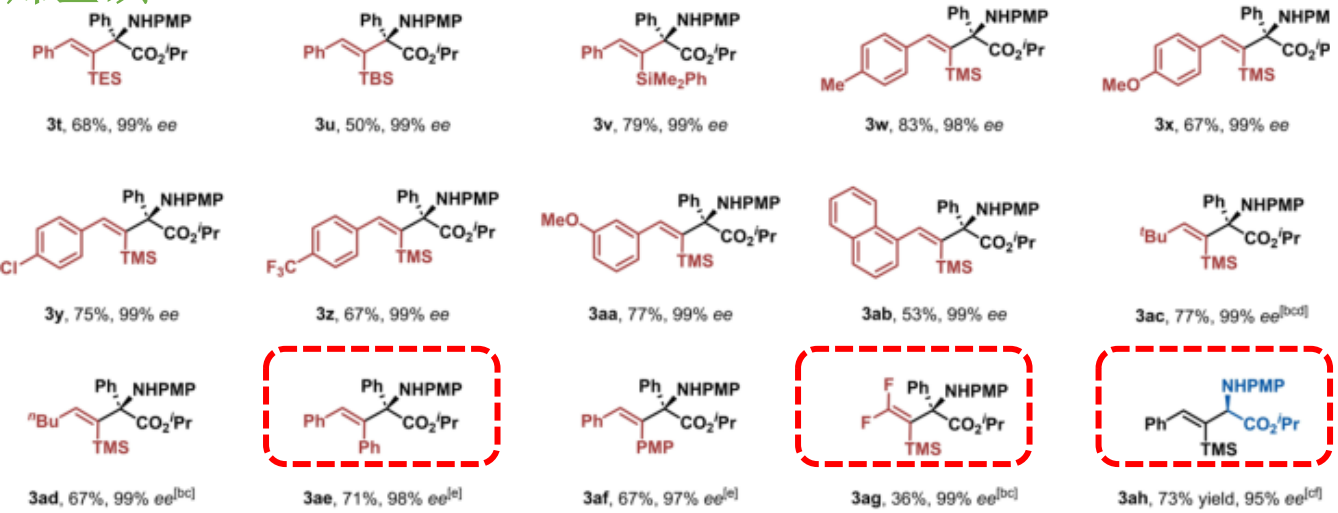
3n, 69%, 99% *ee*[c]

3o, 47%, 99% *ee*[c]

3p, Ar = 4-F-C_6H_4, R = Me, 80%, 99% *ee*
3q, Ar = 3-OCF_3-C_6H_4, R = Et, 71%, 99% *ee*
3r, Ar = 1-Naphthyl, R = Me, 22%, 90% *ee*

3s, 39%, 99% *ee*

烯基碘



3t, 68%, 99% *ee*

3u, 50%, 99% *ee*

3v, 79%, 99% *ee*

3w, 83%, 98% *ee*

3x, 67%, 99% *ee*

3y, 75%, 99% *ee*

3z, 67%, 99% *ee*

3aa, 77%, 99% *ee*

3ab, 53%, 99% *ee*

3ac, 77%, 99% *ee*[bcd]

3ad, 67%, 99% *ee*[bc]

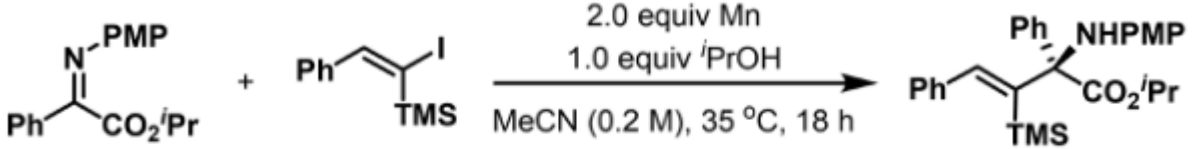
3ae, 71%, 98% *ee*[e]

3af, 67%, 97% *ee*[e]

3ag, 36%, 99% *ee*[bc]

3ah, 73% yield, 95% *ee*[cf]

a) Gram-scale reaction

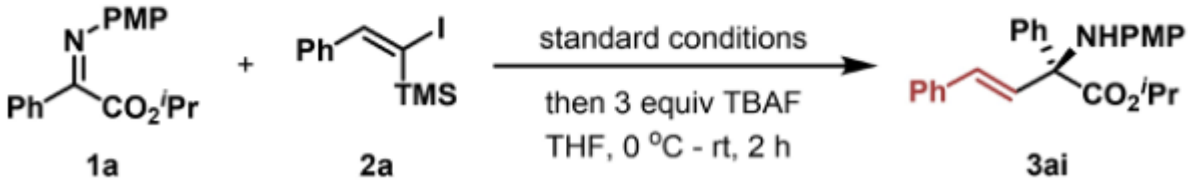


1a
3.0 mmol

2a
(2.0 equiv)

3a
1.26 g, 88%, >99% *ee*

b) *In-situ* removal of TMS group



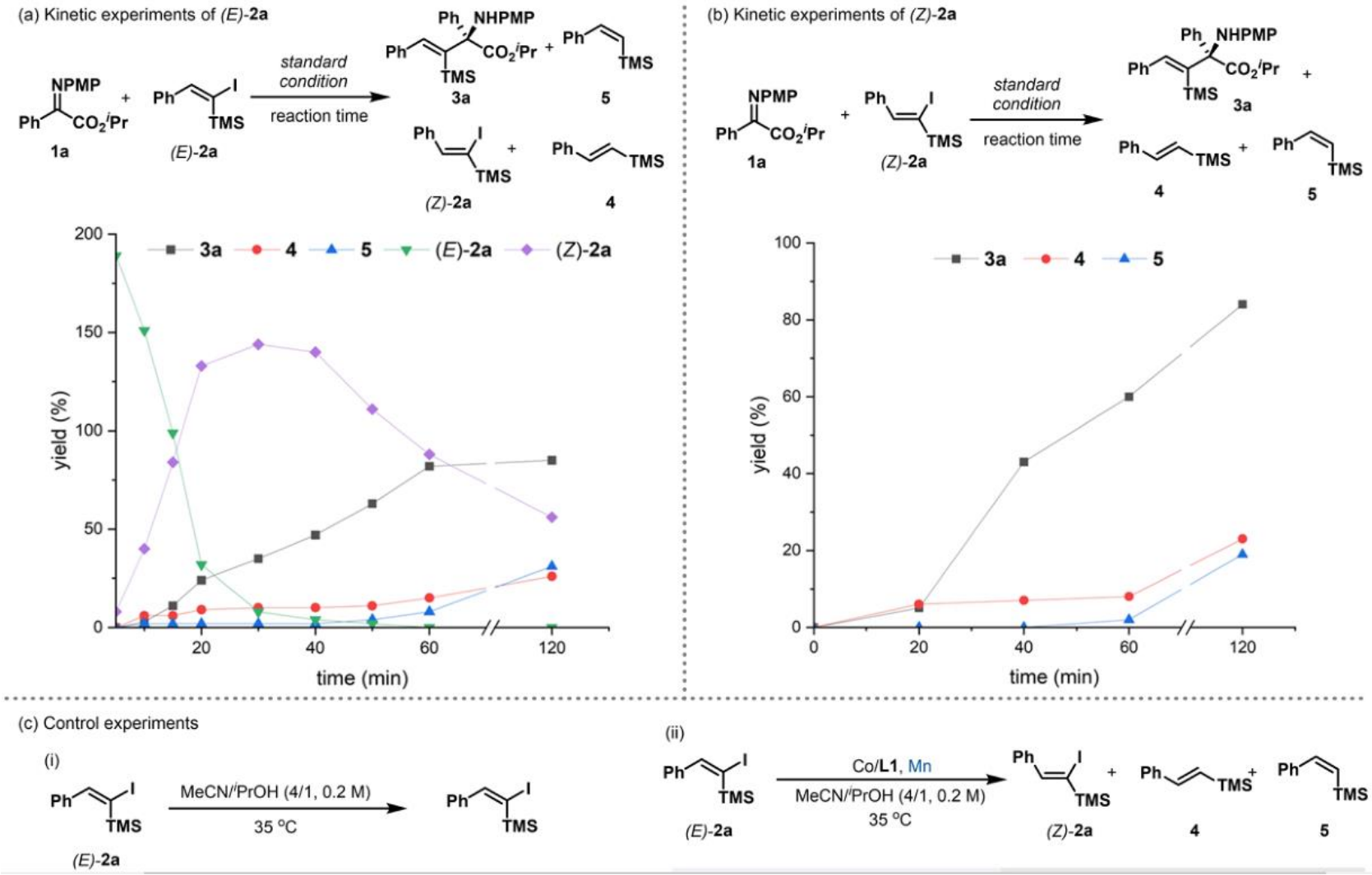
1a

2a
(2.0 equiv)

3ai
80% yield, >99% *ee*

2.2 C=N bonds

实时示踪反应：



生成的(E)-烯基钴的异构化过程达到另一个Z构型的速度远快于加成！

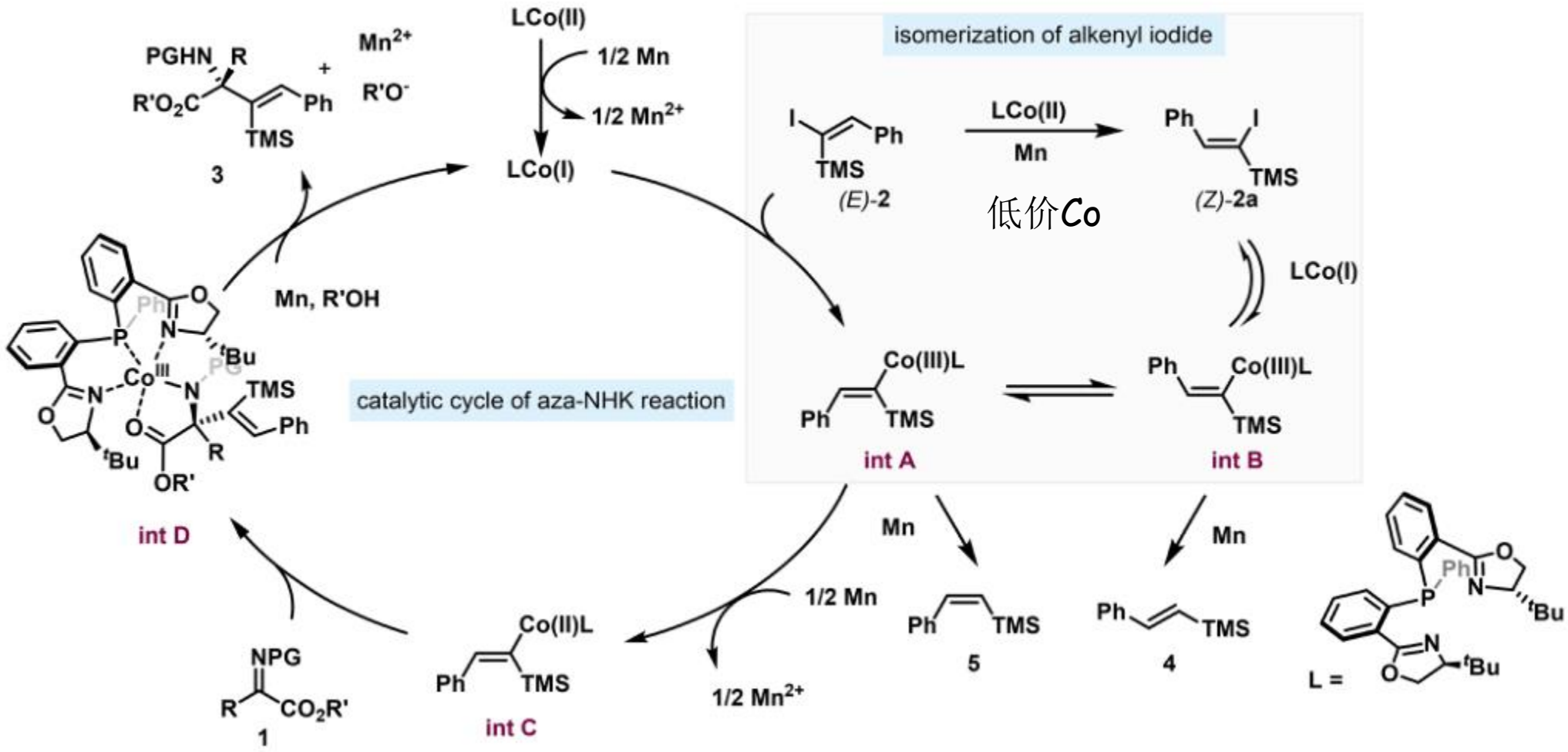
低价Co：碘化烯基异构化的控制

- 不加CoI_2, L1　2.0 equiv Mn　98% of (E)-2a recovered
- 不加Mn　10 mol% CoI_2; 12 mol% L1　98% of (E)-2a recovered

10 mol% CoI_2, 12 mol% L1, 10 mol% Mn	96%	5%	--
10 mol% CoI_2, 12 mol% L1, 2.0 equiv Mn	7%	52%	39%
1.0 equiv [^{t}Bu-NPN^{Ph}-Co^I], w/o Mn	46%	43%	7%

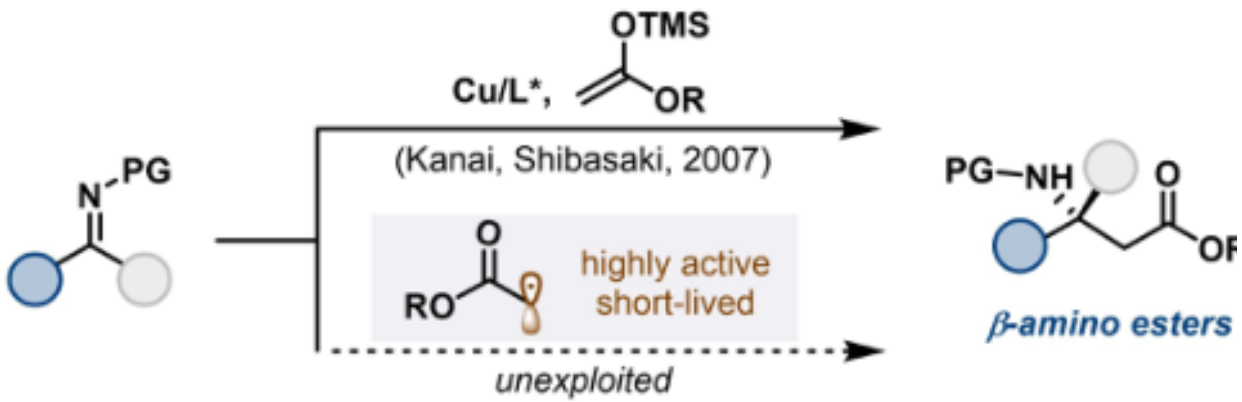
2.2 C=N bonds

(d) Plausible mechanism

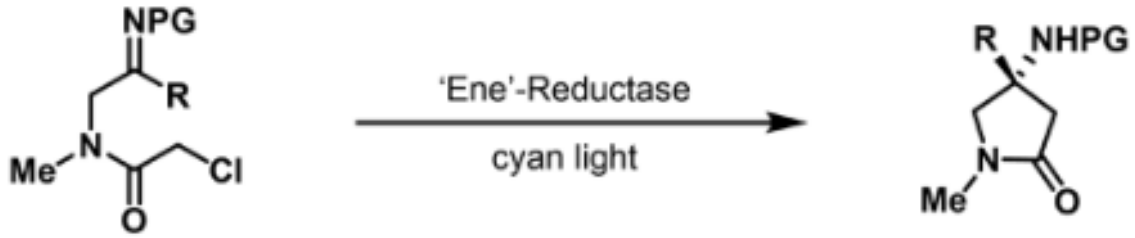


2.2 C=N bonds

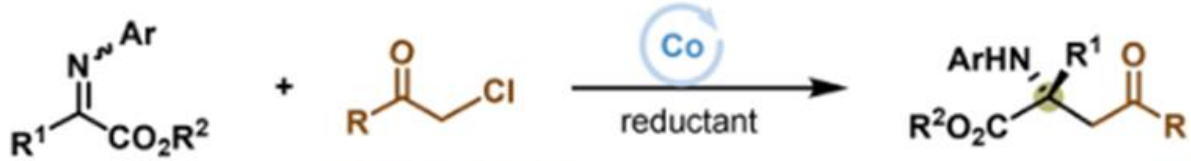
(a) Chiral β-tertiary amino ester synthesis enabled by the stereoselective addition



(b) Enzyme-catalyzed intramolecular asymmetric reductive addition of ketimine with α-chloro amide (Hyster, 2021)



(c) Cobalt-catalyzed intermolecular asymmetric reductive addition of ketimine with α-chloro carbonyl compound (This work)



- transition metal-catalyzed stereoselective addition of α-carbonyl radical
- convenient synthesis of enantioenriched tertiary β-amino acid analogues
- excellent enantioselectivity with broad substrate scope under mild condition

高反应活性的羰基a位自由基：易发生**Reformatsky**加成、自由基对亚胺酯直接加成，降低对映选择性。

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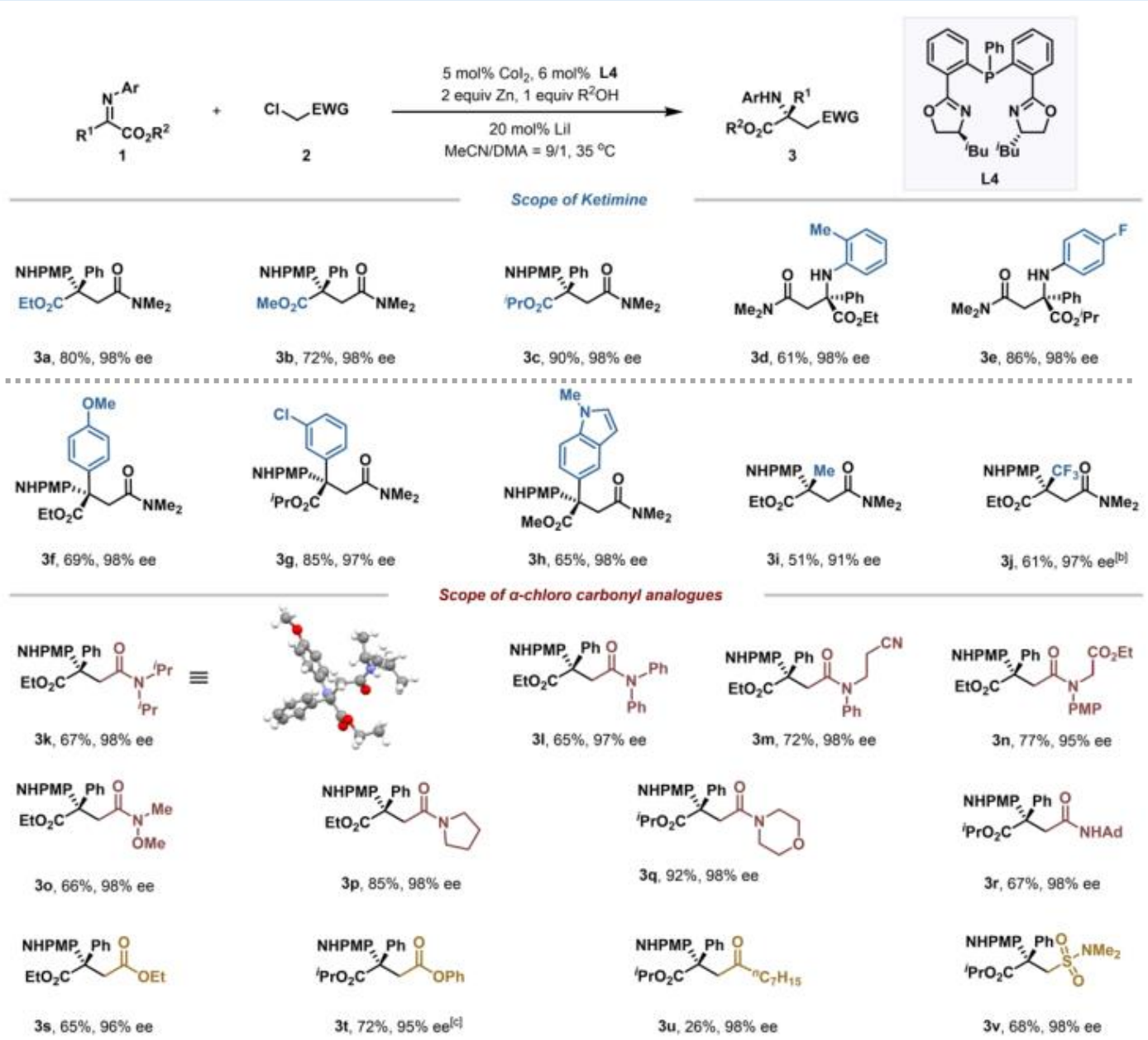
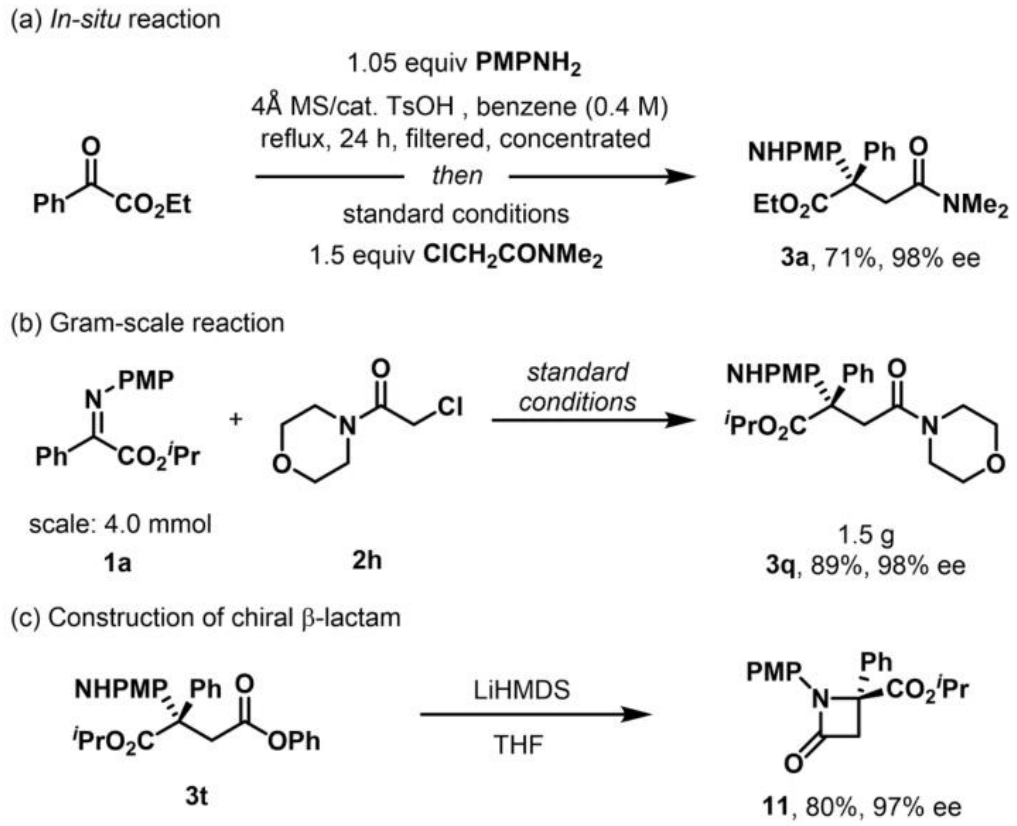
2.2 C=N bonds

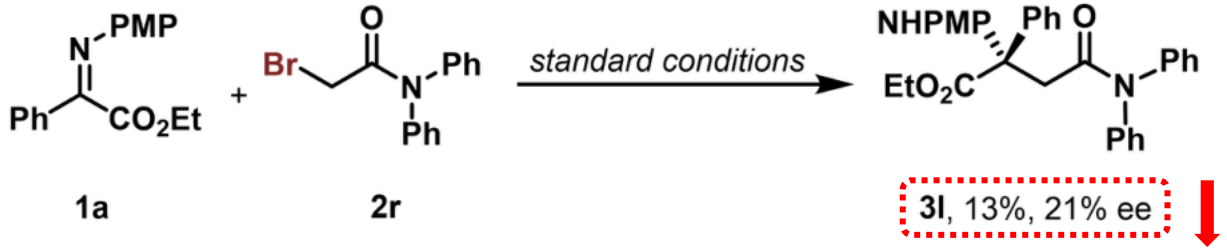




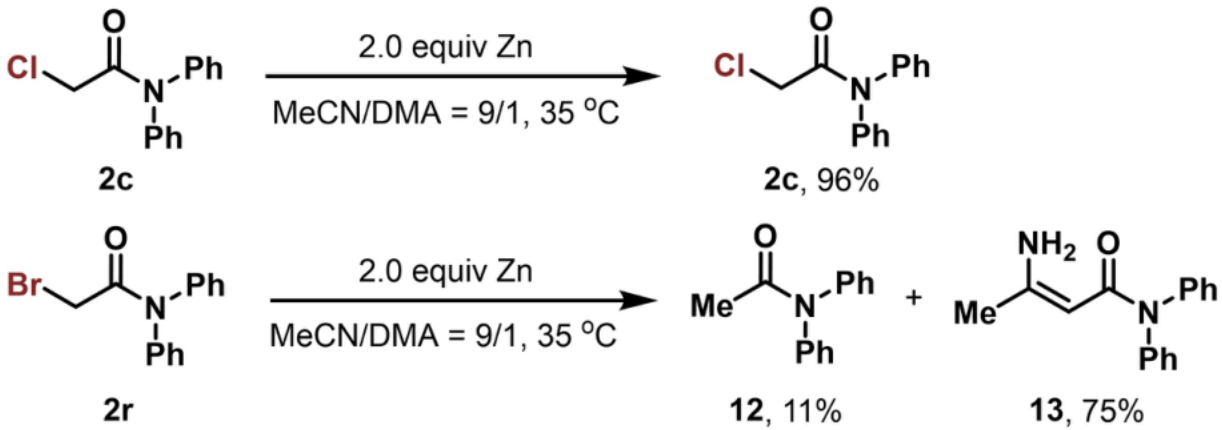
Scheme 4. Synthetic application.

2.2 C=N bonds

(a) Reaction with α-bromoamide as an elecrophile

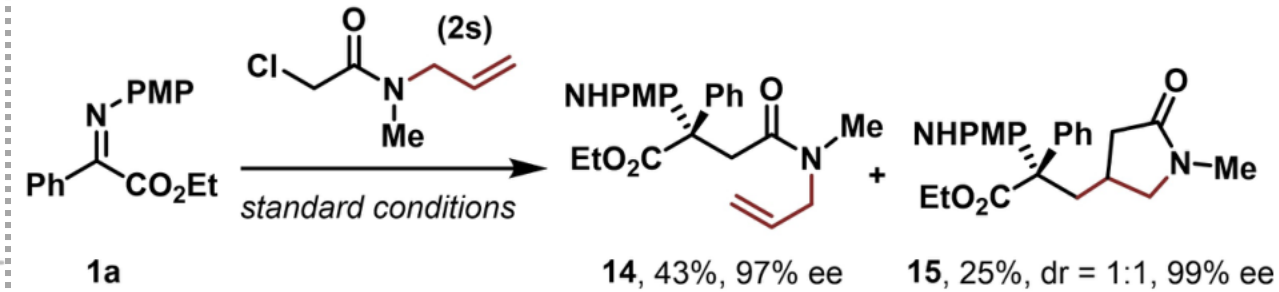


(b) Investigation of Reformatsky reagent formation

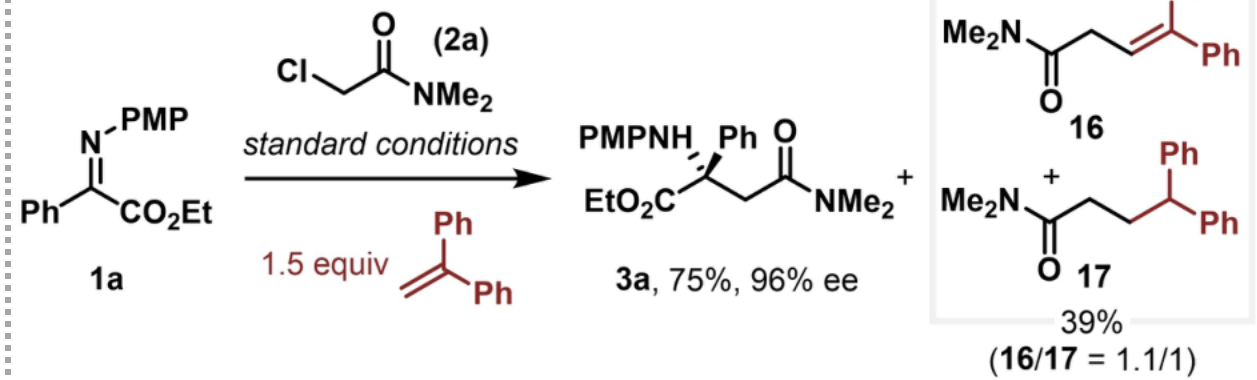


还原自由基加成过程
和经典**Reformatsky**
加成界限的区别

(c) Reaction with alkene substituted α-chloroamide

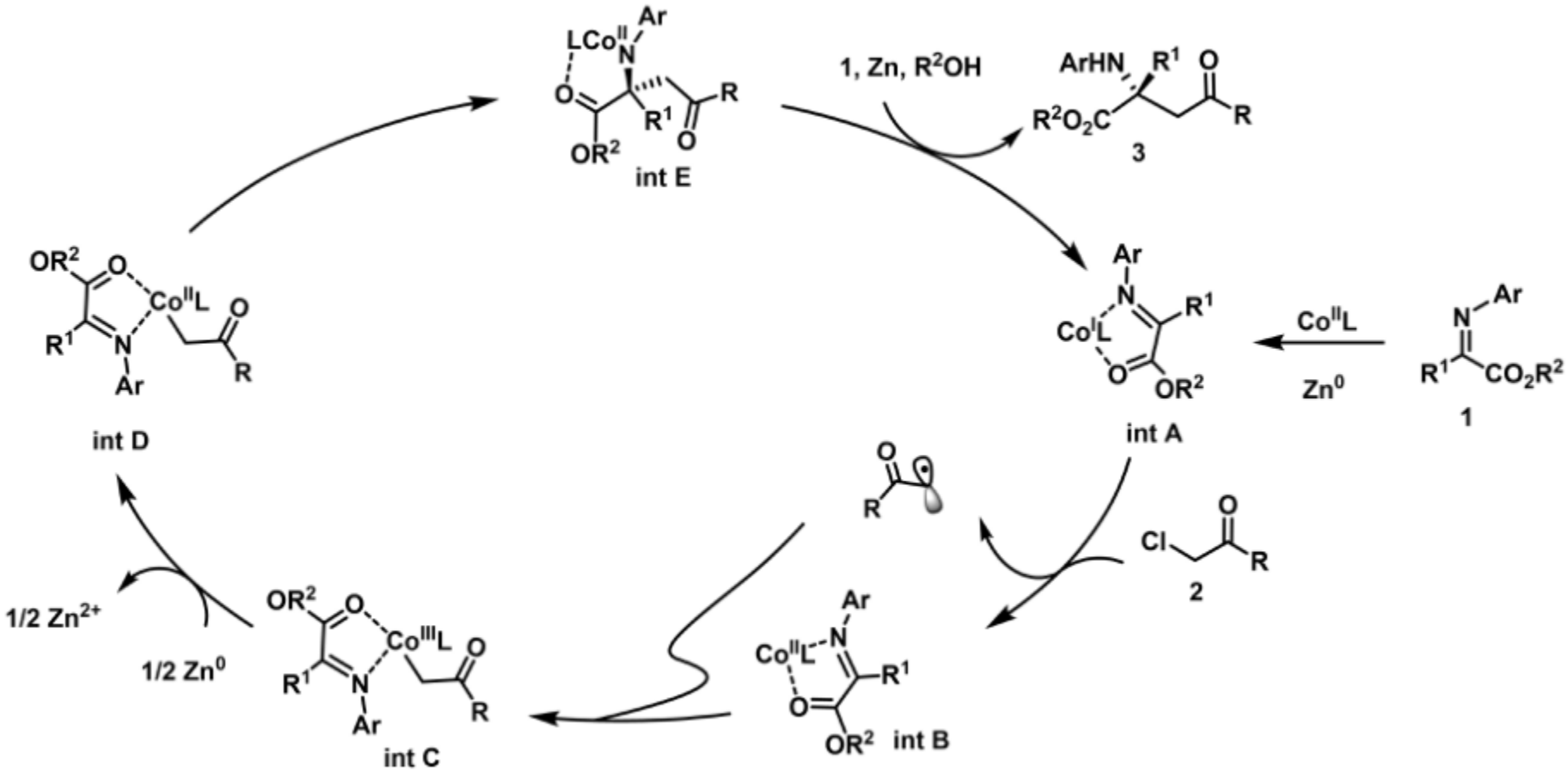


(d) Radical trapping reaction



2.2 C=N bonds

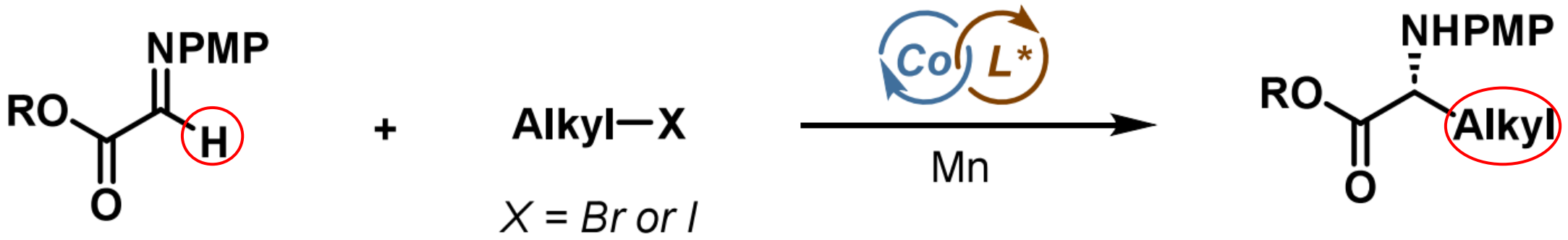
(e) Proposed mechanism



Scheme 5. Mechanistic studies.

2.2 C=N bonds

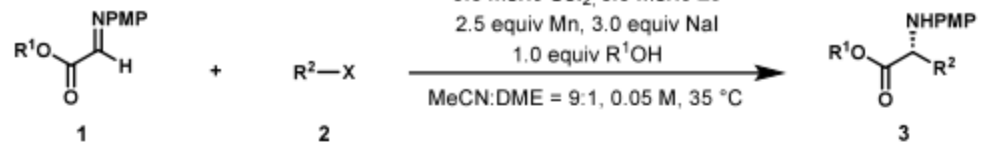
c) This work: cobalt-catalyzed asymmetric aza-Barbier alkylative addition

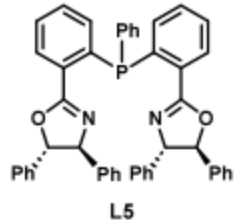


- ***hign functional group tolerance***
- ***modular assembly of exotic α-AAs***
- ***compatibility with 1°, 2°, and 3° alkyl halides***
- ***good to excellent enantioselectivity and yield***

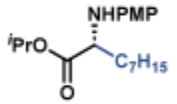
J. Am. Chem. Soc. **2024**, *146*, 25918–25926.

2.2 C=N bonds

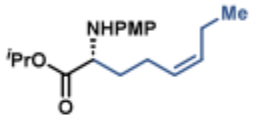




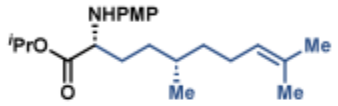
Primary Alkyl Iodide Scope



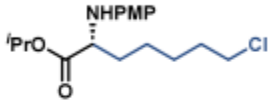
3a, 79%, 95% ee



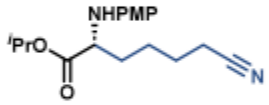
3b, 71%, 91% ee



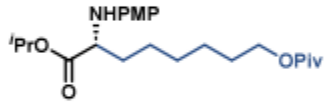
Citronellol analogue
3c, 76%, 96:4 dr



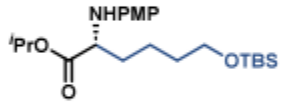
3d, 84%, 94% ee



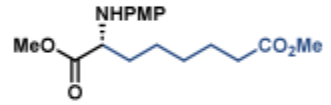
3e, 78%[b], 92% ee



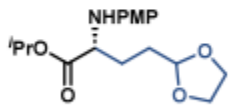
3f, 62%, 91% ee



3g, 73%, 90% ee

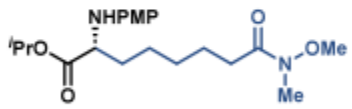


3h, 53%, 90% ee

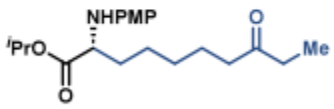


3i, 79%[b], 89% ee

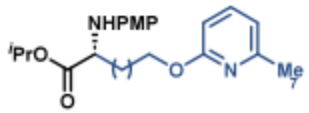
3j, 76%[b], 91% ee



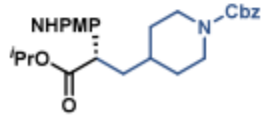
3k, 48%[b], 90% ee



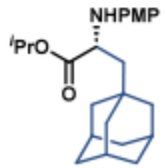
3l, 57%[b],91% ee



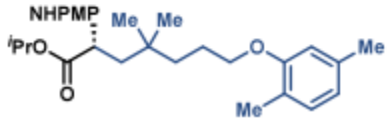
3m, 56%[b], 90% ee



3n, 79%, 90% ee

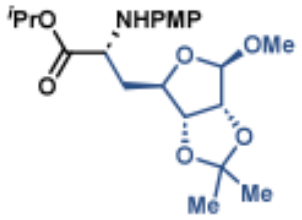


3o, 75%, 99% ee

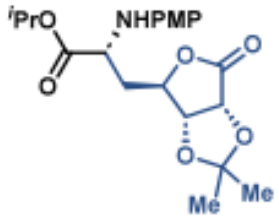


Gemfibrozil analogue
3p, 72%, 98%ee

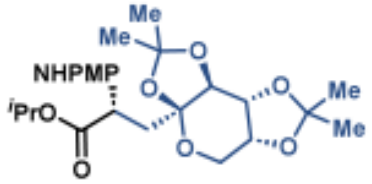
2.2 C=N bonds



Methyl-β-D-ribofuranoside analogue
3q, 63%, 98:2 dr

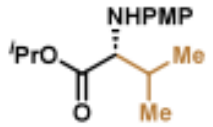


D-Ribonic-γ-lactone analogue
3r, 55%, 96:4 dr

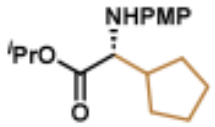


Diacetonefructose analogue
3s, 68%, 95:5 dr

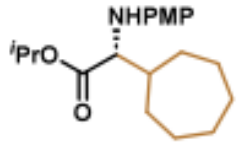
Secondary Alkyl Bromide Scope



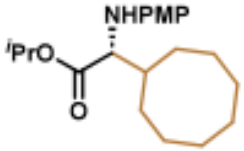
3t, 37%[b], 96% ee



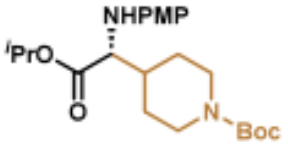
3u, 71%[b], 96% ee



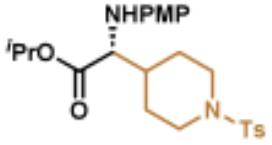
3v, 54%[b], 97% ee



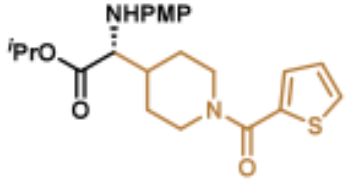
3w, 73%[b], 97% ee



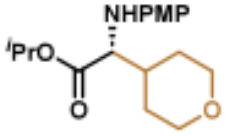
3x, 52%[b], 90% ee



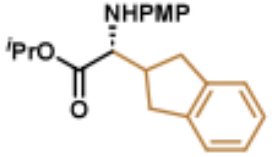
3y, 50%[b], 90% ee



3z, 66%[b], 90% ee

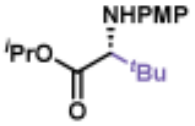


3aa, 44%[b], 93% ee

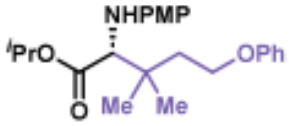


3ab, 64%[b], 91% ee

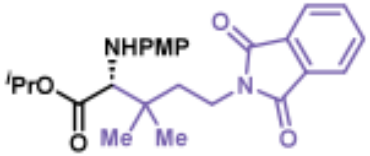
Tertiary Alkyl Bromide Scope



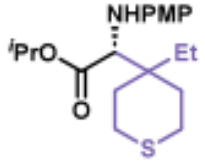
3ac, 58%[b], 92% ee



3ad, 79%[b], 94% ee

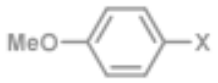


3ae, 80%[b], 94% ee



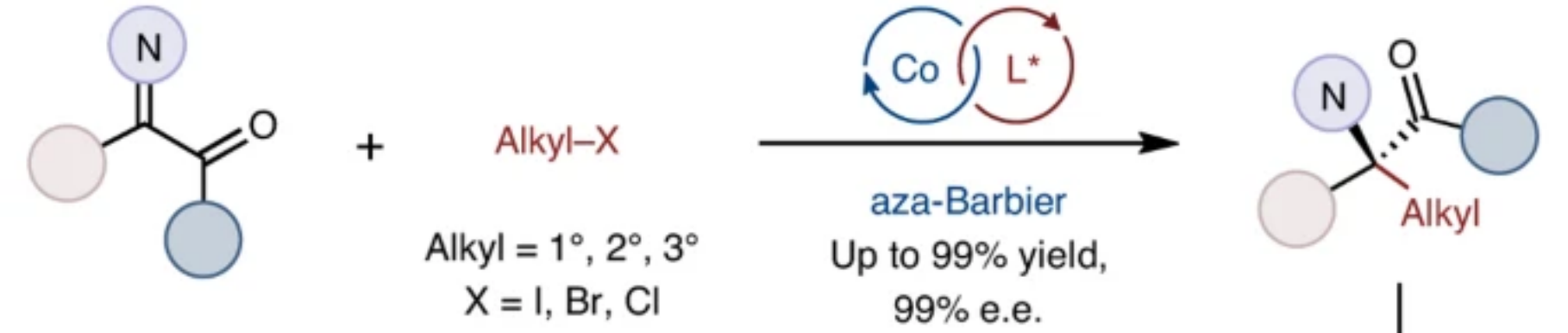
3af, 83%[b], 95% ee

Unsuccessful examples

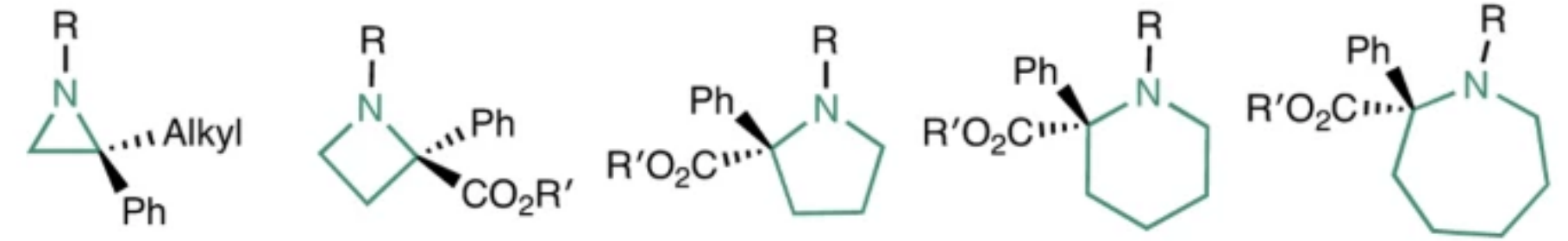


X = Br, I, OTf

2.2 C=N bonds



Modular chiral heterocycle synthesis



■ Facile construction of α-tertiary amino ester ■ Excellent functional group tolerance

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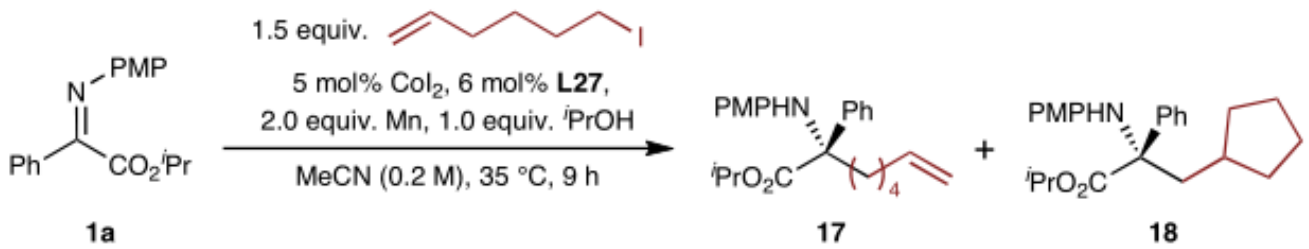
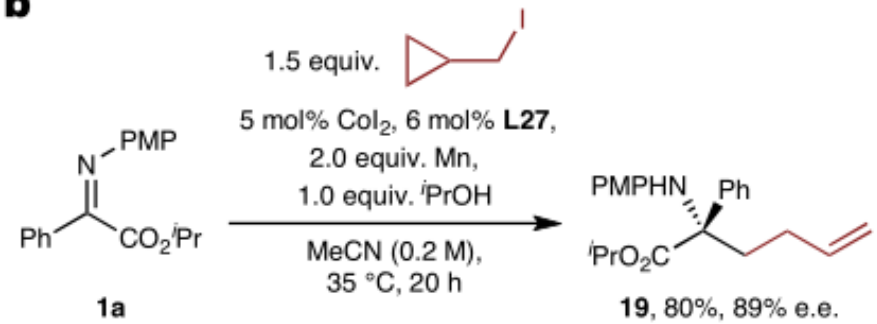
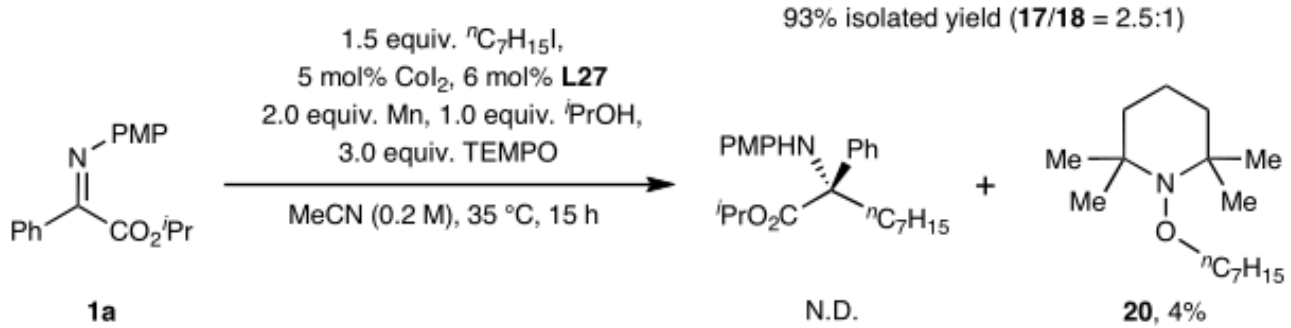
a



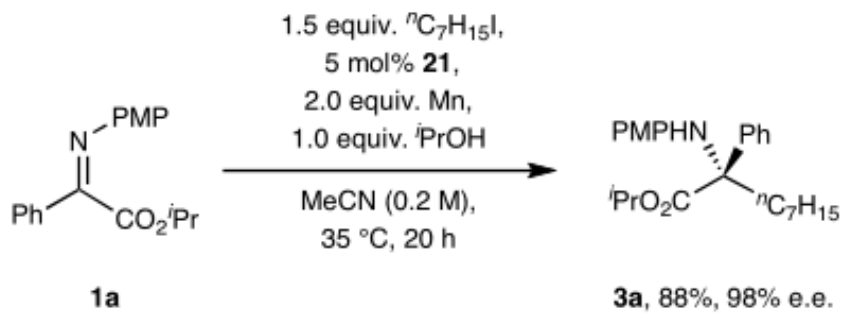
b



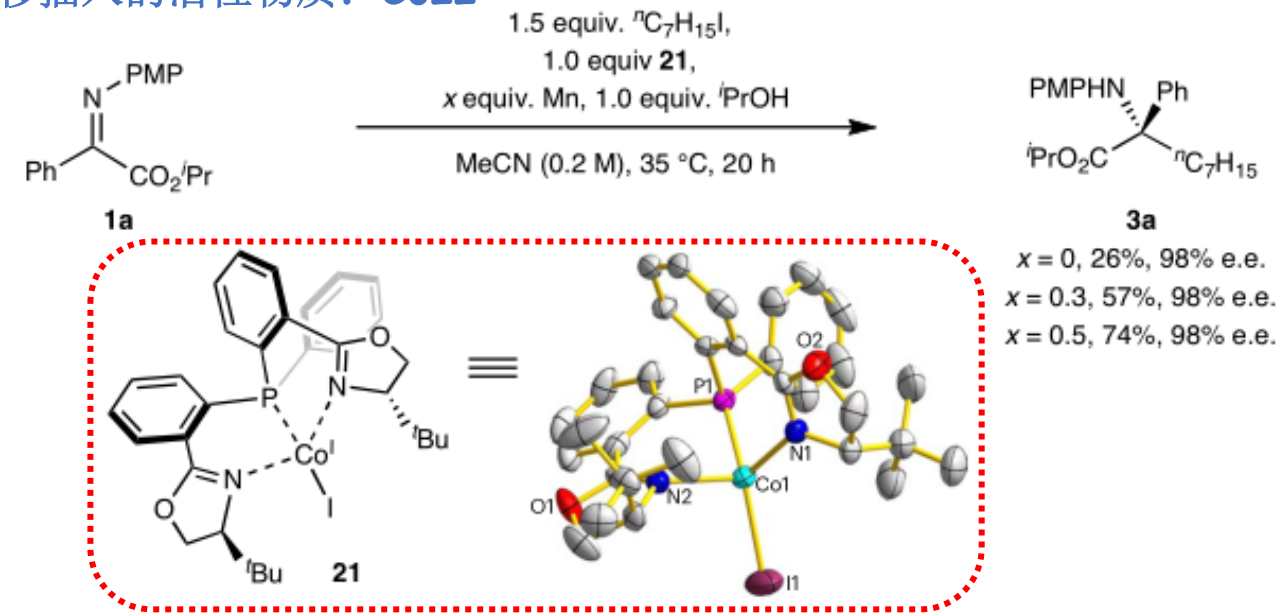
c



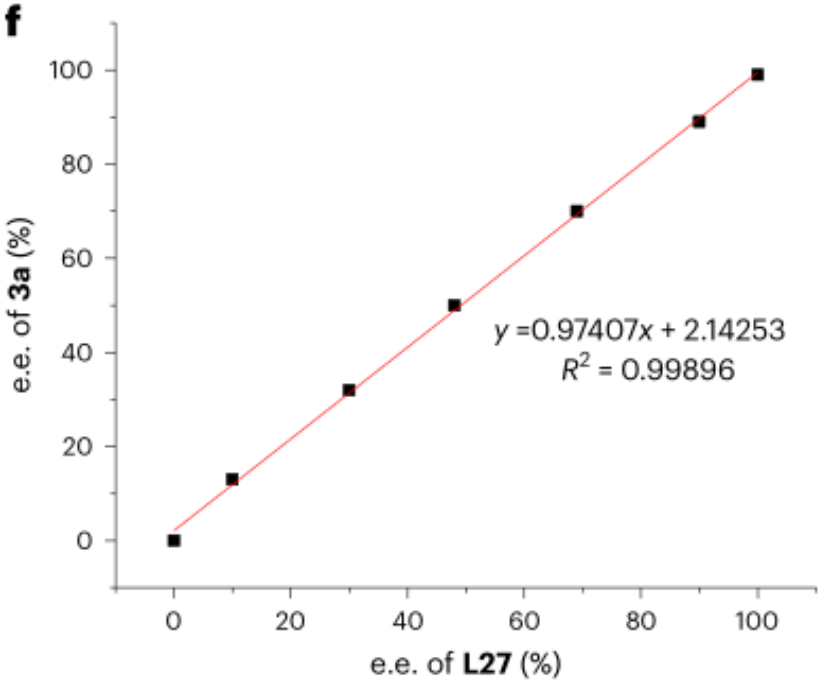
d 反应中间体：**CoI**诱发反应



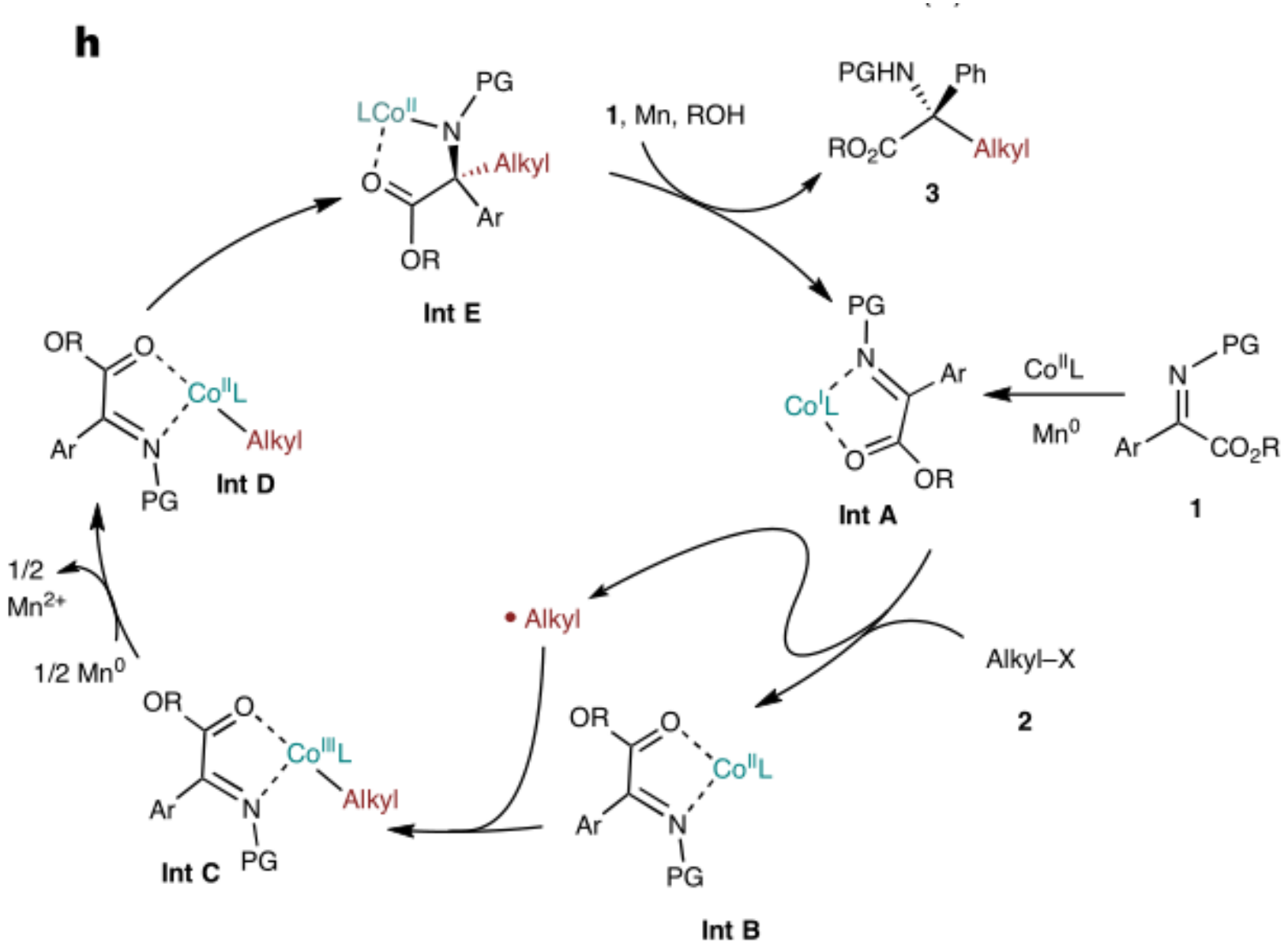
e 迁移插入的活性物质：**CoII**



f

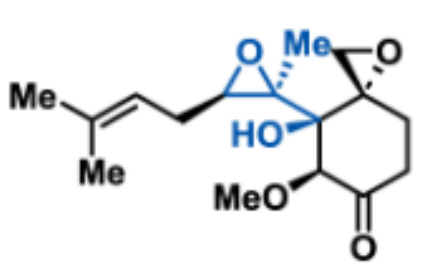


2.2 C=N bonds

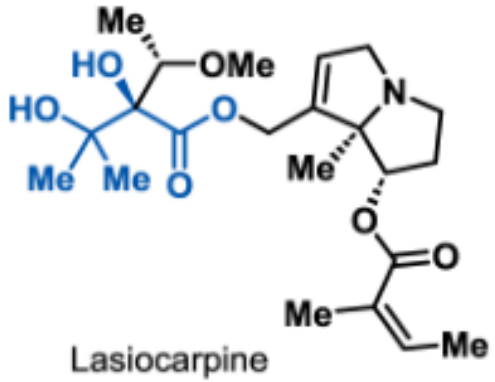

h
PG
LCo^II
N
Alkyl
O
Ar
OR
Int E
1, Mn, ROH
PGHN
Ph
RO2C
Alkyl
3
PG
N
Ar
Co^IL
O
OR
Int A
Co^IIL
Mn^0
PG
N
Ar
CO2R
1
• Alkyl
Alkyl–X
2
OR
O
Co^IIL
Ar
N
PG
Int B
OR
O
Co^IIL
Alkyl
Ar
N
PG
Int C
1/2
Mn^2+
1/2 Mn^0
OR
O
Co^IIL
Alkyl
Ar
N
PG
Int D

2.3 C=O bonds

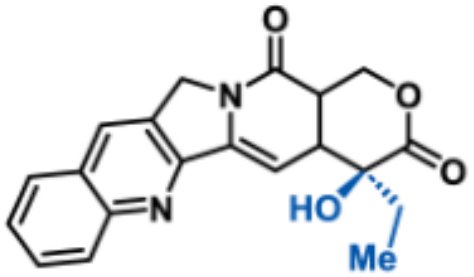
a The prevalence of α-tetrasubstituted chiral alcohol



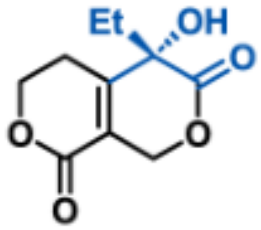
(-)-Ovalicin



Lasiocarpine

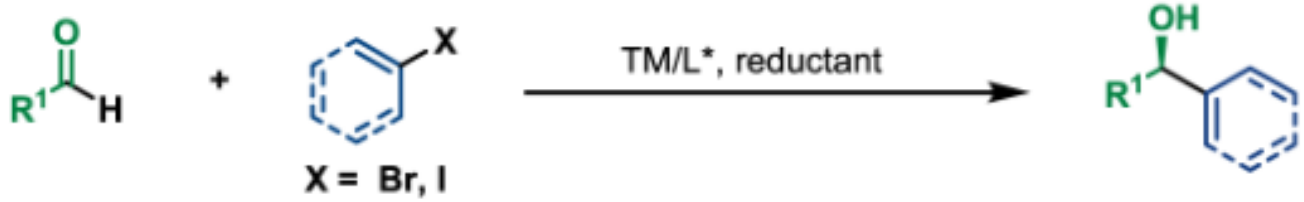


Camptothecin

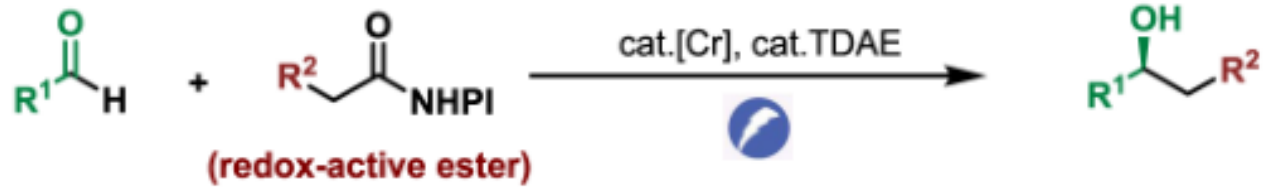


(+)-Gentiolactone

b Catalytic asymmetric addition of aldehyde with alkenyl or aryl halides

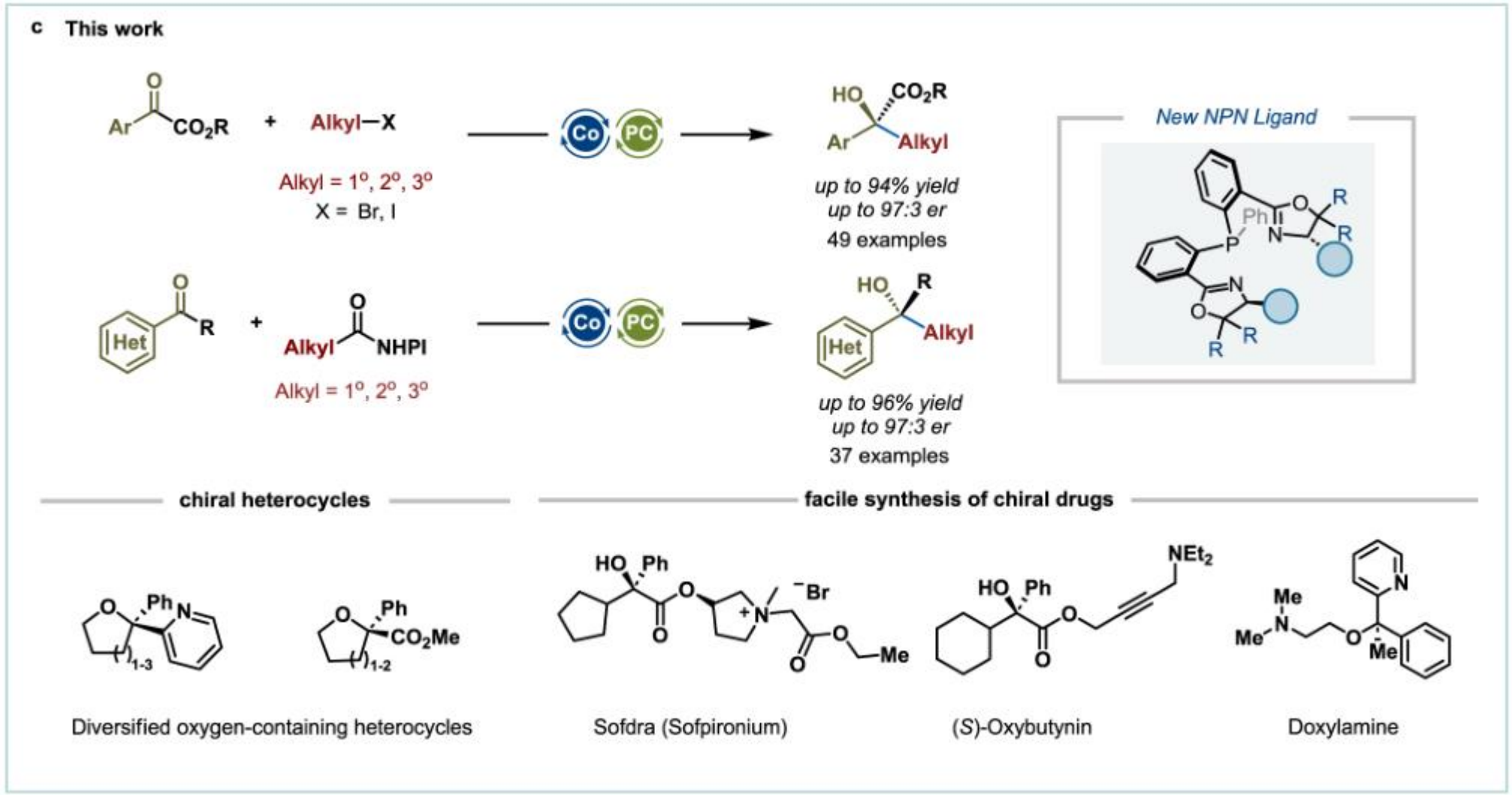


Electrocatalytic asymmetric Nozaki–Hiyama–Kishi reaction of aldehyde



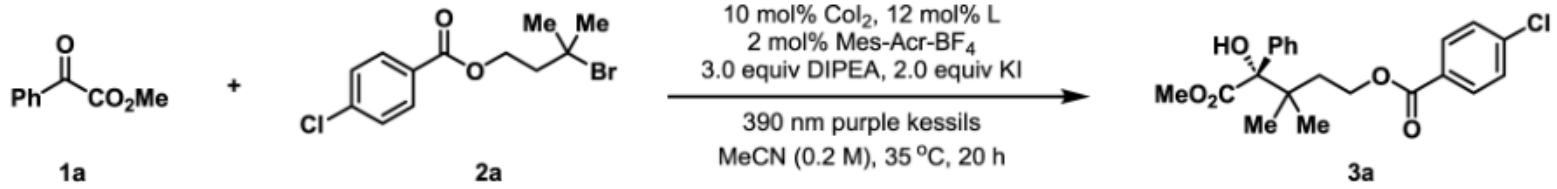
J. Am. Chem. Soc. **2024**, *146*, 28468–28481.

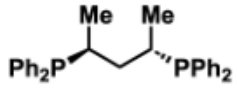
2.3 C=O bonds


c This work
Ar
O
CO2R
+
Alkyl—X
Co
PC
Alkyl = 1°, 2°, 3°
X = Br, I
HO
CO2R
Ar
Alkyl
up to 94% yield
up to 97:3 er
49 examples
New NPN Ligand
Ph
P
N
O
R
Het
Alkyl
NHPI
Alkyl = 1°, 2°, 3°
up to 96% yield
up to 97:3 er
37 examples
chiral heterocycles
facile synthesis of chiral drugs
1-3
1-2
CO2Me
HO
Ph
Br
Me
NEt2
Me
Diversified oxygen-containing heterocycles
Sofdra (Sofpironium)
(S)-Oxybutynin
Doxylamine

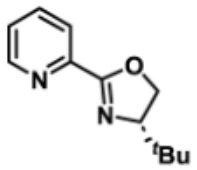
2.3 C=O bonds

Table 1. Optimization of Reaction Conditions[ab]

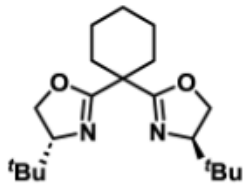




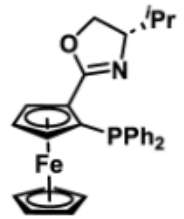
L1, 81%, 44:56 er



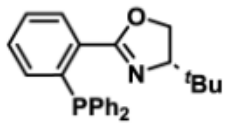
L2, <5%



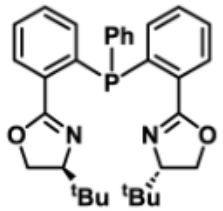
L3, 11%, 56:44 er



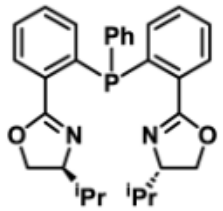
L4, 34%, 56.5:43.5 er



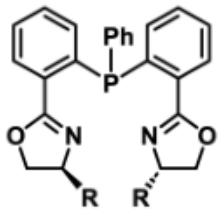
L5, 58%, 65:35 er



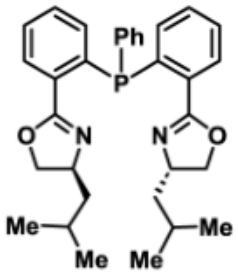
L6, 62%, 87.5:12.5 er



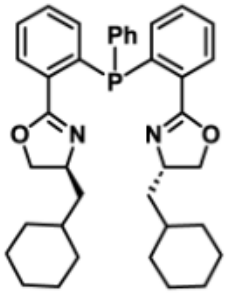
L7, 60%, 80:20 er



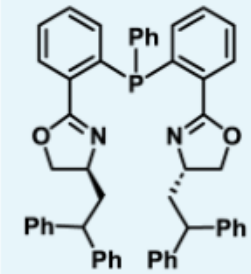
L8, R = Ph, 78%, 89:11 er
L9, R = ^{s}Bu, 63%, 88.5:11.5 er



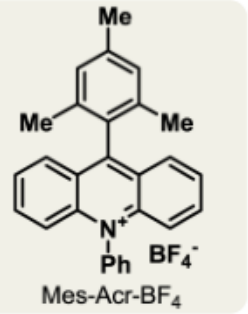
L10, 50%, 90:10 er



L11, 65%, 88:12 er



L12, 85%(85%)[b], 96:4 er



Mes-Acr-BF$_4$
Fukuzumi's catalyst

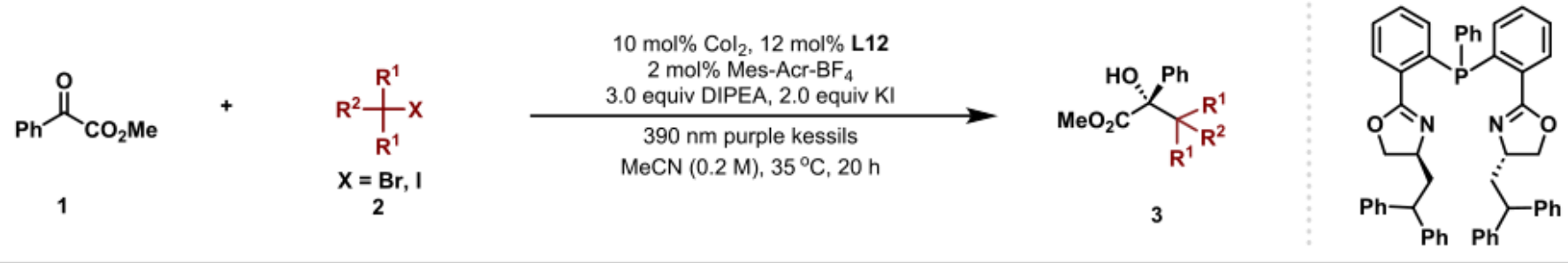
Variations from above
4CzIPN instead of Mes-Acr-BF$_4$
$Ir(ppy)_2(dtbbpy)PF_6$ instead of Mes-Acr-BF$_4$
$Ru(bpy)_3(PF_6)_2$ instead of Mes-Acr-BF$_4$
465 nm blue LED instead of 390 nm purple LED
without KI
7.5 mol % CoI_2, 9 mol % **L12**
alkyl iodide instead of alkyl bromide **2a**

Entry	Yield (%)
1	78
2	68
3	69
4	19
5	20
6	70
7[c]	82

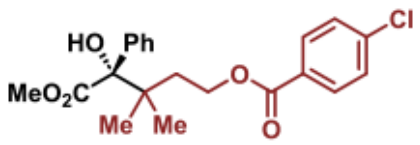
烷基碘化物有相似的效果.

2.3 C=O bonds

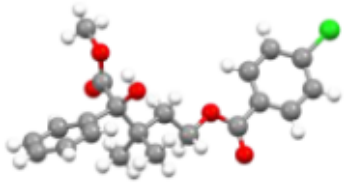
Scheme 2. Substrate Scope of Unactivated Alkyl Halides[ab]



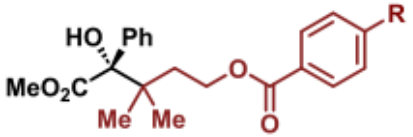
Tertiary alkyl bromide[a]



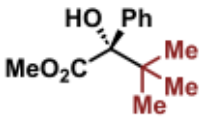
3a, 85%, 96:4 er



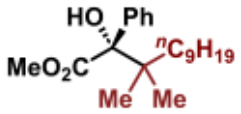
CCDC: 2326190



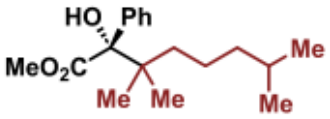
3b, R = CO_2Me, 94%, 96:4 er
3c, R = H, 56%, 95.5:4.5 er
3d, R = OMe, 92%, 95:5 er



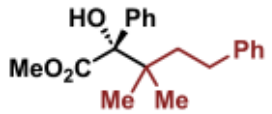
3e, 65%, 95:5 er



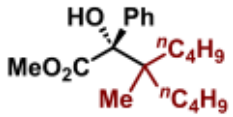
3f, 78%, 95:5 er



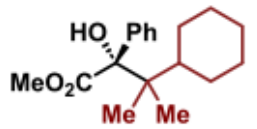
3g, 78%, 96.5:3.5 er



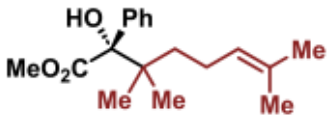
3h, 70%, 94:6 er



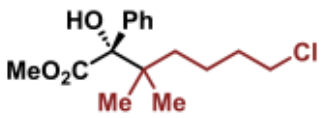
3i, 72%, 96.5:3.5 er



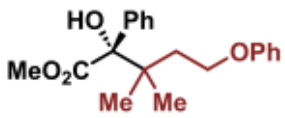
3j, 53%, 96:4 er



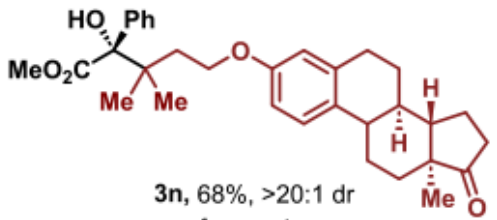
3k, 72%, 95.5:4.5 er



3l, 67%, 96:4 er

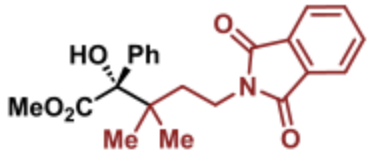


3m, 65%, 96:4 er

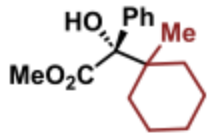


3n, 68%, >20:1 dr
from estrone

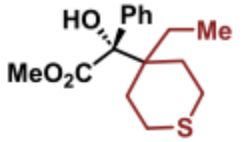
2.3 C=O bonds



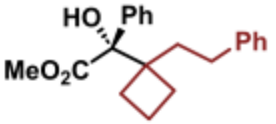
3o, 64%, 96.5:3.5 er



3p, 65%, 95.5:4.5 er

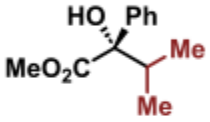


3q, 70%, 95.5:4.5 er

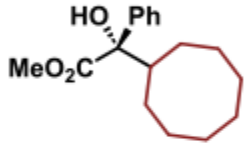


3r, 82%, 95.5:4.5 er

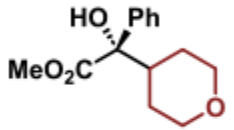
Secondary alkyl iodides[b]



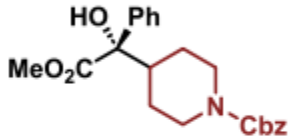
3s, 96%, 93:7 er



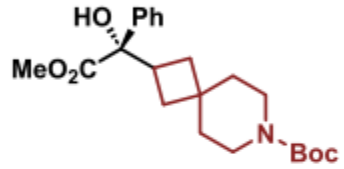
3t, 84%, 92:8 er



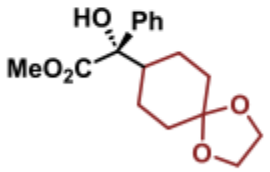
3u, 88%, 93.5:6.5 er



3v, 78%, 94.4:5.5 er

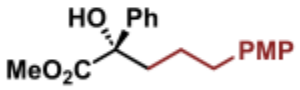


3w, 82%, 92.5:7.5 er

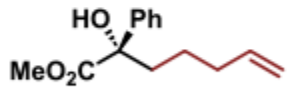


3x, 78%, 91.5:8.5 er

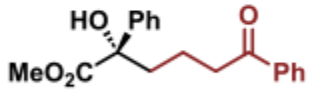
Primary alkyl iodides[b]



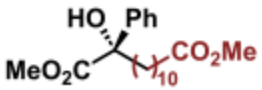
3y, 82%, 93.5:6.5 er



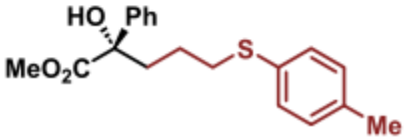
3z, 89%, 93:7 er



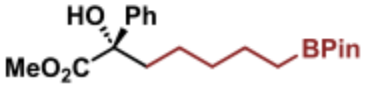
3aa, 74%, 96:4 er



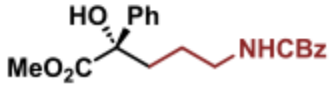
3ab, 78%, 92:8 er



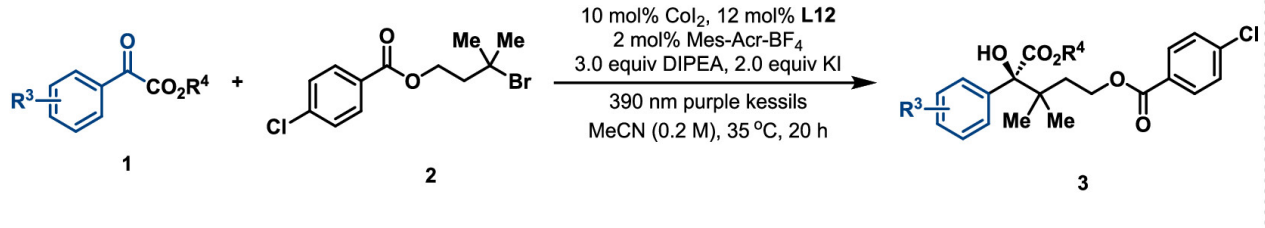
3ac, 71%, 91:9 er

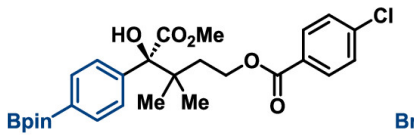


3ad, 76%, 92:8 er

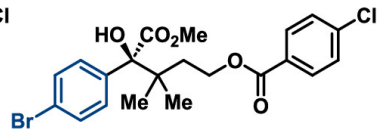


3ae, 63%, 92:8 er

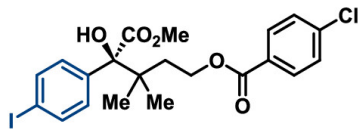




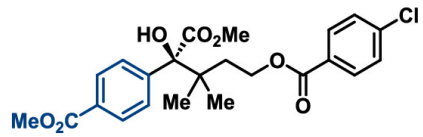
3af, 83%, 96:4 er



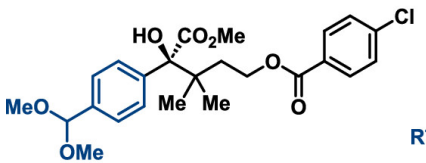
3ag, 76%, 95:5 er



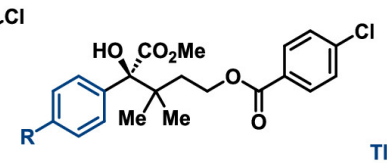
3ah, 89%, 95:5 er



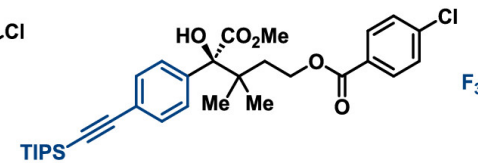
3ai, 85%, 94:6 er



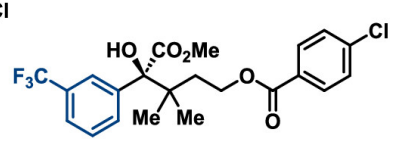
3aj, 82%, 95.5:4.5 er



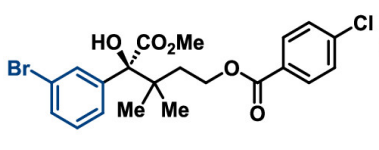
3ak, **R = TMS**, 81%, 95:5 er
3al, **R = SMe**, 87%, 95.5:4.5 er



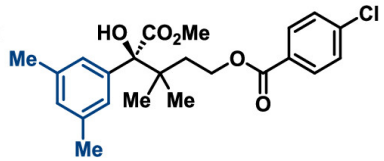
3am, 87%, 97:3 er



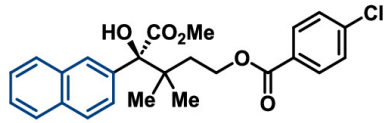
3an, 61%, 95:5 er



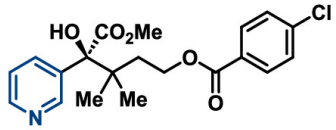
3ao, 54%, 95:5 er



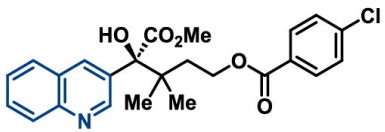
3ap, 78%, 96:4 er



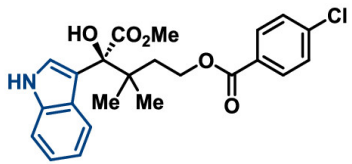
3aq, 89%, 95:5 er



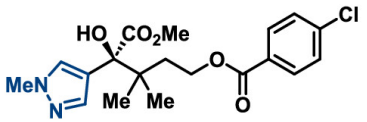
3ar, 75%, 95:5 er



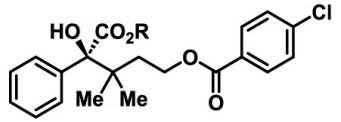
3as, 53%, 93.5:6.5 er



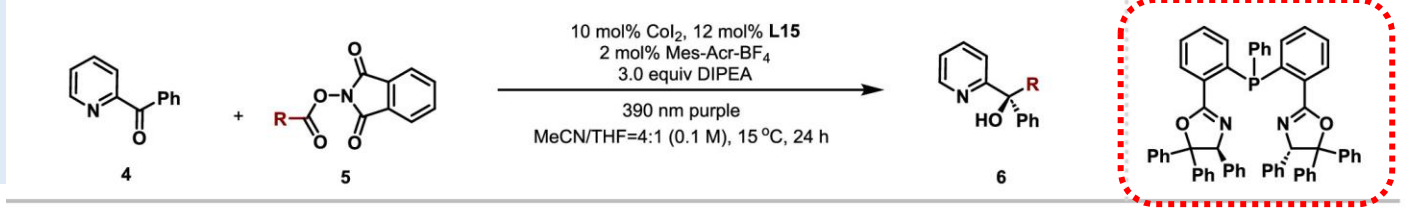
3at, 65%, 96.5:3.5 er



3au, 71%, 95.5:4.5 er

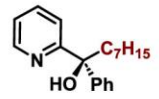


3av, R = ^{i}Pr, 83%, 90.5:9.5 er
3aw, R = Bn, 74%, 94:6 er

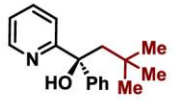


简单更换配体和溶剂

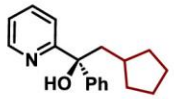
Primary alkyl NHPI esters



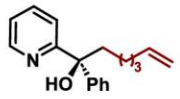
6a, 90%, 96:4 er



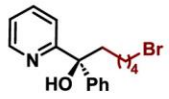
6b, 82%, 96.5:3.5 er



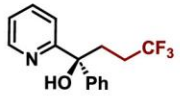
6c, 62%, 96:4 er



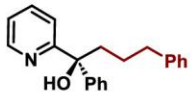
6d, 70%, 94:6 er



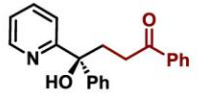
6e, 60%, 96:4 er



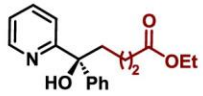
6f, 63%, 97:3 er



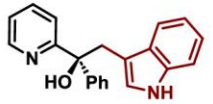
6g, 96%, 95:5 er



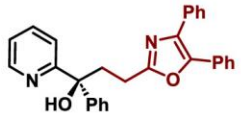
6h, 55%, 95.5:4.5 er[b]



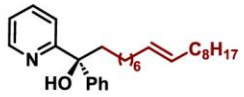
6i, 84%, 95:5 er



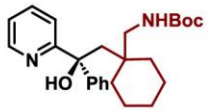
6j, 61%, 95:5 er
from Indole-3-acetic acid



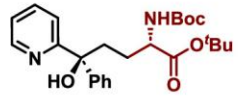
6k, 59%, 95.5:4.5 er
from Oxaprozin



6l, 66%, 94:6 er
from Oleic acid

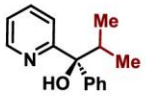


6m, 69%, 91:9 er
from Gabapentin

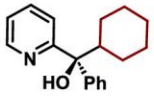


6n, 81%, > 20:1 dr
from L-glutamic acid

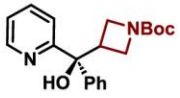
Secondary alkyl NHPI esters



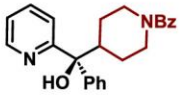
6o, 81%, 94.5:5.5 er



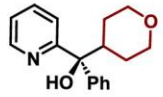
6p, 68%, 95:5 er



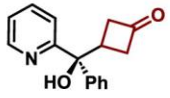
6q, 41%, 96:4 er



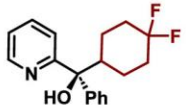
6r, 67%, 96:4 er



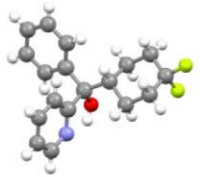
6s, 56%, 93.5:6.5 er



6t, 86%, 95:5 er

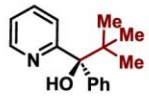


6u, 68%, 94.5:5.5 er



CCDC: 2363999

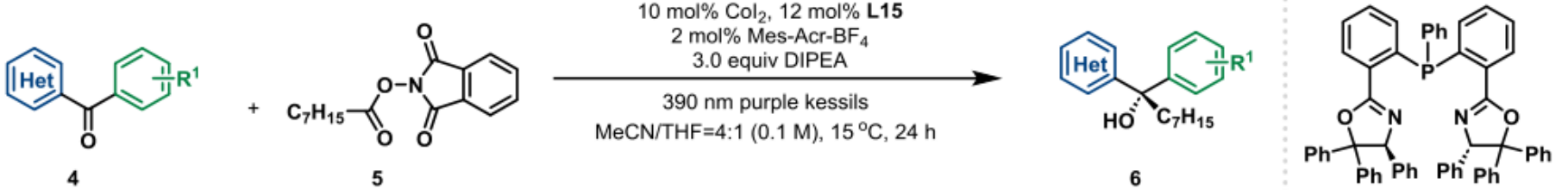
Tertiary alkyl NHPI esters

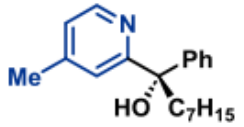


6v, 47%, 86.5:13.5 er

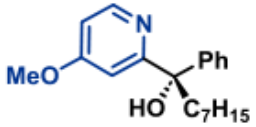
2.3 C=O bonds

Scheme 5. Substrate Scope of Pyridine-Based Ketones[a]

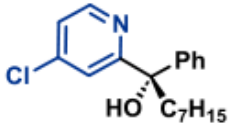




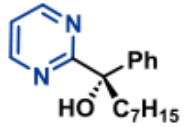
6w, 67%, 96:4 er



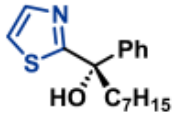
6x, 81%, 95:5 er



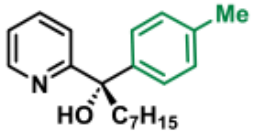
6y, 67%, 97:3 er



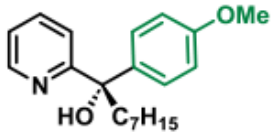
6z, 63%, 97:3 er



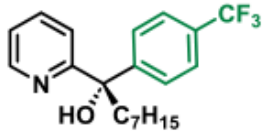
6aa, 62%, 95.5:4.5 er



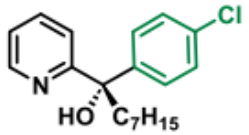
6ab, 79%, 95:5 er



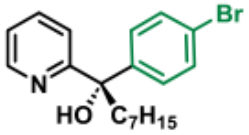
6ac, 74%, 95.5:4.5 er



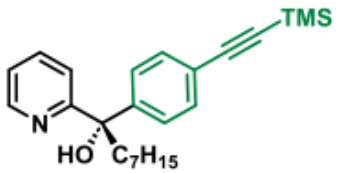
6ad, 51%, 93:7 er



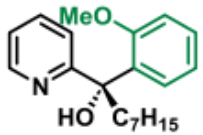
6ae, 46%, 95:5 er



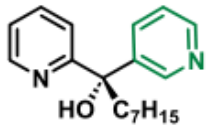
6af, 47%, 94.5:5.5 er



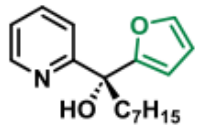
6ag, 53%, 94:6 er



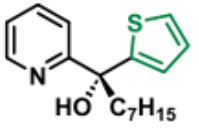
6ah, 46%, 84:16 er



6ai, 68%, 92.5:7.5 er



6aj, 47%, 96:4 er

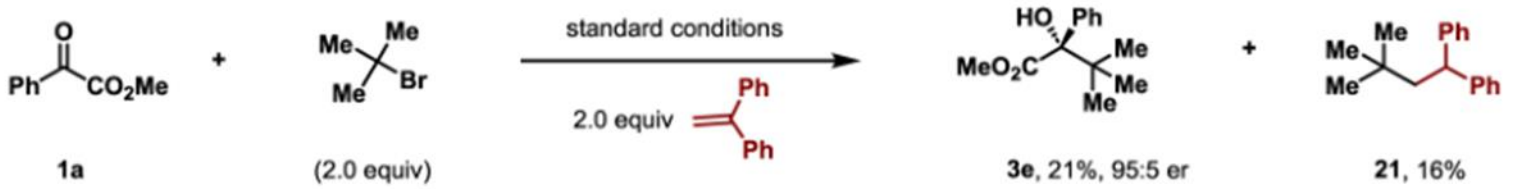


6ak, 76%, 95:5 er

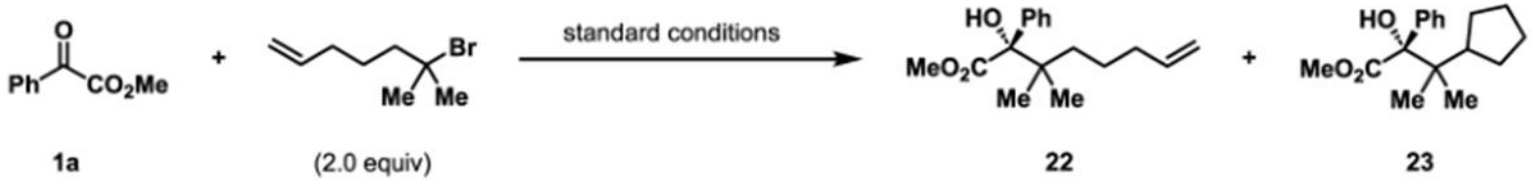
2.3 C=O bonds

Scheme 7. Preliminary Mechanistic Studies

(a) Radical trap reaction

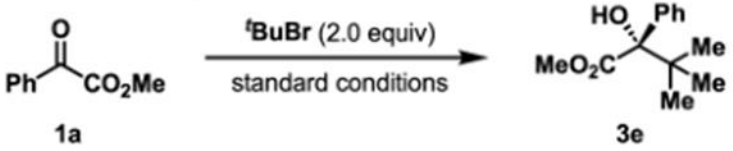


(b) Radical cyclization experiment

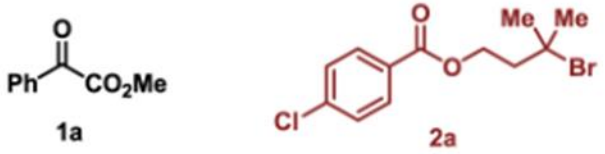


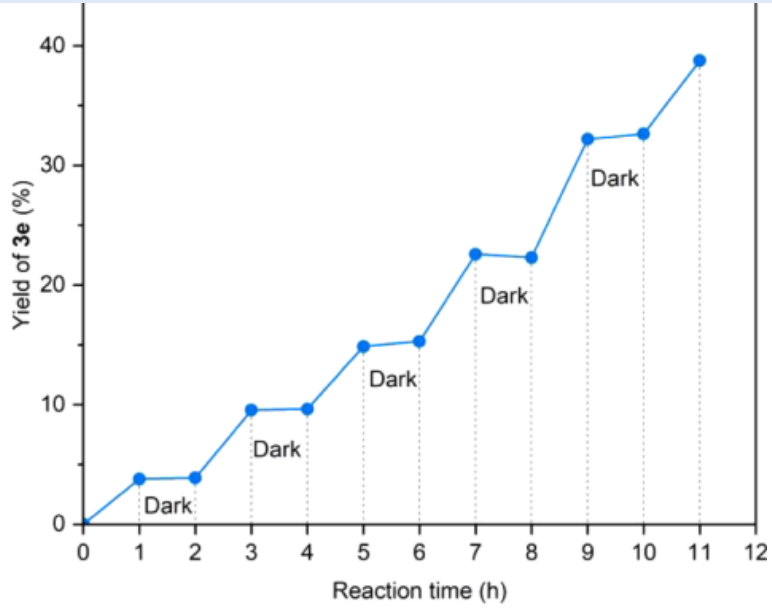
82% isolated yield (**22**:**23** = 2.7:1)

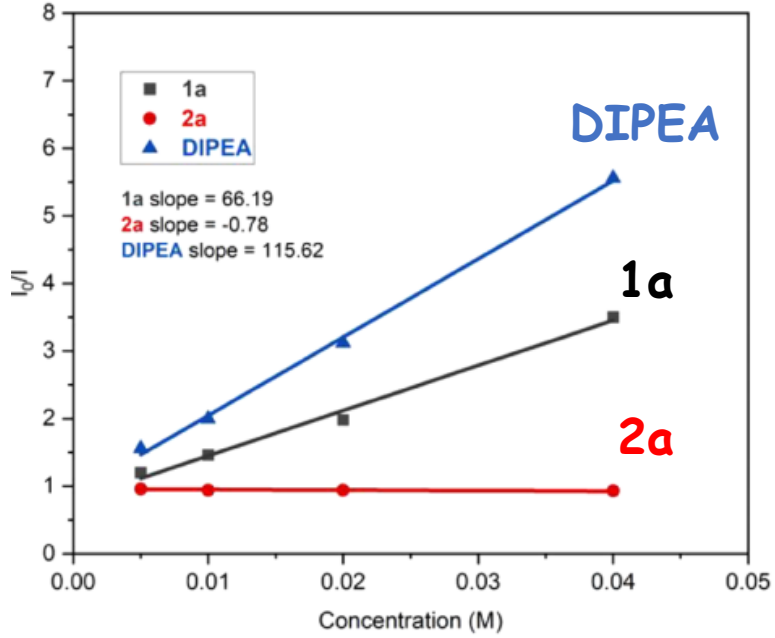
(c) Light on/off study



(d) The Stern–Volmer plots

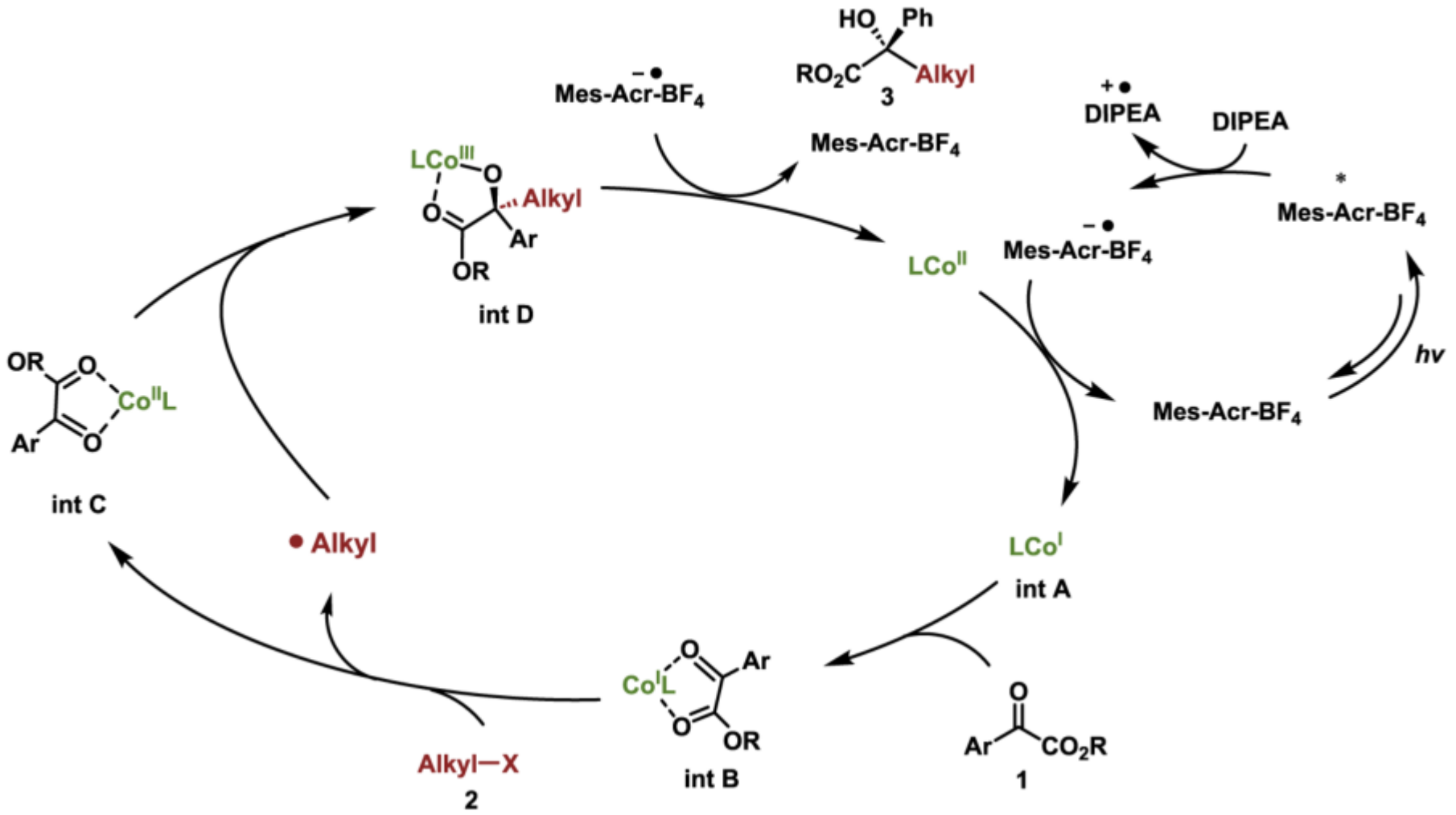






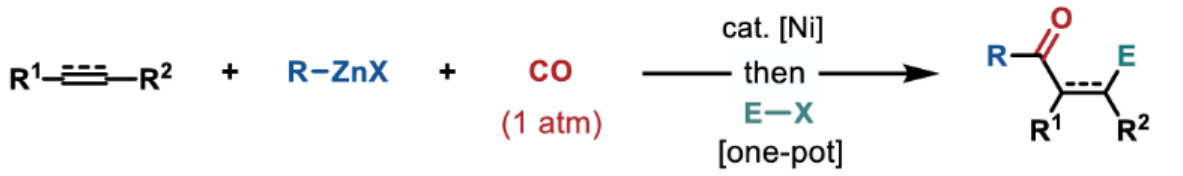
2.3 C=O bonds

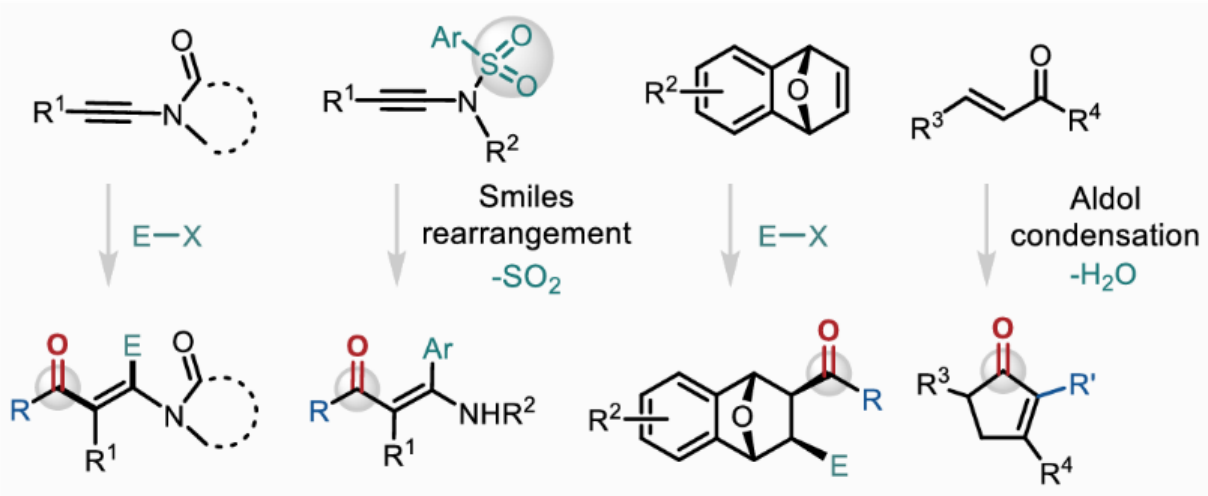
(e) Proposed mechanism



3. Catalytic Carbonylation of 1 atm CO by Nickel

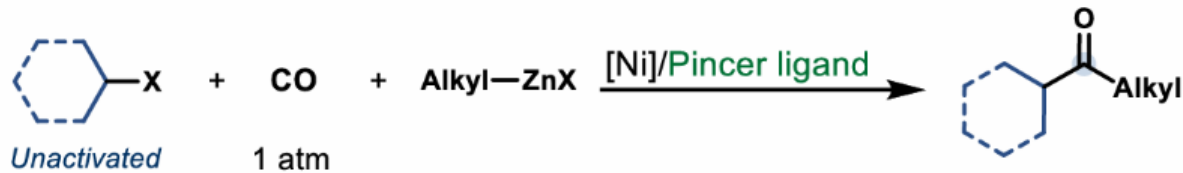
Acylzincation of unsaturated C-C bond



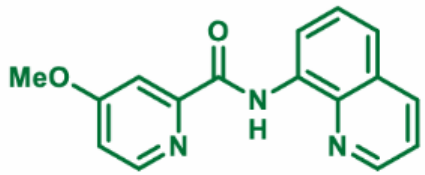


- *in situ* generation of catalytic acyl organometallics
- a new paradigm of carbometallation chemistry

Carbonylative cross-coupling reaction



Pitfall

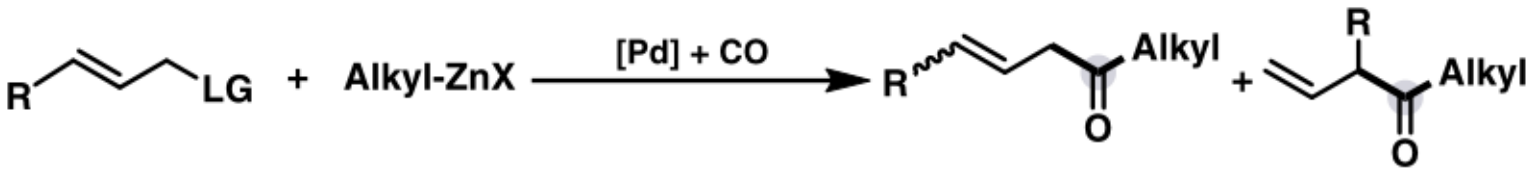


newly developed NN_2-pincer ligand

- the chemoselective three-component carbonylative Negishi cross-coupling reaction.
- overcoming the competing Negishi coupling, the β-hydride elimination, dehalogenation

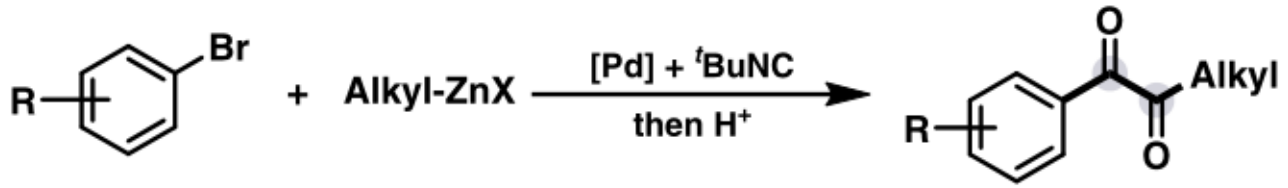
3. Catalytic Carbonylation of 1 atm CO by Nickel

a Pd-catalyzed allylic carbonylative Negishi reaction with CO (Tamaru)



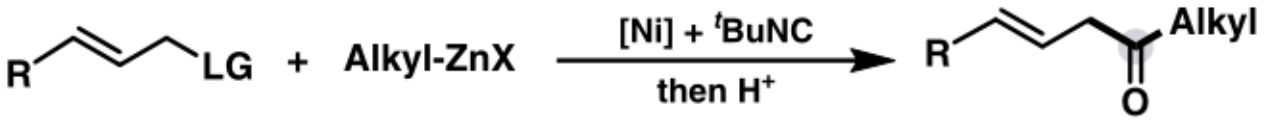
- Poor regioselectivity

b Pd-catalyzed aryl carbonylative Negishi reaction (Dechert–Schmitt and Blackmond)



- Double insertion of ^{t}BuNC
- Challenge for monocarbonylation

c Ni-catalyzed allylic carbonylative Negishi reaction with ^{t}BuNC (this work)



- High regioselectivity
- No polycarbonylation of isocyanide
- High *E*/*Z* selectivity
- No alkene isomerization

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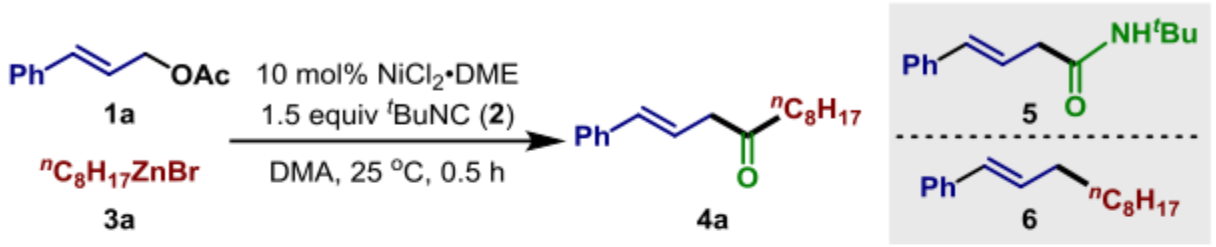
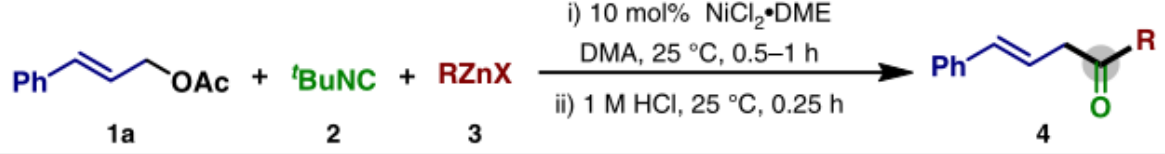
3. Catalytic Carbonylation of 1 atm CO by Nickel

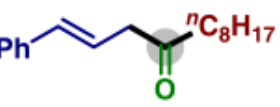
Table 1 Optimization of the reaction conditions.



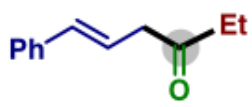
Entry[a]	Catalyst	Ligand	Yield (%)[b]		
			4a	5	6
1	$NiCl_2$·DME	—	90 (86)[c]	ND	1
2	$NiCl_2$·DME	PPh_3	27	10	ND
3	$NiCl_2$·DME	dppf	5	ND	ND
4	$NiCl_2$·DME	Phen	82	3	3
5	$NiCl_2$·DME	SIPr·HCl	87	2	3
6	$Ni(cod)_2$	—	86	6	ND
7	$Pd(dba)_2$	—	4	ND	ND
8	—	—	ND	ND	ND
9[d] *CO*	$NiCl_2$·DME	—	ND	ND	ND

dppf 1,1′-Ferrocenediyl-bis(diphenylphosphine), *SIPr·HCl* 1,3-Bis-(2,6-diisopropylphenyl)imidazolinium chloride, *ND* not determined
[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.3 mmol), **3a** (0.3 mmol), catalyst (0.02 mmol), ligand (0.04 mmol), DMA (2 mL), 25 °C, 0.5 h, and then 1 M HCl (2 mL) was added, 25 °C, 0.25 h
[b]Corrected GC yield
[c]Isolated yield within parentheses in 0.2 mmol scale
[d]The reaction in CO (1 atm) instead of ^{t}BuNC

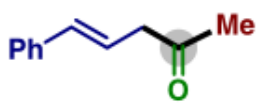




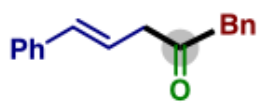
4a, 86%, *E*/*Z* > 20/1



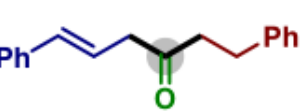
4b, 84%, *E*/*Z* > 20/1



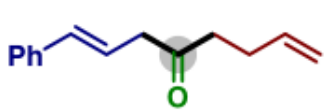
4c, 75%, *E*/*Z* > 20/1



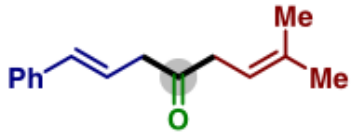
4d, 85%, *E*/*Z* > 20/1



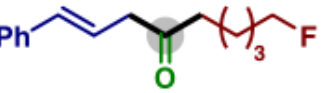
4e, 75%, *E*/*Z* > 20/1



4f, 85%, *E*/*Z* > 20/1

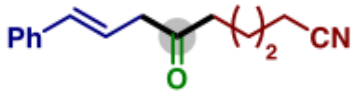


4g, 71%, *E*/*Z* > 20/1

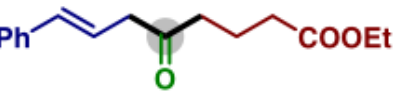


4h, 85%, *E*/*Z* > 20/1

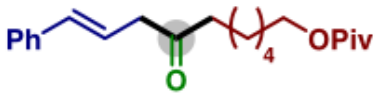
4i, 62%, *E*/*Z* > 20/1



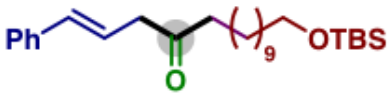
4j, 73%, *E*/*Z* > 20/1



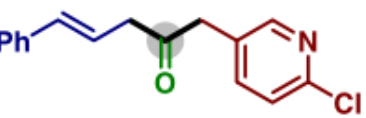
4k, 78%, *E*/*Z* > 20/1



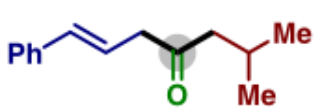
4l, 87%, *E*/*Z* > 20/1



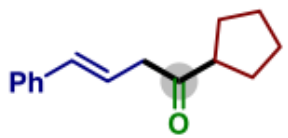
4m, 56%, *E*/*Z* > 20/1



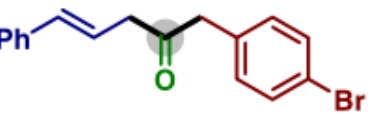
4n, 70%, *E*/*Z* > 20/1



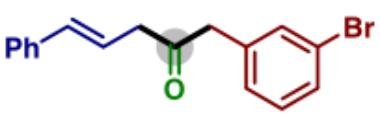
4o, 58%, *E*/*Z* > 20/1



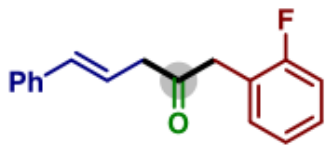
4p, 61%[a], *E*/*Z* > 20/1



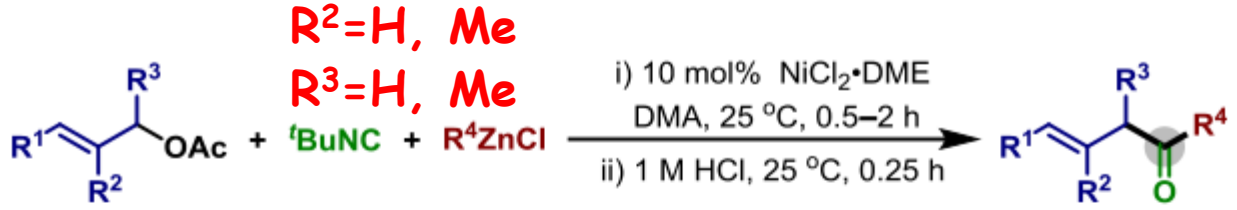
4q, 83%, *E*/*Z* > 20/1

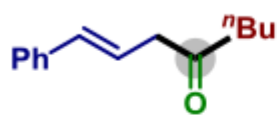


4r, 91%, *E*/*Z* > 20/1

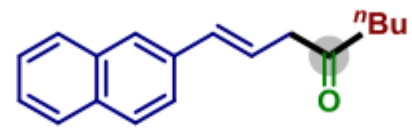


4s, 61%, *E*/*Z* > 20/1

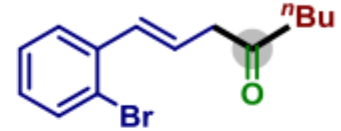




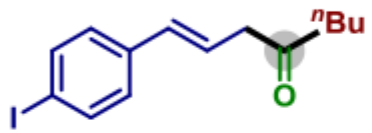
4t, 95%, *E*/*Z* > 20/1



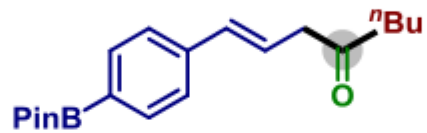
4u, 96%, *E*/*Z* > 20/1



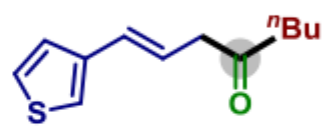
4v, 73%, *E*/*Z* > 20/1



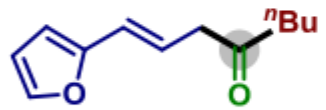
4w, 81%, *E*/*Z* > 20/1



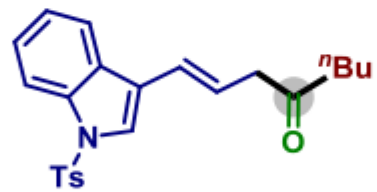
4x, 43%, *E*/*Z* > 20/1



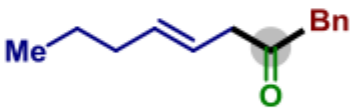
4y, 79%, *E*/*Z* > 20/1



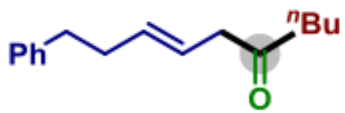
4z, 76%, *E*/*Z* > 20/1



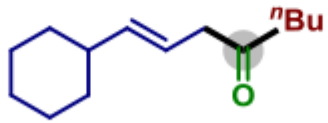
4aa, 80%, *E*/*Z* > 20/1



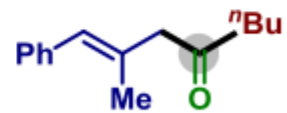
4ab, 76%, *E*/*Z* = 12/1



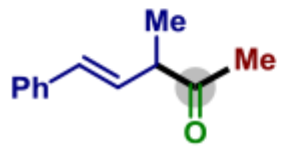
4ac, 82%, *E*/*Z* = 13/1



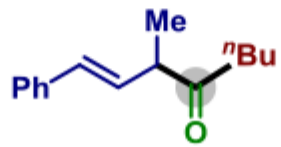
4ad, 73%, *E*/*Z* > 20/1



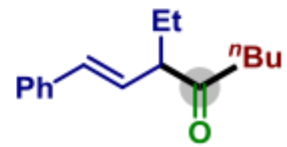
4ae, 57%[a], *E*/*Z* > 20/1



4af, 69%[a,b], *E*/*Z* > 20/1



4ag, 70%[a,b,c]



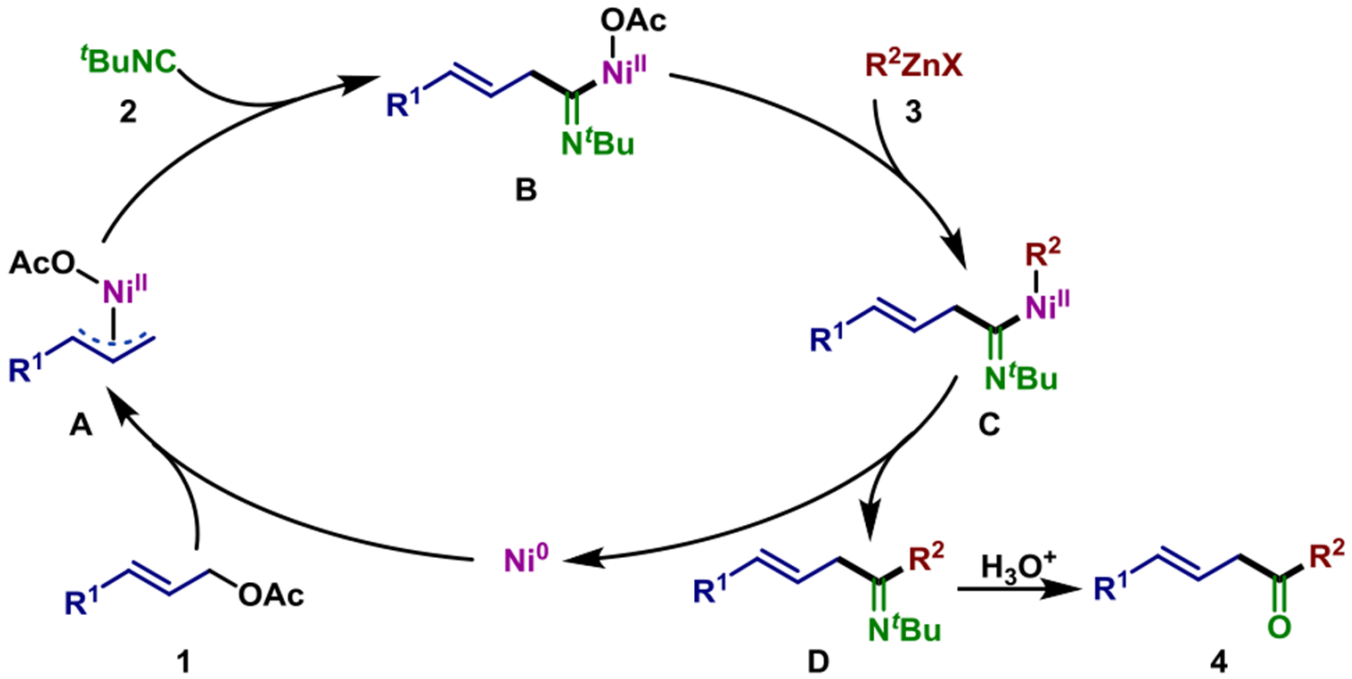
4ah, 84%[a,b,d]

3. Catalytic Carbonylation of 1 atm CO by Nickel

a The reaction proceeds with π-allyl nickel intermediate

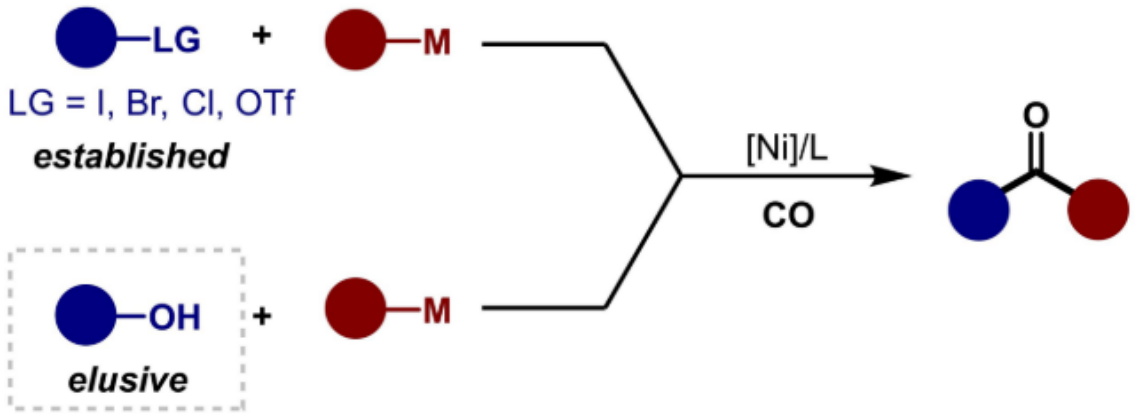
π烯丙基镍中间体进行

自由基中间体

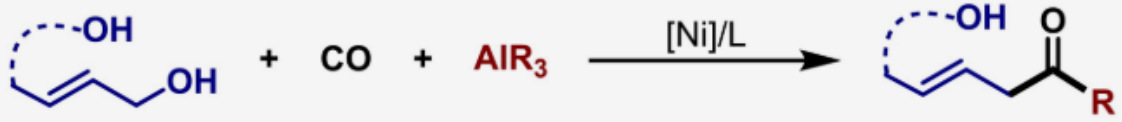


3. Catalytic Carbonylation of 1 atm CO by Nickel

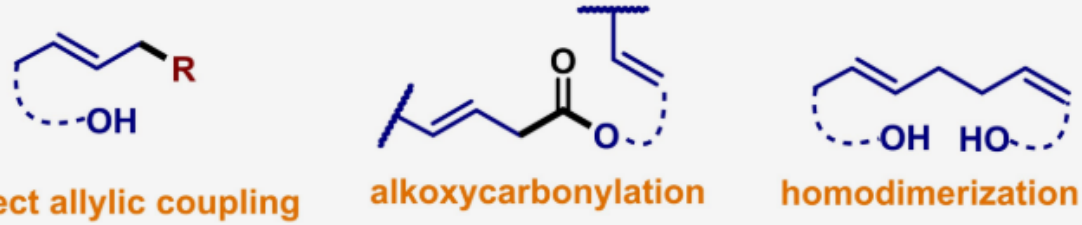
a) Ni-catalyzed carbonylative cross-coupling reactions



b) This work: Ni-catalyzed carbonylative reaction of allylic alcohols

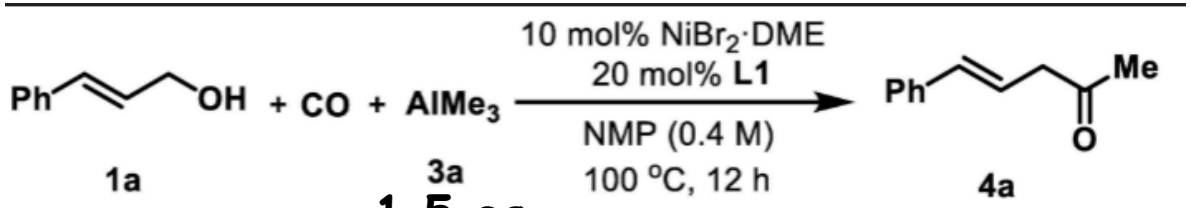


Potential side reaction



direct allylic coupling | alkoxycarbonylation | homodimerization

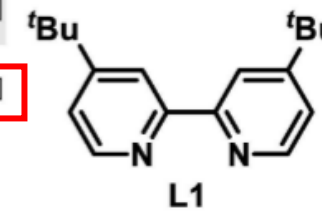
- Two C-C bonds formation
- chemoselective carbonylation
- Dual roles of organoalanes
- Investigation of reactive ADMAL



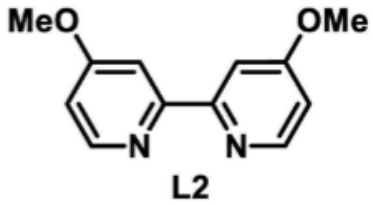
1a 3a 4a

1.5 eq

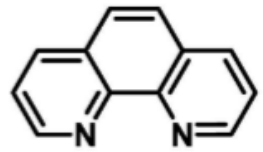
Entry	Deviation from above	4a (%)[b]
1	none	74 (72)[c]
2	$NiCl_2$·DME instead of $NiBr_2$·DME	65
3	$Ni(COD)_2$ instead of $NiBr_2$·DME	37
4	**L2** instead of **L1**	62
5	**L3** instead of **L1**	61
6	DMF as solvent	64
7	THF as solvent	0
8	Toluene as solvent	10
9	NMP (0.1 M)	57
10	NMP (1.0 M)	71
11	2.0 equiv $AlMe_3$	72
12	MeZnCl, MeMgBr, MeLi instead of $AlMe_3$	0
13	**2a** instead of **1a**	74 (72)[c]



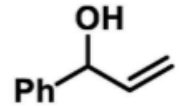
L1



L2



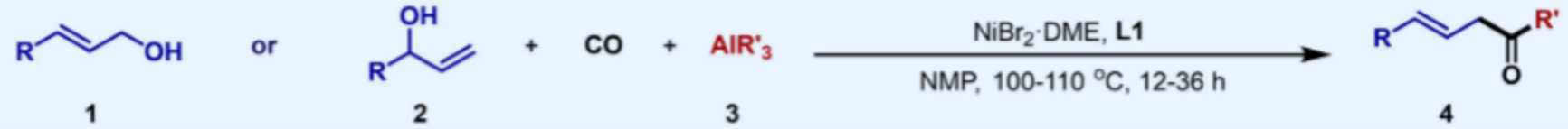
L3

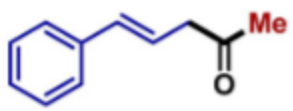


2a

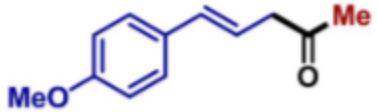
Angew. Chem. Int. Ed. **2022**, *61*, e202210484.

a) Carbonylative cross-coupling of allylic alcohols

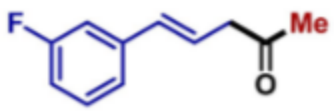




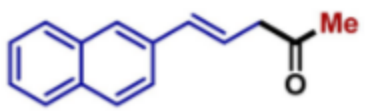
4a, 72%[a,b]



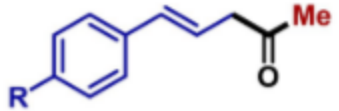
4b, 69%[a] (64%[b])



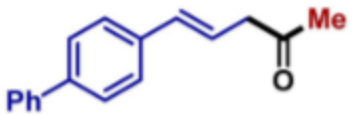
4c, 51%[a] (68%[b])



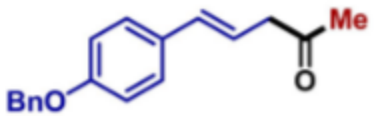
4d, 66%[a,b]



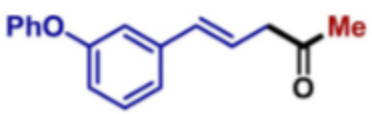
4e, R = Me, 69%[a]
4f, R = ^{i}Pr, 50%[b]
4g, R = ^{t}Bu, 70%[b]



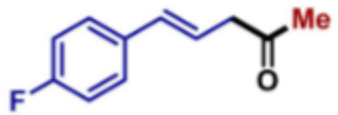
4h, 59%[b]



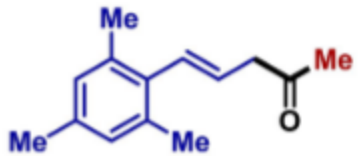
4i, 78%[b]



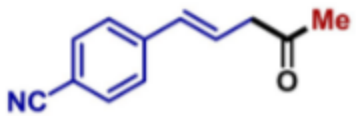
4j, 72%[b]



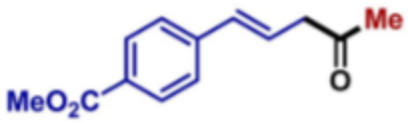
4k, 70%[b]



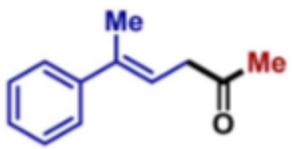
4l, 65%[b]



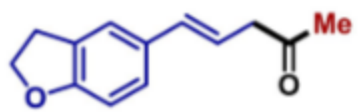
4m, 57%[b]



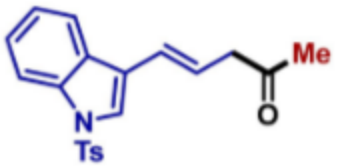
4n, 66%[b]



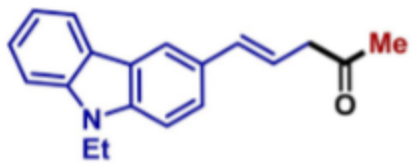
4o, 63%[a]



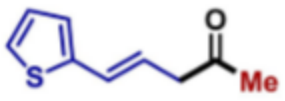
4p, 47%[b]



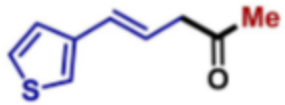
4q, 57%[a]



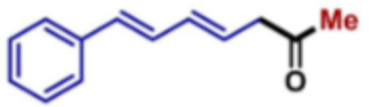
4r, 41%[b]



4s, 43%[b]

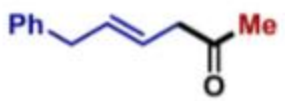


4t, 53%[a]



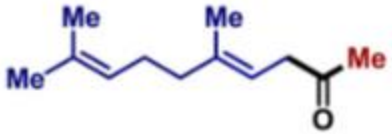
4u, 44%[b]
E/Z = 5/1

4v, 49%[c]
E/Z = 2.6/1

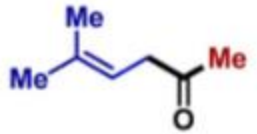


4w, 62%[c]
E/Z = 2.8/1

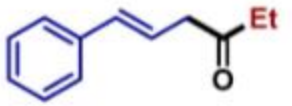
4x, 46%[c]
E/Z = 2/1



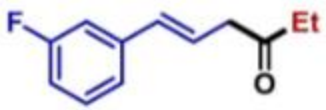
4y, 53%[c]
E/Z = 2.1/1



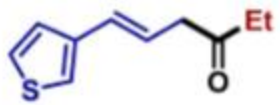
4z, 59%[c]



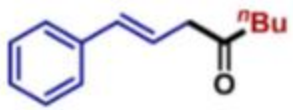
4aa, 75%[a]



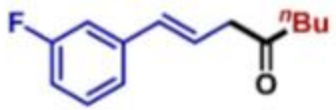
4ab, 47%[a]



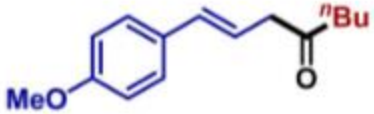
4ac, 62%[a]



4ad, 51%[a]

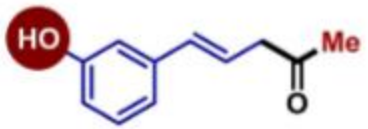


4ae, 52%[a]

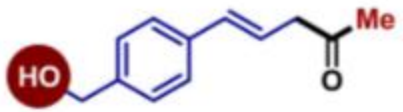


4af, 44%[a]

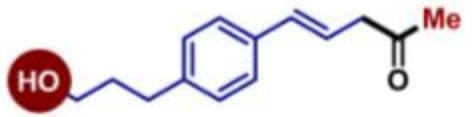
b) Chemoselective carbonylative cross-coupling of diols



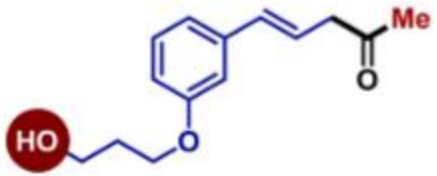
4ag, 72%[b]



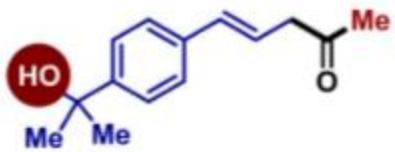
4ah, 49%[b]



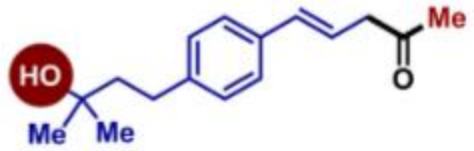
4ai, 66%[b]



4aj, 68%[b]

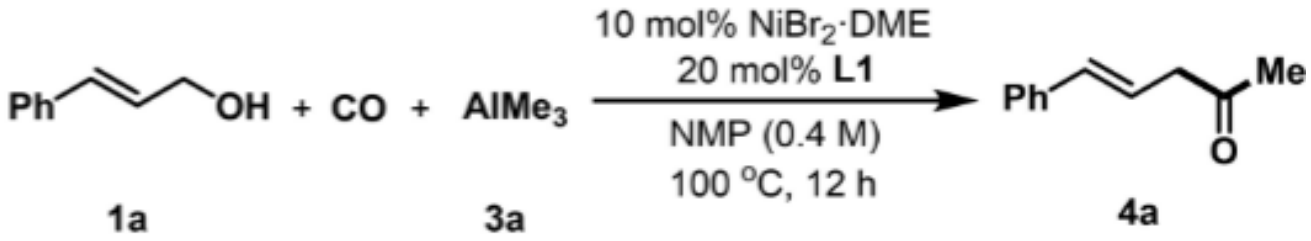


4ak, 45%[b]

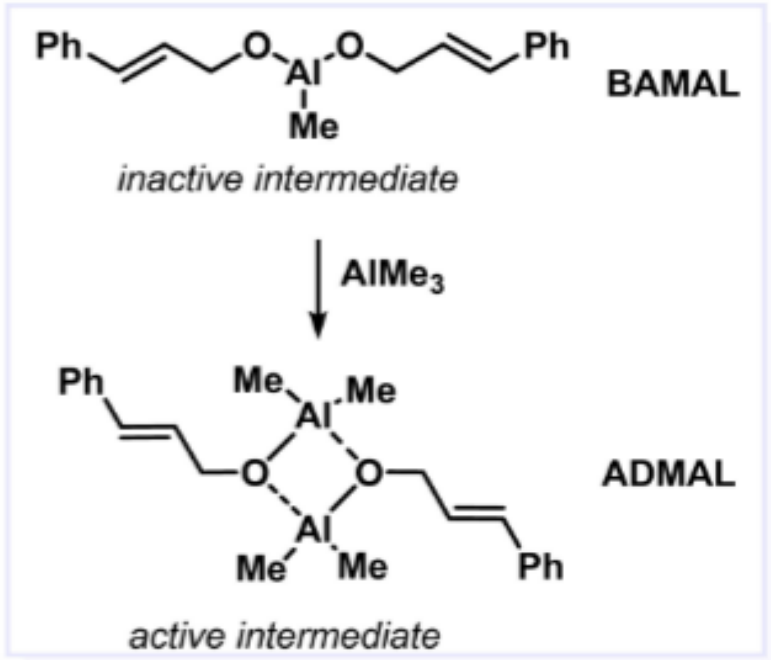


4al, 70%[b]

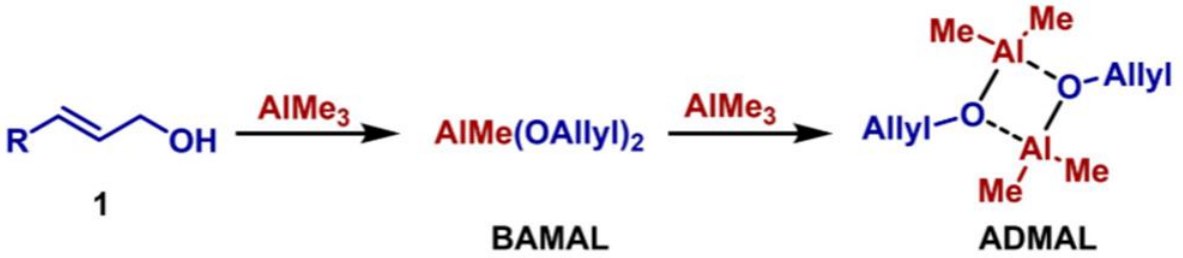
b) Investigation of the amount of $AlMe_3$

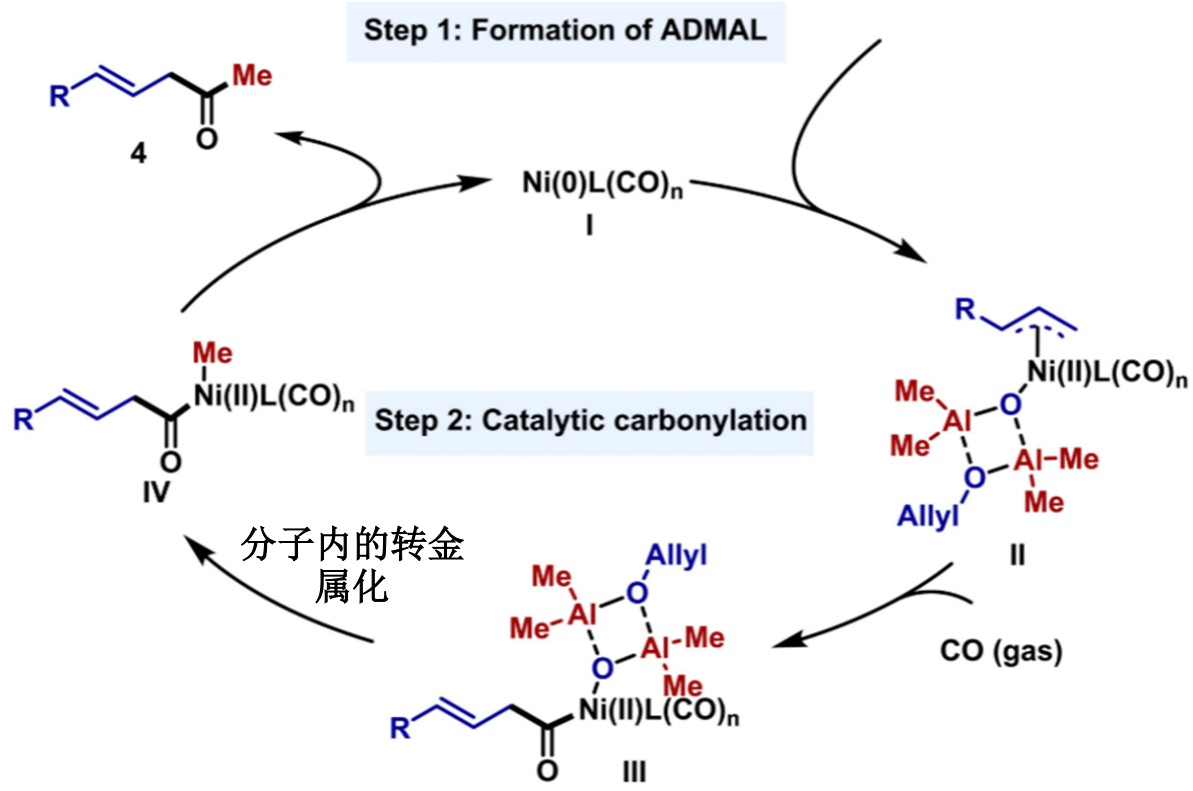


Equiv of 3a	Yield of 4a (%)
0.33	0
0.5	0
0.75	15
1.0	35
1.5	74

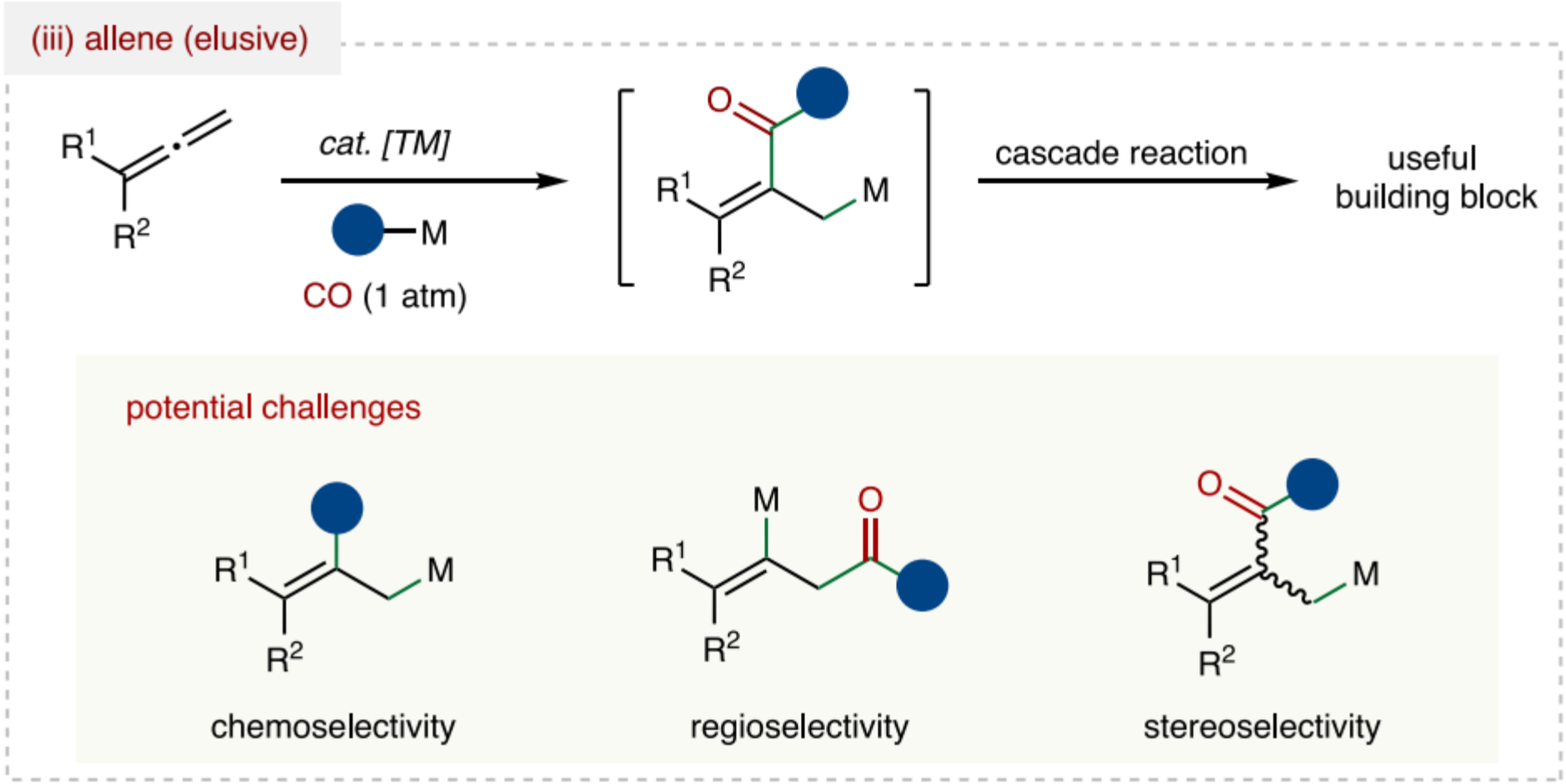


促进*C-O*键氧化断裂的反应中间体

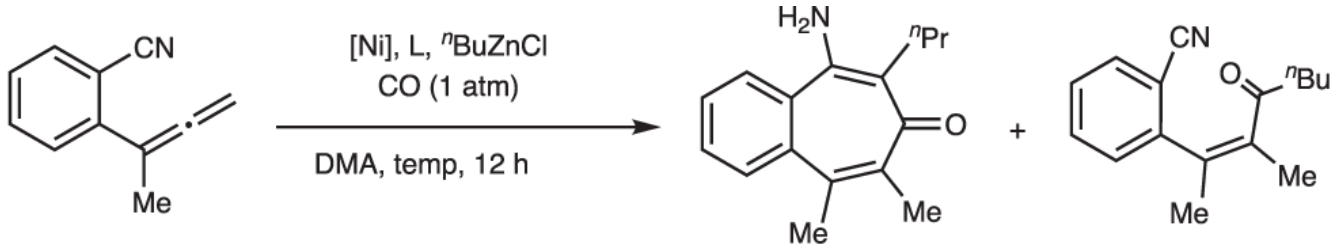




3. Catalytic Carbonylation of 1 atm CO by Nickel

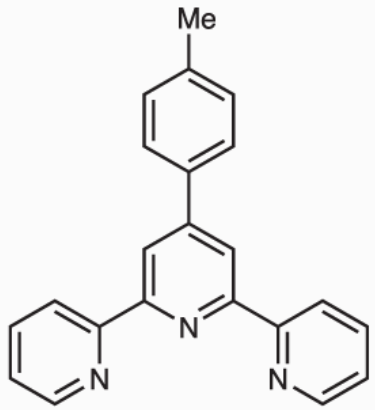


Nat. Commun. 2023, 14, 6960.

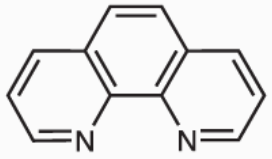


1a **3a** **4a**

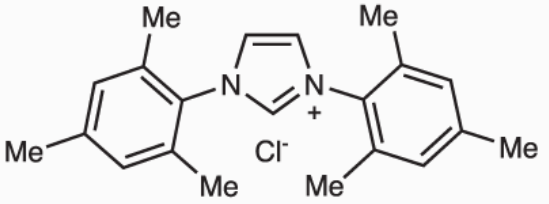
Entry	Ligand	Catalyst	T (°C)	Yield (%)[a] 3a	Yield (%)[a] 4a
	[Ni](0.01 mmol, 10 mol%) and L (0.02mmol, 20 mol%)				
1	**L1**	$Ni(acac)_2$	r.t.	33	28
2	**L1**	$Ni(acac)_2$	40 °C	53	3
3	**L1**	$Ni(acac)_2$	60 °C	51	2
4	**L2**	$Ni(acac)_2$	40 °C	38	7
5	**L3**	$Ni(acac)_2$	40 °C	57	6
6	**L4**	$Ni(acac)_2$	40 °C	61	6
7	**L5**	$Ni(acac)_2$	40 °C	63	7
8	**L6**	$Ni(acac)_2$	40 °C	63	5
9	**L6**	$NiCl_2$•DME	40 °C	61	5
10	**L6**	$NiBr_2$•DME	40 °C	67	2
11[b]	**L6**	$NiBr_2$•DME	40 °C	75 (71)[c]	2
	[Ni] (0.0025 mmol, 2.5 mol%), L6 (0.005 mmol, 5 mol%)				



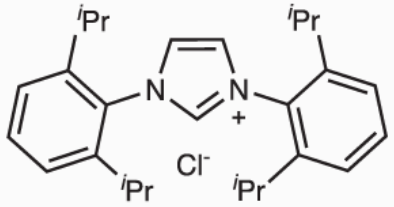
L1



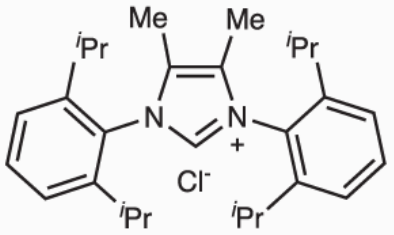
L2



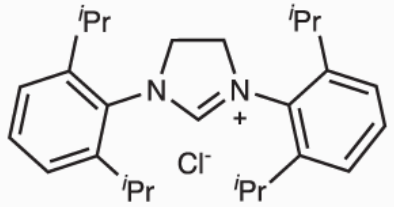
L3



L4

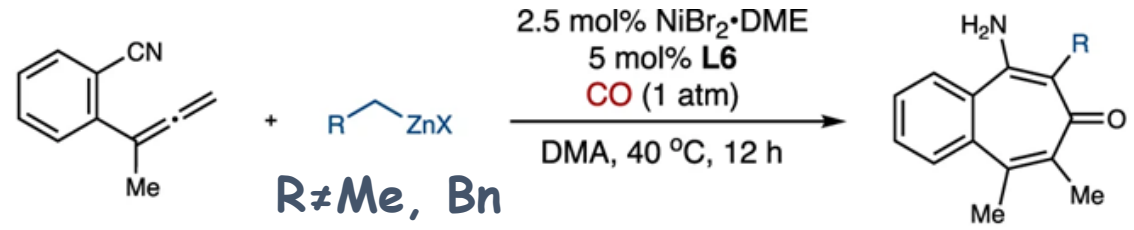


L5



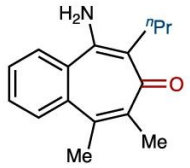
L6

3. Catalytic Carbonylation of 1 atm CO by Nickel

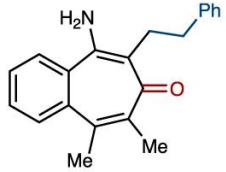


R≠Me, Bn

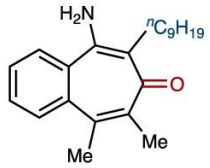
1a **2** **3**



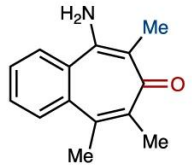
3a, 71%



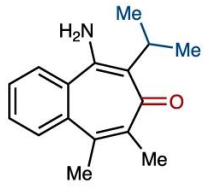
3b, 67%



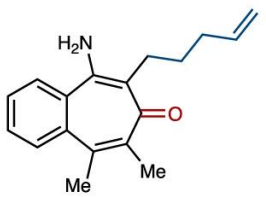
3c, 55%



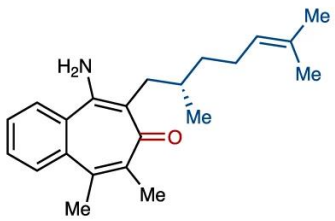
3d, 35%



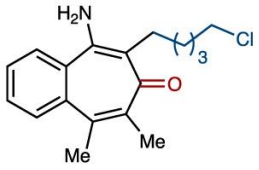
3e, 50%



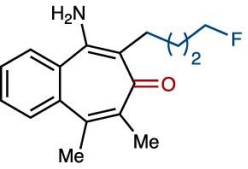
3f, 61%



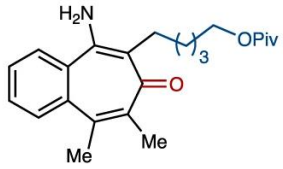
3g, 65%



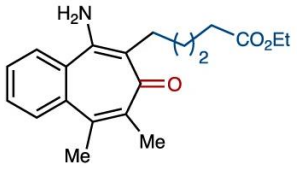
3h, 50%



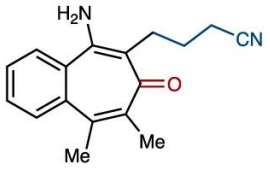
3i, 54%



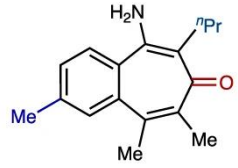
3j, 54%



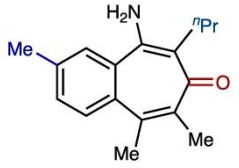
3k, 47%



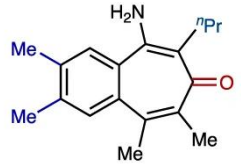
3l, 32%



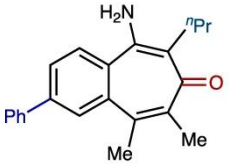
3m, 63%



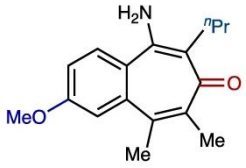
3n, 62%



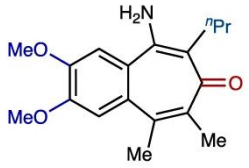
3o, 61%



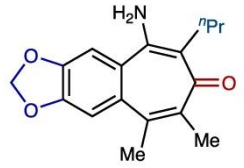
3p, 57%



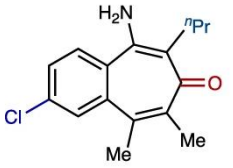
3q, 67%



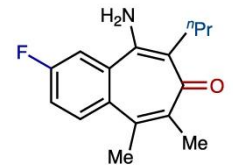
3r, 42%



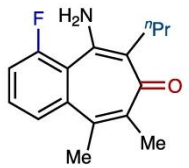
3s, 63%



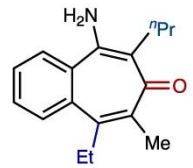
3t, 30%



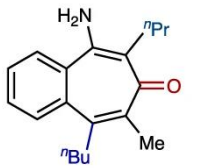
3u, 53%



3v, 32%



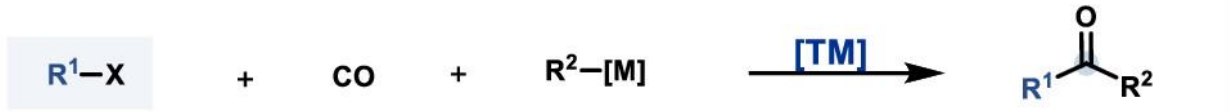
3w, 60%



3x, 51%

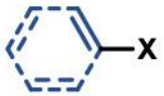
3. Catalytic Carbonylation of 1 atm CO by Nickel

a) Transition metal-catalyzed carbonylative cross-coupling for ketone synthesis

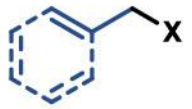


C(sp)-X

C(sp²)-X

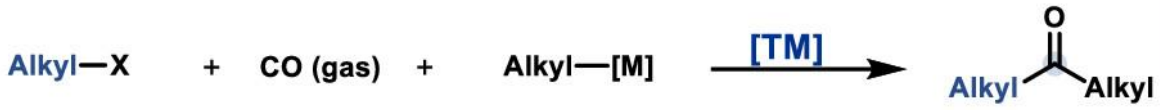


Activated C(sp³)-X



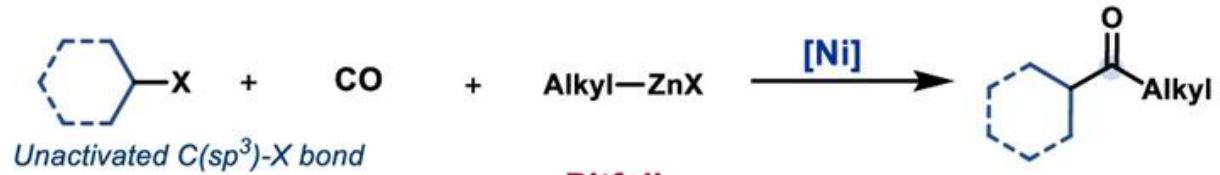
Well-established

b) Transition metal-catalyzed carbonylative cross-coupling of unactivated alkyl electrophiles for dialkyl ketone synthesis



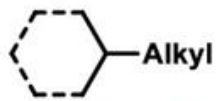
Unmet challenge

ii) Ni-catalyzed carbonylative Negishi coupling of unactivated alkyl-halides with CO



Unactivated C(sp³)-X bond

Pitfall



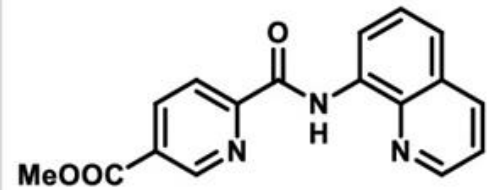
Negishi coupling

reductive dehalogenation

β-H elimination

- New tridentate NNN-pincer ligand
- Mild condition with atmospheric CO gas
- Broad functionality with organozinc reagent
- Facile unsymmetric dialkyl ketone synthesis

New NNN-ligand



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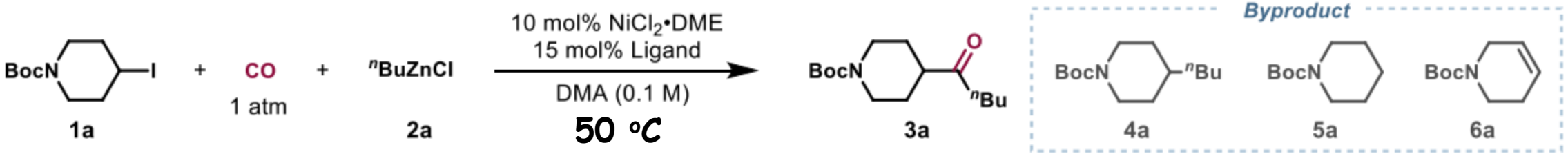
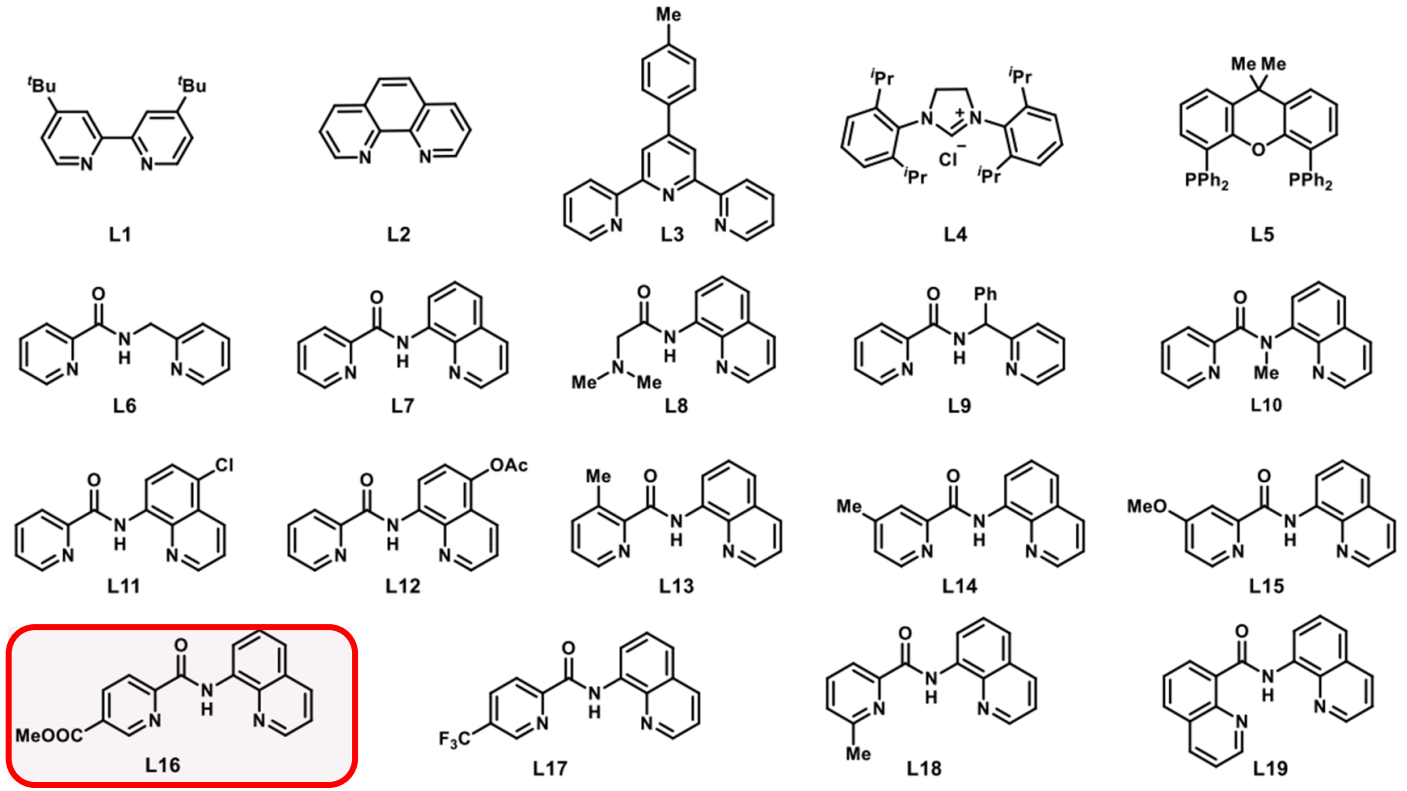
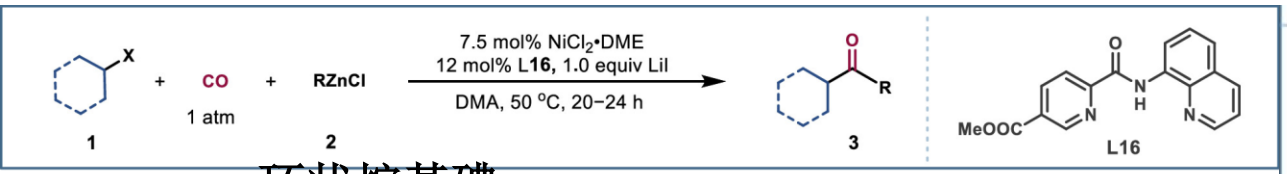
3. Catalytic Carbonylation of 1 atm CO by Nickel





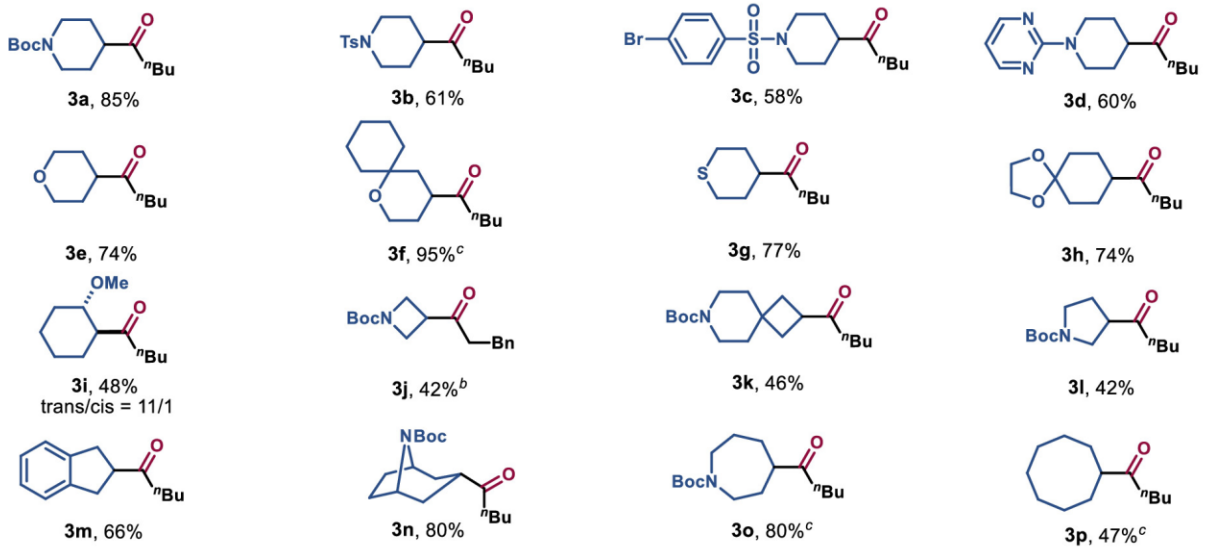
entry	ligand	conversion of **1a** (%)	yield of **3a**/**4a**/**5a**/**6a** (%)[a]
22[c,d]	**L16**	100	90 (85)[e]/0/4/1

3. Catalytic Carbonylation of 1 atm CO by Nickel



环状烷基碘

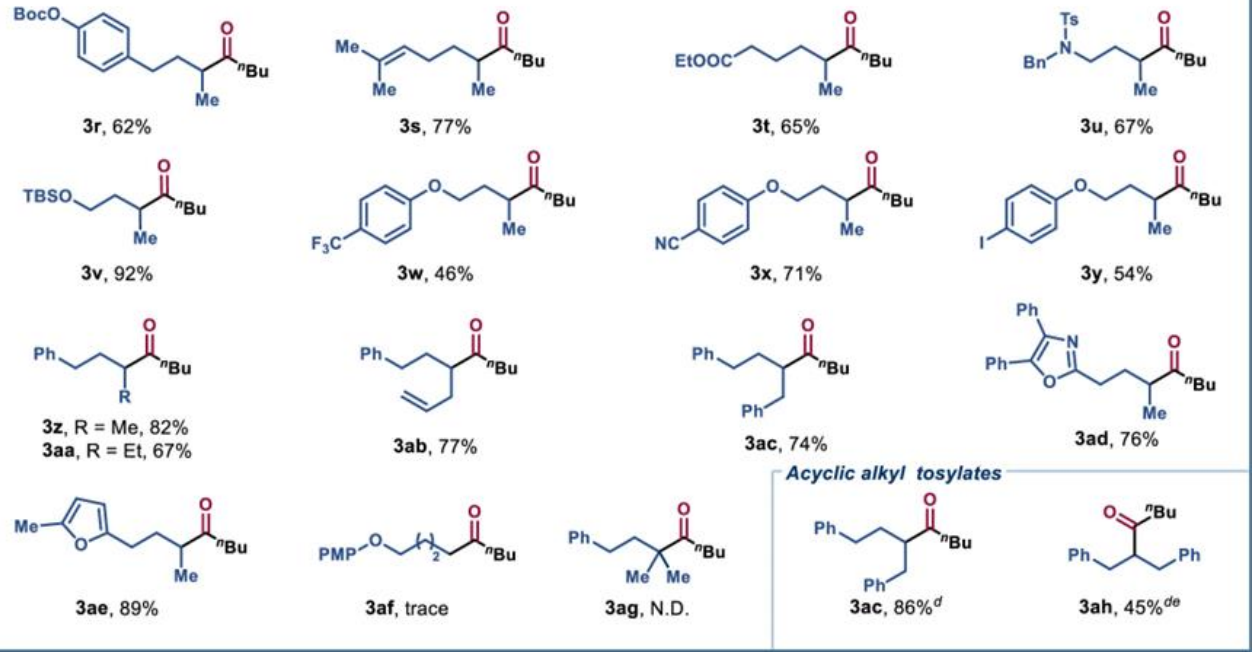
Cyclic alkyl iodides



环状烷基甲苯磺酸酯

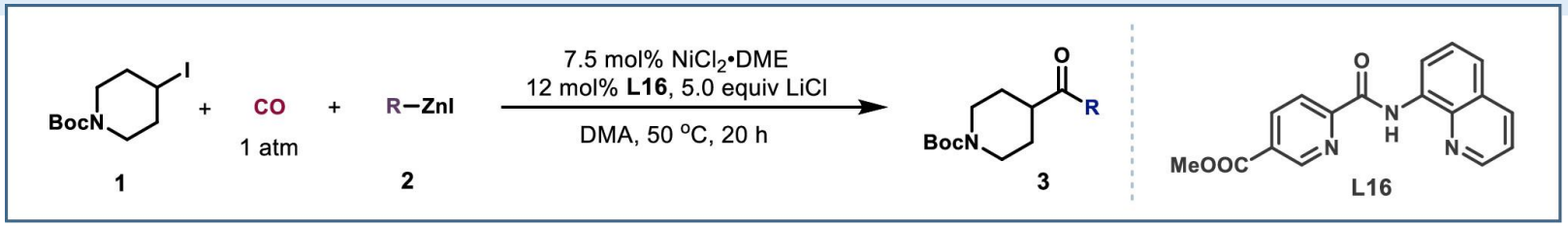
Cyclic alkyl tosylates

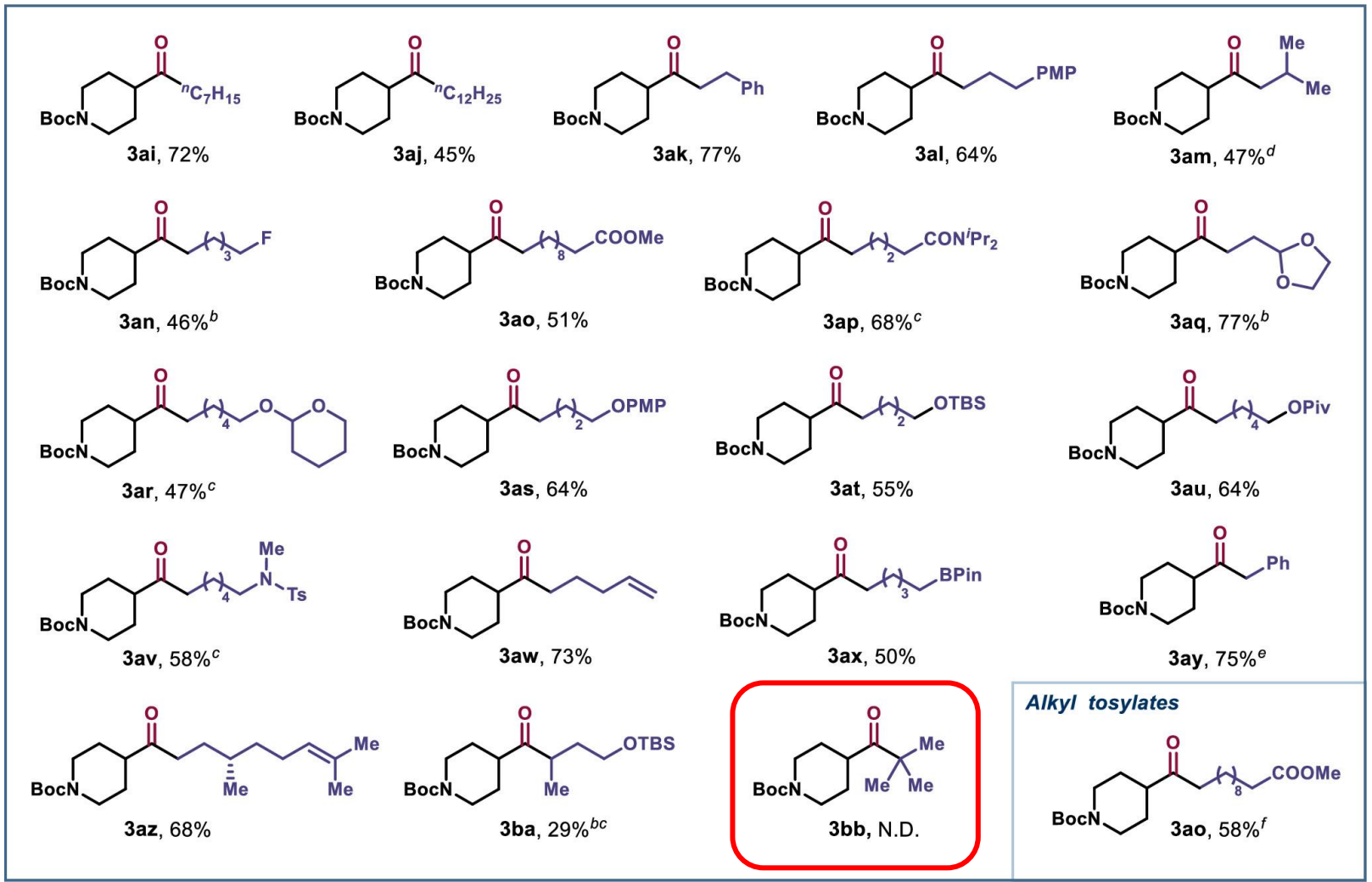
Acyclic alkyl iodides

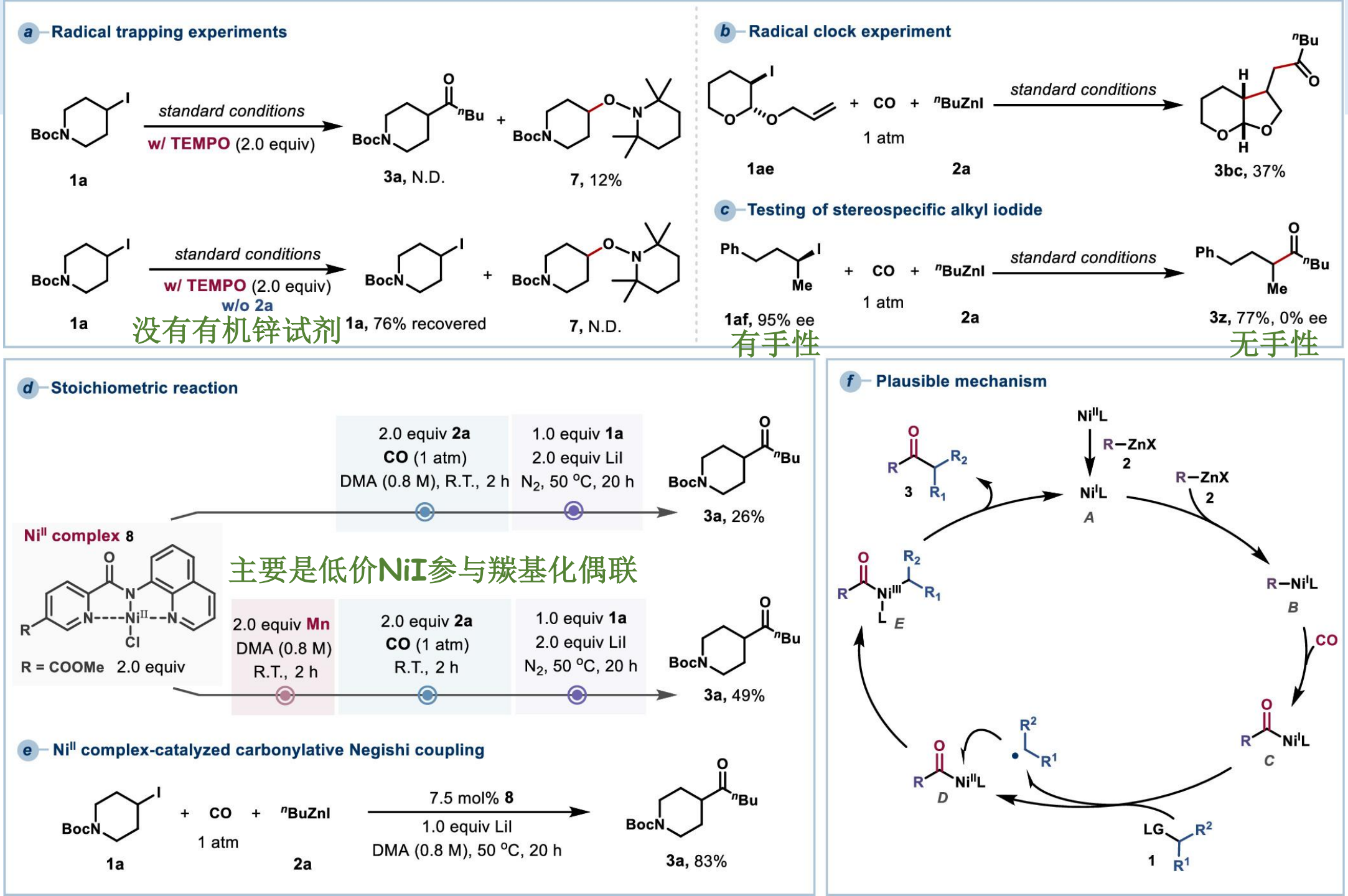


Acyclic alkyl tosylates

3. Catalytic Carbonylation of 1 atm CO by Nickel

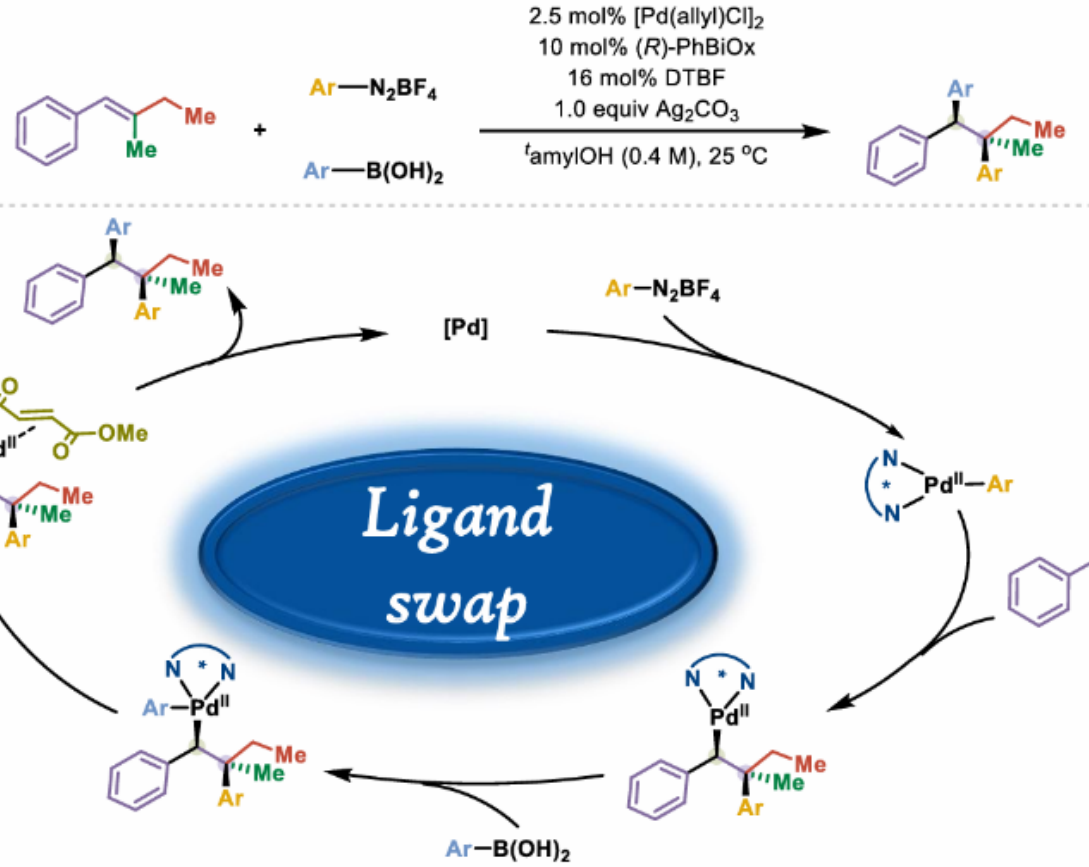





a Radical trapping experiments
standard conditions
w/ TEMPO (2.0 equiv)
1a
3a, N.D.
7, 12%
standard conditions
w/ TEMPO (2.0 equiv)
w/o 2a
1a
1a, 76% recovered
7, N.D.
没有有机锌试剂
b Radical clock experiment
1ae
CO
1 atm
nBuZnI
2a
standard conditions
3bc, 37%
c Testing of stereospecific alkyl iodide
1af, 95% ee
CO
1 atm
nBuZnI
2a
standard conditions
3z, 77%, 0% ee
有手性
无手性
d Stoichiometric reaction
2.0 equiv 2a
CO (1 atm)
DMA (0.8 M), R.T., 2 h
1.0 equiv 1a
2.0 equiv LiI
N2, 50 °C, 20 h
3a, 26%
NiII complex 8
R = COOMe 2.0 equiv
主要是低价NiI参与羰基化偶联
2.0 equiv Mn
DMA (0.8 M)
R.T., 2 h
2.0 equiv 2a
CO (1 atm)
R.T., 2 h
1.0 equiv 1a
2.0 equiv LiI
N2, 50 °C, 20 h
3a, 49%
e NiII complex-catalyzed carbonylative Negishi coupling
1a
CO
1 atm
nBuZnI
2a
7.5 mol% 8
1.0 equiv LiI
DMA (0.8 M), 50 °C, 20 h
3a, 83%
f Plausible mechanism
NiIIL
R–ZnX
2
NiIL
A
R–ZnX
2
R–NiIL
B
CO
NiIL
C
LG
1
NiIIL
D
NiIII
E
3

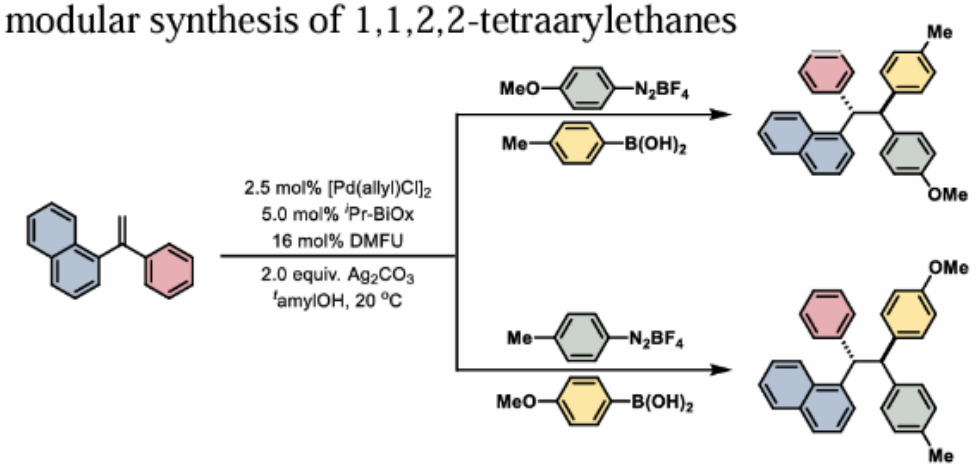
4. Catalytic Intermolecular Cross-Coupling of Olefins

Ligand-swap enabled DF cross-coupling of trisubstituted olefin

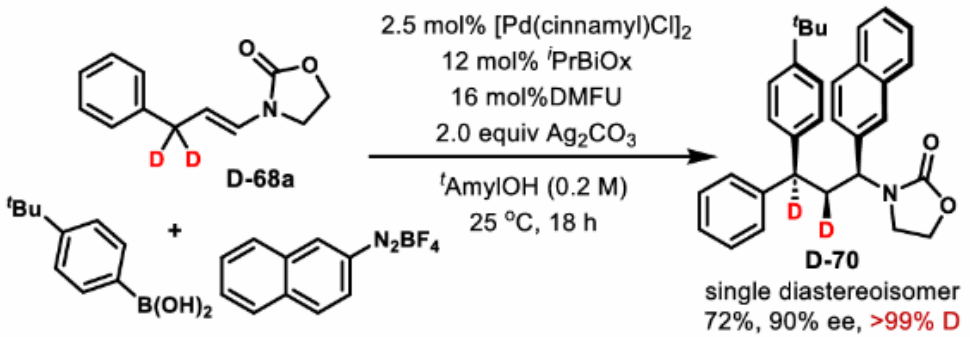


1,1-DF cross-coupling

- modular synthesis of 1,1,2,2-tetraarylethanes

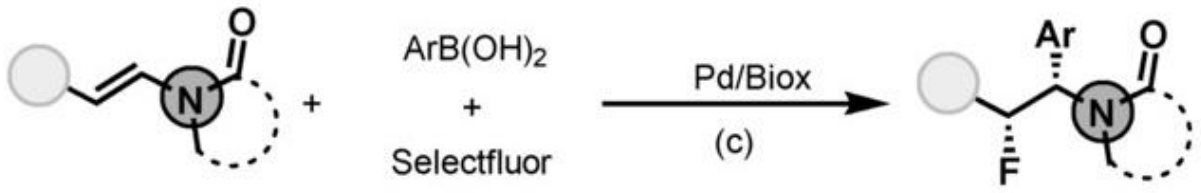


1,3-DF cross-coupling

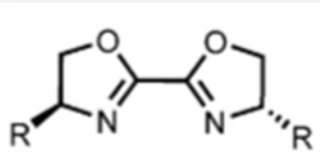


4. Catalytic Intermolecular Cross-Coupling of Olefins

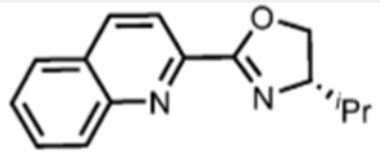
2) This work: Pd-catalyzed asymmetric arylfluorination of internal enamides



- Enantioselective difunctionalization of internal enamides for C-C bond formation
- β-Fluoroamine derivatives with vicinal chiral centers up to 99% *ee*
- High regio-, diastereoselectivities enabled by removable oxazolidinone



R = ^{i}Pr, **L1**
^{i}Bu, **L2**
^{t}Bu, **L3**
Cy, **L4**

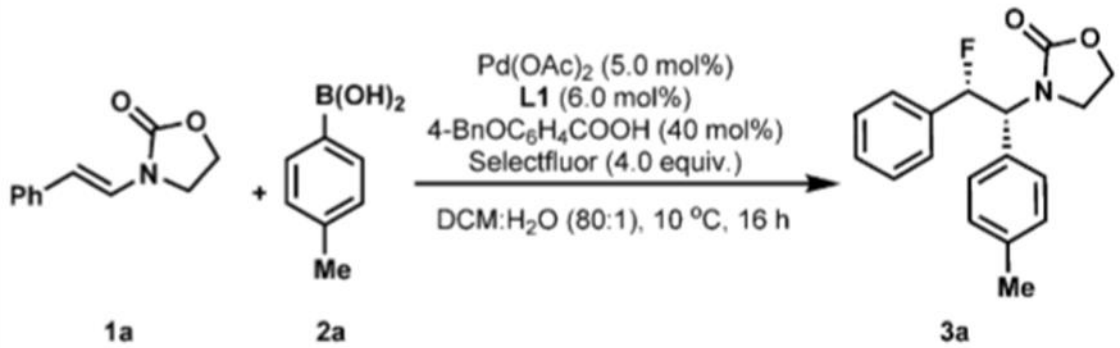


L5

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (2.0 equiv, 0.4 mmol), Selectfluor (4.0 equiv, 0.8 mmol), $Pd(OAc)_2$ (5.0 mol%, 0.01 mmol), ligand (6.0 mol%, 0.012 mmol), 4-(benzyloxy)benzoic acid (40 mol%, 0.08 mmol), DCM:H_2O (v/v) = 80:1 (0.2 M), 10 °C, 16 h. [b] Yield determined by ^{1}H NMR using CH_2Br_2 as the internal standard. [c] Determined by chiral HPLC. [d] Yield of isolated products in parentheses. [e] DCM:H_2O (v/v) = 9:1 (0.2 M). [f] Selectfluor (2.0 equiv, 0.4 mmol). [g] Without 4-(benzyloxy)benzoic acid.

Scheme 1. Enantioselective synthesis of amine derivatives with vicinal stereocenters from alkenes.

Table 1: Optimization of the reaction conditions.[a]



1a **2a** **3a**

Entry	Variation from standard conditions	Yield (%)[b]	*ee* (%)[c]
1	none	84 (75)[d]	98
2	DCM:H_2O (v/v) = 9:1 as solvent	79	98
3	no H_2O	nr	–
4[e]	no 4-$BnOC_6H_4COOH$	77	98
5[e,f]	25 °C instead of 10 °C	20	–
6[e,g]	2.0 equiv Selectfluor	66	98
7[e]	**L2** instead of **L1**	76	98
8[e]	**L3** instead of **L1**	26	–
9[e]	**L4** instead of **L1**	71	95
10[e]	**L5** instead of **L1**	46	-38

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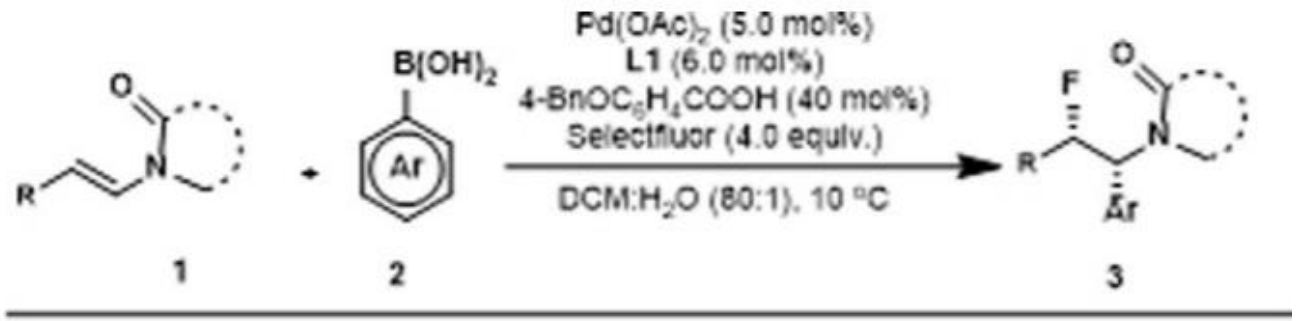
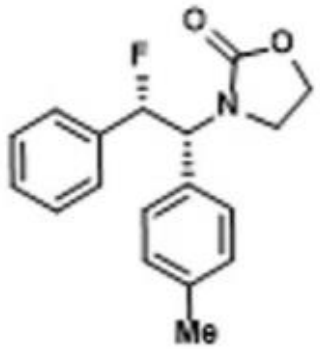
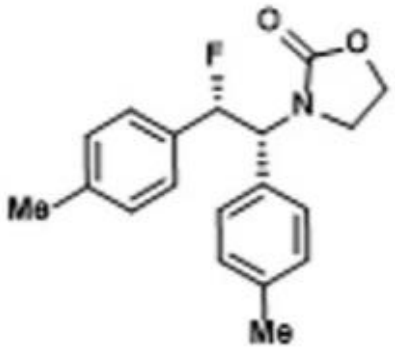
4. Catalytic Intermolecular Cross-Coupling of Olefins



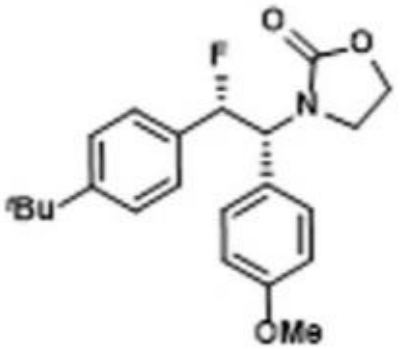
1 2 3



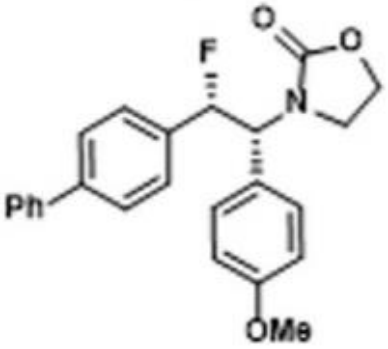
3a, 75%, 98% *ee*
69%, 98% ee[b]



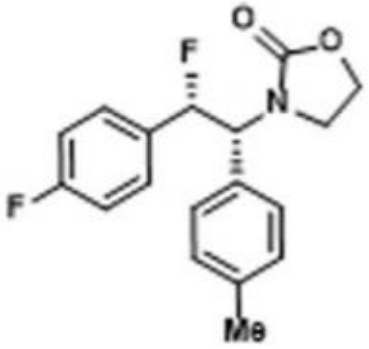
3b, 64%, 99% *ee*



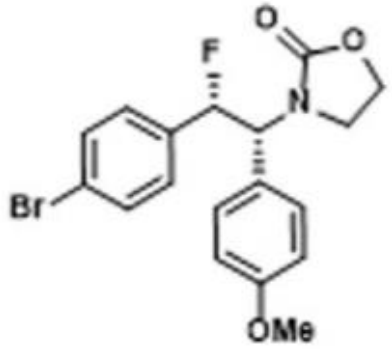
3c, 61%, 96% *ee*



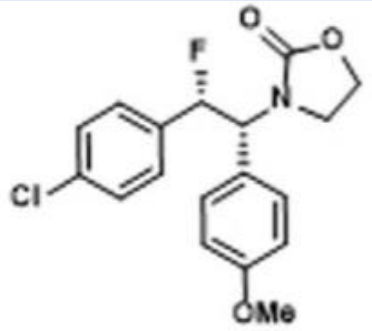
3d, 63%, 94% *ee*



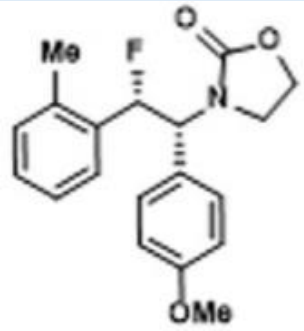
3e, 76%, 99% *ee*



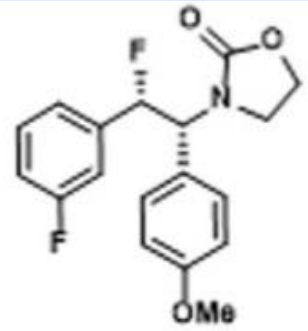
3f, 72%, 98% *ee*



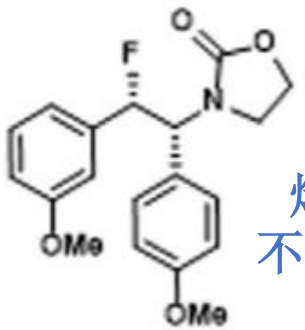
3g, 36%, 88% *ee*



3h, 41%, 95% *ee*

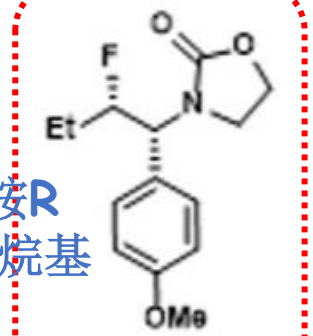


3i, 53%, 98% *ee*

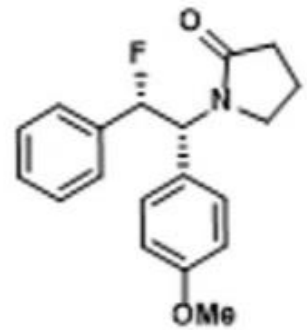


3j, 35%, 96% *ee*

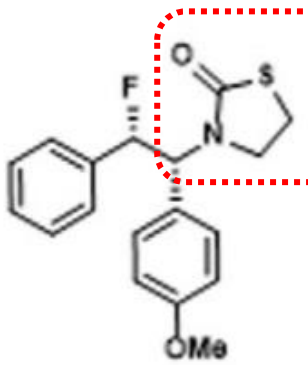
烯酰胺R
不能是烷基



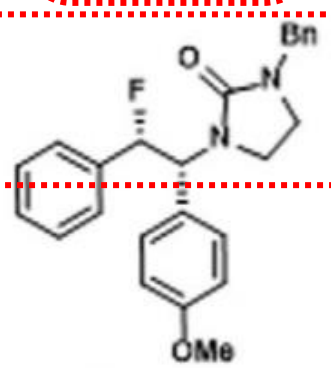
3k, n.d.



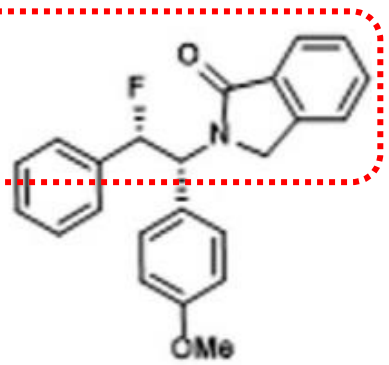
3l, 65%, 99% *ee*



3m, 49%, >99% ee

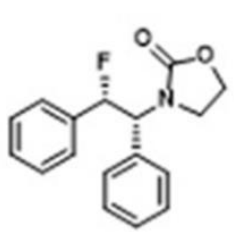


3n, 67%, 99% ee

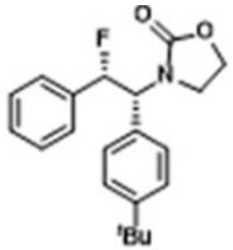


3o, 64%, 98% *ee*

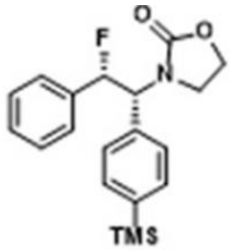
Table 3: Substrate scope of aromatic boronic acids.[a]



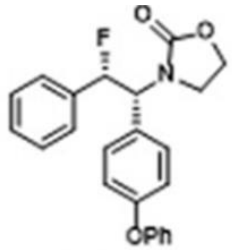
3p, 83%, 93% ee



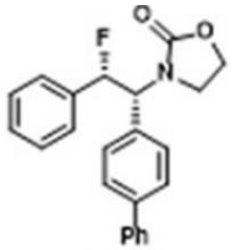
3q, 70%, 97% ee



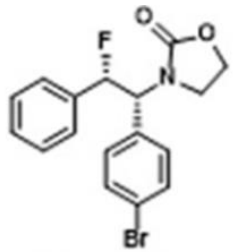
3r, 90%, >99% ee



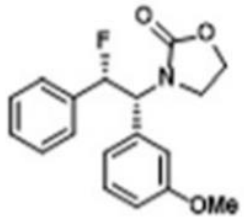
3s, 53%, >99% ee



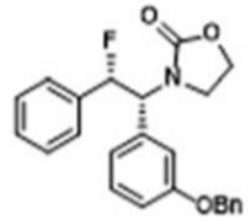
3t, 47%, 97% ee



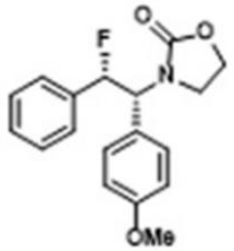
3u, 56%, 92% ee



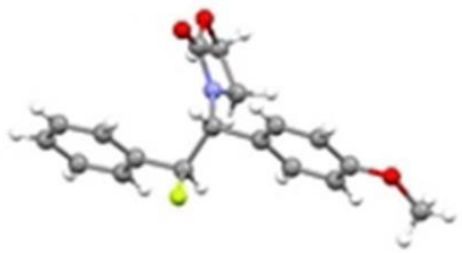
3z, 73%, 99% ee

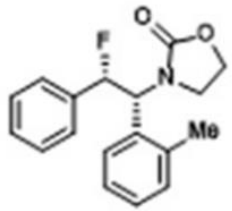


3aa, 59%, 99% ee

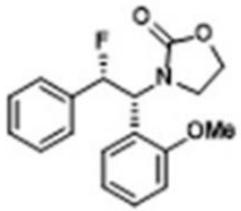


3v, 81%, >99% ee

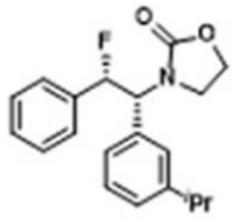




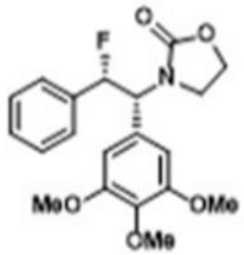
3w, 44%, 93% ee



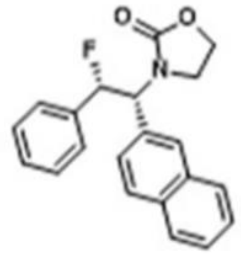
3x, 68%, 88% ee



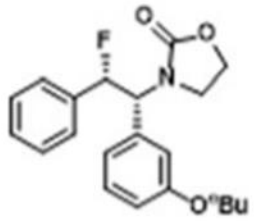
3y, 64%, >99% ee



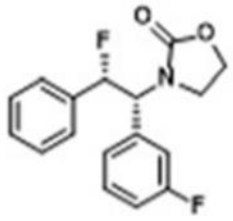
3af, 61%, 94% ee



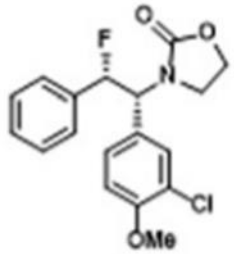
3ag, 51%, >99% ee



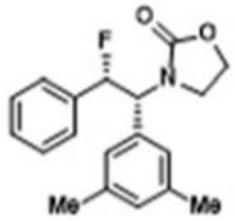
3ab, 74%, 97% ee



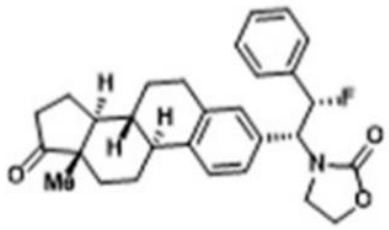
3ac, 69%, 95% ee



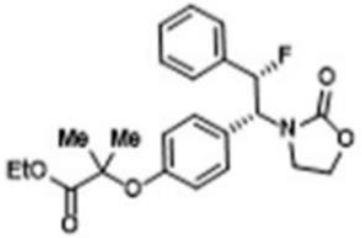
3ad, 53%, 98% ee



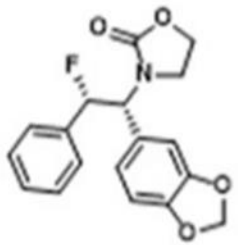
3ae, 89%, 98% ee



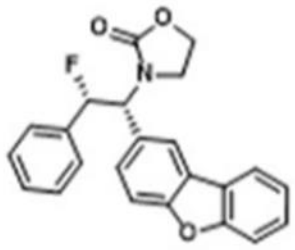
3ak, 62%, >99% ee



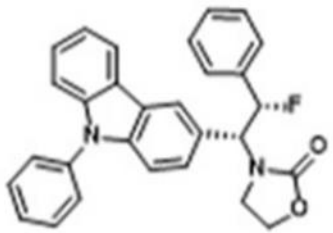
3al, 62%, 97% ee



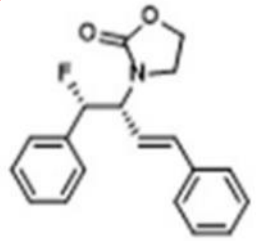
3ah, 48%, 96% ee



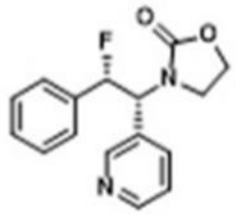
3al, 47%, 98% ee



3aj, 41%, 92% ee



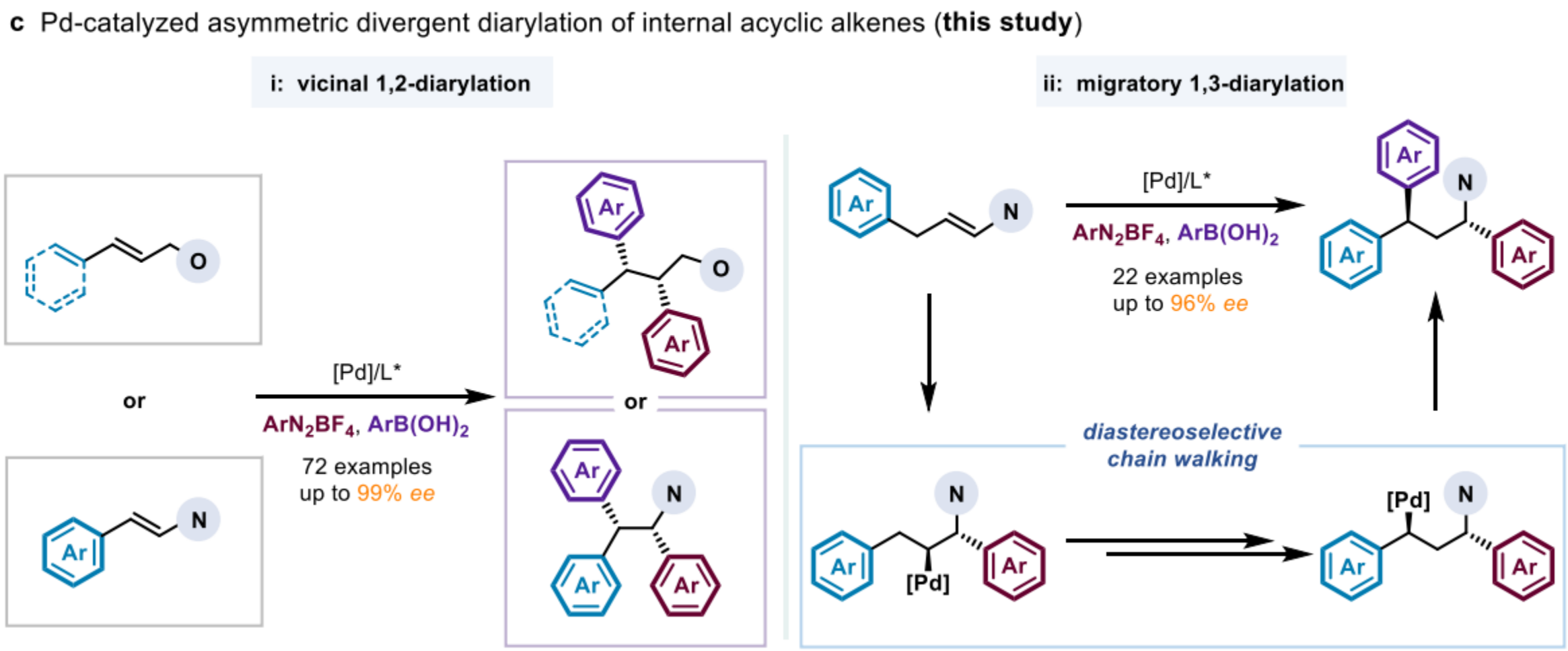
3am, low yield



3an, n.r.

不适用于
苯乙烯基硼酸
和吡啶基硼酸

4. Catalytic Intermolecular Cross-Coupling of Olefins



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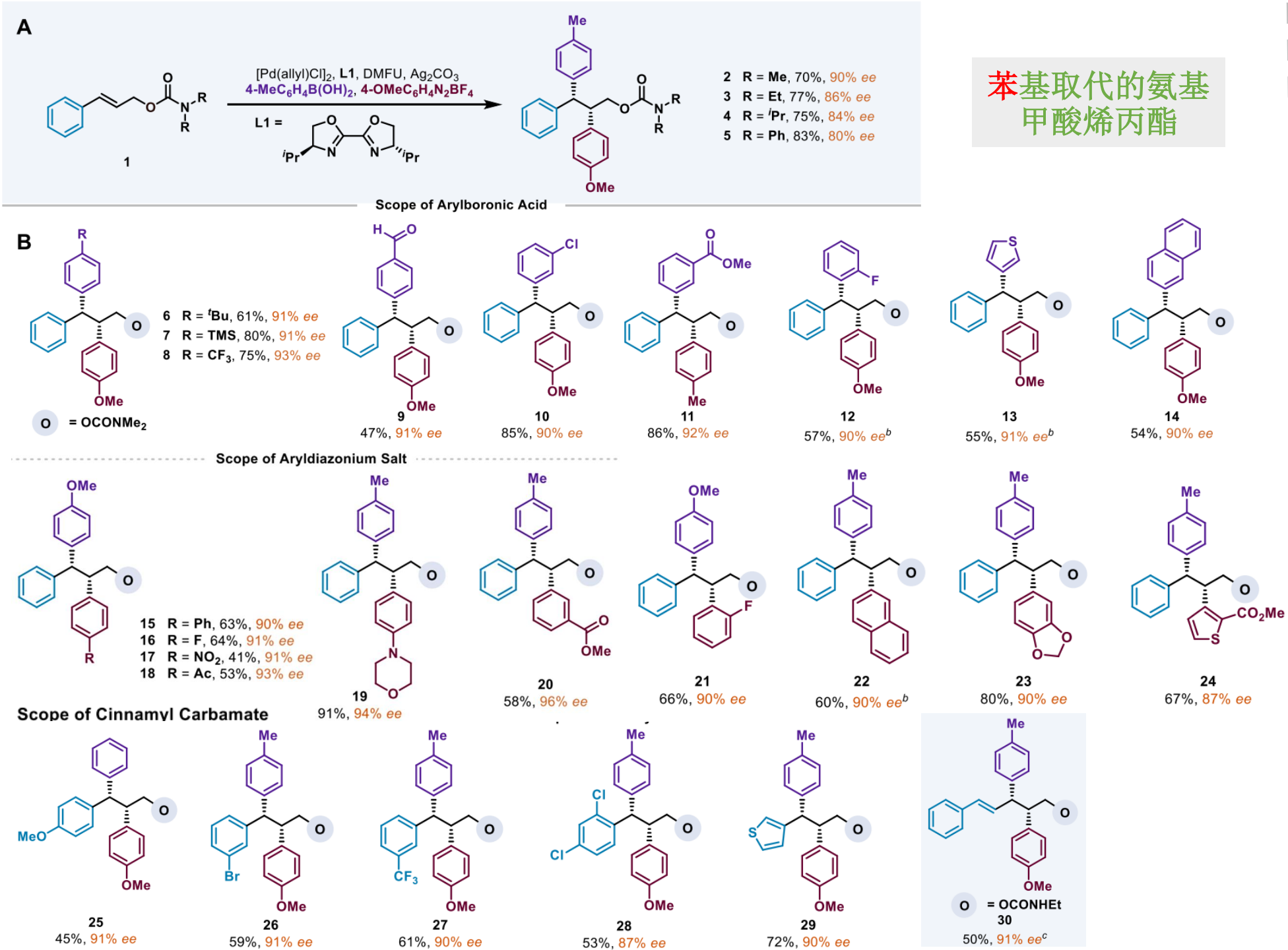
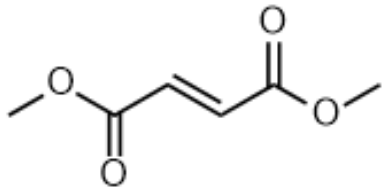
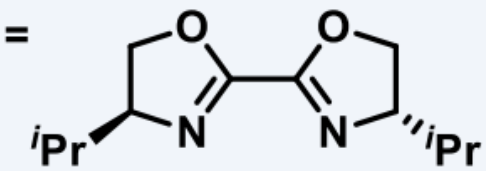


苯基取代的氨基甲酸烯丙酯



DMFU

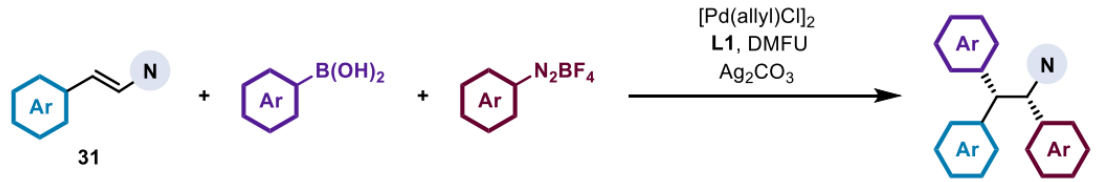
L1 =



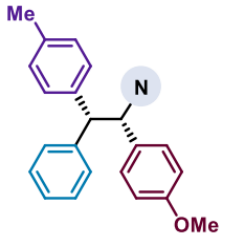
$[Pd(allyl)Cl]_2$

Ag_2CO_3

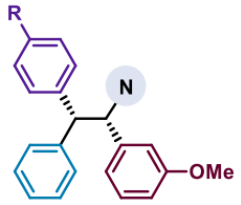
^{t}amylOH



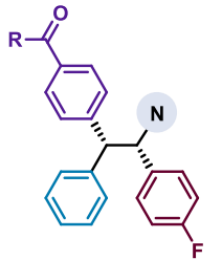
Scope of Arylboronic Acid



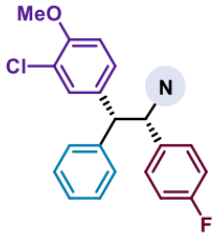
32
71%, 91% *ee*



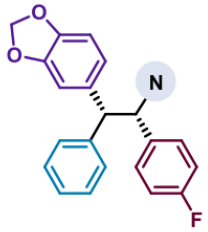
33 R = **OPh**, 71%, 90% *ee*
34 R = **OCF_3**, 56%, 95% *ee*
35 R = **CF_3**, 57%, 97% *ee*



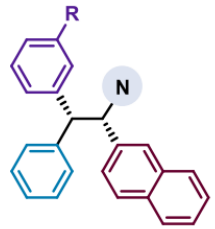
36 R = **Me**, 83%, 93% *ee*
37 R = **H**, 49%, 96% *ee*



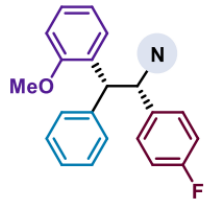
38
81%, 91% *ee*



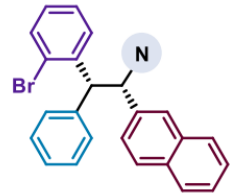
39
65%, 95% *ee*



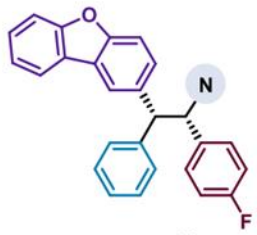
40 R = **Br**, 63%, 99% *ee*
41 R = **CO_2Me**, 75%, 97% *ee*



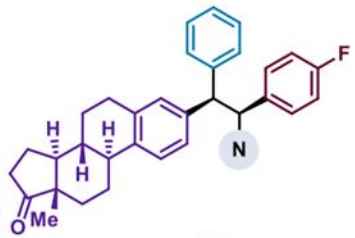
42
74%, 93% *ee*



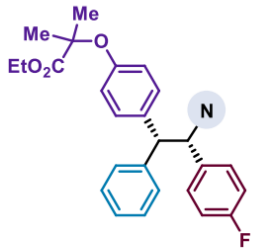
43
69%, 95% *ee*[b]



44
71%, 93% *ee*

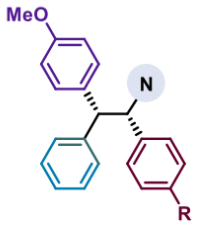


45
80%, 96% *ee*

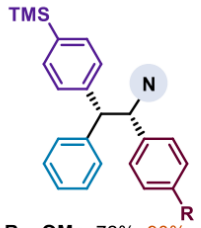


46
75%, 97% *ee*

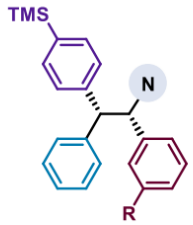
Scope of Aryldiazonium Salt



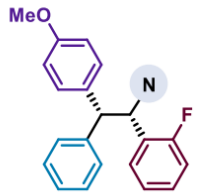
47 R = **Me**, 70%, 96% *ee*
48 R = **Et**, 55%, 97% *ee*



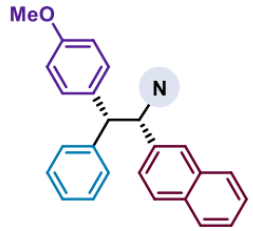
49 R = **OMe**, 72%, 90% *ee*
50 R = **F**, 70%, 96% *ee*
51 R = **Cl**, 62%, 95% *ee*
52 R = **CO_2Me**, 43%, 97% *ee*



53 R = **OMe**, 70%, 95% *ee*
54 R = **CF_3**, 41%, 95% *ee*
55 R = **CO_2Me**, 47%, 92% *ee*

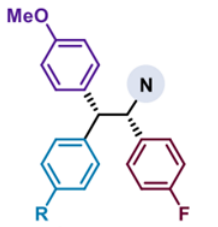


56
47%, 86% *ee*

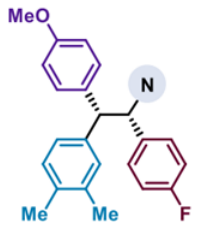


57
74%, 94% *ee*

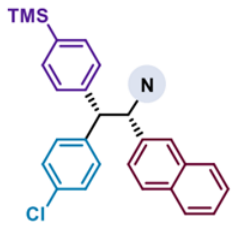
Scope of Internal Enamide



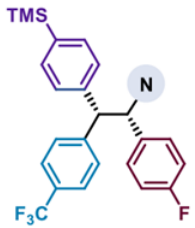
58 R = **^{i}Pr**, 73%, 92% *ee*
59 R = **^{t}Bu**, 65%, 94% *ee*



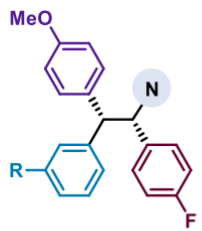
60
68%, 96% *ee*



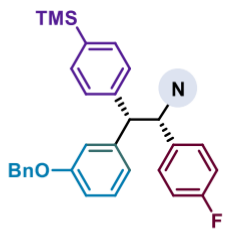
61
55%, 92% *ee*[b]



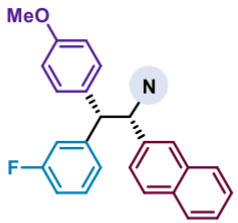
62
51%, 94% *ee*



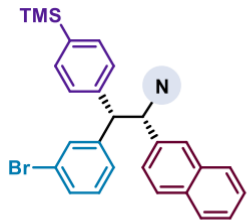
63 R = **OMe**, 67%, 91% *ee*
64 R = **OPh**, 60%, 95% *ee*



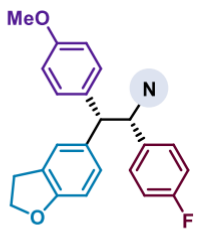
65
55%, 92% *ee*[b]



66
67%, 99% *ee*



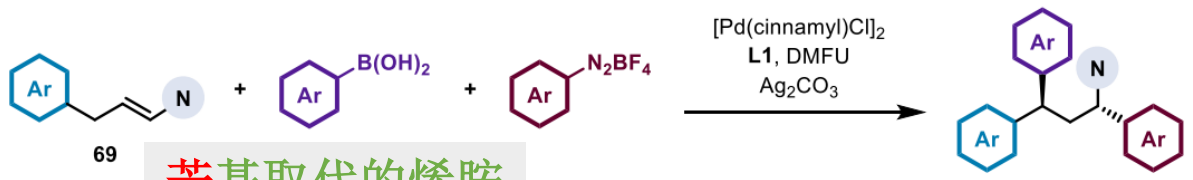
67
69%, 99% *ee*



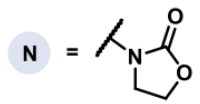
68
55%, 93% *ee*

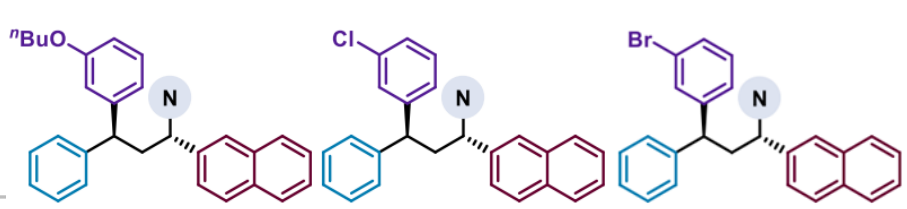
苯基取代的烯胺

$[Pd(allyl)Cl]_2$



苄基取代的烯胺



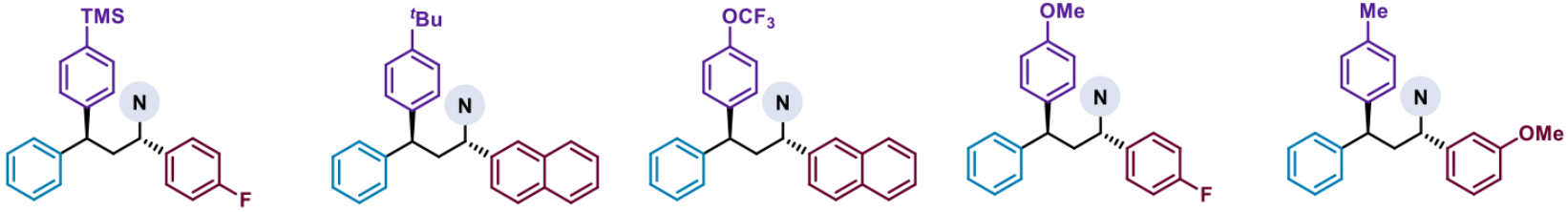


75
54%, 89% *ee*

76
80%, 91% *ee*

77
71%, 90% *ee*

Scope of Arylboronic Acid



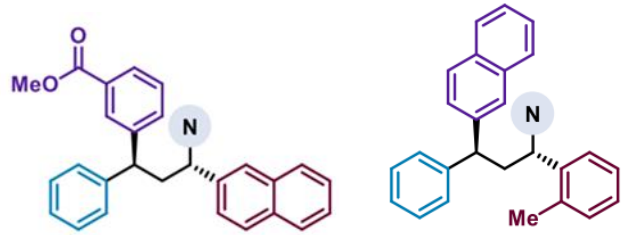
70
73%, 93% *ee*

71
79%, 91% *ee*

72
66%, 90% *ee*

73
72%, 93% *ee*

74
57%, 91% *ee*



78
62%, 88% ee

79
62%, 96% *ee*

Scope of Aryldiazonium Salt

80
53%, 94% *ee*

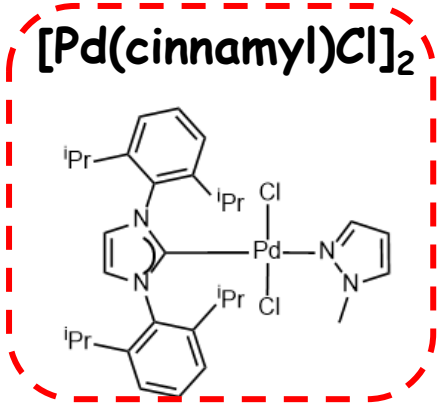
81
47%, 93% *ee*

82
84%, 93% *ee*

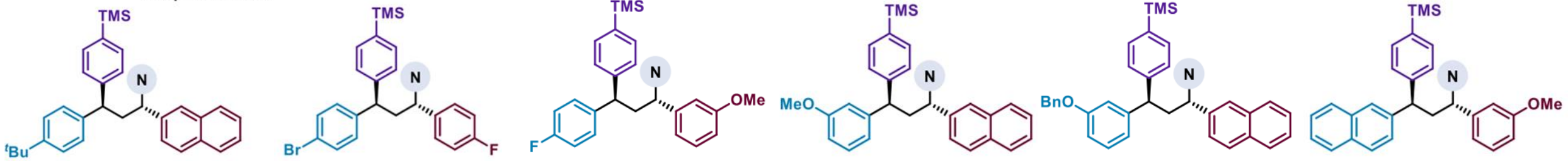
83
71%, 91% *ee*

84
85%, 93% *ee*

85
74%, 89% *ee*



Scope of Internal Enamide



86
61%, 88% *ee*

87
31%, 95% *ee*

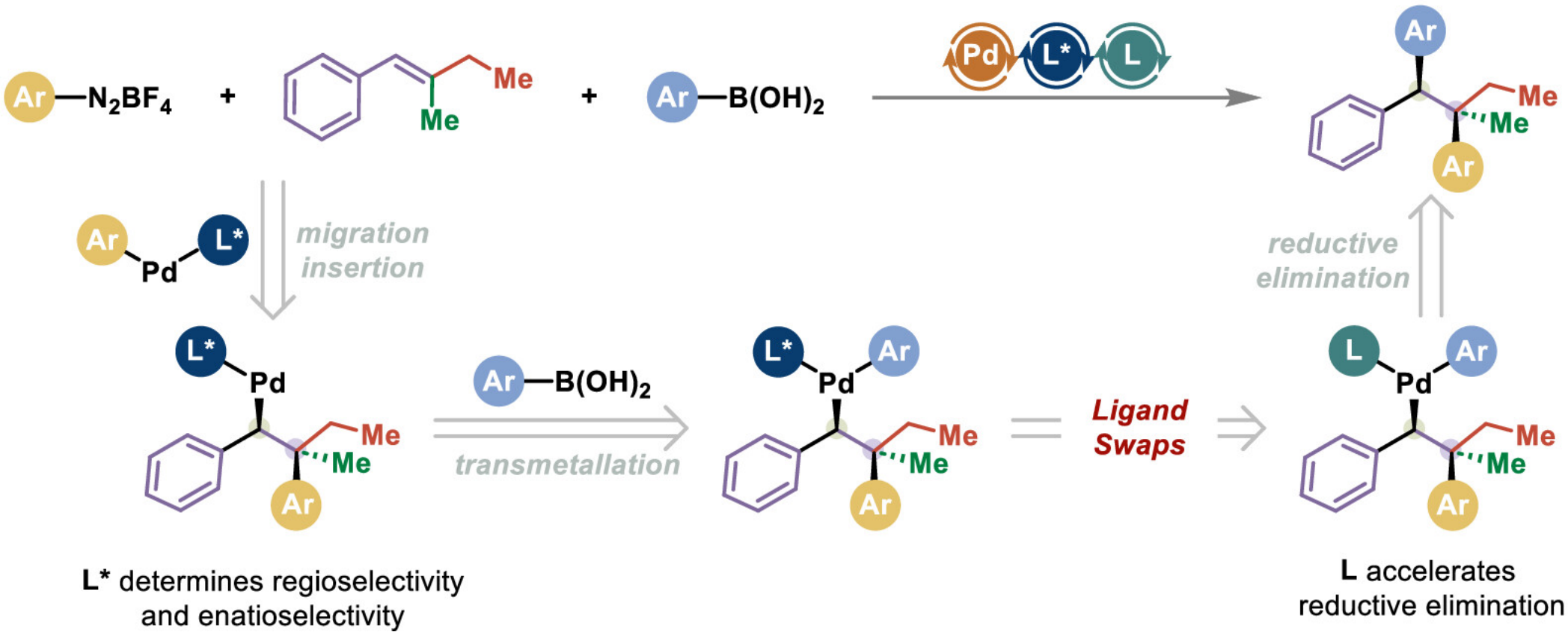
88
73%, 91% *ee*

89
51%, 90% *ee*

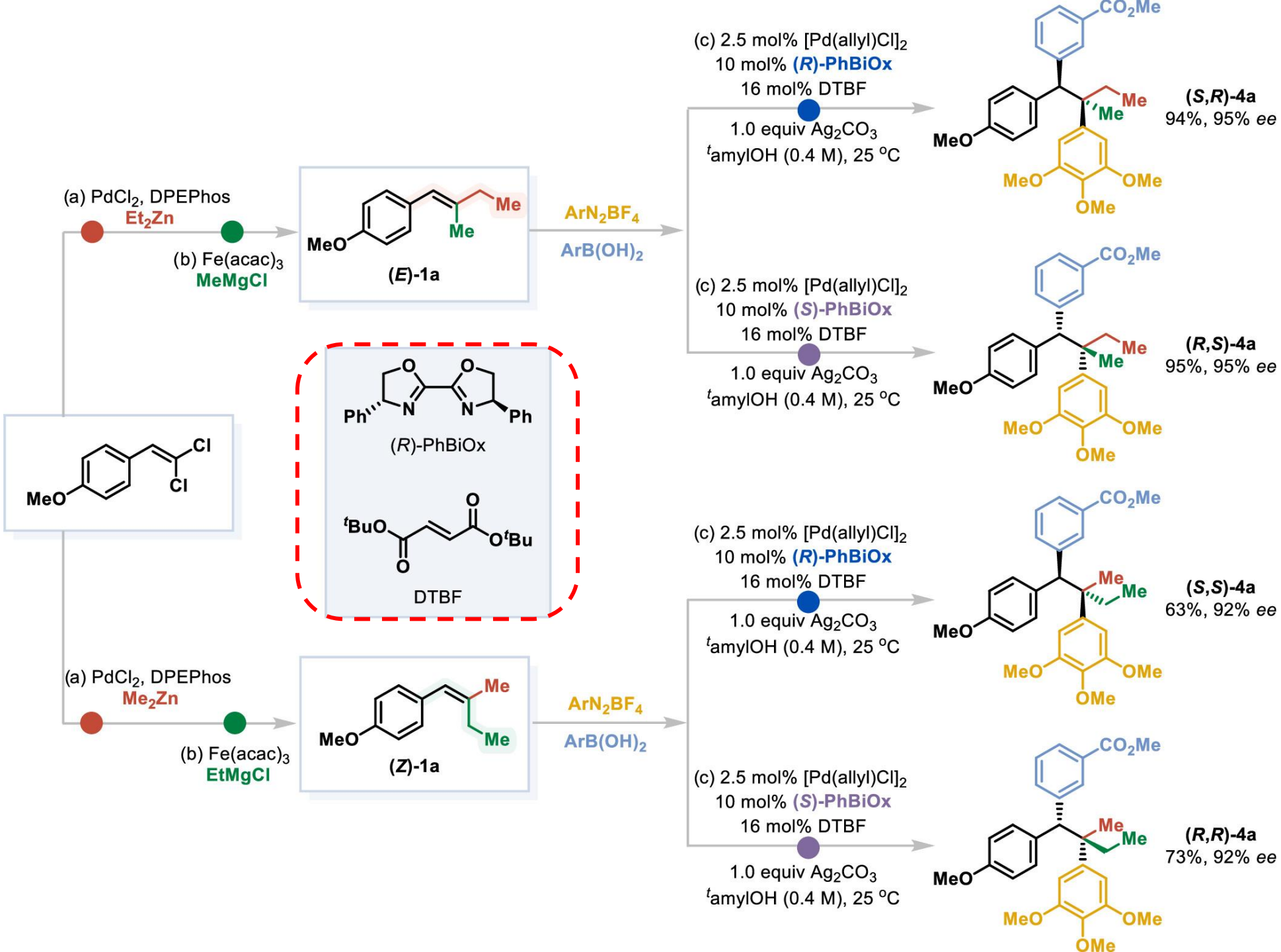
90
49%, 90% *ee*

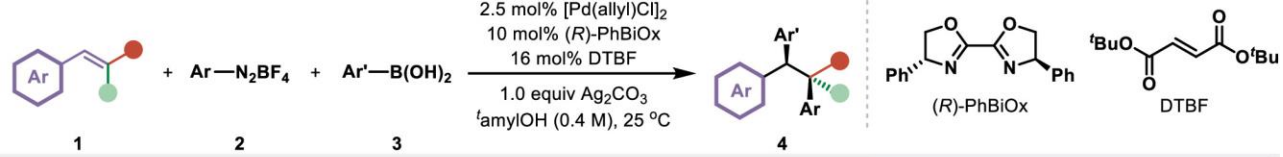
91
61%, 91% *ee*

4. Catalytic Intermolecular Cross-Coupling of Olefins



J. Am. Chem. Soc. **2024**, *146*, *24*, 16892-16901.


(a) PdCl2, DPEPhos
Et2Zn
(b) Fe(acac)3
MeMgCl
(E)-1a
ArN2BF4
ArB(OH)2
(c) 2.5 mol% [Pd(allyl)Cl]2
10 mol% (R)-PhBiOx
16 mol% DTBF
1.0 equiv Ag2CO3
tamylOH (0.4 M), 25 °C
(S,R)-4a
94%, 95% ee
(c) 2.5 mol% [Pd(allyl)Cl]2
10 mol% (S)-PhBiOx
16 mol% DTBF
1.0 equiv Ag2CO3
tamylOH (0.4 M), 25 °C
(R,S)-4a
95%, 95% ee
(R)-PhBiOx
DTBF
(a) PdCl2, DPEPhos
Me2Zn
(b) Fe(acac)3
EtMgCl
(Z)-1a
ArN2BF4
ArB(OH)2
(c) 2.5 mol% [Pd(allyl)Cl]2
10 mol% (R)-PhBiOx
16 mol% DTBF
1.0 equiv Ag2CO3
tamylOH (0.4 M), 25 °C
(S,S)-4a
63%, 92% ee
(c) 2.5 mol% [Pd(allyl)Cl]2
10 mol% (S)-PhBiOx
16 mol% DTBF
1.0 equiv Ag2CO3
tamylOH (0.4 M), 25 °C
(R,R)-4a
73%, 92% ee



1 2 3 4

Ar1 = 3,4,5-triMeOC6H2, Ar2 = 3-CO2MeC6H4

4b
87%, 90% *ee*

4c
56%, 94% *ee*

4d
75%, 92% *ee*

4e
50%, 96% *ee*

4f
57%, 94% *ee*

4g
51%, 97% *ee*

4h
54%, 95% *ee*

4i
62%, 97% *ee*

4j
65%, 98% *ee*

4k
33%, 95% *ee*

4l[a]
53%, 93% *ee*

Ar3 = 4-MeOC6H4, Ar4 = 4-MeC6H4

4m[a]
55%, 96% *ee*

4n[a]
76%, 95% *ee*

4o[a]
38%, 96% *ee*

4p[a]
92%, 91% *ee*

4q[a]
63%, 93% *ee*

4r[a], R = OMe, 49%, 94% *ee*
4s[a], R = Me, 58%, 94% *ee*

4t[a], R = F, 97%, 90% *ee*
4u[a], R = CF_3, 71%, 97% *ee*

4v[a], R = Br, 92%, 90% *ee*
4w[a], R = OBn, 90%, 90% *ee*

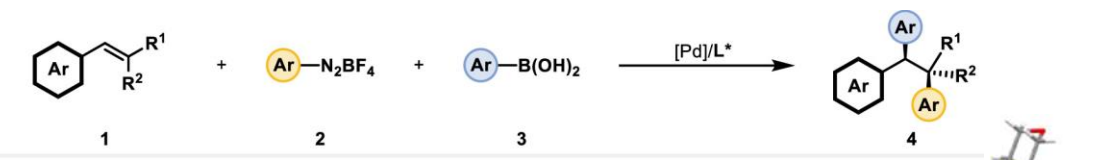
4x[a]
52%, 98% *ee*

4y[b]
47%, 91% *ee*

4z[c]
58%, 89% *ee*

4aa[c]
79%, 95% *ee*

4ab[c]
74%, 95% *ee*



1 2 3 4

4ac
73%, 93% *ee*

4ad
73%, 92% *ee*

4ae
42%, 92% *ee*

Ar = 4-OMeC6H4, Ar3 = 4-MeOC6H4

4af
99%, 91% *ee*

4ag
58%, 88% *ee*

4ah[a]
85%, 95% ee

4ai[a]
62%, 91% ee

4aj[a]

4ak[a]

4al[b]

4am[a]

4an[c]
77%, 91% *ee*

4ao
50%, 92% *ee*

4ap
41%, 95% *ee*

4aq
41%, 92% *ee*

4ar
42%, 94% *ee*

4as[a], R = H, 85%, 91% *ee*
4at[a], R = TMS, 74%, 90% *ee*

4au[a], R = tBu, 70%, 90% *ee*
4av[a], R = nPr, 75%, 92% *ee*

4aw[a], R = OCF_3, 83%, 90% *ee*
4ax[a], R = F, 67%, 92% *ee*

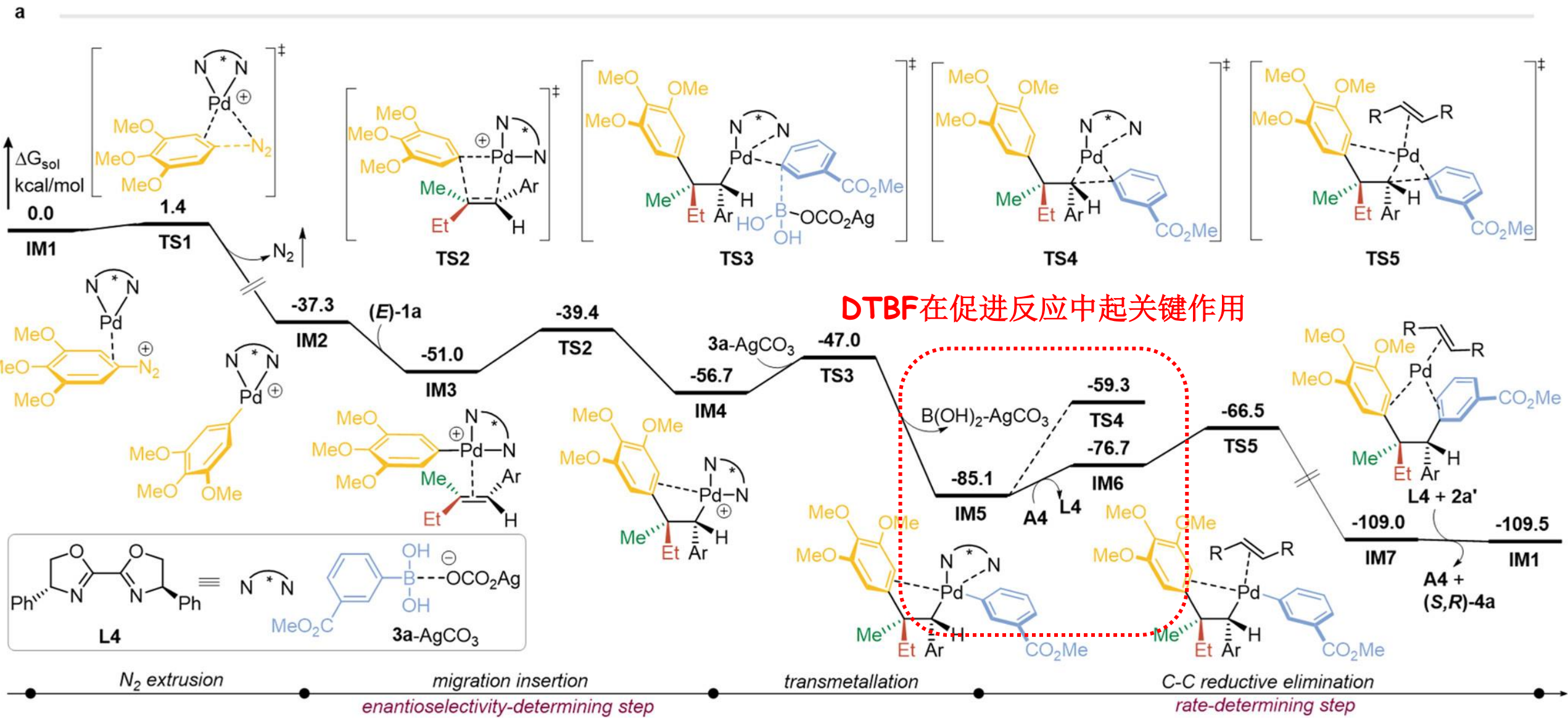
4ay[a]
83%, 90% *ee*

4az[a]
88%, 90% *ee*

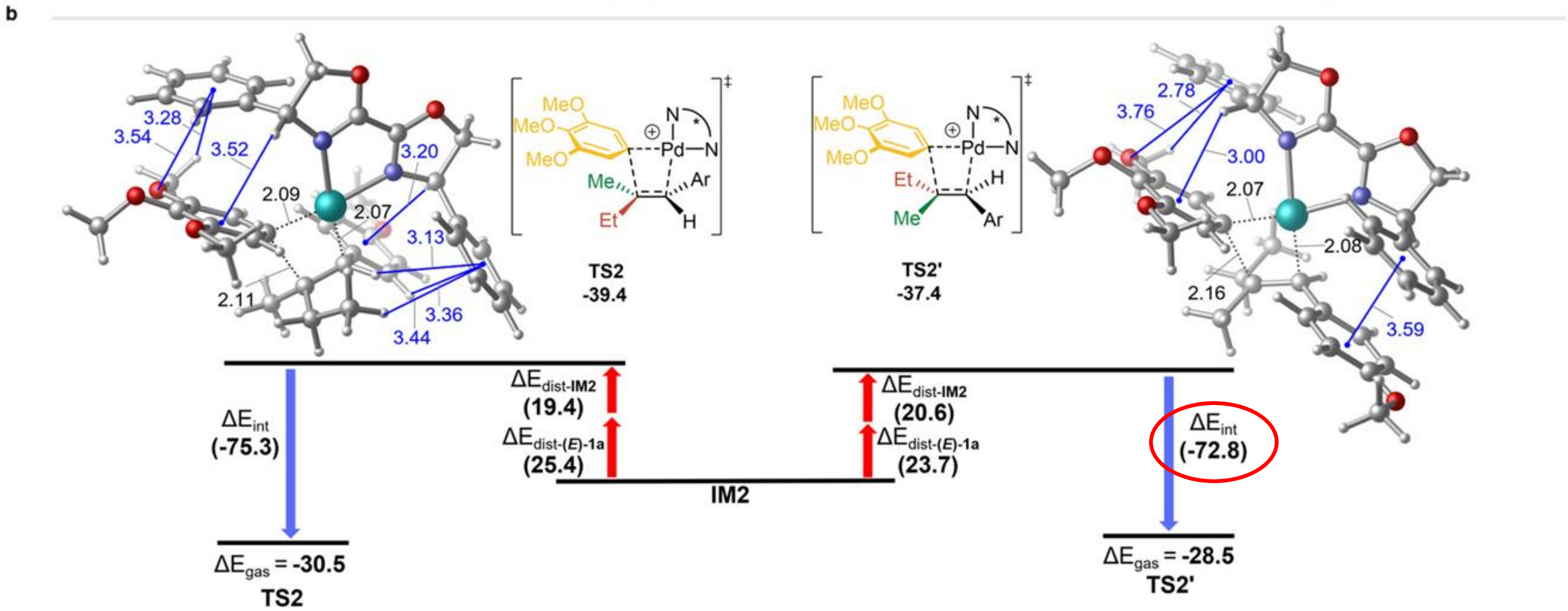
4ba[a]
99%, 92% *ee*

4bb[a]
77%, 92% *ee*

4. Catalytic Intermolecular Cross-Coupling of Olefins



4. Catalytic Intermolecular Cross-Coupling of Olefins



芳香环上的甲氧基与（R）-PhBiOx的苯基之间存在更有效的孤对电子p ···π相互作用

三取代烯烃（E）-1a和（R）-PhBiOx之间的C-H···π相互作用

Thanks for you listening!