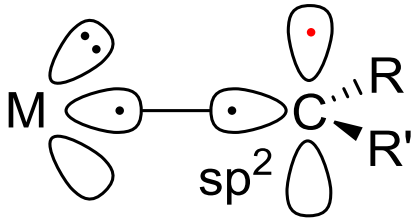
Asymmetric Radical Coupling Reaction Mediated by 'Metal-Carbene Radical'



Carbene radical complex

Lu, Fudong

Feb. 18, 2023

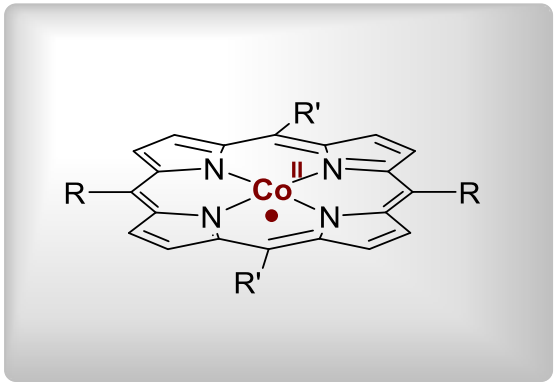
Outline

- ✓ **Background**
  - Overview of 'Metal Carbene'
  - Brief introduction of 'Metal-Carbene Radical' Species
- ✓ **Asymmetric Radical Coupling Mediated by 'Metal-Carbene Radical'**
  - Asymmetric Cyclopropanation and Cyclopropenation
  - Asymmetric intramolecular cyclization
- ✓ **Asymmetric Radical Coupling Mediated by 'Metal-Nitrene Radical'**
  - Asymmetric Olefin Aziridination
  - Asymmetric C–H functionalization (Co, Ru, Fe)
- ✓ **Summary**
- ✓ **Ideas**

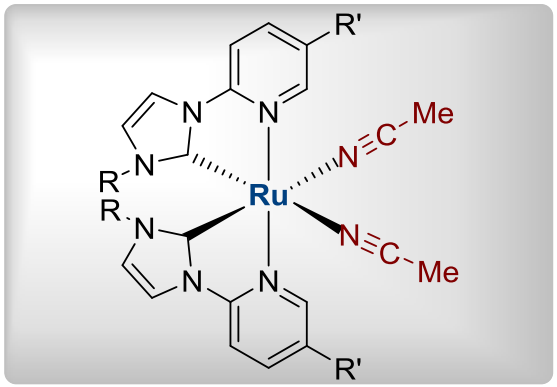
Relevant references:
1) M. P. Doyle et al, *Chem. Rev.* **1998**, *98*, 911–935. 2) M. P. Doyle et al, *Chem. Rev.* **2010**, *110*, 704–724. 3) B. de Bruin et al, *Inorg. Chem.* **2011**, *50*, 9896–9903. 4) X. P. Zhang et al, *Chem. Soc. Rev.* **2011**, *40*, 1899–1909.

Background

- **Brief introduction of authors**



d^7 metal



triplet state 'metal nitrene'

X. Peter Zhang （张小祥）
Boston College

Eric Meggers
University of Marburg

Background

Brief introduction of X. Peter Zhang

X. Peter Zhang
（张小祥）

peter.zhang@bc.edu

Interests：

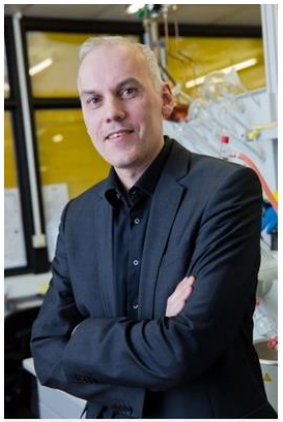
- Radical Reactions
- Metalloradical Catalysis

Homepage:
https://sites.bc.edu/peter-zhang/

- **1985-1988** M.S. Beijing Normal University
- **1991-1996** Ph.D. University of Pennsylvania
  Advisor: Prof. Bradford B. Wayland
- **1996-1999** Postdoc. Massachusetts Institute of Technology, Advisor: Prof. Stephen J. Lippard
- **1999-2001** Postdoc. Massachusetts Institute of Technology, Advisor: Stephen L. Buchwald
- **2001-2006** Assistant Professor, University of Tennessee
- **2006-2015** Associate Professor and Professor, University of South Florida
- **2015-now** Professor, Boston College

Background

Brief introduction of Eric Meggers



Eric Meggers

meggers@chemie.uni-marburg.de

- **1991-1995** B.S. University of Bonn
- **1991-1996** Ph.D. University of Basel, Advisor: Prof. Bernd Giese
- **1999-2002** Postdoc. The Scripps Research Institute, Advisor: Prof. Peter G. Schultz
- **2002-2007** Assistant Professor, University of Pennsylvania
- **2007-now** Professor, University of Marburg

Interests：

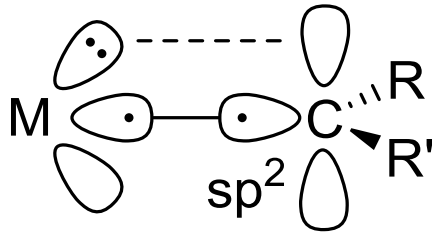
➢ Asymmetric Catalysis with Chiral-at-Metal

Homepage:

https://www.uni-marburg.de/en/fb15/researchgroups/meggers-research-group

Background

Overview of 'Metal Carbene'

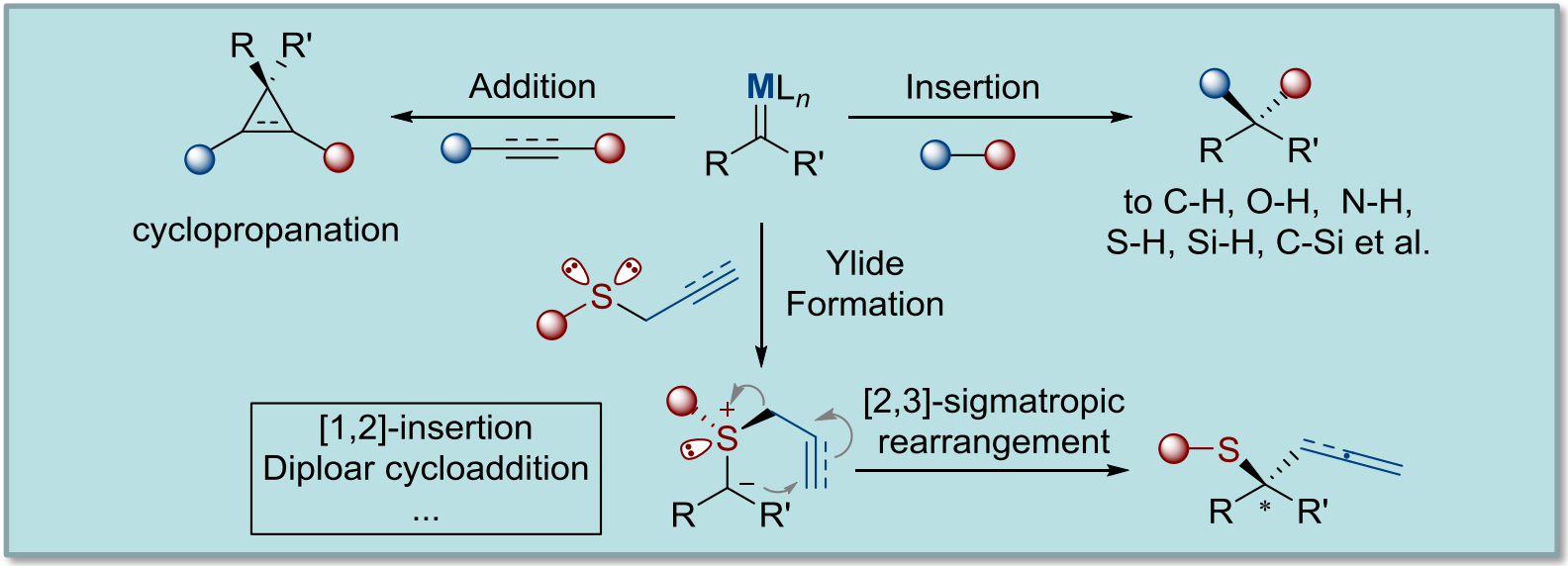


Fischer-type carbene complex

金属的氧化态低
Mo、W、Mn、Fe、Ni 等
卡宾碳带δ⁺电荷，具有亲电性

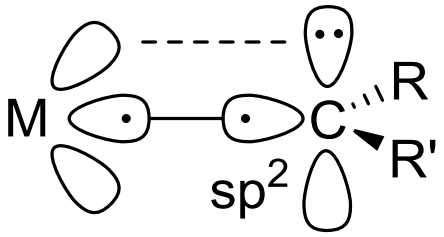
(1) $Cr(CO)_6$ —(1) RLi; 2) Me_3OBF_4)→ $(OC)_5Cr$(R, OMe)

(2) N_2, R, R' —(ML_n, $-N_2$)→ ML_n, R, R'



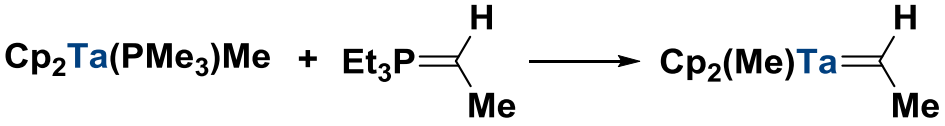
Background

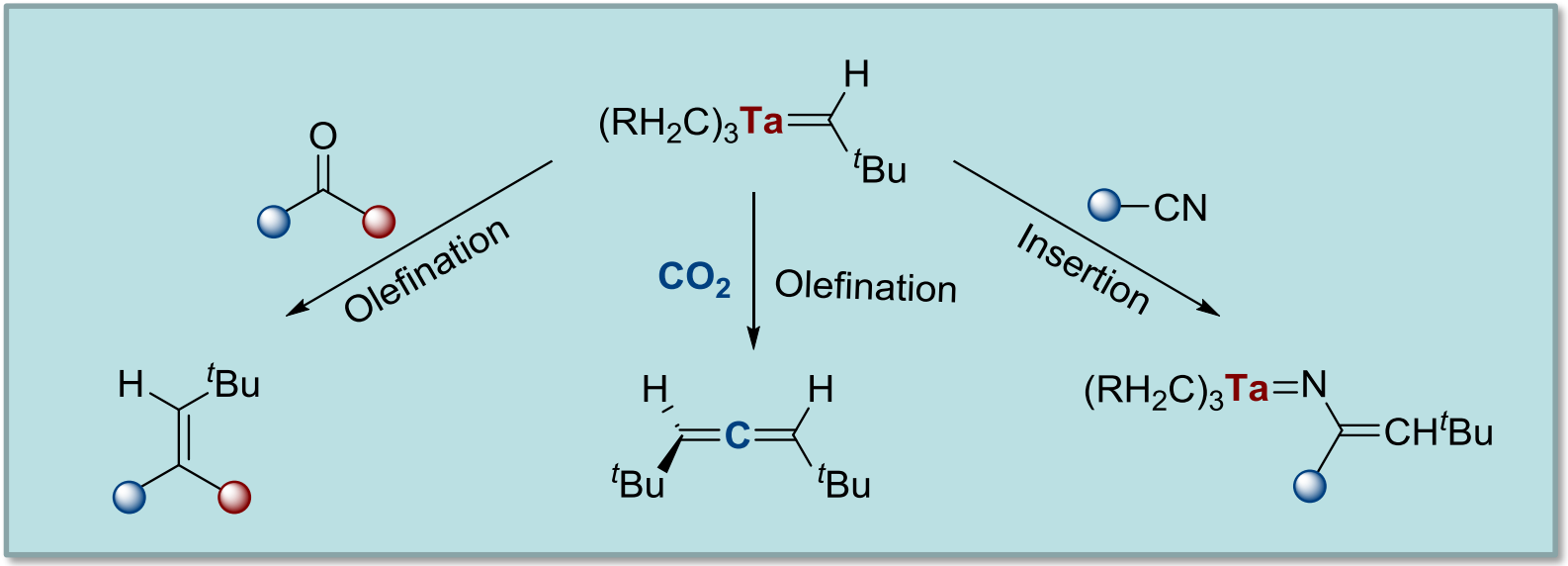
Overview of 'Metal Carbene'



Schrock-type carbene complex

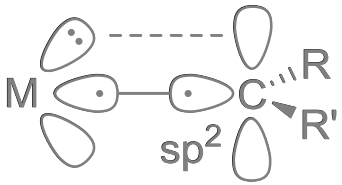
金属的氧化态高
Ti、Ta 等前过渡金属
卡宾碳带δ-电荷，具有亲核性
稳定性较差，其参与的有机反应研究较少



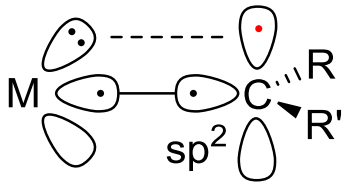


Background

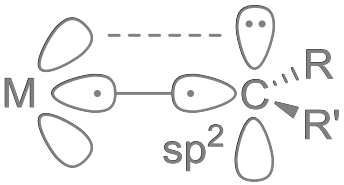
Brief introduction of 'Metal-Carbene Radical' Species



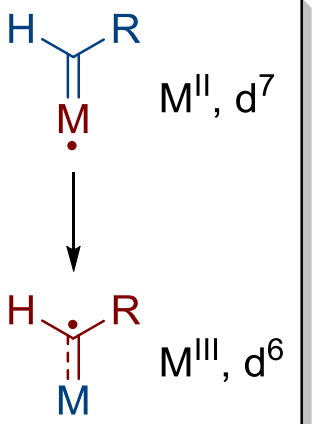
Fischer-type carbene complex

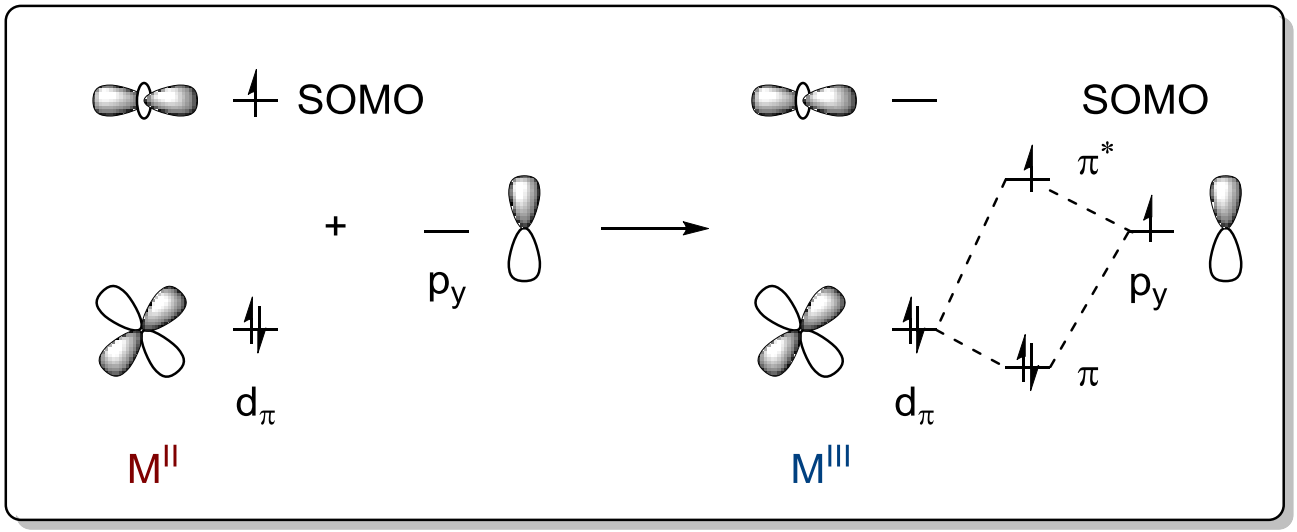


Carbene radical complex



Schrock-type carbene complex

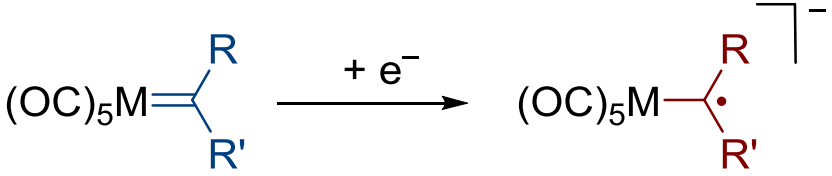




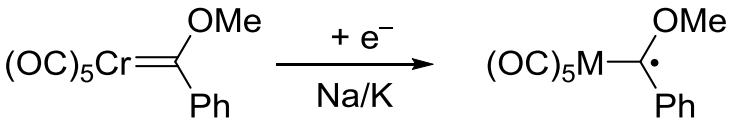
Background

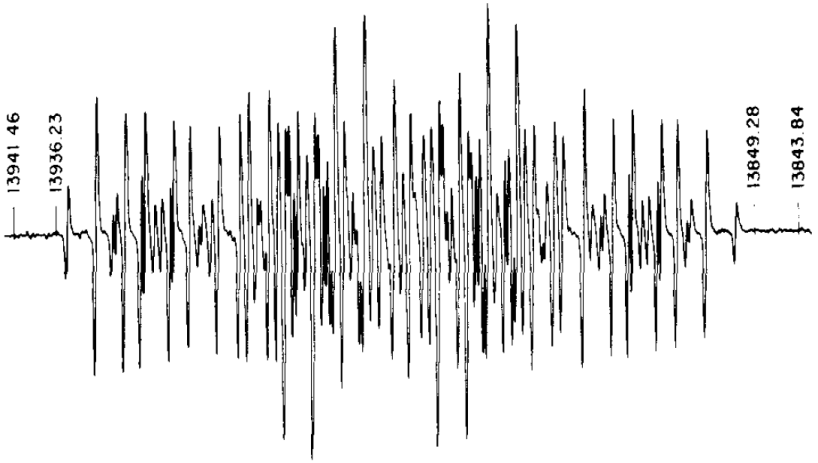
■ Brief introduction of 'Metal-Carbene Radical' Species

***VI B* Metal carbene complexes**



M: Cr, Mo, and W



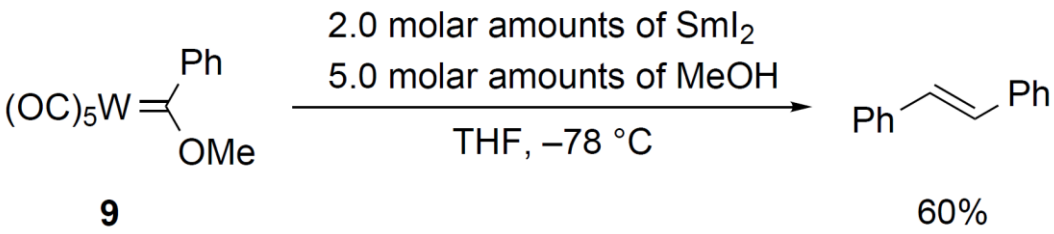


Reduction of the neutral carbene complex with $(\pi\text{-}C_5H_5)Fe(CO)_2Na$ in THF/HMPA at -78 ℃.

P. J. Krusic et al. *J. Am. Chem. Soc.* **1976**, *98*, 2015–2018.

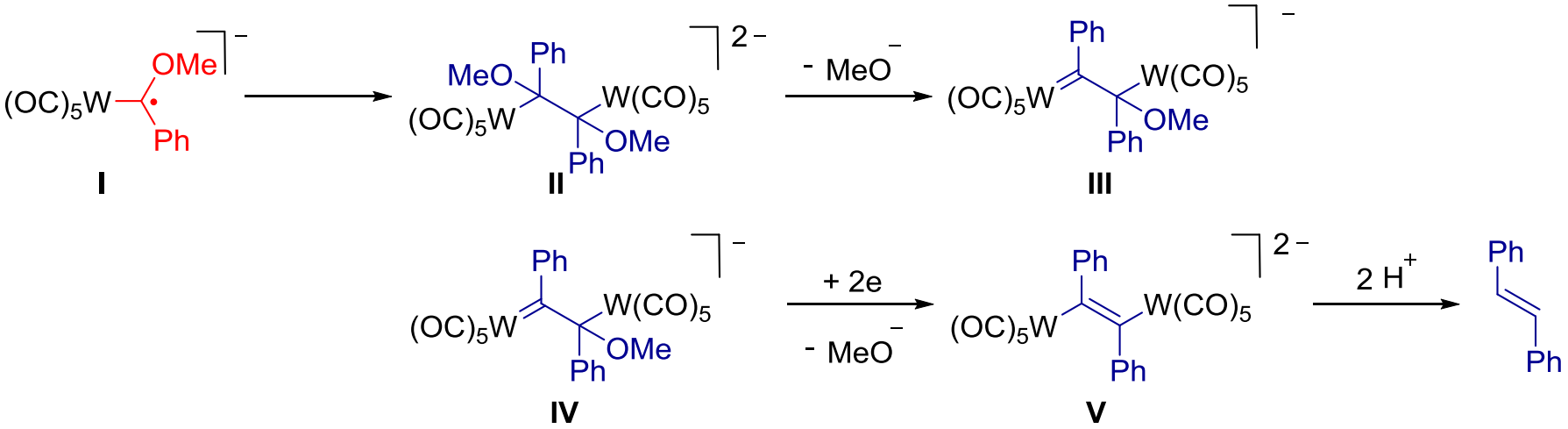
Background

Brief introduction of ‘Metal-Carbene Radical’ Species



9 60%

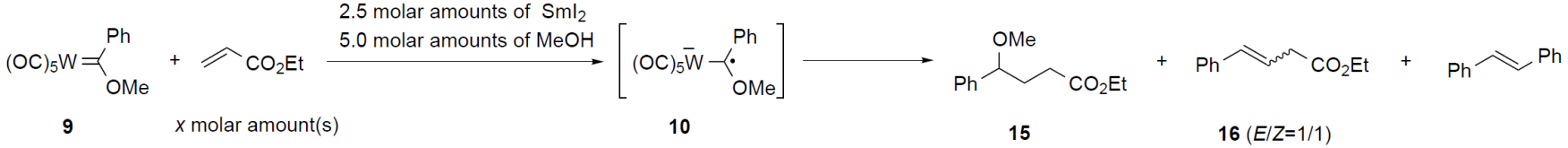
Mechanism



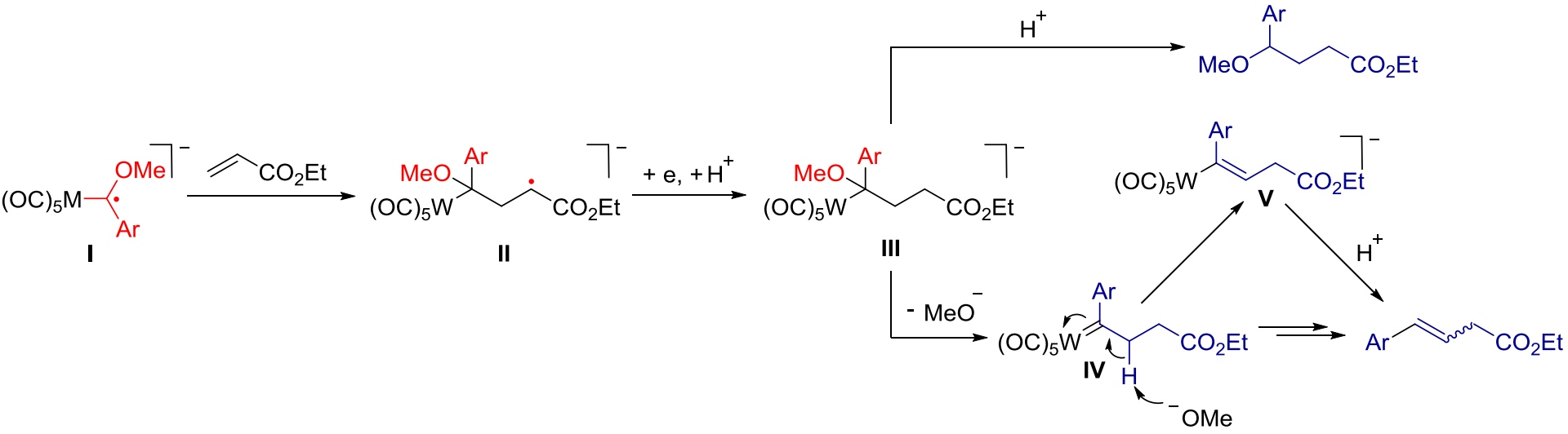
N. Iwasawa et al. *Chem. Eur. J.* **2003**, *9*, 905–914.

Background

Brief introduction of ‘Metal-Carbene Radical’ Species



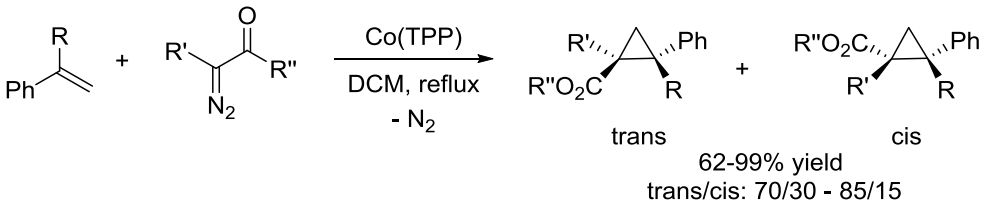
Mechanism



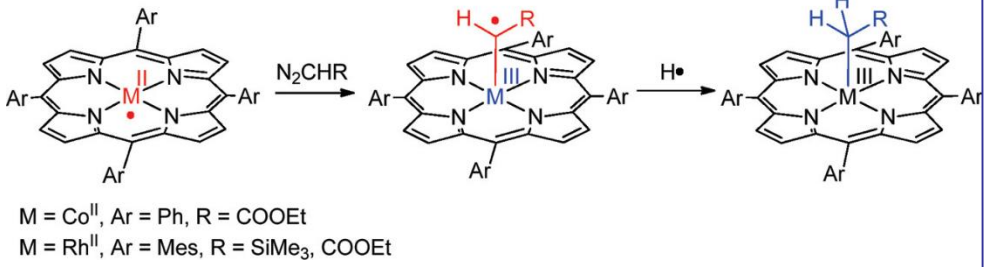
N. Iwasawa et al. *Chem. Eur. J.* **2003**, *9*, 905–914.

Background

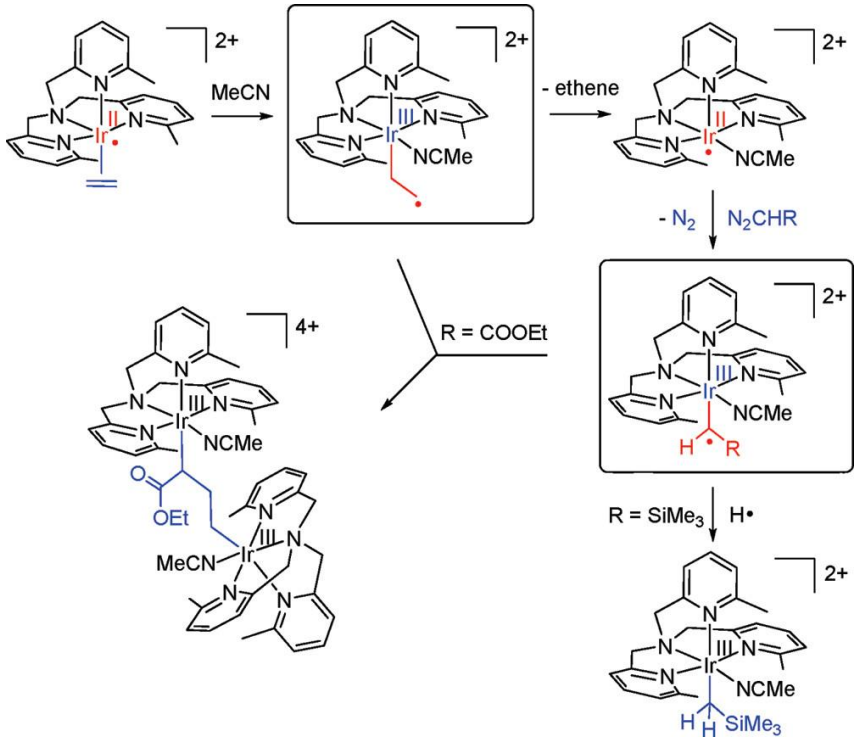
■ Brief introduction of ‘Metal-Carbene Radical’ Species



S. Cenini et al. *Eur. J. Inorg. Chem.* **2003**, 1452–1460.



K. S. Chan et al. *Organometallics* **2007**, *26,* 679–684.

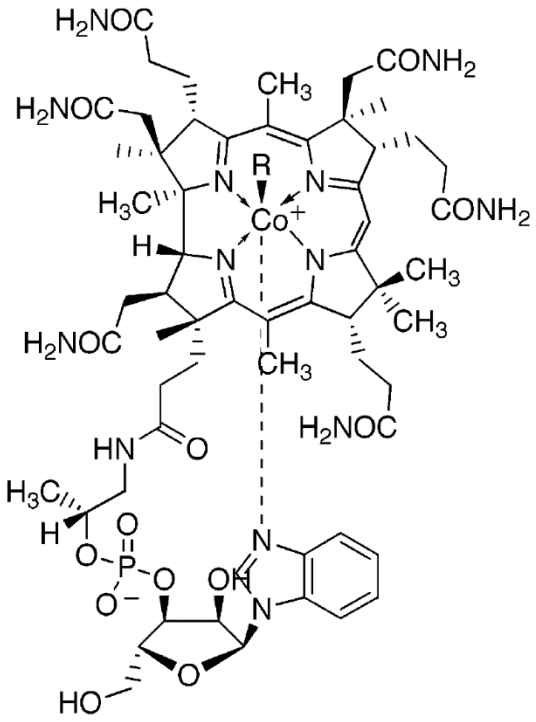


B. de Bruin et al. *Chem. Eur. J.* **2008**, *14*, 7594–7599.

Co(II), Rh(II) and (low-spin) Ir(II) complexes

Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

Asymmetric Cyclopropanation and Cyclopropenation



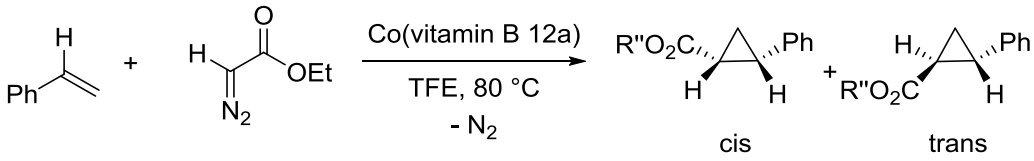
R = CN, Cyanocobalamin, CNCbl;

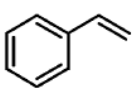
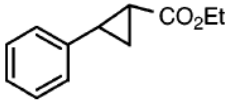
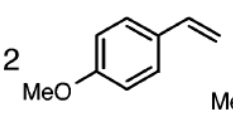
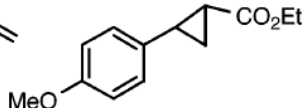
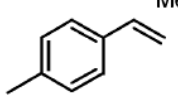
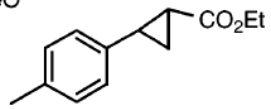
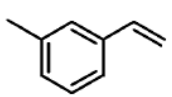
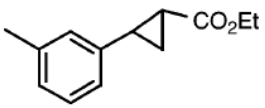
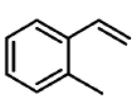
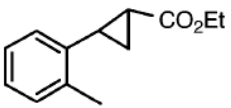
R = CH_3, Methylcobalamin, MeCbl;

R = 5'-deoxyadenosyl, Coenzyme B_{12}, AdoCbl;

R = HO•HCl, Aquocobalamin, B_{12a};

R = e, Cob(II)alamin, B_{12r}.

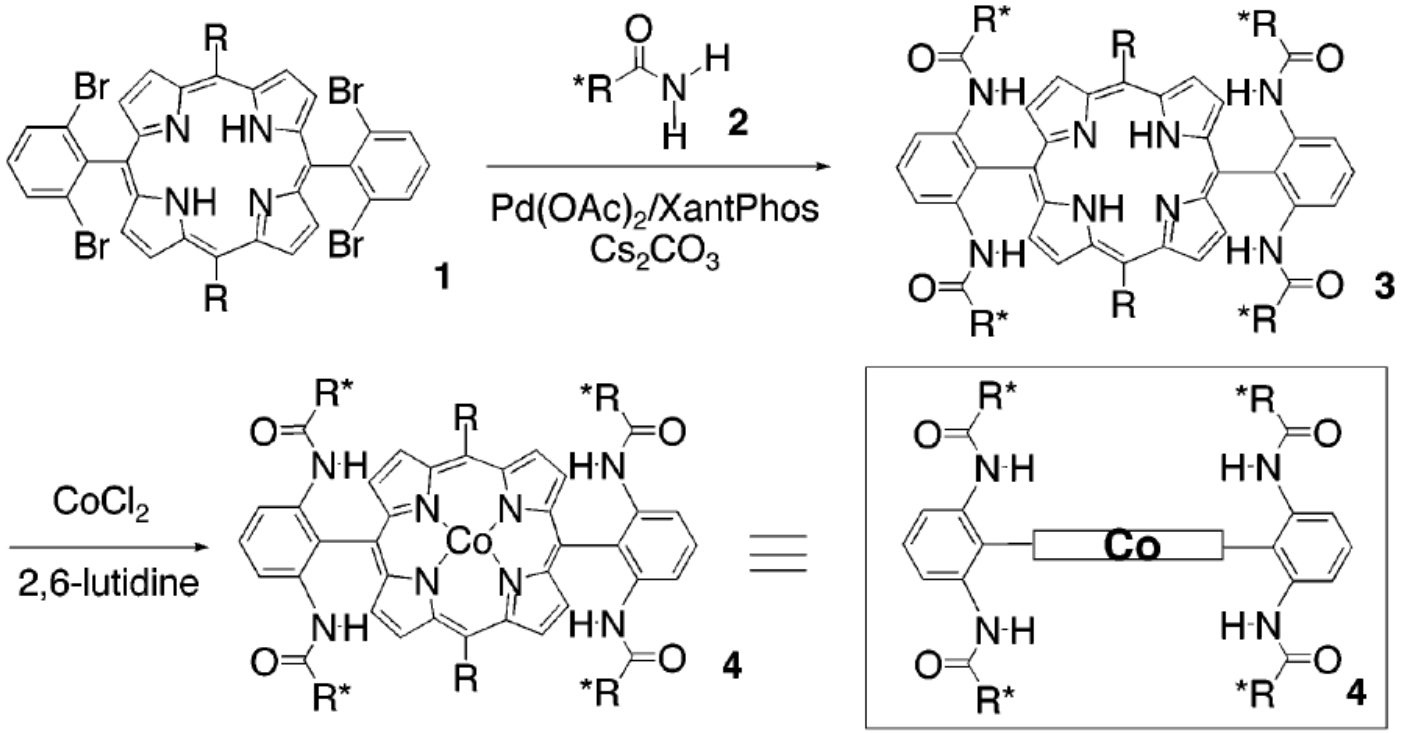


entry	substrate	product	yield (%)[b]	*cis*:*trans*[c]	ee(%)[d]
1			88	61:39	64(54)
2			92	63:37	64(50[e])
3			86	64:36	64(54[e])
4			94	60:40	66(58)
5			88	61:39	NR[f](57[e])

X. P. Zhang et al. *J. Org. Chem.* **2004**, *69*, 2431–2435.

Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

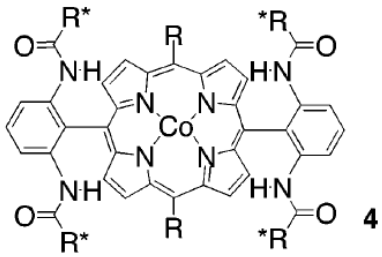
Asymmetric Cyclopropanation and Cyclopropenation



X. P. Zhang et al. *J. Am. Chem. Soc.* **2004**, *126*, 14718–14719.

Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric Cyclopropanation and Cyclopropenation



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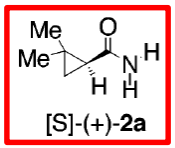
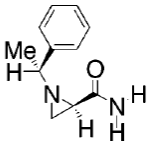
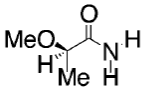


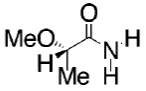
[S]-(+)-**2a**



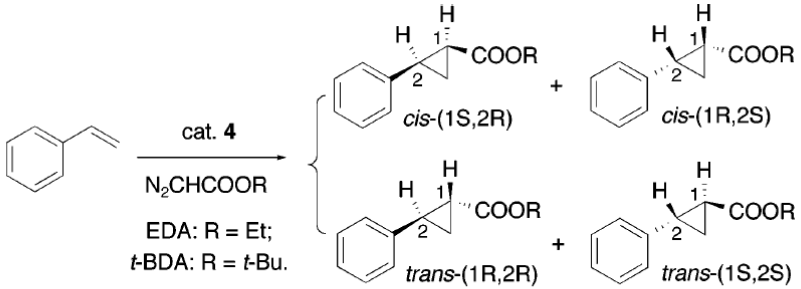
[R,R]-(+)-**2b**



[R]-(+)-**2c**



[S]-(-)-**2d**



entry	R	1	2	3, yield (%)[a]	4, yield (%)[a]
1	Ph	**1a**	**2a**	**3a**, 78	**4a**, 88
2	Ph	**1a**	**2b**	**3b**, 64	**4b**, 86
3	Ph	**1a**	**2c**	**3c**, 75	**4c**, 95
4	Ph	**1a**	**2d**	**3d**, 71	**4d**, 95
5	4-*t*-BuPh	**1b**	**2a**	**3e**, 86	**4e**, 72
6	4-CF_3Ph	**1c**	**2a**	**3f**, 77	**4f**, 95
7	pentaFPh	**1d**	**2a**	**3g**, 46	**4g**, 86
8	4-acetylPh	**1e**	**2a**	**3h**, 66	**4h**, 83
9	2,4,6-triMePh	**1f**	**2a**	**3i**, 84	**4i**, 91
10	2,6-diMeOPh	**1g**	**2a**	**3j**, 59	**4j**, 95
11	3,5-diMeOPh	**1h**	**2a**	**3k**, 88	**4k**, 96
12	3,5-di-*t*-BuPh	**1i**	**2a**	**3l**, 85	**4l**, 91
13	3,5-di-*t*-BuPh	**1i**	**2c**	**3m**, 79	**4m**, 96
14	3,5-di-*t*-BuPh	**1i**	**2d**	**3n**, 72	**4n**, 92
15	4-*n*-heptyl	**1j**	**2a**	**3o**, 74	**4o**, 95
16	H	**1k**	**2a**	**3p**, 79	**4p**, 91

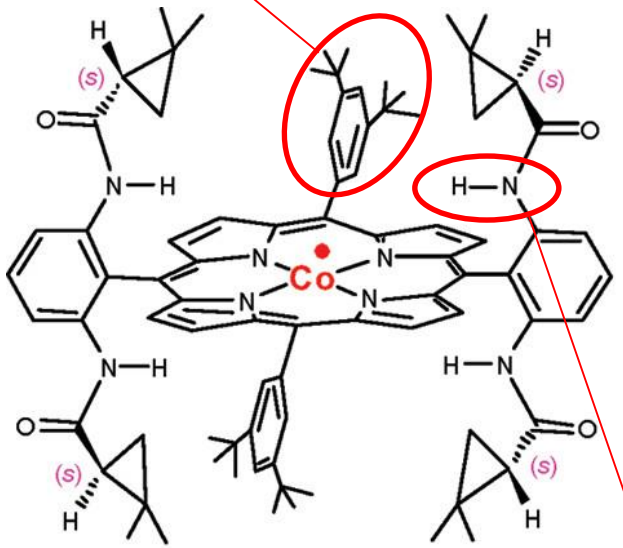
entry	4	diazo	additv	yield (%)[b]	trans:cis[b]	ee (%)[c]	config[d]
1	**4a**	EDA		92 (−)	87:13	31	1*R*,2*R*
2	**4b**	EDA		77 (−)	66:34	35	1*S*,2*S*
3	**4c**	EDA		92 (−)	32:68	48	1*S*,2*R*
4	**4d**	EDA		95 (−)	32:68	51	1*R*,2*S*
5	**4a**	EDA	DMAP	91 (−)	96:04	67	1*R*,2*R*
6	**4c**	EDA	DMAP	52 (−)	44:56	88	1*R*,2*R*
7	**4d**	EDA	DMAP	57 (−)	42:58	89	1*R*,2*R*
8	**4l**	EDA	DMAP	86 (82)	97:03	78	1*R*,2*R*
9	**4l**	*t*-BDA	DMAP	88 (84)	>99:01	95	1*R*,2*R*
10[e]	**4l**	*t*-BDA	DMAP	84 (85)	>99:01	98	1*R*,2*R*
11	**4m**	EDA	DMAP	65 (59)	31:69	92	1*S*,2*R*
12[f]	**4m**	*t*-BDA	DMAP	78 (75)	37:63	96	1*S*,2*R*
13	**4n**	EDA	DMAP	68 (−)	30:70	94	1*R*,2*S*
14[f]	**4n**	*t*-BDA	DMAP	76 (−)	38:62	95	1*R*,2*S*
15	**4o**	EDA	DMAP	80 (−)	96:04	59	1*R*,2*R*
16	**4o**	*t*-BDA	DMAP	73 (−)	99:01	78	1*R*,2*R*

[a] Reactions were carried out at **room temperature** in toluene for 20 h under N_2 with 1.0 equiv of styrene, 1.2 equiv of diazo reagent, and 1 mol% **4** in the presence of 0.5 equiv of additive. [e] Carried out at -20 ° C for 8 h. [f] 5 mol % 4 was used.

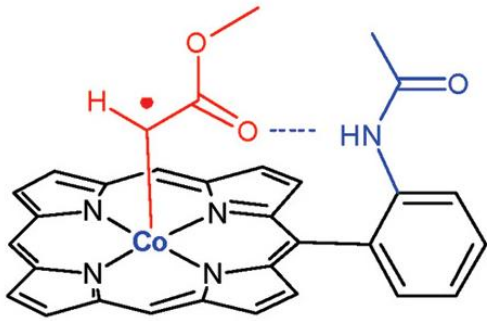
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric Cyclopropanation and Cyclopropenation

Providing a confined, protective, and chiral nanospace around the active site !
Avoiding the side reactions!



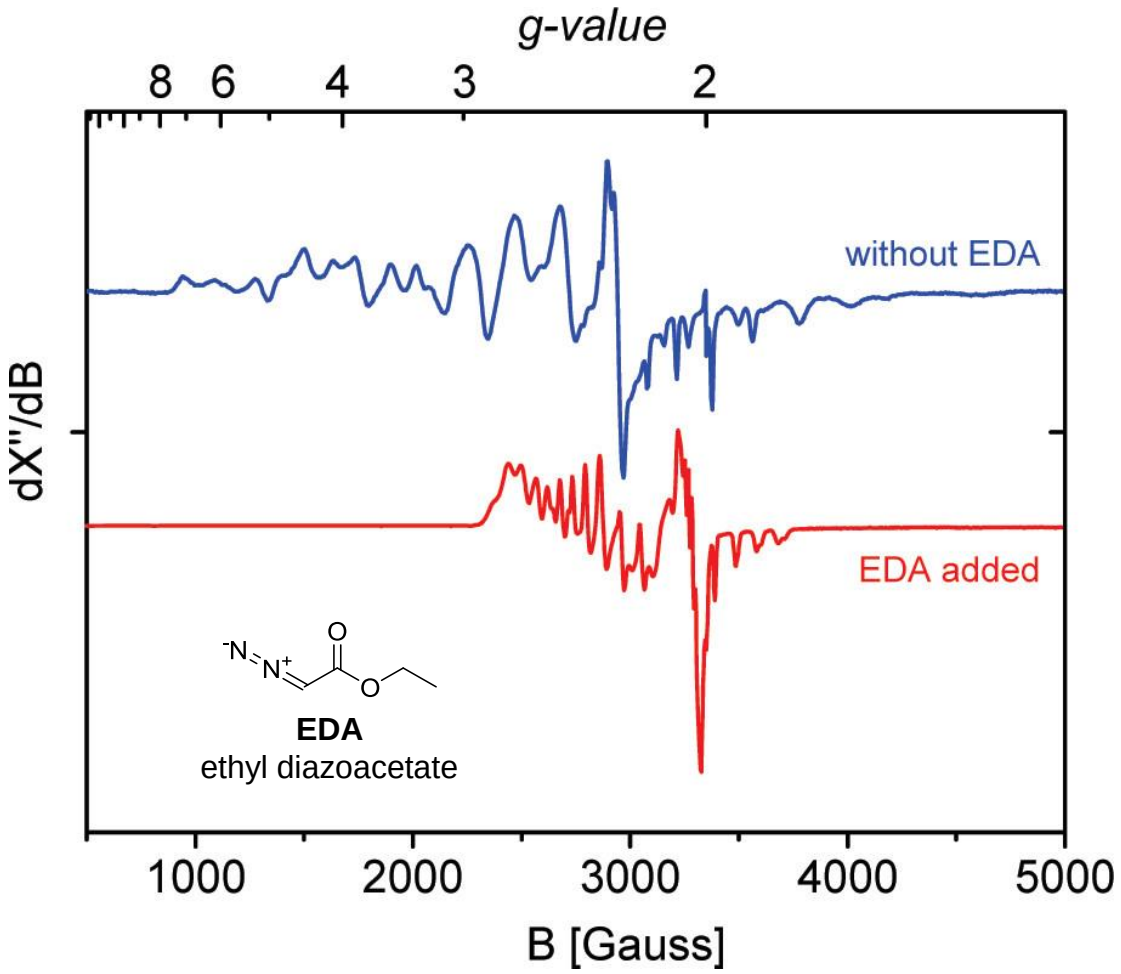
Co(3,5-Di^{t}Bu-ChenPhyrin)

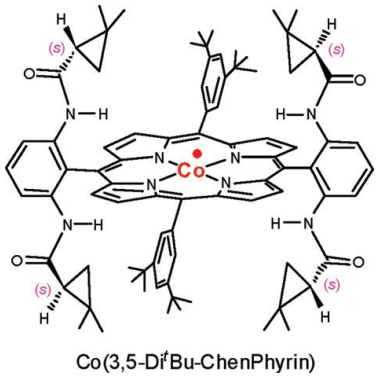


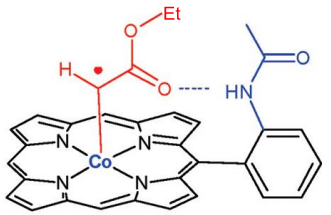
Potential hydrogen-bond donors!
lower the activation barrier,
leading to faster reactions and higher selectivities!

Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric Cyclopropanation and Cyclopropenation



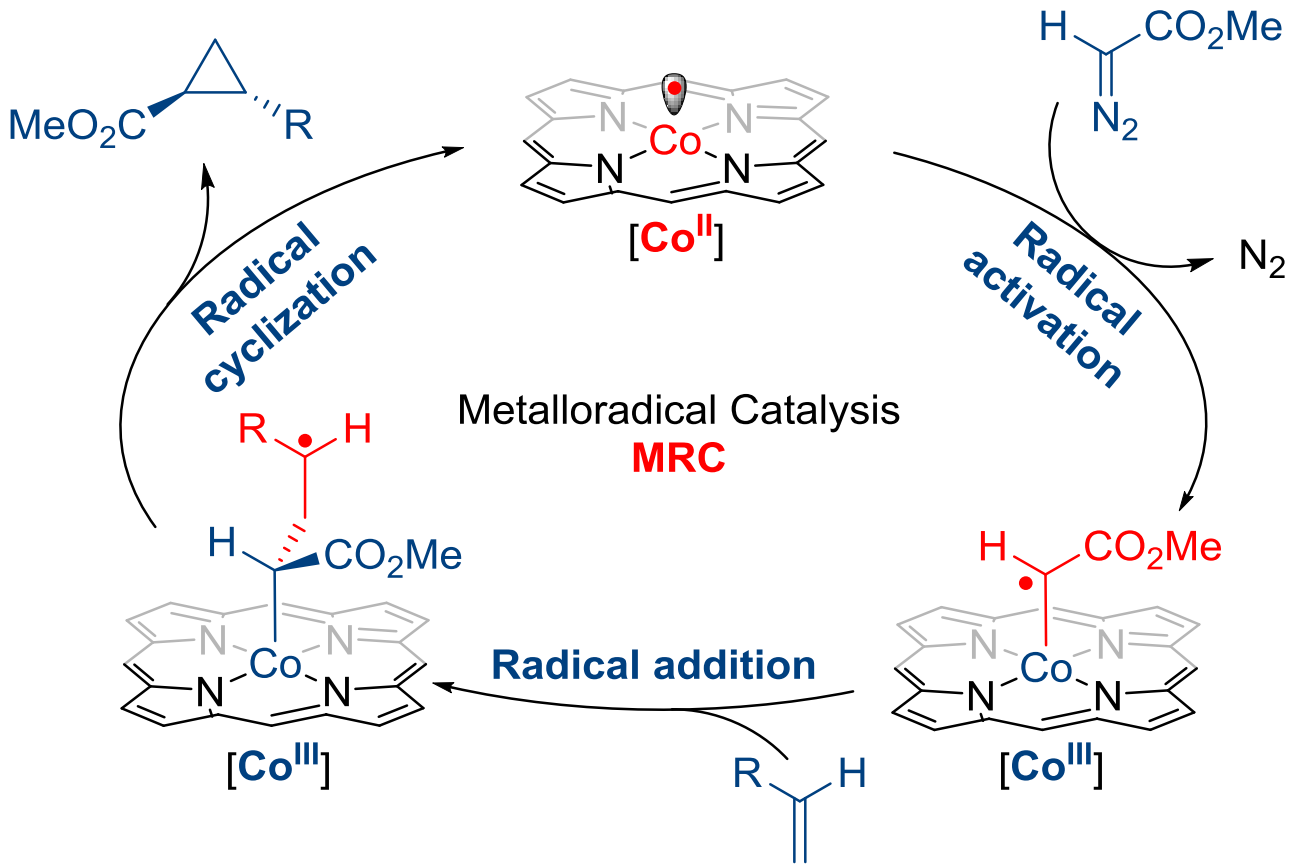




X. P. Zhang et al. *J. Am. Chem. Soc.* **2004**, *126*, 14718–14719.

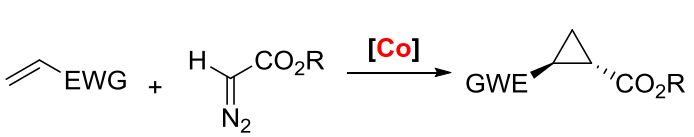
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

- **Asymmetric Cyclopropanation and Cyclopropenation**

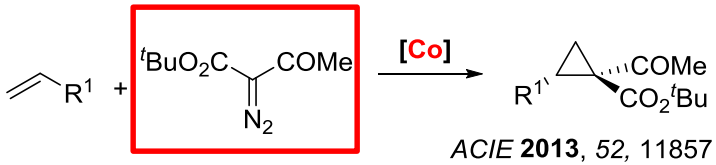


Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

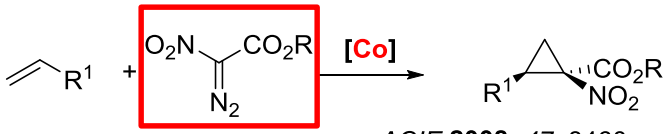
Asymmetric Cyclopropanation and Cyclopropenation



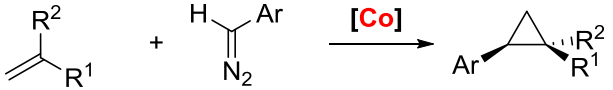
JACS **2007**, *129*, 12704



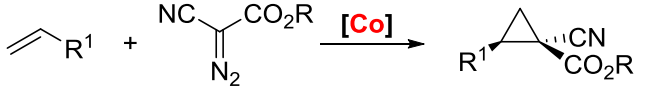
ACIE **2013**, *52*, 11857



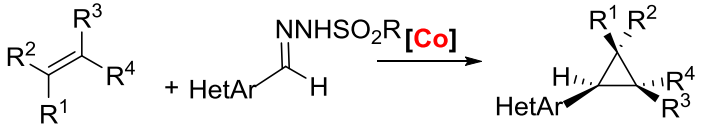
ACIE **2008**, *47*, 8460



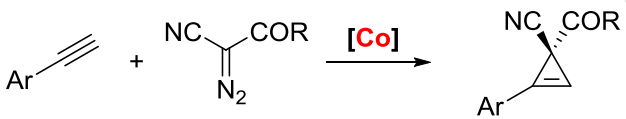
JACS **2017**, *139*, 1049



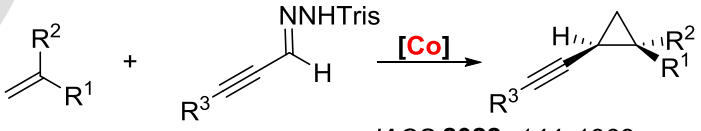
JACS **2010**, *132*, 12796



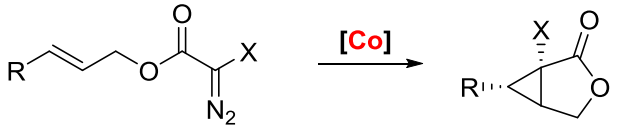
JACS **2021**, *143*, 11141



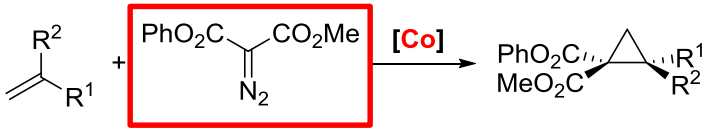
JACS **2011**, *133*, 3304



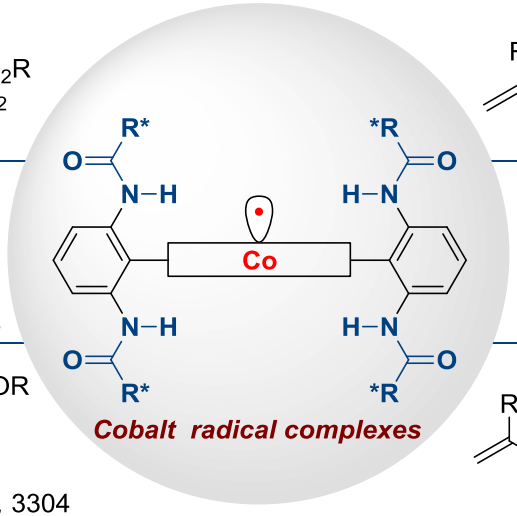
JACS **2022**, *144*, 1368



JACS **2011**, *133*, 15292

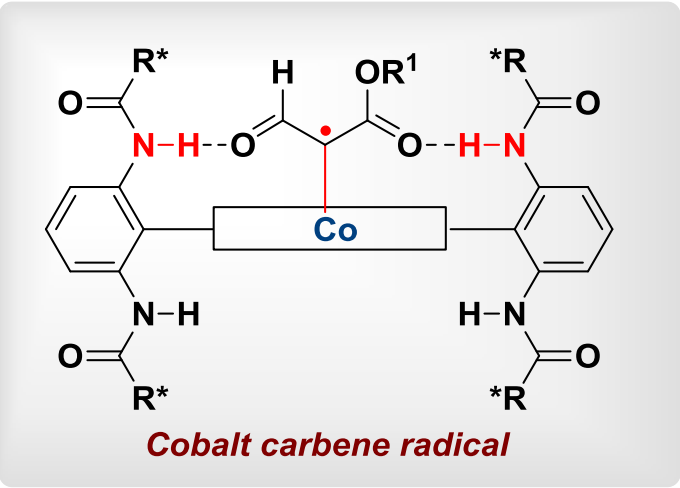


Chem **2022**, *2*, 330

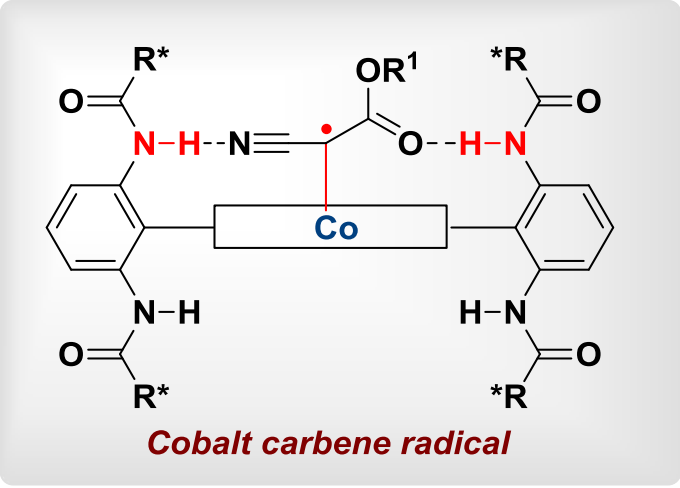


Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

- **Asymmetric Cyclopropanation and Cyclopropenation**



Cobalt carbene radical

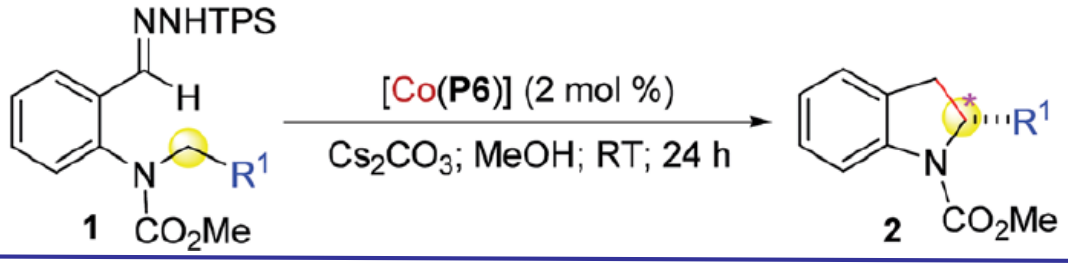


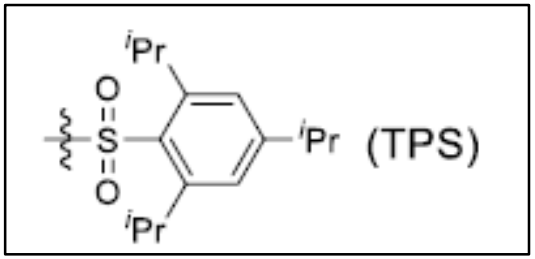
Cobalt carbene radical

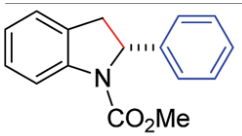
Potential Double H-bonding in '*Cobalt carbene radical' intermediate*

Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric intramolecular cyclization

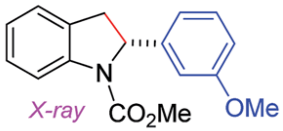




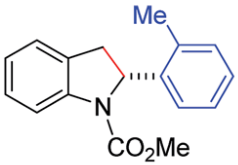


entry 1: **2c**
92% yield, 94% *ee*

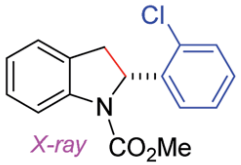
entry 2: **2d**
98% yield, 94% *ee*



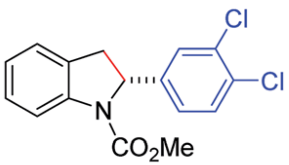
entry 3: **2e**
98% yield, 90% *ee*



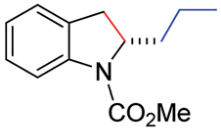
entry 4: **2f**
96% yield, 94% *ee*



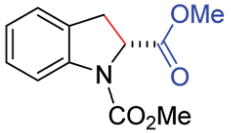
entry 5: **2g**
92% yield, 93% *ee*



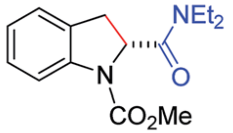
entry 6: **2h**
85% yield, 96% *ee*



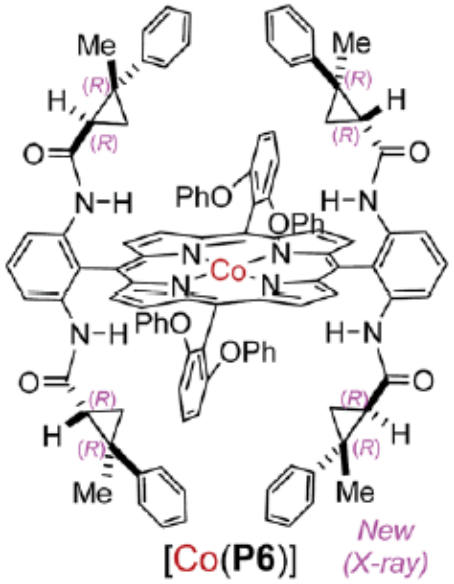
entry 16[b]: **2r**
65% yield, 87% *ee*



entry 17[c]: **2s**
49% yield, 81% *ee*



entry 18[c]: **2t**
92% yield, 68% *ee*



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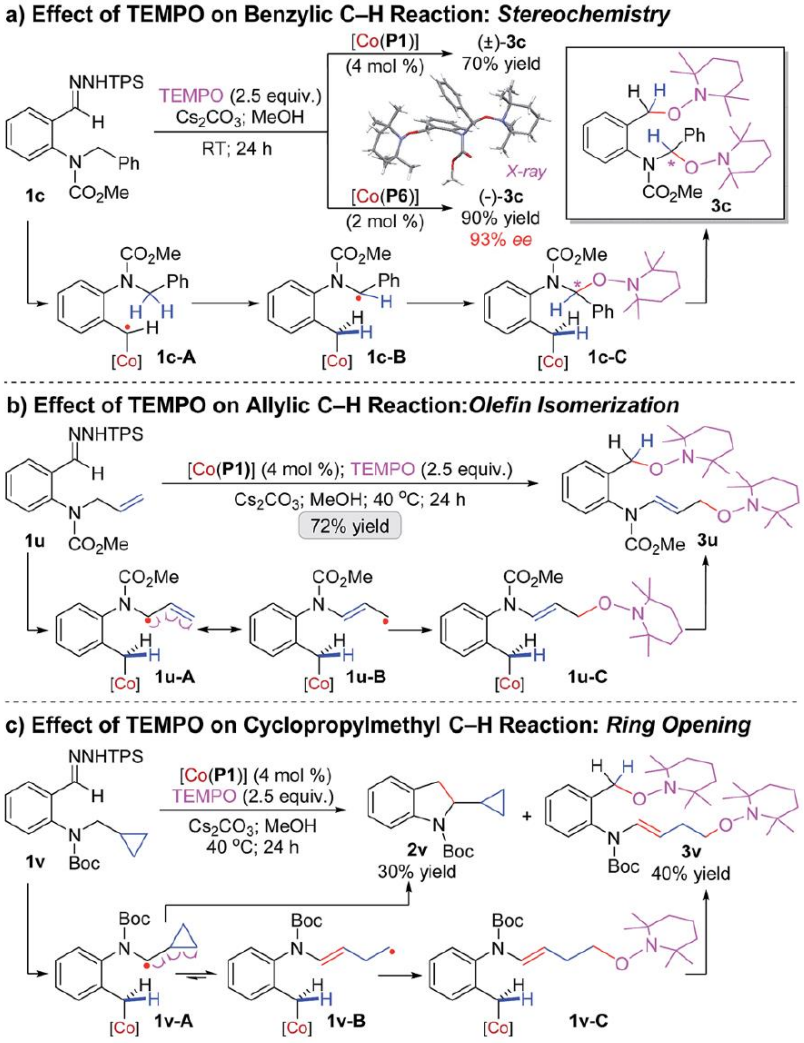
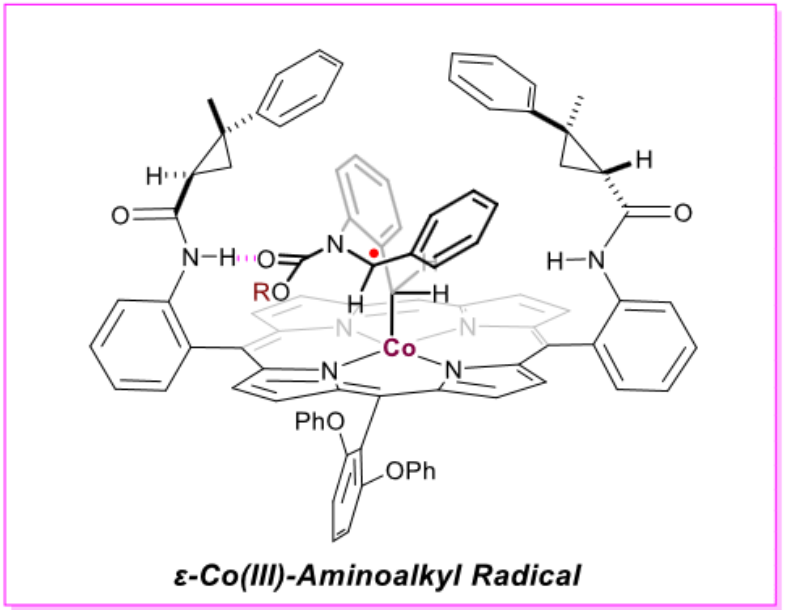
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric intramolecular cyclization





ε-Co(III)-Aminoalkyl Radical

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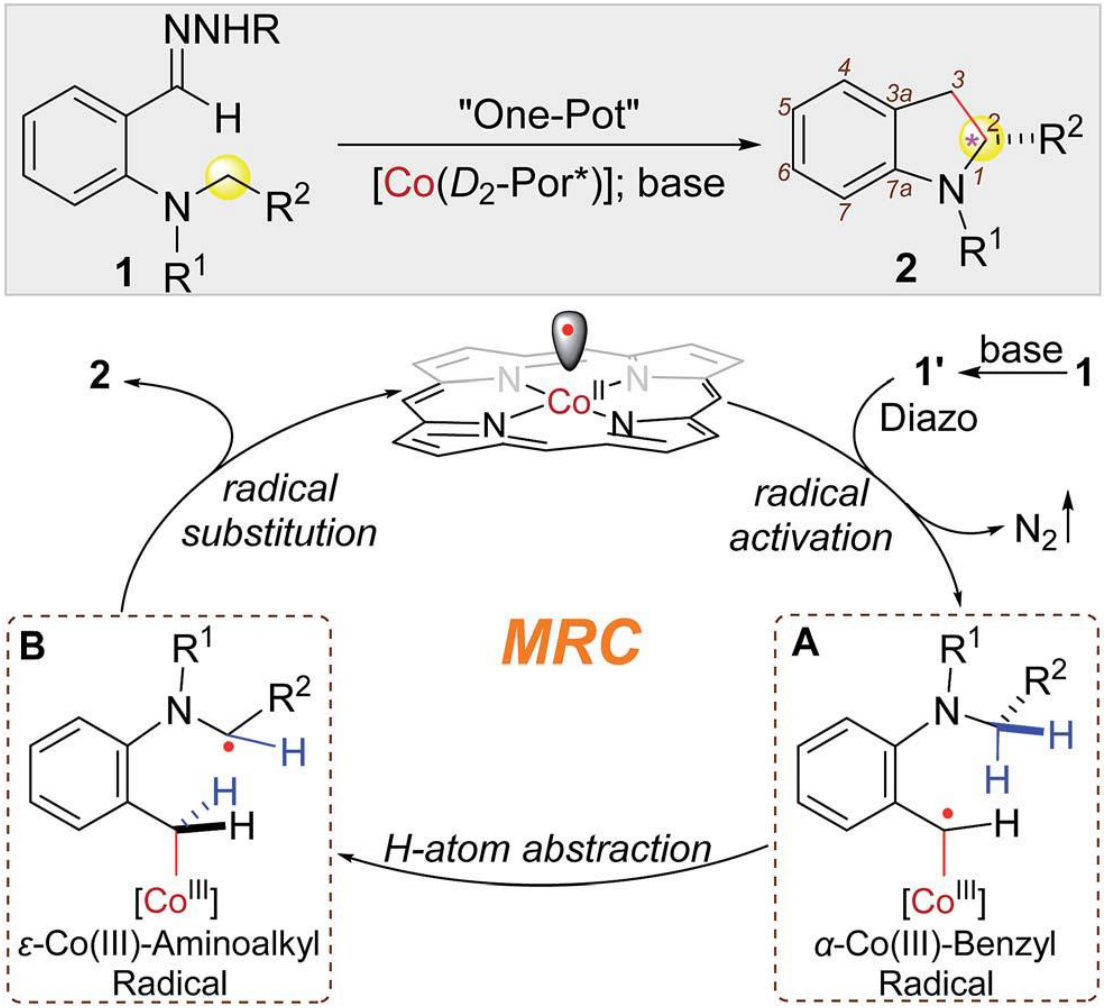
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

- **Asymmetric intramolecular cyclization**



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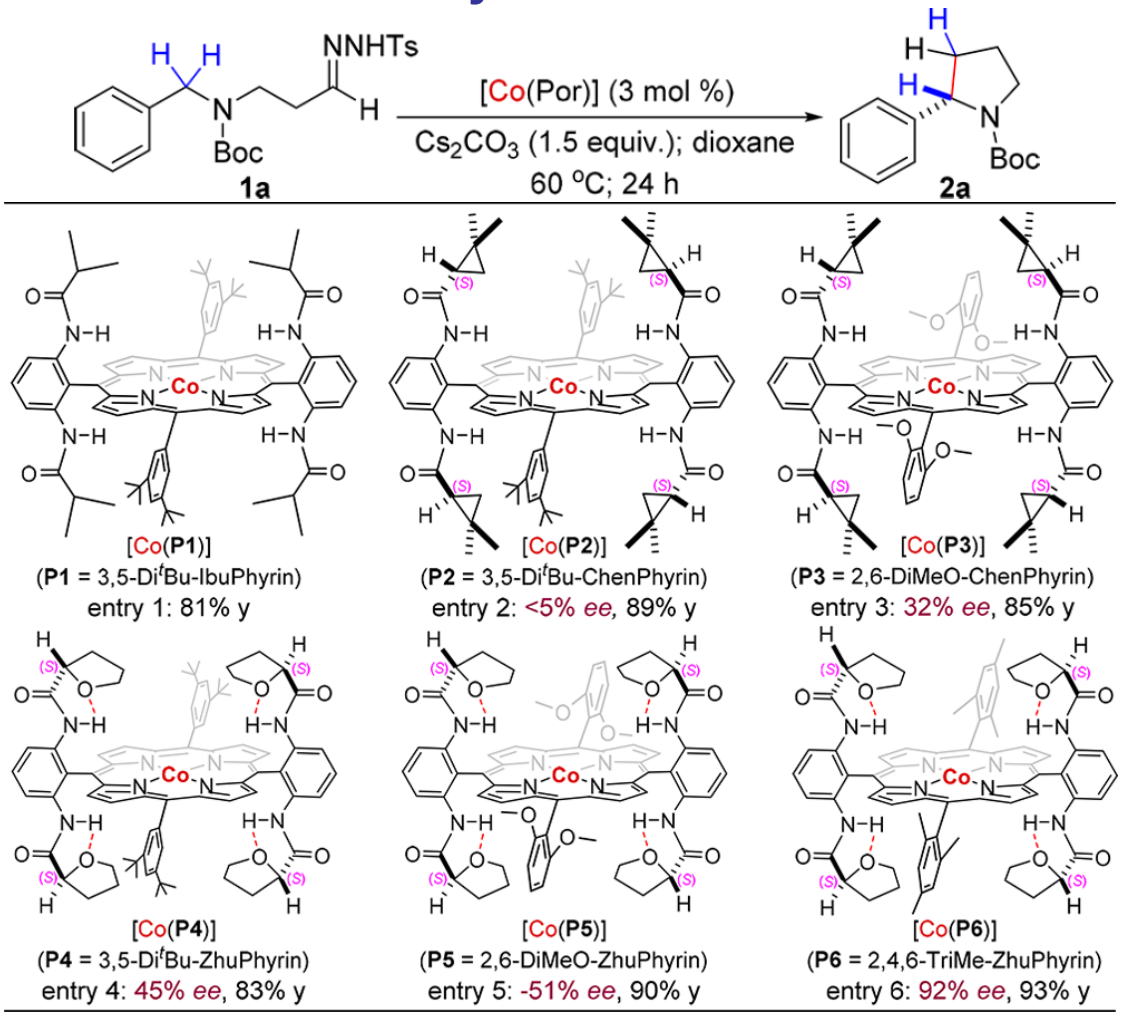
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

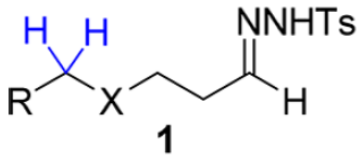
■ Asymmetric intramolecular cyclization



X. P. Zhang et al. *J. Am. Chem. Soc.* **2018**, *140*, 4792–4796.

Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

Asymmetric intramolecular cyclization

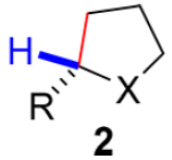


1

[Co(**P6**)] (3 mol %)

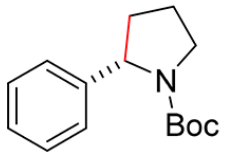
Cs_2CO_3 (1.5 equiv.); dioxane

60 °C; 24 h

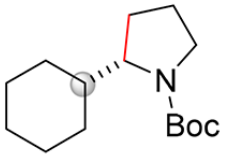


2

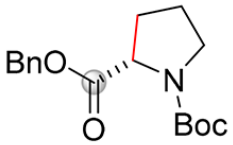
X:
NBoc, O, S, CH_2



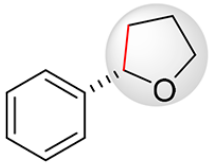
2a
93% y; 92% *ee*



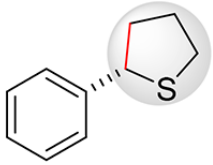
2o
57% y; 88% *ee*



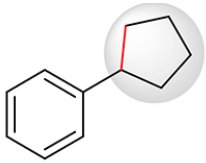
2p
56% y; 82% *ee*



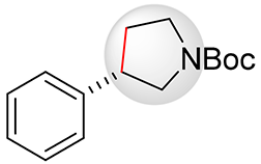
2y
54% y; 85% *ee*



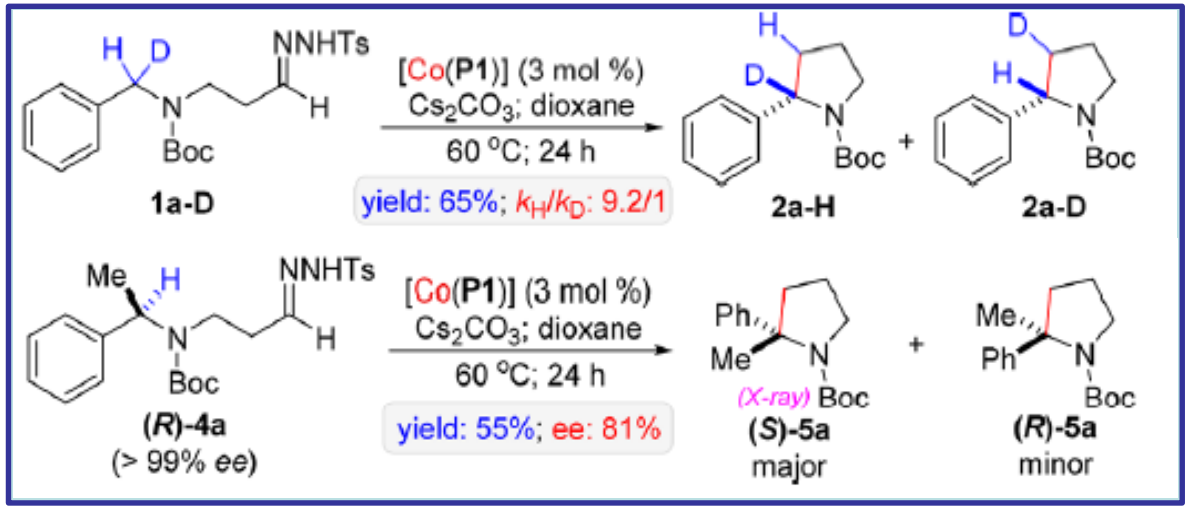
2z
85% y; 91% *ee*

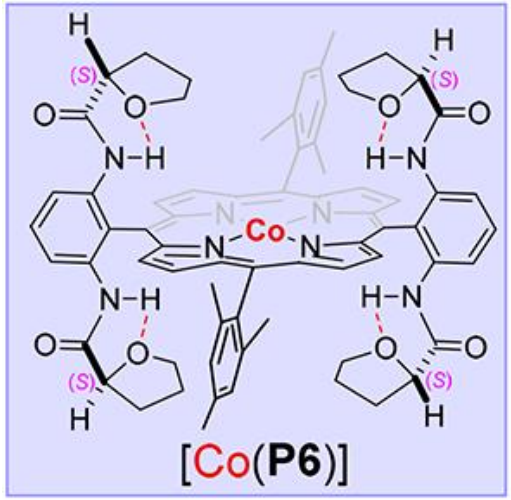


2aa[d]
76% y; *ee*: n/a



2ab
50% y; 67% *ee*





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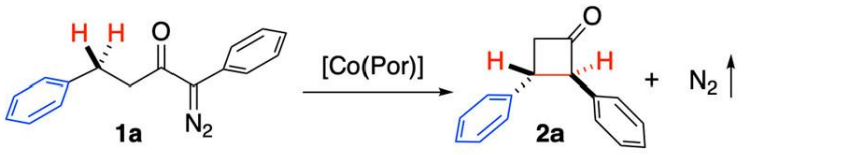
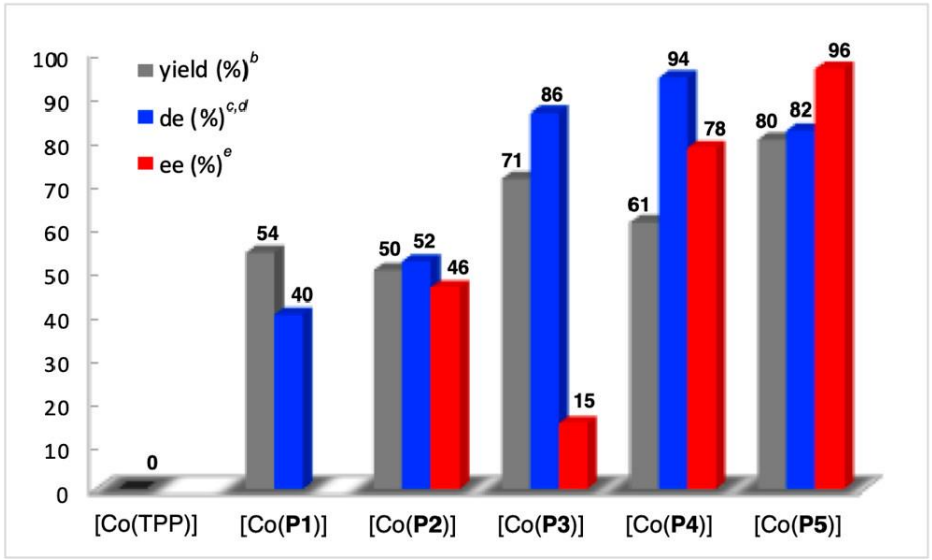
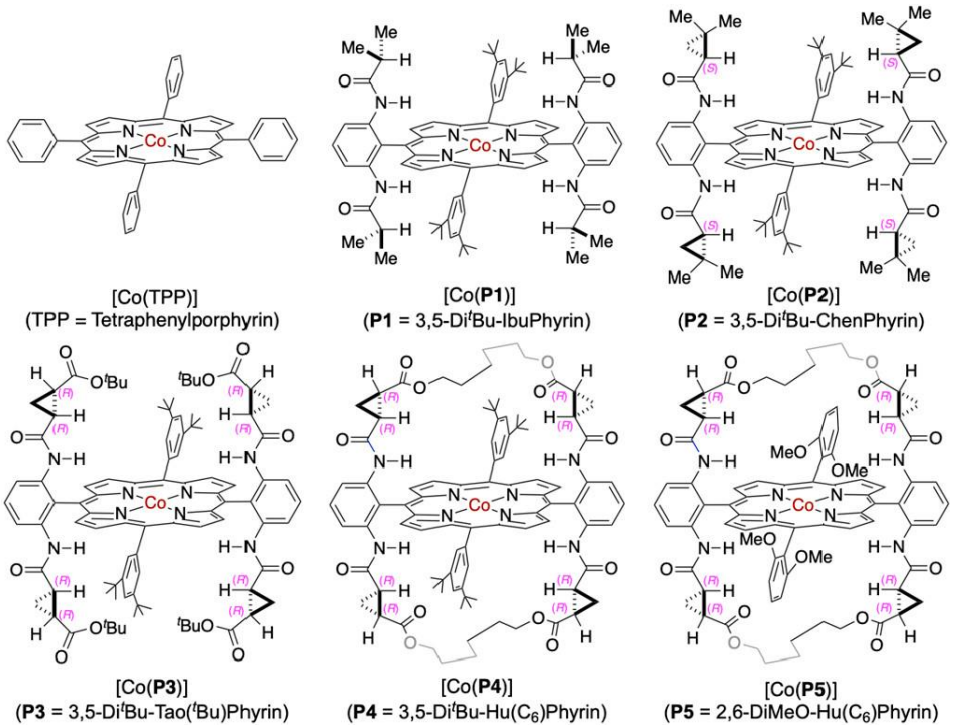
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric intramolecular cyclization







[a]Carried out with 1a (0.10 mmol) using [Co(Por)] (2 mol %) in tert-butyl methyl ether (TBME) (0.5 mL) at 40 ℃ for 12 h. [b]Isolated yield. [c]Diastereomeric excess (de) determined by ^{1}H NMR analysis of crude reaction mixture before purification. [d]Isomerized to trans-enriched products with 96% de after purification by silica gel column chromatography for all catalytic reactions. [e]Enantiomeric excess (ee) of trans-diastereomer determined by chiral HPLC after purification.

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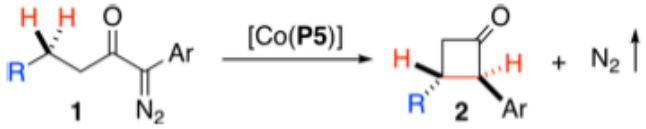
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric intramolecular cyclization



(–)-2a[e] — 1.0 mmol scale
entry 1: 80% yield
98:2 dr (91:9)
96% ee

(–)-2b
entry 2: 70% yield
98:2 dr (87:13)
92% ee

(–)-2c
entry 3: 77% yield
98:2 dr (88:12)
93% ee

(–)-2d
entry 4: 76% yield
95:5 dr (83:17)
70% ee

(–)-2e
entry 5: 71% yield
98:2 dr (89:11)
86% ee

(–)-2f
entry 6: 86% yield
98:2 dr (78:22)
96% ee

(–)-2g
entry 7: 79% yield
99:1 dr (99:1)
90% ee

(–)-2h
entry 8: 81% yield
97:3 dr (86:14)
90% ee

(–)-2i
entry 9: 65% yield
96:4 dr (85:15)
90% ee

(–)-2j[e] — 1.0 mmol scale
entry 10: 76% yield
97:3 dr (90:10)
88% ee

(–)-2k
entry 11: 62% yield
92:8 dr (92:8)
96% ee

(–)-2l
entry 12: 76% yield
95:5 dr (87:13)
92% ee

(–)-2m
entry 13: 70% yield
98:2 dr (97:3)
78% ee

(–)-2n
entry 14: 71% yield
96:4 dr (62:38)
50% ee

(–)-2o
entry 15: 80% yield
72:28 dr (82:18)
73% ee

(–)-2p
entry 16: 75% yield
98:2 dr (92:8)
94% ee

(X-ray) (–)-2q[e,f] — 1.0 mmol scale
entry 17: 93% yield
99:1 dr (97:3)
95% ee

(X-ray) (–)-2r[f]
entry 18: 90% yield
97:3 dr (97:3)
96% ee

(–)-2s
entry 19: 93% yield
98:2 dr (98:2)
95% ee

(–)-2t
entry 20: 52% yield
98:2 dr (88:12)
91% ee

(X-ray) (–)-2u[g]
entry 21: 66% yield
99:1 dr (99:1)
15% ee

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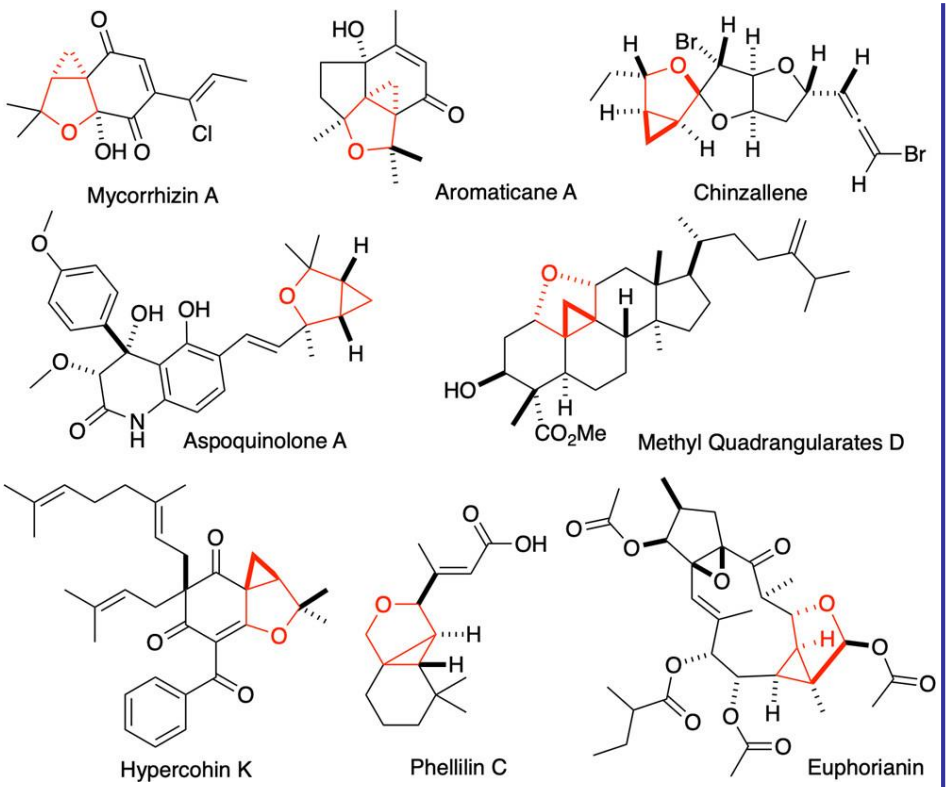
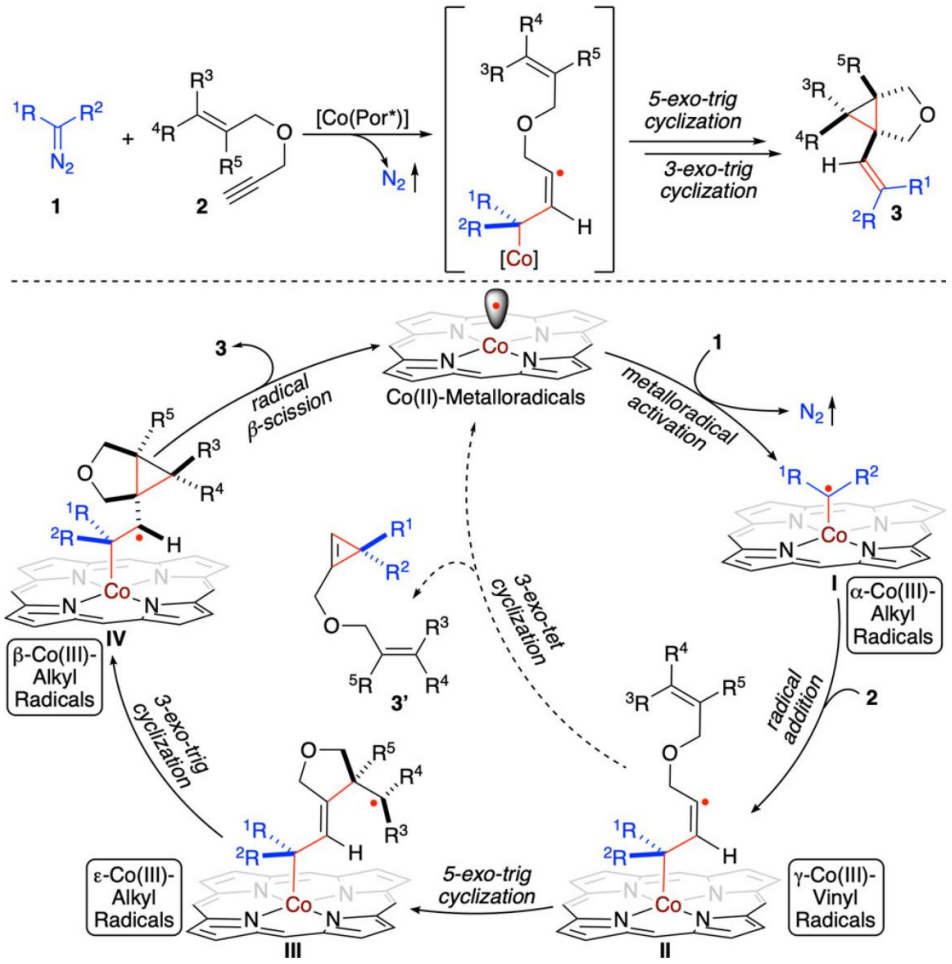
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

■ Asymmetric intramolecular cyclization



Selected examples of natural products and bioactive compounds containing cyclopropane-fused tetrahydrofurans



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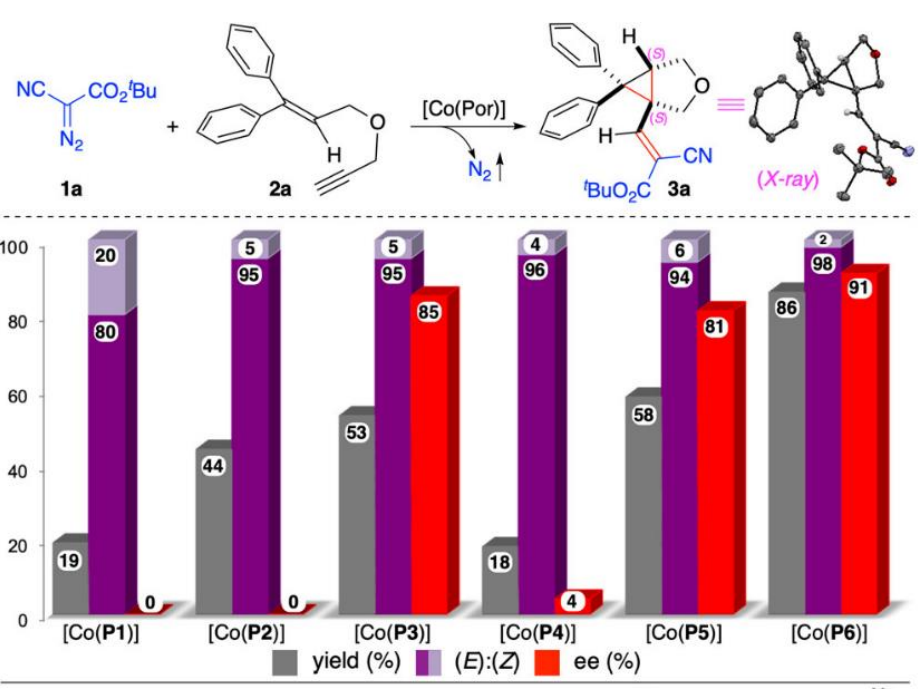
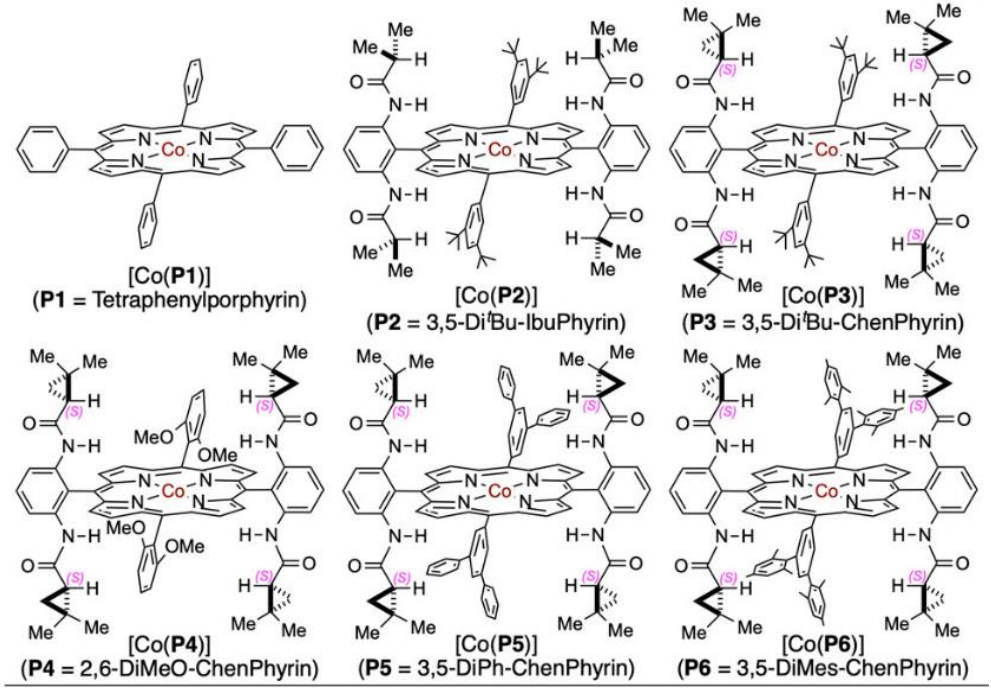
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

- **Asymmetric intramolecular cyclization**





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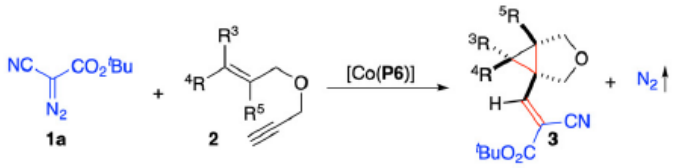
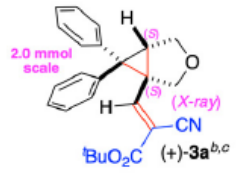
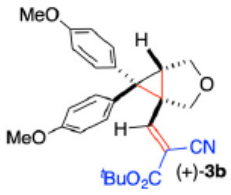
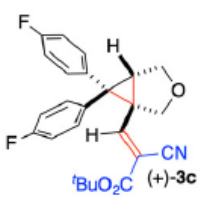
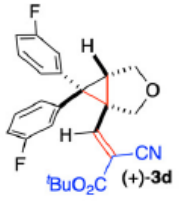
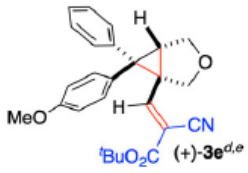
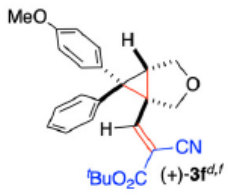
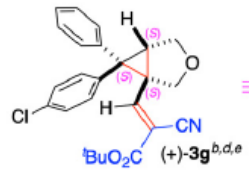
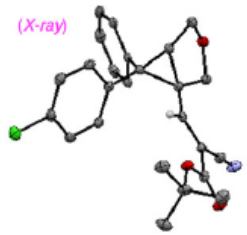
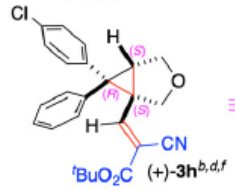
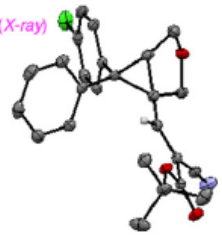
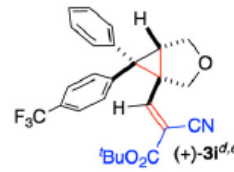
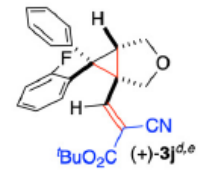
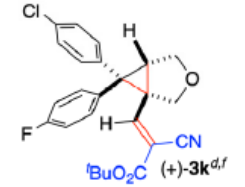
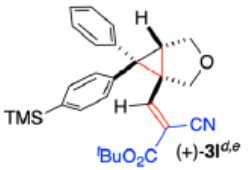
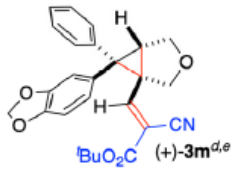
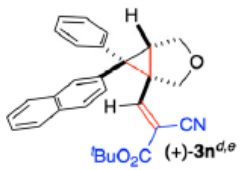
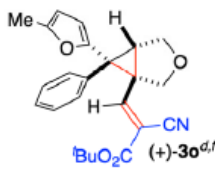
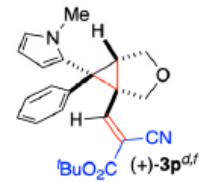
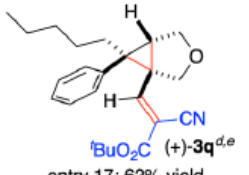
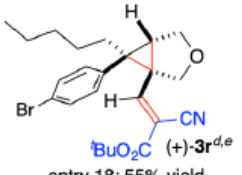
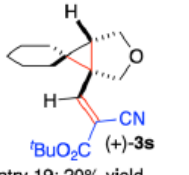
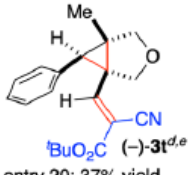
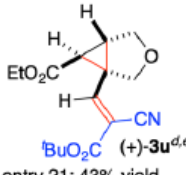
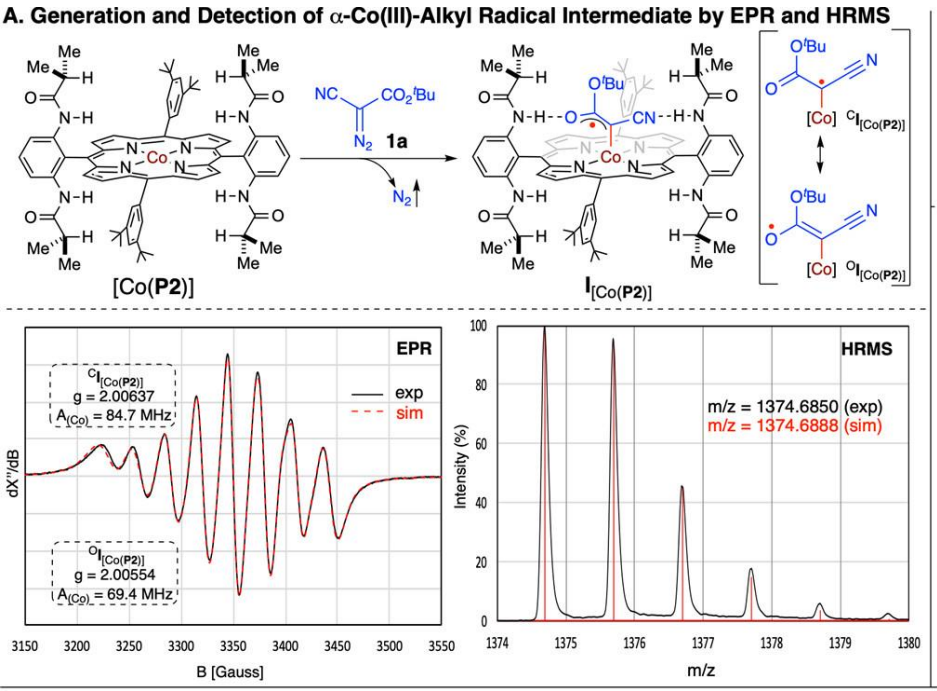
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

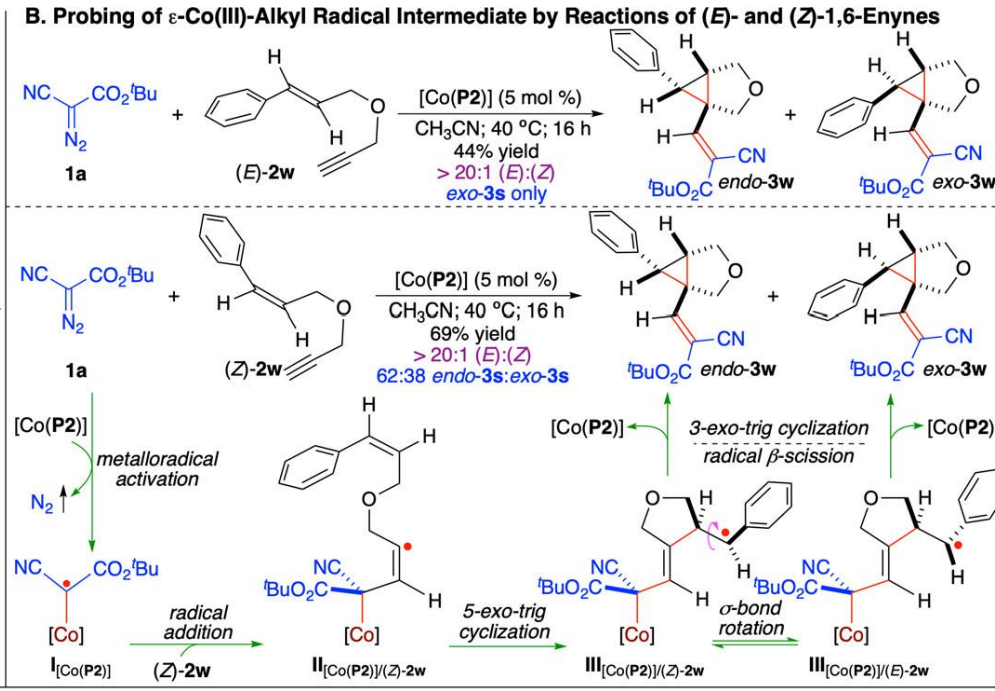


					
2.0 mmol scale; (X-ray); (+)-**3a**[b,c]	(+)-**3b**	(+)-**3c**	(+)-**3d**	(+)-**3e**[d,e]	(+)-**3f**[d,f]
entry 1: 86% yield	entry 2: 61% yield	entry 3: 91% yield	entry 4: 69% yield	entry 5: 84% yield	entry 6: 83% yield
98:2 (*E*):(*Z*); 91% ee	98:2 (*E*):(*Z*); 91% ee	97:3 (*E*):(*Z*); 92% ee	99:1 (*E*):(*Z*); 92% ee	97:3 (*E*):(*Z*); 99:1 dr; 92% ee	97:3 (*E*):(*Z*); 99:1 dr; 95% ee
					
(+)-**3g**[b,d,e]	(X-ray)	(+)-**3h**[b,d,f]	(X-ray)	(+)-**3i**[d,e]	(+)-**3j**[d,e]
entry 7: 76% yield		entry 8: 80% yield		entry 9: 80% yield	entry 10: 50% yield
97:3 (*E*):(*Z*); 99:1 dr; 90% ee		97:3 (*E*):(*Z*); 99:1 dr; 92% ee		98:2 (*E*):(*Z*); 99:1 dr; 94% ee	95:5 (*E*):(*Z*); 99:1 dr; 90% ee
					
(+)-**3k**[d,f]	(+)-**3l**[d,e]	(+)-**3m**[d,e]	(+)-**3n**[d,e]	(+)-**3o**[d,f]	(+)-**3p**[d,f]
entry 11: 79% yield	entry 12: 71% yield	entry 13: 66% yield	entry 14: 68% yield	entry 15: 48% yield	entry 16: 31% yield
98:2 (*E*):(*Z*); 99:1 dr; 89% ee	98:2 (*E*):(*Z*); 99:1 dr; 92% ee	98:2 (*E*):(*Z*); 99:1 dr; 94% ee	97:3 (*E*):(*Z*); 99:1 dr; 91% ee	96:4 (*E*):(*Z*); 99:1 dr; 80% ee	94:6 (*E*):(*Z*); 99:1 dr; 79% ee
					
(+)-**3q**[d,e]	(+)-**3r**[d,e]	(+)-**3s**	(–)-**3t**[d,e]	(+)-**3u**[d,e]	(+)-**3v**[d,e]
entry 17: 62% yield	entry 18: 55% yield	entry 19: 20% yield	entry 20: 37% yield	entry 21: 43% yield	entry 22: 37% yield
95:5 (*E*):(*Z*); 99:1 dr; 83% ee	97:3 (*E*):(*Z*); 99:1 dr; 78% ee	95:5 (*E*):(*Z*); 42% ee	93:7 (*E*):(*Z*); 99:1 dr; 70% ee	95:5 (*E*):(*Z*); 99:1 dr; 10% ee	95:5 (*E*):(*Z*); 99:1 dr; 74% ee

Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

- **Asymmetric intramolecular cyclization**





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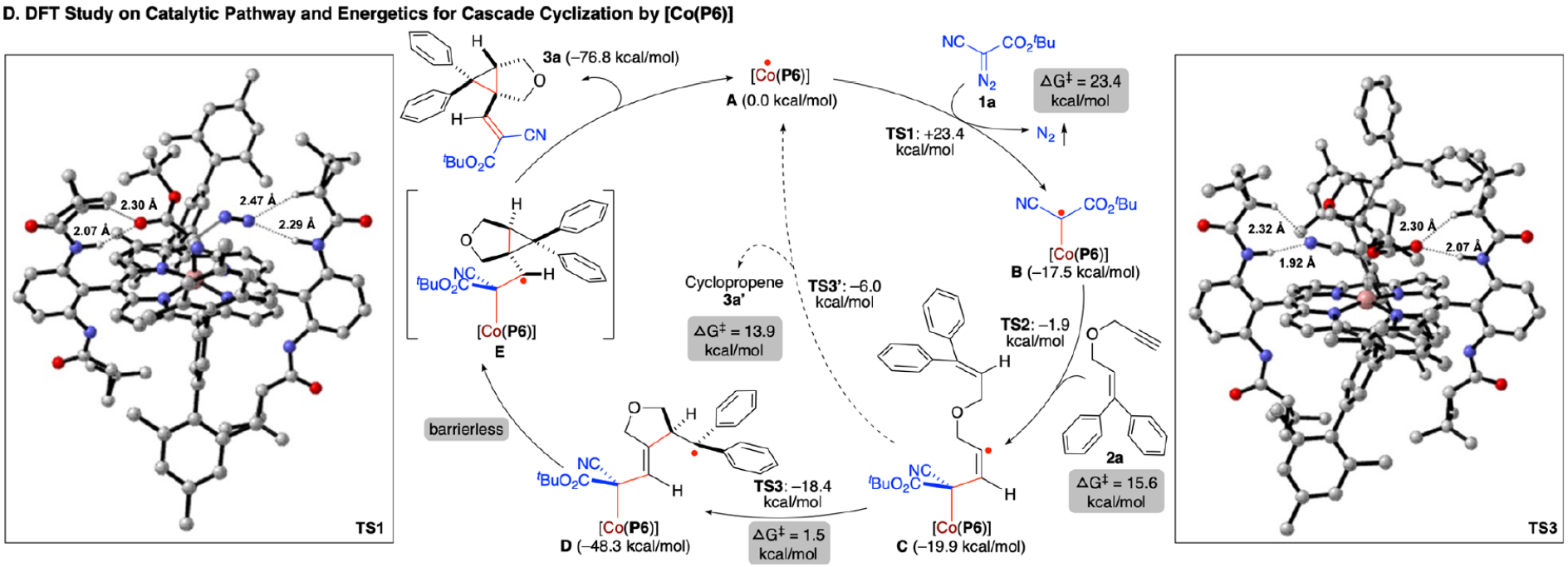
Asymmetric Radical Coupling Mediated by ‘Metal-Carbene Radical’

- **Asymmetric intramolecular cyclization**



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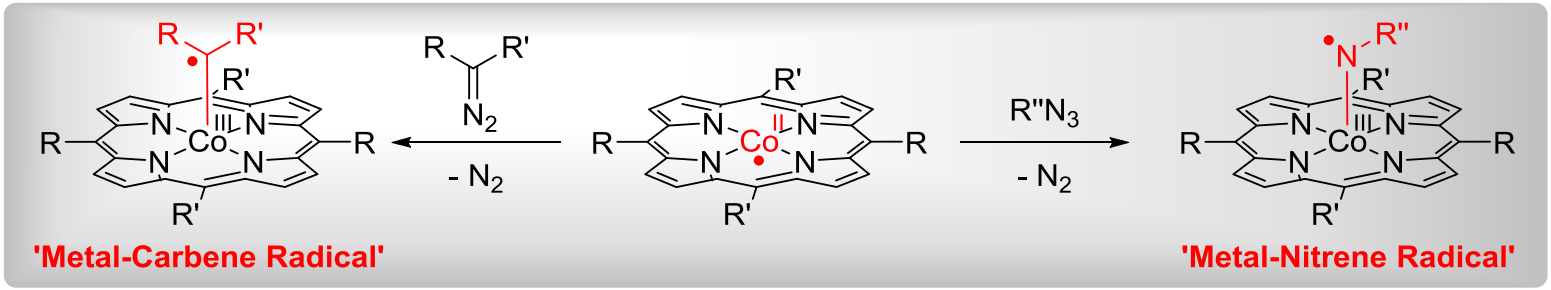
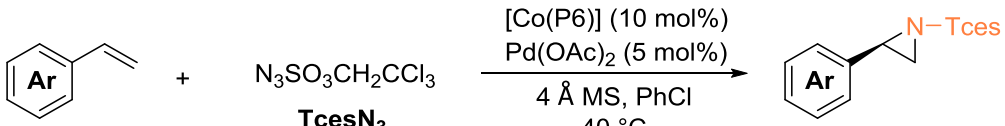
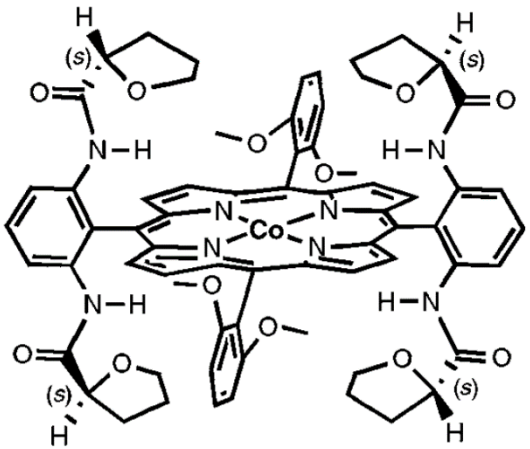
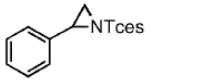
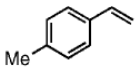
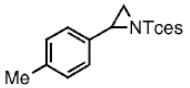
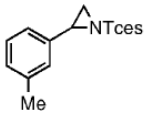
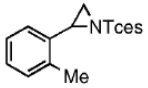
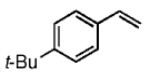
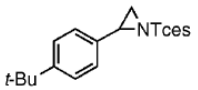
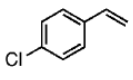
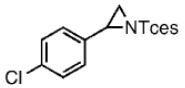
Asymmetric Radical Coupling Mediated by 'Metal-Nitrene Radical'

Asymmetric Olefin Aziridination






[Co(**P6**)] (2,6-DiMeO-ZhuPhyrin)

Entry	Olefin	Aziridine	Temp/°C	Yield[b] (%)	Ee[c] (%)	[α][d]
1			0	91	94	(−)
2			0	89	90	(−)
3[f]			RT	85	82	(−)
4[f]			RT	86	84	(−)
5			0	89	85	(−)
6			0	93	91	(−) (*R*)[e]

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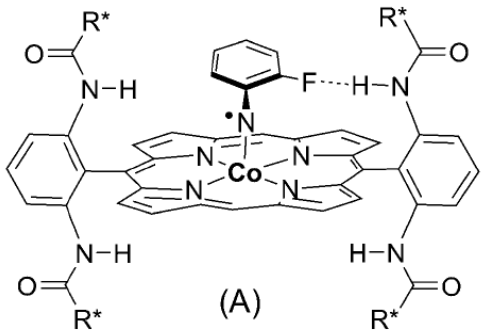
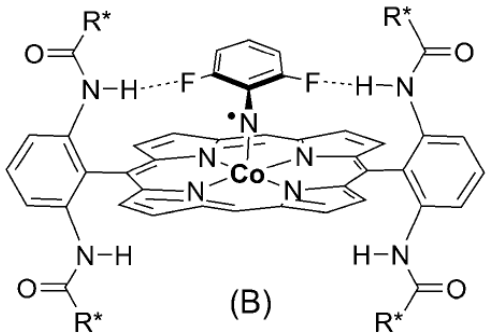
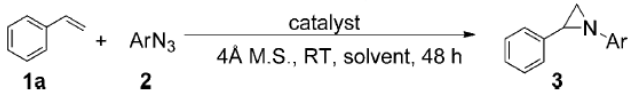
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric Olefin Aziridination

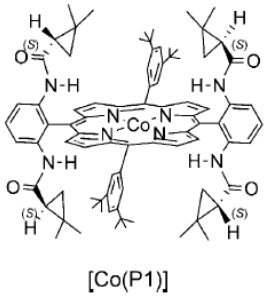


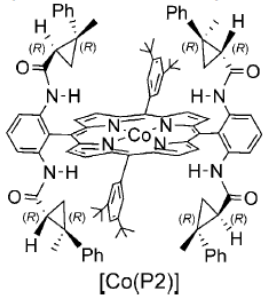


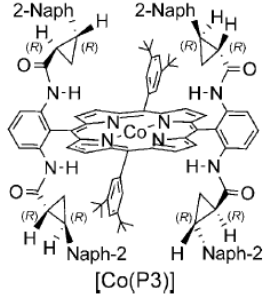


Entry	Catalyst	Ar	Solvent	Yield [%][b]	*ee* [%][c]
1[d]	[Co(P1)]	*o*-FC_6H_4 (**2a**)	PhH	50[e]	−47
2[d]	[Co(TPP)]	*o*-FC_6H_4 (**2a**)	PhH	trace	–
3[d]	[Co(P1)]	2,4,6-$F_3C_6H_2$ (**2b**)	PhH	95	−66
4[d]	[Co(P2)]	2,4,6-$F_3C_6H_2$ (**2b**)	PhH	95	73
5	[Co(P3)]	2,4,6-$F_3C_6H_2$ (**2b**)	PhH	94	90
6	[Co(P3)]	2,4,6-$F_3C_6H_2$ (**2b**)	PhCl	80	91
7	**[Co(P3)]**	**2,4,6-$F_3C_6H_2$ (2b)**	**PhF**	**94**	**92**
8	[Co(P3)]	2,4,6-$F_3C_6H_2$ (**2b**)	hexane	72	90
9	–	2,4,6-$F_3C_6H_2$ (**2b**)	PhH	NR	–

[a] Carried out with olefin (1 equiv, 0.2 M), azide (1.2 equiv), and [Co(D_2-Por*)] (1 mol%). [b] Yields of isolated products. [c] Determined by HPLC on a chiral stationary phase. [d] 2 mol% catalyst loading. [e] Yield determined by ^{19}F NMR spectroscopy. Product mixture contained **2a** (10%), azofluorobenzene (15%), fluoroaniline (10%), and unknown components (15%). Entry in bold marks optimized reaction conditions.







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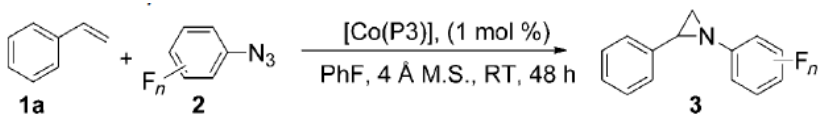
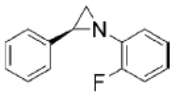
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

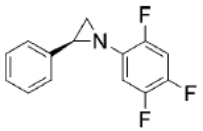
Asymmetric Olefin Aziridination



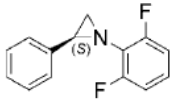
1a + 2 → 3



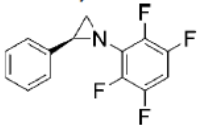
entry 1:[e] **3aa**;
52% yield, 75% *ee*



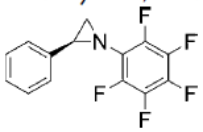
entry 2: **3ac**;
64% yield, 80% *ee*



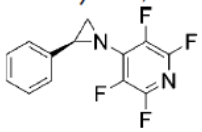
entry 3:[d] **3ad**;
80% yield, 96% *ee*



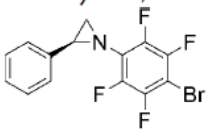
entry 4: **3ae**;
95% yield, 89% *ee*



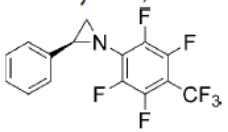
entry 5: **3af**;
99% yield, 92% *ee*



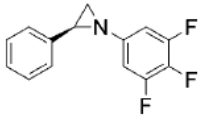
entry 6: **3ag**;
96% yield, 90% *ee*



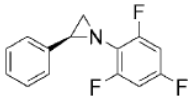
entry 7: **3ah**;
95% yield, 80% *ee*



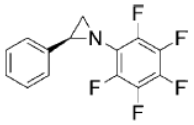
entry 8: **3ai**;
99% yield, 68% *ee*



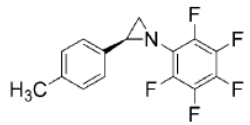
entry 9: **3aj**;
no reaction



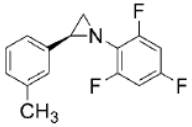
entry 1: **3ab**;
99% yield, 94% *ee*



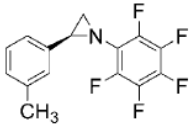
entry 2: **3af**;
99% yield, 92% *ee*



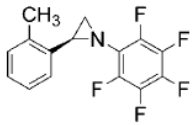
entry 3: **3bf**;
99% yield, 96% *ee*



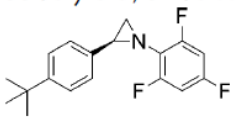
entry 4: **3cb**;
99% yield, 92% *ee*



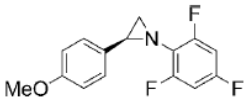
entry 5: **3cf**;
95% yield, 94% *ee*



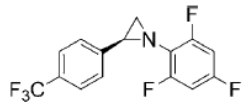
entry 6: **3df**;
99% yield, 87% *ee*



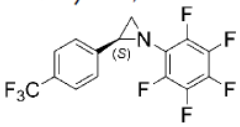
entry 7: **3eb**;
85% yield, 92% *ee*



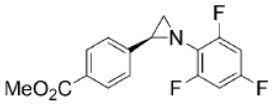
entry 8: **3fb**;
99% yield, 87% *ee*



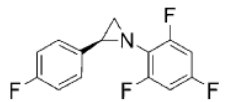
entry 9: **3gb**;
77% yield, 92% *ee*



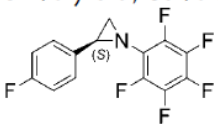
entry 10:[d] **3gf**;
91% yield, 85% *ee*



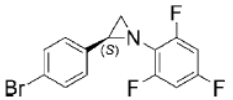
entry 11: **3hb**;
80% yield, 92% *ee*



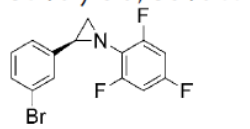
entry 12: **3ib**;
93% yield, 95% *ee*



entry 13:[d] **3if**;
90% yield, 91% *ee*



entry 14:[d] **3jb**;
81% yield, 92% *ee*



entry 15: **3kb**;
82% yield, 93% *ee*

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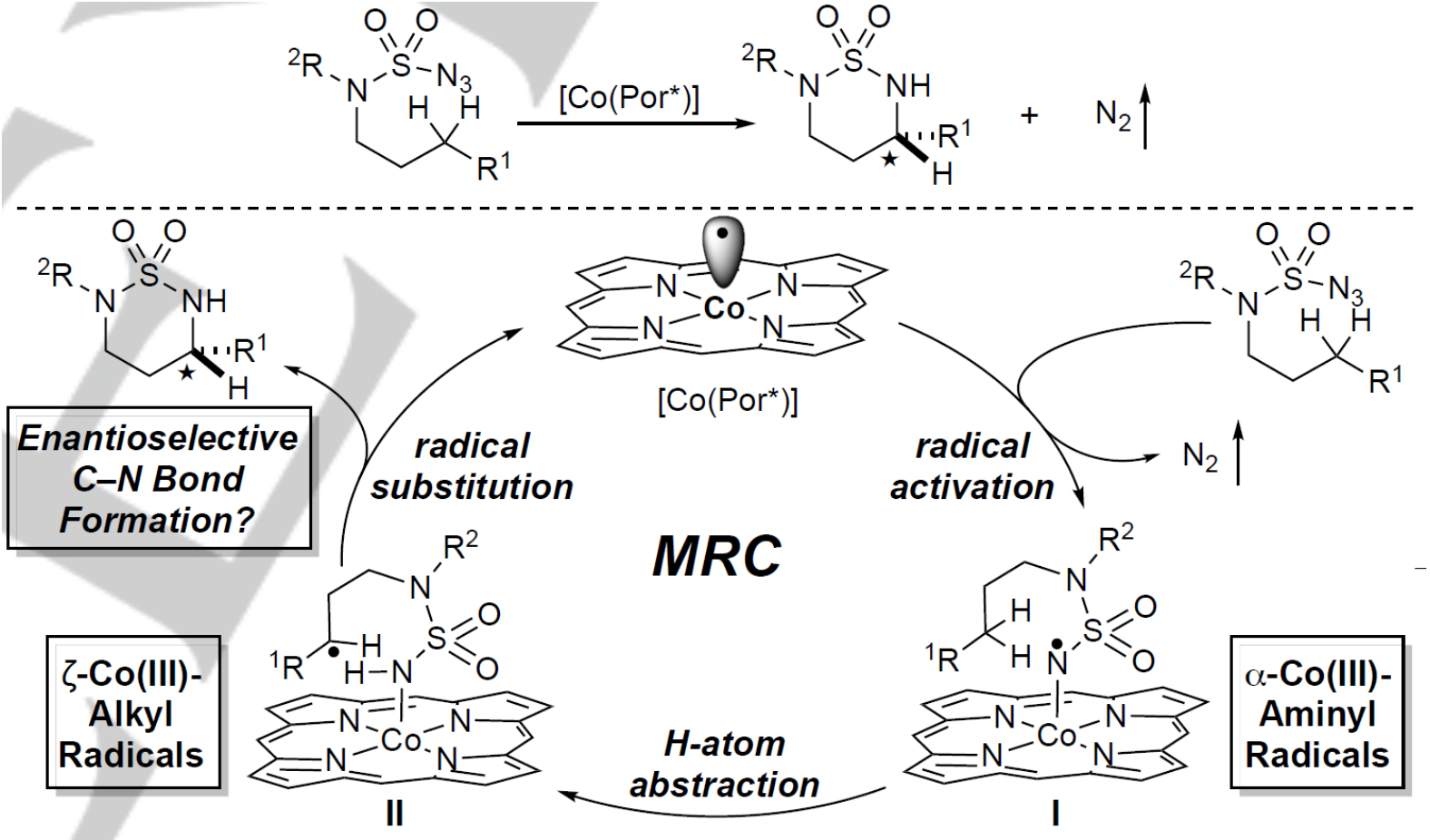
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

- **Asymmetric C−H Functionalization (Co, Ru, Fe)**



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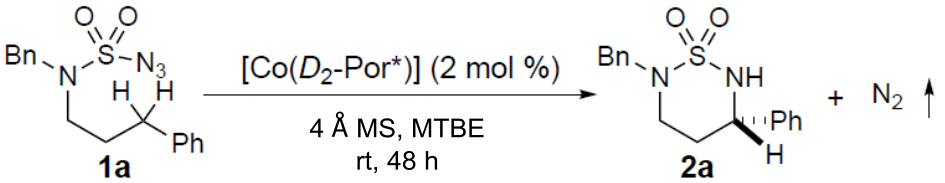
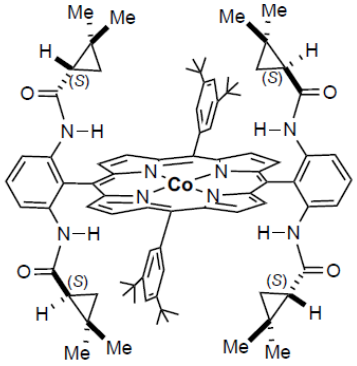
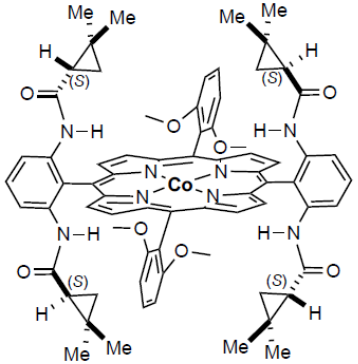
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)

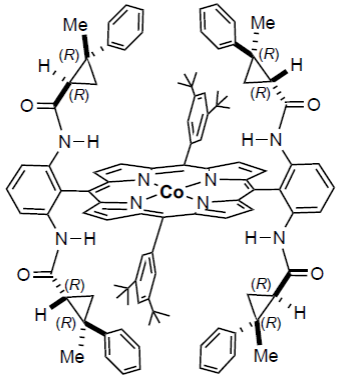




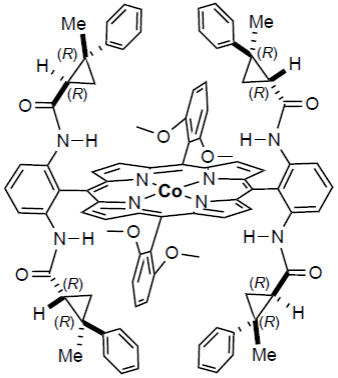
[Co(**P1**)]: 93% yield; −40% ee
(**P1** = 3,5-Di^{t}Bu-ChenPhyrin)



[Co(**P2**)]: 21% yield; −31% ee
(**P2** = 2,6-DiMeO-ChenPhyrin)



[Co(**P3**)]: 90% yield; 50% ee
(**P3** = 3,5-Di^{t}Bu-QingPhyrin)



[Co(**P4**)]: 93% yield; 90% ee
(**P4** = 2,6-DiMeO-QingPhyrin)

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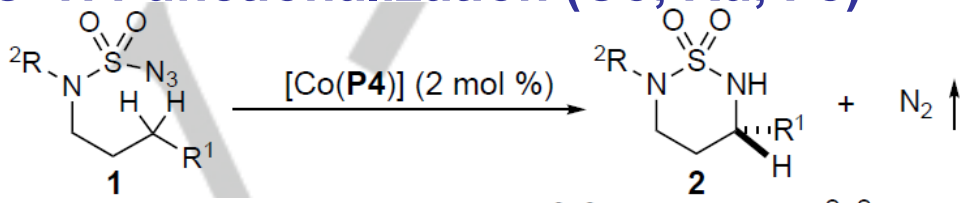
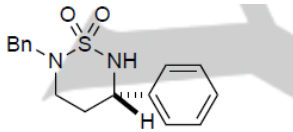
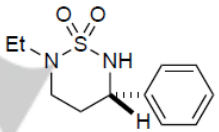
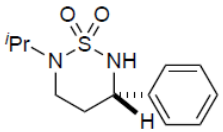
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

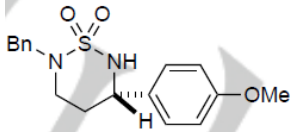
■ Asymmetric C−H Functionalization (Co, Ru, Fe)

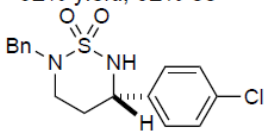


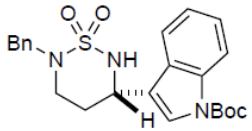

entry 1: (−)-**2a**
93% yield; 90% ee

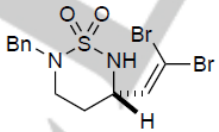

entry 2: (−)-**2b**
92% yield; 92% ee

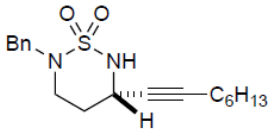

entry 3: (−)-**2c**
89% yield; 93% ee

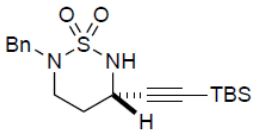

entry 4: (−)-**2d**
93% yield; 84% ee

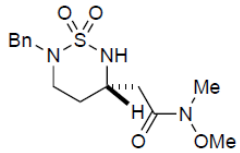

entry 5: (−)-**2e**
91% yield; 92% ee

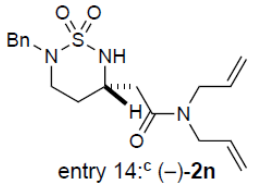

entry 6: (−)-**2f**
94% yield; 96% ee

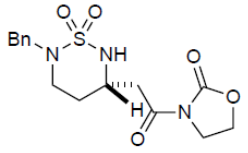

entry 7: (+)-**2g**
72% yield; 94% ee

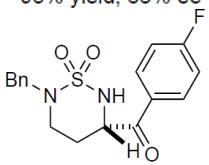

entry 8: (−)-**2h**
88% yield; 89% ee

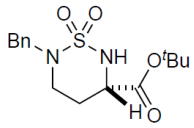

entry 9: (−)-**2i**
88% yield; 93% ee

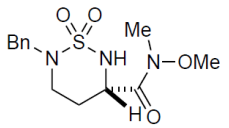

entry 13:[c] (+)-**2m**
93% yield; 88% ee

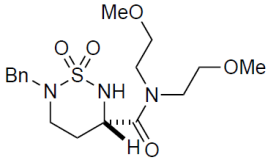

entry 14:[c] (−)-**2n**
91% yield; 89% ee

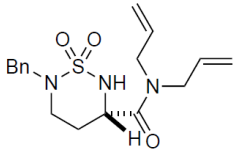

entry 15:[c] (−)-**2o**
93% yield; 86% ee

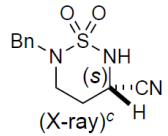

entry 4: (−)-**2s**
92% yield; 98% ee

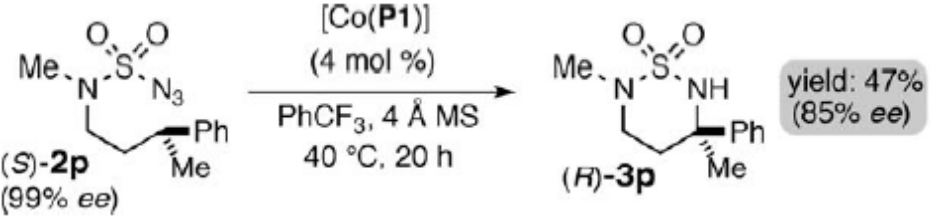

entry 5: (+)-**2t**
95% yield; 96% ee

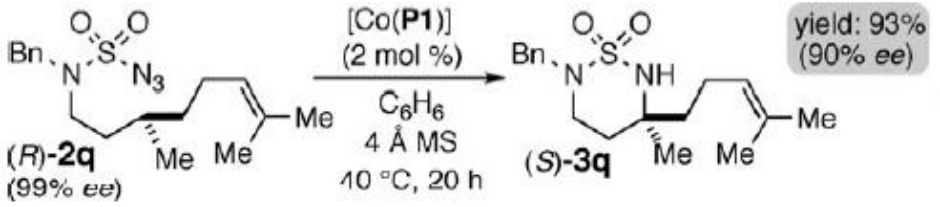

entry 6: (−)-**2u**
92% yield; 91% ee


entry 7: (−)-**2v**
93% yield; 90% ee


entry 8: (−)-**2w**
93% yield; 92% ee

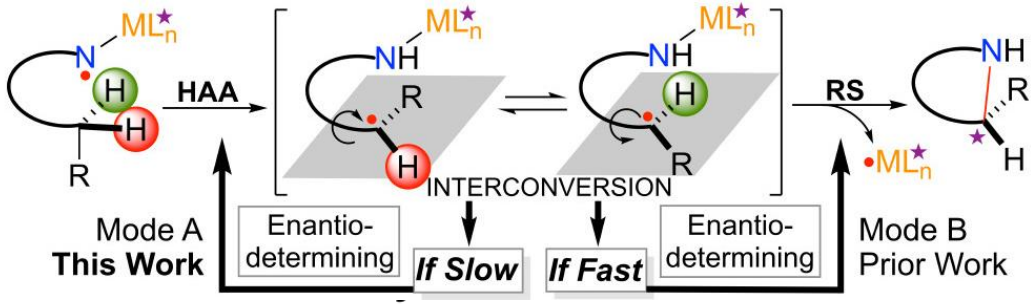

entry 9: (+)-**2x**
88% yield; 83% ee

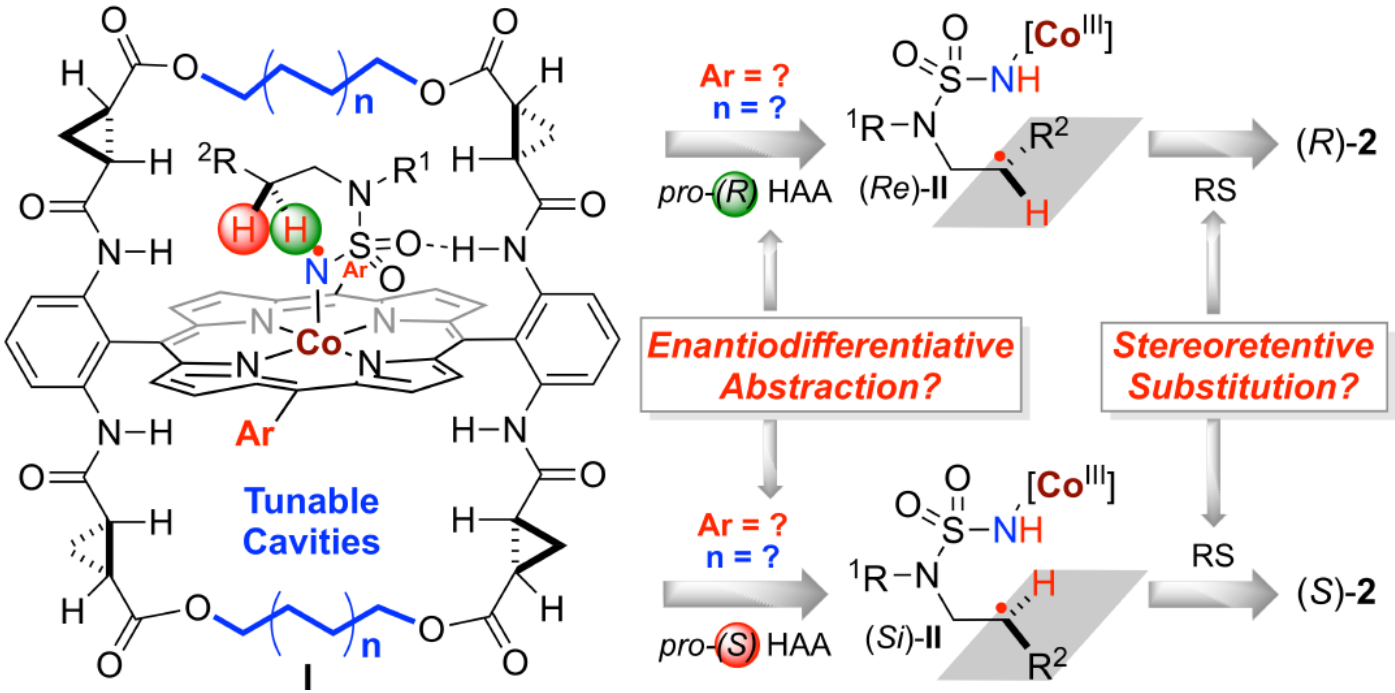




Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)





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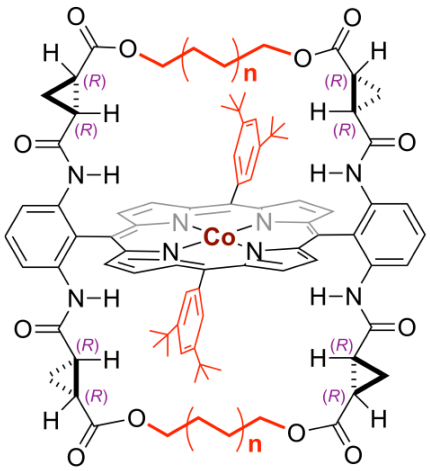
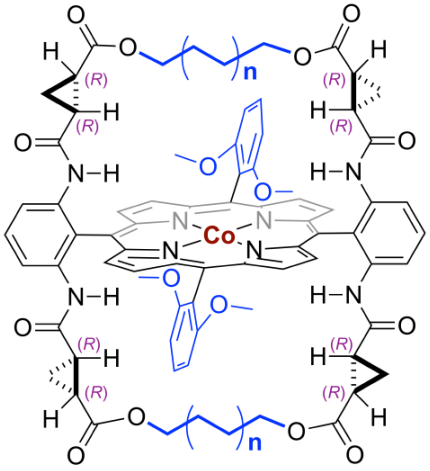
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)



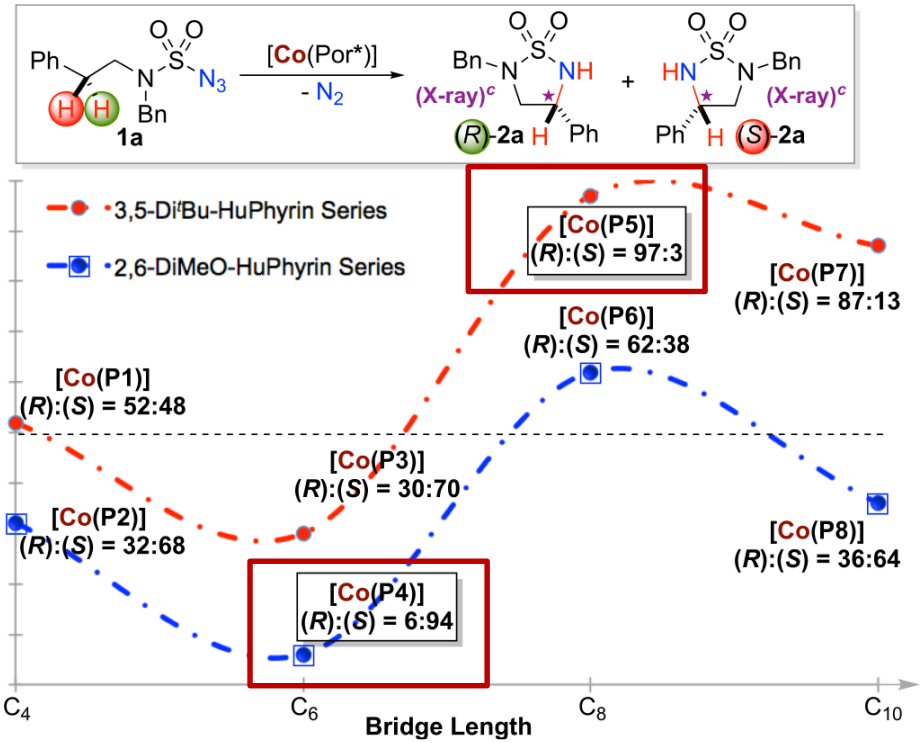


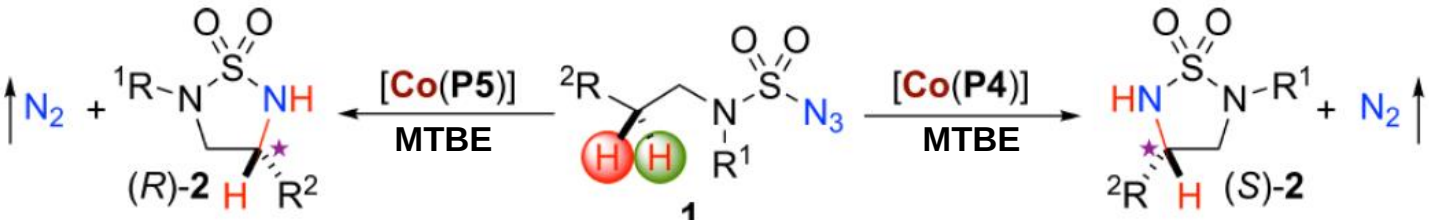
[Co(**P1**)] (**P1**: 3,5-Di^{t}Bu-Hu(C_4)Phyrin) [Co(**P2**)] (**P2**: 2,6-DiMeO-Hu(C_4)Phyrin)

[Co(**P3**)] (**P3**: 3,5-Di^{t}Bu-Hu(C_6)Phyrin) [Co(**P4**)] (**P4**: 2,6-DiMeO-Hu(C_6)Phyrin)

[Co(**P5**)] (**P5**: 3,5-Di^{t}Bu-Hu(C_8)Phyrin) [Co(**P6**)] (**P6**: 2,6-DiMeO-Hu(C_8)Phyrin)

[Co(**P7**)] (**P7**: 3,5-Di^{t}Bu-Hu(C_{10})Phyrin) [Co(**P8**)] (**P8**: 2,6-DiMeO-Hu(C_{10})Phyrin)





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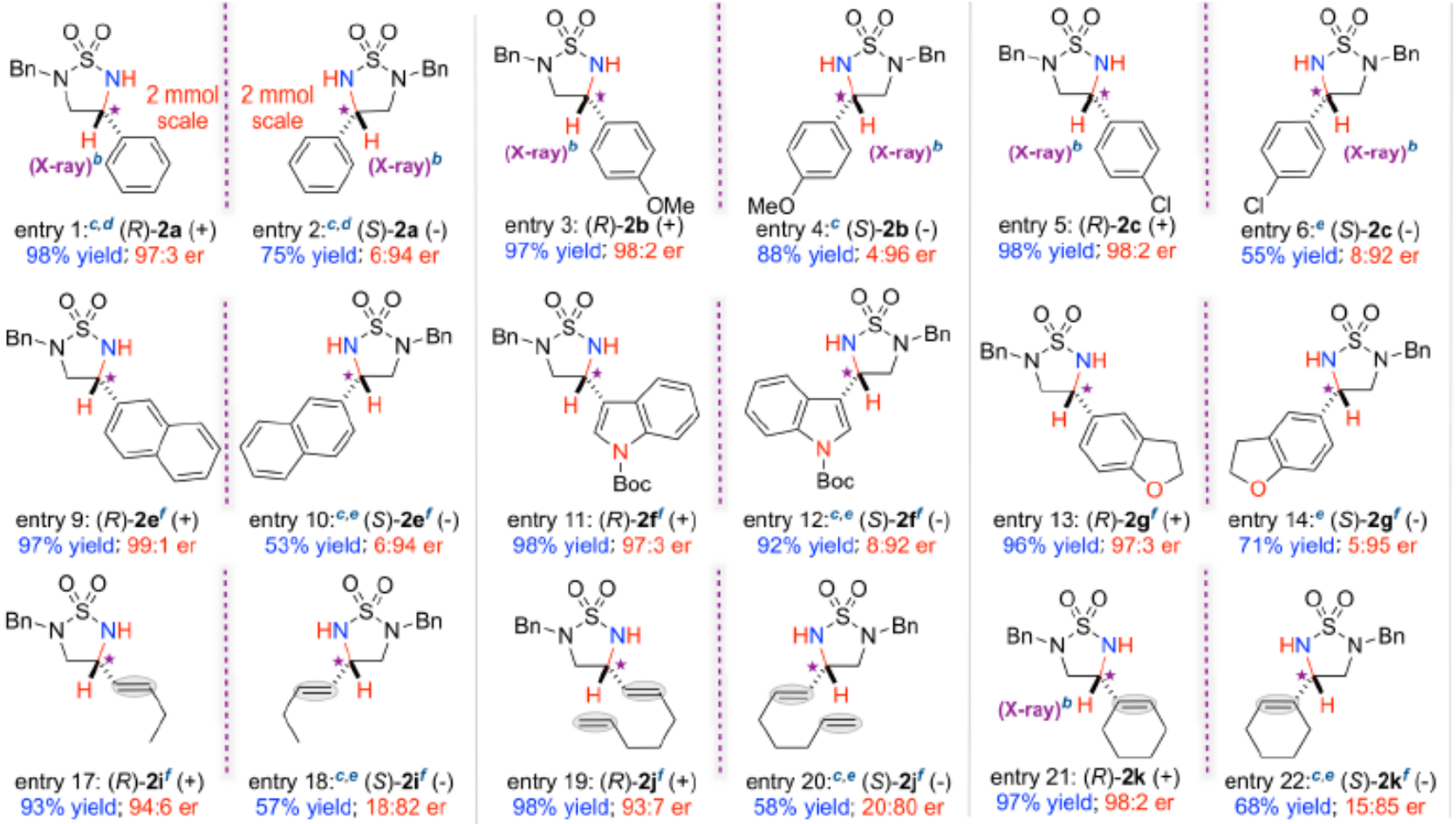

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Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

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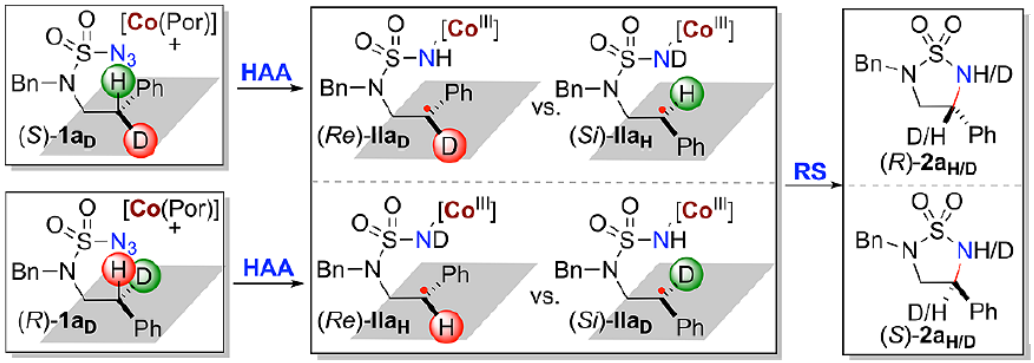
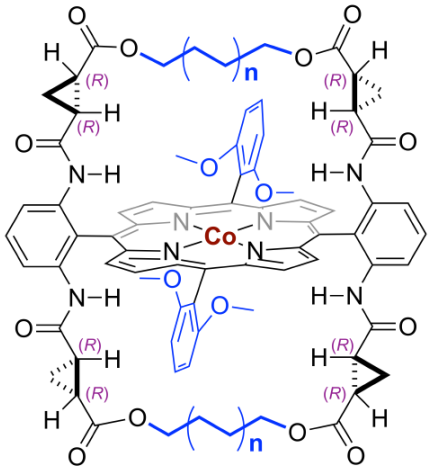
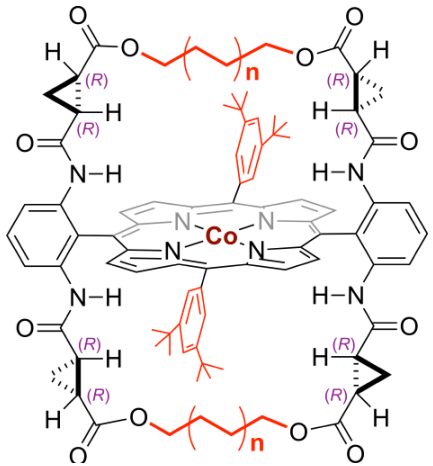


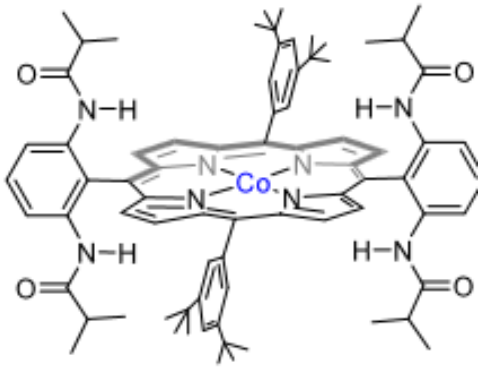
entry	azide	catalyst	KIE[b]	*Re*:*Si* of IIa[c]	ee%[cal,d]	ee%[exp,e]
1	(*S*)-1a$_D$	[Co(**P9**)]	23.0	96:4	92 (*R*)	4 (*R*)
2[f]	(*S*)-1a$_D$	[Co(**P4**)]	2.0	67:33	34 (*R*)	−4 (*S*)
3	(*S*)-1a$_D$	[Co(**P5**)]	96.0	99:1	98 (*R*)	94 (*R*)
4	(*R*)-1a$_D$	[Co(**P9**)]	23.0	4:96	−92 (*S*)	−4 (*S*)
5[f]	(*R*)-1a$_D$	[Co(**P4**)]	61.0	2:98	−96 (*S*)	−94 (*S*)
6	(*R*)-1a$_D$	[Co(**P5**)]	0.8	57:43	14 (*R*)	32 (*R*)



[Co(**P4**)] (**P4**: 2,6-DiMeO-Hu(C_6)Phyrin)



[Co(**P5**)] (**P5**: 3,5-Di^{t}Bu-Hu(C_8)Phyrin)



[Co(**P9**)] (**P9**: 3,5-Di^{t}Bu-IbuPhyrin)

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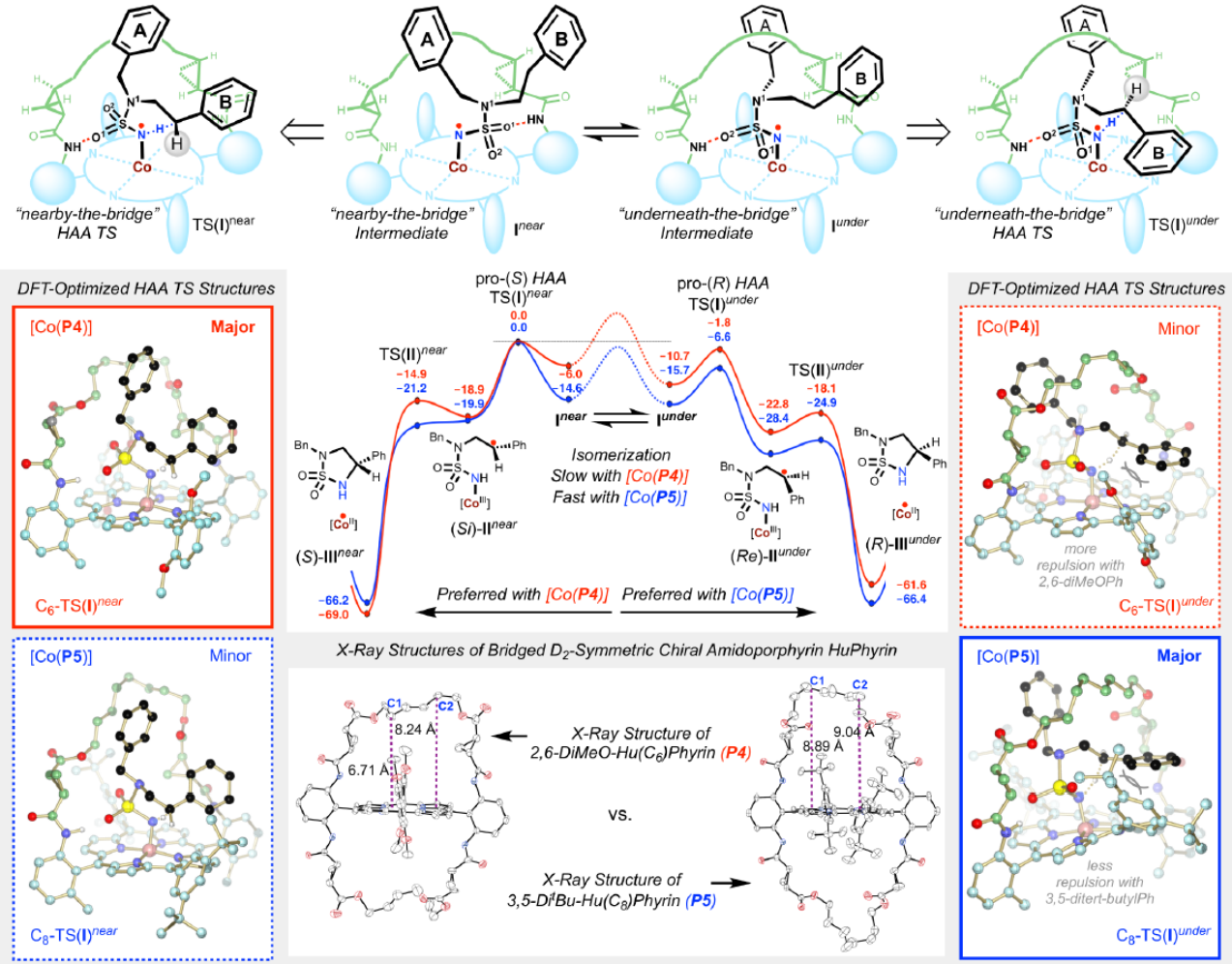
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)



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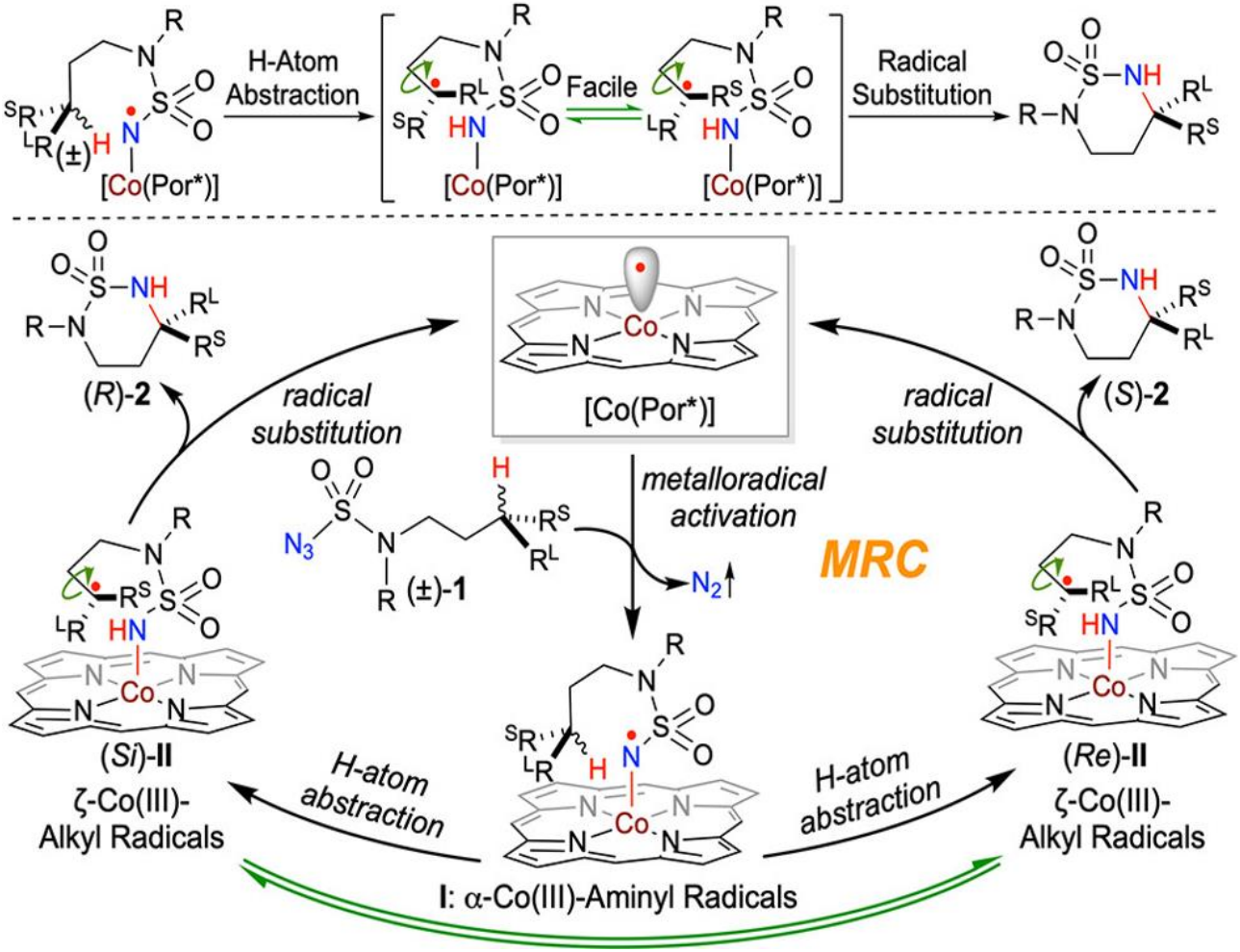
■ Asymmetric C−H Functionalization (Co, Ru, Fe)



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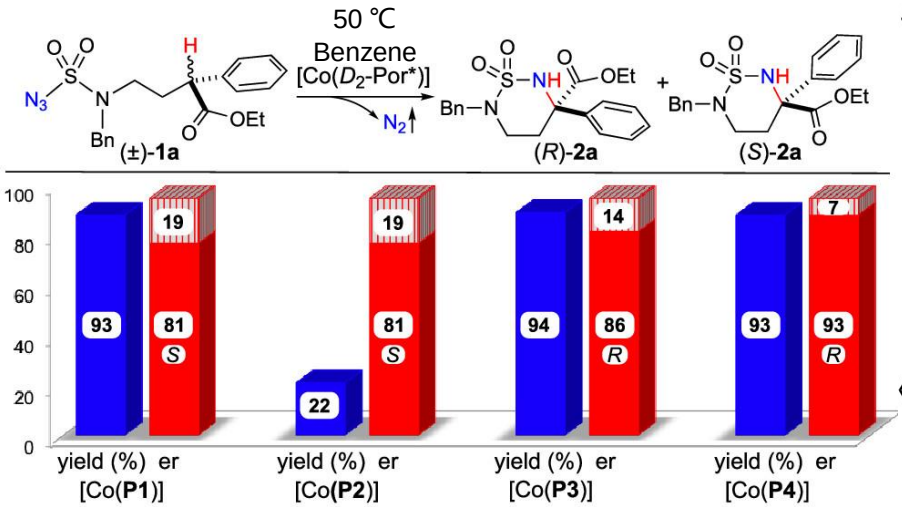
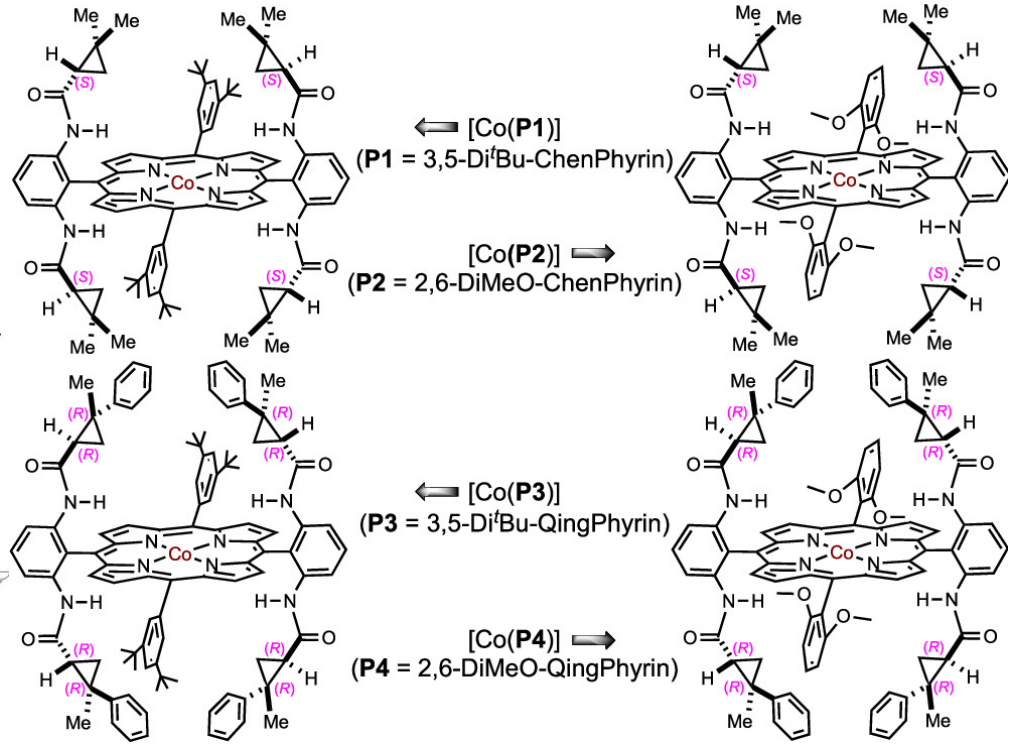
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)





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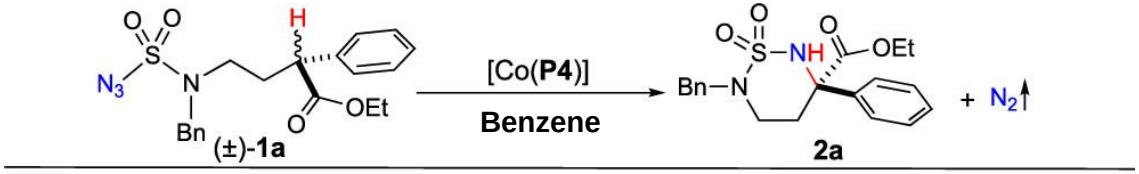
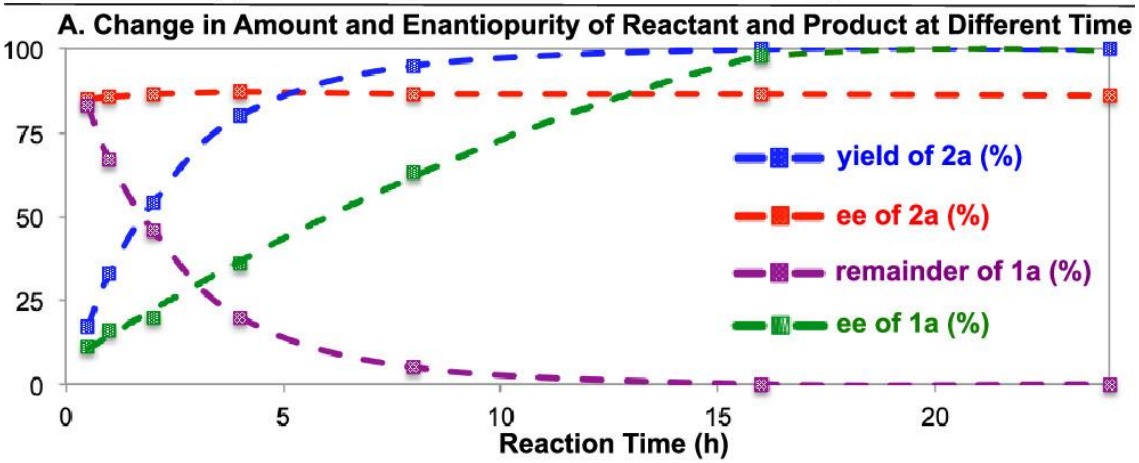
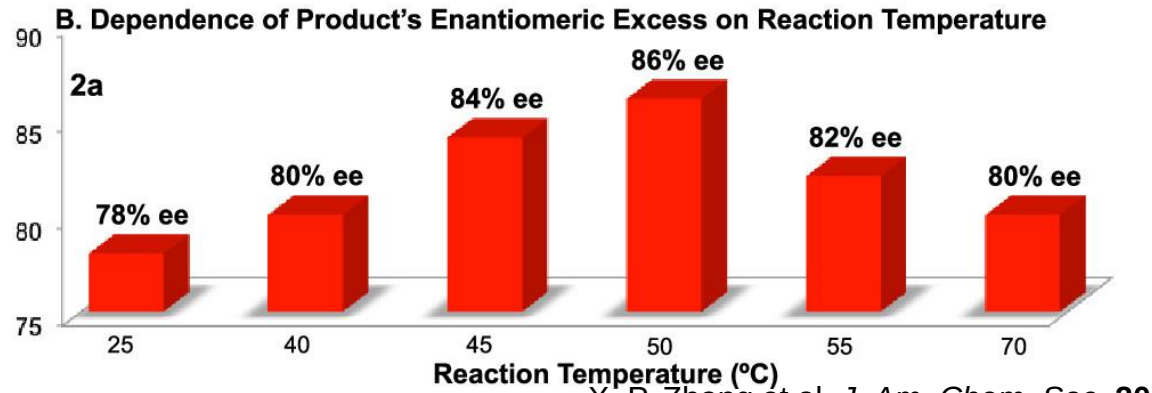
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

- **Asymmetric C−H Functionalization (Co, Ru, Fe)**







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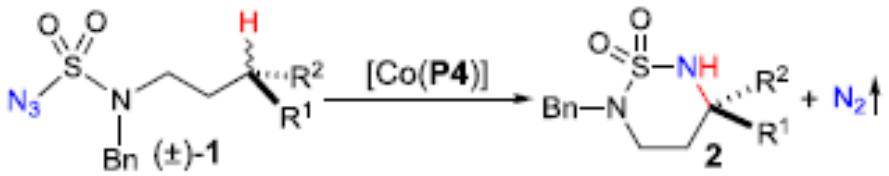
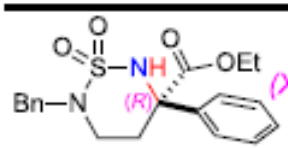
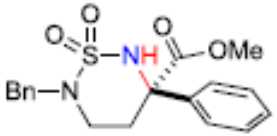
■ Asymmetric C−H Functionalization (Co, Ru, Fe)

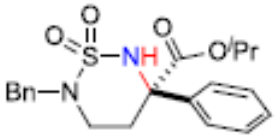




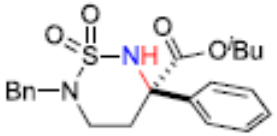
entry 1: (+)-**2a**
93% yield; 93:7 er



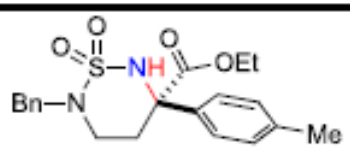
entry 2: (+)-**2b**
91% yield; 91:9 er



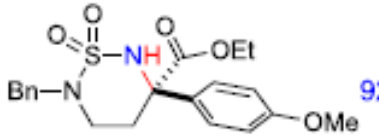
entry 3: (+)-**2c**
90% yield; 90:10 er



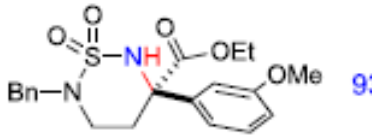
entry 4: (+)-**2d**
92% yield; 89:11 er



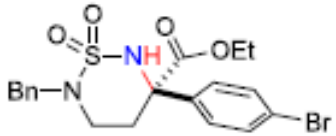
entry 5: (+)-**2e**
95% yield; 92:8 er



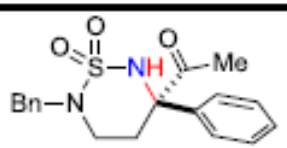
entry 6: (+)-**2f**
92% yield; 92:8 er



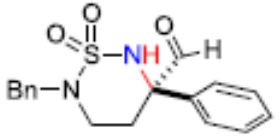
entry 7: (+)-**2g**
93% yield; 90:10 er



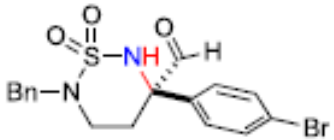
entry 8: (−)-**2h**
95% yield; 92:8 er



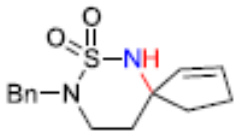
entry 13: (+)-**2m**
94% yield; 83:17 er



entry 14: (+)-**2n**
89% yield; 88:12 er



entry 15: (+)-**2o**
88% yield; 86:14 er



entry 16: (−)-**2p**
93% yield; 74:26 er

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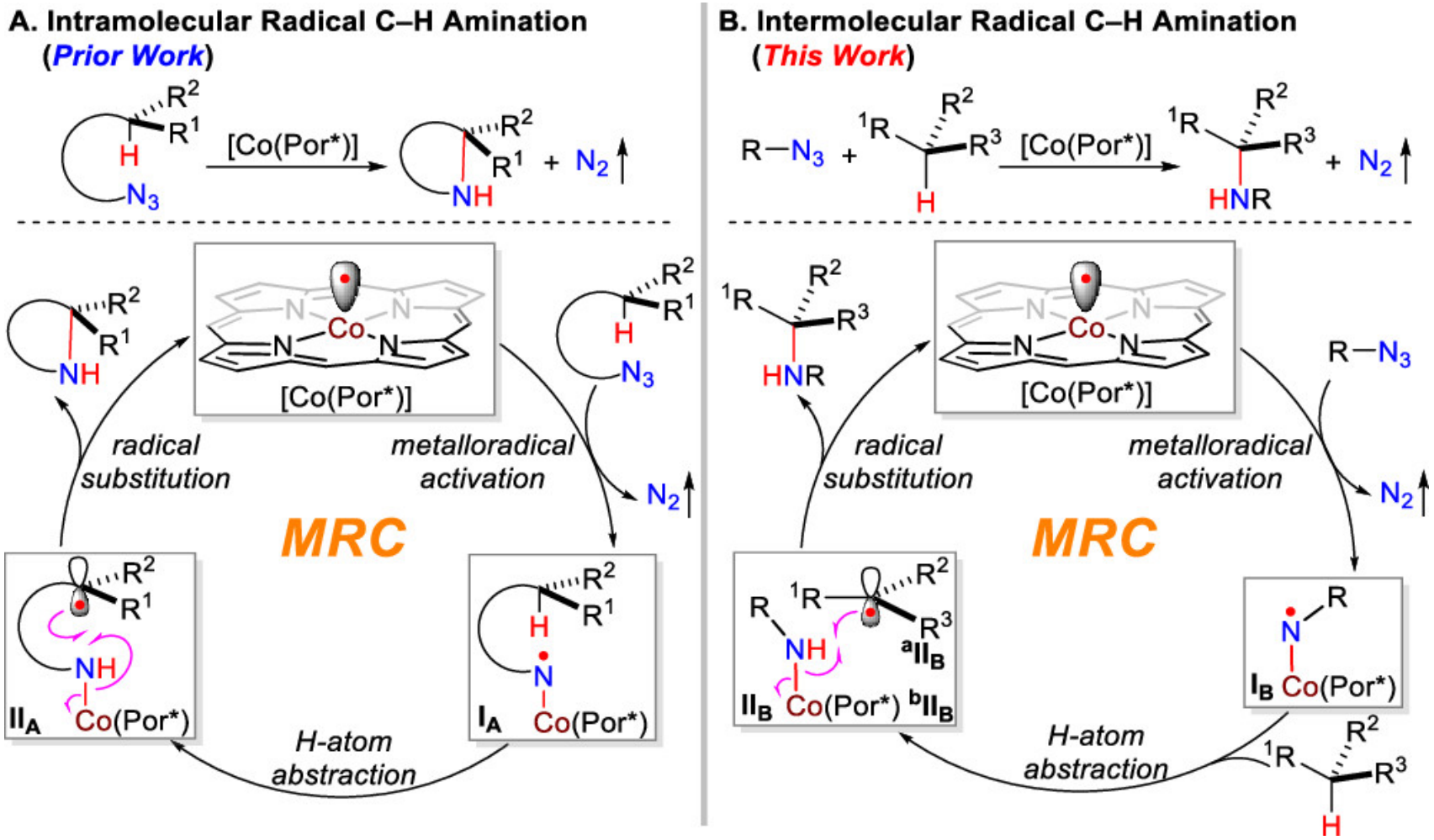
■ Asymmetric C−H Functionalization (Co, Ru, Fe)



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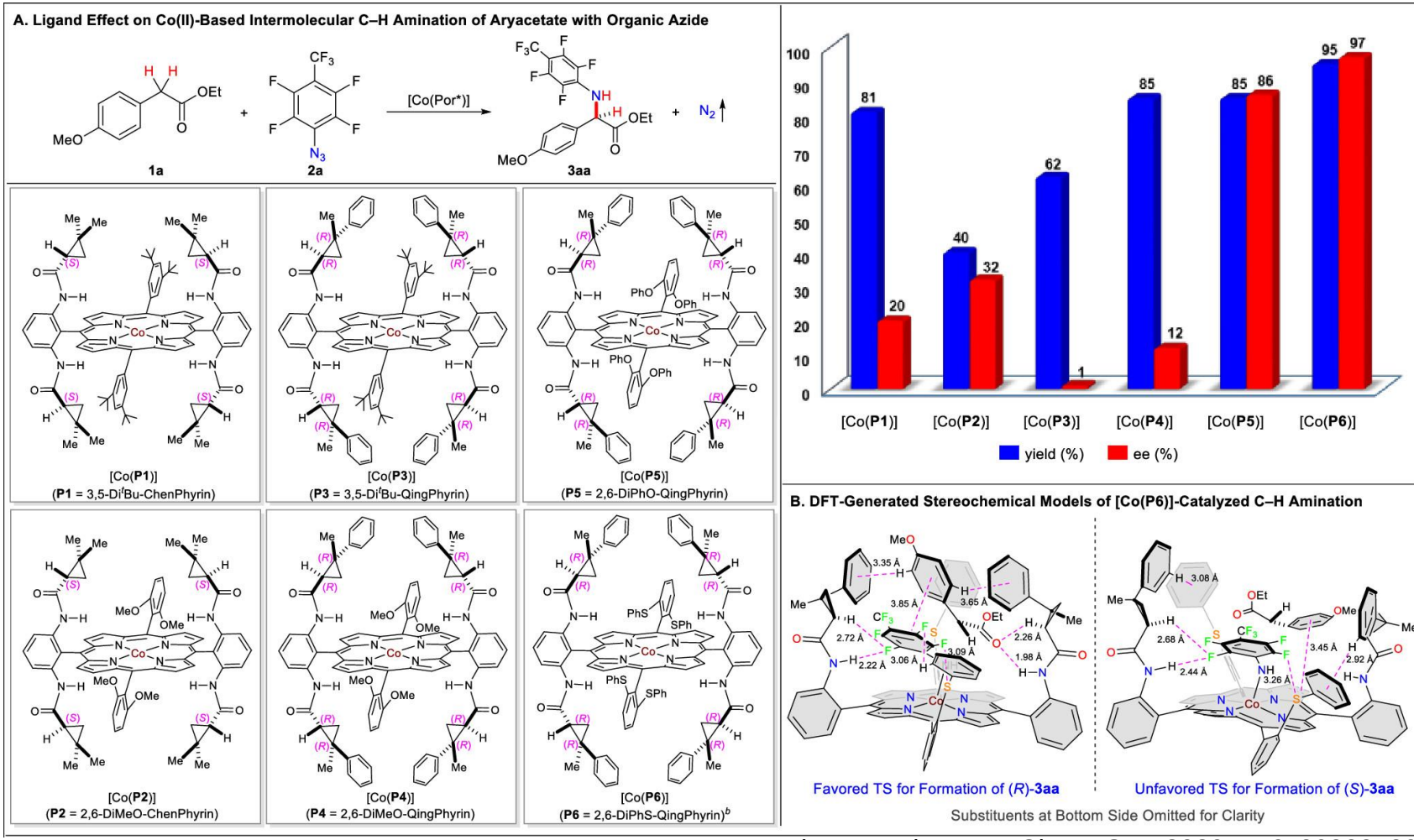
■ Asymmetric C−H Functionalization (Co, Ru, Fe)



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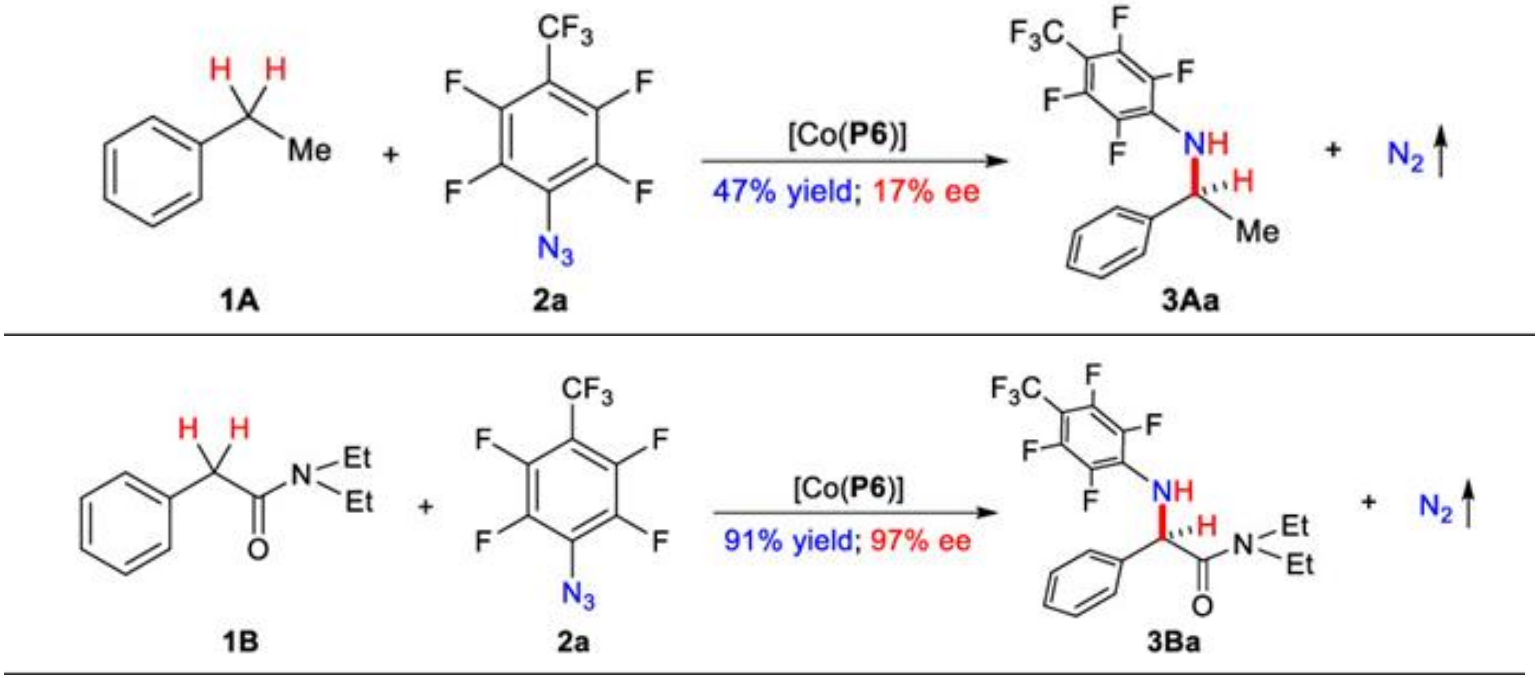

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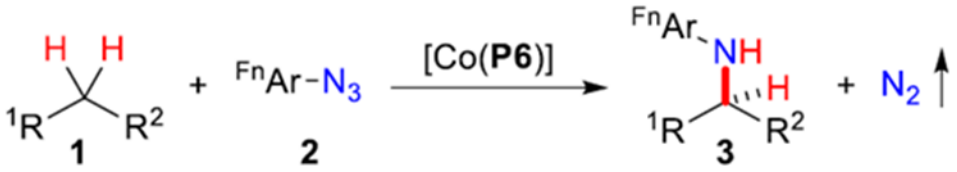
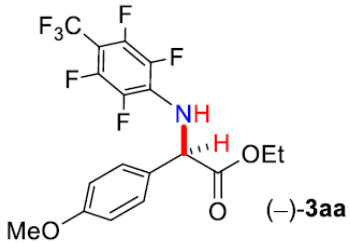
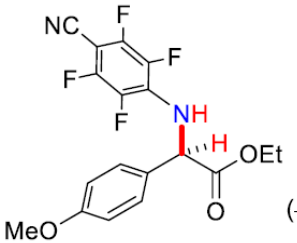


A. Enantioselective C–H Amination of Arylacetate Ester 1a with Various Fluoroaryl Azides



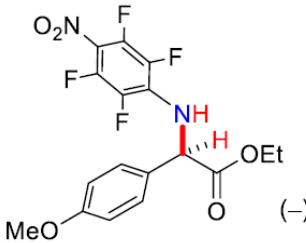
(–)-**3aa**

entry 1: 95% yield; 97% ee



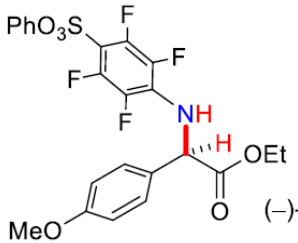
(–)-**3ab**

entry 2: 53% yield; 90% ee



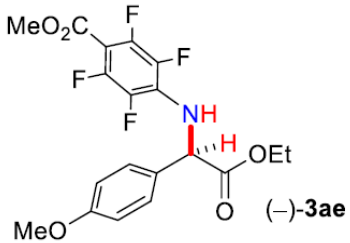
(–)-**3ac**

entry 3: 60% yield; 96% ee



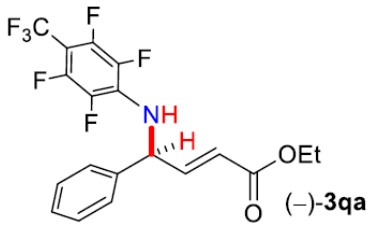
(–)-**3ad**

entry 4: 60% yield; 87% ee



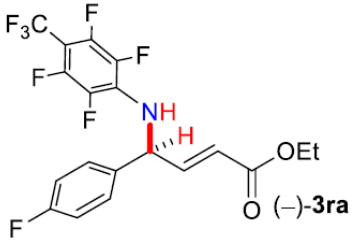
(–)-**3ae**

entry 5: 87% yield; 96% ee



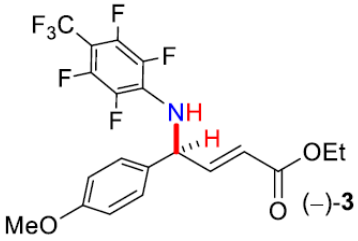
(–)-**3qa**

entry 26: 64% yield; 94% ee



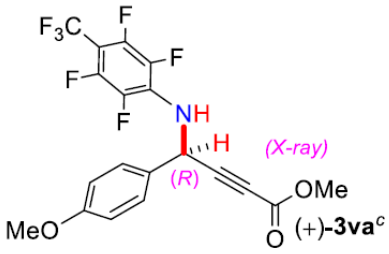
(–)-**3ra**

entry 27: 53% yield; 97% ee



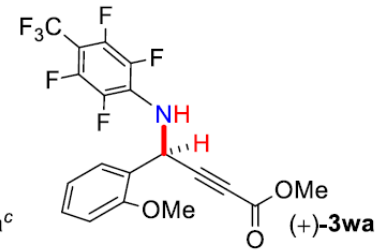
(–)-**3**

entry 28: 70% yield; 95% ee



(+)-**3va**[c]

entry 31: 83% yield; 93% ee



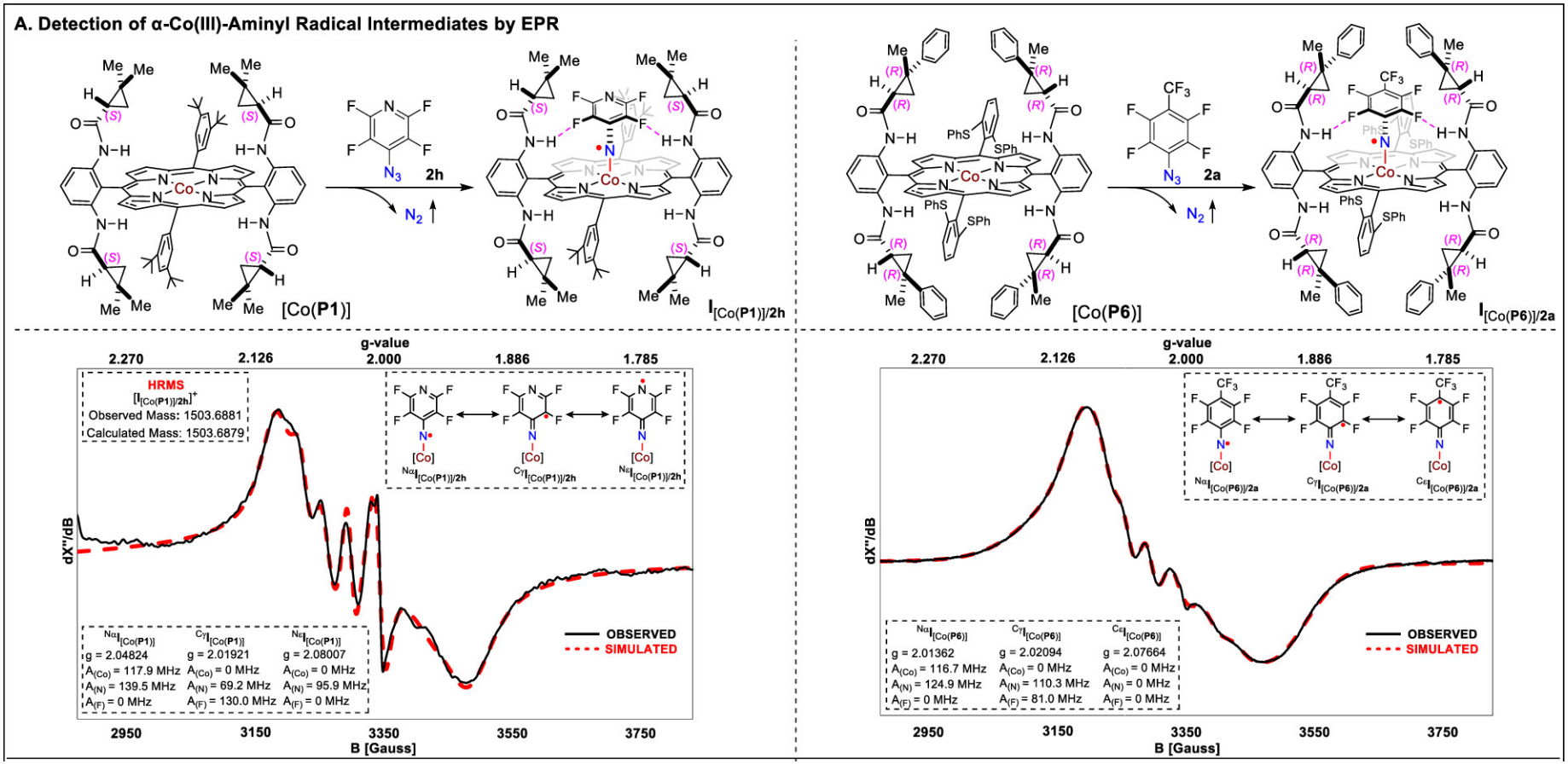
(+)-**3wa**

entry 32: 89% yield; 90% ee

X. P. Zhang et al. *J. Am. Chem. Soc.* **2020**, *142*, 20828–20836.

Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)



X. P. Zhang et al. *J. Am. Chem. Soc.* **2020**, *142*, 20828–20836.

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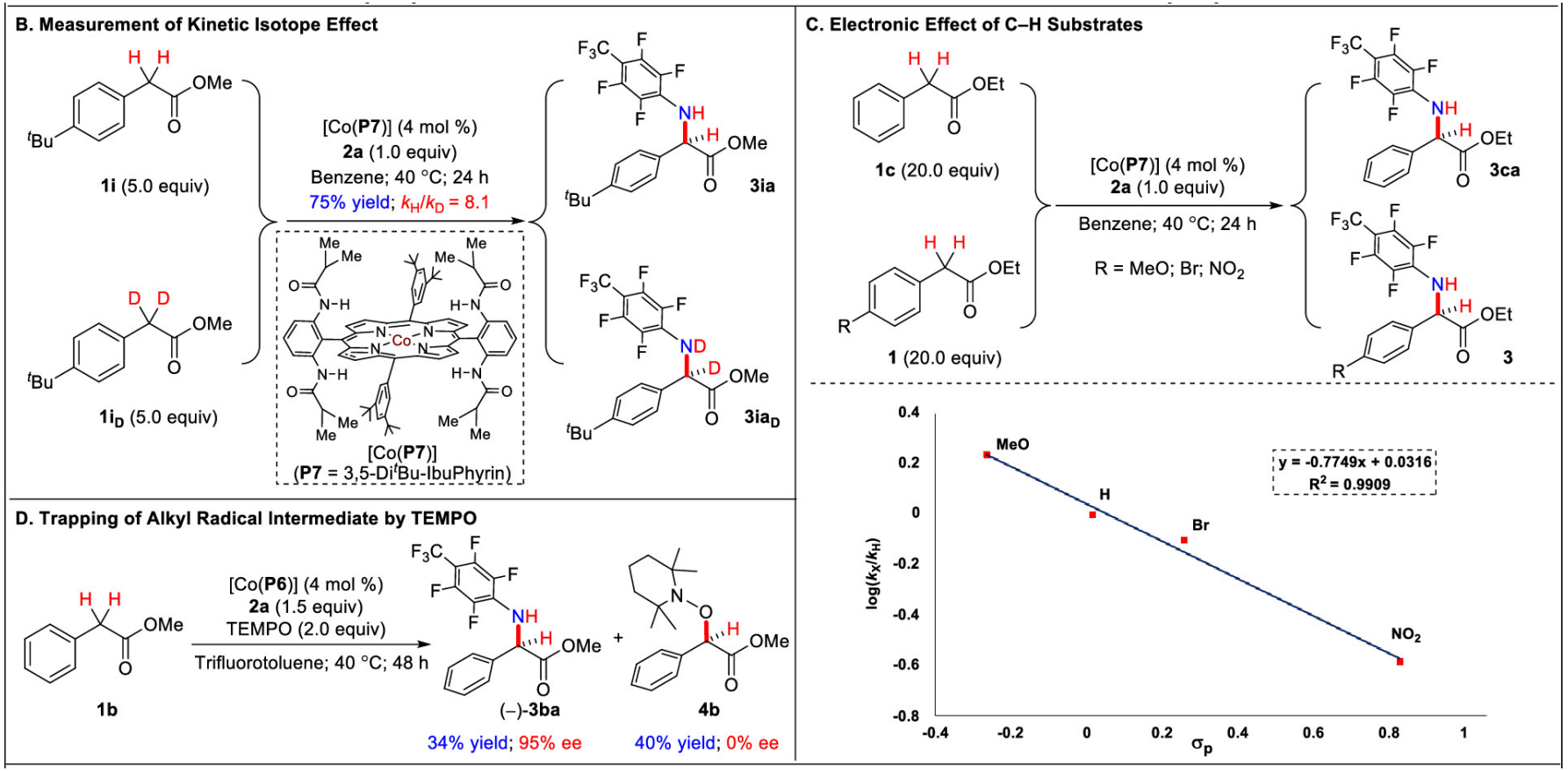

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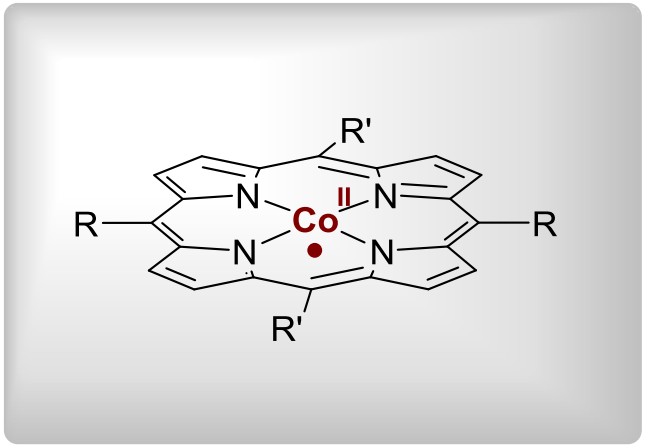
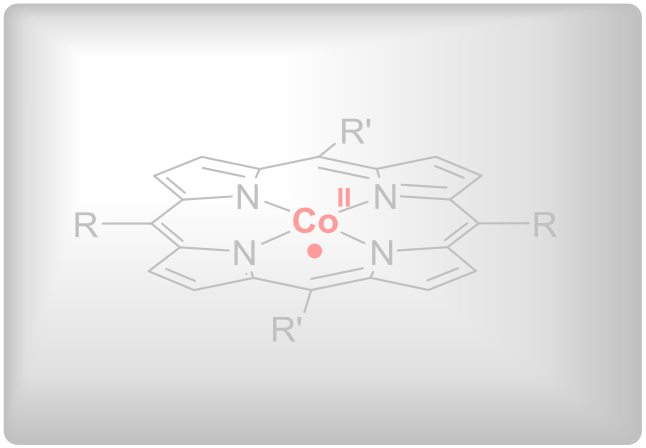
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

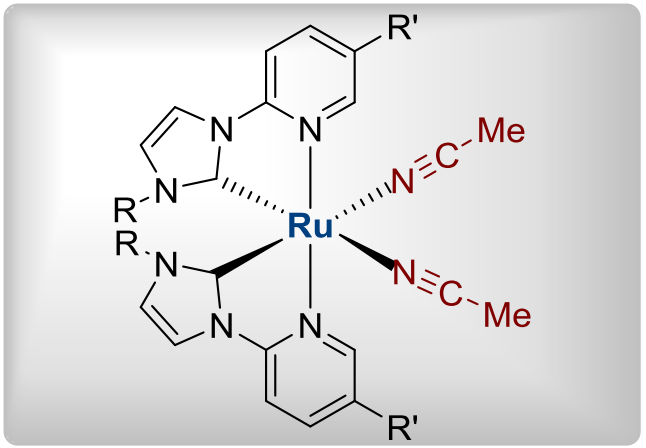


d^7 metal

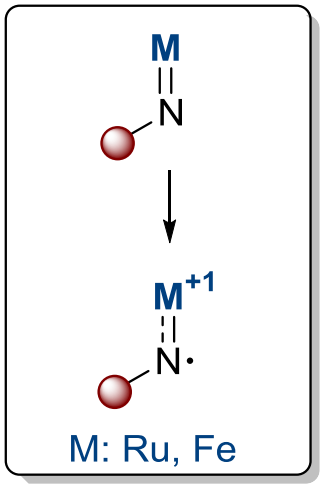
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

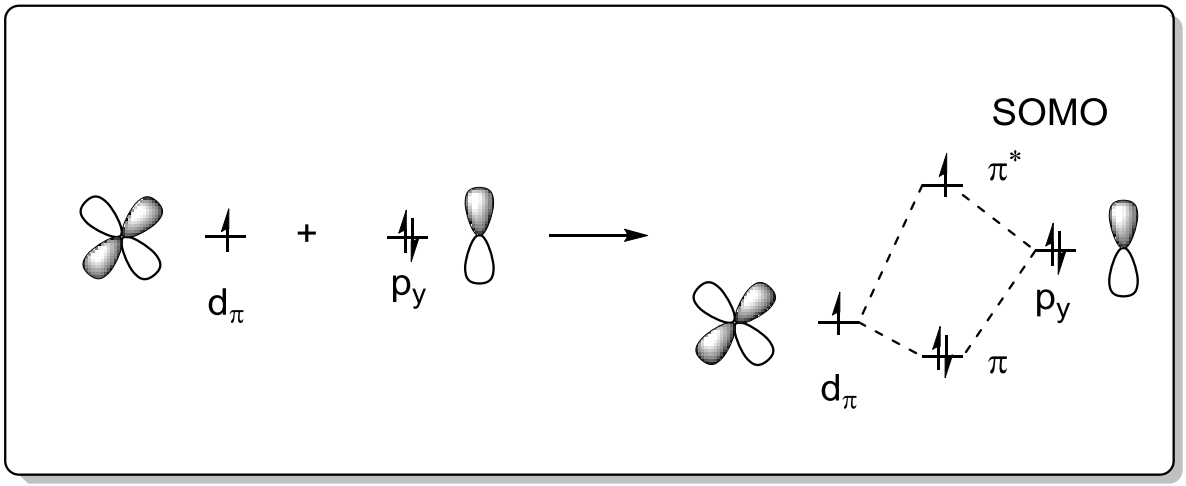


d^7 metal



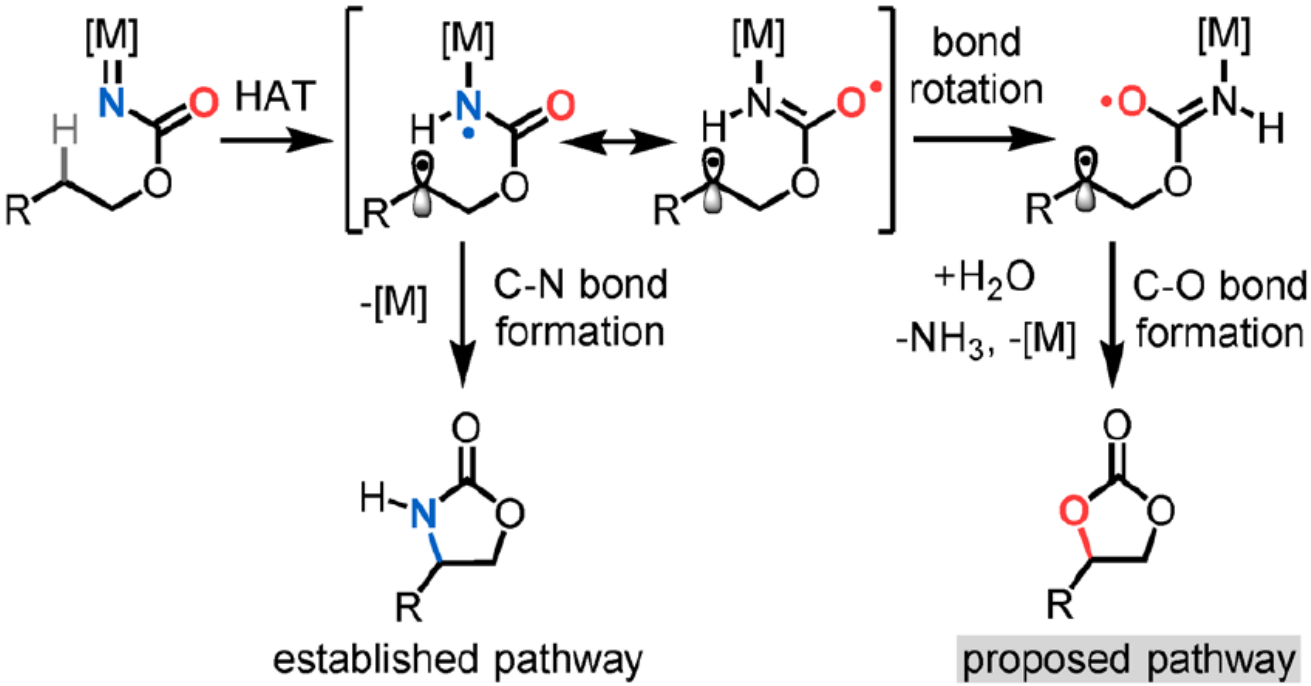
triplet state 'metal nitrene'





Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

- **Asymmetric C−H Functionalization (Co, Ru, Fe)**



E. Meggers et al. *Angew. Chem. Int. Ed.* **2018**, *59*, 21706–21710.

Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

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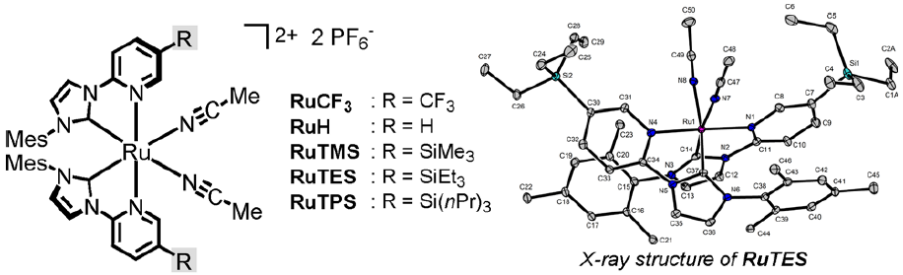
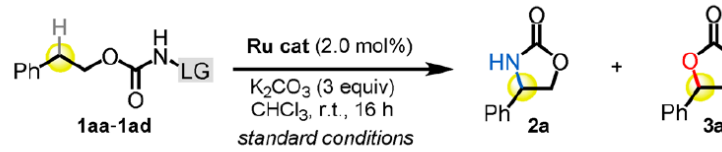
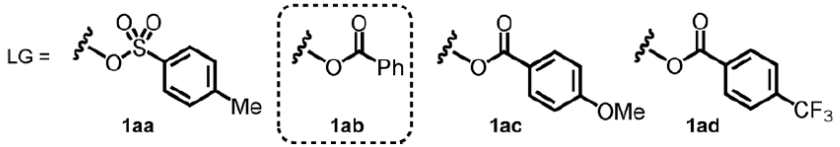


*X-ray structure of **RuTES***





Entry	Catalyst	Substrate	Conditions[b]	Conv. [%][c]	Yield [%][d] 2a	3a
1	**$RuCF_2$**	**1aa**	standard	100	30	0
2	**$RuCF_3$**	**1ab**	standard	100	87	4
3	**RuH**	**1ab**	standard	100	68	18
4	**RuTMS**	**1ab**	standard	100	17	79
5	**RuTES**	**1ab**	standard	100	11	85
6	**RuTPS**	**1ab**	standard	88	12	73
7	**RuTES**	**1ac**	standard	100	10	76
8	**RuTES**	**1ad**	standard	84	14	35
9	**RuTES**	**1ab**	1.0 mol% cat.	79	12	62
10	**RuTES**	**1ab**	1% H_2O added	100	12	81
11	**RuTES**	**1ab**	4 Å MS added	100	14	76
12	**RuTES**	**1ab**	under air	58	10	47
13	**RuTES**	**1ab**	no base	12	5	2

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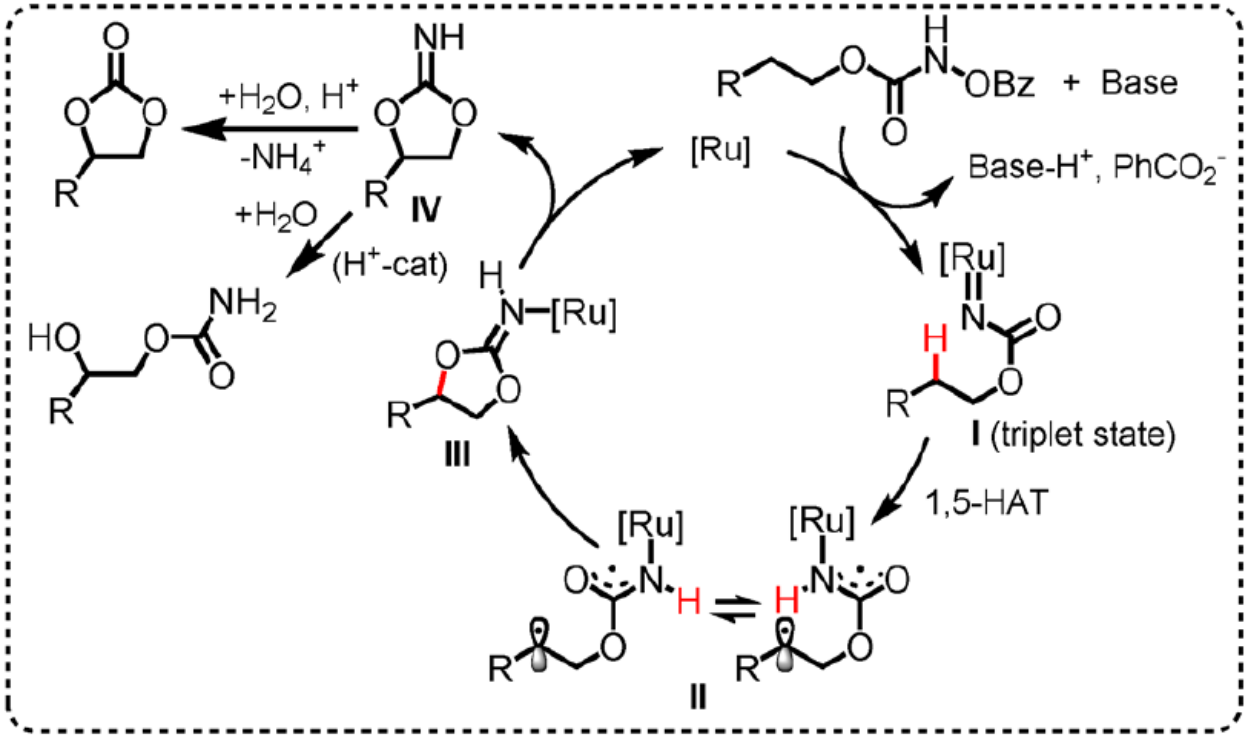
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

- **Asymmetric C−H Functionalization (Co, Ru, Fe)**



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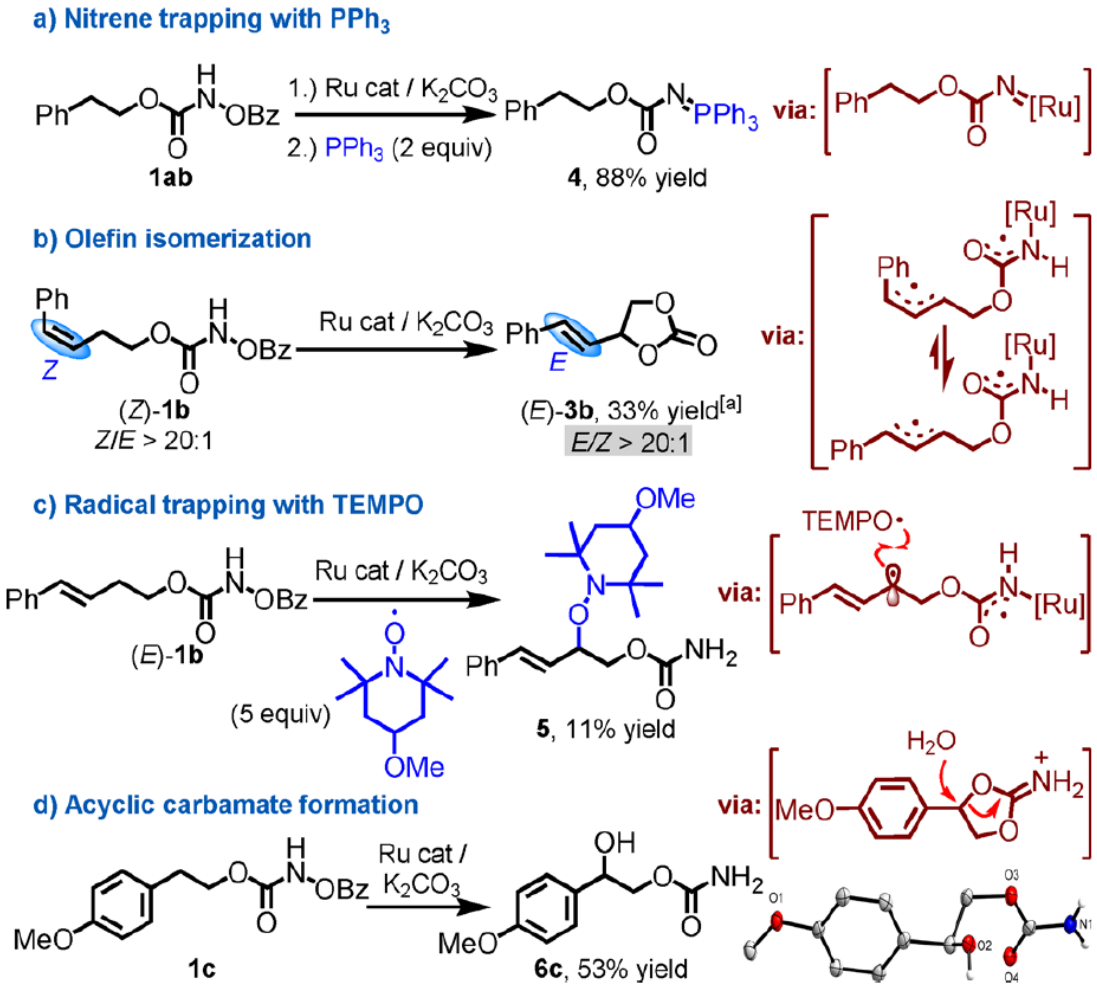
■ Asymmetric C−H Functionalization (Co, Ru, Fe)



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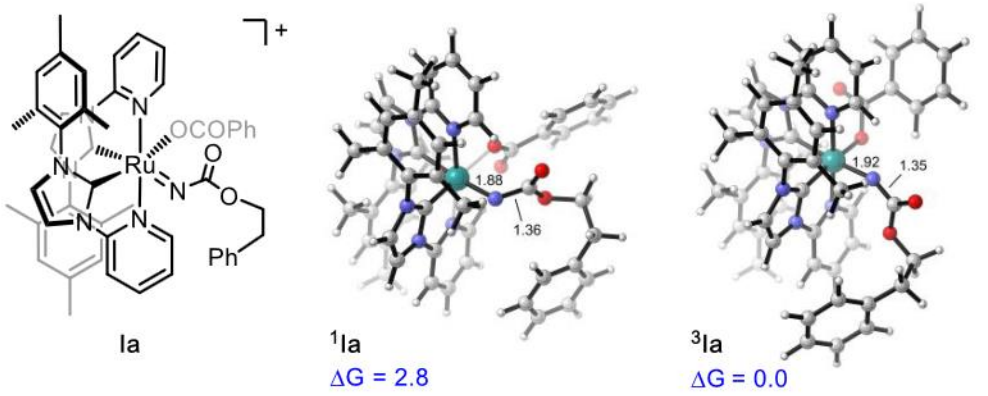
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)

a) Singlet versus triplet ruthenium nitrenoid intermediate



Ia

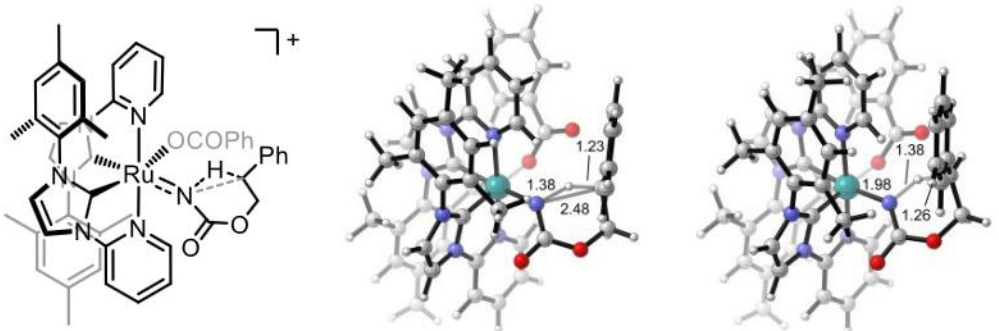
^{1}Ia

ΔG = 2.8

^{3}Ia

ΔG = 0.0

b) Singlet concerted C-H amination versus triplet 1,5-HAT



TS-CHA

^{1}TS-CHA

$\Delta G^{\ddagger}$ = 14.7

^{3}TS-CHA

$\Delta G^{\ddagger}$ = 12.7

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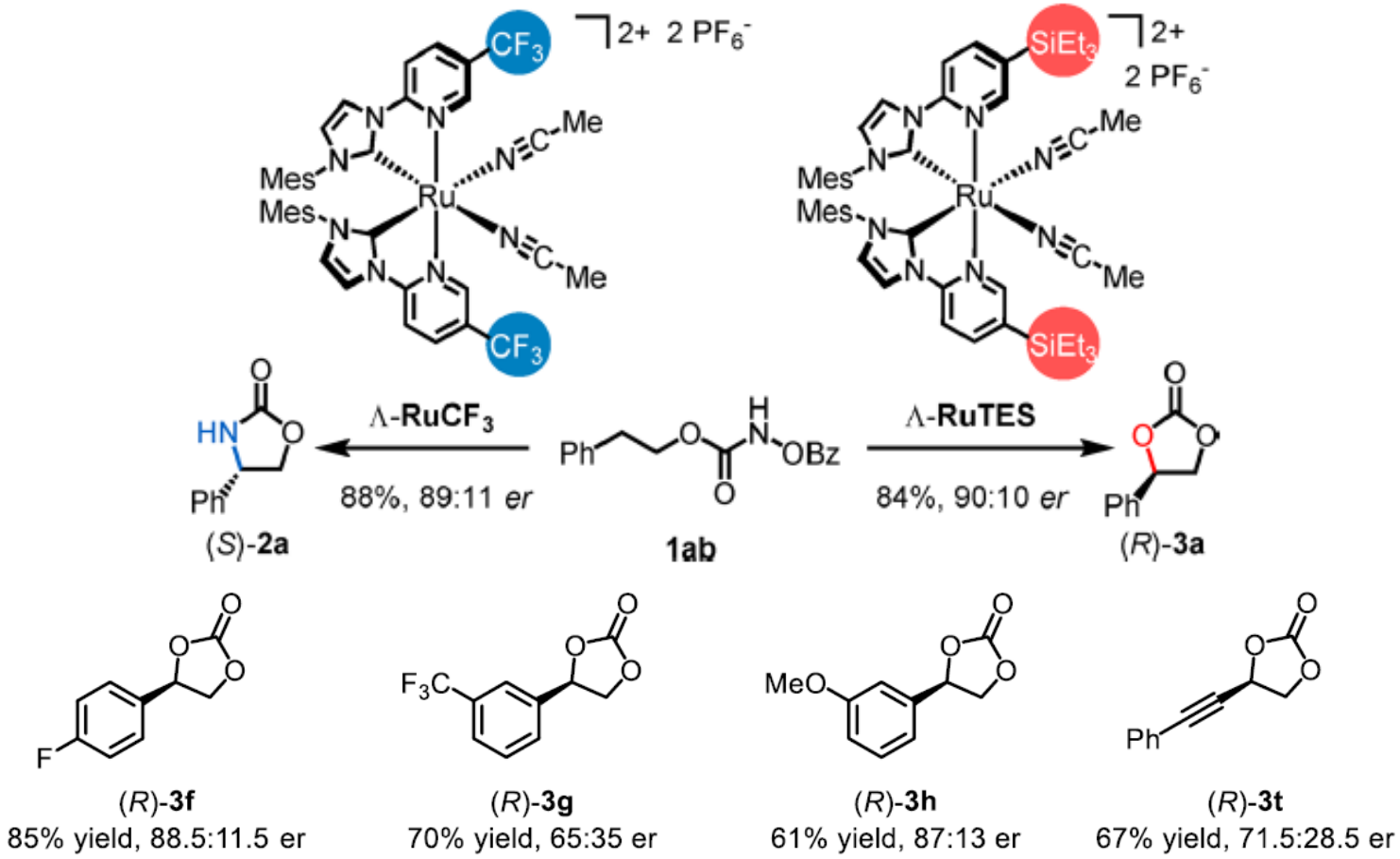
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C−H Functionalization (Co, Ru, Fe)



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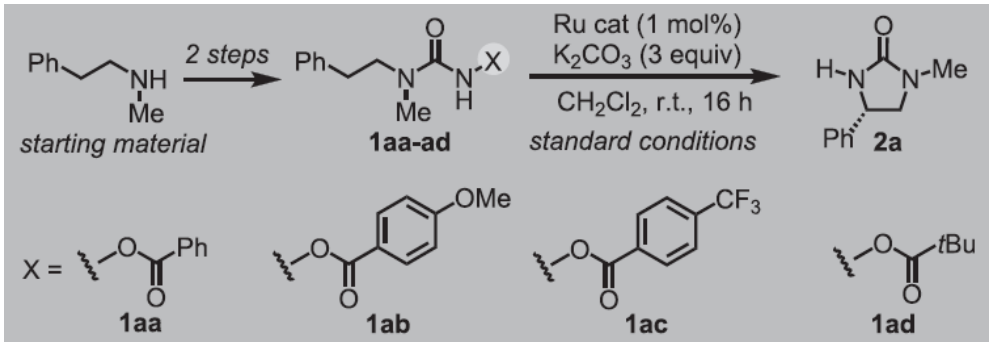
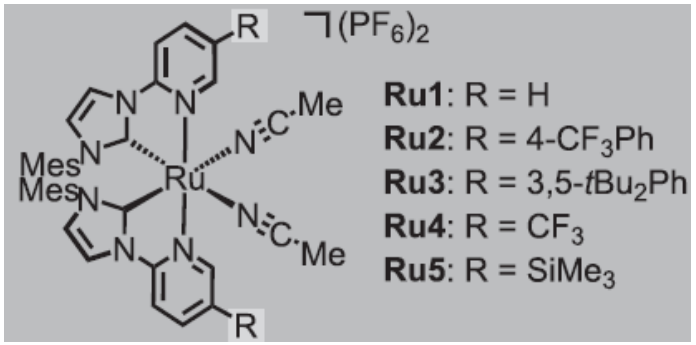
■ Asymmetric C−H Functionalization (Co, Ru, Fe)





Entry	Catalysts	X	Conditions[a,b]	Yield (%)[c]	ee (%)[d]
1	Λ-Ru1	1aa	Standard	100	86
2	Λ-Ru2	1aa	Standard	100	94
3	Λ-Ru3	1aa	Standard	100	95
4	Λ-Ru4	1aa	Standard	100	94
5	Λ-Ru5	1aa	Standard	100 (99)[e]	95
6	Λ-Ru5	1ab	Standard	100	94
7	Λ-Ru5	1ac	Standard	100	94
8	Λ-Ru5	1ad	Standard	27	91
9	Λ-Ru5	1aa	0.5 mol % catalyst)	100	94
10	Λ-Ru5	1aa	0.1 mol % catalyst[f]	100	94
11	Λ-Ru5	1aa	0.05 mol % catalyst[f]	66	93
12	Λ-Ru5	1aa	no base[g]	100	94

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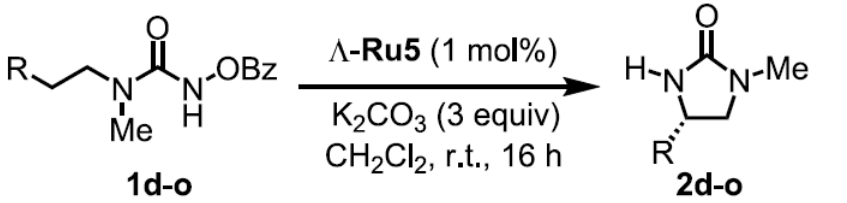
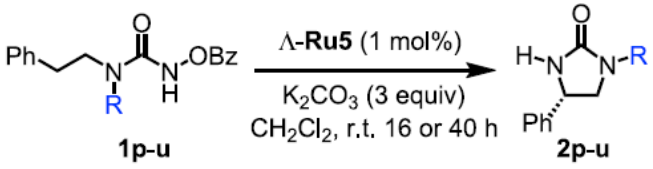
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

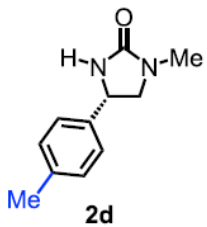
■ Asymmetric C−H Functionalization (Co, Ru, Fe)



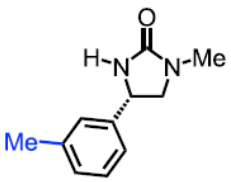
1d-o **2d-o**



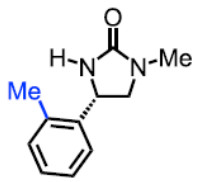
1p-u **2p-u**



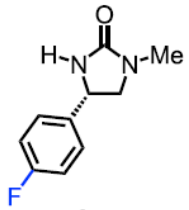
2d
92% yield, 95% ee



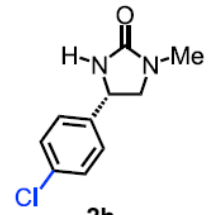
2e
99% yield, 96% ee



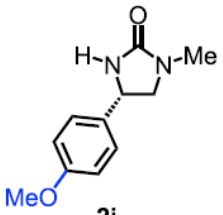
2f
96% yield, 97% ee



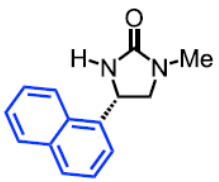
2g
90% yield, 93% ee



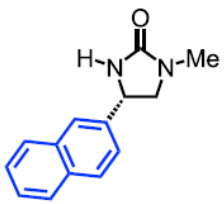
2h
93% yield, 90% ee



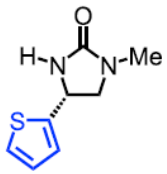
2i
99% yield, 92% ee



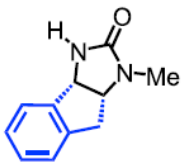
2j
99% yield, 99% ee



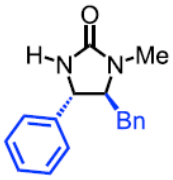
2k
97% yield, 90% ee



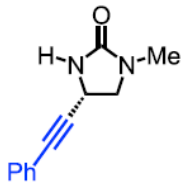
2l
99% yield, 88% ee



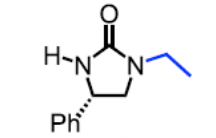
2m[a]
29% yield, 89% ee



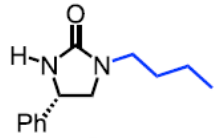
2n
93% yield, 94% ee



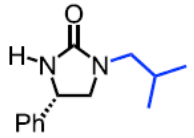
2o[a]
89% yield, 87% ee



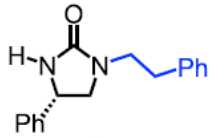
2p[a]
99% yield, 93% ee



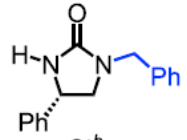
2q[a]
82% yield, 93% ee



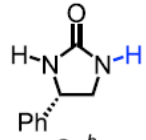
2r[a]
68% yield, 95% ee



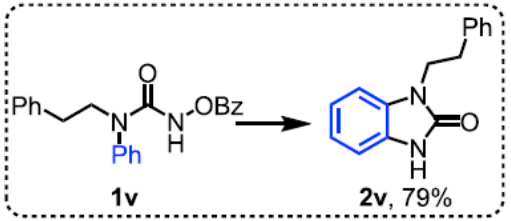
2s[a]
90% yield, 92% ee



2t[b]
37% yield, 93% ee



2u[b]
91% yield, 91% ee



1v **2v**, 79%

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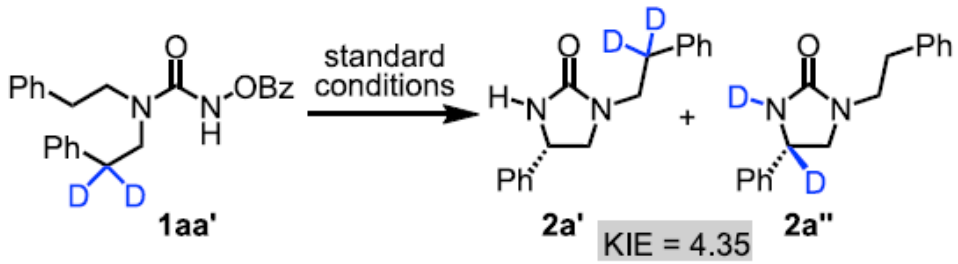
Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

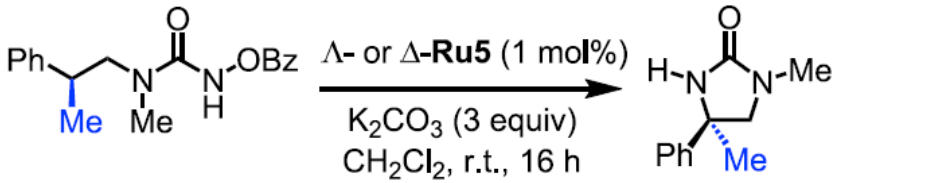
■ Asymmetric C−H Functionalization (Co, Ru, Fe)

A **Kinetic isotope experiment**

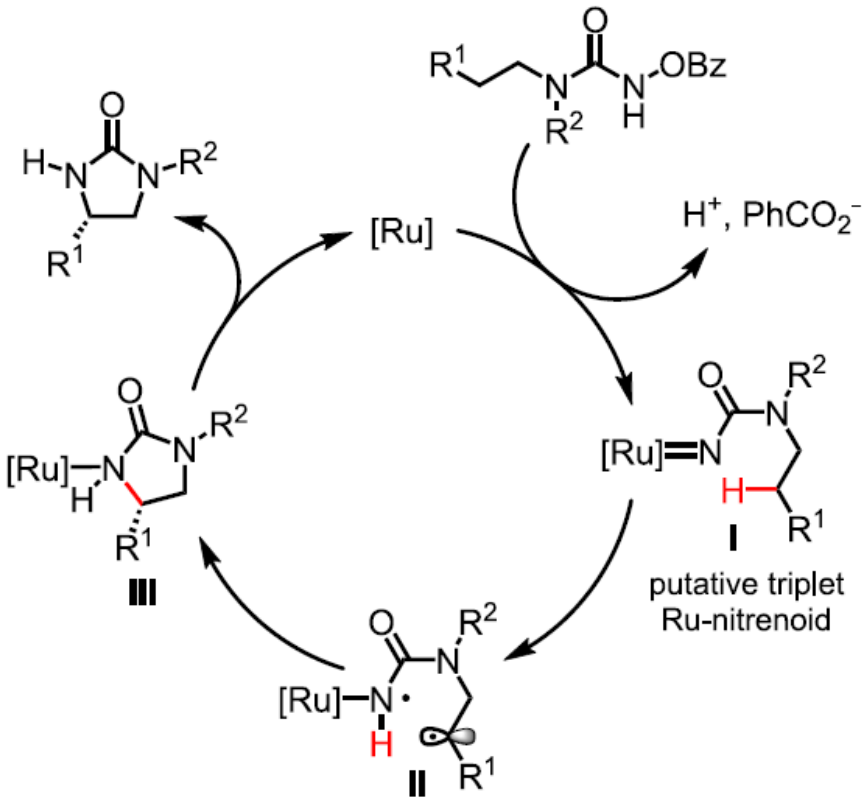


KIE (C-H insertion) = 1.5

C **Stereochemistry**



Mechanism



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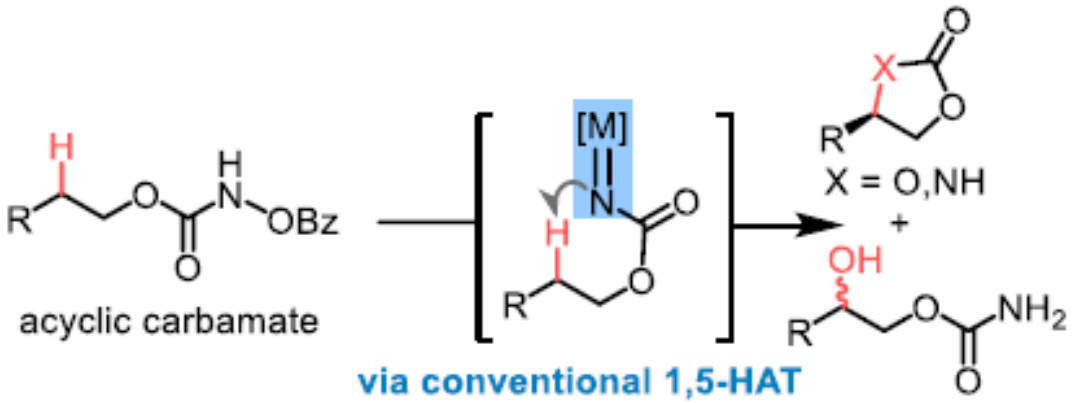
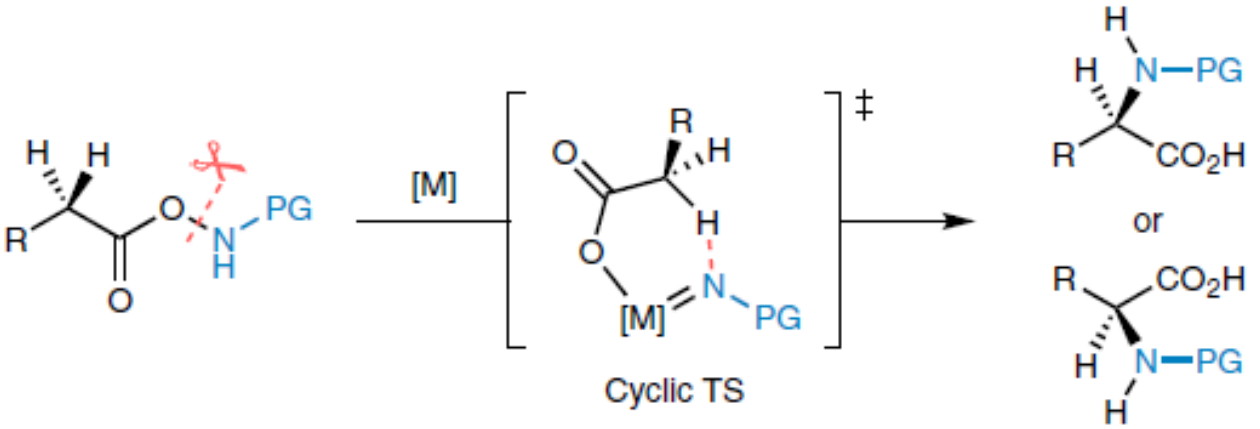
- **Asymmetric C−H Functionalization (Co, Ru, Fe)**

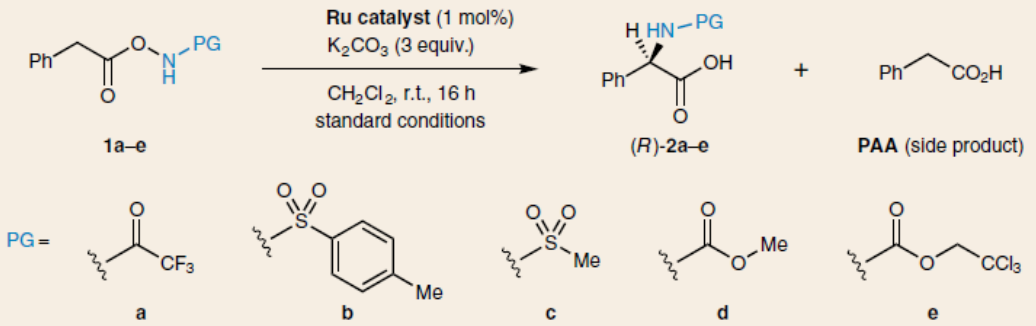


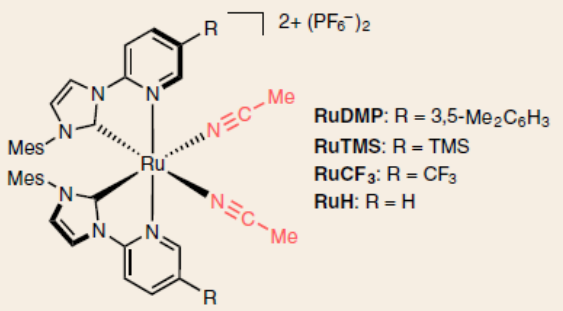


E. Meggers et al. *Nat. Chem.* **2022**, *14*, 566-573.

Asymmetric Radical Coupling Mediated by ‘Metal-Nitrene Radical’

■ Asymmetric C–H Functionalization (Co, Ru, Fe)





Entry	Catalyst	Protecting group (PG)	Conditions[a]	Conversion (%)[b]	Yield of 2 (%)[b]	Yield of PAA (%)[b]	e.e. of 2 (%)[c]
1	Λ-RuDMP	$COCF_3$ (a)	Standard	0	–	–	–
2	Λ-RuDMP	Ts (b)	Standard	37	<5	23	n.d.
3	Λ-RuDMP	Ms (c)	Standard	50	<5	25	n.d.
4	Λ-RuDMP	CO_2Me (d)	Standard	100	86	12	89
5	Λ-RuDMP	Troc (e)	Standard	100	93 (91)[d]	4	95
6	Λ-RuTMS	Troc (e)	Standard	98	80	9	92
7	Λ-$RuCF_3$	Troc (e)	Standard	19	6	5	90
8	Λ-RuH	Troc (e)	Standard	100	85	9	92
9	Λ-RuDMP	Troc (e)	Et_3N as base	100	25	73	95
10	Λ-RuDMP	Troc (e)	Na_2CO_3 as base	99	87	5	95
11	Λ-RuDMP	Troc (e)	THF as solvent	94	15	75	82
12	Λ-RuDMP	Troc (e)	MeOH as solvent	96	0	64	–

[a]Shown are the deviations from the standard reaction conditions. Standard conditions: substrate **1** (0.1 mmol), ruthenium catalyst (1 mol%) and the indicated base (3 equiv.) in the indicated solvent (2 ml, 0.05 M) were stirred at room temperature (25 °C) for 16 h. [b]Conversion and yield were determined by ^1H NMR analysis using hexamethylbenzene as an internal standard. [c]Enantiomeric excess (e.e.) values were determined by HPLC on chiral stationary phases. [d]Yield of the isolated α-amino acid. n.d., not determined; Troc, $CO_2CH_2CCl_3$.

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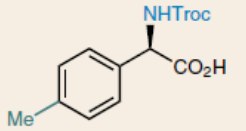
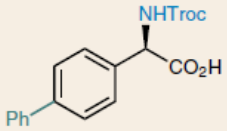
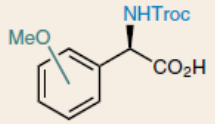


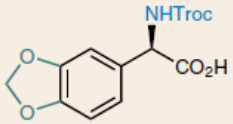
3
86%, 97% e.e.



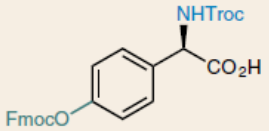
4
86%, 95% e.e.



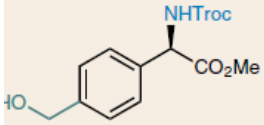
5 (*para*), 96%, 96% e.e.
6 (*meta*), 87%, 96% e.e.
7 (*ortho*), 79%, 85% e.e.



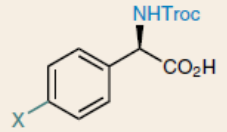
8
56%, 92% e.e.



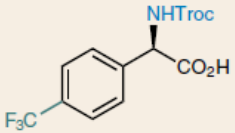
9
83%, 93% e.e.



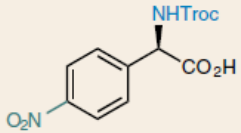
10[a]
64%, 98% e.e.



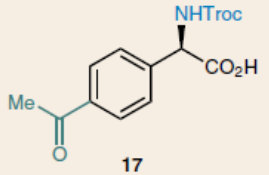
11, X = I, 91%, 94% e.e.
12, X = Br, 93%, 94% e.e
13, X = Cl, 93%, 95% e.e.
14, X = F, 92%, 93% e.e.



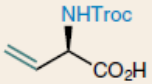
15
87%, 86% e.e.



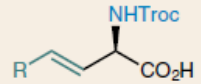
16
73%, 92% e.e.



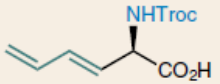
17
79%, 92% e.e.



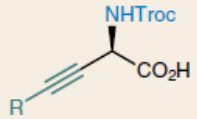
28
62%, 73% e.e.



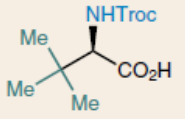
29, R = Et, 83%, 84% e.e.
30, R = ^{i}Pr, 88%, 81% e.e.
31, R = ^{n}Hex, 85%, 82% e.e.
32, R = Ph, 88%, 82% e.e.



33
72%, 81% e.e.

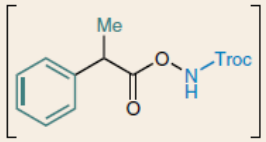


34[c], R = Ph, 46%, 62% e.e.
35[c], R = Et, 63%, 64% e.e.

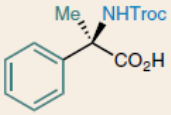


36[d]
20%, 90% e.e.

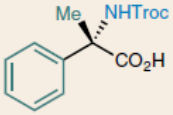
α-Disubstituted amino acids (stereoretentive 1,3-nitrogen shift)



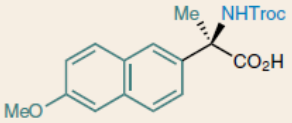
Azanyl ester **37**



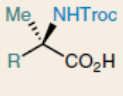
(*R*)-**38**[e]
91%, 98% e.e.[f]



(*S*)-**38**[g]
34%, 28% e.e.



39[f] (86%, 99% e.e.)
from naproxen



40[d,f], R = (*E*)-EtCH=CH, 77%, 87% e.e.
41[d,f], R = Et, 57%, 86% e.e.
42[d,f], R = cyclohexyl, 25%, 92% e.e.

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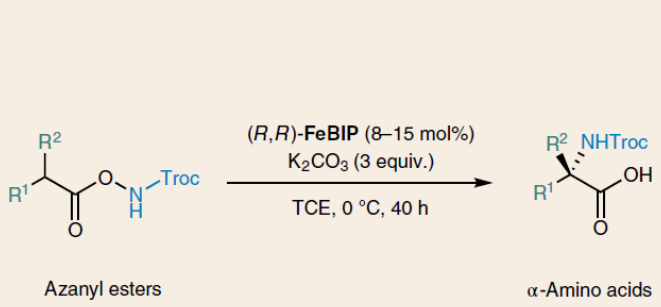
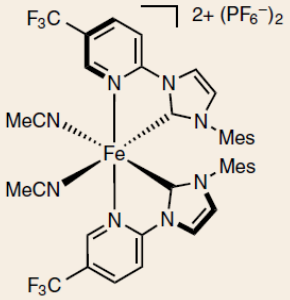
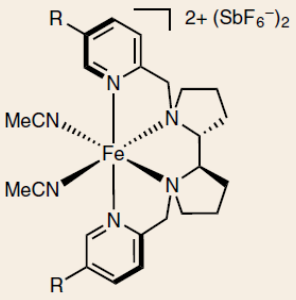


Azanyl esters

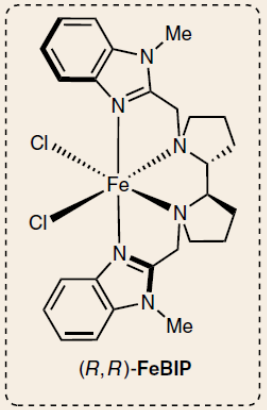
α-Amino acids



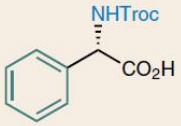
Δ-Fe1



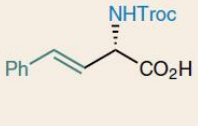
(*R*,*R*)-**Fe2**, R = H
(*R*,*R*)-**Fe3**, R = 2,6-$(CF_3)_2C_6H_3$



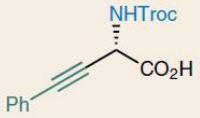
(*R*,*R*)-**FeBIP**



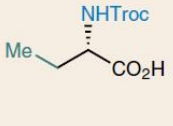
(*S*)-**2e**
Δ-**Fe1** (8 mol%), trace
(*R*,*R*)-**Fe2** (8 mol%), 91%, 15% e.e.
(*R*,*R*)-**Fe3** (8 mol%), 75%, 10% e.e.
(*R*,*R*)-**FeBIP** (8 mol%), 95%, 91% e.e.



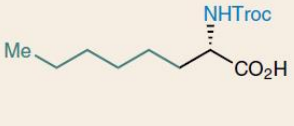
(*S*)-**32**
44%, 86% e.e.



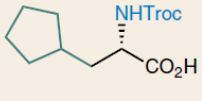
(*S*)-**34**
13%, 44% e.e.



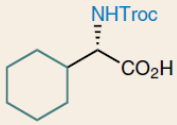
43
62%, 91% e.e.



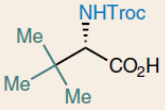
44
75%, 92% e.e.



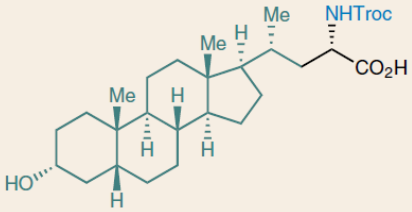
50
65%, 92% e.e.



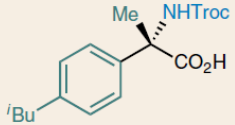
51
48%, 89% e.e.



(*S*)-**36**
56%, 85% e.e.



52[a] (77%, 23:1 d.r.)
from lithocholic acid



53 (70%, 85% e.e.)
from (±)-ibuprofen

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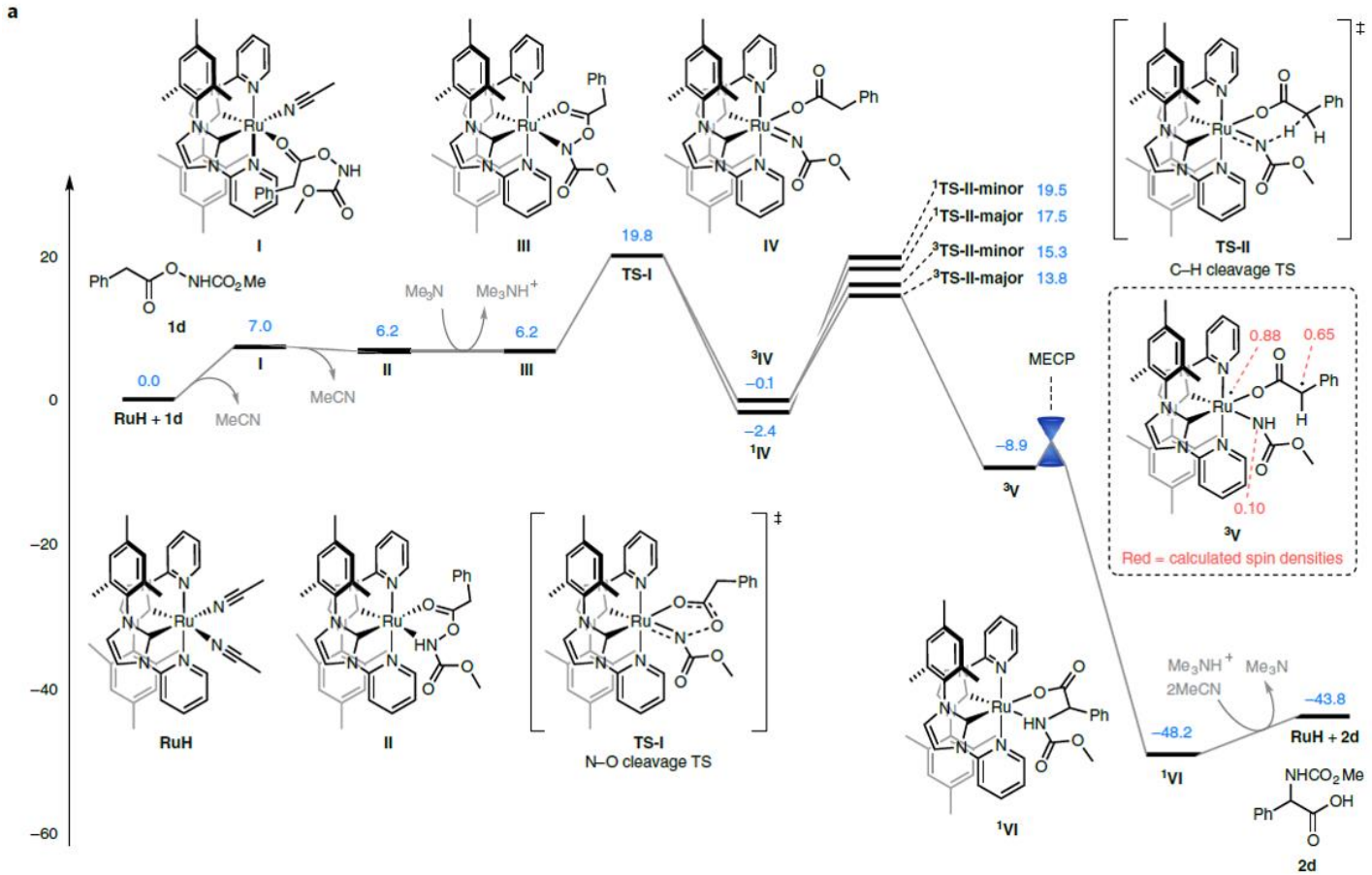
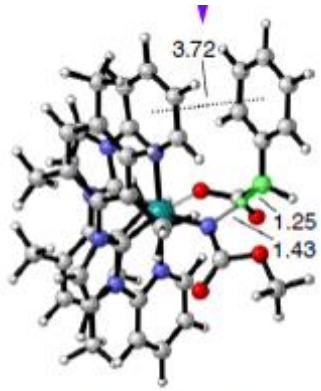
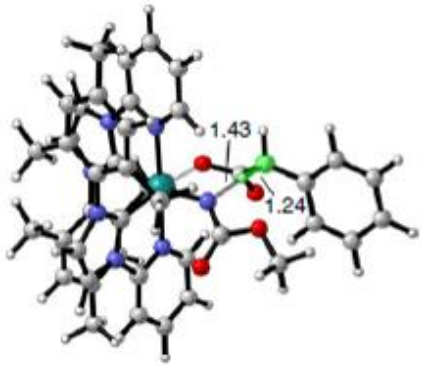




^{3}TS-II-major-Ph

$\Delta\Delta G^{\ddagger} = 0.0$



^{3}TS-II-minor-Ph

$\Delta\Delta G^{\ddagger} = 1.5$

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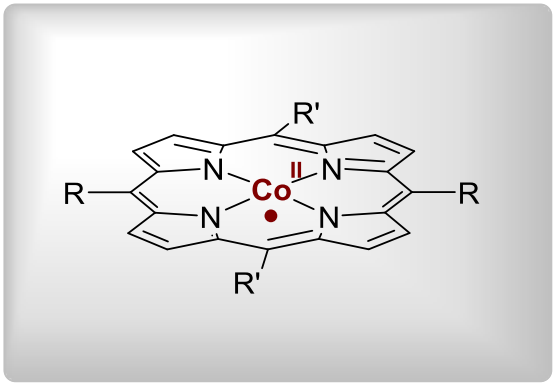
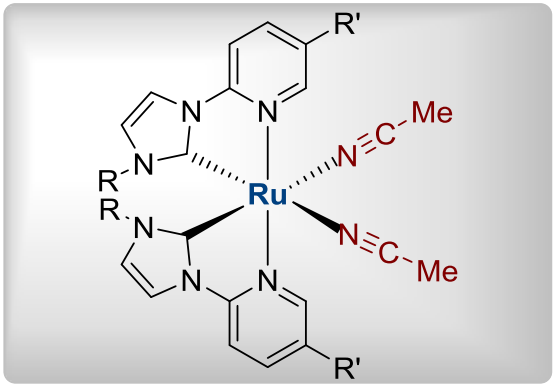
My Comments



d^7 metal



triplet state 'metal nitrene'

- Development and application of ‘metal carbene radical’.
- Highly selective cyclopropanation, cyclopropenation and aziridination.
- It plays an important role in the field of direct asymmetric C-H functionalization.
- More generation methods and reactivity of ‘metal carbene radical’ still need to be explored.

Thanks for your kind attention ！