Catalytic C-C Formation via Cobalt-Carbene Radicals

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Supervisor: Prof. Shengming Ma
Mar 17 2023

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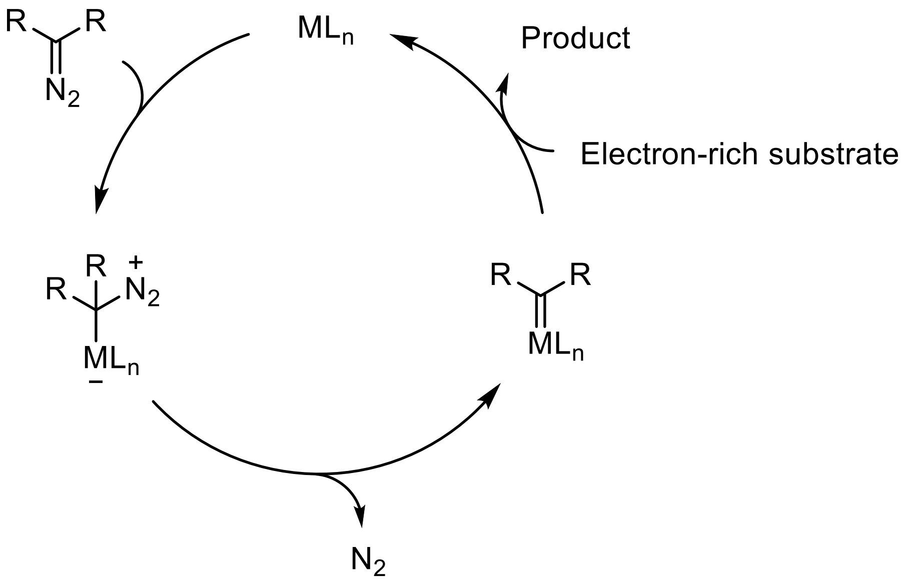
Introduction

1 Introduction

Fischer carbene
electrophilic

Schrock carbene
nucleophilic

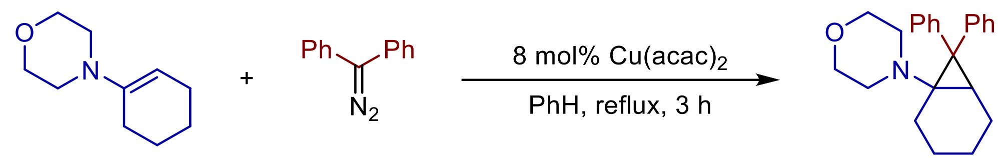
Typical catalytic cycle for metal carbene transformations



E. O. Fischer, *Angew. Chem.* **1974**, *86*, 651-682.
R. R. Schrock, *Acc. Chem. Res.* **1979**, *12*, 98-104.
M. P. Doyle, *Chem. Rev.* **1986**, *86*, 919-939.

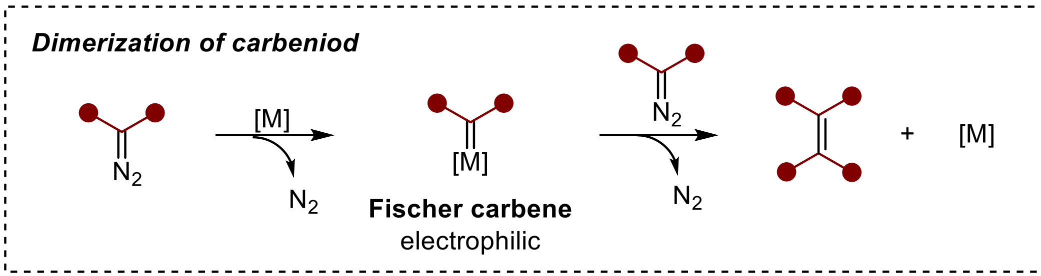
1 Introduction

Homogeneous catalysis for transformation of metal carbene (Nozaki, 1966)

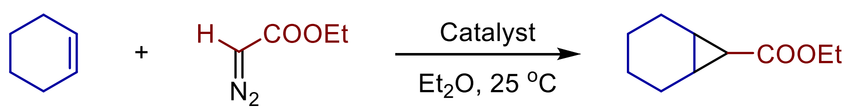


excess

62% yield



Alternative protocol (Doyle, 1981)



0.1 mol

1.0 eq.

Catalyst	Addition rate (mmol/h)	Yield (%)
0.5 mol% $Rh_2(OAc)_4$	10, 5.0	80
0.1 mol% $Rh_6(OAc)_{16}$	5.0, 2.0	43
0.5 mol% $CuClP(O^iPr)_3$	0.25	40

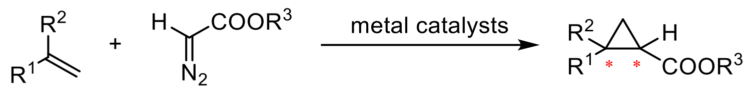
Challenge:

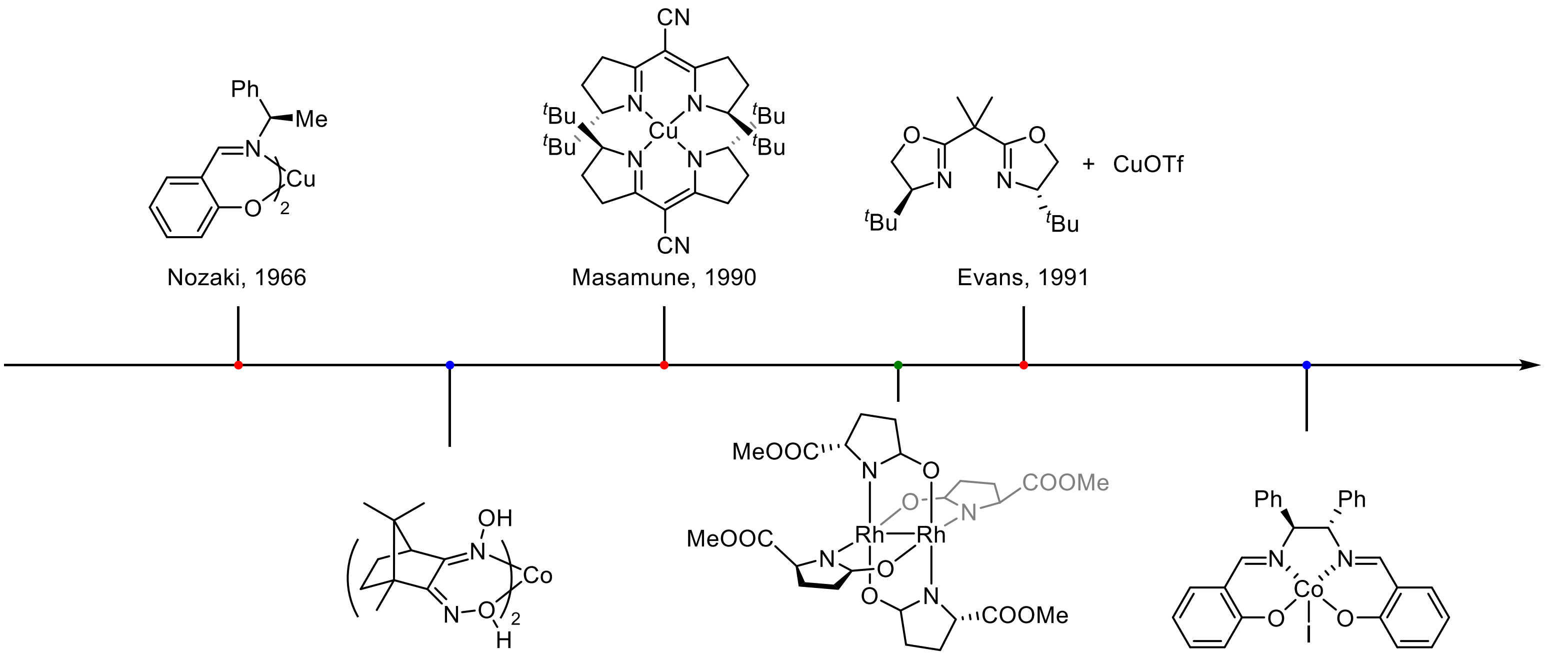
- *Complicated procedure*
- *Only Electron-rich olefins*

H. Nozaki, S. Moriuti, M. Yamabe, R. Noyori, *Tetrahedron Lett.* **1966**, 59-63.
M. P. Doyle, D. van Leusen, W. H. Tamblyn, *Synthesis* **1981**, 787-789.

1 Introduction

Enantioselective cyclopropanation of olefins with diazoacetates





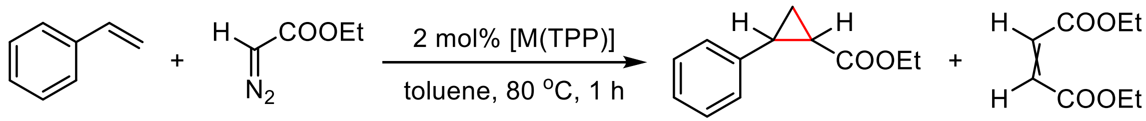
Challenge:

◆ *Lack of strategies with high yield, excellent diastereoselectivity and enantioselectivity*

H. Nozaki, S. Moriuti, H. Takaya, R. Noyori, *Tetrahedron Lett.* **1966**, 5239-5244.
A. Nakamura, A. Konishi, Y. Tatsuno, S. Otsuka, *J. Am. Chem. Soc.* **1978**, *100*, 3443-3449.
R. E. Lowenthal, A. Abiko, S. Masamune, *Tetrahedron Lett.* **1990**, *31*, 6005-6008.
M. P. Doyle, R. J. Pieters, *J. Am. Chem. Soc.* **1991**, *113*, 1424-1426.
D. A. Evans, K. A. Woerpel, M. M. Hinman, M. M. Faul, *J. Am. Chem. Soc.* **1991**, *113*, 726-728.
T. Fukuda, T. Katsuki, *Synlett* **1995**, 825-826.

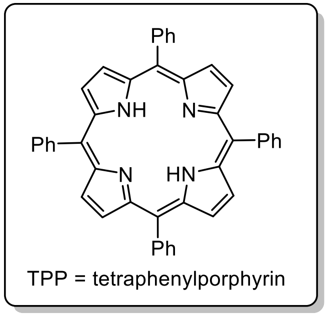
1 Introduction

Cobalt-catalyzed cyclopropanation



1 + **2** (1.2 eq.) → **3** + **4**

Entry	[M(TPP)]	**1**:**3**:**4**	trans:cis of **3**
1	Fe(TPP)Cl	33:36:31	86:14
2	Ru(TPP)(CO)	48:18:34	95:05
3	Rh(TPP)I	28:52:20	64:36
4	Co(TPP)	02:97:01	70:30



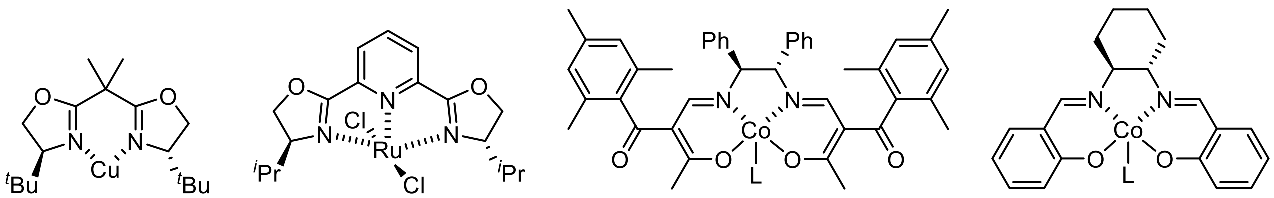
Advantage:

✓ *A practical protocol performed in **one-pot fashion** with **alkene as the limiting reagent.***

L. Huang, Y. Chen, G.-Y. Gao, X. P. Zhang, *J. Org. Chem.* **2003**, *68*, 8179-8184.

1 Introduction

IR: [M] + $N_2CHCOOMe$



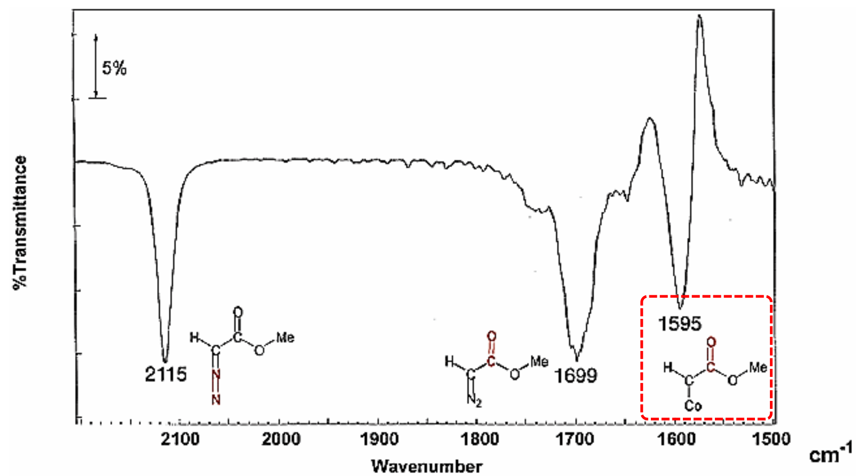
1

2

3 L = *N*-methylimidazole
4 L = Cl

5 L = *N*-methylimidazole
6 L = Cl

Complex	$N_2CHCOOMe$ (**a**)	**1+a**	**2+a**	**3+a**	**4+a**	**5+a**	**6+a**
$\nu_{C=O}$ (cm^{-1})	1699	1650	1651	1595	1600	1601	1617

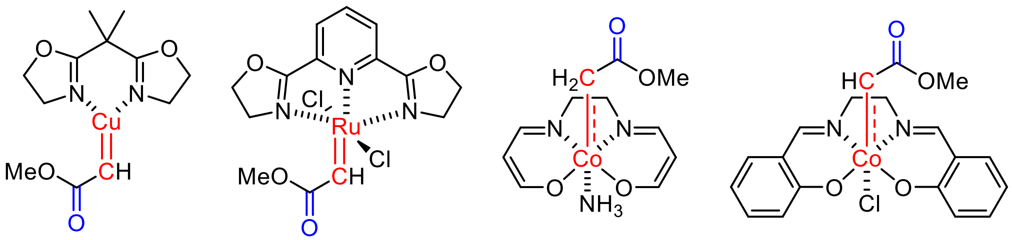


Time-resolved IR-spectrum of the reaction of the cobalt(II) **3** complex and methyl diazoacetate (after 2 min).

T. Ikeno, I. Iwakura, T. Yamada, *J. Am. Chem. Soc.* **2002**, *124*, 15152-15153.

1 Introduction

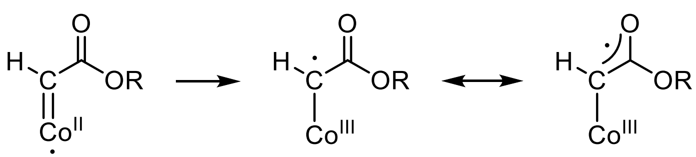
Cobalt-carbene complex with single-bond character



7 **8** **9** **10**

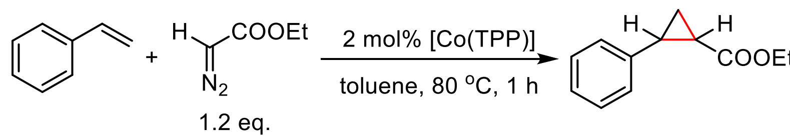
Complex	Bond Order		Bond Distance (Å)	
	M-C	C-O	M-C	C-O
7	1.706	1.812	1.781	1.223
8	1.684	1.847	1.867	1.219
9	0.868	1.391	1.886	1.231
10	0.793	1.415	1.913	1.230

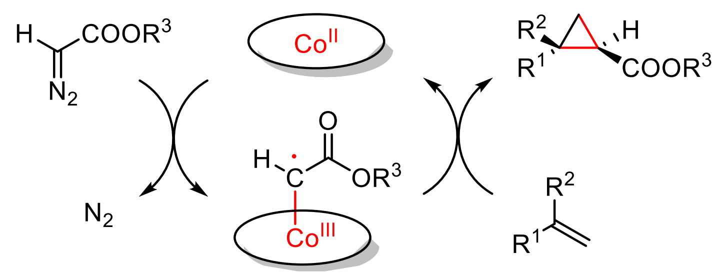
(B3LYP/6-31G*)

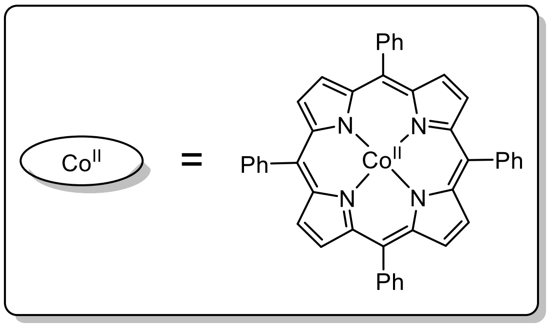


carbene radicals

Proposed mechanism





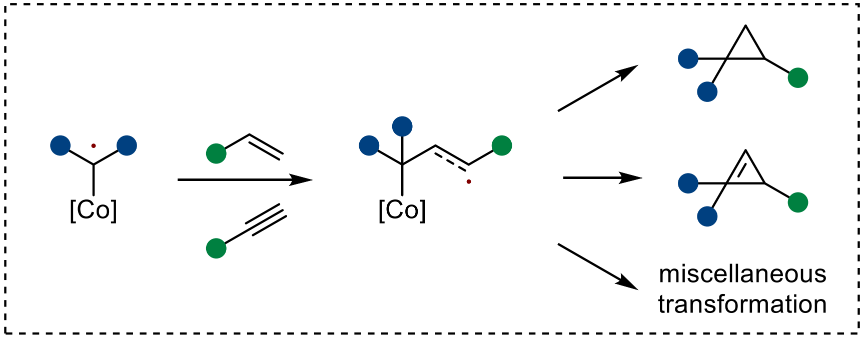


T. Ikeno, I. Iwakura, T. Yamada, *J. Am. Chem. Soc.* **2002**, *124*, 15152-15153.
L. Huang, Y. Chen, G.-Y. Gao, X. P. Zhang, *J. Org. Chem.* **2003**, *68*, 8179-8184.

2.1

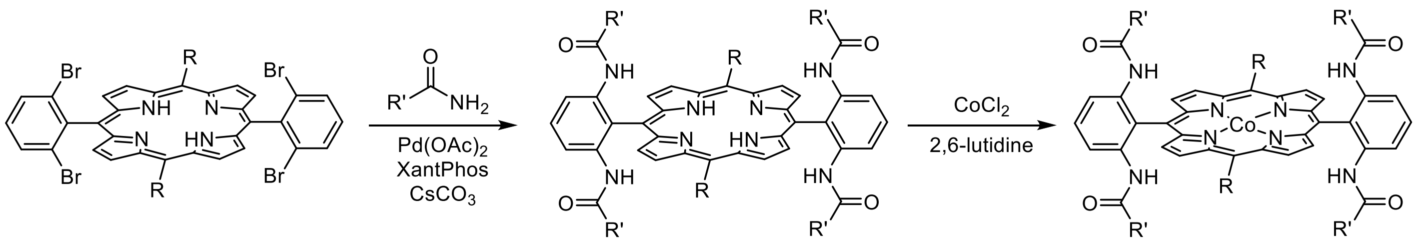
Catalytic C-C Formation via Cobalt-Carbene Radicals

——Addition to Unsaturated Bonds

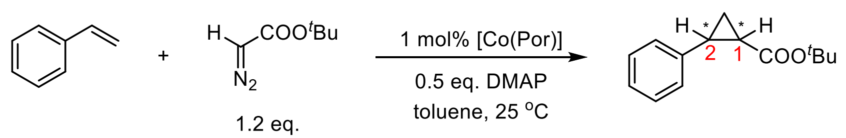


2.1.1 Cyclopropanation

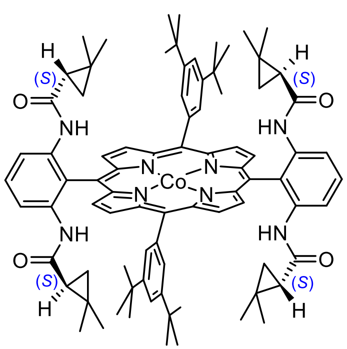
Synthesis of catalysts



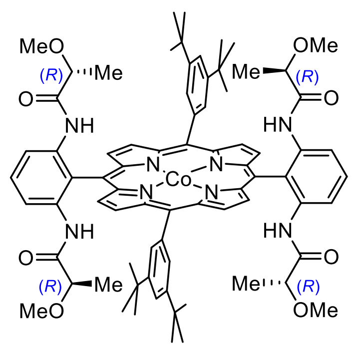
Enantioselective and diastereoselective cyclopropanation



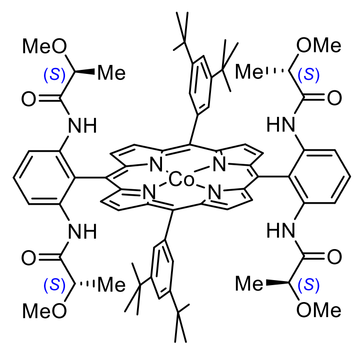
selected examples



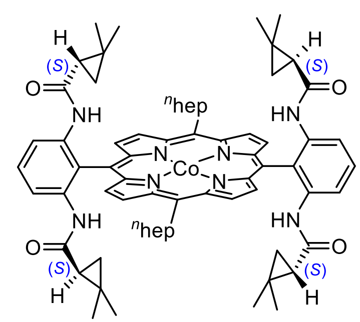
[Co(**P1**)]
config: 1*R*, 2*R*
84% yield
97:3 dr, 98% ee



[Co(**P2**)]
config: 1*S*, 2*R*
78% yield
63:37 dr, 96% ee



[Co(**P3**)]
config: 1*R*, 2*S*
76% yield
62:38 dr, 95% ee

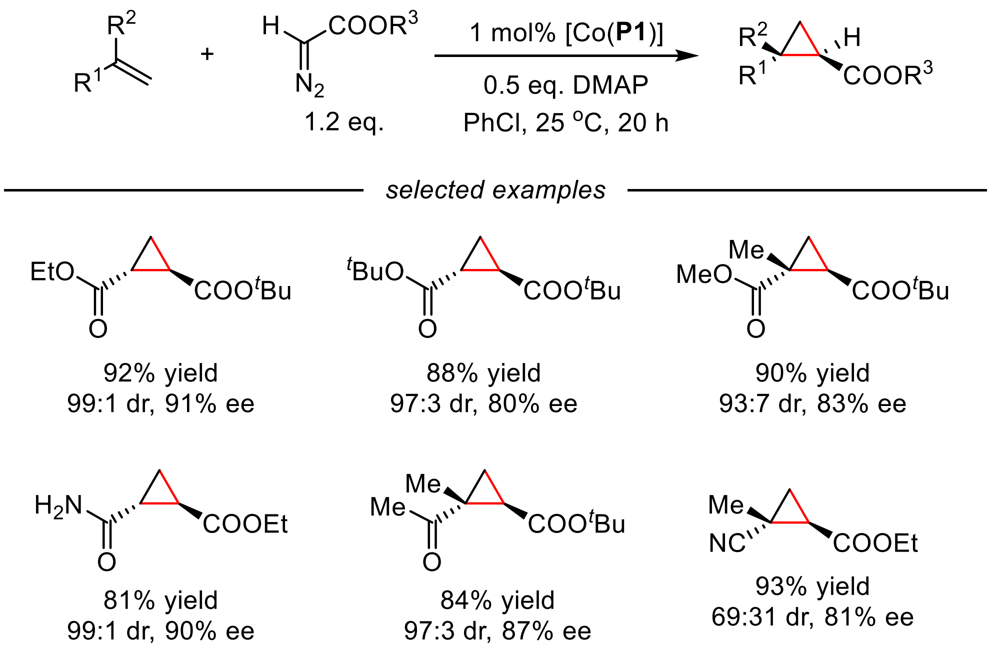


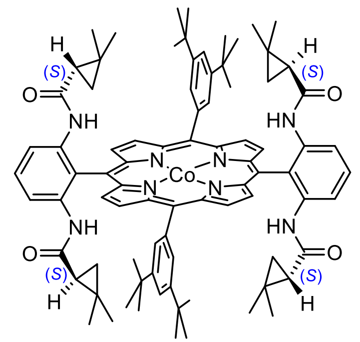
[Co(**P4**)]
config: 1*R*, 2*R*
73% yield
99:1 dr, 78% ee

Y. Chen, K. B. Fields, X. P. Zhang, *J. Am. Chem. Soc.* **2004**, *126*, 14718-14719.

2.1.1 Cyclopropanation

Electron-deficient olefins





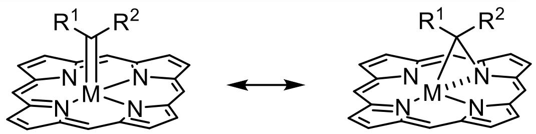
[Co(**P1**)]

P1 = 3,5-Di^{t}Bu-ChenPhyrin

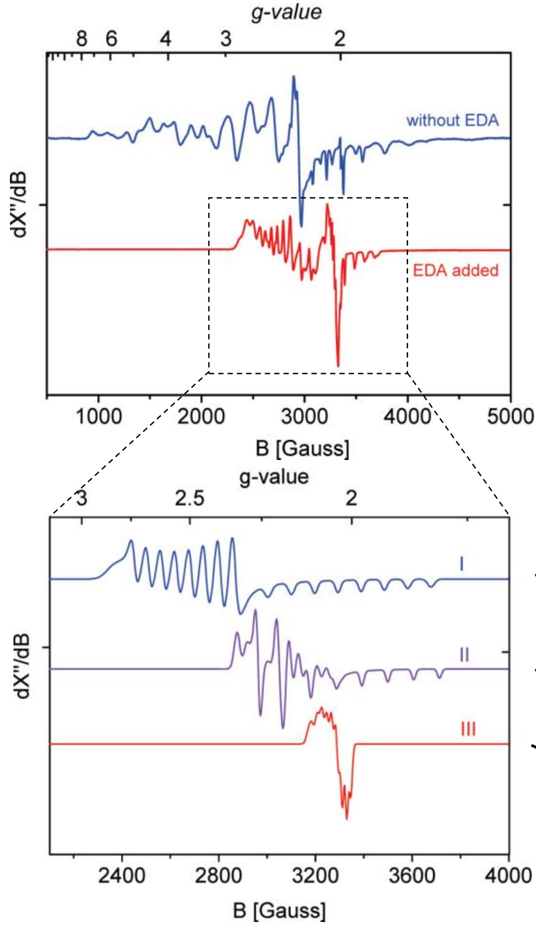
Y. Chen, J. V. Ruppel, X. P. Zhang, *J. Am. Chem. Soc.* **2007**, *129*, 12074-12075.

2.1.1 Cyclopropanation

Hoffmann, 1981



de Bruin & Zhang, 2010

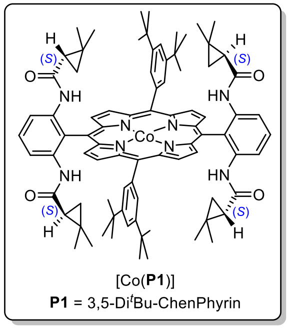


EPR spectrum

[Co(**P1**)]

+

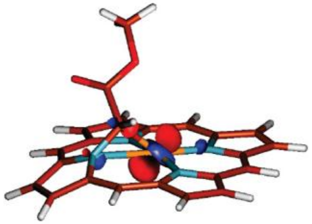
4.0 eq. EDA (ethyl diazoacetate)



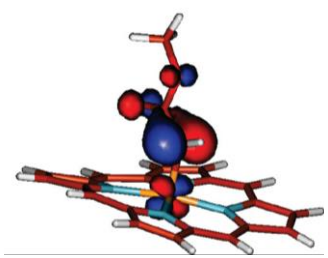
EDA coordinated to cobalt

bridging carbene

terminal carbene



metal-centered radical

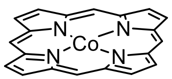


carbene radical

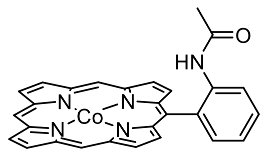
DFT optimized SOMO plots

K. Tatsumi, R. Hoffmann, *Inorg. Chem.* **1981**, *20*, 3771–3784.
W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2010**, *132*, 10891-10902.

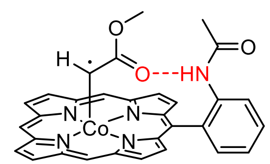
2.1.1 Cyclopropanation



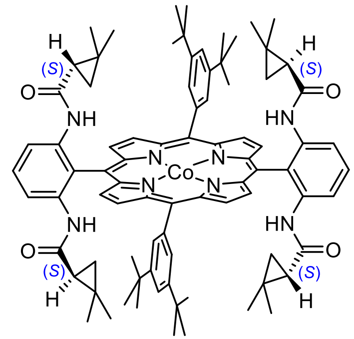
[Co(por)]



[Co(porAmide)]



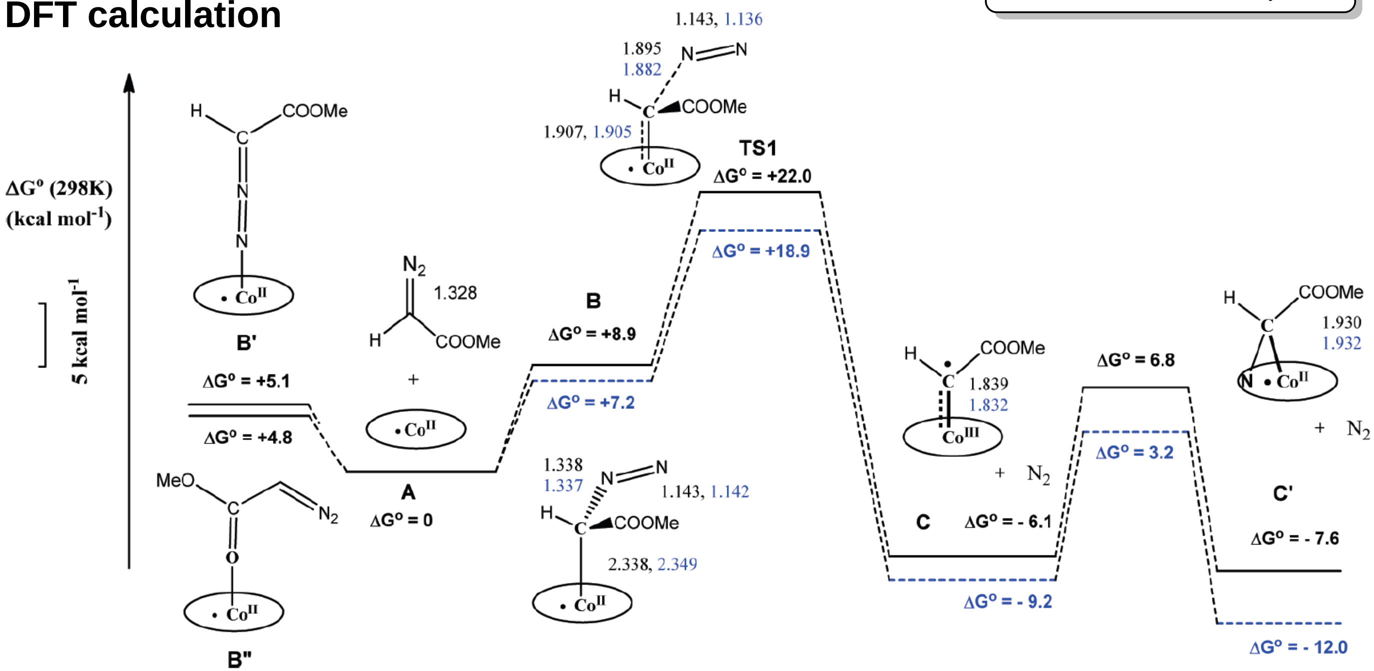
hydrogen bonding



[Co(**P1**)]

P1 = 3,5-Di^{t}Bu-ChenPhyrin

DFT calculation



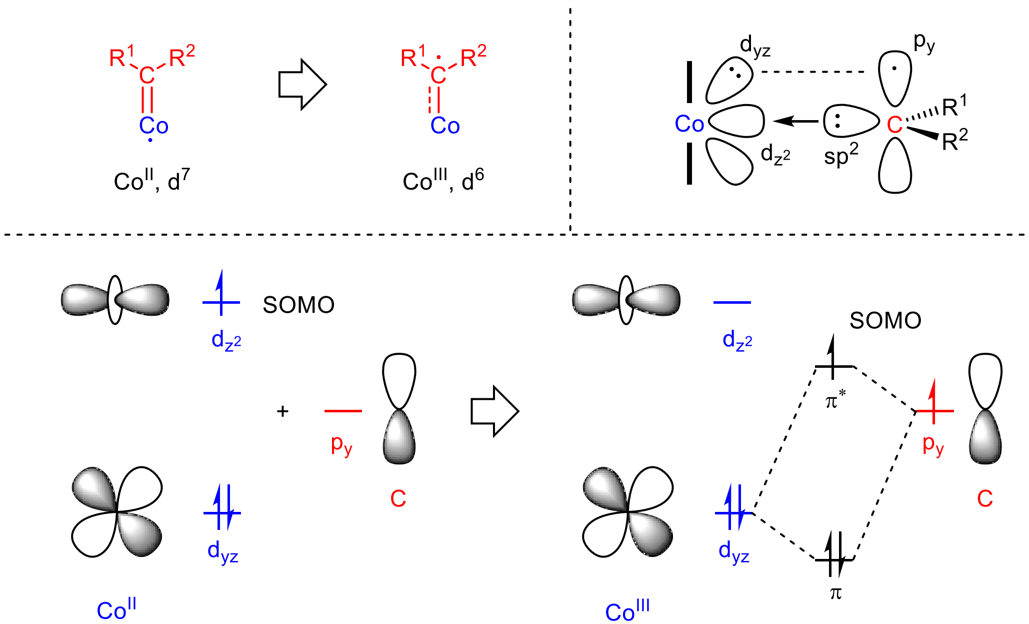
Black: EDA with Co^{II}(por)

Blue: EDA with Co^{II}(porAmide) involving hydrogen bonding

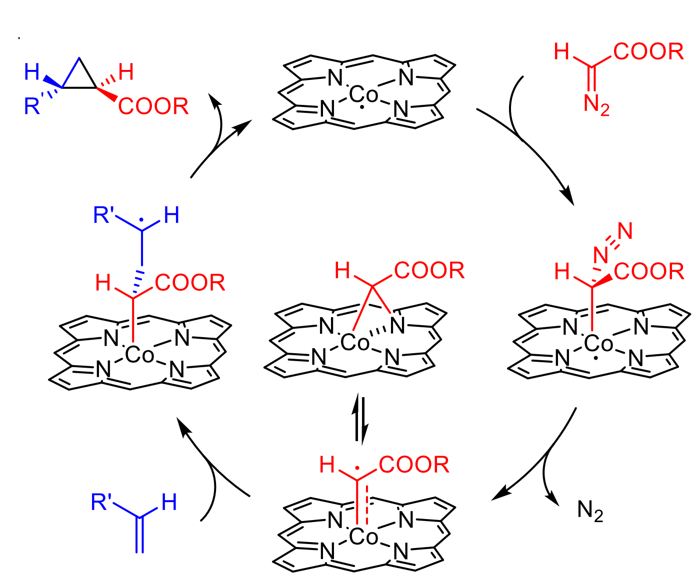
W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2010**, *132*, 10891-10902

2.1.1 Cyclopropanation

A simplified MO bonding model



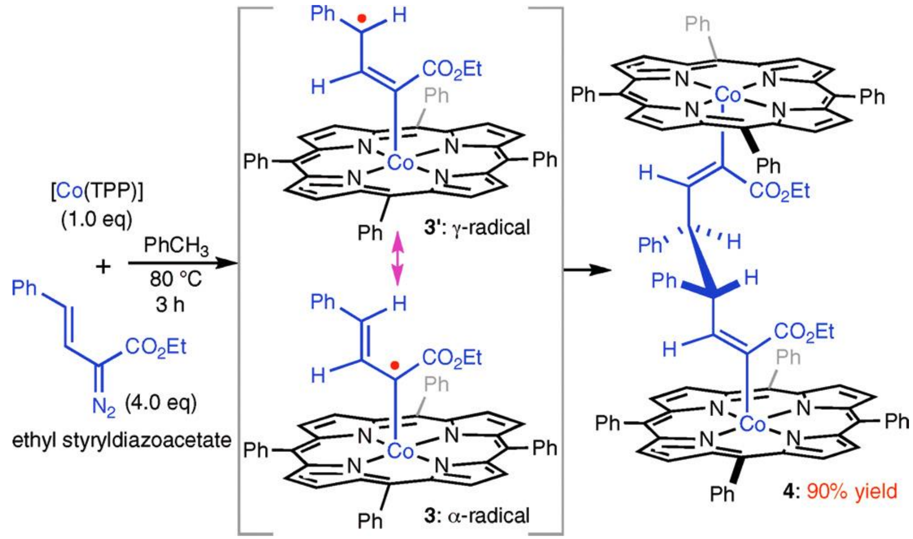
Proposed mechanism

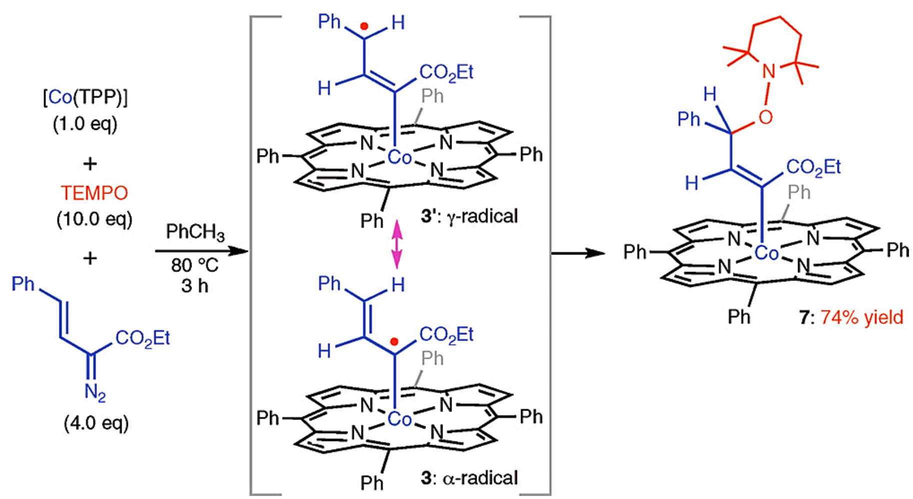


W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2010**, *132*, 10891-10902.

2.1.1 Cyclopropanation

Experimental evidence for cobalt-carbene radicals

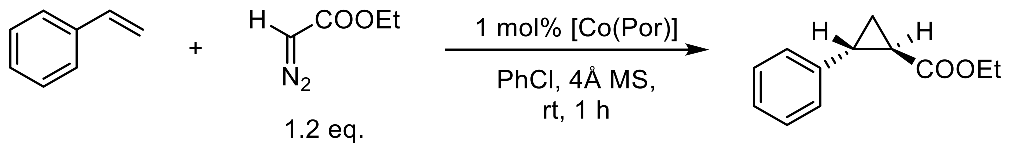


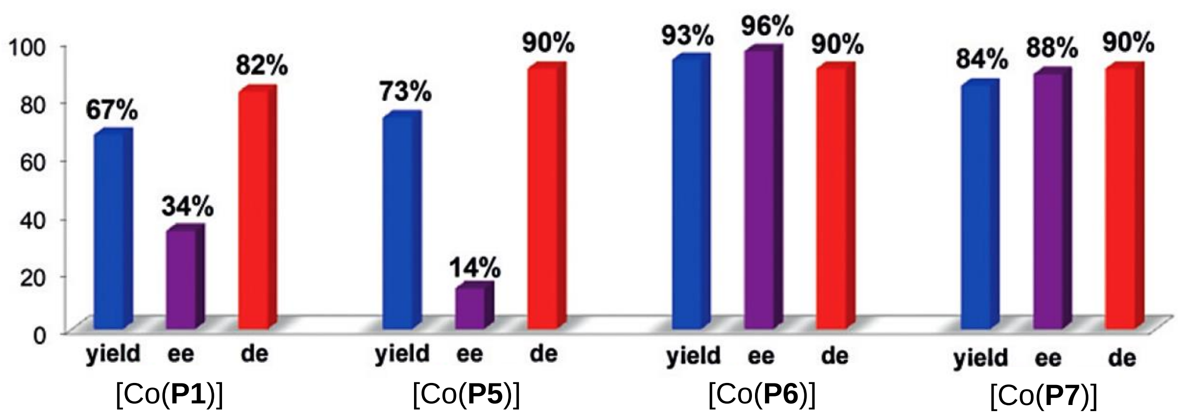


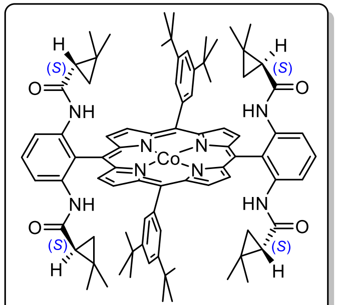
H. Lu, W. I. Dzik, X. Xu, L. Wojtas, B. de Bruin, X. P. Zhang, *Inorg. Chem.* **2011**, *50*, 9896-9903.

2.1.1 Cyclopropanation

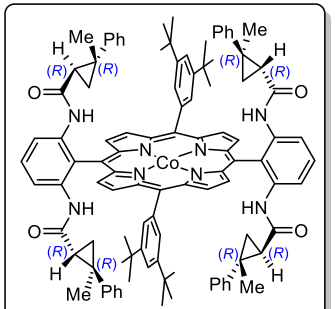
Cavity-like ligand



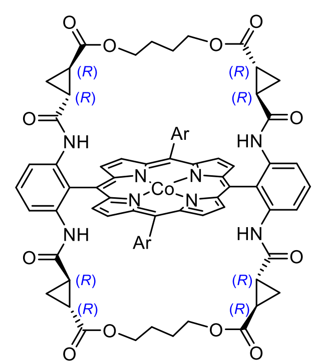




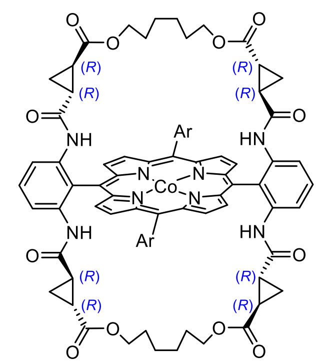
[Co(**P1**)]
P1 = 3,5-Di^{t}Bu-ChenPhyrin



[Co(**P5**)]
P5 = 3,5-Di^{t}Bu-QingPhyrin



[Co(**P6**)]
P6 = 3,5-Di^{t}Bu-Hu(C_4)Phyrin
(Ar = 3,5-di-^{t}butylphenyl)

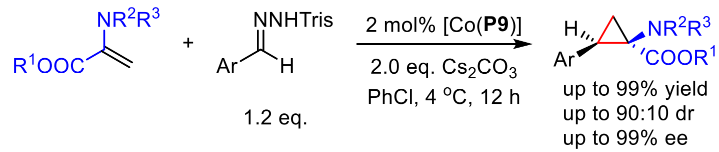


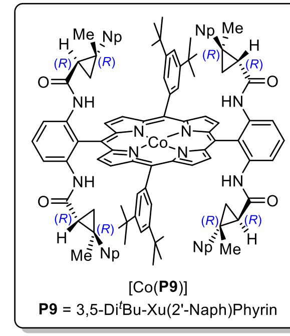
[Co(**P7**)]
P7 = 3,5-Di^{t}Bu-Hu(C_6)Phyrin
(Ar = 3,5-di-^{t}butylphenyl)

Y. Hu, K. Lang, J. Tao, M. K. Marshall, Q. Cheng, X. Cui, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed.* **2019**, *58*, 2670-2674.

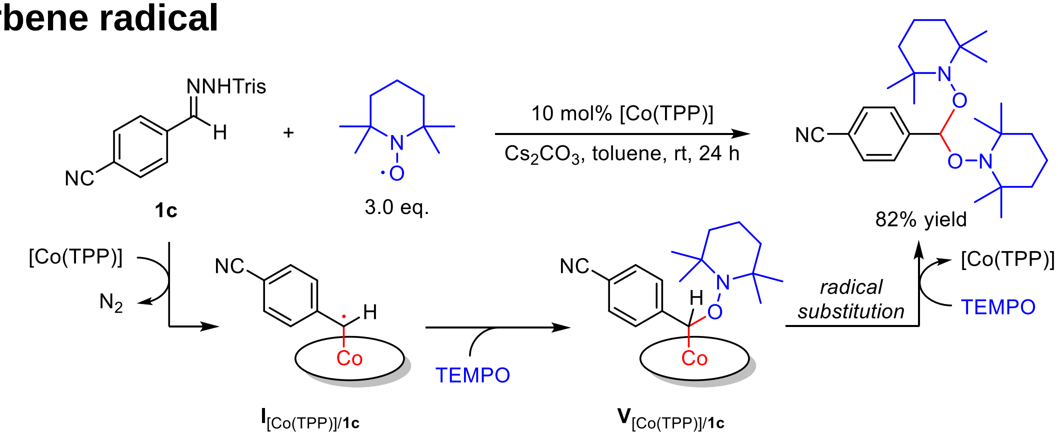
2.1.1 Cyclopropanation

Donor-substituted diazo reagents

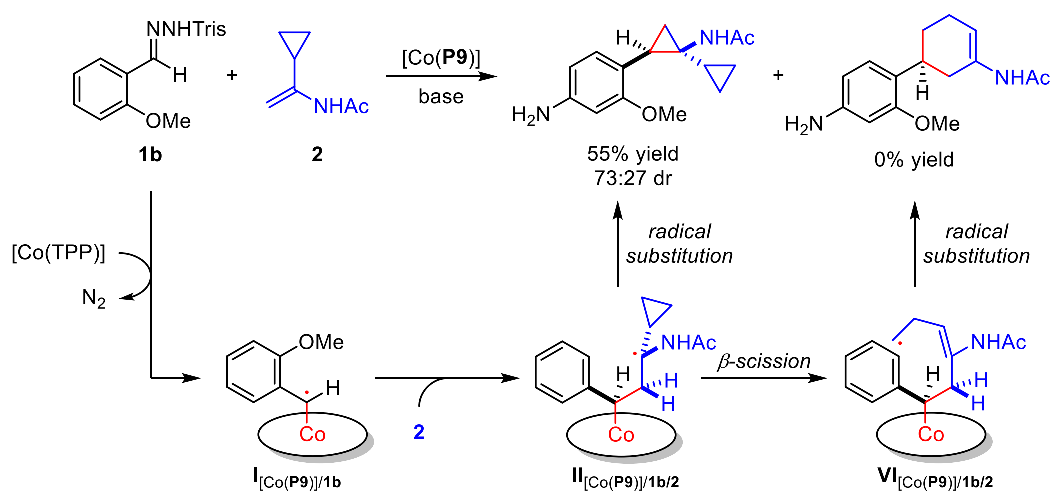




Trapping of carbene radical



Radical clock

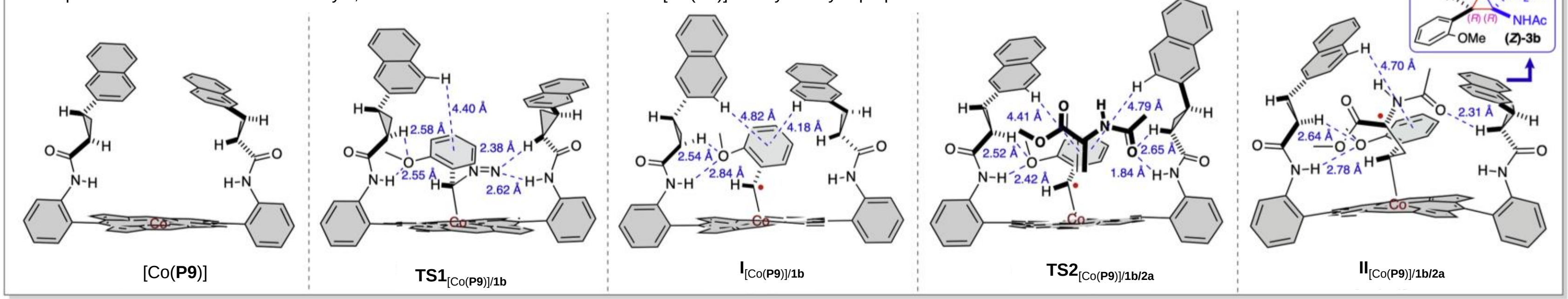


W.-C. C. Lee, D.-S. Wang, C. Zhang, J. Xie, B. Li, X. P. Zhang, *Chem* **2021**, *7*, 1588-1601.

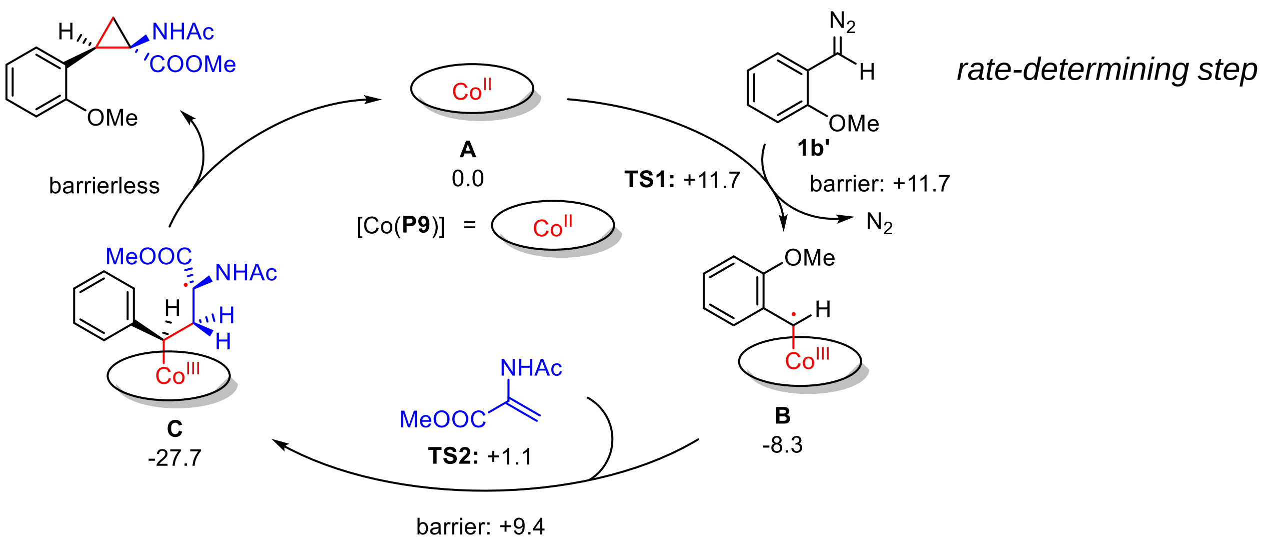
2.1.1 Cyclopropanation

DFT-Optimized models

DFT-Optimized Structure Models of Catalyst, Intermediates and Transition States of [Co(**P9**)]-Catalyzed Cyclopropanation.

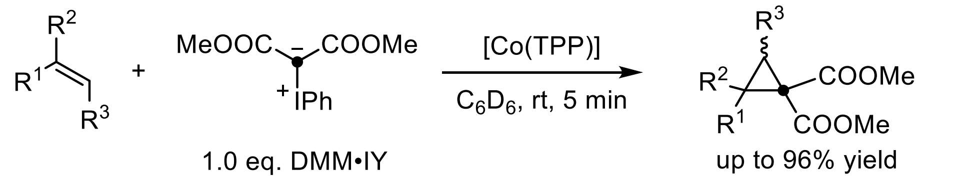


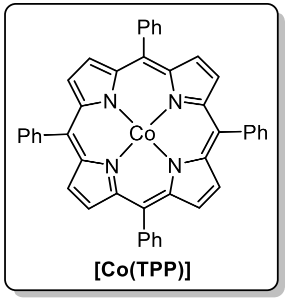
Proposed mechanism



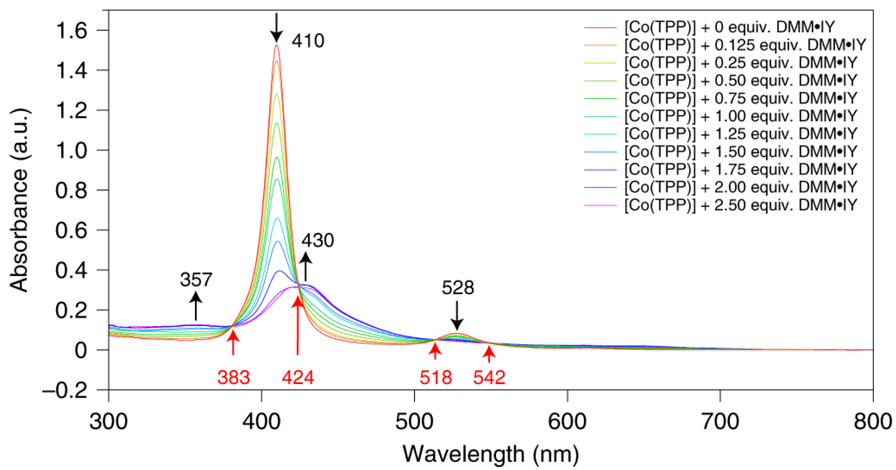
W.-C. C. Lee, D.-S. Wang, C. Zhang, J. Xie, B. Li, X. P. Zhang, *Chem* **2021**, *7*, 1588-1601.

2.1.1 Cyclopropanation

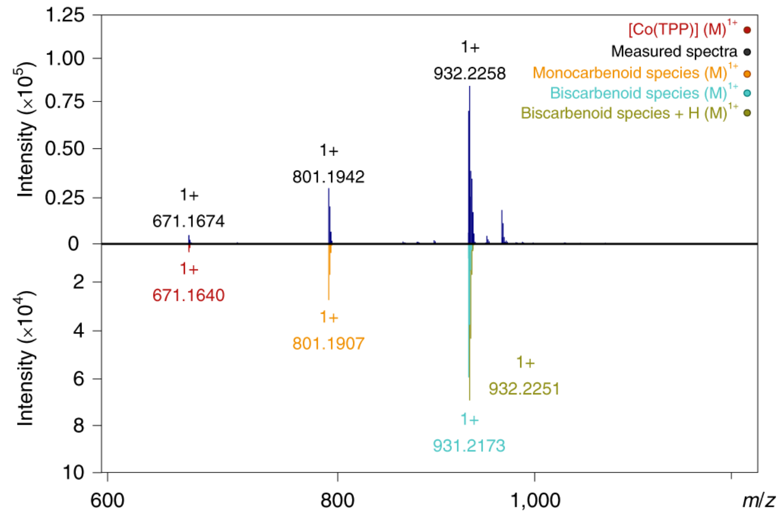




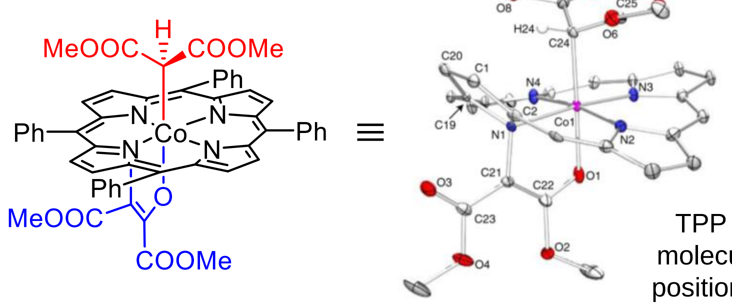
UV/Vis spectra: [Co(TPP)] + x eq. DMM·IY



CSI-HR-MS: [Co(TPP)] + 2.4 eq. DMM·IY



Crystal structure



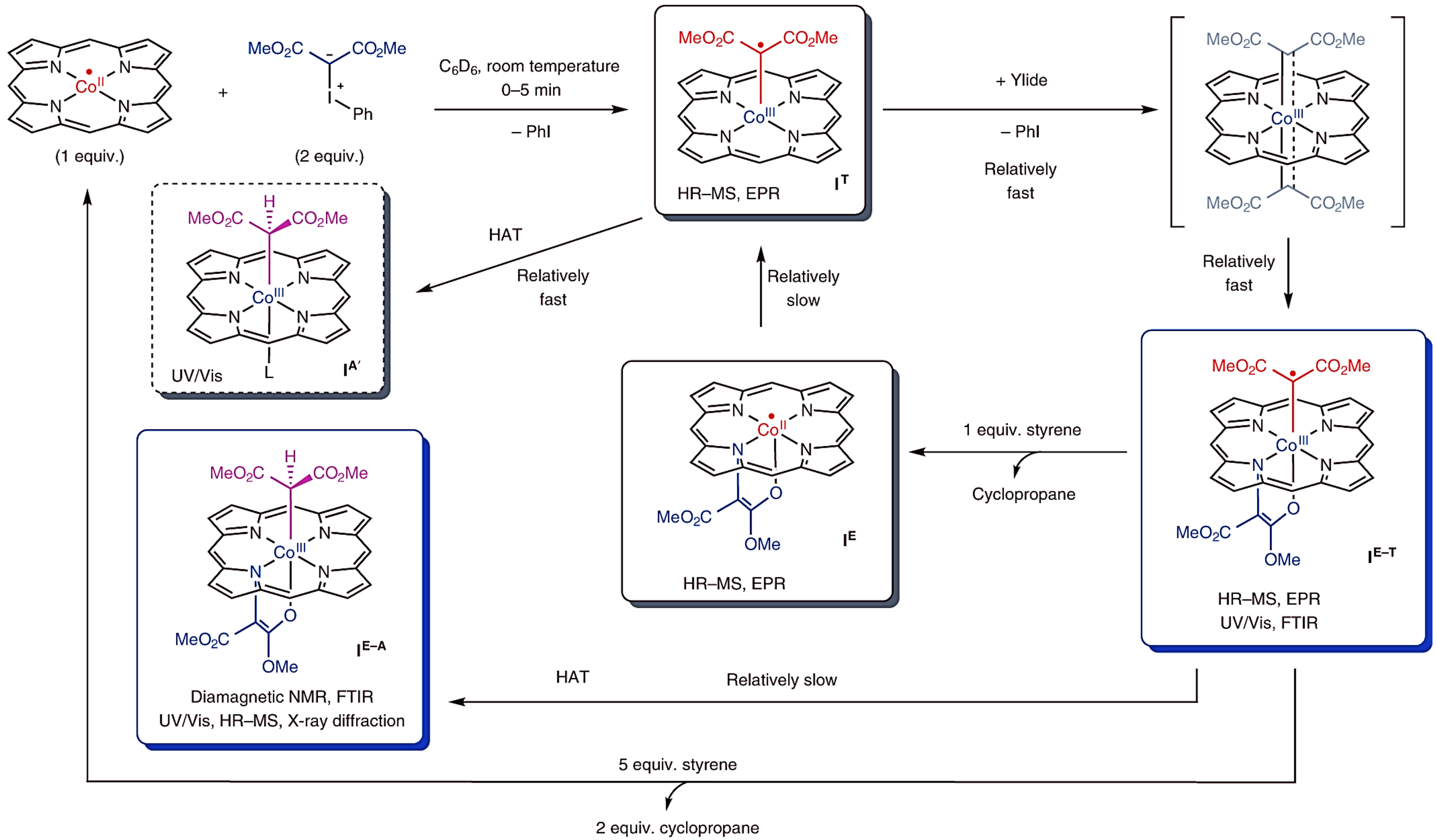
TPP phenyl groups, solvent molecules, disordered O_2–CH_3 positions and all protons except H24 omitted for clarity.

***N*-enolate-carbene radicals**

R. F. J. Epping, M. M. Hoeksma, E. O. Bobylev, S. Mathew, B. de Bruin, *Nat. Chem.* **2022**, *14*, 550-557.

2.1.1 Cyclopropanation

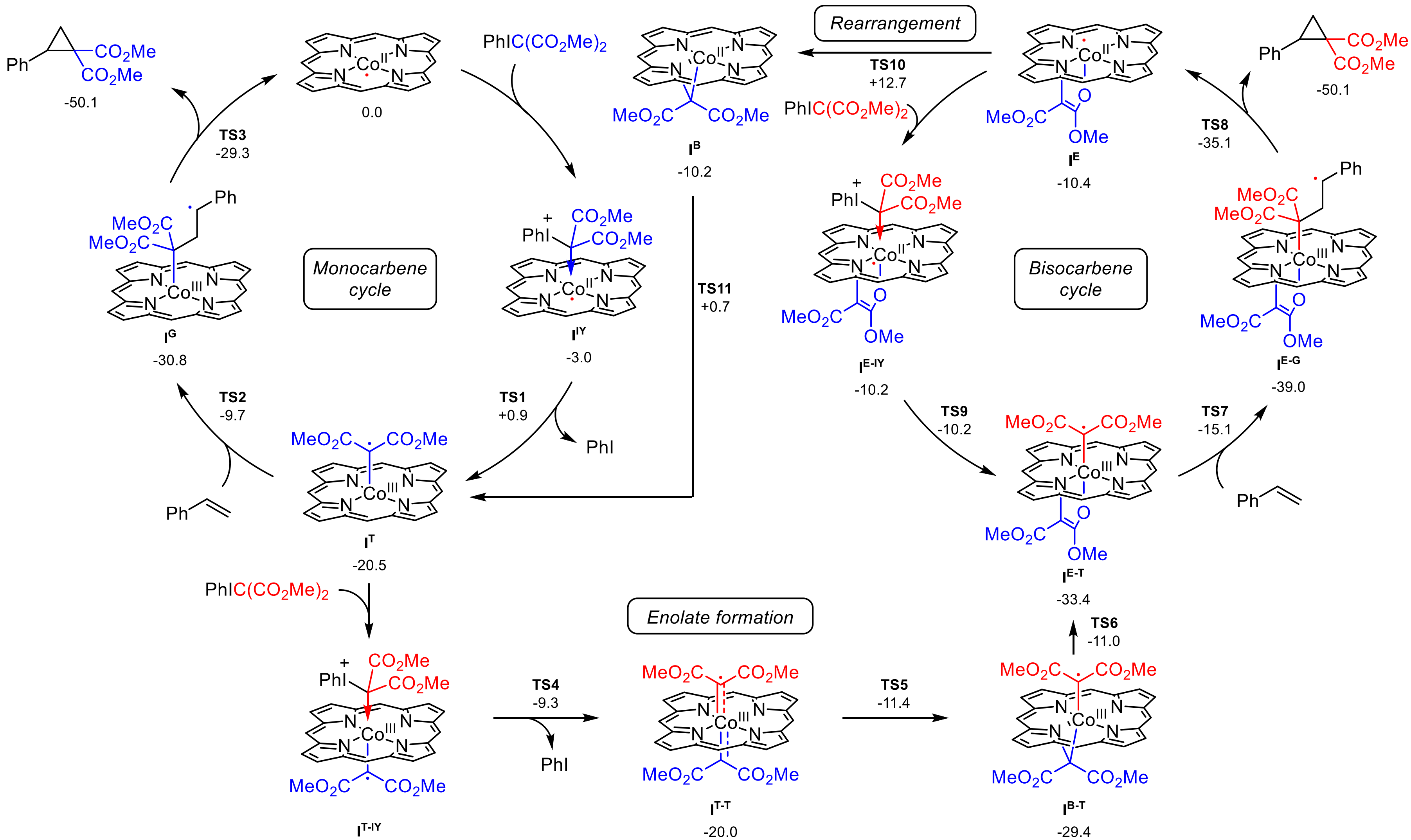
Overview of catalytic intermediates



R. F. J. Epping, M. M. Hoeksma, E. O. Bobylev, S. Mathew, B. de Bruin, *Nat. Chem.* **2022**, *14*, 550-557.

2.1.1 Cyclopropanation

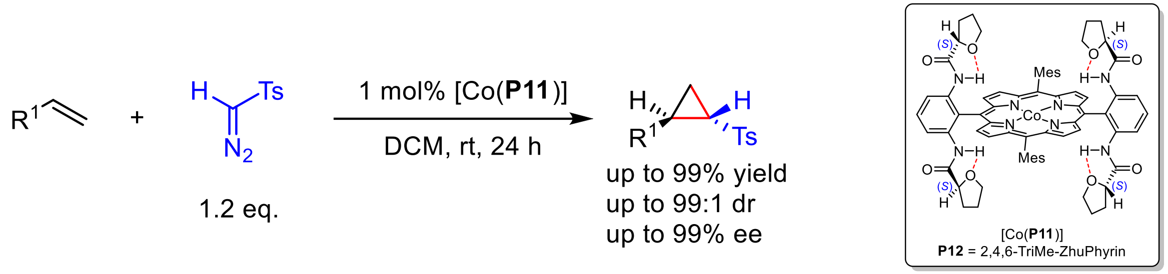
Proposed mechanism



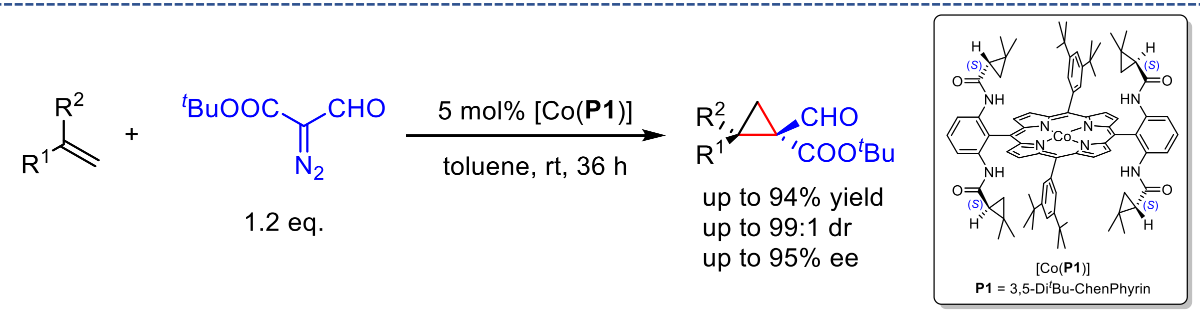
R. F. J. Epping, M. M. Hoeksma, E. O. Bobylev, S. Mathew, B. de Bruin, *Nat. Chem.* **2022**, *14*, 550-557.

2.1.1 Cyclopropanation

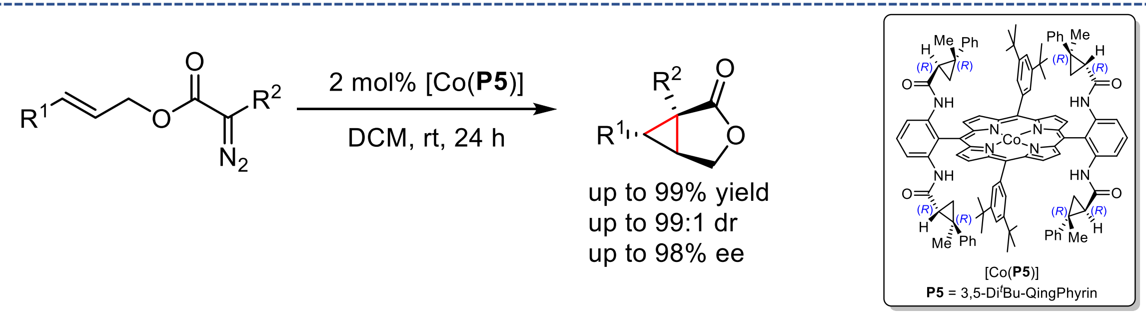
Acceptor-substituted diazo reagents



S. Zhu, J. V. Ruppel, H. Lu, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 5242-5243.



X. Xu, Y. Wang, X. Cui, L. Wojtasb, X. P. Zhang, *Chem. Sci.* **2017**, *8*, 4347-4351.



X. Xu, H. Lu, J. V. Ruppel, X. Cui, S. L. de Mesa, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 15292-15295.

More examples:

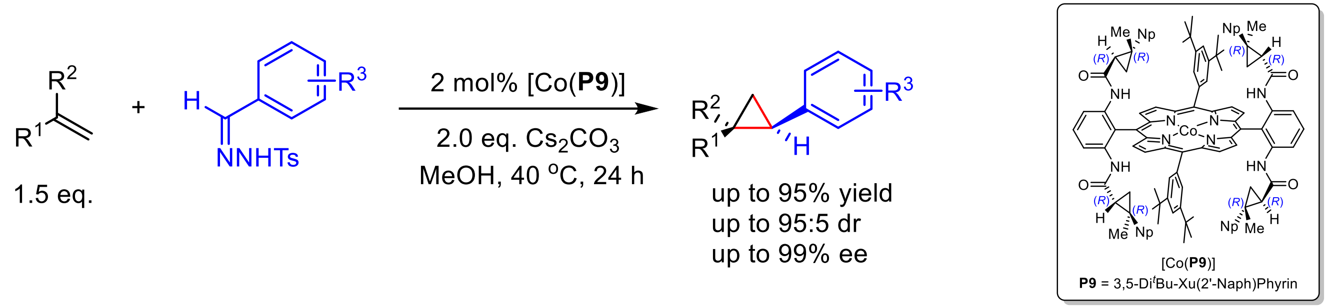
J. V. Ruppel, T. J. Gauthier, N. L. Snyder, J. A. Perman, X. P. Zhang, *Org. Lett.* **2009**, *11*, 2273-2276.

S. Zhu, X. Xu, J. A. Perman, X. P. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 12796-12799.

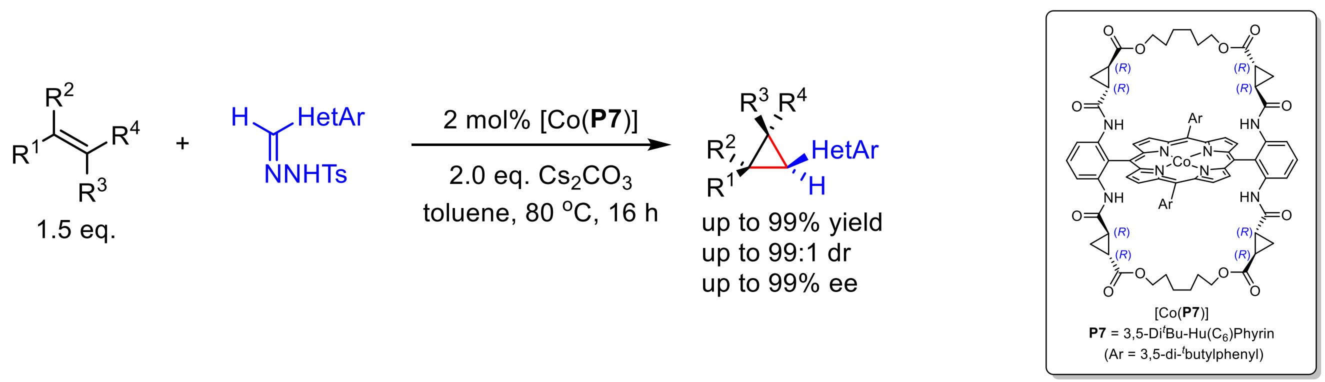
X. Xu, S. Zhu, X. Cui, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 11857-11861.

2.1.1 Cyclopropanation

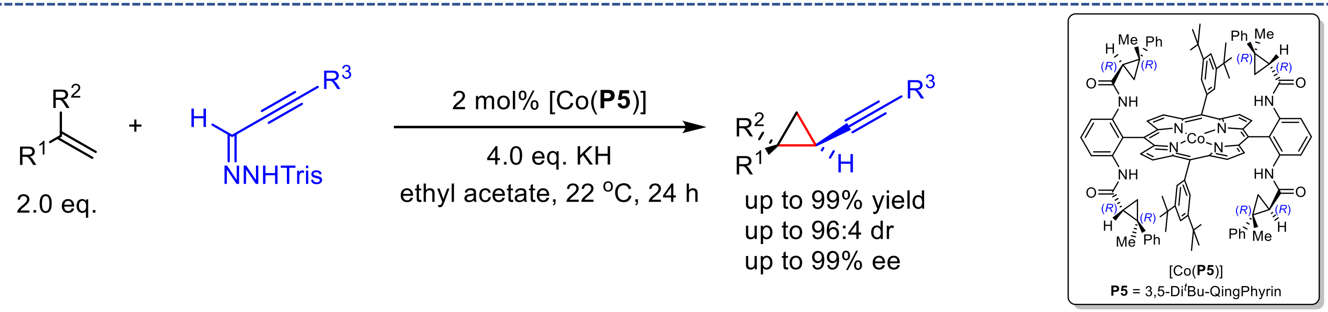
Donor-substituted diazo reagents



Y. Wang, X. Wen, X. Cui, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2017**, *139*, 1049-1052.

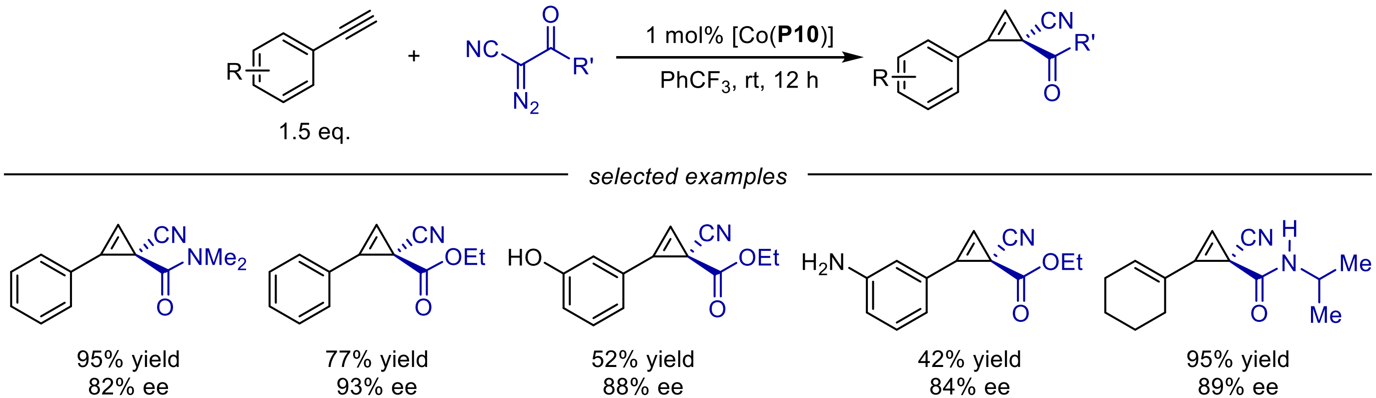


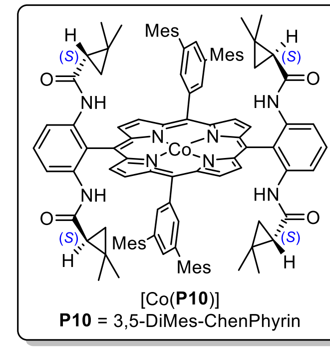
X. Wang, J. Ke, Y. Zhu, A. Deb, Y. Xu, X. P. Zhang, *J. Am. Chem. Soc.* **2021**, *143*, 11121-11129.



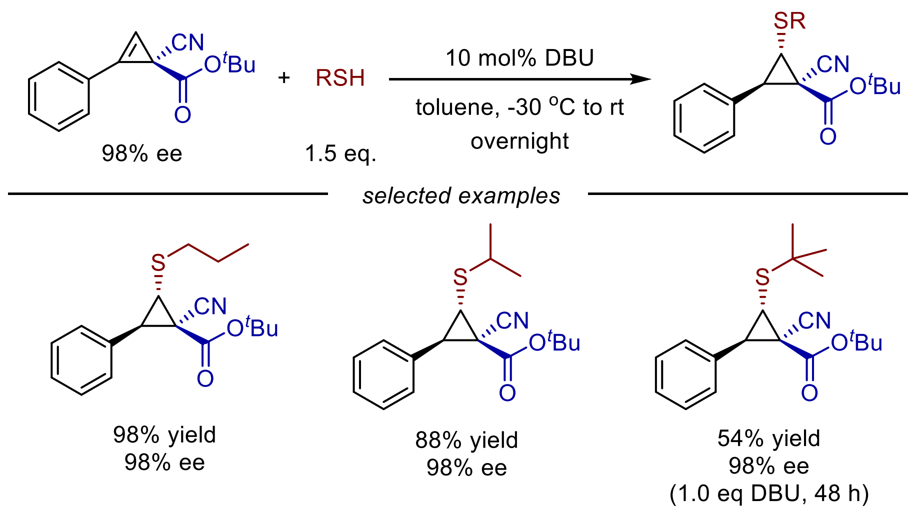
J. Ke, W.-C. C. Lee, X. Wang, Y. Wang, X. Wen, X. P. Zhang, *J. Am. Chem. Soc.* **2022**, *144*, 2368-2378.

2.1.2 Cyclopropenation



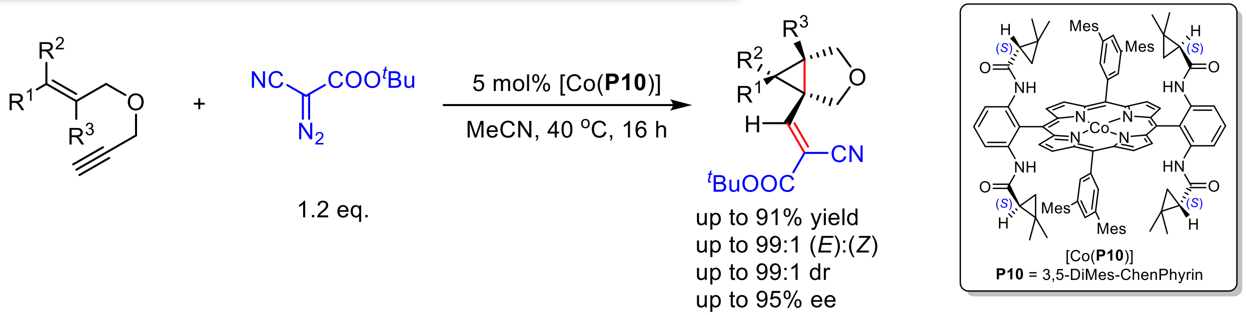


Transformations

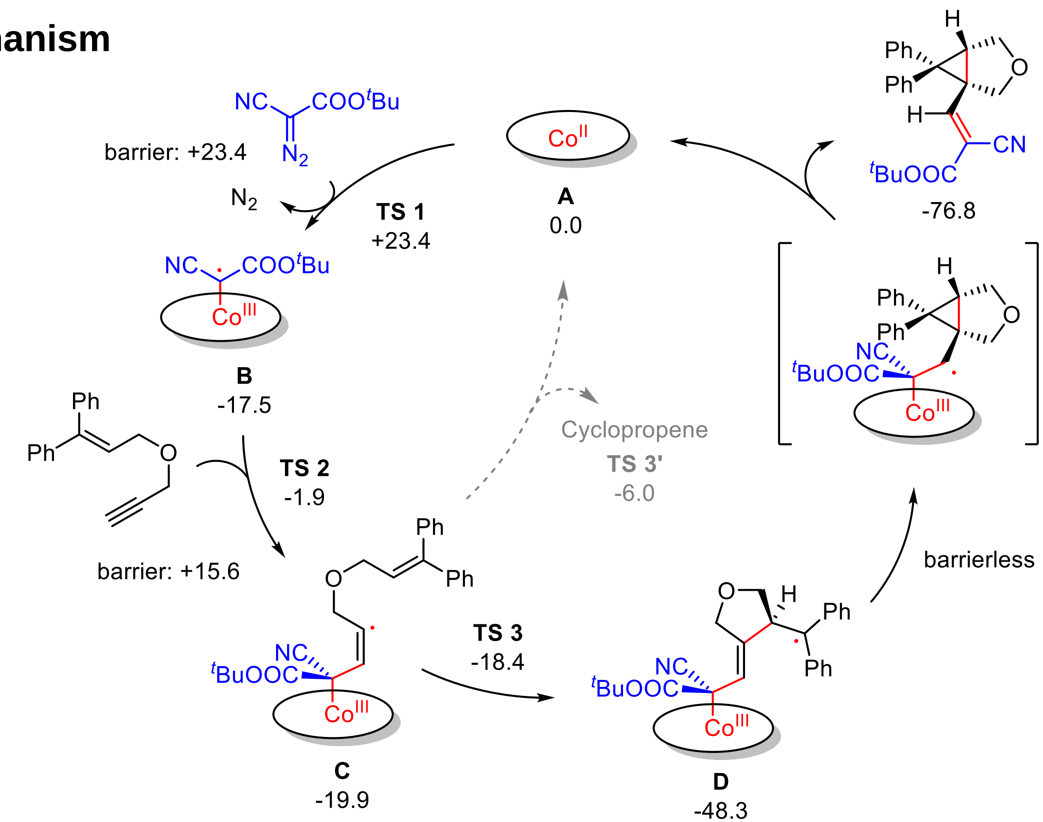


X. Cui, X. Xu, H. Lu, S. Zhu, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 3304-3307.

2.1.3 Miscellaneous Transformation

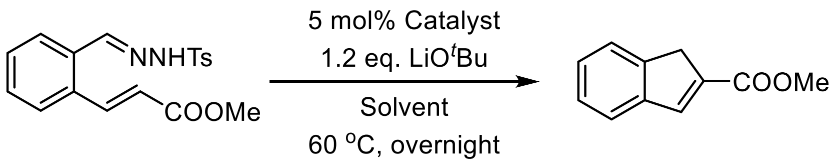


Proposed mechanism



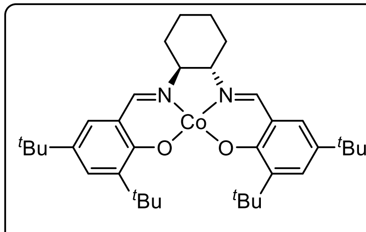
C. Zhang, D.-S. Wang, W.-C. C. Lee, A. M. McKillop, X. P. Zhang, *J. Am. Chem. Soc.* **2021**, *143*, 11130-11140.

2.1.3 Miscellaneous Transformation

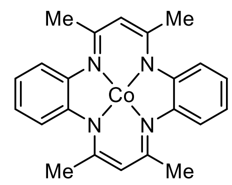


optimization

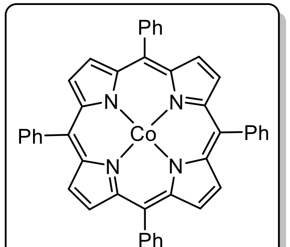
Entry	Catalyst	Solvent	Yield (%)
1	[Co(TPP)]	PhCl	51
2	[Co(salen)]	toluene	0
3	$[Rh_2(OAc)_4]$	toluene	0
4	**[Co(MeTAA)]**	**benzene**	**86**



[Co(salen)]

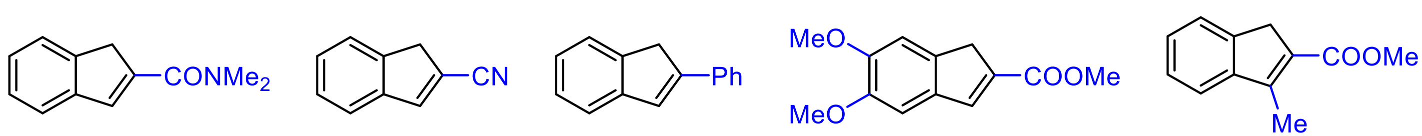


[Co(MeTAA)]



[Co(TPP)]

selected examples

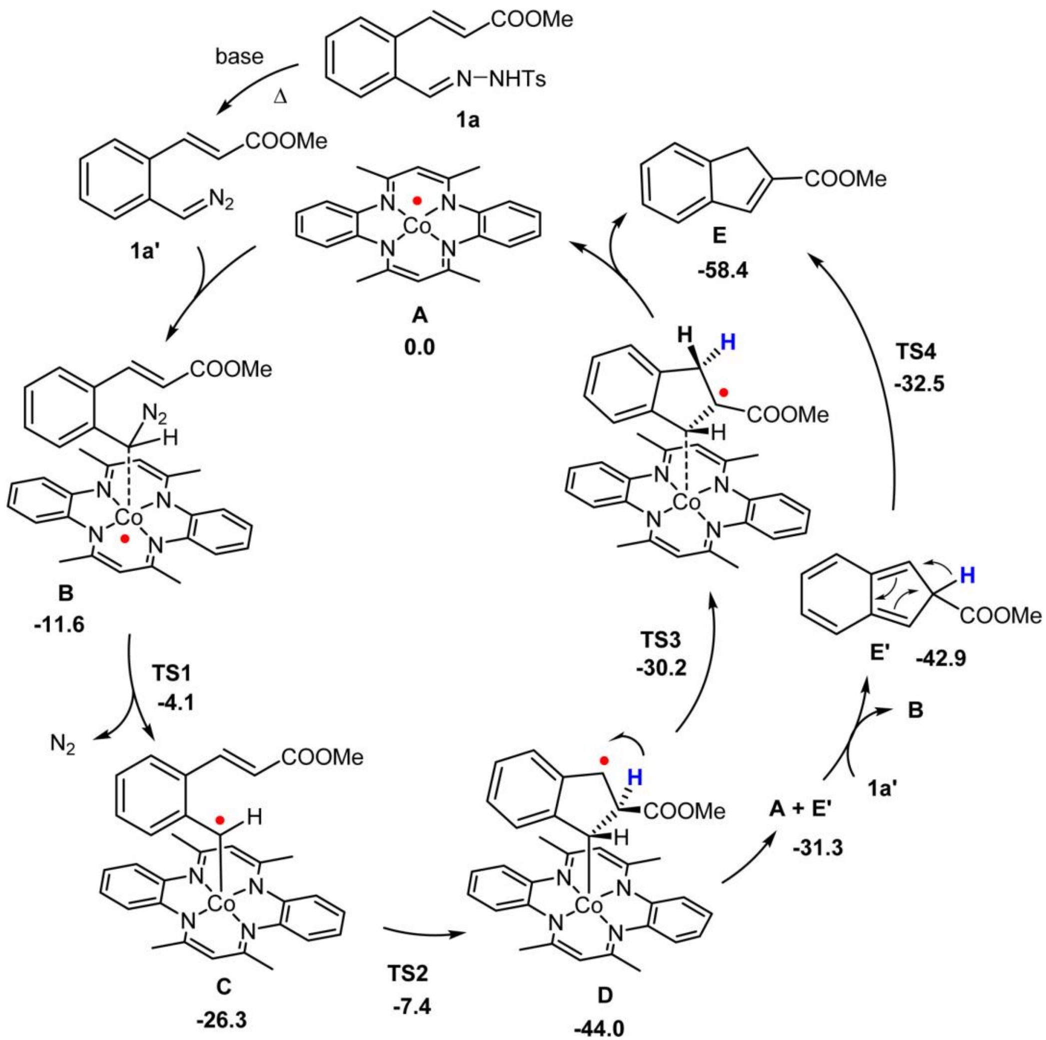


98% yield | 52% yield | 85% yield | 70% yield | 95% yield

B. G. Das, A. Chirila, M. Tromp, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2016**, *138*, 8968-8975.

2.1.3 Miscellaneous Transformation

Proposed mechanism

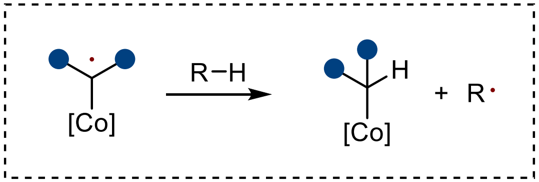


B. G. Das, A. Chirila, M. Tromp, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2016**, *138*, 8968-8975.

2.2

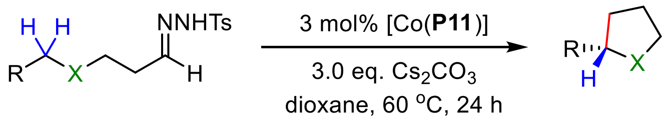
Catalytic C-C Formation via Cobalt-Carbene Radicals

——1,n-Hydrogen Atom Transfer

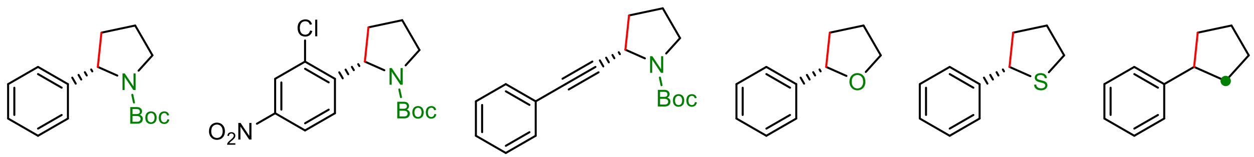


2.2 1,n-Hydrogen Atom Transfer

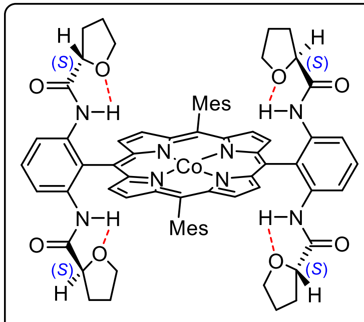
1,5-HAT



selected examples

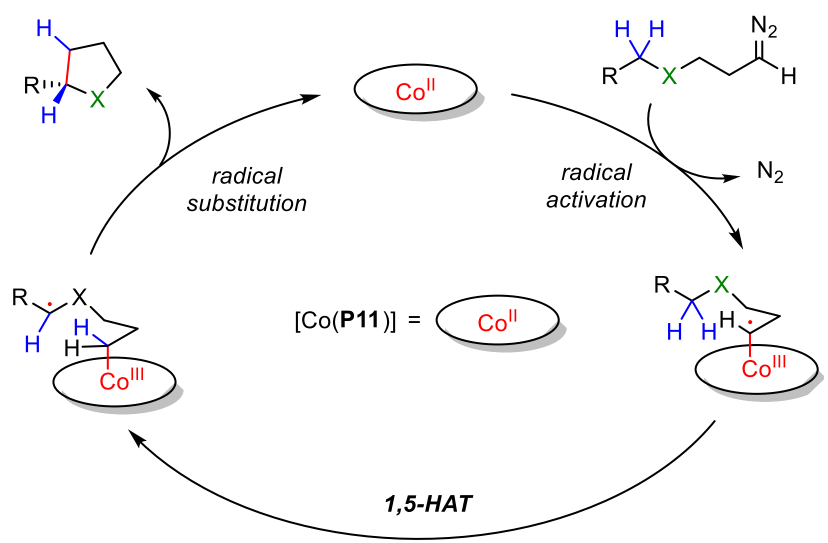


93% yield 92% ee	81% yield 92% ee	60% yield 59% ee	54% yield 85% ee	85% yield 91% ee	76% yield



[Co(**P11**)]
P11 = 2,4,6-TriMe-ZhuPhyrin

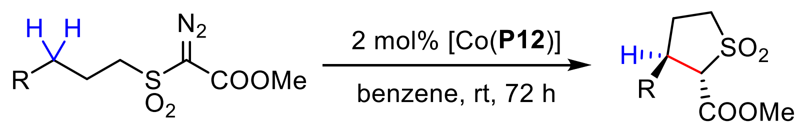
Proposed mechanism



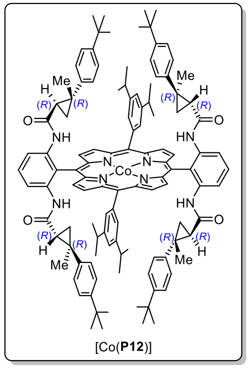
Y. Wang, X. Wen, X. Cui, X. P. Zhang, *J. Am. Chem. Soc.* **2018**, *140*, 4792-4796.

2.2 1,n-Hydrogen Atom Transfer

1,5-HAT
Formation of sulfolanes

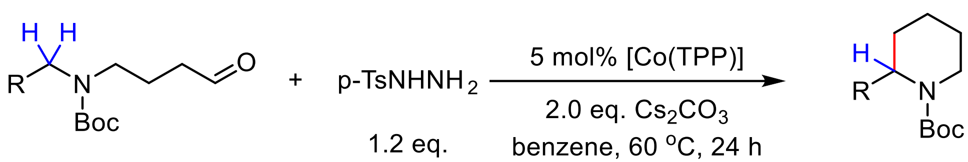


up to 98% yield
up to 97:3 dr
up to 94% ee

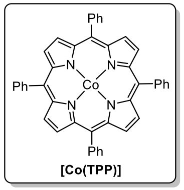


X. Cui, X. Xu, L.-M. Jin, L. Wojtas, X. Pe. Zhang, *Chem. Sci.* **2015**, *6*, 1219-1224.

1,6-HAT
Formation of piperidines

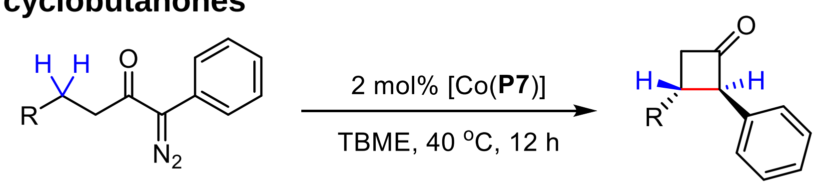


up to 96% yield

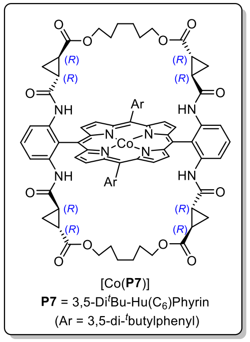


M. Lankelma, A. M. Olivares, B. de Bruin, *Chem. Eur. J.* **2019**, *25*, 5658-5663.

1,4-HAT
Formation of cyclobutanones



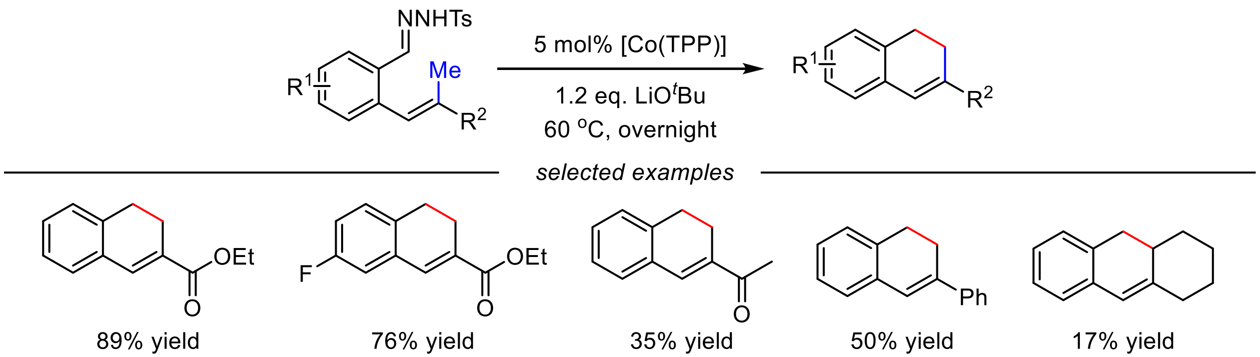
up to 93% yield
up to 99:1 dr
up to 96% ee

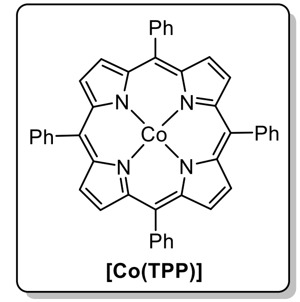


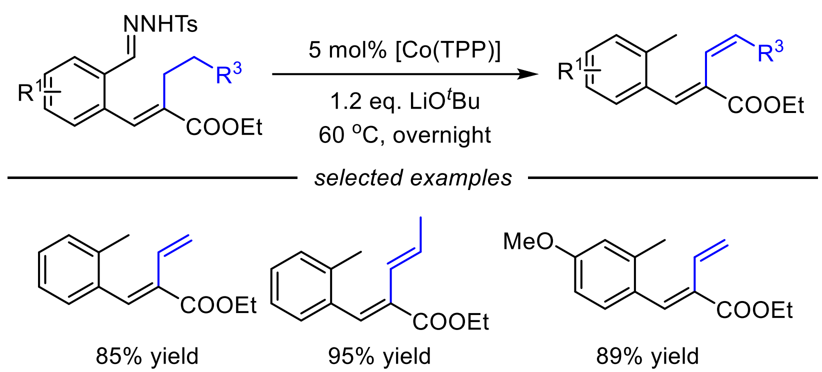
J. Xie, P. Xu, Y. Zhu, J. Wang, W.-C. C. Lee, X. P. Zhang, *J. Am. Chem. Soc.* **2021**, *143*, 11670-11678.

More examples:
A. S. Karns, M. Goswami, B. de Bruin, *Chem. Eur. J.* **2018**, *24*, 5253-5258.
X. Wen, Y. Wang, X. P. Zhang, *Chem. Sci.* **2018**, *9*, 5082-5086.

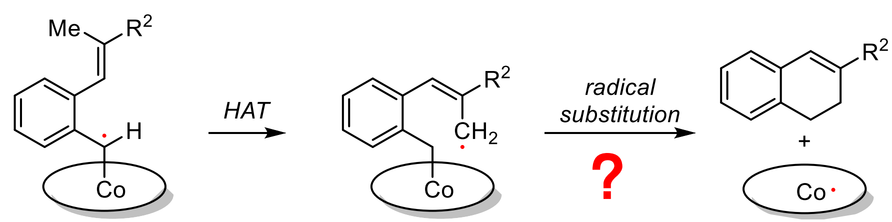
2.2 1,n-Hydrogen Atom Transfer







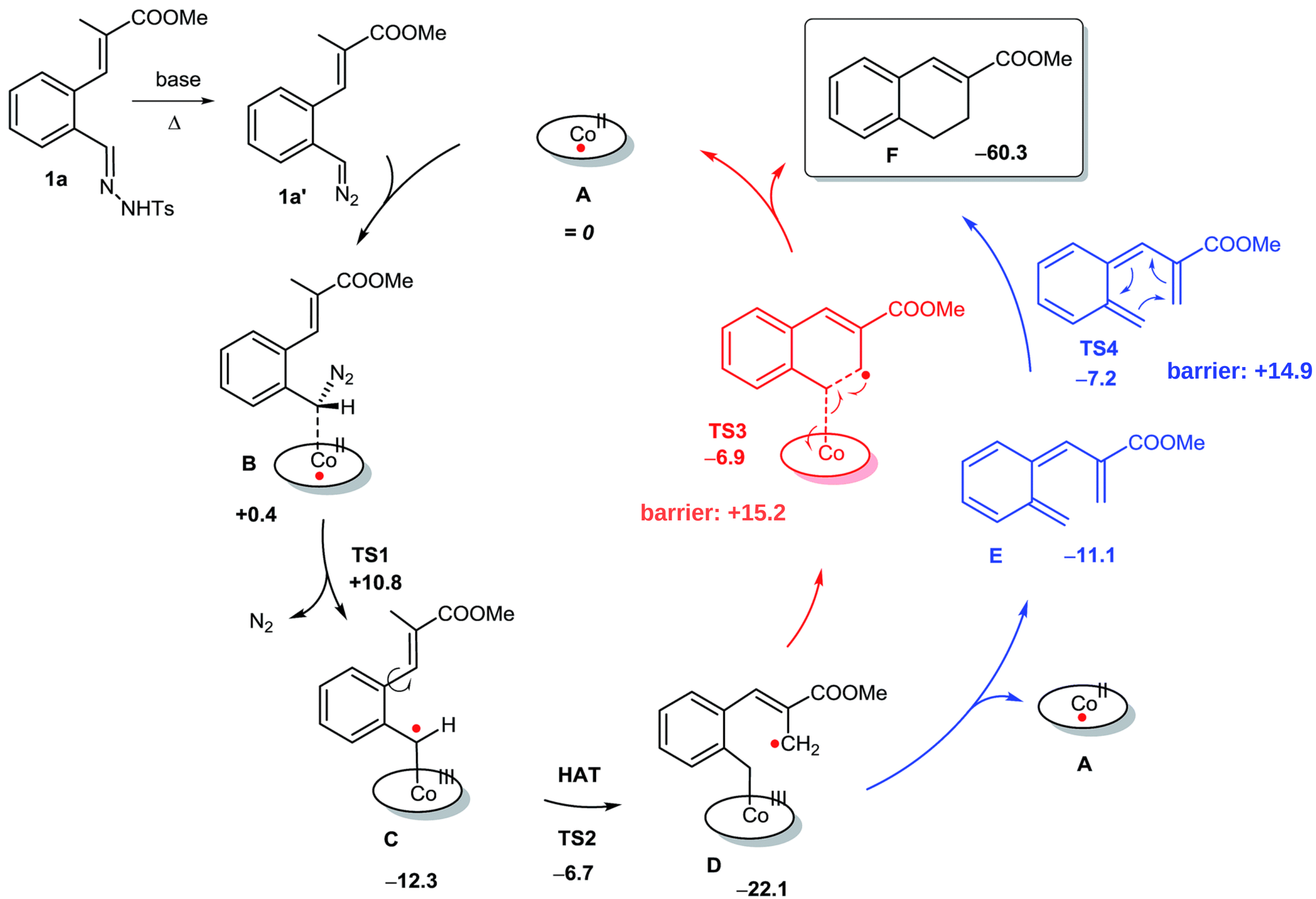
Anticipated pathway



C. te Grotenhuis, B. G. Das, P. F. Kuijpers, W. Hageman, M. Trouwborst, B. de Bruin, *Chem. Sci.* **2017**, *8*, 8221-8230.

2.2 1,n-Hydrogen Atom Transfer

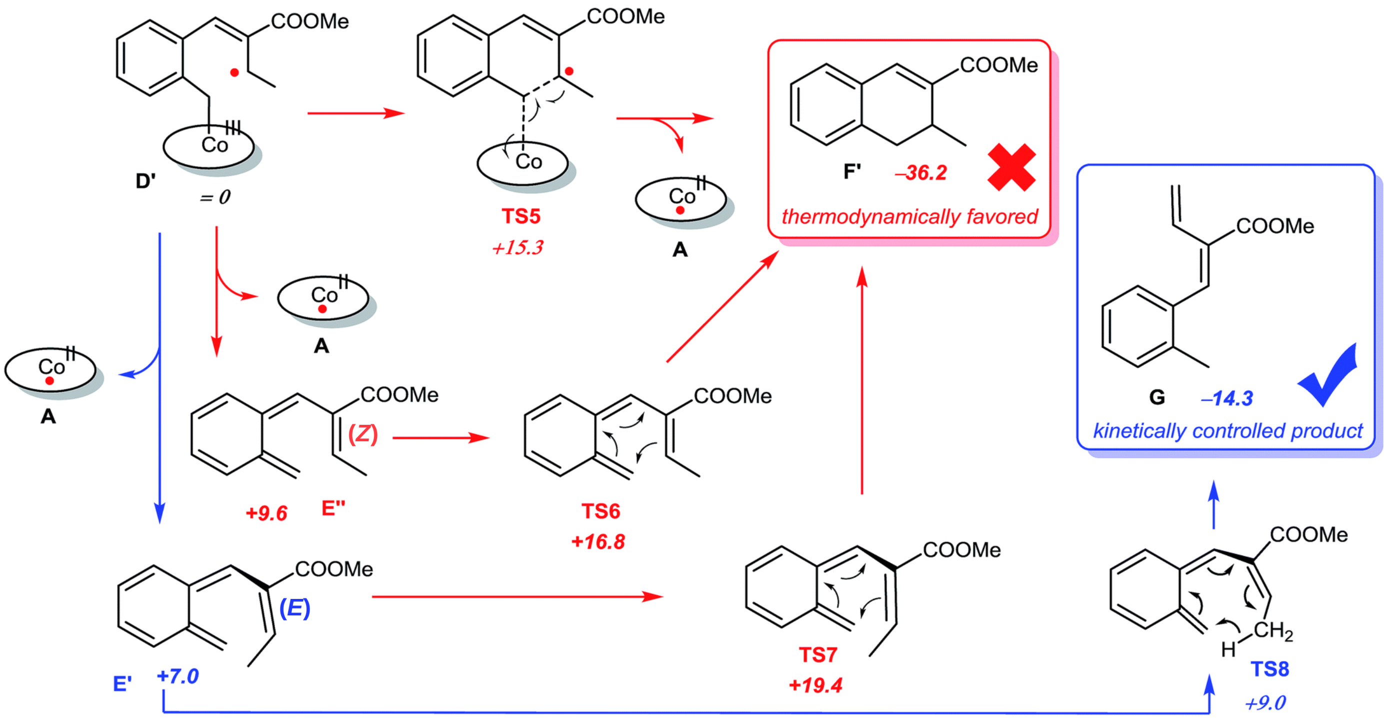
Proposed mechanism



C. te Grotenhuis, B. G. Das, P. F. Kuijpers, W. Hageman, M. Trouwborst, B. de Bruin, *Chem. Sci.* **2017**, *8*, 8221-8230.

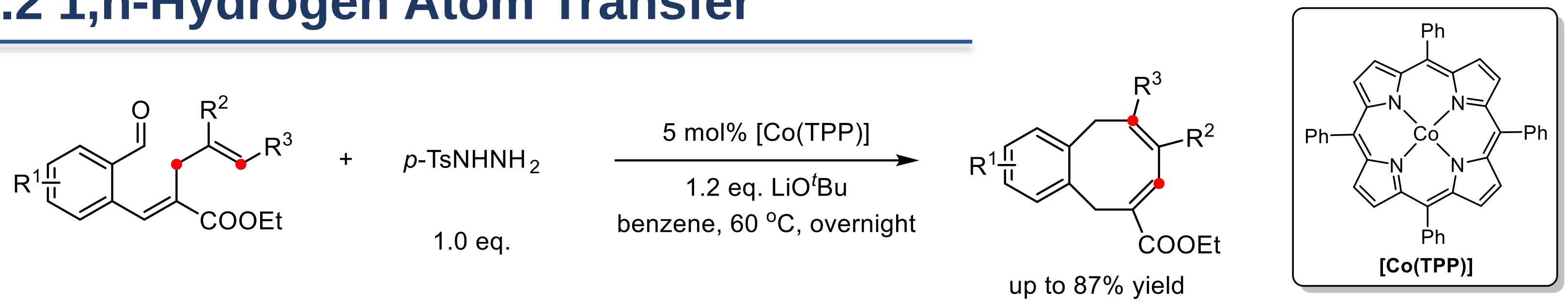
2.2 1,n-Hydrogen Atom Transfer

Proposed mechanism

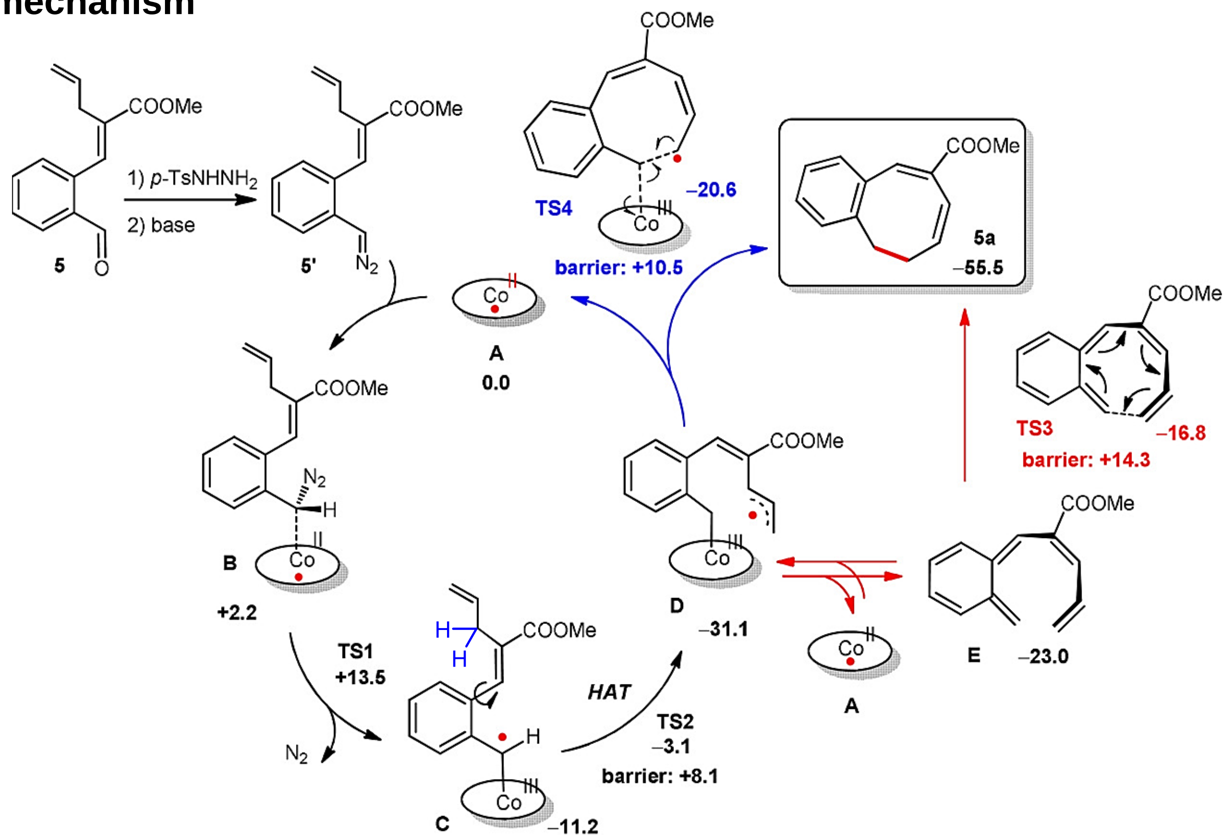


C. te Grotenhuis, B. G. Das, P. F. Kuijpers, W. Hageman, M. Trouwborst, B. de Bruin, *Chem. Sci.* **2017**, *8*, 8221-8230.

2.2 1,n-Hydrogen Atom Transfer



Proposed mechanism

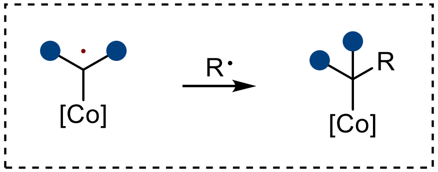


M. Zhou, M. Lankelma, J. I. van der Vlugt, B. de Bruin, *Angew. Chem. Int. Ed.* **2020**, *59*, 11073-11079.

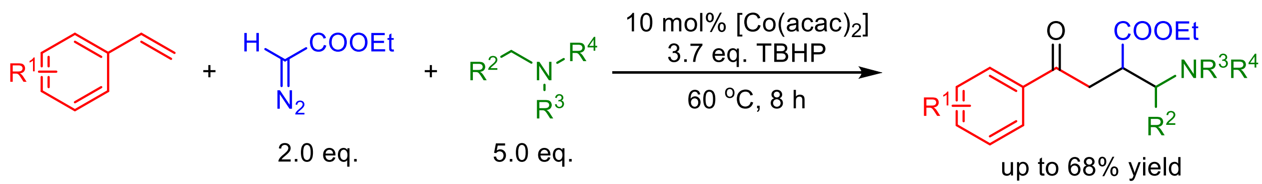
2.3

Catalytic C-C Formation via Cobalt-Carbene Radicals

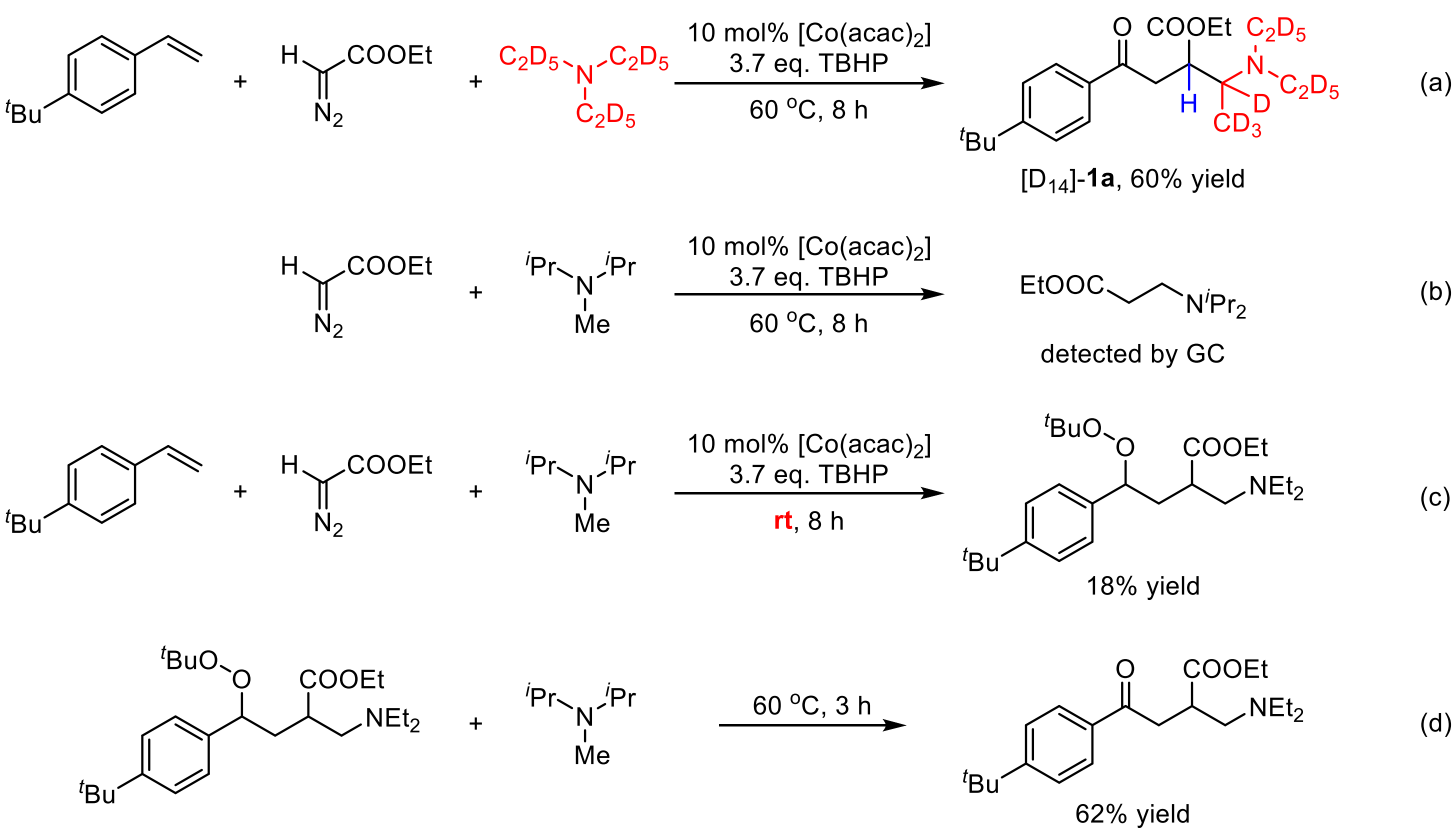
——Radical-Radical Coupling



2.3 Radical-Radical Coupling



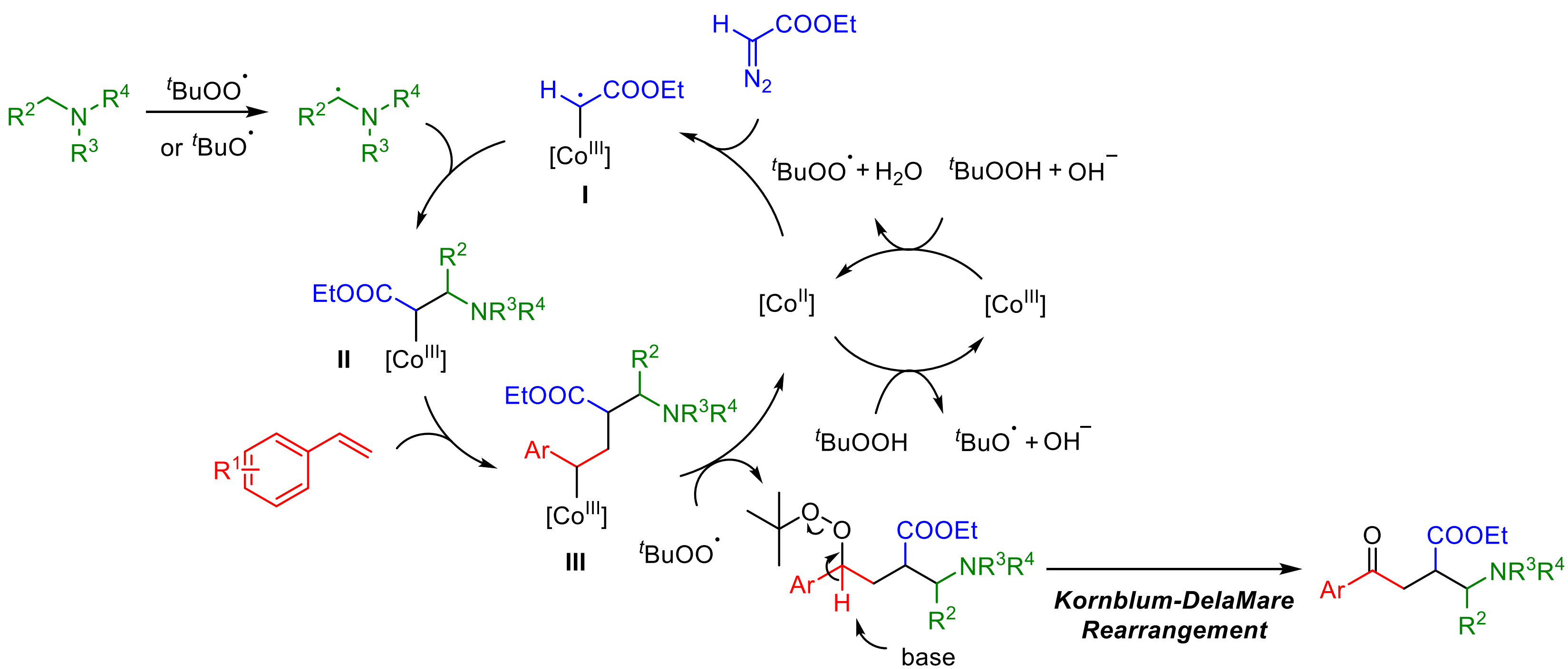
Mechanistic investigations



J. Zhang, J. Jiang, D. Xu, Q. Luo, H. Wang, J. Chen, H. Li, Y. Wang, X. Wan, *Angew. Chem. Int. Ed.* **2015**, *54*, 1231-1235.

2.3 Radical-Radical Coupling

Proposed mechanism



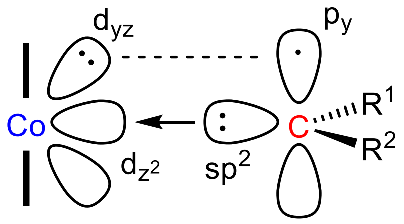
J. Zhang, J. Jiang, D. Xu, Q. Luo, H. Wang, J. Chen, H. Li, Y. Wang, X. Wan, *Angew. Chem. Int. Ed.* **2015**, *54*, 1231-1235.

3

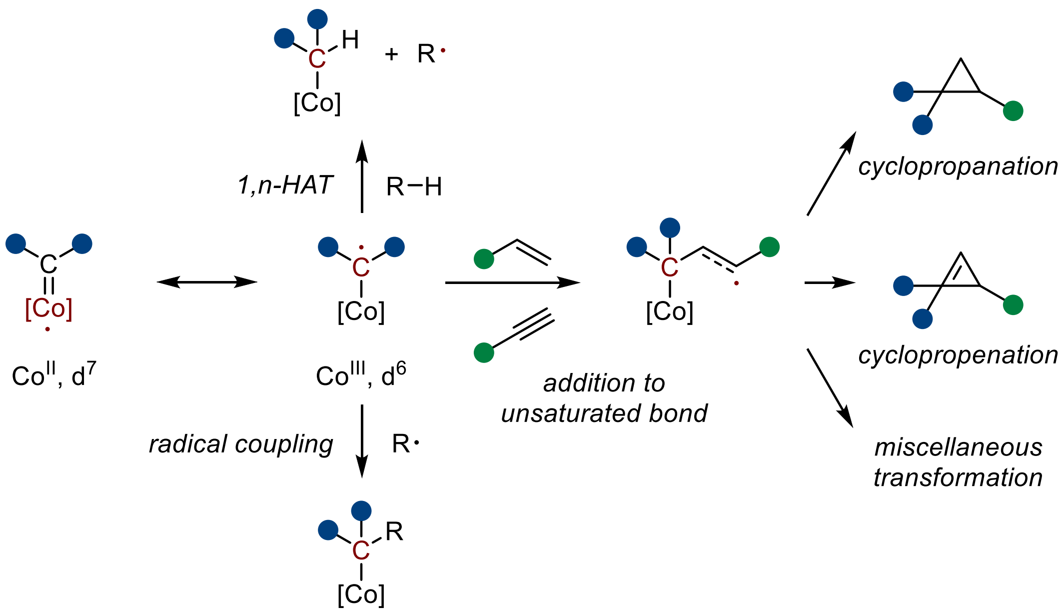
Summary and Outlook

3 Summary and Outlook

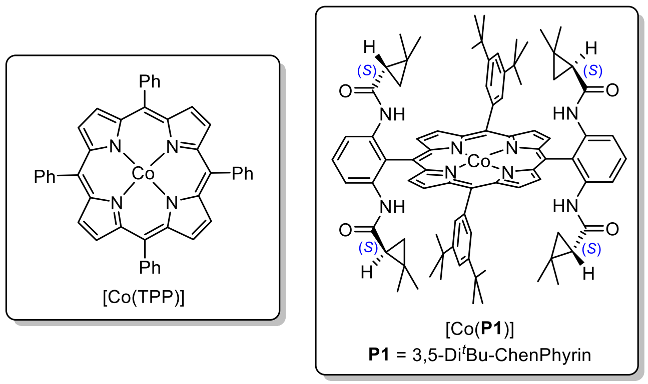
- Carbene-type: more nucleophilic than Fischer carbene
- ✓ *excellent chemoselectivity*
- ✓ *simplified procedure*
- ✓ *broad substrate scopes*
- Radical-type: excellent regio- and stereoselectivity



bonding model

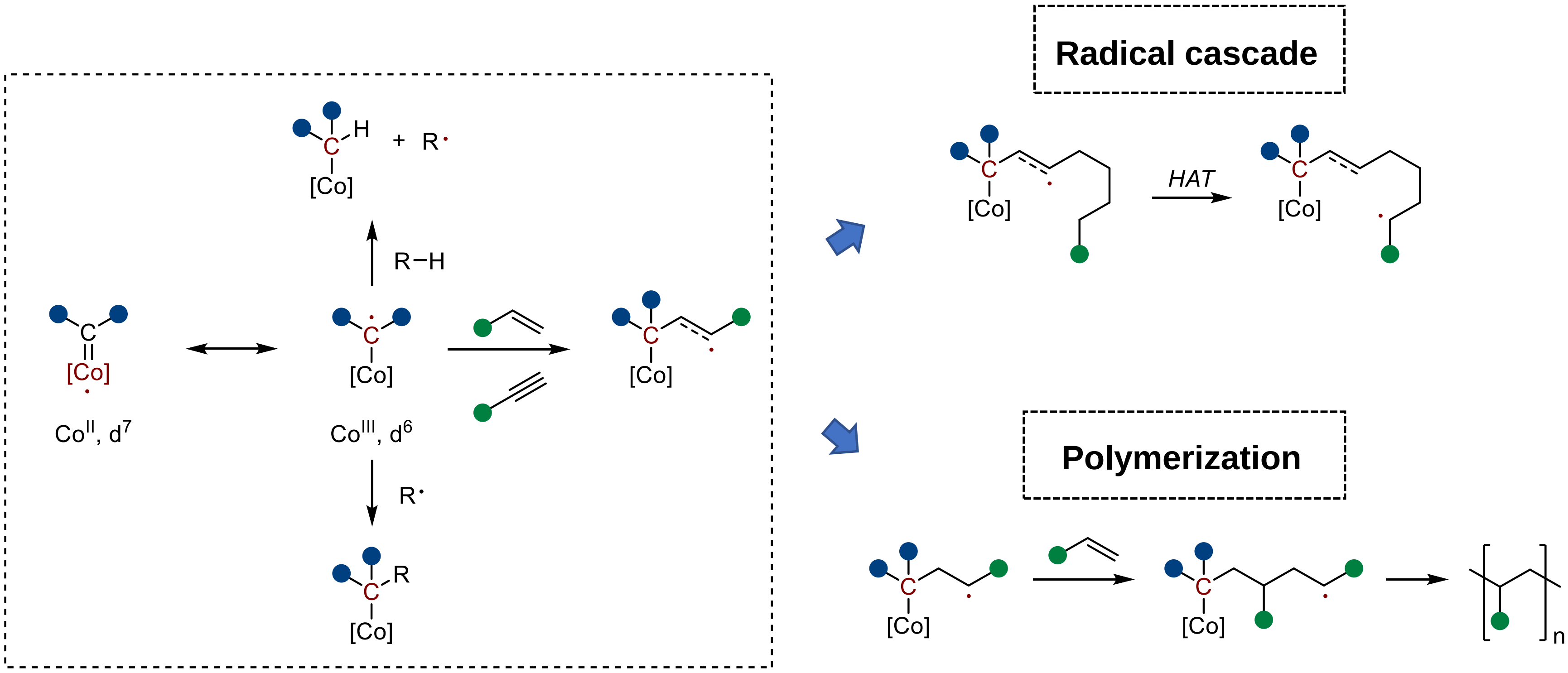


reaction pathways



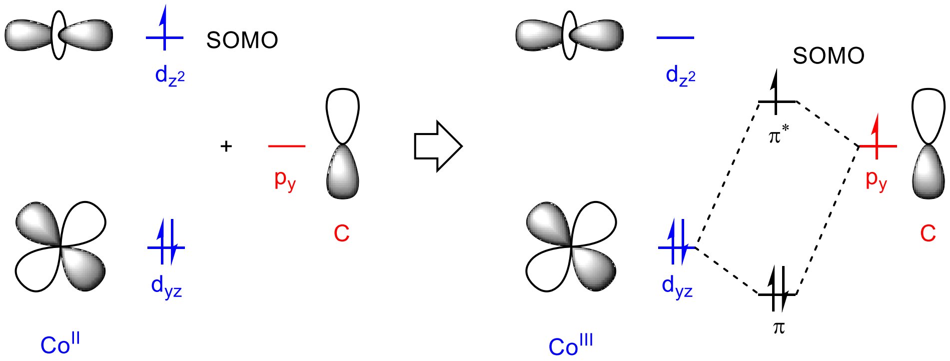
typical catalysts

3 Summary and Outlook



3 Summary and Outlook

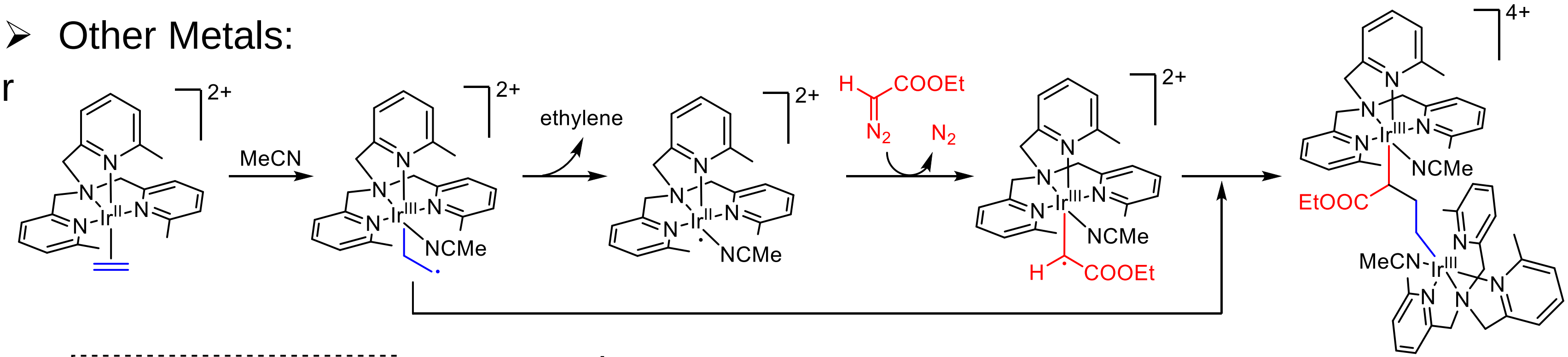
- Why cobalt?



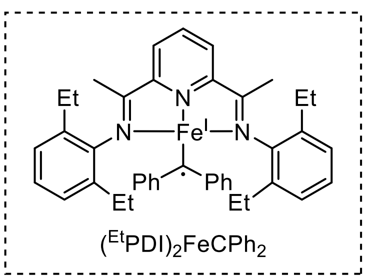
Role of ligands?

- Other Metals:

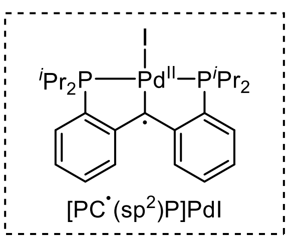
Ir



Fe



Pd



W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2010**, *132*, 10891-10902.
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Thank You

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