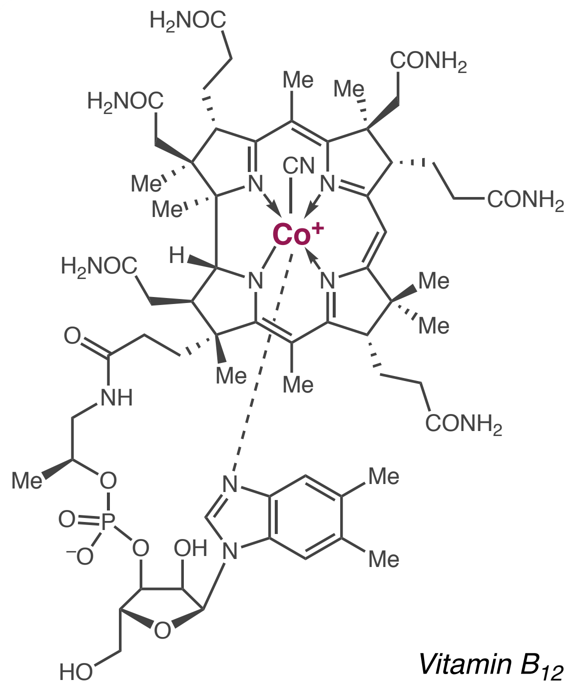
Cobalt in Organic Synthesis



Vitamin B_{12}

Tao Wang

MacMillan Lab Group Meeting

November 29, 2017

Background

Facts about cobalt

27

Co

Cobalt

58.9332

$CoCl_2 \cdot 6H_2O$

Electron configuration	[Ar] $3d^7$ $4s^2$
LD_{50} of cobalt salts	150 – 500 mg/kg
Safety	8th-most-prevalent allergen (1st is nickel)
Nobel Prize	Alfred Werner, 1913 for his contribution to coordination chemistry: proposed correct structure of $[Co(NH_3)_6]^{3+}$

contains ***$CoCl_2$***

$+ H_2O$

Background

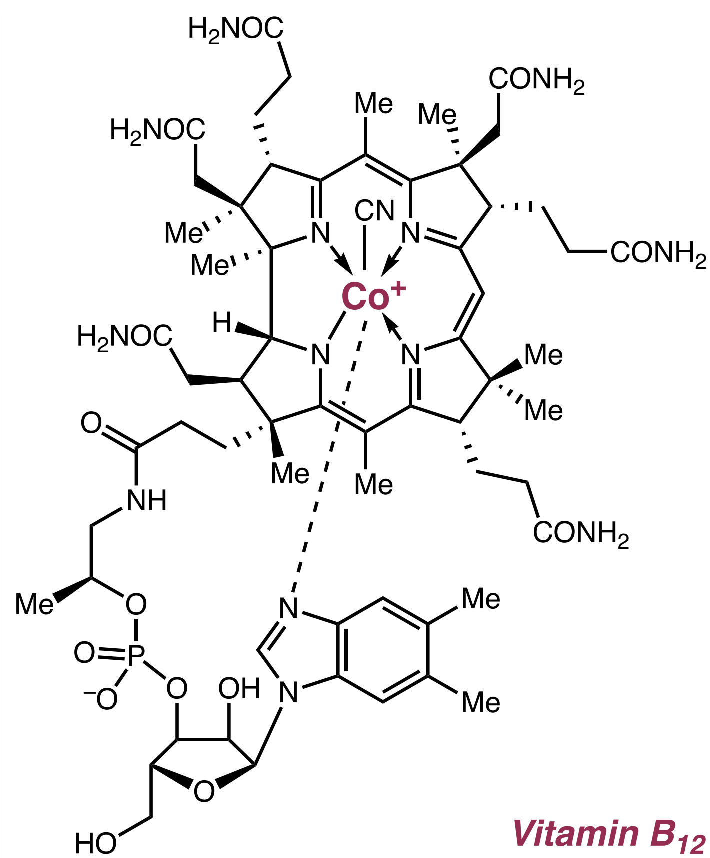
Oxidation state of cobalt

- Most common: +1, +2, +3
- Co(II) forms both Td and Oh complexes (**L** dependent)
- Co(III) prefer Oh complexes

$$Co^{3+}\,(aq) + e^{-} \longrightarrow Co^{2+}\,(aq) \qquad \mathbf{E} = +1.82\ V$$

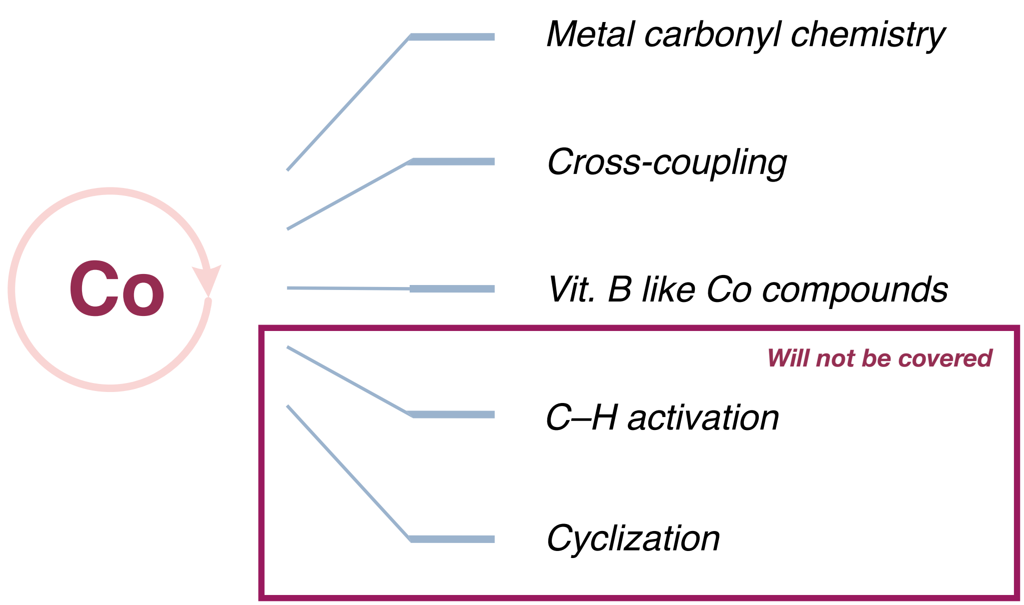
Cobalt in Nature: Vitamin B_{12}

- Most complex of all vitamins
- Play a key role in function of brain and nervous system and the formation of red blood cells
- Isolated in 1948 (Shorb)
- First total synthesis 1972 (Woodward)



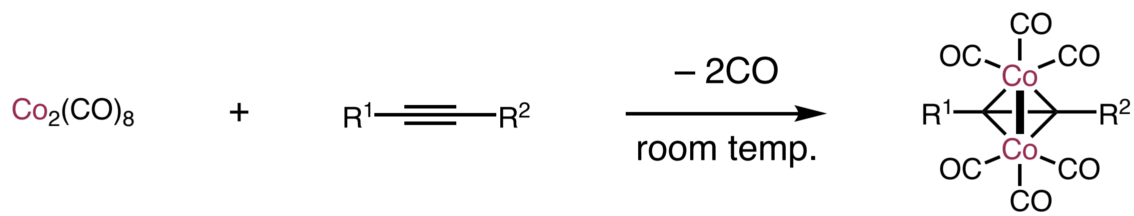
Vitamin B_{12}

Overview of cobalt catalysis

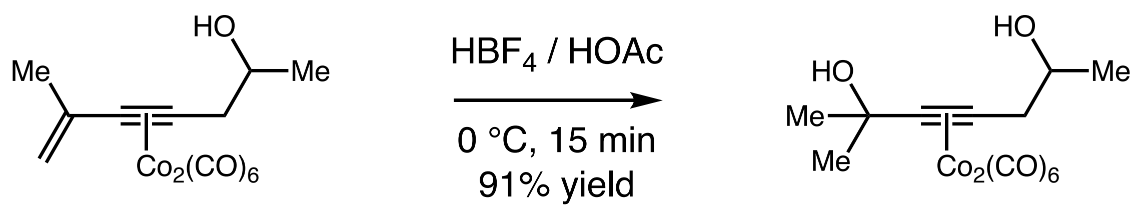


Metal carbonyl chemistry

- Reaction with alkyne



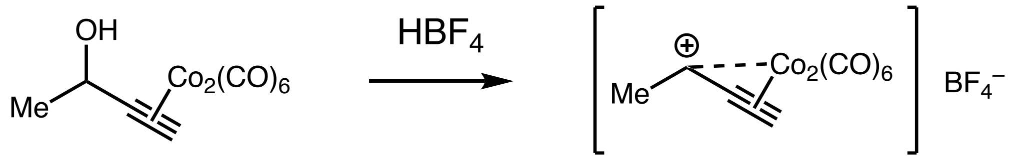
- Serve as an alkyne protecting group



Nicholas, K. M.; Pettit, R. *Tetrahedron Lett.* **1971**, *12*, 3475–3478.

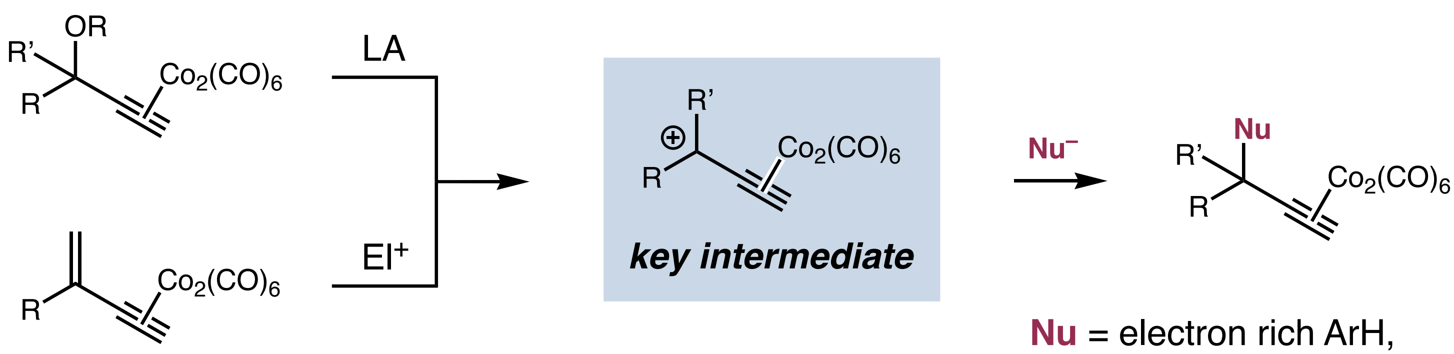
Nicholas reaction

- Highly stable propargylic carbocation



60 grams isolated
burgundy-red salt

- Nicholas reaction

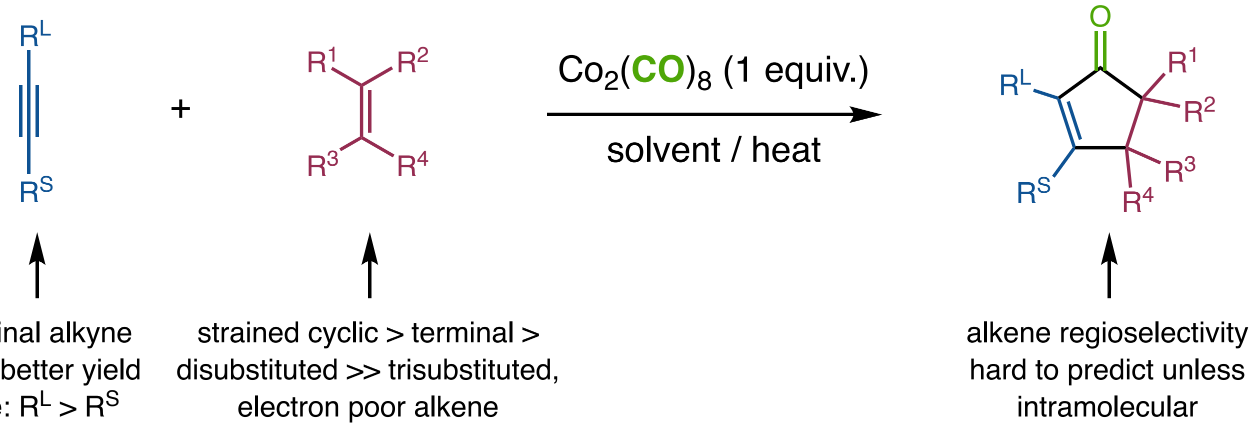


Nu = electron rich ArH, ketone, allyl–SiR_3, and etc.

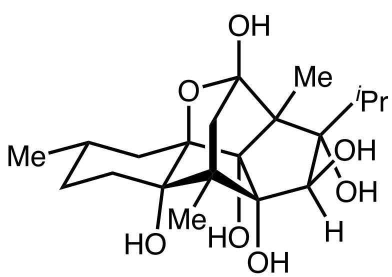
Varghese, V.; Saha, M.; Nicholas, K. M. *Org. Synth.* **1989**, *67*, 141.

Pauson–Khand reaction

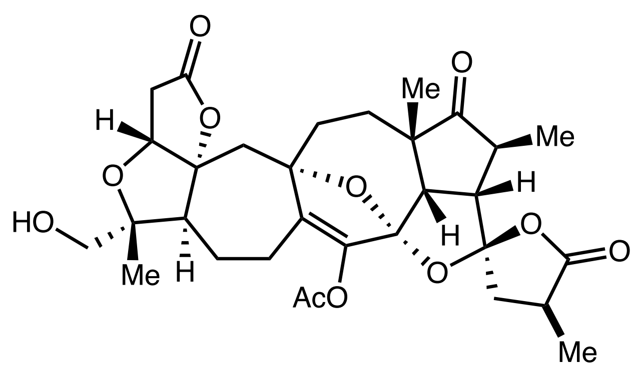
General reaction scheme



Recent total synthesis using Pauson-Khand



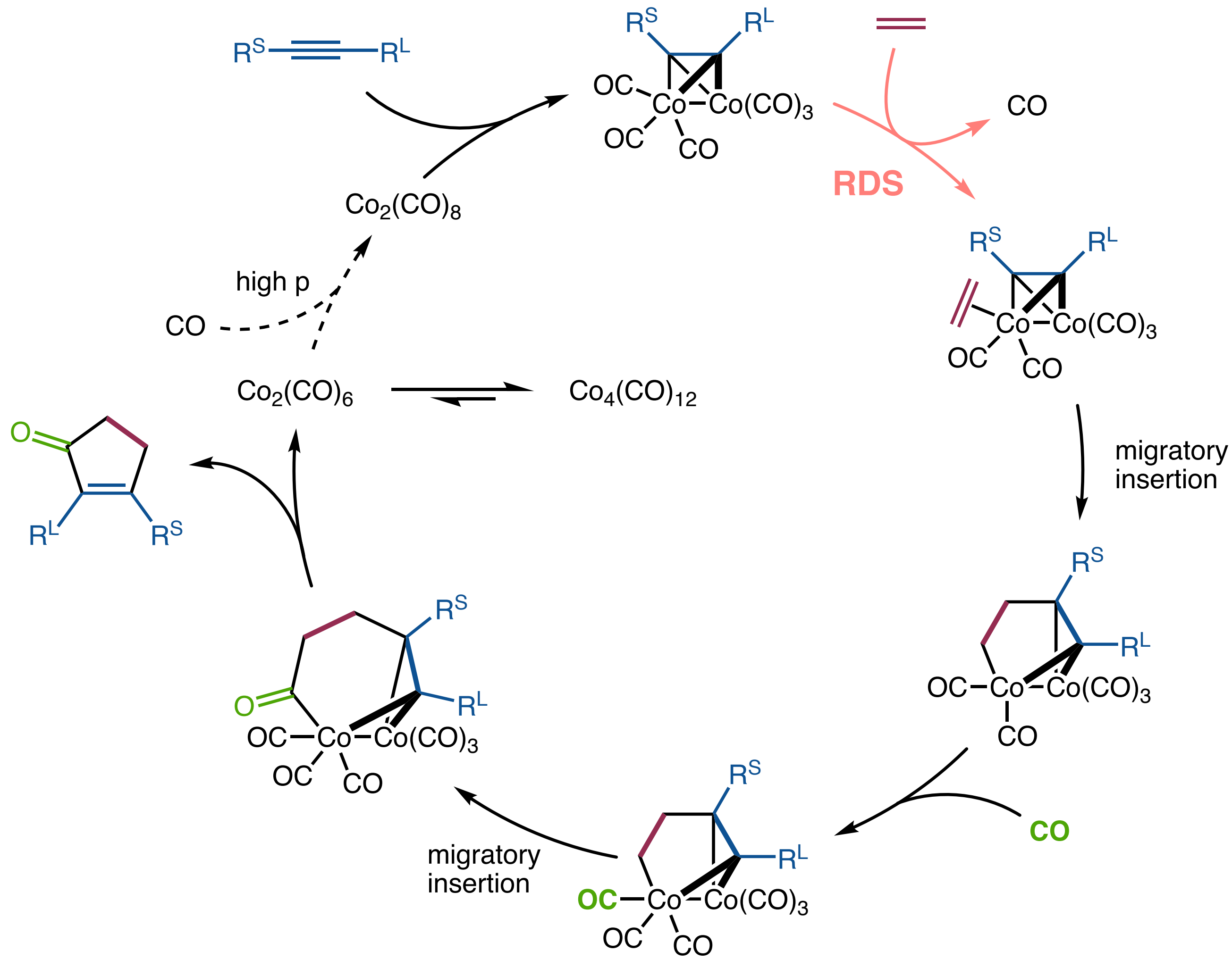
(+)-ryanodol (Reisman 2016)



lancifodilactone G acetate (Yang 2017)

Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1*, **1973**, *0*, 977–981
Chuang, K. V.; Xu, C.; Reisman, S. E. Science **2016**, *353*, 912–915.
Liu, D.–D.; Yang, Z. et al *J. Am. Chem. Soc.* **2017**, *139*, 5732–5735.

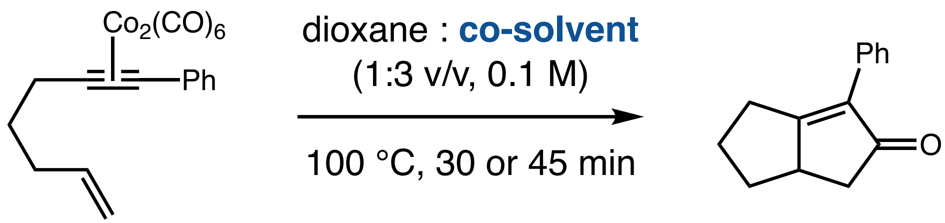
Reaction mechanism



Gibson, S. E.; Mainolfi, N. *Angew. Chem. Int. Ed.* **2005**, *44* 3022–3037.

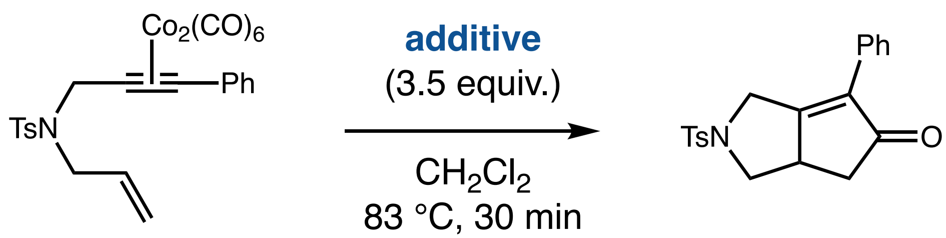
Additives promote CO dissociation

Amine as additive



co-solvent	SM	product
H_2O	91%	0%
1 M $NH_3 \cdot H_2O$	0%	**96%**

Sulfide as additive

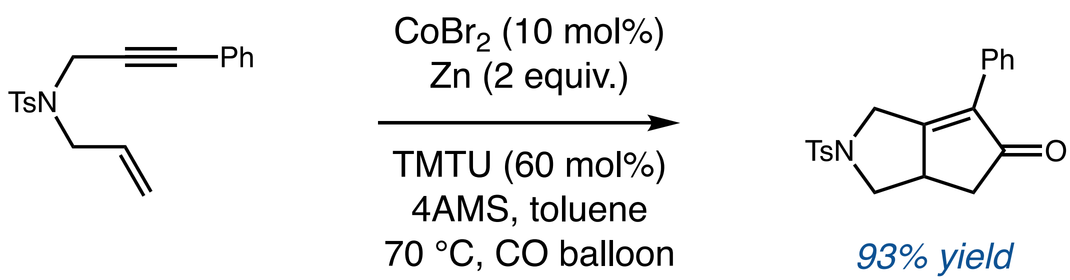


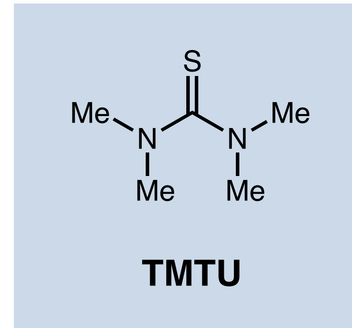
additive	yield
$CyNH_2$	15%
n-BuSMe	**79%**

Sugihara, T. et al. *ACIE*, **1997**, *36*, 2801–2804.
Sugihara, T. et al. *Synlett*, **1999**, *6*, 771–773.

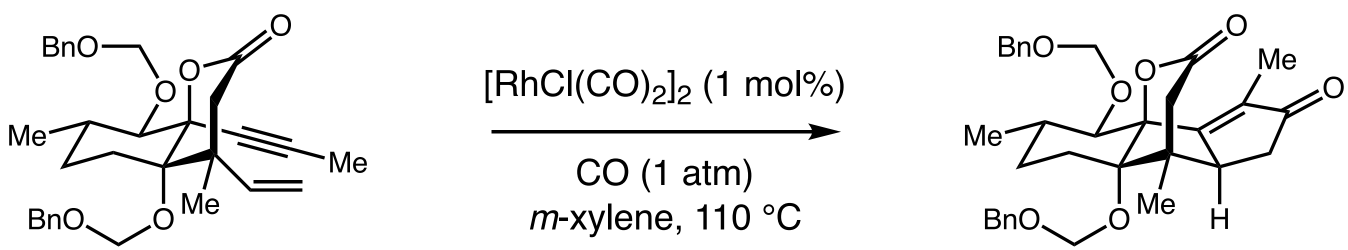
Catalytic Pauson-Khand

Catalytic Pauson-Khand with cobalt





Other metals (eg. Pd, Rh, Ir and etc.) also work



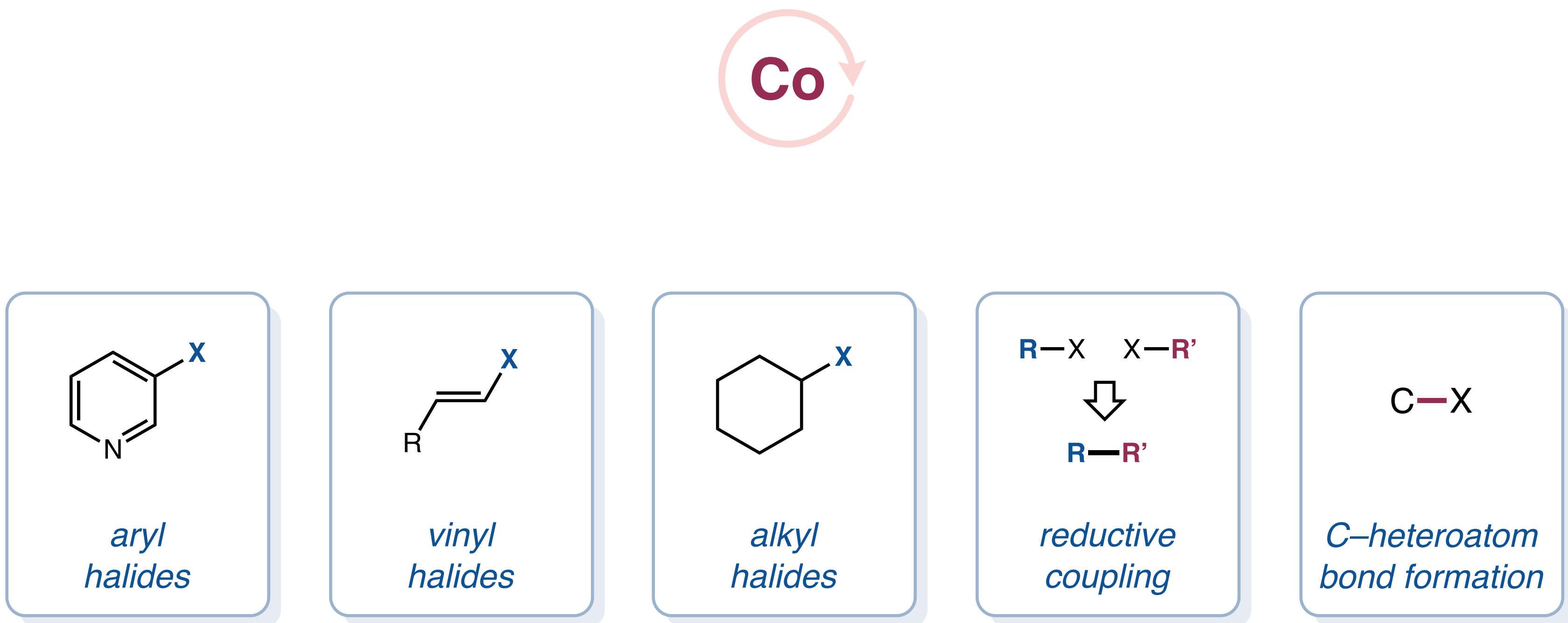
85% yield, > 20:1 dr

- *Catalytic PKR often require fine tuning of reaction conditions*

Wang, Y.; Xu, L.; Yu, R.; Chen, J.; Yang, Z. *Chem. Commun.* **2012**, *48*, 8183–8185.

Chuang, K. V.; Xu, C.; Reisman, S. E. Science **2016**, *353*, 912–915.

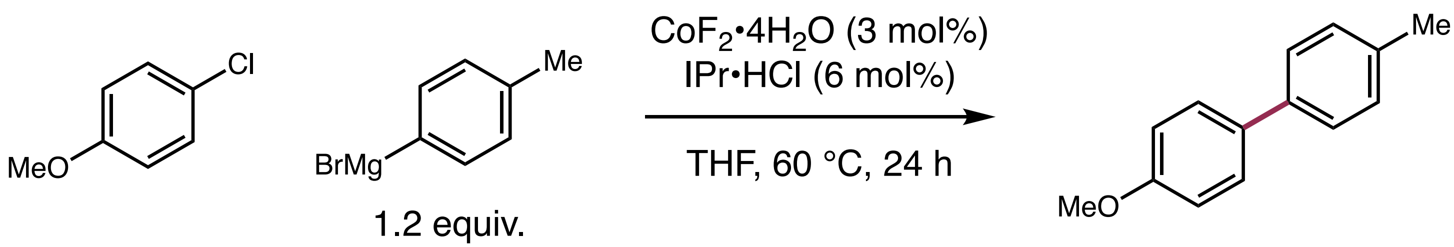
Cobalt catalyzed cross-coupling reactions



Coupling with aryl halides

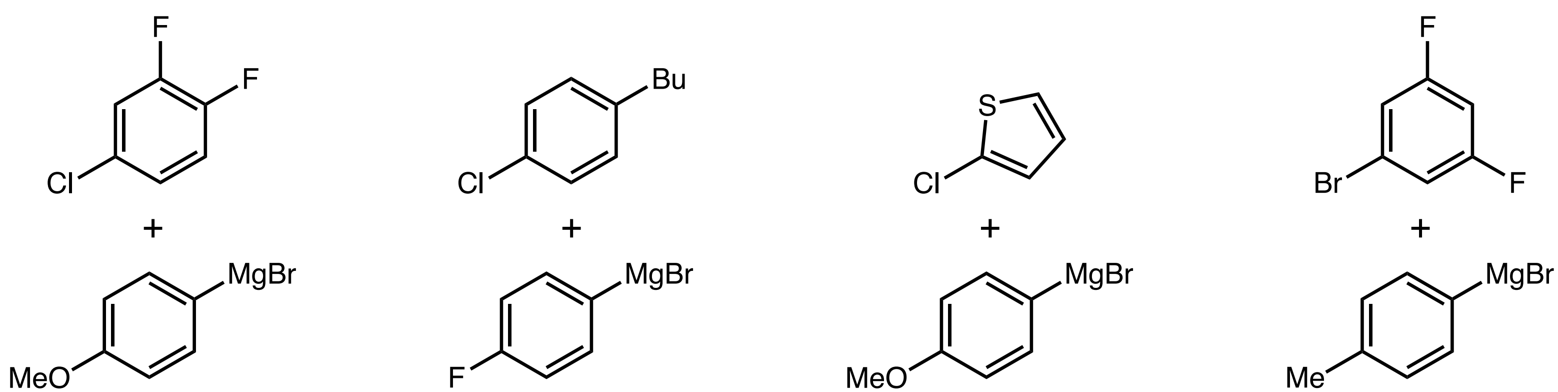
using aryl nucleophiles

Kumada-type coupling



94% isolated yield
(FeF_3: 92%, NiF_2: 88%)

Scope of reaction (Co vs. Ni)



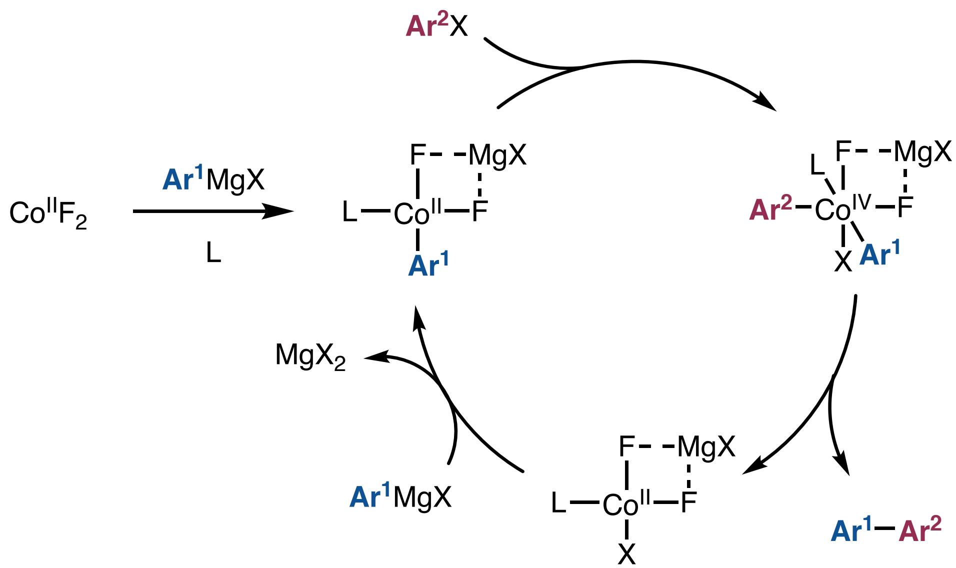
Co: **97%**	Co: **86%**	Co: **95%**	Co: 20%
Ni : 46%	Ni : 39%	Ni : 37%	Ni : **95%**
(C–F red.)	(e^- poor Nuc)	(ArCl recv.)	(Nuc dimerize)

Nakamura, M. et al. *JACS*, **2009**, *131*, 11949–11963.

Coupling with aryl halides

using aryl nucleophiles

- Proposed mechanism



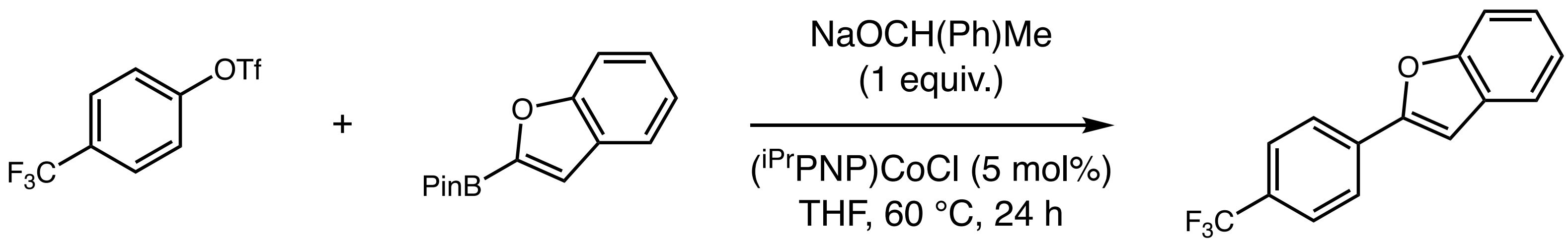
metalate mechanism

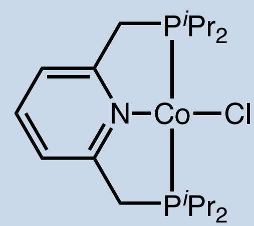
Nakamura, M. et al. *JACS*, **2009**, *131*, 11949–11963.

Coupling with aryl halides

using aryl nucleophiles

- Suzuki-Miyaura-type coupling





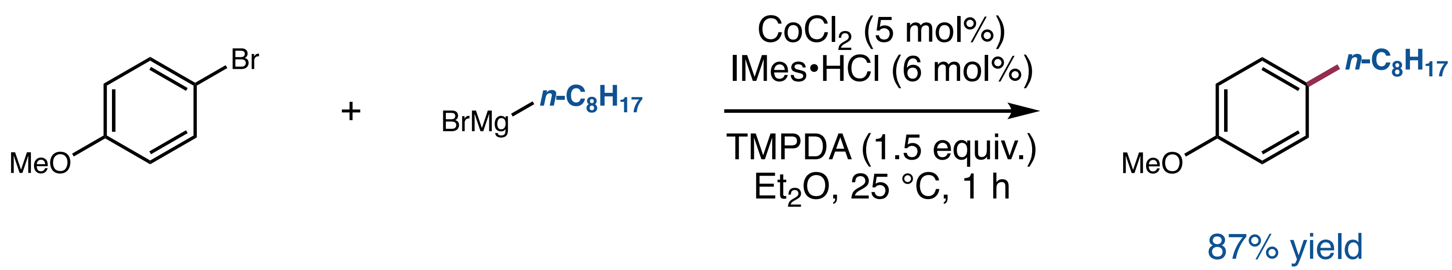
(^{iPr}PNP)CoCl

Neely, J. M.; Bezdek, M. J.; Chirik, P. J. *ACS Cent. Sci.* **2016**, *2*, 935–942.

Coupling with aryl halides

using alkyl nucleophiles

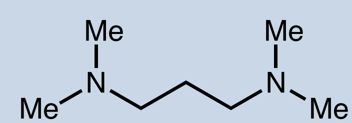
Kumada-type coupling



- The **ONLY** example of Co-catalyzed coupling between ArX and R–M reported to date

"Scope" of nucleophiles

***n*-Bu**MgI	**Me**MgI	**Allyl**-MgBr	***i*-Pr**MgCl
66% yield	0% yield	0% yield	9% yield

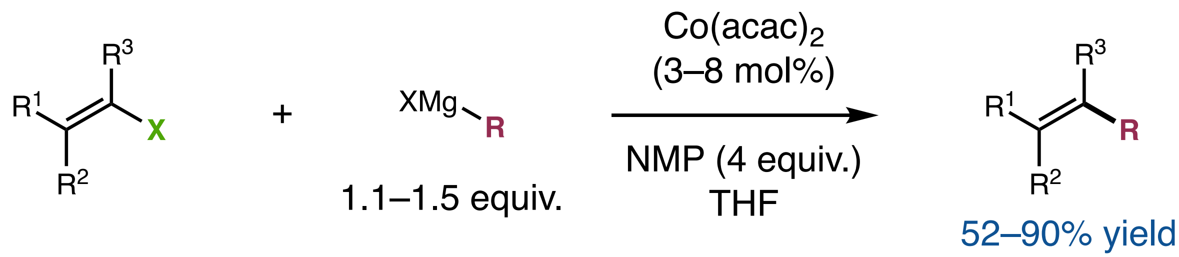


TMPDA

Oshima, K. et al. *Chem. Lett.* **2008**, *37*, 1178–1179.

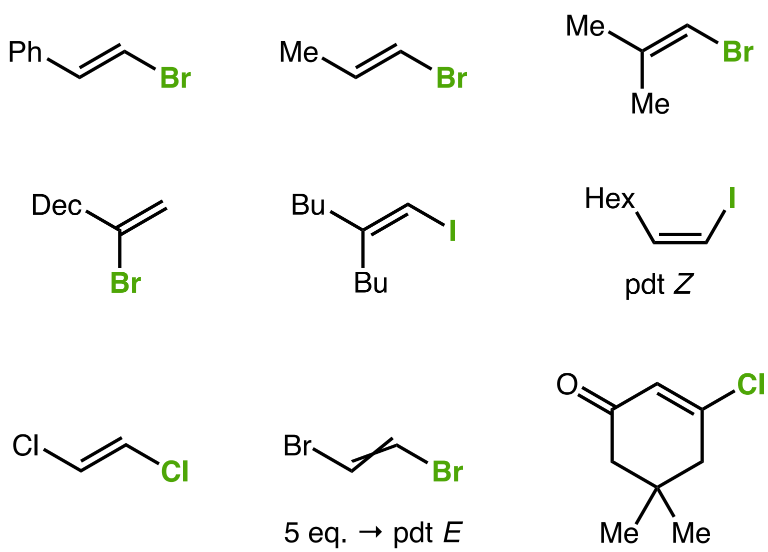
Coupling with vinyl halides

Coupling with $Co(acac)_2$ – THF/NMP system

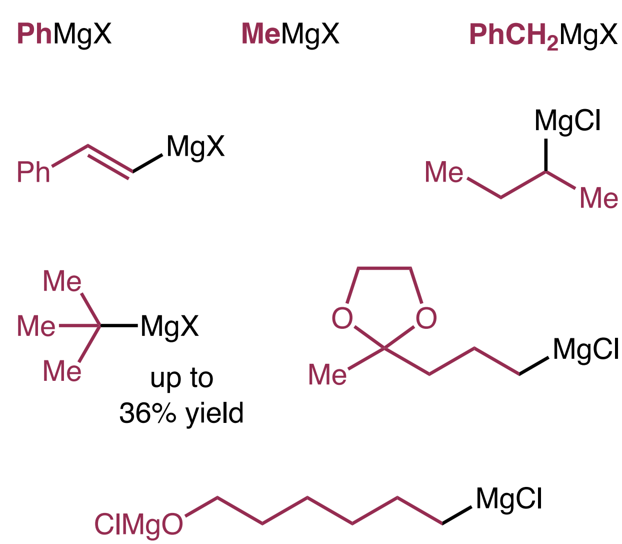


- Addition of NMP is crucial to supress dimerization of Grignard reagent

Scope of halide



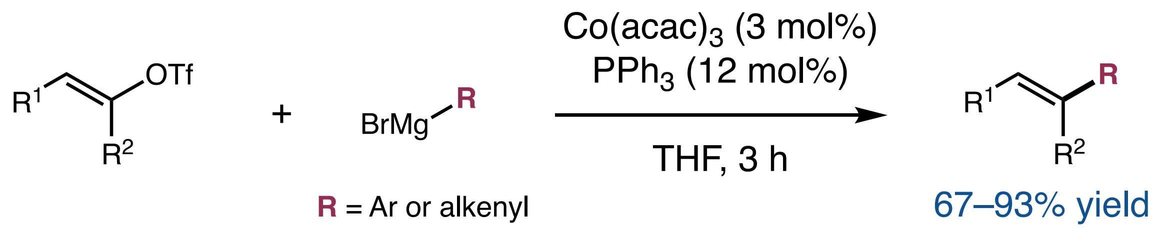
Scope of RMgX



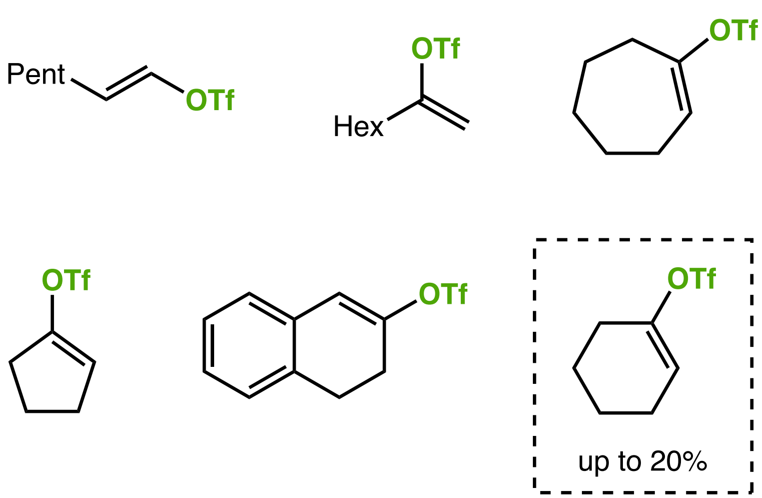
Cahiez, G.; Avedissian, H. *Tetrahedron Lett.* **1998**, *39*, 6159–6162.

Coupling with vinyl halides

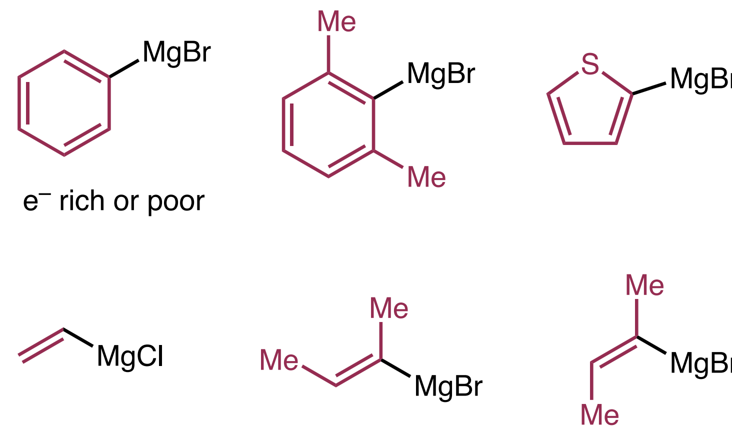
- $Co(acac)_3$–PPh_3 allowed use of triflates as electrophiles



Scope of triflate



Scope of RMgBr



Shirakawa, E.; Imazaki, Y.; Hayashi, T. *Chem. Lett.* **2008**, *37*, 654–655.

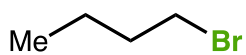
Coupling with alkyl halides

using aryl nucleophiles

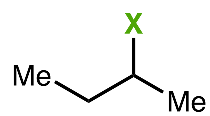
Kumada-type coupling

Alk—Br + **Ar**—MgBr (1.1 equiv.) → [$Co(acac)_3$ (5 mol%), TMEDA (5 mol%); THF, 0 °C, 40 min] → **Alk**—**Ar**

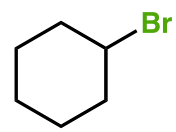
Scope of halide



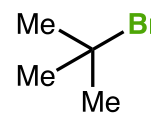
up to 94% y



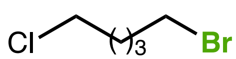
92–94% y (X = I, Br)
4% y (X = Cl)



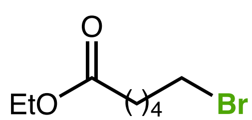
up to 97% y



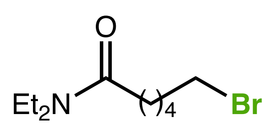
trace



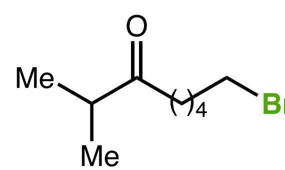
up to 89% y



up to 90%



up to 84% y



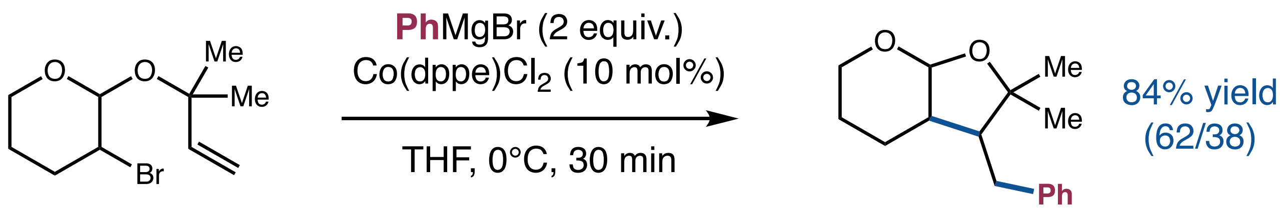
up to 88%

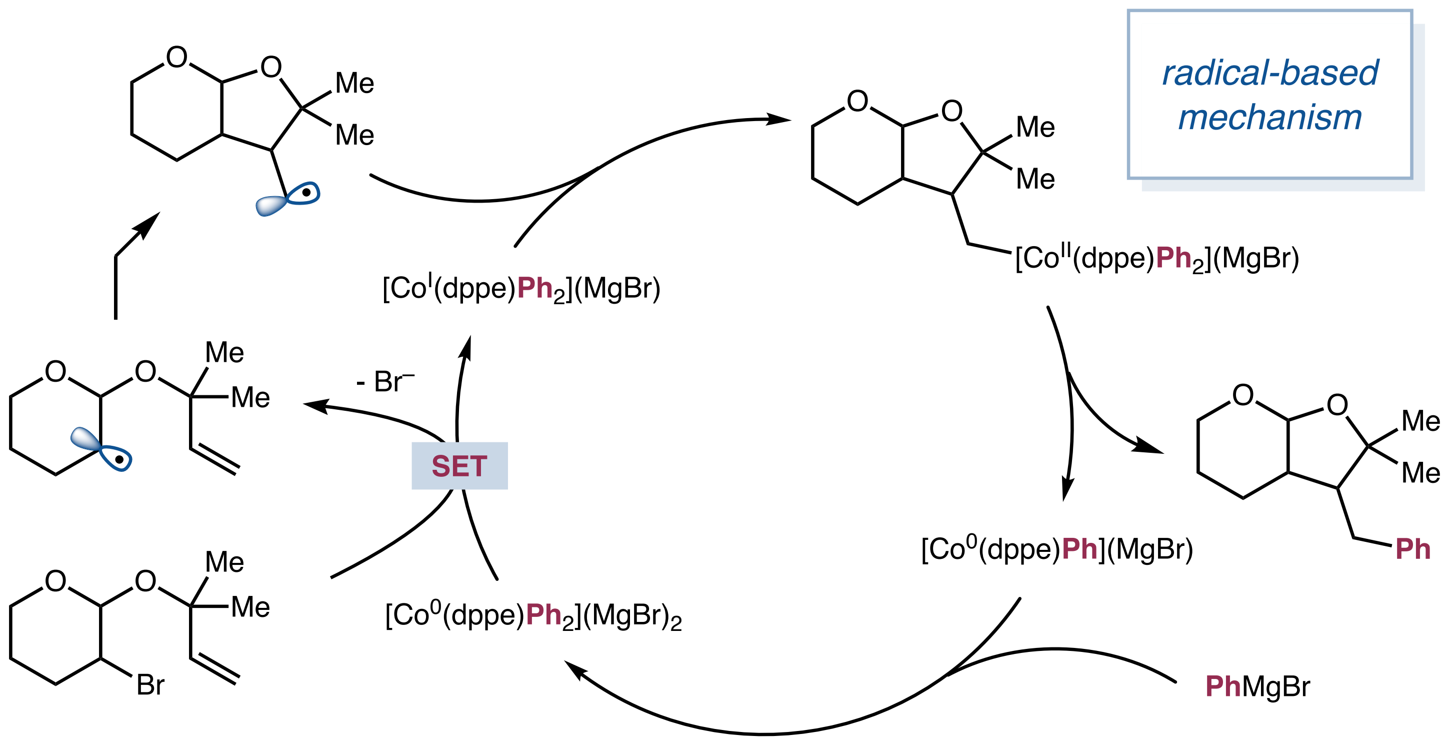
Cahiez, G.; Chaboche, C.; Duplais, C.; Moyeux, A. *Org. Lett.* **2009**, *11*, 277–280.

Coupling with alkyl halides

using aryl nucleophiles

Reaction mechanism



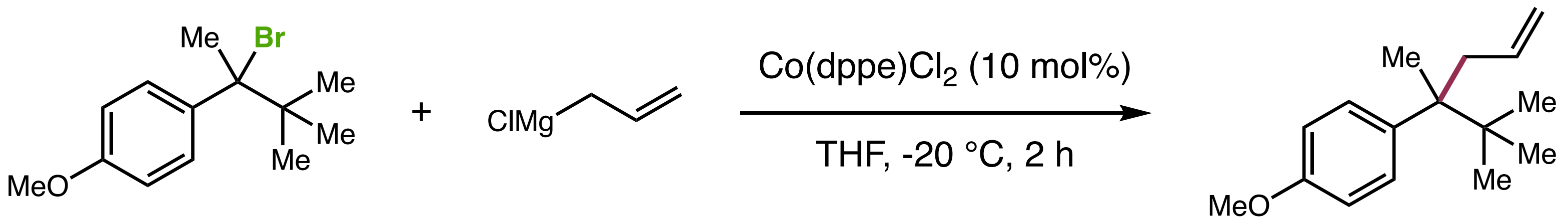


Ohmiya, H.; Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 2207–2213.

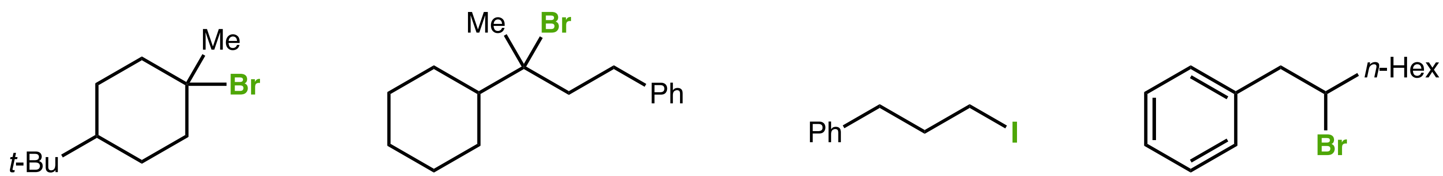
Coupling with alkyl halides

using alkyl nucleophiles

- Allylation works with sterically hindered halides – a “free” radical reaction

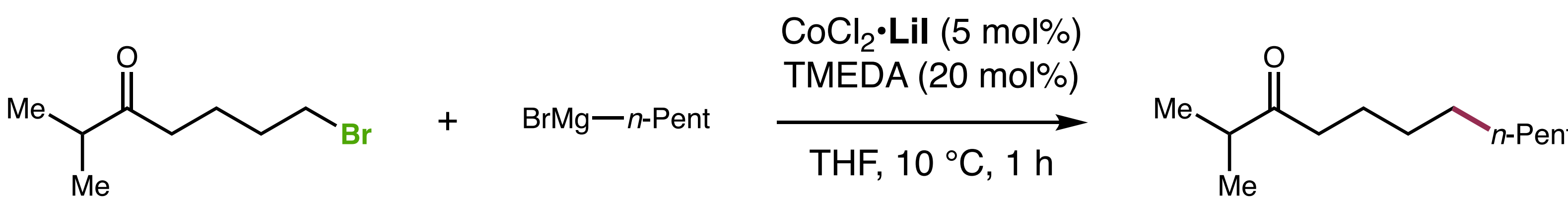


73% yield



76% yield | 83% yield | 82% yield | 84% yield

- Alkyl nucleophiles also works in presence of iodide anion

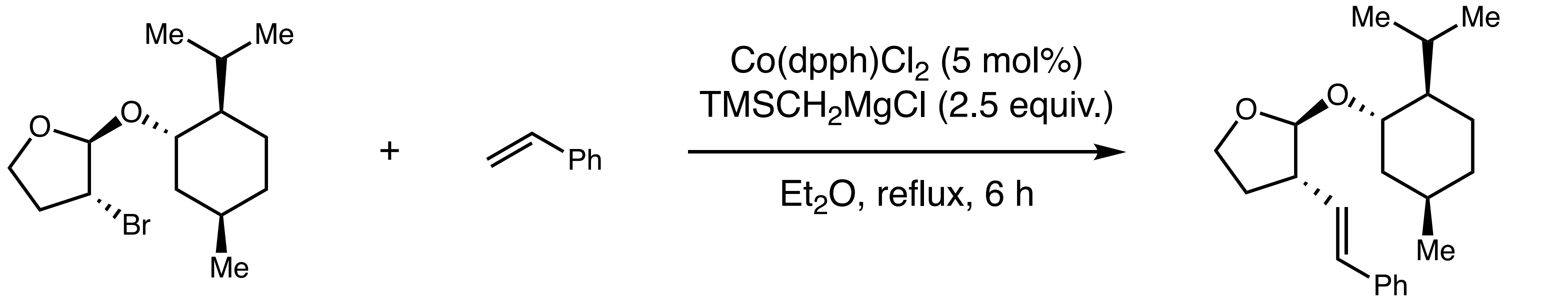


primary, secondary | primary | 73% isolated yield

Oshima, K. *ACIE*, **2002**, *41*, 4137–4139.
Cahiez, G. et al. *Adv. Synth. Catal.* **2008**, *350*, 1484–1488.

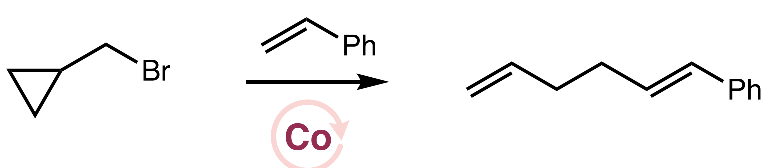
Coupling with alkyl halides

Intermolecular Heck-Type coupling

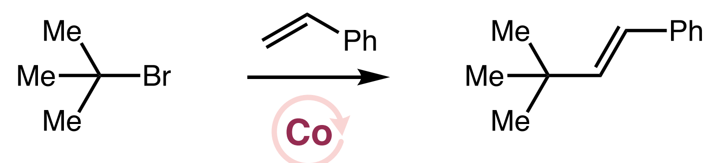


68% yield

Radical nature of the reaction



50% yield

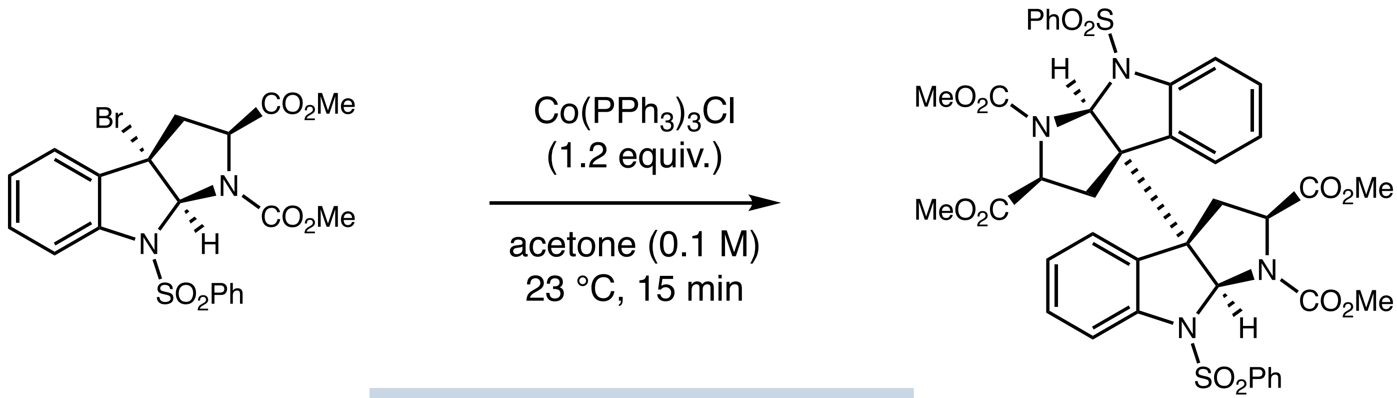


67% yield

Oshima, K. et al. *J. Am. Chem. Soc.* **2002**, *124*, 6514–6515.

Reductive coupling

Dimerization of halides

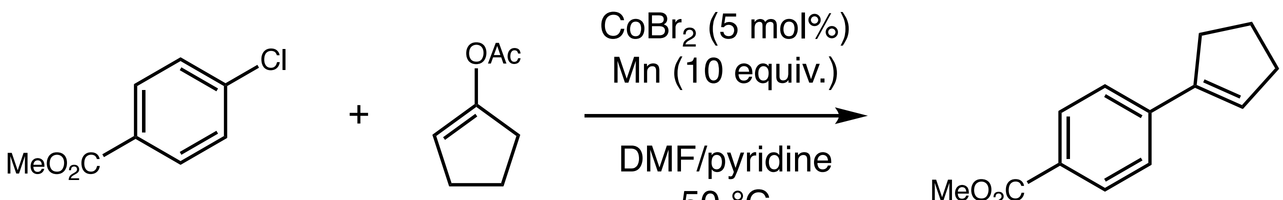


$Mn_2(CO)_{10}$ ⇌ • $Mn(CO)_5$

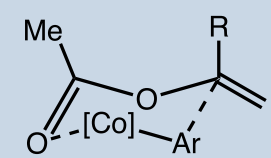
system gave up to 30% yield

60% yield

Aryl chloride/bromide with vinyl acetates



79% yield



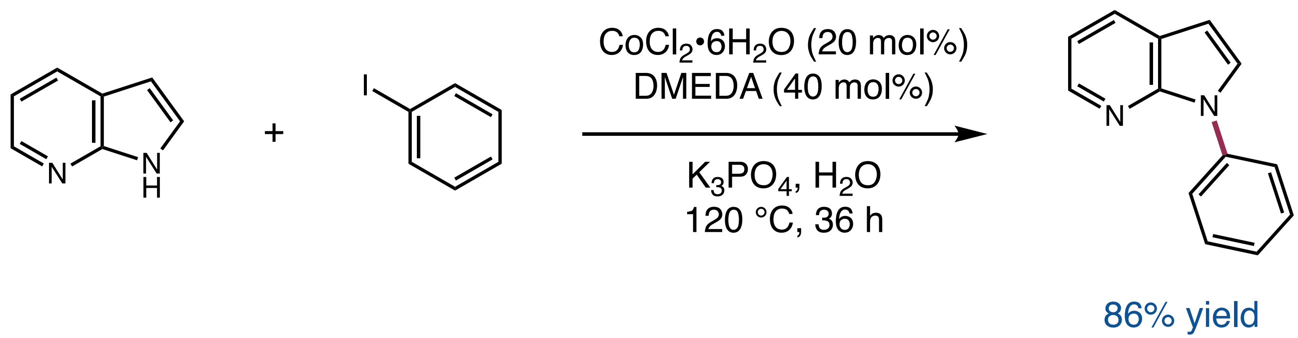
via

Movassaghi, M.; Schmidt, M. A. *ACIE* **2007**, *46*, 3725–3728.

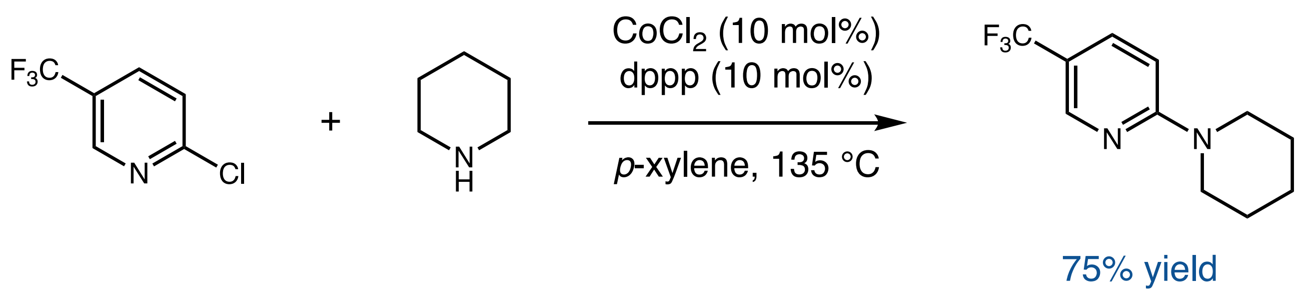
Amatore, M.; Gosmini, C.; Périchon, J. *EJOC* **2005**, 989–992.

C–N bond formation

- Coupling with aryl iodides



- Coupling with chloropyridine

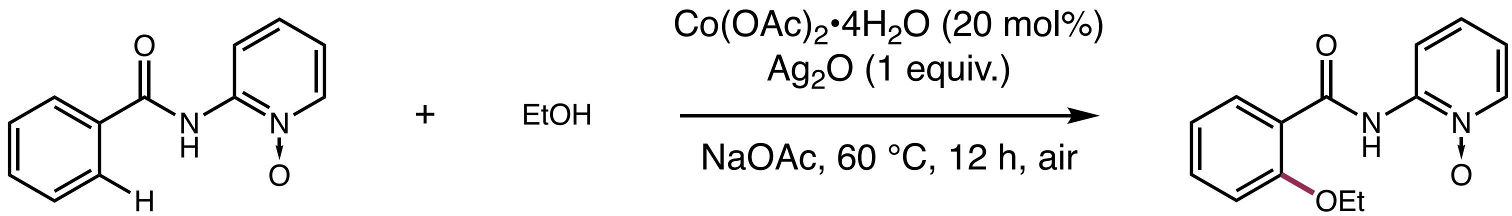


Teo, Y.-C. Chua, G.-L. *Chem. Eur. J.* **2009**, *15*, 3072–3075.

Toma, G.; Fujita, K.; Yamaguchi, R. *Eur. J. Org. Chem.* **2009**, 4586–4588.

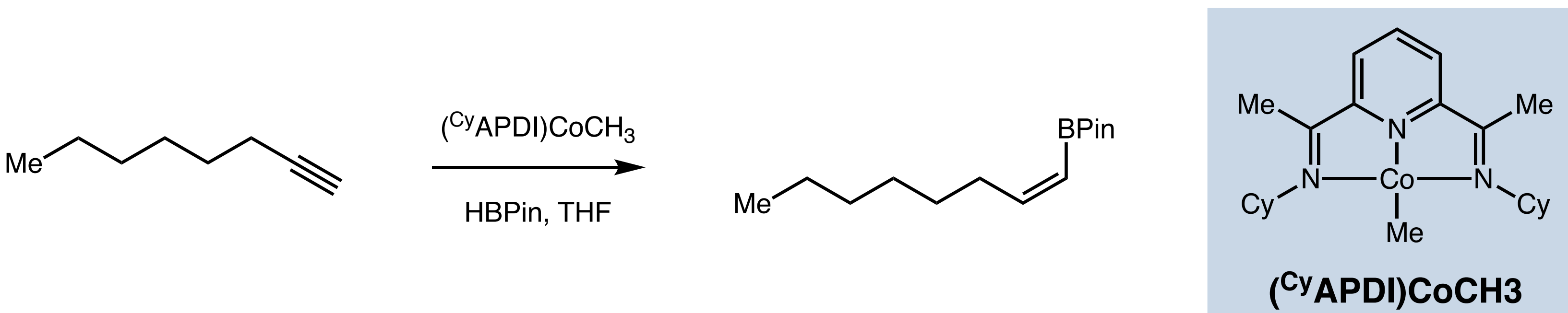
Other C–heteroatom bonds

C–O bond formation



- *Only two reports demonstrated C–O formation via Co catalysis*
- For cobalt–catalyzed C–H activation. See review: *ACS Catal.* **2016**, *6*, 498–525.

C–B bond formation

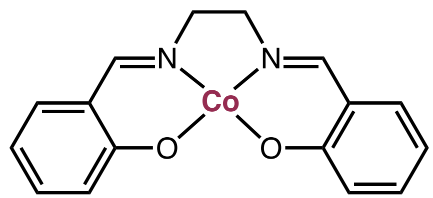


Song, M.–P. et al. *ACIE*, **2015**, *54*, 272–275.

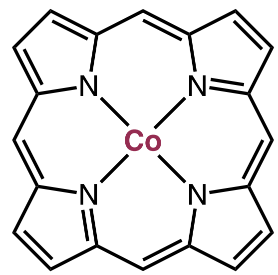
Chirk, P. J. et al. *JACS* **2015**, *137*, 5855–5858.

Vitamin B like Co complexes

- Some vitamin B_{12} like Co compounds



Co(salen)



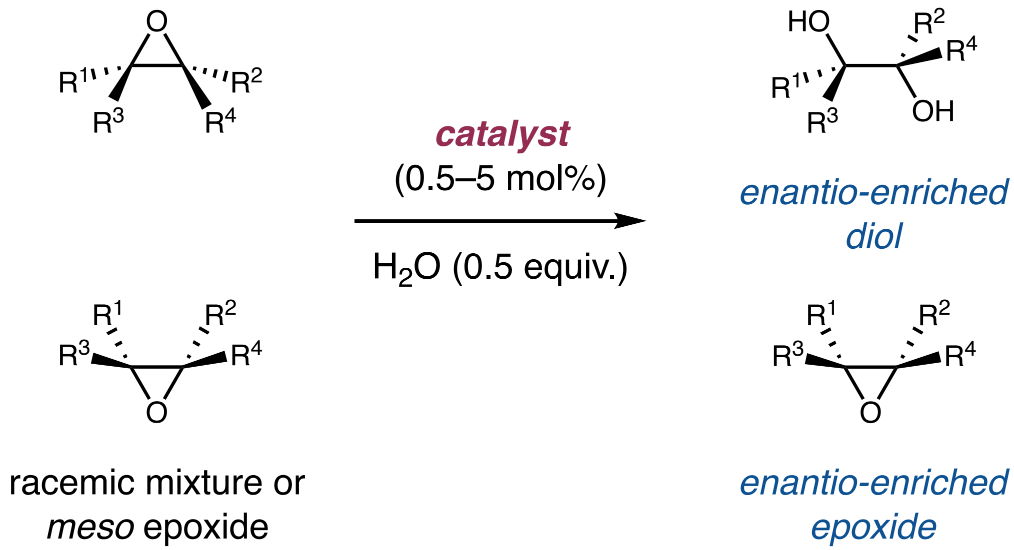
Co porphyrin

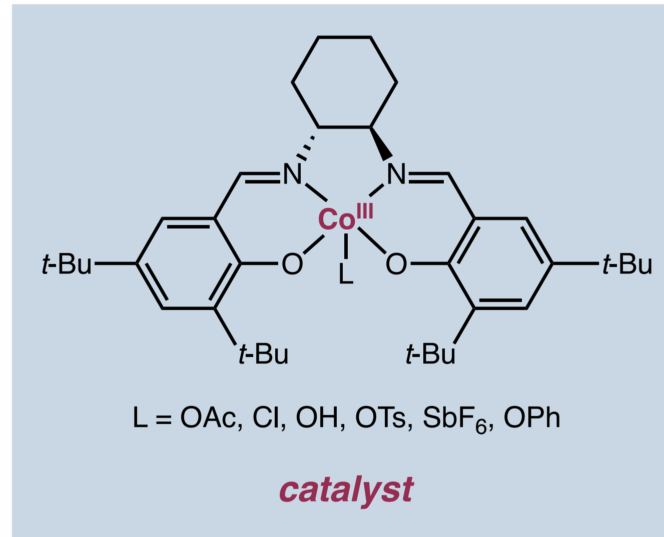
- Enzyme mimics: reversibly binds O_2 replicate certain aspects of vitamin B_{12}
- Jacobsen hydrolytic kinetic resolution

- High "radical character" on Co
- No *cis*–coordination sites available

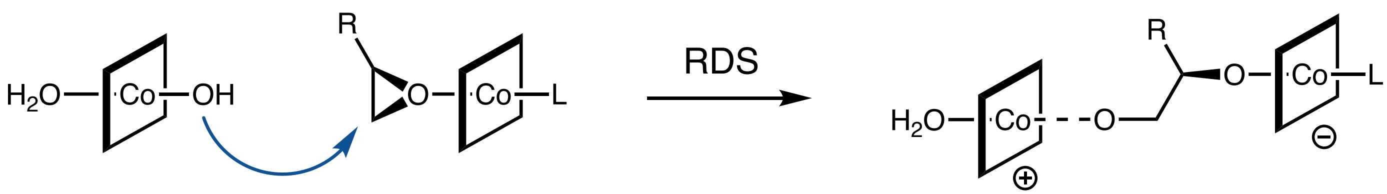
Co^{III}(salen) chemistry

- Jacobsen hydrolytic kinetic resolution





- Mechanism: second order dependence on the catalyst



Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936–938.

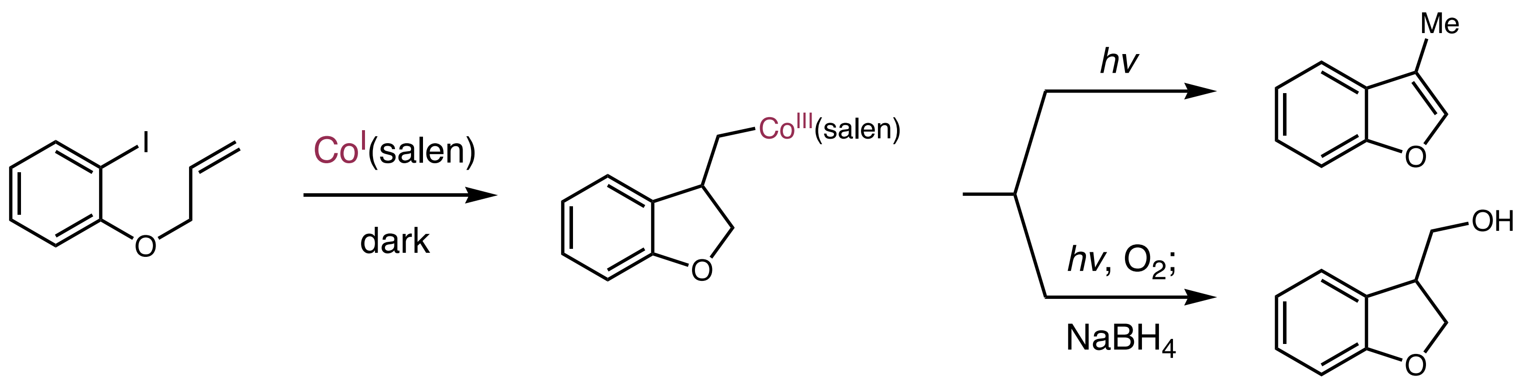
Co(salen) radical chemistry

General reactivity

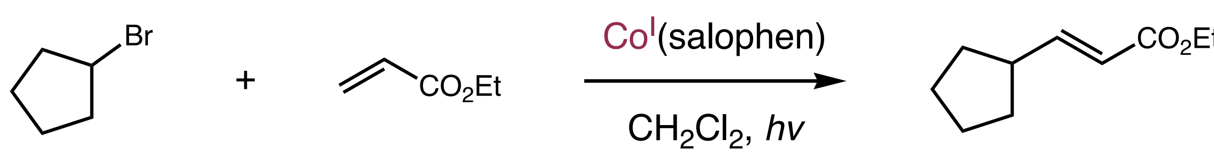
$$Co^{III}\text{–L} \xrightarrow{\text{red.}} Co^{I}\text{–L} \xrightarrow{\text{R–X}} \text{R}\bullet + Co^{II}\text{–L} \underset{\Delta \text{ or } h\nu}{\rightleftharpoons} \text{R–}Co^{III}\text{–L}$$

alkyl or aryl

Aryl halides



Alkyl halides: michael addition

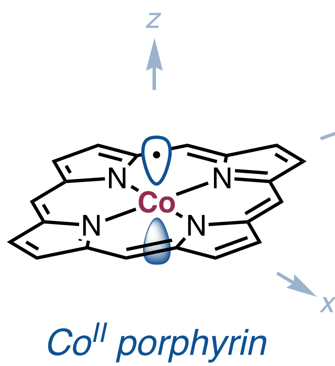


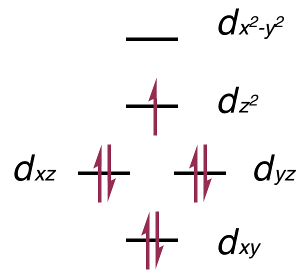
Patel, V. F.; Pattenden, G.; Russell, J. J. *Tetrahedron Lett.* **1986**, 27, 2303–2306.

Patel, V. F.; Pattenden, G. *J. Chem., Chem. Commun.* **1987**, 871–872.

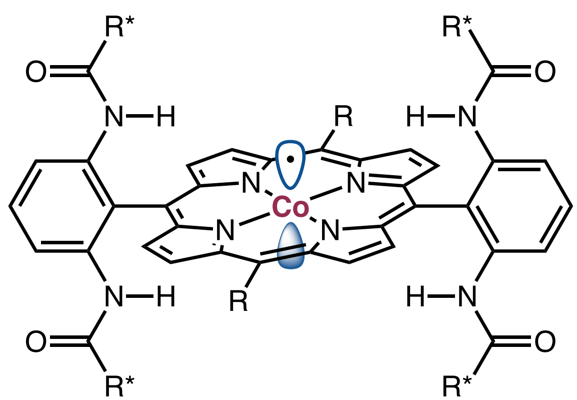
Co^{II}–porphyrin catalysis

- Structure of Co^{II}-porphyrin: metalloradical catalysis (MRC)





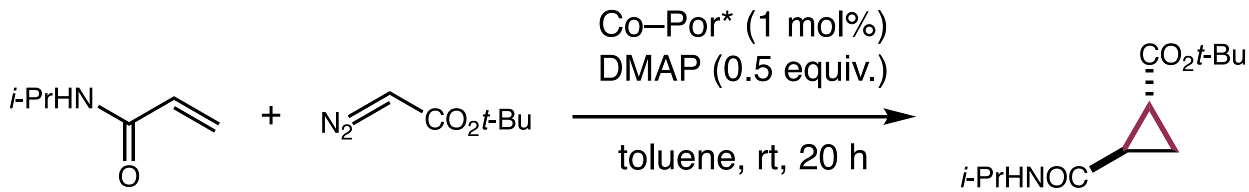
- Porphyrin ligand can be fine tuned and achieve asymmetric catalysis



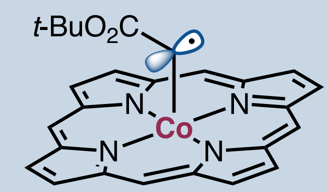
Lu, H.; Zhang, X. P. *Chem. Soc. Rev.* **2011**, *40*, 1899–1909.

Modes of reactions

Cylcopropanation of alkenes

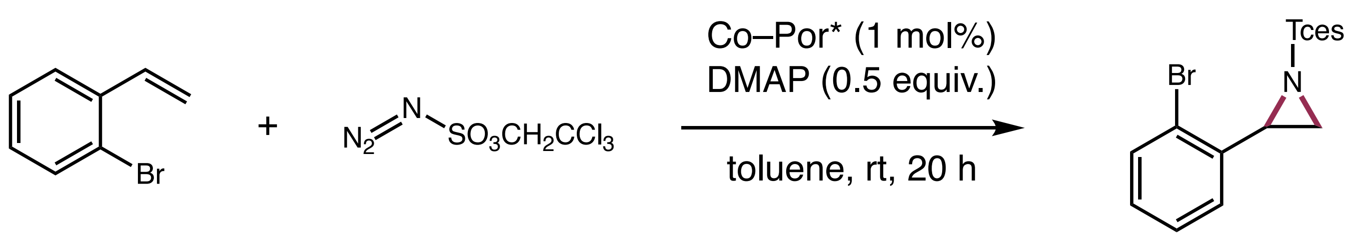


96% isolated yield
99:1 *trans* / *cis*
96% ee



carbene radical

Aziridination of alkenes



92% isolated yield
99% ee

Zhang, X. P. et al. *JACS*, **2007**, *129*, 12074–12075.

Zhang, X. P. et al. *CC*, **2009**, 4266–4268.

Summary

27

Co

Cobalt

58.9332

- Excellent catalyst for carbon–centered radicals reactions

$$\mathrm{Co^{I}{-}L} \xrightarrow{\text{R–X}} \underset{\textit{alkyl or aryl}}{\mathrm{R\bullet}} + \mathrm{Co^{II}{-}L} \underset{\Delta \text{ or } h\nu}{\rightleftharpoons} \mathrm{R{-}Co^{III}{-}L}$$

- Versatile reactivity w/ moderate efficiency. Less studied area.