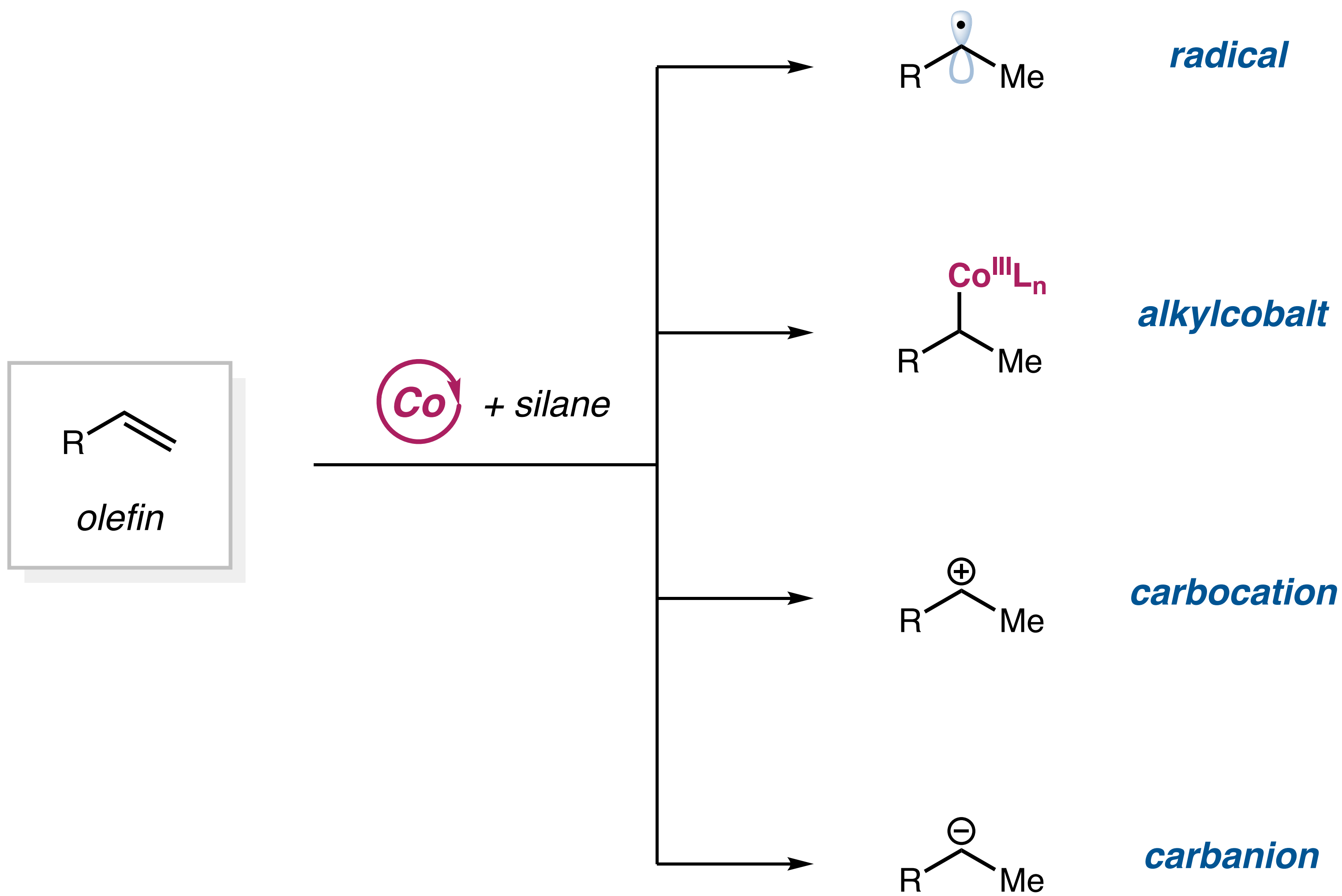
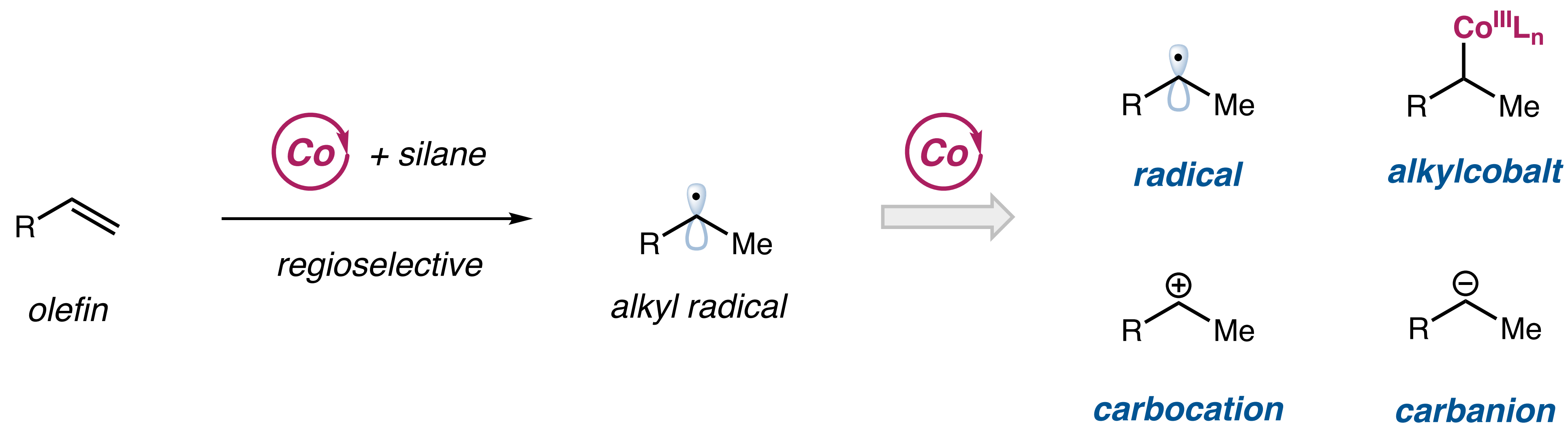
Recent Developments of Cobalt-Catalyzed Hydrofunctionalization of Olefins



Yufan Liang
MacMillan Group Meeting

February 5th, 2020

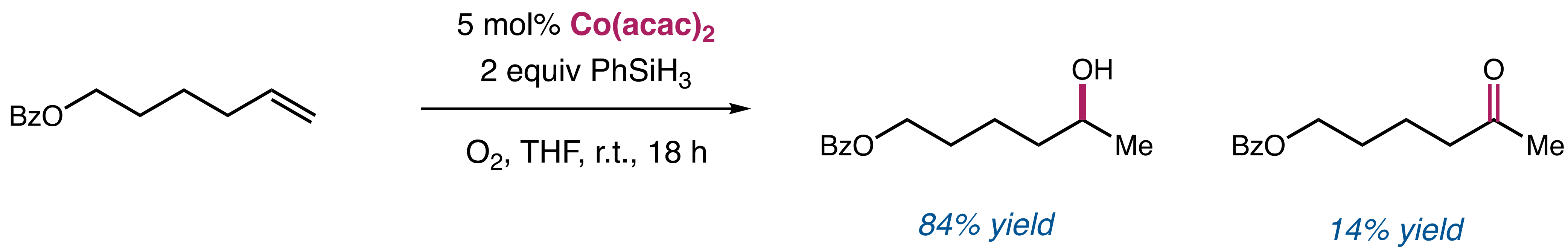
Outline

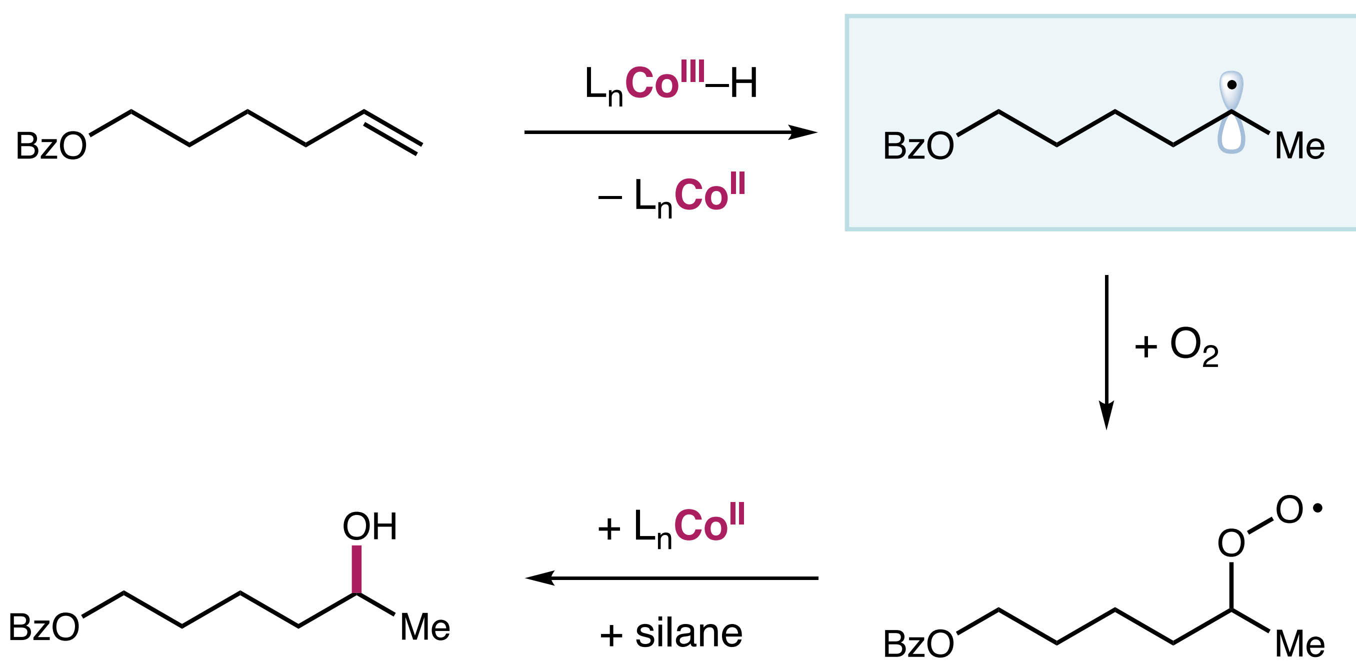


Selected examples from these research groups will be discussed in detail

Prof. Erick Carreira (ETH Zürich)
Prof. Seth Herzon (Yale)
Prof. Ryan Shenvi (Scripps)
Prof. Hiroki Shigehisa (Musashino University, Japan)
Prof. Sergey Pronin (UC Irvine)
Prof. Rong Zhu (Peking University, China)

Mukaiyama Hydration



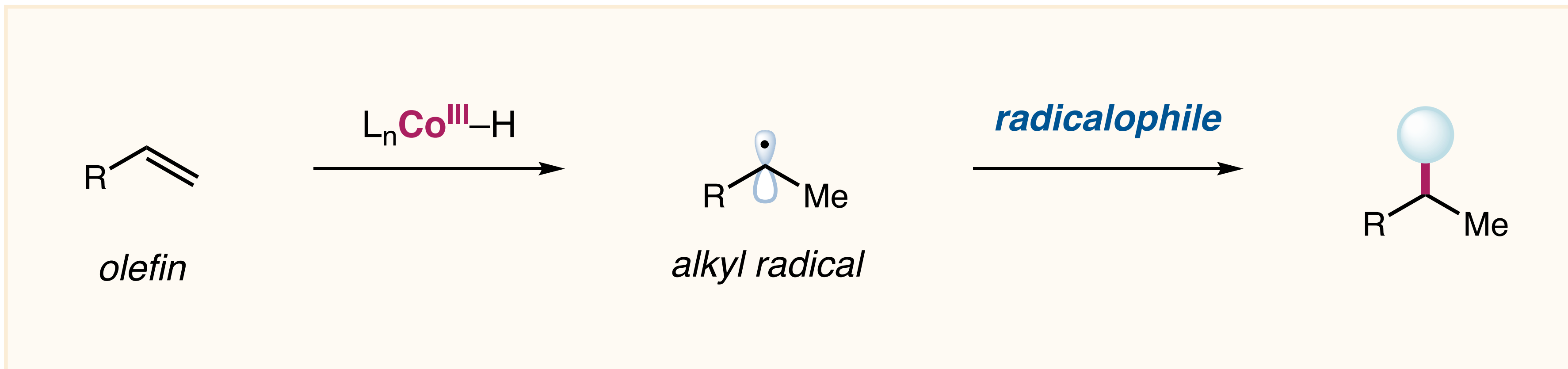


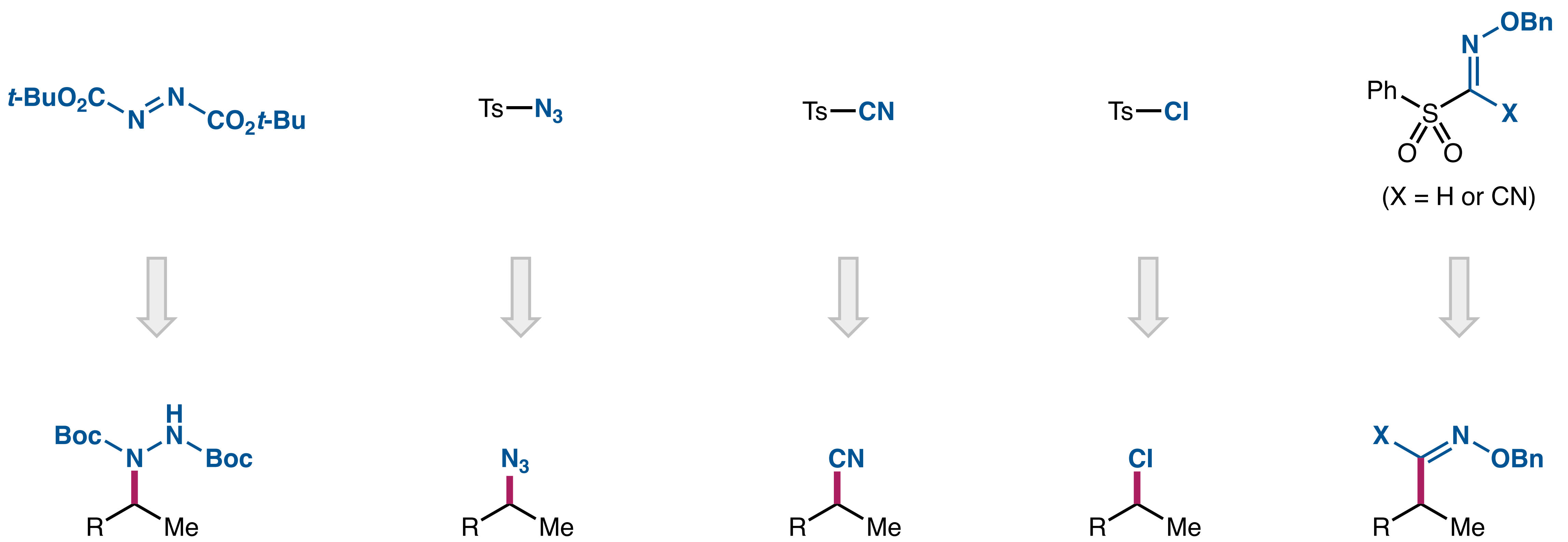
Generating a stable radical

Highly regioselective process

Teruaki Mukaiyama *et al., Chem. Lett.* **1989**, 449; **1989**, 569; **1989**, 573; **1989**, 1071.

Quenching Alkyl Radicals with Radicalophiles: Summary of Carreira's Work





JACS **2004,** 5676
Org. Lett. **2005**, 4249

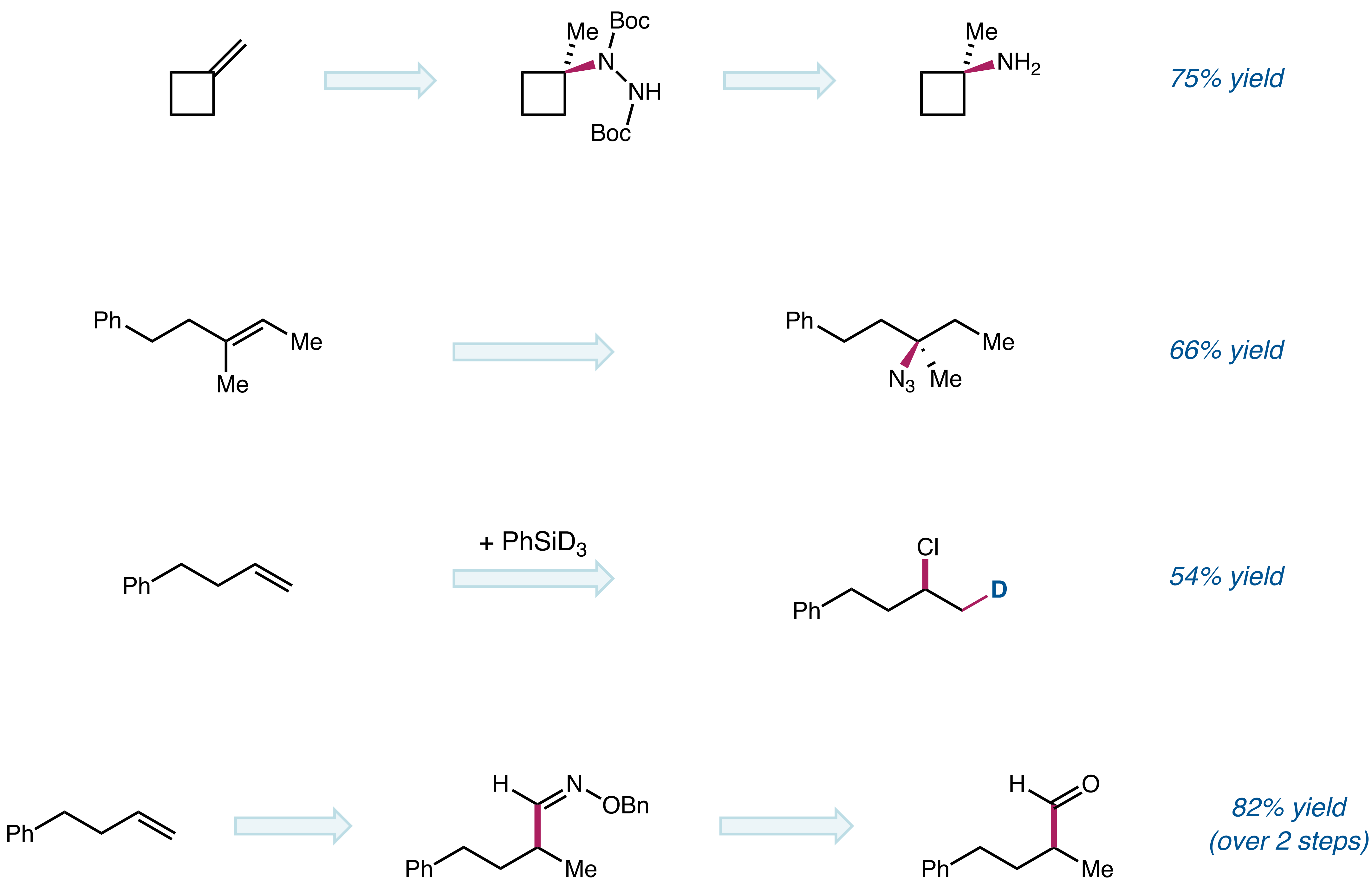
JACS **2005**, 8294
Synthesis **2007**, 3839

ACIE **2007**, 4519

ACIE **2008**, 5758

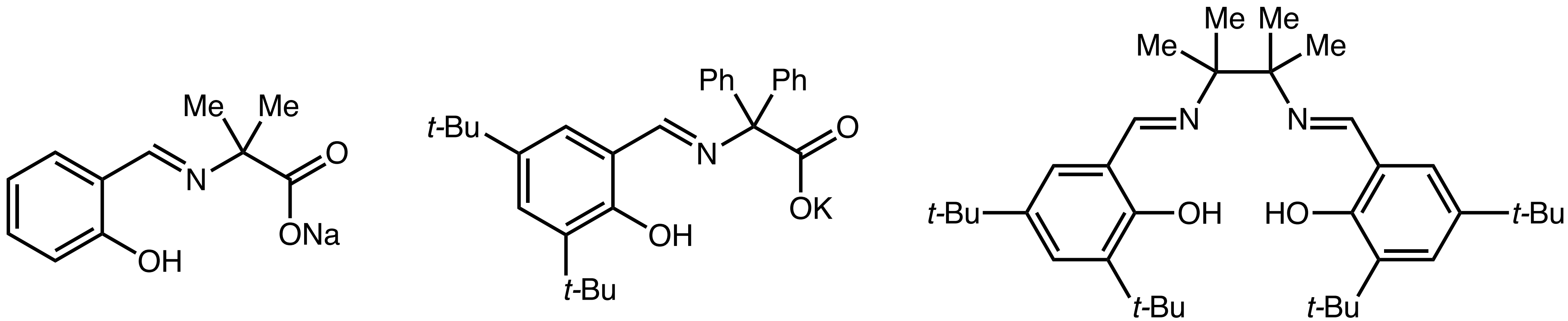
JACS **2009**, 13214

Quenching Alkyl Radicals with Radicalophiles: Selected Examples



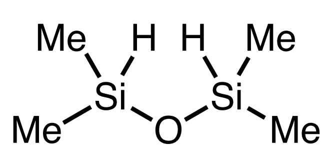
Quenching Alkyl Radicals with Radicalophiles: Important Findings

Ligand



Silane

$PhSiH_3$



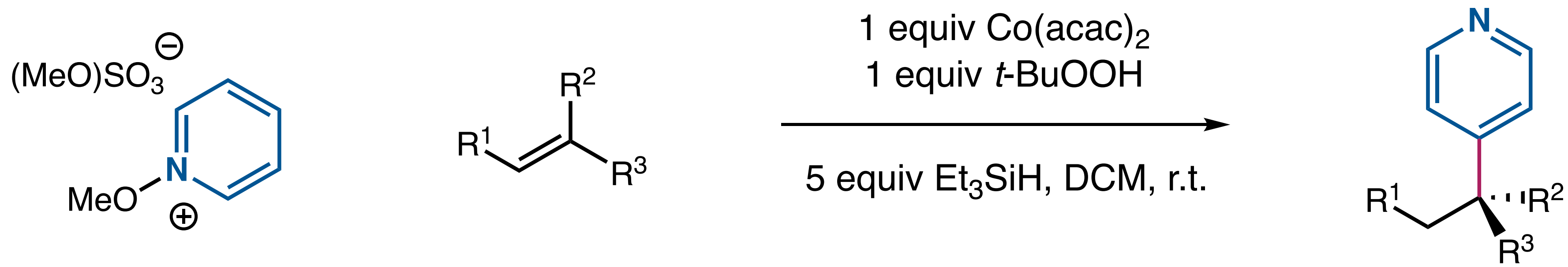
(TMDSO)

- Most commonly used solvent: EtOH
- In some cases, addition of *t*-BuOOH improves efficiency, especially when Co(II) catalyst was used:

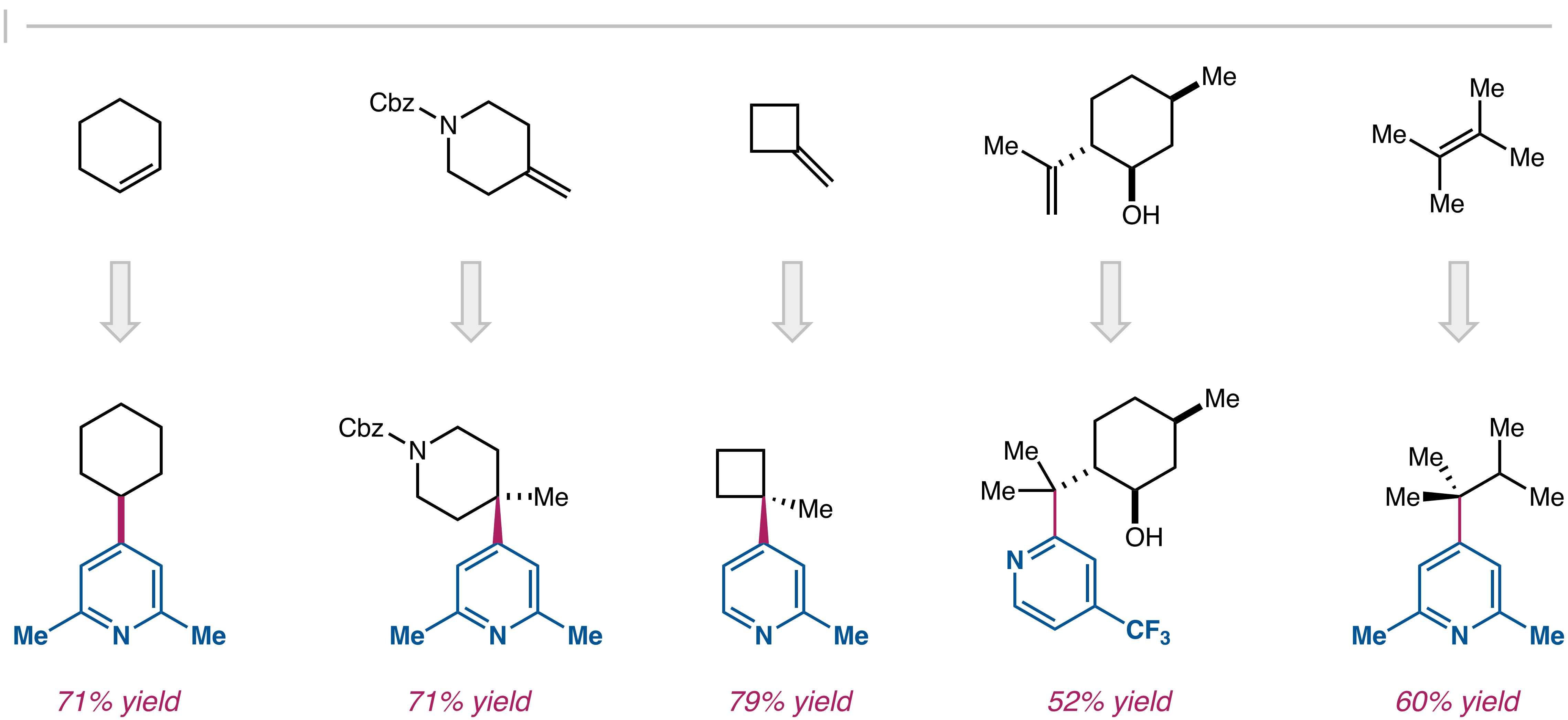
$$L_nCo^{II} \xrightarrow[\text{silane}]{t\text{-BuOOH}} L_nCo^{III}\text{–H}$$

For a full article (including a SAR study of the ligands):
Waser, J.; Gasper, B.; Nambu, H.; Carreira, E. M. *J. Am. Chem. Soc.* **2006**, *128*, 11693.

Quenching Alkyl Radicals with Radicalophiles: Hydroheteroarylation

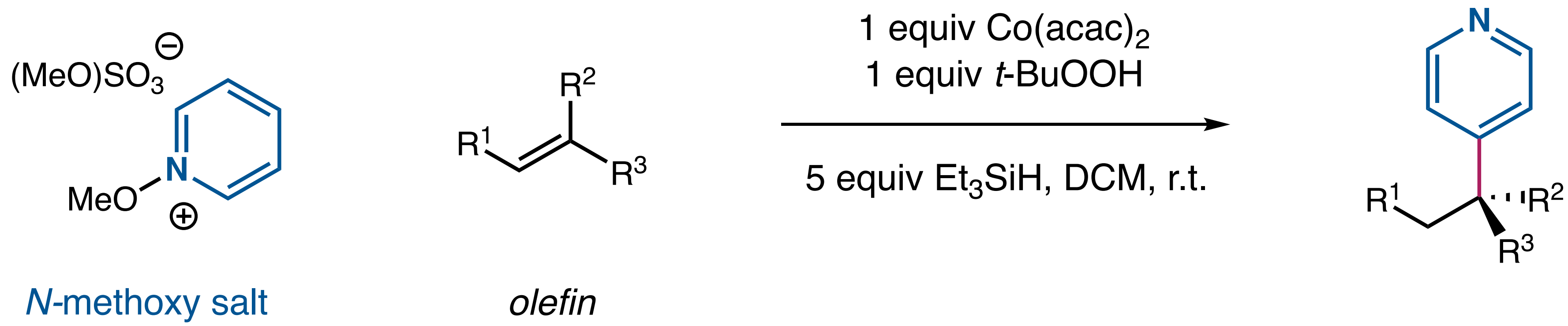


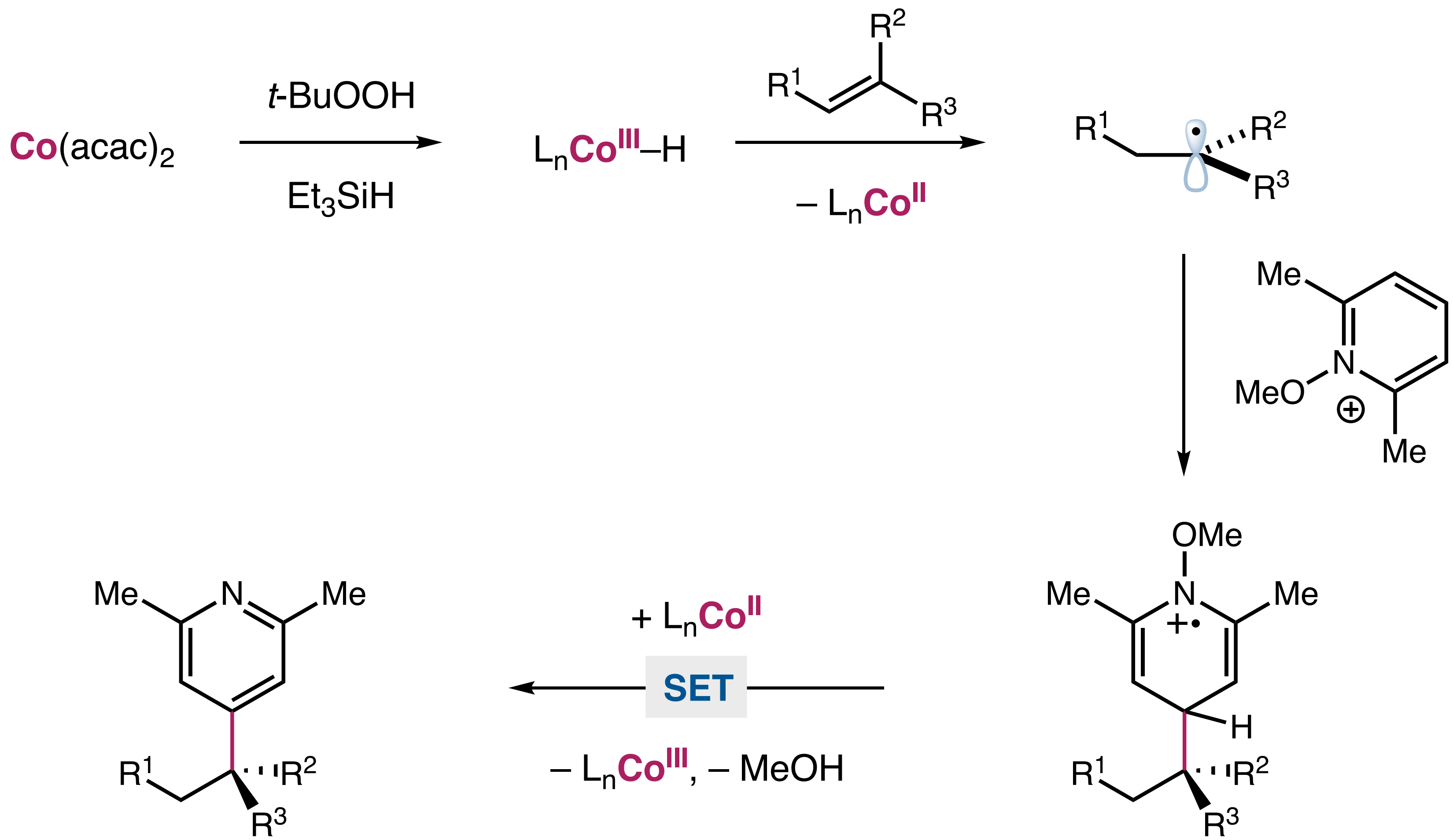
N-methoxy salt — *olefin*



Ma, X.; Herzon, S. B. *J. Am. Chem. Soc.* **2016**, *138*, 8718
Ma, X.; Dang, H.; Rose, J. A.; Rablen, P.; Herzon, S. B. *J. Am. Chem. Soc.* **2017**, *139*, 5998 (full article)

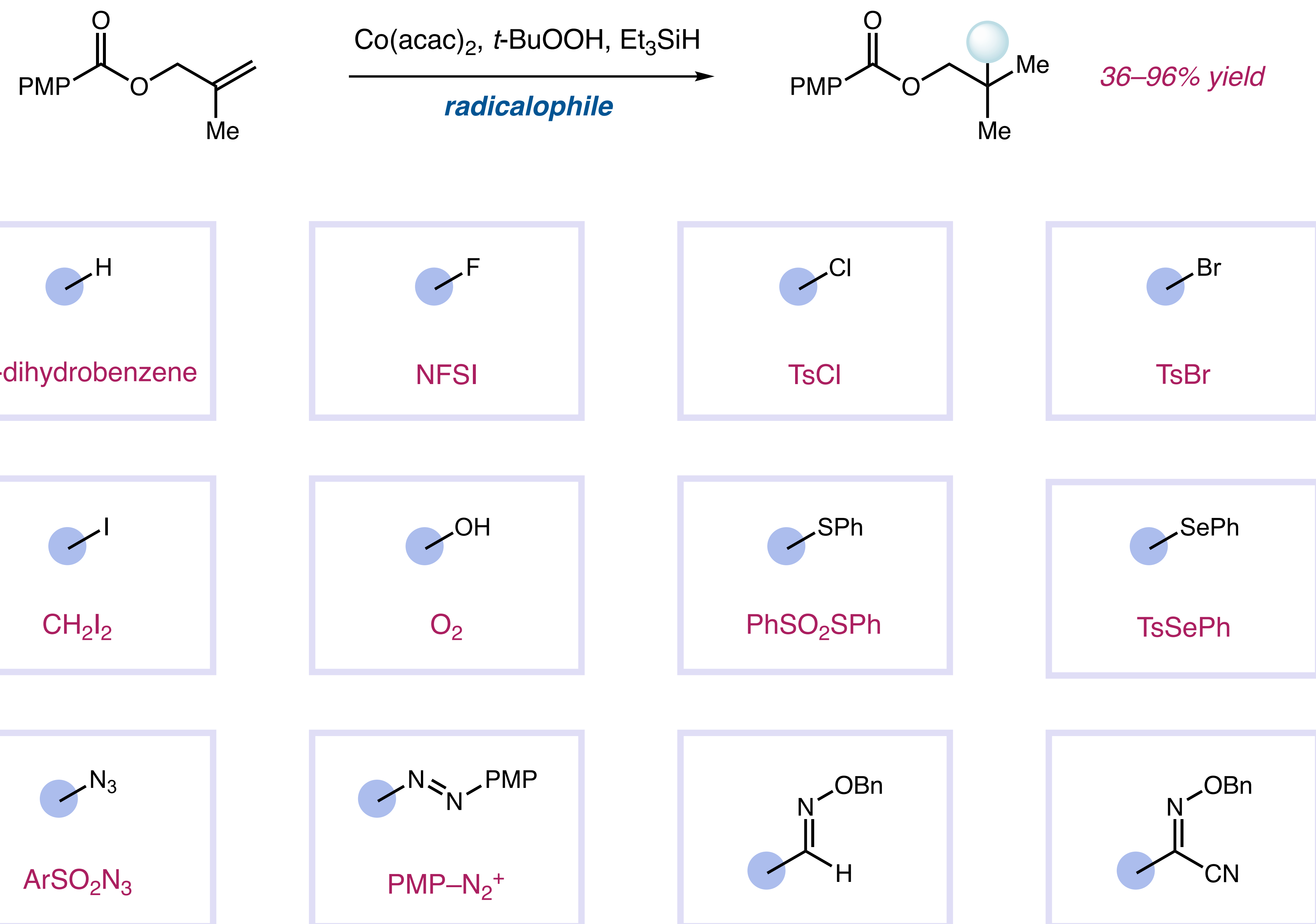
Quenching Alkyl Radicals with Radicalophiles: Hydroheteroarylation





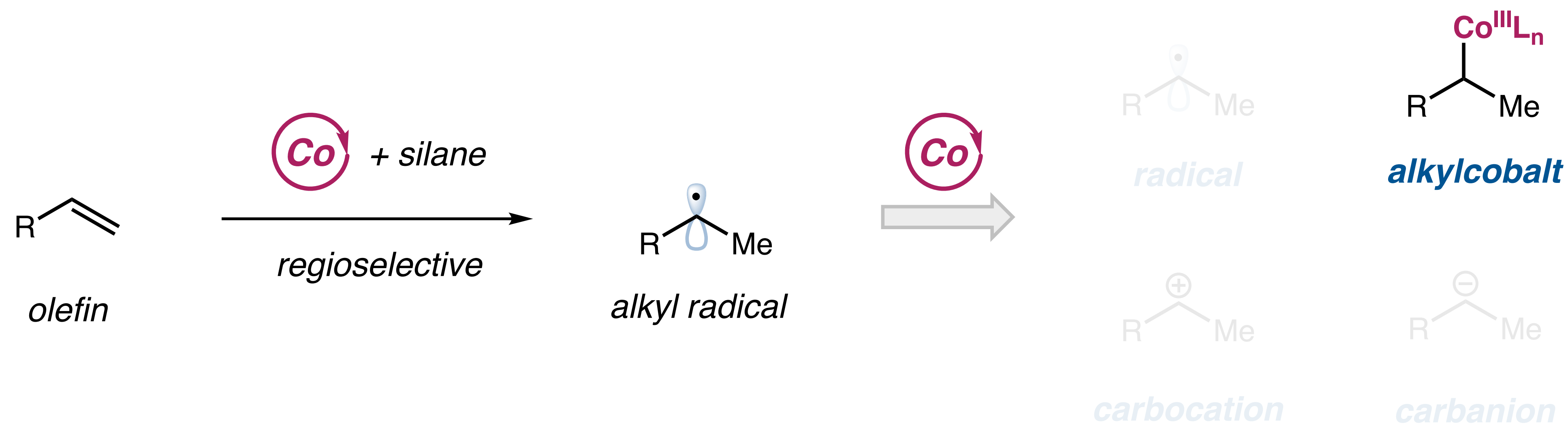
Ma, X.; Herzon, S. B. *J. Am. Chem. Soc.* **2016**, *138*, 8718
Ma, X.; Dang, H.; Rose, J. A.; Rablen, P.; Herzon, S. B. *J. Am. Chem. Soc.* **2017**, *139*, 5998 (full article)

Quenching Alkyl Radicals with Radicalophiles: A Versatile Strategy



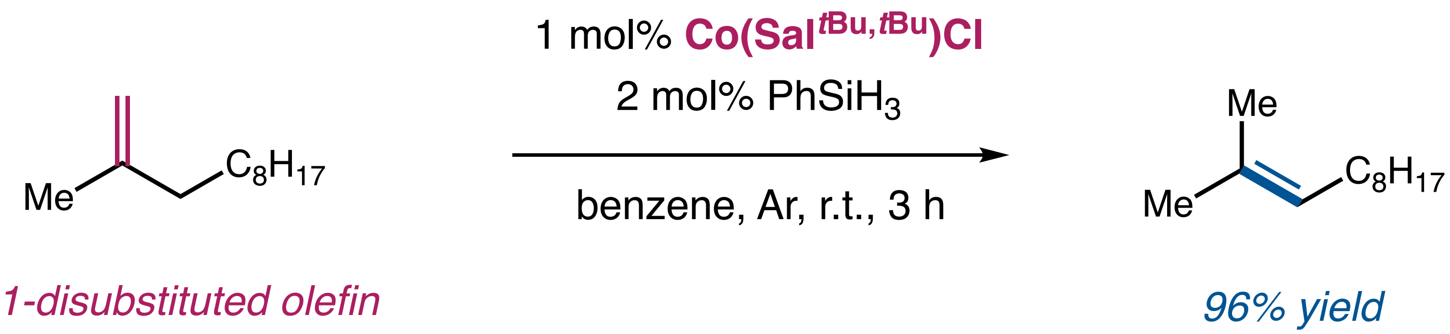
Ma, X.; Herzon, S. B. *Beilstein J. Org. Chem.* **2018**, *14*, 2259

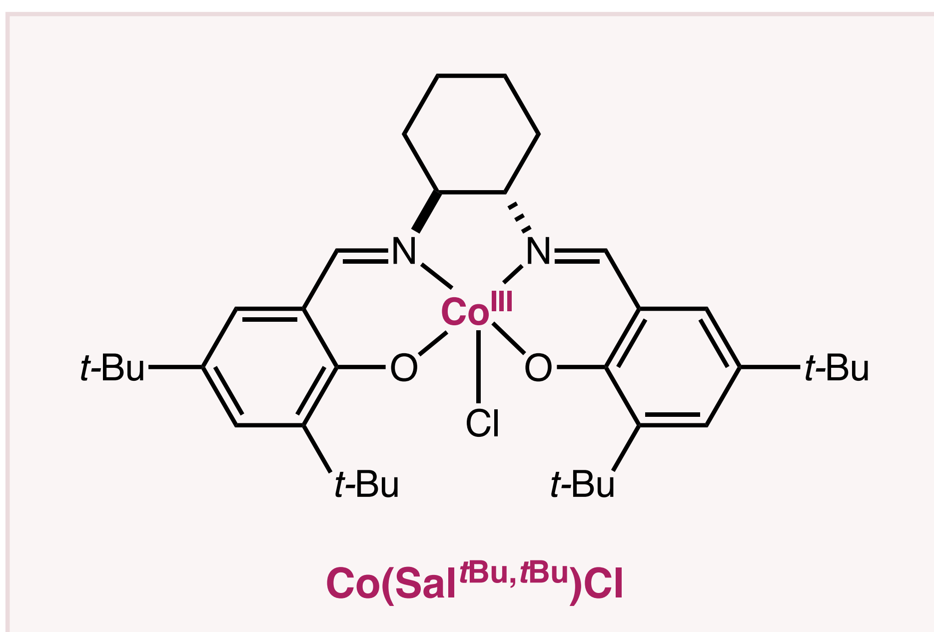
Outline

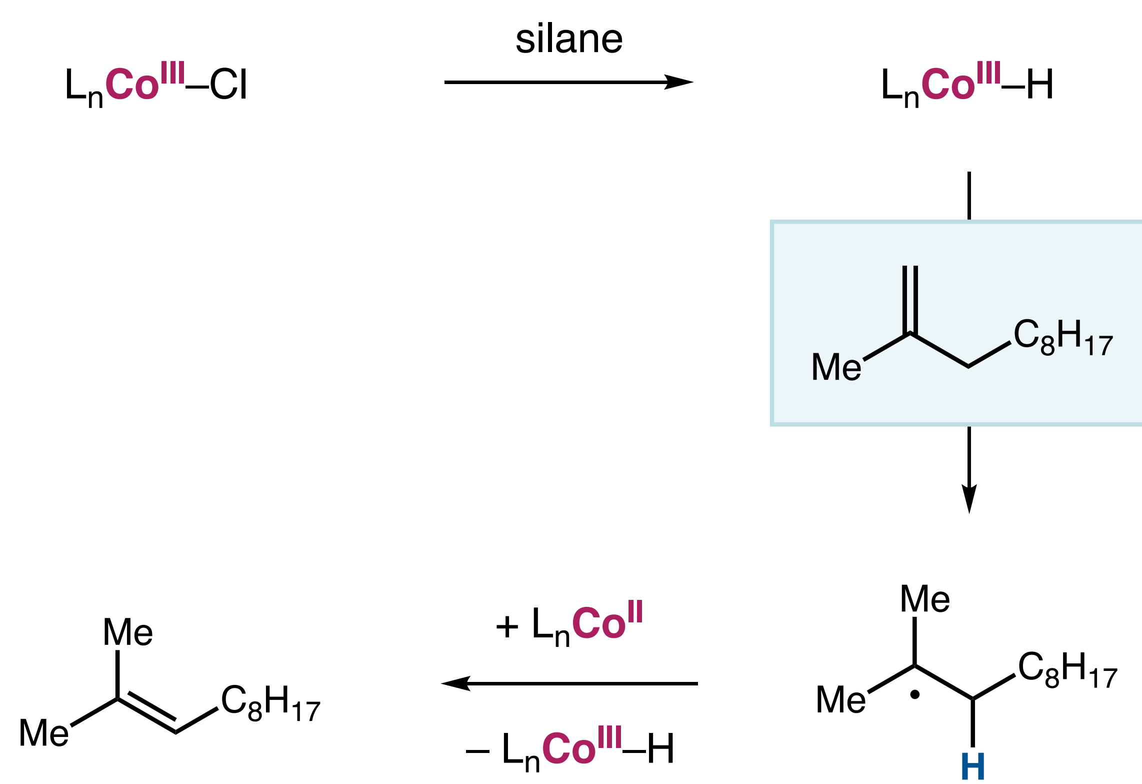


R
olefin
Co
+ silane
regioselective
R
Me
alkyl radical
Co
R
Me
radical
$Co^{III}L_n$
R
Me
alkylcobalt
R
Me
carbocation
R
Me
carbanion

Olefin Isomerization via Reversible HAT

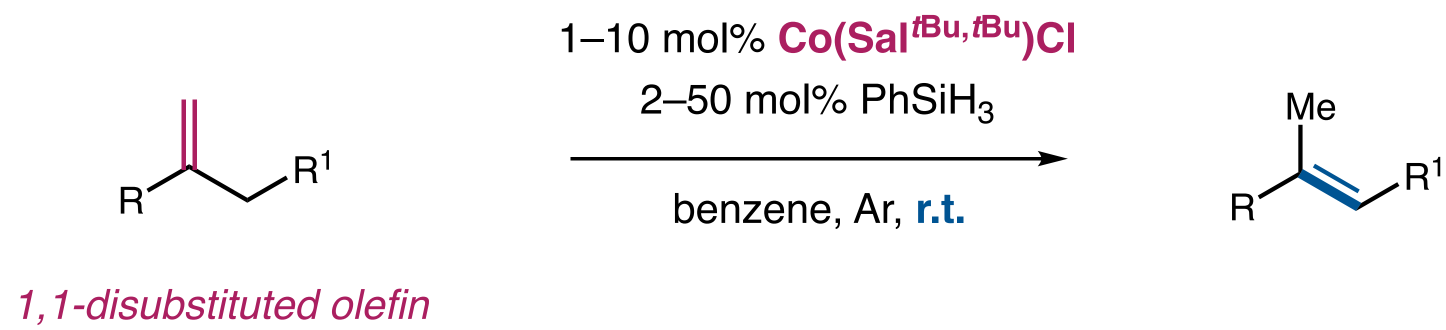


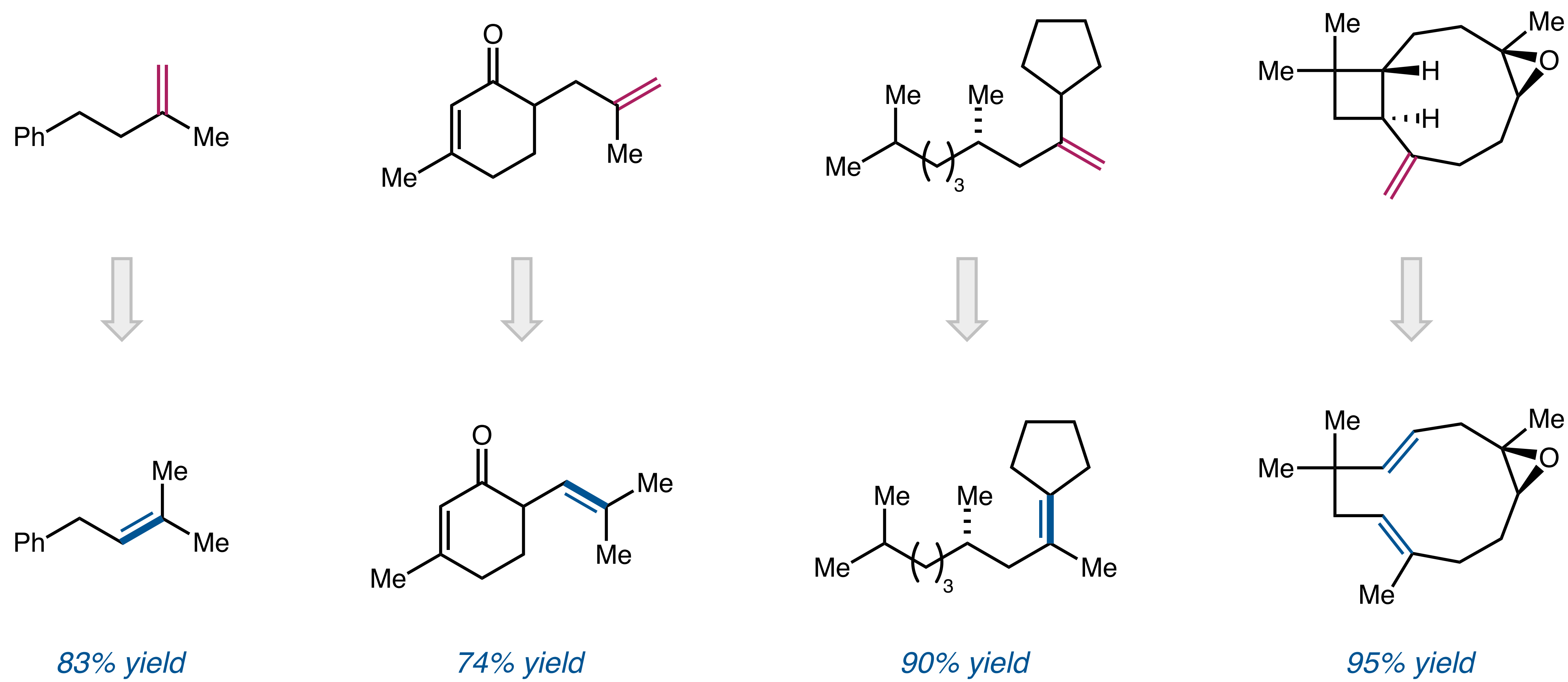




Crossley, S. W. M.; Barabé, F.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 16788

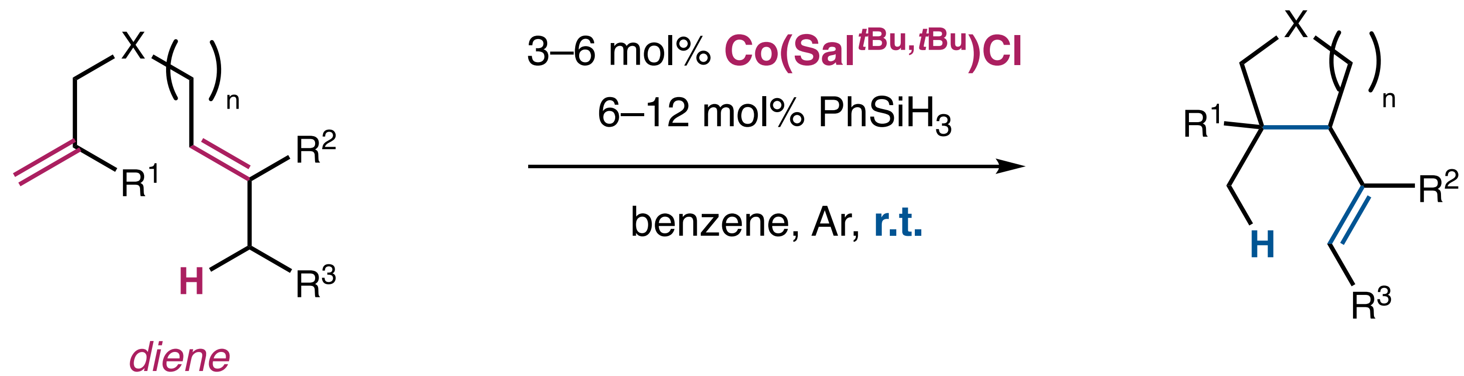
Olefin Isomerization via Reversible HAT

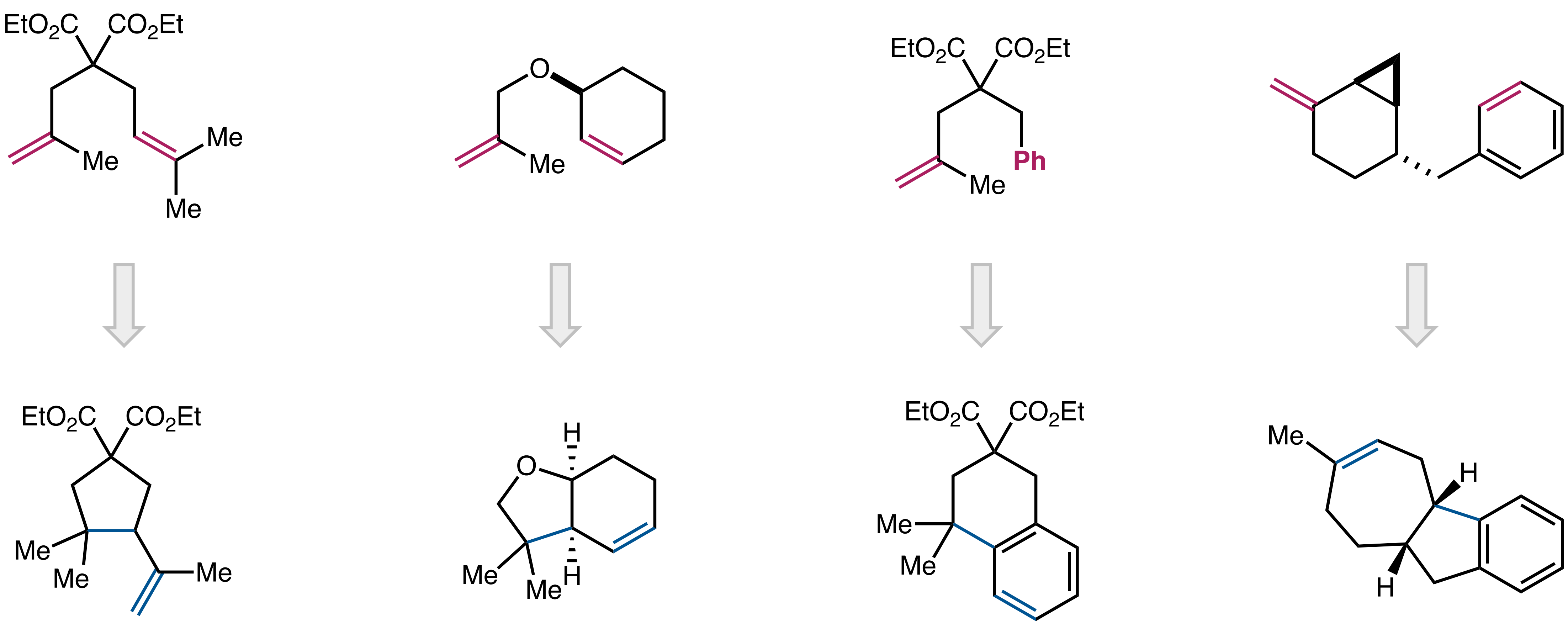




Crossley, S. W. M.; Barabé, F.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 16788

Diene Cycloisomerization via Reversible HAT

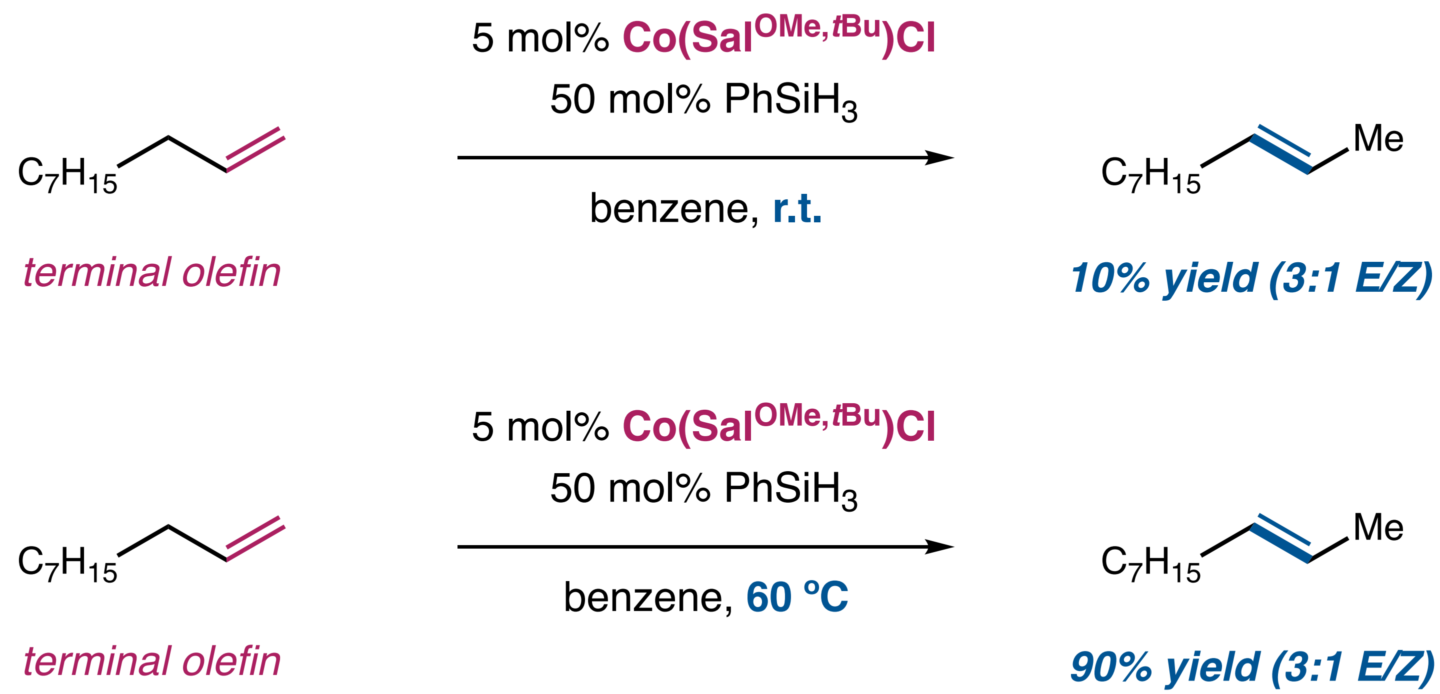


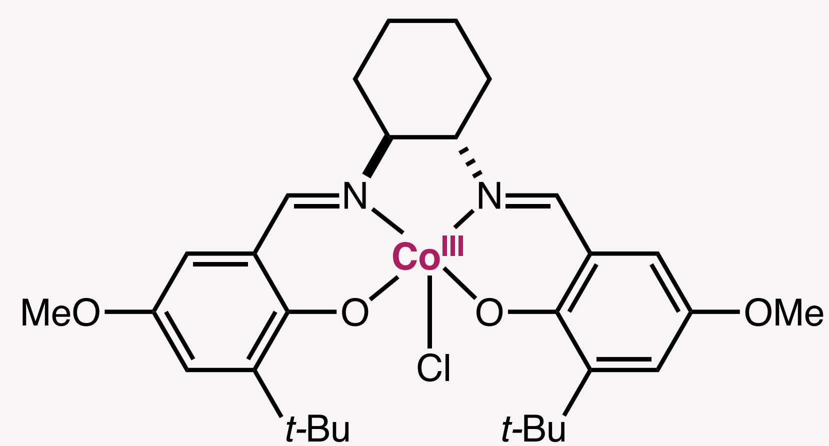


94% yield | *89% yield, >20:1 d.r.* | *92% yield* | *75% yield, >20:1 d.r.*

Crossley, S. W. M.; Barabé, F.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 16788

Terminal Olefin as Substrate: Temperature Effect

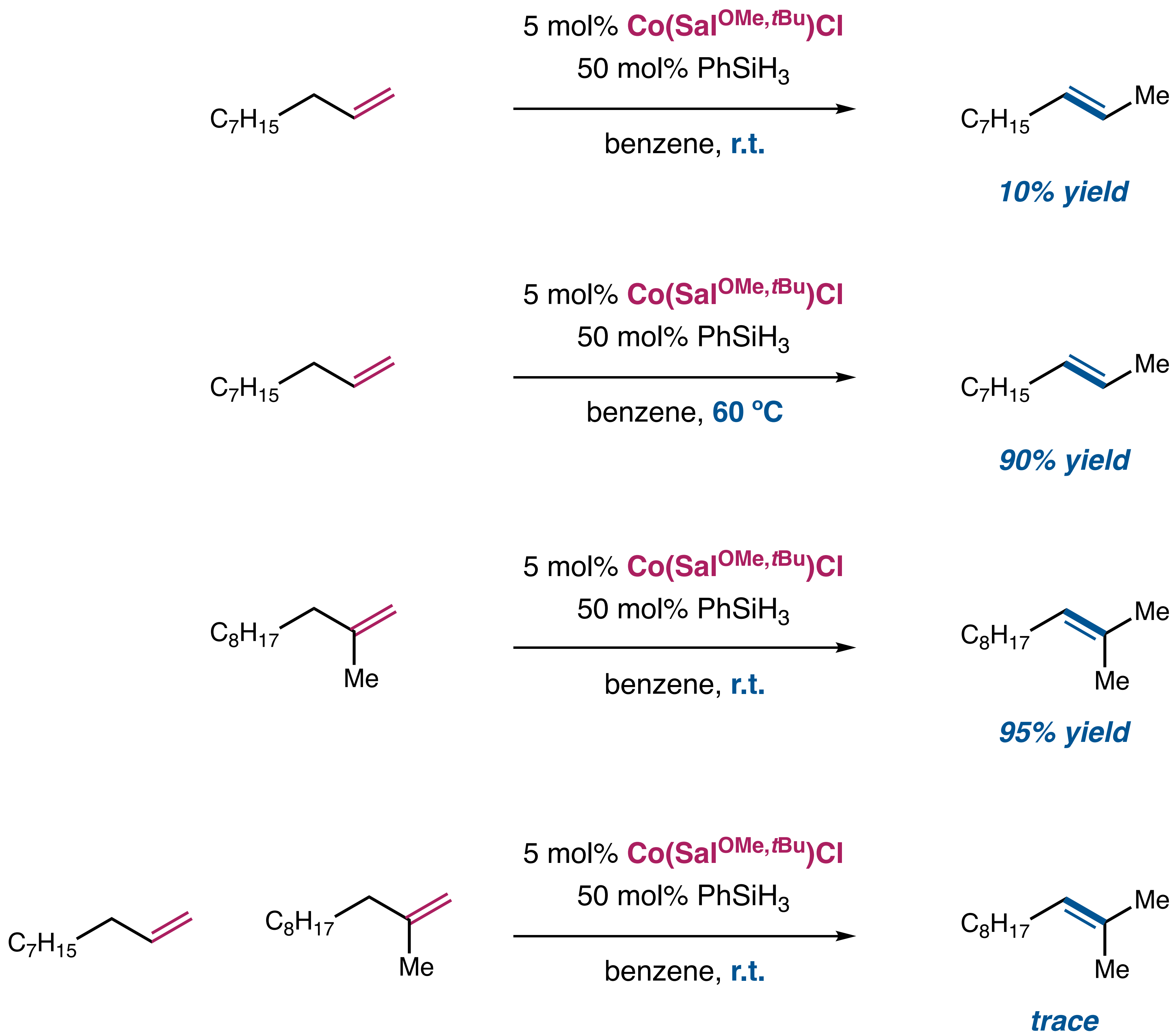




$Co(Sal^{OMe,\mathit{t}Bu})Cl$

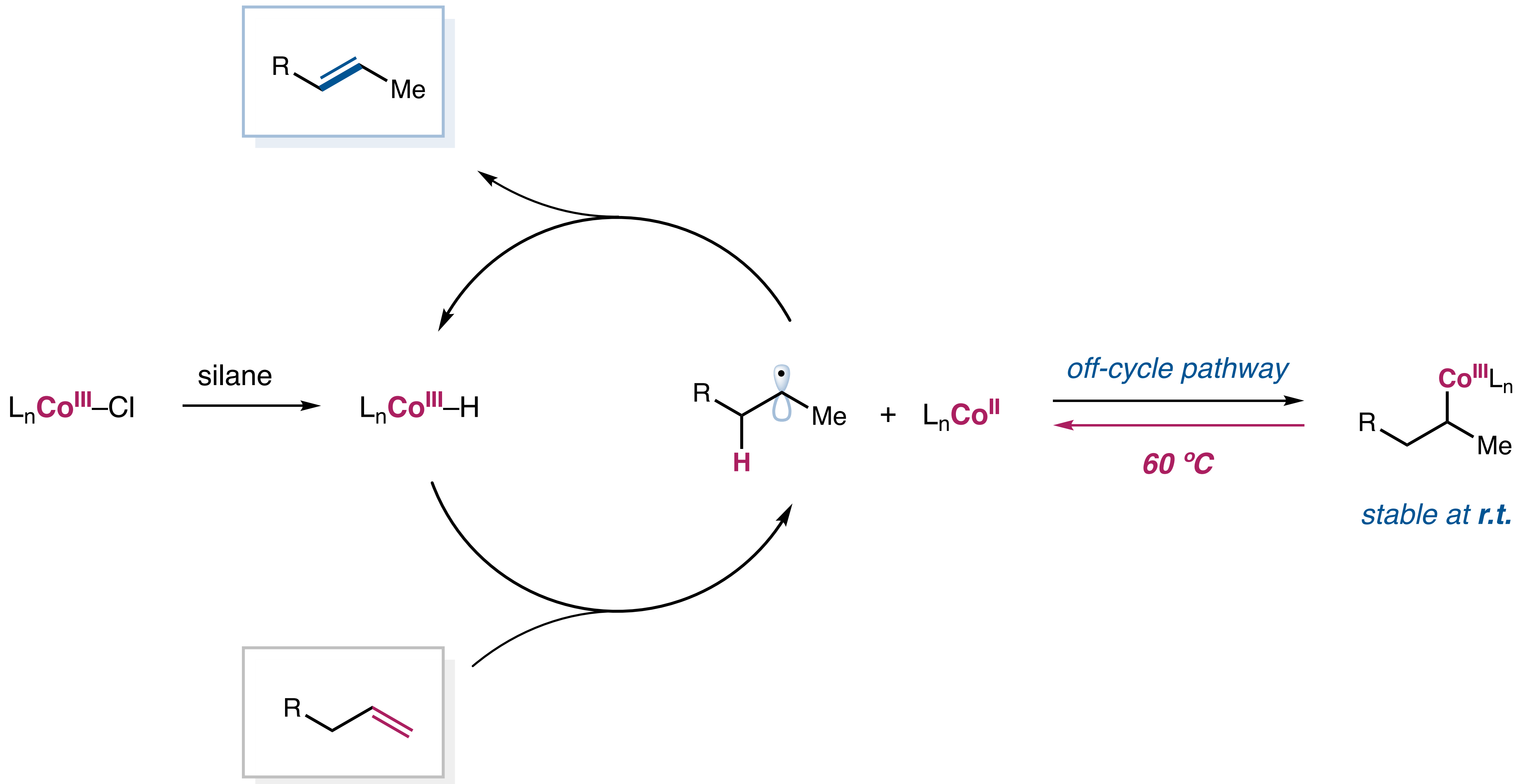
Crossley, S. W. M.; Barabé, F.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 16788

Terminal Olefin as Substrate: Temperature Effect



Crossley, S. W. M.; Barabé, F.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 16788

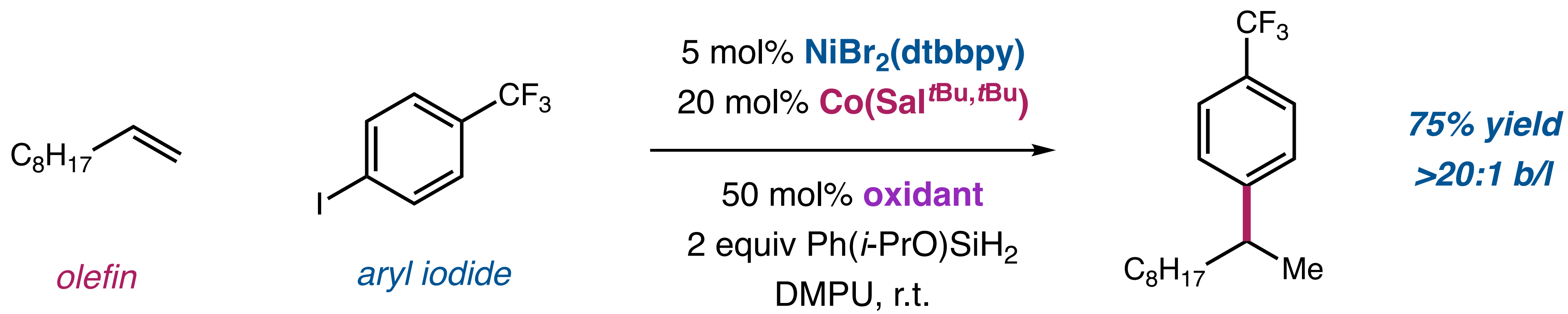
Proposed Mechanism: Off-Cycle Alkylcobalt Species

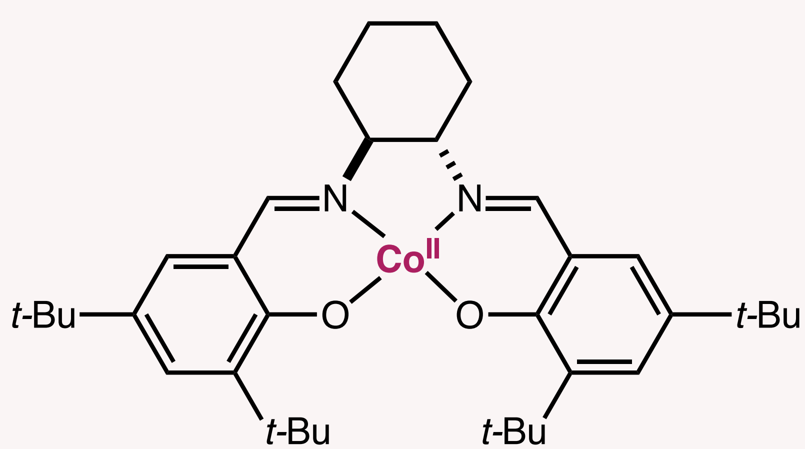


For 1,2-disubstituted olefin, formation of an alkylcobalt species with a tertiaryl alkyl is not favored.

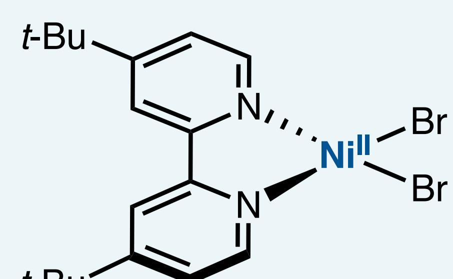
Crossley, S. W. M.; Barabé, F.; Shenvi, R. A. *J. Am. Chem. Soc.* **2014**, *136*, 16788

Olefin Hydroarylation via Dual Nickel and Cobalt Catalysis

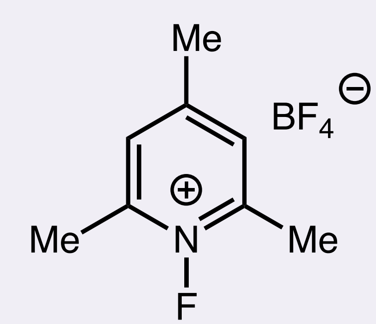




$Co(Sal^{tBu,tBu})$



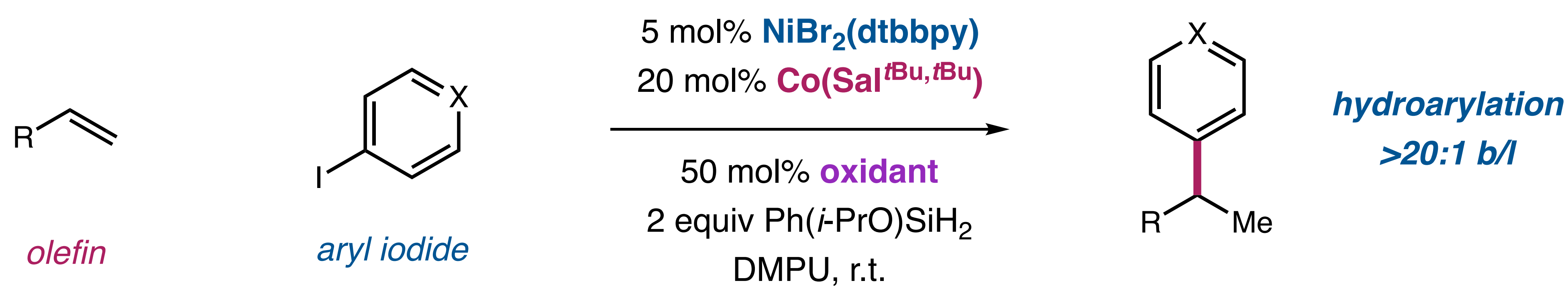
$NiBr_2$(dtbbpy)

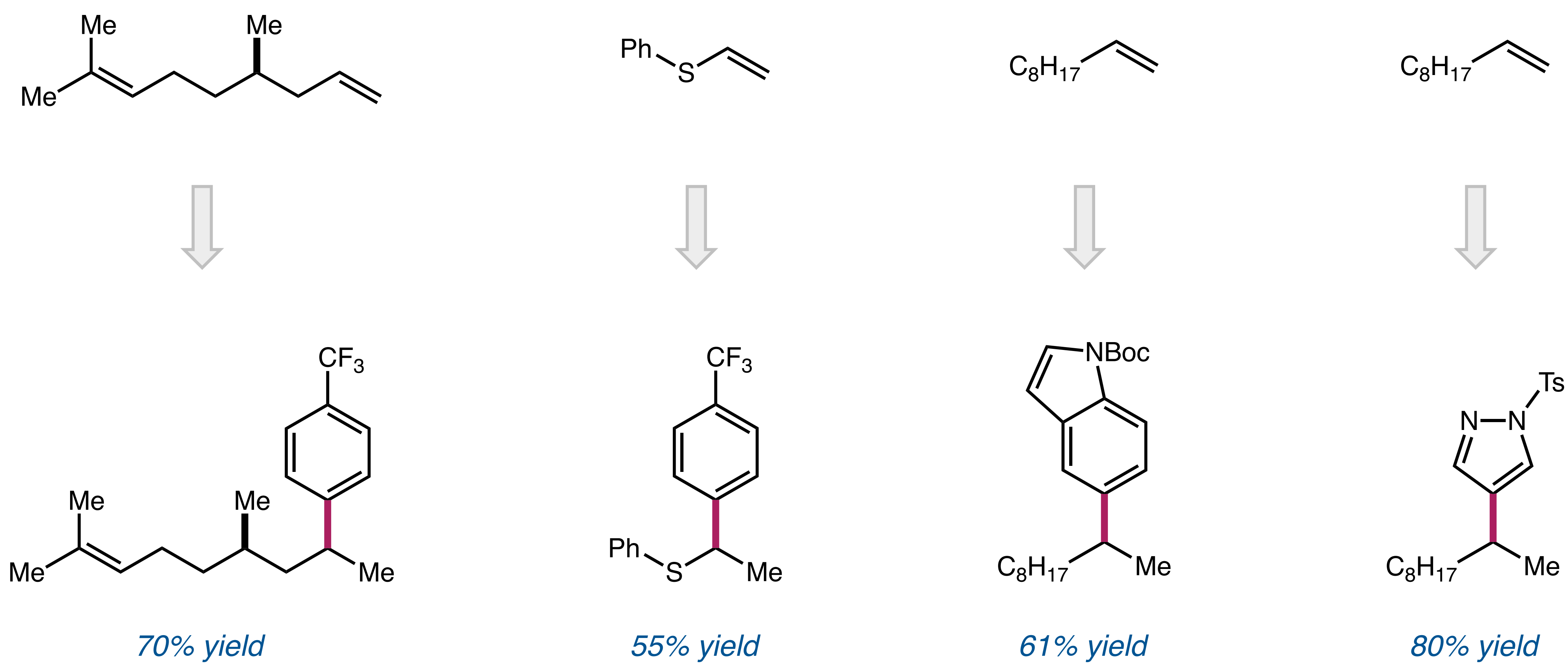


Oxidant

Green, S. A.; Matos, J. L. M.; Yagi, A.; Shenvi, R. A. *J. Am. Chem. Soc.* **2016**, *138*, 12779

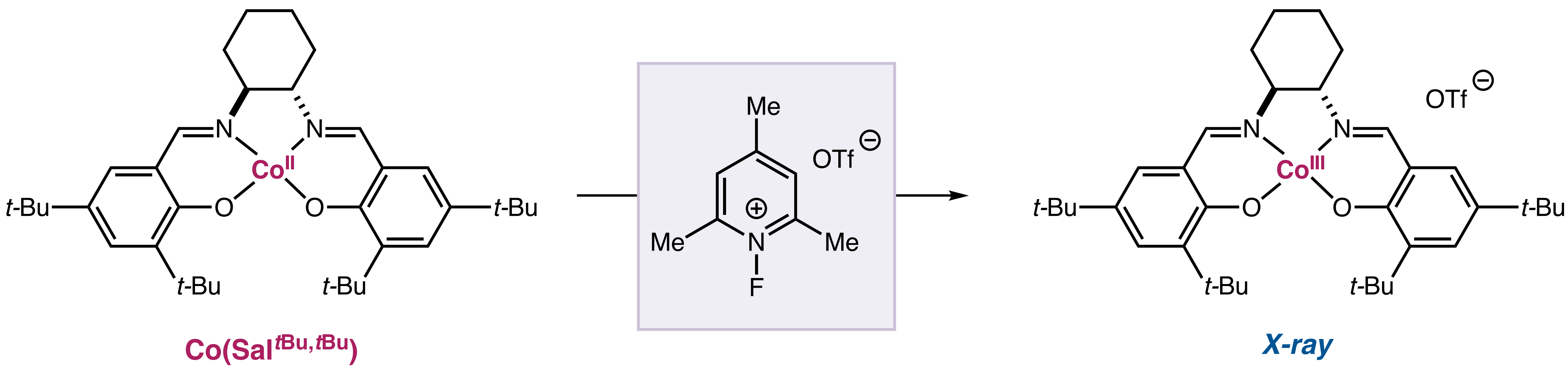
Olefin Hydroarylation via Dual Nickel and Cobalt Catalysis

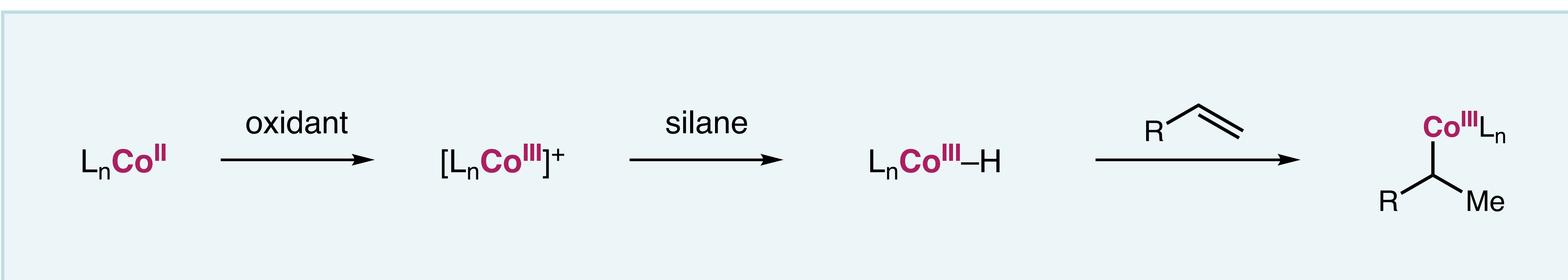




Green, S. A.; Matos, J. L. M.; Yagi, A.; Shenvi, R. A. *J. Am. Chem. Soc.* **2016**, *138*, 12779

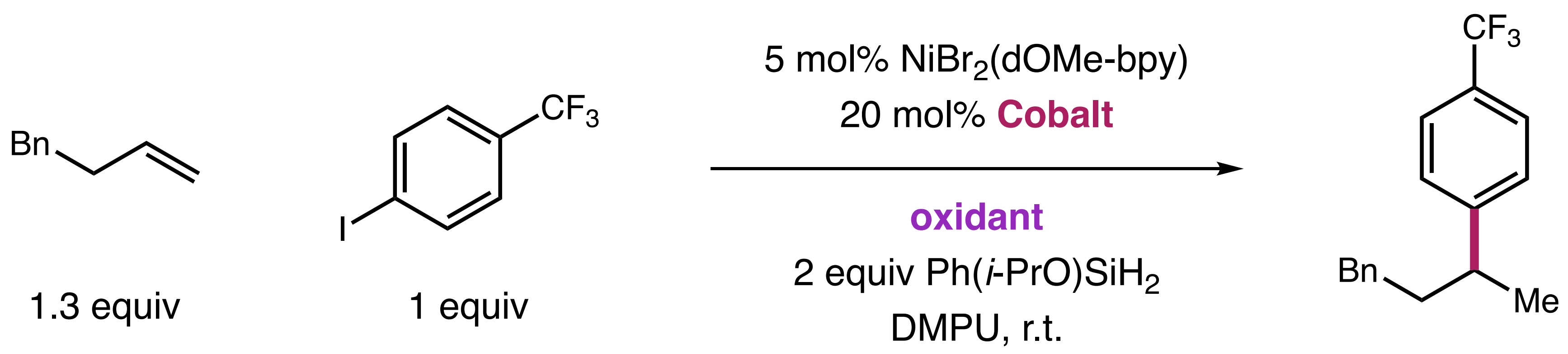
Mechanistic Studies: Roles of the Oxidant





Shevick, S. L.; Obradors, C.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 12056

Mechanistic Studies: Roles of the Oxidant



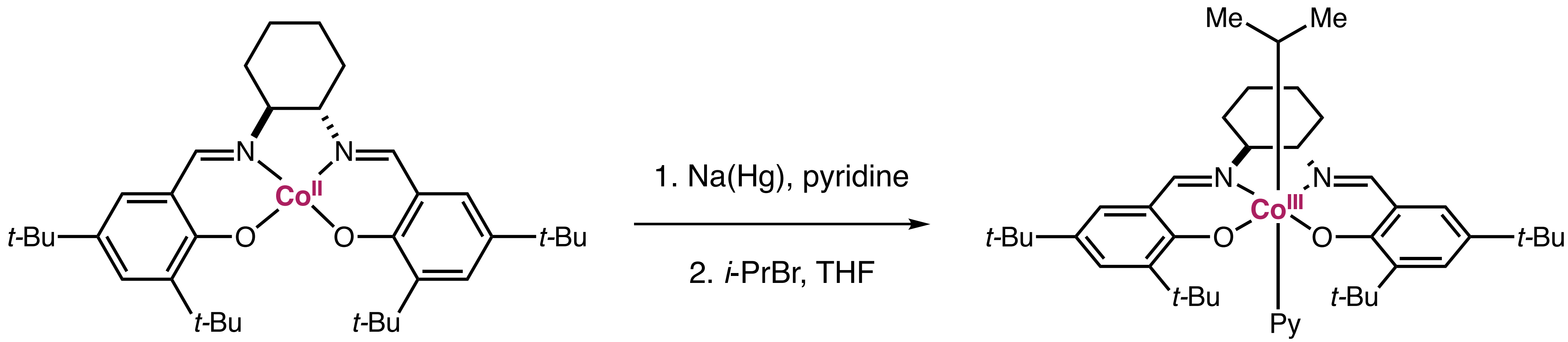
20 mol% **Co^{II}(Sal^{tBu,tBu})**, 50 mol% **oxidant**	***82% yield***
20 mol% **Co^{III}(Sal^{tBu,tBu})(BF_4)**, no **oxidant**	***56% yield***
20 mol% **Co^{III}(Sal^{tBu,tBu})(BF_4)**, 30 mol% **oxidant**	***70% yield***

Roles of oxidant:

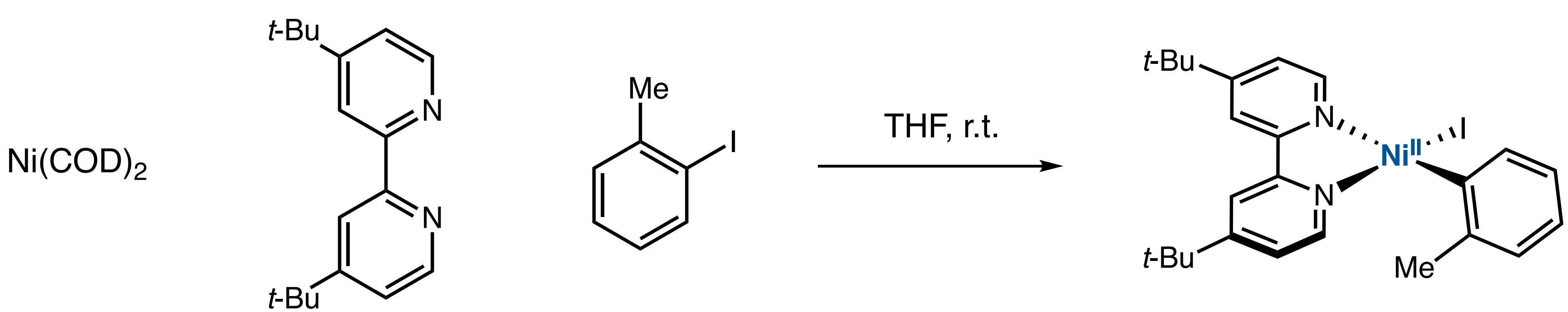
- Generating **Co^{III}** to initiate the reaction
- Reoxidizing **Co^{II}** to the active **Co^{III}** oxidation state

Shevick, S. L.; Obradors, C.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 12056

Mechanistic Studies: Cobalt to Nickel Alkyl Transfer



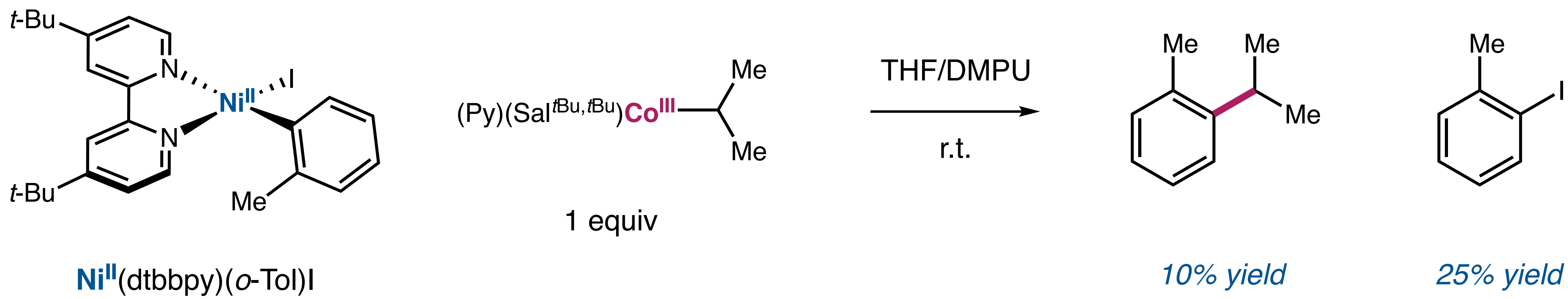
$Co^{II}(Sal^{tBu,tBu})$ $\quad$ $(Py)(Sal^{tBu,tBu})Co^{III}$—*i*-Pr

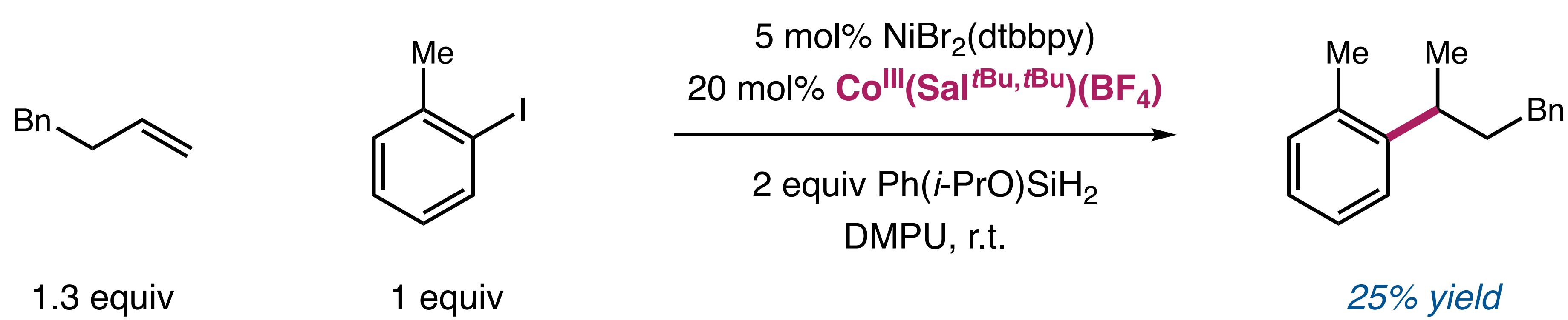


Ni^{II}(dtbbpy)(*o*-Tol)I

Shevick, S. L.; Obradors, C.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 12056

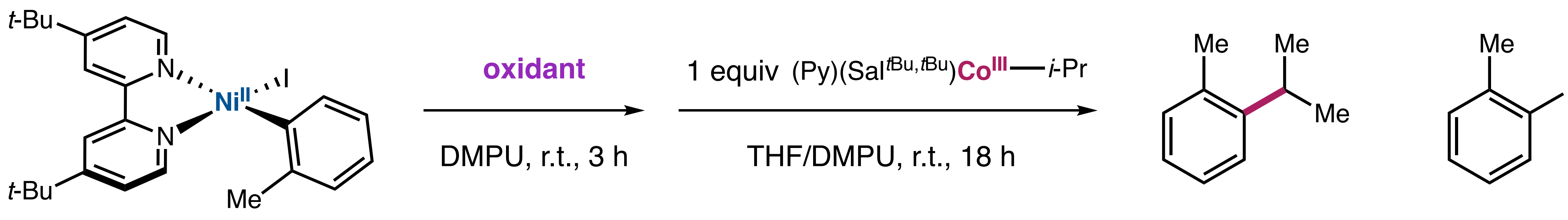
Mechanistic Studies: Cobalt to Nickel Alkyl Transfer



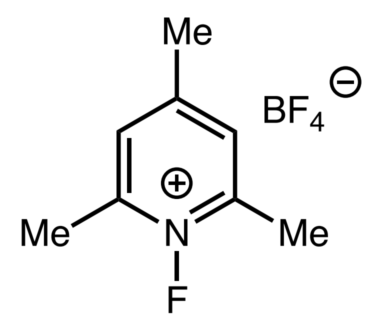


Shevick, S. L.; Obradors, C.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 12056

Mechanistic Studies: Cobalt to Nickel Alkyl Transfer

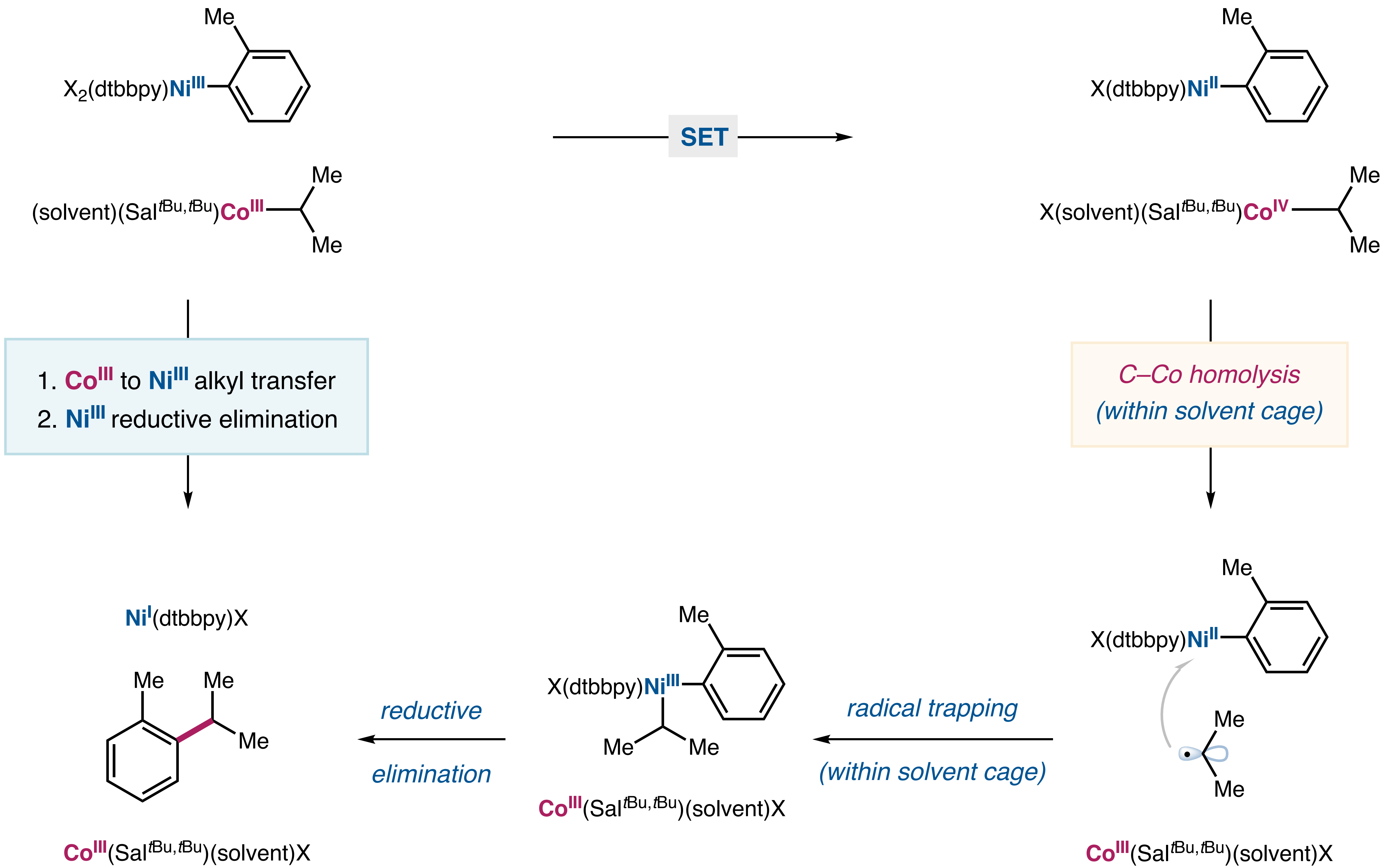


Ni^{II}(dtbbpy)(*o*-Tol)I

oxidant	*yield*	*yield*
none	*10%*	*25%*
1 equiv 	*17%*	*78%*
1 equiv AcFcBF$_4$ (Fe^{III} as oxidant)	*18%*	*18%*
2 equiv AcFcBF$_4$ (Fe^{III} as oxidant)	*41%*	*44%*

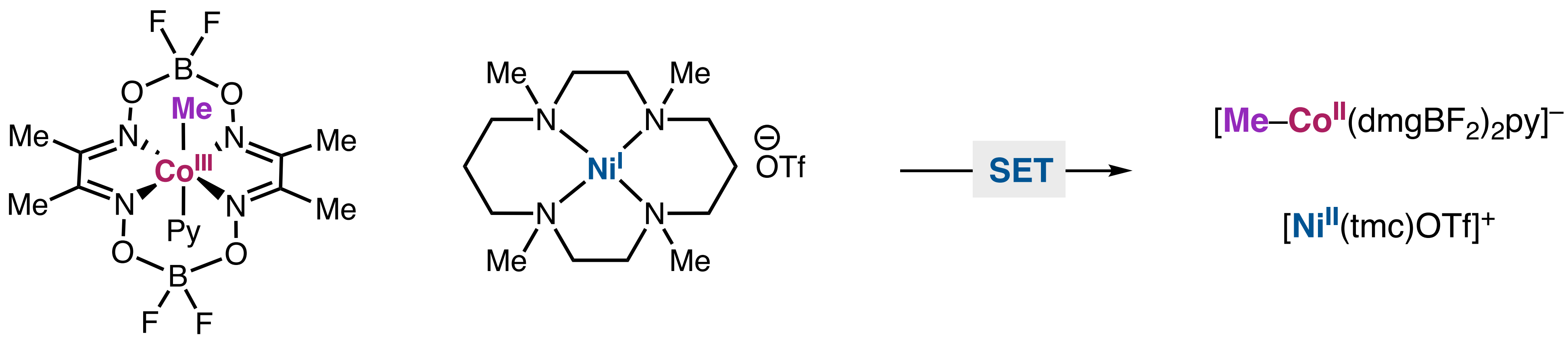
Shevick, S. L.; Obradors, C.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 12056

Mechanistic Studies: Cobalt(III) to Nickel(III) Alkyl Transfer



Shevick, S. L.; Obradors, C.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 12056

Cobalt(III) to Nickel Alkyl Transfer: Literature Precedents



Me–**Co**^{III}(dmgBF$_2$)$_2$py

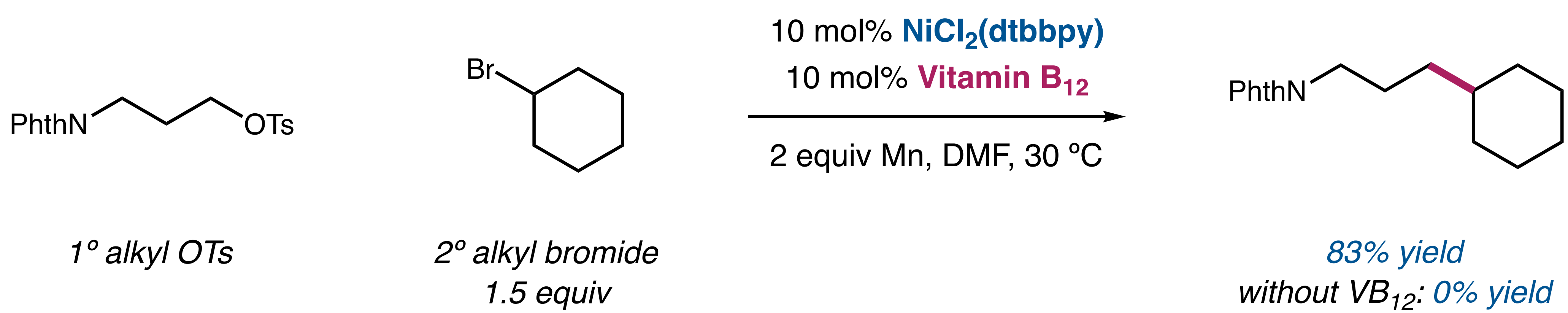
[**Ni**^{I}(tmc)]OTf

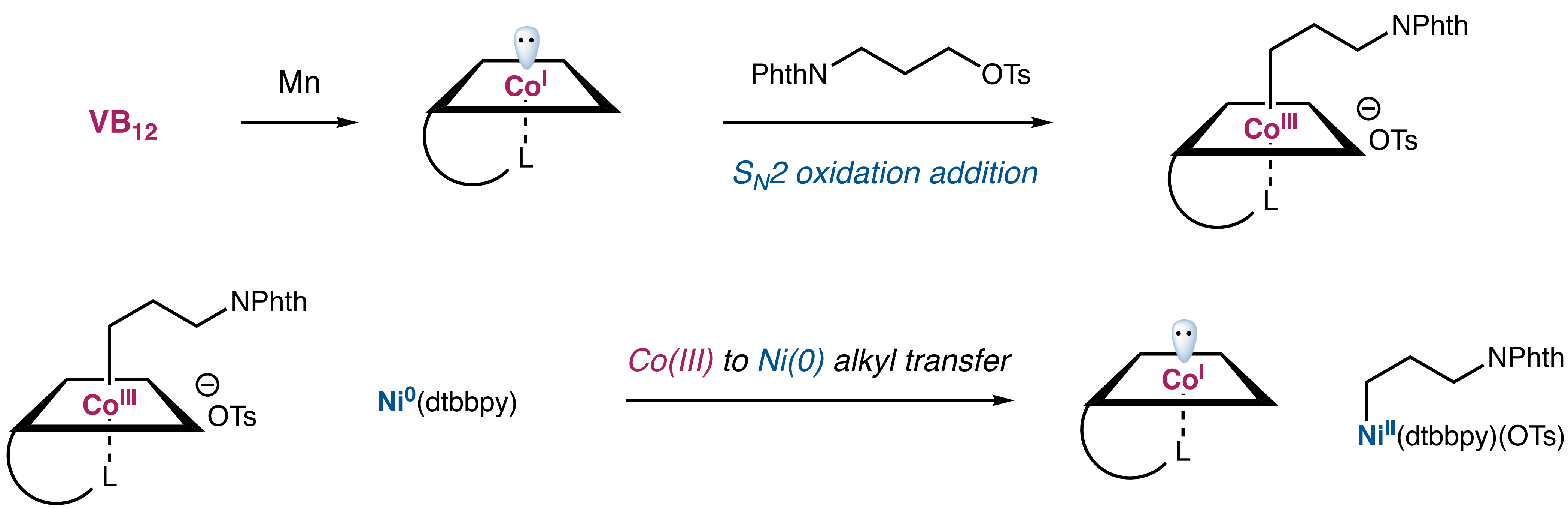
[**Me**–**Co**^{II}(dmgBF$_2$)$_2$py]$^-$ —*C–Co homolysis*→ **Me**• [**Co**^{I}(dmgBF$_2$)$_2$py]$^-$

Me• [**Ni**^{I}(tmc)]OTf —*radical trapping*→ [**Me**–**Ni**^{II}(tmc)]OTf

Ram, M. S.; Riordan, C. G.; Yap, G. P. A.; Liable-Sands, L.;
Rheingold, A. L.; Marchaj, A.; Norton, J. R. *J. Am.Chem. Soc.* **1997,** *119*, 1648

Cobalt(III) to Nickel Alkyl Transfer: Literature Precedents

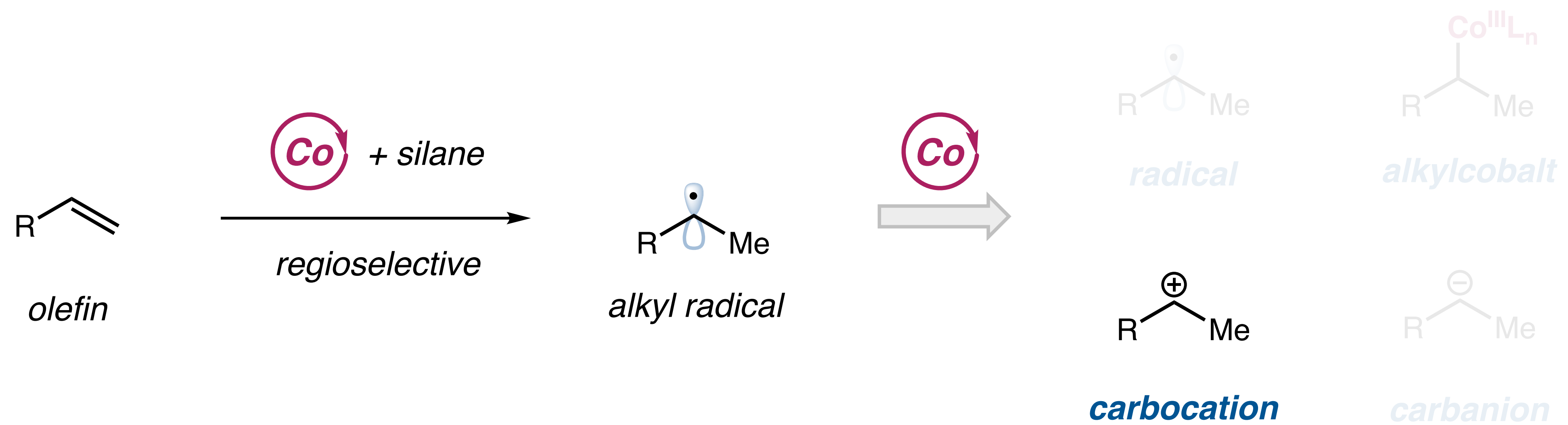




Alternatively, Co(III) to Ni(I)–R alkyl transfer is also feasible

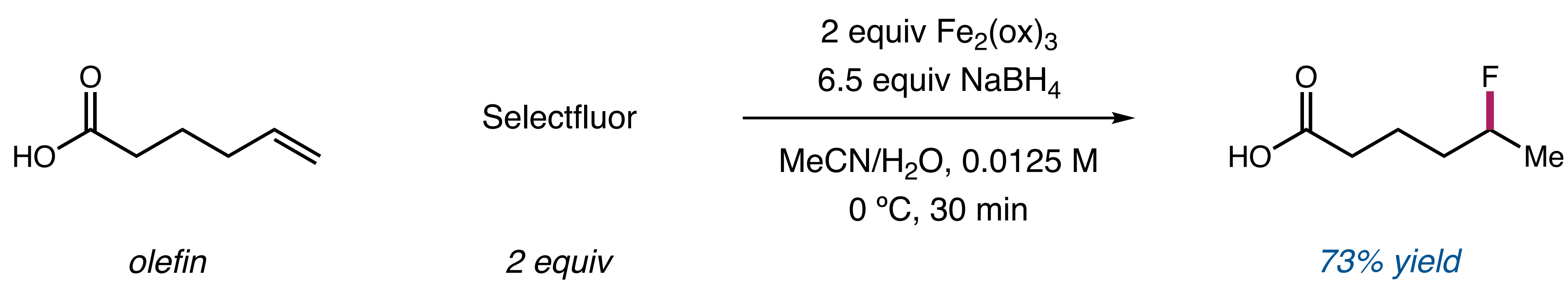
Komeyama, K.; Michiyuki, T.; Osaka, T. *ACS Catalysis* **2019**, *9*, 9285

Outline



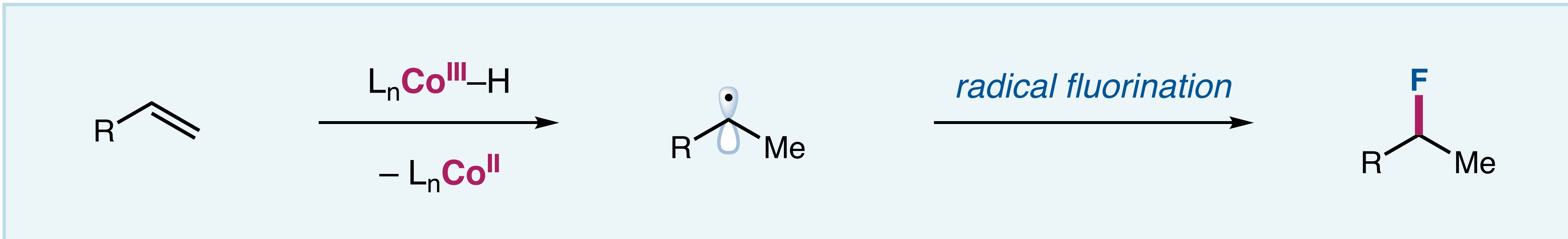
R
olefin
Co + silane
regioselective
R Me
alkyl radical
Co
R Me
radical
Co^{III}L$_n$
R Me
alkylcobalt
R Me
carbocation
R Me
carbanion

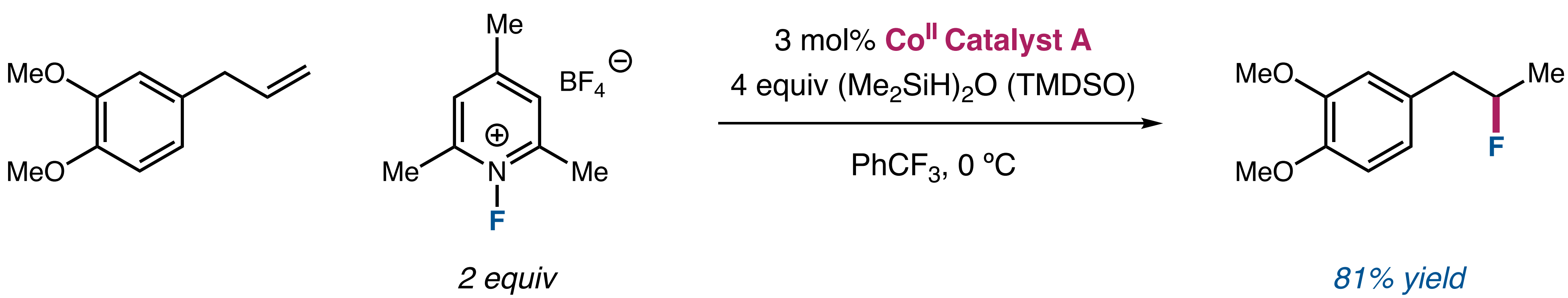
Hydrofluorination of Olefin via Radical Fluorination

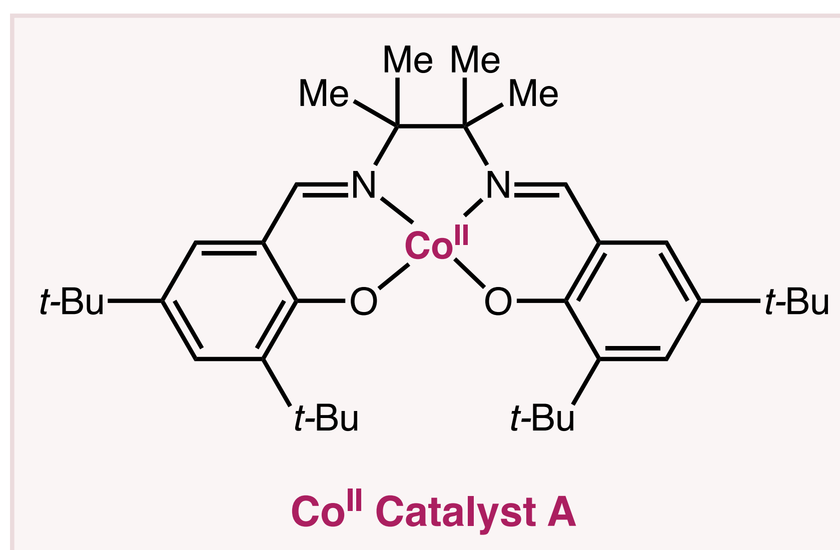


Barker, T. J.; Boger, D. L. *J. Am. Chem. Soc.* **2012**, *134*, 13588

Hydrofluorination of Olefin via Radical Fluorination

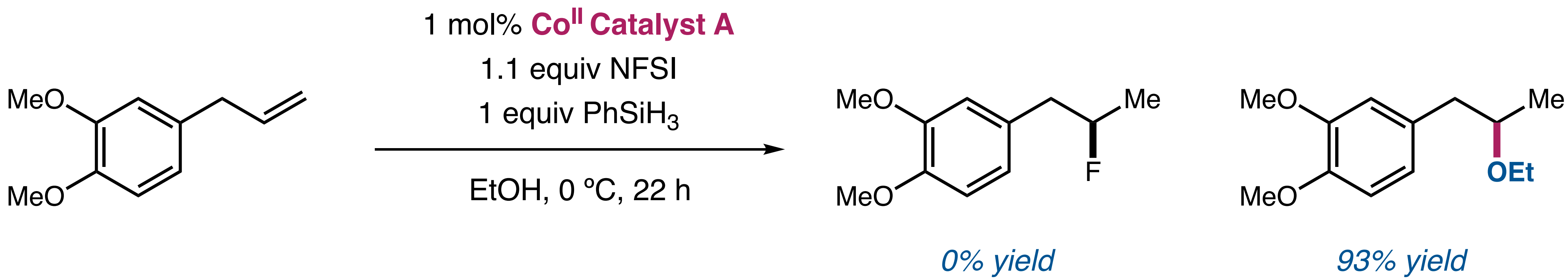


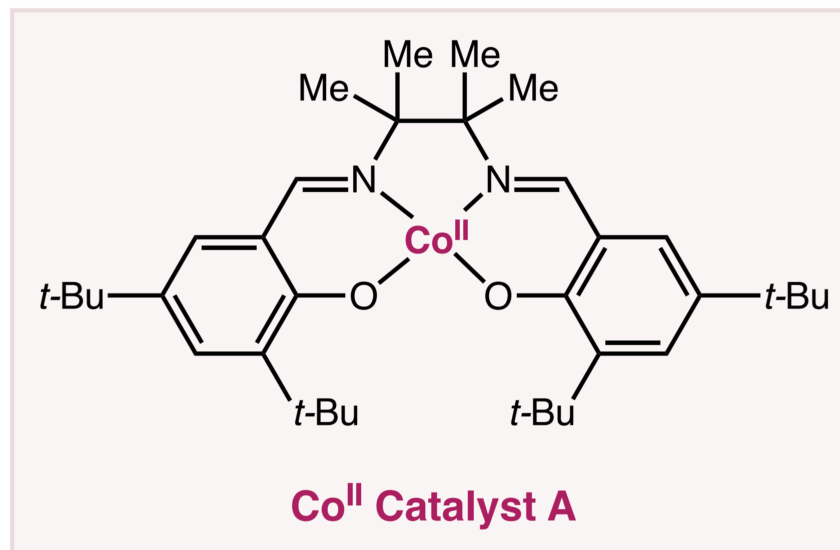


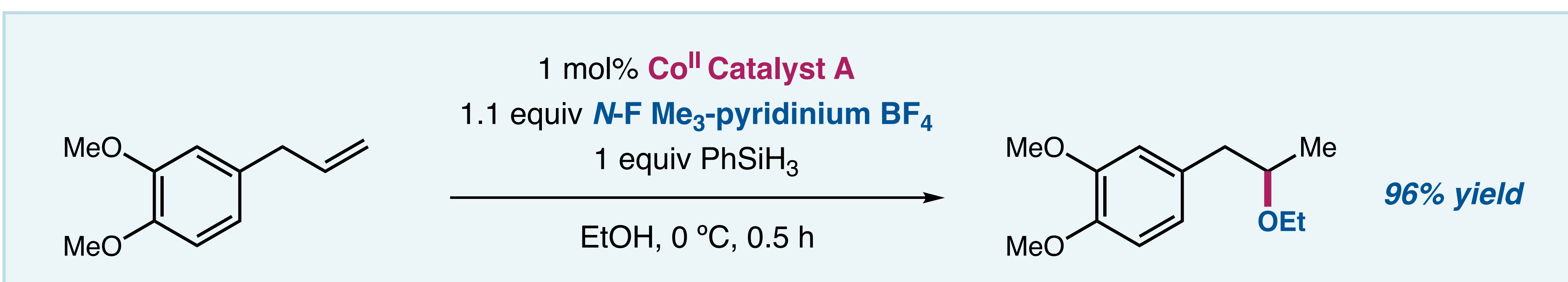


Shigehisa, H.; Nishi, E.; Fujisawa, M.; Hiroya, K. *Org. Lett.* **2013**, *15*, 5158

Hydrofluorination of Olefin: An Happy Accident

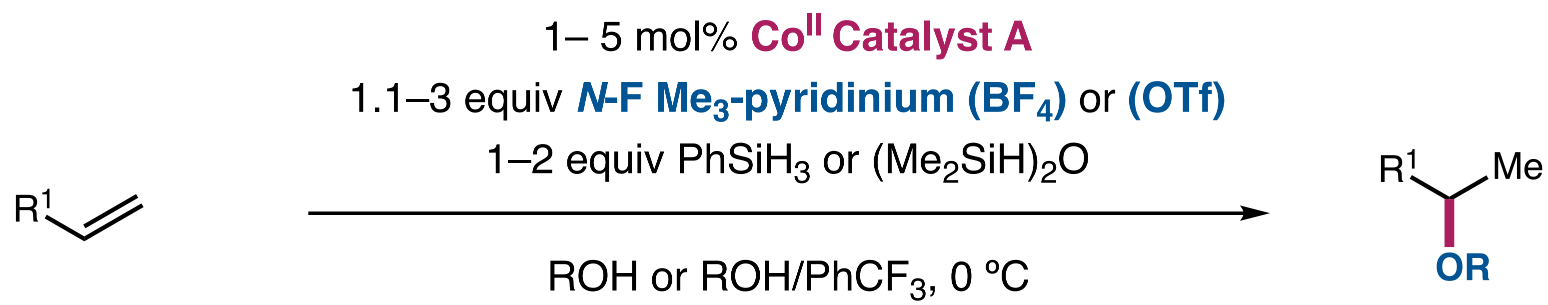


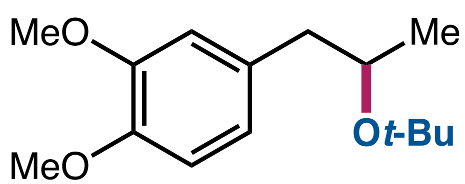




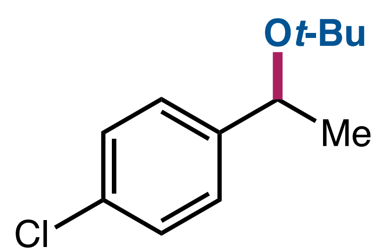
Shigehisa, H. *Chem. Pharm. Bull.* **2018**, *66*, 339
Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306

Hydroalkoxylation of Olefin: Scope

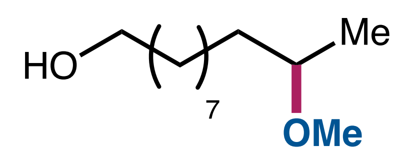




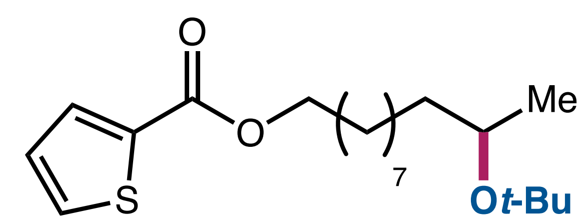
92% yield



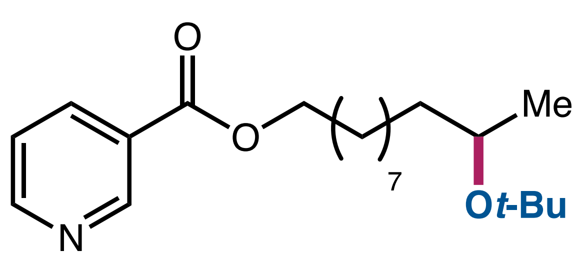
88% yield



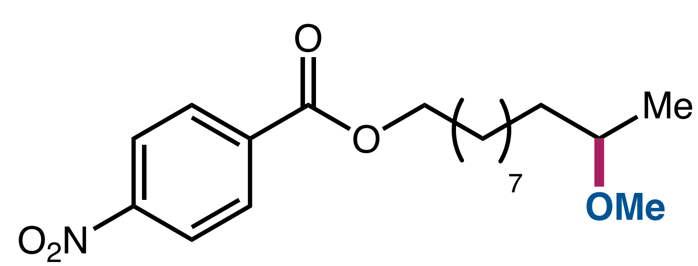
76% yield



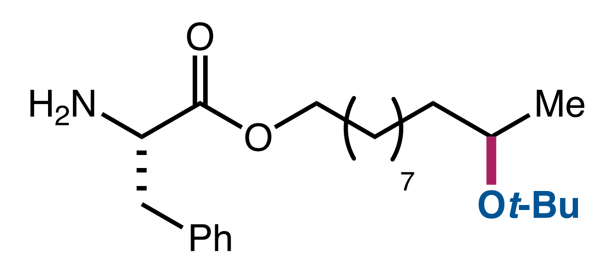
42% yield



7% yield
with MeOH: 33% yield



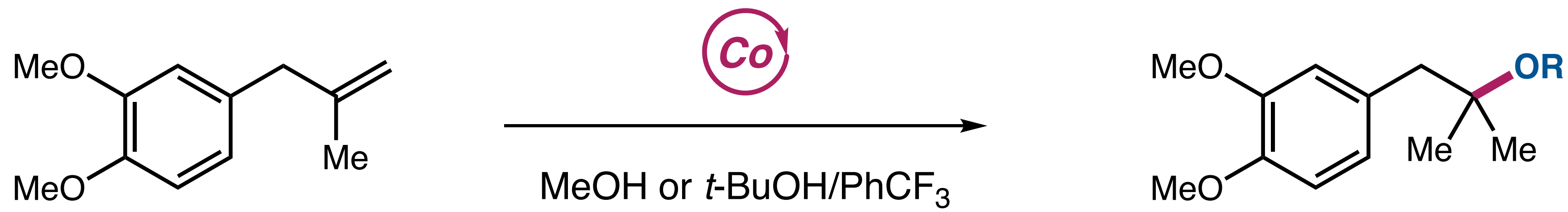
55% yield



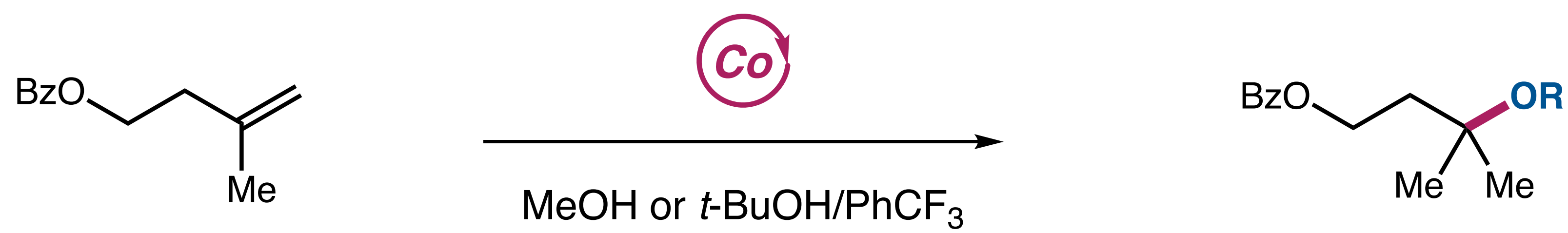
9% yield
with MeOH: 55% yield

Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306

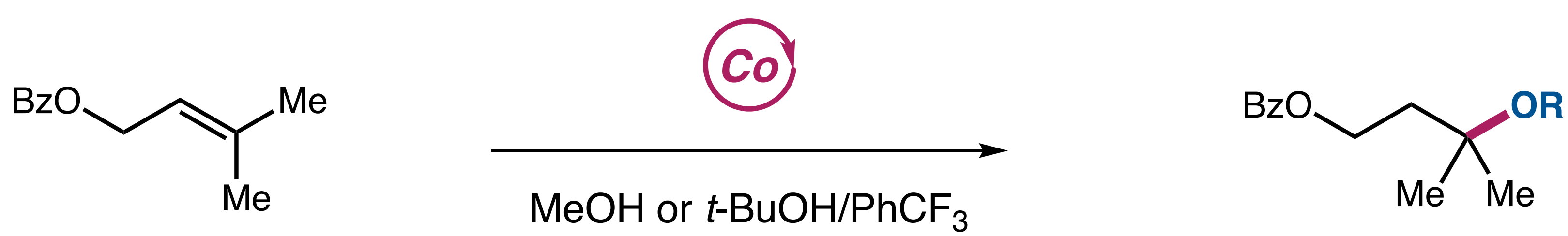
Hydroalkoxylation of Olefin: Tertiary Alkyl C–O Formation



R = Me, *71% yield*
R = *t*-Bu, *34% yield*



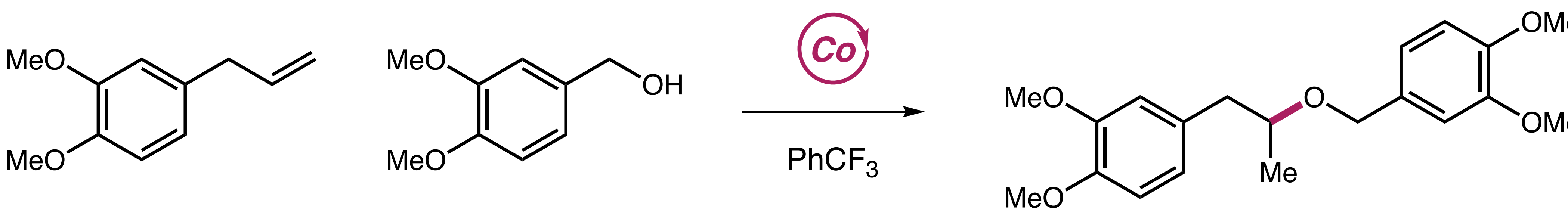
R = Me, *51% yield*
R = *t*-Bu, *34% yield*



R = Me, *57% yield*
R = *t*-Bu, *24% yield*

Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306

Hydroalkoxylation of Olefin: Alcohol not as Solvent

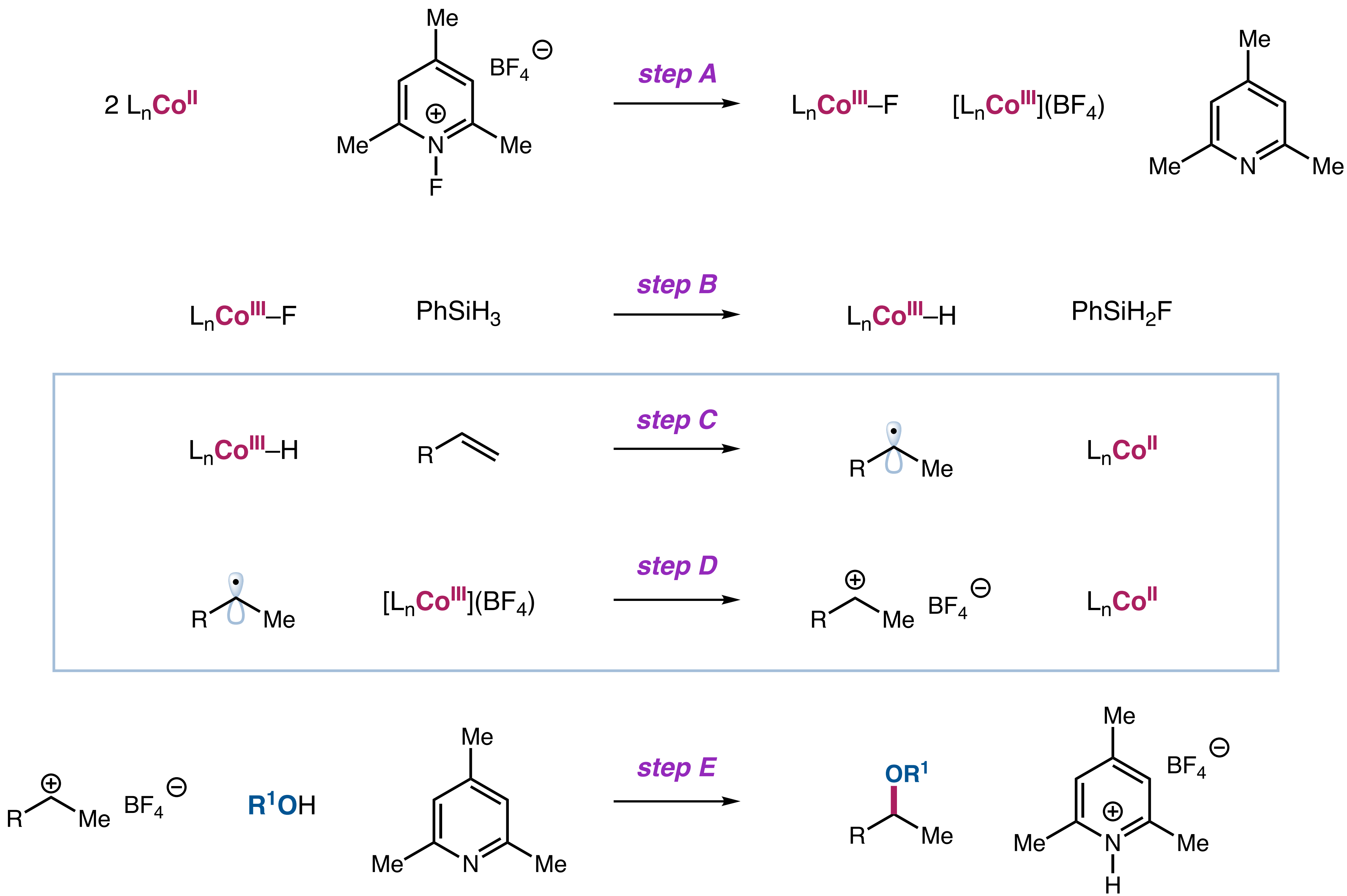


x equiv ***y equiv***

x equiv	***y equiv***	***yield***
1 equiv	*2 equiv*	***79% yield***
2 equiv	*1 equiv*	***80% yield***
1 equiv	*1 equiv*	***67% yield***

Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306

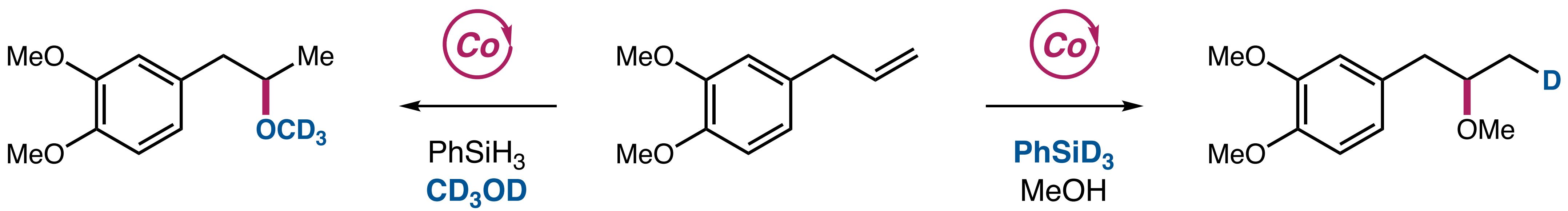
Hydroalkoxylation of Olefin: Proposed Mechanism



Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306

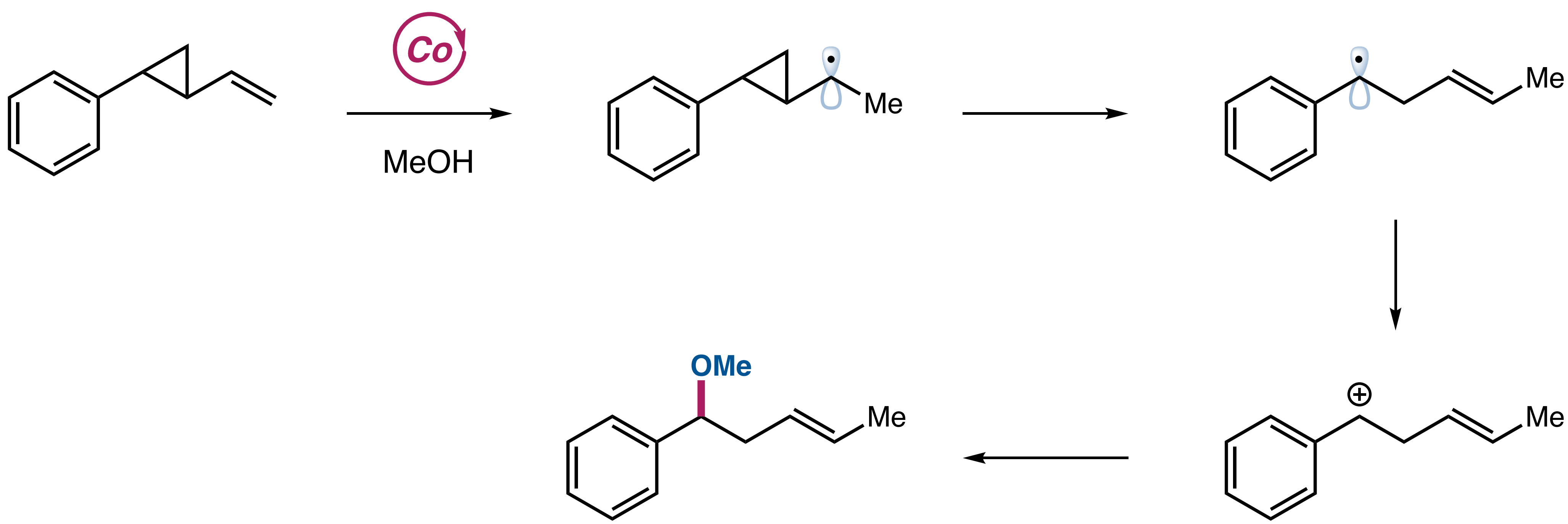
Hydroalkoxylation of Olefin: Mechanistic Studies

Dueterium labeling



90% yield *92% yield*

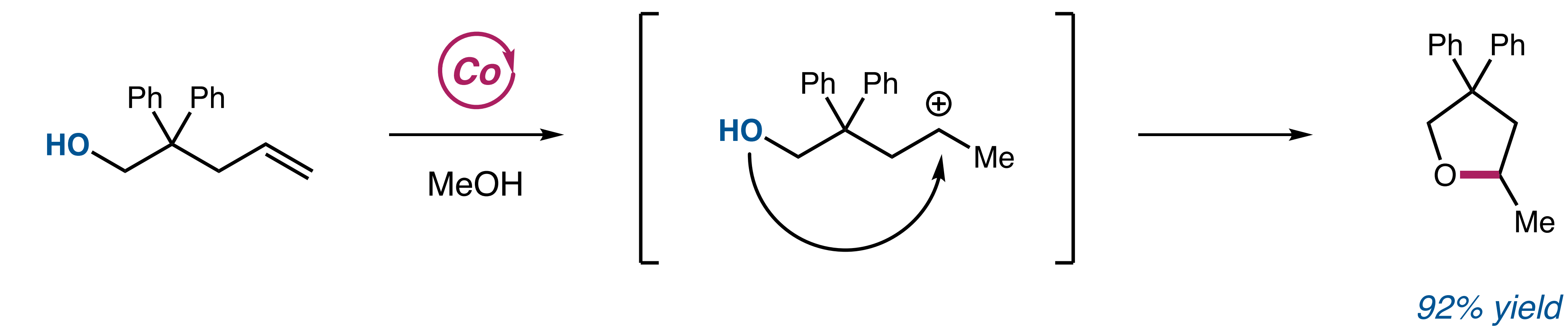
Radical Clock

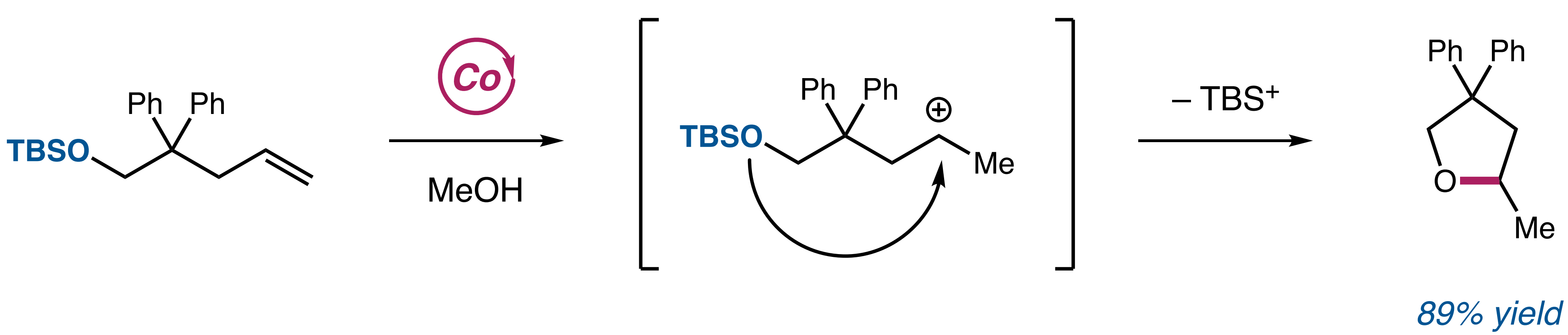


33% yield

Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306

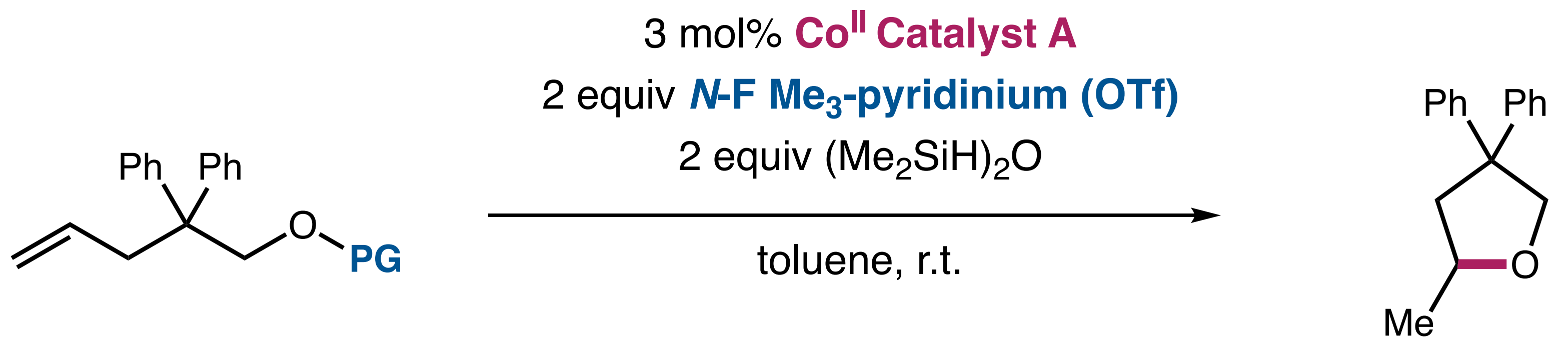
Hydroalkoxylation of Olefin: Mechanistic Studies



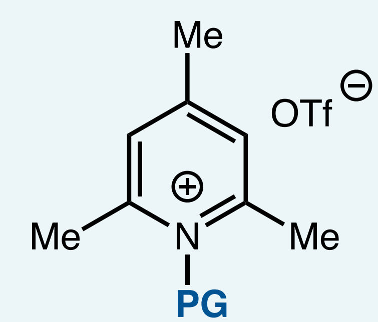


Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306

Intramolecular Hydroalkoxylation of Olefin with Protected Alcohol



PG	time (h)	*yield*
TBS	0.5	*99%*
MOM	0.5	*99%*
MEM	0.5	*97%*
BOM	0.5	*99%*
Bn	1.5	*93%*
Me	1.5	*87%*
Ac	6.5	*27%*

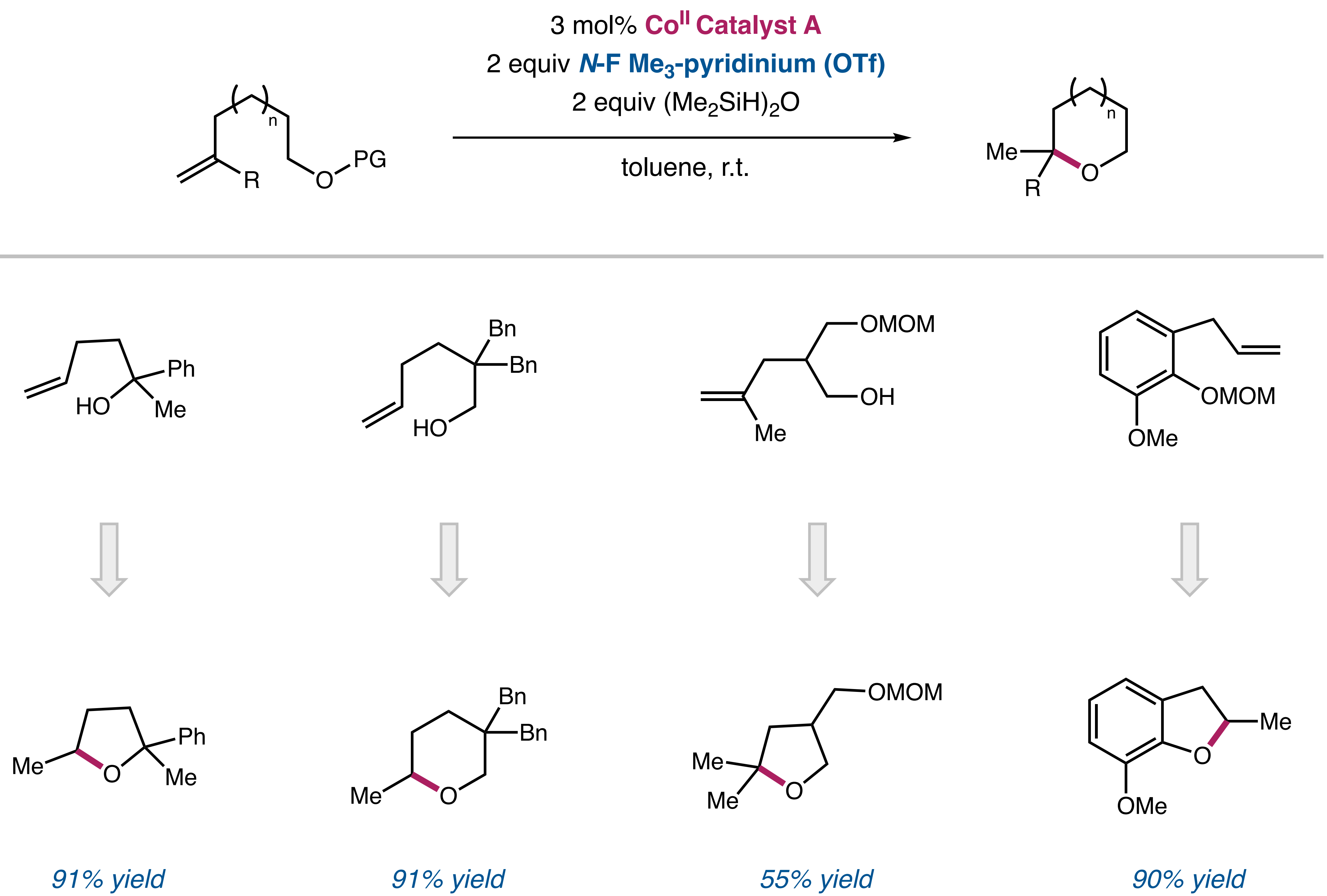


PG = MOM, Bn, Me

major by-product
(>80% yield)

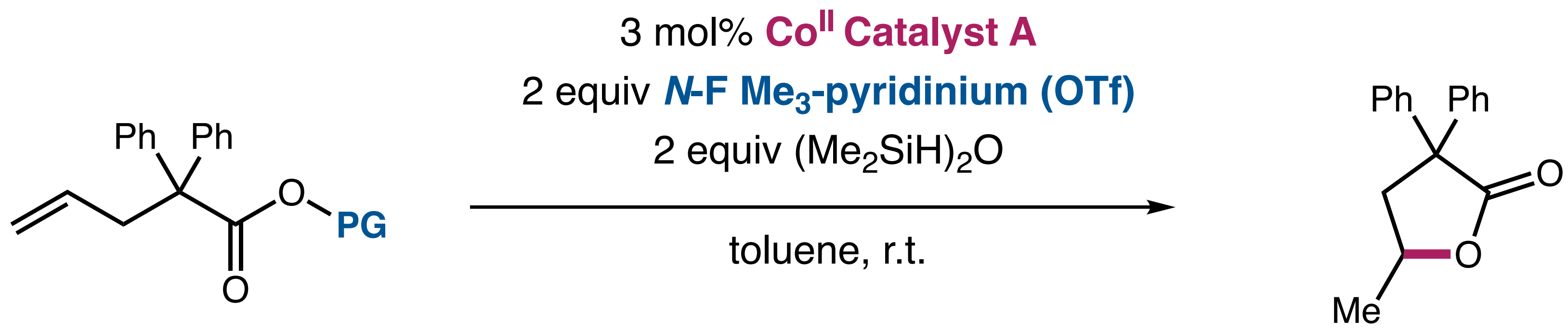
Shigehisa, H. *et. al., J. Am. Chem. Soc.* **2016**, *138*, 10597

Intramolecular Hydroalkoxylation of Olefin with Protected Alcohol



Shigehisa, H. *et. al., J. Am. Chem. Soc.* **2016**, *138*, 10597

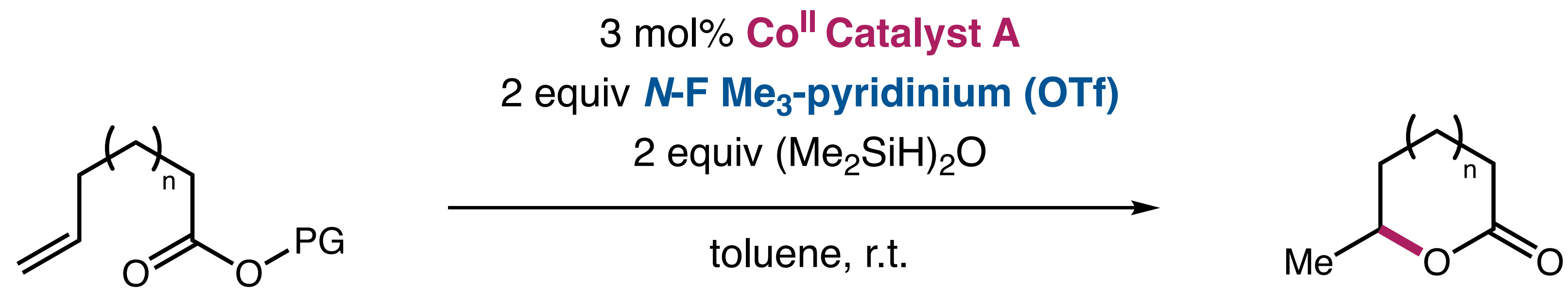
Intramolecular Hydroalkoxylation of Olefin with Acid and Esters

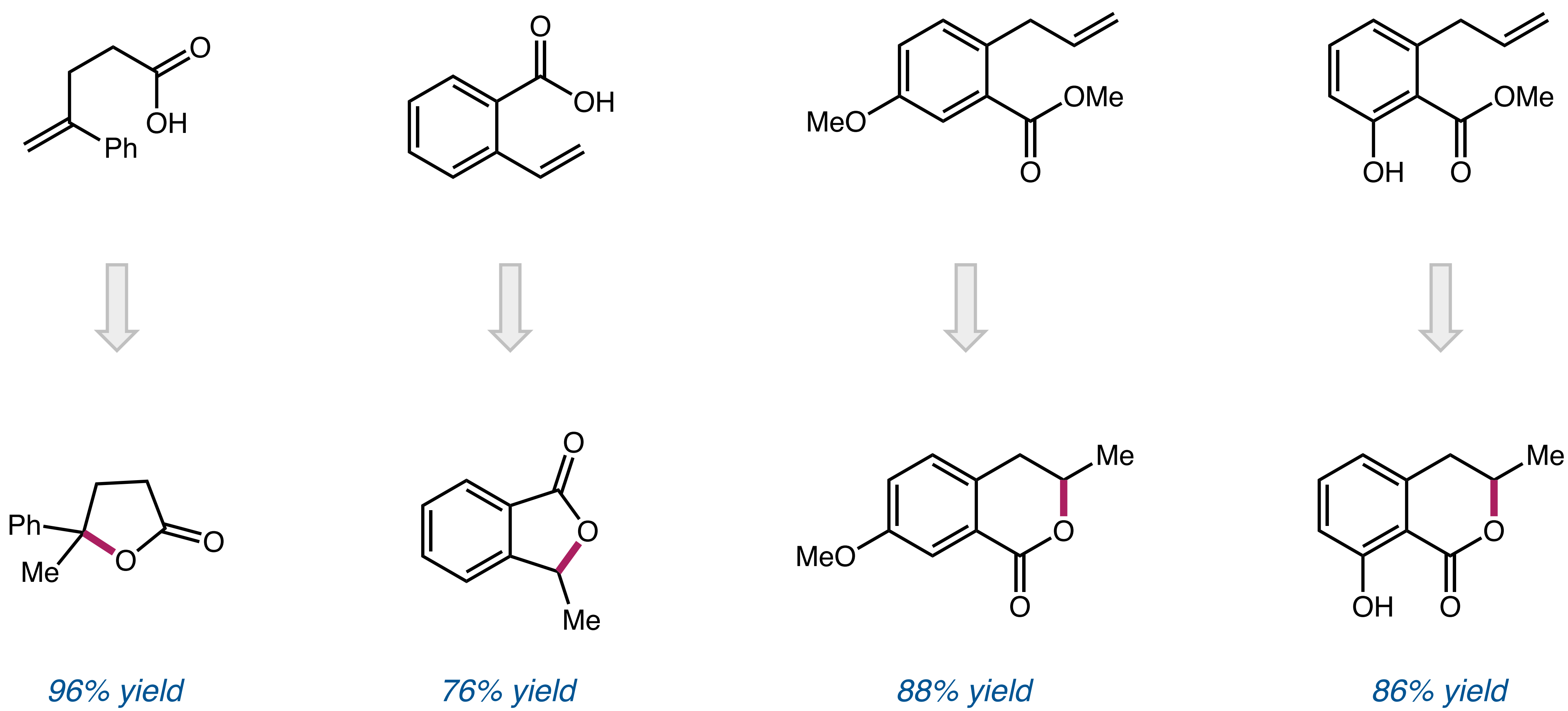


PG	time (h)	*yield*
H	21	*84%*
Me	0.5	*99%*
Et	1	*99%*
Bn	19	*97%*
PMB	3	*99%*
***t*-Bu**	19	*93%*

Shigehisa, H. *et. al., J. Am. Chem. Soc.* **2016**, *138*, 10597

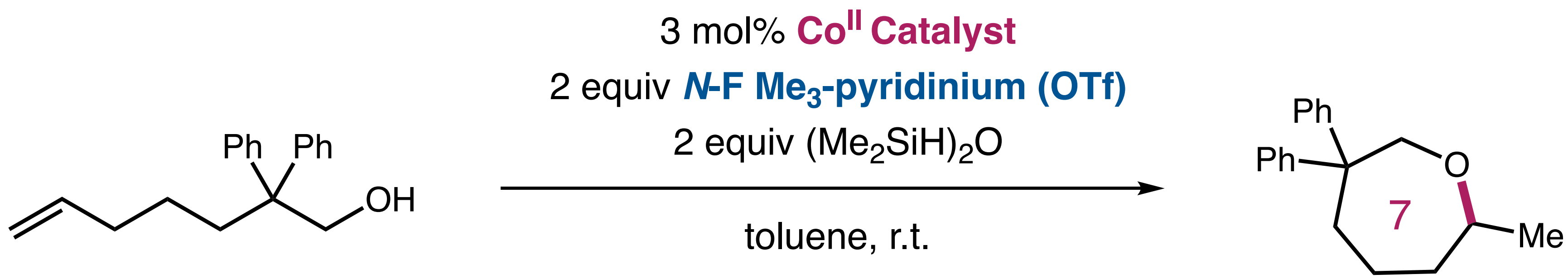
Intramolecular Hydroalkoxylation of Olefin with Acid and Esters

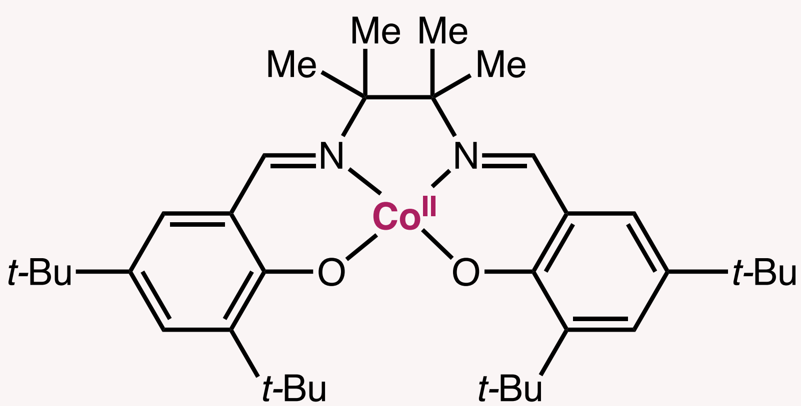




Shigehisa, H. *et. al., J. Am. Chem. Soc.* **2016**, *138*, 10597

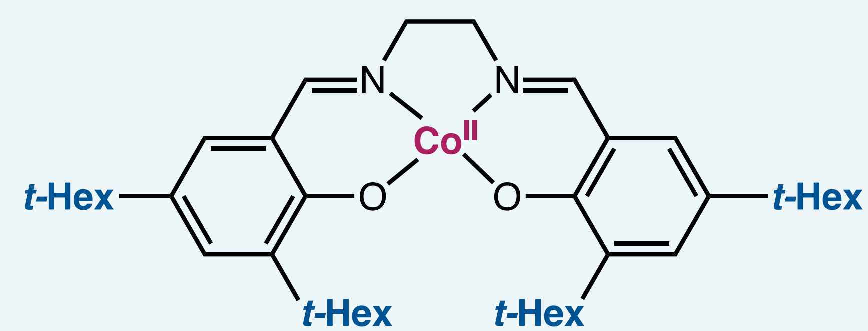
Intramolecular Hydroalkoxylation of Olefin with Acid and Esters





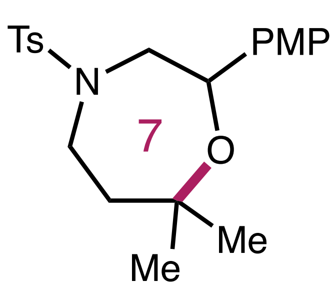
Co^{II} Catalyst A

30% yield

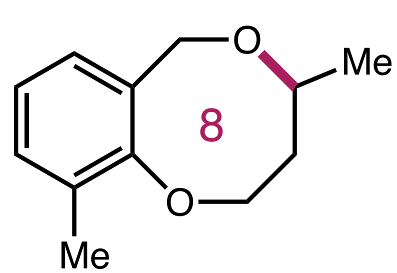


Co^{II} Catalyst B

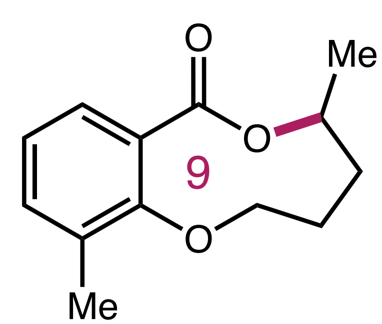
60% yield



69% yield



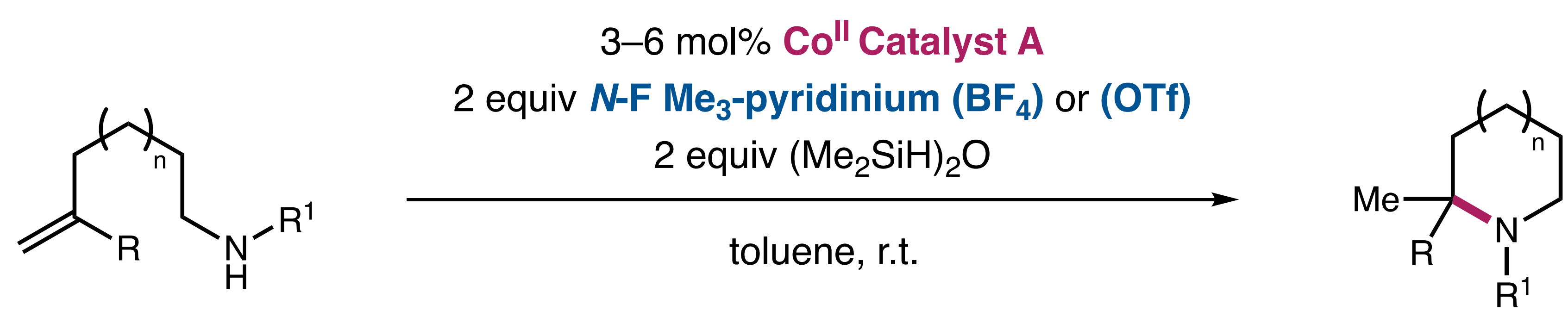
59% yield

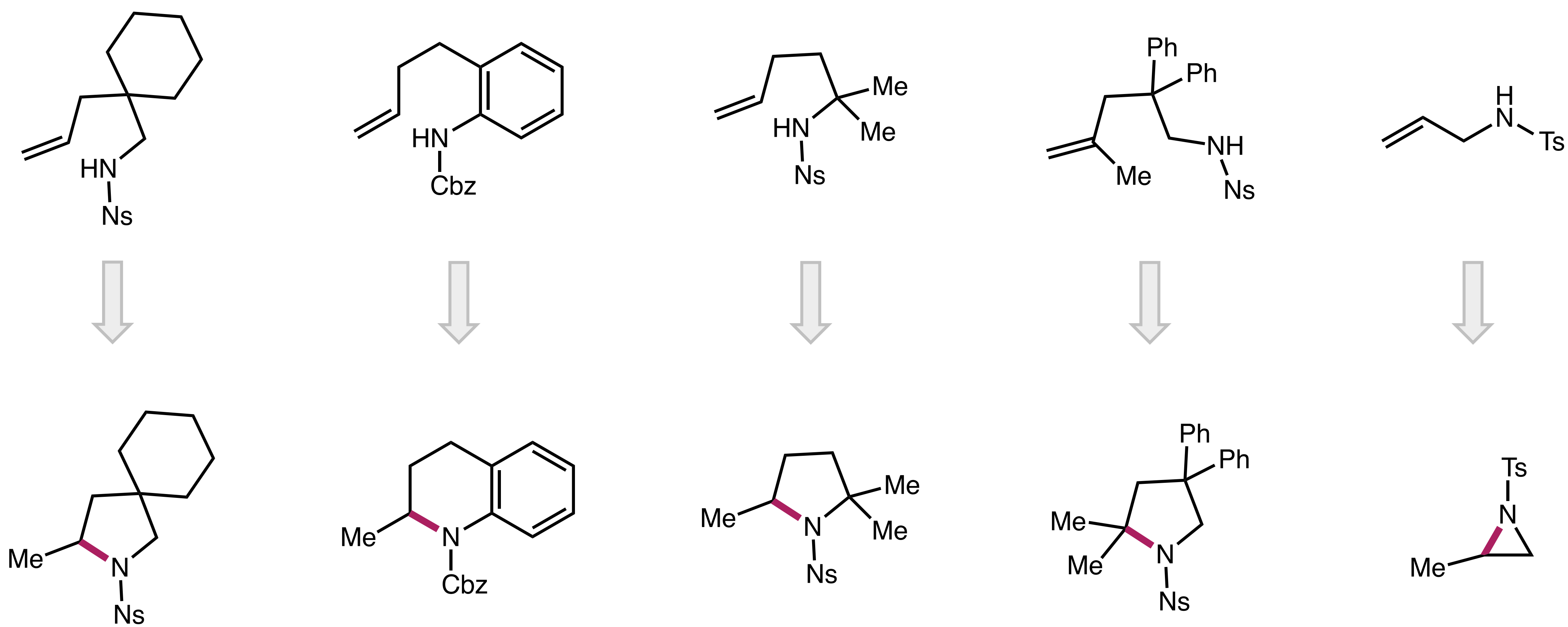


33% yield

Shigehisa, H. *et. al.*, *J. Am. Chem. Soc.* **2016**, *138*, 10597

Intramolecular Hydroamination of Olefin

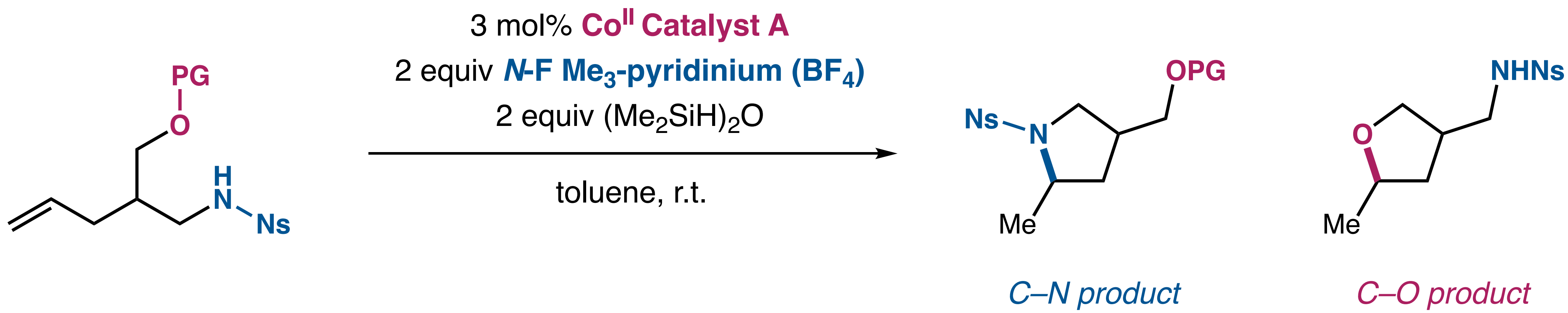




90% yield *55% yield* *68% yield* *42% yield* *56% yield*

Shigehisa, H.; Koseki, N.; Shimizu, N.; Fujisawa, M.; Niitsu, M.; Hiroya, K. *J. Am. Chem. Soc.* **2014**, *136*, 13534

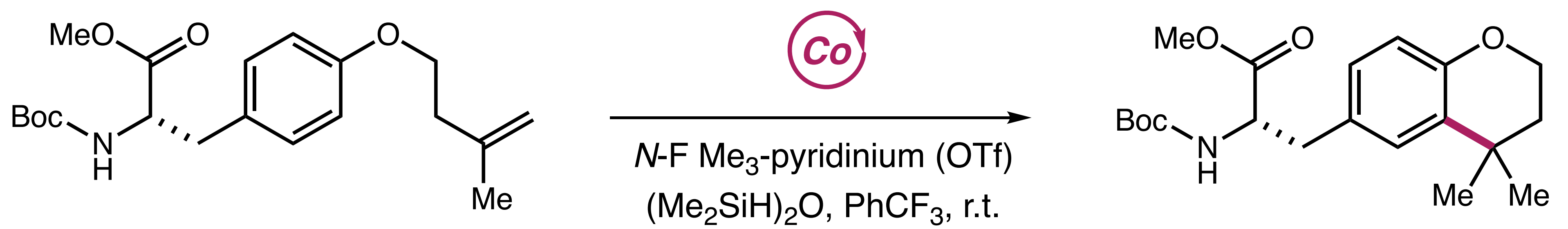
Intramolecular Hydroamination of Olefin: Oxygen v.s. Nitrogen



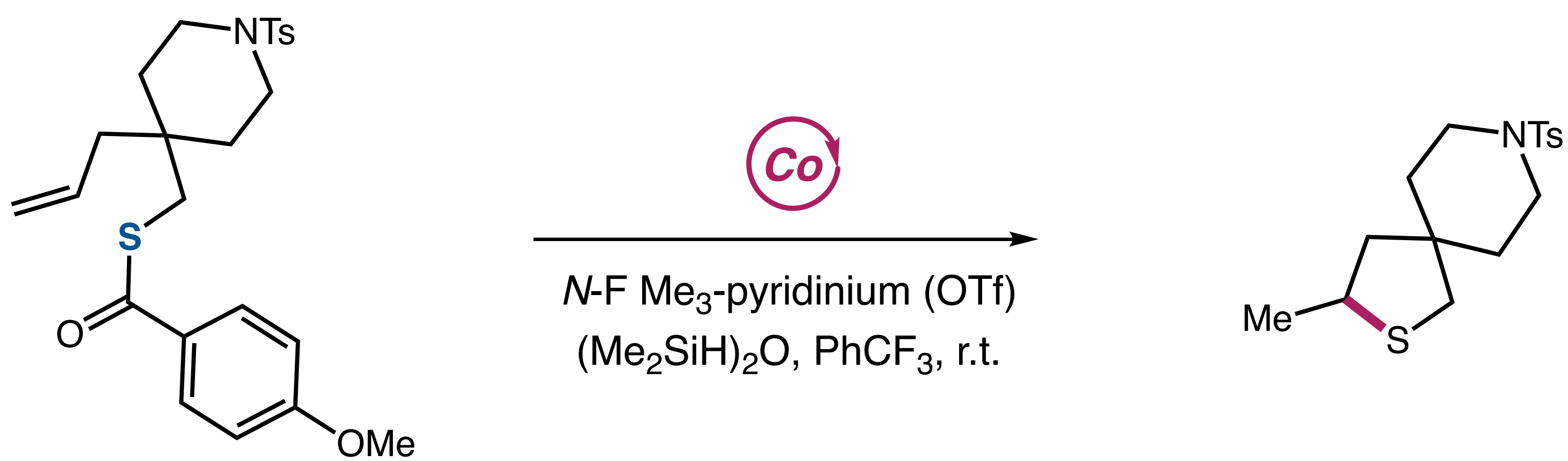
PG	C–N product	C–O product
H	*0%*	*67%*
MOM	*24%*	*54%*
TBS	*43%*	*50%*
Ac	*89%*	*0%*

Shigehisa, H.; Koseki, N.; Shimizu, N.; Fujisawa, M.; Niitsu, M.; Hiroya, K. *J. Am. Chem. Soc.* **2014**, *136*, 13534

Other Applications: Arenes and Thioester as Nucleophiles



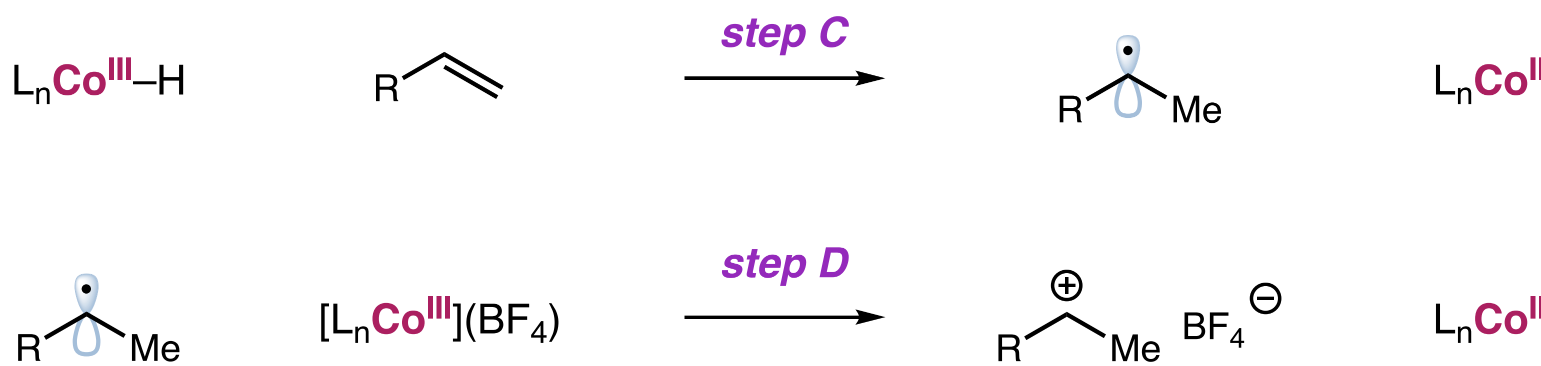
74% yield

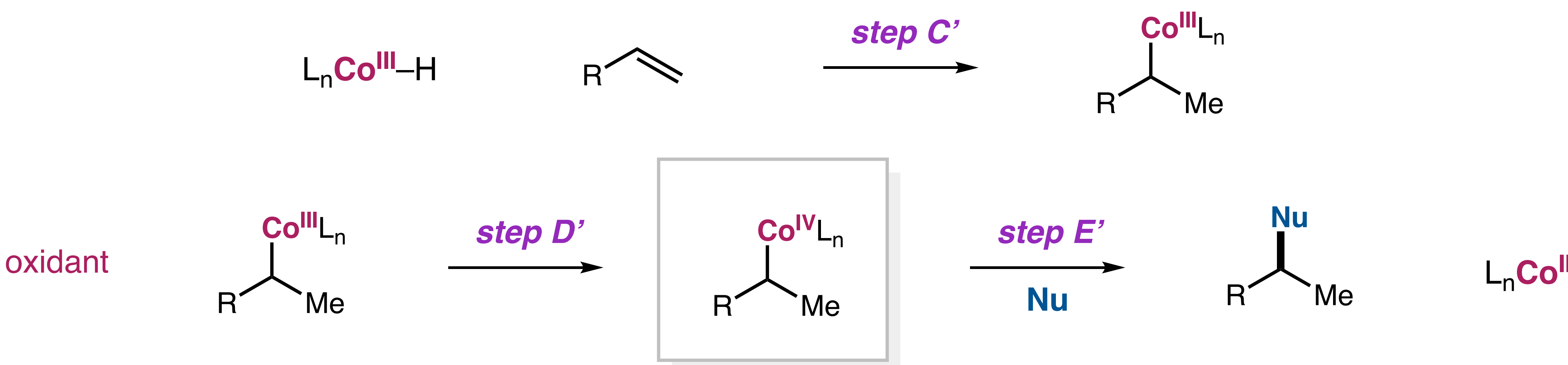


92% yield

Shigehisa, H.; Ano, T.; Honma, H.; Ebisawa, K.; Hiroya, K. *Org. Lett.* **2016**, *18*, 3622
Date, S.; Hamasaki, K.; Sunagawa, K.; Koyama, H.; Sebe, C.; Hiroya, K.; Shigehisa, H. *ACS Catal.* **2020**, *10*, 2039

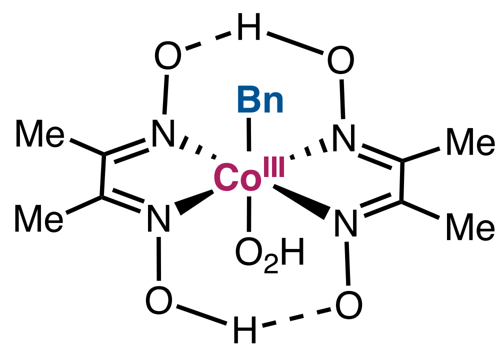
Alternative Pathway to Generate Carbocations: Alkylcobalt(IV)





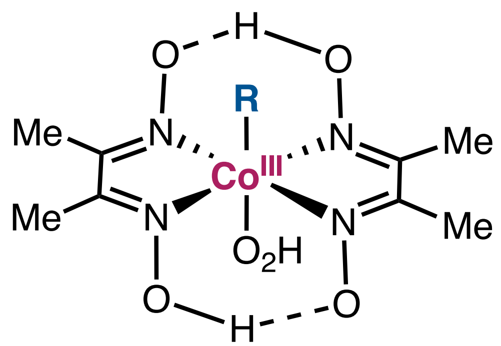
oxidant = *N*-F pyridinium salt *or* $[Co^{III}L_n](BF_4)$

Generation of Alkylcobalt(IV) and Reacting with Nucleophiles: Literature Precedents



Bn–Co^{III}$(dmgH)_2(H_2O)$

Ir^{IV}Cl_6^{2-} —SET→ [Bn–Co^{IV}$(dmgH)_2(H_2O)]^+$ Ir^{III}Cl_6^{3-}

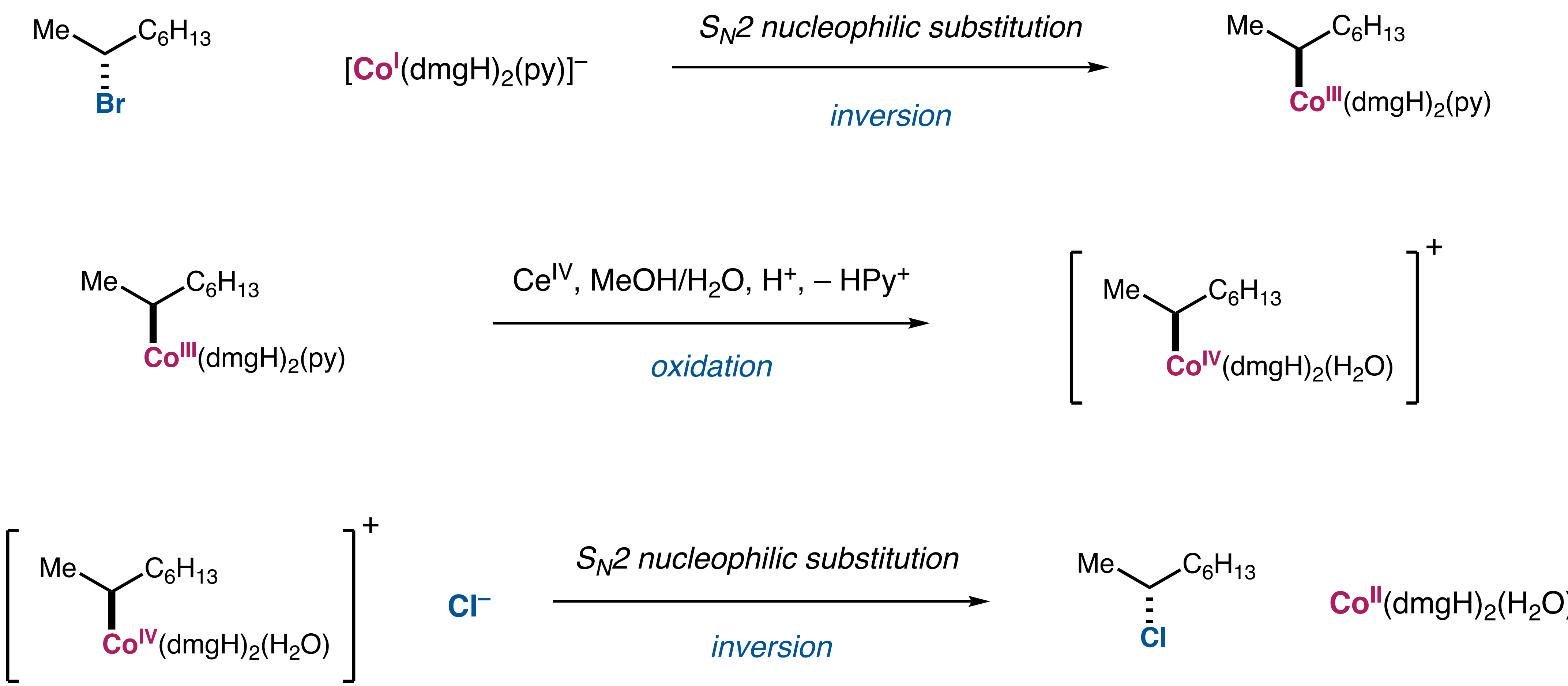


R–Co^{III}$(dmgH)_2(H_2O)$

R	$E_{1/2}^{ox}$ (v.s. SCE, in $HClO_4$ aq.)
Me	0.902 V
Et	0.878 V
n-Pr	0.867 V
i-Pr	0.856 V
Bn	0.859 V

Abley, P.; Dockal, E. R.; Halpern, J. *J. Am. Chem. Soc.* **1972**, *94*, 659
Halpern, J.; Chan, M. S.; Hanson, J.; Roche, T. S.; Topich, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1606

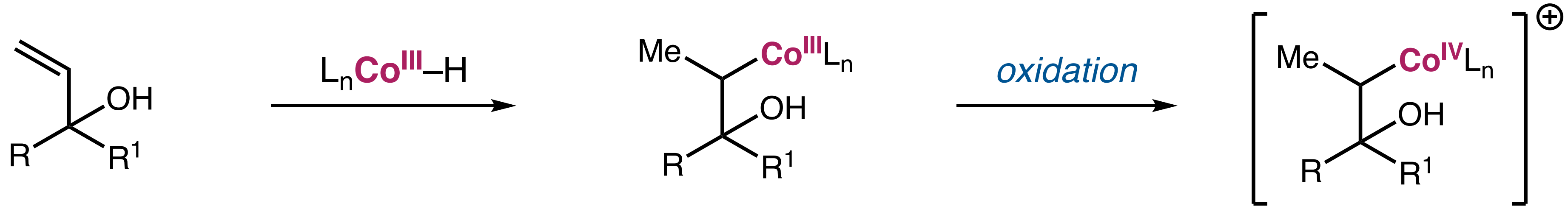
Generation of Alkylcobalt(IV) and Reacting with Nucleophiles: Literature Precedents

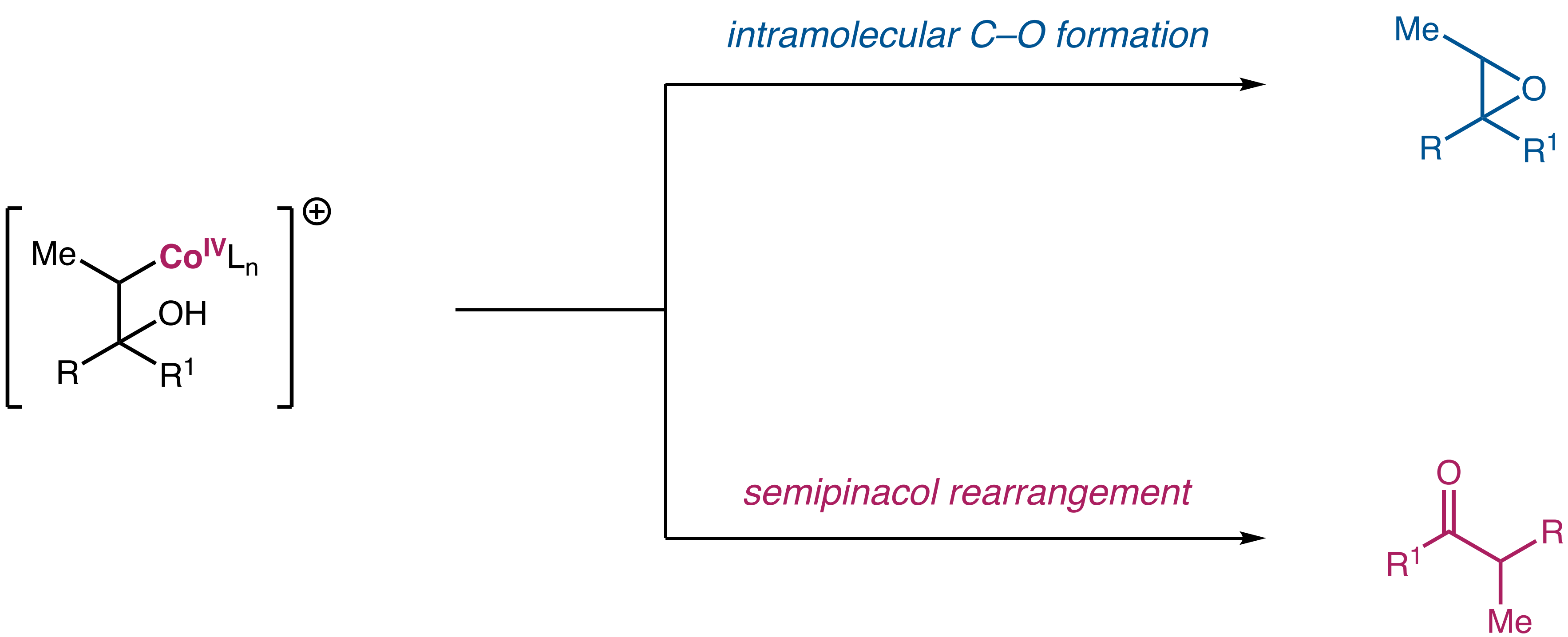


The cobalt part of an alkylcobalt(IV) species is functioning as a great leaving group in S_N2 reactions

Anderson, S. N.; Ballard, D. H.; Chrzastowski, J. Z.; Dodd, D.; Johnson, M. D. *J. Chem. Soc. Chem. Commun.* **1972**, 685
Magnuson, R. H.; Halpern, J.; Levitin, I. Y.; Vol'pin, M. E. *J. Chem. Soc. Chem. Commun.* **1978**, 44

Divergent Pathways of Alkylcobalt(IV) Generated from Allylic Alcohols

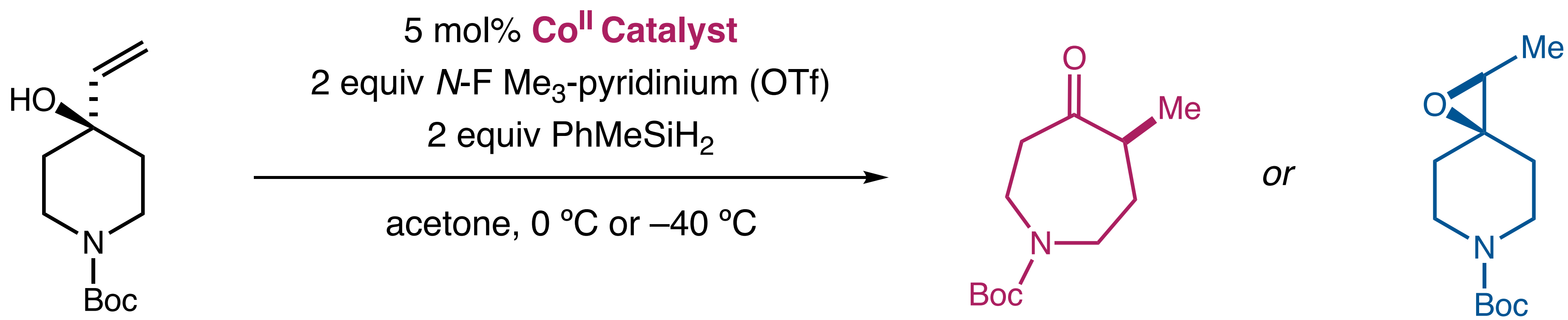


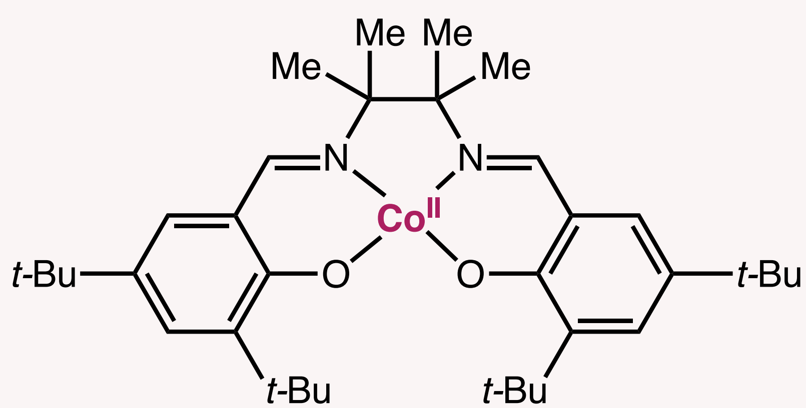


The ligands can serve as a controlling factor for achieving divergent and selective transformations.

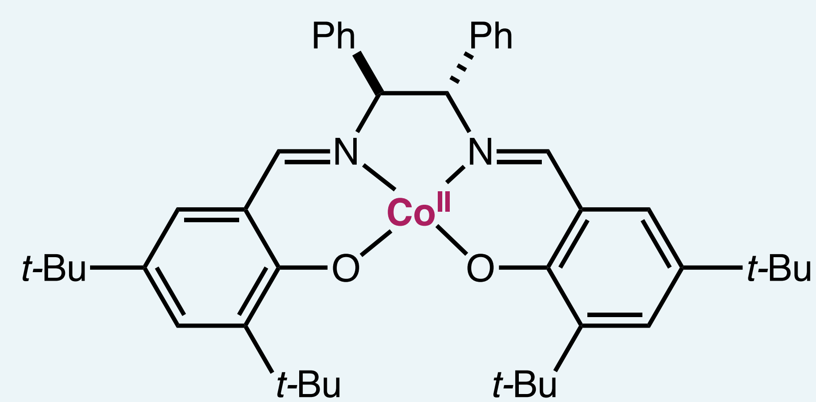
Touney, E. E.; Foy, N. J.; Pronin, S. V. *J. Am. Chem. Soc.* **2018**, *140*, 16982

Divergent Functionalization of Allylic Alcohols





Co^{II} Catalyst A



Co^{II} Catalyst C

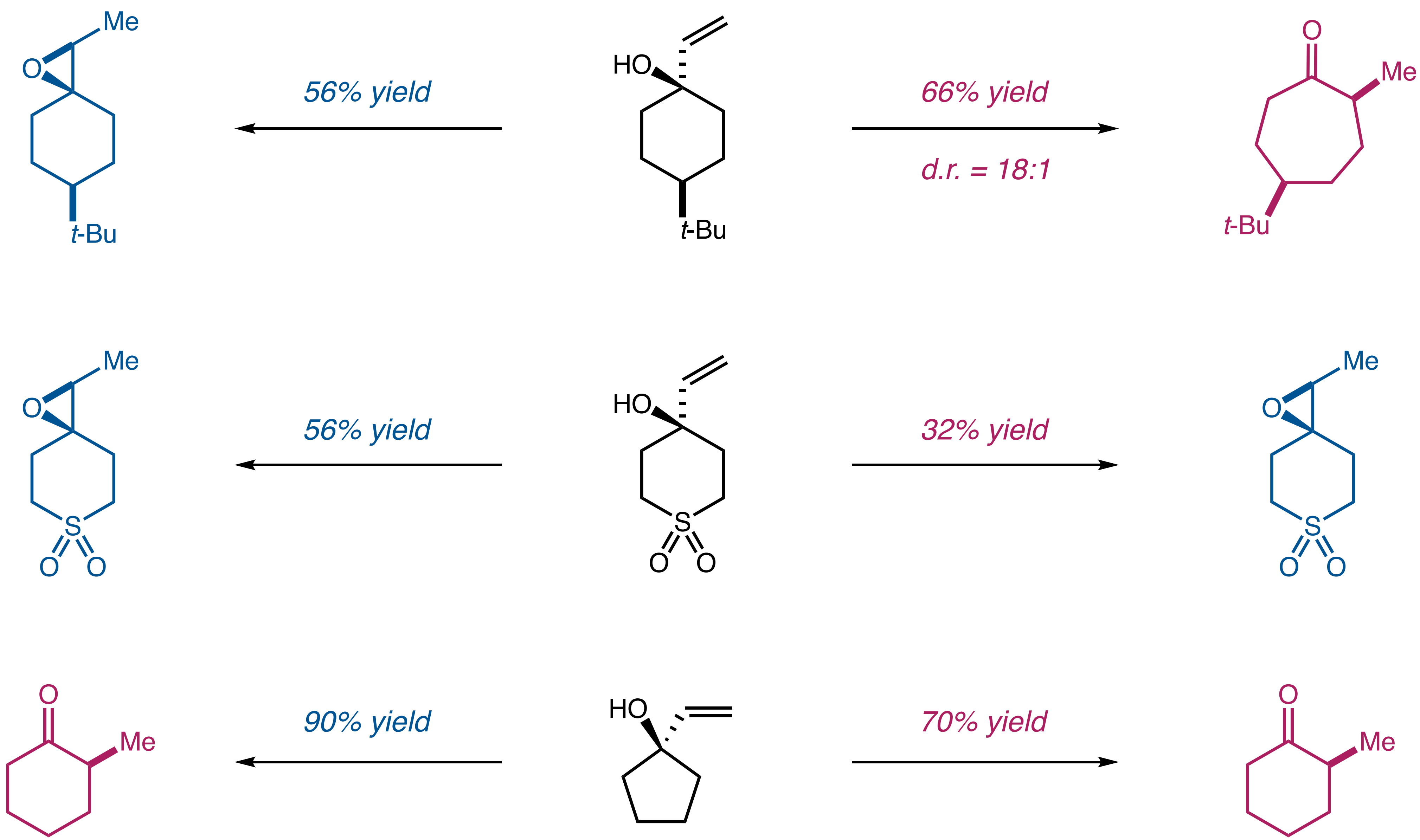
63% yield ketone
(14% epoxide)

84% epoxide
(9% ketone)

Touney, E. E.; Foy, N. J.; Pronin, S. V. *J. Am. Chem. Soc.* **2018**, *140*, 16982

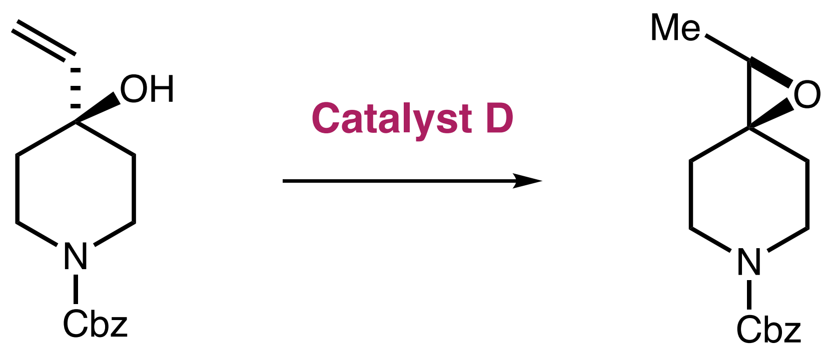
Divergent Functionalization of Allylic Alcohols

With Co^{II} Catalyst C | **With Co^{II} Catalyst A**

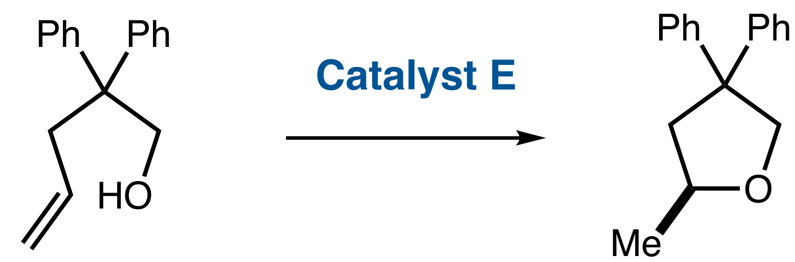


Touney, E. E.; Foy, N. J.; Pronin, S. V. *J. Am. Chem. Soc.* **2018**, *140*, 16982

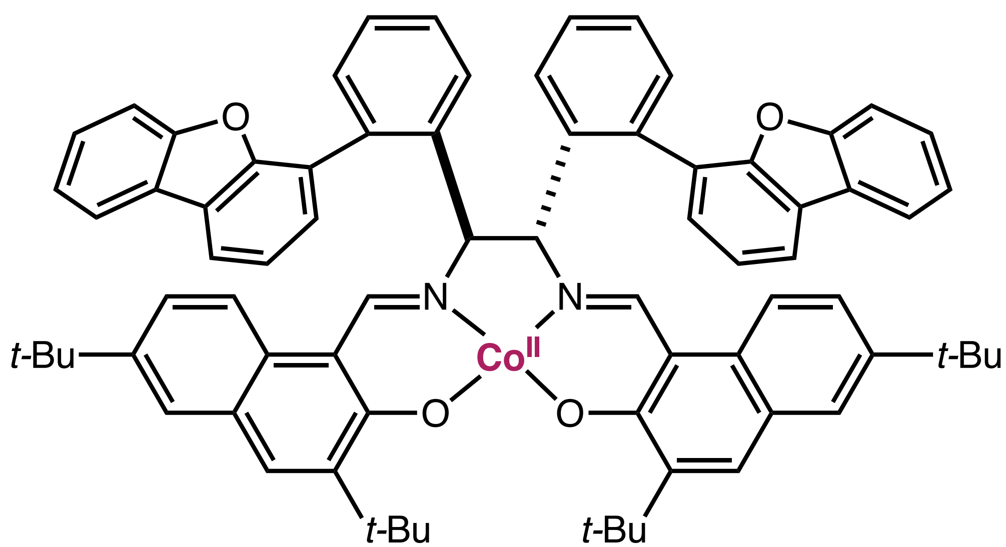
Asymmetric Catalysis for sp^3 C–O Formation using Chiral Salen Ligands



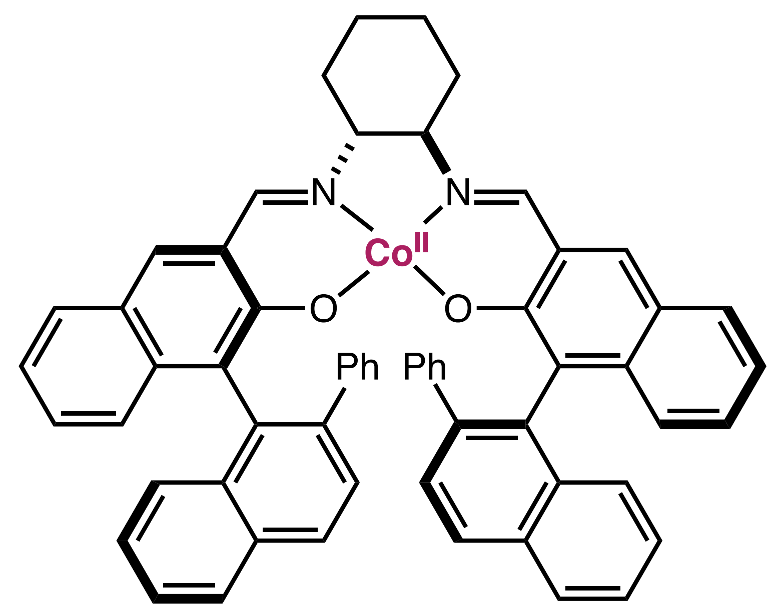
71% yield
89% ee



77% yield
94% ee



Co^{II} Catalyst D

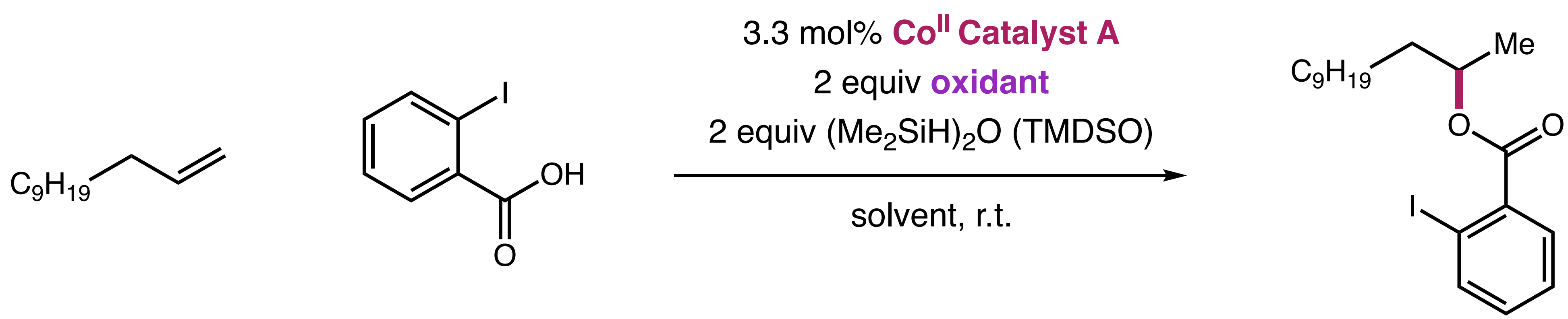


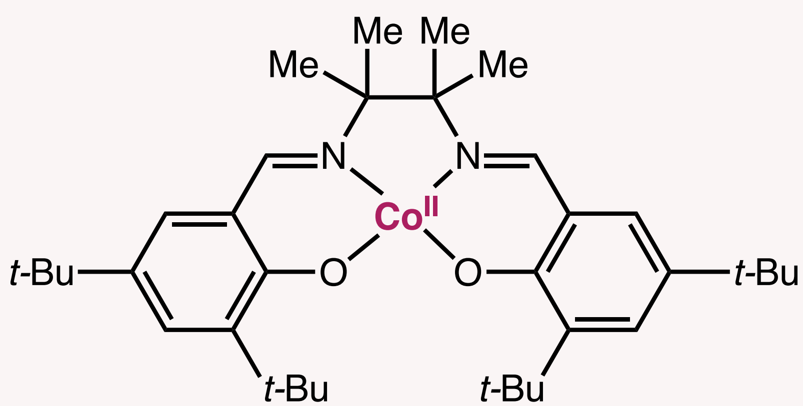
Co^{II} Catalyst E

Discolo, C. A.; Touney, E. E.; Pronin, S. V. *J. Am. Chem. Soc.* **2019**, *141*, 17527
Shigehisa, H. *et. al., Chemrxiv* doi: 10.26434/chemrxiv.9981395.v1

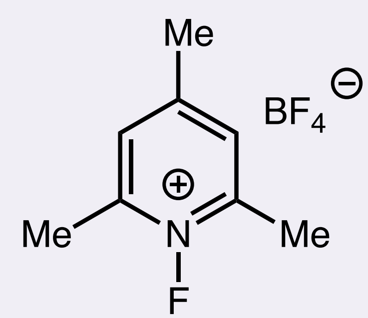
*How to develope **intermolecular** sp^3 C–O and sp^3 C–N formation reactions?*

Intermolecular Hydrofunctionalization using Oxygen and Nitrogen Nucleophiles

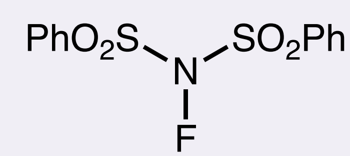




Co^{II} Catalyst A



Oxidant 1

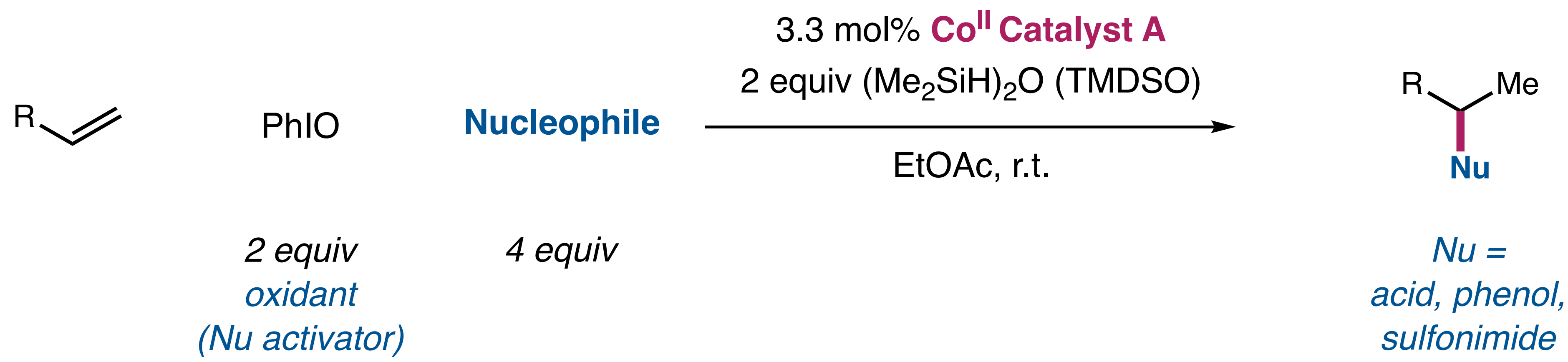


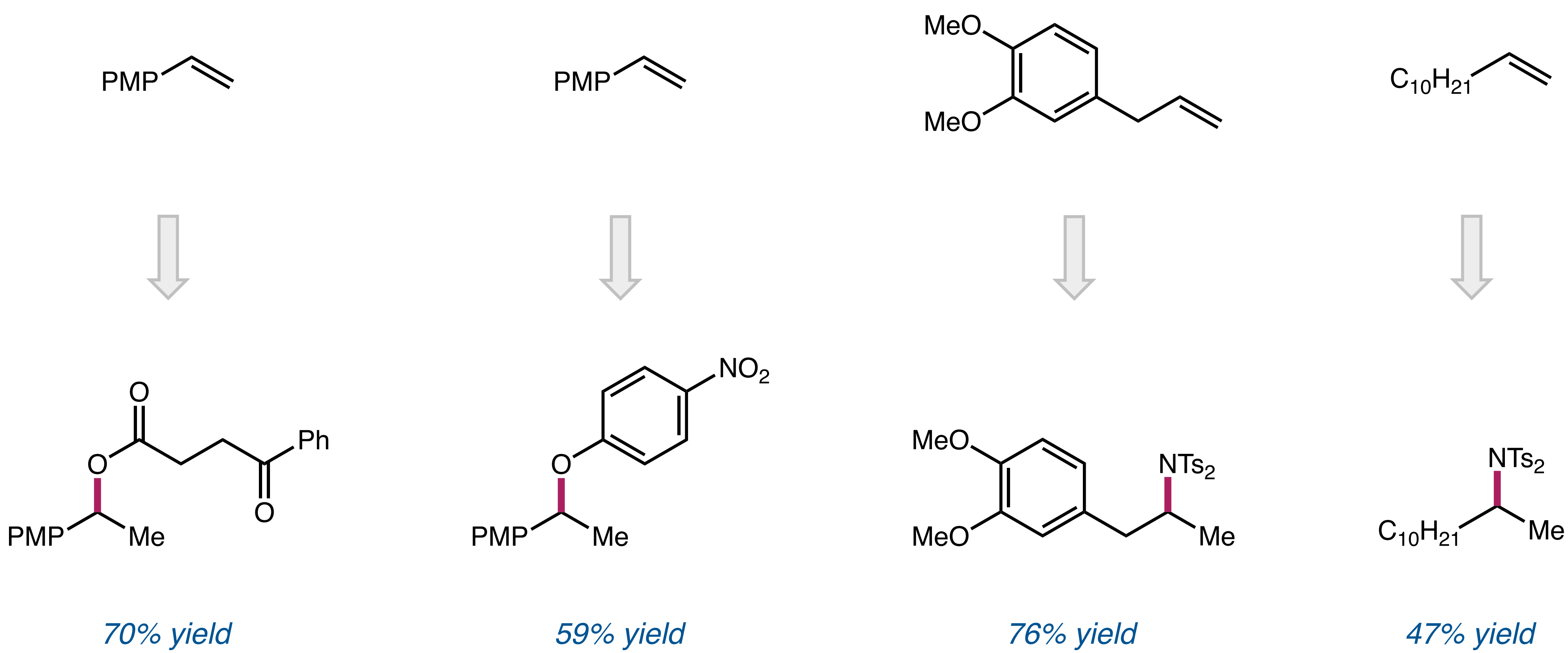
Oxidant 2

<10% yield, under a variety of conditions using either oxidant 1 or 2

Zhou, X.-L.; Yang, F.; Sun, H.-L.; Yin, Y.-N.; Ye, W.-T.; Zhu, R. *J. Am. Chem. Soc.* **2019**, *141*, 7250
Zhu, R. *Synlett* **2019**, *30*, 2015

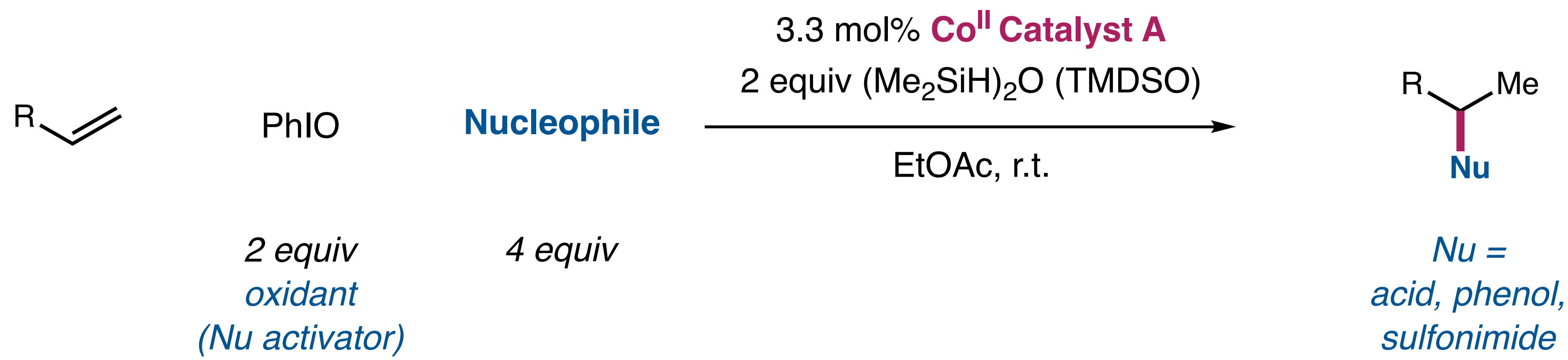
Intermolecular Hydrofunctionalization using Oxygen and Nitrogen Nucleophiles

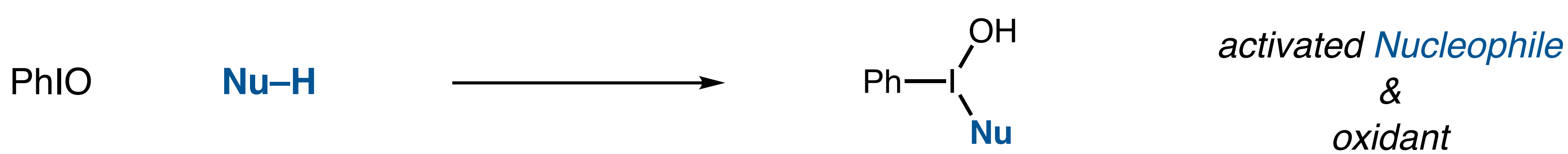


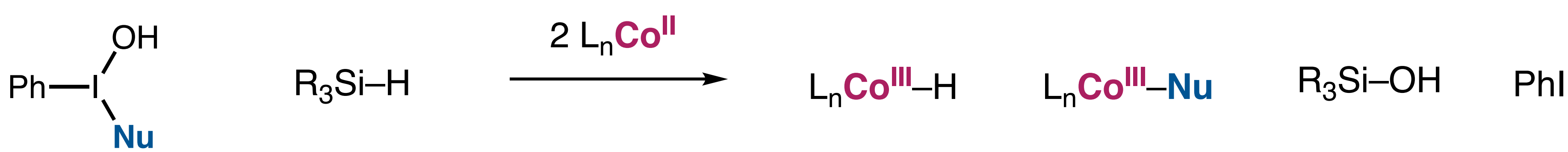


Zhou, X.-L.; Yang, F.; Sun, H.-L.; Yin, Y.-N.; Ye, W.-T.; Zhu, R. *J. Am. Chem. Soc.* **2019**, *141*, 7250

Intermolecular Hydrofunctionalization using Oxygen and Nitrogen Nucleophiles

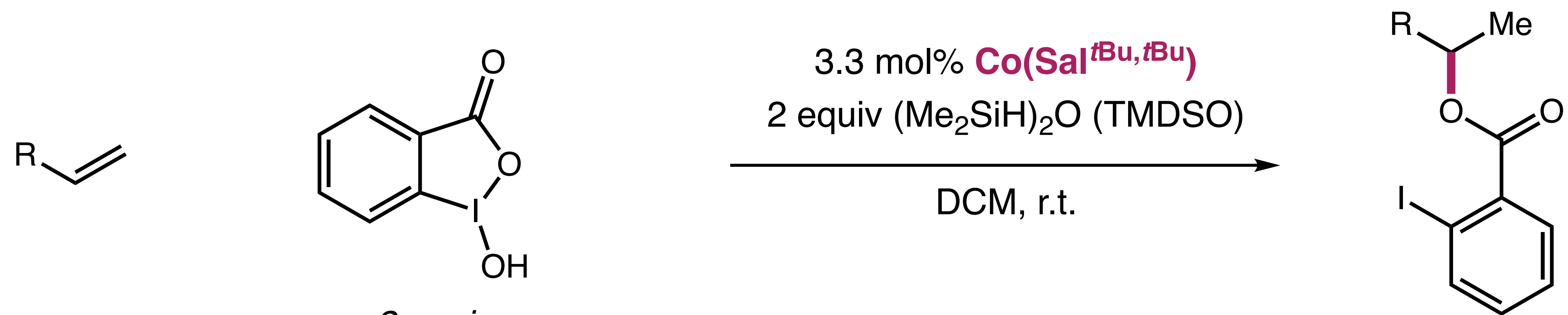




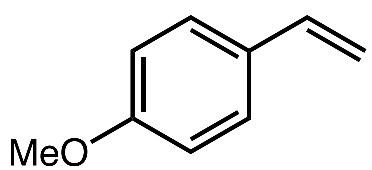


Zhou, X.-L.; Yang, F.; Sun, H.-L.; Yin, Y.-N.; Ye, W.-T.; Zhu, R. *J. Am. Chem. Soc.* **2019**, *141*, 7250

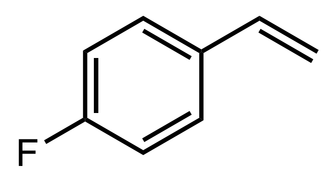
Intermolecular Hydrofunctionalization using Oxygen and Nitrogen Nucleophiles



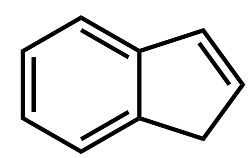
2 equiv
oxidant & Nu



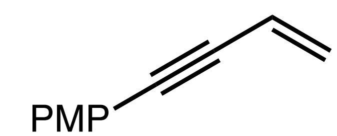
83% yield



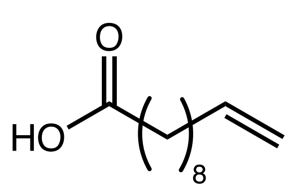
71% yield



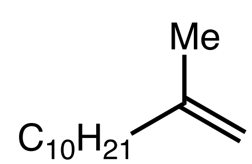
77% yield

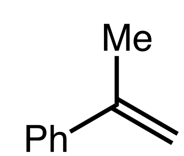


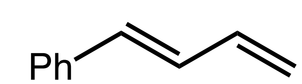
75% yield



65% yield



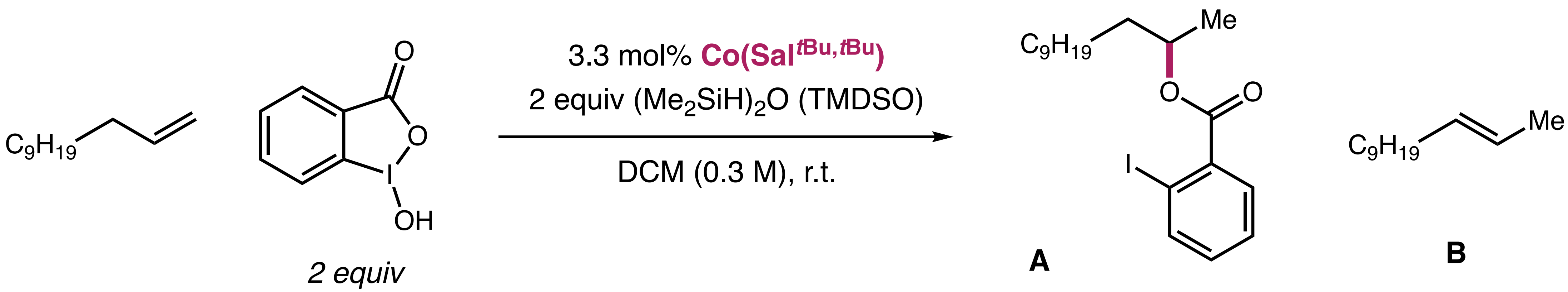




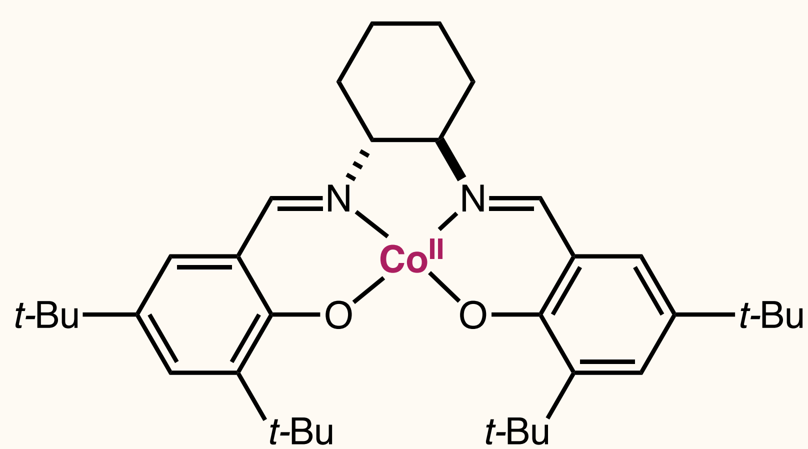
Not applicable (<5% yield)

Zhou, X.-L.; Yang, F.; Sun, H.-L.; Yin, Y.-N.; Ye, W.-T.; Zhu, R. *J. Am. Chem. Soc.* **2019**, *141*, 7250

Optimization: Some Interesting Findings



2nd order in [Co] *1st order in [Co]*

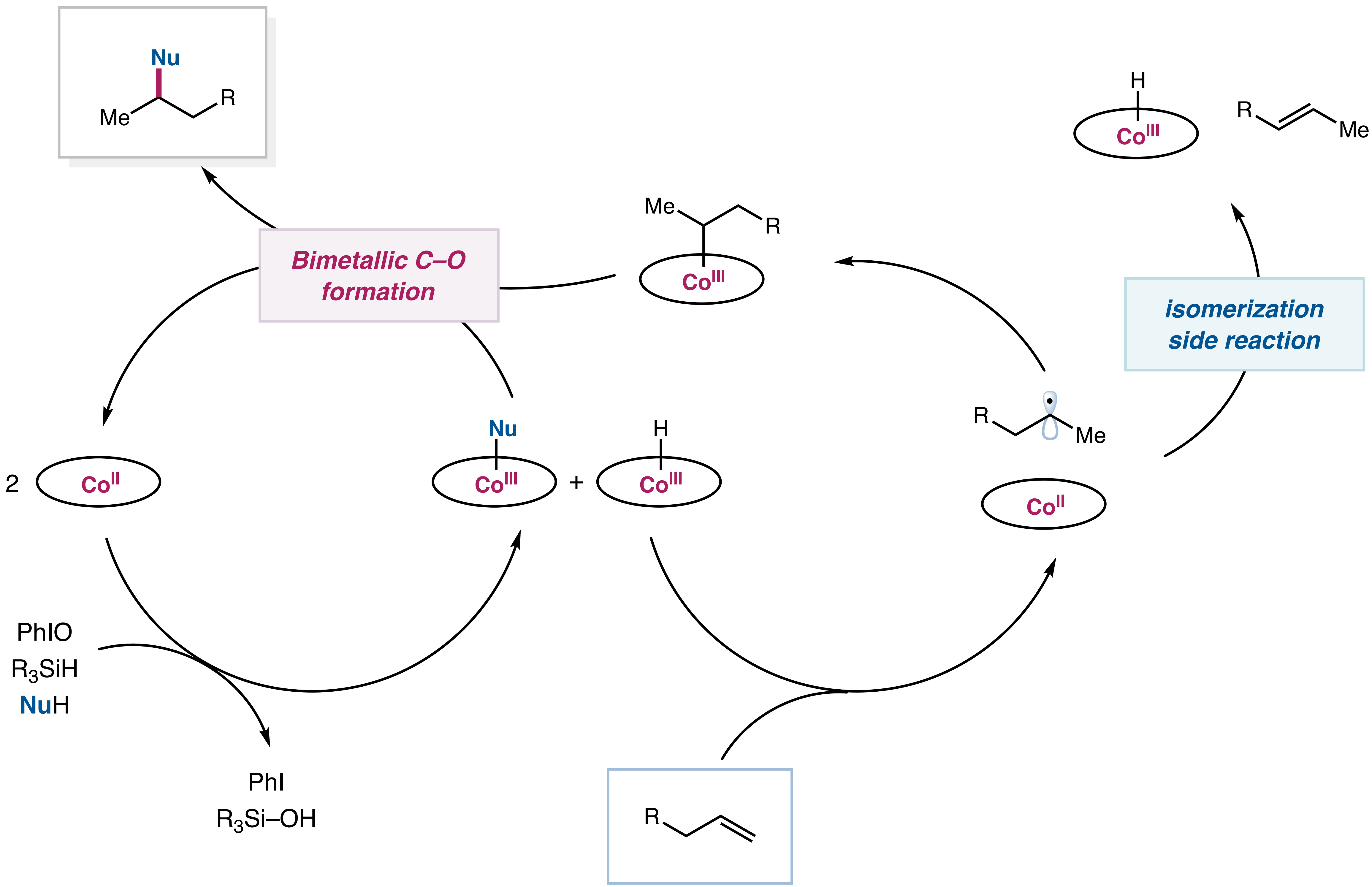


(*R*,*R*)-Co(Sal$^{t\text{Bu},t\text{Bu}}$)

entry	deviation from above	**A** (%)	**B** (%)
1	none	84	16
2	0.1 M instead of 0.3 M	24	10
3	0.1 M, with 10 mol% Co	73	24
4	(*S*,*S*) cobalt catalyst	81	17
5	*racemic* cobalt catalyst	36	15

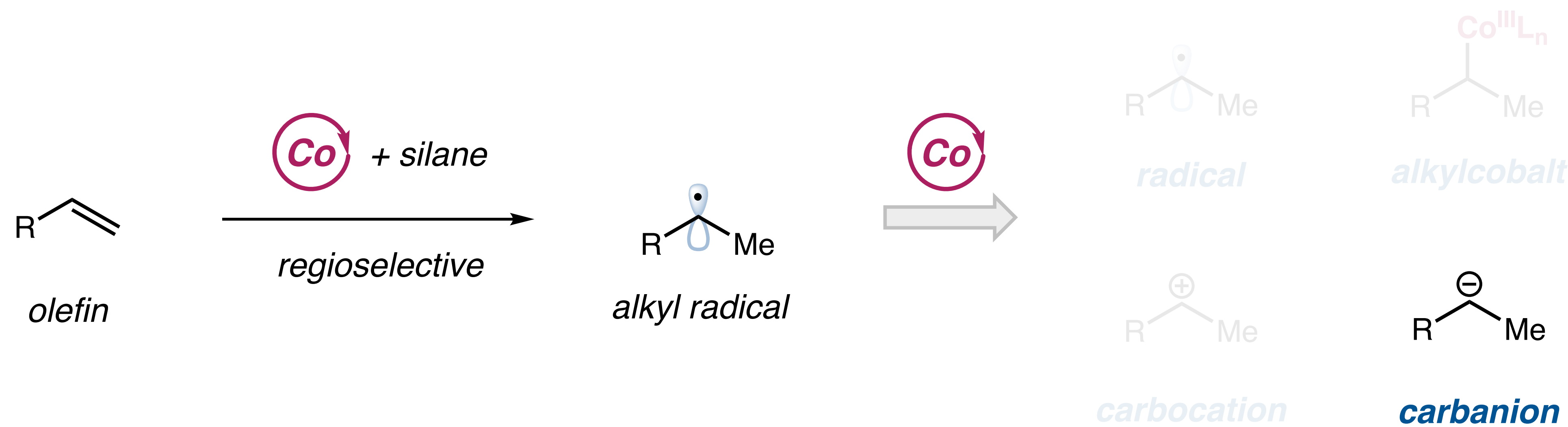
Zhou, X.-L.; Yang, F.; Sun, H.-L.; Yin, Y.-N.; Ye, W.-T.; Zhu, R. *J. Am. Chem. Soc.* **2019**, *141*, 7250

Proposed Mechanism: Bimetallic C–O Formation



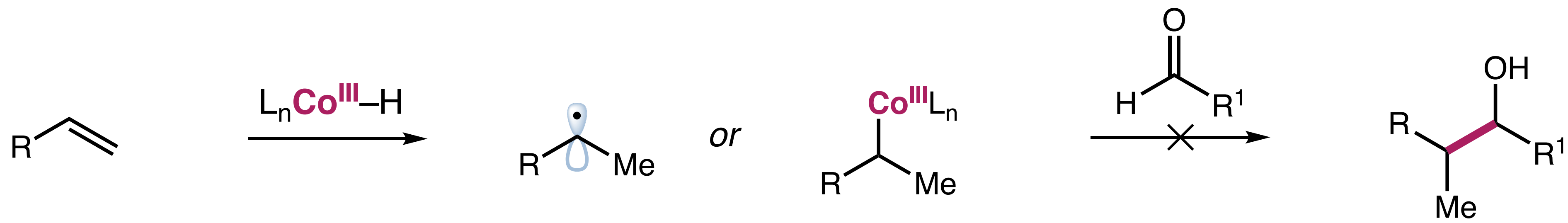
Zhou, X.-L.; Yang, F.; Sun, H.-L.; Yin, Y.-N.; Ye, W.-T.; Zhu, R. *J. Am. Chem. Soc.* **2019**, *141*, 7250

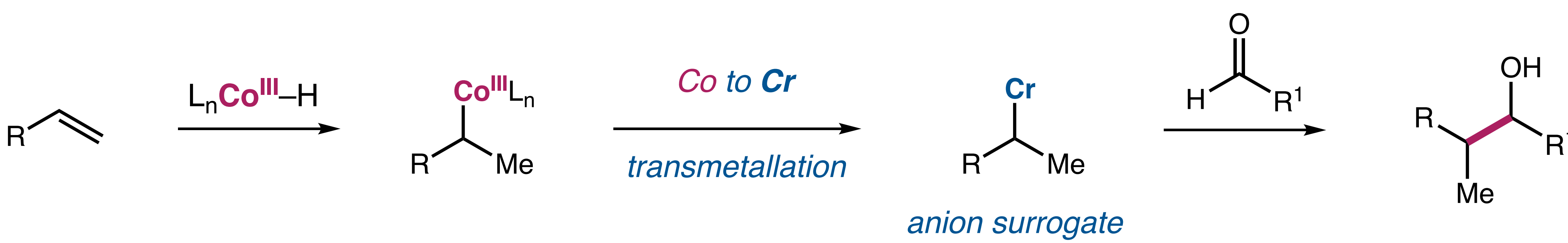
Outline



R
olefin
Co
+ silane
regioselective
R
Me
alkyl radical
Co
R
Me
radical
$Co^{III}L_n$
R
Me
alkylcobalt
R
Me
carbocation
R
Me
carbanion

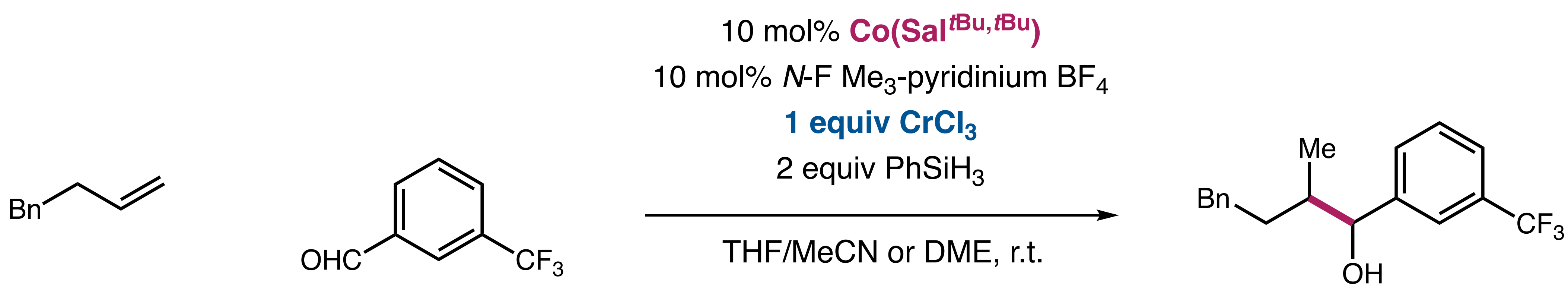
Olefins as Carbanion Precursors



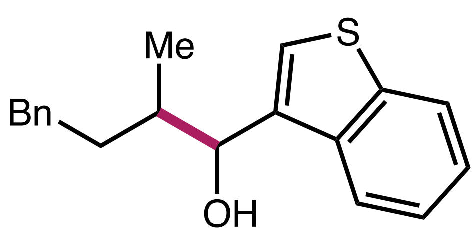


Matos, J. L. M.; Vásquez-Céspedes, S.; Gu, J.; Oguma, T.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 16976

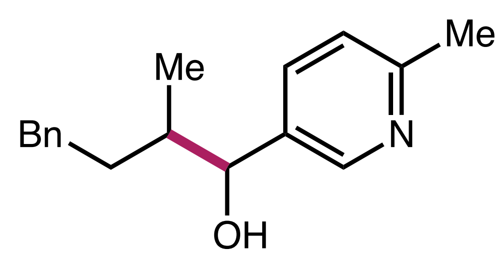
Olefins as Carbanion Precursors



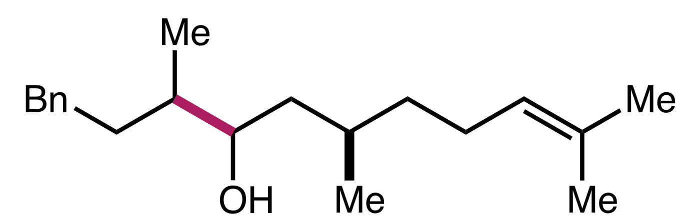
70% yield *(1:1 d.r.)*
*without **Cr**: 0% yield*
*without **$CrCl_2$**: 0% yield*



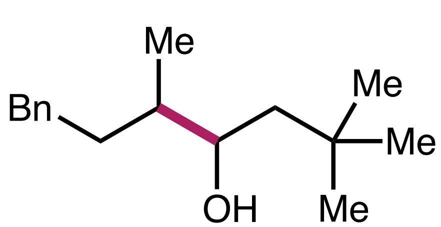
68% yield



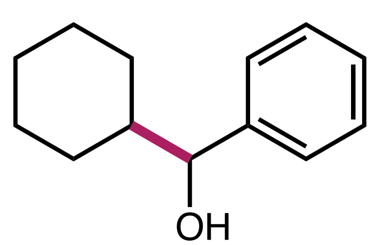
90% yield



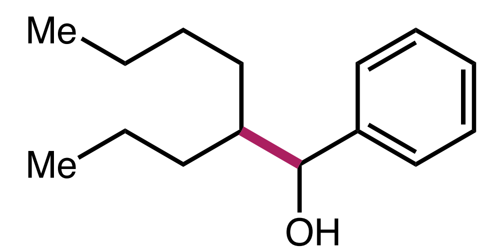
62% yield



84% yield



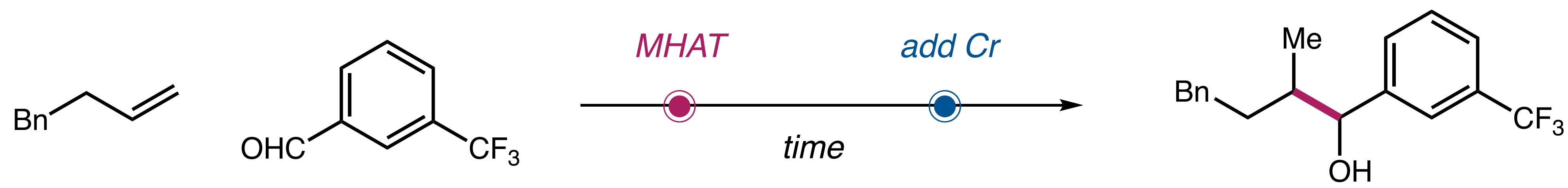
52% yield



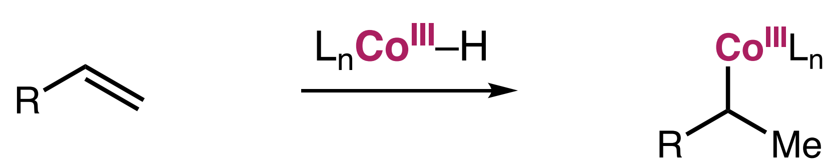
33% yield

Matos, J. L. M.; Vásquez-Céspedes, S.; Gu, J.; Oguma, T.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 16976

Olefins as Carbanion Precursors: Mechanistic Studies



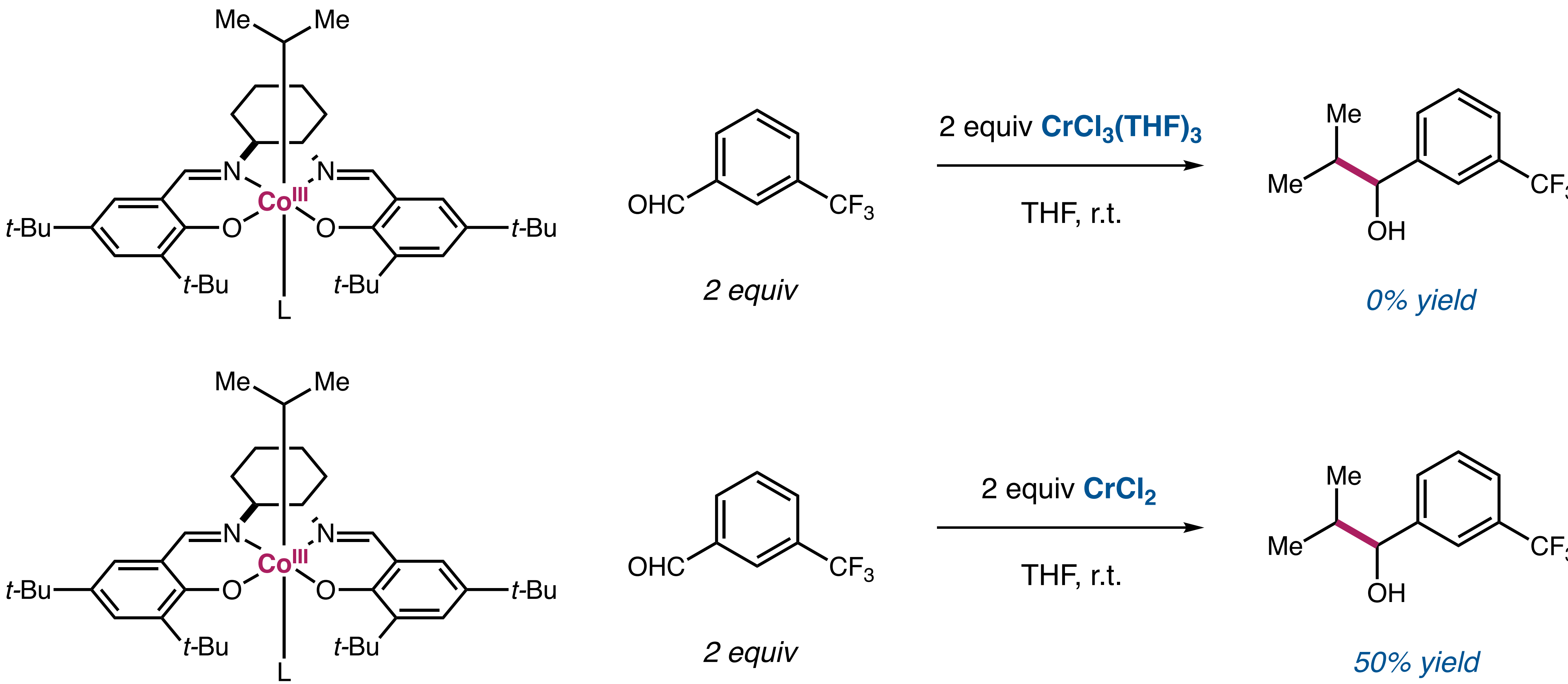
time	*yield*
0 s	*90%*
10 s	*90%*
10 min	*71%*
60 min	*86%*



stable species at r.t. in solution

Matos, J. L. M.; Vásquez-Céspedes, S.; Gu, J.; Oguma, T.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 16976

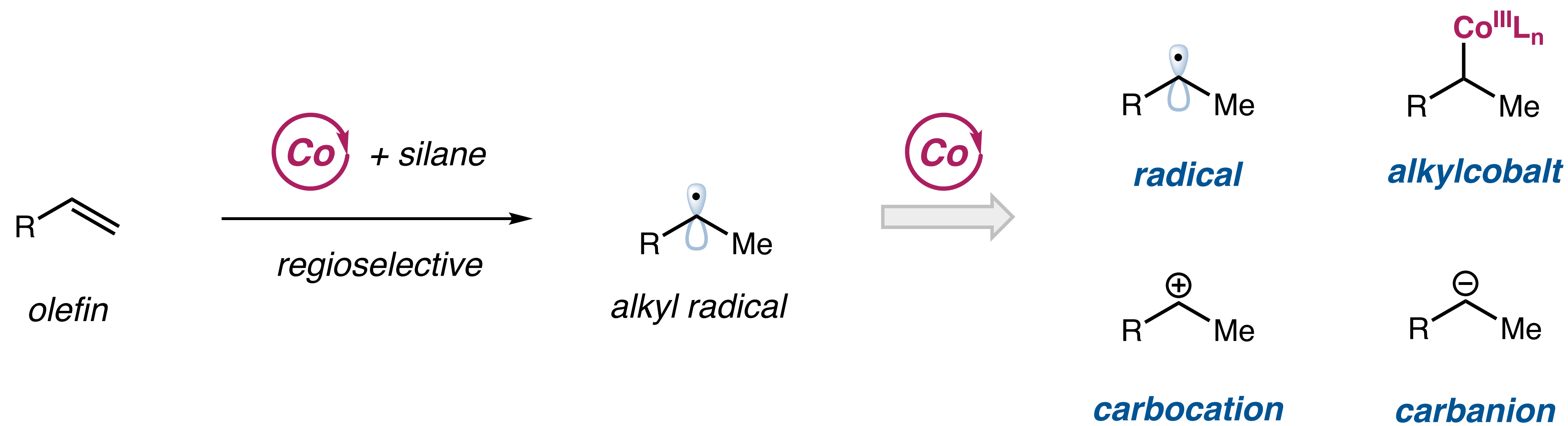
Olefins as Carbanion Precursors: Mechanistic Studies



- Co^{III} to Cr^{II} transmetallation (alkyl transfer)
- Cr^{II} was generated through reduction using silane

Matos, J. L. M.; Vásquez-Céspedes, S.; Gu, J.; Oguma, T.; Shenvi, R. A. *J. Am. Chem. Soc.* **2018**, *140*, 16976

Summary



Reviews for further reading:

Shenvi, R. A. *et. al., Chem. Rev.* **2016**, *116*, 8912
Shenvi, R. A. *et. al., Acc. Chem. Soc.* **2018**, *51*, 2628
Shenvi, R. A. *et. al.,* Chapter 7. Markovnikov Functionalization by Hydrogen Atom Transfer *Organic Reactions*, **2019**, *100*, 383
Shigehisa, H. *Chem. Pharm. Bull.* **2018**, *66*, 339
Zhu, R. *Synlett* **2019**, *30*, 2015

Michiyuki, T.; Komeyama, K. *Asian J. Org. Chem.* **2020**, *9*, 1
"Recent Advances in Four-Coordinated Planar Cobalt Catalysis in Organic Synthesis"