Cobalt in Radical Chemistry

Topic Review

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UNIVERSITÄT
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CONTENTS

Generalities

Cobalt
27
Co
58,933

- Most important transition metal in the developpement of modern coordination chemistry
- Complexes of Co^{III} have also been central to studies the mecanism of ligand substitution and electron transfer in coordination complexe (work of Henry Taube – Nobel Price 1983)
- 33 in abundance of the elements in the earth's crust. Does not exist as free metal in nature.
- Unreactive at air and ambient temperature

Blackman, A. G., *Encyclopedia of Inorganic Chemistry, First Edition.*; John Wiley & Sons, Ltd: Chichester, UK, 2006.

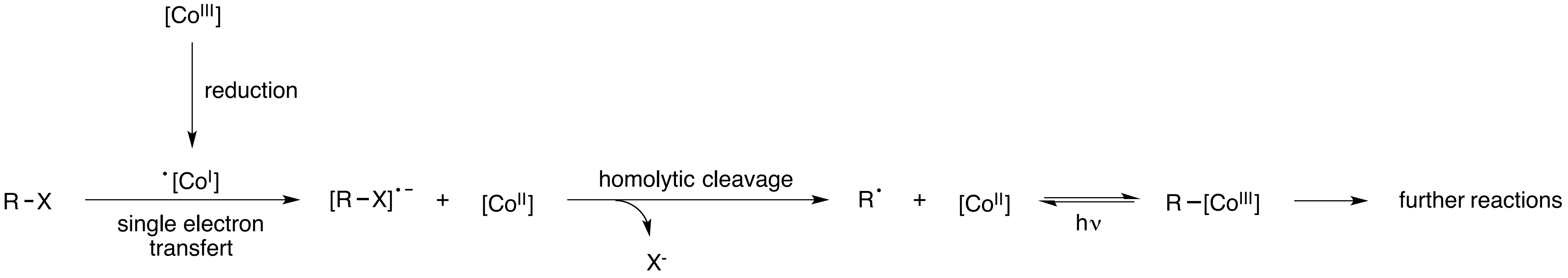
Organocobalt compounds

R –[Co]

> Organo-cobalt complexes are excellent precursos to carbon-centered radicals

> Facile homolytic cleavage (Δ or hv) of a range of alkyl and acyl cobalt complexes and the addition of the resulting carbon-centered radical to carbon-carbon double bond can be carried out by cobalt mediated radical reaction.

> Synthesis of organocobalt species :



$$\begin{tikzcd} & {[Co^{III}]} \arrow[d, "\text{reduction}"] & & & & \\ R-X \arrow[rr, "{^{\bullet}[Co^{I}]}", "\text{single electron transfert}"'] & {} & {[R-X]^{\bullet -} + [Co^{II}]} \arrow[r, "\text{homolytic cleavage}", "-X^{-}"'] & R^{\bullet} + [Co^{II}] \arrow[r, shift left] & R-[Co^{III}] \arrow[l, shift left, "h\nu"] \arrow[r] & \text{further reactions} \end{tikzcd}$$

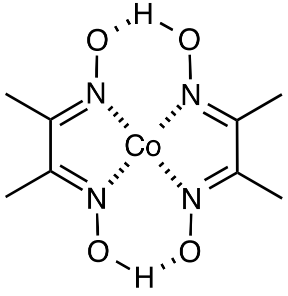
Iqbal, J.; Sanghi, R.; Nandy, J. P. *J. Chem. Soc., Chem. Commun.* **1987**, 871.

Cobalt in Vitamin B_{12}

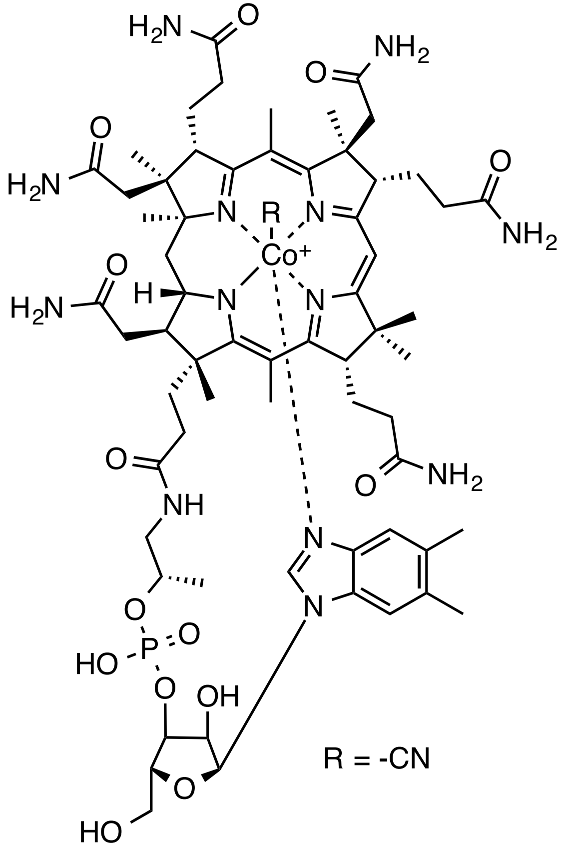
> Co^{III} in a square pyramidale N5 coordination environnement

> First compound with a [M]–C bond in natural product soluble in water.

> Developpement of a simplest model



Cobaloxime



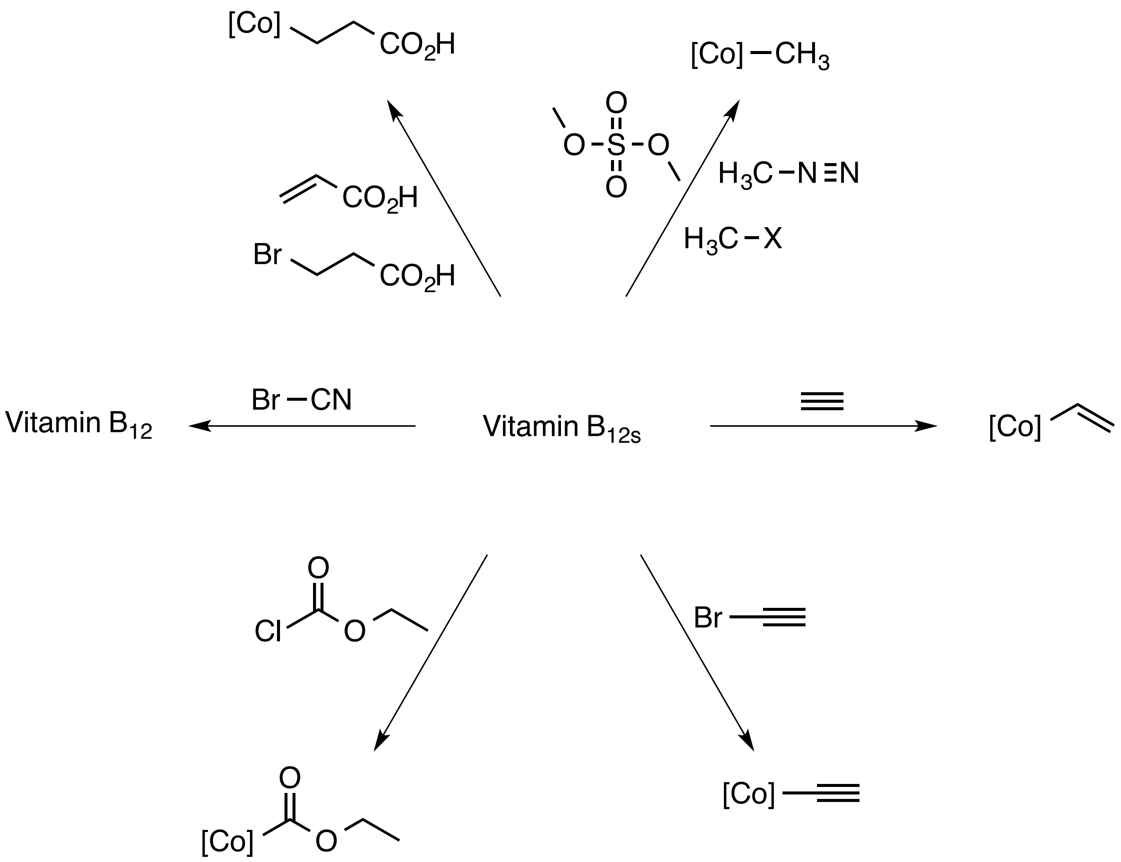
R = -CN

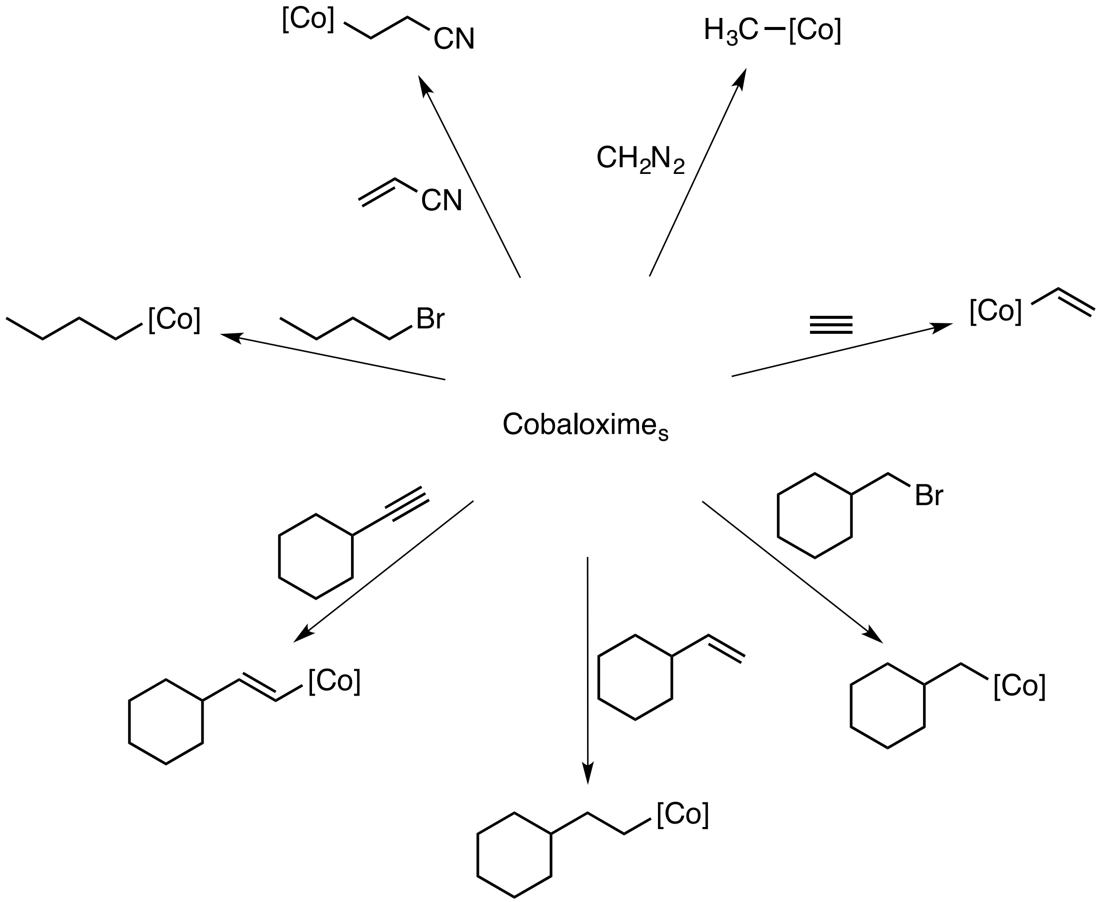
Vitamin B_{12}

> In these compounds the cobalt atom is exactly as in the complexes of vitamin and coenzyme B_{12} group in a ligand field of five nitrogen atoms

Schrauzer, G. N.; Kohnle, J. *Chem. Ber.* **1964**, *97*, 3056.
Schrauzer, G. N. *Acc. Chem. Res.* **1968**, *1*, 97.

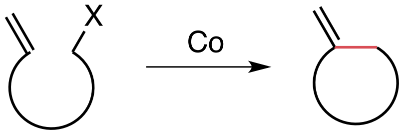
Vitamin B_{12} and Cobaloxime

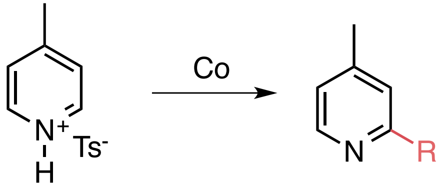




Schrauzer, G. N.; Kohnle, J. *Chem. Ber.* **1964**, *97*, 3056.

Pattenden and Branchaud's chemistry





Gerald («Gerry») Pattenden

- PhD : Queen Mary College of London
- Then lecturer in University College of cardiff followed by Nottingham
- Full Professor in Nothingam university since 1980
- Published over 470 papers

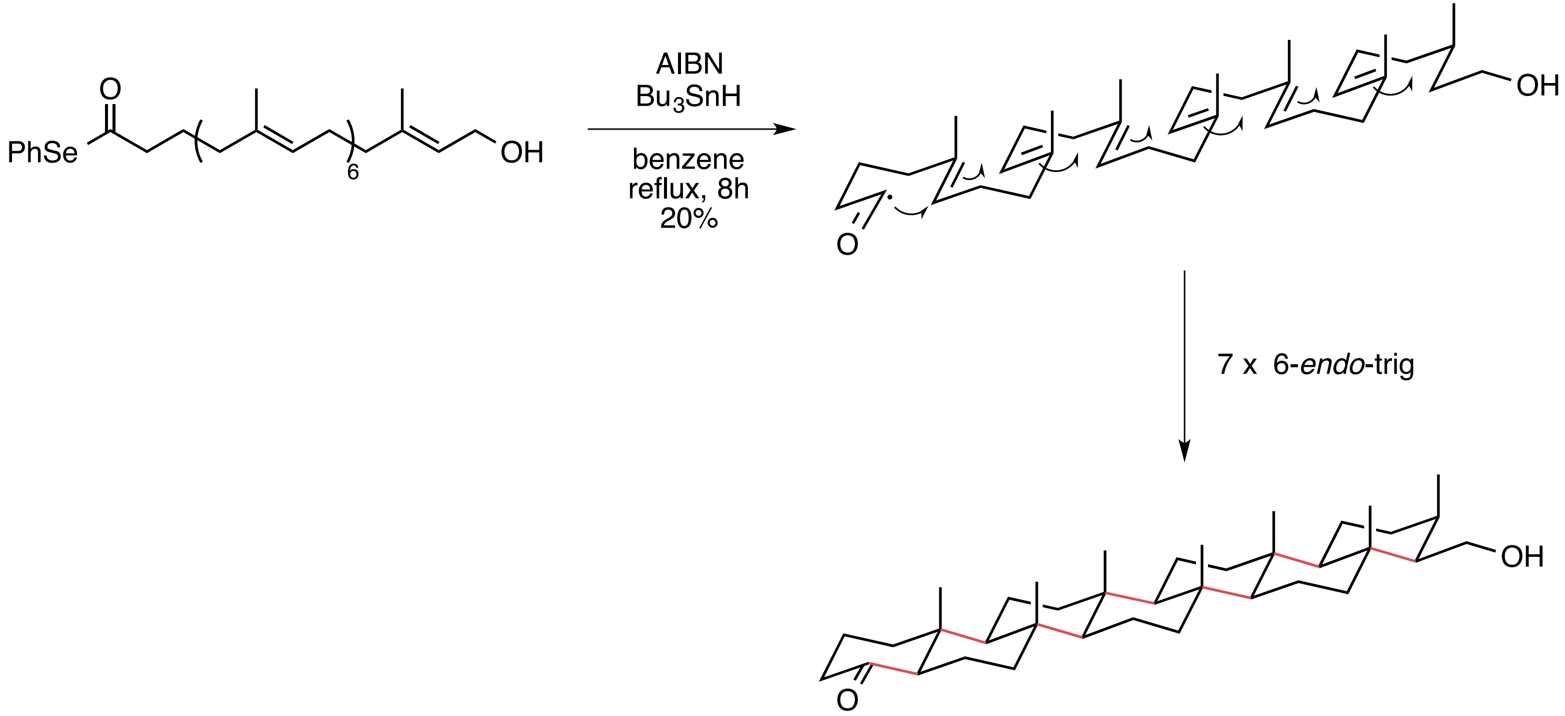
Researches Area :

- Design and development of new and novel organic synthesis methods
- Addressing the total synthesis of natural products
- Problems at the biology/chemistry interface.

Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **2000**, ix.

Pattenden’s Chemistry

- Cascade of seven radical-mediated 6-*endo-trig* cyclisations leading to a unique all-*trans*, *anti* heptacycle



AIBN
Bu_3SnH

benzene
reflux, 8h
20%

7 x 6-*endo*-trig

Handa, S.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1999**, 843.

Bruce Branchaud

- PhD : Harvard University, 1981 (R. B. Woodward).
- Postdoc. : Massachusetts Institute of Technology, 1981-83 (Christopher T. Walsh).
- Professor in Oregon University since 1983.
- Now Professor Emeritus.

- Areas of interest :

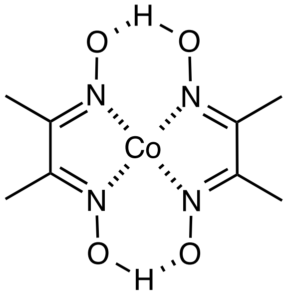
  Synthetic Organic Chemistry,
  Physical/Mechanistic Organic Chemistry,
  Bioorganic Chemistry
  Nanosciences (Synthetic Molecular Motors)
  …

http://chemistry.uoregon.edu/profile/bbranch/

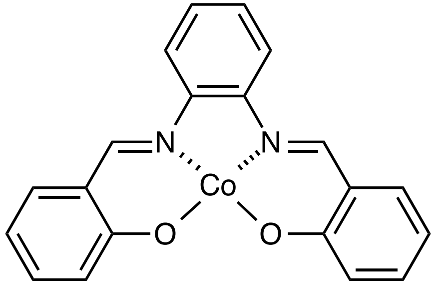
Pattenden and Branchaud’s chemistry

- Synthesis of variety of organocobalt compounds using salen / salophen ligand (Pattenden) and cobaloximes (Branchaud)

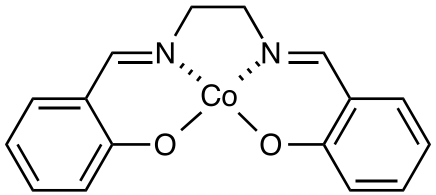
- Exploitation of the weakness of the C-Co bond to generate a cabron centered radical which undergoes a new carbon-carbon bond formation to give a product radical



Cobaloxime



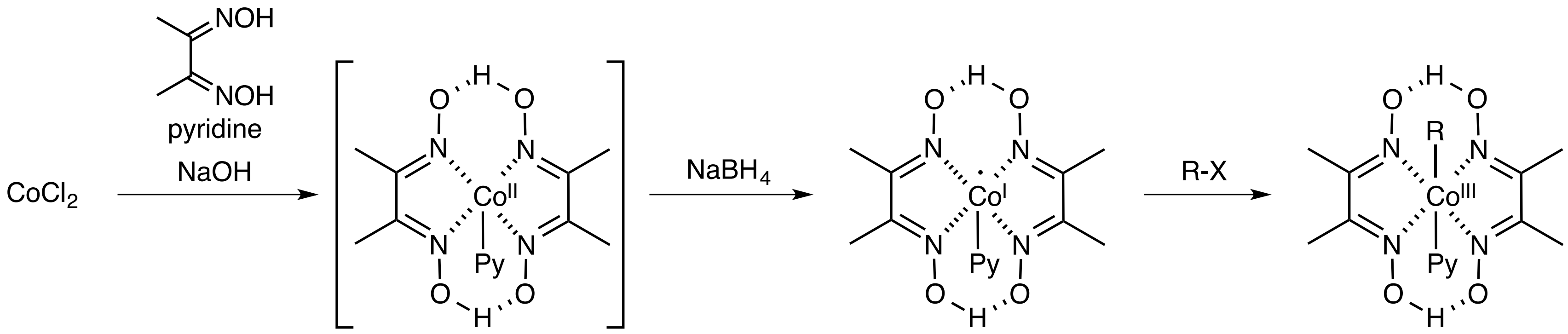
Salophen ligand

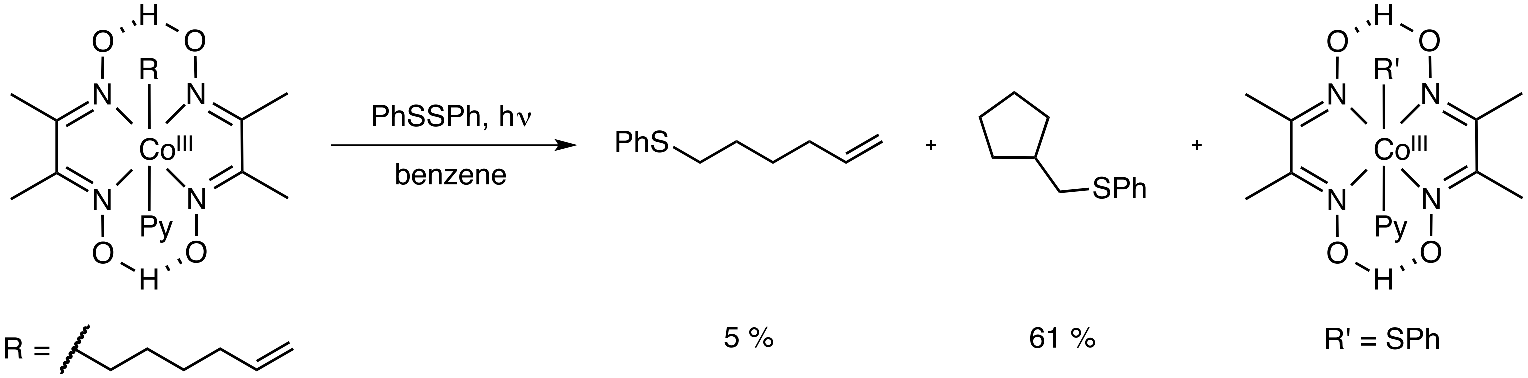


Salen ligand

Iqbal, J.; Sanghi, R.; Nandy, J. P. *J. Chem. Soc., Chem. Commun.* **1987**, 871.

Standard synthesis of Alkyl cobaloximes

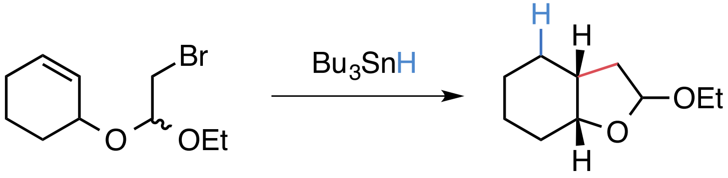




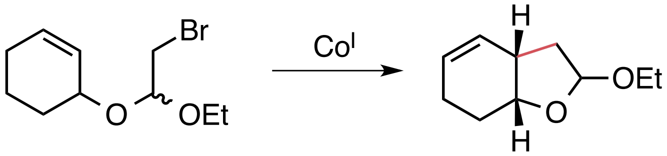
Branchaud, B. P.; Meier, M. S.; Malekzadeh, M. N. *J. Org. Chem.* **1987**, *52*, 212.

Oxidative Free Radical Cyclization

> Reductive free radical cyclization :

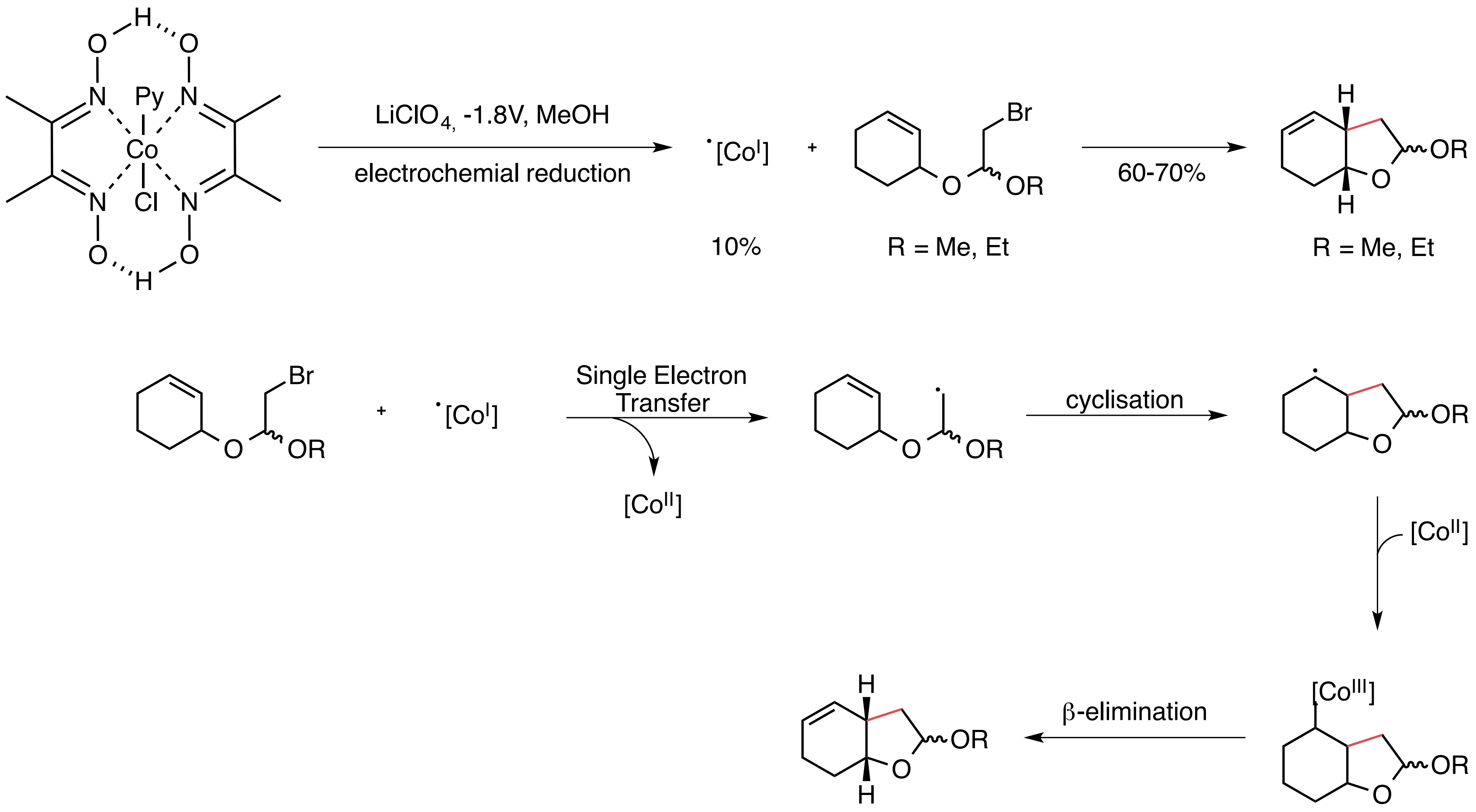


> Oxydative free radical cyclization :



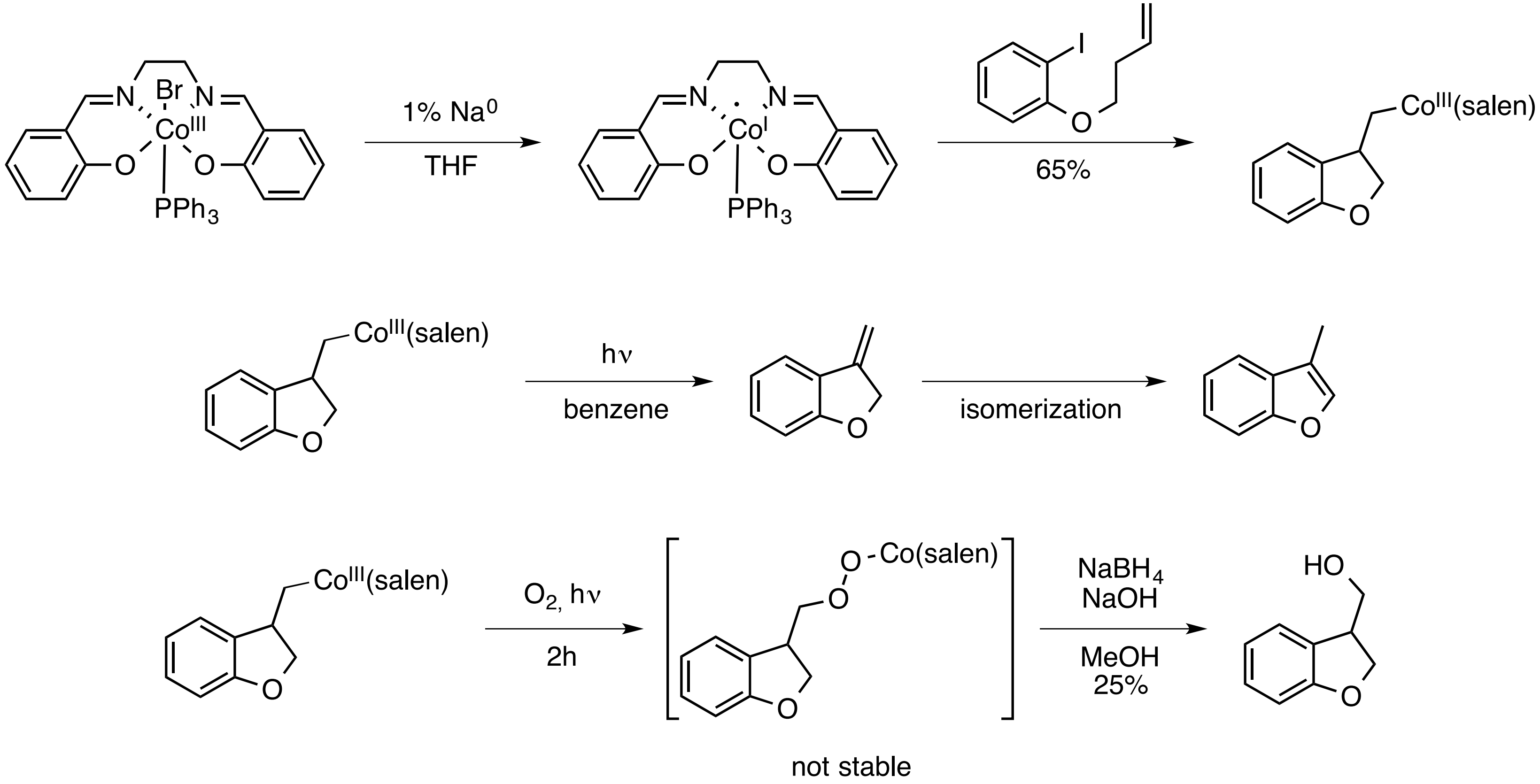
Bhandal, H.; Pattenden, G.; Russell, J. J. *Tetrahedron Letters* **1986**, *27*, 2299.

Oxidative Free Radical Cyclisation



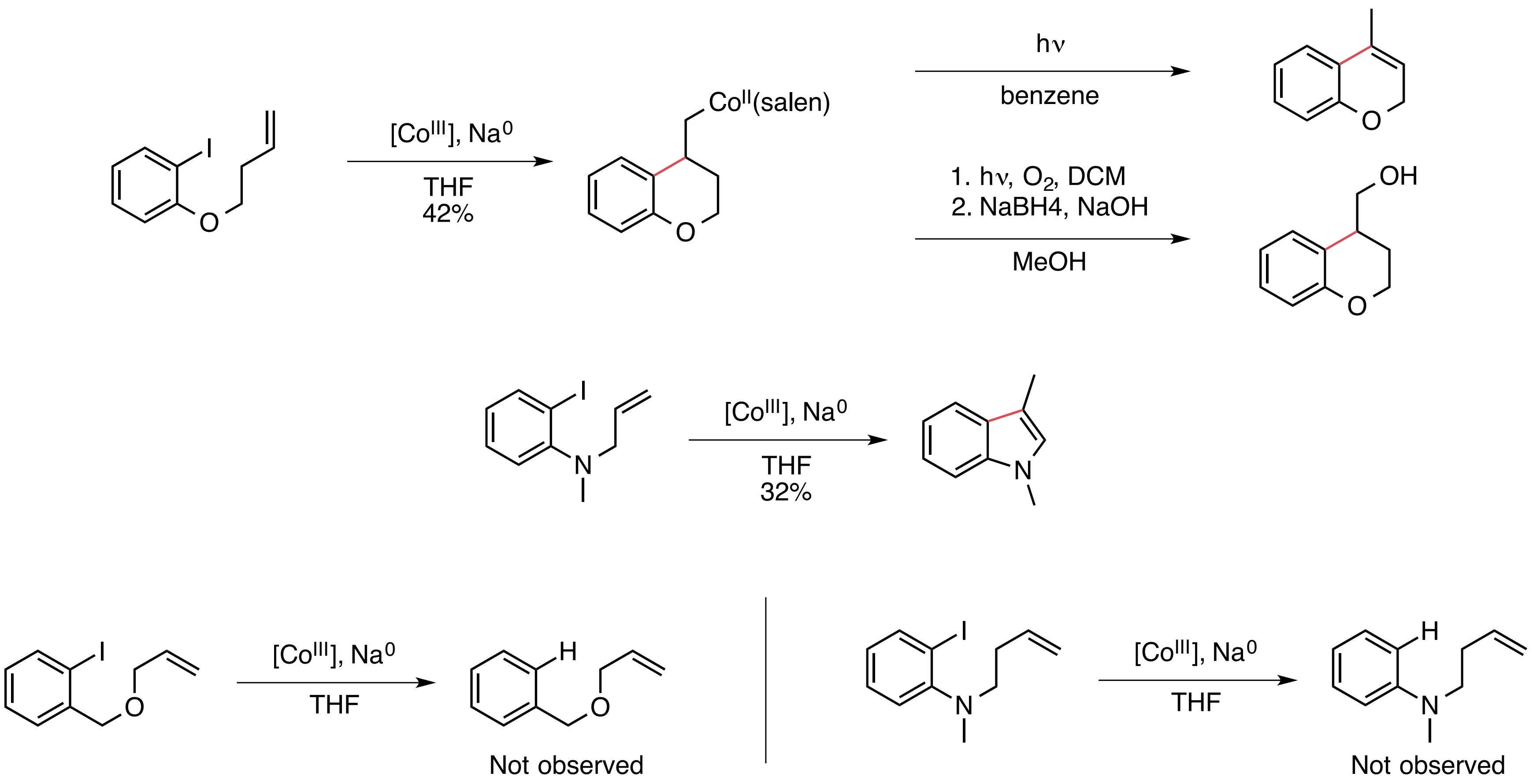
Bhandal, H.; Pattenden, G.; Russell, J. J. *Tetrahedron Letters* **1986**, *27*, 2299.

Synthesis of Heteroaromatics via Oxydative Free Radical Cyclisation



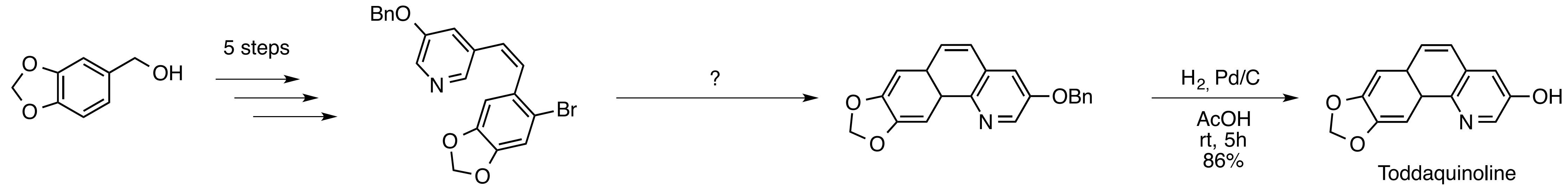
Patel, V. F.; Pattenden, G.; Russell, J. J. *Tetrahedron Letters* **1986**, *27*, 2303.

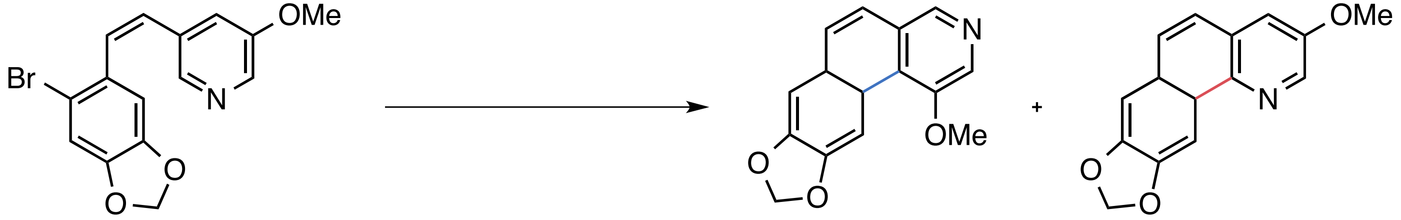
Synthesis of Heteroaromatics via Oxydative Free Radical Cyclisation



Patel, V. F.; Pattenden, G.; Russell, J. J. *Tetrahedron Letters* **1986**, *27*, 2303.

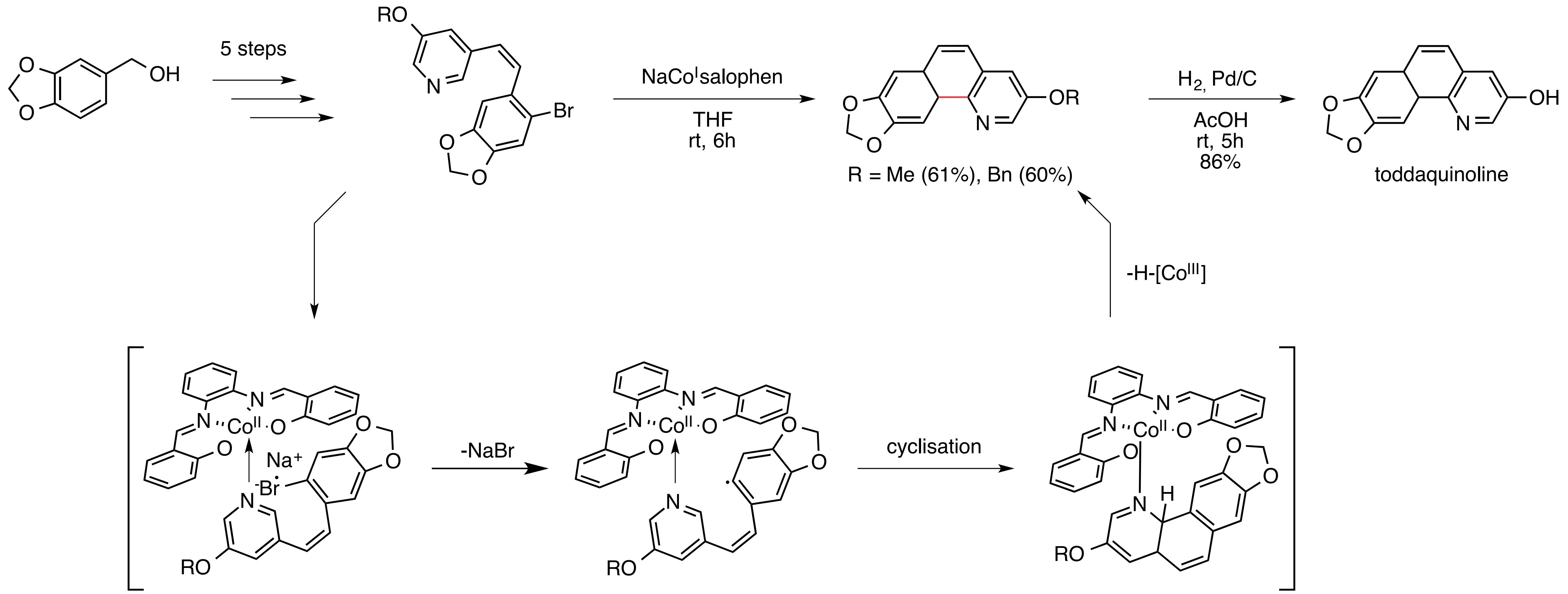
Total Synthesis of Toddaquinoline





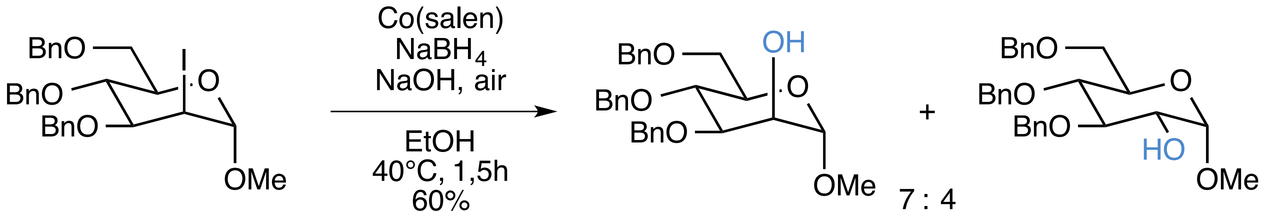
Harrowven, D. C.; Nunn, M. I. T.; Blumire, N. J.; Fenwick, D. R. *Tetrahedron Letters* **2000**, *41*, 6681.

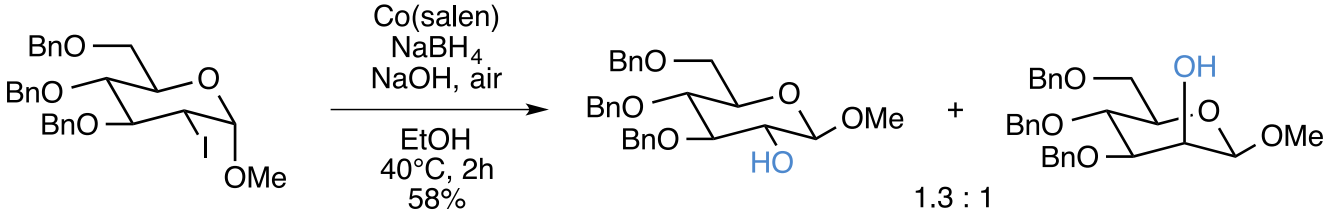
Total Synthesis of Toddaquinoline



Harrowven, D. C.; Nunn, M. I. T.; Blumire, N. J.; Fenwick, D. R. *Tetrahedron Letters* **2000**, *41*, 6681.

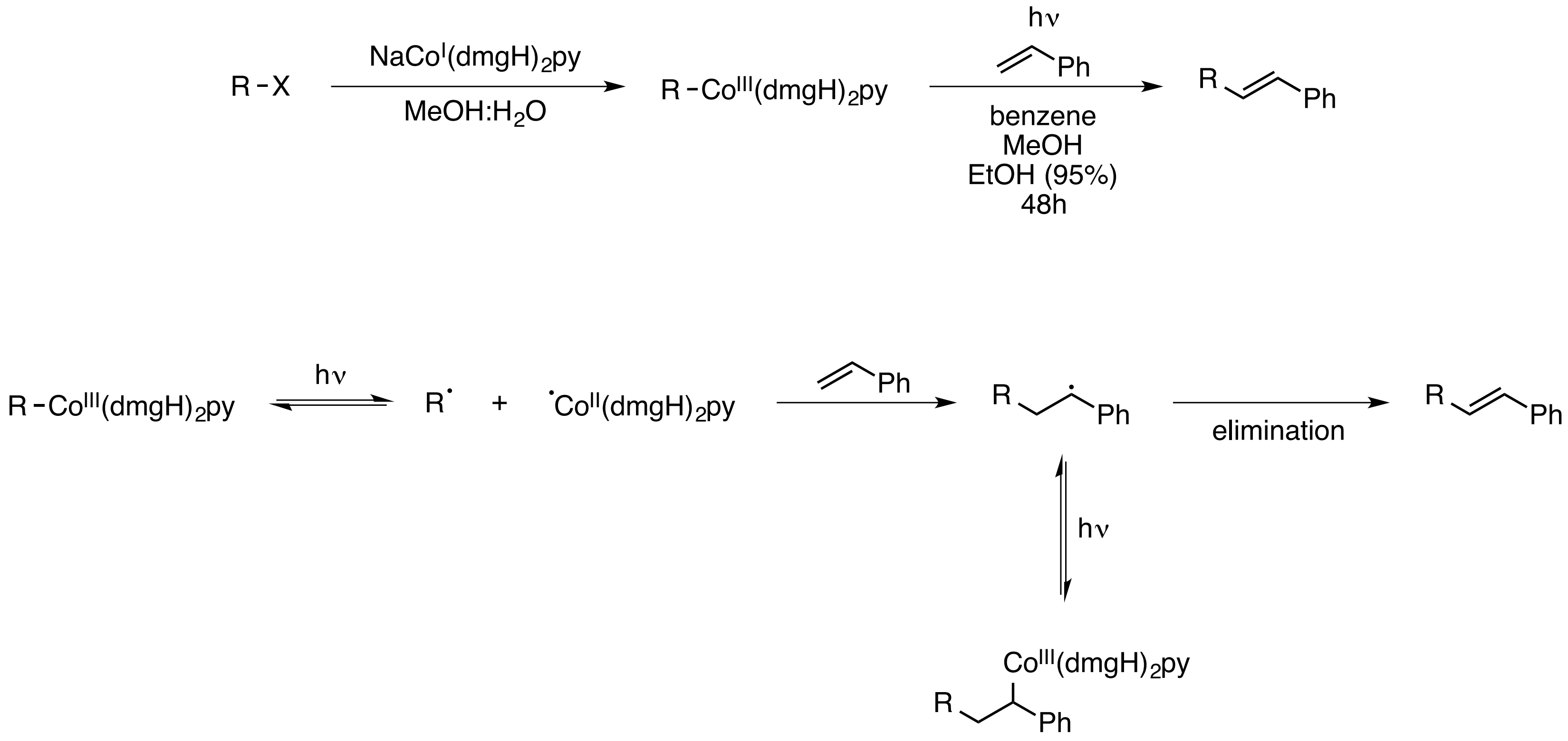
Cobalt-catalysed radical oxygentation with molecular oxygen





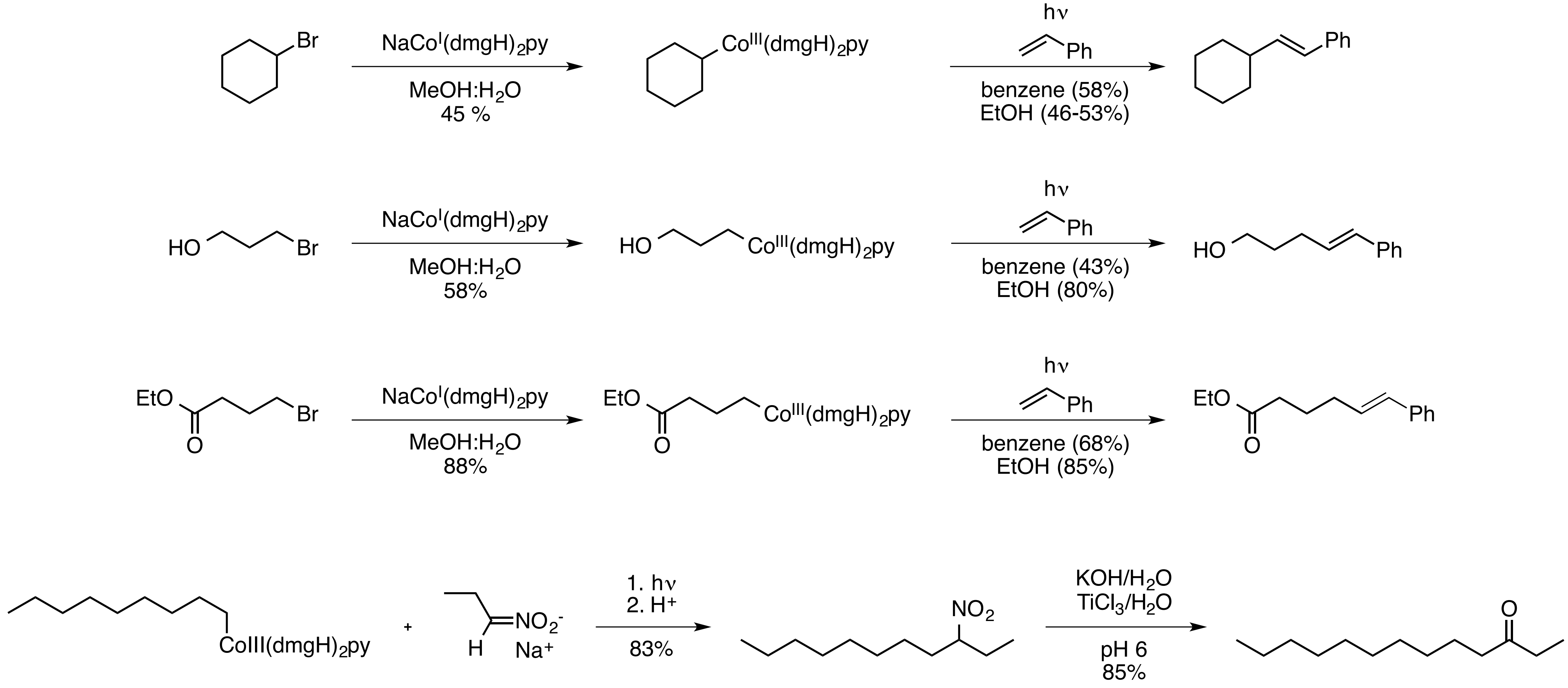
Bamhaoud, T.; Prandi, J. *Chem. Commun* **1996**, 1229.
Bandal, H.; Pattenden, G.; Russell, J. J. *Tetrahedron Letters* **1986**, *27*, 2299.

Alkyl-Alkenyl Cross-Coupling



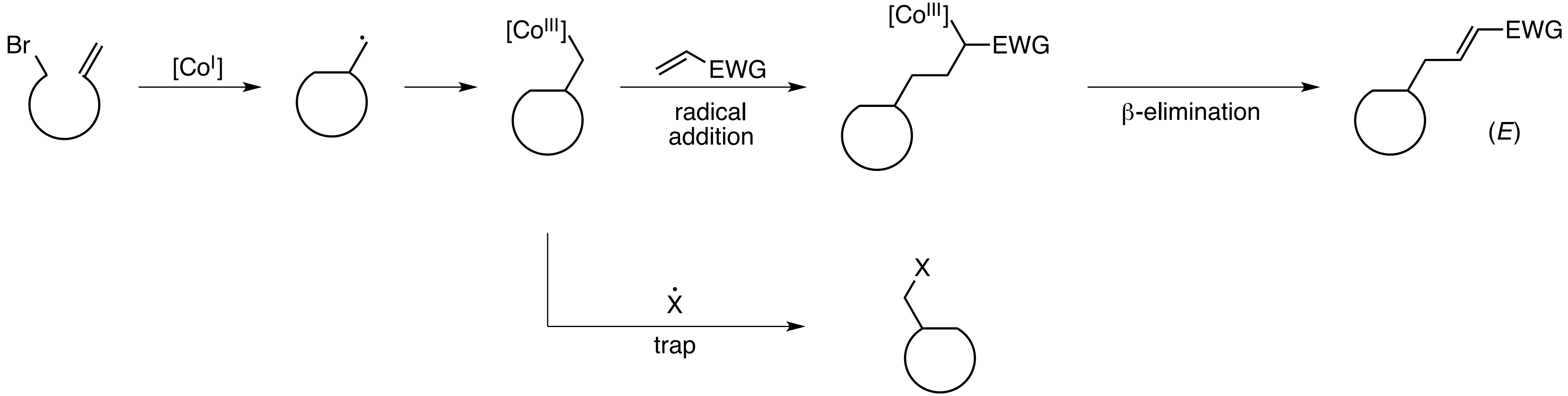
Branchaud, B. P.; Meier, M. S.; Choi, Y. *Tetrahedron Letters* **1988**, *29*, 167.

Alkyl-Alkenyl Cross-Coupling



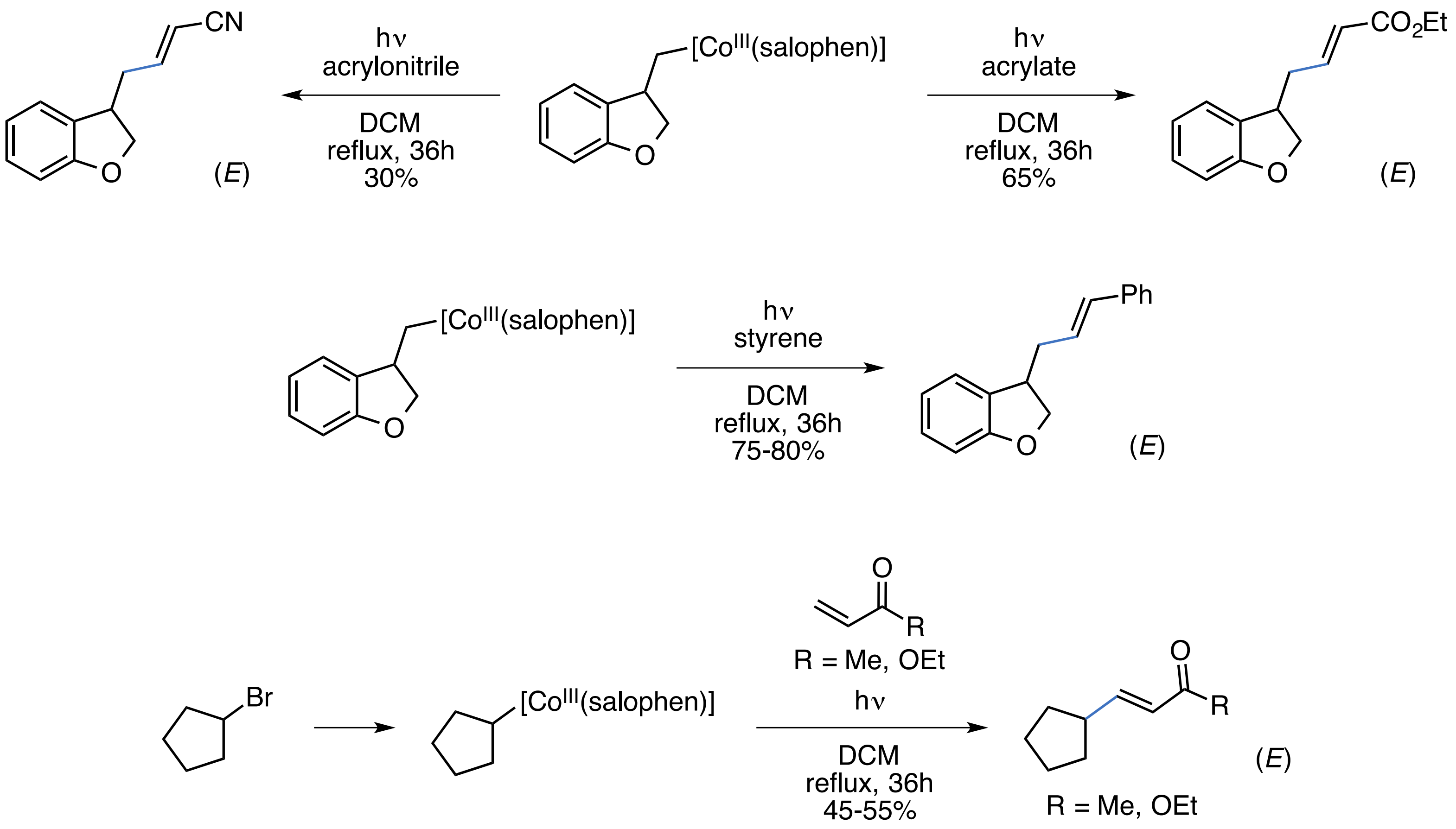
Branchaud, B. P.; Meier, M. S.; Choi, Y. *Tetrahedron Letters* **1988**, *29*, 167.
Branchaud, B. P.; Yu, G. X. *Tetrahedron Letters* **1988**, *29*, 6545.

Radical Michael-Addition Type



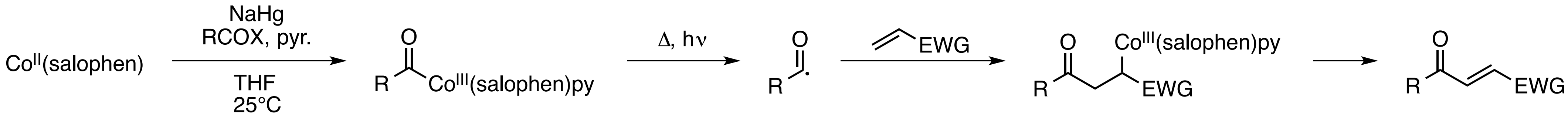
Patel, V. F.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1987**, 871.

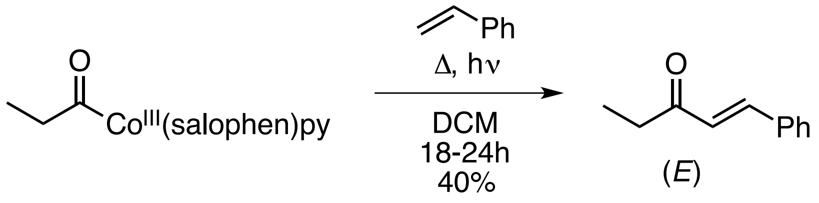
Radical Michael-Addition Type

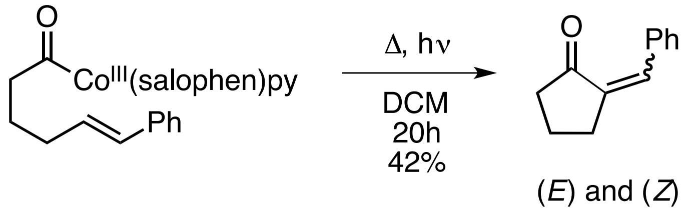


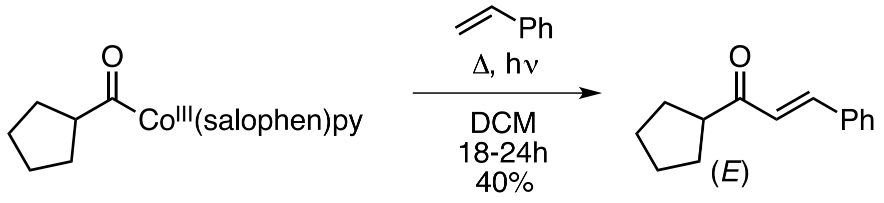
Patel, V. F.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1987**, 871.

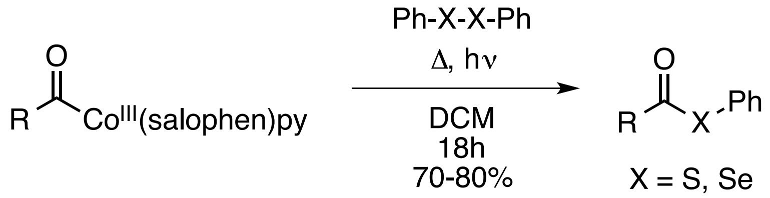
Radical Intermediates for inter- and intra- Molecular Oxidative Michael-Addtition Reaction





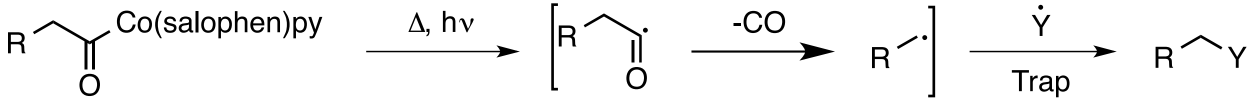


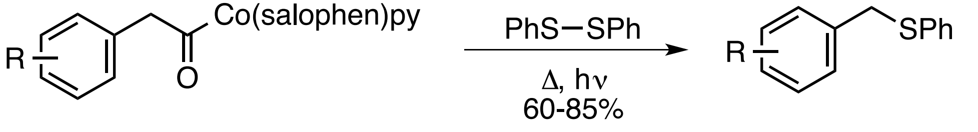




Coveney, D. J.; Patel, V. F.; Pattenden, G. *Tetrahedron Letters* **1987**, *28*, 5949.

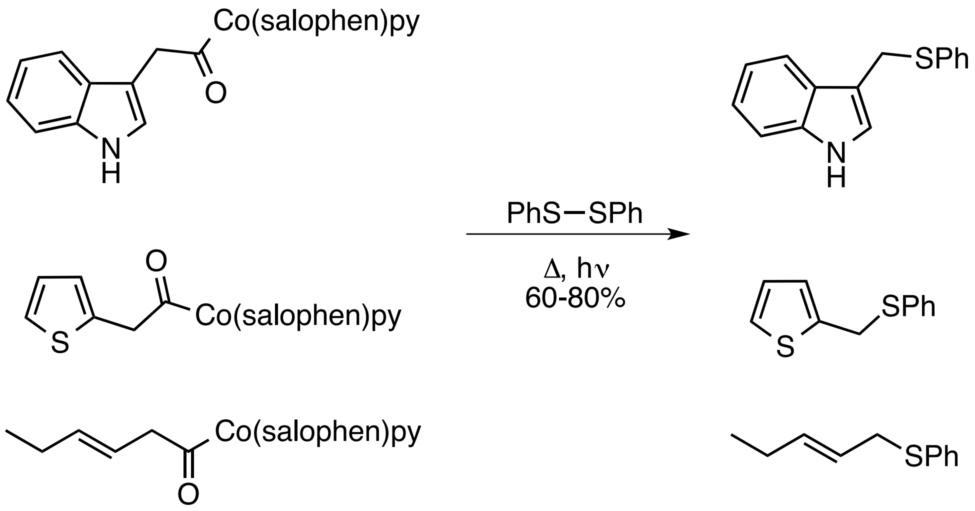
Radical Decarboxylation





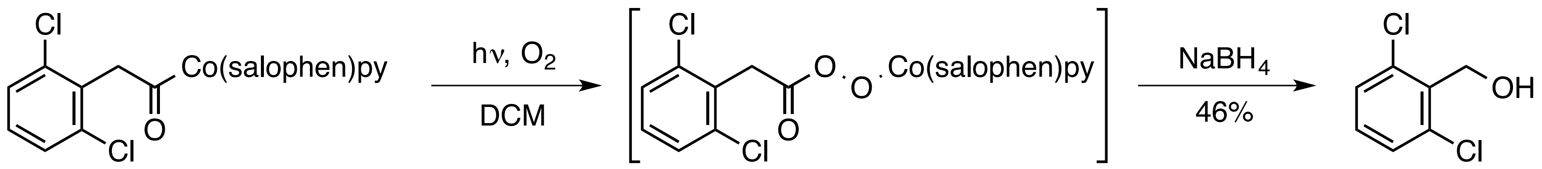
R = H, 4-OMe, 2,6-diCl

R = H, 4-OMe, 2,6-diCl

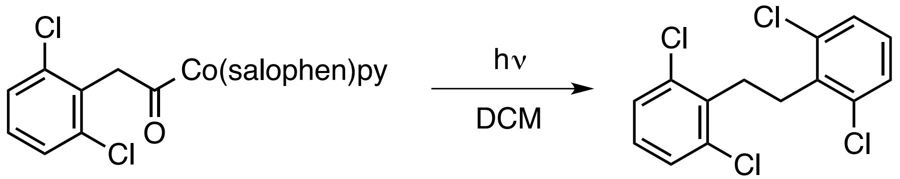


Patel, V. F.; Pattenden, G. *Tetrahedron Letters* **1988**, *29*, 707.

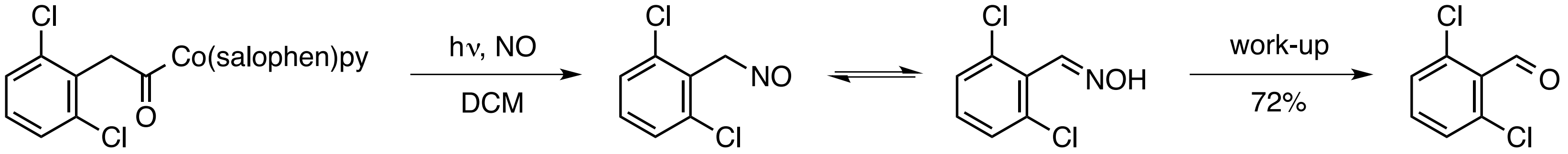
Radical Degradation Of Carboxylic Acids To Functionalised Non-alkanes



- Without trap

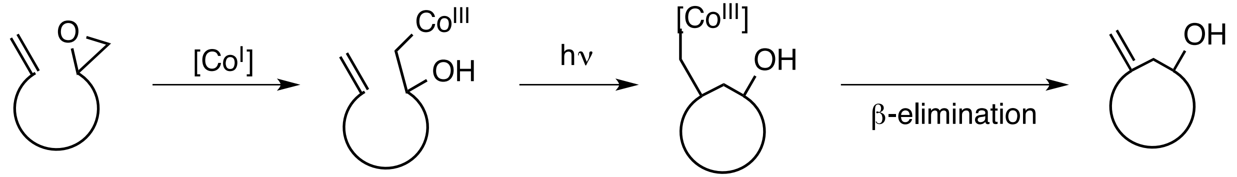


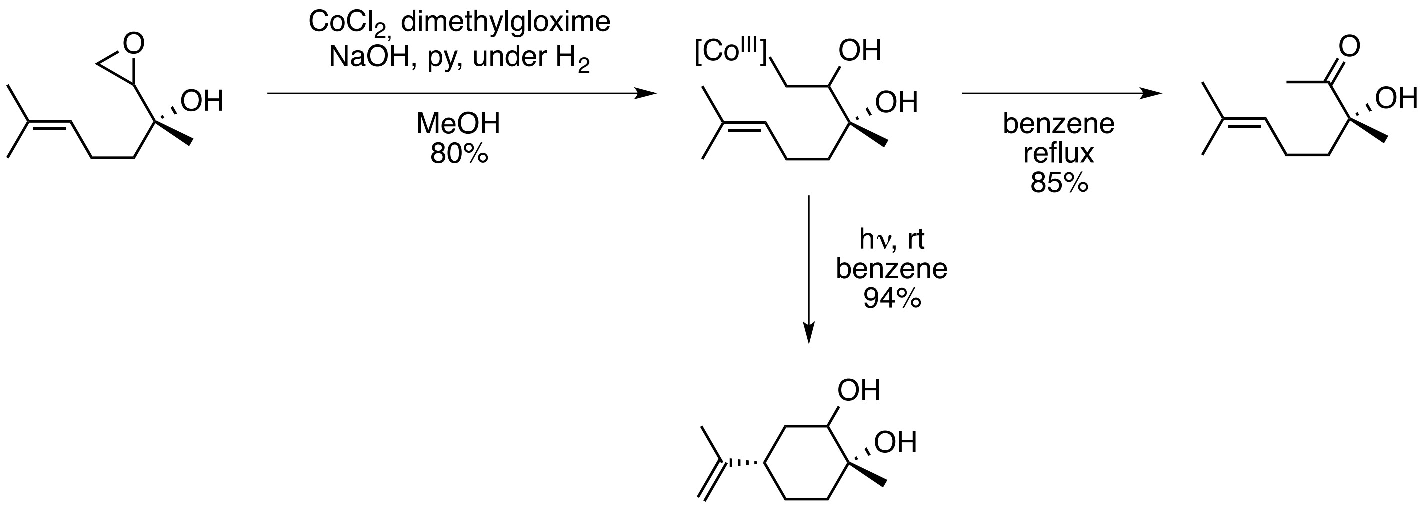
- Generation of an aldehyde



Patel, V. F.; Pattenden, G. *Tetrahedron Letters* **1988**, *29*, 707.

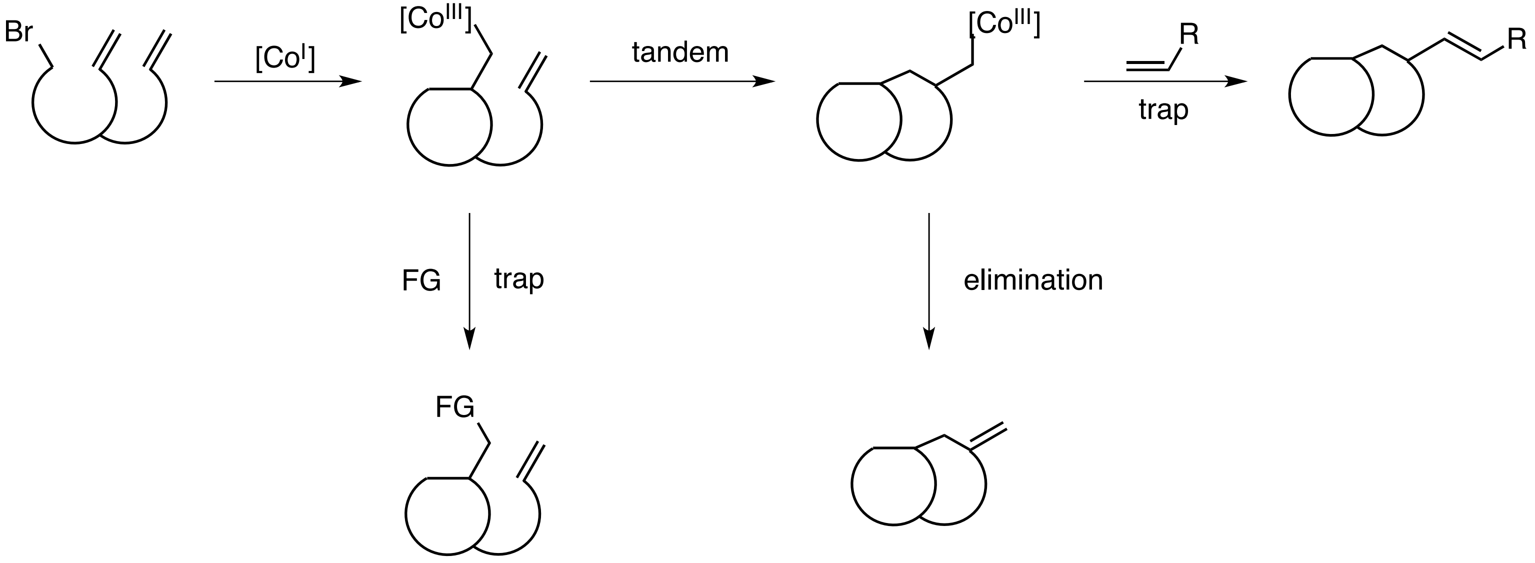
Cobalt mediated cyclisations of epoxy olefins

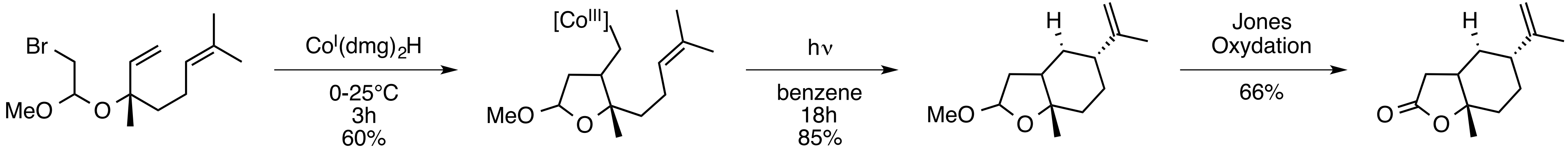




Harrowven, D. C.; Pattenden, G. *Tetrahedron Letters* **1991**, *32*, 243.

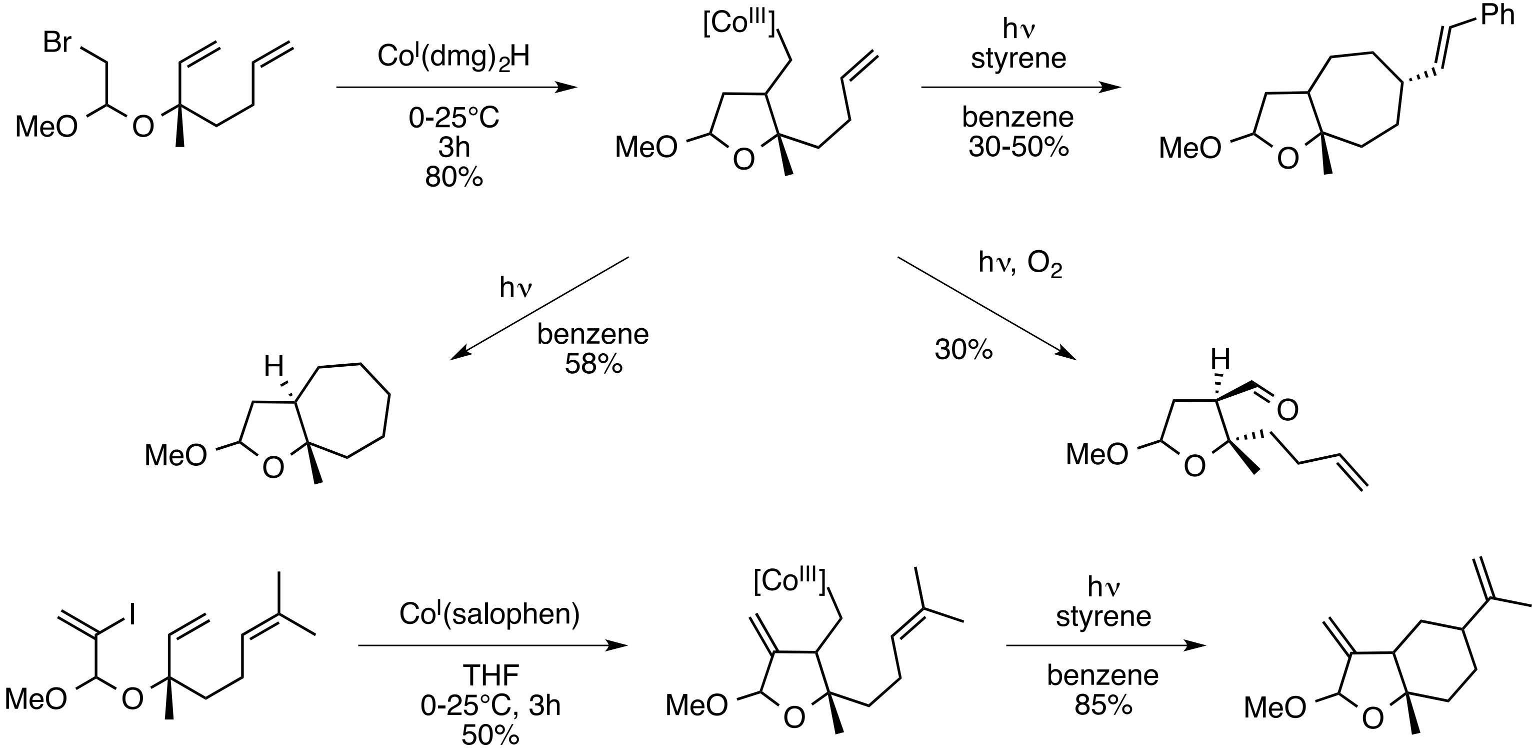
Tandem Radical Cyclisation Reactions



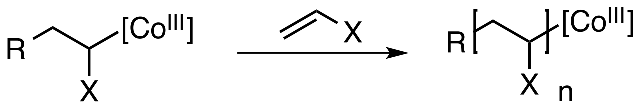


Ali, A.; Harrowven, D. C.; Pattenden, G. *Tetrahedron Letters* **1992**, *33*, 2851.

Tandem Radical Cyclisation Reactions

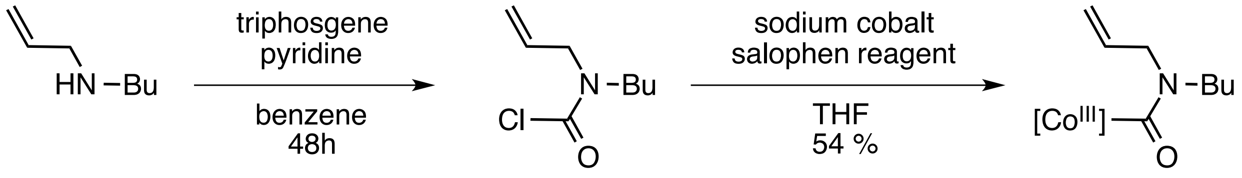


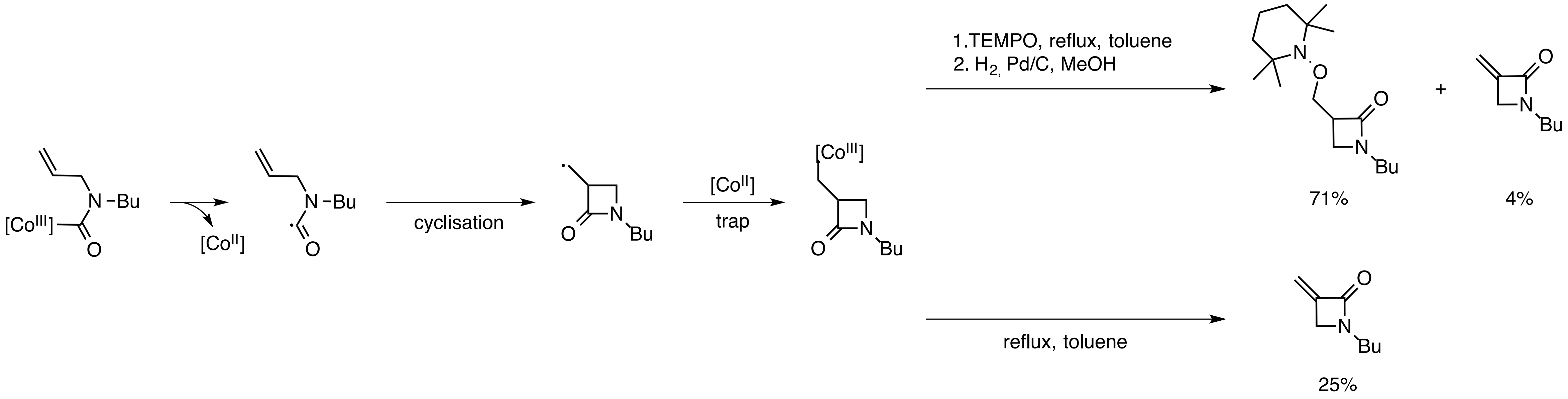
- Also used for polymerization :



Ali, A.; Harrowven, D. C.; Pattenden, G. *Tetrahedron Letters* **1992**, *33*, 2851.
Debuigne, A.; Jérôme, R.; Jérôme, C.; Detrembleur, C. *Cobalt-Mediated Radical Polymerization*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2006; pp 67–79.

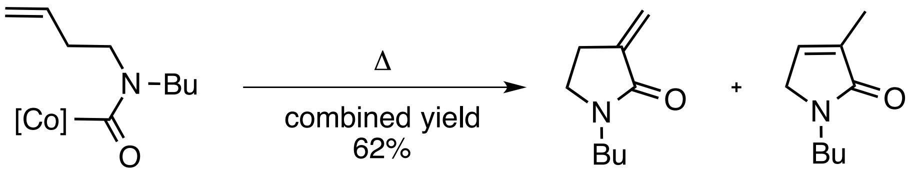
Synthesis of β-lactam

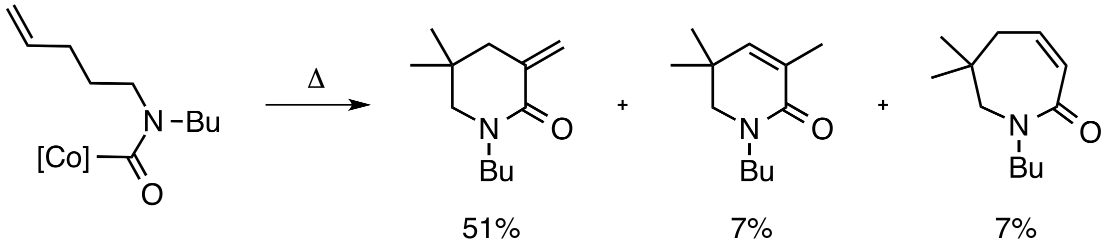




Gill, G. B.; Pattenden, G.; Reynolds, S. J. *Tetrahedron Letters* **1989**, *30*, 3229.

Synthesis of β-lactam

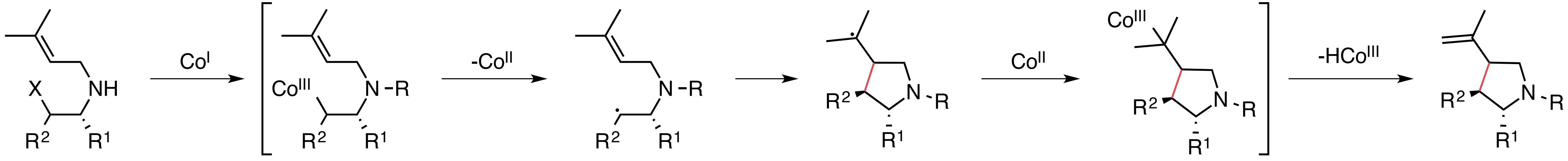




Gill, G. B.; Pattenden, G.; Reynolds, S. J. *Tetrahedron Letters* **1989**, *30*, 3229.

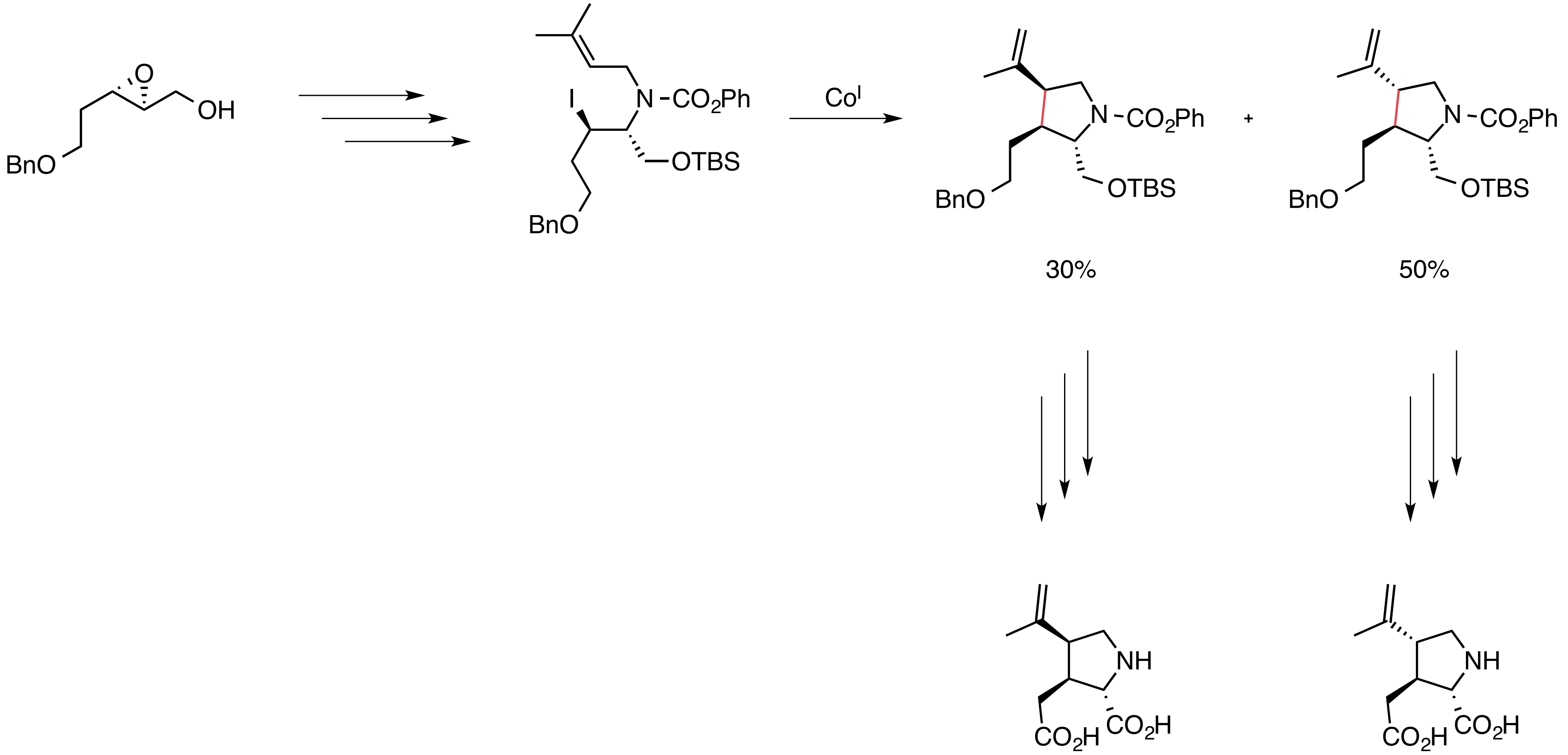
Cobalt-mediated Cyclisation of amino acid derivatives. Application to the Kainiods.

- Enantioselective cyclization :



Baldwin, J. E.; Li, C.-S. *J. Chem. Soc., Chem. Commun.* **1987**, 166.

Cobalt-mediated Cyclisation of amino acid derivatives. Application to the Kainiods.



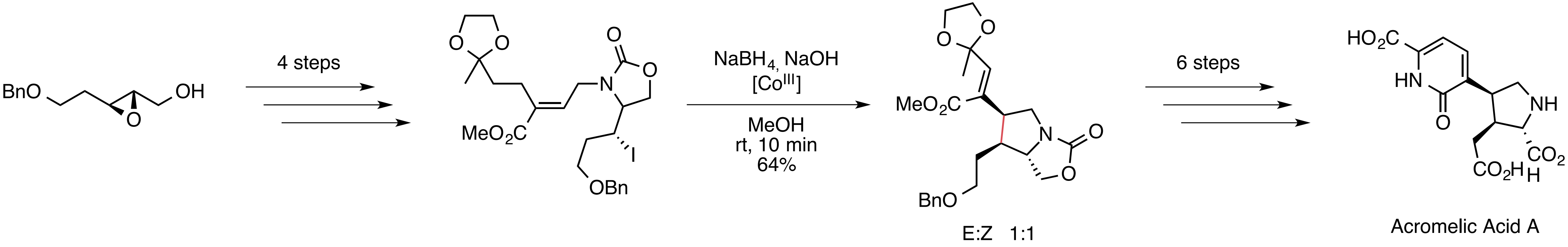
(-)-α-kainic acid

(+)-α-allokenic acid

Baldwin, J. E.; Li, C.-S. *J. Chem. Soc., Chem. Commun.* **1987**, 166.

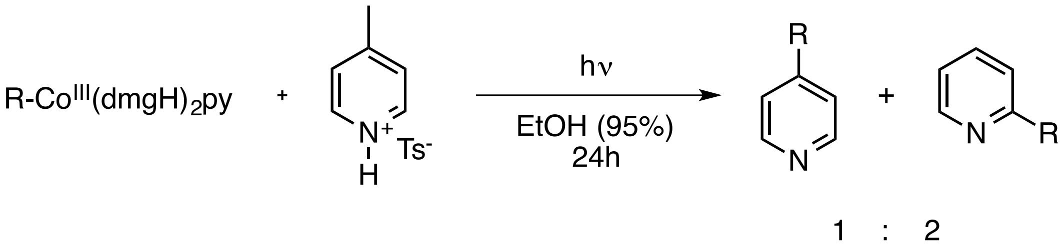
Enantiospecific Synthesis of Acromelic Acid A via a Cobalt mediated Cyclisation Reaction

- Acromelic A : From the poisonous mushroom clitycybe acromelalga
- Extremely potent depolarising activity on glutamate-mediated neurotransmission



Baldwin, J. E.; Li, C.-S. *J. Chem. Soc., Chem. Commun.* **1988**, 261.

Cobaloximes mediated Radical Alkyl-Heteroaromatic Substitution



R = n-$C_{10}H_{21}$ (87%)
c-C_6H_{11} (33-44%)
n-C_3H_6OH (68-80%)

Branchaud, B. P.; Choi, Y. L. *J. Org. Chem.* **1988**, *53*, 4638.

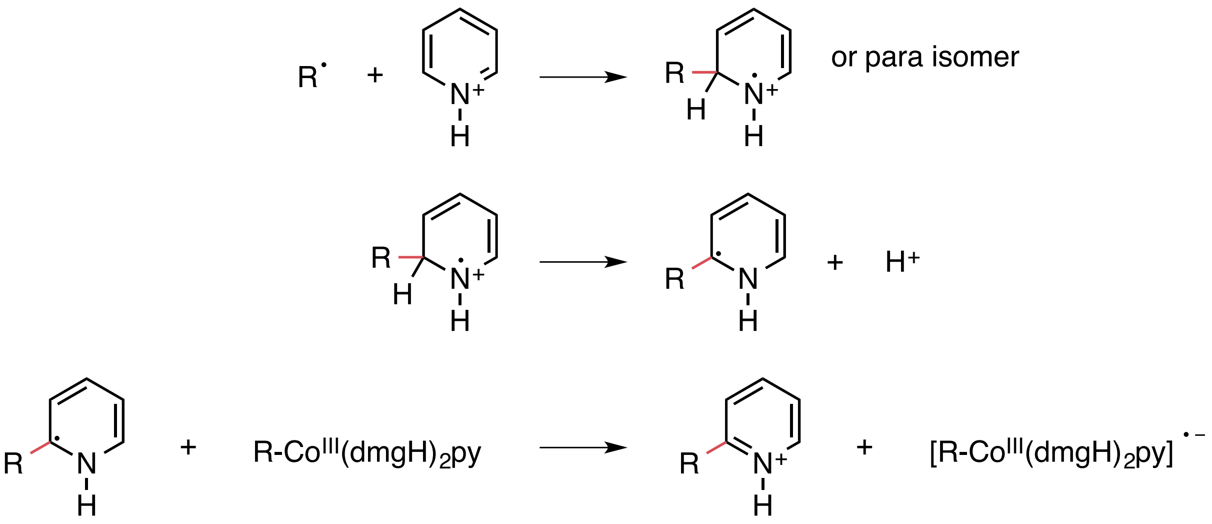
Cobaloximes mediated Radical Alkyl-Heteroaromatic Substitution

> Chain Mecanism

Chain Initiation

$$R\text{-}Co^{III}(dmgH)_2py \xrightarrow{h\nu} R^{\bullet} + {}^{\bullet}Co^{II}(dmgH)_2py$$

Chain Propagation



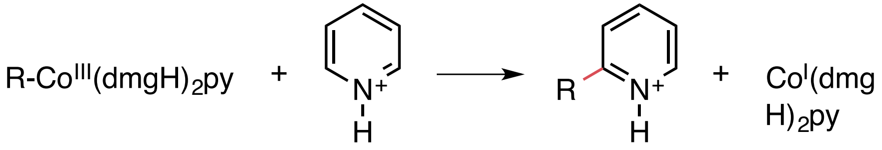
$$[R\text{-}Co^{III}(dmgH)_2py]^{\bullet -} \longrightarrow R^{\bullet} + [Co^{I}(dmgH)_2py]^{-}$$

Cobaloxime disproportionation

$$H^+ + [Co^{I}(dmgH)_2py]^{-} \longrightarrow H\text{-}Co^{III}(dmgH)_2py$$

$$H\text{-}Co^{III}(dmgH)_2py \longrightarrow Co^{I}(dmgH)_2py + H_2$$

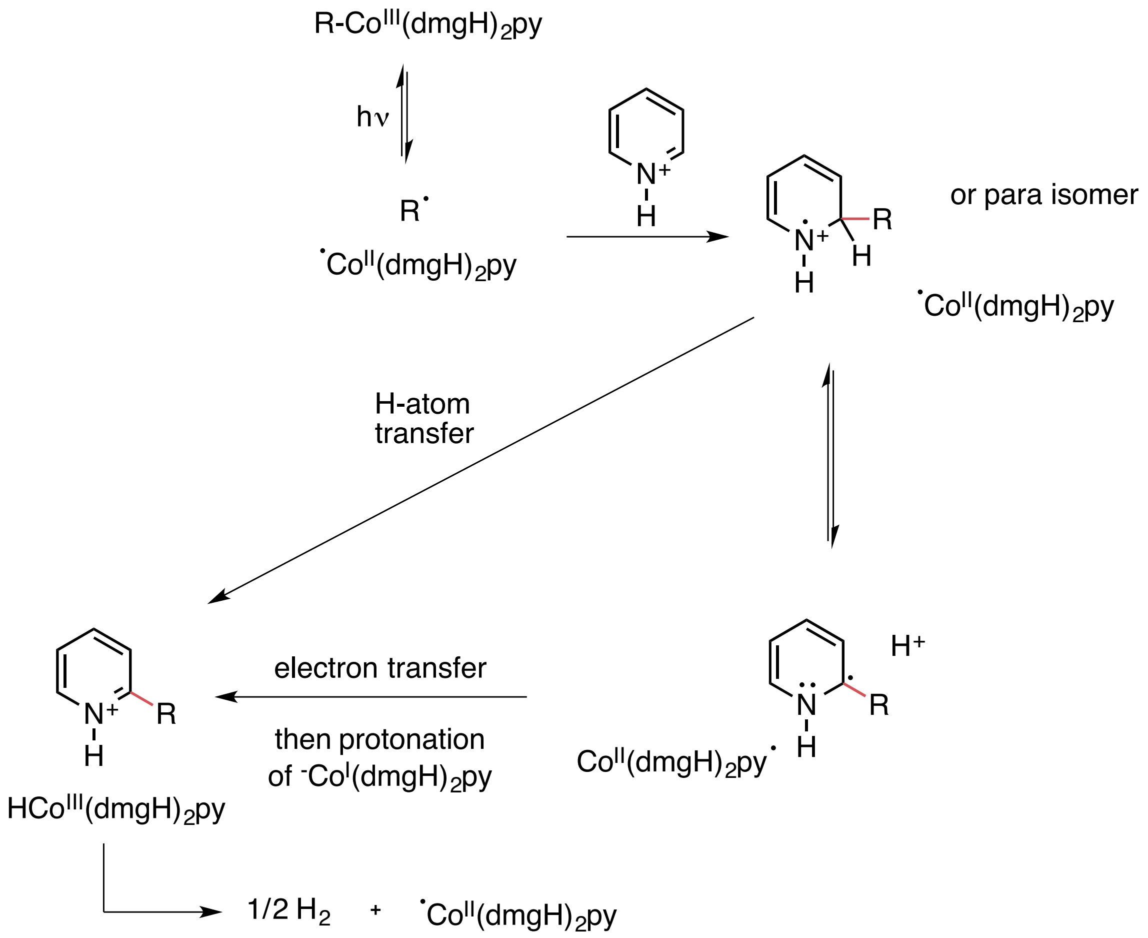
Net reaction



Branchaud, B. P.; Choi, Y. L. *J. Org. Chem.* **1988**, *53*, 4638.

Cobaloximes mediated Radical Alkyl-Heteroaromatic Substitution

- Non Chain Mecanism



$R\text{-}Co^{III}(dmgH)_2py$

hν

$R^{\bullet}$

$^{\bullet}Co^{II}(dmgH)_2py$

or para isomer

$^{\bullet}Co^{II}(dmgH)_2py$

H-atom transfer

H^+

$Co^{II}(dmgH)_2py^{\bullet}$

electron transfer

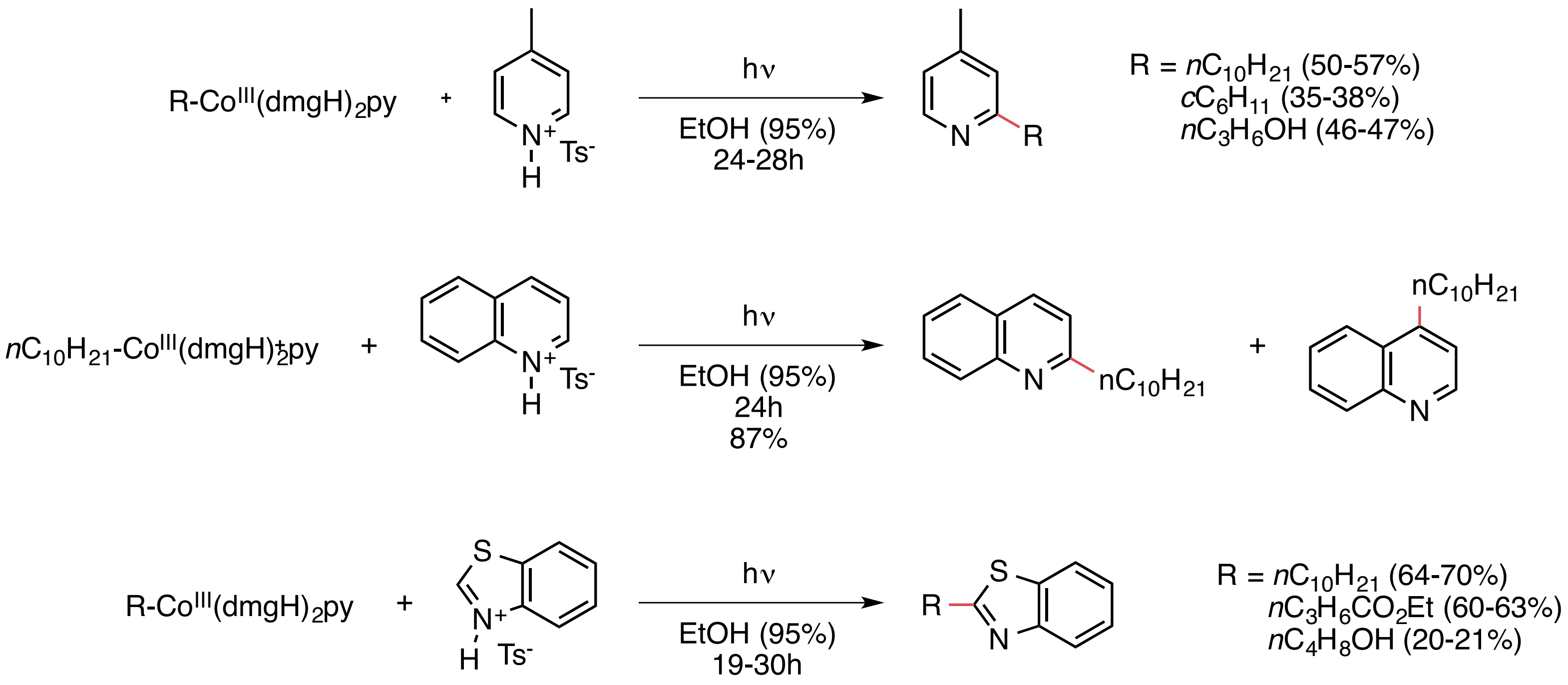
then protonation of $^{-}Co^{I}(dmgH)_2py$

$HCo^{III}(dmgH)_2py$

$1/2\ H_2 + {}^{\bullet}Co^{II}(dmgH)_2py$

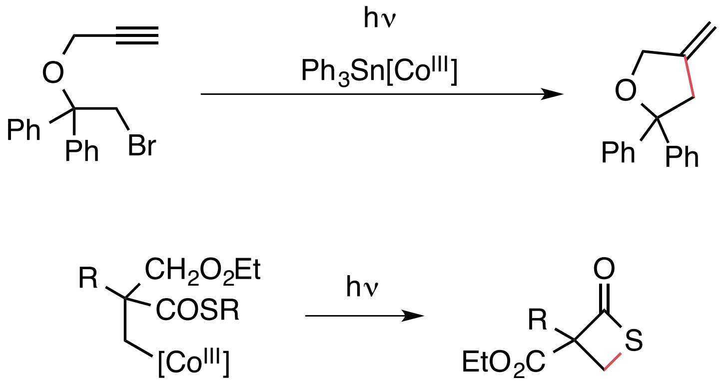
Branchaud, B. P.; Choi, Y. L. *J. Org. Chem.* **1988**, *53*, 4638.

Cobaloximes mediated Radical Alkyl-Heteroaromatic Substitution

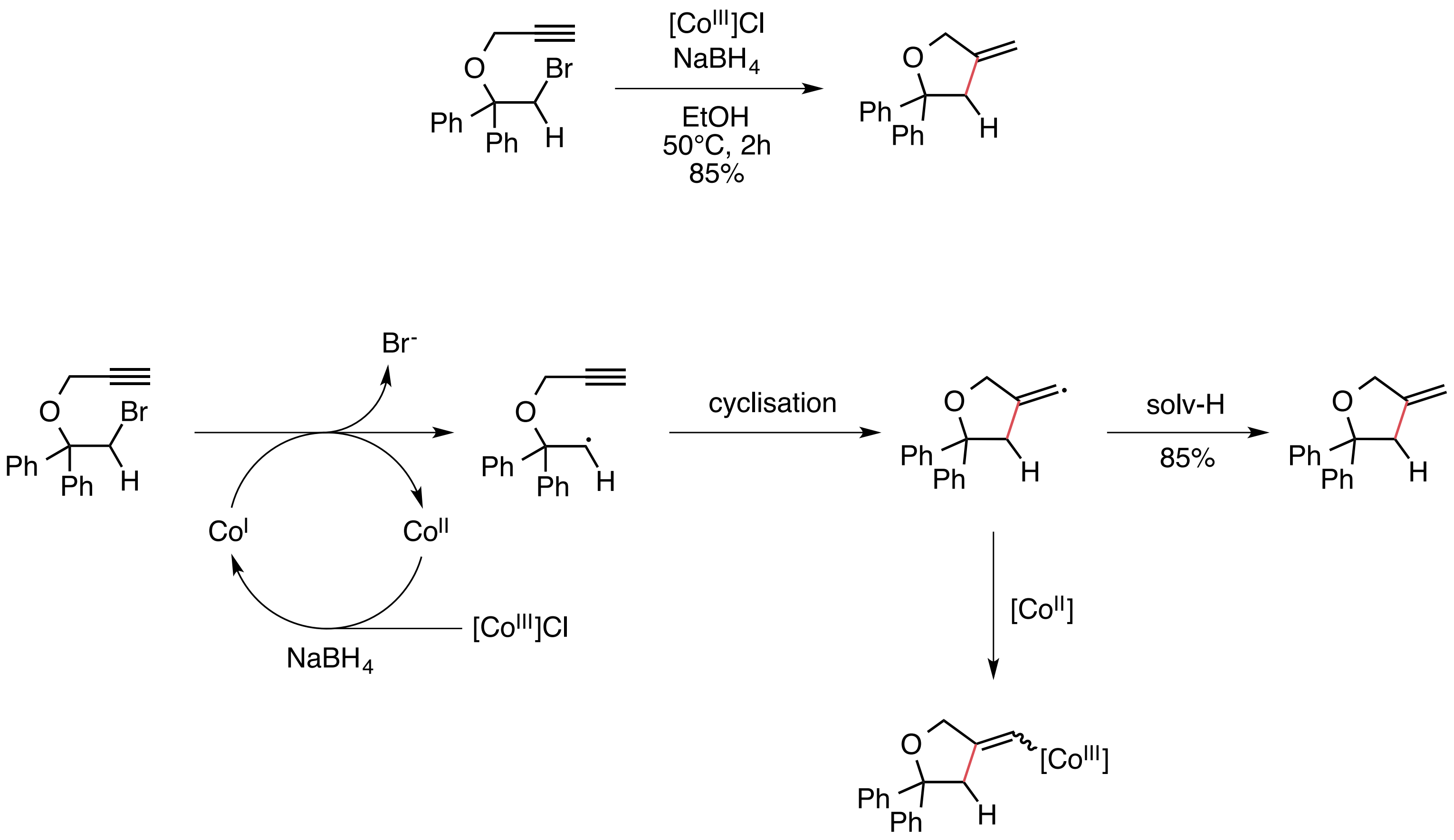


Branchaud, B. P.; Choi, Y. L. *J. Org. Chem.* **1988**, *53*, 4638.

Tada's Chemistry

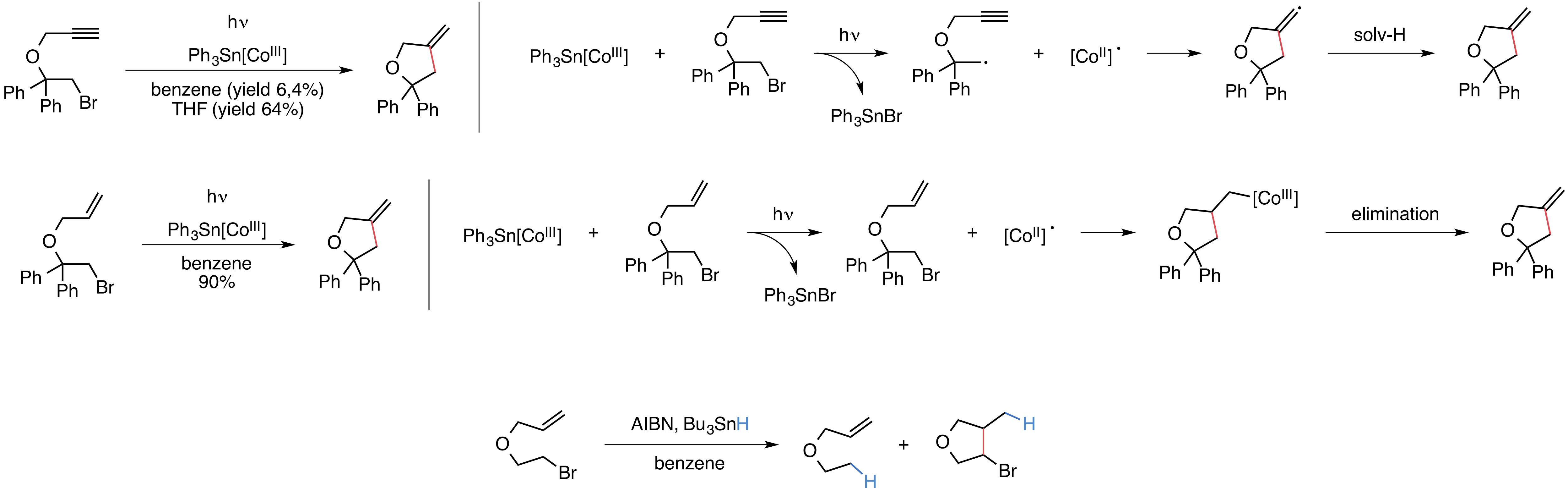


Reductive Cyclization of 2-[(2-Propynyl)oxy]ethyl Bromides



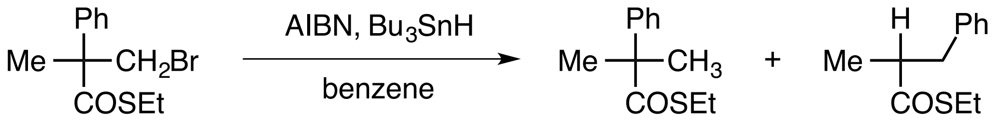
Okabe, M.; Abe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 1775.
Okabe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 5382

(Triphenyltin)cobaxolime as a Reagent for Radical Generation from Bromides



Tada, M.; Kaneko, K. *J. Org. Chem.* **1995**, *60*, 6635.

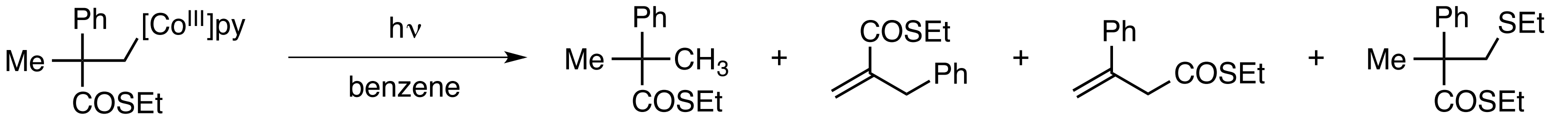
Radical rearrangement of a thioester group mediated by a cobalt complex



1 **2**

[Bu_3SnH]	**1**	**2**
10^{-1} M	100	0
10^{-2} M	72	28
10^{-3} M	21	79

> Phenyl group rearranged more easily than a thioester



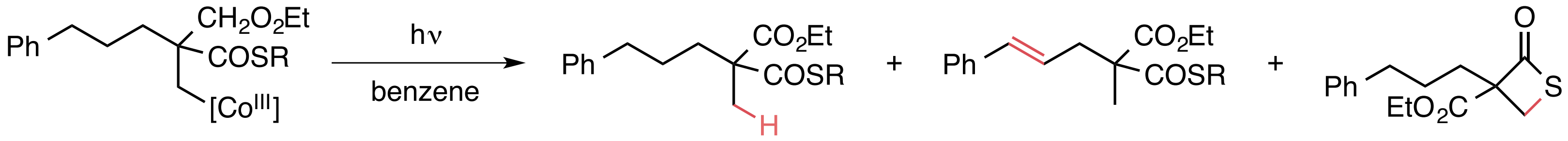
1 **3** **4** **5**

Solvent	**1**	**3**	**4**	**5**
benzene	0	16	27	57
methanol	25	7	18	50
THF	60	8	11	21
chloroform	100	0	0	0

> Involvement of cobalt(II) species in the migration of thioester group

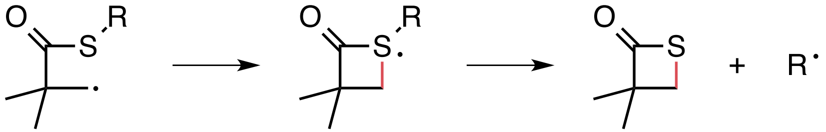
Tada, M.; Inoue, K.; Sugawara, K.; Hiratsuka, M.; Okabe, M. *Chem. Lett.* **1985**, 1821.

Formation of thiolactone by photolyses of organocobaloxime



	Yield			
R = Et	80%	11%	89%	
R = *t*Bu	40%	12%	73%	15%

> Proposed Mecanism



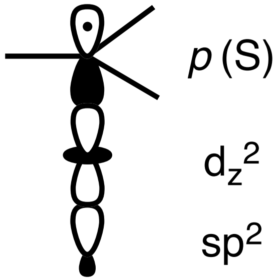
Tada, M.; Nakamura, T.; Matsumoto, M. *J. Am. Chem. Soc.* **1988**, *110*, 4647.

Interactions between the free radical intermediate and the paramagnetic cobalt (II)

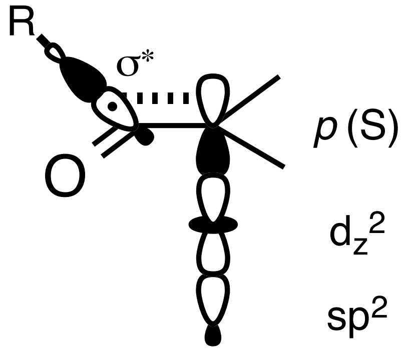
- ESR study showed a coordination between a cobalt(II) complex and sulfur

- Sulfur-coordinated complex is a 19-electron complex

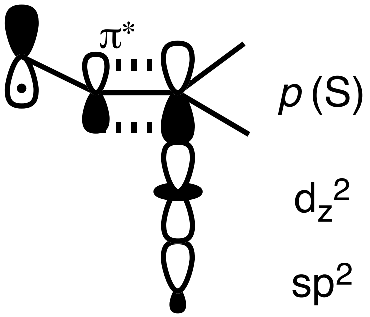
- Axial bond of (S-Co-N) consists of a three-centered five electron bond, which is reinforced by the back donation from cobalt (II).



SOMO
(S-Co-N)



σ^*–SOMO
(S-Co-N)

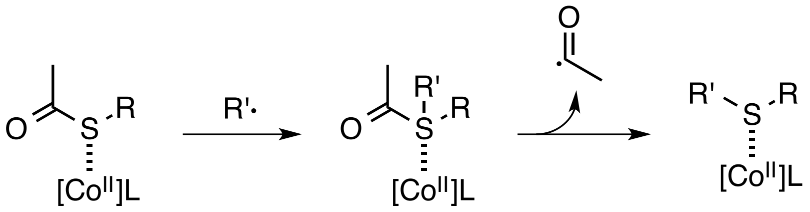


π^*–SOMO
(S-Co-N)

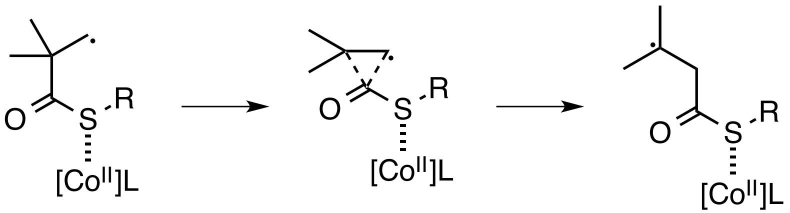
Tada, M.; Shino, R. *Journal of Inorganic Biochemistry* **1991**, *44*, 89.
Tada, M. *Heteroatom Chem.* **2001**, *12*, 204.

Interaction between the free radical intermediate and the paramagnetic cobalt (II)

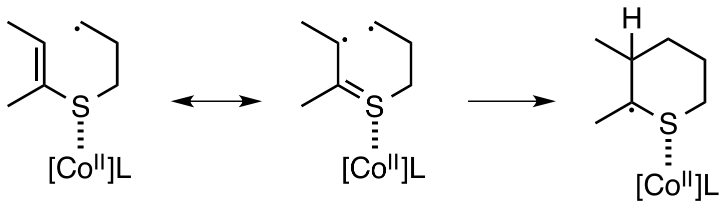
- Free radical substitution on sulfur



- Thioester rearangement

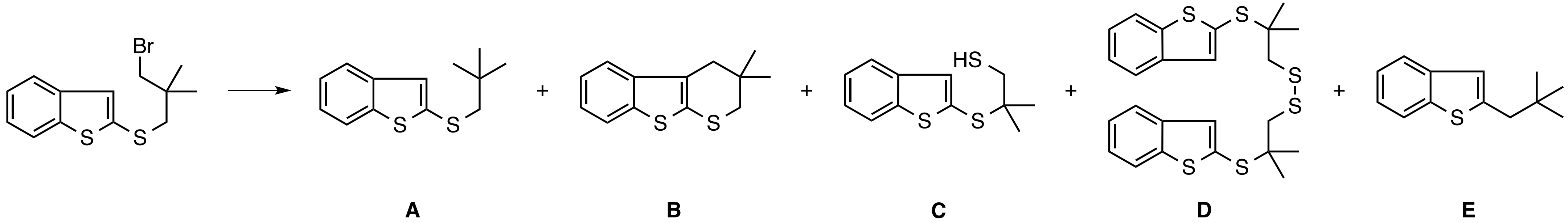


- Ortho addition of an alkyl radical to vinyl sulfides

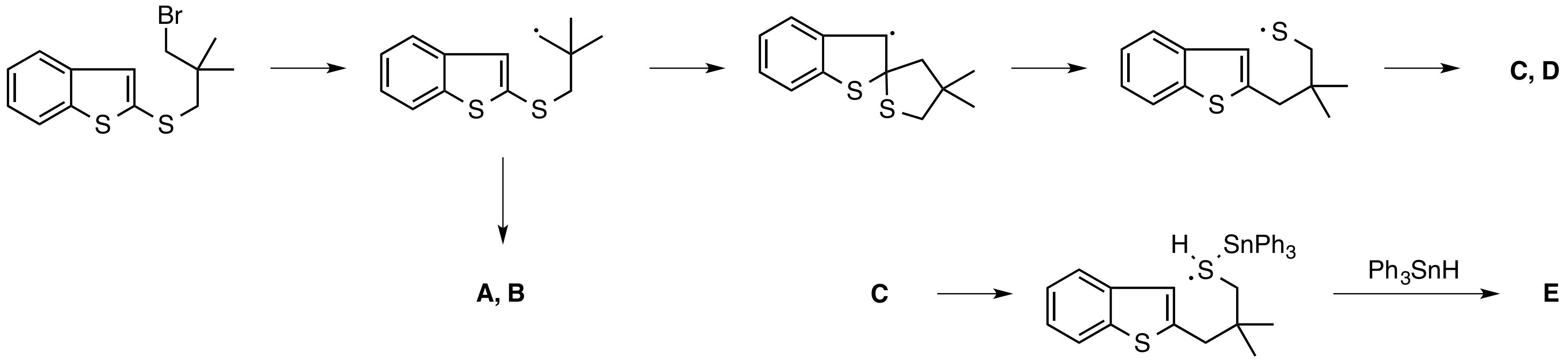


Tada, M. *Heteroatom Chem.* **2001**, *12*, 204.

Ortho vs. *Ipso* Free Radical Addition on Benzothiophene

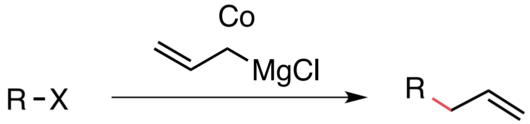


Conditions	*Total Yield (%)*	Product Composition (%)				
		A	**B**	**C**	**D**	**E**
Ph_3SnH - AIBN / 80°C	96	11	-	74	-	15
$Ph_3Sn[Co]L$ / 130°C	87	-	20	-	80	-



Tada, M.; Uetake, T.; Hanaoka, Y. *Chem. Commun* **1999**, 75.
Tada, M. *Heteroatom Chem.* **2001**, *12*, 204.

Oshima’s chemistry

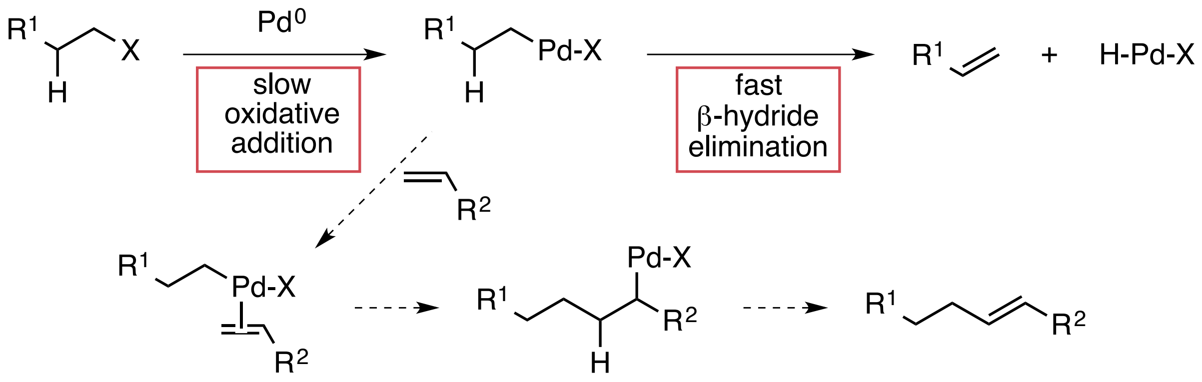


Koichiro Oshima

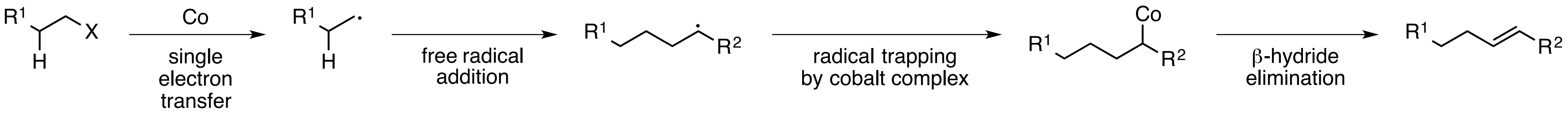
- > PhD under the supervision of Hitosi Nozaki at Kyoto University.
- > Postdoctoral Associate at the MIT during 2 years in the group of Barry Sharpless.
- > Now, Professor at the Graduate School of Engineering at Tokyo.
- > Research Area : deals with the manifold use of main group elements in organic synthesis.

Cobalt Catalyzed coupling reaction of Alkyl halides with Grignard Reagents

> Palladium-catalyzed Heck reaction

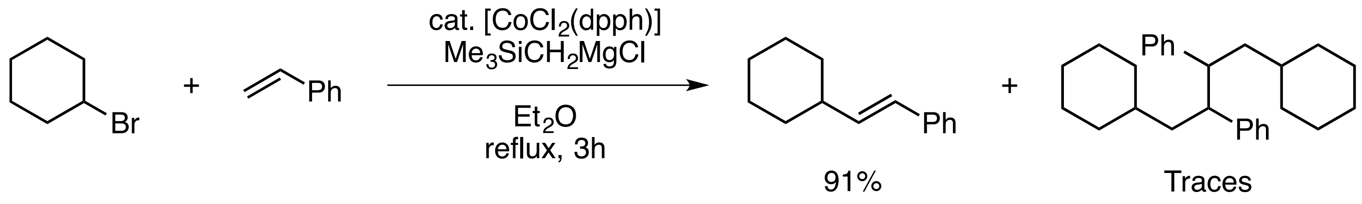


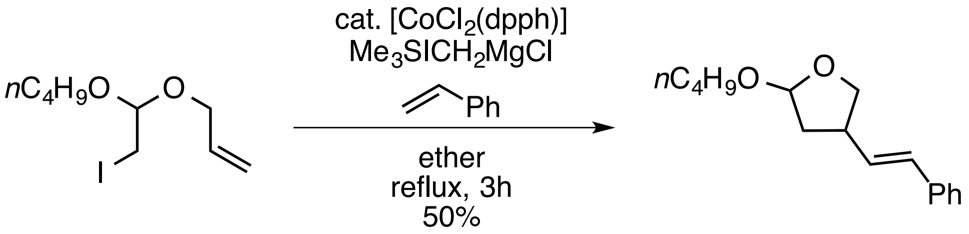
> Cobalt-catalyzed Heck transformation



Affo, W.; Ohmiya, H.; Fujioka, T.; Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K.; Imamura, Y.; Mizuta, T.; Miyoshi, K. *J. Am. Chem. Soc.* **2006**, *128*, 8068.
Tsuji, T.; Yorimitsu, H.; Oshima, K. *Angewandte Chemie International Edition* **2002**, *41*, 4137.

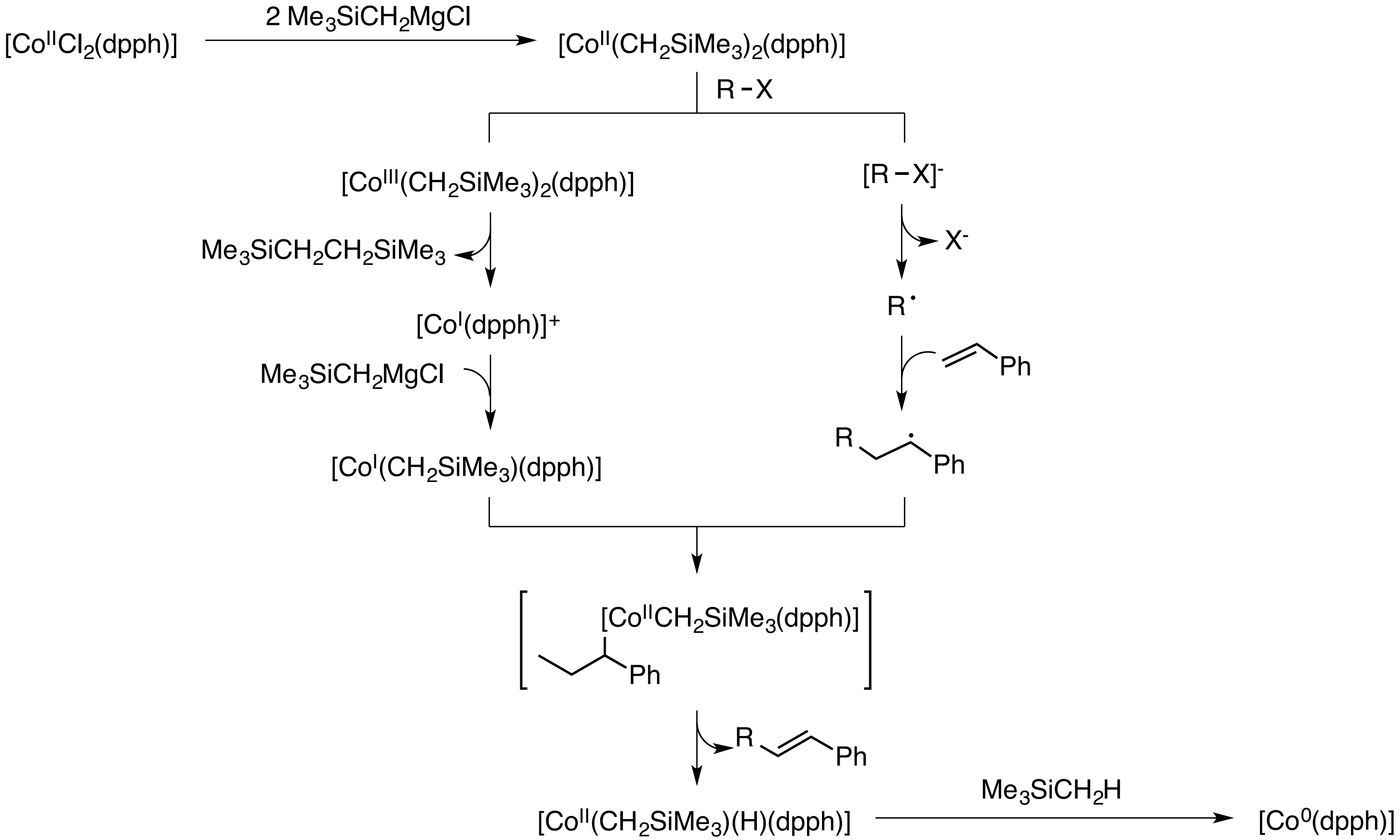
Cobalt Catalyzed coupling reaction of Alkyl halides with Grignard Reagents





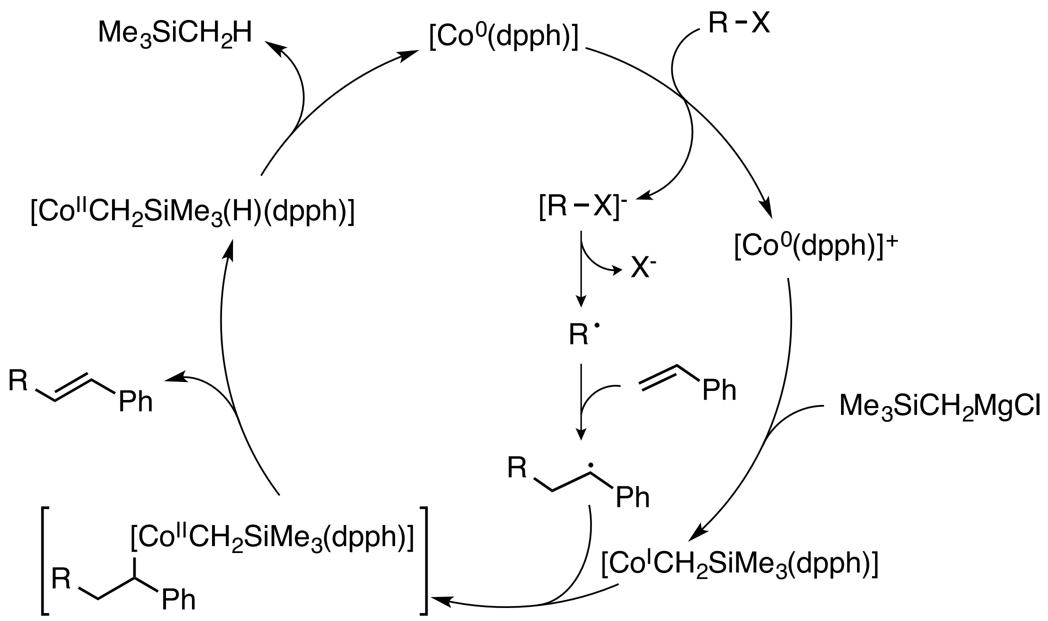
Affo, W.; Ohmiya, H.; Fujioka, T.; Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K.; Imamura, Y.; Mizuta, T.; Miyoshi, K. *J. Am. Chem. Soc.* **2006**, *128*, 8068.

Mecanism of the reaction : Initiation Step



Affo, W.; Ohmiya, H.; Fujioka, T.; Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K.; Imamura, Y.; Mizuta, T.; Miyoshi, K. *J. Am. Chem. Soc.* **2006**, *128*, 8068.

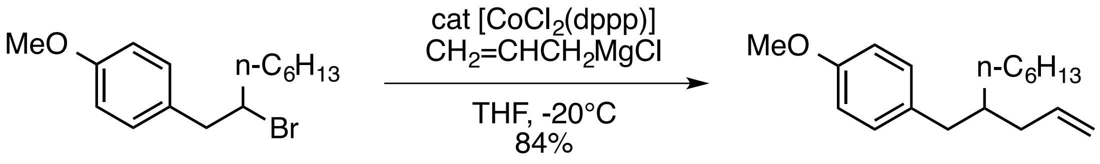
Mecanism of the reaction : Catalytic Cycle



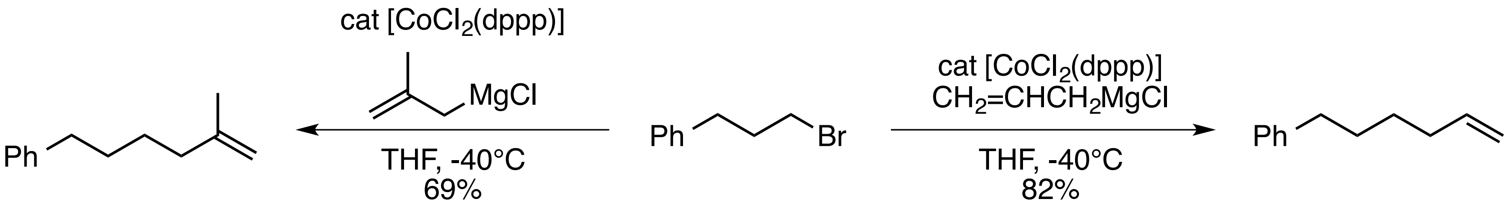
Affo, W.; Ohmiya, H.; Fujioka, T.; Ikeda, Y.; Nakamura, T.; Yorimitsu, H.; Oshima, K.; Imamura, Y.; Mizuta, T.; Miyoshi, K. *J. Am. Chem. Soc.* **2006**, *128,* 8068.

Cobalt-Catalyzed Coupling Reaction of Alkyl Halides with Allylic Grignard Reagents

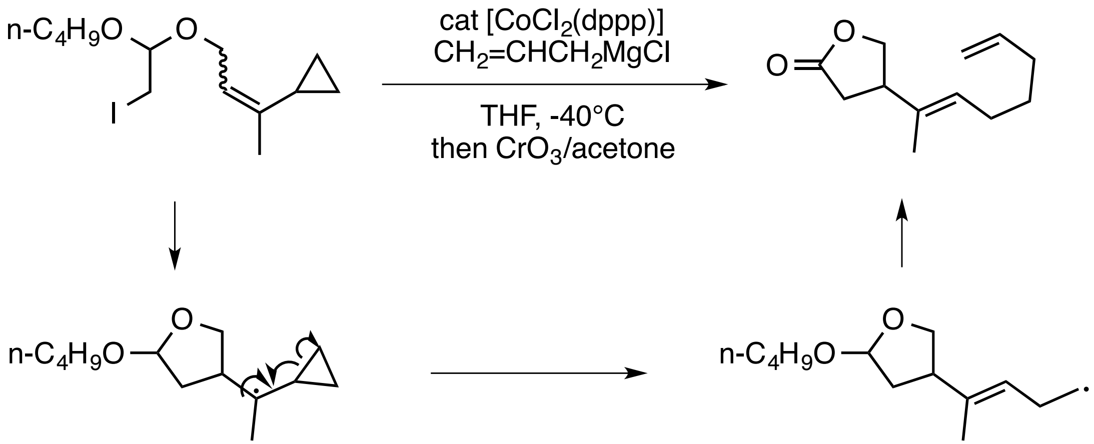
> Primary carbon



> Secondary carbon

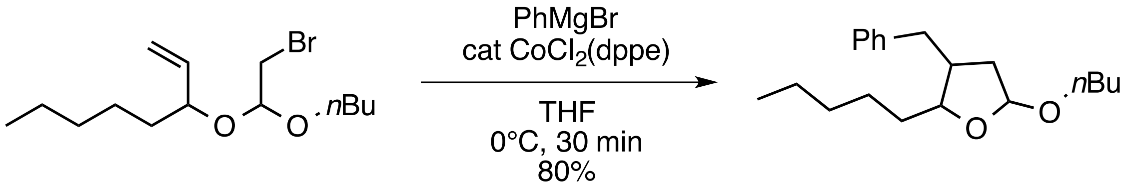


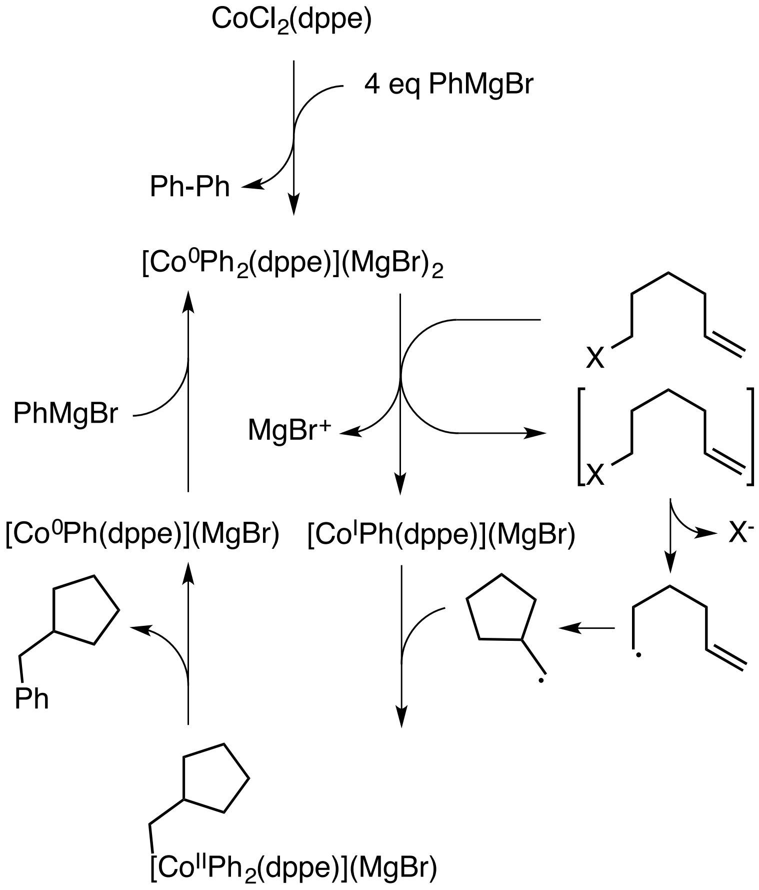
> Tandem cyclization/ cross-coupling reaction



Tsuji, T.; Yorimitsu, H.; Oshima, K. *Angewandte Chemie International Edition* **2002**, *41*, 4137.

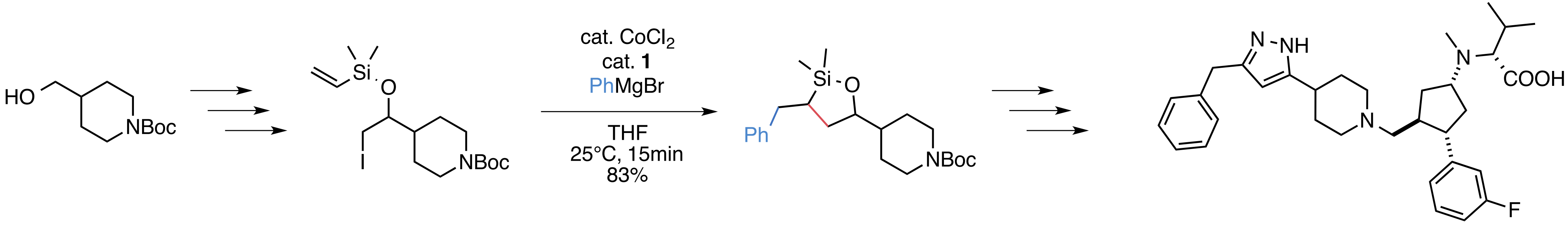
Cobalt-Catalyzed Tandem Radical Cyclization and Cross-Coupling Reaction





Fujioka, T.; Nakamura, T.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2002**, *4*, 2257.

Total Synthesis of an Antagonist of human CCR5 receptor

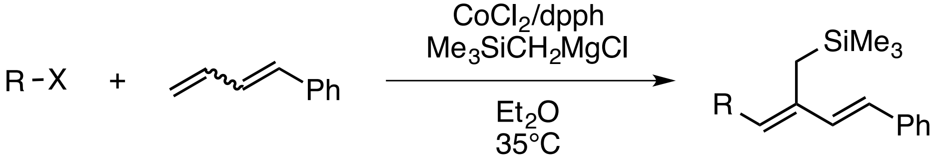


Antagonist of human CCR5 receptor

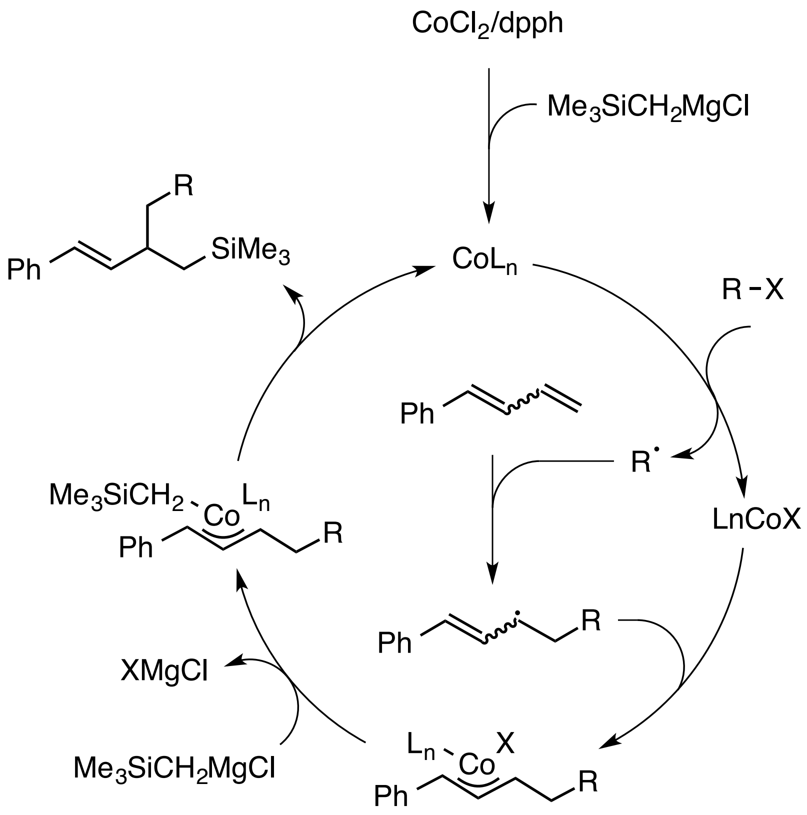
Someya, H.; Kondoh, A.; Sato, A.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Synlett* **2006**, 3061.

Cobalt-Catalyzed Three-Component Coupling Reaction

> Three-Component : Alkyl Halides / 1,3-Dienes / Trimethylsilylmethylmagnesium Chloride

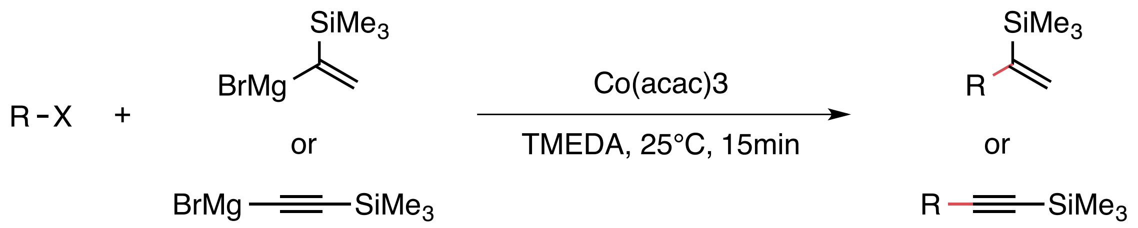


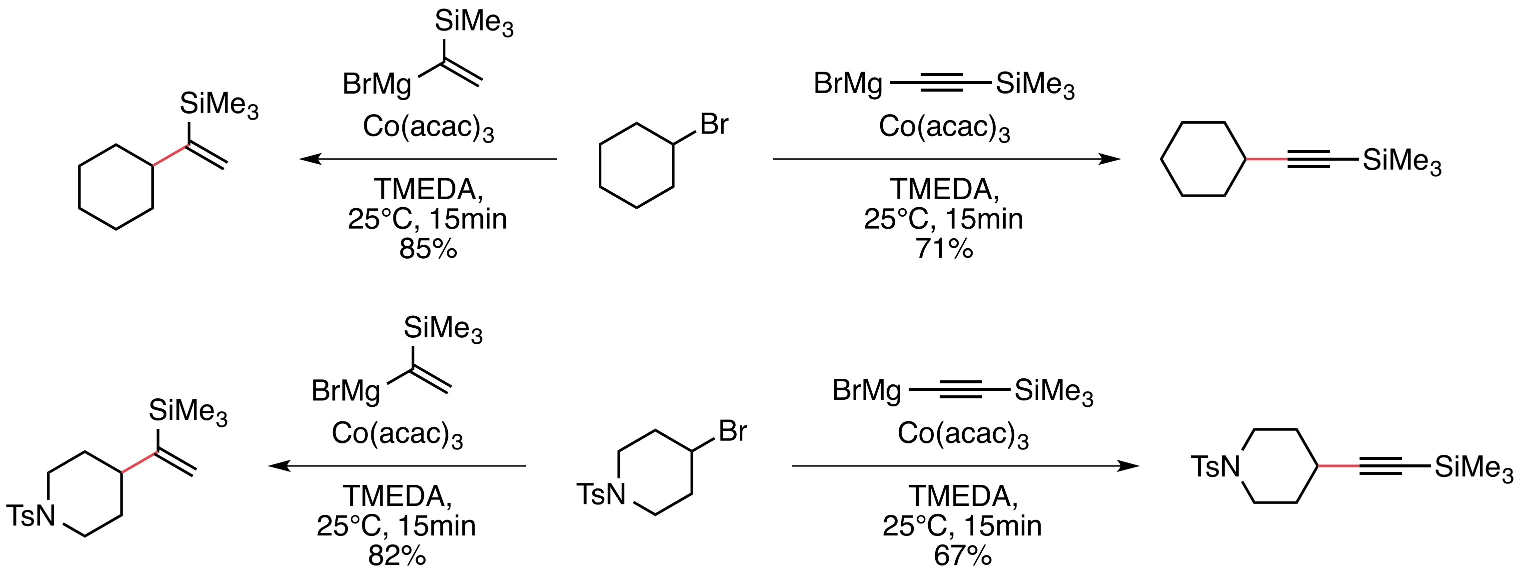
Entry	R-X	Reaction Time (h)	Yield (%)
1	n-$C_{19}H_{19}$Br	2	8400%
2	2-bromoooctane	0.5	87
3	1-bromoadamantane	0.5	93



Mizutani, K.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2003**, *5*, 3959.

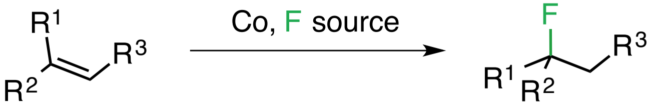
Cobalt-Mediated Cross-Coupling Reactions with Trimethylsilyl reagents



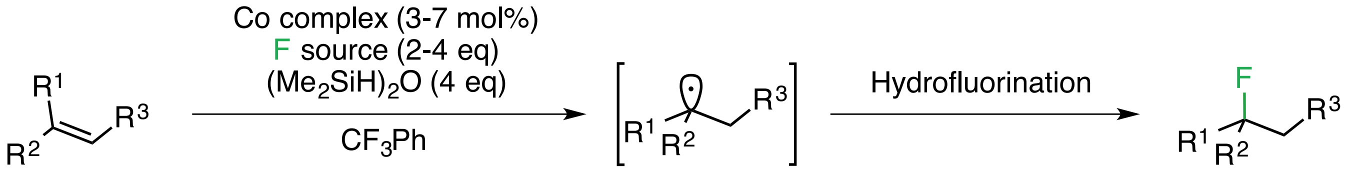


Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2006**, *8*, 3093.

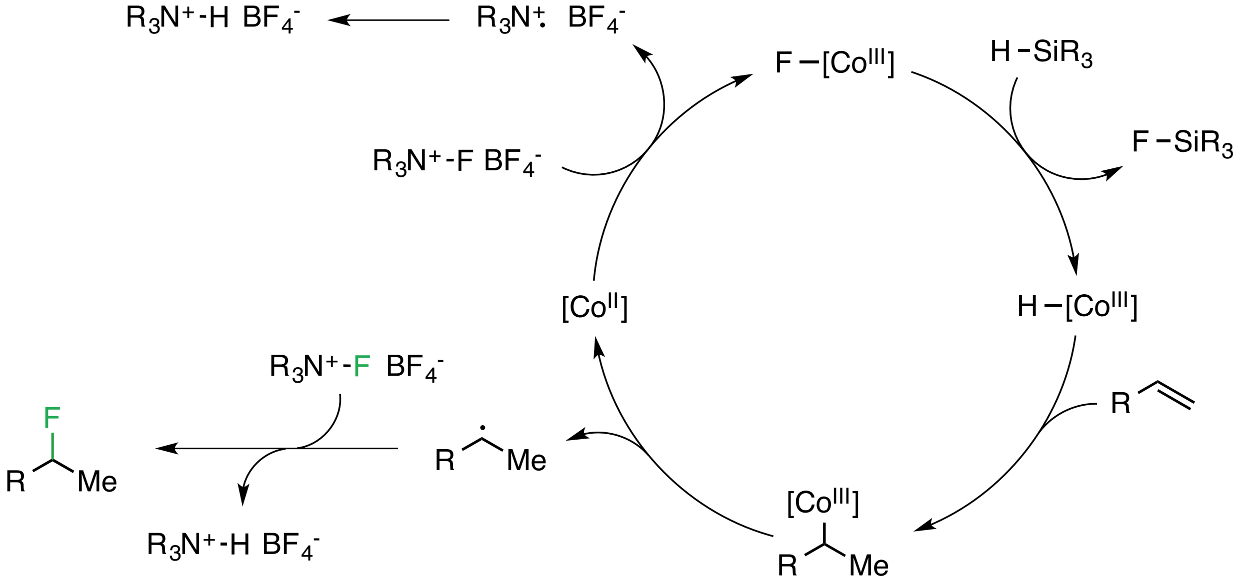
Hydroflurination of Unactivated Olefins

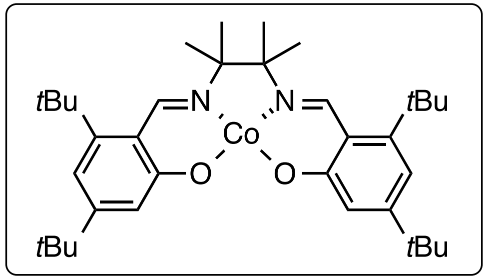


Cobalt-Catalyzed Hydroflurination of Unactivated Olefins



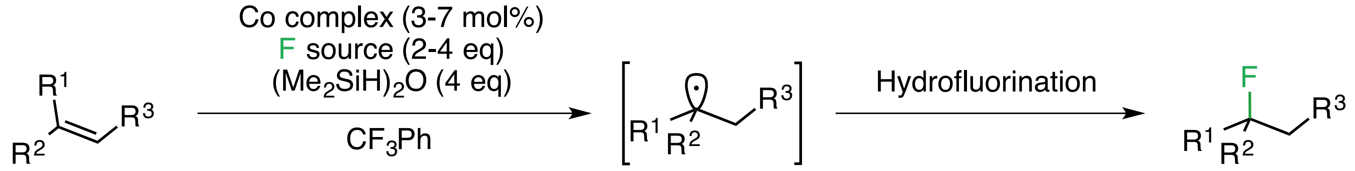
Catalytic / Mild / FG-tolerant / Scalable



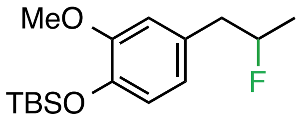


Shigehisa, H.; Nishi, E.; Fujisawa, M.; Hiroya, K. *Org. Lett.* **2013**, *15*, 5158.

Cobalt-Catalyzed Hydroflurination of Unactivated Olefins



Catalytic / Mild / FG-tolerant / Scalable



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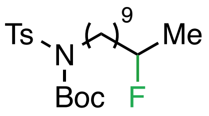

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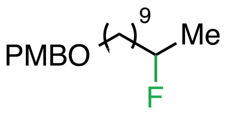

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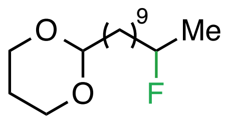
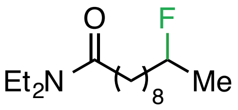


78%



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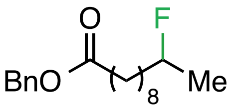
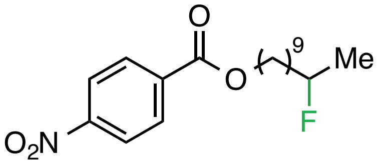
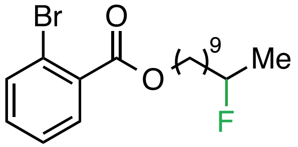


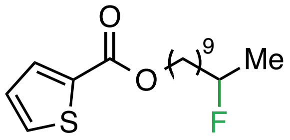
70%



63%



68%



77%

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

What I did not cover

- Andrey's Topic Review :
    - Hydration, Hydrohydrazination, Hydroazidation Reaction
    - Cyclopropanation
- Vitamin B_{12} Chemistry
- Cobalt Porphyrin Chemistry
- Polymerization

Brown, K. L. *Chem. Rev.* **2005**, *105*, 2075

Debuigne, A.; Jérôme, R.; Jérôme, C.; Detrembleur, C. *Cobalt-Mediated Radical Polymerization*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2006; pp 67–79.

Conclusion

> Considerable scope

> Using mild-conditions / compatible with many functionnal groups

> Efficient in cascade and cross coupling reaction

> Efficient hydrofluorination

> No real results yet in asymetric synthesis

Thank you for your attention