

Metalloradicals

Paramagnetic Catalysis

John Thompson
Dong Group Seminar

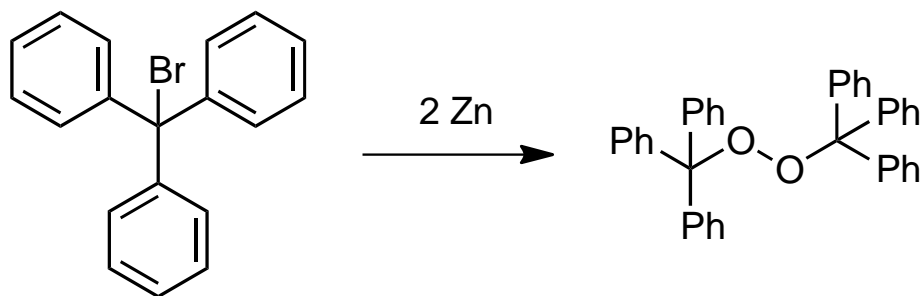
September 12th, 2012

Overview

- I. Historical presence of radicals
- II. Metalloradical background
 - I. Generation
 - II. Defining Characteristics
 - III. Detection
- III. Use in Synthesis
 - I. Mn
 - II. Ru
 - III. Co
 - IV. Rh

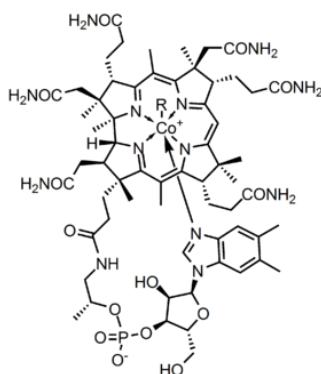
The First Radical

- 1789: Lavoisier used the term radical to explain single electron elements
- 1900: Gomberg isolated first organic free radical



The Radical Story

- 1933: Pfeiffer discovery of the metalloradical
 - Cobalt complex turned red to black through exposure to air



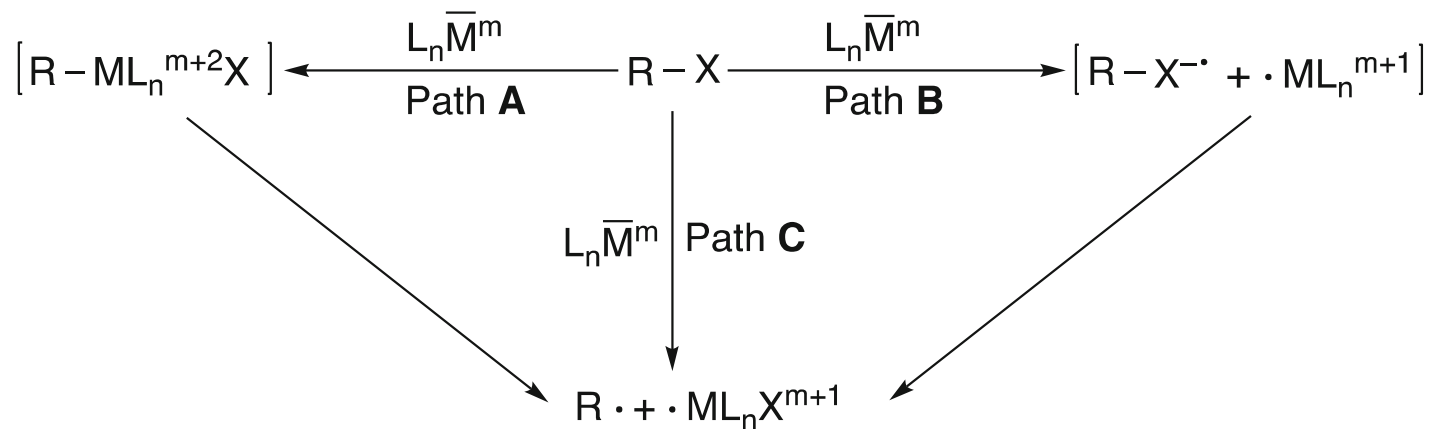
R = 5'-deoxyadenosyl, Me, OH, CN

- 1959: Classification and study of V(CO)₆ radicals

Kealy, T.; Pauson, P. *Nature*. **1951**, *168*, 1039.

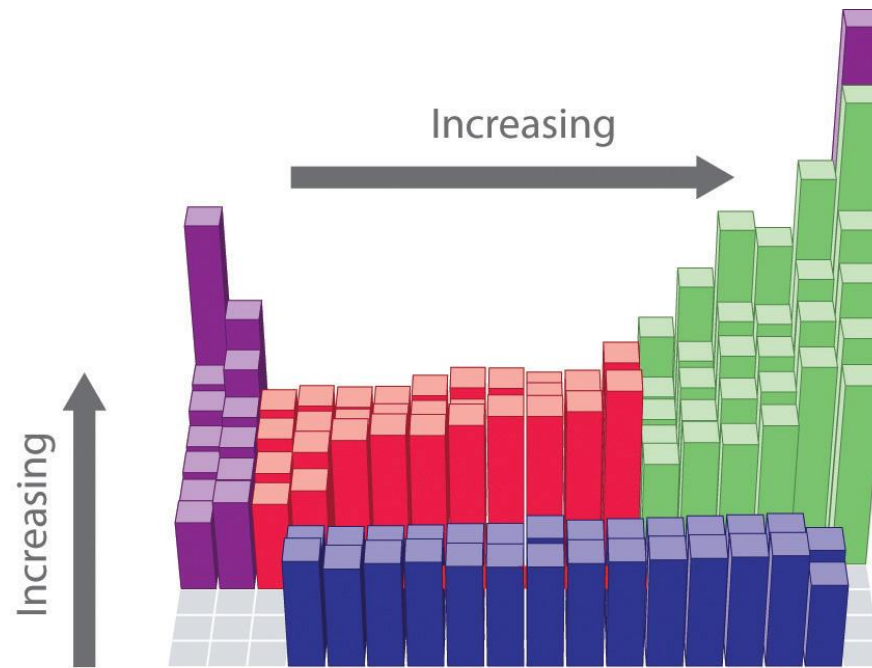
Ercoli, R.; Calderazzo, F.; Alberola, A. *JACS*, **1960**, *82*, 2966.

Transition Metal Reactions



Metal SET Potential

- First ionization potential (electron affinity)

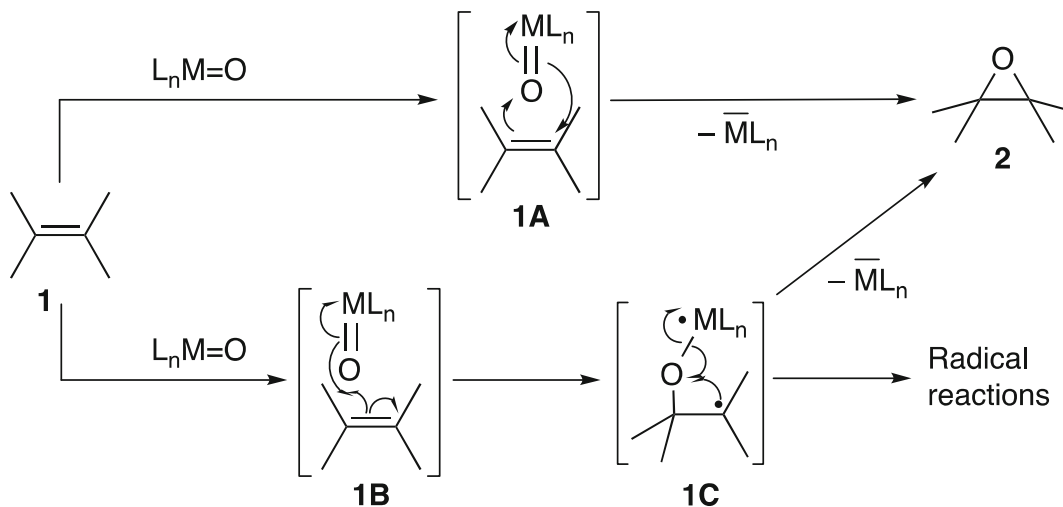


First ionization energy (kJ/mol)

■ s block ■ p block ■ d block ■ f block

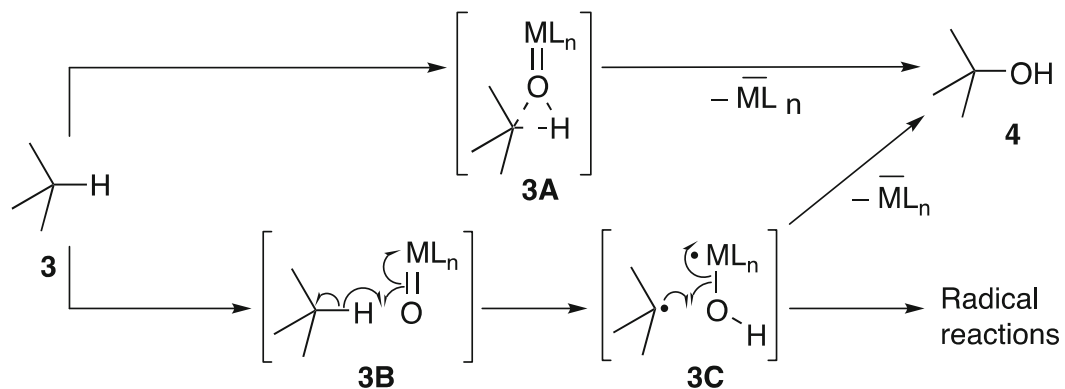
Radical Generation

- Oxidative: High Valent Oxo Compounds

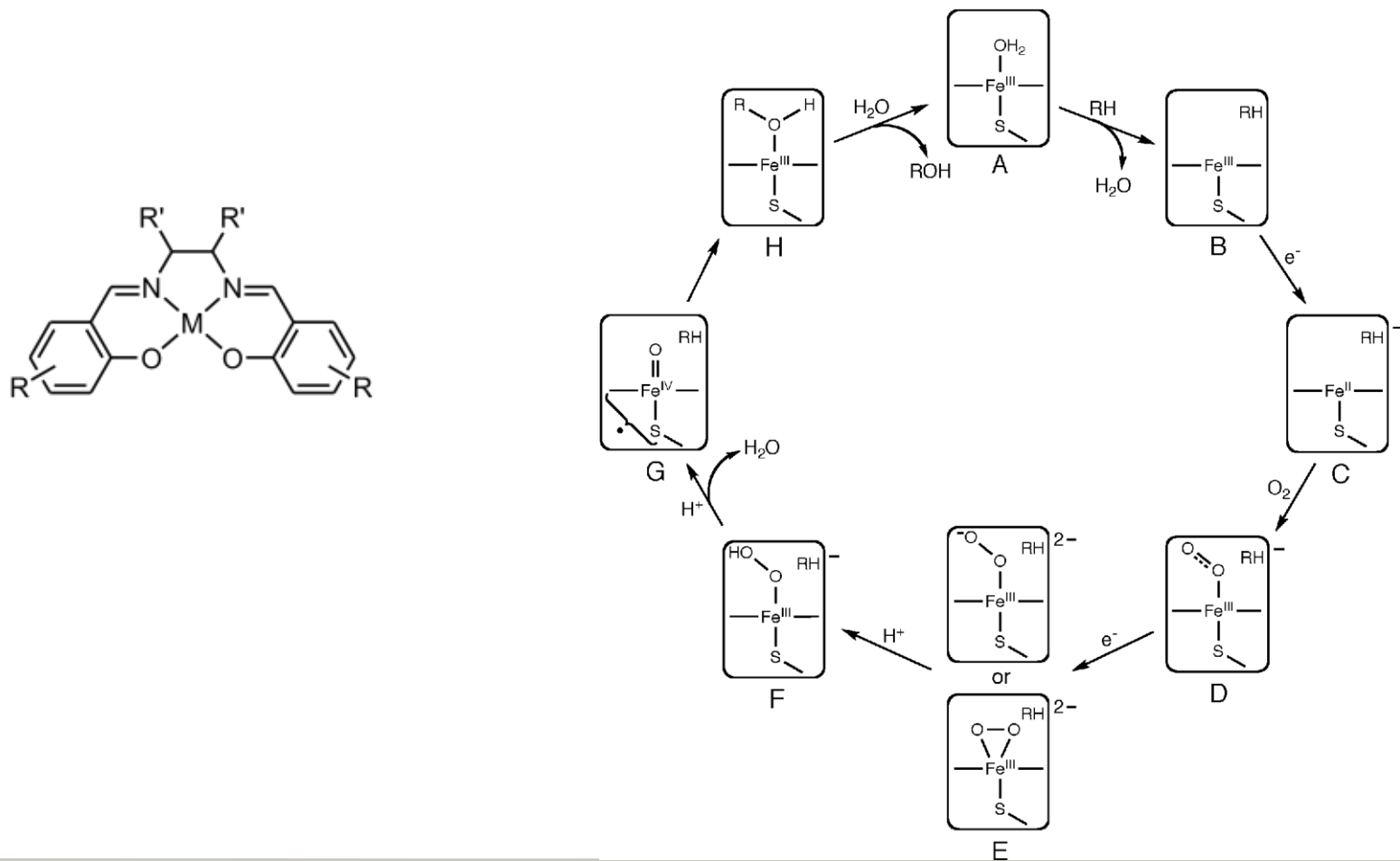


Radical Generation

- Oxidative: High Valent Oxo Compounds

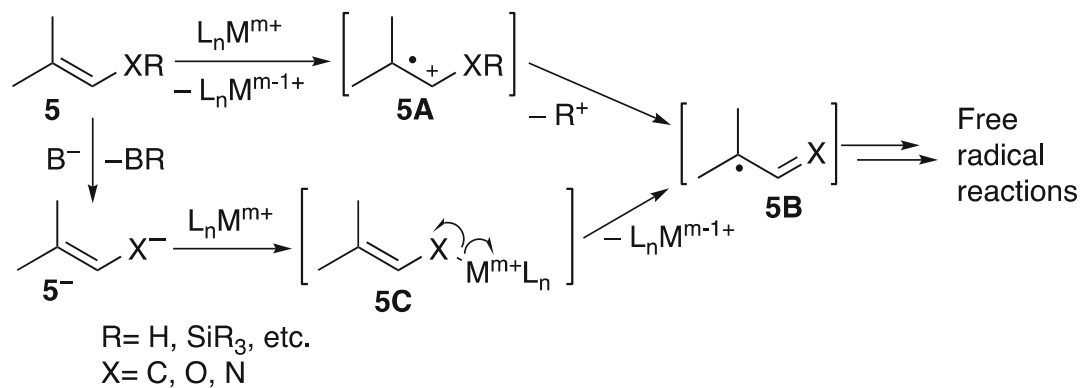


P-450 Cycle



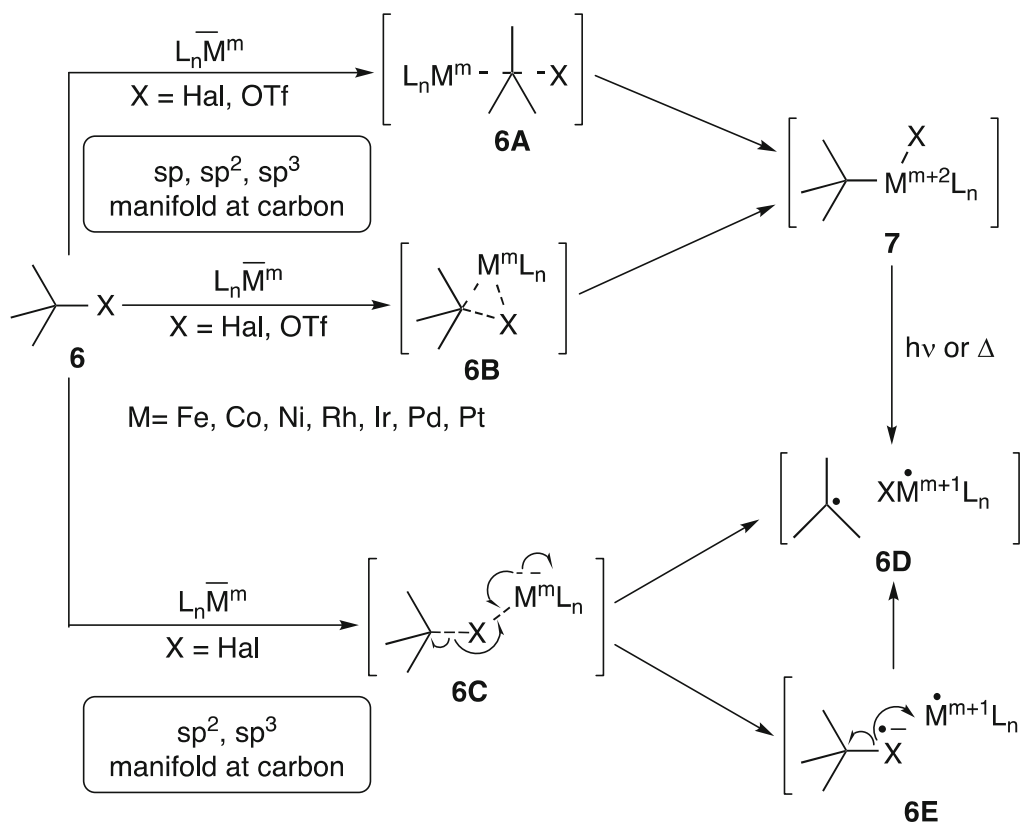
Radical Generation

- Oxidative: Metal Salts or Mn/Fe/Cu/Ag Complexes



Radical Generation

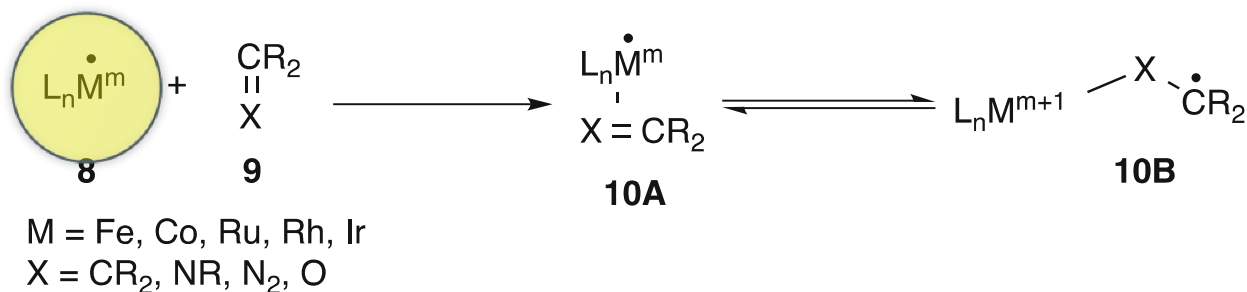
- Reductive:



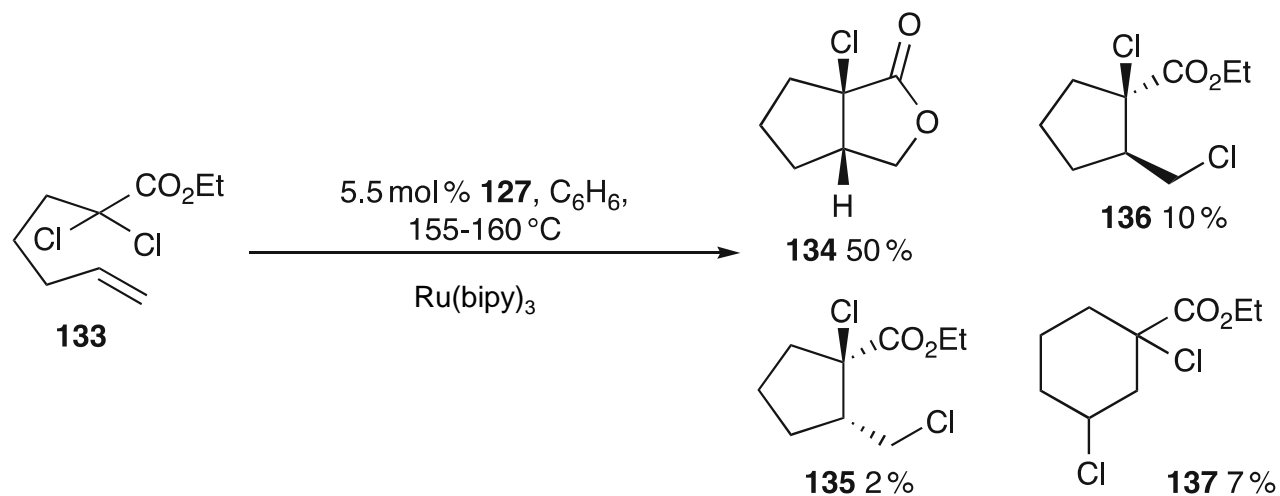
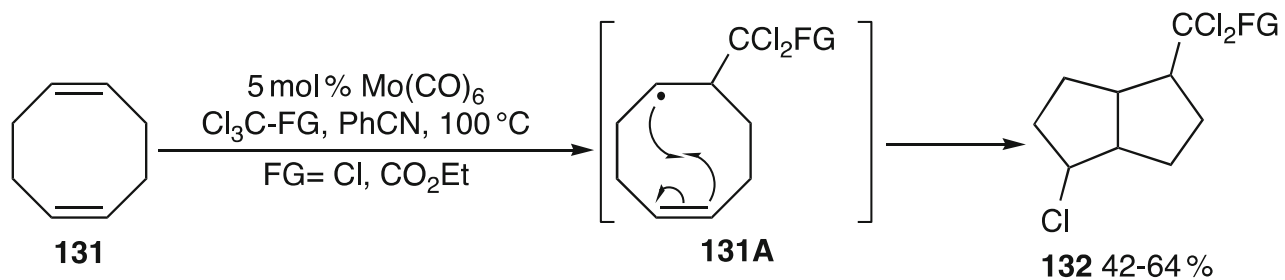
SET:
 Ti, Cr, Mn, Fe, Co,
 Ni, Cu, Ru, Rh,
 Pd, Ag. Or Pt

Radical Generation

- What about a persistent radical?



Example of Metal Initiation



The Metalloradical

- Paramagnetic compounds can transfer electrons to substrates or ligands
 - Redox Noninnocent Ligands: high or low-metal oxidation states allows ligand orbitals to increase and get oxidized
 - Chemically Noninnocent Ligands: ligands play active role in reaction
 - Innocent Radical Ligands: Excludes nitrosyl groups and large extended pi systems (such as fullerenes)
- Paramagnetic radicals have long lifetimes and react often in low concentrations

Detecting Metal Radicals

- Mechanisms are often speculative
- EPR (Electron paramagnetic Resonance)

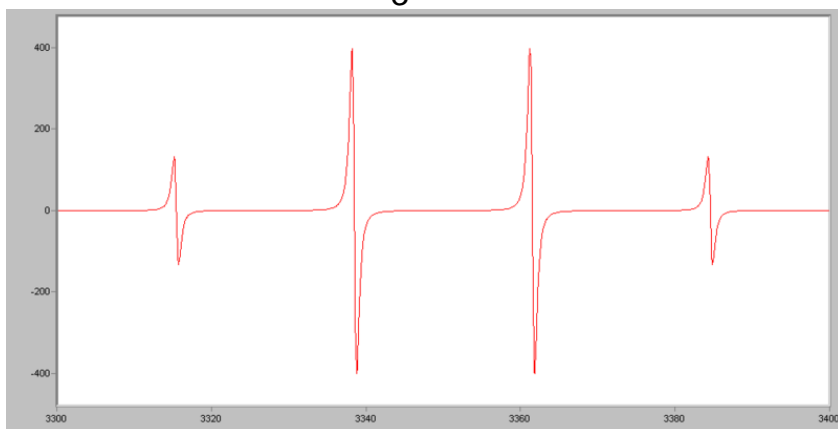
EPR Spectra

- Electron Paramagnetic Resonance (EPR)
- Definitive for resolving location of unpaired electron
- Frequently use frozen solutions
- Relies on microwave radiation to induce resonance of electron spins in a magnetic field
- Free electron in nondegenerate orbital with no mixing with excited states only contributes to its angular momentum, which allows it to be distinguished by EPR
- Metal radicals SOMO mix with empty d orbitals

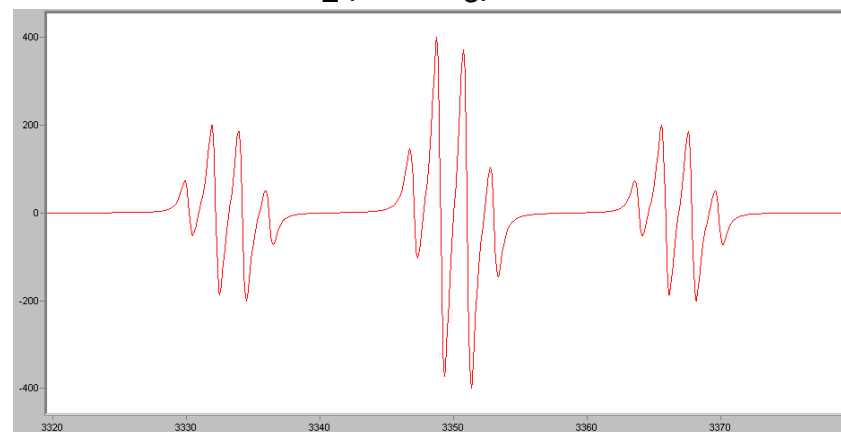
Detecting Metal Radicals

- Mechanisms are often speculative
- EPR (Electron paramagnetic Resonance)

CH₃ radical



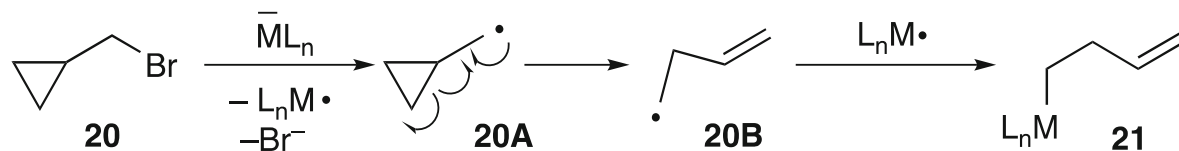
CH₂(OCH₃) radical



Detecting Metal Radicals

- Mechanisms are often speculative
- EPR (Electron paramagnetic Resonance)
- Metal oxidation state changes (color)
- Paramagnetic metal centers
- Radical traps (ex: TEMPO)

- Probes



Key Characteristics

- Generation: through thermal, photochemical, or electrochemical cleavage of metal-metal bonds
 - M-M bonds BDE?
- Stability: normally exist as dimer or with labile ligand, inert atmosphere (not always required), non reactive solvent
- High Reactivity: low activation barriers
 - Mo radical has only 1.2 kcal/mol barrier to H-abstraction

BDE – Quiz!!!!

(will not be graded)

Bond

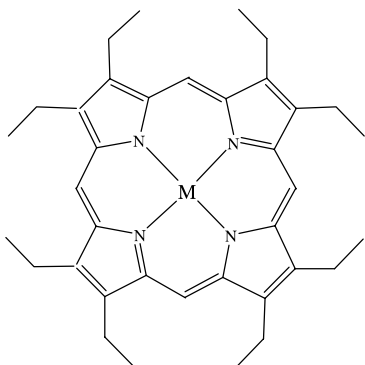
BDE (kcal/mol)

Ph-I

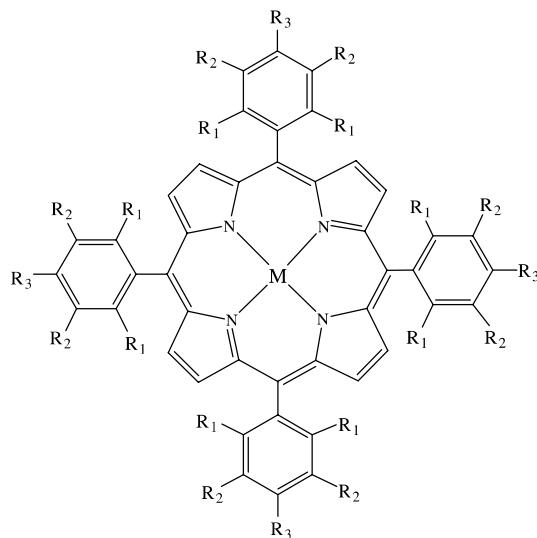
M(CO)_x Radicals Analysis

- V(CO)₆: thermally stable to dimerization, isolable, and 17 e⁻
 - Electron delocalized through CO π network
- Studied radicals of V, Mn, Re, Rh, Os, Co, Cr, W, Fe, and Ru
 - 17 e⁻ metals go through associative and dissociative reactions faster than 18 e⁻ counterparts through possible 19 e⁻ complexes
 - The heavier the metal, the faster the radical reactivity
 - Phosphines:
 - Added electron density on metal increases reactivity
 - Steric bulk hinders

Stabilizing the Rh/Co Radical



(OEP)M



(TPP)*M

(TPP)M: $R_1=R_2=R_3=H$;

(TXP)M: $R_1=R_3=H$, $R_2=CH_3$;

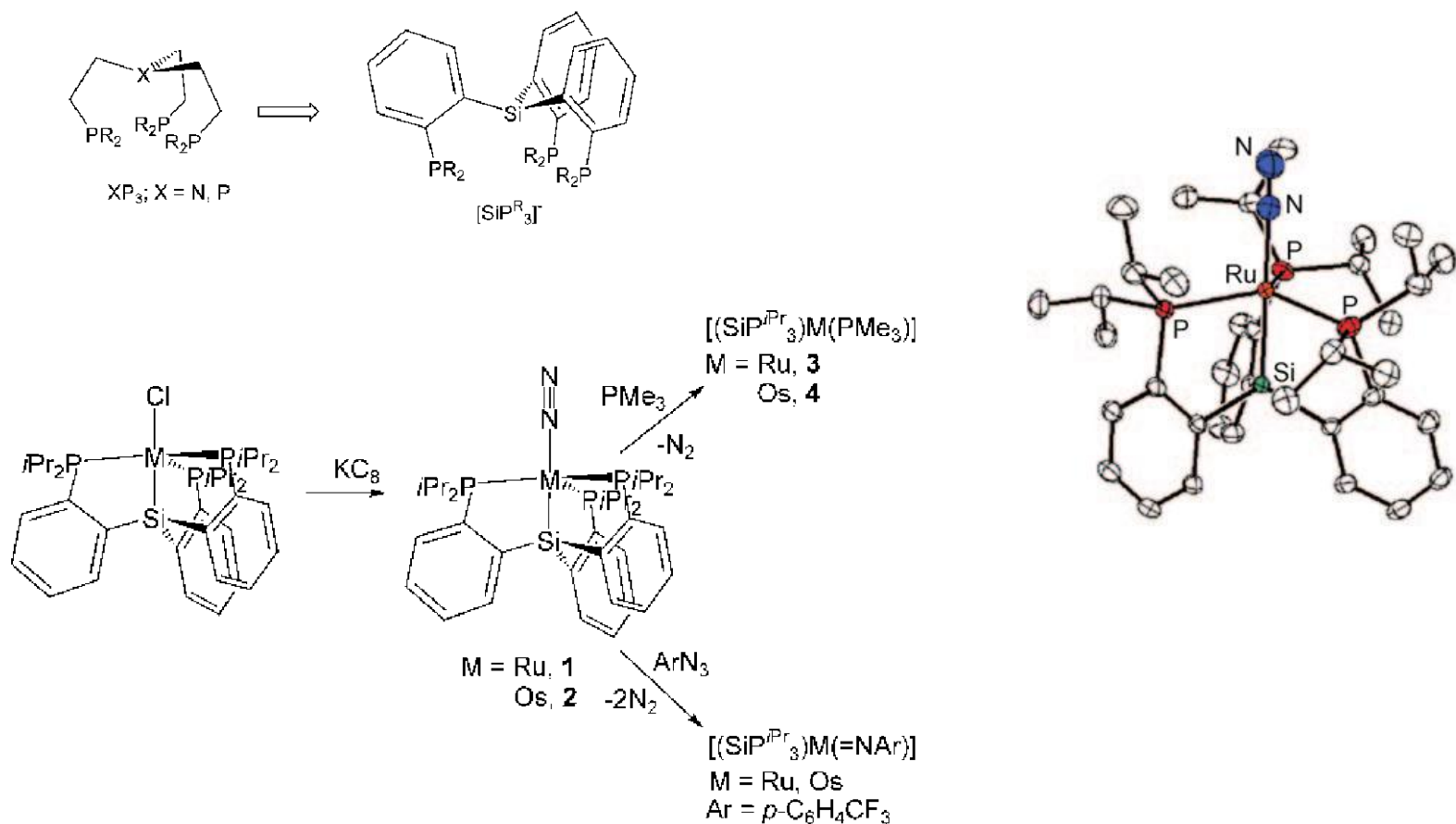
(TMP)M: $R_1=R_3=CH_3$, $R_2=H$;

(TTEPP)M: $R_1=R_3=CH_2CH_3$; $R_2=H$;

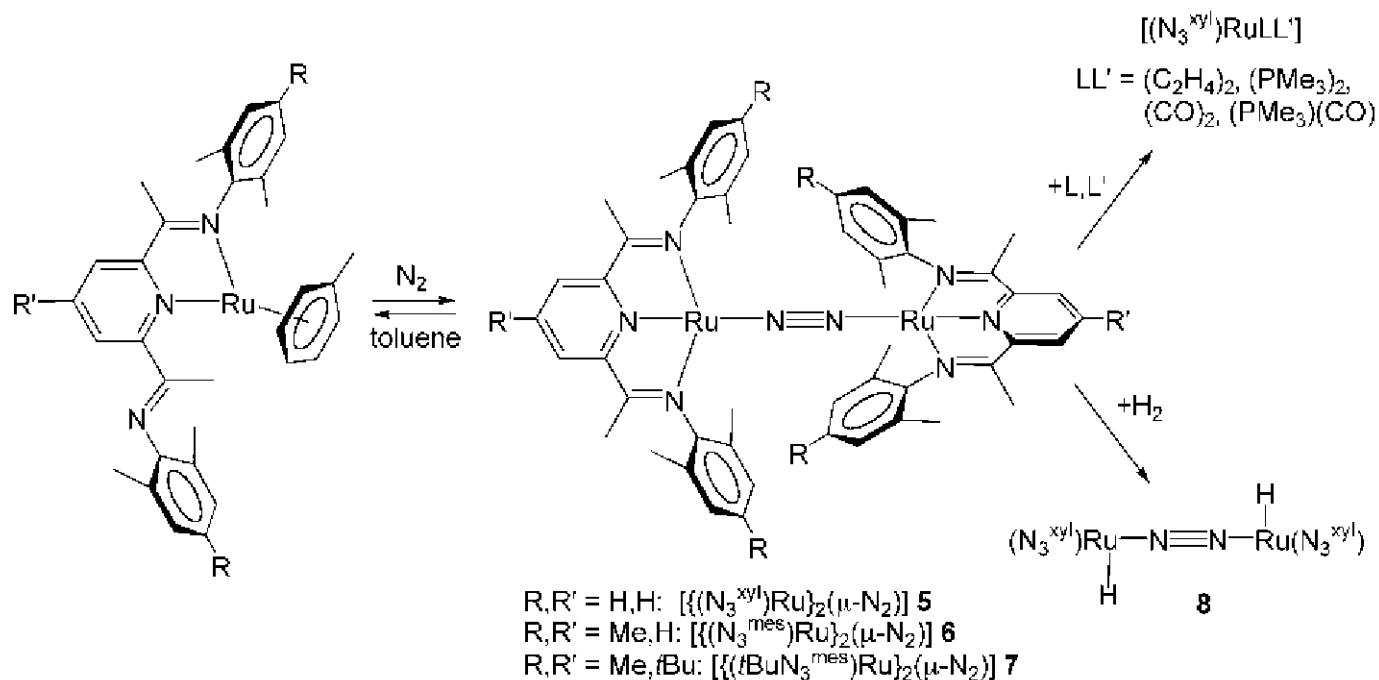
(TTiPP)M: $R_1=R_3=i-Pr$; $R_2=H$;

M = Co, Rh, Ir

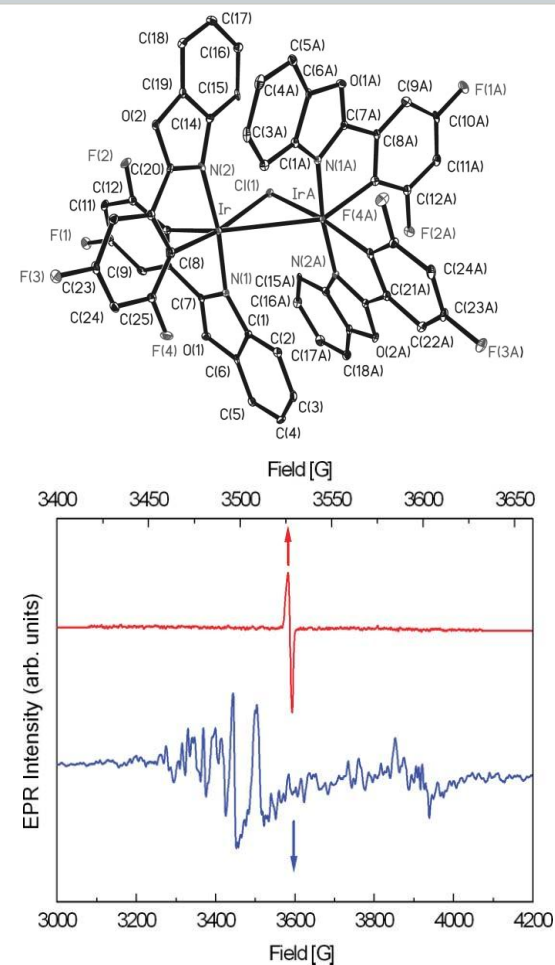
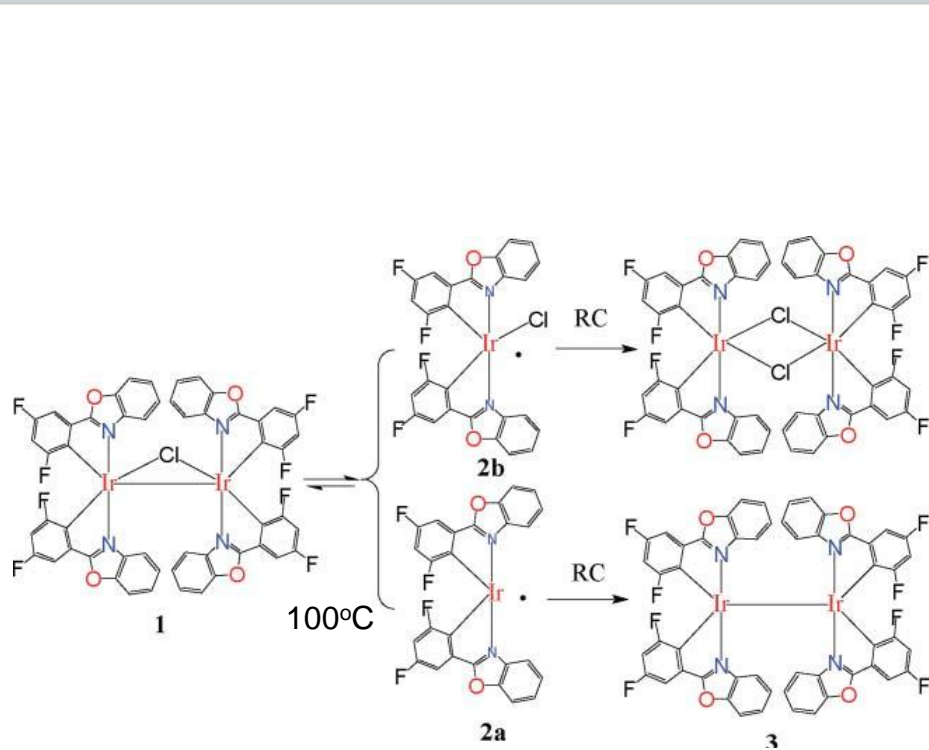
Stabilizing the Ru/Os Radical



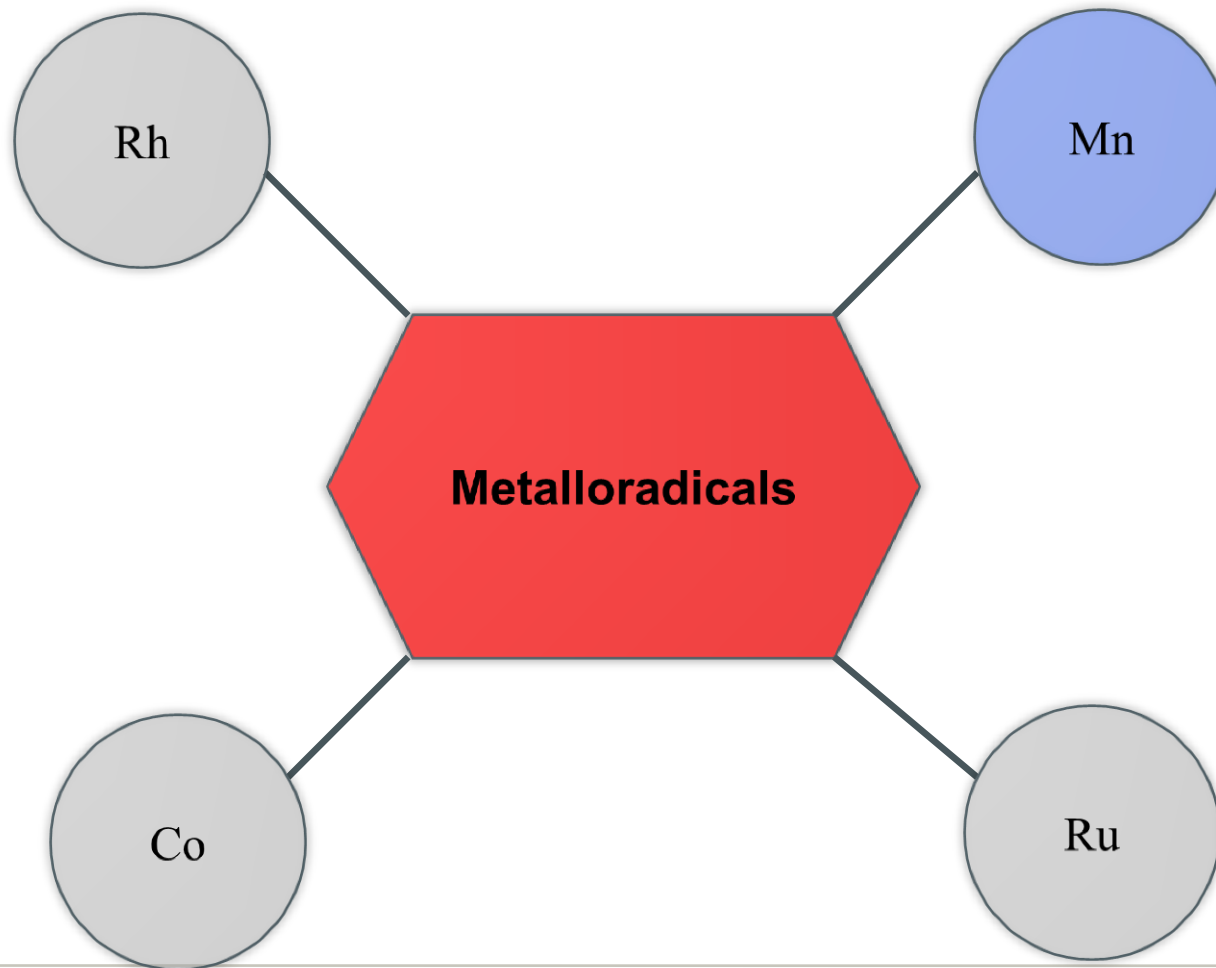
Stabilizing the Ru Radical



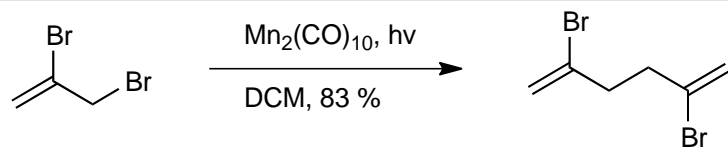
Stabilizing the Radical



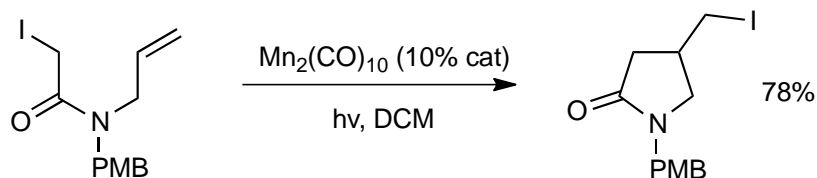
Use in Synthesis



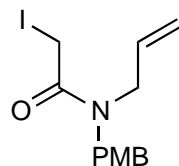
Radical Mn Cyclizations



Xe 300W lamp

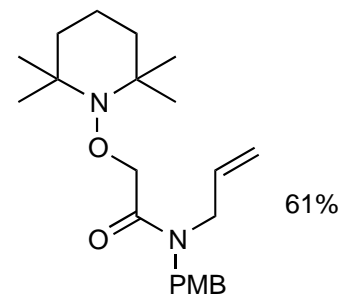


50% Mn had no effect
rt



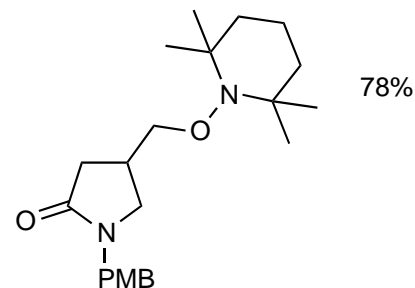
$\text{Mn}_2(\text{CO})_{10}$ (10% cat)

$h\nu$, DCM
TEMPO 1.1 eq

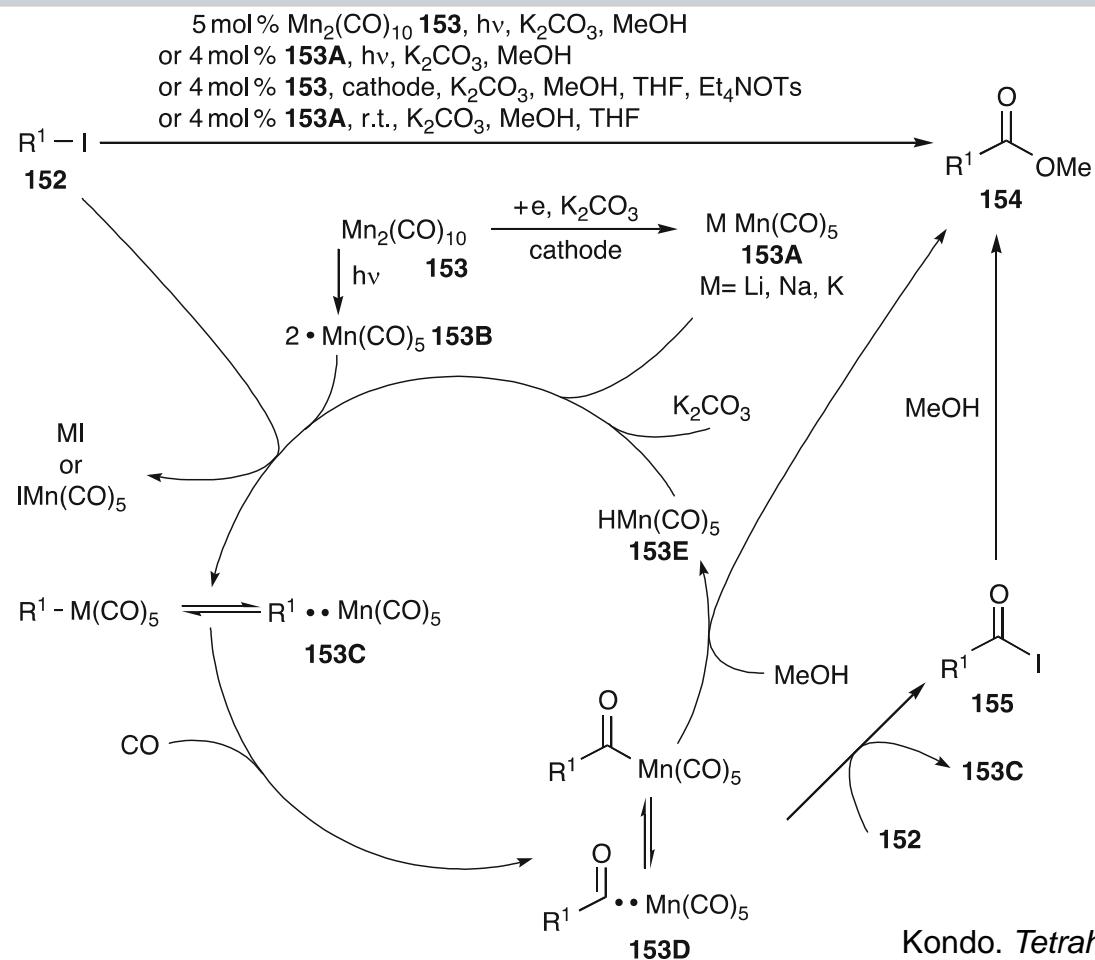


$\text{Mn}_2(\text{CO})_{10}$ (10% cat)

$h\nu$, DCM
TEMPO 1.1 eq



Manganese Radicals

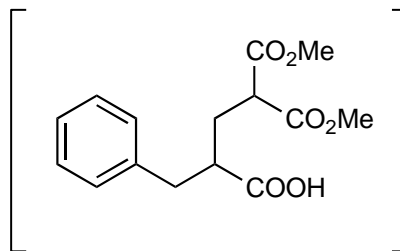
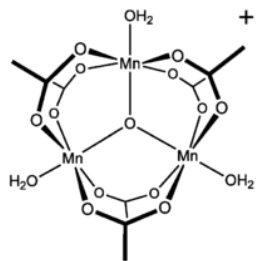
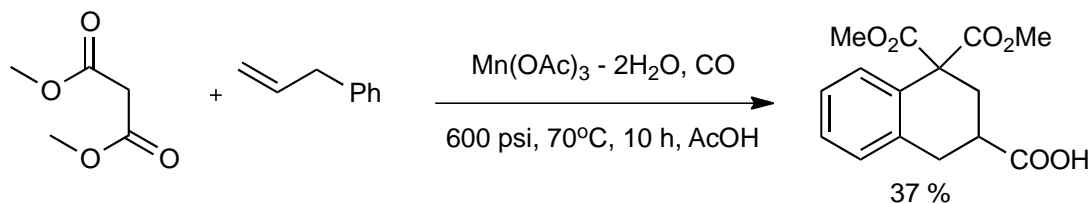
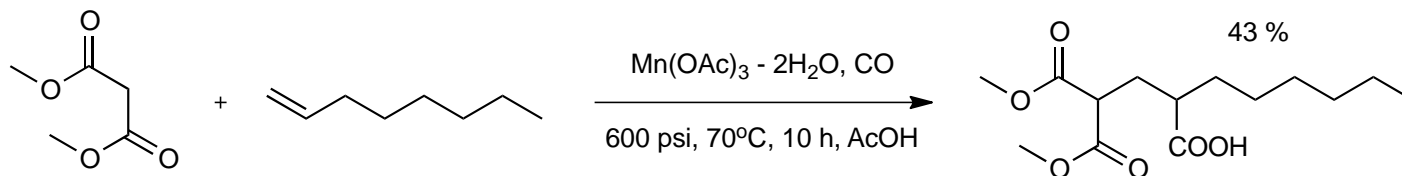
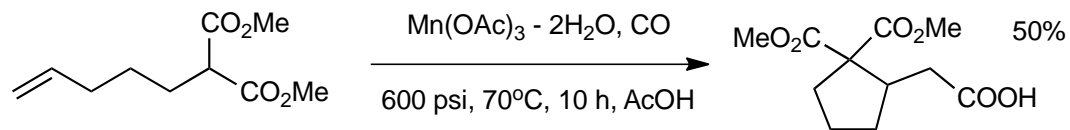


Kondo. *Tetrahedron Lett.* **1988**, 29, 3833.

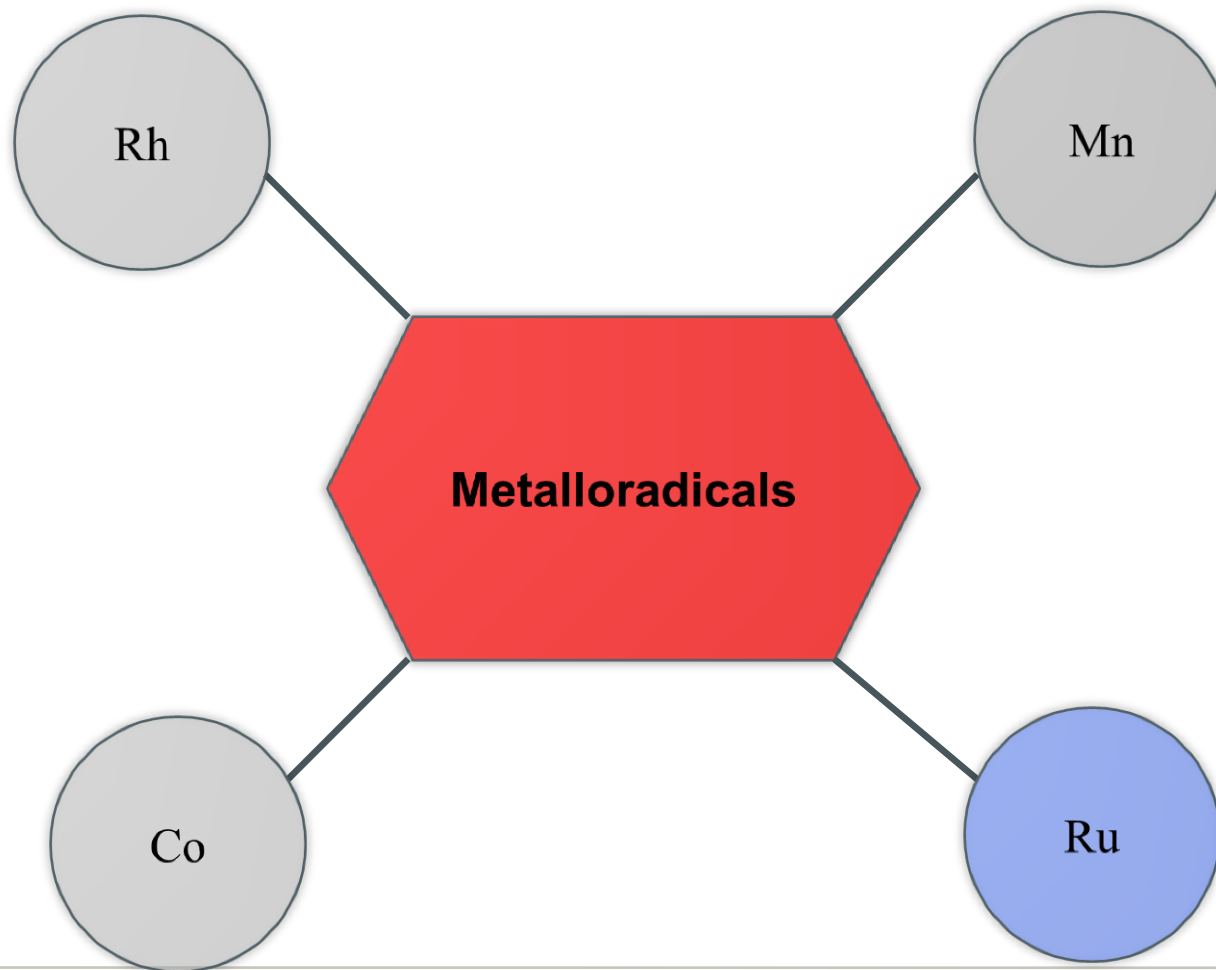
Ryu. *Org. Lett.* **2006**, 8, 1383.

Ryu. *Chem Soc. Rev.* **2001**, 30, 16.

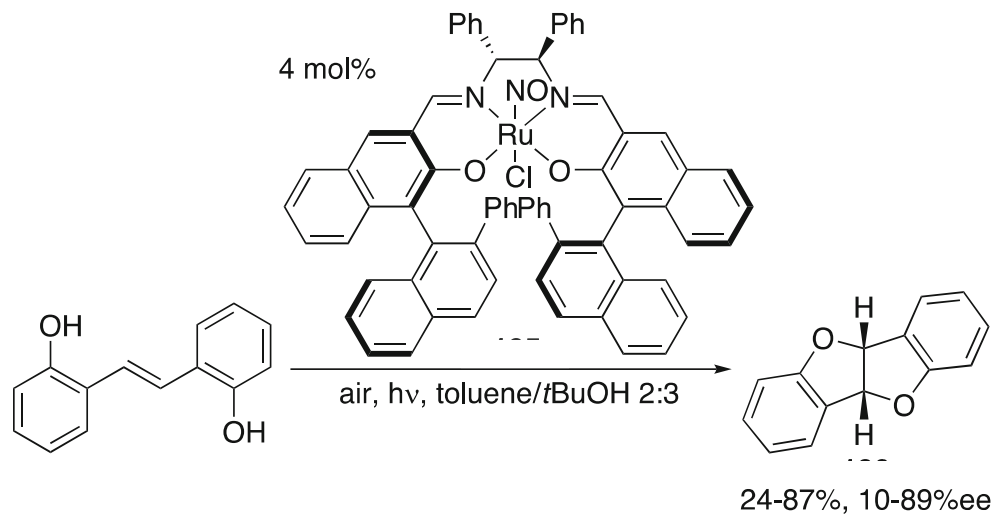
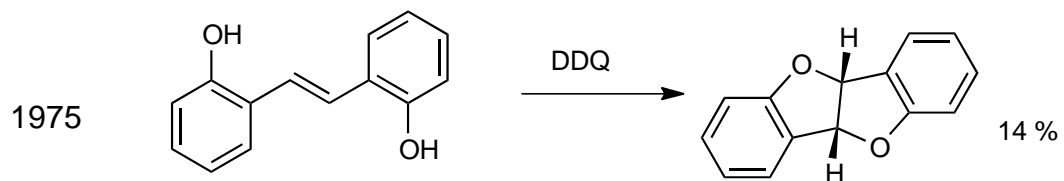
Radical Carbonylative Insertion



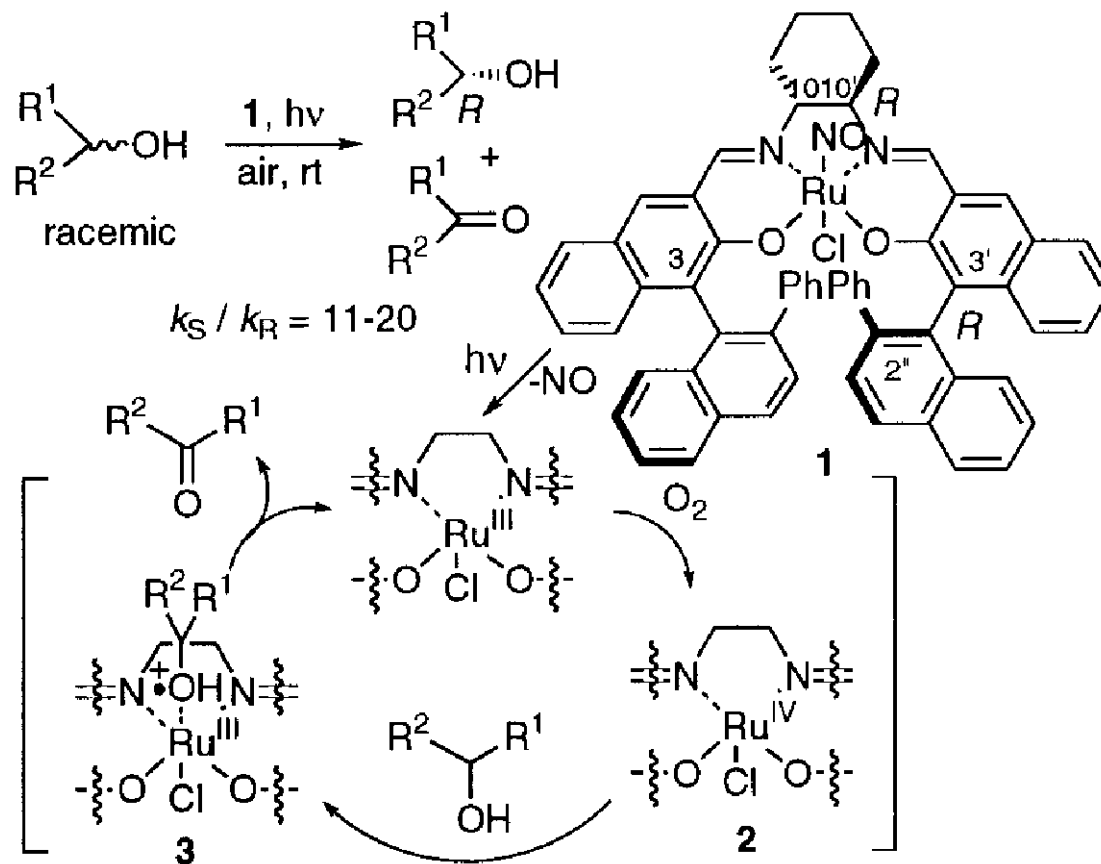
Use in Synthesis



Ru Asymmetric Reaction

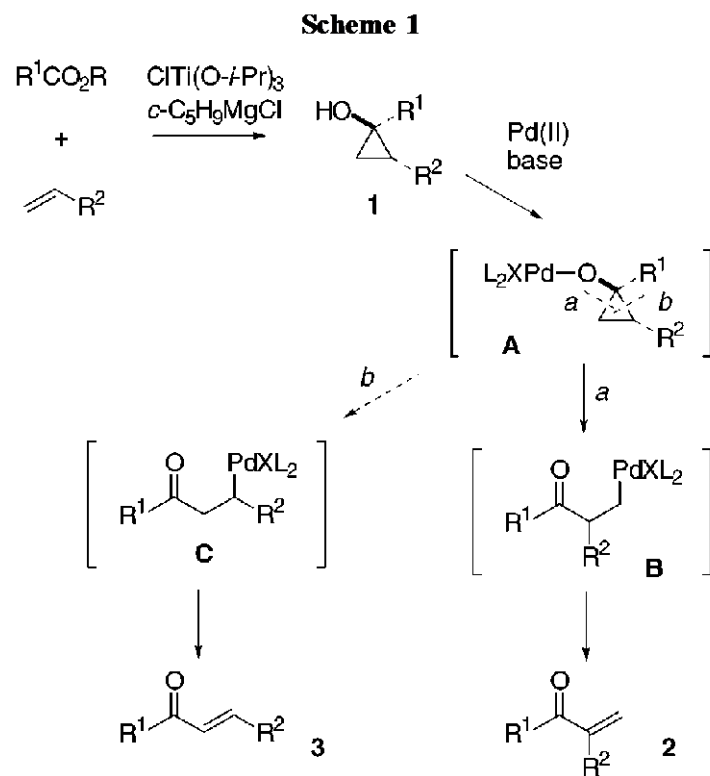


Ru Salen Mechanism

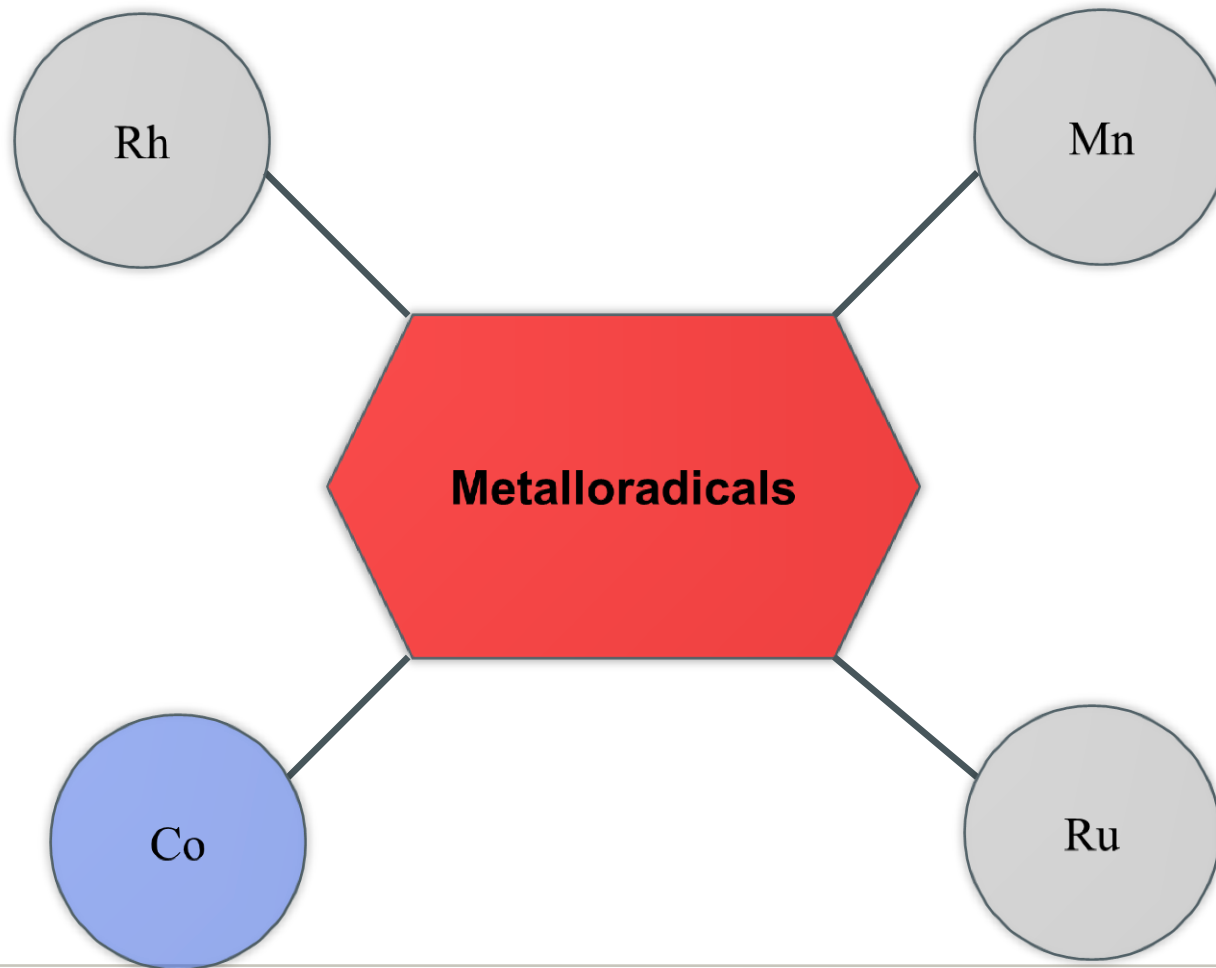


Scheme 1.

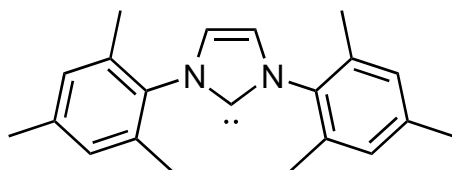
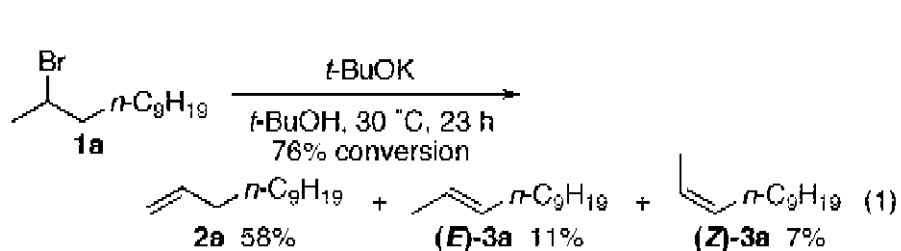
Oxidation of Cyclopropanol



Use in Synthesis



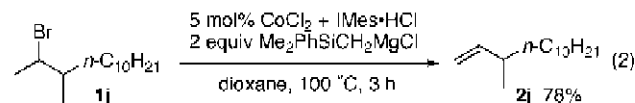
Regioselective Dehydrohalogenation with Co



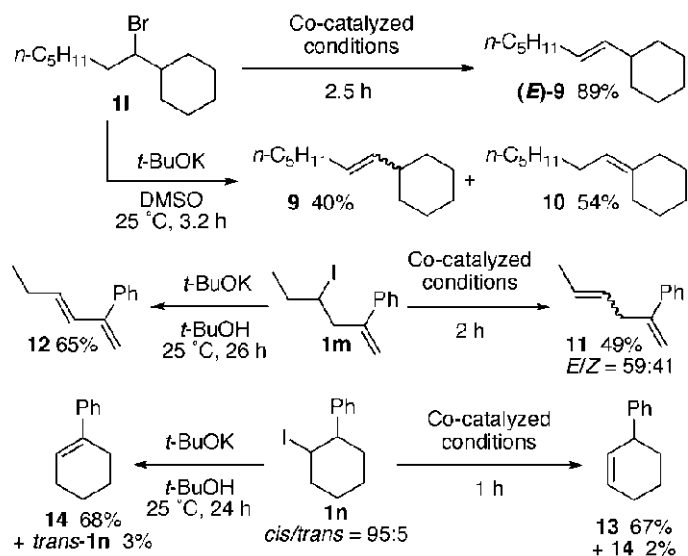
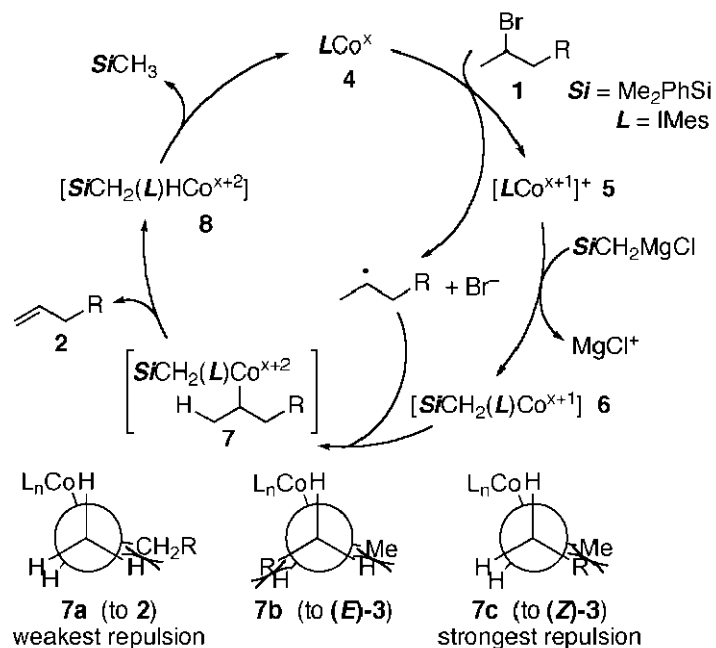
IMES

entry	R	1	time /h	2 /%
1	CH ₂ -1-naphthyl	1b	2	2b , 89
2	(CH ₂) ₈ OSi(<i>t</i> -Bu)Me ₂	1c	1.5	2c , 86 ^a
3	CH ₂ CH ₂ N(CH ₂ Ph)Ts	1d	2	2d , 79
4	CH ₂ CH ₂ OC ₆ H ₄ - <i>p</i> -Cl	1e	1.2	2e , 99
5	CH ₂ OC(d O)Ph	1f	3.4	2f , 81
6	CH ₂ OC(d O)C ₆ H ₄ - <i>p</i> -CF ₃	1g	1.8	2g , 70
7	CH ₂ OC(d O)(2-thienyl)	1h	3	2h , 80
8	CH(<i>n</i> -C ₅ H ₁₁) ₂	1i	1.2	2i , 80

^a (*E*)-CH₃CH(CH₂)₈OSi(*t*-Bu)Me₂ [*E*]-**3c**] was obtained in 4% yield.



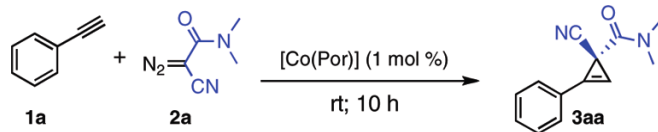
Regioselective Dehydrohalogenation with Co



^a Co-catalyzed conditions: 5 mol% CoCl_2 , 5 mol% IMes HCl , 2 equiv of $\text{Me}_2\text{PhSiCH}_2\text{MgCl}$, dioxane, 25 °C

Cobalt Radicals

Table 1. Reaction Conditions for Cyclopropanation of Phenylacetylene with α -Cyano(*N,N*-dimethyl)diazoacetamide by Cobalt(II) Porphyrins^a



entry	[Co(Por)] ^b	solvent	yield (%) ^c	ee (%) ^d
1	[Co(TPP)]	PhCF ₃	<5	—
2	[Co(P1)]	PhCF ₃	10	71
3	[Co(P2)]	PhCF ₃	95	82
4	[Co(P2)]	PhCl	40	nd ^e
5	[Co(P2)]	PhF	38	nd ^e
6	[Co(P2)]	PhMe	26	nd ^e
7	[Co(P2)]	PhH	45	nd ^e
8	[Co(P2)]	CH ₂ Cl ₂	<5	nd ^e
9	[Co(P2)]	CCl ₄	70	77

^a Reactions were carried out at room temperature for 10 h in one-time fashion without slow addition of the diazo reagent using 1 mol % [Co(Por)] under N₂ with 1.0 equiv of α -cyanodiazo(*N,N*-dimethyl)acetamide and 1.5 equiv of phenylacetylene. Concentration: 0.10 mmol diazo/mL. ^b See Figure 1 for structure. ^c Isolated yields. ^d Enantiomeric excess determined by chiral HPLC. ^e Not determined.

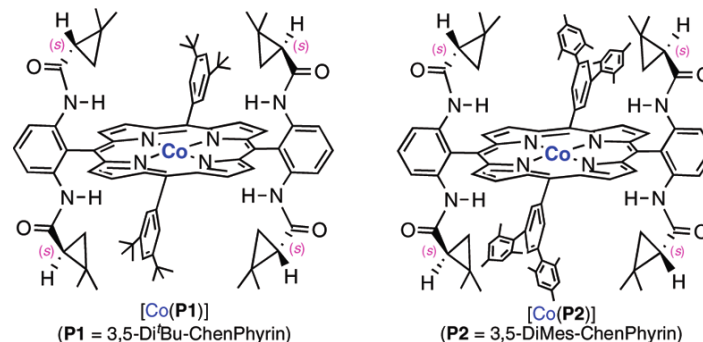
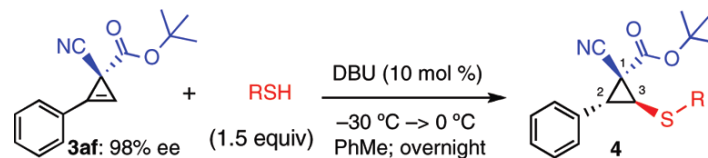
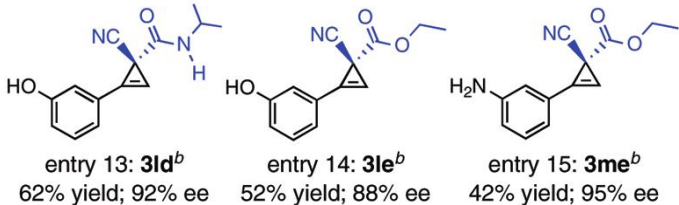
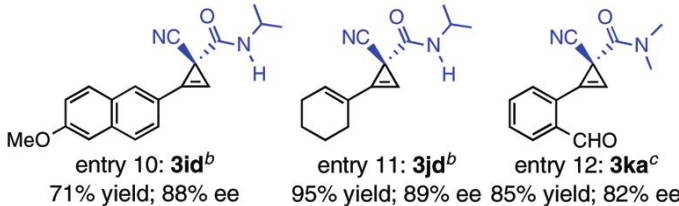
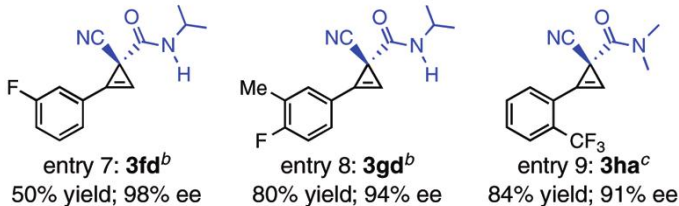
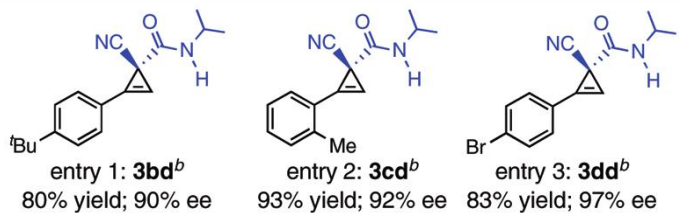
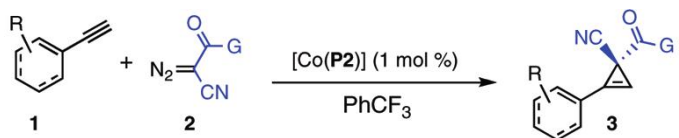


figure 1. Structures of *D*₂-symmetric chiral cobalt(II) porphyrins.

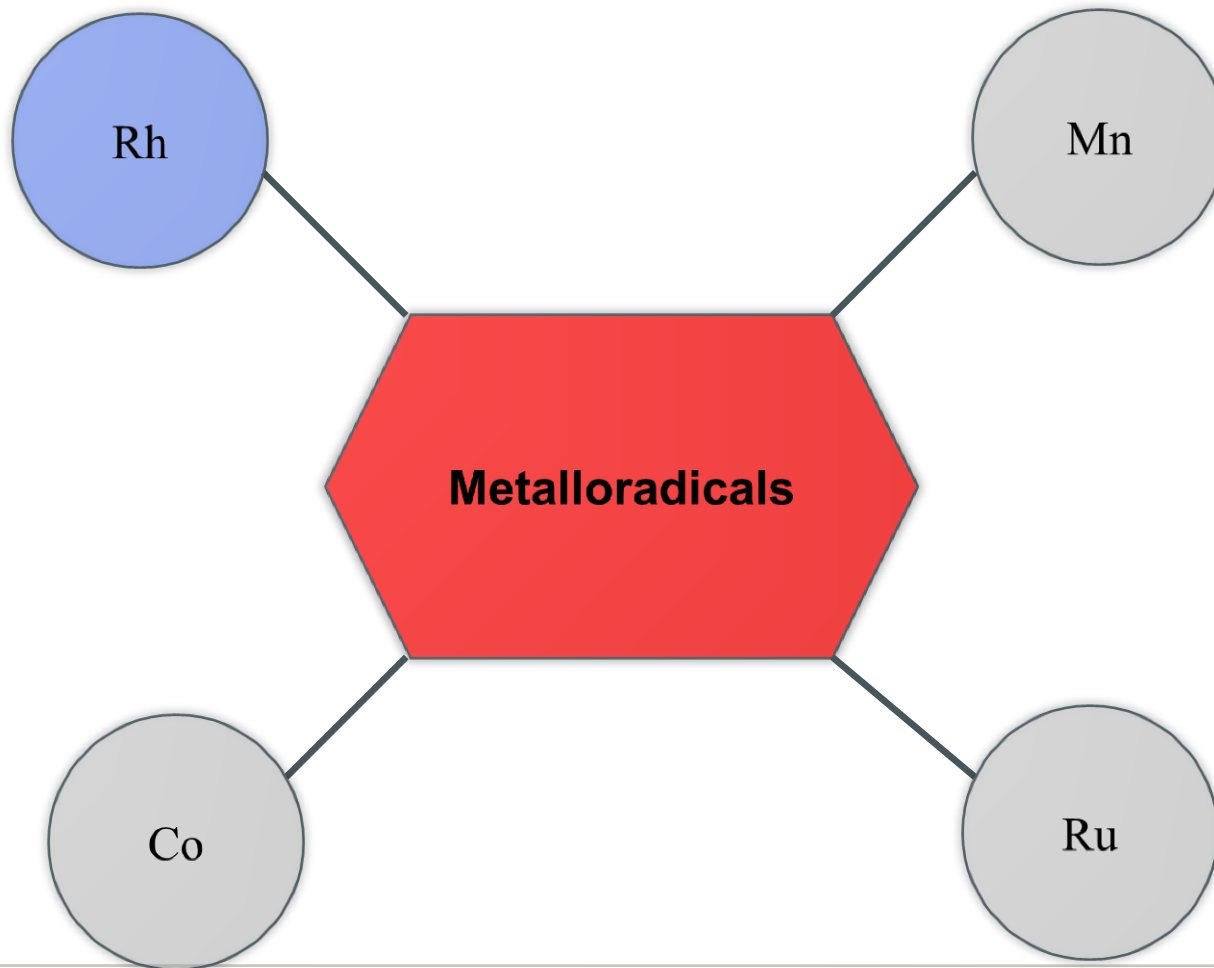
Will discuss mechanism for problem 3!

Hint: porphyrin ligand plays role in mechanism

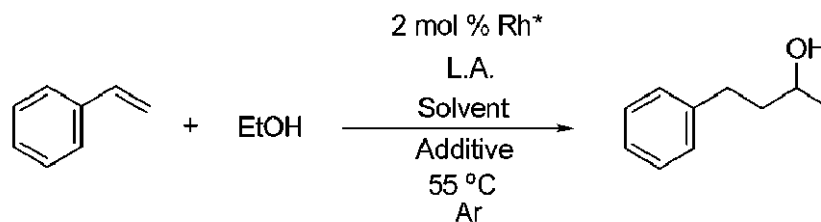


entry	thiol	product	yield (%) ^b	ee (%) ^c
1			98	98 ^d
2			88	98
3 ^e			54	98

Use in Synthesis

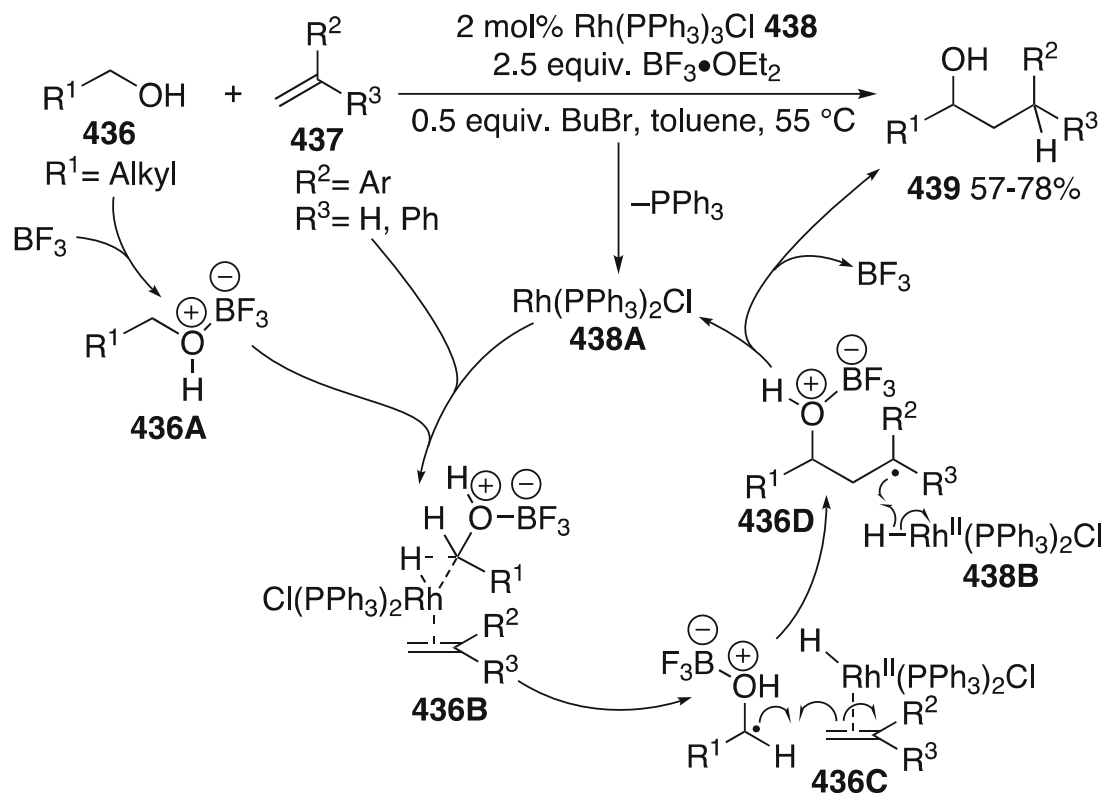


sp^3 - sp^3 Bond Formation through Rh Radicals



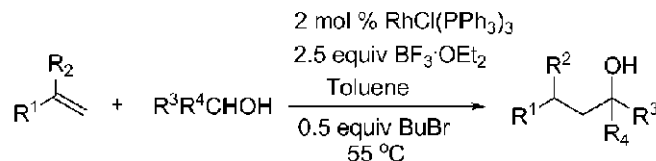
C-C bond formation via C-H bond activation

Lewis Acid Promoted C-H activation through Rh(I)



Shi Substrates

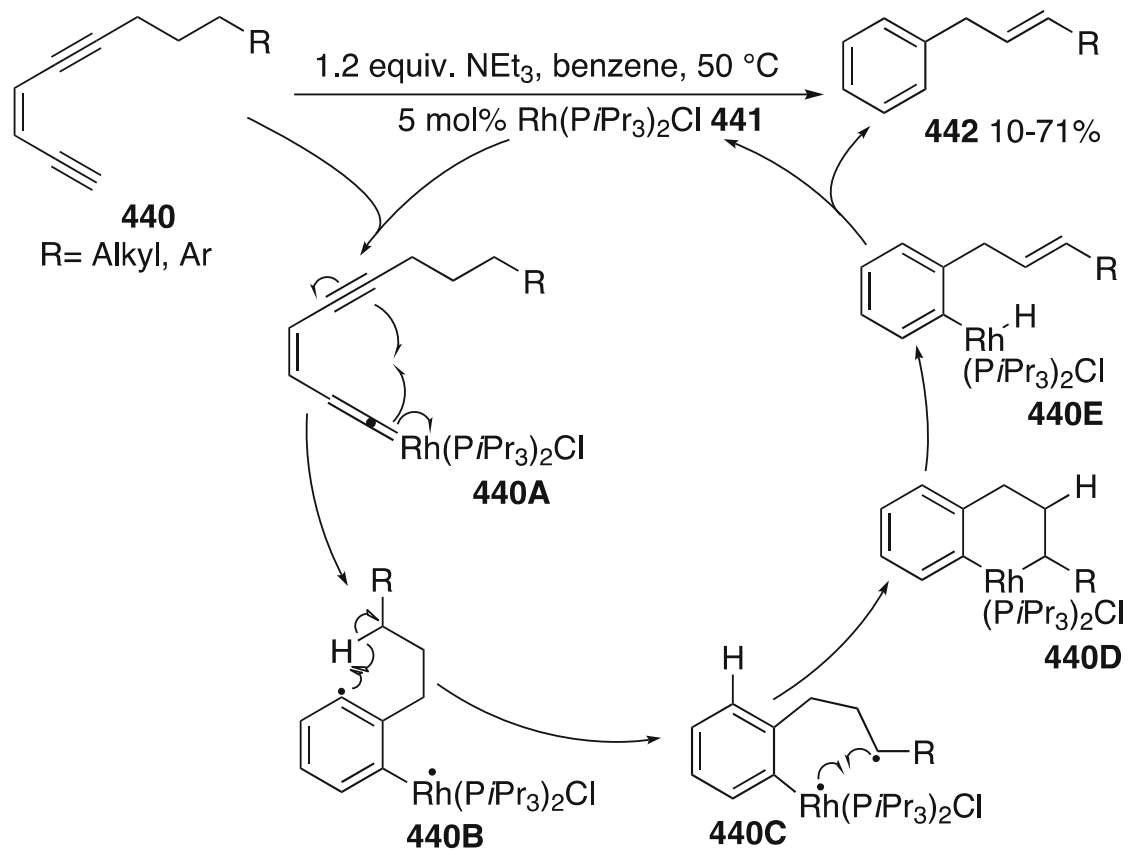
Table 1. Coupling of Alcohols with Olefins^a



entry	olefin (R ¹ , R ²)	alcohol (R ³ , R ⁴)	product	yield (%)
1	R ¹) Ph, R ²) H	R ³) CH ₃ , R ⁴) H	1a	70
2	R ¹) Ph, R ²) H	R ³) <i>n</i> -Pr, R ⁴) H	1b	70
3	R ¹) Ph, R ²) H	R ³) <i>i</i> -Pr, R ⁴) H	1c	68
4	R ¹) Ph, R ²) H	R ³) <i>n</i> -C ₁₃ H ₂₇ , R ⁴) H	1d	74
5	R ¹) 2-MeC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H	1e	65
6	R ¹) 3-MeC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H	1f	78
7	R ¹) 4-MeC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H	1g	63
8	R ¹) 2-OMeC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H		<i>c</i>
9	R ¹) 3-OMeC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H	1h	57
10	R ¹) 4-OMeC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H		<i>c</i>
11	R ¹) 4-(CH ₂ Cl)C ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H	1i	71
12	R ¹) 1-naphthyl, R ²) H	R ³) CH ₃ , R ⁴) H	1j	73
13	R ¹) 2-ClC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H	1k	66
14	R ¹) 2-BrC ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H	1l	64
15	R ¹) 2-NO ₂ C ₆ H ₄ , R ²) H	R ³) CH ₃ , R ⁴) H		<i>d</i>
16	R ¹) Ph, R ²) Ph	R ³) CH ₃ , R ⁴) H	1m	64
17	R ¹) CH ₃ , R ²) CH ₃	R ³) <i>n</i> -C ₇ H ₁₅ , R ⁴) H	1n	31 ^e
18	R ¹) Ph, R ²) H	R ³) CH ₃ , R ⁴) CH ₃		<i>c</i>

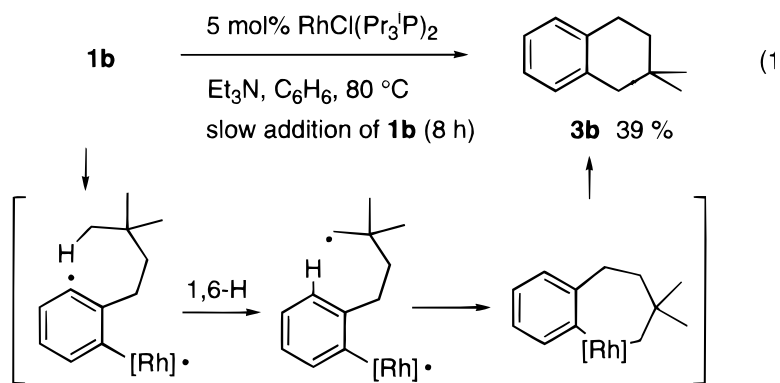
^a For detailed experimental operation, see Supporting Information.
^b Isolated yields of expected products. ^c Complicated products, and no expected products were isolated. ^d No reaction. ^e With 1 equiv of alcohol, 20 equiv of olefin, room temperature.

Rhodium Radical Bergman Cyclization

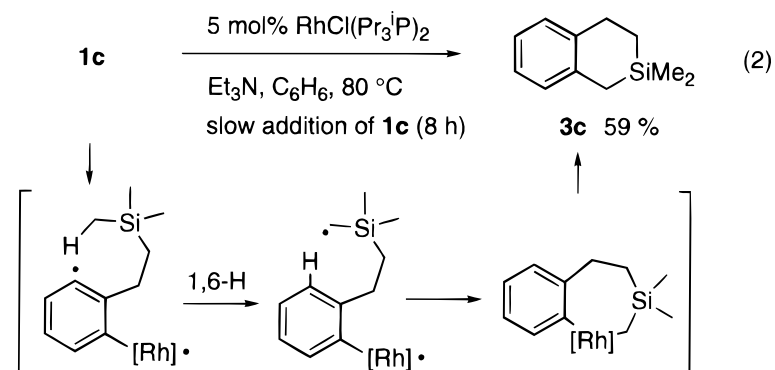


Difference in H-Shift

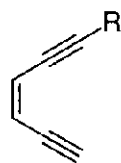
Alkyl



Silyl



Rh Bergman Substrates



1

1a: R = C₆H₁₃

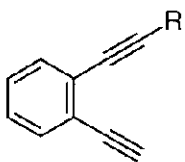
1b: R = CH₂CH₂Bu^t

1c: R = CH₂CH₂SiMe₃

1d: R = CH₂OSiBu^tMe₂

1e: R = CH₂CH₂SiBnMe₂

1f: R = CH₂CH₂SiPrⁱMe₂



2

2c: R = CH₂CH₂SiMe₃

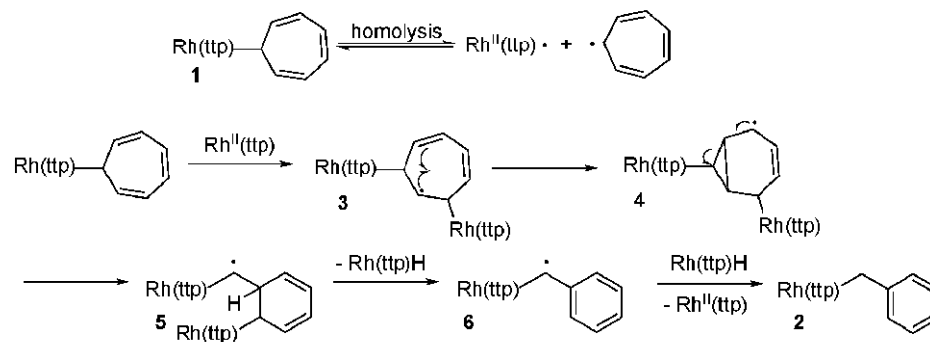
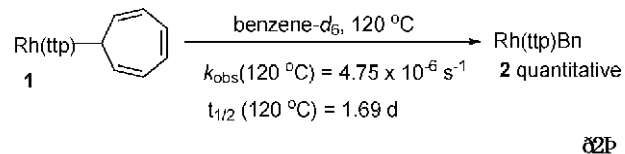
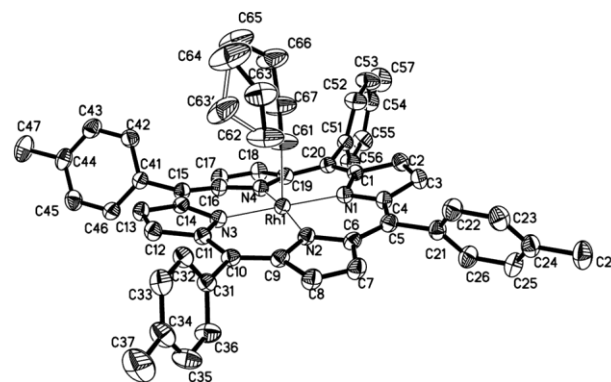
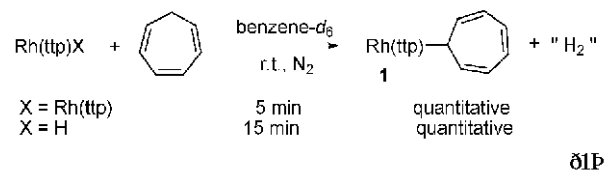
2g: R = CH₂CH₂OSiBu^tMe₂

2h: R = CH₂CH₂OSiPrⁱMe₂

Table 1. Formation of Silacycloalkane and Vinylsilane via 1,6- and 1,7-Hydrogen Transfer

entry	enediyne	products	yield ^a (%)
1	1c	3c	71
2	1d	3d	31 (36) ^b
3	1e	3e	0 (51)
4	2c	4c	48
5	2g	4g	55 (21)
6	1f	5	69 ^c
7	2h	6	42 ^d (21)

Rh(por) Radical



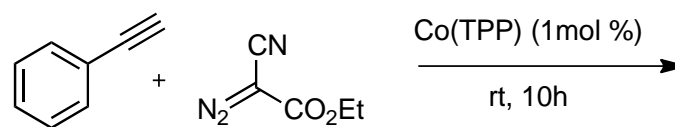
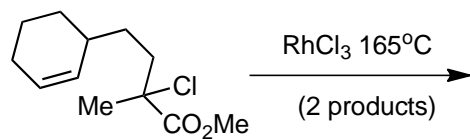
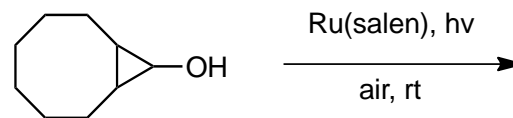
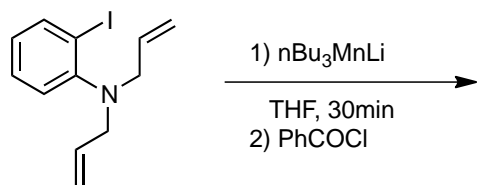
Bimetallo-radicals

- Ti(III)-Rh(I)
- Cr(II)-Co(II)
- Mn(II)-Co(II)
- Mn(II)-Cu(I)
- Ru(II)-Rh(III)

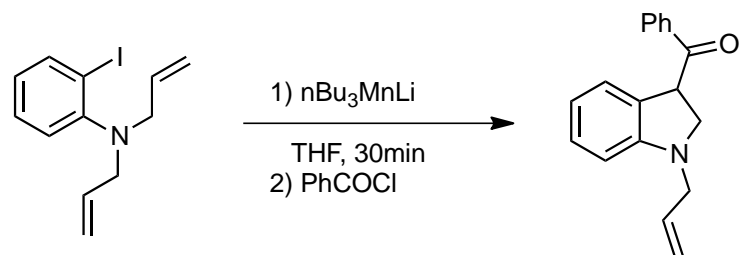
Conclusions

- Offers new alternatives to C-C, C-H and C-X bond formation
- With selective catalyst, mild conditions and fast reactions can be employed for advanced products
- Many common coupling and transformative metal reactions should be tested for radical probes
- Field of organometallic radical chemistry is still young and widely unknown

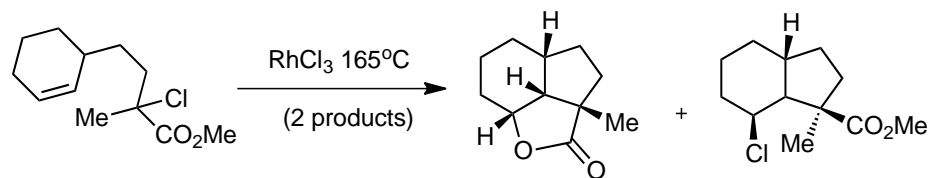
Questions



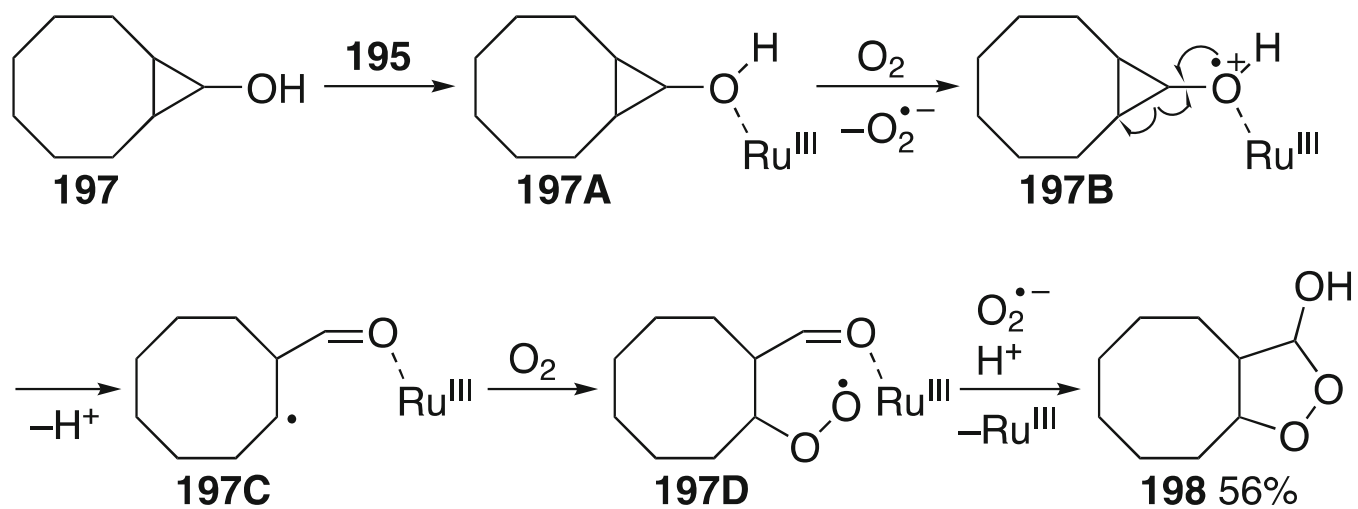
Question 1



J. Org. Chem., Vol. 62, No. 7, 1997 1911



Question 2



Question 3

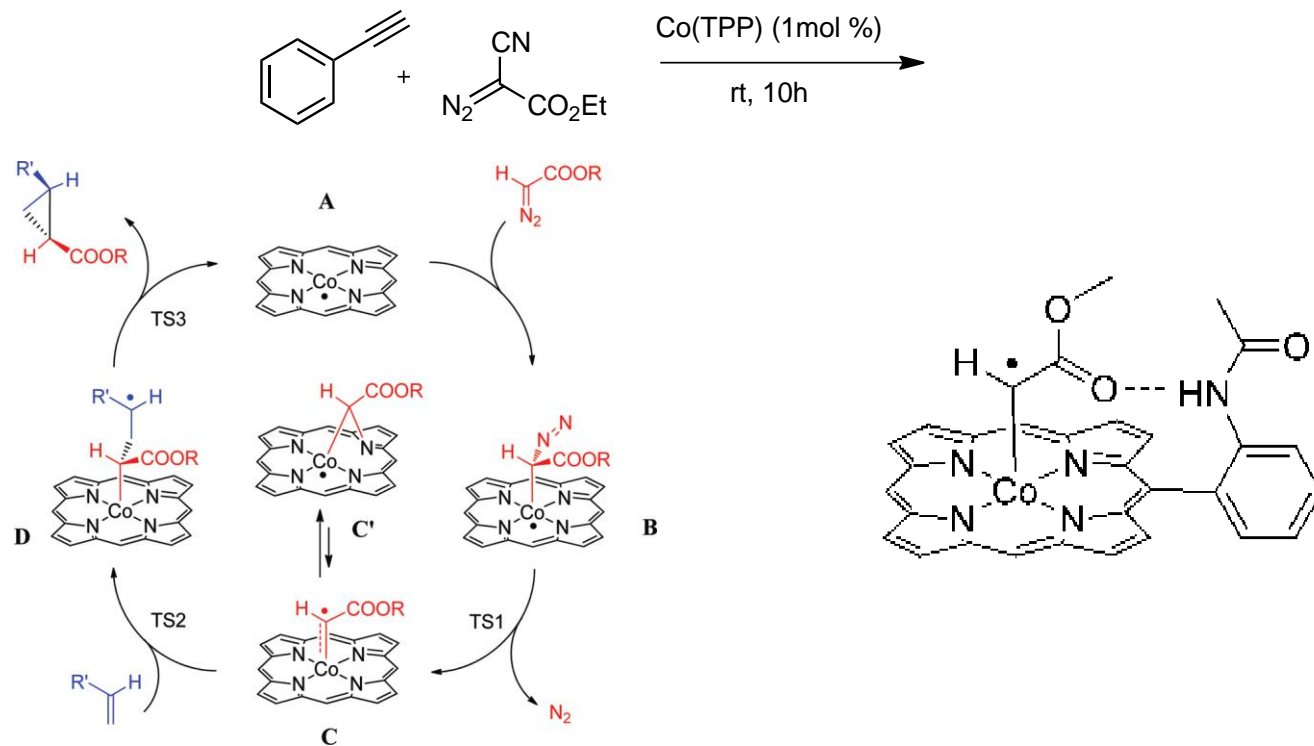
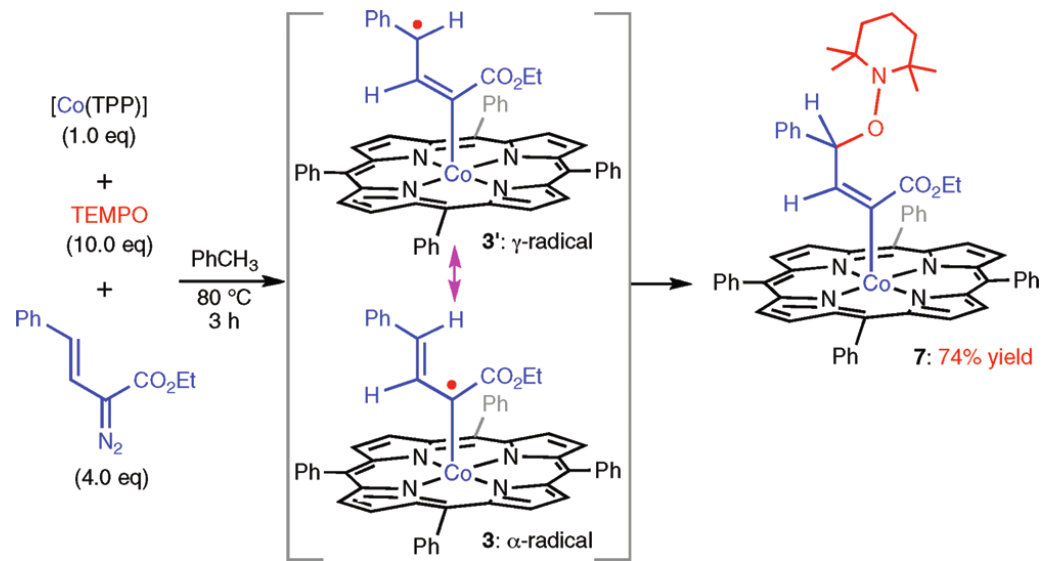


Figure 15. Catalytic cycle for Co(por)-catalyzed cyclopropanation of olefins.



EPR For Metal Radicals

- Generally, electron-spin relaxation processes are faster for metal-centered radicals compared to organic (or ligand) radicals – EPR spectra then are taken under 100K (see broadening at rt)
- Small mixings of the metal SOMO will occur with ligand orbitals
- Metal spin-orbit coupling constants are much larger than light weight organic atoms