Iron Catalysis

Frontier of Chemistry Seminar
Yongzhao Yan
Apr. 26th 2014

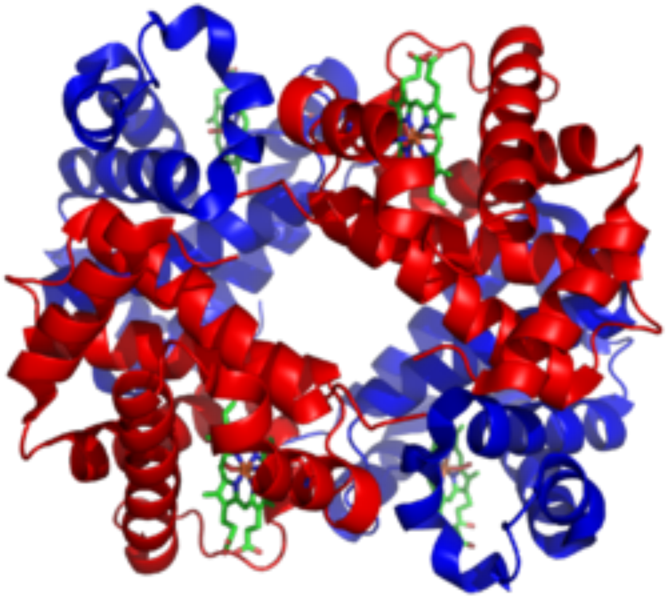
An New Iron Age

- Second most abundant metal in the Earth.
- 1/3 of the mass in the Earth's crust.
- Iron oxide (Fe_3O_4, Fe_2O_3, $FeO(OH)$)

Picture from http://www.meteoritesusa.com/meteorite-information/

An New Iron Age

- Cheap, sustainable and commercially accessible
- Pd, Rh, Ir, Pt and Ru are limited by availability and toxicity
- Iron compounds are relatively nontoxic and common in biological systems
- Hemoglobin



Angew. Chem. Int. Ed. **2008**, *47*, 3317 – 3321

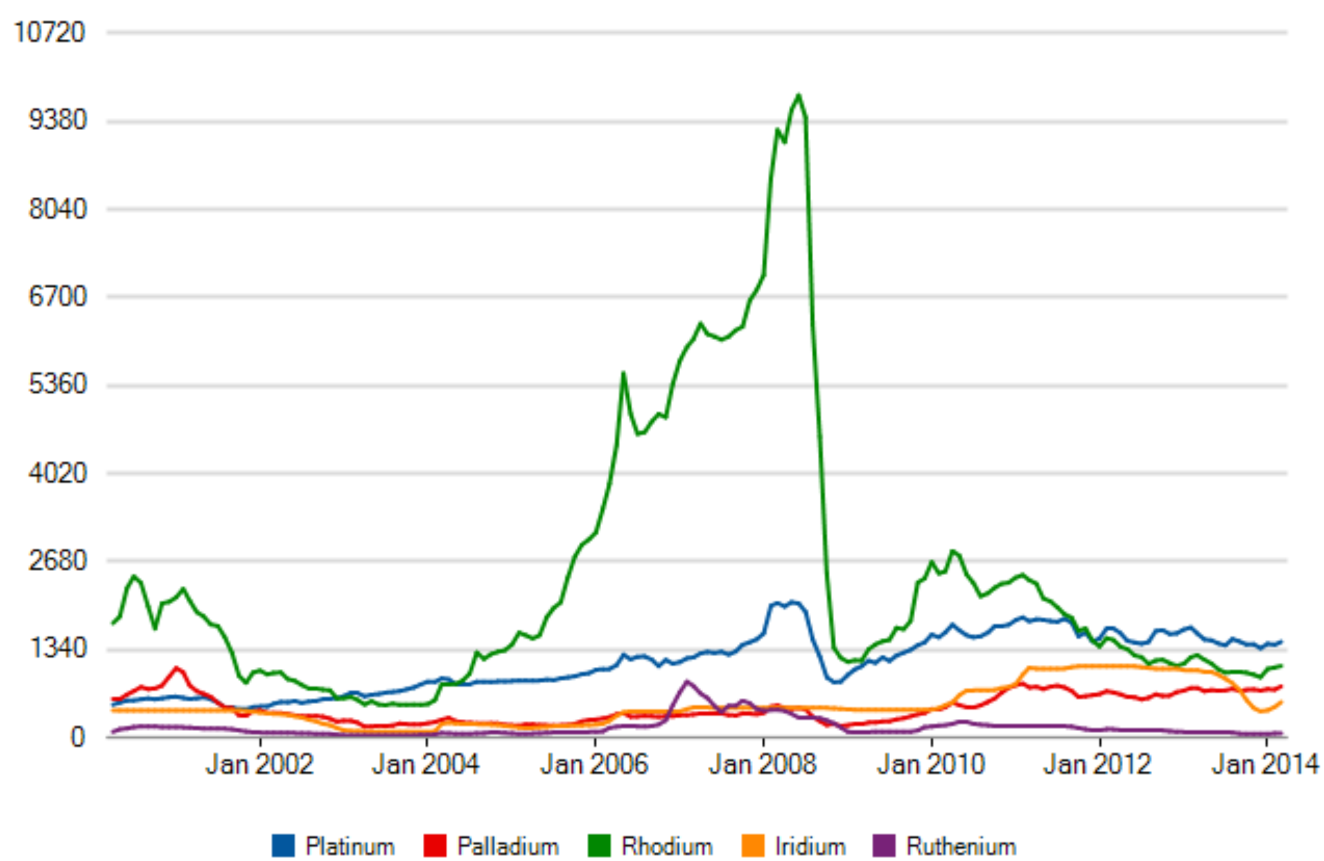
Platinum, Palladium, Rhodium, Iridium, Ruthenium

EXPORT TO PDF | EXPORT TO CSV | EXPORT TO PNG

Monthly Averages between Apr 2000 and Apr 2014

JM Base Price | $/oz

Platinum average: $1139.83
Palladium average: $449.22
Rhodium average: $2387.49
Iridium average: $488.08
Ruthenium average: $159.69



http://www.platinum.matthey.com

An New Iron Age

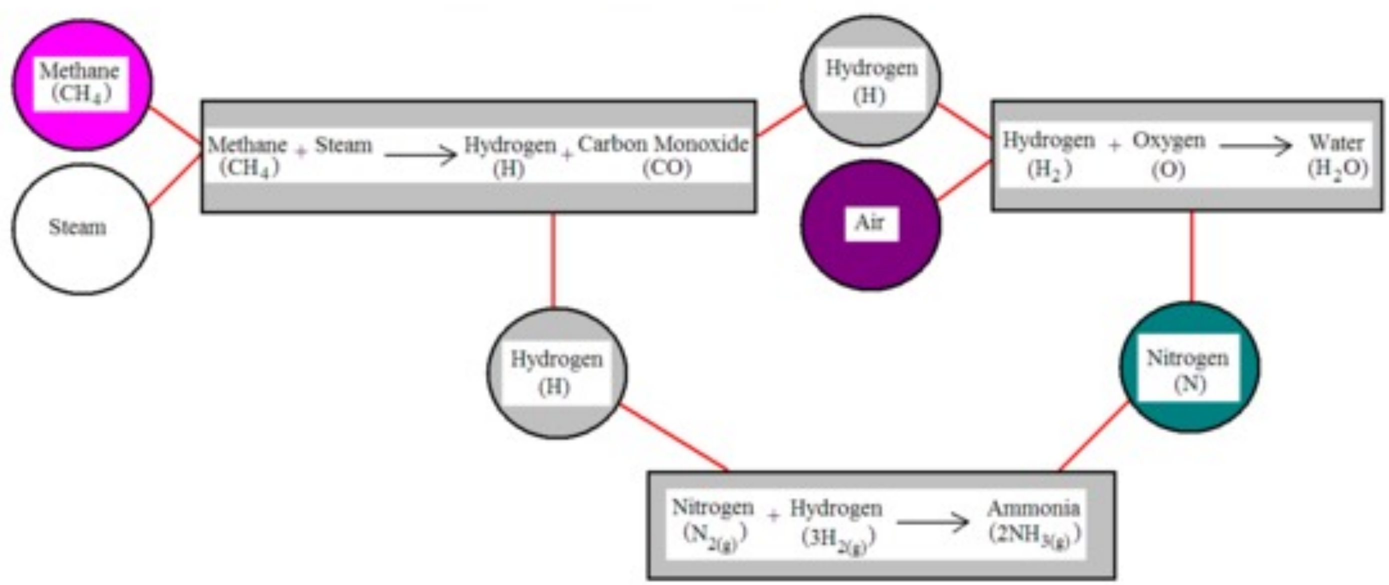
- Despite some well-known applications like Harbor process
- Iron usually is not first choice in terms of catalyst
- Comparing to metals like Pd or Rh, Iron is relatively underdeveloped.

Angew. Chem. Int. Ed. **2008**, *47*, 3317 – 3321

Harbor-Bosch Process

- 3-5% natural gas consumption, 1-2% annual energy supply.
- 80% nitrogen found in human tissue originated from this process.

Haber Process and the Production of Ammonia



Smil, Vaclav (**1999**). Detonator of the population explosion. *Nature* 400:415.
Smil, Vaclav (**2011**). Nitrogen cycle and world food production. *World Agriculture* 2:9-1.
http://chemwiki.ucdavis.edu/Physical_Chemistry/Equilibria/Case_Studies/Haber_Process

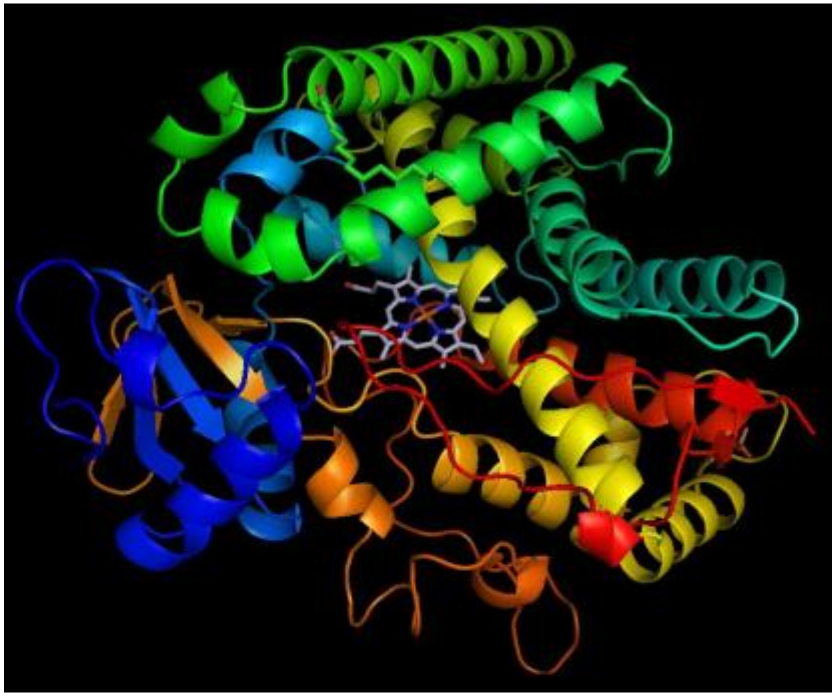
Iron Catalysis

- Iron(II)/Iron(III) oxidation reaction/C-H activation
- Iron-H involved hydrogenation/reduction
- Iron-catalyzed C-C coupling
- Iron-carbene/nitrene

Iron Oxidation

- Cytochrome P450 are redox enzymes
- These enzymes could perform epoxidations, hydroxylations and others
- Many researchers trying to design

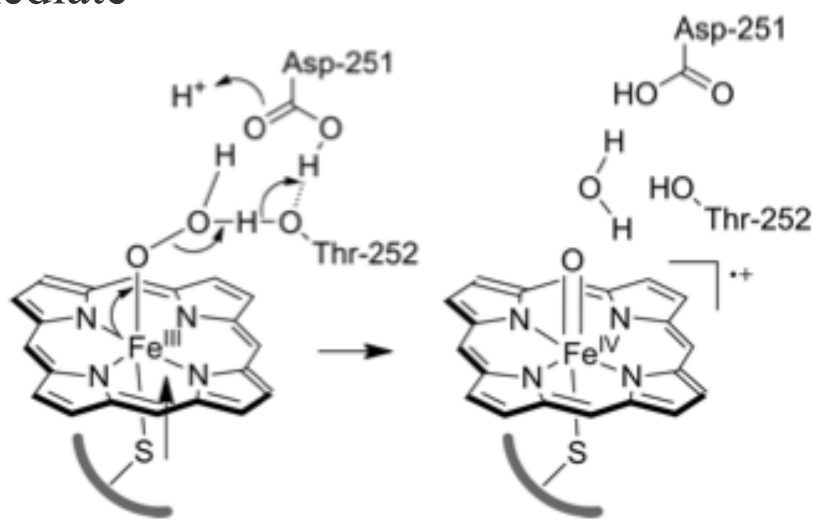
catalysts related to iron porphyrin core.



Chem. Rev. **2013**, *113,* 3248-3296

Iron-Oxo Species

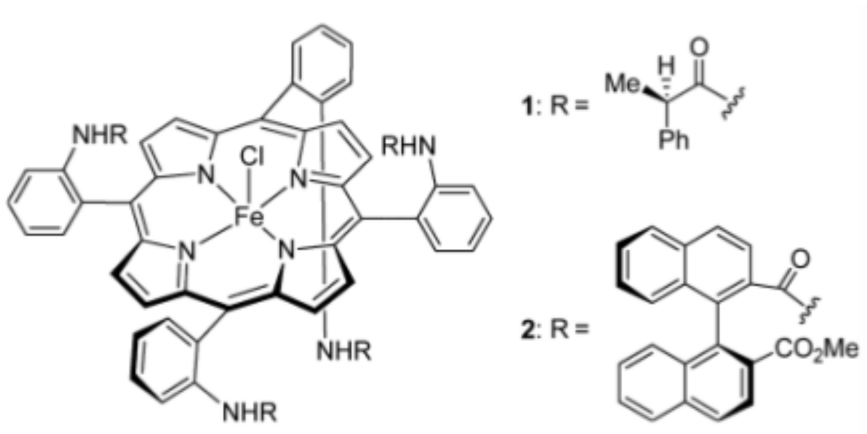
- Iron-oxo species is the key intermediate
- High value ferryl species
- Push-pull effect



Chem. Rev. **2010**, *110*, 949.
Chem. Rev. **2004**, *104*, 3947.

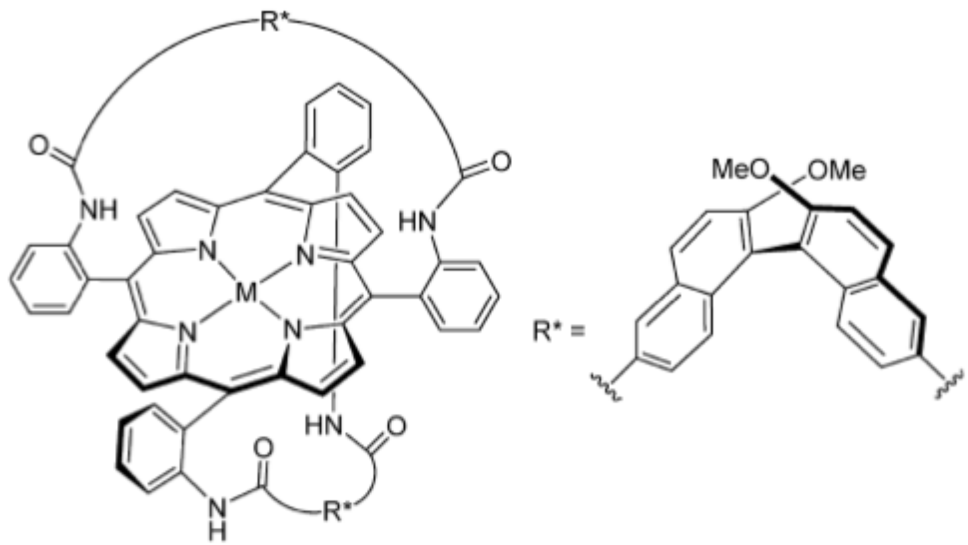
Porphyrin-Based Catalysts

- First example in 1983 by Groves and Myers
- Iodosylbenzene or iodosylmesitylene as the oxygen donors
- Epoxidation *ee* up to 50%



J. Am. Chem. Soc. **1983**, *105*, 5791.

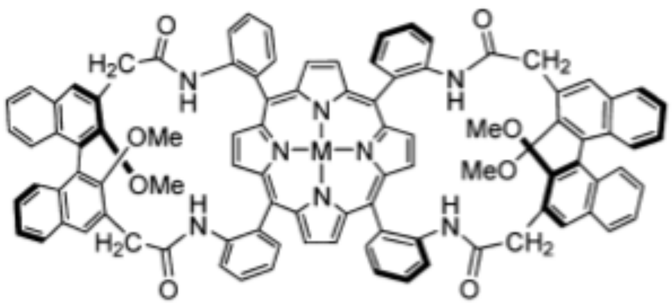
“Vaulted Binaphthyl”



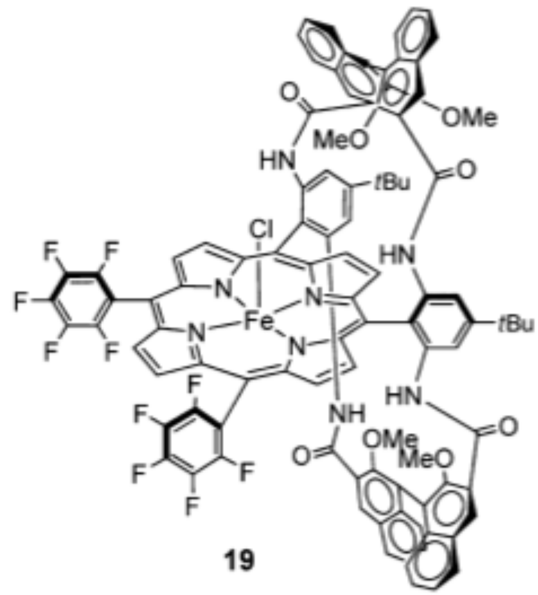
- Epoxidation *ee* 32-70%
- Hydroxylation at benzylic position *ee* 44-72%

J. Org. Chem. **1990**, *55*, 3628.

Porphyrin-Based Catalysts



20 (M = FeCl)



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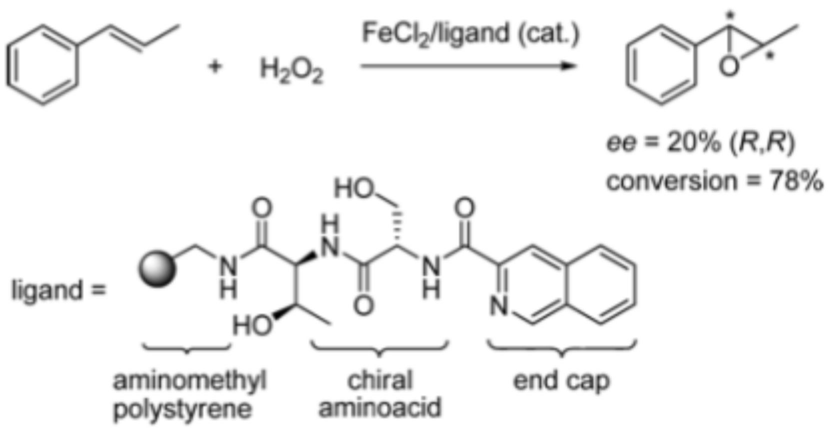
- Epoxidation *ee* up to 97%
- *ee* up to 85%

Polyhedron **2000**, *19*, 581.
Chem. Eur. J. **2004**, *10*, 224.

Non-Porphyrin-Based Catalysts

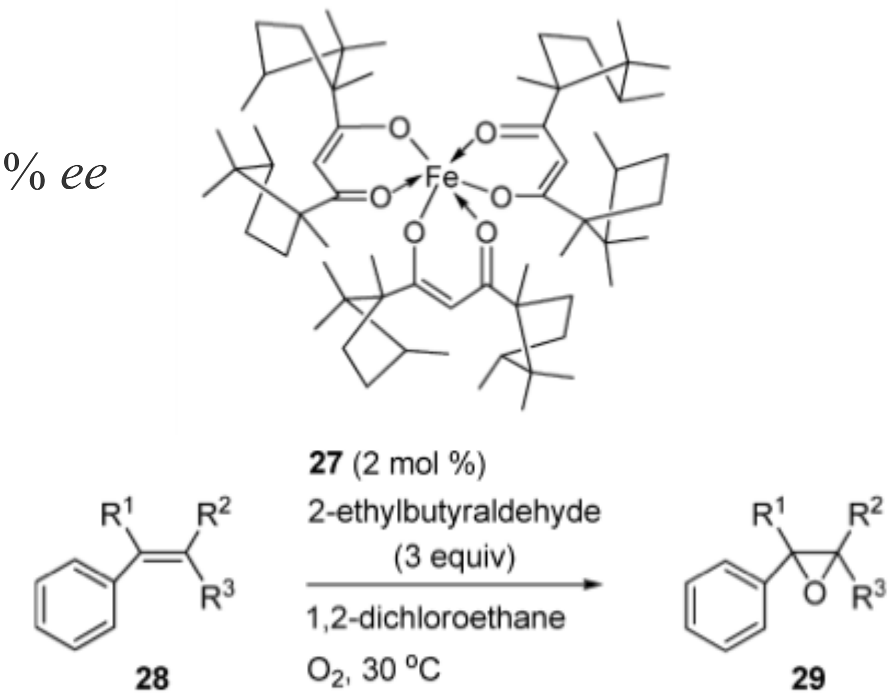
- Using H_2O_2 as oxidant
- A total of 5760 metal ligand combinations were screened.



Angew. Chem., Int. Ed. **1999**, *38,* 937.

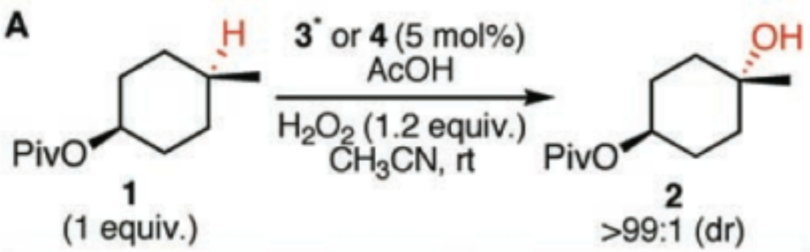
Non-Porphyrin-Based Catalysts

- O_2 as oxidant
- Moderate yield, 47-92% *ee*

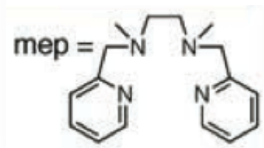


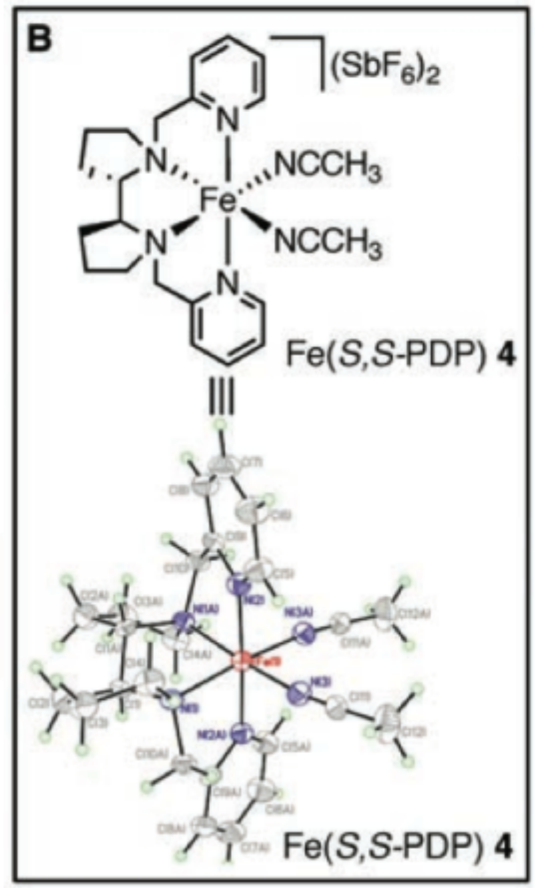
Chin. Chem. Lett. **2005**, *16*, 1467.

White-Chen Catalyst



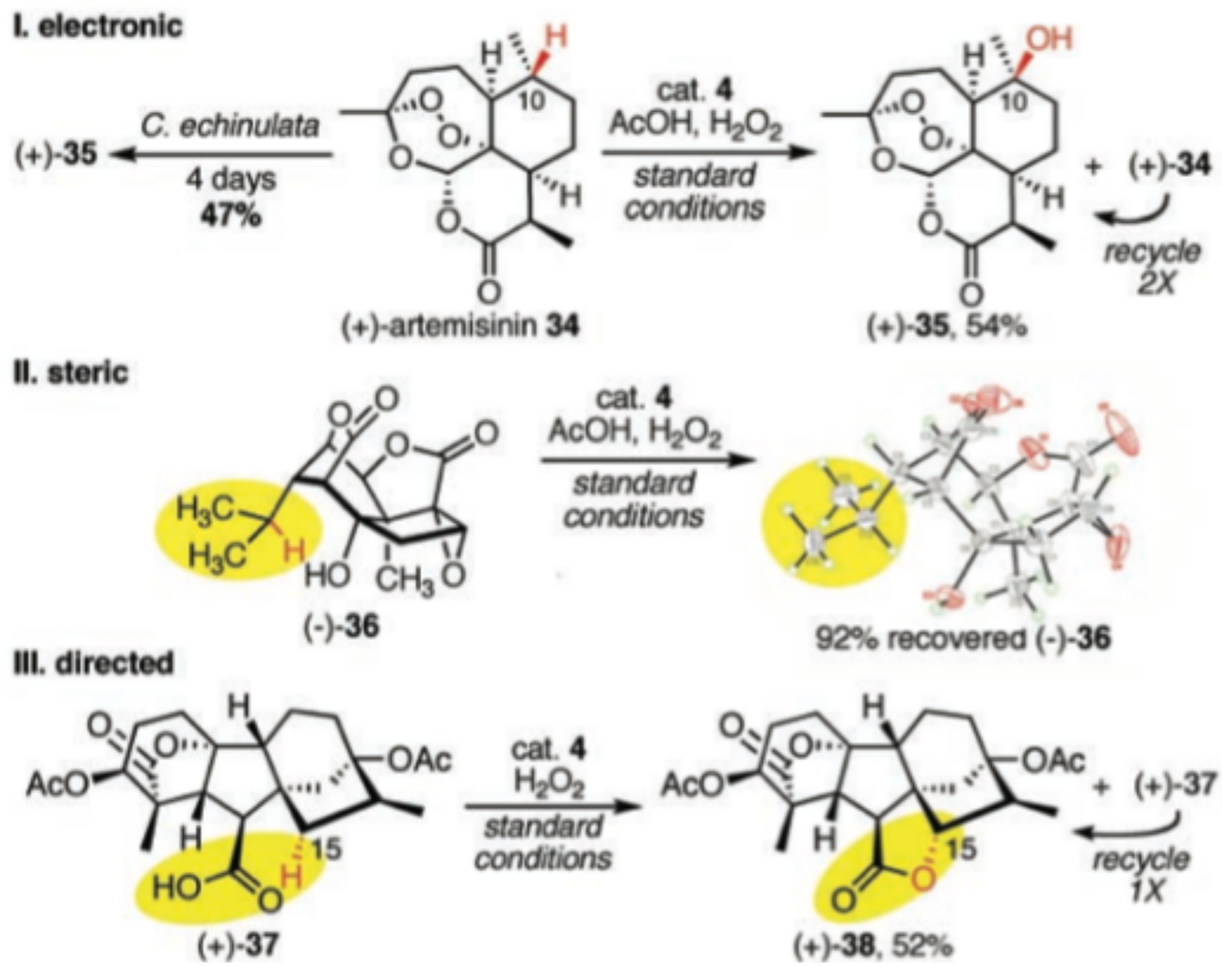
Entry	Catalyst	AcOH (equiv.)	Yield (%)	Conv.† (%)	Select.‡ (%)
1	**3***	0	7	12	56
2	**4**	0	14	15	92
3	**3***	0.5	26	41	62
4	**4**	0.5	38	42	90
5§	**4**	0.5	51	-	-





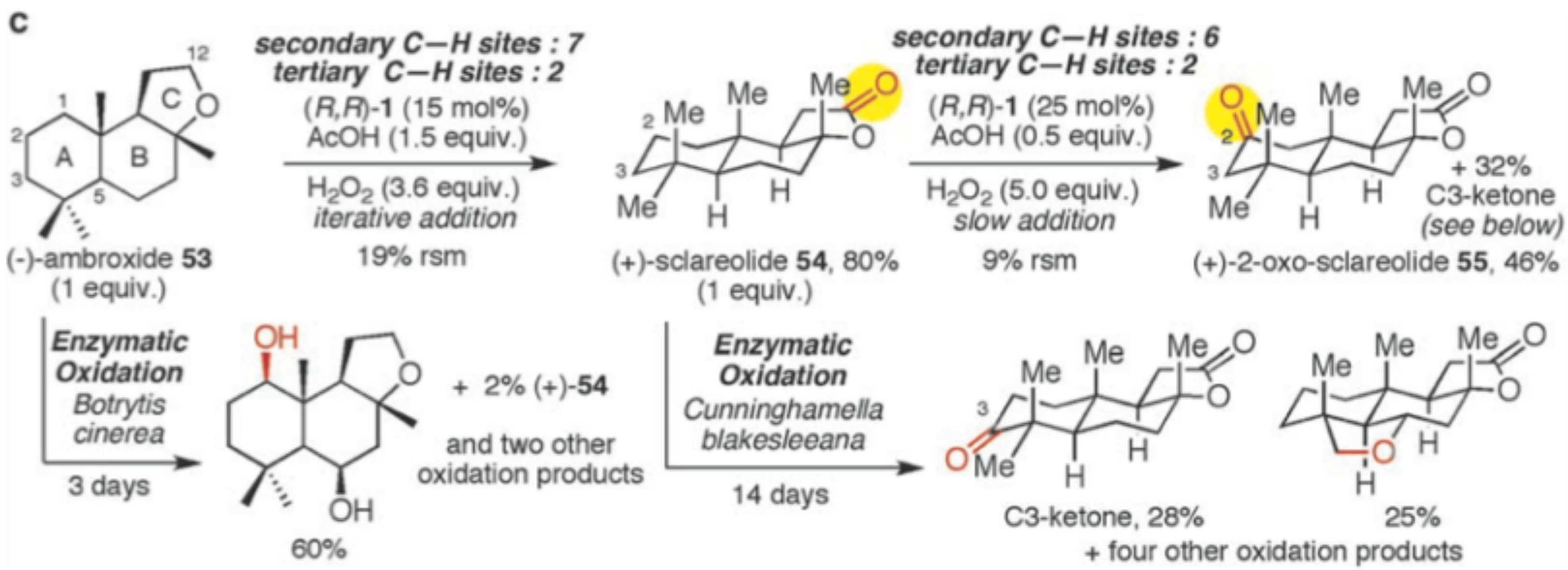
Science **2007**, *318*, 783

White-Chen Catalyst



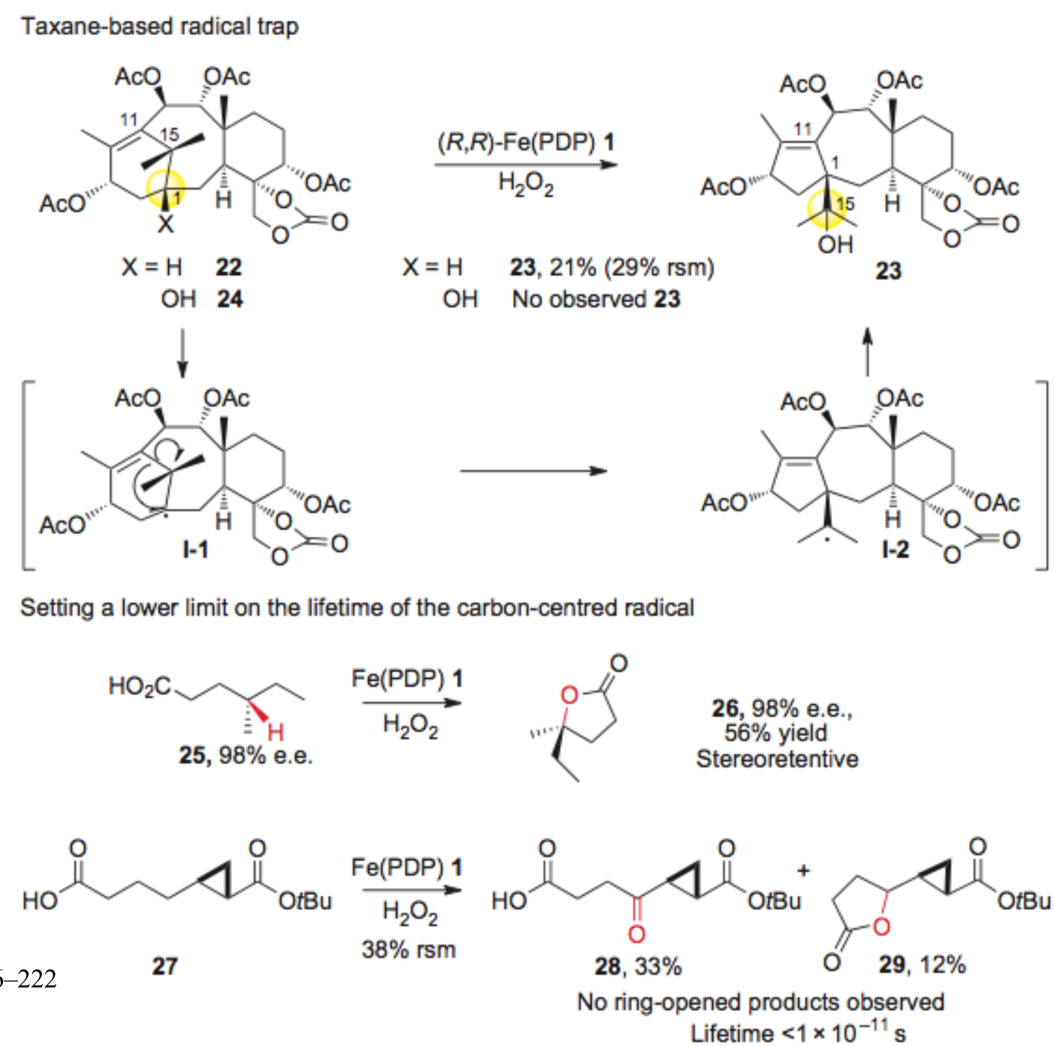
Science **2007**, *318*, 783

White-Chen Catalyst



Science **2010**, *327*, 566

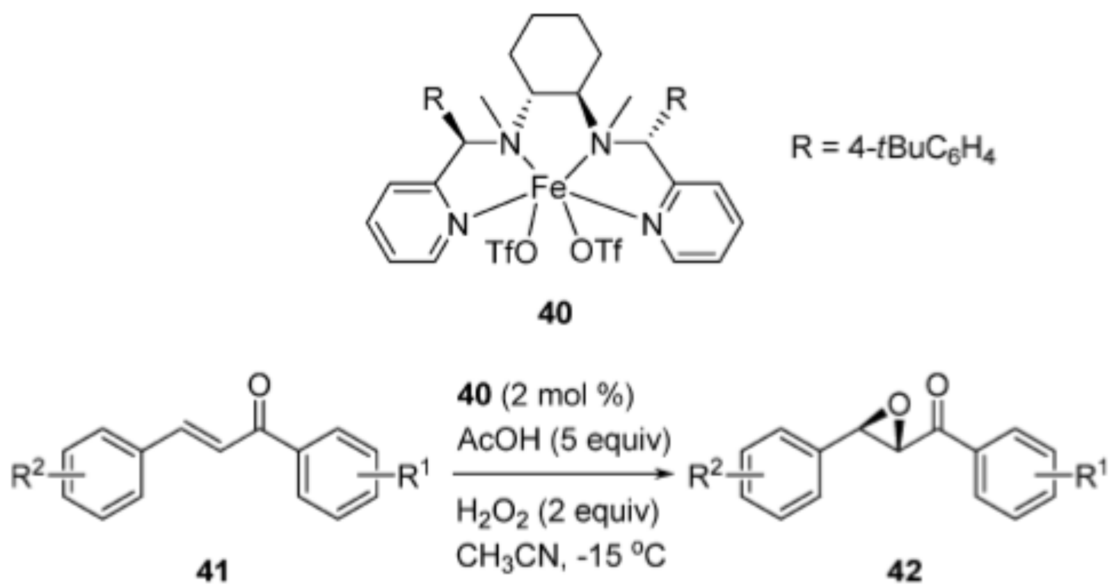
White-Chen Catalyst



Nature Chemistry **2011**, *3*, 216–222

Non-Porphyrin-Based Catalysts

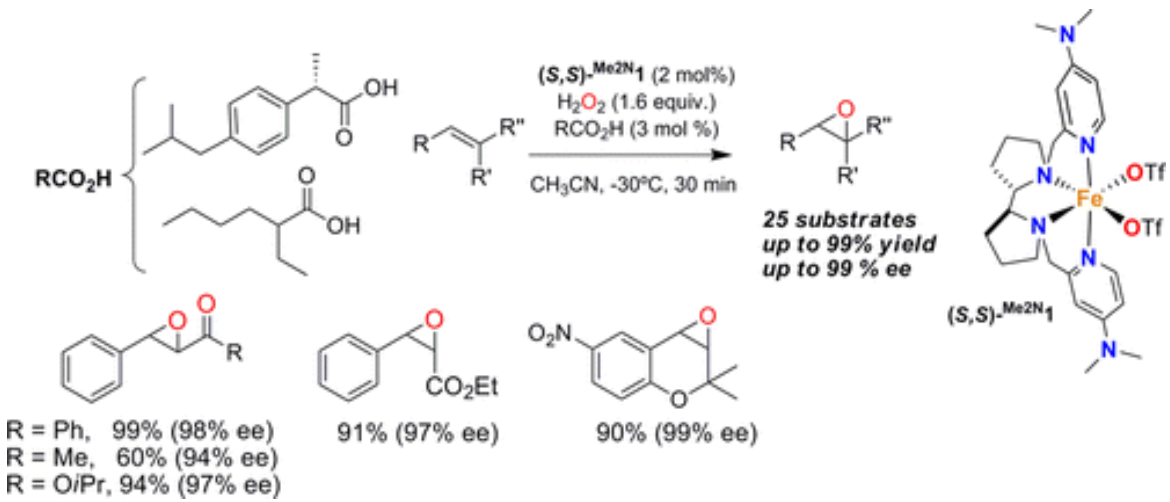
- Moderate to good yields and 74-87% *ee*.
- applicable only to α,β-enones.

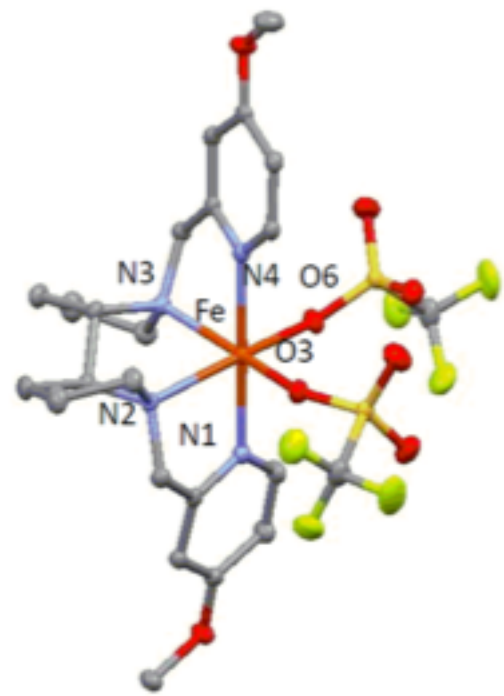


Adv. Synth. Catal. **2011**, *353*, 3014.

Non-Porphyrin-Based Catalysts

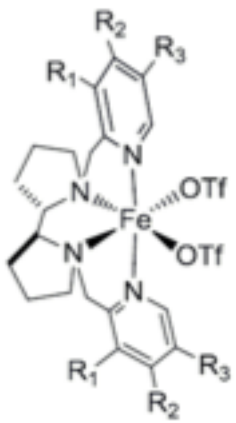
- Carboxylic acid promote acid cleavage of O-O bond
- Electro effects of the ligand



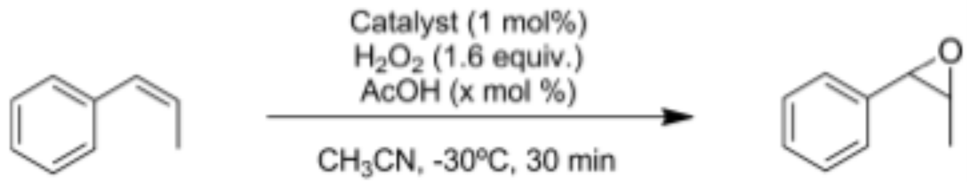


J. Am. Chem. Soc. **2013**, *135*, 14871

Non-Porphyrin-Based Catalysts



X1	R1=R3	R2
Me2N1	-H	-NMe_2
dMM1	-Me	-OMe
MeO1	-H	-OMe
Me1	-H	-Me
H1	-H	-H
Cl1	-H	-Cl
CO2Et1	-H	-CO_2Et

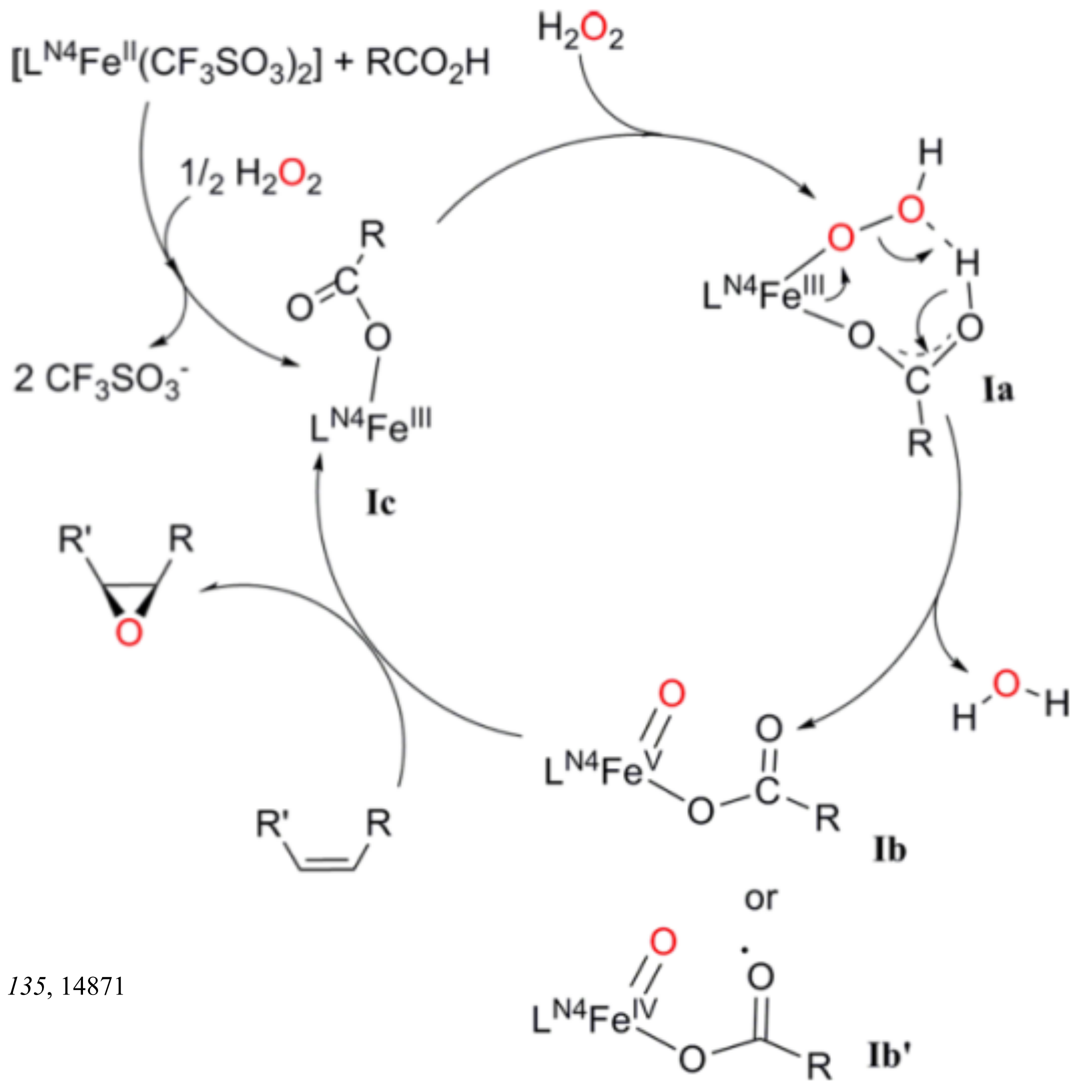


S1

entry	catalyst	AcOH (*x* mol %)	conv (yield, %)	ee (%)
5	^{MeO}**1**	140	64 (37)	39
6	^{dMM}**1**	**140**	97 (81)	40
7	^{Me2N}**1**	**140**	**100 (82)**	**60**
8[b]	^{Me2N}**1**	**140**	**100 (85)**	**61**
9	^{pin}**1**[c]	140	89 (69)	30
10	^{iQuin}**1**	140	80 (46)	20
11	^{dMM}**2**	**140**	82 (55)	32
12	^{Me2N}**1**	**3**	**100 (87)**	**62**
13	^{Me2N}**1**	0	45 (20)	46

J. Am. Chem. Soc. **2013**, *135*, 14871

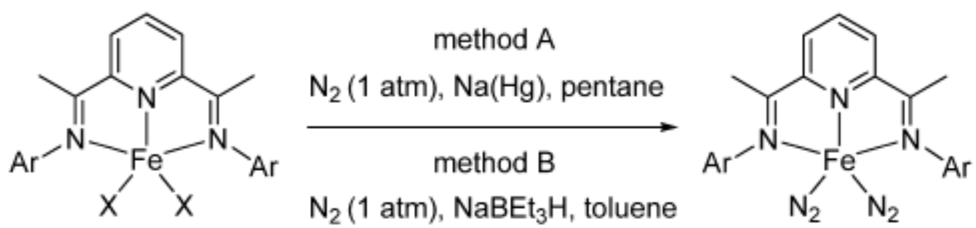
Non-Porphyrin-Based Catalysts



J. Am. Chem. Soc. **2013**, *135*, 14871

Iron Catalyzed Reduction

- Chirik and co-workers synthesized and applied Fe NNN pincer compounds
- Catalyst are capable of hydrogenate alkenes, ketones, imines and etc.



67

X = Cl (or) Br

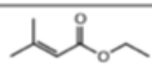
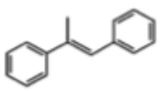
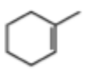
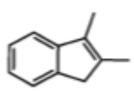
Ar = 2,6-iPr$_2$-C_6H_3

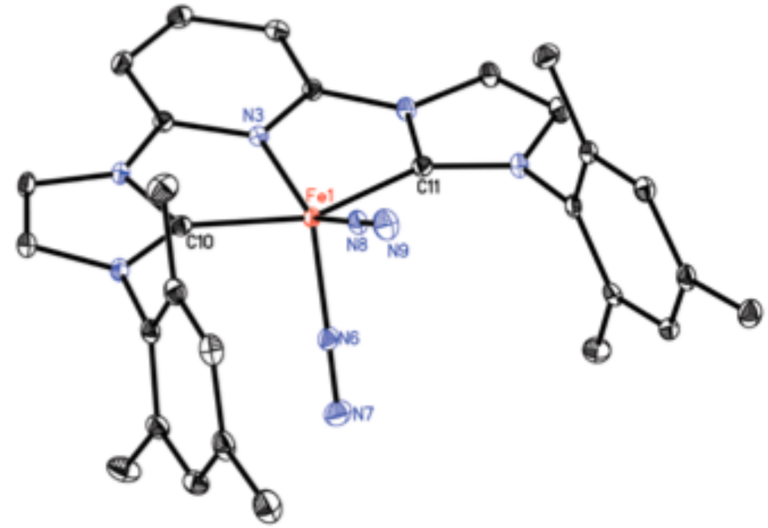
68

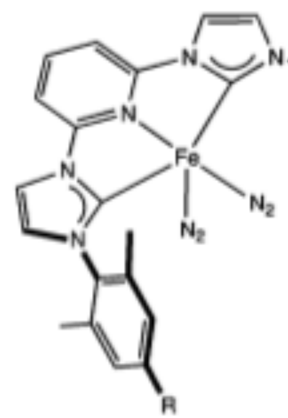
J. Am. Chem. Soc. **2004**, *126*, 13794

Alkene Hydrogenation

- Functional group tolerance and substrate scope
- CNC ligand

Entry	Substrates	Conversion[a] [%] (Reaction time)		
		(^{iPr}CNC)Fe(N_2)$_2$	(^{Me}CNC)Fe(N_2)$_2$	(^{Mes}CNC)Fe(N_2)$_2$
1[b]		> 95 (1 h)	35 (1 h)[e]	35 (1 h)
2[b]		89 (12 h)	> 95 (1 h)	> 95 (1 h)
3[c]		> 95 (15 h)	> 95 (1 h)	> 95 (1 h)
4[b]		20 (24 h)	> 95 (12 h)	> 95 (1 h)
5[b]		4 (48 h)	68 (48 h) 3:1 *cis* : *trans*	60 (48 h) 3:1 *cis* : *trans*
6[c]		0 (24 h)	0 (24 h)	0 (24 h)



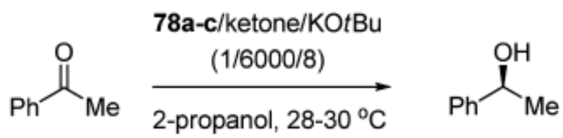


(1)

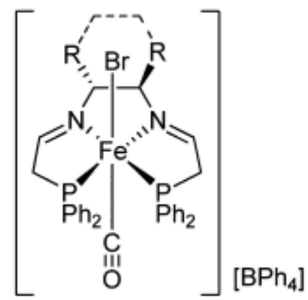
Organometallics **2006**, *25*, 4269.
Organometallics **2008**, *27*, 1470.
ACS Catal. **2012**, *2*, 1760

Transfer Hydrogenation

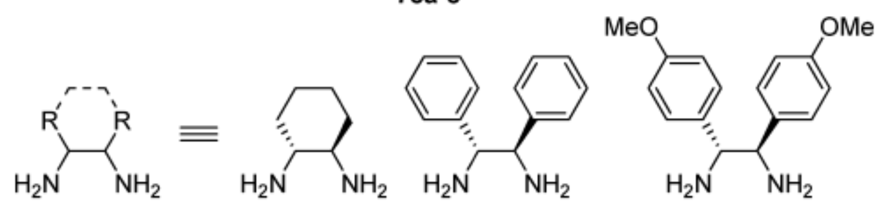
- Homogeneous iron(0) or iron(II) catalyst



Complex	TOF (h^{-1})	*ee* (%)
78a	4.9×10^3	60
78b	2.0×10^4	81
78c	2.0×10^4	82



78a-c

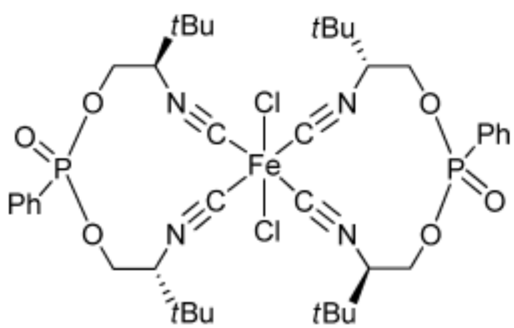


a **b** **c**

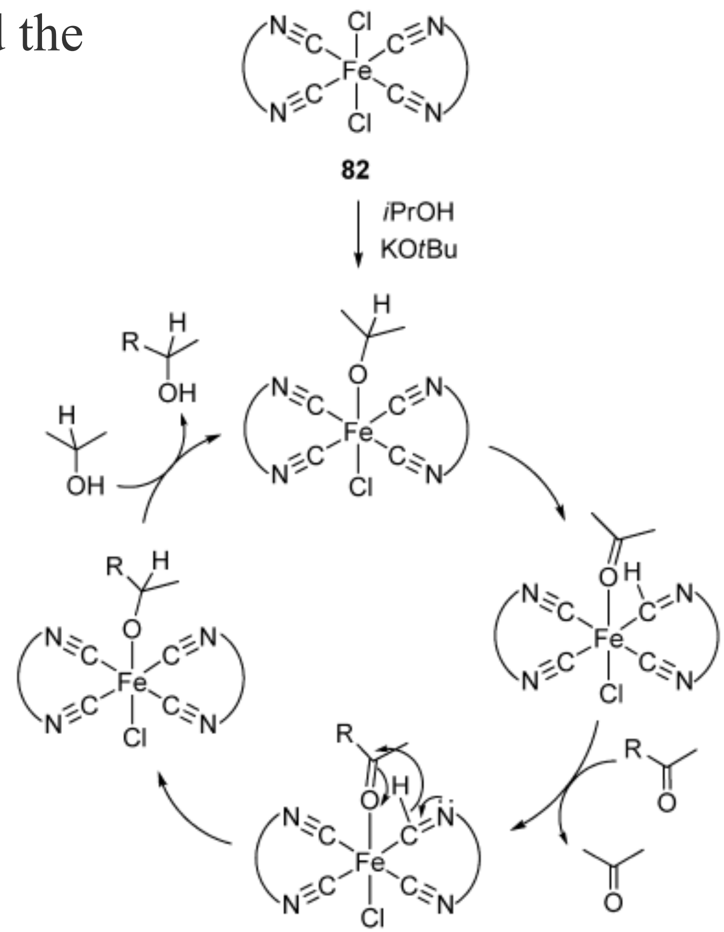
Inorg. Chem. **2010**, *49*, 11039.

Transfer Hydrogenation

- Reiser and co-workers synthesized the iron(II) complex
- Moderate yield with up to 91% *ee*.



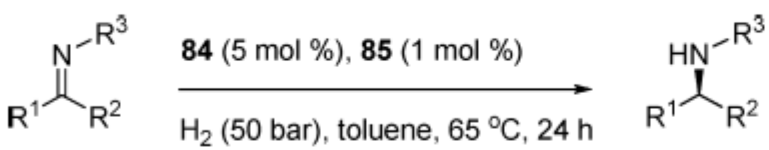
82

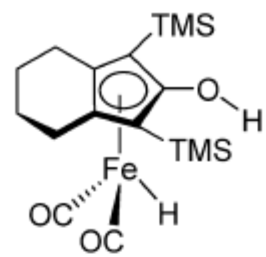


Chem. Commun. **2010**, *46*, 4475.

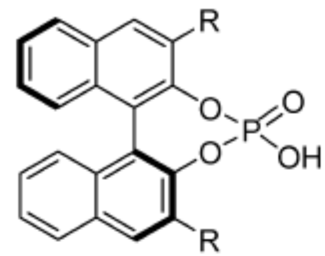
Iron-Hydride Species

- Shvo's catalyst
- High pressure needed, high (70-80%) yield and excellent *ee* (81-99%)

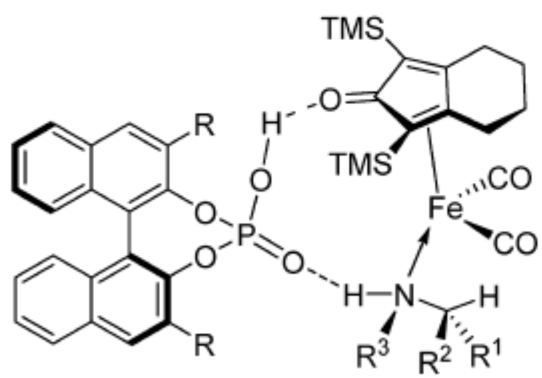




Knölker's complex **84**



85
R = 2,4,6-*i*Pr_3-C_6H_2



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Angew. Chem., Int. Ed. **2011**, *50*, 5120.

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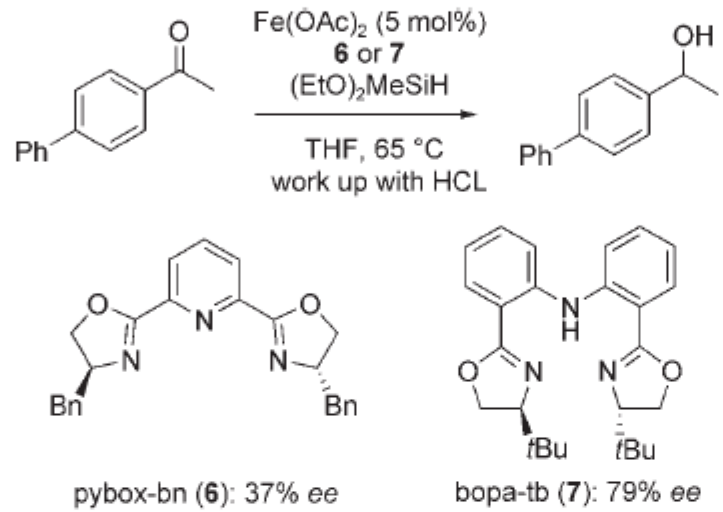
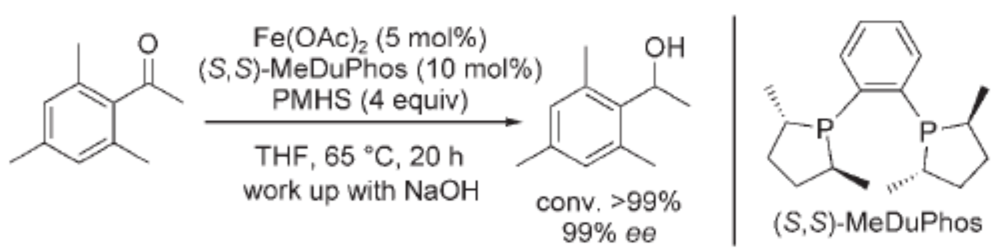
Iron-Catalyzed Hydrosilylation

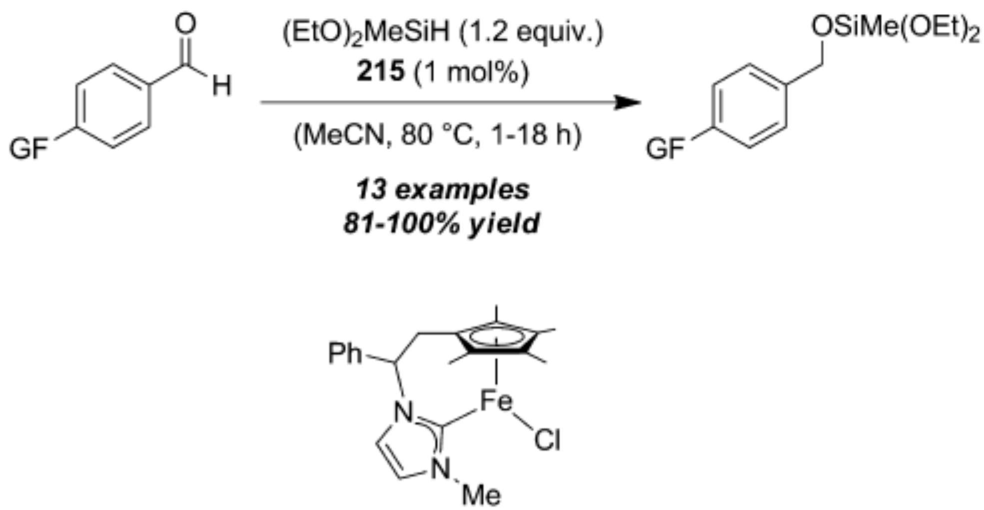




Chem. Commun. **2007**, *7*, 760.
Angew. Chem. Int. Ed. **2008**, *47*, 2497.

Iron-NHC ligand

- Well-defined Fe NHC piano stool complex



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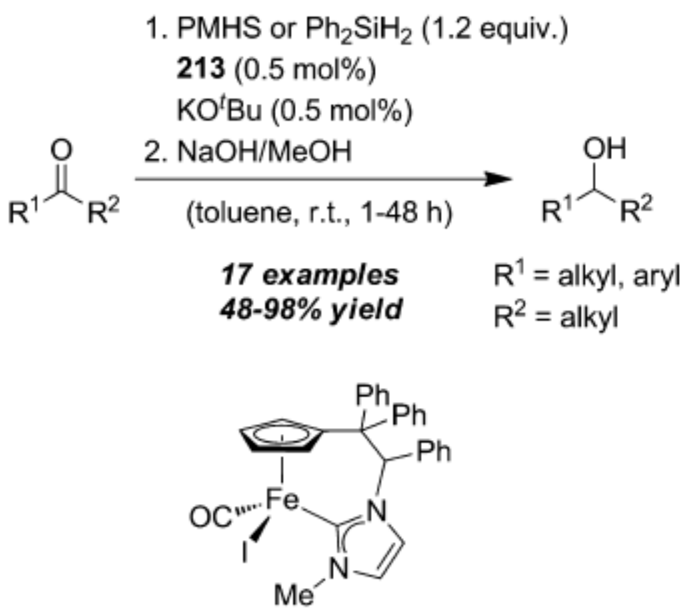
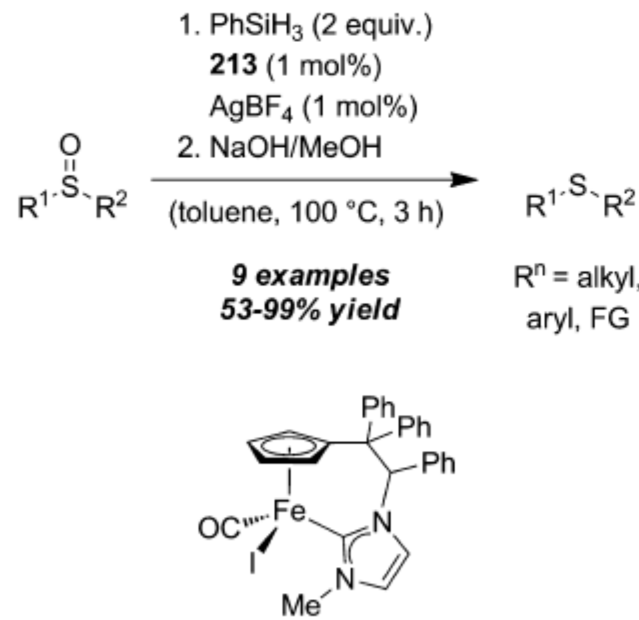
Chem. Commun. **2007**, *7*, 760.
Angew. Chem. Int. Ed. **2008**, *47*, 2497.

Iron-NHC ligand

- Method applied to other reductions with modified catalyst.



213



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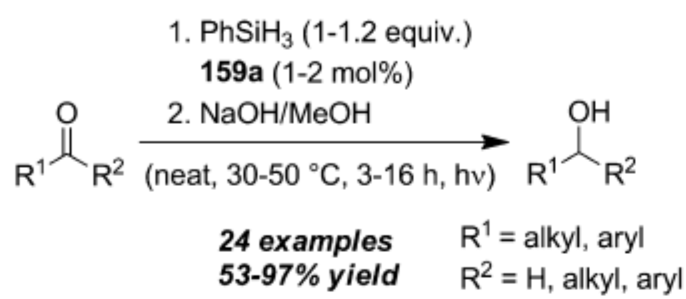
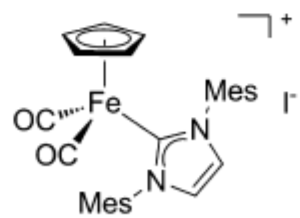
Chem. Commun. **2012**, *48*, 4944.
Catal. Lett. **2013**, *143*,1061

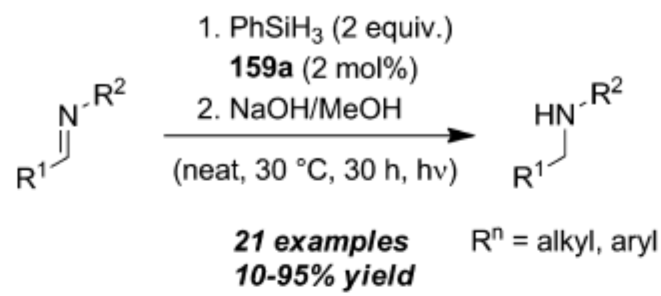
Iron-NHC ligand

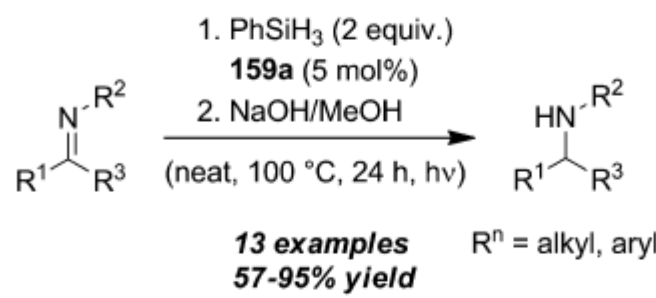
- Visible light irradiation
- Reduction of ketones, imines and amides.





159a

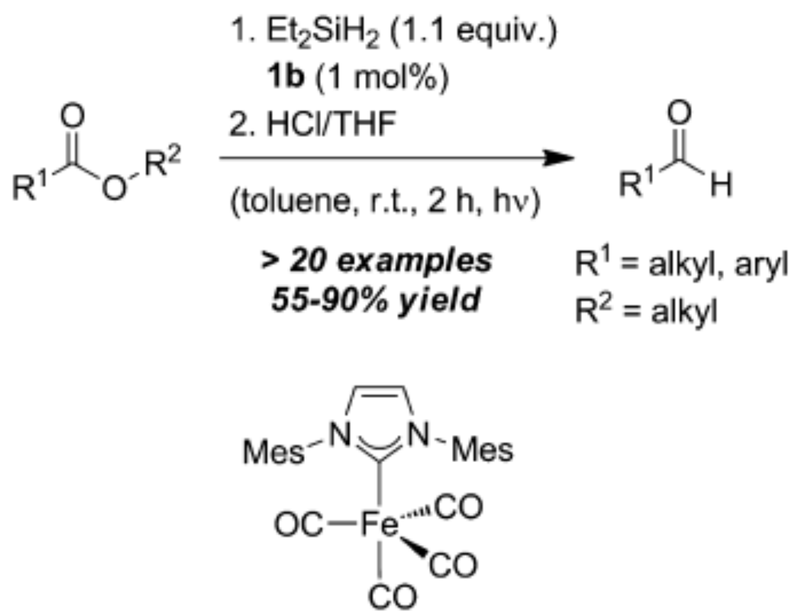




Chem.Commun. **2012**, *48,*151.
Eur. J. Inorg. Chem. **2012**, *2012,* 1333

Iron-NHC ligand

- Chemoselective reduction of esters to aldehyde
- Work with both aromatic and aliphatic esters



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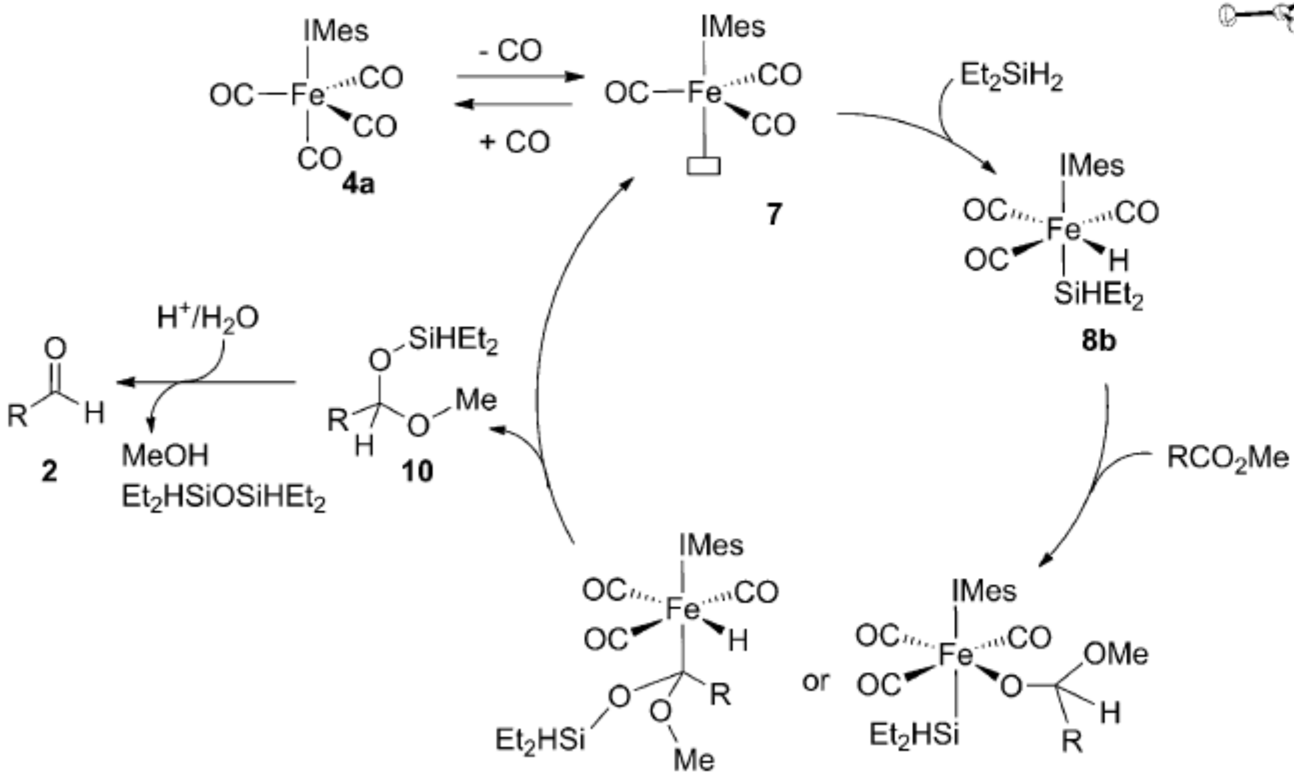
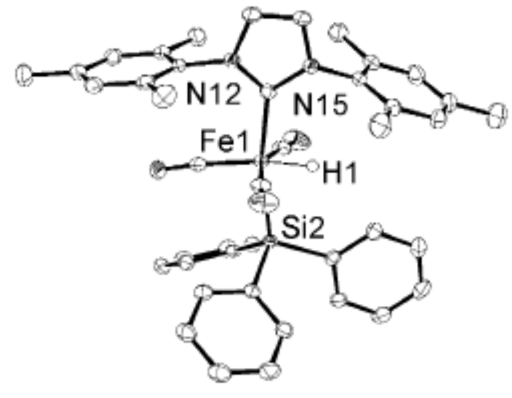
Angew. Chem., Int. Ed. **2013**, *52*, 8045.

Mechanism

- X-ray structure of iron-hydrid intermediate





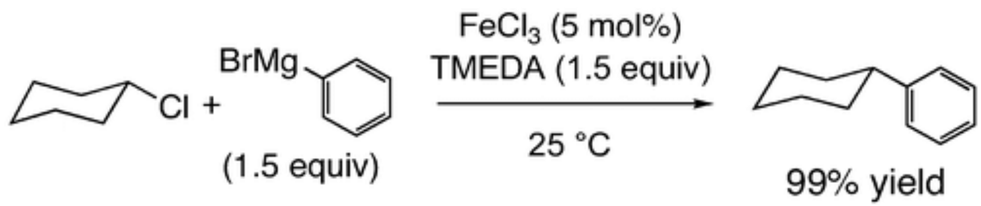
8a

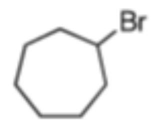
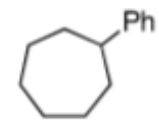
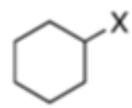
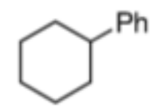
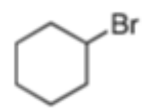
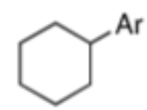
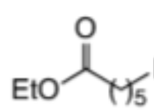
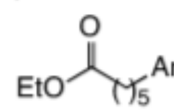
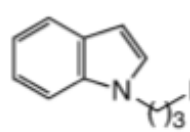
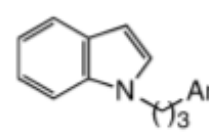
Angew. Chem., Int. Ed. **2013**, *52*, 8045.

Iron C-C Coupling Reaction

- Kumada-Type Coupling
- Oxidative Coupling (C-H activation)
- Reductive Coupling

Kumada-Type Coupling



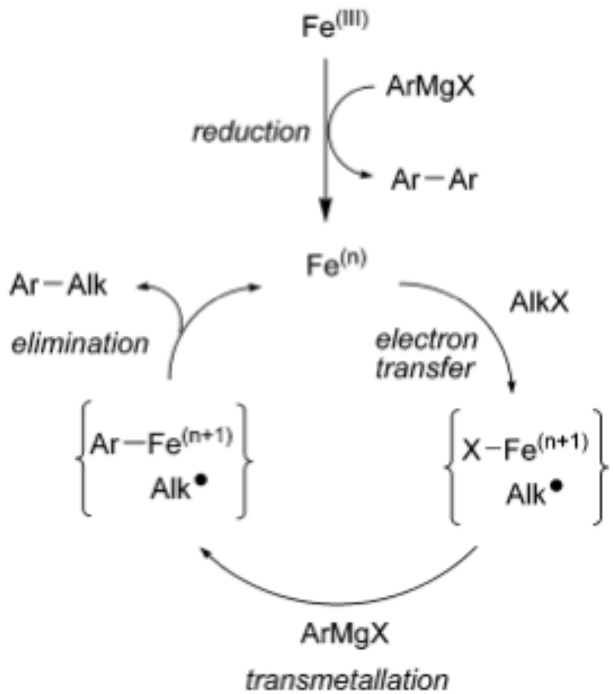
alkyl halide	ArMgBr	product	% yield[c,d]
	Ar = Ph		96 (90)[e,f]
	Ar = Ph		99 (X = I) 99 (X = Br)[e] 99 (X = Cl)[g]
	Ar = 4-MeOC_6H_4 Ar = 4-MeC_6H_4 Ar = 4-$CF_3C_6H_4$ Ar = 2-naphthyl Ar = 1-naphthyl Ar = 2-MeC_6H_4		99[e] 96[e] 67[e,h] 96 97[i] 98[e]
	Ar = 4-MeOC_6H_4		88[e]
	Ar = 4-MeOC_6H_4		87[e]

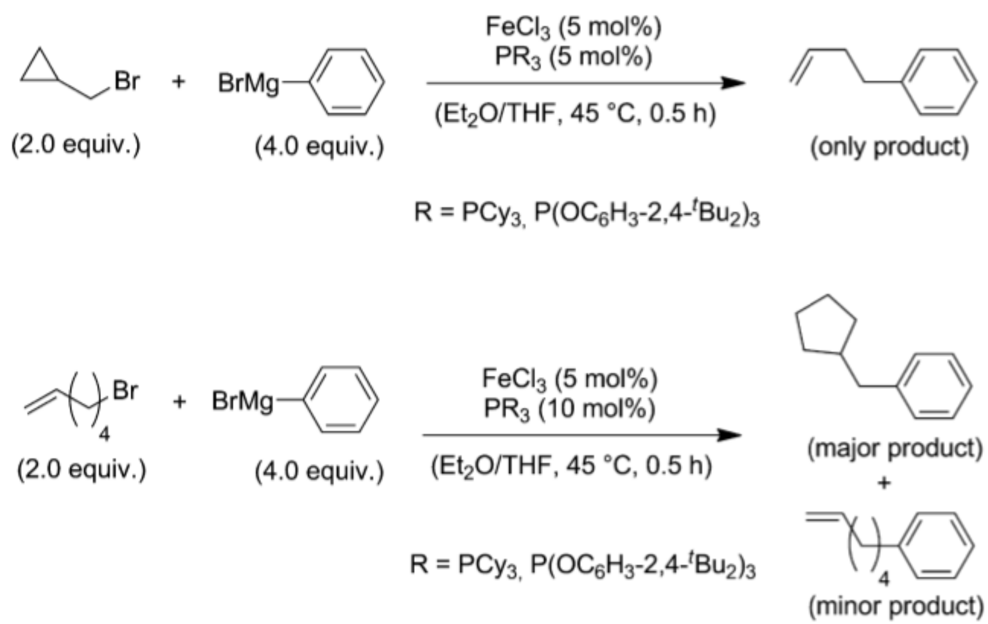
- Funtional group tolerance
- Worked with Cl, Br and I

J. Am. Chem. Soc. **2004**, *126*, 3686

Radical Pathway

- β-elimination

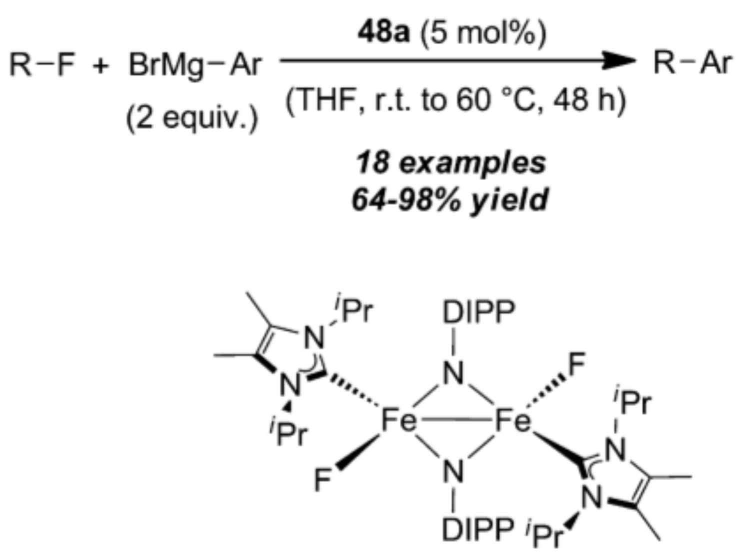




J. Org. Chem. **2006**, *71*, 1104-1110

Kumada-Type Coupling

- Coupling between alkyl fluoride and Grignard reagent

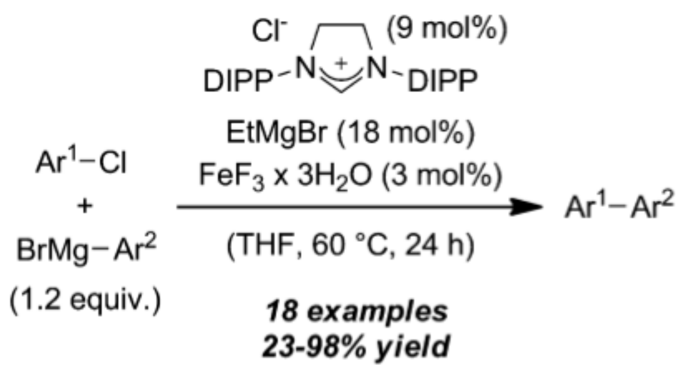


48a

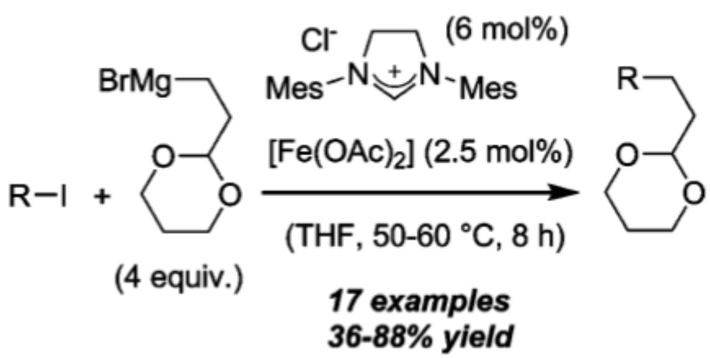
Organometallics **2012**, *31*, 6518.

Kumada-Type Coupling

- Using FeF_3 to overcome homo-coupling issues



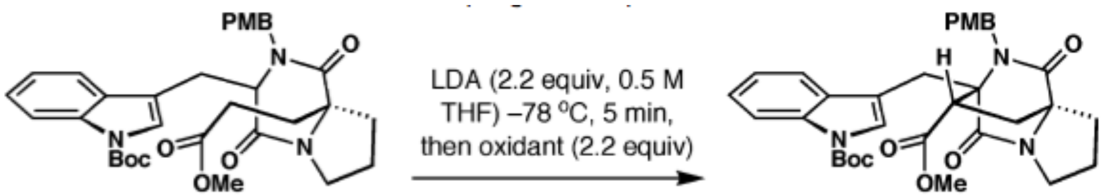
- Alkyl-alkyl coupling



J. Am. Chem. Soc. **2007**, *129*, 9844
J. Am. Chem. Soc. **2009**, *131*, 11949
J. Chem. Sci. **2013**, *4*, 1098

Iron Oxidative Coupling

- Total Synthesis of Avrainvillamide and the Stephacidins

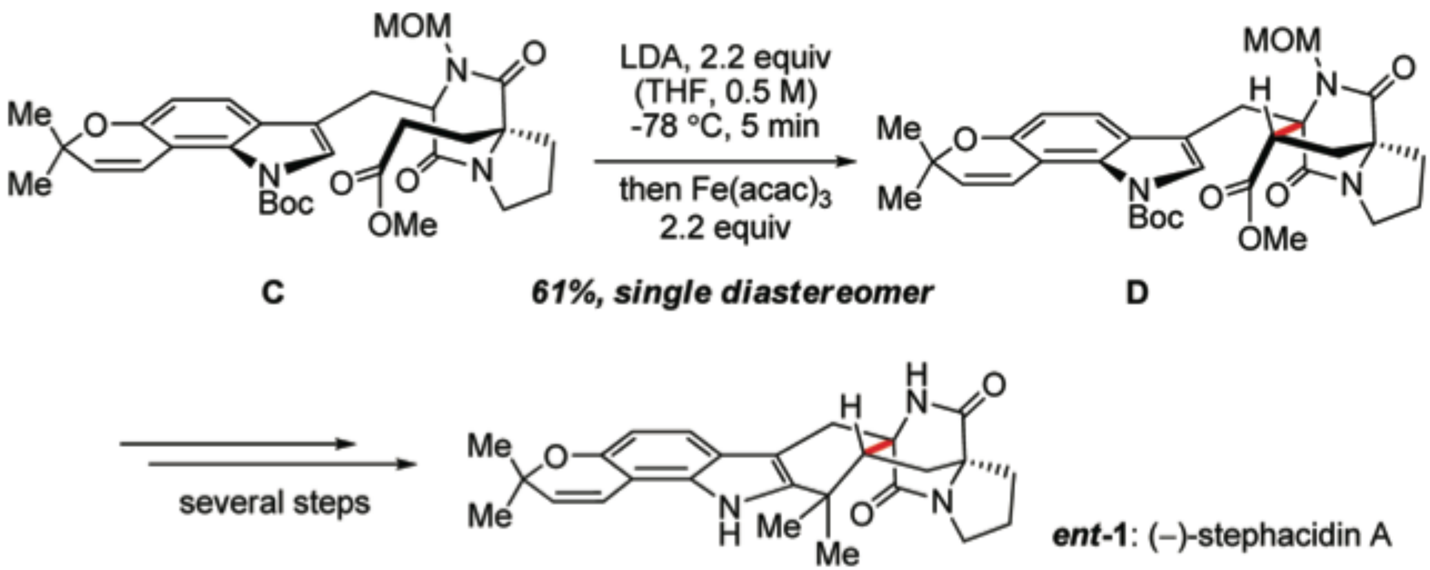


Entry	Oxidant (concentration)	[O] Potential (eV)	Yield[a] (%)
1	I_2 (0.05 M THF)	−0.39	0
2	$FeCl_3$ (0.2 M DMF)	*b*	31
3	$Fe(Cp)_2PF_6$ (0.2 M DMF)	−0.28	26
4	$Fe(acac)_3$ (0.2 M THF)	−1.14	65
5	$CuCl_2$ (0.2 M DMF)	*b*	39
6	$Cu(OTF)_2$ (0.2 M DMF)	*b*	35
7	Cu(4-cyclohexylbutyrate)$_2$ (0.1 M 1:1 THF:DMF)	*b*	19
8	Cu(2-ethylhexanoate)$_2$ (0.1 M THF)	−1.65	29

J. Am. Chem. Soc. **2006**, *128*, 8678

Iron Oxidative Coupling

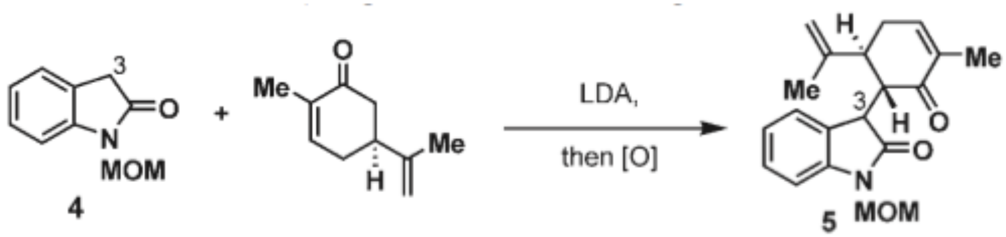
- Gram scale.



J. Am. Chem. Soc. **2006**, *128*, 8678

Iron Oxidative Coupling

- Tuning of the oxidant's oxidation potential

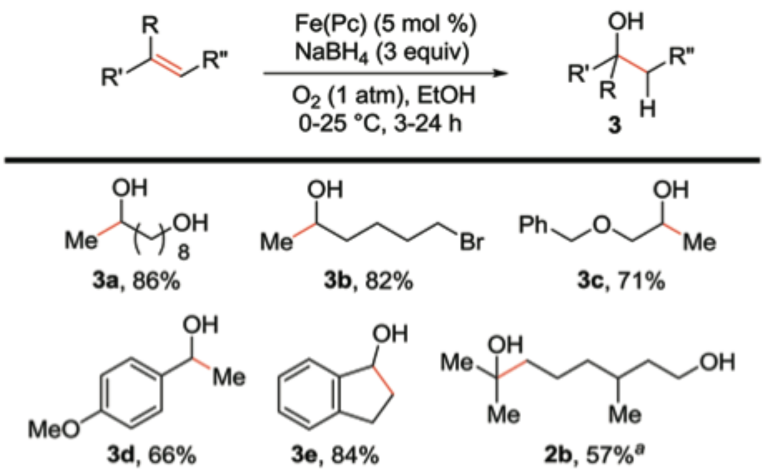


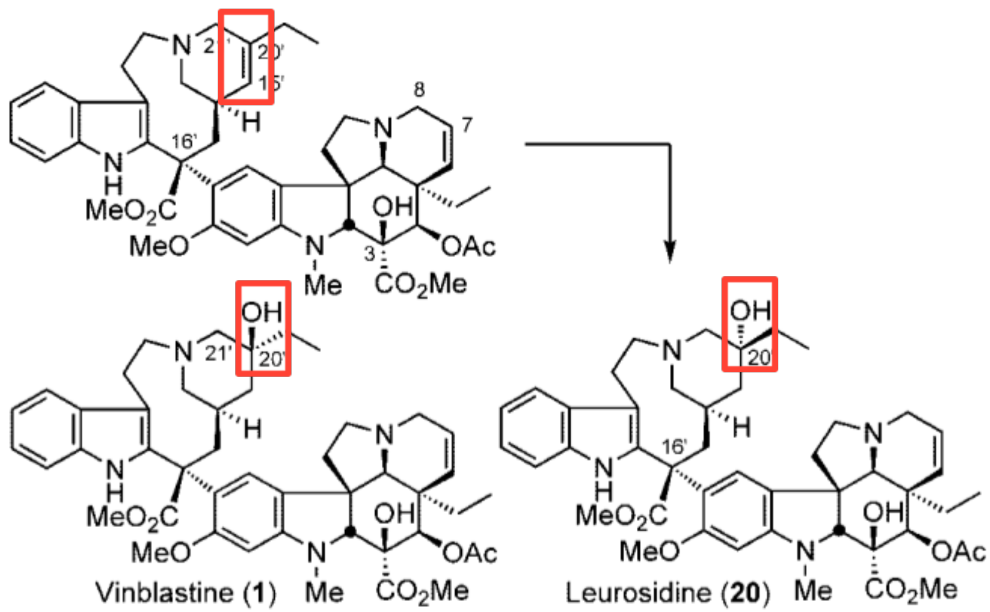
Entry	Oxidant	E_{ox} [eV][b]	Yield [%][c]
1	Cu(2-ethylhexanoate)$_2$	−1.65	15
2	PhI(OAc)$_2$	−1.53	≈10
3	[Fe(acac)$_3$]	−1.14	45
4	Fe(PhCOCHCOMe)$_3$	−1.07	30
5	**Fe(*t*BuCOCHCOCF$_3$)$_3$**	**−0.60**	**83**
6	Fe(MeCOCHCOCF$_3$)$_3$	−0.51	40
7	Fe(C$_{10}$H$_7$COCHCOCF$_3$)$_3$	−0.46	40

J. Am. Chem. Soc. **2008**, *130*, 11546
J. Am. Chem. Soc. **2008**, *130*, 17938
Angew. Chem., Int. Ed. **2006**, *45*, 7083–7086.

Iron Reductive Coupling

- Late stage chemoselective alkene hydration



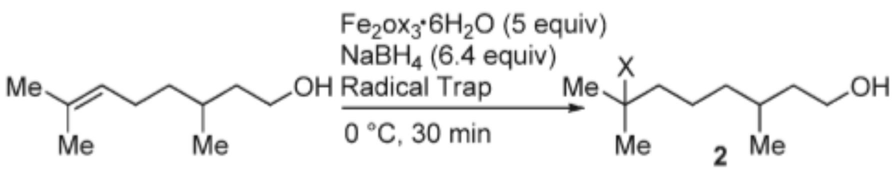


Conditions	Result	
1) $FeCl_3$ (30 equiv) air, 0 °C, 0.1 N HCl–glycine buffer 2) $NaBH_4$ (20 equiv), 0 °C, 30 min	trace **1**	trace **20**
1) $FeCl_3$ (30 equiv), $(CO_2NH_4)_2$ (60 equiv) air, 0 °C, 0.1 N HCl–CF_3CH_2OH 2) $NaBH_4$ (20 equiv), 0 °C, 30 min	35–40% **1**	14–18% **20**
1) $Fe_2(ox)_3$ (30 equiv, suspension) air, 0 °C, 0.1 N HCl–CF_3CH_2OH 2) $NaBH_4$ (20 equiv), 0 °C, 30 min	50% **1**	20% **20**

J. Am. Chem. Soc. **2009**, *131*, 4904
Org. Lett. **2012**, *14*, 1428.

Radical Trap

- Radical intermediate

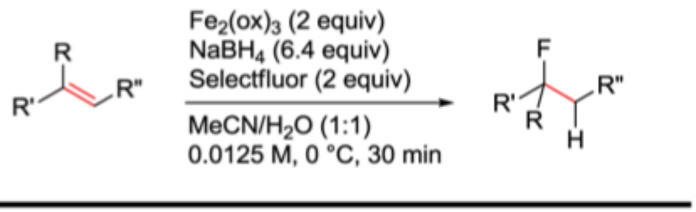


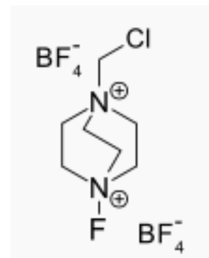
entry[a]	radical trap (equiv)	product	yield
1	NaN_3 (3)	X = N_3, **1a**	88%
2	KSCN (10)	X = SCN, **2a**	77%
3	air	X = OH, **2b**	68%[4]
4	4-$AcNHC_6H_4SO_2Cl$ (5)	X = Cl, **2c**	62%
5	KOCN (10)	X = $NHCONH_2$, **2d**	50%
6	TsCN (4)	X = CN, **2e**	35%
7	TEMPO (3)	X = TEMPO, **2f**[b]	44%[4]
8	$NaNO_2$ (60)	X = NO, **2g**	41%[4]

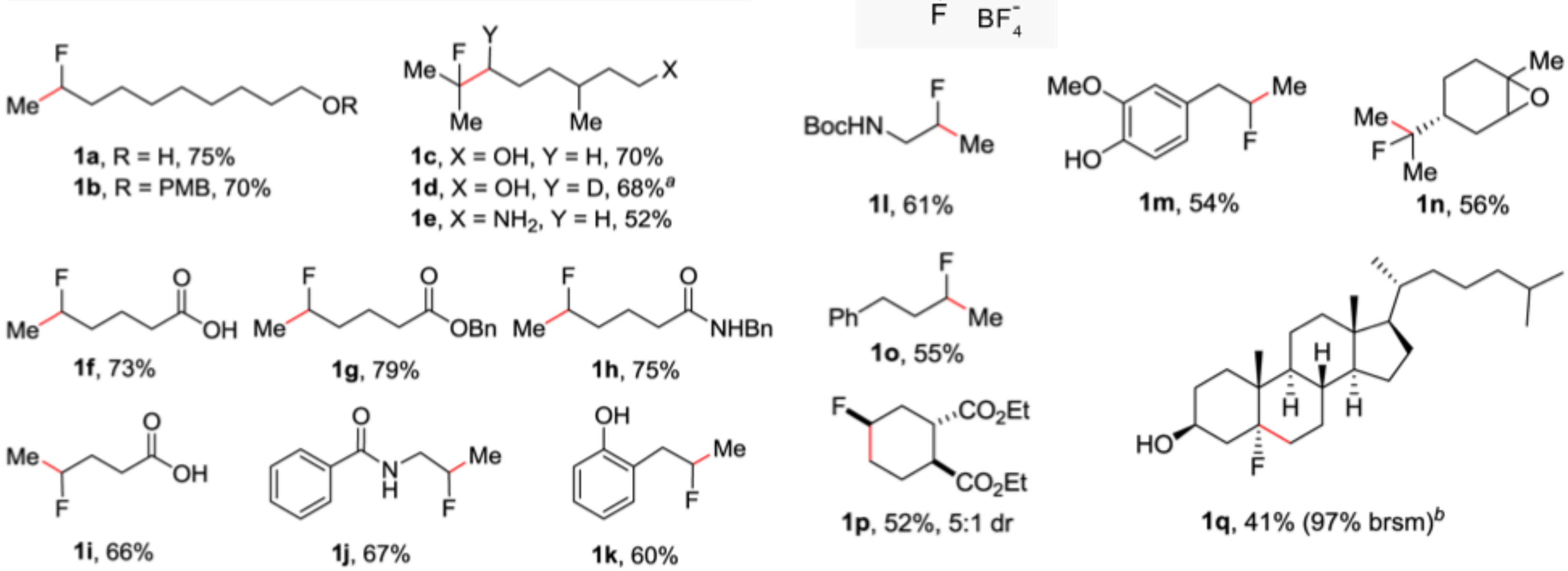
Org. Lett. **2012**, *14*, 1428.

Iron Radical Hydrofluorination

- Hydrofluorination of unactivated alkene





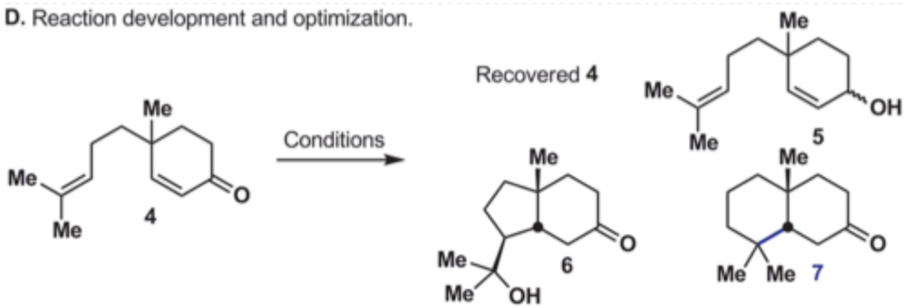


J. Am. Chem. Soc. **2012**, *134*, 13588

Iron Reductive Coupling

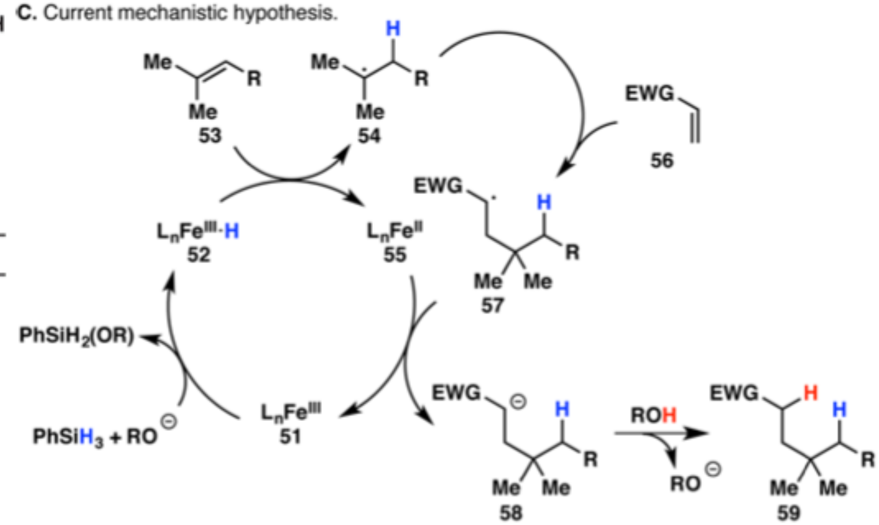
- Trapped by alkenes with EWG

D. Reaction development and optimization.



Entry	Fe(III) Salt	Reductant	Solvent	T (°C)	4[a]	5[a]	6[a]	7[a]
1	$Fe_2(ox)_3{\bullet}6H_2O$ (2.0 equiv)	$NaBH_4$	$EtOH/H_2O$	0	20	5	0	75
2	$Fe_2(ox)_3{\bullet}6H_2O$ (2.0 equiv)	$NaBH(OAc)_3$	THF/H_2O	0 to rt	89	0	5	6
3	$Fe_2(ox)_3{\bullet}6H_2O$ (2.0 equiv)	$(TMS)_3SiH$	THF/H_2O	0 to 60	23	0	77	0
4	$Fe_2(ox)_3{\bullet}6H_2O$ (2.0 equiv)	Et_3SiH	THF/H_2O	0 to 60	0	0	100	0
5	$Fe_2(ox)_3{\bullet}6H_2O$ (2.0 equiv)	$PhSiH_3$	$EtOH/H_2O$	0 to rt	15	0	11	74
6	$Fe(acac)_3$ (1.0 equiv)	Et_3SiH	EtOH	60	100	0	0	0
7	**$Fe(acac)_3$ (1.0 equiv)**	**$PhSiH_3$**	**EtOH**	**60**	**0**	**0**	**0**	**100**
8	**$Fe(acac)_3$ (30 mol%)**	**$PhSiH_3$**	**$EtOH/(CH_2OH)_2$**	**60**	**0**	**0**	**0**	**100**

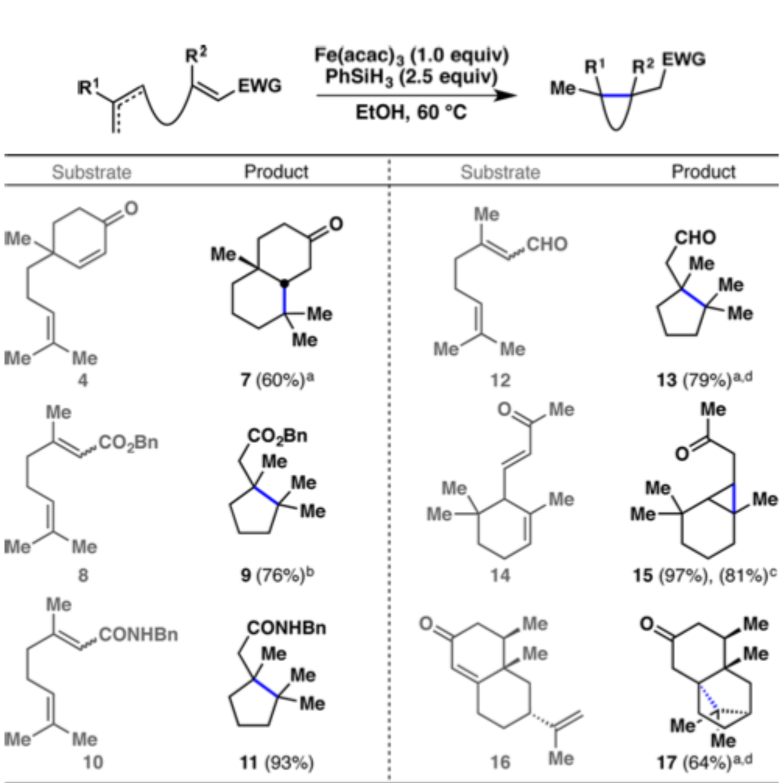
C. Current mechanistic hypothesis.

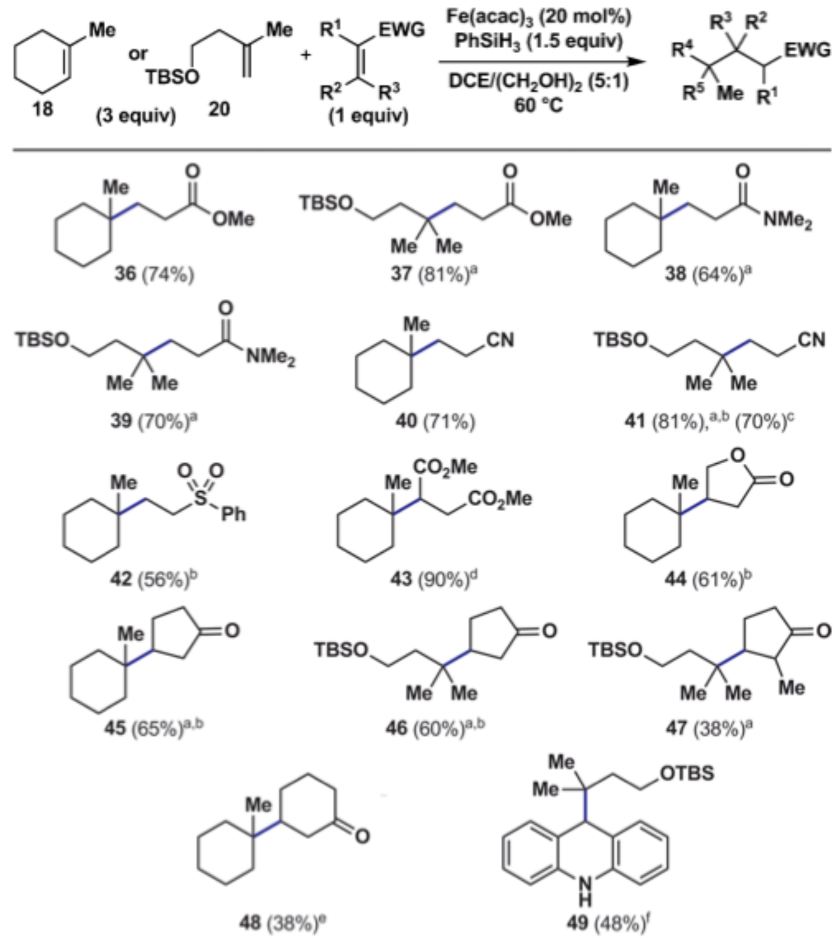


J. Am. Chem. Soc. **2014**, *136*, 1304

Iron Reductive Coupling

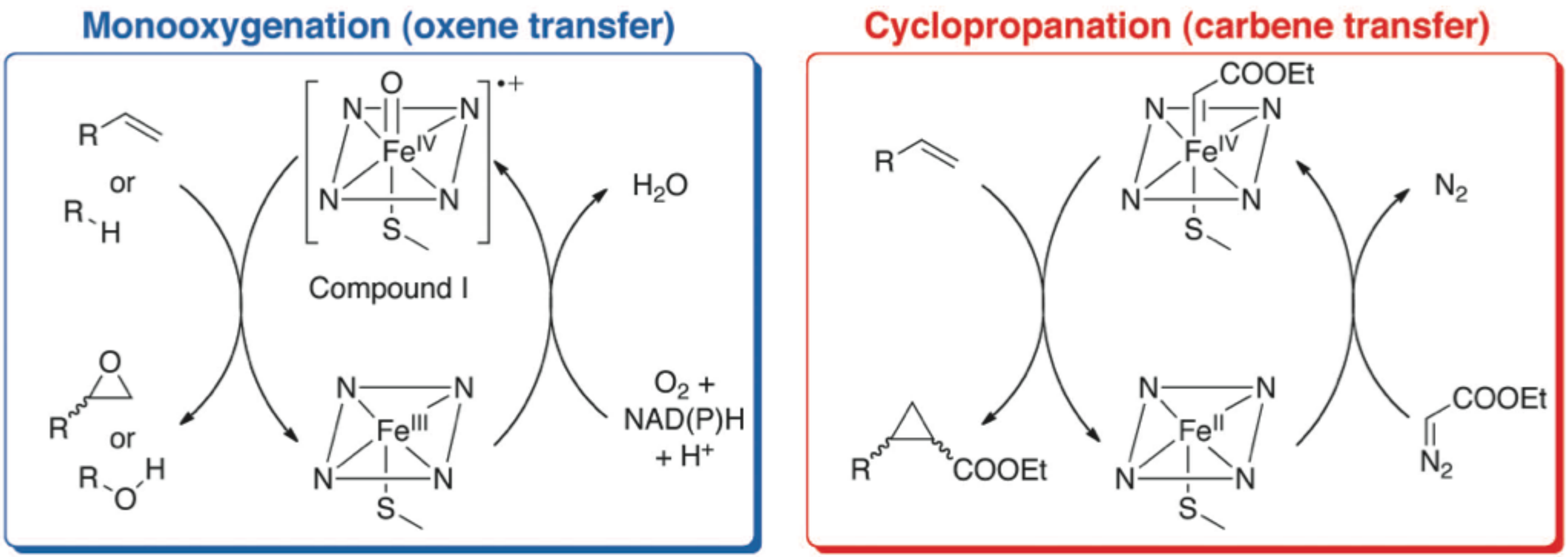
- Work with both intra- and intermolecular fashion





J. Am. Chem. Soc. **2014**, *136*, 1304

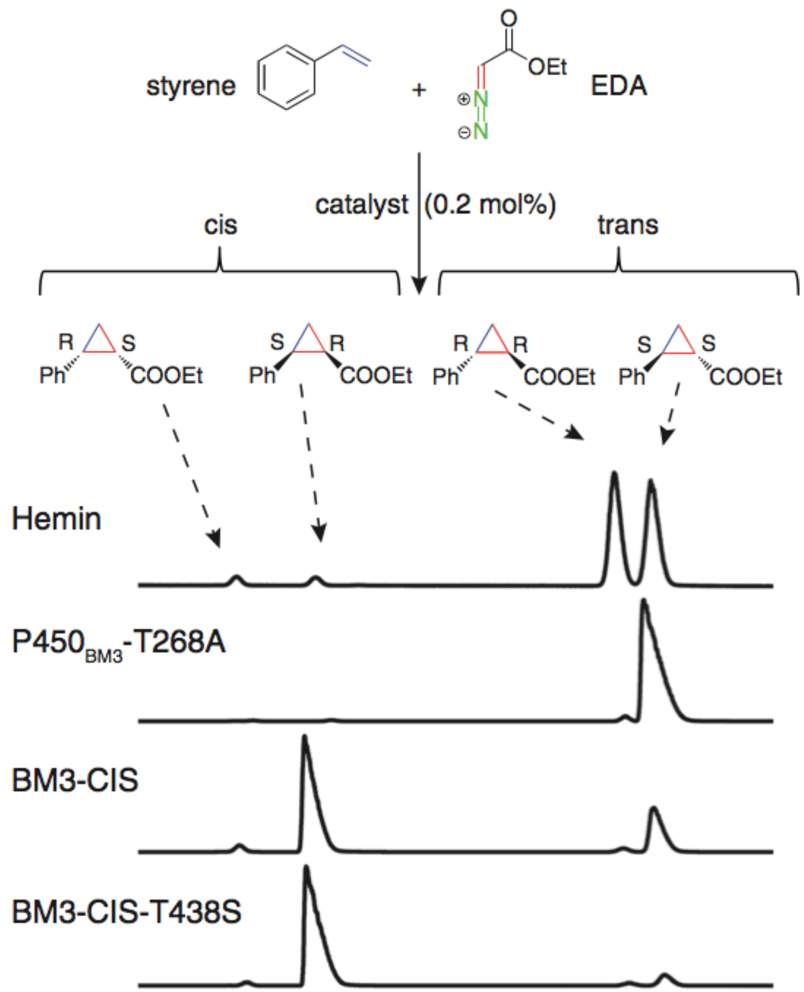
Iron-Carbene Complex



Science. **2013**, *339*, 307

Iron-Carbene Complex

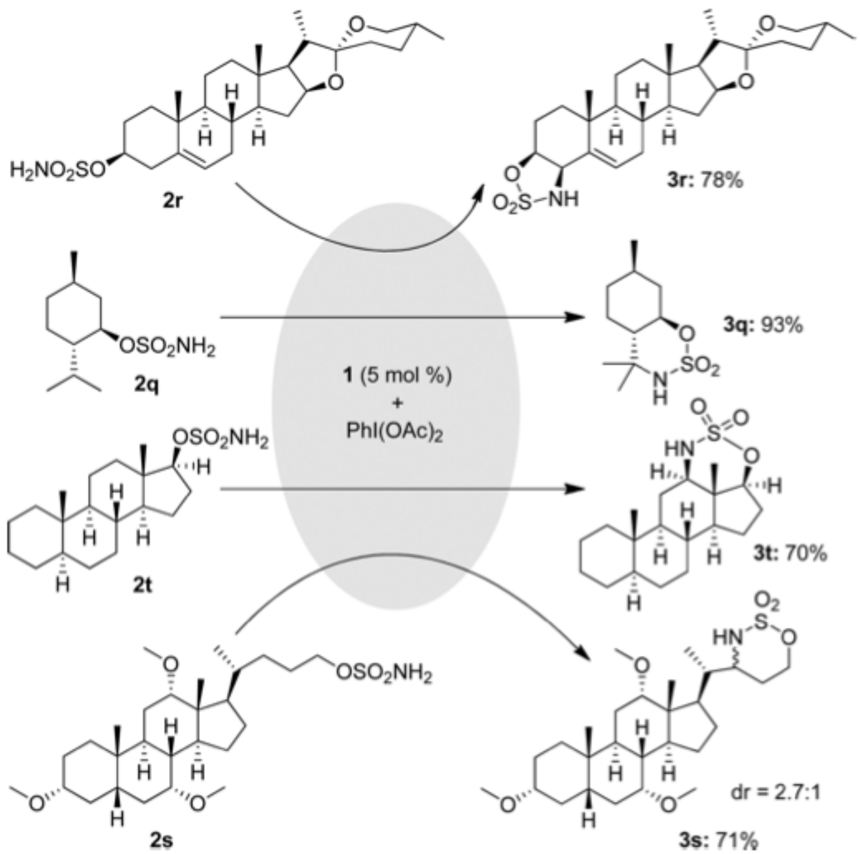
- A simple mutation could result in synthetically useful selectivities
- Directed evolutions can generate a spectrum of highly active catalysts

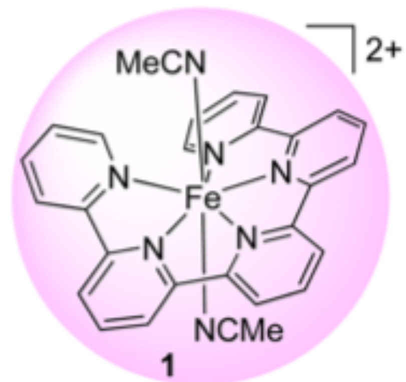


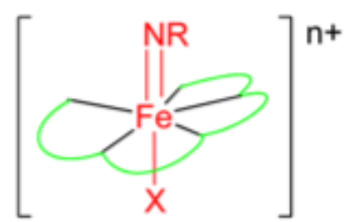
Science. **2013**, *339*, 307

Iron-Nitrene Complex

- Intramolecular nitrene insertion



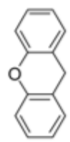
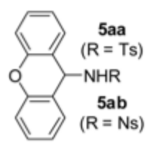
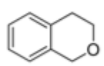
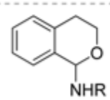
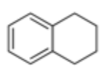
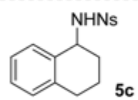
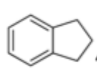
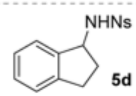
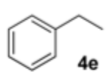
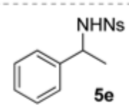
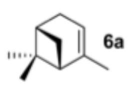
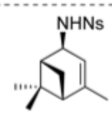
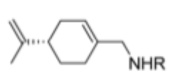


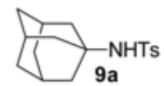
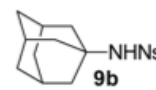
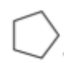
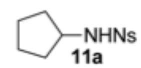
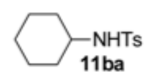
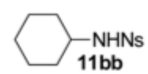
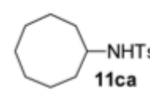
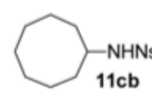


J. Am. Chem. Soc. **2013**, *135*, 7194

Iron-Nitrene Complex

- Intermolecular C-H insertion

entry	substrate	nitrogen source	product	yield (%)[b]
1	 4a	PhI=NTs	 5aa (R = Ts)	75 (5aa)
2		PhI=NNs	5ab (R = Ns)	81 (5ab)
3	 4b	PhI=NTs	 R = Ts 5ba, Ns 5bb	80 (5ba)
4		PhI=NNs		86 (5bb)
5	 4c	PhI=NNs	 5c	76
6	 4d	PhI=NNs	 5d	79
7[c]	 4e	PhI=NNs	 5e	67
8	 6a	PhI=NNs	 7a	53
9	 6b	PhI=NTs	 R = Ts 7ba, Ns 7bb	63 (7ba)
10		PhI=NNs		57 (7bb)

entry	substrate	nitrogen source	conv (%)[b]	product	yield (%)[c]
1	 8	PhI=NTs	73	 9a	63 (86[d])
2	 8	PhI=NNs	75	 9b	51 (68[d])
3[e]	 10a	PhI=NNs	-	 11a	52[f]
4	 10b	PhI=NTs	49	 11ba	33 (68[d])
5	 10b	PhI=NNs	56	 11bb	41 (73[d])
6	 10c	PhI=NTs	52	 11ca	38 (74[d])
7		$PhI(OAc)_2$ + H_2NTs	42		27 (64[d])
8	 10c	PhI=NNs	60	 11cb	49 (82[d])
9		$PhI(OAc)_2$ + H_2NNs	49		37 (76[d])

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Conclusion

- Single electron transfer/mechanism study
- C-H activation
- Enzyme P450 bio-inspired chemistry
- Ligand development: NHC ligand etc.
- Limited substrate scope and functional group tolerance
- Co, Mn and Ni

Reviews

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