First Row TM Catalyzed C-H Activation

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Outline

- 1. Introduction
- 2. Sc catalyzed C-H activation
- 3. Ti catalyzed C-H activation
- 4. V catalyzed C-H oxidation/fluorination
- 5. Mn catalyzed C-H activation
- 6. Fe catalyzed C-H activation
- 7. Ni catalyzed C-H activation
- 8. Summary

Introduction

- First row metal catalyzed C-H activation is much less compare to the second row.
- Most of them are cheaper than the second row.
- V, Mn and Cr are well known to oxidation C-H bonds, but most through radical process, which metal is not attached to

Introduction

- Price comparation: Which metal is the most expensive and which is the least expensive one?
- Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn

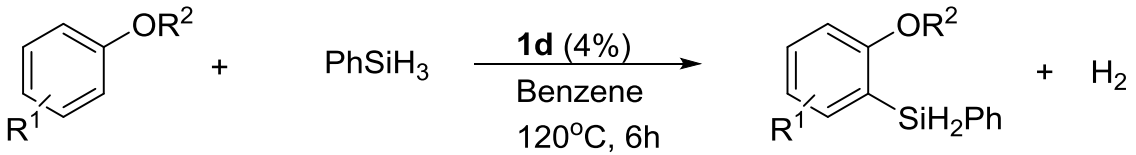
Introduction

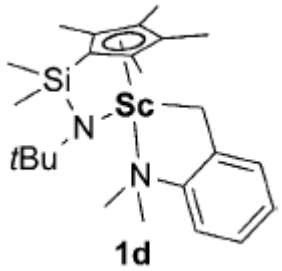
- Price comparation:
- Sc $3123.66/mol
- Co $ 280.22/mol
- V $210.43/mol
- Cr $161.18/mol
- Mn $40.51/mol
- Ti $4.63/mol
- Ni $1.12/mol
- Cu $0.45/mol
- Zn $0.15/mol
- Fe $0.0054/mol

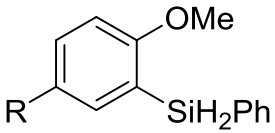
Sc catalyzed C-H activation

- Sc works as LA in most reactions it catalyzed.
- The directed catalytic C-H activation works are all from Zhaomin Hou's group.
- Sc complex can activate methane. These works are from Don Tilley's group.

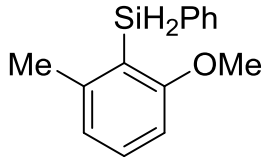
Sc catalyzed C-H activation



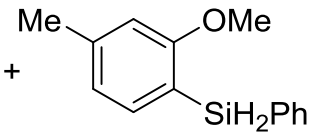




3b when R = Me, yield is 89% (89% GC yield)
3c when R = OMe, yield is 90% (94% GC yield)
3d when R = F, yield is 79% (84% GC yield)
3e when R = Cl, yield is 88% (94% GC yield)
3f when R = Br, yield is 68% (88% GC yield)
3g when R = I, yield is 51% (57% GC yield)
3h when R = SMe, yield is 51% (57% GC yield)
3i when R = NMe_2 , yield is 51% (57% GC yield)

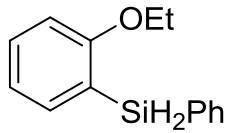


3ja

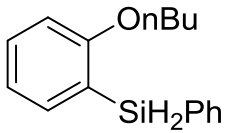


3jb

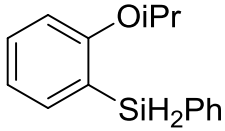
72% yield, **a:b=1:6**



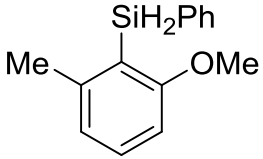
2l
69% (72% GC yield)



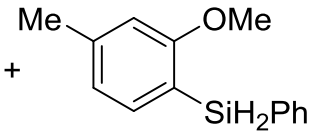
3m
70% (72% GC yield)



3n
17%

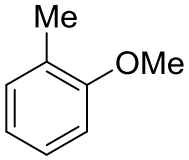


3ka

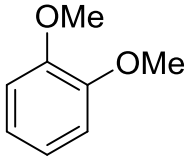


3kb

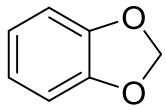
83% yield, **a:b=1.8:1**



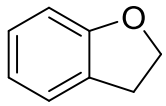
n.r.



n.r.



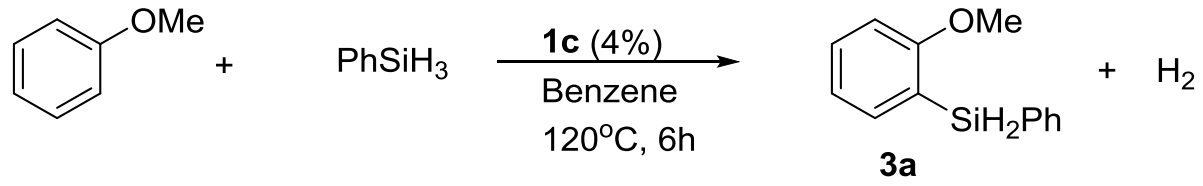
n.r.

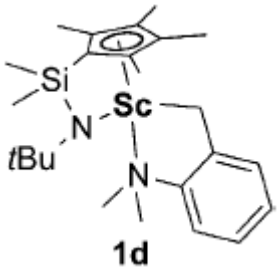


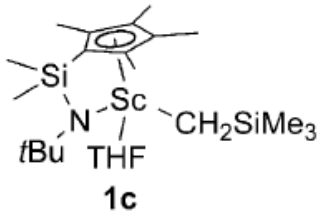
trace

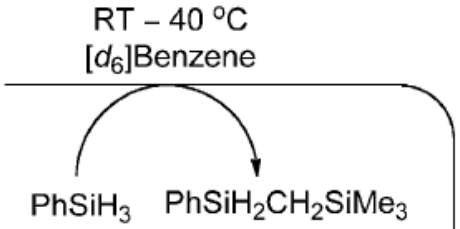
Angew. Chem. Int. Ed. **2011**, *50*, 10720–10723

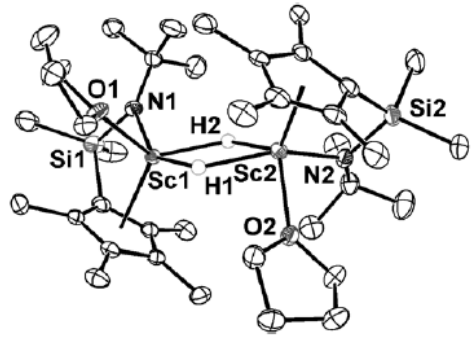
Sc catalyzed C-H activation

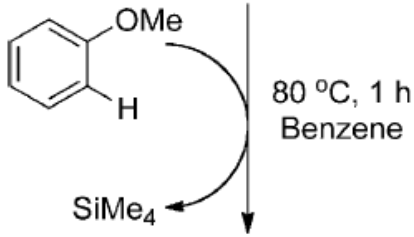


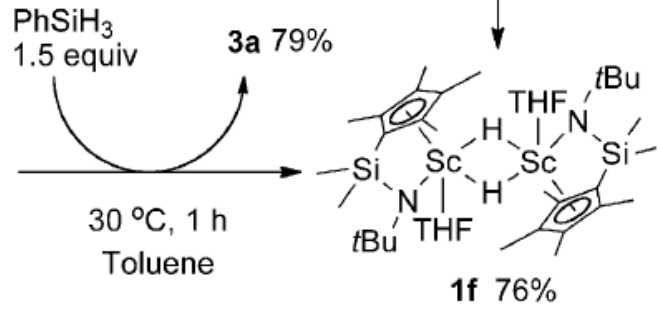


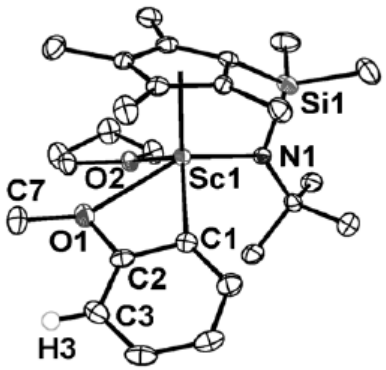


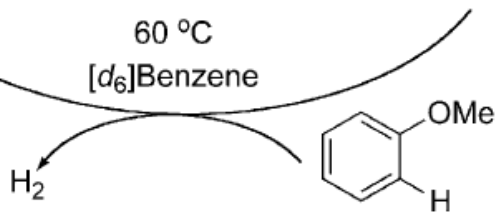












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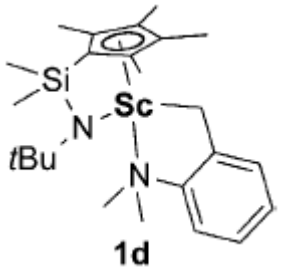
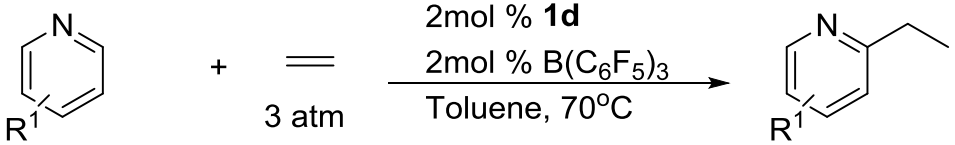
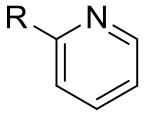
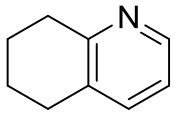


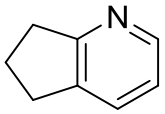




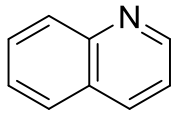
1 when R = Me, yield is 98%, 22h
2 when R = Et, yield is 99%, 8h
3 when R = i-Pr, yield is 96%, 14h
4 when R = t-Bu, yield is 97%, 3h
5 when R = Ph, yield is 98%, 48h
6 when R = Br, yield is 91%, 48h
7 when R = I, yield is 97%, 48h



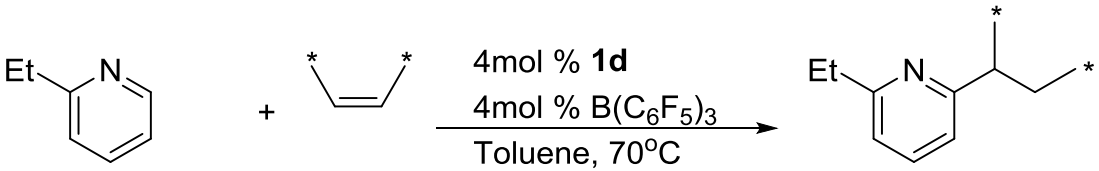
8
96%, 36h

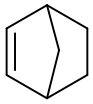


9
94%, 24h

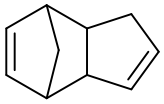


10
86%, 12h

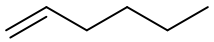




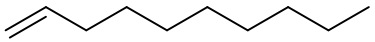
11
98%, 4h



12
99%,12h



13
95%, 32h



14
95%, 48h

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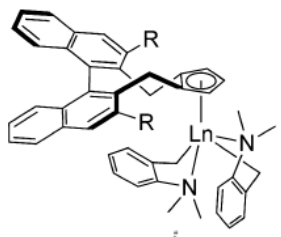
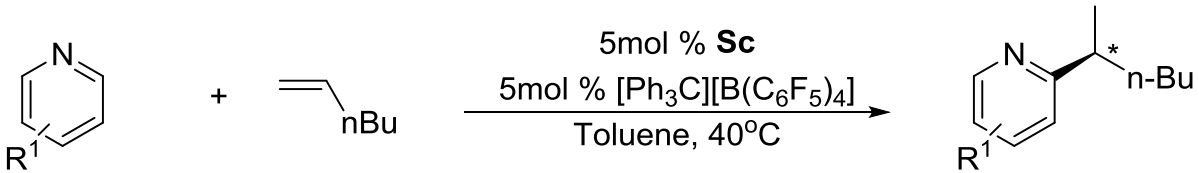
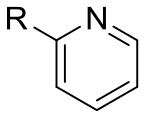
Sc catalyzed C-H activation

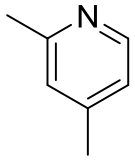


c: R = OSi(^{i}Pr)$_3$
Ln = Sc

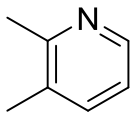




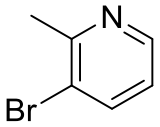
1 when R = Me, yield = 98%, 88% ee, 72h
2 when R = Et, yield = 93%, 86% ee, 72h
3 when R = i-Pr, yield = 94%, 76% ee, 72h
4 when R = t-Bu, yield = 83%, 84% ee, 72h, 15°C
yield = 98%, 56% ee, 24h, 25°C
5 when R = Ph, yield is 94%, 84% ee, 72h
6 when R = Br, yield is 85%, 88% ee, 48h
7 when R = I, yield is 87%, 88% ee, 72h



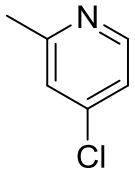
8 93%,
96% ee, 72h



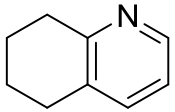
9 95%,
90% ee, 48h



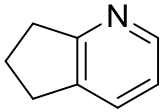
10
95%, 74% ee, 24h
94%, 90% ee, 48h, 25°C



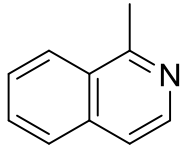
11 91%,
92% ee, 48h



12 93%,
84% ee, 72h

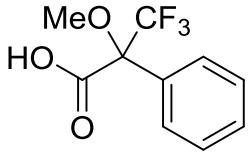


13 **63**%,
86% ee, 96h



14 81%,
94% ee, 72h

a.For entry 3,4, 5, 6, 7, 12,ee was determined by ^{13}C NMR in the presence of Mosher's acid.



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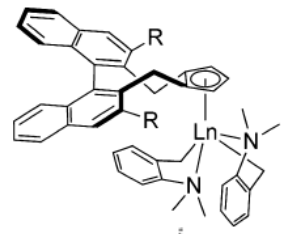
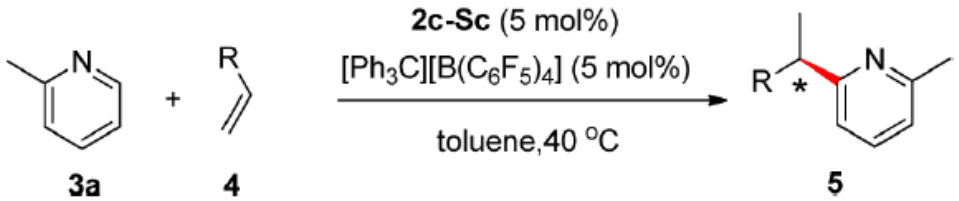
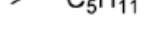
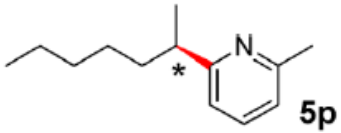
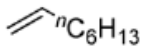
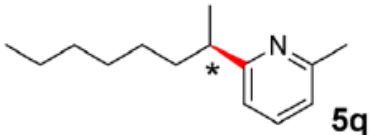
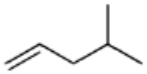
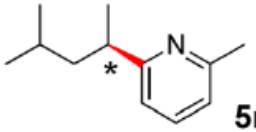
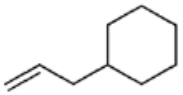
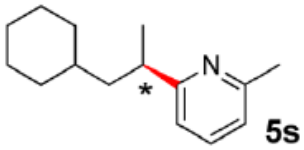
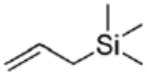
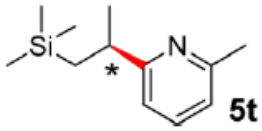
Sc catalyzed C-H activation



c: R = OSi(^{i}Pr)$_3$
Ln = Sc

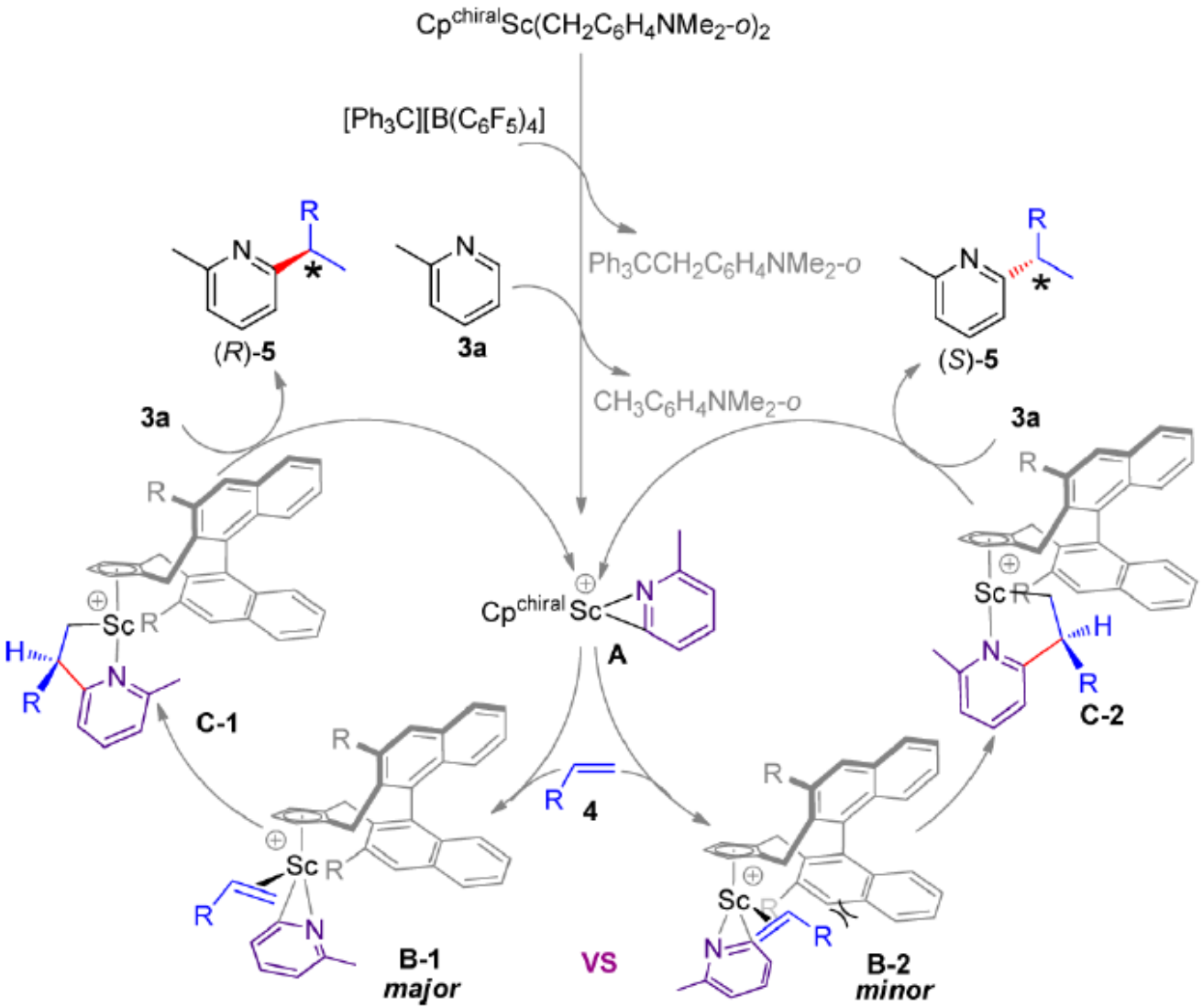


entry	substrate	time (h)	product	yield (%)	er[b]
1		48	 **5p**	92	93:7
2		72	 **5q**	92	93:7
3		96	 **5r**	95	90:10
4		72	 **5s**	94	91:9
5		72	 **5t**	80	86:14

[a]Reaction conditions: **3a** (0.2 mmol), **4** (2 mmol, 10 equiv), **2c-Sc** (5 mol %), $[Ph_3C][B(C_6F_5)_4]$ (5 mol %), toluene (1.0 mL), 40 °C, isolated yield. [b]Determined by chiral HPLC.

J. Am. Chem. Soc. 2014, 136, 12209−12212

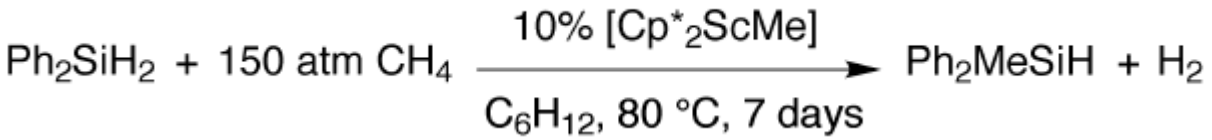
Sc catalyzed C-H activation



J. Am. Chem. Soc. 2014, 136, 12209–12212

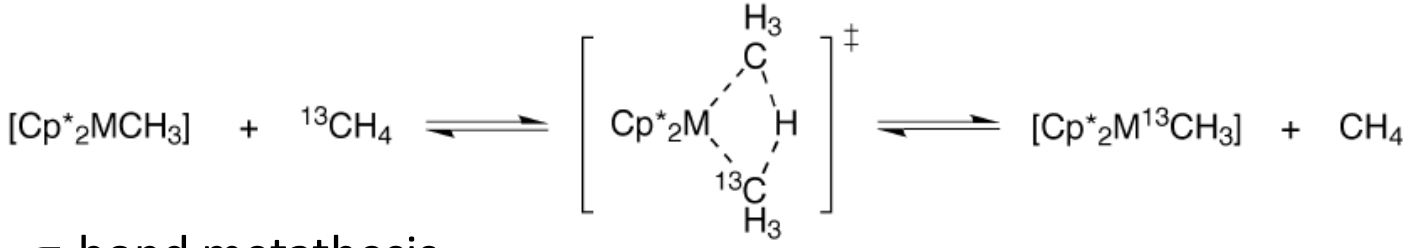
Sc catalyzed C-H activation

- Don Tilley's group



50 turnovers!

After 4 days: 85% 42% 15%

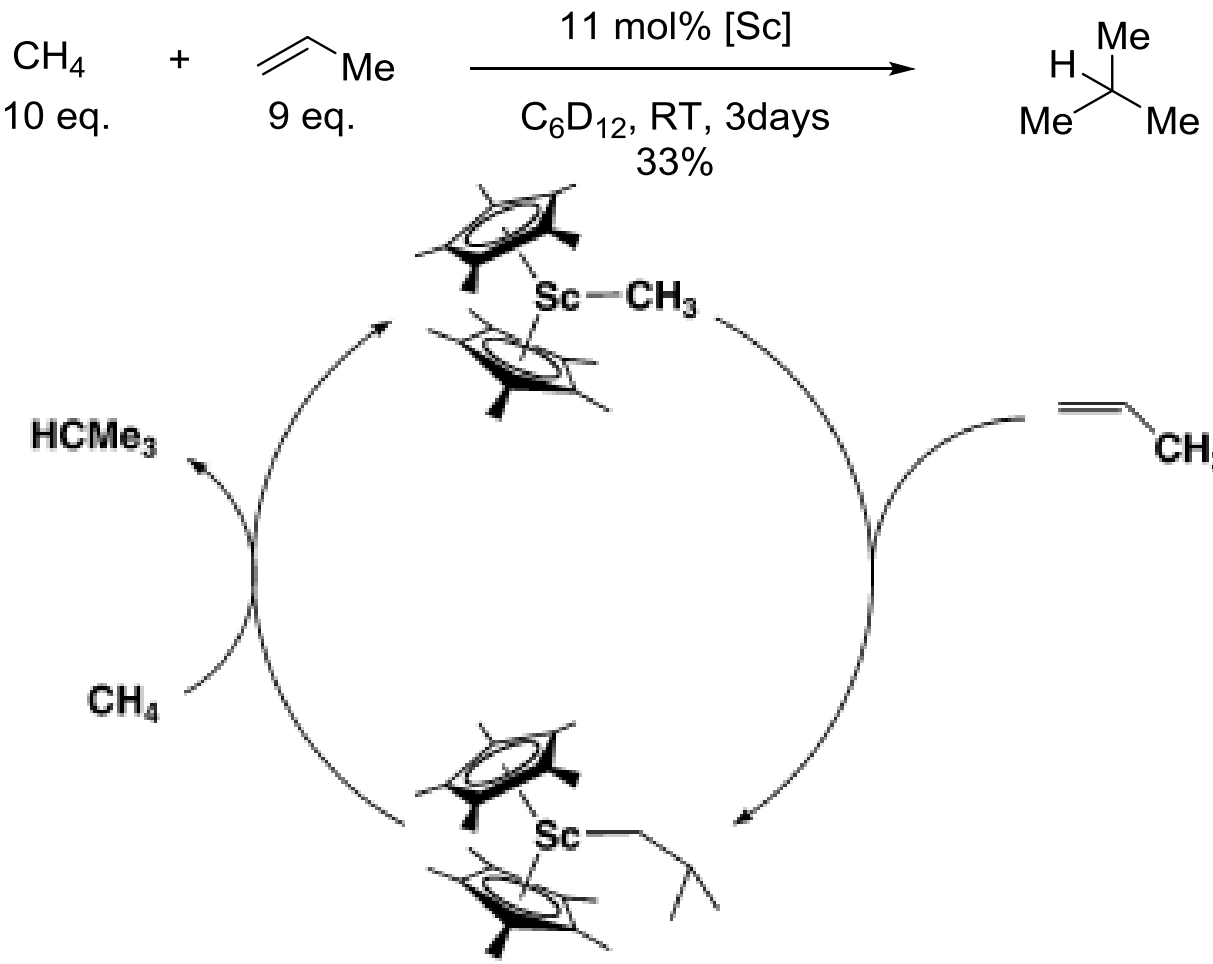


σ-bond metathesis

Angew. Chem. Int. Ed. 2003, 42, No. 7, 803

Sc catalyzed C-H activation

- Don Tilley's group

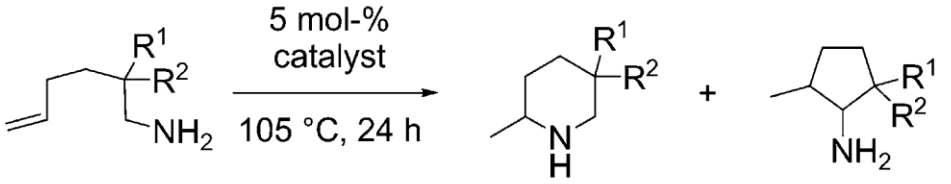


J. AM. CHEM. SOC. 2003, *125*, 7971−7977

Ti catalyzed C-H activation

- Ti works as LA in most reactions it catalyzed.
- Ti is also know for polymerization of alkenes.
- The hydroaminoalkylation reactions presented are all from Sven Doye's group.
- The most common hydroaminoalkylation reactions are catalyzed by Ta.

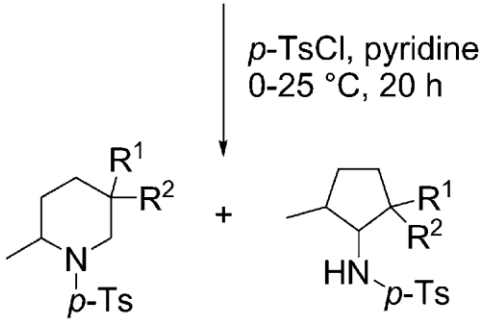
Ti catalyzed C-H activation



16: $R^1 = R^2 = Me$
17: $R^1 = Ph$, $R^2 = Me$

18: $R^1 = R^2 = Me$
20: $R^1 = Ph$, $R^2 = Me$

19: $R^1 = R^2 = Me$
21: $R^1 = Ph$, $R^2 = Me$



22: $R^1 = R^2 = Me$ **23**: $R^1 = R^2 = Me$

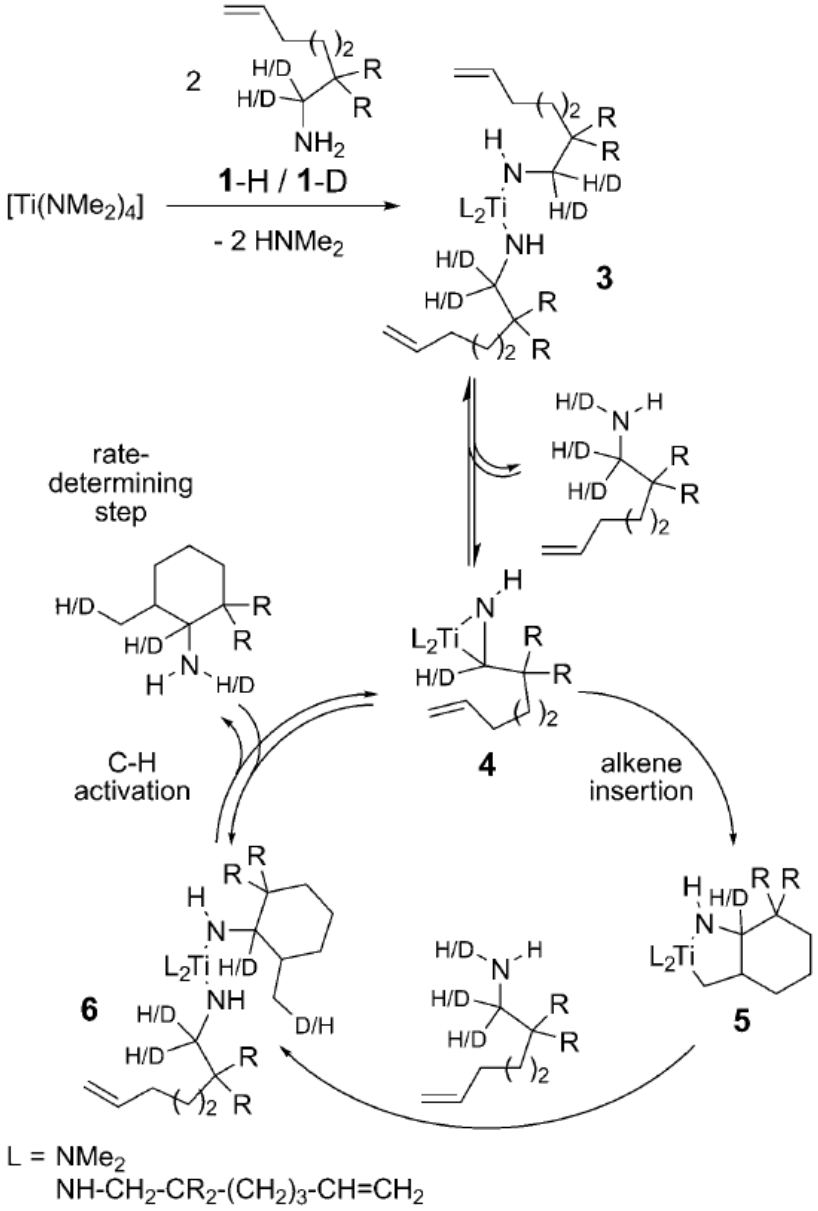
catalyst:	$Ti(NMe_2)_4$	72 %	26 %[a]
	Ind_2TiMe_2	71 %	28 %[a]
	Ind_2ZrMe_2	95 %	-
	Ind_2HfMe_2	24 %	-

24: $R^1 = Ph$, $R^2 = Me$ **25**: $R^1 = Ph$, $R^2 = Me$

catalyst:	$Ti(NMe_2)_4$	79 %[b,c,d]	17 %[b,c,e]
	Ind_2TiMe_2	79 %[b,c,f]	16 %[b,c,e]
	Ind_2ZrMe_2	98 %[c,g]	-
	Ind_2HfMe_2	53 %[c,g]	-

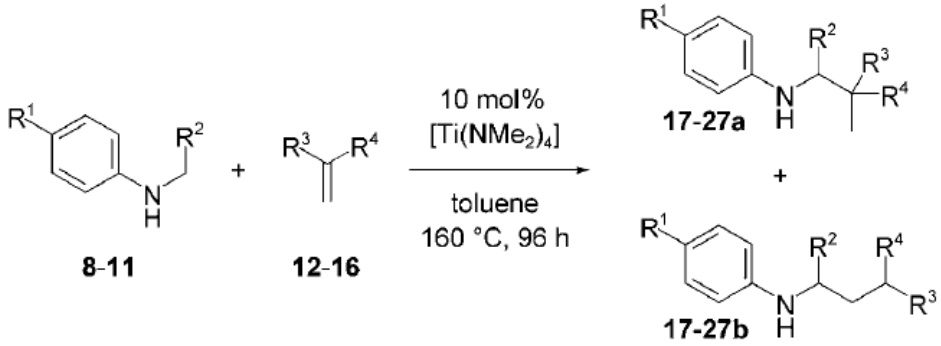
Eur. J. Org. Chem. **2008**, 2731–2739

Ti catalyzed C-H activation



Angew. Chem. Int. Ed. **2011**, 50, 6401 –6405

Ti catalyzed C-H activation

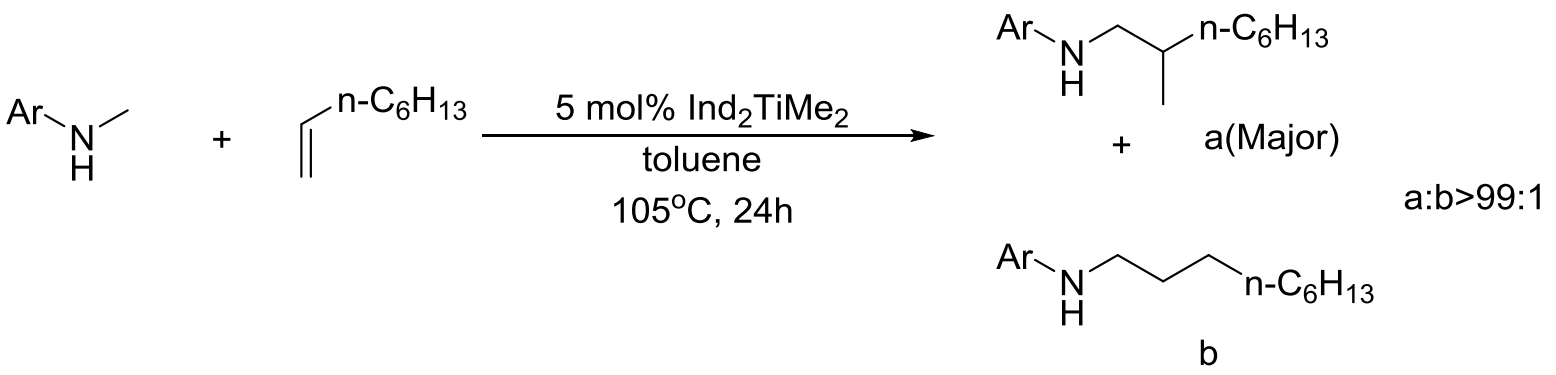


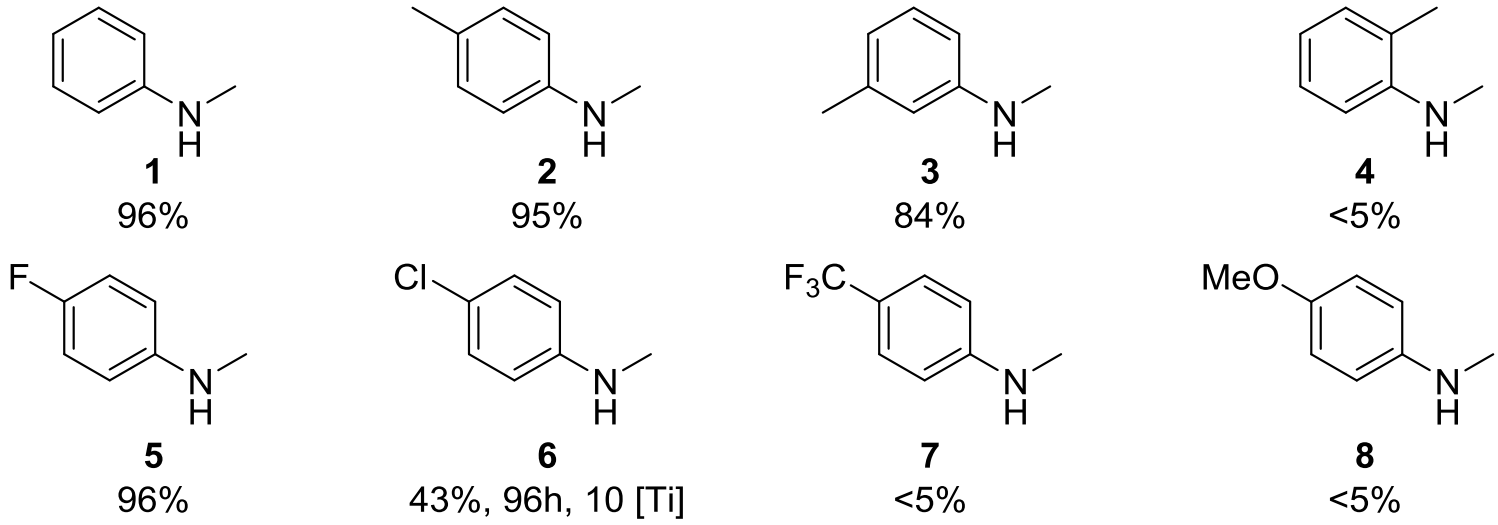
Entry	Amine	R^1	R^2	Alkene	R^3	R^4	Product	Yield **a** + **b** [%][b]	Selectivity **a**/**b**[c]
1	**8**	H	H	**12**	*n*-C_6H_{13}	H	**17a/b**	32	90:10
2	**8**	H	H	**12**	*n*-C_6H_{13}	H	**17a/b**	62[d]	90:10
3	**8**	H	H	**13**	Bn	H	**18a/b**	94	90:10
4	**8**	H	H	**14**	-$(CH_2)_5$-		**19a/b**	–	–
5	**8**	H	H	**15**	Ph	H	**20a/b**	–	–
6	**8**	H	H	norbornene (**16**)			**21**	78	–
7	**9**	Me	H	**12**	*n*-C_6H_{13}	H	**22a/b**	20	95:5
8	**9**	Me	H	**13**	Bn	H	**23a/b**	80	95:5
9	**10**	Me	Et	**12**	*n*-C_6H_{13}	H	**24a/b**	–	–
10	**10**	Me	Et	**13**	Bn	H	**25a/b**	–	–
11	**11**	H	Ph	**12**	*n*-C_6H_{13}	H	**26a/b**	75	1:1
12	**11**	H	Ph	**13**	Bn	H	**27a/b**	84	1:1

[a] Reaction conditions: amine (2.0 mmol), alkene (3.0 mmol), [$Ti(NMe_2)_4$] (0.2 mmol, 10 mol%), toluene (1 mL), 160 °C, 96 h, Bn = benzyl. [b] Yields refer to the total yield of isolated product (**a** + **b**). [c] GC analysis prior to chromatography. [d] Reaction conditions: amine (1.0 mmol), alkene (6.0 mmol), [$Ti(NMe_2)_4$] (0.04 mmol, 4 mol%), 160 °C, 72 h.

Angew. Chem. Int. Ed. **2009**, *48*, 1153 –1156

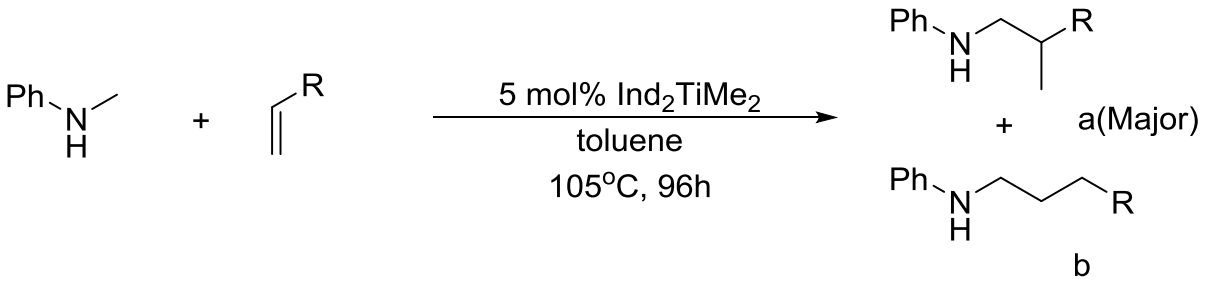
Ti catalyzed C-H activation

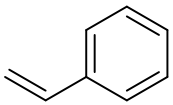




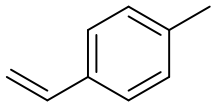
Angew. Chem. Int. Ed. **2010**, *49*, 2626–2629

Ti catalyzed C-H activation

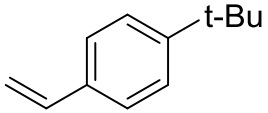




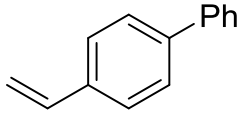
1
96% (85:15)



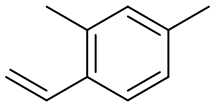
2
99% (90:10)



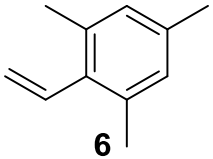
3
97% (87:13)



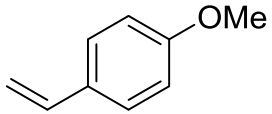
4
97% (82:18)



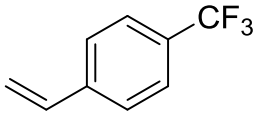
5
94% (75:25)



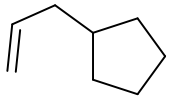
6
<5% (n.d.)



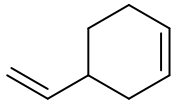
7
95% (92:8)



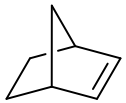
8
<5% (n.d.)



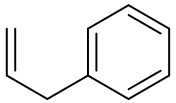
9
93% (>99:1)



10
92% (>99:1)
d.r.=85:15



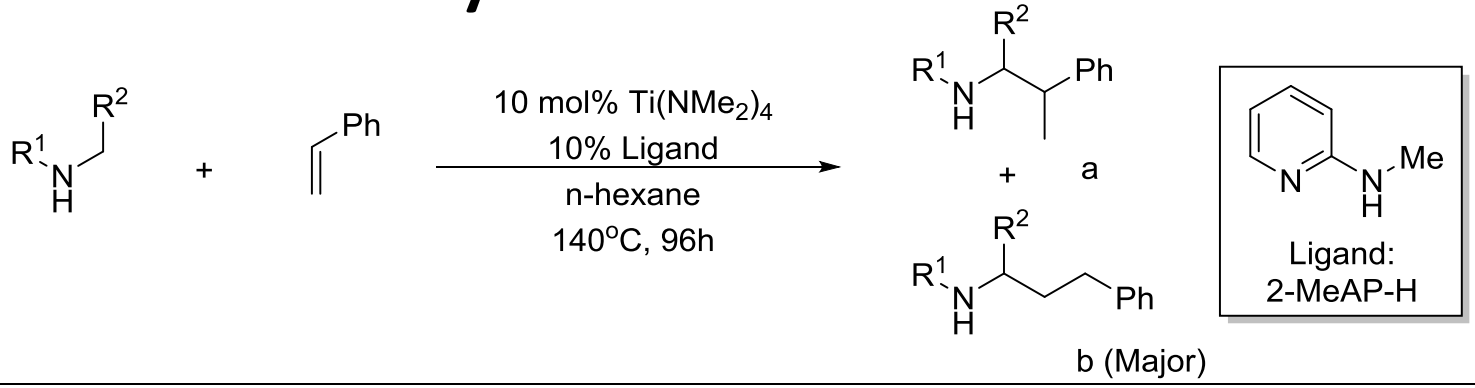
11
12%

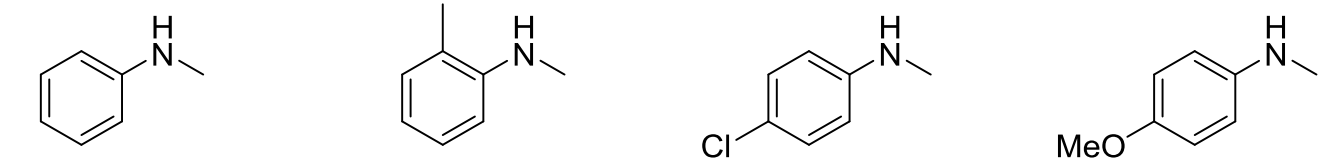


12
40% (92:8)

Angew. Chem. Int. Ed. **2010**, *49*, 2626–2629

Ti catalyzed C-H activation





1
79%(a:b=32:68)

2
31%(a:b=33:67)

3
31%(a:b=43:57)

4
50%(a:b=35:65)

5
61%(a:b=21:79)

6
48%(a:b=9:91)

7
85%(a:b=8:92)

8
71%(a:b=42:58)

9
22%(a:b=20:80)

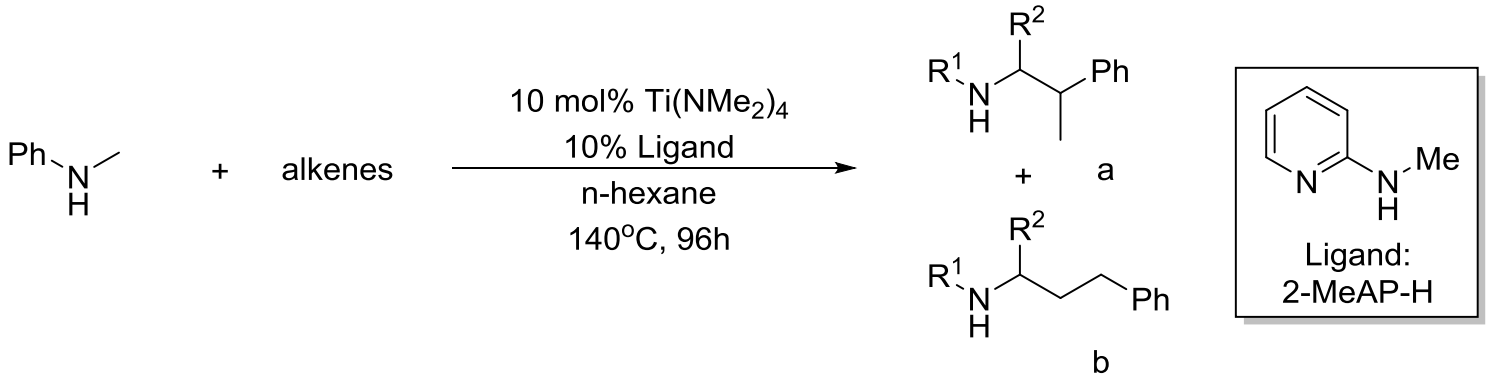
10
69%(a:b=7:93)

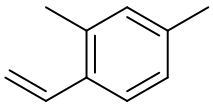
11
17%(a:b=12:88)
20% ligand

12
26%(a:b=15:85)

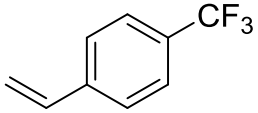
Angew. Chem. Int. Ed. **2013**, *52*, 1806 –1809

Ti catalyzed C-H activation

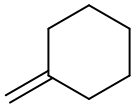




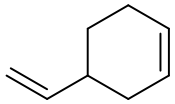
1
49%(a:b=44:56)



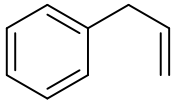
2
31%(a:b=19:81)



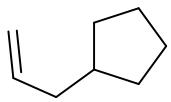
3
16%(a:b>99:1)



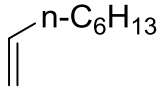
4
69%(a:b=89:11)



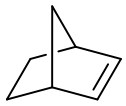
5
91%(a:b=90:10)



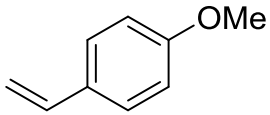
6
85%(a:b=93:7)



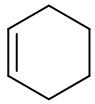
7
99%(a:b=97:3)



8
91%, 20% Ligand



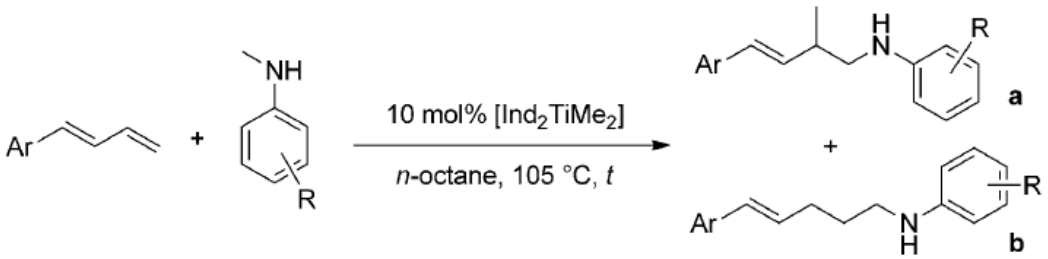
9
n.d.



10
n.d.

Angew. Chem. Int. Ed. **2013**, 52, 1806 –1809

Ti catalyzed C-H activation



Entry	Ar (diene)	R (amine)	t [h]	Yield **a**+**b** [%][a]	Selectivity **a**/**b**[b]
1	Ph (**1**)	H (**2**)	96	84 (**3a**/**b**)[c]	66:34
2	Ph (**1**)	H (**2**)	24	83 (**3a**/**b**)[c]	68:32
3	*o*-Me-C_6H_4 (**4**)	H (**2**)	96	89 (**16a**/**b**)[c,d]	75:25
4	*o*-Me-C_6H_4 (**4**)	H (**2**)	24	85 (**16a**/**b**)[c,d]	75:25
5	*m*-Me-C_6H_4 (**5**)	H (**2**)	96	73 (**17a**/**b**)[c,d]	62:38
6	*m*-Me-C_6H_4 (**5**)	H (**2**)	24	47 (**17a**/**b**)[d]	62:38
7	*p*-Me-C_6H_4 (**6**)	H (**2**)	96	61 (**18a**/**b**)[c]	70:30
8	*m*-MeO-C_6H_4 (**7**)	H (**2**)	96	44 (**19a**/**b**)[c,d]	67:33
9	*p*-MeO-C_6H_4 (**8**)	H (**2**)	96	87 (**20a**/**b**)[c,d]	73:27
10	*p*-Cl-C_6H_4 (**9**)	H (**2**)	96	12 (**21a**/**b**)[c,d,e]	66:34
11	*p*-Cl-C_6H_4 (**9**)	H (**2**)	24	8 (**21a**/**b**)[d,e,f]	66:34
12	*m*-CF_3-C_6H_4 (**10**)	H (**2**)	96	23 (**22a**/**b**)[c,d]	65:35
13	*m*-CF_3-C_6H_4 (**10**)	H (**2**)	24	14 (**22a**/**b**)[d]	66:34
14	2-thiophenyl (**11**)	H (**2**)	96	44 (**23a**/**b**)[c,d]	55:45
15	2-thiophenyl (**11**)	H (**2**)	24	35 (**23a**/**b**)[d]	55:45
16	Ph (**1**)	*m*-Me (**12**)	96	73 (**24a**/**b**)[c,d]	67:33
17	Ph (**1**)	*p*-Me (**13**)	96	85 (**25a**/**b**)[c,d]	65:35
18	Ph (**1**)	*p*-MeO (**14**)	96	23 (**26a**/**b**)[d,g]	60:40
19	Ph (**1**)	*p*-Cl (**15**)	96	6 (**27a**/**b**)	71:29
20	*m*-Me-C_6H_4 (**5**)	*p*-Me (**13**)	96	78 (**28a**/**b**)[c,d]	67:33

Chem. Eur. J. **2013**, *19*, 3833 – 3837

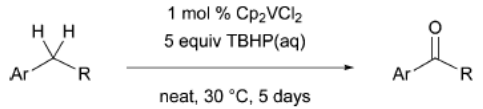
V catalyzed C-H activation

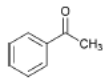
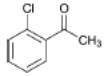
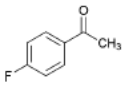
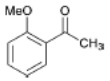
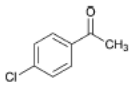
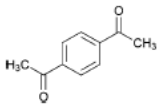
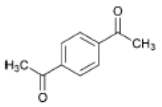
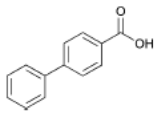
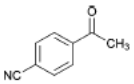
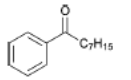
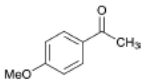
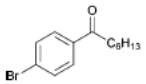
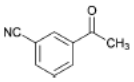
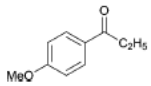
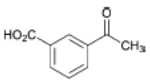
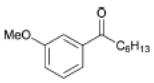
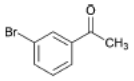
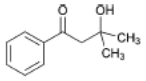
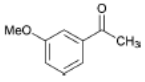
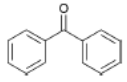
- V is widely use in oxidation of C-H bonds.

Nature Chemistry, ***2010,*** *2, 478.*

- V catalyzed C-H activation is hard to found.
- The two C-H functionalization reactions are from Chuo Chen's group.

V catalyzed C-H oxidation

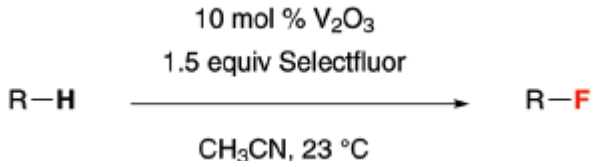


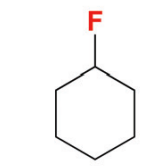
Entry	Ar R	Product	Yield[b]	Entry	Ar R	Product	Yield[b]
1	Ph CH_3		90%	11	2-Cl–Ph CH_3		52%
2	4-F–Ph CH_3		91%	12	2-MeO–Ph CH_3		68%
3	4-Cl–Ph CH_3		86%	13	4-Et–Ph CH_3		86%[c]
4	4-Me(O)C–Ph CH_3		89%	14	4-Ph–Ph H		54% 60%[d]
5	4-NC–Ph CH_3		77%	15	Ph n-C_7H_{15}		57%
6	4-MeO–Ph CH_3		57%	16	4-Br–Ph n-C_6H_{13}		51%
7	3-NC–Ph CH_3		85%	17	4-MeO–Ph n-C_2H_5		49%
8	3-HO_2C–Ph CH_3		91%	18	3-MeO–Ph n-C_6H_{13}		50%
9	3-Br–Ph CH_3		90%	19	Ph $CH_2C(OH)(CH_3)_2$		50%[e]
10	3-MeO–Ph CH_3		80%	20	Ph Ph		95%

[a] All reactions were conducted with 1 mmol of the substrate. [b] Isolated yield. [c] With 2 mol% Cp_2VCl_2 and 10 equiv. TBHP. [d] With acetonitrile (0.2 mL). [e] Yield obtained after TBS protection of the alcohol.

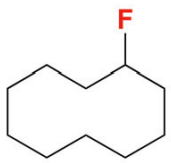
Chem. Sci., 2012, **3**, 2240–2245

V catalyzed C-H Florination

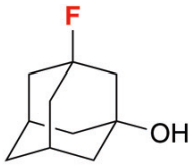




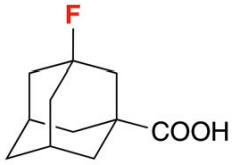
3 (20 h)[b]
70% NMR yield



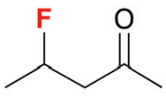
4 (20 h)[b]
61% yield



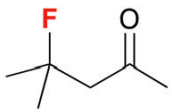
5 (20 h)
74% yield



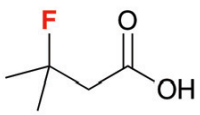
6 (20 h)
70% yield



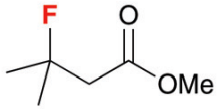
7 (20 h)
47% NMR yield



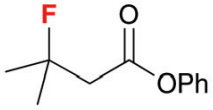
8 (20 h)
78% NMR yield



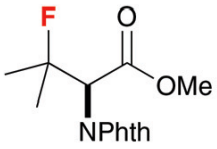
9 (20 h)
63% yield



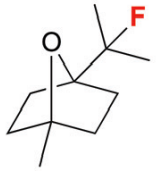
10 (20 h)
85% NMR yield



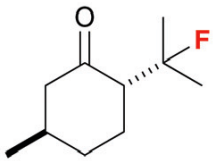
11 (20 h)
12% NMR yield



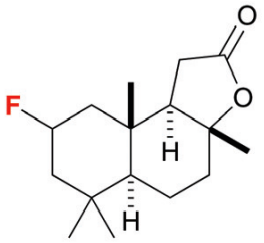
12 (18 h)
46% yield



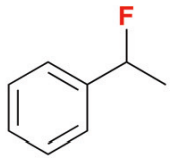
13 (24 h)
53% yield



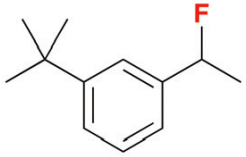
14 (30 h)
75% yield



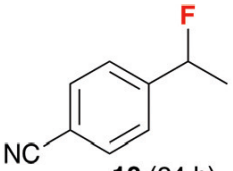
15 (48 h)
61% yield
(α:β = 9:1)



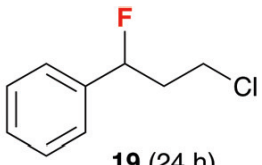
16 (24 h)
67% NMR yield



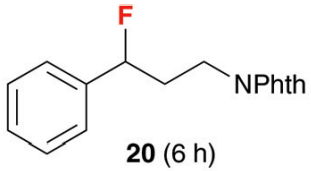
17 (48 h)
47% yield



18 (24 h)
24% yield



19 (24 h)
35% yield



20 (6 h)
43% yield

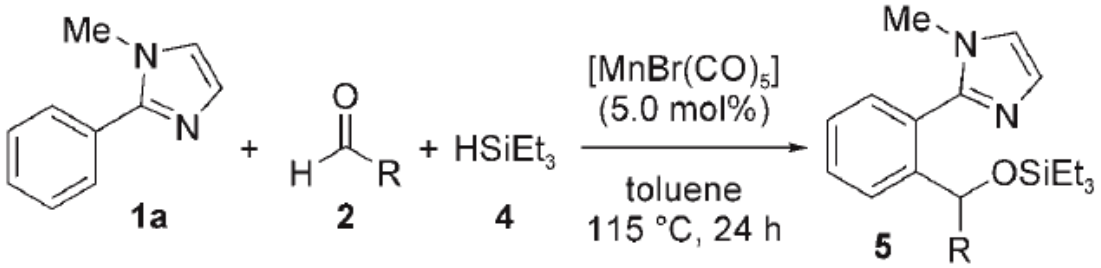
Org. Chem. Front., 2014, **1**, 468–472

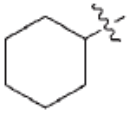
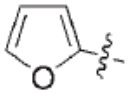
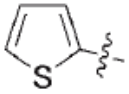
Mn catalyzed C-H activation

- Mn is widely use in oxidation of C-H bonds.
- Mn catalyzed C-H activation is not well developed. Only a few examples.
- The work was discovered by Prof. Takai, and followed by Congyang Wang.

Mn catalyzed C-H Activation

- Kazuhiko Takai and Yoichiro Kuninobu's work



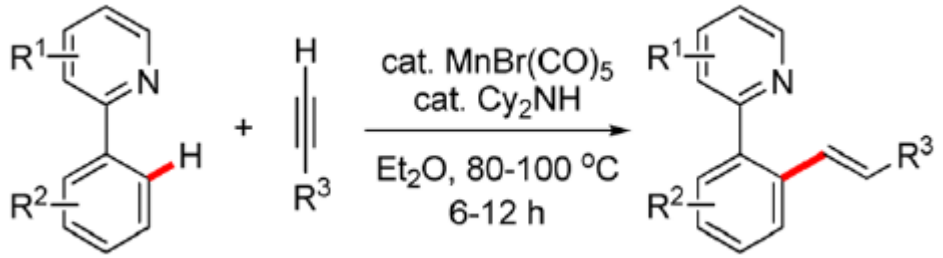
Entry	Substrate	R	Product	Yield [%][b]
1	**2b**	*p*-(MeO)C_6H_4	**5b**	87 (89)
2	**2c**	*p*-(CF_3)C_6H_4	**5c**	87 (89)
3	**2d**	*o*-MeC_6H_4	**5d**	59 (60)
4[c]	**2e**	*n*C_8H_{17}	**5e**	75 (79)
5[c]	**2f**		**5f**	56 (57)
6[d]	**2g**		**5g**	66 (67)
7	**2h**		**5h**	48 (50)

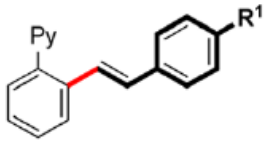
[a] **2** (2.0 equiv); **4** (2.0 equiv). [b] Yield of isolated product. The yield determined by ^{1}H NMR spectroscopy is reported in parentheses. [c] 135 °C. [d] 48 h.

Angew. Chem. Int. Ed. **2007**, *46*, 6518–6520

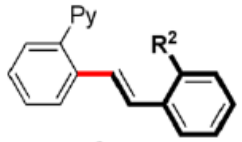
Mn catalyzed C-H Activation

- Wang's work

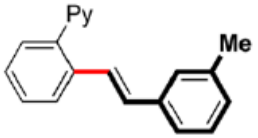




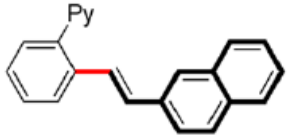
3aa: R^1 = H, 76%
3ab: R^1 = Me, 71%
3ac: R^1 = OMe, 63%[c]
3ad: R^1 = CF_3, 71%
3ae: R^1 = CO_2Me, 66%[d]
3af: R^1 = NO_2, 48%[d]
3ag: R^1 = F, 82%
3ah: R^1 = Cl, 79%
3ai: R^1 = Br, 79%
3aj: R^1 = I, 74%[e]



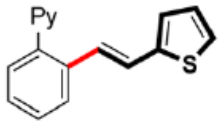
3ak: R^2 = Me, 80%
3al: R^2 = CF_3, 65%



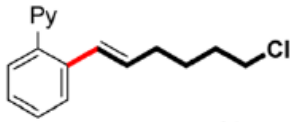
3am: 75%



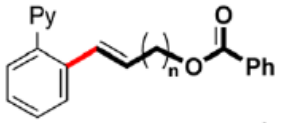
3an: 78%



3ao: 51%[d]



3ap: 68%[d,f]



3aq: n = 1, 48%[d]
3ar: n = 2, 46%[d,g]

[a]Reaction conditions: **1a** (1 mmol), **2** (0.5 mmol), $MnBr(CO)_5$ (0.05 mmol), Cy_2NH (0.1 mmol), Et_2O (1.2 mL), 80 °C, 6 h. [b] Isolated yields of product **3** are shown. [c] **3ac**/**6ac** = 9:1. [d] 100 °C, 12 h. [e] **3aj**/**6aj** = 9:1. [f] **3ap**/**5ap** = 9:1. [g] **3ar**/**5ar** = 8:1.

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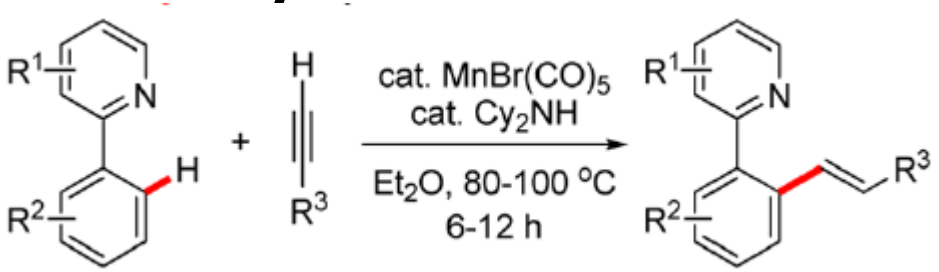
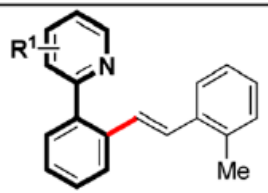
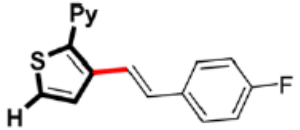
Mn catalyzed C-H Activation

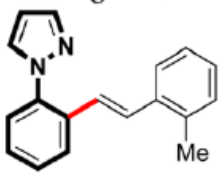




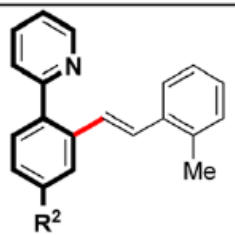
3bk: R^1 = 5-Me, 82%
3ck: R^1 = 5-Ph, 80%
3dk: R^1 = 5-Cl, 80%
3ek: R^1 = 5-CO_2Et, 71%
3fk: R^1 = 4-OMe, 75%
3gk: R^1 = 3-Me,68%



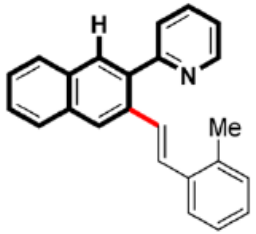
3tg: 51%



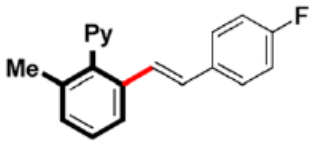
3uk: 77%



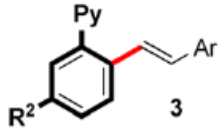
3hk: R^2 = Me, 69%
3ik: R^2 = OMe, 82%
3jk: R^2 = CF_3, 79%
3kk: R^2 = F, 70%
3lk: R^2 = Cl, 72%
3mk: R^2 = Br, 82%
3nk: R^2 = I, 77%



3qk: 75%



3og: 27%



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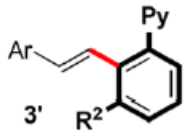

R^2 = Me, Ar = (o-Me)Ph, **3pk**: 86%[c]

R^2 = F, Ar = Ph, **3ra'**: 60%[c], Ar = (o-Me)Ph, **3rk'**: 71%[c]

R^2 = OMe, Ar = (o-Me)Ph, 67% (**3sk**/**3sk'** = 1:2)

[a]Reaction conditions: **1** (1 mmol), **2** (0.5 mmol), $MnBr(CO)_5$ (0.05 mmol), Cy_2NH (0.1 mmol), Et_2O (1.2 mL), 80 °C, 6 h. [b] Isolated yields of **3** are shown. [c] Single product.

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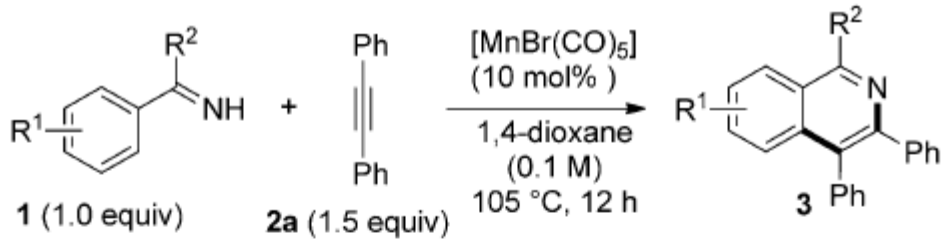
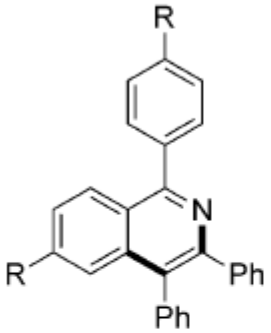
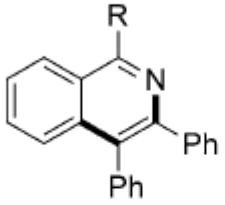
Mn catalyzed C-H Activation



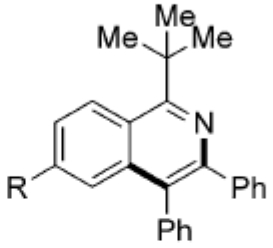
1 (1.0 equiv) **2a** (1.5 equiv) **3**



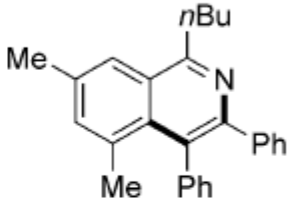
3aa: R = OMe, 89%
3ba: R = F, 75%
3ca: R = H, 63%[a]



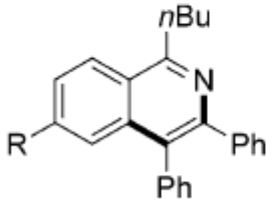
3da: R = *n*Bu, 86%
3ea: R = *i*Pr, 82%
3fa: R = *s*Bu, 87%[b]



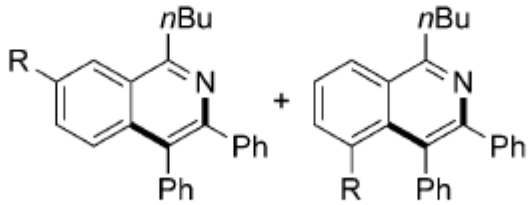
3ga: R = OMe, 93%
3ha: R = NMe_2, 97%



3qa: 48%[a]

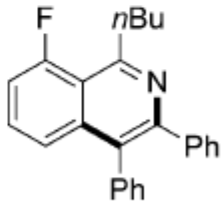


3ia: R = Me, 93%
3ja: R = F, 88%
3ka: R = SMe, 58%
3la: R = Ph, 77%



3 **3'**

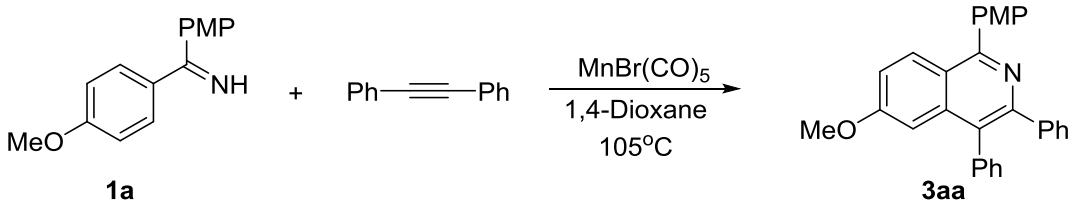
R = Me, 88%, **3ma**:**3ma'** = 8.3:1
R = CF_3, **3na**, 58%
R = OMe, 83%, **3oa**:**3oa'** = 1:1.5
R = F, 86%, **3pa**:**3pa'** = 1:2.7

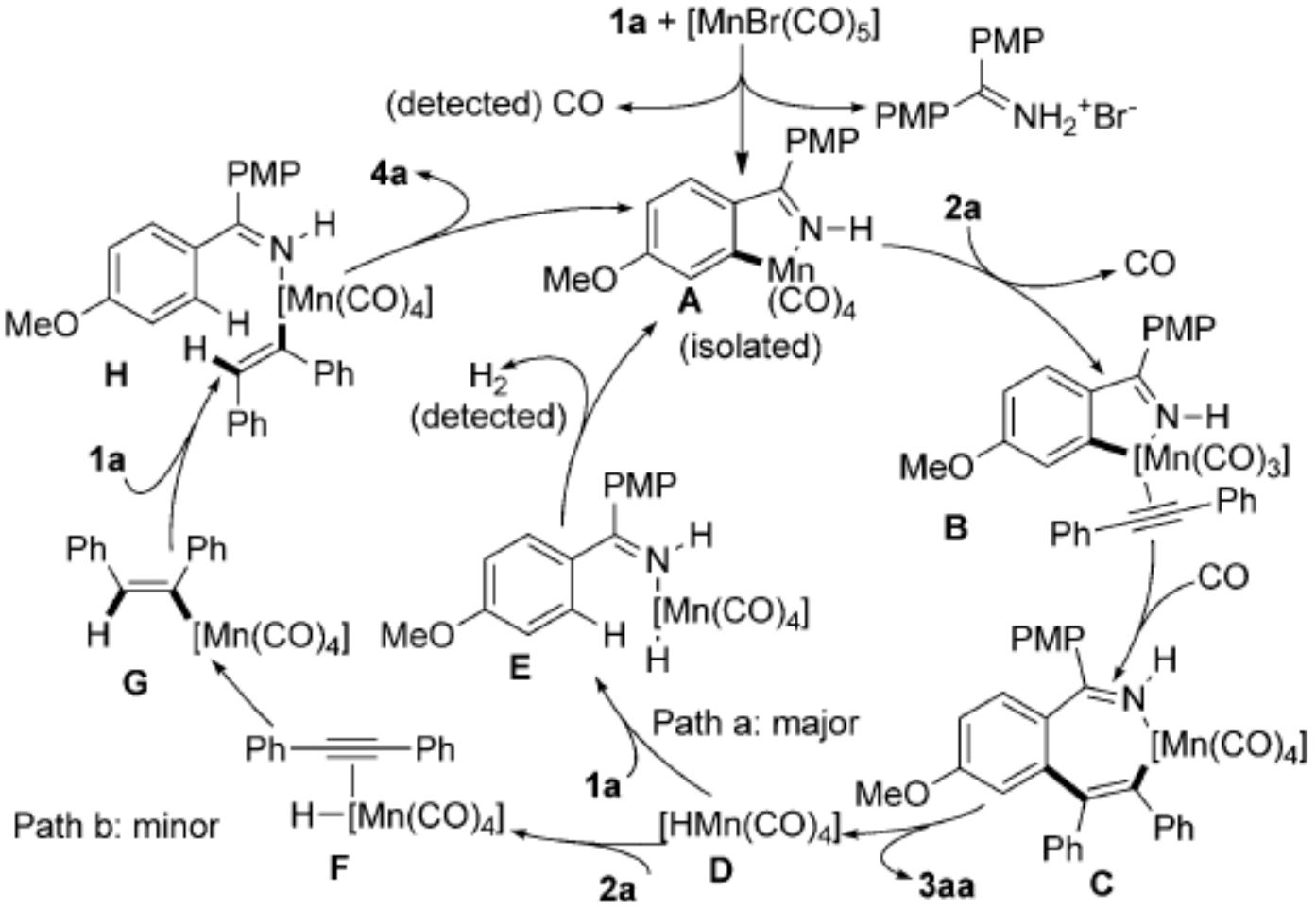


3ra: 75%

Angew. Chem. Int. Ed. **2014**, *53*, 4950–4953

Mn catalyzed C-H Activation





Angew. Chem. Int. Ed. **2014**, *53*, 4950–4953

Fe catalyzed C-H activation

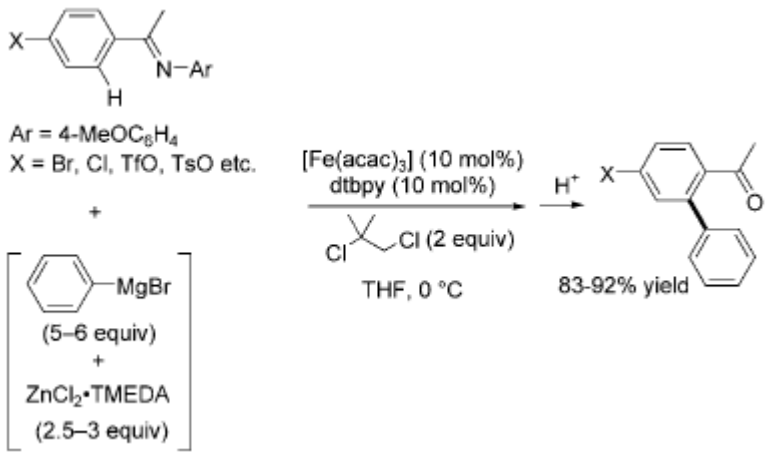
- There are too many Fe catalyzed C-H activation reactions.

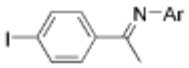
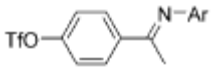
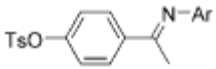
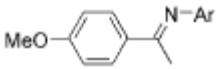
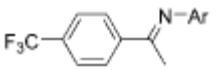
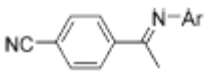
*Zhangjie Shi, Chemical Reviews **2010,** 111, 1293.*

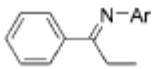
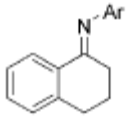
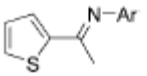
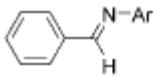
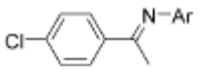
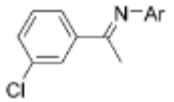
Eiichi Nakamura, *J. Org. Chem.* **2010**, 75, 6061–6067

- The following works are all from Prof. Nakamura's group.

Fe catalyzed C-H Activation

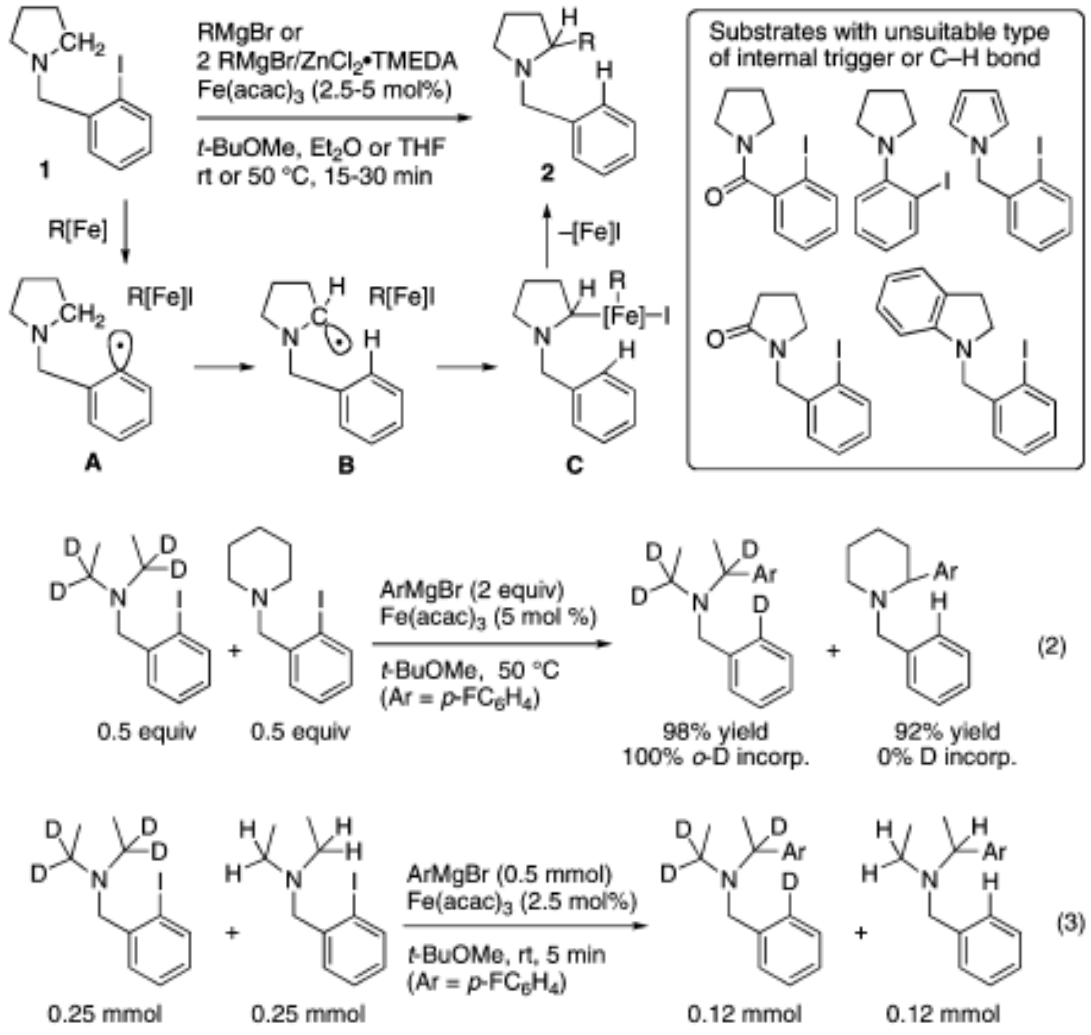


	% yield
	14
	89 (89)
	89
	94
	90
	57

	% yield	
	99	
	93	
	96	
	6 58	mono di
	92	
	87	

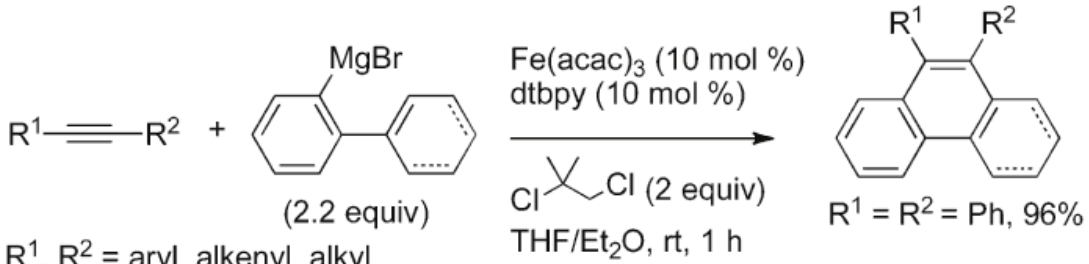
Angew. Chem. Int. Ed. **2009**, *48*, 2925 –2928

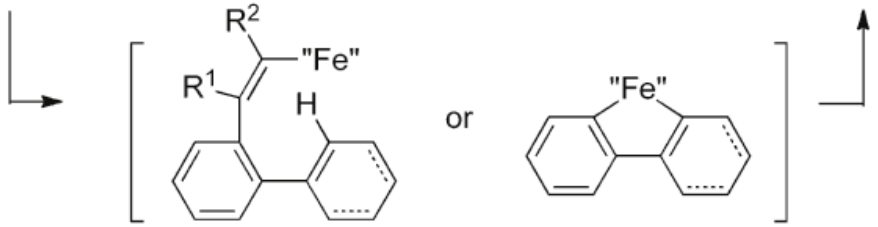
Fe catalyzed C-H Activation

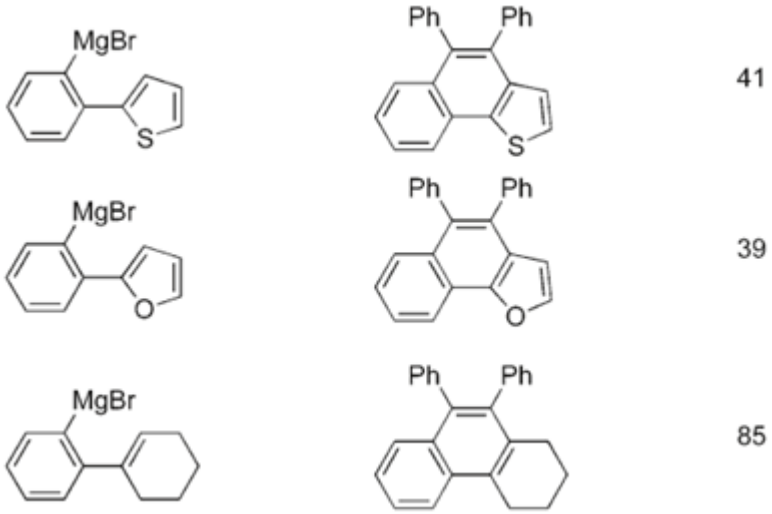


J. AM. CHEM. SOC. 2010, *132*, 5568–5569

Fe catalyzed C-H Activation

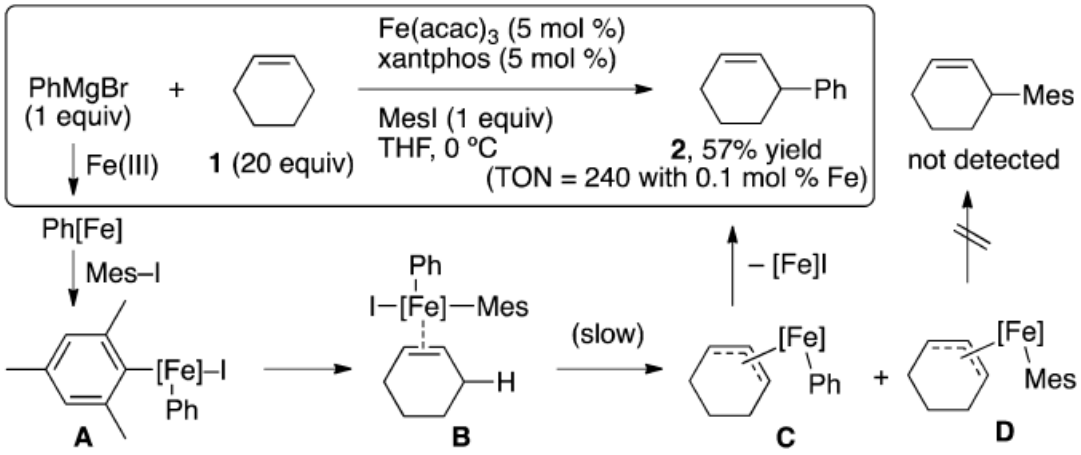


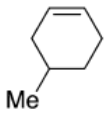
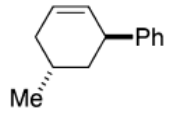
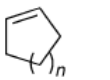
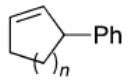
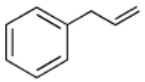
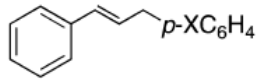
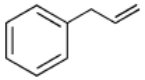
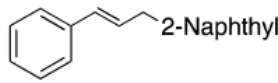
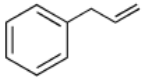
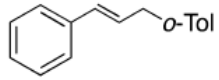
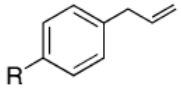
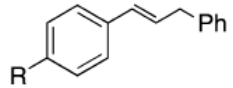
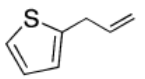
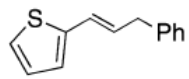




J. Am. Chem. Soc. 2011, 133, 6557–6559

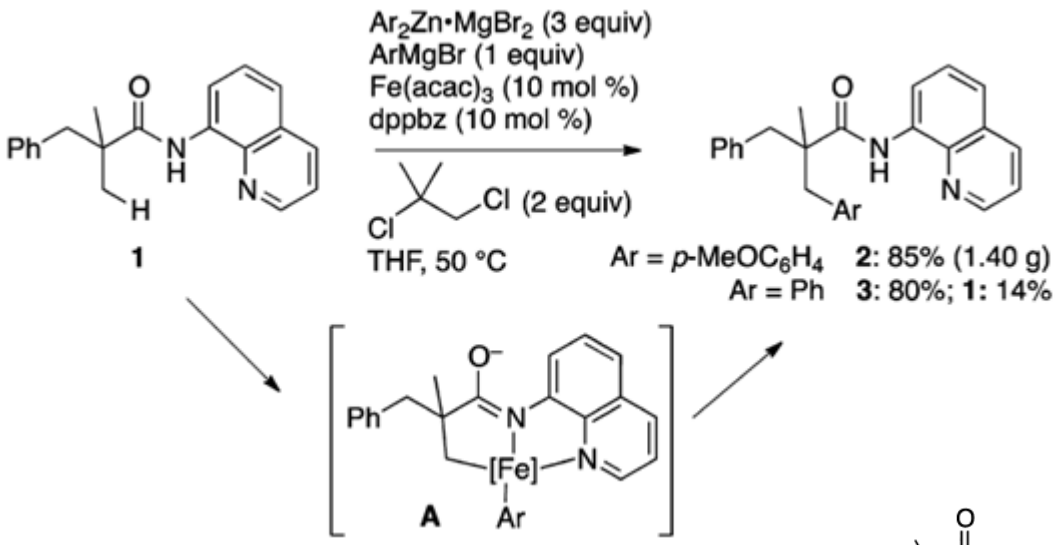
Fe catalyzed C-H Activation

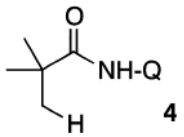
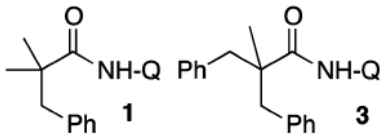
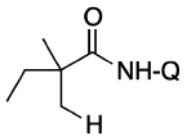
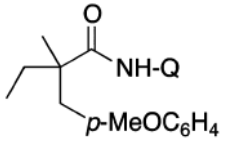
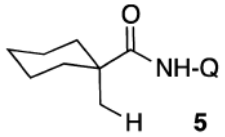
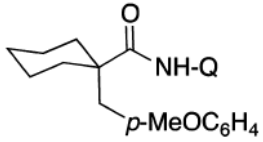
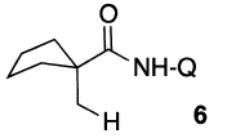
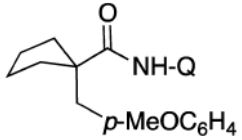


5		**5**	PhMgBr		**6t**	27(+18)[d]/9
6			PhMgBr		n = 1	54/11
7			PhMgBr		n = 3	21/4
8			*p*-XC_6H_4MgBr		X = H	40/8
9					X = Me	40/8
10					X = OMe	31/6
11					X = NMe_2	30/6
12					X = F	42/8
13			2-NaphthylMgBr			18/4
14			*o*-TolMgBr			37/7
15			PhMgBr		R = Me	35/7
16					R = F	37/7
17					R = Cl	27/5
18					R = Br	24/5[e]
19			PhMgBr			34/7

Org. Lett., 2013, 15, 714

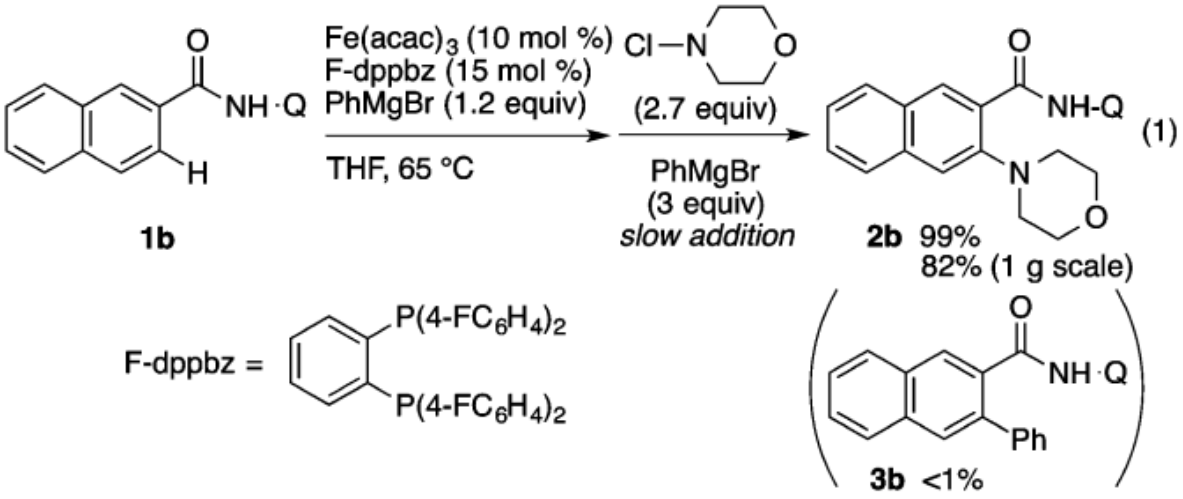
Fe catalyzed C-H Activation

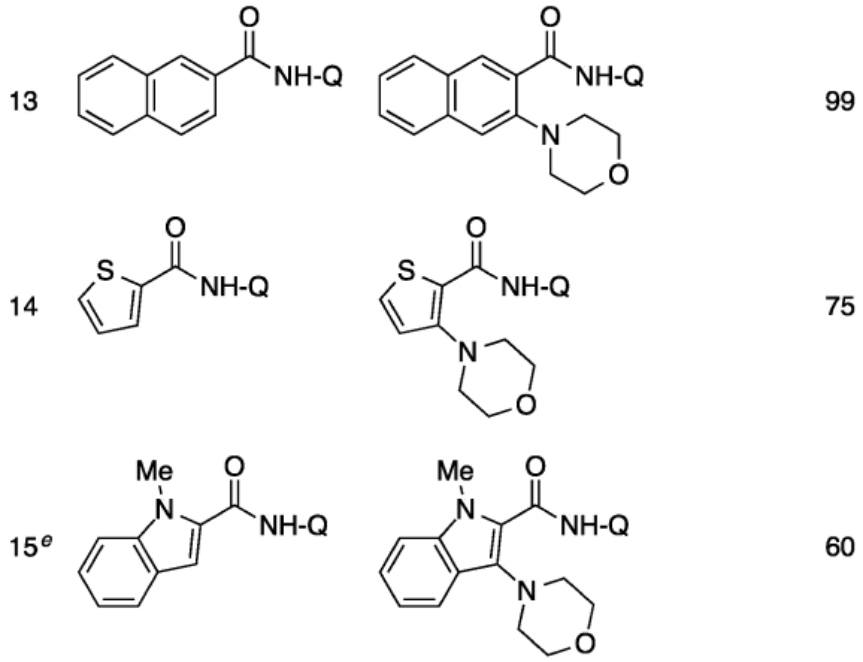


7	 4	 1 3	28+20[d] (33+31)[e]
8			53
9	 5		75
10	 6		69

J. Am. Chem. Soc. 2013, 135, 6030–6032

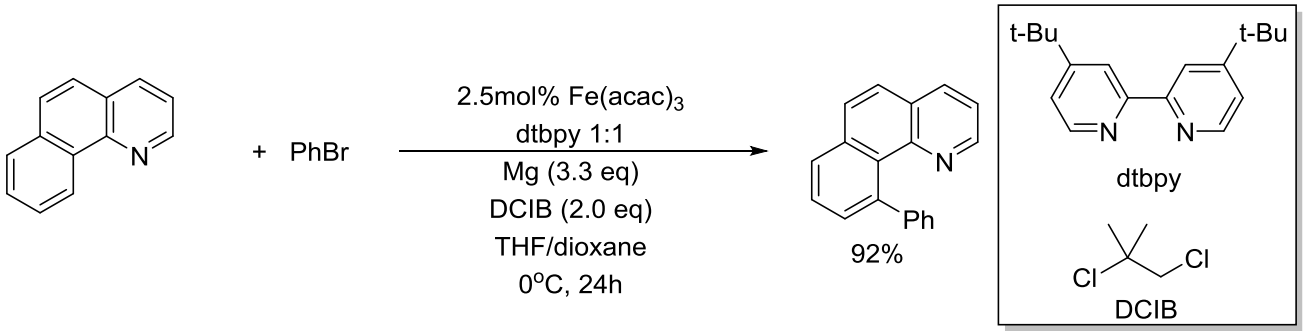
Fe catalyzed C-H Activation



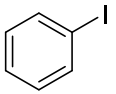


J. Am. Chem. Soc. 2014, 136, 646–649

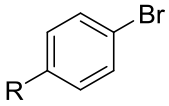
Fe catalyzed C-H Activation



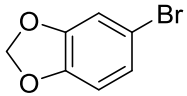
other interesting halide



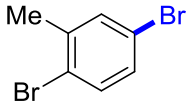
60%



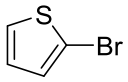
89%, R= OMe
77%, R= CF_3
92%, R= Cl
99%, R= F



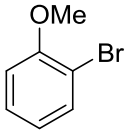
51%



35%



16%

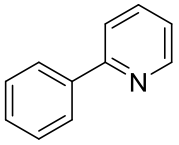


2%

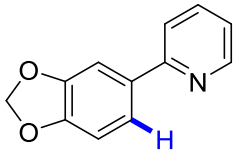
MeI

19%

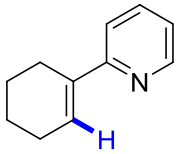
other substrate



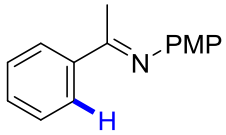
79% mono
9% di



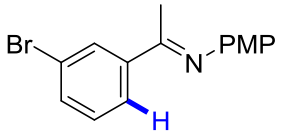
57%



26%



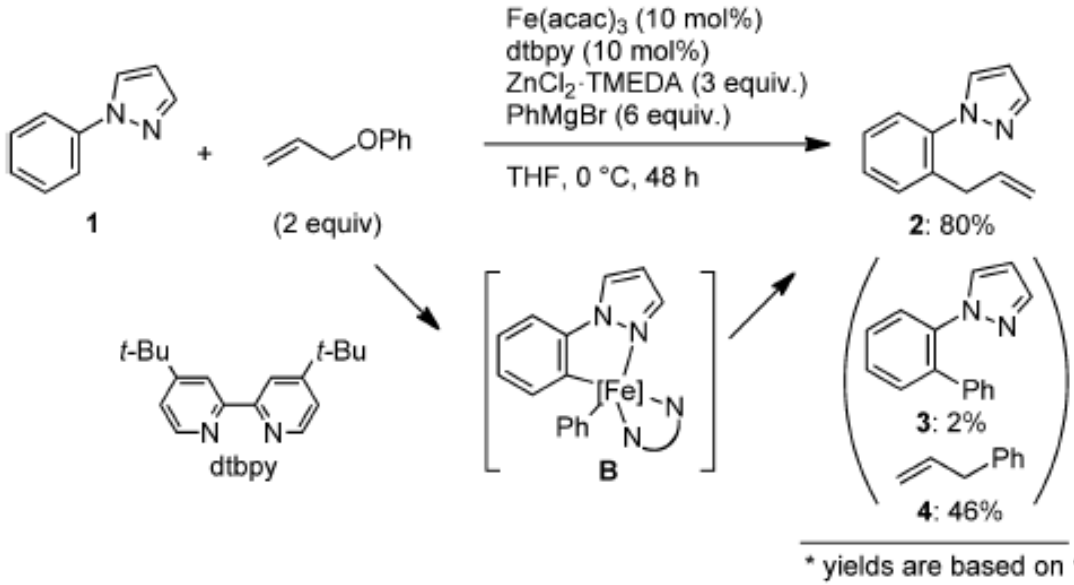
92% ketone

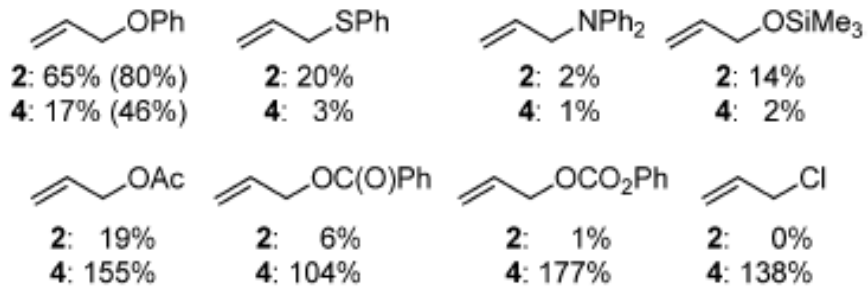


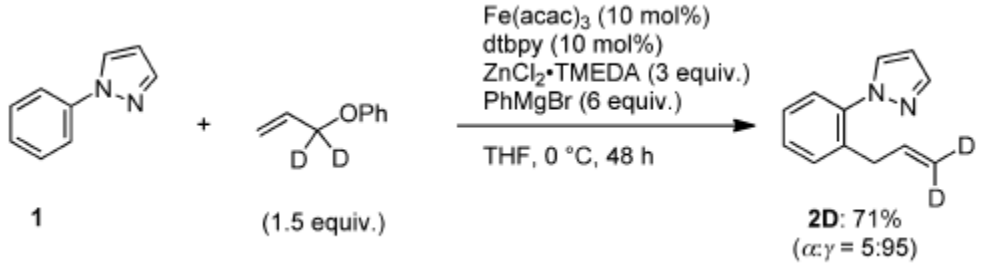
32% ketone

Adv. Synth. Catal. **2012**, *354*, 593–596

Fe catalyzed C-H Activation







Adv. Synth. Catal. **2014**, *356*, 1481 – 1485

Co catalyzed C-H activation

- Huang presented the Co catalyzed C-H activation during his talk.

Yoshikai, N., *Acc. Chem. Res.* **2014**, 47, 1208.

- This Friday, I will present two Co catalyzed C-H activation from Prof. Olafs Daugulis.

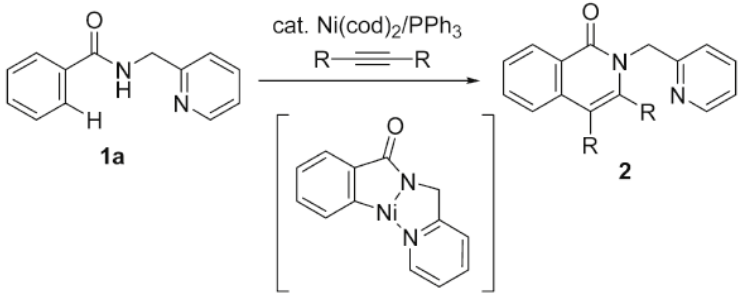
Ni catalyzed C-H activation

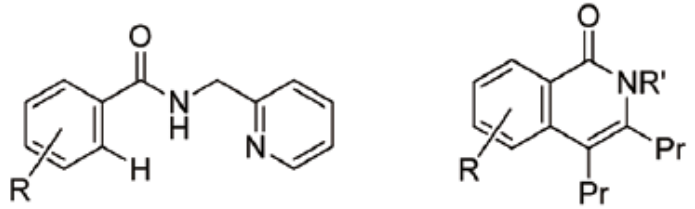
- Ni catalyzed cross coupling reaction was well established.
- For recent Nickel catalysis:

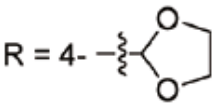
Nature ***2014***, 509, 299.

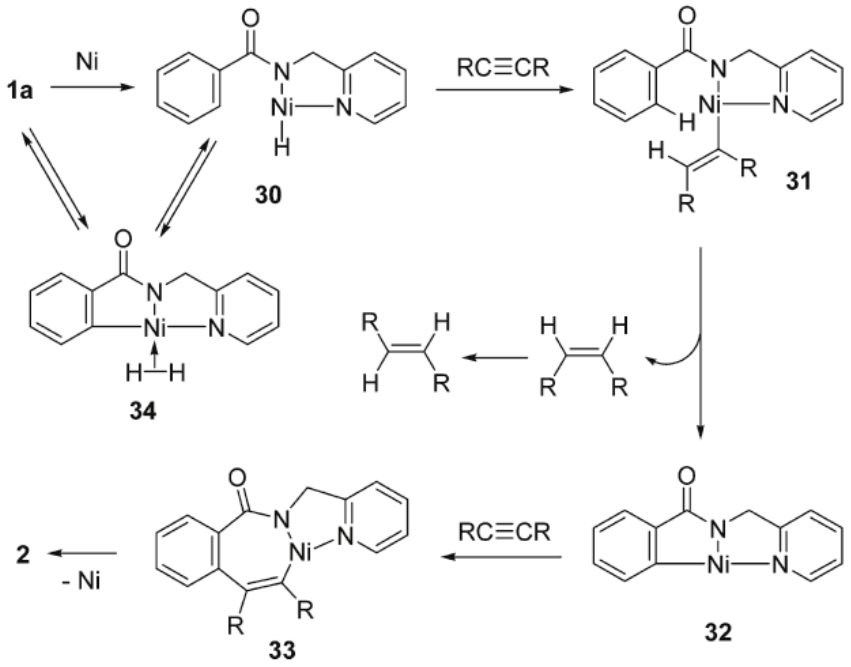
- The following works are all from Prof. Chatani's group.

Ni catalyzed C-H Activation





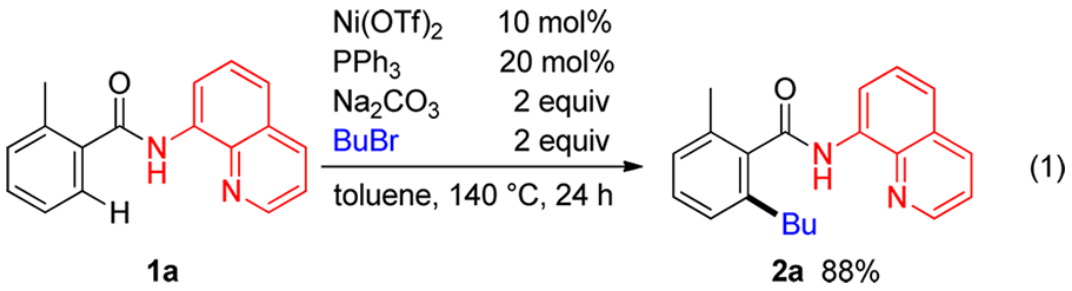
R = H (**1a**)	**2a** 86%
R = 4-CH_3 (**1b**)	**2b** 84%
R = 4-OCH_3 (**1c**)	**2c** 73%
R = 4-NMe_2 (**1d**)	**2d** 69%
R = 4-CF_3 (**1e**)	**2e** 91%
R = 4-Ac (**1f**)	**2f** 85%
R = 4-CN (**1g**)	**2g** 83%
R = 4-  (**1h**)	**2h** 87%
R = 4-Ph (**1i**)	**2i** 87%
R = 2-Ph (**1j**)	**2j** 52%

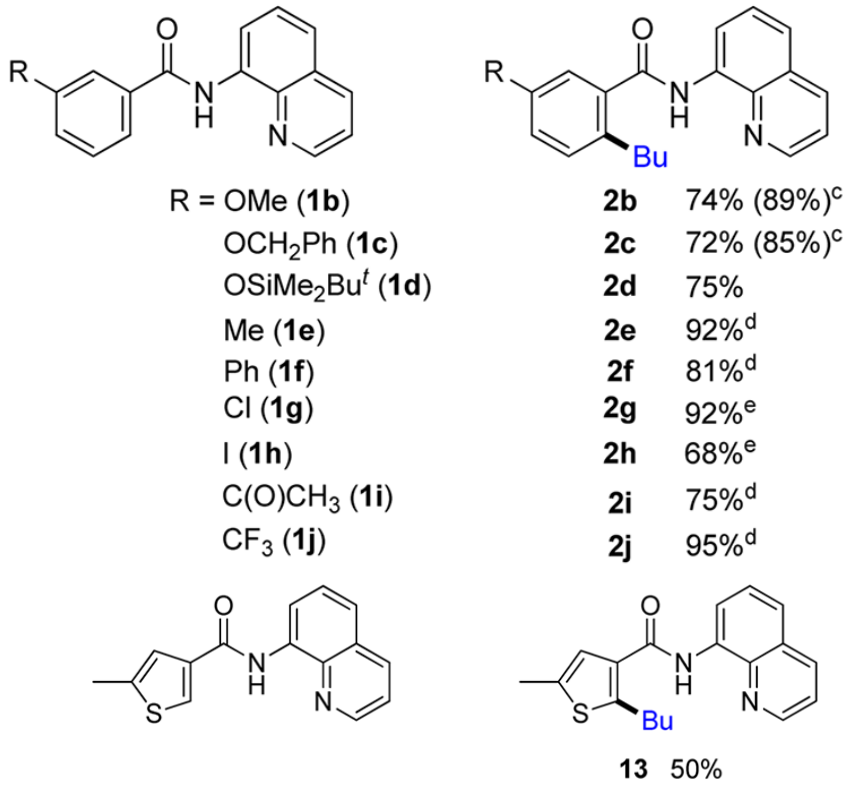


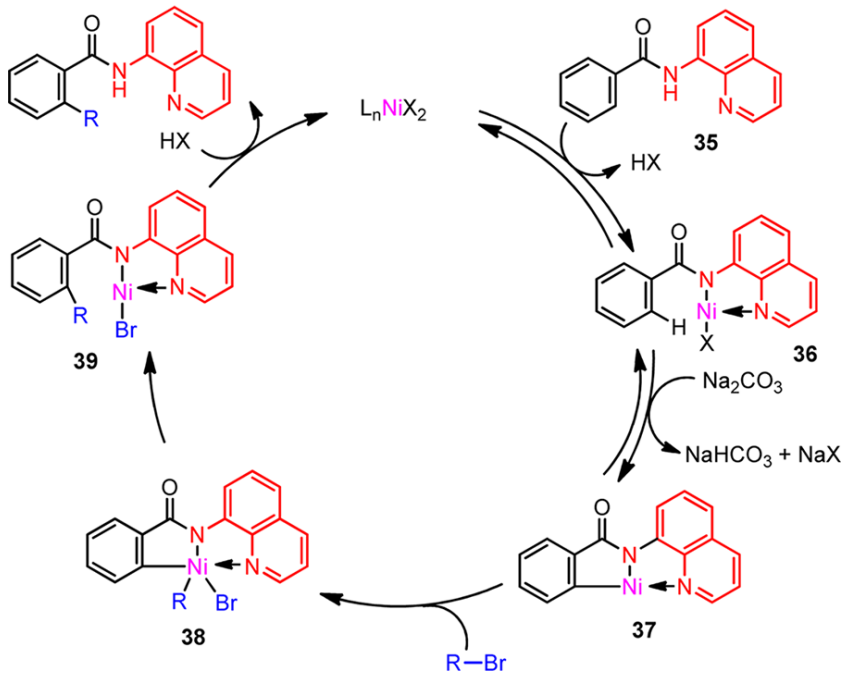
[a] Reaction conditions: amide (0.5 mmol), 4-octyne (1.5 mmol), $Ni(cod)_2$ (0.05 mmol), and PPh_3 (0.2 mmol) in toluene (2 mL) at 160 °C for 6 h. [b] Isolated yields are shown. [c] The ratio of regioisomers is shown in parentheses.

J. Am. Chem. Soc. 2011, 133, 14952–14955

Ni catalyzed C-H Activation



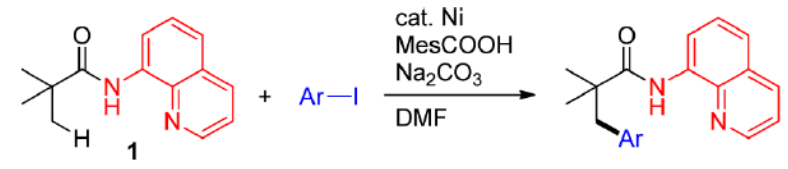




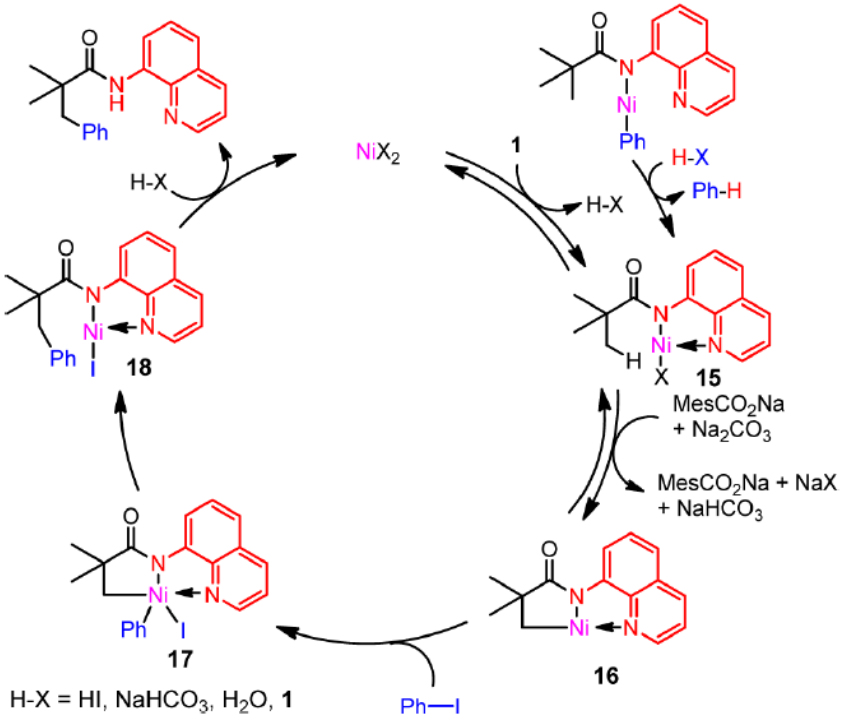
[a] Reaction conditions: amide (0.5 mmol), 4-octyne (1.5 mmol), $Ni(cod)_2$ (0.05 mmol), and PPh_3 (0.2 mmol) in toluene (2 mL) at 160 °C for 6 h. [b] Isolated yields are shown. [c] The ratio of regioisomers is shown in parentheses.

J. Am. Chem. Soc. 2013, 135, 5308–5311

Ni catalyzed C-H Activation



substrate	products[b]		
6a	6b	72% (10%)	Ar = *p*-$MeOC_6H_4$
7a	7b	50% (32%)	
8a	8b	56% (31%)	
9a	9b	29%	9c 54% (6%)
12a	12b	50%[c] 12%[c,d]	12c 33% (15%) cis 62% (0%)[d]
13a	13b	41%[c] 42%[c,d]	13c 8% (40%)[c] 18% (14%)[c,d]



J. Am. Chem. Soc. 2014, 136, 898–901

Cu catalyzed C-H activation

- Cu catalyzed C-H activation reactions are well established.

Acc. Chem. Res., 2012, 45 (6), pp 778–787

Chem. Rev., 2013, 113 (8), pp 6234–6458

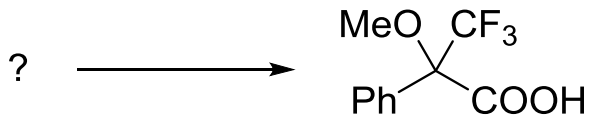
Summary

- 1. Sc and Ti are very lewis acidic, and also oxygenphilic. The ligand development is very important in these type reaction.
- 2. For V, Cr, and Mn, the catalyzed C-H activation reactions are underdeveloped. Use the low-valent species are important.
- 3. For Fe, Co, Ni and Cu system, it is now a rapid growing area.

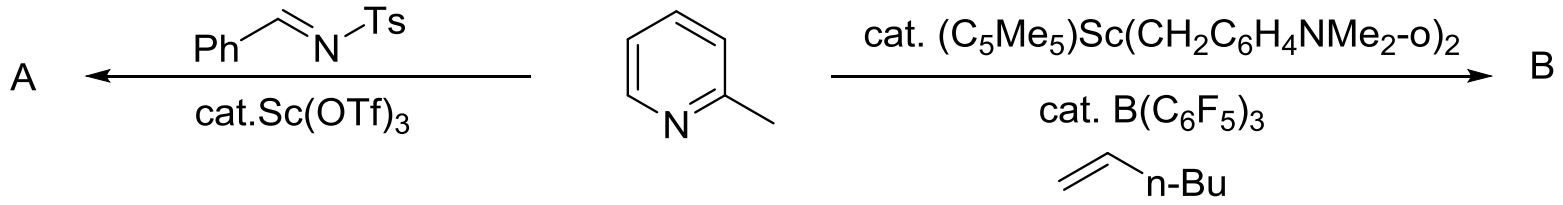
Thanks!

Questions!

1. How to synthesize the Mosher's acid within 3 steps? Question is limited to undergrad and first year.

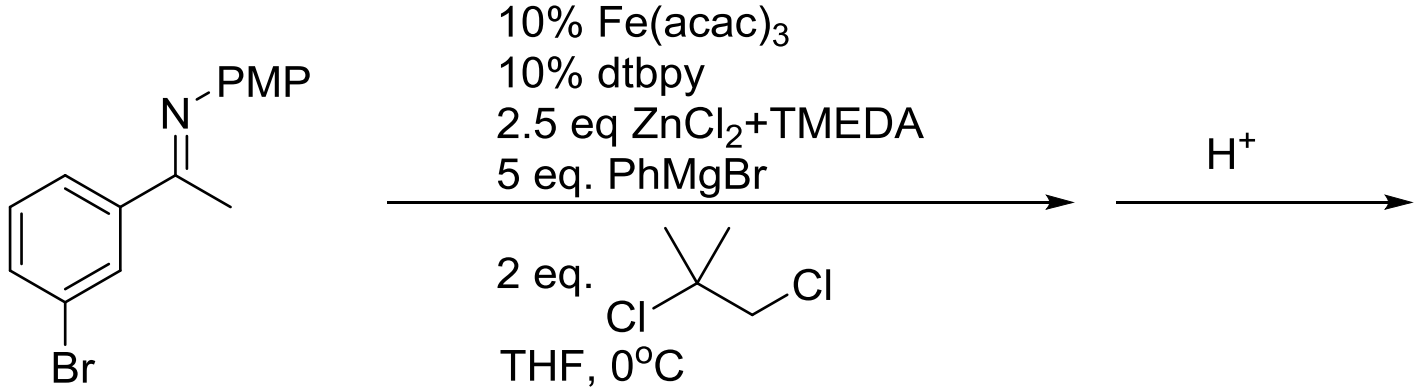


2. Please provide the structure for A and B, and propose a mechanism for both reaction.

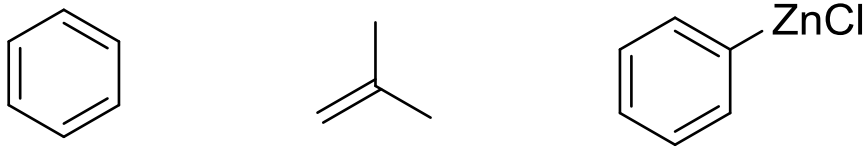


Questions!

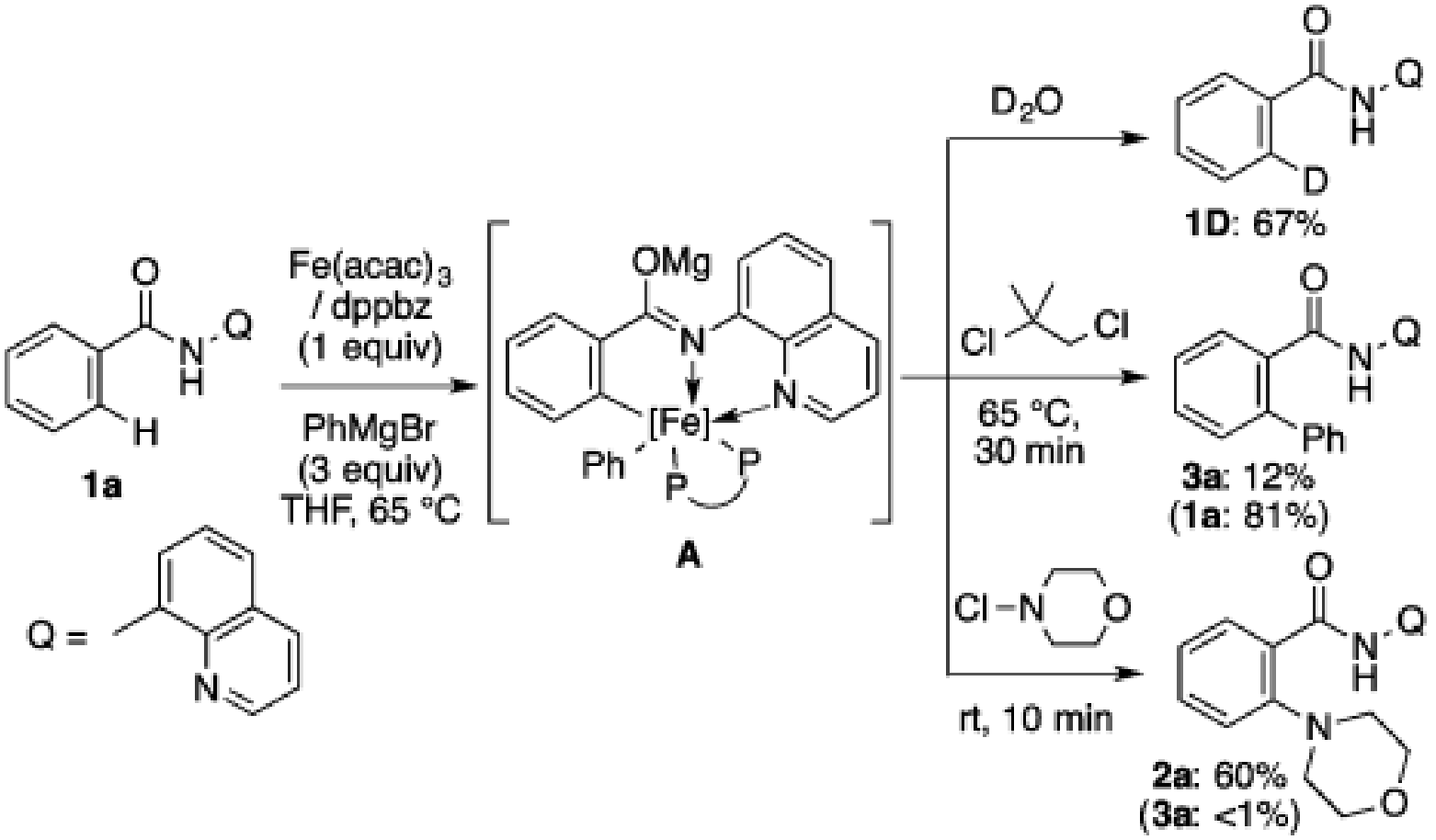
3. Propose a mechanism for the following reaction.



Hint: the prducts of the first step include the following:



Questions!


1a
Fe(acac)3
/ dppbz
(1 equiv)
PhMgBr
(3 equiv)
THF, 65 °C
A
Q =
D2O
1D: 67%
65 °C,
30 min
3a: 12%
(1a: 81%)
rt, 10 min
2a: 60%
(3a: <1%)