同济大学 化学科学与工程学院
School of Chemical Science and Engineering

The Yang Research Group
Precise Synthesis Lab at Tongji University

Masaharu Nakamura Group

姓名：王宁　　指导教师：杨泽鹏 教授

同舟共济

Personal Profile

同济大学 化学科学与工程学院
School of Chemical Science and Engineering

The Yang Research Group
Precise Synthesis Lab at Tongji University

Education

1991

BS from Tokyo University of Science, Department of Science, Applied Chemistry.

1996

PhD from Tokyo Institute of Technology, Graduate School of Science and Engineering.

1993 ~ 1996

JSPS Research Fellow.

April 1996

Assistant Professor at the University of Tokyo, Graduate School of Science, Department of Chemistry.

1999-2000

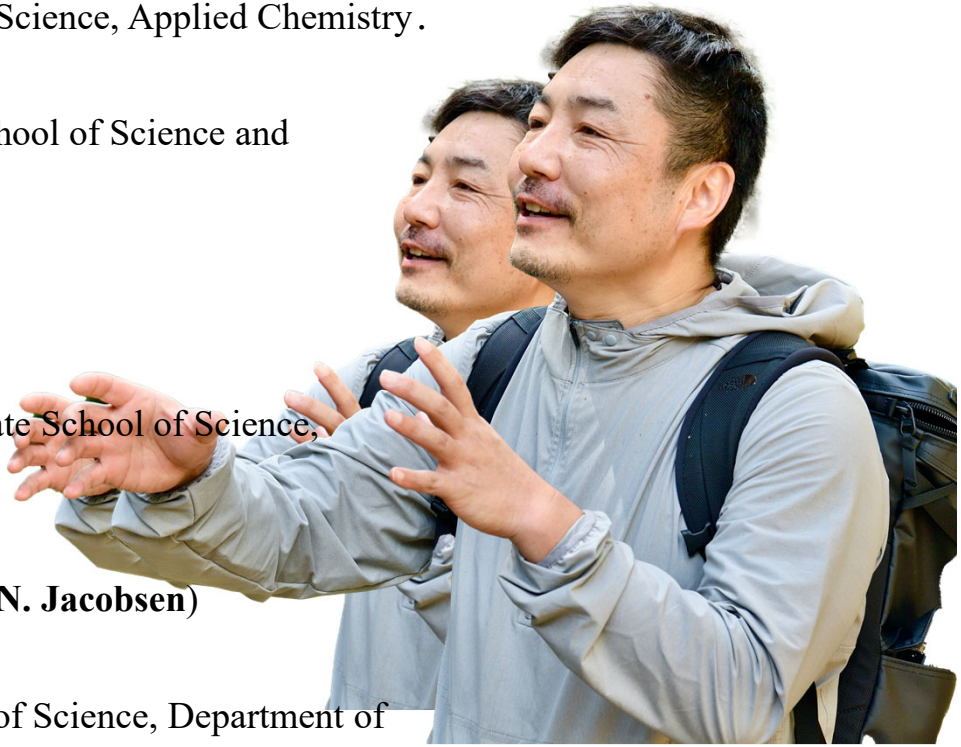
Harvard University PhD Researcher (**Professor Eric N. Jacobsen**)

2002

Lecturer at the University of Tokyo, Graduate School of Science, Department of Chemistry.

Since January 2006

Full Professor at the University of Kyoto, Institute for Chemical Research.



NAKAMURA Masaharu, Ph. D

Background

(a) Features of iron catalysts

Abundance
50000 ppm in earth's crust

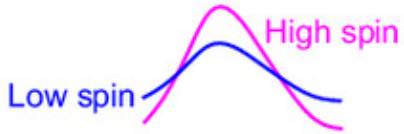
Good biocompatibility
Low toxicity; exist in HGB

Small atomic radius
1.72 Å

Electronic configuration
$1s^2\ 2s^2p^6\ 3s^2p^6d^6\ 4s^2$

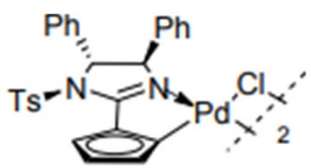
Multiple oxdation state
Fe(-2) to Fe(+6)

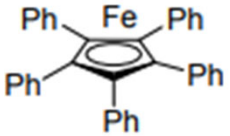
Spin effects in reaction



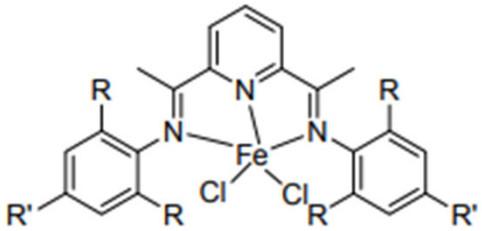
Valence state

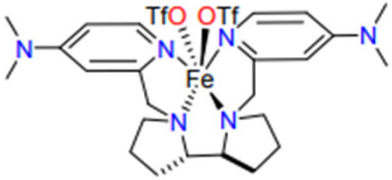
Fe(0) —— Fe(II) —— Fe(III) —— Fe(IV) —— Fe(VI)



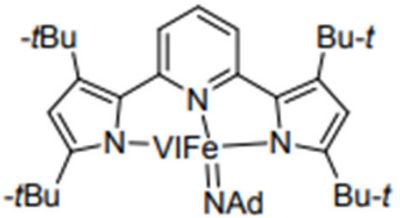


[PPFIP-Cl]$_2$





(*S*,*S*)-Me2N1



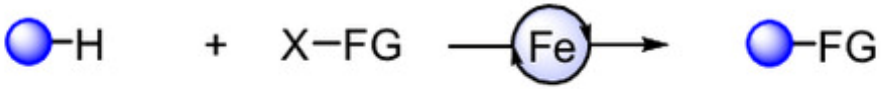
Ad = 1-adamantyl

L.-J. Li, Y. He, Y. Yang, J. Guo, Z. Lu, C. Wang, S. Zhu, S.-F. Zhu, CCS Chemistry 2024, 6, 537-584.

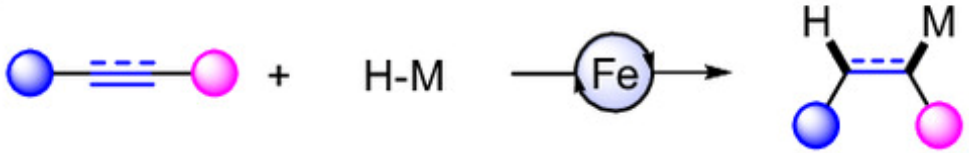
Representive iron-catalyzed Reactions

3.1 Cross-coupling reactions

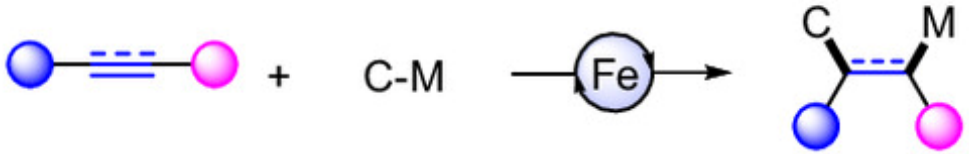
3.2 C-H bond functionalization reactions



3.3 Hydrometalation reactions of alkenes and alkynes



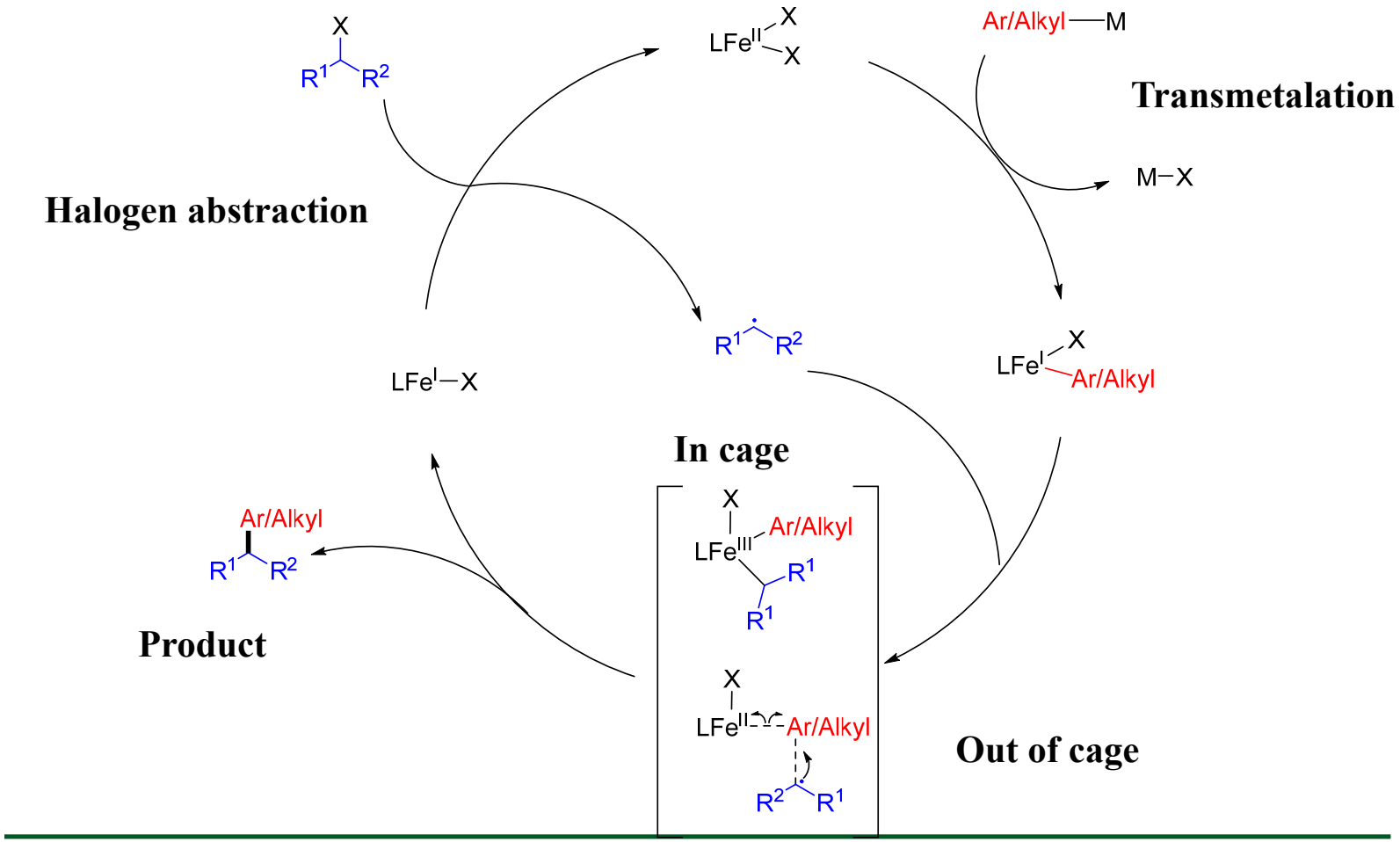
3.4 Carbometalation reactions of alkenes and alkynes



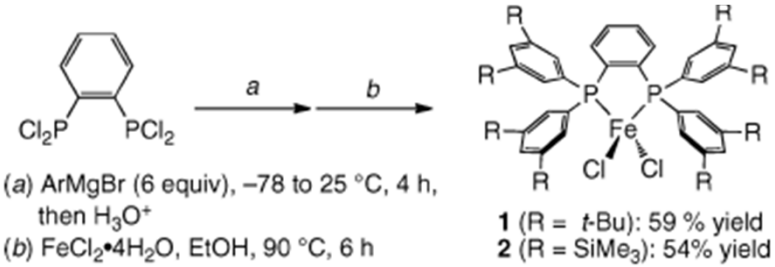
L.-J. Li, Y. He, Y. Yang, J. Guo, Z. Lu, C. Wang, S. Zhu, S.-F. Zhu, CCS Chemistry 2024, 6, 537-584.

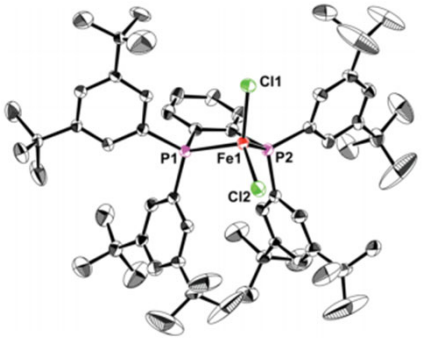
Cross-coupling

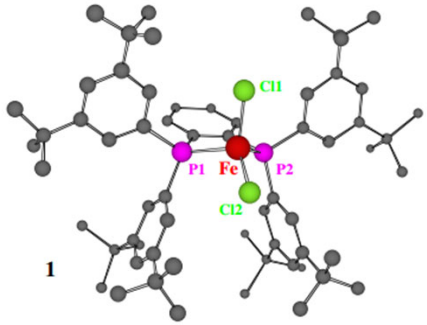
In cage / Out of cage mechanism



sp^2-sp^3 crossing-coupling





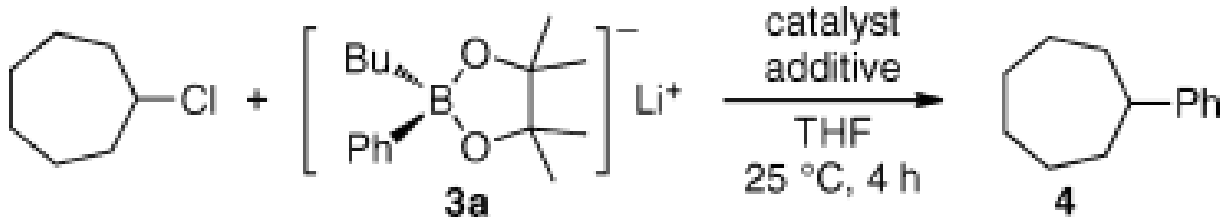


Selected bond lengths	Selected angles
Fe–Cl1 2.2190(14) Å	Cl1–Fe–Cl2 122.16(6)°
Fe–Cl2 2.2172(18) Å	P1–Fe–P2 80.63(4)°
Fe–P1 2.4623(14) Å	
Fe–P2 2.4404(13) Å	

	UB3LYP/ 6-31G(d)	X-ray crystal structure
Fe–Cl1	2.259 Å	2.2190(14) Å
Fe–Cl2	2.238 Å	2.2172(17) Å
Fe–P1	2.495 Å	2.4623(14) Å
Fe–P2	2.484 Å	2.4404(13) Å
Cl1–Fe–Cl	123.507°	122.16(6)°
P1–Fe–P2	81.557°	80.63(4)°

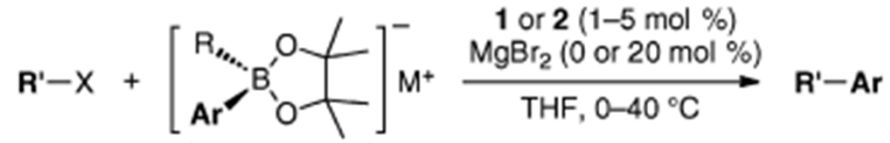
T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono, M. Nakamura, *Journal of the American Chemical Society* **2010**, *132*, 10674-10676.

Condition table

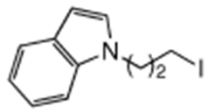
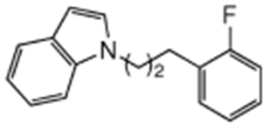
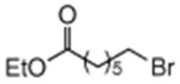
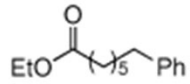
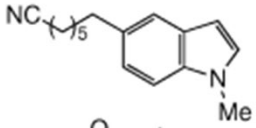
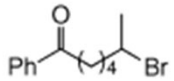
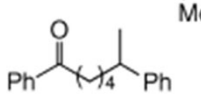
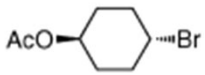
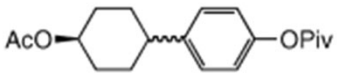
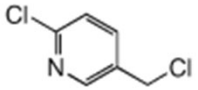
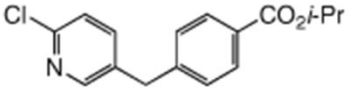
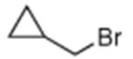
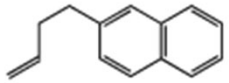
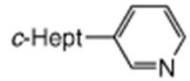


entry[a]	catalyst (3 mol %)	additive (mol %)	yield (%)[b]	recovery (%)[b]
1	$FeCl_3$	TMEDA (200)	0	>99
2	$FeCl_3$	TMEDA (200) + $MgBr_2$ (20)	0	>99
3	$FeCl_2(dppbz)_2$	none	0	>98
4	$FeCl_2(dppbz)_2$	$MgBr_2$ (20)	14	83
5	complex **1**	$MgBr_2$ (20)	**93**	0
6	complex **2**	$MgBr_2$ (20)	**91**	0
7	complex **2**	none	0	>99

T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono, M. Nakamura, *Journal of the American Chemical Society* **2010**, *132*, 10674-10676.

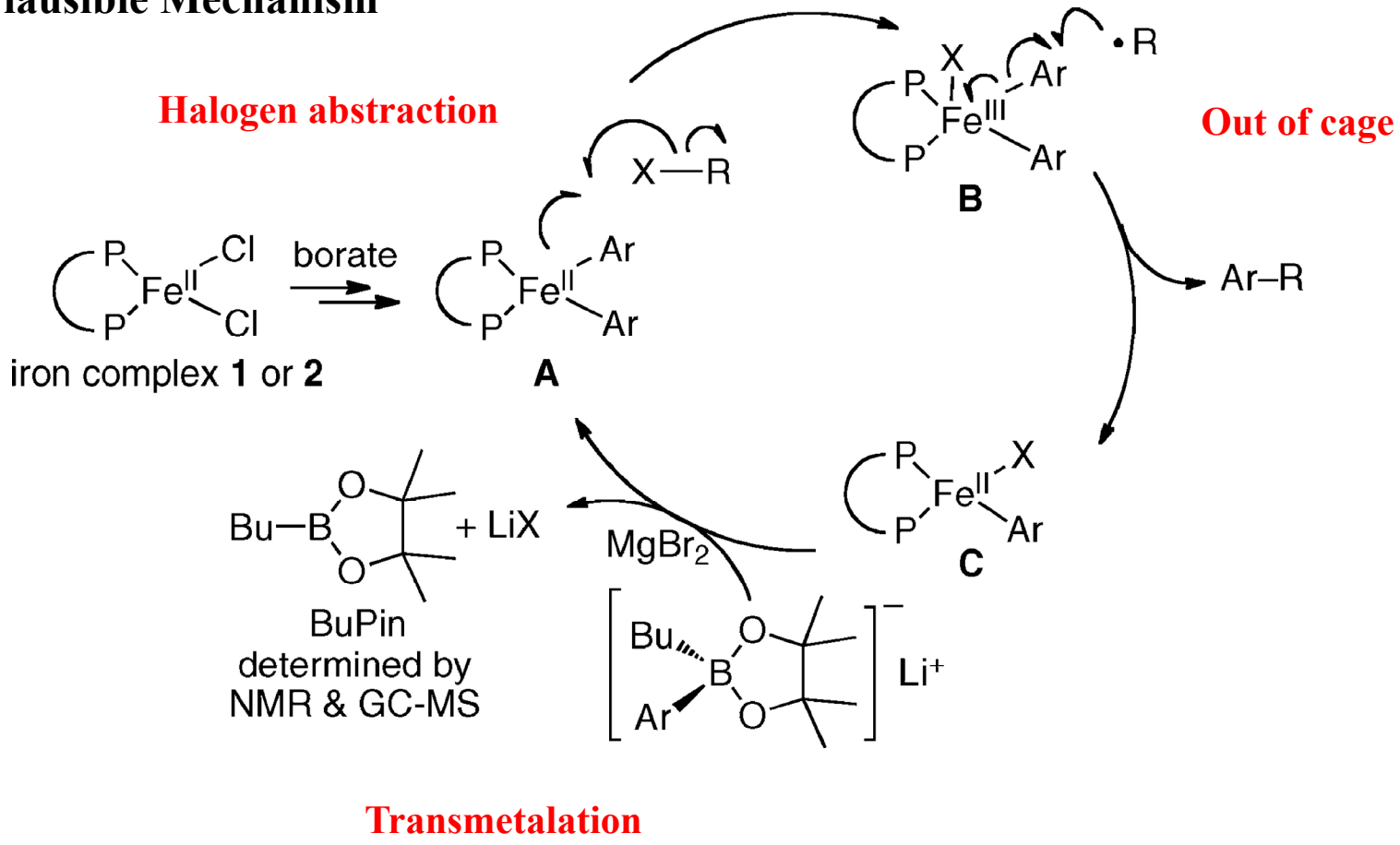


R' = 1°, 2° alkyl, R = Et, Bu, *t*-Bu, Ar = aromatic group, M = Li or MgBr

entry[a]	Alkyl–X	coupling product	yield (%)[b]
1[c]	*c*-Hept—Br	*c*-Hept—R"	99 (R" = H)
2			98 (R" = OMe)
3			94 (R" = NMe_2)
4			77 (R" = Cl)
5[d,e,f]			90 (R" = CO_2Me)
6[d,e,f]			81 (R" = CO_2Et)
7[d,e,f]			74 (R" = CO_2i-Pr)
8		*c*-Hept, F, F, F	83
9			79
10[f,g]	*c*-Hept—Cl	*c*-Hept	93[h]
11			90
12[g]			96
13[e]			65
14[d,e]			83[i]
15[d,f]			86
16			99[j]
17[d]	*c*-Hept—Br		73

T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono, M. Nakamura, *Journal of the American Chemical Society* **2010**, *132*, 10674-10676.

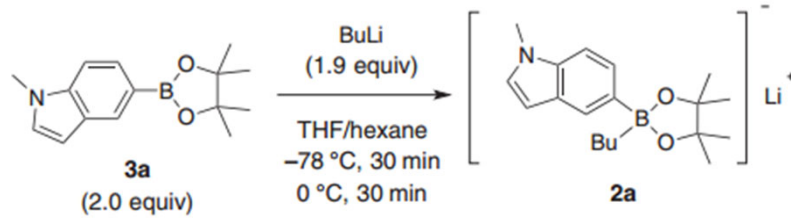
Plausible Mechanism



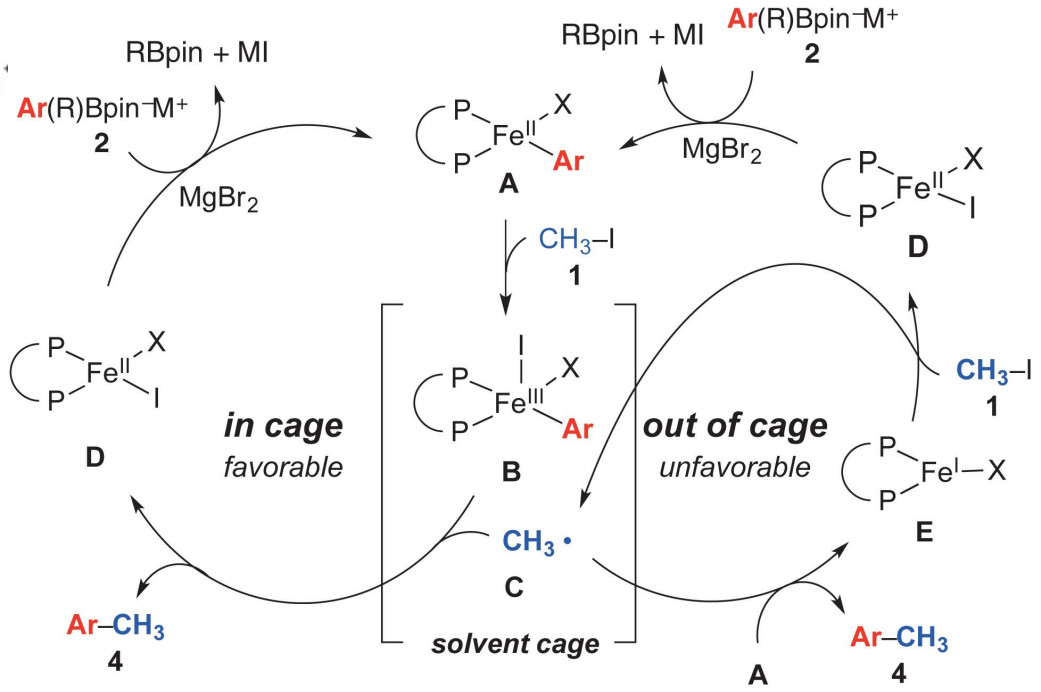
T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono, M. Nakamura, *Journal of the American Chemical Society* **2010**, *132*, 10674-10676.

sp^2-sp^3 crossing-coupling

the first example of iron-catalyzed cross-coupling-based methylations of arylboron compounds



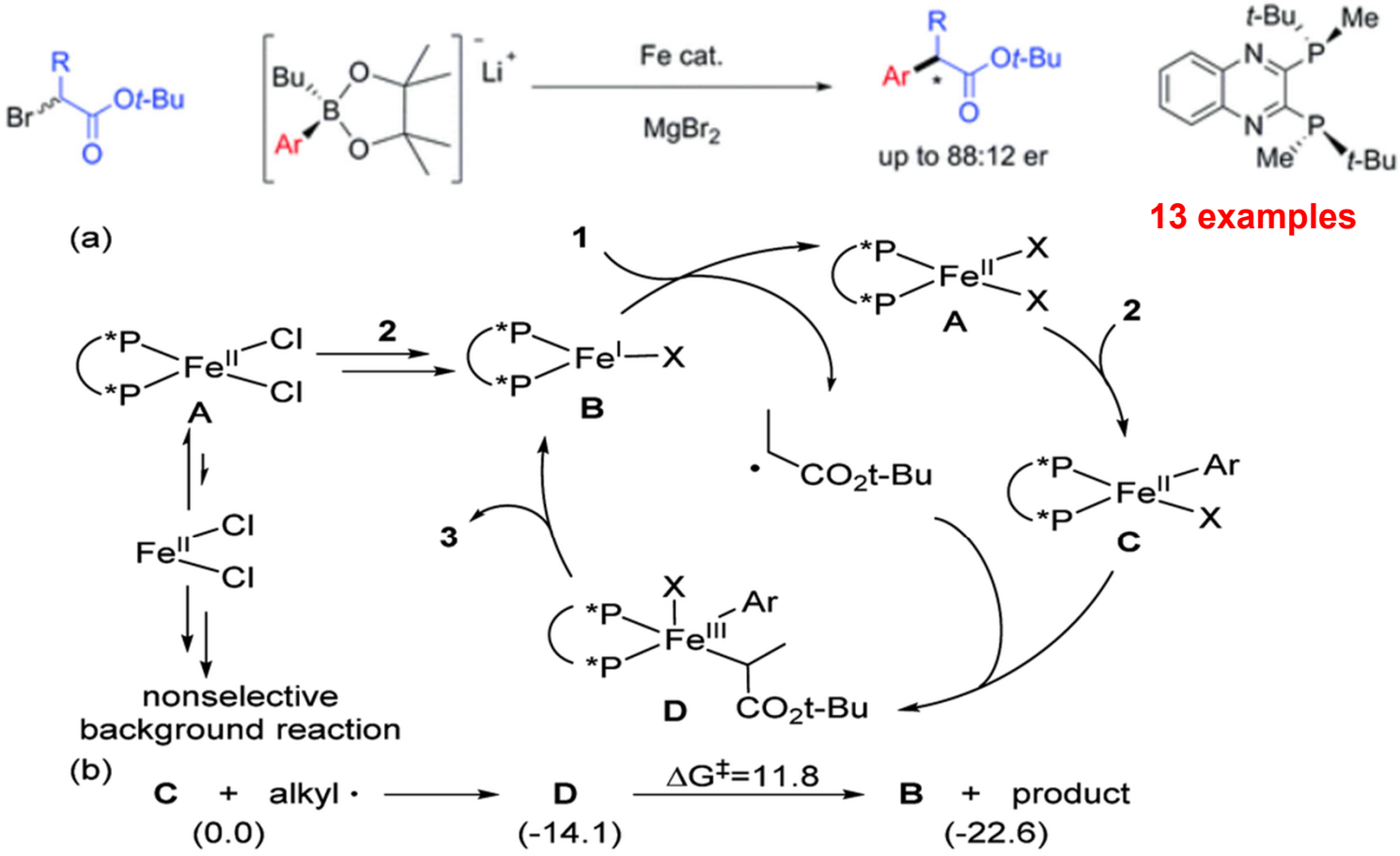
Plausible Mechanism



S. Nakajima, H. Takaya, M. Nakamura, *Chemistry Letters* **2017**, *46*, 711-714.

sp^2-sp^3 crossing-coupling

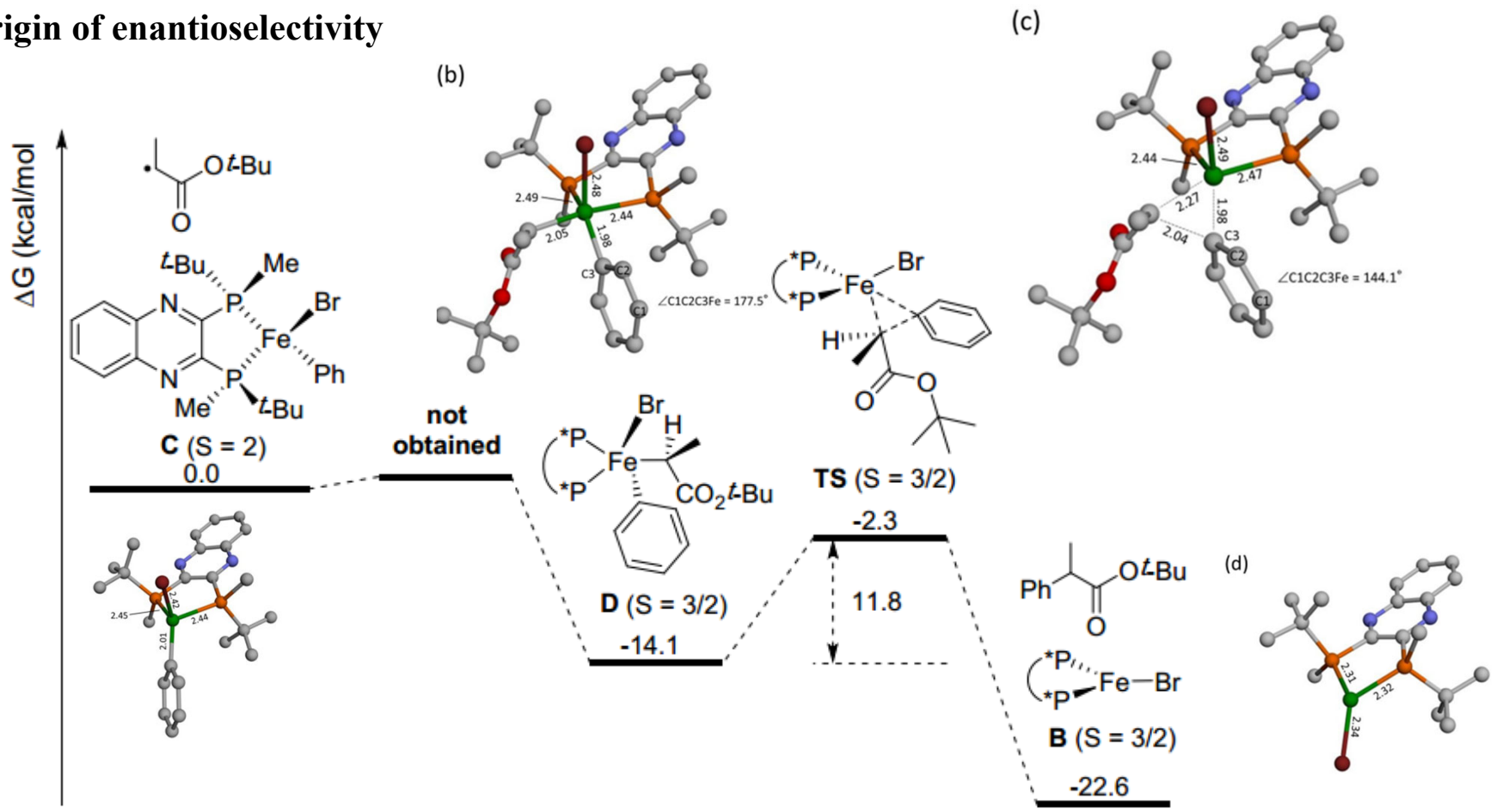
the first examples of iron-catalysed enantioselective couplingsof organoboron reagents



T. Iwamoto, C. Okuzono, L. Adak, M. Jin, M. Nakamura, *Chemical Communications* **2019**, *55*, 1128-1131.

sp^2-sp^3 crossing-coupling

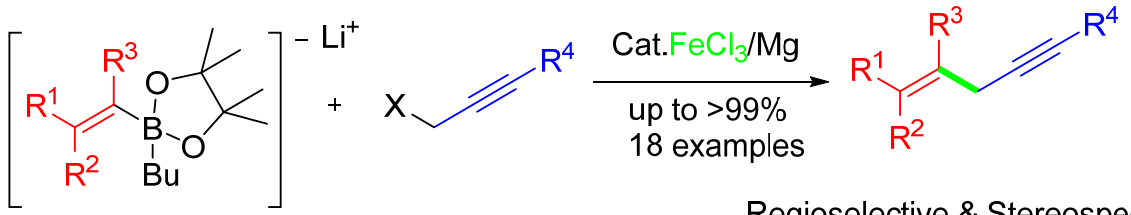
Origin of enantioselectivity



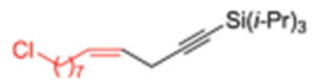
T. Iwamoto, C. Okuzono, L. Adak, M. Jin, M. Nakamura, *Chemical Communications* **2019**, *55*, 1128-1131.

sp^2-sp^3 crossing-coupling

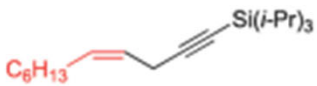
The first iron-catalysed cross coupling of propargyl electrophileswith lithium alkenylborates



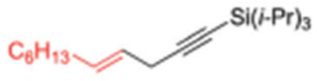
Regioselective & Stereospecific
Functional group tolerance
Ligand-free condition



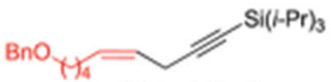
3a, 87%, 2.92g, >99% *Z*[b]



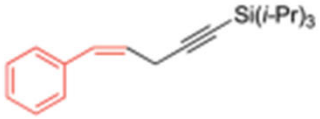
3c, 93%, >99% *Z*



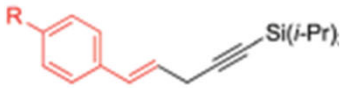
3e, (50%), >99% *E*[c,d]
82%, >99% *E*



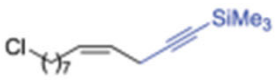
3b, 68%, >99% *Z*



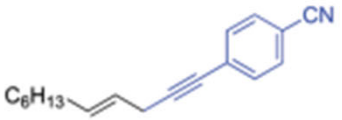
3d, 95%, >99% *Z*



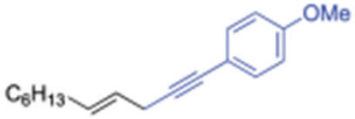
R = OMe: **3f**, 78%, >99% *E*
R = CF_3: **3g**, 86%, >99% *E*



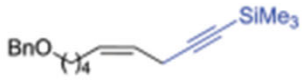
3h, 82%, >99% *Z*
(**3h**:**4h** = 93:7)[e]



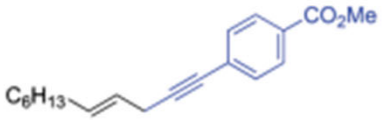
3j, (83%) 28%, >99% *E*[d]



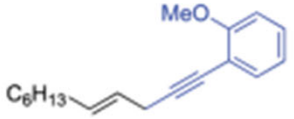
3l, 57%, >99% *E*



3i, 81%, >99% *Z*

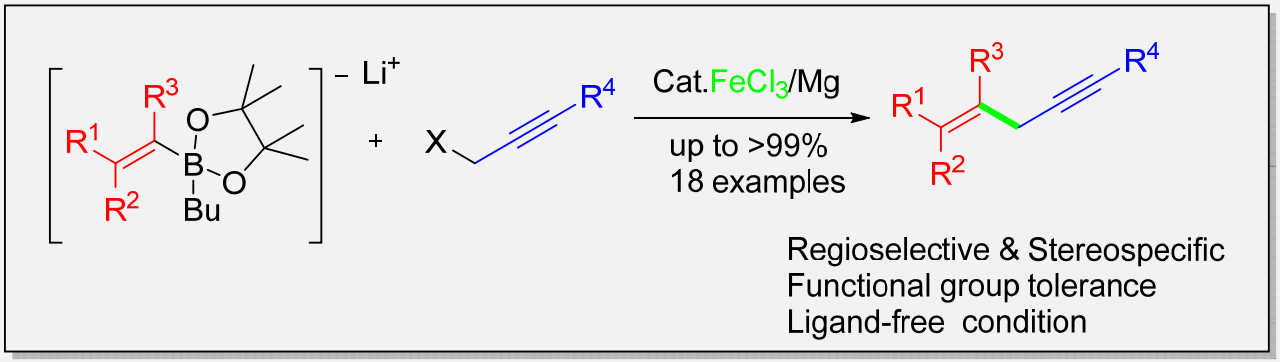


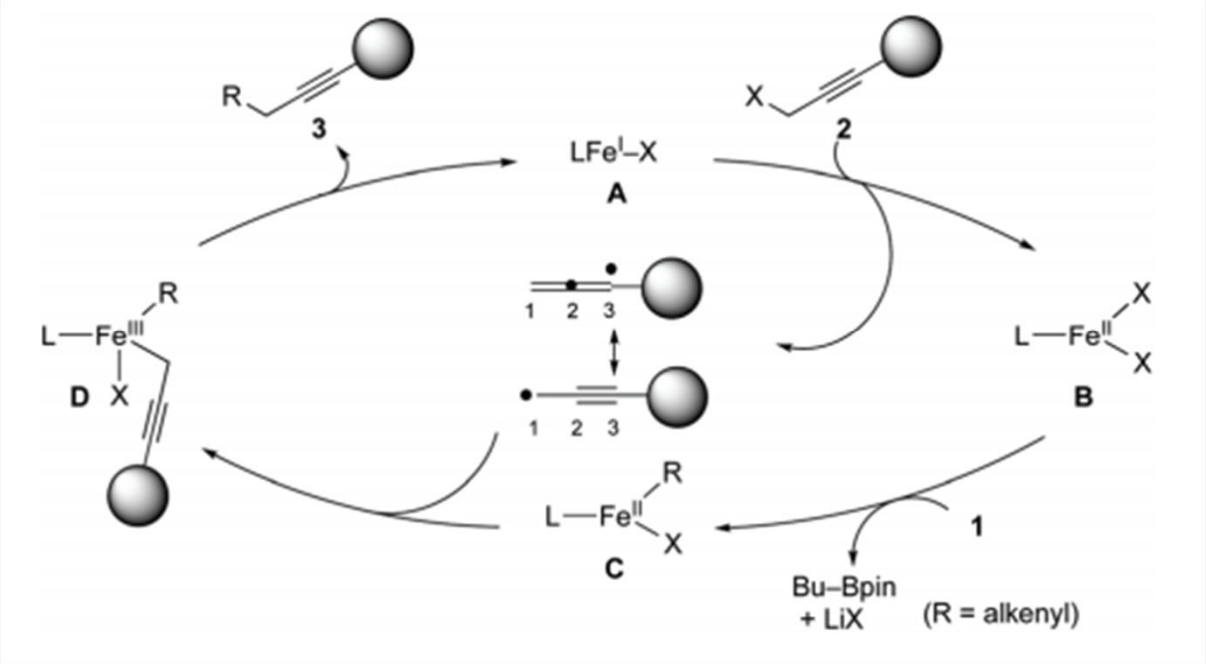
3k, 56%, >99% *E*



3m, 52%, >99% *E*

R. Agata, S. Lu, H. Matsuda, K. Isozaki, M. Nakamura, *Organic & Biomolecular Chemistry* **2020**, *18*.

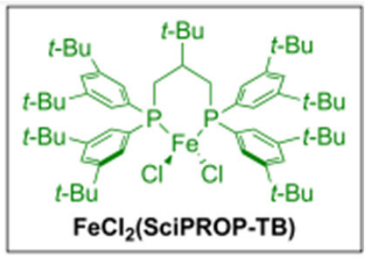


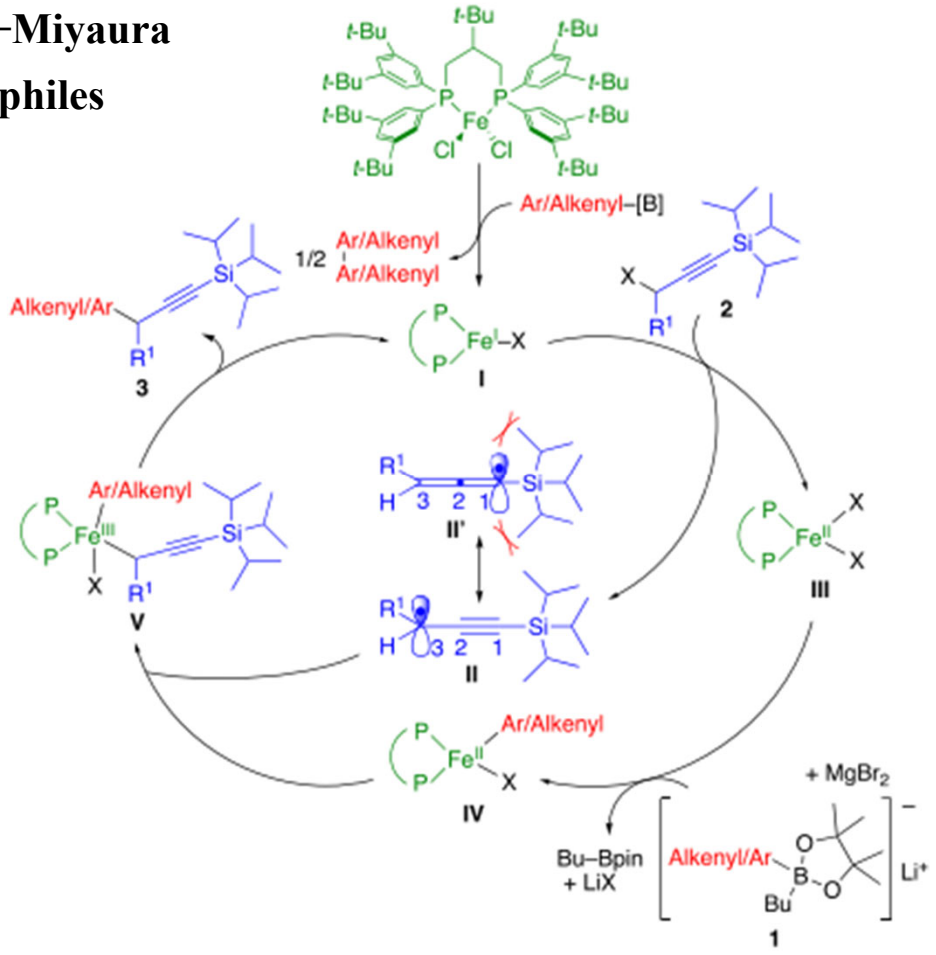


R. Agata, S. Lu, H. Matsuda, K. Isozaki, M. Nakamura, *Organic & Biomolecular Chemistry* **2020**, *18*.

sp^2-sp^3 crossing-coupling

The first iron-catalyzed regioselective Suzuki−Miyaura cross-coupling of secondary propargyl electrophiles with lithium organoborates

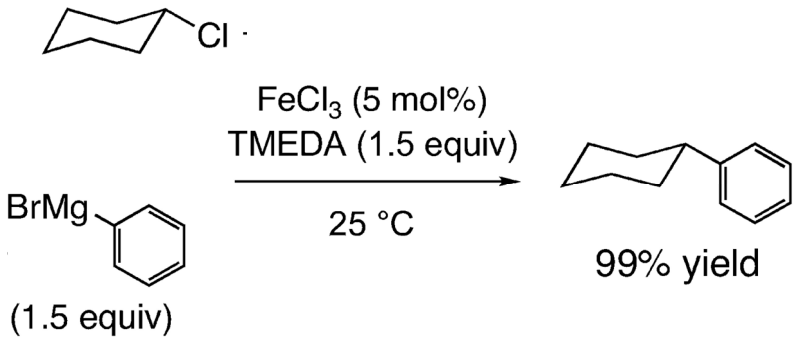


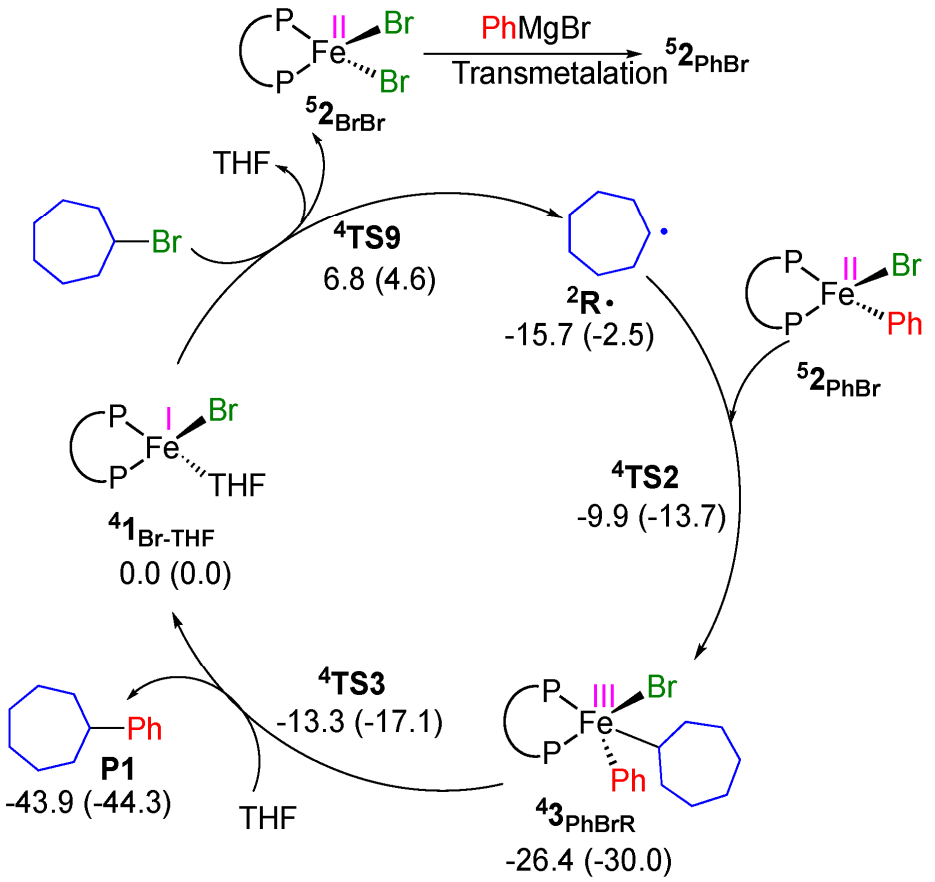


S. Lu, R. Agata, S. Nomura, H. Matsuda, K. Isozaki, M. Nakamura, *The Journal of Organic Chemistry* **2024**, *89*, 8385-8396.

sp^2-sp^3 Cross-coupling

Primary and Secondary Alkyl Halides with Aryl Grignard Reagents

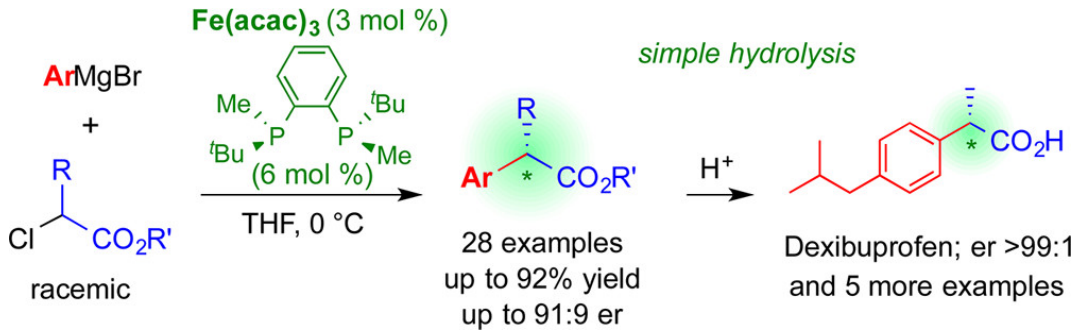




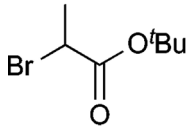
M. Nakamura, K. Matsuo, S. Ito, E. Nakamura, *Journal of the American Chemical Society* **2004**, *126*, 3686-3687.
R. Agata, S. Lu, H. Matsuda, K. Isozaki, M. Nakamura, Organic & Biomolecular Chemistry 2020, 18.

sp^2-sp^3 crossing-coupling

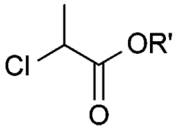
the first example of iron-catalyzed enantioselective cross coupling



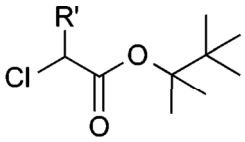
α-Haloalkanoates



1a

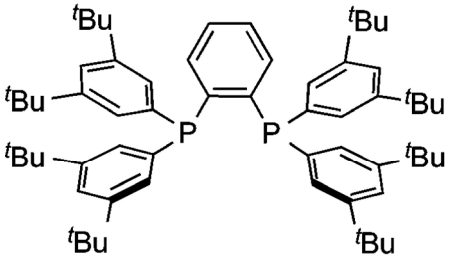


R' = ^{t}Bu: **1b**
R' = ^{i}Pr: **1c**
R' = Et : **1d**



R' = Me: **1e** R' = Et: **1f**
R' = ^{i}Bu: **1g** R' = $MeOCH_2$: **1h**

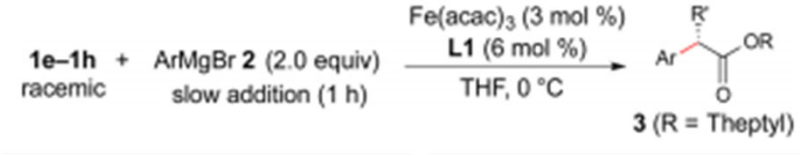
Ligand

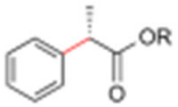
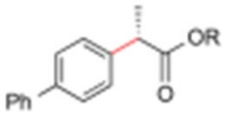
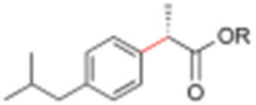
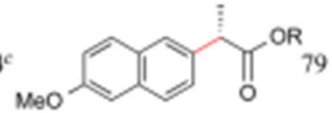
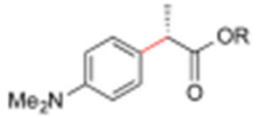


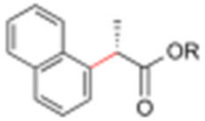
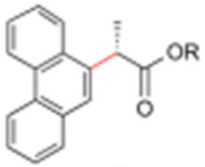
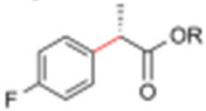
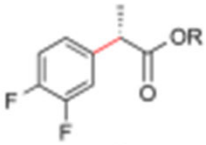
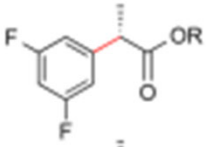
SciOPP

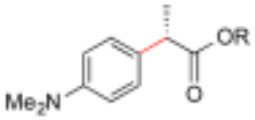
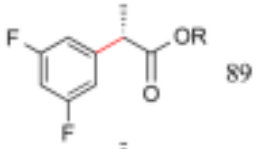
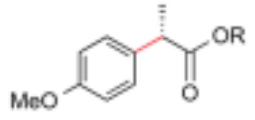
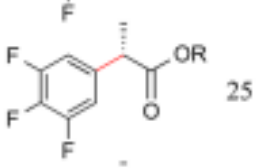
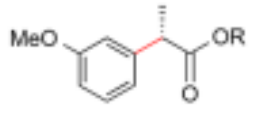
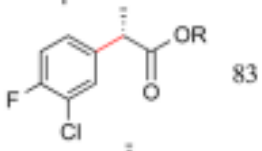
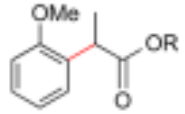
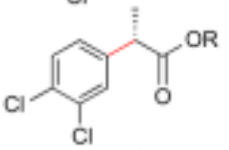
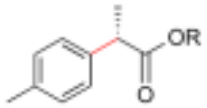
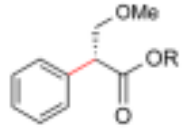
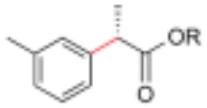
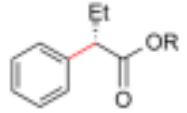
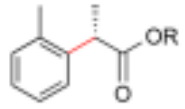
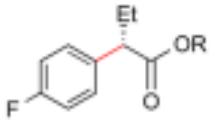
M. Jin, L. Adak, M. Nakamura, *Journal of the American Chemical Society* **2015**, *137*, 7128-7134.

sp^2-sp^3 crossing-coupling



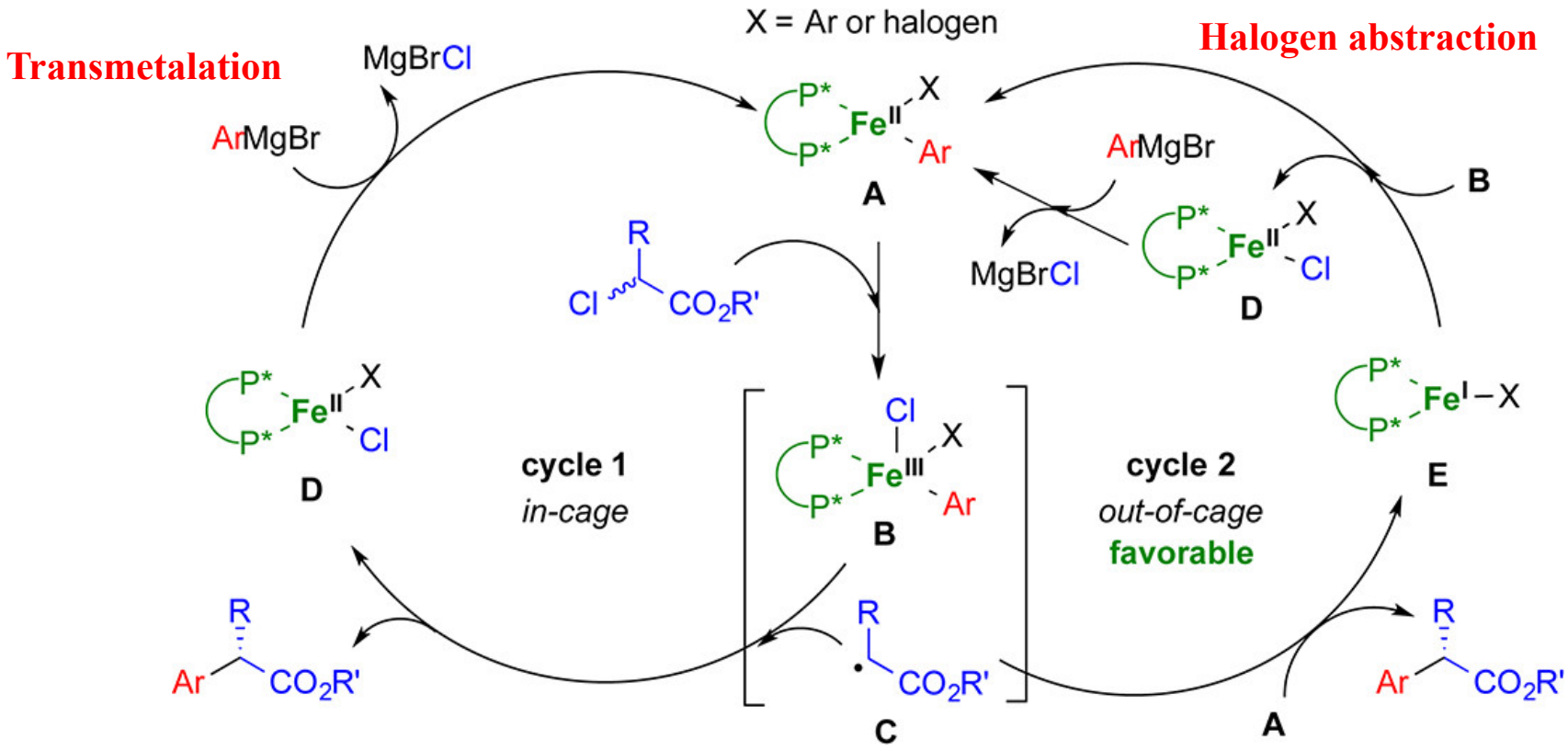
entry	product	% yield (er)[b]
1		82 (90:10)
2[c]		90 (86:14)
3[c]		75 (87:13)
4[c]		79 (87:13)
5		78 (88:12)

entry	product	% yield (er)[b]
15		31 (58:42)
16		81 (74:26)
17		87 (91:9)
18		83 (91:9)
19		89 (90:10)

5		78 (88:12)	19		89 (90:10)
6		78 (88:12)	20		25 (90:10)
7		70 (89:11)	21		83 (91:9)
8		0 (NA)	22		88 (90:10)
9		89 (87:13)	23		42 (77:23)
10		84 (88:12)	24		67 (88:12)
11		38 (84:16)	25		69 (90:10)

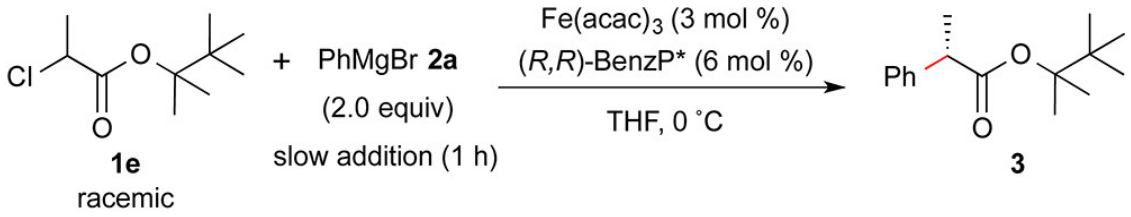
M. Jin, L. Adak, M. Nakamura, *Journal of the American Chemical Society* **2015**, *137*, 7128-7134.

Mechanism

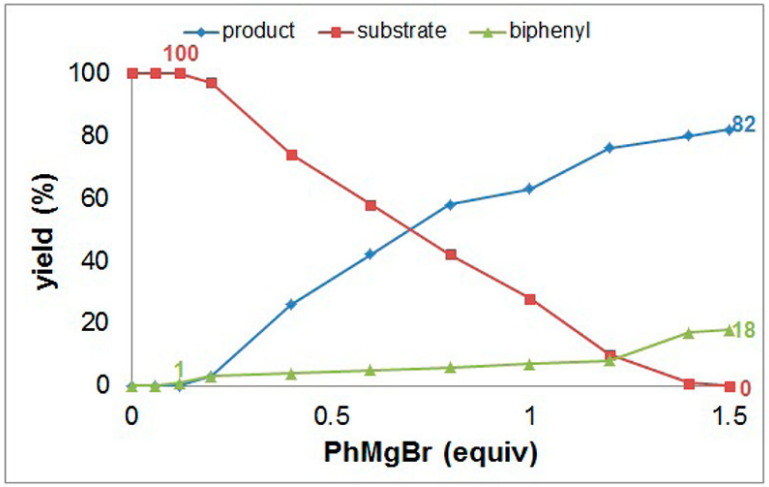


M. Jin, L. Adak, M. Nakamura, *Journal of the American Chemical Society* **2015**, *137*, 7128-7134.

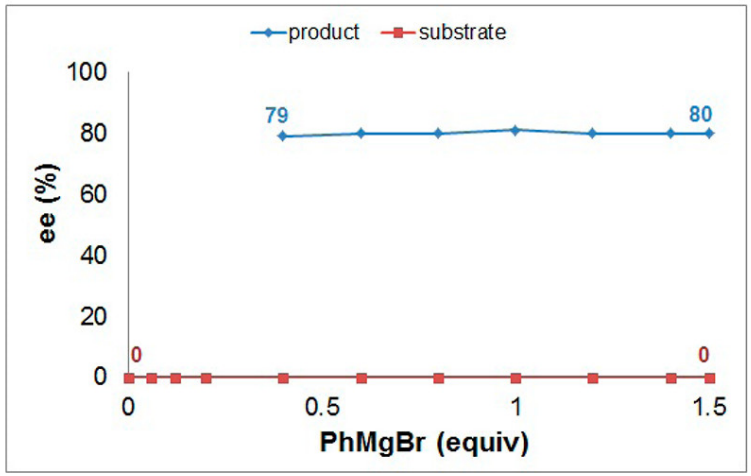
Mechanism



(a)

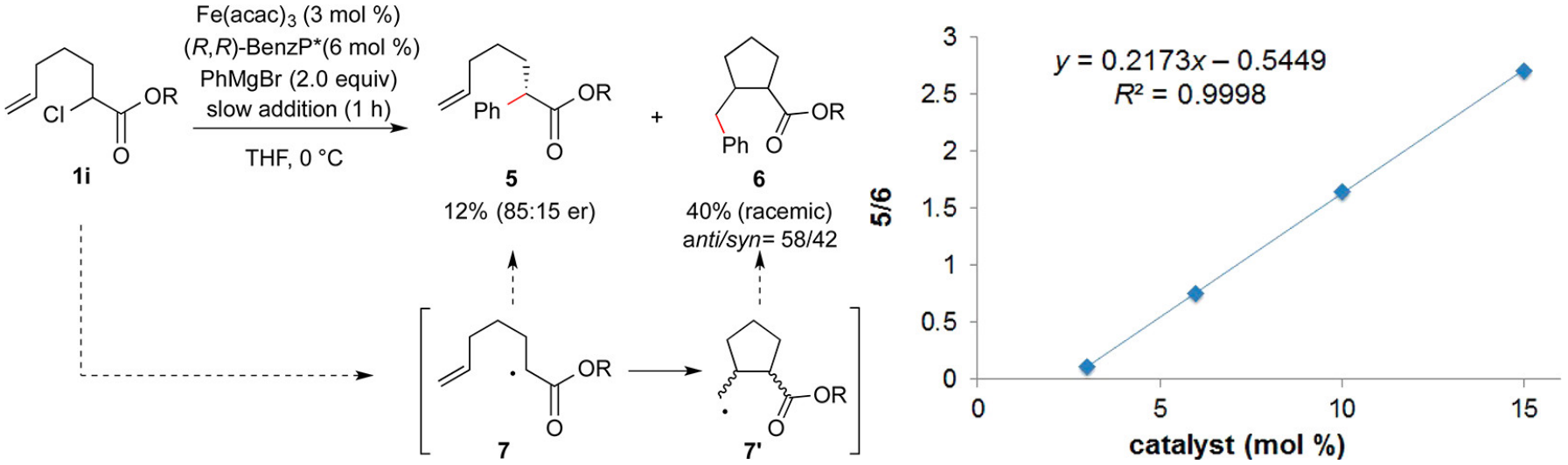


(b)



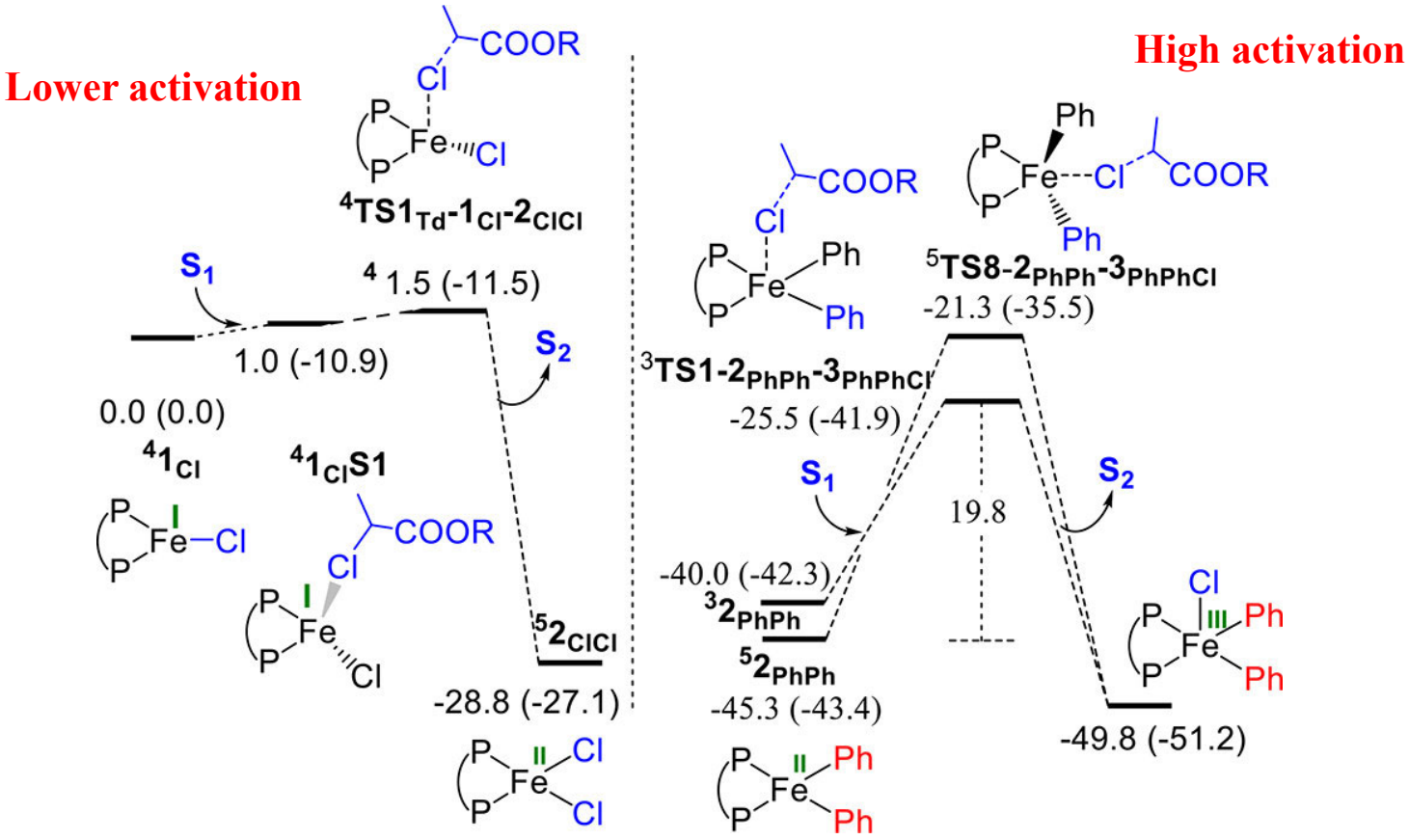
M. Jin, L. Adak, M. Nakamura, *Journal of the American Chemical Society* **2015**, *137*, 7128-7134.

Mechanism



M. Jin, L. Adak, M. Nakamura, *Journal of the American Chemical Society* **2015**, *137*, 7128-7134.

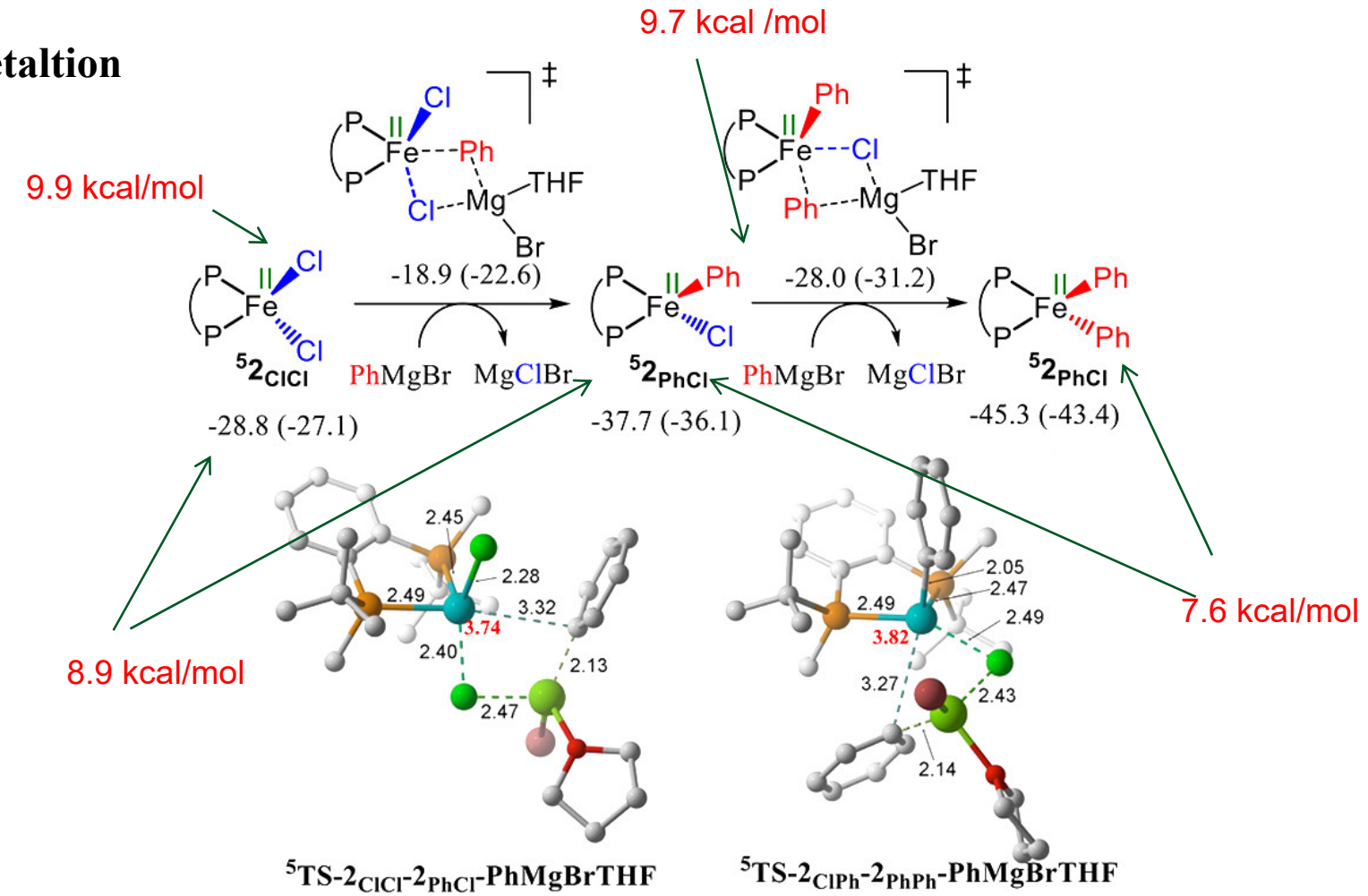
C-Cl activation



A. K. Sharma, W. M. C. Sameera, M. Jin, L. Adak, C. Okuzono, T. Iwamoto, M. Kato, M. Nakamura, K. Morokuma, *Journal of the American Chemical Society* **2017**, *139*, 16117-16125.

sp^2-sp^3 crossing-coupling

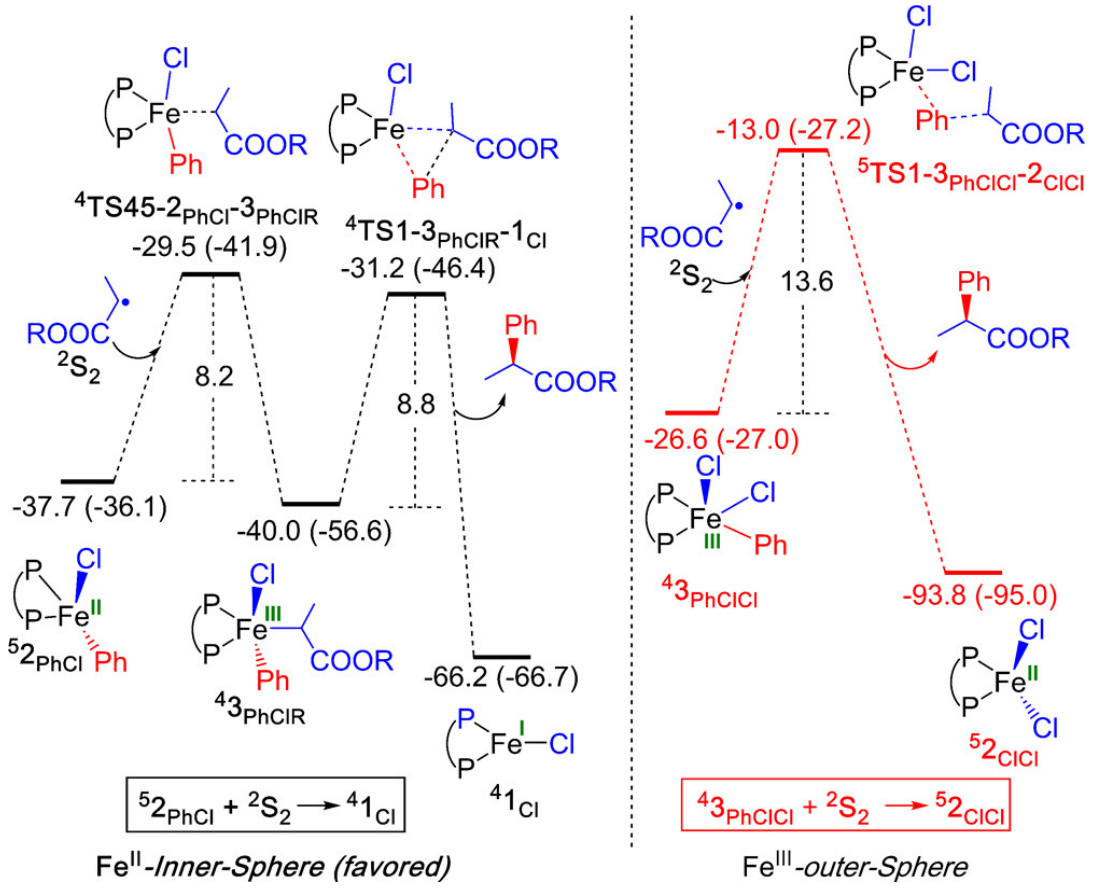
Transmetaltion



A. K. Sharma, W. M. C. Sameera, M. Jin, L. Adak, C. Okuzono, T. Iwamoto, M. Kato, M. Nakamura, K. Morokuma, *Journal of the American Chemical Society* **2017**, *139*, 16117-16125.

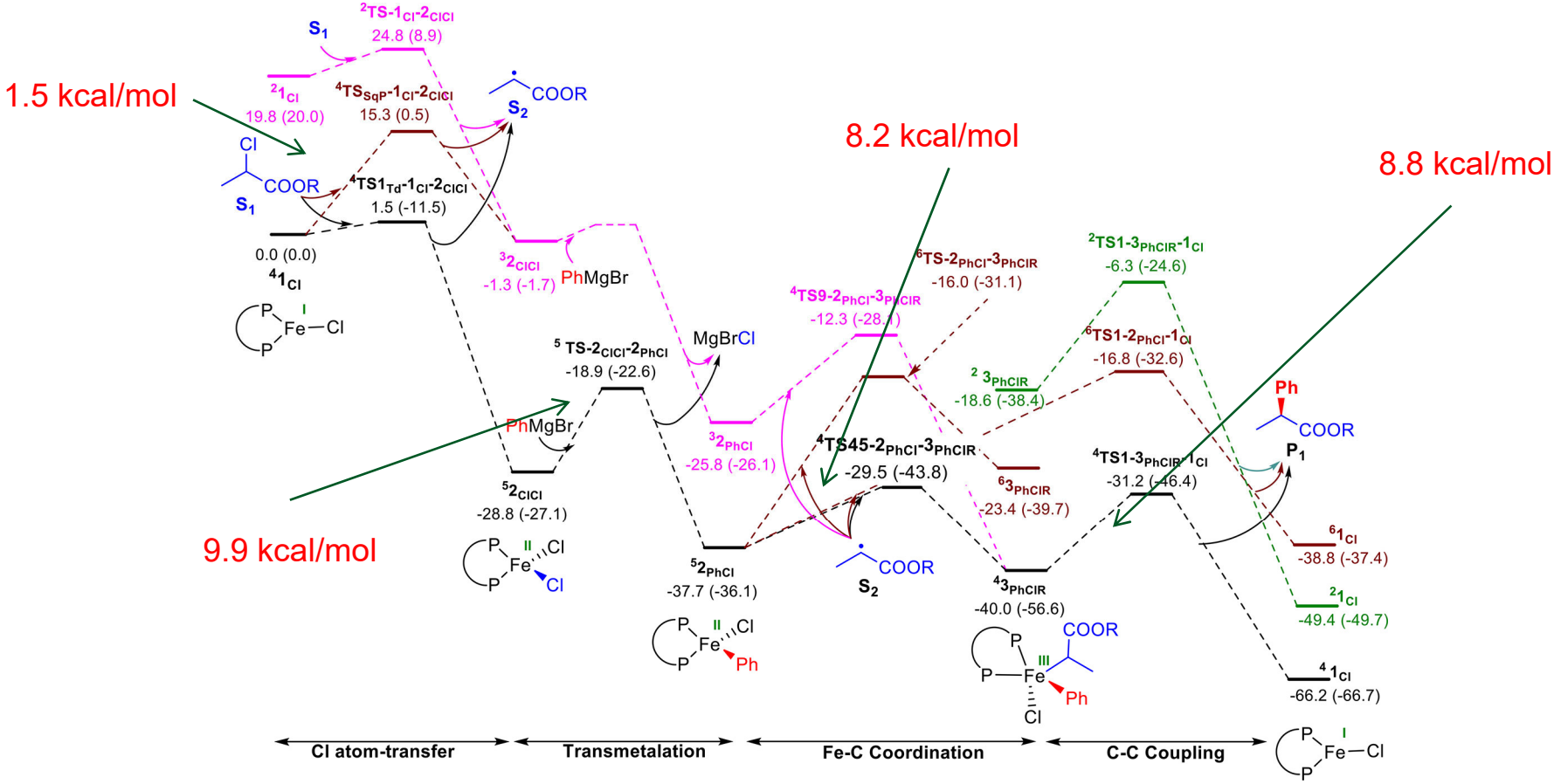
sp^2-sp^3 crossing-coupling

C-C bond formation



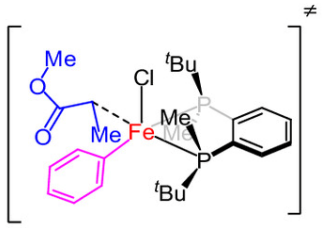
A. K. Sharma, W. M. C. Sameera, M. Jin, L. Adak, C. Okuzono, T. Iwamoto, M. Kato, M. Nakamura, K. Morokuma, *Journal of the American Chemical Society* **2017**, *139*, 16117-16125.

Free energy profile for the favorable reaction pathway (FeI/FeII/FeIII pathway)

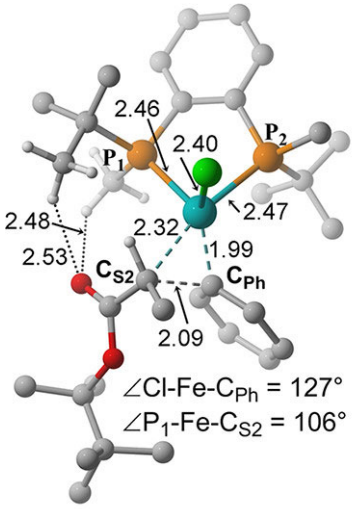


A. K. Sharma, W. M. C. Sameera, M. Jin, L. Adak, C. Okuzono, T. Iwamoto, M. Kato, M. Nakamura, K. Morokuma, *Journal of the American Chemical Society* **2017**, *139*, 16117-16125.

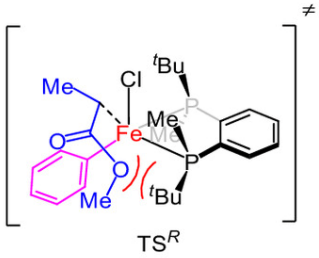
Origin of Enantioselectivity



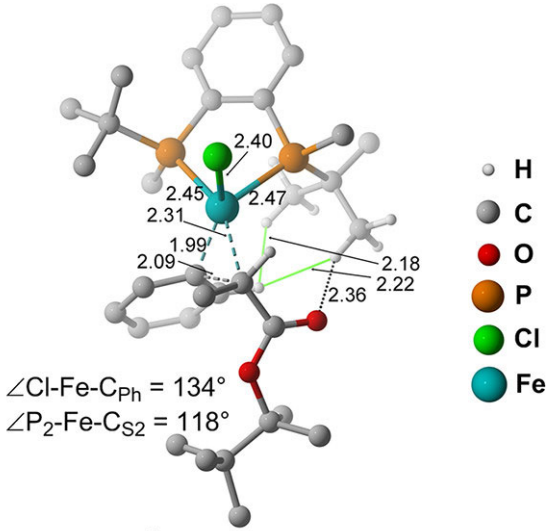
TS^S



^{4}TS1-3$_{PhClR}$-1$_{Cl}$-*S*



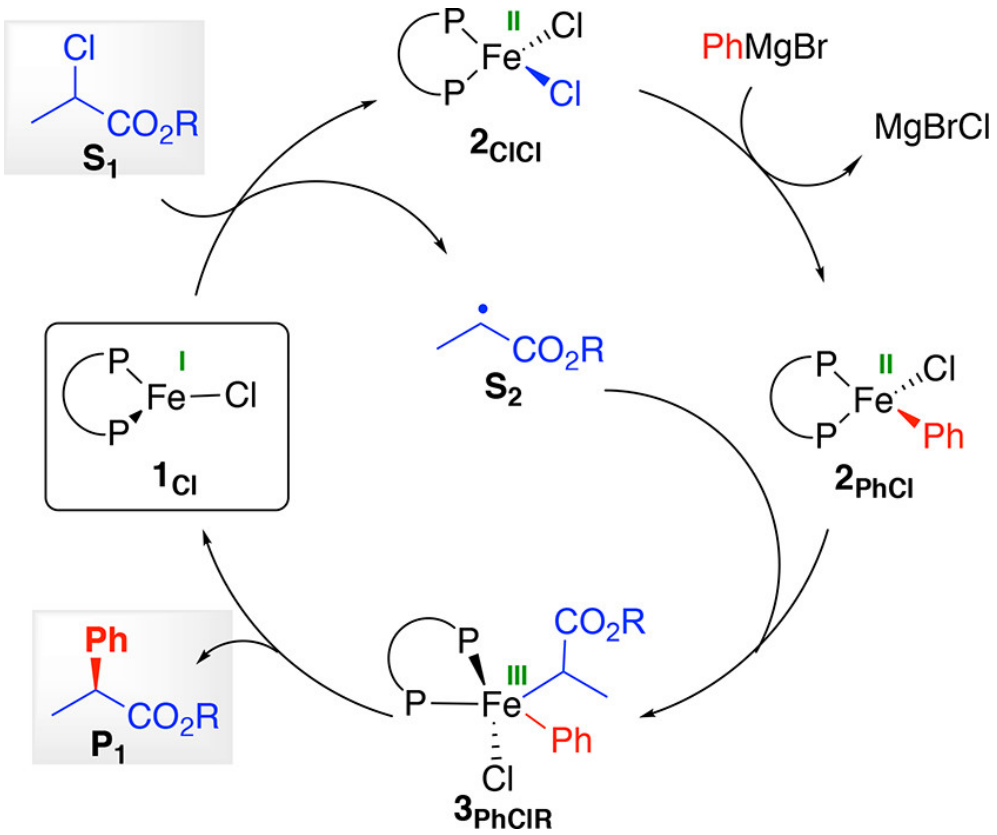
TS^R



^{4}TS2-3$_{PhClR}$-1$_{Cl}$-*R*

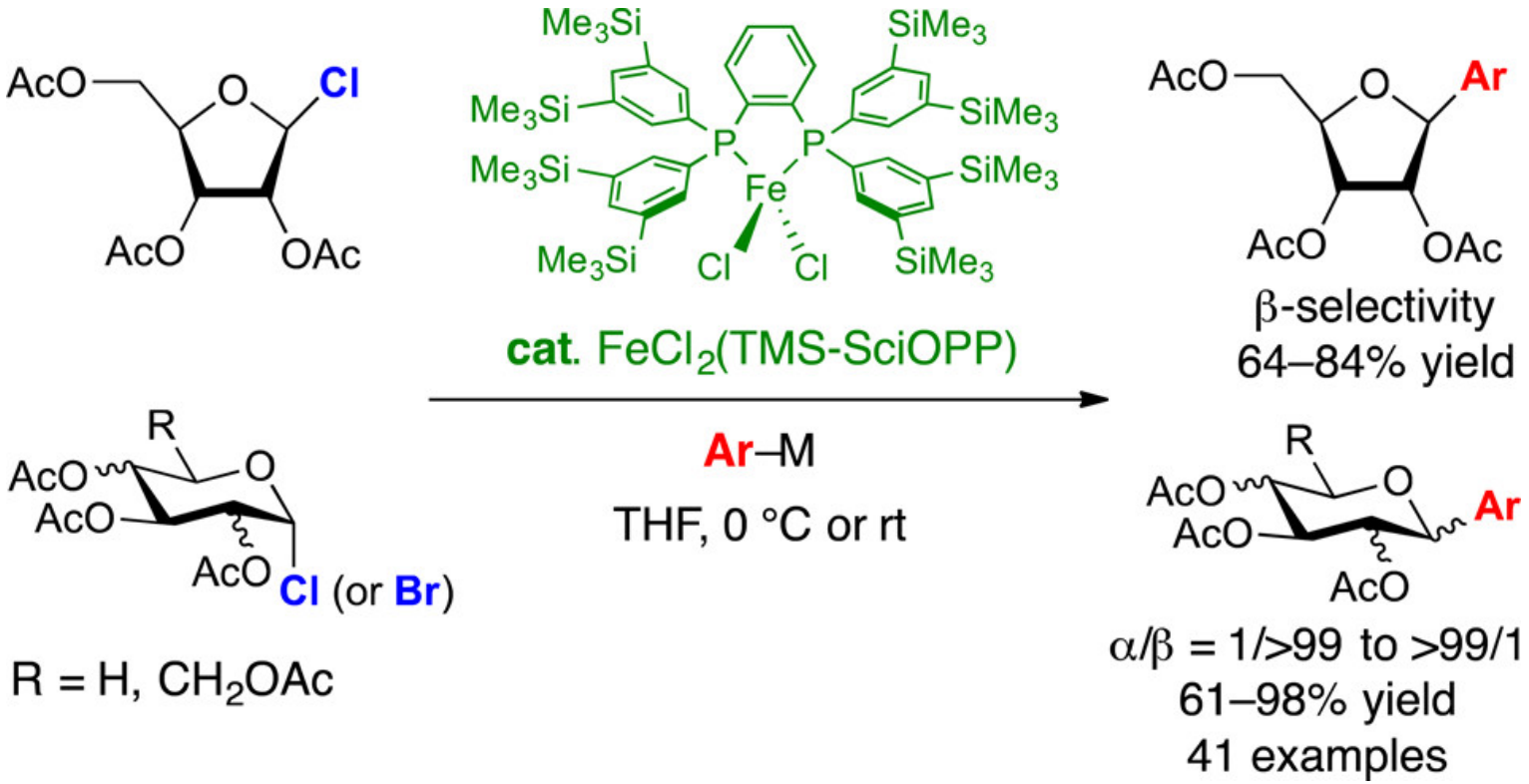
A. K. Sharma, W. M. C. Sameera, M. Jin, L. Adak, C. Okuzono, T. Iwamoto, M. Kato, M. Nakamura, K. Morokuma, *Journal of the American Chemical Society* **2017**, *139*, 16117-16125.

Mechanism



A. K. Sharma, W. M. C. Sameera, M. Jin, L. Adak, C. Okuzono, T. Iwamoto, M. Kato, M. Nakamura, K. Morokuma, *Journal of the American Chemical Society* **2017**, *139*, 16117-16125.

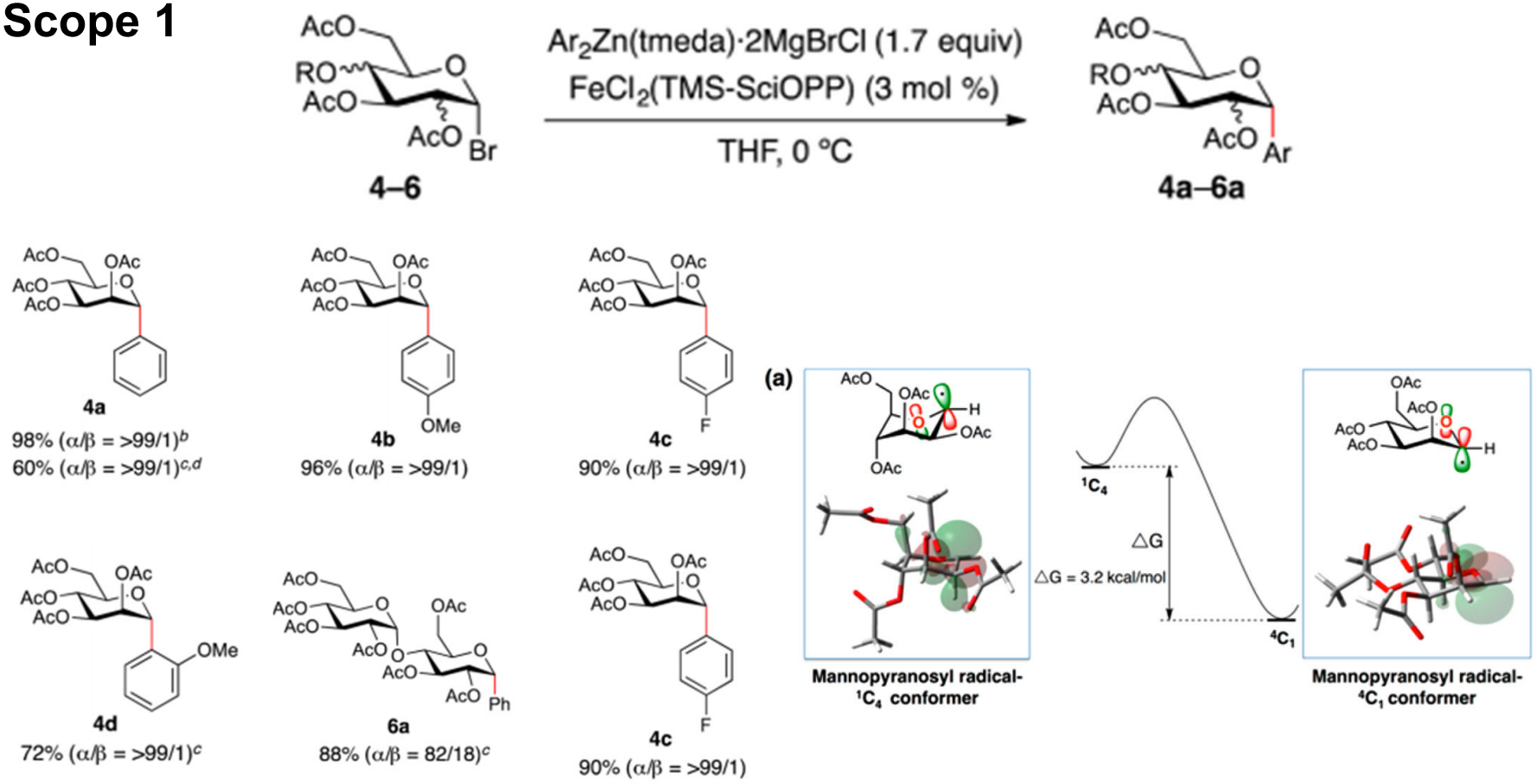
Stereoselective Anomeric Arylation of Glycosyl Radicals



L. Adak, S. Kawamura, G. Toma, T. Takenaka, K. Isozaki, H. Takaya, A. Orita, H. C. Li, T. K. M. Shing, M. Nakamura, *Journal of the American Chemical Society* **2017**, *139*, 10693-10701.

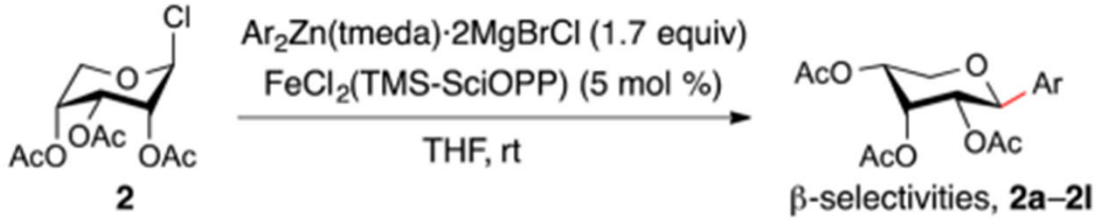
sp^2-sp^3 crossing-coupling

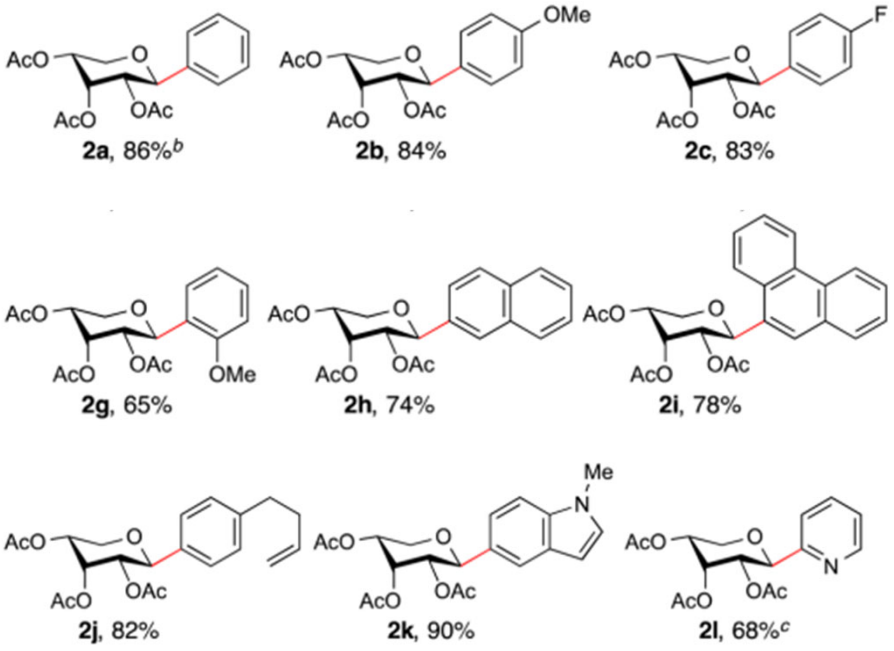
Scope 1

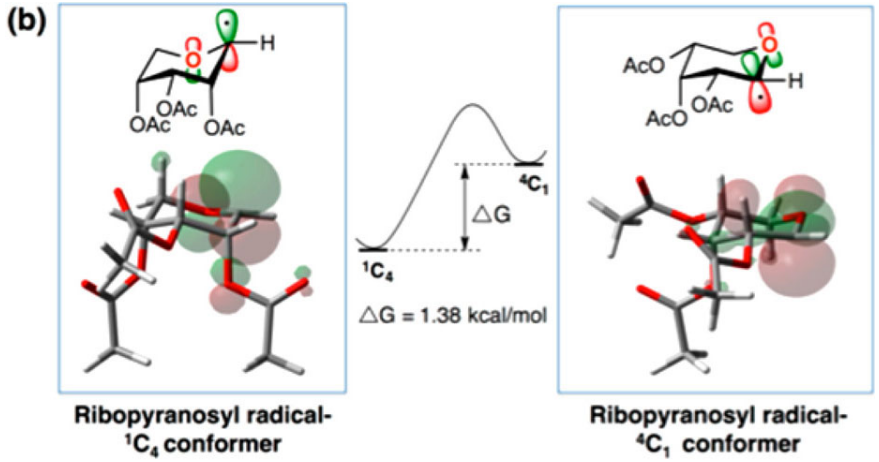


L. Adak, S. Kawamura, G. Toma, T. Takenaka, K. Isozaki, H. Takaya, A. Orita, H. C. Li, T. K. M. Shing, M. Nakamura, *Journal of the American Chemical Society* **2017**, *139*, 10693-10701.

Scope 2

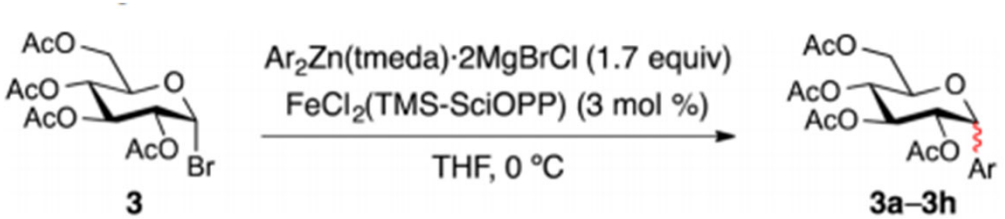


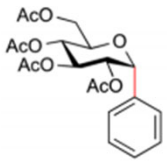




L. Adak, S. Kawamura, G. Toma, T. Takenaka, K. Isozaki, H. Takaya, A. Orita, H. C. Li, T. K. M. Shing, M. Nakamura, *Journal of the American Chemical Society* **2017**, *139*, 10693-10701.

Scope 3

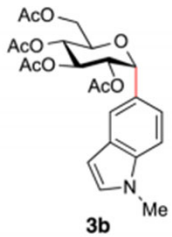




3a

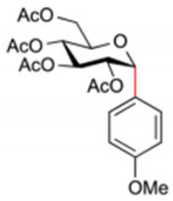
96% (α/β = 73/27)

51% (α/β = 68/32)[b,c]



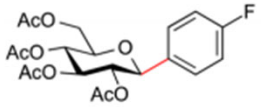
3b

95% (α/β = 74/26)



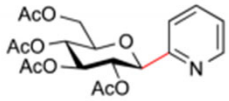
3c

96% (α/β = 56/44)



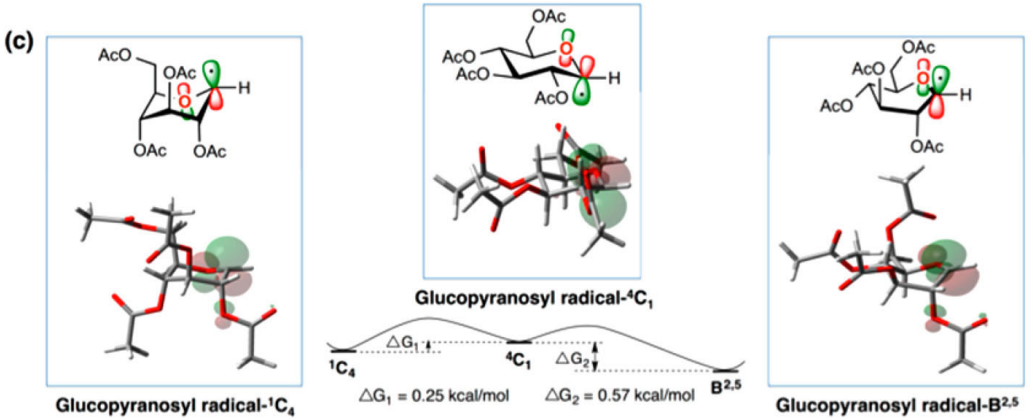
3d

90% (α/β = 46/54)



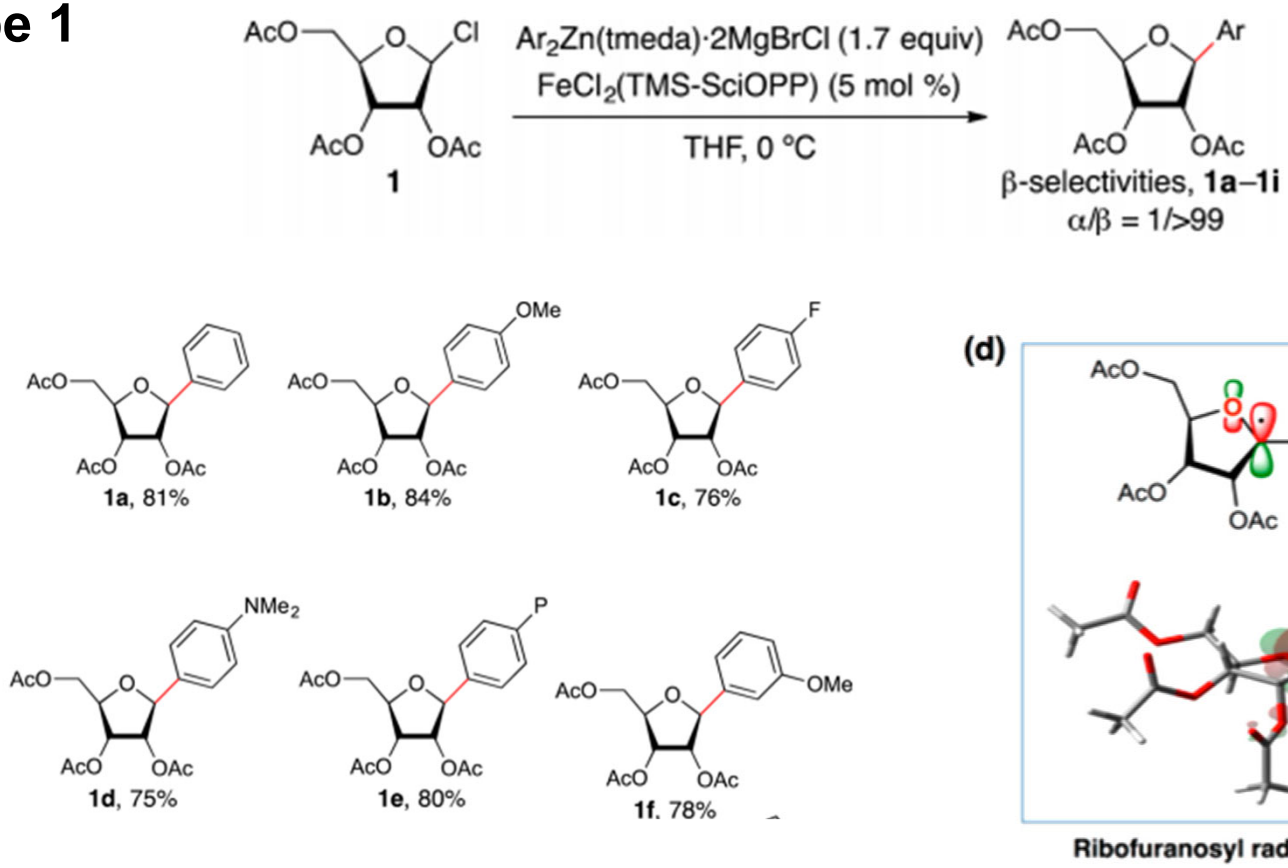
3e

76% (α/β = 25/75)[d]



L. Adak, S. Kawamura, G. Toma, T. Takenaka, K. Isozaki, H. Takaya, A. Orita, H. C. Li, T. K. M. Shing, M. Nakamura, *Journal of the American Chemical Society* **2017**, *139*, 10693-10701.

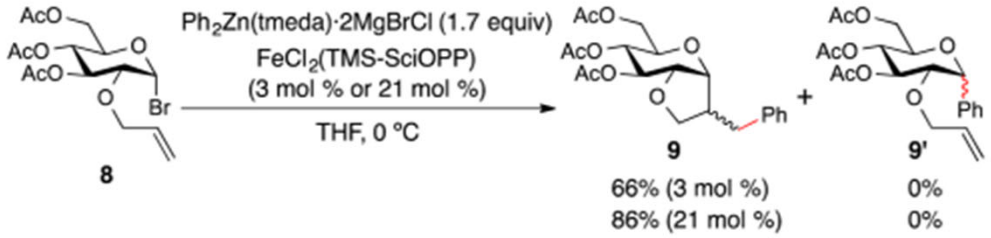
Scope 1



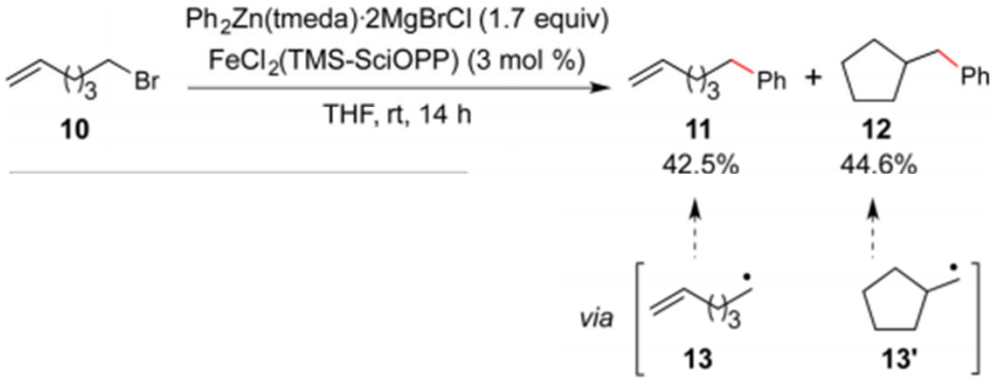
L. Adak, S. Kawamura, G. Toma, T. Takenaka, K. Isozaki, H. Takaya, A. Orita, H. C. Li, T. K. M. Shing, M. Nakamura, *Journal of the American Chemical Society* **2017**, *139*, 10693-10701.

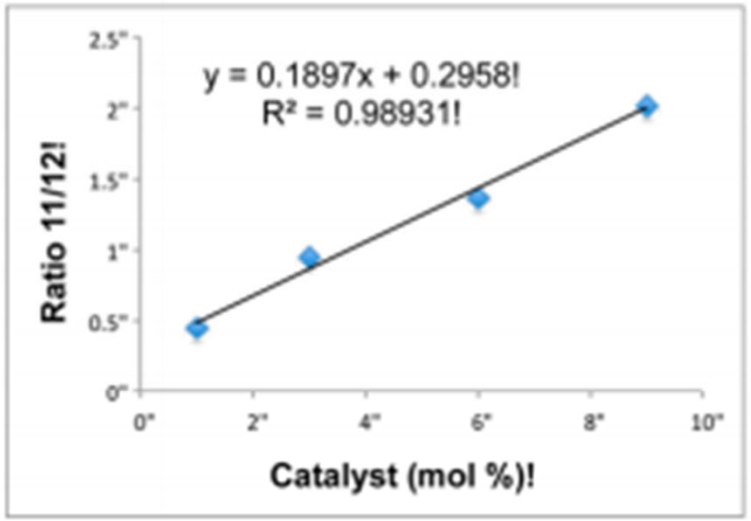
Mechanism

Scheme 1. Cross-Coupling Reaction Using Radical Probe 8



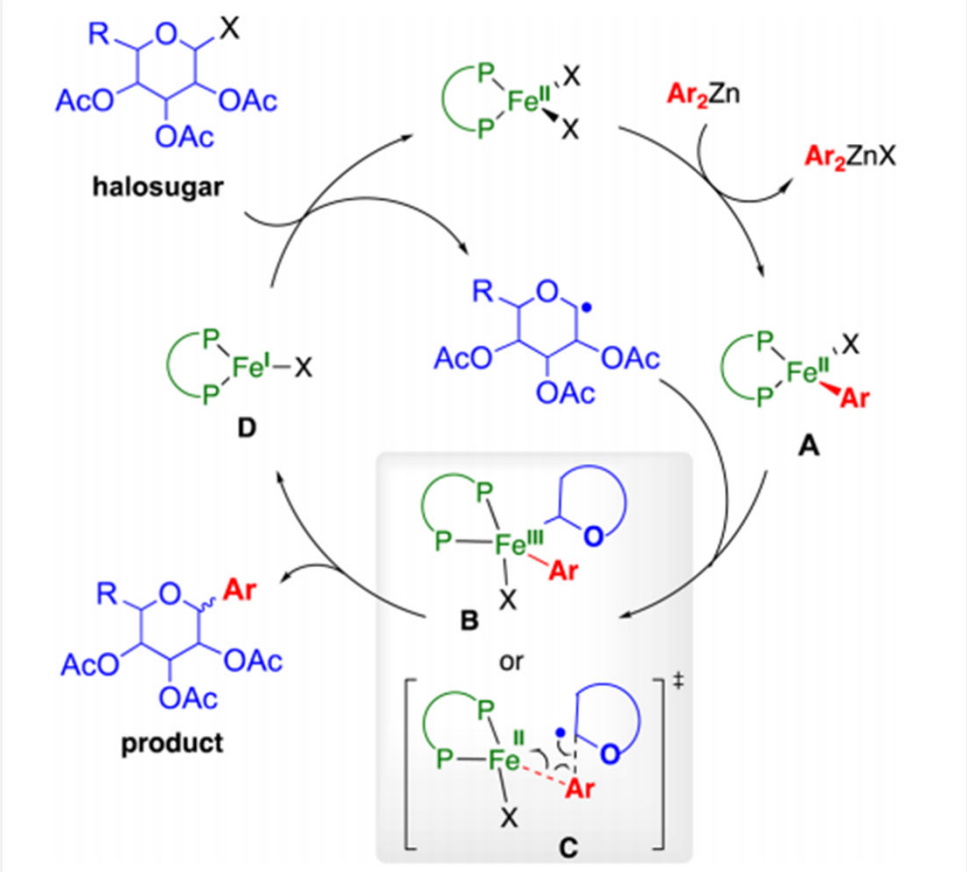
Scheme 2. Cross-Coupling Reaction Using Model Radical Probe 10





L. Adak, S. Kawamura, G. Toma, T. Takenaka, K. Isozaki, H. Takaya, A. Orita, H. C. Li, T. K. M. Shing, M. Nakamura, *Journal of the American Chemical Society* **2017**, *139*, 10693-10701.

Mechanism



L. Adak, S. Kawamura, G. Toma, T. Takenaka, K. Isozaki, H. Takaya, A. Orita, H. C. Li, T. K. M. Shing, M. Nakamura, *Journal of the American Chemical Society* **2017**, *139*, 10693-10701.

A full account of the synthetic scope andmechanistic study of the iron fluoride/SIPr-catalyzed alkyl-aryl coupling reaction

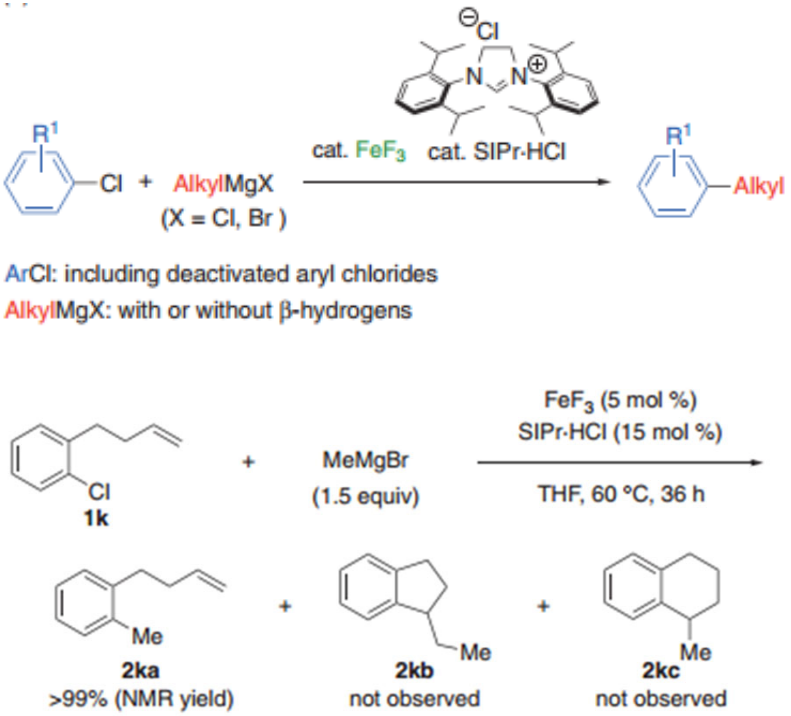
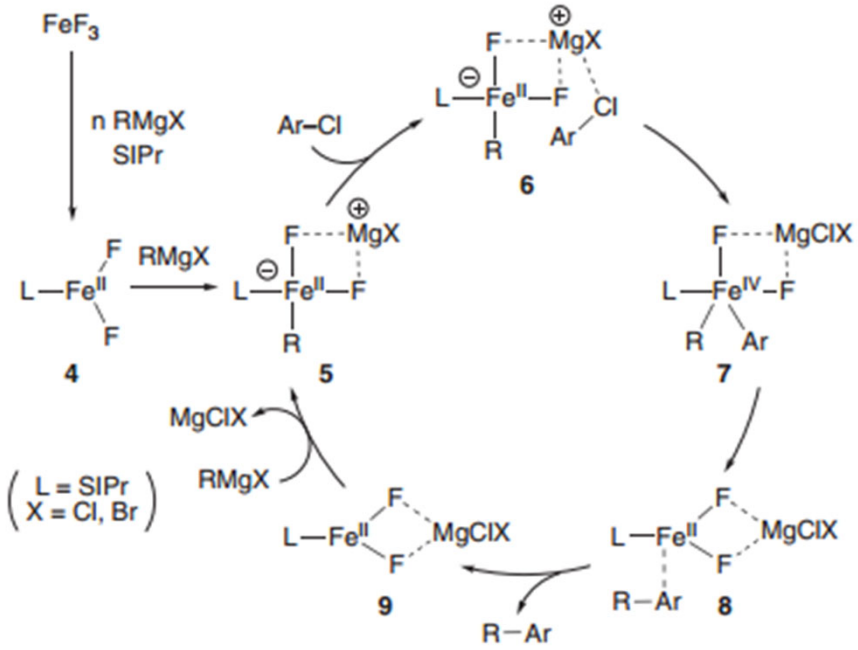


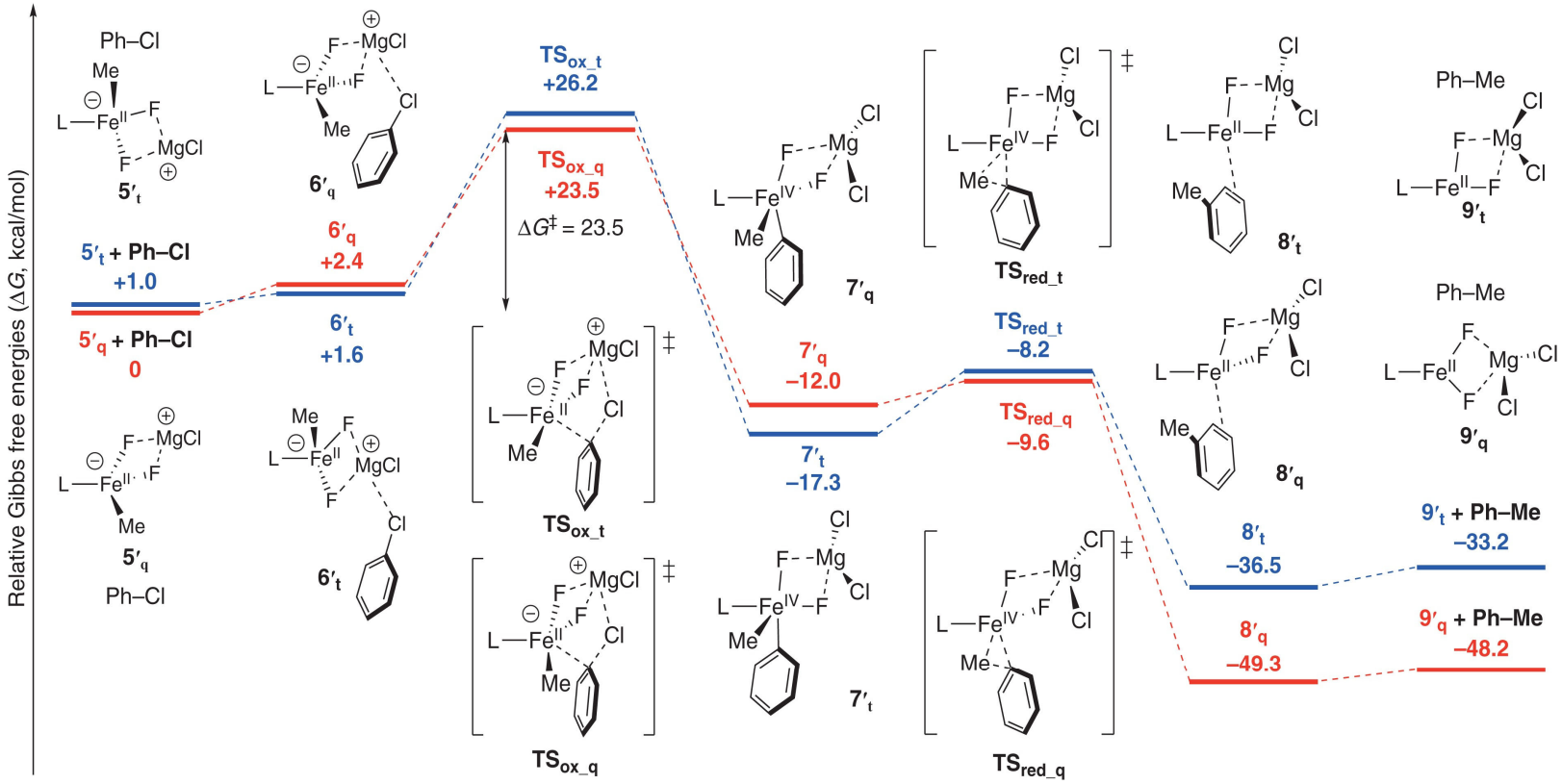
Figure 2. Radical probe experiment.



R. Agata, T. Iwamoto, N. Nakagawa, K. Isozaki, T. Hatakeyama, H. Takaya, M. Nakamura, *Synthesis-Stuttgart* **2015**, *47*, 1733-1740.

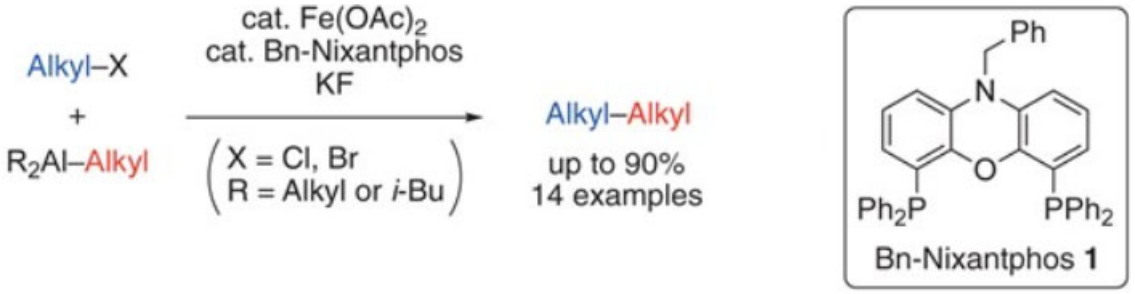
sp^2-sp^3 crossing-coupling

DFT calculation

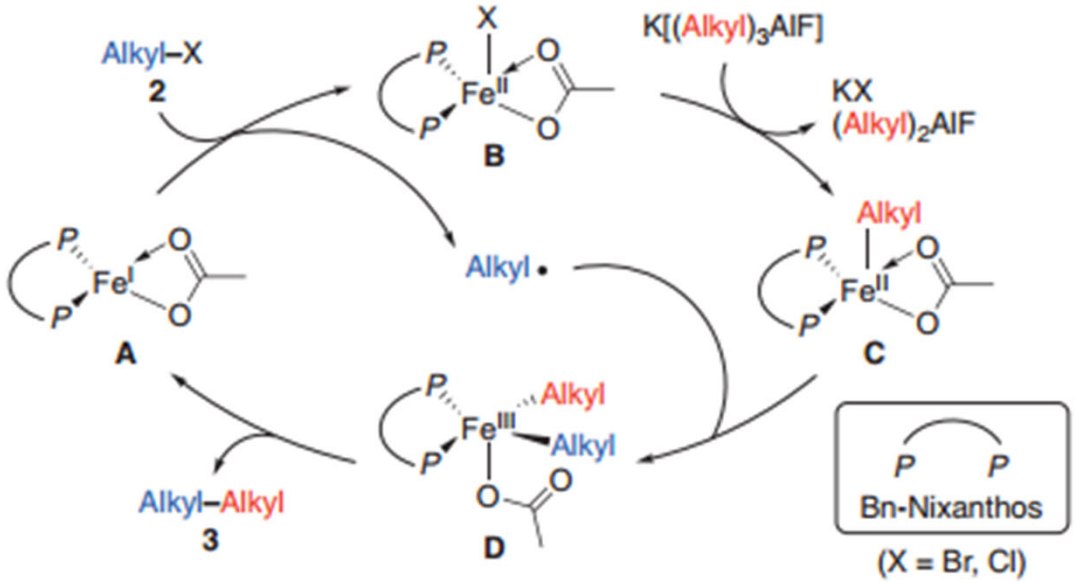


R. Agata, T. Iwamoto, N. Nakagawa, K. Isozaki, T. Hatakeyama, H. Takaya, M. Nakamura, *Synthesis-Stuttgart* **2015**, *47*, 1733-1740.

sp^3-sp^3 crossing-coupling

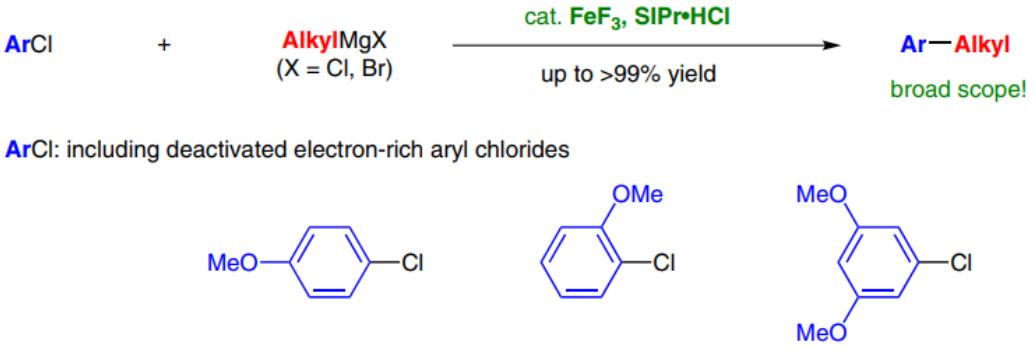


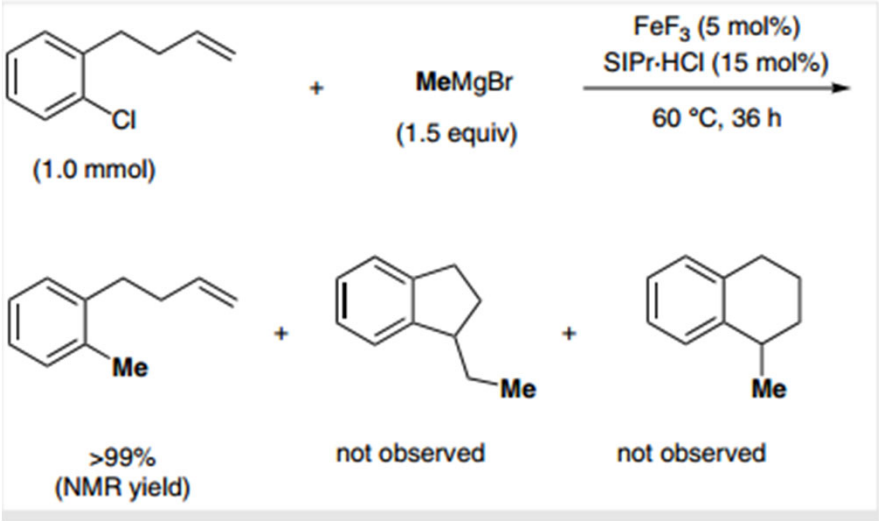
✔ high functional group tolerance: CN, CO_2R, CO_2H, OH, NHR



R. Agata, S. Kawamura, K. Isozaki, M. Nakamura, *Chemistry Letters* **2018**, *48*, 238-241.

sp^2-sp^3 crossing-coupling



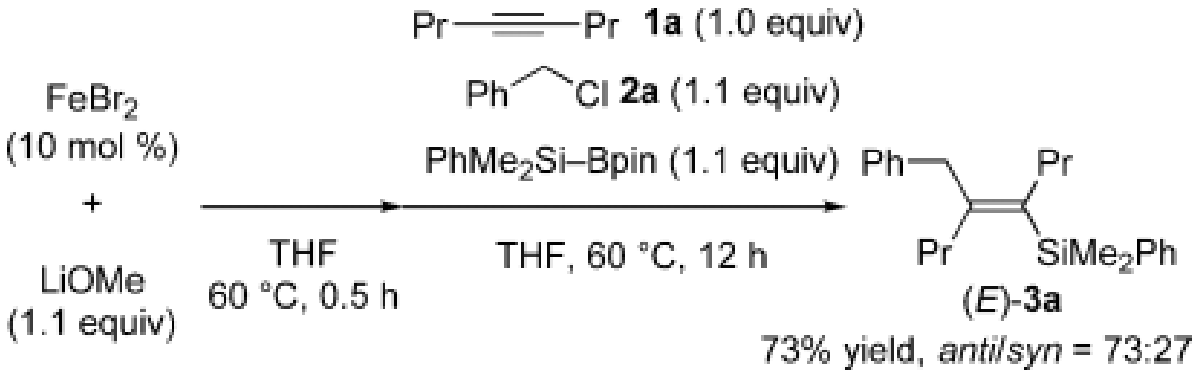


R. Agata, T. Iwamoto, N. Nakagawa, K. Isozaki, T. Hatakeyama, H. Takaya, M. Nakamura, *Synthesis-Stuttgart* **2015**, *47*, 1733-1740.

Carbometalation reactions of alkenes andalkynes

The Yang Research Group
Precise Synthesis Lab at Tongji University

The first iron-catalyzed carbosilylation of alkynes



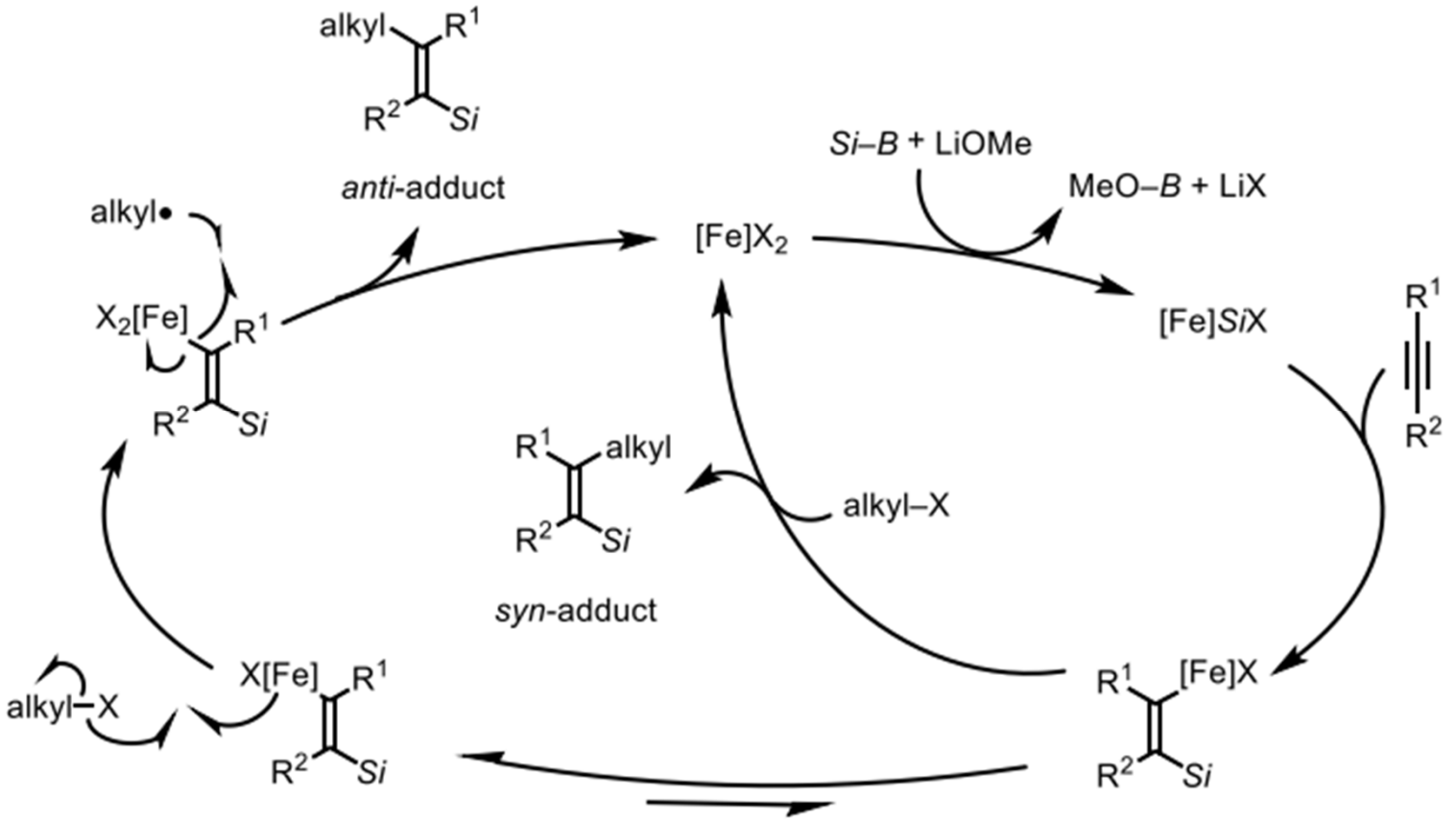
- No need for fouctional group on either alkynes or electrophiles
- Use of alkyl as electrophiles

T. Iwamoto, T. Nishikori, N. Nakagawa, H. Takaya, M. Nakamura, *Angewandte Chemie-International Edition* **2017**, *56*, 13298-13301.

同舟共济

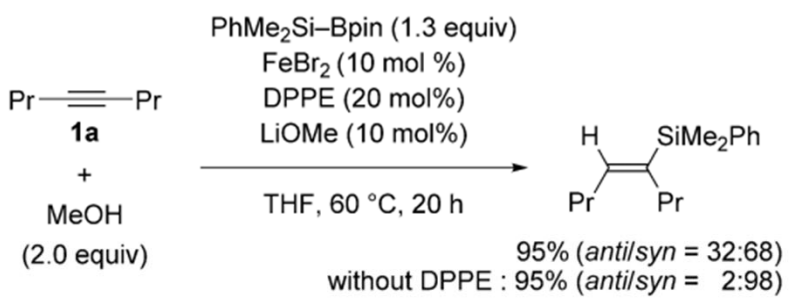
Carbometalation reactions of alkenes andalkynes

the first iron-catalyzed carbosilylation of alkynes

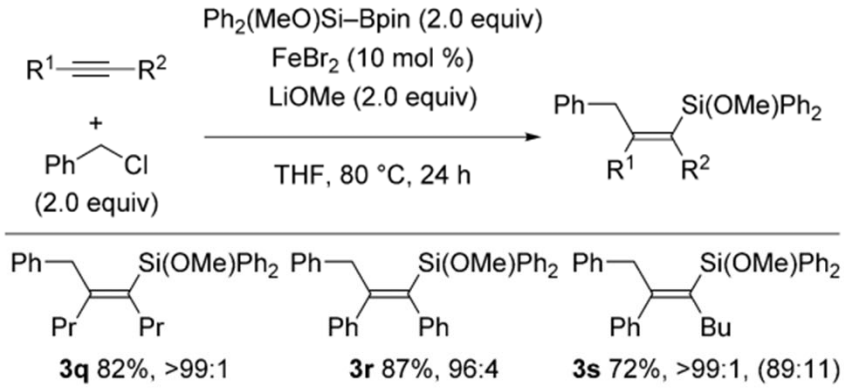


T. Iwamoto, T. Nishikori, N. Nakagawa, H. Takaya, M. Nakamura, *Angewandte Chemie-International Edition* **2017**, *56*, 13298-13301.

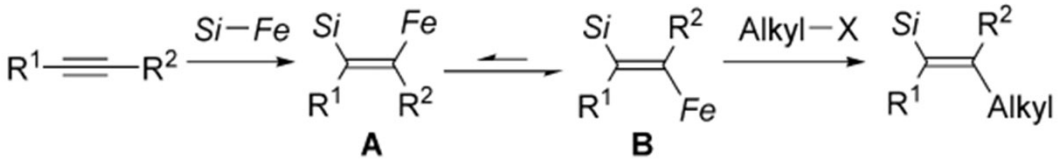
Mechanism



Scheme 3. In situ trapping of the iron intermediate.



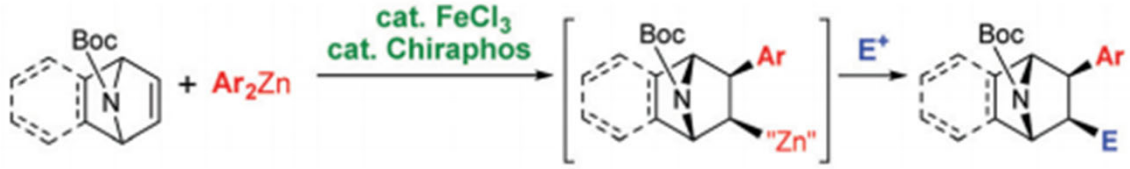
Scheme 5. Iron-catalyzed *syn*-selective carbosilylation of internal alkynes.

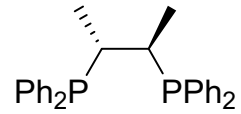


Scheme 4. Proposed mechanism for *anti*-selective carbosilylation.

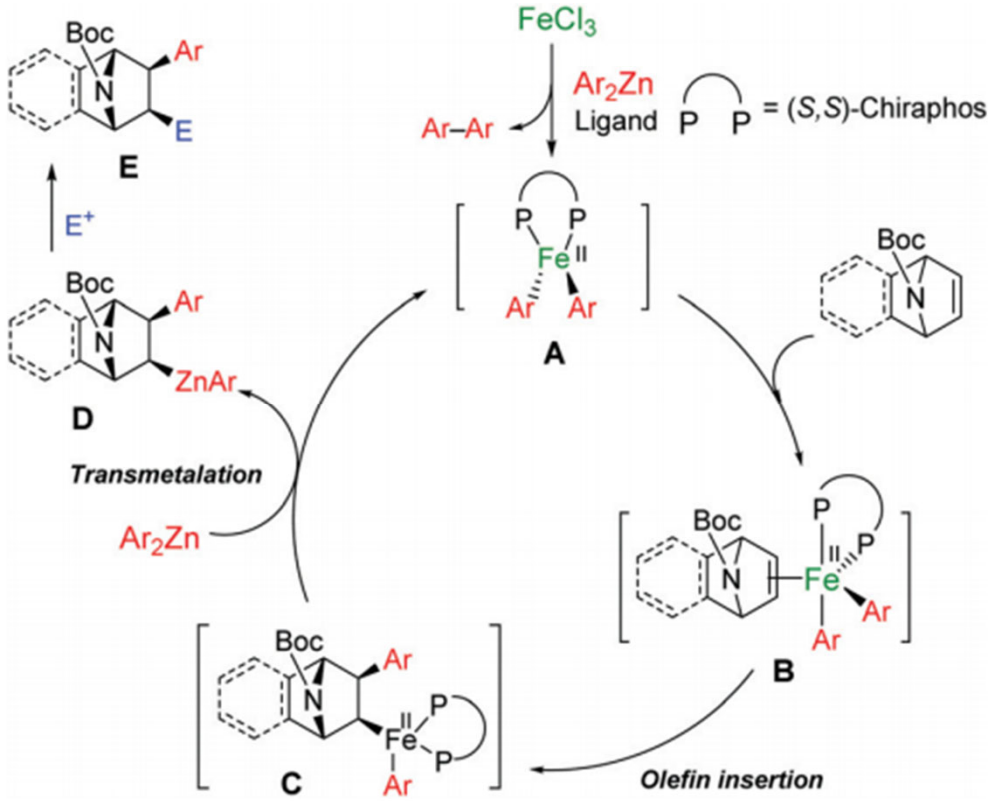
T. Iwamoto, T. Nishikori, N. Nakagawa, H. Takaya, M. Nakamura, *Angewandte Chemie-International Edition* **2017**, *56*, 13298-13301.

Carbometalation reactions of alkenes andalkynes



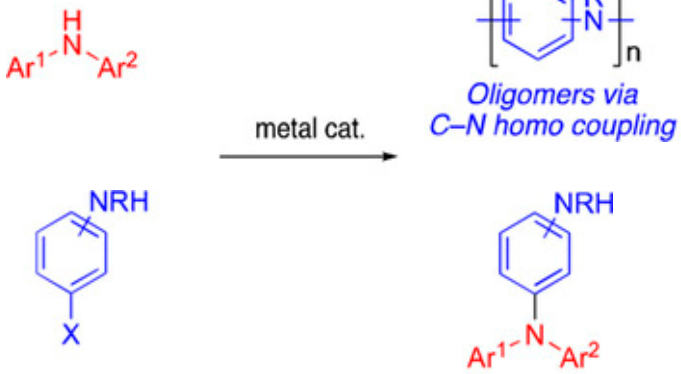


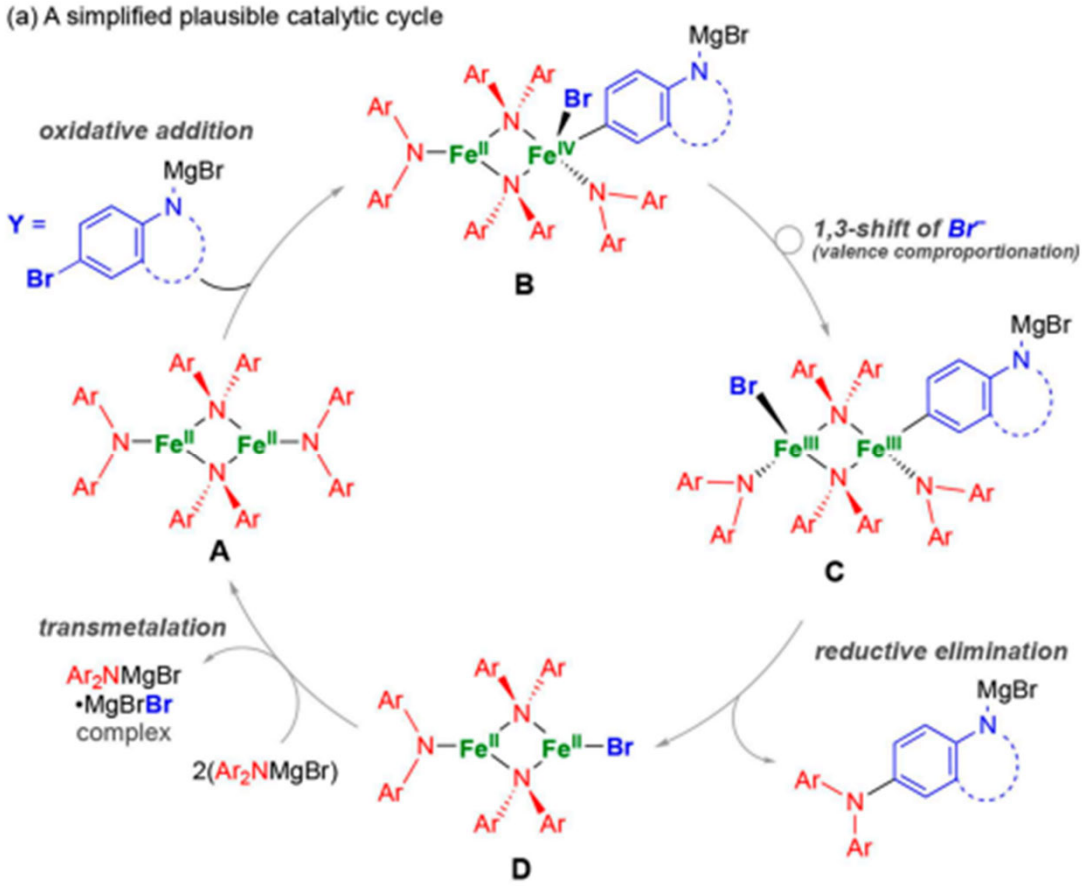
(*S*,*S*)-chiraphos



L. Adak, M. Jin, S. Saito, T. Kawabata, T. Itoh, S. Ito, A. K. Sharma, N. J. Gower, P. Cogswell, J. Geldsetzer, H. Takaya, K. Isozaki, M. Nakamura, *Chemical Communications* **2021**, *57*, 6975-6978.

C-N construction

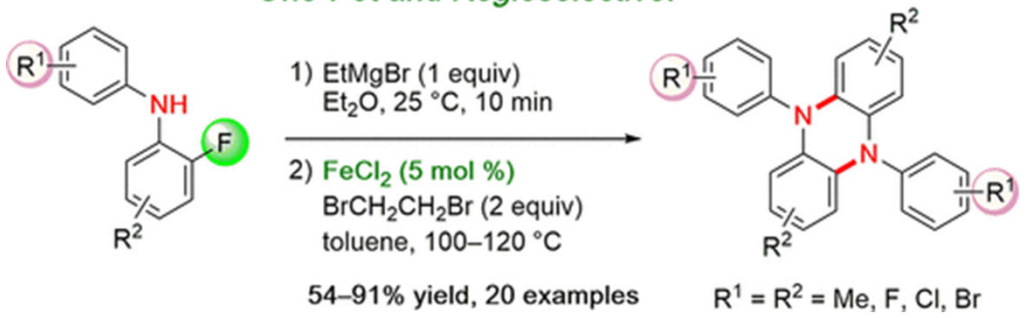


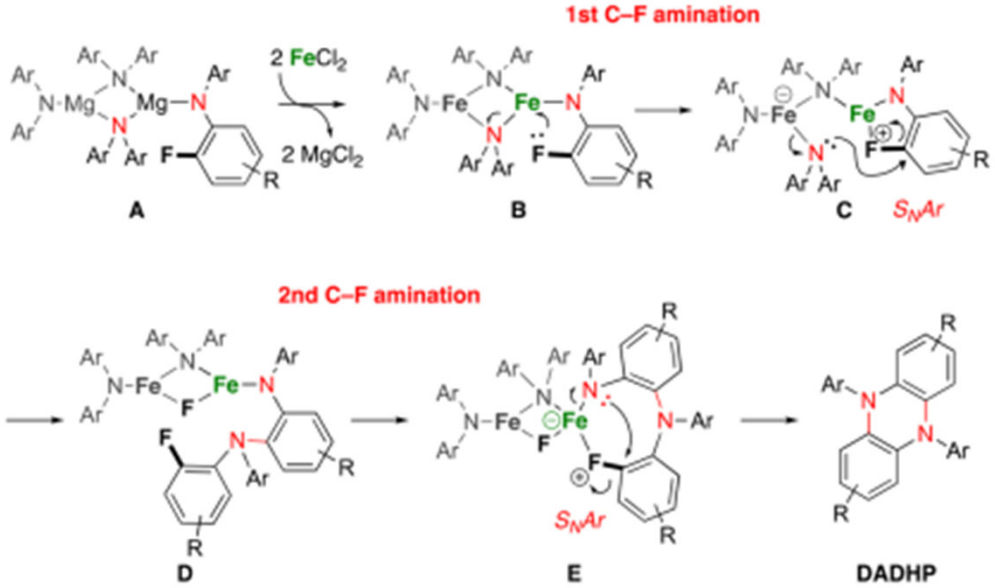


Y. Aoki, T. Toyoda, H. Kawasaki, H. Takaya, A. K. Sharma, K. Morokuma, M. Nakamura, *Asian Journal of Organic Chemistry* **2020**, *9*, 372-376.

C-N construction

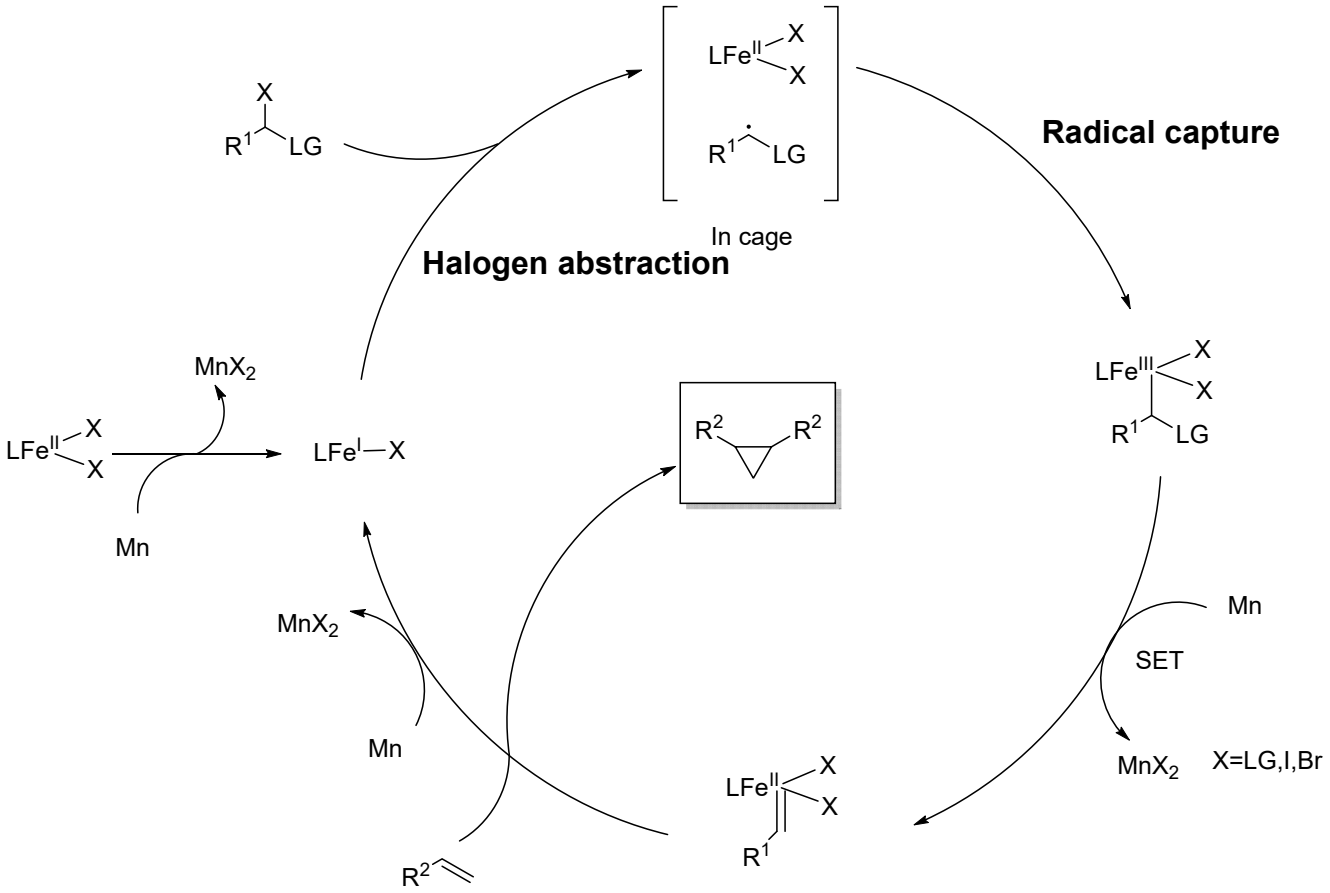
One-Pot and Regioselective!





Y. Aoki, H. M. O'Brien, H. Kawasaki, H. Takaya, M. Nakamura, *Organic Letters* **2019**, *21*, 461-464.

Proposal


Radical capture
In cage
Halogen abstraction
SET
Mn
MnX2
X=LG,I,Br

同济大学 化学科学与工程学院
School of Chemical Science and Engineering

The Yang Research Group
Precise Synthesis Lab at Tongji University

Thank you for listening

姓名：王宁　　指导教师：杨泽鹏 教授

同舟共济