Fe催化C-N键的构建

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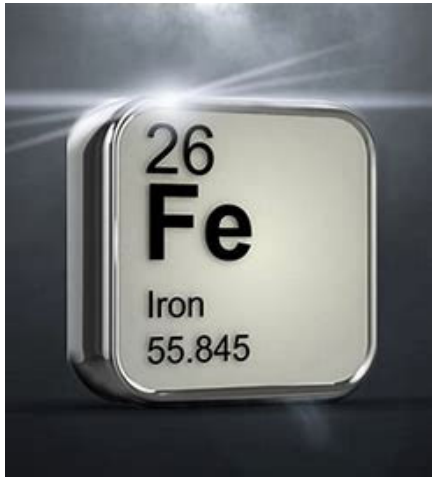
同舟共济

背景介绍

同济大学 TONGJI UNIVERSITY



(a) Features of iron catalysts

Abundance
50000 ppm in earth's crust

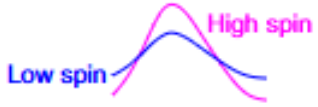
Good biocompatibility
Low toxicity; exist in HGB

Small atomic radius
1.72 Å

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

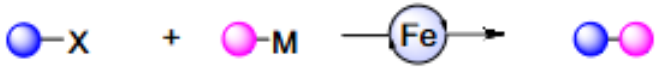
Multiple oxdation state
Fe(-2) to Fe(+6)

Spin effects in reaction

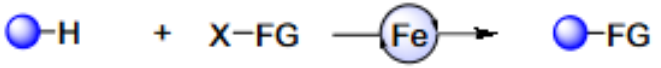


(b) Representative iron-catalyzed reactions

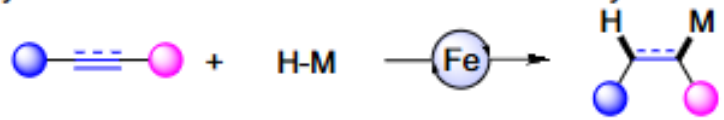
3.1 Cross-coupling reactions



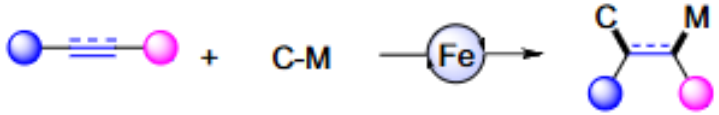
3.2 C-H bond functionalization reactions



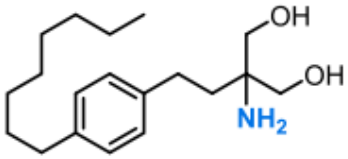
3.3 Hydrometalation reactions of alkenes and alkynes



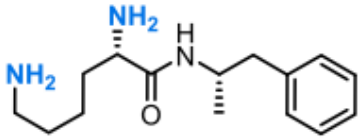
3.4 Carbometalation reactions of alkenes and alkynes



背景介绍

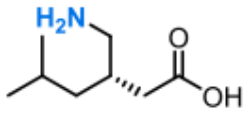


Fingolimod
($2.013 billion in 2022)

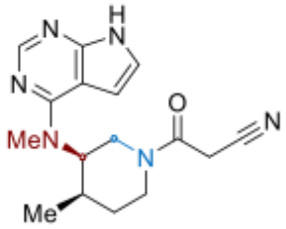


Lisdexamfetamine
($3.219 billion in 2022)

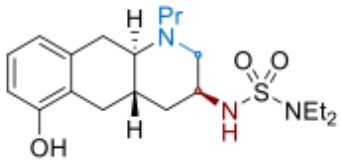
Sitagliptin
($2.813 billion in 2022)



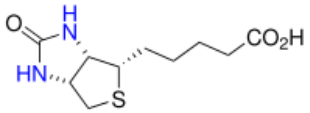
Pregabalin
($632 million in 2022)



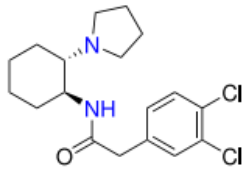
Tofacitinib
JAK inhibitor



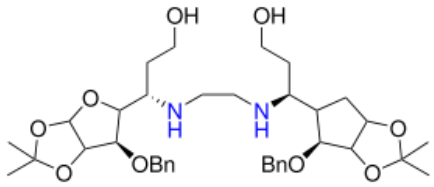
Quinagolide
D_2 receptor agonist



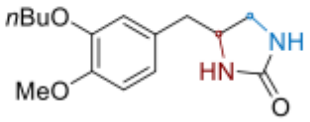
Biotin



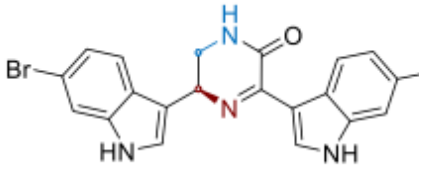
U-50, 488
k agonist



Antitubercular agent



RO 20-1724
PDE4 inhibitor



hamacanthin B
antibacterial

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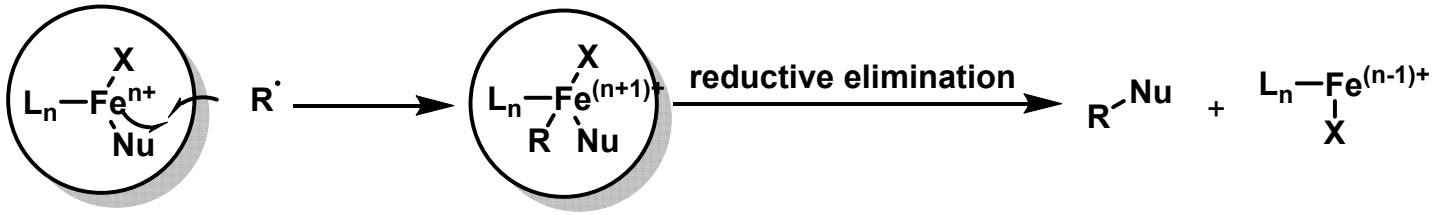
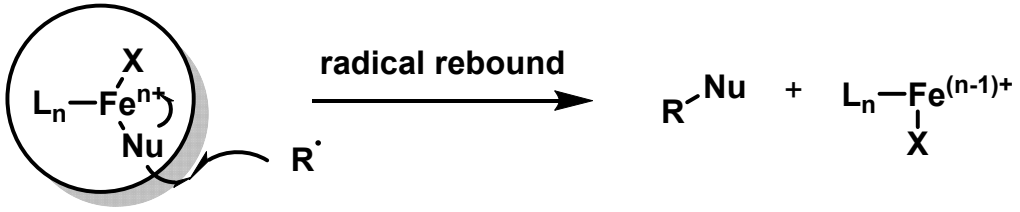
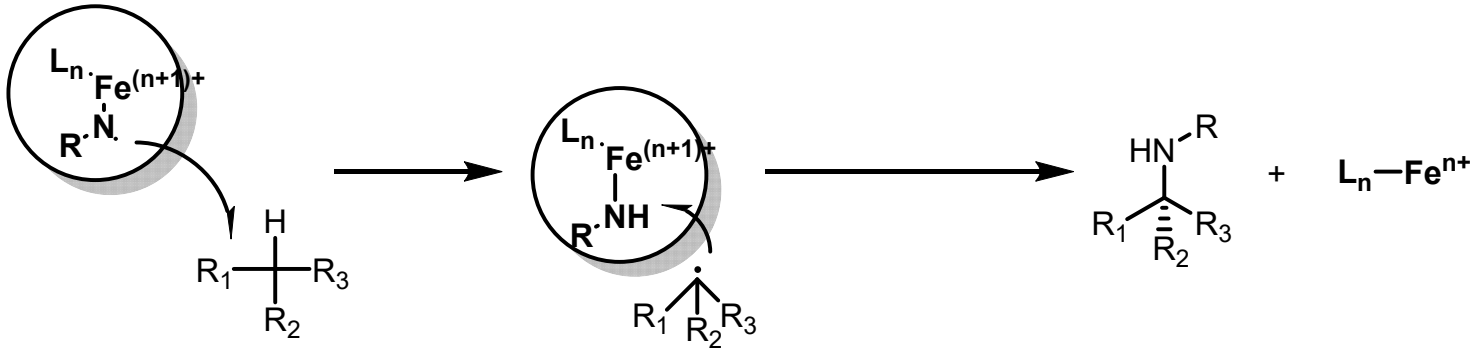
内球催化模式



外球催化模式



铁氮宾中间体



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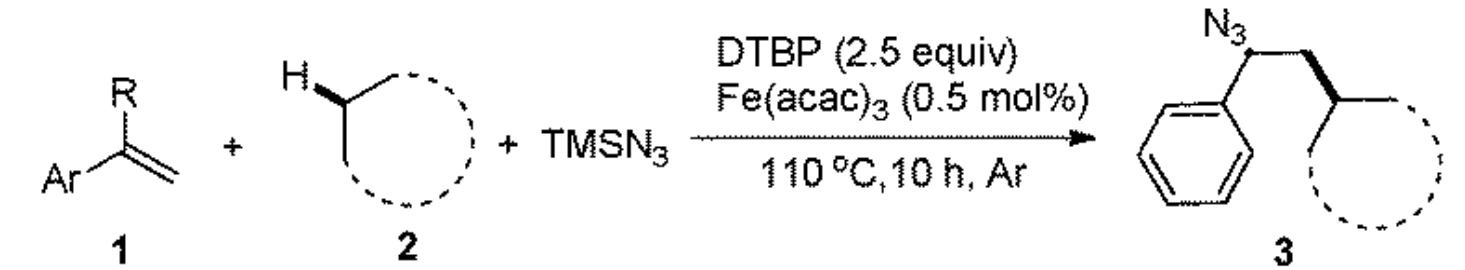
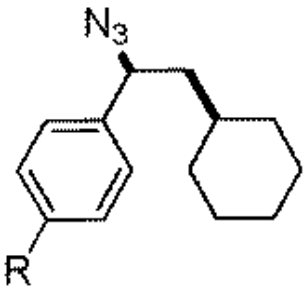
Part 1

外球模式

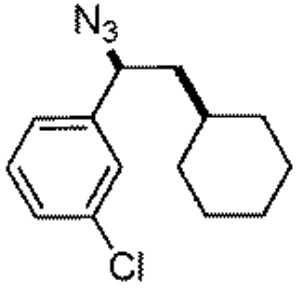
同舟共济

外球模式:Fe催化烯烃/烷烃/$TMSN_3$的三组分叠氮化

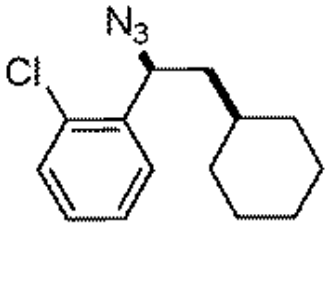




3a, R = H, 74%
3b, R = Me, 68%
3c, R = ^{t}Bu, 92%
3d, R = MeO, 55%
3e, R = CH_2Cl, 56%
3f, R = F, 73%
3g, R = Cl, 68%
3h, R = Br, 60%



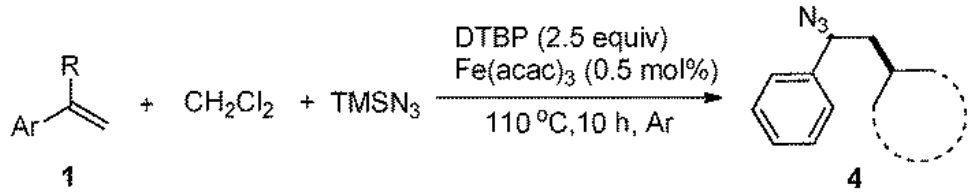
3i, 70%

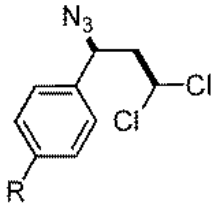


3j, 76%

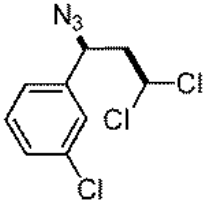
Luo, Y. et al., *Chem. Commun.*, **2018**, *54*, 11013.

外球模式:Fe催化烯烃/烷烃/$TMSN_3$的三组分叠氮化

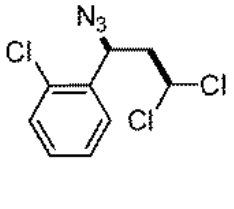




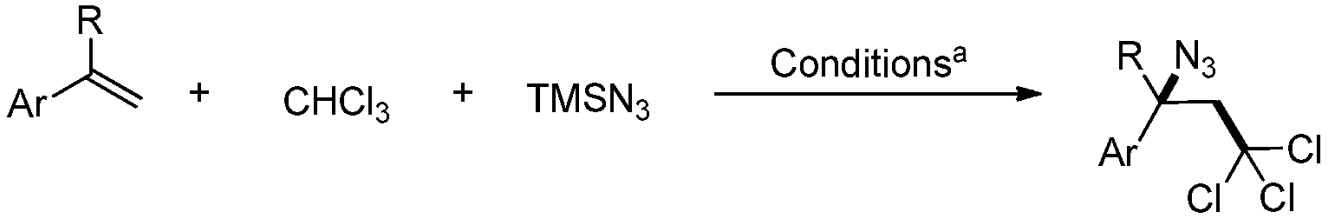
4a, R = H, 75%
4b, R = Me, 71%
4c, R = ^{t}Bu, 82%
4d, R = MeO, 43%
4e, R = CH_2Cl, 64%
4f, R = F, 70%
4g, R = Cl, 72%
4h, R = Br, 65%



4i, 73%



4j, 72%



5a Ar = Ph, R = H, 67%
5b, Ar = 4-$MeOC_6H_4$, R = H, 59%

Luo, Y. et al., *Chem. Commun.*, **2018**, *54*, 11013.

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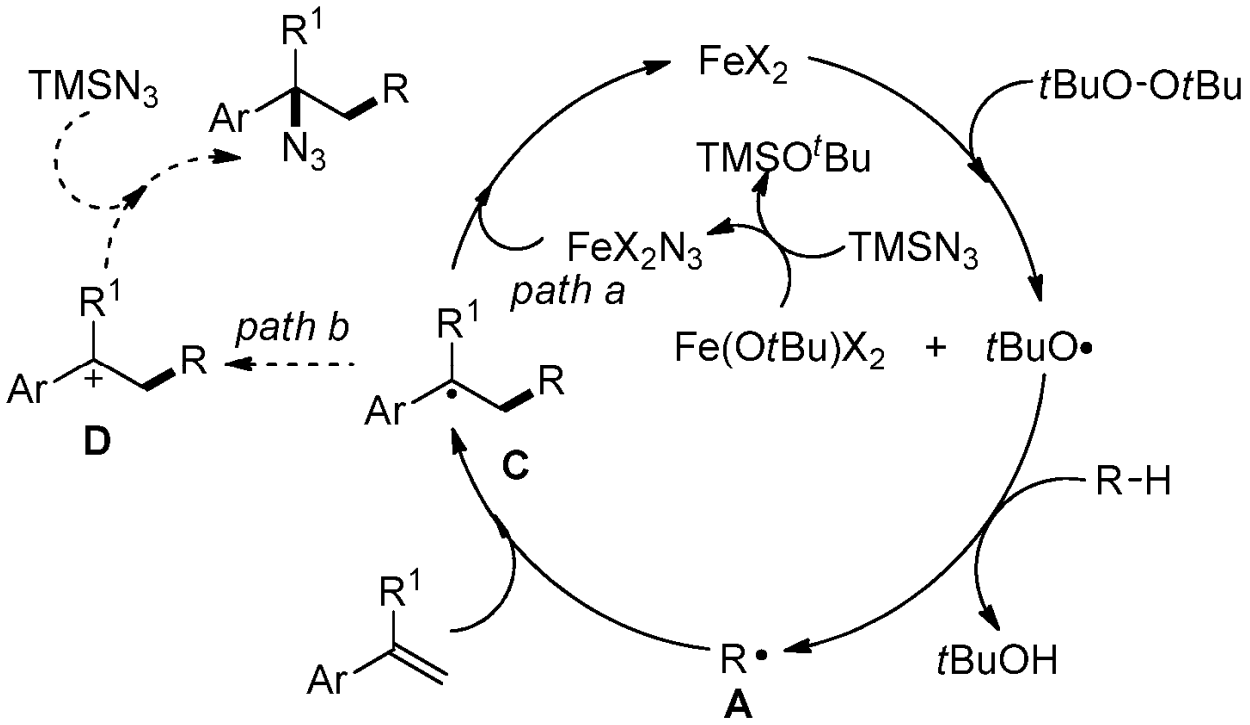
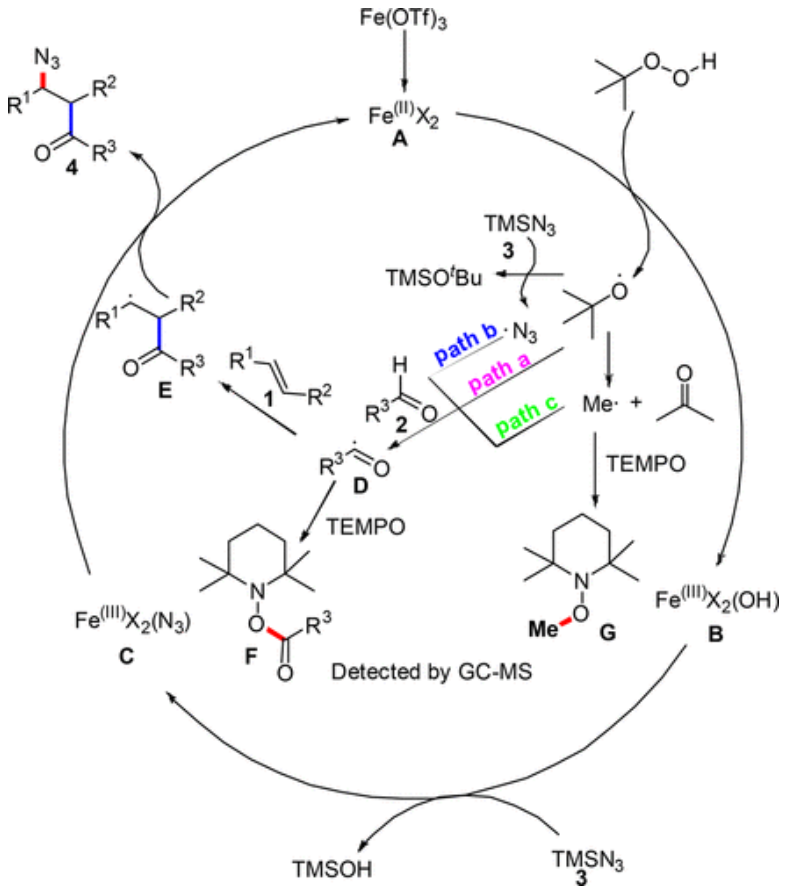


Luo, Y. et al., *Chem. Commun.*, **2018**, *54*, 11013.

外球模式: Bao's work

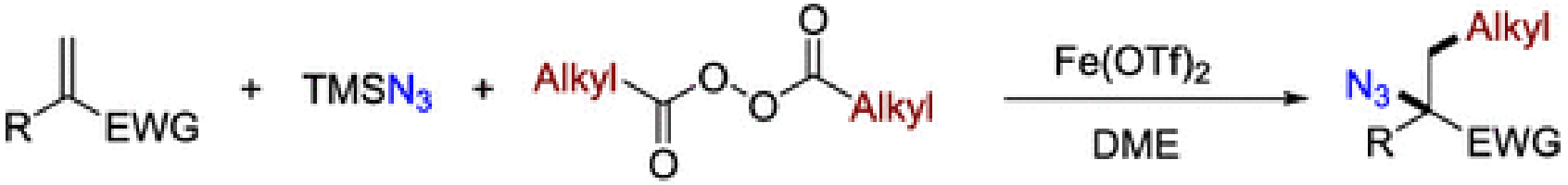
◊ Mild Reaction Conditions ◊ No Additives

◊ Wide Substrate Scope ◊ Precursors of Valuable Compounds

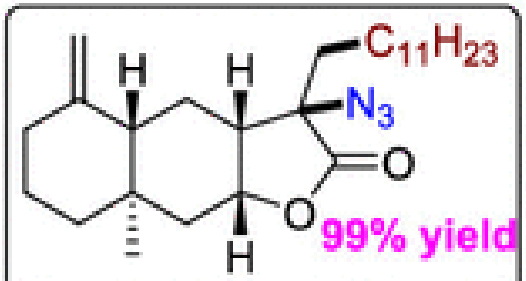


Bao, H.-L. et al., *Org. Lett.* *2019*, **21**, *1*, 256.

外球模式: Bao's work



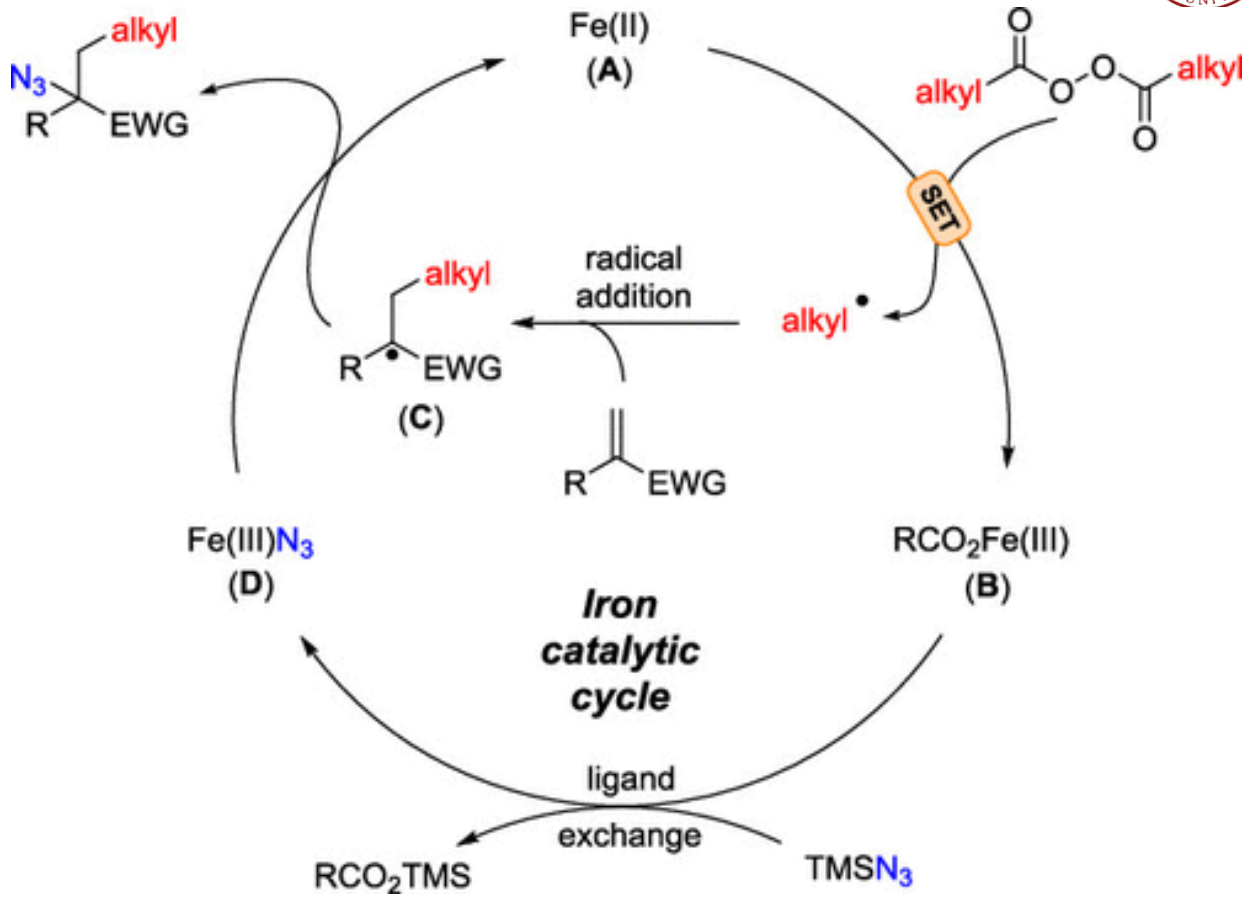
- Iron-catalyzed redox three-component reaction
- Mild reaction conditions
- Excellent functional group tolerance
- Good to excellent yields



direct carboazidation of natural isoalantolactone

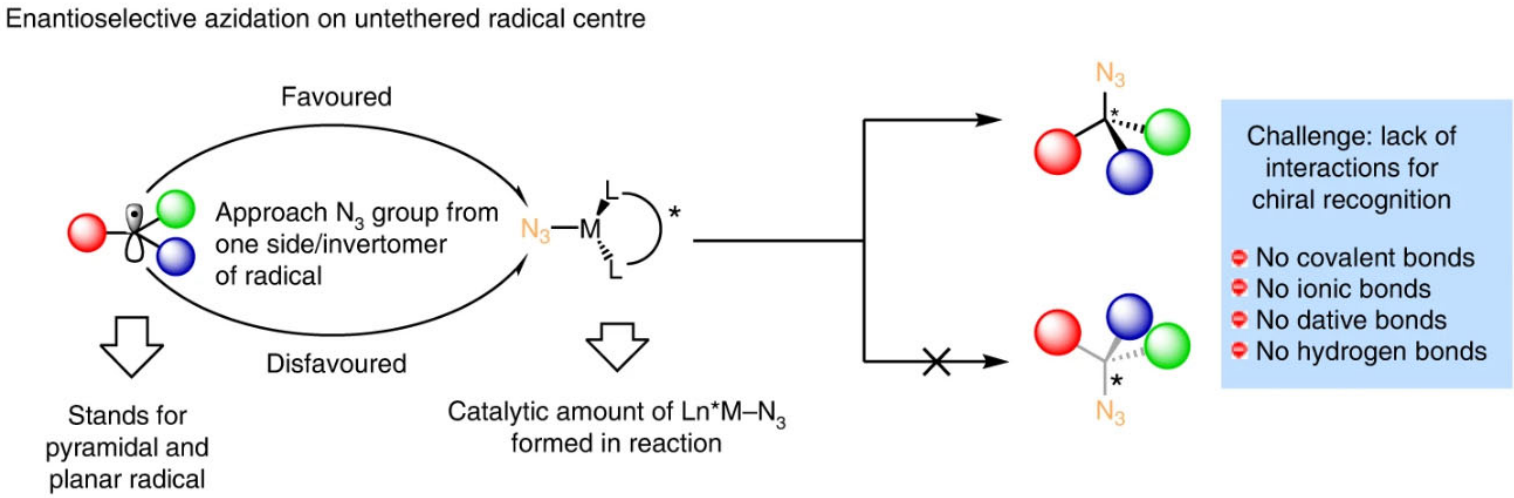
Bao, H.-L. et al., *Org. Lett*. **2020**, *22*, 3195.

外球模式: Bao's work



Bao, H.-L. et al., *Org. Lett*. **2020**, *22*, 3195.

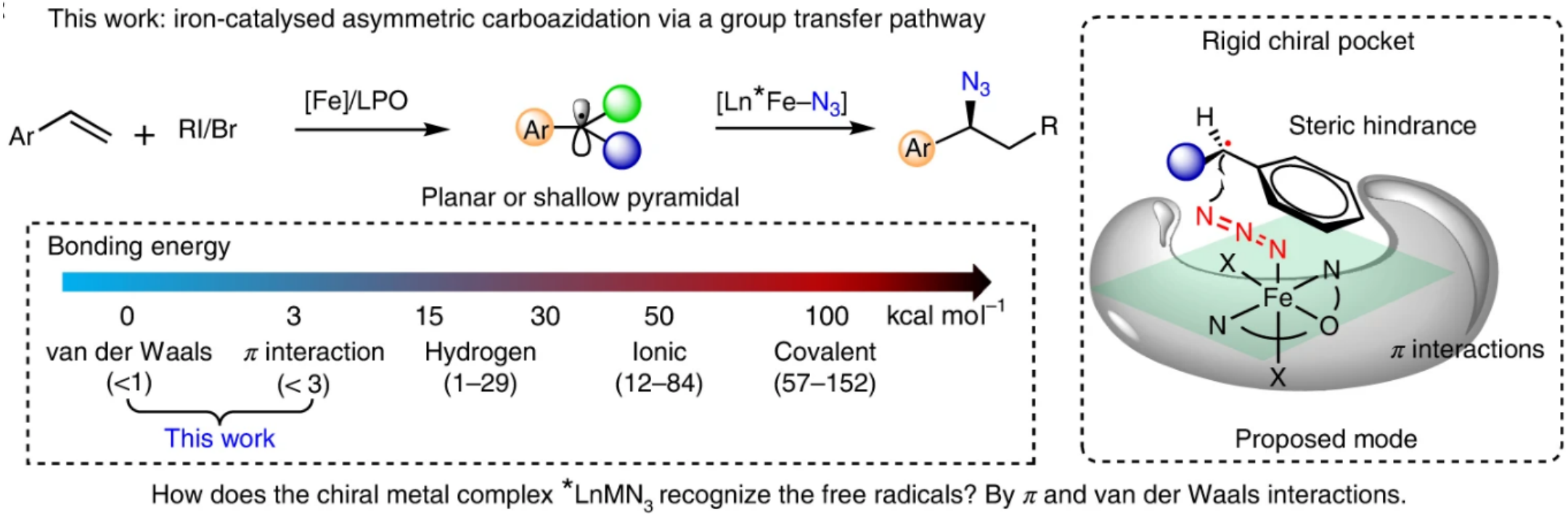
外球模式: Bao's work



- 自由基物种无法通过共价、配位、离子、氢键等传统的中等/强相互作用控制立体结构。
- 自由基叠氮化反应速率非常快，因此需要快速在叠氮反应完成前识别手性，当催化剂和底物自由基物种之间没有相互作用时该过程更难以实现。

Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

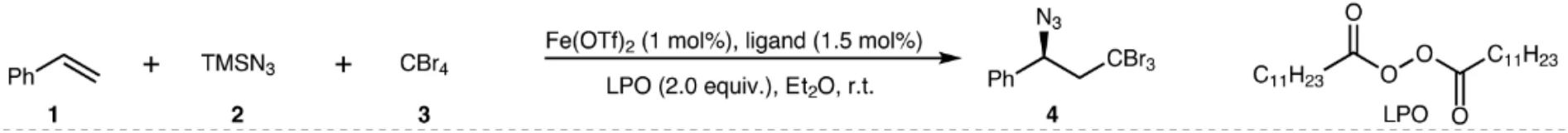
外球模式: Bao's work

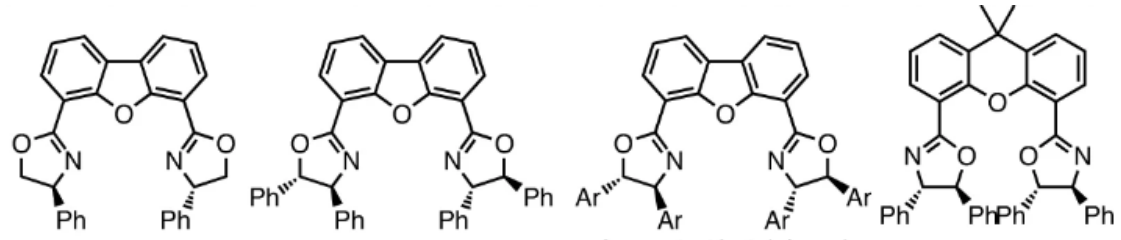


How does the chiral metal complex $^{*}LnMN_3$ recognize the free radicals? By π and van der Waals interactions.

Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

外球模式: Bao's work



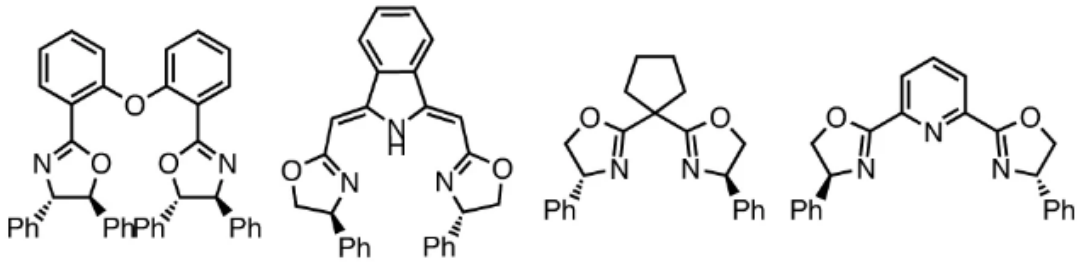


L1
68% yield, 73:27 e.r.

L2
74% yield, 87:13 e.r.

Ar = *p*-*tert*-butylphenyl
L3(HAIXI-*t*Bu)
82% yield, 94:6 e.r.

L4, trace



L5, trace

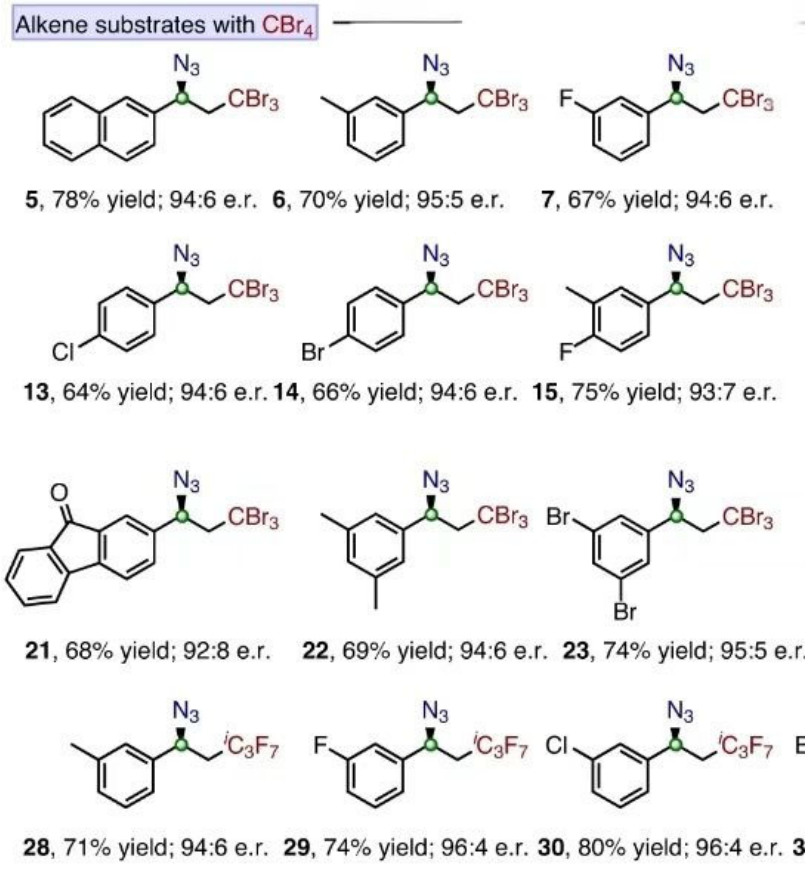
L6 (boxmi), trace

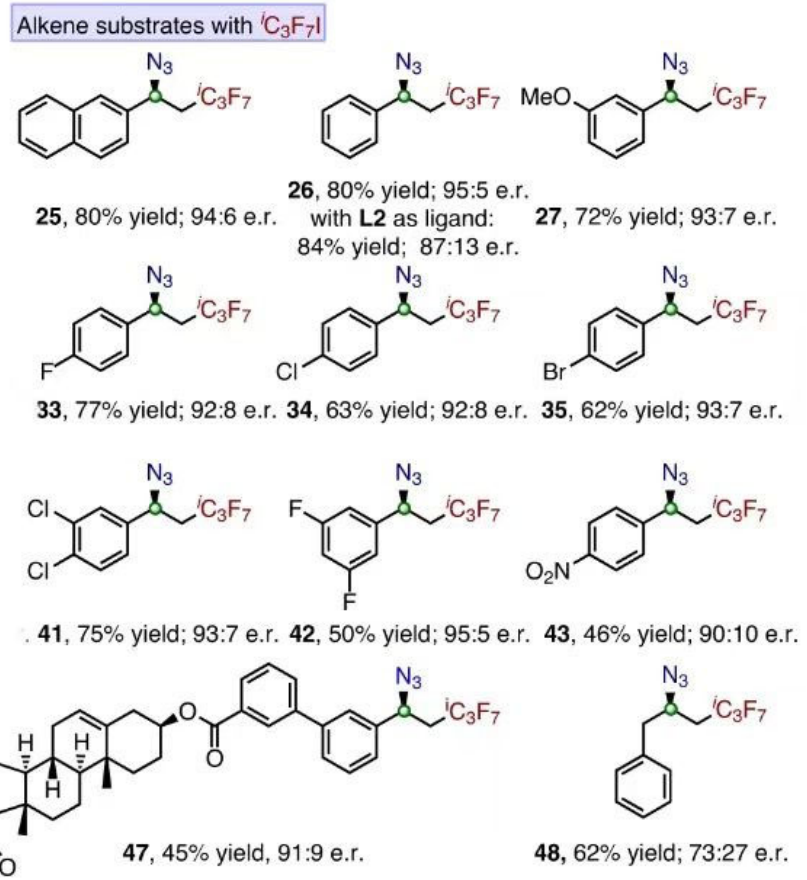
L7
43% yield, 50:50 e.r.

L8 (pybox), trace

Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

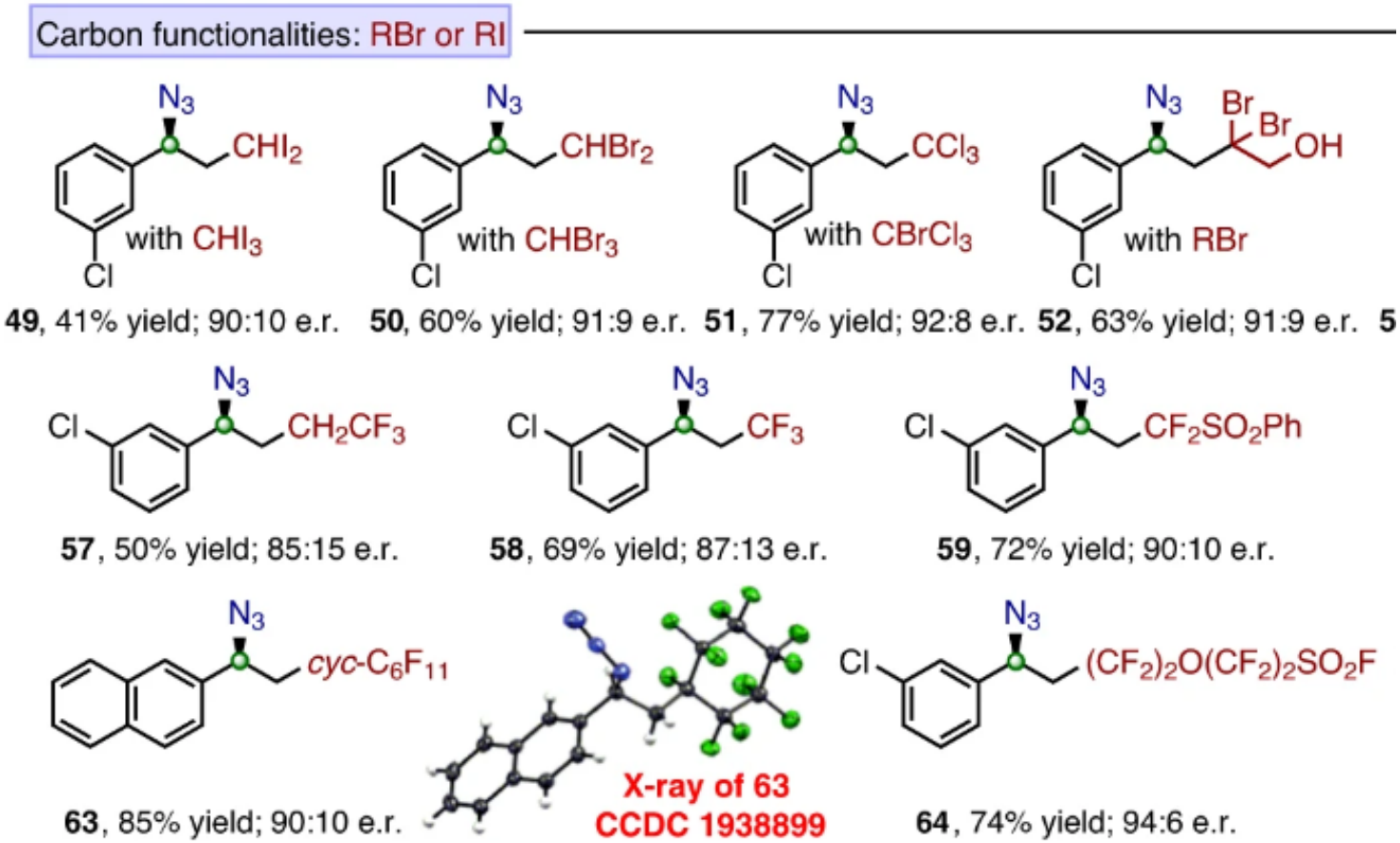
外球模式: Bao's work





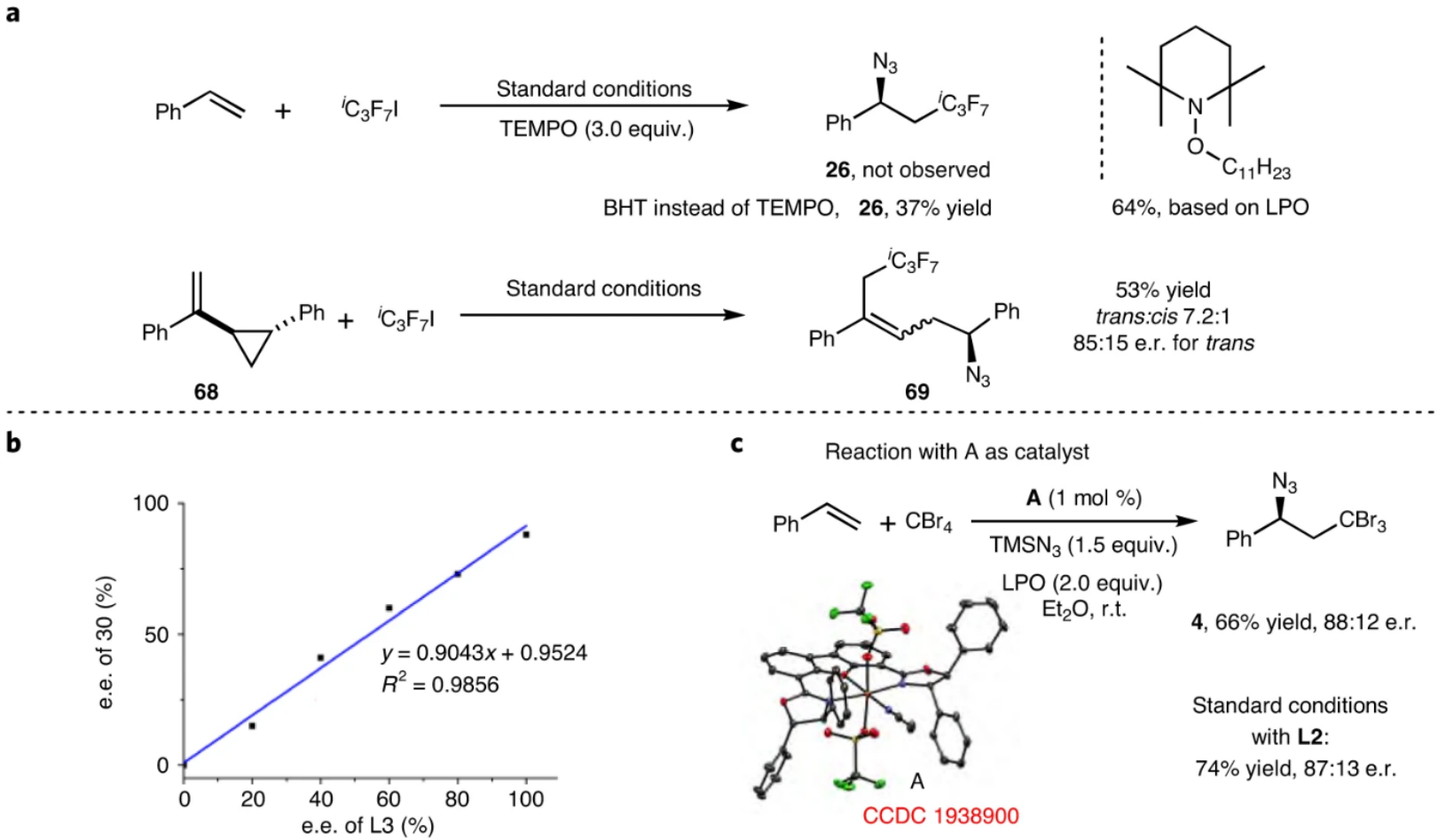
Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

外球模式: Bao's work



Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

外球模式: Bao's work



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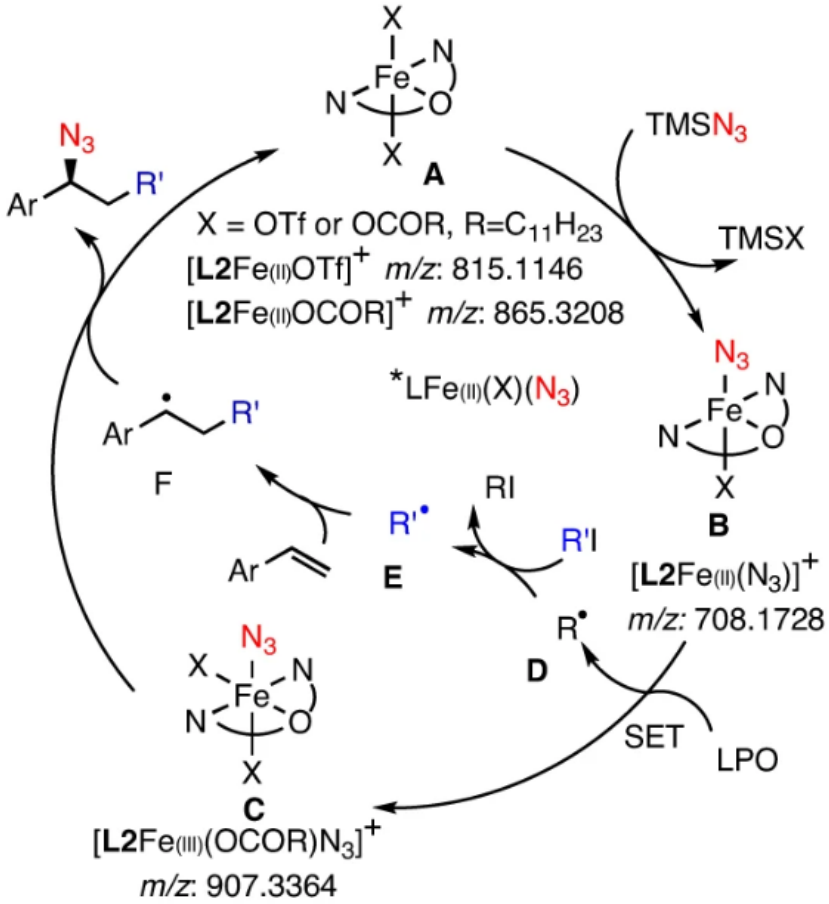
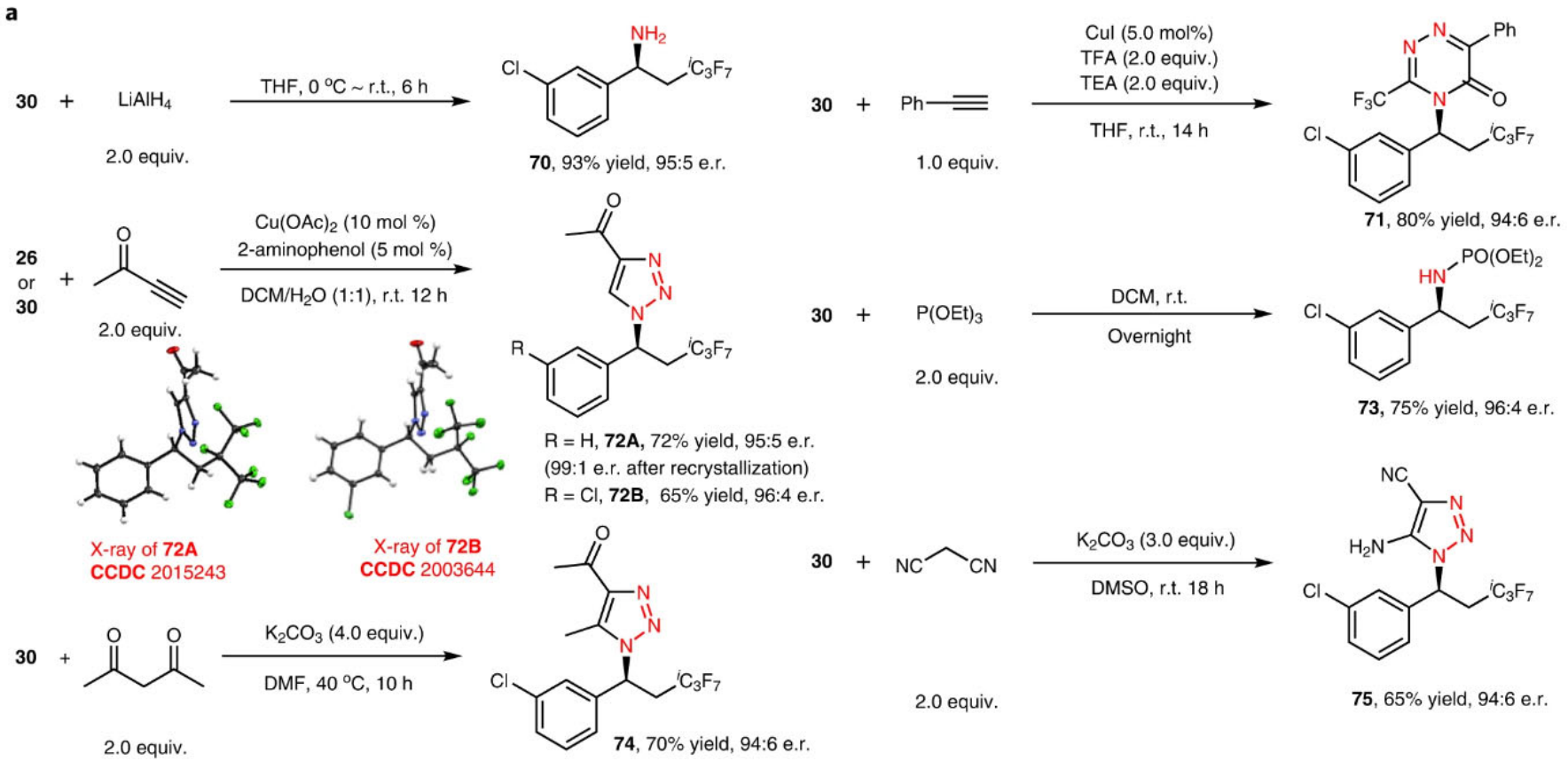


Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

外球模式: Bao's work



Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

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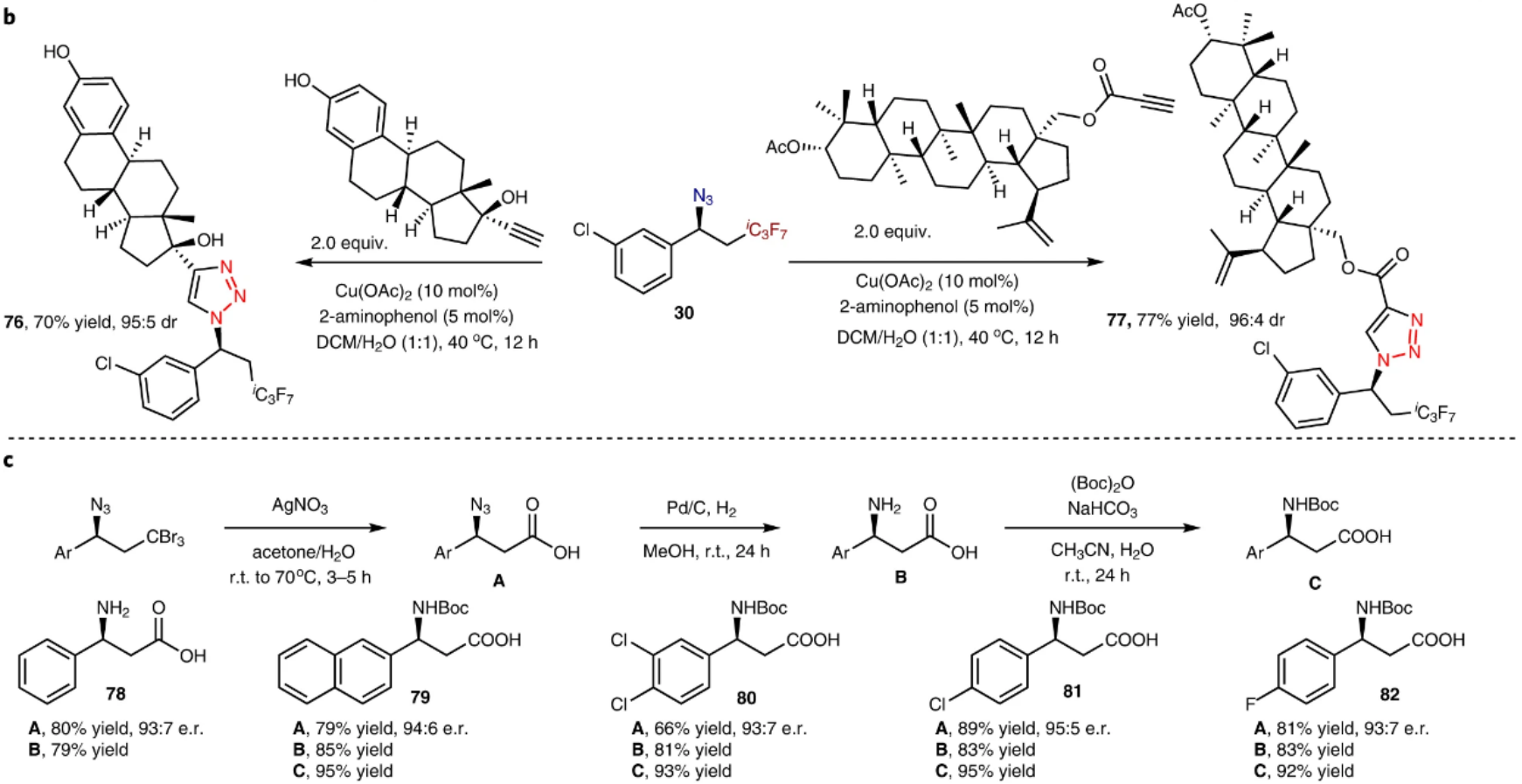

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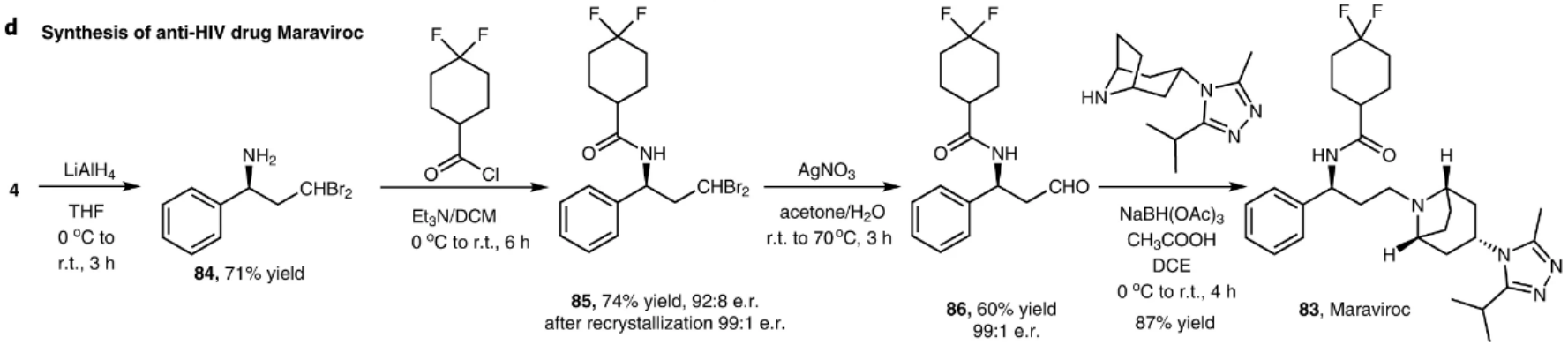
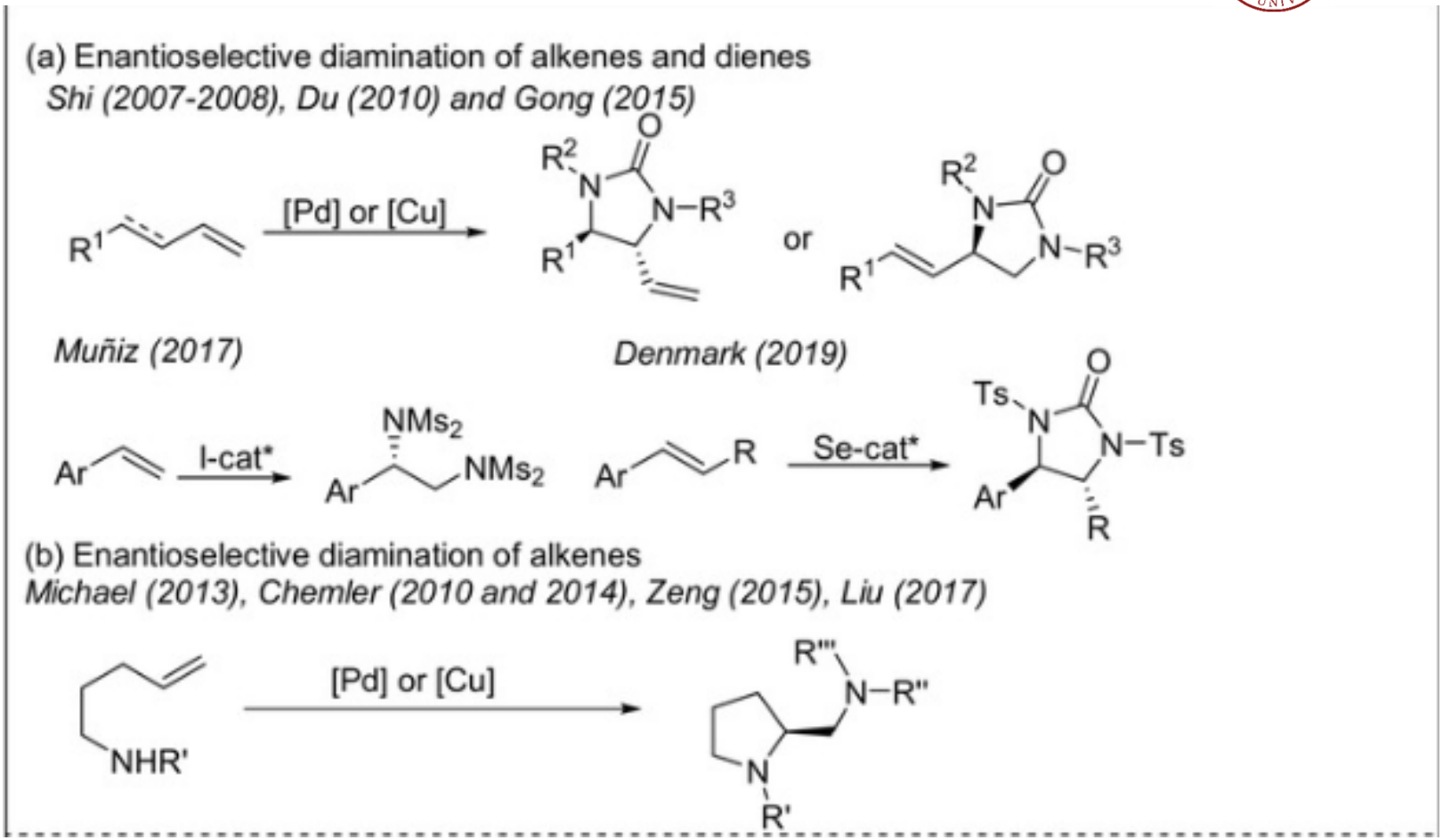


马拉韦罗

- 报道了经外球模式，自由基参与的铁催化烯烃的不对称碳叠氮化反应。
- 利用廉价的工业化学原料得到了有价值的手性卤代有机叠氮化物。
- 该自由基叠氮化反应得到了机理研究的支持，对后续的自由基不对称叠氮化反应有着良好的借鉴意义
- 反应有着良好的实用性，在产物的基础上，合成了一系列含氮化合物、氨基酸衍生物、天然产物衍生物以及抗HIV药物

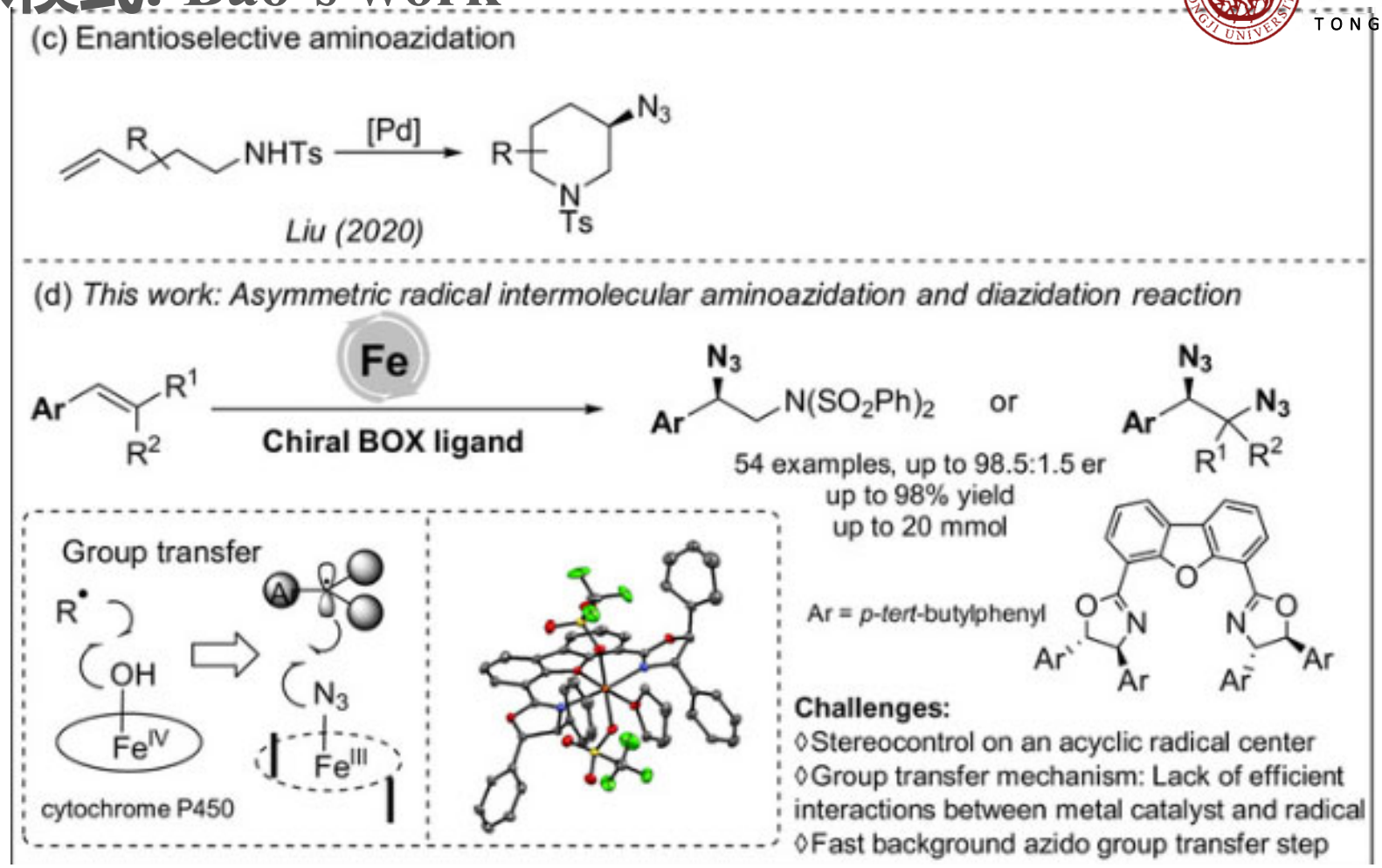
Bao, H.-L. et al., *Nat. Catal.* **2021**, *4*, 28.

外球模式: Bao's work



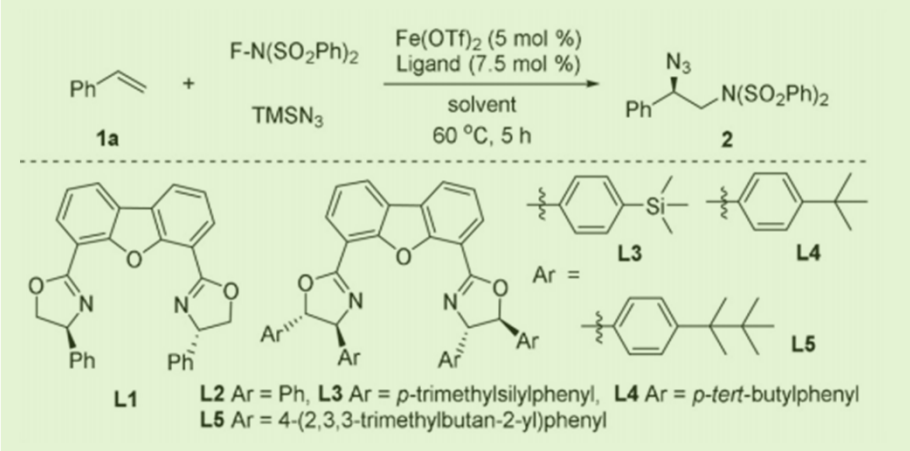
Bao, H.-L. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12455.

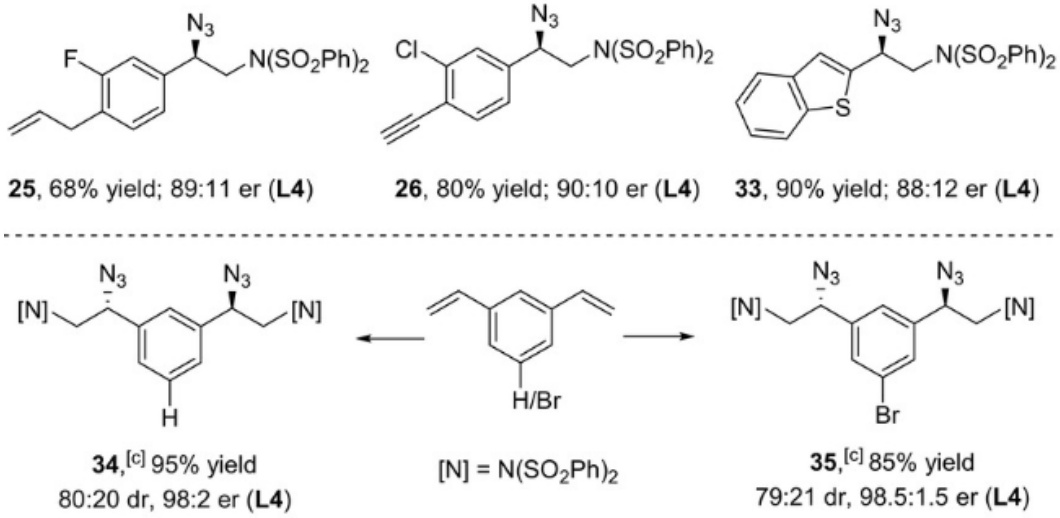
外球模式: Bao's work



Bao, H.-L. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12455.

外球模式: Bao's work





Bao, H.-L. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12455.

外球模式: Bao's work

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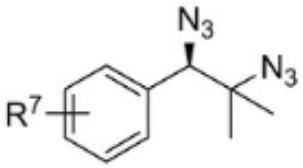
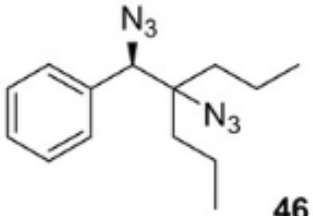
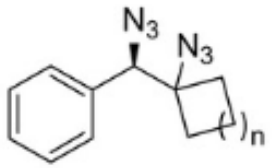
Scope of diazidation with L4 as the ligand



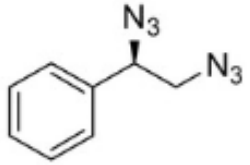
37, R^7 = 3-H, 64% yield; 97:3 er
38, R^7 = 3-CF_3, 55% yield; 93:7 er
39, R^7 = 3-Cl, 58% yield; 97:3 er
40, R^7 = 3-F, 58% yield; 95:5 er
41, R^7 = 3-Br, 75% yield; 95:5 er
42, R^7 = 3-CH_3, 60% yield; 85:15 er
43, R^7 = 3,5-diBr, 55% yield; 88:12 er
44, R^7 = 3,4-diCl, 54% yield; 89:11 er



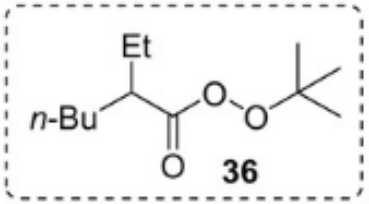
45, 54% yield
92:8 er



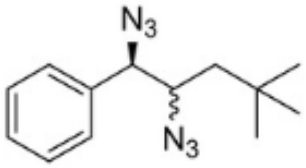
46, n= 1, 75% yield; 95:5 er
47, n= 2, 55% yield; 93:7 er
48, n= 3, 72% yield; 92:8 er
49, n= 5, 80% yield; 92:8 er



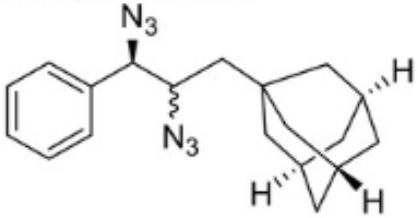
50, 61% yield, 73:27 er



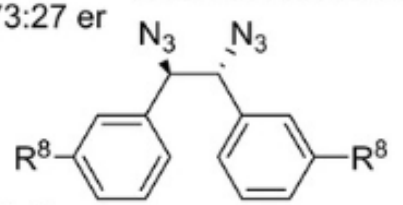
36



51, dr 2:1, 60% yield
major 85:15 er
minor 93:7 er



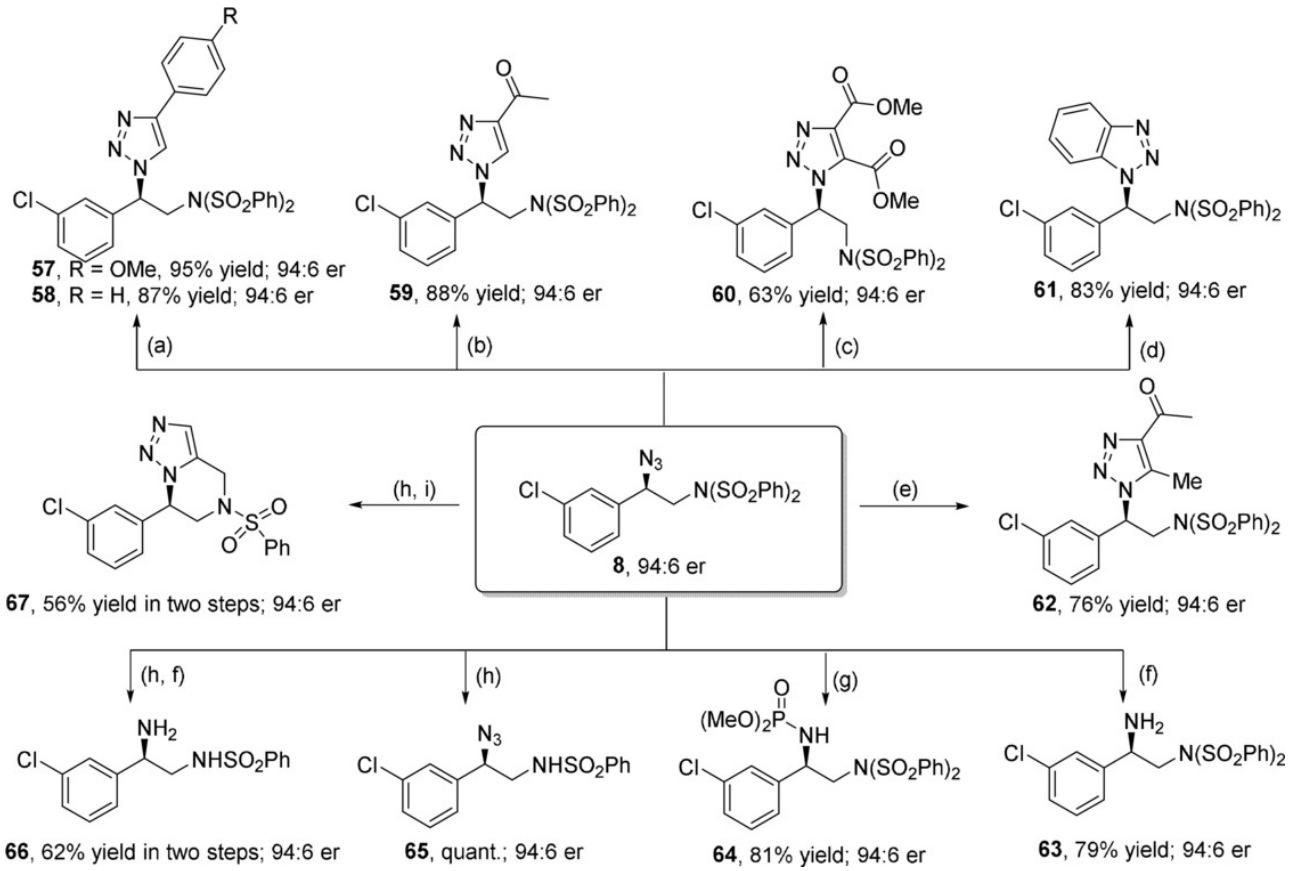
52, dr 3:2, 61% yield
major 85:15 er
minor 92:8 er



53,[d] R^8 = H, dr 1.4:1 (chiral:meso),
73% yield, 92:8 er
54, R^8 = F, dr 1.3:1 (chiral:meso),
78% yield, 90:10 er
55, R^8 = Cl, dr 1:1 (chiral:meso),
67% yield, 88:12 er
56,[d] R^8 = Br, dr 1:1.2 (chiral:meso),
67% yield, 91:9 er

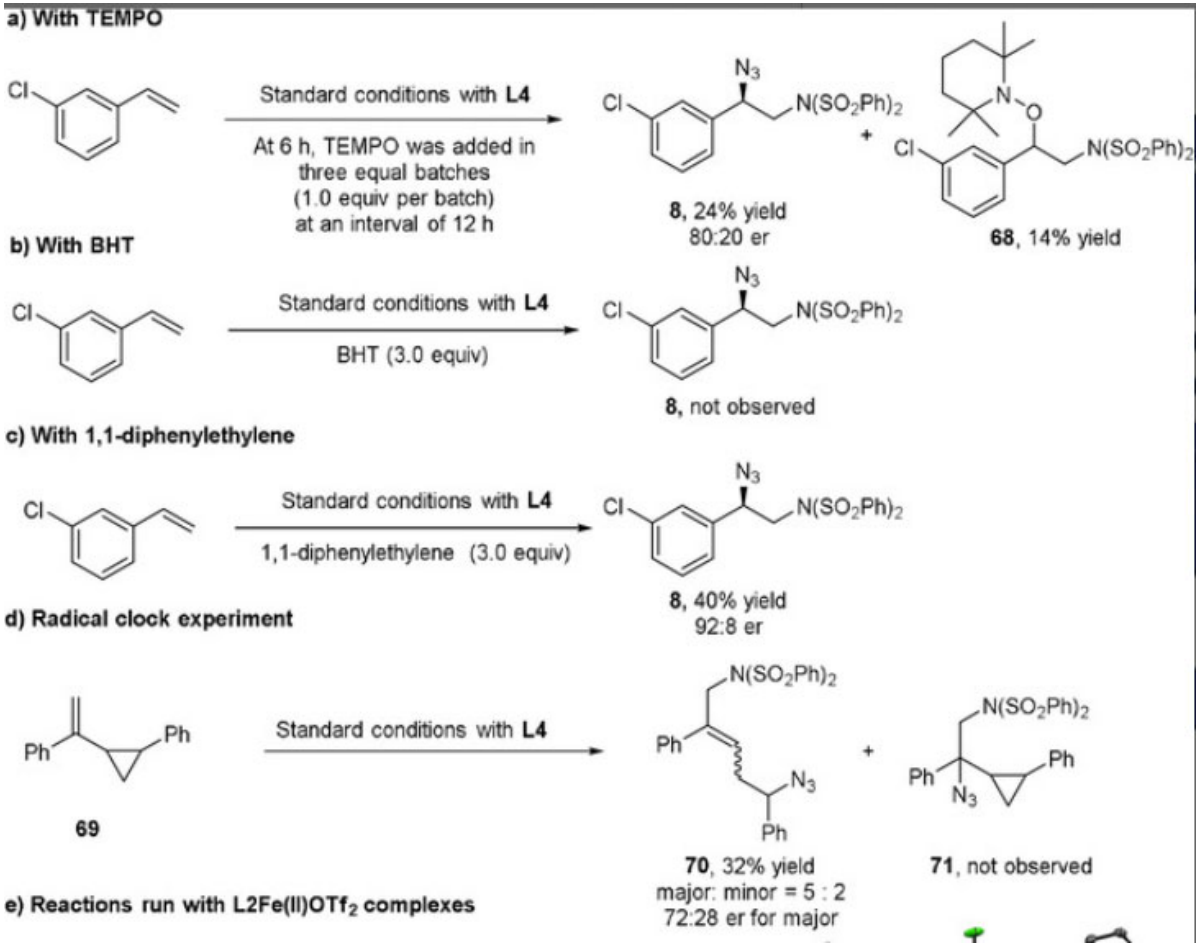
Bao, H.-L. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12455.

外球模式: Bao's work



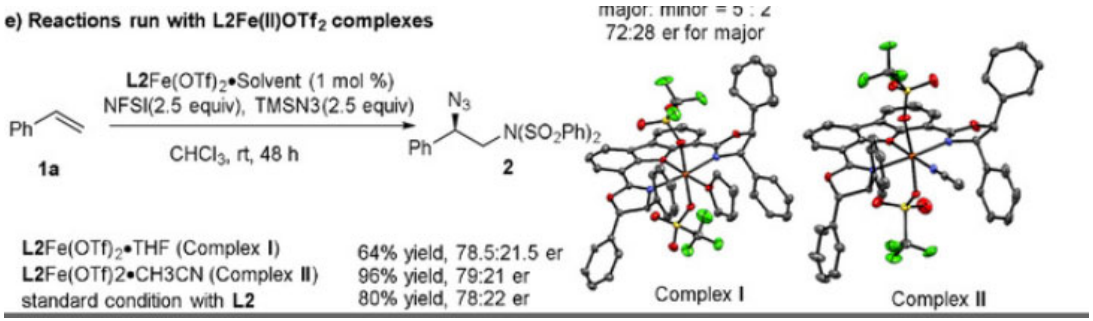
Bao, H.-L. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12455.

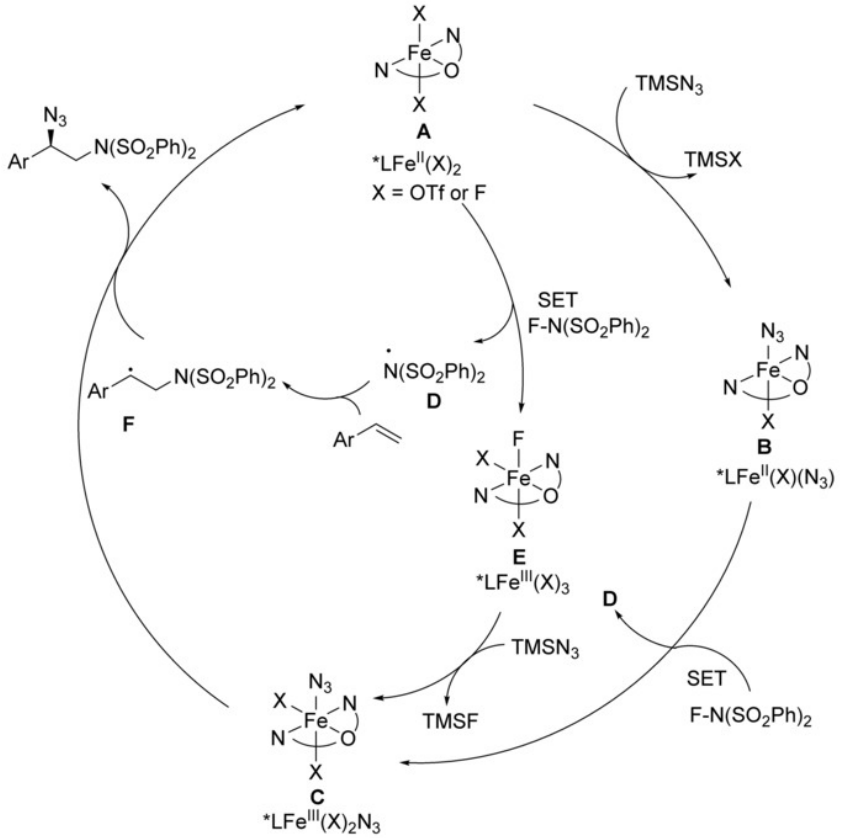
外球模式: Bao's work



Bao, H.-L. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12455.

外球模式: Bao's work

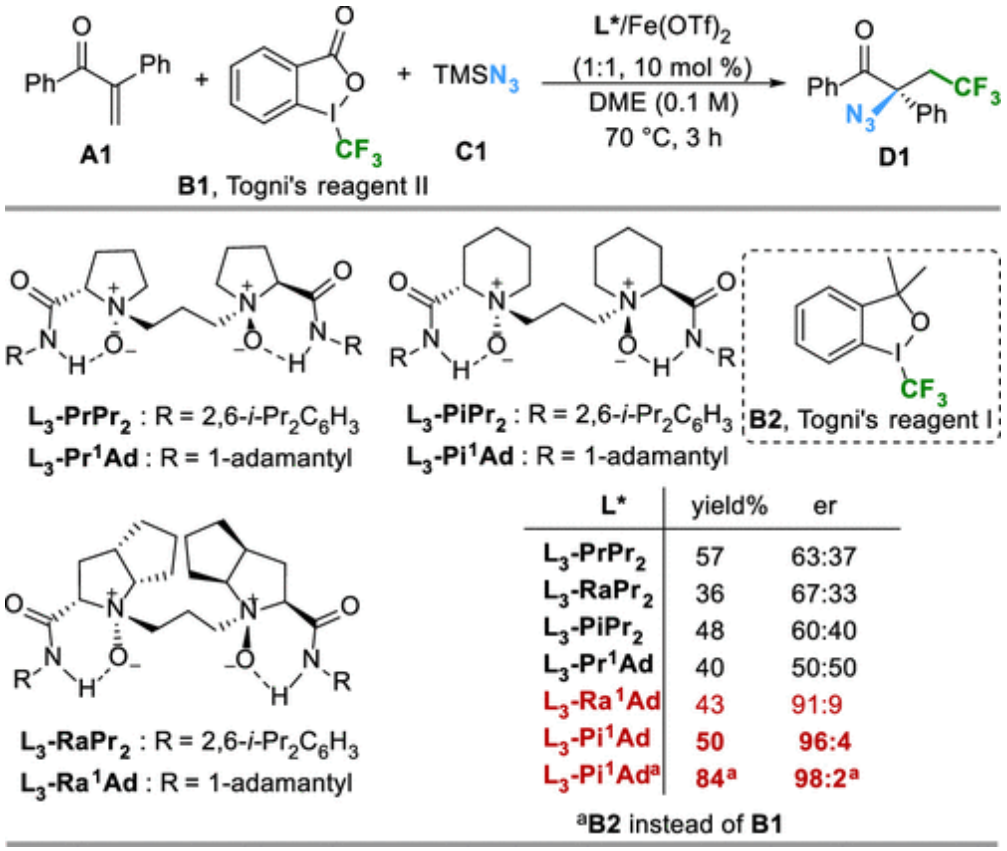




Bao, H.-L. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 12455.

外球模式: Feng's work

α,β-不饱和羰基化合物的不对称自由基碳叠氮化以及双叠氮化反应



L*	yield%	er
L_3-$PrPr_2$	57	63:37
L_3-$RaPr_2$	36	67:33
L_3-$PiPr_2$	48	60:40
L_3-Pr^1Ad	40	50:50
L_3-Ra^1Ad	43	91:9
L_3-Pi^1Ad	50	96:4
L_3-Pi^1Ad[a]	84[a]	98:2[a]

[a]B2 instead of B1

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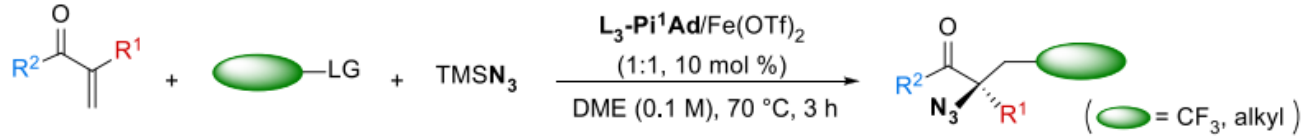
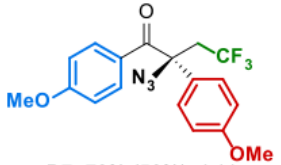
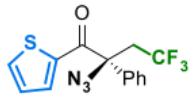
外球模式: Feng's work

α,β-不饱和羰基化合物的不对称自由基碳叠氮化以及双叠氮化反应

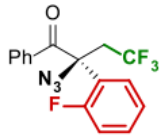




D7, 70% (56%) yield
96.5:3.5 er

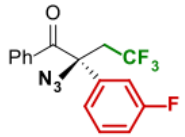


D8, 75% (61.5%) yield
97.5:2.5 er

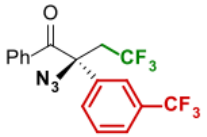


D9, 72% (50%) yield
97:3 er

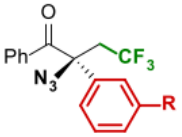
D10, 80% (75.5%) yield
95:5 er



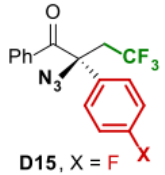
D11, 70% (51.5%) yield
97.5:2.5 er



D12, 66% (38%) yield
96.5:3.5 er

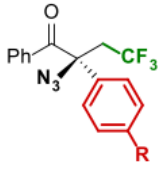


D13, R = Me, 97.5:2.5 er
83% (73.5%) yield
D14, R = MeO, 97.5:2.5 er
76% (61%) yield



D15, X = F
D16, X = Cl
D17, X = Br
D18, X = I

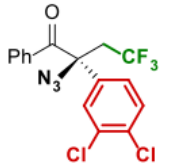
D15, 71% (55%) yield
98:2 er
D16, 70% (54%) yield
97.5:2.5 er
D17, 70% (53%) yield
97:3 er
D18, 74% (56%) yield
96:4 er



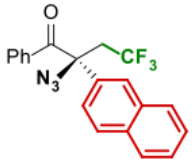
D19, R = Me
D20, R = MeO
D21, R = MeS

D19, 87% (70.5%) yield
97.5:2.5 er
D20, 89% (76%) yield
97:3 er
D21, 77% (57%) yield
98:2 er

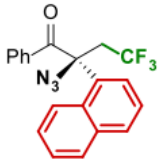
D22, 90% (66%) yield
98:2 er



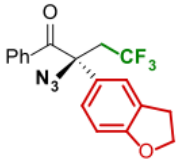
D23, 53% (33%) yield
96.5:3.5 er



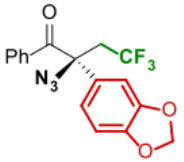
D24, 75% (54%) yield
97.5:2.5 er



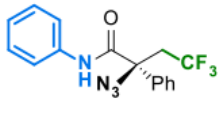
D25, 35% (26%) yield
70.5:29.5 er



D26, 88% (81%) yield
96.5:3.5 er



D27, 94% (80%) yield
97.5:2.5 er



D28, 90% (69%) yield
88:12 er

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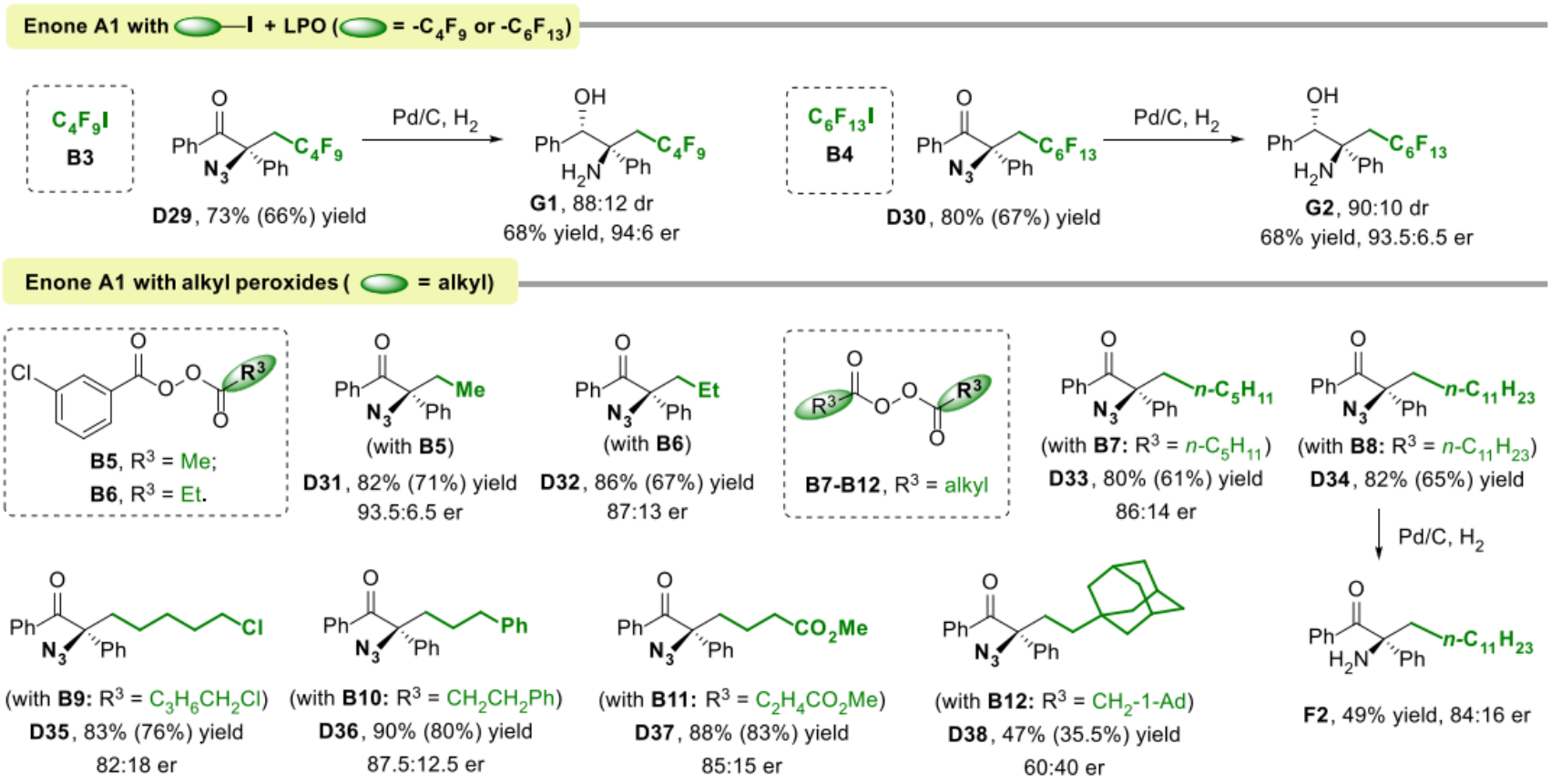
外球模式: Feng's work

α,β-不饱和羰基化合物的不对称自由基碳叠氮化以及双叠氮化反应



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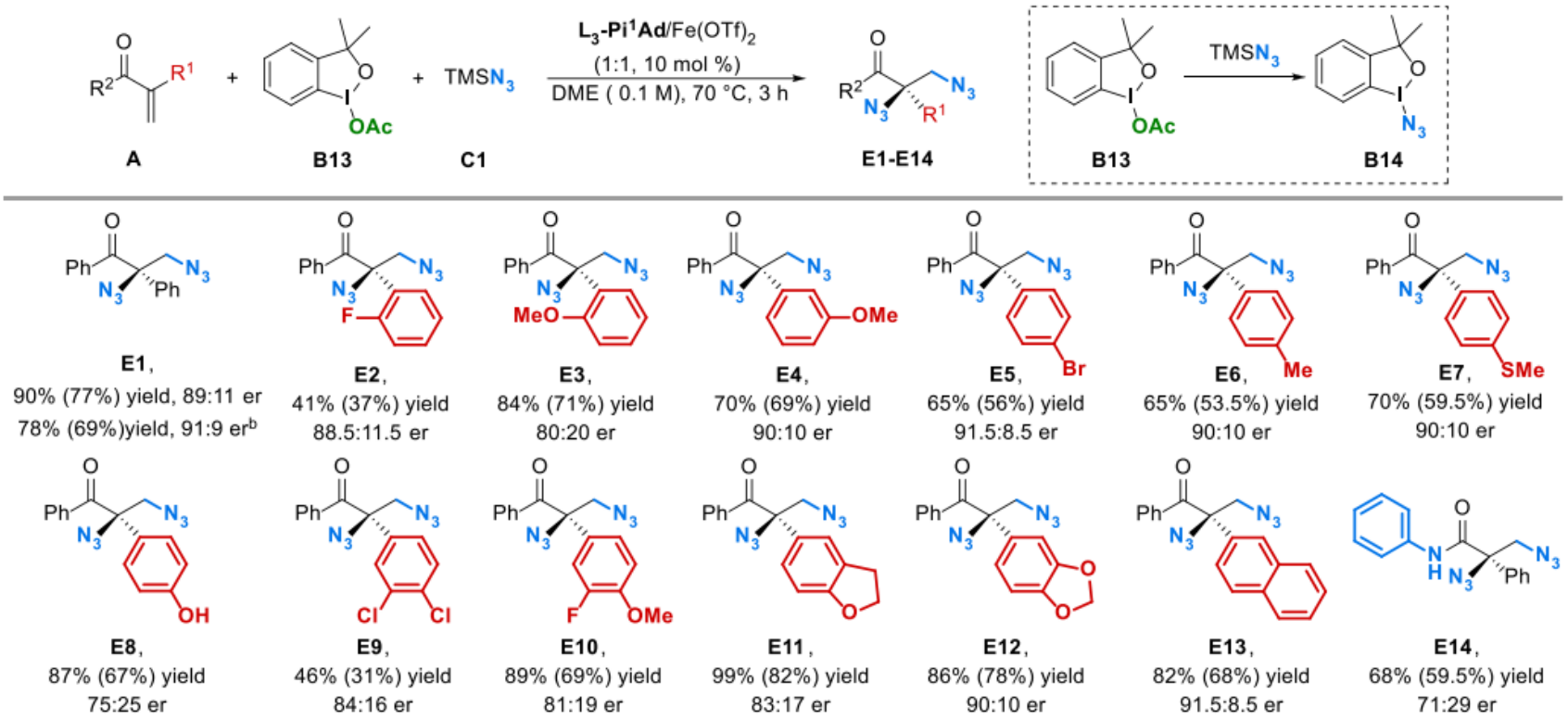

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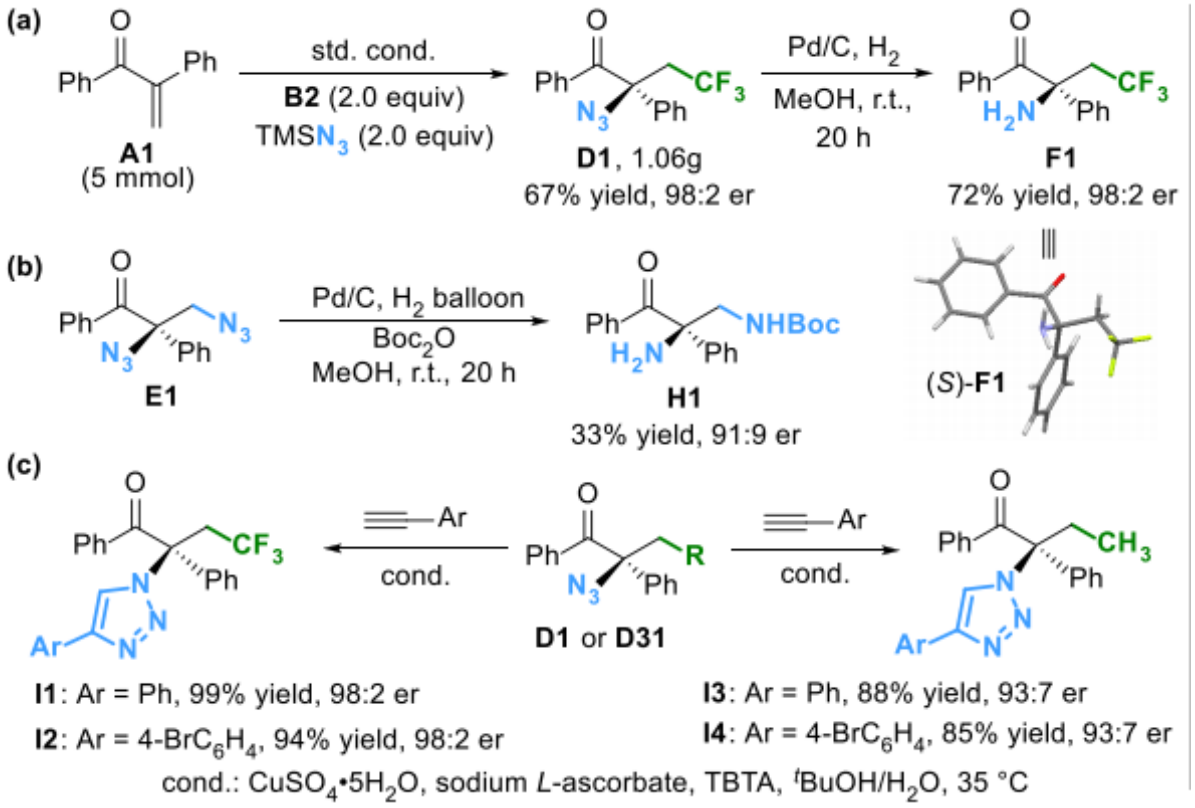

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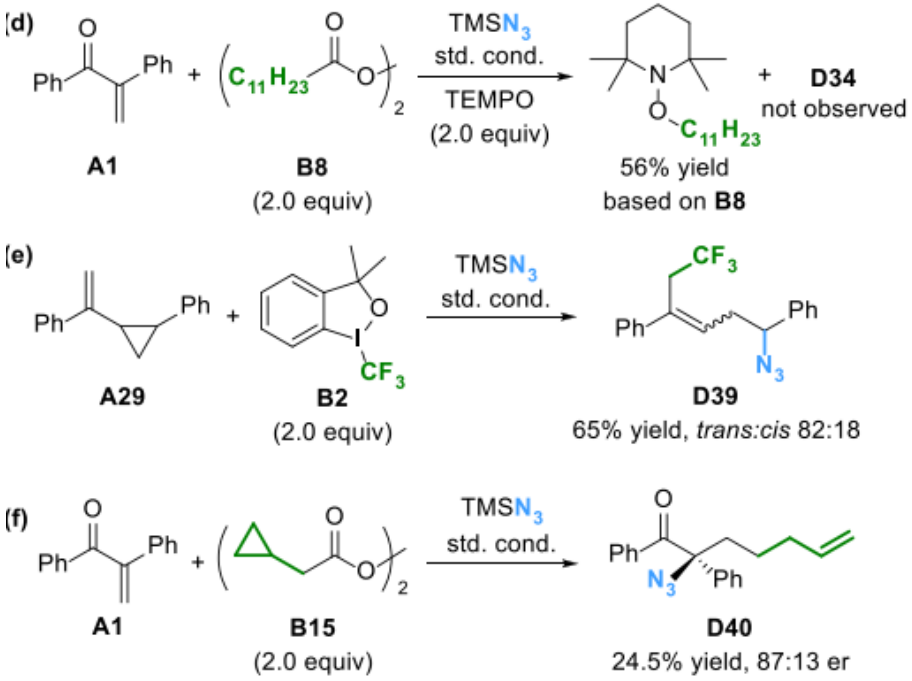

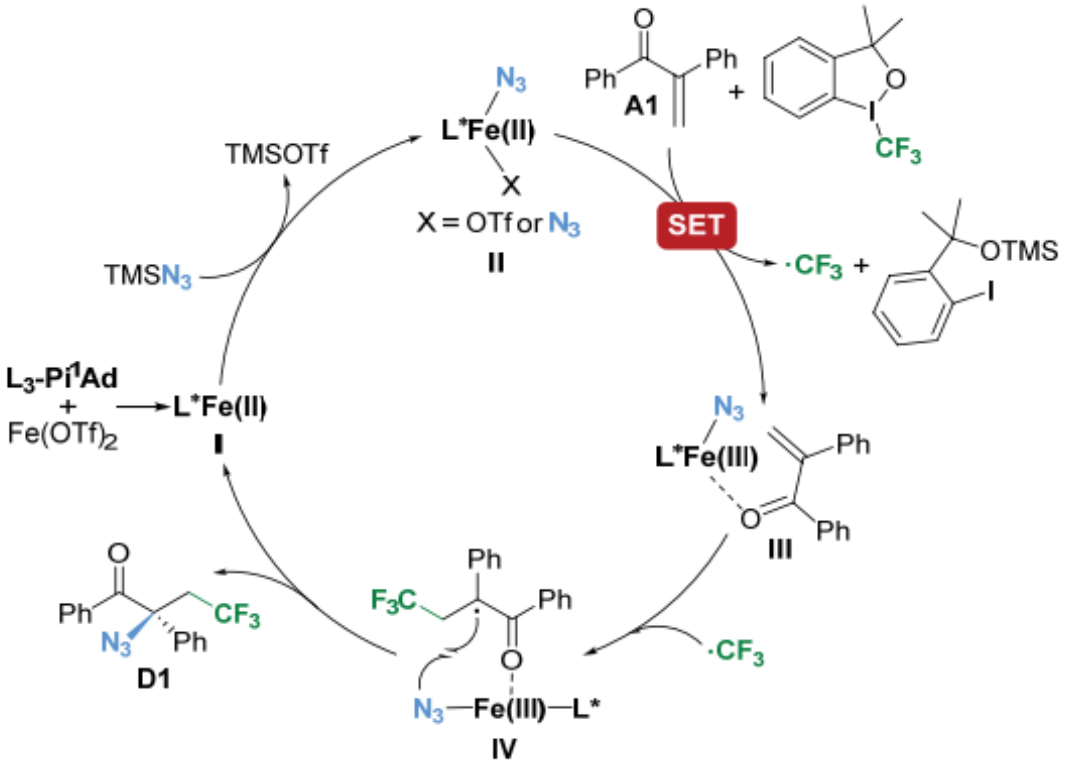

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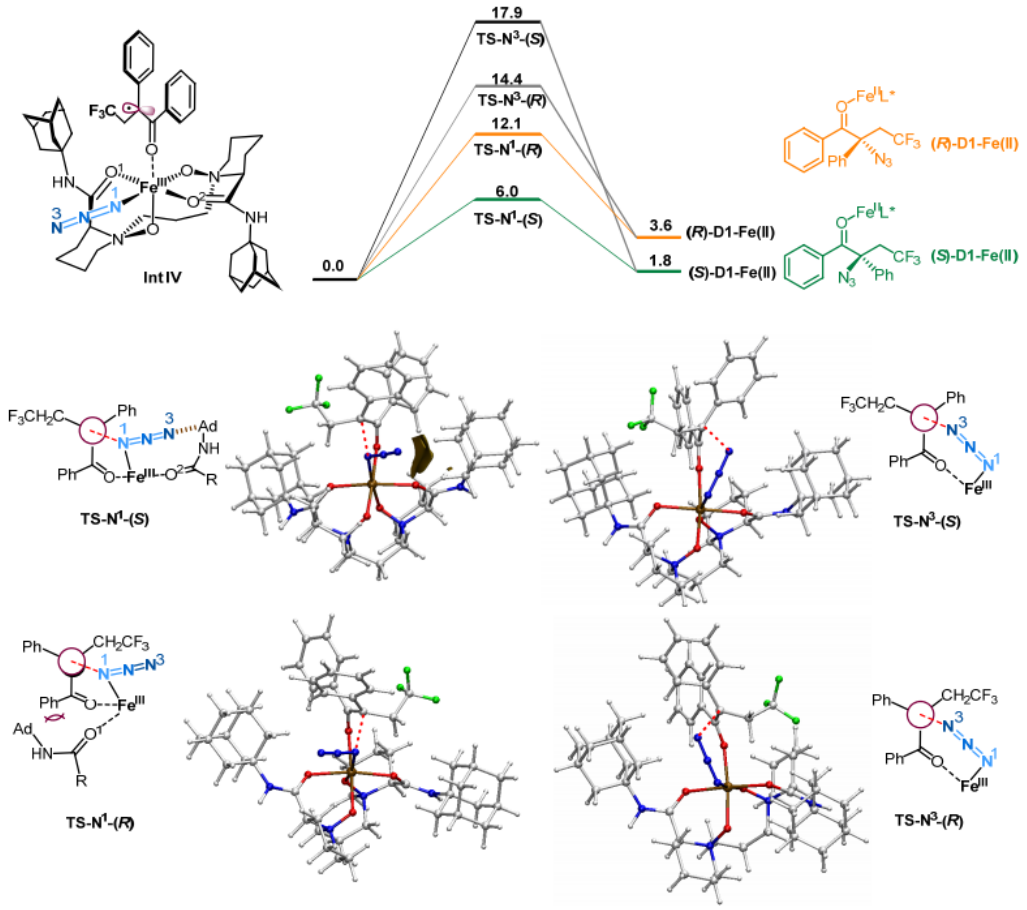
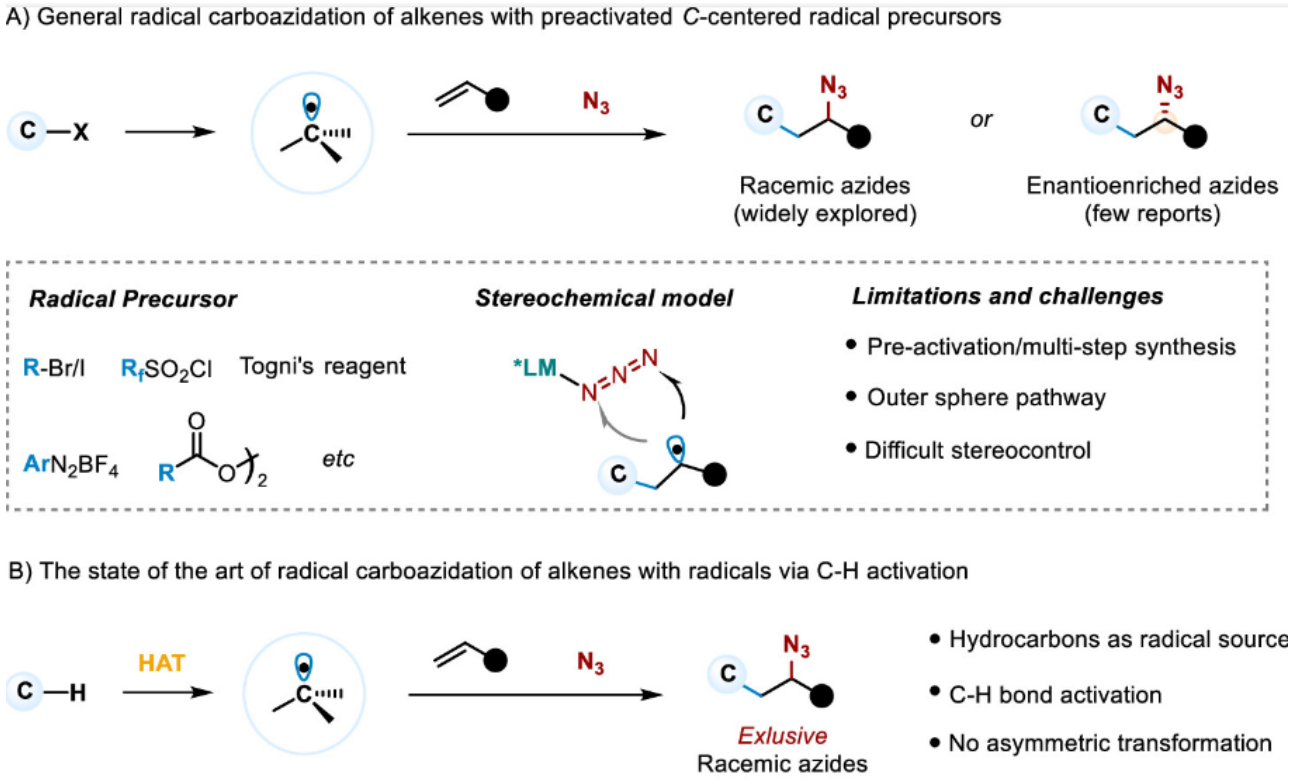


Feng, X.-M. et al., *J. Am. Chem. Soc.* **2021**, *143*, 11856

外球模式: Feng's work

直接活化脂肪族 C-H 键的不对称三组分自由基烯碳叠氮反应



- 预先激活的自由基前体，如烷基卤化物、烷基磺酰氯化物或Togni试剂，是大量需要的，不可避免地导致额外的步骤，降低了整个过程的效率。
- 目前报道的方法主要局限于外消旋，因为催化不对称自由基碳氮化反应涉及外球途径，并且极难立体选择性地构建C−N_3键

Feng, X.-M. et al., *J. Am. Chem. Soc.* **2024**, *146*, 13347

外球模式: Feng's work

直接活化脂肪族 C-H 键的不对称三组分自由基烯碳叠氮反应

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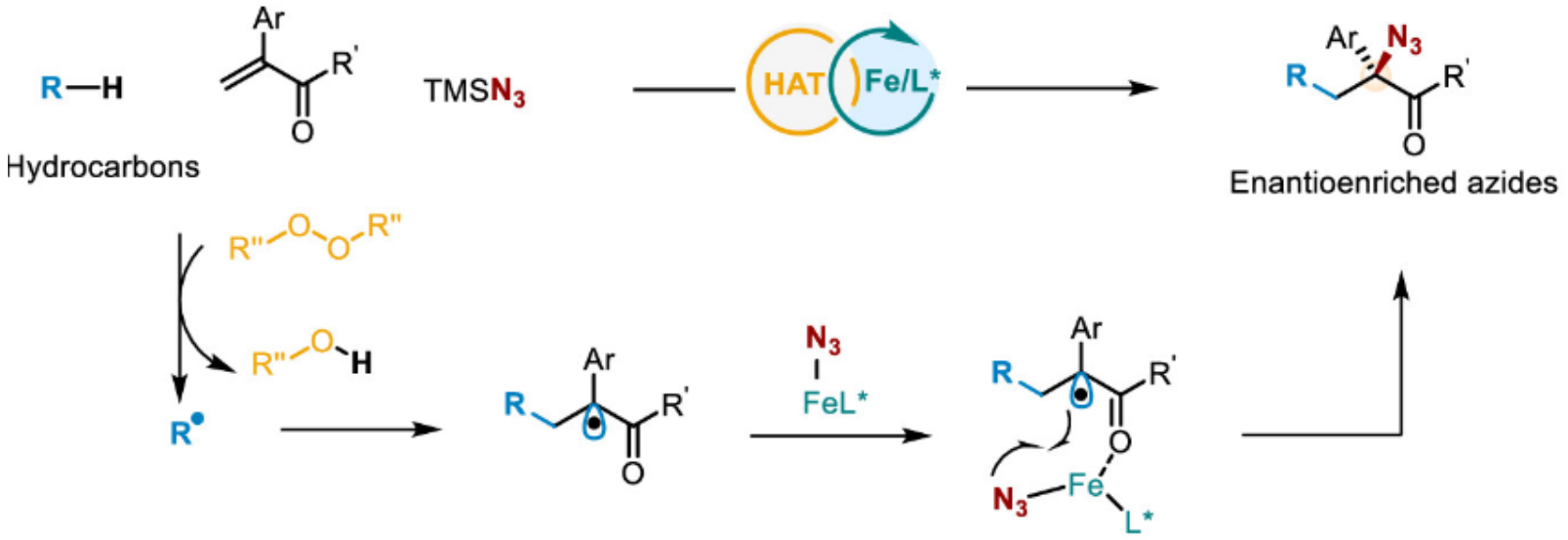
C) *This work*: Iron-catalyzed asymmetric carboazidation of α,β-enones via selective aliphatic C-H activation

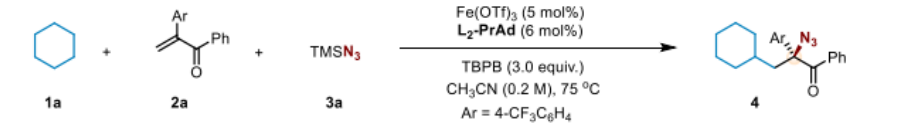


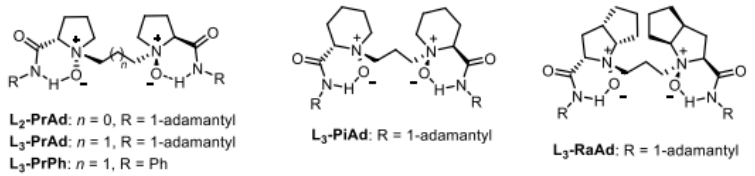
- Abundant hydrocarbons as feedstocks
- Primary, secondary, tertiary radicals
- Catalytic asymmetric radical carboazidation
- HAT catalysis merges chiral iron catalysis

Feng, X.-M. et al., *J. Am. Chem. Soc.* **2024**, *146*, 13347

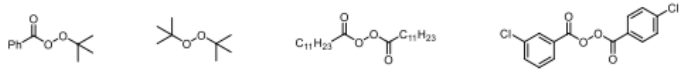
外球模式: Feng's work

直接活化脂肪族 C-H 键的不对称三组分自由基烯碳叠氮反应





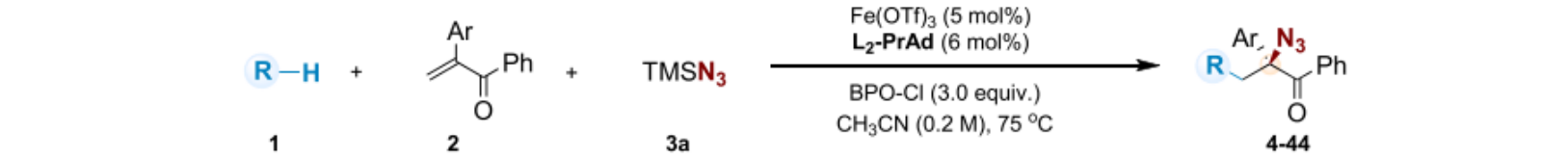
Entry	Deviation from above conditions	**4** (%)	**5** (%)	*er* of **4** (%)
1	None	58	31%	92:8
2	**L_3-PrAd** was used	40	4%	73:57
3	**L_3-PrPh** was used	54	33%	70:30
4	**L_3-PiAd** was used	63	15%	79:21
5	**L_3-RaAd** was used	54	17%	69:31
6	$Fe(OTf)_2$ instead of $Fe(OTf)_3$	46	17%	88:12
7	$Fe(OAc)_2$ instead of $Fe(OTf)_3$	5	trace	50:50
8	$FeCl_2$ instead of $Fe(OTf)_3$	18	trace	50:50
9	DTBP instead of TBPB	5	trace	88:12
10	LPO instead of TBPB	ND	trace	ND
11	BPO-Cl instead of TBPB	64	20%	92:8
12 [b]	Without $Fe(OTf)_3$	trace	trace	50:50
13 [b]	Without **L_2-PrAd**	37%	47%	50:50



Feng, X.-M. et al., *J. Am. Chem. Soc.* **2024**, *146*, 13347

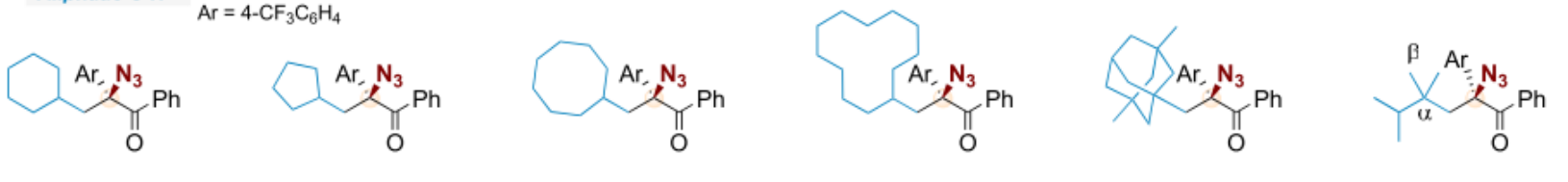
外球模式: Feng's work

直接活化脂肪族 C-H 键的不对称三组分自由基烯碳叠氮反应



Aliphatic C-H

Ar = 4-$CF_3C_6H_4$



4, 56%, 92:8 *er*

6, 65%, 92:8 *er*

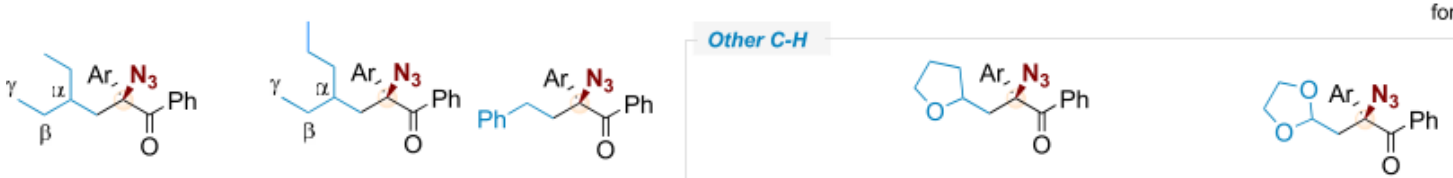
7, 54%, 92:8 *er*

8, 52%, 88:12 *er*

9, 60%, 94:6 *er*

10, 43%, α/β = 2/1
for α-isomer 77:23 *er*

Other C-H



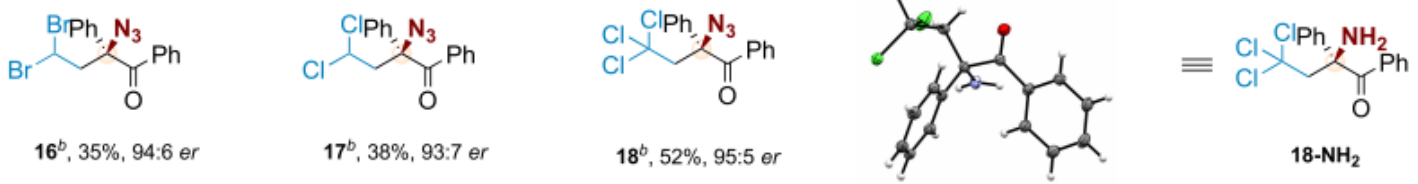
11, 53%
α/β/γ = 1.3/1.6/1

12, 52%
α/β/γ = 1.3/1/1.9

13, 62%, 85:15 *er*

14, 52%, 1:1 *dr*
87:13/86:14 *er*

15, 58%, 95:5 *er*



16[b], 35%, 94:6 *er*

17[b], 38%, 93:7 *er*

18[b], 52%, 95:5 *er*

18-NH_2

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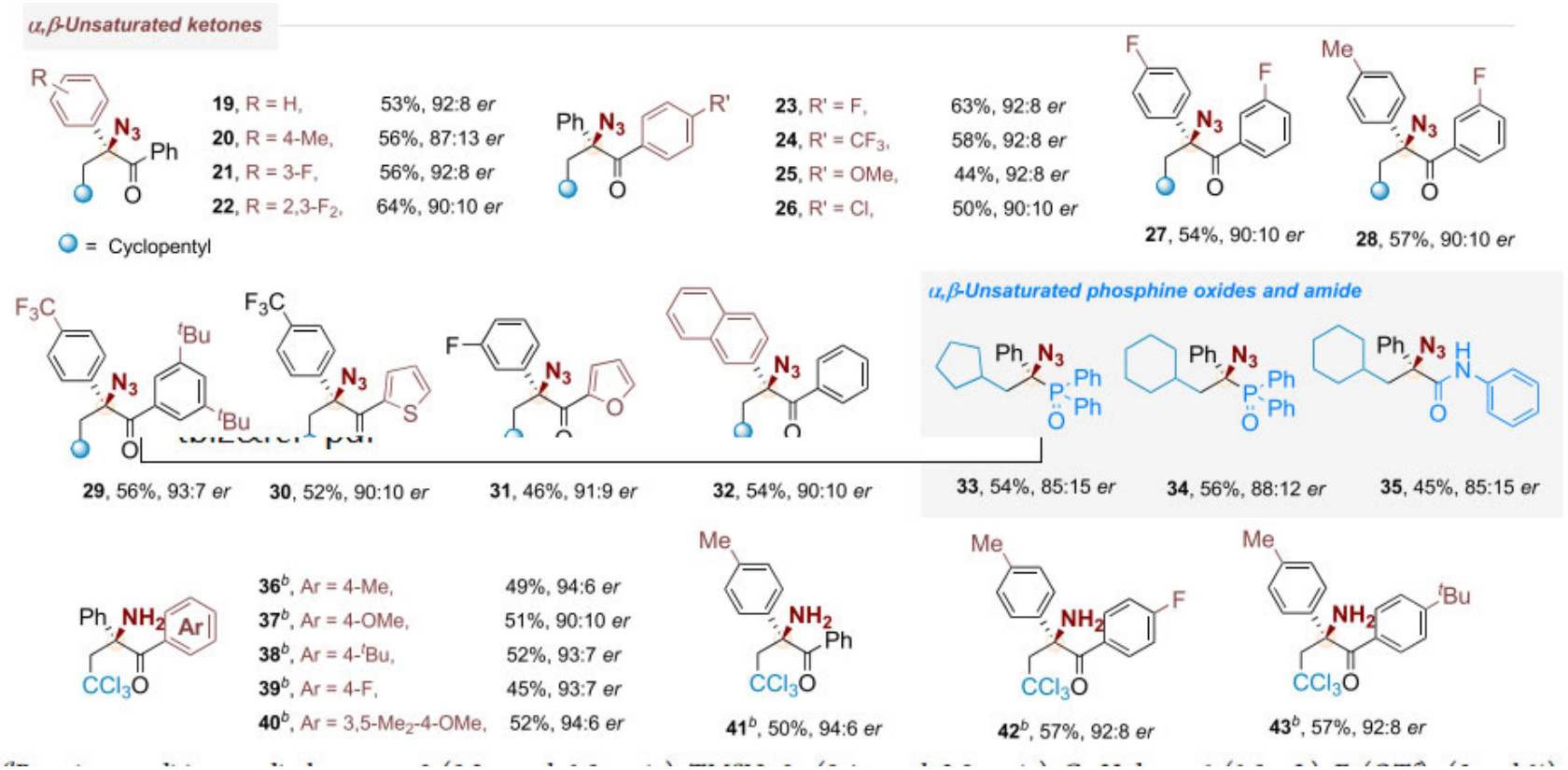

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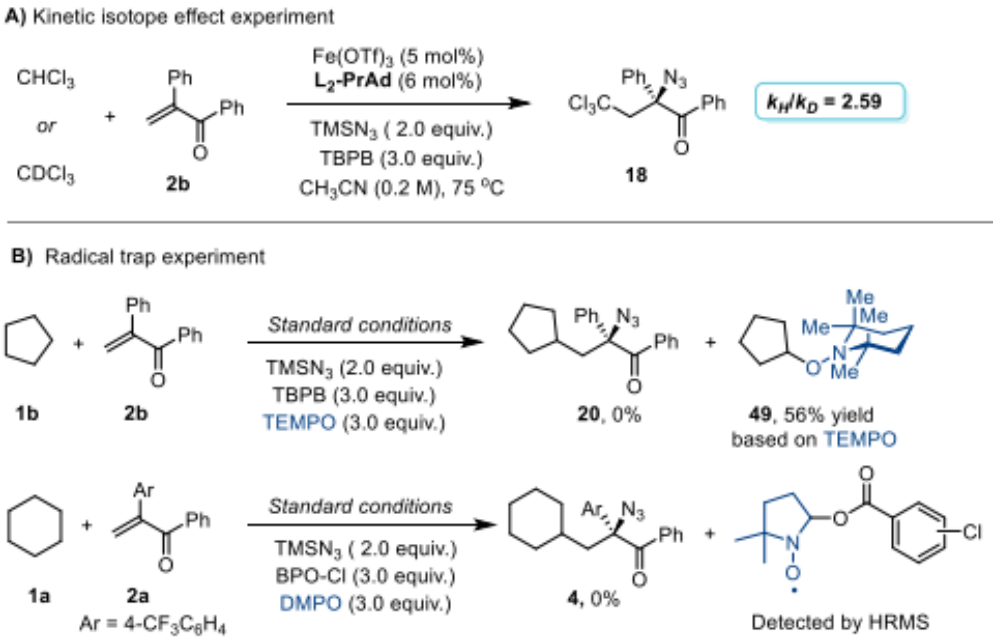

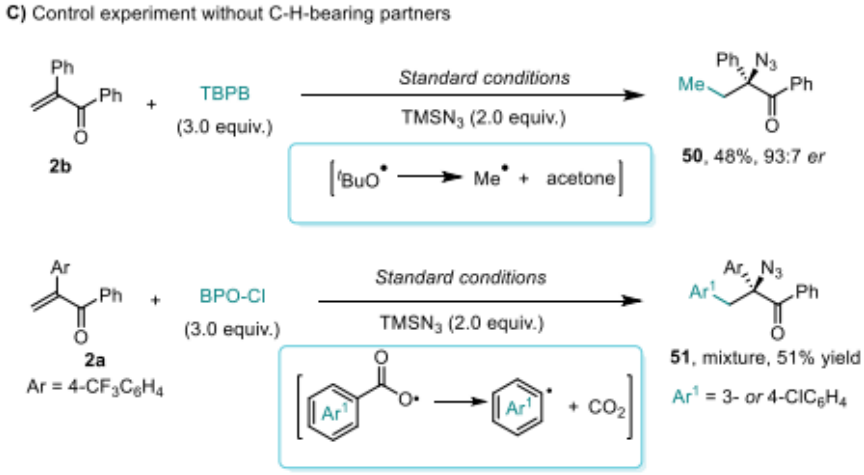

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外球模式: Feng's work

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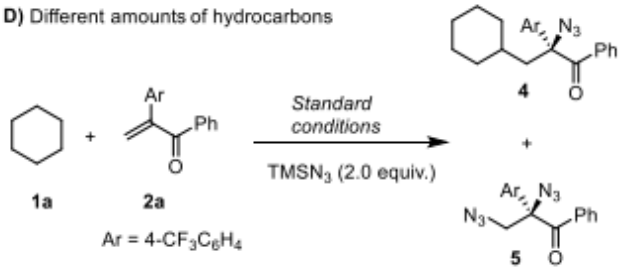
D) Different amounts of hydrocarbons

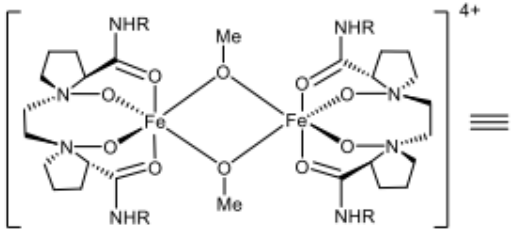


1a 2a

Ar = 4-$CF_3C_6H_4$

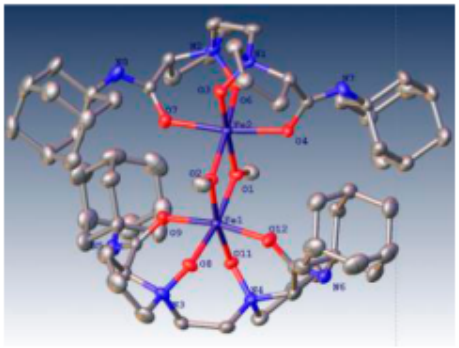
entry	1a	4 (%)	5 (%)	*er* of 4
1	0.1 mL	17%	70%	87:13
2	0.2 mL	29%	45%	91:9
3	0.3 mL	36%	34%	92:8
4	0.4 mL	52%	28%	92:8
5	0.5 mL	64%	20%	92:8

E) Reaction with pre-catalyst

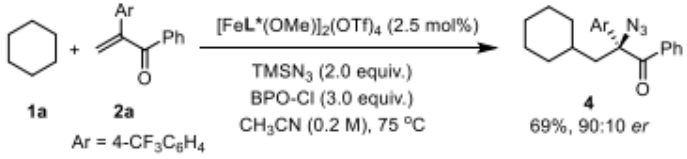


{[Fe**L***(OMe)]$^{2+}$}$_2$ (*Crystallization from methanol*)

L* = **L_2-PrAd** R = 1-adamantyl



CCDC 2347533



1a 2a

Ar = 4-$CF_3C_6H_4$

69%, 90:10 *er*

Standard conditions:

64%, 92:8 *er*

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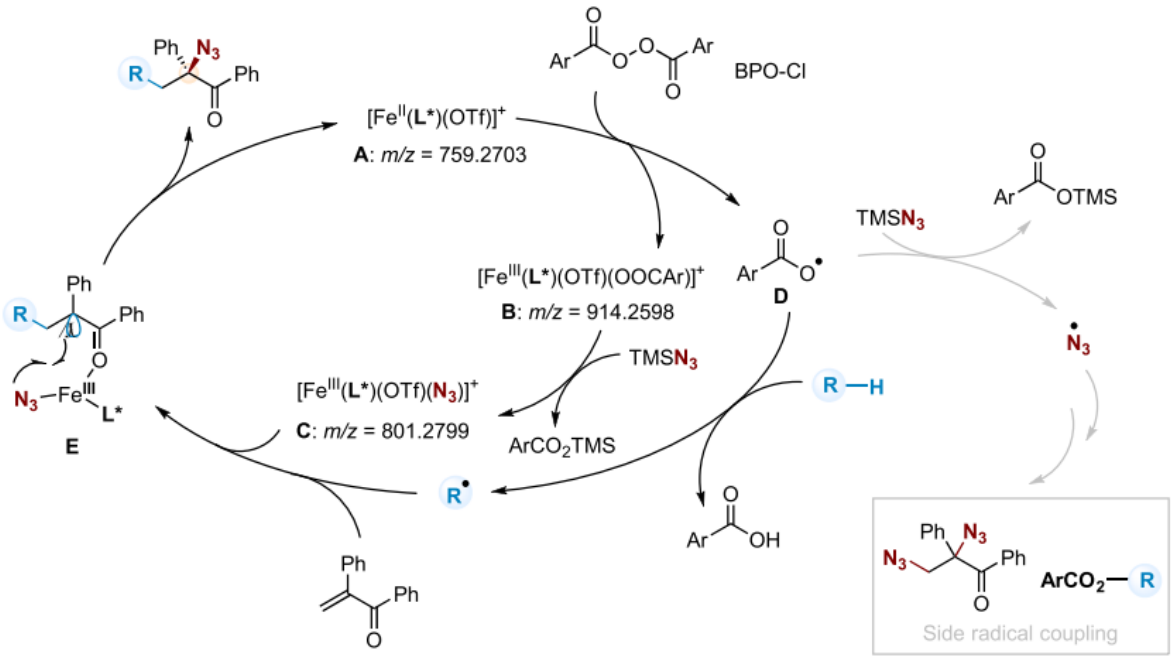


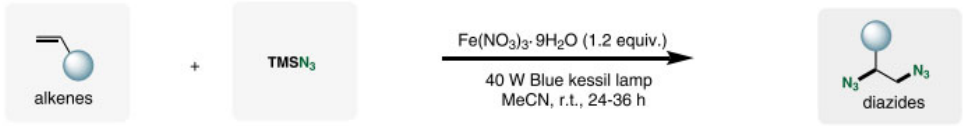
1) 直接使用丰富的碳氢化合物作为烷基化试剂，快速获得有价值的手性季碳中心。

2) 通过Fe(II)/过氧化物介导的分子间HAT过程，形成碳中心自由基，避免了烷基自由基前体的预活化。

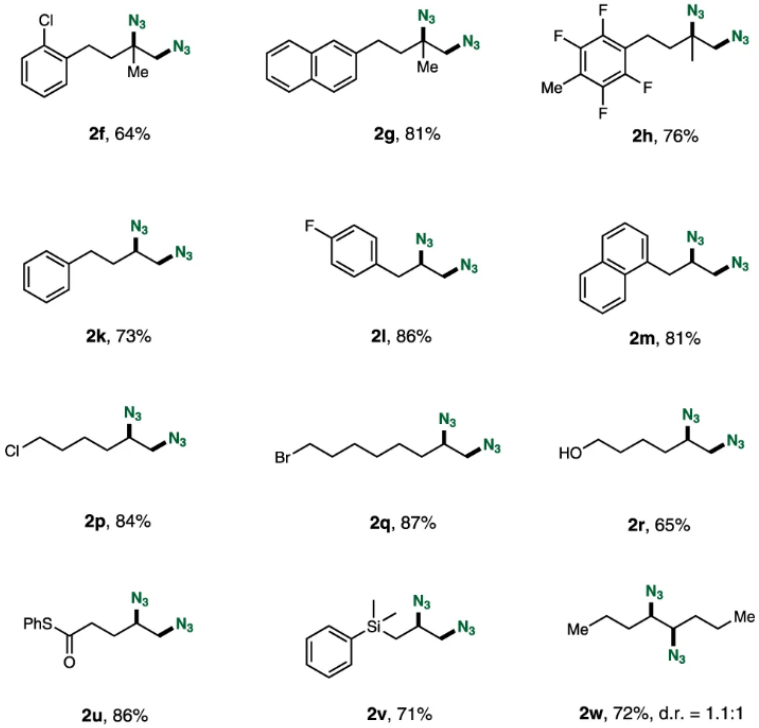
3) 通过手性Fe(III)−N_3配合物介导的不对称分子内叠氮转移过程，得到有价值的手性碳叠氮化化合物。

Feng, X.-M. et al., *J. Am. Chem. Soc.* **2024**, *146*, 13347

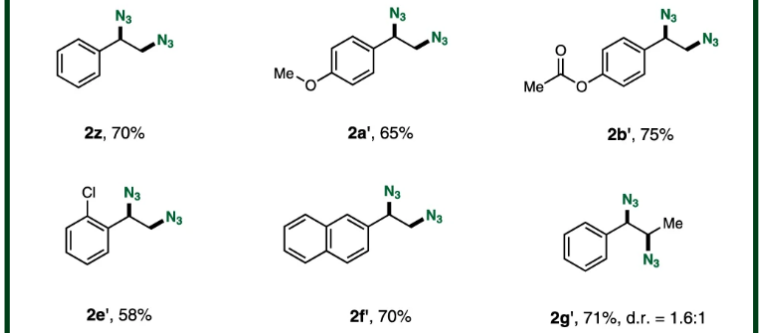
外球模式：Fe介导的LMCT模式下的烯基二叠氮化修饰

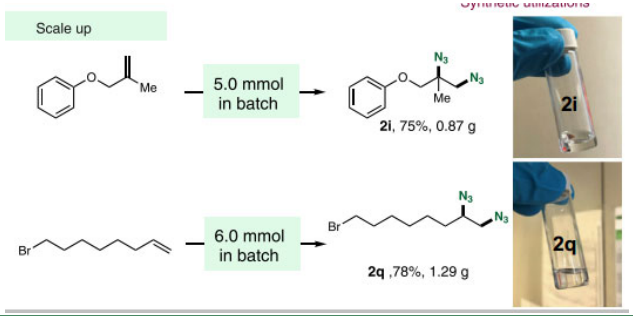


Unactivated alkenes



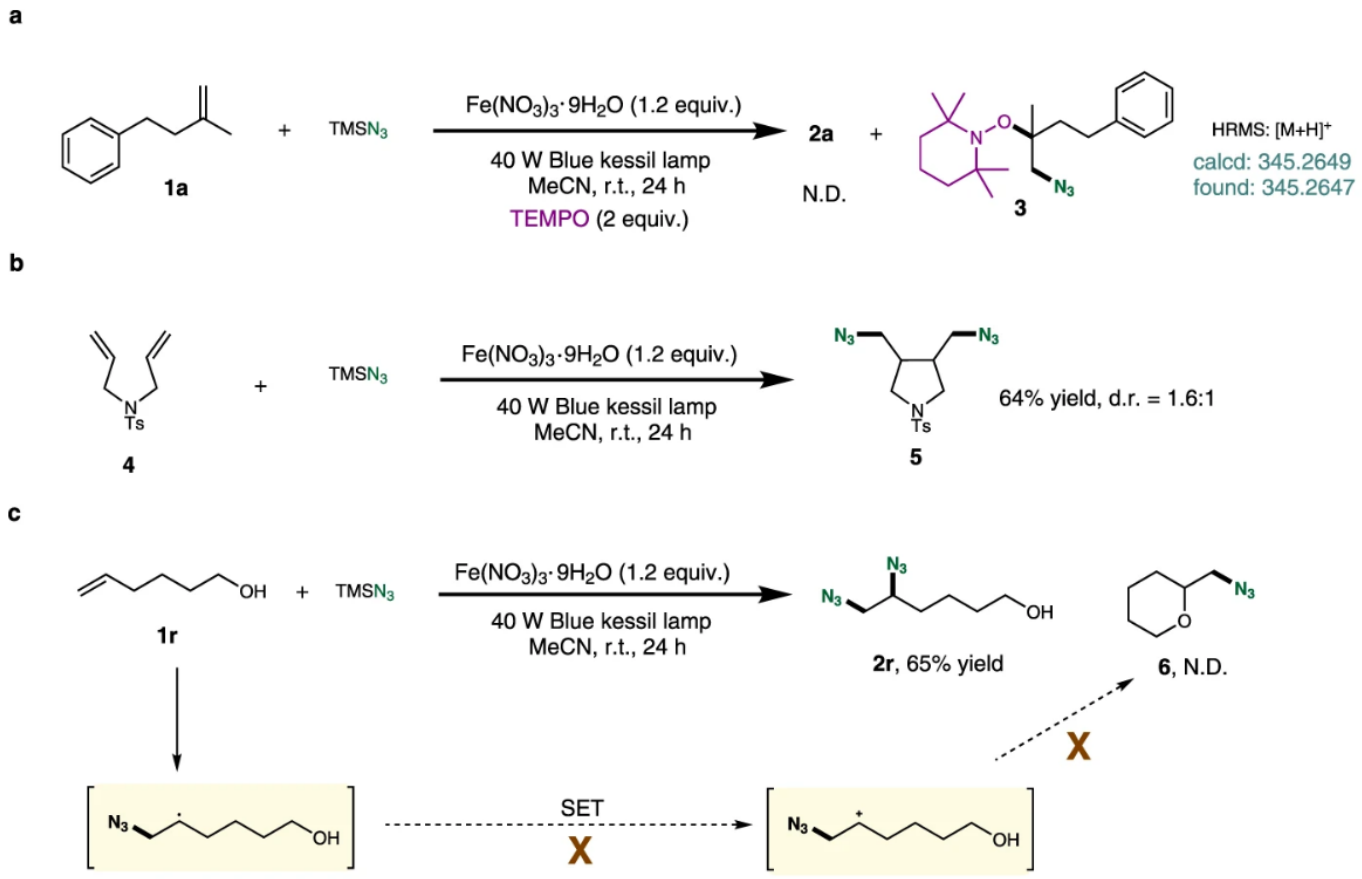
Aromatic alkenes





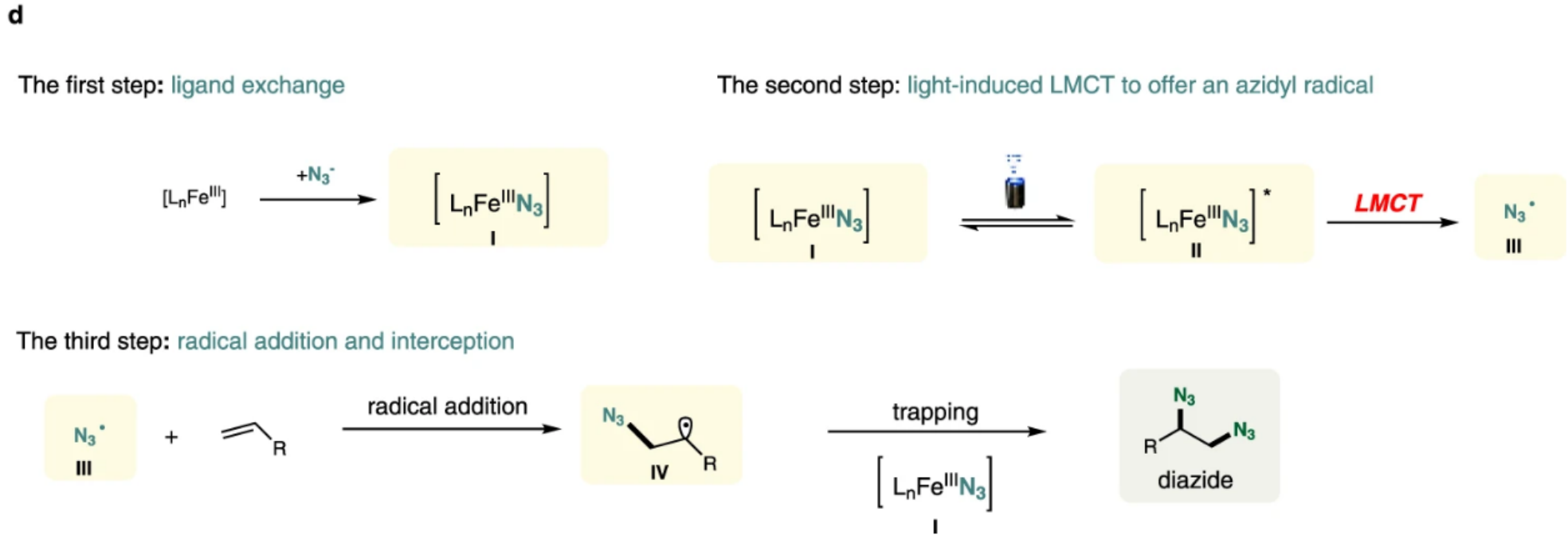
Shi, Y.-M. et al., *Nat. Commun*. **2022**, *13*, 7880.

外球模式：Fe介导的LMCT模式下的烯基二叠氮化修饰



Shi, Y.-M. et al., *Nat. Commun*. **2022**, *13*, 7880.

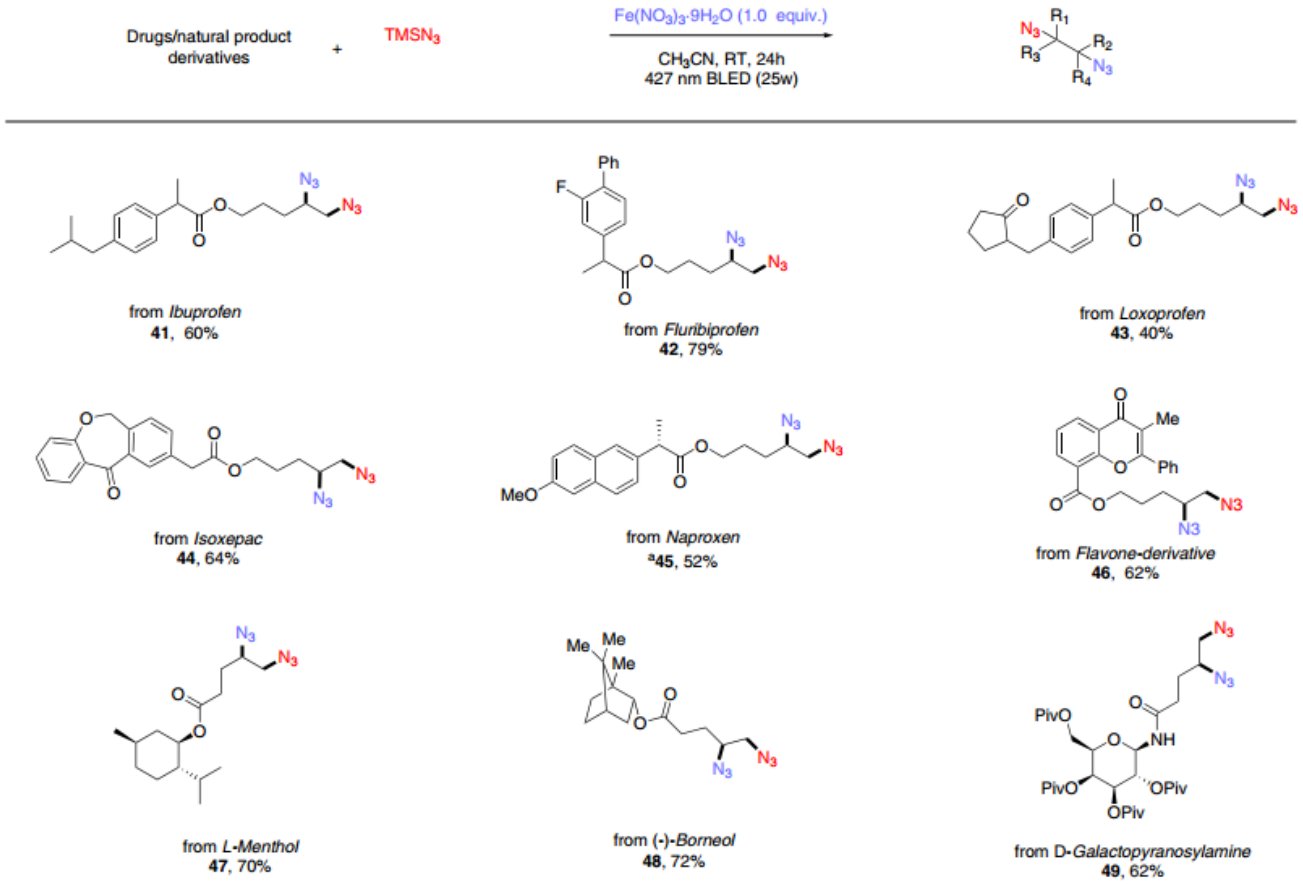
外球模式：Fe介导的LMCT模式下的烯基二叠氮化修饰



避免了使用氧化剂和还原剂，操作简捷，绿色高效，展现出非常好的底物兼容性以及官能团耐受性。同时作者还进行了克级反应的尝试，这些都为后期的药物发现提供了可能。

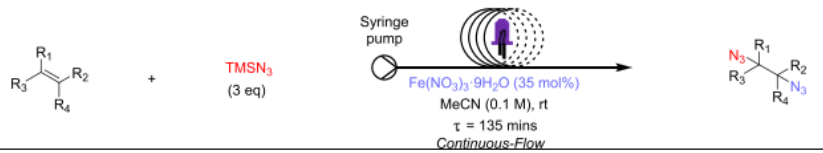
Shi, Y.-M. et al., *Nat. Commun*. **2022**, *13*, 7880.

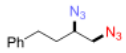
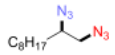
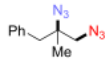
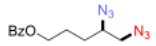
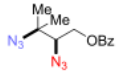
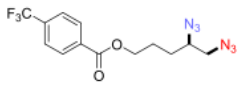
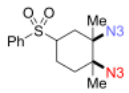
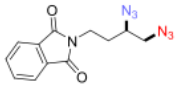
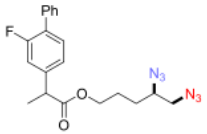
外球模式：Fe介导的LMCT模式下的烯基二叠氮化修饰



West, J. G. et al., *Nat. Commun*. **2022**, *13*, 7881.

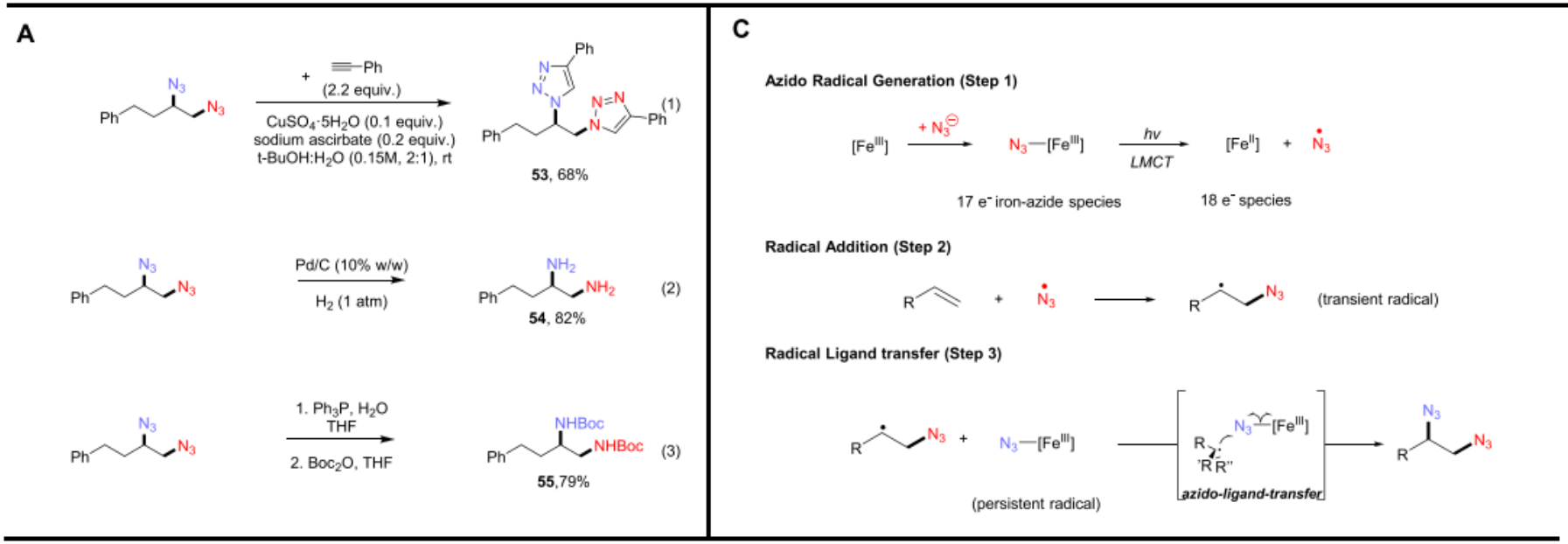
外球模式：Fe介导的LMCT模式下的烯基二叠氮化修饰



Product	Yield (BRSM)[a]	Product	Yield (BRSM)[a]
	70% (92%)		69% (4.2:1) (69%)
	63% (76%)		67% (67%)
	72% (85%) 0.5 mmol scale: 63%[b] (89%)		64% (64%)
	52% (69%)		44% (44%)
	64% (94%)		40% (43%)

West, J. G. et al., *Nat. Commun*. **2022**, *13*, 7881.

外球模式：Fe介导的LMCT模式下的烯基二叠氮化修饰



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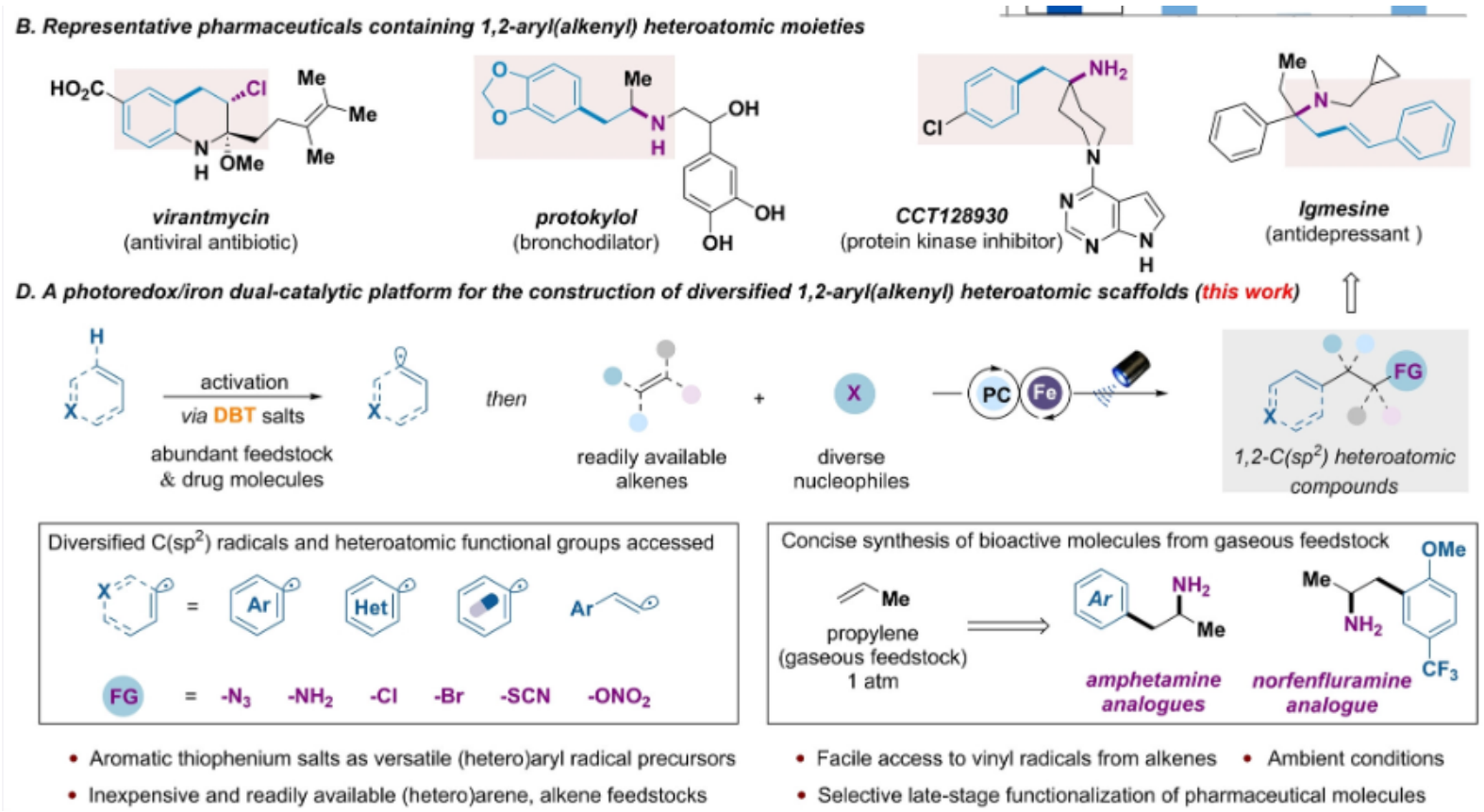
外球模式：Ir/Fe共催化三组分烯烃的芳基杂原子化



Wu, J. et al., *Angew. Chem. Int. Ed.* **2023**, *62*, e202310978.

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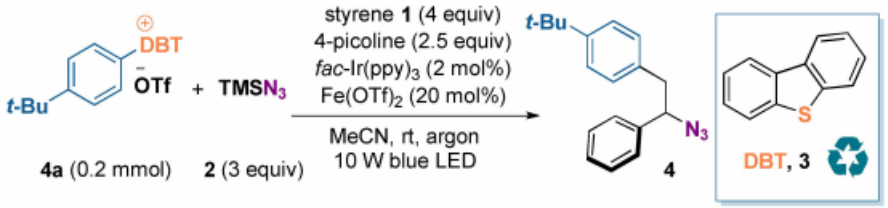

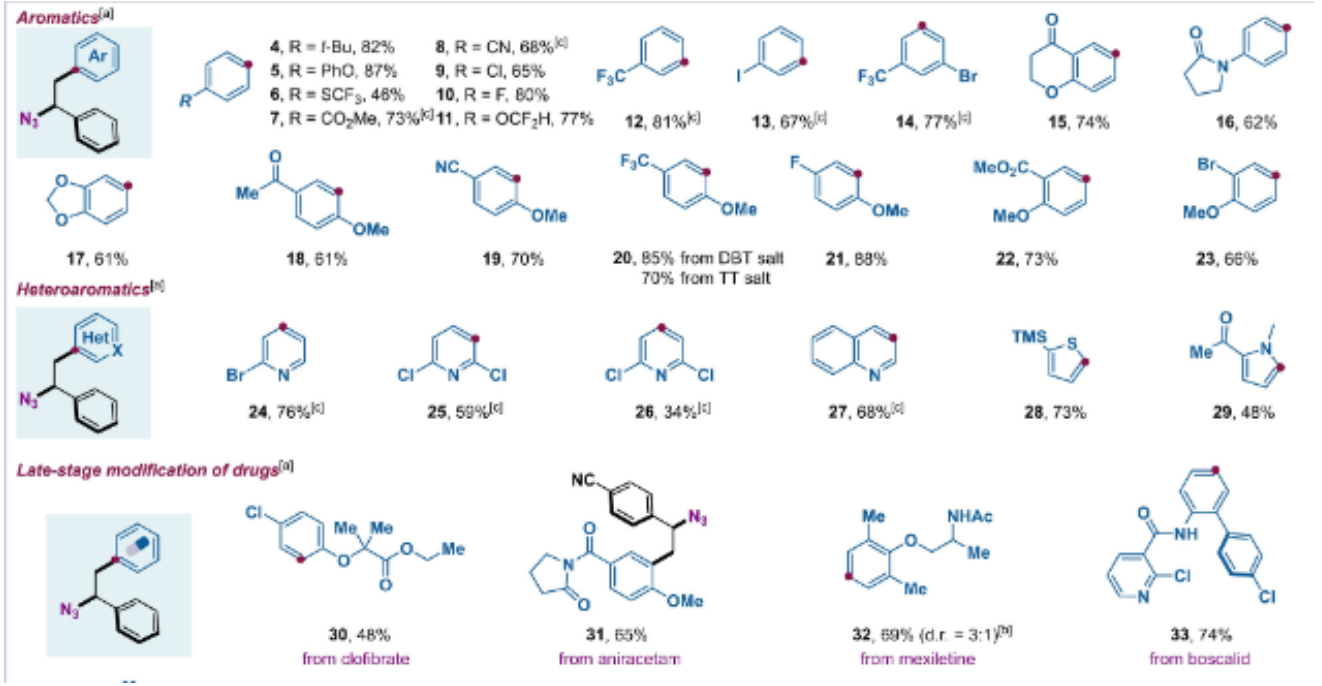

Wu, J. et al., *Angew. Chem. Int. Ed.* **2023**, *62*, e202310978.

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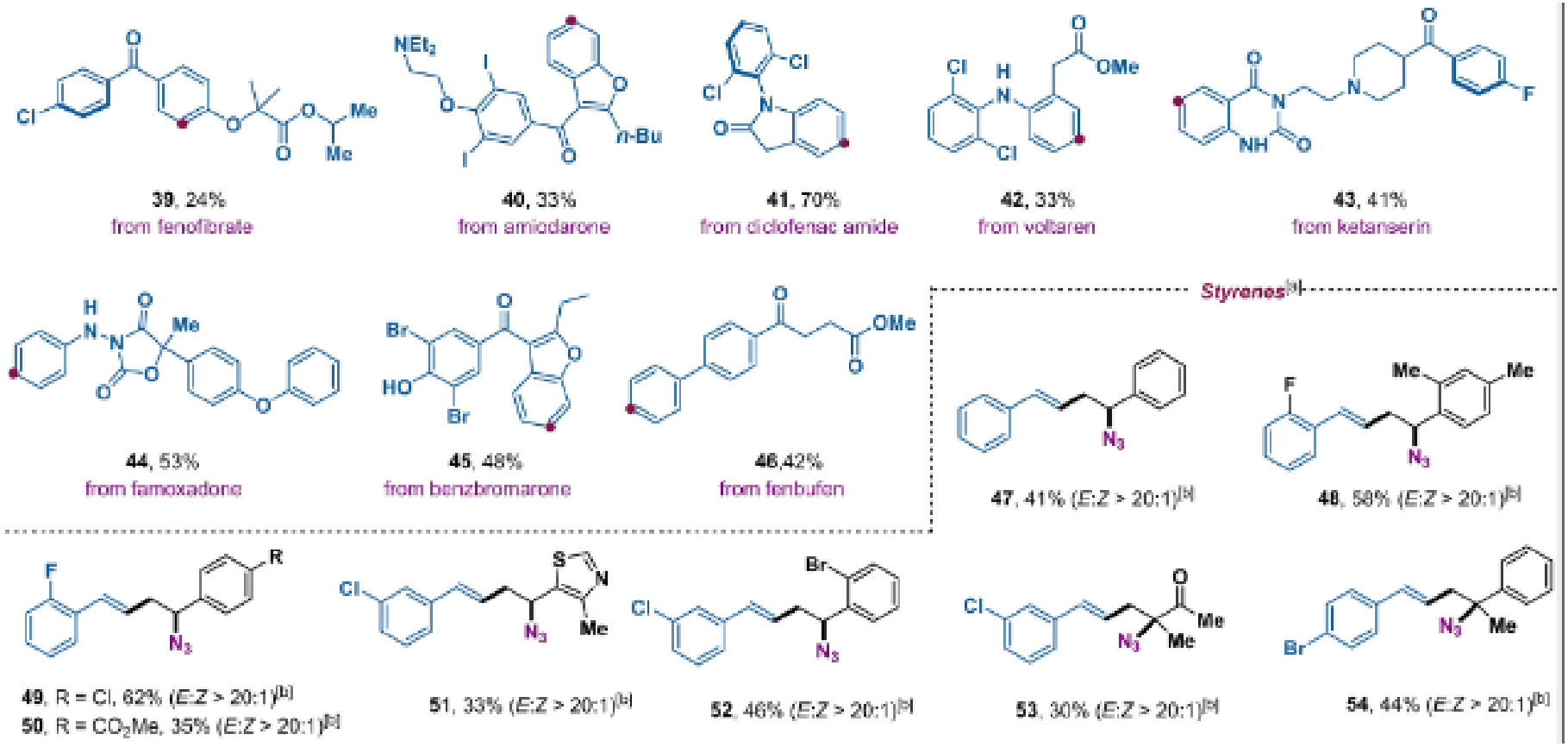

Wu, J. et al., *Angew. Chem. Int. Ed.* **2023**, *62*, e202310978.

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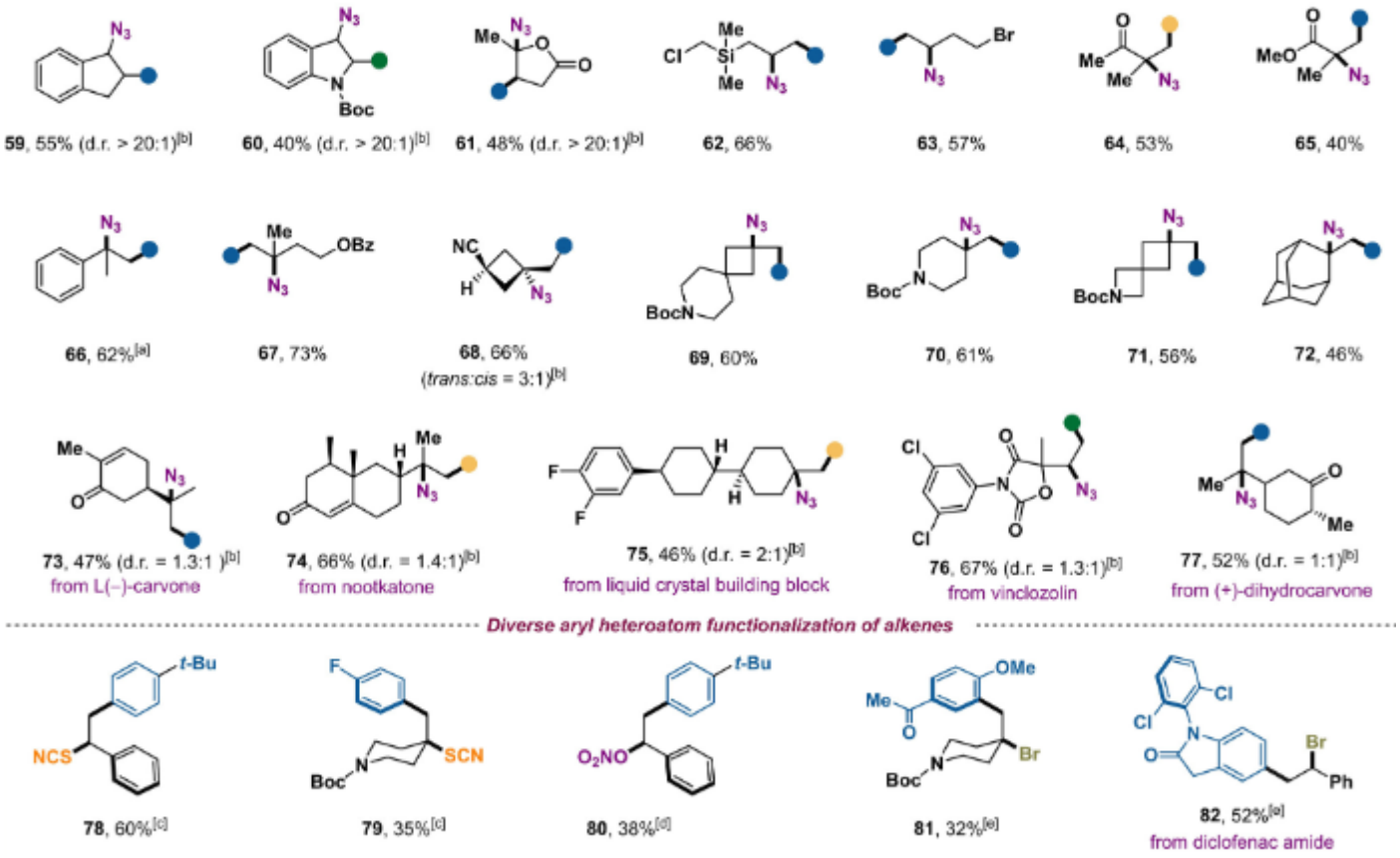

Wu, J. et al., *Angew. Chem. Int. Ed.* **2023**, *62*, e202310978.

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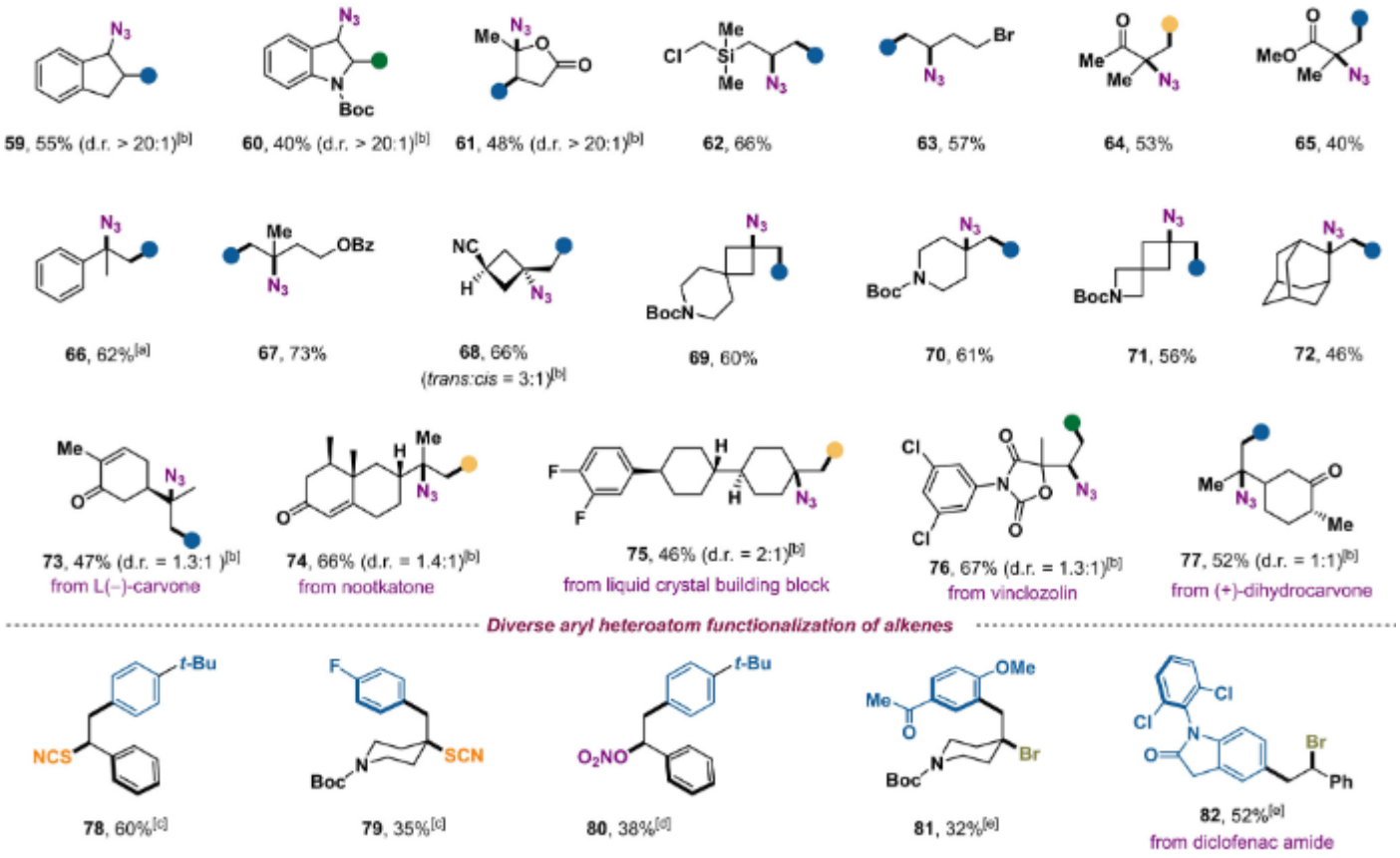

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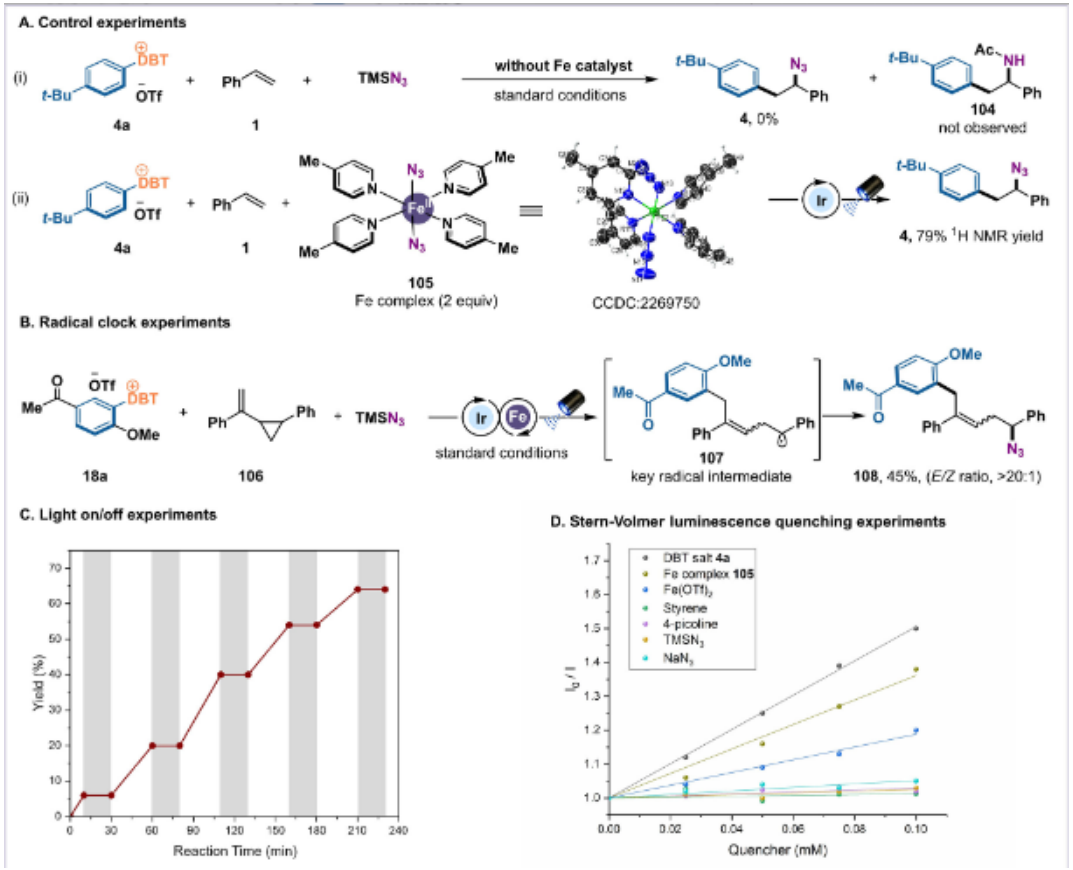

Wu, J. et al., *Angew. Chem. Int. Ed.* **2023**, *62*, e202310978.

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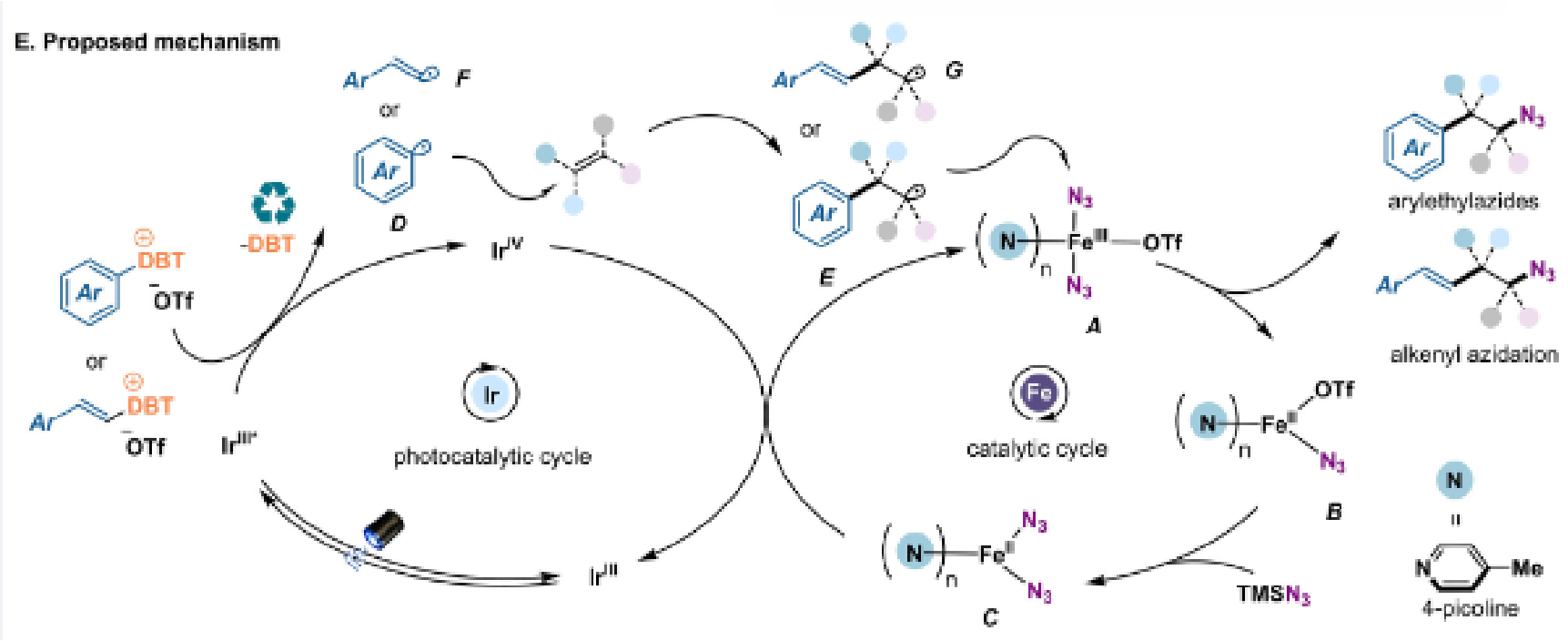
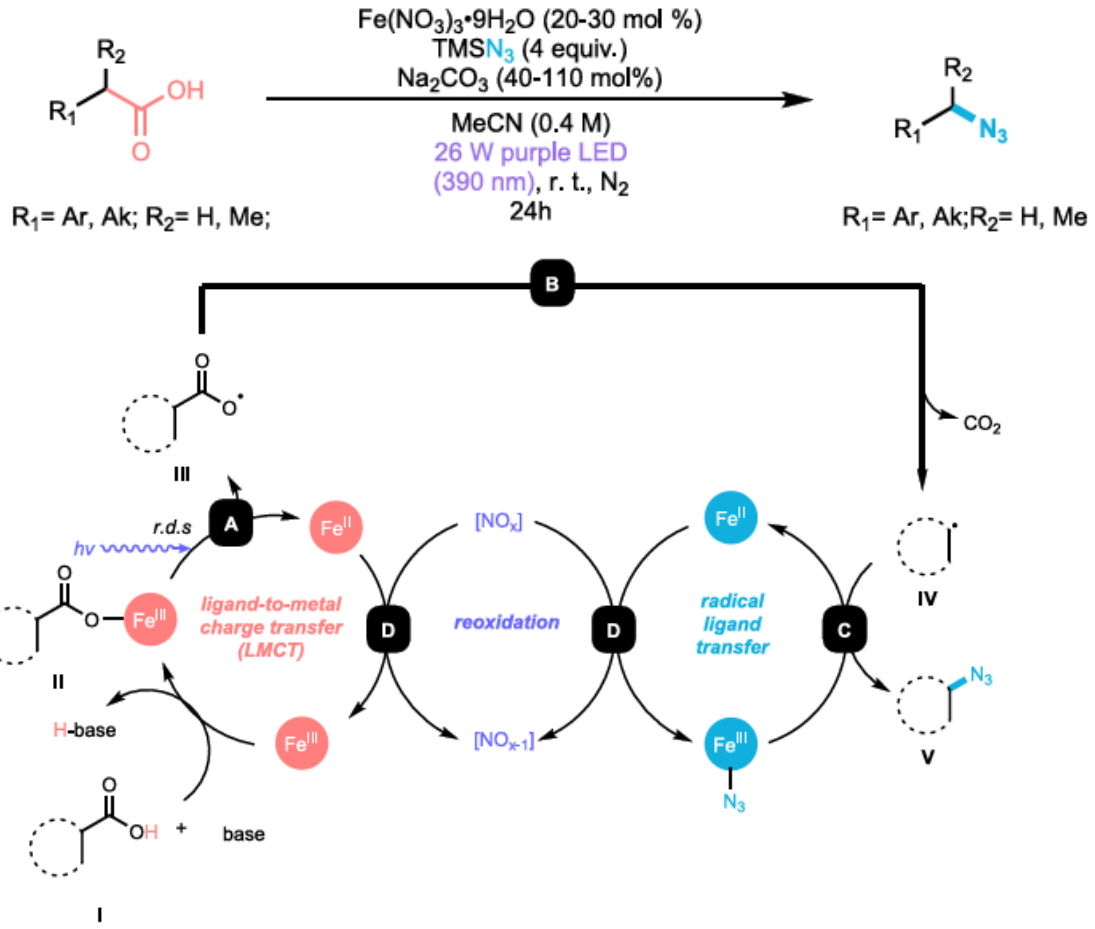


Wu, J. et al., *Angew. Chem. Int. Ed.* **2023**, *62*, e202310978.

外球模式：光/铁共催化脱羧叠氮化



West, J. G. et al., *Chem Catal.* **2023**, *3*, 100603.

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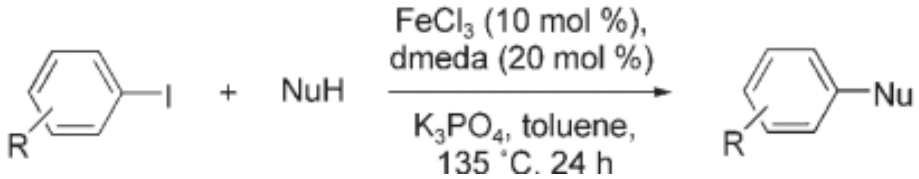
Part 2

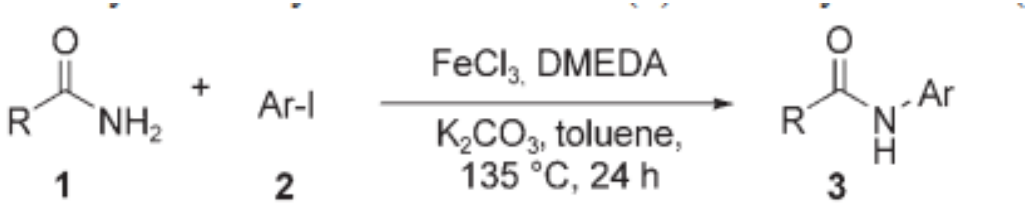
内球模式

同舟共济

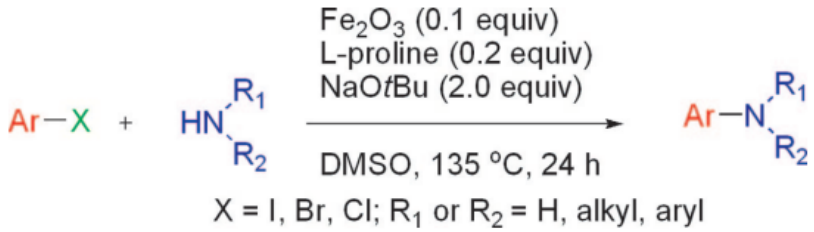
内球模式



Bolm, C. et al., *Angew. Chem. Int. Ed*. **2007**, *46*, 8862.

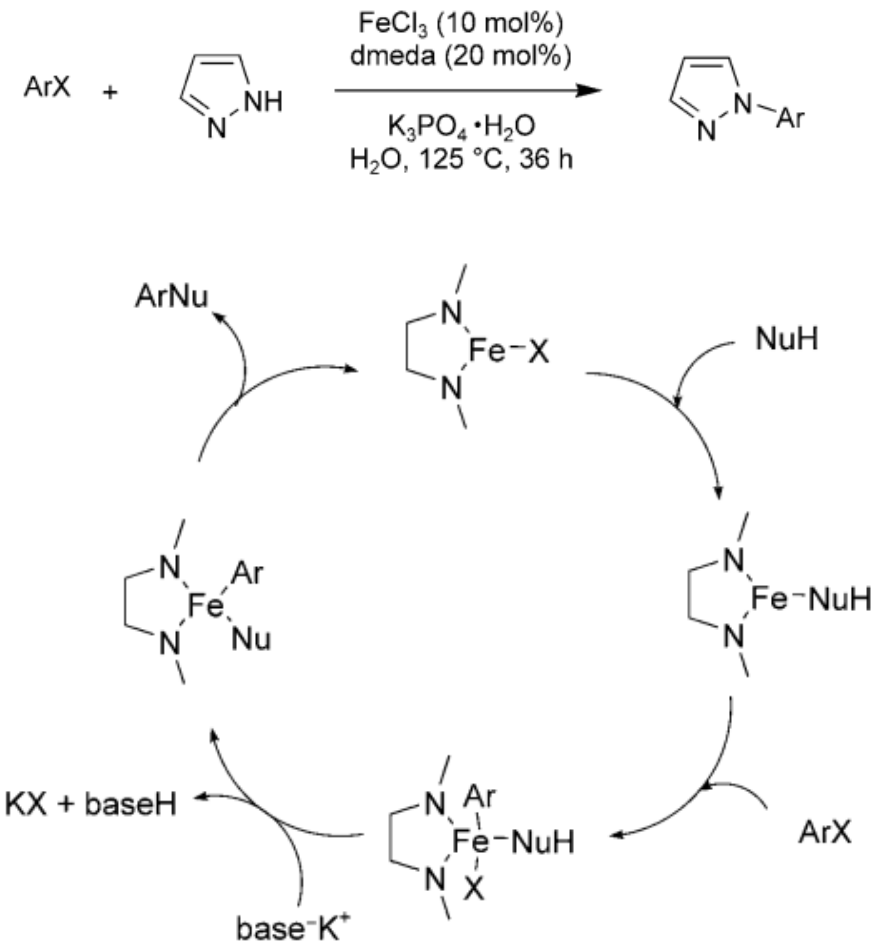


Bolm, C. et al., *Chem. Eur. J*. **2008**, *14*, 3527.



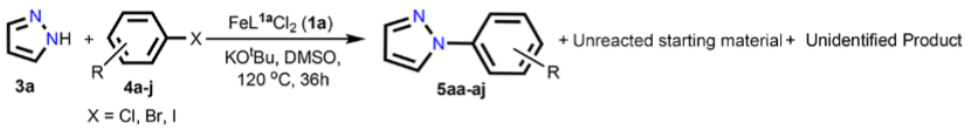
Liu, H. et al., *Org. Lett.* **2008**, *10*, 4513.

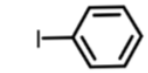
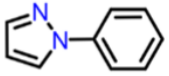
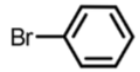
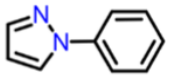
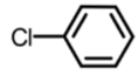
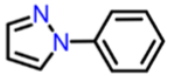
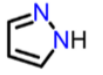
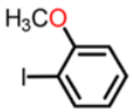
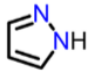
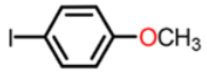
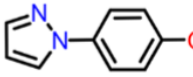
内球模式

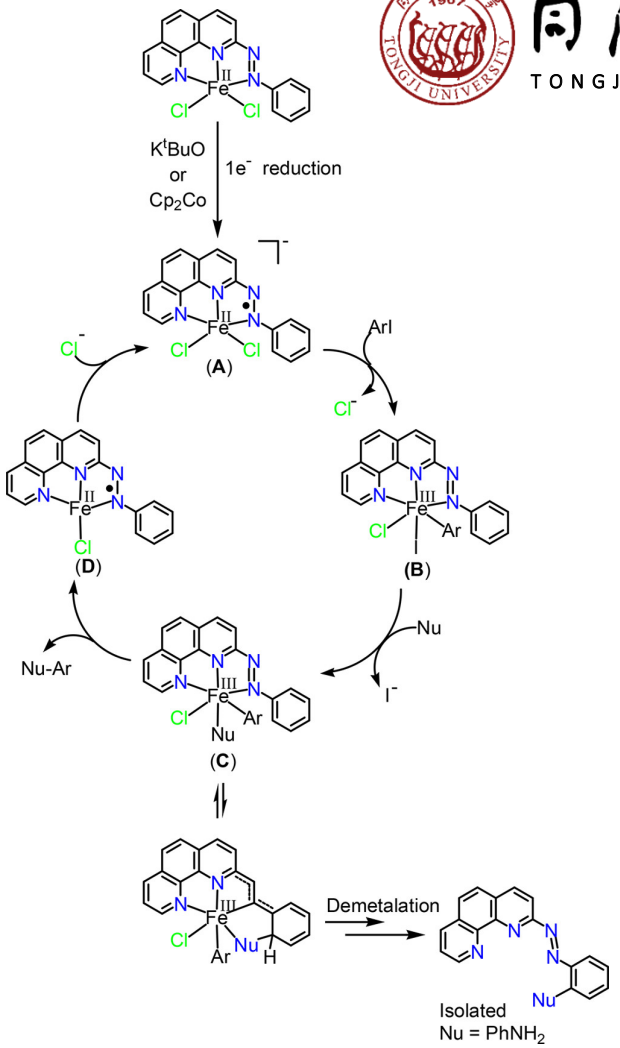


Teo, Y.-C. et al., *Adv. Synth. Catal*. **2009**, *351*, 720.

内球模式

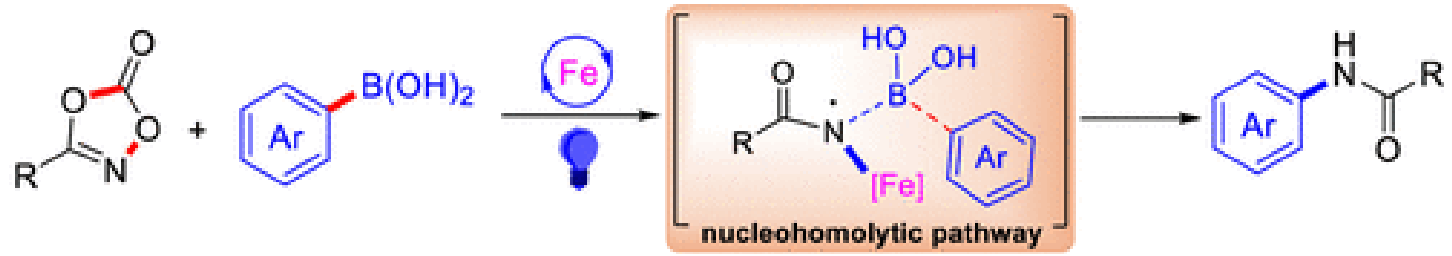


Sl No.	Nucleophile	Iodobenzene	Product		Yield (%)
1				(5aa)	68 (65)
2				(5aa)	40 (35)
3				(5aa)	NR (NR)
4				(5ab)	65 (64)
5				(5ac)	71 (65)



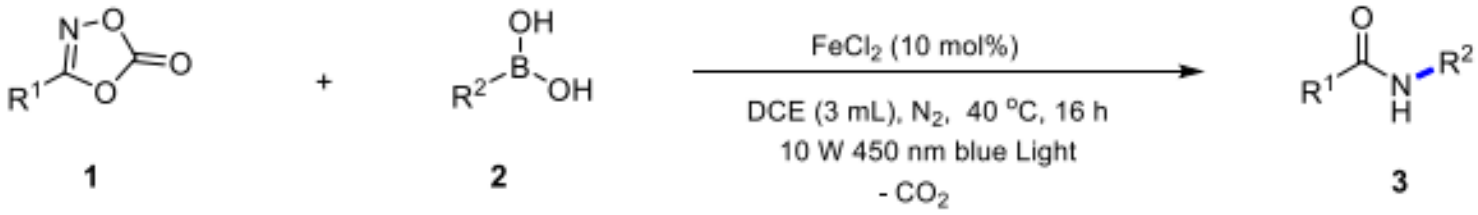
Wong, K.-T. et al., *Org. Lett.* **2010**, *12*, 12.

内球模式：可见光促进铁催化二噁唑酮与芳基硼酸的N-芳基化反应



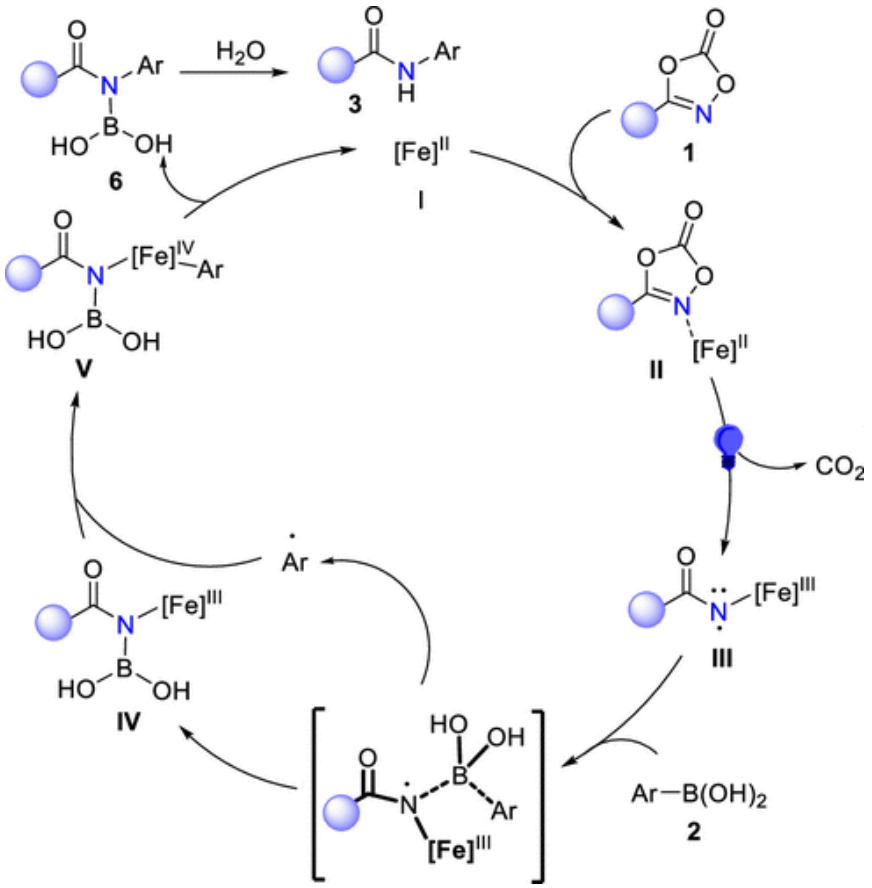
- easily avaliable substrates
- exogenous photosensitizer-free
- broad substrate scope
- first method for *N*-arylation of dioxazolones with arylboronic acids by iron-catalysis

反应条件：



Bao, M. et al., *ACS Catal.* **2021**, *11*, 13955.

内球模式：可见光促进铁催化二噁唑酮与芳基硼酸的N-芳基化反应



Bao, M. et al., *ACS Catal*. **2021**, *11*, 13955.

内球模式：光促进铁催化芳基溴化物和胺之间的C–N偶联反应

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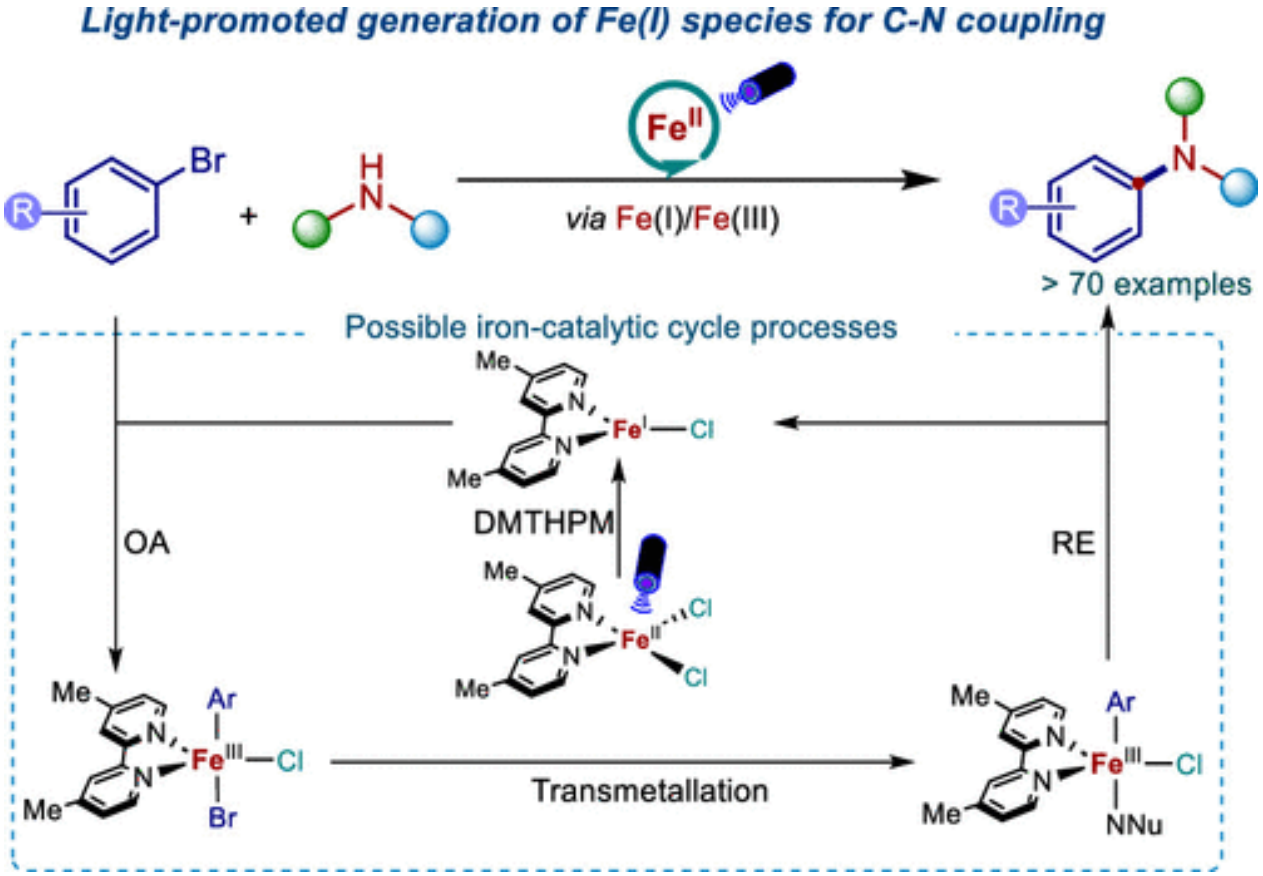
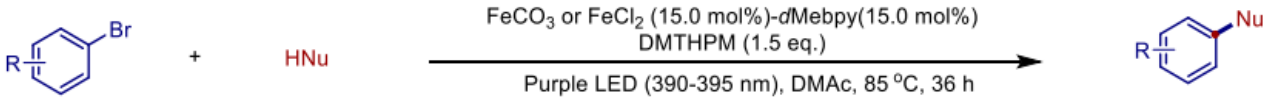
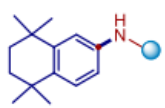
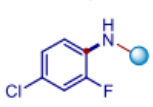


Xue, D. et al., *ACS Catal*. **2024**, *14*, 4968.

内球模式：光促进铁催化芳基溴化物和胺之间的C–N偶联反应

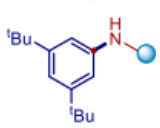



21, 70%



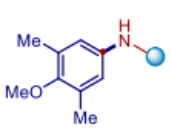
22, 78%

23, 88%

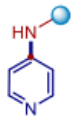


24, 90%

25, 76%

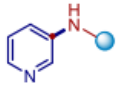


26, 83%

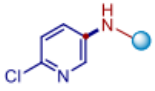


27, 81%

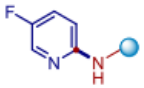
28, 84%



29, 85%



30, 80%



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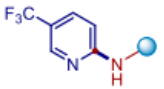
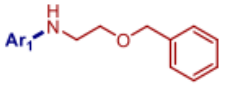


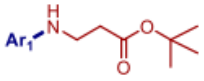
32, 85%



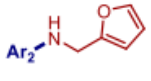
46, 85%[b]

47, 70%[b]

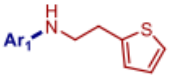
48, 89%[b]



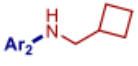
49, 65%[b]



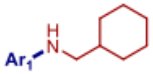
50, 78%[b]



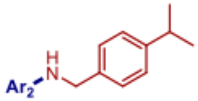
51, 86%[b]



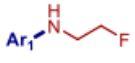
52, 82%



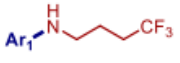
53, 69%[b]



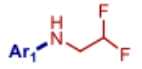
54, 69%



55, 87%[b]



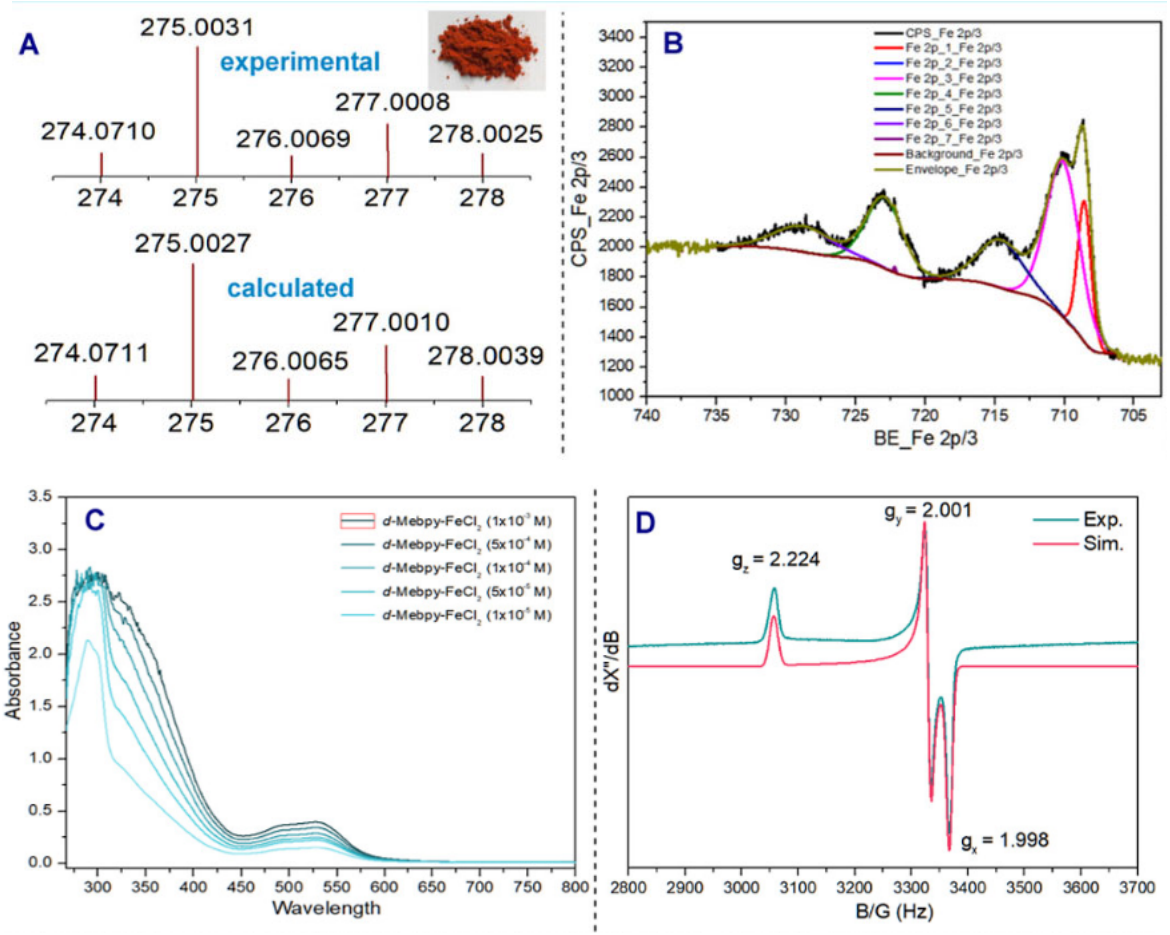
56, 73%[b]



57, 43%[b]

Xue, D. et al., *ACS Catal*. **2024**, *14*, 4968.

内球模式：光促进铁催化芳基溴化物和胺之间的C–N偶联反应

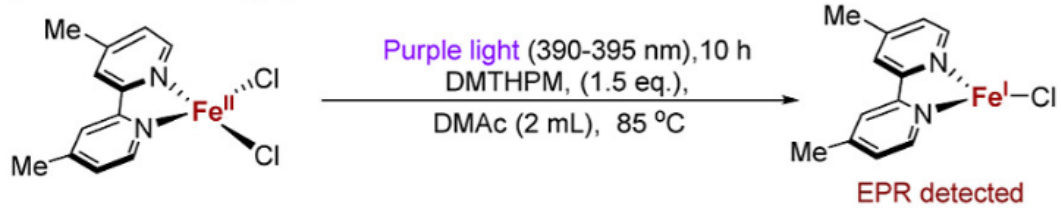


Xue, D. et al., *ACS Catal*. **2024**, *14*, 4968.

内球模式：光促进铁催化芳基溴化物和胺之间的C–N偶联反应

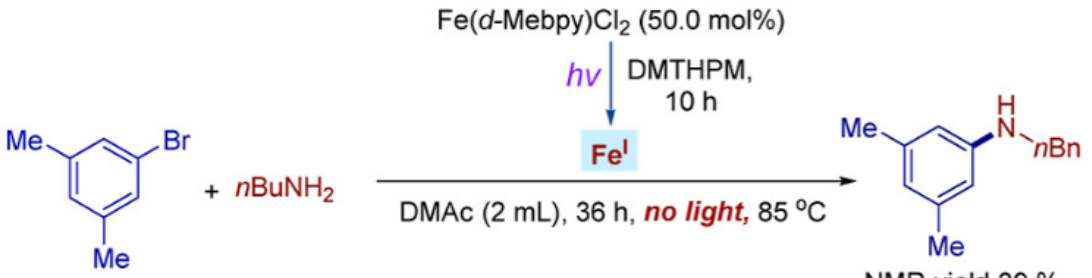
E Amination of aryl halide catalyzed by Fe(I) complex

1) EPR detected Fe(I) species



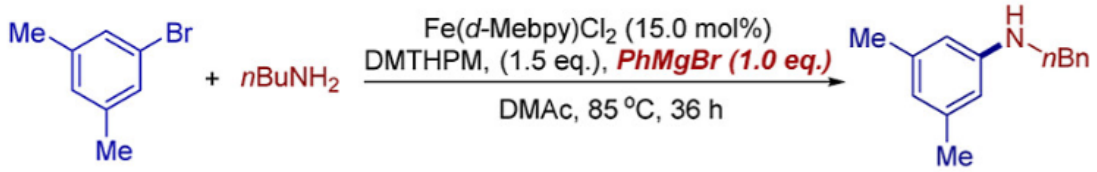
EPR detected

2) Amination of aryl halide catalyzed by Fe(I) complex via light irradiation



NMR yield 39 %

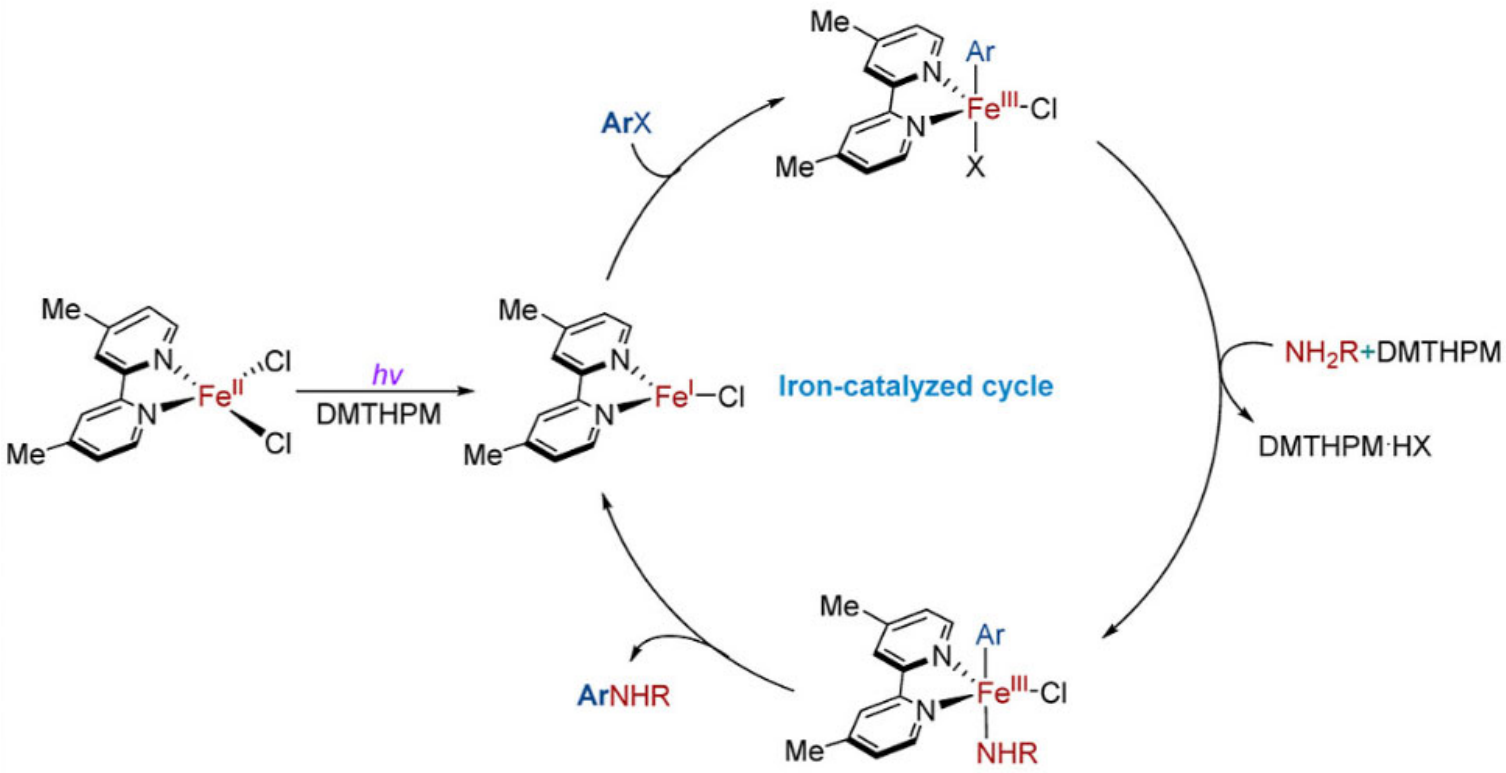
3) Amination of aryl halide catalyzed by Fe(I) complex using PhMgBr as reducing agent



NMR yield 26 %

Xue, D. et al., *ACS Catal*. **2024**, *14*, 4968.

内球模式：光促进铁催化芳基溴化物和胺之间的C–N偶联反应



Xue, D. et al., *ACS Catal*. **2024**, *14*, 4968.

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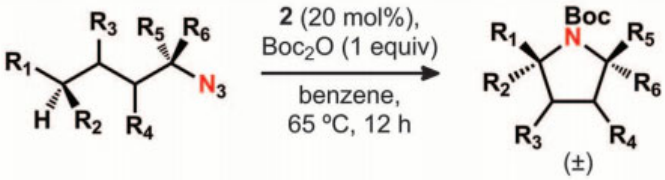
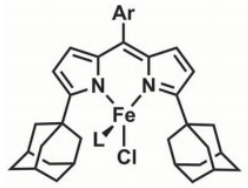
Part 3

铁氮宾中间体

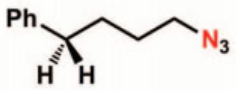
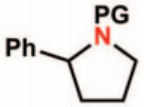
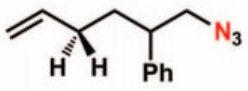
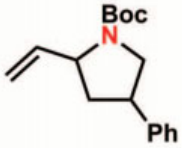
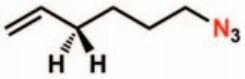
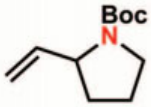
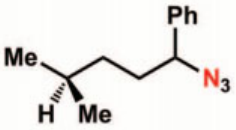
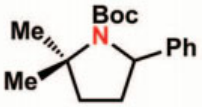
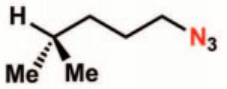
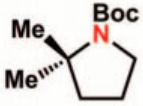
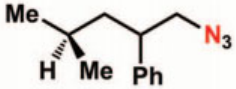
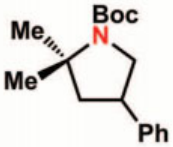
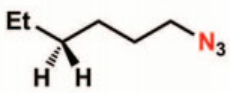
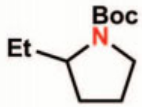
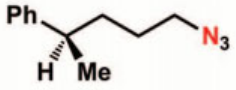
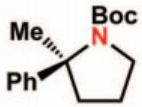
同舟共济

铁氮宾中间体参与



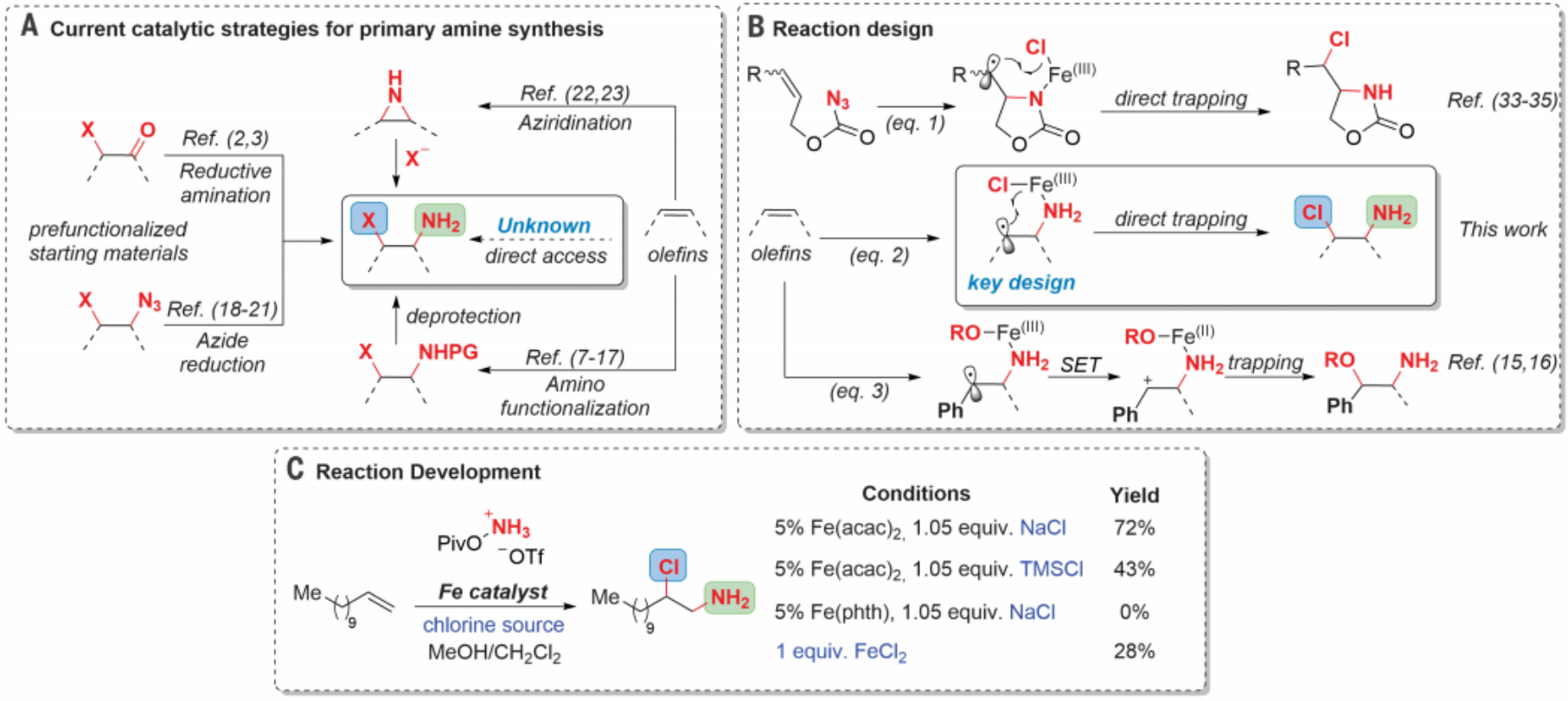


Ar = (**1**) Mes
(**2**) 2,6-$Cl_2C_6H_3$

Entry	Azide	Pyrrolidine	Yield (%)*	Entry	Azide	Pyrrolidine	Yield (%)*
1			98†§ (PG = Fmoc) 93†§ 57‡§ (PG = Boc)	10			66 1:5:1.0 dr
2			72‡§	11			70
3			60§ 49‡§	12			98
4			19‡§	13			75‡ 93% ee

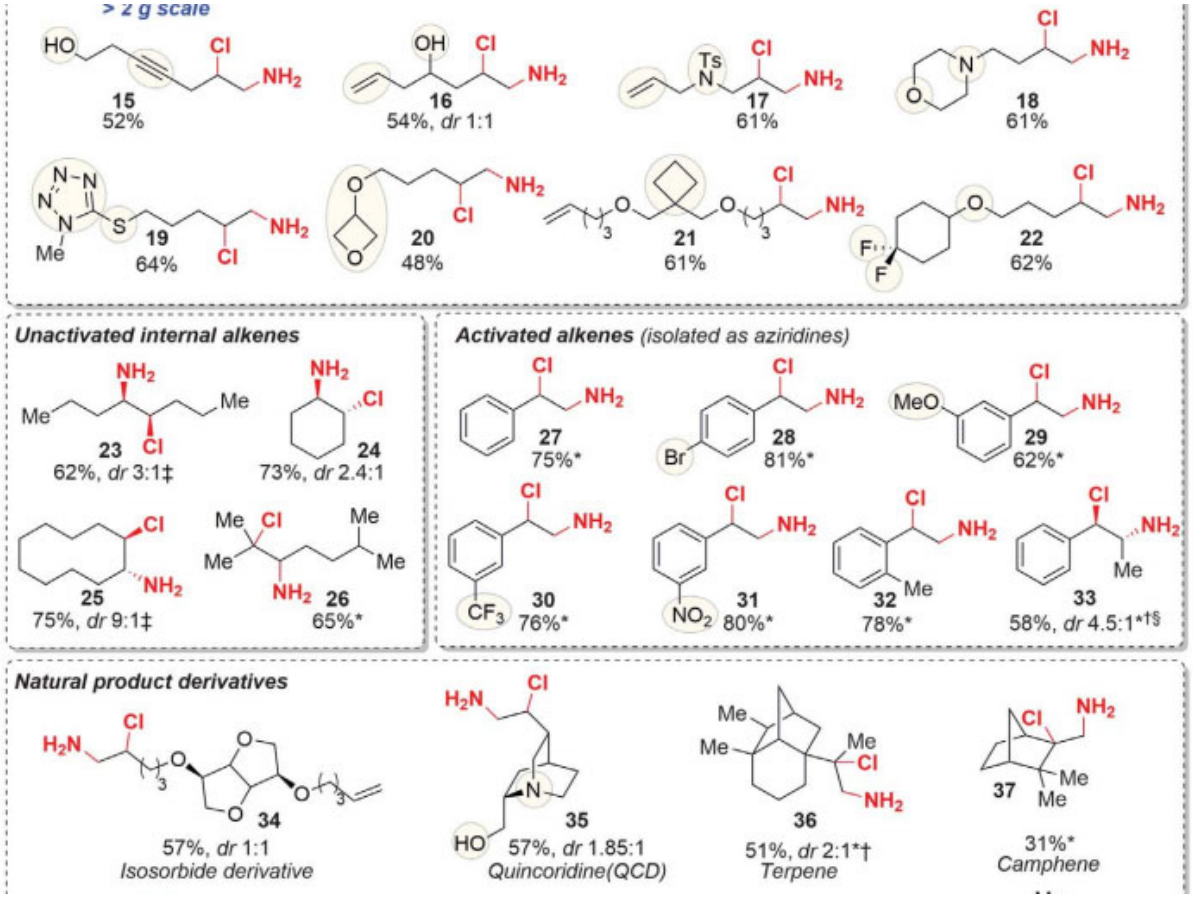
Betley, T. A. et al., *Science* **2013**, *340*, 591.

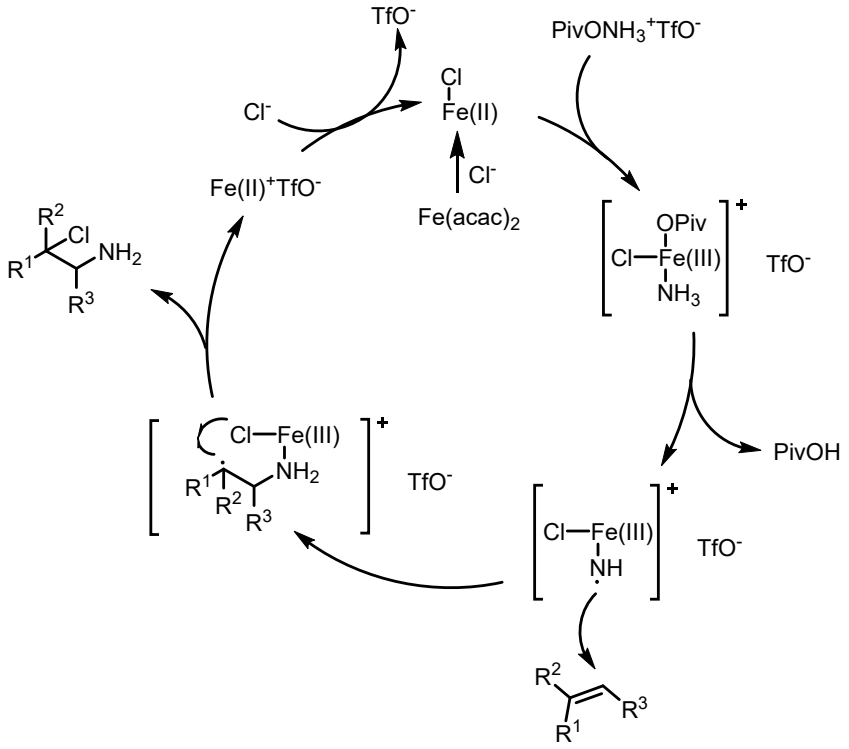
铁氮宾中间体参与



Morandi, B. et al., *Science* **2018**, *362*, 434.

铁氮宾中间体参与

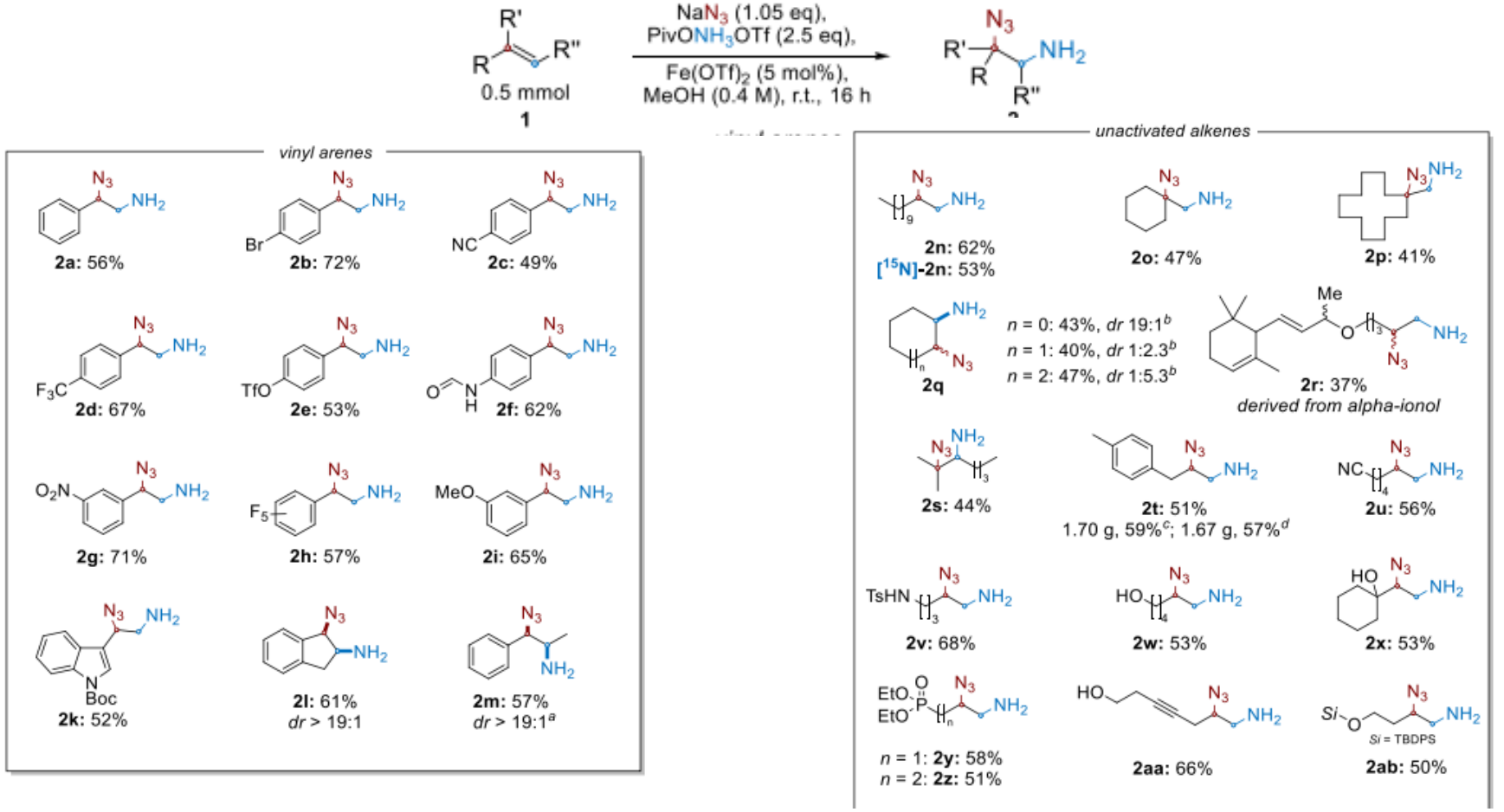




同舟共济

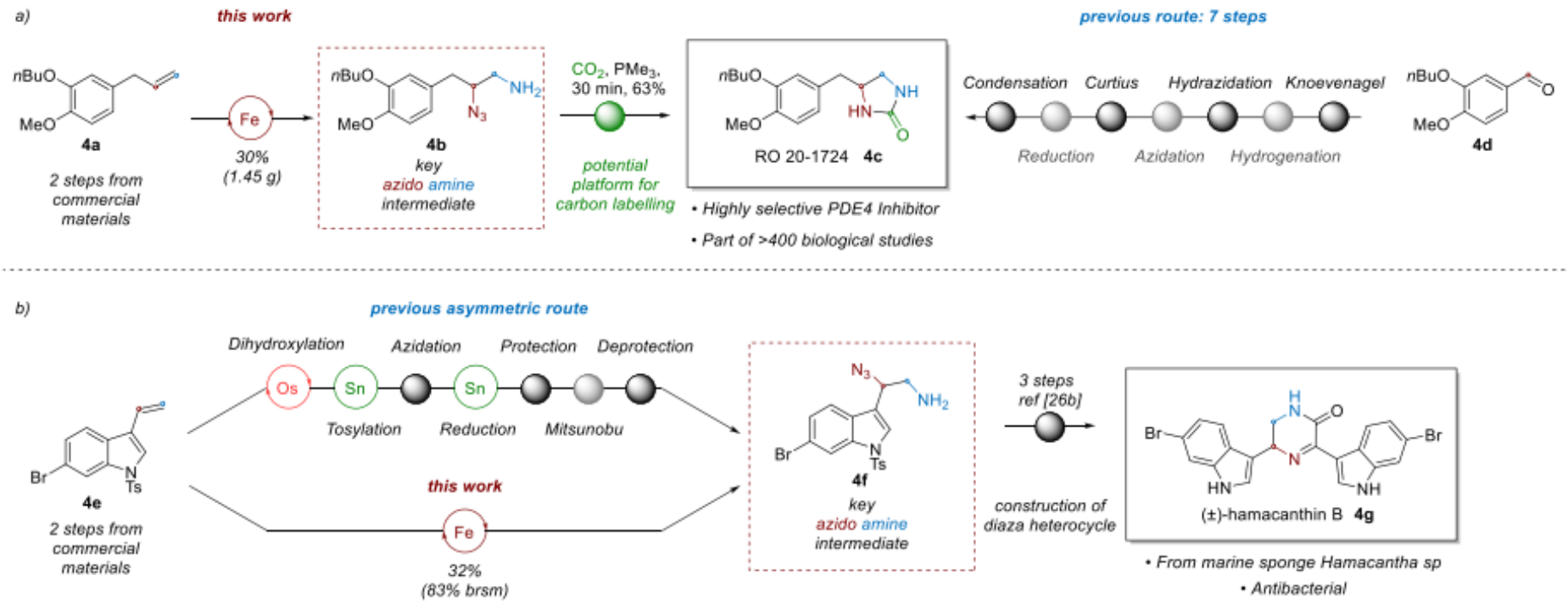
Morandi, B. et al., *Science* **2018**, *362*, 434.

铁氮宾中间体参与



Morandi, B. et al., *J. Am. Chem. Soc.* **2020**, *142*, 21548.

铁氮宾中间体参与



Morandi, B. et al., *J. Am. Chem. Soc.* **2020**, *142*, 21548.

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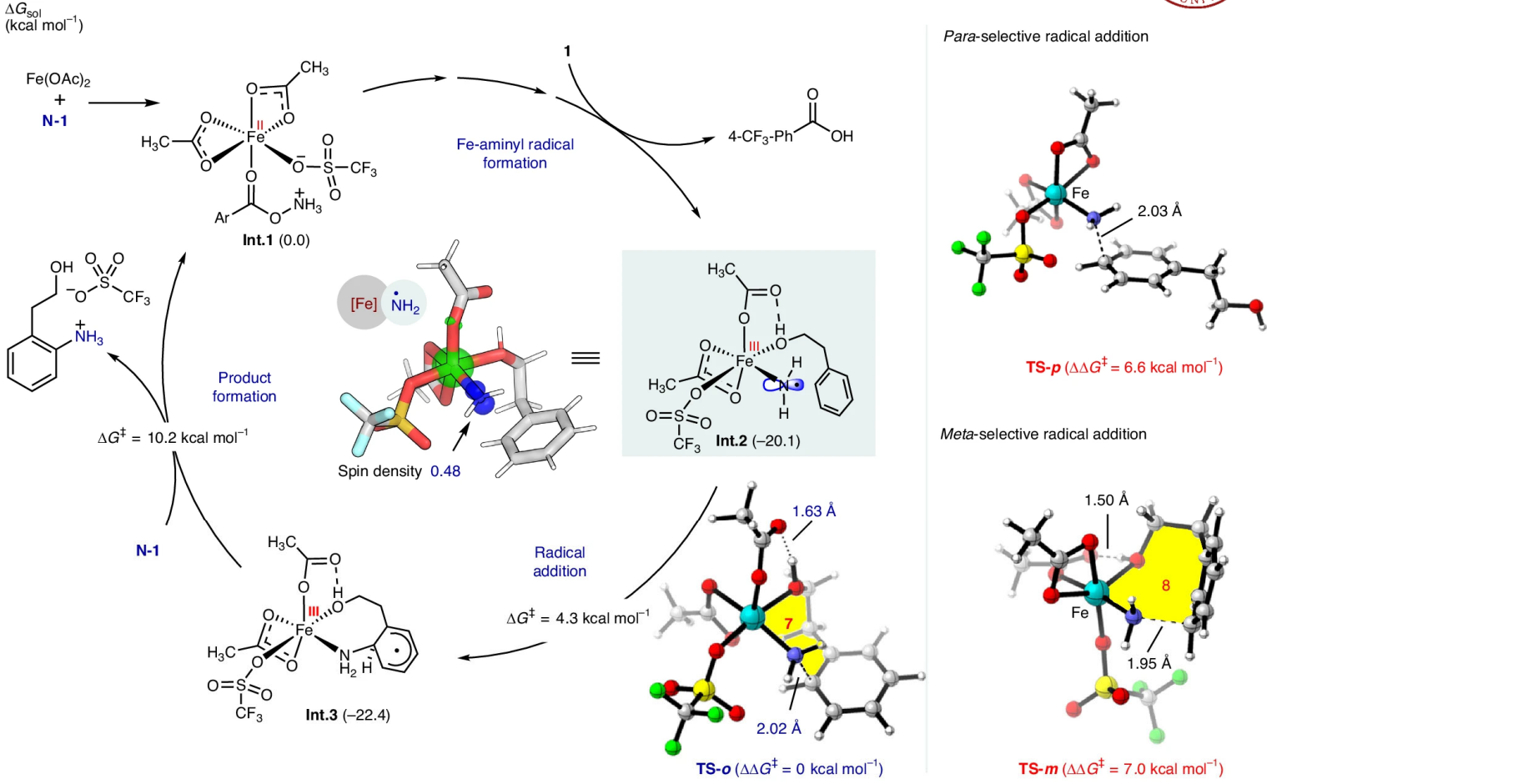
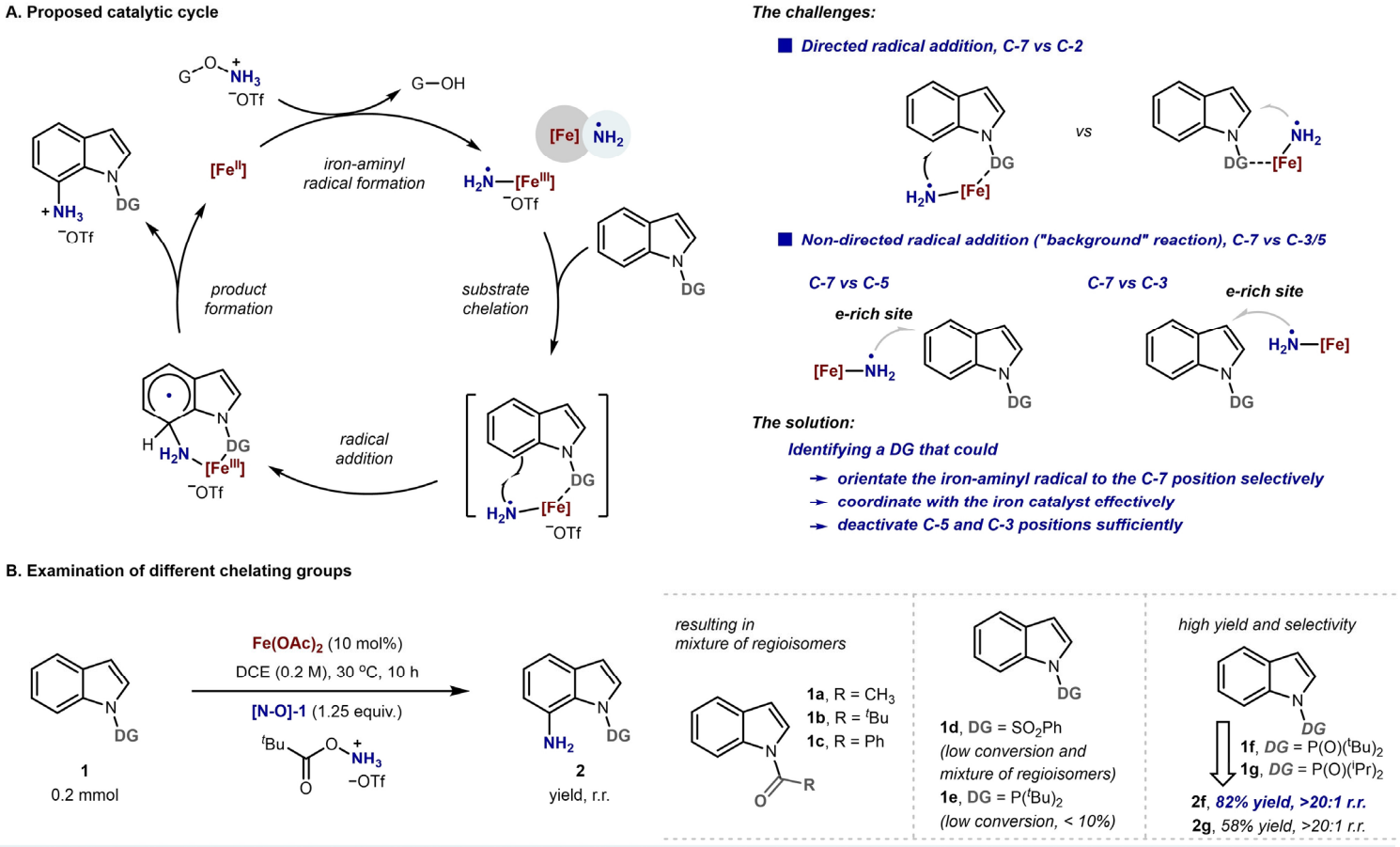


Wang, F. et al., *Nat. Catal.* **2019**, *7*, 636.

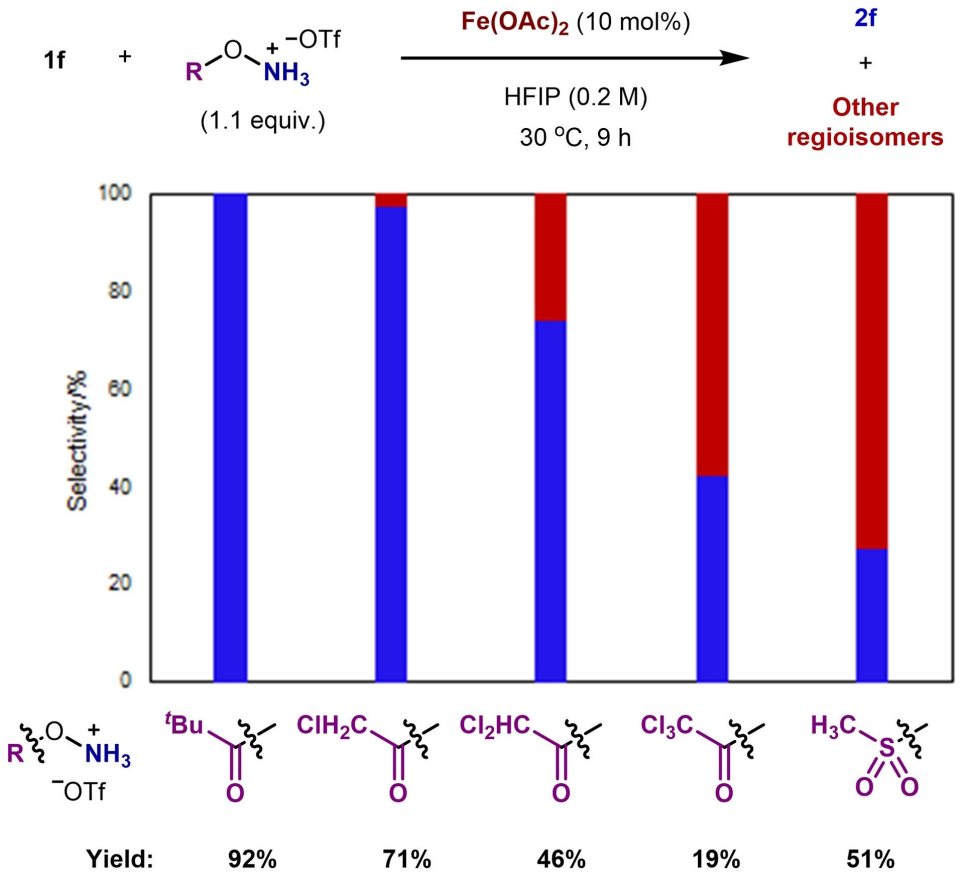
铁氮宾中间体参与



TBPO不仅能够有效地与铁-氨自由基配位，导向C-7位的选择性加成，也能利用其强吸电子特性降低吲哚的电子云密度，减少非导向芳香自由基取代反应的发生。

Wang, F. et al., *Angew. Chem. Int. Ed.* **2024**, e202412103.

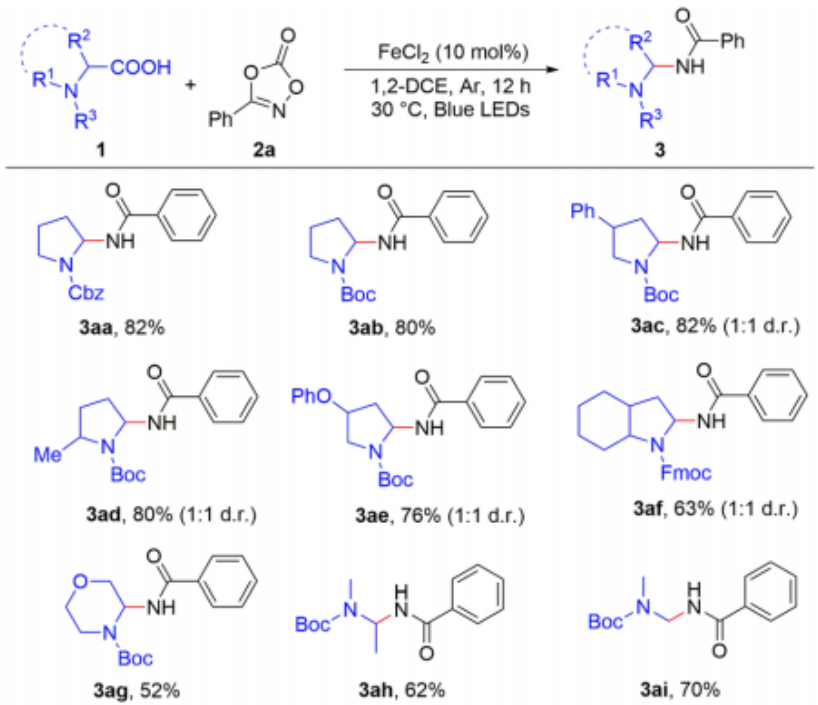
铁氮宾中间体参与

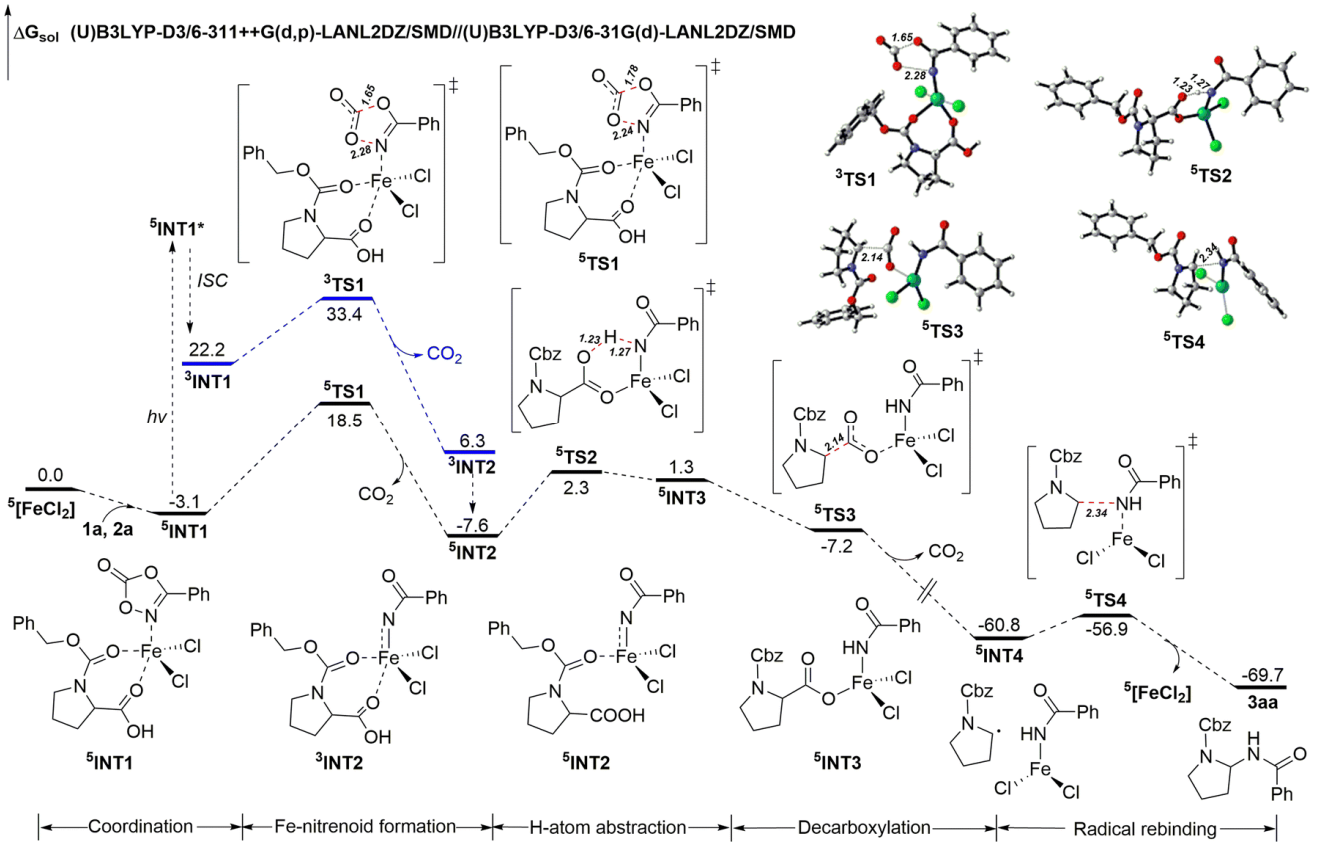


胺化试剂离去基团共轭酸（ROH）的酸性（pKa）与反应的区域选择性之间存在明显的相关性，即：ROH的pKa较大时，反应的区域选择性好；ROH的pKa较小时，反应的区域选择性差。

Wang, F. et al., *Angew. Chem. Int. Ed.* **2024**, e202412103 .

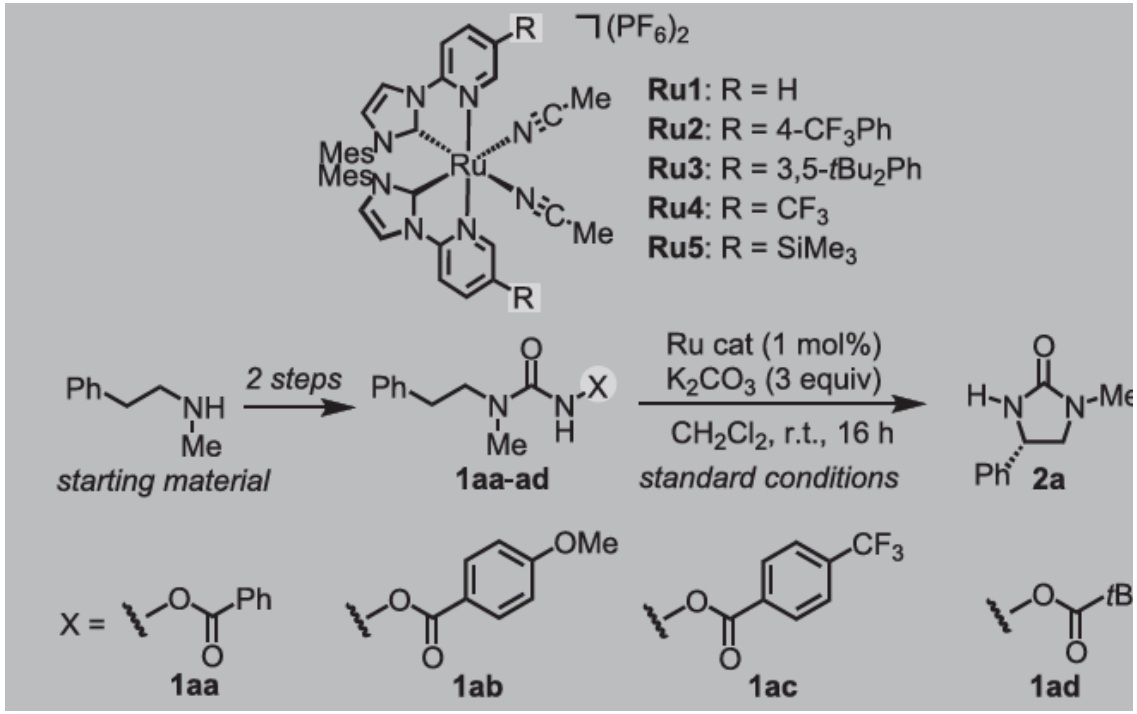
铁氮宾中间体参与

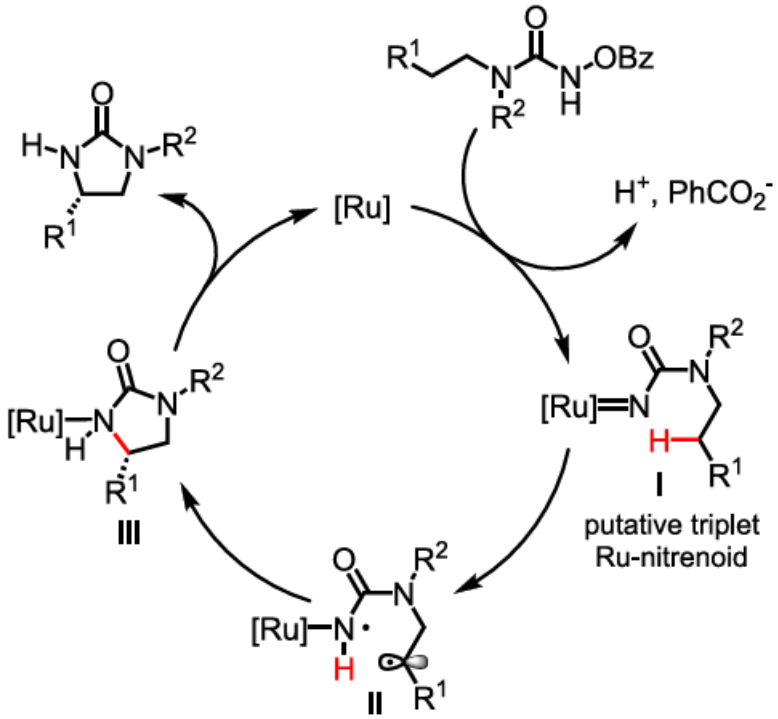




Bao, X.-G. et al., *Chem. Commun.*, **2023**, *59*, 752.

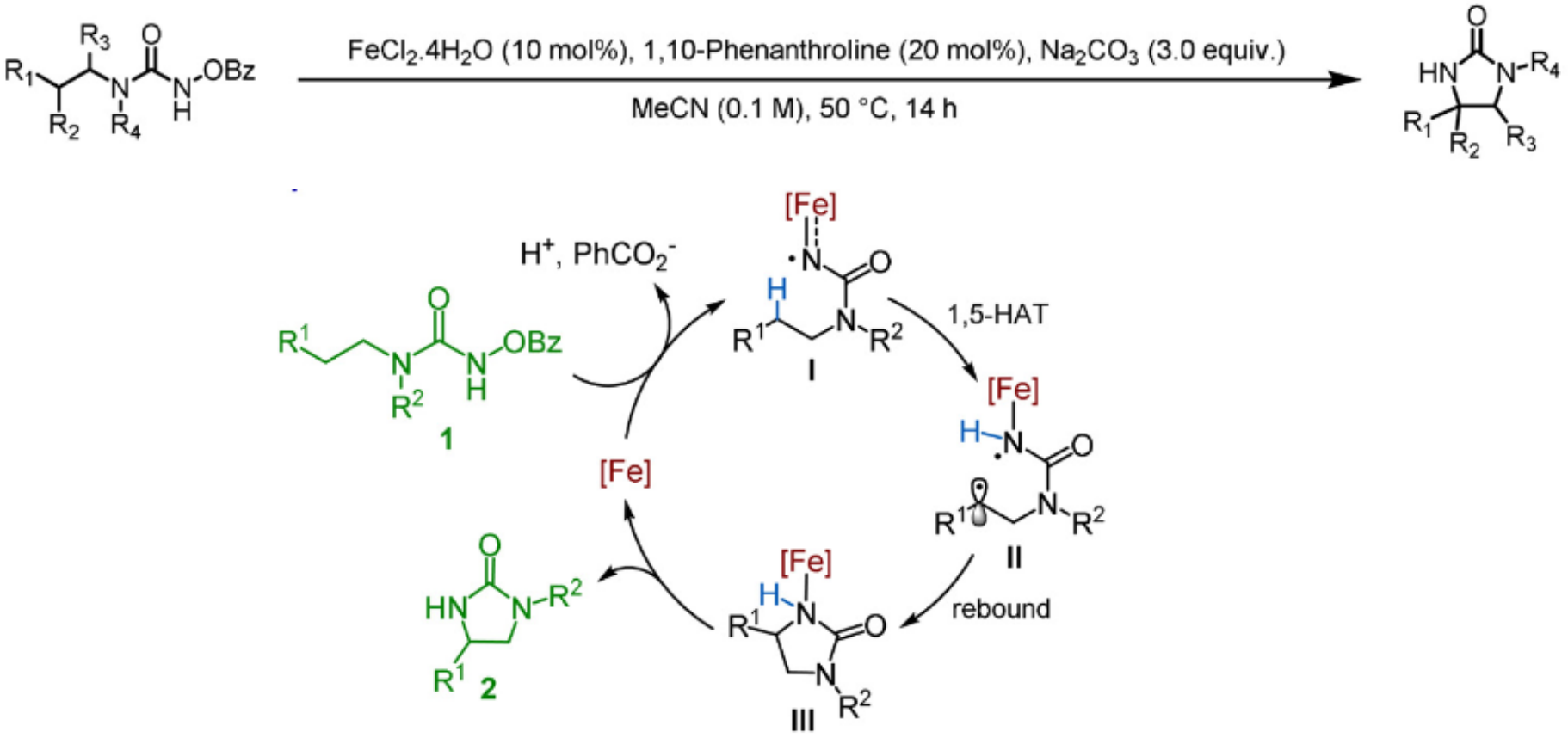
铁氮宾中间体参与





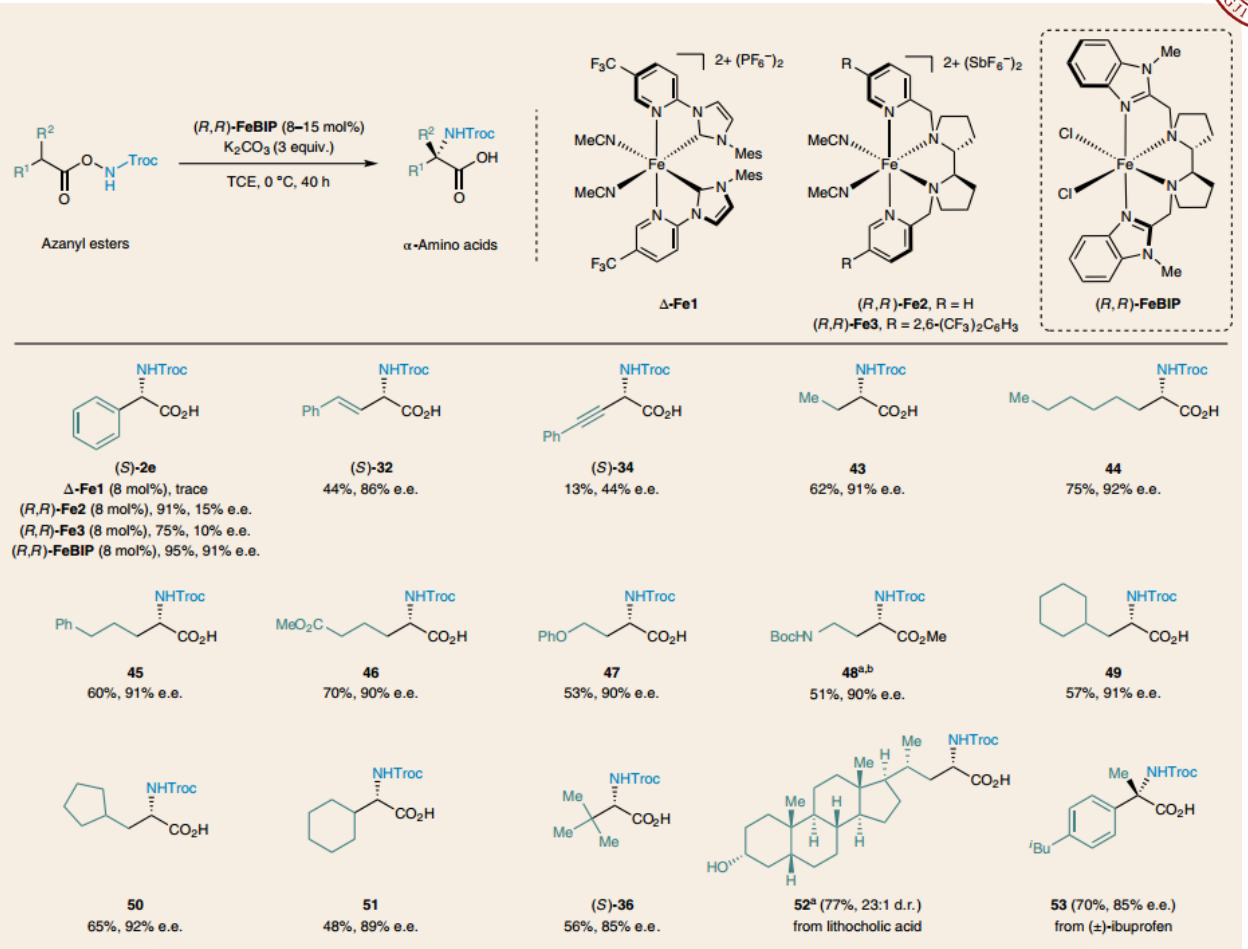
Meggers, E. et al., *Chem*, **2020**, *6*, 2024.

铁氮宾中间体参与



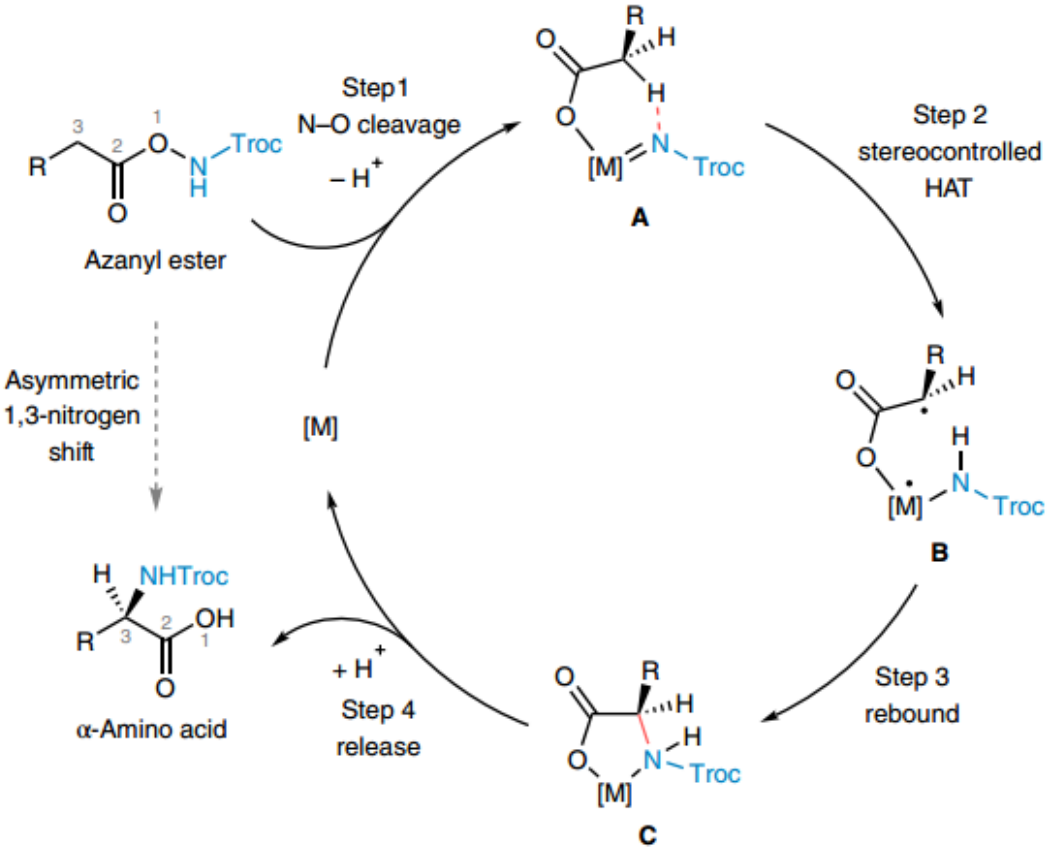
Meggers, E. et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 6314.

铁氮宾中间体参与



Meggers, E. et al., *Nat. Chem*. **2022**, *14*, 566.

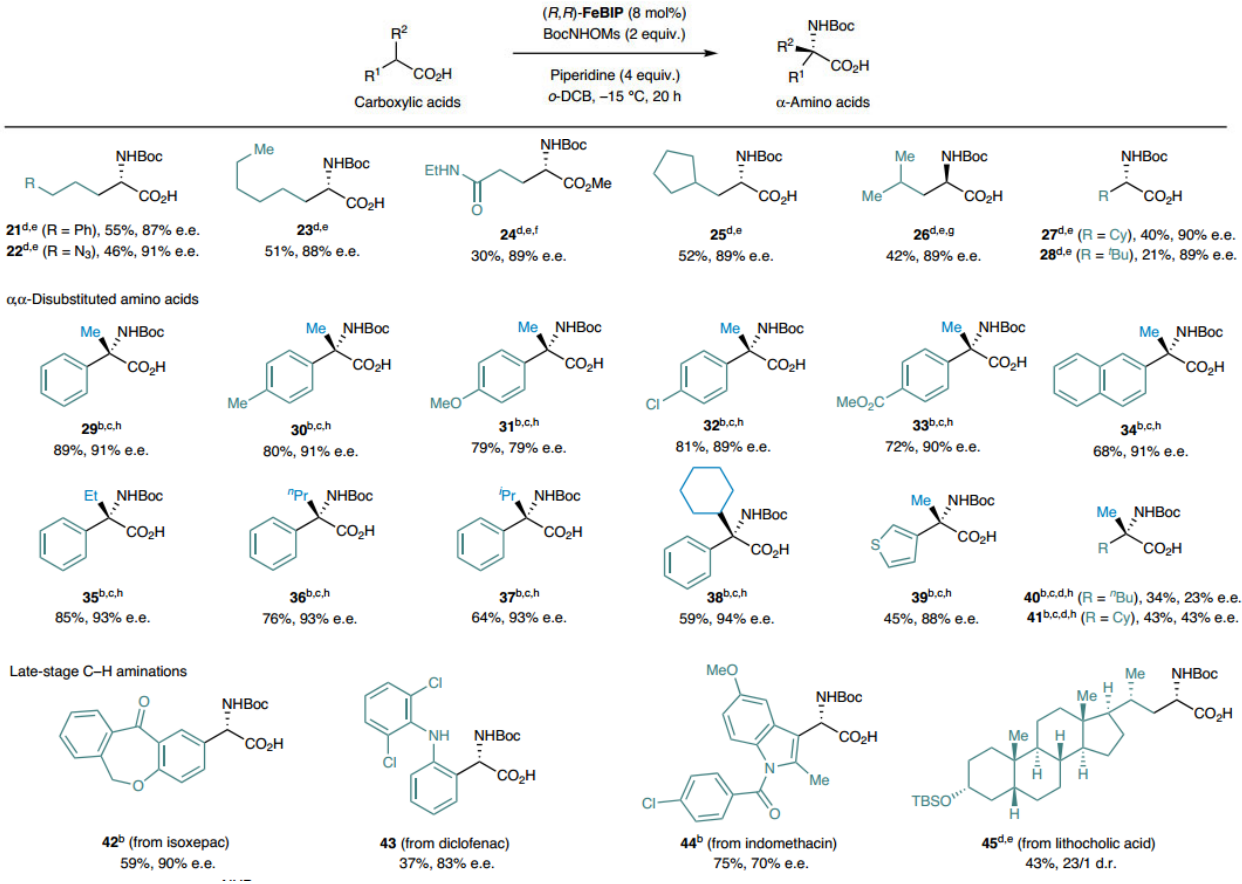
铁氮宾中间体参与



- 本文报道了一种通过1,3-氮迁移的途径，经济实用合成立体选择性α-氨基酸的方案
- 采用丰富的和容易获得的羧酸作为起始原料，首先连接到氮化试剂，然后借助钌或铁催化实现对映选择性的C(sp3)-H胺化
- 该方法具有广泛的应用范围，可以快速获得具有芳基、烯丙基、丙炔和烷基侧链的光学活性α-氨基酸，也可以对含羧酸的药物和天然产物进行后期胺化的立体控制

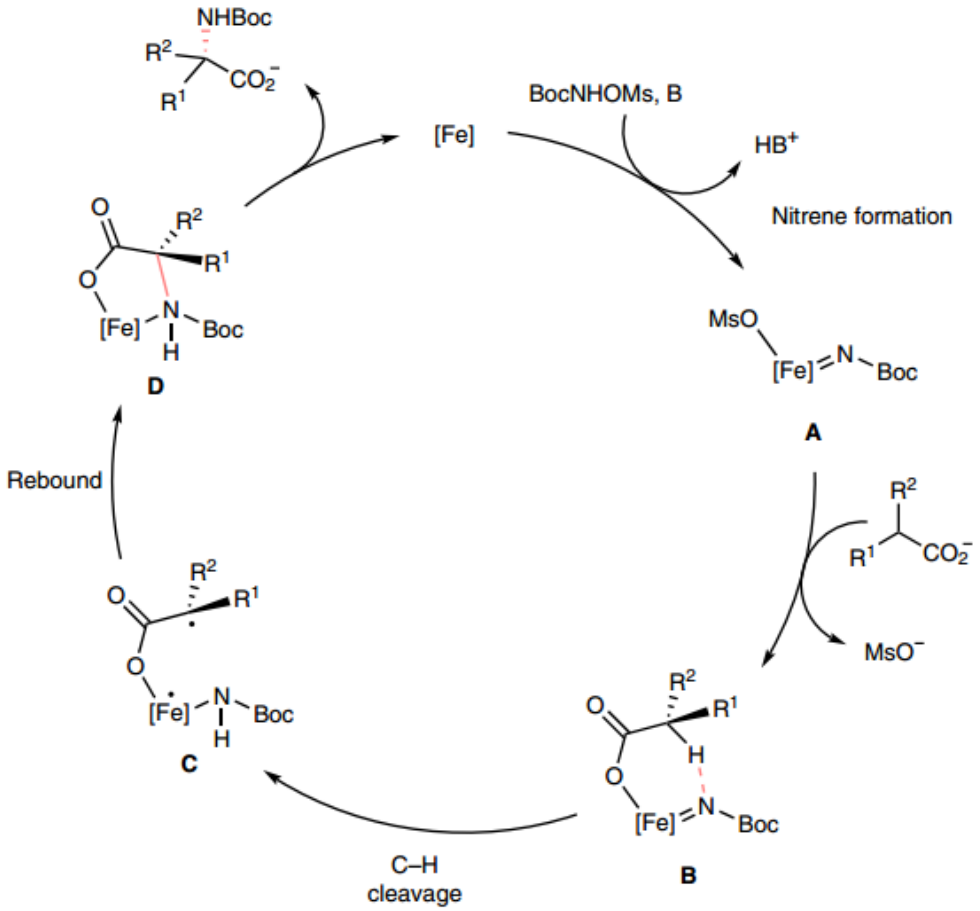
Meggers, E. et al., *Nat. Chem.* **2022**, *14*, 566.

铁氮宾中间体参与



Meggers, E. et al., *Nat. Synth*. **2023**, *2*, 645.

铁氮宾中间体参与



Meggers, E. et al., *Nat. Synth*. **2023**, *2*, 645.

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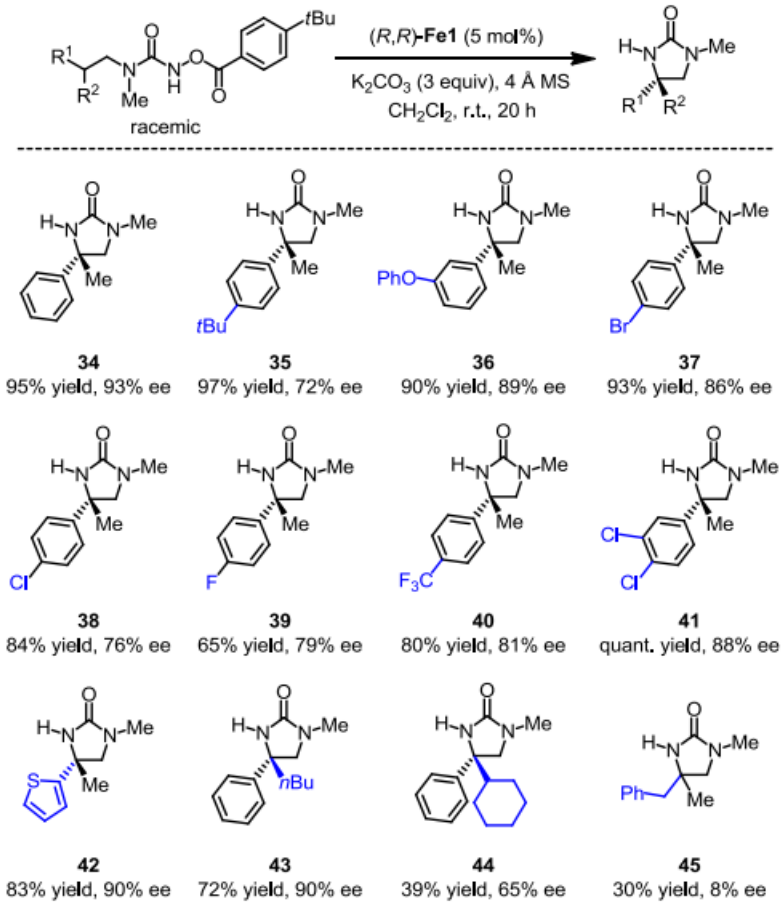

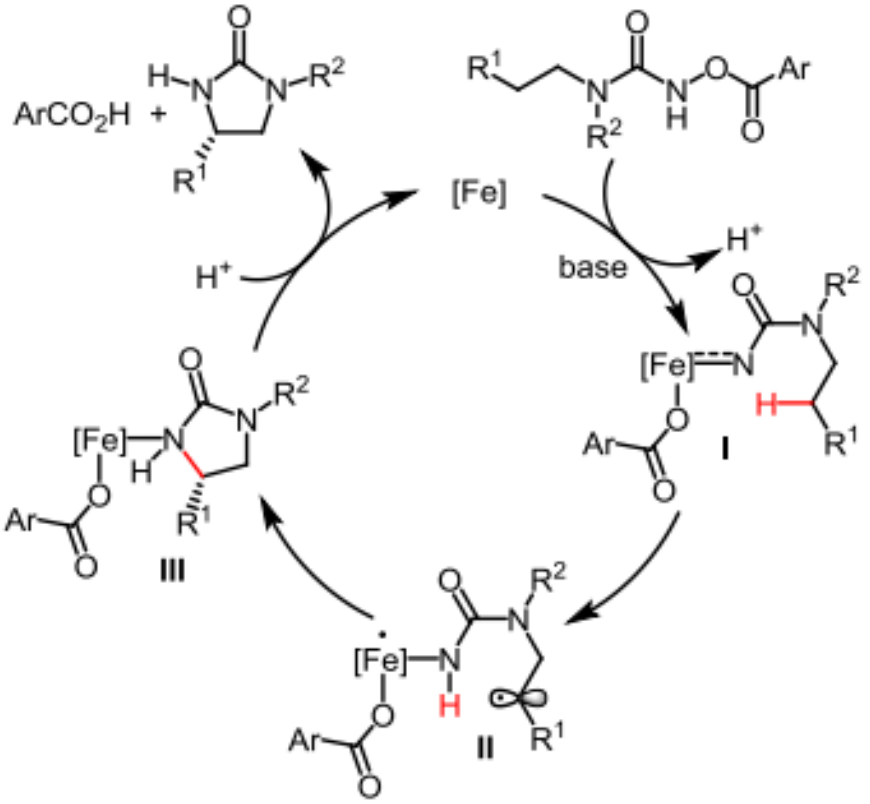

Meggers, E. et al., *Chin. J. Chem.* **2023**, *41*, 2065.

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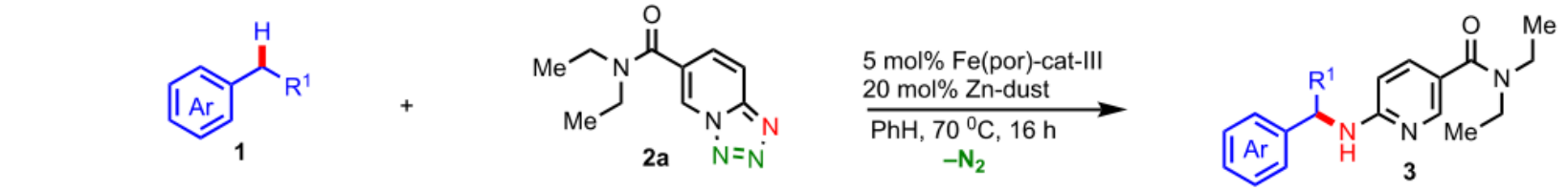
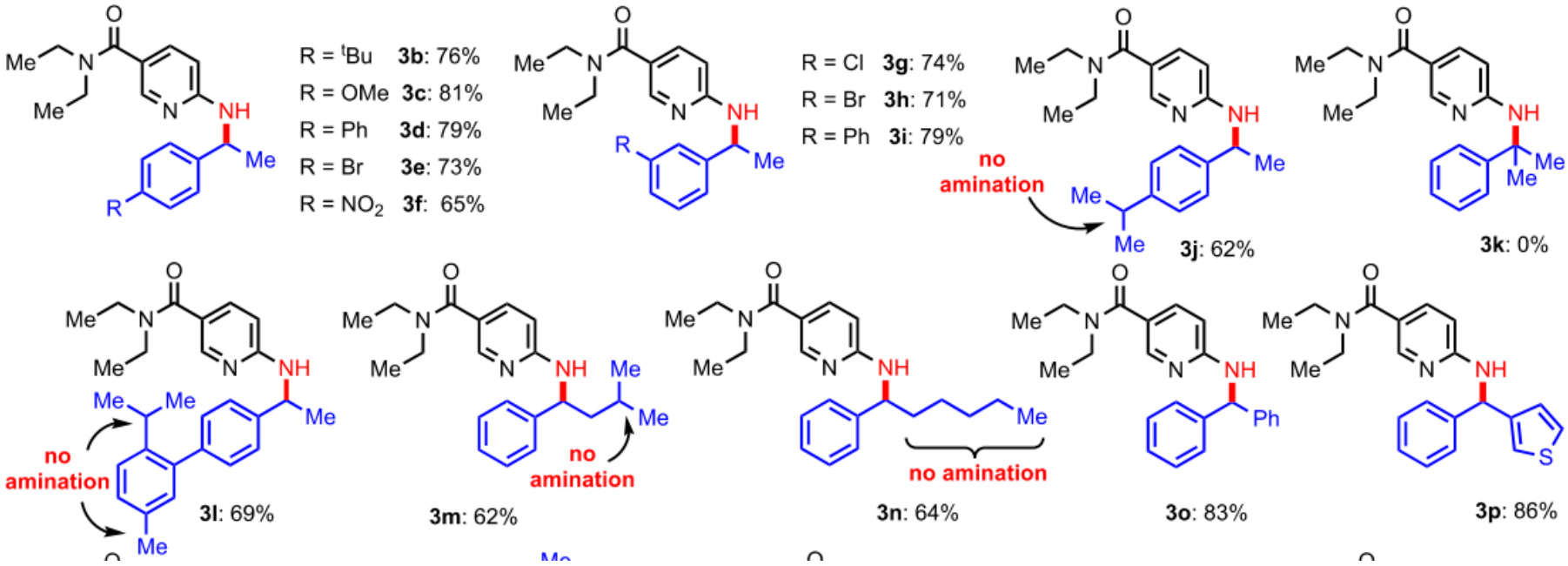
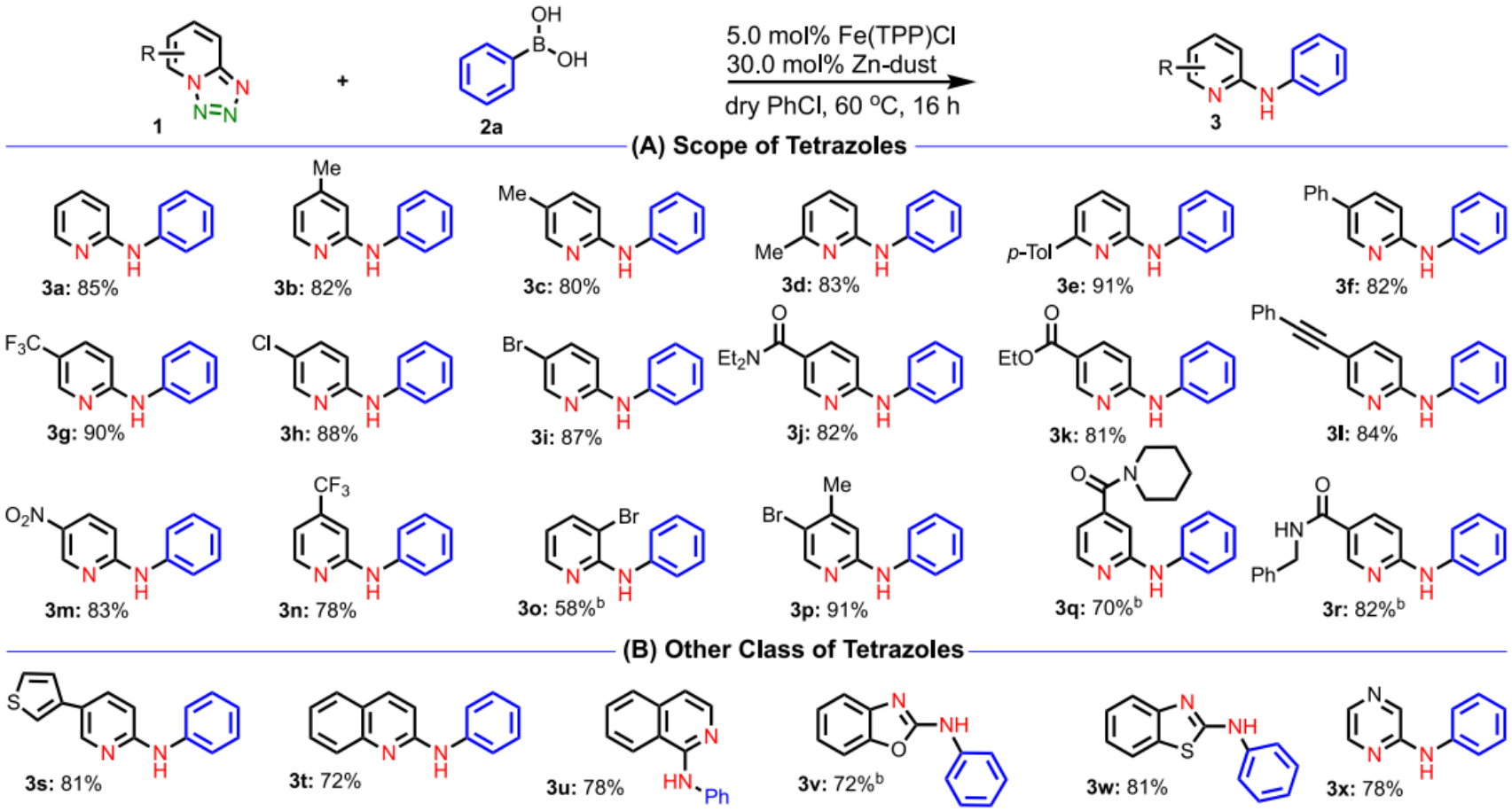




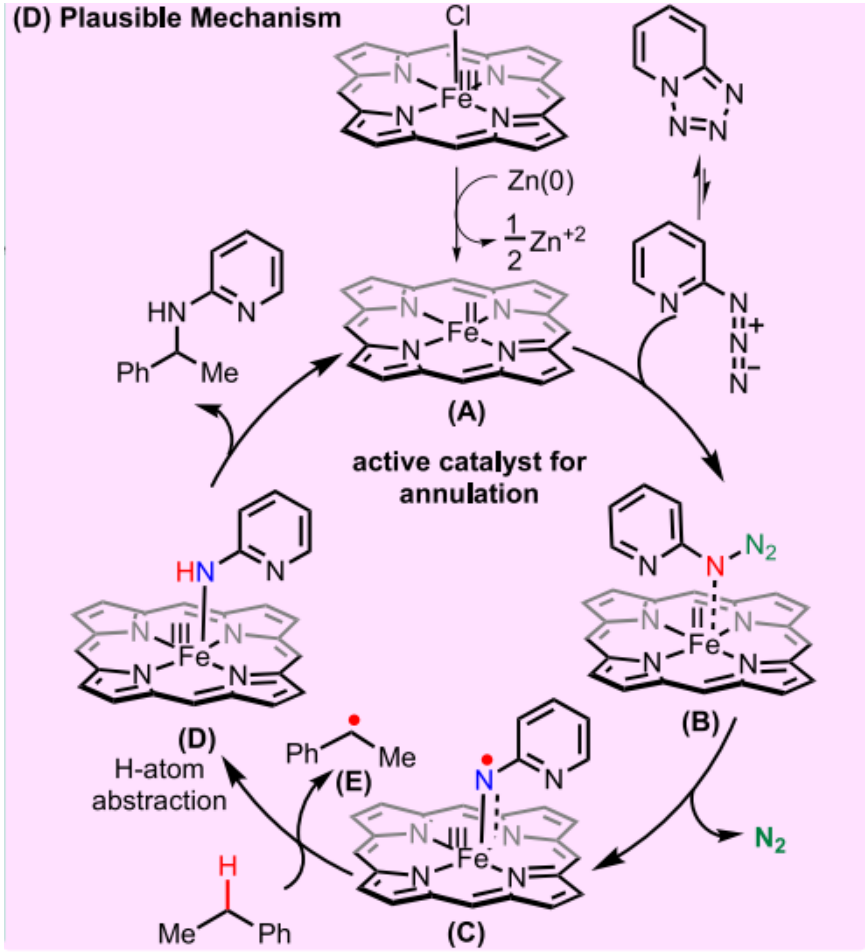
Chattopadhyay, B et al., *J. Am. Chem. Soc.* **2022**, *144*, 21858.

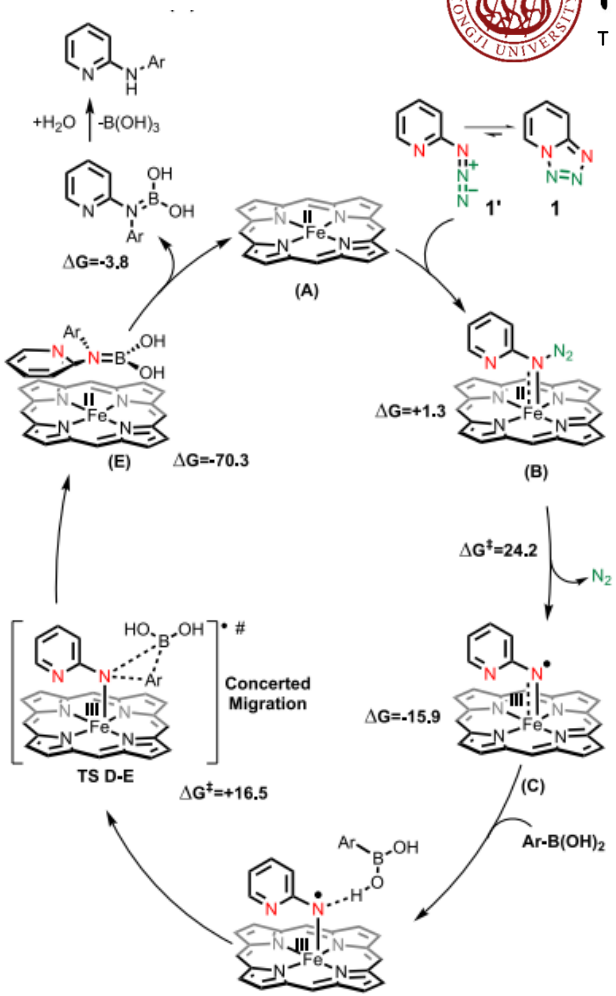
铁氮宾中间体参与



Chattopadhyay, B. et al., *J. Am. Chem. Soc.* **2023**, *145*, 14599.

铁氮宾中间体参与





J. Am. Chem. Soc. **2022**, *144*, 21858; *J. Am. Chem. Soc.* **2023**, *145*, 14599.

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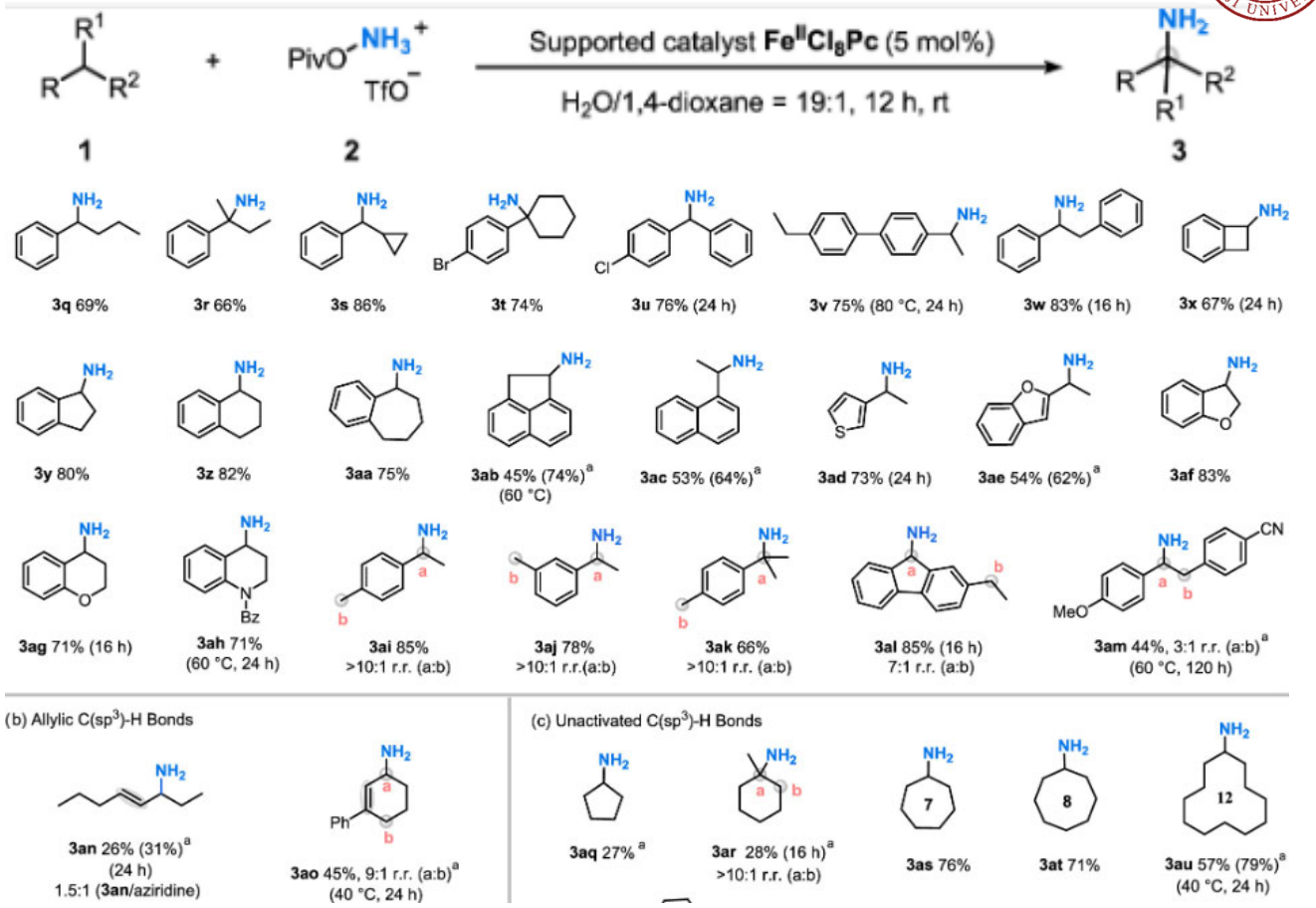

Jia, Z. J. et al., J. Am. Chem. Soc. **2024**, 146, 24863.

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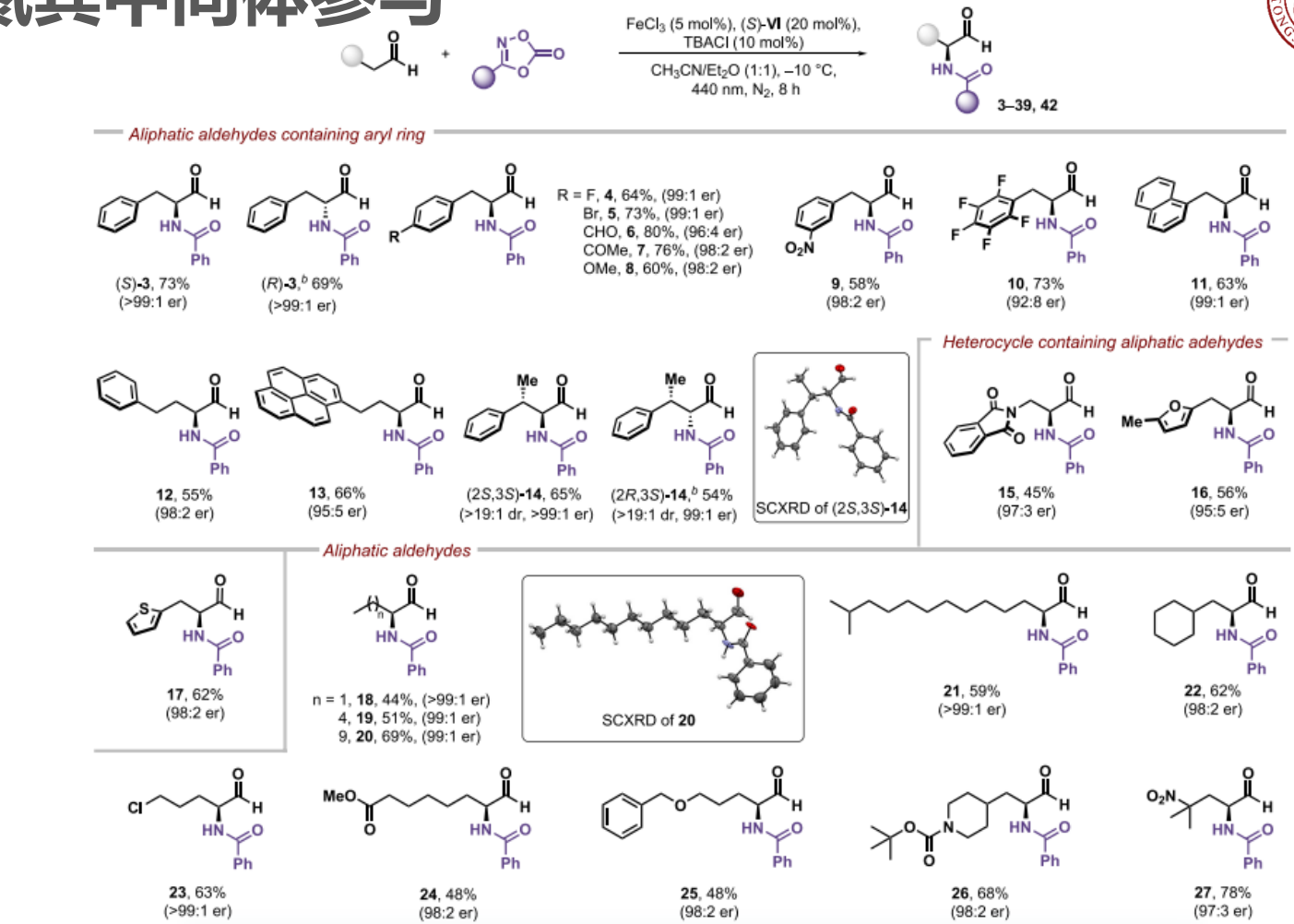

Chang, S. et al., *J. Am. Chem. Soc.* **2024**, *146*, 22172.

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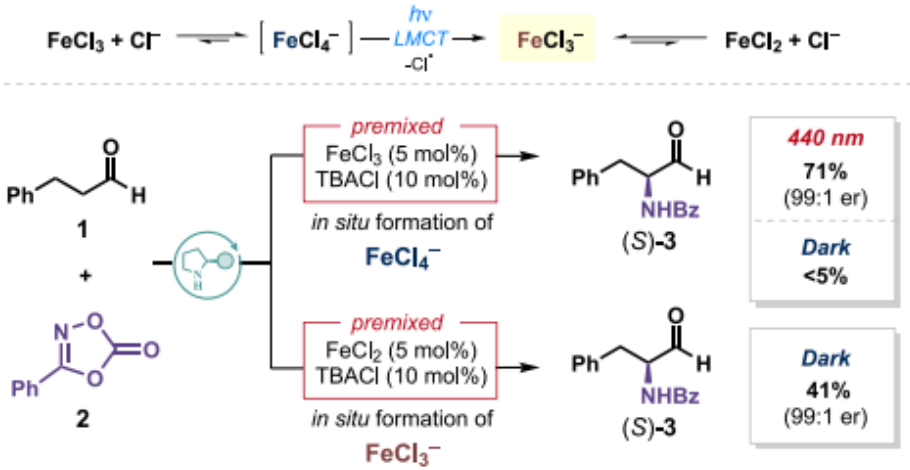
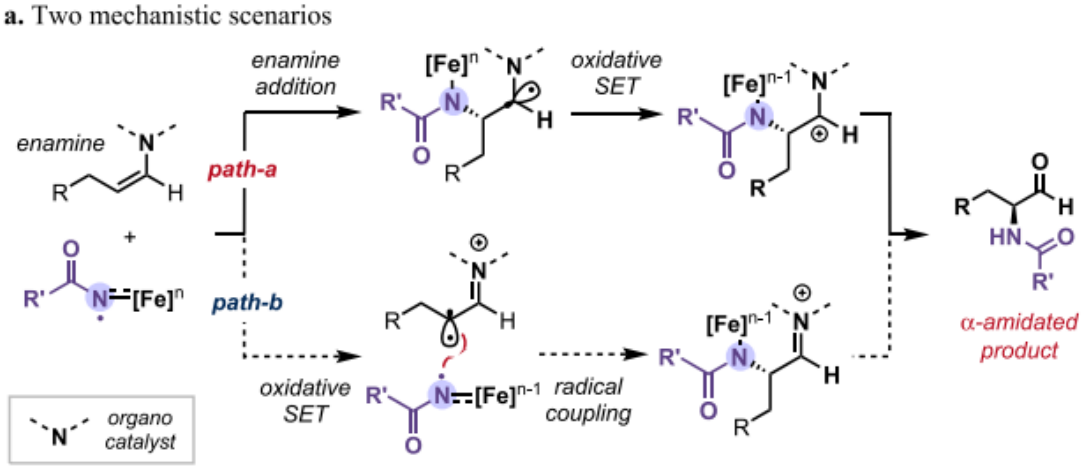
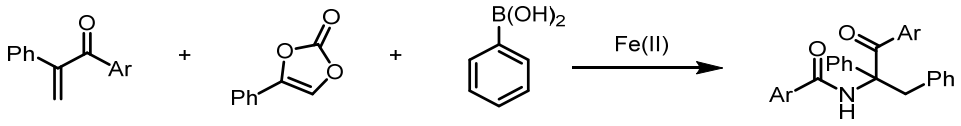




Chang, S. et al., *J. Am. Chem. Soc.* **2024**, *146*, 22172.

Proposal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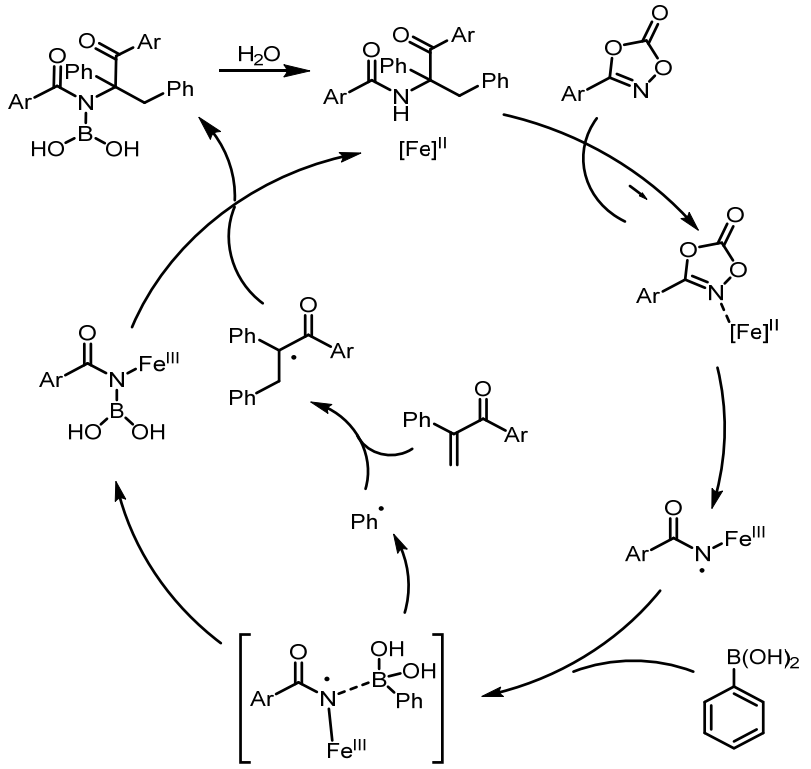
Ar
+
Ph
+
B(OH)2
Fe(II)
Ar
Ph
Ar
Ph


H2O
[Fe]II
[Fe]II
Fe III
Fe III
Fe III
B(OH)2
Ph
Ar

汇报结束 感谢聆听！

X L E R O W J S V] S Y V P M W X I R M R K %

同舟共济