



同濟大學
TONGJI UNIVERSITY



同濟大學 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

王飞课题组相关研究介绍

Topic report

汇报人: 李安妮

时间: 2026.01.09



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金属催化剂调控NCR选择性胺化

第一部分

作者简介

教育经历:

- 2007-2011 青岛科技大学, 本科, 导师: 侯万国 教授
- 2011-2016 中国科学院上海有机所, 博士, 导师: 刘国生 教授

工作经历:

- 2016-2017 中国科学院上海有机所, 研究助理, 导师: 刘国生教授
- 2017-2020 美国University of Wisconsin – Madison, 博士后, 导师: Shannon S. Stahl
- 2021-至今 南开大学化学学院 特聘研究员

研究领域:

有机合成方法学: 自由基化学、不对称催化; 目前聚焦于自由基介导的(对映体)选择性胺化。



王飞 教授

第二部分

脂肪族叠氮化物对未活化烯烃的加氢胺化反应



pubs.acs.org/JACS

Communication

Hydroamination of Unactivated Alkenes with Aliphatic Azides

Si-Ming Jia, Yi-Hang Huang, Zhan-Lin Wang, Fang-Xu Fan, Bo-Han Fan, Hao-Xiang Sun, Hao Wang,*
and Fei Wang*



Cite This: *J. Am. Chem. Soc.* 2022, 144, 16316–16324

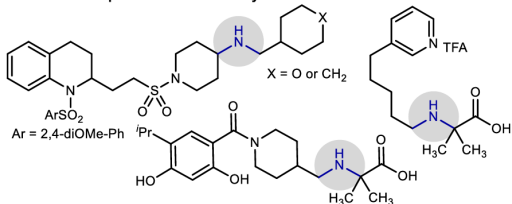


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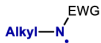
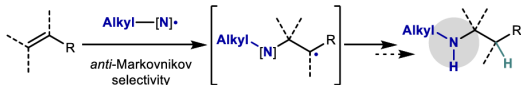
第二部分

脂肪族叠氮化物对未活化烯烃的加氢胺化反应

A. Selected Examples of Bioactive Dialkylamines



B. Dialkylamine Synthesis via NCR-Mediated Alkene Hydroamination (Prior Arts)

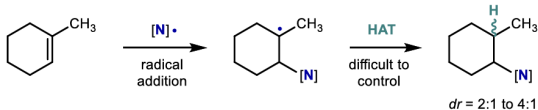


high reactivity
additional PG manipulations

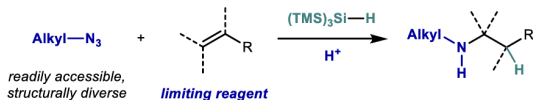


no PG manipulation
using excess alkenes
moderate reactivity with α-olefins

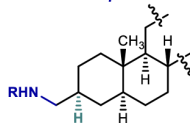
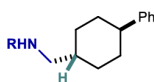
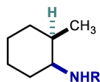
C. A General Limitation in NCR-Mediated Alkene Hydroamination: Poor dr



D. Alkene Hydroamination with Aliphatic Azides (This Work)



- Broad substrate scope
- Mild reaction conditions
- Highly diastereoselective
- Transition metal-free
- Amenable to amination of complex alkenes



第二部分

脂肪族叠氮化物对未活化烯烃的加氢胺化反应

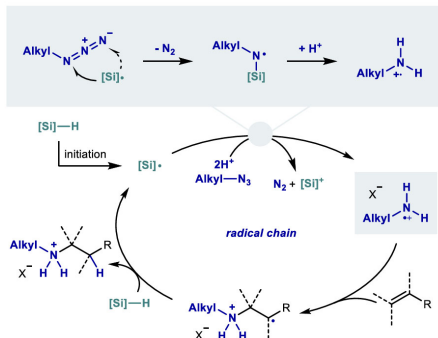


Figure 2. Proposed reaction pathway.

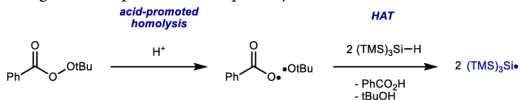


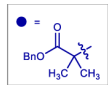
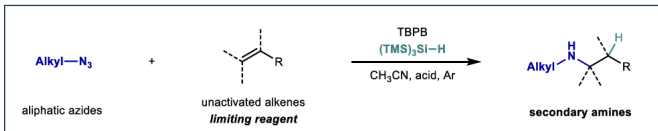
Table 1. Reaction Conditions Examination^a

entry	deviation from the conditions shown above	yield of 4 (%)
1	none	78
2	at room temperature	75
3	TsOH (4.0 equiv) instead of TFA	89
4	TsOH (2.0 equiv) instead of TFA	71
5	CH ₃ SO ₃ H (4.0 equiv) instead of TFA	61
6	using 1.0 equiv of 1 and 3	55
7	using 1.0 equiv of 1 and 3, TsOH (4.0 equiv)	54
8	in the absence of acid	0

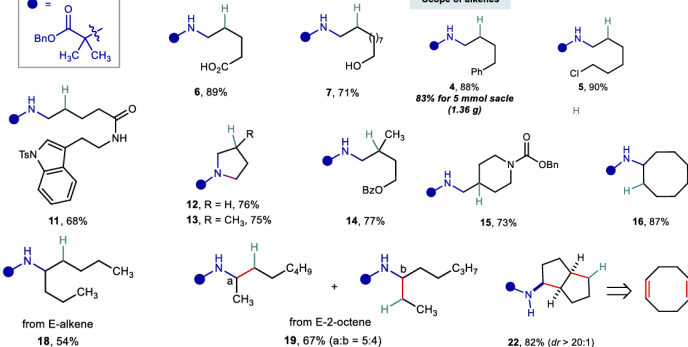
^a¹H NMR yields with 1,3,5-trimethoxybenzene as an external standard.

第二部分

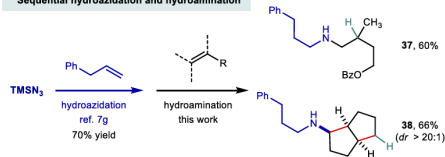
脂肪族叠氮化物对未活化烯烃的加氢胺化反应



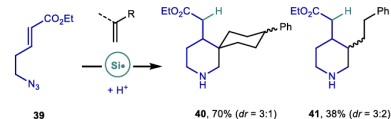
Scope of alkenes



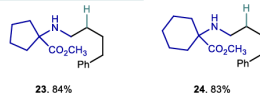
Sequential hydroazidation and hydroamination



Piperidine synthesis via [4+2] annulation



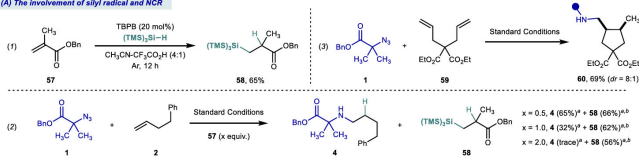
Scope of aliphatic azides



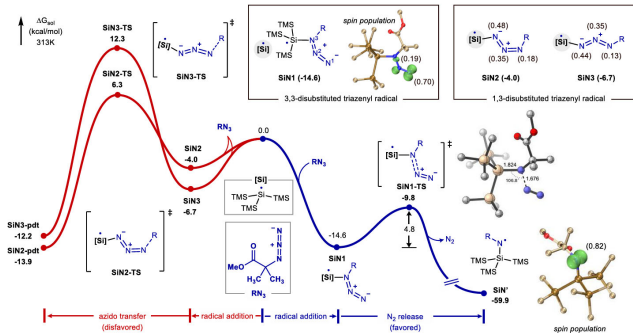
第二部分

脂肪族叠氮化物对未活化烯烃的加氢胺化反应

(A) The involvement of silyl radical and NCR



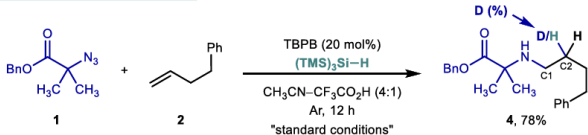
(B) Computational Studies on Azide activation^{c,d}



第二部分

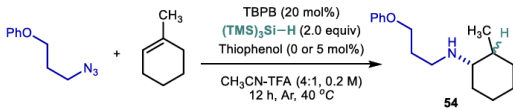
脂肪族叠氮化物对未活化烯烃的加氢胺化反应

(C) Hydrogen atom transfer

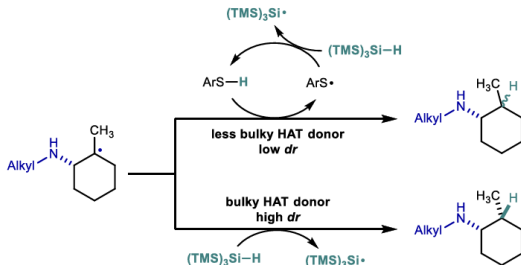


Entry	Deviation from the standard conditions	Yield ^a	D (%)
1	With $(\text{TMS})_3\text{Si-D}$	65%	>95
2	$\text{CD}_3\text{CN-CF}_3\text{CO}_2\text{D}$ (4:1)	72%	<3
3	Entry 2 and 4-F-PhSH (10 mol%)	62%	48
4	Entry 2 and 2,4,6-TRIP-PhSH (10 mol%)	62%	31

(D) Diastereoselectivity rationale



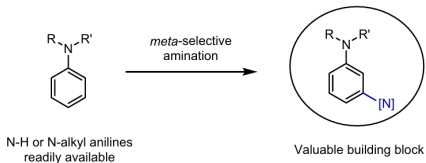
Entry	Conditions	Yield (%) ^a	dr
1	Without thiophenol (standard conditions)	88 (cis) + 3 (trans) (78% isolated yield)	> 20:1
2	With 4-F-PhSH (5 mol%)	58 (cis) + 27 (trans)	~ 2:1
3	With 2,4,6-TRIP-PhSH (5 mol%)	67 (cis) + 18 (trans)	~ 4:1



第二部分

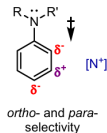
均裂芳香取代中质子化诱导极性翻转实现芳香胺的间位选择性C-H胺化

(b) *meta*-Selective C-H amination of anilines

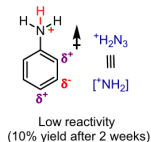


The challenges for electrophilic amination:

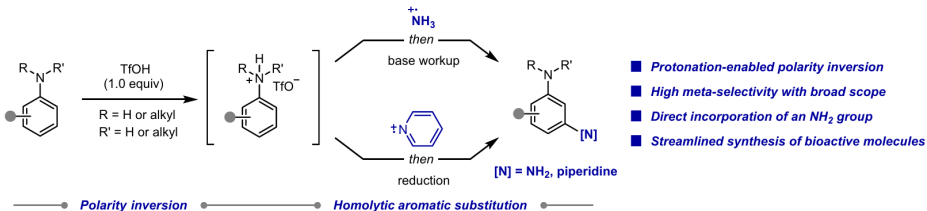
a) The polarity mismatch



b) The low reactivity



(c) A polarity inversion strategy for *meta*-selective amination of anilines with ammoniumyl and pyridinium radicals



第二部分

均裂芳香取代中质子化诱导极性翻转实现芳香胺的间位选择性C-H胺化

Table 1 | Reaction Development

Entry	Substrate	R ¹	R ²	Solvent	Acid	Yield/ 2	2/3
1	1a	H	H	HFIP	No	14%	2:1
2	1a	H	H	HFIP	HCl	N.D.	—
3	1a	H	H	HFIP	H ₂ SO ₄	16%	2:1
4	1a	H	H	HFIP	TFA	30%	2:1
5	1a	H	H	HFIP	MsOH	28%	2:1
6	1a	H	H	HFIP	Tf ₂ NH	42%	4:1
7	1a	H	H	HFIP	TfOH	71%	6:1
8 ^a	1a	H	H	HFIP	TfOH	72%, 65% ^b	6:1
9	1a	H	H	CH ₃ NO ₂	TfOH	10%	1:2:1
10	1a	H	H	CH ₃ OH	TfOH	N.D.	—
11	1a	H	H	CH ₃ CN	TfOH	N.D.	—
12	1a	H	H	THF	TfOH	N.D.	—
13 ^a	1b	CH ₃	H	HFIP	TfOH	67%, 70% ^b	8:1
14 ^a	1c	CH ₃	CH ₃	HFIP	TfOH	87%, 81% ^b	>20:1

Note: Yields and selectivity were determined by ¹H-NMR analysis with CH₂Br₂ as internal standard.

^a With FeSO₄•7H₂O (5 mol %) as catalyst, reaction time is 3 h.

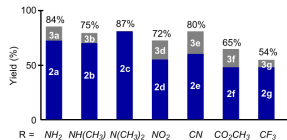
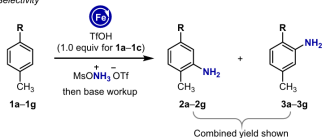
^b Isolated yield.

第二部分

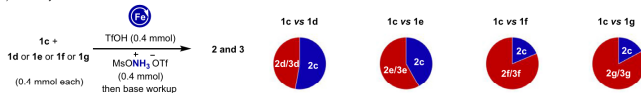
均裂芳香取代中质子化诱导极性翻转实现芳香胺的间位选择性C-H胺化

(a) Comparison of aminium with other electron-withdrawing groups

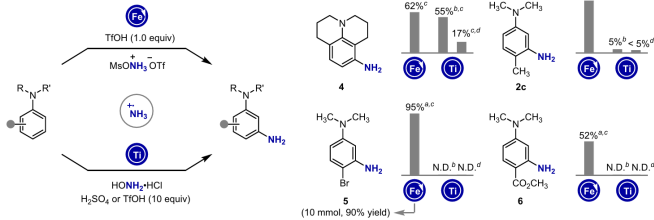
i) Selectivity



ii) Reactivity



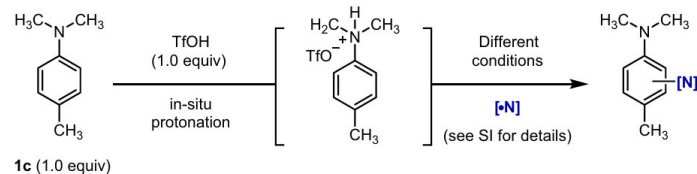
(b) Comparison between iron-catalyzed and titanium(III)-mediated systems



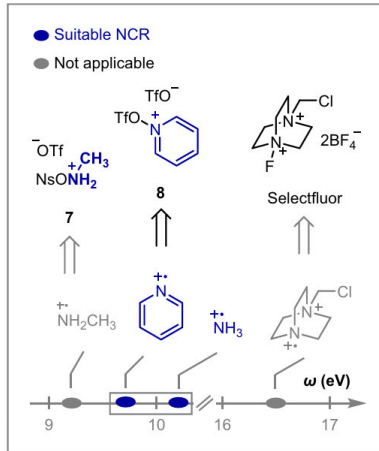
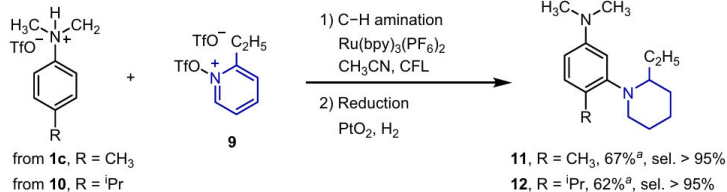
第二部分

均裂芳香取代中质子化诱导极性翻转实现芳香胺的间位选择性C-H胺化

(c) Comparison between different NCRs



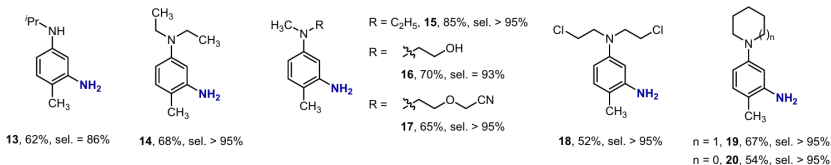
Reactions with pyridinium radical:



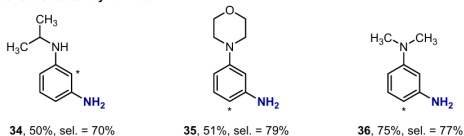
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均裂芳香取代中质子化诱导极性翻转实现芳香胺的间位选择性C-H胺化

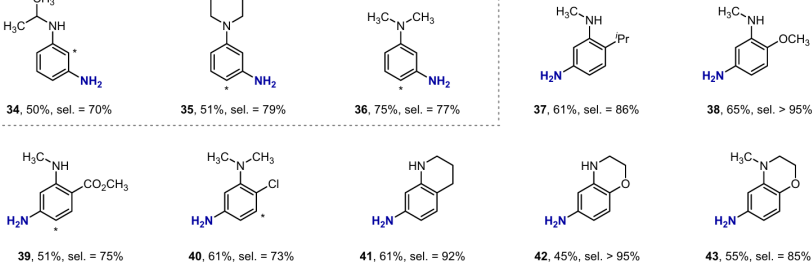
(a) *para*-Substituted aryl amines



(b) Unsubstituted aryl amines



(c) *Ortho*- and di-substituted aryl amines



第三部分

利用铁氨基自由基实现芳烃的位点选择性C-H胺化

[nature](#) > [nature catalysis](#) > [articles](#) > article

Article | Published: 01 April 2024

Site-selective arene C–H amination with iron-aminyl radical

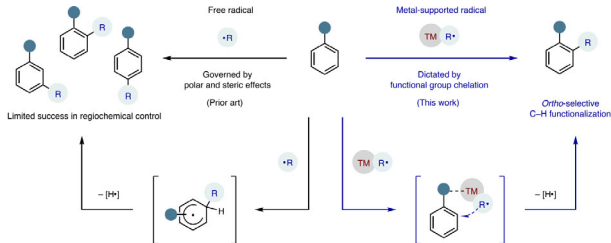
[Chao-Rui Ma](#), [Guan-Wang Huang](#), [Hui Xu](#), [Zhan-Lin Wang](#), [Zheng-Hao Li](#), [Jun Liu](#), [Yin Yang](#), [Gongyu Li](#),
[Yanfeng Dang](#) ✉ & [Fei Wang](#) ✉

[Nature Catalysis](#) **7**, 636–645 (2024) | [Cite this article](#)

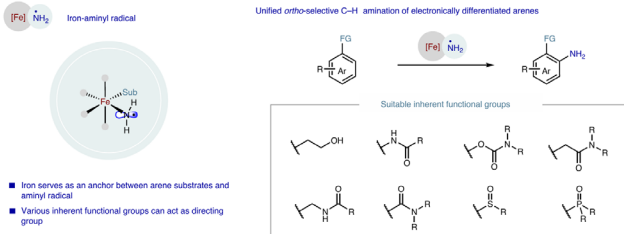
第三部分

利用铁氨基自由基实现芳烃的位点选择性C-H胺化

a The positional selectivity in HAS with free radical and metal-supported radical



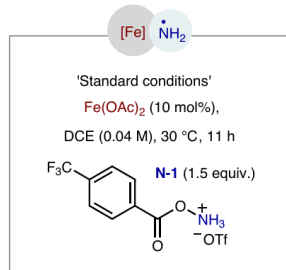
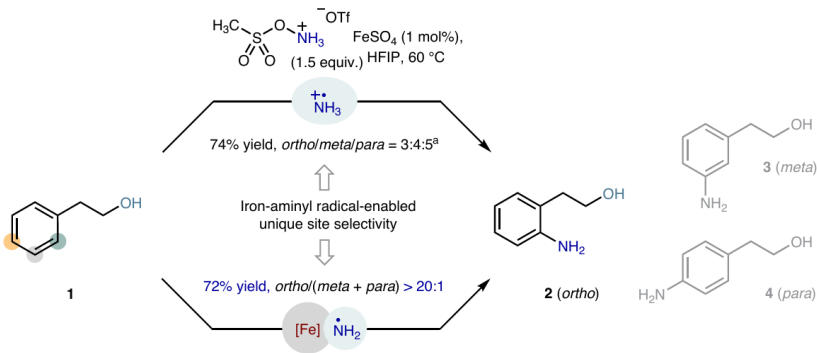
c *Ortho*-selective arene C-H amination with iron-aminyl radical



第三部分

利用铁氨基自由基实现芳烃的位点选择性C-H胺化

a The optimized reaction conditions and site selectivity comparison with existing method via ammoniumyl radical

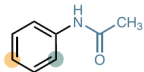


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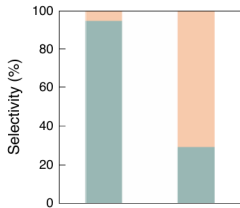
利用铁氨基自由基实现芳烃的位点选择性C-H胺化

b Site selectivity comparison between ammoniumyl radical- and iron-supported NCR-mediated HAS for arene C-H amination

Electron-rich arene



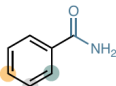
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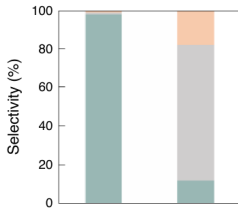
Yield: 6, 97%

44%^b

Electron-deficient arene



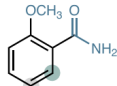
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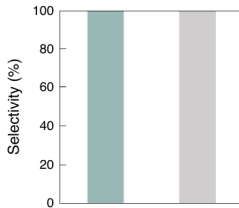
8, 91%

34%^a

Disubstituted arene



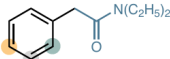
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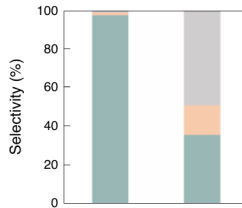
10, 82%

95%^b

Electron-neutral arene



11



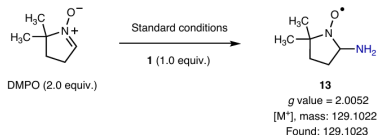
12, 82%

73%^a

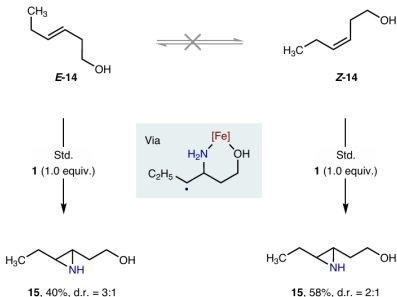
第三部分

利用铁氨基自由基实现芳烃的位点选择性C-H胺化

a EPR analysis of the reaction mixture with DMPO as spin trap

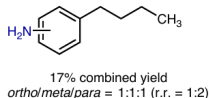


b The reaction of alkenes under standard conditions

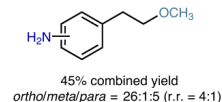


c Control experiments

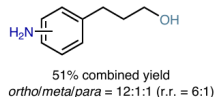
Without chelating group



OCH₃ instead of OH



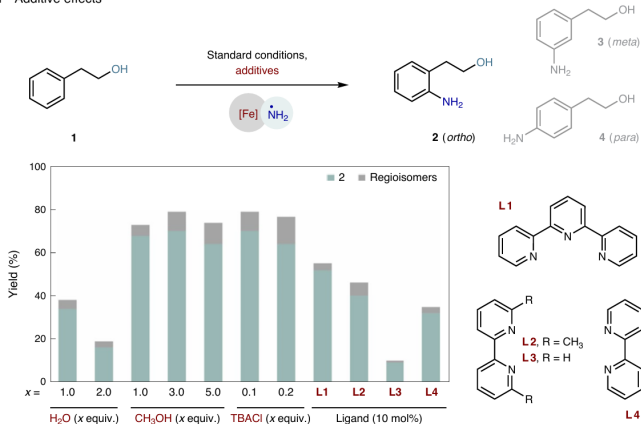
With greater distance



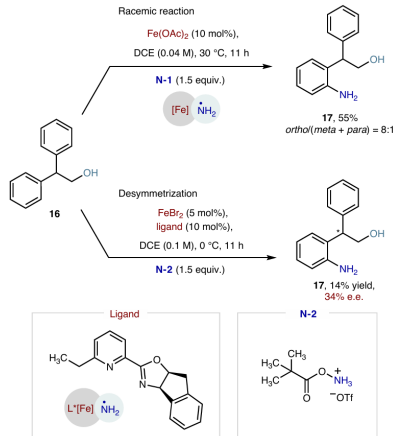
第三部分

利用铁氨基自由基实现芳烃的位点选择性C-H胺化

d Additive effects

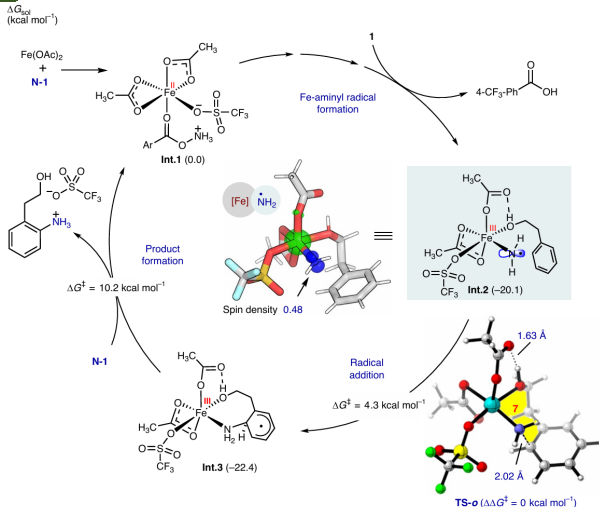


e Preliminary results for desymmetric arene C-H amination

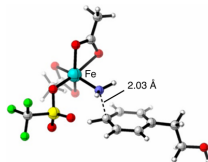


第三部分

利用铁氨基自由基实现芳烃的位点选择性C-H胺化

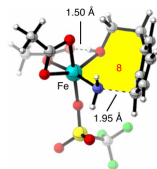


Para-selective radical addition



TS-p ($\Delta\Delta G^{\ddagger} = 6.6$ kcal mol⁻¹)

Meta-selective radical addition



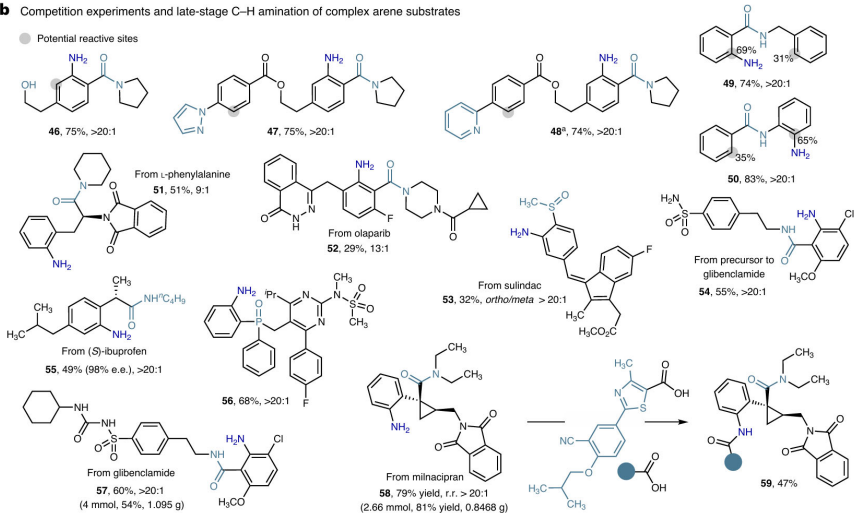
TS-m ($\Delta\Delta G^{\ddagger} = 7.0$ kcal mol⁻¹)

第三部分

利用铁氨基自由基实现芳烃的位点选择性C-H胺化

b Competition experiments and late-stage C-H amination of complex arene substrates

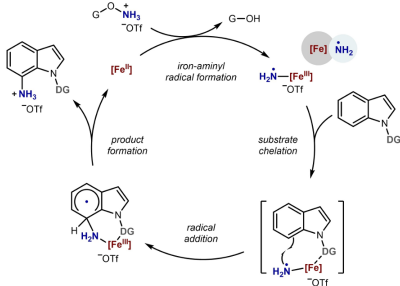
● Potential reactive sites



第三部分

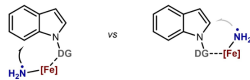
铁催化吲哚的C-7选择性NH₂胺化反应

A. Proposed catalytic cycle

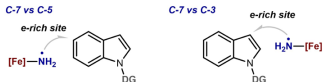


The challenges:

■ Directed radical addition, C-7 vs C-2



■ Non-directed radical addition ("background" reaction), C-7 vs C-3/5

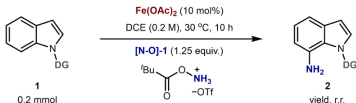


The solution:

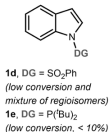
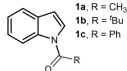
Identifying a DG that could

- orientate the iron-aminyl radical to the C-7 position selectively
- coordinate with the iron catalyst effectively
- deactivate C-5 and C-3 positions sufficiently

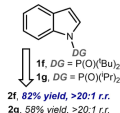
B. Examination of different chelating groups



resulting in
mixture of regioisomers

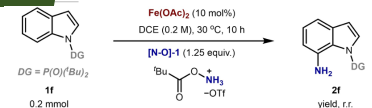


high yield and selectivity



第三部分

铁催化吲哚的C-7选择性NH₂胺化反应



Entry	Solvent	Fe loading	Conversion	Yield of 2f ^a	r.r.
1	DCE	10 mol%	100%	82%	> 20:1
2	PhF	10 mol%	100%	72%	> 20:1
3	MTBE	10 mol%	84%	76%	> 20:1
4	DME	10 mol%	16%	7%	1.4:1
5	THF	10 mol%	12%	3%	-
6	CH ₃ OH	10 mol%	23%	5%	-
7	HFIP	10 mol%	100%	83% (81%) ^b	> 20:1
8 ^c	HFIP	10 mol%	47%	44%	> 20:1
9 ^d	HFIP	10 mol%	87%	80%	> 20:1
10 ^e	HFIP	10 mol%	90%	80%	> 20:1
11 ^f	HFIP	10 mol%	5%	n.d.	-
12 ^g	HFIP	10 mol%	100%	92% (88%) ^h	> 20:1
13 ^g	HFIP	1 mol%	100%	92%	> 20:1
14 ^g	HFIP	0.1 mol%	94%	83%	> 20:1
15 ^{g,i}	HFIP	0.01 mol%	55%	45%	> 20:1
16 ^g	HFIP	-	9%	n.d.	-

aminating reagents:

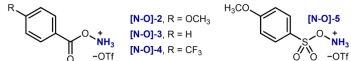


Figure 3. Reaction development. [a] Yields and selectivity were determined by ¹H NMR analysis. [b] Isolated yield in a 0.4 mmol scale. [c] With [N-O]-2. [d] With [N-O]-3. [e] With [N-O]-4. [f] With [N-O]-5. [g] With 1.1 equiv. of [N-O]-1. [h] Isolated yield in a 0.2 mmol scale. [i] The reaction was run for 24 hours. r.r. (regioisomeric ratio) refers to the ratio of the desired C-7 amination product and a sum of the detectable regioisomers.

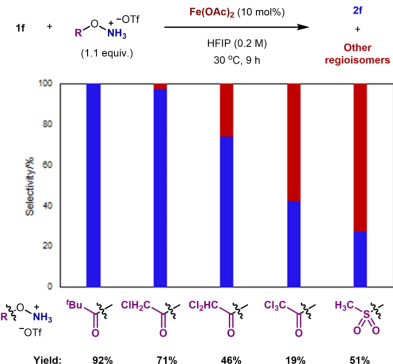


Figure 5. Control experiments with different aminating reagents.

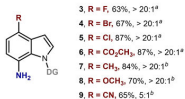
第三部分

铁催化吲哚的C-7选择性NH₂胺化反应

A. Substrate scope



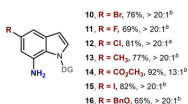
4-Substituted Indoles:



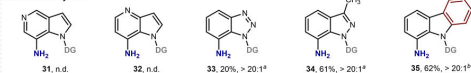
6-Substituted Indoles:



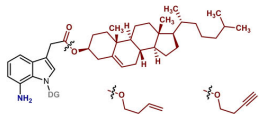
5-Substituted Indoles:



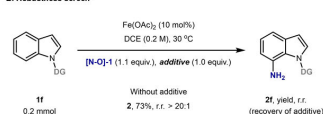
Other heterocycles:



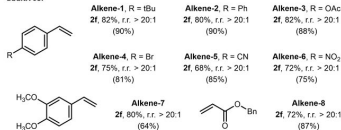
3-Substituted Indoles:



B. Robustness screen^c



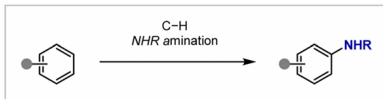
additives:



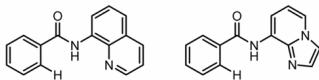
第三部分

铁催化选择性芳香C-H胺化合成N-CD₃芳胺

B. Prior art on aromatic C-H NHR amination (R = alkyl)

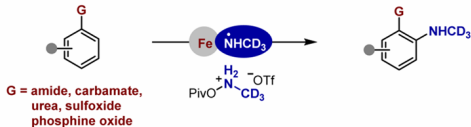


i) C-H metalation (copper catalysis)

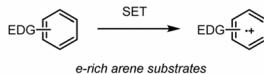


specific directing group required

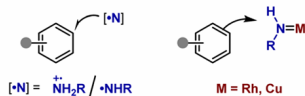
C. Iron-catalysed aromatic C-H NHCD₃ amination of arenes



ii) Arene oxidation to radical cation (photoredox catalysis or via CT complex)



iii) Electrophilic amination (NCRs or protonated metal-nitrenoid)



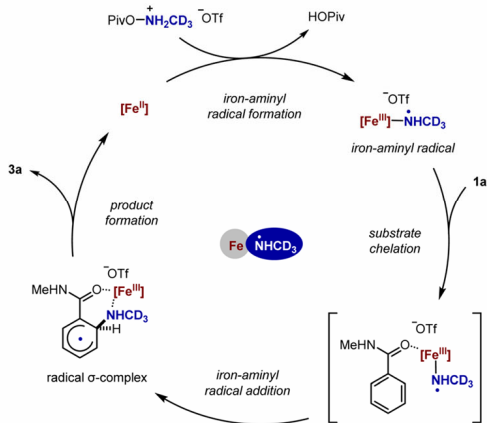
not applicable to *e*-deficient arenes and/or poor regioselectivity

- Direct C-H NHCD₃ amination of arenes
- Inherent functionalities as directing groups
- Excellent ortho-selectivity
- Broad scope and mild conditions

第三部分

铁催化选择性芳香C-H胺化合成N-CD₃芳胺

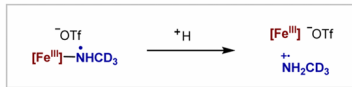
A. Proposed reaction pathway



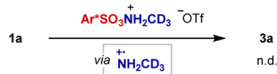
B. Iron-aminyl radical vs aminium radical cation

i) Transforming iron-aminyl radical to aminium radical cation

Entry	Additive	Yield/ 3a ^a
1	-	94%
2	TfOH	n.d.
3	MsOH	n.d.
4	TFA	50%



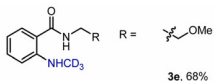
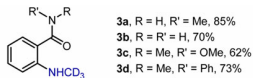
ii) Directly forming aminium radical cation



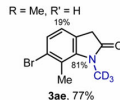
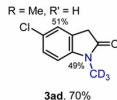
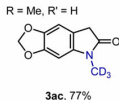
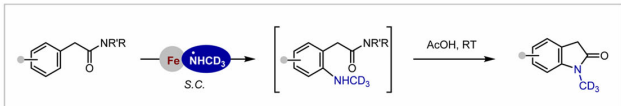
EPR证明NCR参与

第三部分

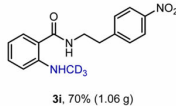
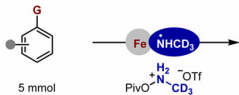
铁催化选择性芳香C-H胺化合成N-CD₃芳胺



一级、二级和三级
苯甲胺的兼容性极
佳



A. Scale-up experiments



第三部分

铁催化配体辅助的烯烃模块化氨化双官能化



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Research Article

Iron-Catalyzed Ligand-Enabled Modular Aminative Difunctionalization of Alkenes

Hao-Xiang Sun,^{||} Guorong Li,^{||} Zhan-Lin Wang,^{||} Shi-Xiong Tang, Zheliang Yuan,^{*} Qian Peng,^{*} and Fei Wang^{*}



Cite This: *ACS Catal.* 2025, 15, 17844–17855

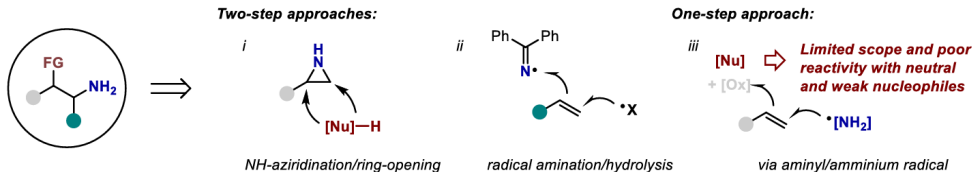


Read Online

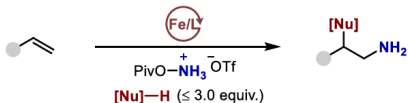
第三部分

铁催化配体辅助的烯炔模块化氨化双官能化

B. Aminative difunctionalization of alkenes to approach primary alkylamines.

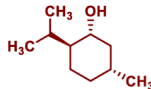


C. This work: Iron-catalyzed modular aminative difunctionalization of alkenes.



- Broad scope of nucleophiles
- One-step and simple operation
- Avoiding the use of nucleophile in large excess

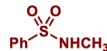
Selected nucleophiles:



alcohol



pyrazole



sulfonamide

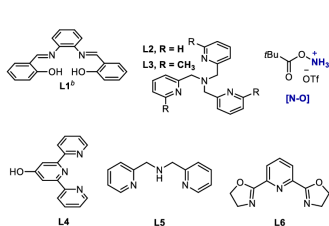
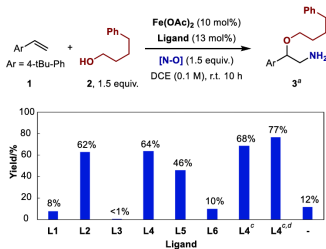


PhCONH₂
benzamide

第三部分

铁催化配体辅助的烯炔模块化氨化双官能化

A. The reaction optimizations.



B. Comparison between Fe(OAc)₂/L4, FePc and Fe(acac)₃ for aminative difunctionalization of alkene.

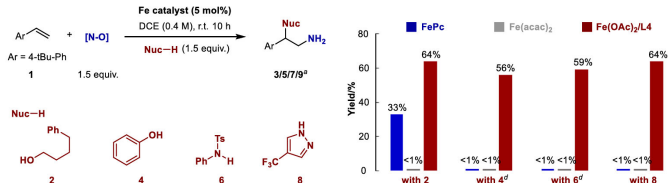
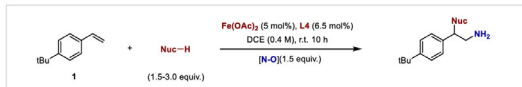


Figure 2. Reaction development and comparison with the existing catalysts for aminative difunctionalization of alkenes. ^aYields were determined using ¹H NMR analysis. ^b10 mol % ligand was used. ^c0.4 M, 5 mol % Fe(OAc)₂, and 6.5 mol % ligand. ^d3.0 equiv of the nucleophile.

第三部分

铁催化配体辅助的烯炔模块化氨化双官能化



phenols



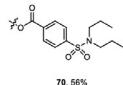
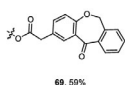
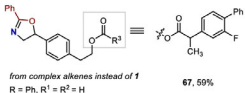
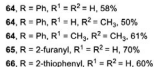
sulfonamides



azoles



amides



B. Alkene scope with 2



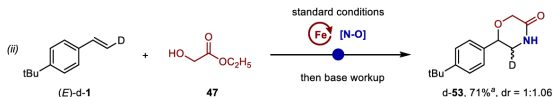
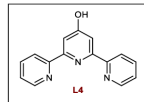
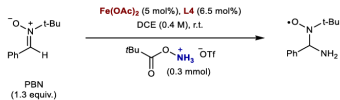
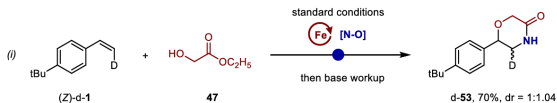
C. Direct access to 6-aryl/morpholin-3-one



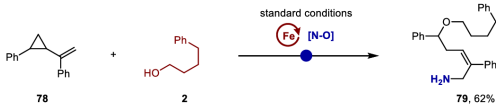
第三部分

铁催化配体辅助的烯炔模块化氨化双官能化

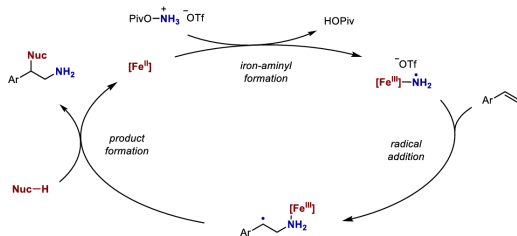
A. Reactions with (Z)- and (E)-d-1.



B. Radical clock experiment.



C. The proposed reaction pathway.



第三部分

通过铁氨基自由基与环丙烯的胺化开环反应立体选择性合成四取代及三取代烯基腈。

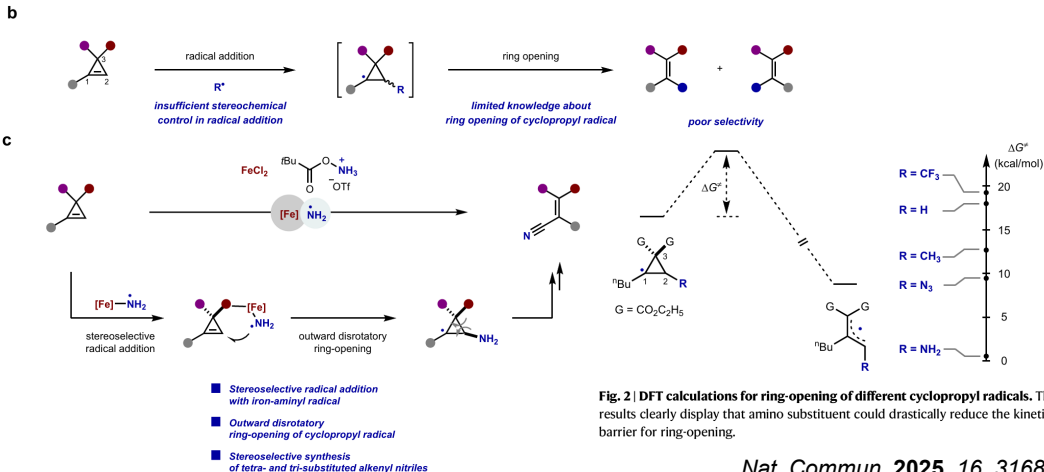
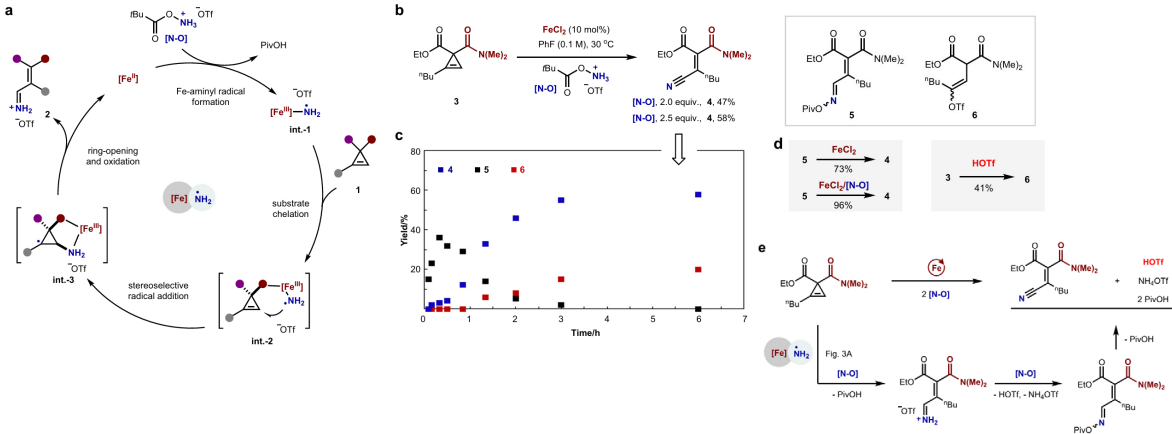


Fig. 2 | DFT calculations for ring-opening of different cyclopropyl radicals. The results clearly display that amino substituent could drastically reduce the kinetic barrier for ring-opening.

第三部分

通过铁氨基自由基与环丙烯的胺化开环反应立体选择性合成四取代及三取代烯基腈。



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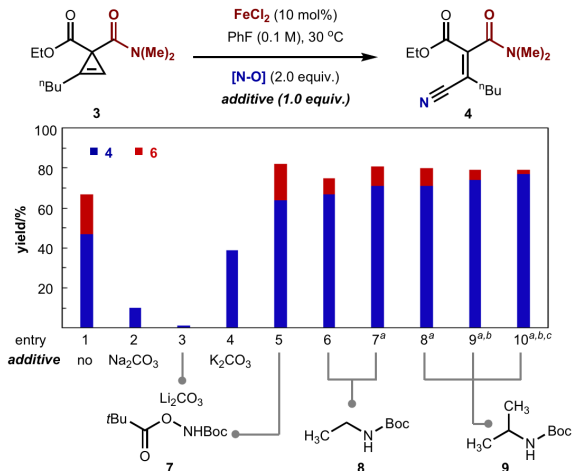
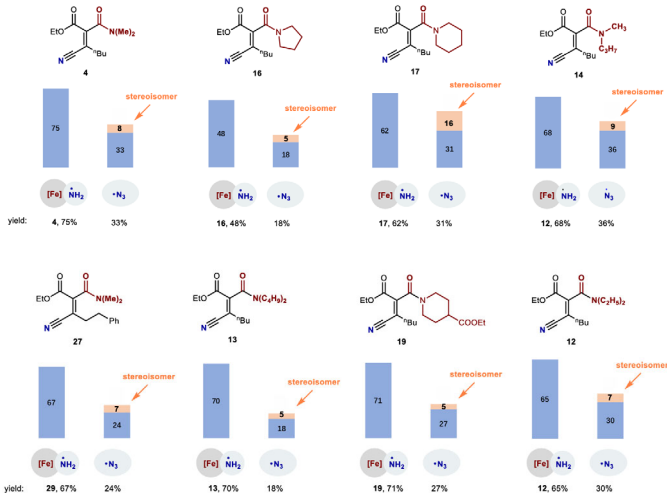
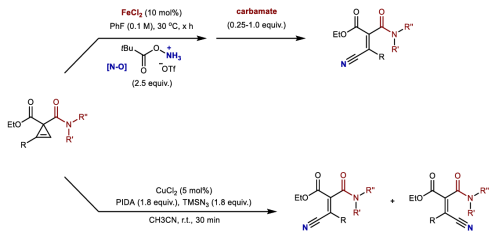


Fig. 4 | Examination of acid scavengers. The additive effect on the reaction. ^aThe additive was added into the reaction mixture after 0.5 h. ^b2.5 equiv. of $[\text{N-O}]$ was used. ^c0.5 equiv. of additive was used. All yields were determined by $^1\text{H-NMR}$ analysis with CH_2Br_2 as internal standard.

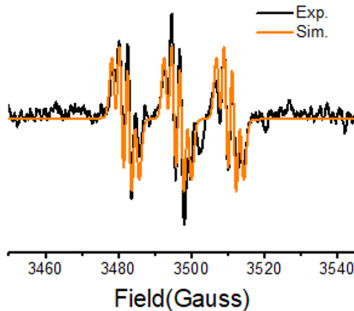
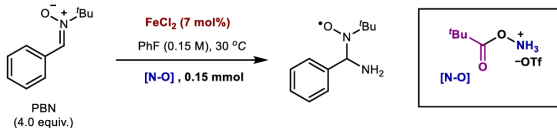
第三部分

通过铁氨基自由基与环丙烯的胺化开环反应立体选择性合成四取代及三取代烯基腈。



第三部分

通过铁氨基自由基与环丙烯的胺化开环反应立体选择性合成四取代及三取代烯基腈。



第三部分

通过铁氨基自由基与环丙烯的胺化开环反应立体选择性合成四取代及三取代烯基腈。

a.

ΔG_{sol} (kcal/mol)

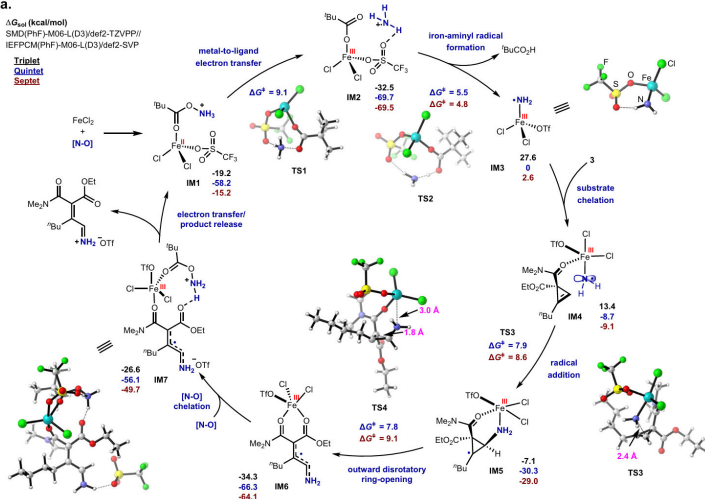
SMD(PhF)-M06-L(D3)/def2-TZVP//

IEFPCM(PhF)-M06-L(D3)/def2-SVP

Triplet

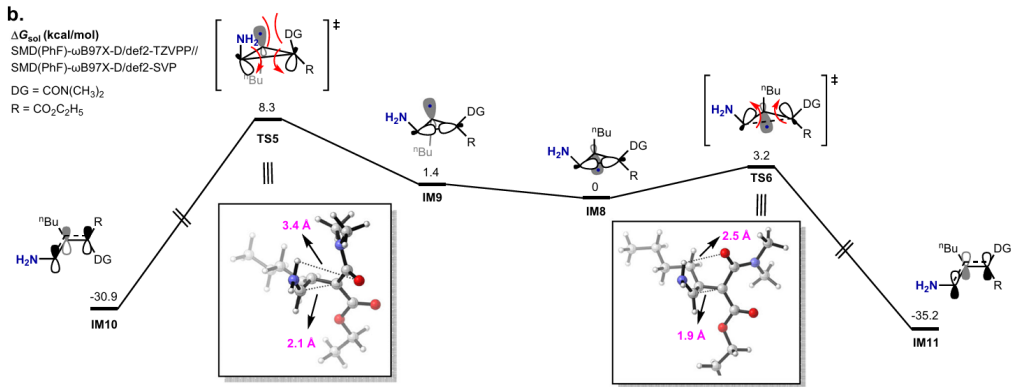
Quintet

Septet



第三部分

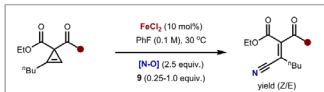
通过铁氨基自由基与环丙烯的胺化开环反应立体选择性合成四取代及三取代烯基腈。



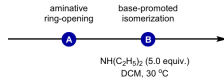
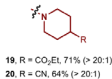
第三部分

通过铁氨基自由基与环丙烯的胺化开环反应立体选择性合成四取代及三取代烯基腈。

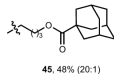
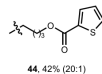
a



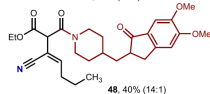
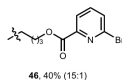
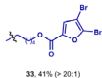
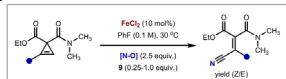
- 4, $\text{R}^1 = \text{R}^2 = \text{CH}_3$, 75% (> 20:1)
10, $\text{R}^1 = \text{R}^2 = \text{H}$, 16%
11, $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{C}_6\text{H}_5$, 51% (> 20:1)
12, $\text{R} = \text{C}_2\text{H}_5$, 65% (> 20:1)
13, $\text{R} = \text{C}_6\text{H}_5$, 70% (> 20:1)



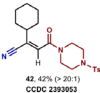
yield from cyclopropene (Z/E)



b



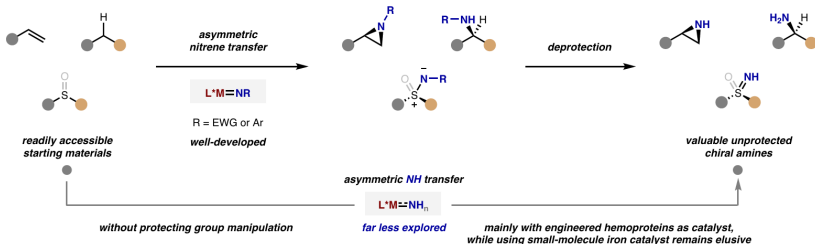
c



第三部分

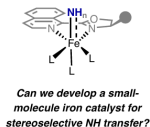
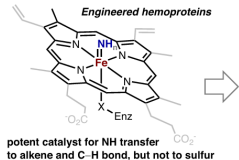
铁催化立体选择性NH转移实现亚砷的动态动力学拆分

a.

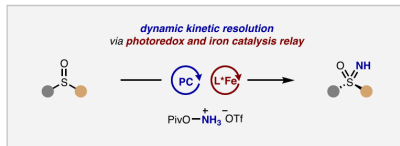


b.

定向进化的血红素蛋白进行酶催化



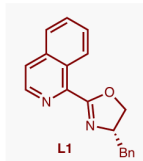
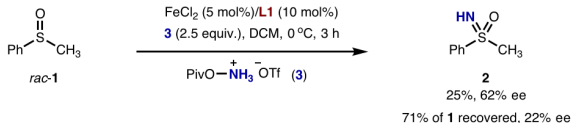
c.



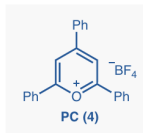
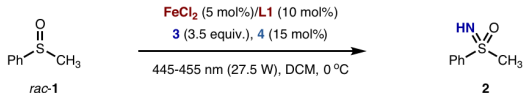
第三部分

铁催化立体选择性NH转移实现亚砷的动态动力学拆分

a. Optimized conditions for kinetic resolution^a



b. Initial trials for dynamic kinetic resolution^a

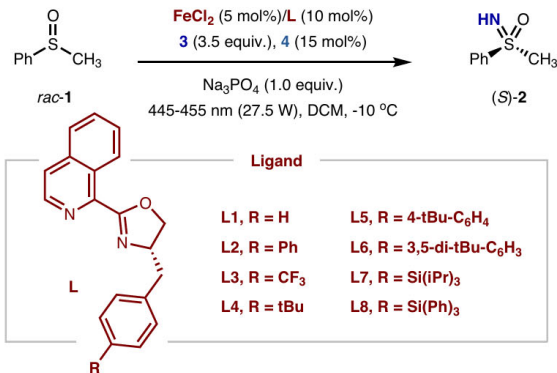


Entry	Conditions	Recovered 1		NH-sulfoximine 2	
		yield/%	ee/%	yield/%	ee/%
1	as above	42%	2%	49%	70%
2	with Na ₃ PO ₄ (1.0 equiv.)	20%	0%	61%	60%
3	with Na ₃ PO ₄ (1.0 equiv.), -10 °C	36%	0%	54%	68%

第三部分

铁催化立体选择性NH转移实现亚砷的动态动力学拆分

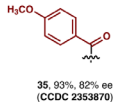
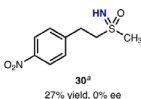
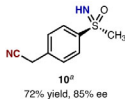
C. Ligand assessment for iron-catalyzed dynamic kinetic resolution^a



Entry	Ligand	NH-sulfoximine 2	
		yield/%	ee/%
1	L1	54%	68%
2	L2	76%	64%
3	L3	41%	64%
4	L4	67%	66%
5	L5	69%	64%
6	L6	67%	74%
7	L7	70%	78%
8	L8	82%	80%
9 ^b	L8	85%	82%

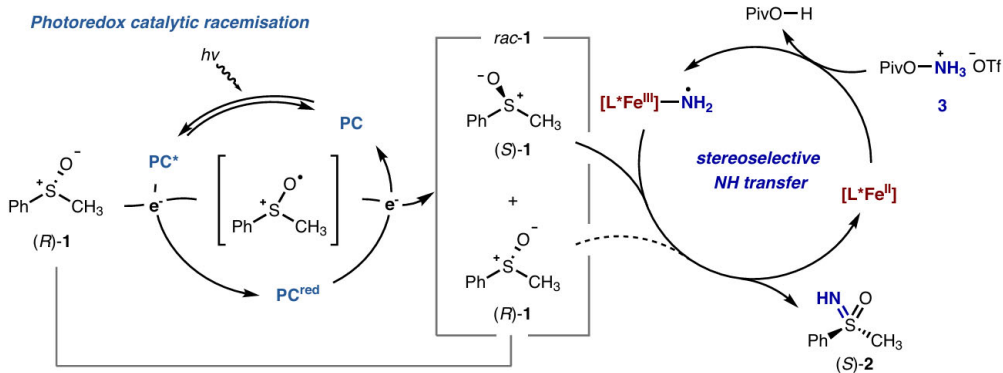
^aThe reactions were performed in 0.05 mmol scale and 10 mM in dichloromethane (DCM) for 3h. All yields were determined by ¹H NMR analysis with CH₂Br₂ as internal standard; ees were measured by HPLC on a chiral phase. ^b5 mM.

铁催化立体选择性NH转移实现亚砷的动态动力学拆分



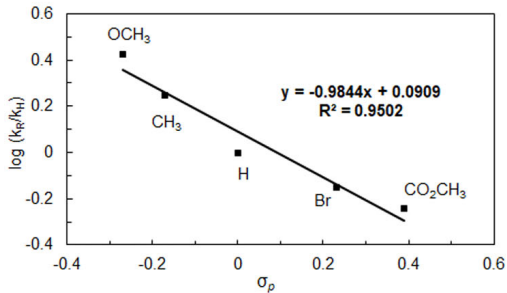
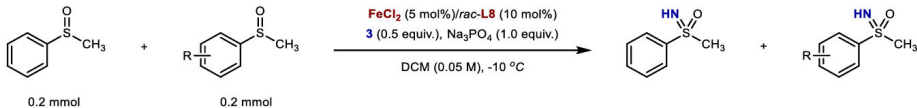
第三部分

铁催化立体选择性NH转移实现亚砷的动态动力学拆分



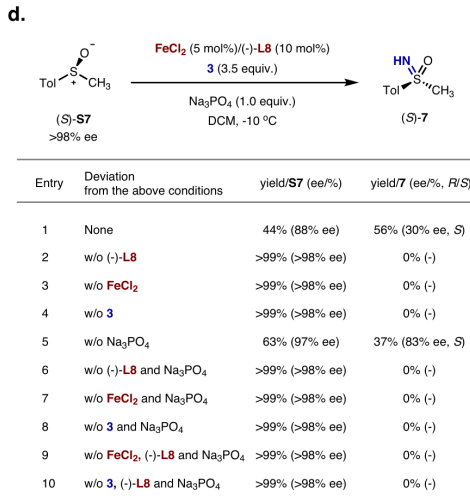
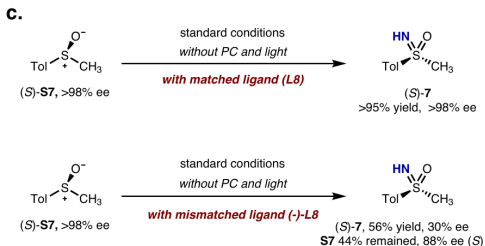
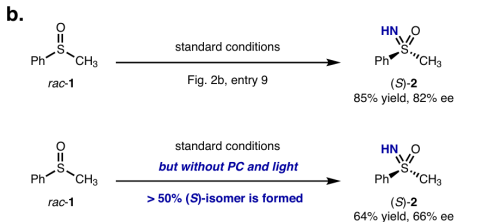
第三部分

铁催化立体选择性NH转移实现亚砷的动态动力学拆分



第三部分

铁催化立体选择性NH转移实现亚砷的动态动力学拆分



第三部分

铁催化芳烃加氧酶代谢氮类似物制备



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Article

Aza Analogs of Arene Oxygenase Metabolization via Iron Catalysis

Si-Ming Jia,[#] Chao-Rui Ma,[#] Shu-Ya Xin, Jin-Kai Cheng, Meng-Meng Ren, and Fei Wang^{*}



Cite This: <https://doi.org/10.1021/jacs.5c19427>

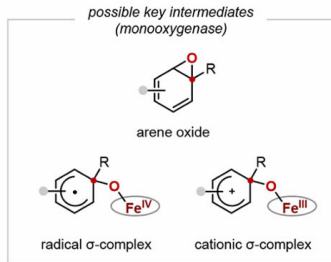
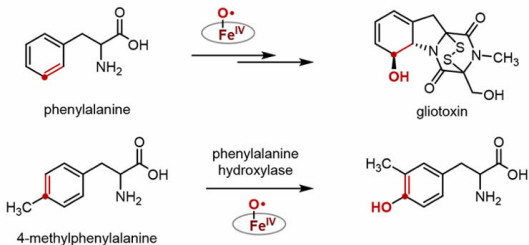
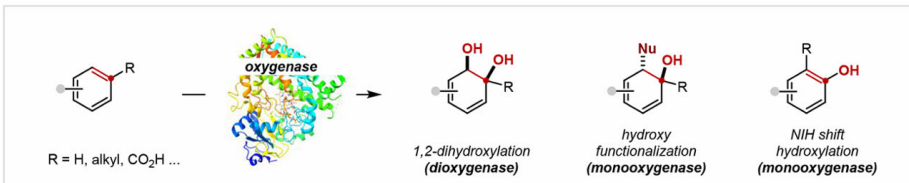


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第三部分

铁催化芳烃加氧酶代谢氮类似物制备

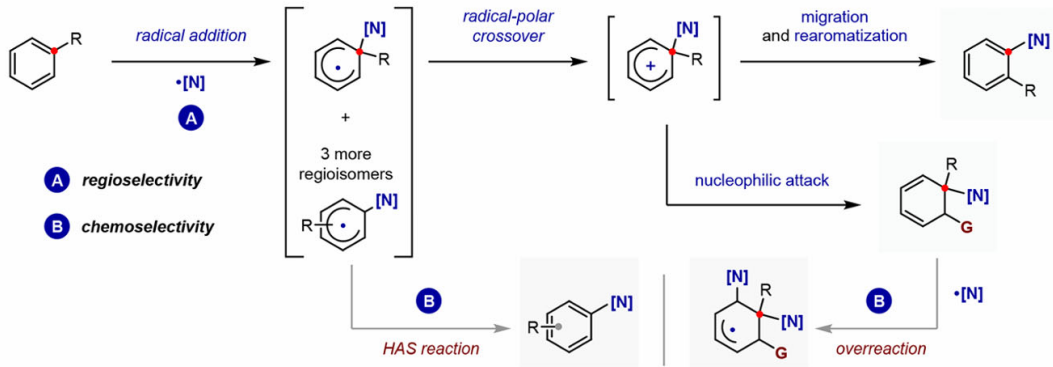
A. Arene metabolism with oxygenase: dearomatization and NIH shift reactions



第三部分

铁催化芳烃加氧酶代谢氮类似物制备

B. Radical-mediated dearomatization/migratory functionalization reactions and potential pitfalls.



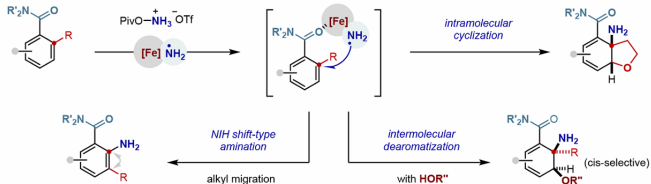
第三部分

铁催化芳烃加氧酶代谢氮类似物制备

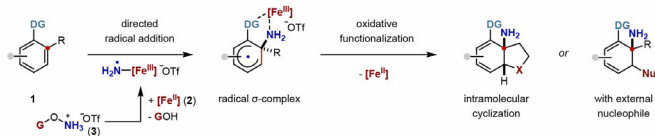
C. Previous work: iron-catalyzed directed radical addition for arene C–H amination.



D. This work: dearomative amination and NIH shift-type amination of arenes facilitated by iron-aminyl radical.



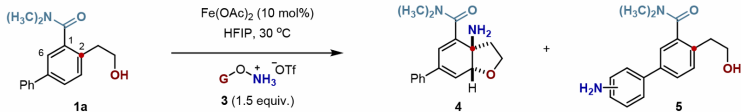
A. Proposed reaction pathway for dearomative amination of arenes



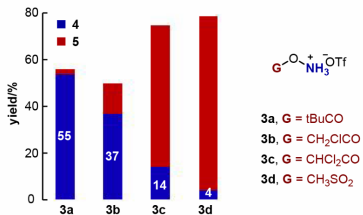
第三部分

铁催化芳烃加氧酶代谢氮类似物制备

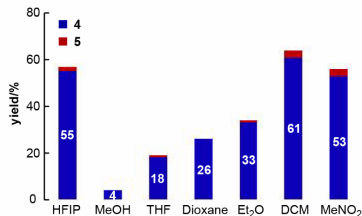
B. Development of dearomative amino-etherification of 1a



i) Effects of aminating reagents^a



ii) The solvent effect (with 3a)^a

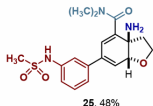
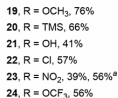
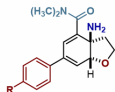
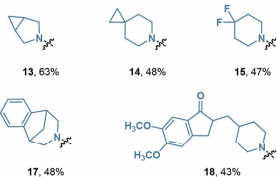
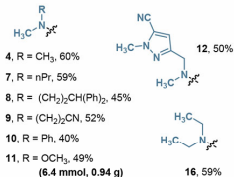
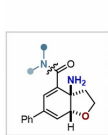
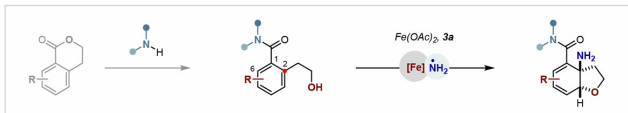


H-OG（离去基团的共轭酸）的高pKa值可能有利于铁-氨基自由基的形成，从而通过底物螯合实现选择性自由基加成。

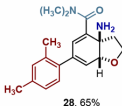
反应中底物与溶剂可能竞争配位铁-氨基自由基，且溶剂分子中的弱C-H键也可能与其发生副反应，导致效率下降。

第三部分

铁催化芳烃加氧酶代谢氮类似物制备



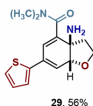
25, 48%



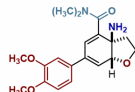
28, 65%



26, 62%



29, 56%



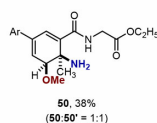
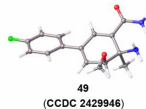
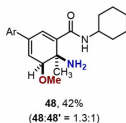
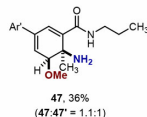
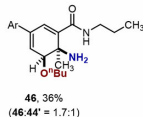
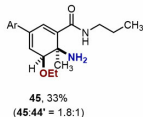
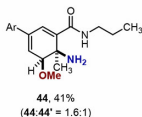
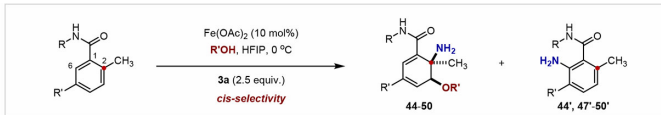
27, 62%



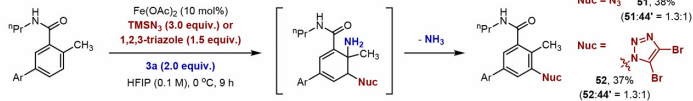
30, 56%

第三部分

铁催化芳烃加氧酶代谢氮类似物制备



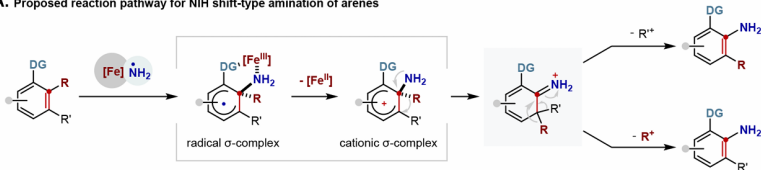
Other nucleophiles



第三部分

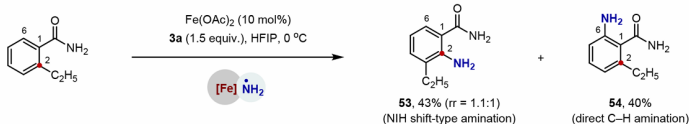
铁催化芳烃加氧酶代谢氮类似物制备

A. Proposed reaction pathway for NIH shift-type amination of arenes

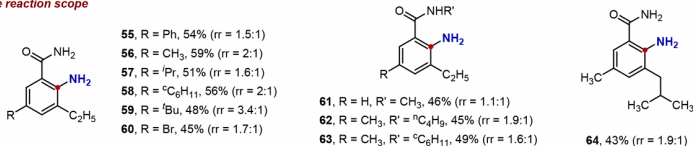


B. Observations of the NIH shift-type amination reactions

i. Alkyl shift



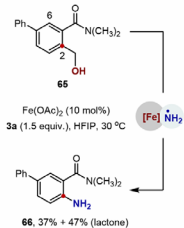
The reaction scope



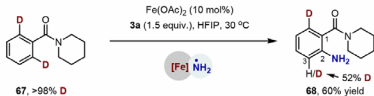
第三部分

铁催化芳烃加氧酶代谢氮类似物制备

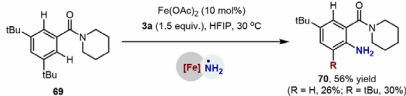
ii. Aminative dealkylation



iii. Deuterium shift

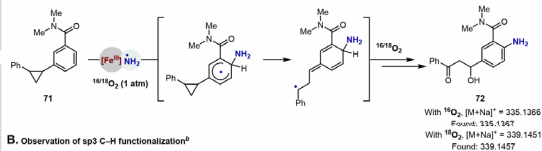


iv. Hydride shift-dealkylation

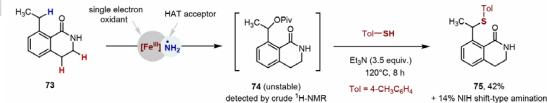


(DMPO) 作为自旋捕获剂进行电子顺磁共振 (EPR) 光谱分析, 证实了 $\cdot \text{NH}_2$ 自由基的参与

A. Radical clock experiment^a

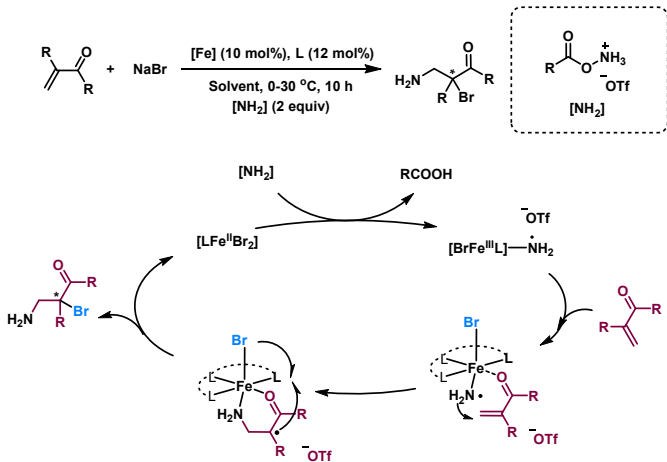


B. Observation of sp³ C-H functionalization^b



芳烃胺化反应可能经历“氢原子攫取→电子转移”路径, 而不是直接的自由基加成。

Proposal





同濟大學
TONGJI UNIVERSITY



同濟大學 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

感谢聆听

Topic report

汇报人：李安妮

时间：2025.12.24