同济大学 TONGJI UNIVERSITY

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

The Yang Research Group
Precise Synthesis Lab at Tongji University

孔望清课题组相关研究介绍

Topic report

汇报人：李安妮

时间：2026.4.17

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第一部分 作者简介

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教育及工作经历：

- 2002-2006 中国地质大学 (武汉), 学士，导师：侯万国 教授
- 2006-2011 浙江大学，博士，导师：麻生明 教授
- 2011-2014 瑞士苏黎世大学 (UZH)，博士后，导师： Cristina Nevado
- 2014-2017 瑞士洛桑联邦理工大学 (EPFL)，博士后，导师：祝介平 教授
- 2017.04-至今 武汉大学高等研究院，教授

研究方向：

（1）金属有机化学：过渡金属不对称催化

（2）自由基化学：发展新的策略实现自由基反应的立体选择性控制

（3）开展具有生物活性天然产物和药物分子的高效合成研究

第二部分

镍催化的活化烯烃通过多米诺环化/交叉偶联的对映选择性还原二芳基化

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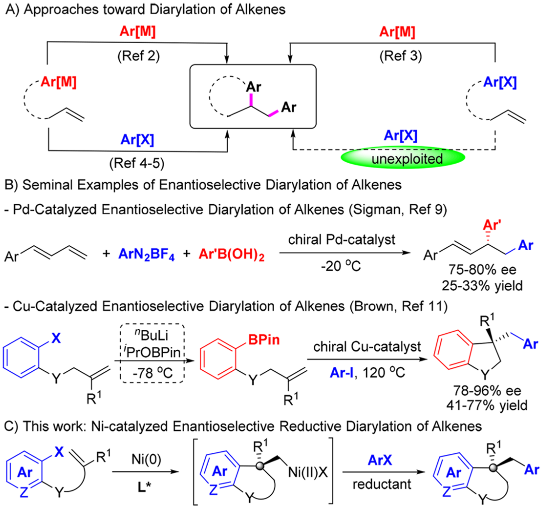
Ni-Catalyzed Enantioselective Reductive Diarylation of Activated Alkenes by Domino Cyclization/Cross-Coupling

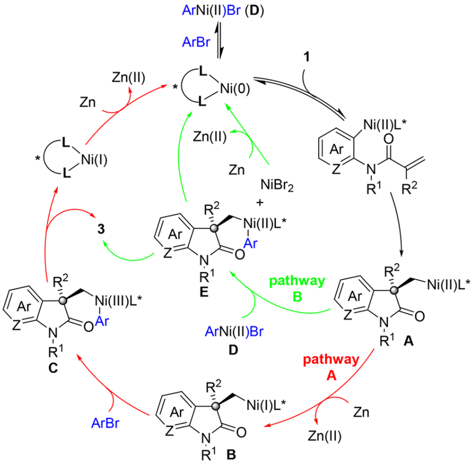
Kuai Wang, Zhengtian Ding, Zhijun Zhou, and Wangqing Kong*

The Institute for Advanced Studies, Wuhan University, Wuhan 430072, People's Republic of China

第二部分 镍催化的活化烯烃通过多米诺环化/交叉偶联的对映选择性还原二芳基化

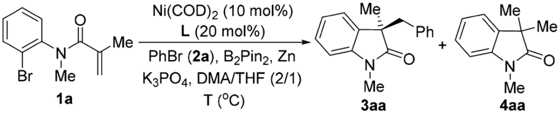


Scheme 6. Proposed Reaction Mechanism

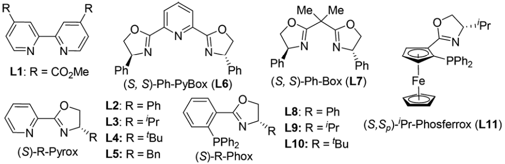


第二部分 镍催化的活化烯烃通过多米诺环化/交叉偶联的对映选择性还原二芳基化

Table 1. Optimization of the Reaction Conditions[a]



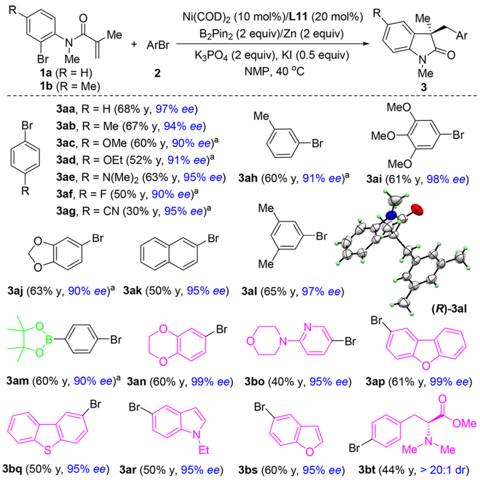
entry	T (°C)	ligand	additive (equiv)	yield of 4aa (%)[b]	yield of 3aa (%)[b]	ee of 3aa (%)[c]
1[d]	100	L1	–	<2	83	–
2	25	L1	–	50	0	–
3	100	L2	–	20	52	44
4	80	L2	–	13	62	45
5	60	L2	–	24	46	52
6	40	L2	–	38	36	62
7	40	L3	–	16	57	16
8	40	L4	–	36	20	41
9	40	L5	–	19	51	28
10	40	L6	–	28	12	0
11	40	L7	–	27	8	6
12	40	L8	–	18	5	n.d.
13	40	L9	–	40	26	77
14	40	L10	–	26	38	90
15	40	L11	–	<2	47	91
16	40	L11	KI (0.5)	<2	63	91
17[e]	40	L11	KI (0.5)	<2	68	97
18[f]	40	L11	KI (0.5)	0	0	–
19[g]	40	L11	KI (0.5)	0	0	–
20	40	–	KI (0.5)	0	0	–
21[h]	40	L11	KI (0.5)	<2	28	97



[a]Reactions were carried out with **1** (0.1 mmol), **2a** (0.4 mmol), $Ni(COD)_2$ (10 mol %), ligand (20 mol %), Zn dust (0.2 mmol), Pin_2B_2 (0.2 mmol), K_3PO_4 (0.2 mmol) in 2 mL solvent for 96 h, unless noted otherwise. [b]Isolated yields. [c]Determined by HPLC analysis with a chiral column. [d]In DMA, 12 h. [e]In NMP. [f]No $Ni(COD)_2$. [g]No Zn^0. [h]No B_2Pin_2. B_2Pin_2 = bis(pinacolato)diboron.

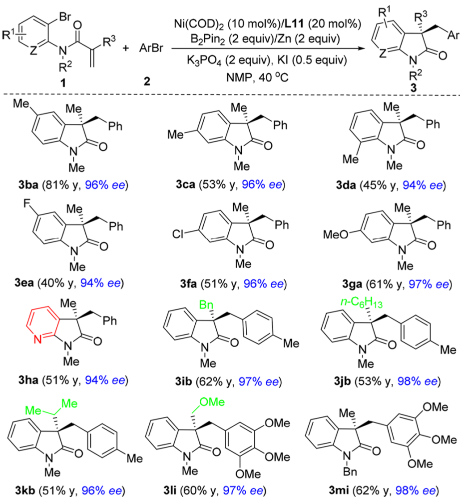
第二部分 镍催化的活化烯烃通过多米诺环化/交叉偶联的对映选择性还原二芳基化

Scheme 2. Substrate Scope of Aryl Bromides 2



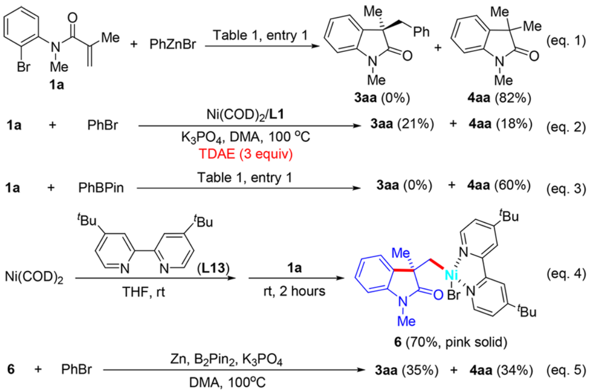
[a]DMA/THF = 2/1

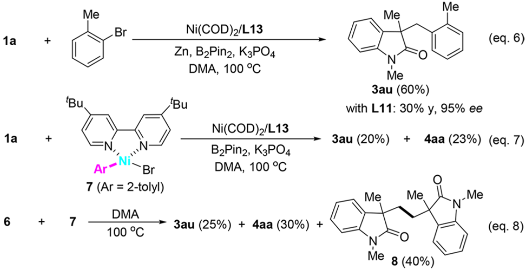
Scheme 3. Substrate Scope of Alkenes 1



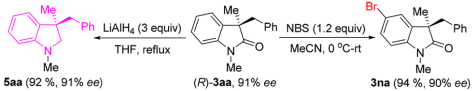
第二部分 镍催化的活化烯烃通过多米诺环化/交叉偶联的对映选择性还原二芳基化

Scheme 5. Mechanistic Study





Scheme 4. Synthetic Conversion of Enantioenriched Oxindoles



第二部分 镍催化的烯烃与二氧化碳的不对称还原性碳羧化反应

Asymmetric Synthesis *Hot Paper*

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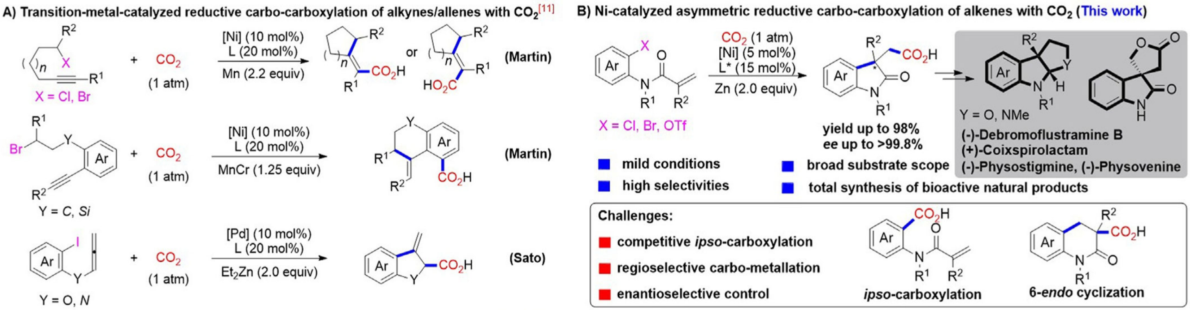
International Edition: doi.org/10.1002/anie.202102769
German Edition: doi.org/10.1002/ange.202102769

Nickel-Catalyzed Asymmetric Reductive Carbo-Carboxylation of Alkenes with CO_2

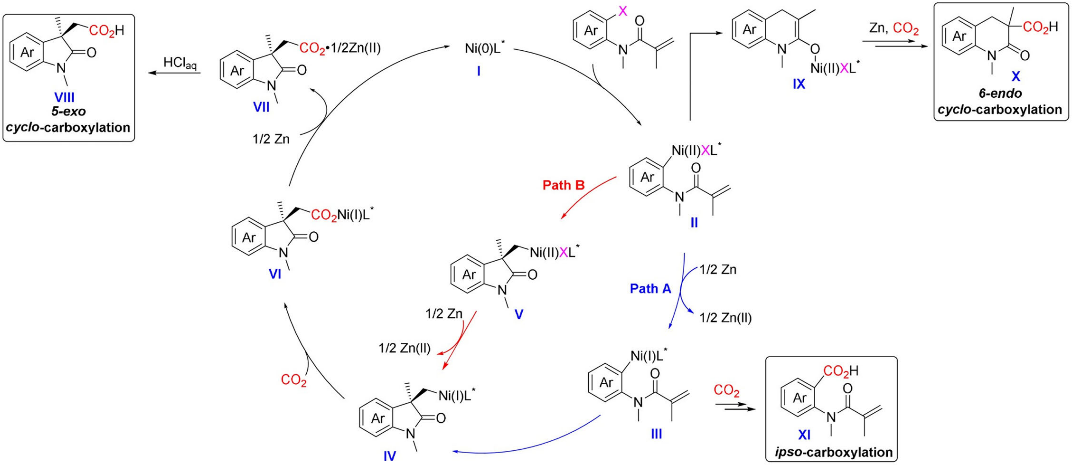
Xiao-Wang Chen, Jun-Ping Yue, Kuai Wang, Yong-Yuan Gui, Ya-Nan Niu, Jie Liu, Chuan-Kun Ran, Wangqing Kong, Wen-Jun Zhou, and Da-Gang Yu**

Dedicated to Professor Peter Kündig and Professor Gerhard Erker on the occasion of their 75th birthdays

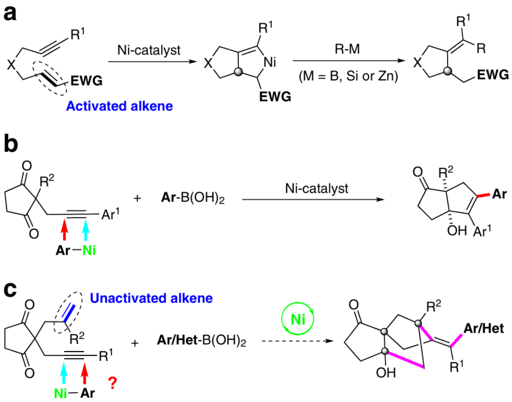
第二部分 镍催化的烯烃与二氧化碳的不对称还原性碳羧化反应

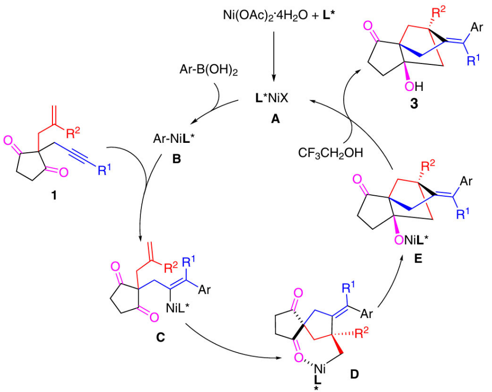


第二部分 镍催化的烯烃与二氧化碳的不对称还原性碳羧化反应



第二部分 通过镍催化的不对称多米诺环化反应合成桥连三环[5.2.1.0^{1,5}]癸烷

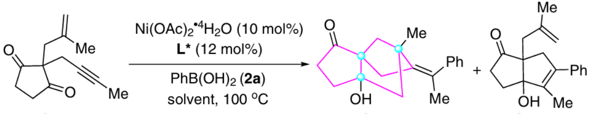




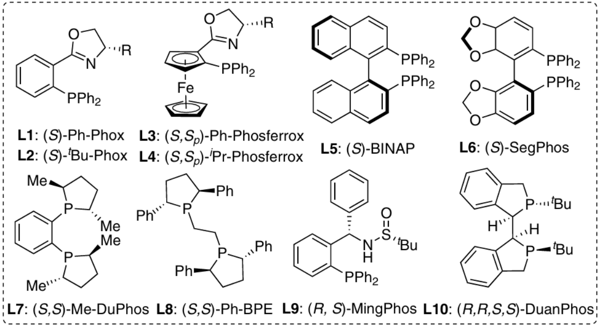
Challenges:
- Regioselective arylnickelation of alkynes
- Low electrophilicity of alkenes compare to ketones
- Enantioselective Heck cyclization

Nat. Commun. **2020**, *11*, 1882-1890.

第二部分 通过镍催化的不对称多米诺环化反应合成桥连三环[5.2.1.0^{1,5}]癸烷



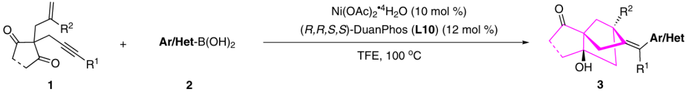
1a 3aa 4aa

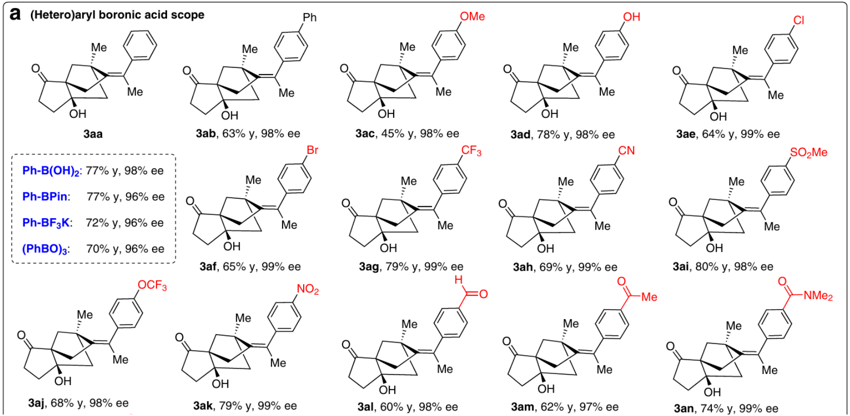


Entry	Ligand	Solvent	Yield of 4aa (%)[b]	Yield of 3aa (%)[b]	ee of 3aa (%)[c]
1	**L1**	MeCN	60	Trace	-
2	**L1**	MeOH	54	Trace	-
3	**L1**	DMF	12	Trace	-
4	**L1**	Toluene	5	Trace	-
5	**L1**	TFE	12	33	71
6	**L2**	TFE	Trace	41	65
7	**L3**	TFE	12	42	76
8	**L4**	TFE	9	46	75
9	**L5**	TFE	24	26	60
10	**L6**	TFE	20	Trace	-
11	**L7**	TFE	Trace	12	25
12	**L8**	TFE	Trace	Trace	-
13	**L9**	TFE	37	Trace	-
14	**L10**	TFE	<1	77	98

TFE 2,2,2-Trifluoroethanol.
[a]Reaction condition: **1a** (0.1 mmol), **2a** (2 equiv), $Ni(OAc)_2.4H_2O$ (0.1 equiv), ligand (0.12 equiv), TFE (1 mL) at 100 °C for 48 h.
[b]yields of isolated products.
[c]Determined by HPLC on a chiral stationary phase.

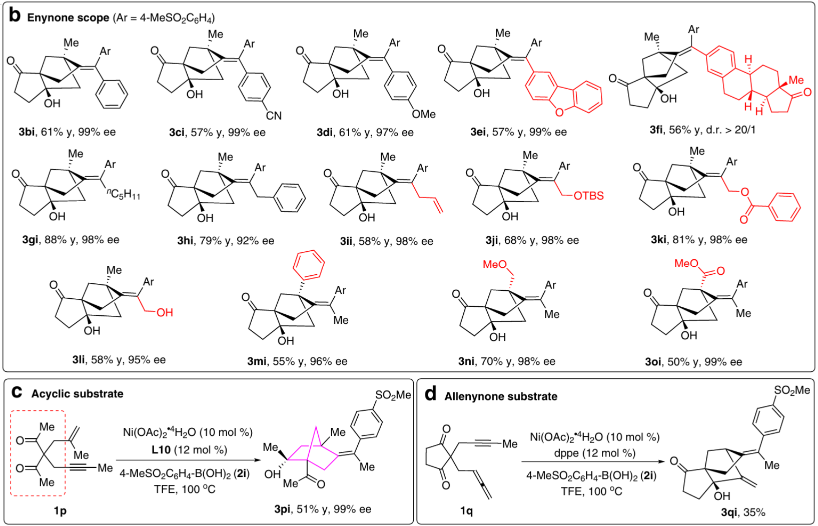
第二部分 通过镍催化的不对称多米诺环化反应合成桥连三环[5.2.1.0^1,5]癸烷



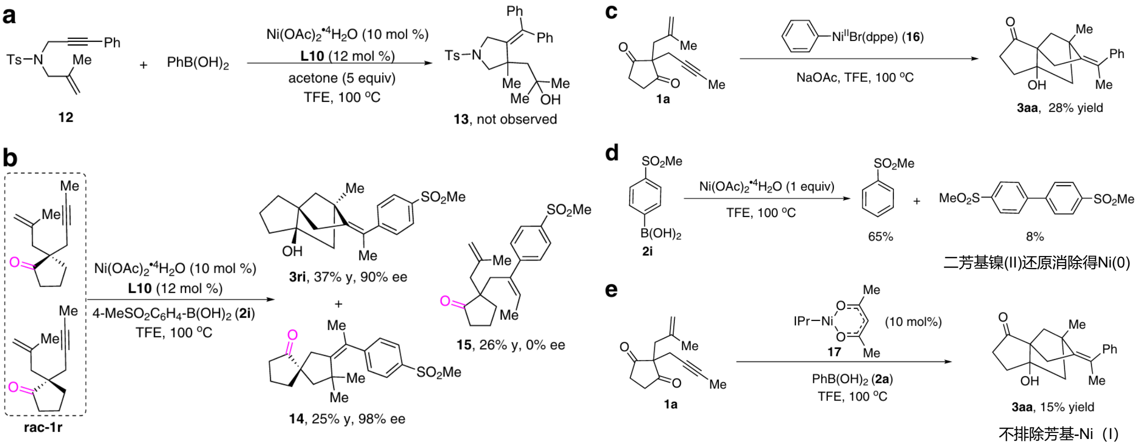


第二部分

通过镍催化的不对称多米诺环化反应合成桥连三环[5.2.1.0^{1,5}]癸烷



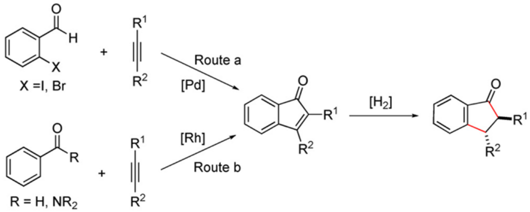
第二部分 通过镍催化的不对称多米诺环化反应合成桥连三环[5.2.1.0^{1,5}]癸烷



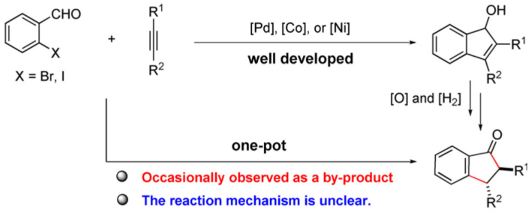
第二部分 基于氢自动转移策略的非对映选择性环化合成茚酮和螺茚酮

(a) Synthetic strategy towards indanones

--Annulation reaction with alkynes to indenones

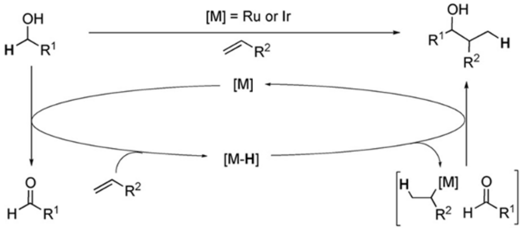


--Annulation of *o*-halobenzaldehydes with alkynes to indenols (Yamamoto, Cheng et al.)



- Occasionally observed as a by-product
- The reaction mechanism is unclear.

(b) Ru- or Ir-catalyzed redox-triggered C-H functionalization of alcohols (Krische)

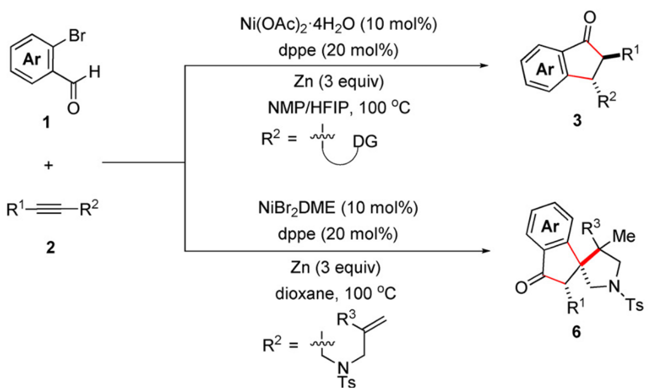


prerequisite:
(1) rare noble metal catalysts: based on Ru, Ir mostly
(2) active π-unsaturated reactants (1,3-dienes, 1,3-enynes or allenes)

Angew. Chem. Int. Ed. **2021**, *60*, 5273–5278.

第二部分 基于氢自动转移策略的非对映选择性环化合成茚酮和螺茚酮

(c) **This work**: Diastereoselective annulation using hydrogen autotransfer strategy



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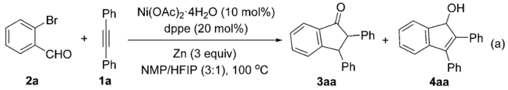
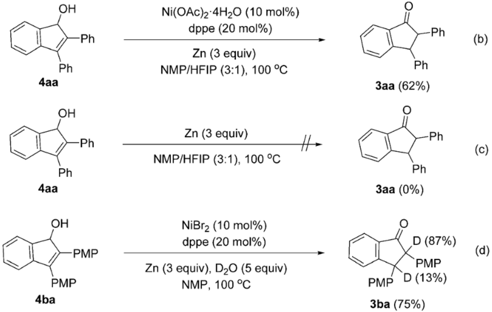
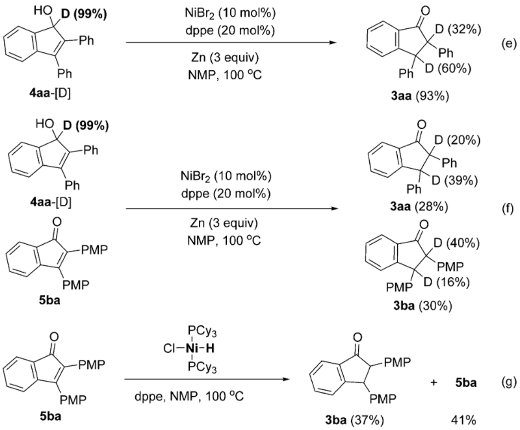
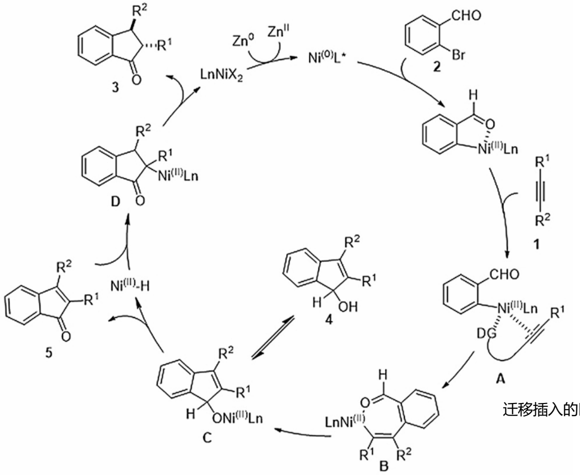


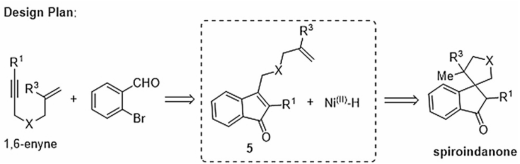
reaction time	yield (%) of **3aa**	yield (%) of **4aa**
12 h	**69**	**21**
36 h	**90**	**0**





第二部分 基于氢自动转移策略的非对映选择性环化合成茚酮和螺茚酮



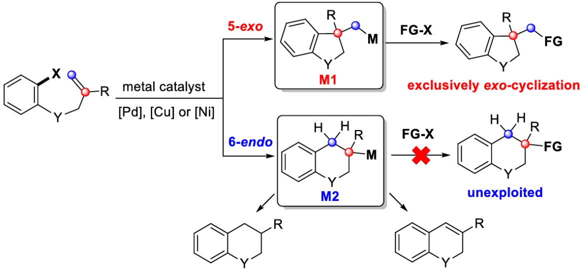


1,6-炔烯的分子内借氢环化

迁移插入的区域选择性由半可逆配体控制

第二部分 镍催化的配体控制的区域发散性还原烯烃双碳官能团化反应

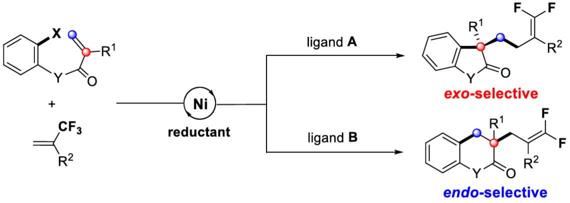
a) Alkene difunctionalization by *exo*-selective cyclization/cross-couplings



Challenges:

- **6-*endo*-Cyclization is kinetically disfavored over 5-*exo*-cyclization**
- **Various side reactions: protonation or β-H elimination**

b) Ligand-controlled regiodivergent alkene difunctionalization reaction

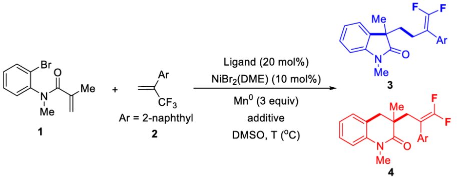


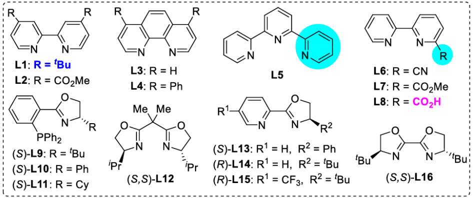
- **Catalyst-controlled**
- **Mild conditions**
- **Excellent regioselectivity**
- **Broad substrate scope**

J. Am. Chem. Soc. **2021**, *143*, 10282−10291.

第二部分 镍催化的配体控制的区域发散性还原烯烃双碳官能团化反应

Table 1. Optimization of the Reaction Conditions[a]

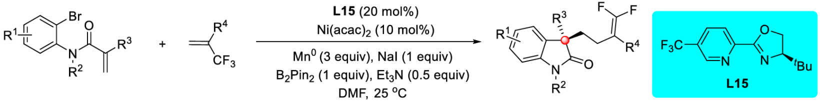


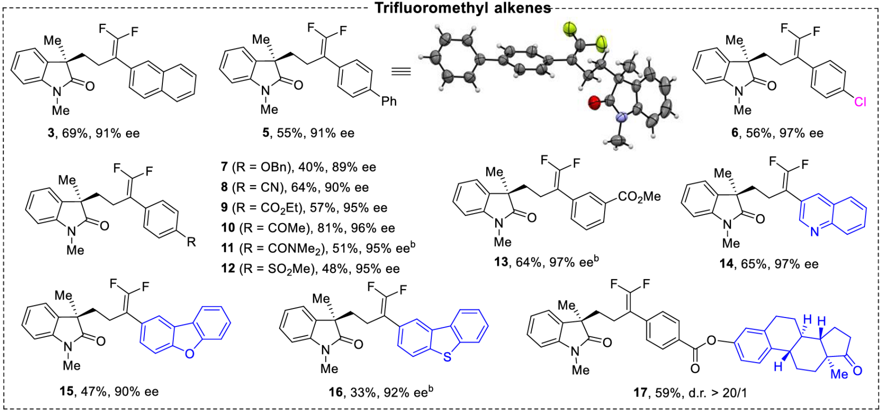


[a]Reaction conditions: **1** (0.1 mmol), **2** (0.2 mmol), $NiBr_2$(DME) (0.01 mmol), ligand (0.02 mmol), Mn^0 powder (0.3 mmol) in DMSO (2 mL) in sealed tube at 60 °C for 48 h. [b]Isolated yield. [c]Determined by HPLC analysis with a chiral column. [d]25 °C. [e]$Ni(acac)_2$ (10 mol %), NaI (0.1 mmol), B_2Pin_2 (0.1 mmol), Et_3N (0.05 mmol) in DMF.

entry	ligand	additive	yield of **3** (%)[b]	ee of **3** (%)[c]	yield of **4** (%)[b]
1	-	-	0	-	0
2	**L1**	-	49	-	< 2
3	**L2**	-	20	-	6
4	**L3**	-	34	-	5
5	**L4**	-	25	-	< 2
6	**L1**	$MgCl_2$	83	-	< 2
7	**L5**	$MgCl_2$	< 2	-	26
8	**L6**	$MgCl_2$	9	-	35
9	**L7**	$MgCl_2$	5	-	32
10	**L8**	$MgCl_2$	< 2	-	77
11	**L8**	-	< 2	-	25
12[d]	**L9**	-	10	36	n.d
13[d]	**L10**	-	48	58	n.d
14[d]	**L11**	-	53	82	n.d
15[d]	**L12**	-	trace	-	trace
16[d]	**L13**	-	38	5	n.d
17[d]	**L14**	-	41	79	n.d
18[d]	**L15**	-	24	87	n.d
19[d]	**L16**	-	trace	-	trace
20[d,e]	**L15**	NaI, B_2Pin_2	62	91	< 2

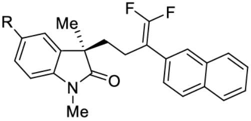
第二部分 镍催化的配体控制的区域发散性还原烯烃双碳官能团化反应





第二部分 镍催化的配体控制的区域发散性还原烯烃双碳官能团化反应

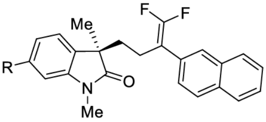
Alkene-tethered aryl bromides



18 (R = Me), 48%, 95% ee[b]

19 (R = OMe), 53%, 96% ee

20 (R = F), 52%, 91% ee[b]

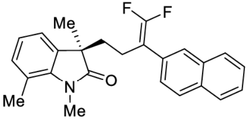


21 (R = Me), 62%, 94% ee[b]

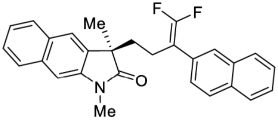
22 (R = OMe), 66%, 94% ee

23 (R = Cl), 51%, 95% ee

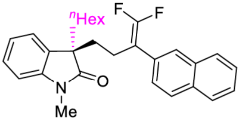
24 (R = Ph), 49%, 93% ee



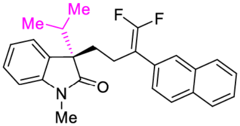
25, 70%, 98% ee



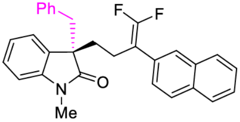
26, 75%, 91% ee



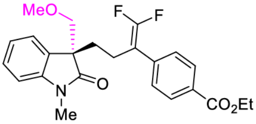
27, 43%, 93% ee[b]



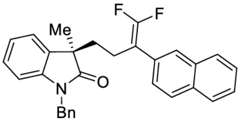
28, 66%, 87% ee



29, 68%, 91% ee

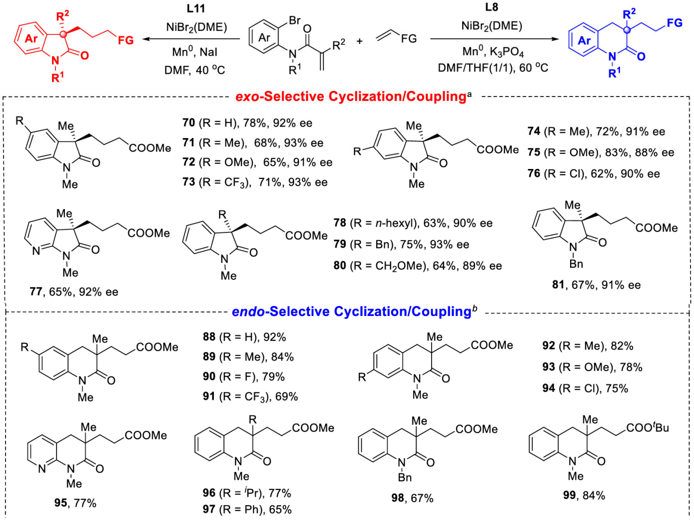


30, 50%, 95% ee



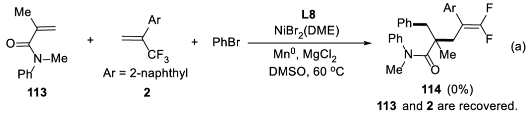
31, 40%, 86% ee[b]

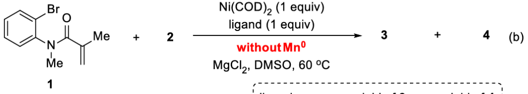
第二部分 镍催化的配体控制的区域发散性还原烯烃双碳官能团化反应



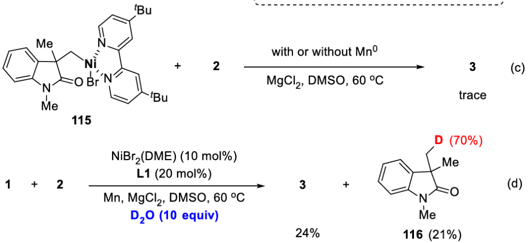
缺电子烯烃也能兼容

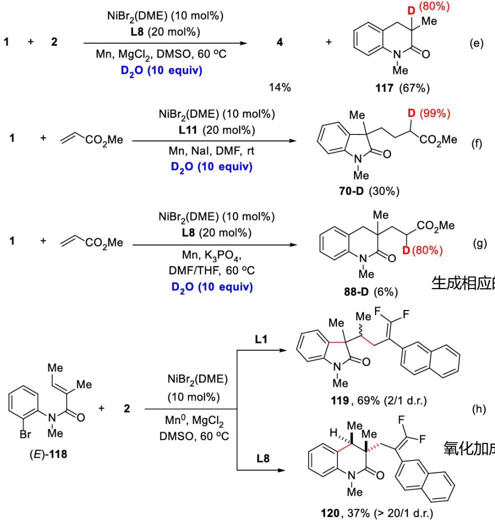
第二部分 镍催化的配体控制的区域发散性还原烯烃双碳官能团化反应





ligand	yield of **3**	yield of **4**
L1	0%	< 2%
L8	0%	**25%**



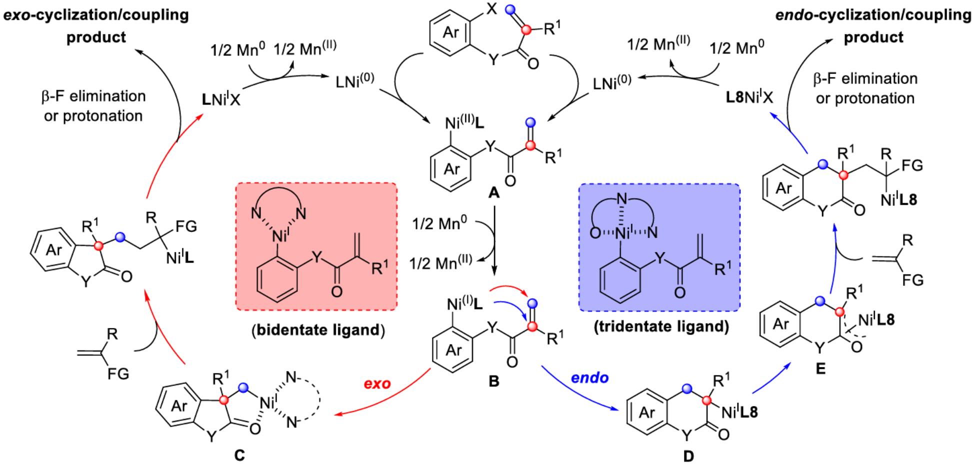


生成相应的镍中间体

氧化加成，迁移插入

第二部分 镍催化的配体控制的区域发散性还原烯烃双碳官能团化反应

Scheme 7. Proposed Mechanism



第二部分 可切换的1,2-重排实现结构多样的含氟骨架的简便合成

JACS JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
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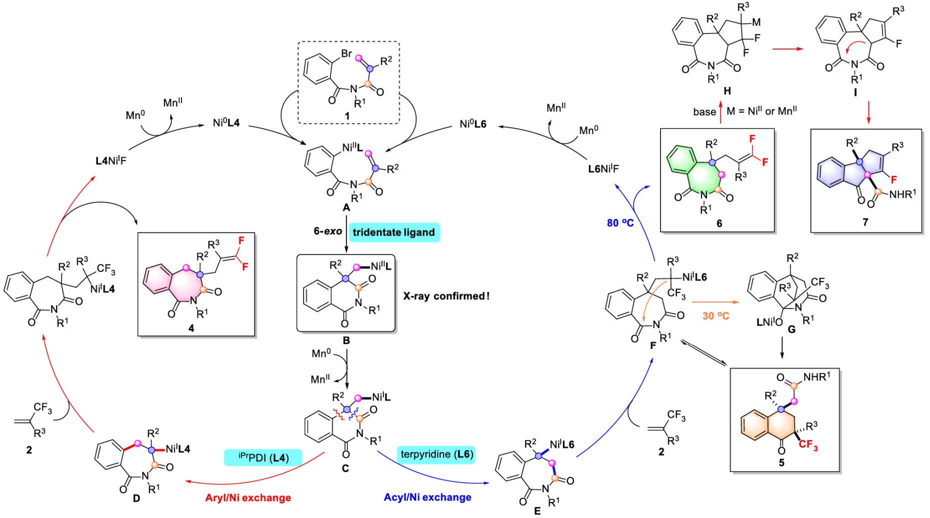
Switchable 1,2-Rearrangement Enables Expedient Synthesis of Structurally Diverse Fluorine-Containing Scaffolds

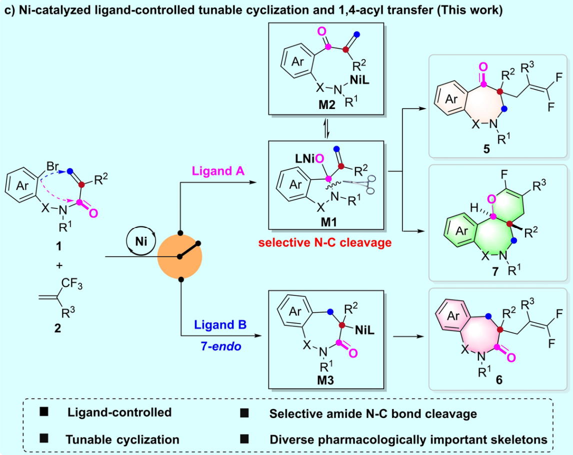
Yuanyuan Ping,§ Qi Pan,§ Ya Guo, Yongli Liu, Xiao Li, Minyan Wang,* and Wangqing Kong*

Cite This: J. Am. Chem. Soc. 2022, 144, 11626−11637 Read Online

第二部分 可切换的1,2-重排实现结构多样的含氟骨架的简便合成



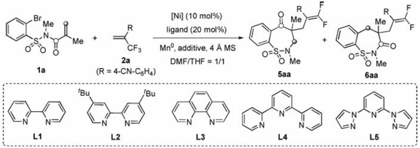
第二部分 镍催化的通过酰胺N-C键断裂触发的可调控环化与1,4-酰基迁移发散合成2-苯并氮杂䓬衍生物



Angew. Chem. Int. Ed. **2022**, *61*, e202201574.

第二部分

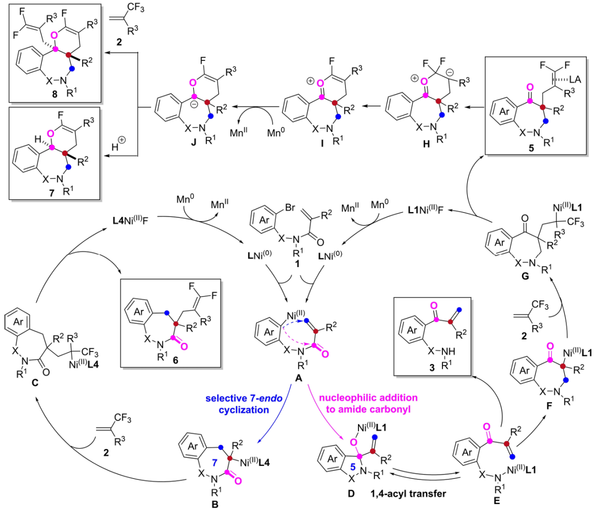
镍催化的通过酰胺N-C键断裂触发的可调控环化与1,4-酰基迁移发散合成2-苯并氮杂草衍生物



entry	[Ni]	ligand	additive	yield of **5aa** [%][b]	yield of **6aa** [%][b]
1	$NiBr_2$·dme	**L1**	–	60	26
2	$NiBr_2$·dme	**L2**	–	57	24
3	$NiBr_2$·dme	**L3**	–	43	32
4	$NiBr_2$·dme	**L4**	–	<**2**	**71**
5	$NiBr_2$·dme	**L5**	–	8	60
6	$Ni(acac)_2$	**L1**	–	53	18
7	$Ni(OTf)_2$	**L1**	–	43	30
8	$Ni(OAc)_2$	**L1**	–	46	32
9[c]	$Ni(acac)_2$	**L1**	–	68	17
10[c]	$Ni(acac)_2$	**L1**	KI	57	12
11[c]	$Ni(acac)_2$	**L1**	$ZnBr_2$	12	37
12[c,d]	$Ni(acac)_2$	**L1**	$MnBr_2$	**78**	<**2**
13	–	**L1**	$MnBr_2$	0	0
14[e]	$Ni(acac)_2$	**L1**	$MnBr_2$	0	0

[a] **1a** (0.1 mmol), **2a** (0.2 mmol), nickel catalyst (0.01 mmol), ligand (0.02 mmol), Mn^0 powder (0.3 mmol), additive (0.2 mmol), 4 Å MS (molecular sieves) (20 mg), DMF/THF = 1/1 (0.05 M) at 60 °C for 48 hours. [b] Isolated yield. [c] DMF/THF = 1/1 (0.025 M). [d] 40 °C. [e] Without Mn^0.

第二部分 镍催化的通过酰胺N-C键断裂触发的可调控环化与1,4-酰基迁移发散合成2-苯并氮杂䓬衍生物



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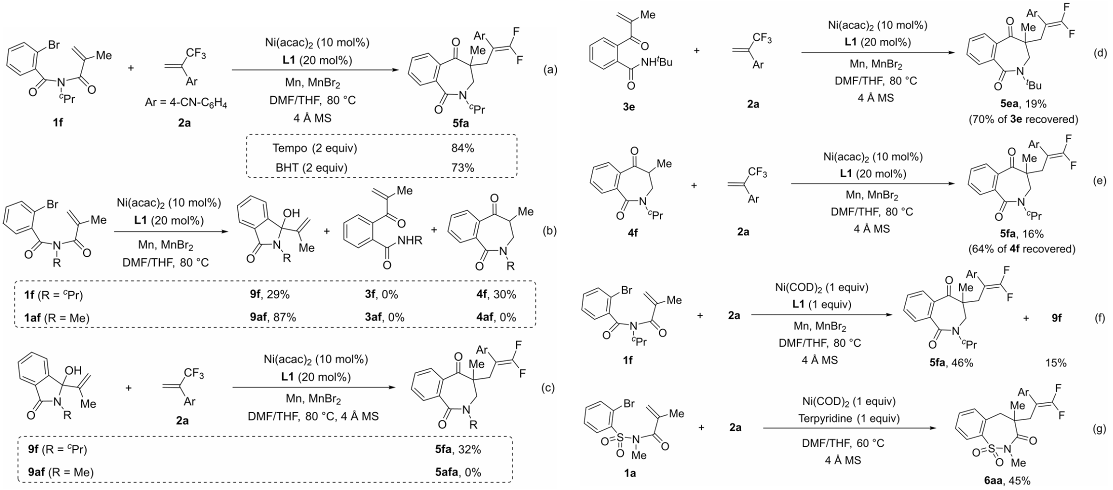
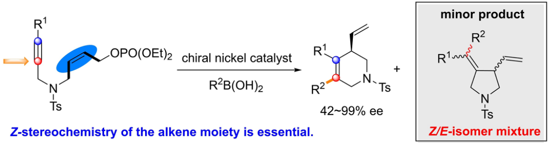
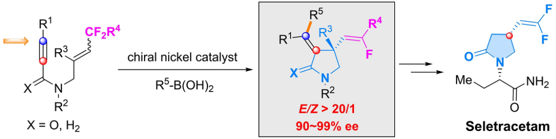


第二部分 镍催化的氟烷基取代的1,6-烯炔的脱氟不对称环化合成塞曲西坦

(a) Synthesis of tetrahydropyridines via allylic alkenylations of *Z*-allylic phosphates (Lam)



(b) Synthesis of 2-pyrrolidones via defluorinative cyclization of 1,6-enynes (This work)

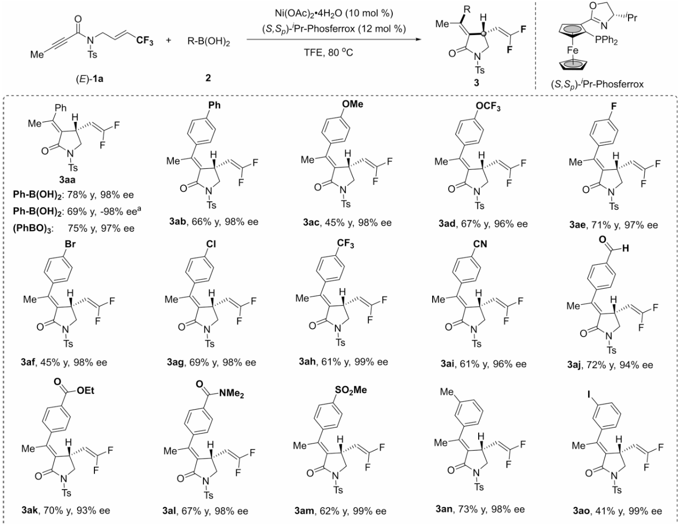


Challenges:

- **Chemoselectivity** (addition to triple bond or double bond)
- **Site-selectivity of alkyne functionalization** (red and blue circles denote sites)
- ***E/Z* selectivity** (reversible *E/Z* isomerization of alkenylnickel species)
- **Enantioselectivity**

Angew. Chem. Int. Ed. **2022**, *61*, e202212664.

第二部分 镍催化的氟烷基取代的1,6-烯炔的脱氟不对称环化合成塞曲西坦



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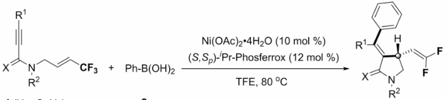
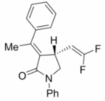
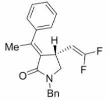


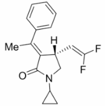
1 (X = O, H_2) **2a** **3**



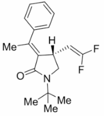
3ba, 57%, 97% ee



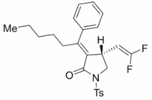
3ca, 62%, 98% ee



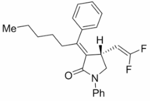
3da, 57%, 98% ee



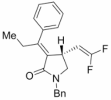
3ea, 55%, 83% ee



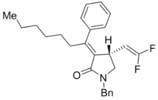
3fa, 84%, 99% ee



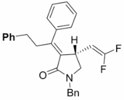
3ga, 60%, 97% ee



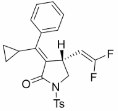
3ha, 60%, 97% ee



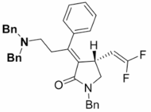
3ia, 68%, 97% ee



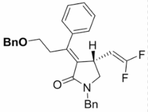
3ja, 66%, 97% ee



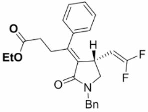
3ka, 50%, 98% ee



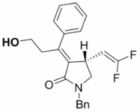
3la, 59%, 97% ee



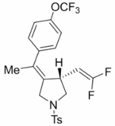
3ma, 62%, 99% ee



3na, 60%, 98% ee

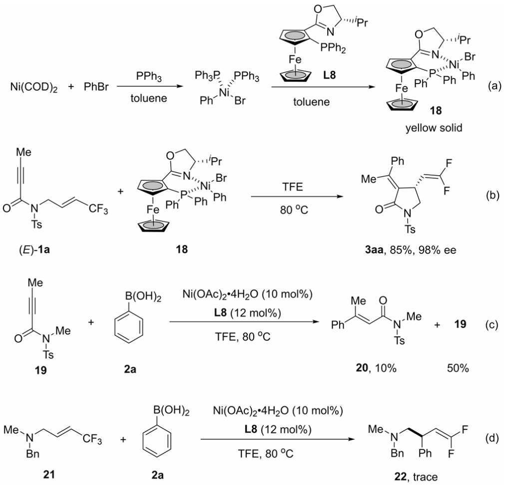


3oa, 62%, 97% ee



3pd, 31%, 98% ee

第二部分 镍催化的氟烷基取代的1,6-烯炔的脱氟不对称环化合成塞曲西坦

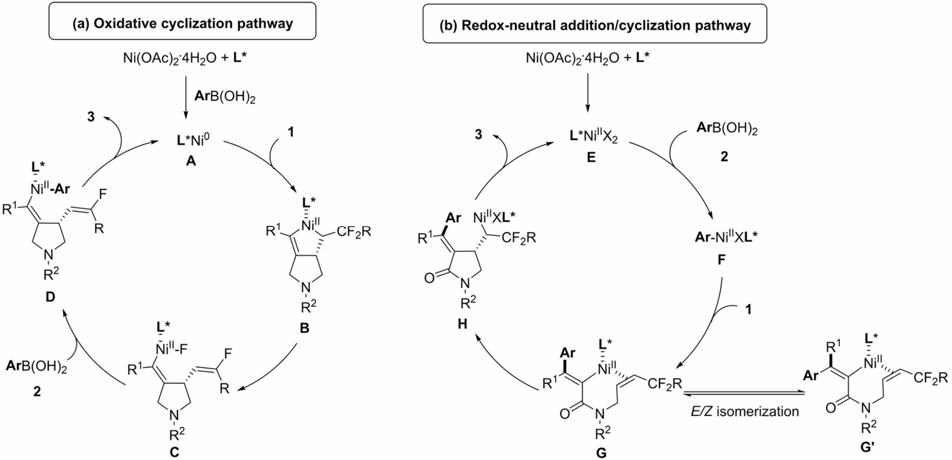


Scheme 6. Mechanistic studies.

催化剂可能需要1,6-炔烯配位，同时三氟甲基烯烃的脱氟可能是反应进行的驱动力

金属未直接加成到烯烃上

第二部分 镍催化的氟烷基取代的1,6-烯炔的脱氟不对称环化合成塞曲西坦



第二部分 镍催化的1,6-烯炔和1,7-烯炔的对映选择性还原环化/酰胺化及胺化

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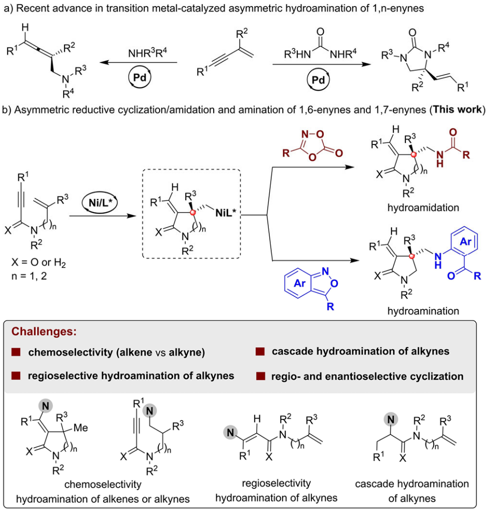
doi.org/10.1002/anie.202413892

Asymmetric Catalysis

Ni-Catalyzed Enantioselective Reductive Cyclization/Amidation and Amination of 1,6-Enynes and 1,7-Enynes

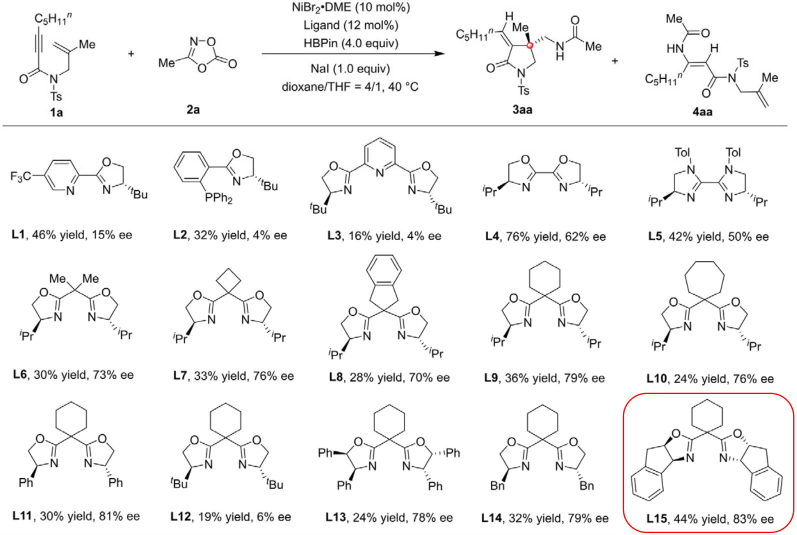
Shengwei Hu+, Xiaoqin Wang+, Tianbao Wu+, Zhengtian Ding, Minyan Wang, and Wangqing Kong**

第二部分 镍催化的1,6-烯炔和1,7-烯炔的对映选择性还原环化/酰胺化及胺化



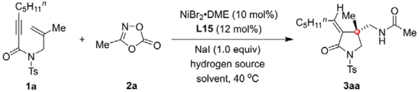
第二部分

镍催化的1,6-烯炔和1,7-烯炔的对映选择性还原环化/酰胺化及胺化



第二部分 镍催化的1,6-烯炔和1,7-烯炔的对映选择性还原环化/酰胺化及胺化

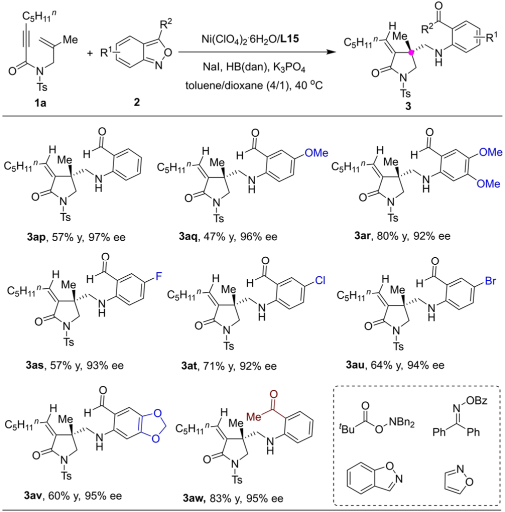
Table 1: Optimization of the reaction conditions.[a]

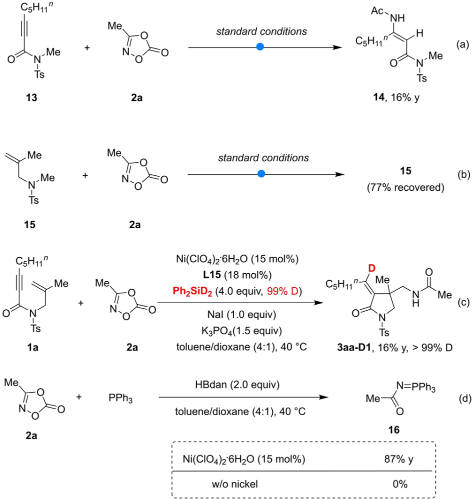


entry	hydrogen source	solvent	yield (%)[b]	ee (%)[c]
1	HBPin	dioxane/THF (4/1)	44	83
2	HBPin	THF	34	55
3	HBPin	MeCN	10	0
4	HBPin	dioxane	41	83
5	HBPin	DCE	40	70
6	HBPin	toluene/dioxane (4/1)	45	86
7	HB(dan)	toluene/dioxane (4/1)	54	90
8	$(EtO)_3SiH$	toluene/dioxane (4/1)	17	89
9	Et_3SiH	toluene/dioxane (4/1)	trace	–
10	Ph_2SiH_2	toluene/dioxane (4/1)	15	–
11	$NaBH_4$	toluene/dioxane (4/1)	trace	–
12[d]	HB(dan)	toluene/dioxane (4/1)	53	97
13[d,e]	HB(dan)	toluene/dioxane (4/1)	68	95

[a] Reactions were carried out with **1a** (0.1 mmol), **2a** (0.4 mmol), $NiBr_2$(DME) (10 mol%), **L15** (12 mol%), NaI (0.1 mmol), hydrogen source (0.4 mmol) in 1 mL solvent at 40 °C, unless noted otherwise. [b] Isolated yield. [c] Determined by HPLC analysis with a chiral column. [d] K_3PO_4 (1.5 equiv) was added. [e] $Ni(ClO_4)_2\cdot6H_2O$ (15 mol%) was used instead of $NiBr_2$(DME). HBDan (Dan = 1,8-diaminonaphthalene); HBPin: pinacolborane.

第二部分 镍催化的1,6-烯炔和1,7-烯炔的对映选择性还原环化/酰胺化及胺化

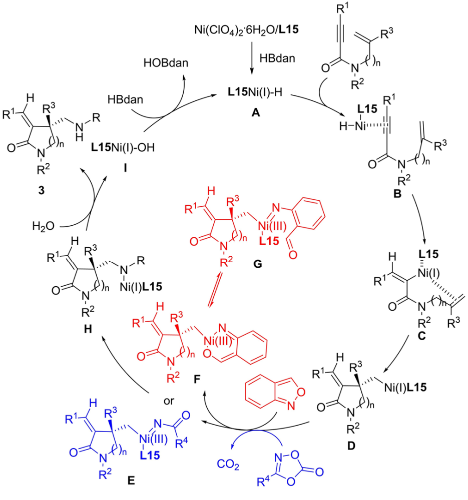




底物与镍之间存在螯合作用，从而控制了炔烃氢胺化的区域选择性。

非线性曲线表明：配体与底物1：1配位

第二部分 镍催化的1,6-烯炔和1,7-烯炔的对映选择性还原环化/酰胺化及胺化



Scheme 9. Proposed mechanism.

第二部分 配体控制的镍催化立体发散性构建1,3-非相邻立体中心

JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
pubs.acs.org/JACS Article

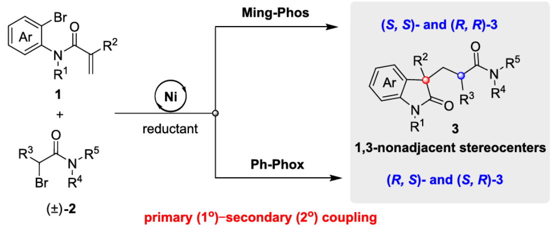
Ligand-Controlled, Nickel-Catalyzed Stereodivergent Construction of 1,3-Nonadjacent Stereocenters

Qi Pan,[∥] Kuai Wang,[∥] Weipeng Xu,[∥] Yuqi Ai, Yuanyuan Ping, Chuhan Liu, Minyan Wang,* Junliang Zhang,* and Wangqing Kong*

Cite This: J. Am. Chem. Soc. 2024, 146, 15453−15463 Read Online

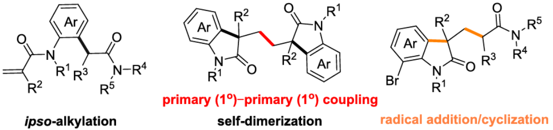
第二部分 配体控制的镍催化立体发散性构建1,3-非相邻立体中心

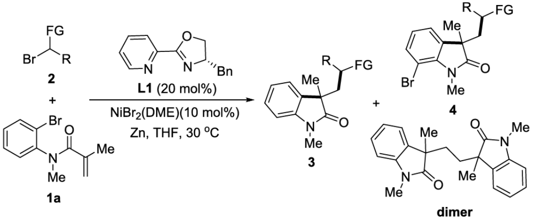
c) Ligand-controlled stereodivergent construction of 1,3-nonadjacent stereocenters



Challenges:

- competitive *ipso*-alkylation
- self-dimerization
- radical addition/cyclization
- enantioselective and diastereoselective control



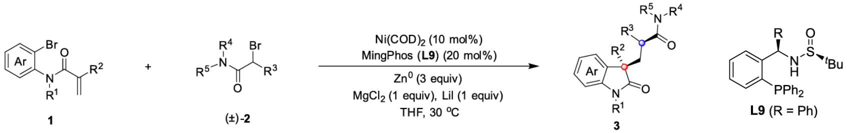


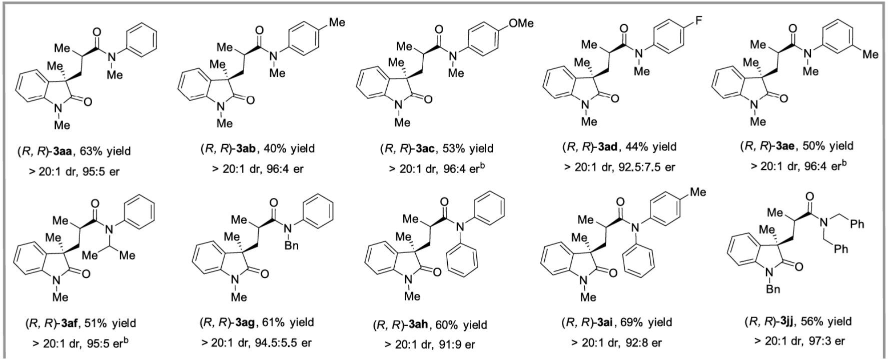
2a (R = Me, FG = CONMePh)	**3aa** (65%) +	**4aa** (trace) +	**dimer** (15%)
2o (R = Me, FG = CO_2Ph)	**3ao** (trace) +	**4ao** (trace) +	**dimer** (55%)
2p (R = $PhCH_2CH_2$, FG = CF_3)	**3ap** (trace) +	**4ap** (trace) +	**dimer** (45%)
2q (R = $PhCH_2CH_2$, FG = CN)	**3aq** (trace) +	**4aq** (45%) +	**dimer** (10%)

Figure 1. Effect of activated secondary alkyl electrophiles.

第二部分 配体控制的镍催化立体发散性构建1,3-非相邻立体中心

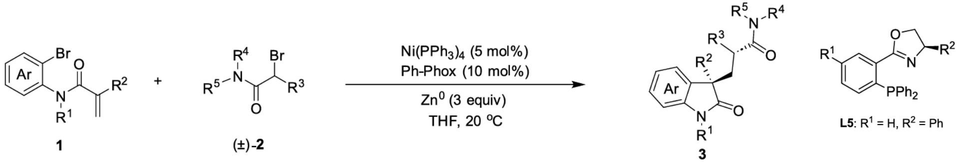
Scheme 3. Substrate Scope for the Synthesis of (*R*,*R*)-3[a]

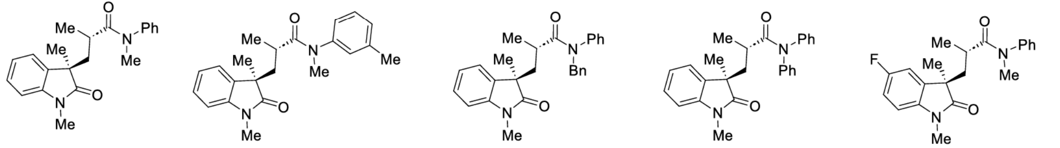




第二部分 配体控制的镍催化立体发散性构建1,3-非相邻立体中心

a) Substrate scope





(*R*, *S*)-**3aa**, 60% yield, 3:1 d.r. (46% yield, 96:4 er)[a]

(*R*, *S*)-**3ae**, 54% yield, 2.9:1 d.r. (40% yield, 96.5:3.5 er)[a]

(*R*, *S*)-**3ag**, 60% yield, 3:1 d.r. (45% yield, 98:2 er)[a]

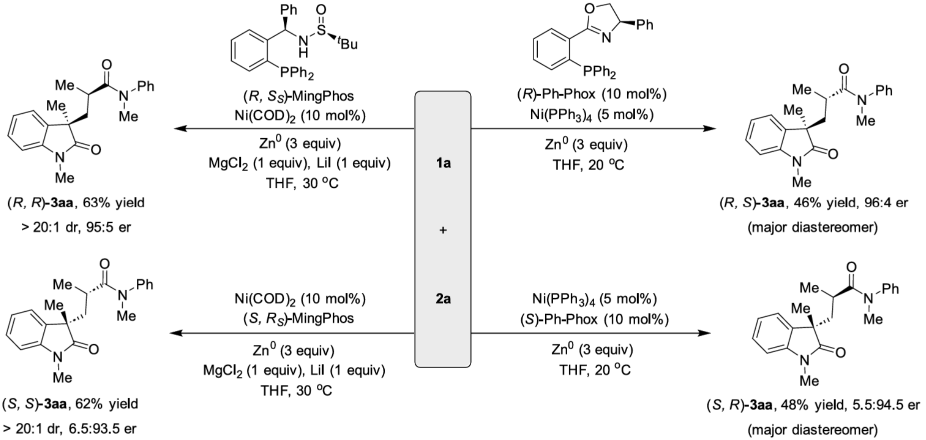
(*R*, *S*)-**3ah**, 50% yield, 3:1 d.r. (38% yield, 95.5:4.5 er)[a]

(*R*, *S*)-**3ca**, 50% yield, 3.2:1 d.r. (38% yield, 96.5:3.5 er)[a]

[a]Values in parentheses represent the isolated yield and enantiomeric ratio (er) of the major diastereomer.

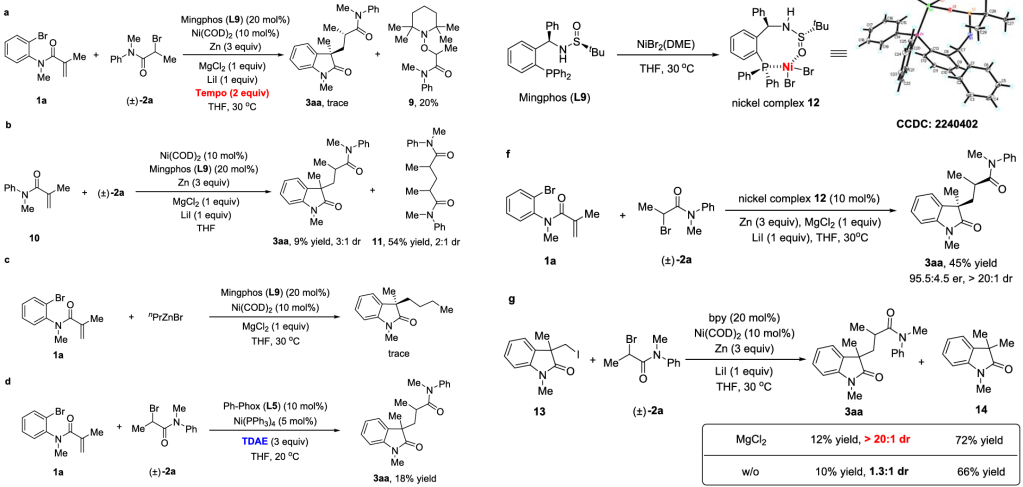
第二部分 配体控制的镍催化立体发散性构建1,3-非相邻立体中心

b) Stereodivergent synthesis of all four stereoisomers of **3aa**



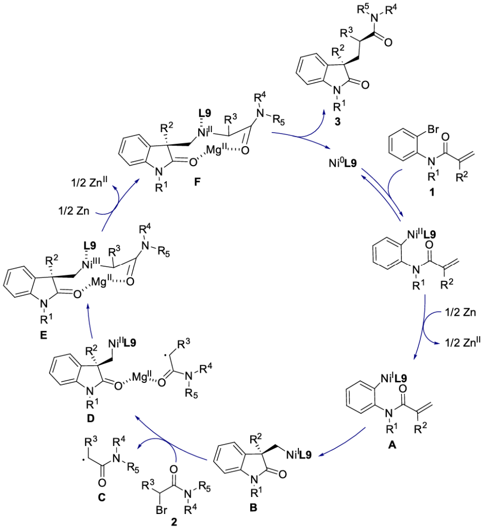
第二部分 配体控制的镍催化立体发散性构建1,3-非相邻立体中心

Scheme 6. Mechanistic Studies



	3aa	14
MgCl2	12% yield, > 20:1 dr	72% yield
w/o	10% yield, 1.3:1 dr	66% yield

第二部分 配体控制的镍催化立体发散性构建1,3-非相邻立体中心



第二部分 使用烯烃对饱和杂环进行直接立体选择性的C(sp³)–H烷基化

nature chemistry

Article https://doi.org/10.1038/s41557-025-01747-6

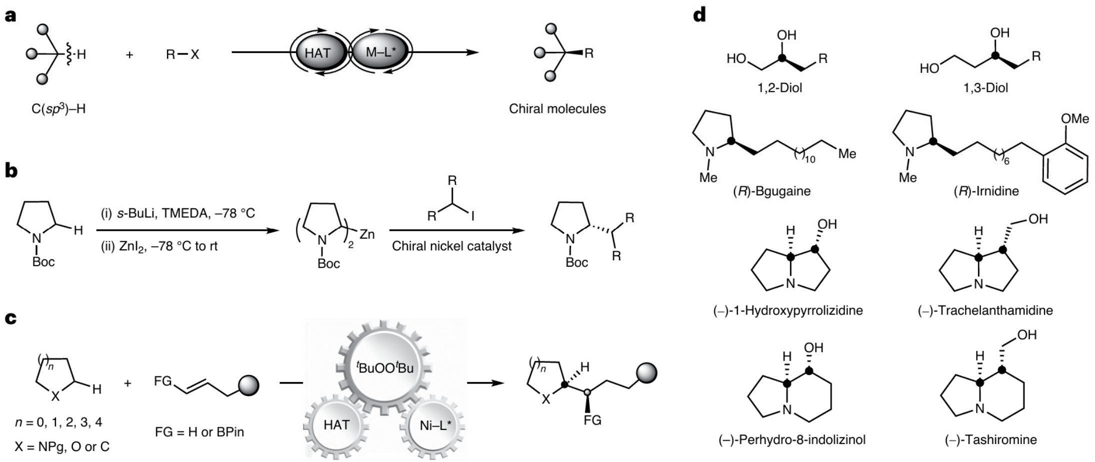
Direct stereoselective C(sp^3)–H alkylation of saturated heterocycles using olefins

Received: 16 July 2024

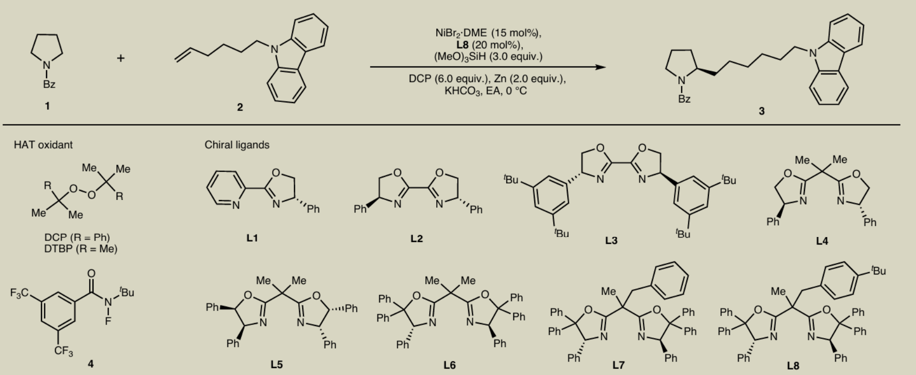
Accepted: 17 January 2025

Zhijun Zhou[1,3], Yang Ke[1,3], Rui Miao[1], Fen Hu[1], Xiaoqin Wang[1], Yuanyuan Ping[1]✉, Sheng Xu[1] & Wangqing Kong[1,2]✉

第二部分 使用烯烃对饱和杂环进行直接立体选择性的C(sp³)–H烷基化



第二部分 使用烯烃对饱和杂环进行直接立体选择性的C(sp³)–H烷基化



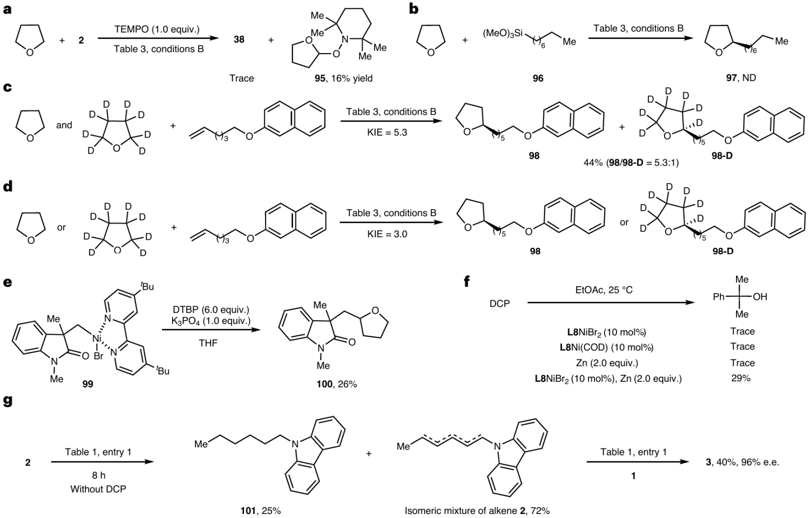
Entry	Variants	Yield (%)[a]	e.e. (%)[b]
1	None	69 (61)	97
2	NFSI instead of DCP	Trace	ND
3	**4** instead of DCP	Trace	ND

第二部分 使用烯烃对饱和杂环进行直接立体选择性的C(sp³)–H烷基化

4	DTBP instead of DCP	53	97
5	BPO instead of DCP	Trace	ND
6	**L1**	Trace	ND
7	**L2**	Trace	ND
8	**L3**	Trace	ND
9	**L4**	Trace	ND
10	**L5**	Trace	ND
11	**L6**	37	87
12	**L7**	58	95
13	PMHS instead of $(MeO)_3SiH$	54	97
14	DEMS instead of $(MeO)_3SiH$	40	97
15	In the dark	68	97
16	Without Zn	40	97
17	Without nickel or silane or DCP	Trace	ND

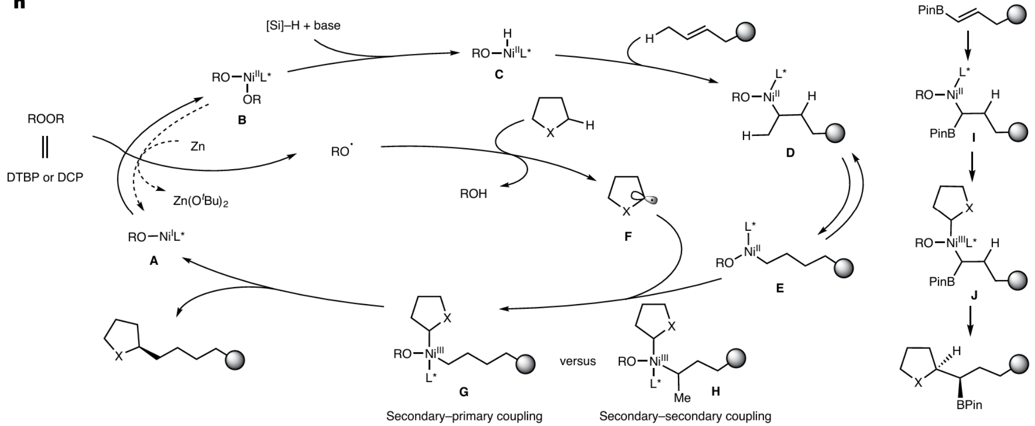
Reaction conditions: **2** (0.1 mmol, 1.0 equiv.), pyrrolidine **1** (0.5 mmol), $NiBr_2$·DME (15 mol%), **L8** (20 mol%), DCP (6.0 equiv.), $(MeO)_3SiH$ (3.0 equiv.), Zn (2.0 equiv.), $KHCO_3$ (1.0 equiv.), EA (50 µl), 0 °C. [a]Determined by gas chromatography using *n*-dodecane as the internal standard. The value in parentheses corresponds to the yield of the isolated product after column chromatography. [b]Determined by HPLC using a chiral stationary phase. Bz, benzoyl; EA, ethyl acetate; ND, not detected.

第二部分 使用烯烃对饱和杂环进行直接立体选择性的C(sp³)–H烷基化



第二部分 使用烯烃对饱和杂环进行直接立体选择性的C(sp³)–H烷基化

h



第三部分 通过直接和选择性活化脂肪族C-H键的三组分烯烃双官能团化

C–H Activation

How to cite: *Angew. Chem. Int. Ed.* **2021**, *60*, 7405–7411
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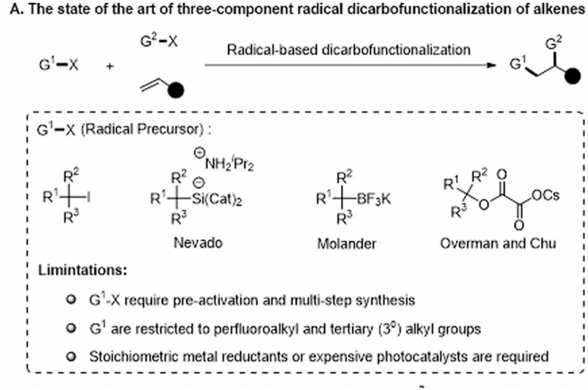
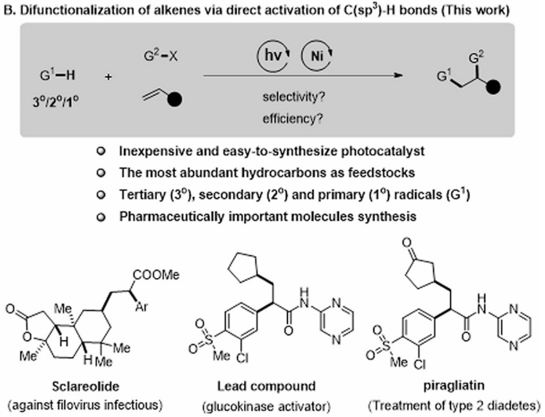
German Edition: doi.org/10.1002/ange.202014632

Three-Component Alkene Difunctionalization by Direct and Selective Activation of Aliphatic C–H Bonds

*Sheng Xu, Herong Chen, Zhijun Zhou, and Wangqing Kong**

第三部分 通过直接和选择性活化脂肪族C-H键的三组分烯烃双官能团化





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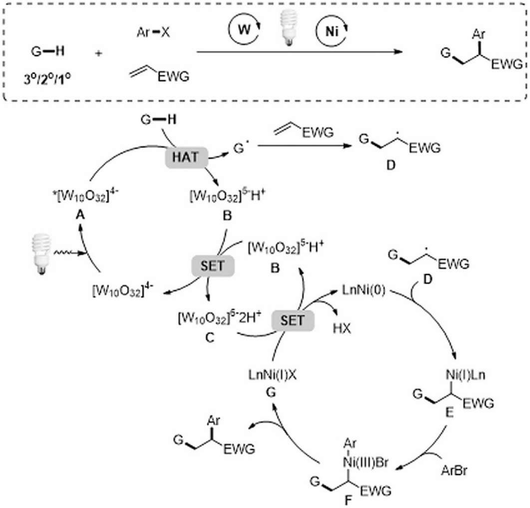


Undesired side reactions:

(1) Arylation of aliphatic C-H bonds

G–Ar

(2) Giese addition

G–CH₂CH₂–EWG

(3) Heck reaction

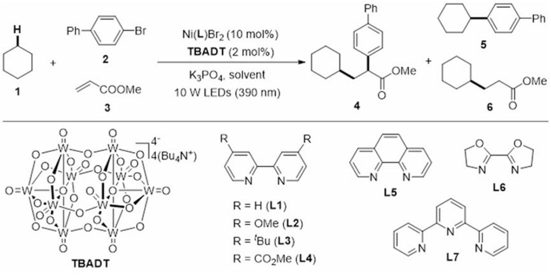
Ar–CH=CH–EWG

(4) Dehalogenation

Ar-H

第三部分 通过直接和选择性活化脂肪族C-H键的三组分烯烃双官能团化

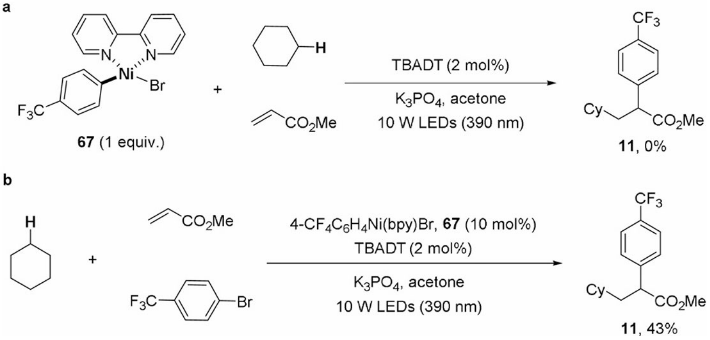
Table 1: Optimization of the reaction conditions.[a]



Entry	Ni(L)Br_2	Solvent	Yield of **4** (%)[b]	Yield of **5** (%)[b]	Yield of **6** (%)[b]
1	**L1**	MeCN	23	30	32
2	**L2**	MeCN	20	30	36
3	**L3**	MeCN	35	15	27
4	**L4**	MeCN	22	18	54
5	**L5**	MeCN	no reaction		
6	**L6**	MeCN	no reaction		
7	**L7**	MeCN	no reaction		
8	**L3**	acetone	57	13	17
9	**L3**	DCM	no reaction		
10	**L3**	DMSO	No reaction		
11[c]	**L3**	acetone	66	6	13
12[d]	**L3**	acetone	71	<2	8
13[d,e]	**L3**	acetone	63	11	5
14[d,f]	**L3**	acetone	61	12	7
15[d]	-	acetone	no reaction		
16[d,g]	**L3**	acetone	no reaction		
17[d,h]	**L3**	acetone	no reaction		

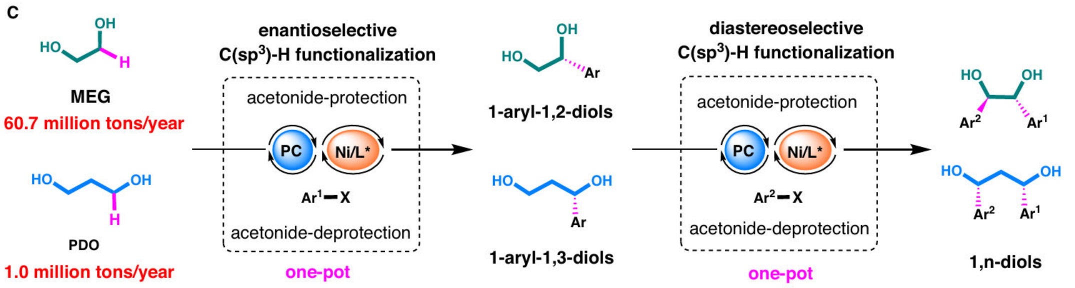
[a] Reactions conditions: **1** (2 mmol), **2** (0.2 mmol), **3** (0.6 mmol), Ni(**L**)Br_2 (10 mol%), TBADT (2 mol%), K_3PO_4 (0.4 mmol) in solvent (2 mL) at 30 °C under irradiation of LEDs (10 W, 390 nm) for 18 hours. [b] Yields of isolated products. [c] Acetone (1 mL). [d] Acetone (0.5 mL). [e] 1.5 E of alkene **3** were used. [f] 5 Equivalents of cyclohexane were used. [g] Without TBADT. [h] Without light.

第三部分 通过直接和选择性活化脂肪族C-H键的三组分烯烃双官能团化



Scheme 6. Mechanistic study.

第三部分 催化立体选择性合成手性1,2-二醇和1,3-二醇的模块化方法



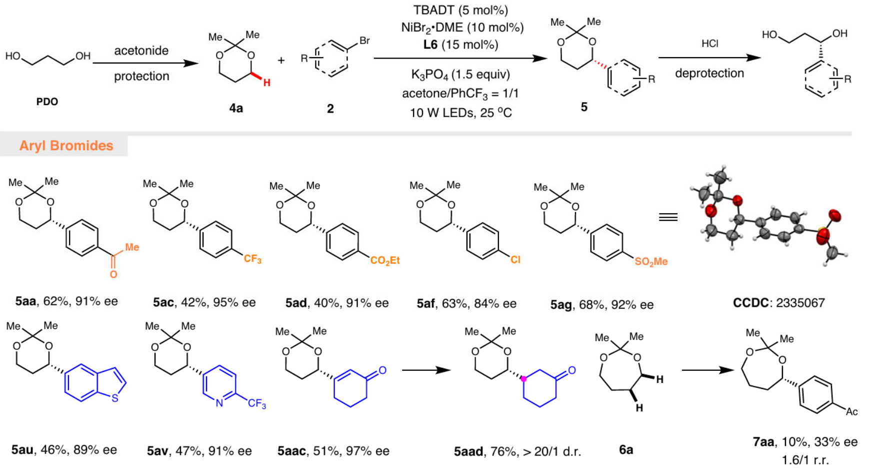
Advantages:

- Abundant C(sp^3)-H feedstocks (MEG and PDO)
- Atom and step economy
- Rapid access to high value-added chiral diols

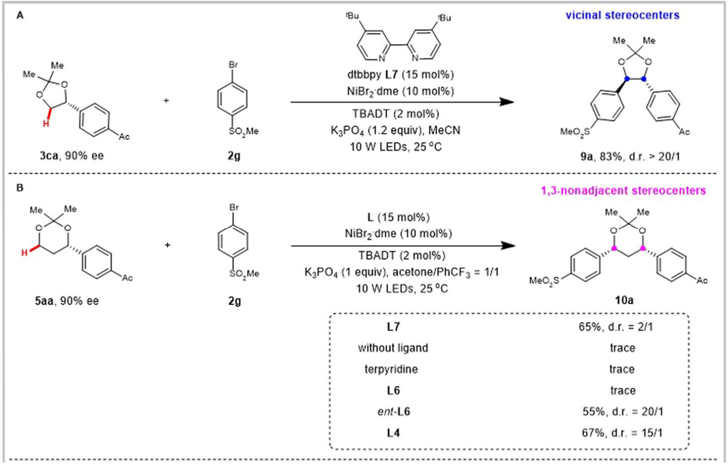
Challenges:

- Regioselectivity, enantioselectivity and diastereoselectivity
- Competitive *O*-arylation of alcohols with aryl bromides
- Optically pure 1,n-*syn*-diols synthesis

第三部分 催化立体选择性合成手性1,2-二醇和1,3-二醇的模块化方法



第三部分 催化立体选择性合成手性1,2-二醇和1,3-二醇的模块化方法



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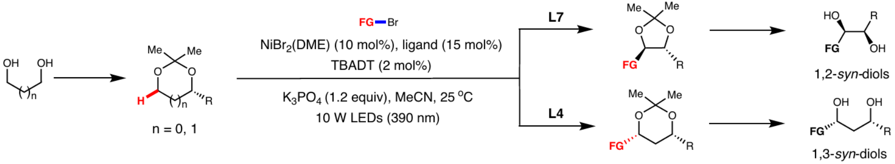
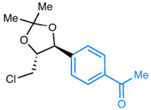
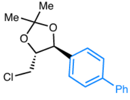


1,2-diols bearing vicinal stereocenters[a]



9b (R = Ac), 88% yield, d.r. > 20/1
9c (R = CN), 83% yield, d.r. > 20/1
9d (R = CO_2Et), 80% yield, d.r. > 20/1
9e (R = SO_2Me), 80% yield, d.r. > 20/1
9f (R = OMe), 70% yield, d.r. > 20/1
9g (R = NHAc), 63% yield, d.r. > 20/1
9h (R = OPiv), 66% yield, d.r. > 20/1



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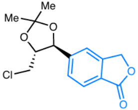
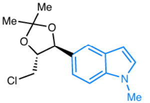
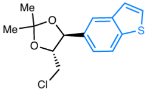
9i, 66% yield, d.r. > 20/1



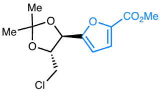
9j, 77% yield, d.r. > 20/1



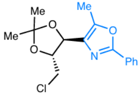
9k, 53% yield, d.r. > 20/1



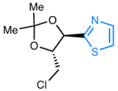
9l, 57% yield, d.r. > 20/1



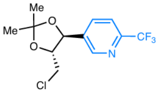
9m, 61% yield, d.r. > 20/1



9n, 51% yield, d.r. > 20/1

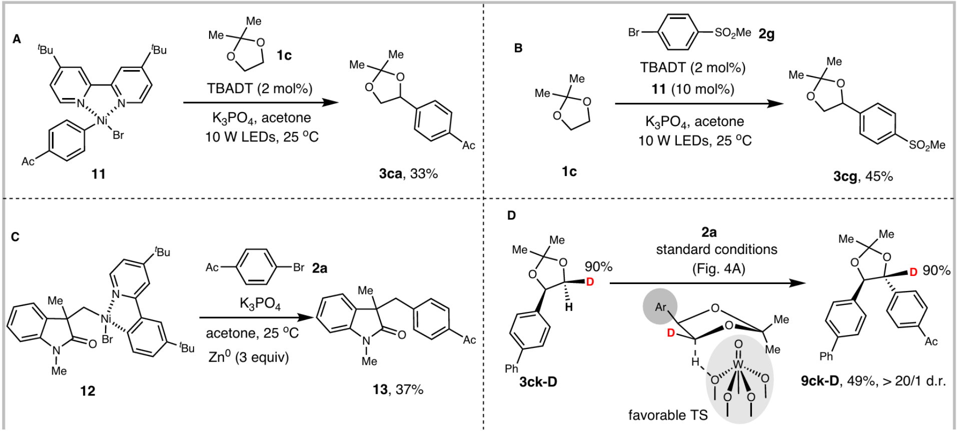


9o, 43% yield, d.r. > 20/1



9p, 85% yield, d.r. > 20/1

第三部分 催化立体选择性合成手性1,2-二醇和1,3-二醇的模块化方法



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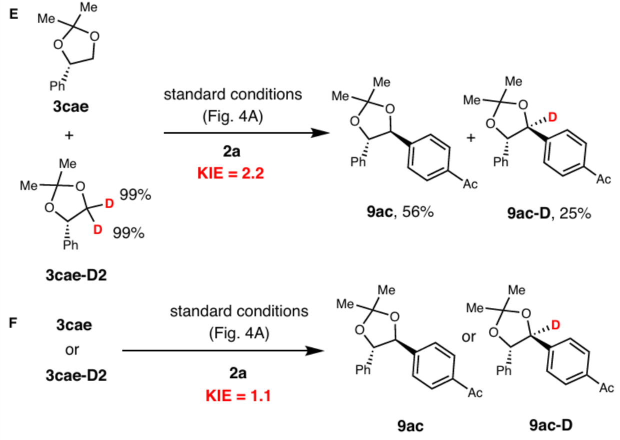

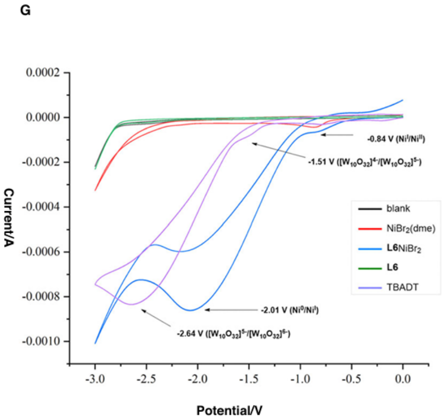

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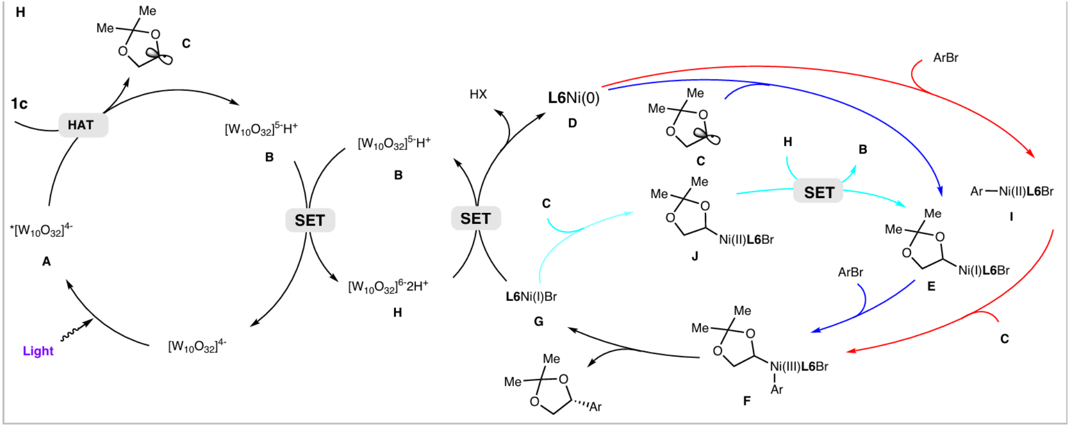

第三部分 通过光诱导氢原子转移/镍双重催化实现氧杂环的对映选择性$C(sp^3)$-H键官能团化

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Article

Enantioselective $C(sp^3)$–H Functionalization of Oxacycles via Photo-HAT/Nickel Dual Catalysis

Sheng Xu, Yuanyuan Ping, Wei Li, Haoyun Guo, Yinyan Su, Ziyang Li, Minyan Wang,*
and Wangqing Kong*

Cite This: *J. Am. Chem. Soc.* 2023, 145, 5231–5241

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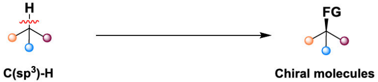
第三部分 通过光诱导氢原子转移/镍双重催化实现氧杂环的对映选择性C(sp³)-H键官能团化

(a) The advantages and challenges of asymmetric C(sp^3)-H functionalization



Advantages:
- Abundant hydrocarbon feedstocks
- Atom and step economy
- Rapid synthesis of valuable chiral molecules

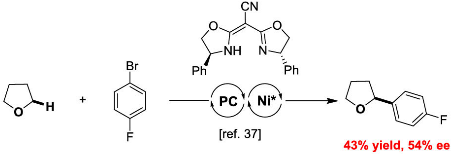
Challenges:
- High bond-dissociation energy
- Site-selectivity
- Asymmetric induction

(b) Enantiofacial differentiation of heterocycles

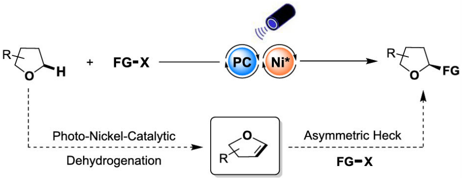
Directing group or structural handle for enantiodifferentiation

Enantiodifferentiation is notoriously difficult to control!

(c) Asymmetric C-H arylation of THF (Martin)

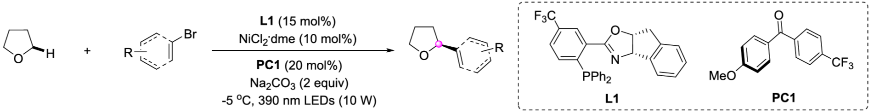


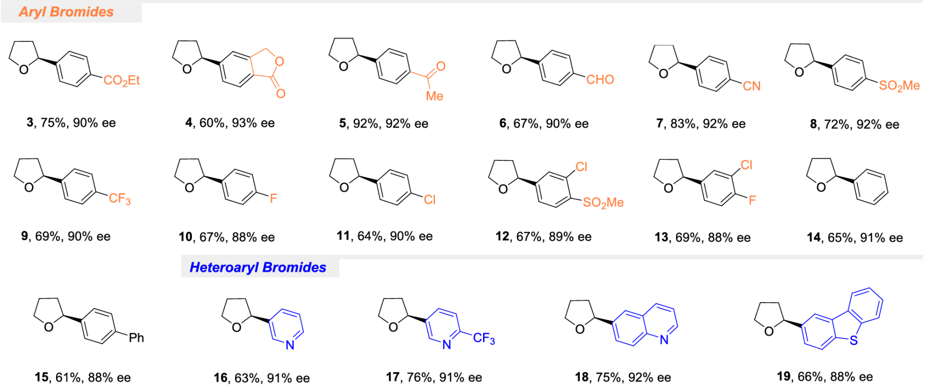
(d) Working Hypothesis: Enantioselective C(sp^3)-H functionalization of oxacycles



- High regioselectivity and enantioselectivity
- Modular access to high value-added chiral oxacycles

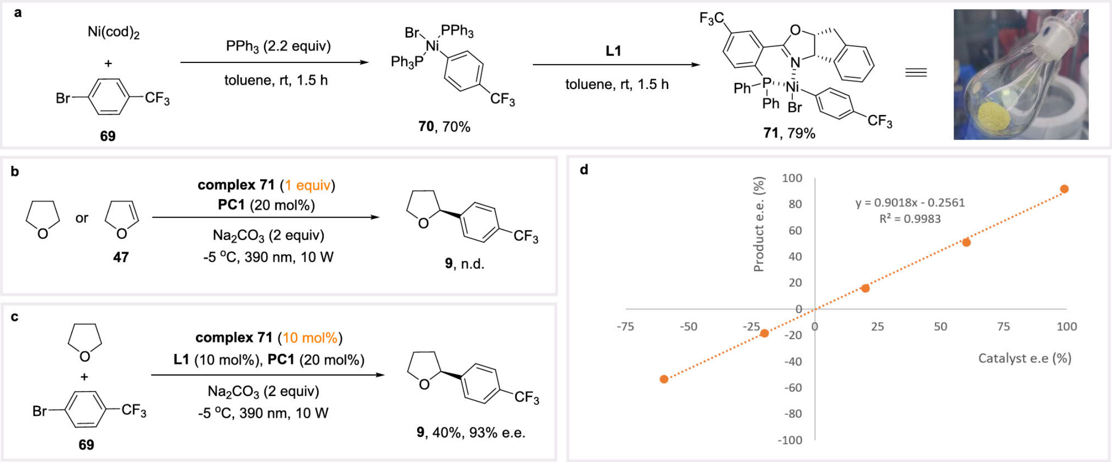
第三部分 通过光诱导氢原子转移/镍双重催化实现氧杂环的对映选择性C(sp³)-H键官能团化





第三部分

通过光诱导氢原子转移/镍双重催化实现氧杂环的对映选择性C(sp³)-H键官能团化



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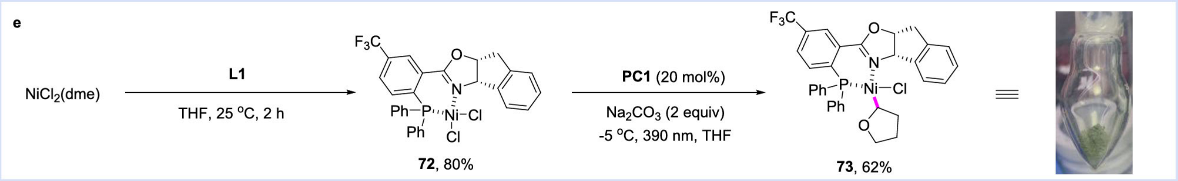

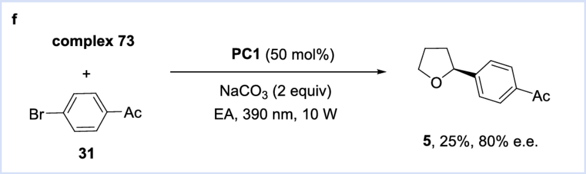

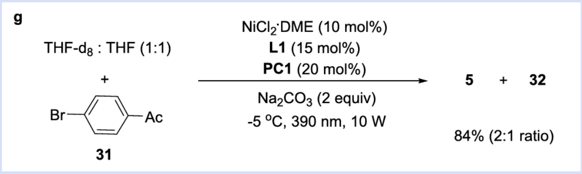

第三部分 醛与多种C(sp³)-H键的直接对映选择性酰基化反应

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Direct and Enantioselective Acylation of Diverse C(sp^3)–H Bonds with Aldehydes

Zhijun Zhou,# Fen Hu,# Xinjing Lin, Yuanyuan Ping,* and Wangqing Kong*

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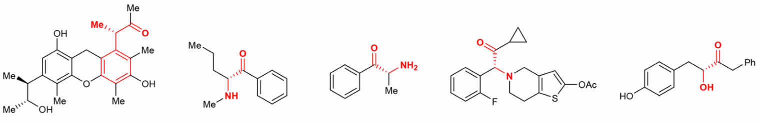
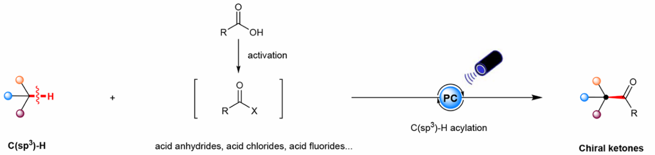
第三部分 醛与多种C(sp³)-H键的直接对映选择性酰基化反应

a. Prevalence of α-aryl, α-amino, and α-oxy ketone moieties in bioactive natural products and pharmaceuticals

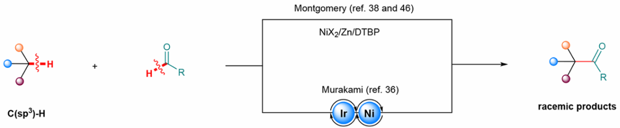


Peniciriols A　Pentedrone　Cathinone　Prasugrel　Kurasoin A

b. Known strategies for photocatalytic enantioselective C(sp³)-H acylation using active acylating agents



c. Cross dehydrogenative coupling of hydrocarbons with aldehydes



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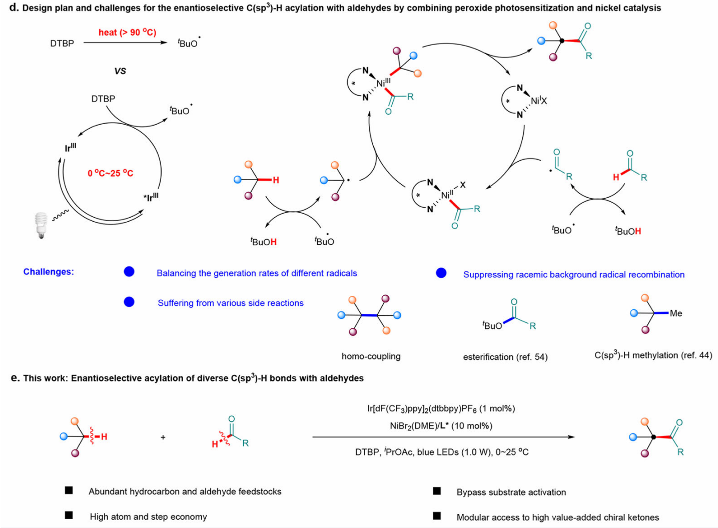

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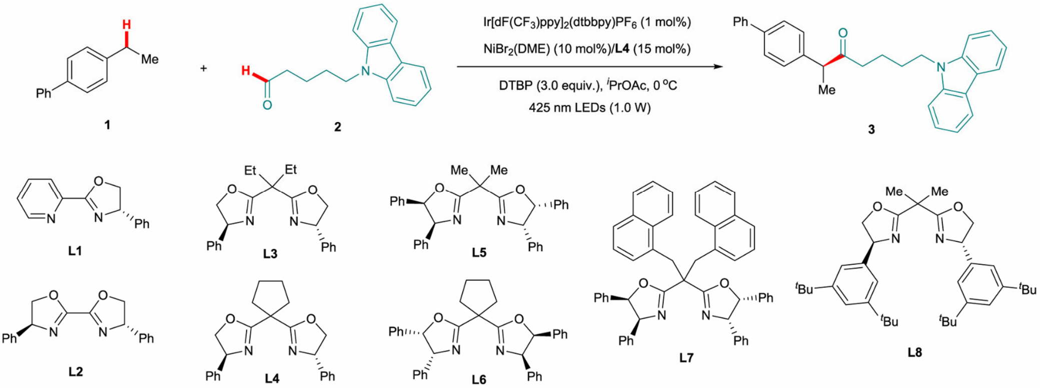

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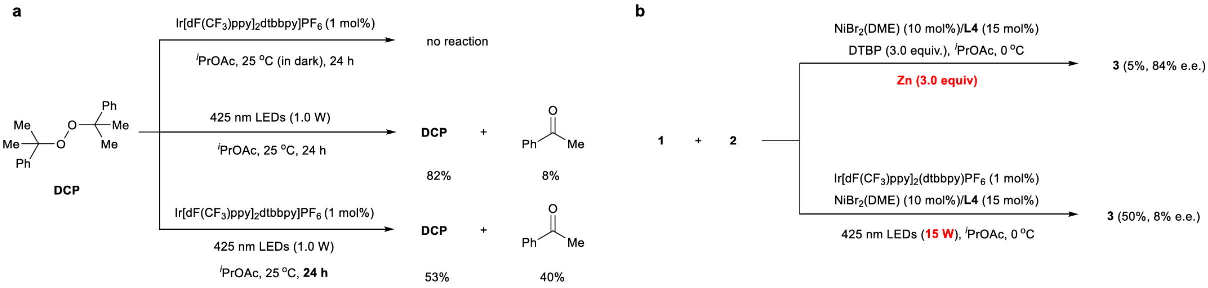

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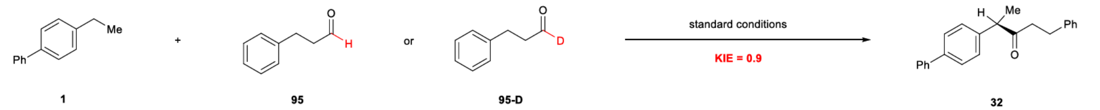
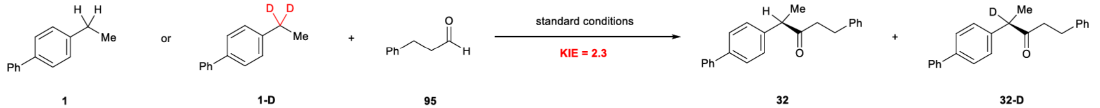
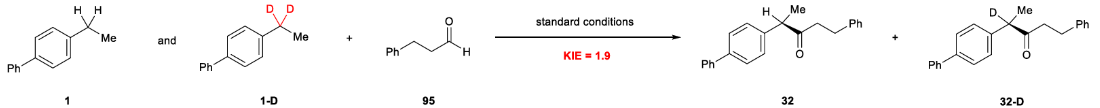
c



d



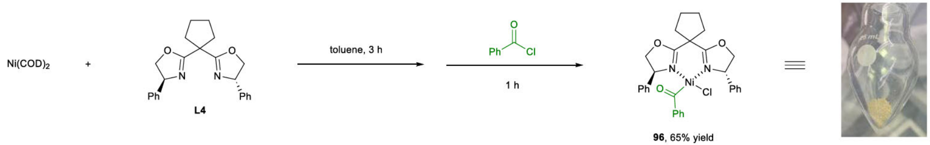
e



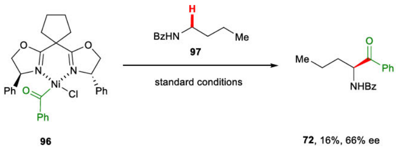
68% (**32**/**32-D** = 1.9/1)

第三部分 醛与多种C(sp³)-H键的直接对映选择性酰基化反应

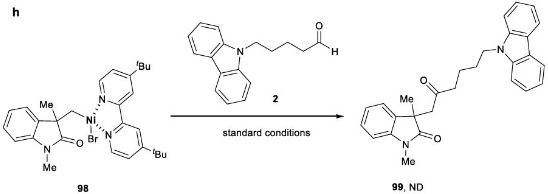
f



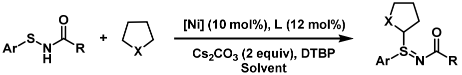
g

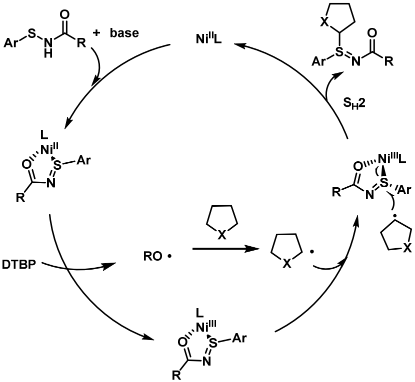


h



Proposal


Ar
S
N
H
O
R
+
X
[Ni] (10 mol%), L (12 mol%)
Cs2CO3 (2 equiv), DTBP
Solvent


+ base
NiIIL
SH2
DTBP
RO •
NiII
NiIII
Ar
O
N
S
R
L
X

同济大学 TONGJI UNIVERSITY

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

The Yang Research Group
Precise Synthesis Lab at Tongji University