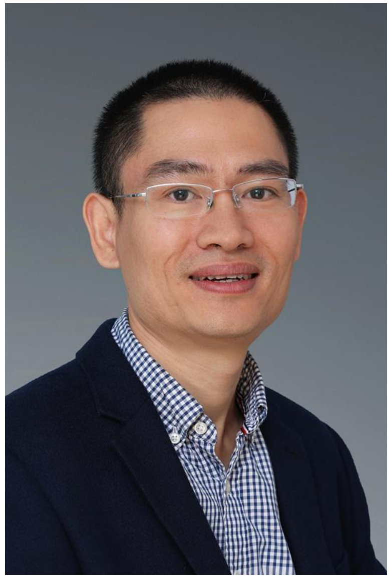
Literature Report IV

Copper-Catalyzed Enantioselective Dehydro-Diels–Alder Reaction: Synthesis of Axially Chiral Carbazoles

Reporter: Kai Xue
Checker: Jian Chen
Date: 2024-10-28

Chen, H.-H.; Chen, Y.-B.; Gao, J.-Z.; Ye, L.-W.; Zhou, B.* *Angew. Chem. Int. Ed.* **2024**, e202411709

CV of Prof. Longwu Ye



Background:

- **1999-2003** B.S., Zhejiang University
- **2003-2008** Ph.D., SIOC, CAS (Prof. Tang Yong)
- **2008-2009** Postdoc., The Scripps Research Institute
- **2009-2011** Postdoc., University of California at Santa Barbara
- **2011-2012** Associate Professor, Xiamen University
- **2012-now** Professor, Xiamen University

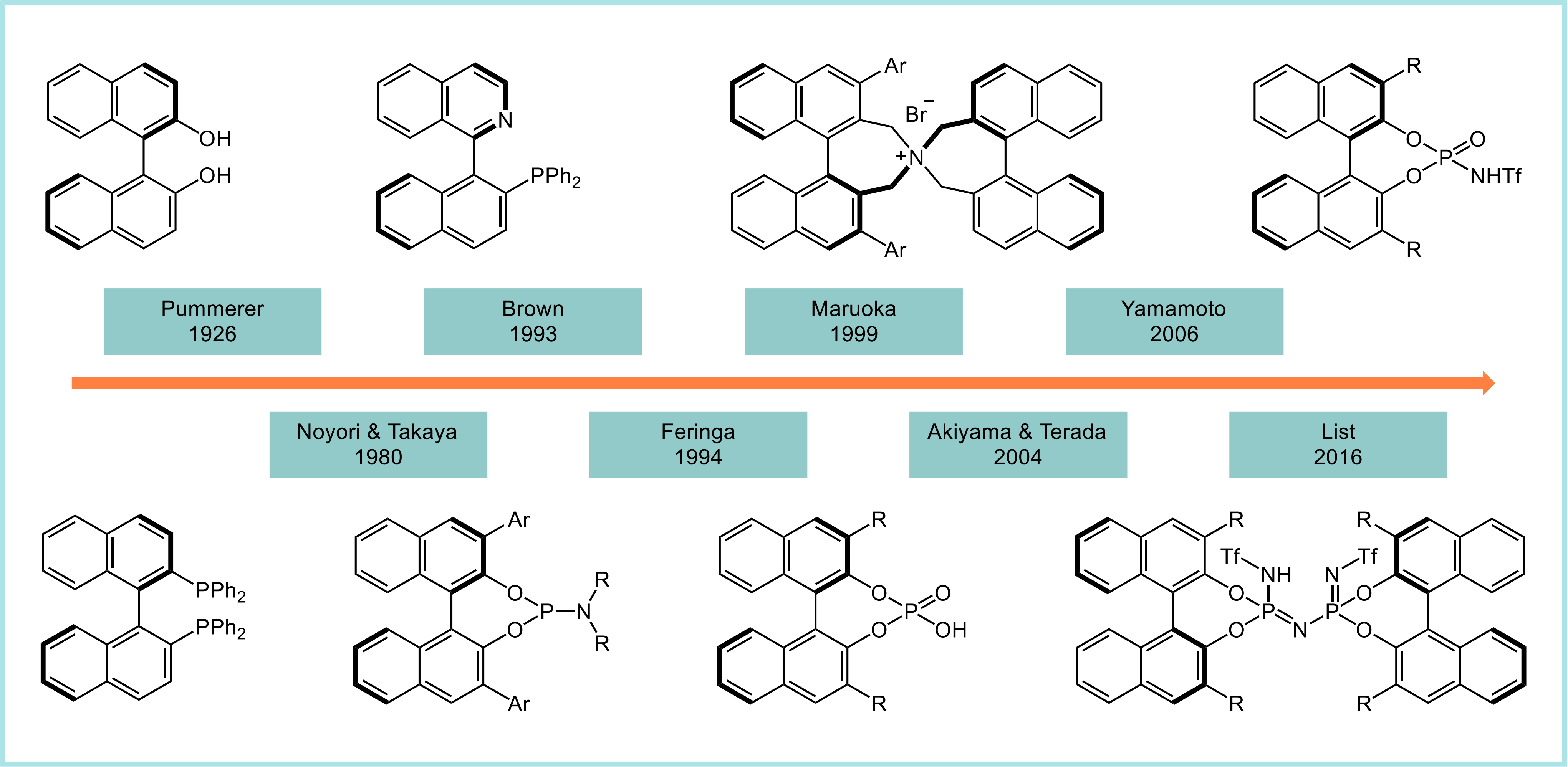
Research:

- **Asymmetric Catalysis**
- **Divergent Heterocycle Synthesis**
- **Total Synthesis of Natural Products**

Contents

Introduction

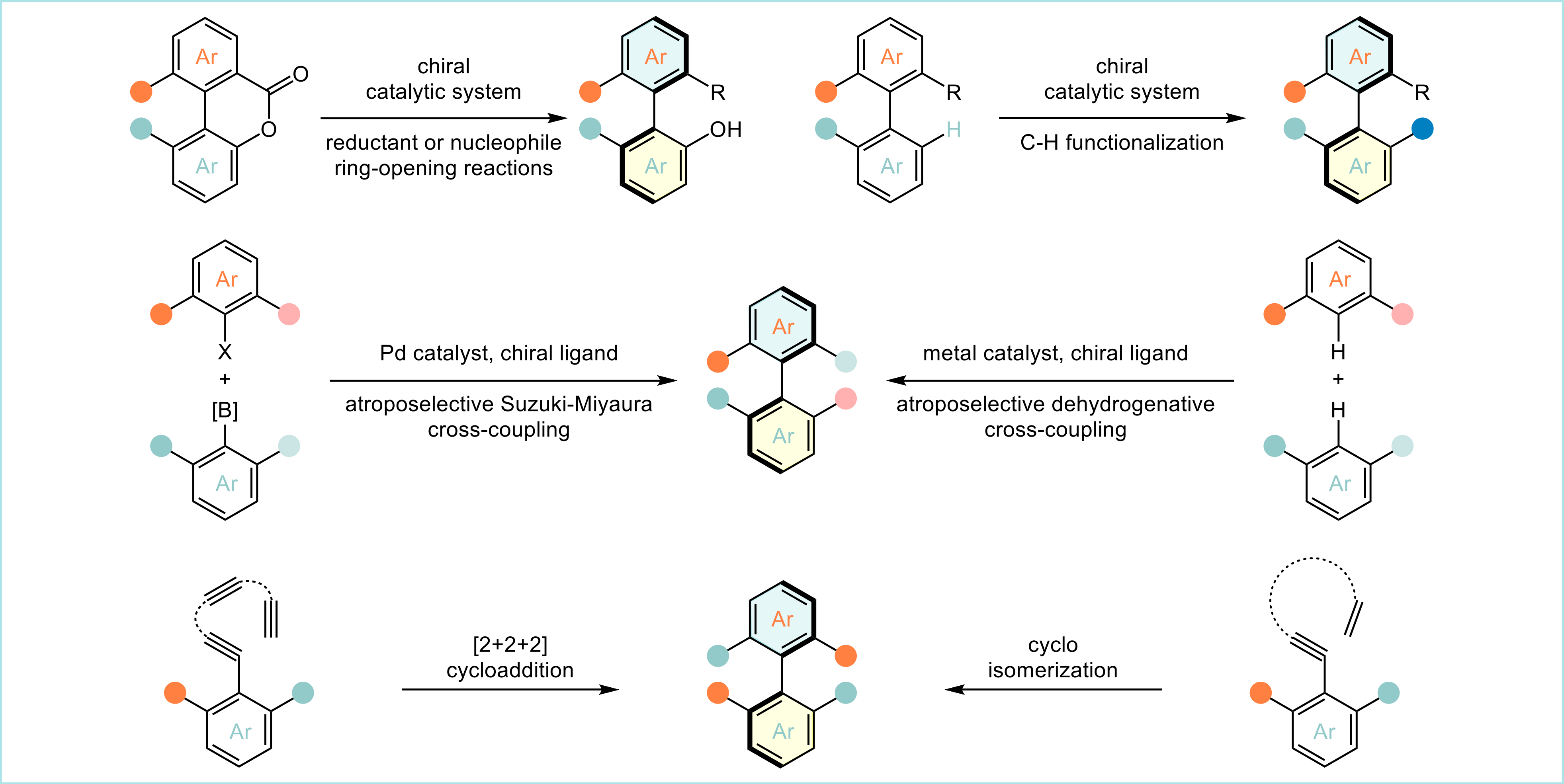
Representative Atropisomeric Ligands and Organocatalysts



Xiang, S.-H.; Ding, W.-Y.; Wang, Y.-B.; Tan, B.* *Nat. Catal.* **2024**, *7*, 483-498

Introduction

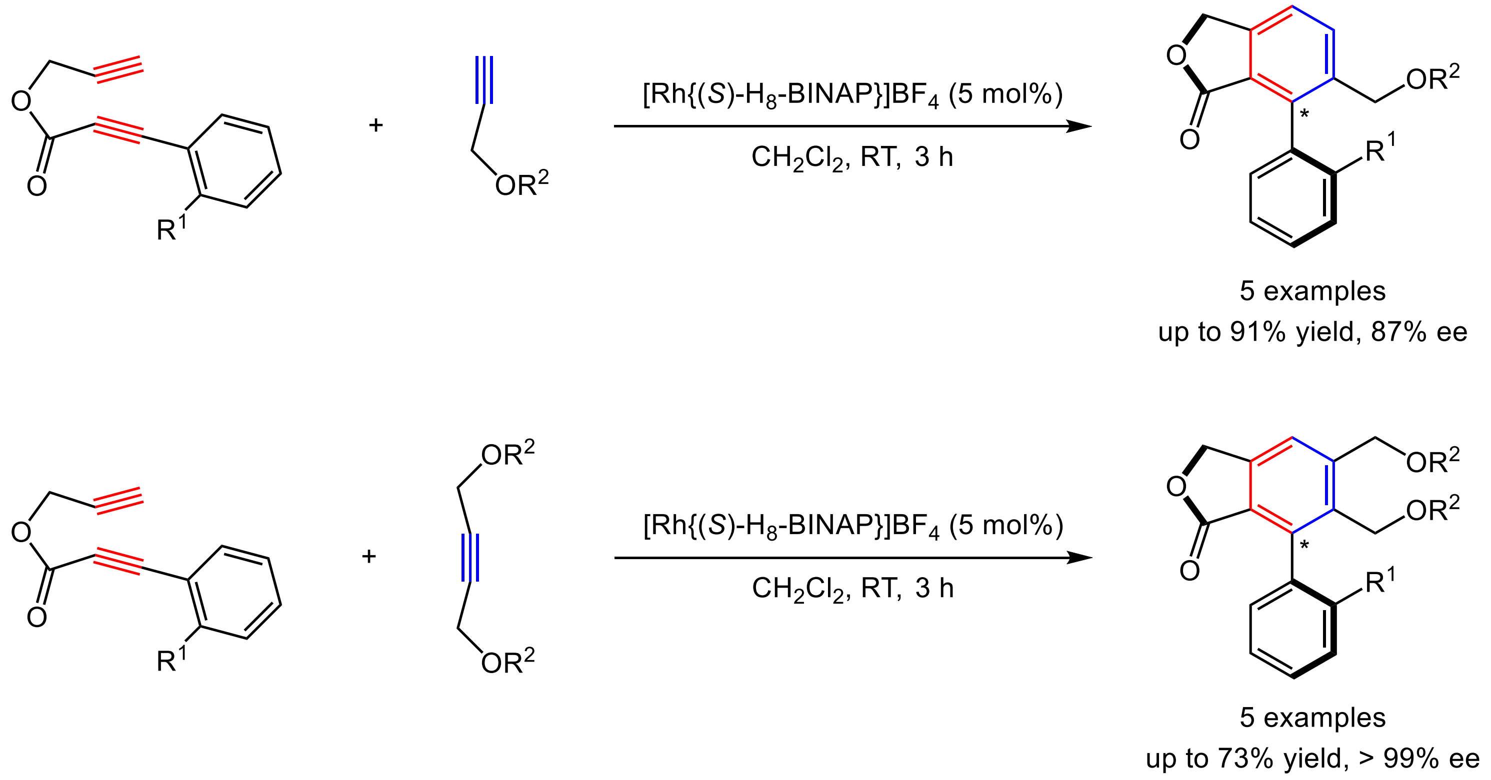
Generation of Axial Chirality along with Benzene-ring Formation



Xiang, S.-H.; Ding, W.-Y.; Wang, Y.-B.; Tan, B.* *Nat. Catal.* **2024**, *7*, 483-498.

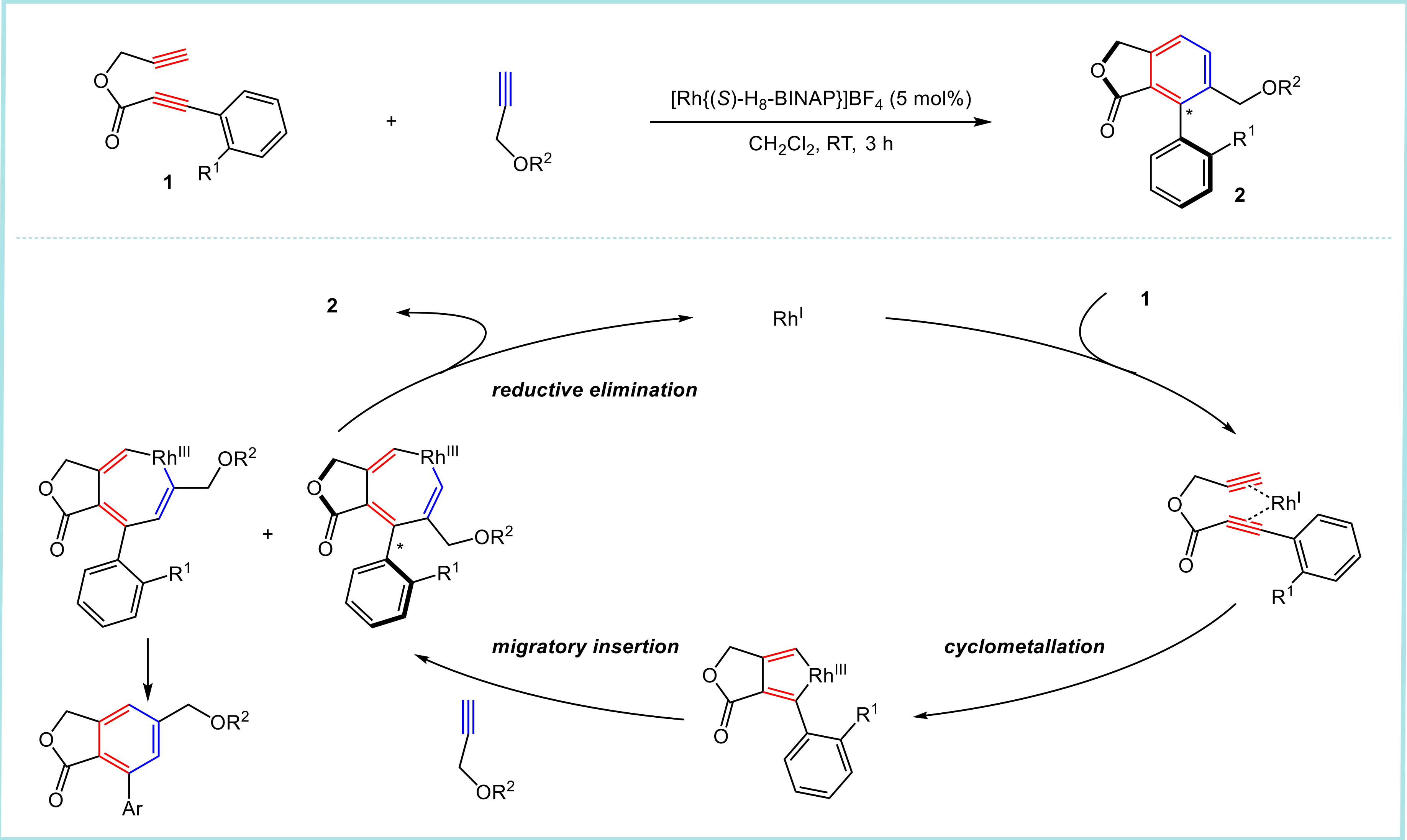
Introduction

Rhodium-Catalyzed Enantioselective [2+2+2] Cycloadditions



Tanaka, K.*; Nishida, G.; Wada, A.; Noguchi, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 6510-6512

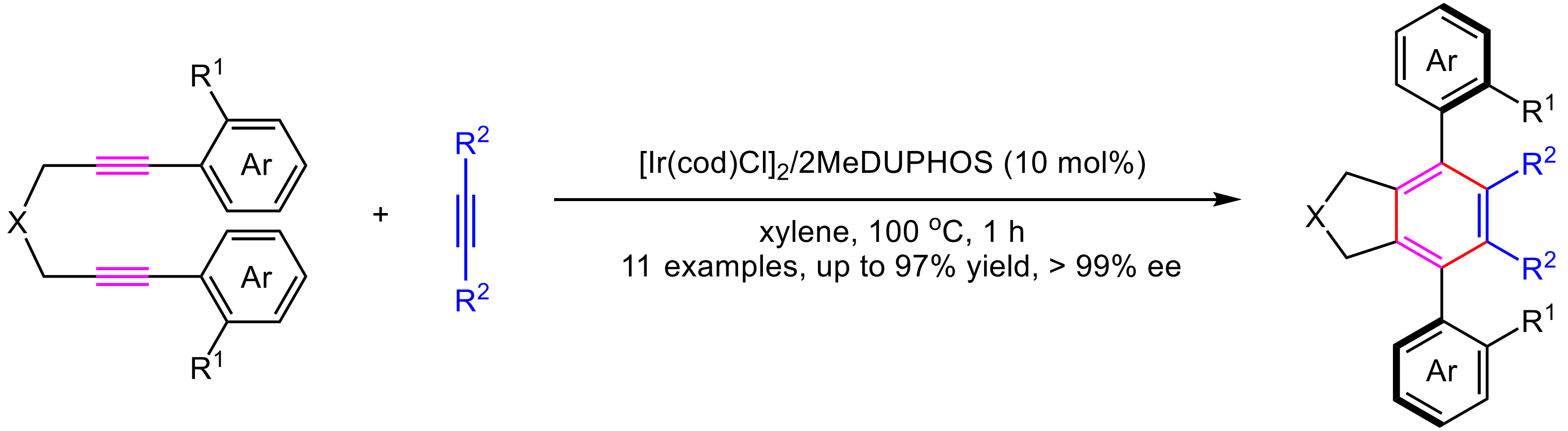
Introduction

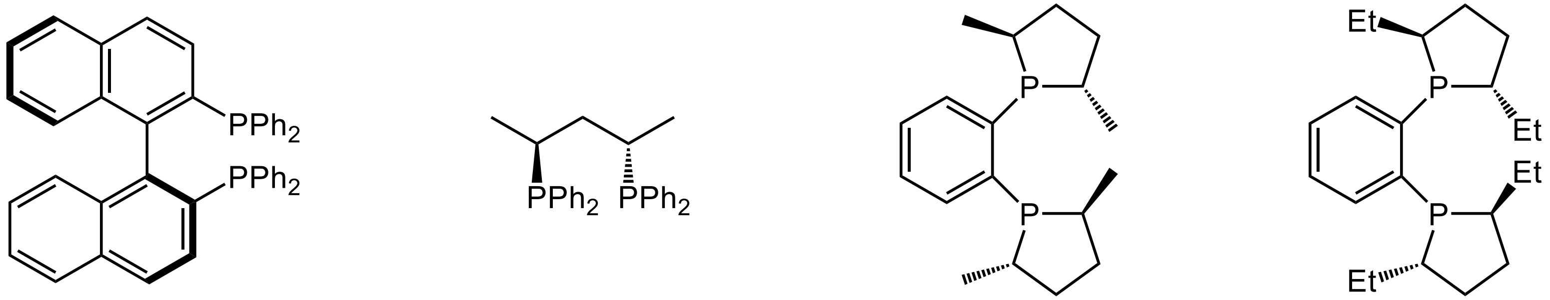


Tanaka, K.*; Nishida, G.; Wada, A.; Noguchi, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 6510-6512

Introduction

Iridium-Catalyzed Enantioselective [2+2+2] Cycloadditions





(*S*)-BINAP
31% yield, 6% ee

(*S*,*S*)-BDPP
39% yield, 51% ee

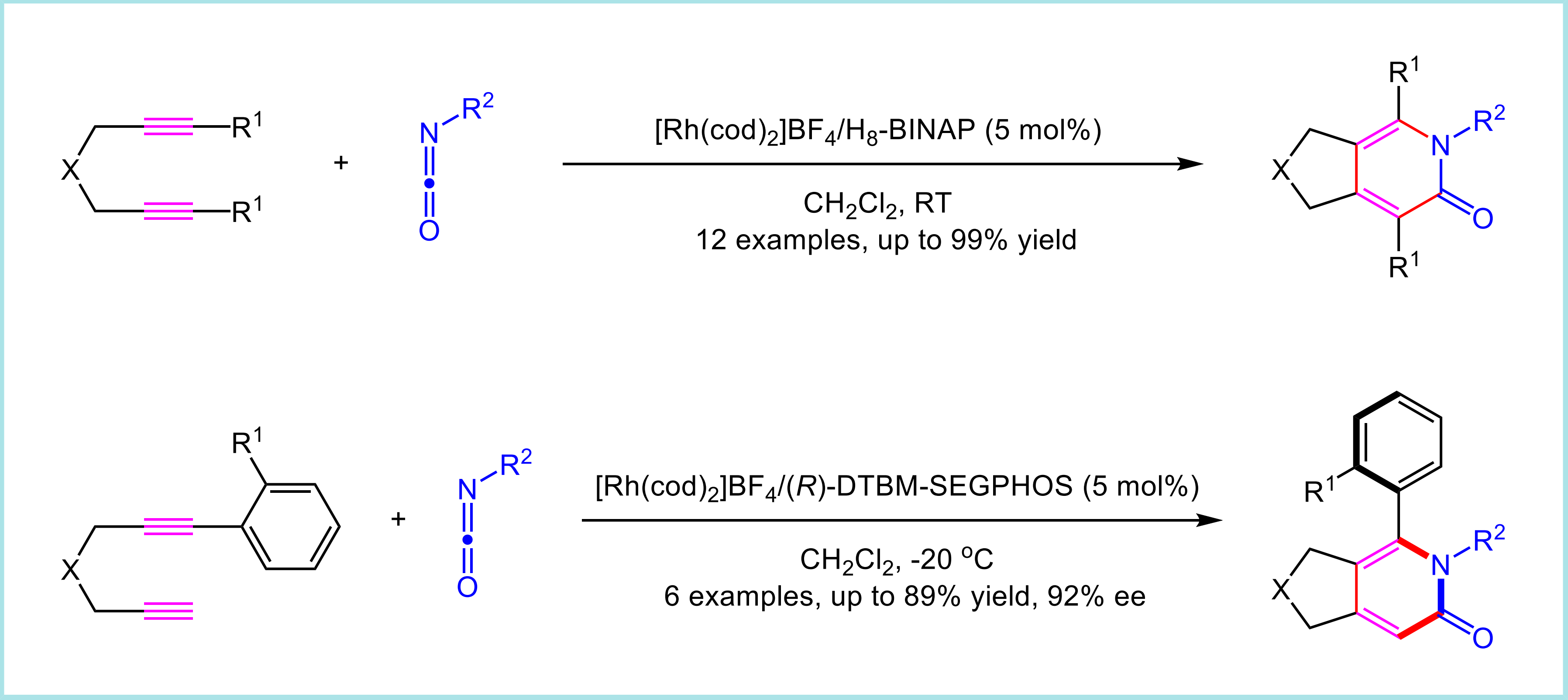
(*S*,*S*)-MeDUPHOS
83% yield, 99.6% ee

(*S*,*S*)-EtDUPHOS
75% yield, 99.8% ee

Shibata, T.*; Fujimoto, T.; Yokota, K.; Takagi, K. *J. Am. Chem. Soc.* **2004**, *126*, 8382-8383

Introduction

Rhodium-Catalyzed Enantioselective [2+2+2] Cycloadditions



Tanaka, K.*; Wada, A.; Noguchi, K. *Org. Lett.* **2005**, *7*, 4737-4739

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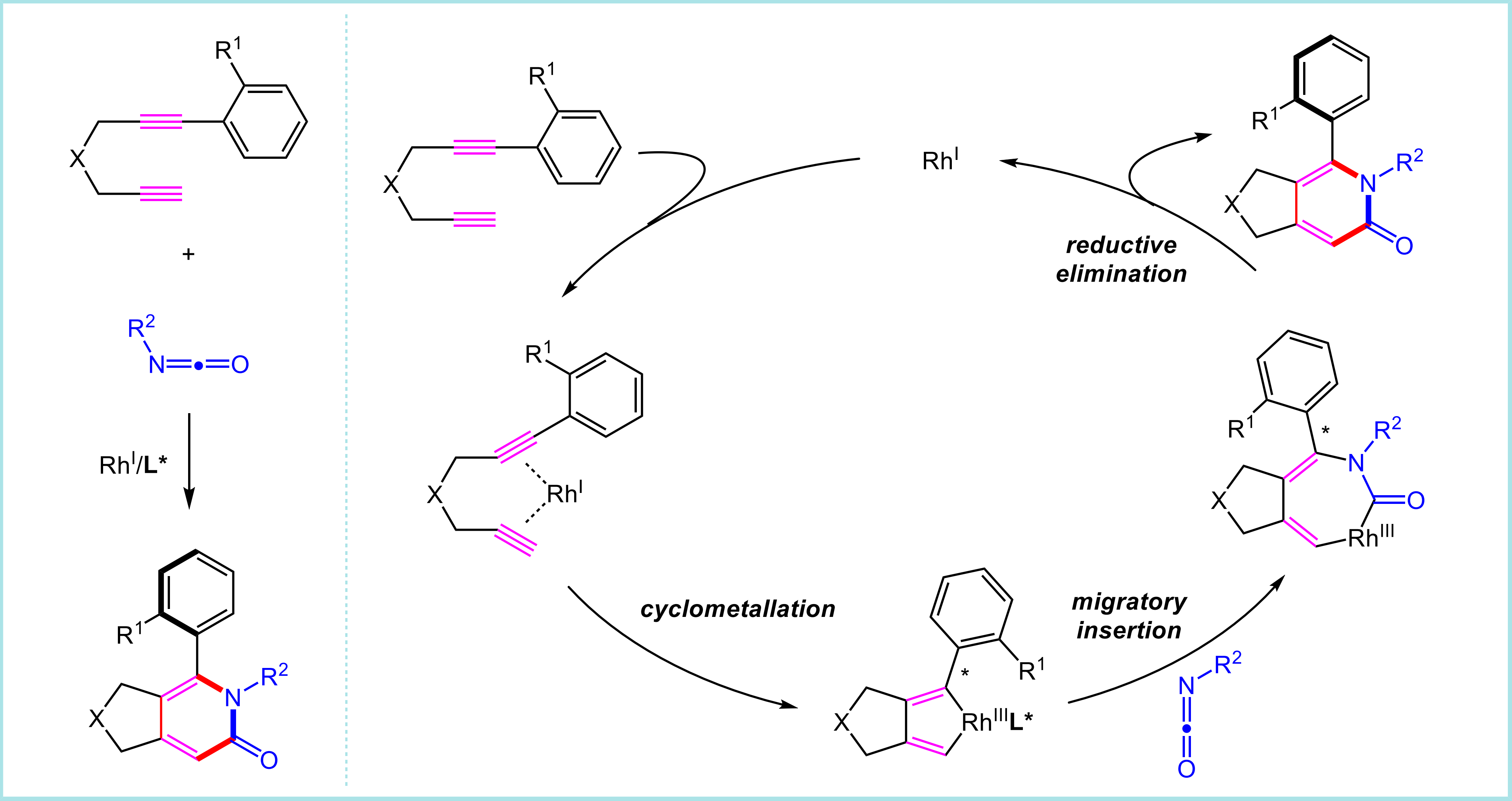
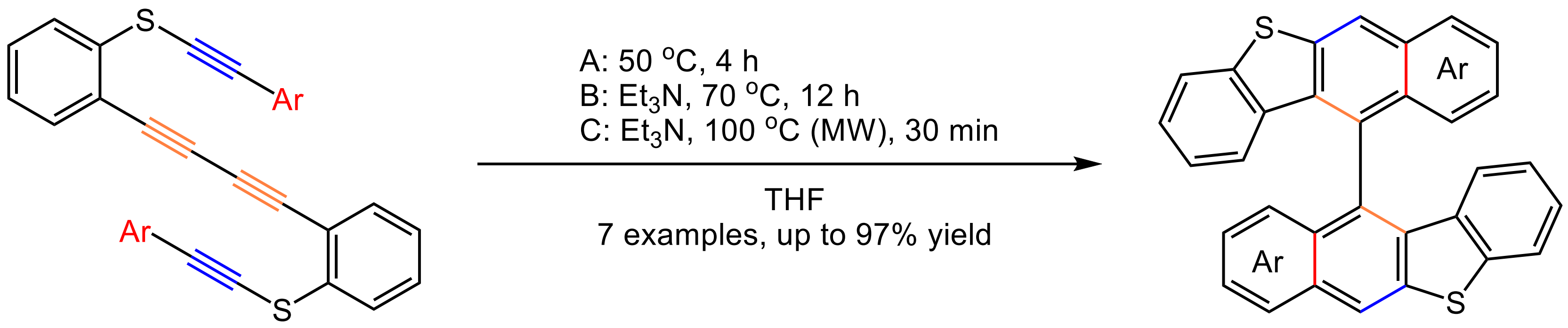


Tanaka, K.*; Wada, A.; Noguchi, K. *Org. Lett.* **2005**, *7*, 4737-4739

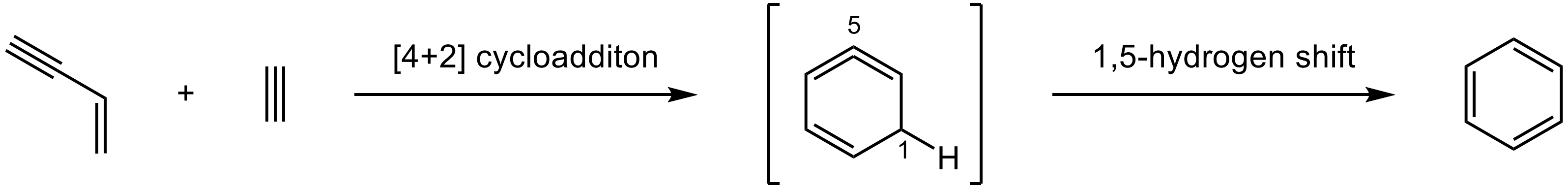
Introduction

Thermal [4+2] Cycloadditions

consecutive intramolecular DDA reactions



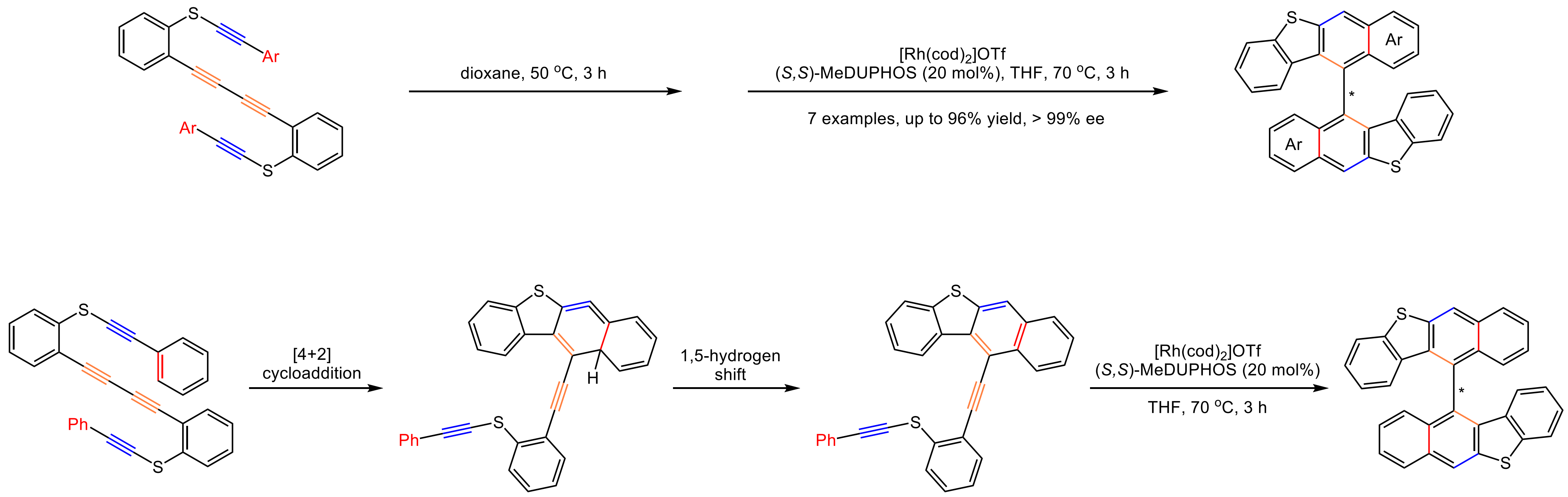
DDA reaction of enyne with alkyne



Shibata, T.*; Sekine, A.; Mitake, A.; Kanyiva, K. S. *Angew. Chem. Int. Ed.* **2018**, *57*, 15862-15865

Introduction

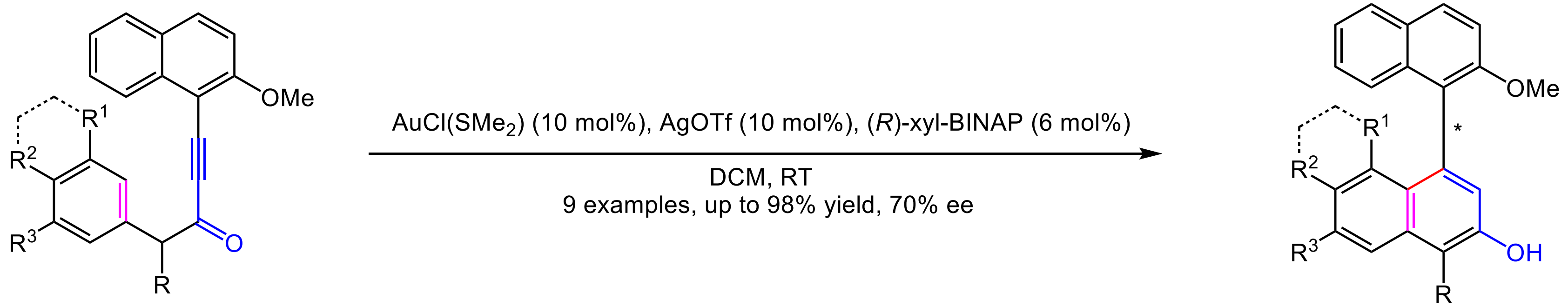
Rhodium-Catalyzed Enantioselective DDA Reactions

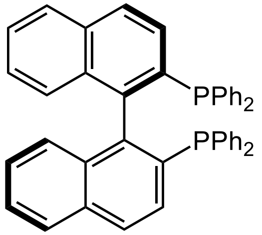


Shibata, T.*; Sekine, A.; Mitake, A.; Kanyiva, K. S. *Angew. Chem. Int. Ed.* **2018**, *57*, 15862-15865

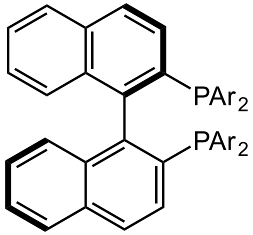
Introduction

Gold-Catalyzed Enantioselective DDA Reactions

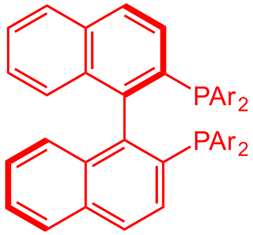




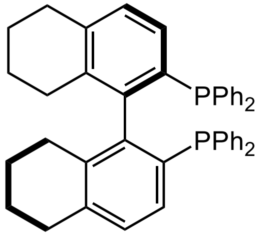
(R)-BINAP
60% yield, 52% ee



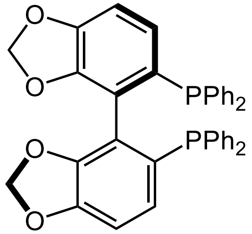
(R)-tol-BINAP Ar = 4-MeC_6H_4
72% yield, 60% ee



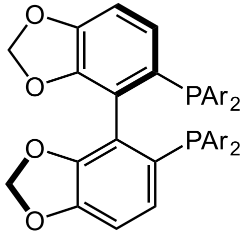
(R)-xyl-BINAP Ar = 3,5-$Me_2C_6H_3$
98% yield, 64% ee



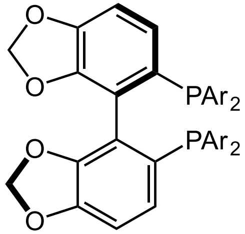
(R)-H_8-BINAP
15% yield, 57% ee



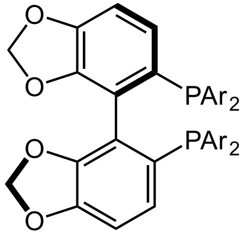
(R)-SEGPHOS
>99% yield, 42% ee



(R)-tol-SEGPHOS Ar = 4-MeC_6H_4
41% yield, 64% ee



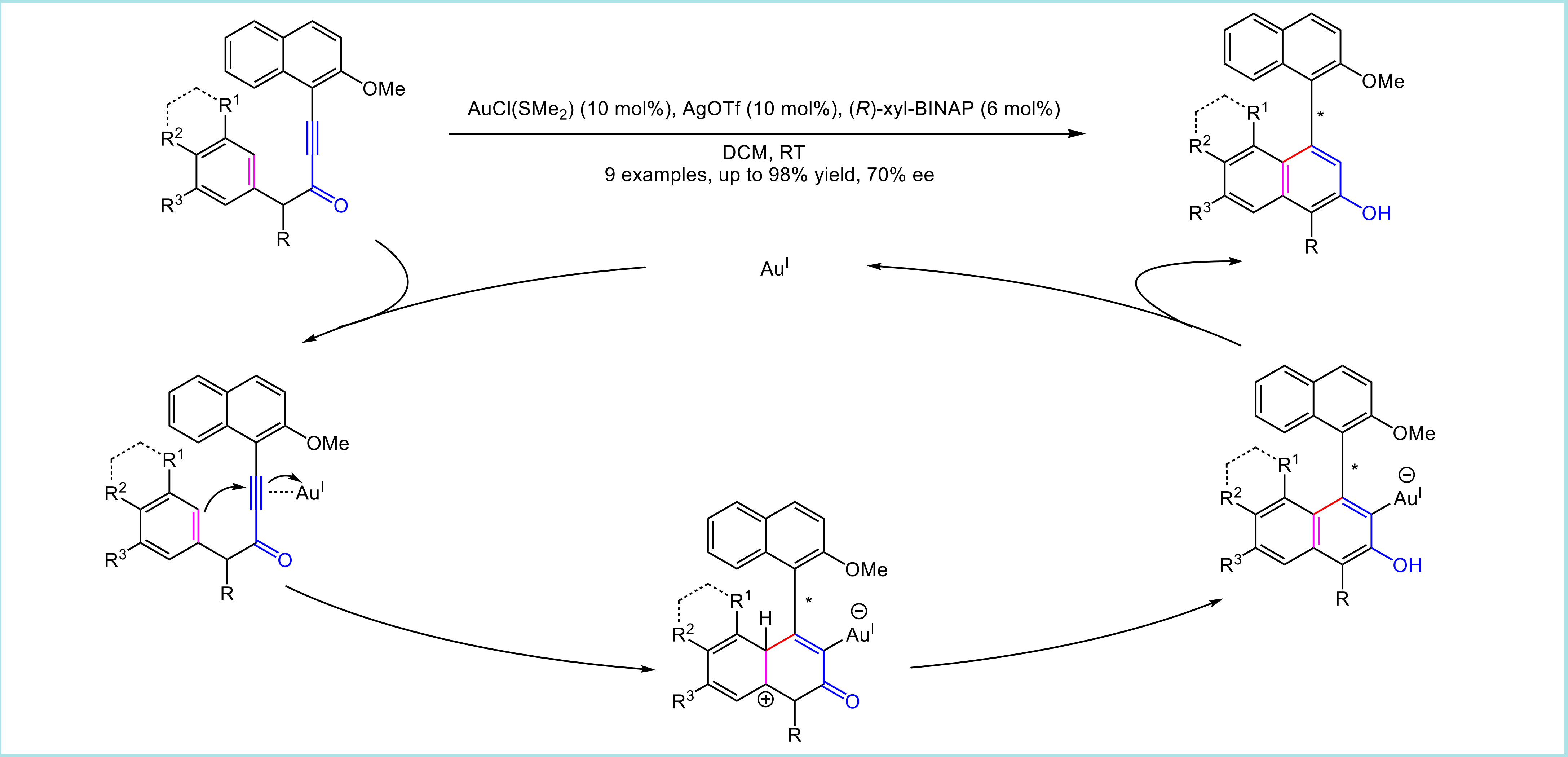
(R)-xyl-SEGPHOS Ar = 3,5-$Me_2C_6H_3$
12% yield, 70% ee



(R)-DTBM-SEGPHOS
Ar = 4-MeO-3,5-^{t}$Bu_2C_6H_2$, 0% yield

Satoh, M.; Shibata, Y.; Kimura, Y.; Tanaka, K.* *Eur. J. Org. Chem.* **2016**, *2016*, 4465-4469

Introduction



Satoh, M.; Shibata, Y.; Kimura, Y.; Tanaka, K.* *Eur. J. Org. Chem.* **2016**, *2016*, 4465-4469

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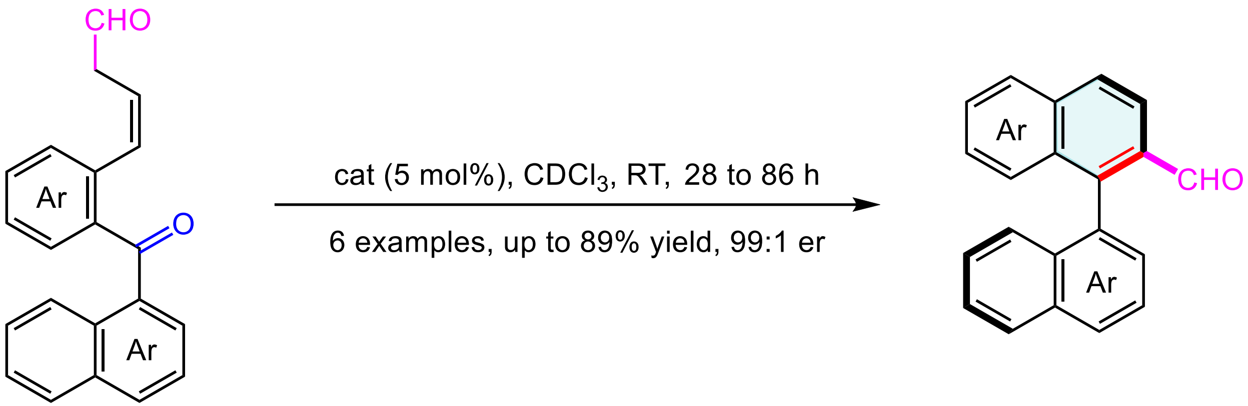
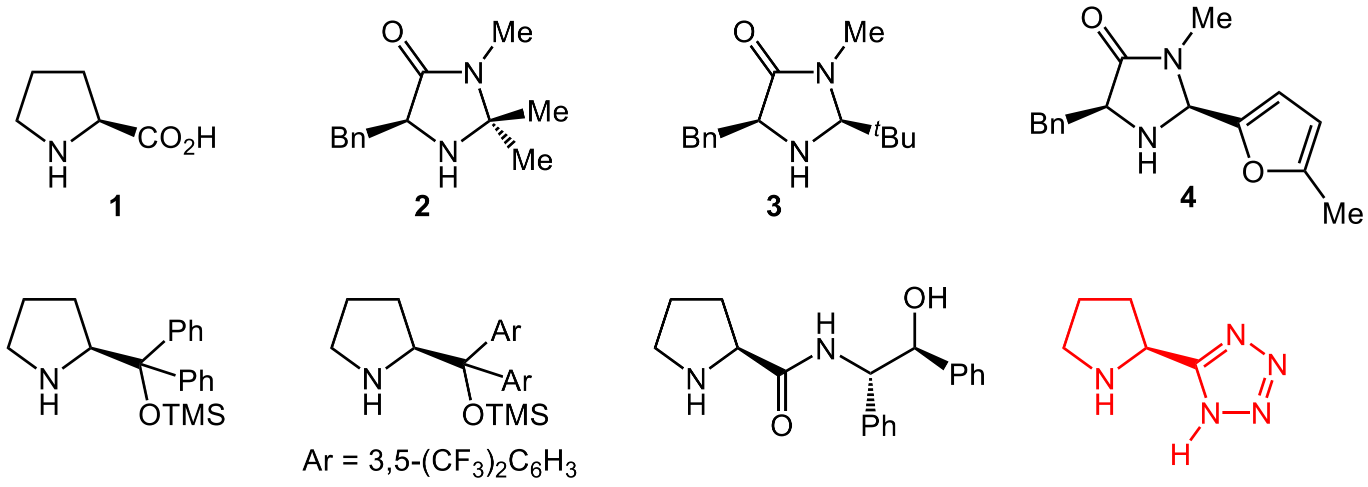
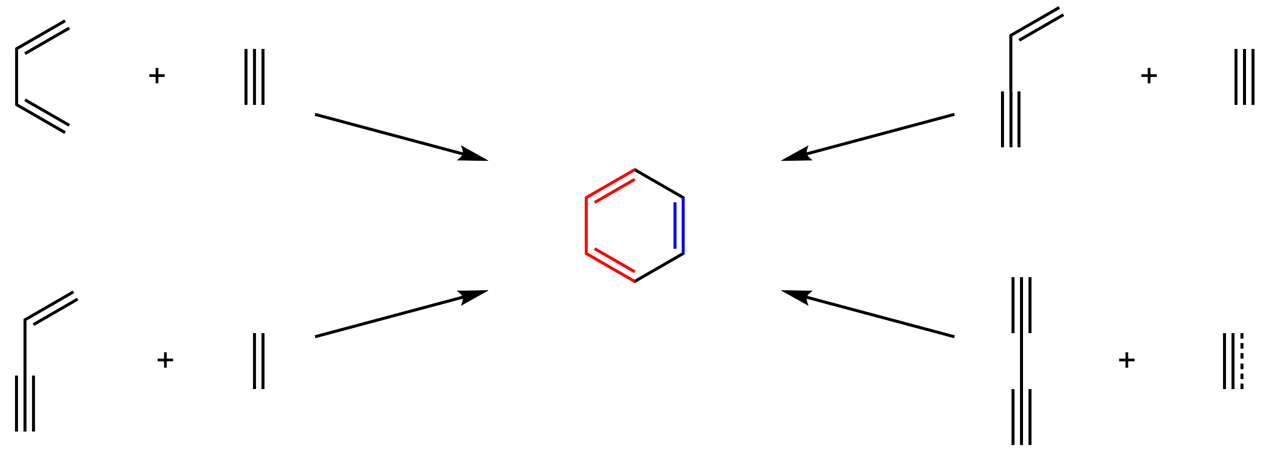




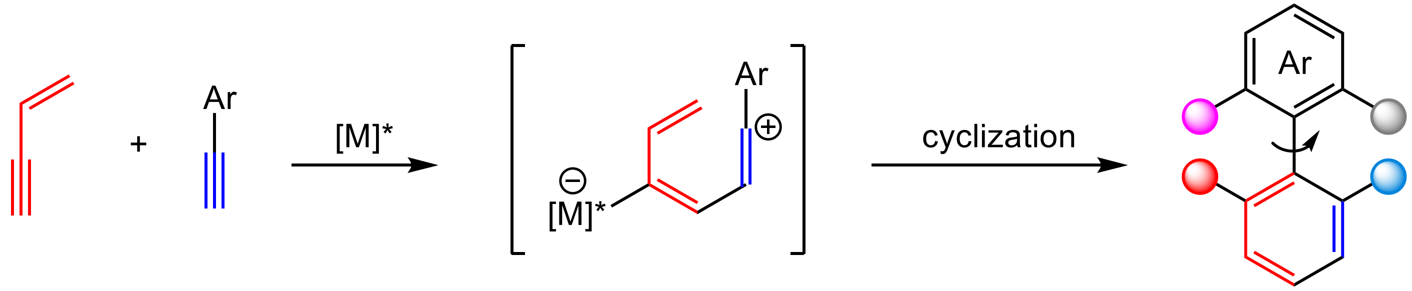
Link, A.; Sparr, C.* *Angew. Chem. Int. Ed.* **2014**, *53*, 5458-5461

Project Synopsis

(a) Dehydro-Diels-Alder (DDA) reaction



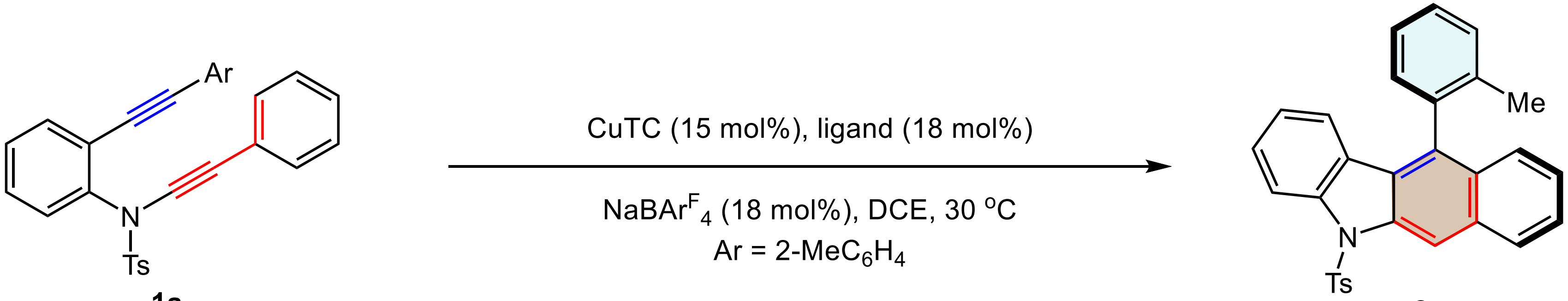
(b) catalytic enantioselective DDA reaction via vinyl cations



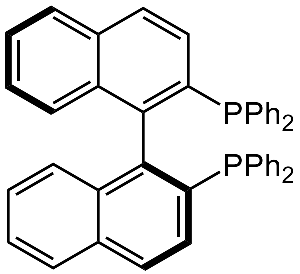
chiral induction model

axial chirality

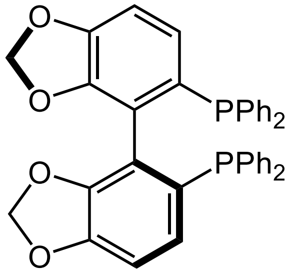
Optimization of the Reaction Conditions



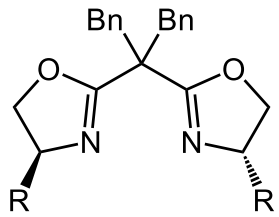
1a **2a**



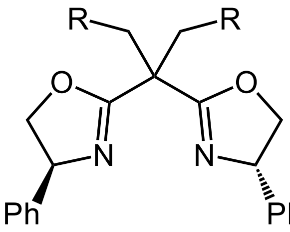
(S)-BINAP (**L1**)
99%, 38.5:61.5 er



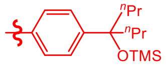
(S)-SEGPHOS (**L2**)
99%, 37.5:62.5 er



L3, R = ^{t}Bu, 92%, 72.5:27.5 er
L4, R = Ph, 92%, 84.5:15.5 er

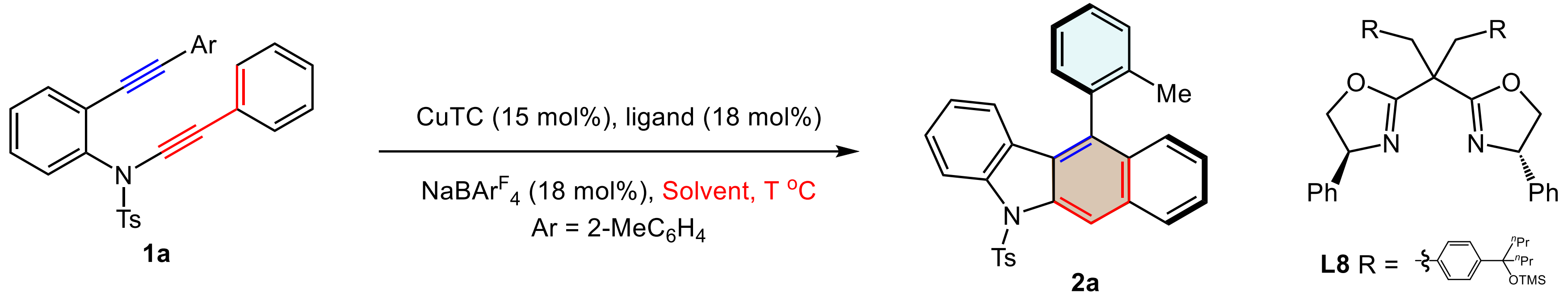


L5, R = 4-Cl-C_6H_4, 88%, 82:18 er
L6, R = 4-Me-C_6H_4, 84%, 84:16 er
L7, R = 4-^{t}Bu-C_6H_4, 98%, 89:11 er

L8, R = 

, 97%, 92:8 er
L9, R = 3,5-Me_2-C_6H_3, 96%, 84.5:15.5 er
L10, R = 2,4,6-Me_3-C_6H_2, 84%, 83:17 er

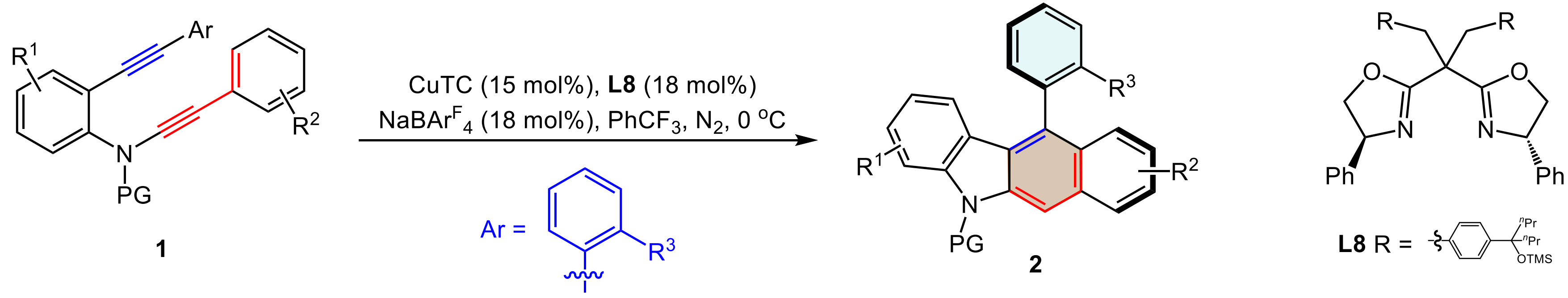
Optimization of the Reaction Conditions

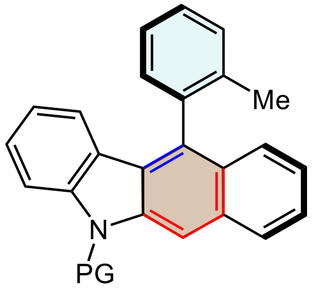


Entry[a]	Solvent	T (°C)	t (h)	Yield (%)[b] (**2a**)	Er (%) (**2a**)[c]
1	DCE	30	4	97	92:8
2	DCM	30	3	98	93.5:6.5
3	THF	30	30	17	50.5:49.5
4	toluene	30	2	97	94:6
5	$PhCF_3$	30	2	99	94.5:5.5
6	$PhCF_3$	15	32	99	95.5:4.5
7	$PhCF_3$	0	90	99	96:4

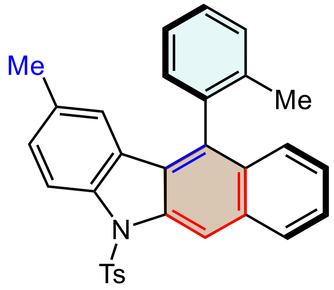
[a]Reaction conditions: **1a** (0.05 mmol), CuTC (0.0075 mmol), ligand (0.009 mmol), $NaBAr^F_4$ (0.009 mol), solvent (2 mL), N_2, 0-30 °C, 2-90 h. [b]Measured by ^1H NMR using 1,3,5-trimethoxybenzene as the internal standard. [c]Determined by HPLC.

Scope for the Formation of Axially Chiral Phenyl Carbazoles

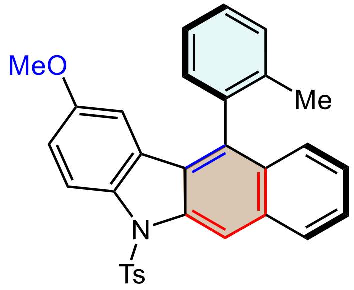




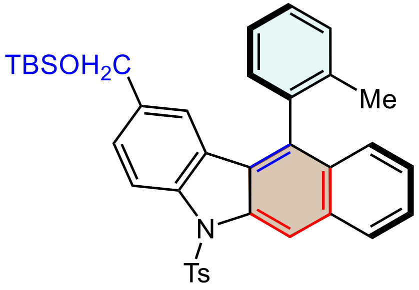
2a, PG = Ts, 99%, 96:4 er (84 h)
2b, PG = Mbs, 98%, 96:4 er (96 h)
2c, PG = SO_2Ph, 98%, 96.5:3.5 er (96 h)
2d, PG = Bs, 96%, 96:4 er (120 h)
2e, PG = Ns, 85%, 94.5:5.5 er (120 h)
2f, PG = Ms, 52%, 96:4 er (144 h)



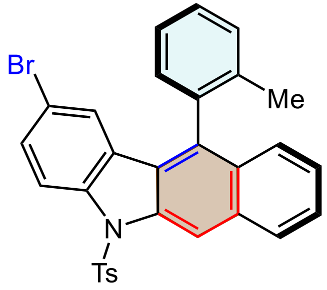
2g, 99%, 96.5:3.5 er (136 h)



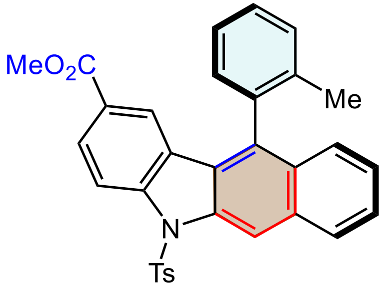
2h, 88%, 96:4 er (138 h)



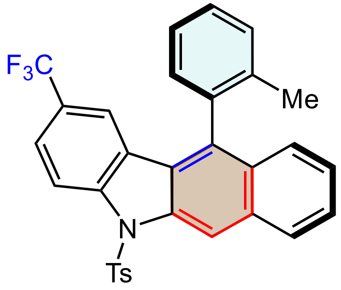
2i, 92%, 97:3 er (141 h)



2j, 99%, 97.5:2.5 er (95 h)

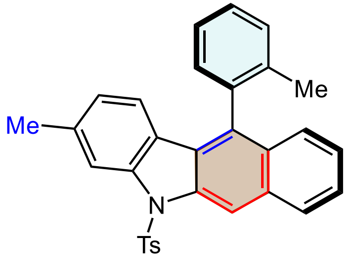


2k, 99%, 95:5 er (95 h)

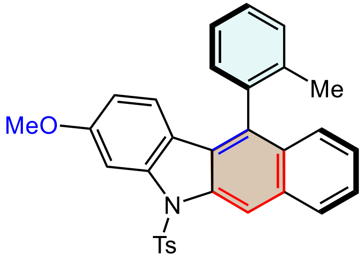


2l, 90%, 95:5 er (90 h)

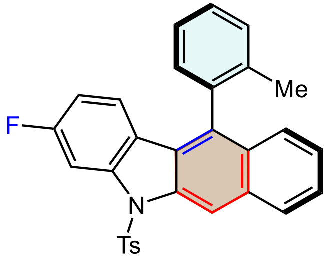
Scope for the Formation of Axially Chiral Phenyl Carbazoles



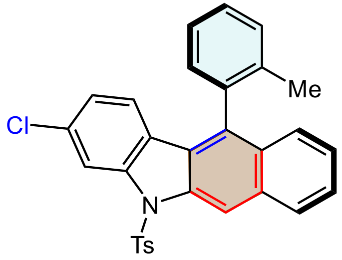
2m, 96%, 96:4 er (108 h)



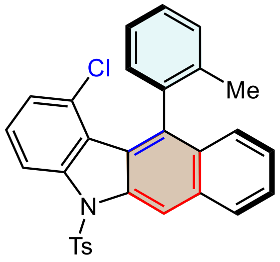
2n, 92%, 96:4 er (131 h)



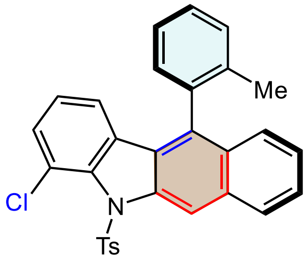
2o, 99%, 95.5:4.5 er (108 h)



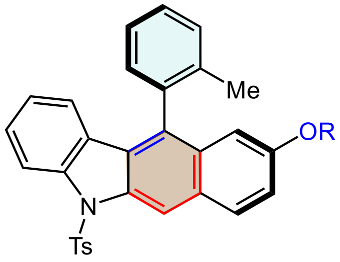
2p, 96%, 95:5 er (123 h)



2q, 69%, 95:5 er (112 h)

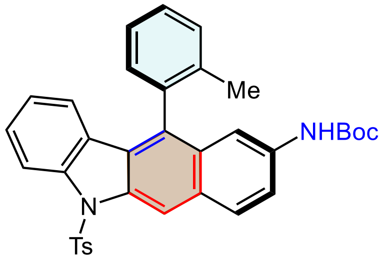


2r, 77%, 91:9 er (144 h)

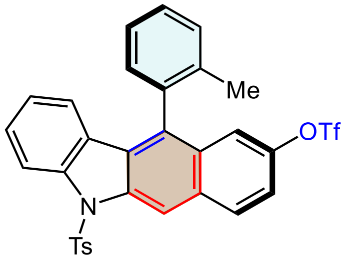


2s, R = Me, 82%, 92:8 er (57 h)

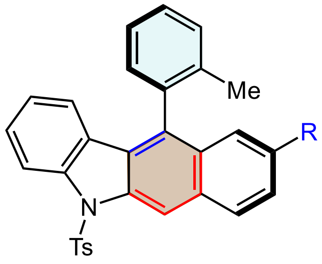
2t, R = TBS, 75%, 92.5:7.5 er (74 h)



2u, 75%, 92:8 er (69 h)

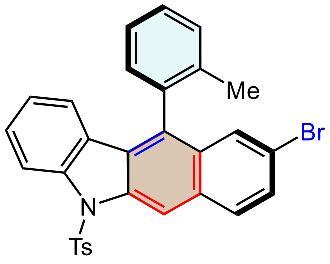


2v, 93%, 99:1 er (42 h)

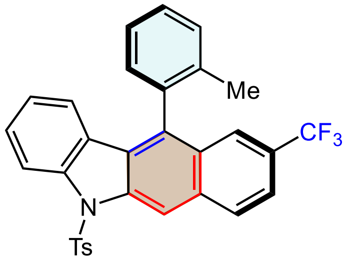


2w, R = F, 97%, 97.5:2.5 er (42 h)

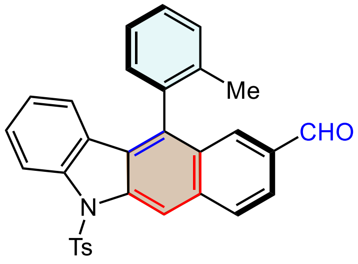
2x, R = Cl, 99%, 97.5:2.5 er (69 h)



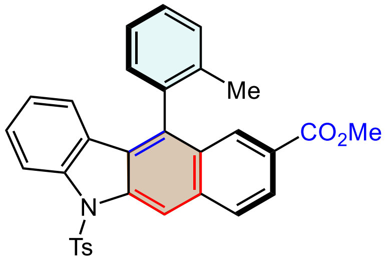
2y, 96%, 97:3 er (33 h)



2z, 99%, 98.5:1.5 er (42 h)

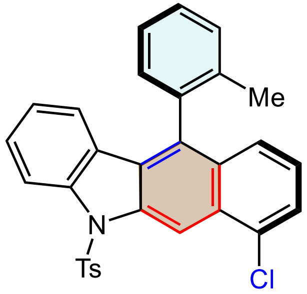


2aa, 99%, 97:3 er (87 h)

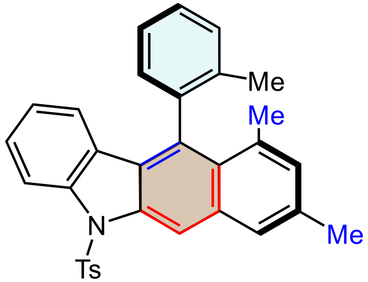


2ab, 98%, 97.5:2.5 er (48 h)

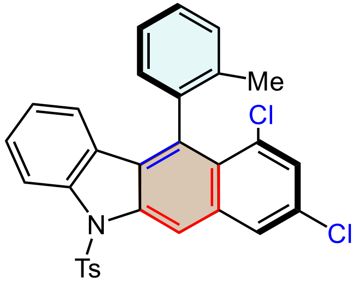
Scope for the Formation of Axially Chiral Phenyl Carbazoles



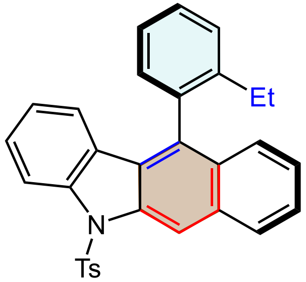
2ac, 85%, 93:7 er (144 h)



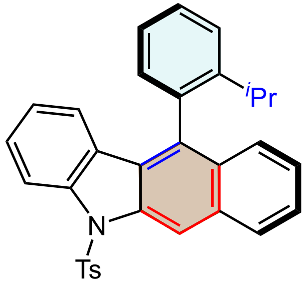
2ad, 89%, 92:8 er (96 h)



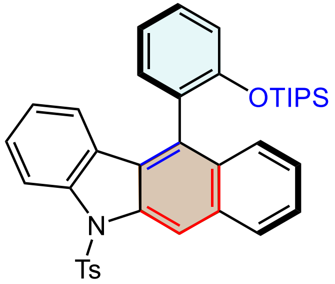
2ae, 96%, 90:10 er (48 h)



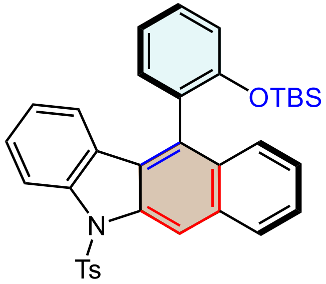
2af, 93%, 96:4 er (90 h)



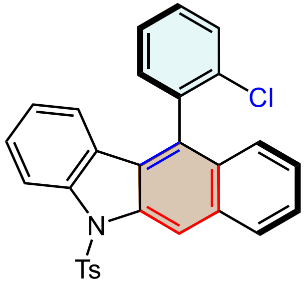
2ag, 94%, 96:4 er (108 h)



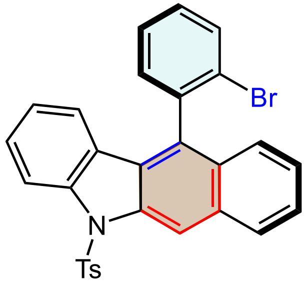
2ah, 91%, 94:6 er (89 h)



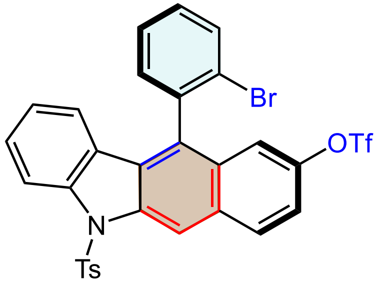
2ai, 82%, 92:8 er (87 h)



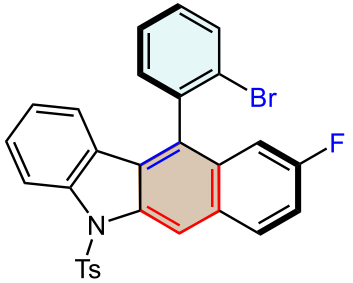
2aj, 95%, 95:5 er (108 h)



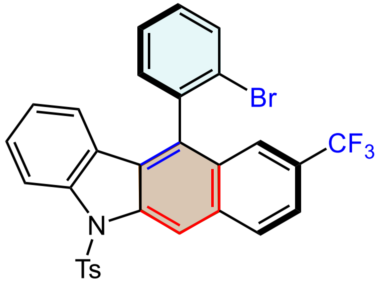
2ak, 96%, 95:5 er (144 h)



2al, 82%, 97:3 er (90 h)

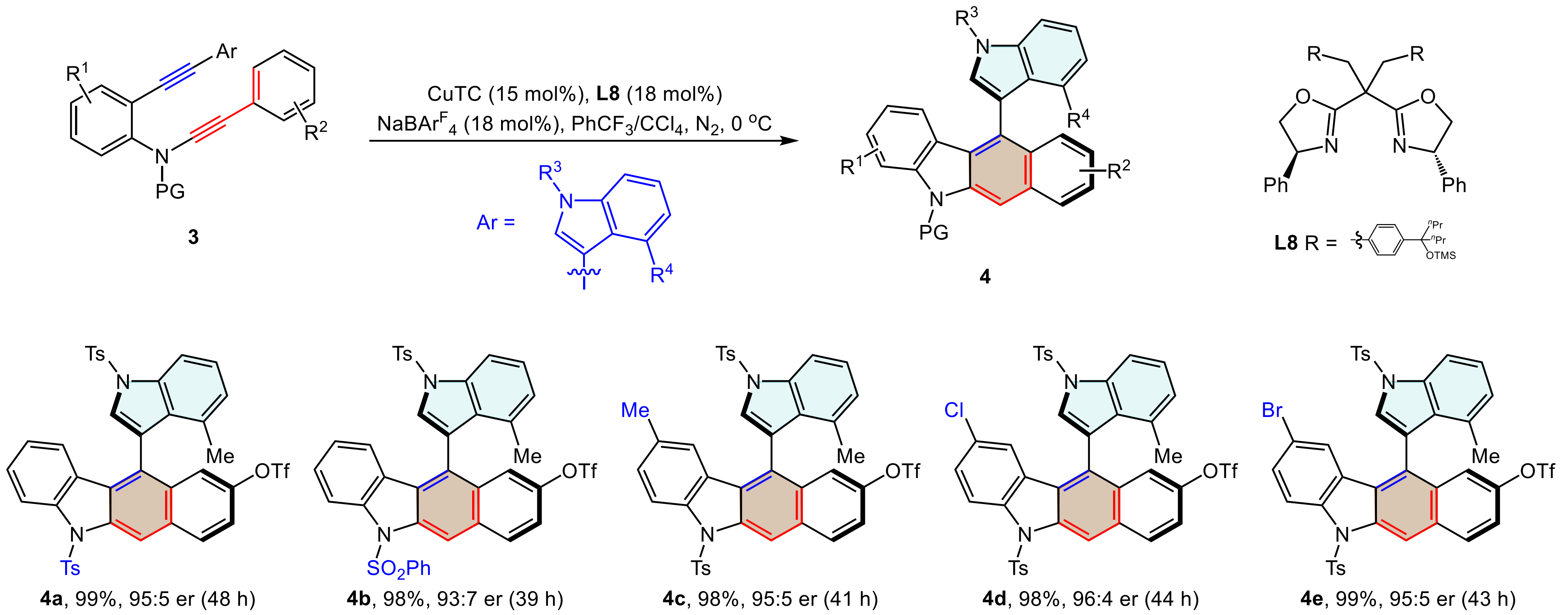


2am, 96%, 97:3 er (95 h)

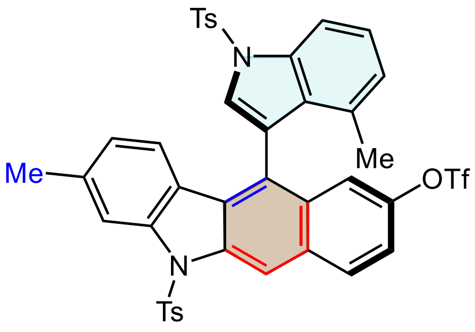


2an, 98%, 98:2 er (120 h)

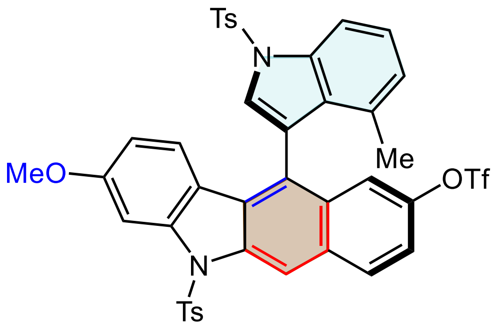
Scope for the Formation of Axially Chiral Indolyl Carbazoles



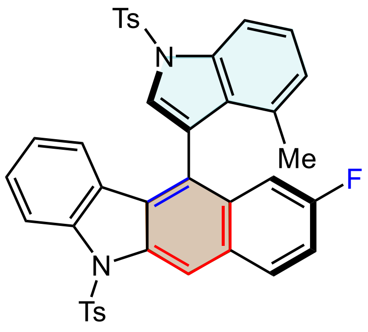
Scope for the Formation of Axially Chiral Indolyl Carbazoles



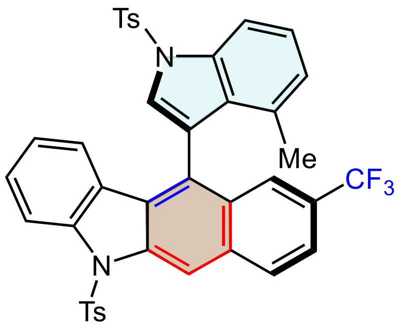
4f, 97%, 95:5 er (43 h)



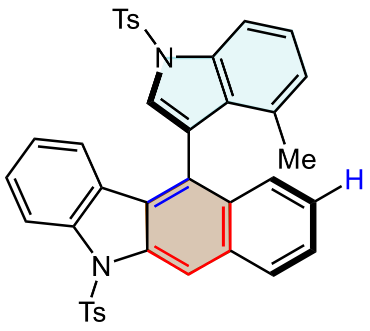
4g, 99%, 92.5:7.5 er (47 h)



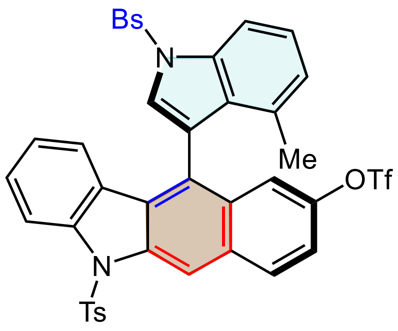
4h, 95%, 93.5:6.5 er (47 h)



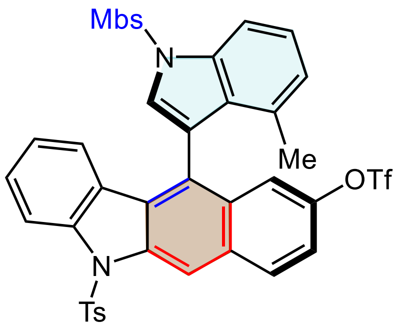
4i, 97%, 91:9 er (72 h)



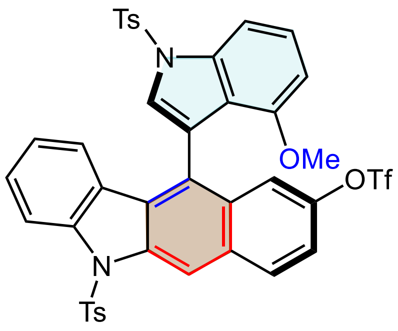
4j, 95%, 89:11 er (44 h)



4k, 97%, 95:5 er (54 h)

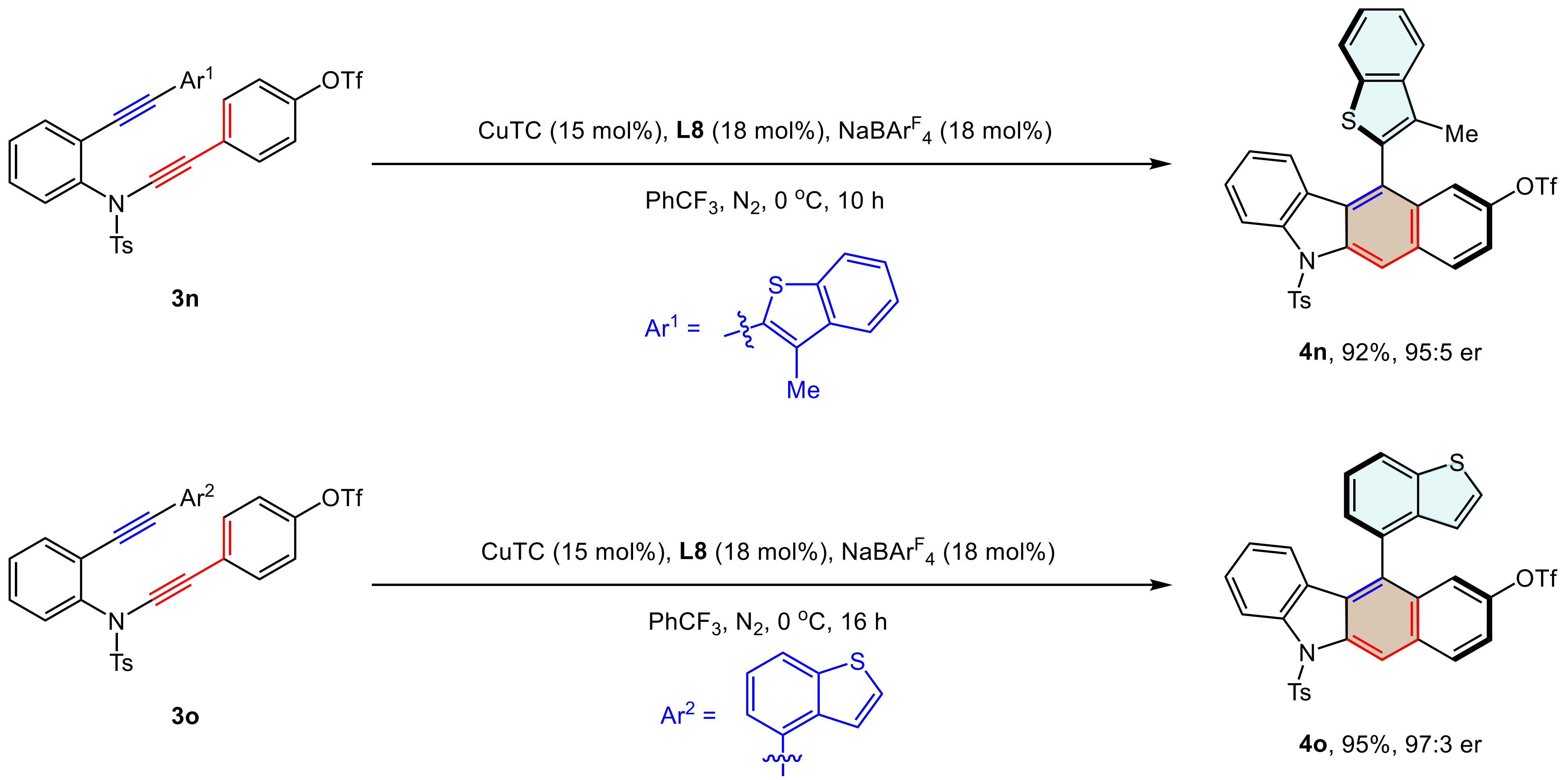


4l, 98%, 95:5 er (29 h)

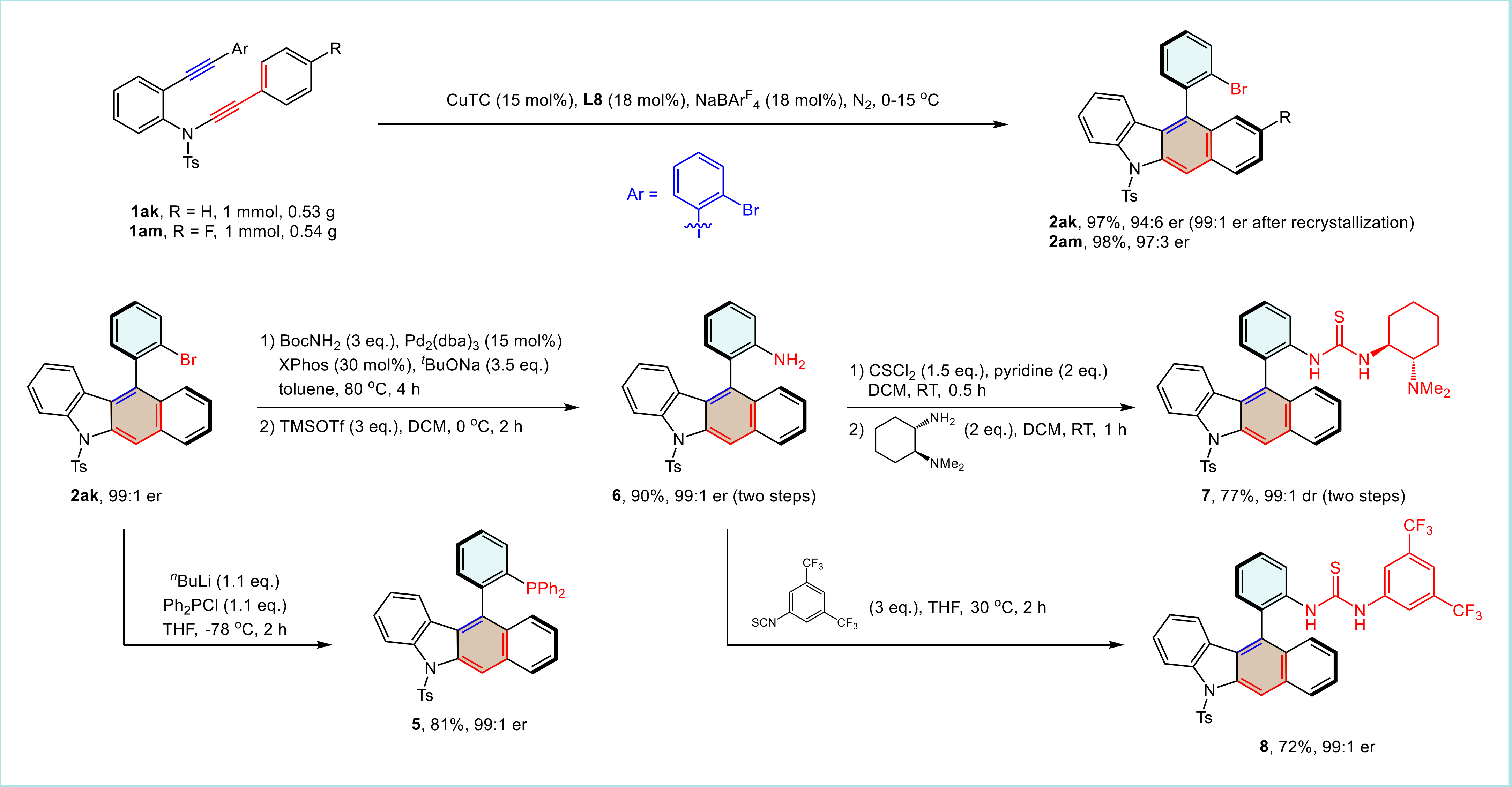


4m, 95%, 91:9 er (42 h)

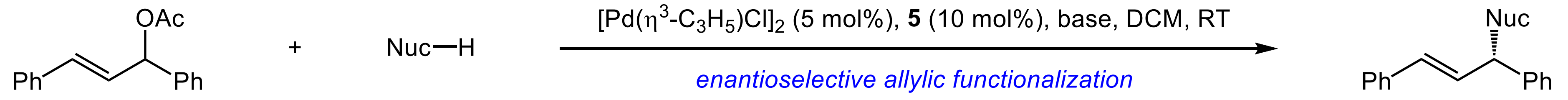
Scope for the Axially Chiral Heteroaryl Atropisomers



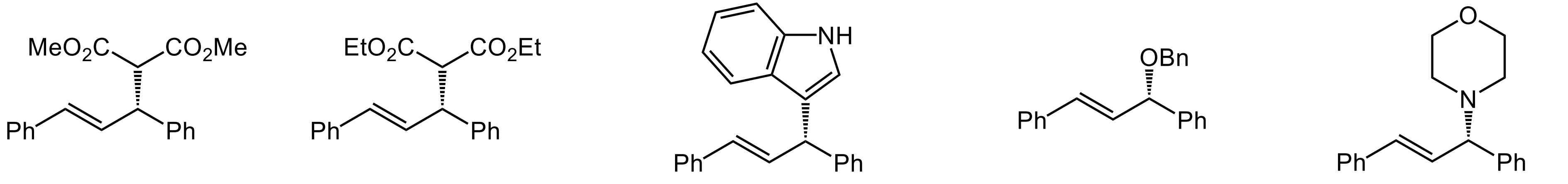
Synthesis of Chiral Ligand and Organocatalyst



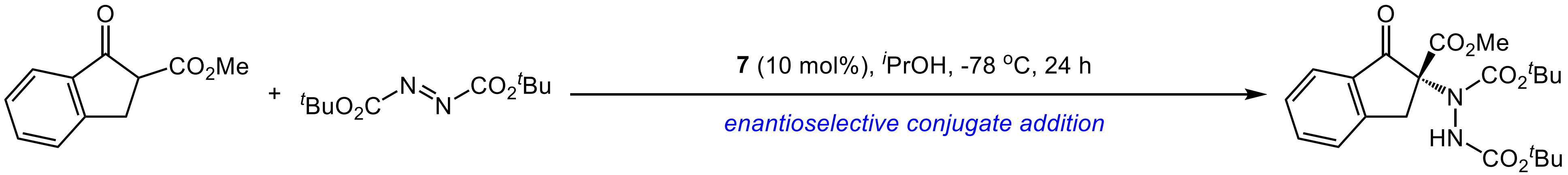
Application in Asymmetric Catalysis



(±)-**9** **10** **11**

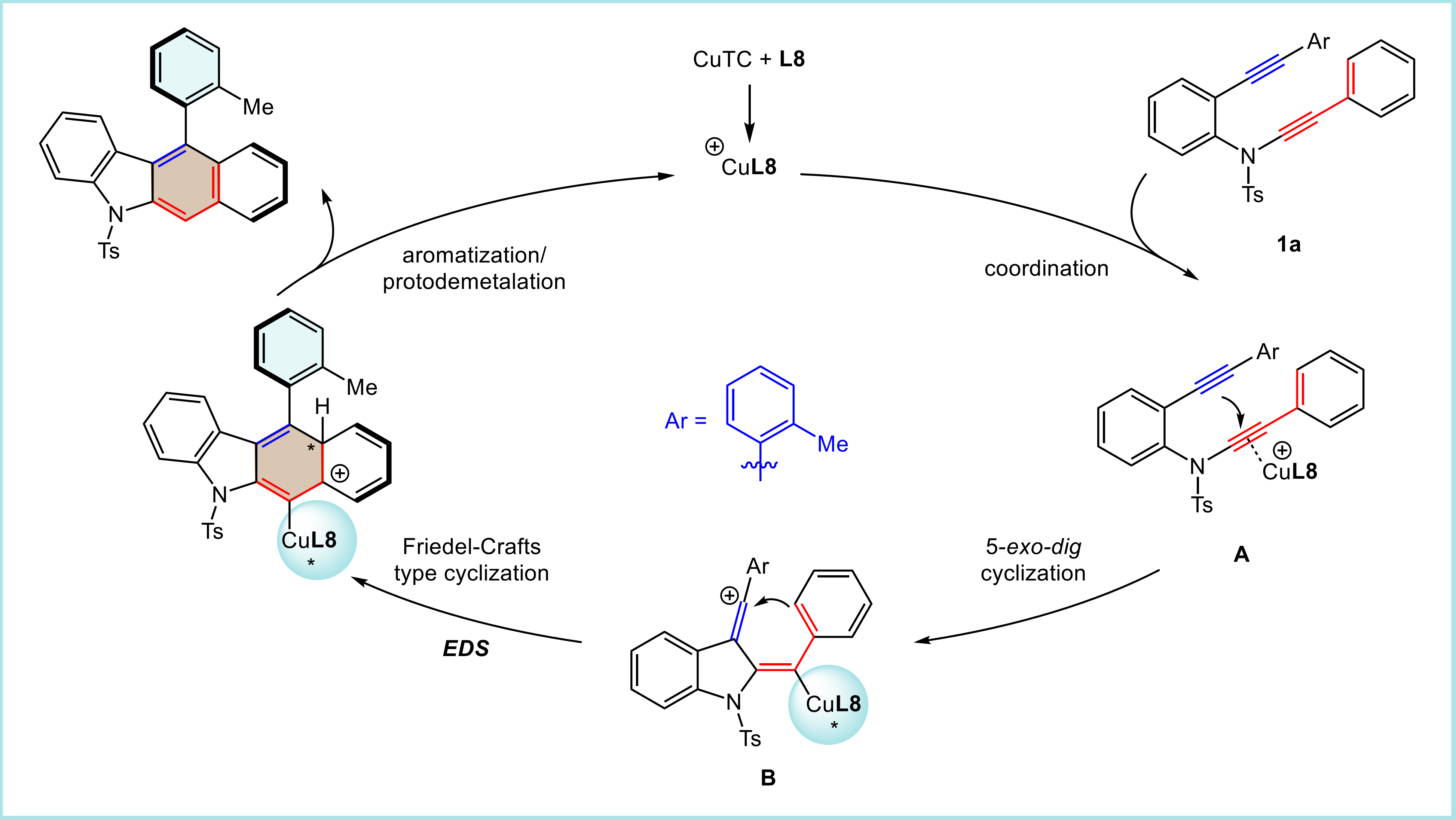


11a, 95%, 96:4 er (2 h) **11b**, 96%, 96:4 er (2 h) **11c**, 96%, 95.5:4.5 er (1.5 h) **11d**, 52%, 96:4 er (36 h) **11e**, 76%, 92:8 er (24 h)

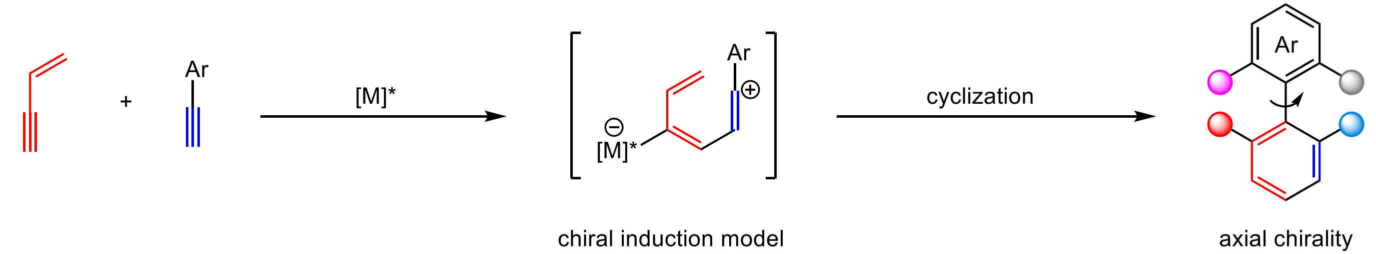


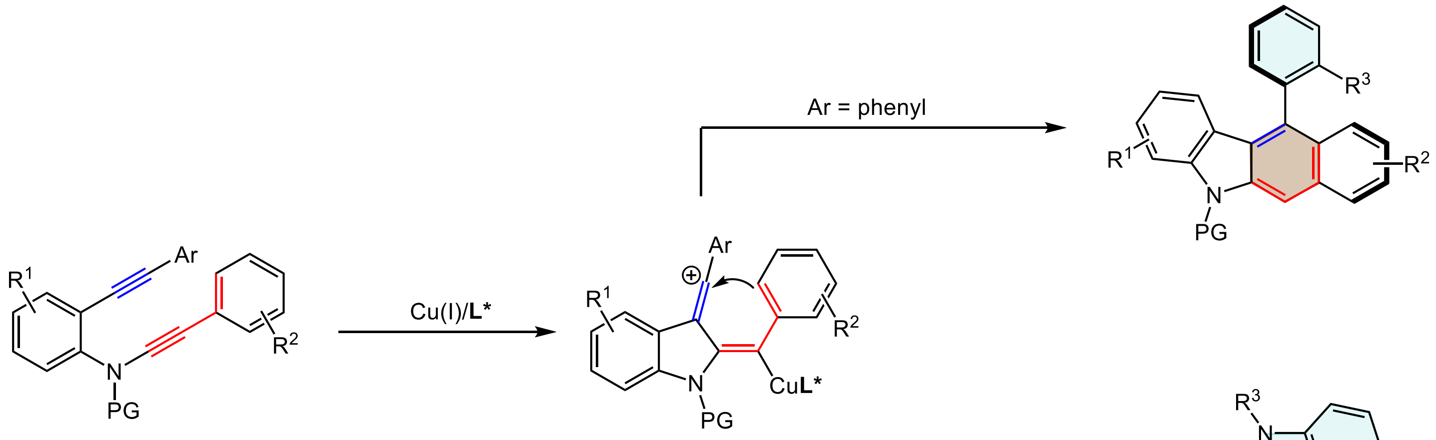
(±)-**12** **13** (1.1 eq.) **14** (99%, 99:1 er)

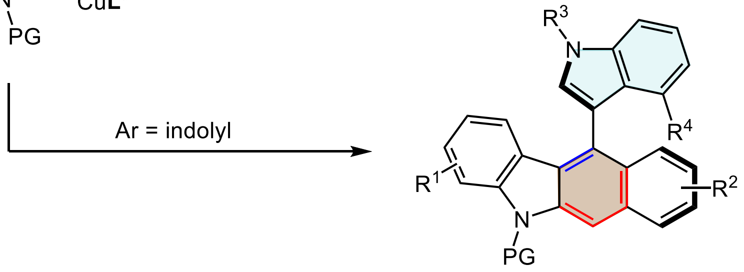
Proposed Mechanism



Summary







- enantioselective DDA reaction
- non-noble metal catalysis
- novel chiral induction model
- useful axially chiral skeletons

Strategy for Writing The First Paragraph

DDA反应提供了制备芳香族化合物的重要途径

↓

不对称DDA反应的例子鲜有报道

↓

引出本文工作

- ✓ The dehydro-Diels-Alder (DDA) reaction refers to the special Diels-Alder (D-A) reaction involving at least one alkyne moiety, which has been developed as an important approach towards aromatic compounds.
- ✓ In 2018, the only catalytic asymmetric example of DDA reaction was reported by Shibata and co-workers. By using 20 mol% of Rh(I) catalyst and chiral bisphosphine ligand, axially chiral bis(benzocarbazole) derivatives were synthesized through the atroposelective reaction of alkynyl sulfides.
- ✓ Therefore, it is imperative to develop a non-noble metal-catalyzed enantioselective DDA reaction, that requires lower catalyst loading and has broader substrate generality and improved utility.

Strategy for Writing The Last Paragraph

总结工作

- ✓ In conclusion, a copper-catalyzed enantioselective DDA reaction has been disclosed *via* the effective enantio-control of vinyl cations, leading to the atom-economical construction of axially chiral phenyl and indolyl carbazoles.

⬇

强调亮点

- ✓ Efforts to examine more chiral induction models to develop broadly useful asymmetric transformations of vinyl cations are ongoing in our laboratory.

Representative Examples

- Therefore, it is imperative to develop a non-noble metal-catalyzed enantioselective DDA reaction. (必要的，势在必行的)
- The enantiocontrol for the transformations of vinyl cations is difficult because of their high reactivities and almost barrierless conversions.(无障碍的;不需要活化能的)
- Efforts to examine more chiral induction models to develop broadly useful asymmetric transformations of vinyl cations are ongoing in our laboratory. (我们的实验室正在努力研究…).

Acknowledgement

Thanks for your attention