Literature Report VI

Organocatalytic Dynamic Kinetic Resolution Enabled Asymmetric Synthesis of Phosphorus-Containing Chiral Helicenes

Reporter: Jian Chen
Checker: Qing-Xian Xie
Date: 2023-12-25

Wu, J.-Q.; Fang, S.; Zheng, X.; He, J.; Ma, Y.; Su, Z.; Wang, T.
Angew. Chem. Int. Ed. **2023**, *62*, e202309515

CV of Prof. Wang Tianli (王天利)

Research:

- Catalytic synthesis methodology
- Green chemistry
- Design and application of phosphonium salt catalyst

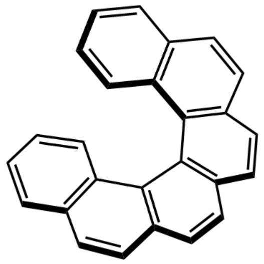
Background:

- **2002-2006** B.S., Sichuan University (Prof. Feng Xiaoming)
- **2006-2011** Ph.D., ICCAS (Prof. Fan Qing-Hua)
- **2011-2012** Assistant Professor, ICCAS
- **2012-2016** Postdoc., National University of Singapore (Prof. Lu Yixin)
- **2016-Now** Professor, Sichuan University

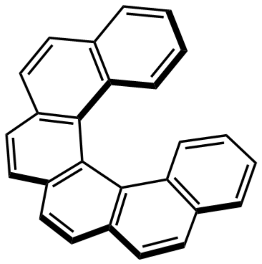
Contents

Introduction

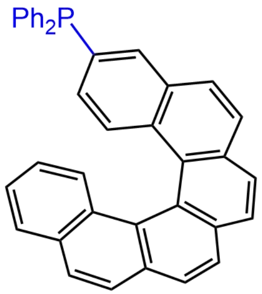
Representative monophosphine-contaning helicenes



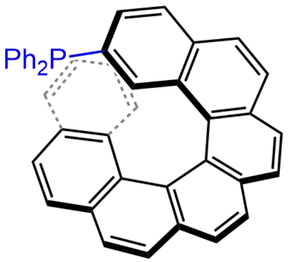
(*P*)-carbo[6]helicene



(*M*)-carbo[6]helicene



(*rac*)-**L1**



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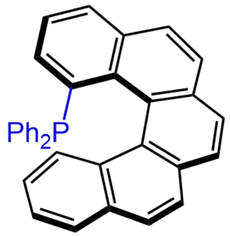

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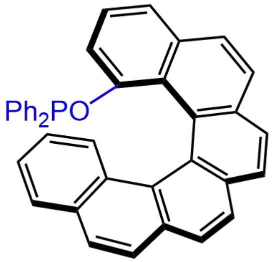
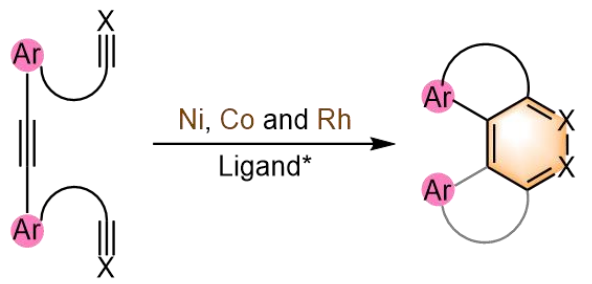


L4

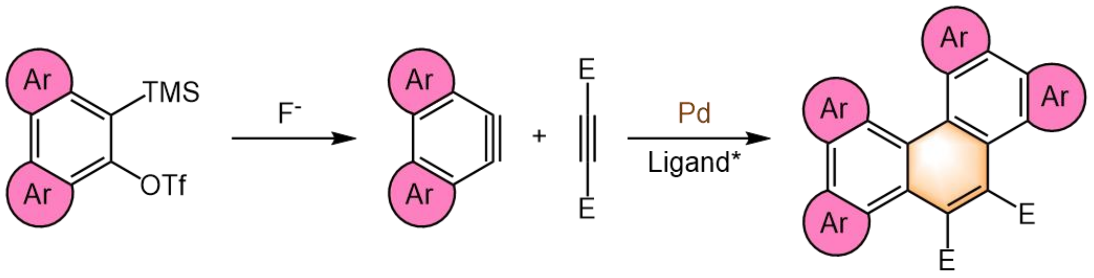
Wang, Y.; Wu, Z.-G.; Shi, F.* *Chem Catalysis* **2022**, *2*, 3077-3111

Metal-Catalyzed Synthesis of Helicenes

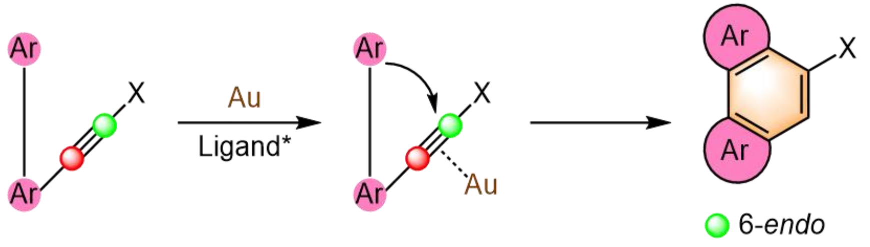
Intramolecular [2+2+2] cycloaddition



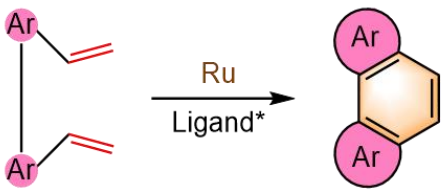
Intermolecular [2+2+2] cycloaddition



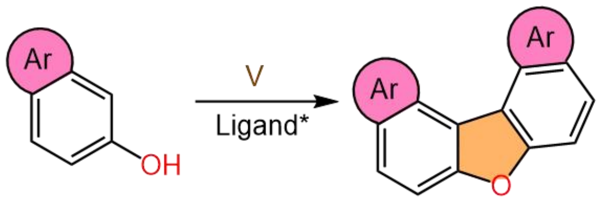
Hydroarylation



Olefin metathesis



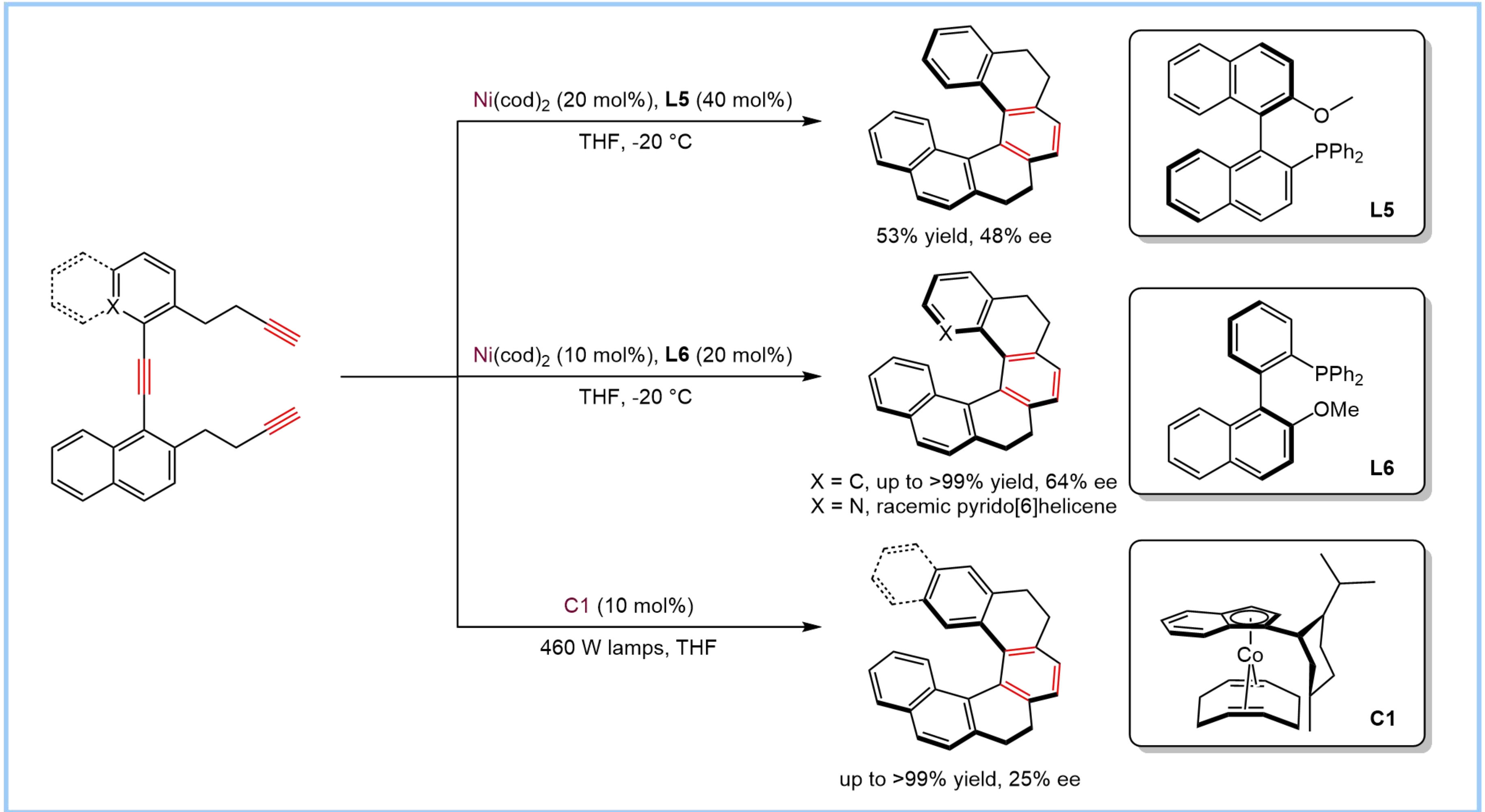
Oxidative coupling



Wang, Y.; Wu, Z.-G.; Shi, F.* *Chem Catalysis* **2022**, *2*, 3077-3111

Metal-Catalyzed Synthesis of Helicenes

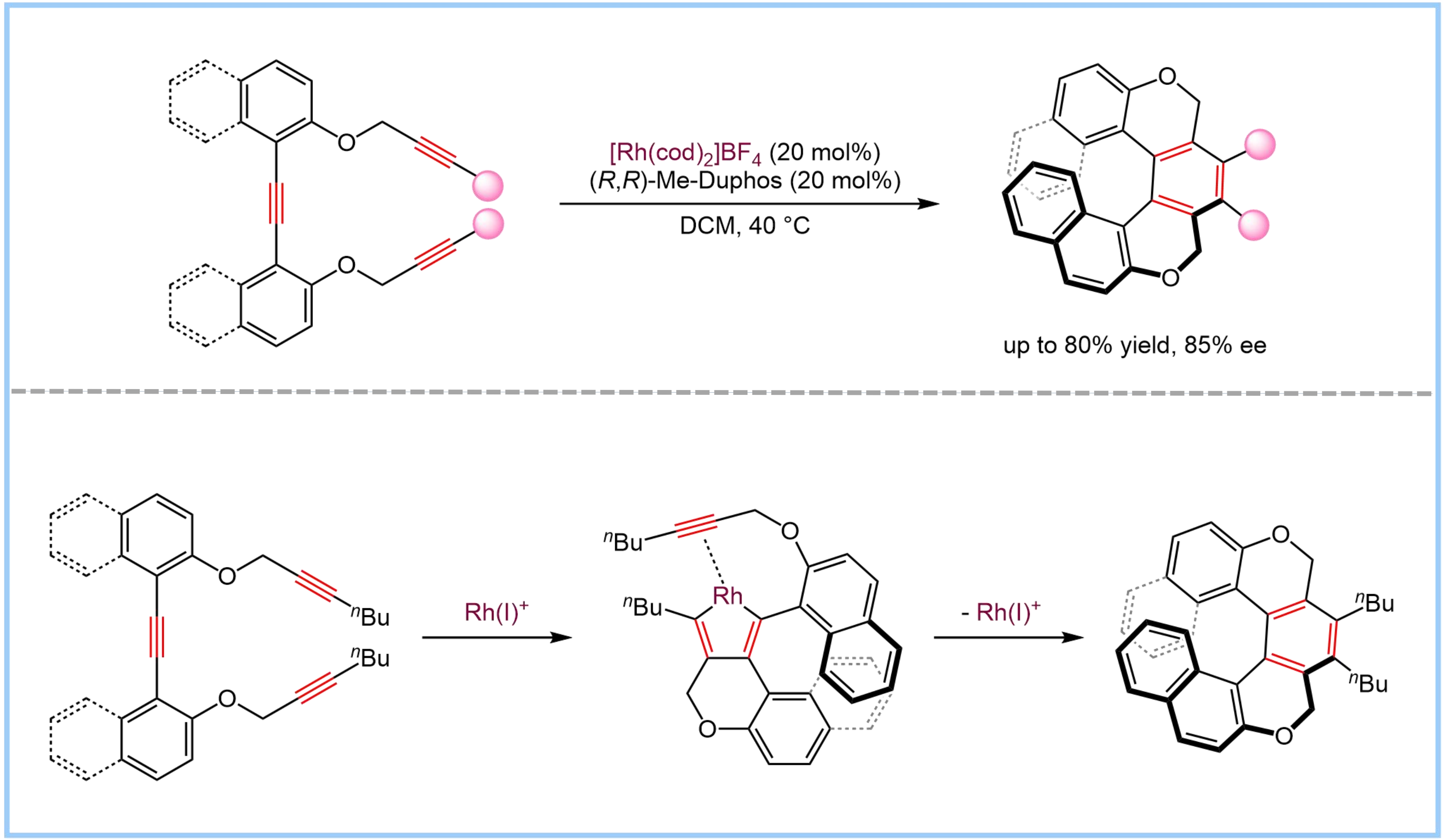
Intramolecular [2+2+2] cycloaddition (Co and Ni)



Stara, I. G. *et al*. *Tetrahedron Letters* **1999**, *40*, 1993-1996; Heller, B. *et al*. *Journal of Organometallic Chemistry* **2013**, *723*, 98-102

Metal-Catalyzed Synthesis of Helicenes

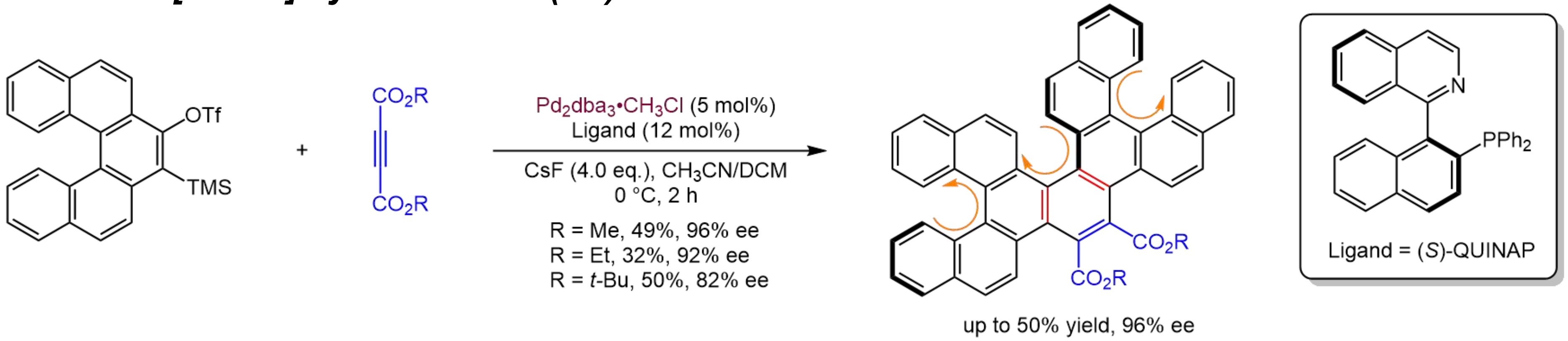
Intramolecular [2+2+2] cycloaddition (Rh)

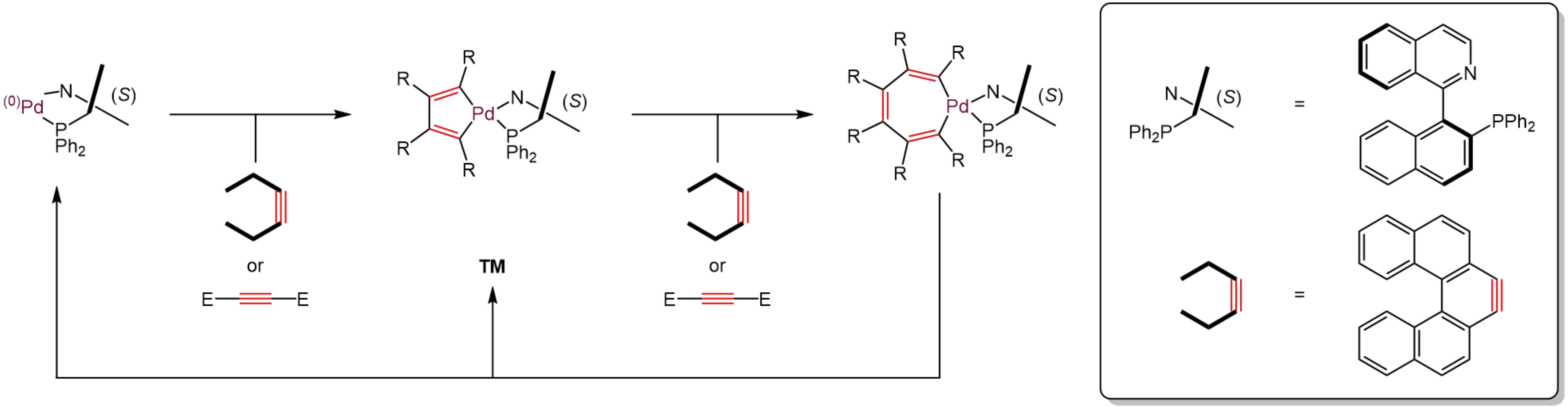


Tanaka, K.*; Kamisawa, A.; Suda, T.; Noguchi, K.; Hirano, M. *J. Am. Chem. Soc.* **2007**, *129*, 12078-12079

Metal-Catalyzed Synthesis of Helicenes

Intermolecular [2+2+2] cycloaddition (Pd)

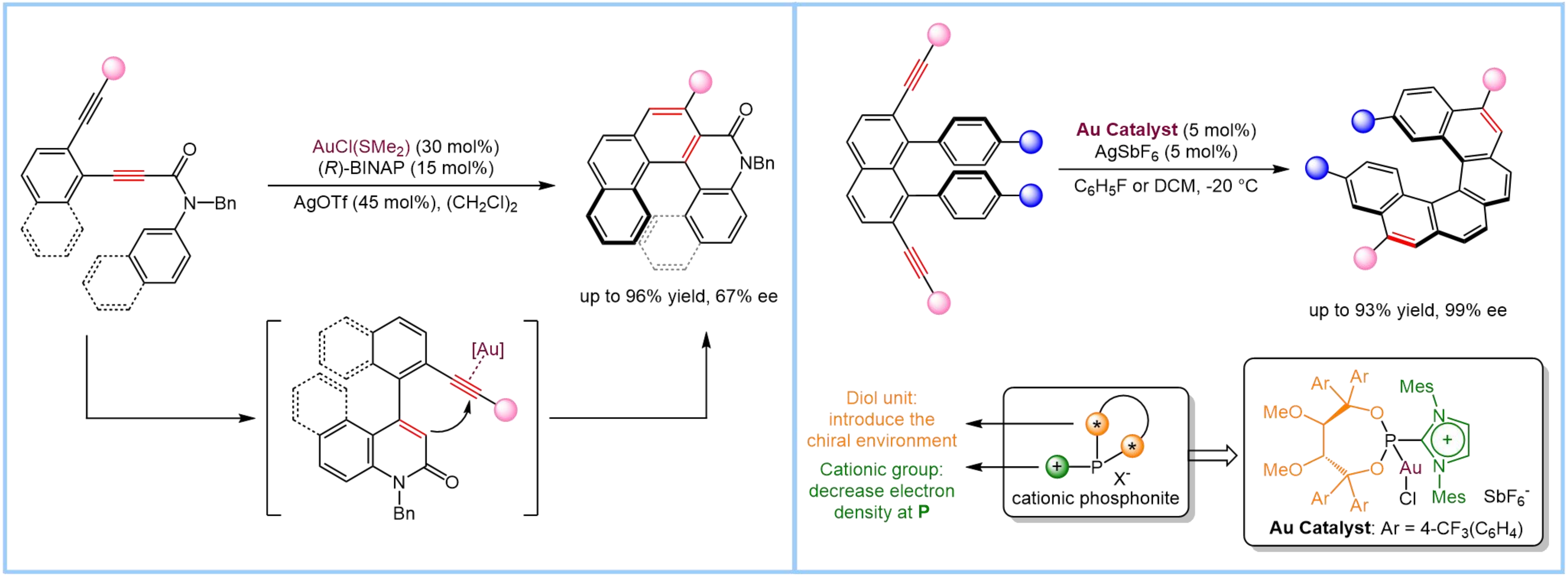




Yubuta, A.; Hosokawa, T.; Gon, M.; Tanaka, K.; Chujo, Y.; Tsurusaki, A.; Kamikawa, K.* *J. Am. Chem. Soc.* **2020**, *142*, 10025-10033

Metal-Catalyzed Synthesis of Helicenes

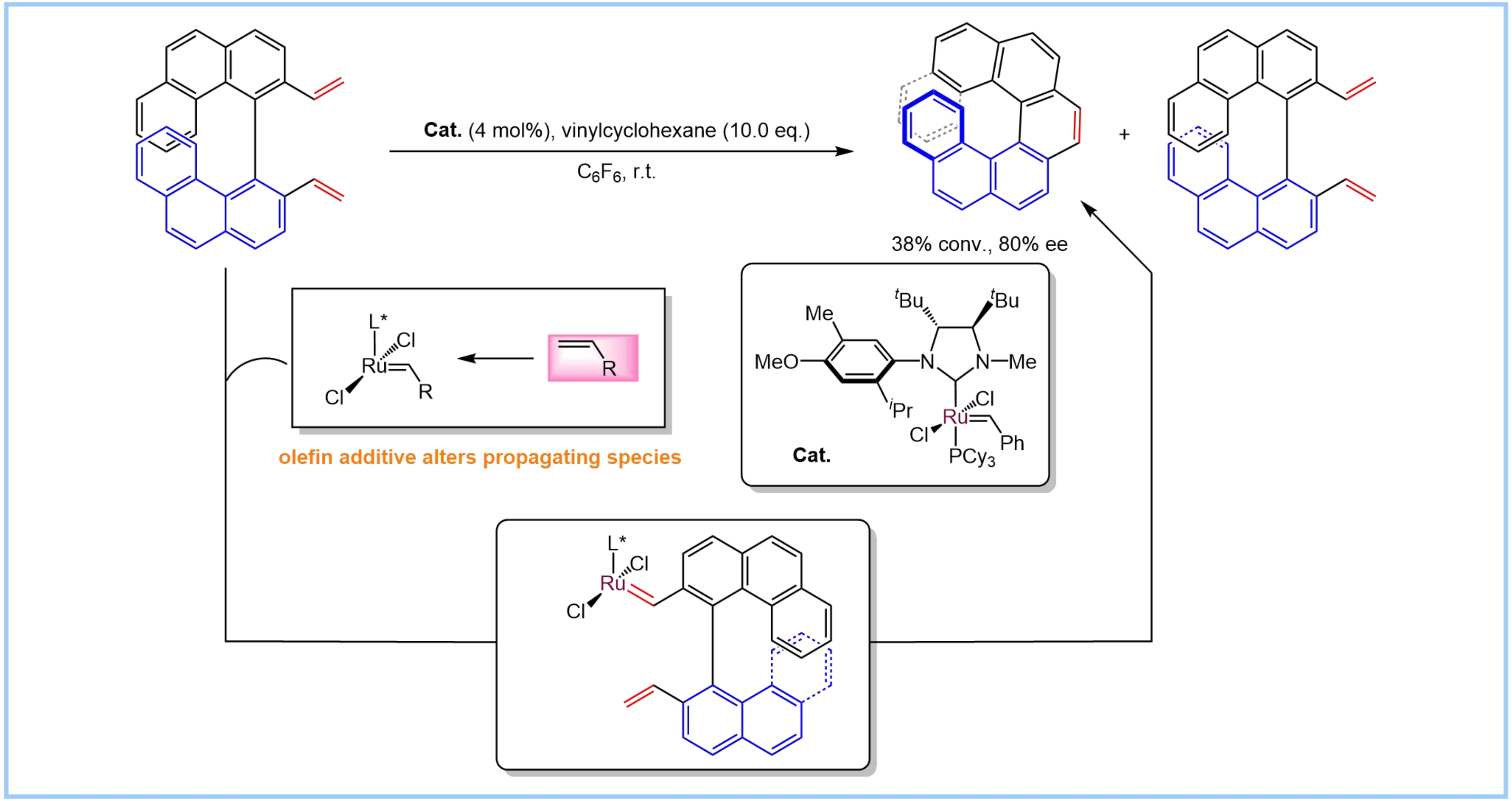
Hydroarylation (Au)



Nakamura, K.; Furumi, S.; Takeuchi, M.; Shibuya, T.; Tanaka, K.* *J. Am. Chem. Soc.* **2014**, *136*, 5555-5558
Gonzalez-Fernandez, E.; Fares, C.; Lehmann, C. W.; Alcarazo, M.* *J. Am. Chem. Soc.* **2017**, *139*, 1428-1431

Metal-Catalyzed Synthesis of Helicenes

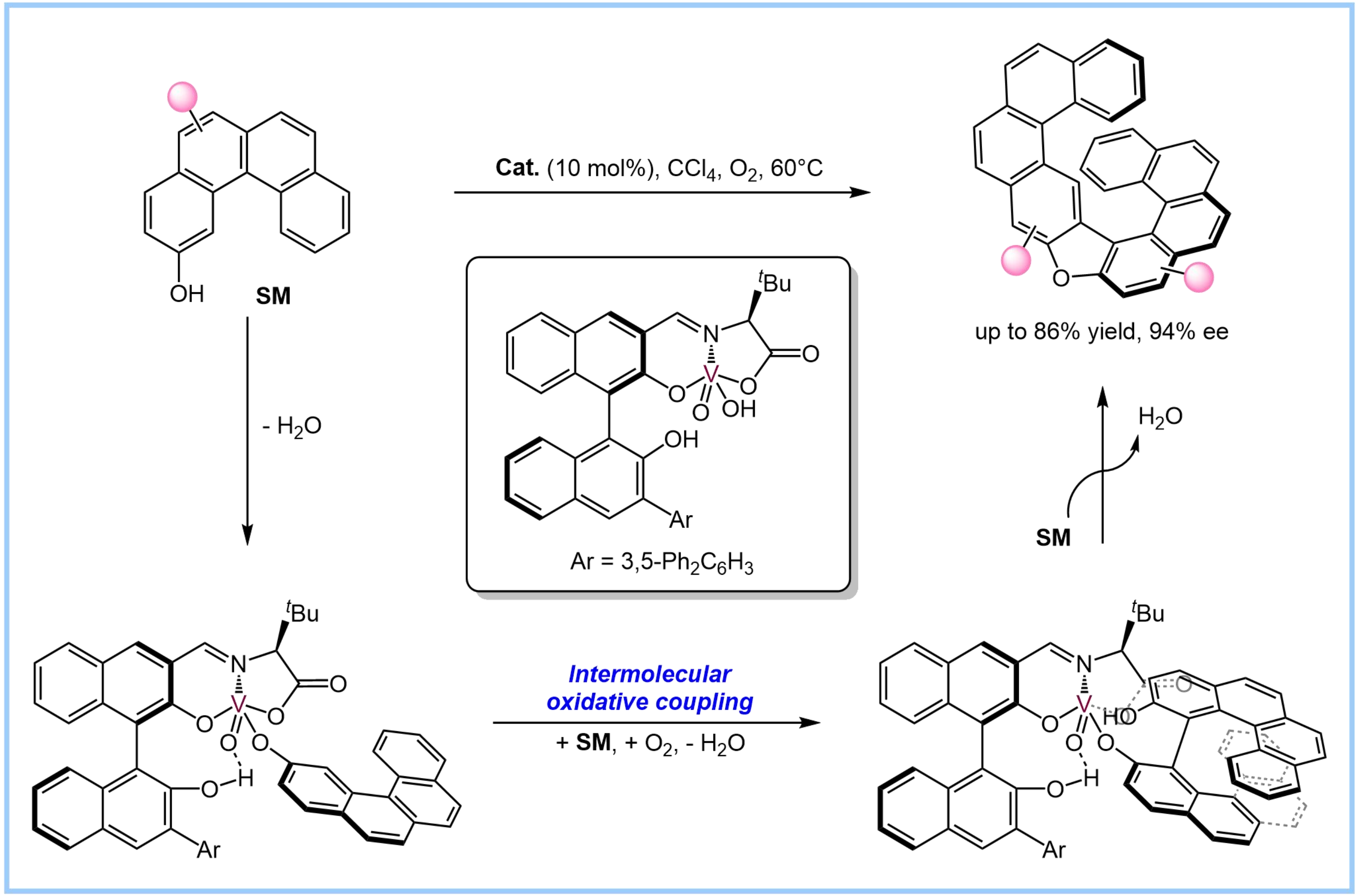
Olefin metathesis (Ru)



Grandbois, A.; Collins, S. K.* *Chem. Eur. J.* **2008**, *14*, 9323-9329

Metal-Catalyzed Synthesis of Helicenes

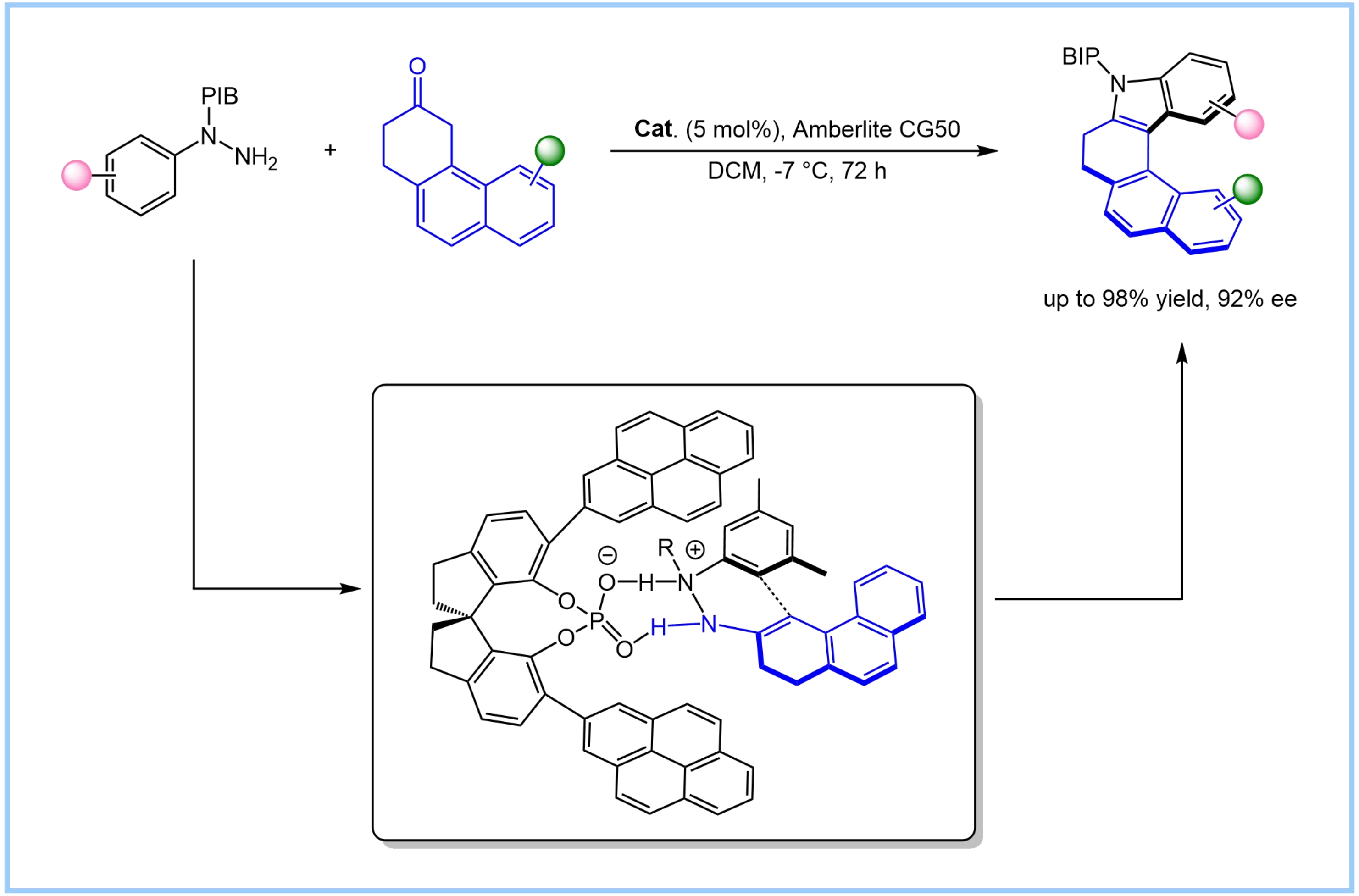
Oxidative coupling (V)



Sako, M.; Takeuchi, Y.; Tsujihara, T.; Kodera, J.; Chujo, Y.; Kawano, T.; Sasai, H.* *J. Am. Chem. Soc.* **2016**, *138*, 11481-11484

Organocatalytic Synthesis of Helicenes

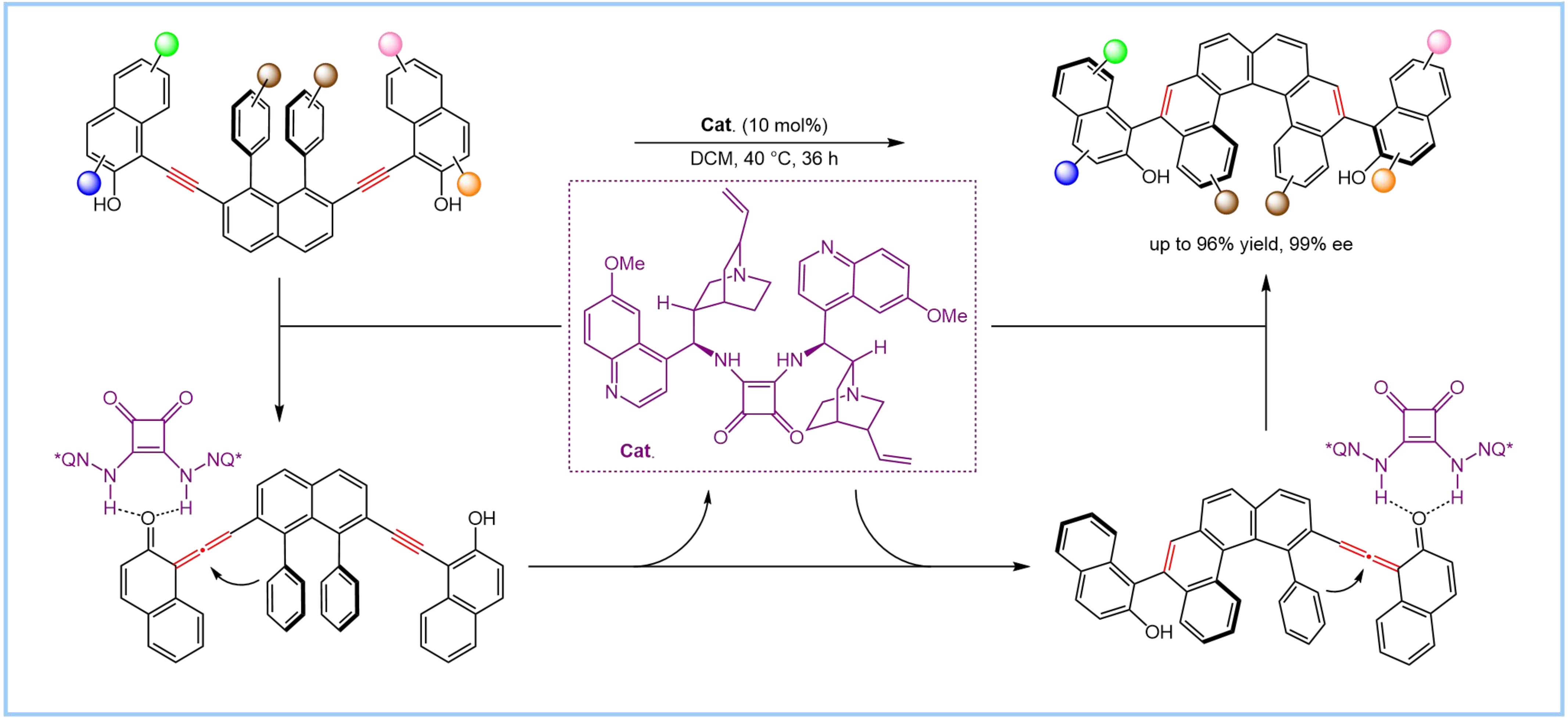
Fisher indole synthesis (CPA catalysis)



Kotzner, L.; Webber, M. J.; Martinez, A.; Fusco, C. D.; List, B.* *Angew. Chem. Int. Ed.* **2014**, *53*, 5202-5205

Organocatalytic Synthesis of Helicenes

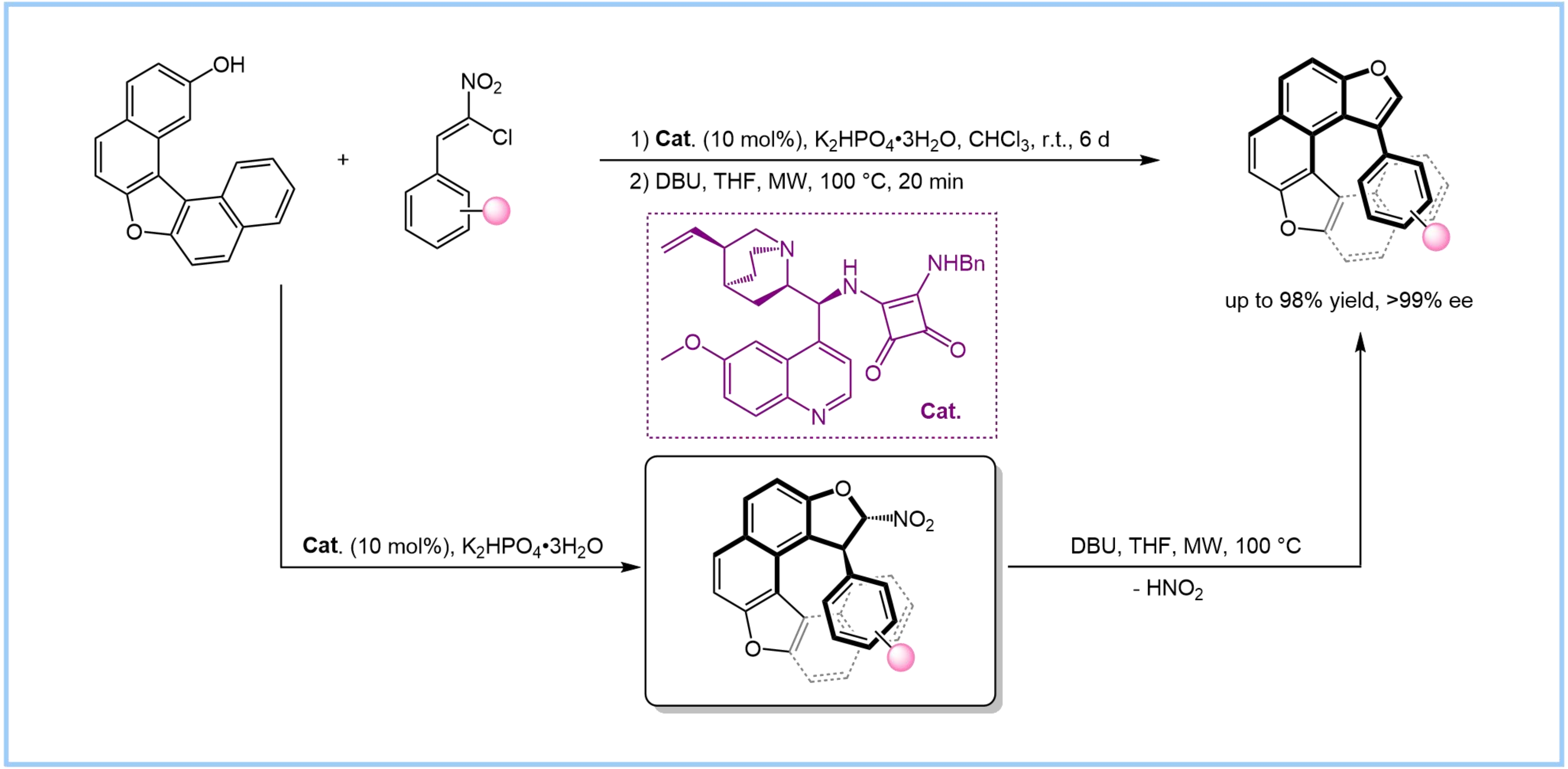
[4+2] Cyclization (Chiral squaramide catalysis)



Jia, S.; Li, S.; Liu, Y.; Qin, W.; Yan, H.* *Angew. Chem. Int. Ed.* **2019**, *58*, 18496-18501

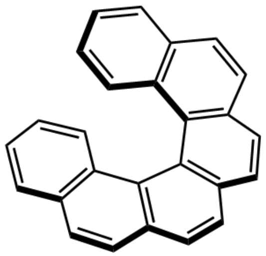
Organocatalytic Synthesis of Helicenes

[3+2] Cyclization (Chiral squaramide catalysis)

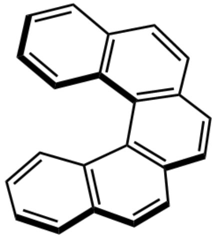


Liu, P.; Bao, X.; Naubron, J.-V.; Chentouf, S.; Humble, S.; Vanthuyne, N.; Bonne, D.* *J. Am. Chem. Soc.* **2020**, *142*, 16199-16240

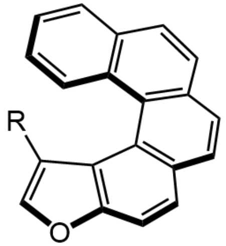
Introduction



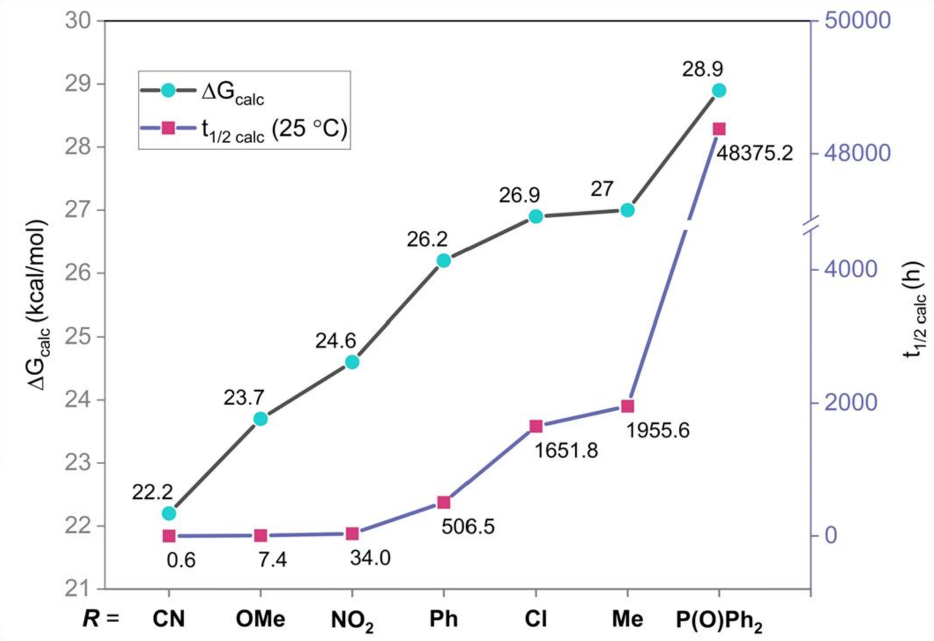
carbo[6]helicene
$\Delta G_{exp}^{‡}$ = 35.9 kcal/mol
$\Delta G_{calc}^{‡}$ = 36.9 kcal/mol
configurationally stable



carbo[5]helicene
$\Delta G_{exp}^{‡}$ = 24.8 kcal/mol
$t^{25}_{1/2}$ calc = 47.5 h
relatively stable

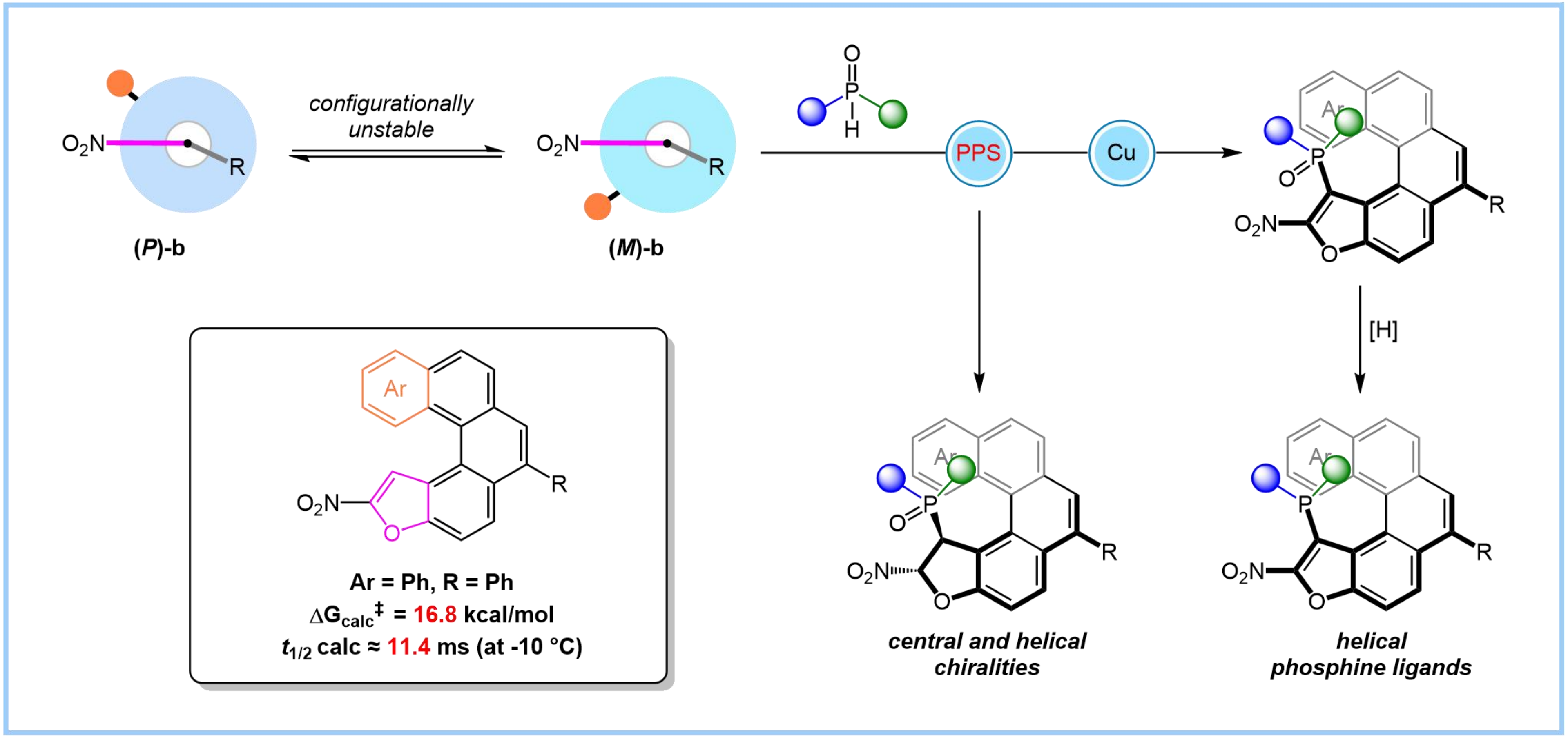


oxa[5]helicene
$\Delta G_{calc}^{‡}$ = 15.7 kcal/mol
$t^{25}_{1/2}$ calc = 36.4 ms (R =H)
unstable

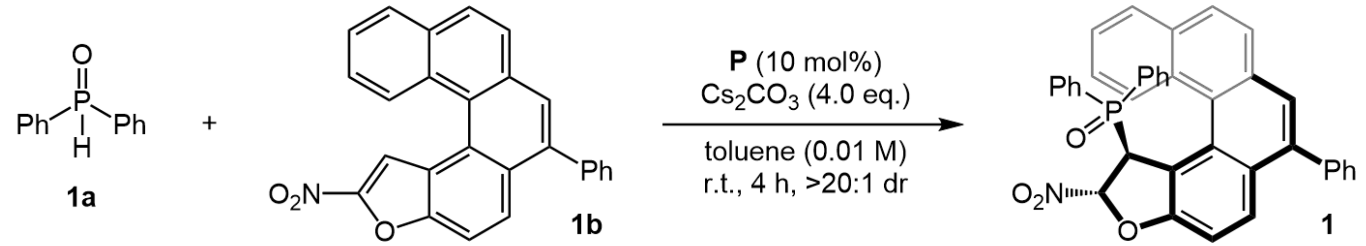


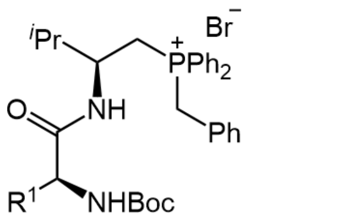
DFT and experiment guided relationship between conformational stability and structures

Project Synopsis

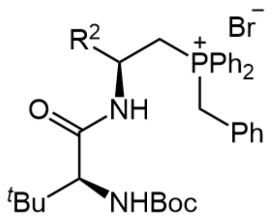


Optimization of Reaction Conditions

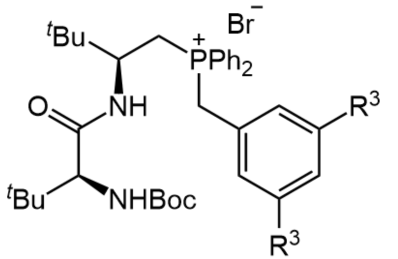




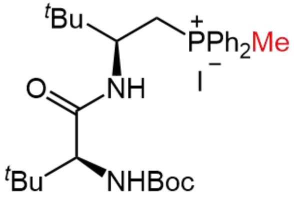
P1: R^1 = Me, 84% yield, 26% ee
P2: R^1 = ^{i}Pr, 88% yield, 46% ee
P3: R^1 = ^{t}Bu, 85% yield, 61% ee



P4: R^2 = Me, 87% yield, 44% ee
P5: R^2 = ^{t}Bu, 87% yield, 80% ee

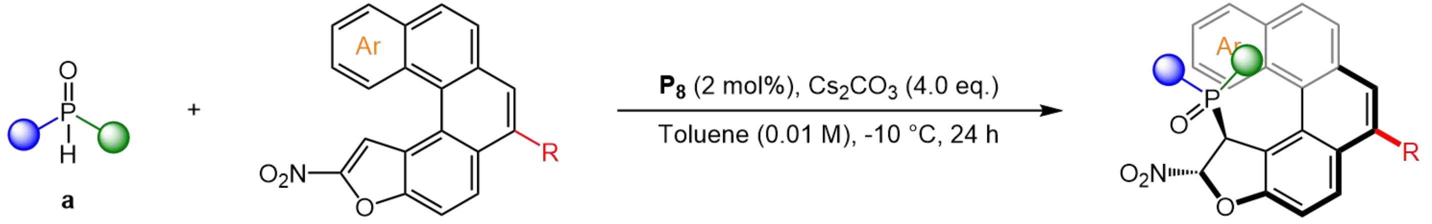


P6: R^3 = Me, 85% yield, 78% ee
P7: R^3 = 3,4,5-OMe-C_6H_2
87% yield, 81% ee

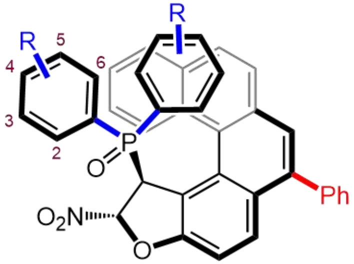


P8
88% yield, 88% ee
90% yield, 91% ee (0 °C, 10 h)
92% yield, 92% ee (-10 °C, 24 h)
92% yield, 92% ee (-10 °C, 24 h, 2 mol%)

Substrate Scope

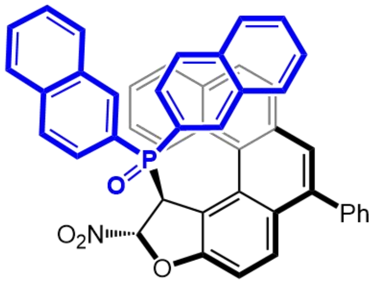


a **b** **1-25**

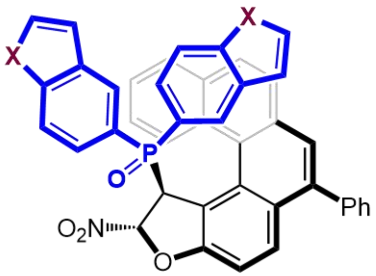


1, R = H, 92% yield, 92% ee
2, R = 3-Cl, 99% yield, 96% ee
3, R = 3-OMe, 98% yield, >99% ee
4, R = 4-F, 97% yield, 94% ee
5, R = 4-Cl, 99% yield, 92% ee
6, R = 4-OMe, 96% yield, 93% ee
7, R = 4-OEt, 96% yield, 96% ee

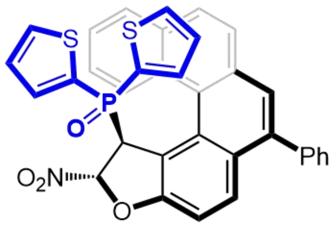
8, R = 4-OPh, 94% yield, 90% ee
9, R = 4-Me, 80% yield, 92% ee
10, R = 4-Et, 82% yield, 87% ee
11, R = 4-Ph, 97% yield, 97% ee
12, R = 3,5-Me, 98% yield, >99% ee
13, R = 3,5-OMe, 99% yield, >99% ee



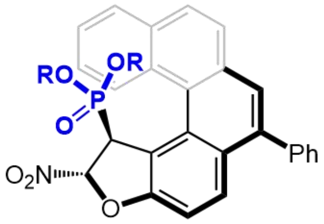
14, 99% yield, >99% ee



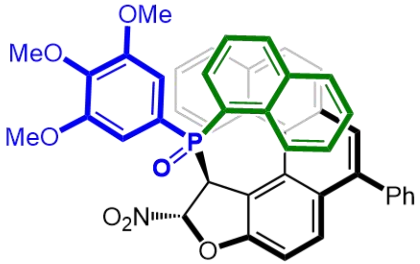
15, X = O, 98% yield, 96% ee
16, X = S, 97% yield, 98% ee



17, 88% yield, 78% ee

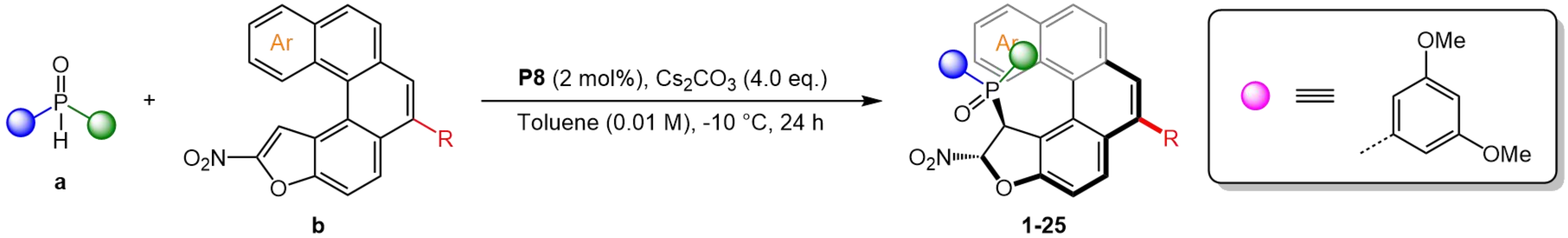


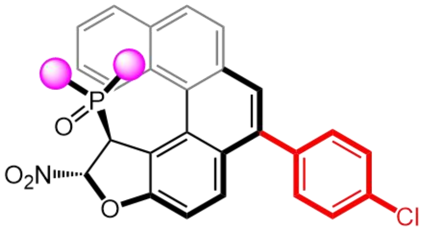
18, R = Me, 88% yield, 92% ee
19, R = Et, 69% yield, 80% ee



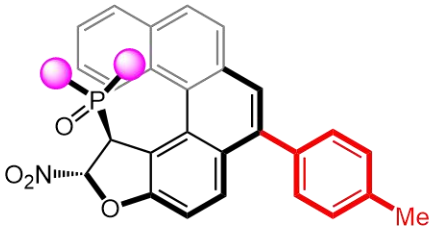
20
89% yield, 5:1 dr, 97% ee (major)

Substrate Scope

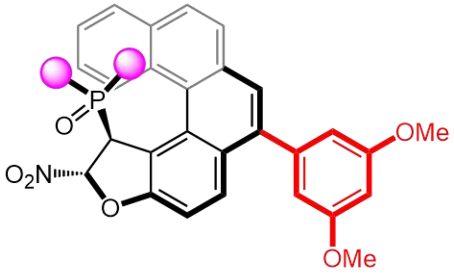




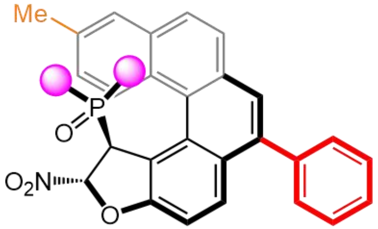
21, 99% yield, >99% ee



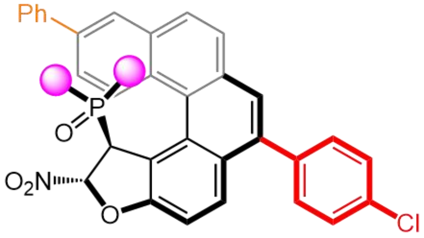
22, 98% yield, 99% ee



23, 97% yield, >99% ee

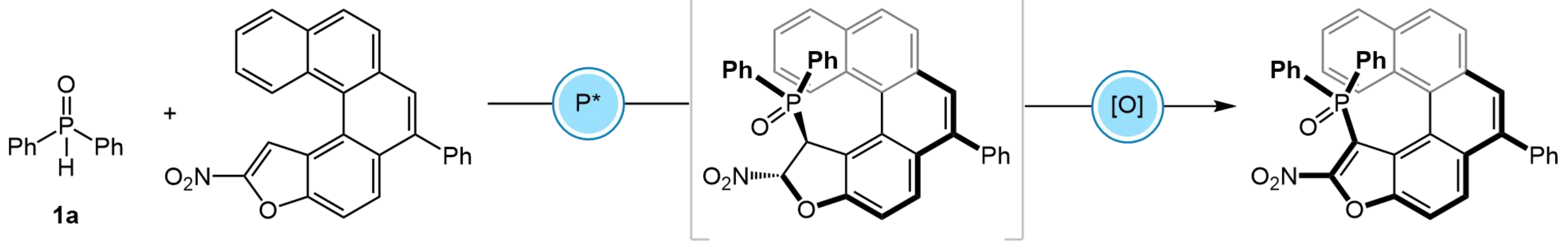


24, 98% yield, >99% ee



25, 97% yield, >99% ee

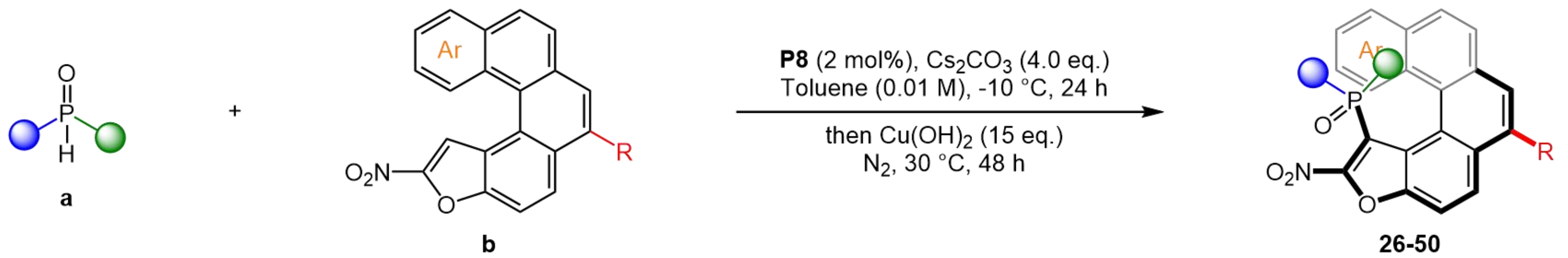
Optimization of Reaction Conditions

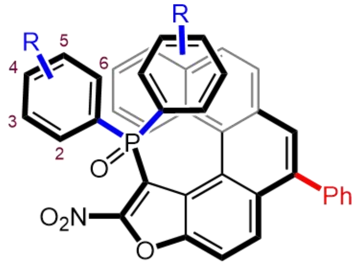


Entry[a]	[O]	Solvent	T (℃) / (h)	Yield (%)	Ee (%)
1	MnO_2	CH_2Cl_2	0 (48)	<5	-
2	$PhI(OAc)_2$	CH_3Cl	0 (48)	<5	-
3	DDQ	CH_2Cl_2	40 (48)	<5	-
4[b]	CAN	$MeCN/H_2O$	r.t. (8)	<5	-
5	Ag_2O	CH_2Cl_2	r.t. (48)	<5	-
6	$Cu(NO_3)_2$	CH_2Cl_2	r.t. (72)	11	92
7[c]	$Cu(OH)_2$	Toluene	30 (48)	85	92

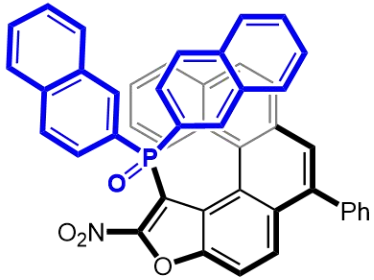
[a] Condition: **1a** (0.12 mmol), **1b** (0.1 mmol), **P8** (0.002 mmol), Cs_2CO_3 (0.4 mmol) in 10 mL toluene at 10 ℃ for 24 h. After the reaction completed, the reaction mixture was filtered to remove Cs_2CO_3, and the residue was directly conducted under the following condition: oxidant (0.5 mmol) in 10 ml solvent. [b] $MeCN/H_2O$ (v/v = 4/1). [c] With $Cu(OH)_2$ (1.5 mmol) under N_2.

Substrate Scope

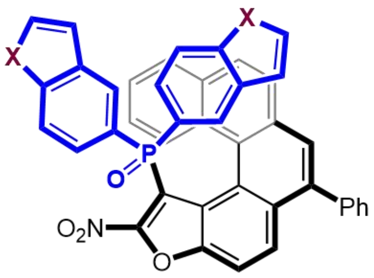




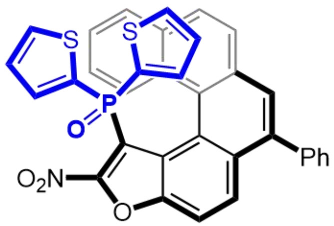
26, R = H, 85% yield, 92% ee
27, R = 3-Cl, 87% yield, 96% ee
28, R = 3-OMe, 83% yield, 98% ee
29, R = 4-F, 90% yield, 95% ee
30, R = 4-Cl, 92% yield, 92% ee
31, R = 4-OMe, 82% yield, 93% ee
32, R = 4-OEt, 81% yield, 95% ee
33, R = 4-OPh, 78% yield, 88% ee
34, R = 4-Me, 76% yield, 92% ee
35, R = 4-Et, 77% yield, 86% ee
36, R = 4-Ph, 77% yield, 97% ee
37, R = 3,5-Me, 89% yield, 99% ee
38, R = 3,5-OMe, 92% yield, >99% ee



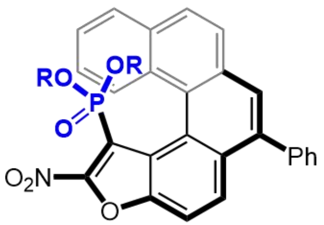
39, 89% yield, >99% ee



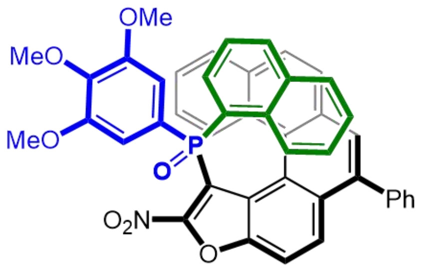
40, X = O, 80% yield, 96% ee
41, X = S, 82% yield, 98% ee



42, 73% yield, 78% ee

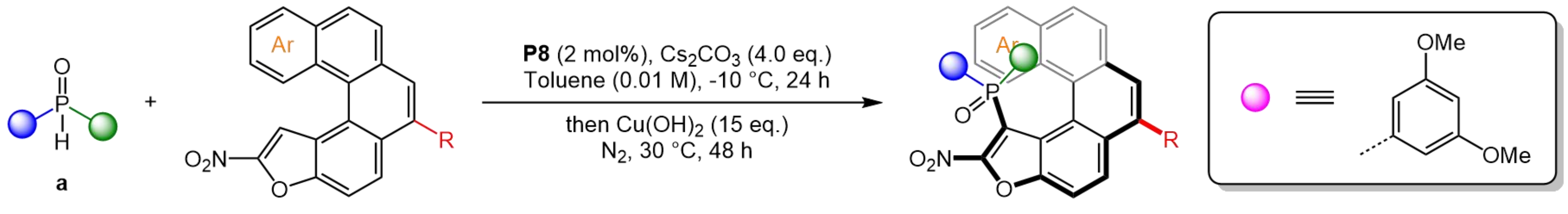


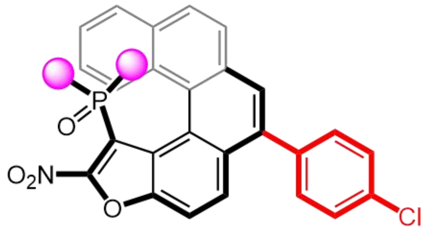
43, R = Me, 86% yield, 92% ee
44, R = Et, 66% yield, 80% ee



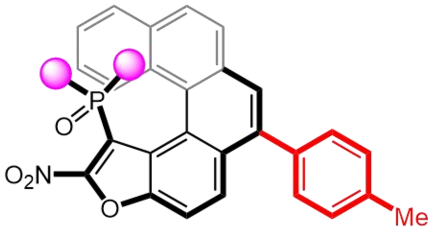
45
73% yield, 5:1 dr, 97% ee (major)

Substrate Scope

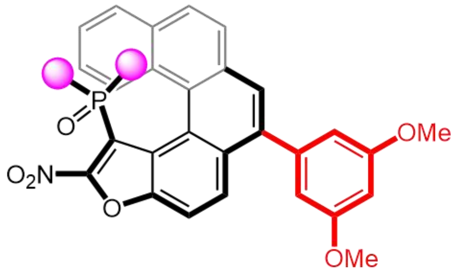




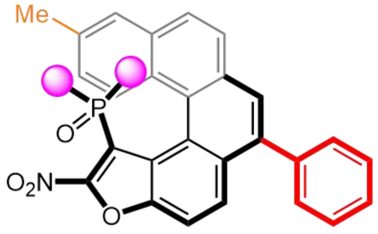
46, 82% yield, >99% ee



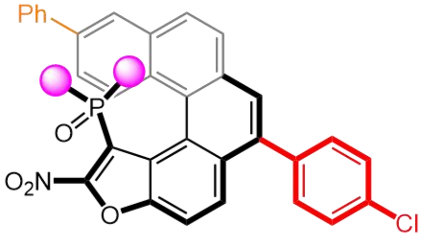
47, 88% yield, >99% ee



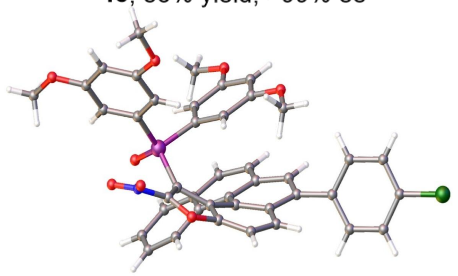
48, 86% yield, >99% ee



49, 79% yield, >99% ee

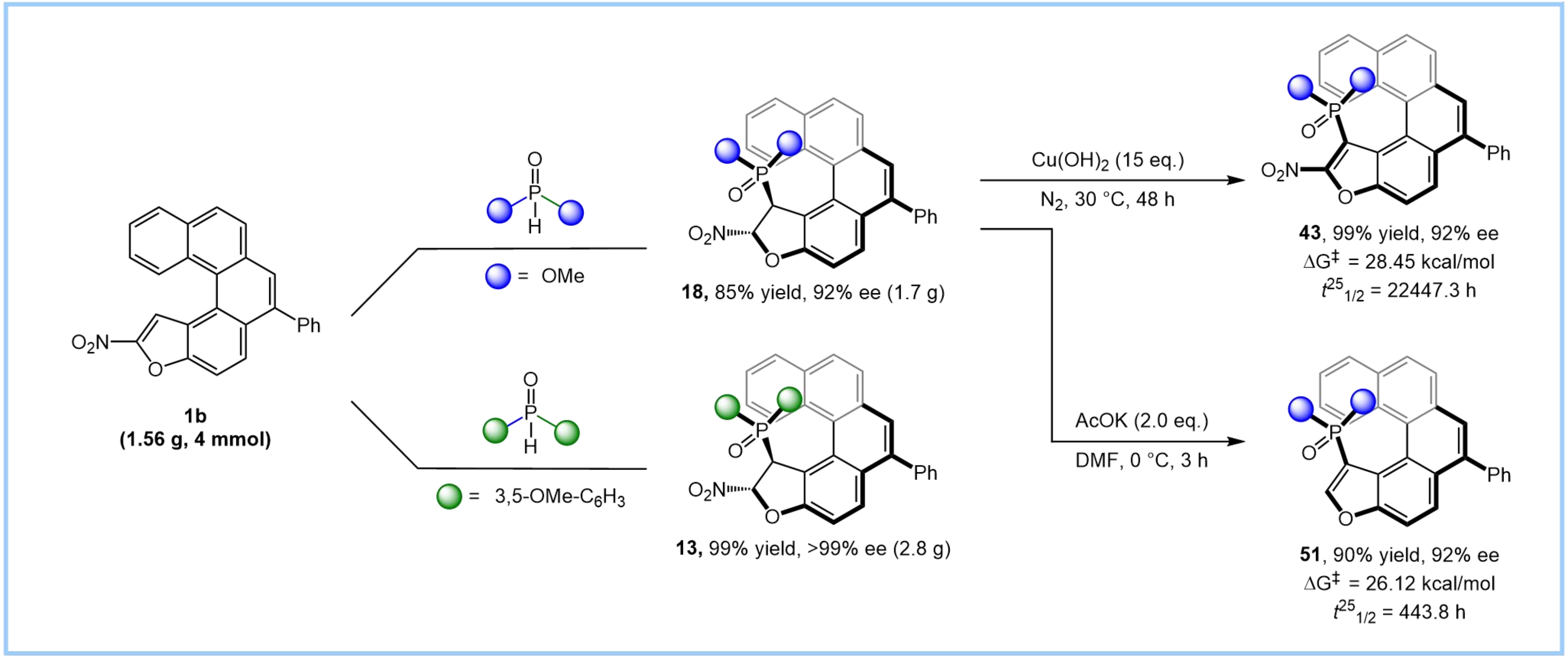


50, 83% yield, >99% ee

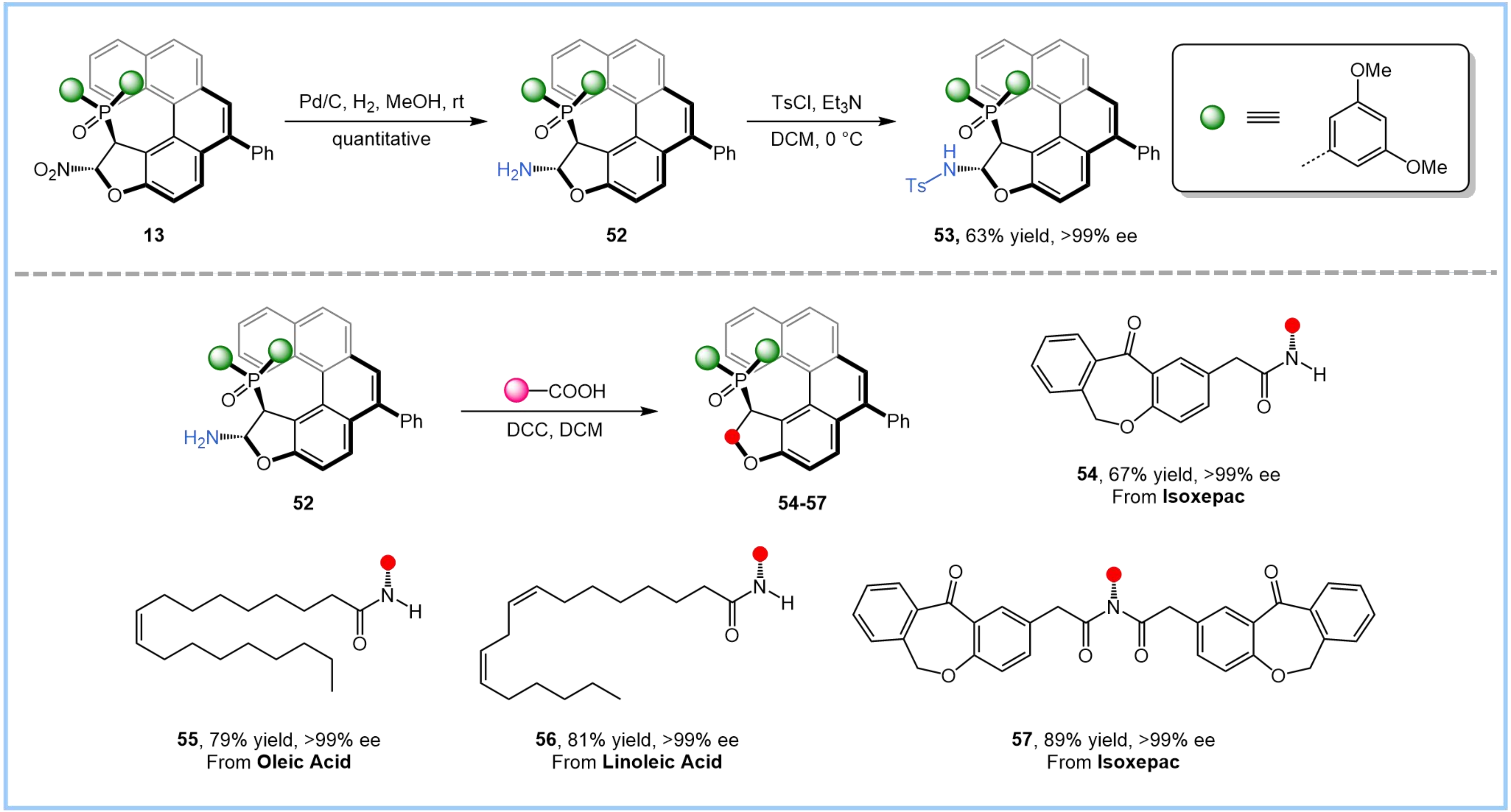


(*M*)-**46**
(CCDC 2245557)

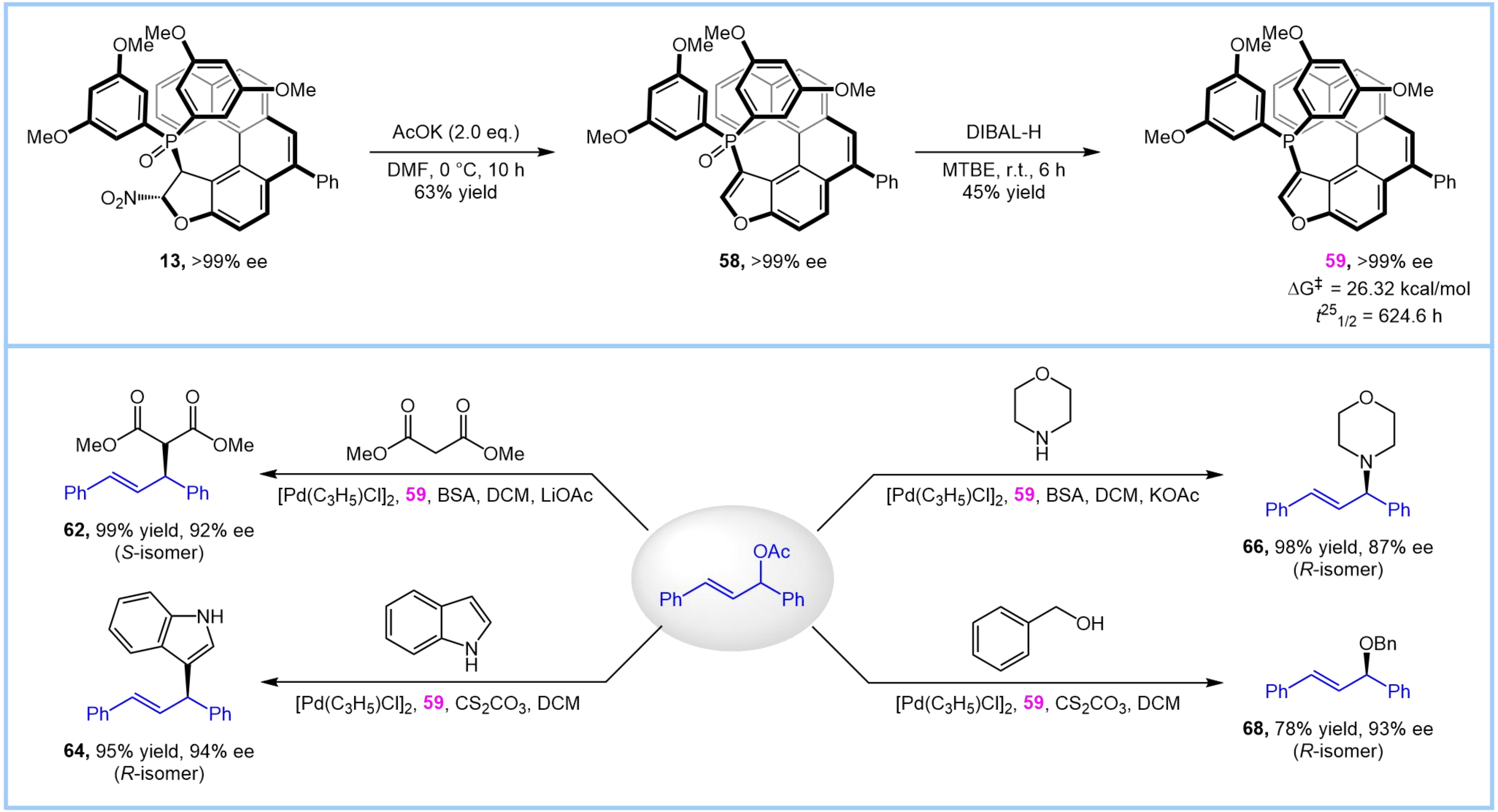
Gram Scale & Transformations of Products



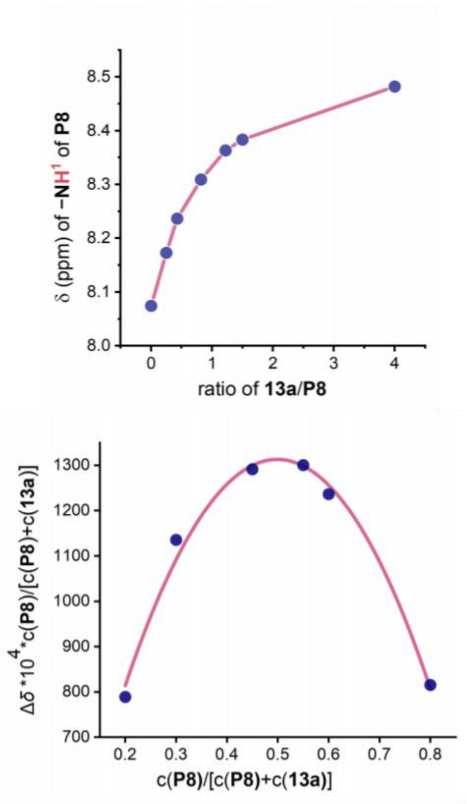
Transformations of Products

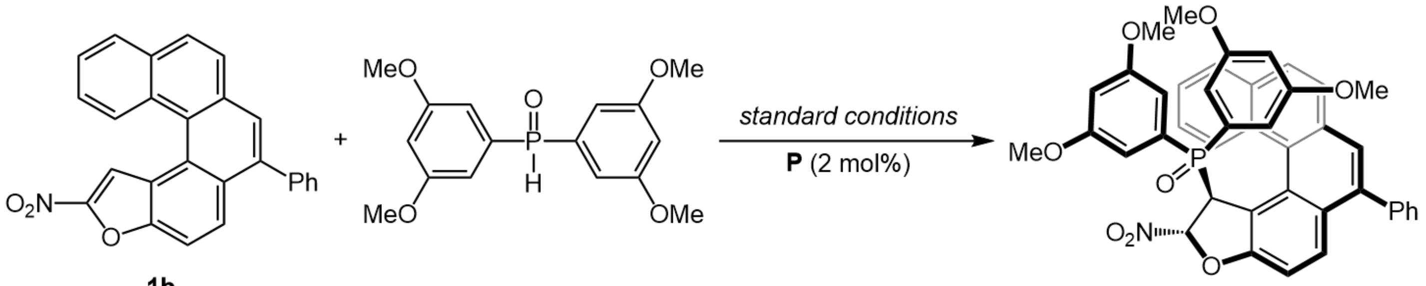


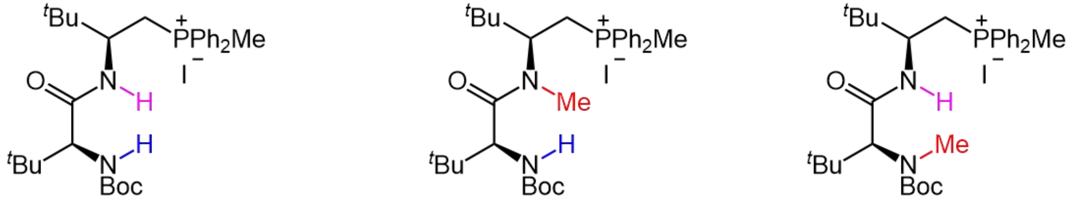
Transformations of Products & Evaluation of 59



Mechanism Study





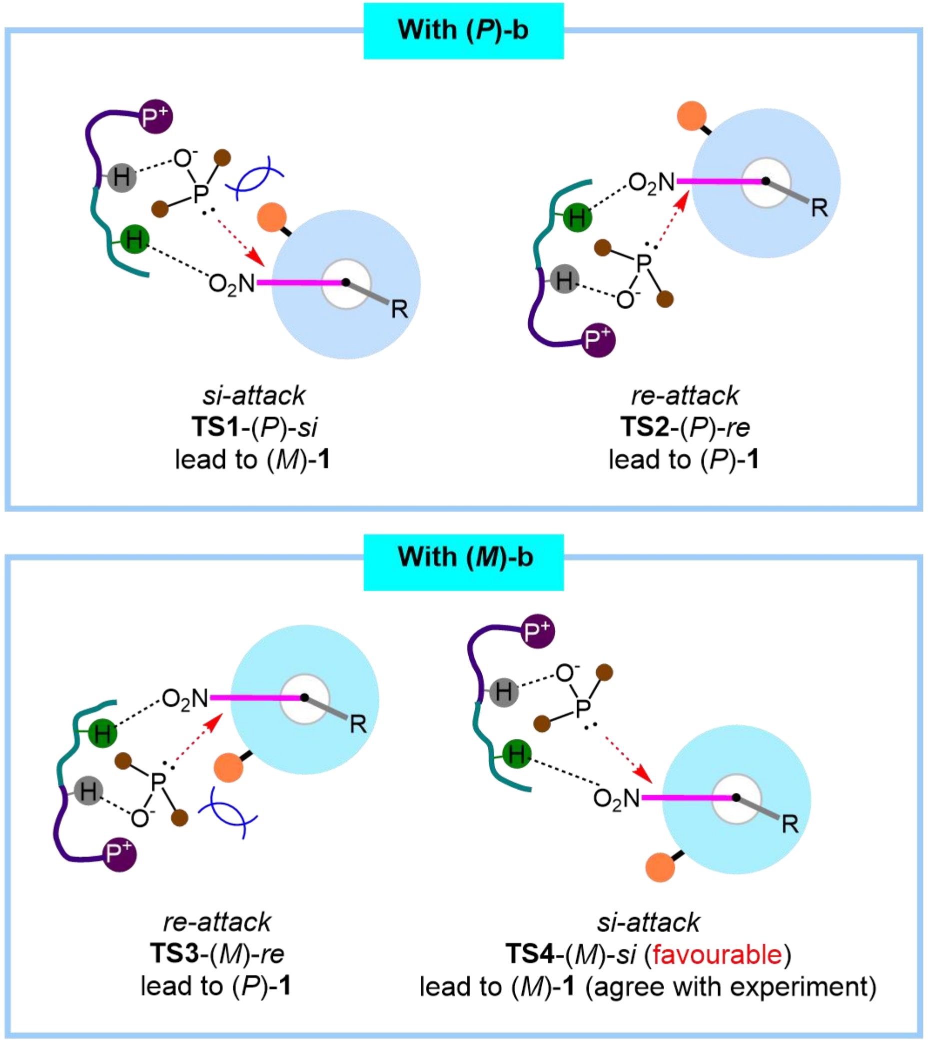


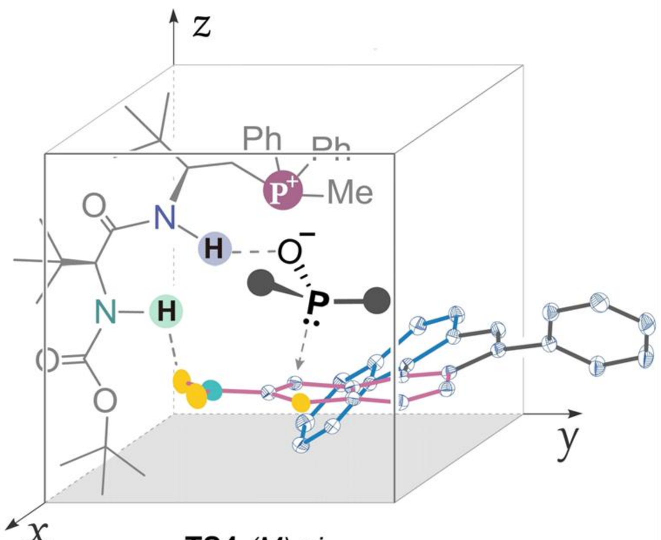
P8
99% yield, >99% ee (toluene)
47% yield, 0% ee (MeOH)

P8-1
96% yield, 14% ee (toluene)

P8-2
97% yield, 72% ee (toluene)

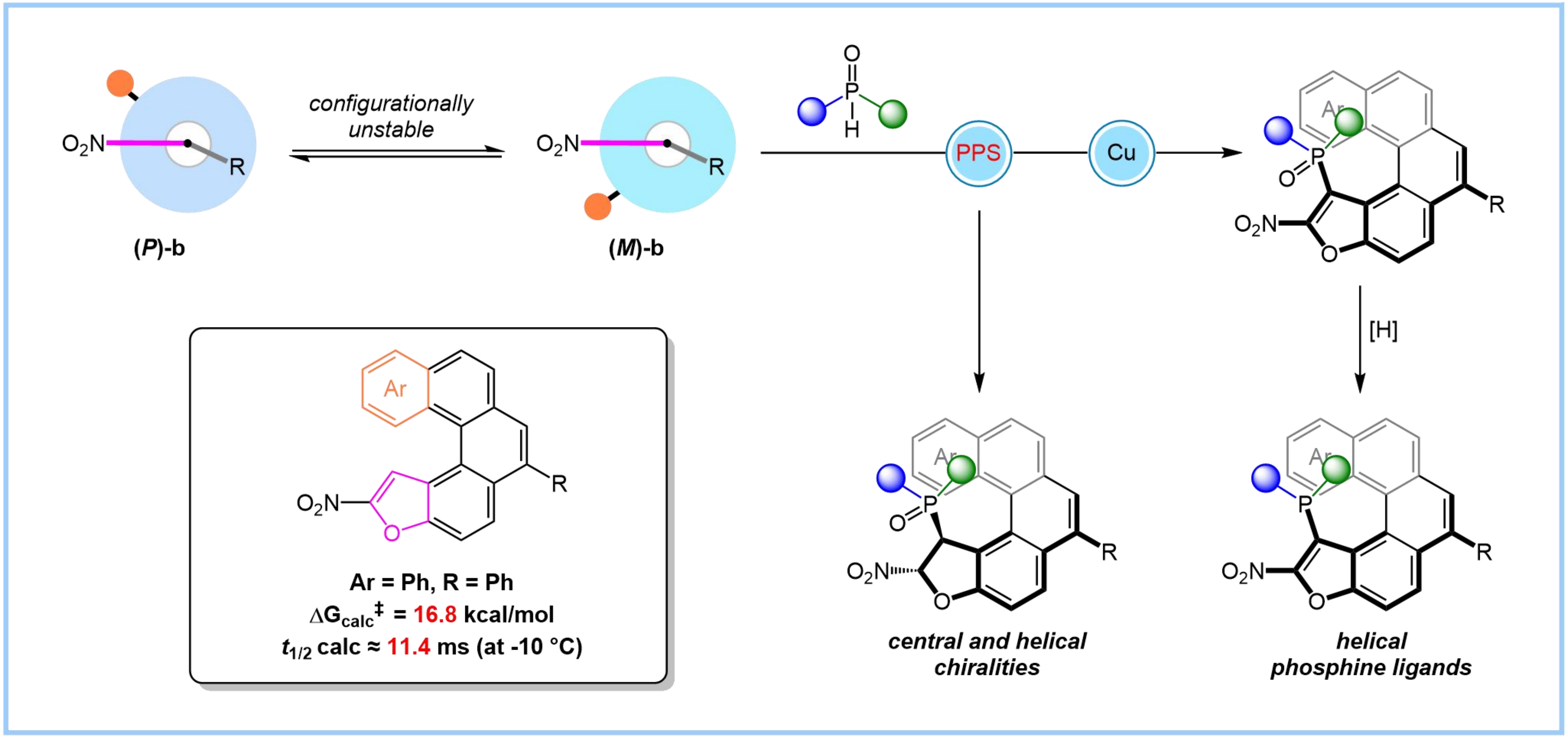
Mechanism Study





TS4-(M)-si

Summary



- Excellent stereoselectivities and reactivities (2 mol% PPS)
- Broad substrate scope and novel phosphorus-containing helicene scaffolds

The First Paragraph

写作思路

螺烯类化合物具有重要的应用价值

↓

过去合成螺烯类化合物的方法

↓

一步合成含膦的螺烯仍是一个挑战

The Last Paragraph

写作思路

总结工作：一步构建含膦的螺烯类化合物

↓

强调亮点：合成的含膦螺烯配体具有实用性

↓

提出展望：进一步发展手性膦盐催化剂的应用

Representative Examples

- Since their discovery by Witte and Meisenheimer in 1903, such distinctive topologies have greatly fascinated chemists due to their superiority in material sciencess. (distinctive: 独特的)

- Amongst them, transition metal-catalyzed enantioselective synthesis of these scaffolds is widely considered the most general approach to date. (Amongst them: 在……之中)

- These limited asymmetric protocols and disproportionate development vastly impose restrictions on their versatility in asymmetric catalysis. (disproportionate: 不成比例的，不均衡的)

Acknowledgment

Thanks
for your attention !