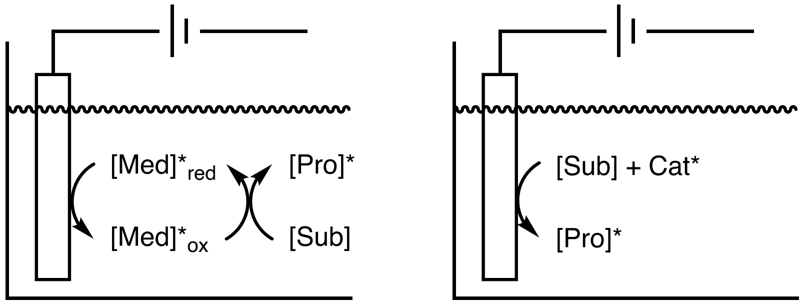
Organocatalytic Electrochemical Reaction



2023/ 10/ 14 (Sat)

Shunsuke Minabe

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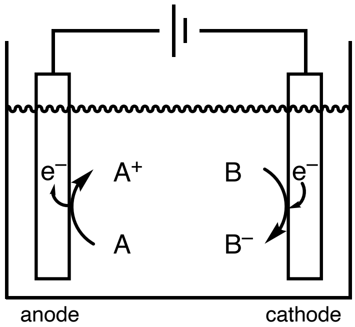
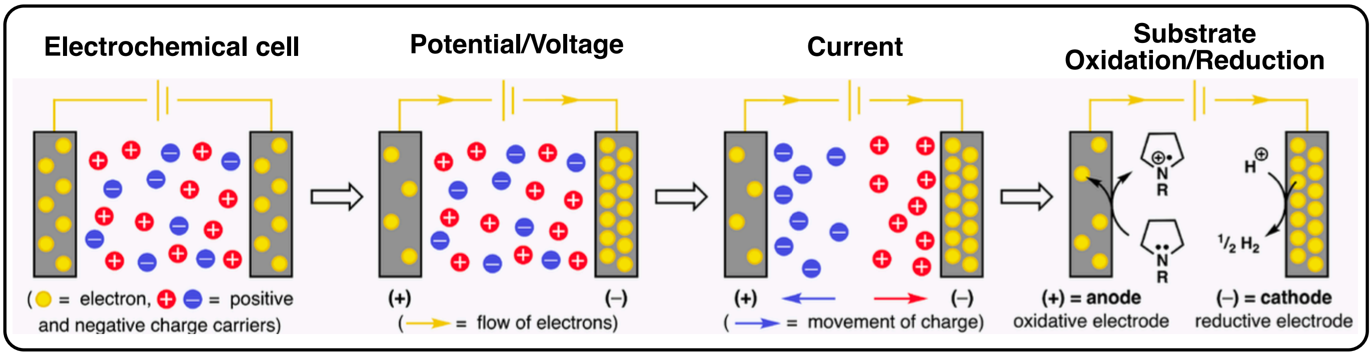
1. Introduction

1-1. Electroorganic Chemistry





Electron transfer between electrode and compound
one electron transfer

Anodic oxidation and cathodic reduction are
Instead of chemical oxidant/reductant

Chemical Oxidant or Reductant

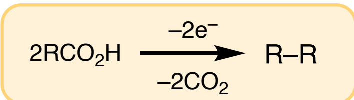
harsh, toxic, expensive, explosiveness, waste

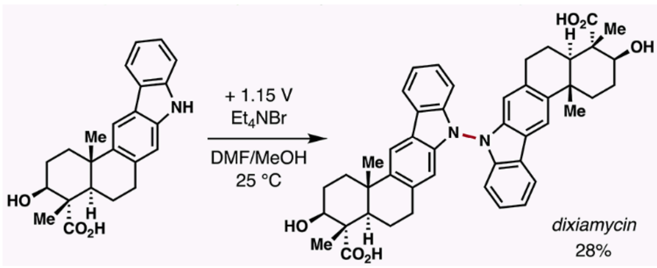
$KMnO_4$, CrO_3, OsO_4, other transition metal, etc.
H_2O_2, Oxone, *m*-CPBA, Selectfluor, etc.

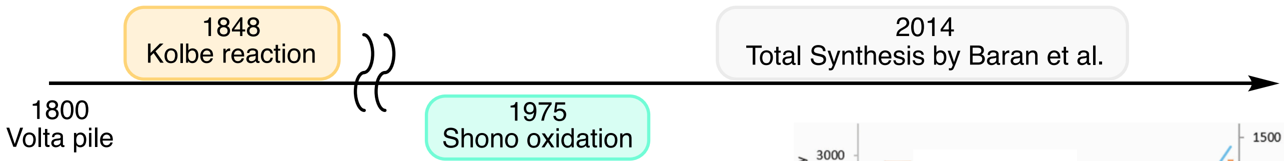
Electrochemistry

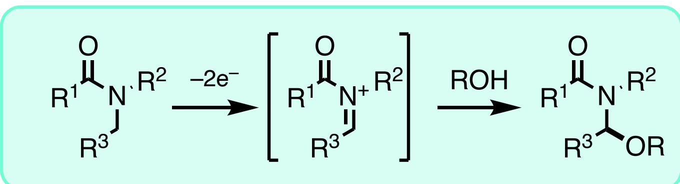
safe, cheap, high energy efficiency
change the potential easly
limitation of reaction condition
solvent, electrolyte (電解質) , electrode (電極)

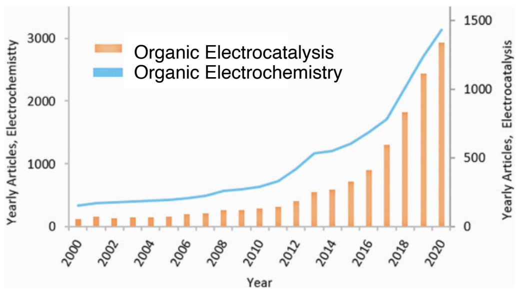
1.2. Development of Electrochemistry









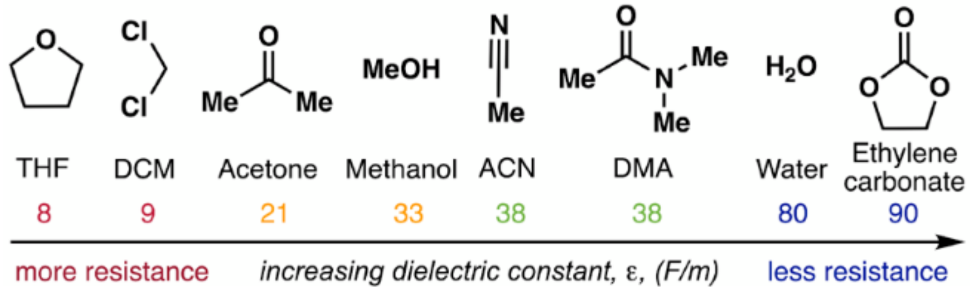


Refference
Baran, P. S. et al. Acc. Chem. Rev. **2017**, *117*, 13230.
Baran, P. S. et al. Acc. Chem. Res. **2020**, *53*, 72.

1. Introduction

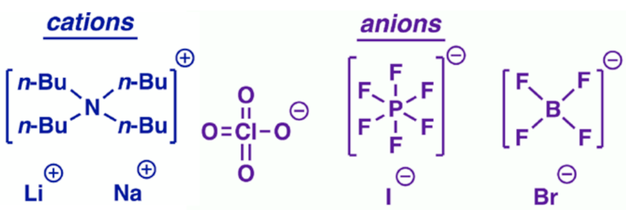
1-3. The Choice of Components

Solvent



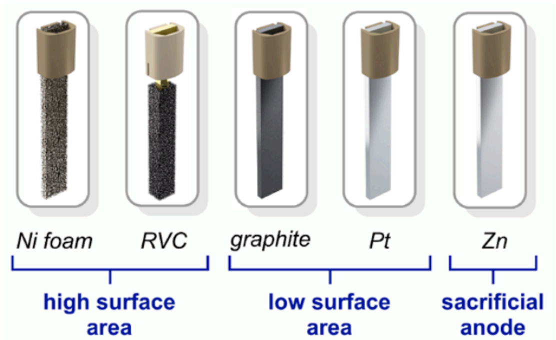
The solvent must dissolve the reagents and elecrtrolyte.
The solvent must be stable under the electrochemical condition.
Polar aprotic are most commonly used.

Electrolyte (電解質)



Electrolyte provide a source of positive and negative ions.
Electrolyte improves conductivity.
Li^+ and Bu_4N^+ salts are commonly used.

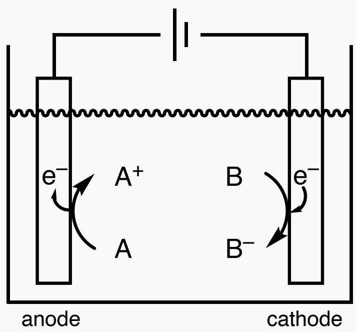
Electrode (電極)



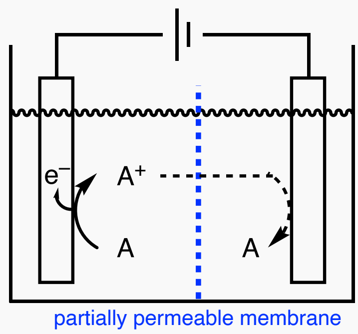
Electron transfer occurs on the electrode surface.
The choice of material affects reactivity/selectivity.

1-4. Various Method

A. Undevided cell



B. Devided cell



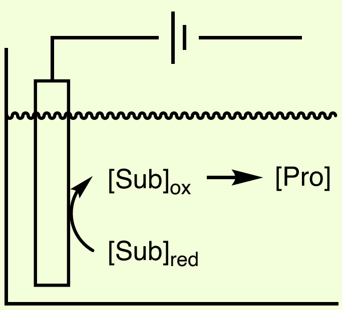
A. Constant Current Electrolysis (CCE)

Maintain current
The potential gradually increases
Easier setup
Over-oxidation/reduction

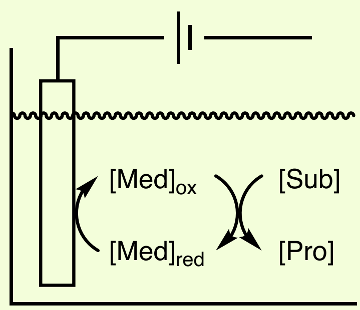
B. Constant Potential Electrolysis (CPE)

Maintain the potential
Higher selectivity
Requires a refference electrode (Ag/AgCl)

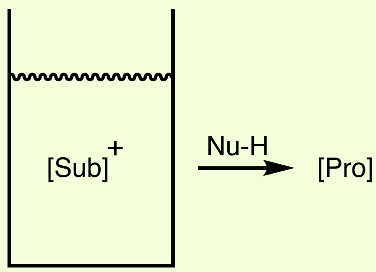
A. Direct Electrolysis



B. Mediated Electrolysis



C. Cation Pool

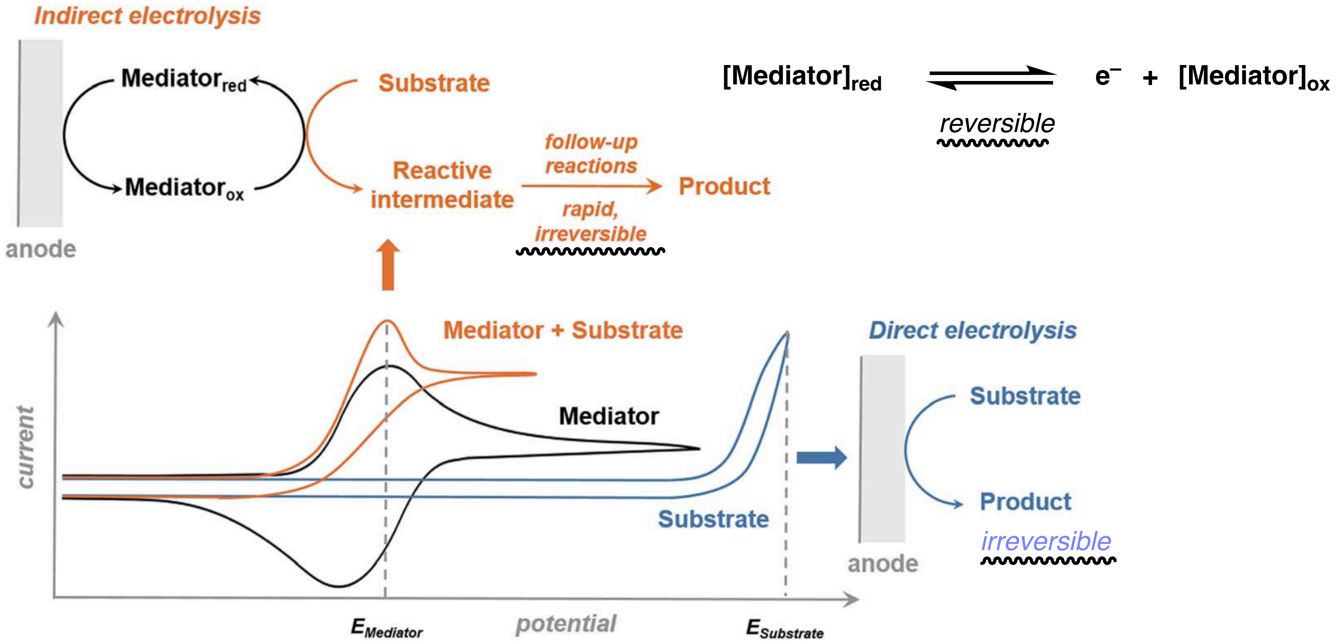


Refference
Baran, P. S. et al. Acc. Chem. Rev. **2017**, *117*, 13230.
Baran, P. S. et al. Acc. Chem. Res. **2020**, *53*, 72.

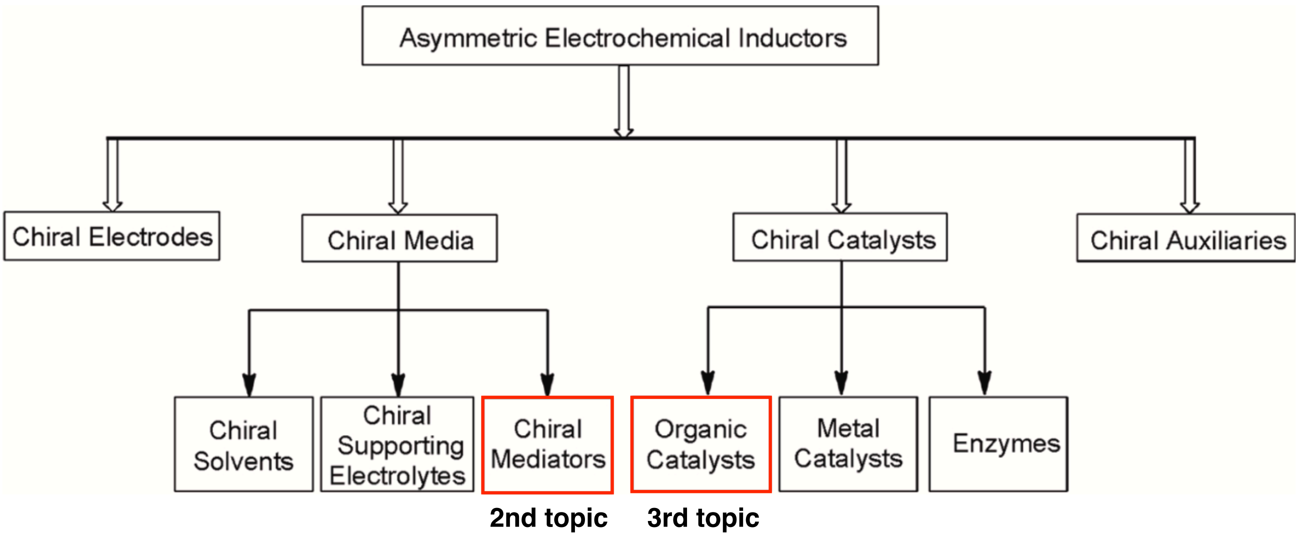
1. Introduction

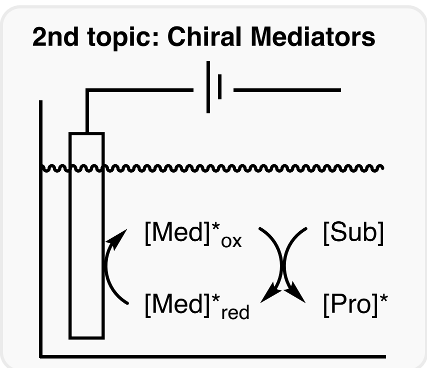
1-5. Cyclic Voltammetry (CV)

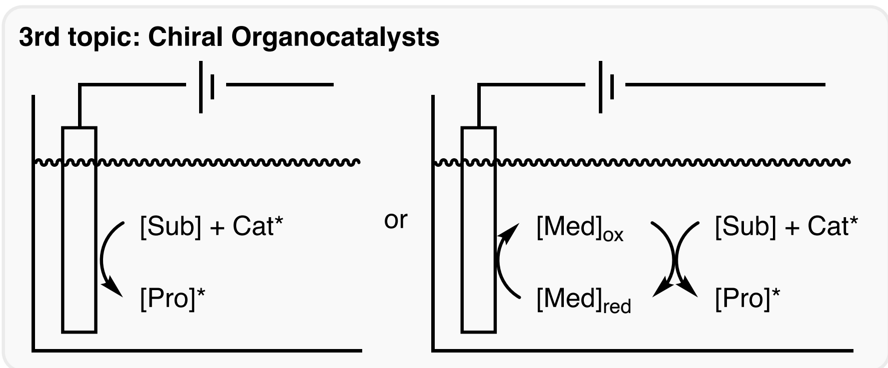
CV is a powerful and popular electrochemical technique commonly employed to investigate the reduction and oxidation processes of molecular species.



1-6. Asymmetric Electrochemical Reactions







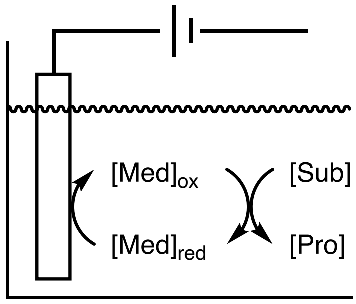
Refference

Berlinguette, C. P. et al. Susteinable Energy Fuels **2018**, *2*, 1905.

Dempsey, J. L. et al. *J. Chem. Educ.* **2018**, *95*, 197.

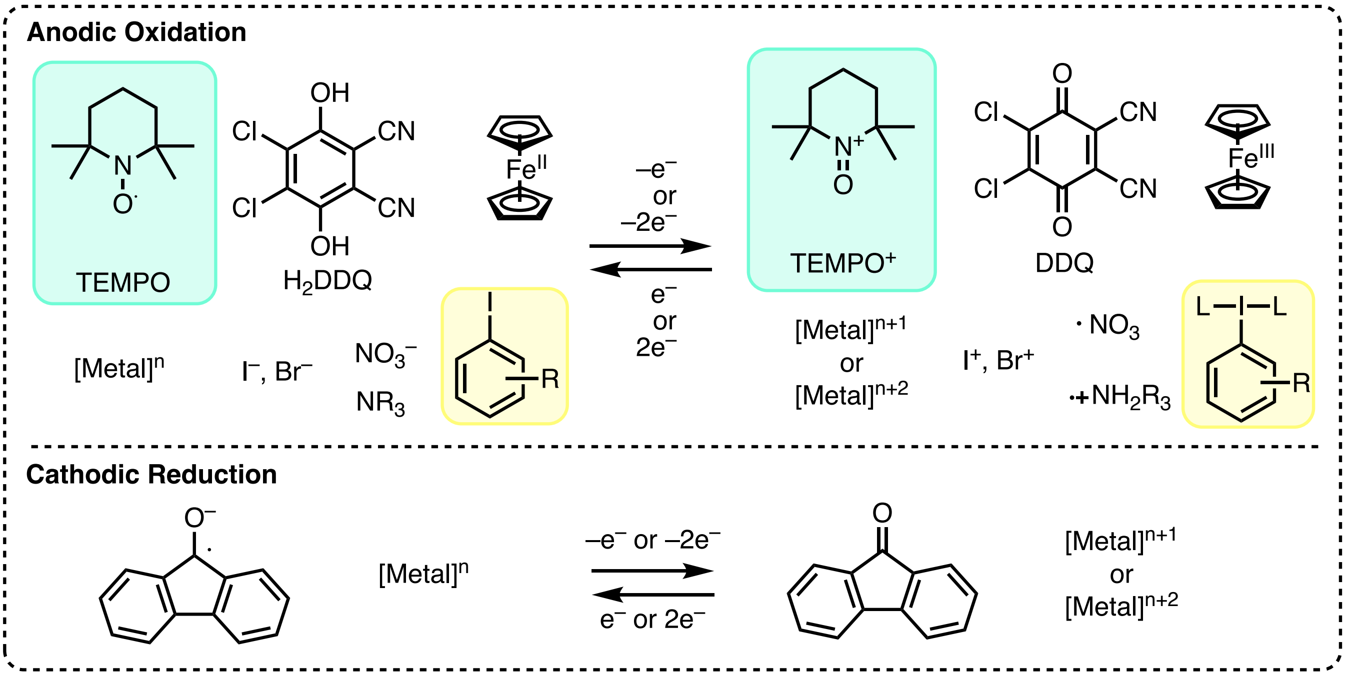
2-Mediators

2-1. Achiral/Chiral Mediators[a]

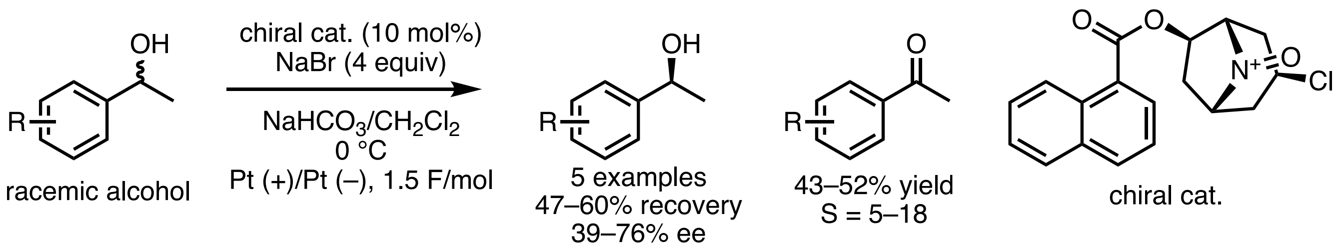


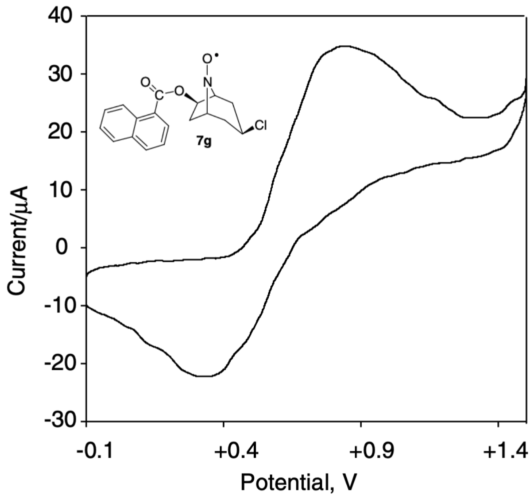
Mediator is "Redox catalyst"

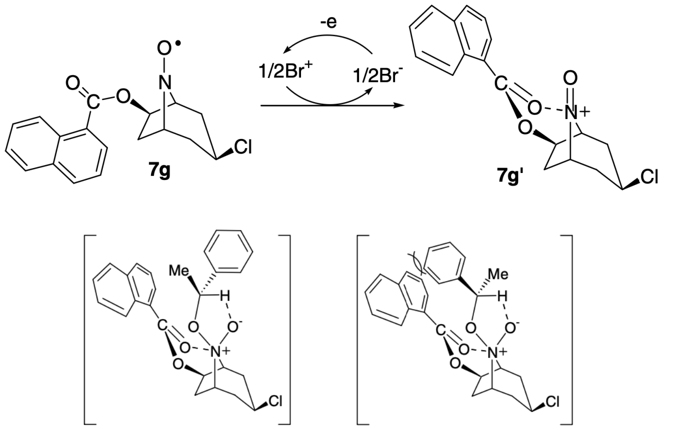
lower oxidation/reduction potential
chemoselective
complex reaction system



2-2. Chiral Azabicyclo-N-oxyls Mediated Catalysis[b]







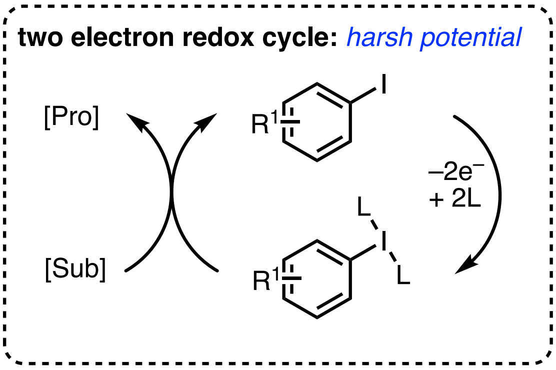
Refference

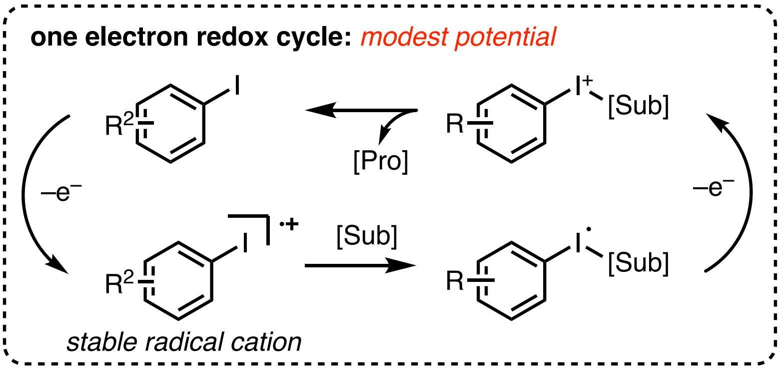
a) Baran, P. S. et al. Acc. Chem. Rev. **2017**, *117*, 13230.

b) Onomura, O. et al. *Tetrahedron Letters* **2008**, *49*, 5247.

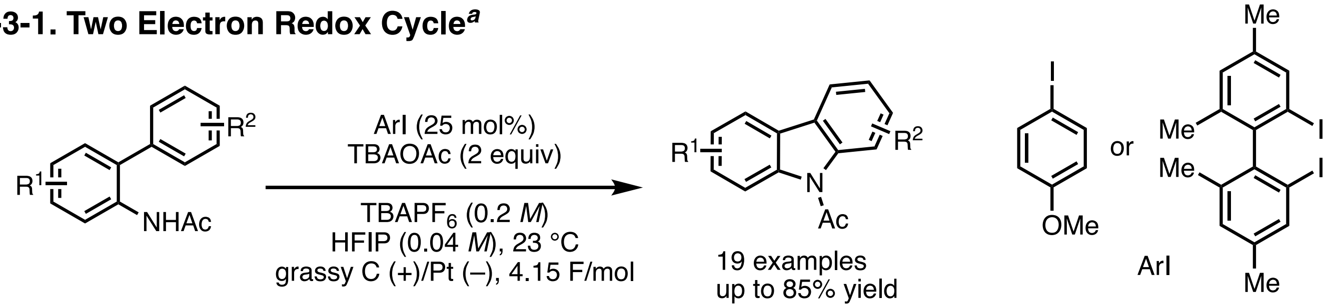
2. Mediators

2-3. Organoiodine(III) Catalysis

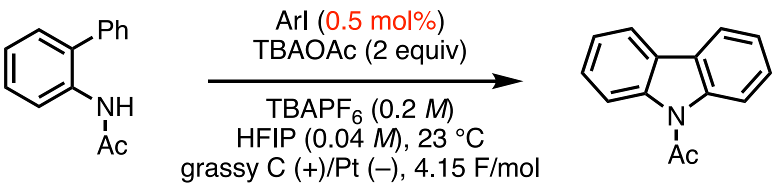


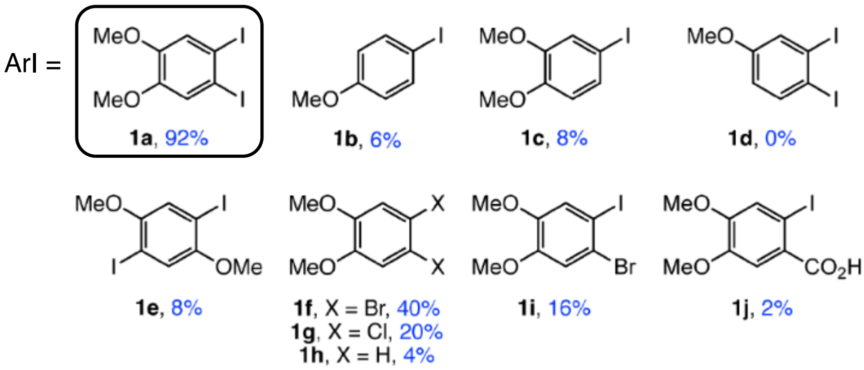


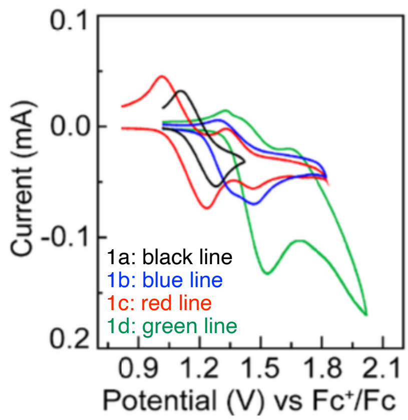
2-3-1. Two Electron Redox Cycle[a]



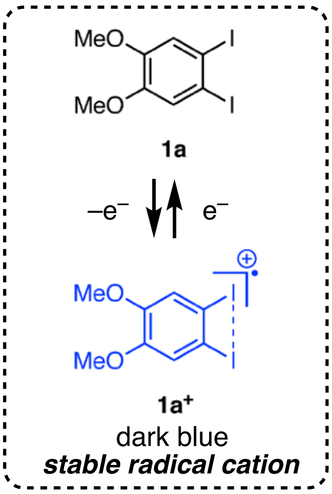
2-3-2. One Electron Redox Cycle (Iodine-Iodine Cooperation)[b]



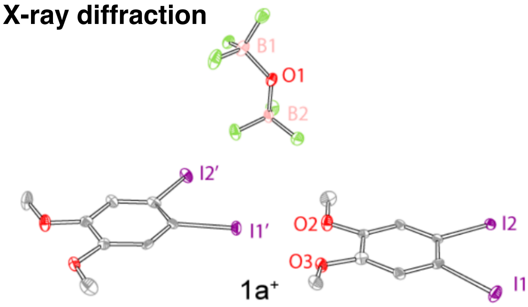




1 (5 mM) in 0.2 M $TBAPF_6$/hfip at 0.1 V/s.

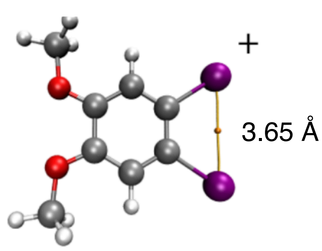


X-ray diffraction



I_1–I_2 = 3.6392 Å

DFT calculation

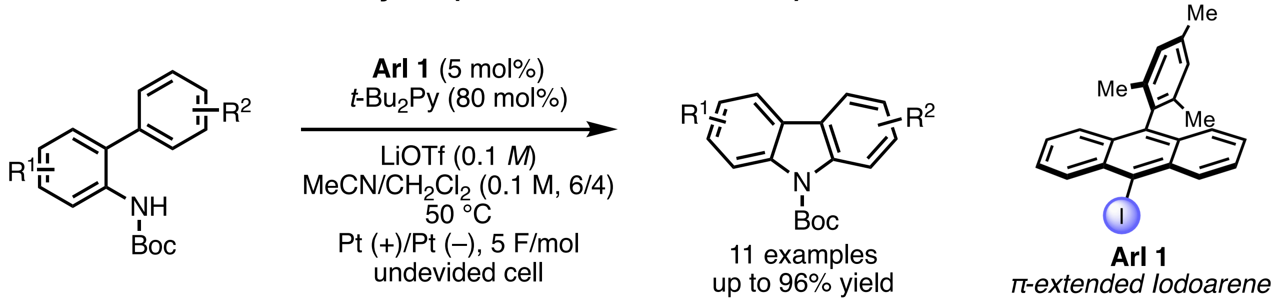


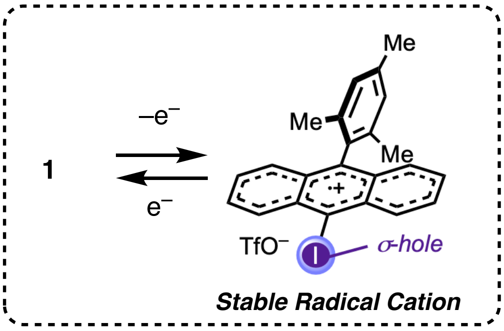
1a'
(1a I–I bond : 3.70 Å)

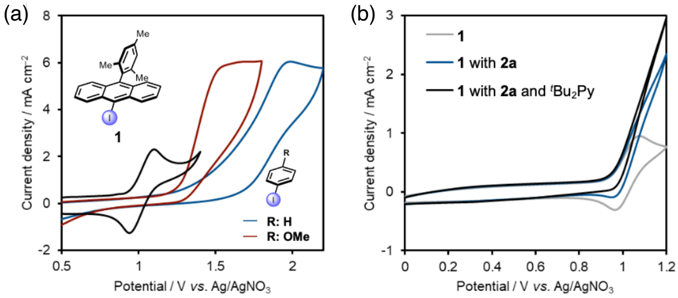
Refference
a) Powers, D. C. et al. *J. Am. Chem. Soc.* **2020**, *142*, 4990.
b) Powers, D. C. et al. *J. Am. Chem. Soc.* **2022**, *144*, 13913.

2. Mediators

2-3-3. One Electron Redox Cycle (π-Extended Iodoarene)[a]

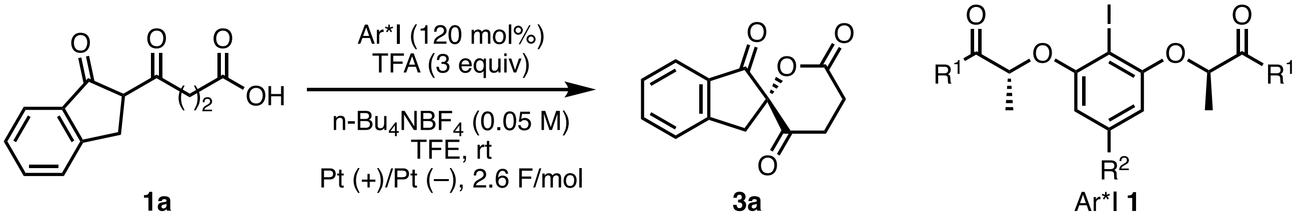






(a) CVs of 5 mM Ar in 0.1 M LiTfO/MeCN+CH$_2$Cl$_2$ (6:4 in vol.) at a scan rate of 0.1 V s–1.
(b) CV in 0.1 M LiTfO/MeCN+CH$_2$Cl$_2$ (6:4 in vol.) at a scan rate of 0.1 V s–1 (1: 1 mM, 2a: 20 mM, tBu$_2$Py: 8 mM).

2-3-4. Chiral Two Electron Redox Cycle[b]



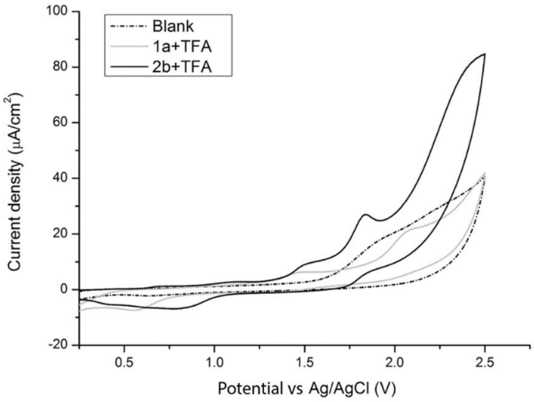
2a R^1 = OMe, R^2 = H: 54% yield, 67% ee

2b R^1 = OMe, R^2 = CO$_2$Me: 70% yield, 71% ee

2c R^1 = O^{t}Bu, R^2 = H: 15% yield, 68% ee

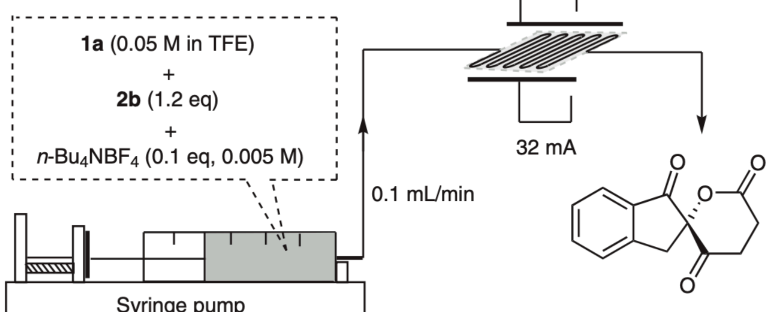
2d R^1 = OBn, R^2 = H: decomposed

2e R^1 = NHPh, R^2 = H: decomposed



Cyclic voltammograms using n-Bu4NBF4 (0.1 M) as electrolyte in TFE at 20 mV s–1, under N2.
Working electrode: glass carbon; refe ence electrode: Ag/AgCl in 3 M NaCl; auxiliary electrode: Pt wire.

Frow microreactor



3a 56%, 55% ee

Refference

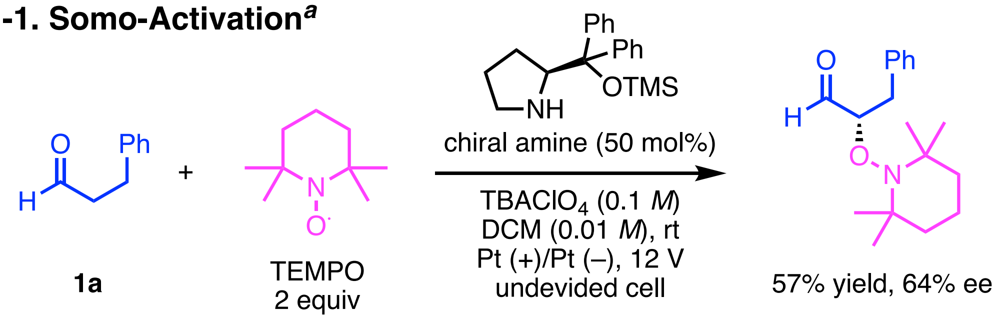
a) Atobe, N.; Shida, N. et al. DOI:10.26434/chemrxiv-2022-sggqd

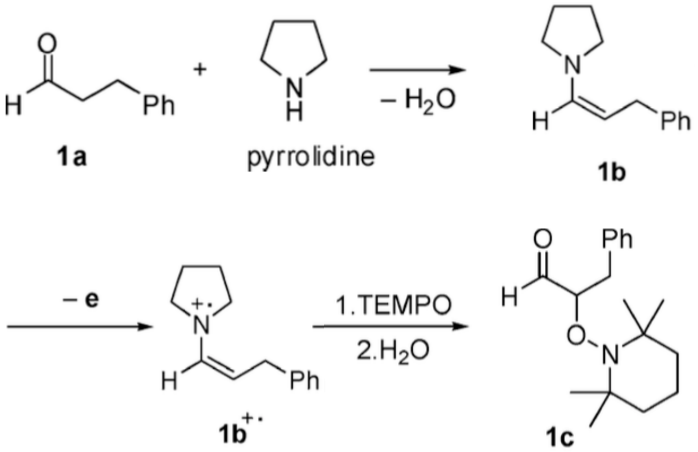
b) Wirth, T. et al. *Synthesis* **2019**, *51*, 276.

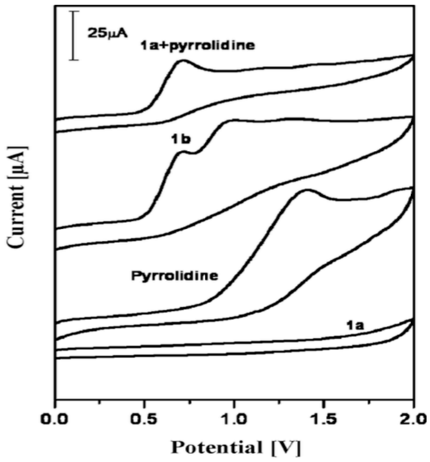
3. Chiral Organocatalysis

3-1. Chiral Enamine Catalysis

3-1-1. Somo-Activation[a]

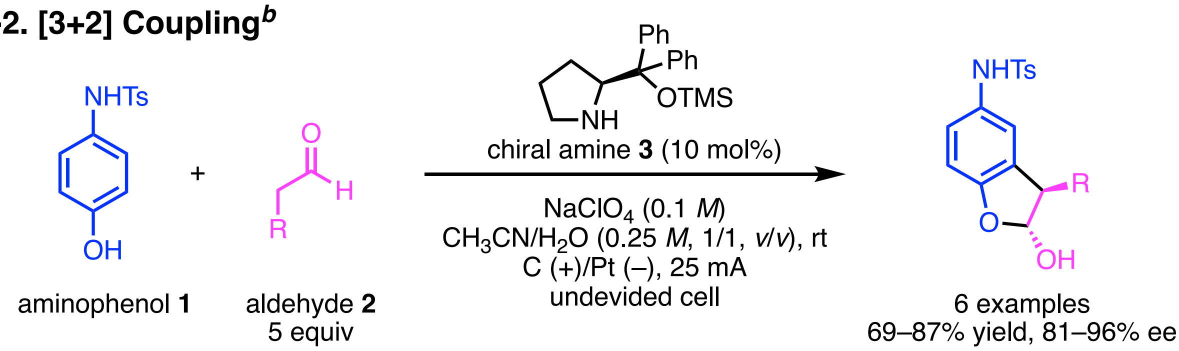


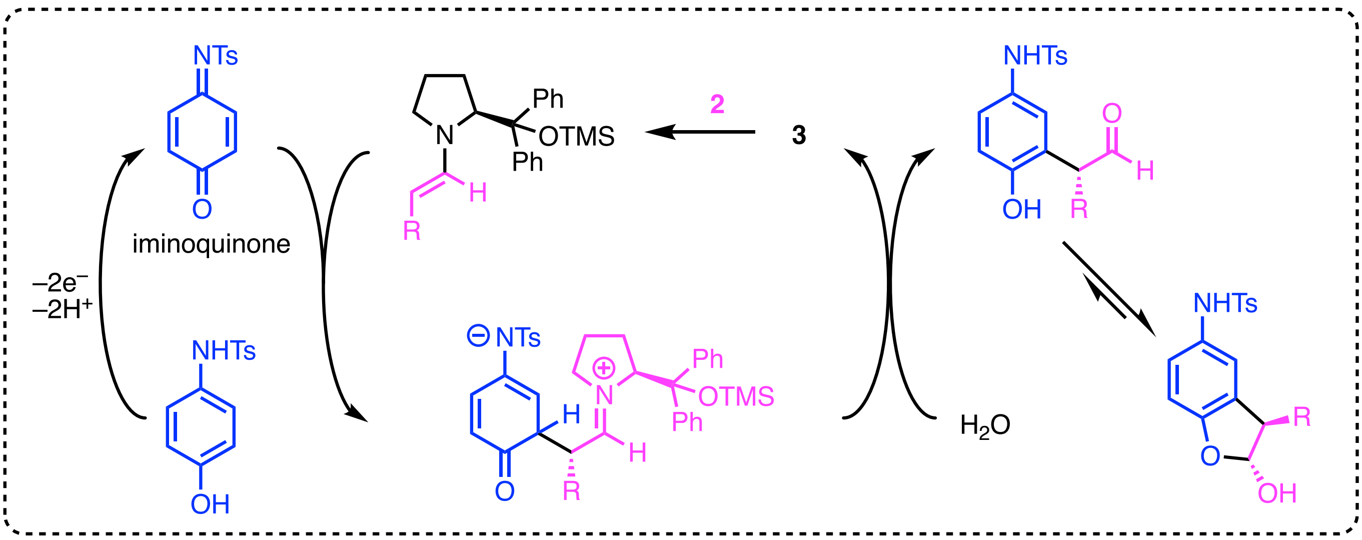




CV of 1a (0.01 *M*), pyrrolidine (0.01 *M*), 1b (0.01 M), and the mixture of 1a (0.01 *M*) and pyrrolidine (0.005 *M*) in 0.1 *M* TBAP dichloromethane solution at a scan rate of 100 mVs^{-1}.

3-1-2. [3+2] Coupling[b]



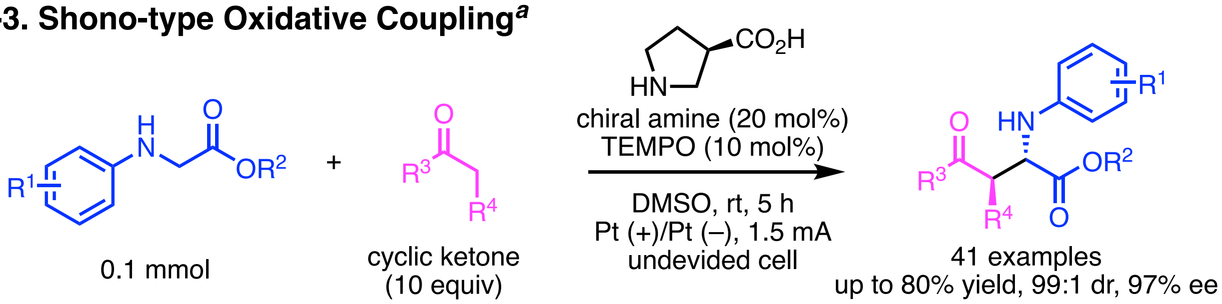


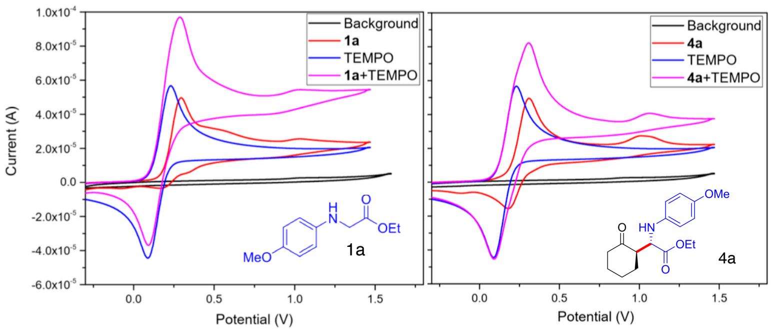
Refference

a) Jang, H.-Y. et. al. *Eur. J. Org. Chem.* **2009**, 5309.
b) Jørgensen, K. A. et. al. *Angew. Chem. Int. Ed.* **2010**, *49*, 129.

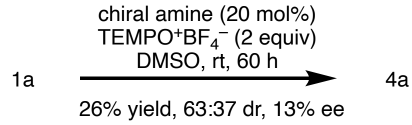
3. Chiral Organocatalysis

3-1-3. Shono-type Oxidative Coupling[a]



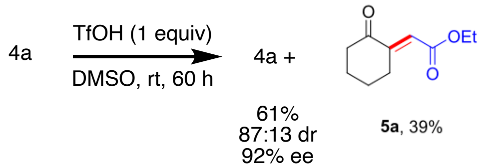


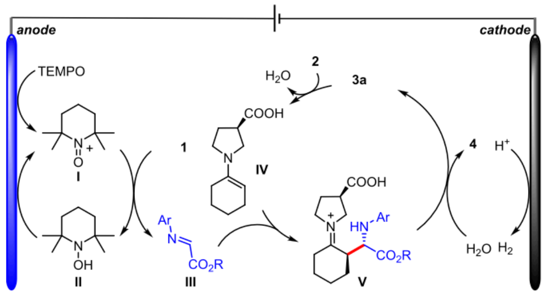
CV analysis on the interaction of 1a/4a with TEMPO in acetonitrile with nBu_4NPF_6 (0.1 *M*) as supporting electrolyte, Pt as working electrode and a platinum wire as counter electrode, scan rate = 100 mV/s.



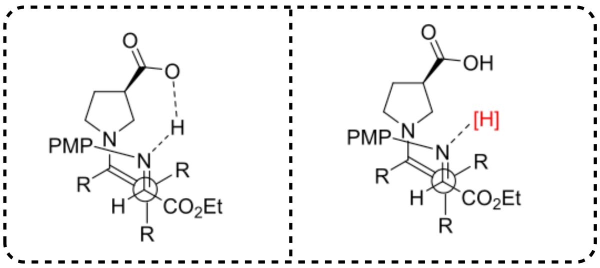
Enfluence of H$^+$

electrochemical condition	
w/o additive	70% yield, 99:1 dr, 97% ee
w TsOH (60 mol%)	83% yield, 61:39 dr, 0% ee

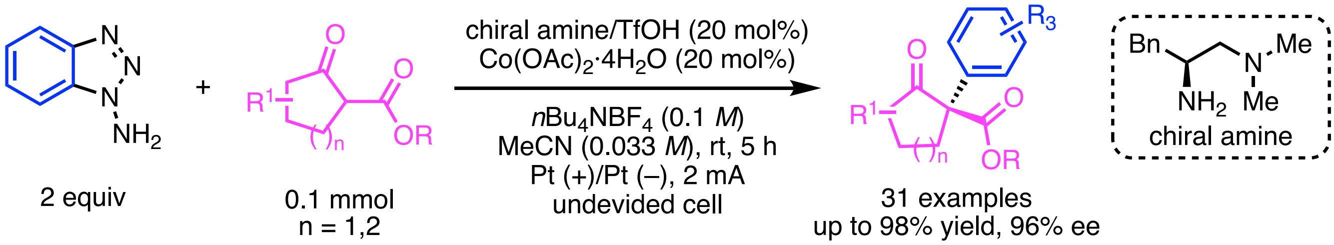


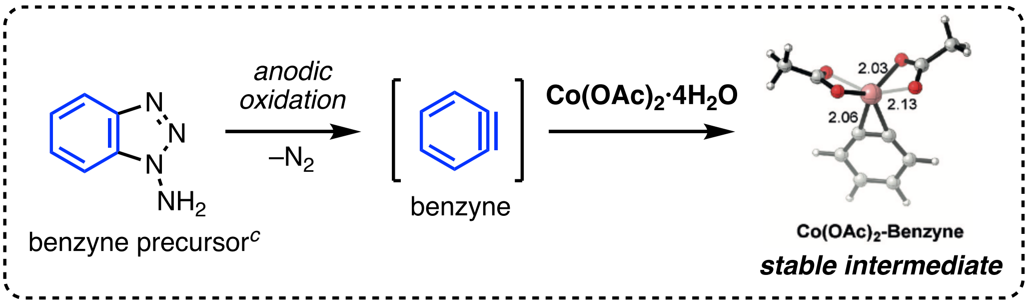


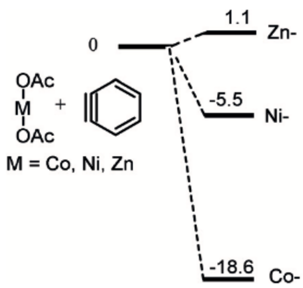
cathode as H$^+$ scavenger



3-1-4. *α*-Arylation of *β*-Ketocarbonyls[b]







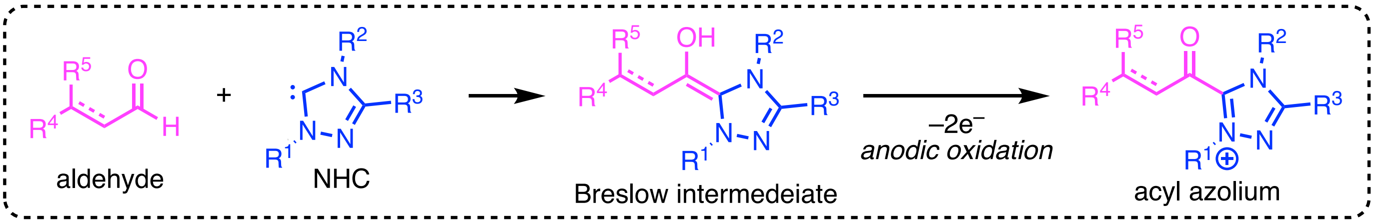
Refference

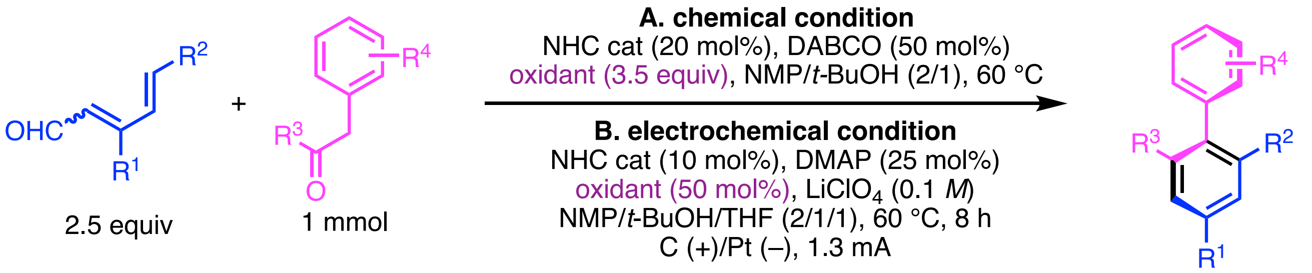
a) Mei, T.-S. et. al. *J. Am. Chem. Soc.* **2021**, *143*, 15599.
b) Luo, S. et. al. *Angew. Chem. Int. Ed.* **2020**, *59*, 14347.
c) Rees, C. W. et al. *J. Chem. Soc.* **1969**, 742.

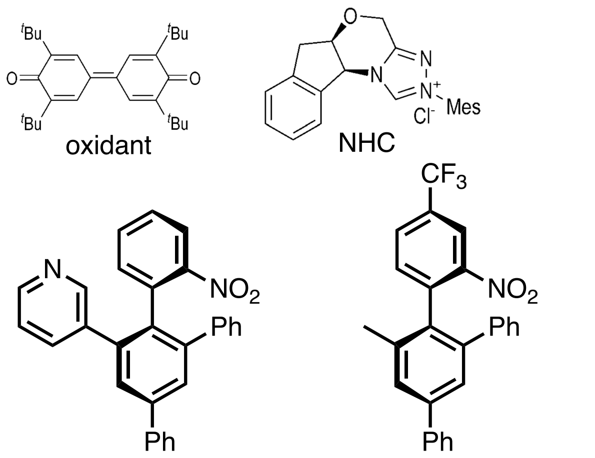
3. Chiral Organocatalysis

3-2 Chiral NHC Catalysis

3-2-1. Electroredox SET[a]



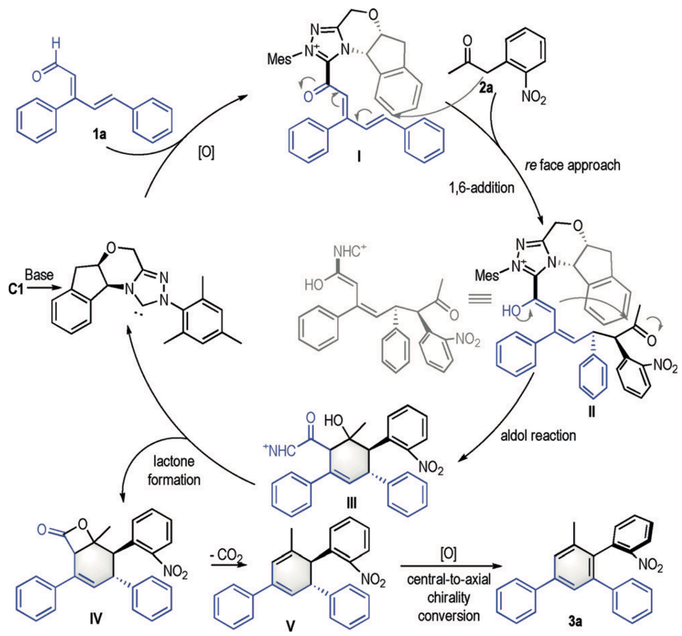




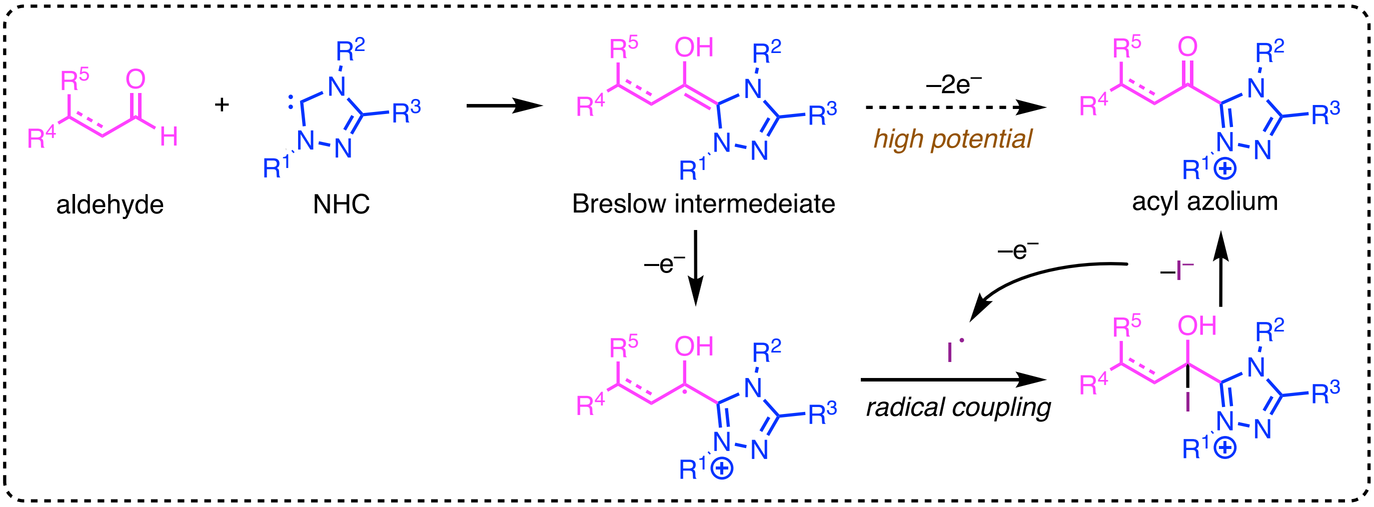
A. 95% yield, 95% ee
B. 75% yield, 95% ee

A. 84% yield, 95% ee
B. 62% yield, 95% ee

Side reaction
· the electrochemical reduction of $-NO_2$
· the formation of 2-methyl indole

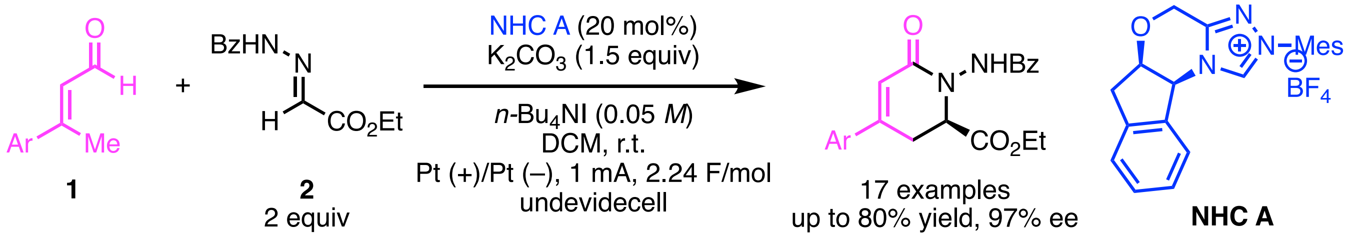


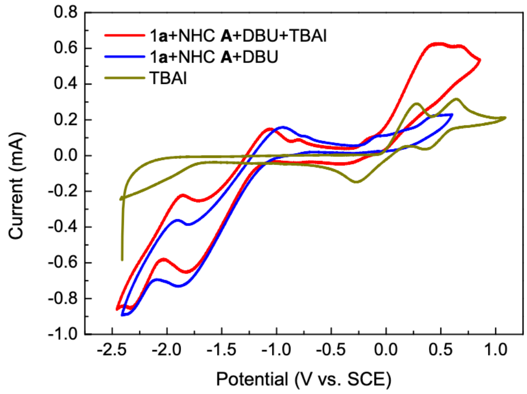
3-2-2. Electroredox SET Mediated by I⁻ [b]



Refference
a) Zhu, T. et. al. *Angew. Chem. Int. Ed.* **2019**, *58*, 17625.
b) Zhu, T. et. al. *Nat. Commun.* **2022**, *13*, 3827.

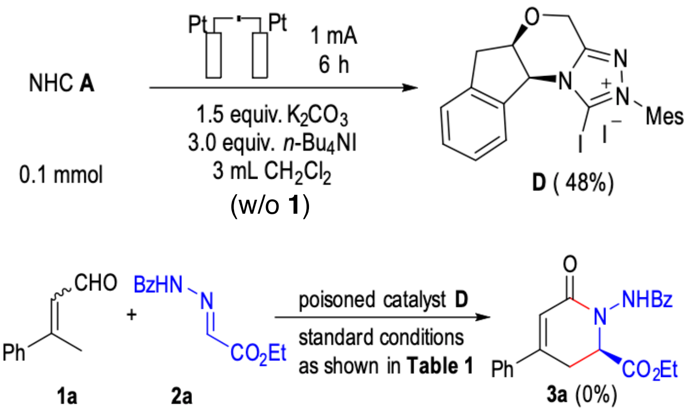
3. Chiral Organocatalysis



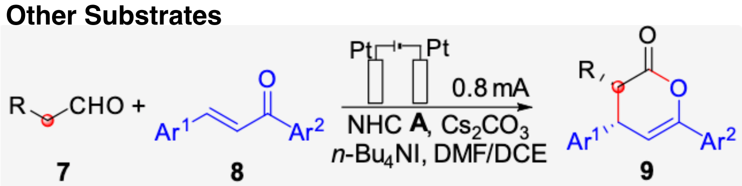


solvent CH_2Cl_2 with 0.1 M n-Bu_4NBF_4 as supporting electrolyte;
brown line: 0.1 mmol n-Bu_4NI;
blue line: 1a (0.3 mmol), NHC A (0.15 mmol), and DBU (0.15 mmol)
red line: 1a (0.3 mmol), NHC A (0.15 mmol), DBU (0.15 mmol) and n-Bu_4NI (0.1 mmol).

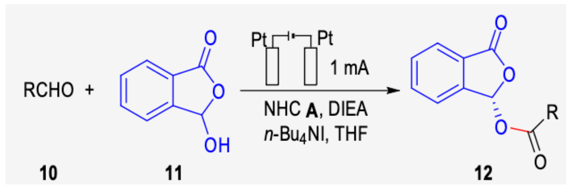
Control Experiment



Other Substrates

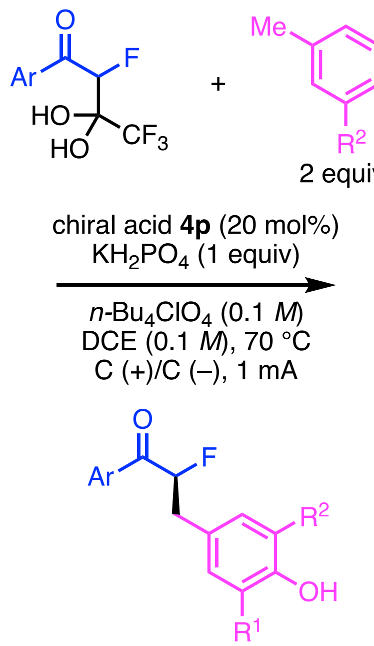


9 examples
up to 68% yield, >20:1 dr, 99% ee

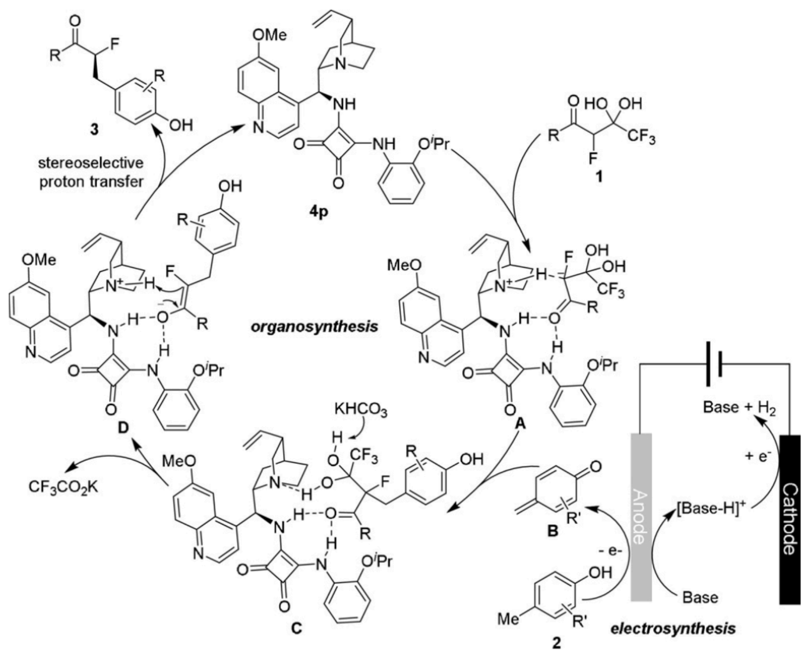


3 examples
up to 84% yield, 96% ee

3-3 Chiral Brønsted Acid Catalysis[a]



29 examples
48–72% yield, 84–95% ee

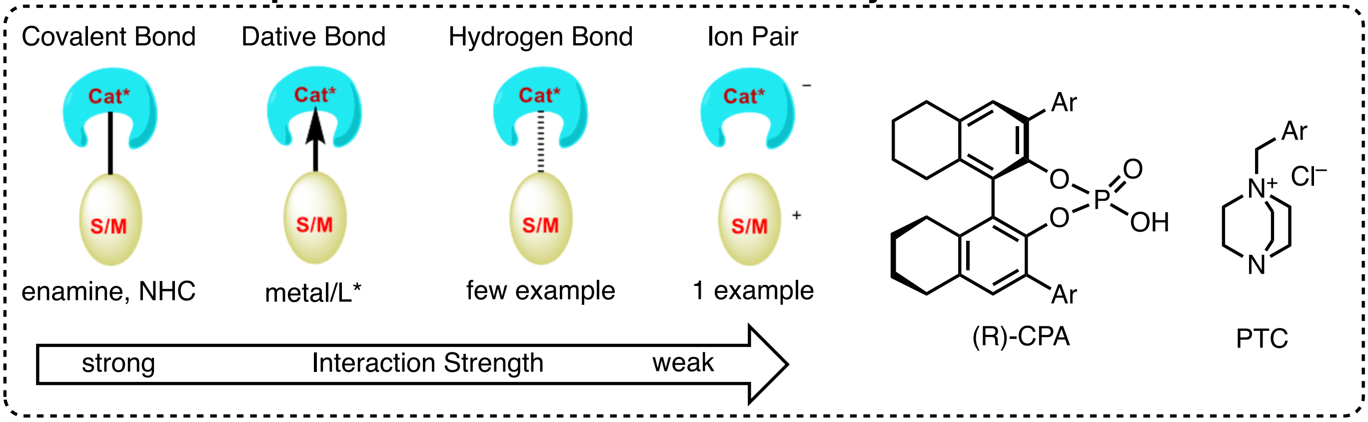


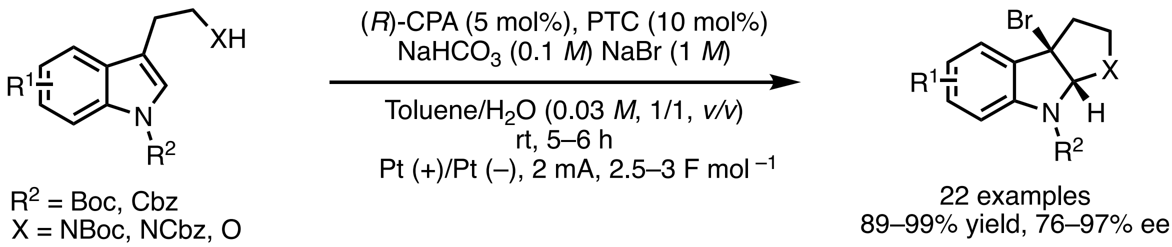
Refference

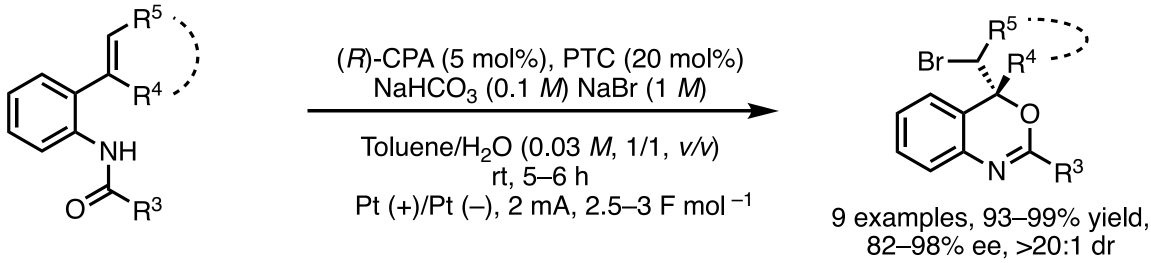
a) Guo, C. et. al. *Angew. Chem. Int. Ed.* **2020**, *59*, 18500.

3. Chiral Organocatalysis

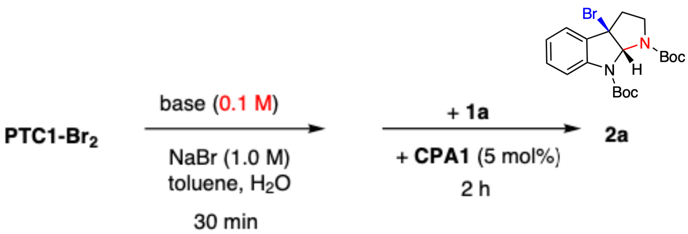
3-4 Chiral Phosphate Anion Phase-Transfer Catalysis



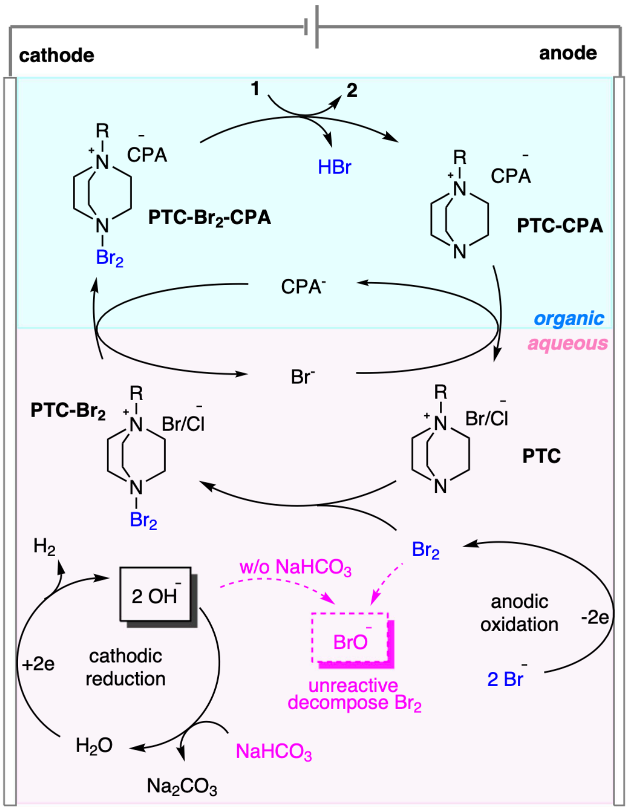




	2a
standard condition	99%, 95% ee
without PTC 1	66%, 25% ee
without $NaHCO_3$	27%, 89% ee
NaCl, NaI instead of NaBr	N.R.
EtOAc instead of toluene	90%, 20% ee



entry	base	**2a** yield, ee
1	$NaHCO_3$	>95%, 92% e.e.
2	NaOH	trace (**1a** remained)
3	NaOH + $NaHCO_3$	>95%, 93% e.e.

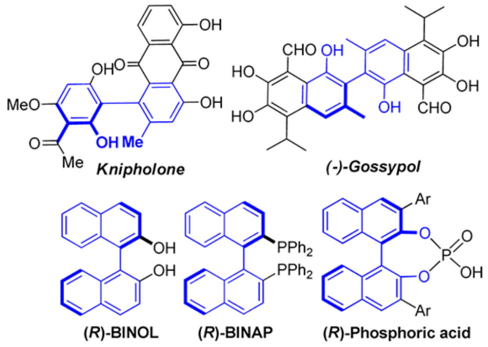


Refference

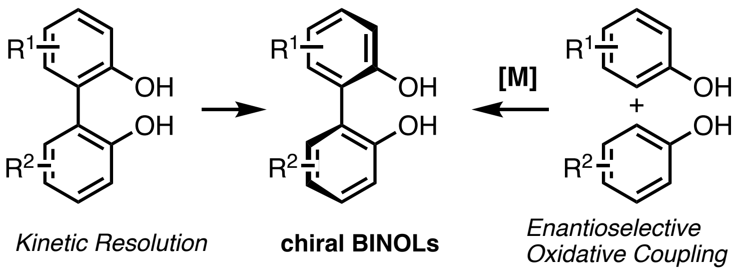
a) Sun. J. et. al. *Nat. Commun.* **2023**, *14*, 357.

4. Proposal

Axially Chiral Biaryls[a]

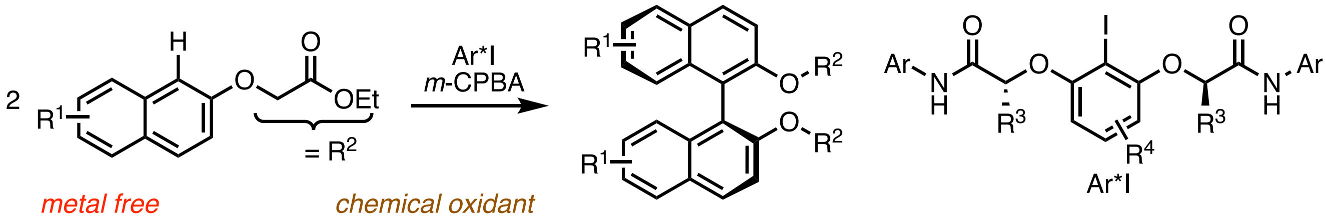


Current Atroposelective Methods[a]



·more efficient ·more Eco-friendly

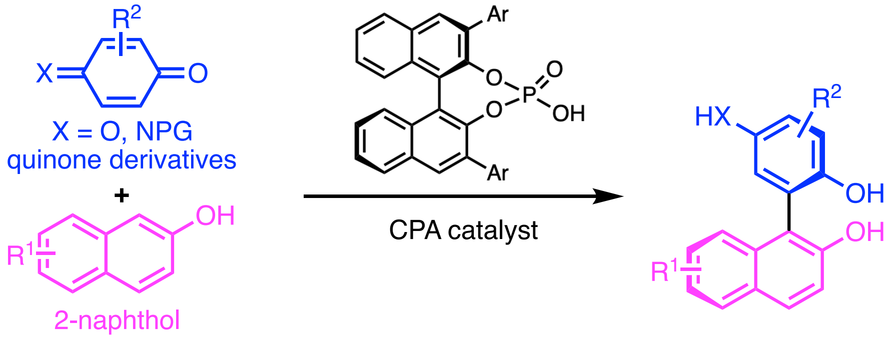
My Researh Topic: Iodine(III) Catalysis (On going)



metal free
oxidative coupling

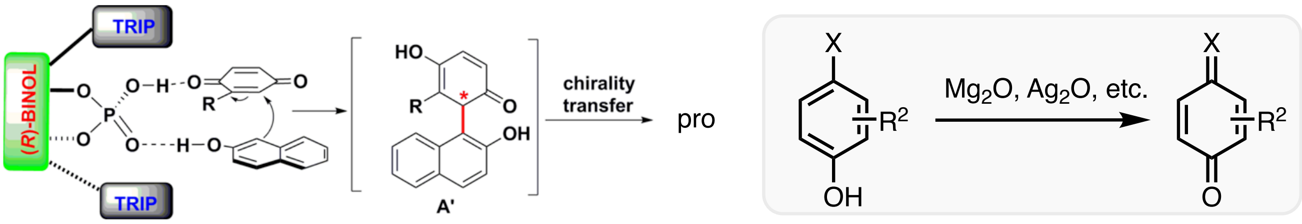
chemical oxidant
only homocoupling

Other approch: Cascade Chirality-Transfer Process[a,b,c]

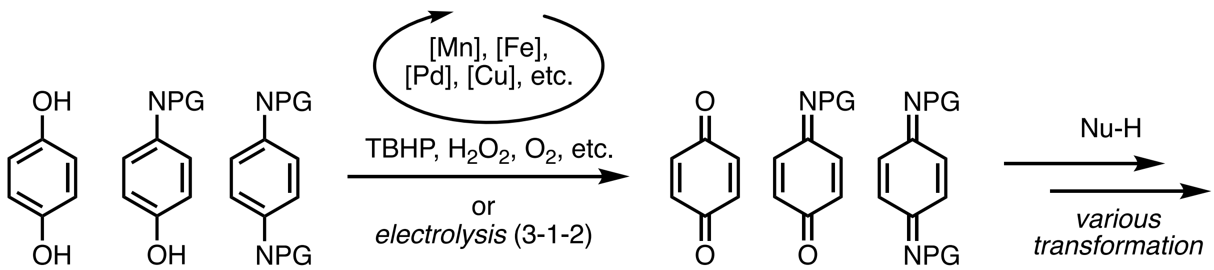


transition metal free
effcient cross coupling

isolated quinone derivatives
limited stable quinone derivatives



Quinone and Its Derivatives[d]



Reference
a) Liu, X.-Y.; Tan, B. et al. *J. Am. Chem. Soc.* **2015**, *137*, 15062.
b) Sun, H.; Xu, Q.-L. et al. *J. Am. Chem. Soc.* **2016**, *138*, 5202.
c) Xiang, S.-H.; Tan. B. et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 11374.
d) Zhong, F.; Zhai, H. et al. *Org. Chem. Front.* **2022**, *9*, 5395.