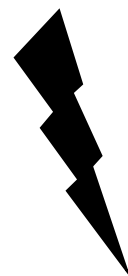


# 电化学合成和电催化

## --Lin Group 文献汇报



**Topic 2021/12/23**  
1852946 · Shenghan Cai

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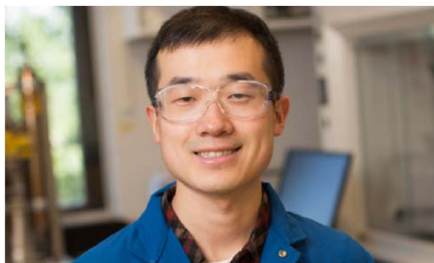
- 电催化
- 自由基氧化还原催化
- 高分子与材料化学(略)

## ■电化学背景知识及Lin Group常用分析方法介绍

- 循环伏安法
- 自由基钟实验

## ■电催化

- 烯烃双官能化



林松(Song Lin)

康奈尔大学化学系助理教授, 有机化学家

#### EDUCATION

- 2013 – 2016 University of California, Berkeley, Postdoctoral Fellow (Advisor: Christopher J. Chang)
- 2008 – 2013 Harvard University, M.A. (2010), Ph.D. (2013) (Thesis Advisor: Eric N. Jacobsen)
- 2004 – 2008 Peking University, B.S. (2008) (施章杰教授)

#### EDITORIAL ROLES

- 2021 – Associate Editor, *Organic Letters*
- 2021 – Early Career Advisory Board, *Chemistry–A European Journal*
- 2019 – 2020 Early Career Advisory Board, *ACS Catalysis*

#### PROFESSIONAL ASSOCIATIONS AND ACTIVITIES

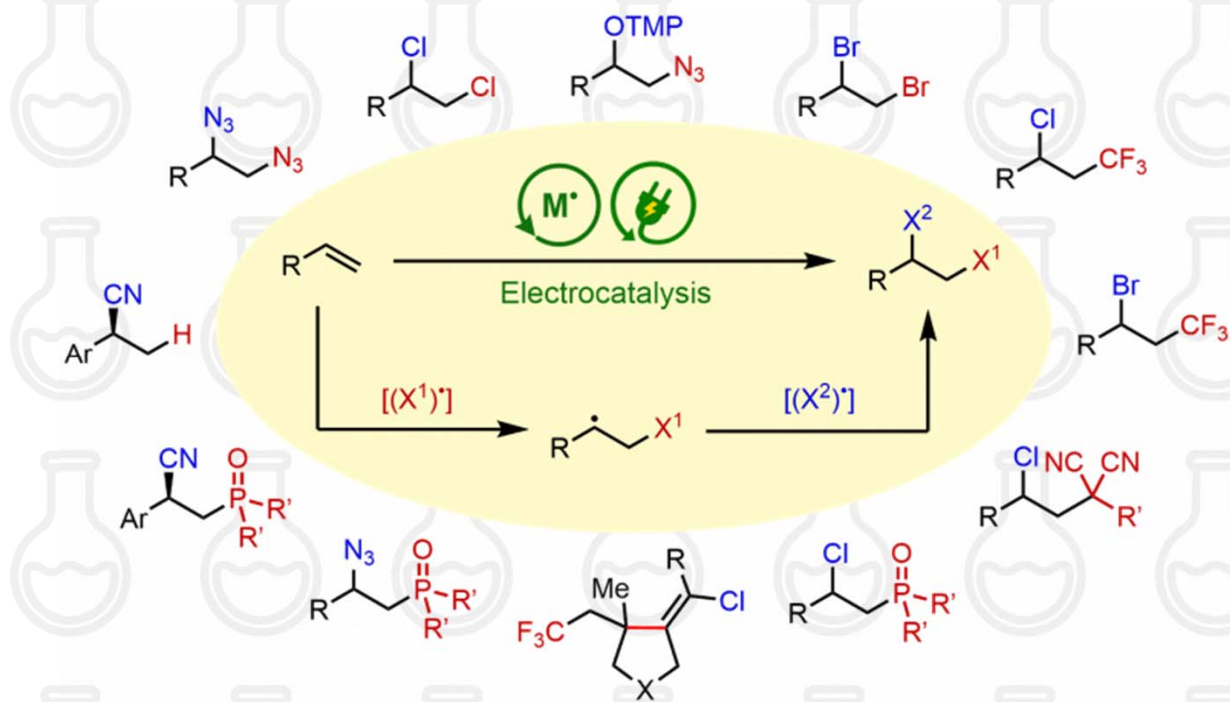
- 2016 – Member, Cornell Center for Materials Research
- 2016 – Faculty Fellow, Atkinson Center for a Sustainable Future
- 2017 – Mentor, Cornell Chemistry-Biology Interface Training Program
- 2019 – 2021 Treasurer, Organic and Biological Electrochemistry Division, Electrochemical Society
- 2021 – Vice Chair, Organic and Biological Electrochemistry Division, Electrochemical Society

# Research Directions

## 电催化

林松教授在过去的几年中，利用电催化作为**烯烃双官能化**的一般方法，开发了一系列不同的电催化反应。

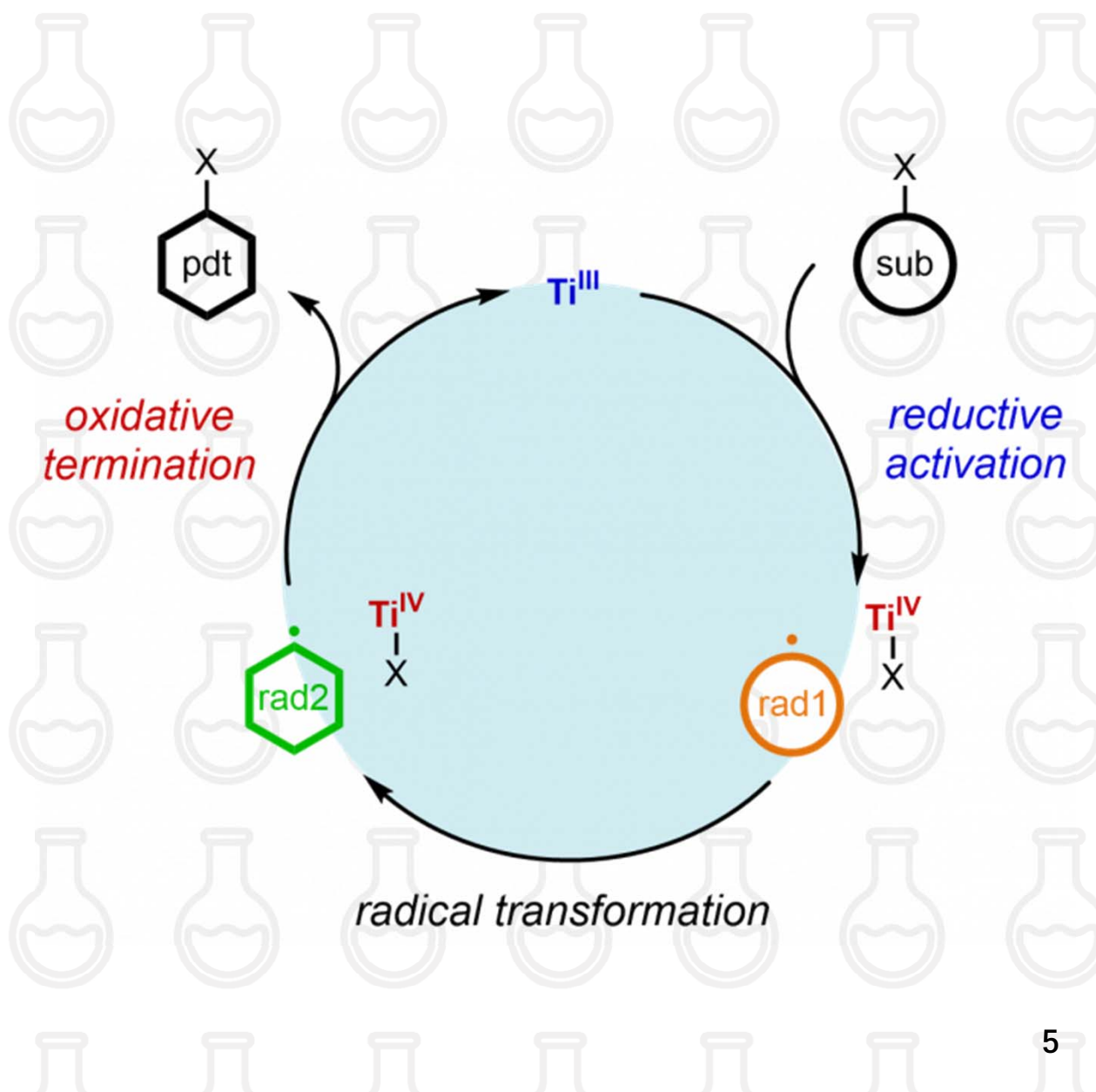
在电极和电源的帮助下，电子成为一种理想的试剂，其电位可以精确地输入。理论上无限的氧化还原范围使电化学能够氧化或还原一些最顽强的化合物。同时，对电极电位的精细控制允许电位差异微小的官能团的化学选择性分化。



## 自由基氧化还原催化

林松教授小组在自由基催化方面的研究工作集中在新型手性催化剂的设计上，该催化剂可以生成稳定自由基中间体，同时可满足复杂结构转化所需的立体和区域控制。

林松教授小组应用该方法用于制备有价值的合成中间体（如多取代的吡咯烷，环戊烷和烯丙基醇）



# 循环伏安法(CV)

循环伏安法控制电极电势以不同的速率，随时间以三角波形一次或多次反复扫描，使电极上能交替发生不同的还原和氧化反应，并记录电流-电势曲线。根据曲线形状可以判断电极反应的可逆程度，中间体、相界吸附或新相形成的可能性，以及偶联化学反应的性质等。

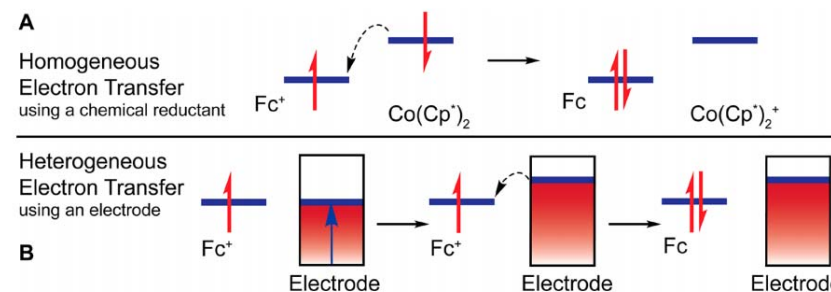


Figure 1. (A) Homogeneous and (B) heterogeneous reduction of  $\text{Fc}^+$  to  $\text{Fc}$ . The energy of the electrons in the electrode is controlled by the potentiostat; their energy can be increased until electron transfer becomes favorable.<sup>4</sup>

## 分子-电极体系

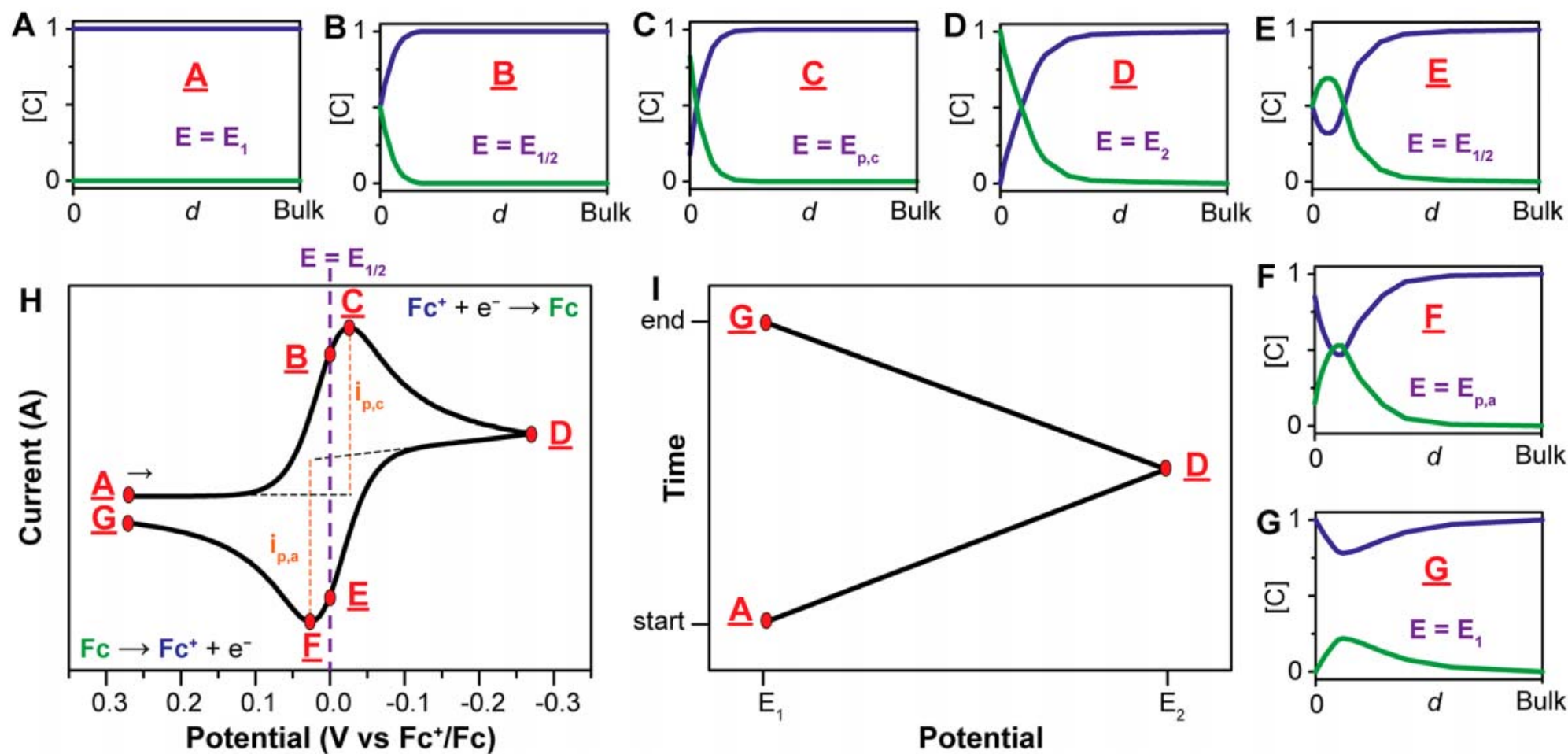
- 当电极的费米能级( $E_F$ )能量高于分子的LUMO轨道能量时，电子从电极转移到分子的LUMO轨道：分子被还原
- 当电极的费米能级( $E_F$ )能量低于分子的HOMO轨道能量时，电子从分子的HOMO轨道转移到电极：分子被氧化

## 电极电势与电荷能量的关系

- 电极电势以正电荷为基准
- 电极电势高：e-能量低，更易接受电子
- 电极电势低：e-能量高，更易给出电子

## $E_F$ 与电极电势( $\varphi$ )的变化相反

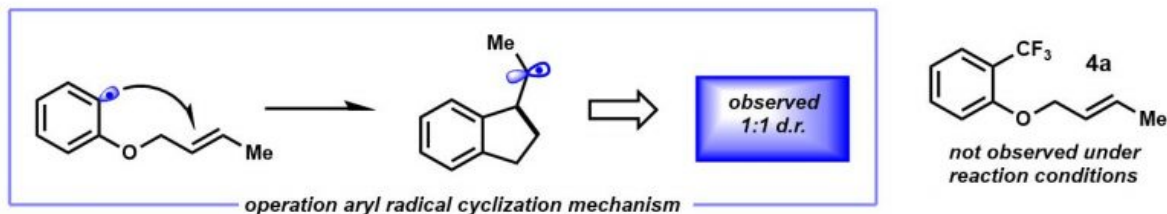
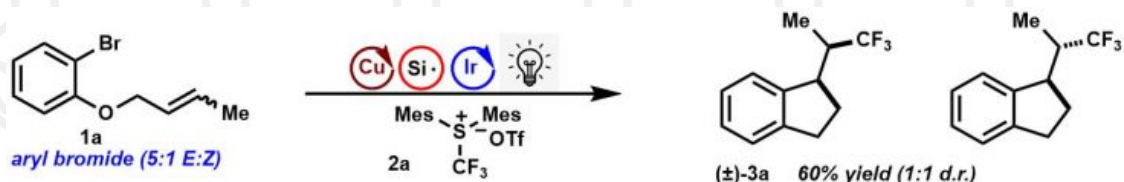
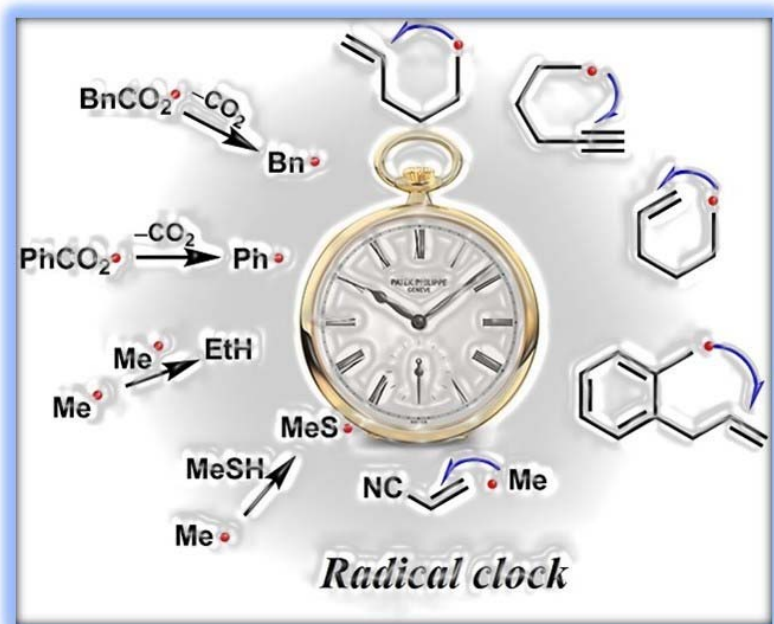
- $\varphi$ 下降，则 $E_F$ 上升
- $\varphi$ 上升，则 $E_F$ 下降



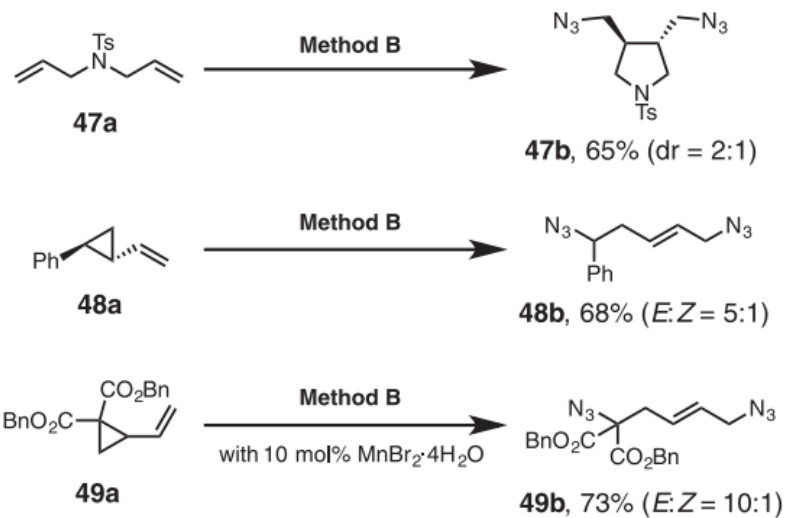
**Figure 3.** (A–G): Concentration profiles (mM) for  $\text{Fc}^+$  (blue) and  $\text{Fc}$  (green) as a function of the distance from the electrode ( $d$ , from the electrode surface to the bulk solution, e.g. 0.5 mm) at various points during the voltammogram. Adapted from Reference 4. Copyright © 2011, Imperial College Press. (H): Voltammogram of the reversible reduction of a 1 mM  $\text{Fc}^+$  solution to  $\text{Fc}$ , at a scan rate of  $100 \text{ mV s}^{-1}$ . (I): Applied potential as a function of time for a generic cyclic voltammetry experiment, with the initial, switching, and end potentials represented (A, D, and G, respectively).

# 自由基机理检测方法

- 自由基捕获试剂
- **自由基钟实验**
- EPR(电子顺磁共振)检测自由基



## 麦克米兰教授使用自由基钟实验



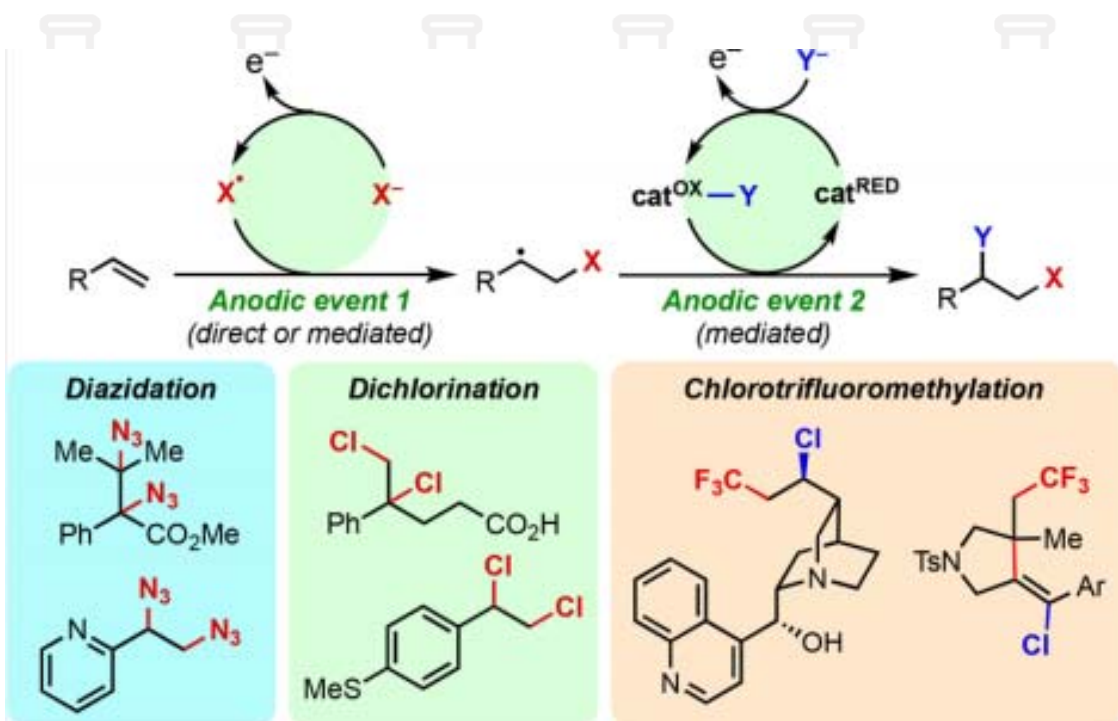
## Lin Group使用自由基钟实验



# An Electrocatalytic Approach to the Radical Difunctionalization of Alkenes

Gregory S. Sauer<sup>†</sup> and Song Lin<sup>\*,†</sup>

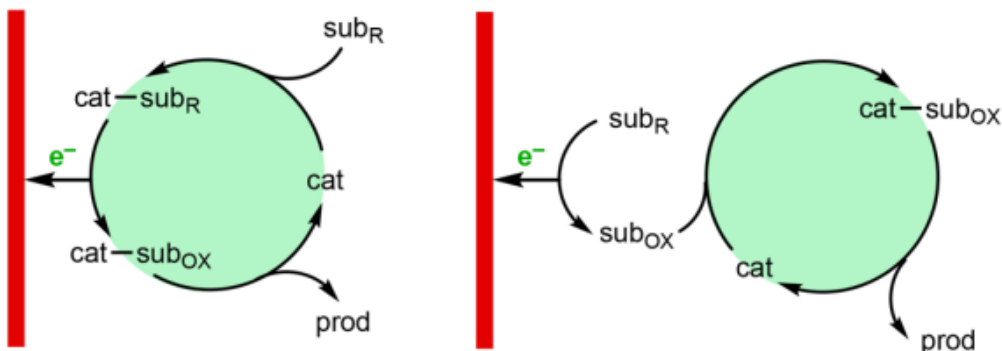
<sup>†</sup>Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States



1. 电极不能控制电子转移后的任何化学步骤的选择性，需要选择正确的催化剂控制下游反应。
2. 电催化合成的关键点在于催化剂的选择以及高活性的电化学中间体的产生

## Scheme 2. Catalysis of Electrochemical Reactions by a Redox-Innocent or Redox-Active Catalyst (Using Anodic Oxidation as an Example)

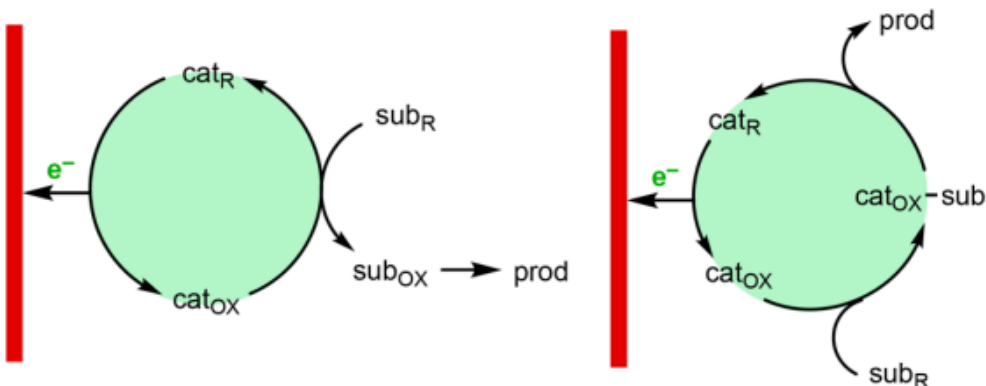
(A) Catalysis of electrochemical reactions by a redox-innocent catalyst



Promoting oxidation (reduction) via HOMO (LUMO) activation

Catalyzing chemical steps post-electron transfer

(B) Catalysis of electrochemical reactions by a redox-active mediator



Mediating electron-transfer only

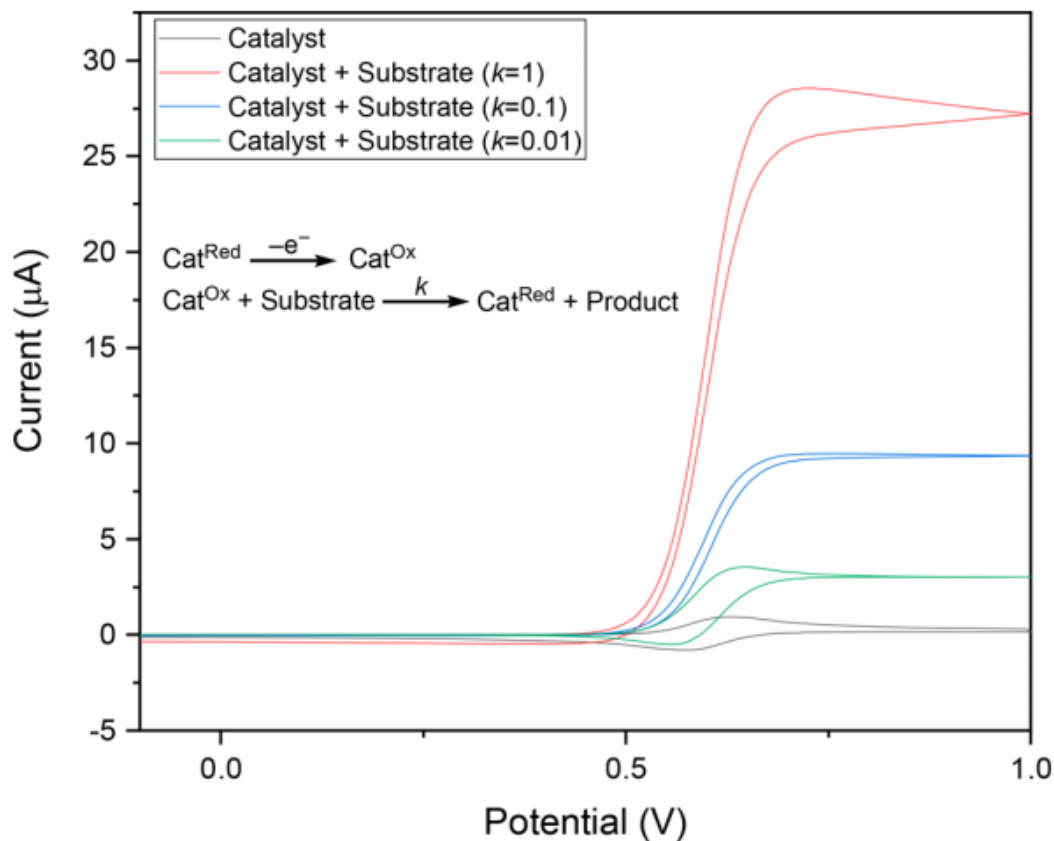
Mediating both electron-transfer and chemical steps

电化学反应的分子催化作用根据催化剂对调节反应活性的作用可分为两类。

第一类是无氧化还原的催化剂，它们不直接参与电极介导的过程。它们通过激活前沿分子轨道（即酸/碱催化）促进电子向或从底物转移，或促进电子转移后的化学步骤。

第二类包括氧化还原活性催化剂，它们直接与电极相互作用并介导电极和底物之间的电子转移，这些催化剂也可能参与后续的化学步骤。

第二类催化剂也被称为电催化剂。电催化剂的鉴定和评价可以很容易地使用循环伏安法(CV)进行，它表征了催化电流的大小和形状。



**Figure 1.** Cyclic voltammety of an electrocatalytic oxidation reaction (simulated using DigiSim). The catalytic turnover manifests as an enhancement of the catalyst oxidation wave. This catalytic current increases as the rate constant ( $k$ ) of the chemical process increases.

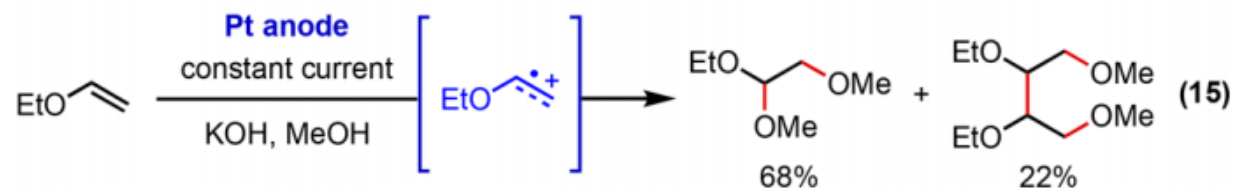
催化转化率表现为催化剂氧化波的增强。这个催化电流随着化学过程的速率常数( $k$ )的增加而增加。

从机理的角度来看，电催化剂在这些反应体系中起着三个关键作用：

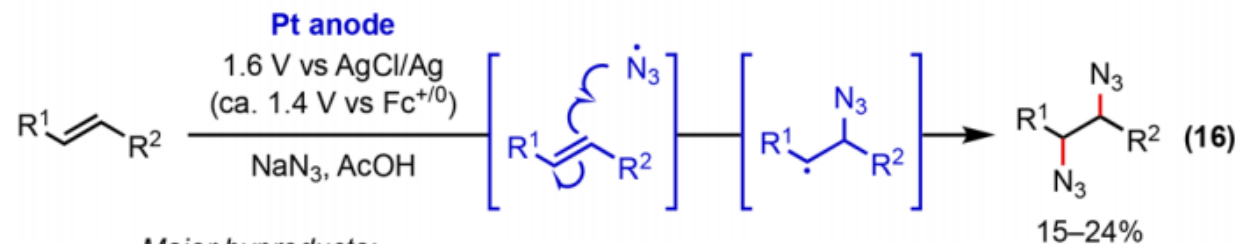
- 介导电子转移以提高电动力学
- 降低自由基生成所需的电势
- 控制电子转移后发生的化学步骤的选择性

## Scheme 6. Electrochemical Alkene Difunctionalization: Radical Cation and Radical Pathways

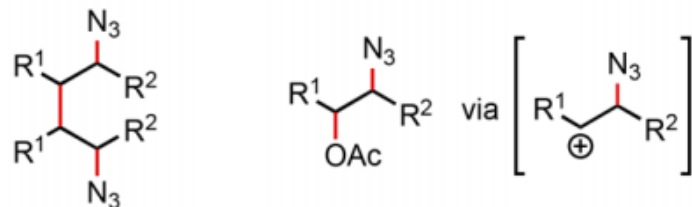
(A) Radical cation pathway for alkene difunctionalization



(B) Radical pathway for alkene difunctionalization



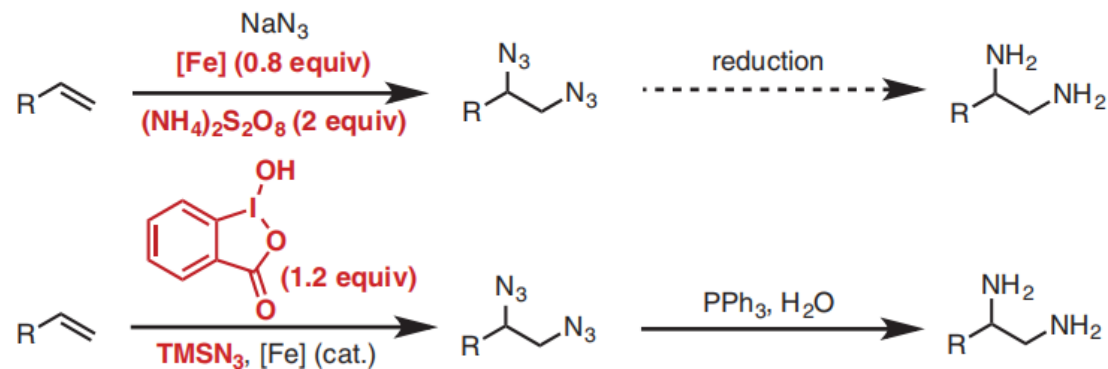
Major byproducts:



# Metal-catalyzed electrochemical diazidation of alkenes

Niankai Fu, Gregory S. Sauer, Ambarneil Saha, Aaron Loo, Song Lin\*

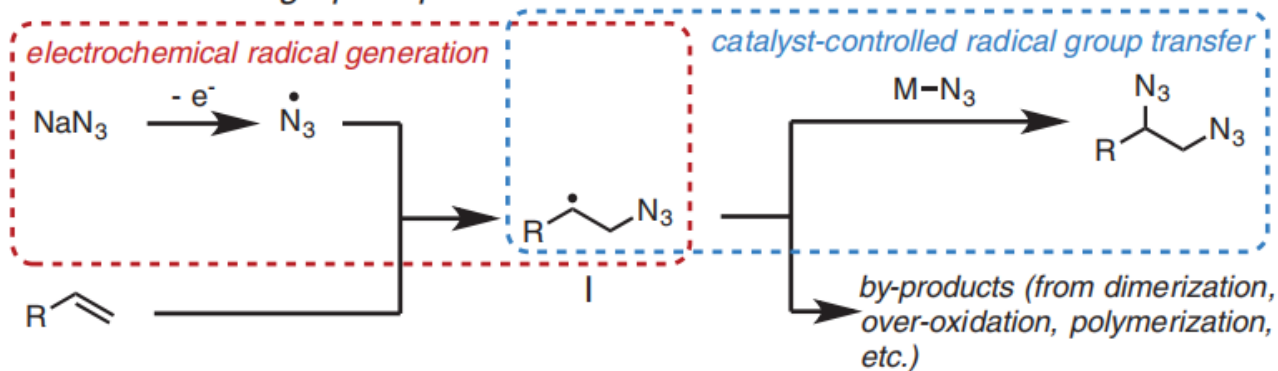
Previous work: examples of alkene diazidation (*refs. 11, 13*)



### C This work: metal-catalyzed electrochemical alkene diazidation



Mechanistic design principle:



$$[E(\text{N}_3\cdot/\text{N}_3^-) = 0.71 \text{ V}]$$

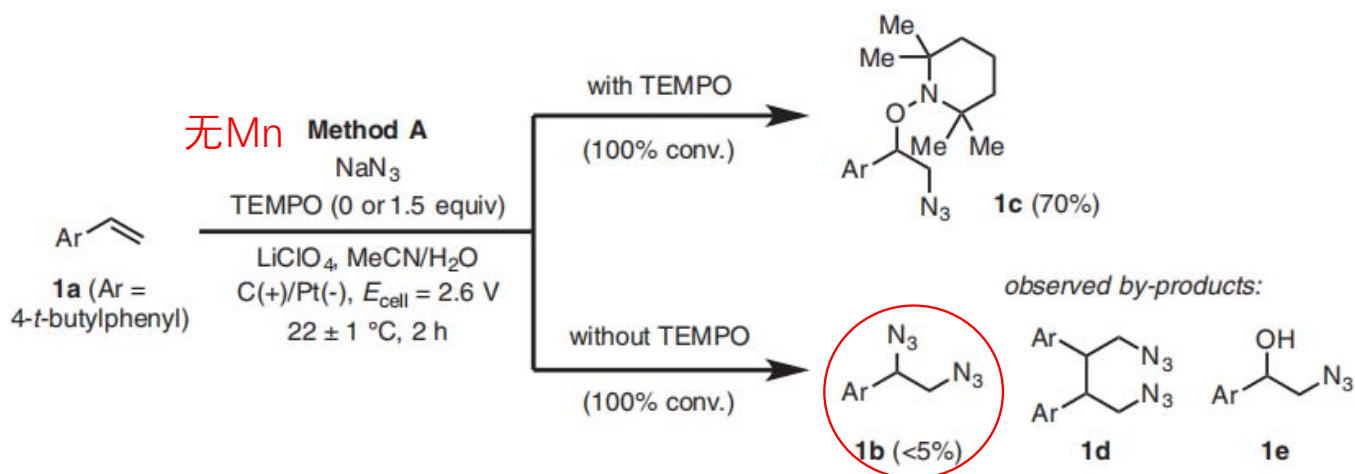
$$[E(\text{styrene radical cation/styrene}) = 1.55 \text{ V}]$$

$$\text{Method A: } E_{\text{cell}} = 2.6 \text{ V} \rightarrow E_{\text{anode}} = 0.75 \text{ V}$$

通过电化学方法产生自由基，使用催化剂控制选择性。

不使用催化剂：

- 自身二聚
- 在阳极上过氧化
- 多聚 (Lin Group使用这种方式合成高分子)



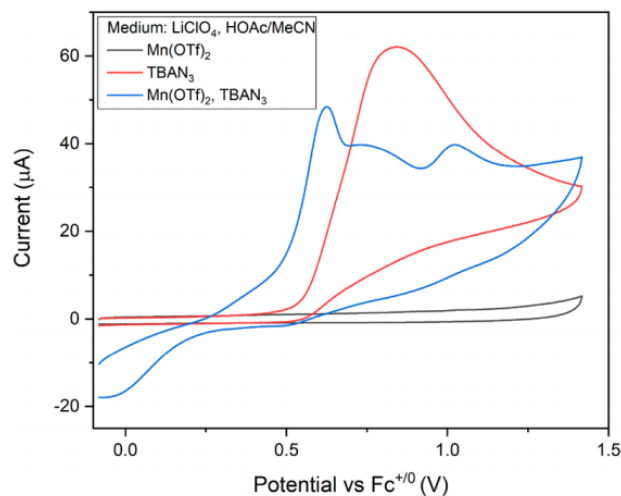
**Fig. 2. Proof-of-concept experiments.** Generation and sequestration of the carbon radical intermediate en route to alkene diazidation are illustrated. h, hour; conv., conversion.



$[E(\text{N}_3^-/\text{N}_3) = 0.71 \text{ V}]$

Method B:  $E_{\text{cell}} = 2.3 \text{ V} \rightarrow E_{\text{anode}} = 0.62 \text{ V}$

苯乙烯 yield = 95%



**Figure 2.** CV data demonstrating the reduced oxidation potential of  $[\text{Mn}^{\text{II}}]-\text{N}_3$  as compared with free  $\text{N}_3^-$  and  $\text{Mn}^{\text{II}}$ .

**Table S1.**

Alkene diazidation under various different conditions

Entry	Variation from standard conditions*	Conversion† (%)	Yield† (%)
1	None	>99	>99 (90)‡
2	Constant electrode potential at 0.72 V	>99	86 [66]§
3	Controlled current at 8 mA	>99	90 [87]§
4	No externally applied potential	<5	<5
5	Graphite as cathode instead of Pt	>99	82
6	Two AA batteries (3 V) as power source	>99	69
7	$\text{FeBr}_2$ instead of $\text{MnBr}_2$	95	<10
8	$\text{Cu}(\text{OAc})_2$ instead of $\text{MnBr}_2$	>99	85
9	$\text{Ni}(\text{OAc})_2$ instead of $\text{MnBr}_2$	83	<10
10	$\text{Mn}(\text{OTf})_2$ instead of $\text{MnBr}_2$	>99	95
11	$\text{Mn}(\text{TPP})$ instead of $\text{MnBr}_2$	>99	64
12	$\text{TBAPF}_6$ instead of $\text{LiClO}_4$	>99	97
13	Reused RVC electrode, no Mn catalyst	15	<5
14	No Mn catalyst	>99	<10

\*

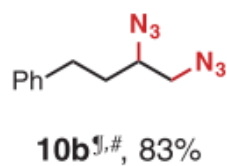
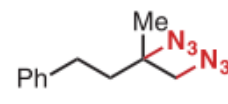
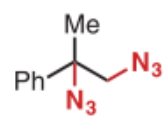
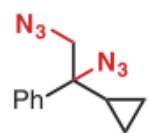
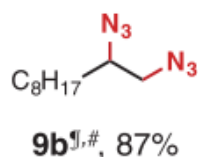
## A Diazidation: alkene substitution pattern and electronic properties\*

### Acyclic alkenes

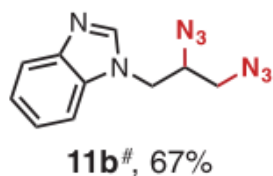
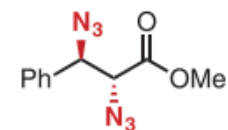
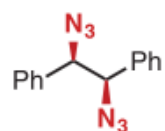
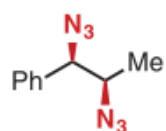
#### Monosubstituted

R = H ( <b>2b</b> )	95%
4- <i>t</i> -Bu ( <b>1b</b> )	90% (92%) <sup>†</sup> [76%] <sup>‡,§</sup>
4-MeO ( <b>3b</b> )	84%
4-F ( <b>4b</b> )	85%
4-Cl ( <b>5b</b> )	86%
3-MeO ( <b>6b</b> ) <sup>§,  </sup>	66%
4-CN ( <b>7b</b> )	70%
2,4,6-Me <sub>3</sub> ( <b>8b</b> )	88%

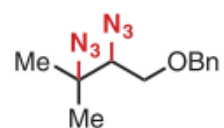
#### 1,1-Disubstituted



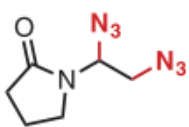
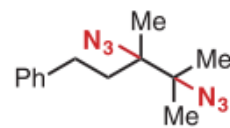
#### 1,2-Disubstituted



#### Trisubstituted

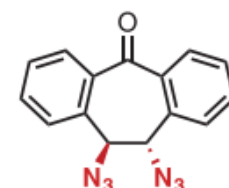
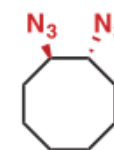
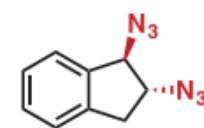


#### Tetrasubstituted

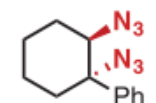
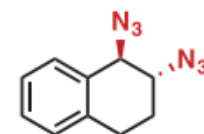


### Cyclic alkenes

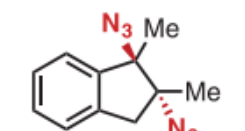
#### Disubstituted



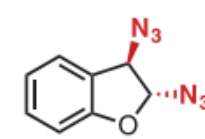
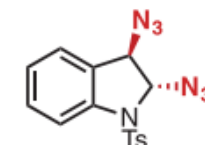
#### Trisubstituted



#### Tetrasubstituted



#### Electron-rich heterocycle



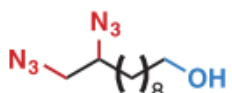


## B Diazidation: functional group compatibility\*

Functional groups sensitive to oxidation

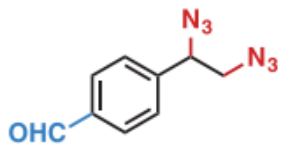
使用最接近循环发生所需的电压，在保证良好反应性的同时不影响易氧化的基团

Alcohol



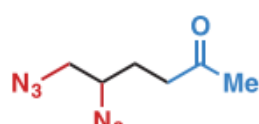
30b<sup>ll</sup>, 81%

Aldehyde



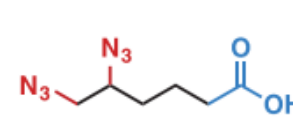
31b, 70%

Enolizable ketone

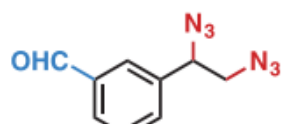


33b<sup>jl, #</sup>, 86%

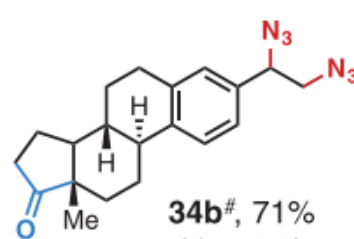
Carboxylic acid



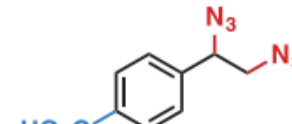
35b<sup>ll</sup>, 78%



32b, 81%

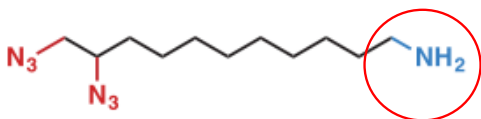


34b<sup>#</sup>, 71%  
(dr = 1:1)

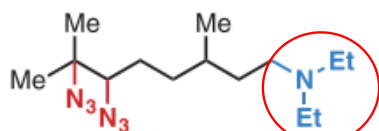


36b, 75%

Amine

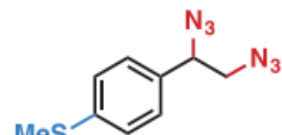


37b<sup>ll</sup>, 77%



38b<sup>ll</sup>, 69% (dr = 1:1)

Sulfide



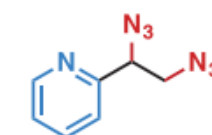
39b, 82%

Alkyne



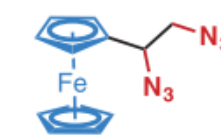
40b, 72%

N-Heterocycle



41b, 95%

Organometallic

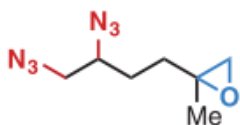


42b, 76%

Functional groups sensitive to nucleophilic substitution

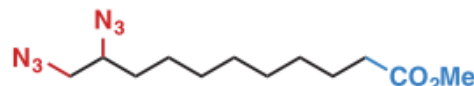
伯胺以及叔胺的氧化电位与Mn(II)-N<sub>3</sub>→Mn(III)-N<sub>3</sub>相当，没有被氧化的原因推测为：由于体系中有乙酸，N与AcOH形成的氢键加大了氧化的难度

Epoxide



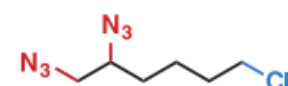
43b<sup>jl, #</sup>, 72% (dr = 1:1)

Ester

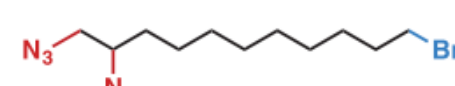


44b<sup>jl, #</sup>, 83%

Alkyl halide

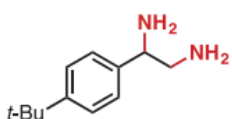


45b<sup>jl, #</sup>, 85%

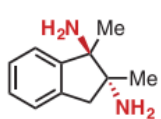


46b<sup>ll</sup>, 79%

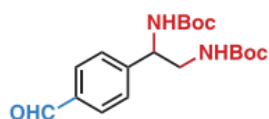
## C Tandem diazidation and reduction\*\*



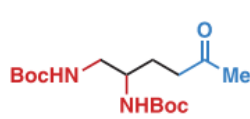
1g<sup>††</sup>, 86%



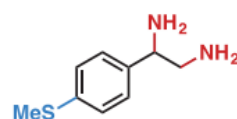
27g, 96%



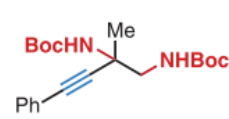
31f<sup>††</sup>, 47%



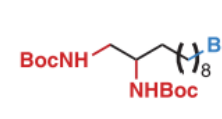
33f<sup>††</sup>, 42%



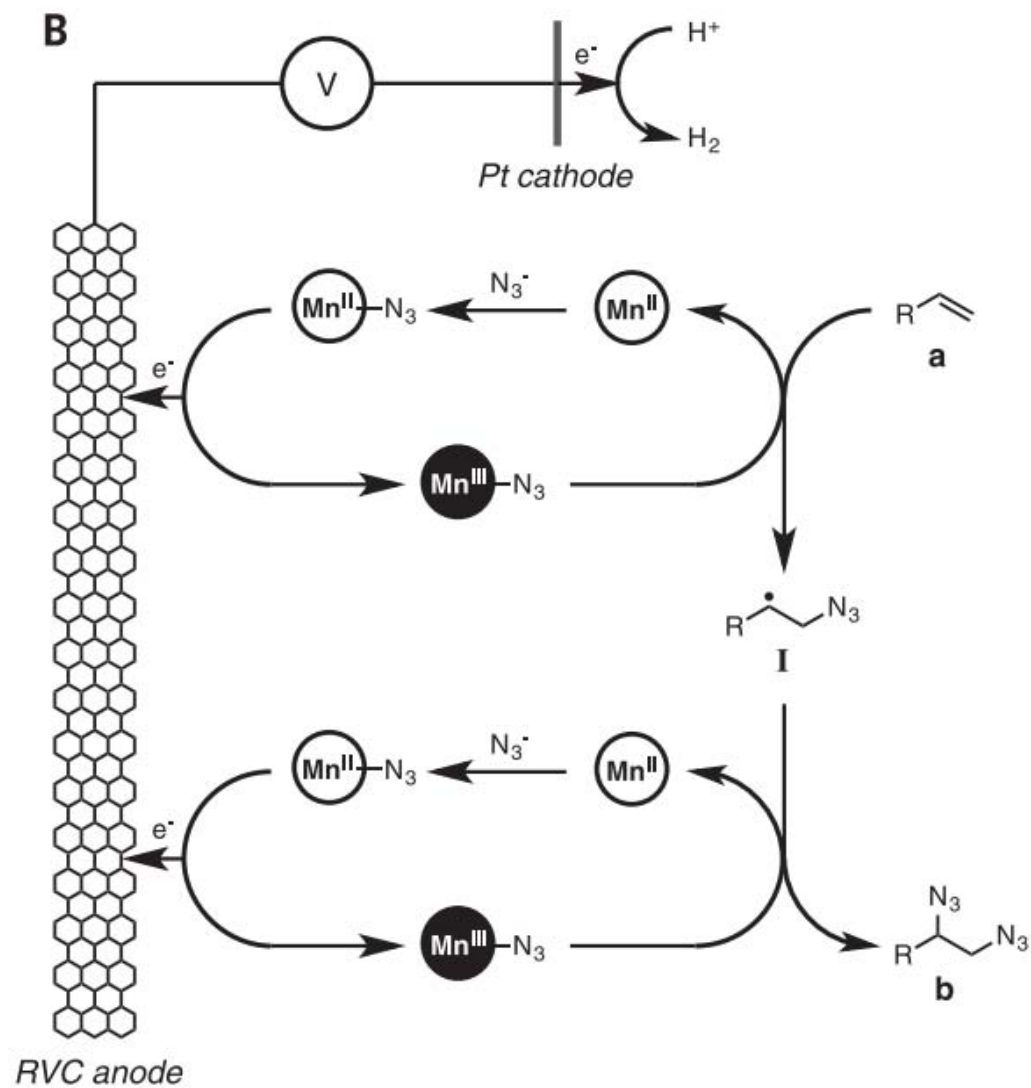
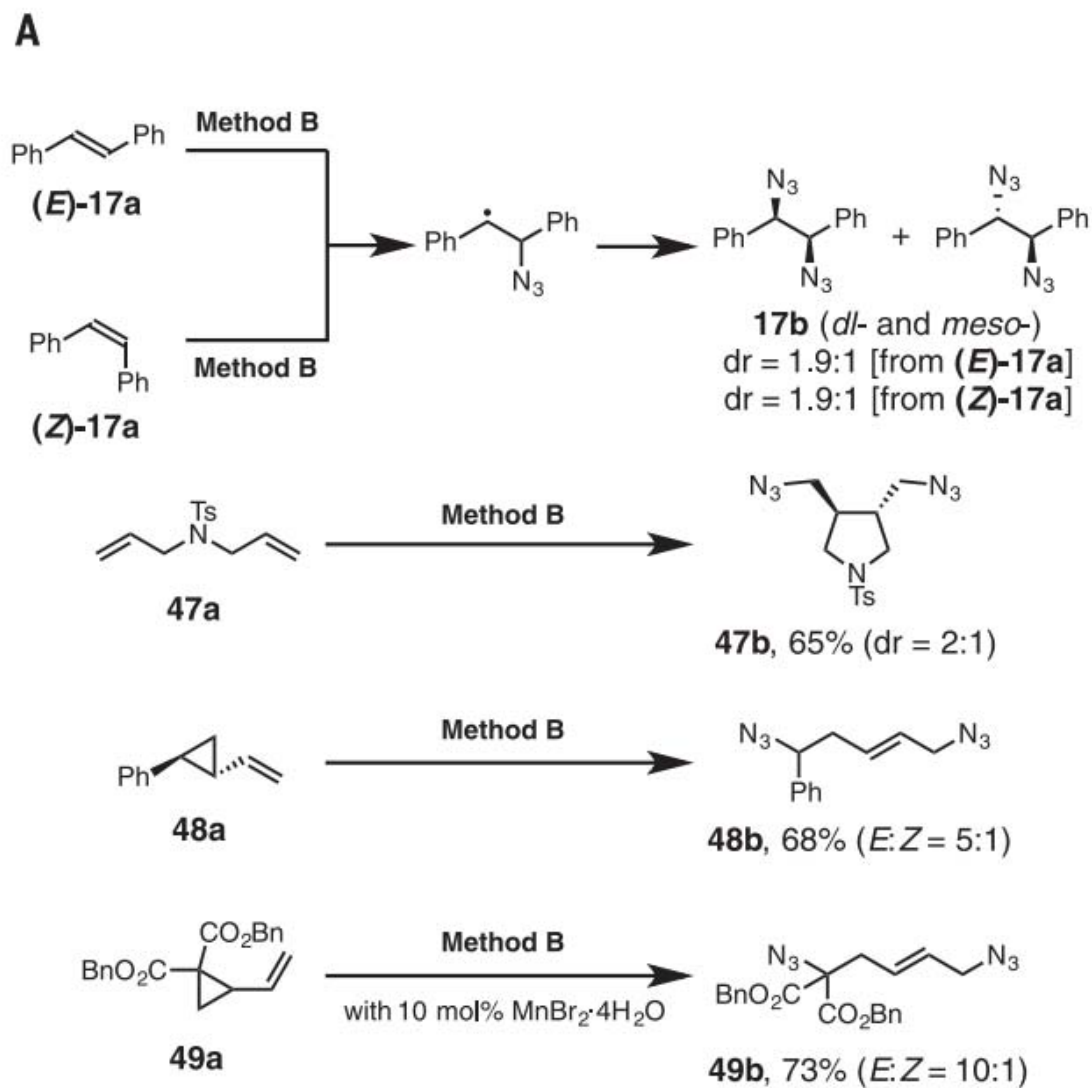
39g<sup>††</sup>, 70%



40f<sup>††</sup>, 67%



46f<sup>††</sup>, 78%



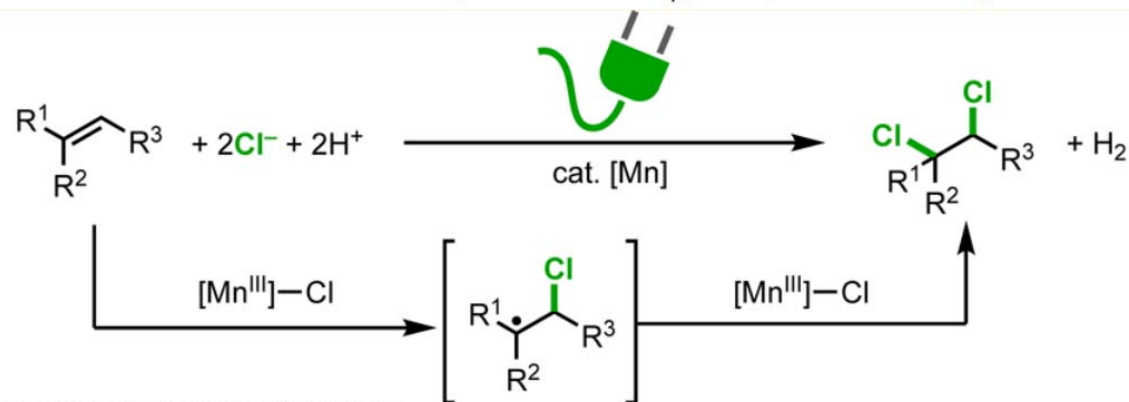
网状碳玻电极

# Electrocatalytic Radical Dichlorination of Alkenes with Nucleophilic Chlorine Sources

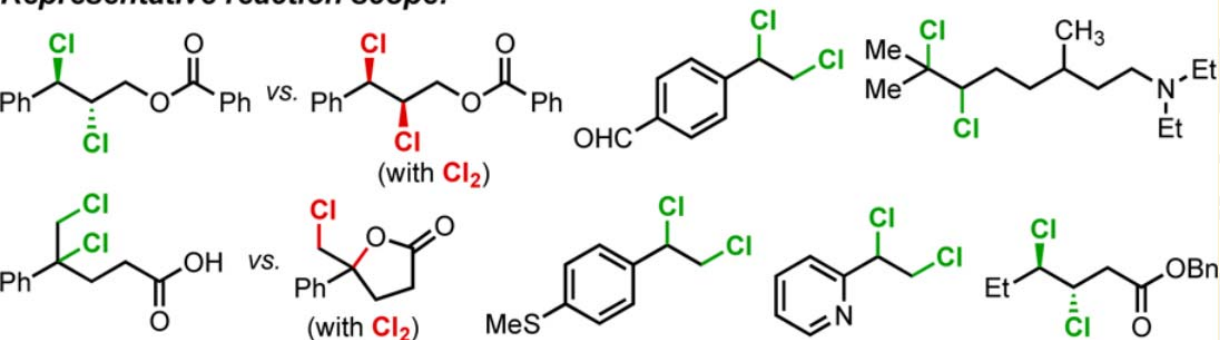
Niankai Fu,<sup>†</sup> Gregory S. Sauer,<sup>†</sup> and Song Lin<sup>\*,†,‡,§</sup>

<sup>†</sup>Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States

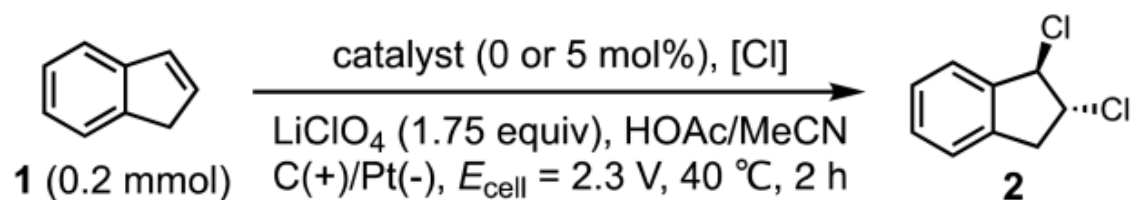
<sup>‡</sup>Atkinson Center for a Sustainable Future, Cornell University, Ithaca, New York 14853, United States



**Representative reaction scope:**



**Table 1. Reaction Discovery and Optimization**



Entry	Cl source	Catalyst	Yield (%) <sup>a</sup>	dr
1	LiCl (4 equiv)	None	16 (32 <sup>b</sup> )	1:1
2	LiCl (4 equiv)	Cu(OTf) <sub>2</sub>	14	1:2
3	LiCl (4 equiv)	Mn(OTf) <sub>2</sub>	63	>19:1
4	MgCl <sub>2</sub> (2 equiv)	Mn(OTf) <sub>2</sub>	89	>19:1
5	CaCl <sub>2</sub> (2 equiv)	Mn(OTf) <sub>2</sub>	<5	ND
6	NaCl (4 equiv)	Mn(OTf) <sub>2</sub>	8	>19:1
7	MgCl <sub>2</sub> (2 equiv)	Mn(OAc) <sub>2</sub> ·4H <sub>2</sub> O	86	>19:1
8 <sup>c</sup>	MgCl <sub>2</sub> (2 equiv)	Mn(OTf) <sub>2</sub>	98	17:1
9	MgCl <sub>2</sub> (1 equiv)	Mn(OTf) <sub>2</sub>	63	>19:1
<b>10</b>	<b>MgCl<sub>2</sub> (3 equiv)</b>	<b>Mn(OTf)<sub>2</sub></b>	<b>92 (90<sup>d</sup>)</b>	<b>&gt;19:1</b>
11 <sup>e</sup>	MgCl <sub>2</sub> (2 equiv)	Mn(OTf) <sub>2</sub>	54	>19:1

$$E(\text{Cl}\cdot/\text{Cl}^-) = 1.56 \text{ V} \rightarrow E_{\text{cell}} = 2.80 \text{ V}$$

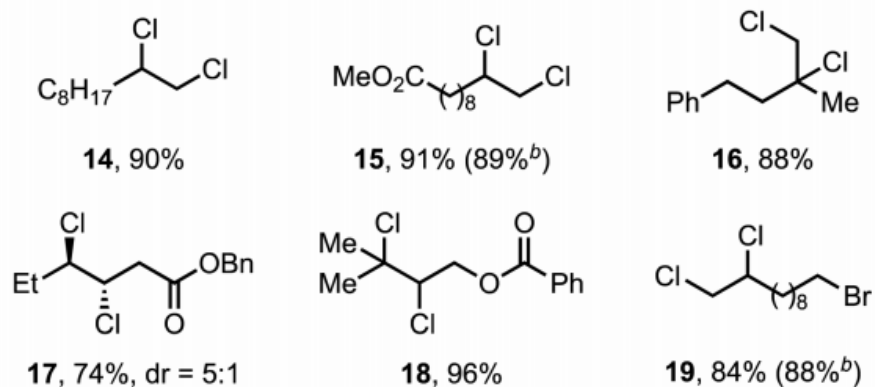
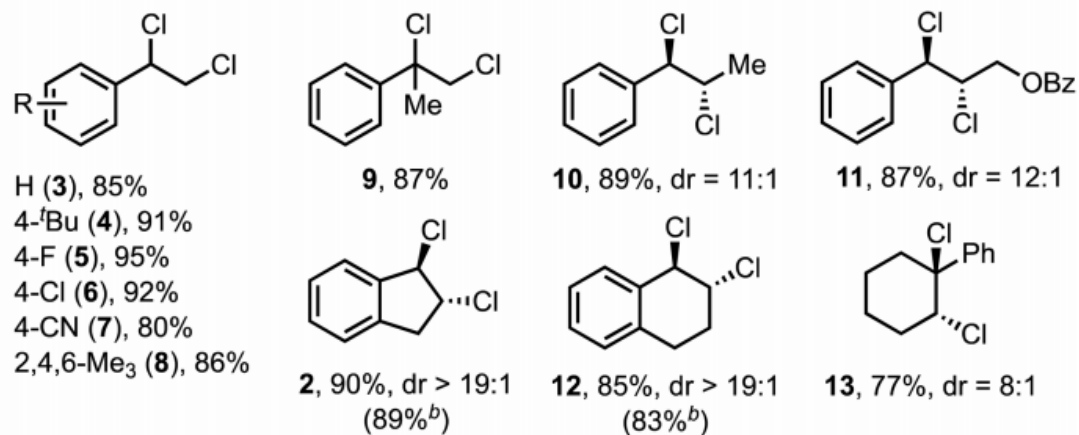
Cu[III]-Cl 体积大, 其中 Cl 比 Cl· 的更具负性, 会与先加成上的 Cl 互相排斥

溶解度太低

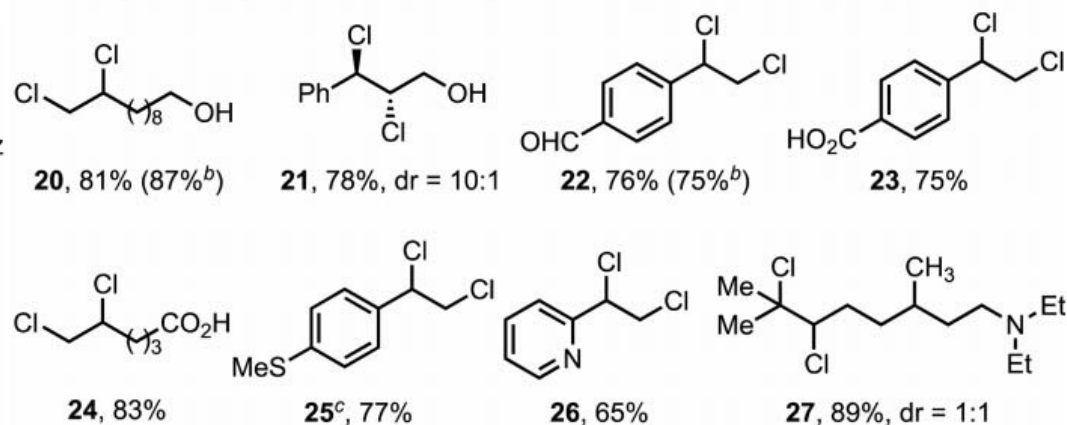
<sup>a</sup>Yields determined with <sup>1</sup>H NMR. <sup>b</sup>E<sub>cell</sub> = 2.8 V. <sup>c</sup>TBAPF<sub>6</sub> instead of LiClO<sub>4</sub> as electrolyte. <sup>d</sup>Isolated yield. <sup>e</sup>E<sub>cell</sub> = 2.1 V.

## Scheme 2. Substrate Scope<sup>a</sup>

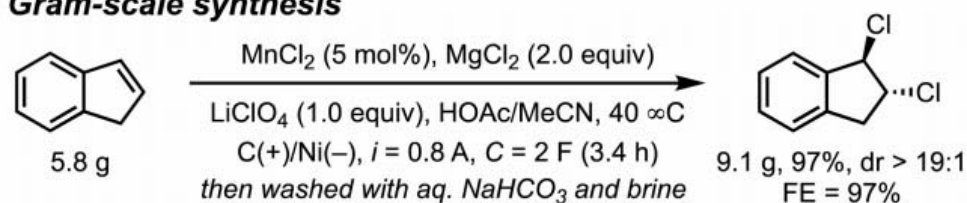
### A. Compatibility with different substitution patterns



### B. Compatibility with oxidatively sensitive functional groups



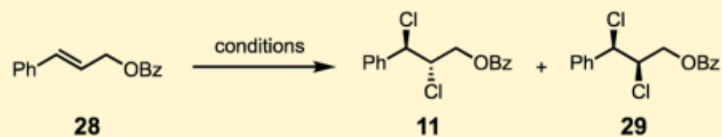
### C. Gram-scale synthesis



<sup>a</sup>Isolated yields are reported. <sup>b</sup>Faradaic efficiency (FE) under a controlled current of 8 mA after passing 2 F charge. <sup>c</sup>With 10 mol % catalyst.

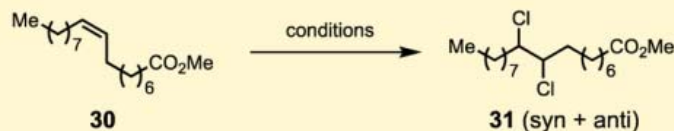
四取代的烯烃无法分离到产物，可能由于不稳定

### A. Diastereoselectivity test

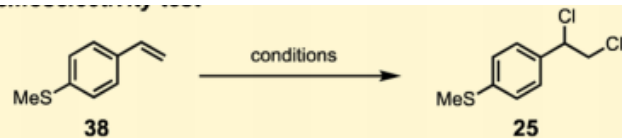


Entry	conditions	yield (%)	11:29
1	Mn(OTf) <sub>2</sub> (5 mol%), MgCl <sub>2</sub> (3.0 equiv), LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN, <b>C(+)/Pt(-), E<sub>cell</sub> = 2.3 V, 40 °C</b>	87	<b>12:1</b>
2	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (1.2 equiv)</b> , LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN	<5	– <sup>a</sup>
3	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	73	<b>1:8<sup>b</sup></b>
4	<b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	70	<b>1:5<sup>b</sup></b>

<sup>a</sup>Not determined. <sup>b</sup>Proposed mechanism for **29** formation:

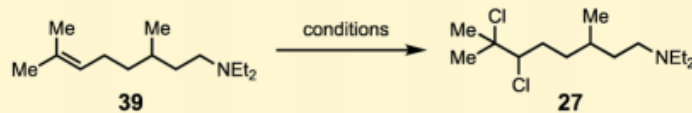


Entry	conditions	yield (%)	syn:anti
5	Mn(OTf) <sub>2</sub> (5 mol%), MgCl <sub>2</sub> (3.0 equiv), LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN, <b>C(+)/Pt(-), E<sub>cell</sub> = 2.3 V, 40 °C</b>	91	<b>1:2</b>
6	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	90	<b>&gt;19:1</b>
7	<b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	92	<b>&gt;19:1</b>



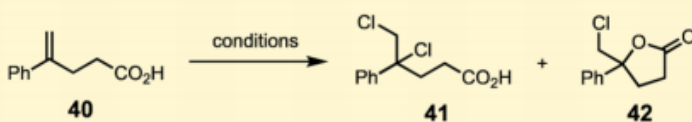
Entry	conditions	yield (%)
1	Mn(OTf) <sub>2</sub> (10 mol%), MgCl <sub>2</sub> (3.0 equiv), LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN, <b>C(+)/Pt(-), E<sub>cell</sub> = 2.3 V, 40 °C</b>	<b>71</b>
2	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (2.0 equiv)</b> , CHCl <sub>3</sub>	<b>&lt;5<sup>a</sup></b>

<sup>a</sup>Full conversion; byproducts observed (see text and SI).



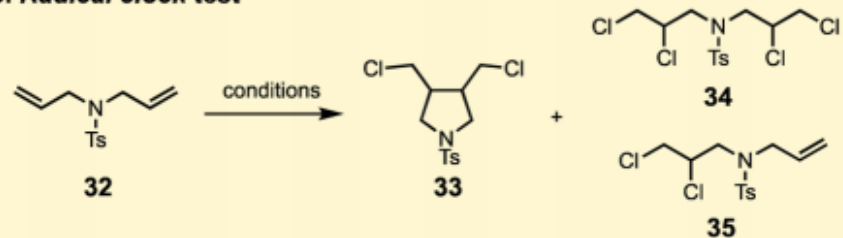
Entry	conditions	yield (%)
3	Mn(OTf) <sub>2</sub> (5 mol%), MgCl <sub>2</sub> (3.0 equiv), LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN, <b>C(+)/Pt(-), E<sub>cell</sub> = 2.3 V, 40 °C</b>	<b>89</b>
4	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	<b>9<sup>a</sup></b>

<sup>a</sup>Full conversion; byproducts observed (see text and SI).



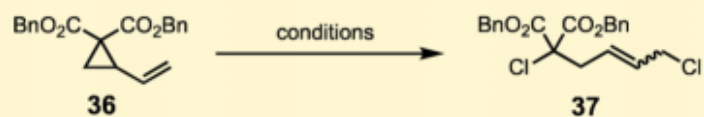
Entry	conditions	41 (%)	42 (%)
5	Mn(OTf) <sub>2</sub> (5 mol%), MgCl <sub>2</sub> (3.0 equiv), LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN, <b>C(+)/Pt(-), E<sub>cell</sub> = 2.3 V, 40 °C</b>	<b>77</b>	<b>10</b>
6	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	<b>16</b>	<b>68</b>

### B. Radical clock test



Entry	conditions	<b>33</b> (%)	<b>34+35</b> (%)
1	Mn(OTf) <sub>2</sub> (5 mol%), MgCl <sub>2</sub> (3.0 equiv), LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN, <b>C(+)/Pt(-), E<sub>cell</sub> = 2.3 V, 40 °C</b>	<b>71<sup>a</sup></b>	<b>&lt;5</b>
2	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	<b>&lt;5</b>	<b>70<sup>b</sup></b>
3	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (2.4 equiv)</b> , CHCl <sub>3</sub>	<b>&lt;5</b>	<b>77<sup>c</sup></b>
4	<b>Cl<sub>2</sub> (2.4 equiv)</b> , CHCl <sub>3</sub>	<b>&lt;5</b>	<b>79<sup>c</sup></b>

<sup>a</sup>Trans/cis = 2:1. <sup>b</sup>**34/35** = 1:1.5. <sup>c</sup>Only **34** observed.



Entry	conditions	yield (%)
5	Mn(OTf) <sub>2</sub> (5 mol%), MgCl <sub>2</sub> (3.0 equiv), LiClO <sub>4</sub> (1.75 equiv), HOAc/MeCN, <b>C(+)/Pt(-), E<sub>cell</sub> = 2.3 V, 40 °C</b>	<b>86<sup>a</sup></b>
6	Mn(OTf) <sub>2</sub> (5 mol%), <b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	<b>&lt;5<sup>b</sup></b>
7	<b>Cl<sub>2</sub> (1.2 equiv)</b> , CHCl <sub>3</sub>	<b>&lt;5<sup>b</sup></b>

<sup>a</sup>E/Z = 8:1. <sup>b</sup>Multiple unidentified products observed with NMR.

### Scheme 4. Proposed Catalytic Cycles

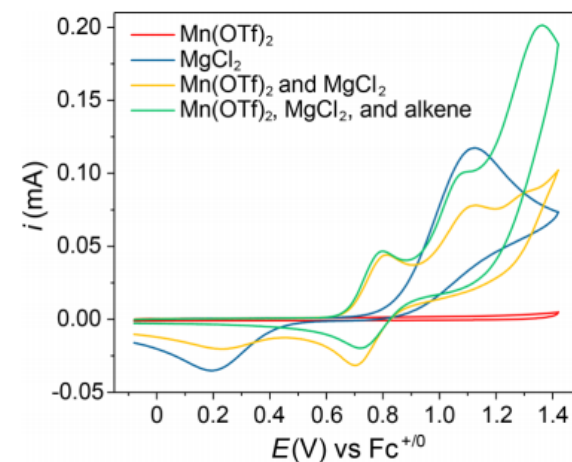
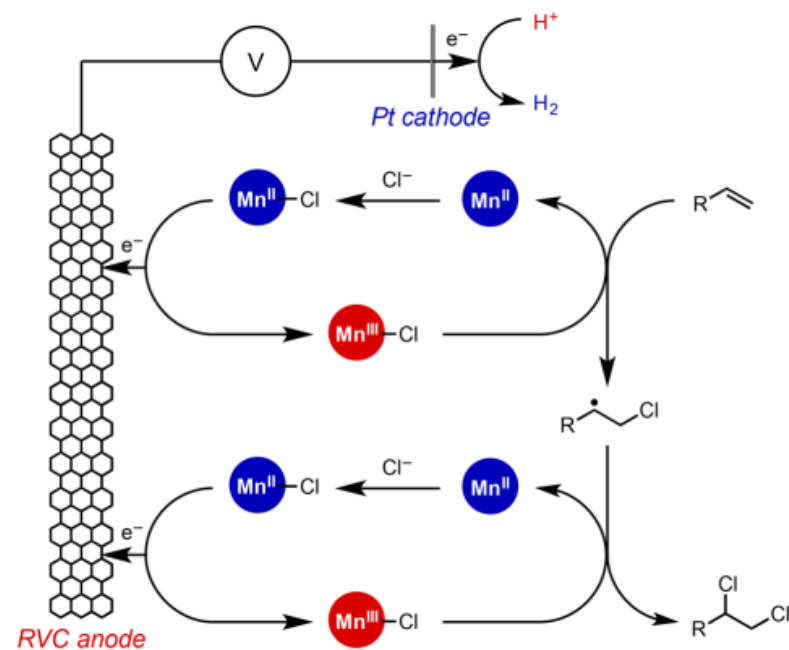


Figure 1. Cyclic voltammetry studies.

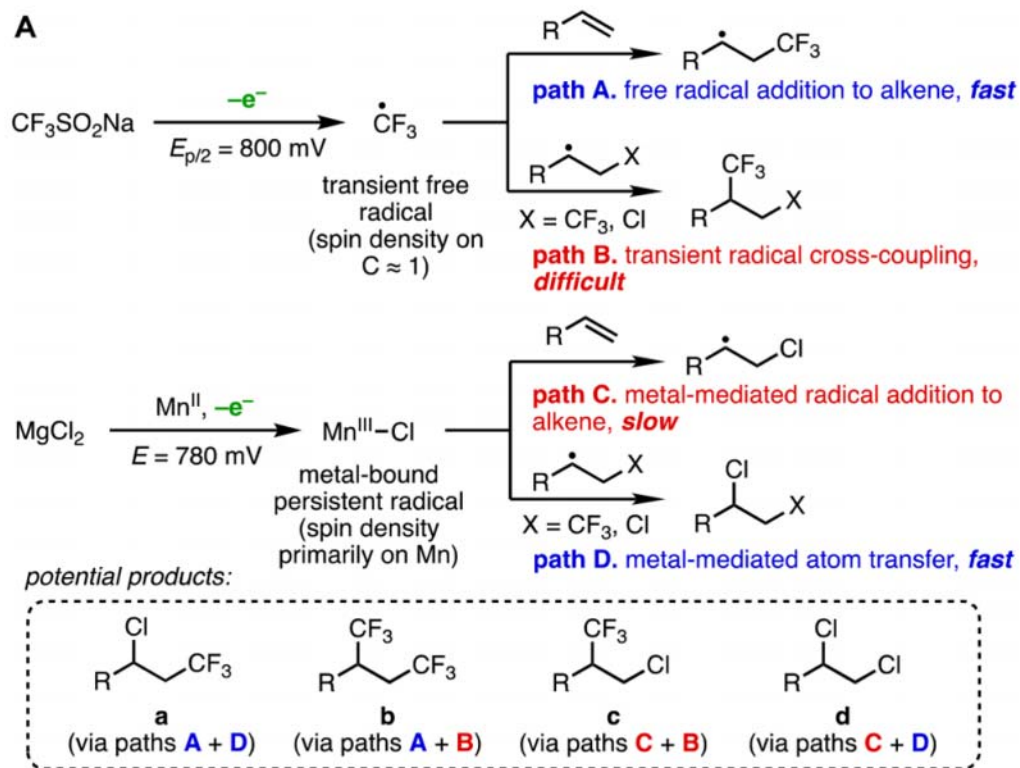


# Anodically Coupled Electrolysis for the Heterodifunctionalization of Alkenes

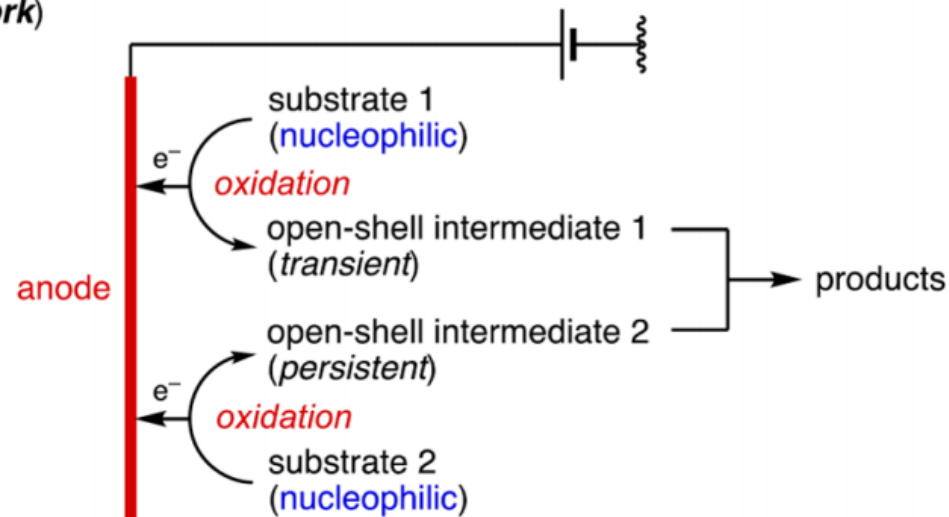
Ke-Yin Ye,<sup>†</sup> Gisselle Pombar,<sup>†,‡</sup> Niankai Fu,<sup>†</sup> Gregory S. Sauer,<sup>†</sup> Ivan Keresztes,<sup>†</sup> and Song Lin<sup>\*,†,‡</sup>

<sup>†</sup>Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States

<sup>‡</sup>Department of Chemistry, University of Central Florida, Orlando, Florida 32816, United States

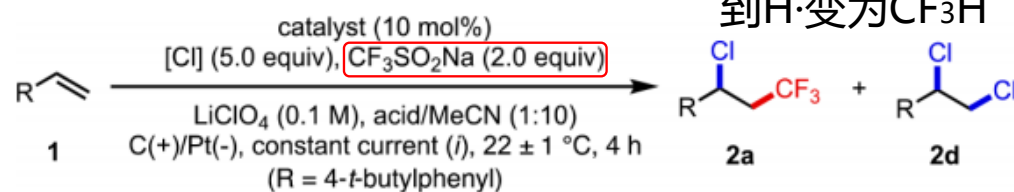


**C.** Anodically coupled electrolysis: merging two distinct oxidative events (*This work*)



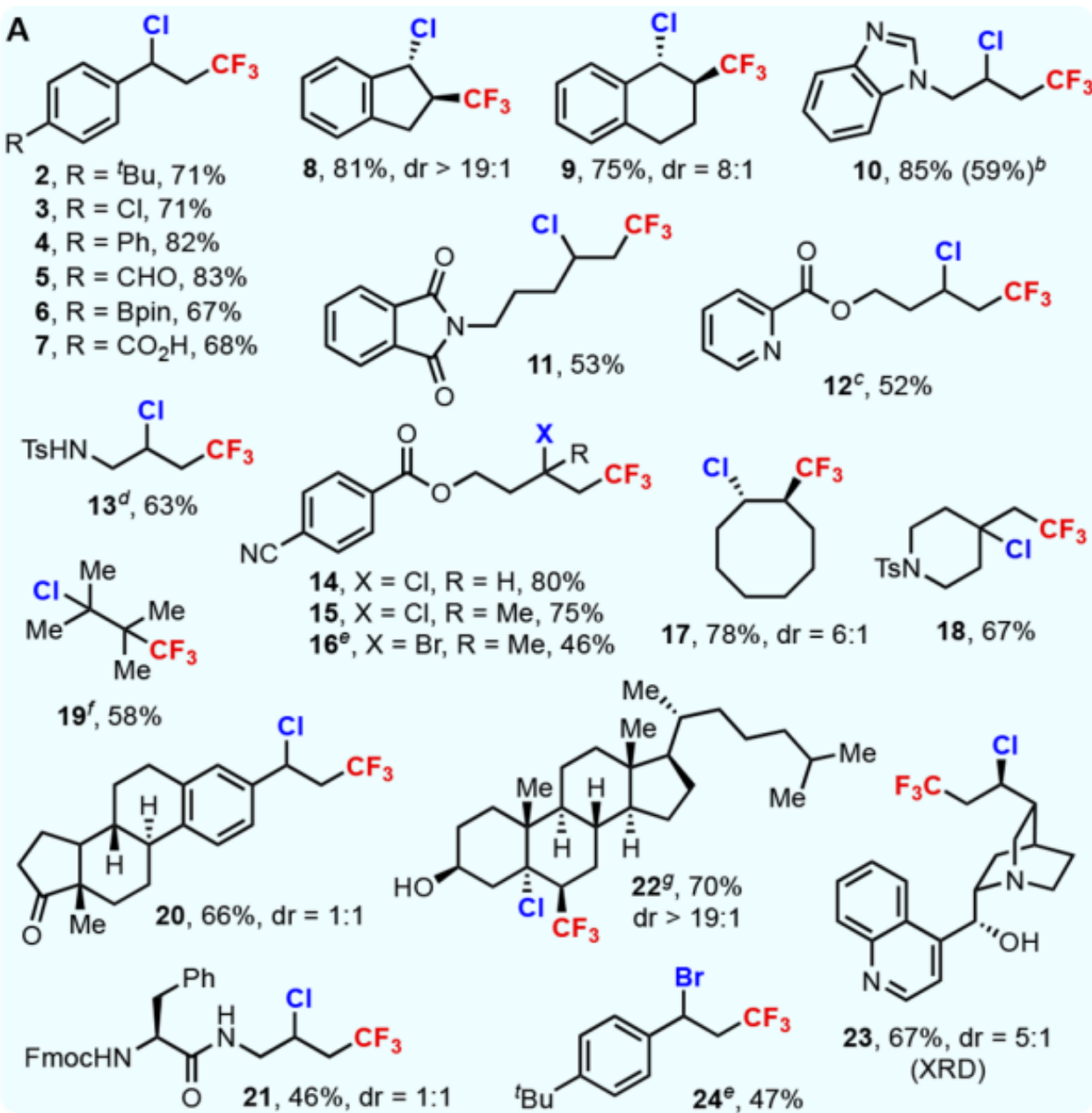


**Table 1. Initial Reaction Discovery and Optimization**



entry	catalyst	[Cl]	acid	<i>i</i> (mA)	$E_{\text{cell},i}$ (V)	2a yield (%) <sup>a</sup>	2a/2d <sup>a</sup>
1	Mn(OAc) <sub>2</sub> <sup>b</sup>	MgCl <sub>2</sub>	HOAc	4	2.08	41	13:1
2	Mn(OAc) <sub>2</sub>	MgCl <sub>2</sub>	HOAc	10	3.00	66 <sup>c</sup>	13:1
3 <sup>d</sup>	None	MgCl <sub>2</sub>	HOAc	10	3.14	<5	– <sup>e</sup>
4	Mn(OAc) <sub>2</sub>	LiCl	HOAc	10	3.20	35	3:1
5	Mn(OAc) <sub>2</sub>	MgCl <sub>2</sub>	CHCl <sub>2</sub> CO <sub>2</sub> H	10	2.67	69	9:1
6	Mn(OAc) <sub>2</sub>	MgCl <sub>2</sub>	CF <sub>3</sub> CO <sub>2</sub> H	10	1.67	71	12:1
7	Mn(OAc) <sub>2</sub>	MgCl <sub>2</sub>	CF <sub>3</sub> CO <sub>2</sub> H	15	2.28	70	13:1
8 <sup>f</sup>	Mn(OAc) <sub>2</sub>	MgCl <sub>2</sub>	CF <sub>3</sub> CO <sub>2</sub> H	15	2.05 <sup>g</sup>	83	19:1
9 <sup>h</sup>	Mn(OAc) <sub>2</sub>	MgCl <sub>2</sub>	CF <sub>3</sub> CO <sub>2</sub> H	15	2.09	82	13:1
10 <sup>i</sup>	Mn(OAc) <sub>2</sub>	MgCl <sub>2</sub>	CF <sub>3</sub> CO <sub>2</sub> H	15	2.02	80	19:1

<sup>a</sup>Determined with NMR. <sup>b</sup>Mn(OAc)<sub>2</sub>·4H<sub>2</sub>O used in all but entry 3. <sup>c</sup>Byproduct 4-*tert*-butyl- $\beta$ -trifluoromethylstyrene also observed. <sup>d</sup>Reaction time 2 h. <sup>e</sup>Not determined. <sup>f</sup>With 0.2 M LiClO<sub>4</sub>. <sup>g</sup>Ending cell voltage 2.49 V. <sup>h</sup>With 3.0 equiv MgCl<sub>2</sub>. <sup>i</sup>With TBAPF<sub>6</sub> as electrolyte.

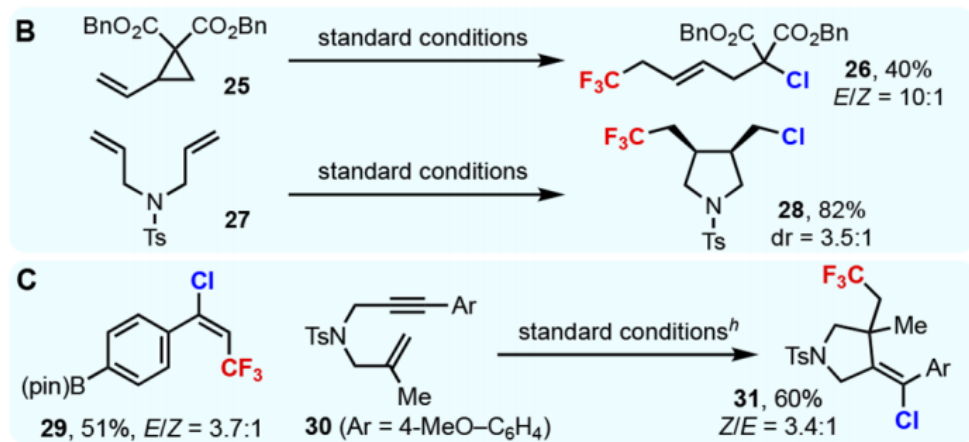


20-23 天然产物

16,24 Cl→Br

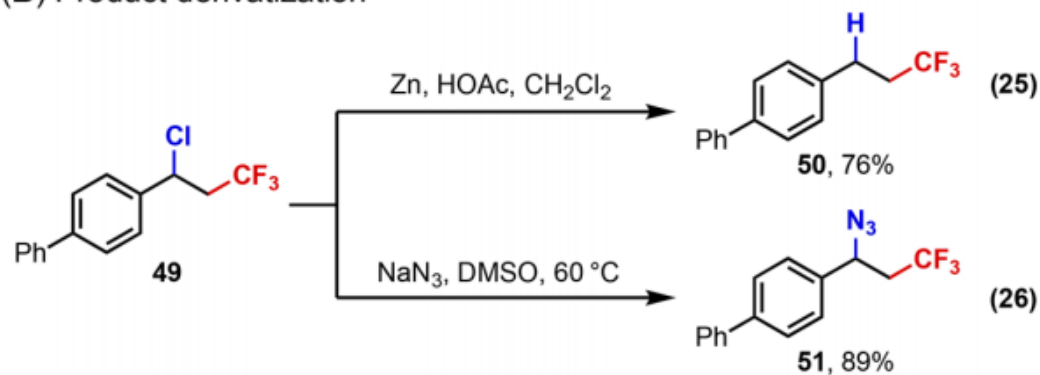
23 敏感基团

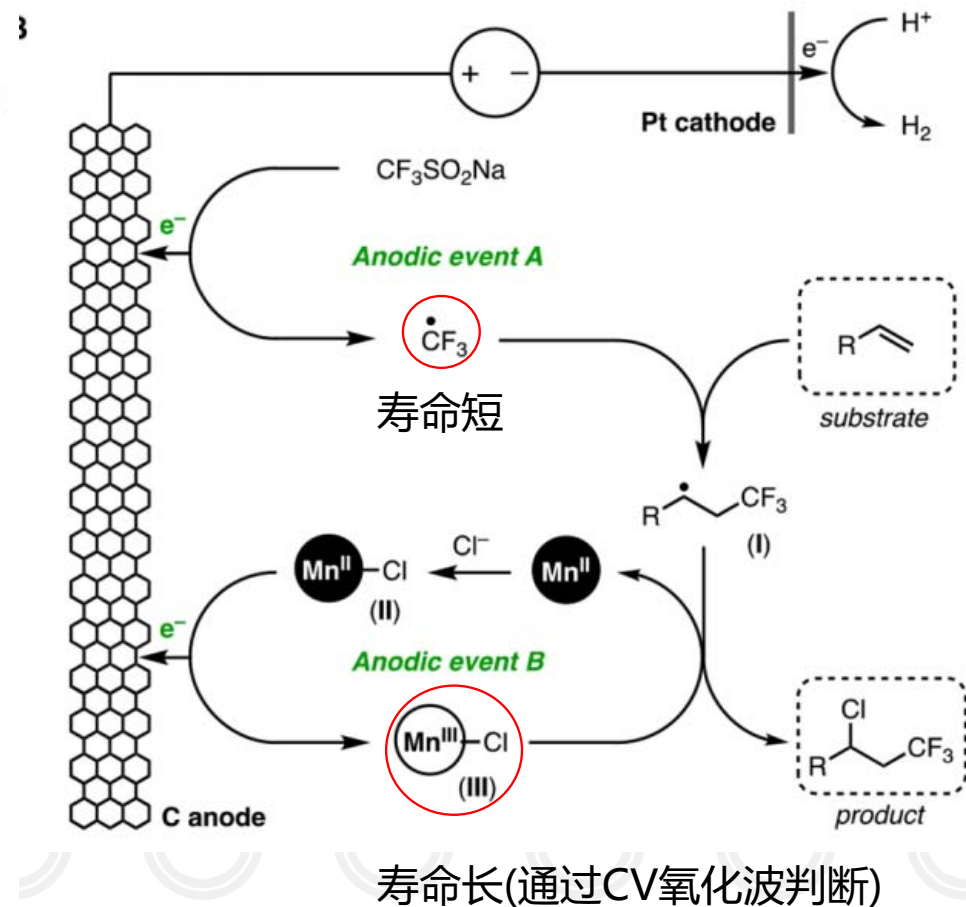
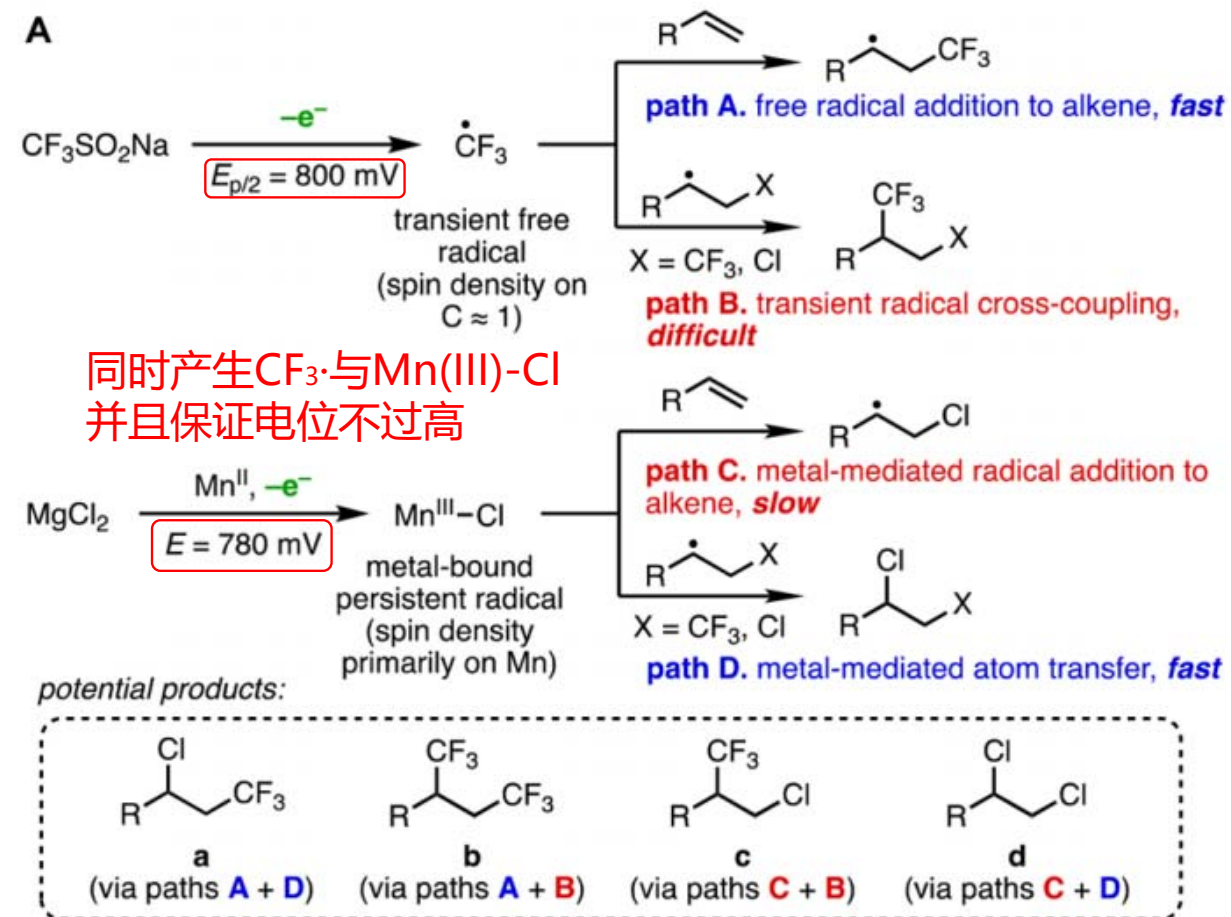
- 富电子的苯乙烯由于芳基发生三氟甲基化不能作为合适的底物
- 含有活泼H的底物由于CF<sub>3</sub>·会得到H·变为CF<sub>3</sub>H，产率降低

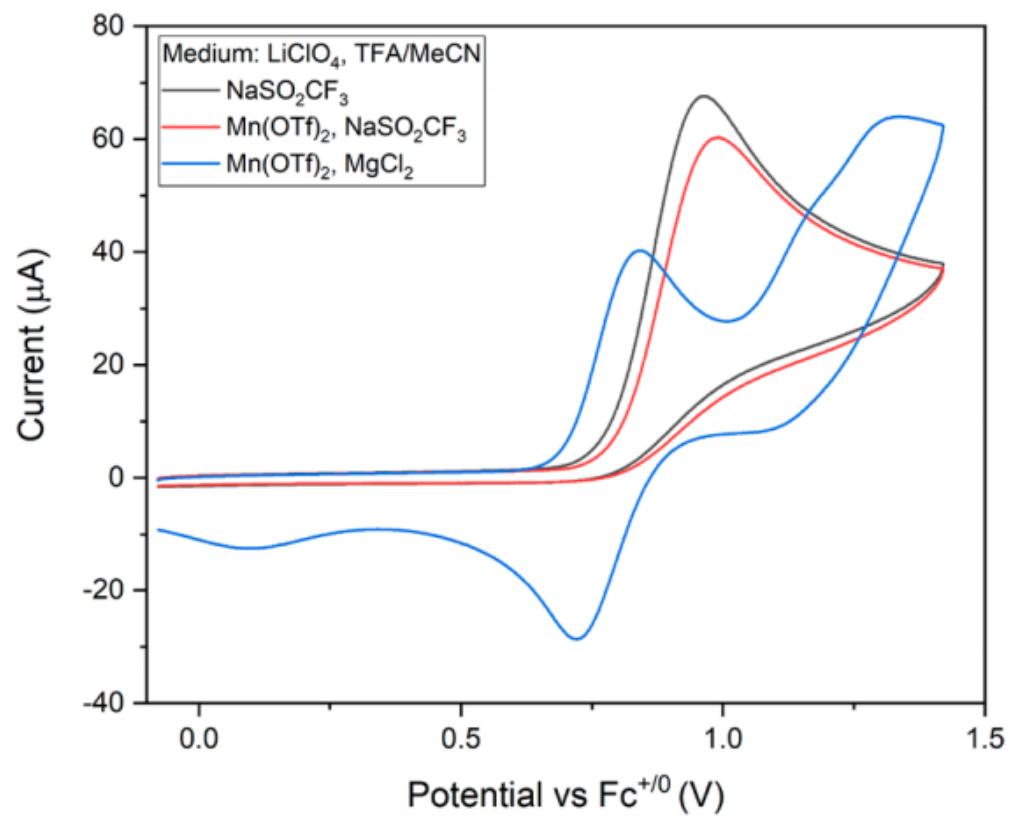


\*Reactions conducted on 0.2 mmol scale, isolated yields reported.  
<sup>b</sup>6.3 mmol scale. <sup>c</sup>The cell voltage controlled at 2.6 V during electrolysis ( $E_{\text{cell}} = 2.6 \text{ V}$ ). <sup>d</sup> $E_{\text{cell}} = 2.1 \text{ V}$ . <sup>e</sup>With 3 equiv KBr instead of MgCl<sub>2</sub> under controlled  $E_{\text{cell}}$  of 2.1 V. <sup>f</sup> $i = 10 \text{ mA}$ , with HOAc instead of CF<sub>3</sub>CO<sub>2</sub>H, yield determined with NMR. <sup>g</sup>0.1 mmol scale with 4 equiv CF<sub>3</sub>SO<sub>2</sub>Na. <sup>h</sup> $i = 8 \text{ mA}$ .

**(B) Product derivatization**



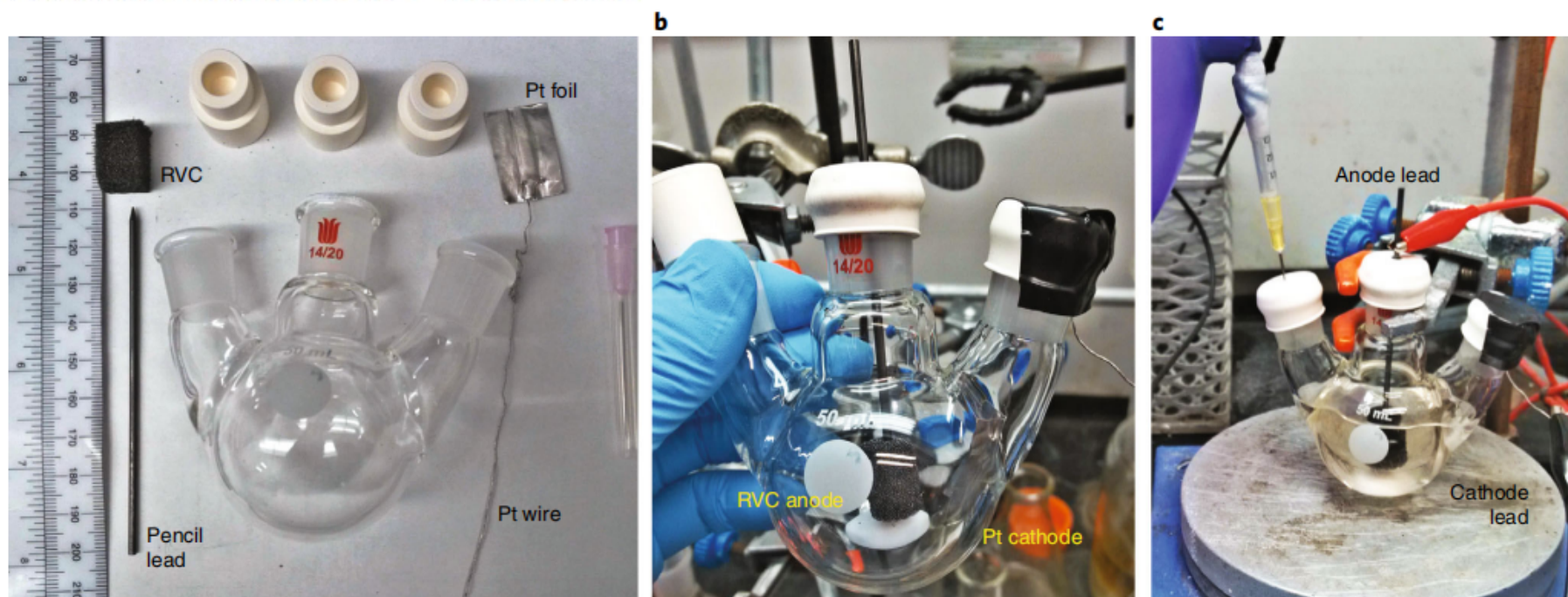




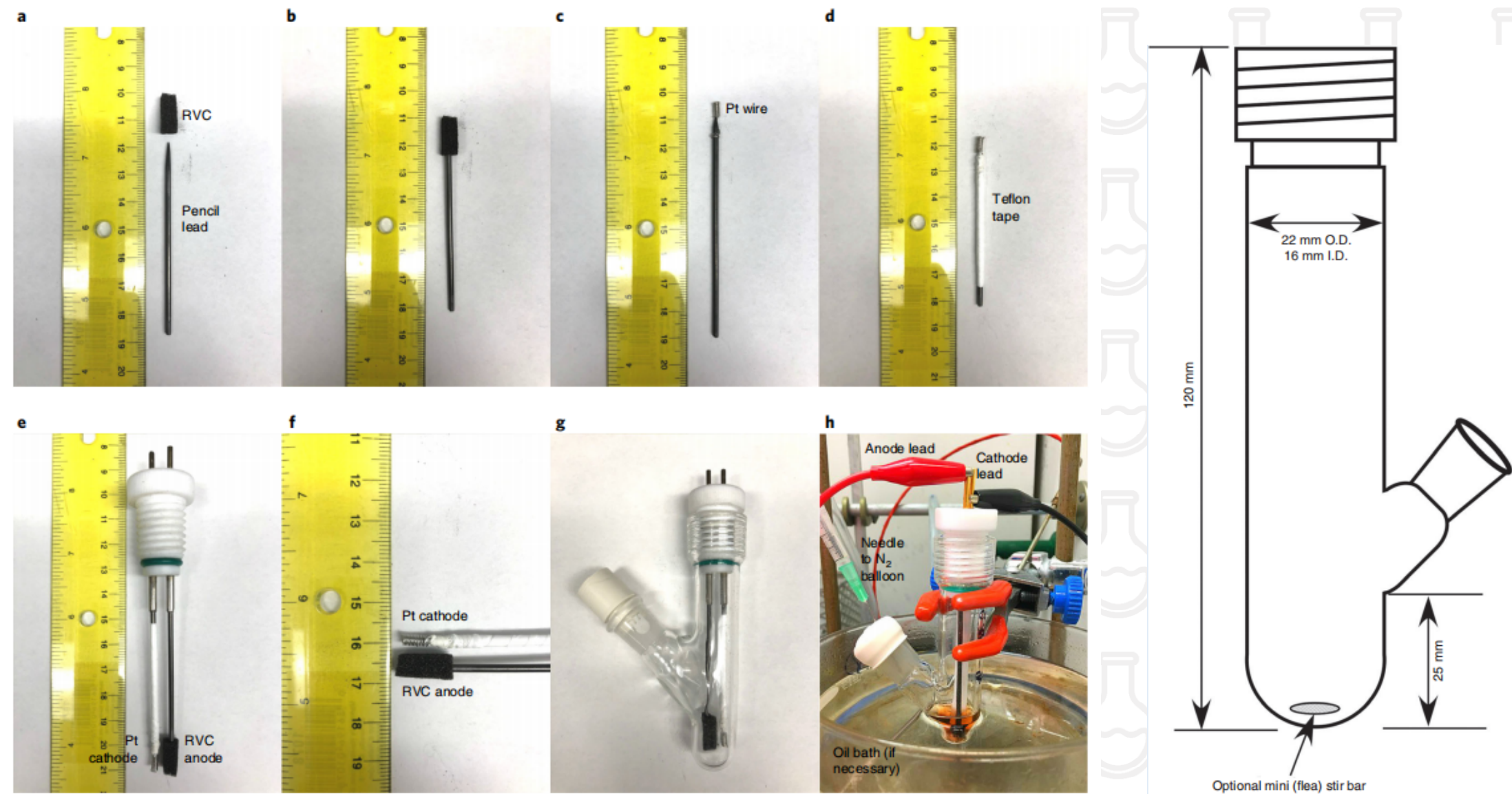
**Figure 4.** CV data demonstrating  $[\text{Mn}^{\text{II}}]\text{-Cl}$  and Langlois reagent are oxidized at similar potentials, enabling anodically coupled electrolysis. Abbreviations: TFA, trifluoroacetic acid.

# A general, electrocatalytic approach to the synthesis of vicinal diamines

Niankai Fu<sup>1,3</sup>, Gregory S. Sauer<sup>1,3</sup> and Song Lin<sup>1,2\*</sup>



**Fig. 4 | Electrolysis setup for 3 mmol scale reactions.** Assemblies of the RVC anode and Pt cathode (a), and the whole electrochemical cell (b,c).

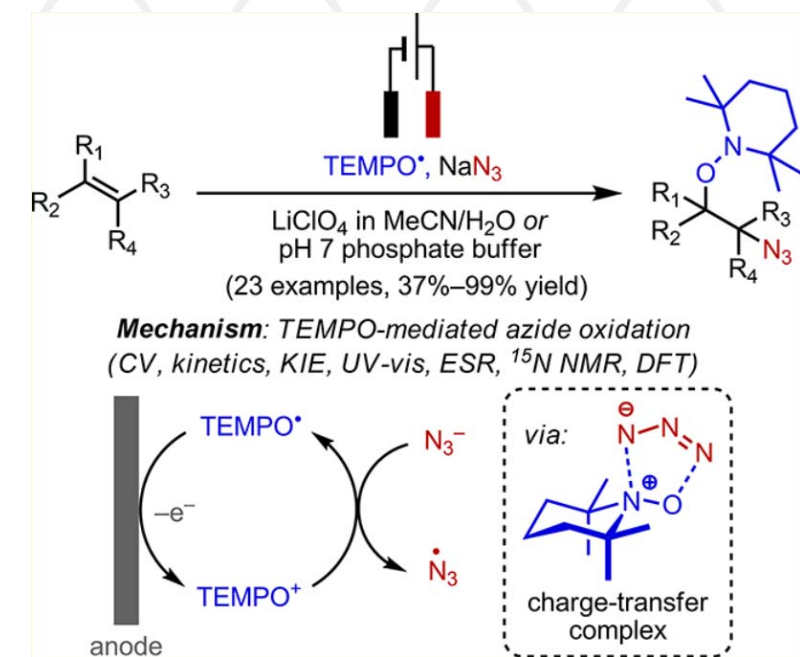


**Fig. 3 |** Electrolysis setup for 0.2 mmol scale reactions. **a-h**, Assemblies of the RVC anode (**a,b**), Pt cathode (**c,d**), the cap (**e,f**), and the whole electrochemical cell (**g,h**).

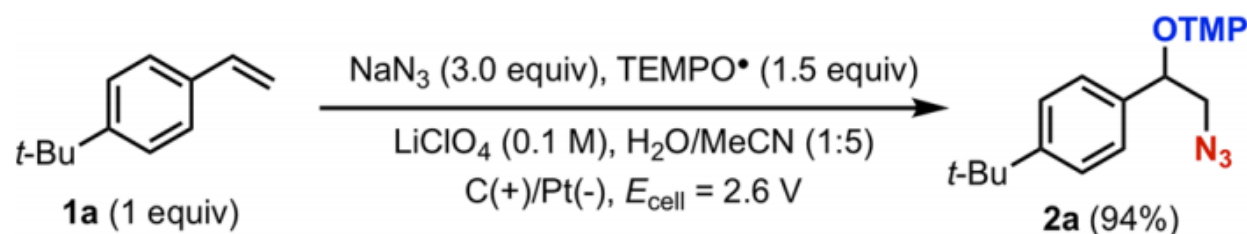
# Electrochemical Azidooxygenation of Alkenes Mediated by a TEMPO–N<sub>3</sub> Charge-Transfer Complex

Juno C. Siu,<sup>1</sup> Gregory S. Sauer, Ambarneil Saha, Reed L. Macey, Niankai Fu, Timothée Chauviré,<sup>1</sup> Kyle M. Lancaster,<sup>1\*</sup> and Song Lin<sup>1\*</sup>

Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States

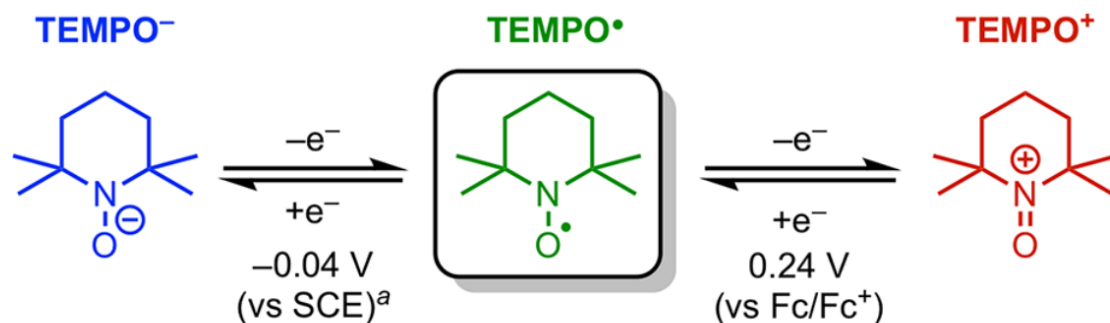


## Scheme 3. Electrochemical Azidooxygenation of Alkenes



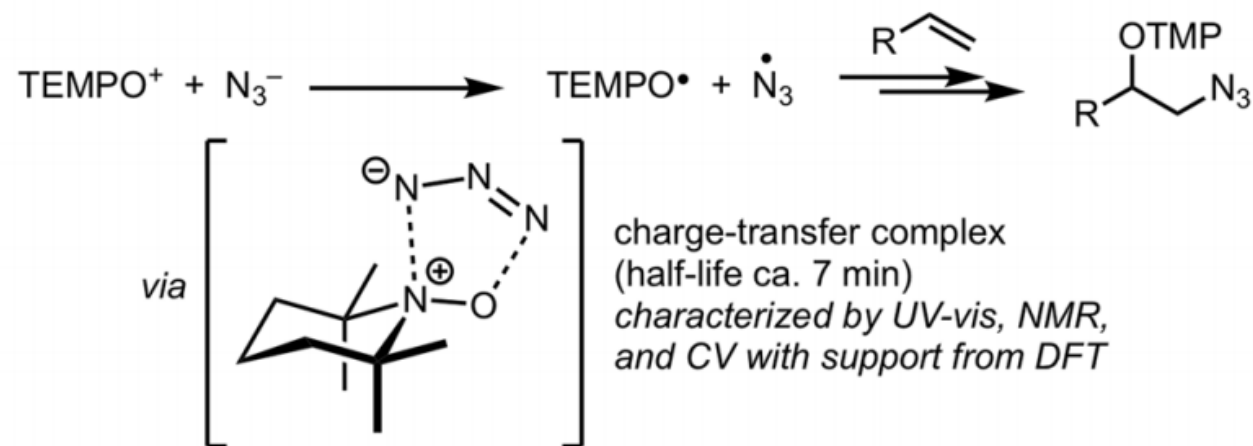


## Scheme 1. Accessible Oxidation States of TEMPO via Single-Electron Oxidation and Reduction Processes



<sup>a</sup>This value was reported in ref 4 and measured in an aqueous buffer.

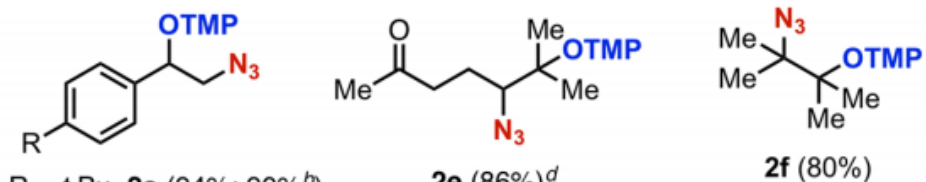
**E. This work:** TEMPO<sup>+</sup> as single-electron oxidant in the azidooxygenation of alkenes (TEMPO<sup>+</sup>/TEMPO<sup>•</sup>, 1e<sup>-</sup>)



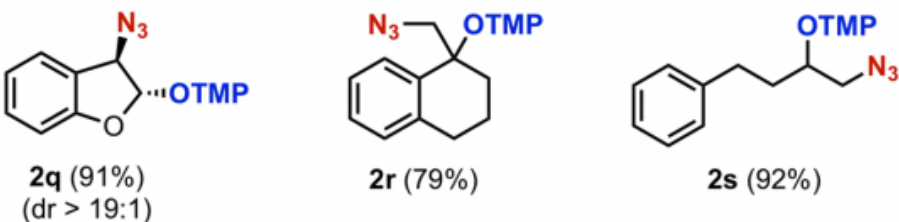
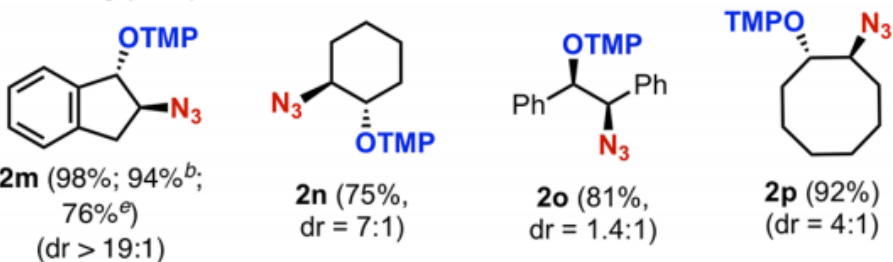
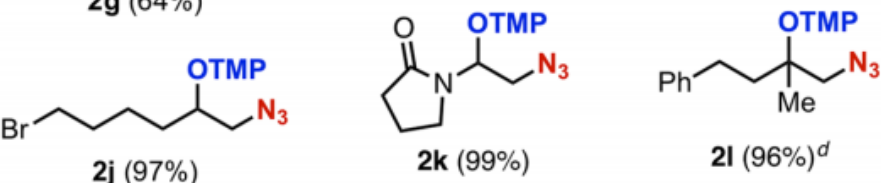
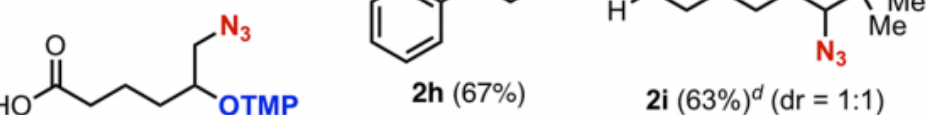
TEMPO的三种价态使得其拥有类似于过渡金属的性质，可以用来催化有机合成反应。

- 温和的单电子/双电子氧化还原剂
- 拔氢

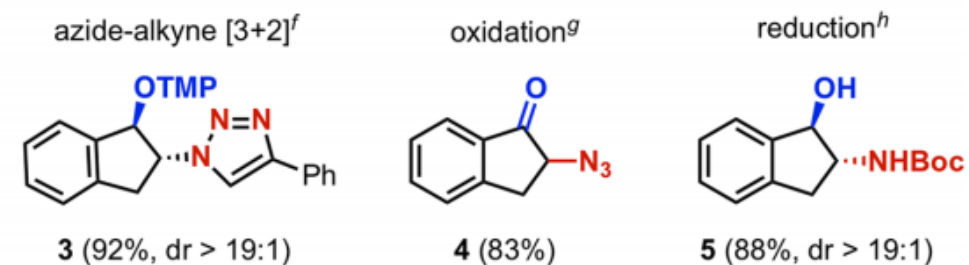
## A. Substrate scope.<sup>a</sup>



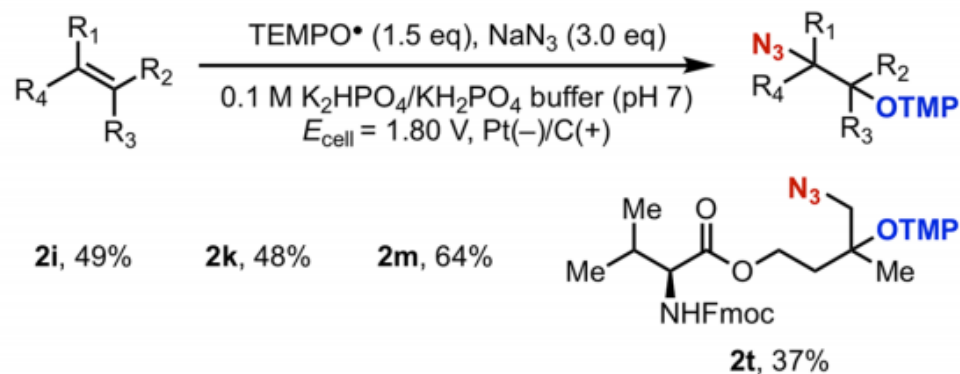
R = *t*-Bu, **2a** (94%; 90%<sup>b</sup>)  
OMe, **2b** (89%)  
Cl, **2c** (92%)  
*p*-CN, **2d** (83%)<sup>c</sup>



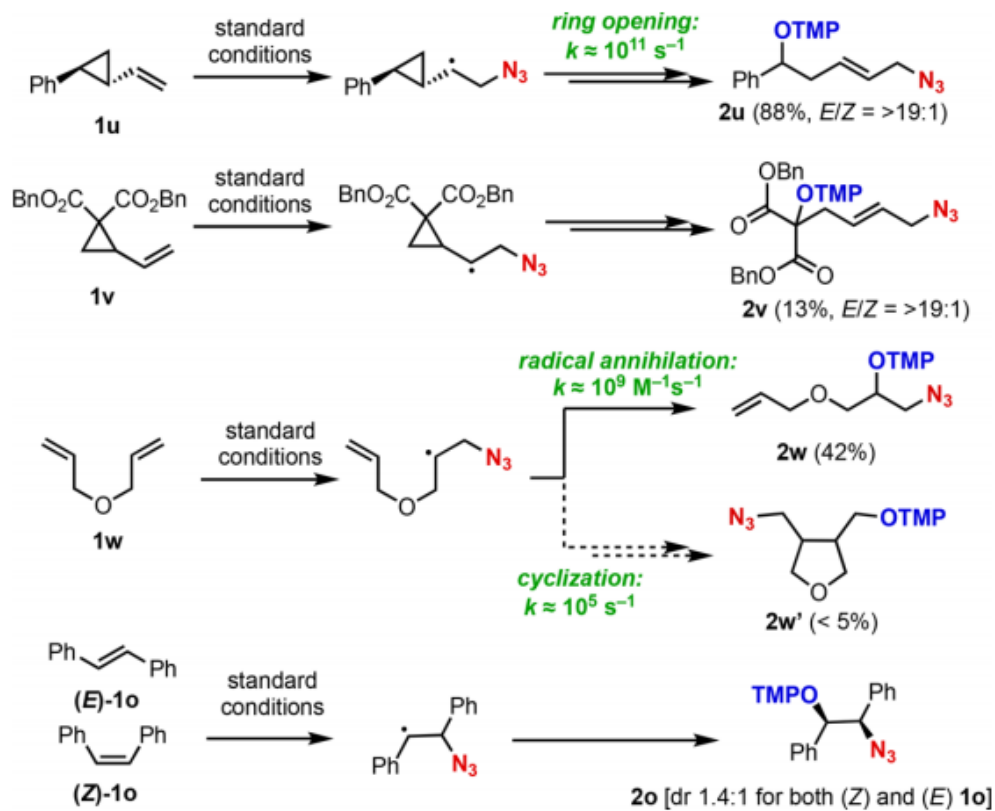
## B. Product derivatization



## C. Substrate scope in biological media

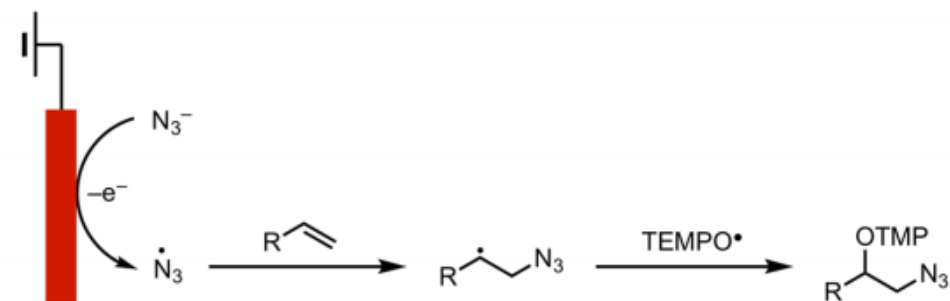


## Scheme 5. Radical Clock Experimental Results



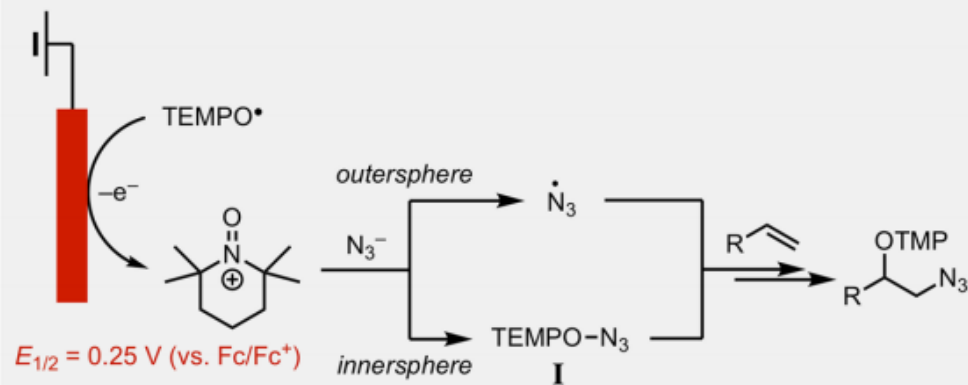
## Scheme 6. Plausible Mechanistic Pathways for the Formation of the Azidyl Radical or Its Equivalent

### Pathway 1a: Direct anodic oxidation of $\text{N}_3^-$

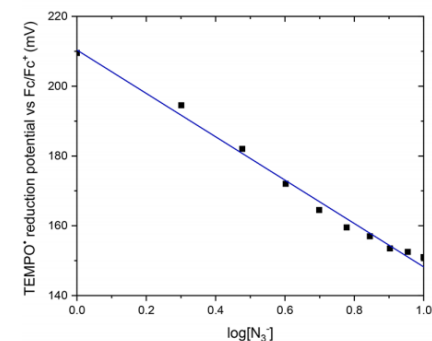
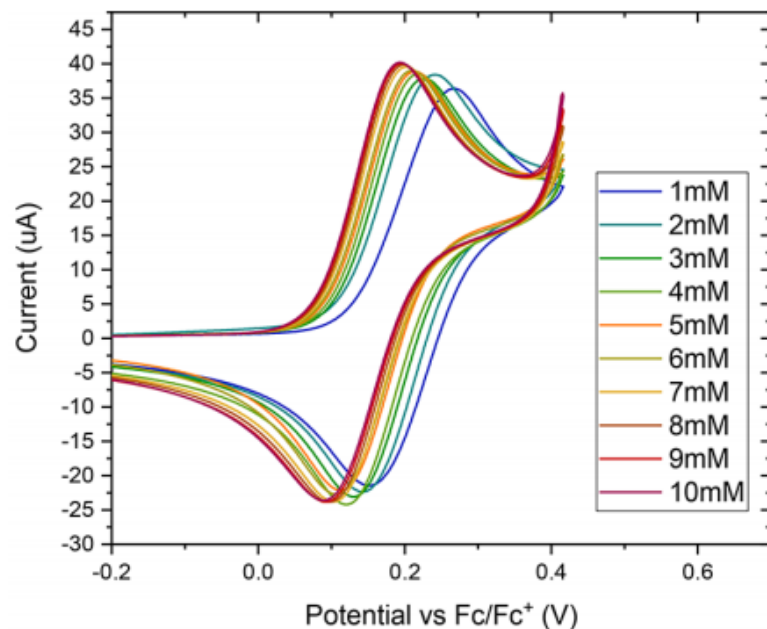
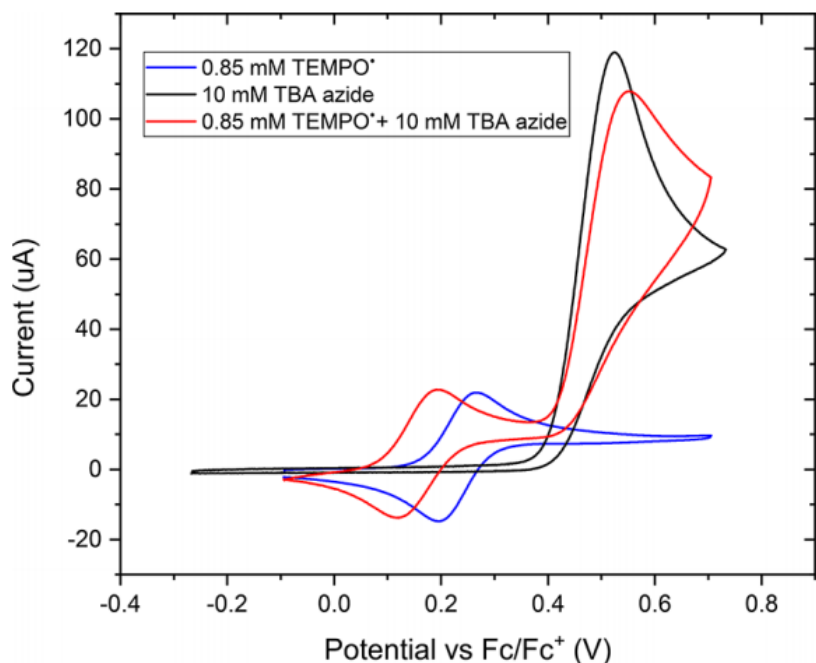


$$E_{\text{p}/2} = 0.45 \text{ V (vs. Fc/Fc}^+) \text{)}$$

### Pathway 1b: TEMPO-mediated oxidation of $\text{N}_3^-$



$$E_{1/2} = 0.25 \text{ V (vs. Fc/Fc}^+) \text{)}$$



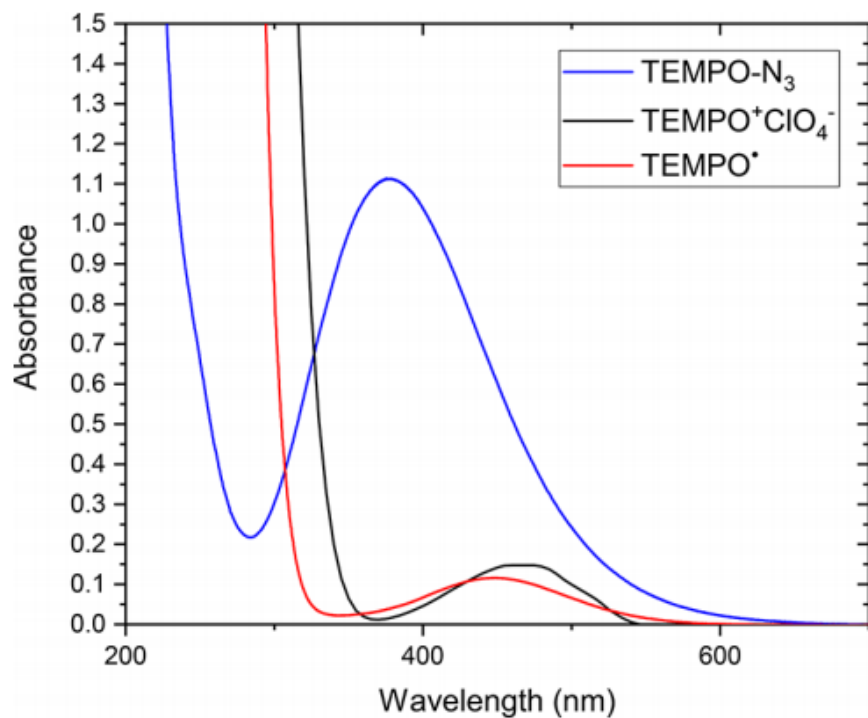
**Figure 1.** Cyclic voltammograms of TEMPO•,  $N_3^-$ , and their mixture.

Nernst 方程将电化学电池的电极电势和物质的标准电势以及氧化物质和还原物质在系统中的平衡相联系。在等式中  $F$  表示法拉第常数,  $R$  是摩尔气体常数,  $n$  代表电子数,  $T$  为温度。

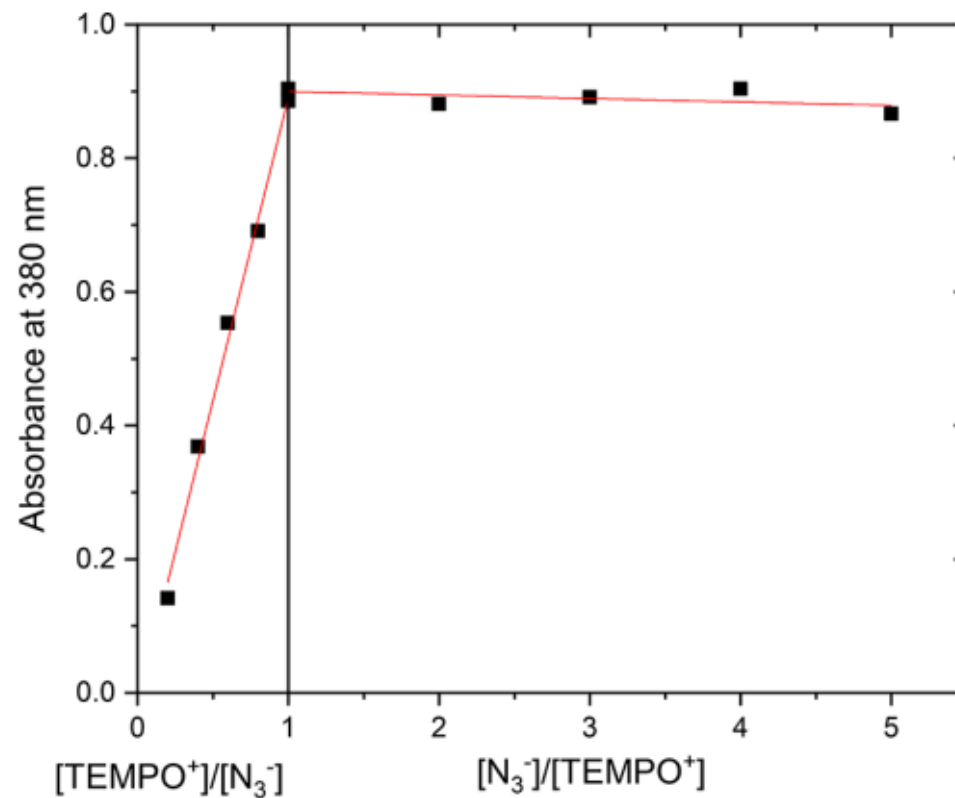
$$E = E^0 + \frac{RT}{nF} \ln \frac{(Ox)}{(Red)} = E^0 + 2.3026 \frac{RT}{nF} \log_{10} \frac{(Ox)}{(Red)}$$

**Figure 2.** Cyclic voltammograms of TEMPO• in the presence of  $N_3^-$  (top), showing a Nernstian dependence of the reduction potential on  $[N_3^-]$  (bottom). The curve depicts a least-squares fit to the function  $f(x) = ax + b$ :  $a = -62 \pm 2$ ;  $b = 210 \pm 2$ ;  $R^2 = 0.990$ .

TBAN<sub>3</sub>的加入使TEMPO•的还原电位下降, 并且下降值符合Nernst方程, 证明反应过程中TEMPO•与N<sub>3</sub><sup>-</sup>形成了较为稳定的中间体



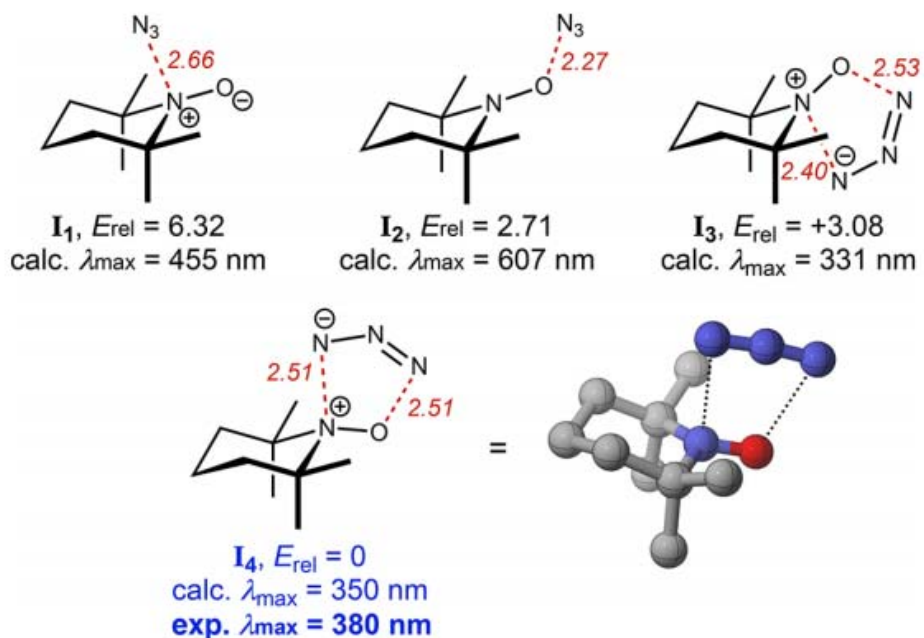
**Figure 3.** UV-vis absorption spectra of TEMPO• (8.6 mM), TEMPO<sup>+</sup>ClO<sub>4</sub><sup>-</sup> (8.6 mM), and the TEMPO-N<sub>3</sub> complex (0.2 mM) in MeCN at room temperature (ca. 22 °C).



**Figure 5.** Titration experiments showing the 1:1 stoichiometry of the TEMPO-N<sub>3</sub> adduct.

紫外动力学测得各物质的吸光度纯谱

紫外吸光度滴定测得化学计量比为1:1(使用TBAN3滴TEMPO+ClO4-, 反滴发现过量的TEMPO+会促进中间体的分解)

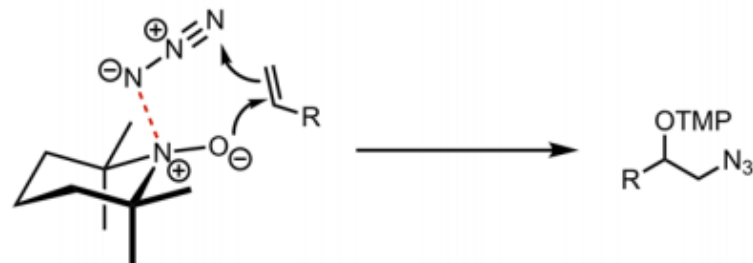


Method	Energy (kcal/mol)			
	I <sub>1</sub>	I <sub>2</sub>	I <sub>3</sub>	I <sub>4</sub>
B3LYP/def2-TZVP, PCM	6.32	2.71	3.10	0
B3LYP/6-311+G**, CPCM	6.18	2.57	3.10	0
B3LYP/cc-pVTZ, PCM	6.90	3.53	3.13	0
M06-2X/def2-TZVP, PCM	6.90	9.45	3.81	0
$\omega$ B97x-D/def2-TZVP, PCM	6.00	7.05	3.20	0

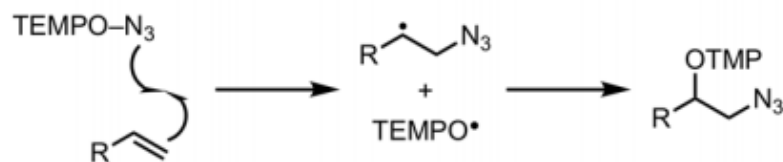
**Figure 6.** Energetically viable structures of the TEMPO–N<sub>3</sub> complex predicted by DFT calculation. All energies are reported in terms of the ground state energy corrected for zero-point energy ( $E + \text{ZPE}$ ).

## Scheme 7. Plausible Mechanistic Pathways for the Reaction between TEMPO–N<sub>3</sub> and Alkenes

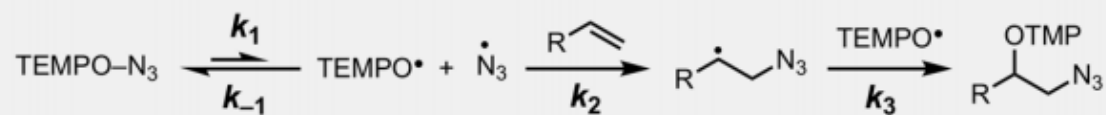
### Pathway 2a: Polar addition

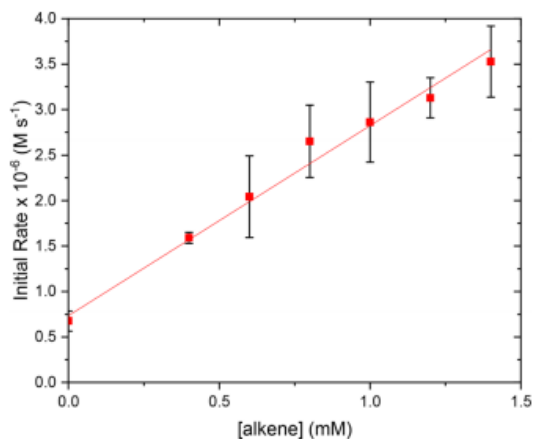


### Pathway 2b: Direct azidyl transfer

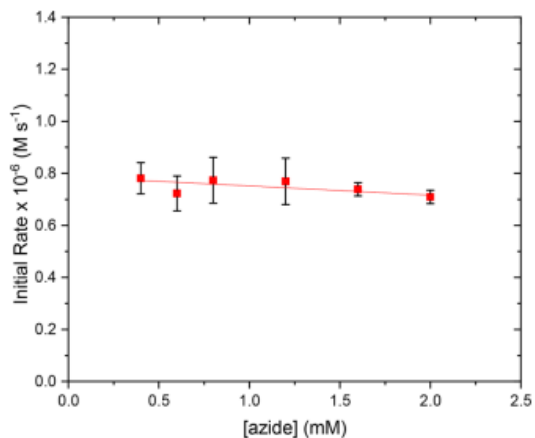


### Pathway 2c: Dissociation–radical addition

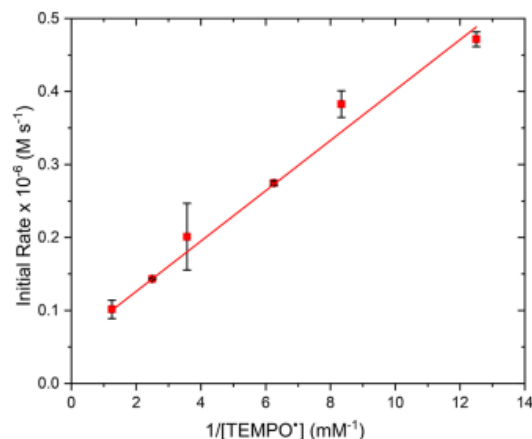




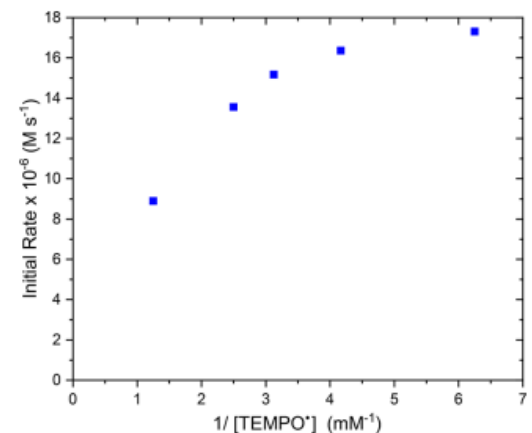
**Figure 8.** Plot of initial rates versus concentration of alkene **II** for the reaction between adduct **I** ( $\text{TEMPO}^+\text{ClO}_4^- + \text{TBAN}_3$ ) and alkene **II**, showing first-order rate dependence on  $[\text{II}]$ . The data point corresponding to  $[\text{II}] = 0$  represents the rate of decomposition of **I** in the absence of **II**. Error bars represent the standard deviation of three independent measurements. The curve depicts an unweighted least-squares fit to the function  $f(x) = ax + b$ :  $a = 2.09 \pm 0.08$ ;  $b = 0.73 \pm 0.04$ ;  $R^2 = 0.993$ .



**Figure 9.** Plot of initial rates versus concentration of  $\text{N}_3^-$  for the reaction between adduct **I** ( $\text{TEMPO}^+\text{ClO}_4^- + \text{TBAN}_3$ ) and alkene **II**, showing zero-order rate dependence on  $[\text{N}_3^-]$ . Error bars represent the standard deviation of three independent measurements. The curve



**Figure 10.** Plot of initial rates versus concentration of  $\text{TEMPO}^*$  for the reaction between adduct **I** ( $\text{TEMPO}^+\text{ClO}_4^- + \text{TBAN}_3$ ) and alkene **II**, showing inverse first-order rate dependence on  $[\text{TEMPO}^*]$ . Error bars represent the standard deviation of three independent measurements. The curve depicts an unweighted least-squares fit to the function  $f(x) = ax^{-1} + b$ :  $a = 0.0345 \pm 0.0008$ ;  $b = 0.057 \pm 0.002$ ;  $R^2 = 0.998$ .

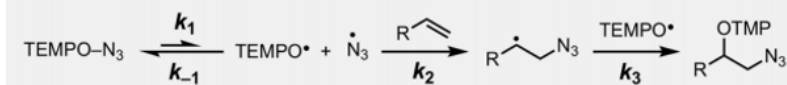


**Figure 11.** Plot of initial rates versus concentration of  $\text{TEMPO}^*$  for the reaction between adduct **I** ( $\text{TEMPO}^+\text{ClO}_4^- + \text{TBAN}_3$ ) and alkene **II** (50 mM). Saturation kinetics were observed when  $\text{TEMPO}^*$  concentration is less than 0.25 mM.

测得该反应反应速率对烯烃为一级，对  $1/[\text{TEMPO}^*]$  为一级，对  $\text{N}_3^-$  为零级

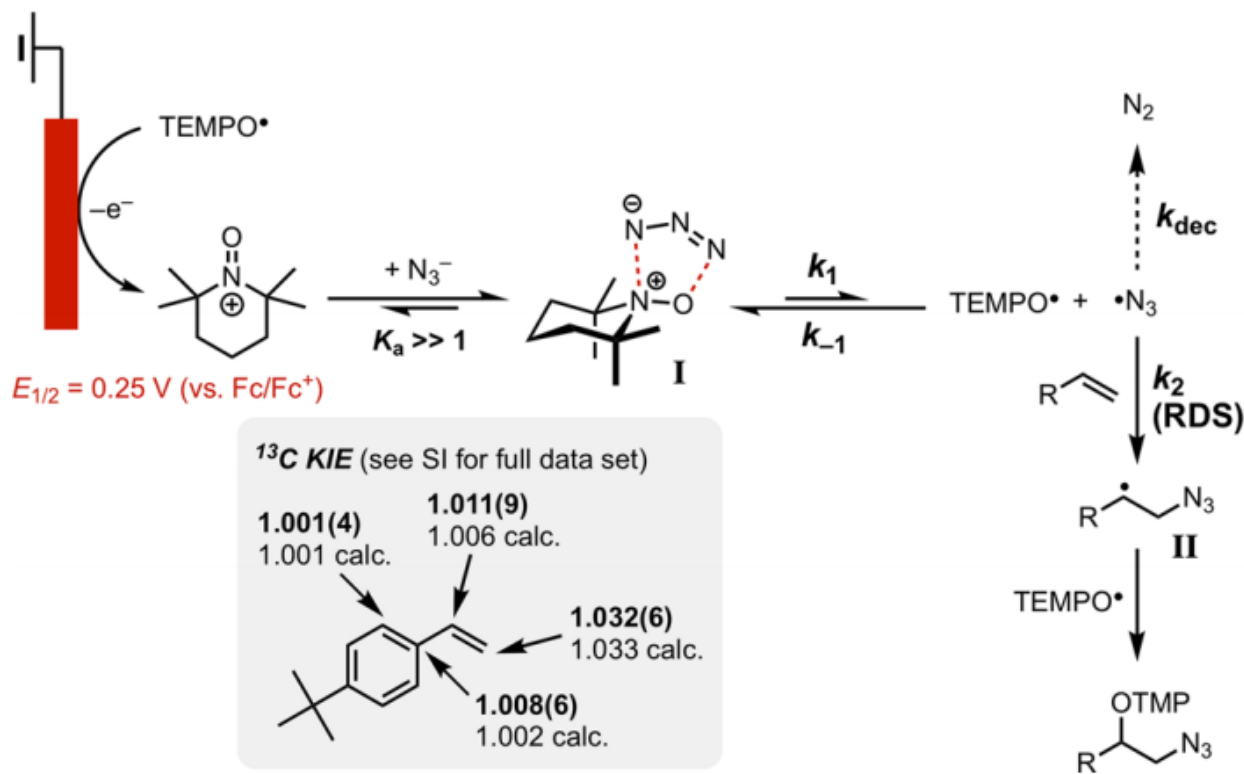
$$\text{rate} = k_{\text{obs}}[\text{alkene}]^1[\text{N}_3^-]^0[\text{TEMPO}^*]^{-1}$$

**Pathway 2c: Dissociation-radical addition**



稳态近似法

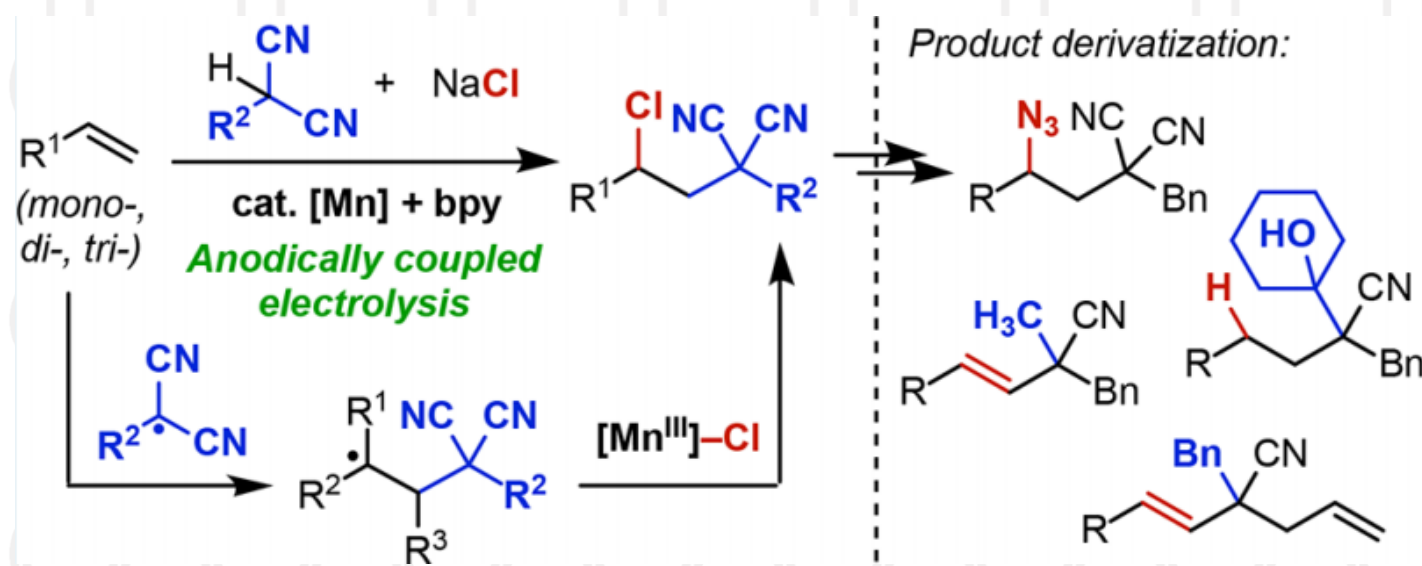
$$\text{rate} = \frac{k_1 k_2 [\text{TEMPO-N}_3] [\text{alkene}]}{k_{-1} [\text{TEMPO}^*] + k_2 [\text{alkene}]}$$



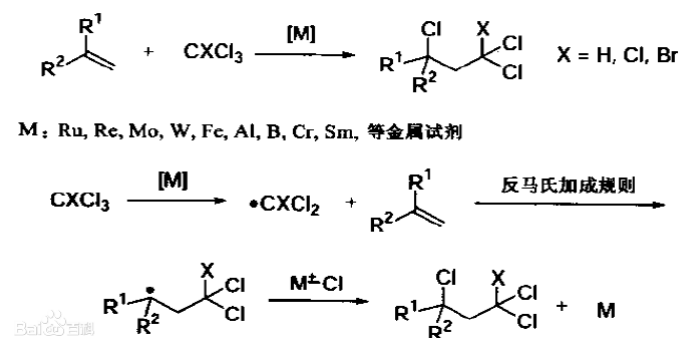
当一个反应进行时, 在速度决定步骤中发生反应物分子的同位素化学键的形成或断裂反应, 将显现出一级同位素效应 (Primary Isotope Effect)。一级同位素效应的机理现已很清楚, 即由于同位素质量不同, 反应物的零点能不同, 从而导致各自的反应速率不同。



## Mn-Catalyzed Electrochemical Chloroalkylation of Alkenes

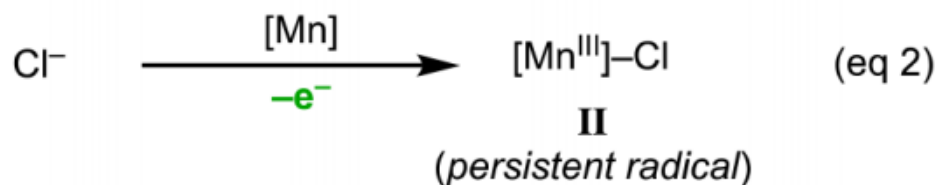
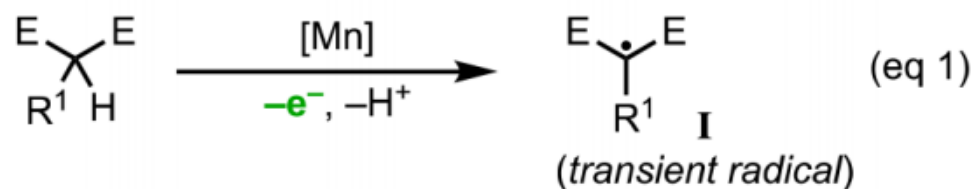
Niankai Fu,<sup>†</sup> Yifan Shen,<sup>†</sup> Anthony R. Allen,<sup>†,‡</sup> Lu Song,<sup>†</sup> Atsushi Ozaki,<sup>†,§</sup> and Song Lin<sup>\*,†</sup><sup>†</sup>Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States<sup>‡</sup>Department of Chemistry and Biochemistry, Oberlin College, Oberlin, Ohio 44074, United States<sup>§</sup>Department of Applied Biological Science, Tokyo University of Agriculture and Technology, Fuchu, Tokyo 183-8509, Japan

## Kharasch Reaction

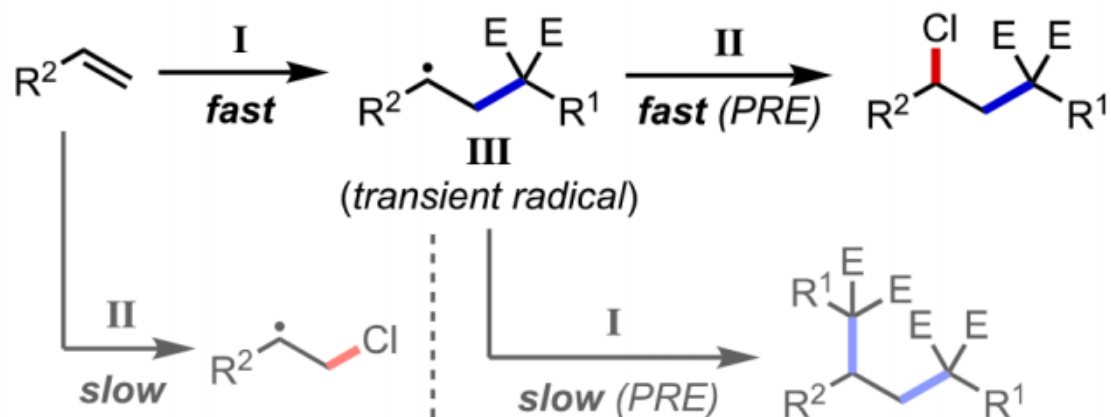


## Scheme 2. Design Principle for the Electrochemical Alkylchlorination of Alkenes<sup>a</sup>

### A. Generation of radical intermediates for alkene chloroalkylation

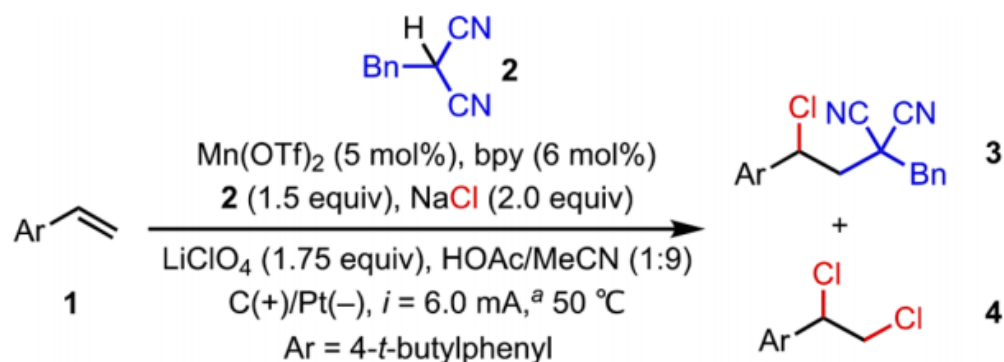


### B. Innate reactivity of transient and persistent radicals determines the selectivity in the radical chloroalkylation



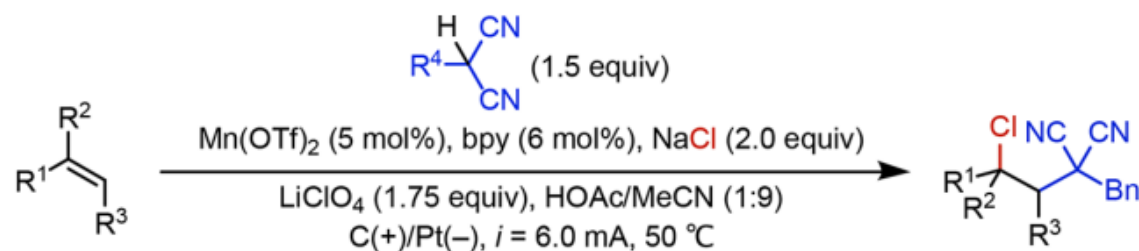
<sup>a</sup>E = electron-withdrawing group. PRE = persistent radical effect.

Table 1. Reaction Optimization<sup>a</sup>

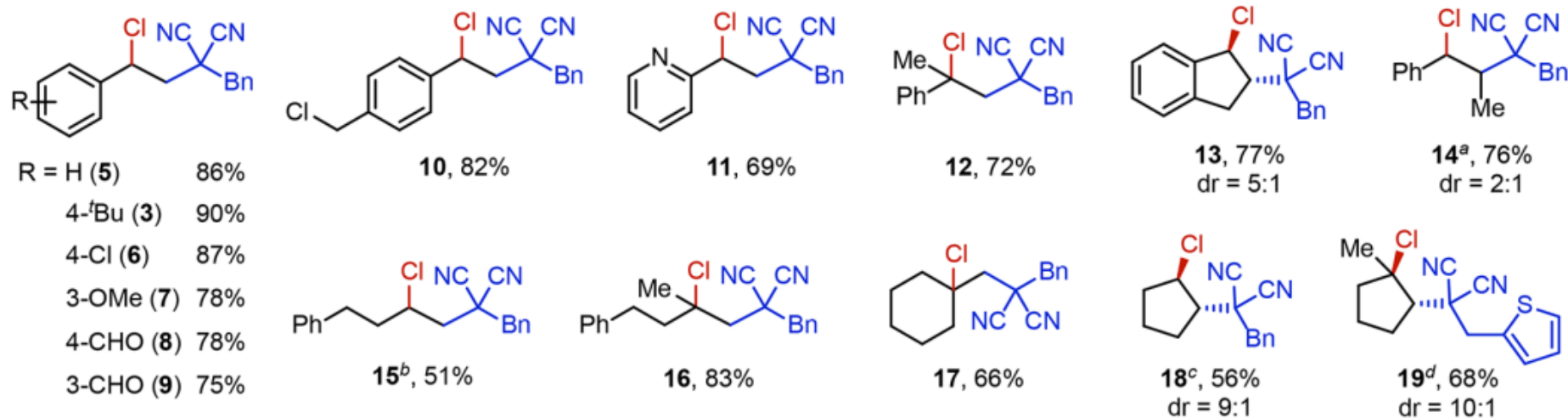


entry	variation from the standard conditions	yield <sup>b</sup> (%)	
		3	4
1	none	94	<5
2	without Mn(OTf) <sub>2</sub>	<5	10
3	without bpy	46	12
4	12 mol % pyridine instead of bpy	47	5
5	control cell voltage at 2.3 V <sup>c</sup>	84	14
6	Control anode potential at 0.62 V <sup>d</sup>	88	<5
7	MgCl <sub>2</sub> instead of NaCl	<5	>99
8	Et <sub>4</sub> N <sup>+</sup> OTs <sup>-</sup> or TBAPF <sub>6</sub> instead of LiClO <sub>4</sub>	87–90	<5
9	Ni foam instead of Pt as cathode	70	<5
10	40 °C instead of 50 °C	68	<5
11	<i>i</i> = 4.0 mA	91	<5
12	<i>i</i> = 8.0 mA	80	<5

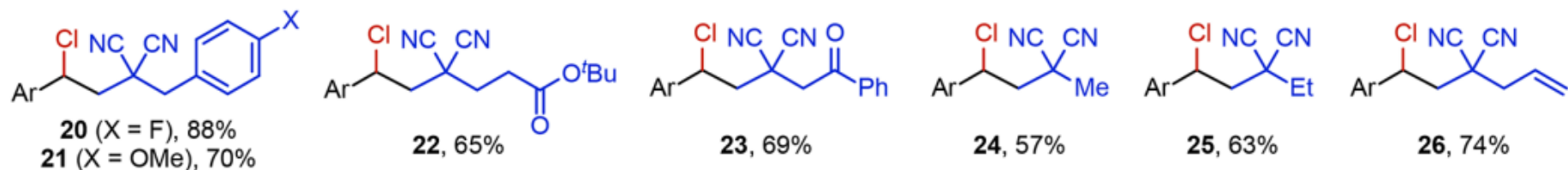
### Scheme 3. Substrate Scope\*



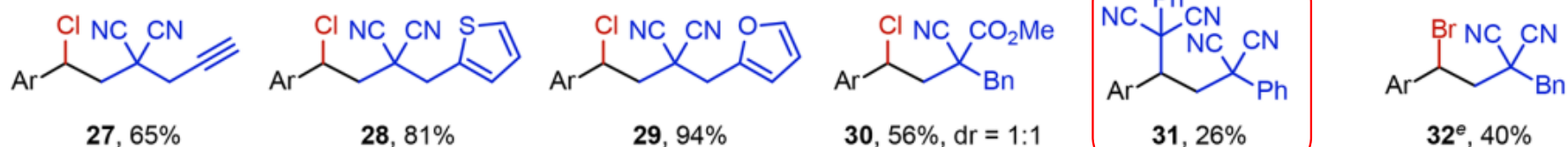
#### A. Scope of alkene (with 2)



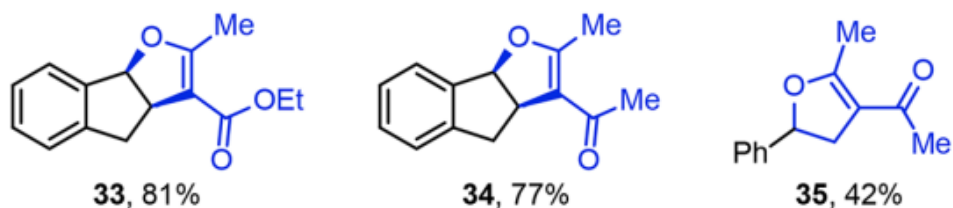
**B. Scope of 2-substituted malononitrile and derivative (with **1**, Ar = 4-*t*-butylphenyl)**



**C. Bromoalkylation (with **1**)**

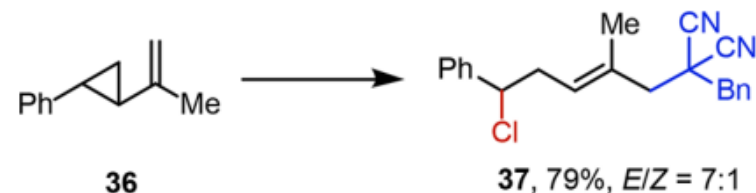


**D. Oxyalkylation**



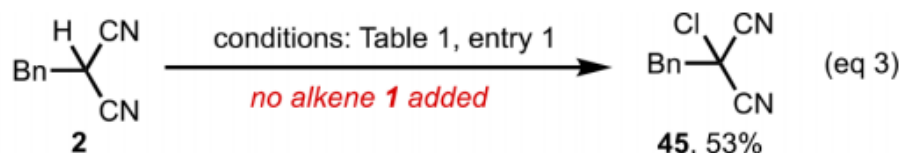
**E. Radical clock**

苯位溴被取代



\*All substrates were electrolyzed at 6.0 mA after 2 F charge was passed; Faradaic yield = product yield. <sup>a</sup>From (*E*)- $\beta$ -methylstyrene. <sup>b</sup>2.5 F charge was passed, Faradaic yield = 41%. <sup>c</sup>Electrolysis at a constant cell voltage of 2.3 V for 2 h. <sup>d</sup>Using the malononitrile as the limiting substrate (1 equiv) in combination with 1.5 equiv of **1**. Using NaBr instead of NaCl at room temperature; 3 F charge was passed, Faradaic yield = 27%.

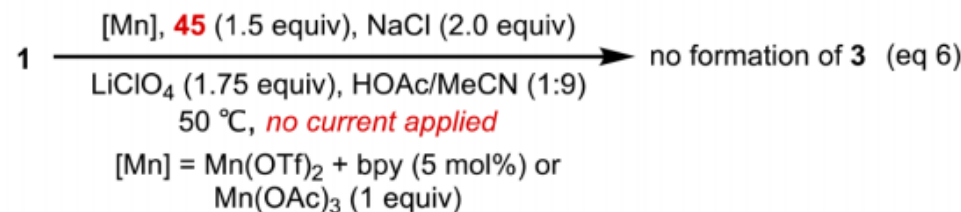
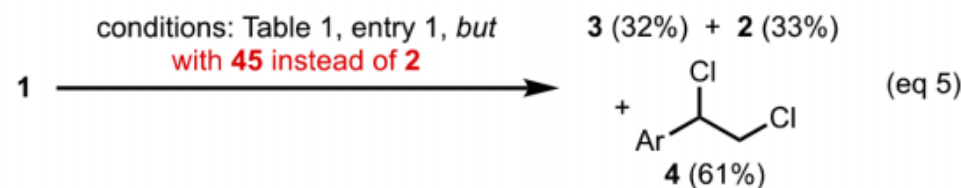
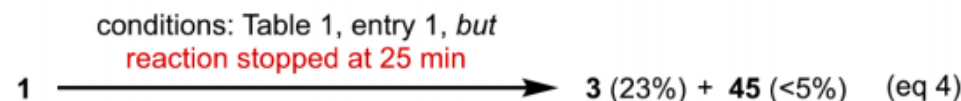
## Scheme 5. Alternative Mechanistic Pathways and Control Experiments<sup>a</sup>



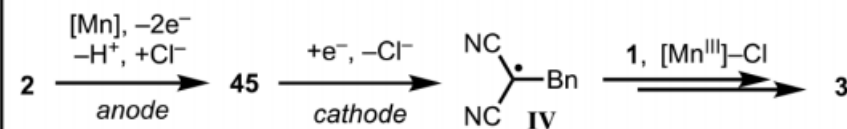
### Alternative path 1: Mn-catalyzed Kharasch-type addition



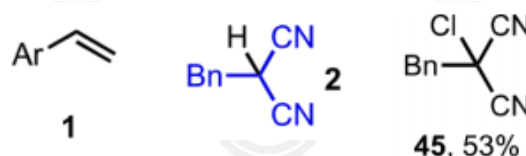
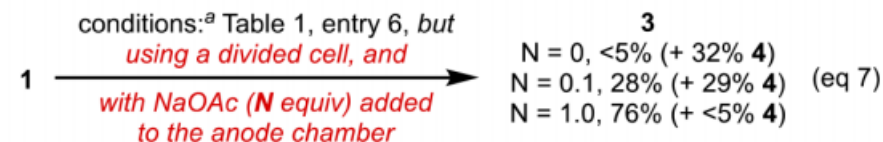
### Control experiments:



### Alternative path 2: Cathode-assisted radical formation



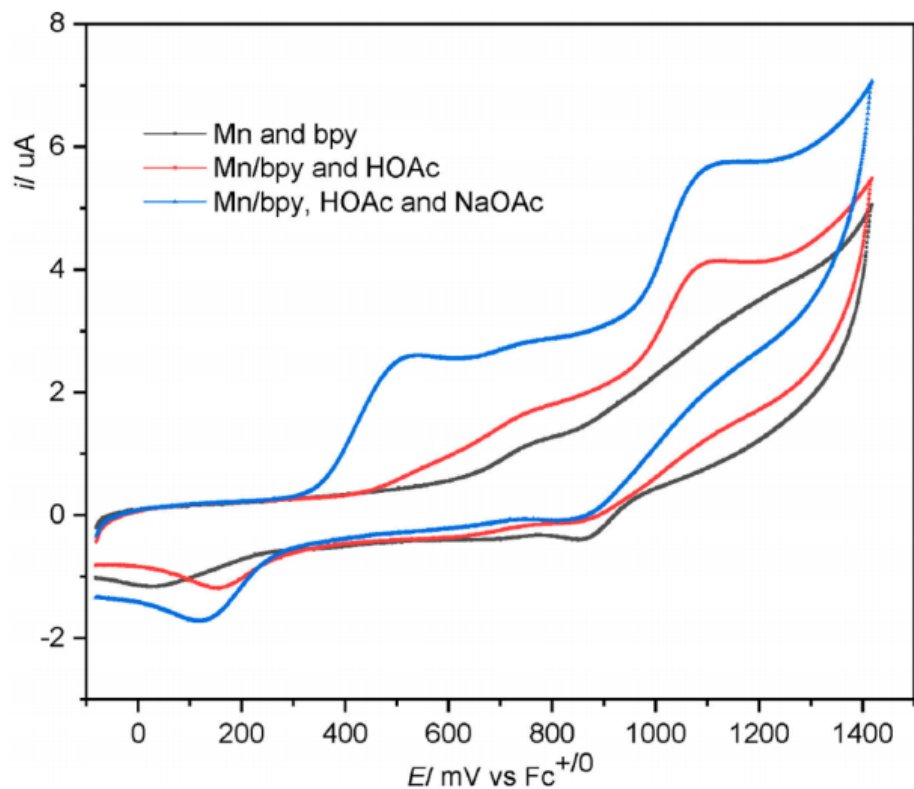
### Control experiments:



CV和电解实验表明，在电解条件下，45可以进行C-Cl键的阴极还原和均裂，形成碳中心自由基IV。

通过使用离子导电玻璃将阳极和阴极分开的装置进行电解，排除了path 2。这种分裂的电解池阻止了阳极产生的45向阴极室的扩散。

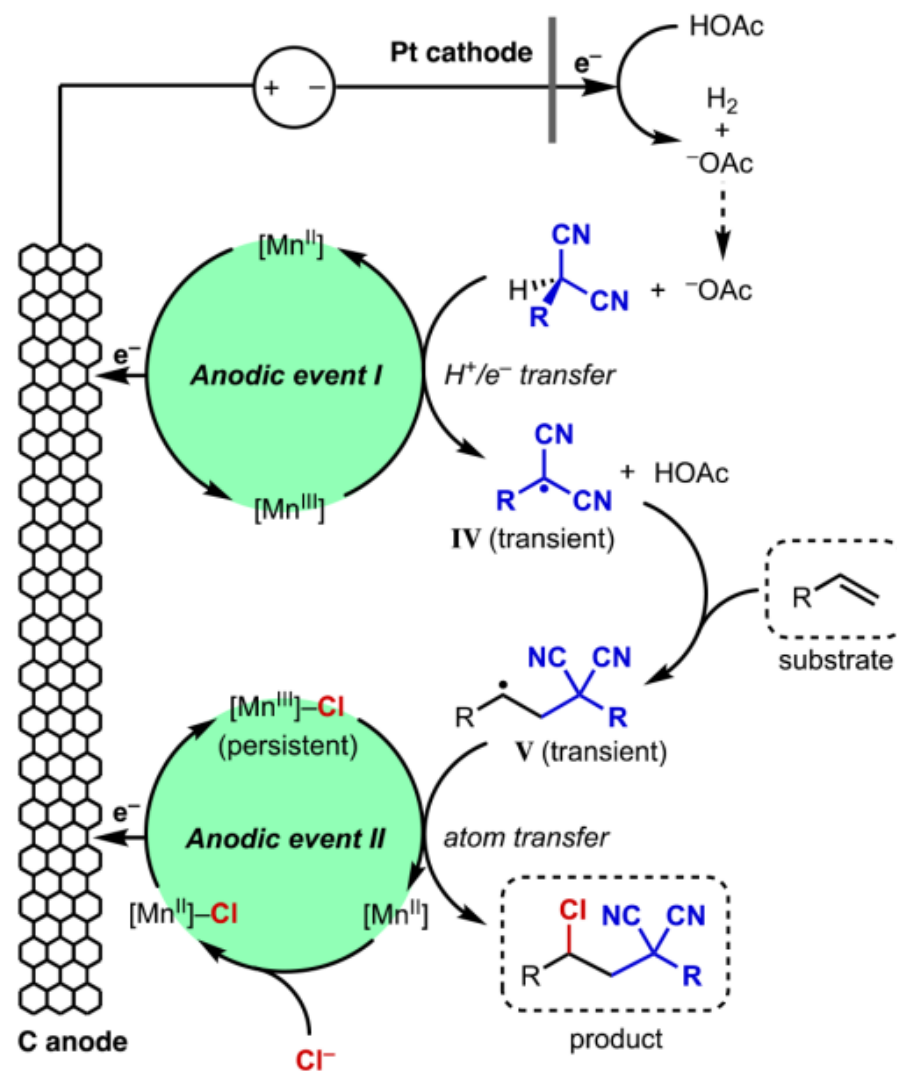
## 加入乙酸钠的原因



**Figure 1.** Cyclic voltammograms of Mn showing the effect of bpy and acetate on the catalyst oxidation. Conditions: glassy carbon as working electrode, Ag/AgNO<sub>3</sub> reference electrode, and a platinum wire counter electrode. LiClO<sub>4</sub> (0.10 M in MeCN), Mn(OTf)<sub>2</sub> (1.0 mM), bpy (1.2 mM), NaOAc (2.0 mM), HOAc (60 mM). Scan rate: 20 mV/s.

OAc<sup>-</sup>可能作为Mn上的附加配体，降低了其氧化所需的电极电势。

## Scheme 7. Proposed Mechanism Involving Catalytic, Anodically Coupled Electrolysis

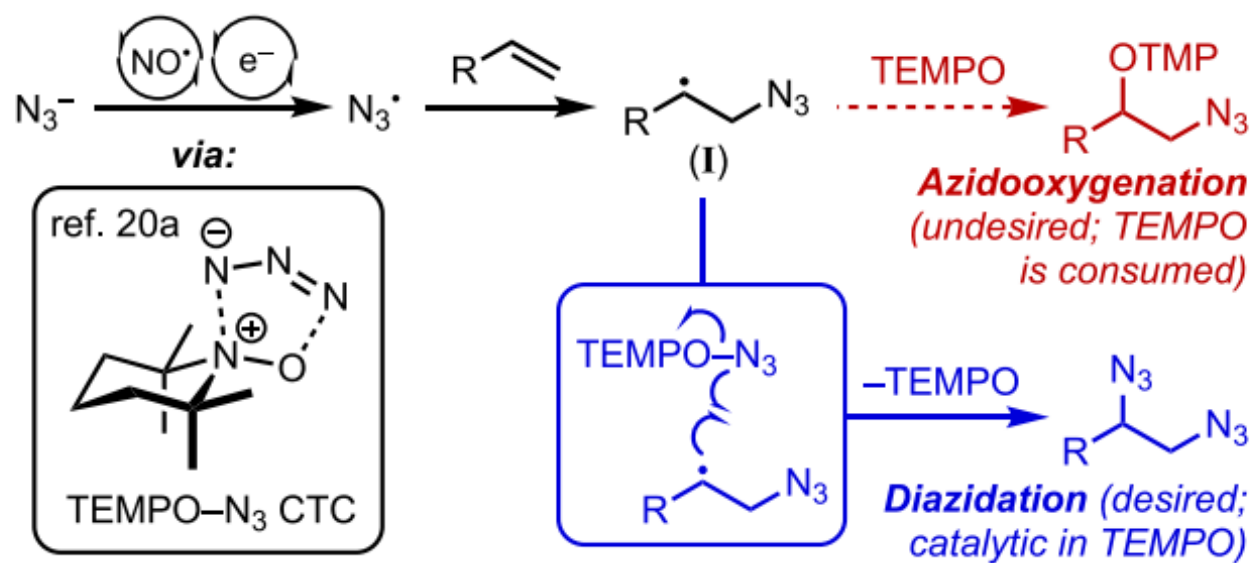


# Aminoxyl-Catalyzed Electrochemical Diazidation of Alkenes Mediated by a Metastable Charge-Transfer Complex

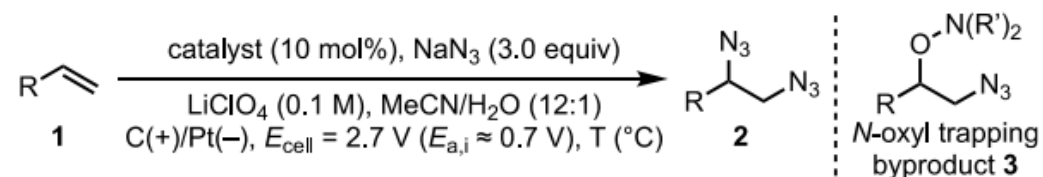
Juno C. Siu,<sup>‡</sup> Joseph B. Parry,<sup>‡</sup> and Song Lin\*<sup>‡</sup>

Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States

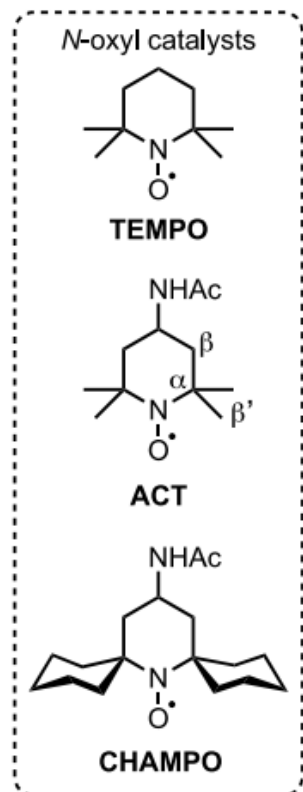
(B) Working mechanistic hypothesis for aminoxyl (NO•)-catalyzed alkene diazidation



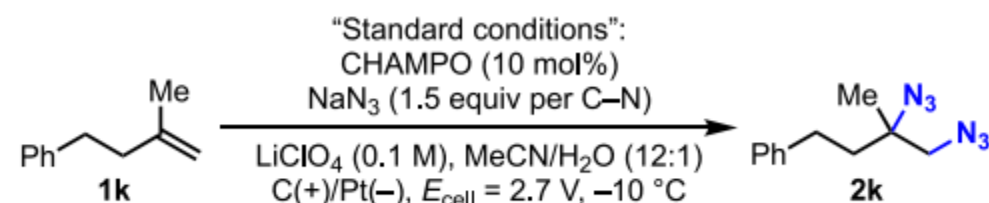
使用TEMPO代替过度金属催化剂  
 用水代替AcOH作为质子源  
 防止Metal-N<sub>3</sub>以及叠氮酸的生成

**Table 1. Reaction Optimization<sup>a</sup>**


Entry	Catalyst	T (°C)	Yield (%)
1 <sup>b</sup>	TEMPO	22	36
2	TEMPO	22	11
3	TEMPO	0	46
4	TEMPO	-10	61
5	ACT	-10	71
6	CHAMPO	-10	97 <sup>c</sup>
7	none	-10	0
8	TEMPO	-10	47
9	ACT	-10	68
10	CHAMPO	-10	87 <sup>c</sup>



<sup>a</sup>Conditions: **1** (0.2 mmol, 1 equiv), NaN<sub>3</sub> (3 equiv; 1.5 equiv per C–N bond), LiClO<sub>4</sub> (1.8 equiv), MeCN/H<sub>2</sub>O (3.8 mL, 12:1); cell voltage ( $E_{\text{cell}}$ ) = 2.7 V; yields determined by <sup>1</sup>H NMR. <sup>b</sup>With 1 equiv TEMPO. <sup>c</sup>Isolated yield.

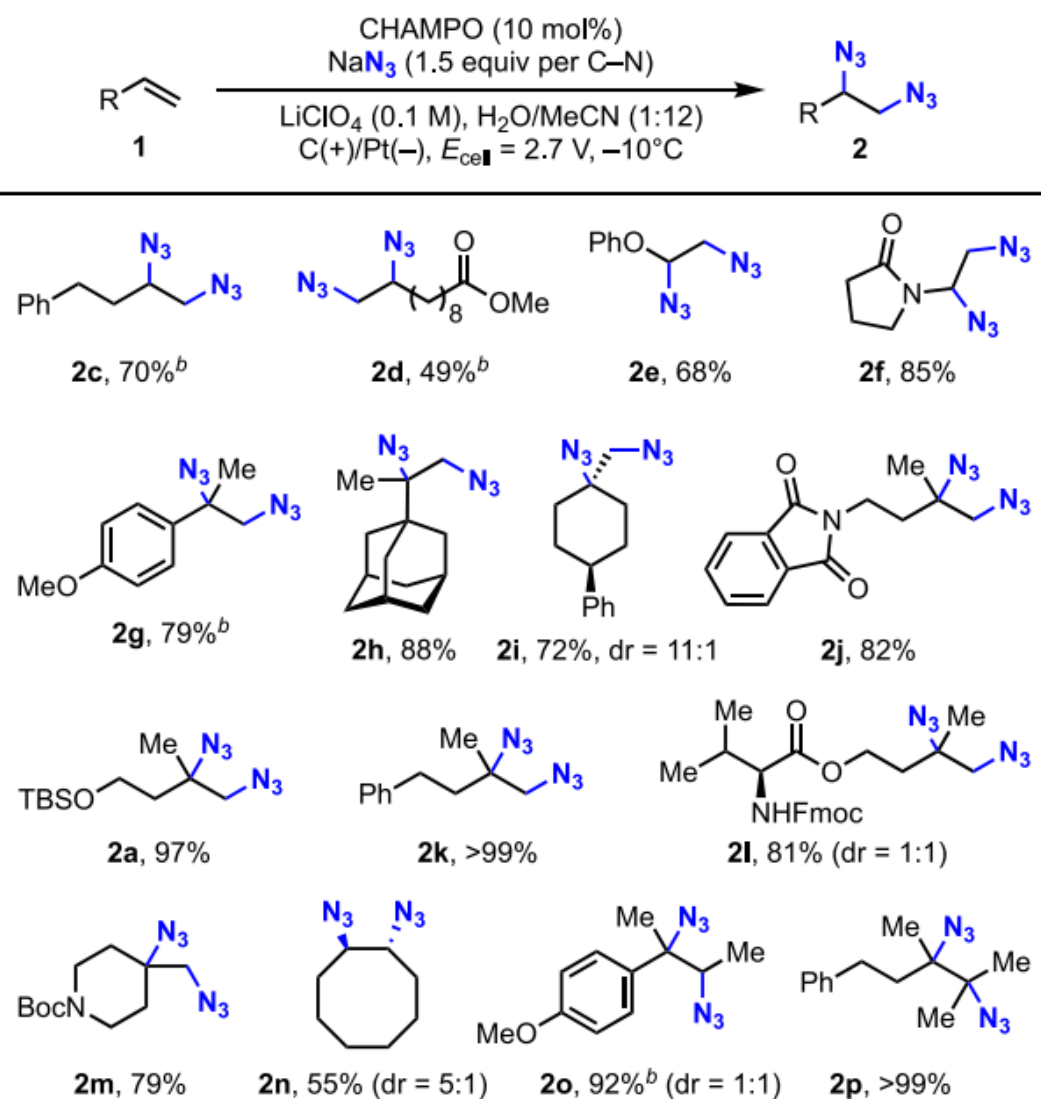
**Table 3. Optimization of the Electrolysis Setup<sup>a</sup>**


entry	variation from “standard conditions”	yield (%)
1	none	>99
2	Ni(–) instead of Pt(–)	92
3	divided cell, constant current of 8 mA	81
4	ElectraSyn 2.0 as power source, 0.3 mmol <b>1k</b>	82
5	AA batteries (×2) as power source	89
6	using TBAPF <sub>6</sub> instead of LiClO <sub>4</sub>	95
7	no LiClO <sub>4</sub> , $E_{\text{cell}} = 3.4 \text{ V}^b$	>99
8	1 mmol scale	69 <sup>c</sup>

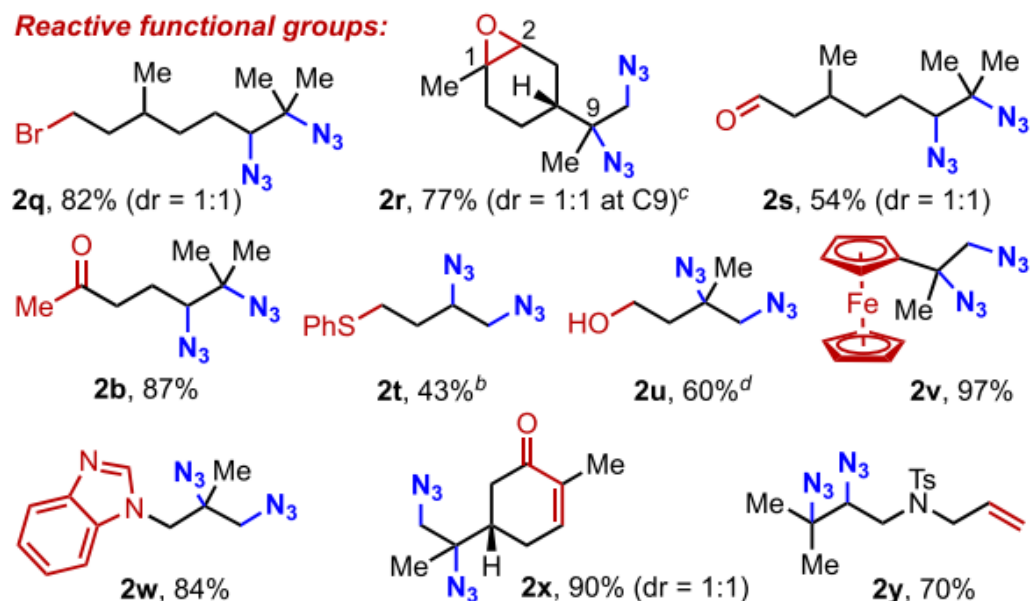
<sup>a</sup>Reaction conditions: see Table 1, entry 6. <sup>b</sup>A higher cell voltage is applied to compensate for the increased solution resistance between cathode and anode. <sup>c</sup>Isolated yield; reaction was carried out at a higher substrate concentration (see SI).



**Table 2. Substrate Scope<sup>a</sup>**



**Reactive functional groups:**

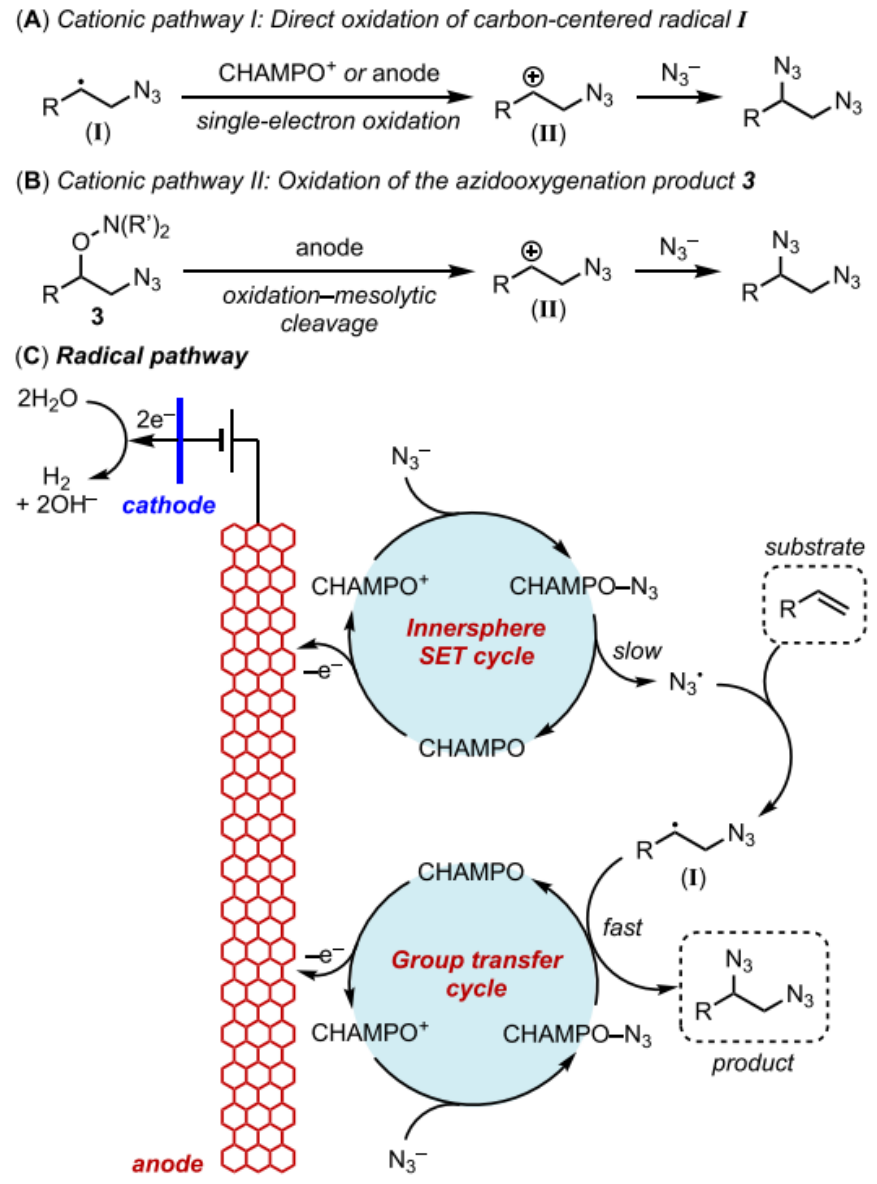


**Product derivatization:**

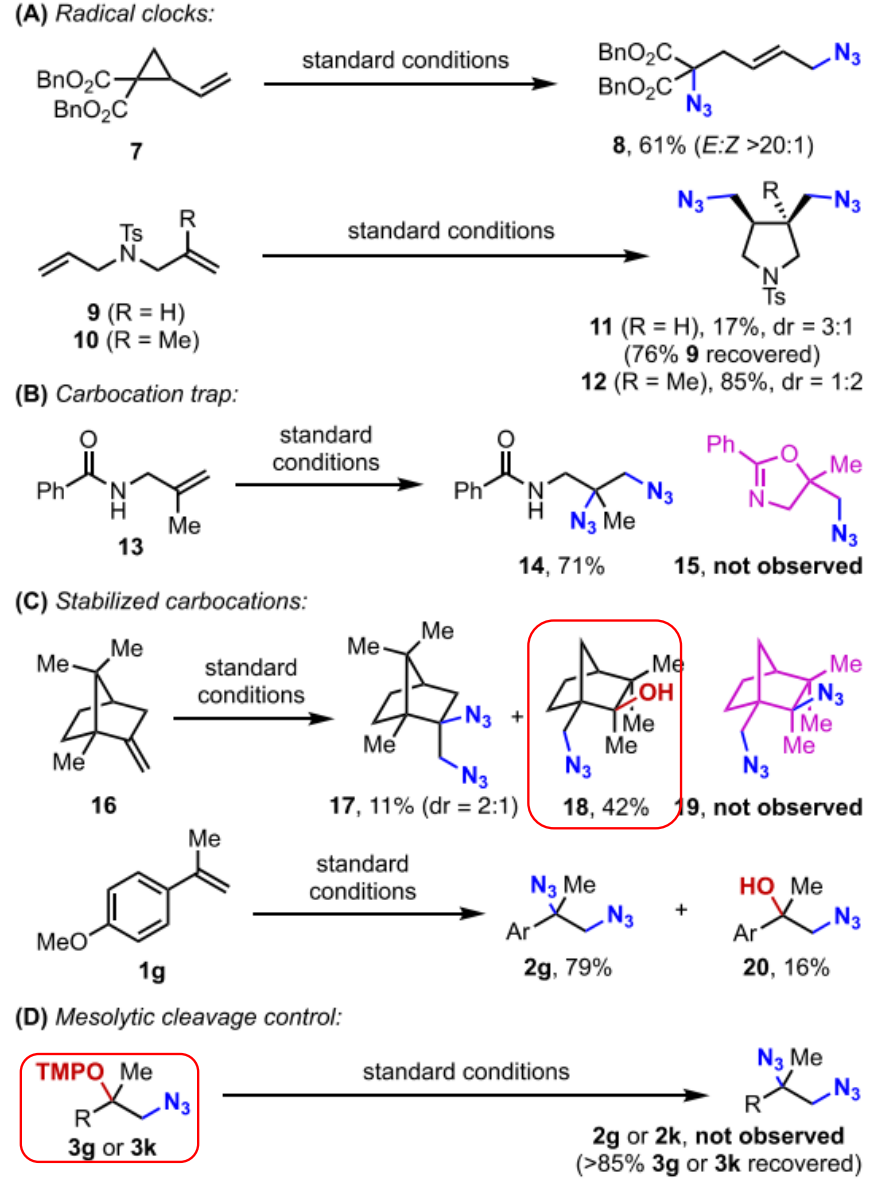


<sup>a</sup>Conditions: **1** (0.2 mmol, 1 equiv), CHAMPO (10 mol %), NaN<sub>3</sub> (3 equiv), LiClO<sub>4</sub> (1.8 equiv), MeCN/H<sub>2</sub>O (3.8 mL, 12:1). <sup>b</sup>15 mol % CHAMPO. <sup>c</sup>Limonene-1,2-oxide (**1r**) was purchased as a pair of diastereomers at C1,2. <sup>d</sup>Determined by <sup>1</sup>H NMR owing to the volatility of the product. <sup>e</sup>Conditions: **2v**, PPh<sub>3</sub>, H<sub>2</sub>O/THF, reflux; then *p*TSA. <sup>f</sup>Conditions: **2k**, PPh<sub>3</sub>, H<sub>2</sub>O/THF, reflux; then Ac<sub>2</sub>O, NEt<sub>3</sub>, DCM, 0 °C. <sup>g</sup>Conditions: **2a**, H<sub>2</sub>, Pd/C, EtOAc, Boc<sub>2</sub>O.

### Scheme 2. Plausible Mechanistic Pathways



### Scheme 3. Mechanistic Probes<sup>a</sup>




有一些烯烃会通过碳正离子中间体反应


18: 碳正离子重排产物(体系中有水, 一旦产生碳正离子就会被水捕捉)

排除TEMPO复合物作为中间体

# Three-Component Chlorophosphinoylation of Alkenes via Anodically Coupled Electrolysis

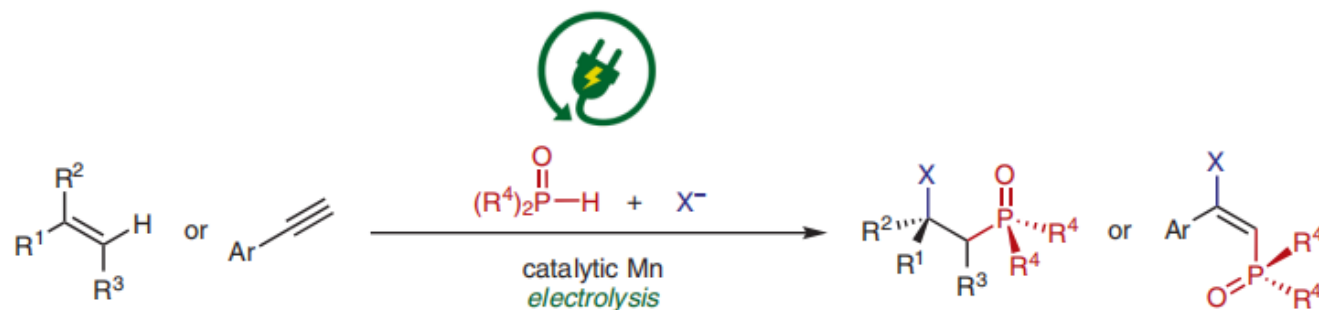
Lingxiang Lu 

Niankai Fu

Song Lin\* 

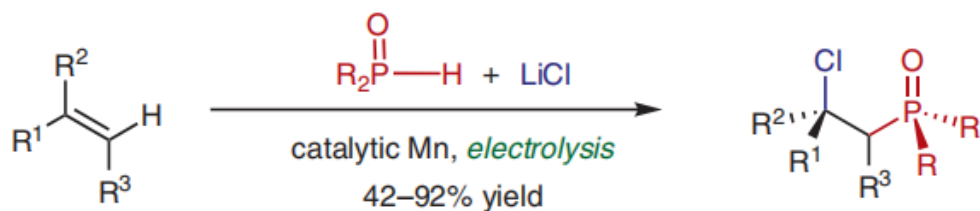
Department of Chemistry and Chemical Biology, Cornell University,  
259 East Avenue, Ithaca, NY 14853, USA  
songlin@cornell.edu

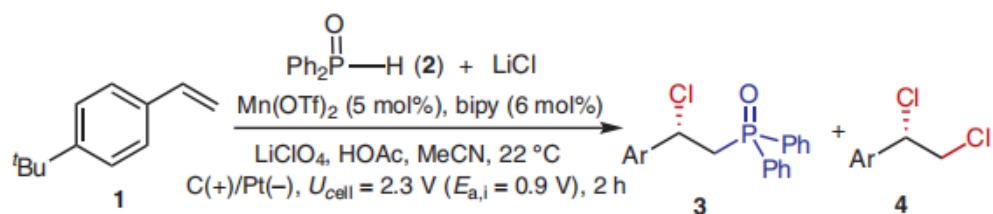
Published as part of the Cluster *Electrochemical Synthesis and Catalysis*



22 examples, 41–92% yield  
(R<sup>1</sup> = aryl, alkyl; R<sup>2</sup> = alkyl, H; R<sup>3</sup> = alkyl, H;  
R<sup>4</sup> = aryl, alkoxy; X = Cl, N<sub>3</sub>)

(C) New reaction: alkene chlorophosphinoylation



**Table 1** Reaction Optimization

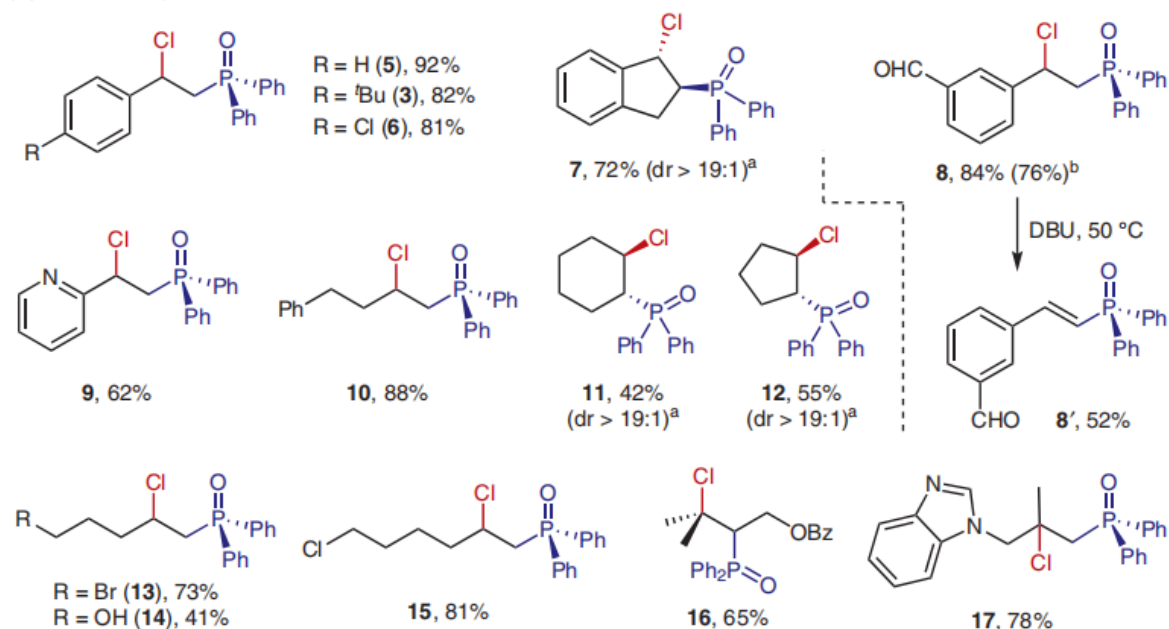
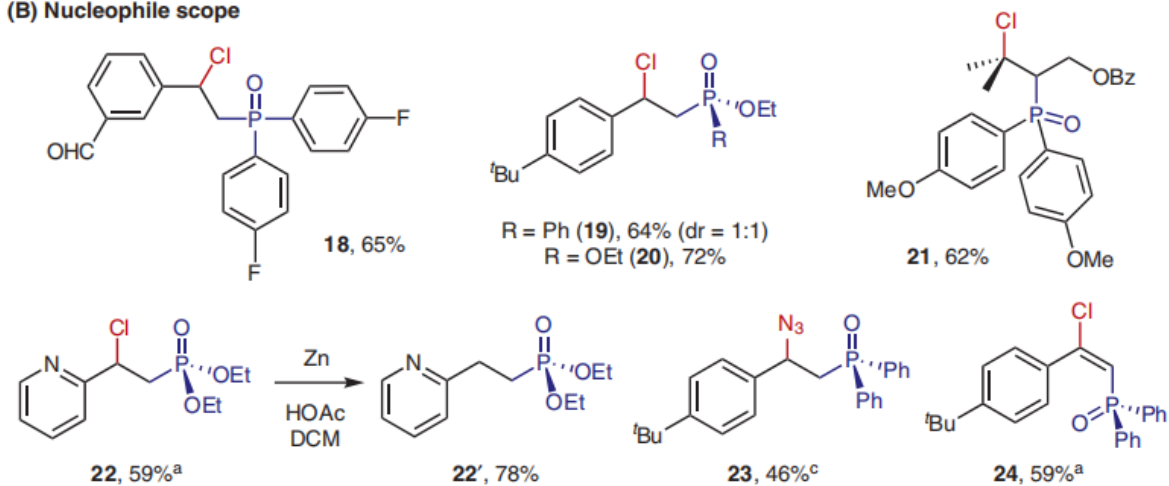
Entry	Variation from optimal conditions	Yield of <b>3</b> (%) <sup>a</sup>	Yield of <b>4</b> (%) <sup>a</sup>
<b>1</b>	none	<b>82</b>	<b>&lt;5</b>
2	without Mn	5	23
3	without bipy	63	8
4	with pyridine (12 mol%) instead of bipy	62	6
5	constant current (5 mA) electrolysis	85	5
6	NaCl instead of LiCl <sup>b</sup>	56	<5
7	TBABF <sub>4</sub> instead of LiClO <sub>4</sub>	75	6
8	LiOTf instead of LiClO <sub>4</sub>	72	<5
9	no LiClO <sub>4</sub> , <i>i</i> = 3 mA (constant current) <sup>c</sup>	55	8
10	Using ElectraSyn 2.0 <sup>d</sup>	84	10

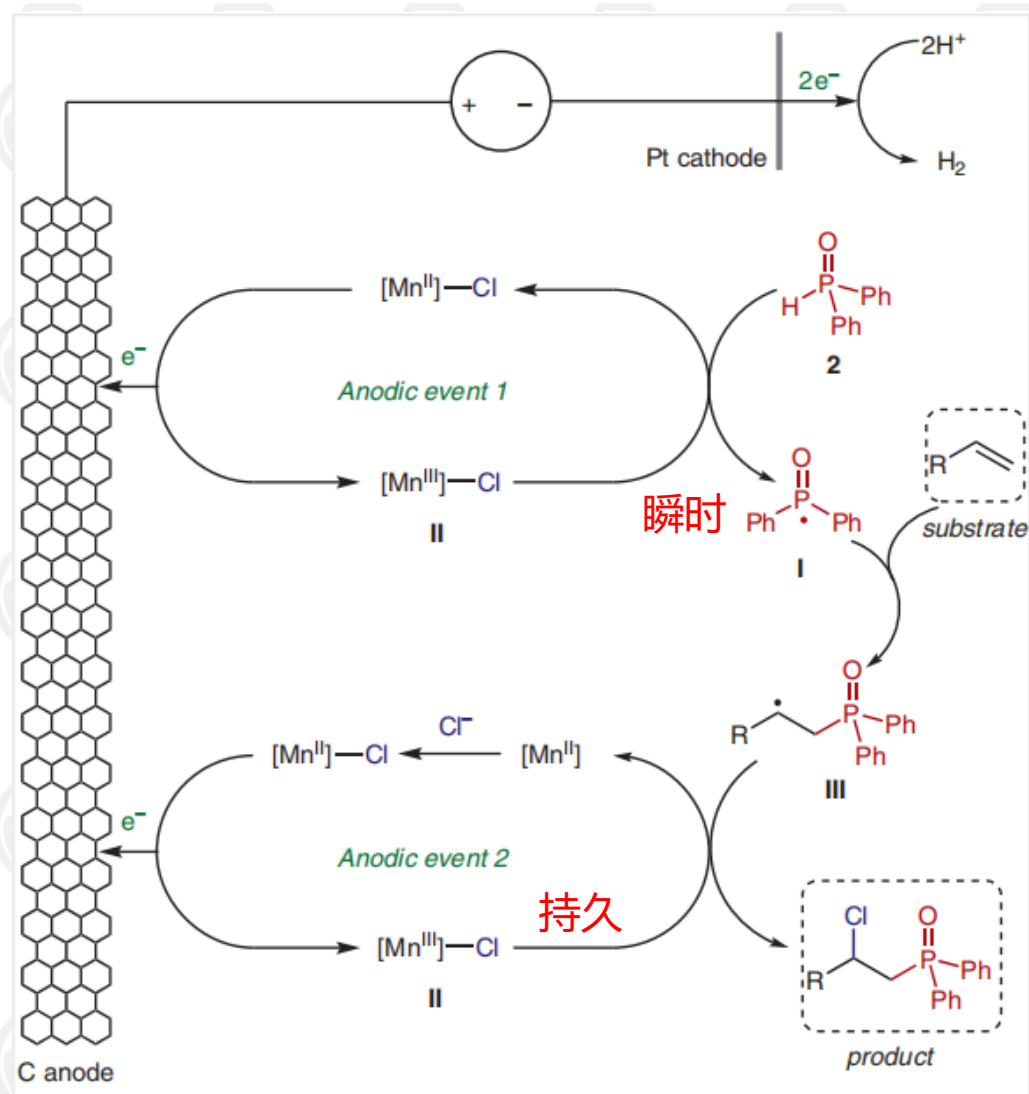
<sup>a</sup> Reactions are conducted on 0.2 mmol scale and yields are determined by <sup>1</sup>H NMR using 1,3,5-trimethoxybenzene as the internal standard.

<sup>b</sup> Reaction at 50 °C.

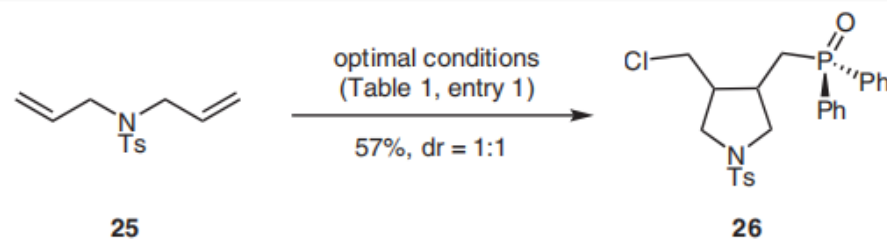
<sup>c</sup> Full cell voltage (*U*<sub>cell</sub>) varies between 2.1 and 2.5 V.

<sup>d</sup> Using 1.5 equiv of **2**, 0.3 mmol scale.

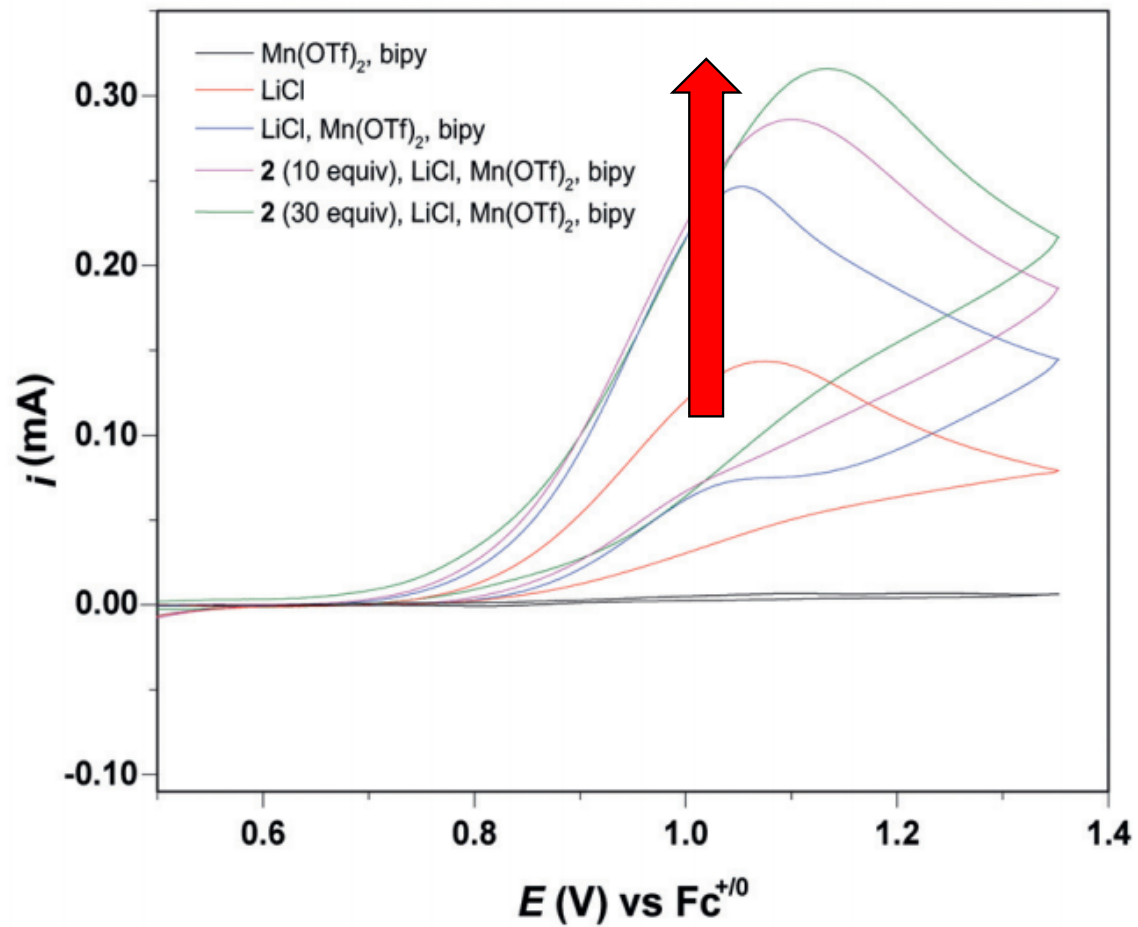
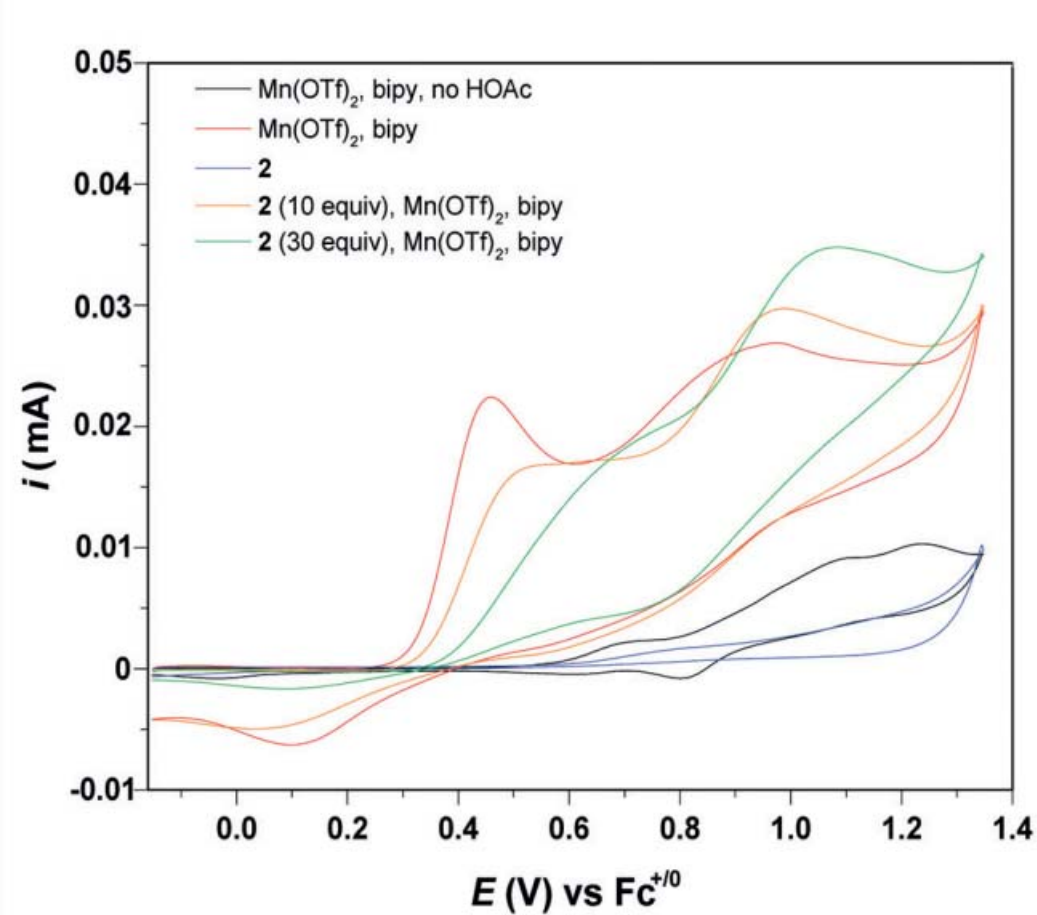
**(A) Alkene scope****(B) Nucleophile scope**



**Scheme 4** Proposed mechanism



**Scheme 3** Radical cyclization experiment



Mn的加入使 $\text{Cl}^- \rightarrow \text{Cl}\cdot$ 的氧化波增强：Mn促进了 $\text{Cl}^-$ 的氧化，生成了 $\text{Mn(III)-Cl}$   
 2的加入使氧化波进一步增强： $\text{Mn(III)-Cl}$ 能够促进2的氧化

# New Bisoxazoline Ligands Enable Enantioselective Electrocatalytic Cyanofunctionalization of Vinylarenes

Niankai Fu,<sup>†</sup> Lu Song,<sup>†</sup> Jinjian Liu, Yifan Shen, Juno C. Siu,<sup>Ⓜ</sup> and Song Lin<sup>\*Ⓜ</sup>

Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States

## (B) New reaction: enantioselective cyanophosphinylation by rational ligand optimization

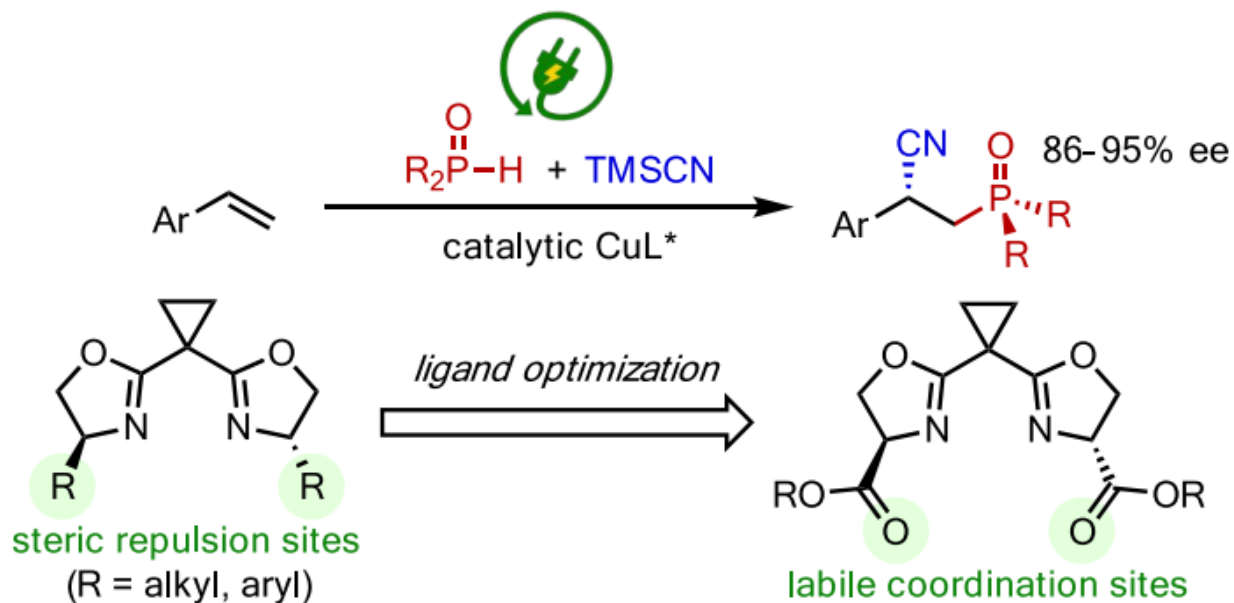
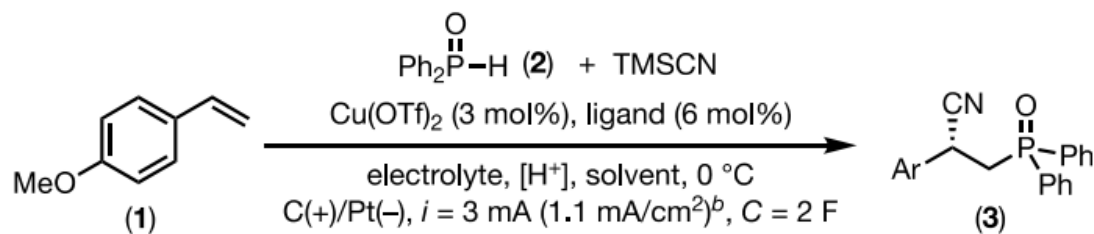
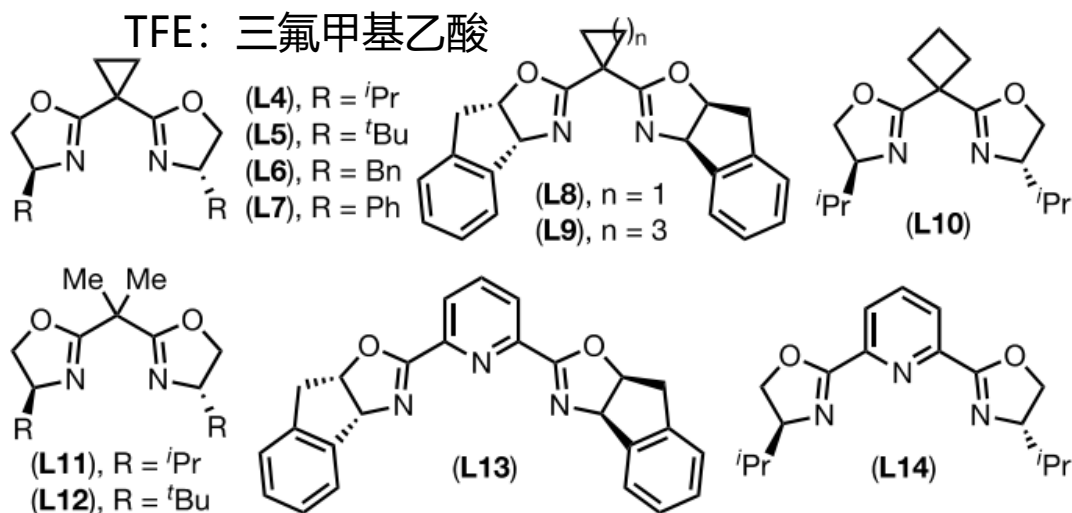


Table 1. Reaction Optimization<sup>a</sup>



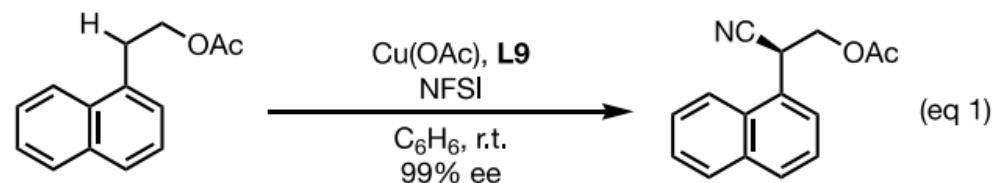
Entry	Ligand	Electrolyte	$[\text{H}^+]$	Solvent	Yield (%)	Ee (%)
1	L4	$\text{LiClO}_4$	HOAc	MeCN	<1	ND
2	L4	$\text{LiClO}_4$	HOAc	DMF	20	79
3	L4	$\text{LiClO}_4$	TFE	DMF	18	76
4	L4	<b>TBABF<sub>4</sub></b>	<b>TFE</b>	<b>DMF</b>	<b>51</b>	<b>84</b>
5	L5-L14	TBABF <sub>4</sub>	TFE	DMF	<10-63	12-79

TFE: 三氟甲基乙酸

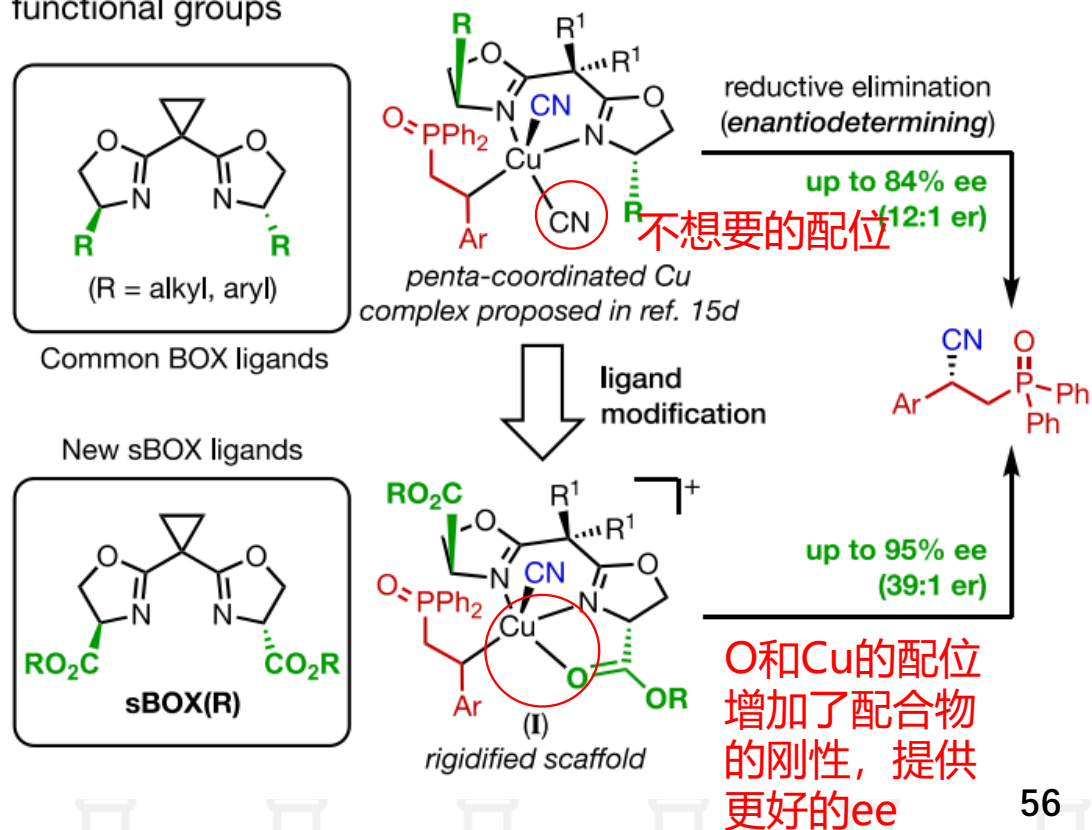


Scheme 2. Development of Serine-Derived BOX Ligands

(A) Enantioselective Cu-catalyzed C–H cyanation by Liu/Stahl<sup>15d</sup>



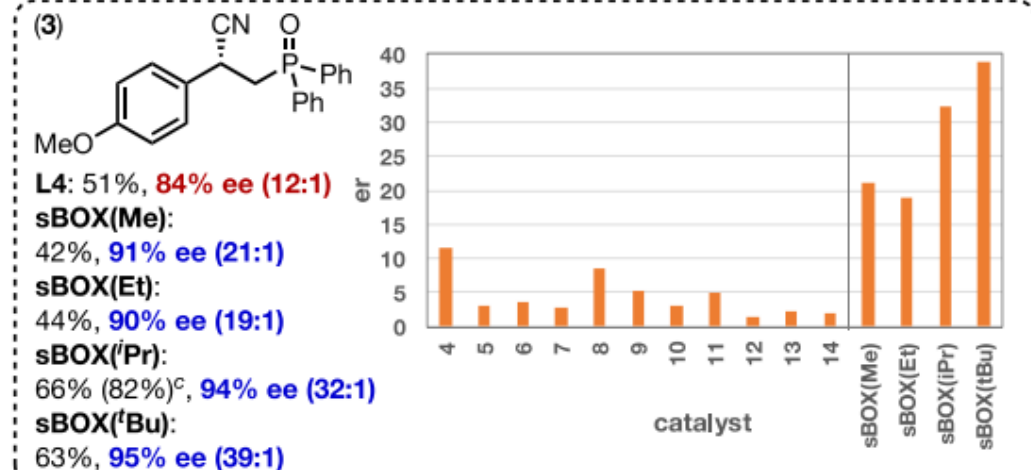
(B) Rational ligand modification: introducing second-sphere functional groups



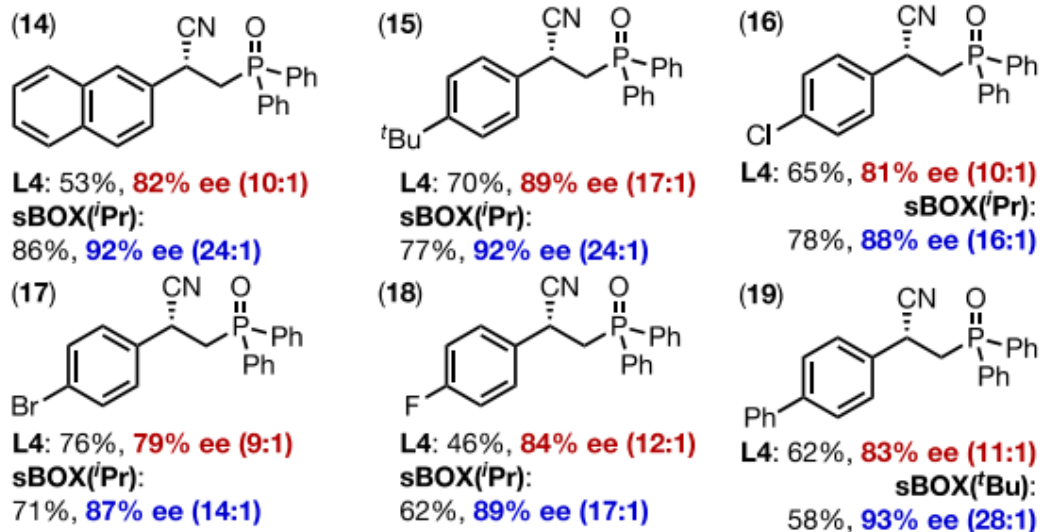


### Scheme 3. Substrate Scope<sup>a</sup>

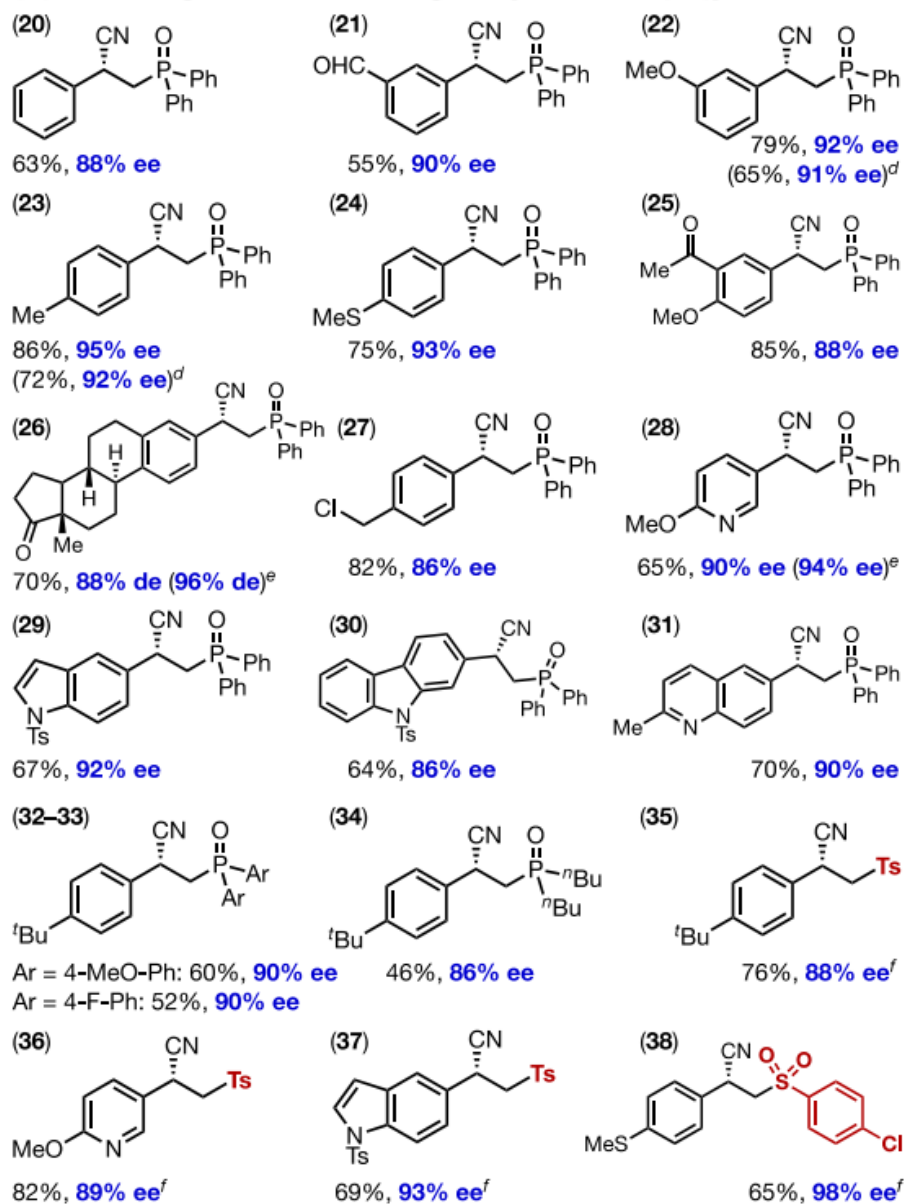
(A) Comparison between sBOX and other oxazoline ligands (numbers in parentheses are er values)<sup>b</sup>



(B) Comparison between ligands 4 and sBOX with other substrates<sup>c</sup>

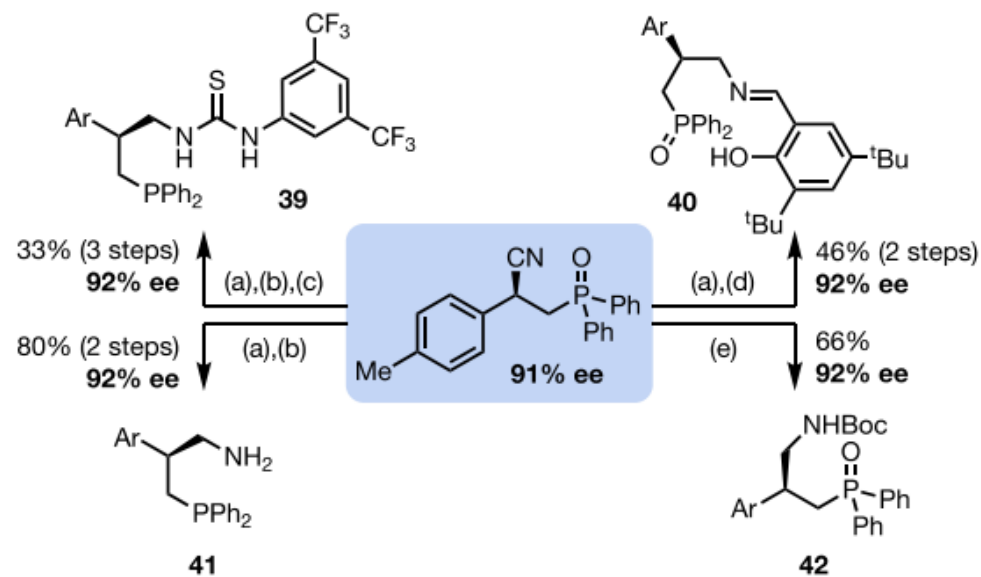


(C) Remaining substrates investigated [with sBOX(iPr)]<sup>c</sup>

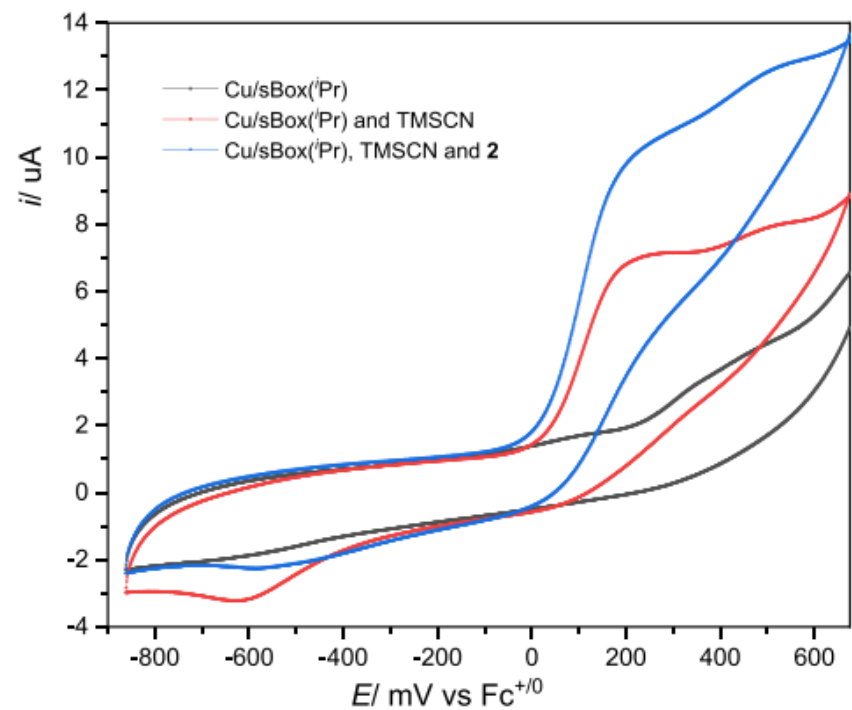
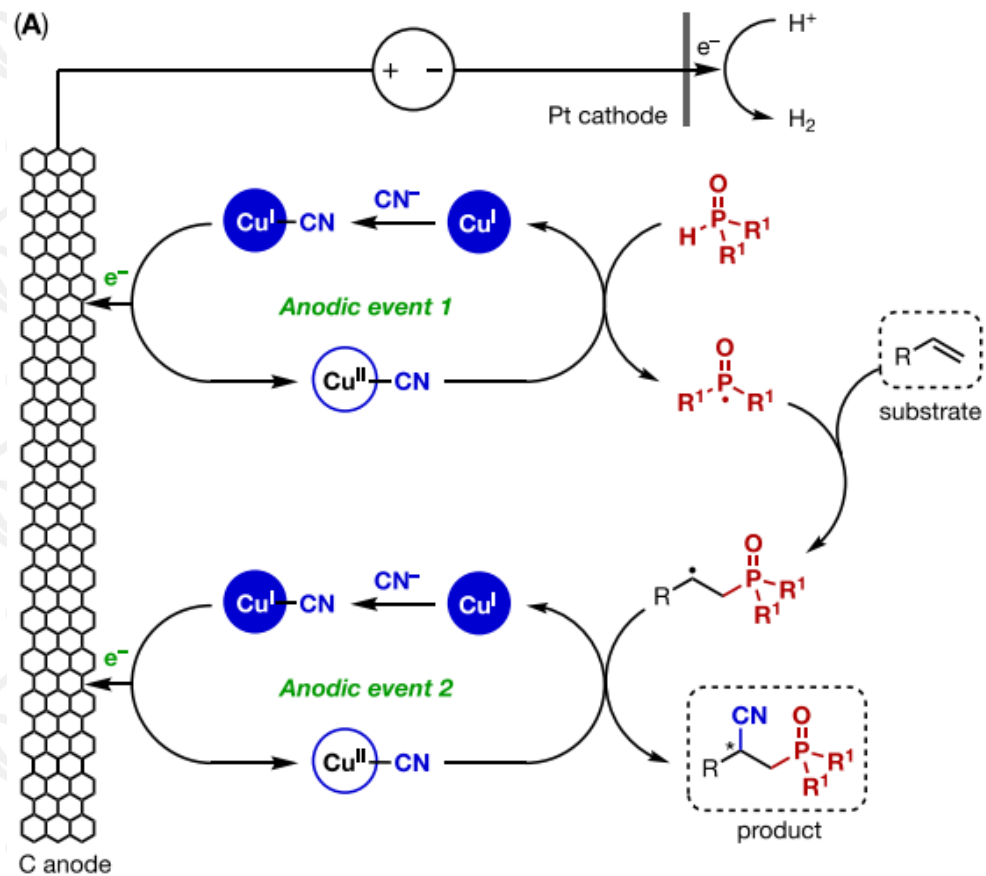


21,24,27  
敏感基团  
保留  
28-31富  
电子以及  
缺电子杂  
环  
32,33取代  
二苯基磷  
34  
二叔丁基  
磷  
35-38  
磺酸

### Scheme 4. Product Derivatization<sup>a</sup>



<sup>a</sup>Reaction conditions: (a) CoCl<sub>2</sub> (cat.), NaBH<sub>4</sub>, MeOH, 0 °C, 83% yield; (b) CeCl<sub>3</sub>, LiAlH<sub>4</sub>, THF, 50 °C, 96% yield; (c) 3,5-Bistrifluoromethylphenyl isothiocyanate, DCM, 42% yield; (d) 3,5-Di-*tert*-butylsalicylaldehyde, EtOH, reflux, 55% yield. (e) NiCl<sub>2</sub> (cat.), NaBH<sub>4</sub>, Boc<sub>2</sub>O, MeOH, 66% yield.



**Figure 1.** (A) Proposed electrocatalytic cycle. (B) Cyclic voltammetry data.

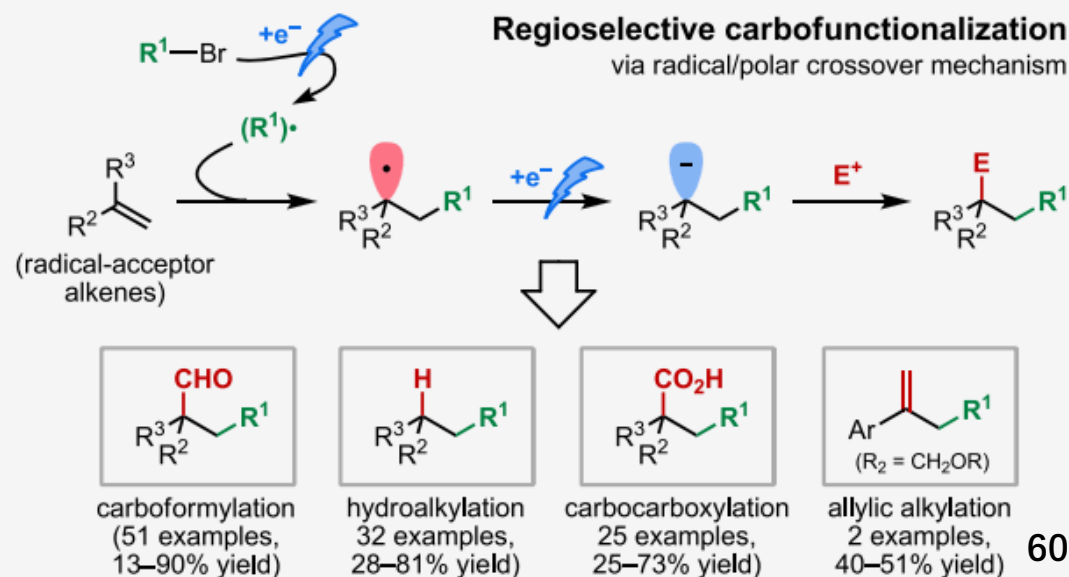
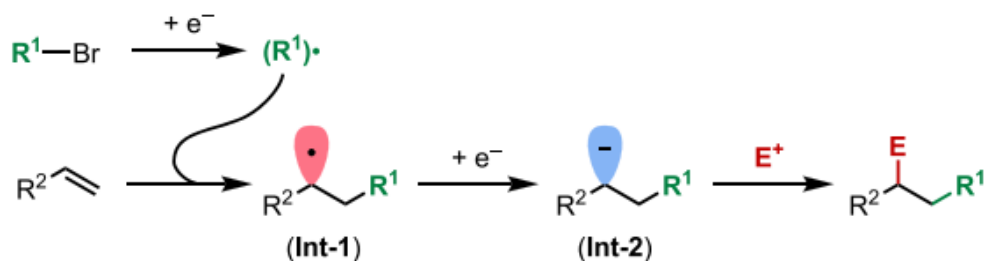
# Electroreductive Carbofunctionalization of Alkenes with Alkyl Bromides via a Radical-Polar Crossover Mechanism

Wen Zhang and Song Lin\*

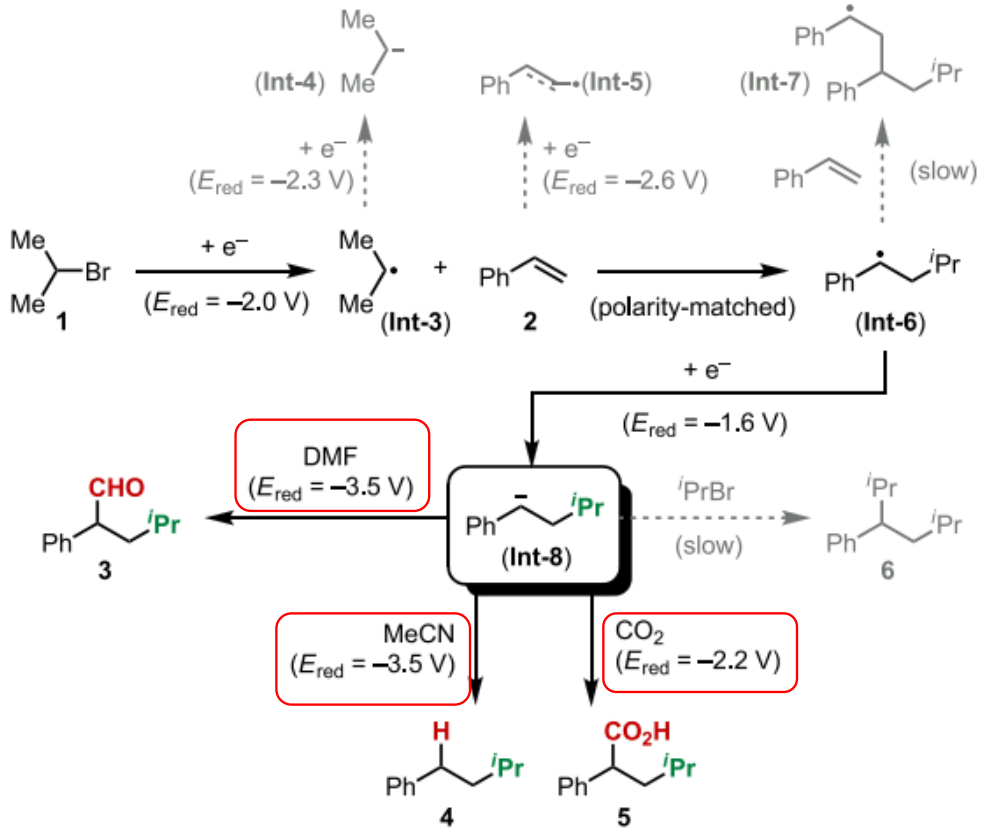


Cite This: *J. Am. Chem. Soc.* 2020, 142, 20661–20670

(C) Electroreductive carbofunctionalization of alkenes with alkyl halides (intermolecular or intramolecular; *this work*)

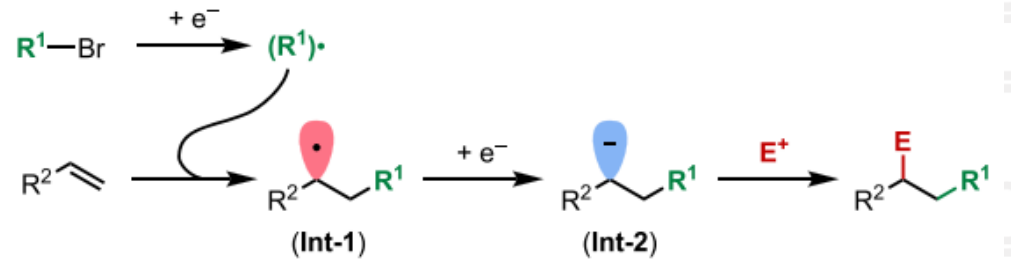


(B) Rationale for reactant choices: a case scenario



作为提供-CHO,-H,-COOH的E+, DMF, MeCN, CO<sub>2</sub>的还原电位低, 对阴极还原表现出惰性

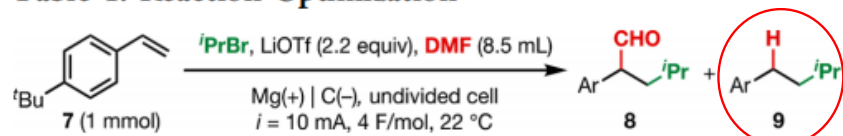
(C) Electroreductive carbonylation of alkenes with alkyl halides (intermolecular or intramolecular; *this work*)



实现预定的方案需要满足:

- R-Br要比烯烃以及E+更易还原
- R·与烯烃结合的速度高于自偶联以及继续还原的速度
- Int 1 优先还原为int 2而不是直接和烯烃反应
- E+比R·更优先与int 2 反应

Table 1. Reaction Optimization<sup>a</sup>



entry	variation from above conditions	conv. of 7 (%)	yield (%)		
			8	9	10
1	none	85	71	7	6
2	2 mol % Co(salen)	93	55	8	<2
3	<sup><i>i</i></sup> PrCl instead of <sup><i>i</i></sup> PrBr	84	9	0	0
4	<sup><i>i</i></sup> PrI instead of <sup><i>i</i></sup> PrBr	99	22	10	35
5	Zn(+) instead of Mg(+)	28	<2	2	0
6	Mg(-) instead of C(-)	38	6	5	0
7	4.2 mL of DMF	99	88	5	6
8	same as entry 7 but with 1.1 equiv of LiOTf	99	89 (86) <sup>b</sup>	4	6
9	same as entry 8 but using a divided cell	90	45	19	14
10	MeCN (4.2 mL) instead of DMF	76	0	65	2
11	same as entry 9 but with Et <sub>2</sub> NH (1.0 equiv)	85	0	77 (73) <sup>b</sup>	3
12	no electricity	2	0	0	0
13	no electricity but with Mg powder	3	0	0	0

反马式产物

最好

entry2: 加入Co(salen)促进7→9, 未奏效

entry3,4: 活性更强的R-Br, R-I不能很好反应

entry5: 用Zn代替Mg作为牺牲阳极, 生成的Zn<sup>2+</sup>在阴极还原, 与原本反应竞争

entry7: DMF在体系中同时充当溶剂与反应物, 体积减半, 浓度上升, 产率更好

entry11: 加入质子供体Et<sub>2</sub>NH, 还原产物大大增加

<sup>a</sup>Reaction conditions: 7 (1 mmol, 1 equiv), <sup>*i*</sup>PrBr (3 equiv), LiOTf (2.2 equiv), DMF (8.5 mL), Mg anode, graphite cathode, undivided cell, constant current *i* = 10 mA, 4 F/mol. Conversion and yield determined by <sup>1</sup>H NMR. <sup>b</sup>Isolated yield.

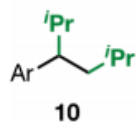
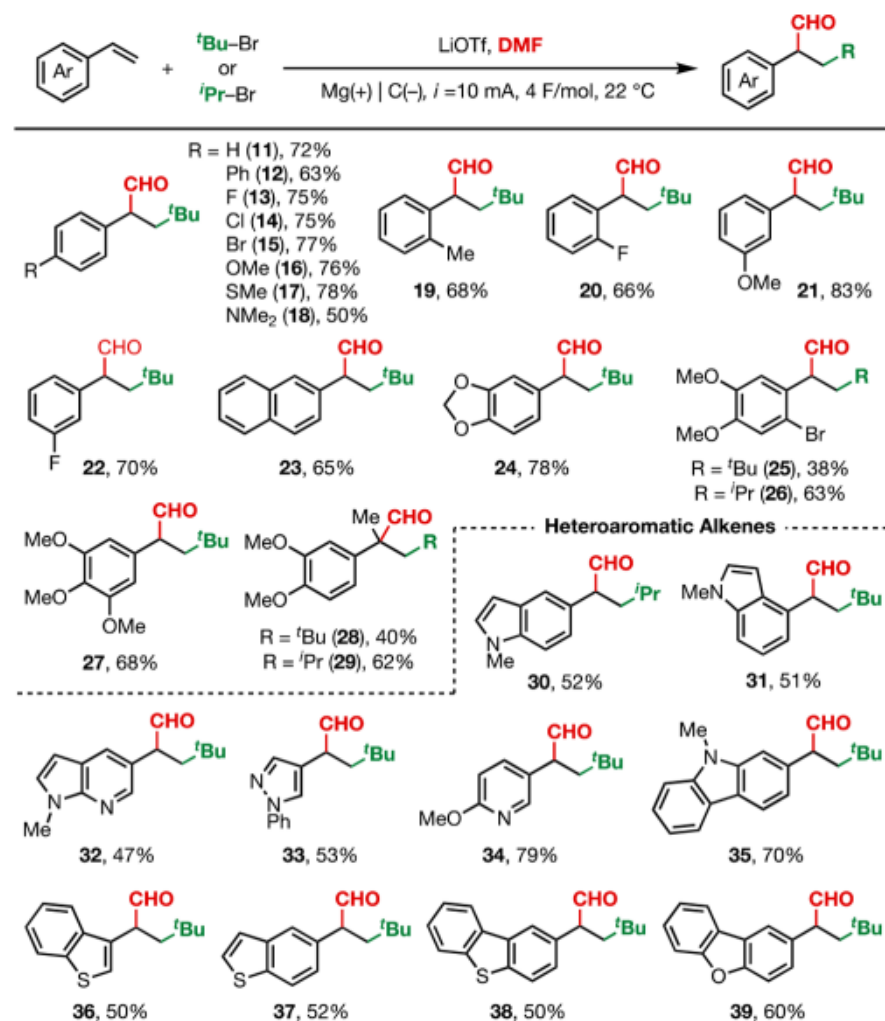
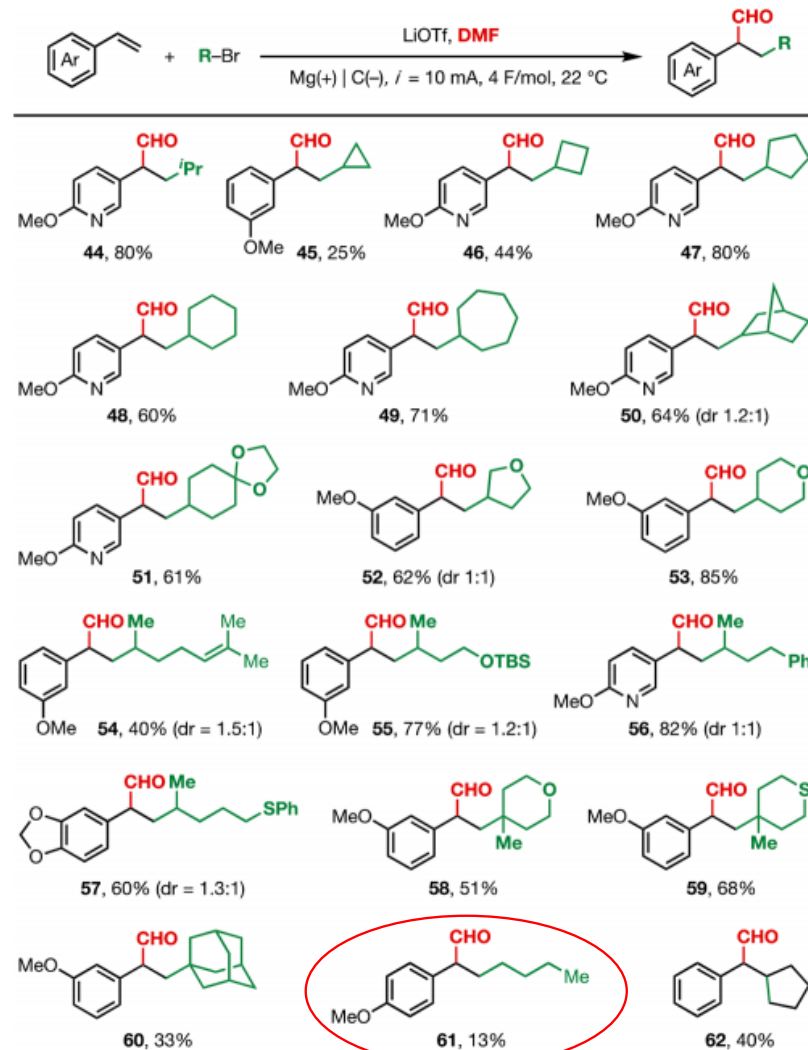


Table 2. Scope of Styrenes for Carboformylation<sup>a</sup>



<sup>a</sup>Reaction conditions: alkene (1 mmol, 1 equiv), alkyl bromides (3 equiv), LiOTf (1.1 equiv), DMF (4.2 mL), Mg plate and graphite plate, undivided cell (ElectraSyn), constant current  $i = 10$  mA, 4 F/mol, 22 °C. Isolated yields are reported.

Table 3. Scope of Alkyl Bromides for Carboformylation<sup>a</sup>



<sup>a</sup>Reaction conditions: alkene (1 mmol, 1 equiv), alkyl bromides (3 equiv), LiOTf (1.1 equiv), DMF (4.2 mL), Mg plate and graphite plate, undivided cell (ElectraSyn), constant current  $i = 10$  mA, 4 F/mol, 22 °C. Isolated yields are reported.

一级溴代物  
还原电位太低，反应性差

Table 4. Substrate Scope of Hydroalkylation<sup>a</sup>

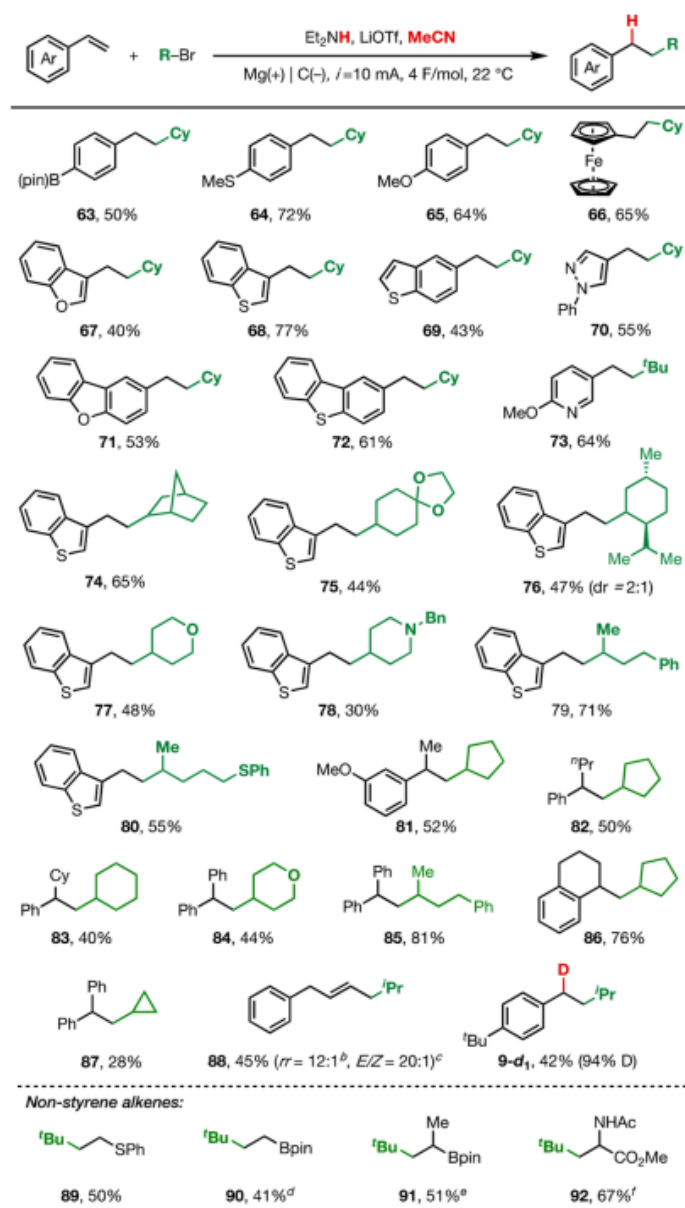
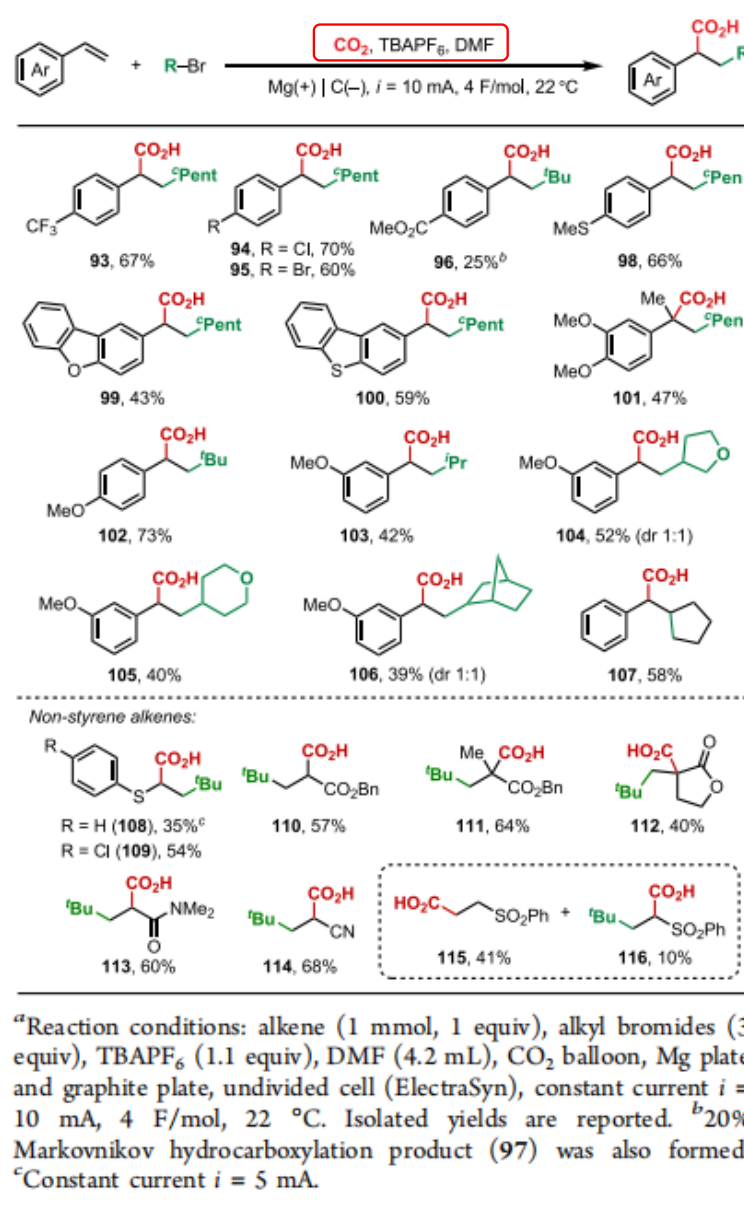
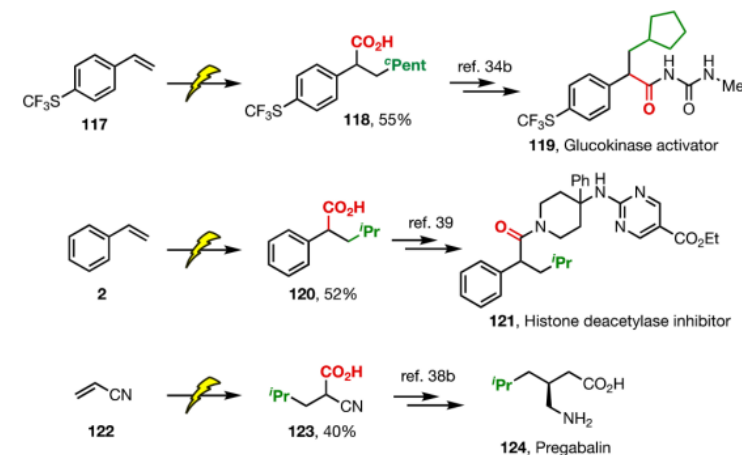


Table 5. Substrate Scope of Carboxylation<sup>a</sup>



CO<sub>2</sub>比DMF更亲电，在上-COOH时可以使用DMF作溶剂，不会有选择性  
问题

Scheme 3. Synthesis of Precursor of Bioactive Molecules

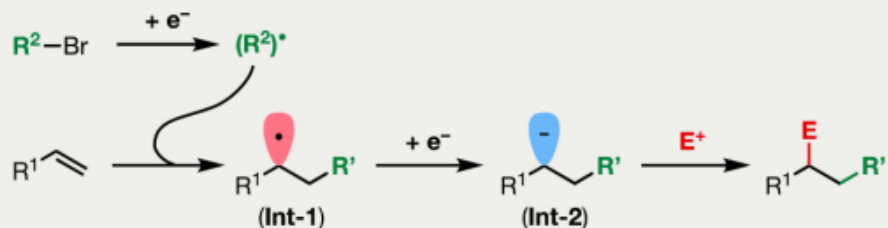


<sup>a</sup>Reaction conditions: alkene (1 mmol, 1 equiv), alkyl bromides (3 equiv), TBAPF<sub>6</sub> (1.1 equiv), DMF (4.2 mL), CO<sub>2</sub> balloon, Mg plate and graphite plate, undivided cell (ElectraSyn), constant current *i* = 10 mA, 4 F/mol, 22 °C. Isolated yields are reported. <sup>b</sup>20% Markovnikov hydrocarboxylation product (97) was also formed. <sup>c</sup>Constant current *i* = 5 mA.

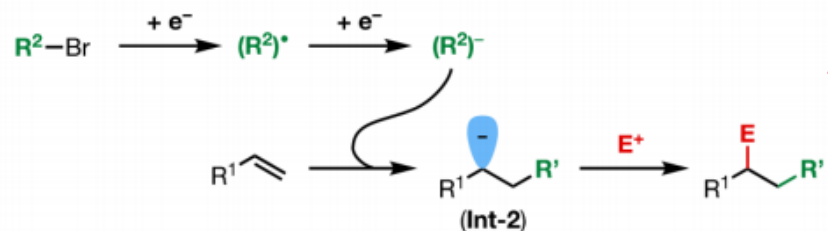


## Scheme 4. Plausible Mechanism

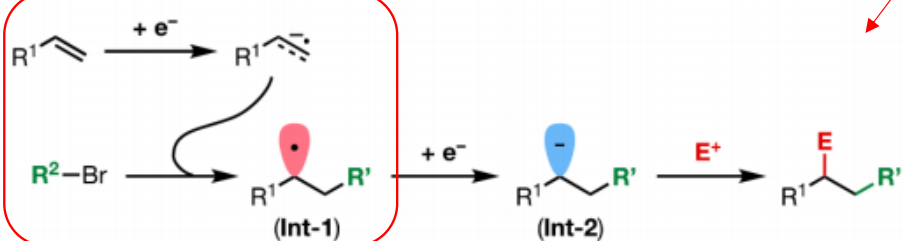
### Pathway A: ECEC radical/polar crossover initiated by alkyl halide reduction



### Pathway B: EEC polar mechanism initiated by alkyl halide 2e-reduction



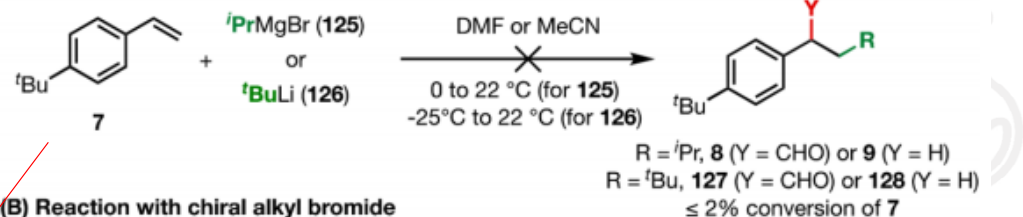
### Pathway C: ECEC radical anion mechanism initiated by alkene reduction



相当于Sn2反应，R2应该会发生手性翻转

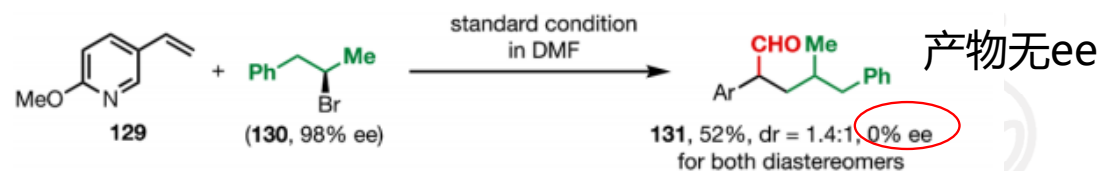
## Scheme 5. Control Experiments for Mechanistic Study

### (A) Direct addition of Grignard and lithium reagent



C-不能直接加成到7上

### (B) Reaction with chiral alkyl bromide



产物无ee

### (C) Radical probe experiment

