# Alternating Current Electrolysis for Organic Synthesis

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# CONTENT

# 1. Background

# Background

- Early explorations of alternating current (AC) electrolysis for organic synthesis

**[1837]**
**De la Rive**
AC was first used for electrolysis of water

**[1880]**
**Drechsel**
AC was postulated to determine rate constants.

**[1939]**
**Shipley**
AC electrolysis of organic compounds (fatty acids, alcohols, aromatic hydrocabons)

**[1956]**
**Wilson**
Kolbe electrolysis of acetate by AC electrolysis

**[1982]**
**Alkire**
AC electrolysis of propylene oxide

**[1984]**
**Fedkiw**
The effect of AC on the selectivity of nitrobenzene reduction

**[1991]**
**Lisius**
Mass transfer is significant in AC electrolysis

Some transformations of small molecules by AC electrolysis

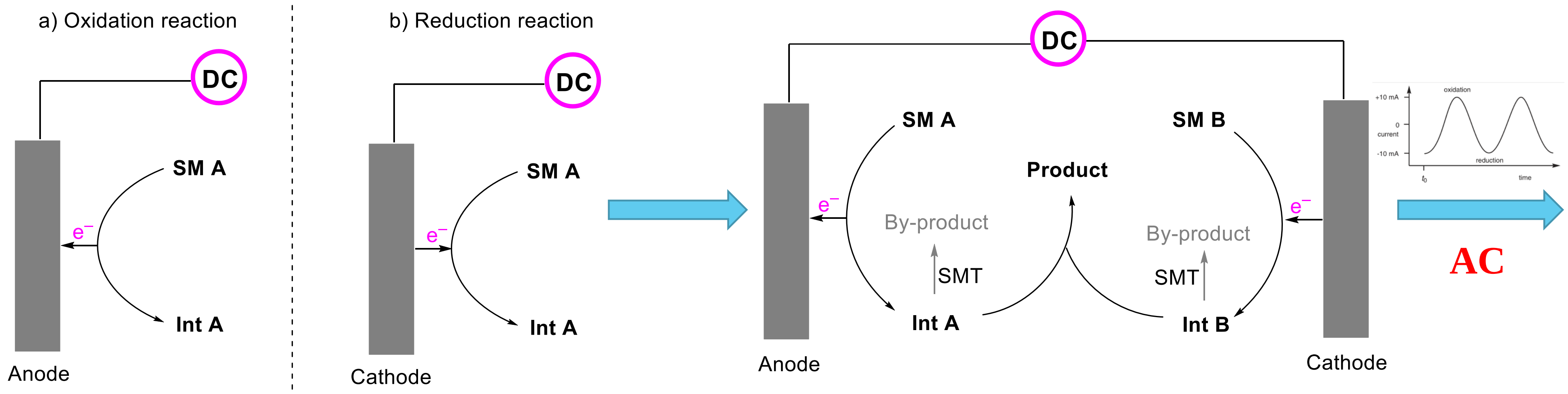
**[1992]**
**Smeltzer, Fedkiw**
A parallel-plate reactor for the electrochemical reduction of nitrobenzene

# Background

■ Recent development of AC electrolysis

**Direct current (DC) electrolysis** → **Alternating current (AC) electrolysis**

**A. One-half-cell reaction** **B. Paired electrolysis**

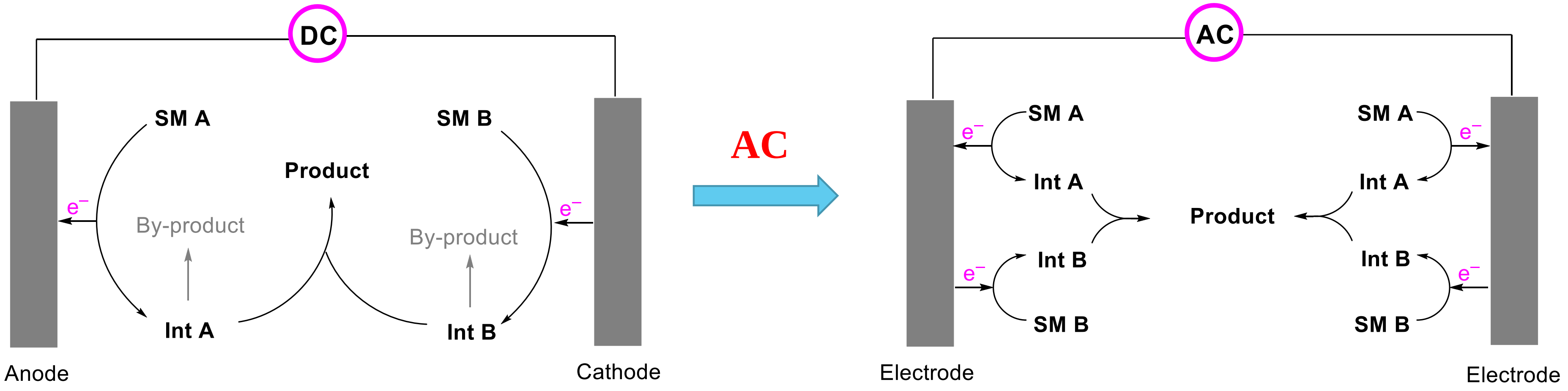



AC-promoted paired electrolysis

- less sustainable than desired
- lower yield due to the conflict between slow interelectrode mass transport and short survival time of intermediates

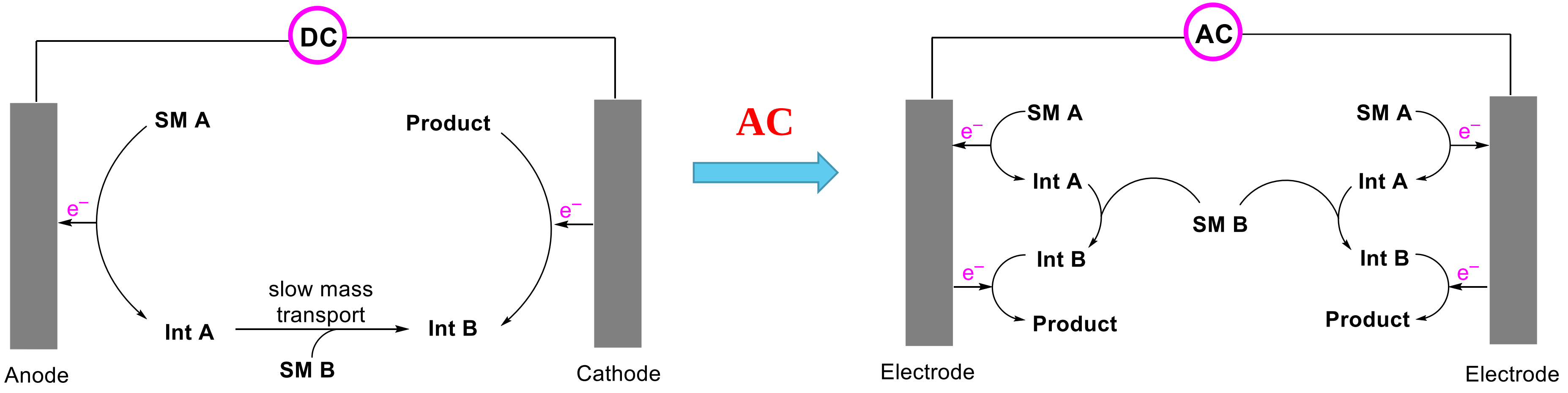
# Background

- AC-promoted paired electrolysis---activation of starting materials/intermediates




Paired electrolysis

AC-promoted paired electrolysis




- change of the polarity of the electrode

# Background

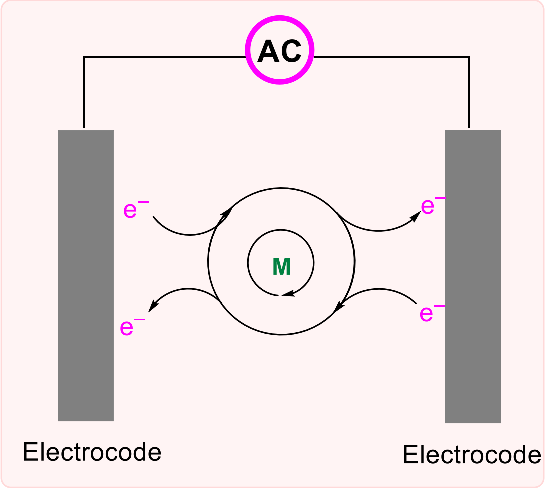
- Different patterns of AC electrolysis

AC electrolysis

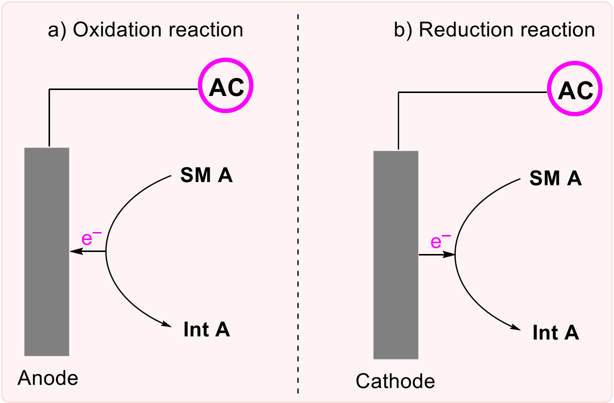
AC-promoted paired electrolysis

Activation of starting materials/intermediates

Activation of metal catalysts

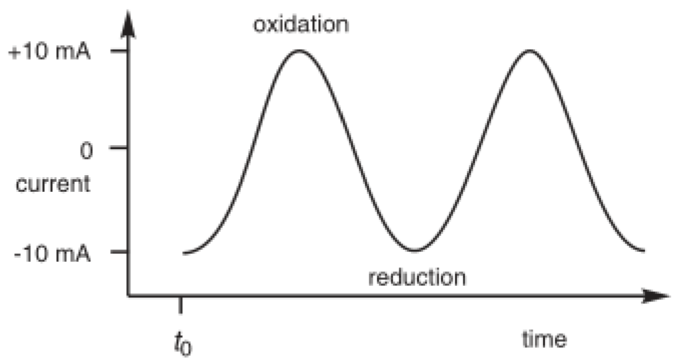



AC-promoted oxidation or reduction reaction on electrodes

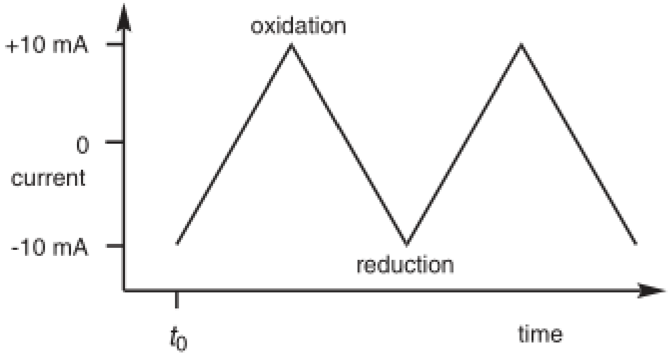


# Background

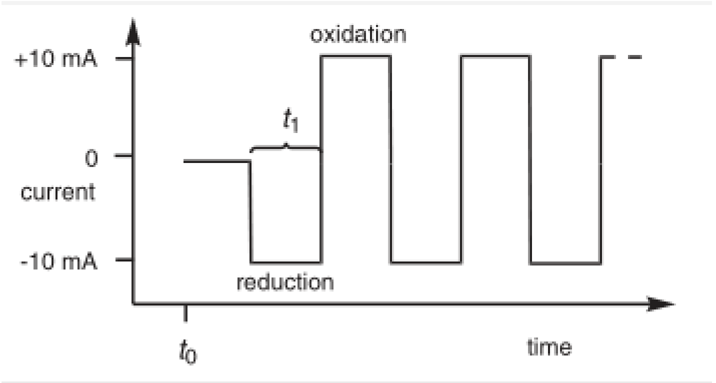
- Different waveforms of AC



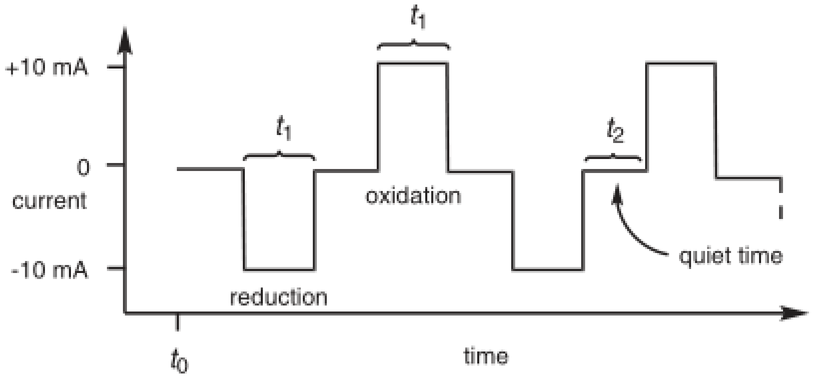

(a) Sinusoidal waveform




(b) Triangular waveform




(c) Square waveform
(rapid alrernating polarity)



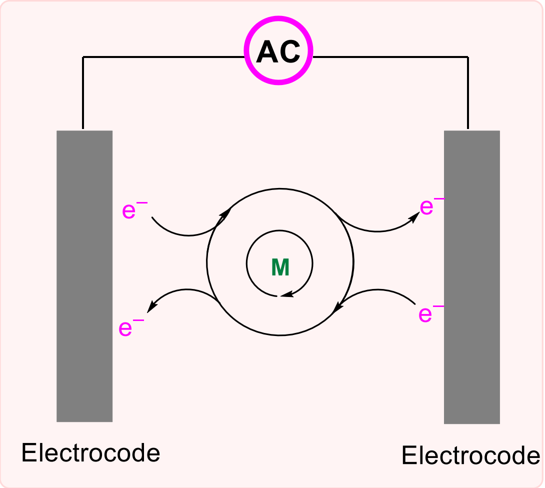

(d) Interrupted square waveform

- AC electrolysis is characterized by a change of polarity of the electrode

# 2.1 AC-promoted paired electrolysis

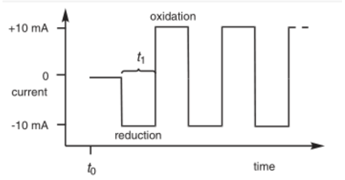
- 2.1.1 Activation of metal catalysts

Activation of metal catalysts

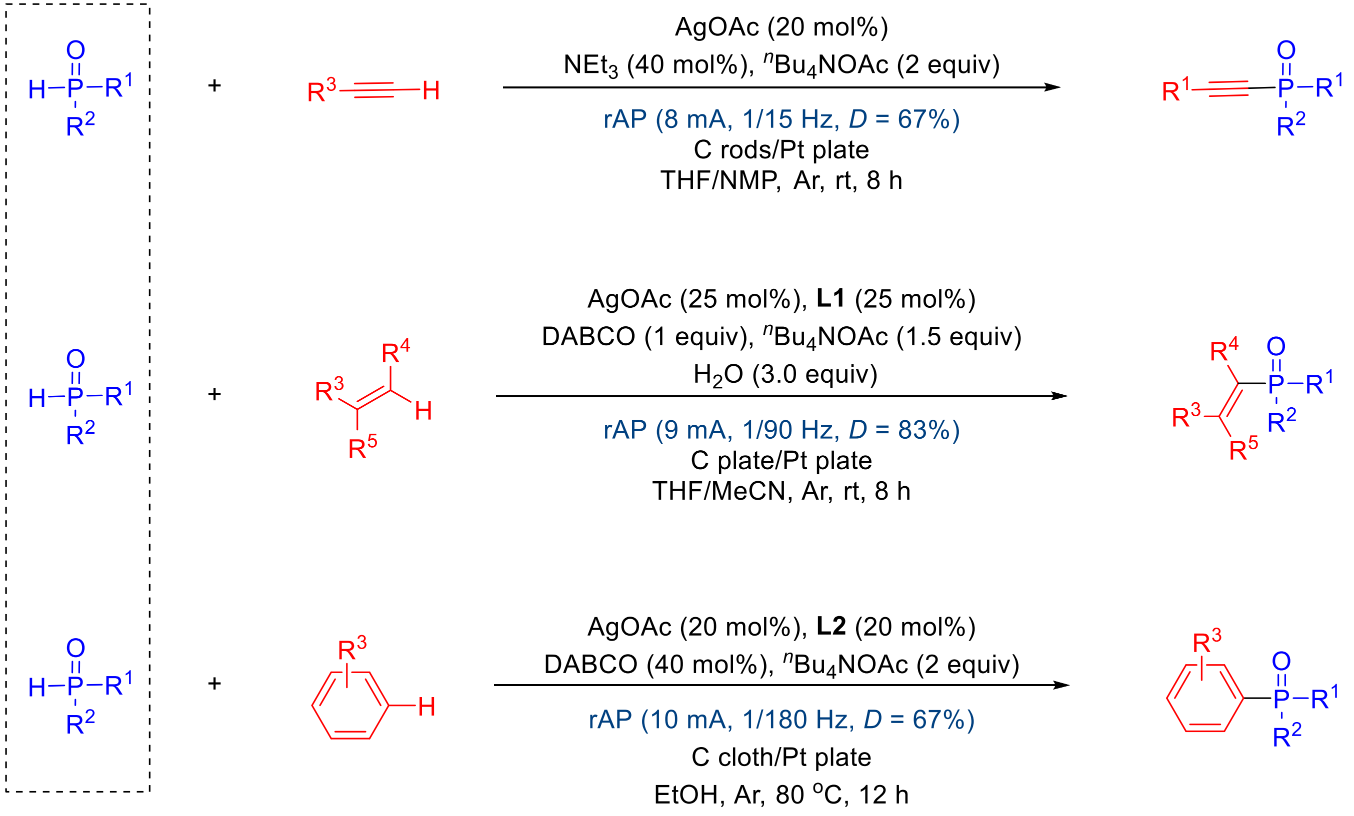


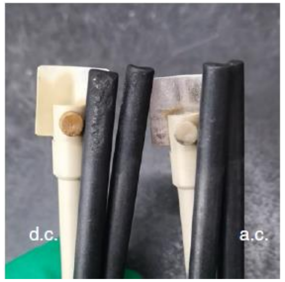
# Activation of metal catalysts

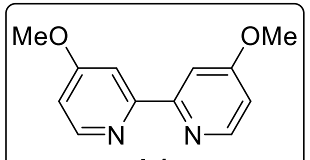
- Asymmetric rAP promoted silver catalysis for C–H phosphorylation



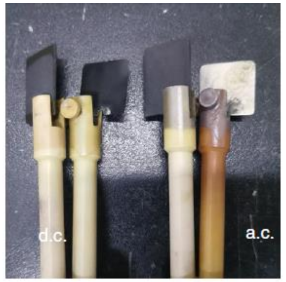
rAP

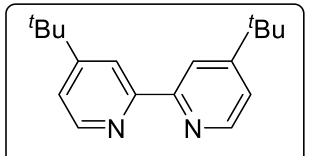


L1



L2

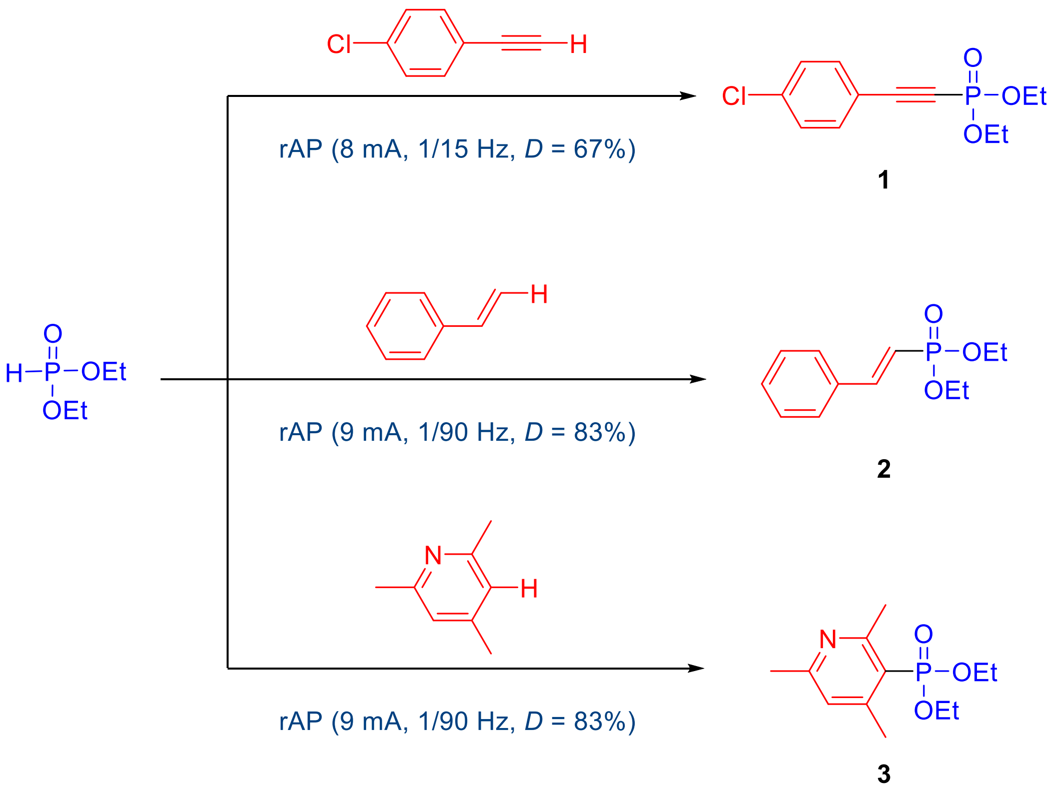

**Overcome the limitation of reductive metal deposition through asymmetric-waveform alternating current electrolysis**

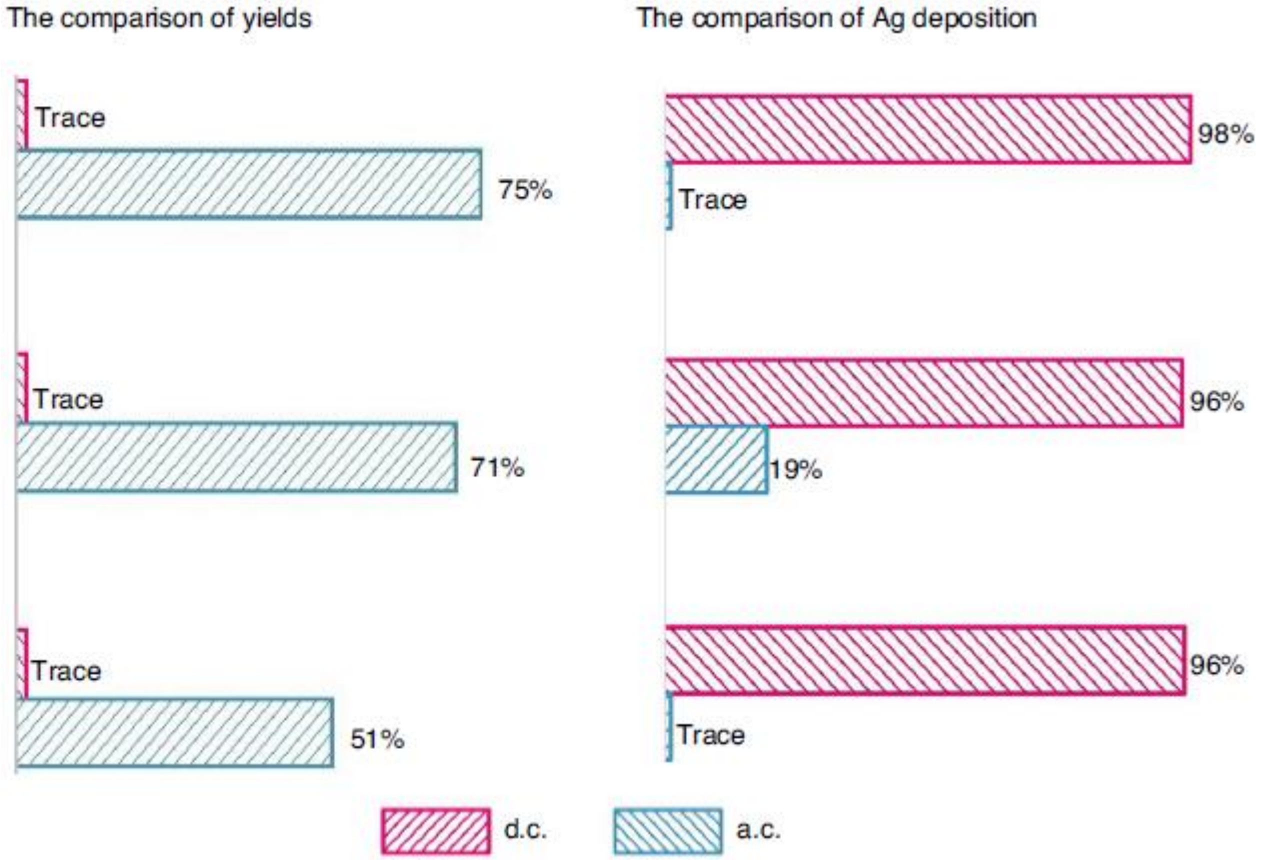
Lei, A. et al. *Nat. Synth.* **2023**, *2*, 172-181

# Activation of metal catalysts

■ Asymmetric rAP promoted silver catalysis for C–H phosphorylation

**A. The comparison between d.c. and a.c.electrolysis**



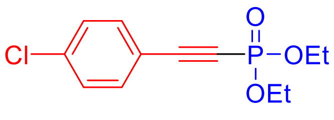




Lei, A. et al. *Nat. Synth.* **2023**, *2*, 172-181

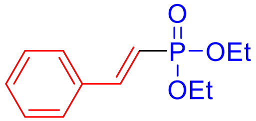
# Activation of metal catalysts

- Asymmetric rAP promoted silver catalysis for C–H phosphorylation

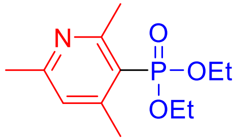
**B. The influence of a.c. parameters**



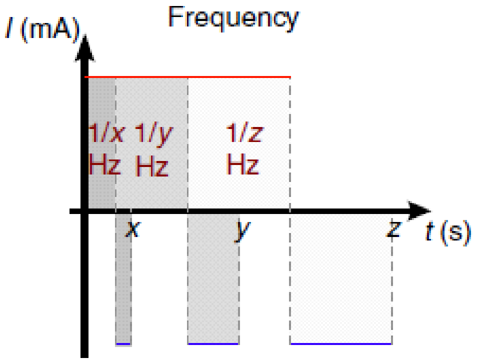

**1**
**Alkynylation**



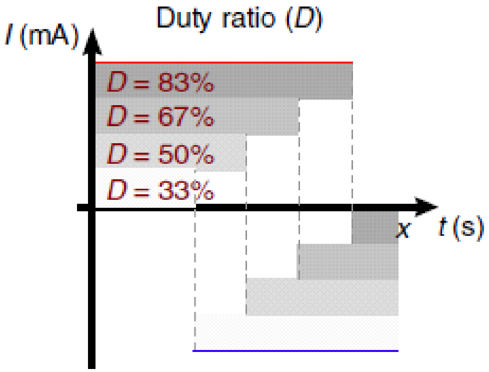

**2**
**Alkenylation**




**3**
**Arylation**




| 1 Alkynylation | 2 Alkenylation | 3 Arylation |
|---|---|---|
| 1/3 Hz: 41% | 1/30 Hz: 51% | 1/90 Hz: 58% |
| 1/15 Hz: 80% | 1/90 Hz: 74% | 1/180 Hz: 71% |
| 1/30 Hz: 47% | 1/180 Hz: 51% | 1/270 Hz: 61% |




| 1 Alkynylation | 2 Alkenylation | 3 Arylation |
|---|---|---|
| *D* = 33%: trace | *D* = 33%: 26% | *D* = 33%: 50% |
| *D* = 50%: 27% | *D* = 50%: 36% | *D* = 50%: 55% |
| *D* = 67%: 80% | *D* = 67%: 53% | *D* = 67%: 71% |
| *D* = 83%: 43% | *D* = 83%: 74% | *D* = 83%: 62% |
| | *D* = 95%: 21% | |

*D*, the ratio of positive half-period to the whole period

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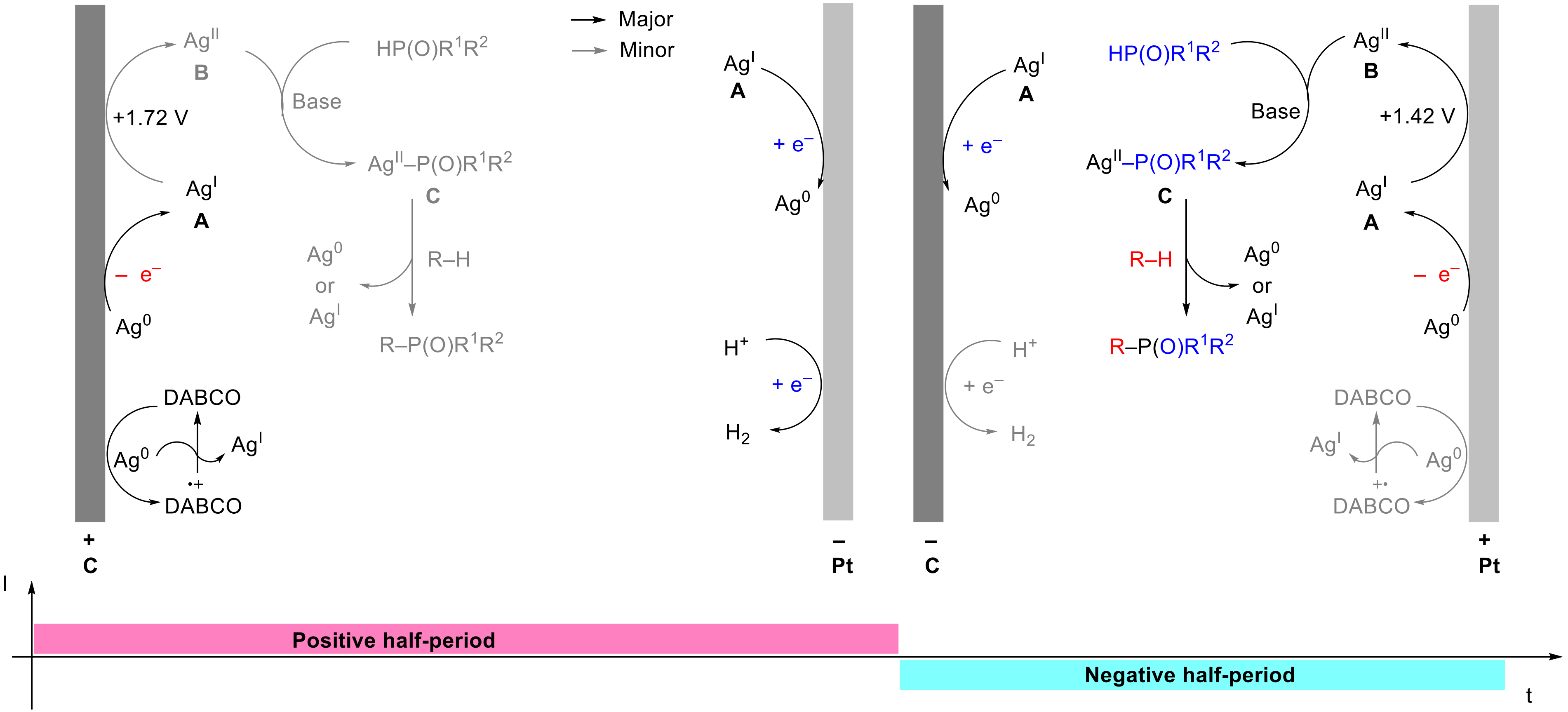
# Activation of metal catalysts

- Asymmetric rAP promoted silver catalysis for C–H phosphorylation

**C. Proposed mechanism**




- The larger number the duty ratio is, the more $Ag^0$ is deposited. If duty ratio (*D*) is more than the critical value, there is too much $Ag^0$ deposited on the Pt electrode, thus hindering the reaction. Because there is not enough time during short negative half-periods for the Pt electrode to oxidize $Ag^0$ to $Ag^{II}$.

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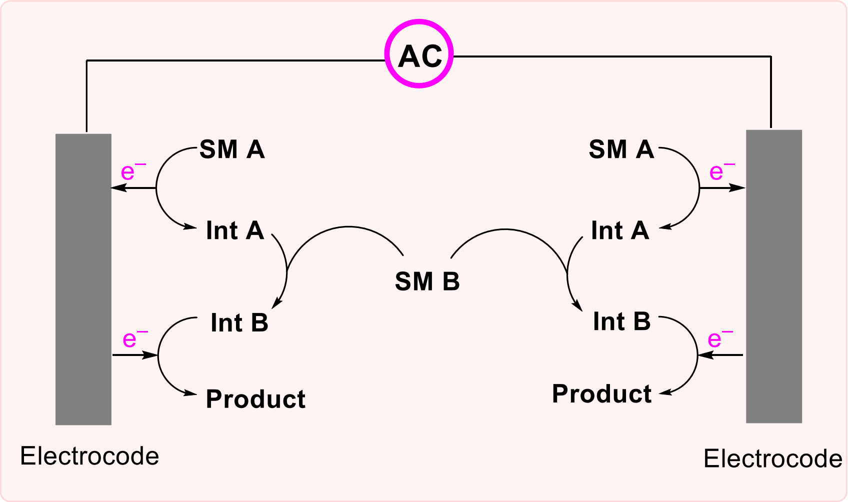
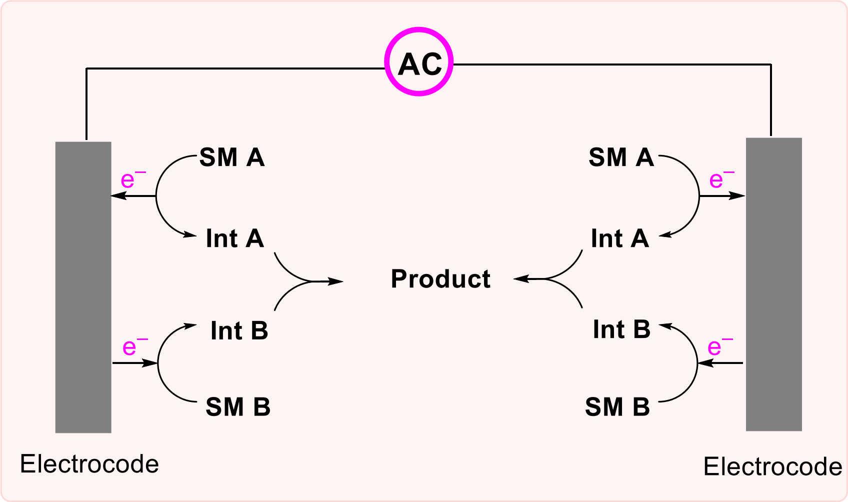
# 2.1 AC-promoted paired electrolysis

- 2.1.2 Activation of starting materials/intermediates

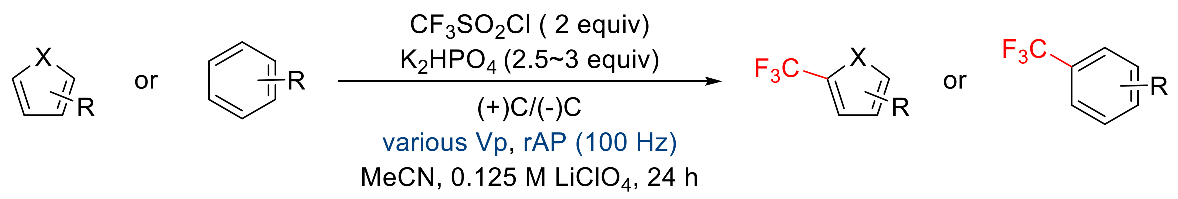
Activation of starting materials/intermediates

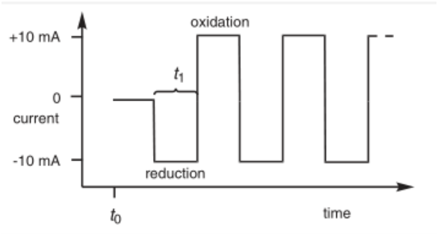


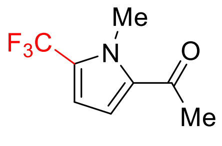
# Activation of starting materials/intermediates

- Trifluoromethylation of (hetero)arenes enabled by rAP

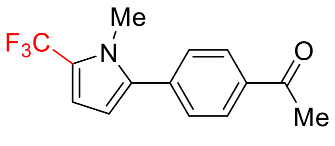


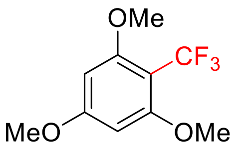

rAP



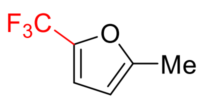
**5**: 84% (4.4 V)



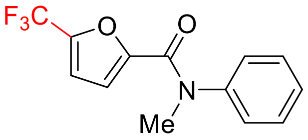
**7**: 61% (2.8 V)



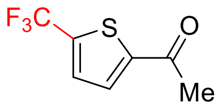
**8**: 42% (4.8 V)



**9**: 43% (2.8 V)



**10**: 43% (3.0 V)



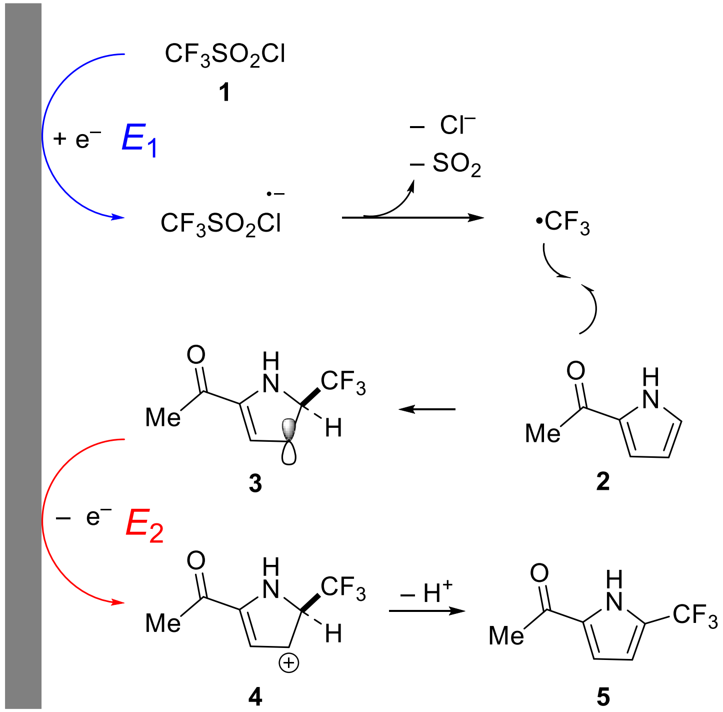
**11**: 28% (4.6 V)

Luo, L. et al. *Org. Lett.* **2020**, *22*, 6719−6723

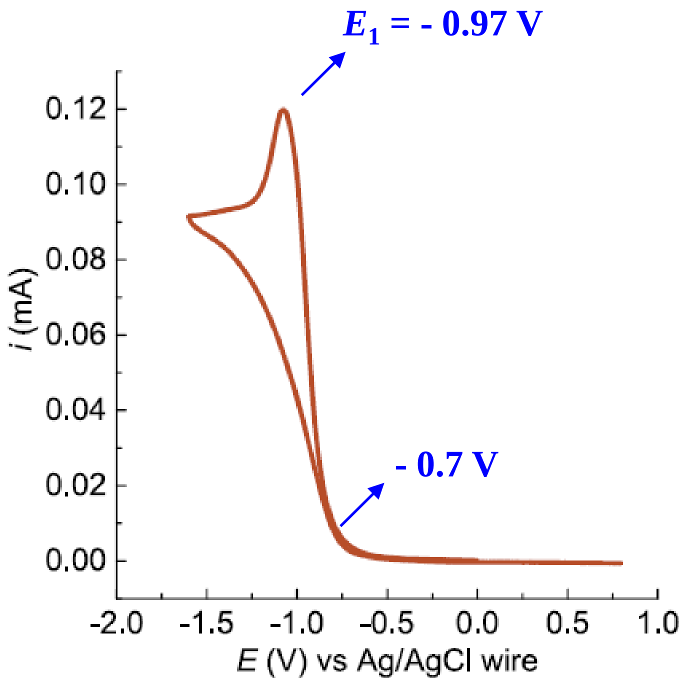
# Activation of starting materials/intermediates

- Trifluoromethylation of (hetero)arenes enabled by rAP

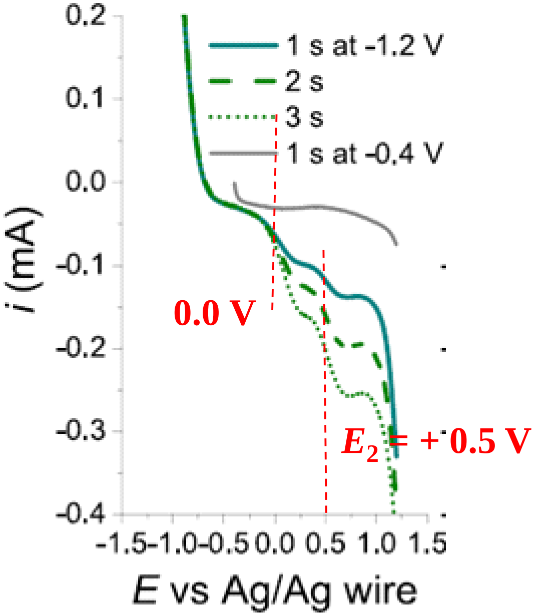
A. Proposed mechanism




B. Cyclic voltammograms of 1 in MeCN




C. Fast-scan linear sweep voltammograms of a mixture of 1 and 2.




**Minimum voltage required for reaction is |-0.7 – 0| = 0.7 V.**
**Thermodynamic voltage: |$E_1$ – $E_2$| = ~ 1.5 V < 4.4 V (optimal voltage)**

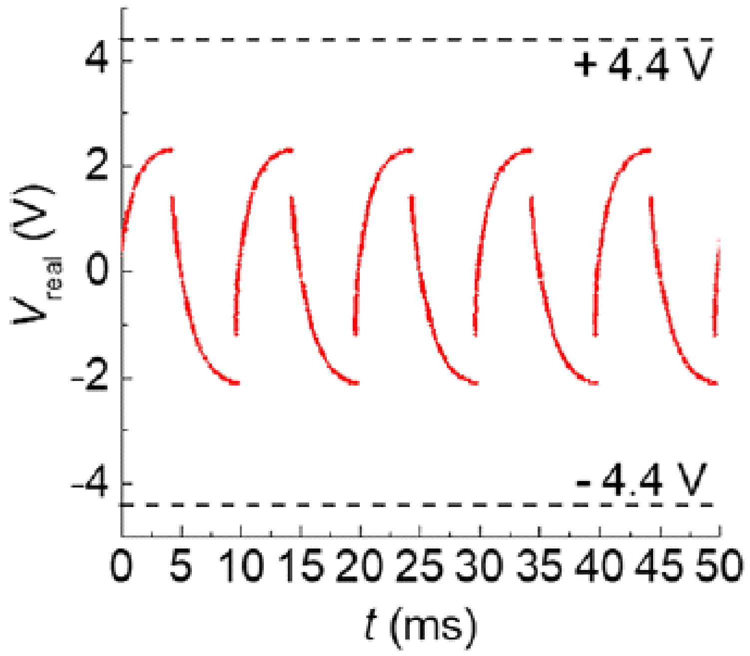
(C). Left panel: Electrode potential was held at −1.2 V for 1, 2, and 3 s followed by sweeping the potential positively to 1.2 at 20 V/s. Concentrations of **1** and **2** were both 0.25 M. Right panel: Different equivalents of **2** to **1** were added, and the holding time at −1.2 V was 3 s. Gray curve: Electrode potential was held at −0.4 V for 1 s before the potential sweep.

Luo, L. et al. *Org. Lett.* **2020**, *22*, 6719−6723

# Activation of starting materials/intermediates

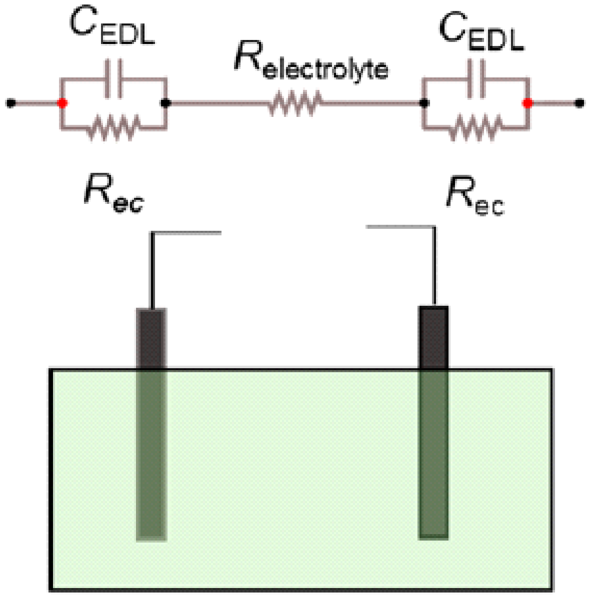
- Trifluoromethylation of (hetero)arenes enabled by rAP

**D. Measured voltage ($V_{real}$)**




$V_p$ = 4.4 V > $|E_1 - E_2|$ = ~ 1.5 V

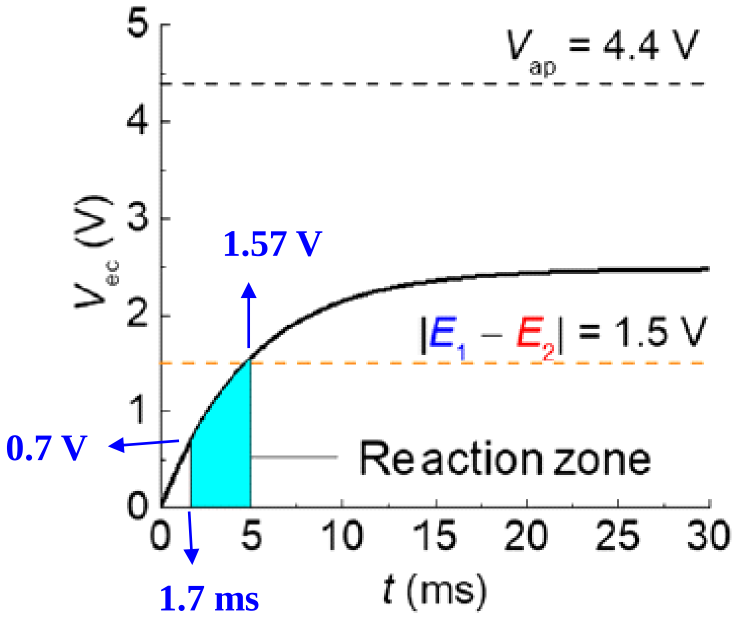
**E. Equivalent circuit**




$C_{EDL}$: electrical double layer capacitor
$R_{ec}$: electrochemical resistor

$R_{electrolyte}$: a constant resistance of electrolyte solution

**F. Theoretical modeling of the voltage ($V_{ec}$)**




$V_p$ (4.4 V), 100 Hz (t/2 = 5 ms)

$$V_{ec} = V_{real,peak}(1 - \exp(-2t/R_{electrolyte}C_{EDL}))$$

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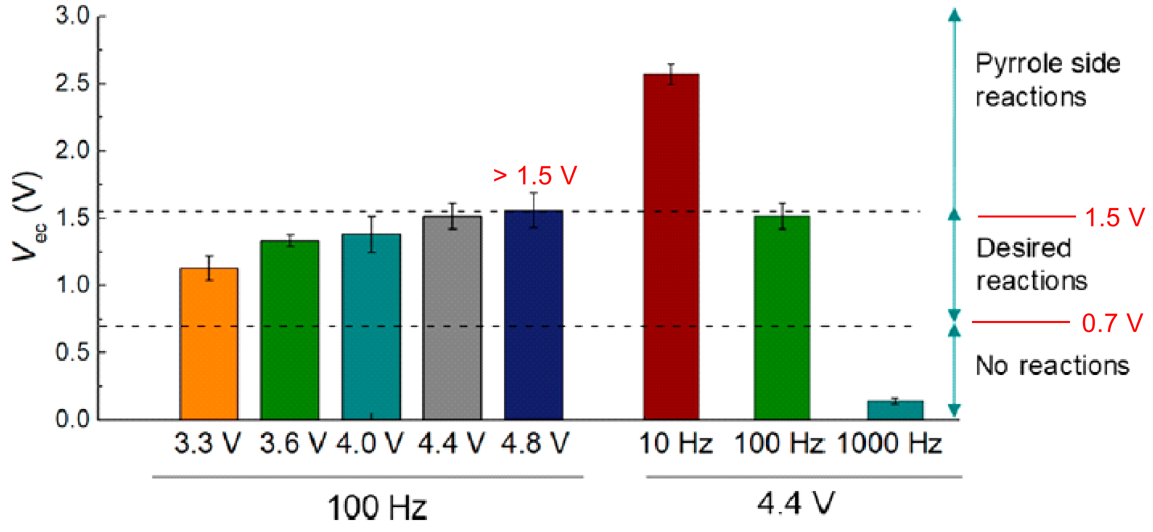
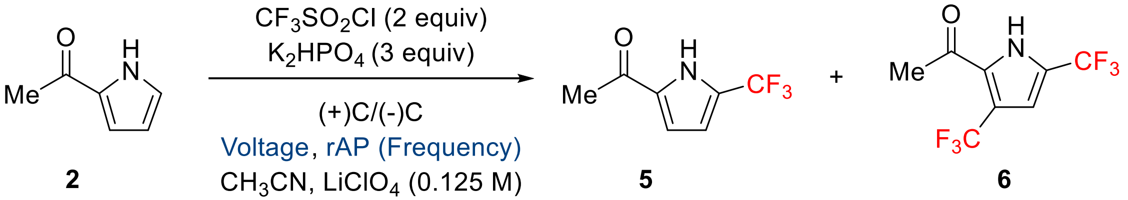
# Activation of starting materials/intermediates

- Trifluoromethylation of (hetero)arenes enabled by rAP

**D. Predicted ranges of $V_{ec}$ at different $V_p$ and $f$**



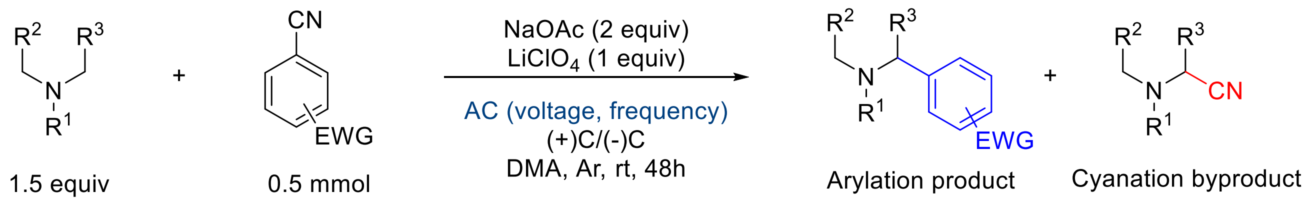

| Entry | $V_p$ (V) | $f$ (Hz) | conversion (%) | yield of **5** (%) | **5**/**6** ratio |
|---|---|---|---|---|---|
| 1 | 3.3 (rAP) | 100 | 6 | | |
| 2 | 3.6 (rAP) | 100 | 27 | | |
| 3 | 4.0 (rAP) | 100 | 48 | 44 | 24/1 |
| **4** | **4.4 (rAP)** | **100** | **100** | **84** | **19/1** |
| 5 | 4.8 (rAP) | 100 | 44 | | 44/1 |
| 6 | 4.4 (rAP) | 10 | 21 | | 0.75/1 |
| 7 | 4.4 (rAP) | 1000 | <1 | | |

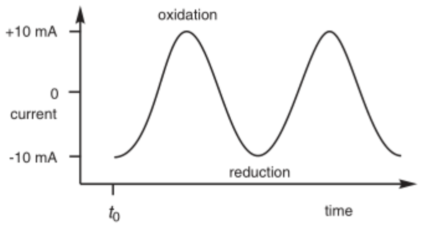
- the desired product **5** was observed at $V_p \geq 3.3$ V
- the product yield increased, and the unreacted **2** decreased until $V_p$ reached 4.4 V
- the chlorination side product was observed at 4.8 V due to the direct oxidation of **2**

Luo, L. et al. *Org. Lett.* **2020**, *22*, 6719−6723

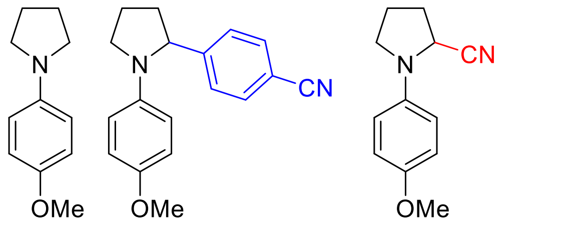
# Activation of starting materials/intermediates

- Selective amine functionalization by alternating current frequency



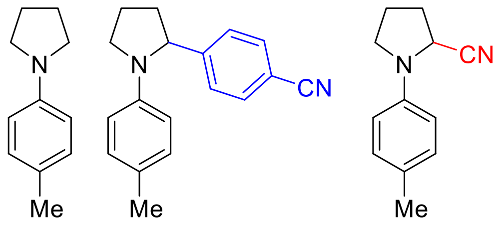



Sinusoidal waveform



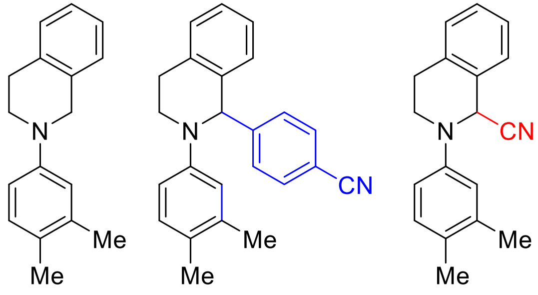
**1** **1a** **1b**

**AC** (10 Hz): 68%, 16% (4.3:1)
**DC**: 30%, 40% (0.8:1)



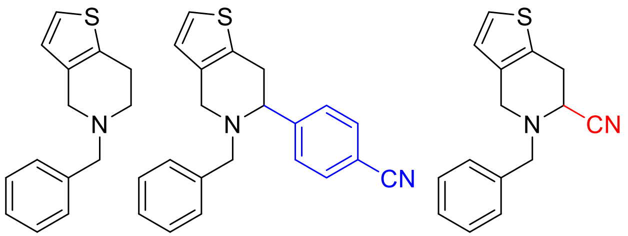
**7** **7a** **7b**

**AC** (450 Hz): 64%, 15% (4.3:1)
**DC**: 14%, 30% (0.5:1)



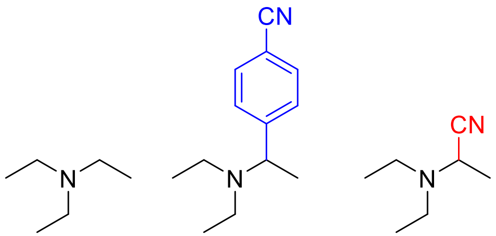
**24** **24a** **24b**

**AC** (250 Hz): 47%, 47% (1:1)
**DC**: 0%, 36% (>99)



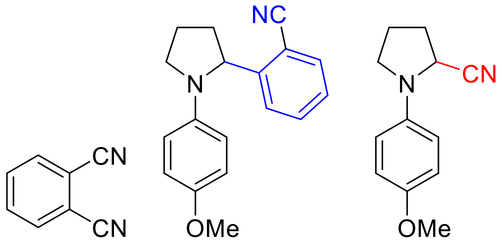
**28** **28a** **28b**

**AC** (200 Hz): 54%, 71% (0.8:1)
**DC**: 17%, 52% (0.3:1)



**32** **32a** **32b**

**AC** (200 Hz): 54%, 0% (>99)
**DC**: 0%, 0%



**35** **35a** **1b**

**AC** (10 Hz): 46%, 14% (3.3:1)
**DC**: 0%, 46% (>99)

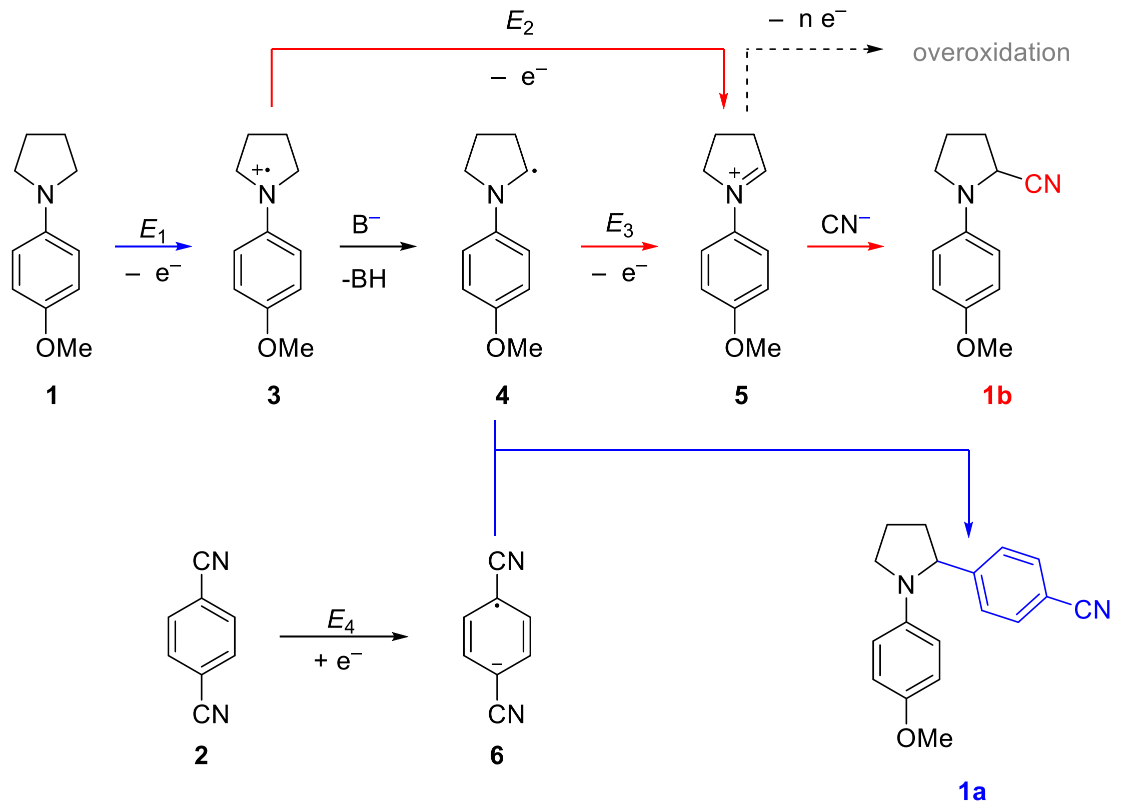
All yields were calculated considering 0.5 mmol of 1,2-dicyanobenzene as the limiting reagent.

Luo, L. et al. *J. Am. Chem. Soc.* **2022**, *144*, 9874−9882

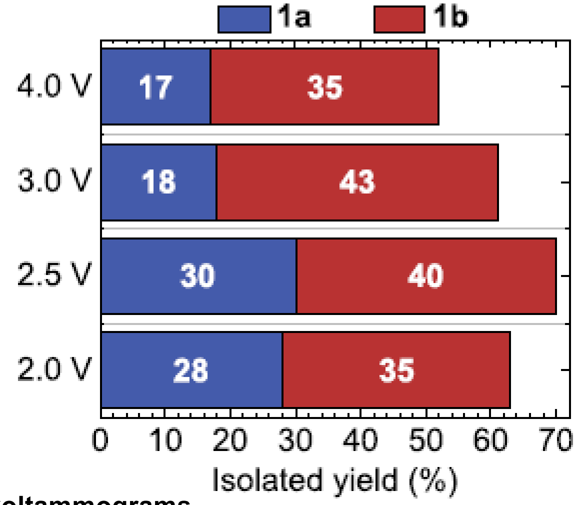
# Activation of starting materials/intermediates

- Selective amine functionalization by alternating current frequency

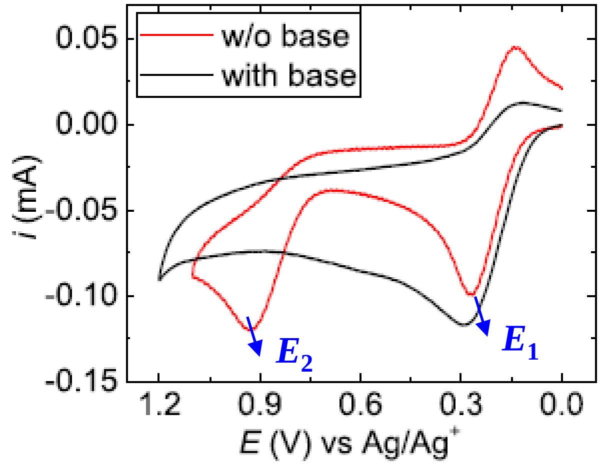
**A. One- and two-electron oxidation pathways**




**B. Isolated yields of 1a and 1b using DC electrolysis at different cell voltages.**




**C. Cyclic voltammograms**




$E_2 >> E_3$

Cyclic voltammograms of **1** in the presence (black) and absence (red) of the base, NaOAc, DMA containing 0.1 M LiClO4. Scan rate: 1 V/s.

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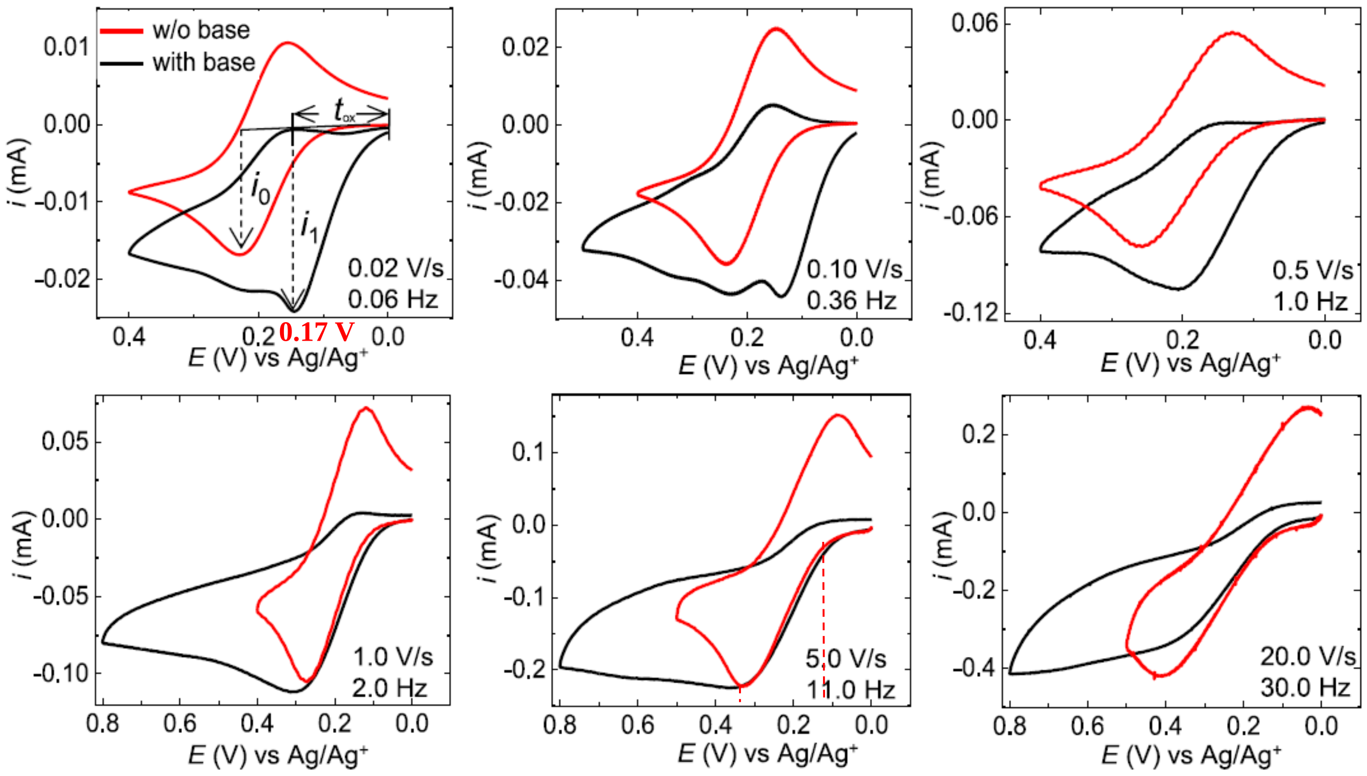
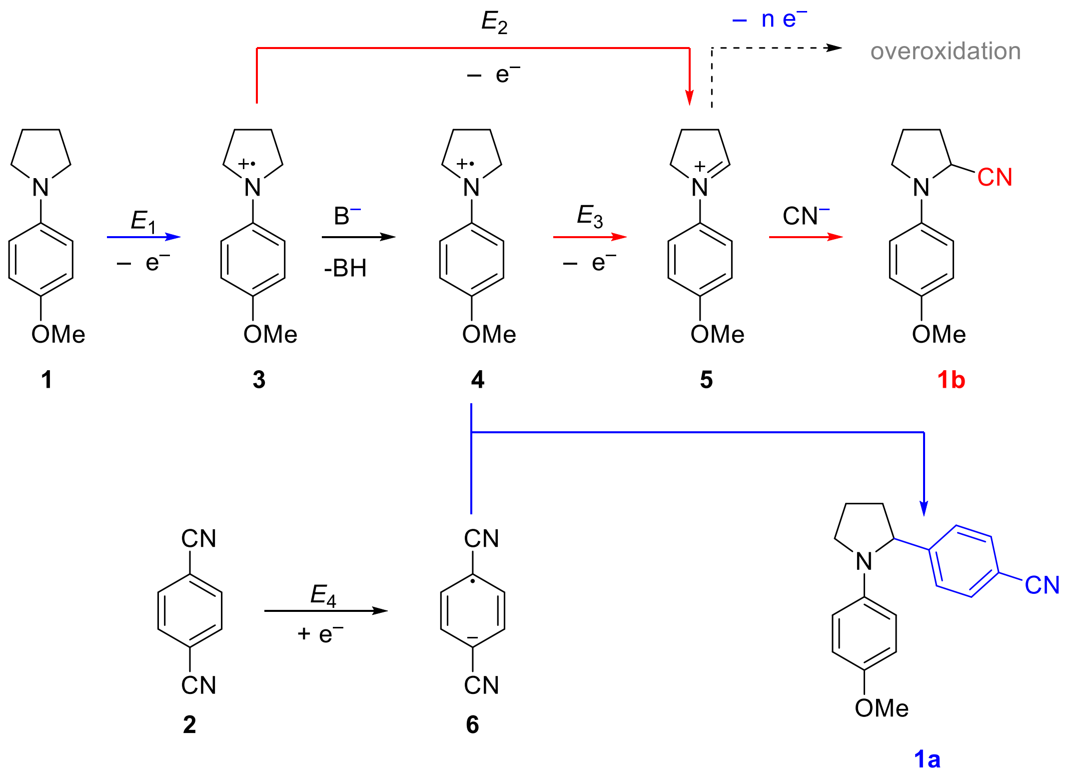
# Activation of starting materials/intermediates

- Selective amine functionalization by alternating current frequency

**D. Cyclic voltammograms of 1 at different scan rates and their equivalent AC frequencies.**




**A. One- and two-electron oxidation pathways**




1) scan rate: 0.02 V/s:
0.17 V/0.02 V/s = 8.5 s
frequency = 1/17 = 0.06 Hz

5) scan rate: 5 V/s:
0.22 V/5 V/s = 45 ms
frequency = 1/90 ms = 11 Hz

$\boldsymbol{i_0}$: $\boldsymbol{E_1}$
$\boldsymbol{i_1}$: $\boldsymbol{E_1}$ + ($\boldsymbol{E_2+E_3}$)

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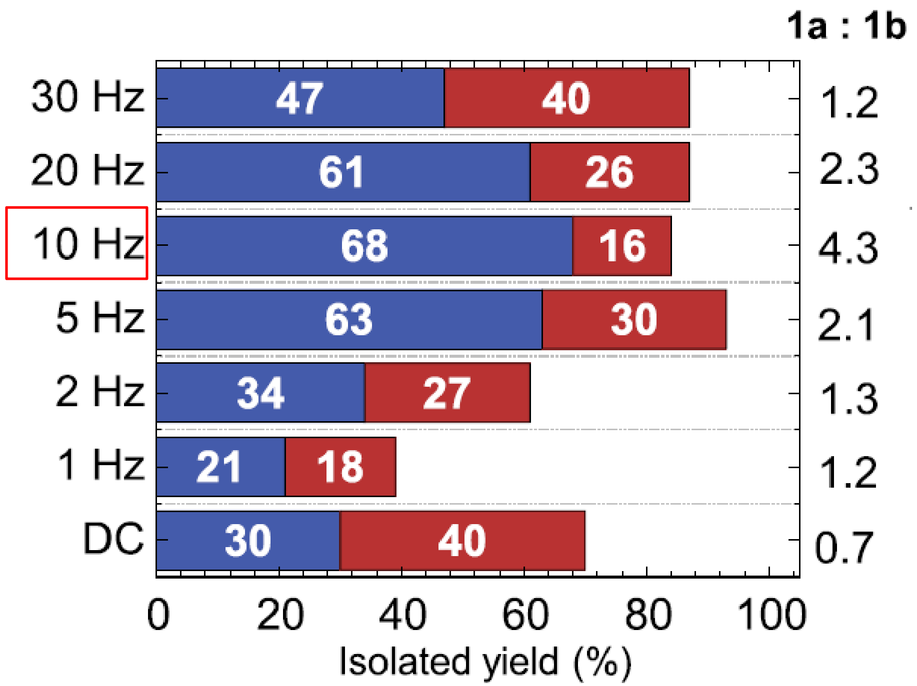
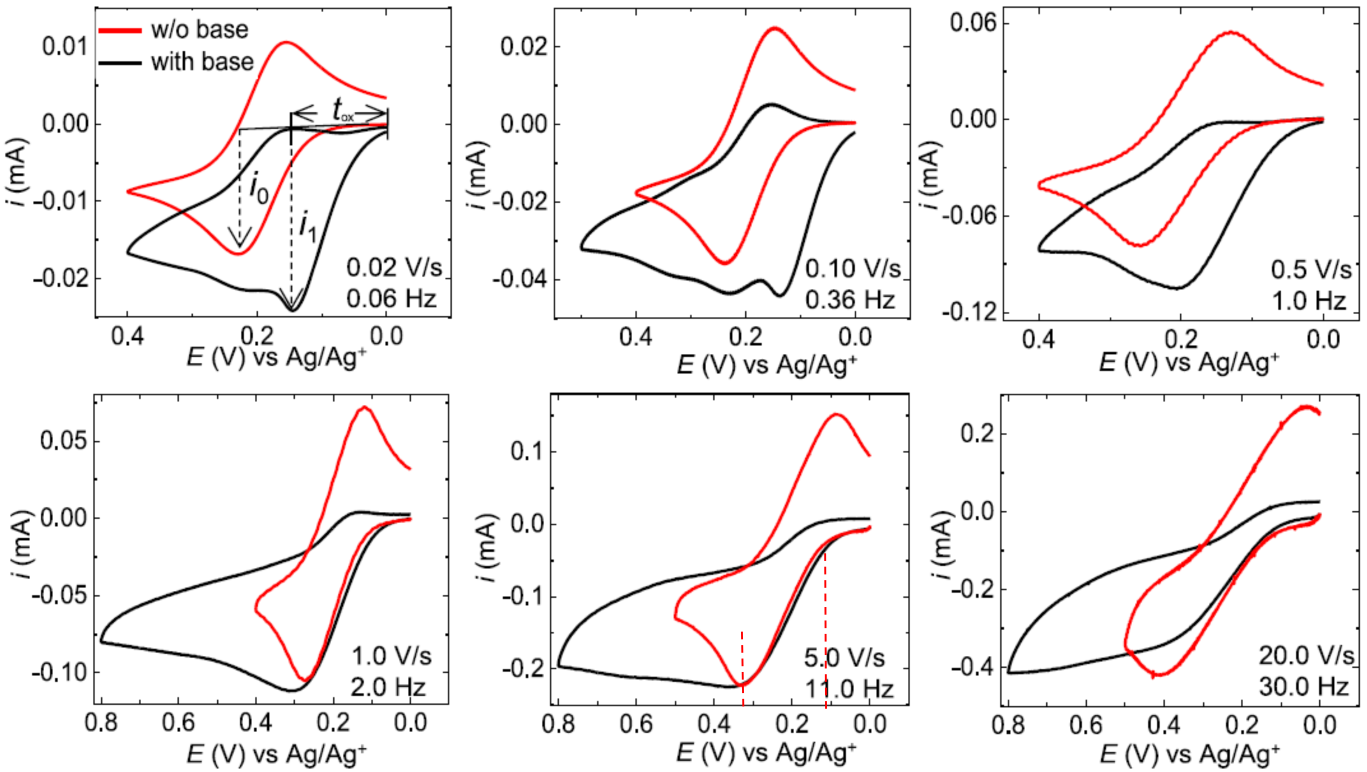
# Activation of starting materials/intermediates

- Selective amine functionalization by alternating current frequency

E. Isolated yields and selectivity of 1a and 1b at different AC frequencies




D. Cyclic voltammograms of 1 at different scan rates and their equivalent AC frequencies.




5) scan rate: 5 V/s:
0.22 V/5 V/s = 45 ms
frequency = 1/90 ms = 11 Hz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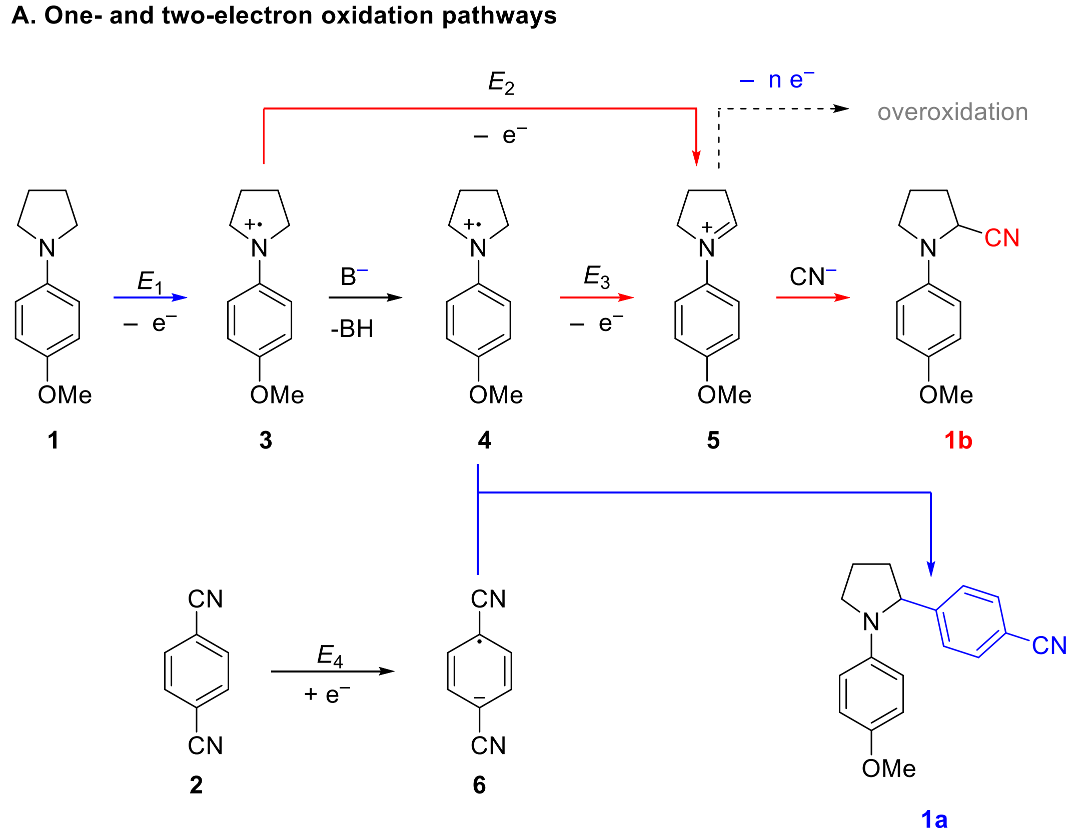
# Activation of starting materials/intermediates

- Selective amine functionalization by alternating current frequency




- Due to the slow deprotonation of **3**, a portion of **3** formed in the positive half-cycle cannot be immediately deprotonated and thus stays intact until the subsequent negative half-cycle.

- In the negative half-cycle, deprotonation continues but the further oxidation of **4** to **5** is prohibited, thereby shifting the product selectivity toward **1a**.

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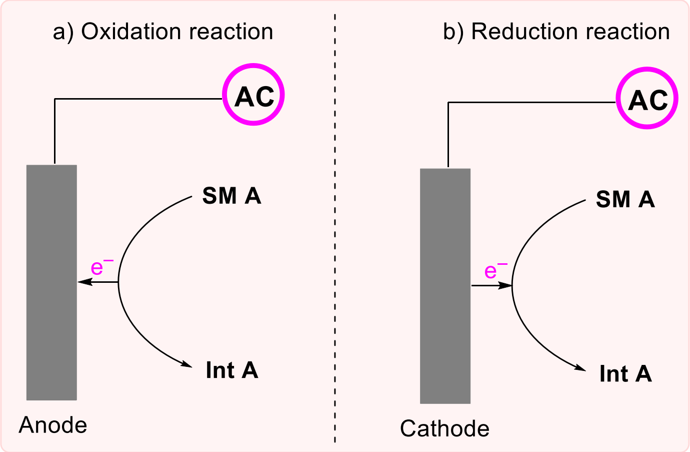
# 2.2 AC-promoted oxidation or reduction reaction on electrodes

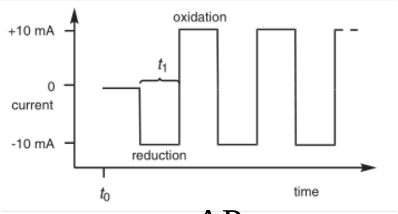
- 2.2 AC-promoted oxidation or reduction reaction on electrodes

AC-promoted oxidation or reduction reaction on electrodes

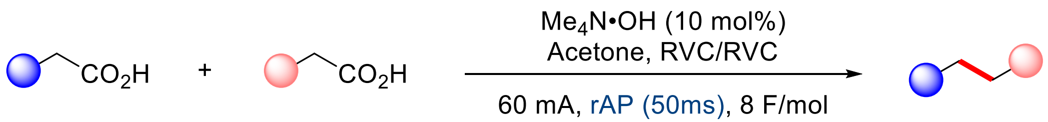


# AC-promoted oxidation or reduction reaction on electrodes

- Overcoming the limitations of Kolbe coupling with waveform-controlled electrolysis

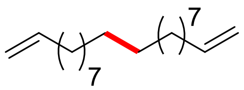



rAP



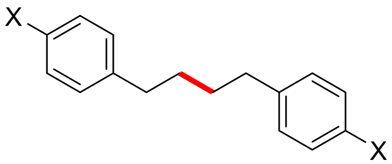

- No activation of carboxylic acids
- No requirement of Pt electrode
- Upconversion of biomass-derived carboxylic acids

Bio-derived



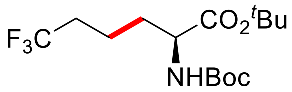

**1**: 63%
**[DC]**: <5%
**[Pt Kolbe]**: 0%
200 mmol: 65%

Bio-derived



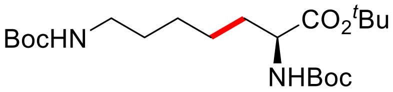

X = Br (**2**) 49%, OAc (3) 42%
**[DC]**: 0% (**2, 3**)
**[Pt Kolbe]**: 0% (**2, 3**)

Trifluoronorleucine




**4**: 58%[a]
25 gram scale: 53%

Lipidic amino acid




**5**: 47%[b]

**[DC]**: the same conditions at 60mA (DC) 8 F/mol instead of rAP. **[Pt Kolbe]**: Pt/Pt electrodes, 10 mol% MeONa, MeOH, 60mA (DC) 8 F/mol

[a] Asp (0.1 mmol,1 equiv.), the second carboxylic acid (6 equiv.) [b] Asp (0.1 mmol,1 equiv.), the second carboxylic acid (3 equiv.)

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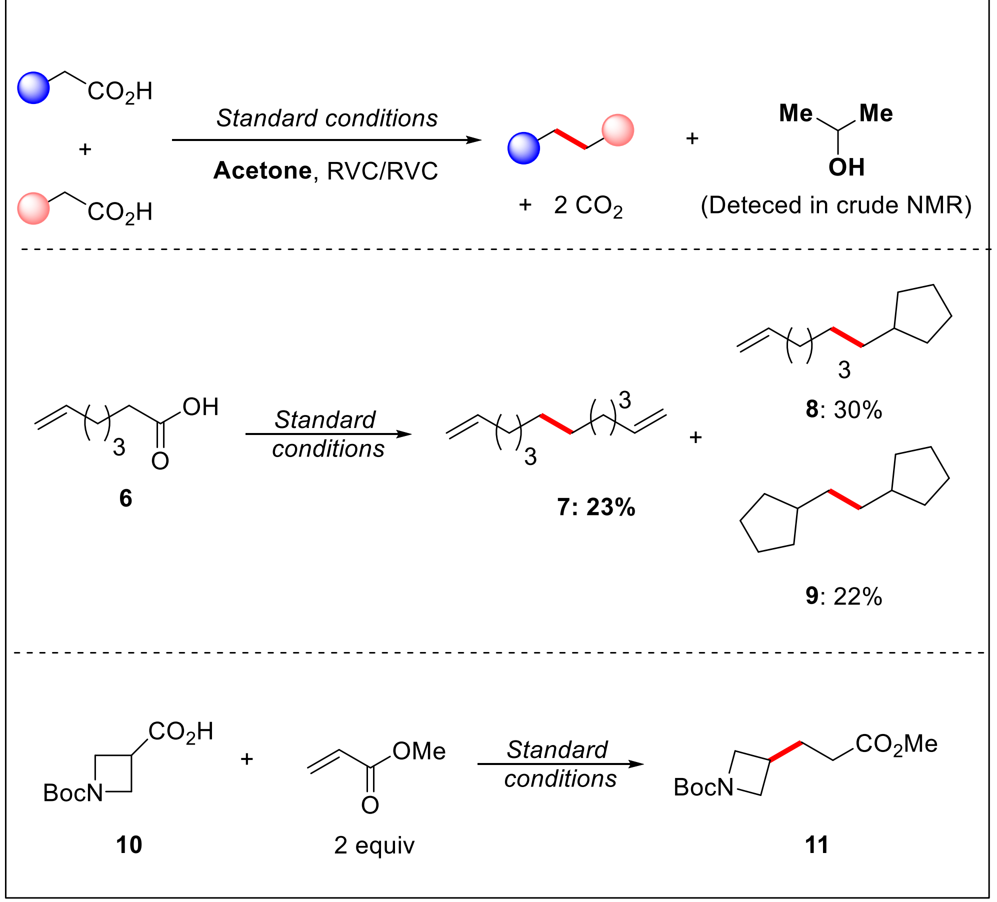
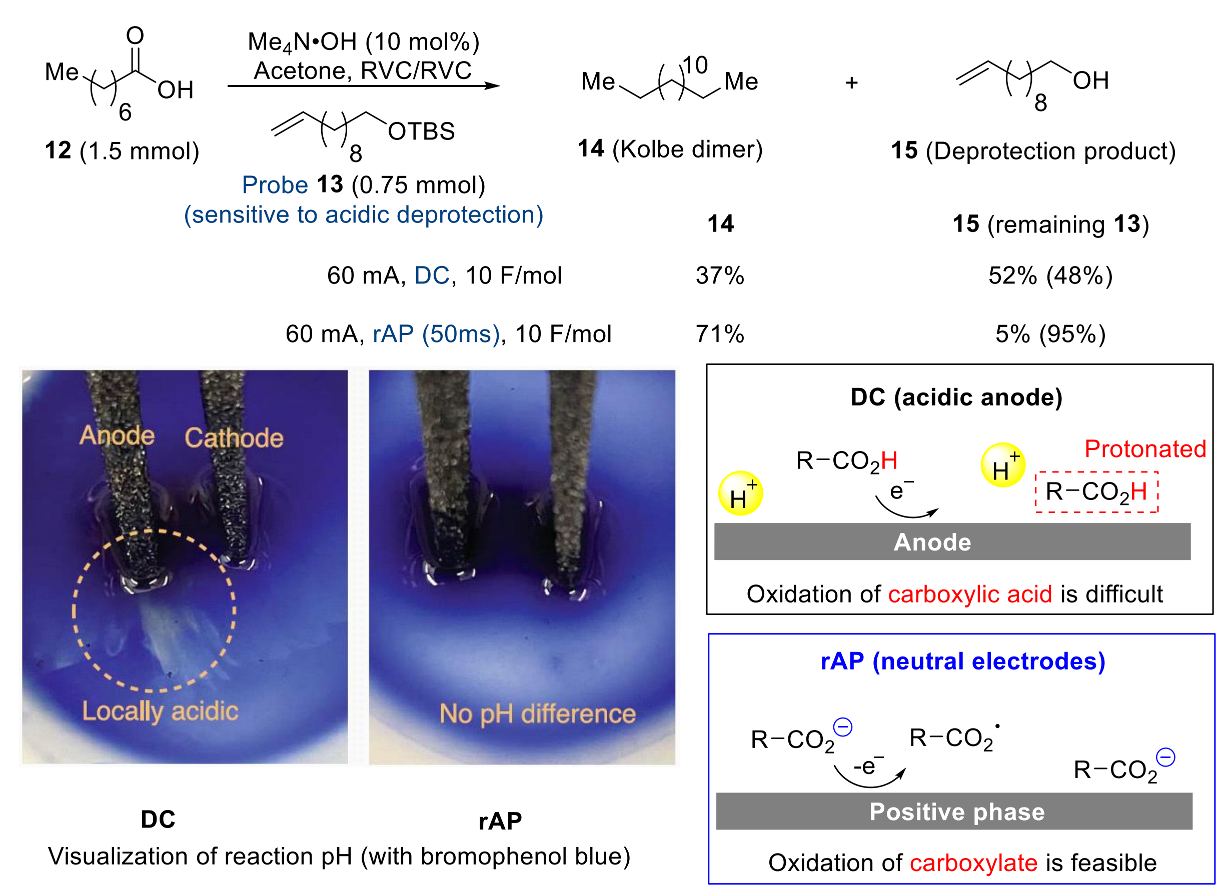
# AC-promoted oxidation or reduction reaction on electrodes

- Overcoming the limitations of Kolbe coupling with waveform-controlled electrolysis ------ **mechanistic studies**

**(a) Overall reaction and proof of free radical generation**



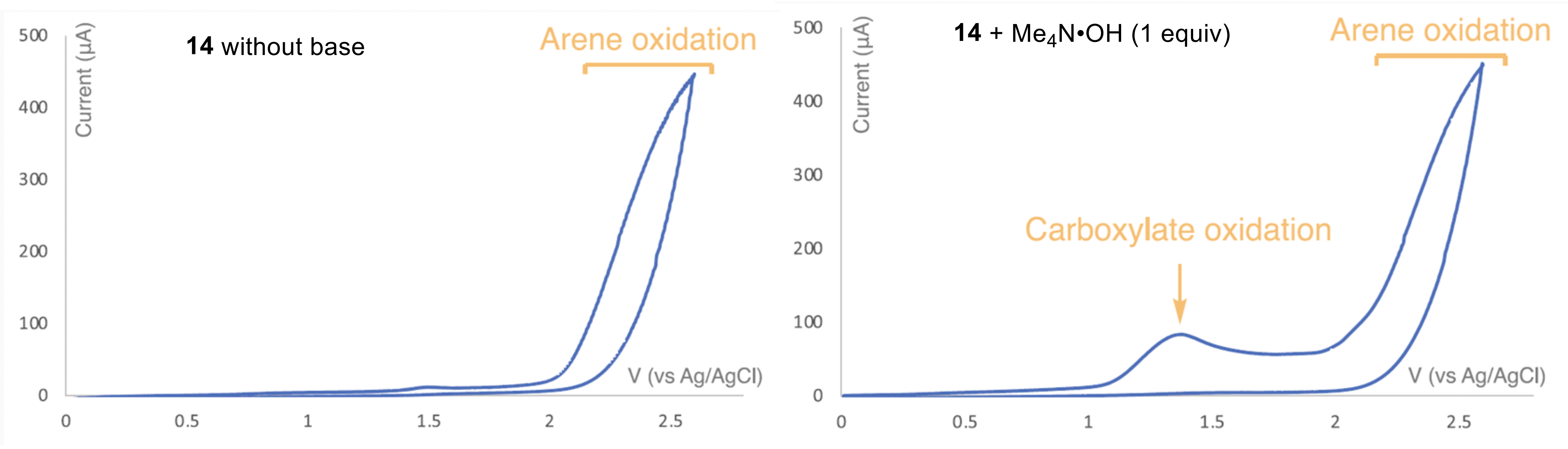

**(b) DC vs. rAP: Differing pH surrounding the electrodes drives reactivity enhancement**

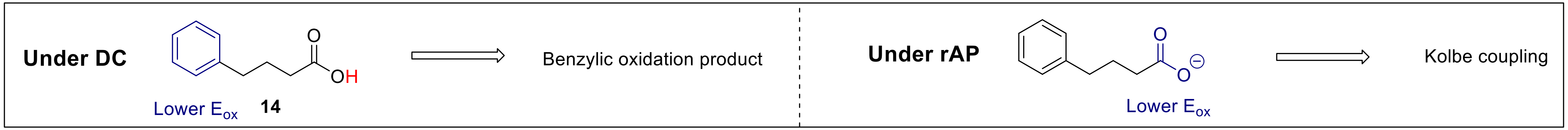



Baran, P. S. et al. *Science* **2023**, *380*, 81-87.

# AC-promoted oxidation or reduction reaction on electrodes

- Overcoming the limitations of Kolbe coupling with waveform-controlled electrolysis ------ **mechanistic studies**
  - (c) Cyclic voltammograms of **14** with or without addition of a base.

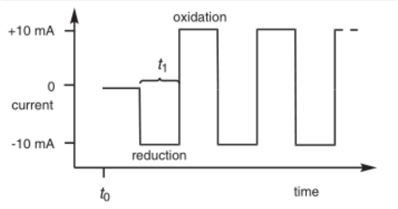


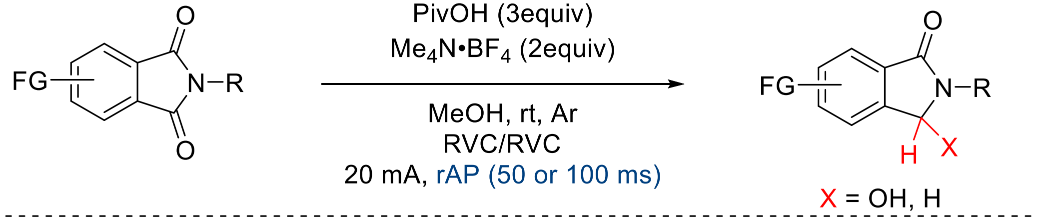

Baran, P. S. et al. *Science* **2023**, *380*, 81-87.

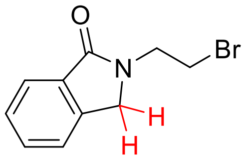
# AC-promoted oxidation or reduction reaction on electrodes

- Chemoselective reduction of phthalimides via rAP

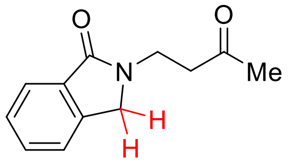



rAP

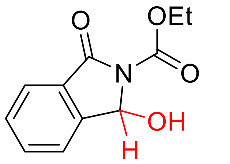


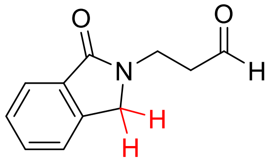
**1**: 53% (DC: <5%)



**2**: 67% (DC: 17%)



**3**: 68% (DC: <5%)



**4**: 45% (DC: 0%)

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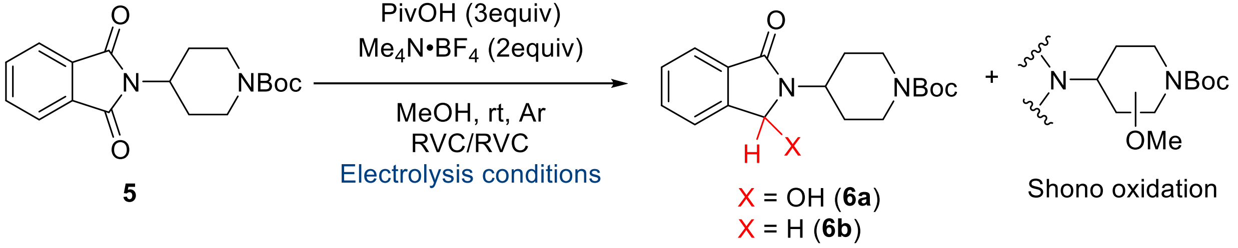
# AC-promoted oxidation or reduction reaction on electrodes

- Chemoselective reduction of phthalimides via rAP




| Entry | Electrolysis conditions | SM% | **6a**% | **6b**% | Shono oxidation |
|---|---|---|---|---|---|
| 1 | 20 mA or 5 mA, DC, 20 F/mol | 0 | 0 | 0 | Yes |
| 2 | 20 mA, rAP (200 ms), 20 F/mol | 0 | 0 | 48 | Yes |
| 3 | 20 mA, rAP (100 ms), 20 F/mol | 0 | 0 | 60 | No |
| 4 | 20 mA, rAP (50 ms), 20 F/mol | 0 | 0 | 62 | No |
| 5 | 20 mA, rAP (33 ms), 20 F/mol | <5 | 74 | 0 | No |
| 6 | 20 mA, rAP (25ms), 20 F/mol | 0 | 82 | 0 | No |
| 7 | 40 mA, rAP (25ms), 20 F/mol | 0 | 0 | 69 | No |
| 8 | 10 mA, rAP (100 ms), 20 F/mol | 0 | 69 | 0 | No |
| 9 | Divided cell, 10 mA, DC, 10 F/mol | 75 | 7 | 0 | No |
| 10 | Zn sacrificial anode, 5 mA, DC, 20 F/mol | 11 | 67 | 0 | No |

- Entries 1-6 : the longer the pulse is, the more redox reactions proceed (an infinite pulse duration being equal to DC).
- Entry 6 vs 7 or entry 3 vs 8: the reduced current efficiency with a short pulse can be increased by larger current.

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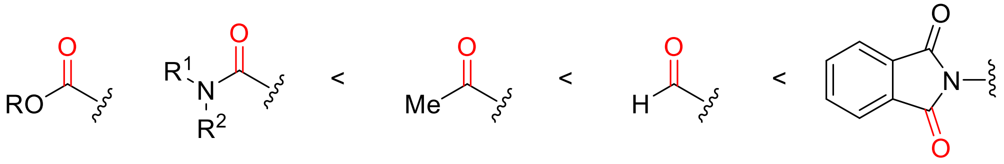
# AC-promoted oxidation or reduction reaction on electrodes

- Chemoselective reduction of phthalimides via rAP

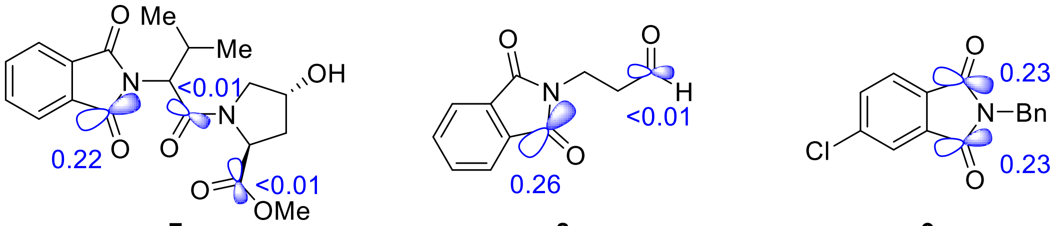
**A. Chemoselectivity follows reduction potential and can be predicted by FMO analysis**

Reduction potential




$E_{red}$ < −2.5 V $E_{red}$ ~ −2.4 V $E_{red}$ ~ −1.8 V $E_{red}$ ~ −1.4 V

LUMO coefficients ($2p_z$)

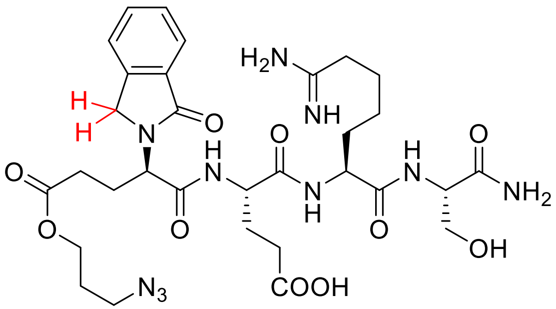



7 8 9

**Exp. results**

| 7 | 8 | 9 |
|---|---|---|
| Reduction of phthalimide | Reduction of phthalimide | Mixture of rigioisomers |

**B. Chemoselective reduction of tetrapeptide 1 with rAP**




Reduction of **1** to **14**
40 mA, rAP (25 ms): 52% NMR (14% isolated)
Complex mixture with DC

rAP chemoselectivety = Redox potential + reaction rate

- rAP would enable differentiation of redox reactions based on their relative reaction rates, not only based on their redox potentials

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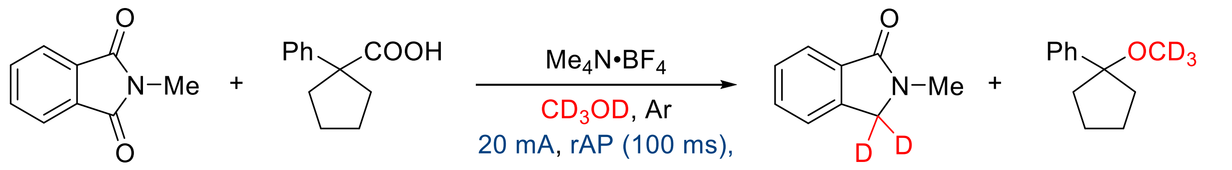
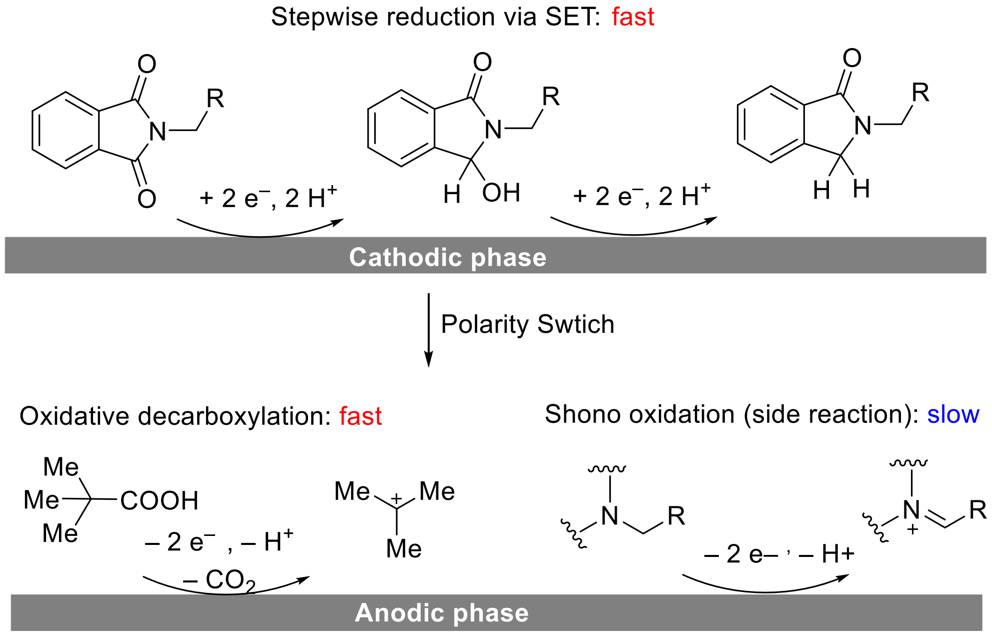
# AC-promoted oxidation or reduction reaction on electrodes

- Chemoselective reduction of phthalimides via rAP

**C. Deuterium labeling study to identify the source of proton and the fate of carboxylic acid**




**D. Proposed mechanism**

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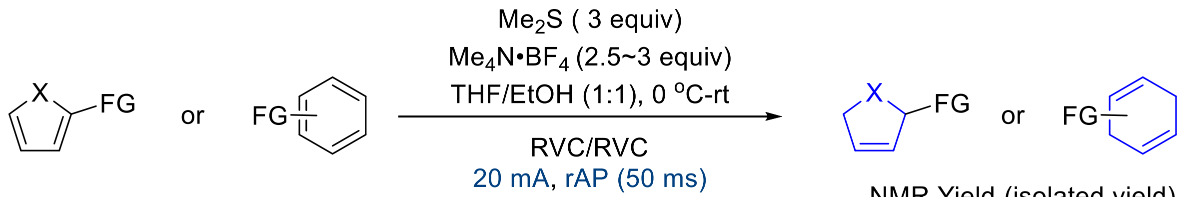
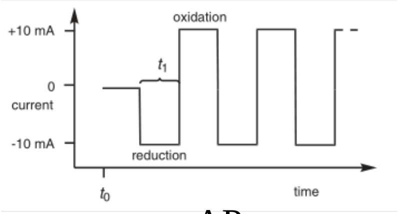
# AC-promoted oxidation or reduction reaction on electrodes

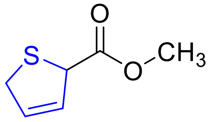
- Chemoselective (hetero)arene electroreduction enabled by rAP



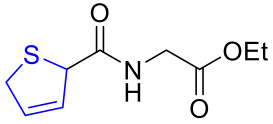

NMR Yield (isolated yield)



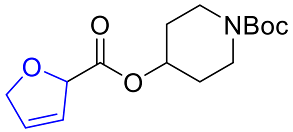

rAP



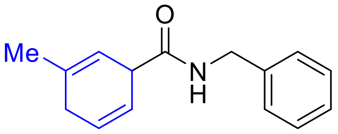

**2**: (83%)
[DC]: <5%



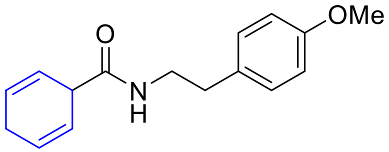

**3**: 67% (62%)
[DC]: 7%



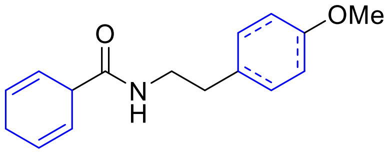

**4**: 67% (56%)
[DC]: <5%




**5**: 43% (42%)
[DC]: <5%




**6**: 44% (39%)
[DC]: <5%




**[Chemical Birch]**: 30% (**5**)
+ 38% over reduction

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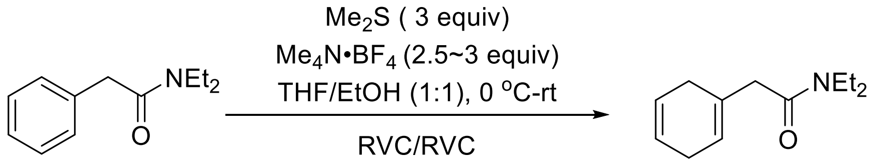
# AC-promoted oxidation or reduction reaction on electrodes

- Chemoselective (hetero)arene electroreduction enabled by rAP

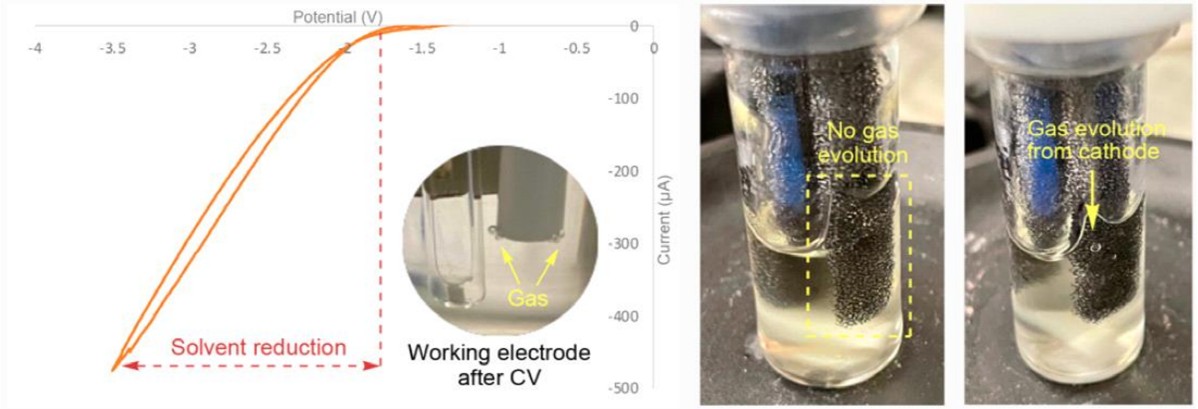
**A. rAP is more reductive than DC**




**7** $E_{red}$ < -3 V

**8**

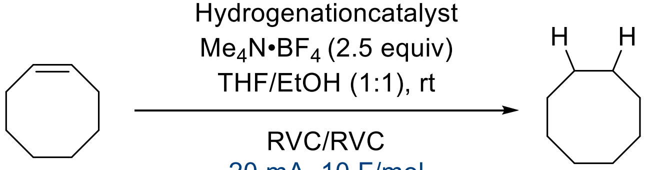
**[rAP]**: 45% (SM 42%)
**[DC]**: <5% (SM 75%)




**CV of reaction solvent (THF/EtOH = 1/1)** **rAP** **DC**

**B. Higher reductive ability by rAP is originated from suppression of H⁺ reduction**

1. Direct detection of $H_2$

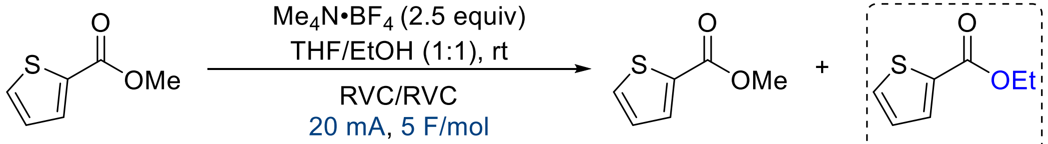



**9** **10**

| | |
|---|---|
| **No Pd/C** | **[rAP]**: 0% (SM >95%)<br>**[DC]**: 0% (SM 63%) |
| **With Pd/C** | **[rAP]**: 0% (SM >95%)<br>**[DC]**: 14% (SM 44%) |

2. pH change in the reaction probed by transesterification

Transesterification




| | **1** | **2** | **11** |
|---|---|---|---|
| **[rAP] (68% conv.)** | | 55% | 0% |
| **[DC] (80% conv.)** | | 17% | 23% |

⇒ rAP creates less basic environment due to the suppression of proton reduction

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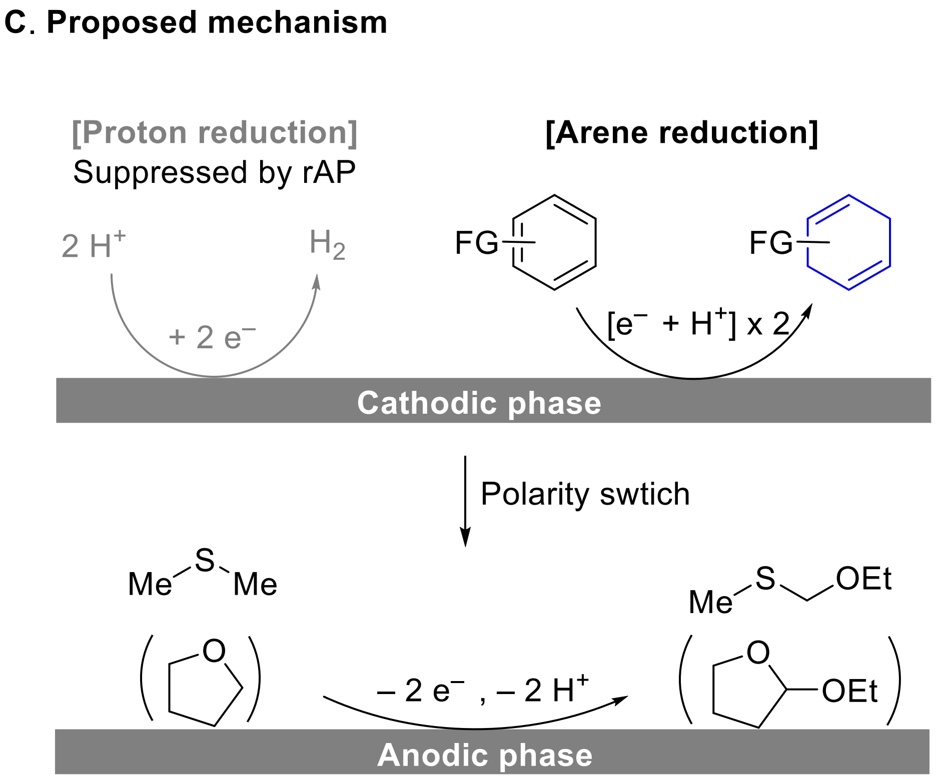
# AC-promoted oxidation or reduction reaction on electrodes

- Chemoselective (hetero)arene electroreduction enabled by rAP




- Proton reduction, a pathway that normally competes to diminish reactivity toward arene reduction, is largely suppressed by applying rAP

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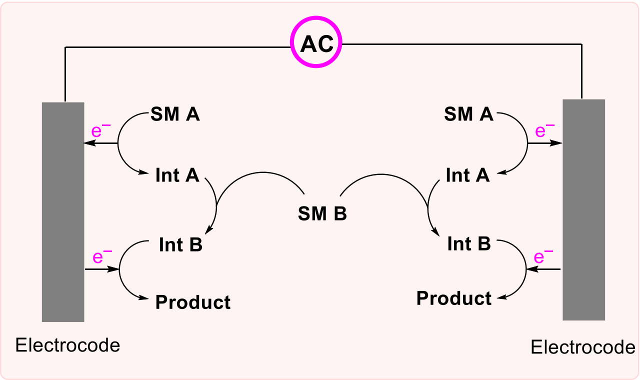
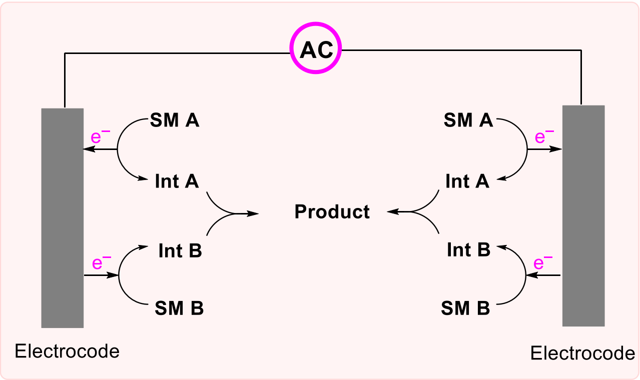
# 3. Summary and outlook

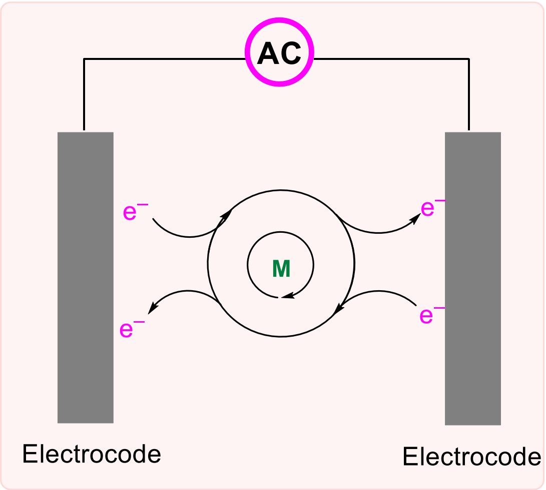
# Summary

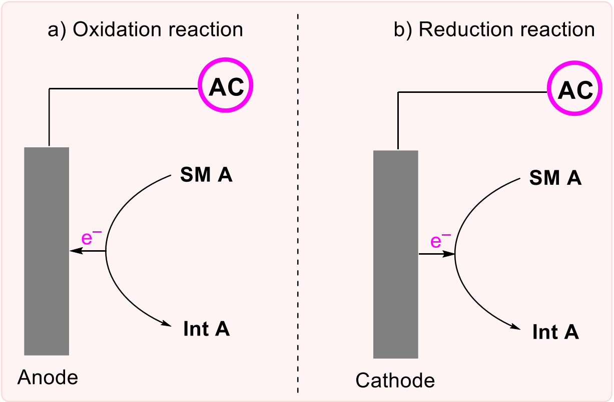
AC electrolysis

- AC-promoted paired electrolysis
  - Activation of starting materials/intermediates
  - Activation of metal catalysts
- AC-promoted oxidation or reduction reaction on electrodes



# Summary

- Advantages and challenges of AC electrolysis

## Advantages

- Realize oxidation and reduction on one electrode
- Minimize over-oxidation/reduction
- Overcome electrode passivation

## Challenges

- How to identify and understand the optimal conditions (i.e., AC frequency and waveform)
- A large reaction parameter space makes the reaction optimization challenging
- Lack of theories to guide the rational design of reaction parameters

# Outlook

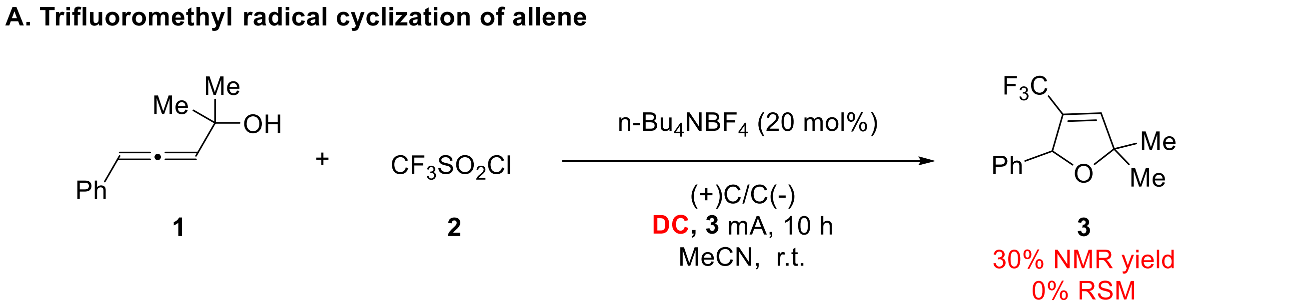
- Future of ACE

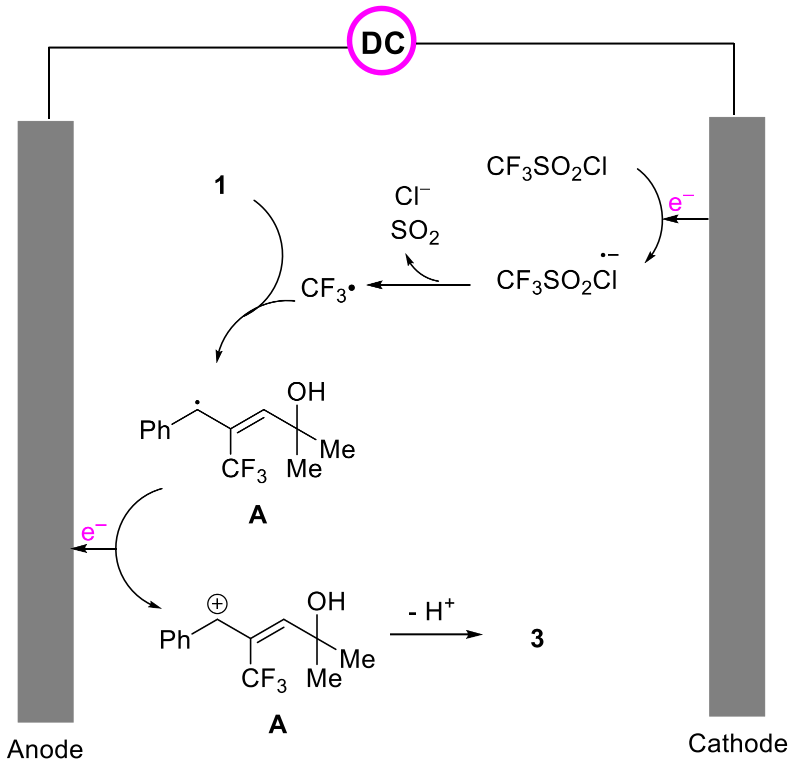
## Future of ACE

- AC electrochemical synthesis in flow
- Asymmetric AC electrolysis
- High-throughput experimentation
- To implement data-derived models through the use of modern artificial intelligence (AI) techniques

# Outlook

- Example---a candidate to use rAP

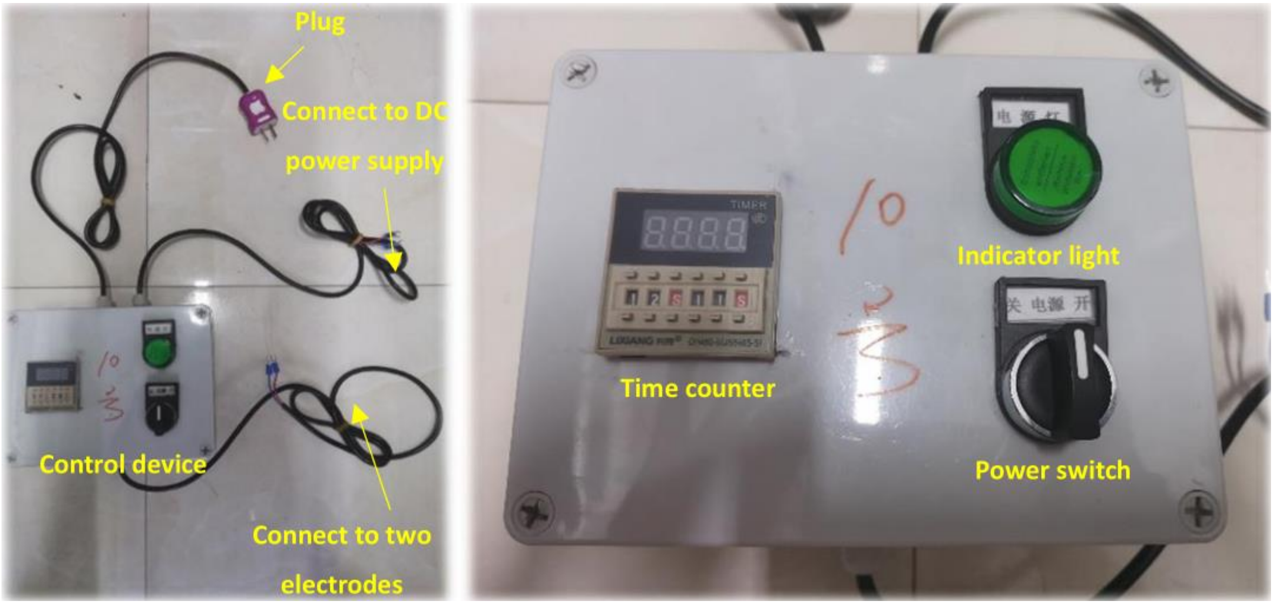



- rAP could prevent decomposition of **1**
- rAP could minimize over-oxidation/reduction of the radical intermediates

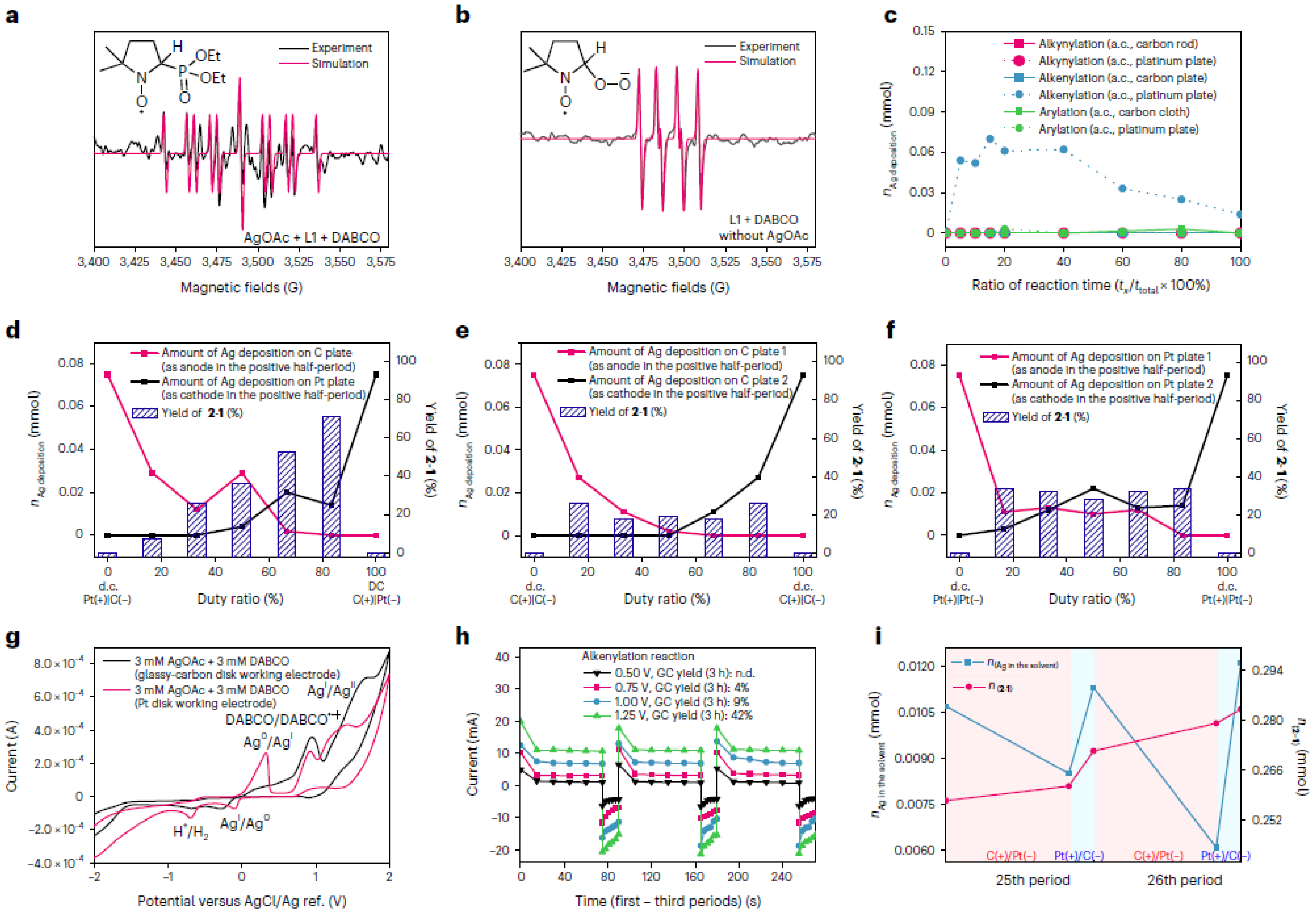
# Thank you for your attention!

# 附录 1




Lei, A. et al. *Nat. Synth.* **2023**, *2*, 172-181

# 附录 1




C: Ag°/Ag$^I$ (0.22 V), DABCO/DABCO$^{•+}$ (0.95 V), Ag$^I$/Ag$^{II}$ (1.72 V), Ag$^I$/Ag$^0$ (-0.29 V) and H$^+$/H$^2$ (-0.68 V)

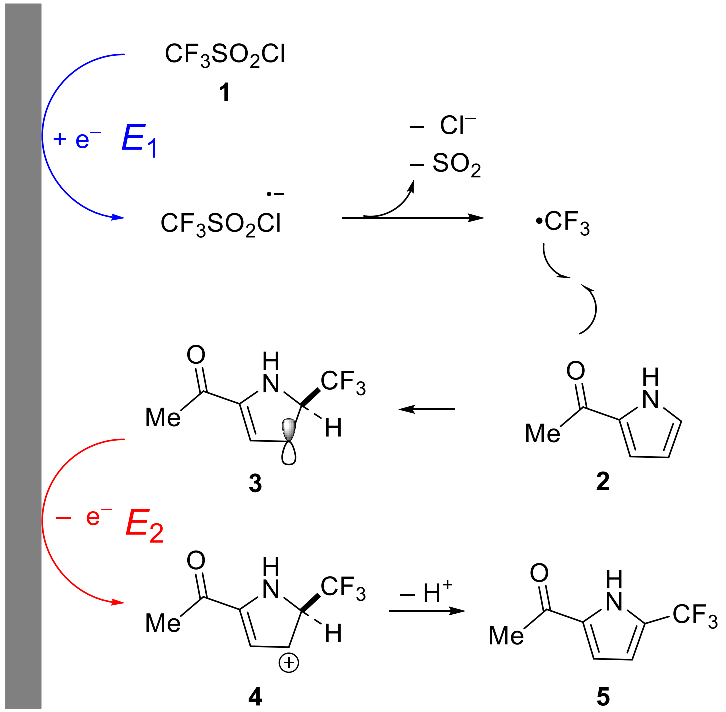
Pt: Ag°/Ag$^I$ (0.32 V), DABCO/DABCO$^{•+}$ (0.93 V), Ag$^I$/Ag$^{II}$ (1.42 V), Ag$^I$/Ag$^0$ (-0.10 V) and H$^+$/H$^2$ (-0.70 V)

Lei, A. et al. *Nature Synthesis* **2023**, *2*, 172-181

# Activation of starting materials/intermediates

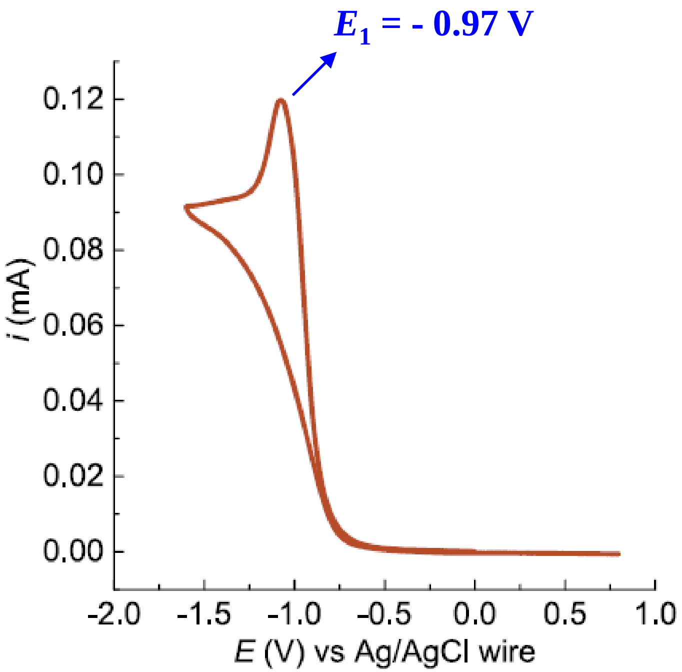
- Trifluoromethylation of (hetero)arenes enabled by rAP

**A. Proposed mechanism**

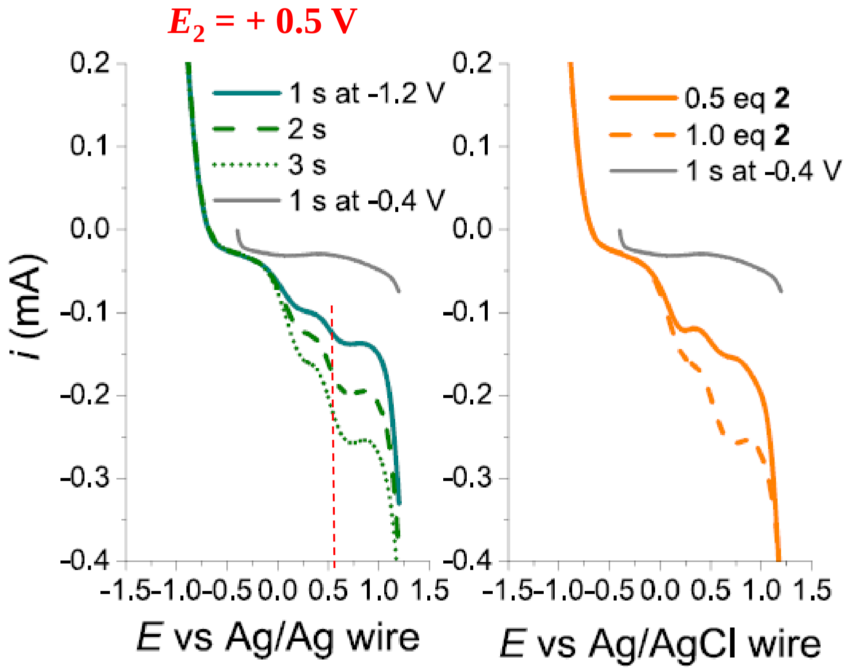



$|E_1 - E_2|$ = ~ 1.5 V

**B. Cyclic voltammograms of 1 in MeCN**




**C. Fast-scan linear sweep voltammograms of a mixture of 1 and 2.**



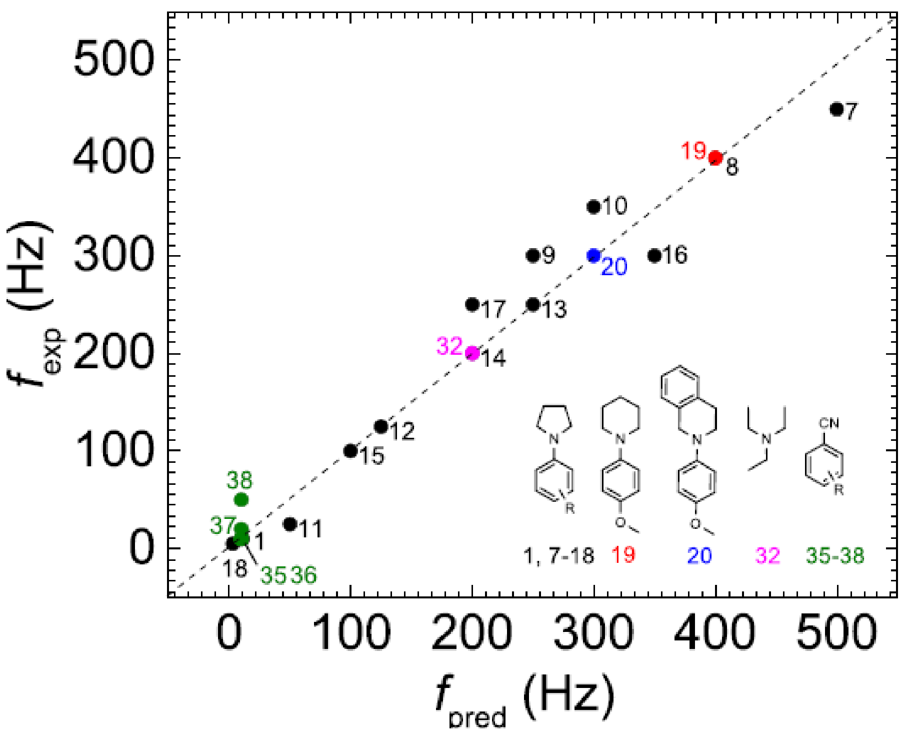

(C). Left panel: Electrode potential was held at −1.2 V for 1, 2, and 3 s followed by sweeping the potential positively to 1.2 at 20 V/s. Concentrations of **1** and **2** were both 0.25 M. Right panel: Different equivalents of **2** to **1** were added, and the holding time at −1.2 V was 3 s. Gray curve: Electrode potential was held at −0.4 V for 1 s before the potential sweep.

Luo, L. et al. *Org. Lett.* **2020**, *22*, 6719−6723

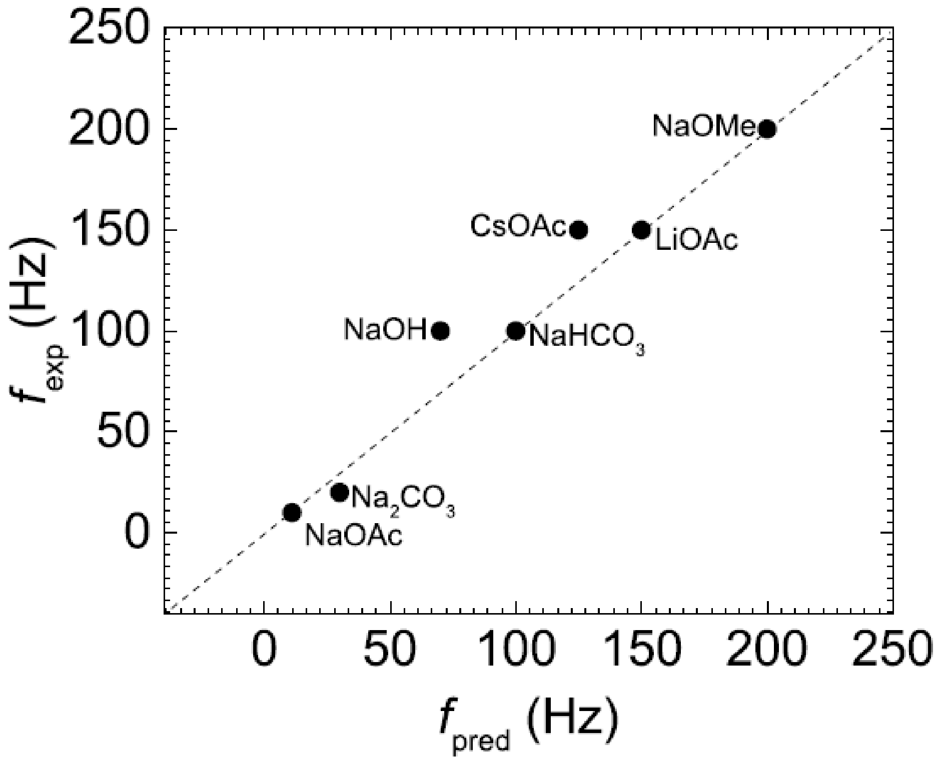
# Activation of starting materials/intermediates

- Selective amine functionalization by alternating current frequency

**E. Plot of $f_{exp}$ vs $f_{pred}$ for various tertiary amines and cyanoaromatics**




**E. Plot of $f_{exp}$ vs $f_{pred}$ pred for 1 with different bases**



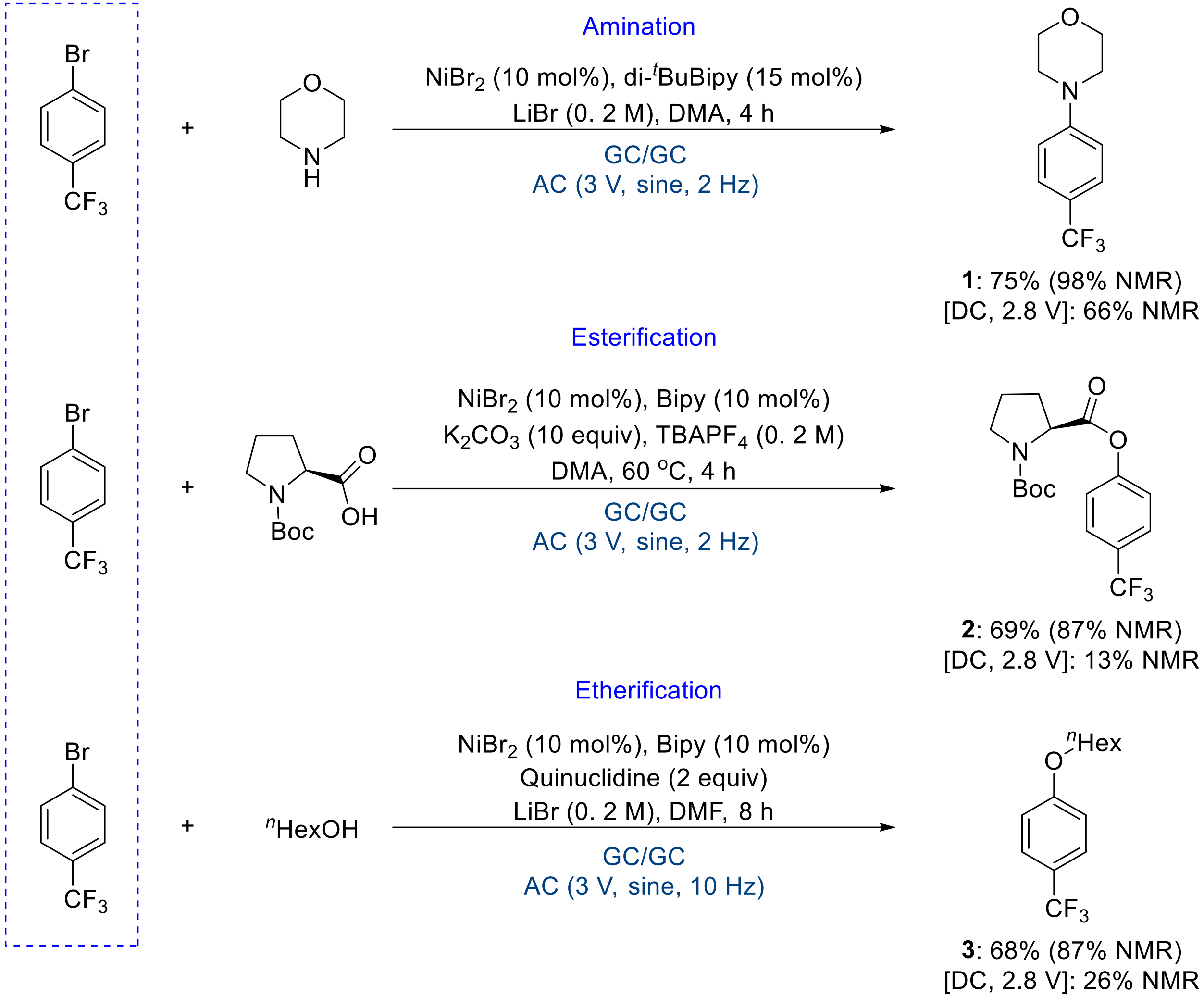

- Base strongly influences $f_{exp}$ : the deprotonation step plays an essential role in controlling the degree of amine oxidation and product selectivity during AC electrolysis.

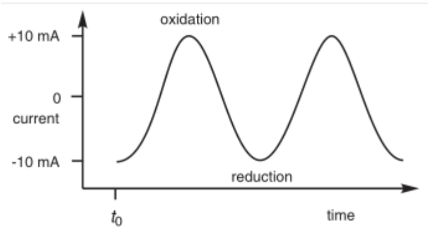
Luo, L. et al. *J. Am. Chem. Soc.* **2022**, *144*, 9874–9882

# Other examples

# Activation of metal catalysts

- Nickel-catalyzed cross-coupling via ACE



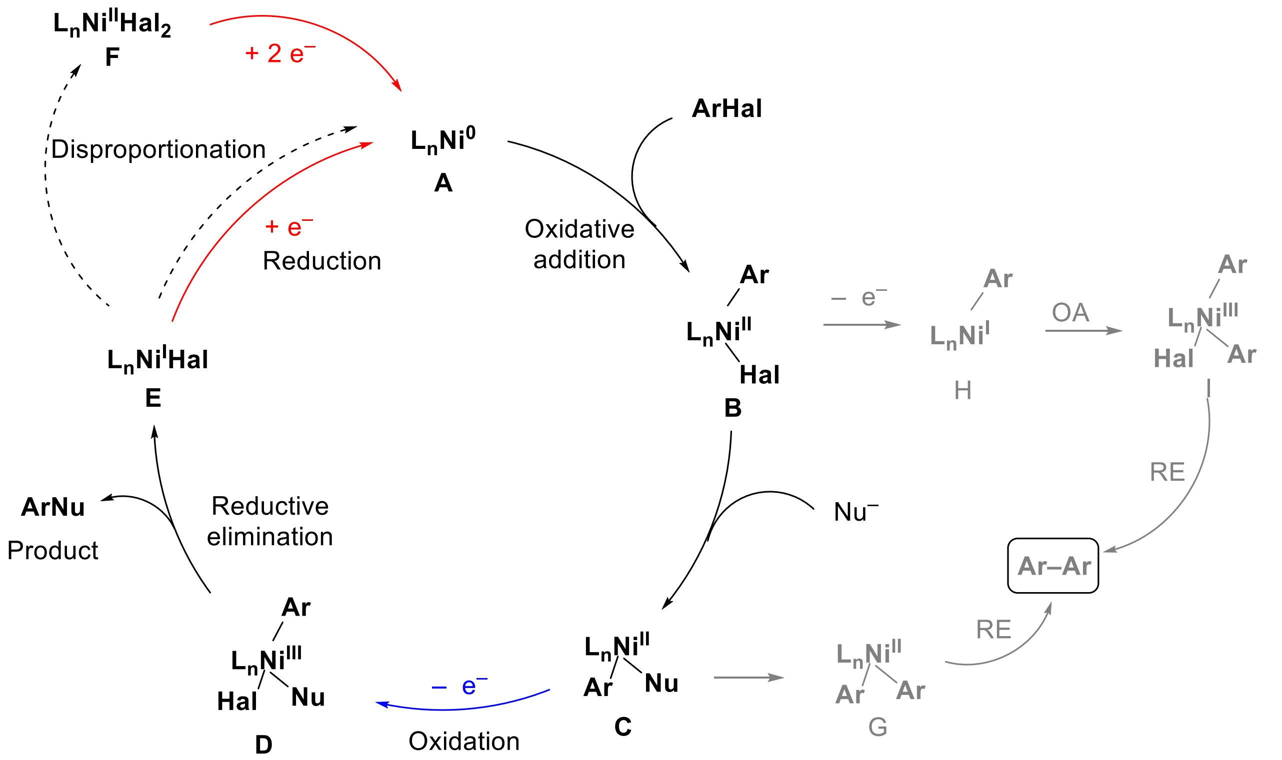

**Sinusoidal waveform**

Semenov, S. N. et al. *J. Org. Chem.* **2021**, *86*, 782−793

# Activation of metal catalysts

- Nickel-catalyzed cross-coupling via ACE

A. Proposed mechanism




**AC vs DC**：

(i) The **shorter lifetime** of $[Ni^{II}L(Ar)(Nu)]$ **(C)** species in the AC than in the DC experiments. $[Ni^{II}L(Ar)(Nu)]$ **(C)** does not have time to transform to the $\mathbf{[NiL(Ar)_2]}$ **(G)** intermediate, which affords diaryl coupling products by reductive elimination

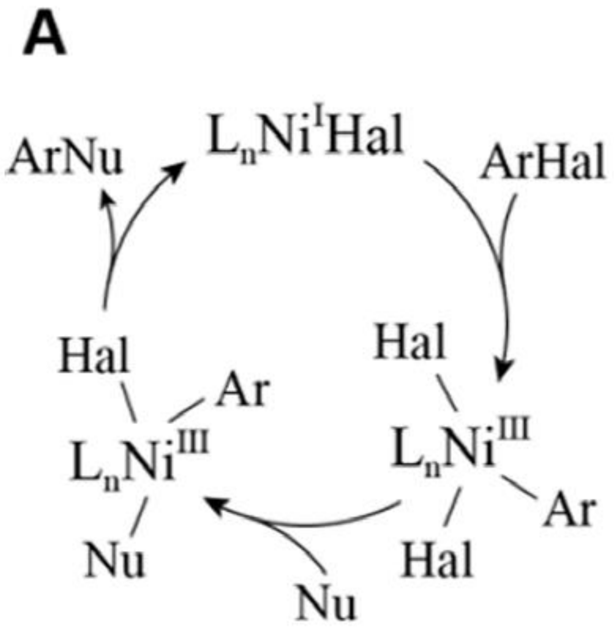
(ii) Fewer chances for the **second oxidative addition** in the AC than in the DC experiments (continuous strongly reducing environment near the cathode.

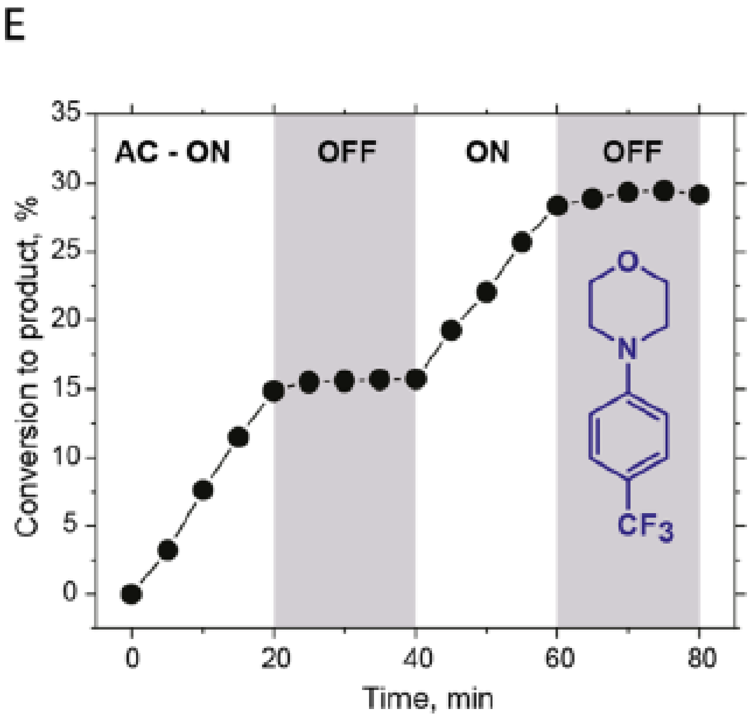
Semenov, S. N. et al. *J. Org. Chem.* **2021**, *86*, 782−793

# Activation of metal catalysts

- Nickel-catalyzed cross-coupling via ACE

**(A) Self-sustainable Ni(III)/Ni(I) cycle**

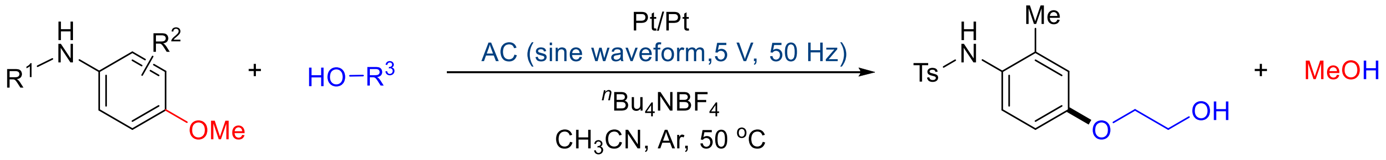


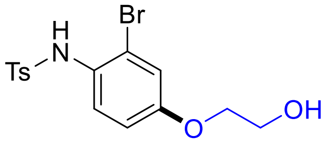




Semenov, S. N. et al. *J. Org. Chem.* **2021**, *86*, 782−793

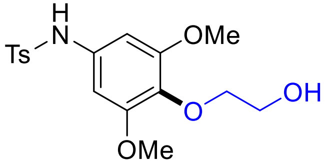
# Activation of starting materials/intermediates

- Formal C−O/O−H cross-metathesis of 4-alkoxy anilines with alcohols via ACE

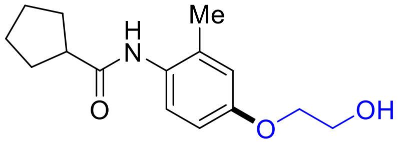


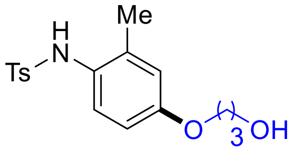
**1:** 72%



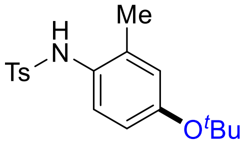
**2:** 50%



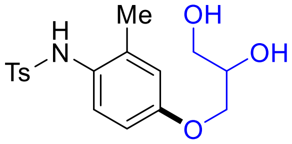
**3:** 87%



**4:** 70%

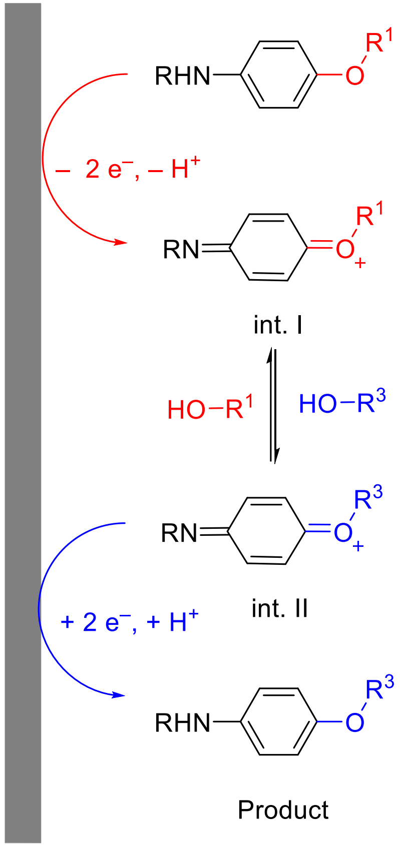


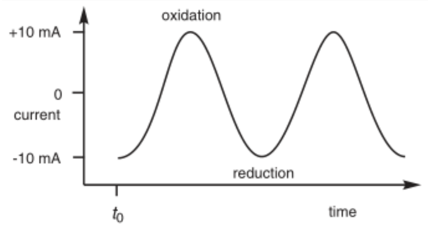
**5:** 65%



**6:** 52%

**A. Proposed mechanism**



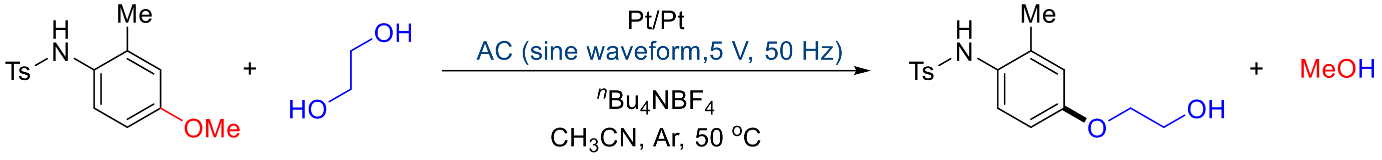

**Sinusoidal waveform**

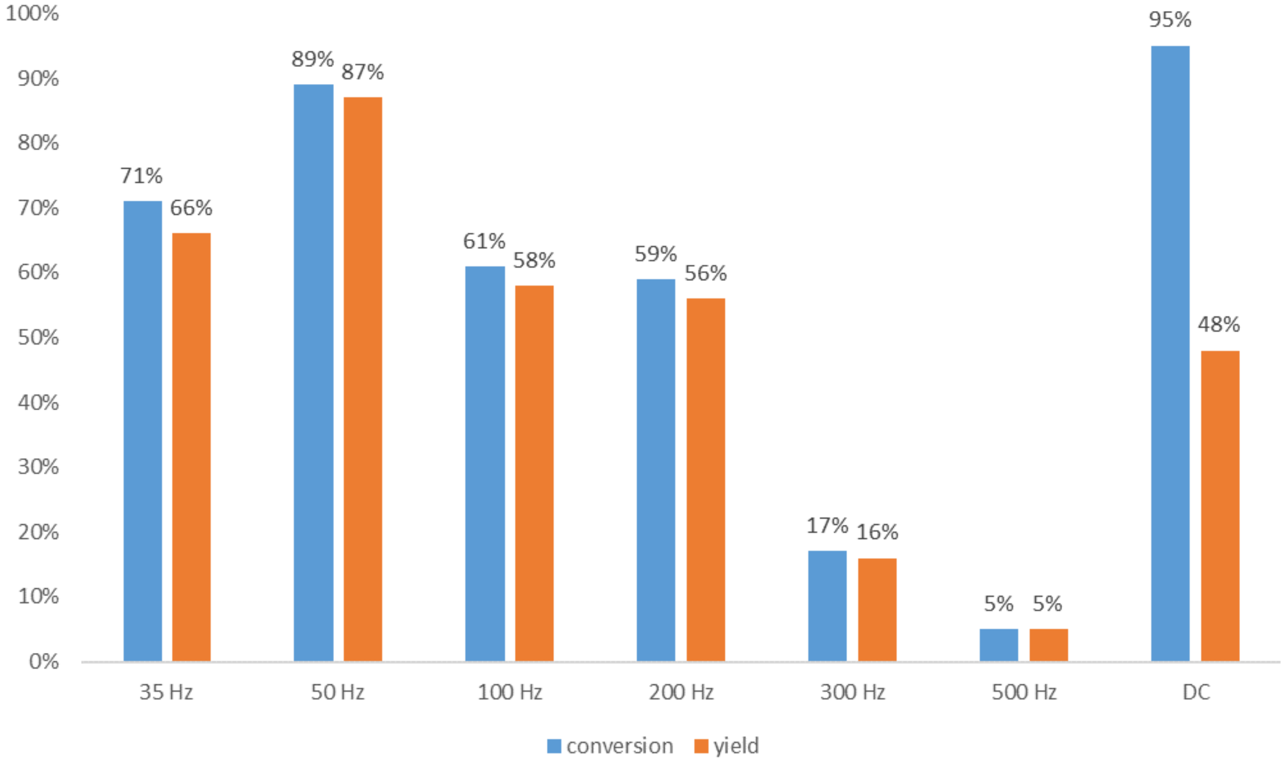
Lei, A. et al. *Angew. Chem. Int. Ed.* **2022**, *61*, e202201543

# Activation of starting materials/intermediates

- Formal C−O/O−H cross-metathesis of 4-alkoxy anilines with alcohols via ACE

**B. The reaction of 3 with 4 in the presence of different AC frequencies and DC**

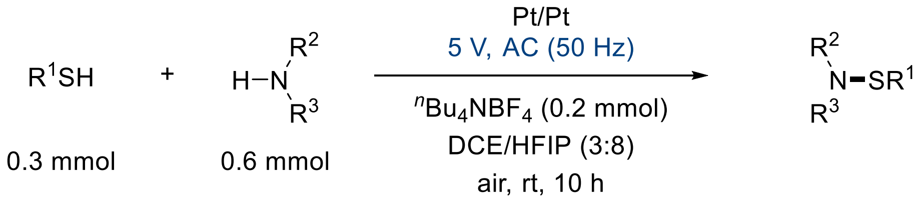


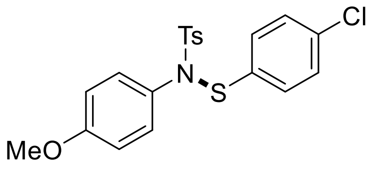




Lei, A. et al. *Angew. Chem. Int. Ed.* **2022**, *61*, e202201543

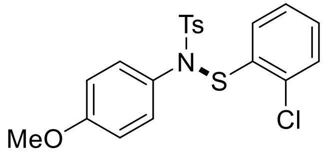
# Activation of starting materials/intermediates

- Radical–radical cross-coupling assisted N–S bond formation using AC

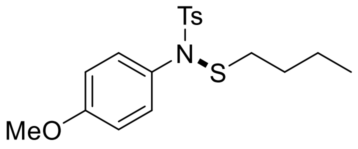


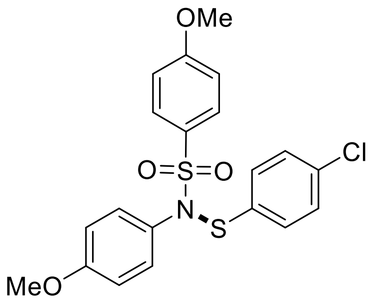

**3**, 93%



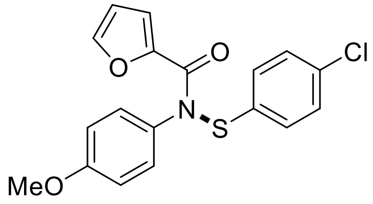

**4**, 93%



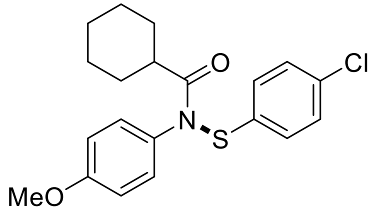

**5**, 63%



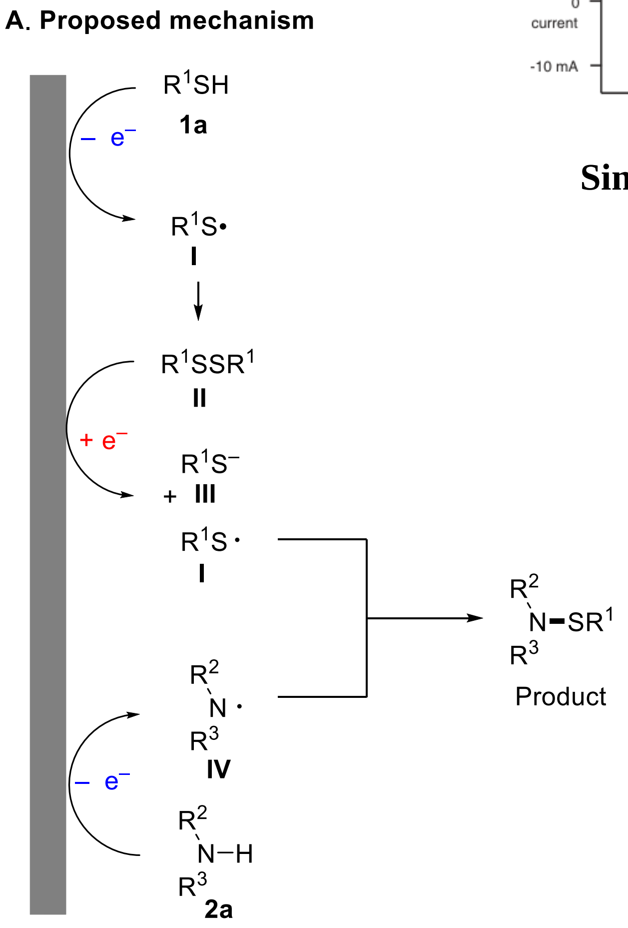

**6**, 83%

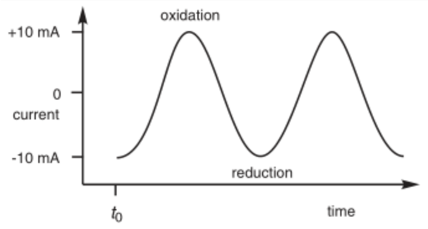



**7**, 61%




**8**, 81%



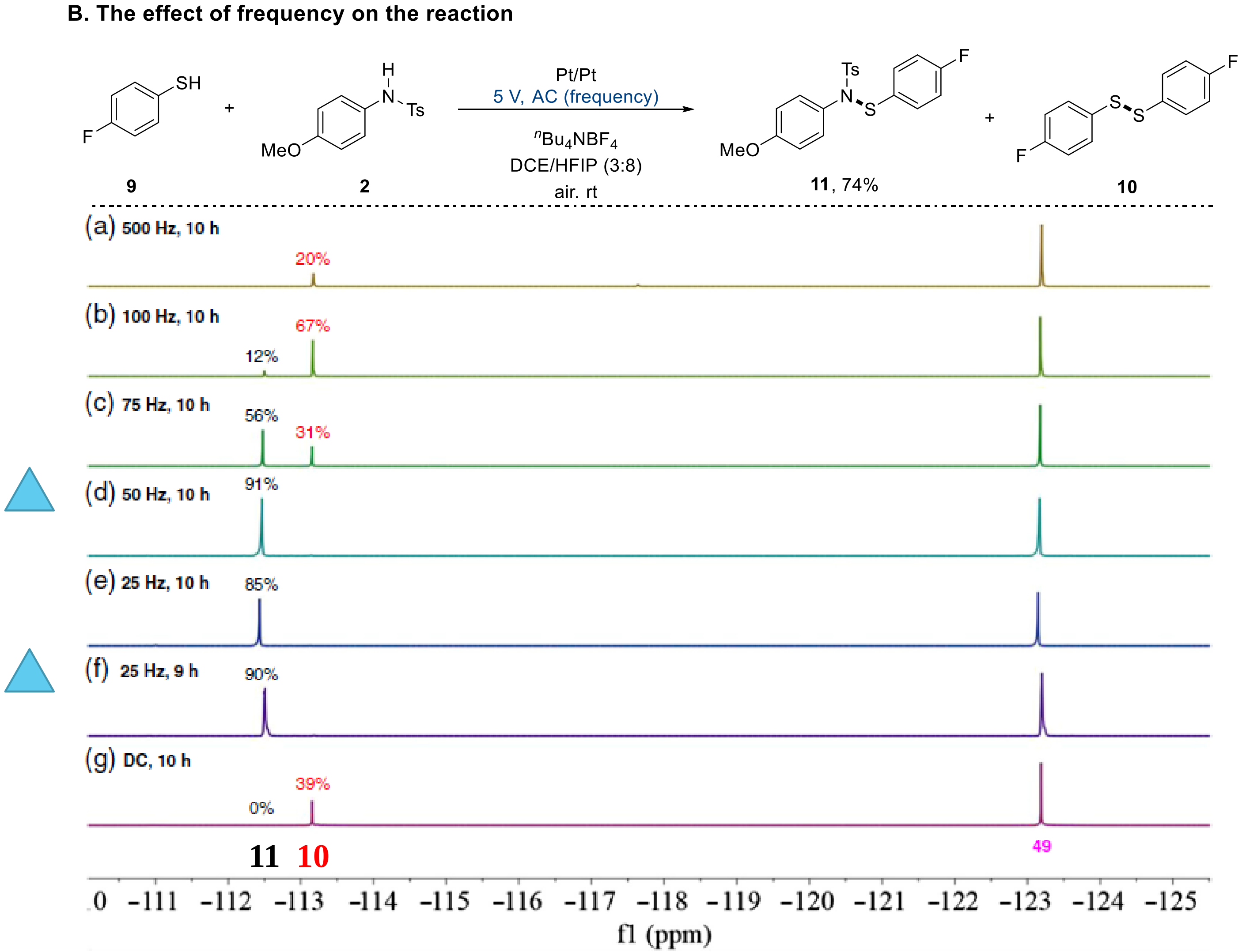




**Sinusoidal waveform**

Lei, A. et al. *CCS Chem.* **2022**, *4*, 2674–2685

# Activation of starting materials/intermediates

- Radical–radical cross-coupling assisted N–S bond formation using AC

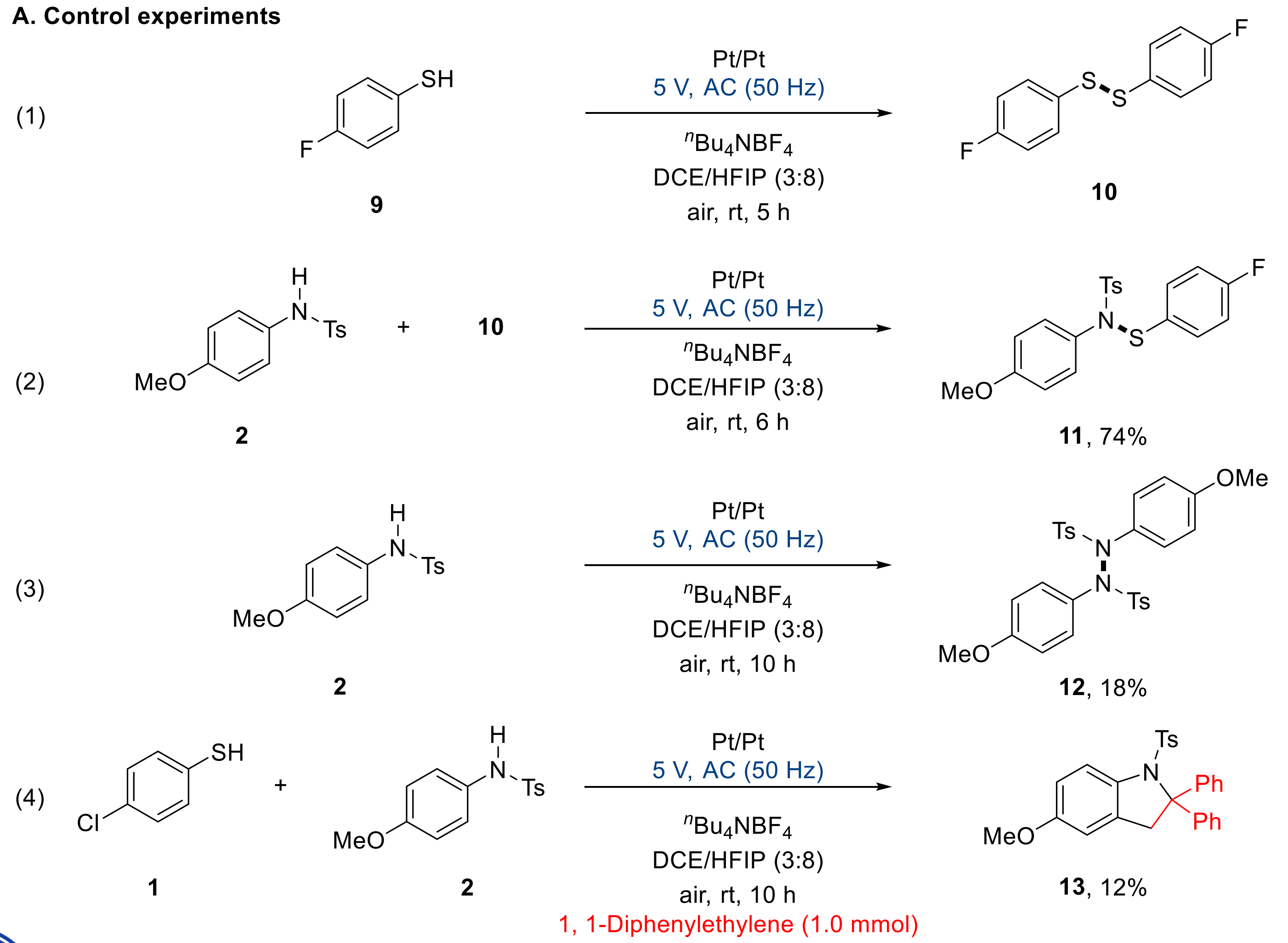


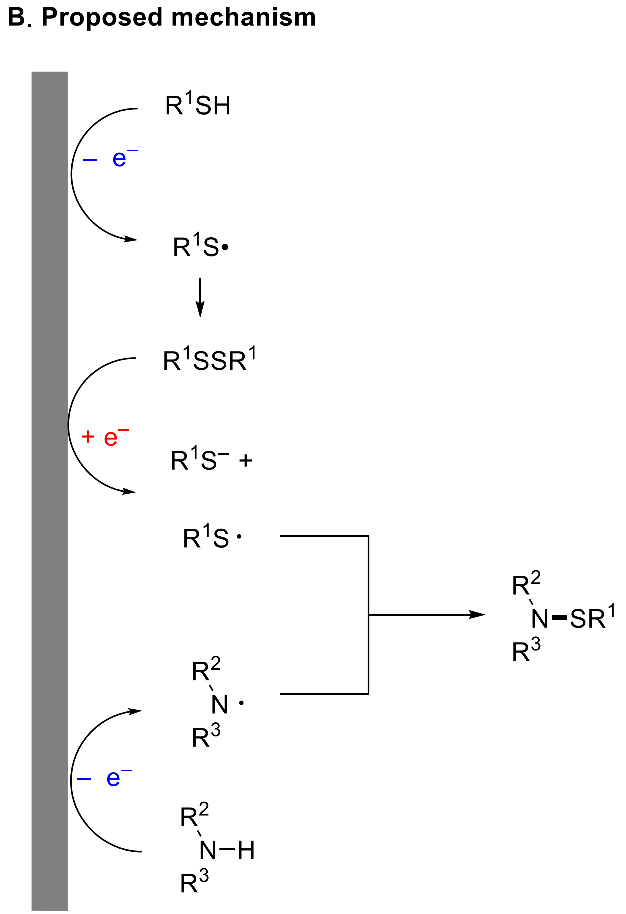


Lei, A. et al. *CCS Chem*. **2022**, *4*, 2674–2685

# Activation of starting materials/intermediates

- Radical–radical cross-coupling assisted N–S bond formation using AC

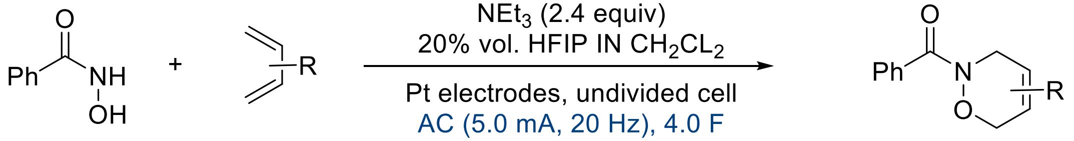


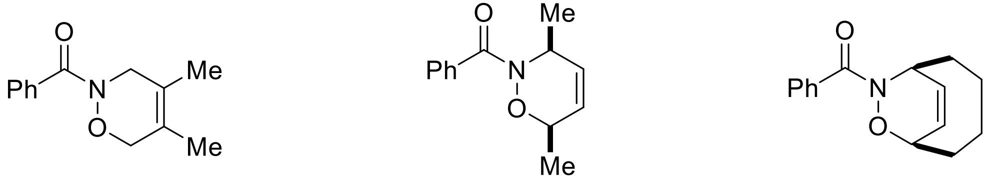




Lei, A. et al. *CCS Chem.* **2022**, *4*, 2674–2685

# AC-promoted oxidation or reduction reaction on electrodes

- Electrochemical oxidation of hydroxamic acids for acyl nitroso Diels–Alder reactions using AC

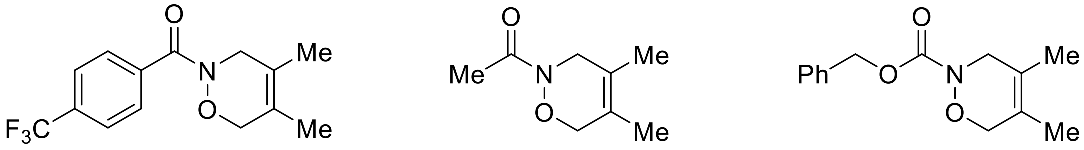



**1:** 85% (95% NMR)
[DC, 2 mA]: 59% NMR
[DC, 5 mA]: 0% NMR

**2**
79%

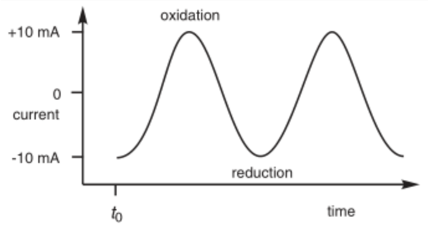
**3**
82%




**4**
89%

**5**
64%

**6**
96%

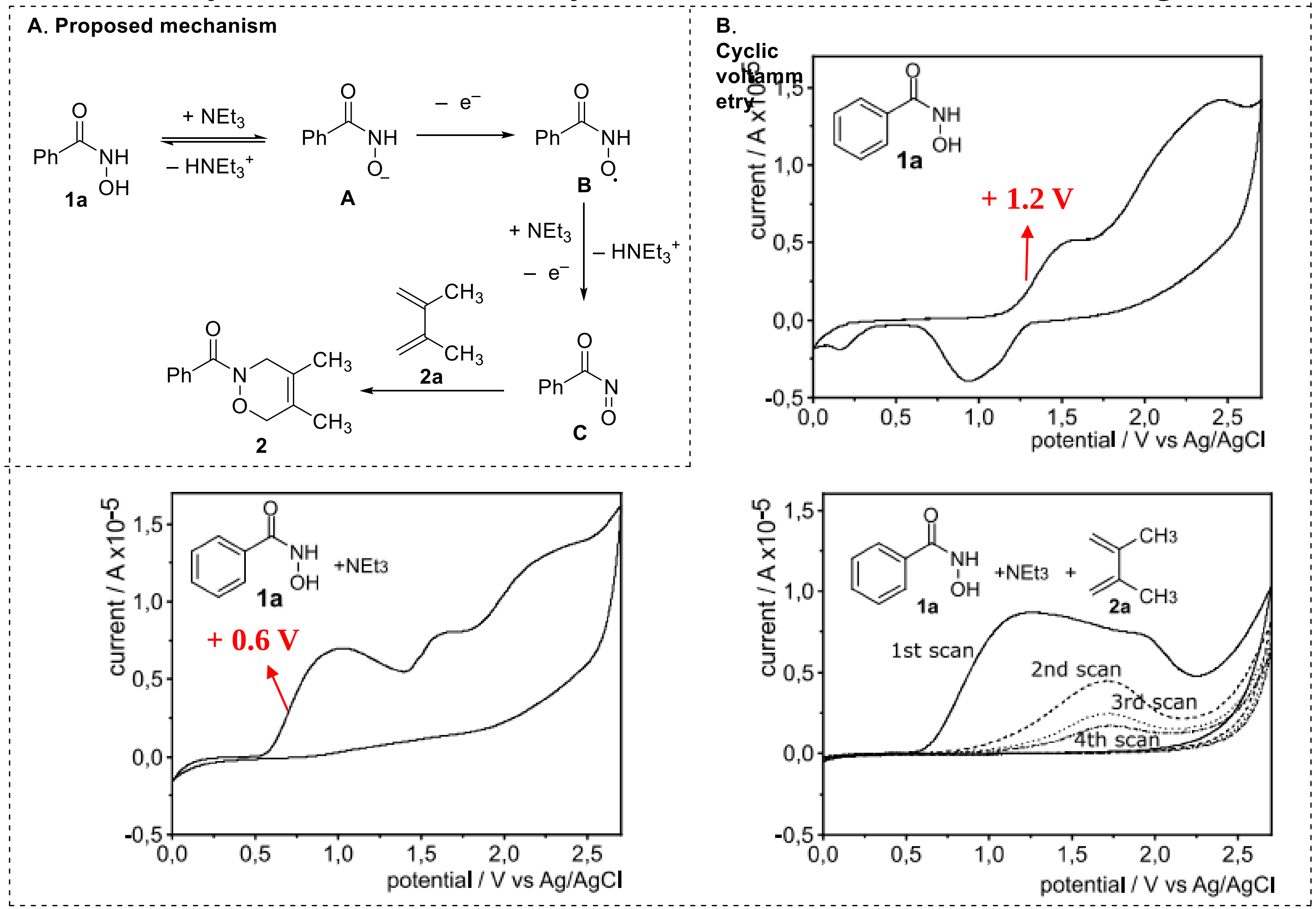



**Sinusoidal waveform**

Hilt, G. et al. *Angew. Chem. Int. Ed.* **2021**, *60*, 20313 –20317

# AC-promoted oxidation or reduction reaction on electrodes

- Electrochemical oxidation of hydroxamic acids for acyl nitroso Diels–Alder reactions using AC




Cyclic voltammograms of 1a/2a/$NEt_3$ in a 0.2 M solution of nBu4NBF4 in 8 mL DCM + 2 mL HFIP at a scan rate of 0.1 V/s at a platinum working electrode (2.0 mm diameter).

Hilt, G. et al. *Angew. Chem. Int. Ed.* **2021**, *60*, 20313 –20317

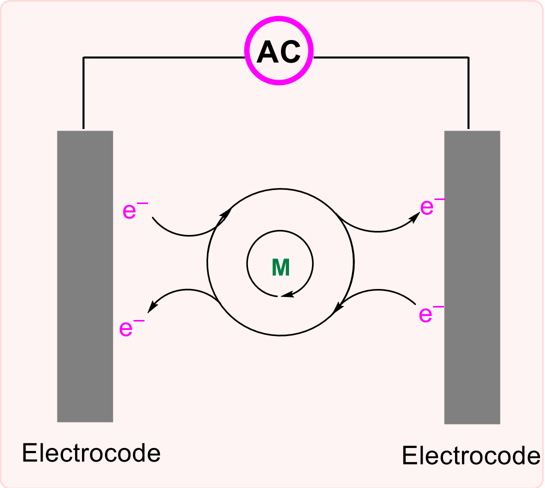
# Summary

- Different patterns of AC electrolysis

AC electrolysis

AC-promoted paired electrolysis

- Activation of starting materials/intermediates
- Activation of metal catalysts




AC-promoted oxidation or reduction reaction on electrodes