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Electrochemical Benzylic C−H Carboxylation

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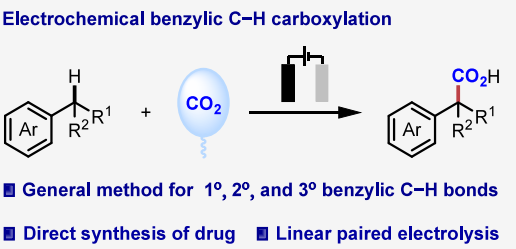
ABSTRACT: Direct benzylic C−H carboxylation stands as a high atom economy, efficient, and convenient route for the synthesis of valuable benzylic carboxylic acids, which are of great significance in many pharmaceuticals and bioactive molecules. However, the inherent inertness of both benzylic C−H bonds and carbon dioxide presents a great challenge for further transformations. Herein, we report our efforts to overcome this obstacle via halide-promoted linear paired electrolysis to generate various benzylic carboxylic acids. Remarkably, this process is transition-metal- and base-free, making it environmentally benign and cost-effective. Besides, it is suitable for constructing a wide range of primary, secondary, and tertiary benzylic carboxylic acids under mild reaction conditions, demonstrating broad substrate scopes and good functional group tolerance. Furthermore, our protocol enables the direct synthesis of some drug molecules, including Flurbiprofen, Ibuprofen, and Naproxen, and facilitates the late-stage modification of complex compounds, showcasing the practical application in synthetic chemistry and underscores its potential to advance the synthesis of benzylic carboxylic acids and related compounds.



INTRODUCTION

Carbon dioxide (CO_2) has emerged as an ideal C1 feedstock due to its abundance, accessibility, and nontoxicity, making it highly attractive for conversion into high-value carboxylic acids.[1] To date, the thermodynamic stability and kinetic inertness of CO_2 have seriously hindered its effective activation and selective conversion. So far, various strategies, including thermochemical,[2] photochemical,[3] and electrochemical[4] approaches, have demonstrated their potential in carboxylation reactions using CO_2 as the carboxyl source. Among these, electrosynthesis has attracted considerable attention due to its controllability, environmental friendliness, and cost effectiveness.[5,6] By use of traceless electrons to achieve the desired CO_2 utilization, electrosynthesis offers promising prospects for the production of valuable carboxylic acids.

Indeed, electrosynthesis has been employed to prepare various types of carboxylic acids, such as aromatic acids, hydroxy acids, and dicarboxylic acids.[4] In which, benzylic carboxylic acids have attracted great attention due to their occurrence in many pharmaceuticals and bioactive molecules, such as Ibuprofen, Naproxen, Flurbiprofen, and other drug intermediates.[4] State-of-the-art electrochemical synthesis of benzylic carboxylic acids focuses on the carboxylation of (pseudo)halides, which usually occurs through electroreduction of (pseudo)halides and the elimination of a leaving group (LG), such as halide, ammonium salt, acetate ion, etc. (Figure 1A).[7] However, the low atom economy of the process strongly inhibits further application. Alternatively, direct electrocarboxylation of benzylic C(sp^3)−H bonds stands out as an ideal and attractive approach, as it increases atom utilization and minimizes waste production.[8] Yet, direct benzylic C−H carboxylation remains a long-term challenge, awaiting solutions, which are mainly due to the inherent inertness of C−H bonds. Early efforts relied on strong base-promoted deprotonation, followed by the nucleophilic attack of CO_2 (Figure 1B, left).[9] More recently, with the revival of photocatalysis,[10] photocarboxylation of benzylic C−H bonds has provided more opportunities to synthesize benzylic carboxylic acids (Figure 1B, right).[11] The synthesis of primary,[11a,b] secondary,[11c] and tertiary[11d,e] benzylic carboxylic acids usually required different photocatalytic systems in the presence of corresponding photocatalysts, transition metals, or hydrogen atom transfer (HAT) reagents. However, a general approach for carboxylation of primary, secondary, and tertiary C−H bonds with CO_2 still remains elusive. Despite these advances, there is a high demand for the development of a greener and general method to synthesize diverse benzylic carboxylic acids from C−H bonds under mild reaction conditions.

Driven by our continued interest in electrochemical carboxylation,[12] herein, we put our efforts in moving this transformation forward by realizing the electrochemical benzylic C−H carboxylation with CO_2 (Figure 1C). Notable features of this strategy include: a) direct carboxylation of benzylic C−H bonds, which maximizes atomic utilization; b) a

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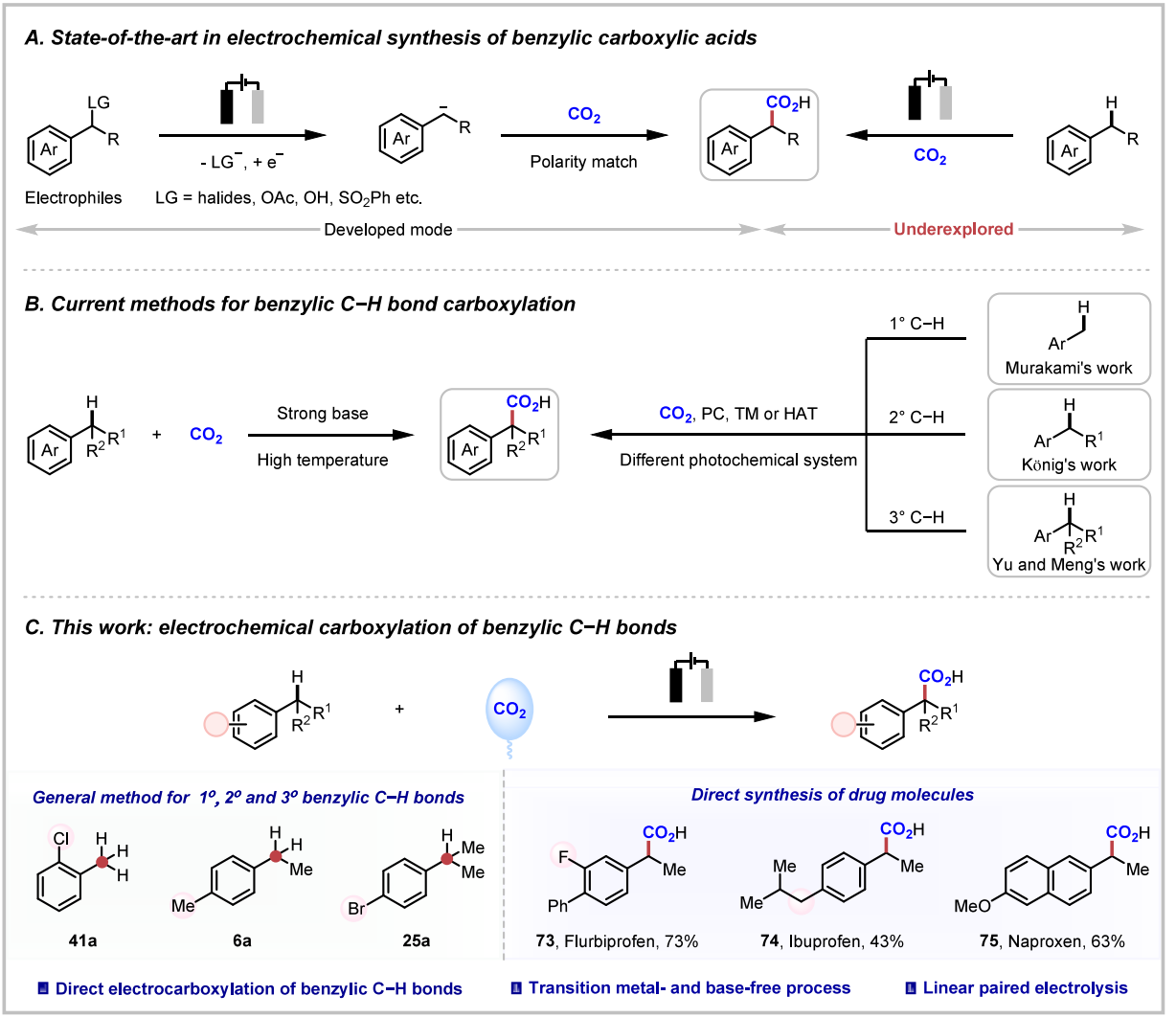

Figure 1. Synthetic approaches to benzylic carboxylic acids. A) **State-of-the-art** in electrochemical synthesis of benzylic carboxylic acids. B) **Current methods** for benzylic C−H bond carboxylation. C) ***This work***: electrochemical carboxylation of benzylic C−H bonds.

general method for the synthesis of primary, secondary, and tertiary benzylic carboxylic acids; c) transition-metal- and base-free process with good functional group tolerance that is compatible with substrates bearing sensitive alkenes, ketones, and halides; d) direct synthesis of drug molecules such as Fenoprofen, Ketoprofen, and Ibuprofen. Besides, this linear paired electrolysis has been promoted by a halide atom in the absence of a sacrificial anode. Moreover, late-stage modification of naturally occurring privileged scaffolds has been demonstrated, thereby showing the potential in broadening the horizon for further applications.

RESULTS AND DISCUSSION

The exploration of the electrochemical benzylic C−H carboxylation is outlined in Table 1, where butylbenzene (**1a**) was used as the model substrates. Several parallel optimizations were conducted to enhance reactivity in an electrochemical setting to its maximum potential. Extensive investigation revealed that the desired benzylic carboxylic acid product **1** could be obtained in 82% yield under a constant current at 20 mA employing 10 mol % NaI in a carbon dioxide-saturated electrolyte solution consisting of $^{n}Bu_4NClO_4$ and 1,2-dichloroethane (DCE). The electrosynthesis was conducted at room temperature with cheap graphite felt (GF) as the anode and a Ni plate as the cathode (Table 1, entry 1). No reaction occurred without an applied current (Table 1, entry 2). What's more, the addition of a catalytic amount of NaI was beneficial for improving reaction efficiency (Table 1, entry 3). We then investigated other halogenated compounds, such as NH_4I, NaBr, $CoBr_2$, and $^{n}Bu_4NI$; however, they resulted in unsatisfactory outcomes (Table 1, entries 4−7). Various electrolytes besides $^{n}Bu_4NBF_4$ proved to be incompatible with the carboxylation reaction (Table 1, entries 8−10). When $^{n}Bu_4NI$ was used as the electrolyte, **1a** was primarily converted into benzylic chlorinated byproduct, with 42% recovery of the starting material (Table 1, entry 8). When DMF was used as the solvent, neither benzylic carboxylated carboxylic acids nor aryl carboxylic acids were detected. Compared to our previous work,[12c] this discrepancy may be attributed to differences in substrate scopes and reaction mechanisms (Table 1, entry 11). In addition, dichloromethane (DCM) was suitable for the transformation (Table 1, entry 12). Cheap Ni plate proved to be the optimal cathode for the carboxylation reaction, and a common active metal anode such as Mg plate resulted in the failure of the reaction (Table 1, entries 13 and 14). No enhancements in reaction efficiency were observed when the

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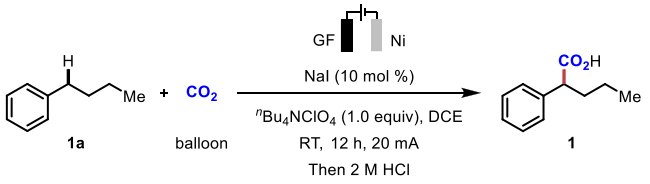
Table 1. Screening of the Reaction Conditions[a]



Entry	Variation	Yield %[b]
1	**None**	**82**
2	w/o electricity	NR
3	w/o NaI	64
4	NH_4I instead of NaI	68
5	NaBr instead of NaI	44
6	$CoBr_2$ instead of NaI	74
7	$^nBu_4NI$ instead of NaI	57
8	$^nBu_4NI$ instead of $^nBu_4NClO_4$	Trace
9	$LiClO_4$ instead of $^nBu_4NClO_4$	NR
10	$^nBu_4NBF_4$ instead of $^nBu_4NClO_4$	32
11	DMF as solvent	NR
12	DCM as solvent	72
13	GF (−) instead of Ni (−)	38
14	Mg (+) instead of GF (+)	NR
15	10 mA instead of 20 mA	66
16	25 mA instead of 20 mA	74
17	Divided cell	ND

[a]Reaction conditions: undivided cell, **1a** (0.3 mmol, 1.0 equiv), CO_2 (balloon), NaI (0.03 mmol, 10 mol %), $^nBu_4NClO_4$ (0.3 mmol, 1.0 equiv), DCE (5.0 mL) under 20 mA constant current at room temperature for 12 h with graphite felt (GF) as the anode and nickel (Ni) plate as the cathode. [b]Yield of isolated product. NR = no reaction. ND = not detected.

current was lowered to 10 mA or raised to 25 mA (Table 1, entries 15 and 16). Experiments with a H-type divided-cell indicated that both anodic oxidation and cathodic reduction played crucial roles in this redox-neutral synthesis. When **1a** was placed solely in either the anodic or cathodic chamber, neither the desired product nor the benzylic chlorinated byproducts were detected in either half-cell. This suggests that the reaction likely proceeds via a linear paired electrolysis mechanism (Table 1, entry 17).[13]

With the optimized conditions established for the benzylic carboxylic acid synthesis, the substrate scope was first explored with substrates bearing benzylic 2° C−H bonds (Figure 2). This method proved to be suitable with substrates bearing different chain lengths (**1**−**3**) and varying levels of steric hindrance (**4** and **5**). This electrochemical strategy also demonstrated high site selectivity in substrates that had more than one possible benzylic site for the synthesis of the desired product. For example, product **6** was constructed with high selectivity, demonstrating that the cleavage of the C(secondary)−H bond was more favorable than that of the C(primary)−H bond during this electrolysis process. Furthermore, the formation of product **7** indicated that the C(secondary)−H bond reacted preferentially over the C(tertiary)−H bond. Substituted ethylbiphenyl and diphenylmethane derivatives offered rapid access to the corresponding carboxylic acid product in yields ranging from 58% to 83%, including the example with an electrochemically sensitive cyano group (**8**−**12**). Inspired by the successful conversion of fluorene to 9-carboxyfluorene **13**, we then tried to extend the substrate scope to cyclic compounds. Four-, five-, and six-membered rings, namely, benzocyclobutene, indan, and tetraline, all reacted smoothly to afford the desired carboxylated products (**14**−**16**). 2-Ethylbenzofuran was a suitable substrate and provided **17** in 56% yield. All-carbon quaternary carboxylic acids are a class of useful compounds but pose great challenges in their synthesis due to their significant steric hindrance and inherent inertness. Encouraged by the aforementioned satisfying results, we further investigated the substrate scope for benzylic 3° C−H bonds. Different cumene derivatives worked well under the standard conditions and delivered **18**−**27** in 48% to 72% yield. Some electrochemical sensitive functional groups, such as ester and bromine, were well-tolerated, offering potential opportunities for further applications. Diarylsubstituted ethane and triphenylmethane, despite their larger steric hindrance, were also reactive and yielded **26** and **27** in acceptable yields. The substrate scope of the electrochemical carboxylation reaction was further explored with substrates containing the benzylic 1° C−H bonds. Various functional groups were tolerated when fixed in the ortho-, meta-, or para- position. Substrate bearing −OMe and $-^t$Bu showed good performance during the electrolysis process (**29**−**31**). When there was more than one benzylic primary C−H bond, the monocarboxylated product **32** was yielded in 75% yield, while the dicarboxylated product could not be detected during the reaction. It was worth mentioning that compound **33a** would be converted to chlorinated tolylacetic acid **33** instead of 4-bromomethylphenylacetic acid, perhaps due to the reactivity of benzyl bromide. Then, we tested some electron-deficient substrates, including compounds bearing trifluoromethyl, ester, cyano, fluorine, chlorine, and bromine, which all worked well in the carboxylation reactions (**34**−**43**). We also devoted effort to expand the scope of biphenylacetic acid derivatives and provided **44**−**53** in 53% to 85% yield. Heterocycle 2-methylthiophene and fused arene 2-methylnaphthalene could couple with CO_2 to afford benzylic carboxylic acids **54** and **55** in moderate yields.

Due to the significant importance of carboxylic acids, direct installation of carboxyl groups on bioactive molecules and their derivatives is of great significance. Our method has proven to be an alternative to the late-stage electrochemical carboxylation of biomolecules. A series of useful biorelevant derivatives, such as Fenofibric acid, Oxaprozin, and Cholesterol, could be coupled with CO_2 efficiently, which resulted in benzylic carboxylic acid analogues **56** to **68** (Figure 3). Notably, substrates with a sensitive ketone, oxazole, pyridine, adamantane, carbohydrate, amide, alkene or acetyl group all showed promising results and furnished the corresponding products in good yields.

In light of the widespread existence of benzylic C(sp^3)−H bonds in natural products and pharmaceuticals,[14] our electrochemical protocol was found to be effective for the direct synthesis of some common drug molecules, such as Fenoprofen **69**, Ketoprofen **70**, and Naproxen **75** (Figure 4). It is worth mentioning that although there were two benzylic C(sp^3)−H bonds in 1-ethyl-4-isobutylbenzene, the highly selective formation of **74** may be attributed to the steric effects. Besides, Repaglinide intermediate **76** and Sitagliptin intermediate **77** further demonstrated the potential application of this electrochemical carboxylation strategy. To further demonstrate the practical application of this methodology, we first conducted a gram-scale experiment of **1a** using a simple two-necked flask, which provided the desired product in 67% yield. Encouraged by the high reaction efficiency, we then

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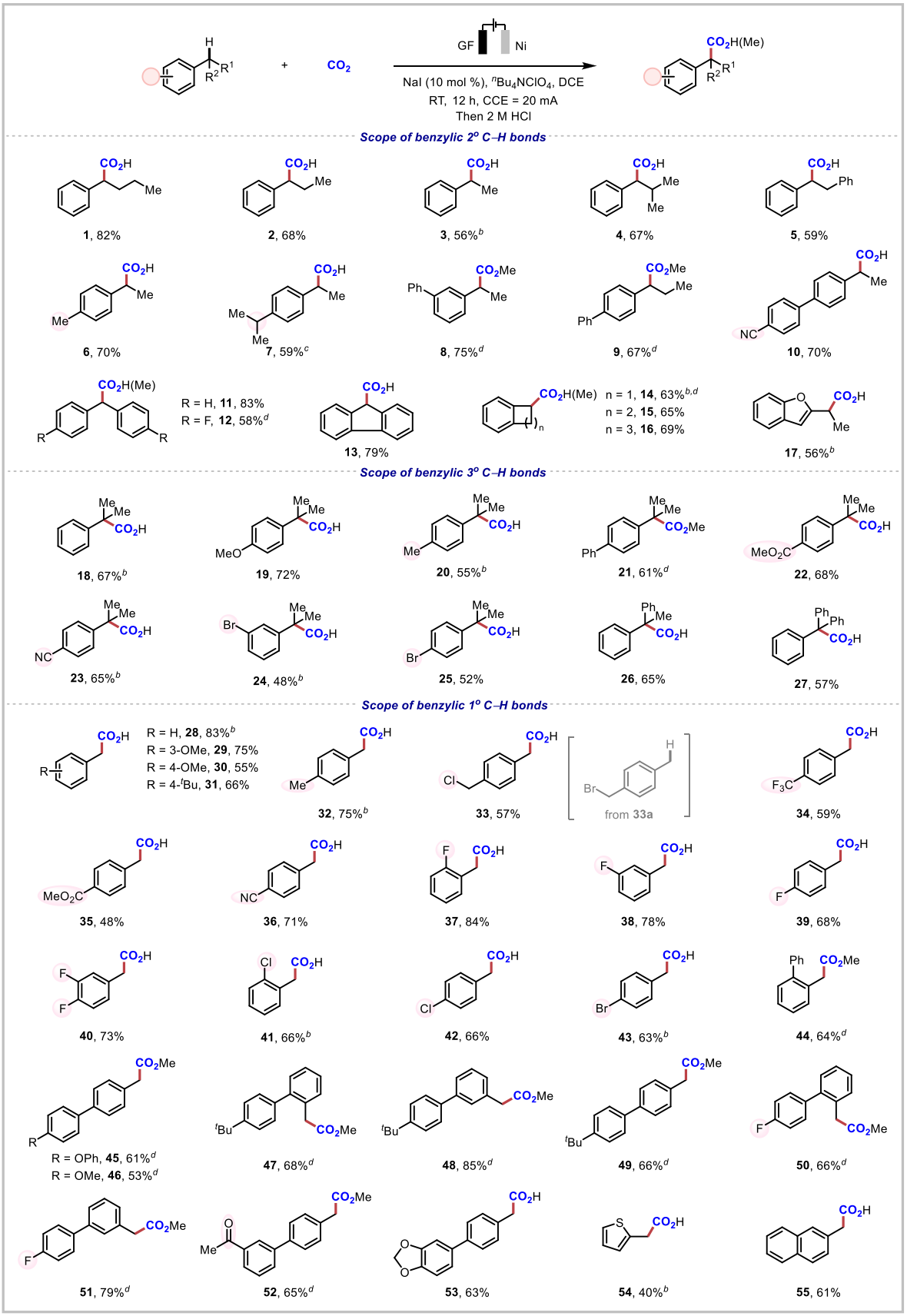

Figure 2. Scope of benzylic C−H bonds. Reaction conditions: [a]substrate (0.3 mmol, 1.0 equiv), CO_2 (balloon), NaI (0.03 mmol, 10 mol %), $^nBu_4NClO_4$ (0.3 mmol, 1.0 equiv), DCE (5.0 mL) under 20 mA constant current at room temperature for 12 h with graphite felt (GF) as the anode and Ni plate as the cathode in an undivided cell. [b]10 mA for 5 h. [c]10 mA for 10 h. [d]Using $TMSCHN_2$ was used as the methylation reagent.

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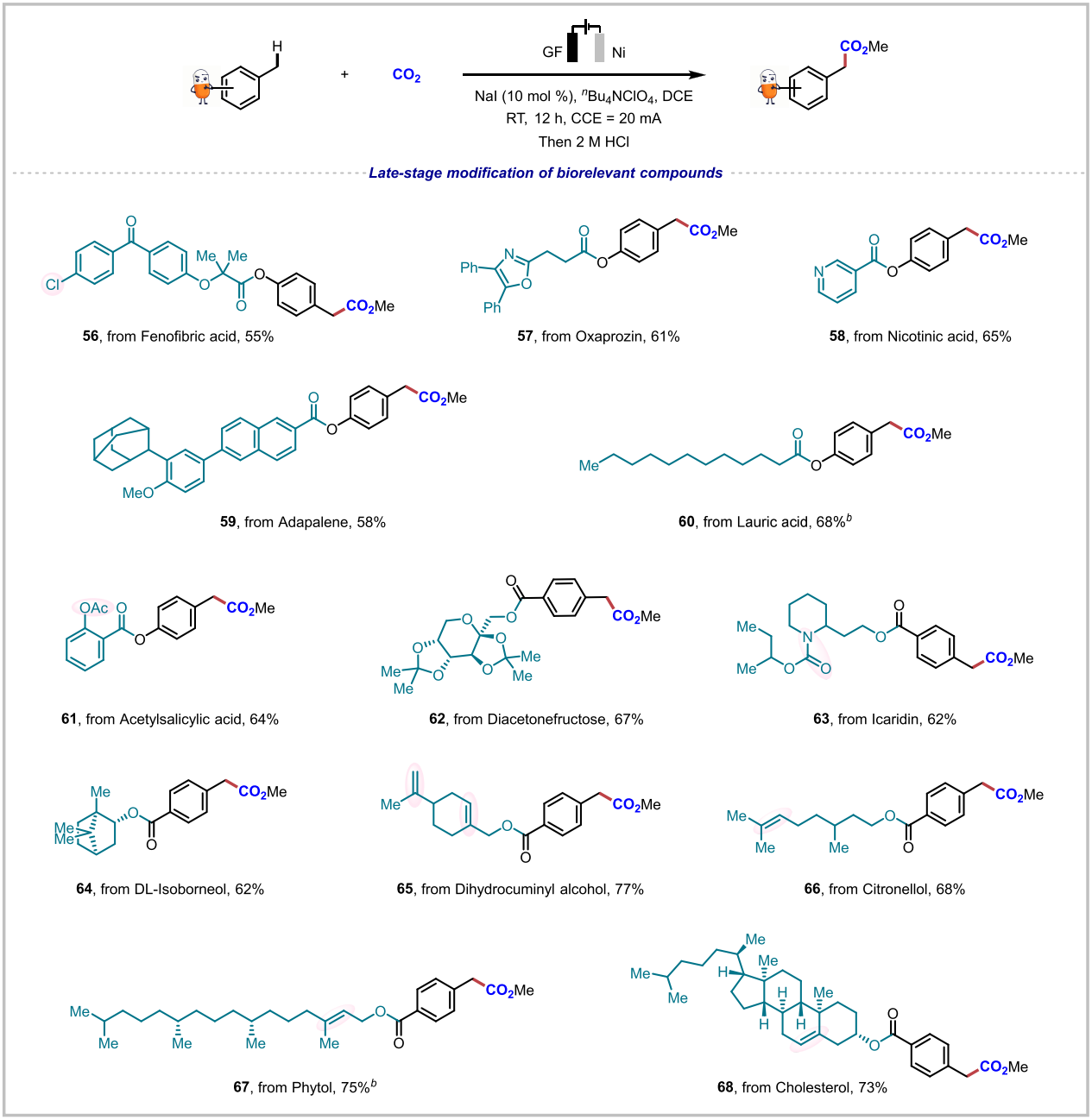

Figure 3. Late-stage modification of biorelevant compounds. Reaction conditions: [a]substrate (0.3 mmol, 1.0 equiv), CO_2 (balloon), NaI (0.03 mmol, 10 mol %), $^{n}Bu_4NClO_4$ (0.3 mmol, 1.0 equiv), DCE (5.0 mL) under 20 mA constant current at room temperature for 12 h with graphite felt (GF) as the anode and Ni plate as the cathode in an undivided cell. Using $TMSCHN_2$ as the methylation reagent. [b]10 mA for 5 h.

evaluated the scalability of direct synthesis of a drug molecule using this carboxylation strategy. The 10 mmol-scale experiment of preparing Biprofen **72** showcased the high step and atom economy of the reaction.

To deepen our understanding of this electrochemical reaction, we initially conducted some radical trapping experiments (Figure 5A). The formation of **1** was completely inhibited when the radical scavenger 2,2,6,6-tetramethyl-1-piperinedinyloxy (TEMPO) was added to the system under the standard conditions, suggesting that the reaction may involve a radical relay process (Figure 5Aa). The presence of TEMPO-adducts **1aA**, **1aB**, and **1aC** was confirmed through high-resolution mass spectrometry (HRMS), demonstrating that benzylic carbon radicals, chlorine radicals, and iodine radicals could be generated during the electrolysis. Radical−radical cross-coupling reaction between **72a** and **78** cumulatively supported the formation of a benzylic carbon radical (Figure 5Ab). The formation of chlorinated product **80-Cl** derived from compound **80** after the removal of the active ester group also indicate the generation of benzylic radicals (Figures 5Ac). Under an Ar atmosphere, once benzylic radicals were generated, they were readily oxidized to carbocations, which then were coupled with chloride ions to produce chlorination products. In addition, the formation of **82** and **83** provided evidence that chlorine radicals may be involved during the process (Figure 5Ad). Furthermore, conventional dichloroethane was replaced with deuterated dichloroethane (d_4-DCE) to investigate the hydrogen source in the reaction

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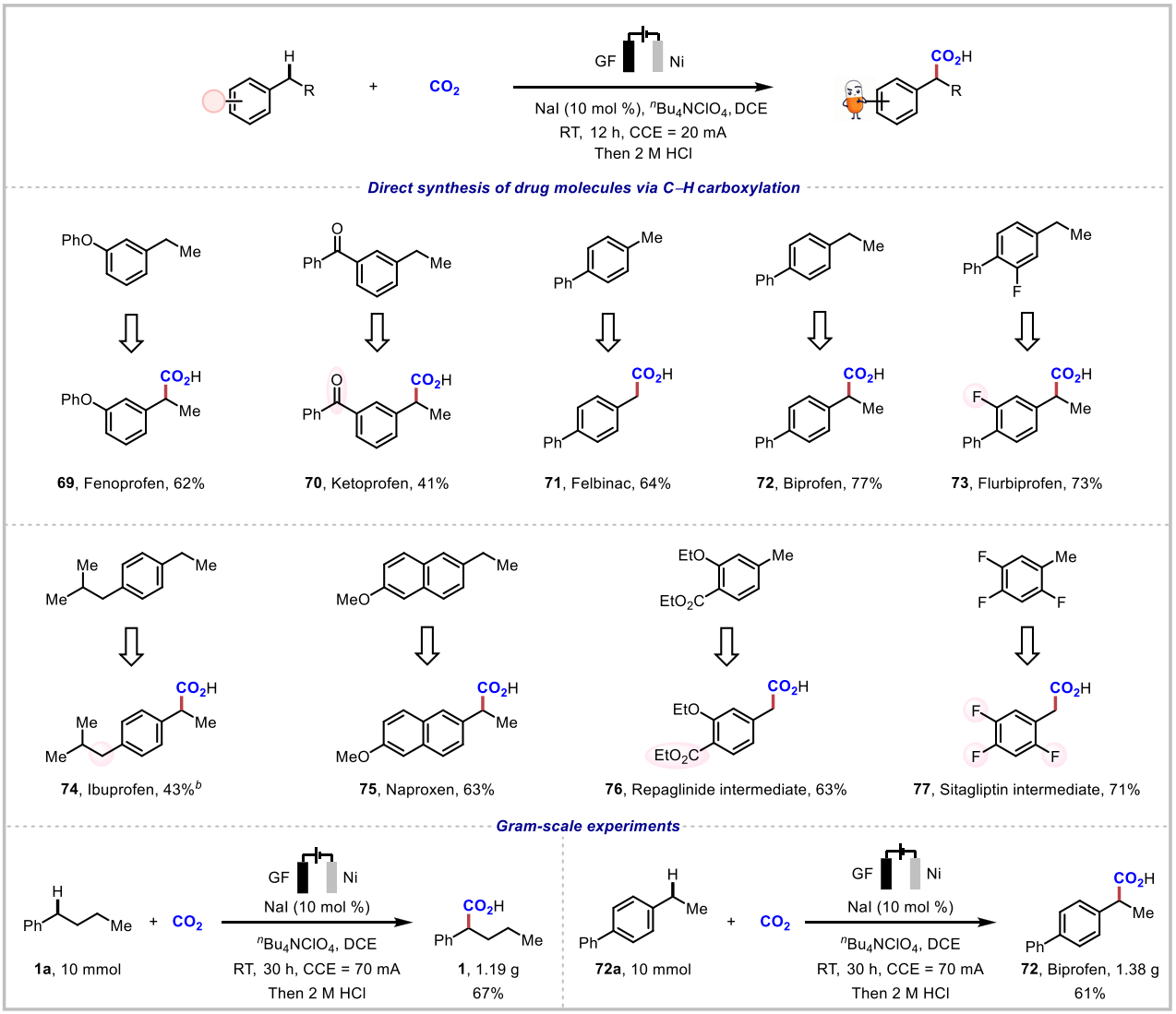

Figure 4. Direct synthesis of drug molecules and gram-scale experiments. Reaction conditions: [a]substrate (0.3 mmol, 1.0 equiv), CO_2 (balloon), NaI (0.03 mmol, 10 mol %), ^{n}Bu$_4$NClO$_4$ (0.3 mmol, 1.0 equiv), DCE (5.0 mL) under 20 mA constant current at room temperature for 12 h with graphite felt (GF) as the anode and Ni plate as the cathode in an undivided cell. [b]10 mA for 5 h. For gram-scale experiments: substrate (10 mmol, 1.0 equiv), CO_2 (balloon), NaI (1 mmol, 10 mol %), ^{n}Bu$_4$NClO$_4$ (10 mmol, 1.0 equiv), DCE (80 mL) under 70 mA constant current at room temperature for 30 h with graphite felt (GF) as the anode and Ni plate as the cathode in an undivided cell.

(please see the Supporting Information for more details). Deuterated product **82-d** could be isolated in 14% yield and 72% deuterium incorporation rate, indicating that the solvent can serve H^+ or D^+ during the electrolysis. Furthermore, the addition of D_2O under the standard conditions resulted in **72a'** in 45% yield and 18% D incorporation, suggesting the possible generation of a benzylic carbon carbanion (Figure 5B). Under standard conditions, the reaction solution becomes acidic after electrolysis, which is likely due to the generation of HCl from the electrolysis of DCE (see the Supporting Information for more details). These additional excess proton sources may compete with D_2O in the reaction, leading to a low ratio of D-incorporation. When substrate **72a** was conducted under an Ar atmosphere, it resulted in benzylic chloride **72a-Cl** in 53% yield (Figure 5Ca). When **72a-Cl** was used as the starting material for carboxylation, **72** was obtained in 28% yield, while **72a-Cl** was recovered in 31% yield, and **72a** was obtained in 35% yield (Figure 5Cb). Cyclic voltammetry experiments revealed that DCE can undergo an initial reduction reaction followed by further oxidation (Figure 5D), while NaI can undergo oxidation in the DCE solution (please see the Supporting Information for more details). Besides, the anode and cathode potentials were monitored separately under standard reaction conditions (see Supporting Information for more details). Initially, the anode potential showed little change, while the cathode potential increased slowly. As electrolysis progressed, the anode potential rose significantly, and the cathode potential stabilized.

On the basis of our mechanistic insights obtained from the above results and relevant studies,[15] a possible mechanism was proposed for the electrochemical carboxylation of benzylic C(sp^3)–H with CO_2 (Figure 5E). DCE is prone to gaining an electron to form a chloride anion, which is subsequently oxidized at the anode. The hydrogen atom transfer (HAT) process between the chlorine radical and substrate **I** provides a benzylic carbon radical **II** and HCl. **III**, formed through the oxidation of **II**, couples with a chloride anion to give benzylic chloride. The in situ-generated **IV** then loses a chloride ion and

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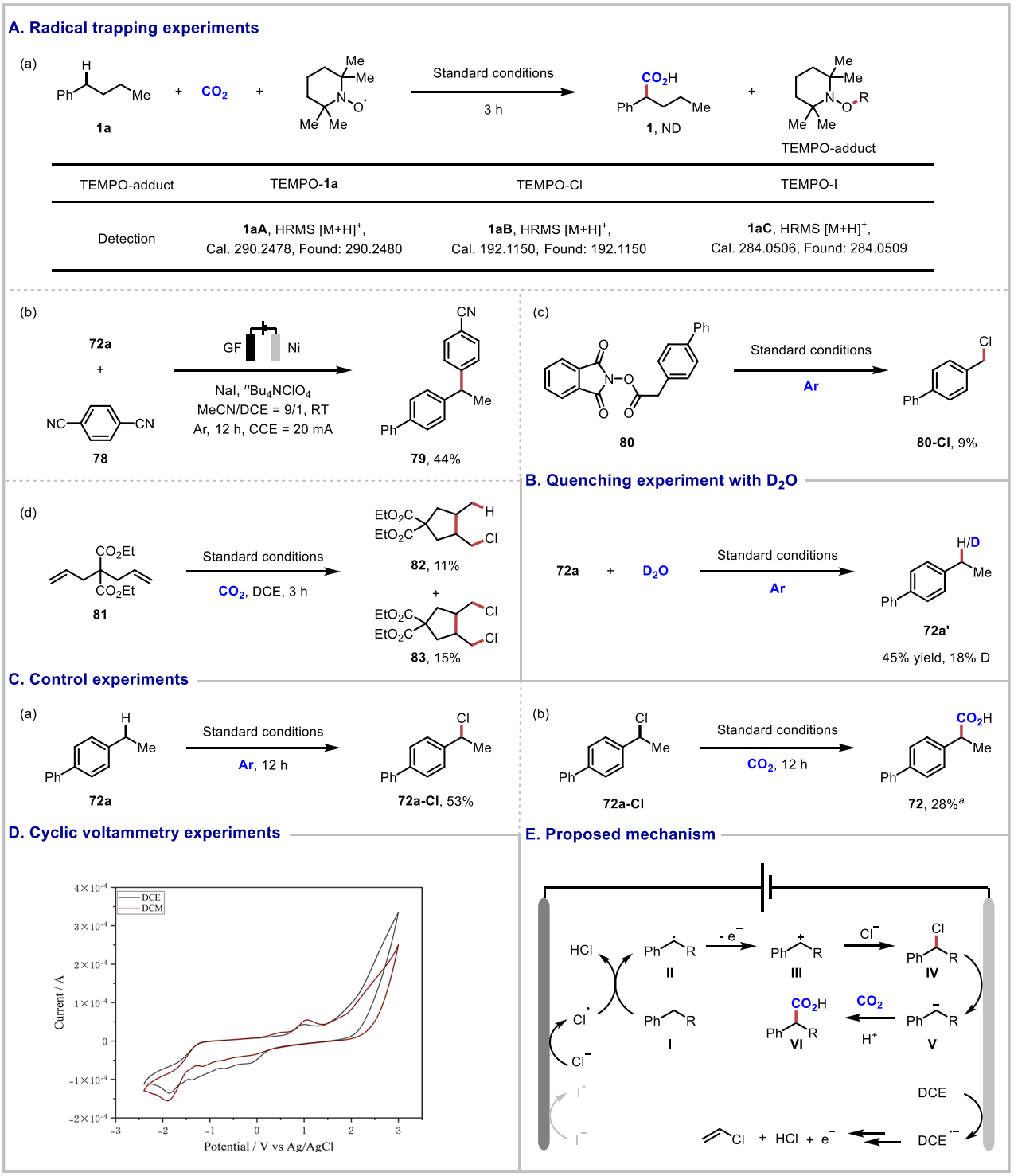

Figure 5. Mechanistic studies and proposed mechanism. A) Radical trapping experiments. B) Quenching experiment with D_2O. C) Control experiments. [a] **72a-Cl** was recovered in 31% yield, and **72a** was obtained in 35% yield. D) Cyclic voltammetry experiments. E) Proposed mechanism.

gains electrons to furnish **V**. The final product is obtained after the nucleophilic attack by CO_2. Besides, the iodine anions derived from the ionization of NaI can also undergo oxidation at the anode.

CONCLUSION

In conclusion, we achieved electrochemical benzylic C−H carboxylation with CO_2, overcoming the inherent inertness of both reactants. This process with high atom-utilization offers a wide substrate scope, which could allow effective construction of primary, secondary, and tertiary benzylic carboxylic acids. Besides, it is compatible with several sensitive functional groups, such as halides, alkenes, and ketones. It is worth noting that our strategy could be applied to the direct synthesis of drugs and late-stage modification of biorelevant compounds under mild conditions. In the absence of sacrificial anodes/

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reagents, transition metals, or strong bases, our protocol offers more opportunities for further applications in a cleaner and more sustainable manner. Detailed mechanistic exploration reveals the proposed mechanism promoted by halide atom to realize the linear paired electrolysis. Further attempts aiming to access other types of electrochemical C−H carboxylation are currently under investigation in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.5c00259.

Experimental details, optimization studies, and characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Sakakura, T.; Choi, J.-C.; Yasuda, H. Transformation of Carbon Dioxide. *Chem. Rev.* **2007**, *107*, 2365−2387. (b) He, M.; Sun, Y.; Han, B. Green Carbon Science: Scientific Basis for Integrating Carbon Resource Processing, Utilization, and Recycling. *Angew. Chem., Int. Ed.* **2013**, *52*, 9620−9633. (c) Aresta, M.; Dibenedetto, A.; Angelini, A. Catalysis for the Valorization of Exhaust Carbon: from CO_2 to Chemicals, Materials, and Fuels. Technological Use of CO_2. *Chem. Rev.* **2014**, *114*, 1709−1742. (d) Maeda, C.; Miyazaki, Y.; Ema, T. Recent progress in catalytic conversions of carbon dioxide. *Catal. Sci. Technol.* **2014**, *4*, 1482−1497. (e) Zhang, L.; Hou, Z. Transition metal promoted carboxylation of unsaturated substrates with carbon dioxide. *Current Opinion in Green and Sustainable Chemistry* **2017**, *3*, 17−21. (f) Song, Q.-W.; Zhou, Z.-H.; He, L.-N. Efficient, selective and sustainable catalysis of carbon dioxide. *Green Chem.* **2017**, *19*, 3707−3728. (g) Wang, S.; Xi, C. Recent advances in nucleophile-triggered CO_2-incorporated cyclization leading to heterocycles. *Chem. Soc. Rev.* **2019**, *48*, 382−404.

(2) (a) Pradhan, S.; Das, S. Recent Advances on the Carboxylations of $C(sp^3)$−H Bonds Using CO_2 as the Carbon Source. *Synlett* **2023**, *34*, 1327−1342. (b) Qiu, L.-Q.; Li, H.-R.; He, L.-N. Incorporating Catalytic Units into Nanomaterials: Rational Design of Multipurpose Catalysts for CO_2 Valorization. *Acc. Chem. Res.* **2023**, *56*, 2225−2240.

(3) (a) Hou, J.; Li, J.-S.; Wu, J. Recent Development of Light-Mediated Carboxylation Using CO_2 as the Feedstock. *Asian J. Org. Chem.* **2018**, *7*, 1439−1447. (b) Yeung, C. S. Photoredox Catalysis as a Strategy for CO_2 Incorporation: Direct Access to Carboxylic Acids from a Renewable Feedstock. *Angew. Chem., Int. Ed.* **2019**, *58*, 5492−5502. (c) Zhang, Z.; Ye, J.-H.; Ju, T.; Liao, L.-L.; Huang, H.; Gui, Y.-Y.; Zhou, W.-J.; Yu, D.-G. Visible-Light-Driven Catalytic Reductive Carboxylation with CO_2. *ACS Catal.* **2020**, *10*, 10871−10885.

(4) (a) Li, C.-H.; Yuan, G.-Q.; Qi, C.-R.; Jiang, H.-F. Copper-catalyzed electrochemical synthesis of alkylidene lactones from carbon dioxide and 1,4-diarylbuta-1,3-diynes. *Tetrahedron* **2013**, *69*, 3135−3140. (b) Muchez, L.; De Vos, D. E.; Kim, M. Sacrificial Anode-Free Electrosynthesis of α-Hydroxy Acids via Electrocatalytic Coupling of Carbon Dioxide to Aromatic Alcohols. *ACS Sustainable Chem. Eng.* **2019**, *7*, 15860−15864. (c) Alkayal, A.; Tabas, V.; Montanaro, S.; Wright, I. A.; Malkov, A. V.; Buckley, B. R. Harnessing Applied Potential: Selective β-Hydrocarboxylation of Substituted Olefins. *J. Am. Chem. Soc.* **2020**, *142*, 1780−1785. (d) Ang, N. W. J.; Oliveira, J. C. A.; Ackermann, L. Electroreductive Cobalt-Catalyzed Carboxylation: Cross-Electrophile Electrocoupling with Atmospheric CO_2. *Angew. Chem., Int. Ed.* **2020**, *59*, 12842−12847. (e) Naito, Y.; Nakamura, Y.; Shida, N.; Senboku, H.; Tanaka, K.; Atobe, M. Integrated Flow Synthesis of α-Amino Acids by In Situ Generation of Aldimines and Subsequent Electrochemical Carboxylation. *J. Org. Chem.* **2021**, *86*, 15953−15960. (f) Sheta, A. M.; Alkayal, A.; Mashaly, M. A.; Said, S. B.; Elmorsy, S. S.; Malkov, A. V.; Buckley, B. R. Selective Electrosynthetic Hydrocarboxylation of α,β-Unsaturated Esters with Carbon Dioxide. *Angew. Chem., Int. Ed.* **2021**, *60*, 21832−21837. (g) You, Y.; Kanna, W.; Takano, H.; Hayashi, H.; Maeda, S.; Mita, T. Electrochemical Dearomative Dicarboxylation of Heterocycles with Highly Negative Reduction Potentials. *J. Am. Chem. Soc.* **2022**, *144*, 3685−3695. (h) Zhang, K.; Liu, X.-F.; Zhang, W.-Z.; Ren, W.-M.; Lu, X.-B. Electrocarboxylation of N-Acylimines with Carbon Dioxide: Access to Substituted α-Amino Acids. *Org. Lett.* **2022**, *24*, 3565−3569. (i) Mondal, S.; Sarkar, S.; Wang, J. W.; Meanwell, M. W. A selective and mild electrochemical defluorinative carboxylation for late-stage $C(sp^3)$−F bond functionalization. *Green Chem.* **2023**, *25*, 9075−9079. (j) Sun, G.-Q.; Yu, P.; Zhang, W.; Zhang, W.; Wang, Y.; Liao, L.-L.; Zhang, Z.; Li, L.; Lu, Z.; Yu, D.-G.; Lin, S. Electrochemical reactor dictates site selectivity in N-heteroarene carboxylations. *Nature* **2023**, *615*, 67−72. (k) Ran, C.-K.; Qu, Q.; Tao, Y.-Y.; Chen, Y.-F.; Liao, L.-L.; Ye, J.-H.; Yu, D.-G. Electro-reductive carboxylation of acyclic $C(sp^3)$−$C(sp^3)$ bonds in aromatic hydrocarbons with CO_2. *Sci. China Chem.* **2024**, *67*, 3366−3372. (l) Yang, D.; Sun, Y.; Feng, N.; Zhong, Y.; Zhou, J.; Zhou, F. Electrochemical Dicarboxylation of Vinyl Epoxide with CO_2 for the Facile and Selective Synthesis of Diacids. *Angew. Chem., Int. Ed.* **2025**, *64*, No. e202419702.

(5) (a) Yan, M.; Kawamata, Y.; Baran, P. S. Synthetic Organic Electrochemical Methods Since 2000: On the Verge of a Renaissance. *Chem. Rev.* **2017**, *117*, 13230−13319. (b) Xiong, P.; Xu, H.-C. Chemistry with Electrochemically Generated N-Centered Radicals. *Acc. Chem. Res.* **2019**, *52*, 3339−3350. (c) Yuan, Y.; Lei, A. Electrochemical Oxidative Cross-Coupling with Hydrogen Evolution Reactions. *Acc. Chem. Res.* **2019**, *52*, 3309−3324. (d) Kingston, C.; Palkowitz, M. D.; Takahira, Y.; Vantourout, J. C.; Peters, B. K.;

Kawamata, Y.; Baran, P. S. A Survival Guide for the "Electro-curious". *Acc. Chem. Res.* **2020**, *53*, 72−83. (e) Röckl, J. L.; Pollok, D.; Franke, R.; Waldvogel, S. R. A Decade of Electrochemical Dehydrogenative C. *C-Coupling of Aryls. Acc. Chem. Res.* **2020**, *53*, 45−61. (f) Novaes, L. F. T.; Liu, J.; Shen, Y.; Lu, L.; Meinhardt, J. M.; Lin, S. Electrocatalysis as an enabling technology for organic synthesis. *Chem. Soc. Rev.* **2021**, *50*, 7941−8002. (g) Shi, S.-H.; Liang, Y.; Jiao, N. Electrochemical Oxidation Induced Selective C−C Bond Cleavage. *Chem. Rev.* **2021**, *121*, 485−505. (h) Zhu, C.; Ang, N. W. J.; Meyer, T. H.; Qiu, Y.; Ackermann, L. Organic Electrochemistry: Molecular Syntheses with Potential. *ACS Central Sci.* **2021**, *7*, 415−431. (i) Cheng, X.; Lei, A.; Mei, T.-S.; Xu, H.-C.; Xu, K.; Zeng, C. Recent Applications of Homogeneous Catalysis in Electrochemical Organic Synthesis. *CCS Chem.* **2022**, *4*, 1120−1152. (j) Liu, Y.; Li, P.; Wang, Y.; Qiu, Y. Electroreductive Cross-Electrophile Coupling (eXEC) Reactions. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202306679. (k) Wang, Y.; Dana, S.; Long, H.; Xu, Y.; Li, Y.; Kaplaneris, N.; Ackermann, L. Electrochemical Late-Stage Functionalization. *Chem. Rev.* **2023**, *123*, 11269−11335. (l) Zeng, W.; Qiu, Y. Electrochemical conversion of organic compounds and inorganic small molecules. *Sci. China Chem.* **2024**, *67*, 3223−3246. (m) Sun, G.-Q.; Liao, L.-L.; Ran, C.-K.; Ye, J.-H.; Yu, D.-G. Recent Advances in Electrochemical Carboxylation with CO_2. *Acc. Chem. Res.* **2024**, *57*, 2728−2745. (n) Gao, R.; Wen, L.; Guo, W. Recent Advances in Electrochemical-Promoted Unactivated C(sp^3)−H Functionalization. *Chin. J. Org. Chem.* **2024**, *44*, 892−902. (o) Li, P.; Wang, Y.; Zhao, H.; Qiu, Y. Electroreductive Cross-Coupling Reactions: Carboxylation, Deuteration, and Alkylation. *Acc. Chem. Res.* **2025**, *58*, 113−129. (p) Zeng, W.; Wang, Y.; Peng, C.; Qiu, Y. Organo-mediator enabled electrochemical transformations. *Chem. Soc. Rev.* **2025**, DOI: 10.1039/D4CS01142B.

(6) (a) Badalyan, A.; Stahl, S. S. Cooperative electrocatalytic alcohol oxidation with electron-proton-transfer mediators. *Nature* **2016**, *535*, 406−410. (b) Fu, N.; Sauer, G. S.; Saha, A.; Loo, A.; Lin, S. Metal-catalyzed electrochemical diazidation of alkenes. *Science* **2017**, *357*, 575−579. (c) Yang, Q.-L.; Li, Y.-Q.; Ma, C.; Fang, P.; Zhang, X.-J.; Mei, T.-S. Palladium-Catalyzed C(sp^3)−H Oxygenation via Electrochemical Oxidation. *J. Am. Chem. Soc.* **2017**, *139*, 3293−3298. (d) Cai, C.-Y.; Xu, H.-C. Dehydrogenative reagent-free annulation of alkenes with diols for the synthesis of saturated O-heterocycles. *Nat. Commun.* **2018**, *9*, 3551. (e) DeLano, T. J.; Reisman, S. E. Enantioselective Electroreductive Coupling of Alkenyl and Benzyl Halides via Nickel Catalysis. *ACS Catal.* **2019**, *9*, 6751−6754. (f) Zhang, L.; Liardet, L.; Luo, J.; Ren, D.; Grätzel, M.; Hu, X. Photoelectrocatalytic arene C−H amination. *Nat. Catal.* **2019**, *2*, 366−373. (g) Liu, C.; Han, S.; Li, M.; Chong, X.; Zhang, B. Electrocatalytic Deuteration of Halides with D_2O as the Deuterium Source over a Copper Nanowire Arrays Cathode. *Angew. Chem., Int. Ed.* **2020**, *59*, 18527−18531. (h) Blum, S. P.; Karakaya, T.; Schollmeyer, D.; Klapars, A.; Waldvogel, S. R. Metal-Free Electrochemical Synthesis of Sulfonamides Directly from (Hetero)arenes, SO_2, and Amines. *Angew. Chem., Int. Ed.* **2021**, *60*, 5056−5062. (i) Chung, D. S.; Park, S. H.; Lee, S.-g.; Kim, H. Electrochemically driven stereoselective approach to syn-1,2-diol derivatives from vinylarenes and DMF. *Chem. Sci.* **2021**, *12*, 5892−5897. (j) Liang, Y.; Shi, S.-H.; Jin, R.; Qiu, X.; Wei, J.; Tan, H.; Jiang, X.; Shi, X.; Song, S.; Jiao, N. Electrochemically induced nickel catalysis for oxygenation reactions with water. *Nat. Catal.* **2021**, *4*, 116−123. (k) Long, C.-J.; Cao, H.; Zhao, B.-K.; Tan, Y.-F.; He, Y.-H.; Huang, C.-S.; Guan, Z. Merging the Non-Natural Catalytic Activity of Lipase and Electrosynthesis: Asymmetric Oxidative Cross-Coupling of Secondary Amines with Ketones. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202203666. (l) Cai, C.-Y.; Zheng, Y.-T.; Li, J.-F.; Xu, H.-C. Cu-Electrocatalytic Diazidation of Alkenes at ppm Catalyst Loading. *J. Am. Chem. Soc.* **2022**, *144*, 11980−11985. (m) Liang, K.; Zhang, Q.; Guo, C. Nickel-catalyzed switchable asymmetric electrochemical functionalization of alkenes. *Sci. Adv.* **2022**, *8*, No. eadd7134. (n) Zhang, J.; Das, B.; Verho, O.; Bäckvall, J.-E. Electrochemical Palladium-Catalyzed Oxidative Carbonylation-Cyclization of Enallenols. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202212131. (o) Chen, M.; Wu, Z.-J.; Song, J.; Xu, H.-C. Electrocatalytic Allylic C−H Alkylation Enabled by a Dual-Function Cobalt Catalyst. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202115954. (p) Huang, C.; Ma, W.; Zheng, X.; Xu, M.; Qi, X.; Lu, Q. Epoxide Electroreduction. *J. Am. Chem. Soc.* **2022**, *144*, 1389−1395. (q) Zhang, B.; Gao, Y.; Hioki, Y.; Oderinde, M. S.; Qiao, J. X.; Rodriguez, K. X.; Zhang, H.-J.; Kawamata, Y.; Baran, P. S. Ni-electrocatalytic Csp^3−Csp^3 doubly decarboxylative coupling. *Nature* **2022**, *606*, 313−318. (r) Zhang, X.; Cheng, X. Electrochemical Reductive Functionalization of Alkenes with Deuterochloroform as a One-Carbon Deuteration Block. *Org. Lett.* **2022**, *24*, 8645−8650. (s) Fan, W.; Zhao, X.; Deng, Y.; Chen, P.; Wang, F.; Liu, G. Electrophotocatalytic Decoupled Radical Relay Enables Highly Efficient and Enantioselective Benzylic C−H Functionalization. *J. Am. Chem. Soc.* **2022**, *144*, 21674−21682. (t) Fang, S.; Zhong, K.; Zeng, S.; Hu, X.; Sun, P.; Ruan, Z. The electrochemically enabled α-C(sp^3)−H azolation of ketones. *Chem. Commun.* **2023**, *59*, 11425−11428. (u) Park, S. H.; Bae, G.; Choi, A.; Shin, S.; Shin, K.; Choi, C. H.; Kim, H. Electrocatalytic Access to Azetidines via Intramolecular Allylic Hydroamination: Scrutinizing Key Oxidation Steps through Electrochemical Kinetic Analysis. *J. Am. Chem. Soc.* **2023**, *145*, 15360−15369. (v) Zhang, S.; Liang, Y.; Liu, K.; Zhan, X.; Fan, W.; Li, M.-B.; Findlater, M. Electrochemically Generated Carbanions Enable Isomerizing Allylation and Allenylation of Aldehydes with Alkenes and Alkynes. *J. Am. Chem. Soc.* **2023**, *145*, 14143−14154. (w) Jiang, Y.-M.; Lin, Y.-Y.; Zhu, L.; Yu, Y.; Li, Y.; Lin, Y.; Ye, K.-Y. A General Electrochemical Synthesis of Sulfonimidoyl Fluorides, Azides, and Acetates. *CCS Chem.* **2024**, *6*, 2021−2030. (x) Wang, T.; He, F.; Jiang, W.; Liu, J. Electrohydrogenation of Nitriles with Amines by Cobalt Catalysis. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202316140. (y) Tang, H.-T.; Zhou, H.-Y.; Pan, Y.-M.; Zhang, J.-L.; Cui, F.-H.; Li, W.-H.; Wang, D. Single-Atom Manganese-Catalyzed Oxygen Evolution Drives the Electrochemical Oxidation of Silane to Silanol. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202315032. (z) Wang, X.-Y.; Pan, Y.-Z.; Yang, J.; Li, W.-H.; Gan, T.; Pan, Y.-M.; Tang, H.-T.; Wang, D. Single-Atom Iron Catalyst as an Advanced Redox Mediator for Anodic Oxidation of Organic Electrosynthesis. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202404295.

(7) (a) Ohkoshi, M.; Michinishi, J.-y.; Hara, S.; Senboku, H. Electrochemical carboxylation of benzylic carbonates: alternative method for efficient synthesis of arylacetic acids. *Tetrahedron* **2010**, *66*, 7732−7737. (b) Senboku, H.; Yoneda, K.; Hara, S. Electrochemical direct carboxylation of benzyl alcohols having an electron-withdrawing group on the phenyl ring: one-step formation of phenylacetic acids from benzyl alcohols under mild conditions. *Tetrahedron Lett.* **2015**, *56*, 6772−6776. (c) Yang, H.; Wu, L.; Wang, H.; Lu, J. Cathode made of compacted silver nanoparticles for electrocatalytic carboxylation of 1-phenethyl bromide with CO_2. *Chin. J. Catal.* **2016**, *37*, 994−998. (d) Senboku, H.; Sakai, K.; Fukui, A.; Sato, Y.; Yamauchi, Y. Efficient Synthesis of Mandel Acetates by Electrochemical Carboxylation of Benzal Diacetates. *ChemElectroChem.* **2019**, *6*, 4158−4164. (e) Yang, D.-T.; Zhu, M.; Schiffer, Z. J.; Williams, K.; Song, X.; Liu, X.; Manthiram, K. Direct Electrochemical Carboxylation of Benzylic C−N Bonds with Carbon Dioxide. *ACS Catal.* **2019**, *9*, 4699−4705. (f) Zhong, J.-S.; Yang, Z.-X.; Ding, C.-L.; Huang, Y.-F.; Zhao, Y.; Yan, H.; Ye, K.-Y. Desulfonylative Electrocarboxylation with Carbon Dioxide. *J. Org. Chem.* **2021**, *86*, 16162−16170.

(8) (a) Horn, E. J.; Rosen, B. R.; Chen, Y.; Tang, J.; Chen, K.; Eastgate, M. D.; Baran, P. S. Scalable and sustainable electrochemical allylic C−H oxidation. *Nature* **2016**, *533*, 77−81. (b) Ackermann, L. Metalla-electrocatalyzed C−H Activation by Earth-Abundant 3d Metals and Beyond. *Acc. Chem. Res.* **2020**, *53*, 84−104. (c) Jiao, K.-J.; Xing, Y.-K.; Yang, Q.-L.; Qiu, H.; Mei, T.-S. Site-Selective C−H Functionalization via Synergistic Use of Electrochemistry and Transition Metal Catalysis. *Acc. Chem. Res.* **2020**, *53*, 300−310. (d) Shen, T.; Lambert, T. H. Electrophotocatalytic diamination of vicinal C−H bonds. *Science* **2021**, *371*, 620−626. (e) Zhang, Z.; Chen, P.; Liu, G. Copper-catalyzed radical relay in C(sp^3)−H functionalization. *Chem. Soc. Rev.* **2022**, *51*, 1640−1658. (f) Zhou, S.;

Zhang, Z.-J.; Yu, J.-Q. Redox-Neutral Copper-Catalyzed Bimodal Dehydrogenation and Lactonization of C(sp^3)−H Bonds. *Nature* **2024**, *629*, 363−369.
(9) (a) Mita, T.; Michigami, K.; Sato, Y. Sequential Protocol for C(sp^3)−H Carboxylation with CO_2: Transition-Metal-Catalyzed Benzylic C−H Silylation and Fluoride-Mediated Carboxylation. *Org. Lett.* **2012**, *14*, 3462−3465. (b) Shigeno, M.; Sasaki, K.; Nozawa-Kumada, K.; Kondo, Y. Double-Carboxylation of Two C−H Bonds in 2-Alkylheteroarenes Using LiO-t-Bu/CsF. *Org. Lett.* **2019**, *21*, 4515−4519. (c) Shigeno, M.; Tohara, I.; Sasaki, K.; Nozawa-Kumada, K.; Kondo, Y. Combined Brønsted Base-Promoted CO_2 Fixation into Benzylic C−H Bonds of Alkylarenes. *Org. Lett.* **2022**, *24*, 4825−4830.
(10) (a) Chan, A. Y.; Perry, I. B.; Bissonnette, N. B.; Buksh, B. F.; Edwards, G. A.; Frye, L. I.; Garry, O. L.; Lavagnino, M. N.; Li, B. X.; Liang, Y.; Mao, E.; Millet, A.; Oakley, J. V.; Reed, N. L.; Sakai, H. A.; Seath, C. P.; MacMillan, D. W. C. Metallaphotoredox: The Merger of Photoredox and Transition Metal Catalysis. *Chem. Rev.* **2022**, *122*, 1485−1542. (b) Holmberg-Douglas, N.; Nicewicz, D. A. *Chem. Rev.* **2022**, *122*, 1925−2016. (c) Dutta, S.; Erchinger, J. E.; Strieth-Kalthoff, F.; Kleinmans, R.; Glorius, F. Energy transfer photocatalysis: exciting modes of reactivity. *Chem. Soc. Rev.* **2024**, *53*, 1068−1089. (d) Cabanero, D. C.; Rovis, T. Low-energy photoredox catalysis. *Nat. Rev. Chem.* **2025**, *9*, 28−45.
(11) (a) Masuda, Y.; Ishida, N.; Murakami, M. Light-Driven Carboxylation of o-Alkylphenyl Ketones with CO_2. *J. Am. Chem. Soc.* **2015**, *137*, 14063−14066. (b) Ishida, N.; Masuda, Y.; Imamura, Y.; Yamazaki, K.; Murakami, M. Carboxylation of Benzylic and Aliphatic C−H Bonds with CO_2 Induced by Light/Ketone/Nickel. *J. Am. Chem. Soc.* **2019**, *141*, 19611−19615. (c) Meng, Q.-Y.; Schirmer, T. E.; Berger, A. L.; Donabauer, K.; König, B. Photocarboxylation of Benzylic C−H Bonds. *J. Am. Chem. Soc.* **2019**, *141*, 11393−11397. (d) focused on the tertiary C−H bonds: Liu, Y.; Xue, G.-H.; He, Z.; Yue, J.-P.; Pan, M.; Song, L.; Zhang, W.; Ye, J.-H.; Yu, D.-G. Visible-Light Photoredox-Catalyzed Direct Carboxylation of Tertiary C-(sp^3)−H Bonds with CO_2: Facile Synthesis of All-Carbon Quaternary Carboxylic Acids. *J. Am. Chem. Soc.* **2024**, *146*, 28350−28359. (e) mainly focused on the tertiary and secondary C−H bonds: Li, J.-L.; Zhang, S.-S.; Jiang, L.-L.; Li, H.-Y.; Zhu, C.-M.; Yuan, P.-F.; Yang, Z.; Yang, X.-L.; Zhong, J.-J.; Meng, Q.-Y. Redox-Neutral Carboxylation of Benzylic Tertiary C−H Bonds with Carbon Dioxide. *Angew. Chem., Int. Ed.* **2025**, *64*, No. e202420852.
(12) (a) Wang, Y.; Tang, S.; Yang, G.; Wang, S.; Ma, D.; Qiu, Y. Electrocarboxylation of Aryl Epoxides with CO_2 for the Facile and Selective Synthesis of β-Hydroxy Acids. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202207746. (b) Wang, Y.; Zhao, Z.; Pan, D.; Wang, S.; Jia, K.; Ma, D.; Yang, G.; Xue, X.-S.; Qiu, Y. Metal-Free Electrochemical Carboxylation of Organic Halides in the Presence of Catalytic Amounts of an Organomediator. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202210201. (c) Zhao, Z.; Liu, Y.; Wang, S.; Tang, S.; Ma, D.; Zhu, Z.; Guo, C.; Qiu, Y. Site-Selective Electrochemical C−H Carboxylation of Arenes with CO_2. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202214710. (d) Wang, Y.; Wang, Q.; Zhu, Z.; Qi, W.; Qiu, Y. Organo-electroreduction enables arylcarboxylation of styrenes. *Sci. China Chem.* **2024**, *67*, 3825−3832.
(13) Nie, L.; Yang, J.; Liu, Z.; Zhou, S.; Chen, S.; Qi, X.; Lei, A.; Yi, H. Linear Paired Electrolysis Enables Redox-Neutral (3 + 2) Annulation of Benzofuran with Vinyldiazo Compounds. *J. Am. Chem. Soc.* **2024**, *146*, 31330−31338.
(14) McGrath, N. A.; Brichacek, M.; Njardarson, J. T. A Graphical Journey of Innovative Organic Architectures That Have Improved Our Lives. *J. Chem. Educ.* **2010**, *87*, 1348−1349.
(15) (a) Liang, Y.; Lin, F.; Adeli, Y.; Jin, R.; Jiao, N. Efficient Electrocatalysis for the Preparation of (Hetero)aryl Chlorides and Vinyl Chloride with 1,2-Dichloroethane. *Angew. Chem., Int. Ed.* **2019**, *58*, 4566−4570. (b) Xu, P.; Chen, P.-Y.; Xu, H.-C. Scalable Photoelectrochemical Dehydrogenative Cross-Coupling of Heteroarenes with Aliphatic C−H Bonds. *Angew. Chem., Int. Ed.* **2020**, *59*, 14275−14280. (c) Levitre, G.; Granados, A.; Molander, G. A. Sustainable photoinduced decarboxylative chlorination mediated by halogen atom transfer. *Green Chem.* **2023**, *25*, 560−565. (d) Wood, D.; Lin, S. Deuterodehalogenation Under Net Reductive or Redox-Neutral Conditions Enabled by Paired Electrolysis. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202218858. (e) Golden, D. L.; Flynn, K. M.; Aikonen, S.; Hanneman, C. M.; Kalyani, D.; Krska, S. W.; Paton, R. S.; Stahl, S. S. Radical chlorination of non-resonant heterobenzylic C−H bonds and high-throughput diversification of heterocycles. *Chem.* **2024**, *10*, 1593−1605.

https://doi.org/10.1021/jacs.5c00259
J. Am. Chem. Soc. 2025, 147, 13461−13470