

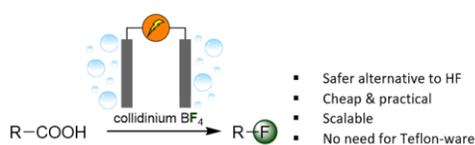
eFluorination using cheap and readily available tetrafluoroborate salts

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Supporting Information Placeholder



ABSTRACT: A practical electrochemical method for the rapid, safer, and mild synthesis of tertiary hindered alkyl fluorides from carboxylic acids has been developed without the need for hydrofluoric acid salts or non-glass reactors. In this anodic fluorination, collidinium tetrafluoroborate acts as both the supporting electrolyte and fluoride donor. A wide range of functional groups has been shown to be compatible, and the possibility of scale-up using flow electrochemistry has also been demonstrated.

Fluorine is an element of significant interest in drug development due to its similar size when compared to hydrogen (1.47 vs 1.20 Å), high electron-withdrawing capacity, and greater lipophilicity. Moreover, C-F bonds are typically more stable than C-H bonds, and efforts to manufacture fluoropharmaceuticals have increased in recent years.¹ It is estimated that 20% of small molecule drugs on the market contain one or more fluorine atoms or fluorinated functional groups.²⁻⁴ Such compounds have shown promise as anaesthetics, antidepressants, anti-inflammatory drugs, and anti-cancer agents.¹⁻⁴

Incorporation of fluorine into potential drug candidates has been shown to improve metabolic stability, positively impact physicochemical properties, and increase the binding affinity to target proteins.¹ It is therefore unsurprising that significant efforts have been undertaken to develop methods for the selective fluorination of organic molecules. These methods fall into one of three categories: nucleophilic (A), electrophilic (B), and radical (C) fluorination (Figure 1). The use of inorganic reagents [e.g. AgF₂, HgF₂, Tl(O₂CCF₃)₃], while easily accessible, is often disfavored due to their high toxicity and poor solubility in organic solvents, resulting in lower reactivity which necessitates harsh reaction conditions.⁵ While XeF₂ has been shown to be a possible alternative to these reagents, its general use has been precluded by its relatively high cost, toxicity, and instability in the presence of moisture.⁶⁻⁸ Similarly, the use of alkali metal salts has shown promise, however, reported substrate scopes are limited.⁹⁻¹¹ Organic fluorination agents such as Selectfluor, NFSI, DAST, and hypervalent iodine reagents are better suited to drug discovery processes, however, their high costs and limited stability often preclude large-scale reactions.¹²⁻¹⁶ Moreover, the synthesis of tertiary alkyl fluorides remains a significant challenge.^{17,18}

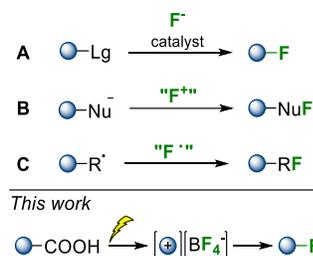


Figure 1. Approaches to fluorination. Nucleophilic (A), electrophilic (B), and radical (C)

Electrosynthesis can provide safer, fast, and economical routes toward various small molecules of interest, including MOM-type ethers,^{19,20} hindered dialkyl ethers,²¹ orthoesters,²² and sulfonyl fluorides.²³ Furthermore, electrochemistry has long been associated with fluorine chemistry.²⁴ Indeed, fluorine gas was initially synthesized through the electrolysis of HF containing traces of KF in 1886, and this remains the favored method for industrial F₂ production. Consequently, considerable time has been invested in developing electrochemical fluorination processes. Perhaps one of the most encountered reactions is the anodic fluorination of organic compounds in the presence of either a fluoride anion or a liquid electrolyte (e.g. Et₄NF·xHF, Et₃N·3HF, HF-pyridine).^{24,25} Unfortunately, these reagents are toxic, and usually require the use of non-glass reactors, which makes them impractical.^{26,27}

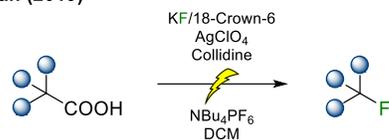
Organic electrosynthesis often uses a supporting electrolyte in vast excess compared to the reagents of interest to render the solution conductive.^{28,29} Commonly encountered supporting electrolytes include perchlorates, triflates, hexafluorophosphates, and tetrafluoroborates.²⁹ We reasoned that aside from

facilitating necessary conductivity, in a similar fashion to the Balz–Schiemann reaction,^{30,31} the use of a fluorinated supporting electrolyte could act as a cheap and safer-to-handle source of fluoride ions.³¹ Additionally, using a weakly coordinating solvent (e.g. dichloromethane) should favor a tight ion pairing between an anodically generated carbocation and the supporting electrolyte's anion, thus limiting unwanted side reactions.

Decarboxylative fluorination, the substitution of a -COOH group with fluorine, has been achieved through the use of Selectfluor and either chemical- or photocatalytic oxidation.^{32–37} However, these methods either require significant quantities of the expensive fluorinating agent,^{32–37} costly photocatalysts,³⁵ or are limited to very specific substrates.^{32,33,37} Moreover, examples of electrochemical decarboxylative fluorination remain rare; necessitate toxic, corrosive, expensive, or potentially explosive reagents; and are limited in terms of substrate scope (Figure 2).^{21,38} Herein we report a complimentary electrochemical methodology for the synthesis of hindered fluorinated centres which aims to reduce the cost and increase the accessibility of this transformation. This is achieved through anodic decarboxylation of tertiary carboxylic acids in the presence of a cheap, bench-stable, and easily accessible fluorinated supporting electrolyte, 2,4,6-collidinium tetrafluoroborate without the need for PTFE reactors.

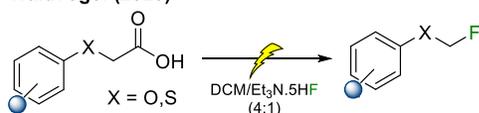
Electrochemical Decarboxylative Fluorination

Baran (2019)



- Only 3 examples
- Excess of expensive additives
- AgClO_4 is potentially explosive

Waldvogel (2020)



- Limited to aryl(thio)ethers
- Uses toxic HF salts
- Requires the use of teflon cells

Figure 2. Electrochemical methods for decarboxylative fluorination

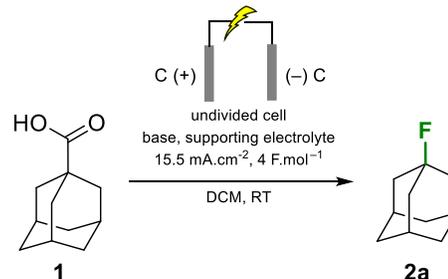
Recently, Baran and co-workers demonstrated the use of electrochemistry to generate carbocations from non-activated aliphatic carboxylic acids using Kolbe/Hofer-Moest chemistry.^{21,39,40} These carbocations were captured by different alcohols to afford a range of hindered ethers, which are challenging to synthesize by conventional means. It was also reported that, in the presence of an excess of KF and 18-crown-6, the carbocations could be trapped to form the corresponding alkyl fluorides. However, only four examples were reported. Moreover, the reaction requires the use of expensive and potentially explosive AgClO_4 as a sacrificial oxidant, and no further investigations or optimisations were reported. Therefore, we hypothesized that a fluorinated salt such as PF_6^- or BF_4^- could advantageously replace the need for a supporting electrolyte, an additional fluoride source, crown ethers and sacrificial oxidant all at once.

Initial analytical and preparative studies focused on the use of collidinium tetrafluoroborate as a supporting electrolyte,

owing to its ease of synthesis and low hygroscopicity compared to traditional supporting electrolytes. Furthermore, the reduction of collidinium serves two purposes: it leads to the generation of hydrogen at the cathode, avoiding any deleterious side reductions and releases collidine, a base that can deprotonate the carboxylic acid, lowering its oxidation potential and favouring its adsorption on the anode. Moreover, collidine itself is known to be stable towards oxidation and therefore is unlikely to result in unwanted side reactions.

Cyclic voltammetry studies of 1-adamantane carboxylic acid (**1**), with ${}^n\text{Bu}_4\text{NPF}_6$ supporting electrolyte in the presence of collidinium tetrafluoroborate, or with collidinium tetrafluoroborate, as the sole supporting electrolyte, were largely unremarkable. This is likely due to the oxidation potential of the carboxylate being higher than the potential associated with solvent breakdown, a well-known phenomenon associated with the Kolbe reaction. The adsorption of the carboxylates onto the anode is a crucial step during their anodic oxidation.⁴¹

Undeterred by this, we continued our investigations using graphite electrodes since they are known to lead to the strong adsorption of organic compounds and favour multielectron transfers. When 3 mL of a 0.07 M solution of **1** was electrolysed with an applied current of 15 mA ($J = 15.5 \text{ mA}\cdot\text{cm}^{-2}$) in the presence of 2,4,6-collidine and collidinium tetrafluoroborate, the corresponding alkyl fluoride, **2a**, could be observed by GC-MS. Optimization studies for this reaction on a larger scale (0.33 mmol in 5 mL vs 0.2 mmol in 3 mL; Scheme 1) revealed that the greatest yield could be obtained using five equivalents of collidinium tetrafluoroborate and electrolysing until a charge of 4 F had been passed (see supporting information).



Scheme 1: Reaction optimization for the synthesis of **2a**

Alternative supporting electrolytes were examined, however, yields of 1-fluoroadamantane (**2a**) were significantly lower. The use of tetraalkylammonium salts led to a high amount of trialkylamine via their cathodic Hofmann degradation. Interestingly, the use of 3 Å molecular sieves to remove water from the cell had little impact on the yield of **2a**, although this could be linked to the choice of substrate. No reaction was observed when the reaction mixture was left to stir without electricity.

With the best conditions in hand, we sought to explore the scope and limitations of our novel electrochemical fluorination approach. A range of tertiary carboxylic acids bearing different functionalities were prepared and subjected to our electrolysis conditions (Figure 3). While, as mentioned before, the fluorination of adamantyl derivatives tolerated the use of non-rigorously dried solvent, the presence of adventitious water was deleterious for the fluorination of non-adamantyl acids. The presence of trace water could preclude formation of the desired alkyl fluoride, as observed by GC-MS studies of the crude mixtures. Consequently, all further electrolyses were conducted in the presence of 3 Å molecular sieves to avoid this eventuality.

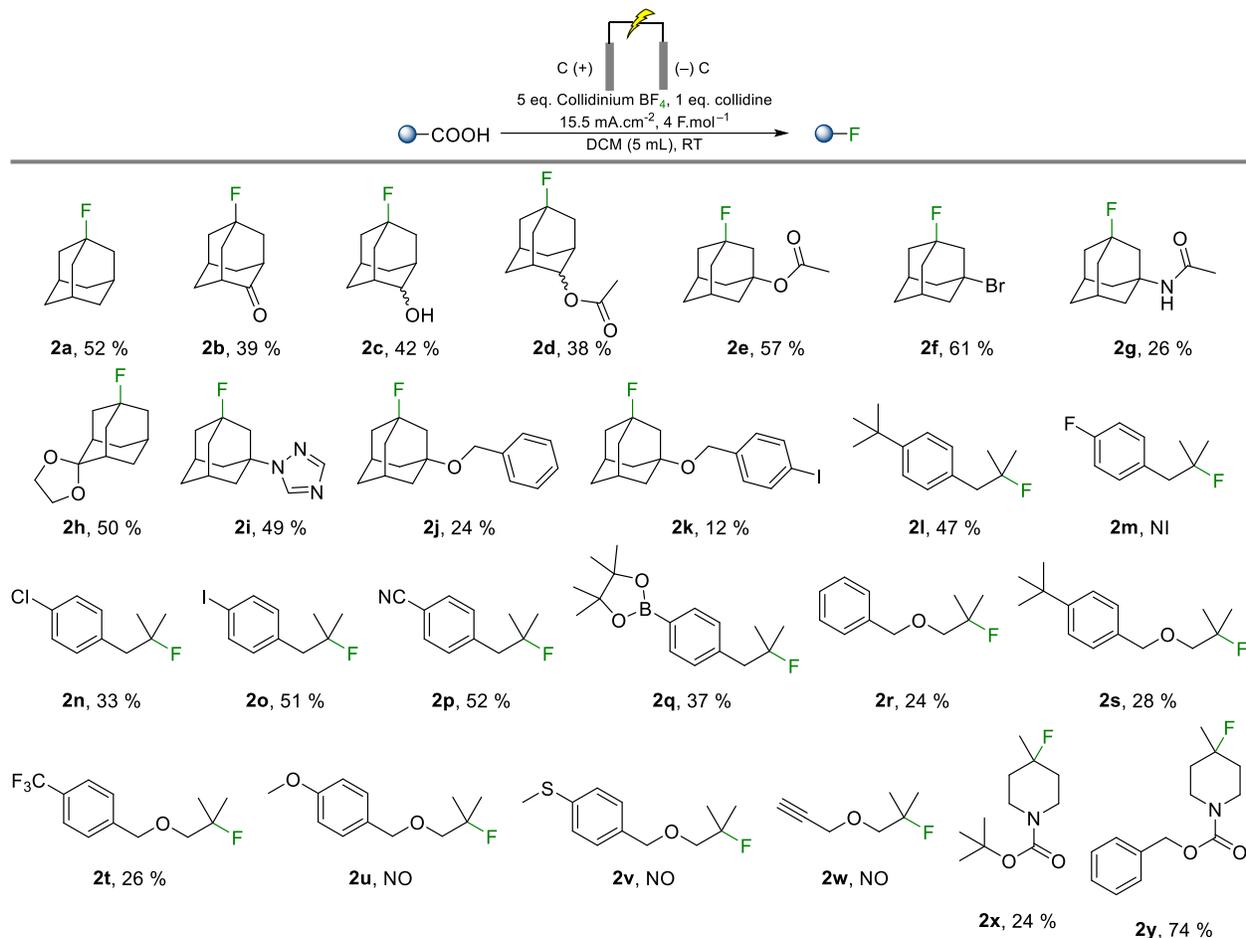


Figure 3. Substrate scope for the synthesis of tertiary alkyl fluorides (0.4 mmol scale). Yields reported for pure isolated products. NI = not isolated (observed by GC-MS). NO = not observed.

A range of carboxylic acids were electrolysed using our conditions, affording the desired fluorinated analogues with moderate to good yields (39–61%), with the corresponding alcohol being the only identifiable by-product by GC-MS. As expected, due to its volatility, **2a** was obtained in a slightly lower yield than that determined by GC-MS. Unprotected ketones (**2b**), esters (**2d**, **2e**), acetals (**2h**) and free alcohols (**2c**) were tolerated, as were halides (**2f**), triazoles (**2i**) and amides (**2g**). The method was then pushed further by electrolysing benzylic derivatives, which are often problematic.^{42,43} Pleasingly only traces of the corresponding benzaldehydes, arising from electrochemical ether cleavage after benzylic oxidation,⁴⁴ were observed in the crude electrolysis mixtures of **2j** and **2k**.

The incorporation of aromatic halides (**2k,m,n,o,t**) had little effect on the fluorination. This is especially surprising in the case of **2o**, since similar substrates are known to be able to generate an iodonium cation under anodic conditions. It should be noted that while **2m** was observed in the crude reaction mixture by TLC and GC-MS, it was too volatile to isolate using standard methods, which precluded its complete characterisation. Excitingly, boronates remained intact after electrolysis (**2q**), opening the possibility of further chemistry (e.g. cross couplings) after fluorination.

Electron-donating groups such as methoxy or thiomethyl favoured benzylic oxidation, thus precluding the formation of the desired alkyl fluorides (**2u**, **2v**), instead giving rise to the

corresponding benzaldehydes, as observed by GC-MS. No reaction was observed with carboxylic acids bearing a propargyl group, with only starting material recovered after extended electrolysis (6 F.mol⁻¹). However, both *N*-Boc and *N*-CBz groups were tolerated (**2x**, **2y**), with no α -oxidation observed by GC-MS, although the volatility of **2x** resulted in a diminished isolated yield. In all cases, complete consumption of the starting material was observed either by TLC or GC-MS analysis; however, isolation and identification of the by-products was unsuccessful.

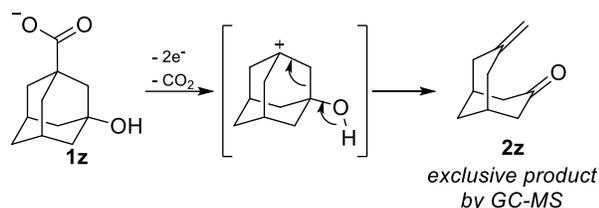
A possible mechanism for the electrochemical synthesis of alkyl fluorides from carboxylic acids is outlined in the supporting information. First, the acid is deprotonated by 2,4,6-collidine to give the corresponding anion. Oxidation, followed by decarboxylation, gives rise to the corresponding tertiary radical which, in turn, is oxidised further to give a tertiary carbocation, which rapidly forms a close ion-pair with BF₄⁻, which is in high concentration in the double layer around the anode. Finally, abstraction of a fluoride from BF₄⁻ by the carbocation give rise to the desired alkyl fluoride and BF₃. An attempt to use BF₃OEt₂ in place of collidinium tetrafluoroborate was unsuccessful.

Evidence for carbocation formation was obtained during the electrolysis of 3-hydroxyadamantane-1-carboxylic acid using our standard conditions. For this compound, electrolysis resulted in no observable formation of fluorinated products. Instead, Grob fragmentation occurs to form enone **2z**, as observed

by GC-MS (Scheme 2). This product formation was not observed for other adamantane derivatives, owing to the structural requirements for fragmentation.

This method is limited to the synthesis of hindered tertiary fluorinated centres. Even though Hofer-Moest oxidations can be used to generate stabilized secondary or primary carbocations like oxocarbenium or benzylic cations, such acid precursors did not undergo fluorination in our case and complete degradation of the substrates was observed. Finally, non-stabilized primary and secondary carbocations are known to be extremely challenging to generate via anodic oxidation of carboxylic acids.

Scheme 2. Proposed fragmentation of 3-hydroxyadamantane-1-carboxylic acid



The plausibility of close ion-pairing between the carbocation and BF_4^- was supported by the electrolysis of **1** in the presence of 5 eq. of collidinium tetrafluoroborate and 5 eq. of cyclohexanol. Given the latter's greater nucleophilicity, exclusive formation of the corresponding ether was expected. However, analysis of the reaction mixture after electrolysis by GC-MS showed the formation of **2a** as the major product and ether **4** as a minor product in a 4:1 ratio (Scheme 3).

Scheme 3. Oxidation of **1** in the presence of cyclohexanol



Finally, we further sought to demonstrate the practicality of our method at a larger scale, both in batch and flow. The synthesis of **2a** was conducted on a 1 mmol scale in batch in 10 mL of DCM and resulted in an excellent yield of 79% after workup. In flow, the current density was the same as in the batch experiments ($15.5 \text{ mA}\cdot\text{cm}^{-2}$), and the flow rate was adjusted to ensure the transfer of $4 \text{ F}\cdot\text{mol}^{-1}$ (cell volume: $225 \mu\text{L}$).

The electrolysis of 1 g of **1** by attachment of a reservoir of the acid in DCM (0.1 M) in the presence of 1 eq. of collidine and 2 eq. of Collidinium tetrafluoroborate was attempted. Decreasing the number of equivalents of Collidinium tetrafluoroborate was necessary to ensure complete dissolution and prevent blockages in the flow system. The application of an 8-bar backpressure helped reduce hydrogen bubble formation, as observed in batch electrolyses, arising from the reduction of collidinium. The desired alkyl fluoride **2a** was isolated in good yield (59%) after workup, therefore further demonstrating the plausibility of reaction scale-up.

In summary, a new electrochemical method to rapidly fluorinate hindered carbon centres has been developed, which is built upon the anodic decarboxylation of substituted carboxylates in the presence of collidinium tetrafluoroborate. This method relies on common chemicals found in most laboratories, lessens the need for expensive, unstable, and toxic fluorinating agents, and can be undertaken in standard glass cells. Good functional group tolerance was observed, and a broad scope of substrates was synthesized. The scalability of this new method has been demonstrated in flow, thus broadening its appeal and utility to the synthetic community.

ASSOCIATED CONTENT

Data Availability

The data underlying this study are available in the published article and its supporting information.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Synthetic procedures, spectral data, and compound characterization (PDF)

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Notes

The authors declare no competing financial interests

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REFERENCES

- (1) Shah, P.; Westwell, A. D. The Role of Fluorine in Medicinal Chemistry. *J. Enzyme Inhib. Med. Chem.* **2007**, *22* (5), 527–540.
- (2) Inoue, M.; Sumii, Y.; Shibata, N. Contribution of Organofluorine Compounds to Pharmaceuticals. *ACS Omega* **2020**, *5* (19), 10633–10640.
- (3) Isanbor, C.; O'Hagan, D. Fluorine in Medicinal Chemistry: A Review of Anti-Cancer Agents. *J. Fluor. Chem.* **2006**, *127* (3), 303–319.
- (4) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. Fluorine in Medicinal Chemistry. *Chem. Soc. Rev.* **2008**, *37* (2), 320–330.
- (5) Caron, S. Where Does the Fluorine Come From? A Review on the Challenges Associated with the Synthesis of Organofluorine Compounds. *Org. Process Res. Dev.* **2020**, *24* (4), 470–480.
- (6) Patrick, T. B.; Johri, K. K.; White, D. H. Fluoro-Decarboxylation with Xenon Difluoride. *J. Org. Chem.* **1983**, *48* (22), 4158–4159.
- (7) Ramsden, C. A.; Shaw, M. M. Fluorodecarboxylation, Rearrangement and Cyclisation: The Influence of Structure and Environment on the Reactions of Carboxylic Acids with Xenon Difluoride. *Tetrahedron Lett.* **2009**, *50* (26), 3321–3324.
- (8) Chatalova-Sazepin, C.; Binayeva, M.; Epifanov, M.; Zhang, W.; Foth, P.; Amador, C.; Jagdeo, M.; Boswell, B. R.; Sammis, G. M. Xenon Difluoride Mediated Fluorodecarboxylations for the Syntheses of Di- and Trifluoromethoxyarenes. *Org. Lett.* **2016**, *18* (18), 4570–4573.
- (9) Sawamura, T.; Takahashi, K.; Inagi, S.; Fuchigami, T. Electrochemical Fluorination Using Alkali-Metal Fluorides. *Angew. Chem. Int. Ed.* **2012**, *51*, 4413–4416.
- (10) Shida, N.; Takenaka, H.; Gotou, A.; Isogai, T.; Yamauci, A.; Kishikawa, Y.; Nagata, Y.; Tomita, I.; Fuchigami, T.; Inagi, S. Alkali Metal Fluorides in Fluorinated Alcohols: Fundamental Properties and Applications to Electrochemical Fluorination. *J. Org. Chem.* **2021**, *86* (22), 16128–16133.
- (11) Shida, N.; Villani, E.; Sanuki, M.; Miyamoto, K.; Gotou, A.; Isogai, T.; Yamauchi, A.; Fuchigami, T.; Tomita, I.; Inagi, S. Bipolar Electrochemical Fluorination of Triphenylmethane and Bis(Phenylthio)Diphenylmethane Derivatives in a U-Shaped Cell. *Electrochemistry* **2021**, *89* (5), 476–479.
- (12) Winterson, B.; Rennigholtz, T.; Wirth, T. Flow Electrochemistry: A Safe Tool for Fluorine Chemistry. *Chem. Sci.* **2021**, *12* (26), 9053–9059.
- (13) Singh, F. V.; Shetgaonkar, S. E.; Krishnan, M.; Wirth, T. Progress in Organocatalysis with Hypervalent Iodine Catalysts. *Chem. Soc. Rev.* **2022**, *51* (18), 8102–8139.
- (14) Doobary, S.; Sedikides, A. T.; Caldora, H. P.; Poole, D. L.; Lennox, A. J. J. Electrochemical Vicinal Difluorination of Alkenes: Scalable and Amenable to Electron-Rich Substrates. *Angew. Chem. Int. Ed.* **2020**, *59* (3), 1155–1160.
- (15) Berger, M.; Lenhard, M. S.; Waldvogel, S. R. Para-Fluorination of Anilides Using Electrochemically Generated Hypervalent Iodoarenes. *Chem. - A Eur. J.* **2022**, *28* (41).
- (16) Umemoto, T.; Yang, Y.; Hammond, G. B. Development of N-F Fluorinating Agents and Their Fluorinations: Historical Perspective. *Beilstein J. Org. Chem.* **2021**, *17*, 1752–1813.
- (17) Chen, H.; Liu, Z.; Lv, Y.; Tan, X.; Shen, H.; Yu, H. Z.; Li, C. Selective Radical Fluorination of Tertiary Alkyl Halides at Room Temperature. *Angew. Chem. Int. Ed.* **2017**, *56* (48), 15411–15415.
- (18) Zhang, W.; Gu, Y.-C.; Lin, J.-H.; Xiao, J.-C. Dehydroxylative Fluorination of Tertiary Alcohols. *Org. Lett.* **2020**, *22* (16), 6642–6646.
- (19) Luo, X.; Ma, X.; Lebreux, F.; Markó, I. E.; Lam, K. Electrochemical Methoxymethylation of Alcohols – a New, Green and Safe Approach for the Preparation of MOM Ethers and Other Acetals. *Chem. Commun* **2018**, *54*, 9969–9972.
- (20) van Melis, C. G. W.; Penny, M. R.; Garcia, A. D.; Petti, A.; Dobbs, A. P.; Hilton, S. T.; Lam, K. Supporting-Electrolyte-Free Electrochemical Methoxymethylation of Alcohols Using a 3D-Printed Electrosynthesis Continuous Flow Cell System. *ChemElectroChem* **2019**, *6*, 4144–4148.
- (21) Xiang, J.; Shang, M.; Kawamata, Y.; Lundberg, H.; Reisberg, S. H.; Chen, M.; Mykhailiuk, P.; Beutner, G.; Collins, M. R.; Davies, A.; Del Bel, M.; Gallego, G. M.; Spangler, J. E.; Starr, J.; Yang, S.; Blackmond, D. G.; Baran, P. S. Hindered Dialkyl Ether Synthesis with Electrogenerated Carbocations. *Nature* **2019**, *573* (7774), 398–402.
- (22) Garcia, A. D.; Leech, M. C.; Petti, A.; Denis, C.; Goodall, I. C. A.; Dobbs, A. P.; Lam, K. Anodic Oxidation of Dithiane Carboxylic Acids: A Rapid and Mild Way to Access Functionalized Orthoesters. *Org. Lett.* **2020**, *22* (10), 4000–4005.
- (23) Laudadio, G.; Bartolomeu, A. de A.; Verwijlen, L. M. H. M.; Cao, Y.; de Oliveira, K. T.; Noël, T. Sulfonyl Fluoride Synthesis through Electrochemical Oxidative Coupling of Thiols and Potassium Fluoride. *J. Am. Chem. Soc.* **2019**, *141* (30), 11832–11836.
- (24) Ignat'ev, N. V. 4 - Electrochemical Fluorination: A Powerful Tool for the Preparation of Organofluorine Compounds. In *Progress in Fluorine Science*; Groult, H., Leroux, F. R., Tressaud, A. B. T.-M. S. P. and R. of F. C., Eds.; Elsevier, 2017; pp 71–123.
- (25) Webb, E. W.; Park, J. B.; Cole, E. L.; Donnelly, D. J.; Bonacorsi, S. J.; Ewing, W. R.; Doyle, A. G. Nucleophilic (Radio)Fluorination of Redox-Active Esters via Radical-Polar Crossover Enabled by Photoredox Catalysis. *J. Am. Chem. Soc.* **2020**, *142* (20), 9493–9500.
- (26) Fuchigami, T.; Inagi, S. Recent Advances in Electrochemical Systems for Selective Fluorination of Organic Compounds. *Acc. Chem. Res.* **2020**, *53* (2), 322–334.
- (27) Heard, D. M.; Doobary, S.; Lennox, A. J. J. 3D Printed Reactionware for Synthetic Electrochemistry with Hydrogen Fluoride Reagents. *ChemElectroChem* **2021**, *8* (11), 2070–2074.
- (28) Kingston, C.; Palkowitz, M. D.; Takahira, Y.; Vantourou, J. C.; Peters, B. K.; Kawamata, Y.; Baran, P. S. A Survival Guide for the “Electro-Curious.” *Acc. Chem. Res.* **2020**, *53* (1), 72–83.
- (29) Leech, M. C.; Lam, K. A Practical Guide to Electrosynthesis. *Nat. Rev. Chem.* **2022**, *6* (4), 275–286.
- (30) Cresswell, A. J.; Davies, S. G.; Roberts, P. M.; Thomson, J. E. Beyond the Balz–Schiemann Reaction: The Utility of Tetrafluoroborates and Boron Trifluoride as Nucleophilic Fluoride Sources. *Chem. Rev.* **2015**, *115* (2), 566–611.
- (31) Yoshida, J.; Ishichi, Y.; Isoe, S. Intramolecular Carbon-Carbon Bond Formation by the Anodic Oxidation of Unsaturated .Alpha.-Stannyl Heteroatom Compounds. Synthesis of Fluorine Containing Heterocyclic Compounds. *J. Am. Chem. Soc.* **1992**, *114* (19), 7594–7595.
- (32) Wang, J.; Scott, A. I. Fluoro-Decarboxylation of Pyroglutamic Acids by F-TEDA-BF₄ - A Convenient General Synthesis of Fluoropyrroles. *J. Chem. Soc., Chem. Commun.* **1995**, 2399–2400.
- (33) Leung, J. C. T.; Chatalova-Sazepin, C.; West, J. G.; Rueda-Becerril, M.; Paquin, J. F.; Sammis, G. M. Photo-Fluorodecarboxylation of 2-Aryloxy and 2-Aryl Carboxylic Acids. *Angew. Chem. Int. Ed.* **2012**, *51* (43), 10804–10807.
- (34) Yin, F.; Wang, Z.; Li, Z.; Li, C. Silver-Catalyzed Decarboxylative Fluorination of Aliphatic Carboxylic Acids in Aqueous Solution. *J. Am. Chem. Soc.* **2012**, *134* (25), 10401–10404.
- (35) Ventre, S.; Petronijevic, F. R.; MacMillan, D. W. C. Decarboxylative Fluorination of Aliphatic Carboxylic Acids via Photoredox Catalysis. *J. Am. Chem. Soc.* **2015**, *137* (17), 5654–5657.
- (36) Katada, M.; Kitahara, K.; Iwasa, S.; Shibatomi, K. Catalyst-Free Decarboxylative Fluorination of Tertiary β -Keto Carboxylic Acids. *Synlett* **2018**, *29* (18), 2408–2411.
- (37) Vincent, É.; Brioché, J. Synthesis of Alkyl Fluorides by Silver-Catalyzed Radical Decarboxylative Fluorination of Cesium Oxalates. *European J. Org. Chem.* **2021**, *2021* (17), 2421–2430.
- (38) Berger, M.; Herszman, J. D.; Kurimoto, Y.; Kurimoto, Y.; De Kruijff, G. H. M.; Schüll, A.; Schüll, A.; Ruf, S.; Waldvogel, S. R. Metal-Free Electrochemical Fluorodecarboxylation of Aryloxyacetic Acids to Fluoromethyl Aryl Ethers. *Chem. Sci.* **2020**, *11* (23), 6053–6057.
- (39) Hofer, H.; Moest, M. Ueber Die Bildung von Alkoholen Bei Der Elektrolyse Fettsaurer Salze. *Justus Liebigs Ann. Chem.* **1902**, *323* (3), 284–323.
- (40) Z. Wang. Kolbe Electrolysis. In *Comprehensive Organic Name Reactions and Reagents*; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2010.

- (41) Schäfer, H. J. Recent Contributions of Kolbe Electrolysis to Organic Synthesis. *Top. Curr. Chem.* **1990**, *152* (4), 91–151.
- (42) Atkins, A. P.; Rowett, A. C.; Heard, D. M.; Tate, J. A.; Lennox, A. J. J. Electrochemical Benzylic C(Sp³)-H Acyloxylation. *Org. Lett.* **2022**, *24* (28), 5105–5108.
- (43) Marko, J. A.; Durgham, A.; Bretz, S. L.; Liu, W. Electrochemical Benzylic Oxidation of C-H Bonds. *Chem. Commun.* **2019**, *55*, 937–940.
- (44) Green, R. A.; Jolley, K. E.; Al-Hadedi, A. A. M.; Pletcher, D.; Harrowven, D. C.; De Frutos, O.; Mateos, C.; Klauber, D. J.; Rincón, J. A.; Brown, R. C. D. Electrochemical Deprotection of Para-Methoxybenzyl Ethers in a Flow Electrolysis Cell. *Org. Lett.* **2017**, *19* (8), 2050–2053.