RSC Advances

ROYAL SOCIETY OF CHEMISTRY

Cite this: *RSC Adv.*, 2024, **14**, 154

Electrochemical oxidative cyclization of *N*-allylamides for the synthesis of CF_3-containing benzoxazines and oxazolines†

Yutian Li,[ac] Li Wang,[ac] Shengbin Zhou,[ac] Guoxue He *[ac] and Yu Zhou *[abc]

Received 25th October 2023
Accepted 7th December 2023

DOI: 10.1039/d3ra07282g

rsc.li/rsc-advances

The introduction of trifluoromethyl ($-CF_3$) groups into compounds is a common synthetic strategy in organic chemistry. Commonly used methods for introducing trifluoromethyl groups are limited by harsh reaction conditions, low regioselectivity, or the need for excess reagents. In this study, a facile electrochemical oxidative and radical cascade cyclization of *N*-(2-vinylphenyl)amides for the synthesis of CF_3-containing benzoxazines and oxazolines was obtained. This sustainable protocol features inexpensive and durable electrodes, a wide range of substrates, diverse functional group compatibility under transition-metal-free, external-oxidant-free, and additive-free conditions, and can be applied in an open environment.

Introduction

Heterocyclic compounds are one of the most important skeletons in organic synthesis, pharmaceutical chemistry, materials science and bioscience. Heterocycles containing N and O atoms play a crucial role in pharmaceuticals and functional molecules.[1] Among these, benzoxazines and oxazolines are common privileged fragments frequently found in pharmaceutical molecules and biologically active compounds with remarkable biological activities,[2] such as anxiolytic,[3] anti-HIV,[4] progesterone receptor agonist,[5] anti-tuberculosis,[6] and anorectant activities[7](Fig. 1).

Generally, the incorporation of fluorinated moieties into molecules can significantly change their physical, chemical, and biological properties. For example, the trifluoromethyl ($-CF_3$) moiety is widely present in a variety of drugs (celecoxib, fluoxetine, and trifloxystrobin *etc.*), which can improve the efficacy, solubility, lipophilicity, metabolic stability, and binding selectivity.[8] Efavirenz containing trifluoromethyl benzoxazine shows potent anti-HIV activity.[4] As a result, the potential values of these trifluoromethylated benzoxazines and oxazolines have attracted significant attention from chemists to develop efficient strategies for the construction of these intriguing molecule scaffolds.[9] Xiao and co-workers reported a visible-light-induced photocatalytic trifluoromethylation of *N*-allylamides for the synthesis of CF_3-containing benzoxazines and oxazolines under Umemoto's reagent and $Ru(bpy)_3(PF_6)_2$ (Scheme 1a).[9m] Similarly, Kumar's group developed a copper-catalyzed approach for construction of trifluoromethylated benzoxazines by using Umemoto's reagent (Scheme 1b).[10] These methods are effective and versatile, but are limited to transition-metal catalysts and Umemoto's reagent as CF_3 sources. In addition, Natarajan and colleagues disclosed a novel 9,10-phenanthrenedione visible-light photocatalysis protocol for the synthesis of trifluoromethylated benzoxazines by using *N*-(2-vinylphenyl)amides and trifluoromethylsulfinate under oxygen atmosphere (Scheme 1c).[9a] Nevertheless, it still requires additional photocatalysts and oxidants. Therefore, it is highly desirable to develop alternatively efficient, sustainable, green, and environmentally friendly synthetic methods avoiding transition metal catalysts and chemical oxidants.

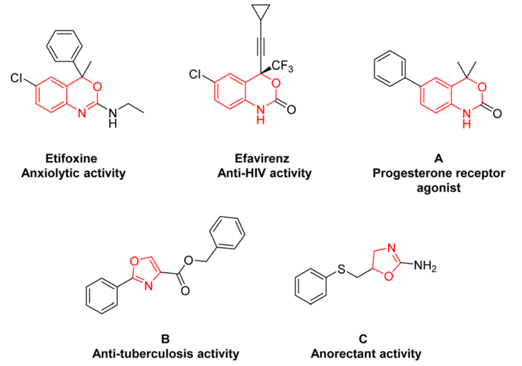


Fig. 1 Bioactive compounds containing benzoxazine or oxazoline motifs.

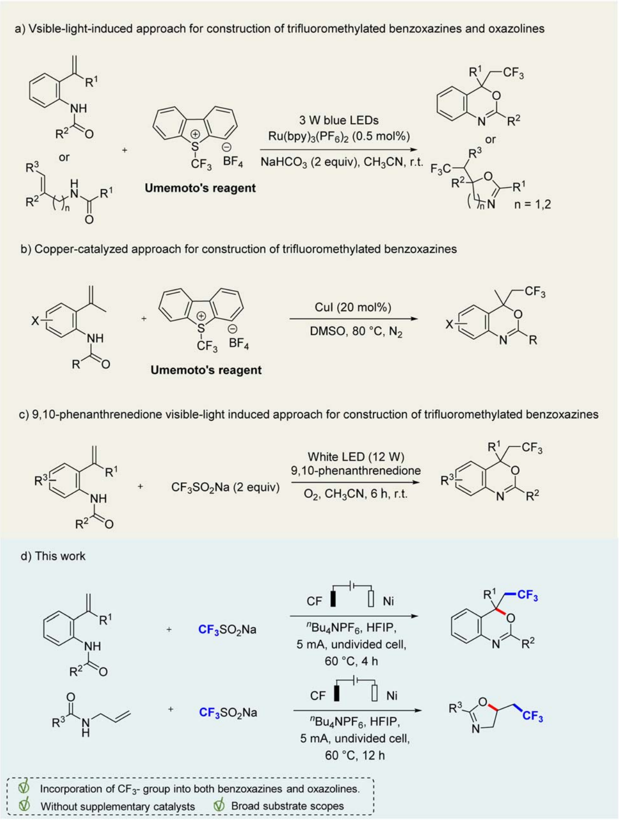
---

[a] School of Pharmaceutical Science and Technology, Hangzhou Institute for Advanced Study, University of Chinese Academy of Sciences, Hangzhou 310024, China. E-mail: heguoxue@ucas.ac.cn

[b] State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China. E-mail: zhouyu@simm.ac.cn

[c] University of Chinese Academy of Sciences, Beijing 100049, China

† Electronic supplementary information (ESI) available. See DOI: https://doi.org/10.1039/d3ra07282g



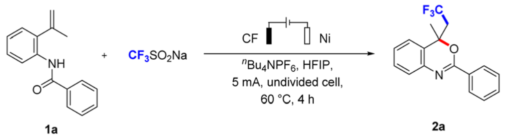
Scheme 1 Strategies for the synthesis of trifluoromethylated benzoxazines.

Organic electrochemistry provides an effective and sustainable strategy for the synthesis of valuable chemicals, employing inexpensive and renewable electrons as redox reagents.[11] In our continuous efforts, our goal is to develop green, metal-free, and efficient methods to construct diversified heterocyclic scaffolds.[12] In our previous work, we reported a direct azidation of benzylic C(sp^3)–H bonds through an electrochemical process.[13] Herein, we'd like to report a new finding to construct trifluorinated benzoxazines and oxazolines through an effective electrochemical strategy, which may use cheap carbon fibre and nickel plates as electrodes in an undivided cell, without any external chemical oxidants, metal catalysts and additives (Scheme 1d). However, while we were preparing this manuscript, a similar work appeared, focusing on the construction of CF_2-substituted benzoxazines,[14] in which the reaction system required trifluoroacetic acid as a catalyst, adding complexity to the reaction system. In contrast, our reaction system is simpler and environmentally benign without the need for a transition metal catalyst or external oxidant, and can proceed smoothly with diverse functional group compatibility.

Results and discussion

Based on the above conception, we have attempted to achieve the CF_3-containing benzoxazines by treatment of *N*-(2-(prop-1-en-2-yl)phenyl)benzamide (**1a**) with CF_3SO_2Na. The reaction was carried out in an undivided cell equipped with a carbon fibre (CF) anode and a nickel plate (Ni) cathode under a constant current of 5 mA (Table 1). The desired product **2a** was obtained in 72% yield when $^nBu_4NPF_6$ was used as the electrolyte in HFIP at 60 °C for 4 h (entry 1). We tried other electrolytes, such as Et_4NBF_4, $^nBu_4NOAc$, $^nBu_4NBr$, and $^nBu_4NI$. Et_4NBF_4 resulted in a significant decrease (entry 2) in yield, only trace of the product was observed when using $^nBu_4NOAc$ and $^nBu_4NBr$ as electrolytes (entry 3), and the product was I-containing benzoxazine derivative when using $^nBu_4NI$ as the electrolyte (entry 4). Besides, the product **2a** also was observed in the absence of electrolyte (entry 5). When we replaced solvent with DMSO (entry 6), CH_3CN (entry 7), CH_3OH (entry 8), and DCE (entry 9), all of them resulted in a slight decrease in the yield. This could be attributed to the ability of HFIP to stabilize radical cation intermediates, thereby aiding in substrate oxidation while preventing the product of overoxidation.[15] We further evaluated other electrode materials, including Pt plate (entry 10), Fe plate (entry 11) as anode, and Fe plate (entry 12), Al plate (entry 13) as cathode, none of them was more effective. We transformed the current to 2 mA (entry 14) or 10 mA current (entry 15), the reaction efficiency was noticeably dropped in 2 mA current. The product **2a** was decreased under 10 mA current, which

Table 1 Optimization of reaction conditions[a]



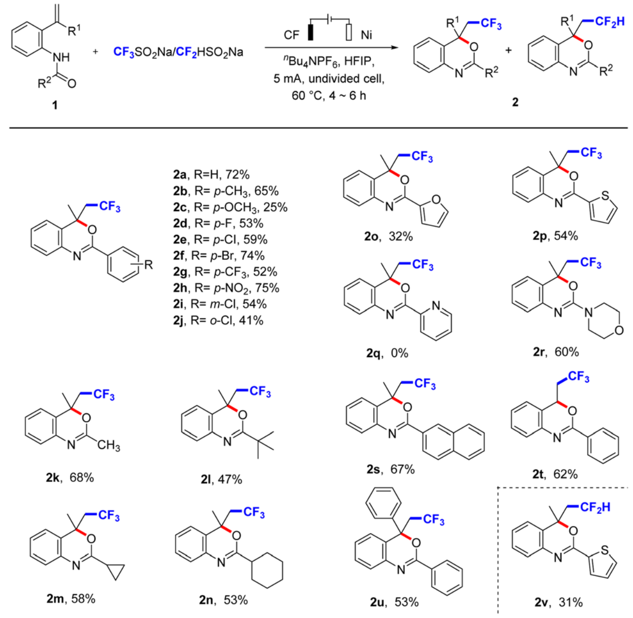
1a **2a**

Entry	Variation from standard conditions	Yield[b] [%]
1	**None**	**72**
2	Et_4NBF_4 as electrolyte	39
3	$^nBu_4NBr$ or $^nBu_4NOAc$ as electrolyte	Trace
4	$^nBu_4NI$ as electrolyte	0
5	No electrolyte	13
6	DMSO as solvent	51
7	CH_3CN as solvent	38
8	CH_3OH as solvent	37
9	DCE as solvent	66
10	Pt plate as anode	25
11	Fe plate as anode	17
12	Fe plate as cathode	29
13	Al plate as cathode	56
14	2 mA	42
15	10 mA	60
16	r.t.	35
17	40 °C	64
18	80 °C	59
19	CF_3SO_2Na (1 equiv.)	63
20	No electricity	0

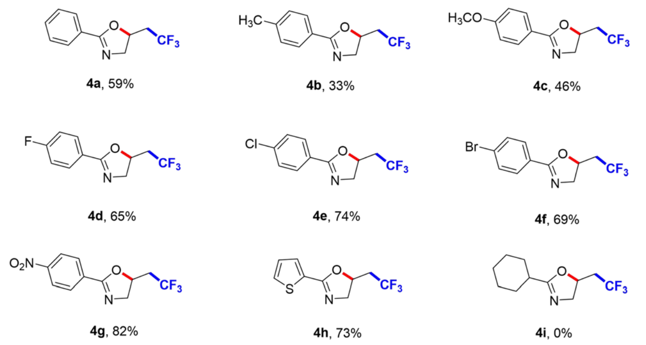
[a] Reaction conditions: undivided cell, **1a** (0.25 mmol), CF_3SO_2Na (0.5 mmol), solvent (6 mL), $^nBu_4NPF_6$ (0.5 mmol), 5 mA, 60 °C, 4 h (3.0 F mol^{-1}). [b] Isolated yield. Under air atmosphere. CF = Carbon fibre (1 × 1 × 0.01 cm), Pt = platinum (1 × 1 × 0.01 cm), Ni = nickel (1 × 1 × 0.01 cm). HFIP, 1,1,1,3,3,3-hexafluoro-2-propanol, DCE, 1,2-dichloroethane.

speculated that high current may cause peroxidation. The reaction temperature also was investigated, which led to lower yields (entries 16–18). When the equivalent of CF_3SO_2Na was reduced to 1, it resulted in a slight decrease in the yield (entry 19). Furthermore, electricity (entry 20) was essential for the process of the reaction.

With the optimal conditions in hand, the substrate scope of CF_3-containing benzoxazines was explored (Scheme 2). Firstly, we introduced electron-donating groups or electron-withdrawing groups into *N*-(2-(prop-1-en-2-yl)phenyl) benzamide (**1a**) and they reacted smoothly to obtain corresponding products **2** in moderate to good yields, such as methyl (**2b**), methoxy (**2c**), and halides (**2d**, **2e**, **2f**, **2i**, and **2j**), especially the strong electron-withdrawing groups trifluoromethyl (**2g**) and nitryl (**2h**) were all tolerant. Besides, we replaced the R^2 group by methyl (**2k**), tertiary butyl (**2l**), cyclopropyl (**2m**), cyclohexyl (**2n**), which reacted smoothly to afford the target product in good yields. Furyl (**2o**) or thienyl (**2p**) was transformed into the desired product in moderate yields, but pyridyl (**2q**) could not produce the target product. We speculated that the electron-withdrawing effect of pyridine made it difficult for **1q** to generate the corresponding intermediate **I** or **II**. We also introduced morpholinyl (**2r**) and naphthyl (**2s**) into R^2 group, the target products were obtained. Further explorations about the R^1 group were hydrogen (**2t**) and phenyl (**2u**), the corresponding target compounds were also generated and showed great compatibility. In this synthetic system, CF_2-substituted benzoxazines were also successfully synthesized using CF_2HSO_2Na as the difluoromethylation reagent (31% yield for compound **2v**), which indicates that the reaction system has good applicability.



Scheme 2 Substrate scope of CF_3-containing benzoxazines. ^{a}Reaction conditions: undivided cell, **1** (0.25 mmol), CF_3SO_2Na/CF_2HSO_2Na (0.5 mmol), $^nBu_4NPF_6$ (0.5 mmol), HFIP (6 mL), under air atmosphere.



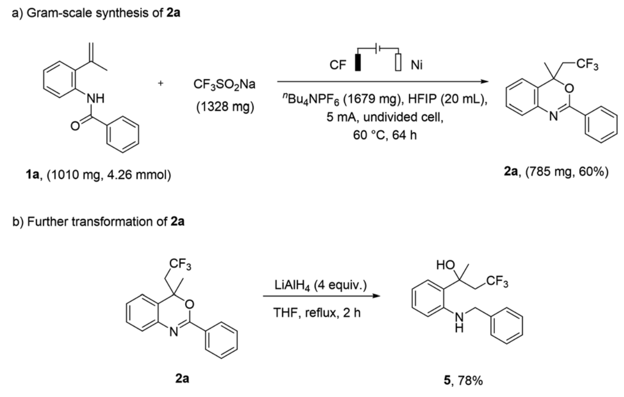
Scheme 3 Substrate scope of CF_3-containing oxazolines. ^{a}Reaction conditions: undivided cell, **3** (0.25 mmol), CF_3SO_2Na (0.5 mmol), $^nBu_4NPF_6$ (0.5 mmol), HFIP (6 mL), under air atmosphere.

We further explored the substrate scope of CF_3-containing oxazolines, and the results were shown in Scheme 3. *N*-allylbenzamide **3a** was reacted with CF_3SO_2Na to access the trifluoromethylation product 2-phenyl-5-(2,2,2-trifluoroethyl)-4,5-dihydrooxazole (**4a**) in 59% yield. *N*-allylbenzamides with various substituents such as methyl (**4b**), methoxy (**4c**), halides (**4d**, **4e** and **4f**) were all tolerant. The benzene rings with electron-deficient nitryl (**4g**) gave 82% yield. Meanwhile, when introducing furyl (**4h**) into the R^3 group, the corresponding target product also was obtained. But introducing cyclohexyl (**4i**) into R^3 group could not produce the target product, which indicated it had a very great influence on this transformation.

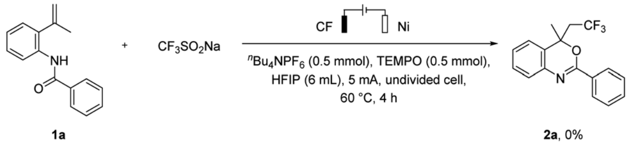
To further evaluate the practicality and potential applications of this method, we performed the reaction on a gram-scale preparation with **1a**, and the yield of product **2a** was 60% under a constant current of 5 mA for 64 h (Scheme 4a). In addition, the product **2a** can be further converted into 2-(2-(benzylamino) phenyl)-4,4,4-trifluorobutan-2-ol (**5**) at a yield of 78% (Scheme 4b).

In order to investigate the possible mechanism of this transition, several control experiments were performed. No desired product was obtained when 2,2,6,6-Tetramethylpiperidoxyl (TEMPO) was added (Scheme 5).

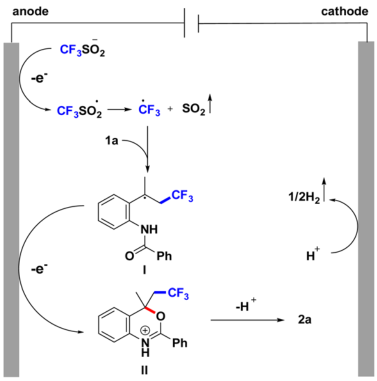
A plausible mechanism for the formation of product has been proposed based on the related reports.[16] As explained in Scheme 6, initially the HFIP undergoes cathodic reduction to



Scheme 4 Gram-scale synthesis and further transformation.



Scheme 5 Control experiments of the reaction.



Scheme 6 Proposal mechanism of the reaction.

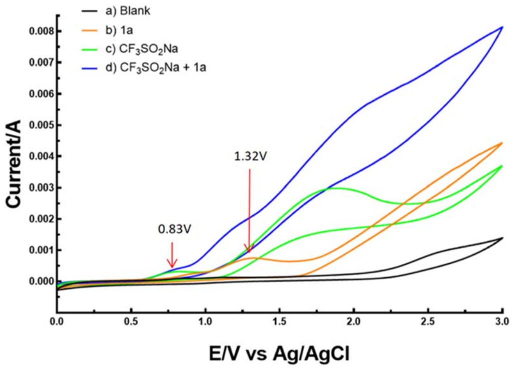


Fig. 2 Cyclic voltammetric experiments of **1a** and CF_3SO_2Na.

generate hydrogen gas at the cathode. At the anode, CF_3SO_2Na produces the CF_3SO_2 radical under anodic oxidation and further forms the CF_3 radical. Subsequently, CF_3 radicals are added to the double bonds of the olefins to generate the alkyl radical intermediate **I**. **I** undergoes a radical cyclization and anodic oxidation to furnish intermediate **II**. Afterwards, the intermediate **II** is finally converted into CF_3-containing benzoxazine **2a** by deprotonation (Scheme 6).

To justify the proposed reaction pathway outlined in Scheme 6, we conducted cyclic voltammetric (CV) experiments. As shown in Fig. 2, the oxidation peak of CF_3SO_2Na was 0.83 V, and **1a** had an oxidation peak of 1.32 V. These results indicated that CF_3SO_2Na was oxidized preferentially at the anode (see the ESI† for details).

Conclusions

In summary, we have developed a mild and efficient electrochemical oxidative and radical cascade cyclization of olefinic amides to afford trifluorinated benzoxazines and oxazolines using cheap and durable nickel plates as electrodes. This paper presents a simple, practical, green and environmentally benign protocol for the synthesis of fluorinated benzoxazines and oxazolines. In the absence of any transition metal catalysts, external oxidizers and additives, this protocol proceeds smoothly with diverse functional group compatibility.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (No. 82130105, 82121005, and 91953108), the research funds of Hangzhou institute for advanced study (No. 2022ZZ01015, 2022ZZ01012, 2022ZZ01019).

Notes and references

1 G. Eichenbaum, J. Zhou, M. F. Kelley, W. Roosen, P. Costa-Giomi, C. Louden, N. A. Di Prospero, G. Pandina, J. B. Singh, L. Ford, J. A. Moyer, T. M. Nork, J. N. Ver Hoeve and G. D. Aguirre, Implications of retinal effects observed in chronic toxicity studies on the clinical development of a CNS-active drug candidate, *Regul. Toxicol. Pharmacol.*, 2014, **69**, 187–200.

2 (*a*) J. Ilaš, Ž. Jakopin, T. Borštnar, M. Stegnar and D. Kikelj, 3,4-Dihydro-2H-1,4-benzoxazine Derivatives Combining Thrombin Inhibitory and Glycoprotein IIb/IIIa Receptor Antagonistic Activity as a Novel Class of Antithrombotic Compounds with Dual Function, *J. Med. Chem.*, 2008, **51**, 5617–5629; (*b*) T. Kline, N. H. Andersen, E. A. Harwood, J. Bowman, A. Malanda, S. Endsley, A. L. Erwin, M. Doyle, S. Fong, A. L. Harris, B. Mendelsohn, K. Mdluli, C. R. H. Raetz, C. K. Stover, P. R. Witte, A. Yabannavar and S. Zhu, Potent, Novel *in vitro* Inhibitors of the Pseudomonas aeruginosa Deacetylase LpxC, *J. Med. Chem.*, 2002, **45**, 3112–3129; (*c*) H. B. Bode, H. Irschik, S. C. Wenzel, H. Reichenbach, R. Müller and G. Höfle, The Leupyrrins: A Structurally Unique Family of Secondary Metabolites from the Myxobacterium Sorangium cellulosum, *J. Nat. Prod.*, 2003, **66**, 1203–1206; (*d*) N. Dias, J.-F. Goossens, B. Baldeyrou, A. Lansiaux, P. Colson, A. Di Salvo, J. Bernal, A. Turnbull, D. J. Mincher and C. Bailly, Oxoazabenzo[de]anthracenes Conjugated to Amino Acids: Synthesis and Evaluation as DNA-Binding Antitumor Agents, *Bioconjugate Chem.*, 2005, **16**, 949–958; (*e*) S. J. Hays, B. W. Caprathe, J. L. Gilmore, N. Amin, M. R. Emmerling, W. Michael, R. Nadimpalli, R. Nath, K. J. Raser, D. Stafford, D. Watson, K. Wang and J. C. Jaen, 2-Amino-4H-3,1-benzoxazin-4-ones as Inhibitors of C1r Serine Protease, *J. Med. Chem.*, 1998, **41**, 1060–1067; (*f*) A. Krantz, R. W. Spencer, T. F. Tam, T. J. Liak, L. J. Copp, E. M. Thomas and S. P. Rafferty, Design and synthesis of 4H-3,1-benzoxazin-4-ones as potent alternate substrate

inhibitors of human leukocyte elastase, *J. Med. Chem.*, 1990, **33**, 464–479.

3 R. Schlichter, V. Rybalchenko, P. Poisbeau, M. Verleye and J.-M. Gillardin, Modulation of GABAergic synaptic transmission by the non-benzodiazepine anxiolytic etifoxine, *Neuropharmacology*, 2000, **39**, 1523–1535.

4 M. M. Bastos, C. C. P. Costa, T. C. Bezerra, F. d. C. da Silva and N. Boechat, Efavirenz a nonnucleoside reverse transcriptase inhibitor of first-generation: Approaches based on its medicinal chemistry, *Eur. J. Med. Chem.*, 2016, **108**, 455–465.

5 (*a*) P. Zhang, E. A. Terefenko, A. Fensome, J. Wrobel, R. Winneker, S. Lundeen, K. B. Marschke and Z. Zhang, 6-Aryl-1,4-dihydro-benzo[*d*][1,3]oxazin- 2-ones: A Novel Class of Potent, Selective, and Orally Active Nonsteroidal Progesterone Receptor Antagonists, *J. Med. Chem.*, 2002, **45**, 4379–4382; (*b*) A. Fensome, R. Bender, R. Chopra, J. Cohen, M. A. Collins, V. Hudak, K. Malakian, S. Lockhead, A. Olland, K. Svenson, E. A. Terefenko, R. J. Unwalla, J. M. Wilhelm, S. Wolfrom, Y. Zhu, Z. Zhang, P. Zhang, R. C. Winneker and J. Wrobel, Synthesis and Structure–Activity Relationship of Novel 6-Aryl-1,4-dihydrobenzo[*d*][1,3]oxazine-2-thiones as Progesterone Receptor Modulators Leading to the Potent and Selective Nonsteroidal Progesterone Receptor Agonist Tanaproget, *J. Med. Chem.*, 2005, **48**, 5092–5095.

6 Z. Jin, Muscarine, imidazole, oxazole and thiazole alkaloids, *Nat. Prod. Rep.*, 2009, **26**, 382–445.

7 E. R. Freiter, A. H. Abdallah and S. J. Strycker, 2-Amino-5-substituted oxazolines and intermediates as potential anorectants, *J. Med. Chem.*, 1973, **16**, 510–512.

8 (*a*) K. Müller, C. Faeh and F. Diederich, Fluorine in Pharmaceuticals: Looking Beyond Intuition, *Science*, 2007, **317**, 1881–1886; (*b*) J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok and H. Liu, Fluorine in Pharmaceutical Industry: Fluorine-Containing Drugs Introduced to the Market in the Last Decade (2001–2011), *Chem. Rev.*, 2014, **114**, 2432–2506; (*c*) Y. Zhou, J. Wang, Z. Gu, S. Wang, W. Zhu, J. L. Aceña, V. A. Soloshonok, K. Izawa and H. Liu, Next Generation of Fluorine-Containing Pharmaceuticals, Compounds Currently in Phase II–III Clinical Trials of Major Pharmaceutical Companies: New Structural Trends and Therapeutic Areas, *Chem. Rev.*, 2016, **116**, 422–518; (*d*) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, Fluorine in medicinal chemistry, *Chem. Soc. Rev.*, 2008, **37**, 320–330.

9 (*a*) P. Natarajan, D. Chuskit, Priya and Manjeet, Transition-metal-free synthesis of trifluoromethylated benzoxazines *via* a visible-light-promoted tandem difunctionalization of o-vinylanilides with trifluoromethylsulfinate, *New J. Chem.*, 2022, **46**, 322–327; (*b*) F. Lu, J. Xu, H. Li, K. Wang, D. Ouyang, L. Sun, M. Huang, J. Jiang, J. Hu, H. Alhumade, L. Lu and A. Lei, Electrochemical oxidative radical cascade cyclization of olefinic amides and thiophenols towards the synthesis of sulfurated benzoxazines, oxazolines and iminoisobenzofurans, *Green Chem.*, 2021, **23**, 7982–7986; (*c*) T.-J. He, W.-Q. Zhong and J.-M. Huang, The synthesis of sulfonated 4H-3,1-benzoxazines *via* an electro-chemical radical cascade cyclization, *Chem. Commun.*, 2020, **56**, 2735–2738; (*d*) Qumruddeen, A. Yadav, R. Kant and C. B. Tripathi, Lewis Base/Brønsted Acid Cocatalysis for Thiocyanation of Amides and Thioamides, *J. Org. Chem.*, 2020, **85**, 2814–2822; (*e*) T.-T. Cao, W.-K. Zhang, F.-H. Qin, Q.-Q. Kang, Y. Dong, Q. Li, C. Kang and W.-T. Wei, Halocyclization of Olefinic 1,3-Dicarbonyls and Olefinic Amides in Aqueous Media Open in Air at Room Temperature, *ACS Sustain. Chem. Eng.*, 2020, **8**, 16946–16951; (*f*) M. Chaitanya and P. Anbarasan, Acid-Mediated Oxychalcogenation of o-Vinylanilides with N-(Arylthio/arylseleno)succinimides, *Org. Lett.*, 2018, **20**, 1183–1186; (*g*) A. Theodorou, I. Triandafillidi and C. G. Kokotos, Organocatalytic Synthesis of Oxazolines and Dihydrooxazines from Allyl-Amides: Bypassing the Inherent Regioselectivity of the Cyclization, *Adv. Synth. Catal.*, 2018, **360**, 951–957; (*h*) T. Liu, D. Zheng, Z. Li and J. Wu, Synthesis of Sulfonated Benzo[*d*][1,3]oxazines by Merging Photoredox Catalysis and Insertion of Sulfur Dioxide, *Adv. Synth. Catal.*, 2018, **360**, 865–869; (*i*) J. Wang, R. Sang, X. Chong, Y. Zhao, W. Fan, Z. Li and J. Zhao, Copper-catalyzed radical cascade oxyalkylation of olefinic amides with simple alkanes: highly efficient access to benzoxazines, *Chem. Commun.*, 2017, **53**, 7961–7964; (*j*) W. Fu, X. Han, M. Zhu, C. Xu, Z. Wang, B. Ji, X.-Q. Hao and M.-P. Song, Visible-light-mediated radical oxydifluoromethylation of olefinic amides for the synthesis of CF2H-containing heterocycles, *Chem. Commun.*, 2016, **52**, 13413–13416; (*k*) J.-F. Zhao, X.-H. Duan, H. Yang and L.-N. Guo, Transition-Metal-Free Oxyfluorination of Olefinic Amides for the Synthesis of Fluorinated Heterocycles, *J. Org. Chem.*, 2015, **80**, 11149–11155; (*l*) H. Yang, X.-H. Duan, J.-F. Zhao and L.-N. Guo, Transition-Metal-Free Tandem Radical Thiocyanooxygenation of Olefinic Amides: A New Route to SCN-Containing Heterocycles, *Org. Lett.*, 2015, **17**, 1998–2001; (*m*) Q.-H. Deng, J.-R. Chen, Q. Wei, Q.-Q. Zhao, L.-Q. Lu and W.-J. Xiao, Visible-light-induced photocatalytic oxytrifluoromethylation of N-allylamides for the synthesis of CF3-containing oxazolines and benzoxazines, *Chem. Commun.*, 2015, **51**, 3537–3540; (*n*) Y.-M. Wang, J. Wu, C. Hoong, V. Rauniyar and F. D. Toste, Enantioselective Halocyclization Using Reagents Tailored for Chiral Anion Phase-Transfer Catalysis, *J. Am. Chem. Soc.*, 2012, **134**, 12928–12931; (*o*) J. G. Yang, X. F. Song, J. Wang, K. Li, X. Y. Chang, L. Y. Tan, C. X. Liu, F. H. Yu, G. L. Cui, G. Cheng, W. P. To, C. L. Yang, C. M. Che and Y. Chen, Highly Efficient Thermally Activated Delayed Fluorescence from Pyrazine-Fused Carbene Au(I) Emitters, *Chem.–Eur. J.*, 2021, **27**, 17834–17842; (*p*) N. Yang, A. N. Li, H. Gao, L. M. Liao, Y. P. Yang, P. L. Wang and H. J. Li, Electrochemical oxidation-induced benzylic C(sp^3)–H functionalization towards the atom-economic synthesis of oxazole heterocycles, *Green Chem.*, 2023, **25**, 5128–5133.

10 S. Jana, A. Ashokan, S. Kumar, A. Verma and S. Kumar, Copper-catalyzed trifluoromethylation of alkenes: synthesis of trifluoromethylated benzoxazines, *Org. Biomol. Chem.*, 2015, **13**, 8411–8415.

11 (*a*) C. Zhu, N. W. J. Ang, T. H. Meyer, Y. Qiu and L. Ackermann, Organic Electrochemistry: Molecular Syntheses with Potential, *ACS Cent. Sci.*, 2021, **7**, 415–431; (*b*) G. M. Martins, G. C. Zimmer, S. R. Mendes and N. Ahmed, Electrifying green synthesis: recent advances in electrochemical annulation reactions, *Green Chem.*, 2020, **22**, 4849–4870; (*c*) N. E. S. Tay, D. Lehnherr and T. Rovis, Photons or Electrons? A Critical Comparison of Electrochemistry and Photoredox Catalysis for Organic Synthesis, *Chem. Rev.*, 2022, **122**, 2487–2649; (*d*) K.-J. Jiao, Y.-K. Xing, Q.-L. Yang, H. Qiu and T.-S. Mei, Site-Selective C–H Functionalization *via* Synergistic Use of Electrochemistry and Transition Metal Catalysis, *Acc. Chem. Res.*, 2020, **53**, 300–310; (*e*) P. Xiong and H.-C. Xu, Chemistry with Electrochemically Generated N-Centered Radicals, *Acc. Chem. Res.*, 2019, **52**, 3339–3350; (*f*) Y. Yuan and A. Lei, Electrochemical Oxidative Cross-Coupling with Hydrogen Evolution Reactions, *Acc. Chem. Res.*, 2019, **52**, 3309–3324; (*g*) S. D. Minteer and P. Baran, Electrifying Synthesis: Recent Advances in the Methods, Materials, and Techniques for Organic Electrosynthesis, *Acc. Chem. Res.*, 2020, **53**, 545–546; (*h*) Y. Jiang, K. Xu and C. Zeng, Use of Electrochemistry in the Synthesis of Heterocyclic Structures, *Chem. Rev.*, 2018, **118**, 4485–4540; (*i*) A. Wiebe, T. Gieshoff, S. Möhle, E. Rodrigo, M. Zirbes and S. R. Waldvogel, Electrifying Organic Synthesis, *Angew. Chem., Int. Ed.*, 2018, **57**, 5594–5619; (*j*) M. Yan, Y. Kawamata and P. S. Baran, Synthetic Organic Electrochemical Methods Since 2000: On the Verge of a Renaissance, *Chem. Rev.*, 2017, **117**, 13230–13319; (*k*) B. A. Frontana-Uribe, R. D. Little, J. G. Ibanez, A. Palma and R. Vasquez-Medrano, Organic electrosynthesis: a promising green methodology in organic chemistry, *Green Chem.*, 2010, **12**, 2099–2119.

12 G. He, J. Ma, J. Zhou, C. Li, H. Liu and Y. Zhou, A metal-free method for the facile synthesis of indanones *via* the intramolecular hydroacylation of 2-vinylbenzaldehyde, *Green Chem.*, 2021, **23**, 1036–1040.

13 G. He, Y. Li, S. Zhou, X. Yang, A. Shang, Y. Wang, H. Liu and Y. Zhou, A Facile Electrochemical Strategy for the Azidation of Benzylic C(sp3)–H Bonds, *Eur. J. Org Chem.*, 2022, **2022**, e202201041.

14 X. Chen, J. Jiang, X.-J. Huang and W.-M. He, Electrochemical oxidative radical cascade reactions for the synthesis of difluoromethylated benzoxazines, *Org. Chem. Front.*, 2023, **10**, 3898–3902.

15 (*a*) L. Eberson, M. P. Hartshorn, F. Radner and O. Persson, Persistent radical cation solutions from the reaction between aromatics and bromine, chlorine or iodine chloride in 1,1,1,3,3,3-hexafluoropropan-2-ol at room temperature, *Chem. Commun.*, 1996, 215–216; (*b*) B. Elsler, A. Wiebe, D. Schollmeyer, K. M. Dyballa, R. Franke and S. R. Waldvogel, Source of Selectivity in Oxidative Cross-Coupling of Aryls by Solvent Effect of 1,1,1,3,3,3-Hexafluoropropan-2-ol, *Chem.–Eur. J.*, 2015, **21**, 12321–12325; (*c*) L. Schulz, M. Enders, B. Elsler, D. Schollmeyer, K. M. Dyballa, R. Franke and S. R. Waldvogel, Reagent- and Metal-Free Anodic C-C Cross-Coupling of Aniline Derivatives, *Angew. Chem., Int. Ed.*, 2017, **56**, 4877–4881; (*d*) L. Schulz and S. R. Waldvogel, Solvent Control in Electro-Organic Synthesis, *Synlett*, 2019, **30**, 275–286.

16 (*a*) S. Zhang, L. Li, J. Zhang, J. Zhang, M. Xue and K. Xu, Electrochemical fluoromethylation triggered lactonizations of alkenes under semi-aqueous conditions, *Chem. Sci.*, 2019, **10**, 3181–3185; (*b*) V. A. Vil, V. M. Merkulova, A. I. Ilovaisky, S. A. Paveliev, G. I. Nikishin and A. O. Terent'ev, Electrochemical Synthesis of Fluorinated Ketones from Enol Acetates and Sodium Perfluoroalkyl Sulfinates, *Org. Lett.*, 2021, **23**, 5107–5112; (*c*) F. Lu, J. Xu, H. Li, K. Wang, D. Ouyang, L. Sun, M. Huang, J. Jiang, J. Hu, H. Alhumade, L. Lu and A. Lei, Electrochemical oxidative radical cascade cyclization of olefinic amides and thiophenols towards the synthesis of sulfurated benzoxazines, oxazolines and iminoisobenzofurans, *Green Chem.*, 2021, **23**, 7982–7986; (*d*) A. Claraz, T. Courant and G. Masson, Electrochemical Intramolecular Oxytrifluoromethylation of *N*-Tethered Alkenyl Alcohols: Synthesis of Functionalized Morpholines, *Org. Lett.*, 2020, **22**, 1580–1584.