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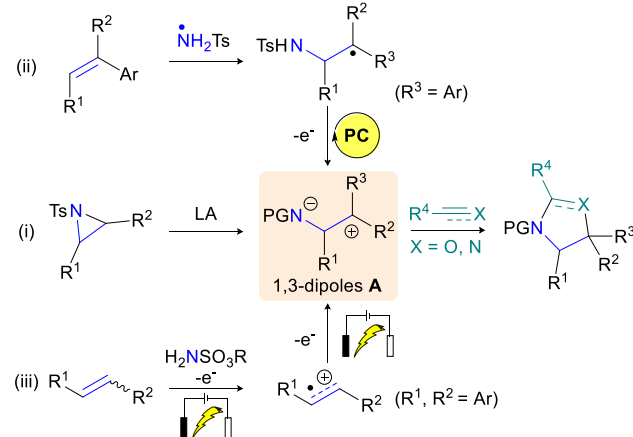
# Electrochemical tandem trifluoromethylation of allylamines /formal (3+2)-cycloaddition for the rapid access to CF<sub>3</sub>-containing imidazolines and oxazolidines

Aur lie Claraz,<sup>\*a</sup> Aur lie Djian,<sup>a</sup> G raldine Masson<sup>\*a</sup>

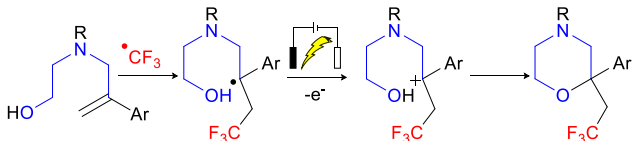
An electrochemical tandem radical trifluoromethylation of allylamines/formal (3+2)-cycloaddition with nitrile and carbonyl compounds has been developed under mild and environmentally benign reaction conditions. Such multicomponent reaction allowed the construction of CF<sub>3</sub>-containing imidazolines and oxazolidines by creating three new bonds from simple and easily available starting materials.

Imidazolines and oxazolidines are important five-membered azacycles existing in a number of natural products and bioactive molecules.<sup>1,2</sup> They also serve as versatile intermediates in organic synthesis and effective ligand in asymmetric catalysis.<sup>3</sup> A considerable effort has been dedicated to the efficient construction of these heterocycles.<sup>4,5</sup> Privileged methods for their syntheses are based on the formal (3+2)-cycloaddition of *N*-tosylaziridines as masked-1,3-dipoles **A** with nitrile or carbonyl compounds (Scheme 1a, eq. (i)).<sup>6,7</sup> Recently, Xu *et al.* have reported a complementary method which involves a photochemical generation of 1,3-dipoles **A** by the addition of *N*-centered radicals to aromatic alkenes followed by single electron transfer oxidation of the resulting  $\beta$ -amino radical intermediate (eq. (ii)).<sup>8</sup> Alternatively, Cheng *et al.* have disclosed an electrochemical formation of 1,3-dipoles **A** through an anodic oxidation of stilbenes, nucleophilic addition of sulfamates and second anodic oxidation step (eq. (iii)).<sup>9</sup> However, little attention has been paid to the synthesis of trifluoromethylated imidazolines and oxazolidines<sup>10</sup> whereas the incorporation of a trifluoromethyl (CF<sub>3</sub>) group<sup>11</sup> may produce heterocycles of high interests for medicinal, agrochemical and synthetic applications. Moreover, most of protocols used for that purpose are limited to the synthesis of 2-imidazolines and 1,3-oxazolidines bearing a CF<sub>3</sub> group at the 2-position. Alternatively, Hanamoto *et al.* have developed elegant methods giving rise to those heterocycles with a CF<sub>3</sub> group at the 5-position but requiring nevertheless the prior preparation of trifluoromethylated aziridines.<sup>12,13</sup> Therefore, the development of novel synthetic methods that allow efficient and rapid access to trifluoromethylated imidazolines and oxazolidines is still highly desirable. Herein, we report an electrochemical three-components tandem process for the preparation of 4-(2,2,2-trifluoroethyl)-2-imidazolines and 4-(2,2,2-trifluoroethyl)-1,3-oxazolidines.

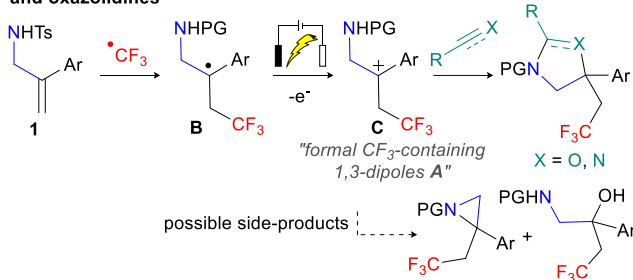
## a) Synthone **A** for the synthesis of imidazolines and oxazolidines



## b) Our previous work : electrochemical oxytrifluoromethylation



## c) This work: electrochemical access to CF<sub>3</sub>-containing imidazolines and oxazolidines



Scheme 1 Synthesis of imidazolines and oxazolidines.

Recently, we have described an efficient electrochemical<sup>14</sup> oxytrifluoromethylation of *N*-tethered alkenyl alcohols using the Langlois reagent<sup>15</sup> as a trifluoromethyl precursor (Scheme 1b).<sup>16–18</sup> On the basis of our previous work, we wished to develop a one-pot electrochemical procedure for the construction of CF<sub>3</sub>-containing 2-imidazolines and 1,3-oxazolidines from easily available allylic amines and Langlois reagent. We envisaged a scenario in which the CF<sub>3</sub> radical generated by electrooxidation could selectively react with *N*-tosyl allylamines **1** and the resulting 1,3-dipole **C**, formed after an additional oxidation step of the radical **B**, could be subsequently engaged in a formal (3+2)-cycloaddition with

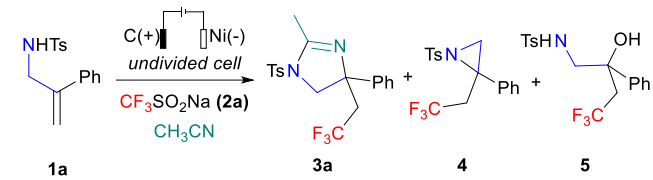
<sup>a</sup>Institut de Chimie des Substances Naturelles, Universit  Paris Saclay, CNRS, UPR2301, 1 Avenue de la Terrasse, 91198 Gif-sur-Yvette cedex, France. E-mail : [geraldine.masson@cns.fr](mailto:geraldine.masson@cns.fr), [aurelie.claraz@cns.fr](mailto:aurelie.claraz@cns.fr).

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nitriles or carbonyls to furnish the desired CF<sub>3</sub>-containing 5-membered heterocycles. However, the development of such approach is not exempt of risk since the highly reactive carbocation **C** could be either intramolecularly trapped by nitrogen to form a trifluoromethylated aziridine<sup>19</sup> or react with traces of water to give an amino-alcohol (Scheme 1c).

To evaluate our proposed approach, we began by examining the reaction of *N*-tosyl allylamine **1a** with the Langlois reagent (**2a**) in a mixture of acetonitrile and dichloromethane using LiClO<sub>4</sub> as supporting electrolyte (Table 1). The mixture was electrolyzed at constant current at room temperature. To our delight, we did form the three-component imidazoline adduct **3a** in 40% yield, together with the aziridine **4** and  $\alpha$ -amino-alcohol **5**.

**Table 1** Optimization of reaction conditions for the synthesis of imidazoline **3a**<sup>a</sup>



Entry	Additive (equiv.)	Yield <sup>b</sup> (%)		
		<b>3a</b>	<b>4</b>	<b>5</b>
1 <sup>c</sup>	-	40	33	13
2	-	54	20	24
3	K <sub>2</sub> CO <sub>3</sub> (1)	49	21	7
4 <sup>d</sup>	-	36	34	17
5	CH <sub>3</sub> COOH (1)	22	22	8
6	CF <sub>3</sub> COOH (1)	45	27	19
7	Bi(OTf) <sub>3</sub> (0.2)	45	19	20
8	Bi(OTf) <sub>3</sub> (1)	48	0	22
9	BF <sub>3</sub> .OEt <sub>2</sub> (0.5)	40	31	17
10	<b>BF<sub>3</sub>.OEt<sub>2</sub> (1)</b>	<b>64 (62)</b>	<b>0</b>	<b>16</b>
11 <sup>e</sup>	BF <sub>3</sub> .OEt <sub>2</sub> (1)	63	0	8
12 <sup>f</sup>	BF <sub>3</sub> .OEt <sub>2</sub> (1)	0	0	0

<sup>a</sup> Reaction conditions: undivided cell, C(+)|Ni(-), **1a** (0.25 mmol), **2a** (0.5 mmol), additive, CH<sub>3</sub>CN (2.5 mL), LiClO<sub>4</sub> (0.2 M), CCE (15 mA), 3.2 F (1 h 25), rt. <sup>b</sup> NMR yield; isolated yield is written between parentheses. <sup>c</sup> CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CN (1:1) instead of CH<sub>3</sub>CN. <sup>d</sup> 2.2 F (1 h) instead of 3.2 F. <sup>e</sup> C(+)|C(-) instead of C(+)|Ni(-). <sup>f</sup> No electricity.

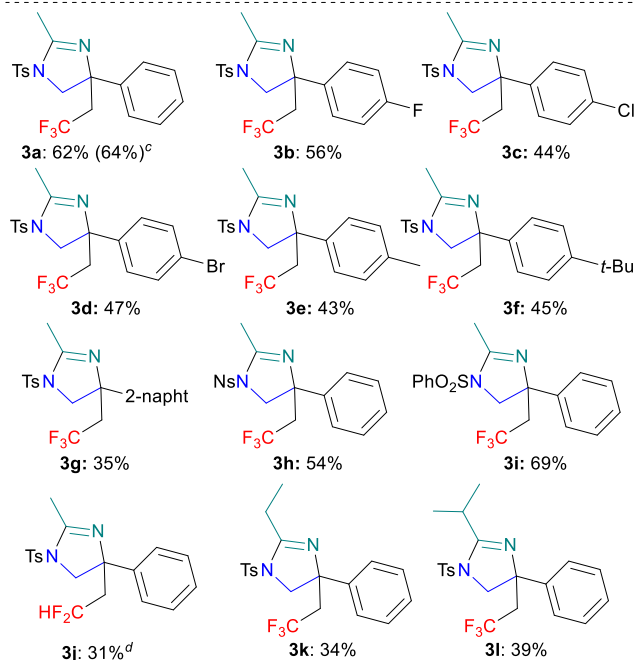
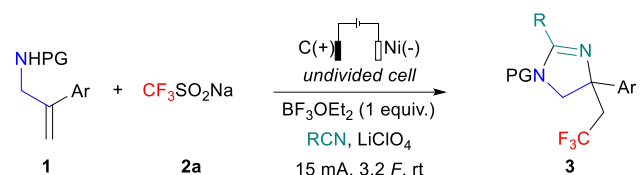
The addition of a base afforded no benefits, while the use of acetonitrile as the sole solvent made a small improvement to the conversion but had little effect on selectivity (entries 2-3). Lower yields were obtained with organic supporting electrolytes.<sup>20</sup> Interestingly, shortening the reaction time afforded a higher amount of aziridine **4** (entries 4 vs 2). This result led us to assume that the formation of imidazoline **3a** might proceed through an aziridine intermediate **4** which then could react with acetonitrile in a formal (3+2)-cycloaddition. Therefore, different acidic additives, which are known to mediate the ring opening of aziridines, were evaluated (entries 5-10).<sup>6</sup> Gratefully, upon adding one equivalent of BF<sub>3</sub>.OEt<sub>2</sub>, the formation of aziridine **4** was totally suppressed and the desired

imidazoline **3a** could be isolated in 62% yield (entry 10).<sup>21</sup> It is also worth mentioning that similar yield was obtained with the cheap graphite electrode as cathode instead of nickel (entry 11).

With the best reaction conditions in hand, the scope of this three-component reaction was examined. As shown in scheme 2, allylamines **1a-f** bearing both electron donating as well as electron withdrawing groups on the aromatic ring reacted smoothly affording the corresponding imidazolines **3a-f** in moderate to good yields. The synthesis of imidazoline **3g** with a 2-naphthyl ring has been also achieved albeit with slightly lower yield. Other sulfonamides such as 2-nosyl and phenyl sulfonyl acted as good reaction partners to form the corresponding imidazolines **3h** and **3i** in 54% and 69% yields, respectively. However, no product was obtained with *N*-benzyl allylic amines, probably due to the direct oxidation of amine at the electrode. Remarkably, this multicomponent reaction could be performed with easily prepared sodium difluoromethylsulfinate **2b**<sup>22</sup> furnishing the desired CF<sub>2</sub>H-containing imidazoline **3j** in 31% yield. Pleasingly, the propionitrile and the sterically hindered *iso*-butyronitrile were found to react with **1a** and Langlois reagent to yield 2-ethyl and 2-isopropyl imidazoline **3k-l**, albeit with slightly lower yields probably due to the lower dielectric constants of these solvents.<sup>23</sup> To demonstrate the synthetic potential of this 3-components tandem protocol, a 1 mmol scale experiment with substrate **1a** was carried out affording the corresponding CF<sub>3</sub>-containing imidazoline **3a** in 64% yield.

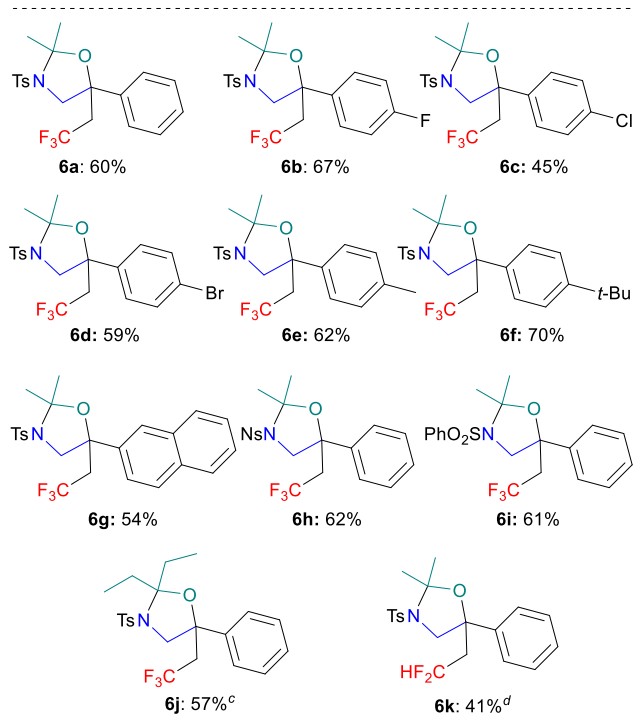
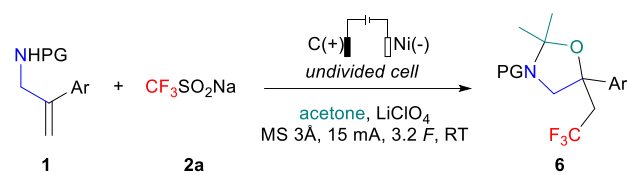
Encouraged by this result, we next sought to extend this electrochemical multicomponent process to carbonyls as dipolarophiles (Table 2). Pleasingly, the reaction proceeded smoothly in acetone as solvent to afford the corresponding oxazolidine **6a** in 49% yield (entry 1) along with amino-alcohol product **5** (29%). Interestingly, no formation of aziridine **4** was detected at the end of the reaction even in the absence of BF<sub>3</sub>.OEt<sub>2</sub> (entry 2). Finally, we were pleased to find that the yield of **6a** increased when molecular sieves were added to trap traces of water present in the reaction media.

A variety of allylamines **1a-i** bearing various aryl rings and aza-protecting groups were subjected to these conditions, furnishing the corresponding CF<sub>3</sub>-containing oxazolidines **6** in up to 70% yields (Scheme 3). Generally, the yields were slightly higher than for the construction of imidazolines. Pleasingly, slight modifications on the reaction conditions permitted the use of pentan-3-one as solvent instead of acetone delivering the corresponding oxazolidine **6j** in good yield (57%). More specifically, with this sterically hindered carbonyl compound, one equivalent of BF<sub>3</sub>.OEt<sub>2</sub> was added at the end of the electrolysis to fully transform the remaining aziridine **4** into the desired 5-membered ring **6j**. CF<sub>2</sub>H-containing oxazolidine **6k** could also be prepared in a decent yield by using sodium difluoromethylsulfinate **2b**.



**Scheme 2** Three-component synthesis of CF<sub>3</sub>-containing imidazolines.<sup>a,b</sup>

<sup>a</sup> Reaction conditions: undivided cell, C(+)|Ni(-), **1a** (0.25 mmol), **2a** (0.5 mmol), BF<sub>3</sub>·OEt<sub>2</sub> (0.25 mmol), RCN (2.5 mL), LiClO<sub>4</sub> (0.2 M), CCE (15 mA), 3.2 F, rt. <sup>b</sup> Isolated yield. <sup>c</sup> Reaction conducted on 1 mmol scale. <sup>d</sup> **2b** instead of **2a**.



**Scheme 3** Three-component synthesis of CF<sub>3</sub>-containing oxazolidines.<sup>a,b</sup>

<sup>a</sup> Reaction conditions: undivided cell, C(+)|Ni(-), **1a** (0.25 mmol), **2a** (0.5 mmol), MS 3A (300 mg), acetone (2.5 mL), LiClO<sub>4</sub> (0.2 M), CCE (15 mA), 3.2 F, rt. <sup>b</sup> Isolated yield. <sup>c</sup> With pentan-3-one instead of acetone, **2a** (0.625 mmol), LiClO<sub>4</sub> (0.4 M), 35 °C, CCE (15 mA), 2.8 F, 35 °C; then BF<sub>3</sub>·OEt<sub>2</sub> (0.25 mmol), overnight, rt. <sup>d</sup> **2b** instead of **2a**.

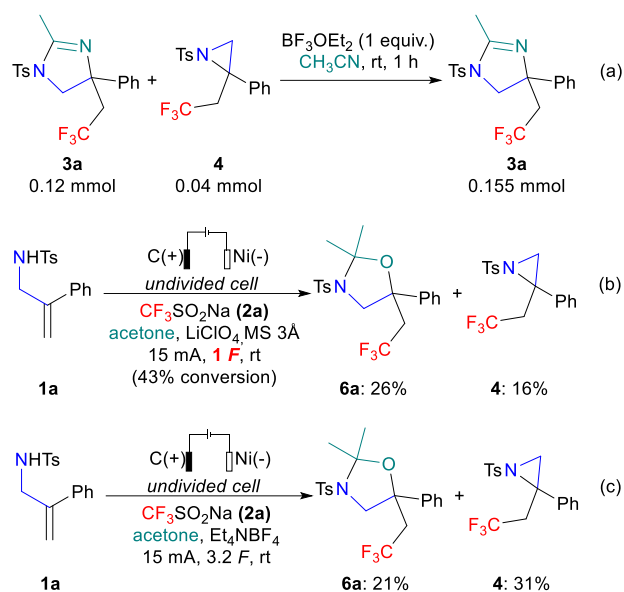
**Table 2** Optimization of reaction conditions for the synthesis of oxazolidines **6a**<sup>a</sup>

Entry	Additive (equiv.)	Yield <sup>b</sup> (%)		
		<b>6a</b>	<b>4</b>	<b>5</b>
1 <sup>c</sup>	BF <sub>3</sub> ·OEt <sub>2</sub> (1)	49	0	29
2	-	52	0	40
3	MS 3A (300 mg)	69 (60)	0	0

<sup>a</sup> Reaction conditions: undivided cell, C(+)|Ni(-), **1a** (0.25 mmol), **2a** (0.5 mmol), additive, acetone (2.5 mL), LiClO<sub>4</sub> (0.4 M), CCE (15 mA), 3.2 F (1 h 25), rt. <sup>b</sup> NMR yield; isolated yield is written between parentheses.

A set of control experiments were conducted to shed light on the reaction mechanism. No reaction occurred in the absence of current (Table 1, entry 12). Measuring the redox behavior of the reagents by cyclic voltammetry analysis revealed that the Langlois reagent **2a** exhibited lower oxidation potentials (1.45 V vs Ag/AgCl) than that of *N*-tosyl allylamine **1a** (2.11 V vs Ag/AgCl).<sup>20</sup> To clarify the role of BF<sub>3</sub>·OEt<sub>2</sub>, the following additional experiment was performed: one equivalent of BF<sub>3</sub>·OEt<sub>2</sub> was added to a mixture of imidazoline **3a** and aziridine **4**. After 1 h, an almost complete conversion of **4** into **3a** was observed (Scheme 4, eq. (a)), thus supporting that BF<sub>3</sub>·OEt<sub>2</sub> works as a Lewis-acid to promote the formal (3+2)-cycloaddition between aziridine **4** and acetonitrile.<sup>6d-h</sup> As mentioned above, no aziridine was observed at the end of the electrolysis when acetone was used as formal dipolarophile. However, when the reaction was stopped at 43% conversion of **1a** (1 F) under optimized conditions, the aziridine **4** was formed in 16% yield (Scheme 4, eq. (b)). This result inferred that aziridine **4** is also a key intermediate in this transformation. Based on this result, we reasoned that the lithium perchlorate electrolyte certainly served<sup>24</sup> to mediate the formal (3+2)-cycloaddition between aziridines and acetone. Indeed, when LiClO<sub>4</sub> was replaced by Et<sub>4</sub>NBF<sub>4</sub> as electrolyte, the aziridine **4**

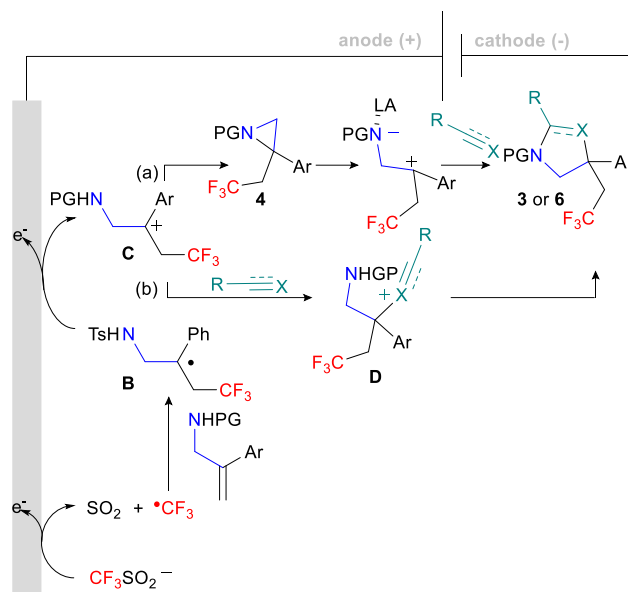
was obtained in 31% yield supporting the crucial role of the lithium cation (Scheme 4, eq. (c)).



**Scheme 4** Control experiments.<sup>a</sup>

<sup>a</sup> Chemical amounts, yields and conversions were determined by <sup>1</sup>H NMR analysis of the crude material using 1,3,5-trimethoxybenzene as an internal standard.

On the basis of the control experiments and the literature,<sup>16-18</sup> a plausible reaction mechanism is outlined in Scheme 5. Initially, the anodic oxidation of Langlois reagent via a single-electron-transfer (SET) can deliver trifluoromethyl radical after fast extrusion of gaseous SO<sub>2</sub>. The regioselective addition of this radical onto the double bond could afford benzylic radical **B**, which can be further oxidized to carbocation **C**. An intramolecular attack of nitrogen atom on **C** could produce aziridine **4**, which subsequently could undergo a formal (3+2)-cycloaddition with nitriles or carbonyls in the presence of a Lewis acid to afford the corresponding imidazolines **3** or oxazolidines **6** (pathway a). The reductions of the proton H<sup>+</sup> and SO<sub>2</sub> would be the counter reactions taking place at the cathode to balance the overall transformation. Nevertheless, at the present stage of the development, we cannot totally exclude an alternative pathway involving a direct addition of nitriles or the acetone on the carbocation **C** followed by attack of sulfonamide on the resulting nitrilium and oxocarbenium ions **D** to form heterocyclic products **3** or **6** (pathway b). Both mechanisms may operate, although the dominant process certainly occurs *via* pathway a.



**Scheme 5** Proposed mechanism.

## Conclusions

In summary, we have developed an electrochemical three-component reaction for the rapid access to new CF<sub>3</sub>-containing imidazolines and oxazolidines from easily prepared allylic amines and cheap Langlois reagent as CF<sub>3</sub> source. This original transformation proceeds through the tandem radical trifluoromethylation of allylic secondary amines/formal (3+2)-cycloaddition with nitrile or carbonyl compounds allowing the creation of three new bonds under mild reaction conditions. This electrochemical process was also applicable to the construction of CF<sub>2</sub>H-containing imidazoline and oxazolidine. Further investigations of new electrochemical multicomponent tandem processes for the construction of heterocycles are currently under way in our laboratory.

## Conflicts of interest

There are no conflicts to declare.

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## Notes and references

- 1 E. Vitaku, D. T. Smith and J. T. Njardarson, Analysis of the structural diversity, substitution patterns, and frequency of nitrogen heterocycles among U.S. FDA approved pharmaceuticals, *J. Med. Chem.*, 2000, **57**, 10257.
- 2 For selected examples with 2-imidazolines, see: (a) L. M. Azevedo, T. A. Lansdell, J. R. Ludwig, R. A. Mosey, D. K. Woloch, D. P. Cogan, G. P. Patten, M. R. Kuszpit, J. S. Fisk and J. J. Tepe, Inhibition of the human proteasome by imidazoline scaffolds, *J. Med. Chem.*, 2013, **56**, 5974; (b) T. A. Davis and J.

- N. Johnston, Catalytic, enantioselective synthesis of stilbene cis-diamines: a concise preparation of (–)-Nutlin-3, a potent p53/MDM2 inhibitor, *Chem. Sci.*, 2011, **2**, 1076; (c) V. Sharma, S. Peddibhotla and J. J. Tepe, Sensitization of cancer cells to DNA damaging agents by imidazolines, *J. Am. Chem. Soc.*, 2006, **128**, 9137; (d) G. Gaba, C. Mohan, Development of drugs based on imidazole and benzimidazole bioactive heterocycles: recent advances and future directions, *Med. Chem. Res.*, 2016, **25**, 173; for selected examples with 1,3-oxazolidines: (e) K. Li, S. Ichikawa, B. Al-Dabbagh, A. Bouhss and A. Matsuda, Function-oriented synthesis of simplified caprazamycins: discovery of oxazolidine-containing uridine derivatives as antibacterial agents against drug-resistant bacteria, *J. Med. Chem.*, 2010, **53**, 3793; (f) J. D. Scott and R. M. Williams, Total synthesis of (–)-tetrazomine. Determination of the stereochemistry of tetrazomine and the synthesis and biological activity of tetrazomine analogues, *J. Am. Chem. Soc.*, 2002, **124**, 2951; (g) L. Yu, W. Zhou and Z. Wang, Synthesis and in vitro antibacterial activity of oxazolidine LBM-415 analogs as peptide deformylase inhibitors, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 1541.
- 3 For selected examples of 2-imidazolines as synthetic intermediates, see: (a) T. Morofuji, A. Shimizu and J.-I. Yoshida, Heterocyclization approach for electrooxidative coupling of functional primary alkylamines with aromatics, *J. Am. Chem. Soc.*, 2015, **137**, 9816; for selected example of 2-imidazolines as chiral auxiliary: (b) P. I. Dalko and Y. Langlois, Stereoselective synthesis of quaternary benzylic carbons using C2 symmetric imidazolines and tetrahydrofuran as electrophile, *J. Org. Chem.*, 1998, **63**, 8107; for selected examples of 2-imidazolines as chiral ligands: (c) C. A. Busacca, D. Grossbach, R. C. So, E. M. O'Brien and E. M. Spinelli, Probing electronic effects in the asymmetric Heck reaction with the BIPI ligands, *Org. Lett.*, 2003, **5**, 595; (d) S. Bhor, G. Anilkumar, M. K. Tse, M. Klawonn, C. Döbler, B. Bitterlich, A. Grotevendt and M. Beller, Synthesis of a new chiral *N,N,N*-tridentate pyridinebisimidazole ligand library and its application in ruthenium-catalyzed asymmetric epoxidation, *Org. Lett.*, 2005, **7**, 3393; (e) K. Hyodo, S. Nakamura and N. Shibata, Enantioselective Aza-Morita–Baylis–Hillman reactions of acrylonitrile catalyzed by palladium(II) pincer complexes having C2-symmetric chiral bis(imidazoline) ligands, *Angew. Chem. Int. Ed.*, 2012, **51**, 10337; for reviews on 1,3-oxazolidines in asymmetric synthesis: (f) C. Wolf and H. Xu, Asymmetric catalysis with chiral oxazolidine ligands, *Chem. Commun.*, 2011, **47**, 3339; (g) C. Agami and F. Couty, The use of *N*-Boc-1,3-oxazolidines as chiral auxiliaries in asymmetric synthesis, *Eur. J. Org. Chem.*, 2004, 677; (h) H. A. McManus and P. J. Guiry, Recent developments in the application of oxazoline-containing ligands in asymmetric catalysis, *Chem. Rev.*, 2004, **104**, 4151; for selected examples of 1,3-oxazolidines as synthetic intermediates: (i) T. Arai, Y. Ogino and T. Sato, Development of a tailor-made bis(oxazolidine)pyridine–metal catalyst for the [3+2] cycloaddition of azomethine imines with propiolates, *Chem. Commun.*, 2013, **49**, 7776; (j) S. Fuse, H. Koinuma, A. Kimbara, M. Izumikawa, Y. Mifune, H. He, K. Shin-Ya, T. Takahashi and T. Doi, Total synthesis and stereochemistry revision of mannopeptimycin aglycone, *J. Am. Chem. Soc.*, 2014, **136**, 12011; (k) S. P. Lathrop; M. Pompeo, W.-T. Chang and M. Movassaghi, Convergent and biomimetic enantioselective total synthesis of (–)-communesin F, *J. Am. Chem. Soc.*, 2016, **138**, 7763; (l) B. Seashor-Ludlow, S. Torrsell and P. Somfai, Addition of azomethine ylides to aldehydes: mechanistic dichotomy of differentially substituted  $\alpha$ -imino esters, *Eur. J. Org. Chem.*, 2010, 3927; for selected examples of 1,3-oxazolidines as chiral auxiliary: (m) A. Tessier, J. Pytkowicz, T. Brigaud, Chiral 4-phenyl-2-trifluoromethyloxazolidine: a high-performance chiral auxiliary for the alkylation of amides, *Angew. Chem. Int. Ed.*, 2006, **45**, 3677; (n) A. Tessier, N. Lahmar, J. Pytkowicz, T. Brigaud, Highly diastereoselective synthetic route to enantiopure  $\beta^2$ -amino acids and  $\gamma$ -amino alcohols using a fluorinated oxazolidine (Fox) as chiral auxiliary, *J. Org. Chem.*, 2008, **73**, 3970; for selected example of 1,3-oxazolidines as chiral ligand: (o) C. Wolf and S. Liu, Bisoxazolidine-catalyzed enantioselective alkynylation of aldehydes, *J. Am. Chem. Soc.*, 2006, **128**, 10996.
- 4 For reviews on 2-imidazolines, see: (a) M. S. Al Mehedi and J. J. Tepe, Recent advances in the synthesis of imidazolines (2009–2020), *Adv. Synth. Catal.*, 2020, DOI: 10.1002/adsc.202000709; (b) H. Liu and D.-M. Du, Recent advances in the synthesis of 2-imidazolines and their applications in homogeneous catalysis, *Adv. Synth. Catal.*, 2009, **351**, 489; for selected examples: (c) D. Gennet, S. Z. Zard and H. Zhang, Amidinyl radicals: new and useful intermediates for the synthesis of imidazolines and imidazoles, *Chem. Commun.*, 2003, 1870; (d) J. M. Concellón, E. Riego, J. Ramón Suárez, S. García-Granda and M. R. Díaz, Synthesis of enantiopure imidazolines through a Ritter reaction of 2-(1-aminoalkyl)aziridines with nitriles, *Org. Lett.*, 2004, **6**, 4499; (e) V. Sharma and J. J. Tepe, Diastereochemical diversity of imidazoline scaffolds via substrate controlled TMSCl mediated cycloaddition of azlactones, *Org. Lett.*, 2005, **7**, 5091; (f) J. Aydin, K. S. Kumar, L. Eriksson and K. J. Szabó, Palladium pincer complex-catalyzed condensation of sulfonimines and isocyanacetate to imidazoline derivatives. Dependence of the stereoselectivity on the ligand effects, *Adv. Synth. Catal.*, 2007, **349**, 2585; (g) N. Elders, R. F. Schmitz, F. J. J. de Kanter, E. Ruijter, M. B. Groen and R. V. A. Orru, A resource-efficient and highly flexible procedure for a three-component synthesis of 2-imidazolines, *J. Org. Chem.*, 2007, **72**, 6135; (h) Q. Zhu and Y. Lu, Facile synthesis of bicyclic amidines and imidazolines from 1,2-diamines, *Org. Lett.*, 2010, **12**, 4156; (i) L. Zhou, J. Zhou, C. K. Tan, J. Chen and Y.-Y. Yeung, *N*-bromosuccinimide initiated one-pot synthesis of imidazoline, *Org. Lett.*, 2011, **13**, 2448; (j) M. R. Kuszpit, W. D. Wulff and J. J. Tepe, One-pot synthesis of 2-imidazolines via the ring expansion of imidoyl chlorides with aziridines, *J. Org. Chem.*, 2011, **76**, 2913; (k) Y. Hu, R. Yi, X. Yu, X. Xin, C. Wang and B. Wan, *O*-Transfer-facilitated cyclizations of propargylamides with TMSN<sub>3</sub>: selective synthesis of tetrazoles and dihydroimidazoles, *Chem. Commun.*, 2015, **51**, 15398; (l) K. Krishna, R. Indranirekha, S. L. Dineshwari, C. S. Roy and P. Phukan, A metal-free protocol for aminofunctionalization of olefins using TsNBr<sub>2</sub>, *J. Org. Chem.*, 2016, **81**, 5423.
- 5 For selected examples of 1,3-oxazolidines, see: (a) V. Sriramurthy, G. A. Barcan and O. Kwon, Bisphosphine-catalyzed mixed double-Michael reactions: asymmetric synthesis of oxazolidines, thiazolidines, and pyrrolidines, *J. Am. Chem. Soc.*, 2007, **129**, 12928; (b) K. S. Williamson and T. P. Yoon, Iron-catalyzed aminohydroxylation of olefins, *J. Am. Chem. Soc.*, 2010, **132**, 4570; (c) L. D. Elliott, J. W. Wrigglesworth, B. Cox, G. C. Lloyd-Jones and K. I. Booker-Milburn, 2,2-Difunctionalization of alkenes via Pd(II)-catalyzed aza-Wacker reactions, *Org. Lett.*, 2011, **13**, 728; (d) A. F. Ward and J. P. Wolfe, Stereoselective synthesis of substituted 1,3-oxazolidines via Pd-catalyzed carboamination reactions of *O*-vinyl-1,2-amino alcohols, *Org. Lett.*, 2011, **13**, 4728; (e) M. B. Shaghafi, R. E. Grote and E. R. Jarvo, Oxazolidine synthesis by complementary stereospecific and stereoconvergent methods, *Org. Lett.*, 2011, **13**, 5188; (f) X. Wu, L. Li and J. Zhang, Nickel(II)-catalyzed diastereoselective [3+2] cycloaddition of *N*-tosyl-aziridines and aldehydes via selective carbon–carbon bond cleavage, *Chem. Commun.*, 2011, **47**, 7824; (g) P. V. Balaji and S. Chandrasekaran, Stereoselective geminal difunctionalization of vinyl arenes

- mediated by the bromonium ion, *Chem. Commun.*, 2014, **50**, 70; (h) A. Kondoh, K. Odaira and M. Terada, *Ring expansion of epoxides under Brønsted base catalysis: formal [3+2] cycloaddition of  $\beta,\gamma$ -epoxy esters with imines providing 2,4,5-trisubstituted 1,3-oxazolines*, *Angew. Chem. Int. Ed.*, 2015, **54**, 11240; (i) V. Satheesh, M. Sengoden and T. Punniyamurthy, "On water" C(sp<sub>3</sub>)-H functionalization/C-O/C-N bonds formations: synthesis of functionalized oxazolines and imidazolines, *J. Org. Chem.*, 2016, **81**, 9792; (j) X. Wu, L. W. Zhou, H.-H. Wu and J. Zhang, Enantioselective [3+2] cycloaddition of azomethine ylides and aldehydes via Ni/bis(oxazoline)-catalyzed ring opening of *N*-tosylaziridines through a chirality transfer approach, *Chem. Commun.*, 2017, **53**, 5661; (k) A. Kondoh, S. Akahira, M. Oishi and M. Terada, Enantioselective formal [3+2] cycloaddition of epoxides with imines under Brønsted base catalysis: synthesis of 1,3-oxazolines with quaternary stereogenic center, *Angew. Chem. Int. Ed.*, 2018, **57**, 6299; (l) V. Satheesh, S. V. Kumar and T. Punniyamurthy, Expedient stereospecific Co-catalyzed tandem C-N and C-O bond formation of *N*-methylanilines with styrene oxides, *Chem. Commun.*, 2018, **54**, 11813; (m) S. Tarannum, S. S. Das, I. A. Wani and M. K. Ghorai, Stereoselective syntheses of highly functionalized imidazolines and oxazolines via ring-opening cyclization of activated aziridines and epoxides with amines and aldehydes, *J. Org. Chem.*, 2020, **85**, 367.
- 6 For reviews: (a) P. Dauban and G. Malik, A masked 1,3-dipole revealed from aziridines, *Angew. Chem. Int. Ed.*, 2009, **48**, 9026; (b) A. L. Cardoso and T. M. V. D. Pinho e Melo, Aziridines in formal [3+2] cycloadditions: synthesis of five-membered heterocycles, *Eur. J. Org. Chem.*, 2012, 6479; for selected examples: (c) M. K. Ghorai, K. Das, A. Kumar and K. Ghosh, An efficient route to regioselective opening of *N*-tosylaziridines with zinc(II) halides, *Tetrahedron Lett.*, 2005, **46**, 4103; (d) B. A. B. Prasad, G. Pandey and V. K. Singh, Synthesis of substituted imidazolines via [3+2]-cycloaddition of aziridines with nitriles, *Tetrahedron Lett.*, 2004, **45**, 1137; (e) V. K. Yadav and V. Sriramurthy, Silylmethyl-substituted aziridine and azetidines as masked 1,3- and 1,4-dipoles for formal [3 + 2] and [4 + 2] cycloaddition reactions, *J. Am. Chem. Soc.*, 2005, **127**, 16366; (f) S. Gandhi, A. Bisai, B. A. B. Prasad and V. K. Singh, Studies on the reaction of aziridines with nitriles and carbonyls: synthesis of imidazolines and oxazolines, *J. Org. Chem.*, 2007, **72**, 2133; (g) N. Hsueh, G. J. Clarkson and M. Shipman, Generation and ring opening of aziridines in telescoped continuous flow processes, *Org. Lett.*, 2015, **17**, 3632; (h) H.-T. Yang, M.-L. Xing, Y.-F. Zhu, X.-Q. Sun, J. Cheng, C.-B. Miao and B.-B. Li, BF<sub>3</sub>·Et<sub>2</sub>O-catalyzed formal [3 + 2] reaction of aziridinofullerenes with carbonyl compounds, *J. Org. Chem.*, 2014, **79**, 1487; (i) B. Kang, A. W. Miller, S. Goyala and S. B. T. Nguyen, Sc(OTf)<sub>3</sub>-catalyzed condensation of 2-alkyl-*N*-tosylaziridine with aldehydes or ketones: an efficient synthesis of 5-alkyl-1,3-oxazolines, *Chem. Commun.*, 2009, 3928; (j) X. Li, X. Yang, H. Chang, Y. Li, B. Ni and W. Wei, A stereoselective and practical synthesis of (*E*)- $\alpha,\beta$ -unsaturated ketones from aldehydes, *Eur. J. Org. Chem.*, 2011, 3122; (k) P.-J. Yang, L. Qi, Z. Liu, G. Yang and Z. Chai, Lewis acid catalyzed dynamic kinetic asymmetric transformation of racemic *N*-sulfonylaziridines, *J. Am. Chem. Soc.*, 2018, **140**, 17211; (l) S. Teranishi, K. Maeda, T. Kurahashi and S. Matsubara, Diastereoselective synthesis of 1,3-oxazolines via cationic iron porphyrin-catalyzed cycloaddition of aziridines with aldehydes, *Org. Lett.*, 2019, **21**, 2593.
- 7 For the generation of  $\beta$ -chloroamines as synthetic equivalent of synthon A from in-situ generated *N*-chloroaziridinium and ensuing formal (3+2)-cycloaddition with acetonitrile, see also: D. Chen, C. Timmons, H.-X. Wei and G. Li, Direct electrophilic diamination of functionalized alkenes without the use of any metal catalysts, *J. Org. Chem.*, 2003, **68**, 5742.
- 8 J.-Q. Chen, W.-L. Yu, Y.-L. Wei, T.-H. Li and P.-F. Xu, Photoredox-induced functionalization of alkenes for the synthesis of substituted imidazolines and oxazolines, *J. Org. Chem.*, 2017, **82**, 243.
- 9 J. Li, W. Huang, J. Chen, L. He, X. Cheng and G. Li, Electrochemical aziridination by alkene activation using a sulfamate as the nitrogen source, *Angew. Chem. Int. Ed.*, 2018, **57**, 5695.
- 10 For 2-(trifluoromethyl)-2-imidazolines derivatives, see: (a) R. N. Johnson and H. M. Woodburn, The reaction of trifluoroacetonitrile with aliphatic diamines, *J. Org. Chem.*, 1962, **27**, 3958; (b) H. Baganz and L. Domaschke, 2-Trifluoromethyl- $\Delta^2$ -imidazolin und - $\Delta^2$ -tetrahydropyrimidin, *Angew. Chem.* 1963, **75**, 1025; (c) H. Jianga, L. Suna, S. Yuana, W. Lua, W. Wana, S. Zhub and J. Hao, A facile one-pot synthesis of 2-fluoroalkyl 1,3-imidazolines and 1,3-oxazolines through imidoyl halide intermediates, *Tetrahedron*, 2012, **68**, 2858; For other CF<sub>3</sub>-containing 2-imidazolines derivatives: (d) C. W. Derstine, D. N. Smith and J. A. Katzenellenbogen, Trifluoromethyl-Substituted Imidazolines: Novel precursors of trifluoromethyl ketones amenable to peptide synthesis, *J. Am. Chem. Soc.*, 1996, **118**, 8485; (e) C. W. Derstine, D. N. Smith and J. A. Katzenellenbogen, Trifluoromethyl-substituted  $\Delta^3$ -imidazolines: synthesis and reactivity, *Tetrahedron Lett.*, 1997, **38**, 4359; (f) H.-Y. Li, I. DeLucca, S. Drummond and G. A. Boswell, Asymmetric synthesis and absolute stereochemistry of 4,4-bis-(trifluoromethyl)imidazoline based ACAT inhibitors, *Tetrahedron*, 1997, **53**, 5359; (g) M.-X. Zhao, H.-L. Bi, R.-H. Jiang, X.-W. Xu and M. Shi, Chinchona alkaloid squaramide/AgOAc cooperatively catalyzed diastereo- and enantioselective Mannich/cyclization cascade reaction of isocyanoacetates and cyclic trifluoromethyl ketimines, *Org. Lett.*, 2014, **16**, 4566; (h) L. Trulli, F. Sciubba and S. Fioravanti, Chiral trans-carboxylic trifluoromethyl 2-imidazolines by a Ag<sub>2</sub>O-catalyzed Mannich-type reaction, *Tetrahedron*, 2018, **74**, 572; for 2-(trifluoromethyl)-1,3-oxazolines: (i) A. Ishii, K. Higashiyama and K. Mikami, Asymmetric addition reactions of Grignard reagents to chiral fluoral hemiacetal: asymmetric synthesis of 1-substituted-2,2,2-trifluoroethylamines, *Synlett*, 1997, 1381; (j) F. Gosselin, A. Roy; P. D. O'Shea, C.-Y. Chen and R. P. Volante, Oxazolidine ring opening and isomerization to (*E*)-imines. Asymmetric synthesis of aryl- $\alpha$ -fluoroalkyl amino alcohols, *Org. Lett.*, 2004, **6**, 641; (k) G. Chaume, M.-C. Van Severen, S. Marinkovic and T. Brigaud, Straightforward synthesis of (*S*)- and (*R*)- $\alpha$ -trifluoromethyl proline from chiral oxazolines derived from ethyl trifluoropyruvate, *Org. Lett.*, 2006, **8**, 6123; (l) F. Huguenot and T. Brigaud, Concise synthesis of enantiopure  $\alpha$ -trifluoromethyl alanines, diamines, and amino alcohols via the Strecker-type reaction, *J. Org. Chem.*, 2006, **71**, 7075; (m) F. Huguenot and T. Brigaud, Convenient asymmetric synthesis of  $\beta$ -trifluoromethyl- $\beta$ -amino acid,  $\beta$ -amino ketones, and  $\gamma$ -amino alcohols via Reformatsky and Mannich-type reactions from 2-Trifluoromethyl-1,3-oxazolines, *J. Org. Chem.*, 2006, **71**, 2159; (n) G. Chaume, O. Barbeau, P. Lesot and T. Brigaud, Synthesis of 2-trifluoromethyl-1,3-oxazolines as hydrolytically stable pseudoproline, *J. Org. Chem.*, 2010, **75**, 4135; (o) H. Zhang, Q. Shen and L. Lu, Highly diastereoselective synthesis of optically pure trifluoromethyl-substituted imidazolidine, oxazolidine and thiazolidine, *Tetrahedron Lett.*, 2011, **52**, 349; (p) G. Chaume, J. Simon, C. Caupène, N. Lensen, E. Miclet and T. Brigaud, Incorporation of CF<sub>3</sub>-pseudoproline into peptides: a methodological study, *J. Org. Chem.*, 2013, **78**, 10144; (q) N. Lensen, J. Marais and T. Brigaud, Straightforward synthesis of novel enantiopure  $\alpha$ -



- trifluoromethylated azetidines 2-carboxylic acid and homoserines, *Org. Lett.*, 2015, **17**, 342; (r) O. Ouerfelli, J. Simon, E. Chelain, J. Pytkowicz, R. Besbes and T. Brigaud, Enantiopure  $\alpha$ -trifluoromethylated aziridine-2-carboxylic acid ( $\alpha$ -TfmAzy): synthesis and peptide coupling, *Org. Lett.*, 2020, **22**, 2946; see also ref. 3m-n.
- 11 For selected reviews, see: (a) K. Muller, C. Faeh and F. Diederich, Fluorine in pharmaceuticals: looking beyond intuition, *Science*, 2007, **317**, 1881; (b) W. K. Hagmann, The many roles for fluorine in medicinal chemistry, *J. Med. Chem.*, 2008, **51**, 4359; (c) D. O'Hagan, Understanding organofluorine chemistry. An introduction to the C–F bond, *Chem. Soc. Rev.*, 2008, **37**, 308; (d) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, Fluorine in medicinal chemistry, *Chem. Soc. Rev.*, 2008, **37**, 320; (e) Y. Zhou, J. Wang, Z. Gu, S. Wang, W. Zhu, J. L. Acenã, 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; (f) N. A. Meanwell, Fluorine and fluorinated motifs in the design and application of bioisosteres for drug design, *J. Med. Chem.*, 2018, **61**, 5822; (g) B. Ameduri, Fluoropolymers: the right material for the right applications, *Chem. Eur. J.*, 2018, **24**, 18830.
  - 12 M. Yoshiki, R. Ishibashi, Y. Yamada and T. Hanamoto, TiF<sub>4</sub>-mediated regioselective cycloaddition of 2-(trifluoromethyl)-*N*-tosylaziridine to nitriles, *Org. Lett.*, 2014, **16**, 5509.
  - 13 R. Maeda, R. Ishibashi, R. Kamaishi, K. Hirotaki, H. Furuno and T. Hanamoto, AgSbF<sub>6</sub>-promoted cycloaddition reaction of 2-trifluoromethyl-*N*-tosylaziridine with aldehydes, *Org. Lett.*, 2011, **13**, 6240.
  - 14 B. A. Frontana-Urbe, R. D. Little, J. G. Ibanez, A. Palma and R. Vasquez-Medrano, Organic electrocatalysis: a promising green methodology in organic chemistry, *Green Chem.*, 2010, **12**, 2099; (b) 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; (c) S. Möhle, M. Zirbes, E. Rodrigo, T. Gieshoff, A. Wiebe and S. R. Waldvogel, Modern electrochemical aspects for the synthesis of value-added organic products, *Angew. Chem. Int. Ed.*, 2018, **57**, 6018; (d) A. Wiebe, T. Gieshoff, S. Möhle, E. Rodrigo, M. Zirbes and S. R. Waldvogel, Electrifying organic synthesis, *Angew. Chem. Int. Ed.*, 2018, **57**, 5595; (e) Y. Jiang, K. Xu and C. Zeng, Use of electrochemistry in the synthesis of heterocyclic structures, *Chem. Rev.*, 2018, **118**, 4485; (f) C. Kingston, M. D. Palkowitz, Y. Takahira, J. C. Vantourout, B. K. Peters, Y. Kawamata and P. S. Baran, A survival guide for the "electro-curious", *Acc. Chem. Res.*, 2020, **53**, 72; (g) J. L. Roedel, D. Pollok, R. Franke and S. R. Waldvogel, A decade of electrochemical dehydrogenative C,C-coupling of aryls, *Acc. Chem. Res.*, 2020, **53**, 45; (h) J. C. Siu, N. Fu and S. Lin, Catalyzing electrocatalysis: a homogeneous electrocatalytic approach to reaction discovery, *Acc. Chem. Res.* 2020, **53**, 547; (i) M. Li, J. Hong, W. Xiao, Y. Yang, D. Qiu and F. Mo, Electrocatalytic oxidative transformation of organic acids for carbon–heteroatom and sulfur–heteroatom bond formation, *ChemSusChem*, 2020, **13**, 1661. For a review on the electrochemical difunctionalization of alkenes: (j) S. G. Sauer and S. Lin, An electrocatalytic approach to the radical difunctionalization of alkenes, *ACS Catal.*, 2018, **8**, 5175; For recent examples on the electrochemical difunctionalization of alkenes: (k) C. Wan, R.-J. Song and J.-H. Li Electrooxidative 1,2-bromoesterification of alkenes with acids and *N*-Bromosuccinimide, *Org. Lett.*, 2019, **21**, 2800. (l) C.-Y. Cai, X.-M. Shu and H.-C. Xu, Practical and stereoselective electrocatalytic 1,2-diamination of alkenes, *Nat. Commun.*, 2019, **10**, 4953. (m) X. Zhang, T. Cui, X. Zhao, P. Liu and Peipei Sun, Electrochemical difunctionalization of alkenes by a four-component reaction cascade Mumm rearrangement: rapid access to functionalized imides, *Angew. Chem. Int. Ed.*, 2020, **59**, 3465.
  - 15 (a) B. Langlois, E. Laurent and N. Roidot, Trifluoromethylation of aromatic compounds with sodium trifluoromethanesulfinate under oxidative conditions, *Tetrahedron Lett.*, 1991, **32**, 7525; (b) for reviews: H. Guyon, H. Chachignon and D. Cahard, CF<sub>3</sub>SO<sub>2</sub>X (X = Na, Cl) as reagents for trifluoromethylation, trifluoromethylsulfenyl-, -sulfenyl- and -sulfonylation. Part 1: Use of CF<sub>3</sub>SO<sub>2</sub>Na, *Beilstein J. Org. Chem.*, 2017, **13**, 2764; (c) C. Zhang, Application of Langlois' reagent in trifluoromethylation reactions, *Adv. Synth. Catal.*, 2014, **356**, 2895; (d) Q. Lefebvre, Toward sustainable trifluoromethylation reactions: sodium triflate under the spotlight, *Synlett*, 2016, **28**, 19.
  - 16 A. Claraz, T. Courant and G. Masson, Electrochemical intramolecular oxytrifluoromethylation of *N*-tethered alkenyl alcohols: synthesis of functionalized morpholines, *Org. Lett.*, 2020, **22**, 1580.
  - 17 For electrochemical trifluoromethylation of alkenes in intermolecular processes, see: (a) J. B. Tommasino, A. Brondex, M. Médebielle, M. Thomalla, B. R. Langlois and T. Billard, Trifluoromethylation reactions with potassium trifluoromethanesulfinate under electrochemical oxidation, *Synlett*, 2002, 1697; (b) W. Jud; C. O. Kappe and D. Cantillo, Catalyst-free oxytrifluoromethylation of alkenes through paired electrolysis in organic-aqueous media, *Chem. Eur. J.*, 2018, **24**, 17234; (c) L. Zhang, G. Zhang, P. Wang, Y. Li and A. Lei, Electrochemical oxidation with Lewis-acid catalysis leads to trifluoromethylative difunctionalization of alkenes using CF<sub>3</sub>SO<sub>2</sub>Na, *Org. Lett.*, 2018, **20**, 7396; (d) K. Y. Ye, G. Pombar, N. Fu, G. S. Sauer, I. Keresztes and S. Lin, Anodically coupled electrolysis for the heterodifunctionalization of alkenes, *J. Am. Chem. Soc.*, 2018, **140**, 2438; (e) Y. Huang, H. Hong, Z. Zou, C. Liao, J. Lu, Y. Qin, Y. Li and L. Chen, Electrochemical vicinal aminotrifluoromethylation of alkenes: high regioselective acquisition of  $\beta$ -trifluoromethylamines, *Org. Biomol. Chem.* 2019, **17**, 5014; (f) X. Sun, H. X. Ma, T. S. Mei, P. Fang and Y. Hu, Electrochemical radical formyloxylat–bromination, –chlorination, and –trifluoromethylation of alkenes, *Org. Lett.*, 2019, **21**, 3167; (g) J.-C. Kang, Y.-Q. Tu, J.-W. Dong, C. Chen, J. Zhou, T. M. Ding, J. T. Zai, Z.-M. Chen and S.-Y. Zhang, Electrochemical semipinacol rearrangements of allylic alcohols: construction of all-carbon quaternary stereocenters, *Org. Lett.*, 2019, **21**, 2536; (h) Z. Guan, H. Wang, Y. Huang, Y. Wang, S. Wang and A. Lei, Electrochemical oxidative aryl(alkyl)trifluoromethylation of allyl alcohols via 1,2-migration, *Org. Lett.*, 2019, **21**, 4619; (i) H. Hong, Y. Li, L. Chen, B. Li, Z. Zhu, X. Chen, L. Chen and Y. Huang, Electrochemical synthesis strategy for C<sub>vinyl</sub>CF<sub>3</sub> compounds through decarboxylative trifluoromethylation, *J. Org. Chem.*, 2019, **84**, 5980.
  - 18 For electrochemical trifluoromethylation of alkenes in intramolecular processes, see: (a) K. Y. Ye, Z. Song, G. Sauer, J. H. Harenberg, N. Fu and S. Lin, Synthesis of chlorotrifluoromethylated pyrrolidines by electrocatalytic radical ene-yne cyclization, *Chem. Eur. J.*, 2018, **24**, 12274; (b) Y.-Y. Jiang, G.-Y. Dou, K. Xu and C.-C. Zeng, Bromide-catalyzed electrochemical trifluoromethylation/cyclization of *N*-arylacrylamides with low catalyst loading, *Org. Chem. Front.*, 2018, **5**, 2573; (c) Z. Zhang, L. Zhang, Y. Cao, F. Li, G. Bai, G. Liu, Y. Yang and F. Mo, Mn-Mediated electrochemical trifluoromethylation/C(sp<sup>2</sup>)–H functionalization cascade for the synthesis of azaheterocycles, *Org. Lett.*, 2019, **21**, 762; (d) Z. Ruan, Z. Huang, M. Xu, G. Mo, X. Tian, X. Y. Yu and L. Ackermann, Catalyst-free, direct electrochemical tri- and difluoroalkylation/cyclization: access to functionalized



- oxindoles and quinolinones, *Org. Lett.*, 2019, **21**, 1237; (e) Z. Li, L. Jiao, Y. Sun, Z. He, Z. Wei and W.-W. Liao, CF<sub>3</sub>SO<sub>2</sub>Na as a bifunctional reagent: electrochemical trifluoromethylation of alkenes accompanied by SO<sub>2</sub> insertion to access trifluoromethylated cyclic *N*-sulfonylimines, *Angew. Chem. Int. Ed.*, 2020, **59**, 7266.
- 19 (a) H. Egami, S. Kawamura, A. Miyazaki and M. Sodeoka, Trifluoromethylation reactions for the synthesis of β-trifluoromethylamines, *Angew. Chem. Int. Ed.*, 2013, **52**, 7841; (b) E. Kim, S. Choi, H. Kim and E. J. Cho, Generation of CF<sub>3</sub>-containing epoxides and aziridines by visible-light-driven trifluoromethylation of allylic alcohols and amines, *Chem. Eur. J.*, 2013, **19**, 6209; (c) S. Kawamura, H. Egami and M. Sodeoka, aminotrifluoromethylation of olefins via cyclic amine formation: mechanistic study and application to synthesis of trifluoromethylated pyrrolidines, *J. Am. Chem. Soc.*, 2015, **137**, 4865; (d) S. Kawamura, K. Dosei, E. Valverde, K. Ushida and M. Sodeoka, *N*-heterocycle-forming amino/carboperfluoroalkylations of aminoalkenes by using perfluoro acid anhydrides: mechanistic studies and applications directed toward perfluoroalkylated compound libraries, *J. Org. Chem.*, 2017, **82**, 12539; (e) X.-X. Liu, J. Jia, Z. Wang, Y.-T. Zhang, J. Chen, K. Yang, C.-Y. He and L. Zhao, Catalyst-free and visible light promoted aminofluoroalkylation of unactivated alkenes: an access to fluorinated aziridines, *Adv. Synth. Catal.*, 2020, **362**, 2604.
- 20 See the supporting information for more details.
- 21 Further attempts to avoid the formation of amino-alcohol **5** by adding various desiccants have failed; see the supporting information for more details.
- 22 Z. He, P. Tan, C. Ni and J. Hu, Fluoroalkylative aryl migration of conjugated *N*-arylsulfonylated amides using easily accessible sodium di- and monofluoroalkanesulfonates, *Org. Lett.*, 2015, **17**, 1838.
- 23 The dielectric constants ( $\epsilon$ ) of acetonitrile, propionitrile and *iso*-butyronitrile are 36.5, 26.5 and 17.9 respectively: H. Schlundt, On the dielectric constants of nitriles, *J. Phys. Chem.*, 1901, **5**, 157. In propionitrile and *iso*-butyronitrile, it was not possible to maintain 15 mA of current.
- 24 For a review on the use of LiClO<sub>4</sub> as a Lewis acid: A. B. Charette and A. Singh, e-EROS Encyclopedia of Reagents for Organic Synthesis, 2007, Lithium perchlorate.