Chemical
Science

ROYAL SOCIETY
OF CHEMISTRY

EDGE ARTICLE

View Article Online
View Journal | View Issue

Check for updates

Cite this: *Chem. Sci.*, 2025, **16**, 14161

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 21st May 2025
Accepted 30th June 2025

DOI: 10.1039/d5sc03674g

rsc.li/chemical-science

Electrochemically promoted defluorinative sulfoximination and fluorosulfonylation of non-activated aryl fluorides at room temperature†

Xianqiang Kong,*[a] Yiyi Chen,[a] Shuangquan Zhang,[a] Kun Feng,[a] Xiaohui Chen,[a] Lin-Hui Dong,[b] Meng-Hua Li,[b] Yuan-Qing Xu[b] and Zhong-Yan Cao*[b]

Due to the high bond dissociation energy and kinetic inertness of the C–F bond, direct activation of inert aryl fluorides for new transformations under mild conditions remains a significant challenge. Although it has been known that single electron reduction can be applied for the activation of inert aryl fluorides at room temperature, the need for very strong reduction conditions along with the competitive side reactions during the reduction process limits the synthetic applications. Herein, by leveraging the advantages of electrosynthesis and the versatile transformation nature of aryl radicals, two types of challenging defluorinative transformations of non-activated aryl fluorides which include sulfoximination *via* cheap nickel catalysis and transition metal catalyst-free fluorosulfonylation at room temperature have been disclosed for the first time. These reactions show good functional group tolerance and can be applied for the late-stage modifications of bioactive derivatives. As for the practical nickel-catalyzed defluorinative sulfoximination, detailed mechanistic studies reveal that after the cathodic reduction of aryl fluorides to form the key aryl radical, subsequent nickel-promoted C–N bond formation *via* paired electrolysis is responsible for the success.

Introduction

The ubiquity and importance of non-activated aryl fluorides in synthetic chemistry have continuously driven the development of efficient transformations under mild conditions.[1] However, their activation has long been a formidable challenge due to the high bond dissociation energy (126 kcal mol^{-1}) and kinetic inertness. While traditional methods typically rely on transition metals to activate the C–F bond *via* oxidative addition (Fig. 1A),[2] recent contributions from the groups of Shibata[3] and Shi[4] have demonstrated that the coordination of simple aryl fluorides with Ru or Rh could deliver η^6-coordinated complexes, facilitating S_NAr substitutions with N- or O-nucleophiles. Nevertheless, the use of harsh conditions such as high temperatures or metallic reagents is often necessary for the above examples.

To develop more robust defluorinative examples under mild conditions, recent advances have uncovered the single electron activation models, enabling some interesting defluorinative transformations even in a catalytic way (Fig. 1A). For example, thanks to the moderate oxidation potential ($E_{ox} = +2.2$ V *vs.* SCE) of aryl fluorides, researchers such as Lambert,[5] Nicewicz,[6] and Jiang[7] have demonstrated that aryl fluorides can be easily oxidized to form electrophilic aryl radical cations, facilitating S_NAr substitutions. Nevertheless, compared with the aforementioned single electron oxidation strategy, the development of a single electron reduction strategy for the defluorinative transformation of inert aryl fluorides lags behind. To date, only visible light-promoted borylation, phosphonylation, arylation, sulfuration and selenization have been reported by König,[8] Jiao,[9] Miyake and co-workers[10] (with moderate yields in most cases) recently, in addition to hydrodefluorination.[11] The difficulty can be attributed to the need for very negative reduction conditions to effectively reduce PhF ($E_{red} = -3.0$ V *vs.* SCE), and the presence of very competitive side reactions such as hydrodefluorination and defluorinative dimerization (to form the corresponding arenes or biaryls) during the reduction process (Fig. 1B),[1g] resulting in limited transformations with limited functional group tolerance.

On the other hand, by borrowing the advantages of electrosynthesis such as tunable and wide redox potential with robust catalytic models under mild conditions, many excellent synthetic methodologies focusing on the use of electrosynthesis to activate and transform inert molecules have been developed recently.[12] Nevertheless, while the reduction of simple fluorobenzenes at the cathode has been observed for more than 50 years,[11b] the potential for using such a convenient activation

---

[a] *School of Chemical Engineering and Materials, Changzhou Institute of Technology, No. 666 Liaohe Road, Changzhou 213032, China. E-mail: kongxq@czu.cn*

[b] *College of Chemistry and Molecular Sciences, Henan University, Kaifeng 475004, China. E-mail: zycao@henu.edu.cn*

† Electronic supplementary information (ESI) available. CCDC 2433423. For ESI and crystallographic data in CIF or other electronic format see DOI: **https://doi.org/10.1039/d5sc03674g**

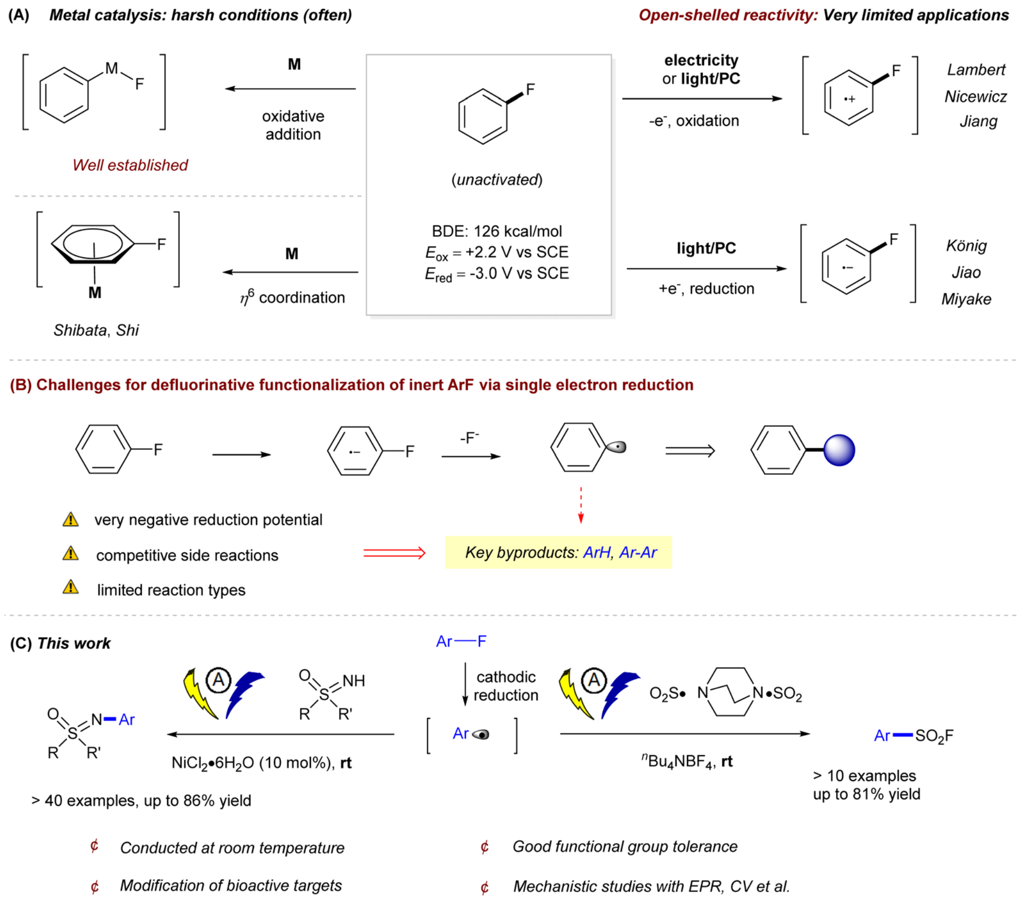


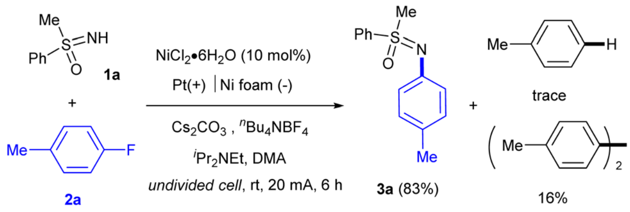
Fig. 1 State of the art for the activation of C–F bonds of inert ArF and our progress.

strategy for defluorative transformations of non-activated aryl fluorides remains underexplored.[13] Herein, coupled with our continuing interest in electrochemically promoted transformations with the involvement of aryl radicals,[14] we envisioned that the exquisite control of cathodic reduction conditions might realize the selective single electron reduction of inert aryl fluorides at first, which could deliver the key aryl radical *via* fragmentation.[1g] After this, by borrowing the versatile chemical transformations of aryl radicals,[15] it might provide an opportunity for developing new defluorinative transformations of inert aryl fluorides at room temperature by overcoming the typically undesired side reactions (*vide anta*). Specifically, the following two kinds of useful yet unknown reactions have been tentatively designed. (1) First of all, guided by known nickel-promoted radical transformations,[16] we thought that the trapping of the aryl radical by nickel species[17] followed by interaction with suitable nucleophiles might constitute a new and efficient solution for achieving the novel defluorination coupling of fluoroarenes at room temperature. Guided by pioneering studies related to the success of nickel-catalyzed C–N bond construction,[17c,18] we have focused our attention on the *N*-arylation of *NH*-sulfoximines since *N*-aryl sulfoximines have found wide applications in organic synthesis, drug discovery, and other fields,[19] as well as the use of non-activated aryl fluorides as the arylation source for the purpose remains elusive.[20] (2) Second, to further demonstrate the synthetic usefulness of such a cathodic reduction strategy, it was further postulated that the trapping of *in situ* formed aryl radicals with stoichiometric amounts of SO_2, followed by fluorination[21] might be able to achieve the unprecedented transition metal catalyst-free defluorinative fluorosulfonylation of inert aryl fluorides at room temperature. Herein, we wish to report these preliminary results. The substrate scope, synthetic applications and the mechanistic studies of these two transformations have been carefully disclosed.

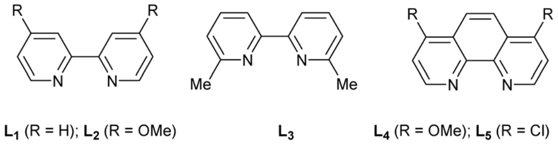
Results and discussion

Condition optimization for *N*-arylation of *NH*-sulfoximines with unactivated aryl fluorides was performed. To explore the feasibility of the designed Ni-catalyzed arylation with aryl fluorides enabled by electrosynthesis, *NH*-sulfoximine **1a** and 1-fluoro-4-methylbenzene **2a** have been chosen as model substrates. After careful screening of various parameters such as nickel source, electrodes, electrolyte, solvent or base, we are pleased to notice that the desired **3a** could be facilely isolated with 83% isolated yield under the optimal mild reaction conditions (Table 1). Both toluene (trace) and 4,4′-dimethyl-1,1′-biphenyl (16%) have been detected as the main byproducts, indicating the involvement of aryl radical species in our system, as well as the

Table 1 Condition optimization for arylation



Entry[a]	Deviation	GC yield of **3a** (%)
1	None	81[b]
2	$NiCl_2$, $NiBr_2$, NiI_2 or $Ni(COD)_2$ instead of $NiCl_2 \cdot 6H_2O$	52/25/trace/trace
3	With **L₁–L₅** (12 mol%)	All trace
4	C(+), RVC(+), Ni foam (+) instead of Pt(+)	Trace/trace/trace
5	C(−), RVC(−) or Pt(−) instead of Ni foam (−)	8/13/trace
6	DMF, DMSO, MeCN, HFIP, CH_2Cl_2 instead of DMA	43/32/0/0/0
7	Na_2CO_3, K_2CO_3 or KOAc instead of Cs_2CO_3	32/23/trace
8	$^nBu_4NPF_6$ or $^nBu_4NBr$ instead of $^nBu_4NBF_4$	25/16
9	No electrolyte, $NiCl_2 \cdot 6H_2O$ or $^iPr_2NEt$	0/0/64
10	0, 15 or 25 mA instead of 20 mA	0/61/trace
11	Mn, Zn instead of electricity	0/0



[a] Standard conditions: Pt anode (1 cm × 0.2 cm) and Ni foam cathode (0.8 cm × 0.2 cm), **1a** (0.30 mmol), **2a** (0.75 mmol), $NiCl_2 \cdot 6H_2O$ (10 mol%), Cs_2CO_3 (2.0 equiv.), $^iPr_2NEt$ (1.5 equiv.), $^nBu_4NBF_4$ (1.0 equiv.), DMA (4 mL) in an undivided cell, 20 mA, 6 h, and argon. [b] Isolated yield.

challenge in achieving the desired transformation. The following five points should be highlighted. (1) First, the use of the simple and cheap $NiCl_2 \cdot 6H_2O$ as a catalyst is essential, as the change to others, such as $NiCl_2$, $NiBr_2$ led to inferior results, and the use of NiI_2 or $Ni(COD)_2$ inhibits the reactivity (entry 2). More interestingly, the addition of bidentate nitrogen-containing ligands, which are commonly used in nickel-catalyzed radical reactions such as **L₁–L₅**, gave only trace **3a** in this system (entry 3). Notably, DMA can serve as a good ligand for $NiCl_2$, which could bind to the nickel center in our case, thereby benefiting the efficiency.[22] Noteworthily, although sulfoximines have been reported as ligands for nickel catalysis,[23] and we also obtained the X-ray structure of the $NiCl_2(\mathbf{1a})_2(H_2O)_2$ complex (CCDC: 2433423†), UV-visible absorption spectra experiments indicate the complete dissociation of the crystal upon mixing with DMA (for details, please see the ESI†). (2) The reactivity diminished significantly when electrodes such as C(+), RVC(+), Ni foam (+), C(−), RVC(−), or Pt(−) were used (entries 4 and 5). (3) Additionally, other solvents (DMF, DMSO, MeCN, HFIP, and CH_2Cl_2), base (Na_2CO_3, K_2CO_3 or KOAc), or electrolyte ($^nBu_4NPF_6$ or $^nBu_4NBr$) proved ineffective (entries 6–8). (4) Control experiments indicated that the nickel catalyst, electric current, electrolyte and additive $^iPr_2NEt$ are all essential for the transformation (entries 9 and 10). (5) Notably, the use of Mn or Zn instead of electricity as a reductant led to the shutdown of the reactivity (entry 11), indicating the importance of electrosynthesis.

Substrate scope evaluation for *N*-arylation

With the optimal conditions in hand, the substrate scope was first evaluated with respect to various aryl fluorides **2** and *NH*-sulfoximines **1**. As shown in Fig. 2, our protocol shows good functional group tolerance, as the introduction of phenyl (**3c**), alkoxyl (**3d–3e**, **3m**, **3n**, and **3t**), phenoxyl (**3f**), ester group (**3g**, **3r**, and **3s**), alkylhydroxyl (**3h**) and Bpin (**3i**) at the *para*- or *meta*-position of fluorobenzene delivered products with 54–86% yields. Noteworthily, the utilization of (*S*)-*NH*-sulfoximine **1b** as the substrate enables the delivery of (*S*)-**3b** without erosion of enantioselectivity. The use of 1,4-, 1,3-difluorobenzene or 1,3,5-trifluorobenzene as substrates enables selective production of the mono-substituted sulfoximines **3j**, **3p** and **3o** with moderate yields (58–71%). Moreover, fluoroarenes bearing substituents at the *ortho*-position are also suitable for the reaction, and the desired **3u–3aa** was obtained with 49–62% yield. In addition, our system is compatible with polyaromatic fluorides, as naphthyl, *O*- or *N*-containing products **3ab–3af** could be easily isolated with 62–79% yields. Next, the scope of sulfoximines with different substituents has been evaluated, as the introduction of methyl, aryl, diaryl or dialkyl groups has a marginal effect on the yields (**3ag–3an**). Although the full conversion of aryl fluorides for products **3y** and **3aa** has been observed, the low yields for these substrates can be partially attributed to the formation of defluorinative byproducts (58% and 51%, respectively) with the remaining **1a** untouched. As for methyl 4-

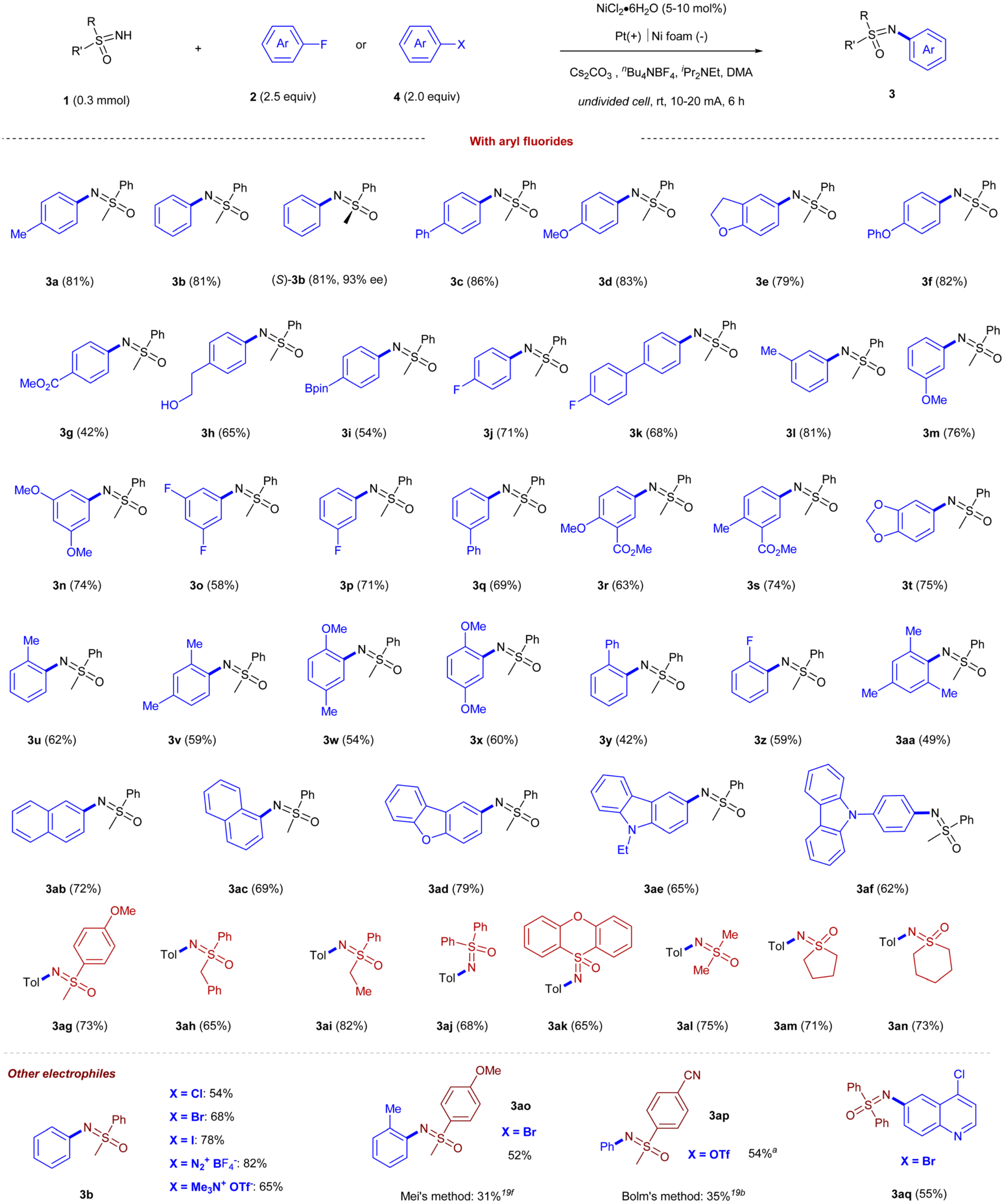


Fig. 2 Ni-catalyzed electrochemical *N*-arylation with versatile aryl electrophiles. Reaction conditions: **1** (0.30 mmol), **2** (0.75 mmol) or **4** (0.60 mmol), NiCl$_2$·6H$_2$O (5–10 mol%), Cs$_2$CO$_3$ (2.0 equiv.), ^{i}Pr$_2$NEt (1.5 equiv.), ^{n}Bu$_4$NBF$_4$ (1.0 equiv.), DMA (4 mL) in an undivided cell, 10–20 mA, 6 h, argon. [a]10-Dicyanoanthracene (40 mol%) was added. For details, please see the ESI.†

fluorobenzoate, low conversion (60%) was observed under standard conditions, along with the formation of 18% of methyl benzoate as the main byproduct.

Encouraged by the above success achieved through the formation of a postulated aryl radical *via* cathodic reduction, we envisioned that the use of other aryl electrophiles with appropriate reduction potential should work similarly in principle. With this in mind, attention was turned to sulfoximination using simple PhCl, PhI, PhN$_2$BF$_4$, and PhNMe$_3$OTf as arylating sources. To our delight, as shown at the bottom of Fig. 2, slightly modified reaction conditions (5 mol% $NiCl_2\cdot 6H_2O$) enabled the formation of the desired **3b** with 54–82% yield across the above electrophiles. Moreover, our system demonstrates superior reactivity for certain substrates compared to existing methods. For instance, while Mei and colleagues reported a yield of only 31% with sterically hindered 1-bromo-2-methylbenzene under their electrochemical conditions,[20f] our system achieved a significantly improved yield of 52% for **3ao**. Similarly, while Bolm and co-workers found that using a phenol-derived electrophile under the catalysis of $Ni(COD)_2$/BINAP (10 mol%) at 110 °C resulted in only a 35% yield,[20b] our approach with phenol-derived PhOTf led to a 53% yield of the same product (**3ap**). In addition, for 6-bromo-4-chloroquinoline, the system preferentially coupled at the bromo moiety, delivering **3aq** in 55% yield.

Substrate scope evaluation for fluorosulfonation

The success of the above defluorinative *N*-arylation prompted us to explore other transformations, leading us to investigate the previously unreported yet synthetically valuable fluorosulfonation of unactivated aryl fluorides. Building on prior work[21] from others and our group, we quickly screened electrochemical conditions and established an optimized protocol (using 0.5 equivalents of DABSO as the SO_2 source, without an added nickel catalyst or base). As shown in Fig. 3, the reaction tolerated a range of *para*- or *meta*-substituted aryl fluorides bearing methyl, methoxy, hydroxyl, fluoro, or 4-fluorophenyl groups, with minimal impact on yield. The desired products **6a–6f** were isolated in 65–81% yield; however, the ester-containing substrate **6g** gave a moderate yield. Notably, *ortho*-substituted aryl fluorides with fluoro, methyl, or methoxy groups (**6h–6j**) also reacted efficiently, albeit in slightly lower yields (58–64%). Additionally, the protocol proved compatible with *O*- or *N*-substituted heterocycles, affording **6k** and **6l** in good yields. Furthermore, the use of 1.0 equivalent of DABSO with prolonged reaction time allows the delivery of the bis-fluorosulfonylation products **6m** and **6n** with moderate yield (see the bottom of Fig. 3). Different from known methods which rely on regioselective bis-sulfonylation under harsh conditions, followed by bis-chlorination and fluorination, our one-pot protocol at room temperature makes it very attractive.[24]

Synthetic applications

To further demonstrate the synthetic utility of our method, we conducted gram-scale reactions and late-stage modifications of bioactive molecules. As shown in Fig. 4A, the *N*-arylation

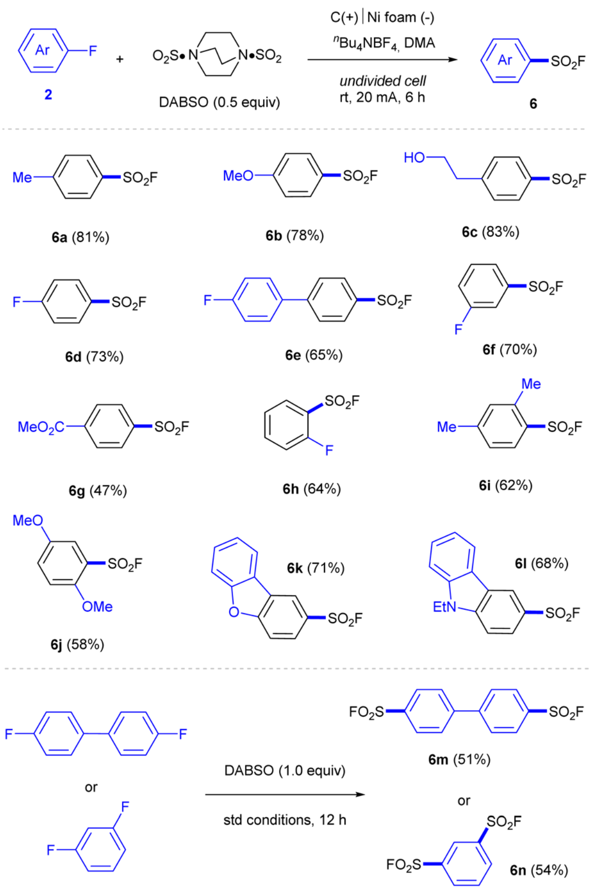


Fig. 3 Fluorosulfonylation with aryl fluorides. Reaction conditions: **2** (0.3 mmol), DABSO (0.15 mmol), $^{n}Bu_4NBF_4$ (1.0 equiv.), DMA (4 mL) in an undivided cell, 20 mA, 6 h, argon. For details, please see the ESI.†

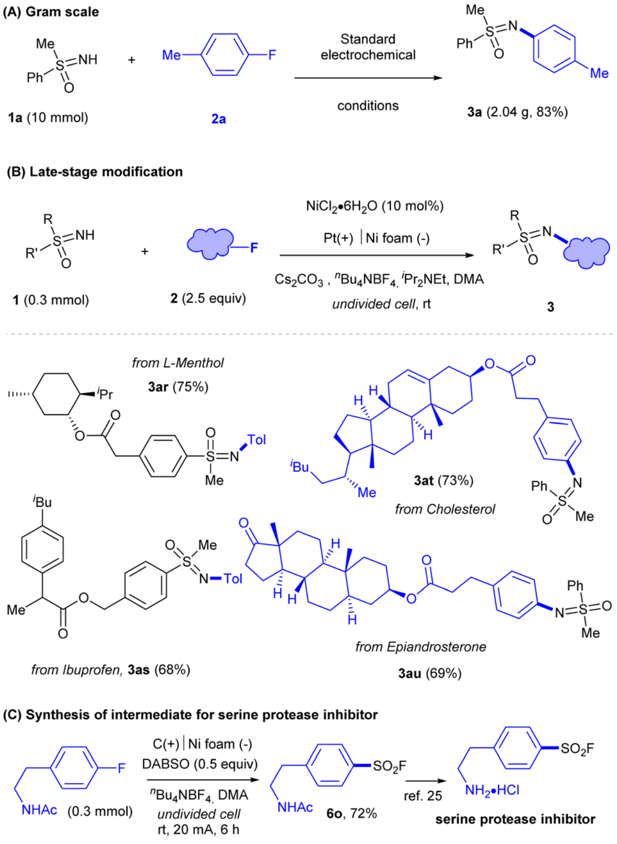


Fig. 4 Synthetic applications. Reaction conditions for late-stage modification: **1** (0.30 mmol), **2** (0.75 mmol), $NiCl_2\cdot 6H_2O$ (10 mol%), Cs_2CO_3 (2.0 equiv.), $^{i}Pr_2NEt$ (1.5 equiv.), $^{n}Bu_4NBF_4$ (1.0 equiv.), DMA (4 mL) in an undivided cell at rt under an argon atmosphere. For details, please see the ESI.†

reaction proceeded efficiently on a gram scale without yield erosion. Moreover, the protocol proved compatible with structurally complex substrates, including those bearing ester and ketone functional groups. Using functionalized aryl fluorides or *NH*-sulfoximines, we successfully obtained derivatives **3ar–3au** in moderate to good yields (Fig. 4B). Furthermore, the current method can be applied for the facile synthesis of **6o**, a key intermediate for the preparation of serine protease inhibitors (Fig. 4C).[25]

Mechanistic studies

To elucidate the reaction mechanism for the *NH*-sulfoximination of 1-fluoro-4-methylbenzene **2a**, we conducted comprehensive experimental investigations (Fig. 5). (1) First, to determine whether the reaction proceeds *via* paired electrolysis, we performed the model reaction in a divided cell, observing a dramatic decrease in yield (16% for **3a**, Fig. 5A). This result confirms that both cathodic and anodic processes are essential for efficient transformation. (2) Second, real-time monitoring of the cathode potential during the course of the reaction revealed values ranging from −15 to −20 V *vs.* Ag/AgCl. This significantly exceeds the reduction potential of **2a** (−2.44 V *vs.* Ag/AgCl, Fig. 5D, curve a), confirming facile electrochemical reduction of the substrate under the reaction conditions. Further evidence was obtained through exhaustive electrolysis of **2a** in the absence of both **1a** and $NiCl_2 \cdot 6H_2O$, which generated toluene (8%) and 4,4′-dimethylbiphenyl (23%) as characteristic reduction byproducts (Fig. 5B). (3) To obtain direct evidence for aryl radical intermediates, we performed a control experiment by using 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) as the radical scavenger. As shown in Fig. 5A, high resolution mass spectrometry (HRMS) indicates the formation of 2,2,6,6-tetramethyl-1-(*p*-tolyloxy)piperidine. Furthermore, by conducting EPR spectroscopy using PBN (*N*-*tert*-butyl-α-phenylnitrone) as a spin trap, characteristic radical adduct signals were observed during electrolysis of **2a**, unambiguously confirming the generation of aryl radical species under reaction conditions (Fig. 5C).[26] (4) Additional cyclic voltammetry studies (*vs.* Ag/AgCl, Fig. 5D) provided further mechanistic insights. $NiCl_2 \cdot 6H_2O$ displayed a well-defined reduction wave at −2.16 V in DMA (curve b), corresponding to the Ni(II)/Ni(I) redox couple.[27] Upon addition of **1a** to the **2a** solution, the catalytic current decreased significantly at −2.64 V (curve c). Subsequent introduction of $NiCl_2 \cdot 6H_2O$ shifted this reduction wave to −2.42 V while substantially increasing the current intensity (curve d). Combining these CV studies with the observed complete loss of reactivity when using $Ni(COD)_2$ as a catalyst (Table 1, entry 2),

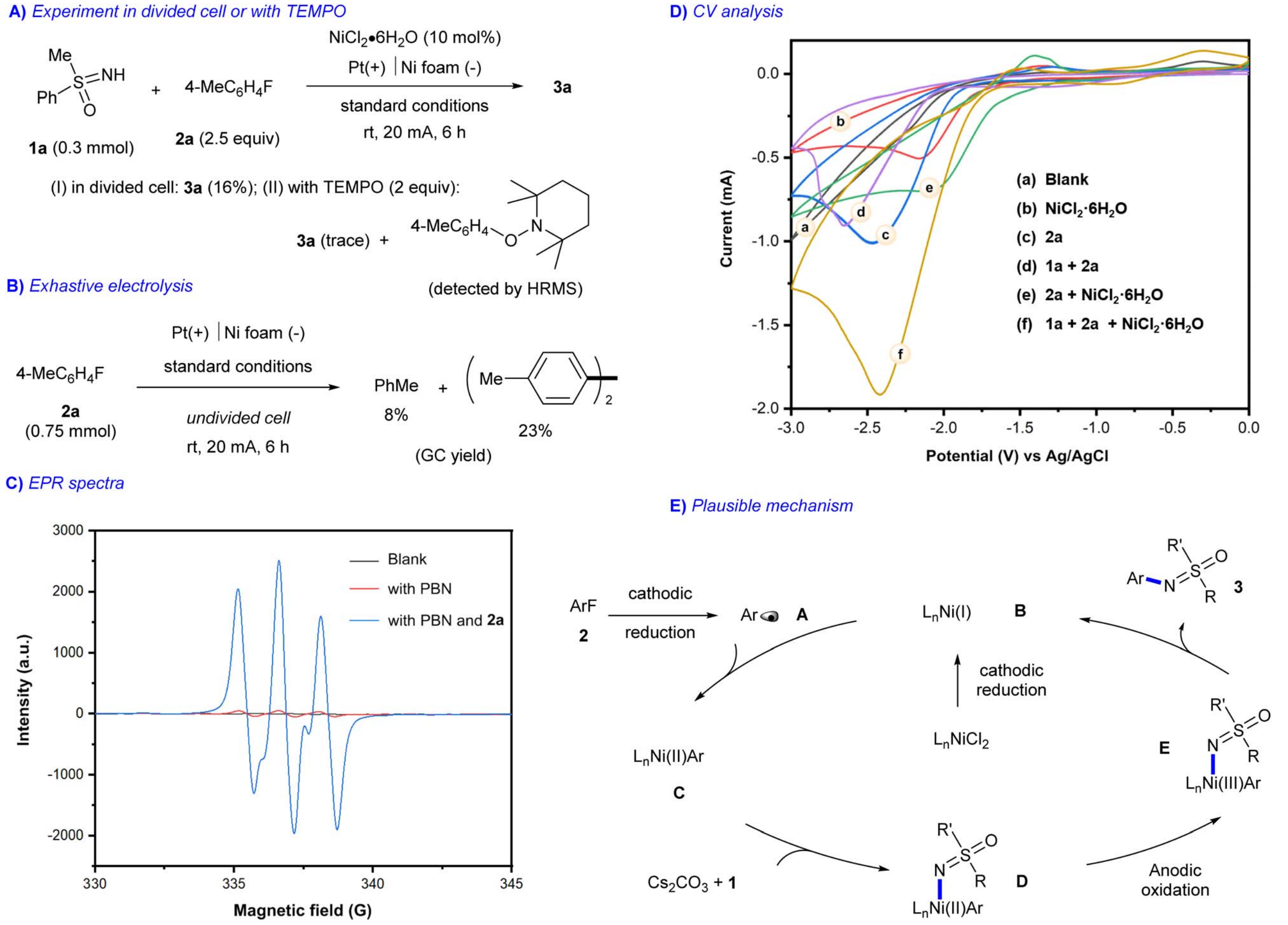


Fig. 5 Mechanistic studies and a plausible mechanism (for details, please see the ESI†).

we propose that a Ni(I) species serves as the active catalytic intermediate. Based on our experimental results and literature precedents,[16,18,20f,g] we propose the catalytic cycle shown in Fig. 5E. Cathodic reduction of both the aryl fluoride substrate and L_nNi(II) generates the key aryl radical intermediate **A** along with the fluoride anion and L_nNi(I) species **B**. Radical trapping by **B** forms the ArNi(II)L_n complex **C**. Subsequent coordination with *NH*-sulfoximine **1**, facilitated by Cs_2CO_3, yields intermediate **D**. Anodic oxidation of **D** produces intermediate **E**. Final reductive elimination affords the desired product **3** while regenerating the active Ni(I) catalyst **B**.

As for the mechanism for defluorinative fluorosulfonylation, based on control experiments (for details, please see the ESI†) and previous studies,[21] we envisioned that after the formation of the aryl radical *via* cathodic reduction, it can be efficiently trapped by SO_2 to form $ArSO_2^{\bullet}$ at first. The combination of $ArSO_2^{\bullet}$ with the radical cation of DABCO formed *via* anodic oxidation followed by nucleophilic substitution with fluoride could deliver the desired product **6**.

Conclusions

In summary, we have developed an electrochemical strategy for the selective cleavage of inert C–F bonds in unactivated aryl fluorides through cathodic reduction at room temperature. This approach, combined with nickel catalysis, has enabled the first successful implementation of direct sulfoximination using aryl fluorides as coupling partners. The protocol demonstrates good substrate scope, accommodating various common aryl electrophiles while exhibiting better reactivity for some challenging substrates compared to existing methods. Furthermore, we have extended this strategy to achieve defluorinative fluorosulfonylation of inert aryl fluorides. The synthetic utility of this methodology has been highlighted through efficient late-stage functionalization of biorelated molecules. Current efforts in our laboratory are focused on expanding this platform to other valuable transformations *via* selective activation of inert electrophiles.

Data availability

ESI is available and includes the experimental procedures, characterization data and crystallographic data for $NiCl_2(\mathbf{1a})_2(H_2O)_2$. Deposition number 2433423 (for $NiCl_2(\mathbf{1a})_2(H_2O)_2$) contains the supplementary crystallographic data for this paper.†

Author contributions

X. K. and Z. C. conceived and directed the project. Y. C., S. Z., K. F., and X. C. discovered and developed the reaction. S. Z., K. F. and L. D. performed the experiments and collected the data. M. L. and Y. X. recorded the X-ray and UV spectra. All authors discussed and analyzed the data. X . K. and Z. C. wrote the manuscript with contribution from other authors.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This project was sponsored by the Natural Science Foundation of Henan (252300421183) and the National Natural Science Foundation of China (22102012, 22202021, 22272011, 22201062, and 22372015). This project was also funded by the China Postdoctoral Science Foundation (2024T170222) and the Postdoctoral Research Grant in Henan Province (HN2024001). This research was sponsored by the Qinglan Project of Jiangsu Province, China, under the leadership of Prof. X. Kong.

Notes and references

1 (*a*) H. Amii and K. Uneyama, *Chem. Rev.*, 2009, **109**, 2119–2183; (*b*) T. Ahrens, J. Kohlmann, M. Ahrens and T. Braun, *Chem. Rev.*, 2015, **115**, 931–972; (*c*) O. Eisenstein, J. Milani and R. N. Perutz, *Chem. Rev.*, 2017, **117**, 8710–8753; (*d*) T. Fujita, K. Fuchibe and J. Ichikawa, *Angew. Chem., Int. Ed.*, 2019, **58**, 390–402; (*e*) H.-J. Ai, X. Ma, Q. Song and X.-F. Wu, *Sci. China: Chem.*, 2021, **64**, 1630–1659; (*f*) Q. Wan, R.-X. Liu, Z. Zhang, X.-D. Wu, Z.-W. Hou and L. Wang, *Chin. J. Chem.*, 2024, **42**, 1913–1928; (*g*) J. L. Röckl, E. L. Robertson and H. Lundberg, *Org. Biomol. Chem.*, 2022, **20**, 6707–6720.

2 (*a*) Y. Kiso, K. Tamao and M. Kumada, *J. Organomet. Chem.*, 1973, **50**, C12–C14; (*b*) X.-W. Liu, J. Echavarren, C. Zarate and R. Martin, *J. Am. Chem. Soc.*, 2015, **137**, 12470–12473; (*c*) T. Niwa, H. Ochiai, Y. Watanabe and T. Hosoya, *J. Am. Chem. Soc.*, 2015, **137**, 14313–14318; (*d*) W.-H. Guo, Q.-Q. Min, J.-W. Gu and X. Zhang, *Angew. Chem., Int. Ed.*, 2015, **54**, 9075–9078.

3 M. Otsuka, K. Endo and T. Shibata, *Chem. Commun.*, 2010, **46**, 336–338.

4 (*a*) Q.-K. Kang, Y. Lin, Y. Li and H. Shi, *J. Am. Chem. Soc.*, 2020, **142**, 3706–3711; (*b*) Q.-K. Kang, Y. Lin, Y. Li, L. Xu, K. Li and H. Shi, *Angew. Chem., Int. Ed.*, 2021, **60**, 20391–20399.

5 H. Huang and T. H. Lambert, *Angew. Chem., Int. Ed.*, 2020, **59**, 658–662.

6 (*a*) V. A. Pistritto, M. E. Schutzbach-Horton and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2020, **142**, 17187–17194; (*b*) W. Chen, H. Wang, N. E. S. Tay, V. A. Pistritto, K.-B. Li, T. Zhang, Z. Wu, D. A. Nicewicz and Z. Li, *Nat. Chem.*, 2022, **14**, 216–223.

7 X. Zhao, L. Bai, J. Li and X. Jiang, *J. Am. Chem. Soc.*, 2024, **146**, 11173–11180.

8 S. Wang, H. Wang and B. König, *Chem*, 2021, **7**, 1653–1665.

9 L. Bai and L. Jiao, *Chem*, 2023, **9**, 3245–3267.

10 X. Liu, A. Sau, A. R. Green, M. V. Popescu, N. F. Pompetti, Y. Li, Y. Zhao, R. S. Paton, N. H. Damrauer and G. M. Miyake, *Nature*, 2024, **637**, 601–607.

11 (*a*) S. H. Langer and S. Yurchak, *J. Electrochem. Soc.*, 1969, **116**, 1228–1229; (*b*) S. Wu, F. Schiel and P. Melchiorre, *Angew. Chem., Int. Ed.*, 2023, **62**, e202306364.

12 (*a*) M. Yan, Y. Kawamata and P. S. Baran, *Chem. Rev.*, 2007, **117**, 13230–13319; (*b*) L. Ackermann, *Acc. Chem. Res.*, 2020, **53**, 84–104; (*c*) J. C. Siu, N. K. Fu and S. Lin, *Acc. Chem. Res.*, 2020, **53**, 547–560; (*d*) C. Ma, P. Fang, Z. Liu, S. Xu, K. Xu, X. Cheng, A. Lei, H. Xu, C. C. Zeng and T.-S. Mei, *Sci. Bull.*, 2021, **66**, 2412–2429.

13 For recent examples focusing on the transformation of activated aryl fluorides, please see: (*a*) O. Allemann, S. Duttwyler, P. Romanato, K. K. Baldridge and J. S. Siegel, *Science*, 2011, **332**, 574–577; (*b*) F. Diness and D. P. Fairlie, *Angew. Chem., Int. Ed.*, 2012, **51**, 8012–8016; (*c*) Y. Lin, M. Li, X. Ji, J. Wu and S. Cao, *Tetrahedron*, 2017, **73**, 1466–1472; (*d*) S. Mallick, P. Xu, E. U. Würthwein and A. Studer, *Angew. Chem., Int. Ed.*, 2019, **58**, 283–287; (*e*) X. W. Liu, C. Zarate and R. Martin, *Angew. Chem., Int. Ed.*, 2019, **58**, 2064–2068; (*f*) Z. You, K. Higashida, T. Iwai and M. Sawamura, *Angew. Chem., Int. Ed.*, 2021, **60**, 5778–5782; (*g*) Y.-J. Chen, W.-H. Deng, J.-D. Guo, R.-N. Ci, C. Zhou, B. Chen, X.-B. Li, X.-N. Guo, R.-Z. Liao, C.-H. Tung and L.-Z. Wu, *J. Am. Chem. Soc.*, 2022, **144**, 17261–17268; (*h*) N. Y. Shin, E. Tsui, A. Reinhold, G. D. Scholes, M. J. Bird and R. R. Knowles, *J. Am. Chem. Soc.*, 2022, **144**, 21783–21790; (*i*) A. Shi, Y. Liu, R. Zhang, Z. Zhu and Y. Qiu, *eScience*, 2024, **4**, 100255; (*j*) Y. Zhang, J. Chen, H. Yao, Y. Wang, H. Liu, L. Wang, N. Huang and N. Wang, *Chin. J. Chem.*, 2025, **43**, 995–1000; (*k*) T. Wang, C. Li, J. Mi, H. Wang, L. Chen, Q. Kong, N. Jiao and S. Song, *CCS Chem.*, 2025, **7**, 392–402.

14 (*a*) X. Kong, Y. Chen, X. Chen, Z.-X. Lu, W. Wang, S.-F. Ni and Z.-Y. Cao, *Org. Lett.*, 2022, **24**, 2137–2142; (*b*) X. Kong, X. Chen, Y. Chen and Z.-Y. Cao, *J. Org. Chem.*, 2022, **87**, 7013–7021; (*c*) X. Kong, Y. Chen, Q. Liu, W. Wang, S. Zhang, Q. Zhang, X. Chen, Y.-Q. Xu and Z.-Y. Cao, *Org. Lett.*, 2023, **25**, 581–586; (*d*) X. Kong, Y. Chen, X. Chen, C. Ma, M. Chen, W. Wang, Y.-Q. Xu, S.-F. Ni and Z.-Y. Cao, *Nat. Commun.*, 2023, **14**, 6933; (*e*) X. Kong, Q. Liu, Y. Chen, W. Wang, H.-F. Chen, W. Wang, S. Zhang, X. Chen and Z.-Y. Cao, *Green Chem.*, 2024, **26**, 3435–3440; (*f*) Y.-Y. Chen, Q. Chen, S. Zhang, K. Feng, Y.-Q. Xu, X. Chen, Z.-Y. Cao and X. Kong, *Org. Lett.*, 2024, **26**, 7555–7559; (*g*) Y. Chen, Q. Chen, S. Zhang, K. Feng, X. Kong, X. Chen, W. Li and Z. Y. Cao, *Org. Biomol. Chem.*, 2025, **23**, 2111–2114.

15 For selected reviews, see: (*a*) I. Ghosh, L. Marzo, A. Das, R. Shaikh and B. König, *Acc. Chem. Res.*, 2016, **49**, 1566–1577; (*b*) N. Kvasovs and V. Gevorgyan, *Chem. Soc. Rev.*, 2021, **50**, 2244–2259; (*c*) D. I. Bugaenko, A. A. Volkov, A. V. Karchava and M. A. Yurovskaya, *Russ. Chem. Rev.*, 2021, **90**, 116; (*d*) A. Das and K. R. J. Thomas, *Chem.–Eur. J.*, 2024, **30**, e202400193; (*e*) X.-Q. Xie, W. Zhou, R. Yang, X.-R. Song, M.-J. Luo and Q. Xiao, *Org. Chem. Front.*, 2024, **11**, 4318–4342.

16 (*a*) L. Yi, T. Ji, K.-Q. Chen, X.-Y. Chen and M. Rueping, *CCS Chem.*, 2021, **4**, 9–30; (*b*) Y. Gong, J. Hu, C. Qiu and H. Gong, *Acc. Chem. Res.*, 2024, **57**, 1149–1162; (*c*) M. C. Franke and D. J. Weix, *Isr. J. Chem.*, 2024, **64**, e202300089.

17 (*a*) S. Ni, J. Yan, S. Tewari, E. J. Reijerse, T. Ritter and J. Cornella, *J. Am. Chem. Soc.*, 2023, **145**, 9988–9993; (*b*) G. Zhang, Z. Luo, C. Guan, X. Zhang and C. Ding, *J. Org. Chem.*, 2023, **88**, 9249–9256; (*c*) S. Ni, R. Halder, D. Ahmadli, E. J. Reijerse, J. Cornella and T. Ritter, *Nat. Catal.*, 2024, **7**, 733–741; (*d*) T. Michiyuki, S. L. Homölle, N. K. Pandit and L. Ackermann, *Angew. Chem., Int. Ed.*, 2024, **63**, e202401198.

18 (*a*) J. P. Wolfe and S. L. Buckwald, *J. Am. Chem. Soc.*, 1997, **119**, 6054–6058; (*b*) S. D. Ramgren, A. L. Silberstein, Y. Yang and N. K. Garg, *Angew. Chem., Int. Ed.*, 2011, **50**, 2171–2173; (*c*) R. A. Green and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2015, **54**, 3768–3772; (*d*) C. M. Lavoie, P. M. MacQueen, N. L. Rotta-Loria, R. S. Sawatzky, A. Borzenko, A. J. Chisholm, B. K. V. Hargreaves, R. McDonald, M. J. Ferguson and M. Stradiotto, *Nat. Commun.*, 2016, **7**, 11073; (*e*) E. B. Corecoran, M. T. Pirnot, S. Lin, S. D. Dreher, D. A. Dirocco, I. W. Davies, S. L. Buchwald and D. W. C. MacMillan, *Science*, 2016, **353**, 279–1613; (*f*) C. Li, Y. Kawamata, H. Nakamura, J. C. Vantourout, Z. Liu, Q. Hou, D. Bao, J. T. Starr, J. Chen, M. Yan and P. S. Baran, *Angew. Chem., Int. Ed.*, 2017, **56**, 13088–13093; (*g*) C.-H. Lim, M. Kudisch, B. Liu and G. M. Miyake, *J. Am. Chem. Soc.*, 2018, **140**, 7667–7673; (*h*) M. S. Oderinde, N. H. Jones, A. Juneau, M. Frenette, B. Aqulia, S. Tentarelli, D. W. Robbins and J. W. Johannes, *Angew. Chem., Int. Ed.*, 2019, **58**, 18859–18863; (*i*) Y. Liu, Y. Sun, Y. Deng and Y. Qiu, *Angew. Chem., Int. Ed.*, 2025, e202504459; for other powerful methods, please see: (*j*) J. Liu, X. Qiu, X. Huang, X. Luo, C. Zhang, J. Wei, J. Pan, Y. Liang, Y. Zhu, Q. Qin, S. Song and N. Jiao, *Nat. Chem.*, 2019, **11**, 71–77; (*k*) J. Liu, C. Zhang, Z. Zhang, X. Wen, X. Dou, J. Wei, X. Qiu, S. Song and N. Jiao, *Science*, 2020, **367**, 281–285; (*l*) C. Li, Z. Yan, B. Wang, J. Li, W. Lyu, Z. Wang, N. Jiao and S. Song, *Chem*, 2023, **10**, 628–643; (*m*) Z. Cheng, K. Huang, C. Wang, L. Chen, X. Li, X. Shan, P. Cao, H. Sun, W. Chen, C. Li, Z. Zhang, H. Tan, X. Jiang, G. Zhang, Z. Zhang, M. Lin, L. Wang, A. Zheng, C. Xia, T. Wang, S. Song, X. Shu and N. Jiao, *Science*, 2025, **387**, 1083–1090.

19 (*a*) V. Bizet, C. M. Hendriks and C. Bolm, *Chem. Soc. Rev.*, 2015, **44**, 3378–3390; (*b*) X. Li, C. Wang and T. Jia, *Chin. J. Org. Chem.*, 2022, **42**, 714–731.

20 For selected examples *via* cross-coupling with organic halides, please see: (*a*) C. Bolm and J. P. Hildebrand, *Tetrahedron Lett.*, 1998, **39**, 5731–5734; (*b*) C. Bolm, J. P. Hildebrand and J. Rudolph, *Synthesis*, 2000, **7**, 911–913; (*c*) Q. Yang, P. Y. Choy, Q. Zhao, M. P. Leung, H. S. Chan, C. M. So, W.-T. Wong and F. Y. Kwong, *J. Org. Chem.*, 2018, **83**, 11369–11376; (*d*) A. Wimmer and B. König, *Org. Lett.*, 2019, **21**, 2740–2744; (*e*) C. Zhu, A. P. Kale, H. Yue and M. Rueping, *JACS Au*, 2021, **1**, 1057–11376; (*f*) D. Liu, Z.-R. Liu, C. Ma, K.-J. Jiao, B. Sun, L. Wei, J. Lefranc, S. Herbert and T.-S. Mei, *Angew. Chem., Int. Ed.*, 2021, **60**, 9444–9449; (*g*) S. A. Fisher, C. M. Simon,

P. L. Fox, M. J. Cotnam, P. L. DeRoy and M. Stradiotto, *Org. Lett.*, 2024, **26**, 1326–1331; with boronic acids, carboxylic acids, or silanes, please see: (*h*) C. Moessner and C. Bolm, *Org. Lett.*, 2005, **7**, 2667–2669; (*i*) C. Wang, H. Zhang, L. A. Wells, T. Liu, T. Meng, Q. Liu, P. J. Walsh, M. C. Kozlowski and T. Jia, *Nat. Commun.*, 2021, **12**, 932; (*j*) P. Xu, W. Su and T. Ritter, *Chem. Sci.*, 2022, **13**, 13611–13616; (*k*) J. Kim, J. Ok, S. Kim, W. Choi and P. H. Lee, *Org. Lett.*, 2014, **16**, 4602–4605; for selected examples *via* C–H functionalization, please see: (*l*) A. Wimmer and B. König, *Adv. Synth. Catal.*, 2018, **360**, 3277–3285; (*m*) W. Su, P. Xu, R. Petzold, J. Yan and T. Ritter, *Org. Lett.*, 2023, **25**, 1025–1029.

21 (*a*) T. Zhong, Z. Chen, J. Yi, G. Lu and J. Weng, *Chin. Chem. Lett.*, 2021, **32**, 2736–2750; (*b*) F. He, Y. Li and J. Wu, *Org. Chem. Front.*, 2022, **9**, 5299–5305; (*c*) T. S.-B. Lou and M. C. Willis, *Nat. Rev. Chem.*, 2022, **6**, 146–162; (*d*) L. Lin, G. Pei, Z.-Y. Cao and S. Liao, *Eur. J. Org Chem.*, 2024, **27**, e202400279; (*e*) H. Zheng, W. Xiao, F. Wu, Y. Ma and C. Liu, *Sci. China: Chem.*, 2025, **68**(5), 1763–1778; (*f*) Y. Tan, L. He and W. He, *Chin. Chem. Lett.*, 2024, **35**, 109986; for selected examples, please see: (*g*) A. T. Davies, J. M. Curto, S. W. Bagley and M. C. Willis, *Chem. Sci.*, 2017, **8**, 1233–1237; (*h*) P. K. T. Lo, Y. Chen and M. C. Willis, *ACS Catal.*, 2019, **9**, 10668–10673; (*i*) G. Laudadio, A. A. Bartolomeu, H. Verwijlen, M. Y. Cao, K. T. Oliveira and T. Noël, *J. Am. Chem. Soc.*, 2019, **141**, 11832–11836; (*j*) T. S.-B. Lou, S. W. Bagley and M. C. Willis, *Angew. Chem., Int. Ed.*, 2019, **58**, 18859–18863; (*k*) Q. Lin, Z. Ma, C. Zheng, X.-J. Hu, Y. Guo, Q.-Y. Chen and C. Liu, *Chin. J. Chem.*, 2020, **38**, 1107–1110; (*l*) X. Nie, T. Xu, Y. Hong, H. Zhang, C. Mao and S. Liao, *Angew. Chem., Int. Ed.*, 2021, **60**, 22035–22042; (*m*) M. Magre and J. Cornella, *J. Am. Chem. Soc.*, 2021, **143**, 21497–21502; (*n*) L. Zhang, X. Cheng and Q.-L. Zhou, *Chin. J. Chem.*, 2022, **40**, 1687–1692; (*o*) P. Wang, H. Zhang, M. Zhao, S. Ji, L. Lin, N. Yang, X. Nie, J. Song and S. Liao, *Angew. Chem., Int. Ed.*, 2022, **61**, e202207684; (*p*) W. Zhang, H. Li, X. Li, Z. Zou, M. Huang, J. Liu, X. Wang, S. Ni, Y. Pan and Y. Wang, *Nat. Commun.*, 2022, **13**, 3515; (*q*) J.-T. Li, X. Zhou, Q.-L. Chen, Z.-D. Chen, G. Lu and J. Weng, *Chem. Commun.*, 2022, **58**, 9409–9412; (*r*) H. Wang, Z. Li, R. Dai, N. Jiao and S. Song, *Chem. Sci.*, 2023, **14**, 13228–13234; (*s*) B. Feng, M. Tang, R. Xiao, Q. Wang, G. Zhu, Z. Zhang, Z. Yuan and Y. Wang, *J. Org. Chem.*, 2025, **90**, 2118–2125; (*t*) B. Zhao, D. Zeng, X. He, J. Li, Y. Lin and K. Ye, *JACS Au*, 2025, **5**, 2359–2367.

22 H. Suzuki and S. Ishiguro, *Inorg. Chem.*, 1992, **31**, 4178–4183.

23 C. Bolm, M. Felder and J. Müller, *Synlett*, 1992, **5**, 439–441.

24 (*a*) C. J. Smedley, A. S. Barrow, C. Spiteri, M.-C. Giel, P. Sharma and J. E. Moses, *Chem.–Eur. J.*, 2017, **23**, 9990–9995; (*b*) J. Dong, K. B. Sharpless, L. Kwisnek, J. S. Oakdale and V. V. Fokin, *Angew. Chem., Int. Ed.*, 2014, **53**, 9466–9470.

25 B. R. Baker and M. Cory, *J. Med. Chem.*, 1971, **14**, 119–125.

26 G. Zhang and I. Hua, *Environ. Sci. Technol.*, 2000, **34**, 1529–1534.

27 Q. Lin, G. Dawson and T. Diao, *Synlett*, 2021, **32**, 1606–1620.