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Introduction

Aliphatic primary amines are prevalent in nature, living organisms, and biologically active molecules.^{1–7} Serving as fundamental building blocks, they find extensive use in synthesizing complex molecules.^{8–14} The cleavage of C(sp³)-N bonds to produce alkyl radicals holds great potential in organic synthesis and drug discovery. However, cleaving the C-N bond in a primary amine (C-NH₂) poses a significant challenge in organic chemistry. This challenge stems from the poor leaving ability of the NH₂ group (C-N BDE = 102 kcal mol⁻¹, pKa = 36) and the free N-H bonds towards oxidation/cross-coupling (N-H BDE = 92 kcal mol⁻¹). In the 1970s, efforts to achieve deamination by sulfonation or pre-functionalization of alkyl amines with 2,4,6-triphenylpyridine salts (Katritzky salts) faced limitations due to strict reaction conditions.¹⁵ Recently, Watson and colleagues reported a milestone study using Katritzky salts to access alkyl radicals *via* a single electron transfer (SET) process.^{16,17} Subsequent developments of amine-derived Katritzky pyridium salts as carbon radical precursors have emerged.^{17–35} Meanwhile, isonitriles and alkyl diazo compounds were also used to achieve various deaminative functionalizations (Fig. 1A and B).^{36,37} In addition, imines could be generated from the corresponding amines with trimethoxybenzaldehyde and applied to a number of photoredox deaminative functionalizations (Fig. 1C).³⁷ Despite these state-of-the-art approaches to achieve deaminative strategies, the pursuit of other readily available surrogates for primary amines remains highly valuable.

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Alkyl bistriflimide-mediated electrochemical deaminative functionalization†

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An efficient electrochemical strategy for the deaminative functionalization of alkyl amines has been described. The alkyl bistriflimides were readily accessed by the treatment of alkyl amines with trifluoromethanesulfonic anhydride and unprecedently employed for C-N bond activation. They can be applied to a range of transformations, including borylation, sulfuration, selenation, sulfonation. Additionally, deaminative esterification and amidation can be performed under catalytic base conditions. The protocol features an undivided cell without the use of transition metal- or photo-catalysts and exhibits high conversion and stability in flow reactors.

Electrochemical synthesis has experienced a new trend of research interest in both research and industry owing to its sustainable and practical nature.^{38–46} In our previous study, Katritzky salts were proven suitable for deaminative functionalization under cell conditions (Fig. 1D).³⁹ However, this strategy could only be applied to secondary alkylamines. Moreover, the expensive pyrylium reagents and the triphenylpyridine by-product restrict the applicability of this method.

To address these issues, we describe a new approach utilizing inexpensive trifluoromethanesulfonic anhydride as an activating reagent. The alkyl bistriflimides undergo mild electrochemical deaminative functionalization in the absence of stoichiometric reductants or transition metal catalysts. In addition, in the presence of a catalytic amount of base, alkyl bistriflimides can undergo ionic reactions, such as Ritter-type reactions (Fig. 1E).

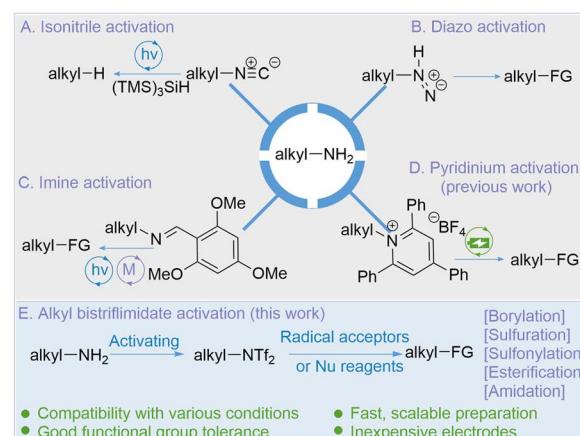


Fig. 1 The strategies of amine activation for deaminative functionalization. (A) Isonitrile activation. (B) Diazo activation. (C) Imine activation. (D) Pyridinium activation. (E) Alkyl bistriflimide activation.



Results and discussion

We began our study with electrochemical deaminative borylation using alkyl bistriflimide (**1**) and B_2Cat_2 (**2**) and treated under constant current electrolysis (CCE) (Table 1). After detailed investigations, we found that the desired alkyl boronate **3** could be obtained in 78% yield under an undivided cell set-up with a magnesium anode and nickel foam cathode at a working current of 20 mA (Table 1, entry 1). Other anode materials, such as zinc, iron, and carbon led to a lower yield (entries 2–4). In the case of carbon as the cathode, a lower yield of 36% was observed (entry 5). Notably, the use of nBu_4NBF_4 instead of TBAI proved to be unfeasible, which indicated that iodide anions were suggested to play an important role in such transformation (entry 6). The presence of air led to a product loss of approximately 15% (entry 7). Control experiments indicate that the electric current is essential (entry 8). Varied current (10 mA and 30 mA) caused decreased yields of the product (entries 9 and 10). The reaction did not occur when B_2Pin_2 was utilized as the boron source (entry 11). Remarkably, activation of the primary alkyl amine with TsCl and preparation as Katritzky salt proved to be impractical under the given reaction conditions, leading to significant challenges in achieving the desired target product (entry 12).

With the optimized conditions in hand, the generality of this electrochemical transformation has been evaluated, as shown in Fig. 2. This protocol exhibited good efficiency toward the borylation of alkyl bistriflimides, showcasing wide functional tolerance and generated borylation products in moderate to high yields. Functional groups, including halides (**4–5**, **8–9**, and

25), trifluoromethyl (**6–7**), ethers (**14**, **16**), esters (**24**), aromatic and heterocyclic (**11–13**, **15**, and **17–20**), cyanides (**31**), naphthalene (**21**), protected alcohols (**29**), and thioether (**32**) could be tolerated in the reaction. This underscores the robustness of our electrochemical methodology. Additionally, recognizing the crucial role of polyboronate compounds in organic synthesis and the limitations of direct synthesis methods, this paper outlines the preparation of diverse diboronate compounds through diamines (**26** and **30**). Secondary alkyl amines were also amenable to this method, as exemplified by 2-amino-4-phenylbutane, which gave product **33** in 45% yield. Cyclic alkylamines, such as cyclohexyl, cyclododecyl and 4-amino-tetrahydropyran, also result in moderate yields of the boronated products (**34–36**).

Having successfully established the C–B bond, we explored the possibility of establishing other C–X bonds within this framework. As depicted in Fig. 3, under the standard conditions, we found that both alkyl and aryl sulfides were generated in high yields (**37** and **41–44**). In addition, we efficiently achieved deaminative selenation (**38**), telluration (**39**), and sulfonylation (**40**), developing a new path for the efficient synthesis of sulfur-containing bioactive molecules.

To further demonstrate the practicality of the deaminative functionalization approach for alkyl bistriflimides, a number of valuable direct transformations were identified. As illustrated in Fig. 4, the reaction of alkyl bistriflimides with amides led to the formation of ester compounds (**45–48**). Notably, alkyl bistriflimides facilitated deamination Ritter reactions, efficiently producing a diverse array of amide compounds, including alkyl and aryl amides (**49–56**). Compared to traditional methods, the avoidance of high temperatures and transition-metal catalysts underscores the practical advantages of this approach.^{47–52} Additionally, to evaluate the compatibility of the deamination process of alkyl bistriflimides across various methodologies, alternative transformations of alkyl bistriflimides were explored, as depicted in Fig. 4C. Compound **1** can undergo nucleophilic substitution with aryl primary amine under catalytic amounts of base to afford secondary amine. Alkyl bistriflimides also participate in reductive cross-coupling reactions under nickel catalysis, yielding a deaminative allylation product (**59**). Furthermore, alkyl bistriflimide **11a** is well-suited to photocatalytic conditions, providing **11** with a 66% yield. Using $(bpy)Cu(CF_3)_3$ as a trifluoromethylating agent, the deaminative trifluoromethylation product (**60**) was obtained with moderate yield.

To explore the reaction mechanism, a series of experiments were conducted. The intermediate verification experiment demonstrated that alkyl bistriflimide (**5a**) was completely converted to alkyl iodide (**5b**) within 2 min, followed by the consumption of **5b** and its conversion into the corresponding product within 40 min (Fig. 5A). The *in situ* observation of compound **5b** via ^{19}F NMR confirms its role as an intermediate product, which can undergo further transformation to yield the subsequent functional group compound (Fig. 5B).^{53,54} The radical trapping experiment with TEMPO under standard conditions resulted in the alkyl adduct **57**, which was detected by HRMS (Fig. 5E). Additionally, the EPR experiments indicate the formation of radicals (for details, see the ESI†). These

Table 1 Optimization of the reaction conditions for electrochemical deaminative borylation

Entry	Modification of standard conditions	Yield ^a [%]
1	None	88 (78 ^b)
2	Using Zn(+) instead of Mg(+)	57
3	Using Fe(+) instead of Mg(+)	69
4	Using C(+) instead of Mg(+)	n.d.
5	Using C(–) instead of Ni(–)	36
6	nBu_4NPF_6 instead of nBu_4NI	Trace
7	Under air	72
8	No current	n.d.
9	10 mA, 1h	50
10	30 mA, 20 min	65
11	B_2Pin_2 instead of B_2Cat_2	n.d.
12	Using alkyl-NTs ₂ or alkyl-Katritzky salts instead of 1	n.d./4

^a Reaction conditions: **1** (0.3 mmol), **2** (1.2 mmol), TBAI (0.9 mmol), DMA (3.0 mL), Ar, at 25 °C under 20.0 mA constant-current conditions in an undivided cell, 30 min. Crude yields were determined by GC using dodecane as an internal standard. ^b The isolated yields were determined.



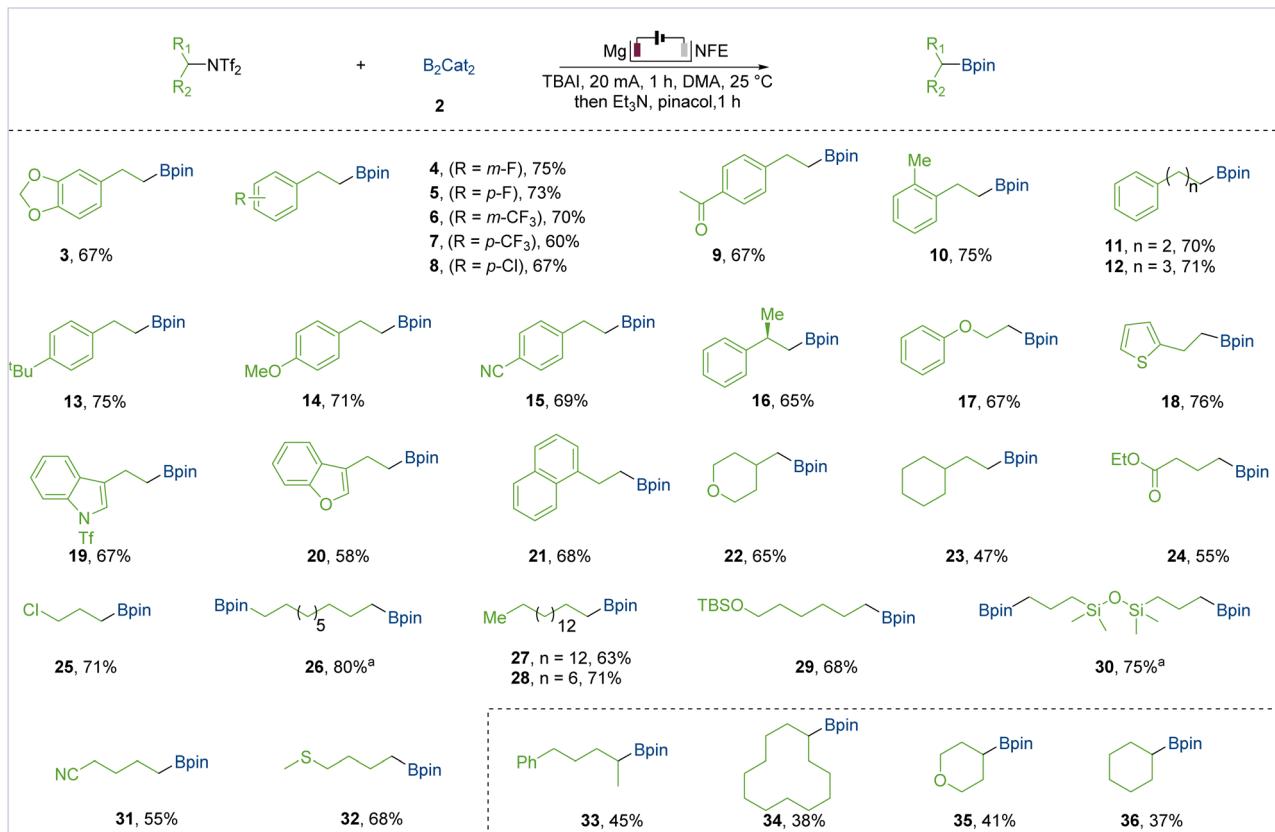


Fig. 2 Scope of the alkyl bis triflimidates. Conditions: alkyl bis triflimidates (0.5 mmol), 2 (2.0 mmol), TBAI (0.9 mmol), DMA (5.0 mL), under an argon atmosphere, 25 °C, 1 h. ^a3 h.

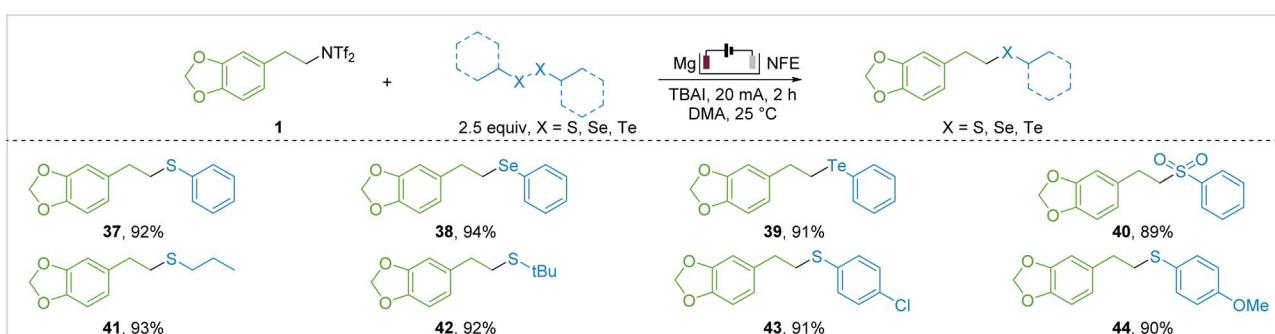


Fig. 3 Electroreductive coupling of disulfides with alkyl bis triflimidates. Conditions: alkyl bis triflimidates (0.2 mmol), disulfides (0.5 mmol), TBAI (0.9 mmol), DMA (3.0 mL), under an argon atmosphere, 25 °C, 2 h.

experiments indicate that the reaction proceeds *via* a radical pathway. The CV experiments were performed to verify the species undergoing cathodic reduction. The reduction potential of the alkyl bis triflimidate **8a** (−3.6 V) was higher than that of compound **8b** (−3.1 V), indicating that the direct reduction of alkyl bis triflimidate to radicals is challenging, whereas **8b** is more likely to be reduced to generate alkyl radicals, according to the literature (Fig. 5C).^{55,56} Next, the reaction was conducted in a flow system, and a microfluidic electrochemistry platform was introduced for scale-up reactions. At a flow rate of 0.025 mL min^{−1} and an electrolysis current of 10 mA, we

obtained a yield of 76% for the product comparable to those obtained in batch (Fig. 5D). To corroborate the applicability of this protocol, a 3 mmol-scale reaction was carried out, yielding the boronated product in 75% within 5 h at 100 mA (Fig. 5F). Furthermore, utilizing a one-pot synthesis approach, the boronated product could be produced in 43% yield, demonstrating the practicality of this method under the given reaction conditions (Fig. 5G).

Based on previous reports and the above experiments, we propose a possible mechanism as shown in Fig. 5H.^{57–61} The reaction is initiated with rapid iodination of alkyl

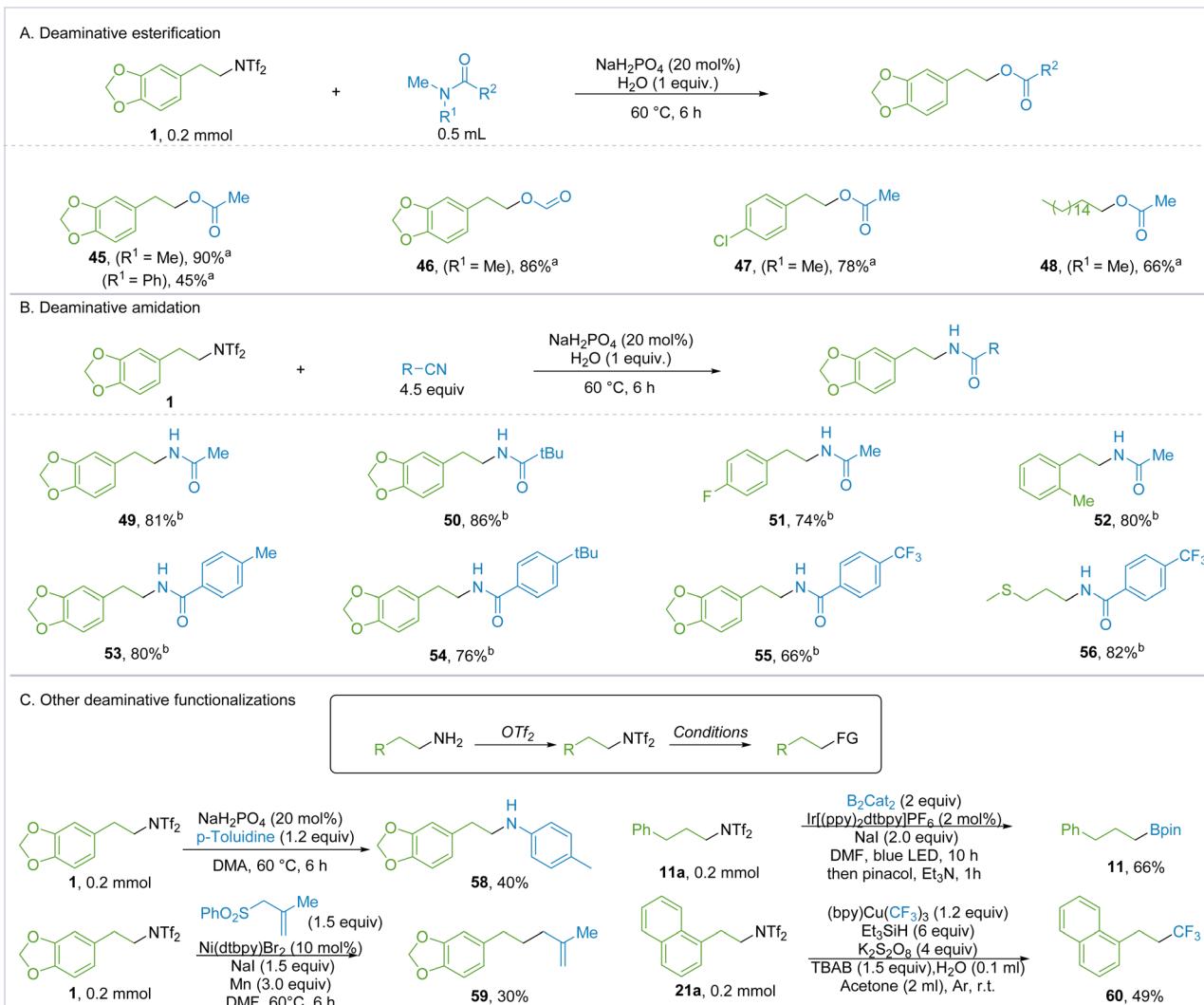


Fig. 4 Deaminative functionalization. (A) Deaminative esterification. (B) Deaminative amidation. (C) Other deaminative functionalizations.

^aConditions: alkyl bistriflimides (0.2 mmol), amide (0.5 mL), NaH₂PO₄ (20 mol%), H₂O (0.2 mmol), 60 °C, 6 h. ^bConditions: alkyl bistriflimides (0.2 mmol), cyanide (0.9 mmol), NaH₂PO₄ (20 mol%), H₂O (0.2 mmol), 60 °C, 6 h.

bistriflimide to generate alkyl iodide. Meanwhile, DMA with 1 equivalent of B₂cat₂ forms complex **A** and undergoes single-electron reduction at the cathode to form radical anion **B**. Subsequently, this radical may undergo two different paths. In path a, the reaction of the alkyl radical with **A** gives the alkyl boronate product and **C/D**, which is eventually oxidized by alkyl iodide to form **E** and an alkyl radical. In path b, radical–radical cross-coupling of the alkyl radical and **B** furnishes the alkyl boronate and complex **F**.

Experimental

General procedure for the synthesis of products 3–32.

Condition A

Tetrabutylammonium iodide (TBAI) (332 mg, 0.9 mmol), 2,2'-bis-1,3,2-benzodioxaborole(B₂cat₂) (477 mg, 2.0 mmol), alkyl bistriflimides (0.5 mmol) and DMAc (5 mL) were taken in a tube and placed in a glove box. A magnesium plate (52.5 × 8 ×

2 mm) was used as the anode, a foamed nickel electrode (52.5 × 8 × 2 mm) was used as the cathode and then the reaction mixture was electrolyzed at a constant current of 20 mA for 30 min. Afterwards, a solution of pinacol (2.0 mmol, 4.0 equiv., 236 mg) in triethylamine (1.0 mL) was added to the electrolyzer cell and the reaction mixture was kept stirring at room temperature for 1 h. The mixture was then quenched with ethyl acetate, dried onto silica gel, and purified by rapid column chromatography.

General procedure for the synthesis of products 33–36.

Condition B

An oven dried tube flask equipped with a stir bar placed in a glove box was charged with amine (0.5 mmol, 1.0 equiv.), CH₂Cl₂ (1 mL, 0.5 M) and Et₃N (0.28 mL, 1 mmol, 2.0 equiv.). The flask was cooled to −78 °C, and trifluoromethanesulfonic anhydride (0.26 mL, 0.42 g, 1.5 mmol, 3.0 equiv.) was added

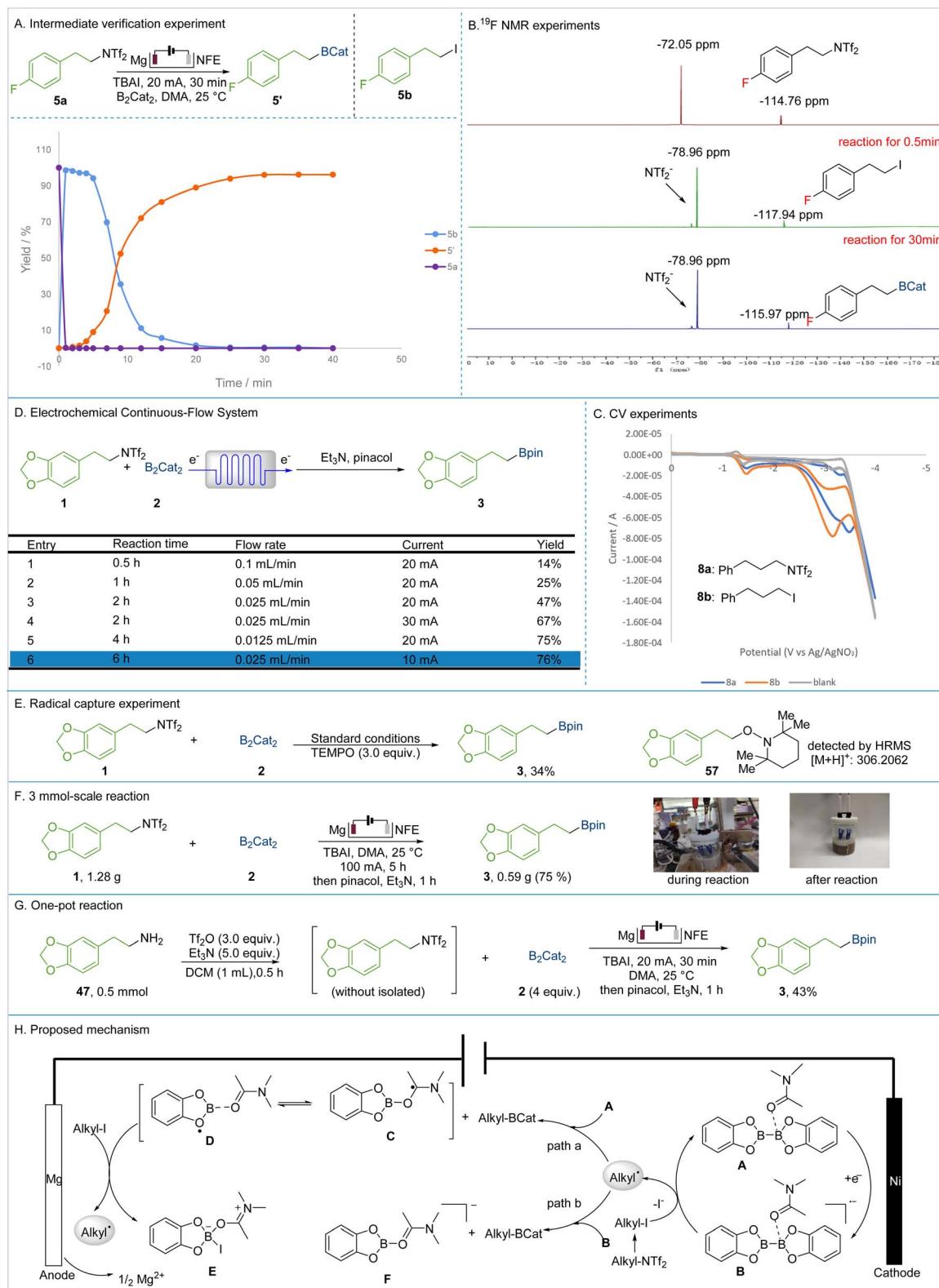


Fig. 5 Mechanism study and application. (A) Intermediate verification experiment. (B) ^{19}F NMR experiments. (C) CV experiments. (D) Electrochemical continuous-flow system. (E) Radical capture experiment. (F) 3 mmol-scale reaction. (G) One-pot reaction. (H) Proposed mechanism.

dropwise. The reaction was stirred vigorously at $-78\text{ }^\circ\text{C}$ for 0.5 h. Then NaI (135 mg, 0.9 mmol), B_2Cat_2 (477 mg, 2.0 mmol), and DMAc (3 mL) were taken in a tube and placed in a glove box.

A magnesium plate ($52.5 \times 8 \times 2\text{ mm}$) was used as the anode, a foamed nickel electrode ($52.5 \times 8 \times 2\text{ mm}$) was used as the cathode and then the reaction mixture was electrolyzed at

a constant current of 20 mA at 60 °C. Afterwards, a solution of pinacol (2.0 mmol, 4.0 equiv., 236 mg) in triethylamine (1.0 mL) was added to the electrolyzer cell and the reaction mixture was kept stirring at room temperature for 1 h. The mixture was then quenched with ethyl acetate, dried onto silica gel, and purified by rapid column chromatography.

Conclusions

In conclusion, we have developed an efficient and operationally simple deaminative protocol for constructing C-X bonds, which complements the diverse functionalization of alkylamines. Under mild electrochemical conditions, deaminative borylation, sulfuration, selenation and sulfonation were shown to be possible applications. Furthermore, scale-up reactions and continuous-flow reactions have demonstrated the applicability of this deaminative borylation strategy. Mechanistic studies indicate that iodide anions play a crucial role in the deaminative process. Additionally, esterification and amidation could be performed under catalytic base conditions.

Data availability

The data supporting this article have been included as part of the ESI.†

Author contributions

H. S., J. L., and J. X. conducted all experiments and characterized the novel compounds. X. T., Y. W., S. N., and Y. P. designed the experiments and wrote the manuscript.

Conflicts of interest

The authors declare no competing interests.

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