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ARTICLE

Electrosynthesis deamination functionalization via C-N bond cleavage and radical formation

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The C-N bond cleavage of amines has gained attention in the scientific community due to their numerous synthetic applications. In the traditional methods, the requirements for toxic oxidants and costly catalysts affect their cost-effectiveness and sustainability. However, recent advances in synthetic organic electrochemistry allow for the in-situ activation of the C-N bonds, affording different functionalizations under mild reaction conditions and with a shorter reaction time. In light of the ever-increasing importance of electrosynthesis spanning most disciplines of the chemical sciences, we review the recent development of electrochemically promoted radical deamination functionalization over the past decade years (from 2015 to 2025). Special emphasis is put on various electrochemical transformation paths and proposed mechanisms.

1. Introduction

Amines constitute a foundational class of organic compounds with significant structural diversity and broad applications across pharmaceuticals, agrochemicals, fine chemicals, dyes, and functional materials. The C-N bond, as one of the most prevalent chemical linkages, is ubiquitous in organic molecules and biological macromolecules. Its formation and transformation represent pivotal research domains in organic synthesis, organometallic chemistry, and biochemistry.[1] The precise addition and removal of chemical functionalities in sophisticated molecular settings is a highly sought but challenging goal for organic chemists, essential for flexible molecular decoration. However, the high bond dissociation energy (102.6 ± 1.0 kcal·mol^{-1}) of C-N bonds and the fact that NH_2-is virtually non-viable as a leaving group pose a persistent challenge for their selective cleavage. [2] Thus, converting the NH_2 group into a versatile and modular leaving group is highly desirable. Current strategies primarily rely on functional group activation, wherein amines are converted into activated intermediates such as diazonium salts,[3] hydrazines,[4] Katritzky salts,[5] or ammonium salts.[6] These modifications facilitate subsequent C-N bond cleavage and enable the construction of novel bonds. However, the majority of traditional C-N bond cleavage methods require a chemical reductant or transition metal catalyst, photocatalyst, or organocatalyst. Therefore, the search for new "green" processes to achieve the cleavage of C-N bonds has become a hot topic in the development of new methods.

Organic electrochemistry[7] leverages electrical energy as a renewable and clean synthetic driving force, as same as the wind and solar. By utilizing electrons and electron holes as traceless redox equivalents, it eliminates the need for stoichiometric chemical oxidants or reductants, positioning itself as an emerging environmentally sustainable paradigm in synthetic chemistry. This approach significantly enhances atom economy while diminishing dependence on fossil-derived energy resources. Through precision modulation of electrical input via optimized electrochemical conditions (e.g., current, voltage, current density, electrode, electrolyte, reaction temperature), electrochemical systems enable controlled reaction pathway steering. Due to the multiple Redox conditions be allowed to exist simultaneously, this facilitates stabilization of transient intermediates and enhanced selectivity, while occasionally unlocking unconventional mechanistic pathways.[8] Many researchers are therefore working eagerly to discover new reaction patterns and make previously known reactions electrochemically accessible.

In fact, significant advancements in the fields of C-N bond activation and electrochemical synthesis over recent decades, a large number of high-quality works have been reported. However, only a few examples can be compatible with electrochemical conditions and achieve stable conversion. Additionally, radical type reagents are very easily activated through the electrode single-electron transfer redox process. For this reason, we focus on electrochemical synthesis strategies and review the electrochemical radical deamination functionalization methods established in the past decade (from 2015 to 2025) using a wide range of nitrogen-containing

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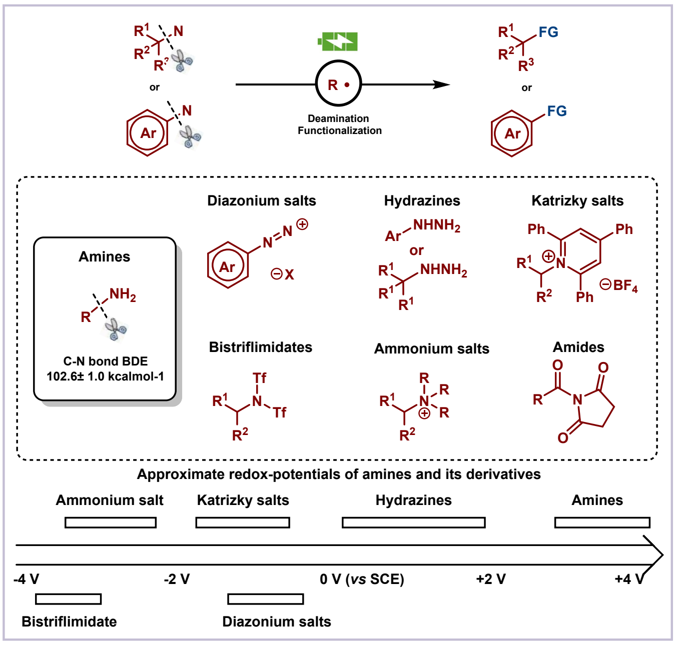
compounds, including diazonium salts, hydrazines, Katritzky salts, bistriflimidates and other nitrogen sources.

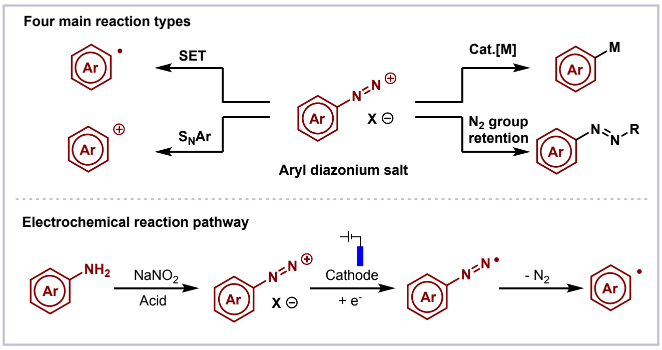


Scheme 1. Electrosynthesis deamination functionalization via C-N bond cleavage

2. Electrosynthetic deamination via aryl diazonium salts

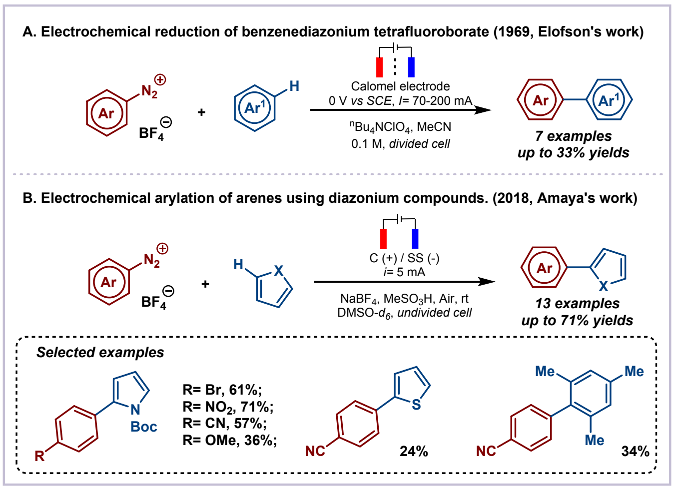
Compared to the C-halide (Br/I) bond, the C-N bond exhibits significantly shorter bond lengths, lower polarizability, and greater chemical inertness.[9] Consequently, chemical transformations reliant on C-N bond cleavage remain a substantial challenge in synthetic chemistry. The initial report by Griefs in 1858,[10] a series of prominent named reactions associated with aryl diazonium salts, which conveniently synthesized from the corresponding anilines, have been discovered and developed over the past centuries. Especially, the seminal discovery by Traugott Sandmeyer in 1884[11] established a transformative paradigm for converting aryldiazonium salts into aryl halides, enabling regioselective substitution at the diazonium site. Moreover, those century-old transformation include, Pschorr reaction (1896),[12] Gomberg-Bachmann reaction (1924),[13] Balz-Schiemann reaction (1927),[14] and Meerwein arylation (1939)[15] are still widely used in modern organic synthesis in academic and industrial Settings to this day for its exceptional regioselectivity and broad functional group tolerance.

There are four main reaction types of aryl diazonium salts, including aryl radical transformations via single-electron transfer (SET) processes, aryl cation transformations via nucleophilic aromatic substitution processes (S_NAr), transition-metal-catalyzed processes, and transformations with retention of the dinitrogen group.[16] Given the mechanistic constraints of electrochemistry, aryl diazonium cations readily undergo direct SET reduction at the cathode surface, forming diazo radicals. These intermediates spontaneously release nitrogen gas, producing aryl radicals primed for subsequent reaction transformation (Scheme 2).



Scheme 2. The reaction pathway of aryl diazonium salts

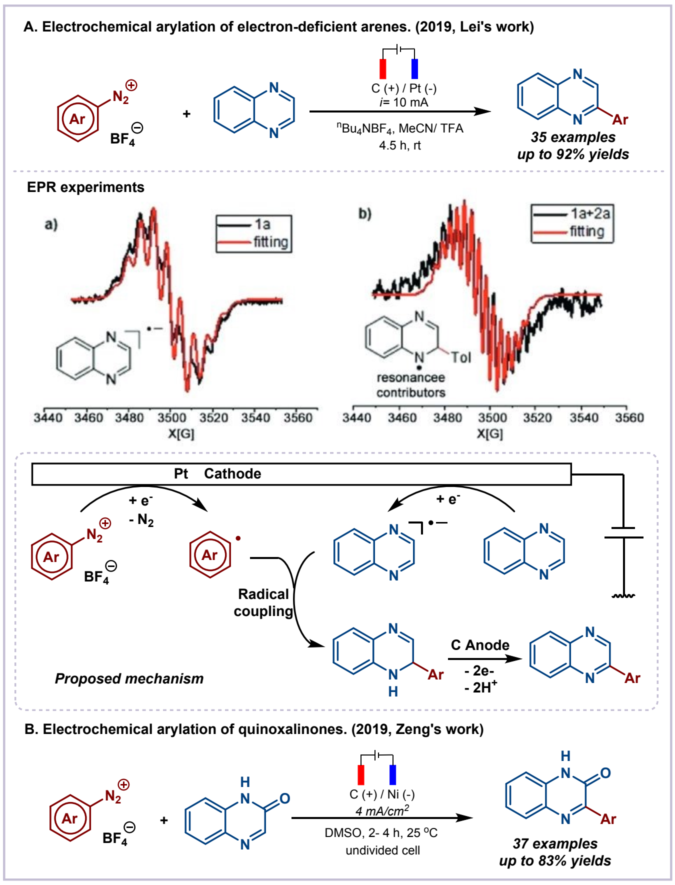
2.1 Electrochemical-mediated C(sp²)-C(sp²) bond formation via aryl diazonium salts



Scheme 3. Electrochemical-mediated aryl C-C bond formations with aryl diazonium salts

The earliest report on the electrochemical synthesis involving aryl diazonium salts was pioneered by Elofson and co-workers in 1969.[17] Their study demonstrated that aryl-aryl coupling reactions could be achieved under electrochemical conditions using diazonium tetrafluoroborate as the aryl radical source, employing tetrabutylammonium perchlorate as the electrolyte and acetonitrile as the solvent with a standard calomel electrode in a divided cell. This approach successfully facilitated coupling across seven aromatic substrates, including benzene, toluene, anisole, benzonitrile, nitrobenzene, bromobenzene and naphthalene. However, this methodology exhibited limitations in regioselectivity and yields (below 33% yields) (Scheme 3A). Since then, the field of electrochemical aryl-aryl coupling via diazonium salts experienced a prolonged quiescent period until 2018, when the Amaya's group developed a controlled electrochemical Gomberg-Bachmann reaction strategy for synthesizing heteroaromatic hydrocarbons by employing an undivided electrolytic cell with a carbon cathode and stainless steel anode.[18] This methodology utilized DMSO-d_6

as the solvent, sodium tetrafluoroborate as the supporting electrolyte, and methanesulfonic acid as an additive. Notably, this method achieved heteroaromatic coupling with enhanced functional group tolerance toward electron-deficient substituents (e.g., nitro, cyano, and halogens), yielding significantly higher efficiencies compared to electron-rich aromatic substrate (Scheme 3B).



Scheme 4. Electrochemical-mediated Minisci-type arylation with aryl diazonium salts

In 2019, a new approach for the electrochemical Minisci-type arylation of various electron-deficient arenes with aryldiazonium salts was demonstrated by Lei and co-workers, providing the 35 examples in up to 92% yield.[19] Utilizing tetrabutylammonium tetrafluoroborate as the supporting electrolyte and a mixture of MeCN/ TFA as the co-solvent, the arylation product of quinoxaline was obtained under 10 mA constant current for 4.5 hours. To prove the possible radical reaction pathway conjecture, the controlled experiments conducted by the author. EPR experiments were conducted in a divided cell and it was concluded that quinoxaline was reduced in the cathodic chamber, forming a quinoxaline radical that generated an EPR peak at g = 2.0040, 2 AN = 6 G, 6 AH = 6 G. Moreover, a cyclic voltammetry study suggested that quinoxaline in the presence of TFA was initially protonated and then reduced at -0.34 V. Based on the above results, the author proposes a possible mechanism in Scheme 4A that quinoxaline and diazonium salts respectively undergo SET reduction at the C cathode to form the corresponding quinoxaline radical anion and aryl radical. Subsequently, a radical coupling process is carried out to obtain a coupling intermediate. Then, deprotonation and re-aromatization processes are successively completed under two anodic oxidation actions, ultimately resulting in the target product. With similar operating principles to those proposed by Zeng[20] and co-workers in the same year, but the difference was that their electrochemical Minisci-type arylation of quinoxalinones with aryldiazonium salts in the absence of an external supporting electrolyte (Scheme 4B).

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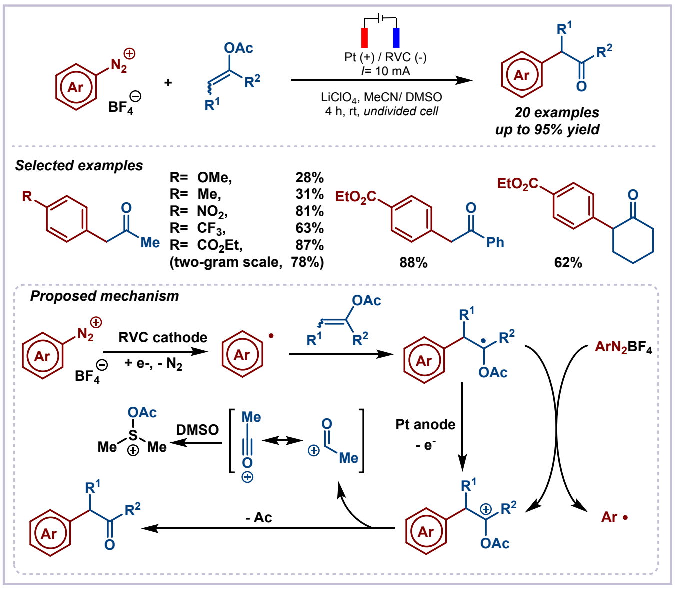
2.2 Electrochemical-mediated C(sp^2)-C(sp^3) bond formation via aryl diazonium salts



Scheme 5. Electrochemical-mediated Csp^2-Csp^2 bond coupling of enol acetates

In 2022, Wang and co-workers reported a green, economical electrosynthesis process for ketone *α*-arylation, achieved by reacting aryl diazonium salts with enol acetates at room temperature without bases or metal catalysts.[21] The optimized reaction conditions included lithium perchlorate as the supporting electrolyte, a mixture of CH_3CN/DMSO (v/v=5: 1) as the co-solvent and a constant current of 10 mA in an undivided cell equipped with a Pt plate anode and an RVC cathode. Enhanced yields were observed for *para*-substituted aryl diazonium salts bearing electron-withdrawing groups (such as ester, cyano, nitro, trifluoromethyl) compared to those with electron-donating groups (such as methoxy, methyl). Significantly, this methodology proved applicable to an in-situ one-pot diazotization/electrochemical approach, and it achieved a 76% yield in a gram-scale synthesis of the target compound from enol acetate and aryldiazonium salt by using the cheap graphite plate electrodes instead of expensive RVC electrodes. On the basis of control experiments, a reaction mechanism is proposed which involves the initial reduction of aryl diazonium salts at the RVC cathode's surface to generate corresponding phenyl diazo radicals. Then, the aryl radical adds to enol acetate to generate carbon radical intermediate. Subsequently, this intermediate is oxidized at the anode to

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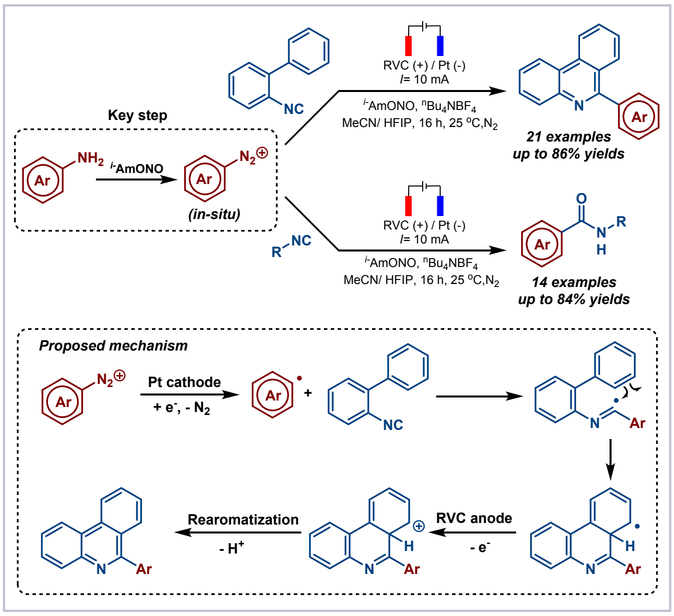
afford the corresponding cation intermediate. Finally, the required α-arylation product was obtained through the departure of an acyl cation (Scheme 5).



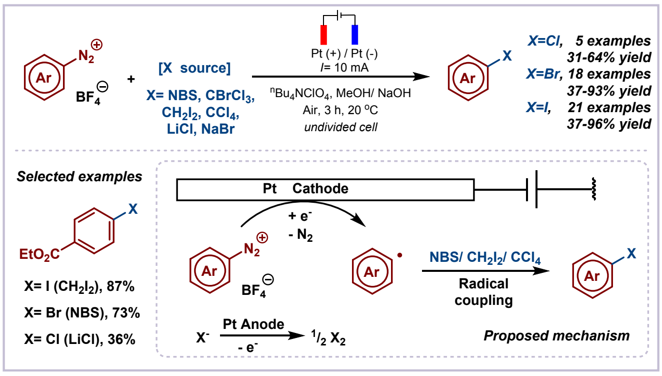
Scheme 6. Electrosynthesis of phenanthridines via 2-isocyanobiphenyls and aromatic amines

In 2021, Sharma et al. utilized the electrochemical method to synthesis the phenanthridines by the coupling of amines and 2-isocyanobiphenyls in a simple undivided cell.[22] From the perspective of possible mechanism, the key step to the success of the reaction lies in the in-situ formation of the aryl diazonium salt of aniline and amyl nitrite in the reaction system. Subsequently, the aryl diazonium salts are reduced at the Pt cathode to release nitrogen gas and aryl radicals. Notably, the aryl radical undergoes preferential capture by aryl isonitrile, followed by anodic oxidation and re-aromatization affords the phenanthridines. Conversely, alkyl isonitrile capture diverts the pathway toward amide formation (Scheme 6).

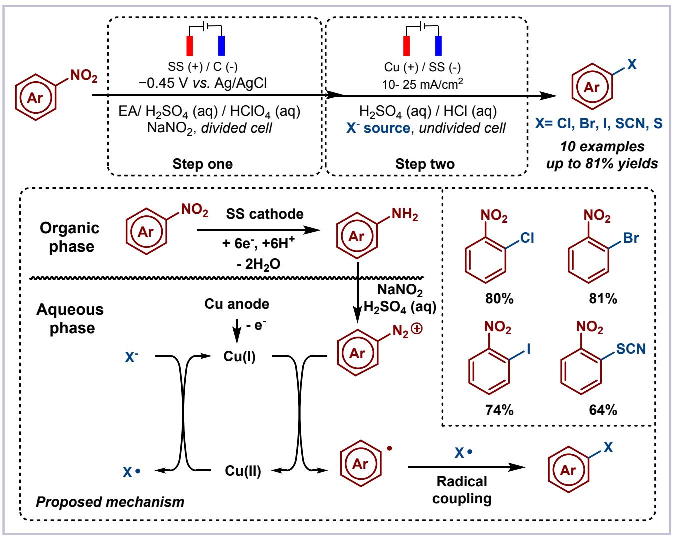
2.3 Electrochemical-mediated C-X bond formation via aryl diazonium salts

The classical Sandmeyer reaction represents a fundamentally important method to convert an aryl amine to an aryl halide via the intermediacy of a diazonium salt, including a copper metal mediated process (Gattermann reaction),[23] diazotization in organic phases (Doyle diazotization),[24] a Cu(I)-catalyzed process[25] and acetate-facilitated metal-free halogenation.[26] Critically, the incompatibility of transition metal reagents or halogenated reagents with electrochemical conditions has greatly limited the development of electrochemical Sandmeyer reactions.

In 2018, Mo and co-workers reported a general electrochemical strategy for the Sandmeyer reaction, using a simple and inexpensive halogen source, such as NBS, $CBrCl_3$, CH_2I_2, CCl_4, LiCl and NaBr for the halogenation of aryl diazonium salts.[27] Due to the advantage of electrochemical strategies, aryl diazonium salts can easily generate the key aryl radicals from cathode electrons and capture halogen radicals directly from halogen sources. However, aryl iodides and aryl bromides are more readily available than aryl chlorides, which may be affected by the differences in the activity of halogenation reagents and operating conditions. To prove the scalability of this electrochemical strategy, a gramscale reaction was successfully performed and its potential for future industrial applications was demonstrated. Importantly, mechanistic studies, including in situ EPR, support a single-electron reduction pathway for the electrochemical halogenation of diazonium salts. This method complements Sandmeyer reactions, potentially paving the way for other metal-free transformations (e.g. noble metal-free trifluoromethylation) in the near future. (Scheme 7).



Scheme 7. Electrochemical-mediated Sandmeyer reaction with aryl diazonium salts



Scheme 8. Electrochemical-mediated heterogeneous Sandmeyer reaction of nitroaromatics

An uncommon one-pot two-phase electrochemical reduction of aryl diazonium salts derived from nitrobenzenes to aryl halidess were reported by Wang in 2022 (Scheme 8).[28] To ensure success, the author adopted the Step-by-step reaction strategy. Firstly, the author respectively used a carbon electrode and a stainless-steel electrode as the cathode and anode, which were respectively located in the divided cells of the ethyl acetate/water ($HClO_4$ 0.25 M, $NaNO_2$ 1.5 equiv., H_2SO_4 1.2 M)

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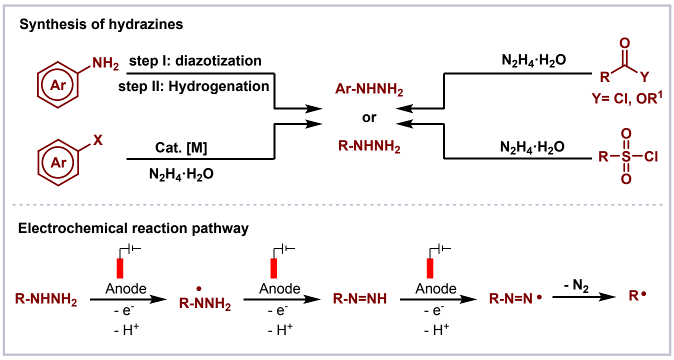
co-solvent system, with a cell voltage of -0.45 V. This process ensures the in-situ conversion of the nitro group to the diazo group and the transfer from the organic phase to the aqueous phase. Next, the aqueous solution containing HCl, HBr, KI or NaSCN was added to the above solution and electrolysis was completed under constant current conditions at a copper anode/stainless steel cathode. Key to this strategy is the use of available copper rod as anode, which serves as an electrode and a catalyst by electrogenerating copper(I) ions species and then oxidizing aryl diazonium salts generates the corresponding aryl radicals. Notably, this unique work synthesizes haloaryl compounds in a two-phase system at room temperature using either galvanic or electrolytic cells, achieving higher yields than previous approaches.

3. Electrosynthetic deamination via hydrazines

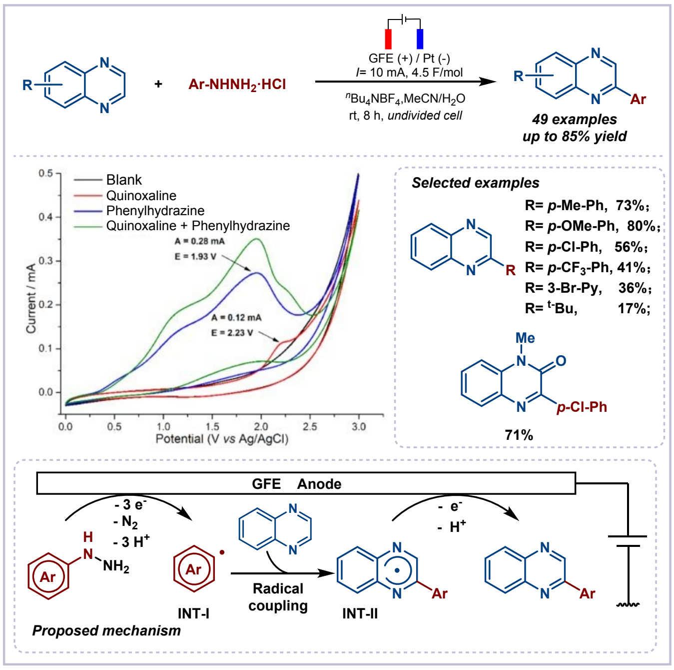


Scheme 9. The synthsis and electro-transformations of hydrazines

Hydrazines are characterized by their unique C-N bond architecture and have emerged as promising reagents in contemporary coupling chemistry. These reactions exploit C-N bond cleavage to achieve flexible and synthetically diverse reaction systems. Relative to traditional electrophilic partners such as halogenated hydrocarbons, hydrazines present superior operational advantages, such as low cost, easy accessibility (derived from aniline, aryl halide, ester or acyl halide), and minimized environmental impact. In particular, the corresponding carbon radicals and nitrogen are released by electrochemical oxidation activation (Scheme 9). There is a growing demand for the development of strategies to achieve the transformation and utilization of hydrazines.

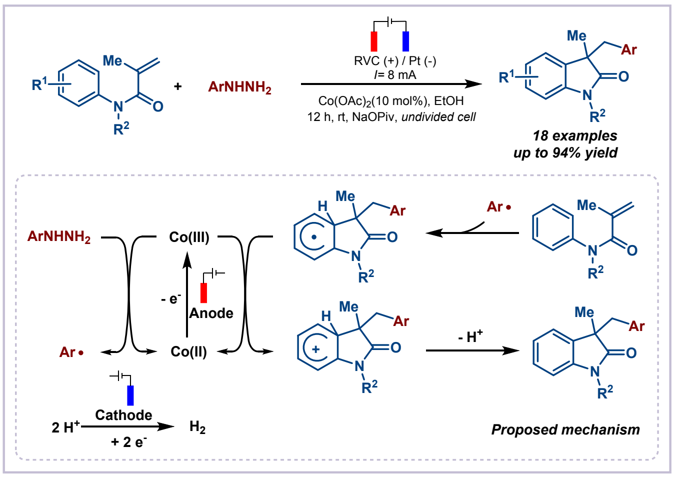
3.1 Electrochemical applications of aryl hydrazines

Radical oxidative coupling reactions are interesting alternatives to well-established methods for the formation of C–C and C–X bonds, contributing numerous significant innovations to synthetic chemistry. In 2022, Li and Zhou et al. revealed a practical and scalable protocol for electrochemical arylation of quinoxalin(on)es with arylhydrazine hydrochlorides in an undivided cell, providing 45 corresponding products in moderate to good yields (Scheme 10).[29] Electron-rich alkenes afforded high yields of product, while moderate yields were observed for electron-deficient alkenes. The reaction is significantly accelerated using microwave irradiation. Although, this method exhibits high efficiency, easy scalability, and broad functional group tolerance, alkyl hydrazines are not suit for this condition due to the tendency of alkyl radicals to oxidize into cations. Cyclic voltammetry experiments found that quinoline presented an oxidation peak at E= +2.23 V *vs* Ag/AgCl, which which are much higher than that of aryl hydrazine (E= +1.93 V *vs* Ag /AgCl), indicating that aryl hydrazine is preferentially oxidized by the electrode. The authors proposed a reaction mechanism initiating with the oxidation of arylhydrazine at the graphite anode, which forms the aryl radical intermediate **INT-I** via deprotonation, three-electron loss, and N_2 release. This radical subsequently adds to quinoxaline to yield intermediate **INT-II**. Following further single-electron oxidation and deprotonation, the arylation product is afforded. Concurrently, hydrogen ions are reduced at the Pt cathode to form H_2. It should be noted that since the radical-radical coupling between azo and aryl radicals is inevitable, the use of an excess of arylhydrazine is proposed to suppress this side reaction and improve the arylation efficiency.



Scheme 10. Electrochemical oxidative C-H arylation of quinoxalines and quinazolinones

In 2018, Yu and co-workers developed a series of substituted oxindoles were facilely synthesized via electrochemical cobalt-catalyzed C-H or N-H oxidation between N-arylacrylamides and arylhydrazines or potassium alkyltrifluoroborates under mild conditions (Scheme 11).[30] The optimized reaction conditions included $Co(OAc)_2$ (10 mol%) as the catalyst, NaOPiV as the additive, EtOH as the effective solvent system and 8 mA constant current between a RVC anode and a Pt cathode in an undivided cell over 12 h at room temperature. To gain a deeper insight into the mechanistic pathways of this oxidative annulations, control experiments(such as radical inhibition experiment and gas-chromatographic headspace analysis) were conducted, demonstrating the radical pathway and the existence of molecular nitrogen and hydrogen as the byproducts. Mechanistically, anodic oxidation converts Co(II) species to Co(III) species, which act as an oxidant to indirectly generate aryl radicals from aryl hydrazine. The generated aryl radical adds to *N*-aryl acrylamide, followed by intramolecular cyclization. The resulting radical intermediate is then oxidized by Co(III) via a single-electron transfer path to form an aryl cation, which subsequently undergoes deprotonation to yield oxindoles.



Scheme 11. Electrochemical Co-catalyzed coupling of *N*-arylacrylamides with arylhydrazines

In addition to radical addition with an alkene moiety, an electrooxidative carbonylative Sonogashira-type cross-coupling reaction of arylhydrazines and alkynes has also been realized, achieving the synthesis of functionalized ynones under the relative low CO atmosphere with moderate to excellent yields (Scheme 12).[31] The proposed reaction pathway includes the precursor of the active catalyst Pd(II) formed by electro-oxidation of Pd(0) species reacted with arylhydrazines to give the **INT-I** species, along with the release of N_2 and the insertion of CO into the C-Pd bond of the **INT-I** species generated the **INT-II** species. Then, the **INT-II** intermediate is react with terminal alkynes to give the **INT-III** intermediate. Ultimately, Reductive elimination occurred to afford the corresponding ynones and Pd(0) species. Notebly, another possible initial source of Pd(0) species might be generated from Pd(II) catalyst by the reduction of NH_4I in the presence of CO. This transformation would contribute significantly to the development of electrochemical carbonylative Sonogashira-type reactions.

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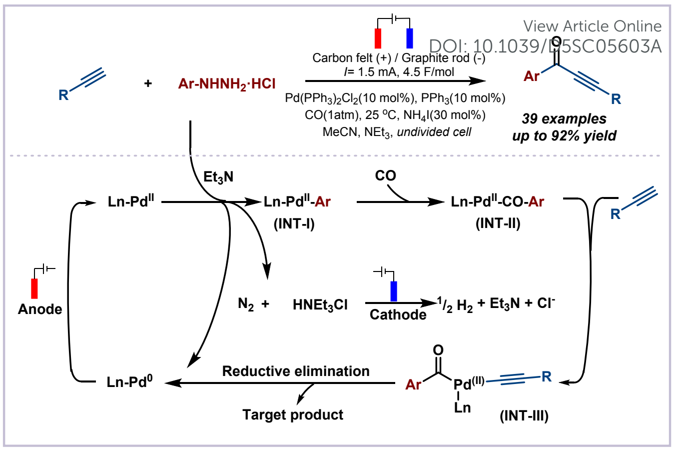
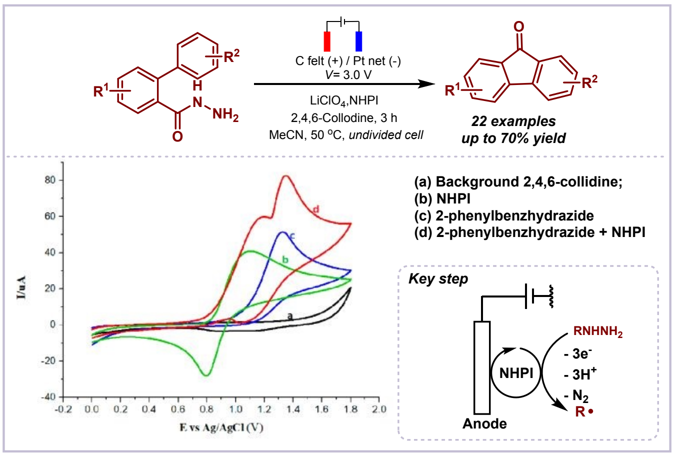


Scheme 12. Electrochemical Pd-catalyzed coupling of alkynes with arylhydrazines

3.2 Electrochemical applications of acyl hydrazine



Scheme 13. Electrochemical synthesis of fluorenone derivatives from arylhydrazides

Cyclization of Aryl hydrazines with functionalized alkenes or alkynes has provided a facile and expeditious route to assembly of five- or six-membered rings, particularly for heterocyclic scaffold. This route usually proceeds through a radical cyclization pathway or transitionmetal-catalyzed condition. An *N*-Hydroxyphthalimide (NHPI)-mediated electrochemical method for the oxidative denitrogenation of aroylhydrazides to afford acyl radicals with high efficiency in 2021 (Scheme 13).[32] Zeng and Xu described this electrochemical method features external oxidant-free and transition metal-free conditions. The in situ generated acyl radicals could be intramolecularly trapped to give fluorenones with high efficiencies. After extensive optimization, the author found that the use of the catalytic amount of 2,4,6-collidine as the base makes this method more attractive for the synthesis of fluorenones. To prove the possible radical reaction pathway conjecture, the controlled experiments conducted by the author. A cyclic voltammetry study suggested that NHPI was initially oxidized at +1.05 V *vs* Ag/AgCl (curve b) and aroylhydrazides showed an oxidation potential at 1.38 V *vs* Ag/AgCl (curve c). These results reveal that the oxidation of NHPI is preferable to anodic oxidation of aroylhydrazides. However, the CV of the 1:1 mixture of NHPI

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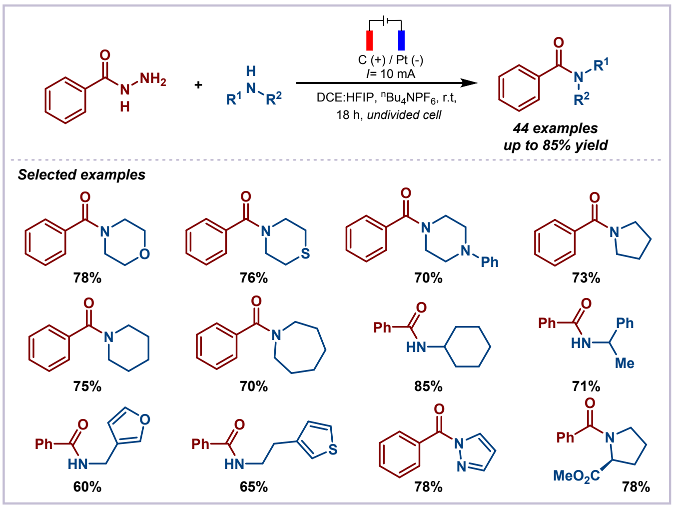
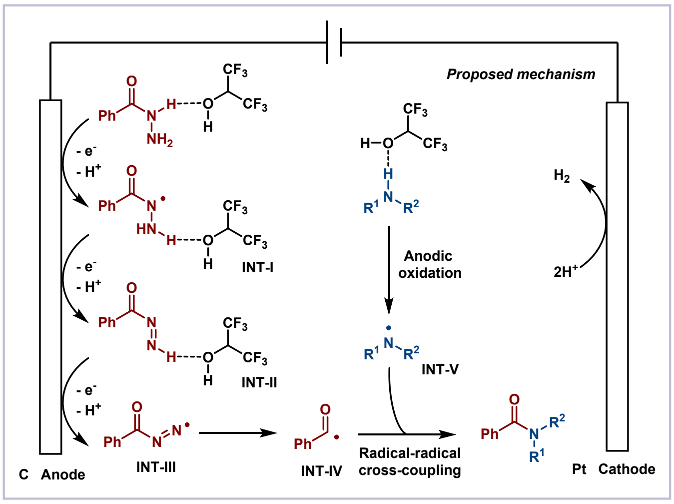
and aroylhydrazides showed a catalytic current, while the reductive current of NHPI disappeared (curve d), which results from the hydrogen atom transfer (HAT) process between Phthalimide N-Oxyl (PINO) and aroylhydrazides to regenerate NHPI. Based on the above results, a plausible mechanism was proposed that the reaction success hinged critically on the preferential electrochemical oxidation of acyl hydrazine to generate acyl radicals.



Scheme 14. Electrochemical deamidation coupling with hydrazine and amine



Scheme 15. Proposed mechanism

One year later, An electrochemical amidation of benzoyl hydrazine/ carbazate and 1°/ 2° amine as coupling partners via concomitant cleavage and formation of C(sp^2)-N bonds has been achieved by Patel and co-workers (Scheme 14).[33] This reaction generated both acyl and *N*-centered radicals from benzoyl hydrazines and amines via the simultaneous cleavage and formation of C(sp^2)-N bonds. Broad substrate scope was observed for both the benzoyl hydrazine/ carbazate and amine (aromatic or aliphatic) components under this catalytic system. Significantly, the process produced only environmentally benign nitrogen and hydrogen gas as by-products. To further demonstrate the synthetic utility of this methodology, a gram-scale (10 mmol) reaction of benzoyl hydrazine with morpholine proceeded for 32 hours to yield morpholino(phenyl)methanone in 70% isolated yield. Remarkably, the practical applicability of this electrochemical radical coupling strategy was successfully extended to the synthesis of bezafibrate, a commercially available fibrate drug widely used for the treatment of hyperlipidemia.

The authors propose a plausible reaction mechanism for the crucial bifunctional hexafluoroisopropanol (HFIP). First, the reaction begins with HFIP-solvent hydrogen-bonding activation of the benzoyl hydrazine, enabling anodic electrochemical oxidation to form the *N*-centered diazanyl radical **INT-I**. Subsequently, Intermediate **INT-I** then undergoes a two-step anodic oxidation sequence, progressing through intermediate **INT-II** to yield the diazene radical intermediate **INT-III**. Cleavage of the C-N bond within **INT-III** releases molecular nitrogen (N_2) and produces the benzoyl radical **INT-IV**. Simultaneously, an H-bonding interaction and anodic oxidation generate the N-centered radical intermediate **INT-V**. Finally, radical–radical cross-coupling between **INT-IV** and **INT-V** delivers the desired products (Scheme 15).

3.3 Electrochemical conversion of hydrazine carbamates

Compared with aryl hydrazine, there are only a few reports and applications of alkyl hydrazine under the electrochemical condition. In 2020, Wang and co-workers established that electrochemical oxidation efficiently affords key alkyl radical intermediates concurrent with N_2 and CO_2 elimination (Scheme 16).[34] This green electrochemical approach leverages sequential anodic oxidative fragmentation to access primary/secondary/tertiary alkyl radicals, enabling direct functionalization of diverse nitrogen-containing heteroarenes and some nature products (e.g. benzoquinoxalinones, pyrazinones, quinazolinones, isoquinolines, phthalazines, quinazolines, phenanthridines, caffeine, provost, borneol) in moderate to good yields with high stereoselectivity. Key to this reaction's success is alkyl carbazates's low oxidation potential (E_{OX} = +1.4 V *vs* SCE), facilitating its anodic oxidation to release electrons, protons, N_2 and CO_2. The generated radicals then undergo Minisci-type coupling with nitrogen-containing heterocycles.

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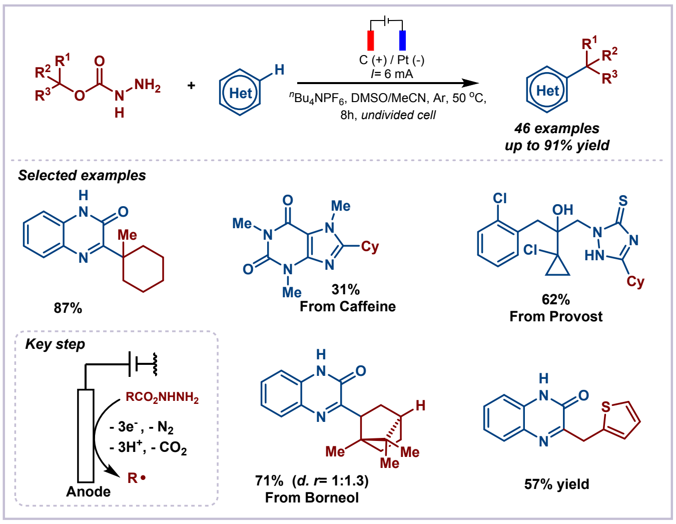
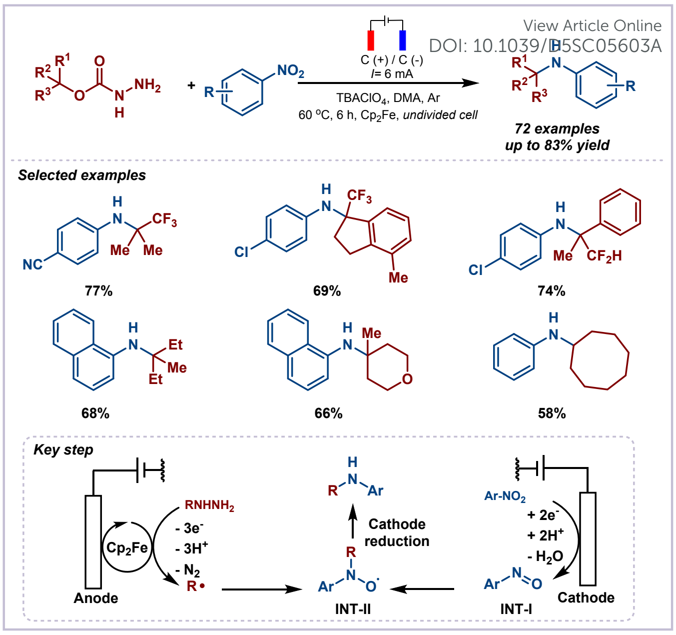


Scheme 16. Electrochemical Minisic reaction

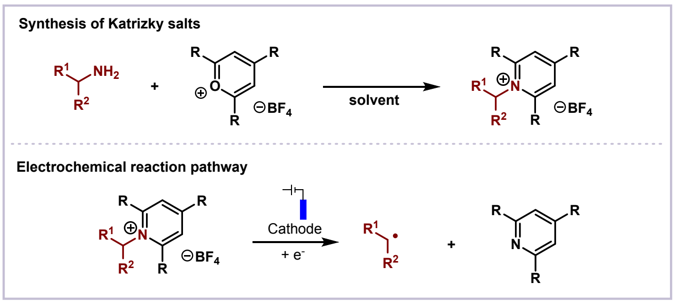
More recently, the same group achieved a general electrochemical deoxygenative C-N bond coupling of alkyl carbazates with nitroarenes (Scheme 17).[35] This strategy enabled the conversion of diverse primary, secondary, and tertiary alkyl carbazates into valuable alkylamines, including substrates bearing α-CF_3, α-CF_2H, and benzyl groups. The reaction proceeded with broad substrate scope and mild conditions, demonstrating significant potential for sustainable synthesis. With the combination of flowchemistry strategy, the gram-scale electrochemical C-N bond coupling of alkyl carbazates with nitroarenes was realized under continuous-flow conditions, enabling overall reaction times of 20 h. To expand the application range of the substrate and enhance the conversion efficiency, the authors added ferrocene as an oxidation medium to the reaction system. The paired electrolysis mechanism of this reaction was shown in Scheme 17. Initially, a part of alkyl carbazates were multistep oxidized at anode, and the remaining part were initial oxidized at the anode involves Cp_2Fe (0.42 V), regenerating Cp_2Fe^+. The generated alkyl radicals are captured by an in situ-generated nitroso species **INT-I** (from cathodic nitrobenzene reduction), forming intermediate **INT-II**. Subsequent cathodic reduction of intermediate **INT-II** ultimately delivers the amine products. In fact, the mismatched reactivity of alkyl radicals and nitrogen sources has been addressed by paired electrolysis, providing a powerful and versatile tool for the streamlined access to a wide array of amine compounds on a preparative scale, especially for the advancements in the synthesis of α-fluorinated amines.



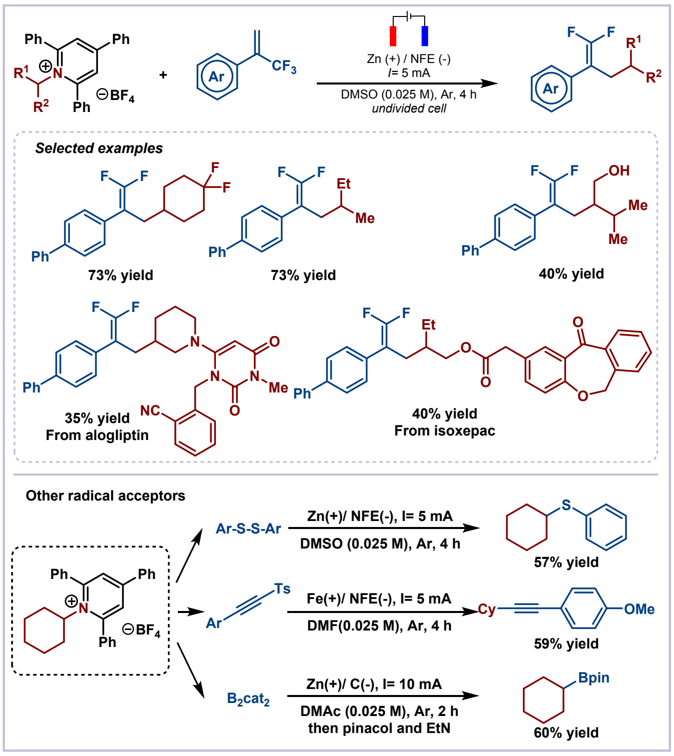
Scheme 17. Electrochemical C-N bond coupling of hydrazine carbamates with nitroaromatics

4. Electrosynthetic deamination via Katritzky salts

Due to the low redox potentials, Katritzky salts (E_{red} = -0.92 V *vs* SCE) are more reactive compared to NHP-ester (E_{red} = -1.28 V *vs* SCE), and halogens (E_{red} = -1.7 to -2.2 V *vs* SCE), and it provide a new suite precursor in selective radical alkylation. As early as 1970s, Katritzky[36] and co-workers first found that 2,4,6-trimethylpyrylium tetrafluoroborate can convert alkyl amines into bench-stable, bulky pyridinium salts in a single step. Katritzky salts effectively reduce the energy of the C(sp^3)-N bond, opening up the prospect of functionalization by the breakup of C(sp^3)-N bond under mild reaction circumstances. Primary amine-derived Katritzky pyridium salts have been employed as carbon radical surrogates for transition-metal catalysis and photoredox chemistry. Previous approaches[37]on reductive cross-coupling of Katritzky salts required expensive photocatalysts, electron donor-acceptor (EDA) complexes or heavy metal catalystsfor the single electron transfer process. The analogous SET outcome could be achieved by cathodic reduction without chemical catalyst loading (Scheme 18).



Scheme 18. The reaction pathway of Katritzky salts



Scheme 19. Electrochemical deaminative functionalization of Katritzky salts with radical acceptors

In 2021, Wang's team first demonstrated a metal-free electrochemical reductive deaminative C(sp^3)-C(sp^3) bond cross-coupling of Katritzky salts with various radical acceptors.[38] In that work, many gem-difluoroalkenes were synthesized under the electrochemical reductive conditions. The results showcased that a diversity of secondary Katritzky salts were verified for this electrolytic protocol, providing the cross-coupling products in moderate to excellent yields. It is worth mentioning that no Ni-catalyst was involved in this reaction and C-N scission in this conversion could be mediated by Zinc anode serves as the sacrificial electrode, which significantly improved the atomic economy and reduced the consumption of fossil fuels. Moreover, C(sp^3)-C(sp^3), C(sp^3)-C(sp^2), C(sp^3)-C(sp), C-S, and C-B bonds were also successfully constructed. This deaminative functionalization, facilitated by rapid molecular diffusion across microfluidic channels, demonstrates practicality that outperforms conventional electrochemistry setups (Scheme 19).

Nickel-catalyzed coupling reactions are important synthetic tools for the construction of carbon-carbon and carbon-heteroatom bonds, owing to advantages, such as low cost, wide substrate compatibility, and mild reaction conditions. However, the favorable reduction potential of Katritzky salts ($E_{1/2}$≈ -1.4 V *vs* Fc/Fc^+) poses a particular challenge for electroreductive Ni catalysis (-1.7 V *vs* Fc/Fc^+) that Katritzky salts reduce faster than Ni intermediates or typical alkyl electrophiles (e.g., alkyl halides, redox-active esters), generating off-cycle byproducts via dihydropyridyl trapping or alkyl radical dimerization/reduction. Moreover, successful catalysis critically depends on balancing the rate of aryl halide oxidative addition with the alkylpyridinium salt activation step.

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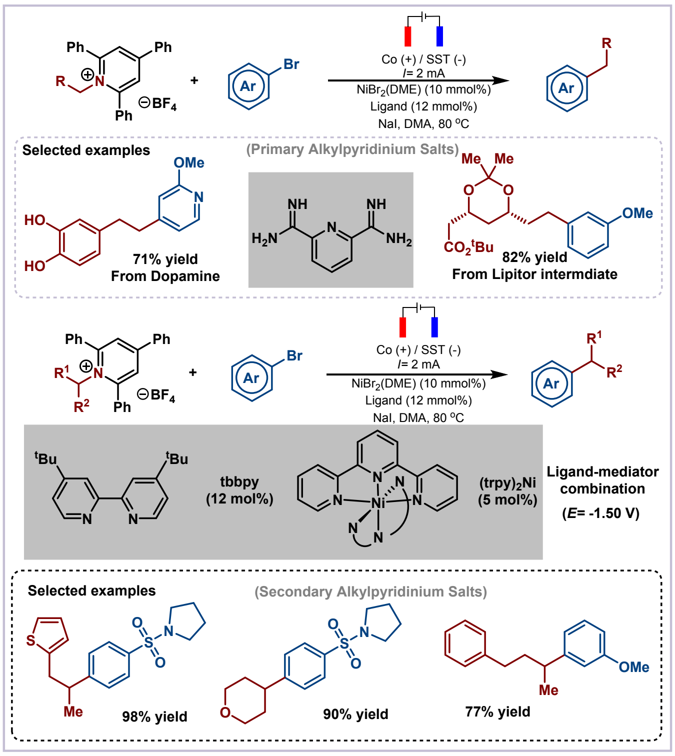

Scheme 20. Nickel-catalyzed electroreductive coupling of Katritzky salts with aryl halides

In 2023, the first electroreductive couplings of alkylpyridinium salts with aryl bromides, leveraging state-of-the-art high-throughput experimentation (HTE) for electrochemical reaction development was disclosed by Sevov, Watson, and Kalyani (Scheme 20).[39] First, the author optimized the conditions with the help of high-throughput technology and determined that such telescoped methods are effective to leverage the amine building blocks for library synthesis in the context of medicinal chemistry applications (over 50 drug examples). Second, they embarked on the elucidation of scope and generality of the electrochemical reductive cross-coupling by surveying the reaction of alkylpyridinium salt with diverse aryl- and heteroaryl bromides, furnishing the desired products in good to excellent isolated yields. Next, they re-optimized conditions for reactions of secondary alkylpyridinium salts detailly and the ligand-mediators were found to be critical to achieving high product yields. Finally, the author conducted a multidimensional library synthesis of 48 distinct products via the reductive cross-coupling of 6 aryl bromides against 4 primary and 4 secondary alkylpyridinium salts using HTE-Chem. Excitingly, microscale HTE further demonstrated the synthetic value of this method by enabling the efficient construction of extensive libraries of cross-coupled products, a key advantage for material-sparing discovery in medicinal chemistry, and this strategy highlights the power of HTE technologies for enabling new pharmaceutically relevant electrochemical transformations that provide complementary efficiency or chemical space access to their nonelectrochemical counterparts.

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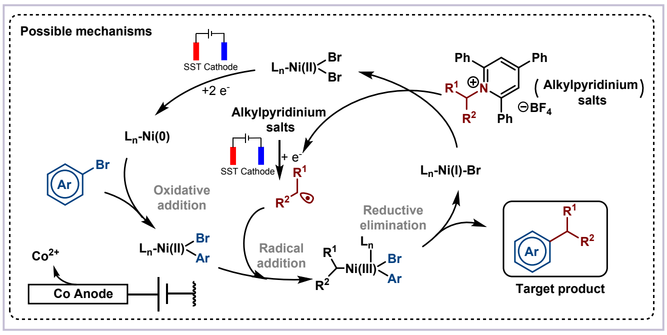
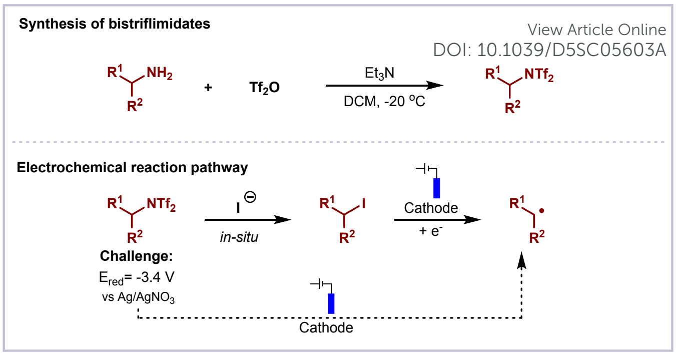


Scheme 21. Proposed mechanism

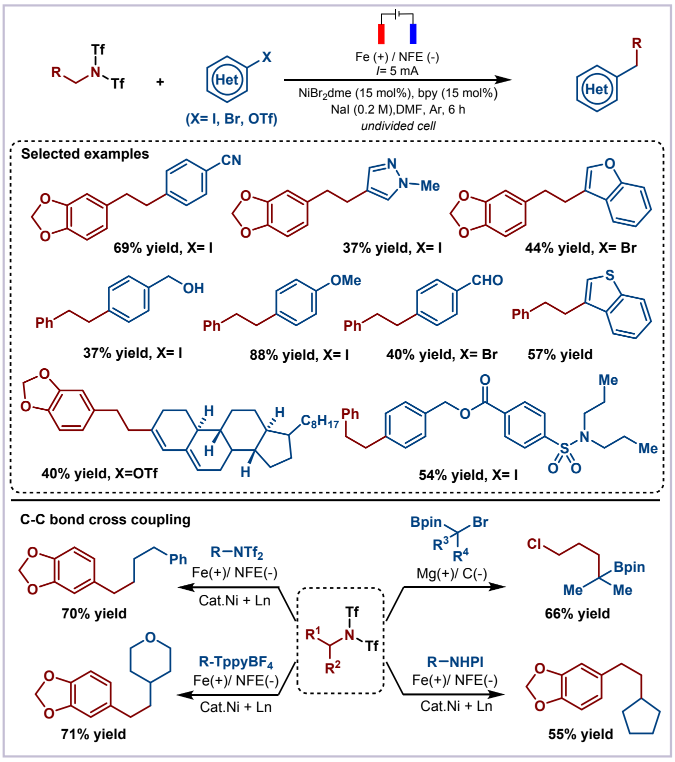
As shown in Scheme 21, the proposed mechanism starts with the formation of an carbon radical by single-electron transfer (SET) from the excited state of SST cathode to the alkylpyridinium salts, or alkylpyridinium salts oxidise the Ni(I) reactive species to obtain the corresponding carbon radical intermediates and Ni(II) intermediates, which are cathodically reduced to Ni(0) intermediates, and then oxidatively adducted with bromobenzene to obtain the Br-Ni(II)-Ar intermediates, which trap free carbon radicals to form the unstable Ni(III) intermediates and undergo a rapid reductive elimination, resulting in C(sp^2)–C(sp^3) coupling products and Ni(I) reactive species. Notably, this one-step paired electrolysis can avoid the isolation of frequently toxic alkyl halides, and the use of stoichiometric Zn, Mg or Mn in reductive cross-couplings. Regarding substrate generality, this methodology demonstrates broad applicability across three key dimensions: i) facilitating coupling reactions between diverse primary/secondary amines and aryl bromides, ii) enabling efficient synthesis of structurally complex natural product derivatives, and iii) permitting precise modifications of pharmacologically active scaffolds. The protocol exhibits moderate to excellent functional group compatibility while maintaining satisfactory stereochemical control.

5. Electrosynthetic deamination via bistriflimidates

Although bistriflimidates could be readily synthesized on a gram scale using amines and trifluoromethanesulfonic anhydride as starting materials, with triethylamine as the base and dichloromethane as the solvent at -20°C, its direct electrochemical transformation via cathodic reduction presents a significant challenge. This difficulty arises from its exceptionally high reduction potential (E_{red}= -3.4 V *vs* Ag/AgNO$_3$), which prevents direct radical generation.[40] Consequently, the electrochemical pathway for bistriflimidates involves a two-step sequence: (i) priority conversion to the corresponding alkyl iodide (E_{red} = -3.1 V *vs* Ag/AgNO$_3$), and (ii) subsequent cathodic reduction of alkyl iodide to generate the target radical species for further reaction (Scheme 22).



Scheme 22. The reaction pathway of bistriflimidates



Scheme 23. Eelectrochemical C-C bond coupling of alkyl bistriflimides with aryl halides

In 2024, Wang and Hong collaborated to develop a new alkyl bistriflimides reagent, which were unprecedentedly employed for C-N bond activation (Scheme 23).[41] Alkyl amines are efficiently converted to alkyl bistriflimides via trifluoromethanesulfonic anhydride, serving as superior electrophiles over traditional Katritzky salts or redox-active imines. This replaces toxic stoichiometric metal reductants (e.g., Mn, Zn) with electricity, aligning with green chemistry principles. The methodology enables diverse C(sp^3)-C(sp^3) and C(sp^3)-C(sp^2) bond formations with broad compatibility. It couples alkyl bistriflimides with alkyl halides, aryl/heteroaryl halides, alkenyl triflates, Katritzky salts and NHPI esters, achieving moderate to excellent yields. The broad substrate scope, excellent functional group tolerance, and mild reaction conditions collectively underscore the practicality and effectiveness of this methodology. Beyond expanding the toolbox for C-C bond construction, this work establishes a sustainable strategy for employing amine-derived precursors in organic synthesis.

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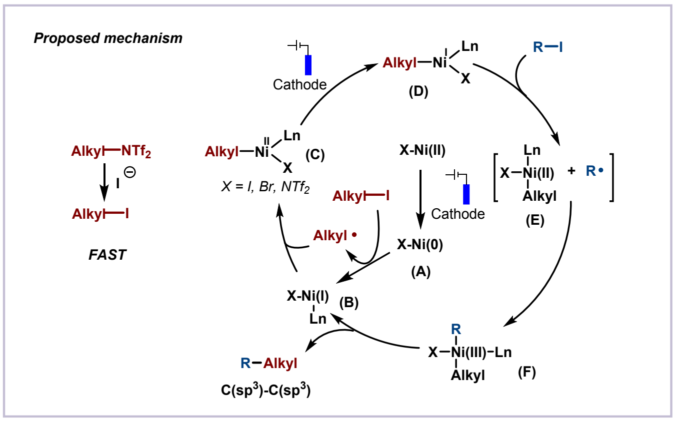
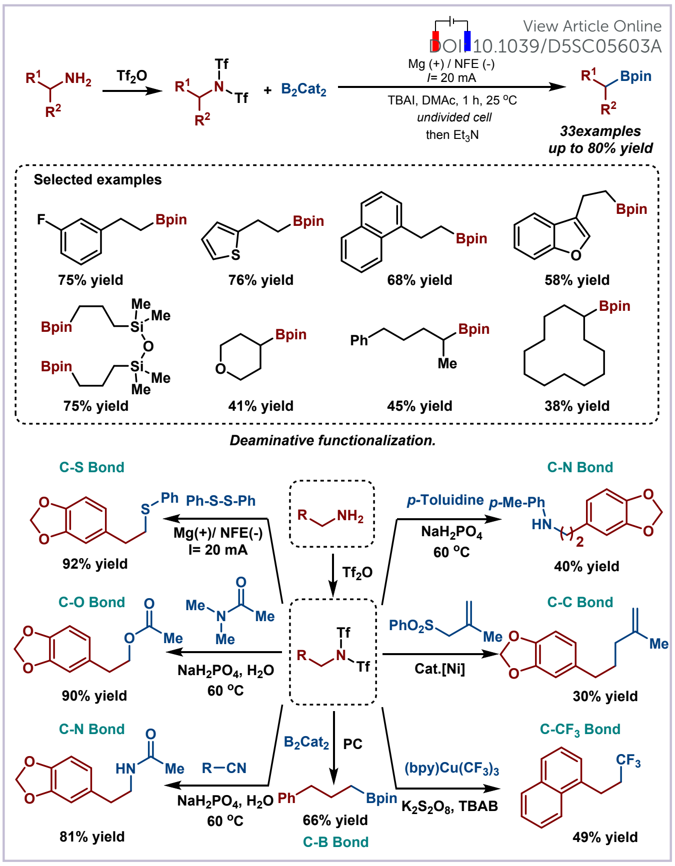


Scheme 24. Proposed mechanism

This approach avoids stoichiometric oxidants, expensive catalysts (e.g., Pd, Ru) and neutral by-product interference. Reactions proceed at room temperature under constant current (5 mA) using inexpensive electrodes (Mg anode/Ni foam cathode) and NaI as a critical electrolyte. Alkyl bistriflimides react rapidly via an S_N2 mechanism to generate key alkyl iodide intermediates in the presence of iodide ions. The proposed catalyst pathway initiates with the electrochemical reduction of Ni(II) to generate a low-valent Ni(0) species **A**. This Ni(0) complex subsequently undergoes single-electron transfer (SET) with alkyl iodides, yielding alkyl radicals while oxidizing to Ni(I) species **B**. Species **B** participates in radical addition to form alkyl-Ni(II) intermediate **C**. **A** second electroreduction event then reduces **C** to Ni(I) species **D**. Crucially, **D** engages in oxidative addition with an additional halide substrate, forming Ni(III) species **F**. The cycle concludes with reductive elimination from **F**, releasing the C(sp^3)-C(sp^3) cross-coupled product and regenerating the Ni(I) catalyst (Scheme 24).

Later, the same groups demonstrated that the more efficient C-B bond cross-coupling reaction could be extended to alkyl bistriimidate and B_2cat_2.[40] After detailed investigations, the author found that the desired alkyl boronate 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. This protocol exhibited good efficiency toward the borylation of alkyl bistriimidates, showcasing wide functional tolerance and generated borylation products in moderate to high yields. Notably, the reaction time only requires 1 hour. In addition to C-B bond formations through electrosynthesis, subsequent interception by various nucleophiles provides the remote C-C, C-S, C-O, and C-N bond formation products, and bistriimidates have also been explored as radical initiates to allow the regioselective cleavage of C-N bonds and the preparation of trifluoromethylated derivatives in the presence of $CuCF_3$. The author proposed this strategy features an undivided cell without the use of transition metal- or photo-catalysts and exhibits high conversion and stability in flow reactors (Scheme 25).



Scheme 25. Eelectrochemical C-B bond coupling of alkyl bistriflimides with B_2cat_2

6. Electrosynthetic deamination via other nitrogen sources

Apart from the above-mentioned deoxygenation reagents, other nitrogen sources (such as quaternary ammonium salts, amides) have made significant contributions in the field of electrochemical deoxygenation functionalization.

In 2019, Manthiram and co-workers provides a new design strategy for electrochemical carboxylation which utilizes the benzyltrimethylammonium bromide intermediate as a substrate for carboxylation (Scheme 26).[42] The optimized conditions called for reaction in an undivided cell with a Pt anode and a C cathode in the presence of benzylammonium salt (0.15 mmol), CO_2 bubbling, and $^nBu_4PBF_4$ as electrolyte in DMF (0.1 M) electrolysis of -4.5 V cell voltage at room temperature for 4 h. Compared to previous transition-metal-catalyzed carboxylations, this electrochemical method avoid using stoichiometric metals as reducing agents. By employing trimethylamine (in situ generated from the substrate) as an anodically oxidizable sacrificial agent, this method avoids traditional sacrificial anodes while achieving high current efficiency, suppressed overoxidation, and broader substrate compatibility. The proposed mechanism involves concurrent electrode processes: cathodic reduction of ammonium salt generates benzyl radical **INT-I**, which undergoes further reduction to anion **INT-II** followed by carboxylation to 2-phenylacetate **INT-III**. Simultaneously, trimethylamine **INT-IV**

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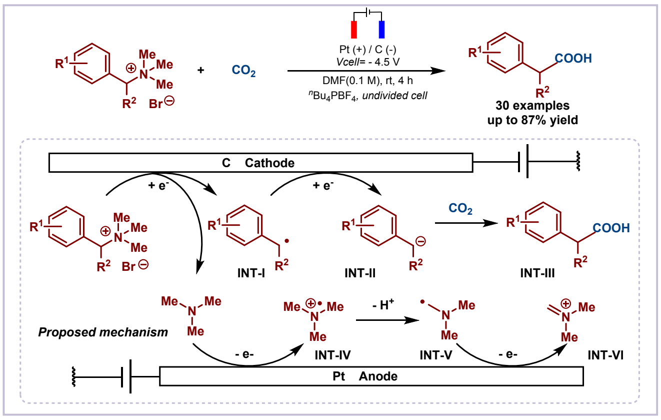
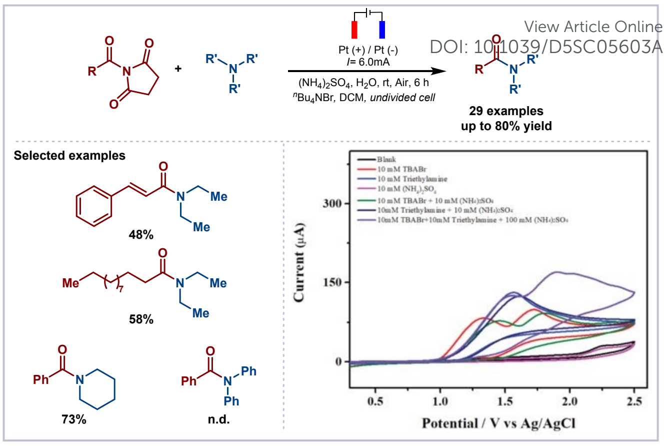
liberated through reductive C-N cleavage diffuses to the anode, oxidizing to radical cation **INT-V**, eventually further loses electrons to form iminium cation **INT-VI**. Taken together, this method proceeds through C-N bond cleavage and subsequent CO_2 insertion, eliminating the need for stoichiometric metal reductants, sacrificial anodes, or purification by column chromatography. Both primary and secondary benzylammonium substrates were carboxylated with high selectivity and afforded products in moderate to excellent yields. The reaction also demonstrated excellent functional group tolerance. Given its user-friendly nature, this system holds promise for application in the synthesis of diverse aliphatic carboxylic acids and dicarboxylic acids.

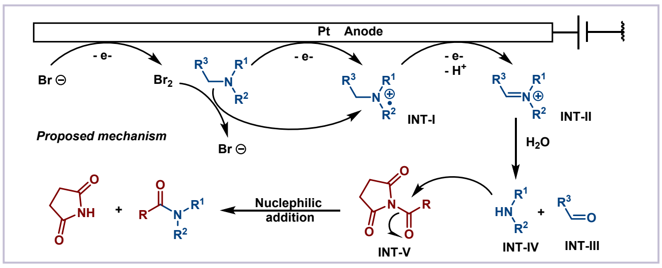


Scheme 26. Electrochemical carboxylation of benzylic C-N bonds with CO_2

Wang and Luo have developed a novel and efficient electrochemical oxidative transamidation of tertiary amines with N-acyl imides, offering advantages over traditional metal catalysis or emerging visible light catalysis by eliminating the need for metal catalysts and oxidants.[43] After extensive optimization, $^nBu_4NBr$ as the supporting electrolyte, $(NH_4)_2SO_4$ as an additive, and DCM/ H_2O as the effective solvent system furnished the desired product by employing a constant current of 6 mA between Pt (anode) and Pt (cathode) over 6 hours at room temperature in an undivided cell. The reaction proceeded smoothly to generate the desired transamidation products under transition metal-free and photocatalyst-free conditions with good functional group compatibility (including alkyl, halogen, alkene and heteroaromatic-ring-based N-acyl-imides) in moderate to good yields. Unfortunately, triarylamine cannot serve as an ideal nitrogen source to complete the conversion under these conditions (Scheme 27).



Scheme 27. Electrochemical oxidative transamidation of tertiary amines with *N*-acyl imides



Scheme 28. Proposed mechanism

Moreover, cyclic voltammetry (CV) analysis under standard conditions produced oxidation peaks at +1.29 V, +1.57 V, +1.75 V *vs* Ag/AgCl, indicating bromine anions are first oxidized to molecular bromine and then involved in the oxidation of triethylamine. The mechanism commences with anodic bromide oxidation generating Br_2, which migrates to the organic phase oxidizing trimethylamine to intermediate **INT-I** while regenerating Br^- to sustain a catalytic bromine cycle. Concurrently, trimethylamine undergoes direct anodic oxidation via single-electron transfer and α-hydrogen loss at the tertiary amine center to yield **INT-I**. This intermediate sequentially transforms into unstable iminium ion **INT-II**, which undergoes hydrolytic fragmentation to aldehyde **INT-III** and secondary amine **INT-IV**. Finally, nucleophilic attack by **INT-IV** on activated tertiary amide **INT-V**, followed by N-deprotection, furnishes transamidation product. It presents a novel approach for the cleavage and conversion of C-N bonds, with the potential to pave the way for the design and improvement of synthetic pathways (Scheme 28).

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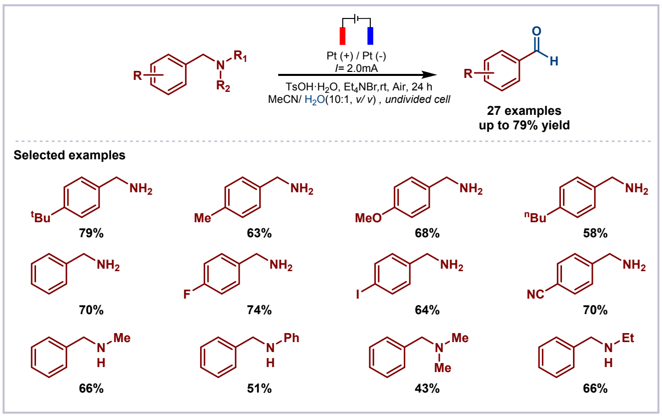
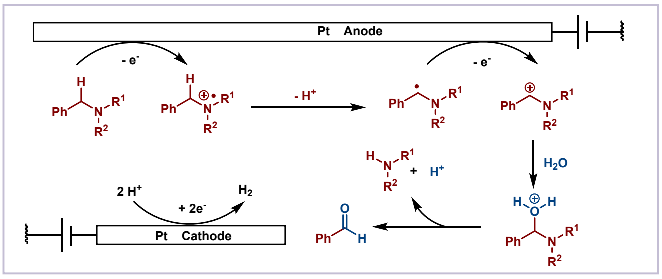


Scheme 29. Electrochemical selective oxidative cleavage of benzyl C-N bond



Scheme 30. Proposed mechanism

Apart from the above reports, an uncommon efficient electrochemical method for the oxidative cleavage of C-N bonds under mild conditions using water as the oxygen source was furnished by Liu and Xia (Scheme 29).[44] The optimized reaction conditions includ Et_4NBr as the electrolyte, a 10: 1 (*v/v*) mixture of MeOH/ H_2O as the effective solvent system, a constant current of 2.0 mA and duration of 24 h in an undivided cell setup assembly with Pt as the anode and cathode. With the optimal conditions in hand, the substrate scope of this protocol was investigated, the author found that benzylamines bearing electron-donating groups and electron-withdrawing groups at the para position of the benzene ring are converted to the corresponding aldehyde compounds with moderate to good yields. Additionally, disubstituted benzylamines, *N*-substituted and *N, N*-disubstituted benzylamines also tolerate this transformation to afford the corresponding compounds. In order to further explore the reaction mechanism, butylhydroxytoluene (BHT) was added under standard conditions, the yield of the product was significantly reduced, which implied the possible involvement of radical species in the reaction. In CV analysis, the addition of TsOH·H_2O and H_2O was able to cause a significant emergent oxidation peak at +3.2 V, proving that the reaction could proceed via the oxidation of benzylamine. The transformation mechanistically involves a single-electron transfer (SET) between benzylamine salts and an in situ generated nitrogen radical cation. This initiates concurrent deprotonation and radical 1,2-migration to afford an *α*-aminoalkyl radical intermediate. Subsequent anodic oxidation of this radical generates a benzyl cation, which undergoes nucleophilic trapping by H_2O. TsOH·H_2O-mediated dissociation of the resulting aminol liberates the target carbonyl product (Scheme 30).

7. Conclusions and perspectives

Radical reactions are the heart of modern synthetic chemistry. The generation of radicals via electrochemical strategies is efficient and mild, compared with the traditional methods with the use of stoichiometric chemical oxidants or reductants. However, many aspects of the electrosynthesis deamination functionalization via C-N bond cleavage and radical formation are still not purely understood and still far from being well developed. The discussion of electrosynthesis deamination functionalization reaction, in particular, the electro-redox generation of radical intermediates from redox-active amines and the subsequent reactions, as well as the reaction mechanism have been presented in this review.

Despite significant advancements and achievements being made in this area, there is still room for further exploration, which is mentioned as follows; (a) Electrochemical construction of diverse C-Y (e.g., C-Si, C-P, C-N_3) bonds based on redox-active amines and established reaction types would undoubtedly expand the research horizon in this area. (b) Develop and explore the deamination properties and electrochemical applications of new deamination reagents reagents, such as imines, amides, azo, azide. (c) There are no reports on chiral control through redox-active amines using electrochemistry. (d) The electrochemical three-component reaction using redox-active amines as a radical precursor are underexplored. (e) The reports involving direct electrochemical deamination of amines are scanty. Overall, we believe that the electrosynthesis deamination functionalization will play a major role in complementing the growing repertoire of residuespecific modifications and bioconjugation approaches which are driving innovation in organic synthesis, medicinal chemistry, and chemical biology in the next future, and hope this review will receive significant attention and contribute to further achievement on this topic.

Author Contributions

Investigation, J. D. ,Y. S and W. C.; writing- review & editing, Z. Z.; supervision, W. Z. and Y. W.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (a) P. Ruiz-Castillo and S. L. Buchwald, Applications of palladium-catalyzed C–N cross-coupling reactions, *Chem. Rev.* 2016, **116**, 12564−12649. (b) B. Alcaide, P. Almendros and C. Aragoncillo, β-Lactams: Versatile building blocks for the stereoselective synthesis of non-β-Lactam products, *Chem. Rev.*, 2007, **107**, 4437–4492. (c) H. Lin, S. Liu, Q. Li, Q. Zhang, L. Yang, T. Wang and J. Luo, Electrochemical oxidative transamidation of tertiary amines with N-acyl imides to access amide compounds, *Synth. Commun.*, 2023, **53**, 1412–1425. (d) Y. Liu and H. Ge, Site-selective C–H arylation of primary aliphatic amines enabled by a catalytic transient directing group, *Nature Chem*, 2017, **9**, 26–32. (d) V. R. Pattabiraman, Rethinking amide bond synthesis. *Nature* 2011, 480, 471–479.

2 C. Ghiazza, T. Faber, A. Gómez-Palomino and J. Cornella, Deaminative chlorination of aminoheterocycles, *Nat. Chem.*, 2022, **14**, 78–84.

3 (a) A. Roglans, A. Pla-Quintana and M. Moreno-Mañas, Diazonium salts as substrates in palladium-catalyzed cross-coupling reactions, *Chem. Rev.*, 2006, **106**, 4622–4643. (b) E. F. V. Scriven and K. Turnbull, Azides: their preparation and synthetic uses, *Chem. Rev.*, 1988, **88**, 297–368. (c) Y. Su, X. Sun, G. Wu and N. Jiao, Catalyst-controlled highly selective coupling and oxygenation of olefins: a direct approach to alcohols, ketones, and diketones, *Angew Chem Int Ed*, 2013, **52**, 9808–9812. (d) F. Mo, G. Dong, Y. Zhang and J. Wang, Recent applications of arene diazonium salts in organic synthesis, *Org. Biomol. Chem.*, 2013, **11**, 1582.

4 (a) P.-K. C. Huang and E. M. Kosower, Properties of phenyldiimide, *J. Am. Chem. Soc.*, 1967, **89**, 3910–3911. (b) T. Jiang, S.-Y. Chen, G.-Y. Zhang, R.-S. Zeng, J.-P. Zou, CoPc-catalyzed selective radical arylation of anilines with arylhydrazines for synthesis of 2-aminobiaryls, *Org. Biomol. Chem.* 2014, **12**, 6922. (c) P. Chauhan, M. Ravi, S. Singh, K. S. Raju, V. Bajpai, B. Kumar, P. P. Yadav, Palladium and copper-catalyzed ligand-free coupling of phenylhydrazines in water, *RSC Adv.* 2014, **4**, 43336. (d) J.-B. Liu, F.-J. Chen, N. Liu, J. Hu, Palladium-catalyzed Heck coupling of arylhydrazines via C–$NHNH_2$ bond activation, *RSC Adv.* 2015, **5**, 45843.

5 (a) Y. Pang, D. Moser and J. Cornella, Pyrylium salts: selective reagents for the activation of primary amino groups in organic synthesis, *Synthesis*. 2019, **51**, A-O. (b) O. A. Tikhanova, D. I. Bugaenko and A. V. Karchava, Recent progress in functionalization of the pyridine ring through C−S bond formation under transition metal catalyst free conditions, *Adv Synth Catal*, 2024, **366**, 1467–1483. (c) B. Saxena, R. I. Patel and A. Sharma, Recent advances in electron donor-acceptor (EDA)-complex reactions involving quaternary pyridinium derivatives, *Adv Synth Catal*, 2023, **365**, 1538–1564.

6 (a) Wang Y., Li F. and Zeng Q., Advances in formation of C-X bonds via cleavage of C-N bond of quaternary ammonium salts, *Acta Chim. Sinica*, 2022, **80**, 386. (b)T. Ikeda, T. Masuda, M. Takayama, H. Adachi and T. Haino, Solvent-induced emission of organogels based on tris(phenylisoxazolyl)benzene, *Org. Biomol. Chem.*, 2016, **14**, 36–39. (c) H. Ogawa, Z.-K. Yang, H. Minami, K. Kojima, T. Saito, C. Wang and M. Uchiyama, Revisitation of organoaluminum reagents affords a versatile protocol for C–X (X = N, O, F) bond-cleavage cross-coupling: a systematic study, *ACS Catal.*, 2017, **7**, 3988–3994.

7 (a) R. Francke and R. D. Little, Redox catalysis in organic electrosynthesis: basic principles and recent developments, *Chem. Soc. Rev.*, 2014, **43**, 2492. (b) E. J. Horn, B. R. Rosen and P. S. Baran, Synthetic organic electrochemistry: an enabling and innately sustainable method, *ACS Cent. Sci.*, 2016, **2**, 302–308. (c) C. Sandford, M. A. Edwards, K. J. Klunder, D. P. Hickey, M. Li, K. Barman, M. S. Sigman, H. S. White and S. D. Minteer, A synthetic chemist's guide to electroanalytical tools for studying reaction mechanisms, *Chem. Sci.*, 2019, **10**, 6404–6422. (d) H. Mei, R. Pajkert, L. Wang, Z. Li, G.-V. Röschenthaler and J. Han, Chemistry of electrochemical oxidative reactions of sulfinate salts, *Green Chem.*, 2020, **22**, 3028–3059. (e) K.-J. Jiao, Y.-K. Xing, Q.-L. Yang, H. Qiu and T.-S. Mei, Site-selective C–H functionalization via synergistic use of electrochemistry and transition metal catalysis, *Acc. Chem. Res.*, 2020, **53**, 300–310. (f) Z. Zou, W. Zhang, Y. Wang and Y. Pan, Recent advances in electrochemically driven radical fluorination and fluoroalkylation, *Org. Chem. Front.*, 2021, **8**, 2786–2798. (g) Y. Wang, J. Xu, Y. Pan and Y. Wang, Recent advances in electrochemical deoxygenation reactions of organic compounds, *Org. Biomol. Chem.*, 2023, **21**, 1121–1133.

8 (a) G. Hilt, Convergent paired electrolysis for the three-component synthesis of protected homoallylic alcohols, *Angew. Chem. Int. Ed.*, 2003, **42**, 1720–1721. (b) L. Zhang and X. Hu, Nickel catalysis enables convergent paired electrolysis for direct arylation of benzylic C–H bonds, *Chem. Sci.*, 2020, **11**, 10786–10791. (c) S. Rodrigo, C. Um, J. C. Mixdorf, D. Gunasekera, H. M. Nguyen and L. Luo, Alternating current electrolysis for organic electrosynthesis: trifluoromethylation of (hetero)arenes, *Org. Lett.*, 2020, **22**, 6719–6723. (d) Z. Li, W. Sun, X. Wang, L. Li, Y. Zhang and C. Li, Electrochemically Enabled, Nickel-catalyzed dehydroxylative cross-coupling of alcohols with aryl halides, *J. Am. Chem. Soc.*, 2021, **143**, 3536–3543. (e) Z. Zou, H. Li, M. Huang, W. Zhang, S. Zhi, Y. Wang and Y. Pan, Electrochemical-promoted nickel-catalyzed oxidative fluoroalkylation of aryl iodides, *Org. Lett.*, 2021, **23**, 8252–8256.

9 S. Smołka and K. Krukiewicz, Catalyst design through grafting of diazonium salts—a critical review on catalyst stability, *Int. J. Mol. Sci.*, 2023, **24**, 12575.

10 Griefs, P. Vorläufige Notiz über die Einwirkung von salpetriger Säure auf Amidinitro- und Aminitrophenylsäure. *Justus Liebigs Ann. Chem.* 1858, **106**, 123−125.

View Article Online
DOI: 10.1039/D5SC05603A

11 (a) T. Sandmeyer, Ueber die ersetzung der amidgruppe durch chlor in den aromatischen substanzen, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 1633–1635. (b) T. Sandmeyer, Ueber die ersetzung der amid-gruppe durch Chlor, brom und xyan in den aromatischen substanzen, *Ber. Dtsch. Chem. Ges.*, 1884, **17**, 2650–2653.

12 R. Pschorr, Neue synthese des phenanthrens und seiner Derivate, *Ber. Dtsch. Chem. Ges.*, 1896, **29**, 496–501.

13 M. Gomberg and W. E. Bachmann, The syhthesis of biaryl compounds by means of the diazo reaction, *J. Am. Chem. Soc.*, 1924, **46**, 2339–2343.

14 G. Balz and G. Schiemann, Über aromatische fluorverbindungen, I.: ein neues verfahren zu ihrer darstellung, *Ber. dtsch. Chem. Ges. A/B*, 1927, **60**, 1186–1190.

15 H. Meerwein, E. Büchner and K. Van Emster, Über die einwirkung aromatischer diazoverbindungen auf *α, β*-ungesättigte carbonylverbindungen, *J. Prakt. Chem.*, 1939, **152**, 237–266.

16 F. Mo, D. Qiu, L. Zhang and J. Wang, Recent development of aryl diazonium chemistry for the derivatization of aromatic compounds, *Chem. Rev.*, 2021, **121**, 5741–5829.

17 F. F. Gadallah and R. M. Elofson, Arylation of aromatic compounds by electrochemical reduction of benzenediazonium tetrafluoroborate in aprotic solvents, *J. Org. Chem.*, 1969, **34**, 3335–3338.

18 D. Hata, M. Tobisu and T. Amaya, Electrolytic cross-coupling of arenediazonium salts and heteroarenes, *Bull. Chem. Soc. Jpn.*, 2018, **91**, 1749–1751.

19 P. Wang, Z. Yang, Z. Wang, C. Xu, L. Huang, S. Wang, H. Zhang and A. Lei, Electrochemical arylation of electron-deficient arenes through reductive activation, *Angew Chem Int Ed*, 2019, **58**, 15747–15751.

20 Y. Jiang, G. Dou, L. Zhang, K. Xu, R. D. Little and C. Zeng, Electrochemical cross-coupling of C(sp2)–H with aryldiazonium salts via a paired electrolysis: an alternative to visible light photoredox-based approach. *Adv. Synth. Catal*. 2019, **361**, 5170 – 5175.

21 P. Zhou, Y. Liu, Y. Xu and D. Wang, Electrochemical synthesis for *α*-arylation of ketones using enol acetates and aryl diazonium salts, *Org. Chem. Front.*, 2022, **9**, 2215–2219.

22 B. K. Malviya, K. Singh, P. K. Jaiswal, M. Karnatak, V. P. Verma, S. S. Badsara and S. Sharma, Catalyst-free synthesis of phenanthridines via electrochemical coupling of 2-isocyanobiphenyls and amines, *New J. Chem.*, 2021, **45**, 6367–6378.

23 L. Gattermann and A. Cantzler, Zur kenntniss der aromatischen Isocyanate, *Ber. Dtsch. Chem. Ges.*, 1892, **25**, 1086–1091.

24 M. P. Doyle, J. F. Dellaria, B. Siegfried and S. W. Bishop, Reductive deamination of arylamines by alkyl nitrites in N, N-dimethylformamide. A direct conversion of arylamines to aromatic hydrocarbons, *J. Org. Chem.*, 1977, **42**, 3494–3498.

25 C. P. Beletskaya, A. S. Sigeev, A. S. Peregudov and P. V. Petrovskii, Catalytic sandmeyer bromination, *Synthesis 2007, **16**, 2534–2538*.

26 D. A. Leas, Y. Dong, J. L. Vennerstrom and D. E. Stack, One-pot, metal-free conversion of anilines to aryl bromides and iodides, *Org. Lett.*, 2017, **19**, 2518–2521.

27 Q. Liu, B. Sun, Z. Liu, Y. Kao, B.-W. Dong, S.-D. Jiang, F. Li, G. Liu, Y. Yang and F. Mo, A general electrochemical strategy for the sandmeyer reaction, *Chem. Sci.*, 2018, **9**, 8731–8737.

28 H. Goljani, Z. Tavakkoli, A. Sadatnabi and D. Nematollahi, Two-Phase Electrochemical generation of aryldiazonium salts: application in electrogenerated copper-catalyzed sandmeyer reactions, *Org. Lett.*, 2020, **22**, 5920–5924.

29 S. Song, X. Shi, Y. Zhu, Q. Ren, P. Zhou, J. Zhou and J. Li, Electrochemical oxidative C–H arylation of quinoxalin(on)es with arylhydrazine hydrochlorides under mild conditions, *J. Org. Chem.*, 2022, **87**, 4764–4776.

30 Y. Yu, P. Zheng, Y. Wu and X. Ye, Electrochemical cobalt-catalyzed C–H or N–H oxidation: a facile route to synthesis of substituted oxindoles, *Org. Biomol. Chem.*, 2018, **16**, 8917–8921.

31 Y. Wu, L. Zeng, H. Li, Y. Cao, J. Hu, M. Xu, R. Shi, H. Yi and A. Lei, Electrochemical palladium-catalyzed oxidative sonogashira carbonylation of arylhydrazines and alkynes to ynones, *J. Am. Chem. Soc.*, 2021, **143**, 12460–12466.

32 H. Zhang, T. Wang, K. Xu and C. Zeng, N-Hydroxyphthalimide-mediated electrochemical denitrogenation of aroylhydrazides to generate acyl radicals and their applications in the syntheses of fluorenones, *J. Org. Chem.*, 2021, **86**, 16171–16176.

33 T. Alam, A. Rakshit, H. N. Dhara, A. Palai and B. K. Patel, Electrochemical amidation: benzoyl hydrazine/carbazate and amine as coupling partners, *Org. Lett.*, 2022, **24**, 6619–6624.

34 Y. Gao, G. Wu, L. Yu, Y. Wang, Y. Pan, Alkyl carbazates for electrochemical deoxygenative functionalization of heteroarenes, *Angew Chem Int Ed*, 2020, **59**, 10859-110863.

35 J. Xu, Y. Liu, Q. Wang, X. Tao, S. Ni, W. Zhang, L. Yu, Y. Pan and Y. Wang, Electrochemical deoxygenative amination of stabilized alkyl radicals from activated alcohols, *Nat Commun*, 2024, **15**, 6116.

36 B. Bapat and C. A. Ramsden, Pyridines as leaving groups in synthetic transformations: nucleophilic displacements of amino groups, and novel preparations of nitriles and isocyanates, *Tetrahedron Lett.*, 1976, **31**,2691-2694.

37 (a) F. T. Pulikottil, R. Pilli, R. V. Suku and R. Rasappan, Nickel-catalyzed cross-coupling of alkyl carboxylic acid derivatives with

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DOI: 10.1039/D5SC05603A

pyridinium salts via C–N bond cleavage, *Org. Lett.*, 2020, **22**, 2902–2907. (b) L. Zhang, D. Liang, Y. Wang, D. Li, J. Zhang, L. Wu, M. Feng, F. Yi, L. Xu, L. Lei, Q. Du and X. Tang, Caged circular siRNAs for photomodulation of gene expression in cells and mice, *Chem. Sci.*, 2018, **9**, 44–51. (c) M. Ociepa, J. Turkowska and D. Gryko, Redox-activated amines in Csp3–Csp and Csp3–Csp2) bond formation enabled by metal-free photoredox Catalysis, *ACS Catal.*, 2018, **8**, 11362–11367. (d) H. Yue, C. Zhu, L. Shen, Q. Geng, K. J. Hock, T. Yuan, L. Cavallo and M. Rueping, Nickel-catalyzed C–N bond activation: activated primary amines as alkylating reagents in reductive cross-coupling, *Chem. Sci.*, 2019, **10**, 4430–4435.

38 Y. Liu, X. Tao, Y. Mao, X. Yuan, J. Qiu, L. Kong, S. Ni, K. Guo, Y. Wang and Y. Pan, Electrochemical C–N bond activation for deaminative reductive coupling of Katritzky salts, *Nat Commun*, 2021, **12**, 6745.

39 J. Fu, W. Lundy, R. Chowdhury, J. C. Twitty, L. P. Dinh, J. Sampson, Y. Lam, C. S. Sevov, M. P. Watson and D. Kalyani, Nickel-catalyzed electroreductive coupling of alkylpyridinium salts and aryl halides, *ACS Catal.*, 2023, **13**, 9336–9345.

40 H. Shu, X. Tao, S. Ni, J. Liu, J. Xu, Y. Pan and Y. Wang, Alkyl bistriflimidate-mediated electrochemical deaminative functionalization, *Chem. Sci.*, 2025, **16**, 2682–2689.

41 X. Tao, W. Lee, Z. Xu, H. Shu, Q. Wang, S. Ni, Y. Pan, S. Hong and Y. Wang, Reductive deaminative cross-coupling of alkyl bistriflimides enabled by electrocatalysis, *Sci. Adv.*, 2024, **10**, eads5410.

42 D.-T. Yang, M. Zhu, Z. J. Schiffer, K. Williams, X. Song, X. Liu and K. Manthiram, Direct electrochemical carboxylation of benzylic C–N bonds with carbon dioxide, *ACS Catal.*, 2019, **9**, 4699–4705.

43 H. Lin, S. Liu, Q. Li, Q. Zhang, L. Yang, T. Wang and J. Luo, Electrochemical oxidative transamidation of tertiary amines with N-acyl imides to access amide compounds, *Synth. Commun.*, 2023, **53**, 1412–1425.

44 J. Huang, X. Li, P. Liu, Y. Wei, S. Liu and X. Ma, Selective oxidative cleavage of benzyl C–N bond under metal-free electrochemical conditions, *Molecules*, 2024, **29**, 2851.

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DOI: 10.1039/D5SC05603A

Data Availability Statement

This study did not generate any new datasets. All data analyzed are from publicly available sources, as cited in the manuscript.