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Green advancements towards the electrochemical synthesis of heterocycles

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Heterocyclic chemistry is a large field with diverse applications in the areas of biological research and pharmaceutical advancement. Numerous initiatives have been proposed to further enhance the reaction conditions to reach these compounds without using harmful compounds. This paper focuses on the recent advances in the eco-friendly and green synthetic procedures to synthesize N-, S-, and O-heterocycles. This approach demonstrates considerable potential in accessing such compounds while circumventing the need for stoichiometric quantities of oxidizing/reducing agents or catalysts containing precious metals. Merely employing catalytic quantities of these substances proves sufficient, thereby offering an optimal means of contributing to resource efficiency. Renewable electricity plays a crucial role in generating environmentally friendly electrons (oxidant/reductant) that serve as catalysts for a series of reactions. These reactions involve the production of reactive intermediates, which in turn allow the synthesis of new chemical bonds, enabling beneficial transformations to occur. Furthermore, the utilization of metals as active catalysts in electrochemical activation has been recognized as an effective approach for achieving selective functionalization. The aim of this review was to summarize the electrochemical synthetic procedures so that the undesirable side reactions can be considerably reduced and the practical potential range of the chemical reactions can be expanded significantly.

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Introduction

Significant progress in electrochemical engineering technology in the past thirty years has facilitated the creation of alternative approaches to mitigate and avoid the production of harmful pollutants that negatively impact the environment. Implementing this method in reality poses challenges, and it is more practical and achievable to utilize technologies that can reduce and transform pollutants into environmentally benign by products. This article explores different approaches to the electrosynthesis of heterocyclic molecules. Electrochemical technologies have played a vital role in developing methods to remove harmful gasses such as carbon dioxide, nitrous oxides, and sulfur dioxide. This strategy effectively prevents energy waste and minimizes the release of greenhouse gas emissions.

The chemical sector makes a significant contribution to global pollution. In response to increasingly strict and strictly enforced environmental regulations, the chemical industry should adopt the following guidelines in the 21st century and beyond: (1) prioritize waste avoidance and minimization, (2) eliminate, recover, and recycle waste, (3) achieve environmentally acceptable and harmless waste disposal, (4) significantly reduce the generation of pollutants and energy consumption in the chemical process industry, without involving the combustion of fossil fuels, and (5) promote the generation and storage of clean energy.

Due to the immense applicability of the heterocyclic compounds, the synthesis and alteration of heterocyclic structures often takes place in conditions that may require the use of toxic substances such as acids or bases the requirement of high temperatures to generate the desired heterocyclic system. By utilizing the electron as a reactant, the need for further chemicals is eliminated, making the process of disposing, recycling, and recovering of treated solutions more straightforward. The broad versatility of electrochemical processes in both their electrosynthesis and elimination, recovery, recycling within the process industry stems from the fact that electrons can be easily removed by oxidation or reduction, unlike conventional chemicals. This can be accomplished by utilizing electrode materials that possess high resistance to oxidation or reduction and employing inert electrolytes that can tolerate electrode potentials ranging from +3 V to −3 V compared to the standard calomel electrode. Reduction may be achieved with a power that is equivalent to or superior to that of Na or Li-metals in amine solvents, and oxidations can be carried out at the chemical fluorine level. The electron is an inexpensive, versatile, and highly pure reagent. The use of electrons as reagents to induce

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chemical changes offers several advantages. Firstly, it is cost-competitive compared to alternative processes. Secondly, it allows for selective chemistry, meaning that specific reactions can be targeted. Thirdly, it has broad applicability, making it suitable for a wide range of reactions. Fourthly, it results in less pollution compared to most competing processes. Fifthly, it requires lower temperature conditions compared to equivalent techniques, especially those involving high temperatures. Sixthly, the involved equipment and operations are mainly simple and, if properly inexpensive or designed compared to conventional technologies. Lastly, the foremost electrochemical parameters, potential and current, are particularly compatible for data acquisition, process automation, and control.

Scientists have mostly focused their efforts on developing sustainable and environment friendly technologies that adhere to both economic and environmental constraints, by avoiding the use of harmful substances.[1] In the years to come, there shall be a growing interest in the utilization of organic electrochemical synthesis as a versatile and potent approach for constructing heterocyclic structures.[2–5] This method has demonstrated superior efficiency and selectivity compared to traditional synthetic methods. Moreover, it is worth to notice that the green methodologies involved in the electrosynthesis complies with nine out of the **12** principles of green chemistry, as depicted in Fig. 1. Agricultural chemicals, physiologically active natural organic compounds, and pharmaceuticals contain at least one heterocyclic ring.[6,7] Electricity-initiated biological transformations possess intrinsic sustainability and environmental benefits, as they only necessitate mild operating conditions.[8,9]

Nevertheless, there are certain apprehensions that arise when employing an electrochemical process in chemical transformations. One notable concern pertains to the necessity of possessing a comprehensive electrochemical apparatus, which is commonly associated with substantial expenses for both acquisition and operation. Moreover, the utilization of a supporting electrolyte is commonly employed to facilitate e-transfer in a solution. The selection of a suitable solvent for electrosynthesis can be a complex task due to the usage of poorly conductive solvents such as tetrahydrofuran and toluene. The electrochemical reactions involving the use of metal catalysts within easily accessible undivided cells are somewhat restricted because of its tendency to get readily reduced to zero-valent metals at the cathode. Additionally, when chemical and electrical reactions are conducted in split cells, the use of expensive ion exchange membranes becomes necessary in order to separate the negative and positive electrodes.[10] The use of an electrochemical process in chemical transformations raises

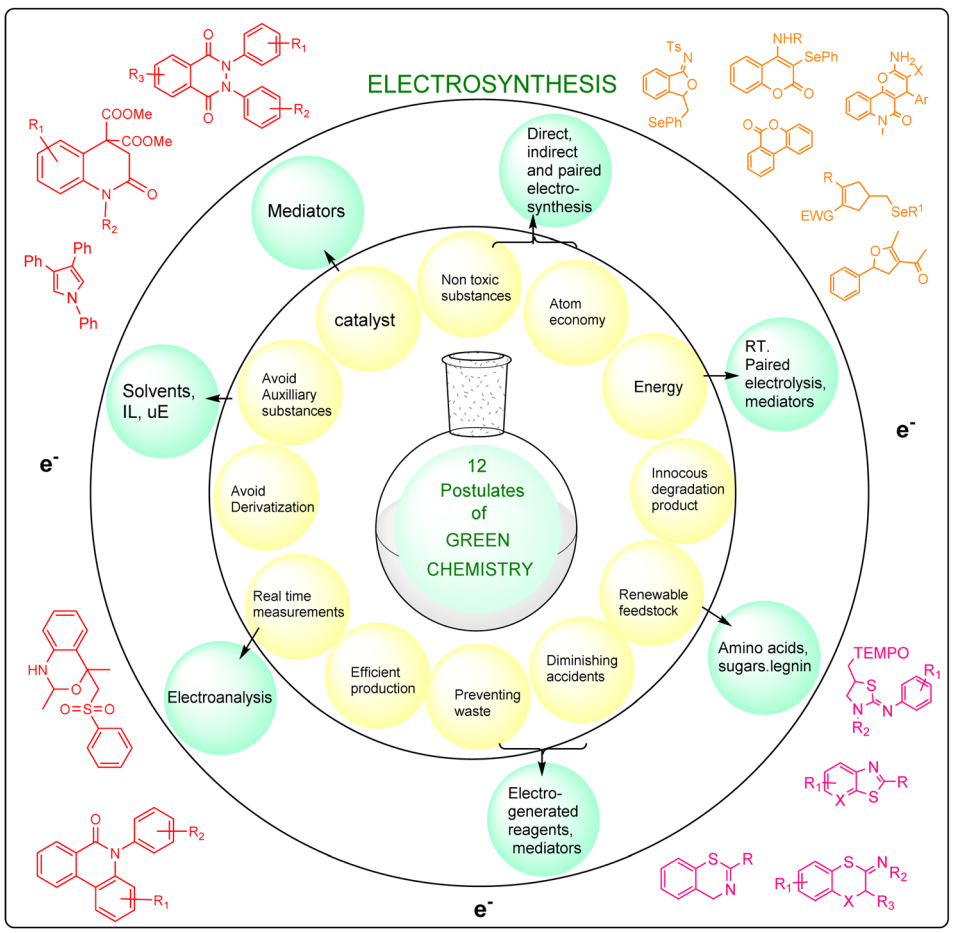
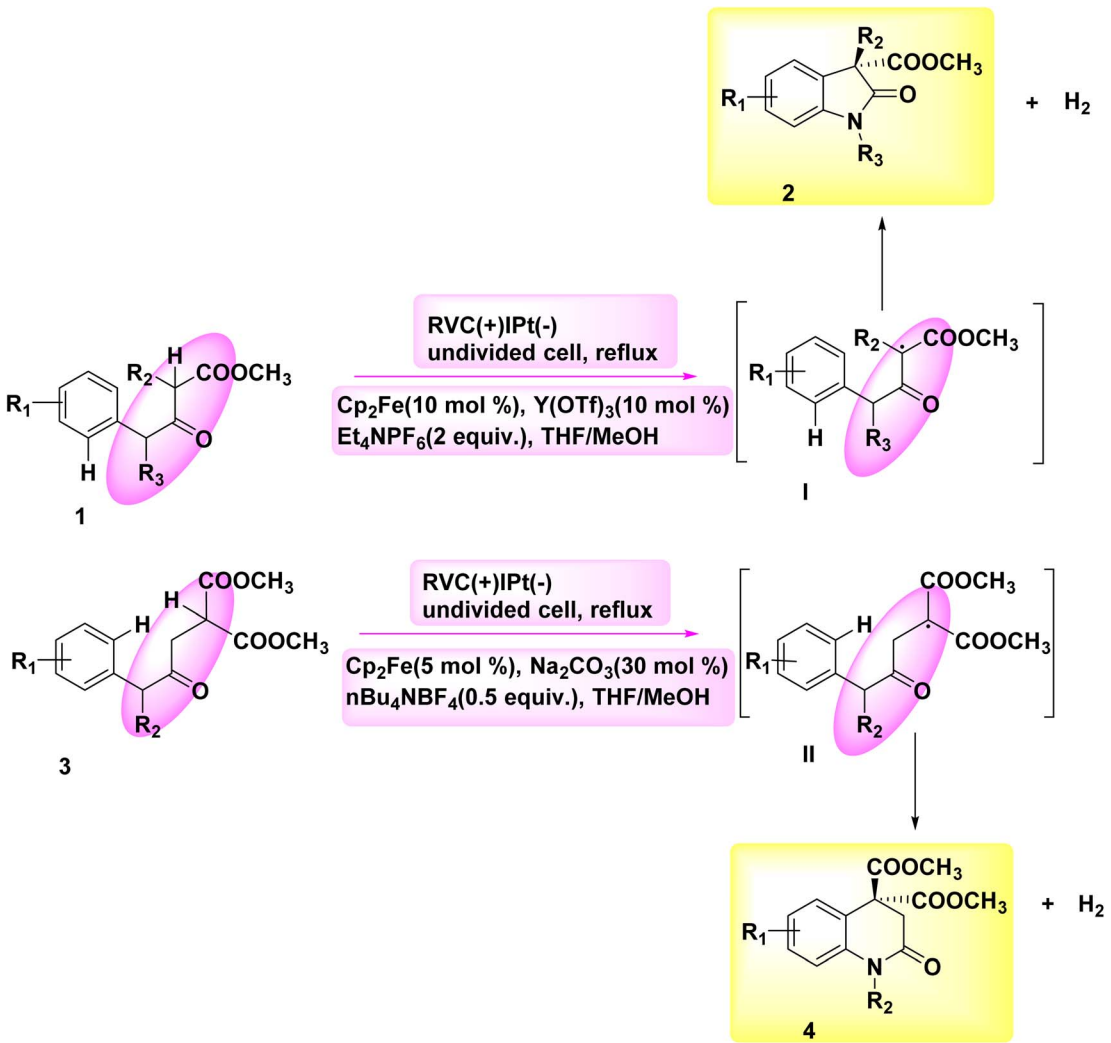


Fig. 1 Relationship between 12 postulates of green chemistry and 9 principles of electrosynthesis.

a number of apparent issues, such as the need for extensive electrochemical equipment that is often expensive to purchase and maintain. The selection of solvent can be difficult in electrosynthesis since toluene, tetrahydrofuran, and other less conductive solvents are utilized. Furthermore, a supporting electrolyte is typically employed to aid electron transit in solution. The majority of metallic ions are easily reduced at the cathode to zero-valent metals, which restricts the use of metal catalysts in electrochemical reactions occurring in easily accessible undivided cells. Additionally, while customizing the electronic configuration to achieve the best binding, thermodynamics, and even predictive manipulations are also challenging. Another obstacle that lies in the occurrence of side reactions, is the reduction in the current efficiency which can lead to deterioration of the electrode.

Electrochemical synthesis has experienced rapid development in recent years, contrasting with the previously steady evolution. The concept of utilizing electricity in organic synthesis has emerged as a new era with expanding opportunities and advantages. The drive to create cleaner and more cost-effective synthetic methods has insisted chemists to explore novel approaches for activating organic molecules. Electrosynthesis stands out as one of the most cost-effective and environmentally friendly techniques, as it enables oxidations and/or reductions to be conducted without the requirement for additional chemical reagents. Minimizing the number of stages results in energy conservation, contributing positively to both environmental sustainability and the economic evaluation of manufacturing processes.

Electrochemical processes have inherent advantages over conventional reagent-based methods, while transforming renewable biogenic compounds and natural raw materials into complex compounds with high added value, such as pharmaceuticals or other chemicals and natural products. Now a days electrocatalysis integrated with electrosynthesis is becoming an emerging trend. This includes utilization of flow chemistry for scaling up the processes to enhance efficiency and sustainability. Moreover, there is a focus on incorporating new synthetic feedstocks to further diversify the scope of electrochemical reactions.[11]



Scheme 1 Electrochemical synthesis of oxindole ring compounds 2 and 4.

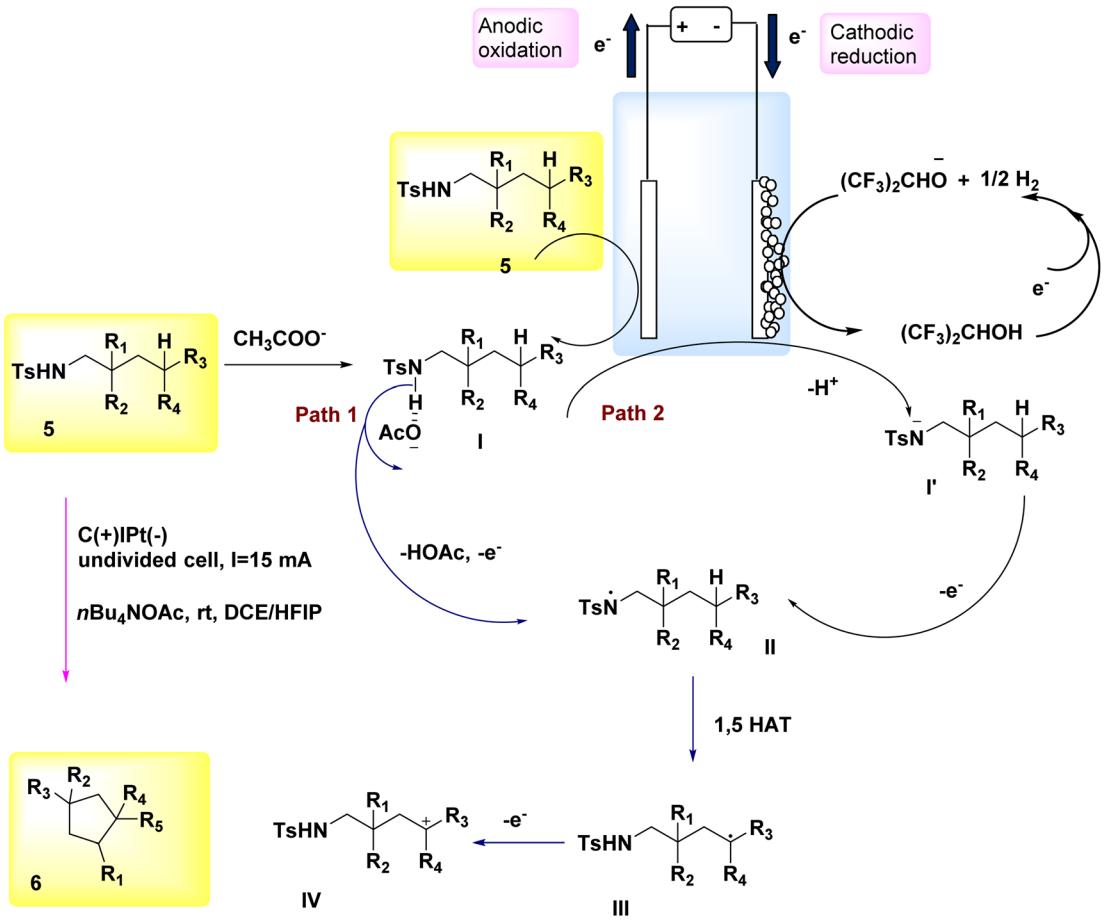
In this article, we aim to provide a comprehensive overview of the advancements achieved in the electrochemical synthesis of N-, S-, and O-heterocyclic compounds using intermolecular and intramolecular cyclization reactions over the past few years.

Electrosynthesis of N-heterocycles

The significance of N-containing heterocyclic compounds in the field of biomedicine[12] has led to the advancement of synthetic techniques employed in their synthesis. In the year 2018, Wu and colleagues published a study documenting the electrochemical reaction employed for the intramolecular cross-coupling of C(sp^3)–H and C(sp^2)–H bonds. The catalyst used in this reaction was Cp_2Fe, as illustrated in Scheme 1. A family of oxindole cycle of $C_8H_{12}O_3$ compounds **2** and **4** was synthesized with high efficiency.[13]

In 2018, Hu *et al.* introduced an alternative technique for the electrochemical synthesis of N-heterocycles, Scheme 2. One of the techniques employed in the synthesis of nitrogen-containing compounds with high saturation involves the cross-coupling of C(sp^3)–H and N–H bonds. Typically, supplementary oxidizing agents or halogenated compounds are required in such processes. The authors have presented a commendable study on the electrochemical synthesis of a five-membered ring, demonstrating the absence of additional oxidants or hazardous chemicals. A significant yield of pyrrolidine **6** was achieved from sulfonamide **5**, resulting in the generation of a substantial family of pyrrolidine compounds. The process of electrolysis was conducted in an undivided cell utilizing a cathode made of Pt plate and an anode composed of a carbon rod. Tetrabutylammonium acetate has the ability to form intermolecular H_2-bonds with amide molecules, hence aiding in the breaking of the nitrogen–hydrogen bond. Furthermore, it is employed as an electrolyte in several applications. In this approach, the inclusion of additional oxidants and the *N*-halogenation step can be omitted. The production of benzylic and non-activated primary, secondary, and tertiary C(sp^3)–H amination can be achieved with favorable yields.[14–16]

The process was initiated by the formation of bonding complexes between sulfonamide **5** and acetate. The formation of the N-centered radical intermediate **II** was initiated by a process of single electron oxidation occurring at the anode (path 1). A carbon-centered radical **III** was formed as a result of the 1,5-HAT reaction, where a carbon–hydrogen bond was cleaved by an aminyl radical. Subsequently, the radical species underwent oxidation to yield the C-cation intermediate **IV**. The cyclization product **6** is formed as a result of the nucleophilic attack and subsequent proton eliminations of the sulfonamide.



Scheme 2 Electrochemical synthesis of substituted pyrrolidine **6** with its proposed mechanism.

In the framework of the reaction phase, the concurrent reduction of protons at the cathode would result in the production of molecular H_2. This process eliminates the need for a stoichiometric external oxidant. The alkoxide that is generated has the ability to deprotonate the substrate, leading to the creation of N anion **I′**. This intermediate can then undergo rapid oxidation on the (+), culminating in the synthesis of the N-centered radical intermediate **II** (path 2)

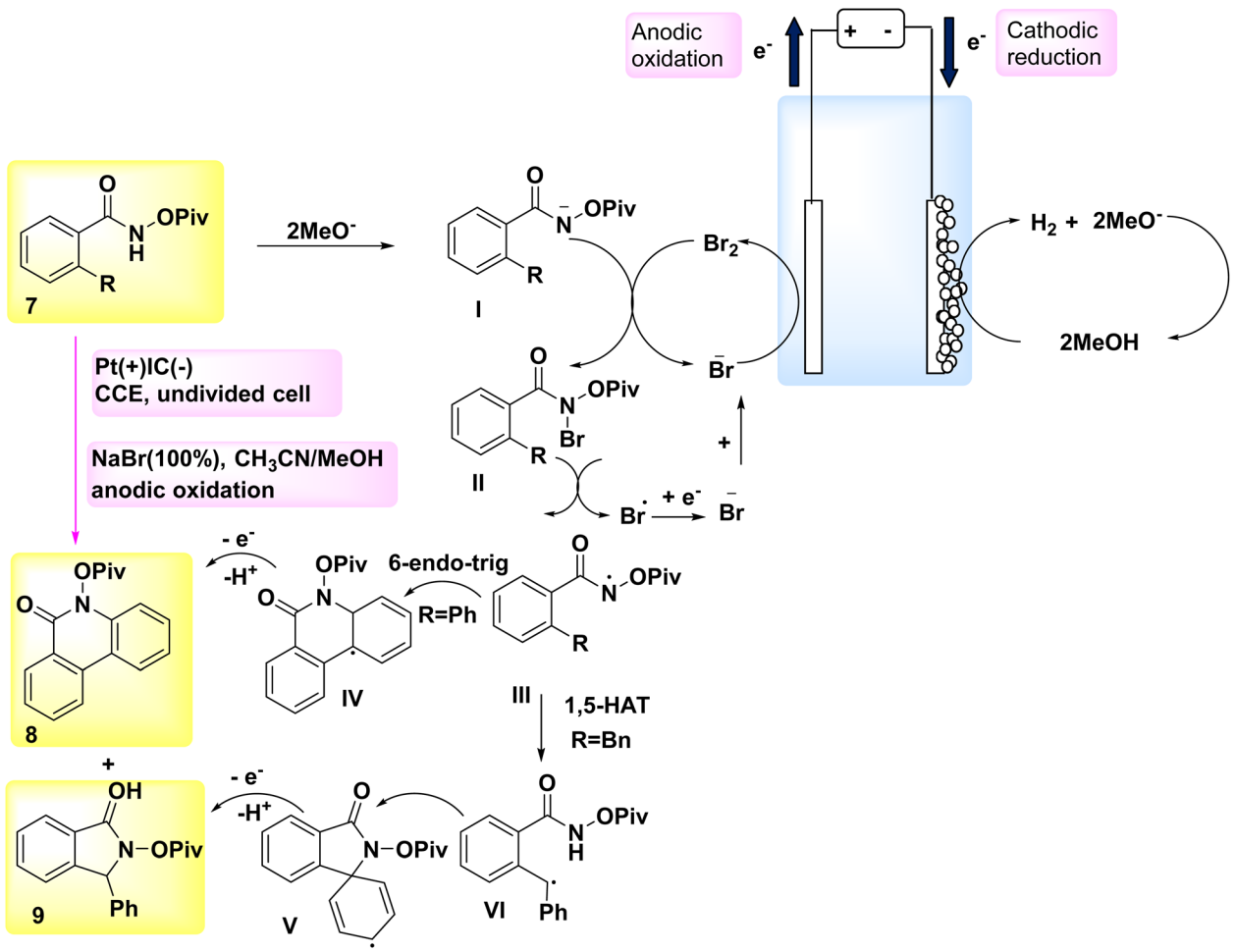
In the year 2018, a novel approach was employed for the generation of *N*-acyloxy NH_2s electrochemically, marking the first instance of utilizing an inner-sphere electron-transfer mechanism for this purpose (Scheme 3). A cellular system consisting of a cathode made of graphite (C) and an anode made of Pt (Pt) was utilized. The NH_2s that are generated *in situ* undergo intramolecular C(sp^2/sp^3)–H aminations in the presence of NaBr, which serves as both an electrolyte and catalyst. This reaction leads to the formation of quinolinone **8** and indolinone **9** products, exhibiting remarkable regio- and chemoselectivities.[17,18]

A hypothetical method was built based on the findings from these results and relevant studies (Scheme 3). Intermediate **II** is formed when a methoxide ion (MeO^-), which acts as an electrogenerated base, is present, and it facilitates the collection of anodically produced Br_2 by the substrate **7**.

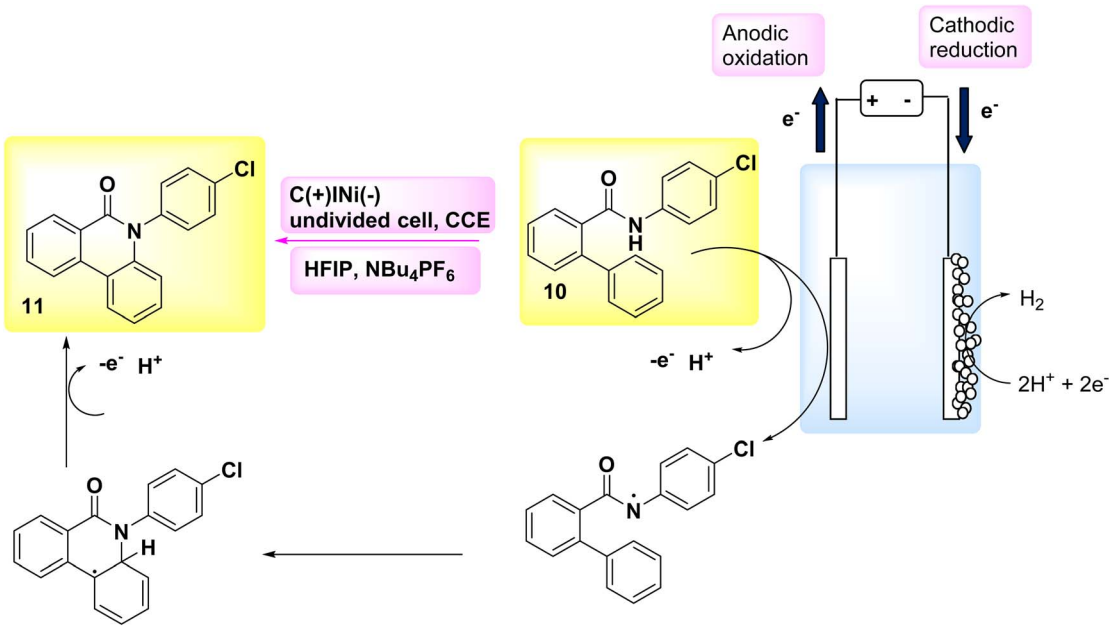
After the cleavage of the nitrogen and bromine bonds, the formation of *N*-acyloxy amidyl **III** occurs, which then undergoes cyclization by a 6-*endo*-trig mechanism to produce intermediate **IV**. The generation of Br-radicals was seen in the cyclic voltammetry tests, providing evidence for the breaking of the nitrogen-bromine (N–Br) bond. The presence of steric hindrance caused by the –OPiv group effectively mitigates the formation of an undesired intermediate.

The aromatization process ultimately converts intermediate **IV** into the sp^2 carbon–hydrogen amination product **8**. The postulated mechanism for the development of benzylic radical **VI** in the sp^3 carbon–hydrogen amination process involves a 1,5-H_2 atom transfer. The benzylic radical **VI** undergoes further oxidation and then undergoes intramolecular cyclization, resulting of product **9** formation.

In the year 2018, an alternative technique for electro-anodic oxidation was employed in order to establish a novel and enduring supply of N arylphenanthredin-6-one derivatives. The conversion of $C_{19}H_{15}NO$ **10** to N, C coupled product **11** (Scheme 4) is achieved using an undivided Teflon cell equipped with cathodic graphite and anodic nickel electrodes. The solvent used in this study is 1,1,1,3,3,3-hexafluoroisopropanol. The utilization of a moderator is not obligatory in conjunction with



Scheme 3 Electrochemical synthesis of quinolinone **8** and indolinone **9** with its proposed mechanism.



Scheme 4 Electrochemical synthesis of *N*-arylphenanthredin-6-one **11** with its proposed mechanism.

this system owing to its exceptional electrical efficiency. An accessible or cost-effective method for synthesizing this category of chemicals is facilitated by readily obtainable and economical initial reactants. The production of a diverse array of derivatives is achievable, and the identification of valuable functionalities that facilitate subsequent reactions is acknowledged. The scalability of this technology allows for effortless adjustments in both larger and smaller scales.[19]

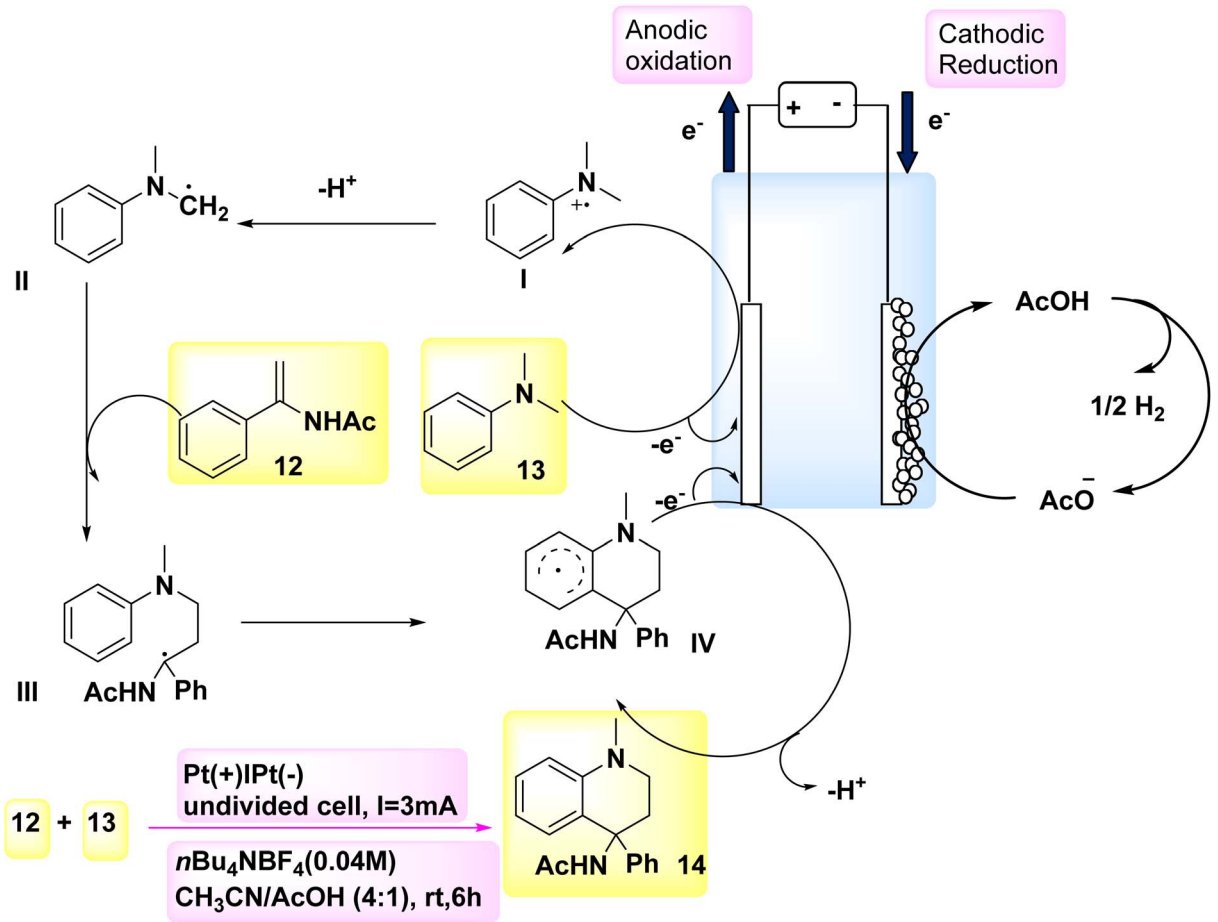
Scheme 4 illustrates the proposed procedure for the synthesis of compound **11**. The initiation of cyclization occurs through the oxidation of the substrate at the anode electrode, at which the generation of an NH_2 **I** is seen. The anilide could be deprotonated by an 1,1,1,3,3,3-hexafluoroisopropanolanion that is generated *in situ*. The *N*-aryl system has the ability to provide stabilization to the NH_2. In this particular situation, the NH_2 establishes a nitrogen, carbon link with the second phenyl moiety of the biphenyl scaffold, which is unsubstituted. Consequently, a radical is formed within the lactam system. The product **11** undergoes a secondary oxidation phase, subsequent to which a proton extrusion occurs.

According to a paper in 2018, the oxidative [4 + 2] annulation method, specifically Scheme 5, was identified as an efficient method for the rapid synthesis of six-membered heterocycles. In this methodology, tertiary anilines and alkenes engage in an [4 + 2] electrochemical annulation process, resulting in the formation of tetrahydroquinolines in a homogeneous manner, without the requirement of metallic catalysts or external oxidizing agents. In order to assess the reaction conditions, model substrates DMA **13** and $C_{10}H_{11}NO$ **12** were employed. $C_{18}H_{20}N_2O$ **14** may be synthesized with a 72% yield in an undivided cell by employing nBu$_4$NBF$_4$ as the CH_3CN/AcOH and electrolyte as cosolvents for a duration of 6 hours.[20,21]

Scheme 5 presents a possible mechanism along with its synthesis for the reaction involving compound **12** and compound **13**. Initially, the oxidation of **13** occurs, resulting in the generation of a radical cation. This radical cation can be stabilized by acetic acid, thereby facilitating the anodic reaction. The tertiary-amino carbon radical is formed through a process involving resonance of the radical cation followed by deprotonation. The radical **II** has the potential to engage in a radical addition reaction with **12**. The intended product **14** will be generated during the subsequent anodic oxidation, wherein an intramolecular cyclization process is taken part in by the resulting radical species **III**. The production of H_2 gas occurs by the concurrent (−) reduction of acetic acid.

In the year 2018, two interrelated electrochemical techniques utilizing Co catalysts were employed for the synthesis of substituted oxindoles through radical pathways. The effectiveness and environmental friendliness of the electrochemical Co-catalyzed system were described, as it achieved high yields of arylation **18** or alkylation **19** compounds at ambient temperature without the need for stoichiometric oxidants. Several substituted oxindoles were synthesized using electrochemical reactions of *N*-arylacrylamides **15** with either potassium alkyltrifluoroborates **17** or arylhydrazines **16** in environmentally friendly conditions. The reaction is carried out using platinum as the cathode and reticulated vitreous carbon as the anode. The absence of oxidants in these two reactions has support a groundbreaking approach for the synthesis of novel radical oxidative couplings. Furthermore, the synthesis of molecules possessing an all-carbon chiral core can potentially be achieved using a Co-catalyzed radical reaction involving the reaction between *N*-arylacrylamides and potassium alkyltrifluoroborates. These two unique approaches for acquiring substituted oxindoles are anticipated to yield advantageous outcomes in the field of organic synthesis.[22]

The anodic oxidations of phenylhydrazine **16** or $C_7H_7BF_3K$ **17** were facilitated by Co salts. This resulted in the formation of



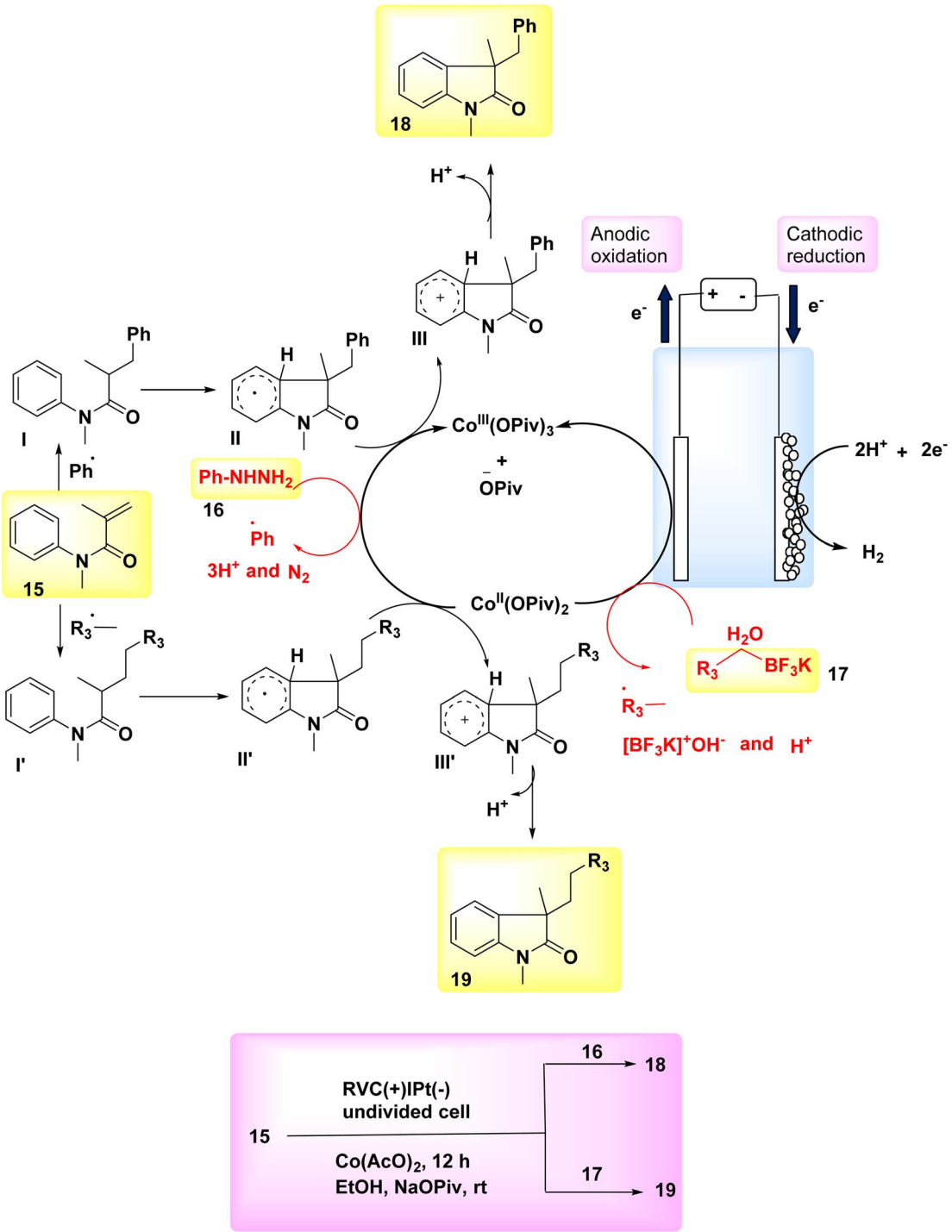
Scheme 5 Electrochemical synthesis of *N*-(1-methyl-4-phenyl-1,2,3,4-tetrahydro-quinolin-4-yl)acetamide **14** with its proposed mechanism.

benzyl or phenyl free radicals, which subsequently acted as catalysts for the reaction (Scheme 6-**I**). The process of cathodic reduction is responsible for the production of molecular H_2 as depicted in Scheme 6-**II**. The compound $Ph^{\bullet}$ or $Ph-CH_2^{\bullet}$ was subjected to a direct assault by **17** throughout the reaction, resulting in the formation of radical intermediate **I** or **I′**. Subsequently, an intramolecular cyclization process was employed to generate radical **II** or **II′**. After the transfer of a solitary electron from cobalt III to cobalt II, the anode undergoes oxidation, resulting in the fabrication of the oxidized radical **II** or **II′** and the formation of the cationic intermediate **III** or **III′**. In the final step, deprotonation was employed to facilitate the conversion of intermediate **III** or **III′** into the desired products **18** and **19**, respectively (as seen in Scheme 6-**III**).

In the year 2018, researchers employed electrochemical synthesis as a means to generate a novel and environmentally friendly method for obtaining phthalazin-1,4-diones **21**. This approach can effectively circumvent the use of hydrazine chemicals, as it is used in many of the synthetic procedures for the incorporation of pyrazole ring in the hybrid multi-component drug synthesis.[23–25] They have been shown to have substantial toxicity or carcinogenic qualities.

The experimental procedure involved the utilization of a single, non-partitioned cell including graphite (+) and a Pt (−). The solvents employed were 1,1,1,3,3,3-hexafluoroisopropanol and NBu_4PF_6. The starting material used in this study was phthaldianilide **20**, as depicted in Scheme 7. The utilization of this method presents a valuable alternative to the traditional synthetic route due to its utilization of easily accessible and cost-effective starting materials. The utilization of a straightforward configuration, the exclusion of metallic catalysts and organic oxidizers, and the availability of electrode materials that can be scaled up and have a prolonged lifespan, facilitate convenient and enduring accessibility to this particular category of substrates. A N–N connection with an anodic character is formed. This methodology facilitates the synthesis of a diverse array of derivatives, hence enabling the incorporation of valuable functionalities that can support subsequent reactions. Additionally, this approach offers the opportunity to obtain nonsymmetrical compounds.[26,27]

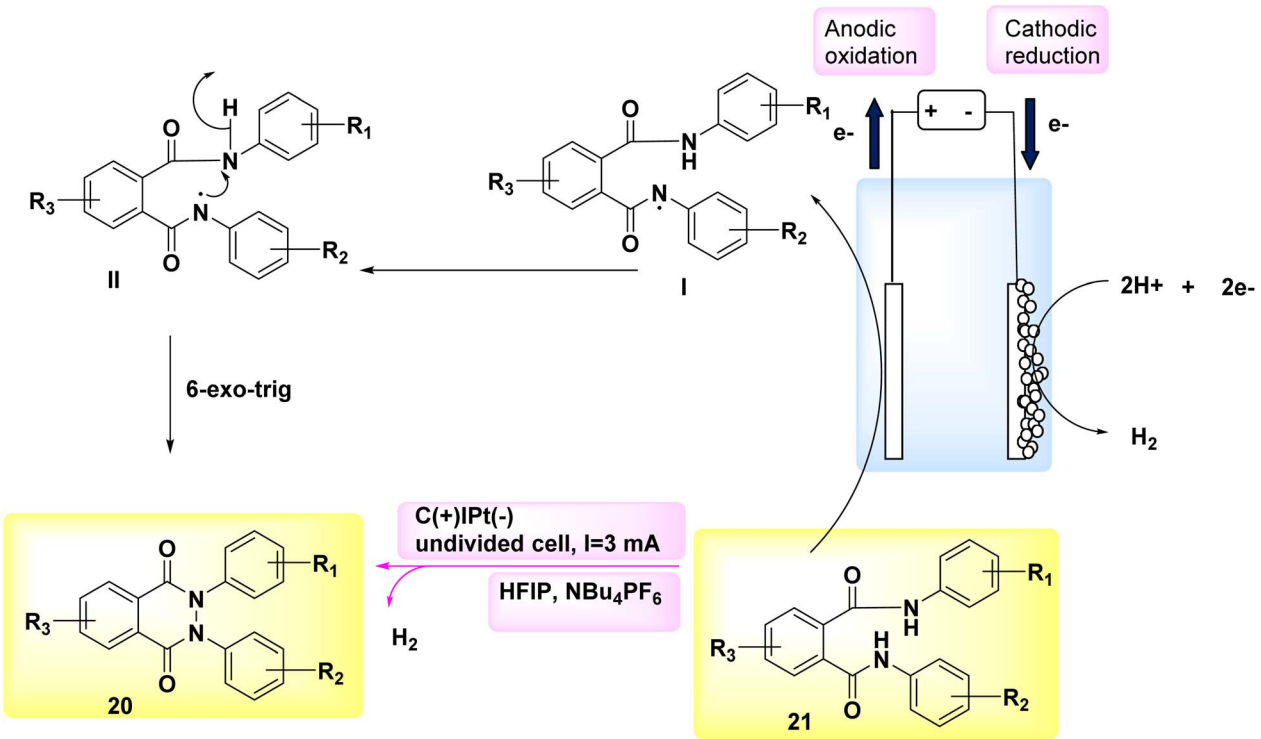
The year 2018 witnessed the evoluation of a systematic and stereoselective approach for the synthesis of indolines and azaindolines **23**. This method used the (3 + 2) annulation of heteroarylaminesintramolecular dehydrogenation **22** with coupled substituted alkenes. The reaction was facilitated by the use of oxidizing agents or metal catalysts Scheme 8. The procedure employs a cascade radical cyclization mechanism to produce C–C and C–N bonds sequentially. The initial phase of



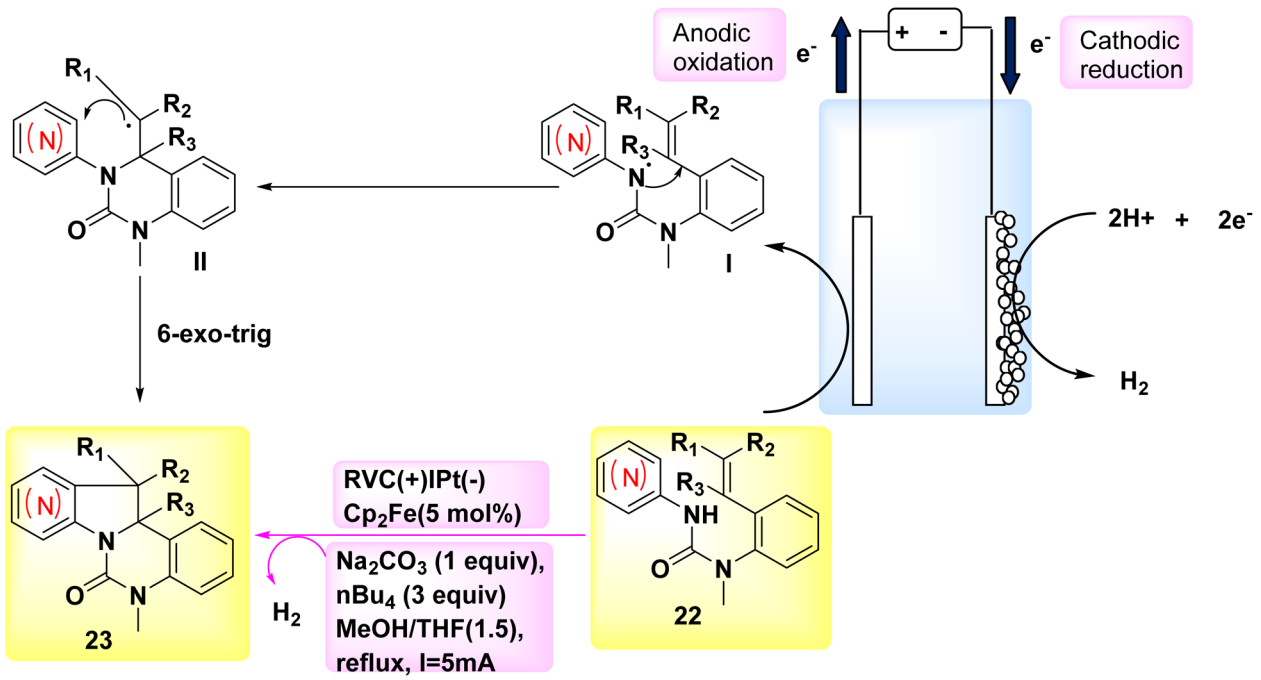
Scheme 6 Electrochemical arylation **18** and alkylation **19** products with its proposed mechanism.

the bicyclization process facilitates the production of a 6-membered ring, hence ensuring the effective evoluation of the subsequent C–C bond, which plays a crucial role in the overall effectiveness of the annulation. The electrosynthetic approach enables the complete synthesis of (±)-hinckdentine using commercially available components.[28]

In the year 2018, a radical cyclization cascade, namely a 5-*exo*-trig or 7-*endo*-trig mechanism, was utilized for the electrochemical synthesis of 7-membered carbocycles, denoted as compound **25** in Scheme 9. The initial cyclization step of the cascade process results in the formation of a five-membered ring, accompanied by the transposition of the radical center and the remaining alkene. The *trans*-configuration of the molecule induces a region-selective 7-endo cyclization of the 6-heptenyl radical. The experiment was performed within a single



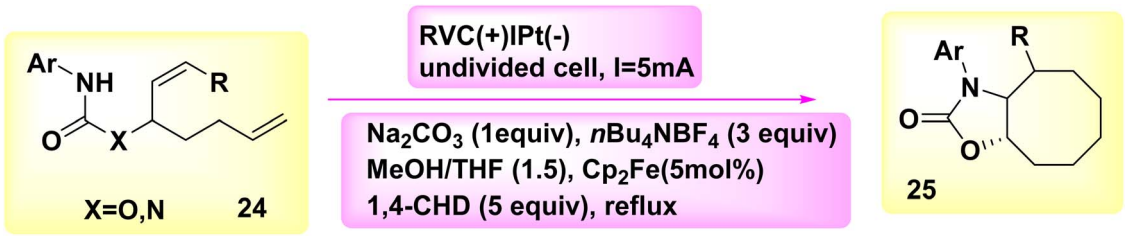
Scheme 7 Electrochemical synthesis of phthalazin-1,4-diones **21** with its proposed mechanism.



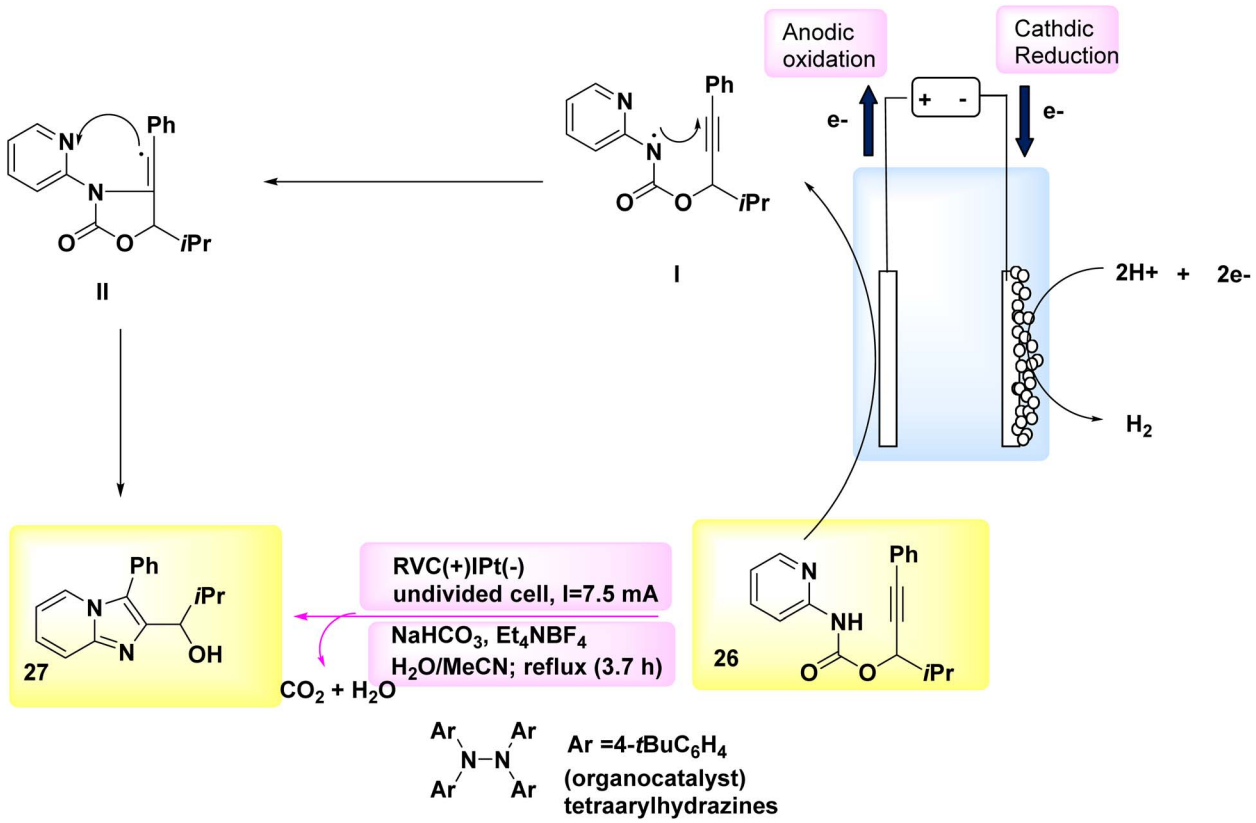
Scheme 8 Electrochemical synthesis of azaindolines **23** with its proposed mechanism.

cell, utilizing a solvent mixture of tetrahydrofuran and methanol, with nBu$_4$NBF$_4$ serving as the electrolyte.[29]

The synthesis of chiralaxial imidazopyridine-containing biaryls involves a series of events that proceed through a radical cyclization cascade mechanism.[30] A novel and groundbreaking C–N linked cyclization technique, known as regiospecific [3 + 2] annulations, was utilized in the electrochemical synthesis of imidazo-fused N-heteroaromatics.[31] The electrosynthesis process was made possible in 2018 due to the evolution of a tetra-arylhydrazine catalyst that generates NH_2

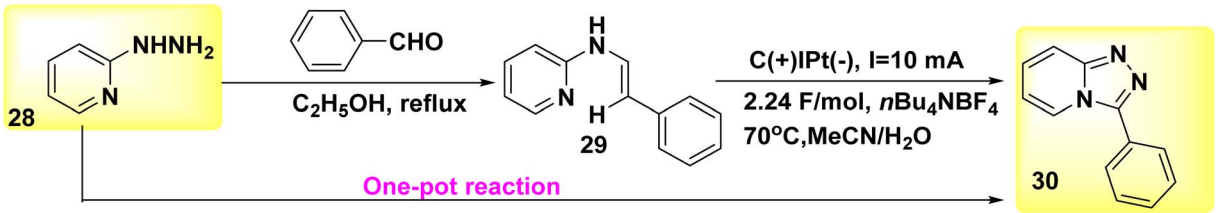


Scheme 9 Electrosynthesis of 7 membered functionalized carbocycles **25**.

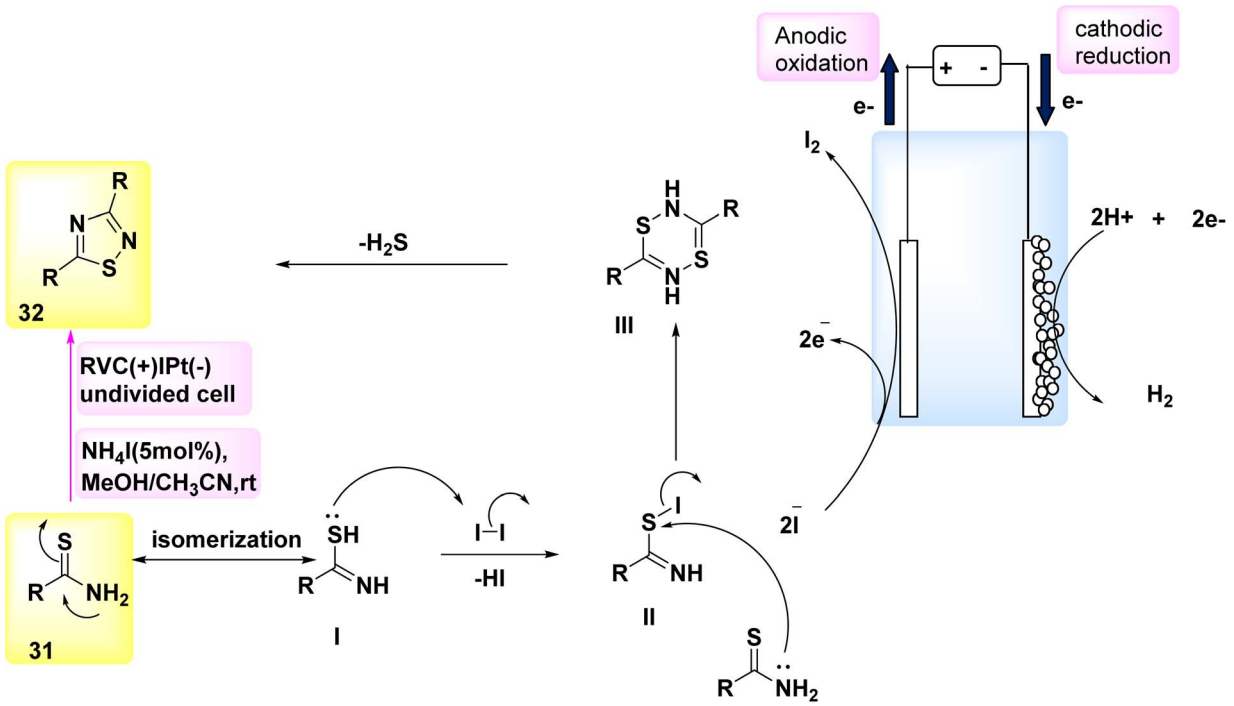


Scheme 10 Electrochemical synthesis of fused imidazo–pyridine **27** with its proposed mechanism.

and the subsequent discovery of the distinct reactivities exhibited by nitrogen and C-centered radicals in constructing C–N links. In order to achieve this purpose, a readily accessible carbamate **26** was employed as a representative substrate. An undivided cell, equipped with a reticulated vitreous carbon-anode and a Pt-cathode, was utilized to evaluate various electrolysis conditions. The most favorable outcomes were obtained when a steady current was applied to the electrolysis of **26** in a mixed solvent of CH_3CN and H_2O, while under reflux conditions and in the presence of tetraarylhydrazines-catalyst. Despite the fact that tetraarylhydrazines are readily accessible, they have not been employed as a redox catalyst in any known



Scheme 11 Electrochemical synthesis of 1,2,4-tetrazolo [4,3-α]pyridines **30**.



Scheme 12 Electrochemical synthesis of 3,5-disubstituted-1,2,4-thiadiazoles **32** with its proposed mechanism.

instances.[32,33] The imidazopyridine compound **27** (Scheme 10) was successfully extracted with a yield of 89% under the given conditions.[34]

A reagent-free intramolecular dehydrogenative carbon–nitrogen cross-coupling technique for mild electrolysis was discovered in 2018 (Scheme 11). The synthesis of valuable $C_6H_5N_3$ **30** and their derivatives can be achieved by a convenient one-pot technique using readily available aldehydes and 2-hydrazinopyridines **28**. This synthetic approach is both atom- and step-economic. The approach described herein, which may be easily implemented on a gram scale in the absence of oxidizing agents or metallic catalysts, applies to a wide range of functional groups. The present study employed a novel methodology for the synthesis of Xanax, a widely prescribed medicine, along with subsequent late-stage functionalization to introduce chemical heterogeneity in pharmacologically significant lead compounds.[35]

The year 2018 witnessed the evoluation of a method for synthesizing 3,5-disubstituted-1,2,4-thiadiazoles using an electrochemical process involving the NH_4I-mediated dimerization of thioamides **31** (Scheme 12).

The electrosynthesis technique described in this study employs NH_2I as both a catalyst and electrolyte. Notably, this method eliminates the need for oxidizing agents, hence enabling the synthesis of a diverse array of 1,2,4-thiadiazole molecules. The procedure serves as a demonstration of the electrochemical formation of S–N bonds.[32]

In the year 2018, significant progress was achieved in the field of electrochemical reactions for the synthesis of functionalized tetrazoles, with a particular emphasis on their ecological compatibility. The simple reaction did not require oxidants or metal catalysts, and a range of chemicals were deemed suitable under the favorable conditions.

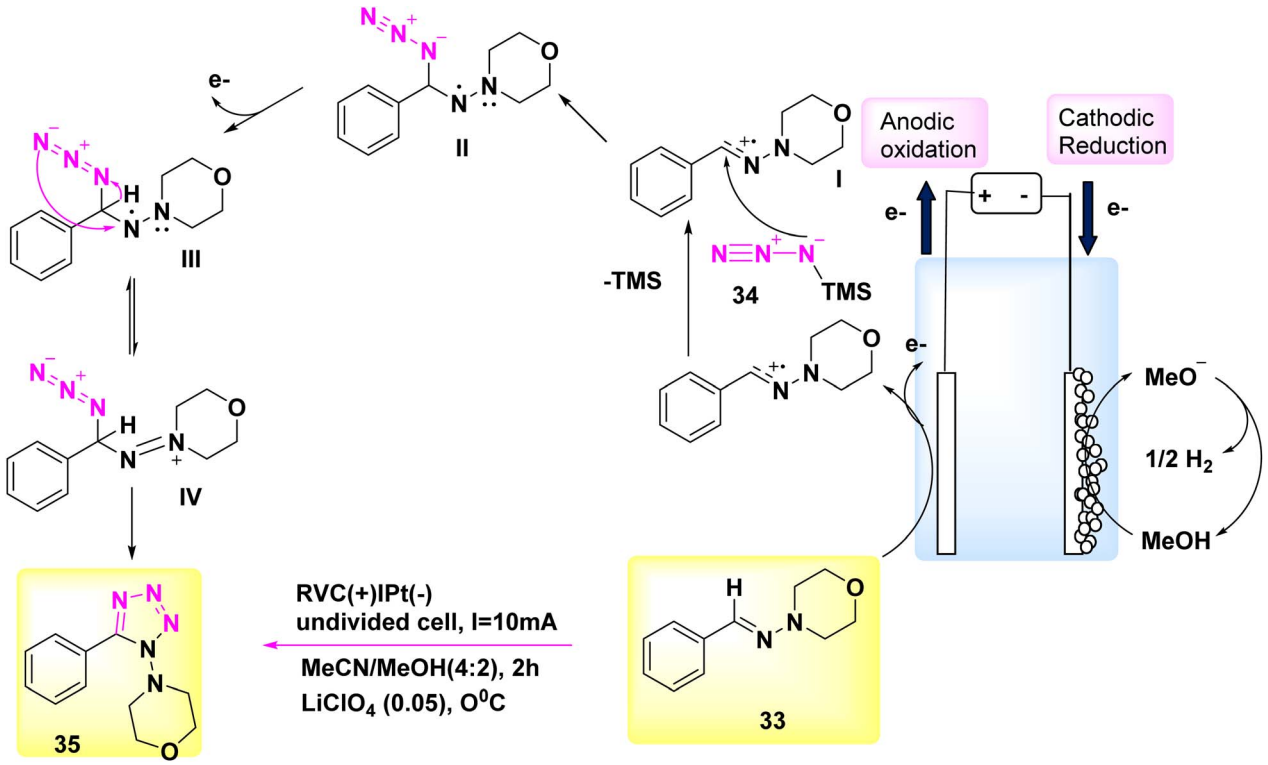
Significantly, this reaction can be conveniently conducted in a singular vessel or on a scale of grams. Additional applications of this inovationare currently being evaluated.[33] The electrochemical reaction was conducted in a basic undivided cell under conditions of continuous current.

The anode is composed of reticulated vitreous carbon, whilst the (−) consists of a Pt-plate. Tetrazole **35** was successfully combined with a high yield of 90% using the process of electrolyzing hydrazone **33** and $TMSN_3$ **34** at a temperature of 0 °C. This reaction took place in a solvent mixture consisting of CH_3CN and CH_3OH.

In this experiment, the electrolyte employed was lithium perchlorate ($LiClO_4$) as described in Scheme 13.

The author presents a viable technique in Scheme 13. The formation of carbocation intermediate **I** can occur through anodic oxidation of **33**. Subsequently, this intermediate can react with $TMSN_3$ to establish a carbon–nitrogen bond, resulting in the generation of intermediate **II**. Afterwards, the anode has the potential to undergo oxidation of the N-centered radical, resulting in the development of intermediate **III**. This intermediate exhibits resonance with **IV**. After intramolecular deprotonation and cyclization, facilitated by the methoxide ion generated during the cathodic reduction of CH_3OH, compound **III**/**IV** undergoes a conversion process resulting in the production of tetrazole product **35**.

In the year 2018, a novel electrochemical methodology was employed to achieve the initial direct aziridination of alkenes, with potential applicability to styrenes bearing multiple substituents. $C_3H_2F_6O$ sulfamate **37** was employed as



Scheme 13 Electrochemical synthesis of 1,5-disubstituted tetrazole **35** with its proposed mechanism.

a nucleophilic N-source. The mechanistic experiments suggest that the electrochemical process involves the sequential production of two carbon-nitrogen bonds, facilitated by the interaction between cationic carbon species or sulfamate.

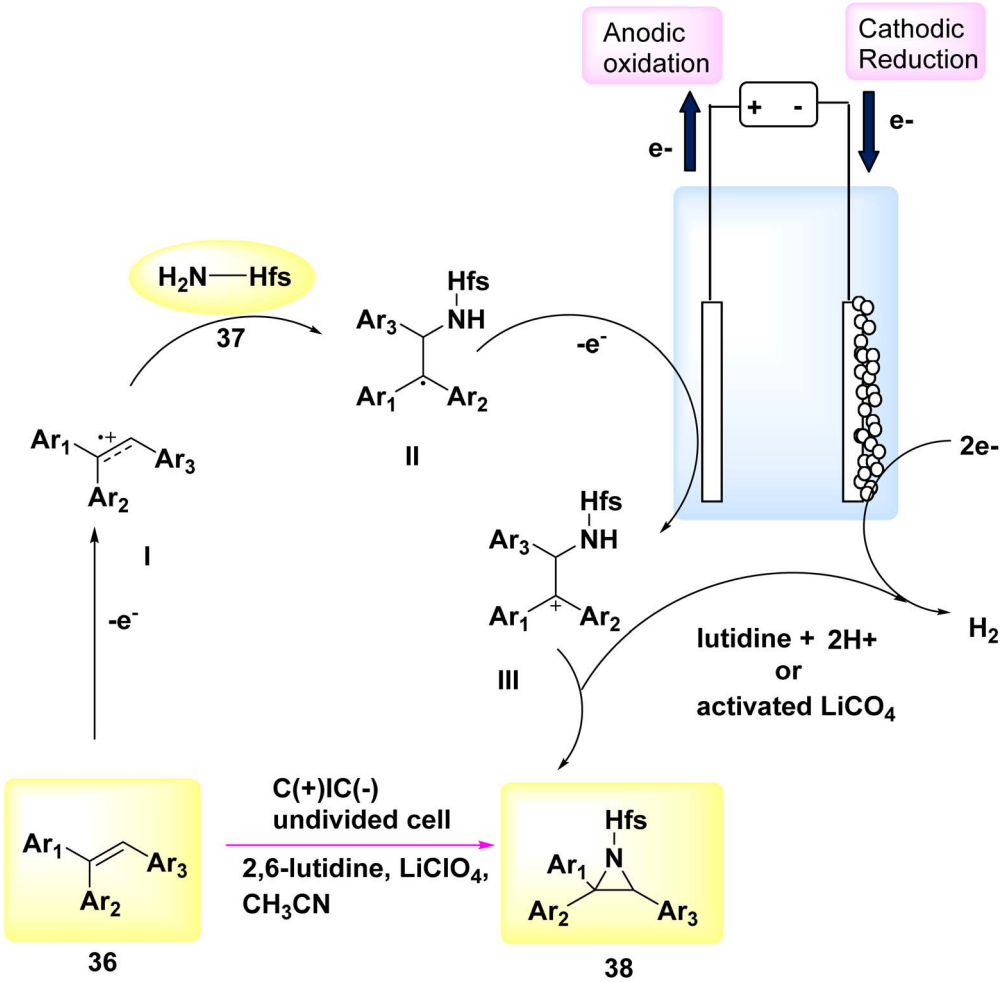
In order to assess the feasibility of this approach, a group of **36** subjects were subjected to electrochemical methods at a voltage of 5 V, utilizing $LiClO_4$ as the electrolyte. Graphite felt electrodes were employed, and the experiment was conducted in the presence of sulfamate 37 dissolved in C_2H_3N. The aziridine **38** was obtained with a yield of 87% using 2,6-lutidine as a base, as described in Scheme 14.[36]

A proposal was made to establish a reaction route, as seen in Scheme 14. The alkene undergoes an anodization process, leading to the generation of carbocation radical **I**. The sulfamate nucleophile is introduced, and lutidine is employed as a deprotonating agent, leading to the formation of a neutral radical species **II**. This species is subsequently oxidized on the anode, resulting in the production of carbocation **III**. The aziridine product **38** is ultimately achieved by the process of ring closure. Lutidine is regenerated at the cathode through the process of H_2 release. Furthermore, the cathode discharge process can involve the utilization of $LiClO_4$, activated potassium benzyl trifluoroborate, or CH_3CN.

In the year 2018, a method based on electrochemical reactions was employed to illustrate the dehydrogenative carbon–hydrogen/nitrogen–hydrogen [4 + 2] annulation of amides **39** utilizing either ethylene **40** or ethyne **41**. Nevertheless, there are only a limited number of methodologies that can be employed to introduce ethylene or ethyne into intricate chemical structures. The compound $Co(acac)_2$ was effectively employed as a catalyst in the existence of NaOPiv and undivided electrolytic conditions for the reaction involving ethylene **40**. Under the conditions of a constant current electrolysis of 4.0 mA, a significant yield of 89% for the cyclization product **42** was obtained after 4 hours. The electrochemical procedure required the use of the aminoquinoline leading group, as the presence of pyridine or pyridine-*N*-oxide as directing groups did not yield any favorable result. The selection of a Co catalyst precursor had a pivotal role in achieving a high reaction yield. An experiment was conducted using a 5 mmol scale reaction in a bigger divided cell with a constant current of 30 mA (Scheme 15). Both the (+) and (−) electrodes were constructed using carbon fabric. Fortunately, a significant amount of 0.90 grams, which accounts for 66% of the initial 56 grams, was successfully removed following a 13 hours electrolysis process.[37]

One of the most straightforward methods for synthesizing CO compounds involves the utilization of oxidative carbonylation with CO (Scheme 15), a process that is facilitated by transition metals as catalysts. In the year 2018, the intramolecular CH/NH carbonylation process was successfully conducted using anodic oxidation, with $C_{17}H_{14}N_2O$ **39** as the chosen substrate. At a constant current of 15 mA, an isolated yield of **43** with an efficiency of 85% could be achieved using electrolysis. The catalyst $Co(OAc)_2 \cdot 4H_2O$ exhibited the most superior performance.[38]

In light of the mentioned results, a putative mechanism is proposed for Scheme 15. By utilizing NaO–Piv·H_2O, it is possible to synthesize Co(II) complex **I** as a bidentate N-



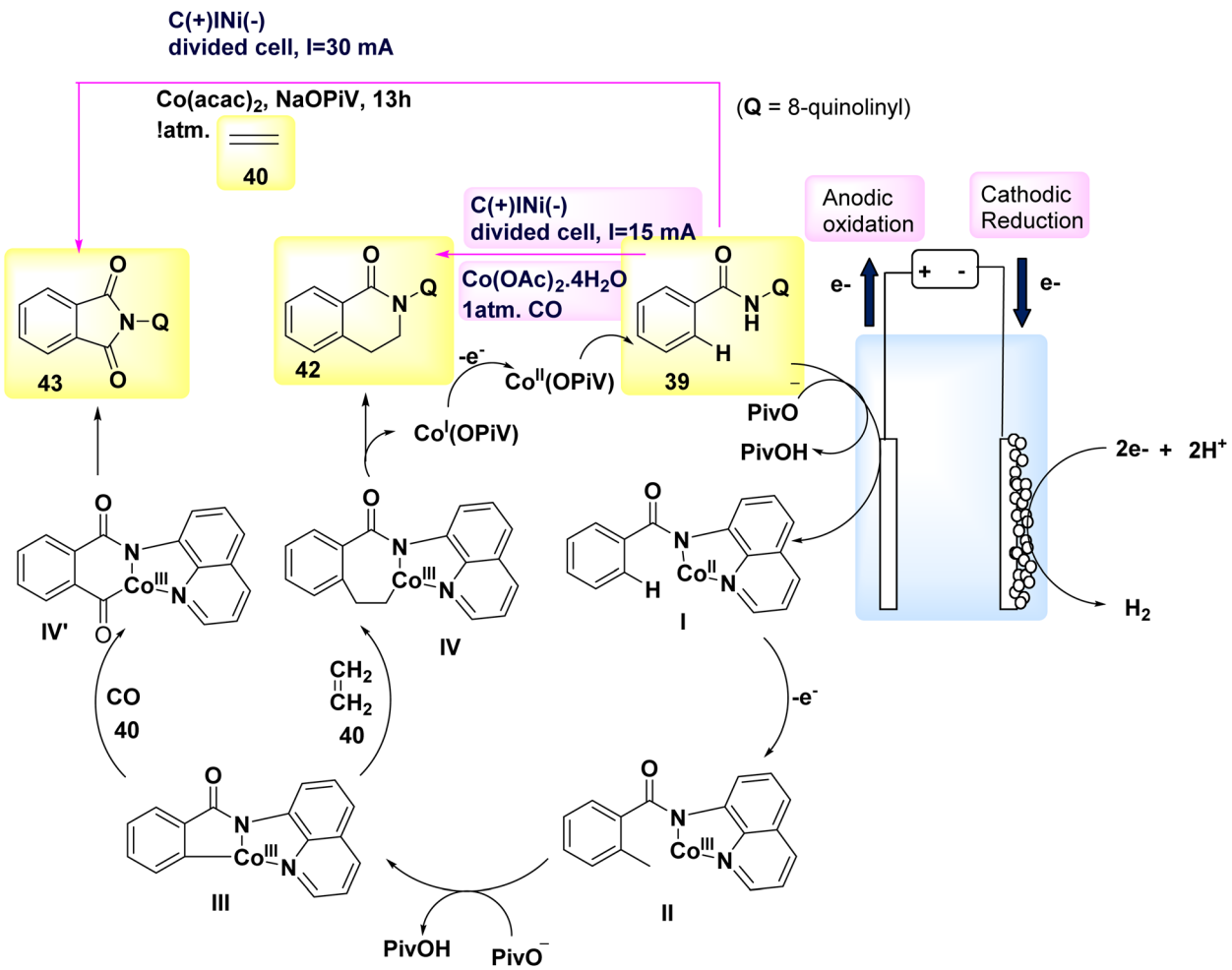
Scheme 14 Electrochemical synthesis of aziridine **38** with its proposed mechanism.

coordinated Co(II) complex, which first coordinates with **39**. Subsequently, the anode facilitates the direct oxidation of complex **I**, resulting in the production of Co(III) complex **II**. Complex **II** undergoes intramolecular carbon–hydrogen activation facilitated by NaOPiv·H_2O, resulting in the formation of cyclic Co(III) complex **III**. The final products, denoted as **42** and **43**, are synthesized through the processes of ethylene **40** or CO-insertion and the subsequent reductive elimination of the Co(III) species. To restore the Co(II) catalyst, the Co(I) species generated during reductive exclusion undergo oxidation at the C-anode. The presence of a considerable quantity of H_2 gas in the reaction system, as detected by gas chromatography following the cessation of the reaction, suggests that the cathodic reaction most likely involves proton reduction.

In the year 2018, a series of experiments involving competition, KIE measurements, and cyclic voltammetry investigations were conducted in order to gain a better understanding of the carbon–hydrogen/nitrogen–hydrogen annulation process. These investigations resulted in the identification of key mechanistic insights, which in turn led to the evoluation of a schematic representation (Scheme 16). This illustration depicted the formation of an intermediate molecule, denoted as **I**, followed by the alkyne addition **46** to generate the crucial intermediate **II**. Through the process of reductive elimination, the required product **47** or **48** is respectively synthesized.[39]

In the year 2018, allenes were employed for the purpose of electrochemically activating C–H bonds, which were afterwards connected to Co catalysis with a high degree of versatility. Therefore, under mild circumstances, the process of allene **50** annulations was successfully achieved, specifically targeting carbon–hydrogen/nitrogen–hydrogen functionalizations. The reactions exhibited favorable levels of chemo-, site-, and regioselectivity. The conversion of Substrate **49** into product **51** occurs. The discovery was made that employing a reduced vanadium compound (RVC) as an anode yielded favorable results. Furthermore, it was shown that various Co-salts might potentially serve as the precatalyst. The electrochemical activation of C–H bonds demonstrated efficacy when employing various solvents, such as polar protic alcohols, tetrahydrofuran (THF), and dichloromethane (CH_2Cl_2). Hence, the utilization of MeOH as the solvent and sodium pivalate as the additive yielded the most optimal reaction conditions, as depicted in Scheme 17.[40]

The described mechanism is mentioned in Scheme 17, depending on both experimental and theoretical mechanistic



Scheme 15 Electrochemical synthesis of 2-(quinolin-2-yl)-3,4-dihydroisoquinolin-1(2*H*)-one **42** and 2-(quinolin-2-yl)isoindoline-1,3-dione **43** with its proposed mechanism.

investigations. It facilitates the process of achieving a successful BIES–carbon–H_2 scission by utilizing carboxylate assistance. The *exo*-methylene isoquinolone **III** is synthesized through the reaction of allene **50** and subsequent reductive elimination, resulting in the isomerization and formation of product **51**.

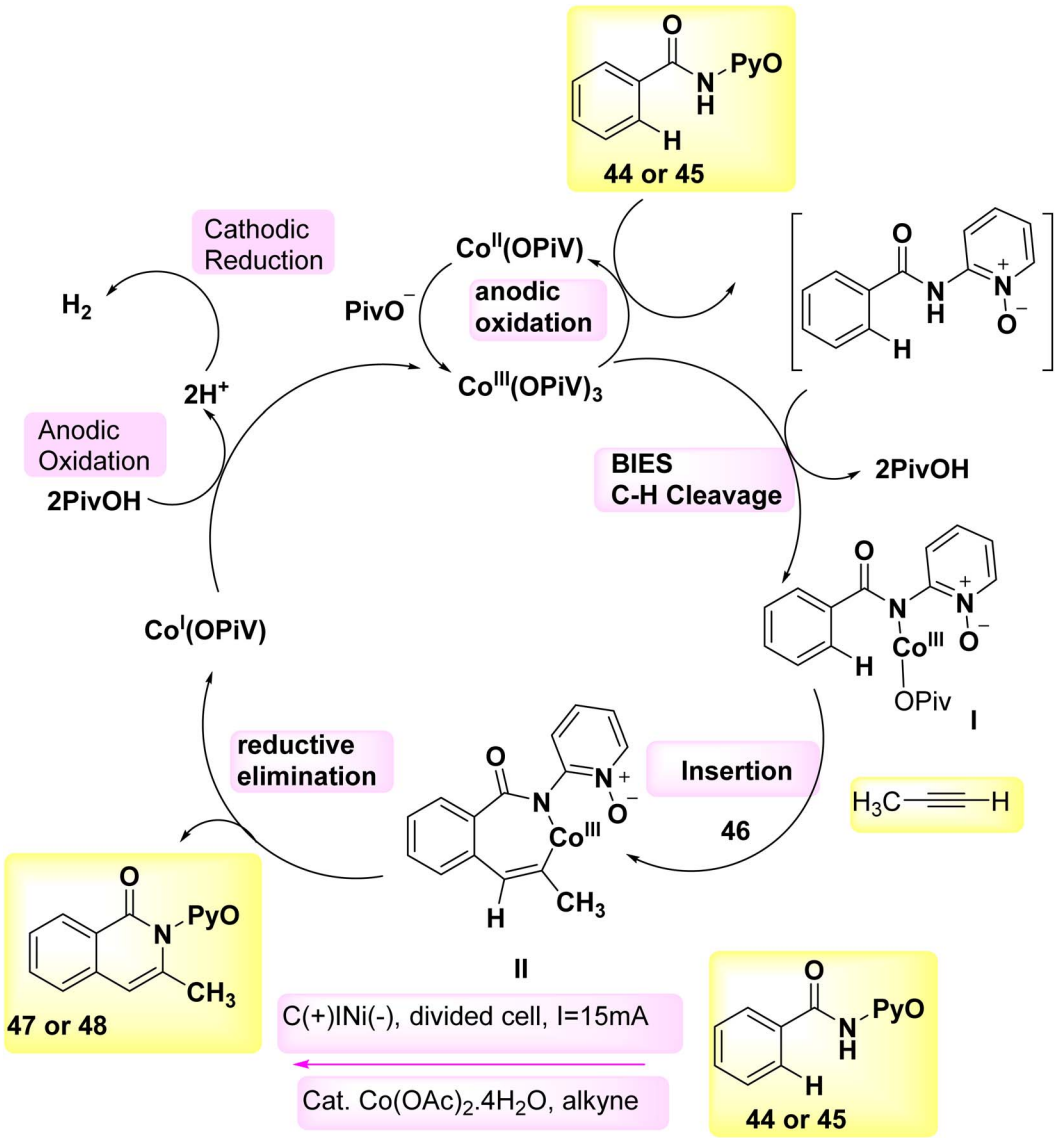
Subsequently, the pivotal process of anodic oxidation effectively restores the active Co catalyst, resulting in the sole byproduct of H_2 gas.

The year 2018 witnessed the demonstration of the utilization of flexible Co-catalyzed activation and annulation of internal alkynes **53** and **52** for the purpose of achieving substituted isoquinolone product **54**. The electro-oxidative carbon–hydrogen activation array was demonstrated using earth abundant Co catalysts in an undivided cell arrangement. The reaction parameters were kept at a very low level, and the experiments were conducted at room temperature. The exclusive production of H_2 gas as a byproduct is achieved through the utilization of electrochemical Co catalysis, which involves the prevention of metallic oxidizing agents.[41]

Scheme 18 has presented a plausible mechanism, drawing upon the fundamental research conducted. Initially, the process of anodic oxidation is employed to generate the Co(III) salt with catalytic properties. Afterwards, the process of carbon–hydrogen coation, facilitated by carboxylate, results in the formation of Co(III) species **I**. After the process of migratory insertion, the formation of Co(III) complex **II** occurs. The process involves the concurrent release of isoquinolone **54** and Co(I) intermediate, which is then followed by reductive elimination. The process of anodic oxidation was employed for the purpose of regenerating Co(III) carboxylate, a compound known for its catalytic properties.

In general, Co-electrocatalysis circumvents the need for employing costly and hazardous oxidizing agents in stoichiometric quantities, hence producing H_2.

In the year 2018, researchers discovered that ethyl naphthalen-1-ylcarbamate **55** can be simply used to electro-oxidatively annulate alkyne **53**. The rhodium(III) catalysts commonly utilized shown a lack of efficacy in generating the desired product, resulting in a mere 70% yield. DMF and *t*-AmOH were identified as solvents that yielded favorable outcomes among a set of conventional solvents. However, it was found that the inclusion of $C_2H_3KO_2$ in a solvent blend



Scheme 16 Electrochemical synthesis of isoquinolones **47** and pyridones **48** with its proposed mechanism.

consisting of *t*-ammonium hydroxide and H_2O proved to be the most efficacious.[42]

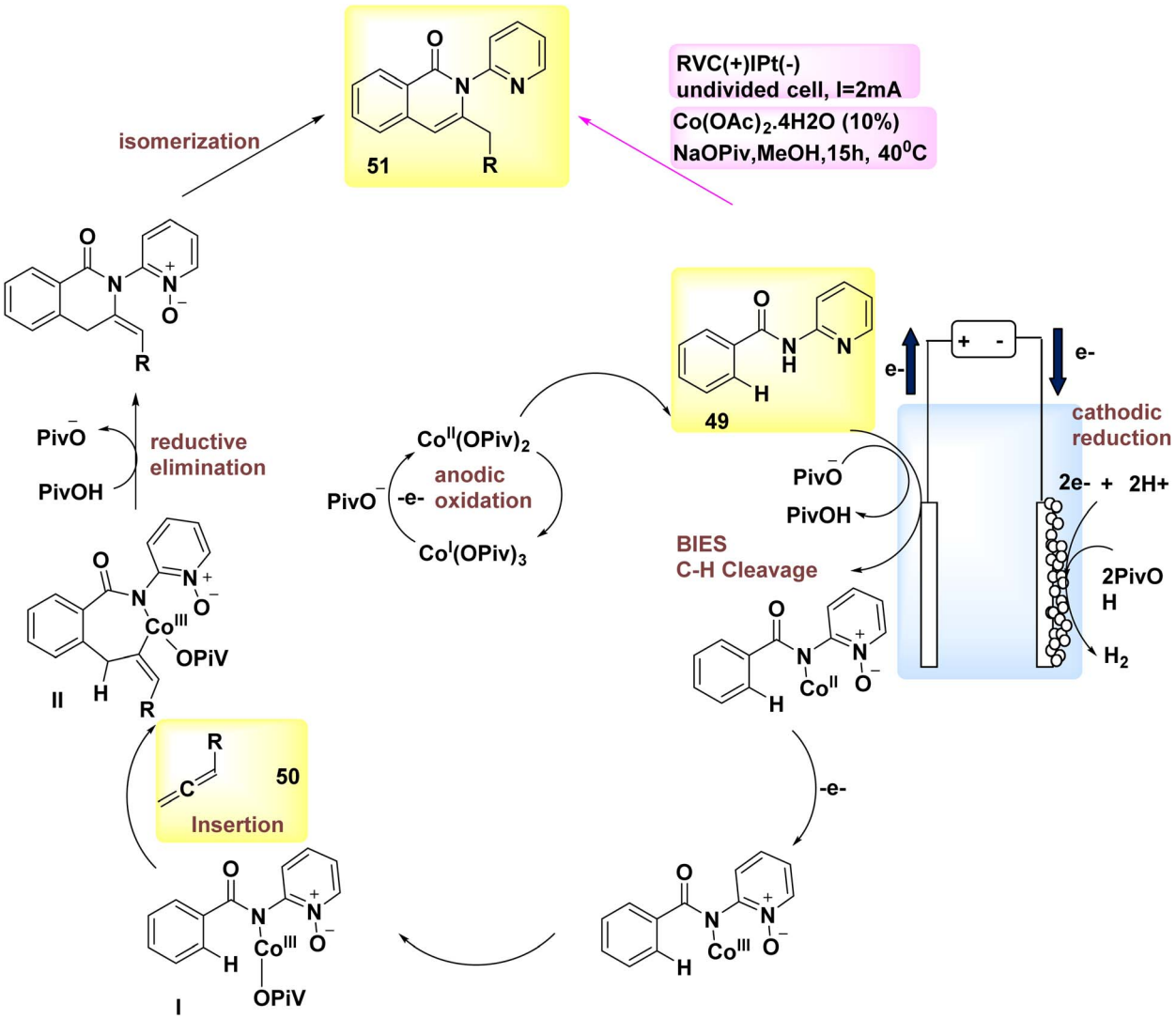
According to mechanistic study, it has been proposed that the initiation of a viable catalytic cycle can be achieved through the facile activation of an organometallic CH bond (as seen in Scheme 19).

Therefore, the reaction yields ruthena(II) cycle **I** and two equivalents of COOH. The ruthena(II) cycle **III**, consisting of seven members, is then obtained through alkyne inclusion. This cycle is rapidly converted into Ru(0) sandwich complex **IV** *via* reductive elimination.

Catalytic reduction produces just molecular H_2 as a byproduct in a stoichiometric way, whereas anodic oxidation is principally responsible for the crucial reoxidation of the resulting Ru(0) complex **IV**. In the year 2018, a novel approach was developed to synthesize fluorinated dibenzazepines **59** by the discovery of a previously unidentified difluoromethylation reagent, $CF_2HSO_2NHNHBoc$ **58** (Scheme 20).

In order to generate the compound with a molecular weight of **59**, the CF_2H radical, which is generated in the presence of ferrocene, engages in a unique alkyne reaction at **57**. This reaction is followed by homolytic aromatic substitution process, resulting in the formation of a seven-membered ring. The stereoselective synthesis of fluorinated dibenzazepine **59** (yield = 70%) was successfully accomplished through the electrolysis of amide **57**, which served as the radical acceptor and carried a terminal alkynyl group. The aforementioned reaction takes place in the presence of methanol at 70 °C temperature, employing ferrocene (Cp_2Fe) as the mediator.[43]

Scheme 20 provides a viable explanation for the formation of fluorinated dibenzazepine **59**. The initial stage of the electrolytic reaction involves the oxidation of Cp_2Fe to Cp_2Fe^+. The process of cathodic reduction of CH_3OH results in the formation of H_2 gas (H_2) and methoxide ions (MeO^-). Consequently, the oxidation of the conjugate base of **58** by Cp_2Fe^+ likely facilitates the production of diazene **III**, maybe in conjunction



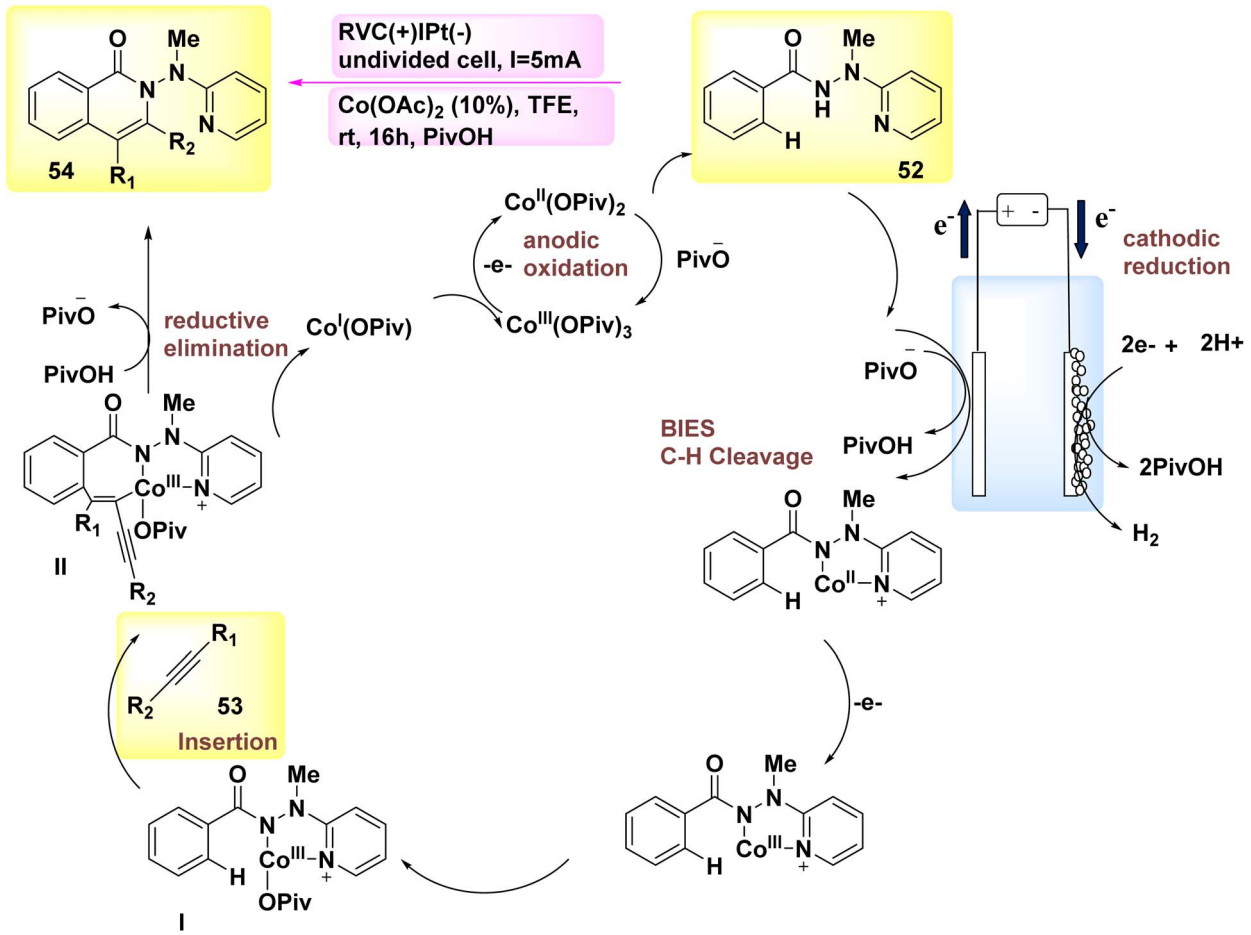
Scheme 17 Electrochemical synthesis of carbon–hydrogen annulation product **51** with its proposed mechanism.

with N-radical **II**. The occurrence of current efficiency can be attributed to the reduction of Cp_2Fe^+ to Cp_2Fe at the cathode within an undivided cell. Upon the decomposition of **III**, the CF_2H radical is generated, which subsequently engages with **57** to yield vinyl radical **IV**. Based on computational simulations (Scheme 20), it was determined that the 7-ortho cyclization (path-a) exhibited a higher kinetic preference in the present process compared to the 6-*ipso* cyclization (path-b) or 1,5-H abstraction (path-c). To generate the radical intermediate **V**, the C-radical **IV** proceeds along a regio- and stereoselective pathway, designated as path-a. The dibenzazepine product **59** is ultimately formed through the process of rearomatization of **V**, which occurs as a result of the removal of an electron (e^-) and a proton (H^+).

The electrocatalytic synthesis of chlorotrifluoromethylated pyrrolidine derivatives has been documented in the years 2018 and 2020. The process of anodically linked electrolysis involves the simultaneous generation of two reactive radical species at the anode, followed by their subsequent convergence and beneficial reaction. This procedure enables the desired outcome to be achieved. The addition of these intermediates to the alkene is regulated by a redox-active Mn catalyst. The eneyne cyclization products can be synthesized with a high degree of stereoselectivity in relation to the alkene geometry by employing 2,2′-bipyridine as the ligand. Remarkably, when subjected to only slightly modified reaction conditions, the 1,6-enyne substrates **60** underwent difunctionalization, resulting in the formation of chlorotrifluoromethylated pyrrolidines **61**. In this experimental protocol, lithium perchlorate ($LiClO_4$) was employed as the electrolyte, while a combination of CH_3COOH and CH_3CN served as the solvent within an undivided cell.

The reaction is conducted at a temperature of 22 °C for a duration of 3 hours. In this particular instance, the utilization of the (bpy)-bidentate ligand significantly enhanced the stereochemical properties of the products **61**, as depicted in Scheme 21.[44,45]

A cyclic system was developed Scheme 21 for the purpose of facilitating the electrochemical ene-yne cyclization. Anodically



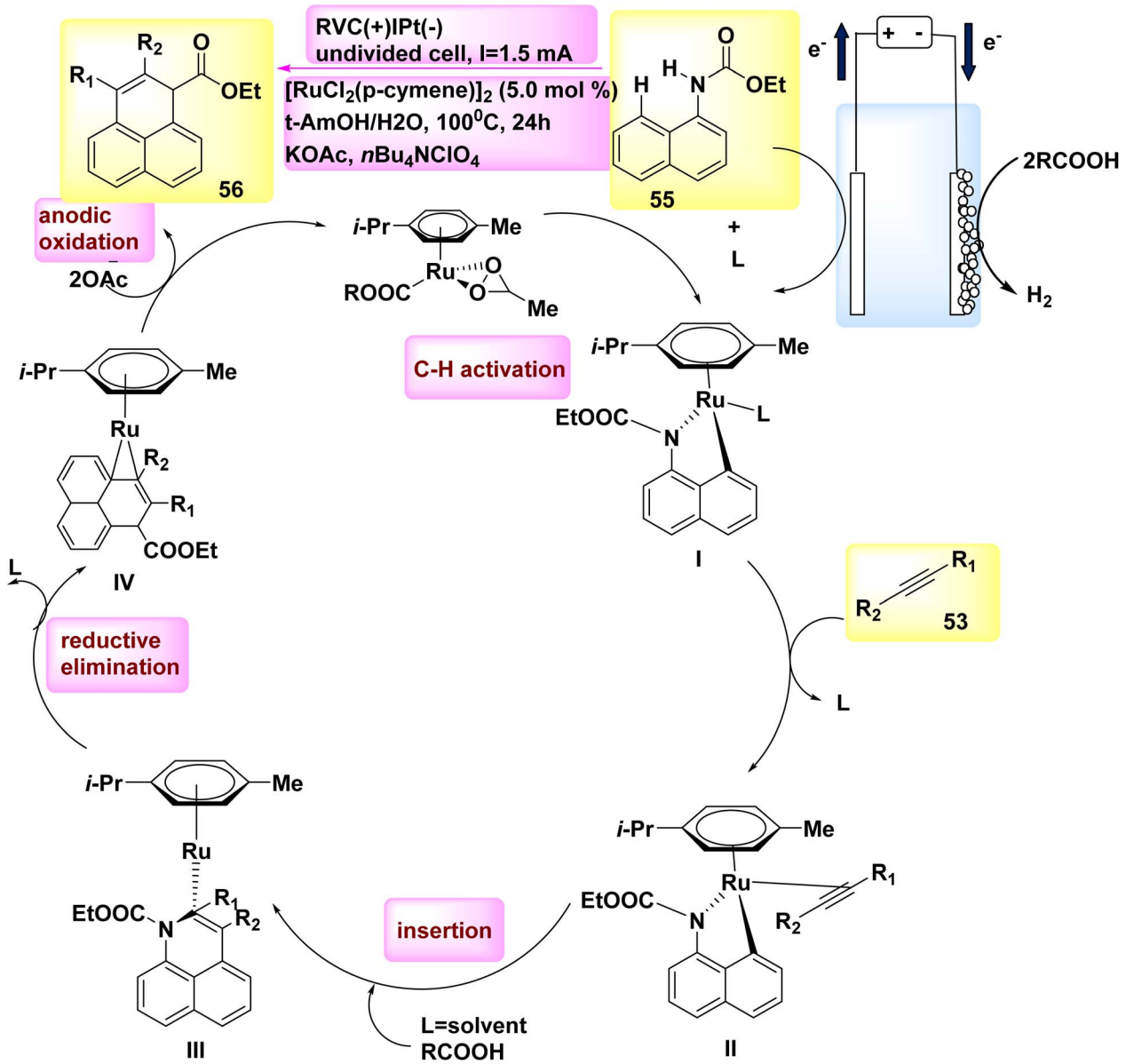
Scheme 18 Electrochemical synthesis of substituted isoquinolone **54** with its proposed mechanism.

connected electrolysis facilitates the participation of catalysts and functional group donors in promoting the anodic events A and B. A C-centered radical with sp^3 hybridization is formed through the addition of the transitory and highly reactive CF_3 radical to the trisubstituted alkene **60**. The aforementioned intermediate is subsequently subjected to an intramolecular addition reaction with the alkyne, resulting in the formation of an intermediate containing an alkenyl radical, denoted as **II**. The highly reactive C-centered radical is employed in close proximity to an open-shell metal complex ([Mn^{III}]–Cl), where it undergoes a conversion into an alkenyl chloride **61** through a radical atom transfer process. In the present experimental protocol, the catalyst experiences a process of single-electron oxidation at the electrode, leading to a subsequent transition back to the Mn^{II} oxidation state.

In 2019, Gao and colleagues published an exceptional method for synthesizing pyrrole derivatives. Pyrroles **64** were synthesized in an undivided cell utilizing a carbon plate as the anode and a Pt cathode. By subjecting easily obtainable arylacetaldehydes **62** and primary amines **63** to electrolysis at a constant current of 10 mA, a wide range of C_4H_5N derivatives were produced in high yields (Scheme 22). In addition, in humble settings, this reaction may exhibit robust resistance to functional groups and consistent reproducibility.[46]

In the year 2019, an electrolytic operation was successfully conducted without the presence of an external oxidant and the utilization of a catalyst. The approach involves a controlled and straightforward electrolysis process of sodium sulfinates **31**. This is carried out in an undivided cell, utilizing a solvent mixture of methyl cyanideor water, along with the addition of Et_4NClO_4 salt as an electrolyte. The electrochemical trifluoromethylation and cycling of *N*-arylacrylamide **65** were conducted under conditions of constant current, utilizing CF_3-SO_2Na **66**. This notion has the potential to be applied to a diverse array of functional categories. A yield of 74% was achieved in the synthesis of the desired compound, $C_{12}H_{11}F_3INO$ **67** (Scheme 23).[47]

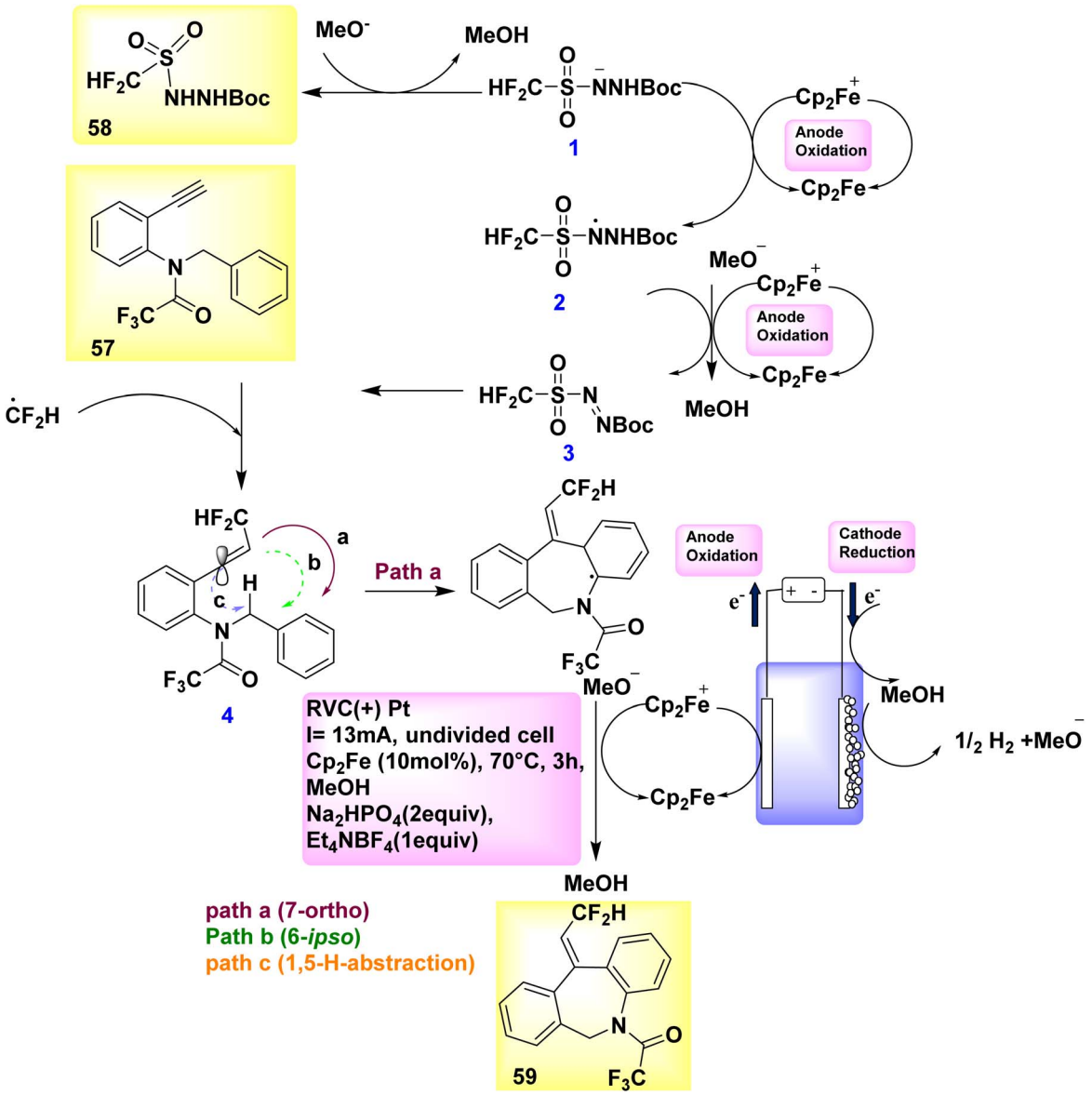
A corresponding radical is generated in a desulfurative process, leading to the conversion of sulfinate anion **I** into CF_3 radical. Within the specified location, the CF_3 radical initiates an assault on the alkene **65**, resulting in the formation of intermediate **II**. Subsequently, intermediate **II** undergoes a transformation process, leading to the formation of intermediate **III**. Under conditions of anodic oxidation, a higher degree of aromatization leads to the formation of the same product **67**. At the cathode, the process of reduction occurs where H_2 cations undergo simultaneous reduction, resulting in the production of molecular H_2.



Scheme 19 Electrochemical synthesis of rhodium(III) catalysed annulated product **56** with its proposed mechanism.

In the year 2019, Hu *et al.* introduced a novel methodology for synthesizing N–O heterocycles. A Cu-catalyzed electrosynthesis was employed to develop an aza-Wacker cyclization process. The utilization of this tandem methodology enables the occurrence of substrate transformations that yield R – intermediates, so significantly broadening the scope of action. Alkene-substituted oxazolone **69** was synthesized under moderate conditions. The experiment commenced by employing electrochemical oxidative amination on crotyl *N*-phenylcarbamate **68**, utilizing a Cu catalyst. It was found that the target compound **69** could be synthesized under ambient conditions using a partitioned cell setup. The experimental setup included CH_3OH as the solvent, C-fiber as the electrode, $LiClO_4$ as the electrolyte, diacetoxycopper as the catalyst, sodium acetate as the base, and a constant current of 3 mA.[48]

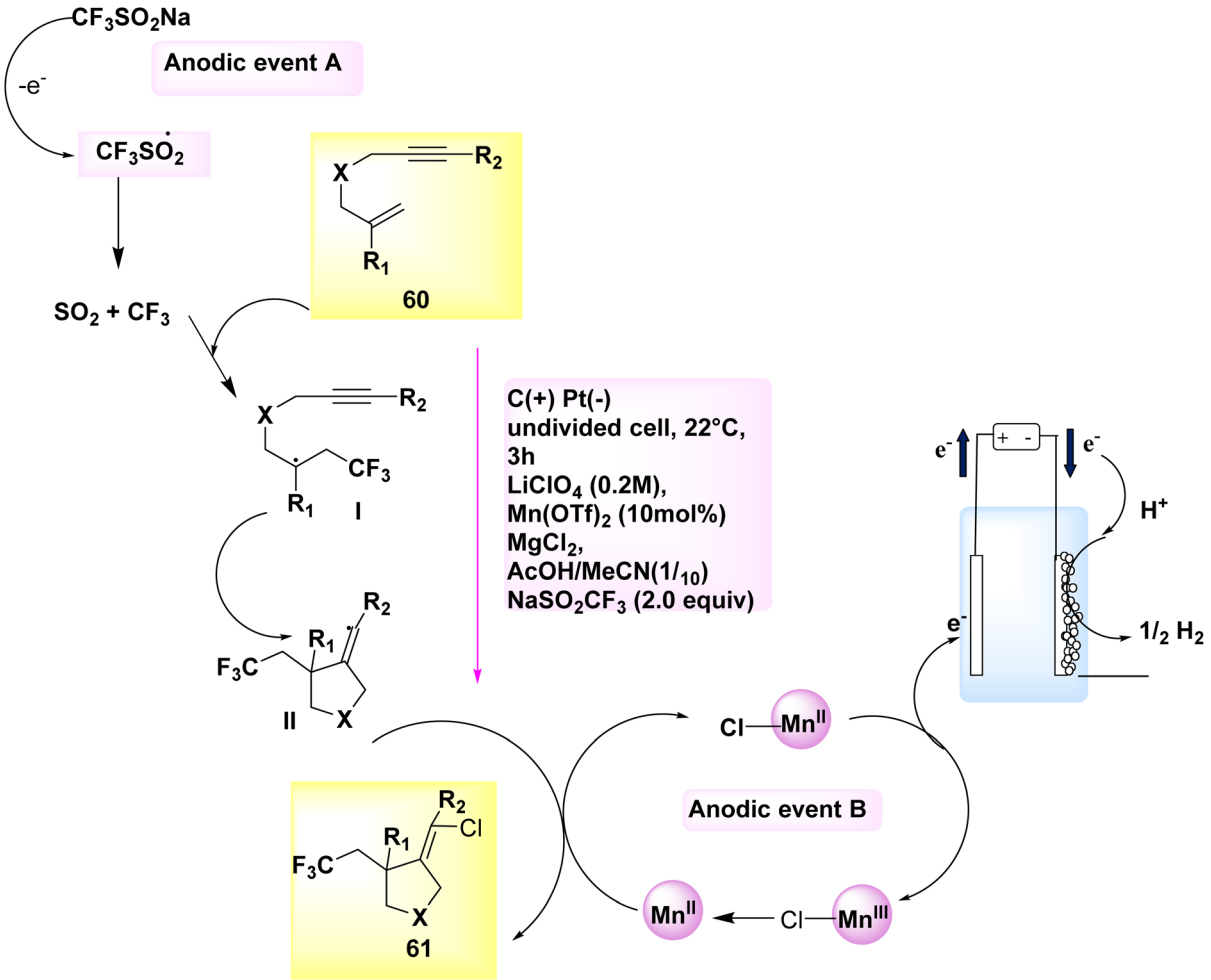
The aforementioned observations described as the basis for the evoluation of the electrochemical formal called aza-Wacker cyclization mechanism, as depicted in Scheme 24. Initially, substrate **68** undergoes a reaction with the base, **I**, resulting in the formation of an adduct. Subsequently, this adduct is subjected to oxidation at the anode, leading to the generation of an NH_2, denoted as **II**. The radical undergoes cyclization to yield radical **III**, which is subsequently captured by copper(II) to form copper(III) alkyl intermediate **IV**. After undergoing a base-catalyzed elimination reaction, the resulting product is identified as product **69**, which leads to the formation of a copper(I) species. In order to reinitiate the catalytic cycle, the latter undergoes oxidation at the electrode, resulting in the constitution of copper(II).



Scheme 20 Electrochemical synthesis of fluorinated dibenzazepine **59** with its proposed mechanism.

In the year 2019, there was a proposal to utilize a dehydrogenative cyclization cascade for the synthesis of benzimidazolone and benzoxazolone derivatives with high levels of substitution. This approach involves the generation of homo- and heterocyclic ringed structures. The benzimidazolone **71** and benzoxazolone **73** are fundamental structures found in various pharmaceutical drugs. The process of biscyclization/dehydrogenation involves the conversion of arylamine-tethered 1,5-enynes into functionalized benzanellated heterocycles, exhibiting precise control over regioselectivity. The mechanism of H_2 evolution is responsible for driving electricity-powered oxidative reactions, hence eliminating the need for metal catalysts and oxidants altogether. The electrochemical dehydrogenative interconversion of an easily accessible urea substrate **70** was investigated in Scheme 25. In order to mitigate the susceptibility of compound **72** to base-promoted ionic hydroamidation, deliberate efforts were made to exclude any base additions.

In contrast, the substrate exhibits stability even in an acidic milieu. Researchers successfully synthesized the benzimidazolone product **71** with a yield of 83% by performing an electrolytic method at a temperature of 100 °C. In this experimental procedure, a consistent current of 10 mA was utilized, along with $C_2HF_3O_2$ as an additive and dimethylformamide as the solvent. The anode used was made of reticulated vitreous C, while the (−) was composed of Pt. One possible approach for synthesizing functionalized benzoxazolones **73** from propargylic carbamates **72** involves employing an electrochemical cyclization cascade, Scheme 25. The yield was notably enhanced by conducting the electrochemical process in a solvent of TFE and including $C_2H_4O_2$ as an addition while maintaining a temperature of 80 °C.[49]



Scheme 21 Electrochemical synthesis of chlorotrifluoro methylated pyrrolidines **61** with its proposed mechanism.

To generate an NH_2, the arylamine moiety **70** of the starting material is initially subjected to anodic oxidation, followed by deprotonation, and subsequently undergoes a 5-*exo*-dig cyclization to form a vinyl radical **II**. The intramolecular 6-*endo*-trig cyclization of **II** leads to the formation of **III**, which possesses an acyclic carbon structure. As an alternative, compound **II** can undergo a 5-*exo*-trig cyclization reaction to yield compound **IV**. Subsequently, compound **IV** can be transformed into compound **III** through the involvement of an intermediate a tricyclic radical **V**. The vinyl radical cyclization typically results in the formation of both the 6-endo and 5-exo products, namely **71** and **73**, in combination.

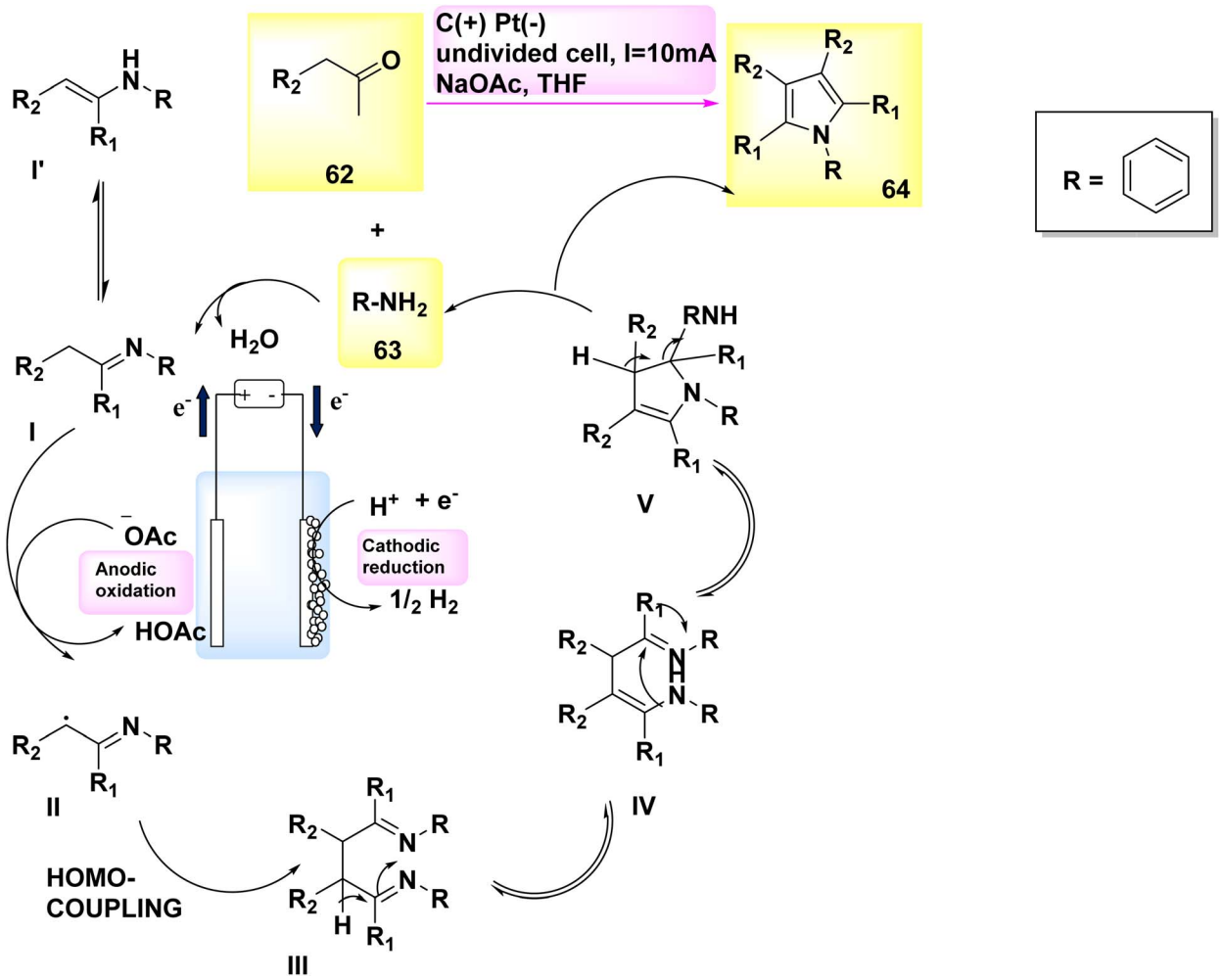
The electrochemical dehydrogenative cyclization of *N*-benzylamides **74** was observed in the year 2019. In an undivided cell at room temperature, a Pt-plate anode and a graphite rod cathode were utilized. A steady current of 10 mA was supplied for duration of 2 hours. The inhibition of oxidative degradation of the products was effective, resulting in the production of 4*H*-1,3-benzoxazines **75**, Scheme 26, irrespective of the substituents at the benzylic position. The proposed methodology has the ability to synthesize 4*H*-1,3-benzothiazines **75**.[50]

The substrate **74** under went oxidation of its benzylic moiety by electrolysis conditions, resulting in the radical cation **I** formation. Subsequently, this radical cation underwent cyclization and deprotonation, leading to the formation of the intermediate radical **II**. Ultimately, the compound underwent oxidation followed by rearomatization, resulting in the formation of the cyclic product with a yield of 89%.

In the year 2019, a cupra electro-catalyzed electrolytic approach was successfully employed to synthesize isoindolones of significant synthetic importance. In a simplified and uncomplicated cellular configuration, Cu work as a catalyst for the electro-oxidative activation of CH or NH bonds in benzamide **76** when combined with terminal alkyne **77**.

Cu(II) acetate, which is characterized by its flexibility, affordability, and non-toxicity, is utilized as a catalyst. The optimal conditions for synthesizing isoindolone **78** were determined to be at a temperature of 100 °C in dimethylacetamide, utilizing catalytic amounts of $Cu(OAc)_2 \cdot H_2O$ and NaOPiv as the most effective additive.[51]

A potential catalytic cycle was proposed, supported by thorough mechanistic research. The cycle initiates with the coupling of substrate **76** and concludes with the oxidation of



Scheme 22 Electrochemical synthesis of 1,3,4-triphenyl pyrrole **64** with its proposed mechanism.

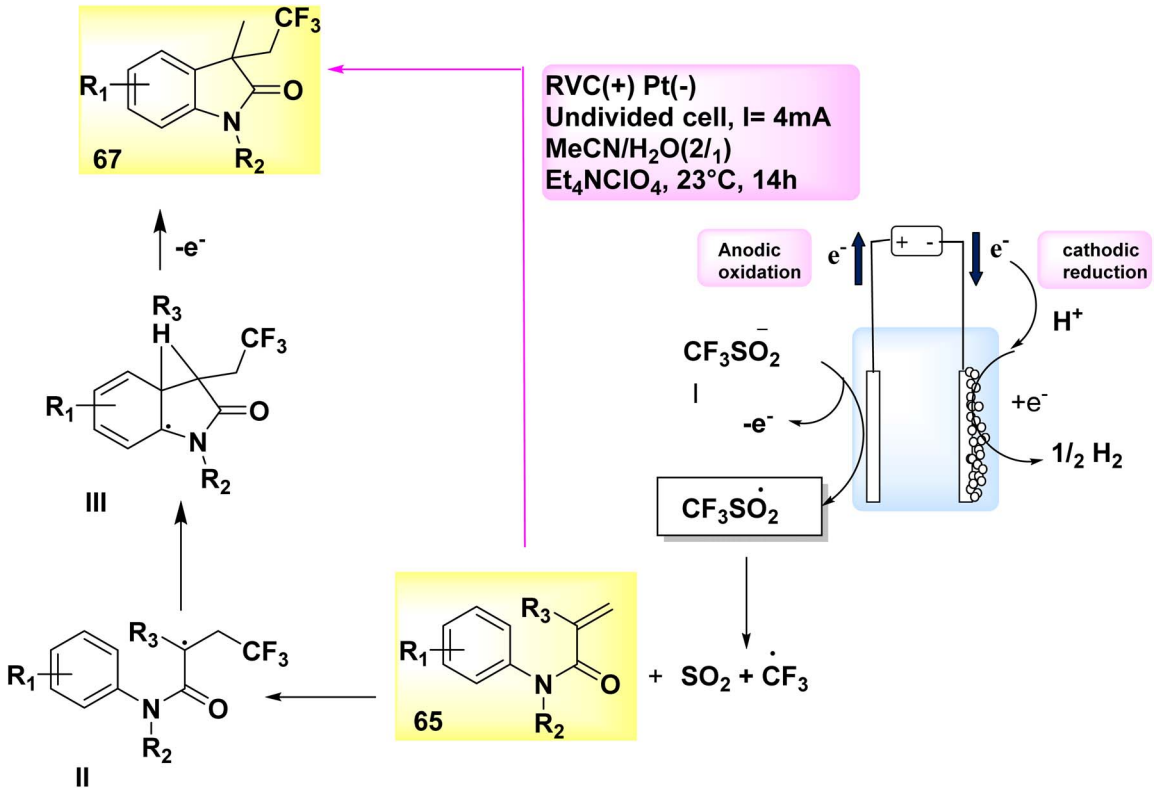
Cu(II) to generate the active catalytic Cu(III) carboxylate species Scheme 27. The Cu(III) intermediate **IV** is then formed through a direct CH activation when the electron-deficient benzamide **II** is present with a carboxylate. The alkynylated arene **VII** is synthesized through the metallization of the terminal alkyne **77** with the assistance of carboxylate, followed by reductive elimination to create the desired isoindolon **78**. The Cu(I) complex is oxidized at the anode to regenerate the catalytically active Cu(III) species.

The electrocatalytic process of C–H activation using isocyanides is being investigated. At ambient temperature, in the absence of oxidizing agents, the readily accessible Co-catalysts also facilitate efficient electrooxidation carbon–hydrogen/nitrogen–hydrogen functionalization of benzhydrazides **52** employing cost-effective CO. The metallic electrocatalysis is facilitated by the utilization of a detachable pyridyl support in a practical undivided cell configuration. This design allows for a cost-effective method to synthesize physiologically significant imidates **93** and **94**. In a broad sense, the utilization of electricity hinders the activation of CH bonds by equimolar amounts of d-and f-block elements, which are both costly and detrimental. However, this hindrance can be overcome with the use of a lasting Co catalyst that is abundant in the Earth's aqueous environment. The observation that only benzhydrazides **52** shown the capability to facilitate the insertion of isocyanide highlights the inherent challenges associated with the Co-electrooxidative C–H activation mechanism (Scheme 28).[52]

A possible catalytic cycle was described based on mechanistic discoveries Scheme 29. An intermediate, referred to as **II** or **II′**, is generated through the process of simple carboxylate-assisted CH activation. Additionally, a six-membered Co(III) cycle, known as **III** or **III′**, is also synthesized. The formation of **III**/**III′** is achieved through consecutive migrating insertion. The production of the necessary products, specifically **79** or **80**, is achieved by the process of reductive elimination. This process also results in the formation of Co(I) species.

In conclusion, the utilization of anodic oxidation serves as a means to regenerate the catalytically active Co(III) carboxylate complex. This approach eliminates the requirement for costly and dangerous metal oxidants, while generating molecular H_2 as the individual byproduct.

In the year 2019, a comprehensive electrocatalytic strategy (Scheme 30) was formed for the CH/NH annulation process.



Scheme 23 Electrochemical synthesis of 1,3-dimethyl-3-(2,2,2-trifluoroethyl)indolin-2-one **67** with its proposed mechanism.

This technique utilized economical and easily accessible Co salts.

The discovery of diynes **81** has been unveiled. The electro-oxidative Co-catalysis occurred in a elementary undivided cell at benign reaction conditions, demonstrating outstanding compatibility with various functional groups. The utilization of electricity obviates the need for potentially dangerous and/or costly chemical substances. The experiment involved the utilization of a reticulated vitreous C(+) and a Pt(−). The reaction was carried out in a solvent known as TFE at a temperature of 60 °C.[53,54]

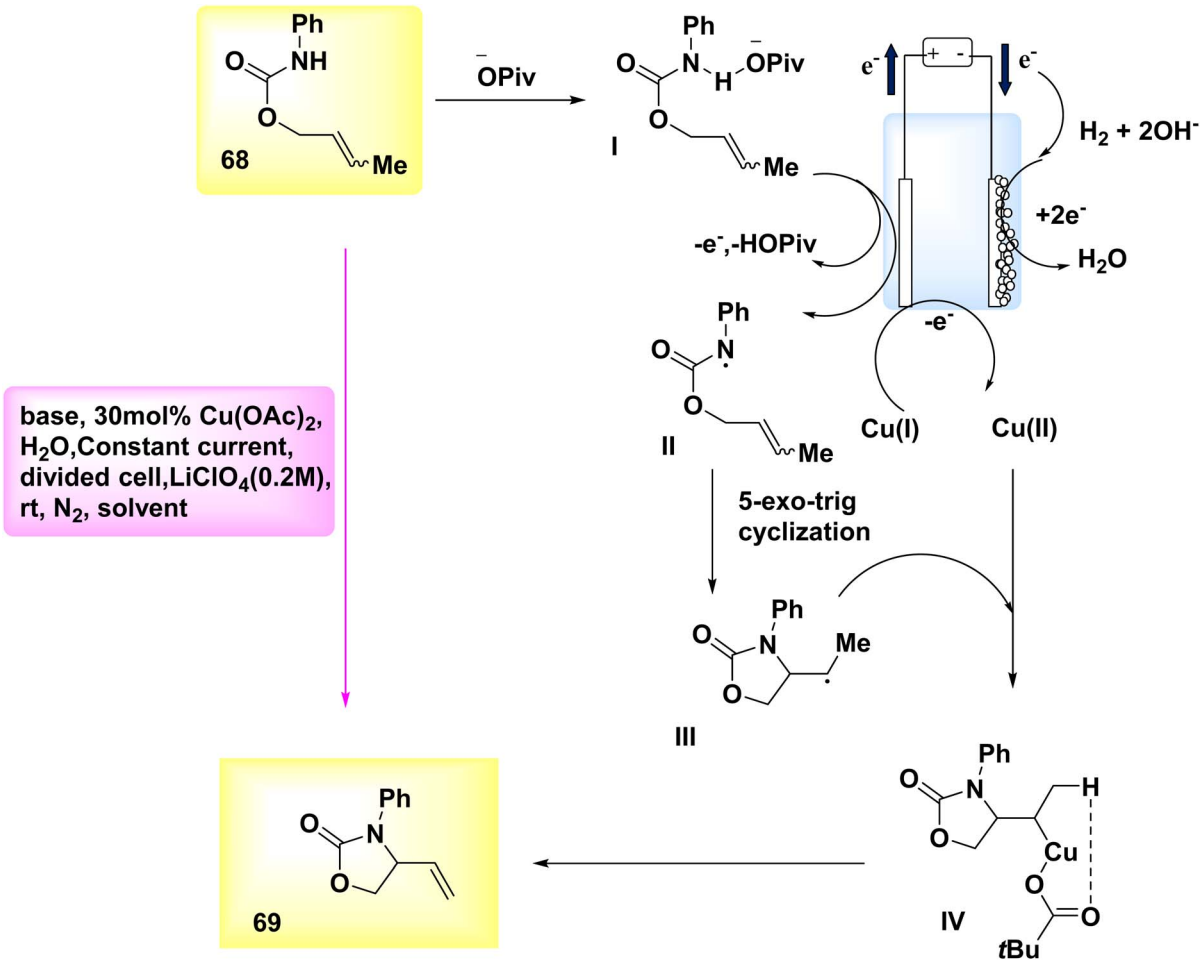
The initial step in the production of the catalytically efficient Co(III) salt involves the utilization of anodic oxidation. The subsequent step involves the generation of Co(III) species through a direct C–H Coation process with carboxylate support. The synthesis of Co(III) complex **II** proceeds through migratory insertion, wherein the Co(I) intermediate and isoquinolone **82** compound are simultaneously released, developed by reductive elimination. The Co(III) carboxylate, which exhibited catalytic activity, was restored through the process of anodic oxidation. In general, Co-electrocatalysis is capable of generating H_2 without the need for stoichiometric quantities of expensive and hazardous oxidizing agents.

Aza-PAHs, nitrogen-doped polycyclic aromatic hydrocarbons, find extensive applications within the realm of materials research. In the year 2019, a method including the utilization of annulation or Rh-catalyzed activation was employed to achieve the electrochemical synthesis of polycyclic aromatic hydrocarbons. The regio and chemo selectivity observed in this study was attributed to the functional properties of *o*-methyl amidoxime. Amidoxime **83** and diphenylacetylene **84** were employed as initiators for the reaction to achieve the intended objective. The target product **85** was isolated through the utilization of KOAc as a base, methanol as a solvent, and a current of 2 mA. The results demonstrated that the inclusion of a little amount of R-carboxylic yielded favorable results, with $(CH_2)_6(CH)_3(CCO_2H)$ acid exhibiting the most significant effects.

The effectiveness of the process was further improved by the utilization of a rhodium catalyst with a positive charge. This catalyst facilitated the synthesis of product **85** with a yield of 90% at a temperature of 35 °C (Scheme 31).[55]

In 2019, significant advancements were made in the field of metallaelectro-catalyzed annulations and activation. Consequently, a variety of carbon–hydrogen/nitrogen–hydrogen functionalizations were found to be feasible, both intramolecularly and intermolecularly, for alkyne **87** annulations. These functionalizations demonstrated significant levels of durability, sensitivity, and selectivity towards functional groups. The electrochemical reaction between imidate **86** and asymmetrical alkyne **87** resulted in the formation of the desired isoquinoline **88** with a yield of 90% (Scheme 32). In the experimental setup, methanol (CH_3OH) is employed as the solvent, catalyst, while NaOPiv and PivOH are introduced. Additionally, Pt-plate and GF are utilized as the negatively and positively charged electrodes, respectively, in an undivided cell configuration.[56]

Scheme 33 proposes a plausible mechanism. The compound $Cp^*Rh(OPiv)_2$ **I** is synthesized through the interaction of NaOPiv



Scheme 24 Electrochemical synthesis of alkene-substituted oxazolone **69** with its proposed mechanism.

with a catalyst precursor. This resulting compound then reacts with substrate **86**, leading to the formation of the cyclometalated complex **II** *via* a straightforward CH-activation process. The rhoda(III) cycle **IV** is then generated by the processes of alkyne coordination **III** and migrating insertion.

The rhoda(IV) cycle **V** efficiently generates intermediate **VI** by the process of anodic oxidation. The regeneration of catalyst **I** is subsequently facilitated through anodic oxidation, a process that can be accelerated by the presence of oxygen. Aerobic and anodic oxidations have been identified as potential mechanisms for the reoxidation of Rh **II**–Rh **III**. The rhoda(III) cycle **IV** has the capability to directly provide product **88**, along with a diminished amount of Rh (rhodium) that has the potential to undergo reoxidation.

The process of cathodic proton reduction exclusively yields molecular H_2 as a stoichiometric byproduct, a conclusion that has been substantiated through meticulous headspace gas chromatography examination.

In the year 2019, a novel method for direct electrochemical synthesis was developed, which involved the breakage of carbon–carbon bonds without the need for a catalyst (Scheme 34). The most favorable outcomes were achieved with the direct electrolysis of substrate **89** under a consistent current of 8 mA, utilizing a blended electrolyte solution composed of MeCN/H_2O and nBu$_4$NBF$_4$.

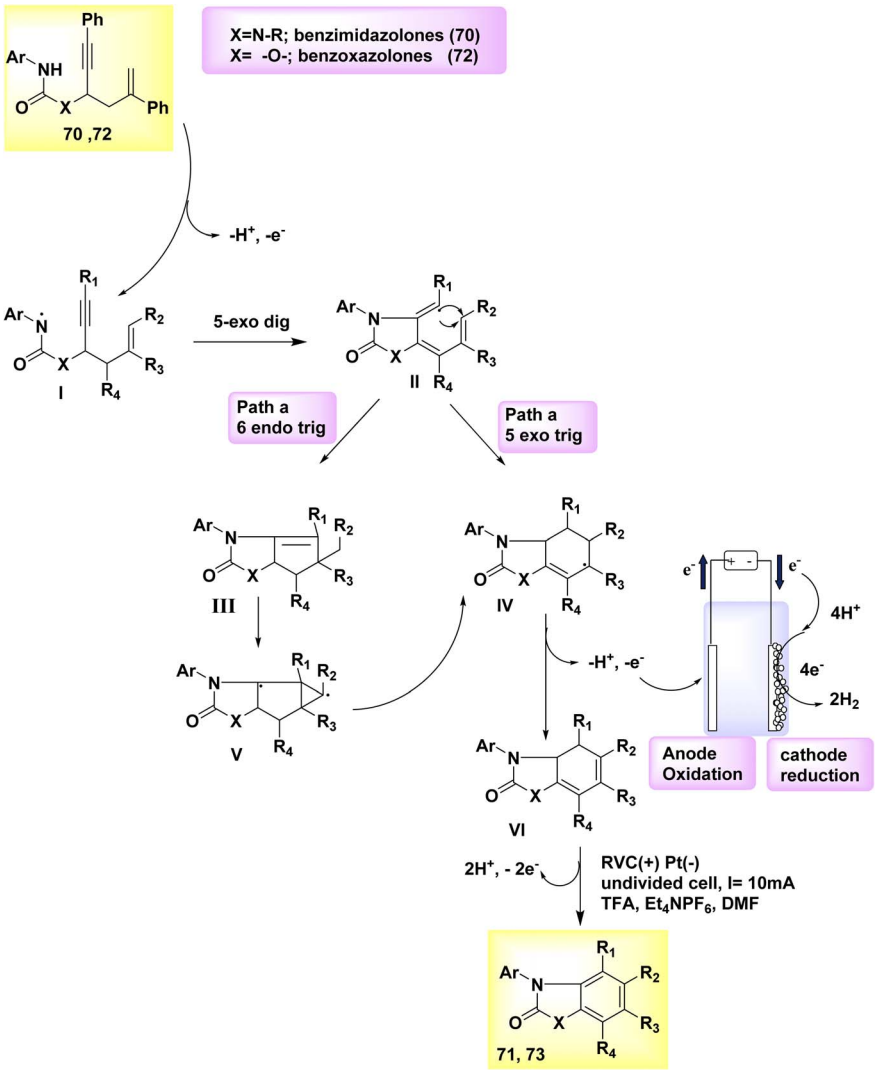
The 9-membered lactam **90** was obtained with a yield of 98% without the use of any extra bases or catalysts.[57]

A mechanism that is considered feasible is suggested, drawing upon our mechanistic discoveries (Scheme 34). The NH bond in compound **89** undergoes anodic oxidation, resulting in the formation of intermediate **I**. The intermediate undergoes cyclization, resulting in the formation of radical **II**. This radical then undergoes selective cleavage of a C–C bond, leading to the production of radical **III**. Ultimately, the medium-sized lactam **90** can be synthesized through the oxidation of the ketyl radical **III** *via* the transfer of a single electron, followed by proton loss.

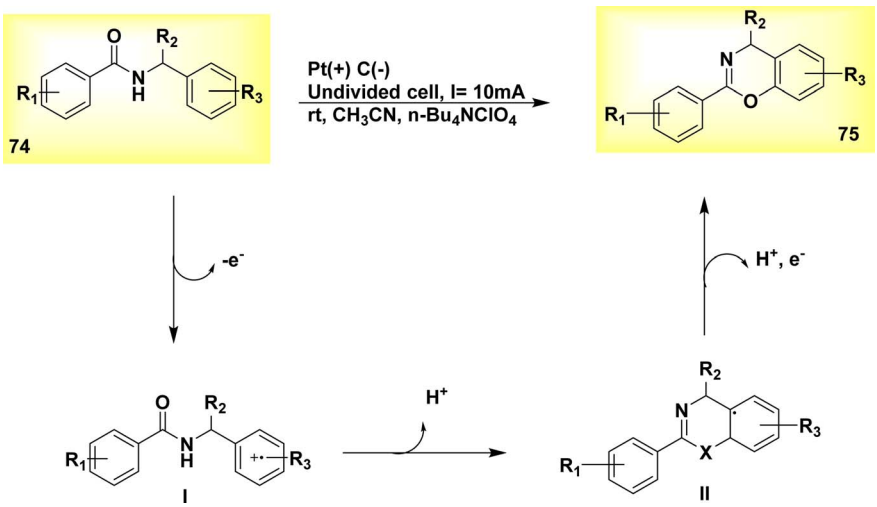
Nevertheless, the possibility of the cationic pathway cannot be disregarded due to the presence of two closely spaced oxidative waves at **89** in the CV.

In the year 2020, the author and their colleagues presented a viable approach for the electrochemical synthesis of sulfonated 4*H*-3,1-benzoxazines. *N*-(2-(prop-1-en-2-yl)phenyl)benzamide was reacted with *p*-toluenesulfonylhydrazine to produce sulfonated 4*H*-3,1-benzoxazine in a yield of 78% (Scheme 35).

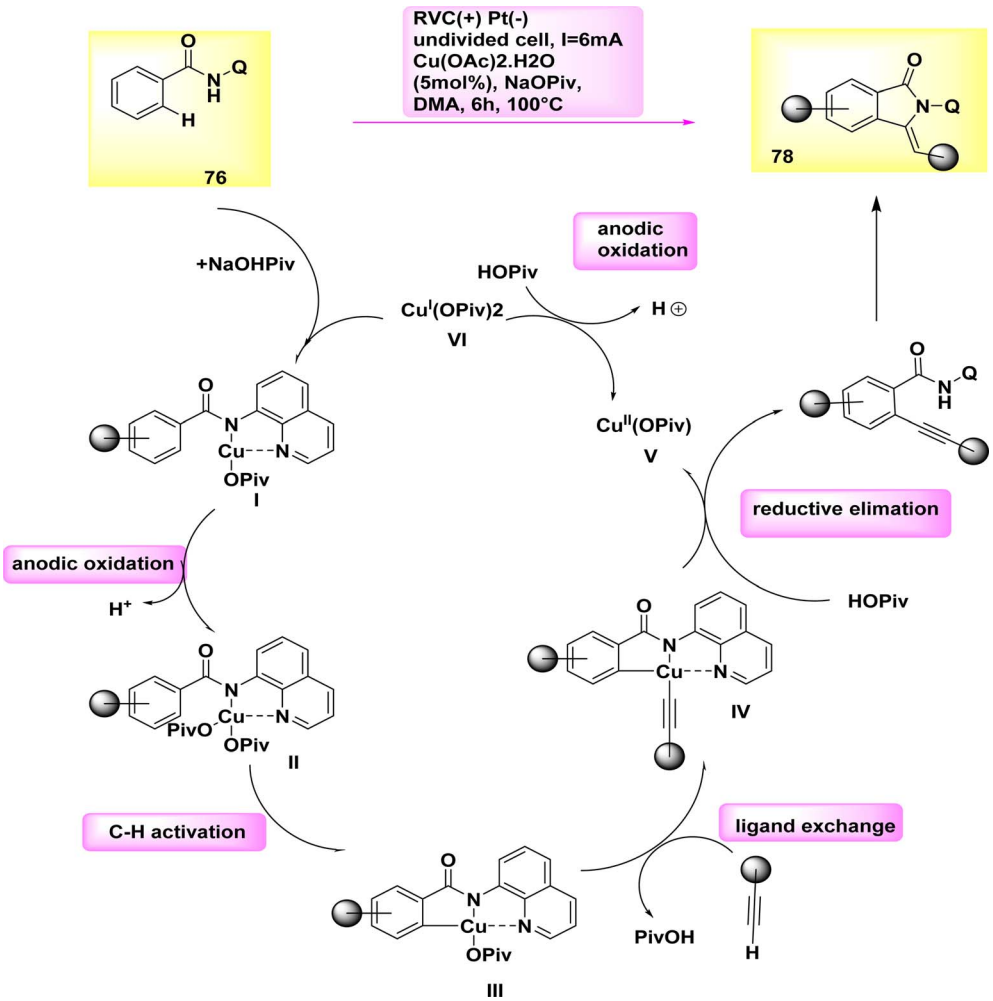
The most favorable outcome was achieved by performing the reactions in an undivided cell with a carbon rod as the anode



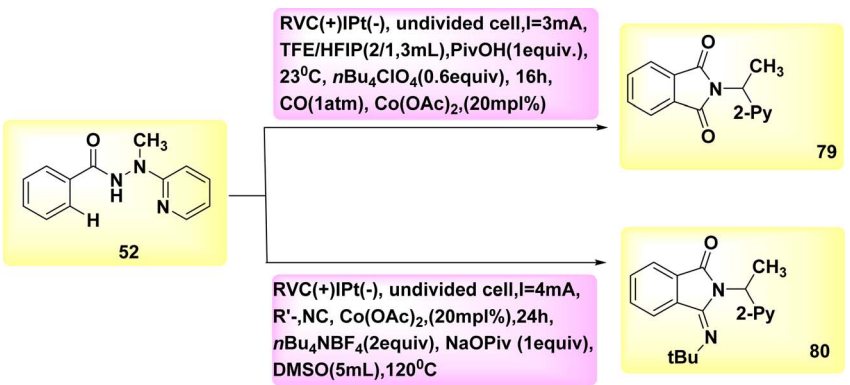
Scheme 25 Electrochemical synthesis of benzimidazolone 71 and benzoxazolone 73 with its proposed mechanism.



Scheme 26 Electrochemical synthesis of benzimidazolone 71 and benzoxazolone 73 with its proposed mechanism.



Scheme 27 Electrochemical synthesis of isoindolone **78** with its proposed mechanism.

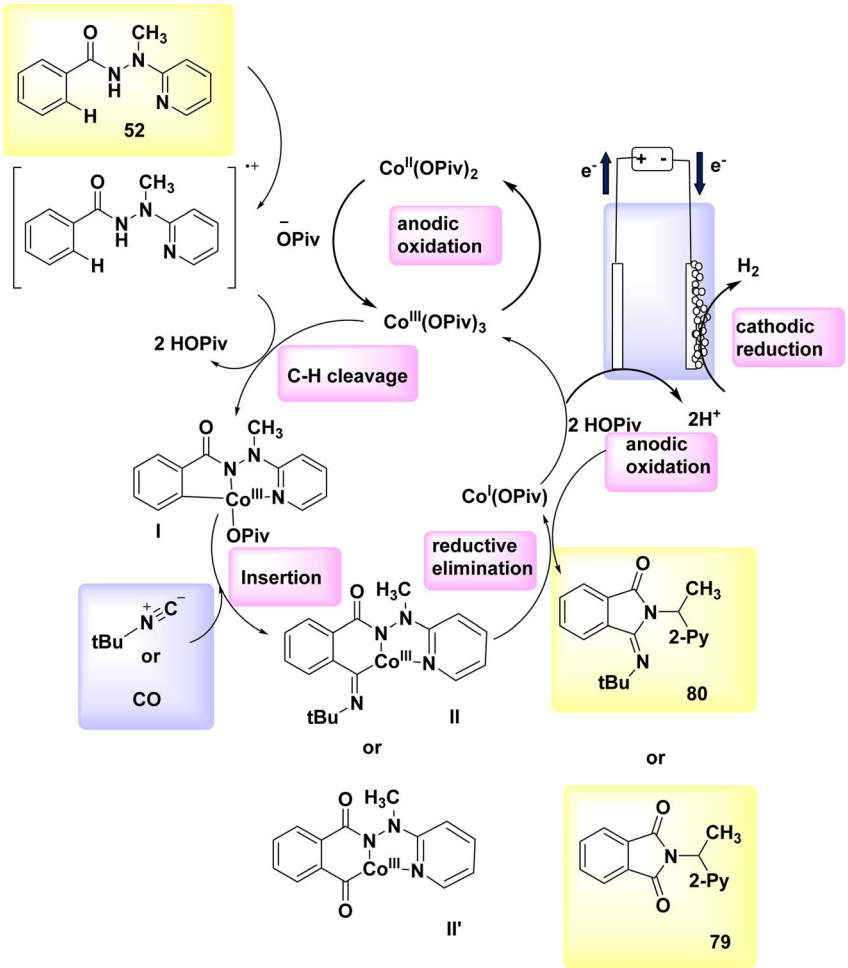


Scheme 28 Electrochemical synthesis of substituted cyclic imidates **79** and **80**.

and a Pt foil as the cathode. The cell was filled with anhydrous MeCN and nBu$_4$NBF$_4$ was used as the electrolyte. The reactions were carried out under galvanostatic conditions at ambient temperature.

The approach exhibits a larger range of substrate compatibility, accommodating diverse functional groups, and operates at ambient temperatures without the need for metal catalysts or external oxidizing agents.[58]

The electro-oxidation and deprotonation of $CH_3C_6H_4SO_2$-$NHNH_2$ **92** led to the generation of the corresponding sulfonyl radical **II**, which subsequently resulted in the liberation of N_2. The sulfonyl radical **II** was subsequently reacted with alkene **91**



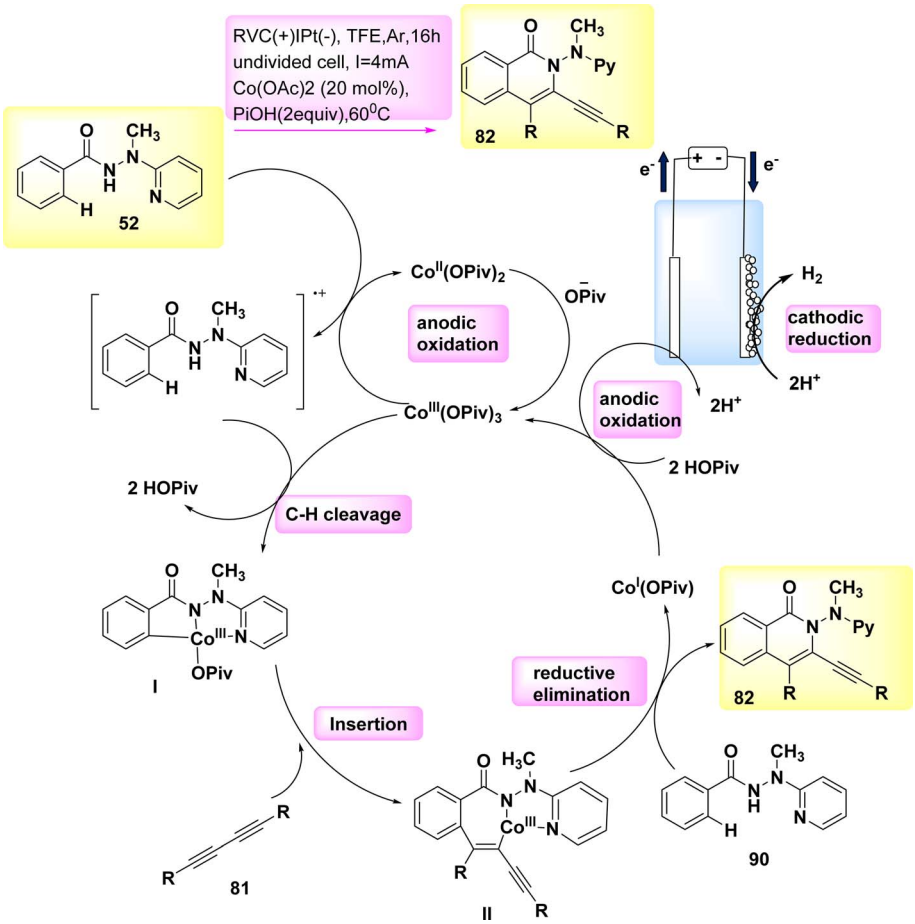
Scheme 29 Electrochemical synthesis of substituted cyclic imidates **79** and **80** with its proposed mechanism.

to generate the radical intermediate **III**. The radical intermediate **III**, might subsequently undergo quick oxidation at the anode, resulting in the generation of the corresponding carbon cation, referred to as **IV**. The sulfonated 4*H*-3,1-benzoxazine **93** was synthesized through a series of reactions involving nucleophilic attack and subsequent deprotonation. The protons underwent synchronous transformation into H_2 through cathodic reduction, Scheme 35.

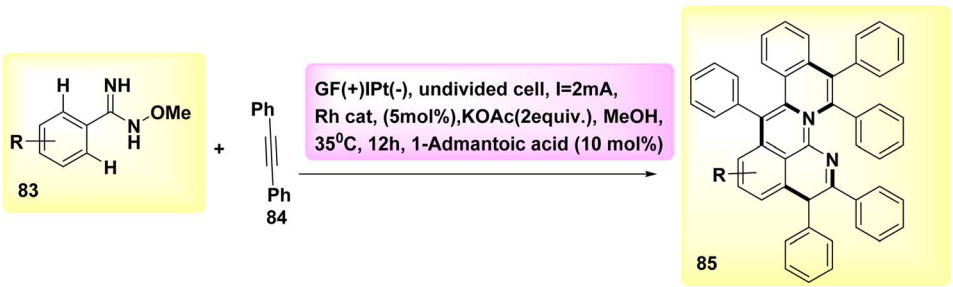
In a study conducted by He *et al.* in 2018 and 2020, the authors documented the synthesis of pyrrolidines **96** and tetrahydropyridines **97** derivatives using a dehydrogenative annulations technique. This method utilized readily available chemicals, Scheme 36. In this methodology, the utilization of a catalytic quantity of a redox catalyst based on phenothiazine facilitates efficient and selective intermolecular radical reactions of $C_8H_{12}O_3$ compounds. The utilization of this approach is currently under consideration as a means to promote diverse oxidative radical processes of 1,3-dicarbonyl molecules.[59,60] In this study, the electrolysis of *N*-allyl amide **94** with dimethyl malonate **95** was conducted. The optimal reaction system was identified as HCO_2Na (0.3 equivalents) serving as the base additive, along with phenothiazine (20 mole%) acting as the redox catalyst. This system was employed in a refluxed mixture of *t*BuOMe, MeCN, and H_2O, with a ratio of 20 : 3 : 1. The pyrrolidine derivative **96** was synthesized, resulting in a yield of 70%, using the given conditions. A reverse voltage converter (RVC) anode and a Pt (Pt) cathode were employed.

The utilization of a β-ketoester as the coupling partner in the reaction led to the production of a tetrahydropyridine product **97** by a (4 + 2) annulation process, without the generation of a pyrrolidine derivative **96**. The reaction involving the annulation of methyl acetoacetate (a β-ketoester) with an enyne exhibited a unique outcome, resulting in a 13% yield of pyrrolidine and a 53% yield of C_5H_9N product. It is noteworthy to mention that these annulations were not dependent on the use of sodium formate and were advantageous in terms of reduced current densities.

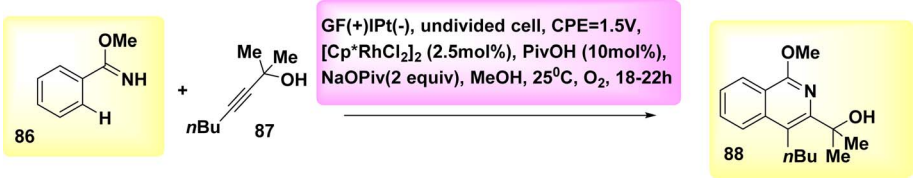
The study's findings have presented a beneficial mechanistic approach in Scheme 36. The initial stage of the process involves the anodic oxidation of A, resulting in the formation of the radical cation $A^{\bullet+}$. Simultaneously, at the cathode, a process takes place where water is reduced to OH^- ion and H_2 gas. The H_2 gas then deprotonates the 1,3-dicarbonyl molecule **95**, resulting in the formation of the anion **I′**, which possesses



Scheme 30 Electrochemical synthesis of isoquinolone **82** with its proposed mechanism.

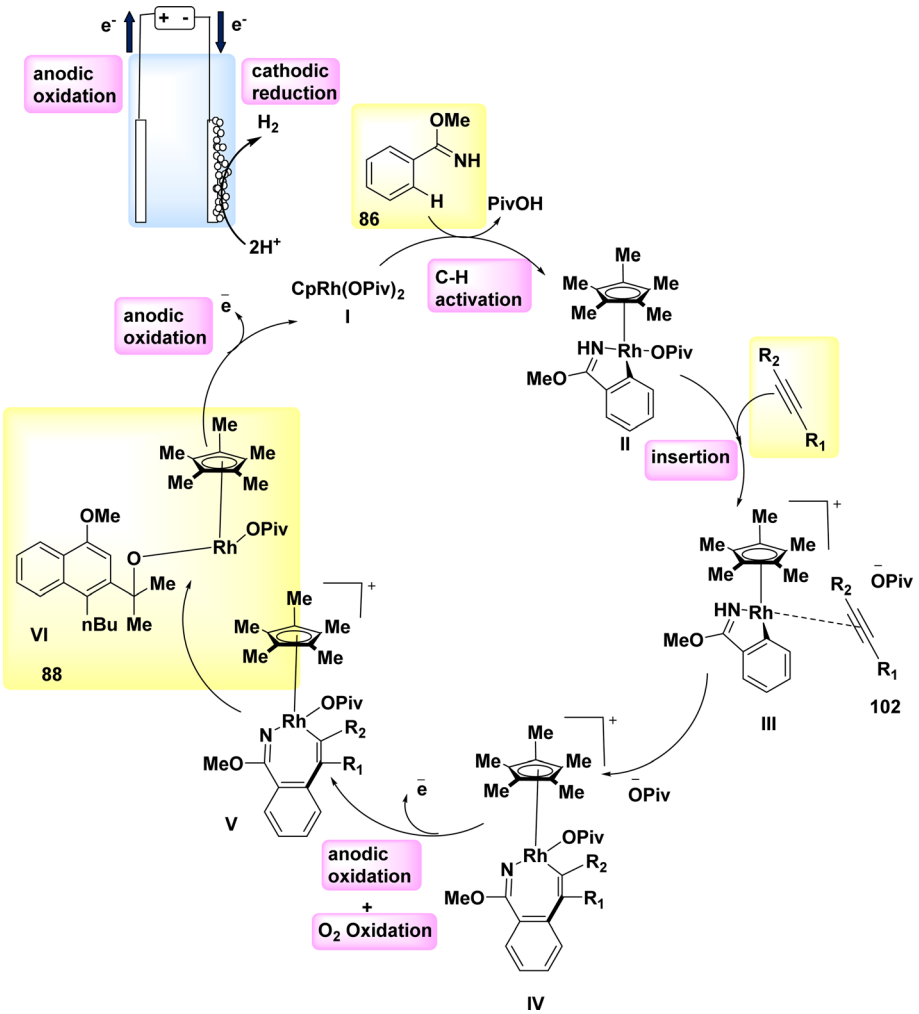


Scheme 31 Electrochemical synthesis of nitrogen-doped polycyclic aromatic hydrocarbons (aza-PAHs) **85**.



Scheme 32 Electrochemical synthesis of isoquinoline **88**.

a higher oxidizability. The process of single-electron transfer results in the development of a radical **II′**. This radical then combines with the alkenyl group of the *N*-allyl amide **94**, leading to the generation of a tertiary C-radical **I**. Intermediate **I** undergoes intramolecular oxidation and subsequent entrapment of its carbonyl group, rather than the Co of the 1,3-



Scheme 33 Electrochemical synthesis of isoquinoline **88** with its proposed mechanism.

dicarbonyl moiety, resulting in the formation of compound **II**. The reaction involving the removal of the tertiary butyl group yields a cyclic carbamate **III**.

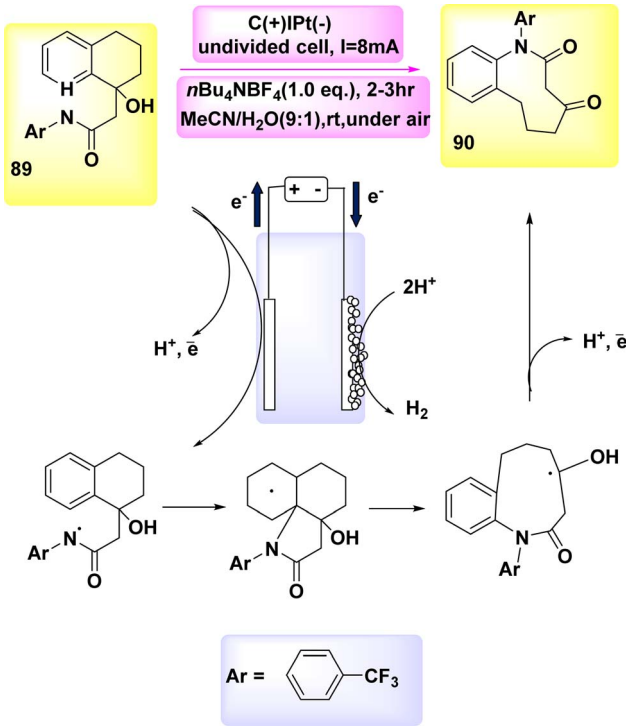
Amides can undergo a reaction with water or hydroxide ion, resulting in the formation of a secondary amine. This secondary amine can then participate in a C(sp^3)–H/N–H cross coupling reaction, leading to the formation of the depicted product **96** (where R═OCH_3). Alternatively, in the presence of intramolecular dehydration, the secondary amine can generate tetrahydropyridine **97** (where R═CH_3).

The 5-*exo*-dig cyclization of NH_2s was employed in the year 2020 to successfully synthesize oxazol-2-ones **99** and imidazole-2-ones **99′**, Scheme 37. The electrosynthesis process relies on the dual functionality of TEMPO as both an O_2-atom donor and a redox facilitator in the formation of NH_2I. The reactions are conducted in a straightforward experimental arrangement under gentle operating conditions.[61]

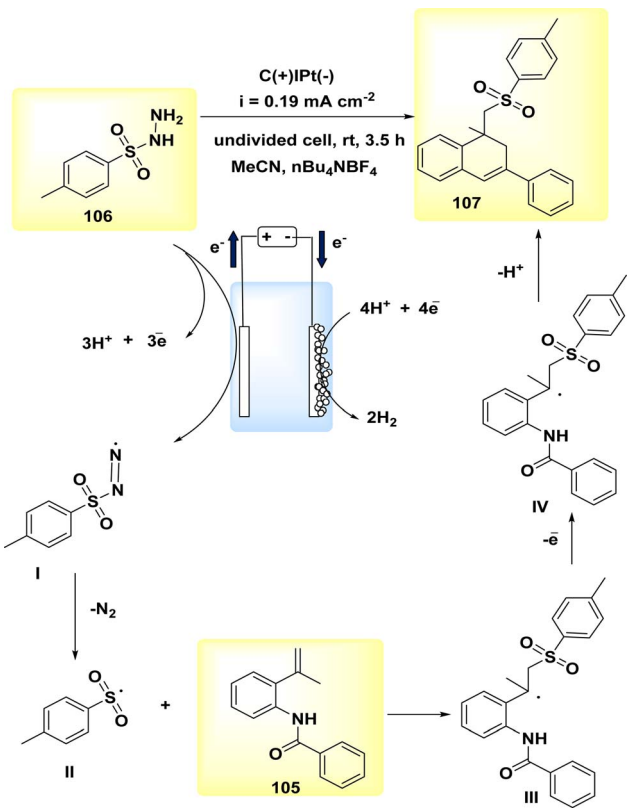
The broad and useful procedure of electrochemically forming isoxazolidine-fused isoquinolin-1(2*H*)-ones **101** through the employment of NH_2s has been documented in 2020 Scheme 37. In the optimization experiment, the compound $C_{17}H_{15}NO_2$ **100** was chosen as the outline molecule. The intended oxidation-induced intramolecular annulation product **101** was successfully synthesized with a yield of 93% under a constant current of less than 2 mA and using nBu$_4$NBF$_4$ as the electrolyte.[62]

Scheme 38 presents a viable technique. Initially, the process involves the cathodic reduction of ethanol, resulting in the formation of ethoxide ions. Subsequently, these ethoxide ions undergo deprotonation, leading to the generation of anion **I**. Subsequently, the anion **I** undergoes selective oxidation in order to produce radical **II**. The compound **II** participates in the 5-*exo*-dig annulation reaction, resulting in the formation of radical **III**. Subsequently, a second annulation reaction occurs, leading to the generation of delocalized radical **IV**. Ultimately, the process of electron-oxidation leads to the rearomatization of **IV**, resulting in the formation of compound **101**.

The year 2020 witnessed the presentation of a very adaptable and potent method for the electrochemical production of Zincke intermediate **I**, which carries a double positive charge. The compound known as phenoxy-acetate **102** exhibited notable reactivity in the context of 2-fold amination reactions. The pyridinium intermediates **I** release amines that induce the



Scheme 34 Electrochemical synthesis of 9-membered lactam **90** with its proposed mechanism.



Scheme 35 Electrochemical synthesis of sulfonated 4*H*-3,1-benzoxazines **93** with its proposed mechanism.

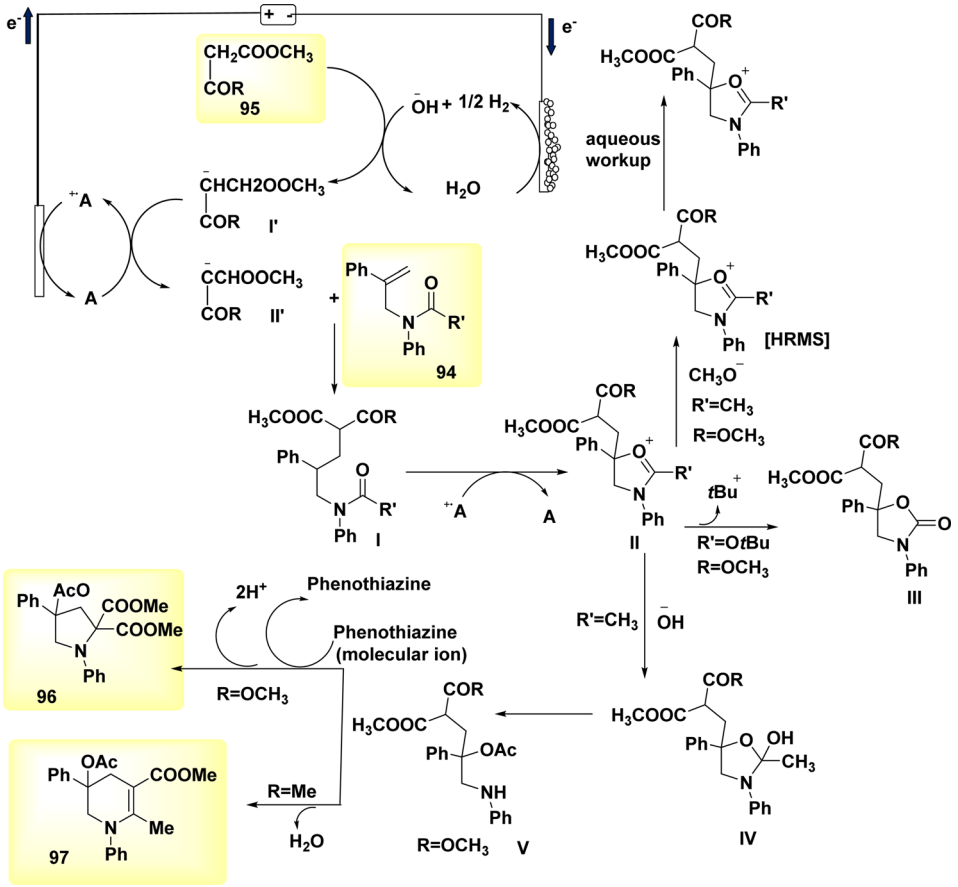
development of an intramolecular heterocycle **103**. A two-step amination process, which demonstrated a yield of 90%, was discovered, Scheme 38. This process is characterized by its lack of reliance on metal catalysts or leaving groups, rendering it a unique and robust approach. The best settings for electrolysis involve a divided cell arrangement with an isostatic graphite-(+) and Pt-cathode, a Thomapor-separator, and a two-step electrolysis process. The first step involves a current density of 5 mA cm^{-2} and a total charge of 3.4 F, while the second step involves a current density of 10 mA cm^{-2} and a total charge of 2.1 F. These electrolysis conditions are conducted at a temperature of 25 °C.[63]

When pyridine is present, the process of anodic oxidation of compound **102** typically leads to the formation of pyridinium intermediates **I**, which are positively charged and exhibit a relatively high level of stability. In the subsequent stage, species **I** undergo a treatment with pyridine, followed by the extraction of an aromatic primary amine group. The ester functionality of phenoxy acetate derivative **102** has the potential to stabilize compound **I** through various interactions, such as π–π, π-non-bonding, or nonbonding cationic connections. Enhanced oxidation reactions can potentially be facilitated by the stability of the e^--deficient substituent. The aforementioned contacts serve the purpose of concealing the positive charge, mitigating shielding effects, diminishing the influence of electron withdrawal, and facilitating increased oxidation of **I**, as illustrated in Scheme 39.

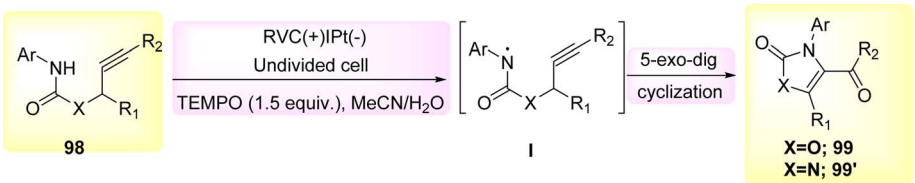
The catalysis of C–H functionalization by Co has occurred as a groundbreaking approach for chemical synthesis in the year 2020. In this study, the synthesis of biologically significant isoquinolones **107** and pyridines **108** was achieved by the utilization of aryl and alkenyl amides **104** or **105**, which were derived from pyridine *N*-oxide. This synthesis method involved C–H or N–H activation, and the use of Co-electrocatalysis. The results of this study demonstrated the potential of Co-electrocatalysis in the synthesis of these important compounds, Scheme 40. The transition was observed at ambient temperature under highly mild reaction conditions and resulted in high yields in a solvent mixture containing H_2O. A cellular system consisting of a single cell is utilized, wherein the cathode is composed of Ptand the anode is composed of RVC. This system is employed to facilitate the operation for duration of 16 hours at a temperature of 23 °C. Consequently, a novel approach has been developed to establish a comprehensive resource economy. This approach utilizes renewable green power as a redox agent, which operates in redox mediator-free conditions and only generates valuable H_2.[64–66]

The experimental conditions for the reaction (Scheme 40-path a) were kept constant, except for the substitution of an RVC anode with a GF anode. This modification resulted in product yields ranging from 70%–76%.[67]

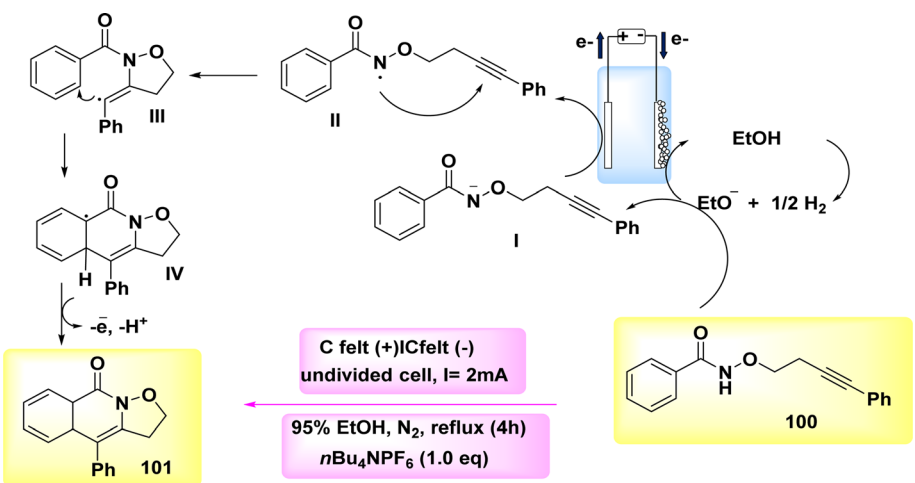
The utilization of glycerol derived from biomass as a medium for electrochemically facilitated CH activation pathways has not been previously recorded in academic literature. The utilization of renewable energies for the formation of C–C or NC bonds, without the production of molecular H_2 as a byproduct, has contributed to the advancement of resource efficiency. The



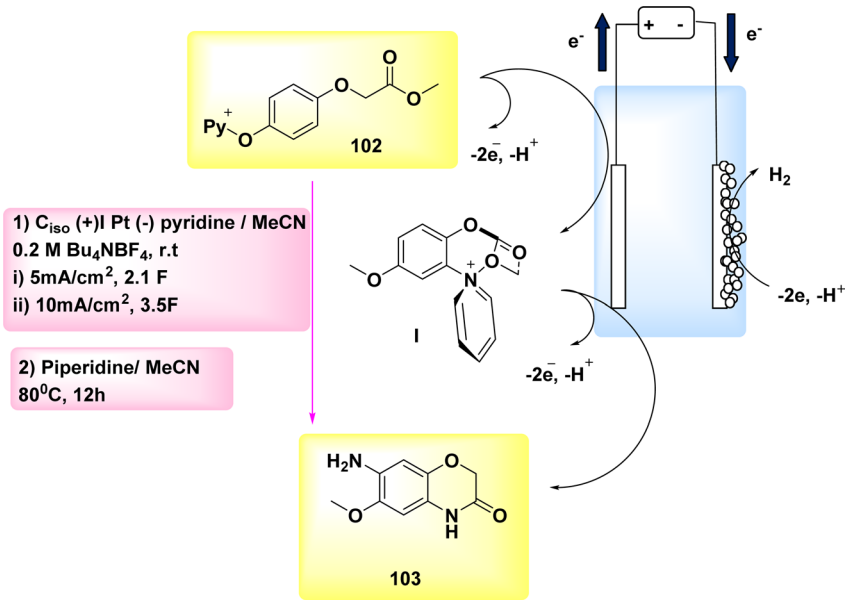
Scheme 36 Electrochemical synthesis of pyrrolidine **96** and tetrahydropyridine **97** with its proposed mechanism.



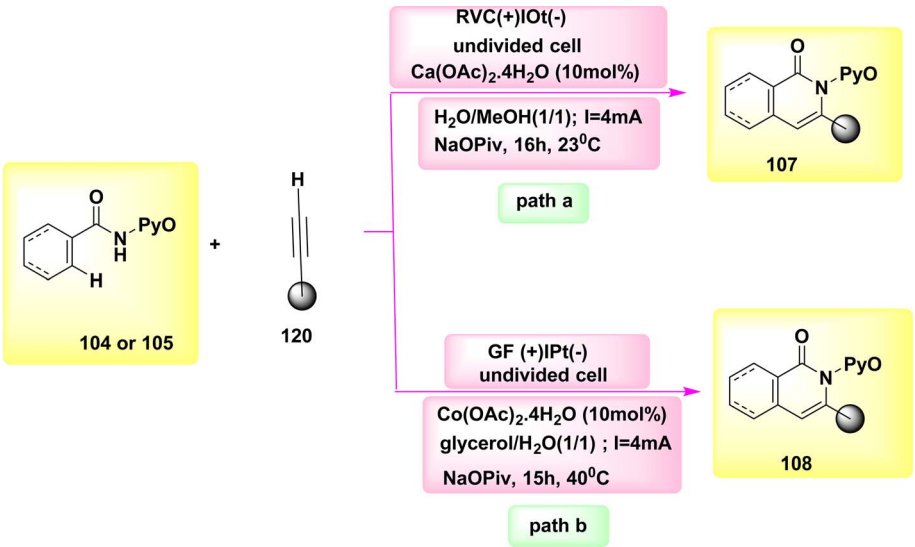
Scheme 37 Electrosynthesis of oxazol-2-ones **99** and imidazole-2-ones **99′**.



Scheme 38 Electrochemical synthesis of isoxazolidine-fused isoquinolin-1(2*H*)-ones **101** with its proposed mechanism.



Scheme 39 Electrochemical synthesis of 2*H*-benzo[b][1,4]oxazine-3(4*H*)-one **103** with its proposed mechanism.

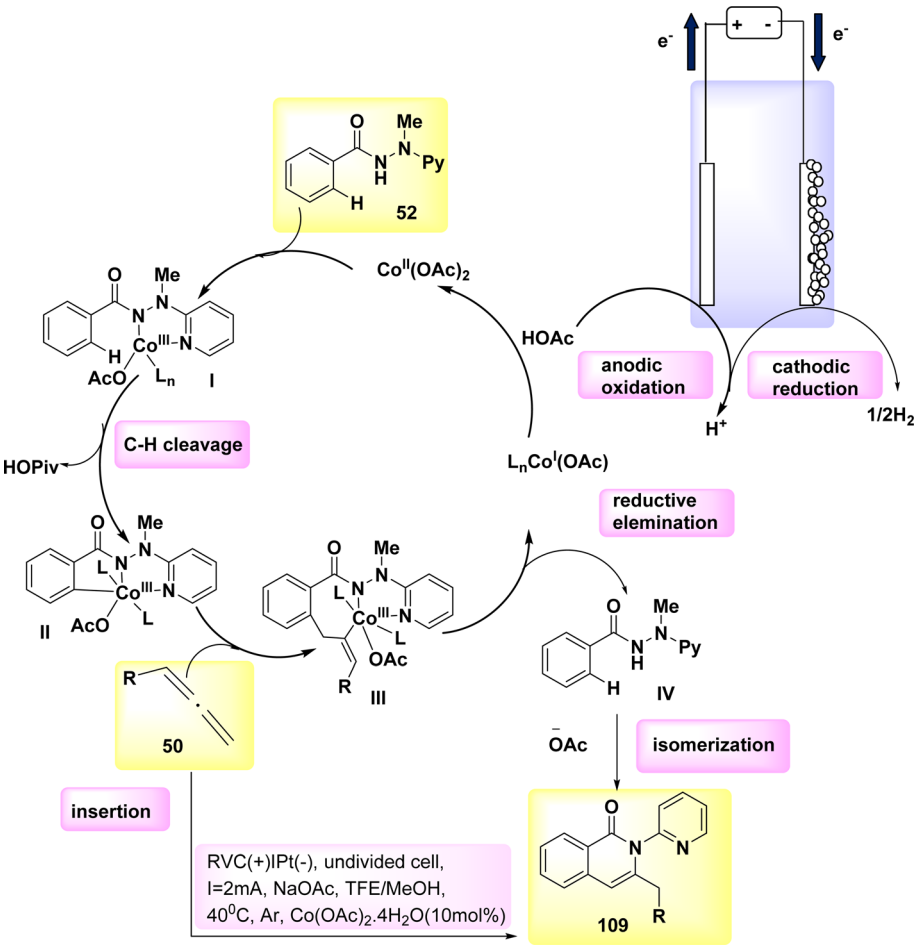


Scheme 40 Electrochemical synthesis of isoquinolones **107** and pyridines **108** with its proposed mechanism.

utilization of a Co catalyst devoid of Cp* has facilitated the achievement of sustainable C–H activation of amides, eliminating the need for the use of detrimental metal oxidants. The carbon–hydrogen/nitrogen–hydrogen functionalization process was successfully carried out in an aqueous glycerol solution at a temperature of 40 °C. Significantly, previous studies have demonstrated the feasibility of conducting electrocatalytic C–H activations through the utilization of sustainable solar and wind energy sources. The integration of renewable solvents and alternative energy sources in molecular catalysis, specifically through Scheme 40-path b, holds promise for advancing the evoluation of more sustainable future energy economies.[68]

In 2020, the feasibility of electro-oxidative Co catalysis was achieved (Scheme 41). The electrochemical activation of carbon-hydrogen bonds in compound **52** using allene **50** was conducted in an undivided cell configuration, resulting in significant levels of chemoselectivity and regioselectivity. The intended regioselective carbon–hydrogen annulation product **109** was obtained in a yield of 91% when either $C_2H_3F_3O$ or CH_3OH was employed as the solvent. The yield of the synthesis was significantly enhanced when conducted at a temperature of 40 °C. Upon analysis of substitute additives, it was shown that sodium acetate NaOAc had a slightly superior performance compared to NaOPiv and PivOH.[69]

A plausible catalytic cycle was suggested and is depicted in Scheme 41, building upon the previously discussed mechanistic findings. The electrooxidative CH activation was catalyzed by anodic oxidation, subsequently leading to a carboxylated-



Scheme 41 Electrochemical synthesis of carbon–H_2 annulation product **109** with its proposed mechanism.

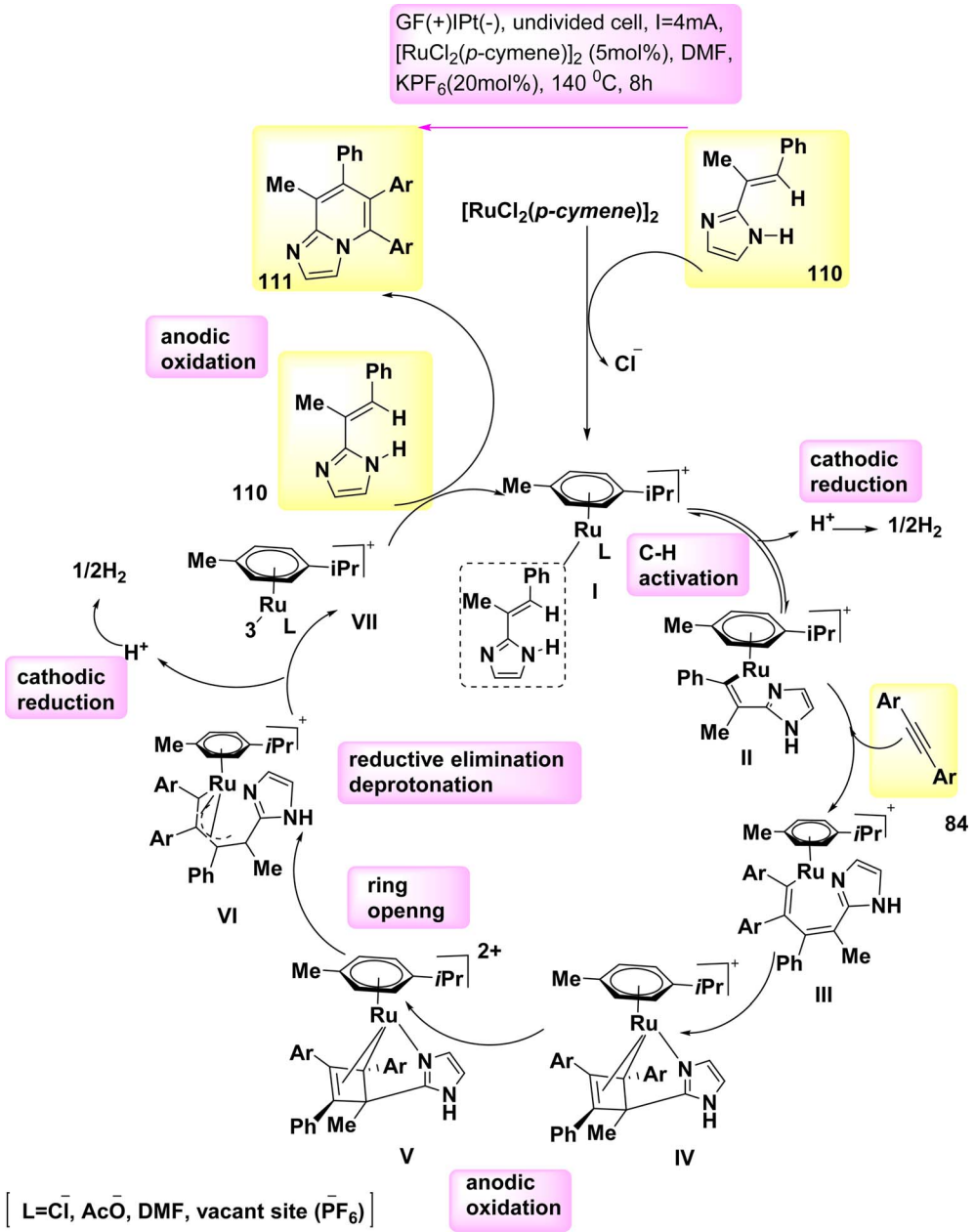
assisted BIES CH cobaltation process, resulting in the formation of Co(III) complex **II**. The Co(I) complex and exomethylene isoquinolone **IV** were synthesized using a subsequent reductive elimination process and regioselective allene insertion. This reaction pathway allowed for the isomerization of the resulting compounds, ultimately yielding the desired product **109**. The process of anode oxidation was employed to reconstruct the Co(III) complex **I**, which is essential for catalytic activity. This step completes the overall catalytic cycle. In general, the cobalt-electrocatalysis approach effectively circumvented the utilization of chemical oxidants, resulting in the production of just molecular H_2 as waste.

In 2020, observed the discovery that, in the absence of metallic oxidizing agents, imidazoles **110** and alkynes **84** can go through a Ru(Ru)-catalyzed electrosynthesis process to produce a range of N-fused[5,6]-bicyclic heteroarenes **111** through electrochemical carbon–hydrogen/nitrogen–hydrogen annulation that is selective and sensitive. To get the intended result, an indivisible cell configuration with a Pt-(−) and GF-(+) is employed **111**. But when compared to other solvents, DMF yielded the greatest results.[70]

Based on the mechanistic findings (Scheme 42), it is proposed that the catalytic cycle commences with a rapid organometallic CH activation. Consequently, the production of **II** occurs. The $C_{12}H_{16}N_2Ru_2$ **IV** is subsequently synthesized using alkyne coordination and migratory insertion processes, followed by anodization to yield the Ru(III) complex **V**. The formation of **VI** occurs through a process known as ring opening of **V**. The formation of Ru(I) complex **VII** occurs through a process of oxidation-induced reductive elimination, followed by subsequent anodic reoxidation.

In the year 2021, a transformation involving the conversion of a linear molecule known as BrHN into a cyclic structure, **112**, Scheme 43, was successfully achieved. The β-lactams, also referred to as azetidin-2-ones, are a class of heterocyclic compounds characterized by a four-membered ring structure and the presence of an amide. Elaborating on the significance of this category of compounds in the realm of antibiotics is deemed unnecessary due to their widespread recognition within the biomedical sciences.[71]

A facile electrochemical synthesis of β-lactams has been successfully accomplished using constant current electrolysis in a suitable solvent with a volatile organic compound (VOC)-supporting electrolyte solution containing $C_4H_{12}^+$ salt. This method involves the addition of bromoamides **113** and results in the production of an electrogenerated base. By employing this approach, the necessity for bases and probases is circumvented, leading to the attainment of high yields of β-lactams **112**

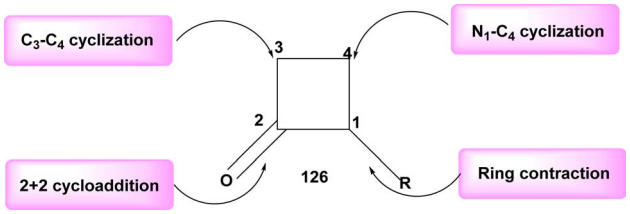


Scheme 42 Electrochemical synthesis of bridge head N-fused[5,6]-bicyclic heteroarenes **111** with its proposed mechanism.

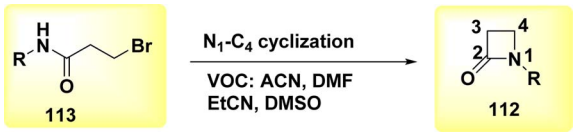
(Scheme 44). Typically, **113**, which possess a leaving group in the β-position, can undergo deprotonation at the N atom under normal circumstances. This deprotonation generates a (−)ion that facilitates internal nucleophilic displacement, ultimately yielding the corresponding β-lactams.

The cyclization of a linear bromoamide **113** can be achieved by deprotonating a carbon atom. In this particular situation, the attainment of suitable acidity necessitates the utilization of ethoxy-carbonyl, which functions as an electron-withdrawing group. The generation of N-heterocyclic carbene (Scheme 45) occurs by the reduction of $BMIm^+$ at the negative electrode. The NHC can function as both a nucleophile and a base. In this context, it acts as a deprotonating agent for the bromoamide **113**, leading to the evoluation of a ring structure. Carbenes have demonstrated efficacy and environmental compatibility as valuable instruments for conducting chemical synthesis. The electrochemical technique described in this study offers a simplified process as it does not necessitate the use of any probase other than the IL solvent. The initial IL cation is generated by the NHC when it acts as a base in practice. The yields of β-lactams **112** are also satisfactory when the internal displacement occurs at a CBr site that is disubstituted, regardless of the nitrogen terminus.

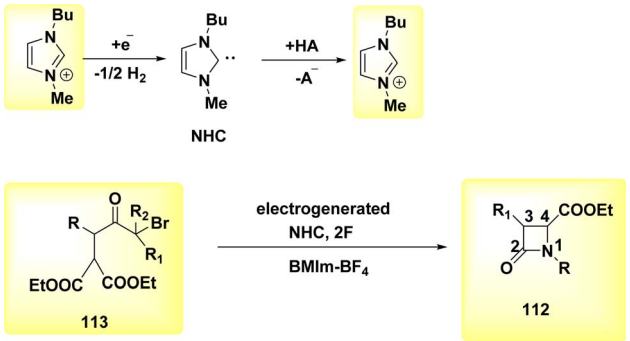
[2 + 2], the most widely recognized method for synthesizing β-lactams **112** is through the cycloaddition reaction, specifically the Staudinger reaction, involving imine **114** and ketene,



Scheme 43 Synthesis of azetidin-2-ones **112**.



Scheme 44 Electrochemical synthesis of azetidin-2-ones **112**.



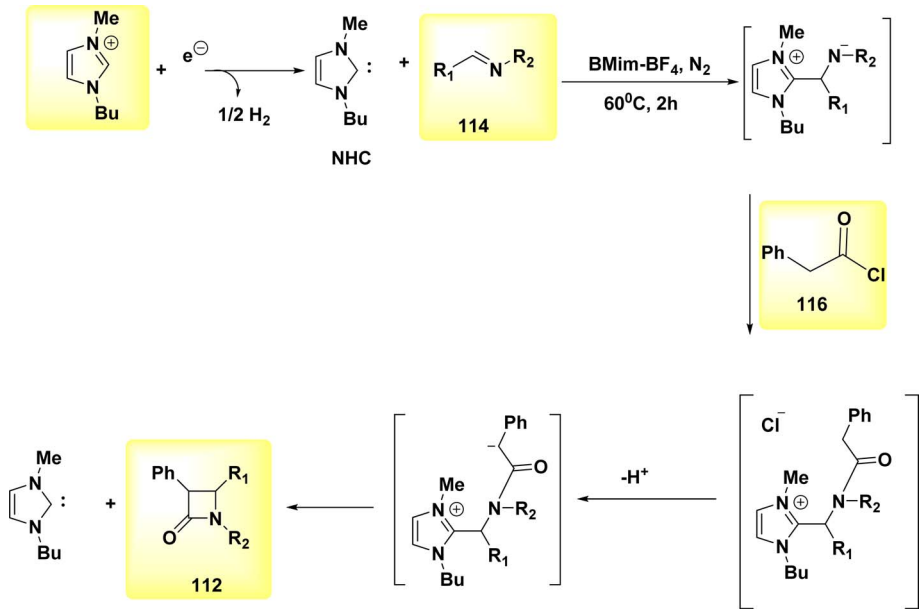
Scheme 45 Electrochemical synthesis of azetidin-2-ones **112**.

Scheme 46. The ketene, known for its inherent instability, is commonly generated through the *in situ* dehydrohalogenation of a suitable acyl halide **115**.

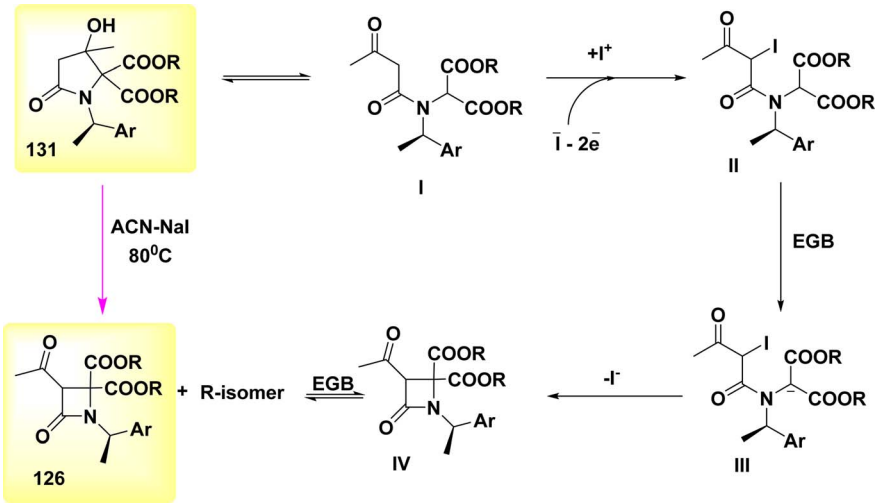
The stereochemical outcome of the occurrence is not neglected due to its unexpected character. Indeed, it is possible to achieve either a concerted or two-step process in the final β-lactam **112**, depending on the varying relative configurations. During the electrosynthesis process of the ionic liquid BMIm-BF_4, the formation of *cis*-lactams was shown to occur predominantly, with the preference being determined by the configuration of the nitrogen atom. However, due to the varying amount of NHC, the inclusion of Et_3N (an external base) was required to achieve good yields. The imine **114** (Scheme 46) was activated by the electrogenerated NHC, which functioned as botha nucleophile and a base in the reaction. This finding eliminates the possibility of a coordinated mechanism.[72]

The final electrochemical step employed in the production of β-lactams **112** entails the induction of ring contraction by anodic means. The electrochemical approach anticipated the potential to generate the active "I^+" in its original location through anodic oxidation of I^- from the supporting electrolyte, while inadvertently forming an electrogenerated base at the cathode. The reaction was conducted in acetonitrile at a temperature of 80 °C in the presence of chiral pyrrolidones **117**, resulting in a high yield (Scheme 47).

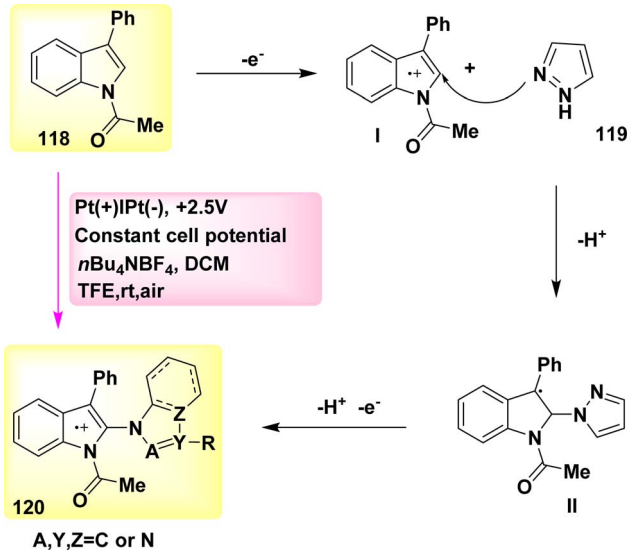
The electroactive species in question is the I-anion, which undergoes oxidation to become "I^+" and subsequently reacts with the open form of iodide to generate the corresponding α-I^-. The compound known as β-lactam **112** is synthesized through the process of intramolecular iodide translocation and subsequent base deprotonation. It is highly probable that this reaction occurs with equal amounts of the R- and S-forms at the C_3 position.



Scheme 46 Electrochemical synthesis of azetidin-2-ones **112** with proposed mechanism.



Scheme 47 Electrochemical synthesis of azetidin-2-ones **112** with proposed mechanism.



Scheme 48 Electrochemical synthesis of 2-heteroaryl-$C_{16}H_{13}NO$ **120** with proposed mechanism.

The process of equilibration in alkaline solutions results in the formation of the S-diastereoisomer as the predominant product. This particular isomer can be obtained in a pure state by the process of crystallization, as it exhibits the highest level of thermodynamic stability.

In the year 2021, Zhou[73] and colleagues presented a novel electro-oxidative method for the formation of C–N bonds. This strategy was shown to be suitable for large-scale synthesis, enabling the synthesis of several compounds (Scheme 48). The initial step was the coupling of the model substrate $C_{16}H_{13}NO$ **118** with a substituted pyrazole **119**. This reaction was carried out using an undivided cell, where Pt served as both the cathode and anode.

The best condition was eventually produced by employing a solvent mixture of dichloromethane/tetrafluoroethylene, nBu_4NBF_4 as the electrolyte, and a reaction mixture containing 0.5 mmol of compound **118** and 0.5 mmol of compound **119**. The reaction was conducted at room temperature under atmospheric conditions. The product with the designation **120**, which exhibited a yield of 69%, was subjected to separation.[73]

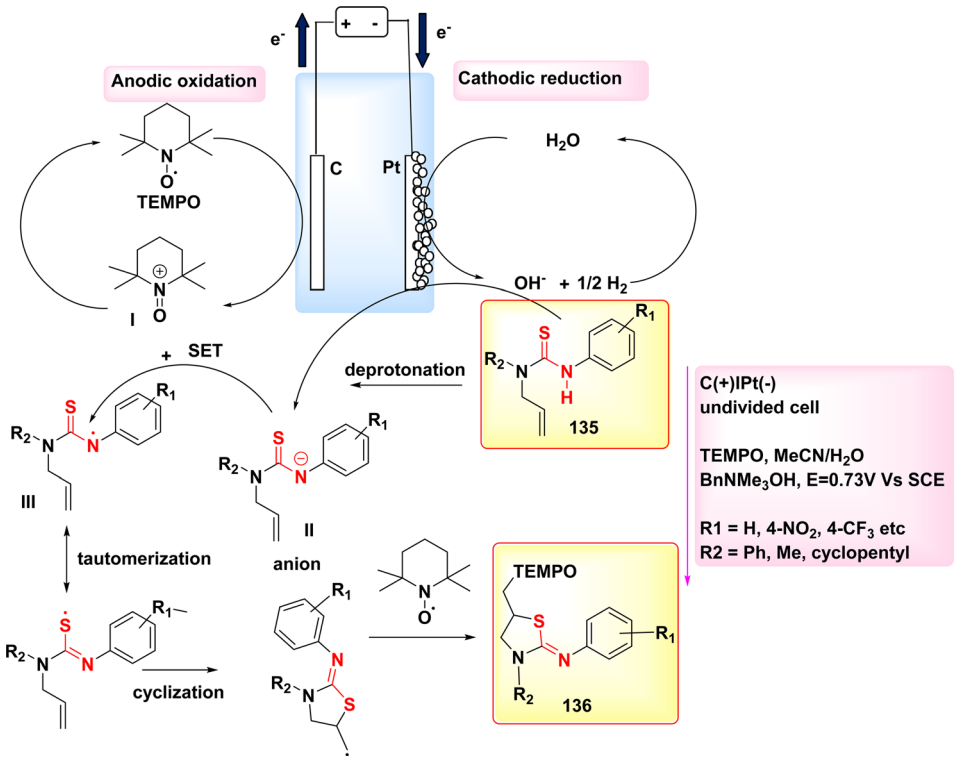
This study presents a feasible mechanistic approach for the electrochemical oxidative azolation of indoles **118**, which is based on thorough mechanistic investigations and pertinent literature sources (Scheme 48). Due to its comparatively lower oxidative potential in comparison to pyrazole **119**, indole **118** exhibits anodic oxidation as its initial reaction. This leads to the intermediate **I** formation, which subsequently engages in nucleophilic addition with **118**, leading in the elimination of a proton and the formation of radical intermediate **II**. In order to obtain the desired isolated product **120**, it is necessary to subject the radical intermediate to subsequent oxidation and tautomerization processes.

Electrosynthesis of S-heterocycles

The S-heterocycles, including derivatives of thiazole-2-imine **136**, has exhibited a significant rise in their pharmacological utilization owing to their noteworthy therapeutic capabilities, such as analgesic properties, anti-inflammatory effects, kinase inhibition activities, antibacterial attributes,[79] antifungal properties,[74] and melanin reduction activity.[75]

M. Islam *et al.* described the electrochemical synthesis of $C_3H_6N_2S$ **136** from thiourea-tethered terminal alkenes **135** in 2019.[76] The electrolysis was carried out in a flow-reactor system, employing, $C_9H_{18}NO^{\bullet}$ as a redox catalyst. The catalyst acts as a nucleophilic reagent according to the mechanism proposed (Scheme 49).

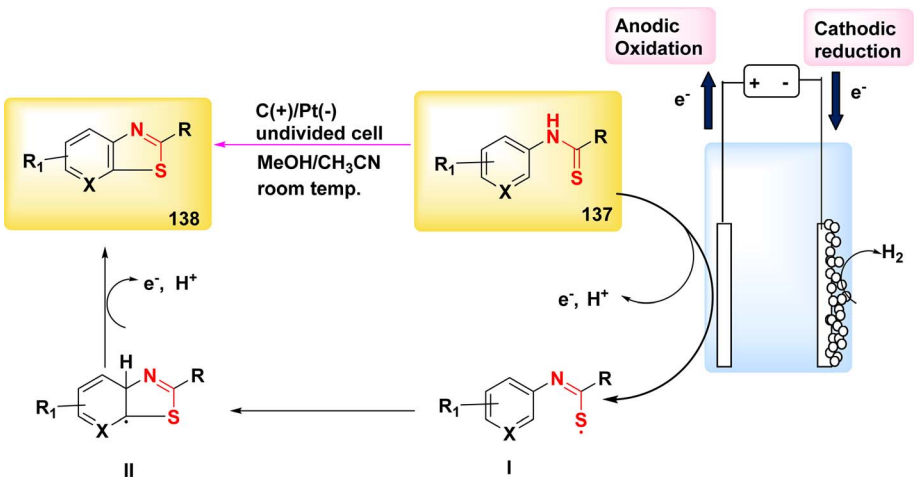
The process of cathodic reduction involves the conversion of water into hydroxide ions (OH^-) and H_2 gas (H_2), while the subsequent anodic oxidation involves the conversion of tropospheric emission: monitoring of pollution into oxo-ammonium ion **I**. Phenylurea undergoes deprotonation through the action



Scheme 49 Electrochemical synthesis with the proposed mechanism of thiazolidin-2-imines **136**.

of the hydroxide ion, leading to the formation of an anion **II** centered on the nitrogen atom. A nitrogen-centered radical **III**, which is lacking in electrons, is formed through a subsequent SET reaction between an anion **II** and an intermediate **I**. This process serves to regenerate the TEMPO radical molecule. The compound known as thiazolidin-2-imine **136** exhibits a N-radical tautomerization process in the presence of the thiocarbonyl group, resulting in the formation of a sulfur radical. The aforementioned radical undergoes cyclization, resulting in the formation of another radical at the terminal carbon. This radical then interacts with the tropospheric emission: monitoring of pollution radical molecule, leading to the production of the difunctionalized oxysulfurization product **136.**

Folgueiras-Amador *et al.* in 2018, devised a novel method to enable continuous flow of electrochemical dehydrogenative C–S bond formation, without the need of a catalyst or a supporting electrolyte. The conversion of a diverse array of *N*-arylthioamides **137** to their corresponding benzothiazoles **138** has been achieved with excellent yields and great current efficiency (Scheme 50). The experiment involved utilizing a Pt plate as the cathode and carbon as the anode. The reaction was conducted within an undivided cell under conditions of a consistent



Scheme 50 Electrochemical synthesis of benzothiazoles **138** with its proposed mechanism.

current. The authors have shown that this transformation is achieved exclusively by the utilization of a solvent of high laboratory quality and electricity, without the need of a degassing or a flux environment. It examines three advantages of employing electrochemistry in flow systems: (i) the ability to scale up the reaction without necessitating a larger reactor; (ii) the feasibility of conducting a reaction without the need for a supporting electrolyte; and (iii) the substantial influence of utilizing a well-designed reaction solution, which can be achieved through the implementation of flow systems.[77]

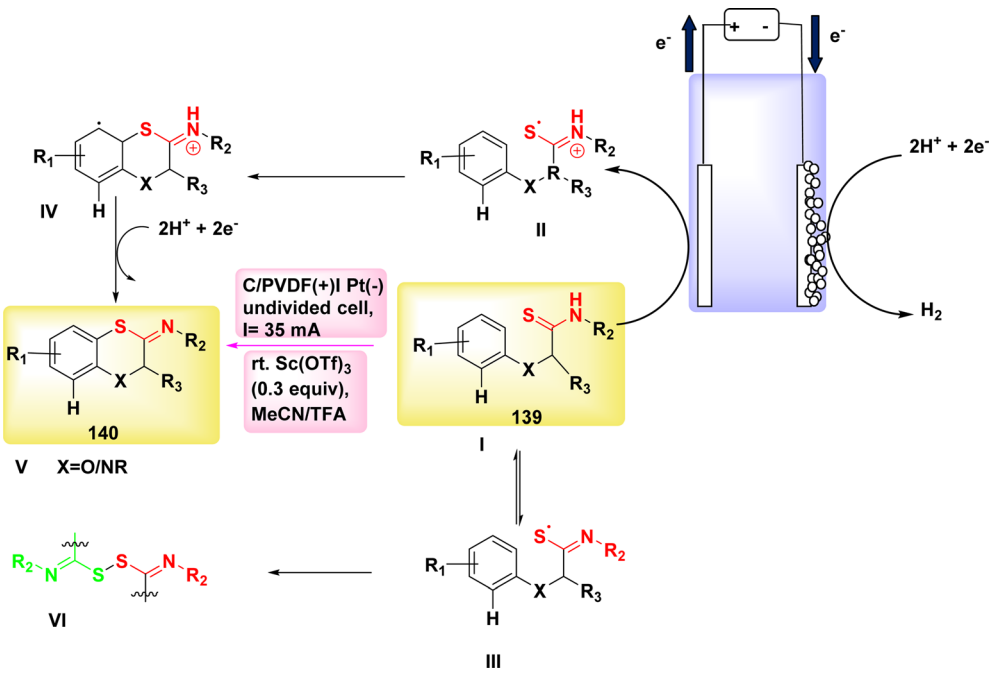
It was proposed that the anodic oxidation served as the initial step in the sequence of reactions involving thioamide derivatives **137**, leading to the formation of radical intermediates **I** and **II**. The final compound **138** is obtained through cyclization and subsequent deprotonation (Scheme 50).

C. Huang *et al.* in 2019 synthesized the six-membered heterocyclic ring in C_8H_6OS and C_8H_7NS through the utilization of intramolecular dehydrogenative C–S coupling.[78] The avoidance of oxidative desulfurization, which is a common side reaction for thioamides **139**, is achieved by carrying out the reactions within an acidic flow cell. The selection of the model substrate, thioamide **139**, was made in order to determine the optimal reaction conditions. The electrolysis was conducted using a flow electrolytic cell equipped with a polyvinylidene fluoride (PVDF) anode loaded with carbon and a Pt-(cathode). Extensive experimentation revealed that the implementation of a continuous-flow electrolytic technique, utilizing a mixture of solvents including MeCN and TFA in a ratio of 9 : 1, in the existence of $Sc(OTf)_3$, resulted in the successful extraction of C_8H_6OS **140** with a yield of 73%.

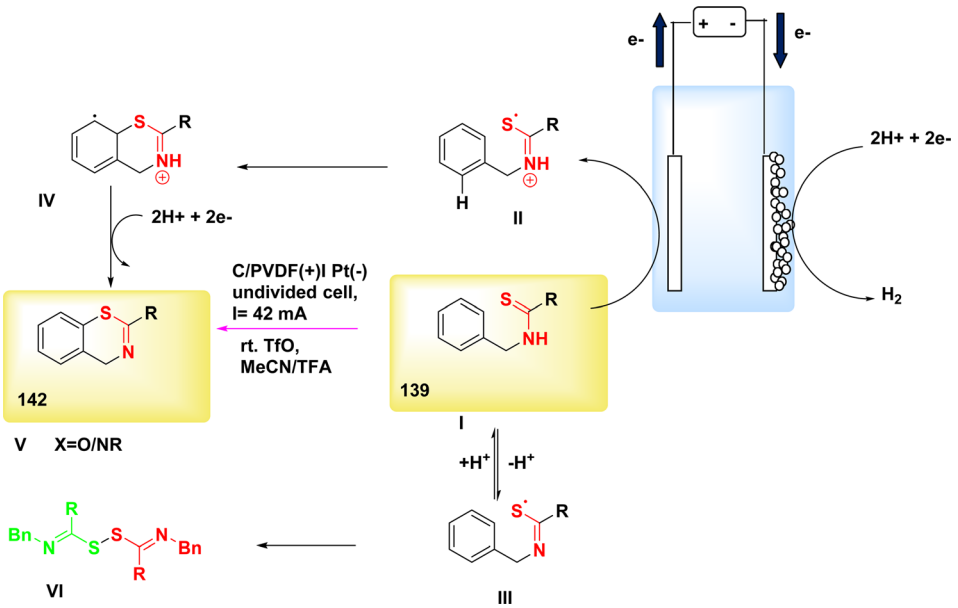
The generation of SNH_2 cation **II**, illustrating the observed concordance between the neutral SNH_2 **III** and the thioamide substrate **I** which is attributed to the outcomes of a one-electron anodic oxidation process. The ultimate outcome, denoted as **V**, is achieved through the process of radical cyclization, which is subsequently followed by oxidative rearomatization. The expectation is that cyclization *via* the protonated radical **II** will exhibit more efficacy compared to cyclization *via* the neutral species **III**. This is due to the higher electrophilicity of the S-radical in intermediates **II**, rendering it more reactive towards the phenyl ring than the S-radical in intermediates **III**. It is probable that TFA undergoes ligand exchange with $Sc(OTf)_3$ inside the reaction mixture, resulting in the formation of the more potent acid, TfOH. This enhances the level of protonated form **II**. The radical **III** has the ability to undergo dimerization and hydrolysis reactions, resulting in the formation of desulfurization product **140** by a slow cyclization process (Scheme 51).

In a study conducted in 2019, a range of functionalized 1,3-benzothiazines **142** were synthesized using an acidic flow cell (Scheme 52). This method effectively prevents oxidative desulfurization, a common undesired side reaction observed in thioamide processes. The SNH_2 cation is widely believed to be the pivotal intermediate. The electrolytic process was conducted within a flow cell, utilizing a Pt cathode and a carbon anode that was impregnated with $-(C_2H_2F_2)_n^-$. An assessment of the Rx^n conditions was conducted, encompassing several parameters such as current (42 mA), flow rate (0.3 mL min^{-1}), additives, and solvent (TfOH, 0.06 M) in MeCN. It was determined that this particular set of conditions yielded the most favorable outcome.

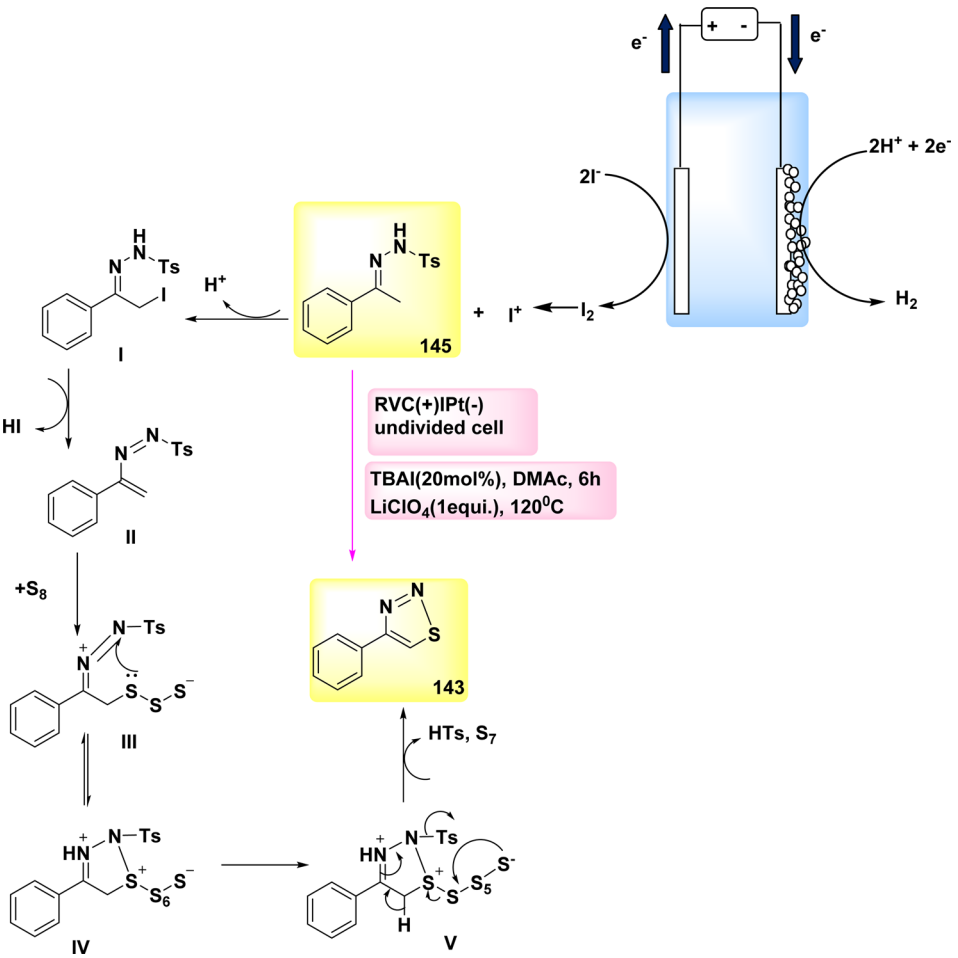
The inclusion of trifluoromethanesulfonic acid (TfOH) resulted in an increase in the conductivity of the reaction solution, eliminating the need for any additional supporting salt. Under the given conditions, the reaction of **139** resulted in



Scheme 51 Electrochemical synthesis of 1,4-benzoxathiin **140** with its proposed mechanism.



Scheme 52 Electrochemical synthesis of 1,3-benzothiazines **142** with its proposed mechanism.



Scheme 53 Electrochemical synthesis of 1,2,3-thiadiazoles **145** with its proposed mechanism.

the formation of the intended product **142** with a satisfactory yield.[80]

At the anode, the thioamide **I** undergoes oxidation through SET to generate radical cation **II**. Subsequently, radical cation **II** undergoes cyclization and oxidative aromatization, resulting in the formation of the ultimate heterocycle **V**. The removal of a proton from the intermediate **II** results in the formation of **III**, which exhibits a lower susceptibility to cyclization compared to **II**. The process of dimerization of radical **III** can lead to the development of radical **VI**, which subsequently undergoes hydrolysis to yield desulfurized material. The introduction of trifluoromethanesulfonic acid (TfOH) leads to a more advantageous equilibrium on compound II, resulting in a decrease in the process of desulfurization.

According to a report in 2019, the introduction of sulfur element **144**, to *N*-tosylhydrazones **143** leads to the formation of $C_2H_2N_2S$ through the utilization of an electrochemical method that does not require the presence of metals or oxidants (Scheme 53).

The coupling reaction involved the combination of tosylhydrazone **143**, derived from acetophenone, with sulfur **144**. The annulation product **145** was synthesized with an 80% yield by employing a catalyst of TBAI (tetrabutylNH$_2$I) at a concentration of 20 mol%, along with $LiClO_4$ as the electrolyte, in a DMAc (dimethylacetamide) solvent. The reaction was carried out at a temperature of 120 °C for duration of 6 hours.[86]

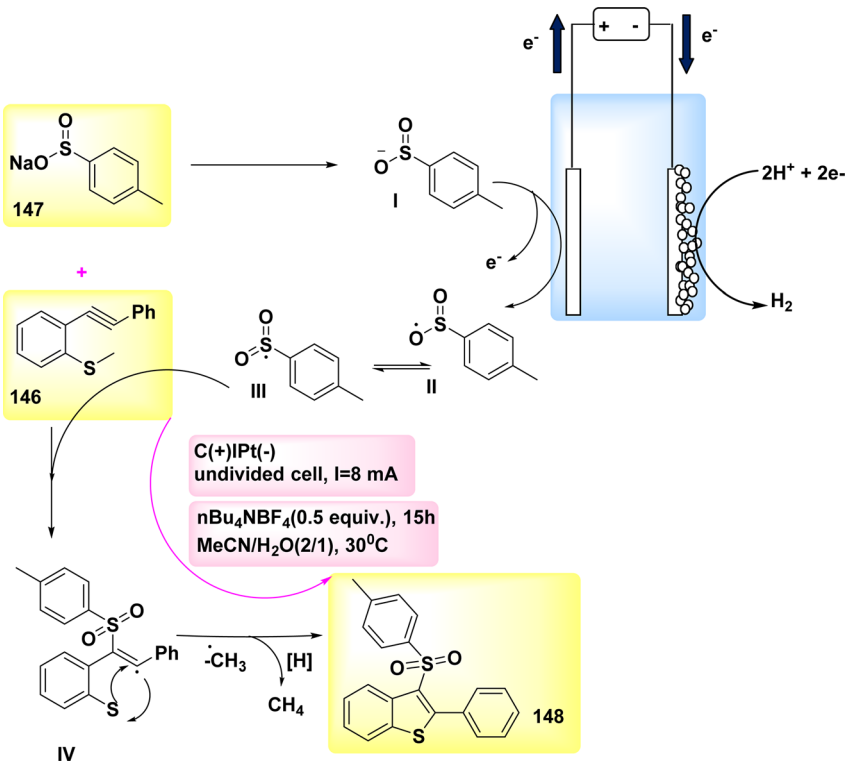
The process of electrochemical oxidation at the anode resulted in the production of I_2 through the oxidation of $2I^-$. This I_2 was then effectively transformed into I^- and I^+ ions. The conversion of acetophenone tosylhydrazone **143** into intermediate **I** was achieved through α-iodation, whilst the formation of azoalkene **II** occurred *via* HI elimination.

The completion of the reaction cycle can be achieved through the utilization of various methods, which involve the continued oxidation of the generated iodine anions. Zwitterion **III** was synthesized through the addition of sulfur (S_8) to azoalkene **II**. The aforementioned compoundundergoes a process of cyclization, resulting in the development of intermediate **V**. The intended product **145** was ultimately synthesized through the elimination of S_7 and TsH.

H_2 production was achieved through reduction at the cathode, so completing the electrochemical cycle.

In the year 2021, a viable and ecologically sustainable electrochemical method was developed for the synthesis of C-3-sulfonated benzothiophenes **148**. This method was conducted under conditions that did not require the use of oxidants or catalysts. The reaction involved the combination of 2-alkynylthio-anisoles **146** with sodium sulfinates **147**. Sulfonated benzothiophenes with notable and useful functional groups have been successfully synthesized under conditions of consistent current, resulting in moderate to high yields. A single, unpartitioned cell was utilized for the reaction, with a graphite rod employed as the anode and Pt utilized as the cathode (Scheme 54).

The electrolyte employed in this study was nBu$_4$BF$_4$ at a concentration of 2.5 mmol. The solvent system consisted of a mixture of CH_3CN and H_2O in a ratio of 2 : 1. To achieve a yield of 68% for product **148**, the mixture was subjected to agitation



Scheme 54 Electrochemical synthesis of C-3-sulfonated benzothiophenes **148** with its proposed mechanism.

at a temperature of 30 °C and electrolyzed for 15 hours using a current of 8 mA within an oil bath.[81]

Scheme 54 depicts a possible mechanistic route for the electrocatalytic sulfonylation process. The reaction phase was initiated by the oxidation of sodium *p*-tolylsulfinate **147** at the positive electrode, resulting in the formation of radical intermediate **II** or **III** through the loss of an electron. Resonance structures can be observed between the arylsulfonyl radicals **III** and **II**. The formation of the intermediate vinyl radical **IV** occurs through the intermolecular radical addition of sulfonyl radical **III** to the alkynyl molecule of **146**. Subsequently, the methylthio-moiety initiates an assault on intermediate **IV**, resulting in the liberation of the desired product **148** and the emission of a methyl radical. The H_2 present in the reaction mixture then undergoes a reaction with the methyl radical, resulting in the formation of methane.

Electrosynthesis of O-heterocycles

O-Heterocycles constitute a significant class of biologically active compounds. One possible explanation for this phenomenon could be the inherent prevalence and wide-ranging physiological roles of these entities, which are harnessed in the advancement of novel pharmaceuticals.[82]

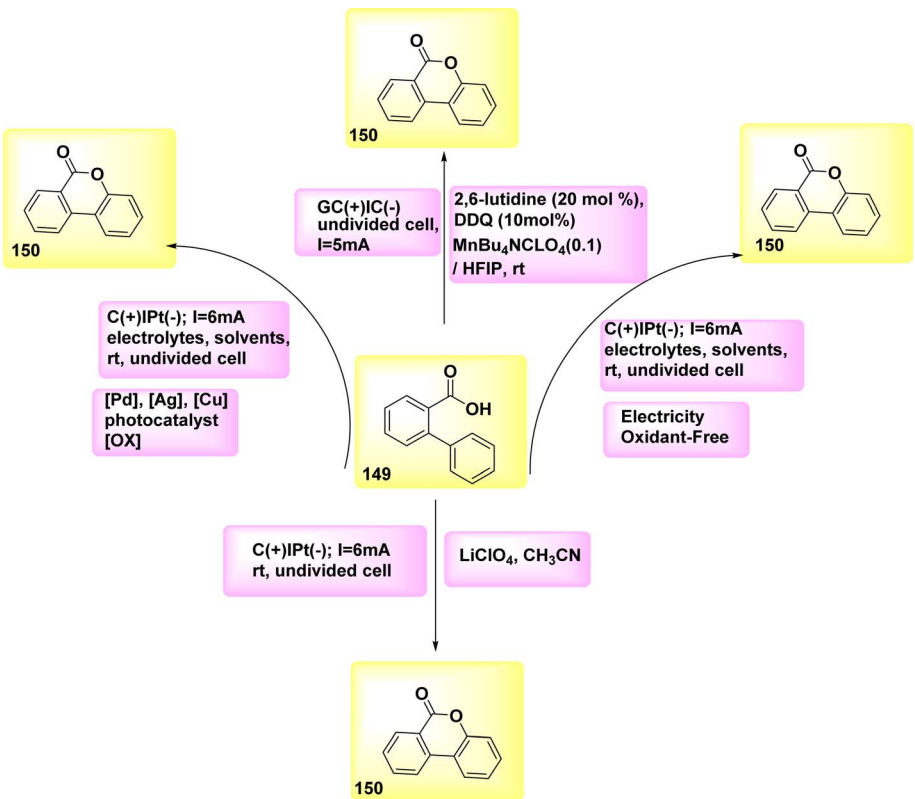
In 2018, Li and colleagues published a series of O-heterocycles (Scheme 56). The electro-synthesis described in this study involves the utilization of $C_8Cl_2N_2O_2$ as a redox-mediator and low-cost glassy carbon electrodes. This setup facilitates the intramolecular lactonization process of $C_{13}H_{10}O_2$ derivatives **149**, resulting in the production of a diverse range of 6*H*-benzo[*c*]chromen-6-ones 150 with high efficiency.[83] The experiment was conducted at ambient temperature using $C_{13}H_{10}O_2$ **149** as a representative substrate in an undivided cell containing a MeCN/$LiClO_4$ electrolyte solution. This resulted in the production of the desired chemical **150**.

The process commences with the compound $C_8Cl_2N_2O_2$ facilitating a homogenous electron transfer from **149** to radical **I**. This subsequently enables the regeneration of DDQ through anodic oxidation. The addition of radical **I** to an arene ring results in the development of intermediate **II**. The aryl radical **II** underwent anodic oxidation once again, resulting in a yield of **150**. The inclusion of 2,6-lutidine in the system will enhance the process of linked electron-transfer by promoting the deprotonation of both **149** and intermediate **II**.

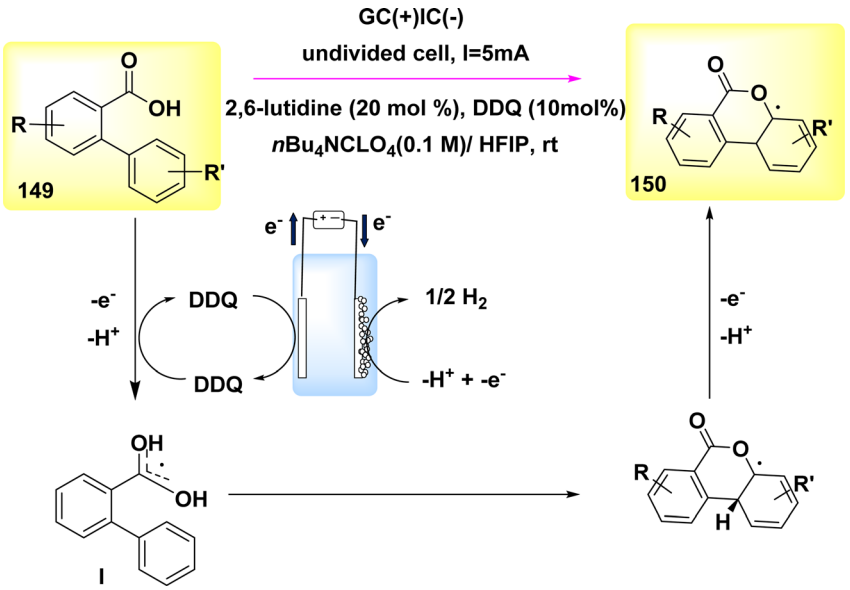
In a similar vein, Shao *et al.*[84] (2018) have shown the electrochemical oxidative coupling within the same framework (Scheme 55 c).

The electrochemical synthesis of lactones **150** has been achieved using 2-arylbenzoic acids **149**. The C–H or O–H cross-coupling reaction of $C_{13}H_{10}O_2$ acid **149** can be successfully conducted under mild conditions, both with and without the need for excess oxidants and metallic species. This can be performed by utilizing anodic oxidation and cathodic H_2 development in a straightforward undivided cell.

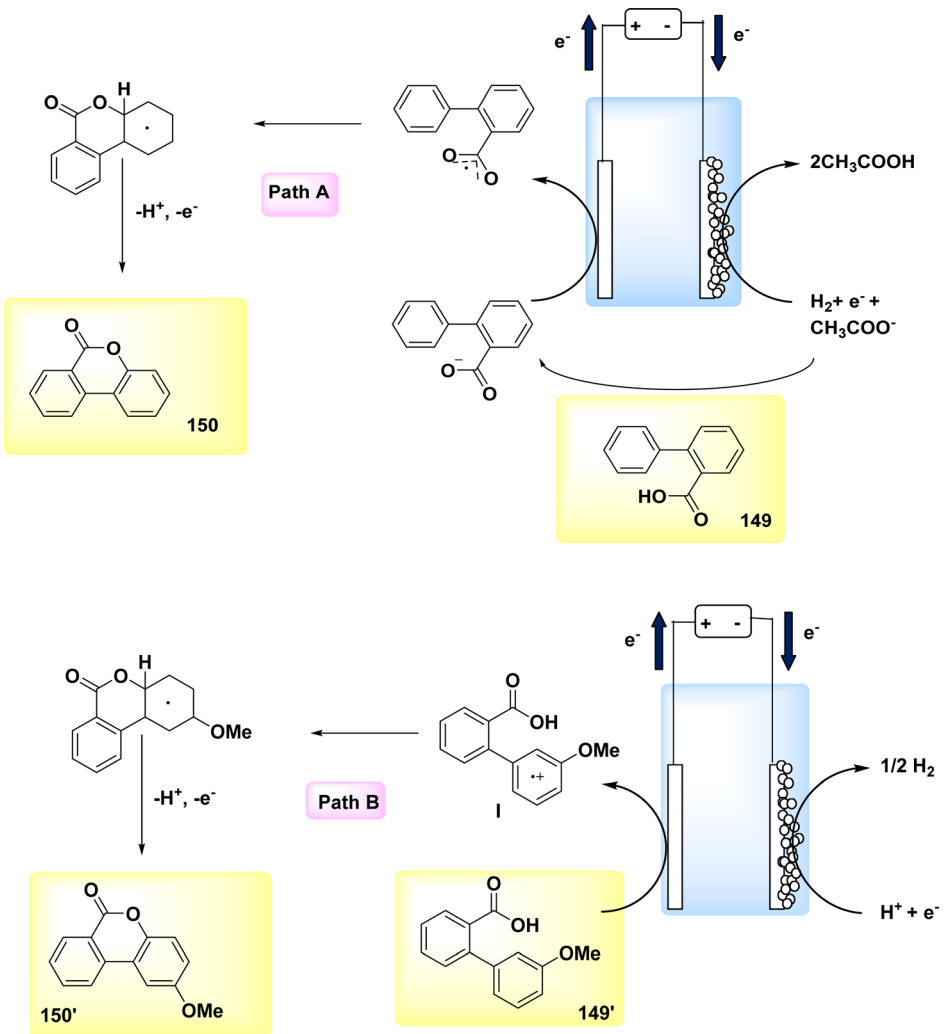
Various $C_{12}H_{16}O_2$ acids have been found to generate the corresponding lactones with yields ranging from 30% to 90%



Scheme 55 Electrosynthesis of 6*H*-benzo[*c*]chromen-6-ones **150**.



Scheme 56 Electrosynthesis of 6*H*-benzo[*c*]chromen-6-ones **150** with its proposed mechanism.



Scheme 57 The electrosynthesis of 6*H*-benzo[*c*]chromen-6-one **150** and its CH_3O^- derivative **150′** with its proposed mechanism.

when utilizing an inexpensive and environmentally friendly Na_2SO_4 aqueous solution as a supporting electrolyte. The aforementioned reaction has a considerable degree of utility in natural product synthesis, demonstrating exceptional efficiency when performed on a gram scale.[84]

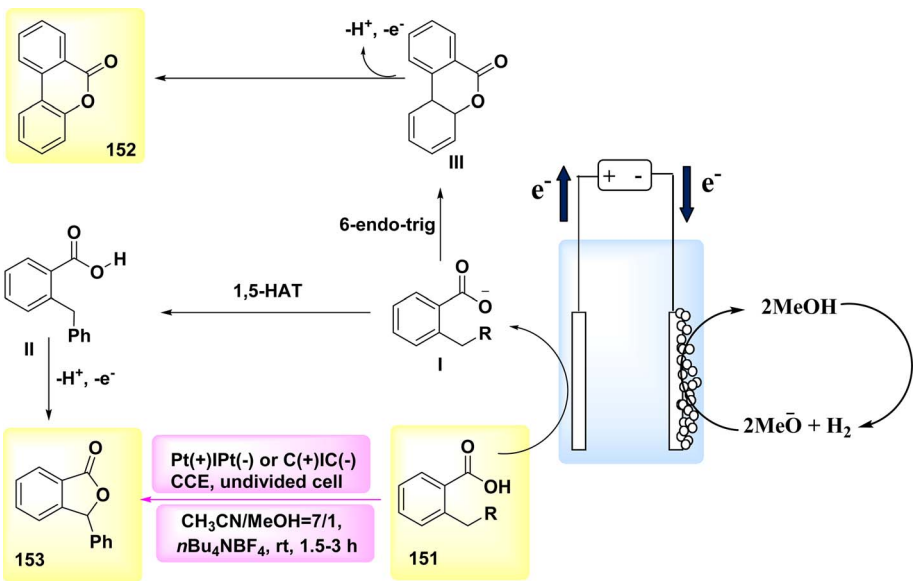
Path B exhibits selectivity towards substrates that possess a methoxy group, namely those with a **149′** configuration. The formation of the radical cation **I** occurs when an anode, which is a positively charged electrode, undergoes single electron transfer oxidation of **149′**. The aromatic ring radical cation that is generated is subsequently subjected to assault by the carboxyl group, leading to the formation of intermediate **II**. The radical adducts **II** undergo rapid aromatization and deprotonation through anode oxidation, resulting in the formation of the desired product **150′**. In contrast, in path A, the process involves the elimination of H_2 from the R–COOH at the cathode or the exclusion of a proton through the electro-generated CH_3COO–. This leads to the formation of compound **III**, which is subsequently oxidized to carboxyl radical **IV** through anode oxidation. The intermediate **V**, which undergoes cyclization, is rapidly converted into an aromatic compound through a single electron transfer process. Subsequently, the compound is deprotonated through anode oxidation, resulting in the formation of the desired product **150**. This product is then subjected to intramolecular assault by a carboxyl radical. The simultaneous cathodic process in both processes A and B involved the reduction of H^+ ions to produce H_2 gas (Scheme 57).

The year 2018 witnessed the demonstration of the electrosynthesis of aromatic lactones 150 by the process of dehydrogenative cyclization. This methodology, which relies on electrochemical techniques, was shown to be highly effective and dependable, as depicted in Scheme 55. The electrochemical technique described in this study is both innovative and advantageous, since it has the potential to be scaled up to 100 grams while operating within reasonable constraints. Interestingly, the utilization of substrates that incorporate heterocycles has the potential to enhance the efficiency of this particular process. Graphite or Pt was employed as the cathode and anode, respectively, in the electrochemical carbon–oxygen cyclization reaction of $C_{13}H_{10}O_2$ acid **149**. By subjecting the system to a constant current of 6 mA, the desired product with a yield of 91% was successfully obtained at ambient temperature. A comprehensive depiction of this particular approach has already been elucidated in path A of Scheme 57.[85]

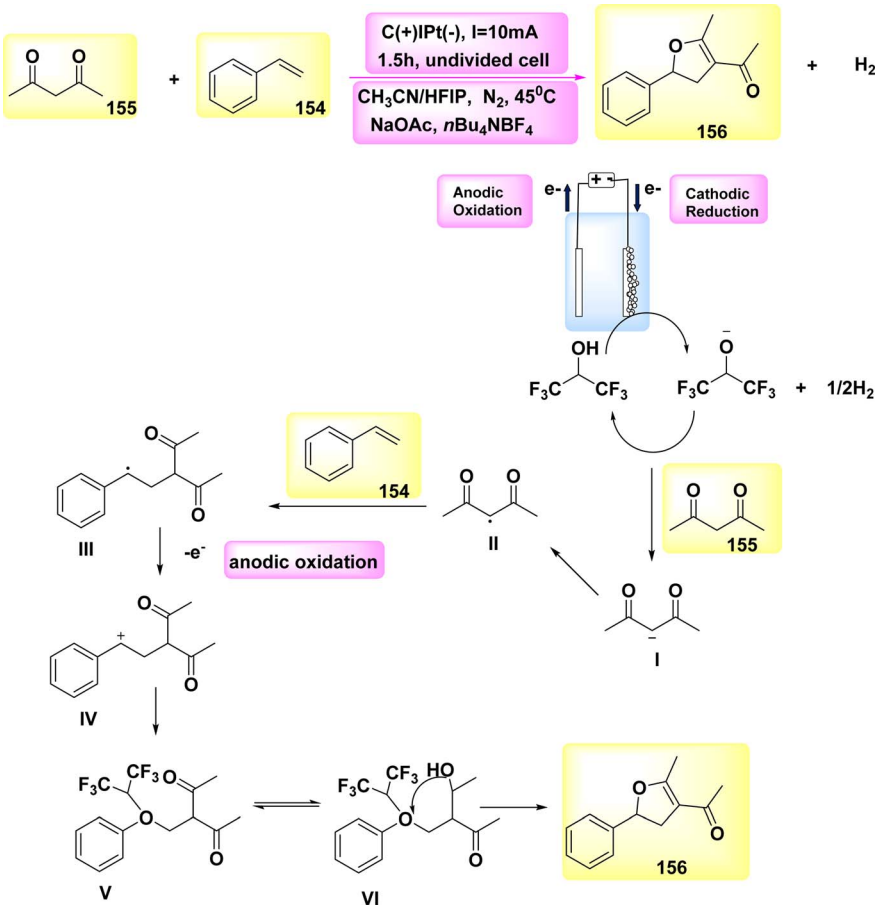
In the year 2018, a highly effective electrochemical method was developed for the direct lactonization process, demonstrating exceptional regioselectivity, without the need for external oxidants or metals. Under conditions of steady current, the cyclization of 2-biphenylcarboxylic acid **151** occurs readily. In this particular situation, the electrolyte used was tetrabutylammonium tetrafluoroborate (nBu$_4$NBF$_4$), while the solvent system consisted of a combination of methanol and methyl cyanide. The experimental setup involved an undivided cell furnished with a Pt/C-anode and cathode. The scalability of the newly developed methodology was demonstrated utilizing a simple method (Scheme 58) on a 40 g scale.[86]

The carboxylate radical **I** exhibits divergent pathways, which are contingent upon the structural characteristics of the substrate. The evoluation of intermediate **III** is achieved through a 6-*endo*-trig cyclization. Upon lactonization of the C(sp^3)–H link, a H_2-atom transfer takes place, resulting in the formation of a stable benzyl radical **II**. In due course, radicals **III** and **II** undergo a process where they undergo the loss of an e$^-$ and a proton, resulting in the evoluation of products **152**and **153**, respectively.

According to Xiong *et al.* (2019), the electrochemical formation of dihydrofuran derivatives **115** was observed in Scheme 59. A significant quantity of **156** was obtained in high yield by the reaction of styrene derivatives **154** and acetylacetone **155**. In the experiment an undivided cell is used, with a Pt plate as the



Scheme 58 Electrosynthesis of substituted coumarin **152** and tetrahydrofuranone **153** with its proposed mechanism.



Scheme 59 Electrochemical synthesis of substituted dihydrofuran **156** with its mechanism.

cathode, carbon serving as the anode, and CH_3CN/1,1,1,3,3,3-hexafluoroisopropanol as the solvent and electrolyte. A steady current of 10 mA was utilized.[87]

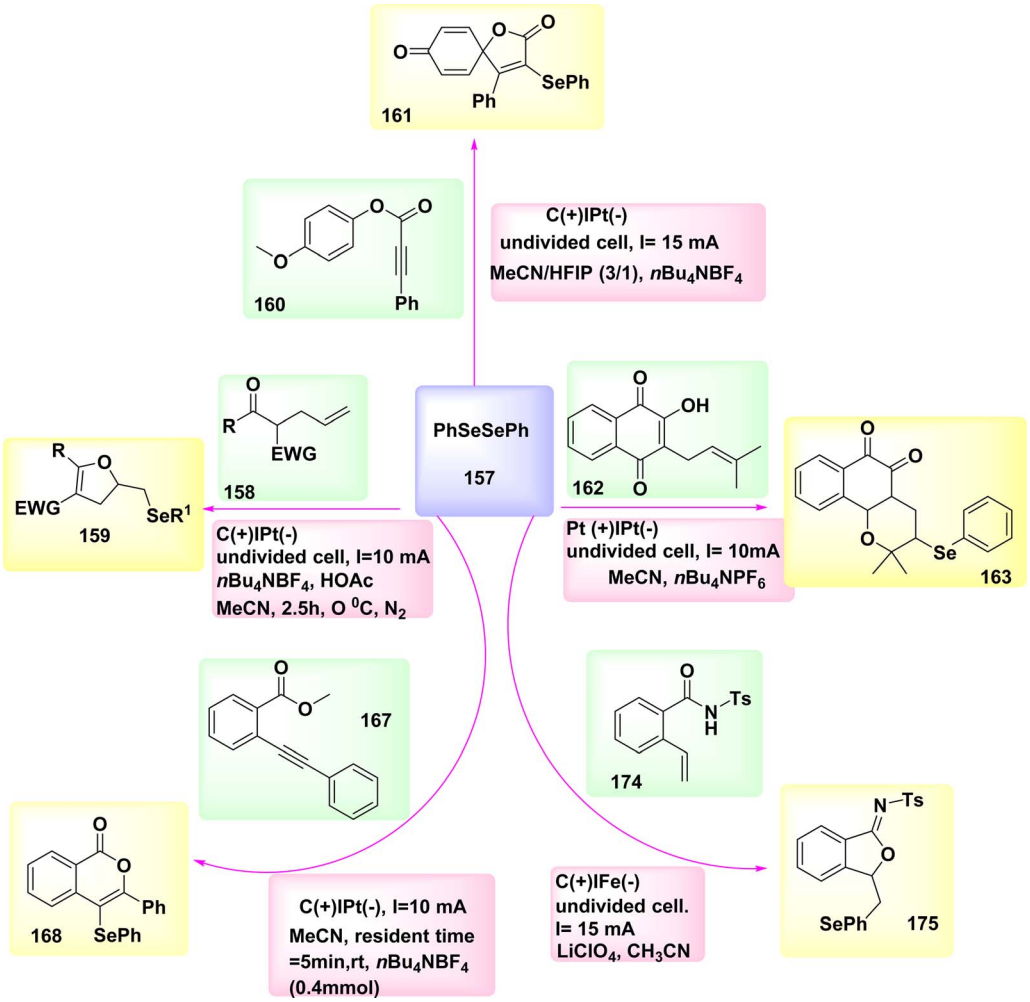
By the acetylacetone deprotonation **155** using the base NaOAc or alkoxide, the acetylacetone anion is generated. Subsequently, this anion undergoes oxidation, ensuing the formation of small quantities of the electrophilic C radical **II**. The stability of this radical can be enhanced by 1,1,1,3,3,3-hexafluoroisopropanol, leading to an anodic event. The C radical **II** subsequently has a reaction with styrene **154**, resulting in the formation of the benzylic radical **III**. This radical is then subjected to oxidation at the anode, leading to the generation of the benzylic cation **IV**. The intermediate **V**, which is likely to undergo tautomerization to **VI**, initiates an intermolecular nucleophilic attack to release the molecular target **156**. This process can be additionally stabilized by the 1,1,1,3,3,3-hexafluoroisopropanolcluster.

In the year 2019, researchers were able to successfully carry out electrochemical oxidation of olefinic carbonyls **158** using readily available diselenides **157**. This process enabled theecologically friendly, immediate formation of C–Se and C–O in a configuration. Using substrates **157** and **158**, the electrochemical oxidative cyclization reaction was initiated, Scheme 60. The final product was successfully obtained with a Pt-sheet (−) and a graphite-rod(+), utilizing nBu$_4$NBF$_4$ as the electrolyte, acetonitrile as the solvent, andacetic acid as an additive, resulting in a high yield.

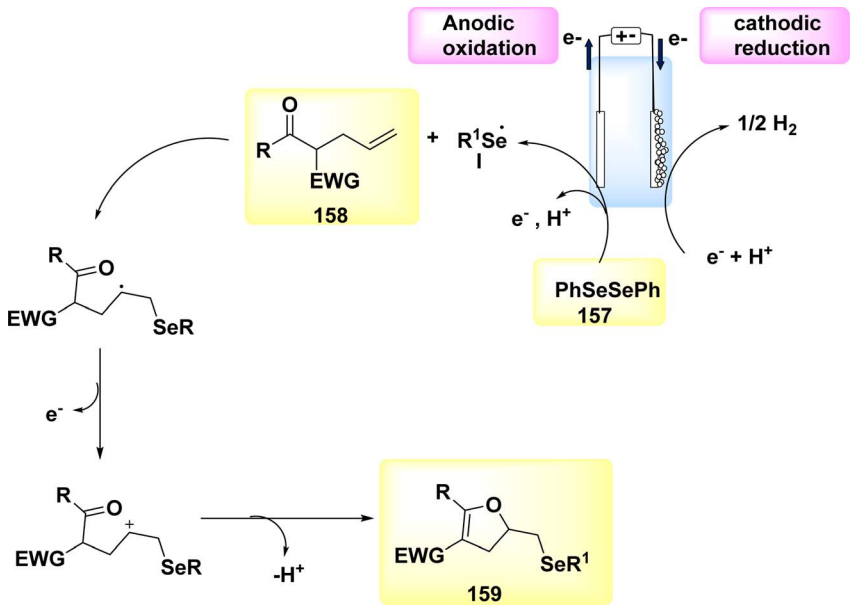
Using an innovative chelation technique, a diverse range of selenodihydrofurans **159** and selenooxazolines with fragile heterocycles, moderate carbon-iodide bonds, and additional $C_2H_3^{\cdot}$ groups were synthesized. This process occurs by preventing the presence of exogenous metallic and oxidizing substances.[88]

Scheme 61 illustrates the proposed pathway for the aforementioned reaction. The compound **158** undergoes a reaction with phenyl selenium radical **I**, resulting in the formation of alkyl radical **II**. Subsequently, the removal of one electron from alkyl radical **II** leads to the formation of cation **III**. The desired product **159** is obtained through a rapid ring closure, subsequent nucleophilic assault on the carbonyl oxygen atom, and deprotonation.

For the synthesis of spiro[4.5]trienones, a novel and ecologically sustainable approach has been developed in the year 2020, as outlined in Scheme 60. The process, which exhibited moderate regulation, was conducted within a single, undivided cellular unit. $C_{16}H_{12}O_3$ **160** and diphenyl diselenide **157** were chosen as the experimental compounds for the synthesis of 3-selenated spiro[4.5]trienones **161**. The reaction was carried outusing a Pt cathode and a graphite anode under constant



Scheme 60 Electrochemical synthesis of substituted selenated dihydrofuran **159**, 3-selenated spiro[4.5]trienones **161**, selenium-containing naphthoquinones **163**, isocoumarin **168**, and selenatedisobenzofuran **175**.



Scheme 61 Electrochemical synthesis of substituted selenated dihydrofuran **159** with its mechanism.

current conditions of 15 mA. The electrolyte utilized in the CH_3CN/1,1,1,3,3,3-hexafluoroisopropanol reaction was nBu$_4$-NPF$_6$, resulting in a yield of 84% for the required product **161**. Furthermore, substantial quantities of additional analogous compounds were produced.[89]

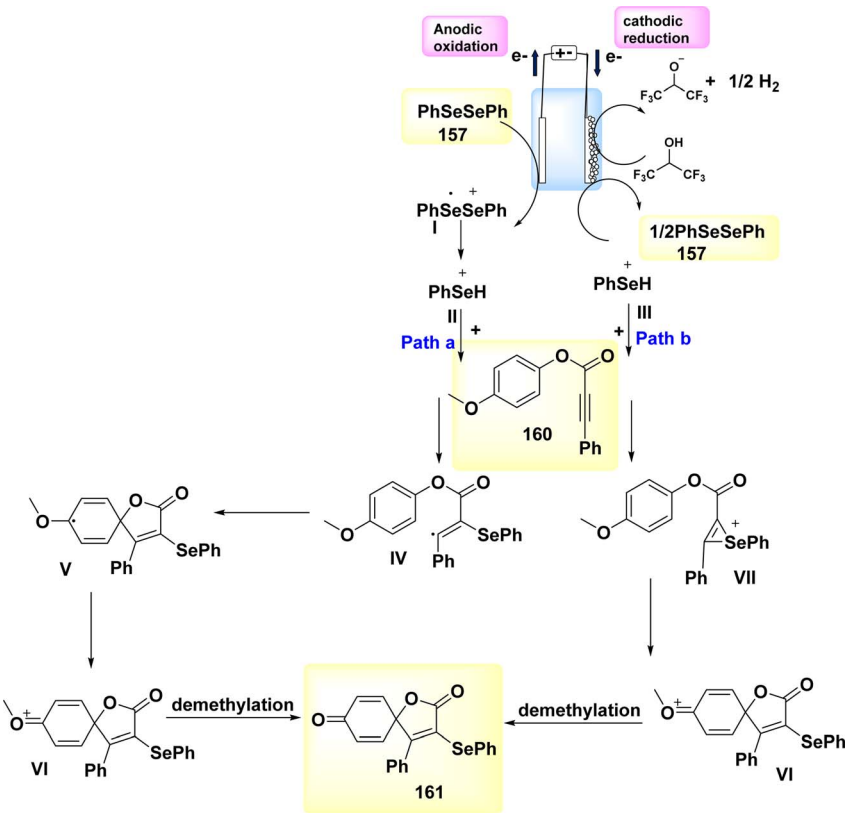
A possible reaction mechanism for the electrochemical transition is shown in Scheme 62. The first oxidation of diphenyl diselenide **157** results in the formation of the cationic radical intermediate **I**. Subsequently, this intermediate undergoes decomposition, giving rise to the generation of radical **II** and cation **III**. Subsequently, the carbon–carbon triple bond, the C_6H_5ClSe radical **II** reacts with **160** undergo a radical addition process, resulting in the construction of vinyl radical **IV**. By the presence of a 5-membered ring str. and the inherent stability of the resonant free radical, known as the $C_2H_3^{\cdot}$ **IV**, the intramolecular spirocyclization to form compound **V** is typically facilitated. At the (+) further oxidation of intermediate **V**, resulted in the production of intermediate **VI**, which is an oxygenium cation. Finally, the formation of product **161** occurs by following path A, by the demethylation of cation **VI** and the subsequent dearomatization of the aromatic ring. In contrast, it is important to acknowledge that the formation of intermediate **VII** may potentially occur by the combination of **160** and phenyl selenium cation **III**. The cyclic selenium cation undergoes intramolecular assault by an aromatic ring possessing a high electron density, resulting in the formation of intermediate **VI**. Consequently, demethylation of intermediate **VI** occurs, leading to the production of product **161** through path B.

The manufacture of selenium-containing naphthoquinones **163** in the year 2020, is accomplished by the electrochemical selenation process in undivided electrochemical cells (Scheme 60). By employing nBu$_4$NPF$_6$ as the electrolyte and applying a current of 10 mA for a reaction time of 1 hour, this efficient and environmentally friendly technology achieves a yield of **163** (yield = 93%) without the use of oxidizing agents.[90]

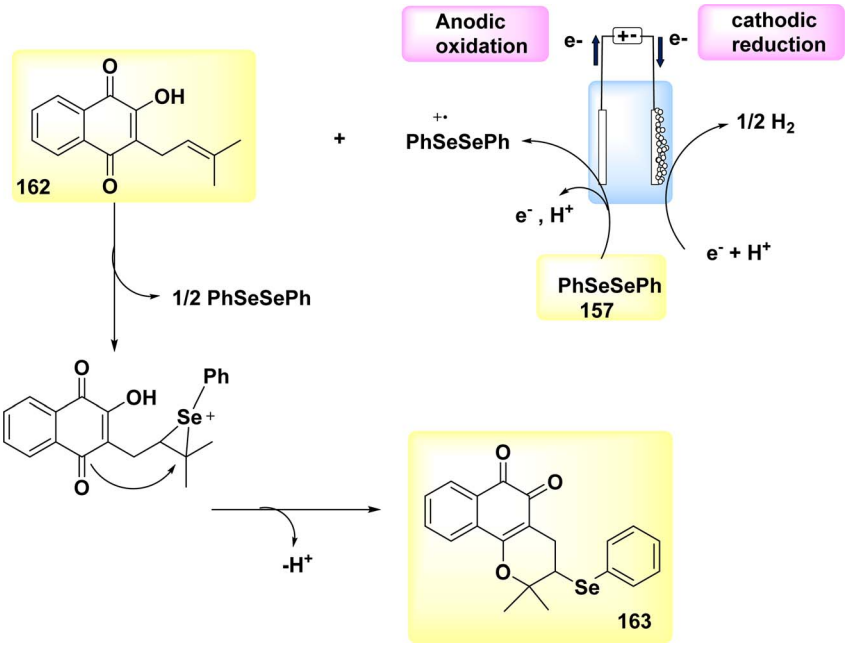
The mechanism for the electrosynthesis of naphthoquinones containing selenium, as hypothesized, is presented in Scheme 63.

The inclusion of lapachol **163** resulted in the observation of a novel anodic reaction occurring at a potential of $E_p = 1.55$ V *vs.* the SCE. The oxidation process of product **163** can be observed at the anode, as evidenced by a distinct study conducted on product **163**. The presence of both the supplementary anodic incident and the diminishing cathodic incident at higher scan rates suggests that the lapachol **162** and selenium-di-cation **II** undergo rapid carbophilic reactions to form cationic intermediate **III**. This intermediate then undergoes nucleophilic cyclization, resulting in the production of product **163** and diselenide **157**.

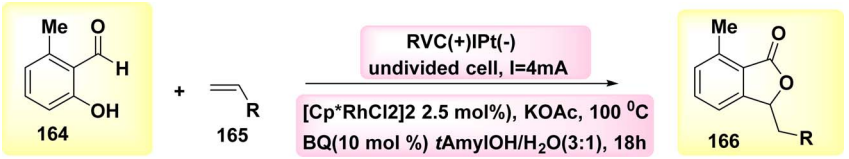
The phenomenon of Ir catalyzed electrocatalysis was observed in the year 2020. This fabrication serves as an example of a user-friendly material that exhibits high stereo- and chemoselectivity (Scheme 64). The reaction between alkene **165** and 2-hydroxybenzaldehyde **164** results in the formation of substituted isobenzofuran-1(3*H*)-one **166**. The electrolyte employed in the experiment is potassium acetate, and the



Scheme 62 Electrochemical synthesis of 3-selenated spiro[4.5]trienones **161** with its proposed mechanism.



Scheme 63 Electrochemical synthesis of selenium-containing naphthoquinones **163** with its proposed mechanism.

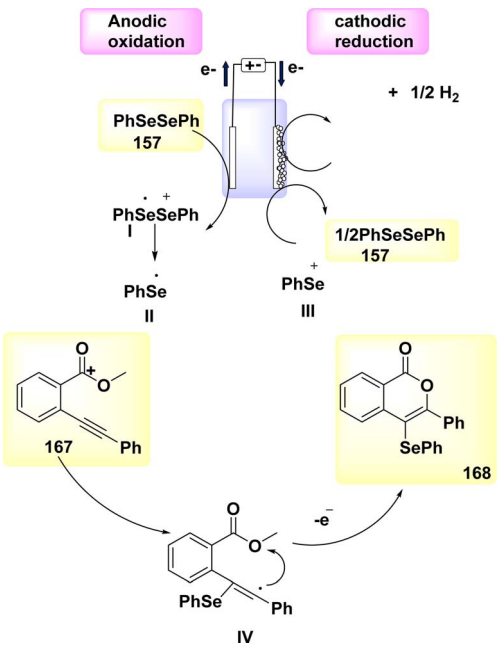


Scheme 64 Electrosynthesis of substituted isobenzofuran-1(3*H*)-one **166**.

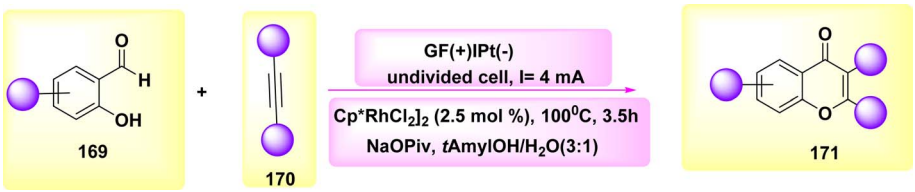
process takes place within an undivided cell at a temperature of 100 °C for a duration of 18 hours.[61,62]

In the year 2020, to initiate an oxidative cyclization process involving *o*-(1-alkynyl) benzoate and radicals, a persistent electrochemical microreactor was utilized. The production of isocoumarin **168** (Scheme 60) can be achieved by non oxidant and a metal-free technique. Despite the absence of recent advancements in post processing techniques, the potential for further evoluation in greening this synthesis method remains significant, primarily driven by the improved chemical efficacy. In addition, the scalability of events can be achieved through the implementation of a continuous electrochemical process, resulting in extreme yields of the intended product. This highlights the considerable potential of this approach for future applications in industrial production. **157** and $C_{16}H_{12}O_2$ **167** are reacted with two equivalents of nBu$_4$NBF$_4$ in the presence of acetonitrile as the solvent. The amalgamated solution was introduced into the electrochemical microreactor, where a reaction took place under the conditions of a flow rate of 45 L min^{-1} and a current of 10 mA. A target product yield of 92% can be attained, resulting in the production of **168**.[91]

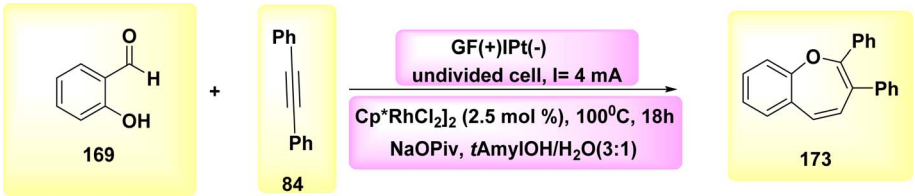
The intricate mechanism is elucidated by Scheme 65. Initially, diphenyl selenide **157** undergoes oxidation at the anode, thereby producing a cationic radical intermediate **I**. A phenyl-selenium radical **II** and a phenyl-selenium cation **III** is



Scheme 65 Mechanism of formation of isocoumarin **168**.

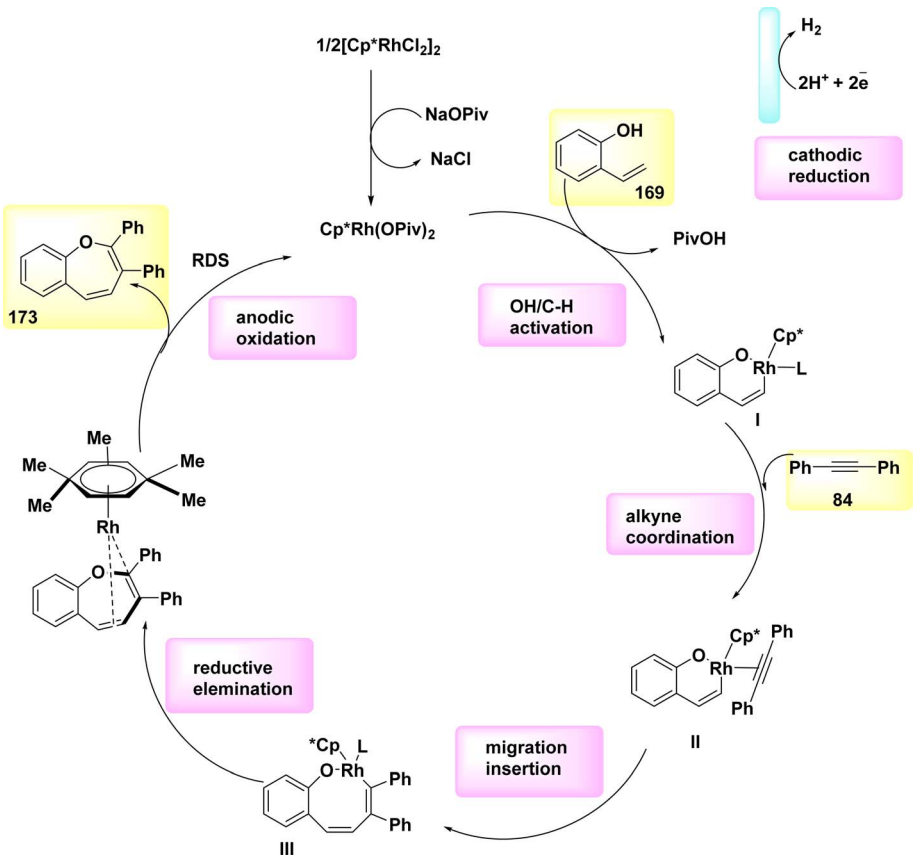


Scheme 66 Electrosynthesis of 4*H*-chromen-4-one **171**.



Scheme 67 Electrosynthesis of benzoxepine **173**.

generated by the cleavage of the intermediate **I**. Subsequently, the C_6H_5Se cation **III** under went reduction at the cathode to form diphenyl-selenide. Simultaneously, phenyl-selenium radicals reacted with the carbon–carbon triple bond of *o*-(1-alkynyl) benzoates **167**, resulting in the formation of the remarkably regioselective vinyl radical **IV**. The intramolecular cyclization of the vinyl group, which is formed *in situ*, is further facilitated by its contact with the –OMe moiety. This process results in the production of the final product **168** and the liberation of the methyl cation. This cation subsequently undergoes a reaction with the OH^- ion present in the solvent, resulting in the evoluation of CH_3OH.



Scheme 68 Electrosynthesis of benzoxepine **173** with its proposed mechanism.

A C_6H_5Se radical **II** and a C_6H_5Se cation **III** is created by the cleavage of the intermediate **I** (Scheme 66).

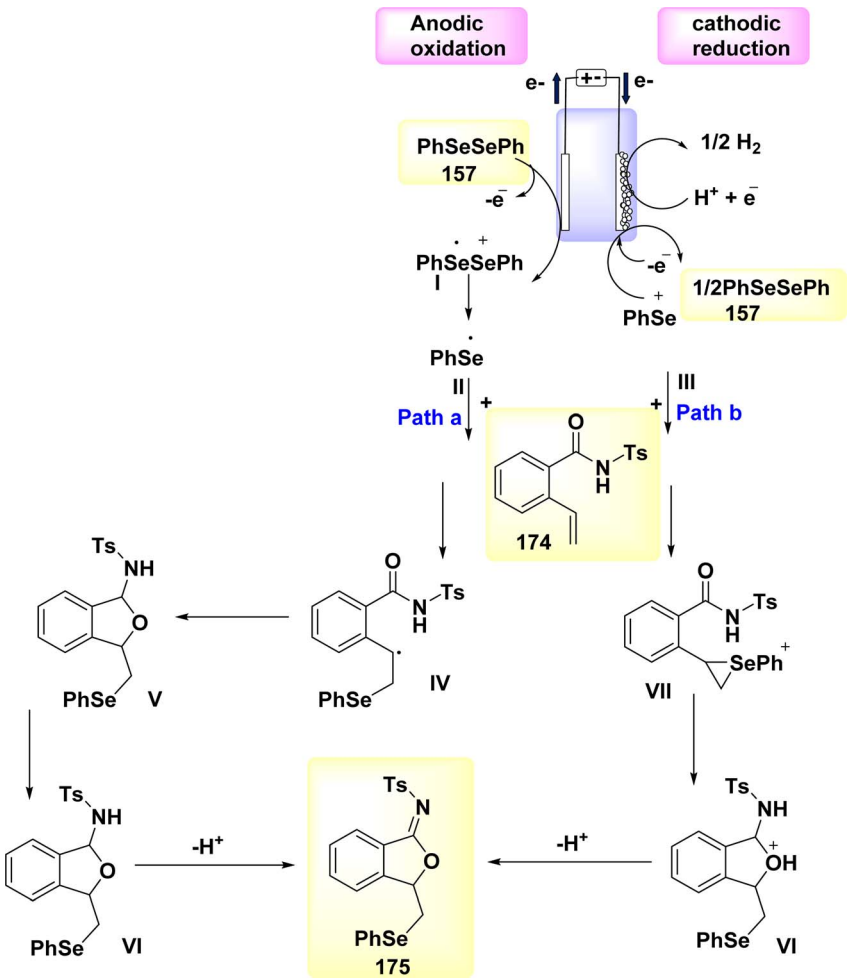
The year 2021 witnessed a proposal on the possibility of synthesizing chromones through the gradual process of electroformyl C–H activation. Electrocatalysis was conducted using a cell that consisted of an undivided compartment, wherein GF-anode and a Pt-cathode were employed. A 10 mL cell was packed with a mixture containing 2-hydroxybenzaldehyde **169**, alkyne **170**, sodium pivalate (an electrolyte), $[Cp^*RhCl_2]_2$ (a catalyst), and *t*-AmylOH/H_2O (4.0 mL, 3 : 1) as the solvent. In order to synthesize the target compounds **171**, an electrocatalytic process was conducted at a temperature of 100 °C using an undivided cell setup. The cell consisted of a GF-anode and a Pt-cathode, and a constant current of 4 mA was applied during the reaction.[92]

The year 2021 seen the documentation of valuable 7-membered benzoxepine **171** frameworks formed *via* metal-catalyzed [5 + 2] cyclo additions (Scheme 67). The alkyne annulation method exhibits a broad substrate scope and relies solely on the utilization of electricity as an oxidizing agent. In the electrochemical [5 + 2] cycloadditions, an undivided cell configuration was employed, utilizing graphite as the (+) material and Pt plate as the (−) material. The reactants involved in this process were 2-vinylphenol (**172**) and diphenylacetylene (**84**). The target product **173** was obtained with a yield of 88% after subjecting it to rigorous testing using 4-methoxyphenyl-3-phenylpropiolate dimer as the catalyst and sodium pivalate as the electrolyte in a solvent system consisting of *t*AmOH–H_2O at a temperature of 100 °C for a duration of 18 hours.[93]

A potential catalytic cycle is outlined in Scheme 68, whereby the initial step involves the activation of an O_2–N_2 or H–H bond to generate a rhodacycle **I**. Complex **IV** is formed through the process of alkyne coordination-insertion, which subsequently undergoes reductive-elimination, resulting in the production of intermediate **III**.

In the final analysis, the Rh I species undergoes oxidation to Rh III at the anode, resulting in the liberation of product **173**. Simultaneously, molecular H_2 is generated as a byproduct at the (−).

In 2021, Bian *et al.* introduced an alternative methodology for the production of O-heterocycles. In this experiment, the oxidation of $C_{16}H_{15}NO_3S$ **174** and diphenyl diselenide **157** in an electrochemical microreactor occurs. The microreactor consisted of a graphite as anode and an iron as cathode. The outcome of the

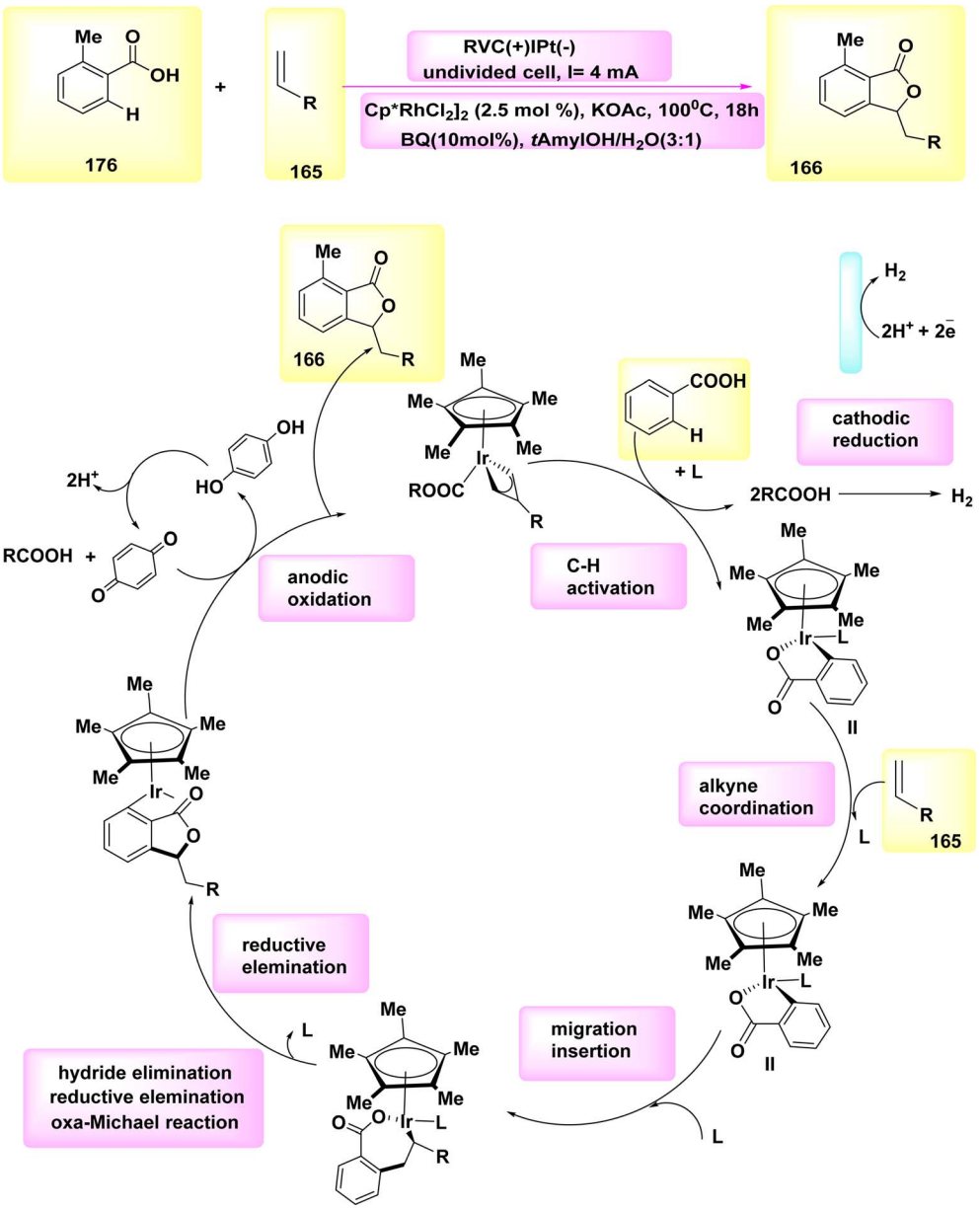


Scheme 69 Electrosynthesis of selenated isobenzofuran **175** with its proposed mechanism.

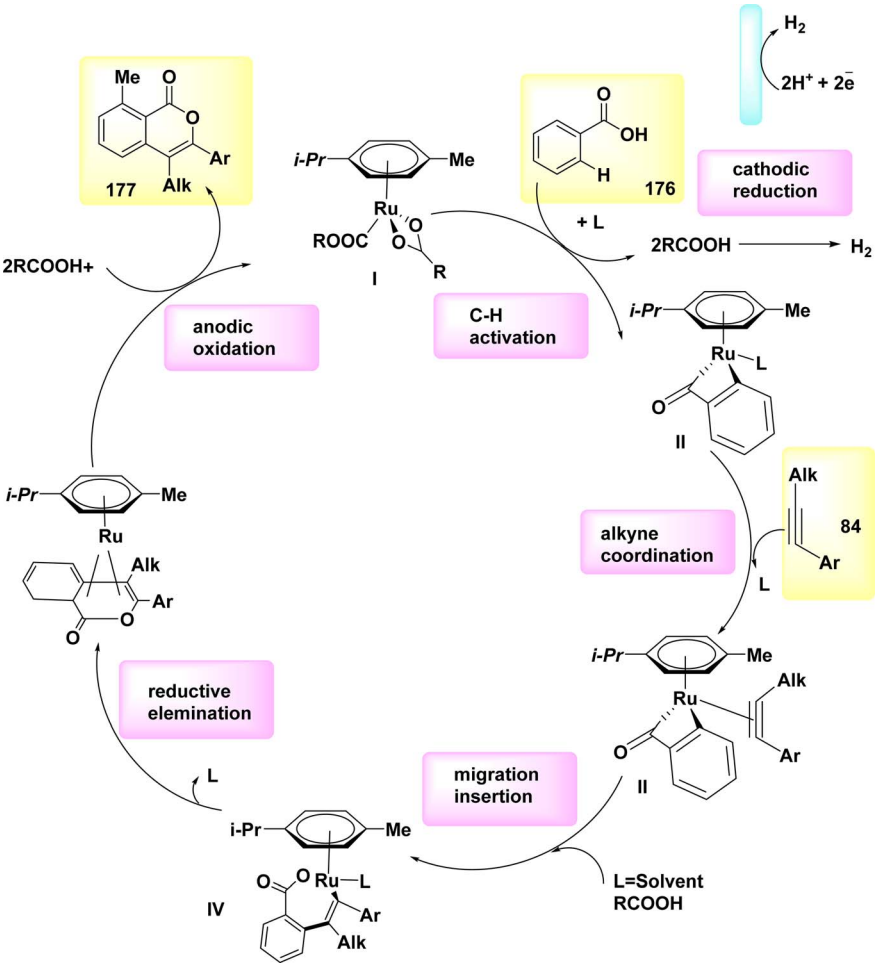
reaction was the production of selenated isobenzofuran **175**. Initially, a series of solvents were examined in an experiment conducted using a constant current of 15 mA and $LiClO_4$ as the electrolyte. The desired iminoisobenzofuran product **175** was successfully synthesized with high efficiency when CH_3CN was used as the solvent. Subsequently, several electrolytes with supporting properties were subjected to testing. By excluding the use of metals and oxidants, this methodology enabled the synthesis of a diverse range of iminoisobenzofuran derivatives with remarkable yields, as seen in Scheme 69. The utilization of a continuous-flow system in conjunction with electrochemical techniques effectively addresses the challenge of upscaling a batch-type electrolysis process.[94]

The experiment showcased the occurrence of transition using benzoic acid **176**, which exhibited weak coordination. The optimal approach for achieving the desired product **166** was utilizing a solvent mixture of *t*-AmOH and H_2O, with the addition of KOAc, within an undivided cell configuration that was user-friendly. The inclusion of ferrocene/*p*-benzoquinone (catalytic mediators) in the process may lead to a substantial enhancement in overall efficacy, when compared to the catalytic effects of Rh[95] and Ru.[96,97]

In the years 2018, 2020, and 2021, it is quite probable that an Ir(Ir)-catalyzed cycle was launched to facilitate the process of organometallic carbon–hydrogen functionalization, as depicted in Scheme 70. The construction of a 7-membered Ir(III) cycle **IV** is subsequently achieved through the process of alkene **168** insertion. Subsequently, this process progresses by reductive elimination and β-hydride elimination to generate intermediate **V**. The catalytic reoxidation of intermediate **V** to generate the



Scheme 70 Electrosynthesis of substituted isobenzofuran-1(3*H*)-one **166** with its proposed mechanism.



Scheme 71 Mechanism for the synthesis of 1*H*-isochromen-1-one **177**.

active molecule **I** is facilitated by *p*-benzoquinone. The process of anodic oxidation is occurring on the recently formed hydroquinone.[62,66,91,96,98]

The utilization of a Ru catalyst was initially documented in 2018 and subsequently in 2021, as outlined in Scheme 71. The sole oxidizing agent employed in this study was electrical energy, which served to activate the carbon–hydrogen bond. The emission of H_2 gas occurred as a by product. The catalyst employed in this procedure had no discernible response to the presence of water and air.

The most favorable outcomes were obtained while doing the experiment in a solvent mixture consisting of *t*AmOH or H_2O, supplemented with NaOPiv. The reaction conditions facilitate the conversion of biphenylacetylene **84** and benzoic acid **176** into substituted 1*H*-isochromen-1-one **177**.[97–99]

A pragmatic catalytic cycle should begin with a direct organometallic C–H activation, as suggested (Scheme 71). Consequently, the ruthena(II) cycle **II** is formed along with two equivalents of carboxylic acid. The migration of alkyne insertion subsequently provides the **IV**. The reductive elimination process is rapidly executed in this cycle, resulting in the formation of complex **V**. (+) oxidation accomplishes the reoxidation of complex **I**.

Conclusion and future perspective

This article primarily examines notable advancements towards the chemical synthesis of heterocycles including nitrogen (N), sulfur (S), and oxygen (O). There is also ongoing discourse over the recognized mechanics of heterocycle evoluation. Organic electrochemistry originated in the 19th century and continues to be a much unexplored area of research. Electrosynthesis is a process that facilitates the selective creation of N-, S-, and O-heterocyclic molecules. This approach presents a less severe situation, decreases the quantity of steps, and gives alternate pathways in comparison to traditional synthesis. Redox reactions are ideal for electrolysis because they involve both reduction and oxidation events happening simultaneously at the (+) and (−), respectively, at the time of the electrolytic process.

The utilization of electricity as an alternate method presents a convenient and efficient approach in terms of atom utilization and cost-effectiveness for the formation of molecules.[93] Although substantial advancements have been made in this particular area of study, certain challenges persist, notably the need for substantial doses of supporting electrolytes. Under the growing realm of emphasis on environmentally friendly

synthesis methods continuous-flow electrochemistry in electrolyte-free conditions is a significant area of concentration.[100] Moreover, the recent integration of photochemistry and electrosynthesis has facilitated the evoluation of homogeneous photo electrocatalysis, which exhibits remarkable redox potentials and eliminates the requirement for aggressive chemical redox reagents.[101]

Nevertheless, the synthesis of cathodic heterocycles seems to be a rare phenomenon, as the majority of recorded electrochemical heterocyclic syntheses are attributed to anodic oxidation. This observation suggests that there exist numerous unexplored domains and opportunities for further investigation within this field. The domain of electro-organic synthesis is experiencing growth, and it is anticipated that further evaluations in electro-reductive methodologies will enhance its scope and provide valuable resolutions to synthetic challenges.[102] There are further captivating advancements that are anticipated, like the utilization of sustainable solvents and sustainable energy sources.[103] It can be reasonably inferred that the implementation of unique bioderived reaction process medium will advance in parallel with the advancement of innovative heterocyclic reactions.[104] There is potential for further advancements in the recycling of transition metals through the utilization of anodic oxidation. The future holds the potential for the advancement of catalyst designs, which will contribute to the expansion of regio- and stereoselective bond functionalizations.[105]

Electrochemistry is rapidly transitioning from its conventional use to specialized chemical production in a preventive capacity, as well as in recycling and environmental remediation in a curative capacity. Electrochemistry offers a viable alternative to numerous perilous, challenging, and costly procedures across various industries. It is expected to have a significant impact on the advancement of more efficient and cleaner and processes across several industries involved in the production or utilization of chemicals, as it has the potential to address environmental concerns.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

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