Arenes / (Hetero)Arenes C–H Functionalization Under Synergistic Conditions: Electrochemistry, Photoelectrochemistry & Flow Technology

Ayesha Murtaza,[a] Zia ulhaq,[b] Bahareh Shirinfar,[c]* Sadia Rani,[d] Samina Aslam,[d] Guilherme M. Martins,[e,f] and Nisar Ahmed[f]*

[a]Department of Chemistry, Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan 64200, Pakistan.
[b]Chemical Engineering Department, Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan 64200, Pakistan.
[c]Department of Chemistry, University of Bath, BA2 7AY, Bath, United Kingdom.
[d]Department of Chemistry, The Women University Multan, Multan 60000, Pakistan.
[e]Department of Chemistry, Federal University of Sao Carlos – UFSCar, 13565-905 São Carlos - SP, Brazil.
[f]School of Chemistry, Cardiff University, Main Building Park Place, Cardiff, CF10 3AT, United Kingdom.
*E-mail: AhmedN14@cardiff.ac.uk (NA), shirinpostech@gmail.com (BS)

Keywords: C–H functionalization; Flow electrosynthesis; Photoelectrocatalysis; Metalla-electrocatalysis; Organo-electrocatalysis

Table of Contents (TOC):
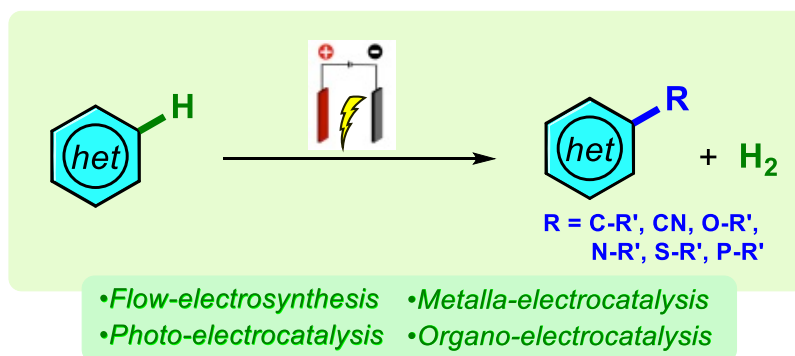
Herein, we review and summarize the recent advances in the electrochemical functionalization of C-H arenes / (hetero)arenes via batch, continuous flow, metalla-, photo- and organo-electrocatalysis reactions. The application of merging techniques to accelerate organic transformations in environmentally benign conditions is highlighted, seeking to serve as inspiration enabling tools in the field of organic chemistry.

Abstract:

The electrochemical generation of molecular complexity via C–H bond transformations without pre-functionalization of molecules, stoichiometric amounts of oxidizing/reducing species or precious metal catalysts, represent a highly sustainable technology and green methodology of contributing toward resource economy. Thus, renewable electricity provides clean electron (oxidant/reductant) that initiate a reaction cascade via producing reactive intermediates that facilitate in the building of new bonds for valuable chemical transformations. The application of modern enabling strategies (electrochemistry, photochemistry & microfluidics) in organic transformations will accelerate the process to achieve sustainable C–H bond activation and to access valuable chemicals, pharmaceuticals, and fine chemicals under safe & environmentally friendly conditions. Herein, we discussed enabling tools and technologies used for the recent C–H bonds functionalization of Arenes / (Hetero)Arenes.

Introduction

In recent years, there has been a correlation between the implementation of new technologies and quality compliance in scientific research[1–3]. With the growing concern about the environment and the impacts on nature during chemical processes, the industry is constantly highlighting the need for synthetic methods with less residue formation. Considering this, chemists are seeking to develop synthetic methods to reduce or, even more desirable, avoid the generation of waste[4]. Thus, the development and integration of new technologies in organic synthesis, as well as the use of more efficient and environmentally friendly routes are desirable. The electrochemical coupling via anodic oxidation of R−H stands out for generating only hydrogen gas as waste via cathodic reduction, in which compared to other methods that generate large amounts of by-products, the electrochemical oxidative method delivers the same product in environmentally friendly conditions[5–6].

Commonly, to favor a chemical transformation it is necessary for an atom susceptible to cleavage, substitution, addition or migration. The C−H functionalization may represent a change in this logic, since it is possible to obtain a functionalization of C−H bonds even in the presence of apparently more reactive functional groups,[7–8] however regio- and chemoselectivity

represent the greatest challenges for chemists. This process can be induced by an external energy source, a neighbor functional group with the electronic or steric features, and/or an external agent, making a specific atom more reactive for synthetic transformation[9]. Several reports describe progress using electrosynthesis for the functionalization of C−H bonds, increasing the selectivity, making cleaner, more efficient, safer, and often avoiding the use of external oxidizers[10–13], being an emerging strategy for the discovery of new molecules, also of great interest to the medicinal chemistry[14–15]. Many organic synthesis techniques can be elegantly coupled with the electrolytic cell, such as batch[16–17], continuous flow[18–20], microwave[21–23] or photochemical reactions[24–25]. Likewise, electrosynthetic processing of organic chemicals on an industrial scale has been carried out, with the production of compounds such as sorbitol, mannitol, benzidine, hydroquinone, 1,4-dihydronaphthalene, salicylic aldehyde, chloroform, iodoform, vanillin, pinacol, chloral, indigo, etc[26].

To help the reader understand the technique of electrosynthesis, we recommend the review article recently published by Gerhard Hilt[27] which highlights the basic strategies and types of applications in organic electrochemistry, as well as the article published by Charlotte Willans and co-workers[28] that aims to facilitate new synthetic chemists explore electrosynthesis. Likewise, we highlight an interesting discussion on the advantages of electrosynthesis compared to traditional methods, presented by Lei and Yuan[6].

Herein, this review article aims to provide an overview of recent advances in electrochemical arenes/(hetero) arenes C–H functionalization through batch reactions, continuous flow, metalla-, photo- and organo-electrocatalysis. The development of methodology and mechanistic studies was emphasized, seeking to provide inspiration for future synthetic applications in the field of electrosynthesis in organic chemistry.

1. Arene C–H Functionalization via batch electrochemistry

In the past ten years, C–H functionalization technologies have advanced significantly, as evidenced by the large number of publications that have been made in the literature and are attracting significant interest from researchers in various fields[29–31]. While the majority of the reported protocols execute C–H functionalization procedures in batch conditions[29]. So neither

flow nor batch is novel concepts. Although flow chemists advocate getting rid of "outdated" batch technology, it's crucial to recognize batch's genuine use. Batch is the mainstay of what we perform as synthetic chemists, we were raised on it. The basic concept is the same whether producing a medication in a research facility in milligrams or scaling it up to tons. Combine certain ingredients, stir, if required, heat, and then take out of the pot for purification. It is a tried-and-true strategy. It also works. It allows you to perform a wide range of tasks without requiring you to learn numerous new skills. However, it can be highly inefficient in a world with narrow profitability margins and environmental concerns.

Batch technology is well-known, straightforward and versatile. The same batch reactor design is used for process development from the lab to the production scale, which speeds up research and lowers costs. The most cost-effective approach to carry out many chemical operations is still batch technology. In order to explain the C–H functionalization via batch electrochemistry, in 2018, Gooßen and co-workers reported that an open, simple and undivided electrochemical cell using sodium cyanide(NaCN) as the reagent allows for the electrochemical C–H cyanation of arenes and heteroarenes to occur at room temperature in methanol(MeOH). Adsorbed cyanide maintains the quality of the platinum electrodes, enabling the conversion of a remarkable variety of electron-rich substrates all the way down to dialkylarenes. Due to the abundance of nucleophilic cyanide sources and the difficulty of handling and storing electrophilic cyanide reagents, electrochemical oxidation would be a highly advantageous technique for aromatic C–Hcyanations. The benzonitrile**2**, along with hydrogen and one equivalent of base, would result from the electrochemical coupling of NaCN with1,3-Dimethoxybenzene**1** in 84% yield as a single isomer using methyl alcohol with low water content. NaCN was selected as cyanide source because it is non-volatile from a safety standpoint and because its ionic nature allows us to avoid using more expensive supporting electrolytes. At a current of 20 mA for four hours, galvanostatic electrolysis was performed[32].
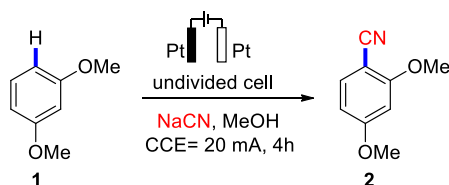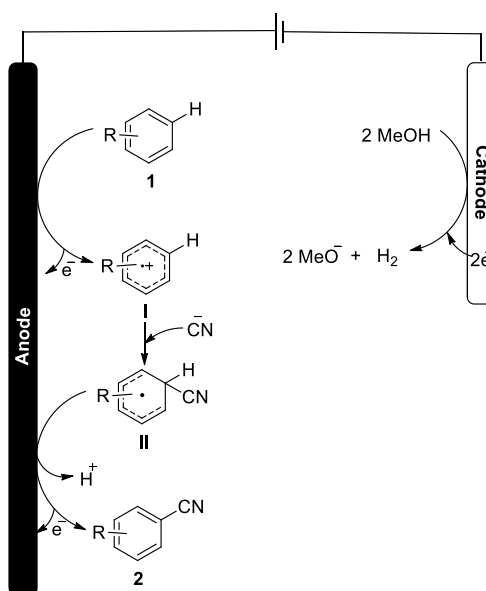

Scheme 1: Electrochemical Synthesis of arylnitrile**2** under constant current electrolysis(CCE).

Hydrogen cyanide can be used to refill the cyanide electrolyte, providing the possibility of industrial C–Hcyanation without the use of salt (Scheme 2).
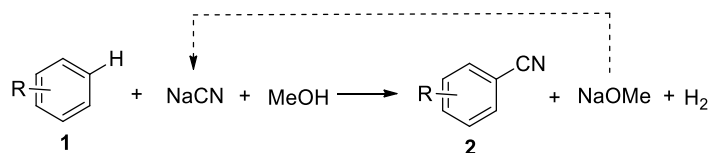

Scheme 2: Perspective industry process: combining electrolytic H_2 evolution with anodic cyanation

The arene underwent sequential anodic oxidation to produce radical cation**I**, which was then attacked by the cyanide nucleophile to produce cyclohexadienylradical**II**, which experienced additional oxidation to produce benzonitrile**2** (Scheme 3).


Scheme 3: Proposed mechanism for the **e**lectrochemical Synthesis of arylnitrile**2**

The 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) aryl ethers**4** were electrochemically obtained by Waldvogel and co-workers employing boron-doped diamond (BDD) electrodes in up to 59% of yield. Triethylamine(Et$_3$N) was employed as a base because, when combined with HFIP, it creates a highly conductive medium, eliminating the need for additional supporting electrolytes. Design of Experiment (DoE) methodologies were used to optimise the synthesis and provide a thorough understanding of the importance of the experimental parameters[33].
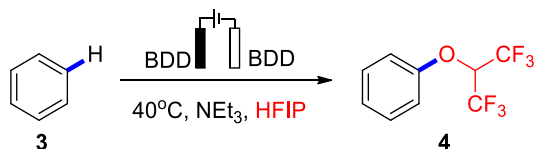
Scheme 4: Electrochemical Synthesis of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) aryl ethers**4**

A procedure for the dehydrogenative C(sp^2)–H/N–H cross-coupling between arenes/alkenes and sulfonimides that is brought on by electrochemical oxidation has been developed. It was possible to complete this reaction without the need of a transition metal catalyst or a stoichiometric extra oxidant. A wide range of aryl sulfonimides and alkenylsulfonimides could be obtained using the electro-synthetic approach. The simplicity with which the reaction can be scaled up shows this technique's potential for synthetic synthesis. The electro-oxidative C–H imidation using naphthalene**5**(0.4mmol) as a template platform and dibenzenesulfonimide**6** (1.5equiv.) as the nitrogen supply were considered. By utilising a carbon rod-anode and a platinum plate-cathode in an undivided cell with a constant current of 10 mA for 4 hours at room temperature, the cross-coupling product**7** may be produced in acetonitrile with a 43% pure yield. The electrolyte and base utilised were both tetrabutylammonium acetate. A mix-solvent system, DCM/MeCN/HFIP = 20:4:1, provided the greatest result (76% isolated yield)[34].
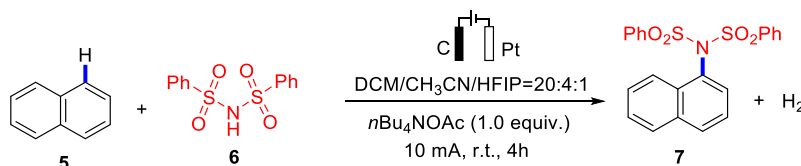
Scheme 5: Electrochemical Synthesis of N-(naphthalen-1-yl)-N-(phenylsulfonyl)benzenesulfonamide**7**

A possible mechanism was predicted (Scheme 6). Tetrabutylammonium acetate and the dibenzenesulfonimide N–H bond would first create a hydrogen-bonded complex **I**. The resultant adduct **I** would go through a coordinated proton-coupled electron transfer event along with a single electron oxidation on the anode, which would cause the N–H bond to homolyze and result in the generation of the crucial sulfonimidyl radical intermediate **II**. A new C–N bond and a vicinal radical **III** with a carbon core were produced by the following radical addition to

naphthalene. The radical species was subsequently subjected to further oxidation in order to produce a carbon cation intermediate **IV**, which was subsequently aromatized in order to produce the aryl C(sp^2)–H imidation product**7** via proton deletion. During the course of the reaction, concurrent cathodic reduction of the obtained protons would produce hydrogen gas, avoiding the need for an external oxidant to complete the transformation.
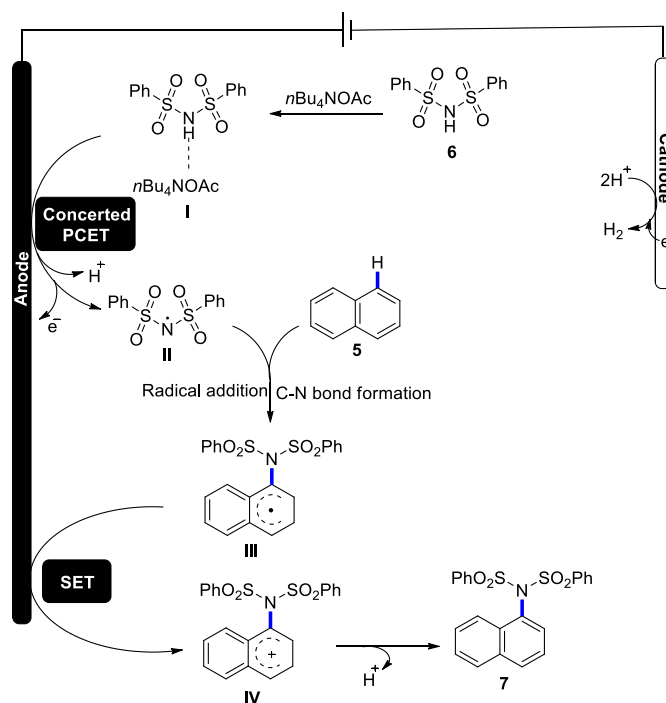
Scheme 6: Proposed mechanism for the electrochemical Synthesis of N-(naphthalen-1-yl)-N-(phenylsulfonyl)benzenesulfonamide**7**

Sulfones are extremely adaptable basic components that have several uses in the pharmaceutical, agrochemical, and functional industries[35]. Lei and co-workers proposed an oxidatively C–H sulfonylate anilines electrochemically without the use of a metal catalyst or external oxidant. When methylnitrile, water, and acetic acid (10.2 mL, 9/1/0.2, v/v/v) are used as the solvent and various sodium sulfinates as the electrolyte, the necessary products can be produced in an undivided cell at 18mA constant current for two hours with up to 96% yield[36].Using nBu$_4$NBF$_4$ as the electrolyte and CH$_3$CN/H$_2$O as co-solvents for 3 hours in an undivided cell (a three-necked round-bottomed flask) furnished with a carbon rod anode and a platinum plate

cathode. In 2019, Wu and co-workers reported the preparation of an anodic C–H sulfonylation product in 2019 with a 91% yield[37].
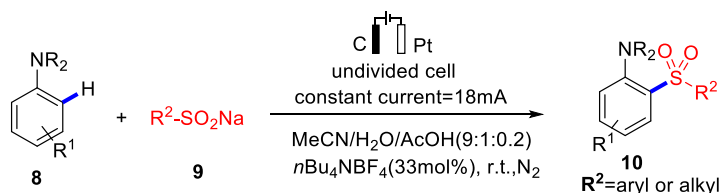
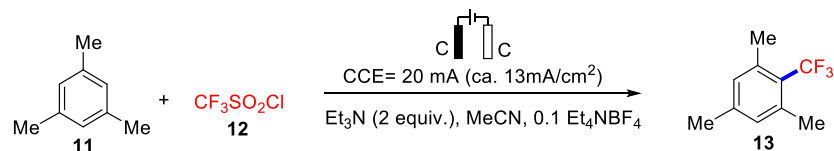**Scheme 7:** Electrochemical Synthesis of sulfonylate aniline**10**

The suggested mechanism in Scheme 8 is as follows. First, the anodic oxidation of sulfinate salts produces the arylsulfonyl radical **IV**. Aniline**8** underwent oxidation at the same moment, resulting in radical cation**I**. Then, through tautomerization, radical cation**I** would yield radical cation**II**. Arylsulfonyl radical **IV** and radical cation**II** undergo radical/radical cross-coupling before being successively deprotonated and aromatized to produce the required sulfonated aniline**10**. During the reaction, the co-solvent water or acetic acid may be reduced at the cathode to produce hydrogen gas(Scheme 8).
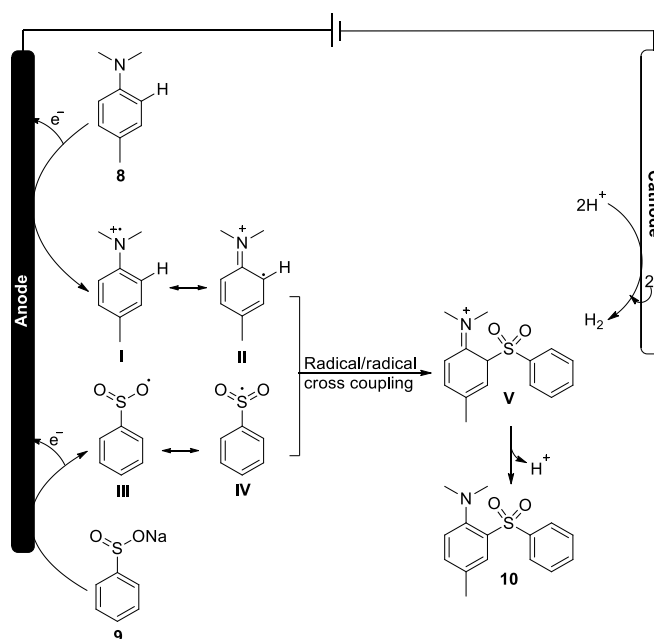
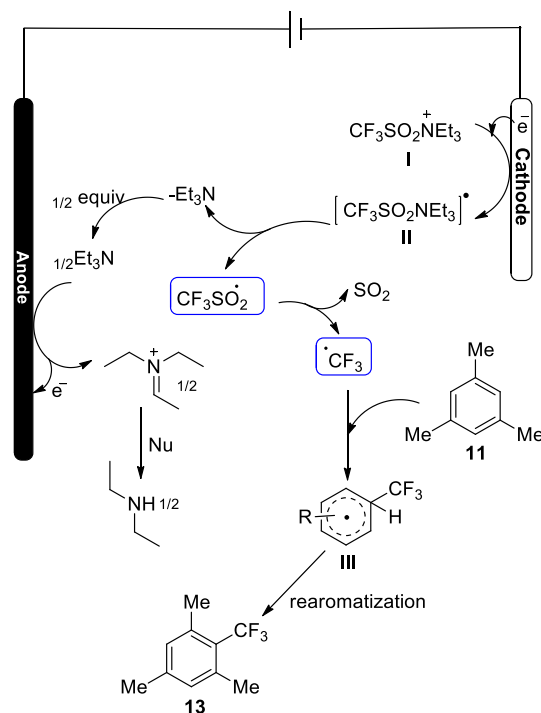**Scheme 8:** Proposed mechanism for the electrochemical Synthesis of sulfonylate aniline**10**

Recently, Cantillo and co-workers described for the first time that arenes and heteroarenes undergo cathodic-trifluoromethylation. Mesitylene**11** was used as a template platform (Scheme

9), and graphite was used as the anode and cathode materials in an undivided cell arrangement (IKA ElectraSyn 2.0). In order to elucidate the oxidation product of the amine, in addition to Et$_3$N, other bases were investigated. Likewise, assays with MeCN-d$_3$ helped to understand the electrochemical trifluoromethylation reaction[38].

Scheme 9: Electrochemical synthesis of trifluoromethyl arene**13**

The suggested reaction mechanism calls for a change that would mostly occur on the cathode surface (Scheme 10). A neutral radical is produced when trifluoroammonium complex **I** is reduced by one electron. The process is based on an electrochemical reduction of an unstable triflyltriethylammonium complex produced in-situ from triflyl chloride and triethylamine, which results in the production of CF$_3$ radicals that are captured by arenes on the cathode surface.

Scheme 10: Proposed mechanism for theelectrochemical synthesis of trifluoromethyl arene**13**

Even having a long history, electroorganic synthesis did not for a very long time contribute to the main stream of chemical study. This is most often caused by a lack of tools and established

procedures. However, organic electrochemistry is currently experiencing a revival, and a wide variety of intriguing electrochemical transformations and techniques have been devised, not just for academic reasons but also for massive industrial production. Electrochemical processes can be naturally green, environmentally safe, and simple to manage to reach high degrees of selectivity, depending on the source of electricity. Furthermore, it is possible to produce and consume hazardous reagents and reactive or unstable intermediates in a secure manner. Electrochemical flow cells can be used to overcome some of the drawbacks of conventional batch-type electrochemical processes, such as the constrained electrode surface, the requirement for supporting electrolytes, and the challenges of scaling up[39]. High surface-to-volume ratios in microreactors make it possible to precisely manage the temperature, residence duration, flow rate, and pressure. Furthermore, handling of small amounts, improved mass and heat transmission, and effective mixing reduce safety issues and simplify scaling-up procedures. In contrast to conventional batch-type electrolysis cells, electrolysis under flow circumstances lowers the likelihood of over oxidation because the reaction mixture is flown continually out of the reactor[27].

Pumping the reactant solution into an assembly of two electrodes with a generally modest interelectrode gap is all that is necessary to perform electrolysis under flow circumstances. Because of the reduced ohmic resistance caused by the close proximity of the two electrodes, electrolysis can be performed with very little or no supporting electrolyte. Figure 1 depicts a schematic illustration of such a reaction arrangement.
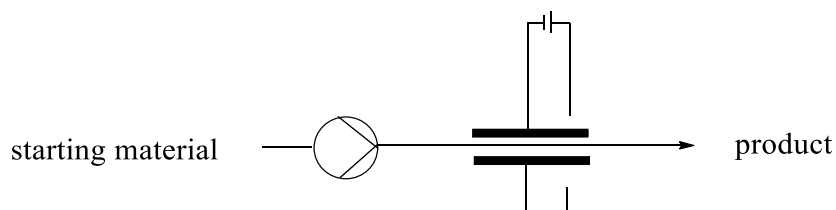

Figure 1: Schematic representation of electrolysis under flow conditions

## 2. Arene C–H Functionalization via flow-electrochemistry

The interest in electrochemical C–H functionalization in organic synthesis is expanding quickly. The flow electrolysis procedure is more environmentally friendly and allows for optimum atom economy. As a result, reaction times can be speedier, workplaces can be safer, and selectivities

can be higher. With the use of this innovation, the issue of over-oxidation can be mitigated, and side products may even not form at all. Electrochemical processes can now be controlled without the requirement for a purposefully supplied supporting electrolyte thanks to flow electro-reactors, which have electrodes that are closely placed where the diffusion layers meet to generate the desired result. Despite its many benefits, this approach is only employed in a small number of chemical and pharmaceutical firms because of the elaborate and costly setting. The creation of insoluble substances as the primary or by-product, which might interfere with uniform flow, is one of the many difficulties that restrict the use of flow electrochemistry in the industrial field. Additionally, other gases including H_2 or N_2 are formed during electrochemical synthesis, which results in a gas-liquid phase and affects the product's quality. The implementation of electro-flow methodologies will undoubtedly benefit from additional advancement and research of micro-reactors with simple setup and affordable electrochemical flow microreactors[40].

It is of special industrial significance since 3,3′,5,5'-Tetramethyl-2,2′-biphenol is well known for being an exceptional fundamental basis for ligands in transition-metal catalysis. In highly modular narrow gap flow electrolysis cells, the dehydrogenative anodic homocoupling of 2,4-dimethylphenol **14** is shown to scale up successively from the laboratory scale to the technically applicable scale. Up to 62% of the necessary biphenol might be produced. The electrolysis of **14** was completed using HFIP as solvent at a temperature of 50°C in order to transfer the electrosynthesis of **15** into the 2cm x 6cm flow electrolysis cell. Bromination can be efficiently controlled as a side reaction by supplying H_2O to the electrolyte. For both electrodes, glassy carbon was utilized as the electrode material. To get the most thorough conversion to the intended **15**, a small excess of charge of 1.2F was introduced. 6.1 mA/cm^2 of applied current was a moderate amount. Additionally, a higher flow rate in the cascade mode can effectively convey the resultant gaseous hydrogen(H_2) out of the flow cell [41].

The anode material was changed from glassy carbon to BDD with the goal of creating an all-encompassing procedure that is also appropriate for other phenols. Because stainless steel is affordable and has a minimal impact on electrolysis, it was recommended as the cathode material. Me-Bu$_3$NO$_3$SOMe was used as a supportive electrolyte throughout the electrolysis

process and was used in pure HFIP without any other additives. Additionally, electrolysis in cascade mode might greatly boost the output of 62%[42].
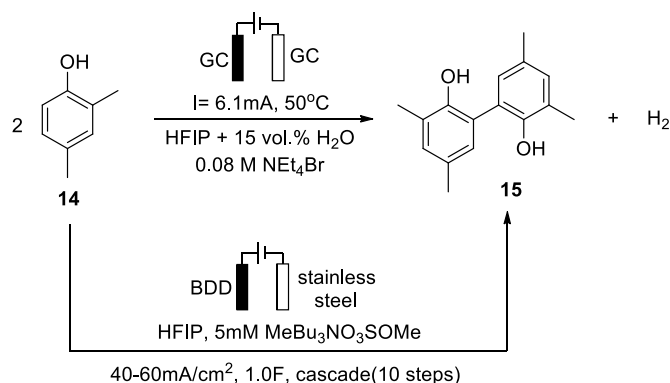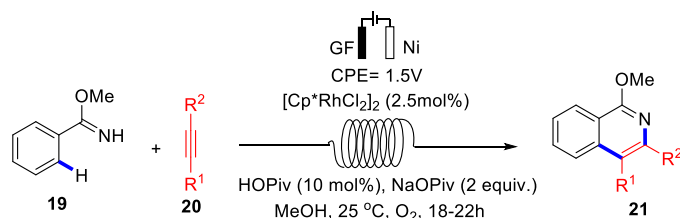

Scheme 11: Electrochemical Synthesis of 3,3′,5,5'-Tetramethyl-2,2′-biphenol**15**

Instead linear and oligomericbyproducts, like ortho, meta-coupling product **16**, and diaryl ether **17**, can be obtained under neutral to acidic conditions in addition to the required bi-phenol **15**. This substantially relies on the regioselectivity of the phenoxy radical **I** action. A dehydrotrimer of 2,4-dimethylphenol **18**as well as oligomeric compounds can develop because**15** is susceptible to overoxidation[42].
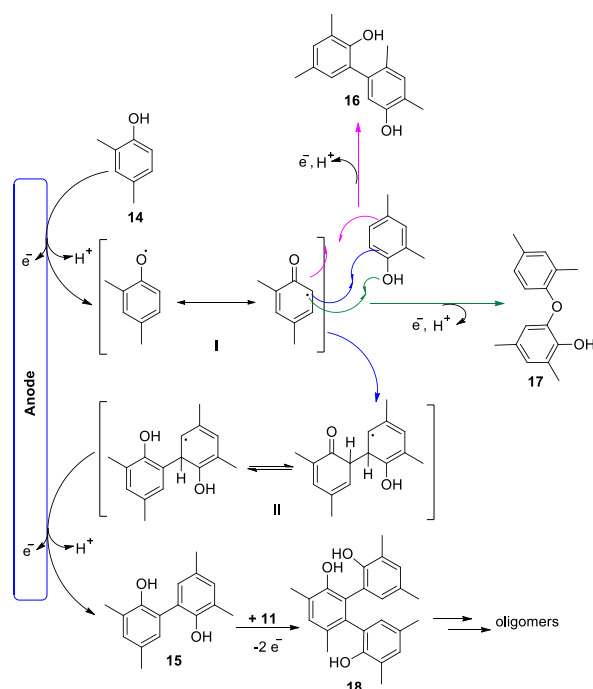
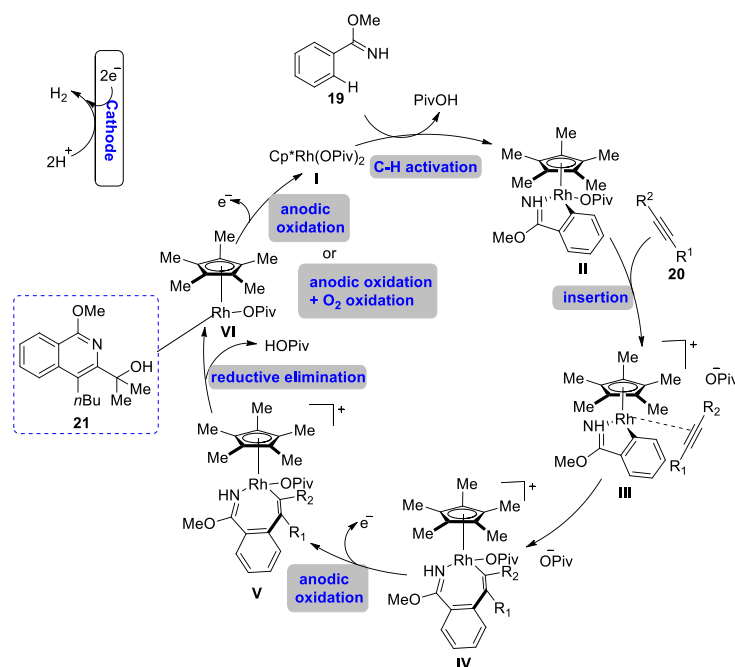**Scheme 12:** Proposed mechanism for the electrochemical Synthesis of 3,3′,5,5'-Tetramethyl-2,2′-biphenol**15**

The intended isoquinoline**21** was synthesized by focusing experiments on the envisioned rhodaelectro-catalyzed C–H annulation with imidate**19** and unsymmetrical alkyne **20** in batch, adopting methanol as the solvent, 2.5 mol% [RhCp*Cl$_2$]$_2$ as the catalyst, sodium pivalate and pivalic acid as additives under air in an undivided cell, employing graphite felt(GF) anode and Nickel plate cathode. With this improved flow cell in hand, additional tuning allowed for the production of product **21** in 83% yield at a constant potential of 1.5 V and a flow rate of 400 L/min while operating under 1atm of oxygen at room temperature[40,43].

Scheme 13: Electrochemical Synthesis of isoquinoline**21**

A realistic catalytic cycle is suggested based on the mechanistic investigations and is shown in Scheme 14. Cp*Rh(OPiv)$_2$ **I**, which is obtained via ligand exchange between the catalytic

precursor and NaOPiv, is then directed by substrate **19** to supply the cyclometallated rhodium complex **II** through simple C–H activation. Rhoda(III)cycle **III** is then produced by alkyne coordination and migratory insertion. Rhodium(II) intermediate **V** is produced fast by anodic oxidation of rhodium(IV)cycle **IV**. The catalyst **I** is then regenerated via anodic oxidation, which can be quickened by oxygen. Aerobic and anodic oxidation appear to be plausible processes for the rhodium(II)-rhodium(III) reoxidation phase. Preventing cathodic reduction of extremely reactive rhodium intermediates, most likely rhodium(II) species, is another benefit of molecular oxygen. In contrast, rhoda(III)cycle **VI** can also produce product **21** directly together with a reduced rhodium species that may reoxidize at the anode. Overall, cathodic proton reduction produces only molecular hydrogen as a stoichiometric by-product, and rigorous head-space GC analysis has proven this to be the case.

Scheme 14: Proposed mechanism for the electrochemical Synthesis of isoquinoline **21**

Due to their advantageous excited-state characteristics, such as their high reduction potential and long lifespan, acridinium dyes are one of the most commonly investigated groups of organic photocatalysts. Modulating their catalytic performance through a structural change is still difficult. Xu and co-workers described a site-selective late-stage C(aryl)–H functionalization of the acridinium core using a continuous-flow, two-step method for the production of

functionalized acridiniumphotocatalysts has been disclosed. The parent acridinium dye is consecutively pumped through a photoreactor to achieve cross-coupling with an organotrifluoroborate and an electrochemical reactor for electrocatalytic dehydrogenation in order to perform the alkylation. A variety of different alkyl groups can be introduced at the 3-position of the acridinium dye using the two-step automated technique. A second alkylation of 3-alkylated acridinium salts in the flow system results in 3,6-disubstituted acridinium dyes. The reactor system comprises of an electrolytic microreactor and a photoreactor consisting of perfluoroalkoxy (PFA) tubing tied around blue light-emitting diodes (LEDs). It can be difficult to work with salts in microflow reactors because particles can precipitate and clog the microchannels.**22**(0.05M) and *t*Bu-BF$_3$K (0.075M) was dissolved in MeCN/H$_2$O (5:1) and fed into the reactor system to assure the solubility of salts. The 3,4-dihydroacridine **25** resulting from the photoreactor was difficult to oxidize and needed deprotonation to produce 3,10-dihydroacridine **26**, which is easily oxidized. In order to combine with the photoreactor's eluent before entering the electrochemical reactor, pyridine (Py) was delivered via pump B together with the electrocatalyst 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO). In these circumstances, a 91% yield of the required acridinium**24** was isolated[44].
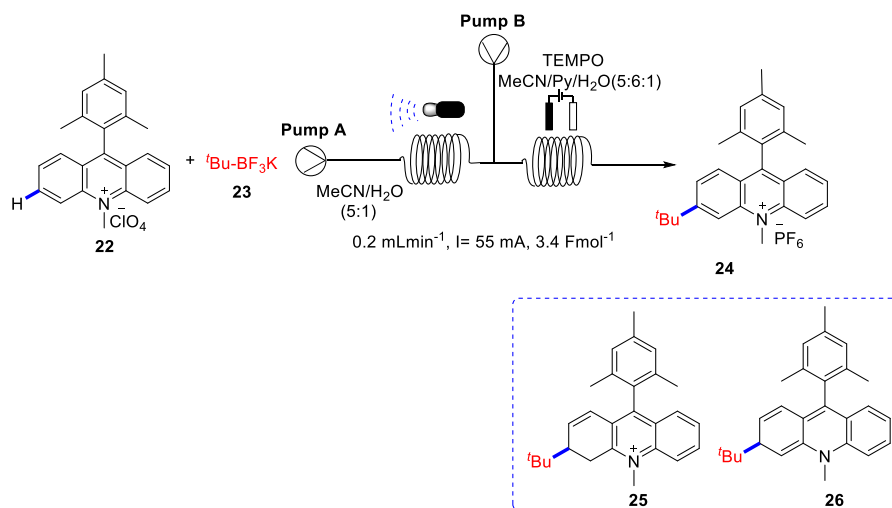
Scheme 15: Electrochemical Synthesis of 3-alkylated acridinium salts**24**, **25** and **26**

Due to the widespread use of organophosphorus compounds in chemistry, biology, and the sciences of materials, it is crucial to create effective and sustainable processes for the creation of carbon-phosphorus bonds[45,46]. Xu and co-workers disclose an electrochemical C–H

phosphorylation reaction of arenes in continuous flow without the use of a catalyst or external oxidant for the manufacture of aryl phosphorus compounds. In spite of extensive research on P-radicals, the formation of the C–P bond involves the reaction of arenes with anodically produced P-radical cations and a class of reactive intermediates. The gentle electro-synthesis conditions and strong reactivity of P-radical cations allow for both selective late-stage functionalization of complex natural products and bioactive chemicals as well as efficient reactions of arenes with a variety of electronic characteristics. An undivided continuous flow electrochemical cell with a graphite anode, a platinum cathode, and a flow channel carved out of a fluorinated ethylene propylene spacer with a 0.25 mm thickness was used to conduct the electrolysis. When a solution of benzoate **27** (1 equiv.), trialkylphosphite $P(OR)_3$ (5 equiv.), HBF_4 (2 equiv.), and H_2O (2 equiv.) in MeCN was run through the flow cell at 0.2 mL/min, an ideal 70% yield of phosphonate**29** was produced[11].
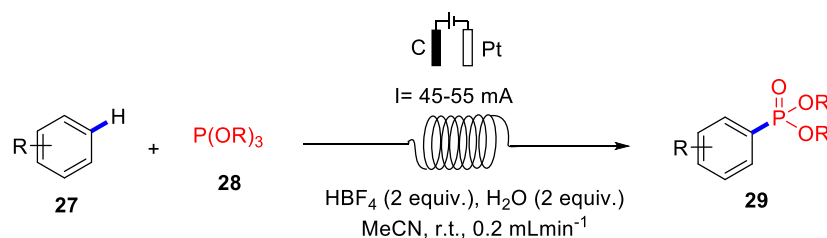
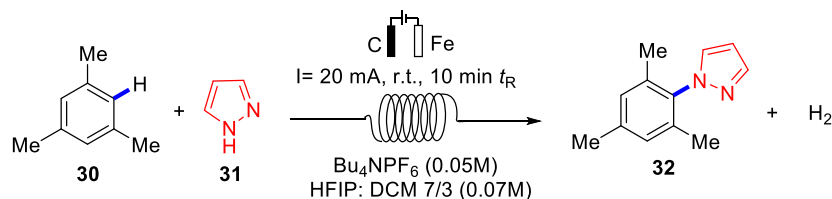**Scheme 16:** Electrochemical Synthesis of phosphonate**29**

The mechanism of phosphorylation via C–H bond functionalization has been suggested(Scheme 17). Trialkylphosphite**28** is first oxidised on the anode to produce P-radical cation**I**, which then interacts with arene**27** to produce distal radical cation**II**. In order to create phosphonium**III**, the latter is further oxidised on the anode and then deprotonated. Phosphonium**III** then loses an alkyl group to a nucleophilic species in the reaction mixture, such as H_2O or alcohol created from the hydrolysis of $P(OR)_3$, or during the workup, in order to produce the final phosphonate product **29**. Protons, the most readily reduced component in the reaction mixture, receive electrons at the Pt cathode in these acidic circumstances to produce hydrogen gas. Acidic additive HBF_4 prevents unintended cathodic reduction of electron-deficient molecules like **III** and **29** by promoting hydrolysis of $P(OR)_3$ and acting as a proton source for H_2 evolution. By reversibly forming an adduct **IV**with radical cation**I**, the $HPO(OR)_2$ produced

in situ by the hydrolysis of P(OR)$_3$ delays the breakdown of **I**and prolongs the time needed for its reaction with the arene.
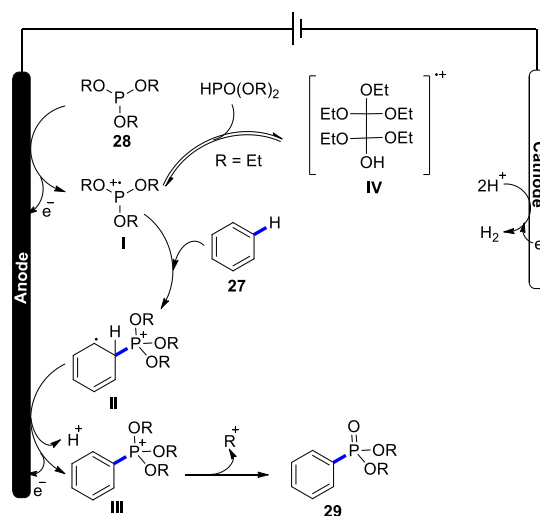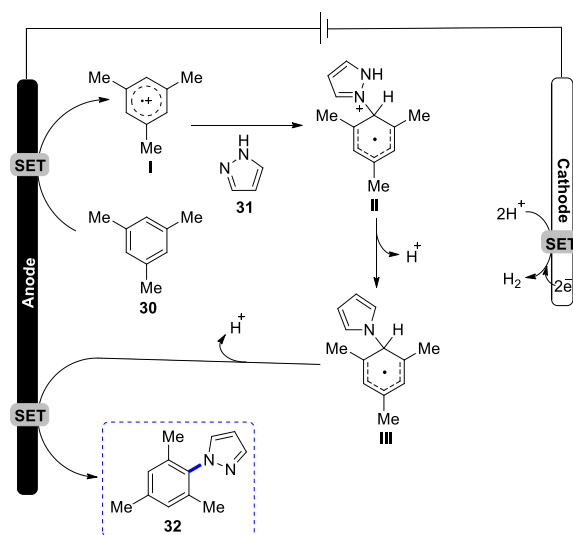

Scheme 17: Proposed mechanism for the electrochemical synthesis of phosphonate**26**

In a microflow reactor, aryl azoles**32** were synthesised electrochemically for the first time time by Nöel and co-workers. Considering that the reaction depends on the anodic oxidation of the arylderivatives, no homogeneous transition-metal-based catalysts are needed, which makes these substrates suitable to C–H functionalization with azoles**31**. It is envisaged that this electrochemical azolation technique would be used in contemporary medicinal chemistry settings due to its operational simplicity and sped-up reaction times. Carbon anode and stainless steel cathode in the electrochemical microflow reactor were separated by a Teflon gasket, resulting in an interelectrode gap of 250μm m and a volume of 700μL. A solution of pyrazole(1.0 equiv.) and 1,3,5-trimethylbenzene**30** (6 equiv.) in hexafluoro-2-propanol (HFIP)/CH$_2$Cl$_2$ (7:3) could be subjected to the galvanostatic conditions (20mA, equivalent to 0.71 mA cm^{-2} and 2.6 F mol^{-1}) for just 10 minutes before 67% of the required cross-coupled product **32** could be isolated[47].

Scheme 18: Electrochemical Synthesis of aryl azole**32**

The arene is oxidised at the graphite anode (+2.07 vs saturated calomel electrode (SCE) for mesitylene) to produce the aryl radical cation **I**, according to the mechanism that has been hypothesised to operate in the electrochemical flow reactor (Scheme 19). The subsequent attack on this molecule by the nucleophilic azole can result in the creation of the new C–N bond. After losing a second proton and an electron, **II** will produce the radical species **III** by a deprotonation phase, which will eventually give rise to the azolated product **32**. As a synthetically advantageous consequence of the cathodic process, protons are reduced to create molecular hydrogen.


Scheme 19: Proposed mechanism for the electrochemical synthesis of aryl azole **32**

3. Arene C–H Functionalization via Metalla-electrocatalysis

Conventional techniques primarily rely on using stoichiometric levels of harmful and costly metal and chemical oxidants, despite their overall sustainability. Unwanted by-products are being produced in the meantime, which is troublesome for the scaling up process. However, a more effective method for achieving selective functionalizations has been shown to be electrochemical C–H activation via catalyst control strategy employing metals as mediators (instead of electrochemical substrate control approach). Thus, indirect electrolysis improves the potential range and reduces the likelihood of adverse responses. Here, we provide a summary of the metallaelectrocatalysis procedure for functionalization and activation of inert C–H bonds. These Metalla-electrocatalyzed C–H bond functionalizations are described in terms of the

production of C–C and C–X bonds (where X is one of the halogens, N, O, or P)[48]. Better chemoselectivities with a wide tolerance of sensitive functionalities are how one can describe the electrooxidative C–H transformations in the presence of metal catalysts. Additionally, metalla-electrocatalysis integration with flow and photochemistry will enable safe and efficient scale-up in the future and may potentially improve reaction kinetics, timings, and yields in order to address sustainability and green chemistry concerns[49].

Shi and co-workers reported an electrochemical method for promoting directed C–H alkynylation with terminal alkyne by iridium catalysis. In this study, Ir(III) intermediate, which was identified by X-ray crystallography, was anodized to facilitate reductive elimination and to produce the necessary coupling products in good yields (up to 95%) without the use of any additional external oxidants. With 2.5% [Cp*IrCl$_2$]$_2$, KOPiv acting as the base and electrolyte in methanol under argon, the reaction's ideal conditions are made clear. The target product **35** was obtained in a 92% isolated yield when the reaction was carried out with RVC as the anode and Pt as the cathode under constant current conditions of 5mA for 8 hours at room temperature. With H$_2$ as the sole by-product, this transformation works well for a variety of directing groups and allows for practical oxidative C–C bond synthesis[50].
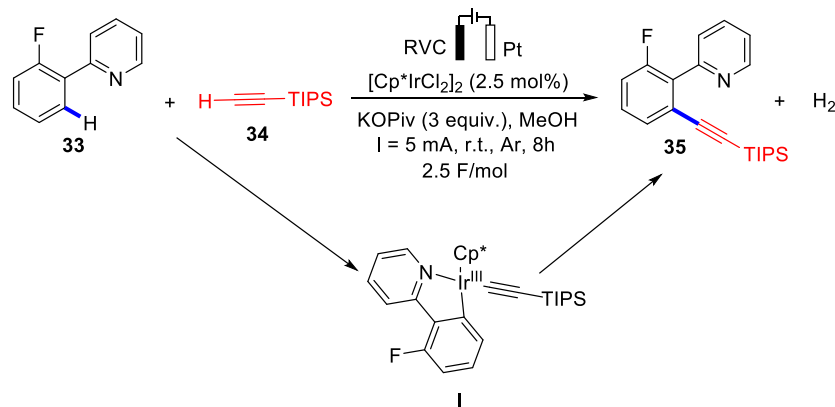
Scheme 20: Electrochemical Synthesis of alkynyl arene**35**

Earth-abundant nickel catalysts were used to produce C–H phosphorylation with waste-free power acting as the redox mediator. Arylphosphonates, phenylphosphine oxides, and diazaphospholidine oxides of significance to bioactive chemicals and materials were successfully obtained by the strong nickela-electrooxidative C–H activation of arenes, heteroarenes, and olefins. The electrooxidative C–P synthesis with guanidine assistance avoided chemical oxidants.

By using X-ray diffraction analysis, catalytically important nickel(II) and nickel(III) intermediates were identified and thoroughly characterised. It has been documented that nickela-electrooxidative C–H phosphorylation of benzamide**36** occurs non-sequentially with an undivided cell using unmasked phosphonate**37**. The desirable product **38** was successfully obtained in high yields using a graphite felt (GF) anode and a nickel (Ni) foam cathode in the presence of the organic base 1,1,3,3-tetramethylguanidine (TMG) as an additive and Ni(DME)Cl$_2$ as a catalyst[50].
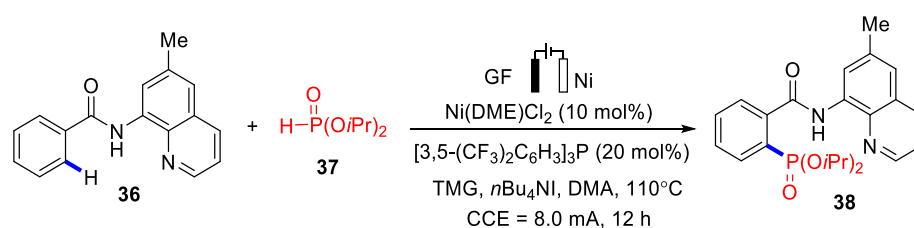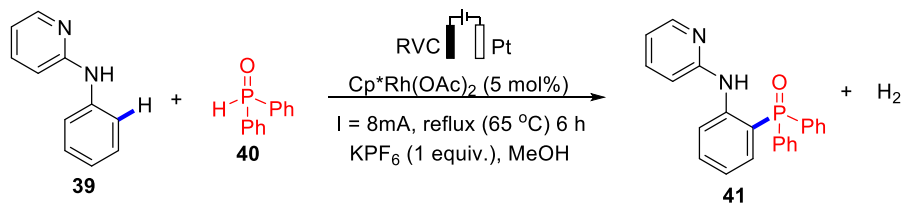

Scheme 21: Electrochemical synthesis of Arylphosphonate**38**

In Scheme 22, a possible catalytic cycle is shown. Coordination of substrate **36** and anodic oxidation at Ni(III)**II** results in first C–H activation. Later coordination of phosphonate**37** prepares Ni(IV)**V** for an oxidation-induced reductive elimination. It is suggested that the TMG addition will help **VII** form by facilitating coordination. The phosphine is postulated to stabilise an off-cycle species rather than directly take part in an on-cycle event, hence increasing the overall electrochemical stability. Through cathodic reduction, these newly generated protons provide hydrogen gas.
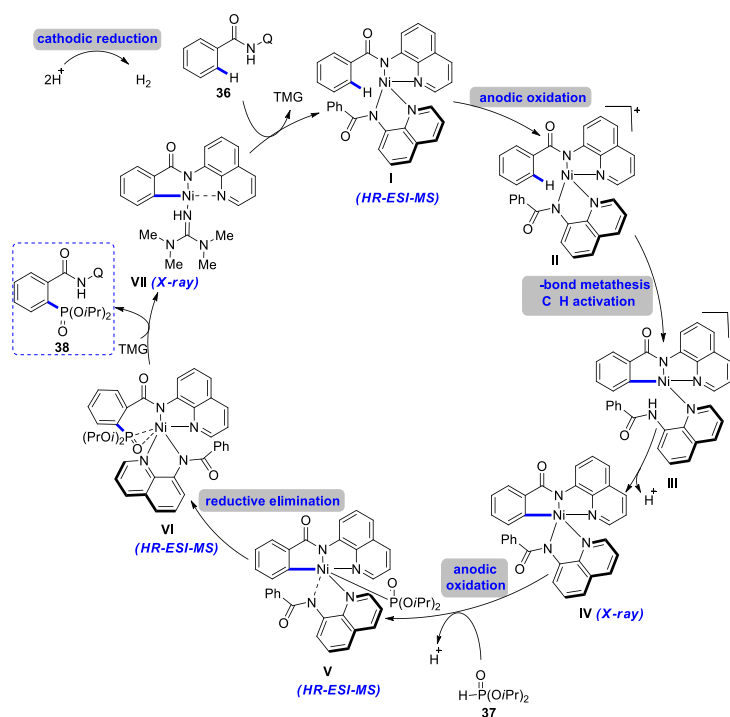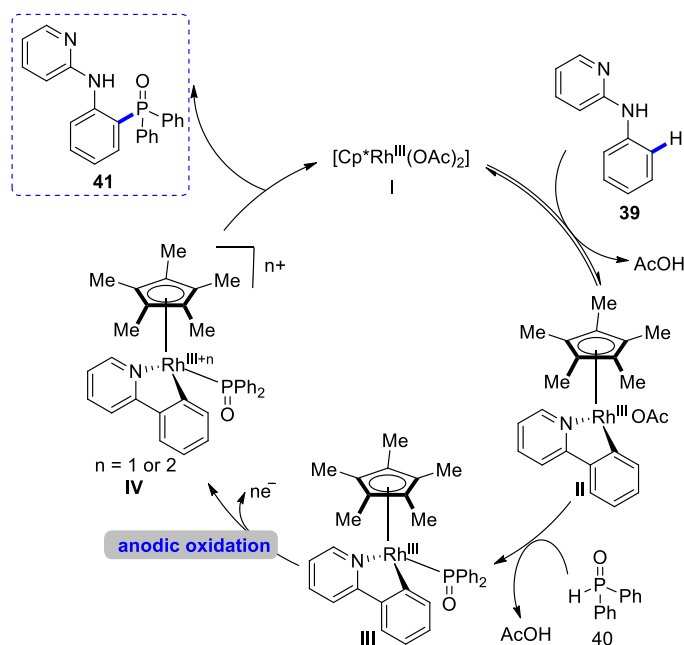
Scheme 22: Proposed mechanism for the electrochemical synthesis of Arylphosphonate**38**

In 2020, Xu and co-workers proposed aryl C–H phosphorylation under Rh^{III} catalysis without the need of stoichiometric metal oxidants. The reaction occurs via H_2 generation. The technique is beneficial for generating triarylphosphine oxides from diarylphosphine oxides, which are frequently challenging coupling partners for transition metal catalysed C–H phosphorylation processes. It is compatible with a variety of aryl C–Hand P–H coupling partners. These investigations begin by first enhancing the electrochemical conditions for the previously unreported phosphorylation of N-(2-pyridyl)aniline**39** with diphenylphosphine oxide**40**. An undivided cell furnished with a RVC-anode and a Pt-cathode was used to conduct the electrosynthesis. The reaction mix consisting of KPF_6-supporting salt (1 equiv.), methanol-solvent, and Cp*Rh(OAc)$_2$(5 mol%)-catalyst produced the best results at 65°C and a constant current of 3 mA. The required phosphorylated product**41** was recovered in 75% of yield under these circumstances[51].
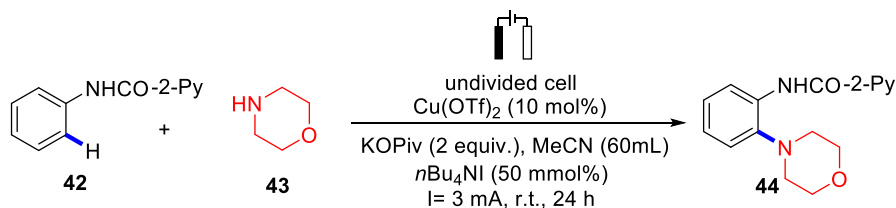
Scheme 23: Electrochemical synthesis of phosphorylated arene**41**

Scheme 24 illustrates a potential mechanism for the electrochemical C–H phosphorylation process using the manufacturing of **41**. The rhodacycle **II** is formed through the simple and reversible cyclorhodation of the *ortho* C–H bond of 2-phenylpyridine. The more oxidizable organometallic complex **III** is produced by ligand exchange between **II** and **40**, which is followed by oxidation-induced reductive elimination to give the C–H phosphorylation product **41** and either a Rh^{III} or Rh^{II} complex, depending on the oxidation state of **IV**. How many electrons **III** loses before the reductive elimination is currently unknown. External electron or proton acceptors are not necessary at the cathode since protons are reduced there to produce hydrogen gas.

Scheme 24: Proposed mechanism for the electrochemical synthesis of phosphorylated arene**41**

Metal catalyzed electrochemical C–H amination is an highly demanded transformation owing to the dominance of heteroarylamines and arylamines in pharmaceuticals and natural products. The electrochemical C–H aminations of arenes catlyzed by cobalt with secondary amines was independently developed by Ackermann[52] and Lei group[53]. An environmentally acceptable alternative to traditional procedures that call for caustic stoichiometric chemical oxidants is electrochemical oxidation. However, up to now, most C–H functionalizations combining transition-metal catalysis and electrochemical methods have mostly relied on precious metals and divided cells[54]. The first examples of room-temperature electrochemical C–H aminations of arenes with copper as the catalyst using undivided electrochemical cells was proposed by Mei and co-workers in 2018, offering a workable solution for the production of arylamines[55]. These results provide up a novel route for electrochemical C–H functionalization processes mediated by transition metals. N-phenylpicolinamide**42** and morpholine**43** were initially used as reaction partners, and several reaction conditions were investigated in order to achieve the expected electrochemical C–H amination in an undivided cell. After thorough optimization, it was shown that under constant-current electrolysis at 3.0 mA, 10 mol% Cu(OTf)$_2$, 50 mol% n-Bu$_4$NI (redox mediator), and 2 equiv of KOPiv in MeCN for 24 hours, 86% isolated yield of the desired product **44** could be produced[55]. The aminated products might be obtained in good to excellent yields if the arenes exhibited various functional groups which are well-tolerated such as silyl, ether, alkyl, hyddroxyl, alkyne, trifluoromethyl, alkene, thioether and halogen etc.,

Scheme 25: Electrochemical synthesis of arylamine**44**

Experimental findings are used to offer a viable mechanism for the Cu(II)-catalyzed electrochemical C–H amination (Scheme 26). The copper(II) catalyst first works in conjunction with an amine and substrate**42** to produce copper(II) complex **I**. Iodine radical then oxidises copper(II) complex**I** to produce Cu(III) species **II**. According to kinetic studies, the catalytic cycle's rate-determining step is the production of Cu(III). The next step involves a single electron transfer (SET), which produces intermediate **III** from complex **II**. Species **IV** is developed by an

intramolecular amine transfer to the radical-cation intermediate and a second SET event, which liberates the aminated product **44** and creates a Cu(I) species. Cu(II) catalyst is renewed following anodic oxidation, concluding the catalytic cycle.
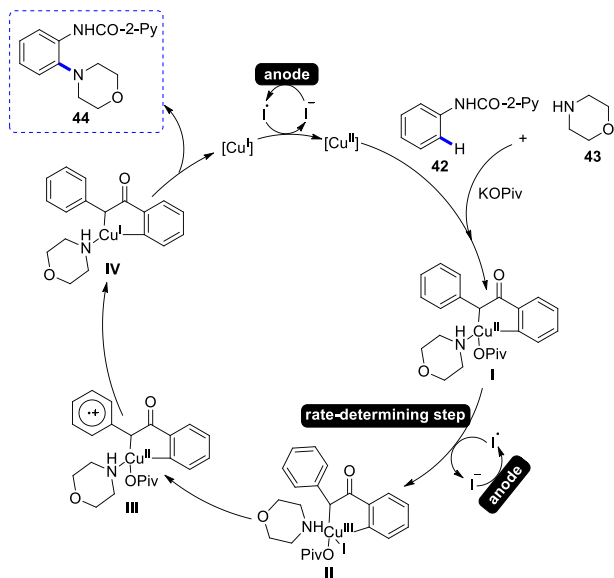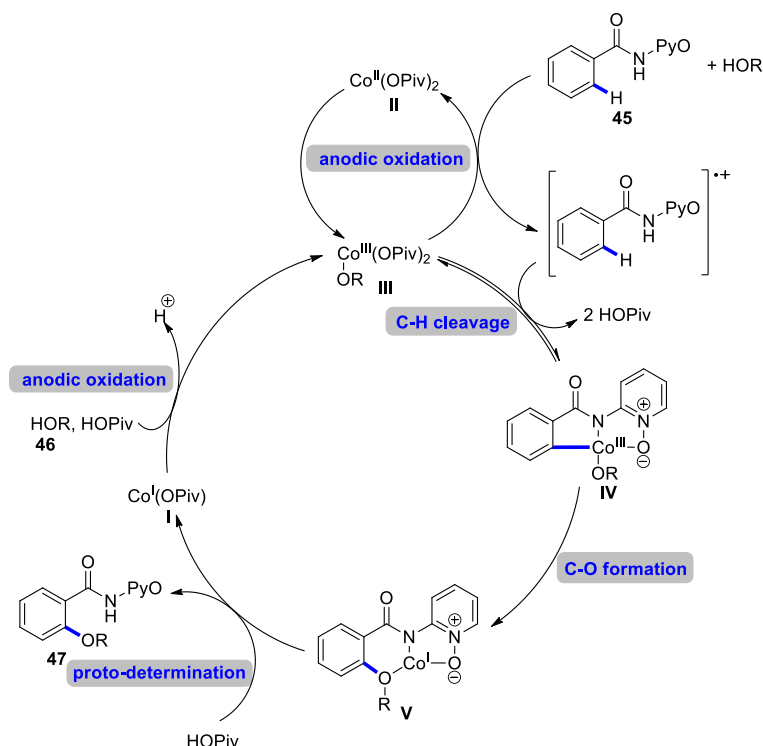

Scheme 26: Proposed mechanism for the electrochemical synthesis of arylamine**44**

Cobalt mediated C–H oxygenation was performed by Ackermann and co-workers. Large substrate scope was a highlight of the reliable electrochemical C–H functionalization, and mechanistic analyses supported a simple C–H cleavage. By avoiding the use of stoichiometric silver(I) oxidants under ambient circumstances, the electrochemical cobalt-catalyzed C–H oxygenation was successful on arenes and alkenes with excellent degrees of positional and diastereo-selectivity. Using an RVC-anode(+) and a platinum-cathode(–), the electrochemical oxygenation was accomplished at 23°C, applying 3.6 F/mol delivering the product **45**. Co(OAc)$_2$ was the best cobalt precursor out of a representative group, with NaOPiv as the preferred base[56].
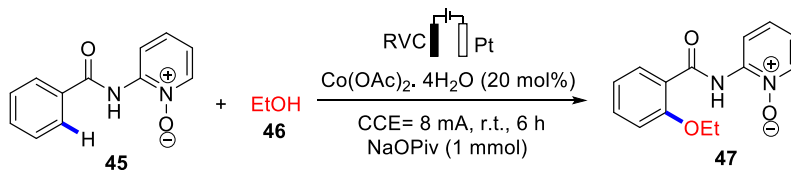
Scheme 27: Electrochemical synthesis of alkyl aryl ether**47**

Focusing on fundamental research, a possible catalytic cycle that would start with the electrochemical SET of the aromatic benzamide**45** by anodic oxidation and end with the creation of a simple electrochemical catalyst has been proposed (Scheme 28). Following that, proximity-induced chelation aids in C–O production, ensuring high positional selectivity. The final result is the release of the desired product **47**, and anodic oxidation is used to renew the catalytically active cobalt(III) species.


Scheme 28: Proposed mechanism for the electrochemical synthesis of alkyl aryl ether**47**

For organic synthesis, the electrochemical C–H functionalization reactions catalyzed by palladium have appeared as an appealing tool. The distinct potential of electricity as a green terminal oxidant is highlighted by the fact that other regularly used chemical oxidants, such as PhI(OAc)$_2$, t-BuOOAc, or NaNO$_3$/O$_2$, delivered the desired productin noticeably lower yields. Mei and co-workers reported the oxidative C(sp^2)–H methylation**52**(yield= 89%)and benzoylation**50**(yield = 65%) of oxime ether**48** with methyltrifluoroborates**51**and benzoyl acetic acids**49**, respectively, based on their preliminary findings (Scheme 28-a and 28-b). By using anodic oxidation, first instance of Pd(II)-catalyzed C(sp^2)–H methylation and acylation was disclosed. This procedure represents an environmentally friendly way for cross-coupling

potassium trifluoroalkylborates and α-keto acids with C(sp²)–H bonds, as opposed to traditional procedures that call for strong chemical oxidants.Oxime ether**48** was selected as the substrate for the reaction with potassium trifluoromethylborat (CH₃BF₃K) under electrochemical conditions in order to study the formation of C(sp²)–C(sp³) bonds. The monomethylated product**52** was produced in 76% (89% GC yield) by treating**48** (0.3 mmol) with MeBF₃K (2 equiv) in the presence of Pd(OAc)₂ (10 mol%) under constant-current electrolysis conditions at 1.5 mA (J = 0.75 mAcm⁻²)[57].

The acetoxylation of C(sp²)–H bonds with palladium has a successful electrochemical technique. The disadvantages of conventional acetoxylation techniques that use stoichiometric oxidants are overcome by this reaction, which proceeds at a low temperature without the use of harmful oxidants. Because the oxime moiety can be easily controlled and has a large amount of derivation potential, it was decided to employ oxime**48**as the substrate for the reaction under electrochemical circumstances to study the production of C(sp²)–O bonds. Fortunately, a 75% isolated yield (scheme 28-c) of the monoacetoxylated product**53** was produced by the reaction of **48** with 10 mol% Pd(OAc)₂ in the presence of 1 equiv of tetrabutylammonium acetate under constant-current electrolysis conditions at 1.0 mA (J = 0.75 mA/cm²[58]**.
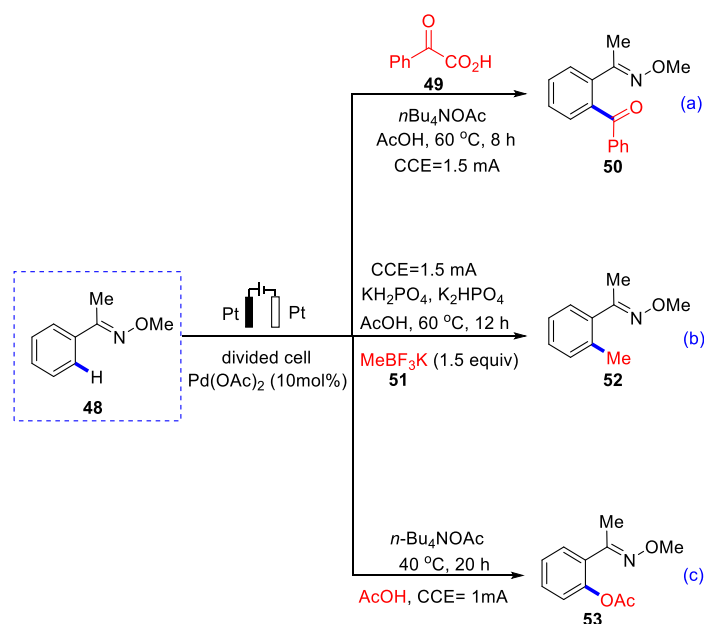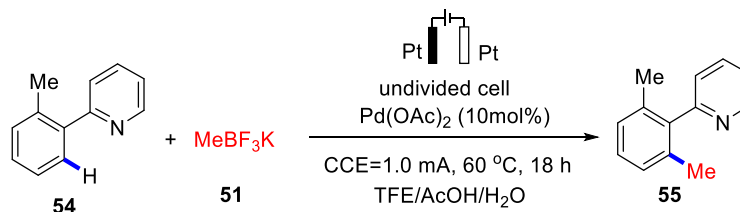

Scheme 29: Electrochemical synthesis of benzoyl**50**, methyl**52** and acetyloxy**53** derivatives of arenes

The first example of Pd-catalyzed aryl C–H cross coupling raction with alkyl boron and alkyl tin reagents, reported by Yu and co-workers in 2006 (Scheme 30)[59–61]. However, many examples of aryl C–H couplings catalyzed by Pd using organoboron reagents have been established. In orgnic synthesis, these tranformations possess remarkable importance in convenient construction of C–C bonds, however, in these system the practical disadvantage is the requirement of the constituents of the transition metal chemical oxidant in stoichiometric amont. Thus, there is highly demand to devloped the novel oxidation set-up, so elecrochemical C–H bond functionalization catalyzed by transition metal has developed as an appealing tool in organic synthesis and by-products, side reactions can be eliminated because it avoids the use of toxic and dangerous chemical oxidants[62–63].
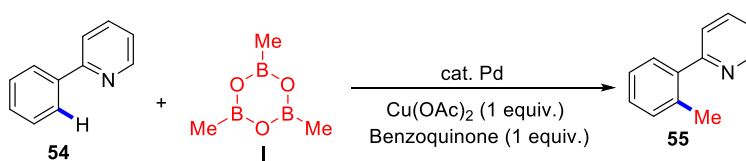
Scheme 30: Pioneering work on Pd-catalyzed C(sp2) –H cross-couplings

MeBF$_3$K and 2-(o-tolyl)pyridine**54** were employed as reaction partners to test different reaction conditions for the electrochemical C–H alkylation in an undivided cell. After significant optimization, it was discovered that a TFE/AcOH/H$_2$O solution (2 mL/2 mL/0.5 mL) containing 10 mol% Pd(OAc)$_2$ and 2 equivalents of MeBF$_3$K could provide a 70% isolated yield of the target product**55** when electrolyzed at constant current at 1.0mA[64].

Scheme 31: Electrochemical synthesis of alkyl arene**55**

A viable mechanism for the Pd(II)-catalyzed C(sp^2)–H methylation via electrochemical oxidation is postulated in light of the aforementioned experimental findings (Scheme 32). Initial coordination of the palladium catalyst with a nitrogen atom in substrate**48** places it close to the ortho-C–H bond. The next step is C(sp^2)–H activation, which results in palladacycle**III**. Then **III**

might either undergo a transmetallation with MeBF₃K under anodic oxidation to yield a Pd(III) or Pd(IV) intermediate **IV** or react with a methyl radical generated in-situ from MeBF₃K. Ultimately, a reductive elimination would be performed on the high-valent palladium intermediate to release the methylated product**52** and regenerate Pd(II) species. We could not, however, exclude out the likelihood that this alkylation was catalysed by Pd(II)/Pd(0) at this time. The N atom of the oxime first aligns with Pd(II) to produce the acetyloxy derivative, which is proceeded by a rate-determining C–H activation to produce the intermediate **III**. At the anode, this Pd(II) complex undergoes direct oxidation to produce Pd(IV) complex **IV**. The catalytic cycle is subsequently completed by reductive elimination of the intermediate **IV** to yield the desired product**53**.
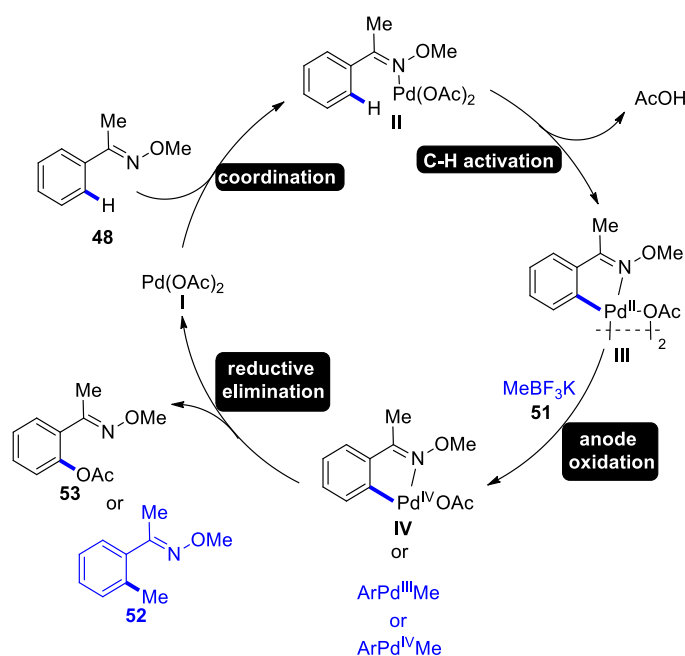
Scheme 32: Proposed mechanism for the electrochemical synthesis of methyl and acetyloxyarenes

Cobalt metal displayed numerous advantages in contrast to other noble metals like unique catalytic reactivity, low toxicity and cost. Recently, C–H alkoxylation, arylation and amination reaction catalysed by cobalt have been widely stated. So there is need to seek an efficient oxidant free cobalt catalytic system, substrates could be oxidized directly or indirectly at anode under electrolytic conditions. Though, most of the metal catalysts are disposed to be reduced at cathode, thus lose their catalytic reactivity. Using divided cell, continuous endeavours have been

devoted in order to progressing the transition-metal-catalysed electroxidative C-H functionalization[65–66]. Cobalt-catalyzed C–H amination of arenes is a method for making valuable arylamines that has been created using an eco-friendly electrochemical process. Diverse arenes and alkylamines are investigated in divided cells to provide C–N formation products without the need for external oxidants, which prevents the development of undesirable by-products and demonstrates high atom economy. Importantly, the reaction can be efficiently extended to the gram level. As common substrates, N-(quinolin-8-yl)thiophene-2-carboxamide**56**and morpholine**57**are used. In the presence of 20 mol% Co(OAc)$_2$.4H$_2$O and 1 equiv. NaOPiv.H$_2$O in methylnitrile at 65°C, 74% isolated yield of the target molecule **58** could be achieved by constant-current electrolysis at 10 mA for 3 hours[53].
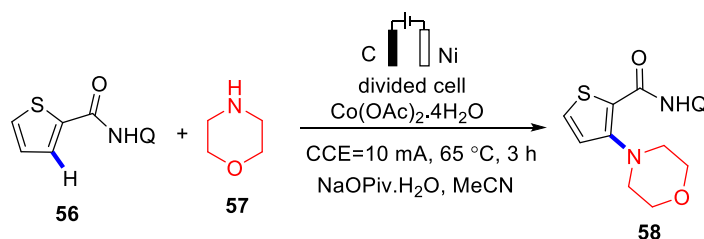
Scheme 33: Electrochemical synthesis of arylamine**58**

There have been two possible mechanisms examinedon the basi of literature results[67–69]. Co(III)-complex**II** was produced by Path-a, in which Co(II) was oxidised to Co(III) at the anode. Next, Co(III) coordinated to N-(quinolin-8-yl)benzamide**56**. Path-b: Prior to electrolysis, Co(II) coordinated to **56** in the presence of a base to produce Co(II)-complex **I**. At the anode, this Co(II)- complex **I**underwent oxidation to produce Co(III)- complex **II**. In the presence of base, C–H activation occurred, morpholine attacked Co(III)-complex **II** to create Co(III)-complex **III**, which was then reductively eliminated to release the targeted output and Co(I) species. To conclude the entire catalytic cycle of Co, the Co(I) species was re-oxidized to Co(II) at the anode.
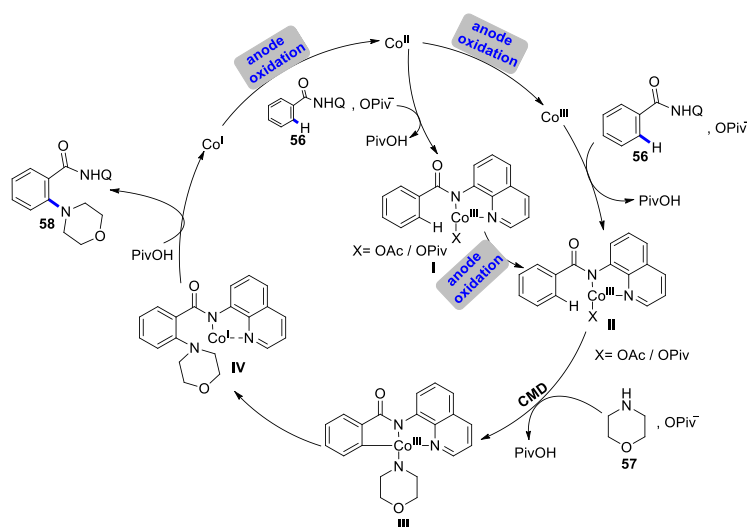
Scheme 34: Proposed mechanism for the electrochemical synthesis of arylamine**58**

Jutand and co-workers in 2007 reported the first Pd-catalyzed electroxidative C (sp^2)-H alkenylation[70]. So, there is demanding to develop economically transition metal catalysed electroxidative C-H functionalization.Under anodic oxidation conditions, ortho-selective chlorination of N-quinolinylbenzamide derivatives**59** with hydrochloric acid was accomplished. The selective chlorination was successful when the directing group 5,7- dichloro-8-quinolinyl was used. Vismodegib was also successfully synthesised in two steps utilising the electrochemical C–H chlorination with palladium as the catalyst. Then, it was looked at how the *o*-methylbenzamide derivative**59** reacted. The ortho chlorination product**60** was produced via the reaction of 0.20 mmol of **59** with 10 mL of DMF over a 12-hour period at 2.5 mA in an isolated yield of 86%[60].
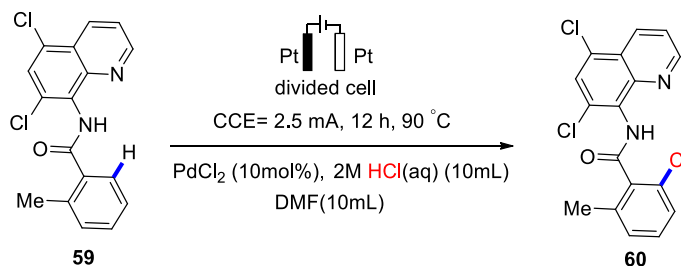
Scheme 35: Electrochemical synthesis of *o*-chlorinated N-quinolinylbenzamide derivatives**60**

According to proposed mechanism (Scheme 36), the palladium-catalyzed electrochemical C–H chlorination is thought to happen by first selectively cleaving the ortho C–H bond of

benzamide**59** and then reacting with electrochemically produced chlorinating species (Cl$^+$ or an analogous species).
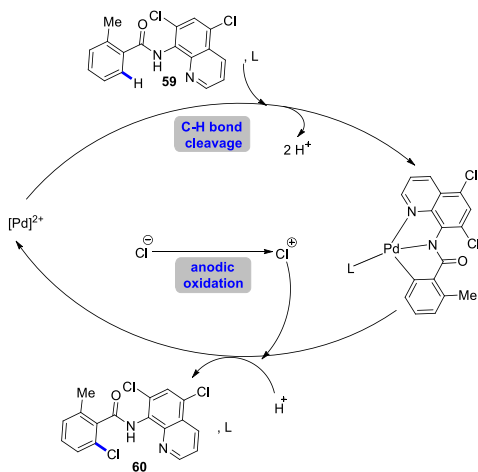
Scheme 36: Proposed mechanism for the electrochemical synthesis of *o*-chlorinated N-quinolinylbenzamide derivatives**60**

It has become clear that metal-catalyzed chelation-aided C–H olefinations are effective methods for creating functionalized alkenes. Here, benzamide**61** and styrene**62** were subjected to a Rhoda-electrocatalyzed C–H activation/alkenylation process in the presence of [Cp*RhCl$_2$]$_2$ (2.5 mol%) and NaOPiv in *t*-AmOH/H$_2$O (3:1), which produced product**63** with a 73% isolated yield. The product **63** was purified in an 85% yield when the alkenylation procedure was carried out at a scale of 1 mmole. Thus, the olefinations of difficult electron-poor benzamides were carried out under electrochemical conditions in a totally dehydrogenative manner, avoiding stoichiometric chemical oxidants, and with hydrogen gas as the only by-product. This adaptable alkenylationreaction uses electricity as a green oxidant and has a wide range of substrates[73].
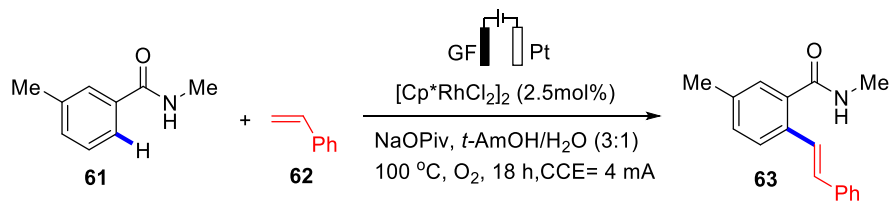
Scheme 37: Electrochemical synthesis of alkenyl arene**63**

Rhodacycle **I** is formed, as shown in scheme 38, by directed cyclorhodation at the ortho-position after the N-atom of amide**61**is coordinated to Cp*Rh^{III}. Then, alkene**62** insertion takes place to

produce intermediate **II**, which proceeds through β- hydrogen elimination to create **63** along with a rhodium(II) species that is created after the N-atom in **III** is broken up. The catalytic cycle is finished when the rhodium(II) species is reoxidized to rhodium(III) at the anode, producing molecular hydrogen(H_2) as a byproduct at the cathode.
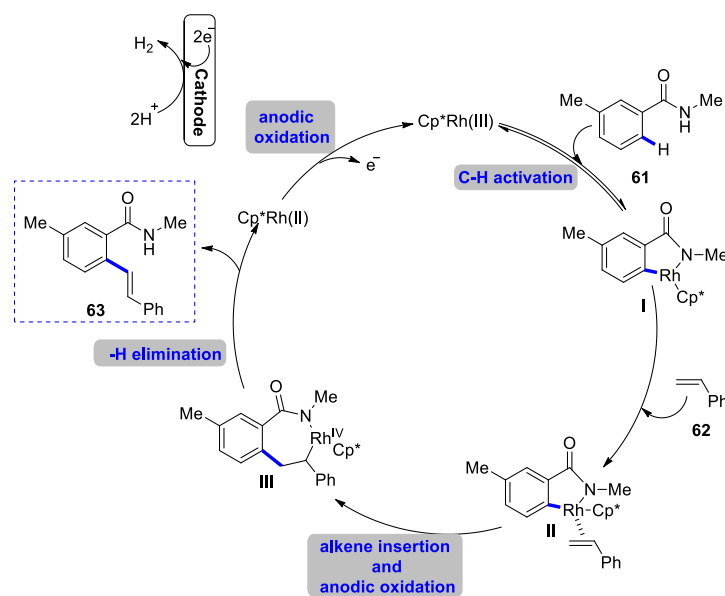
**Scheme 38:** Proposed mechanism for the electrochemical synthesis of alkenyl arene**63**

The electrochemical C–H allylation with non-activated alkenes was made possible by versatile and powerful cobalt catalysis. Ackermann and co-workers described an electro-oxidatively C–H allylate benzamide**64** with unactivated alkene**65** in a very user-friendly undivided cell setup. NaOPiv emerged as the best additive among many others. As a result, in the solvent γ-valerolactone(GVL) formed from biomass, allylated benzamide**66** was produced with high degrees of chemo-, position-, and regio-selectivityin 60% output. With H_2 as the sole byproduct, the cobaltaelectro-catalysis generally accomplished resource economy by eliminating the usage of stoichiometric chemical oxidants[74].
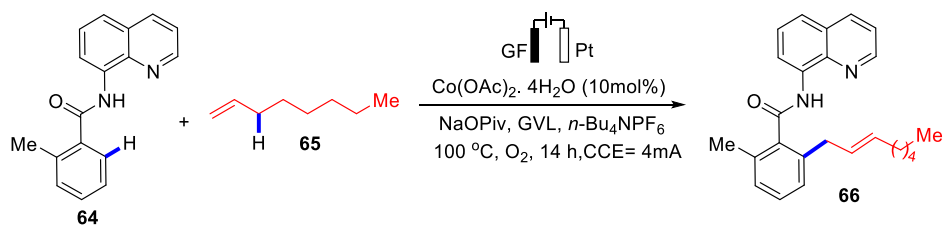
Scheme 39: Electrochemical synthesis of allylated benzamide**66**

A base-assisted internal electrophilic-type substitution mechanism for the crucial C–H activation step was strongly supported by thorough mechanistic analyses. A possible catalytic cycle for the cobalt-catalyzed electrochemical C–H allylation has been provided in Scheme 40 based on mechanistic findings. The 5-membered cobaltacycle **III**, which in a competition experiment may have a heteroleptic coordination environment, is formed first by anodic cobalt oxidation, which prepares the way for an effective BIES C–H scission with carboxylate assistance. To create the conformationally stiff 7-membered metallacycle **V**, 1,2-migratory insertion of **IV** with the non-activated alkenes **65** is made possible by alkene co-ordination. Third, in order to produce the desired allylated product, the seven-membered metallacycle **V** primarily undergoes β-hydride removal from the allylic proton. Eventually, anodic oxidation is used to regenerate the active cobalt(III) catalyst **II**.H$_2$ generation is the only stoichiometric by-product of the cathodic half-reaction.
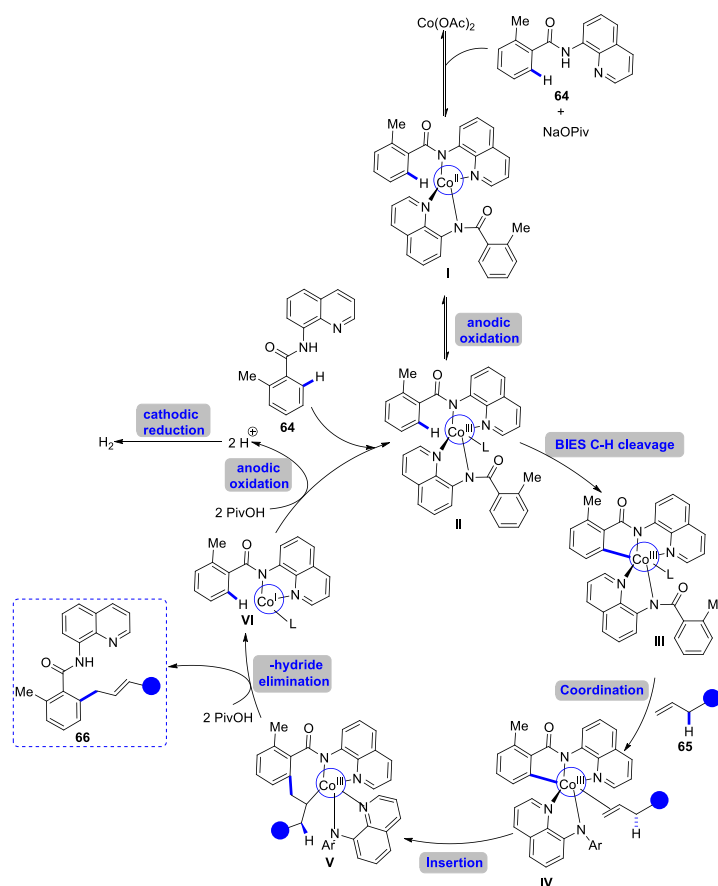
Scheme 40: Proposed mechanism for the electrochemical synthesis of allylated benzamide**66**

Additionally, the same author reported an electrochemical cobalt-catalyzed C–H acyloxylation. Because there were no expensive silver oxidants present, flexible cobalt electrocatalysis allowed for long-lasting C–H oxygenations of substituted benzamides**67**, with the only waste being molecular hydrogen. The C–H acyloxylation reaction was characterised by broad applicability in γ-valerolactone, a renewable solvent generated from biomass. Using affordable cobalt(II) salts and Na₂CO₃ as the preferred base, the required benzoxylation product **69**with a 66% yield was produced in an undivided cell arrangement at 80°C[75].
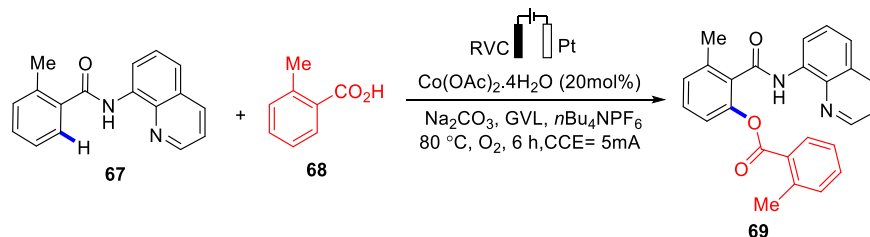
Scheme 41: Electrochemical synthesis of benzoxylation product**69**

A catalytic cycle that is thought to be started by the electrochemical production of the catalytically competent cobalt(III) species **IV** via anodic oxidation has been postulated based on mechanistic results. Following that, salt metathesis with carboxylic acid**68** results in the cobalt(III) intermediate **III**, whereas carboxylate-assisted C–H activation yields the cyclometalated complex **I**. Reductive elimination creates a cobalt(I) species **III** and yields the desired product**69**. By anodic oxidation, the catalytically active cobalt(III) complex **IV** is ultimately replenished.
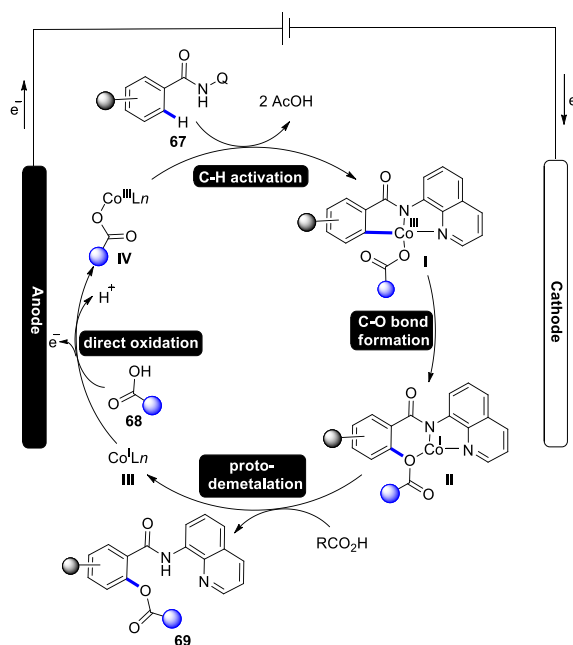
Scheme 42: Proposed mechanism for the electrochemical synthesis of benzoxylation product**69**

4. Arene C–H Functionalization via photo-electrocatalysis

For the conversion of solar energy into chemical fuels, the photoelectrochemical (PEC) cells are widely examined[75]. This protocol is effectively applied in several pharmaceutical molecules for late stage functionalization owing to broad scope of this method. Usually, a photoanode is used for the oxidation of water to produced oxygen and photocathode is used for the reduction of water to produced hydrogen (Figure 3). On light illumination, a high oxidizing or reducing power might be generated under mild conditions using PEC cell and they are well appropriated to catalyse the redox transformations of organic molecules to produced high value added chemicals (Figure 3). Recently, for the oxidation of benzylic alcohol[76], cyclohexane[77], furan[78], 5-hydroxymethylfurfural[79] and tetralin[80], the oxidizing power of photoanodes like WO_3 and $BiVO_4$ was exploited. However, the broad scope for the synthetic methodologies of functional organic molecules utilizing PEC cells remains unexplored.
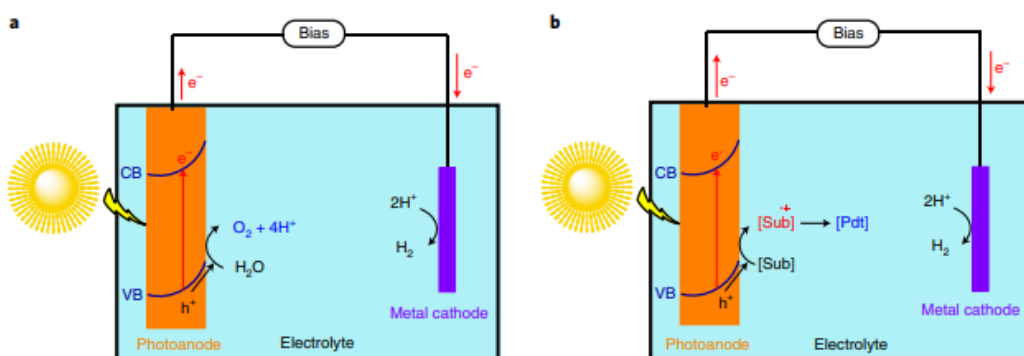
Figure 2: PEC cells: (a) Cell for water oxidation, **(b)** Cell for oxidative transformations of organic substrates, **CB:** conduction band, **VB:** valence band[81].

Building on the groundwork laid by early pioneers in the fields of radical chemistry and photochemistry, so-called visible light, or photoredox catalysis has become a potent tool in organic synthesis. The quick construction of complicated products on the road to new regions of chemical space is made possible by photoredox chemistry, which also creates new bonds via open shell pathways. Through a variety of synthetic transformations, including but not limited to cross-coupling, C–H functionalization, alkene and arene functionalization, and trifluoromethylation, photocatalysts can open up access to completely new, previously inaccessible bond formations in the presence of visible light. Academic research teams, industrial chemists, and academic-industrial partnerships have all used photocatalysis with success. These

efforts have led to new synthetic disconnections, inventive techniques, and a better mechanistic understanding of photoredox processes[82].

MacMillan and co-workers demonstrated the synthesis of several 3,6-functionalized acridinium photocatalysts via site-selective late-stage C–H alkylation. Following 0.5 hours of blue LED irradiation, the addition of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) as the redox catalyst and KPF$_6$ as the supporting electrolyte induced the addition of organotrifluoroborate to**70** to occur. The intended 3-alkylated acridinium product**71** was obtained in high to excellent yields (73-97%) during electrolysis of the resulting reaction mixture at a constant current of 10 mA without the presence of any other region-isomers. The 3,6-dialkylated acridinium product**72** can be produced in a good yield by repeating these settings.These reactions exhibit high scalability as well as broad functional group suitability. By adding a variety of electrically and sterically varied substituents to the cores of acridinium dyes, a synthetic technique makes it simple to adjust the photocatalytic capabilities of these dyes. The advantages of the structural variation in improving photocatalytic efficiency are revealed by the catalytic uses of the newly produced acridinium dyes in a benchmark process[83].
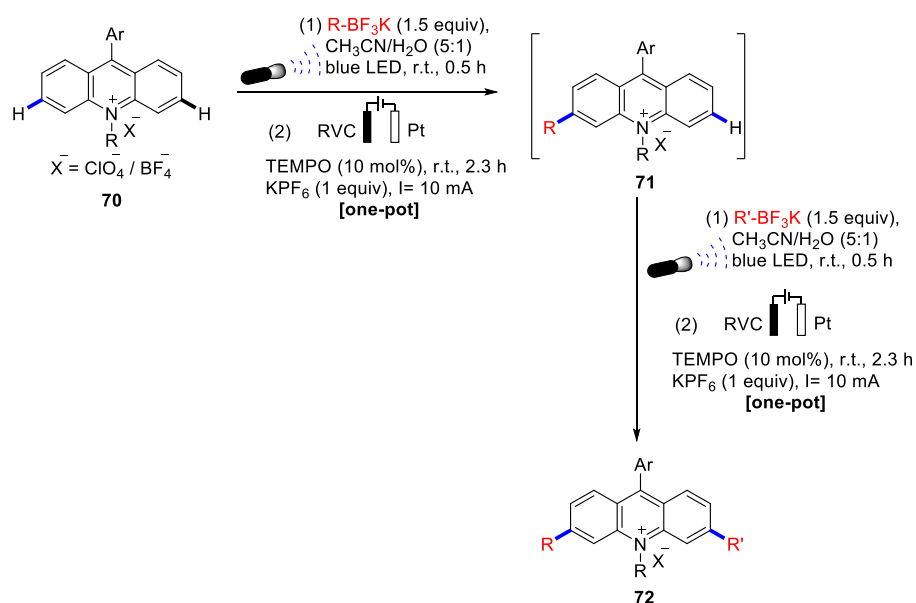
Scheme 43: Electrochemical synthesis of 3,6-dialkylated acridinium product**72**

The C–H alkylation of acridinium dyes was hypothesised as a possible process (Scheme 44). When excited acridinium**70** reacts with tBu-BF$_3$K in a SET reaction, it produces the radicals tBu• and **I**, which go via cross-coupling to produce 3,10-dihydroacridine**II**. Due to its smaller conjugation system and lack of reactivity, 3,4-dihydroacridinium**III** is produced by protonating **II**. It does not go through additional alkylation. While **II** ($E_{1/2}$ = 0.27 V vs SCE) is considerably easier to oxidise than **III** ($E_{1/2}$ = 2.10 V), **III** can revert to **II** by deprotonation by OH$^-$, which is produced by cathodic reduction of solvent H$_2$O. The electrocatalytic process results in the synthesis of alkylated acridinium product **71** by the TEMPO-mediated oxidation of **II**.
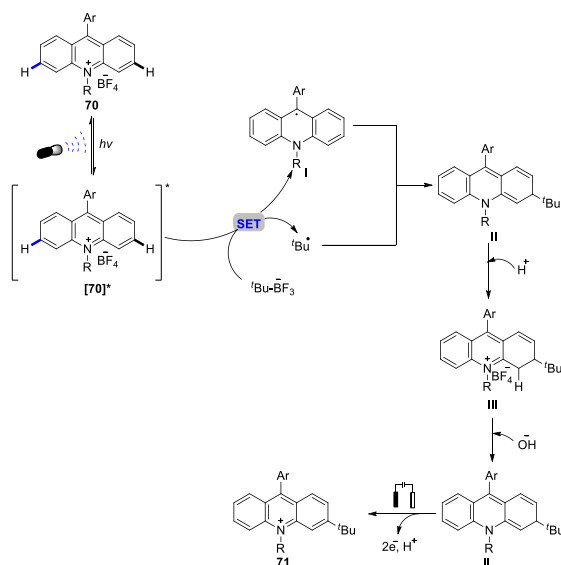
Scheme 44: Proposed mechanism for the electrochemical synthesis of 3-alkylated acridinium product**71**

The trifluoromethylated compounds exhibits inimitable lipophilicity as well as bioactivity and thus highly demanded in pharmaceutical industries and medicinal chemistry[54]. Moreover, in contrast to conventional methods these trifluromethylations have made the modifications to electrosynthesis and photoreodox catalysis[83]. Additionally, Schefoldused vitamin B$_{12}$as an electro-photo catalyst and explained the nucleophilic acylation of Michael olefins. An refined example of electrophotochemical transformations were described very recently by the researchers Stahl[84–85], Lambert[86] and Hu[87] on the sustainability of C–H activation persuaded through photocatalysis. Arene C–H trifluoromethylation with the Langlois reagent CF$_3$SO$_2$Na$_2$(2 equiv.) has been made possible by electrophotochemistry under benign reaction conditions. The CF$_3$ radical was produced without the need of chemical oxidants thanks to the

combination of electrosynthesis and photoredox catalysis. Undivided cells were used for the electrophotochemistry, which made it possible to tackle difficult C–H trifluoromethylations of inactive arenes and heteroarenes like the easily available mesitylene**72**. A broad range, encompassing electron-rich and electron-deficient benzenes as well as naturally occurring heteroarenes, highlighted the robustness of the electrophotochemical manifold. A platinum plate cathode and a graphite feeling (GF) anode were used in the orientation investigations, along with a cost-effective $LiClO_4$ additive and [Mes-Acr$^+$] ClO_4^- as a photocatalyst (PC) in methylcyanide at 23°C room temperature[40,63].
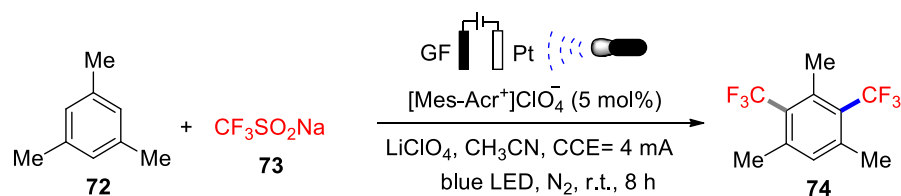
Scheme 45: Electrochemical synthesis of trifluoromethyl arene**74**

A potential mechanism was presented in Scheme 46 based on mechanistic discoveries. The oxidised excited state Mes-Acr$^+$ * is produced when the organic dye Mes-Acr$^+$ is first exposed to radiation. The acridinyl radical and the CF_3SO_2 radical are produced by a SET reaction between Mes-Acr$^+$* and the sulfinate anion. The ground state catalyst Mes-Acr$^+$ is then renewed by anodic electrooxidation of the acridinyl radical. The trifluoromethyl radical attacks substrate **72** simultaneously, creating aradical **I** that then undergoes SET oxidation to create the cationic Wheland complex **II**. A might also undergo direct oxidation at the anode in the interim. In the end, proton abstraction produces the desired product**74**, whereas at the cathode, protons are reduced to produce H_2.
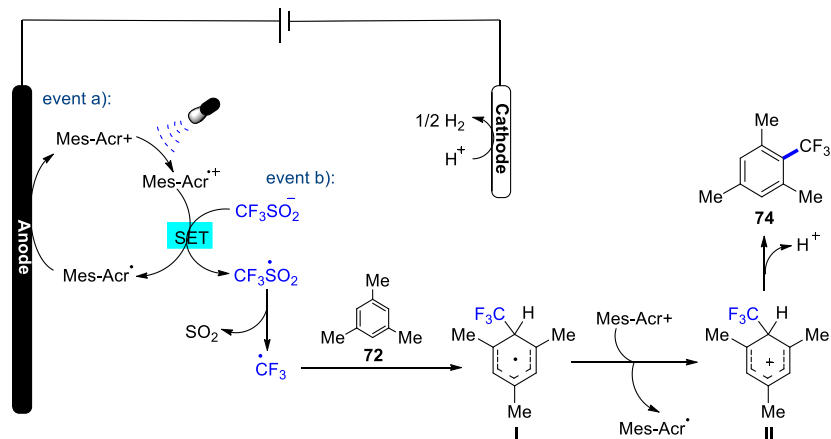
Scheme 46: Proposed mechanism for theelectrochemical synthesis of trifluoromethyl arene**74**

It has been created to trifluoromethylate and perfluoroalkylate aromatic compounds electrochemically using a vitamin B_{12} derivative as a cobalt-based catalyst. An effective technique for adding trifluoromethyl and perfluoroalkyl groups to aromatic compounds that works by creating radical intermediates in an electrocatalytic process when there is a catalytic amount of **75**. Fluoroalkylating reagents (R_fI) such as heptafluoropropyl iodide, trifluoroiodomethane, nonafluorobutyl iodide, henicosafluorodecyl iodide, and heptadecafluorooctyl iodide which are easy to use and affordable, are employed in this reaction. The 1,3,5-trimethoxybenzene **76** and n-C_3F_7I model reaction in this work has been revealed utilising an electrochemical approach. Cyclic voltammetry revealed that the reduction potential of the central cobalt ion (Co(II)/Co(I)) in the **75** was -0.61V vs. Ag/AgCl in methanol. To get a greater yield, the reaction conditions were improved. When exposed to visible light at ambient temperature, after 9 hours, 100% substrate conversion at a potential of -0.8 V vs. Ag/AgCl was achieved, yielding the desired product **77** in 84% of the cases[89].
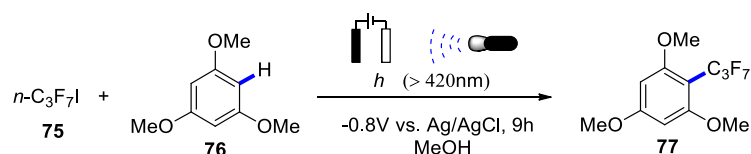
Scheme 47: Electrochemical synthesis of 2-heptafluoropropyl1,3,5-trimethoxybenzene**77**

Co(I) was first obtained from Co(II) via controlled-potential electrolysis at -0.8 V vs. Ag/AgCl, and Co(I) then interacted with R_fI to swiftly produce the Co(III)-R_f complex (Scheme 48). The compound then emitted an R_f radical when exposed to visible light. In order to deliver

the desired product**77**, the produced R$_f$- Trimethoxybenzene radical then reacted with non-activated substrates such arenes and heteroarenes. This reaction was followed by a one-electron oxidation and proton loss. This is the first report of catalytic trifluoromethylation and perfluoroalkylation processes employing vitamin B$_{12}$ derivatives, despite the fact that trifluoromethyl- and fluoroalkyl-cobalamines have been created and described by Geremia and co-workers.
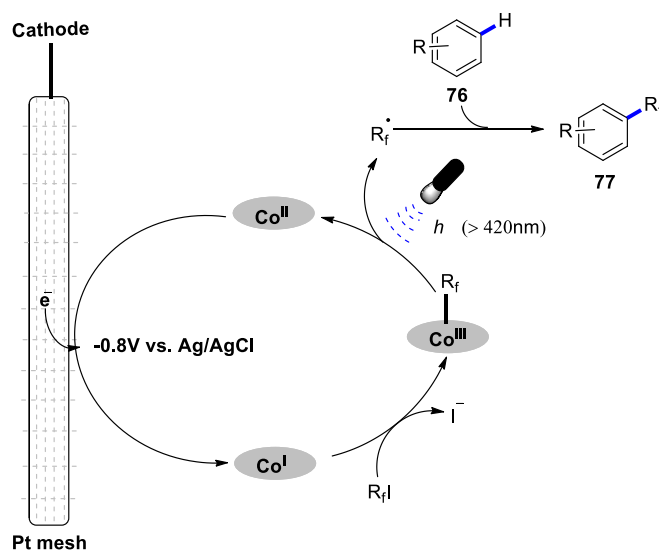
Scheme 48: Proposed mechanism for the electrochemical synthesis of 2-heptafluoropropyl1,3,5-trimethoxybenzene**77**

Now a days, for the synthesis of organic compounds through photoelectrocatalytic approach to non-directed arene C–H amination has an attractive method[89]. To conduct the C–H amination in PEC set-up, involves the use of haematite (α-Fe$_2$O$_3$) which is an earth abundant and strong photoanode (Figure 3). For the solar-driven water oxidation, haematite has been broadly investigated due to its high stability, appropriate band gap of 2.1 eV for strong light absorption and low cost[90]. The heterogenous nature of photoelectrocatalysis and and the stability of haematite in a PEC cell suggest impending advantages in the separation of product and life time of catalyst. Due to light ingathering the photoelectrocatalysis comsumes less amount of energy, if compared it with direct electrocatalysis. Consequently, this presented method is operationally simple and thus might be utilized in the synthesis of wide range of nitrogen-containing

heterocycles which are considered to be advantageous in the discovery of drug. Remarkably, for many substrates reverse selectivity is attained in contrast to previously described electrochemical and photoredox methods[91–92]. For late-stage functionalization of pharmaceuticals molecules, the utility of this method is broadly exercised by several examples.

For C–H amination reaction, the C–H/N–H coupling of anisole with pyrazole was investigated using nanostructured haematite[93] and under a blue light emitting diode (LED) the reaction was performed with a constant potential. With the photocurrent at about 2~3 mA cm^{-2}, the potential was set at 0.73V against a ferrocene/ferrocenyl (Fc/Fc$^+$) after some investigation and the reaction time period was set to about 10 hours. The tetrabutylammonium hexafluorophosphate (TBAPF$_6$) was initially used as electrolyte. Various organic solvents were experienced which benefit the organic media for the PEC oxidation, inspired after the work of Berlinguette and co-workers. In direct electrochemical oxidation[94], the choice of solvent acetonitrile (CH$_3$CN) was found to be ineffective. The yield and selectivity were increased using LiClO$_4$ as the electrolyte and HFIP/methanol(4:1) as the solvent. The achievement of unusual ortho selectivity was most likely made possible by a hydrogen-bonding interaction between the substrates and the co-solvent, hexafluoroisopropanol. From this profile, the analysis of the rate order was convoluted by mass transfer to the photoanode, it was apparently observed that reaction began to down after about 6 hours. After ten hours of time period the substrate anisole remained about 10% only but improving the reaction time beyond ten hours had partial impact on the yield. Without prefunctionalizing the substrates, a variety of heterocycles having an aryl C–N moiety can be made from basic arenes and azoles. The test reaction for the C–H amination was the C–H/N–H coupling of anisole**78**(0.2mmol) with pyrazole**79**(2 equiv.)[81].
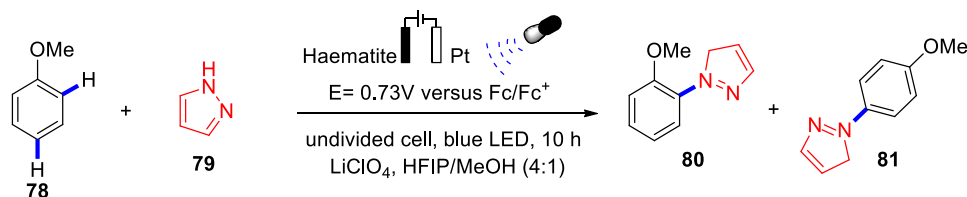
Scheme 49: Electrochemical synthesis of arene C–H amination products **80** and **81**

The photoelectrocatalysis has been explained by a reasonable mechanism (Scheme 50). Holes are produced at the valence band when haematite is illuminated. An electron-rich arene is converted by the holes into a radical cation that interacts electrophilically with an azole to

produce intermediate **I**. Proton loss from **I** results in the intermediate **II**, which, after being oxidised and having one proton removed, produces the amination product. **II** may be oxidised at the photoanode either by the photogenerated holes or by a methoxy radical that may also be produced there. When photoexcited electrons migrate from the haematite's conduction band to the counter electrode and reduce protons into dihydrogen gas, the photoelectrocatalysis is said to be complete.
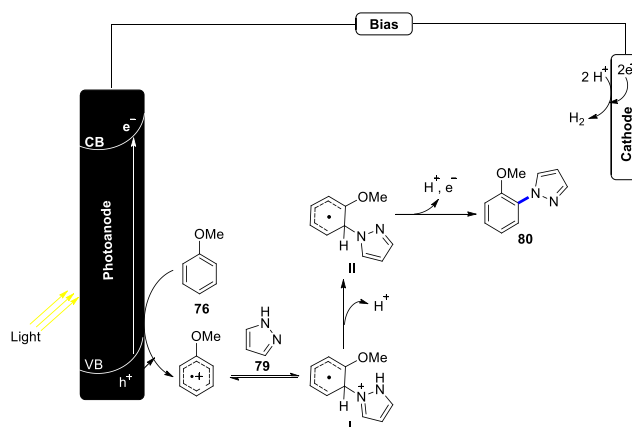
Scheme 50: Proposed mechanism for the electrochemical synthesis of arene C–H amination products **80** and **81**

Lambert and co-workers proposed a heterofunctionalization of arenes via electrophotocatalysis, arenes undergo hydroxylation, amination and alkoxylation free of oxidants (Scheme 51).First, the electrophotocatalytic coupling of benzene **82** and water **83** (50 equiv.) provided phenol **84** by applying 10 mol% of 2,3-dichloro-5,6-dicyanoquinone (DDQ) at a controlled potential of 1.5 V in a undivided cell (carbon cathode, Pt anode), under visible light irradiation (blue LED strip), in the presence of LiClO₄ and acetic acid[95].
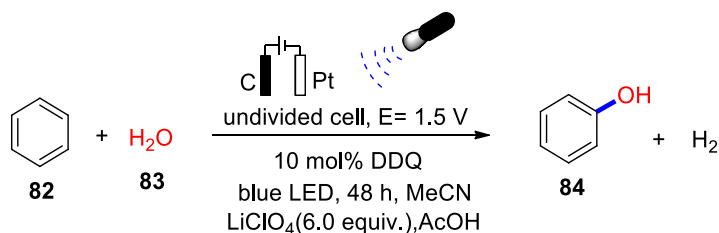
Scheme 51: Electrochemical synthesis of phenol**84**

Additionally, reactions of benzene**82**(0.4mmol)with different alcohols, amines, and carboxylic acids produced the aryl ether**85**, aryl amines**87**, and ester**86** products, respectively(Scheme 52)[95].
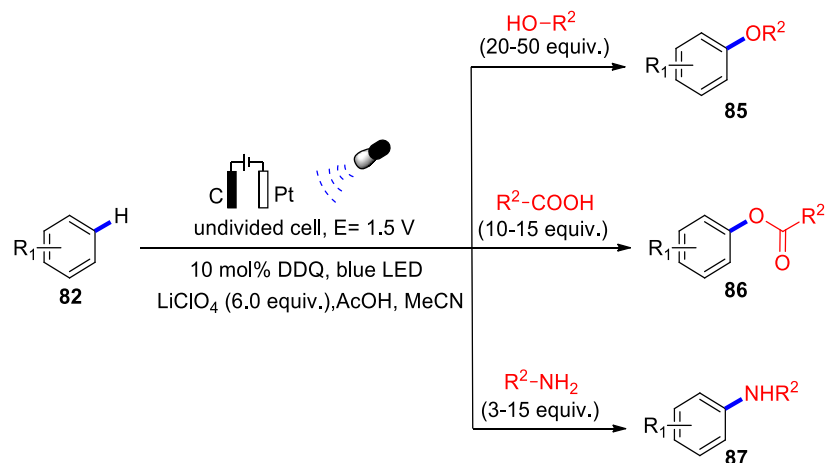
Scheme 52: Electrochemical synthesis of aryl ether**85**, ester**86** and aryl amine**87** products

The photoexcited DDQ causes single electron transfer (SET) oxidisation of an arene**82** to produce a radical cation **IV** that is capable of nucleophilic capture. The main distinction is that DDQ **I** would be produced by anodizing the reduced DDQH$_2$ **III**, and the electrochemical reaction would be finished by cathodizing protons to produce H$_2$. Therefore, the use of a conventional oxidant like TBN is not necessary with this electrophotocatalytic arrangement.
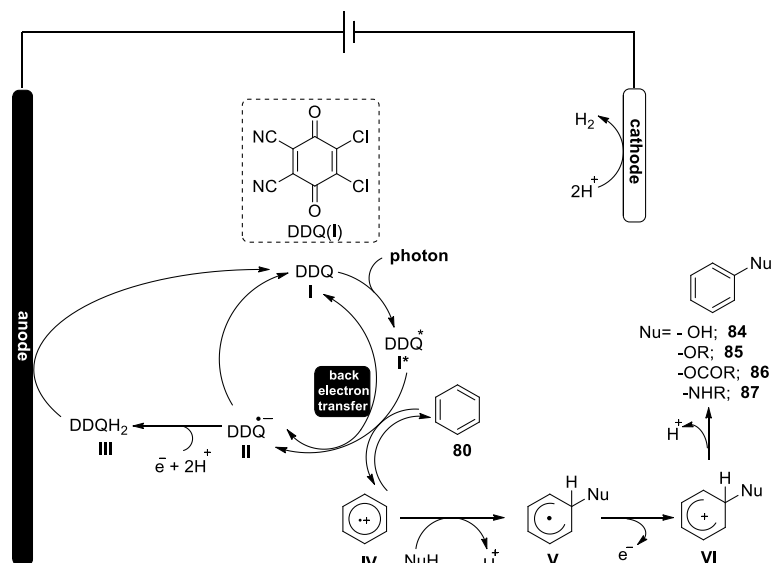
Scheme 53: Proposed mechanism for the electrochemical synthesis of phenol**84**, aryl ether**85**, ester**86** and aryl amine**87** products

Simple access to functionalized heteroarenes from commercially accessible materials is made possible by dehydrogenative cross-coupling of heteroarenes with aliphatic C–H bonds. Standard procedures use stoichiometric chemical oxidants when heated or exposed to light. Without the need of metal catalysts or chemical oxidants, an effective photoelectrochemical dehydrogenative cross-coupling of heteroarenes and $C(sp^3)$–H donors through H_2 evolution has been accomplished by Xu and co-workers, combining electrochemistry and photochemistry. As a model reaction, the dehydrogenative cross-coupling of 2-phenylquinoline**88** and cyclohexane**89** has been studied (Scheme 54). After initial optimization, a photoelectrochemical reaction using LEDs (392 nm, 10 W) and an undivided cell with a reticulated vitreous carbon (RVC) anode and a Pt cathode produced the desired product**90** in 92% yield.HCl(6 equiv) and Et₄NCl (0.3 equiv) were used in the reaction mixture as an acid and chloride source, respectively, in methylnitrile(CH₃CN)[96].
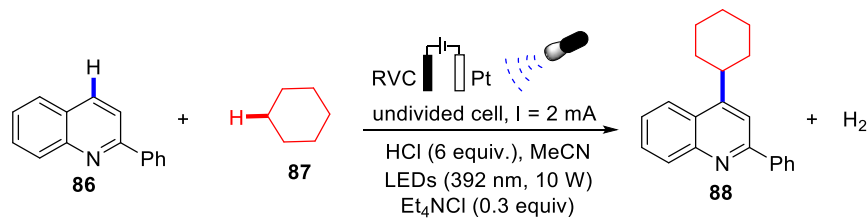
Scheme 54: Electrochemical synthesis of alkylarene**90**

The C(sp³)–H donor is mechanically changed into a nucleophilic C-radical through the transfer of a hydrogen and chlorine atom, which is created by light irradiating anodically generated Cl_2 from Cl^-. To produce alkylated heteroarene compounds, the C-radical is subsequently subjected to radical substitution with the heteroarene.
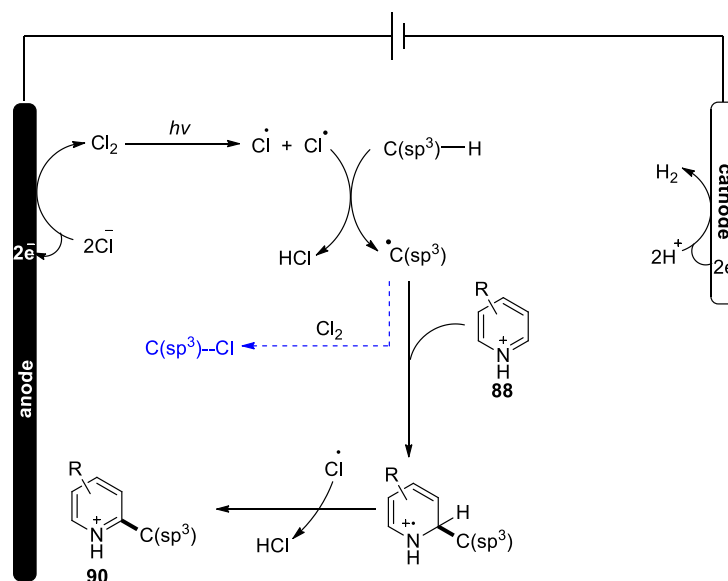
Scheme 55: Proposed mechanism for the electrochemical synthesis of alkylarene**90**

5. Arene C–H Functionalization via organo-electrocatalysis

In developing novel and challenging organic transformations, the revitalization of photo-redox catalysis and organocatalysis, both areas individually experienced enormous success, even in the greatly stereoselective manners. For the successful implementation of α-functionalization of amines and carbonyl compounds, the merger of visible light catalysis by asymmetric organocatalysis has turned out as an operative strategy. Newly, organocatalysis have revealed extraordinary compatibility with electrochemistry to yield stimulating organic transformations, which appears challenging to realize in the absence of catalytic systems. Several practical problems in terms of organic synthesis could be resolved with the applications of photoredox, organo- and electrocatalysis which offers several advantages and could lead to the development of novel organic transformations[97].

In the development of electrolysis, the toxic and dangerous redox reagents can be substituted by electric current or produced in situ, it is acknowledged as an environmentally friendly and safe methodology. This is all due to the fact that the need for excess amounts of supporting electrolytes comprises a severe drawback. From the reaction mixture the supporting electrolyte must be separated as the completion of reaction takes place, unless it is reused and recovered, thus it constitutes a cause of leftover. The tetraalkylammonium salts are often used, due to their good solubility in organic solvents and maximum electrochemical stability. However, as the reaction has completed, the good solubility of an electrolyte often leads to difficulties with the separation of the salts from the products. By the use of redox mediators, further separation issue is initiated. The electron transfer between substrate and electrode is facilitated by the use of such mediators, thus also influence the selectivity of the electrosynthetic methodology. As both the mediators and supporting electrolyte represent an expense factor and source of waste, therefore for industrial applications their reuse and recovery in terms of various cycle is highly demanded.

With regard to electrosynthesis thus by unlocking the potential of iodine(I)/iodine(III) redox couple, Francke and co-workers developed a mediator based on compound **91** (Scheme 56), containing a redox active unit of 4-iodopheny moiety, which is joined to a quaternary ammonium group and serves as a supporting electrolyte[98].
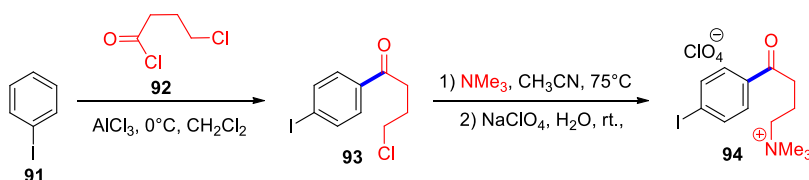
Scheme 56: Synthesis of the Redox-active supporting electrolyte **94**

After complete transformation with a substrate, it facilitates the reuse and separation of redox active salt as shown in (Scheme 56). For the mediated electrochemical processes, fluorinated alcohols were targeted as solvents depicted in (Scheme 57). Due to the excellent electrochemical properties such as anodic stability and high conductivity, the first fluorinated solvents such as 1,1,1,3,3,3-2,2,2-trifluoroethanol (TFE) or hexafluoroisopropanaol (HFIP)are renowned. In the electrochemical generation of active form of mediator, alcohol is expected to play an active role by stabilizing iodine(III)(Structure **95** in Scheme 57). Additionally, due to the positive influence of fluorinated alcohols on the selectivity of transformations and rate containing ionic or radical

intermediates, thus it frequently employed in iodine(III) mediated reactions. At the end, as cathodic half reaction the selective proton reduction is feasible due to the rather low pK_a values of fluorinated alcohols, thus during electrochemical process produced H_2 as by-product.
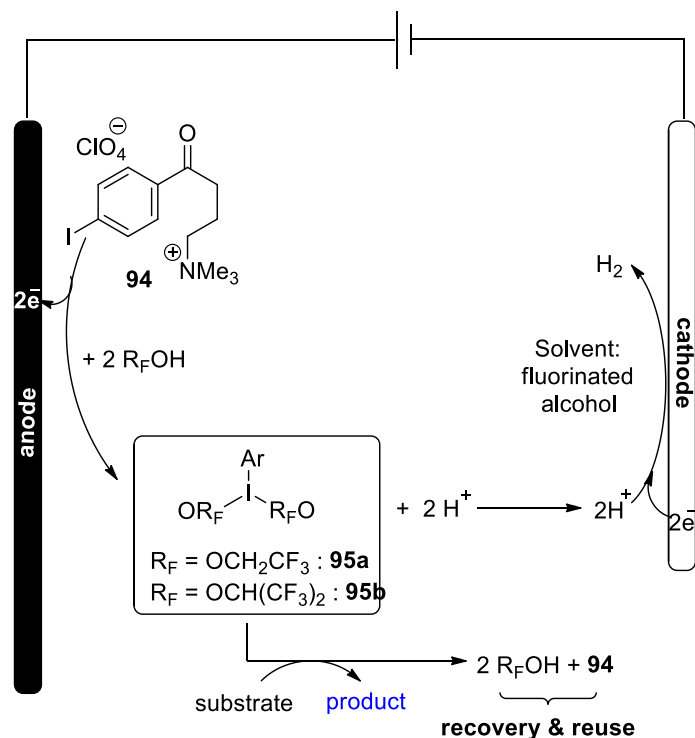
Scheme 57: Concept for the electrochemical generation of an Iodine(III) species and the subsequent use for chemical Transfeormations

The concentration of **94**, current density, and electrolysis conditions have been optimised for the electrode material. It was discovered that using a glassy carbon working electrode in conjunction with a platinum counter electrode in an undivided cell while using a current density of 15 mA/cm^2 results in an optimum Faradaic efficiency of 70% (0.2 M solution of **94** in HFIP). With these refined parameters at hand, research into potential applications began with direct oxidative C–N bond forming reactions that had previously been reported in the context of other hypervalent iodine reagents. Through the intramolecular cyclization of 2-(N-acetylamino)-biphenyls**96**, N-acetyl carbazoles**97** have been created[98].
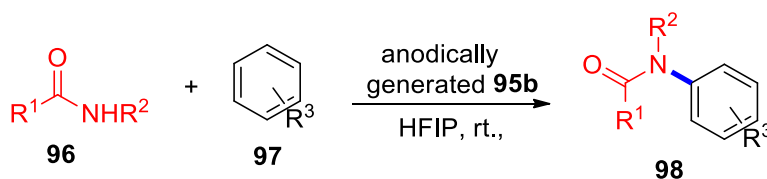
Scheme 58: Electrochemical synthesis of N-acetyl carbazoles **98**

Conclusion & Perspective

a. Advantages of electrosynthesis compared to traditional methods

Electrosynthesis has several benefits, one of which is that it is environmentally benign. There are various factors that should persuade chemists to employ organic electrosynthesis from the perspective of practical operation. For instance, electrochemical processes typically show strong functional group tolerance in the absence of exogenous oxidants or reductants. Electrochemical reactions are typically carried out in milder conditions compared to traditional procedures, which frequently proceed at elevated temperature or pressure, offering an energy-saving alternative. Due to their high reaction efficiency, electrochemical processes typically have quick reaction times. Further reducing the reaction time is possible by tuning the current. The electrochemical system's capacity for oxidation or reduction can be optionally changed by adjusting the current or voltage, enabling processes that aren't possible with chemical oxidants or reductants. Electrochemical processes can be quickly stopped at any time by flipping the power switch, unlike conventional reactions that typically need quenching. Last but not least, the majority of electrochemical reactions may be readily scaled up and have enormous potential for commercial applications. For instance, the industrialization of the electrochemical synthesis methods for 1,4-dicyanobutane, sebacic acid, etc. has been effective[6].

The application of electrosynthesis proposes overcoming some limitations of the directed C–H functionalizations. For example, in molecules containing nitrogen or sulphur that will coordinate strongly with metallic catalysts, possibly poisoning the catalyst or functionalizing C-H in an unwanted position [99,100]. The use of electrosynthesis provides greater control of the reaction medium by electrical voltage, allowing the acceleration or stabilization of synthetic intermediates. In electrosynthesis, substrates can undergo redox processes directly at the

electrodes, or even better redox control of the reaction mediators can be achieved by controlling the applied electrical potential. We can also mention a better control of the substrate with fluorinated solvents, allowing the modulation of the nucleophilicity and stabilization of the intermediates [101].

b. Practical limitations of electrosynthesis

Despite many benefits, there are some disadvantages to using electrosynthesis in organic chemistry. For instance, a whole electrochemical device is required, and both its cost and maintenance are often expensive. Additionally, a supporting electrolyte must typically be used to facilitate the transmission of electrons in solution, and because solvents like tetrahydrofuran, toluene, etc. are poorly conductive, choosing a solvent for electrosynthesis can occasionally be challenging. The use of metal catalysts in electrochemical reactions under readily accessible undivided cells is relatively limited because most metal cations are readily reduced at the cathode to zero-valent metals, and when electrochemical reactions are carried out in divided cells, expensive ion exchange membranes are required for separating anode and cathode[6].

c. Use of enabling tools in arenes/(hetero)arenes C–H functionalization

The arenes/(hetero)arenes C–H functionalization has emerged as an elegant strategy in organic synthesis, and with technological advances as new tools, the perspective is of greater achievements for synthetic chemistry. Currently, it is observed that laboratories are being gradually updated with equipment to absorb these demands, such as flow systems, electrochemical, photochemical, ultrasound and microwave reactors, automation, etc. For this, a growing collaboration with engineers, computer scientists, electrical technicians, software developers and other areas of chemistry is required.

The modern world and its sustainable development trends are forcing the chemical industry to improve in an environmentally friendly direction and meet the requirements of "green chemistry." Additionally, it is worth mentioning the various advantages of electrochemical reactions, such as high yields, higher selectivity and mild reaction conditions provide an environmentally friendly route. In this sense, the electrochemical arenes/(hetero)arenes C–H

functionalization methods in batch reactions, continuous flow, metalla, photo and organo-electrocatalysis were widely discussed in this review.

Acknowledgment

References

[1]   D. E. Fitzpatrick, C. Battilocchio, and S. V. Ley, "Enabling technologies for the future of chemical synthesis," *ACS Cent. Sci.*, vol. 2, no. 3, pp. 131–138, 2016, doi: 10.1021/acscentsci.6b00015.

[2]   S. L. Luiz F. T. Novaes#, Jinjian Liu#, Yifan Shen#, Lingxiang Lu#, Jonathan M. Meinhardt, "Electrocatalysis as an enabling technology for organic synthesis," *Chem Soc Rev*, vol. 50, no. 14, pp. 7941–8002, 2021, doi: 10.1039/d1cs00223f.Electrocatalysis.

[3]   L. F. T. Novaes, J. Liu, Y. Shen, L. Lu, J. M. Meinhardt, and S. Lin, "Electrocatalysis as an enabling technology for organic synthesis," *Chem. Soc. Rev.*, vol. 50, no. 14, pp. 7941–8002, 2021, doi: 10.1039/D1CS00223F.

[4]   V. Srivastava, "Grand Challenges in Chemical Treatment of Hazardous Pollutants," *Front. Environ. Chem.*, vol. 2, no. November, pp. 1–4, 2021, doi: 10.3389/fenvc.2021.792814.

[5]   H. J. Schäfer, "Contributions of organic electrosynthesis to green chemistry," *Comptes Rendus Chim.*, vol. 14, no. 7–8, pp. 745–765, 2011, doi: 10.1016/j.crci.2011.01.002.

[6]   Y. Yuan and A. Lei, "Is electrosynthesis always green and advantageous compared to traditional methods?," *Nat. Commun.*, vol. 11, no. 1, pp. 2018–2020, 2020, doi: 10.1038/s41467-020-14322-z.

[7]   K. Peng and Z. Dong, "Recent Advances in Cross-Dehydrogenative Couplings (CDC) of C−H Bond in Aqueous Media," *Adv. Synth. Catal.*, vol. 363, no. 5, pp. 1185–1201, Mar. 2021, doi: 10.1002/adsc.202001358.

[8]   J. A. Labinger and J. E. Bercaw, "Understanding and exploiting C–H bond activation," *Nature*, vol. 417, no. 6888, pp. 507–514, May 2002, doi: 10.1038/417507a.

[9]   J. A. Ellman, L. Ackermann, and B.-F. Shi, "The Breadth and Depth of C–H Functionalization," *J. Org. Chem.*, vol. 84, no. 20, pp. 12701–12704, Oct. 2019, doi: 10.1021/acs.joc.9b02663.

[10]   G. M. Martins, N. Sbei, G. C. Zimmer, and N. Ahmed, "C-H Activation/Functionalization via Metalla-Electrocatalysis," in *Electrocatalysis*, IntechOpen, 2021, p. 10.5772/intechopen.95517.

[11]   S. Z. & H.-C. X. * Hao Long, Chong Huang, Yun-Tao Zheng, Zhao-Yu Li, Liang-Hua Jie, Jinshuai Song, "Electrochemical C–H phosphorylation of arenes in continuous flow suitable for late-stage functionalization," *Nat. Commun.*, vol. 12, pp. 1–7, 2021, doi: 10.1038/s41467-021-26960-y.

[12]   M. Oliva, G. A. Coppola, E. V. Van der Eycken, and U. K. Sharma, "Photochemical and Electrochemical Strategies towards Benzylic C−H Functionalization: A Recent Update," *Adv. Synth. Catal.*, vol. 363, no. 7, pp. 1810–1834, Mar. 2021, doi:

10.1002/adsc.202001581.

[13] C. Ma, P. Fang, and T.-S. Mei, "Recent Advances in C–H Functionalization Using Electrochemical Transition Metal Catalysis," *ACS Catal.*, vol. 8, no. 8, pp. 7179–7189, Aug. 2018, doi: 10.1021/acscatal.8b01697.

[14] T. Gul, R. Bischoff, and H. P. Permentier, "Electrosynthesis methods and approaches for the preparative production of metabolites from parent drugs," *TrAC Trends Anal. Chem.*, vol. 70, pp. 58–66, Jul. 2015, doi: 10.1016/j.trac.2015.01.016.

[15] R. Jana, H. M. Begam, and E. Dinda, "The emergence of the C–H functionalization strategy in medicinal chemistry and drug discovery," *Chem. Commun.*, vol. 57, no. 83, pp. 10842–10866, 2021, doi: 10.1039/D1CC04083A.

[16] C. Zhu, N. W. J. Ang, T. H. Meyer, Y. Qiu, and L. Ackermann, "Organic Electrochemistry : Molecular Syntheses with Potential," *ACS Cent. Sci.*, vol. 7, pp. 415–431, 2021, doi: 10.1021/acscentsci.0c01532.

[17] M. Yan, Y. Kawamata, and P. S. Baran, "Synthetic Organic Electrochemical Methods since 2000: On the Verge of a Renaissance," *Chem. Rev.*, vol. 117, no. 21, pp. 13230–13319, 2017, doi: 10.1021/acs.chemrev.7b00397.

[18] S. Maljuric, W. Jud, C. O. Kappe, and D. Cantillo, "Translating batch electrochemistry to single-pass continuous flow conditions: an organic chemist's guide," *J. Flow Chem.*, vol. 10, no. 1, pp. 181–190, 2020, doi: 10.1007/s41981-019-00050-z.

[19] T. Noël, Y. Cao, and G. Laudadio, "The Fundamentals behind the Use of Flow Reactors in Electrochemistry," *Acc. Chem. Res.*, vol. 52, no. 10, pp. 2858–2869, 2019, doi: 10.1021/acs.accounts.9b00412.

[20] A. A. Folgueiras-Amador and T. Wirth, "5 Electrosynthesis in Continuous Flow," in *Flow Chemistry in Organic Synthesis*, Stuttgart: Georg Thieme Verlag, 2018, pp. 147–189.

[21] Y.-C. Tsai, B. A. Coles, R. G. Compton, and F. Marken, "Microwave Activation of Electrochemical Processes: Enhanced Electrodehalogenation in Organic Solvent Media," *J. Am. Chem. Soc.*, vol. 124, no. 33, pp. 9784–9788, Aug. 2002, doi: 10.1021/ja026037w.

[22] M. Matsuhisa *et al.*, "Hole Accumulation at the Grain Boundary Enhances Water Oxidation at α-Fe $_2$ O $_3$ Electrodes under a Microwave Electric Field," *J. Phys. Chem. C*, vol. 124, no. 14, pp. 7749–7759, Apr. 2020, doi: 10.1021/acs.jpcc.9b11179.

[23] L. Rassaei, R. G. Compton, and F. Marken, "Microwave-Enhanced Electrochemistry in Locally Superheated Aqueous−Glycerol Electrolyte Media," *J. Phys. Chem. C*, vol. 113, no. 8, pp. 3046–3049, Feb. 2009, doi: 10.1021/jp900116k.

[24] T. Hardwick and N. Ahmed, "C-H Functionalization via Electrophotocatalysis and Photoelectrochemistry: Complementary Synthetic Approach," *ACS Sustain. Chem. Eng.*, vol. 9, no. 12, pp. 4324–4340, 2021, doi: 10.1021/acssuschemeng.0c08434.

[25] J. Liu, L. Lu, D. Wood, and S. Lin, "New Redox Strategies in Organic Synthesis by Means of Electrochemistry and Photochemistry," *ACS Cent. Sci.*, vol. 6, no. 8, pp. 1317–1340, Aug. 2020, doi: 10.1021/acscentsci.0c00549.

[26] C. A. C. Sequeira and D. M. F. Santos, "Electrochemical routes for industrial synthesis," *J. Braz. Chem. Soc.*, vol. 20, no. 3, pp. 387–406, 2009, doi: 10.1590/S0103-50532009000300002.

[27] G. Hilt, "Basic Strategies and Types of Applications in Organic Electrochemistry," *ChemElectroChem*, vol. 7, no. 2, pp. 395–405, Jan. 2020, doi: 10.1002/celc.201901799.

[28] C. Schotten, T. P. Nicholls, R. A. Bourne, N. Kapur, B. N. Nguyen, and C. E. Willans, "Making electrochemistry easily accessible to the synthetic chemist," *Green Chem.*, 2020,

doi: 10.1039/D0GC01247E.

[29]   S. Santoro, F. Ferlin, L. Ackermann, and L. Vaccaro, "C-H functionalization reactions under flow conditions," *Chem. Soc. Rev.*, vol. 48, no. 10, pp. 2767–2782, 2019, doi: 10.1039/c8cs00211h.

[30]   H. M. L. Davies and D. Morton, "Recent Advances in C-H Functionalization," *J. Org. Chem.*, vol. 81, no. 2, pp. 343–350, 2016, doi: 10.1021/acs.joc.5b02818.

[31]   S. Govaerts, A. Nyuchev, and T. Noel, "Pushing the boundaries of C–H bond functionalization chemistry using flow technology," *J. Flow Chem.*, vol. 10, no. 1, pp. 13–71, 2020, doi: 10.1007/s41981-020-00077-7.

[32]   A. Davit Hayrapetyan and b] and L. J. G. Raja K. Rit,[a] Markus Kratz,[b] Kristina Tschulik, "Electrochemical C H Cyanation of Electron-Rich Hetero Arenes." pp. 11288–11291, 2018.

[33]   M. Dörr, J. L. Röckl, J. Rein, D. Schollmeyer, and S. R. Waldvogel, "Electrochemical C−H Functionalization of (Hetero)Arenes—Optimized by DoE," *Chem. - A Eur. J.*, vol. 26, no. 45, pp. 10195–10198, 2020, doi: 10.1002/chem.202001171.

[34]   X. Hu, G. Zhang, L. Nie, T. Kong, and A. Lei, "Electrochemical oxidation induced intermolecular aromatic C-H imidation," *Nat. Commun.*, vol. 10, no. 1, 2019, doi: 10.1038/s41467-019-13524-4.

[35]   S. Liang, K. Hofman, M. Friedrich, J. Keller, and G. Manolikakes, "Recent Progress and Emerging Technologies towards a Sustainable Synthesis of Sulfones," *ChemSusChem*, vol. 14, no. 22, pp. 4878–4902, 2021, doi: 10.1002/cssc.202101635.

[36]   F. Lu *et al.*, "Electrochemical Oxidative C−H Sulfonylation of Anilines," *Asian J. Org. Chem.*, vol. 8, no. 10, pp. 1838–1841, 2019, doi: 10.1002/ajoc.201900447.

[37]   Y. C. Wu, S. S. Jiang, S. Z. Luo, R. J. Song, and J. H. Li, "Transition-metal- and oxidant-free directed anodic C-H sulfonylation of N, N-disubstituted anilines with sulfinates," *Chem. Commun.*, vol. 55, no. 61, pp. 8995–8998, 2019, doi: 10.1039/c9cc03789f.

[38]   W. Jud, S. Maljuric, C. O. Kappe, and D. Cantillo, "Cathodic C-H Trifluoromethylation of Arenes and Heteroarenes Enabled by an in Situ-Generated Triflyltriethylammonium Complex," *Org. Lett.*, vol. 21, no. 19, pp. 7970–7975, 2019, doi: 10.1021/acs.orglett.9b02948.

[39]   V. Shlyannikov, "Nonlinear stress intensity factors in fracture mechanics and their applications," *Procedia Struct. Integr.*, vol. 2, pp. 744–752, 2016, doi: 10.1016/j.prostr.2016.06.096.

[40]   T. Pokhrel, B. K. Bijaya, R. Giri, A. Adhikari, and N. Ahmed, "C−H Bond Functionalization under Electrochemical Flow Conditions," *Chem. Rec.*, vol. 22, no. 6, 2022, doi: 10.1002/tcr.202100338.

[41]   M. Selt, B. Gleede, R. Franke, A. Stenglein, and S. R. Waldvogel, "Electrosynthesis of 3 , 3 ′ , 5 , 5 ' -Tetramethyl-2 , 2 ′ -biphenol in Flow," *J. Flow Chem.*, 2020.

[42]   B. Gleede, M. Selt, R. Franke, and S. R. Waldvogel, "Developments in the Dehydrogenative Electrochemical Synthesis of 3,3′,5,5′-Tetramethyl-2,2′-biphenol," *Chem. - A Eur. J.*, vol. 27, no. 32, pp. 8252–8263, 2021, doi: 10.1002/chem.202005197.

[43]   W. Kong *et al.*, "Flow Rhodaelectro-Catalyzed Alkyne Annulations by Versatile C-H Activation : Mechanistic Support for Rhodium (III / IV)," *J. Am. Chem. Soc.*, 2019, doi: 10.1021/jacs.9b07763.

[44]   H. Yan, S. Zhu, and H. C. Xu, "Integrating Continuous-Flow Electrochemistry and Photochemistry for the Synthesis of Acridinium Photocatalysts Via Site-Selective C–H

Alkylation," *Org. Process Res. Dev.*, vol. 25, no. 12, pp. 2608–2613, 2021, doi: 10.1021/acs.oprd.1c00038.

[45]   Y. H. Budnikova, E. L. Dolengovsky, M. V Tarasov, and T. V Gryaznova, "Recent advances in electrochemical C-H phosphorylation," *Frontiers in chemistry*, vol. 10. FRC Kazan Scientific Center of RAS, Arbuzov Institute of Organic and Physical Chemistry, Kazan, Russia., p. 1054116, 2022, doi: 10.3389/fchem.2022.1054116.

[46]   N. Sbei, G. M. Martins, B. Shirinfar, and N. Ahmed, "Electrochemical Phosphorylation of Organic Molecules," *Chem. Rec.*, vol. 20, no. 12, pp. 1530–1552, 2020, doi: 10.1002/tcr.202000096.

[47]   L. Buglioni, M. Beslać, and T. Noël, "Dehydrogenative Azolation of Arenes in a Microflow Electrochemical Reactor," *J. Org. Chem.*, vol. 86, no. 22, pp. 16195–16203, 2021, doi: 10.1021/acs.joc.1c01409.

[48]   H. Yi *et al.*, "Recent Advances in Radical C-H Activation/Radical Cross-Coupling," *Chem. Rev.*, vol. 117, no. 13, pp. 9016–9085, 2017, doi: 10.1021/acs.chemrev.6b00620.

[49]   G. C. Z. and N. A. Guilherme M. Martins, Najoua Sbei, "C-H Activation/Functionalization via Metalla-Electrocatalysis," *Intech*, vol. 11, p. 13, 2016, [Online]. Available: https://www.intechopen.com/books/advanced-biometric-technologies/liveness-detection-in-biometrics.

[50]   X. Ye *et al.*, "Facilitating Ir-Catalyzed C-H Alkynylation with Electrochemistry: Anodic Oxidation-Induced Reductive Elimination," *ACS Catal.*, vol. 10, no. 20, pp. 11693–11699, 2020, doi: 10.1021/acscatal.0c03207.

[51]   Z. J. Wu *et al.*, "Scalable Rhodium(III)-Catalyzed Aryl C−H Phosphorylation Enabled by Anodic Oxidation Induced Reductive Elimination," *Angew. Chemie - Int. Ed.*, vol. 58, no. 47, pp. 16770–16774, 2019, doi: 10.1002/anie.201909951.

[52]   C. Tian, L. Massignan, T. H. Meyer, and L. Ackermann, "Electrochemical C−H/N−H Activation by Water-Tolerant Cobalt Catalysis at Room Temperature," *Angew. Chemie*, vol. 130, no. 9, pp. 2407–2411, 2018, doi: 10.1002/ange.201712647.

[53]   X. Gao, P. Wang, L. Zeng, S. Tang, and A. Lei, "Cobalt(II)-Catalyzed Electrooxidative C-H Amination of Arenes with Alkylamines," *J. Am. Chem. Soc.*, vol. 140, no. 12, pp. 4195–4199, 2018, doi: 10.1021/jacs.7b13049.

[54]   F. Kakiuchi and T. Kochi, "New strategy for catalytic oxidative CH functionalization: Efficient combination of transition-metal catalyst and electrochemical oxidation," *Chem. Lett.*, vol. 49, no. 10, pp. 1256–1269, 2020, doi: 10.1246/CL.200475.

[55]   Q. L. Yang, X. Y. Wang, J. Y. Lu, L. P. Zhang, P. Fang, and T. S. Mei, "Copper-Catalyzed Electrochemical C-H Amination of Arenes with Secondary Amines," *J. Am. Chem. Soc.*, vol. 140, no. 36, pp. 11487–11494, 2018, doi: 10.1021/jacs.8b07380.

[56]   N. Sauermann, T. H. Meyer, C. Tian, and L. Ackermann, "Electrochemical Cobalt-Catalyzed C-H Oxygenation at Room Temperature," *J. Am. Chem. Soc.*, vol. 139, no. 51, pp. 18452–18455, 2017, doi: 10.1021/jacs.7b11025.

[57]   C. Ma *et al.*, "Palladium-catalyzed C-H activation/C-C cross-coupling reactions: Via electrochemistry," *Chem. Commun.*, vol. 53, no. 90, pp. 12189–12192, 2017, doi: 10.1039/c7cc07429h.

[58]   Y. Q. Li, Q. L. Yang, P. Fang, T. S. Mei, and D. Zhang, "Palladium-Catalyzed C(sp2)-H Acetoxylation via Electrochemical Oxidation," *Org. Lett.*, vol. 19, no. 11, pp. 2905–2908, 2017, doi: 10.1021/acs.orglett.7b01138.

[59]   X. Chen, C. E. Goodhue, and J. Yu, "Palladium-Catalyzed Alkylation of sp 2 and sp 3 C -

H Bonds with Methylboroxine and Alkylboronic Acids : Two Distinct C - H Activation Pathways," *J. Am. Chem. Soc.*, vol. 128, pp. 12634–12635, 2006.

[60] B. R. Rosen, L. R. Simke, P. S. Thuy-boun, D. D. Dixon, J. Yu, and P. S. Baran, "C-H Functionalization Logic Enables Synthesis of (+) -Hongoquercin A and Related Compounds," *Angew. Chemie - Int. Ed.*, vol. 52, pp. 7317–7320, 2013, doi: 10.1002/anie.201303838.

[61] J. Wippich, I. Schnapperelle, and T. Bach, "ChemComm Regioselective oxidative Pd-catalysed coupling of alkylboronic acids with pyridin-2-yl-substituted," *Chem. Commun*, vol. 51, pp. 3166–3168, 2015, doi: 10.1039/c4cc10144h.

[62] S. Mçhle, M. Zirbes, E. Rodrigo, T. Gieshoff, A. Wiebe, and S. R. Waldvogel, "Modern Electrochemical Aspects for the Synthesis of Value-Added Organic Products Angewandte," *Angew. Chemie - Int. Ed.*, vol. 57, pp. 6018–6041, 2018, doi: 10.1002/anie.201712732.

[63] S. Tang, Y. Liu, and A. Lei, "Electrochemical Oxidative Cross-coupling with Hydrogen Evolution : A Green and Sustainable Way for Bond Formation," *CHEMPR*, no. 2017, pp. 1–19, 2018, doi: 10.1016/j.chempr.2017.10.001.

[64] Q. L. Yang *et al.*, "Palladium-Catalyzed Electrochemical C-H Alkylation of Arenes," *Organometallics*, vol. 38, no. 6, pp. 1208–1212, 2019, doi: 10.1021/acs.organomet.8b00550.

[65] C. Ma, P. Fang, T. Mei, C. Ma, P. Fang, and T. Mei, "Recent Advances in C-H Functionalization Using Electrochemical Transition Metal Catalysis," *Am. Chem. Soc.*, 2018, doi: 10.1021/acscatal.8b01697.

[66] T. H. Meyer and L. Ackermann, "Electrochemical Cobalt-Catalyzed C–H Activation," *Chem. - A Eur. J.*, 2018, doi: 10.1002/chem.201802706.

[67] D. Kalsi and B. Sundararaju, "Cobalt Catalyzed C − H and N − H Bond Annulation of Sulfonamide with Terminal and Internal Alkynes," *Org. Lett.*, pp. 3–6, 2015, doi: 10.1021/acs.orglett.5b03142.

[68] J. Ni, J. Li, Z. Fan, and A. Zhang, "Cobalt-Catalyzed Carbonylation of C(sp 2) − H Bonds with Azodicarboxylate as the Carbonyl Source," *Org. Lett.*, vol. 2, pp. 8–11, 2016, doi: 10.1021/acs.orglett.6b03111.

[69] R. N. and C. M. R. V. Neetipalli Thrimurtulu, "Cobalt-Catalyzed Aryl C−H Activation and Highly Regioselective Intermolecular Annulation of Sulfonamides with Allenes Received," *Chem. Commun*, 2017, doi: 10.1039/C6CC08622E.

[70] C. Amatore, C. Cammoun, and A. Jutand, "Electrochemical Recycling of Benzoquinone in the Pd / Benzoqui- none-Catalyzed Heck-Type Reactions from Arenes," *Adv. Synth. Catal.*, vol. 349, pp. 292–296, 2007, doi: 10.1002/adsc.200600389.

[71] U. Dhawa, N. Kaplaneris, and L. Ackermann, "Green strategies for transition metal-catalyzed C-H activation in molecular syntheses," *Org. Chem. Front.*, vol. 8, no. 17, pp. 4886–4913, 2021, doi: 10.1039/d1qo00727k.

[72] M. Konishi, K. Tsuchida, K. Sano, T. Kochi, and F. Kakiuchi, "Palladium-Catalyzed ortho-Selective C-H Chlorination of Benzamide Derivatives under Anodic Oxidation Conditions," *J. Org. Chem.*, vol. 82, no. 16, pp. 8716–8724, 2017, doi: 10.1021/acs.joc.7b01137.

[73] Y. Zhang, J. Struwe, and L. Ackermann, "Rhodium-Catalyzed Electrooxidative C−H Olefination of Benzamides," *Angew. Chemie - Int. Ed.*, vol. 59, no. 35, pp. 15076–15080, 2020, doi: 10.1002/anie.202005257.

[74] U. Dhawa, C. Tian, W. Li, and L. Ackermann, "Cobalta-Electrocatalyzed C-H Allylation with Unactivated Alkenes," *ACS Catal.*, vol. 10, no. 11, pp. 6457–6462, 2020, doi: 10.1021/acscatal.0c01436.

[75] C. Tian, U. Dhawa, J. Struwe, and L. Ackermann, "Cobaltaelectro-Catalyzed C—H Acyloxylation," *Chinese J. Chem.*, vol. 37, no. 6, pp. 552–556, 2019, doi: 10.1002/cjoc.201900050.

[76] Y. Tachibana, L. Vayssieres, and J. R. Durrant, "Artificial photosynthesis for solar water-splitting," *Nat. Photonics*, vol. 6, pp. 511–518, 2012, doi: 10.1038/NPHOTON.2012.175.

[77] H. Tateno, Y. Miseki, and K. Sayama, "Photoelectrochemical oxidation of benzylic alcohol derivatives on BiVO 4 / WO 3 under visible light irradiation," *ChemElectroChem*, vol. 4, pp. 3283–3287, 2017, doi: 10.1002/celc.201700710.

[78] H. Tateno, S. Iguchi, Y. Miseki, and K. Sayama, " Photo-Electrochemical C−H Bond Activation of Cyclohexane Using a WO 3 Photoanode and Visible Light ," *Angew. Chemie*, vol. 130, no. 35, pp. 11408–11411, 2018, doi: 10.1002/ange.201805079.

[79] H. Tateno, Y. Miseki, and K. Sayama, "Photoelectrochemical dimethoxylation of furan via a bromide redox mediator using a BiVO4/WO3 photoanode," *Chem. Commun.*, vol. 53, no. 31, pp. 4378–4381, 2017, doi: 10.1039/c7cc01190c.

[80] H. G. Cha and K. S. Choi, "Combined biomass valorization and hydrogen production in a photoelectrochemical cell," *Nat. Chem.*, vol. 7, no. 4, pp. 328–333, 2015, doi: 10.1038/nchem.2194.

[81] L. Zhang, L. Liardet, J. Luo, D. Ren, M. Grätzel, and X. Hu, "Photoelectrocatalytic arene C–H amination," *Nat. Catal.*, vol. 2, no. 4, pp. 366–373, 2019, doi: 10.1038/s41929-019-0231-9.

[82] C. K. Prier, D. A. Rankic, and D. W. C. MacMillan, "Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis," *Am. Chem. Soc.*, vol. 113, no. 7, pp. 5322–5363, 2013.

[83] H. Yan, J. Song, S. Zhu, and H. C. Xu, "Synthesis of Acridinium Photocatalysts via Site-Selective C–H Alkylation," *CCS Chem.*, vol. 3, no. 12, pp. 317–325, 2021, doi: 10.31635/ccschem.021.202000743.

[84] Z. Tang, K. Mo, X. Ma, J. Huang, and D. Zhao, "para-Selective Radical Trifluoromethylation of Benzamide Derivatives via Iminium Intermediates," *Angew. Chemie*, vol. 134, no. 36, 2022.

[85] T. Zhang, X. Guo, Y. Shi, C. He, and C. Duan, "Dye-incorporated coordination polymers for direct photocatalytic trifluoromethylation of aromatics at metabolically susceptible positions," *Nat. Commun.*, vol. 9, no. 1, 2018, doi: 10.1038/s41467-018-05919-6.

[86] F. Wang and S. S. Stahl, "Merging Photochemistry with Electrochemistry: Functional-Group Tolerant Electrochemical Amination of C(sp3)−H Bonds," *Angew. Chemie - Int. Ed.*, vol. 58, no. 19, pp. 6385–6390, 2019, doi: 10.1002/anie.201813960.

[87] H. Huang and T. H. Lambert, "Electrophotocatalytic SNAr Reactions of Unactivated Aryl Fluorides at Ambient Temperature and Without Base," *Angew. Chemie - Int. Ed.*, vol. 59, no. 2, pp. 658–662, 2020, doi: 10.1002/anie.201909983.

[88] Y. Qiu, A. Scheremetjew, L. H. Finger, and L. Ackermann, "Electrophotocatalytic Undirected C−H Trifluoromethylations of (Het)Arenes," *Chem. - A Eur. J.*, vol. 26, no. 15, pp. 3241–3246, 2020, doi: 10.1002/chem.201905774.

[89] M. J. Hossain, T. Ono, K. Wakiya, and Y. Hisaeda, "A Vitamin B12 derivative catalyzed electrochemical trifluoromethylation and perfluoroalkylation of arenes and heteroarenes in

organic media," *Chem. Commun.*, vol. 53, no. 79, pp. 10878–10881, 2017, doi: 10.1039/c7cc06221d.

[90] H. Xu, X. Qiao, S. Yang, and Z. Shen, "Cu-catalyzed direct amidation of aromatic C-H bonds: An access to arylamines," *J. Org. Chem.*, vol. 79, no. 10, pp. 4414–4422, 2014, doi: 10.1021/jo5003592.

[91] and B.-J. H. Andebet Gedamu Tamirat, John Rick, Amare Aregahegn Dubale, Wei-Nien Su, "Using hematite for photoelectrochemical water splitting: a review of current progresses and challenges," *Nanoscale Horizons*, 2016, [Online]. Available: http://dx.doi.org/10.1039/C6NH00140H.

[92] K. Sivula, F. Le Formal, and M. Grätzel, "Solar water splitting: Progress using hematite (α-Fe 2O3) photoelectrodes," *ChemSusChem*, vol. 4, no. 4, pp. 432–449, 2011, doi: 10.1002/cssc.201000416.

[93] K. A. Margrey, J. B. McManus, S. Bonazzi, F. Zecri, and D. A. Nicewicz, "Predictive Model for Site-Selective Aryl and Heteroaryl C-H Functionalization via Organic Photoredox Catalysis," *J. Am. Chem. Soc.*, vol. 139, no. 32, pp. 11288–11299, 2017, doi: 10.1021/jacs.7b06715.

[94] S. D. Tilley, M. Cornuz, K. Sivula, and M. Grätzel, "Light-Induced Water Splitting with Hematite: Improved Nanostructure and Iridium Oxide Catalysis," *Angew. Chemie*, vol. 122, no. 36, pp. 6549–6552, 2010, doi: 10.1002/ange.201003110.

[95] H. Huang and T. H. Lambert, "Electrophotocatalytic C−H Heterofunctionalization of Arenes," *Angew. Chemie - Int. Ed.*, vol. 60, no. 20, pp. 11163–11167, 2021, doi: 10.1002/anie.202100222.

[96] P. Xu, P. Y. Chen, and H. C. Xu, "Scalable Photoelectrochemical Dehydrogenative Cross-Coupling of Heteroarenes with Aliphatic C−H Bonds," *Angew. Chemie - Int. Ed.*, vol. 59, no. 34, pp. 14275–14280, 2020, doi: 10.1002/anie.202005724.

[97] Y. Hussain, D. Sharma, N. Kotwal, I. Kumar, and P. Chauhan, "Stereoselective Oxidative Mannich Reaction of Ketones with Dihydrodibenzo-Oxazepines via a Merger of Photoredox-/Electro-Catalysis with Organocatalysis," *ChemSusChem*, vol. 15, no. 12, 2022, doi: 10.1002/cssc.202200415.

[98] T. Broese and R. Francke, "Electrosynthesis using a recyclable mediator-electrolyte system based on ionically tagged phenyl iodide and 1,1,1,3,3,3-hexafluoroisopropanol," *Org. Lett.*, vol. 18, no. 22, pp. 5896–5899, 2016, doi: 10.1021/acs.orglett.6b02979.

[99] Liu, Yue-Jin, Xu, Hui, Kong, Wei-Jun, Shang, Ming, Dai, Hui-Xiong, Yu, Jin-Quan, "Overcoming the limitations of directed C–H functionalizations of heterocycle", *Nature,* vol. 515(7527), pp. 389–393, 2014, doi:10.1038/nature13885.

[100] Engle, Keary M, Mei, Tian-Sheng, Wasa, Masayuki, Yu, Jin-Quan, "Weak Coordination as a Powerful Means for Developing Broadly Useful C–H Functionalization Reactions", *Accounts of Chemical Research,* vol. 45(6), pp.788–802, 2012, doi:10.1021/ar200185g.

[101] Schulz, Lara, Waldvogel, Siegfried, "Solvent Control in Electro-Organic Synthesis", *Synlett,* (), s-0037-1610303, 2018, doi:10.1055/s-0037-1610303.

Corresponding Author's Profile:

Nisar Ahmed *obtained his PhD in organic chemistry with Brain Korea BK21 fellowship from POSTECH, Korea. Then, he moved to the University of Zurich, Switzerland for a postdoctoral stay with a Novartis Fellowship. Subsequently, he joined the University of Bristol as a research associate. Further, he started his academic career at Cardiff University (2017 - present), United Kingdom. His fields of research include synthesis of value-added chemicals, fine chemicals, and pharmaceuticals with special focus on inert bonds activations using modern synthetic tools such as electrochemistry, photochemistry, sonochemistry, flow technology, digital & automation chemistry, and reaction engineering.*