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C–H Functionalisation via Electrophotocatalysis and Photoelectrochemistry: Complementary Synthetic Approach

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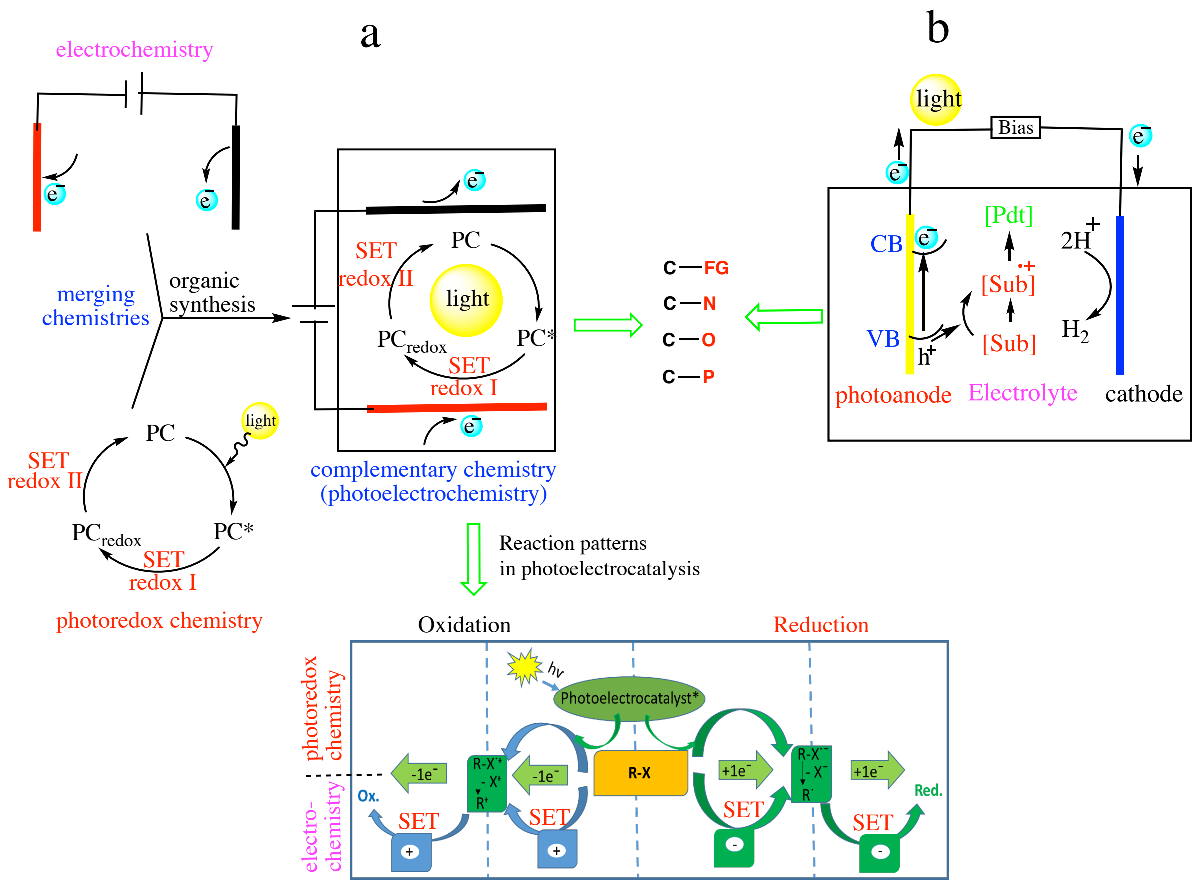
Abstract

Photoelectrochemical (PEC) cells are well documented as an important tool for energy and environmental applications. Most commonly used to produce hydrogen fuel from water splitting, PEC cells have also been directed towards pollutant degradation, carbon dioxide reduction and the production of solar fuels. Their application in organic synthesis, however, remains in its infancy. Motivated by the desire for green and sustainable synthetic methods, the merger of photochemistry and electrochemistry is envisaged to become a new strategy to accompany the modern organic chemists. PEC cells are desirable due to the abundance, convenience, inexpensive and clean nature of sunlight, the rich variety of photoelectrode materials and redox mediators as well as their ability to utilise mild reaction conditions. This perspective article describes some of the recent developments in PEC-driven organic synthesis by combining electrochemistry and photoredox catalysis in a single system. Specific emphasis has been given for reactions concerning C-H activations, whereby new chemical bonds are forged, whether they be for the late stage functionalisation of interesting compounds or the conjoining of two molecular building blocks. This combination is emerging as a powerful system that can achieve reactions that previous methodologies would find difficult or impossible, and can do so in an environmentally friendly, energy saving manner with high atom- and step-economies.

Introduction

Photocatalysis is a captivating technique in chemistry and organic synthesis, largely attributed to its employment of renewable visible light that acts as an effective tool to induce single electron transfer (SET) steps in cross-coupling reactions.[1–7] Energy is selectively transferred to the catalyst rather than the substrate, therefore, unwanted side reactions such as decomposition of desired compounds can be avoided.[1,7–11] Unfortunately, energy constraints of the visible light, (400-700 nm, 1.8-3.1 eV) poses a problem as it is typically insufficient for many challenging chemical transformations (e.g. production of glucose from H_2O and CO_2),[12–14] and is further hampered by intersystem crossing and nonradiative losses. For instance, potentials of +2.4–3.5 V vs. SCE and -2.6–3.4 V vs. SCE are required for many SET oxidations and reductions, respectively.[13] This means that many compounds cannot be activated by phototcatalysis, leading to the requirement for external oxidants/reductants to achieve redox-neutral reactions, which can introduce hazards and generate by-products, thus damaging chemoselectivity.[13,15–17]

Green electrochemistry, on the other hand, can overcome this limitation by using safer, alternative oxidants/reductants with electricity as the traceless redox agent.[18–27] An example would be protons which are effective as the terminal oxidant and produce hydrogen as the predominant by-product. At the anode and cathode, respectively, oxidation and reduction occur simultaneously. Furthermore, these can occur in the same system (undivided cell) or in one that is separated into two individual components (divided cell). Similar to photocatalysis, the same open-shell intermediates are generated from electron exchange at the electrode surface in an electrochemical system. However, in opposition, this is usually followed by a second SET in the same direction in electrochemistry due to the harsher redox conditions.[28] The applied potential employed by electrocatalysis gave the technique traction as a powerful tool which can prevent electrode passivation, eliminate the need for external oxidants, improve electron transfer kinetics and impart the catalyst with selectivity and tunability.[29] Thus, many electrosynthetic transformations have been realised such as C-H activations,[30] direct C-H oxidations,[31] and alkene functionalisations.[32,33] The ability of electrochemistry to choose any potential is arguably its biggest advantage, allowing access highly reactive intermediates at extreme potentials (without the dependence on excited states)[34] with the tolerance of the solvent being the redox windows only limit.[1] However, the constant application of high potentials can result in undesirable reactions near the surface of the electrode, damaging yields, chemoselectivities and functional group tolerance (from overpotentials). Electrochemically generated radicals can easily undergo radical homo-coupling, over-oxidation/reduction (e.g. radicals at the cathode reduced to anions), and inefficient mass transfer at the electrode/bulk solution interface leads to electrode passivation.[35] Moreover, a high ohmic drop between the two electrodes in an organic solvent system (in conjunction to one that is aqueous) means that high potentials are required for acceptable conversions.[1,36,37] The drop can be decreased with a high supporting electrolyte concentration (n-Bu_4NPF_6), however, one that is amphiphilic can be difficult to separate from the desired product. Therefore, what is needed is something that can access an extreme redox potential under mild conditions without over-exerting the intermediates.



Scheme 1: **a**. *Electrochemically mediated photocatalysis: merging of photoredox chemistry with electrochemistry in organic synthesis to yield the photoelectrochemical method; SET (single electron transfer), PC (photocatalyst), R-X (substrate)* ***b****. Interfacial electro-photocatalysis: Photoelectrochemical cells (PECs) using a photoelectrode for oxidative organic transformations. (****Lower part****). In an electrochemical process, the intermediates are generated upon the exchange of an electron at the surface of an electrode. However, at variance with photocatalysis, the involved intermediates usually undergo a second electron transfer in the same direction because of the strong oxidizing/reducing conditions.*

In the leap towards green and sustainable chemistry both electrochemistry and photoredox catalysis have received much attention in the past decade.[38–45] They are often mentioned and compared together because of their close similarities, such as the generation of open shell intermediates via SET methods, enabling transformations to be translated from one to the other and to allow easy access to radical intermediates for organic synthesis. To date, the constructive merging of photochemistry and electrochemistry is in its infancy states, particularly when compared to the constituent parts (**Scheme 1**). However, it does possess the opportunity to use the advantages of one to compensate for the weaknesses of the other, thereby realising a powerful new tool for green chemistry with the possibility of unlocking novel reaction pathways that are not possible with each individual methodology.[44] Photoelectrochemical (PEC) cells have been of interest to multiple disciplines to tackle modern energy and environmental issues through the conversion of solar energy to electricity, to produce hydrogen from the water splitting reaction and the reduction of CO_2. Typically, solar photons strike a photoelectrode emerged in an electrolyte solution, generating electron-hole pairs. These then direct the redox reaction by reducing water to oxygen and protons at the cathode and oxidising protons to hydrogen at the anode.[46] These same electron-hole pairs, which are generated under mild conditions with high oxidising/reducing power, can also be used to drive organic reduction and oxidation reactions to high-value targets. Precise control over reaction progress and selectivity can subsequently be achieved using the electrons, photons and photoelectrode properties (i.e. band position, morphology and composition).

This branch of chemistry has developed from the desire to create green catalysts for the splitting of water that are inexpensive (e.g. no noble metals), highly active and display long-term activity. Many PEC semiconductor electrodes are burdened with low photo-water splitting efficiency due to material degradation, poor light absorption, charge separation and transportability. Recently however, waste-yeast biomass supports decorated with Ru single-atoms and nanoparticles and Fe-based materials has been reported for cathode and anode electrodes to produce hydrogen and oxygen from water, respectively.[47] This study is interesting because the living organism yeast (rich in phosphorus, carbon, sulphur and nitrogen) provided several positive attributes including eco-friendly chemistry, good electrical conductivity, functional group tolerance that allows strong interaction with metal ions, low cost, nontoxic, easy availability, degrades easily and has a bio-composition (DNA, proteins, lipids, etc.). Moreover, for the hydrogen evolution reaction and in addition good activity and a long cycle life (10,000 cyclic voltammetry (CV)), with respect to overpotential, Tafel slope, exchange current density and durability, the Ru-catalyst managed to outperform the 20wt% Pt/C catalyst and the Fe-anode showed good activity of the oxygen evolution reaction. This was attributed to the supports good conductivity, synergy between single atoms and nanoparticles, a large porous surface area with lots of catalytically active sites, and fast charge transfer kinetics. Other attempts involving semiconductor electrodes to improve performance by mitigating electron-hole recombination and poor light absorbance is to decorate with single atoms and p- and d-block elements (noble metals Pt, Pd, Ru, Ir, Au, Ag as well as Fe, Co, Ni, Cu, Mo, Bi, W and their respective alloys),[48] graphene and other nanomaterials. To improve the PEC conversion efficiency, activity, light absorption spectrum, reduce recombination etc. semiconductors can be functionalised with 0D quantum dot nanomaterials such as CdS, graphene, graptitic carbon nitride (g-C_3N_4), Co_3O_4 and 1D nanotubes (carbon, TaON), nanowires (SiC, Fe_2O_3, CdS, ZnO) and nanorods (WO_3, ZnO, TiO_2/TiO_2).[48] 2D materials such as MoS_2, g-C_3N_4, TiO_2, and hematite can lead to enhanced photoactivity due to high surface areas and thin sheets providing greatly reduced resistance and access to UV light. Moreover, graphene is often referred to as a “wonder material” due to its variety of exciting properties arising from a single atomic layer of sp^2-hydridised carbon atoms π-conjugated with a large surface area and excellent electrical conductivity and mechanical strength. Graphene’s properties allow it to act as a protective layer over a semiconductor to hinder photocorrosion and to enhance catalytic activity by reducing charge recombination, provide a large area for adsorption, improve charge transfer at interfaces and to and from the semiconductor and provide more photocatalytically active centres. 3D nanostructures may also be used to enable easy diffusion pathways, reduce electrolyte/electrode distances and offer high-temperature photoactivity (e.g. dendritic α-Fe_2O_3).[48]

Moreover, PEC systems can be constructed with heterogeneous photoelectrodes and homogeneous catalysts, hence the generation of a chromophore in solution is possible if so desired. Clean energy from the light and electricity not only reduce the required external bias, saving electricity and reducing the chances of the chemoselectivity being negatively affected due to unfavourable side reactions, but also eliminate the need of chemical oxidants/reductants. Thus, the environmental impact of organic redox reactions is reduced, the milder conditions can broaden the functional group tolerance, redox window (allowing access to high redox potentials), increase atom economies and still enable net-oxidative photochemical processes, e.g. C-H alkylation of heteroarenes.[28] PEC cells do, however, require a more complex setup than photocatalysis and electrochemistry; equipment is not yet standardised and their use for organics is limited.

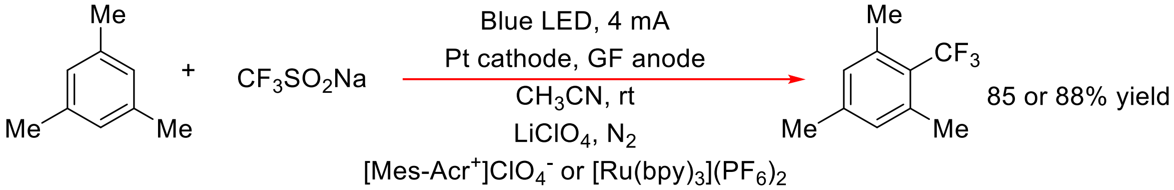
Combining photocatalysis with electrochemistry are expected to broaden the redox window of SET processes, increase atom economy, energy/ money savings and improve selectivities and functional group tolerance by using milder conditions. The applicability may also extend to difficult SET chemistries such as direct reductions of ethers, amides, sulphides, sulfoxides, Si-X (X=Cl, F, OR, $OSiR_3$) and direct oxidations such as hydrocarbons, carbonyls, fluorinated aromatics and sulfones.[1] Electrophotochemistry occurs when there is an interdependent relationship between constituent components, i.e. photoexcitation of electrochemically generated ions. This can allow a large redox window of SET reactions by the generation of super-oxidants and reductants and thus perform processes at potentials beyond the capabilities of organic solvents in each individual process. In addition, this method can appeal to industry and sustainability by alleviating the need for a sacrificial agent. Interfacial photoelectrochemistry on the other hand is the same process, but with reactions occurring at semiconductor photoelectrodes. Compared to electrophotochemistry it has a disadvantage in that some photoanode materials can photocorrode in the aqueous solvents, nor can it attain the very high redox potentials, thus loses an energy benefit. However, it is advantageous in the sense that is does not need to form a chromophore, it is difficult to measure redox potentials when they lie outside the redox window of the solvent, can interact with compounds that do not absorb visible light, and can use the visible light energy to reduce the high external bias applied to electrode, thus reducing electricity-induced electrode damage and improving energy efficiency and selectivity. Most of its application has been realised for simple chemical transformations but as progress is made, in time interfacial photoelectrochemistry will extend to more complex substrates. For both techniques, addressing certain challenges will be needed to propel photoelectrochemical organic transformations into a highly established methodology. One will be the more rigorous control experiments, highlighting the benefit and necessity for both light and electricity. Another will be the standardisation of equipment since many of the current PEC syntheses are performed in custom-built electrochemical glassware that can be irradiated with light. That being said commercially available water splitting PEC cells can be adapted for transformations in organic solvents and continuous flow technology can be incorporated to remove the current problems of scalability in batch reactors as well as to improve the kinetics and transmission of light and electrons.

The nomenclature “photoelectrocatalysis” is associated with interfacial photoelectrocataysis, also commonly used in physical chemistry, i.e. concerning the water splitting reaction, and has been used for a longer time, while “electrophotocatalysis” is used for electrochemically-mediated photocatalysis. However, IUPAC defines photoelectrochemistry as a “term applied to a hybrid field of chemistry employing techniques which combine photochemical and electrochemical methods for the study of the oxidation-reduction chemistry of the ground or excited states of molecules or ions. In general, it is the chemistry resulting from the interaction of light with electrochemical systems.” Therefore, photoelectrochemistry technically coverers both photoelectrocatalysis and electrophotocatalysis, however, in organic chemistry it is now being associated with photocurrent generation and reaction at semiconductor electrodes and hence, interfacial photoelectrocatalysis. In the absence of the heterogeneous semiconductors with the reaction performing in solution with homogenous catalysts, electrophotocatalysis is the term commonly used.[49]

Recent breakthroughs indicate that the enabling technology could open up a plethora of green, sustainable reactions, many of which could be non-redox neutral, yet to be explored, and transformations not possible in the absence of light and electricity. Several examples have already been reported, employing photoanodes such as $BiVO_4$ and WO_3, to afford various solar-induced organic transformations.[46] Herein, we have directed our attention of the combing of electrochemistry with photoredox catalysis to the activation of C-H bonds. This is because direct C-H functionalisations are an established process during the synthesis of important organic molecules, and have been known to improve reaction atom- and step economies.[50] C-H functionalisations are a very important way of making important organic compounds by combining two molecular building blocks or later stage functionalisations (e.g. of pharmaceuticals). C-H bonds are commonplace in every organic molecule and yet are also infamous for being notoriously stable. To be able to selectively swap one of these hydrogens for something specifically desired by the chemist is a difficult task. However, to do so allows us to manipulate molecules at will, something that is of particular interest for the large-scale functionalisation of simple alkanes and the creation of more complex, highly functionalised value-added compounds such as pharmaceuticals and agrochemicals. When C-H activations took their initial strides 25 years ago it was evident that a catalytic system would be needed to overcome the challenge of selectivity and efficiency. To date we are still progressing towards such a catalytic system with a high enough turnover to be industrial practical. By gaining better understandings of homogeneous and heterogeneous catalytic systems, that the goal that C-H functionalisations will one day be a useful, commonplace methodology will be realised on a practical scale. We show that attractive solutions to challenging problems are revealed via this new catalytic tool, which opens the door to SETs that utilise the unique reactivity's of open shell intermediates that were not previously possible.[51] We envision that photoelectrochemistry will be a great new asset to organic synthesis and reveal an element of sustainability, such as the formation of radical intermediates and hydrogen gas.

Electro-photochemical C-H bonds Transformations

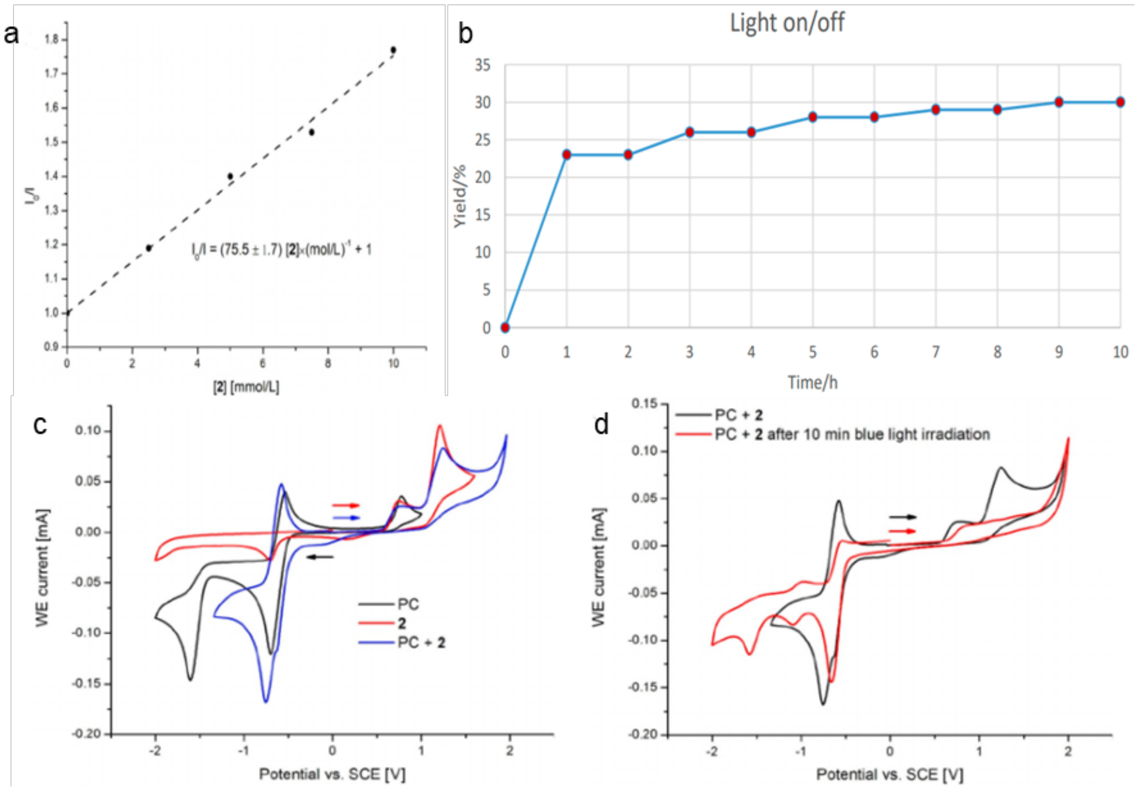
Electrochemically-mediated photocatalysis: C(sp^2)-H Functionalisation



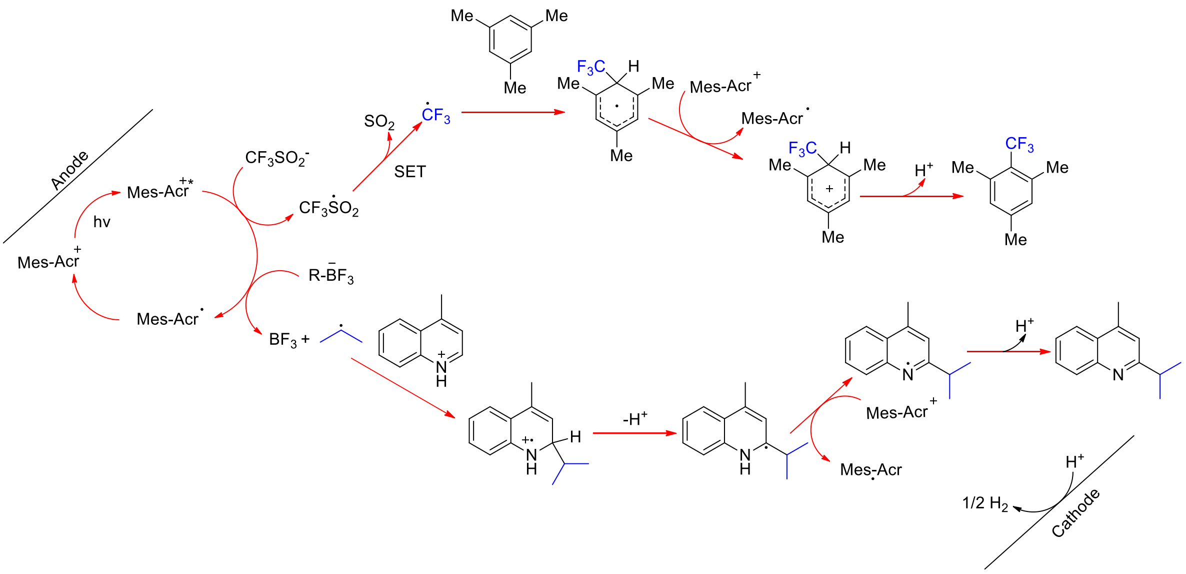
Scheme 2: *Electrophotochemical undirected C-H trifluoromethylation of an unactivated arene.*

It was through the combination of photo- and electro-chemistry that enabled the first electrophotochemical undirected C-H trifluoromethylation of unactivated arenes and heteroarenes (**Scheme 2**).[52] The cheap Langlois reagent CF_3SO_2Na allowed CF_3 radicals to be generated under mild conditions without the need for toxic and expensive chemical oxidants. This is attractive because pharmaceutical/ medicinal chemistry industries are interested in the unique bioactivity and lipophilicity of trifluoromethylated compounds.[53–55] In an undivided cell, CF_3SO_2Na was combined with the readily available mesitylene with Pt (cathode), graphite felt (GF, anode), CH_3CN (solvent) and $LiClO_4$ (additive). It was found that photocatalysts $[Mes\text{-}Acr^+]ClO_4^-$ or $[Ru(bpy)_3](PF_6)_2$ worked well, giving yields of 85 and 88%, respectively, while the addition of light and electricity were paramount to this success. The importance of light was evidenced by monitoring the conversion profile of the trimethylation via a Stern–Volmer plot analyses (**Scheme 3a**), which revealed effective fluorescence quenching of MesAcr*, predominantly by CF_3SO_2Na, accounting for reaction suppression in the absence of light. Moreover, on/off experiments demonstrated that transformation suppression was also apparent in the absence of electricity (**Scheme 3b**). Taking the organic dye Mes-Acr$^+$ as the example, light excitation oxidised it to its excited state of Mes-Acr^{+*} at the anode, which was then involved in a single electron transfer (SET) process with the sulfonate anion to produce the acridinyl and the CF_3SO_2 radical (**Scheme 4, top route**).[52] CF_3● radicals were then efficiently generated from the latter with the loss of SO_2, attributed from CV

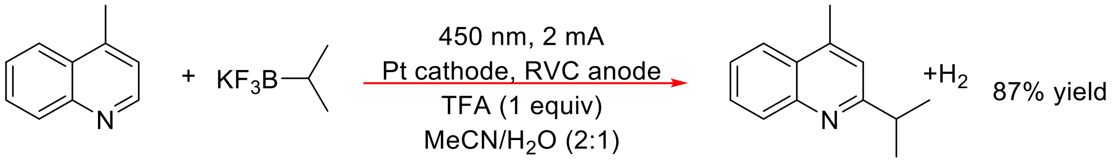
(**Scheme 3c** and **d**) studies whereby a reductive current was observed at E_{onset}= 0.57 V vs. SCE (trimethylation observed at E_{onset}=+1.02 V vs.SCE). The spectra remained the same after the addition of the photocatalyst, however, under blue light irradiation displayed the consumption of CF_3SO_2 to give the radical via oxidation at E_{red}=+2.06 V vs. SCE, suggesting the presence of CF_3● radicals, which readily performed intermolecular oxidative C–H transformations; proton reduction to H_2 occurred at the cathode. Toleration of a board substrate scope was subsequently discovered (e.g. ester, amide, and acetyl substituents), including naturally occurring heteroarenes, electron-rich and electron-poor benzenes with high regioselectivity. Further utility was demonstrated with the efficient late-stage trifluoromethylations of naturally occurring motifs such as caffeine, pentoxifylline, doxofylline, theobromine, methyl estrone, and tryptophan derivatives. Finally, these batch results paved the way for a corresponding continuous flow methodology that displayed high efficiency and utilised on-line flow-NMR which gave support for SET processes.



Scheme 3. ***a***. *Stern-Volmer plot analysis of fluorescence quenching of* $[Mes\text{-}Acr^+]ClO^{4-}$ *with* CF_3SO_2Na; ***b***. *Light on/off experiments;* ***c*** *and* ***d***. *Cyclic voltammagrams with substrates (5 mmol/L), LiClO4 (100 mmol/L), MeCN, 100 mV/s; 2 =* CF_3SO_2Na*, PC = photocatalyst. Reproduced from ref* 52, Copyright (2020) John Wiley & Sons.



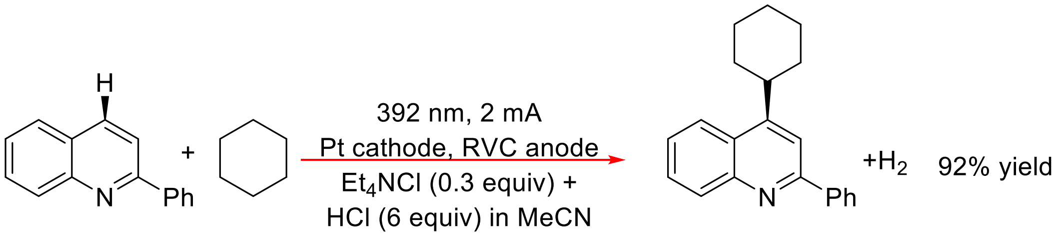
Scheme 4: *Proposed mechanisms for electrophotochemical C–H trifluoromethylation of mesitylene with the Langlois reagent (****top route****) and C–H alkylation of lepidine with potassium isopropyltrifluoroborate (****bottom route****) proceeding via a Minisci-type reaction.*



Scheme 5: *Photoelectrochemical C-H alkylations of a heteroarene with an organotrifluoroborate.*

The merger of photoredox catalysis and electrocatalysis has led to chemical-oxidant free Minisci-type reactions for electrophotochemical C-H alkylations of heteroarenes with organotrifluoroborates (**Scheme 5**) and carboxylic acids.[56] Alkyl radicals are generated from a variety of heteroarenes efficiently and functionalised from primary, secondary and tertiary organotrifluoroborates. Typically, the generation of alkyl radicals via electrochemical means is plagued by undesirable reactions such as overoxidation to carbocations (non-Kolbe electrolysis), reacting, and therefore passivating, the electrode surfaces and radical-radical dimerization (Kolbe reaction).[56–58] Overoxidation is a common problem for redox catalysis because the oxidation potentials of many common radial precursor is higher than that of many alkyl radicals.[57,59–61] Here, however, this was observed to occur in regio- and chemoselective manners, whereby the alkyl radicals readily underwent intermolecular oxidative transformations without being overoxidised to carbocations. Electrolysis with the assistance of light from a 20 W LED (blue) was initially applied to the alkylation of lepidine with potassium isopropyltrifluoroborate, in an undivided cell that used a Pt cathode and a reticulated vitreous carbon (RVC) anode. An optimised solvent system of MeCN/H_2O (2:1) at rt with TFA (acid additive), Et_4NBF_4 (supporting electrolyte) and the organic dye [Mes-Acr$^+$]ClO_4^- (catalyst) led to an 87% yield of the product. Importantly, product formation was significantly hampered in the absence of light, electricity or catalyst, thus illustrating the importance of the merger. The reaction could even be conducted without Et_4NBF_4 (80% yield) and in air, albeit with a lower yield (63%). Other, lower redox potential catalysts were found to be less efficient.

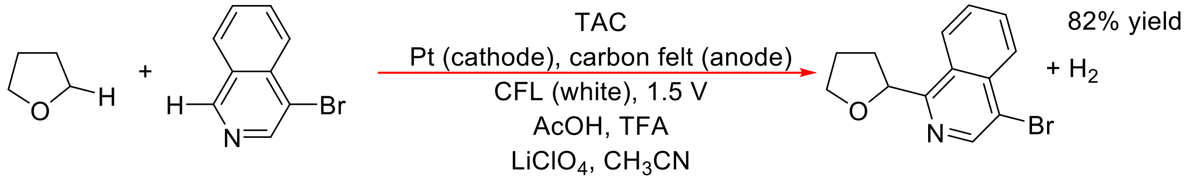
Nevertheless, a broad scope of heteroarenes and organotrifluoroborates were well tolerated, including secondary alcohols, alkynes, amines and tertiary amines, all of which are prone to overoxidation during electrolysis. This, and the following C-C bond formations typically occur via a Minisci-type mechanism.[62] A carbon-centred radical (C-radical) is conjoined to an electron-deficient heteroaromatic compound, which is attractive since a broad scope of heterocycles can therefore be incorporated. The C-radical precursors are mostly used due to their availability, non-toxicity, structural diversity and affordability, however, they are typically produced with stoichiometric amounts chemical oxidants (gives rise to atom economic, safety and environmental issues). The oxidants may be something like peroxide, hypervalent iodine or persulfate, that are exposed to light or heat to promote hydrogen atom transfer (HAT) to cleave a C-H donor to produce the radical.[63] However, using electrochemistry to replace these oxidants is an exciting way forward to unlock a greater range of chemical moieties and improve chemioselectivity. This example, shown in **Scheme 4** (**bottom route**), is a Minisci-type reaction where the catalyst, Mes-Acr$^+$, is irradiated to its excited, highly oxidising state (Mes-Acr^{+*}, E_{red} = 2.06 V vs SCE in MeCN). An SET between Mes-Acr^{+*} and the organotrifluoroborate forms the alkyl radical and the stable Mes-Acr$^{\bullet}$ (which is oxidised at the anode to reform the ground state Mes-Acr$^+$). The C-radical can then react with the protonated heteroarene, which is followed by the loss of a proton and then an electron to afford the product.



Scheme 6: *Electrophotochemical dehydrogenative cross-coupling of 2-phenylquinoline with cyclohexane.*

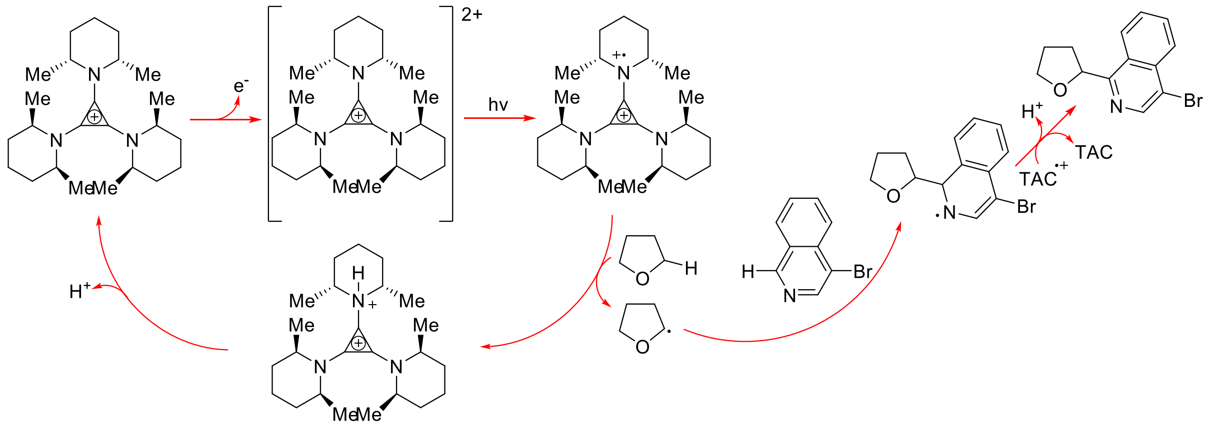
Xu *et al*. extended this work to another elegant strategy whereby electrochemistry and photochemistry have been combined in a single system for the dehydrogenative cross-coupling of C(sp^2)-H heteroarenes and C(sp^3)-H donors (**Scheme 6**).[63] Heteroarenes are important components of functional materials, pharmaceutical and bioactive compounds,[64,65] and combining them with dehydrogenative cross-coupling with aliphatic C-H bonds provides an excellent way of functionalising their C-H bonds via the creation new C-C bonds. It should be noted that this can be done using readily available starting materials with high step and atom economies.[66] Photochemical methods alone have reported this, although they require cobalt catalyst that lead to the reduction and elimination of alkyl radicals.[67] Electrochemical methods have achieved efficient acylation of heteroarenes[68] and C-H fluroalkylation[69] but have failed when it comes to election-poor heteroarenes and C(sp^3)-H due to oxidation difficulties with the coupling partners and election-rich alkyl radicals oxidising to carbocations.[70] The electrophotochemical system comprised an undivided cell with 10 W LEDs (392 nm), a Pt cathode, RVC anode and a MeCN solvent containing Et_4NCl and HCl.[63] Proton reduction at the cathode, in combination with anodic Cl^- oxidation to Cl_2, revealed the evolution of H_2 with independence from additional chemical oxidants or metal catalysts. A yield of 92% was obtained for an initial, optimised cross-coupling of cyclohexane with 2-phenylquinoline. Similarly to the above, no product formation occurred in the absence of light, electricity or acid, and the mechanism is quite similar. Moreover, performing the reaction in air, thereby leaving oxygen in the system, still gave a good yield of 80%. Further investigations revealed that a broad scope of both C(sp^3)-H and heteroarene species could be well tolerated (listed in ref [63]).

As a final proof-of-concept a synthesis was scaled up to the gram and even decagram scale when using a continuous flow setup. This eliminated the disadvantages of batch scale-up such as poor light penetration through the solution due to the reactors low surface-area-to-volume ratio, making it hard to balance the kinetics of electro- and photochemistry.



Scheme 7: *Electrophotocatalytic C−H Functionalisation of an ethers with an isoquinoline.*

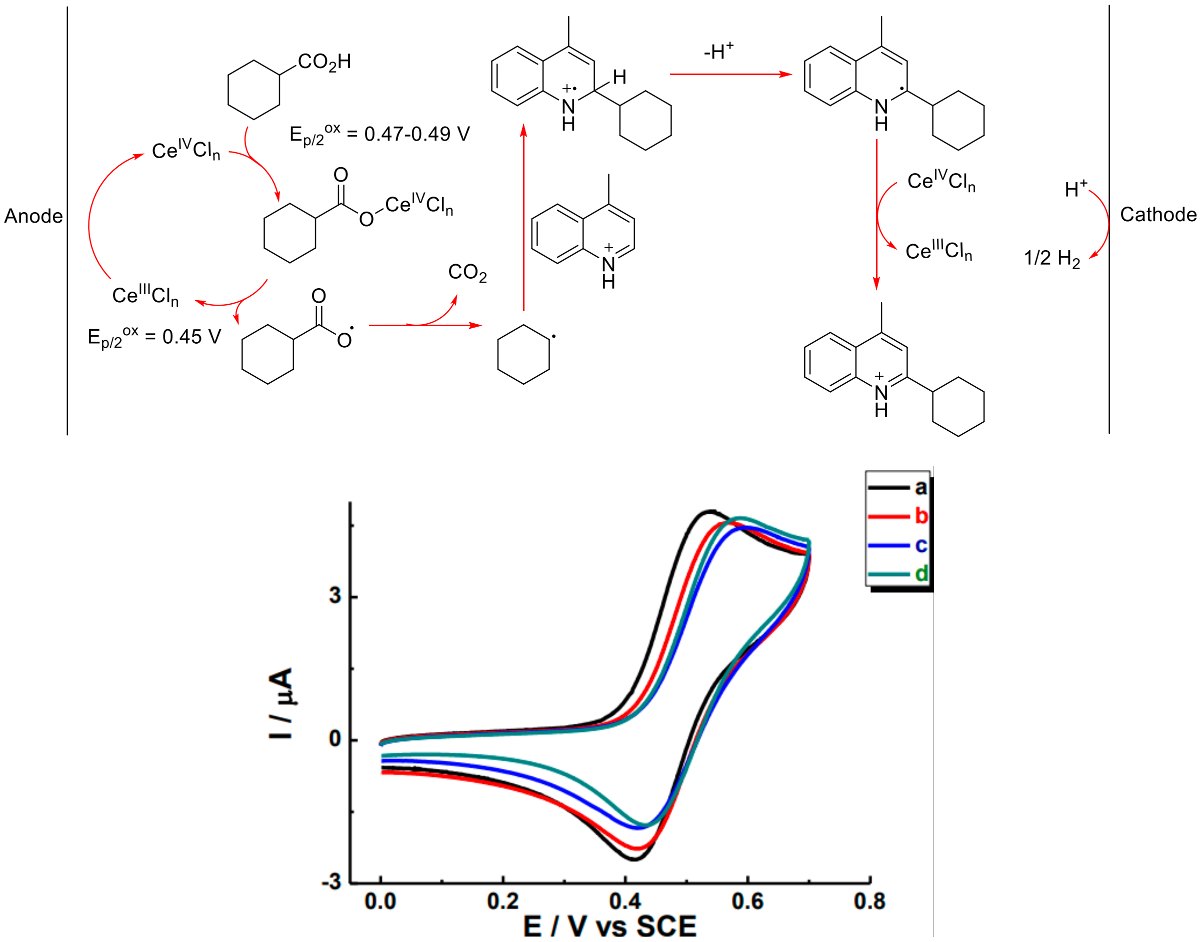
Alternatively, one of the nitrogen substituents in the photoexcited radical cation of trisaminocyclopropenium (TAC) has been determined to possess aminyl radical cation character that could impart the catalyst with a new reactivity function by enabling it to act as a HAT acceptor.[71] This premise is supported when considering the sterically hindrance nature of TAC, since HAT reactions are sensitive to steric effects,[72,73] and therefore, TAC may enforce reactions between chemically similar (but structurally different) C-H bonds regioselectively. To prove this, regioselective catalysis of important reactions concerning C-H functionalisation of ethers, in a single electrophotocatalytic system employing TAC, has been performed (**Scheme 7**).[71] In accordance with other highlighted studies combining electro- and photochemistry, additional chemical oxidants were able to be excluded. Not only do the results concur with the above hypothesis, they reveal a diverse arsenal of organic transformations initiated by this novel activation event. Ethers could then be coupled with a variety of other compounds such as isoquinolines, azols, pyrazoles, purines, alkanes and alkenes. Reaction probing began with the coupling THF and 4-bromoisoquinoline in an undivided cell with a cell voltage of 1.5 V, while light compact fluorescent light (CFL), acetic acid, and CF_3CO_2H. The optimised Minisci reaction (**Scheme 8**) afforded the product in 82% yield using 8 mol % of the catalyst and 36 h reaction time; this was completely dependent (≤5% yield) on the attendance of light, electricity and catalyst. On/off experiments demonstrated that light and electricity were paramount to the success of the reaction as well as eliminating the possible idea that the transformation proceeded by a radical chain process. A larger voltage of 3 V produced a mixture of unidentifiable products. In terms of regioselectivity of C-H bods: almost no regioselectivity was observed for substrates with only slight steric differences, primary were favoured over tertiary (only primary functionalised products detected), secondary favoured over tertiary (no reaction with tertiary), and secondary were favoured over primary. This was likely due to an intermediate secondary carbon radical having a greater stability which outweighed differences in steric environment.[71] Moreover, C-N bonds were able to be formed with similar conditions to C-C bond formations, but with CF_3CO_2H replaced with acetic acid and a 2 V cell voltage.



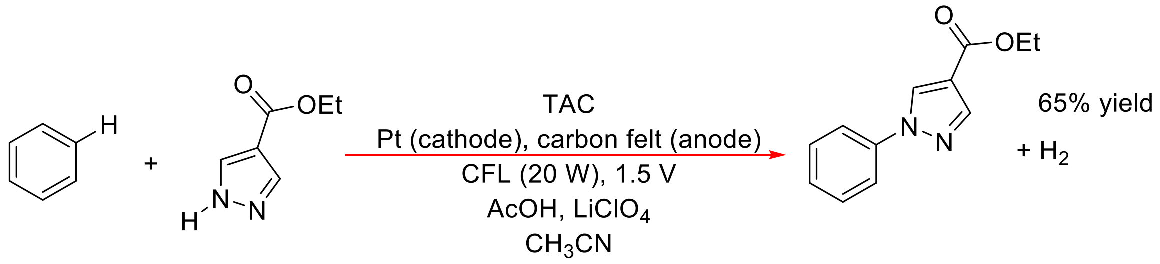
Scheme 8: *Mechanism electrophotocatalytic Minisci reaction using a TAC catalyst for the C-H functionalisation of ethers with isoquinolins.*

Electrochemically-mediated photocatalysis: C(sp^3)-H Functionalisation

Continuing on similar lines, C-C bonds may also be constructed by decarboxylative C–H functionalisation reactions which, like the above, are attractive due to desirable step- and atom-economies, as well as pervasiveness of carboxylic acids and C–H bonds. Ideally, these reactions would be conducted in the absence of chemical oxidants with the assistance of hydrogen evolution. Such was the case for the groups of Li *at al.*[67] and Ackermann *et al.*[74] where they employed photocatalysis for heteroarene C-H alkylation but only achieved a limited reaction scoped. Xu *et al.* have attempted to solve this challenge via an oxidant-free electrophotochemical approach whereby organotrifluoroborates have been replaced with carboxylic acids for decarboxylative C–H alkylation and carbamoylation of heteroarenes with carboxylic acids, oxamic acids and the release of H_2.[75] In agreement with the above, only when the strengths of electrochemistry and photocatalysis were combined did the efficiency of the reactions become acceptable. Decarboxylation was directed by the efficiency and selectivity of photocatalysis while proton reduction was promoted by electrochemistry which enabled a diverse range of carboxylic and oxamic acids to be cross-coupled with a large scope of heteroarenes. This included several drug molecules e.g. the direct alkylation of fasudil tolerated in 96% yield. Although the alkaline additive Cs_2CO_3 has been used in previous photocatalytic works,[76] the catalyst that was revealed to be efficient in the presence of the HCl acid additive was the inexpensive $CeCl_3{\bullet}7H_2O$.[75] Initial studies for the decarboxylative alkylation of lepidine with cyclohexanecarboxylic acid (**Scheme 9**) under a 10 W LED (392 nm) in a solvent system of HFIP/TFE (3:2) in an undivided cell with *n*Bu_4NCl as supporting electrolyte and Pt (cathode) and Ni or Cu (anode) gave a 91% yield. These conditions formed the basis for the larger scope testing, which was eventually confirmed to allow scale up to gram and decagram scales and for late stage drug functionalisation.



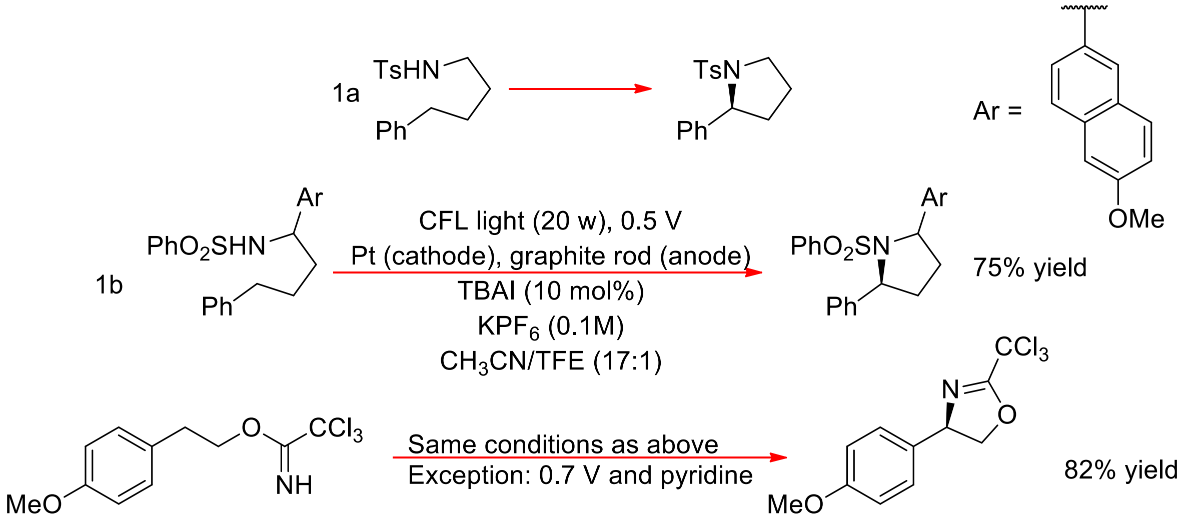
Scheme 9: *Plausible mechanism for direct electrophotochemical decarboxylative C–H alkylation of lepidine with cyclohexanecarboxylic acid. Cyclic voltammogram. a) $CeCl_3 \cdot 7H_2O$ (3.0 mM), $^nBu_4NCl$ (9.0 mM), $E_{p/2ox}$ = 0.45 V; b) $CyCO_2H$ (3.0 mM), $CeCl_3 \cdot 7H_2O$ (3.0 mM), $^nBu_4NCl$ (9.0 mM), $E_{p/2ox}$ = 0.47 V; c) $CyCO_2H$ (15.0 mM), $CeCl_3 \cdot 7H_2O$ (3.0 mM), $^nBu_4NCl$ (9.0 mM), $E_{p/2ox}$ = 0.49V; d) $CyCO_2H$ (30.0 mM), $CeCl_3 \cdot 7H_2O$ (3.0 mM), $^nBu_4NCl$ (9.0 mM), $Ep_{/2ox}$ = 0.49V. CV reproduced with permission from ref* 75, Copyright (2020) John Wiley & Sons.

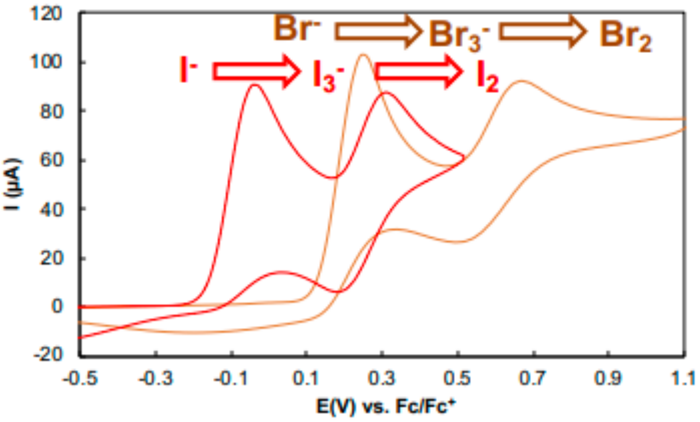


Scheme 10: *Trisaminocyclopropenium (TAC) mediated electrophotocatalytic C–H/N–H coupling of benzene and pyrazole.*

Due to the prevalence of amines and nitrogen heterocycles found in pharmaceuticals and natural products,[77–79] another similar area of interest is the direct dehydrogenative amination of sp^3 C-H bonds. An example is the Hofmann- Löffler–Freytag (HLF) reaction[80,81] which has several variations including stepwise ET-PT-ET (electron transfer, proton transfer),[82] proton-coupled electron transfer (PCET),[82] and one that is bromide-mediated, the latter two of which are followed by a key 1,5-HAT step.[83,84] A significant problem with these, however, is that electron transfer from an organic species requires a large electrode voltage that results in overoxidation or decomposition. A possible correction is use an aminoxyl or imidoxyl species because they are electron-proton transfer mediators that, in conjunction to non-mediated processes, can reduce electrode potentials by >1 V for oxidations.[31,85] Even so, this progress is not sufficient since functional group tolerance is still limited by high potentials for HAT mediators.[82,85,86]

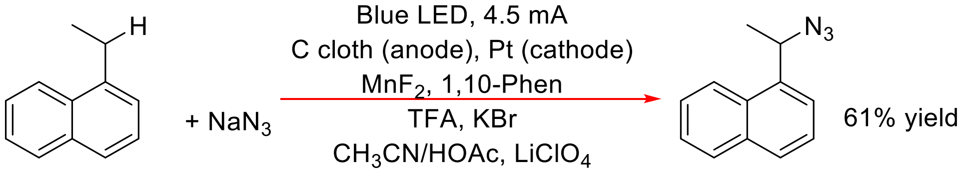
When used together, electrochemistry and photochemistry can transfer their energy to generate catalysts more potent that those obtained when they are performed separately. Lambert *et al*. reported that TAC could act as a potent selective oxidation electrophotocatalyst that could be oxidised ($E_{1/2}$ = +1.26 V vs SCE)[87–90] to an air-stable radical dication (seen by a colourless to deep red change).[29] Visible light then excites the radical dication to a species with oxidising power of 3.33 V vs SCE, a value higher than several others.[2] This oxidising power was sufficient enough to oxidise a range of challenging substrates (i.e. benzene and its halogenated derivatives) via SET so that they could undergo C-H/C-N coupling with azoles. This premise was initiated with the challenging Nicewciz-type oxidation of benzene (2.48 V vs SCE) coupling to pyrazole, which achieved a 65% yield with a cell voltage of 1.5 V and a 23 W CFL in acetonitrile with acetic acid (**Scheme 10**). The authors were enthralled to note that without light, electricity of catalyst the reaction did not occur. Moreover, the chemical oxidant oxygen was not used, nor was TEMPO which would have been typically employed as a co-catalyst during photocatalysis. A higher potential of 3 V led to a significantly decreased yield and the formation of polymeric material. Divided and undivided cells were utilised to prove that a diverse scope of arenes and nitrogen heteroaromatics could be well tolerated, with the divided cell being optimal for the coupling of benzene and halogenated benzenes, and the undivided cell optimal for alkylated benzenes. This can be viewed through the consumed current of the divided cell (2.05 F/mol – adheres to the theoretical value) and the undivided cell (3.44 F/mol).[29] The oxidising power of the diradical was also able to incorporate strongly deactivated arenes into the scope (albeit with lesser performance). The excess charge consumption was attributed to the unproductive, competing reaction of the radical dication back to TAC. In addition, this work represents only one of a few cases during photocatalysis where a doublet excited state have been employed.





Scheme 11: *Electrophotochemical iodide-mediated HLF-type sp*^{3} *C–H amination of two N-alkyl sulfonamide derivatives and an imidate nucleophile-containing substrate proceeding via iodide-mediated coupling. CVs of iodide and bromine (for comparison) using a platinum wire (counter electrode) and a glassy carbon disk working electrode, the latter potentials measured versus a Ag/AgNO*$_3$ *reference electrode (internal solution, 0.1 M Bu*$_4$*NClO*$_4$ *and 0.01 M AgNO*$_3$ *in CH*$_3$*CN). The redox potential of ferrocene/ferrocenium (Fc/Fc*$^+$*) was measured (same experimental conditions) and used to provide an internal reference.* CV reproduced with permission from ref 91, Copyright (2019) John Wiley & Sons.

On the other hand, iodide as the mediator, in combination with electrophotochemistry has been reported as a good alternative to reduce applied voltages via photolysis contributing to homolysis of intermediate N-I bonds, forming an N-centred radical that then takes part in the 1,5-HAT step to form an alkyl radical.[91] Performing sp^3 C-H/N-H amination in this way allowed Wang and Stahl to lower the necessary electrode potential,[91] due to the redox potential of I_3^- /I_2 being lower by 1-1.5 V compared to those for the PCET and ET-PT-ET, and *ca.*0.2-0.6 V lower compared to that of the most commonly used electrochemical C-O oxidation HAT reagent, phthalimido-N-oxyl (PINO) generated from N-hydroxyphthalimide (NHPI).[91] The light-induced homolysis is also advantageous as it did not promote the N-iodo intermediate to undergo β-elimination to form HI and imine. Beginning with the three aforementioned HLF reactions (ET-PT-ET, PCET, and Br-mediated mediated electrochemical HLF reaction) with two N-alkyl sulfonamide derivatives **1a** and **1b**, but **1b** with an electron-rich substituent was almost completely converted into a complex mixture of products (**Scheme 11**). Next, these reactions were probed under electrophotochemcial conditions utilising an undivided cell, 0.5 V, CFL, 10% tetrabutylammonium iodide (TBAI, mediator), KPF_6 (electrolyte), Pt (cathode), graphite rod (anode) and TFE in CH_3CN (solvent). This iodide-mediated coupling led to a 75% yield for the previously failed **1b** N-alkyl sulfonamide derivative. Moreover, these conditions were applied for the C-H amination of an imidate nucleophile-containing substrate and gave a 54% yield, which was further optimised to 82% with 0.7 V and pyridine. No product was observed in the absence of light. It's worth noting that the estimated sulfonamide and imidate N-H bond dissociation energies are > 100 kcal/mol compared to NHPI O-H (*ca.*88 kcal/mol), indicating that the created N-centred radicals are stronger H-acceptors than PINO.[92,93] For completion, a number of substrates with electron-poor and electron-rich (typically participate in unwanted side reactions at high potentials) moieties were shown to be compatible with this low-potential iodide-mediated approach.[91] The CVs shown is **Scheme 11** illustrate the low redox window needed to regenerate the I_2 at the anode (0.3–0.7 V vs. Fc/Fc$^+$). Potent oxidants that enabled the dehydrogenative coupling were able to be formed at the lower potentials and thus revealed a good functional group tolerance.



Scheme 12: *Manganese-catalysed oxidative photoelectrochemical azidation of 1-ethylnaphthalene with* NaN_3.

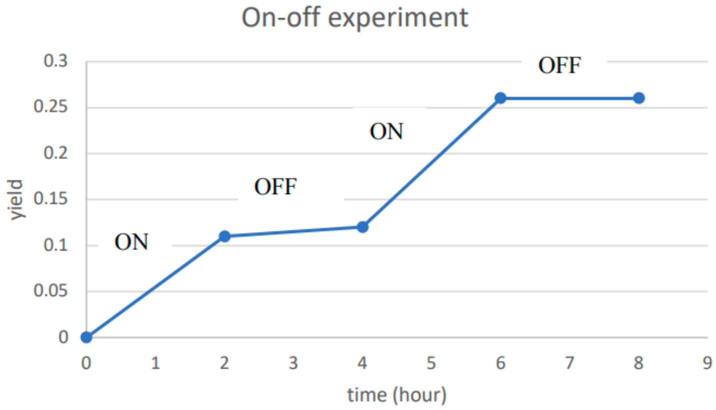


Figure 1. *On-Off measurements for Mn-catalysed PEC azidation of 1-ethylnaphthalene with* NaN_3*. Reproduced from ref 94, Copyright (2020) American Chemical Society.*

Azide groups are another attractive motif due to their ability to be turned into amines, amides, triazoles, aziridines and imines[95,96] and thus selectively incorporating them into C(sp^3)-H bonds in a sustainable way is of great importance to chemical biology, organic and pharmaceutical synthesis.[97–99] This has been achieved using a PEC cell with NaN_3 via manganese-catalysed oxidative azidations of a range of C(sp^3)-H bonds and late stage functionalisation of drug-like molecules.[94] Unlike typical electrochemical amination methods this approach does not need stoichiometric amounts of chemical oxidants (i.e. iodine (III) or NFSI) nor is its applications confined to C(sp^3)-H bonds adjacent to special benzyl C(sp^3)-H bonds or N or O atoms. Initial optimisation gave a 61% yield for the reaction between 1-ethylnaphthalene and NaN_3 (**Scheme 12**) in a system consisting of blue LED light irradiation, a constant current of 4.5 mA, carbon cloth (anode), Pt (cathode), MnF_2 (manganese catalyst), 1, 10-Phen (ligand), p-fluronone (photocatalyst), CH_3CN (9.5 mL)/HOAc (0.5 mL) (solvent), $LiClO_4$ (electrolyte), TFA (acid) and KBr (additive). In the absence of light some product formation was still observed at a low yield of 28% (**Figure 1**) and no product formation occurred without electricity. This method was then found to be well tolerant for a range of aliphatic, as well as secondary and tertiary benzylic C(sp^3)-H bonds and bioactive materials. After these were produced in moderate to excellent yields, the potential applications of the system was further demonstrated by scaling up to the gram-scale.

Interfacial photoelectrocatalysis

A popular catalyst for PEC oxidations is $BiVO_4$, which has found utility in forming value-added chemicals. For example nanoporous $BiVO_4$ nanoarrays in a H-type cell drove the PEC oxidation of glycerol (main by-product from biodiesel production) to 1,2-dihydroxyacetone (DHA) (widely used in the cosmetic, pharmaceutical, fine chemical, and food industries).[100] Glycerol oxidation was achieved with a 51% selectivity towards DHA with a photocurrent density, in acidic medium (pH = 2) under AM 1.5G light, of 3.7 $mAcm^{-2}$ at a potential of 1.2 V vs. RHE. This corresponded to 200 mmol per m^2 h^{-1} at an overall Faradaic efficiency of *ca.*30%. A by-product of this was glyceric acid (another valuable derivative) which may increase the selectivity of value-added compounds to *ca*.60%. Formic acid and glycolic acid (trace) were also detected, along with CO_2, CO, H_2O_2 and O_2 from further oxidation of liquid products and water. Moreover, the photocurrent and selectivity towards desired organics was found to decrease with increased pH (**Figure 2a** and **b**), with almost complete oxidation of glycerol with *ca*.99% Faradaic efficiency at pH = 12. High selectivity, efficiency and stability against photocorrosion was also observed at pH =2 under ambient temperature and pressure. It was noted that in the absence of light under electrochemical conditions glycerol oxidation to DHA did occur, but at a very low efficiency. The PEC mechanism for reaction shown in **Figure 2c** and **d** which was drawn from the conclusion that when 10% $H_2{}^{18}O$ was used to label the electrolyte, DHA in the form of $C_3H_6O_2{}^{18}ONa$ was detected. The oxygen in DHA therefore comes from the water in the electrolyte which probably oxidised the C(sp^3)- β-hydroxy to C(sp^2)-carbonyl group. Overall, it is speculated that glycerol is adsorbed onto $BiVO_4$ and oxidised by radicals formed by photogenerated holes, reacts with water followed by dehydreation to form DHA; this pathway is similar to the formation of glyceric acid and formic acid via further oxidation of glyceraldehyde.

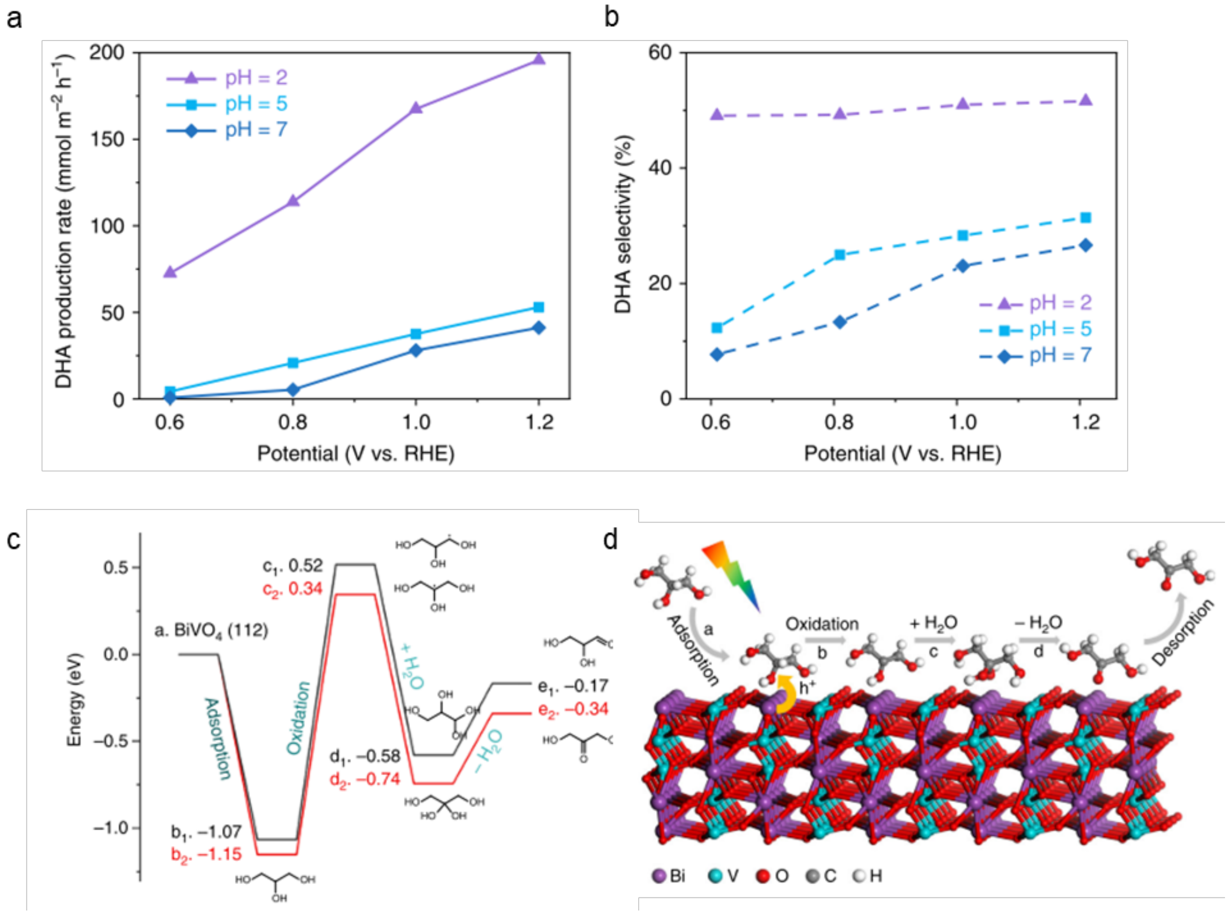
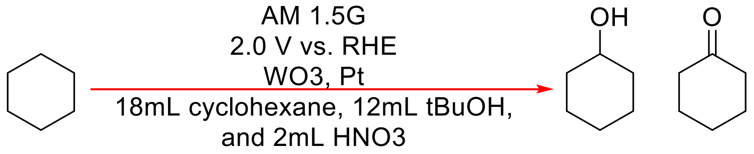


Figure 2. **a**. *Production rate and* **b**. *selectivity of DHA production.* ***c.*** *Energy profile of glycerol oxidation on $BiVO_4$. Black and red correspond to reactions taking place at the terminal and middle carbon, respectively.* ***d***. *Schematic illustration showing PEC reaction mechanism of the oxidation of glycerol to DHA. Reproduced from ref* 100, Copyright (2019) Springer Nature.

In another PEC oxidation $BiVO_4$ was found to resist photocorrioisn significantly more in MeCN rather than in water. There is a counter argument due increased resistance of the organic media (~20 mV), however, this was deemed admissible for the transformations. These involved PEC oxidations of benzyl alcohol, cyclohexene and tetralin (usually necessitates precious metals and toxic chemicals) with a $BiVO_4$ photoanode, 100 W Xe lamp fitted with an

AM1.5G filter and N-Hydroxysuccinimide (NHS) to mediate hole-transfer, and for the latter two, tert- butyl hydroperoxide (^{t}BuOOH) was required as an external oxygen source. These oxidations could, however, be performed under electrochemical conditions only. Nevertheless, it is noteworthy to mention that the added benefit of the PEC system arises from the energy saving ability of the method, requiring 1.0 V less potential than the electrochemical system, translating to 60% energy savings.



Scheme 13: PEC C-H activation of cyclohexane to KA oil over a WO_3 photoanode.

Similar energy saving C-H oxidations have been reported by Tateno and Sayama, such as the C-H activation of cyclohexane (normally difficult due to a high dissociation energy of 439 kJmol^{-1}) to form a mixture of cyclohexanol and cyclohexanone (**Scheme 13**), aka KA oil (ketone-alcohol oil).[101] Here, another heterogeneous catalyst used in photoelectrochemistry to complete an important (and in this case difficult) reaction is porous WO_3, due to its direct band gap of *ca*. 2.58 eV. C-H cleavage induced by an SET process at the porous photoanode converts cyclohexane into a cyclohexyl radical, which is activated by oxygen to give a cyclohexylperoxyl radical which is converted into KA oil. With the combination of photoirradiation and an applied bias, the applied bias of above 2.0 V for the linear sweep voltammograms of a cyclohexane-based electrolyte solution could be reduced by the light energy at a current density of 0.5 mAcm^{-2}. Without light, no product was formed, without electricity some product was formed, but at a greatly reduced rate (<8 mmolh^{-1}); the influences of light and electricity can be viewed in **Figure 3**. Moreover, a Faradaic efficiency of 76% and partial oxidation selectivity of 99% were obtained (without by-product formation i.e. bicyclohexyls), along with high incident photon-to-current efficiencies (IPCE) of 57% and 24%, at 365 and 420 nm, respectively.

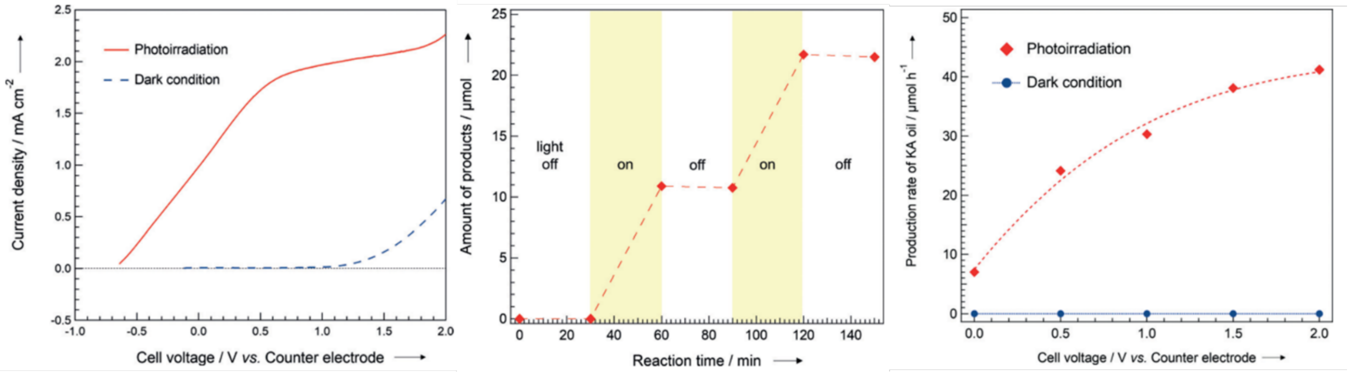


Figure 3. *Linear sweep voltammograms with AM 1.5G light and dark under air and scan rate of 10 mV s^{-1}. The effect of light irradiation and applied bias dependence of on PEC oxidation of cyclohexane to KA oil in constant potential mode at a cell voltage of 0.5 V or 0-2.0 V vs. counter electrode. WO_3 (working electrode), Pt (counter electrode), 10 ml cyclohexane: 12 ml tBuOH: 2 ml HNO_3 (electrolyte). Reproduced with permission from ref* 101, Copyright (2018) John Wiley & Sons.

This work can be furthered to include a $BiVO_4/WO_3$ photoanode for the PEC dimethoxylation of furan, which was mediated by bromide ions to achieve an 84% yield and Faradaic efficiency of up to 99% at low applied potential (+0.1 V vs. SHE).[102] Under the same conditions in the absence of light, the oxidation current and methoxylated product were hardly observed. In the dark at +1.2 V vs. SHE, an oxidation an current could then be observed, however, AM 1.5G could shift this nearly to 0 V vs. SHE, thereby demonstrating then energy saving capabilities of the PEC method. The authors continued to work with the $BiVO_4/WO_3$ photoanode and performed the first PEC organic transformation with PINO, formed by the oxidation of NHPI.[103] PINO then serves as a catalyst for the abstraction of the C-H hydrogen from organic bond scission. Concurrently, the oxidation potential for PINO is greater than that for other electron transfer mediators such as TEMPO and N-hydroxysuccinimide (NHSI), and can therefore preform difficult chemical reactions including oxidation of relatively inert hydrocarbons. As such, the selective oxidation of cyclohexane to 2-cyclohexene-1-one was conducted, and occurred with a Faradaic efficiency >99% with a low applied bias. Interestingly, the oxidation potential was much lower, decreasing from +2.4 V to +0.5 V vs. $Ag/AgNO_3$, with the use of light compared to conventional electrochemical reactions. Moreover, this oxidation potential was slightly increased when cyclohexene was introduced, attributed to the concentration of NHPI increasing from reaction of PINO with cyclohexene on the surface of the catalyst. This method also displayed future promise by realising reaction with several *N*-oxyl radicals and cycloalkenes.

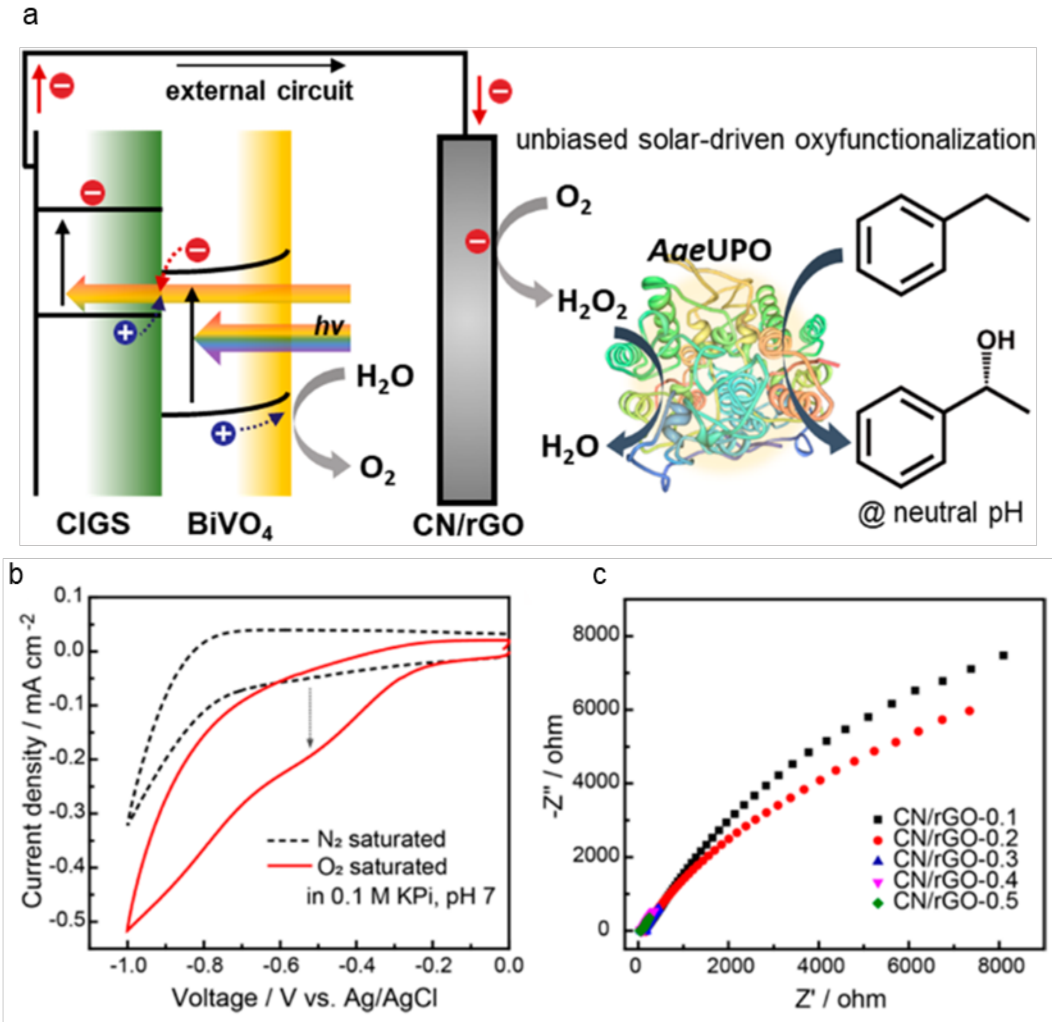
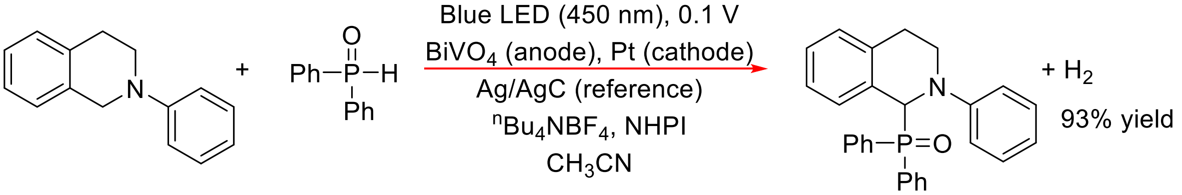


Figure 4: **a.** *Unbiased PEC cell using a solar cell,* $BiVO_4$ *photoanode, carbon nitride/reduced graphene oxide cathode, water and light to promote oxyfunctionalisations of C-H bonds.* ***b.*** *Corresponding CV of 0.2wt% CN/rGO-0.2 electrode measured in* O_2*- and* N_2*-saturated 0.1 M*

KPi buffer (pH 7.0) at a scan rate of 50 mV s−1 and ***c.*** *Nyquist curves of 2 cm*^{2} *(area) CN/rGO-n electrodes measured in a 0.1 M KPi buffer (pH 7.0) at an applied bias of −0.3 V (vs Ag/AgCl). Reproduced from ref* 104*, Copyright (2019) American Chemical Society.*

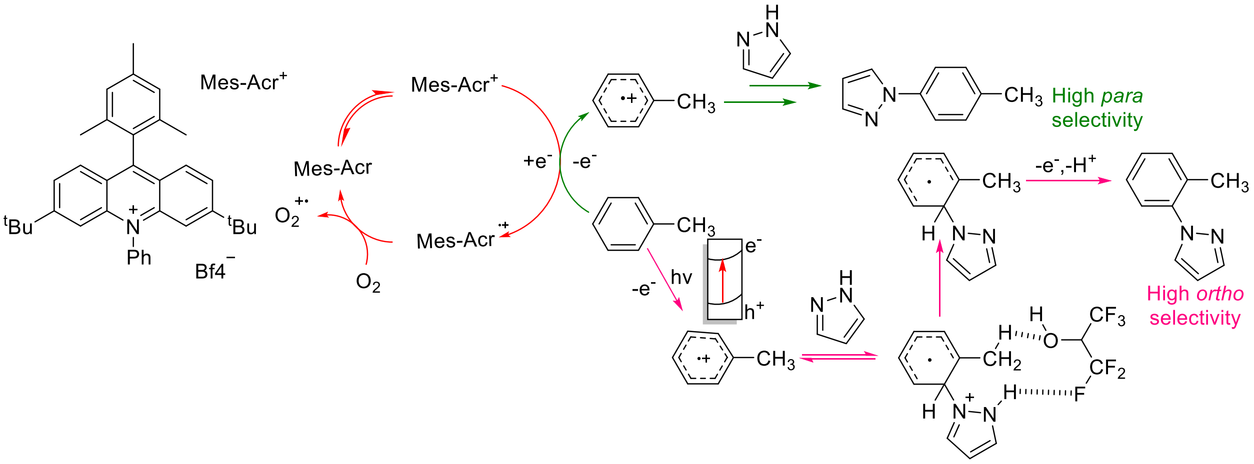
In 2019 Park *et al.* reported a peroxygenases catalysed selective oxyfunctionalisation of C-H bonds via the generation of in situ H_2O_2 through the use of a tandem PEC with a FeOOH/n-$BiVO_4$ photoanode and a graphitic carbon nitride/reduced graphene oxide (CN/rGO) cathode (**Figure 4a**).[104] Excitingly, an external bias was not required because the system employed a Cu(In,Ga)Se_2 (CIGS) solar cell with a band gap of 1.1 eV, thus maximising the amount of solar energy to be converted. Water oxidation at the photoanode and concurrent H_2O_2 generation via O_2 reduction at the cathode, using only water and solar energy in the absence of an applied potential, was tested for the selective hydroxylation of ethylbenzene to (R)-1-phenylethanol, catalysed by the biocatalyst peroxygenase from Agrocybe aegerita (AaeUPO). The thin-film CIGS solar cell could then provide sufficient photovoltage to fulfil the thermodynamic requirements for a spontaneous reaction. The FeOOH co-catalyst and $BiVO_4$ were chosen as a suitable band gap catalyst (~2.5 eV for the nanostructure) with good photochemical stability in aqueous environments. A 0.4 wt% loading of GO was found to optimal; CV suggested cathodic O_2 reduction due to increased cathodic currents in oxygen (compared to N_2)-saturated solutions (**Figure 4b**), the peak current density of CN/rGO increased from -0.2 to -0.53 from 0.2-0.5 wt% (with negligible difference between 0.4 and 0.5 wt%), double-layer capacitance increased by a factor of 29 and the EIS spectra suggested a decrease in charge transfer resistance from 0.1-to 0.5 wt% (**Figure 4c**), respectively, indicating that rGO facilitates efficient charge transfer to solution. Increased loading of GO will cause blocking of active sites. The CN/rGO cathode is therefore, praised for significantly increasing the electrical conductivity and the specific surface areas of the cathode hybrid, enabling high O_2 reduction activity. This unbiased system was observed to generate H_2O_2 and (R)-1- phenylethanol at a rate of 2.8 mM h^{-1} cm^{-2} and 0.89 mM h^{-1}, respectively, the latter being 4.2 times faster than when in the absence of the solar cell. No (R)-1- phenylethanol was produced in the absence of light, AeaUPO or oxygen. Hydroxylation occurred with high enantioselectivity (ee > 99%), a turnover frequency (TOF) of 12.9 s^{-1} and total turnover number (TTN) of 43,300. This TOF is noted to be much larger than other H_2O_2-generating PEC platforms such as Flavin-hybridised carbon nanotube cathode (1 s^{-1}).[105] By physically separating the anodic and cathodic reactions, oxidation of H_2O_2 at the anode and enzyme degradation at the cathode were avoided. Thus, this approach provides an ecologically and economically promising strategy to yield C-H oxyfunctionalisations using light and water whilst avoiding the accumulation of by-products.[104]



Scheme 14: *Photoelectrochemical P-H/C-H dehydrogenation cross-coupling of N-phenyl tetrahydroisoquinoline with diphenyl-phosphine oxide.*

The photoanode $BiVO_4$ has also been incorporated into a PEC system for P-H/C-H dehydrogenation cross-coupling with the evolution of hydrogen. In doing so C-P bonds in organophosphates can be synthesised in a cleaner, more energy efficient manner without metal catalysts, chemical oxidants or directing groups (as would be the case for electrochemistry). C-P bonds are of particular interest due to their ubiquitous presence in materials chemistry, agrochemistry and biochemistry. In an undivided cell using $BiVO_4$ as the photoanode and NHPI as the mediator, Wu *et al.* were able to afford a 93% yield from the cross coupling of N-phenyl tetrahydroisoquinoline with diphenyl-phosphine oxide (**Scheme 14**).[106] This was furthered to include a range of organophosphates in good to excellent yields, displaying a board substrate scope and good functional group tolerance. What is interesting here is that, compared to a purely electrochemical system, nearly 90% of the external input bias is saved when light was involved. A similar yield was obtained (88%) with a glassy carbon anode, however, the PEC cell took the centre stage by requiring only 0.1 V compared to 1.5 V vs. Ag.AgCl, thereby demonstrating its energy saving ability.

PEC C-H amination reactions have also been recently carried out by Hu *et al.* A novel set of high *ortho* selective non-directed aminaitions of arenes and pyrazols using the inexpensive, Earth abundant hematite as the photoelectrode were realised.[107] Haematites 2.1 eV bandgap suitable for light absorption, in combination with its high oxidising potential (2.3 V vs. SCE), which is similar to organic photoredox catalysts, i.e. acridinium was promising for the C–H/N–H coupling of anisole with pyrazole. In an undivided cell with a Pt cathode, $LiClO_4$ as the electrolyte, HFIP/MeOH (4:1) as the co-solvent, a blue LED (0.7 V) as the light source and a photocurrent of 2~3 mA cm^{-2}, an *ortho/ para* ratio of 6:1 was obtained along with a 77% yield. Notably, there were no side products detected after the reaction, only unreacted species which is in opposition to electrochemistry where trimerisation due to overoxidation is observed. This method was expanded to include a wide array of C-N containing molecules and could be used for the late stage functionalisation of several pharmaceutical compounds in up to 89% yield. Without the light component, higher electrochemical potentials were required, leading to side product formation and poorer yields. Both *ortho* and *para* configurations are expected, however, the domination of the former is an unusual phenomena since steric hindrance typically favours the *para* in electron-rich C-H aminations. The reason has been attributed to the *ortho* pyrazole intermediate species being stabilised by hydrogen bonding to the hexafluoroisopropanol co-solvent. The mechanistic rational for this is displayed in **Scheme 15**, within which both the typical photoredox catalysed *para* dominating route (green) and the new PEC, solvent stabilised *ortho* route (pink) are shown.



Scheme 15: *Mechanistic rational for the PEC C-H amination revealing the conventionally para dominating pathway (green) and ortho dominating pathway (pink). The ortho intermediate can be seen hydrogen bonding (dashed lines) to the hexafluoroisopropanol co-solvent, thereby stabilising the intermediate.*

Ref	Scheme	Reaction without light	Reaction without electricity	Yield	Efficiency	Selectivity	Energy input	Catalyst
52	2	No	No	85%	36%	93%	Blue LED 4.0 mA	Mes-Acr$^+$
56	5	Suppression (4% yield)	Suppression (14% yield)	87%	High	High*	Blue LED 450 nm 2 mA	Mes-Acr$^+$
63	6	No	No	92%	High	High*	392 nm 2 mA	None
71	7	No (<5%)	No (<5%)	82%	Na	High*	CFL 1.5V	TAC
74	9	No	No (<5%)	91%	High	High*	392 nm 2 mA	$CeCl_3$●$7H_2O$
29	10	No	No 3.0 V very low yield; mostly polymer	65%	High	High*	CFL 1.5V	TAC
91	11	No	-	75%	Good	High*	CFL 0.5 V	I_3^-/I_2
94	12	Low 28%	-	61%	Good	High*	Blue LED 4.5 mA	MnF_2 1,10-Phen
100	Figure 2	No	No	200 mmol m^{2}h^{-1}	30-99%	50-60%	AM 1.5G 1.2 V	$BiVO_4$
101	13	No	Little (<8 mmolh^{-1})	41.2 mmol h^{-1}	76%	99%	AM 1.5G 2.0 V vs. RHE	WO_3
104	Figure 4	No	- CIGS solar cell built in	0.89 mM h^{-1}	High	>99% ee	Visible light CIGS solar cell	FeOOH/ n-$BiVO_4$
106	14	No	No	93%	High	High*	Blue LED 450 nm 0.1 V	$BiVO_4$
107	15	No	No	77%	35%	High*	Blue LED 0.73 V	Hematite

Table 1. *Performance data for the above listed schemes and figures. * By-products: unreacted substrate +* H_2.

From **Table 1** it is clear that the method of combining electrochemistry with photocatalysis is a powerful one that can achieve good yields, efficient and selectivities of reactions that may not be possible by each lone strategy. A range of catalysts and PEC systems are beginning to be employed whilst keeping the door open for more discoveries. A large redox window have been evidenced,[1] difficult C-H activations have been realised and energy saving attributed have now made themselves apparent. With more attention to this upcoming synthetic approach the goal of practical scale transformations is looking like a real possibility.

Conclusion

We have highlighted recent examples of organic C-H activations driven by the creative adoption of electrochemistry and photoredox catalysis in the same system. The combination shows that photoelectrochemical cells, along with their photovoltaic effect, water splitting and solar fuel production, can now include organic synthesis to their repertoire. Applicable to homogeneous and heterogeneous catalytic systems, this emerging yet promising approach is receiving growing attraction due to its nature of using the advantages of one method to overcome the shortcomings of the other. This has enabled reactions to occur in the absence of chemical oxidants/reductants, incorporation of modified photoelectrodes, the generation of more potent homogeneous catalysts compared to electrochemistry or photochemistry, and specific requirements of specific reactions to be met. As a consequence, synthetic organic processes that are not possible during each individual approach are achievable with this combined strategy. Furthermore, in the future, integration with continuous flow chemistry will enable safe and efficient scale-up and may even improve reaction times, kinetics, yields and transmission of light/electrons through the solution. Overall, PEC cells will become of great interest to a number of interesting areas including synthetic, materials and energy-related chemistry.

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Conflicts of Interest

The authors declare no conflict of interest.

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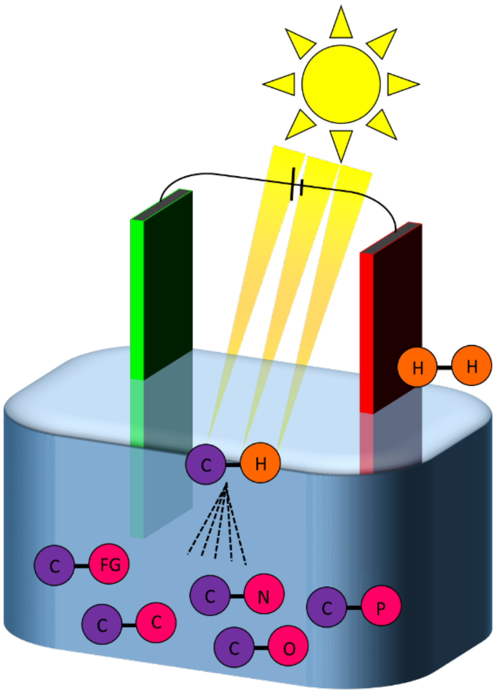

Herein, the recent developments of C-H activation / functionalisation via electrophotocatalysis and photoelectrochemistry have been described. Through this complementary chemistry difficult C-H organic transformations are possible with high atom- and step-economies.

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