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Renewable resources for sustainable metallaelectro-catalysed C–H activation

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The necessity for more sustainable industrial chemical processes has internationally been agreed upon. During the last decade, the scientific community has responded to this urgent need by developing novel sustainable methodologies targeted at molecular transformations that not only produce reduced amounts of byproducts, but also by the use of cleaner and renewable energy sources. A prime example is the electrochemical functionalization of organic molecules, by which toxic and costly chemicals can be replaced by renewable electricity. Unrivalled levels of resource economy can thereby be achieved *via* the merger of metal-catalyzed C–H activation with electrosynthesis. This perspective aims at highlighting the most relevant advances in metallaelectro-catalysed C–H activations, with a particular focus on the use of green solvents and sustainable wind power and solar energy until June 2020.

1 Introduction

During the last decades, research in academia and agrochemical and pharmaceutical industries has increasingly focused on the development of resource-economical,[1] synthetic methodologies, reducing the amount of byproducts while enabling more efficient molecular transformations of decreased environmental impact.[2–5] In line with the UN-sustainability goals,[6]

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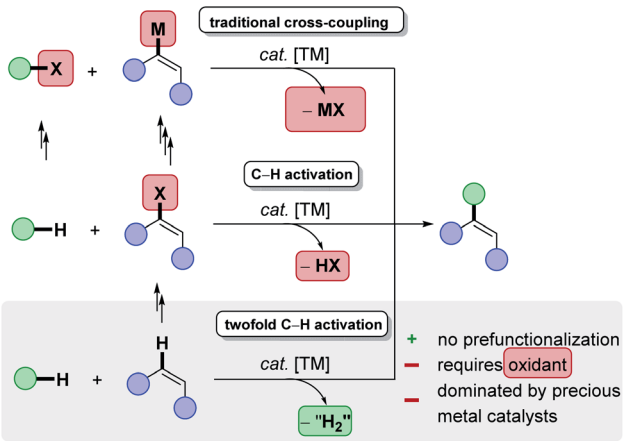
catalysis[7] represents an indispensable tool for process chemists by providing access to unique bond-forming transformations not only with a high atom economy.[8] Indeed, the required reaction temperature and the amount of otherwise needed stoichiometric reagents, can be minimized.[9,10] As a result, scientists have focused their efforts towards the avoidance of waste product formation and more efficient resource utilization in molecular sciences.[11] Therefore, ambitious guidelines have been set in place to define these challenges, such as the twelve-principles of green chemistry,[12,13] or circular chemistry.[14]

In this context, C–H activation constitutes one of the most promising strategies for directly forming new chemical bonds and consequently synthesizing novel organic compounds in a sustainable and step efficient fashion,[15–22] in line with the principles of green chemistry.[23] For example, in stark contrast to classical metal-catalysed cross-coupling reactions,[24] the direct conversion of otherwise inert C–H bonds circumvents the laborious prefunctionalisation of synthetic building blocks and avoids by-product generation (Scheme 1).[25]



Scheme 1 Twofold C–H activation as step and resource economical alternative to cross-coupling reactions.

Although classical C–H activation avoids the prefunctionalisation of one coupling partner, additional steps are required to synthesise often required organic electrophiles, such as organic halides.[26] In theory, the most atom- and step-economic approach would be the cross-dehydrogenative coupling (CDC),[27] or twofold C–H activation, since formally molecular hydrogen would be generated as the sole byproduct. Despite tremendous successes in the field of twofold C–H activations, the latter predominantly suffers from harsh reaction conditions, such as high reaction temperatures, toxic, halogenated solvents, precious transition metal catalyst, stoichiometric amounts of often ecologically damaging and cost-intensive oxidants, thus compromising the overall sustainability of twofold C–H activations. A remarkable progress has been made by the replacement of the commonly used fossil-based and often toxic solvents, with biomass-derived solvents, thereby considerably reducing the ecological footprint.[28,29] Furthermore, recent accomplishments, especially with Earth-abundant base metal catalysts has indicated the great potential towards an overall resource-economic functionalisation of ubiquitous C–H bonds (Scheme 2).[30] Despite of these notable advances, one challenge – the requirement of chemical oxidants – remained largely unsolved until recently.[31,32]

Meanwhile, organic electrochemistry has experienced a renaissance during the recent years and evolved from a underappreciated technique into an attractive concept in academia and industries.[33–40] Through the use of electrochemistry it is possible to direct sustainable power, harvested from sunlight, wind, biomass or hydropower, towards the desired

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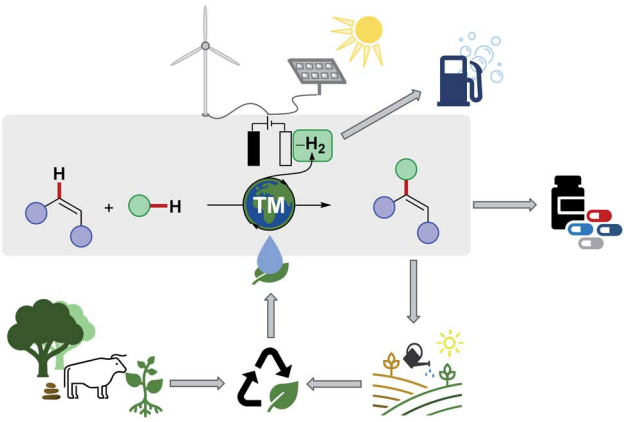
Lutz Ackermann studied chemistry at the Christian-Albrechts-University Kiel and obtained his PhD in 2001 with Alois Fürstner at the MPI für Kohlenforschung in Mülheim/Ruhr. He was a postdoctoral fellow with Robert G. Bergman (UC Berkeley) before initiating his independent research in 2003 at the Ludwig-Maximilians University München, supported within the Emmy Noether Program of the DFG. In 2007, he became full professor at the Georg-August-University Göttingen, where he served as the Dean of Research and Dean of Chemistry as well as the director of the Wöhler Research Institute for Sustainable Chemistry. The development of novel concepts for homogeneous catalysis and their applications to late-stage peptide diversification by bond activation, and electrocatalysis are among his main current research interests.



Scheme 2 Electrochemical C–H activation in biomass-derived solvents, powered by renewable energy sources, catalysed by Earth-abundant catalyst.

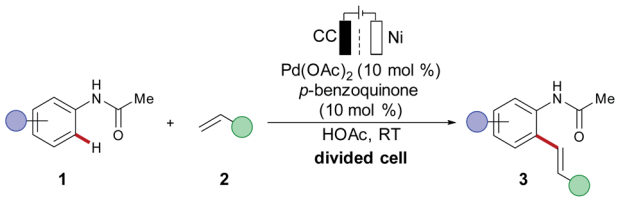
chemical transformation drastically improving the overall environmental footprint of the required chemical transformation.[41,42] Consequently, scientists enabled to facilitate catalytic reactions through the use of electricity for the assembly of chemical compounds or renewable fuels,[43] based on greenhouse gases such as carbon dioxide (CO_2).[44–46] Furthermore, more complex synthetic tasks can be tackled with the aid of electrosynthesis,[47] and recent successes in synthetic organic electrochemistry, have emerged as a strong testament to the versatility of electrochemically promoted organic transformations (Scheme 2).[38,48–52]

The advantages of the merger of C–H activation with electrochemistry include the replacement of chemical redox reagents and the discovery of new synthetic methodologies such as twofold C–H activations amongst others.[53–57] The only by-product formed – molecular hydrogen gas – can further be used as a sustainable energy source[58] or utilized in various chemical reduction reactions, ideally by paired electrolysis.[59]

Within this perspective, key examples highlight the recent developments in metallaelectro-catalysed C–H activation, with a major focus on Earth-abundant base metal catalysis, biomass-derived reaction media, and the combination of sustainable power sources for overall resource economic chemical bond transformations until June 2020.[1,31,32,51]

2. Merger of electrochemistry and C–H activation

Oxidative transformations commonly employ chemical oxidants and thus generate stoichiometric amounts of by-products, which reduces the atom- and resource-economy of the process at hand.[1] As a more sustainable alternative, anodic oxidation can be used with molecular hydrogen as the sole by-product formed through cathodic reduction. Direct anodic oxidation for metal-catalysed redox reactions was early realized in 1987 by Tsuji, for a modification of the Wacker reaction, using anodic oxidation with benzoquinone as a redox mediator.[60] In 2007, Amatore and Jutand reported an



Scheme 3 Early work on palladaelectro-catalysed C–H activation.

electrochemically-modified Fujiwara–Moritani alkenylation of acetanilides **1** with alkene **2** (Scheme 3).[61] A divided cell setup was used to prevent the deposition of palladium black on the cathode. A catalytic amount of *p*-benzoquinone served as a shuttle for the electrons between the anode and the metal catalyst to reoxidise the palladium(0) species to the catalytically relevant palladium(II) complex. Indeed, this otherwise powerful approach has an adverse impact on the overall atom economy. Instead, the direct anodic oxidation of the metal catalyst on the electrode surface to achieve a proton-coupled electron transfer (PCET) in C–H activation is more desirable, yet significantly more challenging (*vide infra*).

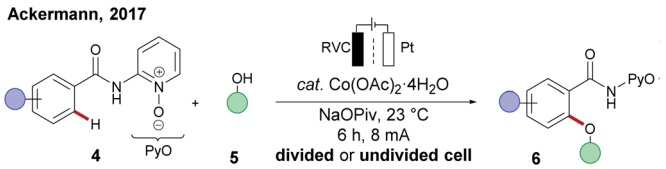
In this context, Mei disclosed a palladium-catalysed C–H acetoxylation, for which the catalyst was directly oxidized at the electrode surface.[62] However, palladium-catalysed electrochemical transformations including halogenations[63] and alkylations[64] commonly required a more complex divided cell set up. In order to circumvent the problems accompanied by a divided cell setup, the Ackermann group introduces an unprecedented, user-friendly undivided cell arrangement for performing rhoda-[65] and ruthena-electro-catalysed[66] C–H/C–H activation and C–H/O–H annulation reactions respectively. Subsequently, other 4d and 5d metals including ruthenium,[66–70] rhodium[71–75] and iridium[76–78] were explored for electrochemical C–H activations.

Electrochemical 3d base metal-catalysed oxidative C–H activation

The preference for 3d base metals over precious 4d and 5d metals in organic catalysis is due to several reasons including (a) low costs (b) environmentally-benign nature (c) Earth abundant (d) generally less toxic than 4d and 5d metals, and arguably intellectually most notably (e) mechanistically unique pathways in molecular transformations. In recent years, 3d metals[30] have experienced tremendous applications to metal-catalysed C–H activations, featuring the power of copper,[79] iron,[80,81] manganese,[82,83] cobalt[84–86] and nickel.[87,88] Despite significant advances in this field, the use of renewable electricity to power oxidative and redox-neutral C–H activations remained elusive until 2017.

Cobalt-catalysed electrooxidative C–H activation

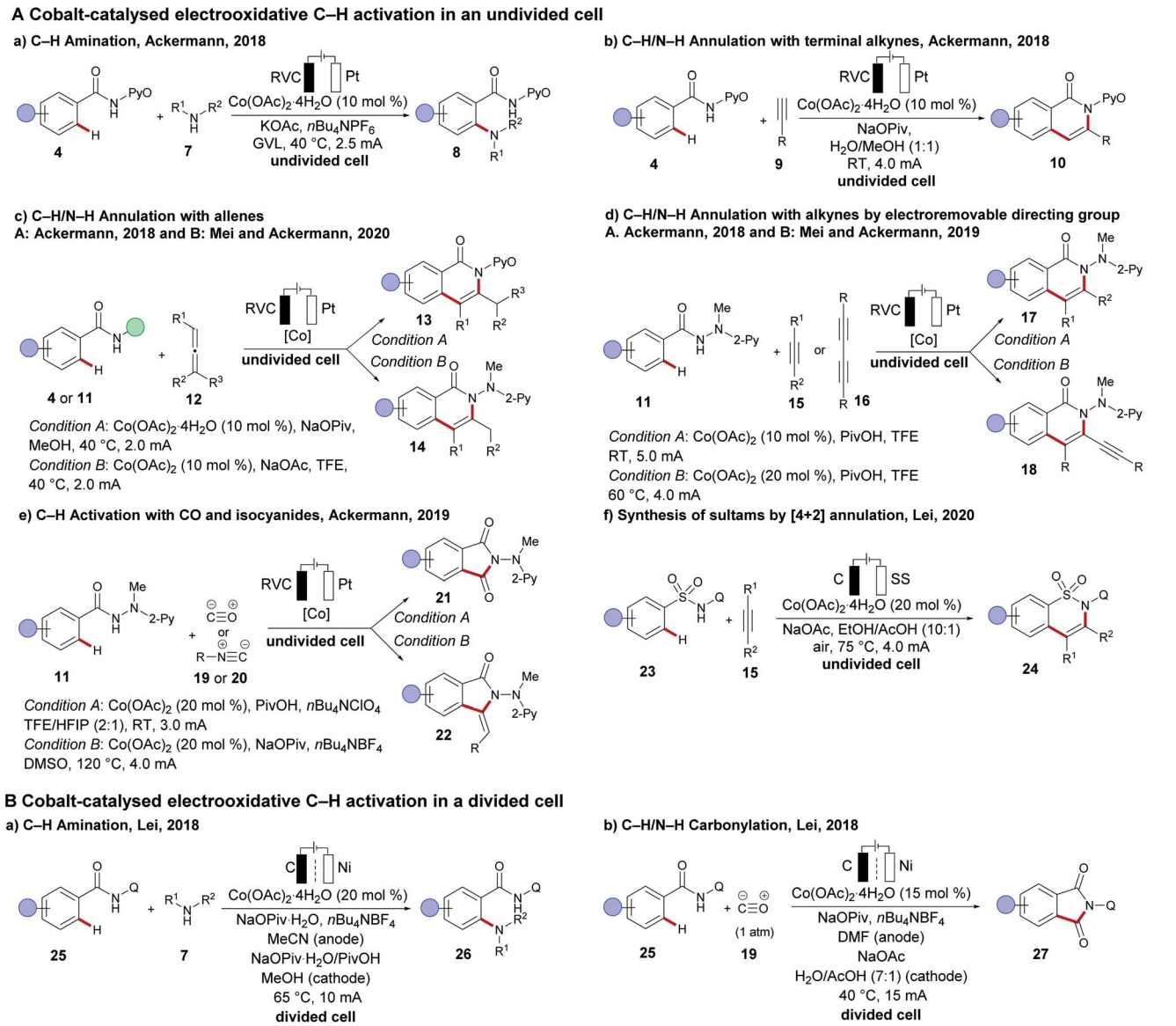
In 2017, the Ackermann group disclosed the merger of electrochemistry with 3d metal-catalysed C–H activation.[89,90] The strategy provided access to the desired C–H oxygenated products **6** at ambient temperature from a variety of amides **4** using



Scheme 4 Merger of electrochemistry with cobalt-catalysed C–H oxygenation.

primary alcohols **5** with the assistance of a pyridine *N*-oxide amide (Scheme 4). Inspired by this finding, cobalt-catalysed oxidative C–H transformations were heavily explored with the aid of electricity as a green oxidant. Herein, operationally simple undivided cells were predominantly used by the Ackermann group for numerous C–H transformations, such as C–H amination,[91] C–H/N–H annulations with allenes,[92,93] alkynes[94,95] and bis-alkynes[96] and C–H annulation reactions with carbon monoxide **19** or isocyanides **20**[97] (Scheme 5A(a–e)). Although the initial finding on C–H oxygenation was assisted by pyridine *N*-oxides **4**, later an electro-removable hydrazide **11** proved viable likewise.[95] In contrast, the Lei group employed thereafter a rather complex divided cell setup to achieve oxidative cobalt catalysis under electrochemical conditions namely for C–H aminations, alkyne annulations[98] and a C–H/N–H carbonylation of quinoline amides **25** (Scheme 5B).[99,100] Very recently the same group have developed a [4 + 2] annulation method for the synthesis of sultams **24** using the undivided cell setup (Scheme 5A(f)).[101]

Despite of extensive reports on cobaltaelectro-catalysed transformations, until recently, there was only very little understanding on the exact working mode of these novel transformations. Moreover, these reactions are mechanistically

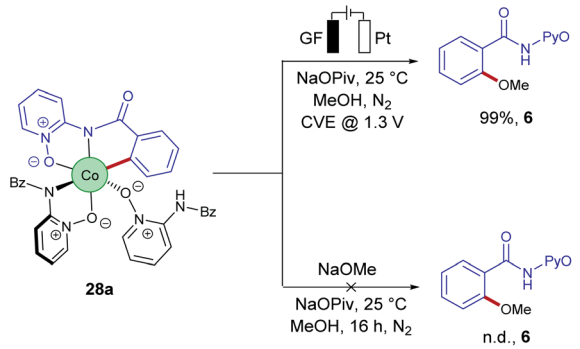


Scheme 5 Recent advances on cobaltaelectro-catalysed C–H activation (A) in an undivided cell setup; (B) in a divided electrolysis setup.

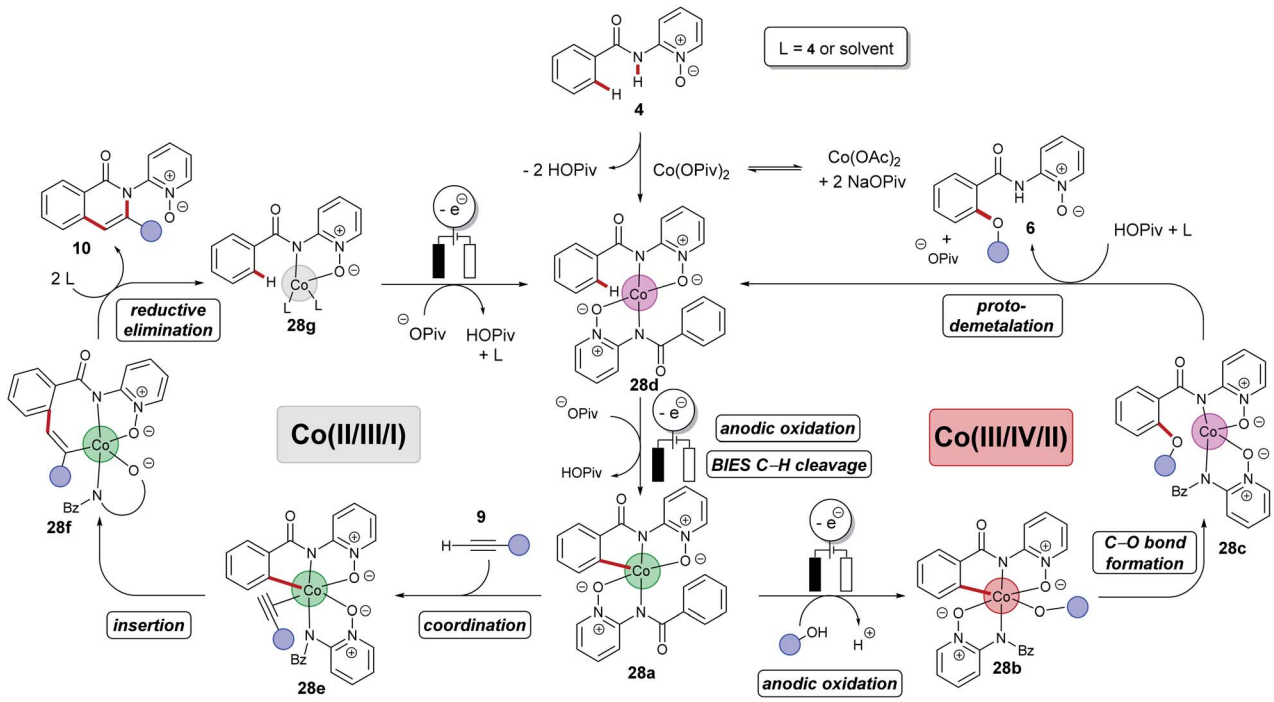
intriguing as they can be performed under exceedingly mild conditions, in stark contrast to reactions performed with chemical oxidants. Rather these reactions were suggested to occur *via* a cobalt(II/III/I)-catalytic cycle involving a base-assisted internal electrophilic-type substitution (BIES) type C–H activation. However, the role of the electricity presumably only served as a green oxidant to reinitiate the catalytic turnover by anodic oxidation of the reduced cobalt-species. To shed light on the mechanism of the cobaltaelectro-catalysed C–H activation, very recently a detailed mechanistic study was performed by the Ackermann group.[53] Here, key cyclometalated cobalt(III) complexes were synthesized with the aid of potentiostatic electrolysis and were subjected to detailed mechanistic studies. A series of stoichiometric reactions were performed with the isolated cobalt(III) complex **28a** and the results revealed that in the case of alkoxylation, a second oxidation was required, whereas for alkyne annulation reactions, the product was formed without any further oxidation (Scheme 6). This observation indicated that the alkyne annulation reactions are likely to proceed *via* a cobalt(II/III/I) manifold, which is in agreement with the previously proposed oxidative cobalt catalysis (Scheme 7, left cycle).[53] However, the authors proposed the cobaltaelectro-catalysed C–O forming reaction to proceed *via* an oxidatively-induced reductive elimination from a high-valent cobalt(IV) complex. Their hypothesis was further supported by means of cyclic voltammetry (CV) (Fig. 1).

When the CV-experiments were performed at lower temperatures, a reversible redox event was observed, which could be assigned to the transient generation of high-valent Co(IV) intermediates.

Based on their mechanistic studies a cobalt(III/IV/II) manifold was put forward for the electrocatalytic C–H alkoxylations, which was further supported by DFT calculations for an oxidatively-induced reductive elimination. In this new mechanism, a C–H activation takes place after anodic oxidation to the active cobalt(III) catalyst with a BIES mechanism to generate intermediate **28a** (Scheme 7, right cycle). It is noteworthy that this scenario likely proceeds within a concerted PCET, which contrasts with the previously reported mediated anodic reoxidation of palladium complexes (*vide supra*, Scheme 3). The subsequent anodic oxidation results in a highly reactive cobalt(IV) complex **28b** which is followed by a facile reductive elimination leading to cobalt(II) intermediate **28c**. A proto-demetalation releases the product and the reduced cobalt(II) species **28d**. Finally, anodic oxidation and subsequent C–H activation regenerates the catalytically competent cobalt(III) intermediate **28a.**



Scheme 6 Stoichiometric reactions with cyclometalated [Co(III)] complex **28a**.



Scheme 7 Proposed catalytic cycle for cobaltaelectro-catalysed C–H alkoxylations.

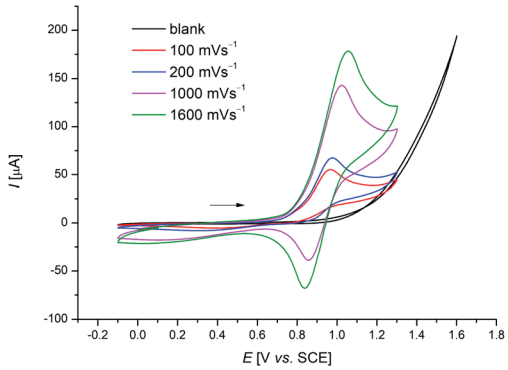


Fig. 1 Cyclic voltammograms of cobaltacycles [Co(III)] in MeOH (3.5 mM) at different scan rates. The voltammograms were recorded in 0.1 M [n-Bu_4N][PF_6] at 273 K.

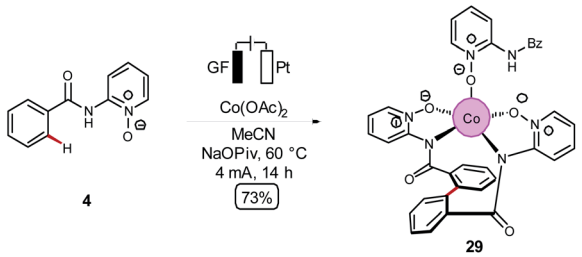
A cobalt(III/IV/II) catalytic cycle seems likewise plausible for the cobaltaelectro-catalyzed amination, as multiple oxidations appear prior entering the catalytic cycle similar as in the C–O forming reaction.[89,91] The potential of the amination reaction is lower than for the latter reaction. However, the estimated bond dissociation energy of R_2N–H is lower than of RO–H suggesting that its oxidation (*via* a bidirectional PCET reaction) appears at lower potential.[102]

The Ackermann group was further able to use the mechanistically gained insights in the high-valent cobaltaelectro-catalyzed C–H activation to develop an unprecedented twofold C–H/C–H arylation of benzamides **4** (Scheme 8).

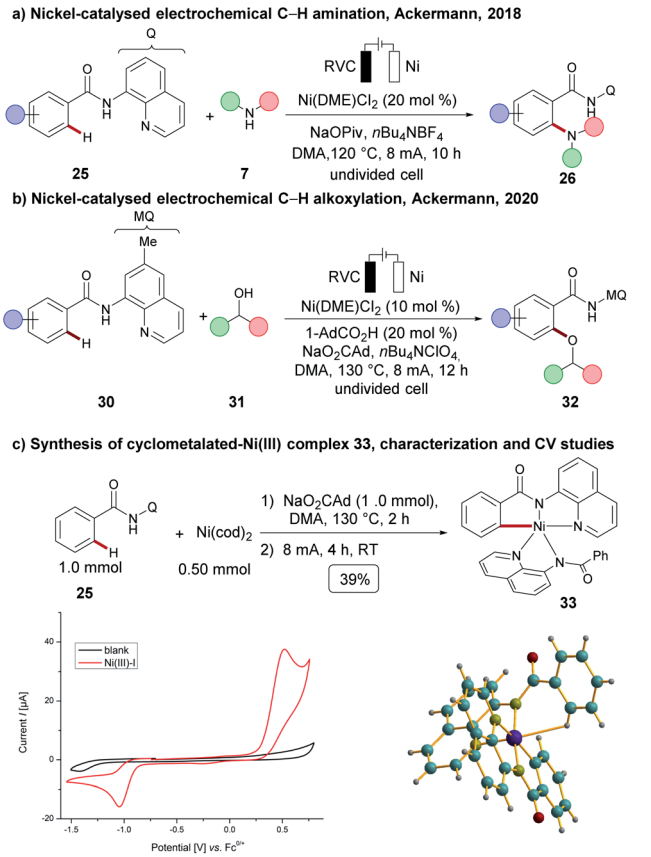
This study, among others[56,57] demonstrates how electrochemical manipulation of the oxidation states of the metal catalyst by single-electron transfer (SET) processes, offers the possibility to access new mechanistic pathways that were previously inaccessible.

Nickelaelectro-catalyzed C–H activation

A plethora of C–H activations have been realized by palladium catalysis.[17] Nickel catalysts feature advantages in contrast to palladium, including its low costs, Earth-abundant nature, as well as being generally less toxic.[103] However, an electrochemical C–H activation[104] using nickel catalysis was unprecedented until very recently when Ackermann and coworkers achieved an electrochemical C–H amination of benzamides **25** with cyclic and acyclic secondary amines **7** (Scheme 9).[105] C–H amination products **26** were hence obtained by chelation



Scheme 8 Cobaltaelectro-induced twofold C–H/C–H arylation.

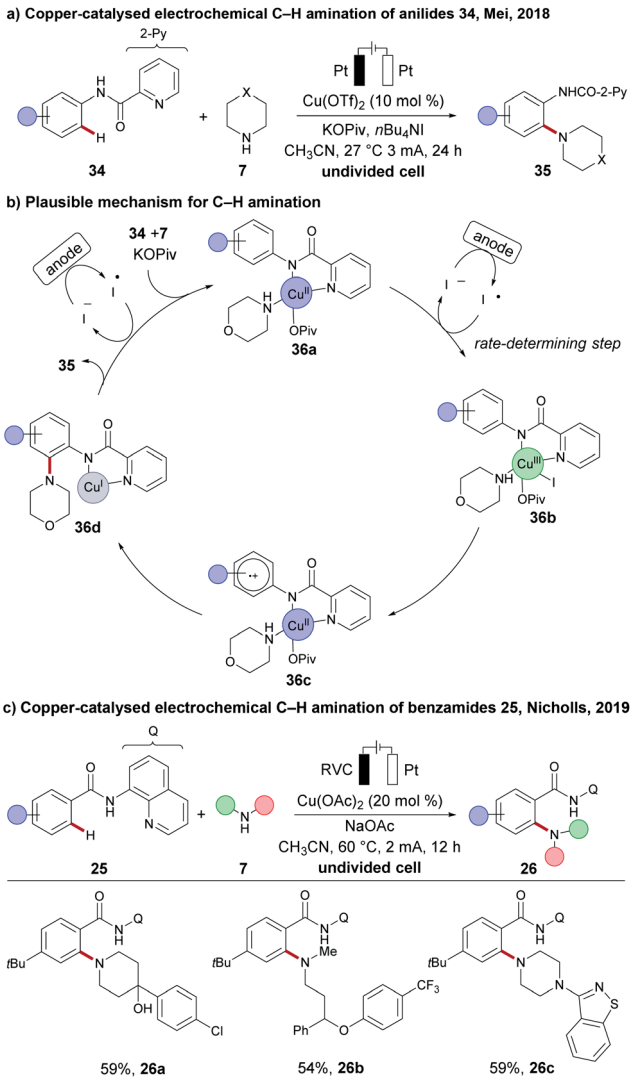


Scheme 9 Nickel-catalysed electrooxidative C–H activation.

assistance without the necessity of additional chemical oxidants. Cyclic voltammetry studies suggested a possible nickel(IV) intermediate and hence an oxidatively-induced reductive elimination step was proposed to be operative. The most recent notable advancement in electrooxidative nickel catalysis was again made by the Ackermann group. Thus, they disclosed an electrochemical C–H oxygenation of diversely decorated benzamides **30** with a wealth of secondary alcohols **31**, which otherwise were not viable with any other chemical oxidant or transition metals, such as palladium, cobalt, copper, among others.[54] As to the reaction mechanism, a cyclometalated nickel(III) complex **33** was independently synthesised. As a result of detailed mechanistic studies, an oxidatively-induced reductive elimination step at a nickel(III) complex **33** was suggested experimentally, and computational studies at the PBE0/Def2TZVP level of theory indicated that a non-innocent ligand effect was of relevance for the SET-oxidation.

Copper-catalysed electrooxidative C–H activation

Due to the low costs and high natural abundance of copper, a number of copper-catalysed or copper-mediated C–H activations have been reported.[30,79] Furthermore, simple copper salts or complexes have often served as the oxidants in oxidative transformations. Despite these precedents, the merger of electrosynthesis with copper-catalysed C–H activation remained dormant until very recently. Thus, the Mei group reported on



Scheme 10 Copper-catalysed electrochemical C–H activation. (a) C–H amination of anilides **34**. (b) Mechanistic proposal. (c) C–H amination of quinoline amides **25**.

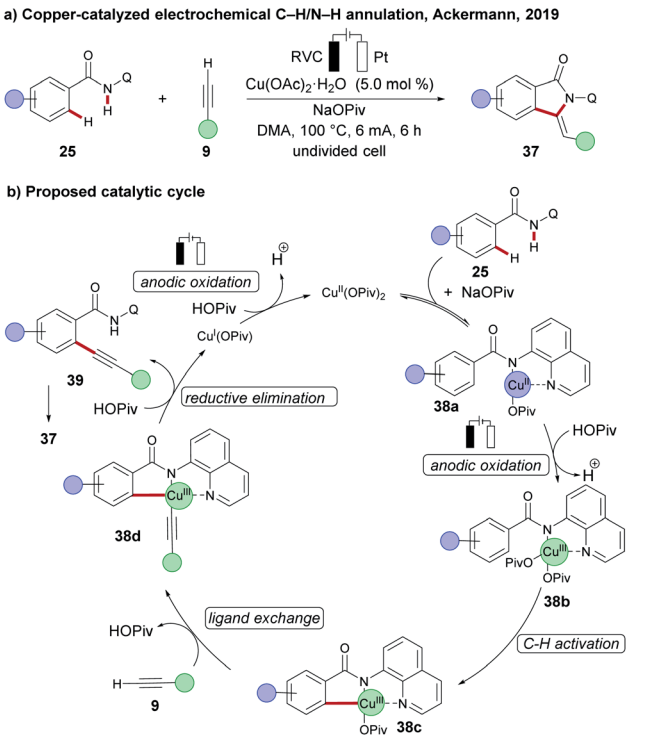
the copper-catalysed electrochemical C–H amination of anilides **34**, using various cyclic secondary amines **7** as the coupling partner (Scheme 10).[106] An undivided cell setup was used to access densely decorated the *ortho* C–H amination products **35**. Here, tetrabutylammonium iodide (TBAI) acted as a redox mediator to shuttle the electrons between the anode and the reduced copper complex. Based on insightful mechanistic studies, a radical mechanism was proposed. The active catalyst features a copper(II) species that is coordinated by anilide **34** and amine **7** to form the copper(II) intermediate **36a**, which then undergoes oxidation to copper(III) species **36b** by the iodine radical. According to kinetic studies, the formation of the copper(III) species **36b** is expected to be the rate-limiting step. A single-electron-transfer (SET) at the copper(III) complex **36b** forms the proposed radical copper(II) intermediate **36c**. Intramolecular amine transfer and subsequent electron transfer forms the copper(I) intermediate **36d**. Finally, the product **35** is released and the resulting copper(I) is oxidized by the iodine mediator to regenerate the active copper(II) catalyst. Thereafter, a redox mediator-free cupraelectro-catalysed C–H transformation was reported by Nicholls for quinoline amides **25**. The C–H amination products **26** could only be obtained in moderate yields at elevated temperatures of 60 °C and with higher catalyst loading (20 mol%), albeit with a broad scope, including active pharmaceutical ingredients (APIs), such as antipsychotic Haloperidol **26a**, Perospirone **26c** and antidepressant Fluoxetine **26b**.[107]

Concurrently, the Ackermann group reported on the first cupraelectro-catalyzed C–C formation by C–H activation on amides **25** with terminal alkynes **9** in a simple undivided cell setup (Scheme 11a).[108] Their mechanistic findings for redox mediator-free conditions comprise an electrochemical C–H alkynylation under copper catalysis, followed by a base-mediated cyclization of alkyne **39** to the annulation products **37** (Scheme 11b). Moreover, the strategy was operative up to gram scale without loss of catalytic efficacy.

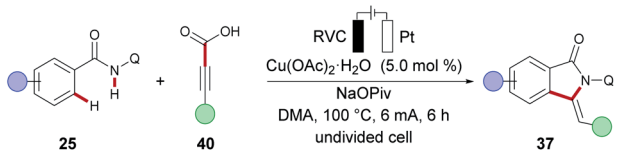
Furthermore, electrochemical C–H/C–C cleavage was realized with alkyne carboxylic acids **40** to deliver the annulation products **37** upon decarboxylation in good yields and with high *E*/*Z* selectivity (Scheme 12).

Iron-catalysed electrooxidative C–H activation

Iron being the most abundant transition metal in the earth's crust and having less toxicity compared to other transition metals, can have a remarkable impact on C–H activation. However, the predominant requirement of dichloroisobutane (DCIB) as a sacrificial stoichiometric oxidant made iron-



Scheme 11 (a) Copper-catalysed electrochemical C–C formation by C–H activation. (b) Proposed mechanism.

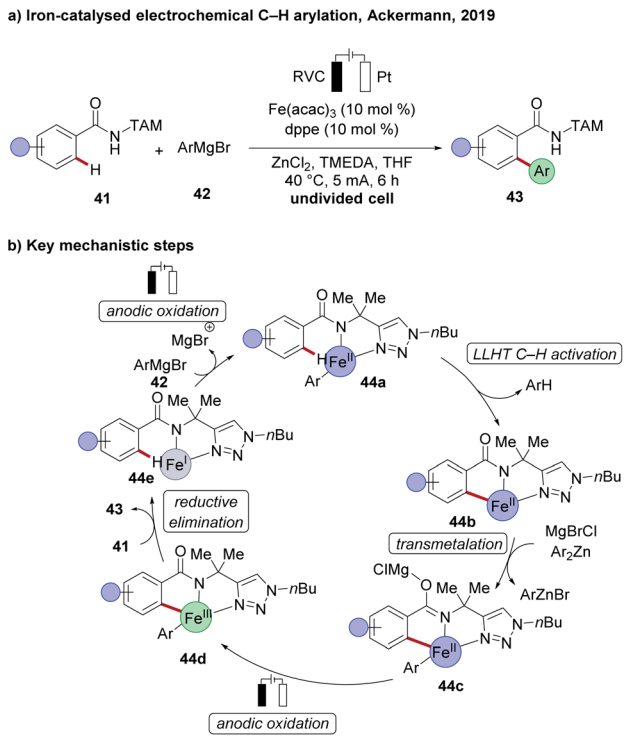


Scheme 12 Copper-catalysed C–H/N–H annulation of benzamides *via* C–C cleavage.

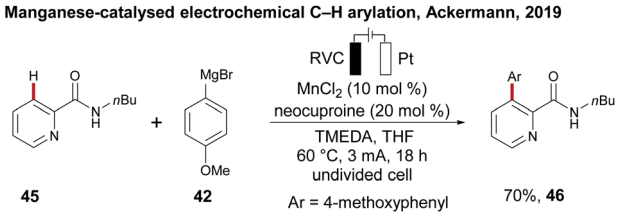
catalysed oxidative C–H activation rather unattractive.[30] This longstanding problem in iron catalysis was solved recently by successfully replacing the chemical oxidant DCIB through carefully chosen electrochemical reaction conditions by the Ackermann group. A chelation assisted C–H arylation of TAM-amide **41**, using arylating reagent **42** under electrochemical iron catalysis, enabled the formation of arylated products **43** in excellent yield, with a broad scope (Scheme 13a).[109] Detailed mechanistic studies proved indicative of an iron(II) complex as the active catalyst. The proposed catalytic cycle involves first a ligand-to-ligand hydrogen transfer (LLHT), followed by transmetalation to generate complex **44c** and the key subsequent anodic oxidation to deliver the iron(III) complex **44d**, which finally undergoes reductive elimination to deliver the desired product **43** (Scheme 13b).

Manganese-catalysed electrooxidative C–H activation

While the electrochemical C–H activation with 3d metal catalysts has been established in recent years as a green method, an approach for the merger of manganese-catalysed oxidative C–H



Scheme 13 (a) Electrochemical C–H arylation under iron catalysis. (b) Key mechanistic steps.



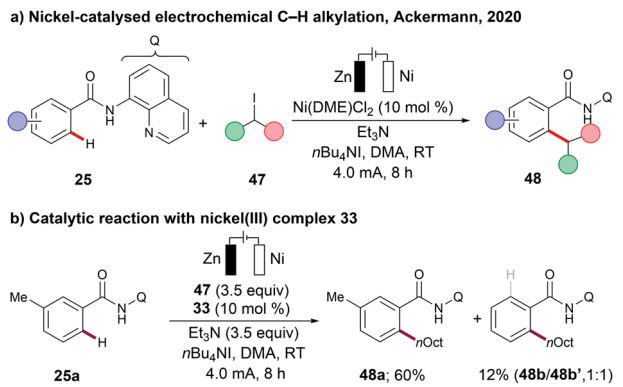
Scheme 14 Electrochemical C–H arylation under manganese catalysis.

transformations with electrosynthesis was not achieved until recently. As a proof-of-concept, in the same study Ackermann first reported on electrosynthesis with environmentally-benign manganese catalysis for a C–H arylation of pyridine amide **45** with arylating reagent **42** in 70% yield of **46**.[109] The reaction proceeded in an undivided cell under zinc additive free conditions, being indicative of the unique potential of manganaelectro-catalyzed C–H activation (Scheme 14).

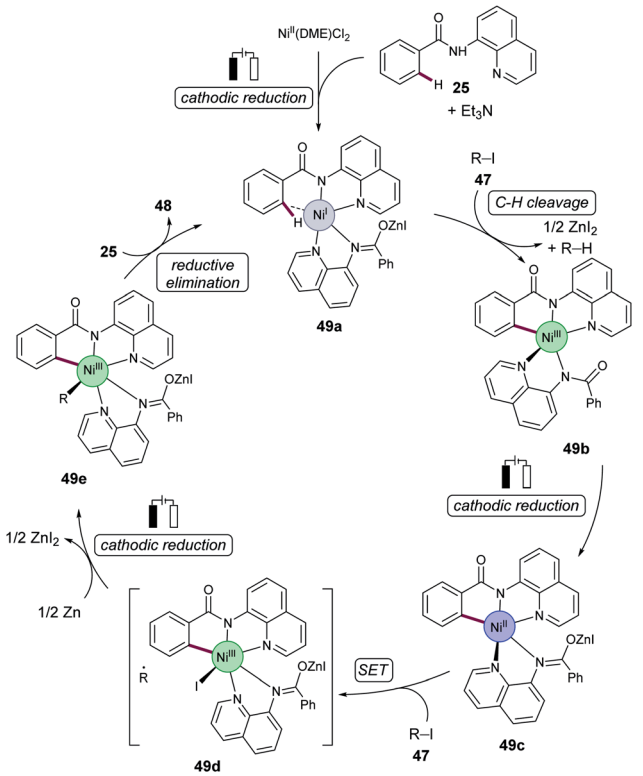
Electrochemical net redox-neutral C–H activation: nickel-catalysed electrochemical C–H alkylations

In oxidative C–H transformations, electricity serves as an oxidant, and plays a crucial role in terms of lowering the activation energy, which then facilitates the desired transformations. In contrast, net redox-neutral nickel-catalysed C–H activation reactions do not require a stoichiometric oxidant, but were largely limited to harsh reaction conditions. Specifically nickel-catalysed C–H alkylations require strong bases, such as lithium *tert*-butoxide (LiO*t*Bu) or lithium bis(trimethyl)silylamide (LiHMDS), and high reaction temperatures of 140–160 °C, translating into a significantly reduced substrate scope.[87]

Very recently, the Ackermann group have demonstrated that nickel-catalysed C–H alkylations can be achieved under mild reaction conditions at room temperature using Et_3N as a mild base (Scheme 15a).[55] Both primary and secondary alkylation proceeded efficiently, using the corresponding alkyl iodides **47** as the alkylating reagents. It is further noteworthy to mention that chain-walking[110,111] – commonly observed in nickel-catalysed cross-coupling reactions – was not observed under



Scheme 15 (a) Nickel-catalysed electrochemical C–H alkylation. (b) Catalytic reaction with nickel(III) complex **33**.



Scheme 16 Proposed catalytic cycle for nickelaelectro-catalysed C–H alkylations.

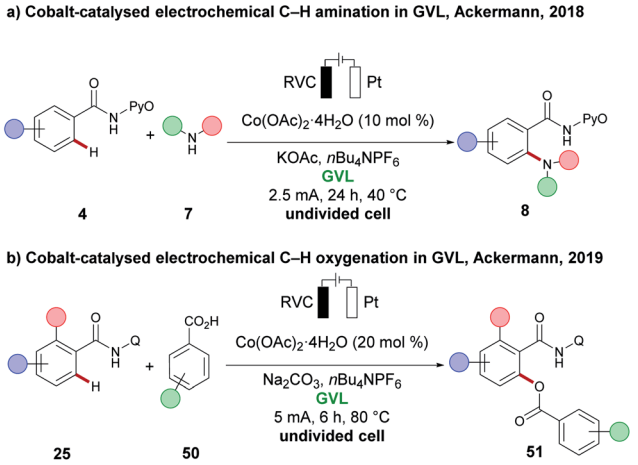
the optimized reaction conditions.[55] The organometallic nature of the transformation was further supported by the independently prepared cyclometalated nickel(III) complex **33**, which was found to be catalytically competent under the electrochemical conditions (Scheme 15b).

Based on detailed mechanistic studies,[55] the authors proposed a nickel(I/III/III) manifold. A cyclometalated nickel(III) complex **49b** was formed which was then reduced at the cathode to produce the nickel(II) intermediate **49c**. Following a single electron transfer (SET), and addition of **47**, gives the nickel(III) complex **49d**. Complex **49d** then undergoes cathodic reduction, followed by radical recombination, which generates nickel(III) intermediate **49e**. Subsequent reductive elimination, and coordination of substrate **25**, releases the C–H alkylation product **48** and regenerates the catalytically competent nickel(I) intermediate **49a** (Scheme 16).

3 Renewable solvents in electrochemical C–H activation

γ-Valerolactone (GVL)

γ-Vialerolactone (GVL) has gained significant attention in recent years as a potential green and renewable reaction medium for C–H activation reactions.[29] GVL can be produced from levulinic acid, obtained upon degradation of lignocellulose biomass.[112] It is characterised by a low toxicity, it is non-flammable, shows good chemical stability, and its

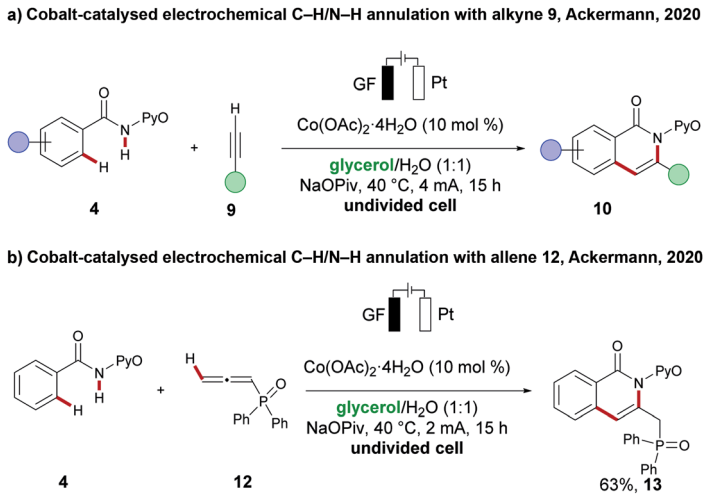


Scheme 17 (a) Cobalt-catalysed electrochemical C–H amination in GVL. (b) Cobalt-catalysed electrochemical C–H oxygenation in GVL.

biodegradable nature renders it a suitable alternative for polar aprotic, non-renewable, toxic and often flammable solvents, such as DMF, DMA and NMP. GVL was first used in electrochemistry for C–H activation by the group of Ackermann in a cobalt-catalysed C–H amination reaction (Scheme 17a).[91] To overcome the low conductivity, nBu_4NPF_6 was added as conducting salt. Under the reaction conditions, various aromatic and heteroaromatic amides **4** were aminated, with various cyclic secondary amines **7** to furnish the *ortho* C–H aminated products **8** with high reaction efficacy. Later, the same group found that GVL again was the optimum solvent for a cobaltaelectro-catalysed C–H oxygenation, using various benzoic acids **50** (Scheme 17b).[113] An *ortho*-substituent to the amide **25** was found to be useful in order to obtain the desired C–H oxygenation products **51** in good yield and high selectivity.

Glycerol

Glycerol is produced as a by-product from biodiesel synthesis and can be obtained at a low cost. Several features, including low toxicity, a high boiling point, and its biocompatibility make it a potential green alternative solvent for numerous transformations.[114,115] However, a major disadvantage arises from its high viscosity which results difficulties in mixing and diffusion of reactants inside this reaction medium and must be solved for using glycerol as a green solvent in electrochemistry. Due to its high polarity, it is miscible with water and thereby the viscosity of the overall mixture can be reduced, which now transforms it in a suitable protic solvent.[116] Indeed, this strategy was in a proof-of-concept validated by the Ackermann group earlier this year. They could successfully replace non-renewable solvents for electrochemical transformations with identical and even better reaction efficacy using a mixture of glycerol/water as the renewable solvent of choice. Furthermore, their approach did not require electrolytes, which further boosts the catalyst's sustainability. In the first case, they performed a cobalt-catalysed oxidative C–H/N–H annulation of amides **4** with alkynes **9** (Scheme 18a).[117] An improved yield of the



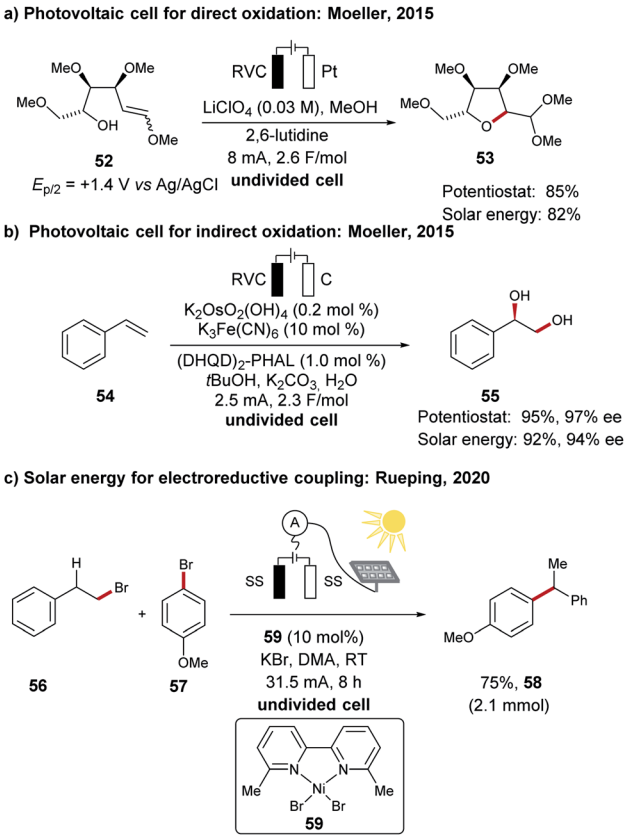
Scheme 18 Cobaltaelectro catalysis in glycerol/H_2O. (a) Alkyne annulation. (b) Allene annulation.

annulation products **10** was observed in the glycerol/water solvent mixture. They also explored the C–H/N–H annulation reaction of amides **4** with allenes **12** (Scheme 18b), which transformed the substrates in slightly reduced yield to product **13**, compared to the previously published solvent system.

4 Renewable energy sources in organic electrochemical transformations

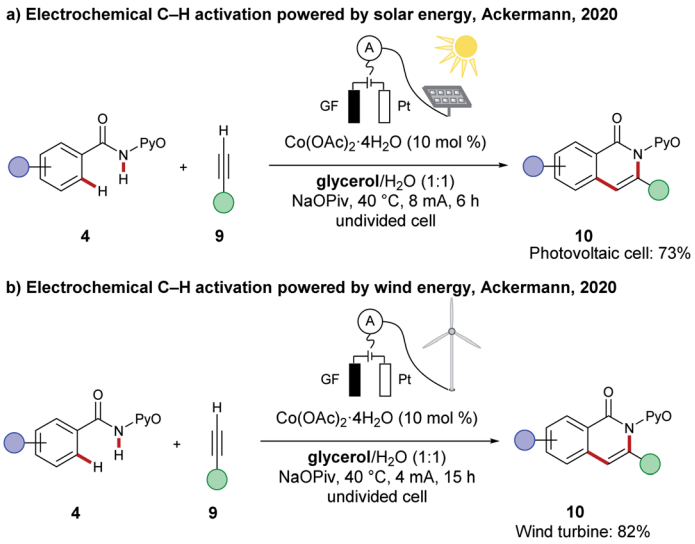
In order to meet the increasing demand of global energy consumption, fossil fuels are not adequate and therefore the direct utilization of renewable energies has become a highly demanding field of research.[41–43,118,119] Hydrogen production from water will certainly have a high impact, however, this requires the associated oxygen evolution reaction (OER) which is characterized by a high overpotential.[120–123] In this regard electrosynthesis has been identified as a powerful tool for direct conversion of electricity to high-value chemicals, rather than producing oxygen with a lower economical footprint.[124]

The direct utilization of sunlight for chemical energy conversion is an active research field.[125] Although its impact in organic syntheses has been realized by the development of suitable photocatalysts for energy and electron transfer reactions,[126] it is unfortunately often limited to the use of energy-intensive light sources of a specific wave length.[127–129] In this context, the direct utilization of solar energy for electrosynthesis was reported by Moeller for oxidative transformations with a crystallin silicon photovoltaic module (Scheme 19a).[130,131] In a representative example the direct oxidative cyclization of **52** to the tetrahydrofuran derivative **53** was achieved. A similar photovoltaic device was also used for the catalyst regeneration in an asymmetric dihydroxylation of **54** to form chiral alcohol **55** by means of anodic oxidation (Scheme 19b).[130] Recently, the group of Rueping has demonstrated the use of solar energy for the reductive nickel-catalyzed cross-electrophile coupling between halides **56** and **57** to form the chain-walking product **58** (Scheme 19c).[111]



Scheme 19 Selected examples for the direct utilization of solar energy in chemical transformations.

To guarantee full resource economy of C–H activations, the merger of electrochemistry with Earth-abundant 3d base metal catalysis have made a notable impact (*vide supra*). However, in a recent proof-of-concept study, the Ackermann group showed that the direct utilization of renewable energies for oxidative C–H transformations by renewable energy sources, such as solar energy and wind energy, is indeed viable. Here, the



Scheme 20 Electrochemical C–H activation powered by renewable electricity.

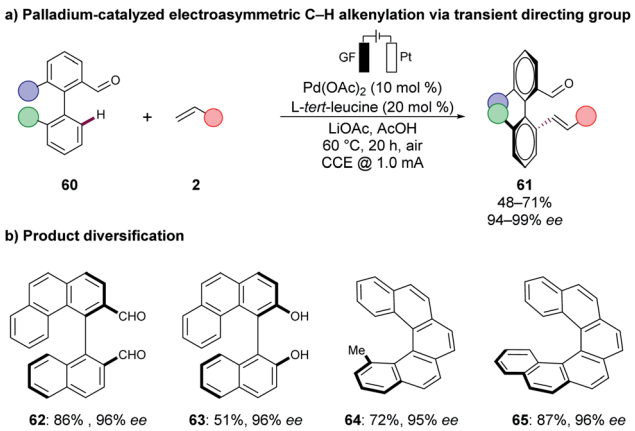
cobaltaelectro-catalysed C–H/N–H annulation of amide **4** with alkyne **9** in biomass derived glycerol served as model reaction and was powered by either a commercially available photovoltaic module or a commercially available wind turbine (Scheme 20).[117]

5 Summary and outlook

Metallaelectro-catalysed C–H activations have significantly improved the sustainability and resource-economy of organic synthesis by the direct utilisation of renewable energy sources, Earth-abundant metal catalyst, and the employment of biomass-derived solvents. Herein, we have discussed, in the first part, cost-effective, less-toxic and mechanistically less explored 3d base metal-catalysed transformations that with the aid of electrochemistry enabled unexplored mechanistic pathways, such as oxidatively-induced transformations can be revealed. In the second part, biomass-derived solvents such as GVL and glycerol have proven to be viable solvents in cobaltaelectro-catalysed C–H transformations, and thus further improved the overall sustainability of the methodology. Polar protic solvents, such as glycerol, serve as an excellent reaction medium for organic electrochemical synthesis as no additional electrolyte is needed. Finally, the direct utilization of renewable energies, such as solar or wind energy, have served as an ideal proof-of-concept for the robustness of the method.

Overall, the recent state-of-the-art allows an environmentally-benign strategy for C–H activation with molecular hydrogen being produced as the sole by-product. The proper utilization of the on-site generated hydrogen gas for further useful transformations may lead to complete electron economy by paired electrolysis, which has barely been explored[59] and thus enables synthetic strategies in a circular fashion. Paired electrolysis could further be used for a combined strategy in organic CO_2 functionalisation and fixation.[132,133] However, unsolved challenges remain for the broader implementation of metallaelectro-catalysed C–H activations. For instance, in most of the presented studies, a bidentate directing group was required to stabilise the often high-valent metal-catalyst. Innovative ligand design will therefore be mandatory to overcome this challenge to adjust the reactivity of the 3d metal catalysts. Here precious metal-catalysts show a significantly higher robustness as was presented in recent reports by the group of Ackermann,[48] using chiral amino-acids as transient directing groups in asymmetric palladaelectro-catalysed C–H olefinations.[134] Thus, axially-chiral biaryls **61** were accessed from the biaryl aldehydes **60** *via* atroposelective C–H alkylations under electrochemical conditions (Scheme 21a). Moreover, the thus-obtained biaryls **61** were readily converted into the diversified axially-chiral biaryl compounds **62**, **63** and helicenes **64**, **65** (Scheme 21b).

Furthermore, the concept has mainly been applied to C(sp^2)–H bonds, while transformations of C(sp^3)–H by means of electrocatalysis are less explored.[135] On a different note, sensitive



Scheme 21 Palladaelectro-catalyzed atroposelective synthesis.

reactions may not tolerate polar protic solvent conditions, hence, additional electrolytes are necessary to reduce the electrochemical cell resistance. Here, notable innovative concepts, including the combination of electrochemistry with recently introduced findings in micellar catalysis,[136,137] ionic liquids[138] or flow chemistry[75,139] are expected to gain further prominence. Moreover, the recent merger of photochemistry with electrosynthesis enabled homogenous photoelectrocatalysis with outstanding redox potentials, thus avoiding drastic chemical redox reagents.[140] This innovative strategy was successfully implemented in selective C–H alkylations of heteroarenes,[141] as well as in otherwise challenging C–H trifluoromethylations of various (het)-arenes.[142]

Conflicts of interest

There are no conflicts to declare.

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