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Green chemistry: Electrochemical organic transformations via paired electrolysis

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Abstract:

Paired electrolysis is highly valuable from the viewpoint of efficiency as well as atom and energy economies. In order to optimise the latter two for chemical reactions, the development of paired electrochemical processes is necessary. When both of the electrodes in an electrochemical cell (divided and undivided) are applied as working electrodes, and both sides of the processes (oxidation and reduction) yield valuable compounds, this ideal electrolysis phenomena is defined as paired electrosynthesis. This paired electrolysis offers the opportunity to reduce the spent energy and time, when compared with a single electrolysis system that is only used to achieve a product of interest, while ignoring the other side of the electrolysis (anodic or cathodic). In an ideal case, 200% current efficiency could be achieved during paired electrosynthesis using cathodic and anodic processes to provide the same product. Paired electrosynthesis is a highly efficient green process and therefore, is beneficial for preserving resources and minimising waste. However, while a paired electrosynthesis is beneficial, both oxidation and reduction processes must be compatible to counter the yield losses, and equally ease separation and purification of both sides of the electrode products. Greater efforts are required to perform paired electrosynthesis with a more systematic and rational approach to achieve optimal products under paired conditions. Nevertheless, new computational tools could be applied for assistance in this matter. There is a considerable level of adventure in designing new paired electrosynthetic processes and accompanying opportunities to design innovative and powerful synthetic strategies. Herein, an overview of several examples of paired electrosyntheses and their advantages are summarised that will aid researchers to both develop a greater understanding of this subject and subsequently employ paired electrolysis for green and sustainable synthesis of organic molecules.

Introduction

Developments in the methodology of organic electrochemistry are still continuing to emerge,¹ due to electrochemistry presenting itself as a green, modern, and safe technique to achieve a diverse range of chemical transformations.²⁻³ The primary reactant to perform such chemistry is the humble electron that can be used as an inherently clean alternative for an oxidant or chemical reducing agent. Electrosynthesis is an excellent way of minimising energy consumption and can also be used successfully for the *in-situ* production of hazardous and unstable reagents, in addition to maximising energy efficiency. Different electrosynthetic methods have been used, such as direct oxidation⁴ or reduction of substrates,⁵ indirect electrolysis (mediated or catalysed),⁶⁻¹¹ or by electrogenerated bases such as CH_3CN ,¹²⁻¹⁷ DMSO, or DMF.¹⁸ The process of paired electrosynthesis has been known for a long time as a convenient and practical methodology,¹⁹ the appellation of which has been to describe electrochemical processes in which both the reaction at the anode and the reaction at the cathode contribute usefully to the formation of the product(s). The literature, however, predominantly reports reaction at only one electrode,²⁰⁻²¹ either anodic oxidation or cathodic reduction (**Fig. 1**). Hence, the reaction products from one of these is usually wasted. In contrast, paired electrolysis could maximise energy efficiency by using both cathodic and anodic reactions without waste and undesirable products. As shown in **Fig. 2**, the total energy required to drive any electrolysis reaction is defined by the potential difference needed for accomplishing both the oxidation and the reduction half reactions.²²

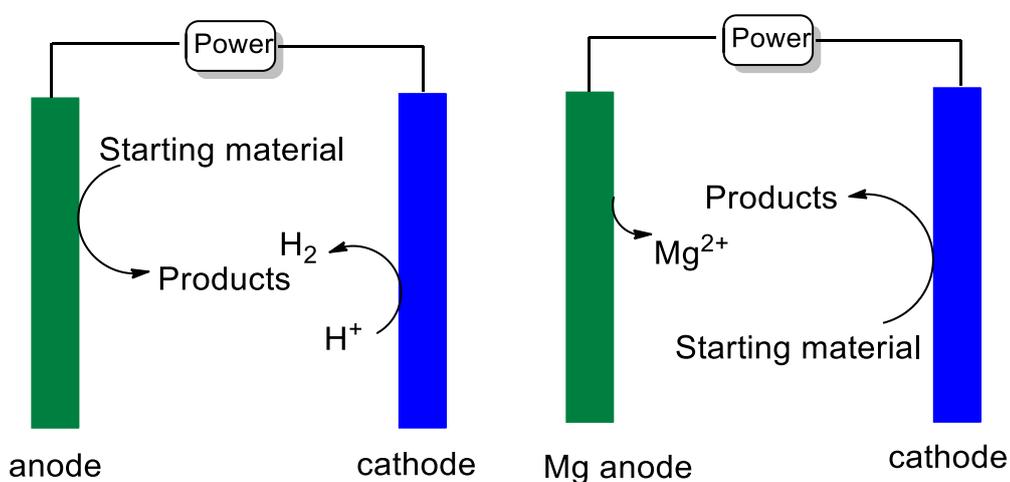


Fig. 1 The formation of a desired product at only one electrode (by oxidation or by reduction).

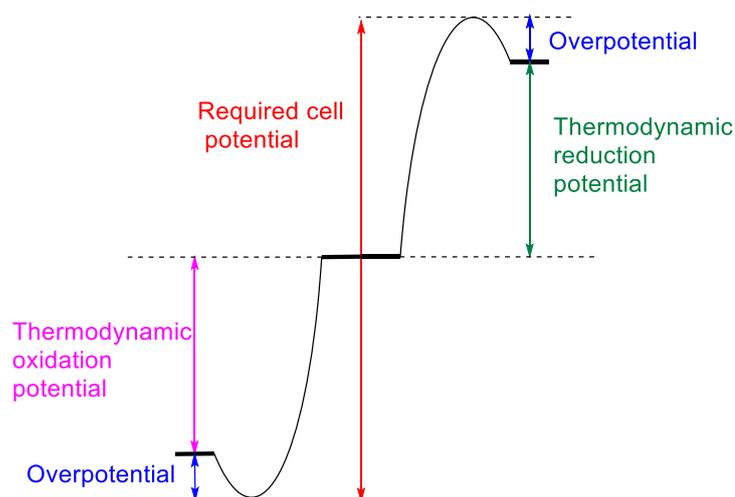


Fig. 2 Energy requirements for electrolysis. Reproduced from ref 22, Copyright (2021) John Wiley & Sons.

One of the vital bottlenecks in paired reactions is the electrode material/processes' selectivity,²³⁻²⁵ which has to be chosen to allow the formation of a product without further undesired side reactions. Typically, paired reactions are classified into four types: convergent, parallel, divergent, and linear paired electrolysis (**Fig. 3**). For the *convergent paired electrolysis*, the intermediates formed on the anode and cathode react together to provide the desired product (**Fig. 3a**). In *parallel paired electrolysis*, the anode and cathode reactions are simultaneous, but non-interfering or reacting; two different products can be obtained from two different starting substrates (**Fig. 3b**). In *divergent paired electrolysis*, one starting material is reduced as well as oxidised, providing two different products (**Fig. 3c**). In *linear paired electrolysis*, one product will be obtained by the substrate's oxidation, followed by reduction, or vice versa (**Fig. 3d**).

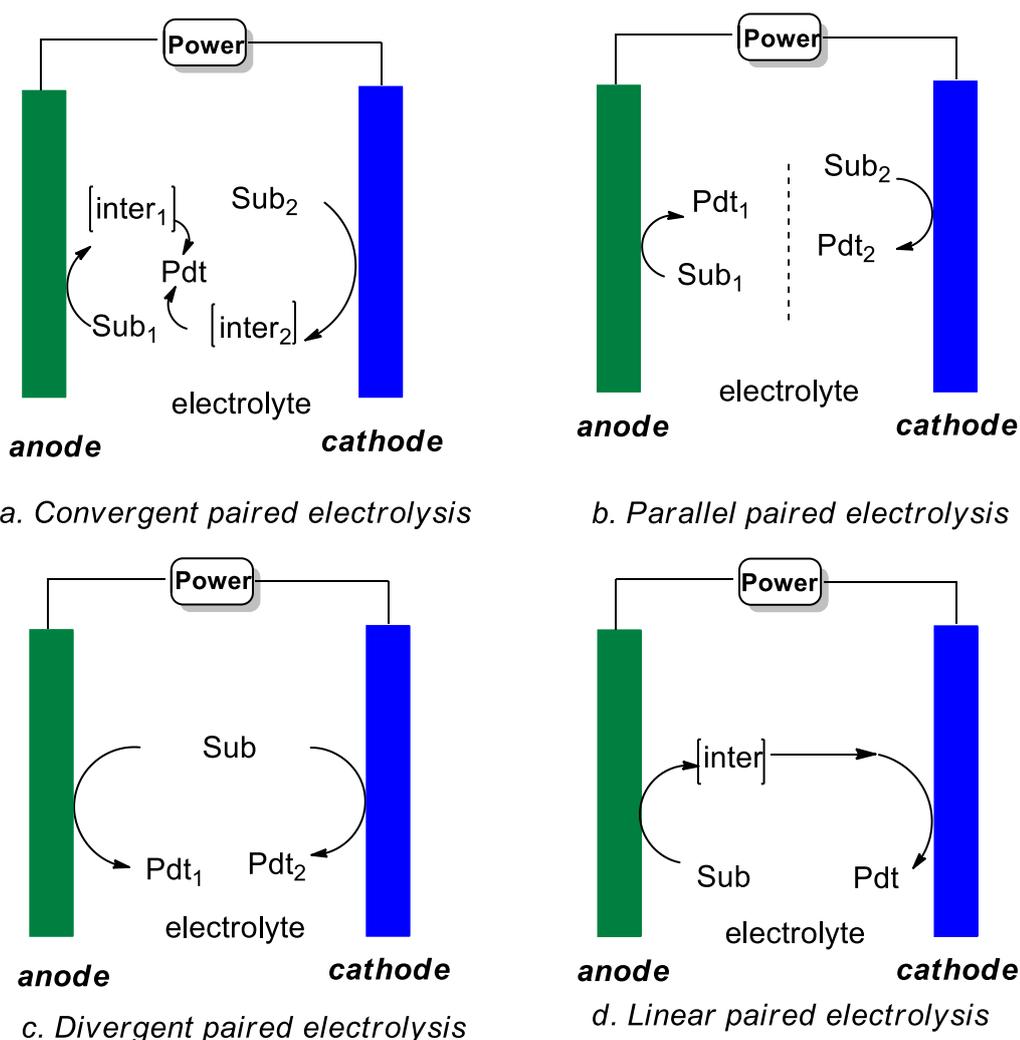


Fig. 3 Types of paired electrolysis: **a.** Convergent paired electrolysis, **b.** Parallel paired electrolysis, **c.** Divergent paired electrolysis, **d.** Linear paired electrolysis; intermediate = [inter]; substrate = Sub; product = Pdt

In electrochemical reactions, more consideration is given to optimize the efficiency of atom usage without paying similar attention to optimizing the use of energy. Equally, the part of the energy associated with the counter reaction is simply overlooked. However, to optimize both the atom and energy economy of a reaction, the development of paired electrolysis is important to maximize the outcome (oxidation and reduction products), thereby maximizing the energy efficiency of the reaction. To make paired electrochemical process a sustainable, the number of things could be considered such as i) sustained electrolysis ii) maximum faradaic yield iii) optimized power conversion efficiency iv) current matching of the half-reactions in an electrolysis cell v) chemical compatibility between half-reactions vi) formation of products with high value than the chemical reactants, vii) renewably sourced chemical feedstocks viii) design of modified and selective electrodes to avoid unwanted reactions.²⁶⁻²⁷ These adaptations in electrolysis could improve the atom economy at the possible expense of energy economy. This increased sustainable phenomenon of paired electrolysis can be implemented within larger synthetic setup where the reagent produced from paired electrolysis further can be used for another possibly non-electrochemical reaction and so on more chemical transformations are achievable. By pairing electrode processes at a closely spaced anode and cathode such as in micro-flow reactors where the diffusion layer of anode and cathode overlap to give the desired product and paired

electrochemical processes can now be managed without the need for a deliberately added supporting electrolyte. The product is obtained directly by solvent removal and without laborious separation phases, which is of considerable benefit in chemical syntheses.²⁸

Generally, paired electrolysis is economical for a number of reasons. i) The energy consumption considerably reduces. The reaction takes place simultaneously at the working- and counter-electrode and this fact offers the prospect to reduce energy and time by pairing the two processes so that the chemicals formed at each electrode are valuable. Thus, the yields may increase past 100%, thereby maximising the energy efficiency. Moreover, in case of microflow when inter-electrodes distance is very short, paired electrolysis can now be accompanied without supporting electrolyte and the diaphragm at low overpotential. ii) Theoretically, in an ideal case to provide the product, current efficiencies can be achieved with a value of up to 200%, since the current efficiency is equal to the mole of products per unit of charge used in the electrochemical cell (when a mole of electrons is passed through the electrochemical cell and both electrodes accomplish valuable chemical transformations, the overall yield is simply the total of the respective yields of the reactions that occur at each electrode). In some cases, hydrogen is evolved at a cathode in protic solvents like water or methanol, along with desired anodic products. The evolving hydrogen can be economical and utilized as fuel material. iii) The process costs and resources that can be saved once both sides of the electrochemical cell are used instead of a separate arrangement or an additional cell/ reactor with extra electrodes, electrolytes and vessel space. iv) Maximum atom economies are also possible because the formation of wastes/side products are minimised. Furthermore, fewer separation and synthetic steps are required. However, reaction control is critical in paired electrolysis, and therefore, the cell and the setup have to fit for each target reaction. Work-up, product isolation and purification are important for a successful synthesis and can be even more problematic in a paired synthesis. The paired reaction has been successfully utilised in industrial production, such as for the paired electrosynthesis of nylon 6,6,²⁹ the parallel paired reaction for the formation of 1-butyl-4-(dimethoxymethyl)benzene and isobenzofuran-1(3*H*)-one,³⁰ the electroformation of gluconic acid and sorbitol via divergent electrolysis of glucose,³¹ the formation of glyoxylic acid via convergent paired electrolysis,³² the electrocatalytic convergent paired degradation of *Para*-dinitrobenzene,³³ the electrosynthesis of methyl ethyl ketone via linear paired electrolysis,³⁴ and the use of electrogenerated azobenzene as a base to achieve ethyl hexanoate.³⁵ Recently, we have published review articles emphasising the importance of organic electrochemistry for the synthesis of heterocyclic compounds,³⁶⁻³⁷ annulation reactions,³⁸ alkyne functionalisation,³⁹ alkene difunctionalisations⁴⁰ and the electrochemical phosphorylation of organic compounds.⁴¹ In 1999, Chou and co-workers reviewed the types of paired electrolysis,⁴² in 2017 the Pletcher group⁴³ reviewed the advantage of flow electrolysis cells for paired synthesis, the basic strategies of paired reactions were reviewed by Hilt in 2019,⁴⁴ and in 2020, the Nanda group reviewed the key parameters of paired electrolysis.⁴⁵ However, looking at these reviews, we found that they do not contain the new examples of paired electrolysis reactions. It is for this reason that we would like to add the recent developments of paired reactions. Herein we review an updated summary of recent developments in convergent, divergent, parallel, and linear paired electrolysis.

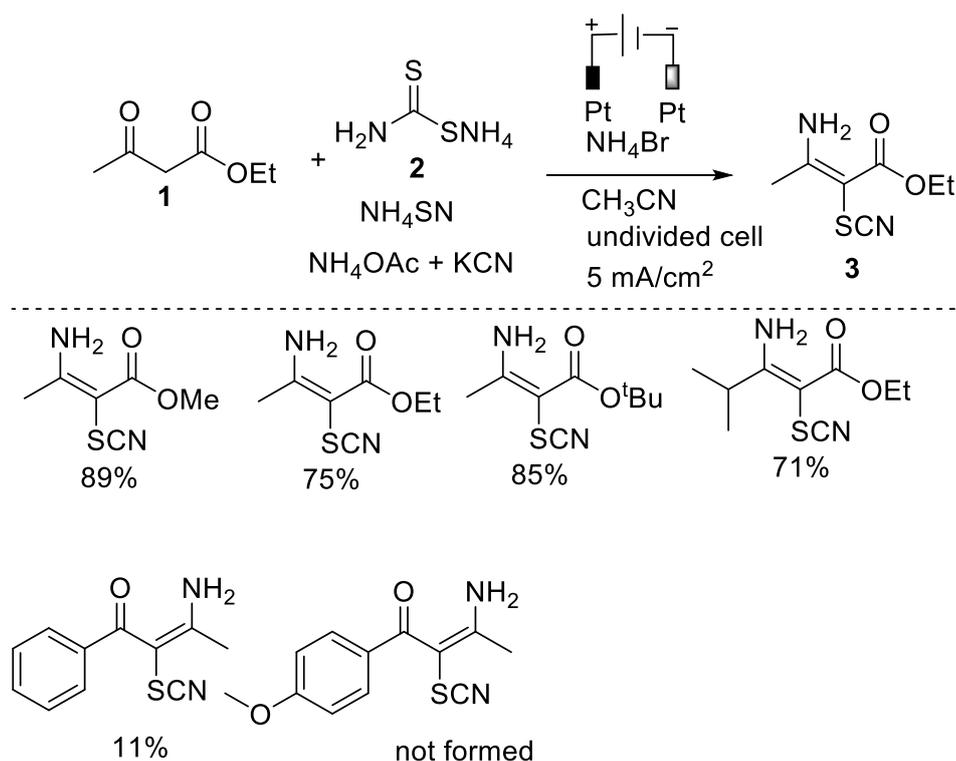
Paired electrolysis for organic transformations

Convergent paired electrolysis

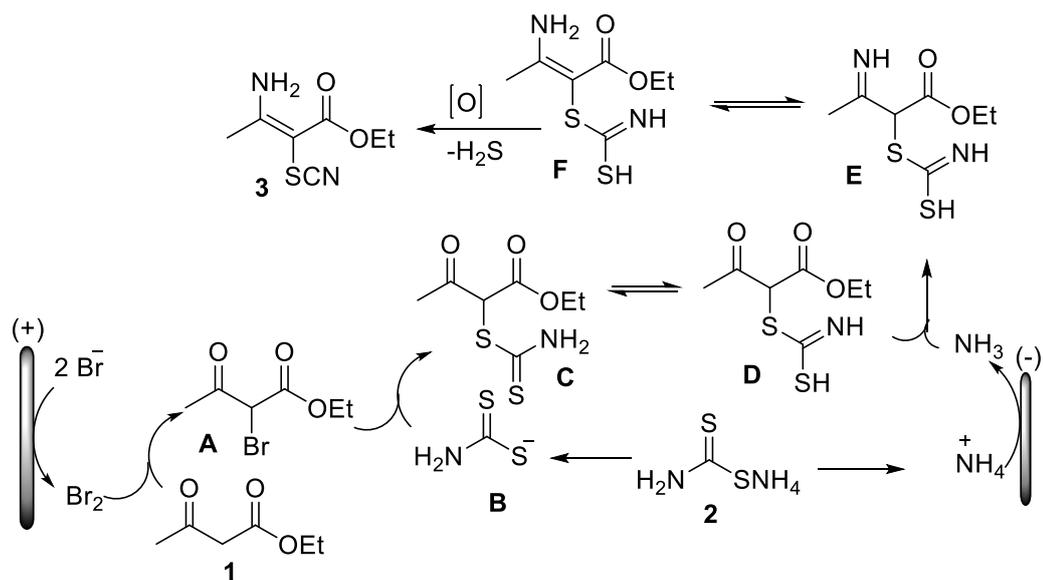
Convergent paired synthesis has been reported in two types; mediated and non-mediated synthesis. Both were successfully used to manage different reactions, such as cross-coupling reactions, amino-oxygenation reactions, and arylation reactions.

Mediated electrolysis

In the last few years there is a growing number of reported electrocatalysed convergent paired syntheses. In 2016, the Zeng group reported an efficient synthesis method for the convergent paired electrolysis of 3-amino-2-thiocyanato-unsaturated carbonyl derivatives **3** using NH_4Br as the mediator and an electrolyte (**Scheme 1**).⁴⁶ The reaction proceeded in an undivided cell at room temperature in acetonitrile, at a constant current using platinum plates as both electrodes. Under mild conditions, ethylacetoacetates **1** and ammonium carbamodithioates **2** (or ammonium acetate with potassium isocyanate) afforded a broad scope of the desired products **3** in good yields of up to 89%. Aromatic 1,3-dicarbonyl compounds were also tested for this transformation. It was found that, starting with phenylbutane-1,3-dione as a substrate, the reaction proceeded sluggishly, and only 11% of the desired product was formed. However, when ethyl 3-(4-methoxyphenyl)-3-oxopropanoate was used, the desired product was not formed. It was also demonstrated that 20 mol% of Et_4NBr as a redox catalyst worked well in this transformation, giving moderate to good yields for the final products. The reaction took place both at the anode and cathode (**Scheme 2**), to achieve 200% electrolysis efficiency. The authors suggested that the cascade of reactions began with the anodic oxidation of bromide (Br^-) to give the bromine molecule (Br_2), which reacted with substrates **1** to provide the intermediate **A**. Then the substrate **2** dissociated to afford the anion intermediate **B** and ammonium cation. Then intermediate **B** attacked **A** to give intermediate **C** and its tautomer **D**. Concurrently, on the cathode, the ammonium cation is reduced to generate NH_3 , which reacted with **D** to afford **E** and its tautomer **F**. Further anodic oxidation of **F** led to the final product **3** after the removal of H_2S .



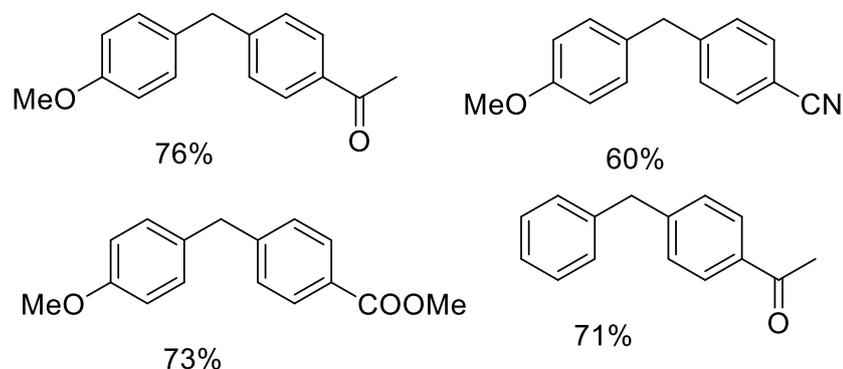
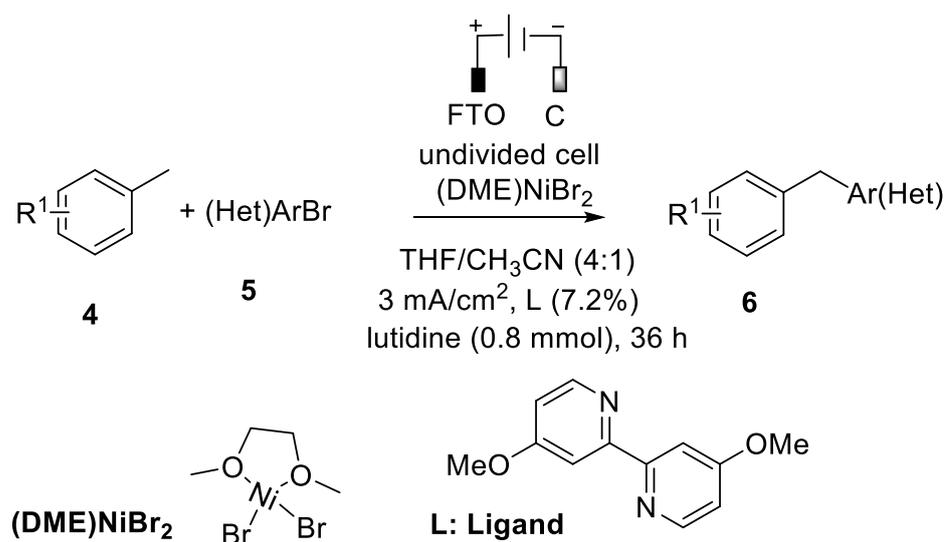
Scheme 1. The convergent paired electrolysis of 3-amino-2-thiocyanato-unsaturated carbonyl derivatives.



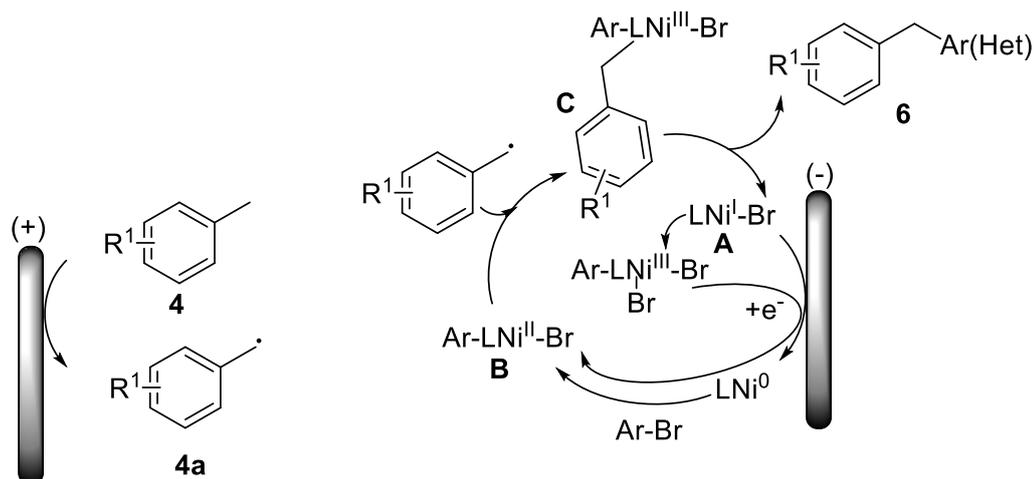
Scheme 2. Plausible mechanism for the convergent paired electrolysis of 3-amino-2-thiocyanato-unsaturated carbonyl derivatives.

Another case of electro-coupling reactions for the paired formation of C-P or C-Se bond owes its success to the use of a Ni-catalyst;⁴⁷ of which the electricity was found to be a good alternative when generating the unstable Ni^{III} intermediate. Based on the experimental mechanistic investigations, it was demonstrated that the simultaneous anodic oxidation of Ni^{II} to Ni^{III} and cathodic reduction of Ni^{I} to Ni^0 occurred with high energy efficiency. In this context and recently in 2020, Hu and co-workers achieved an excellent method for Ni-catalysed convergent paired electrosynthesis for the direct arylation of benzylic C-H bonds.⁴⁸ Under mild conditions, different toluene derivatives **4** and substituted aryl bromides **5** could

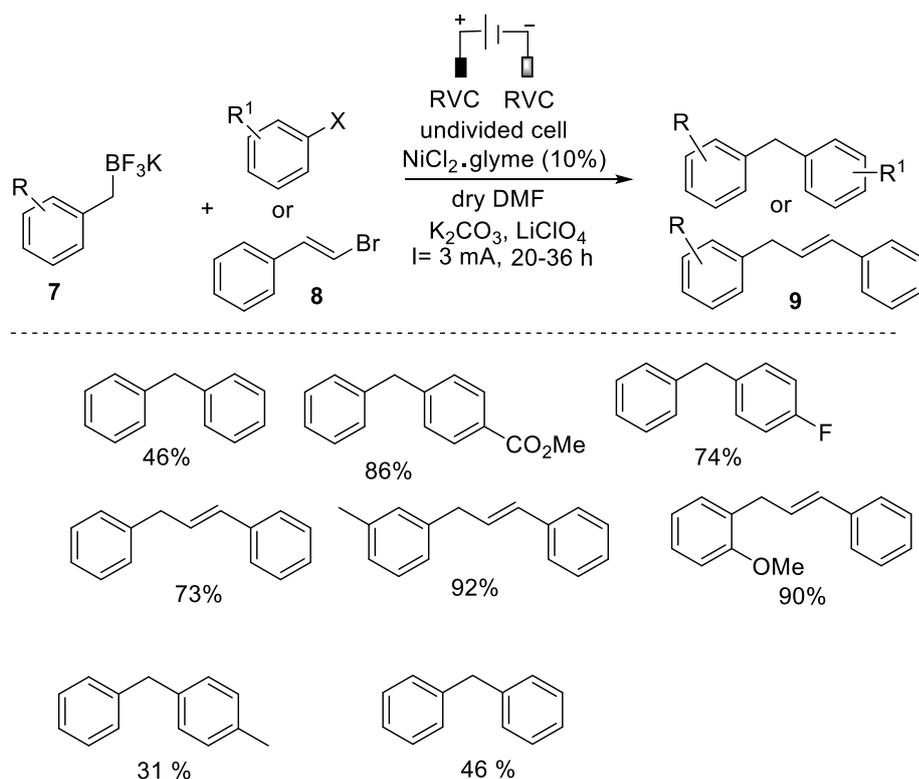
afford a large scope of diarylmethane derivatives **6** in moderate to good yields of up to 76% (**Scheme 3**). The electrolysis was conducted in an undivided cell at a constant current in THF/CH₃CN using fluorine-doped tin oxide (FTO) as the anode and carbon fibre as the cathode. The optimal yields were obtained by using the combination of 4,4'-dimethoxy-2,2'-bipyridine as a ligand (L) and Nickel(II) bromide ethylene glycol dimethyl ether complex ((DME)NiBr₂) as a catalyst. Other solvents and different electrodes were found to be less efficient. Importantly, aryl bromide bearing electron-donating groups were tolerated in this transformation in the presence of Ni(acac)₂ as a catalyst instead of (DME)NiBr₂. The weakness of this transformation being with toluene derivatives containing an electron-withdrawing group such as F and Cl, which could only be arylated when they were used in a higher excess (10 equiv.) As an improvement of the convergent electrochemistry, the authors suggested the following plausible mechanism (**Scheme 4**). At the anode, the oxidation of toluene **4** gave the benzyl radical **4a**. This radical was trapped by an LNi^{II}ArBr **B** to give intermediate **C**. The latter underwent reductive elimination to give the final product. **A** could be converted to **B** either by oxidation addition of ArBr followed by cathodic reduction or by reduction to form Ni⁰ followed by oxidation addition of ArBr. Very recently, independently of works Hu's group, Liu and co-workers also reported an elegant approach for an Ni-catalysed electrochemical method for C(sp²)-C(sp³) cross-coupling convergent paired reactions.⁴⁹ Under mild conditions, potassium benzyltrifluoroborate derivatives **7** and halogen derivatives **8** could afford a broad scope of desired products **9** in good yields of up to 92% (**Scheme 5**). The reaction proceeded in an undivided cell at a constant current of 3 mA, with dry DMF as a solvent, in the presence of LiClO₄ as an electrolyte, using reticulated vitreous carbon (RVC) as both electrodes. Different substituted aromatics groups with electron-donating and electron-withdrawing substituents were well tolerated in this transformation. The results show that when electron-rich substrates were used, the desired product was formed with a low yield of 31% and 46%. A very important notification was demonstrating the potential application of this Ni-cross-coupling methodology. The authors exploited the synthesis of pharmaceutical molecules containing the diphenylmethane structural component. Beclobate analog **I** and Bifemelane **II**, an antidepressant, were synthesised with 74% and 56% overall yield, respectively (**Scheme 6**). As an improvement for this transformation, the authors suggested the following plausible mechanism (**Scheme 7**). The catalytic cycle commenced with the cathodic reduction of Ni^{II} species **A** to Ni^I species **B**, which coordinated with the substrate **8** by a further oxidative addition to provide the complex Ar-Ni^{III} **C**. **C** was subsequently reduced on the cathode to generate the intermediate Ar-Ni^{II} **D**. Meanwhile at the anode, the substrates **7** was oxidised to provide the radical **E**. Then **D** combined with **E** to form Ar-Ni^{III}-Bn species **F**. Finally, **F** underwent reductive elimination to provide the cross-coupling product **9** and regenerated the Ni^I catalyst.



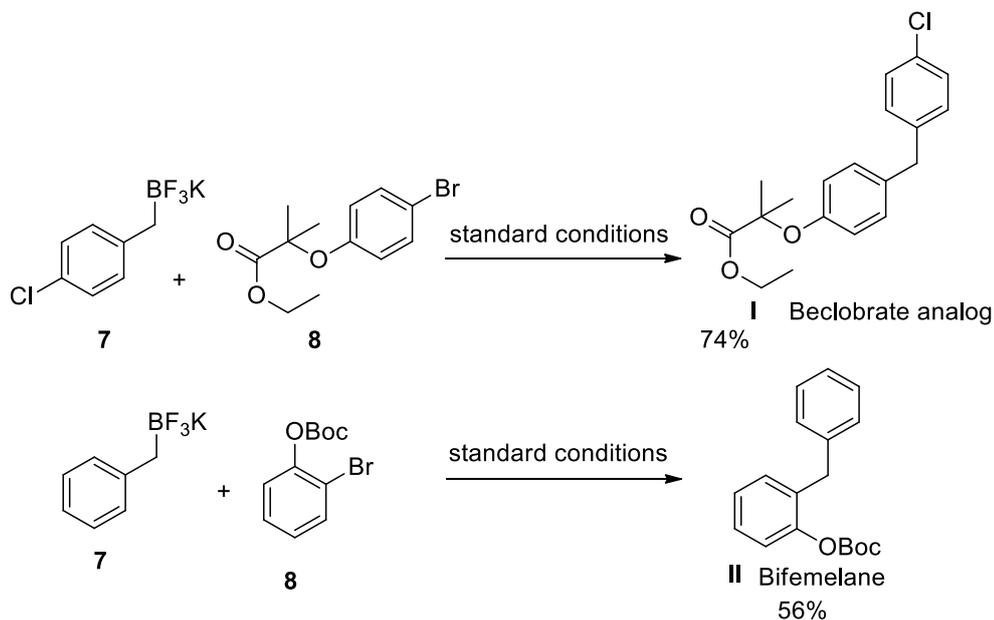
Scheme 3. Ni-catalysed convergent paired electrosynthesis for the direct arylation of benzylic C-H bonds.



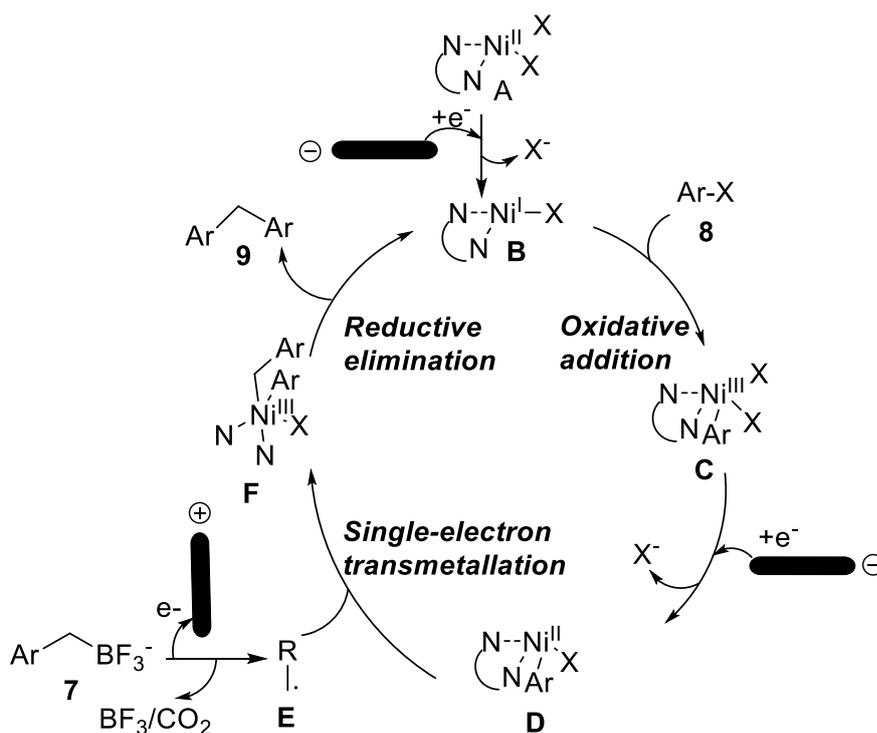
Scheme 4. Plausible mechanism for the Ni-catalysed convergent paired electrosynthesis for the direct arylation of benzylic C-H bonds.



Scheme 5. The Ni-catalysed electrochemical method for C(sp²)–C(sp³) cross-coupling convergent paired reactions.

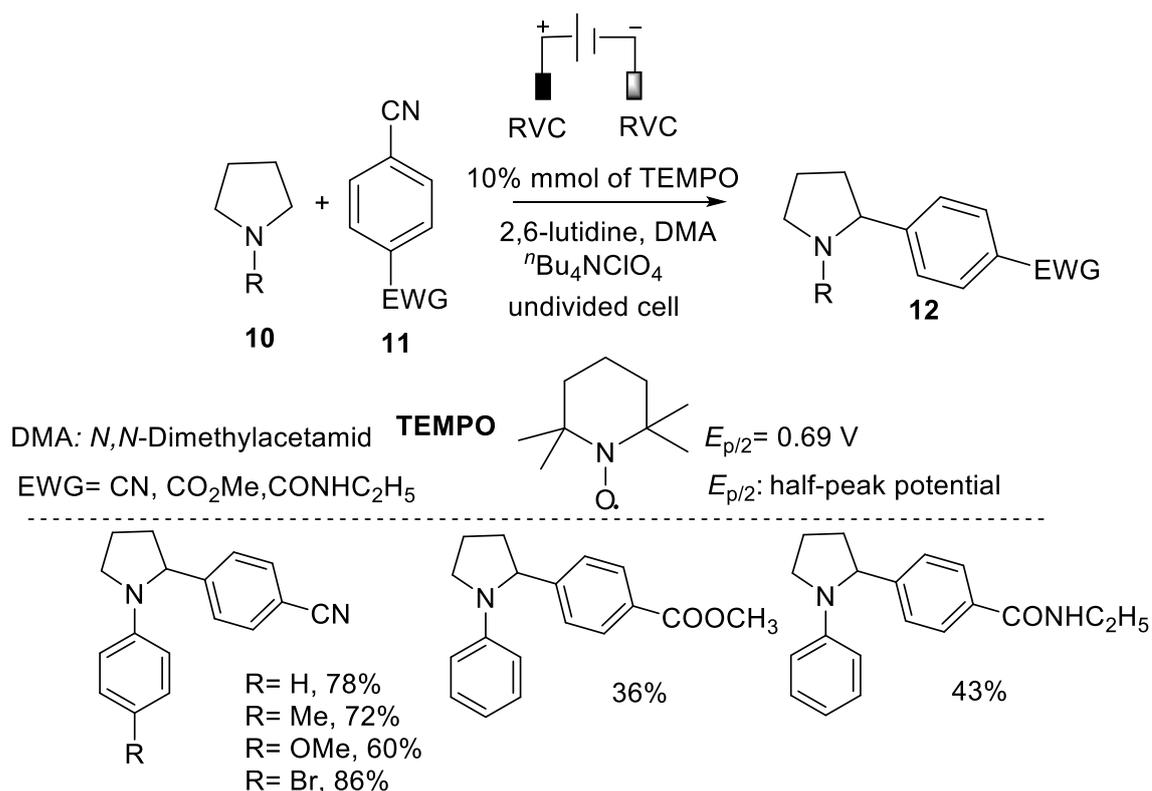


Scheme 6: Applications of the Ni-catalysed electrochemical C(sp²)–C(sp³) cross-coupling reaction. Electrosynthesis of pharmaceutical molecules Beclobrate analog (I) and Bifemelane (II).

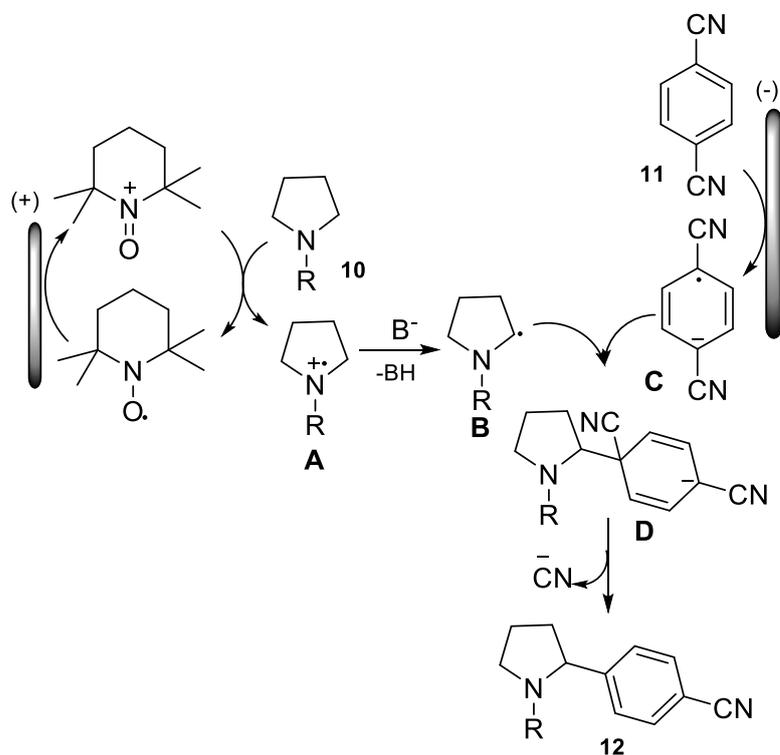


Scheme 7. Plausible mechanism for Ni-catalysed electrochemical method for C(sp²)–C(sp³) cross-coupling convergent paired reactions.

In 2019, Ye and co-workers reported an interesting TEMPO-mediated convergent paired electrolysis for the synthesis of pyrrolidinbenzoxonitrile derivatives **12**.⁵⁰ The cross-coupling reaction was performed for the arylation of cyclic tertiary amine **10** by dicyanobenzene derivatives **11**. The aromatic groups with electron-donating moieties such as Me, MeO and electron-withdrawing groups (EWG) such as Cl, Br, and CO₂Me, were tolerated in this transformation with yields of up to 86% (**Scheme 8**). The transformation's weakest results were for some electron-deficient heteroaromatic compounds, such as 4-cyanopyridine, 1-isoquinolinecarbonitrile, 2-chlorobenzoxazole, and 2-chlorobenzothiazole, which were not compatible with this convergent paired synthesis. The reaction proceeded in an undivided cell at a constant current in *N,N*-dimethylacetamide (DMA) in the presence of 2,6-lutidine as a base, using carbon electrodes as both anode and cathode. The plausible convergent mechanism in **Scheme 9** shows that firstly, TEMPO was oxidised on the anode to produce TEMPO⁺. This then catalysed the oxidation of tertiary amine **10** to produce intermediate radical cation **A**, which was then deprotonated by a base to give amino radical **B**. Concurrently, on the cathode, substrates **11** were reduced to form anion radical **C**, which coupled with **B** to produce intermediate **D**. Finally, the elimination of a CN anion gave the final products **12**.



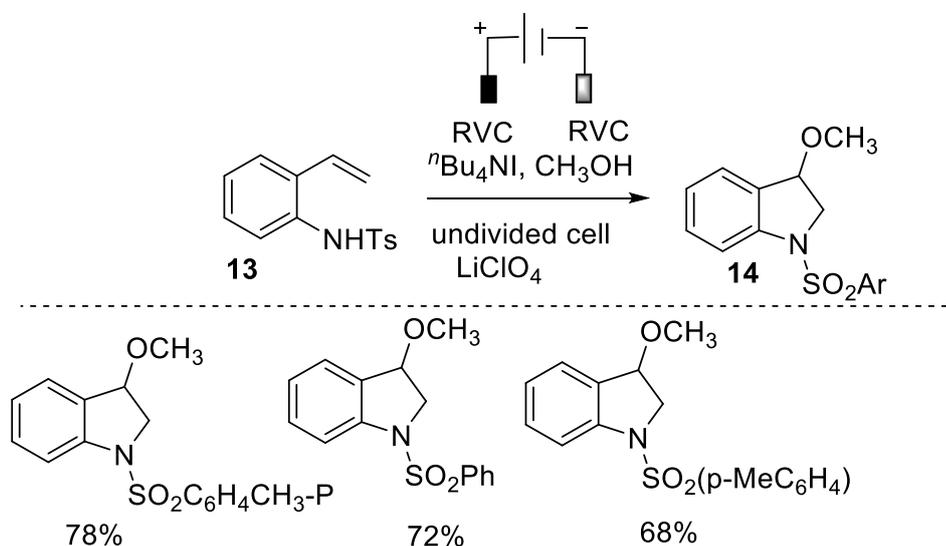
Scheme 8. TEMPO-mediated convergent paired electrolysis for the synthesis of pyrrolidinbenzoxonitrile derivatives.



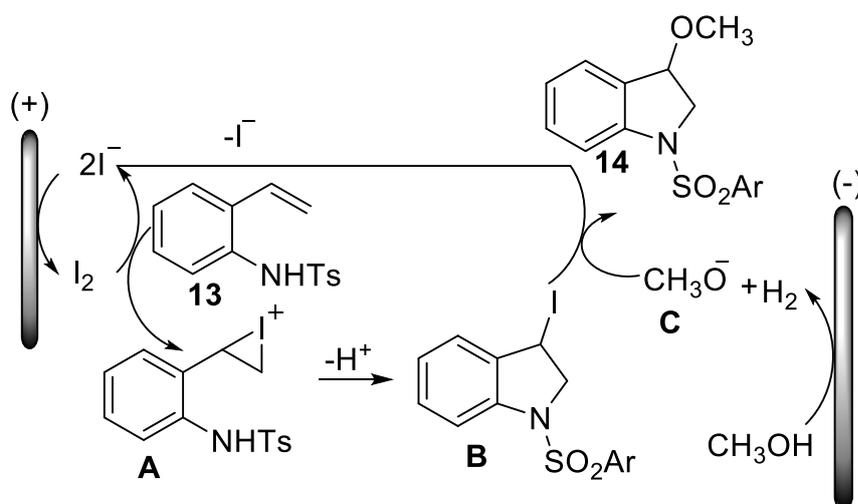
Scheme 9. Plausible mechanism for TEMPO-mediated convergent paired electrolysis for the synthesis of pyrrolidinbenzoxonitrile derivatives.

Iodide-mediated convergent paired synthesis of indoline **14** has been described by Liang and co-workers in 2016.⁵¹ Under mild conditions, the electrolysis of toluenesulfonamide derivatives **13** in an undivided cell with graphite plates as the electrodes provided the

desired products **14** in moderate to good yields, with a wide range of functional groups tolerated (**Scheme 10**). The results show that the combination of $n\text{Bu}_4\text{NI}$ as a redox catalyst with MeOH as a solvent affords the optimal yields. Several catalysts were tested, such as KI, NaI, or NH_4I ; notably lower yields were obtained compared to $n\text{Bu}_4\text{NI}$. The authors attributed this result by the good solubility of $n\text{Bu}_4\text{NI}$ in CH_3OH compared to other salts. Moreover, the reaction could not be conducted with NaCl, NaBr, or NH_4Br as the redox catalyst. For the reaction protocol, with the redox catalyst, the electrolyte LiClO_4 was used to increase the conductivity of the reaction medium. However, large quantities of it led to separation problems and the production of unwanted waste materials. The convergent paired plausible mechanism is shown in **Scheme 11**. The reaction began with the anodic oxidation of iodide, leading to molecule iodine, which reacted with the substrate **13** to provide cyclic iodonium intermediate **A**. Then, the intramolecular nucleophilic attack of the sulfonamide nitrogen on the cyclic iodonium gave the cyclic intermediate **B**. Meanwhile, on the cathode methanol was reduced to form methoxide anion **C**. Finally, the coordination of **B** with **C** gave the final product **14**.

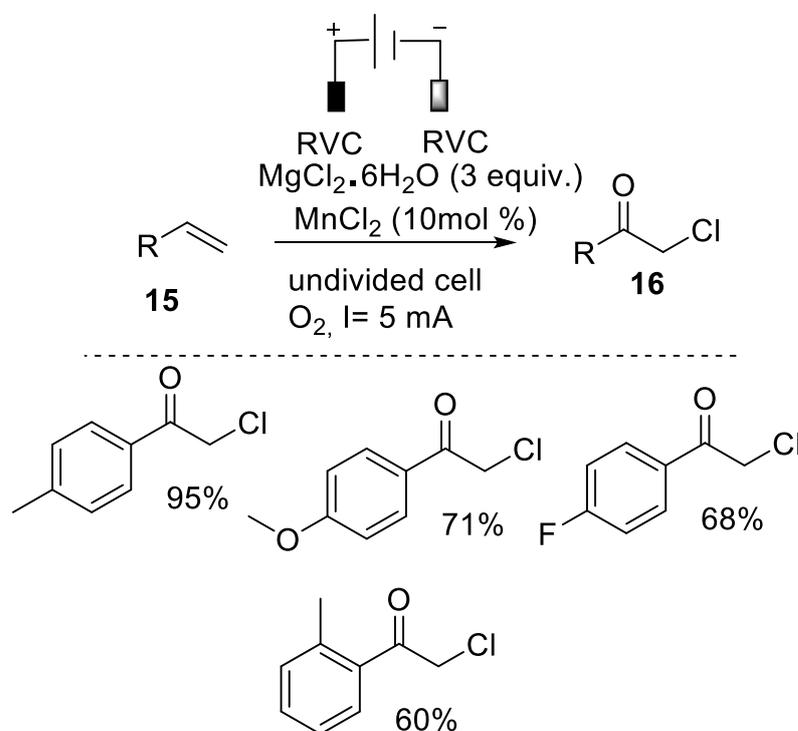


Scheme 10. Iodide-mediated convergent paired synthesis of indoline.

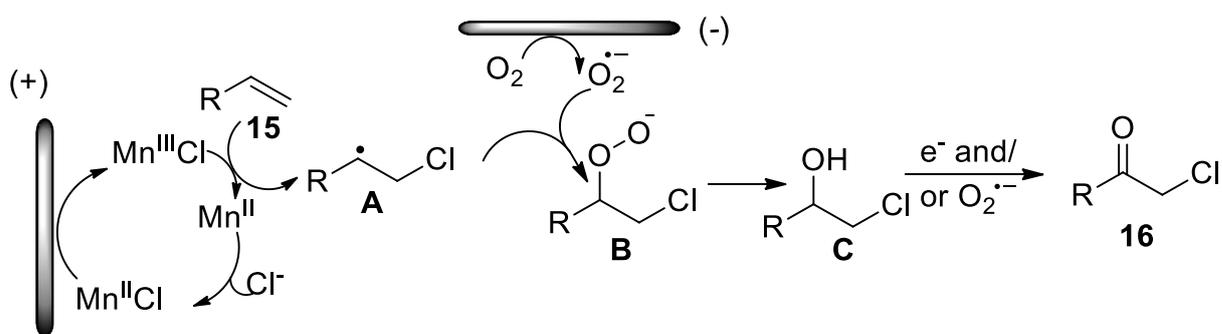


Scheme 11. Plausible mechanism for iodide-mediated convergent paired synthesis of indoline.

Manganese (Mn)-mediated convergent paired electrosynthesis was reported in 2019 by the Chen group to synthesise chloroacetophenone derivatives **16** (Scheme 12).⁵² Electrolysing styrene derivatives **15** in the presence of O₂ gas and MgCl₂ at a constant current afforded a large family of desired products **16** in good yields. Different functional groups such as MeO, Me, F could be tolerated in this transformation with yields of up to 90%. The reaction proceeded in an undivided cell equipped with RVC as anode and cathode, using acetone-DCM/LiClO₄ as a solvent/electrolyte, for 12 h. Acetone and acetonitrile were found to be less efficient; the authors attributed their unsuccessful use to their conductivity. Notably, the experimental results show that electrolytes played a key role in this transformation, i.e. if tetrabutylammonium tetrafluoroborate (ⁿBu₄NBF₄) and potassium hexafluorophosphate (KPF₆) were employed, the desired product was formed with 10% and 32%, respectively. The authors proposed the following convergent paired mechanism (Scheme 13). The transformation commenced with the anodic oxidation of Mn^{II}Cl to yield Mn^{III}Cl. Then styrene derivatives **15** reacted with Mn^{III}Cl to give intermediate **A**. Simultaneously, at the cathode O₂ was reduced to form superoxide, which reacted with **A** to form intermediate **B**. This later decomposed to form compound **C** which, after further oxidation (on the anode or by O₂), gave the final products **16**.

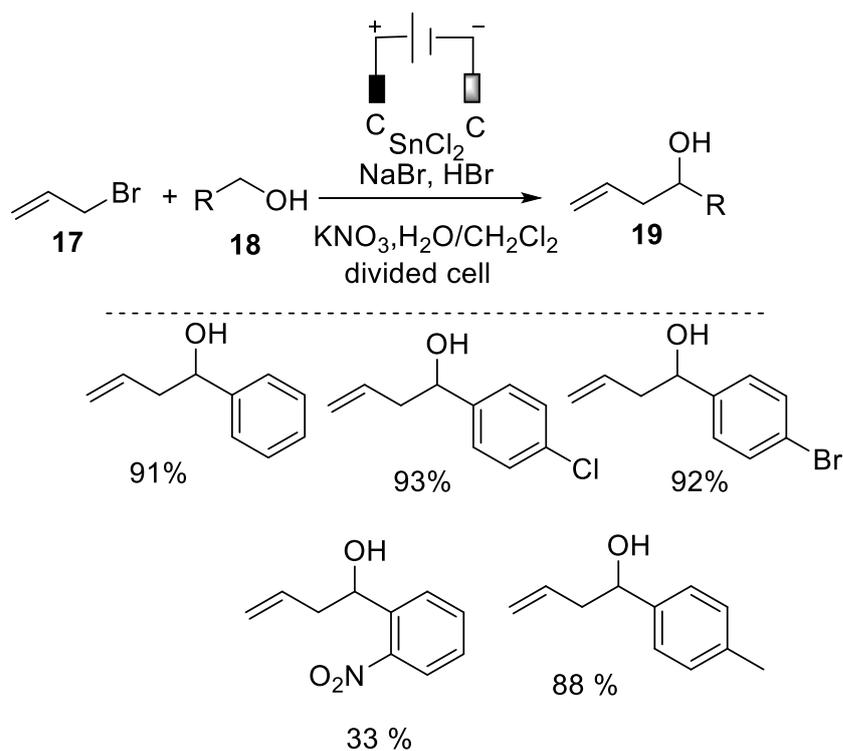


Scheme 12. Manganese (Mn)-mediated convergent paired electrosynthesis of chloroacetophenone derivatives.

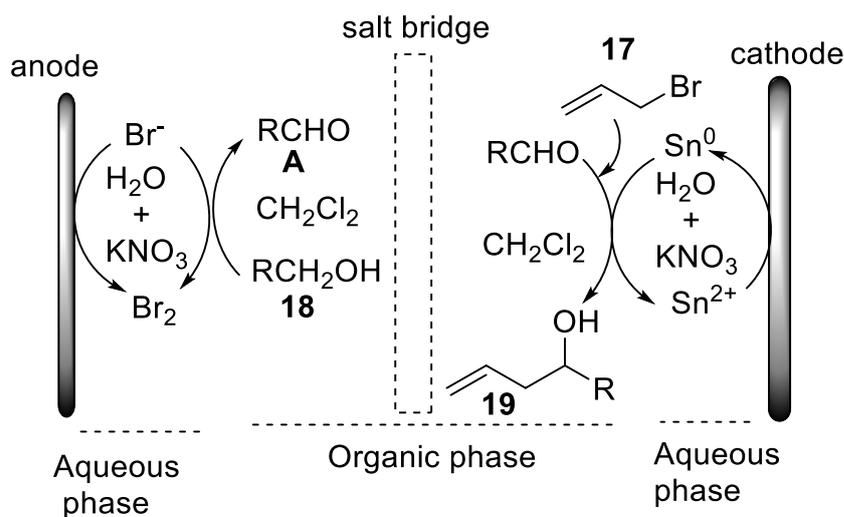


Scheme 13. Plausible mechanism for (Mn)-mediated convergent paired electrosynthesis of chloroacetophenone derivatives.

Zhang and co-workers reported the mediated paired electrosynthesis of homoallylic alcohols **19** in 2010.⁵³ The reaction proceeded with Br^- as a catalyst for the oxidation and Sn as a reduction catalyst (**Scheme 14**). Alcohols **18** with propargylic bromide **17** provided desired products **19** in good yields of up to 93%. It was found that para- NO_2 and para- CH_3 substituents on the benzylic alcohol gave lower yields. However, ortho- NO_2 substitution had a negative effect on this allylation. The reaction was conducted in a divided cell using graphite electrodes as both electrodes in a mixture of water and dichloromethane as a solvent, under a controlled potential. The applied potential should be exactly 0.6 V. When it was below 0.6 V, Sn^{2+} was reduced slowly on the cathode, coating on the electrode tightly, making it difficult for the tin to peel off from the electrode into the solution and retarding further electrolysis. At the same time on the anode, Br^- could not be oxidised. When the potential was over 0.6 V vs. SCE, by-products were formed. Importantly, reducing the amount of SnCl_2 and NaBr didn't affect the yielding reaction, and could be reused five times without loss in catalytic activity. The convergent paired mechanism of this methodology in **Scheme 15** shows that the reaction started at the anode, by the oxidation of Br^- to Br_2 , which mediated the alcohols oxidation to the corresponding aldehyde **A**. Meanwhile at the cathode, Sn^{2+} is reduced to Sn, which catalysed the reaction between allyl bromide **17** and carbonyl compounds **A** to provide the final product **19**.



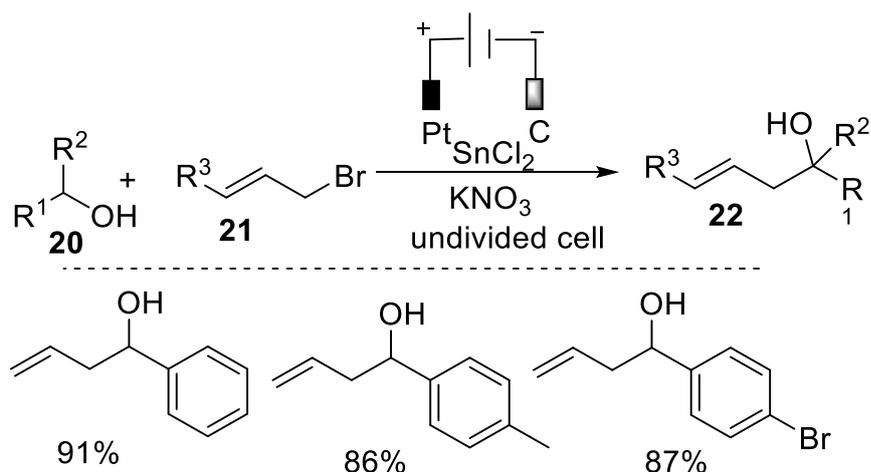
Scheme 14. The mediated paired electrosynthesis of homoallylic alcohols.



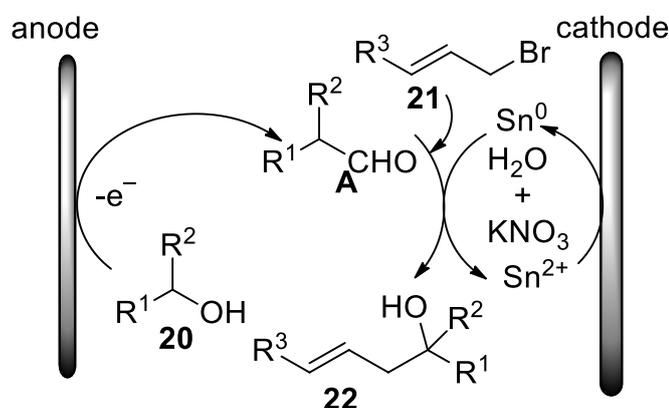
Scheme 15. Plausible mechanism for the mediated paired electrosynthesis of homoallylic alcohols.

Given the considerable interest the Zhang group had in homoallylic alcohol formation⁵⁴ in the presence of some catalytic redox mediator,⁵³ such as SnCl₂ and NaBr, they recently attempted the electrosynthesis of homoallylic alcohols from alcohols directly to exclude the oxidation reaction catalyst (**Scheme 16**).⁵⁵ The authors proved that a platinum anode can oxidise the alcohols **20** to the corresponding aldehyde **A** under catalyst-free conditions. The reaction was performed in an undivided cell at a constant current for 6 h. The results show that high yields were obtained when KNO₃ was used as an electrolyte and by the combination of the platinum anode with a carbon cathode. **Scheme 17** shows the plausible mechanism for the paired synthesis; the reaction started with the oxidation of alcohols **20** without a catalyst to give the corresponding aldehyde **A** after losing two electrons, whereas

the cathodic reduction of SnCl_2 provides Sn. Then the formed aldehyde **A** reacted with Sn and allyl bromide **21** to provide the final product **22**.



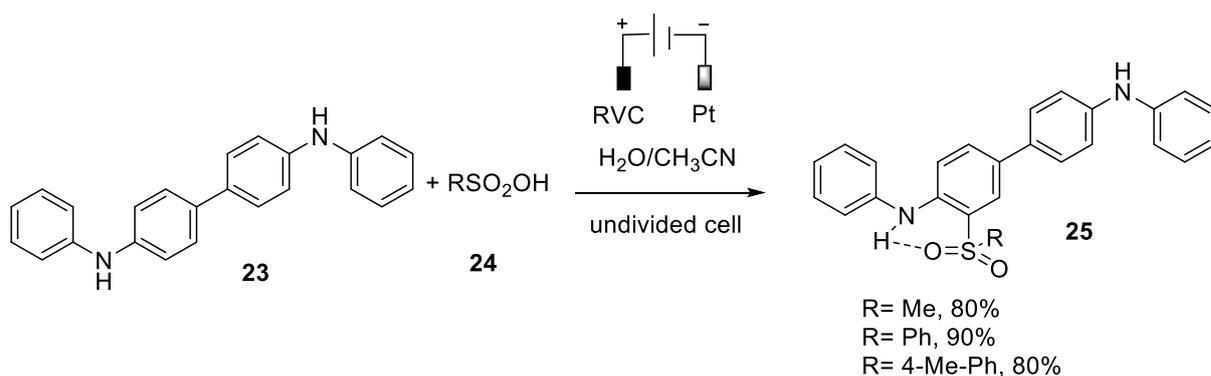
Scheme 16. The paired electrosynthesis of homoallylic alcohols.



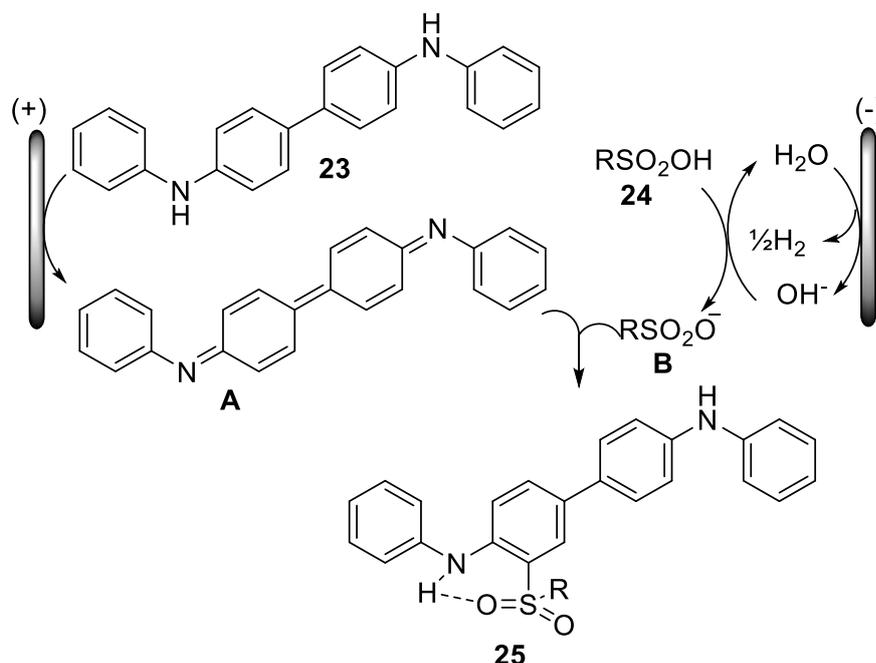
Scheme 17. Plausible mechanism for the paired electrosynthesis of homoallylic alcohols.

Non-mediated electrolysis

In 2016 the Nikpour group reported an excellent approach for the convergent paired electrosynthesis of *N,N'*-diphenyl-3-sulfonyl-biphenyl-diamines (**Scheme 18**).⁵⁶ Under mild condition, *N,N'*-diphenylbenzidazine **23** and sulfinic acids **24** afforded a limited scope of four families of desired products **25** with yields of up to 90%. The electrolysis was performed in an undivided cell at a constant current equipped with a graphite plate as anode and a platinum plate as the cathode. The experimental study showed that high yields were obtained with current densities of 0.4 mA cm^{-2} . With lower current densities the oxidation step of **23** is difficult to carry out and gives lower yields. Higher current densities resulted in the occurrence of some side reactions such as the oxidation of water, the nucleophile and the product, and consequently, a decrease in the product yields and energy efficiencies. The convergent paired mechanism in **Scheme 19** shows that firstly, *N,N'*-diphenylbenzidazine **23** was oxidised at the anode to form intermediate **A**, while at the cathode, water was reduced to provide the hydroxide anion OH^- . This latter deprotonated sulfinic acid **24** to produce the anion intermediate **B**, which condensed with **A** to provide the final product **25**.

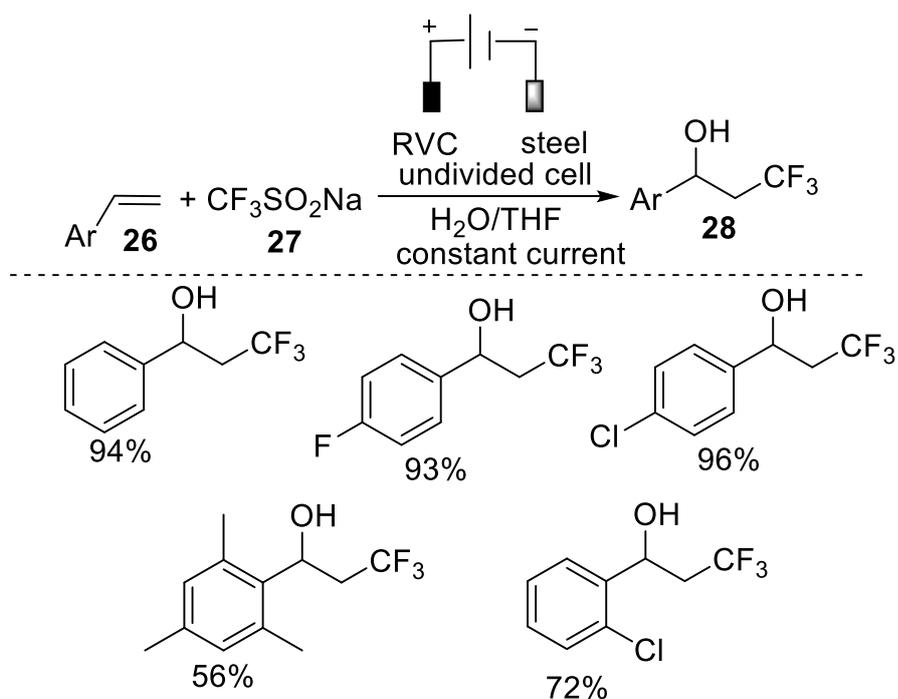


Scheme 18. Convergent paired electrolysis of *N,N'*-diphenyl-3-sulfonyl-biphenyl-diamines.

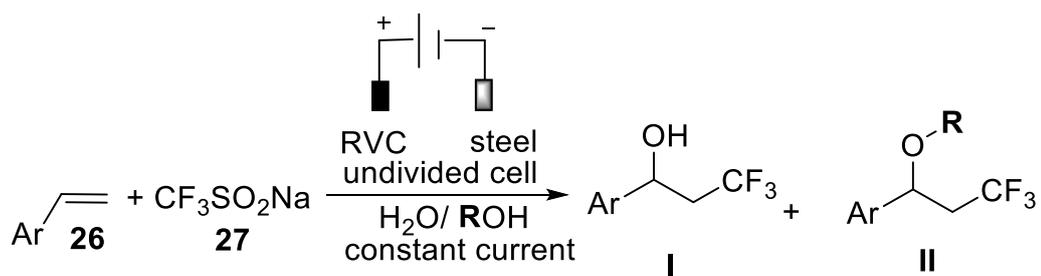


Scheme 19. Plausible mechanism for convergent paired electrolysis of *N,N'*-diphenyl-3-sulfonyl-biphenyl-diamines.

In 2018 the Cantillo group reported an elegant strategy for catalyst-free convergent paired electro-synthesis of 1-hydroxy-2-trifluoromethyl derivatives **28**.⁵⁷ Sodium triflate **27** with alkene **26** derivatives afforded a large variety of desired products **28** in moderate to good yields (**Scheme 20**). The reaction was conducted in an undivided cell equipped with a carbon anode and a steel cathode, at a constant current using the mixture of THF/ H₂O as a solvent. The authors also tested the reactions in alcohols as nucleophilic solvents to evaluate the extent of alkoxytrifluoromethylation production (**Scheme 21**). The proportion of alkoxytrifluoromethylated compounds **I** and **II** due to their low boiling points. **Scheme 22** demonstrates the plausible mechanism for the convergent paired reaction. The reaction commenced by the anodic oxidation of triflate anion **27** to give a radical intermediate **A** that decomposed to form radical CF₃ with the release of SO₂. Then, CF₃ radical reacted with alkene **26** to form intermediate **B**, which after further oxidation, gave intermediate cation **C**. At the same time on the cathode, water was reduced to hydroxide anion. The latter combined with **C** to provide the final product **28**.

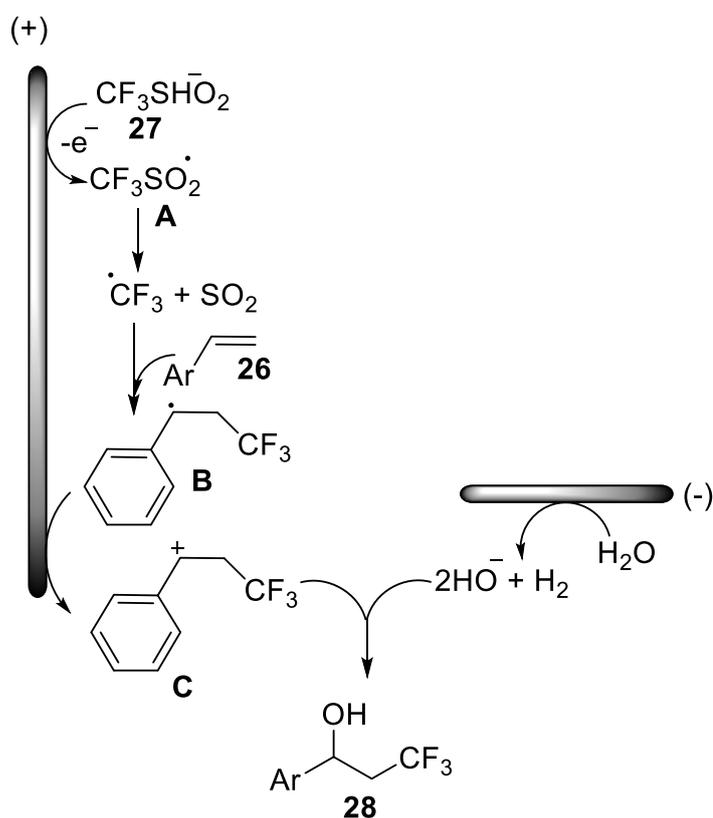


Scheme 20. Convergent paired electrosynthesis of 1-hydroxy-2-trifluoromethyl.



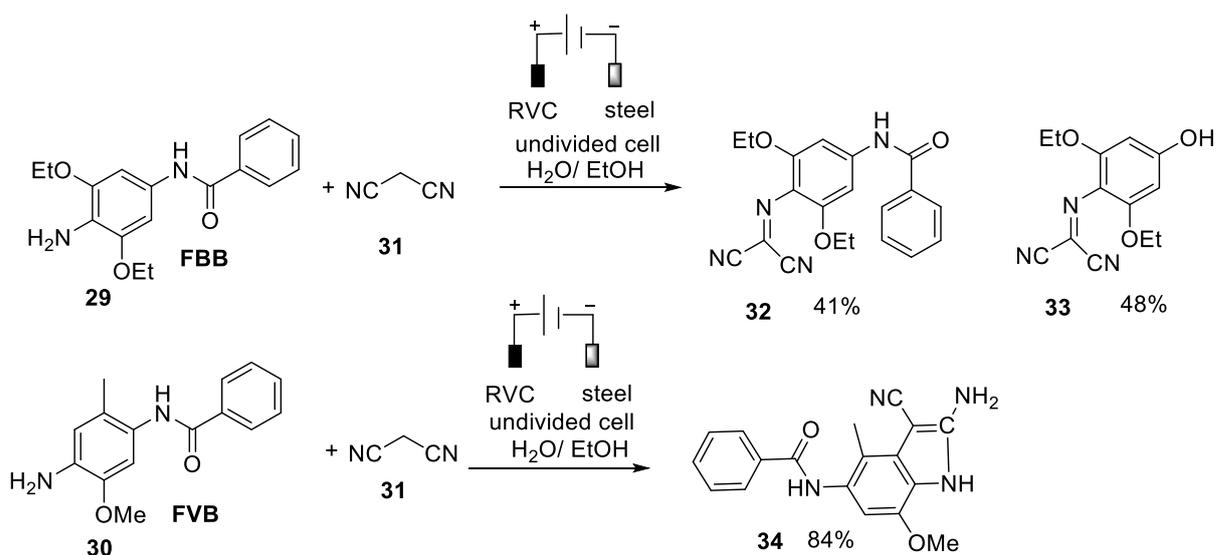
	R= Me	R= Et	R= <i>i</i> Pr
ratios	10:1	7:1	3:1
yields	59%	23%	17%

Scheme 21. Reactions in alcohols as nucleophilic solvents.

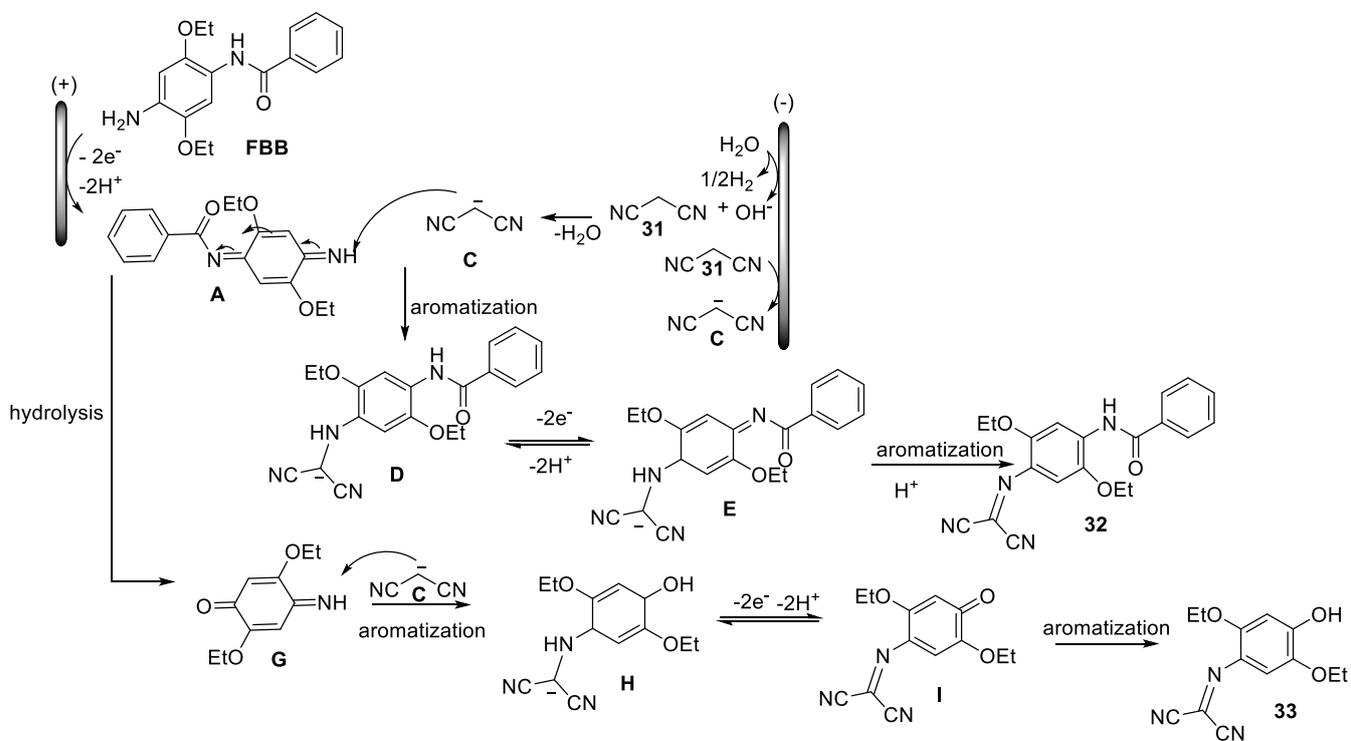


Scheme 22. Plausible mechanism for convergent paired electrosynthesis of 1-hydroxy-2-trifluoromethyl.

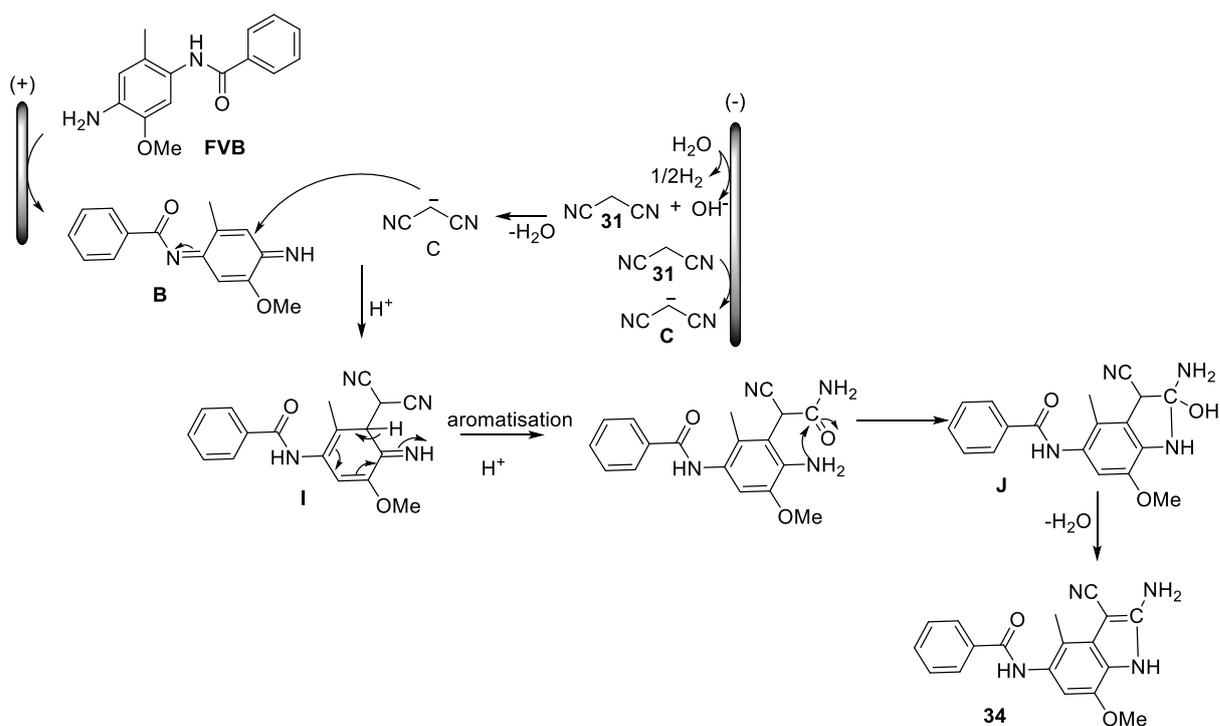
Recently in 2018, Alizadeh and co-workers reported an excellent convergent paired synthesis of phenylcarbonimidoyl dicyanide dyes (**Scheme 23**).⁵⁸ The oxidation of **FVB 30** or **FBB 29** in the presence of malononitrile **31** provided the desired products **32**, **33** and **34** in moderate to good yields. The electrolysis was performed in an undivided cell equipped with a carbon anode and a steel cathode in H₂O/EtOH as a solvent at the applied potential for 0.45 and 0.35 V vs Ag/AgCl when **FBB** and **FVB** substrate were used, respectively. The results showed that **33** exhibits high affinity for nylon and wool fabrics and found that the colour fastness of this dye to rubbing and washing is excellent. It should be noted that antibacterial experiments on **33** and **32** show that these compounds do not have any antibacterial activity at 30 µg/mL against *Salmonella enteritidis* and *Escherichia coli* (Gram-negative), *Bacillus cereus*, and *Staphylococcus aureus* (Gram-positive). The mechanism of this transformation is convergent (**Scheme 24**, **Scheme 25**). At the anode, the oxidation of **FVB** (or **FBB**) provided the intermediate **A** (or **B**). At the cathode, two reactions are possible for the formation of malononitrile anion **C**: i) direct formation via direct reduction of malononitrile **31** on the cathode or ii) by cathodic reduction of water, which afforded a hydroxide anion that can deprotonate malononitrile **31** to form the anion **C**. Then this reacted with **A** to form the intermediate **D** which after further oxidation followed by the aromatisation provided the product **32** (**Scheme 24**). The hydrolysis of **A** followed by the Michael addition reaction of **C** generating anion intermediate **H**, after which further oxidation followed by the aromatisation, provided the product **33**. The addition of **B** to **C** provided the intermediate **I** (**Scheme 25**), which, after aromatisation and hydrolysis, led to intermediate **J**. Subsequent cyclisation and dehydration of **J** led to the product **34**.



Scheme 23. Convergent paired synthesis of phenylcarbonimidoyl dicyanide dyes.

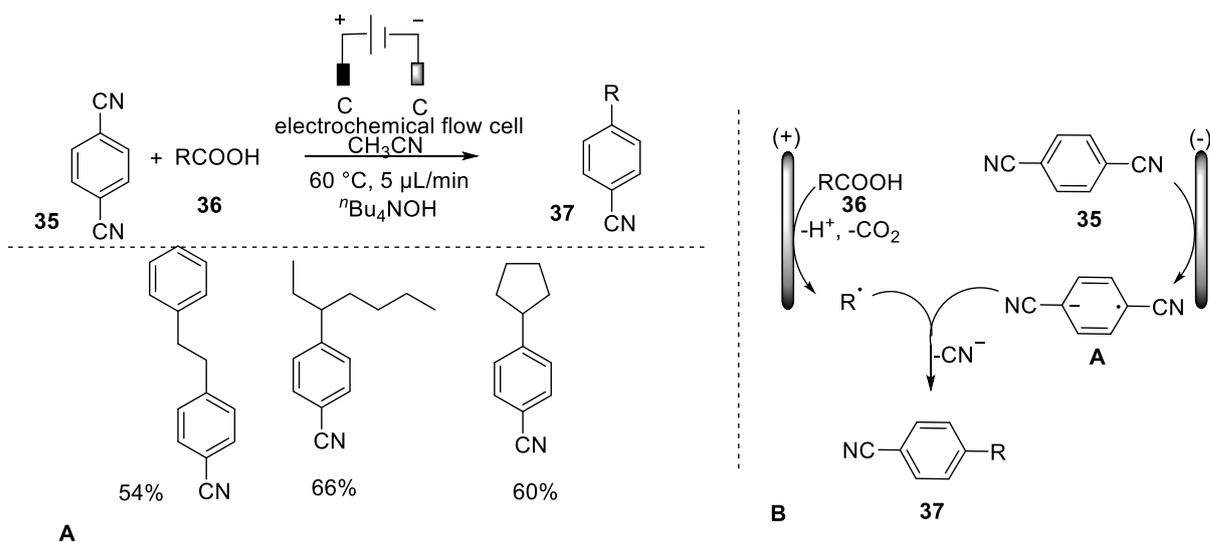


Scheme 24. Plausible mechanism for convergent paired synthesis of phenylcarbonimidoyl dicyanide dyes **32** and **33**.

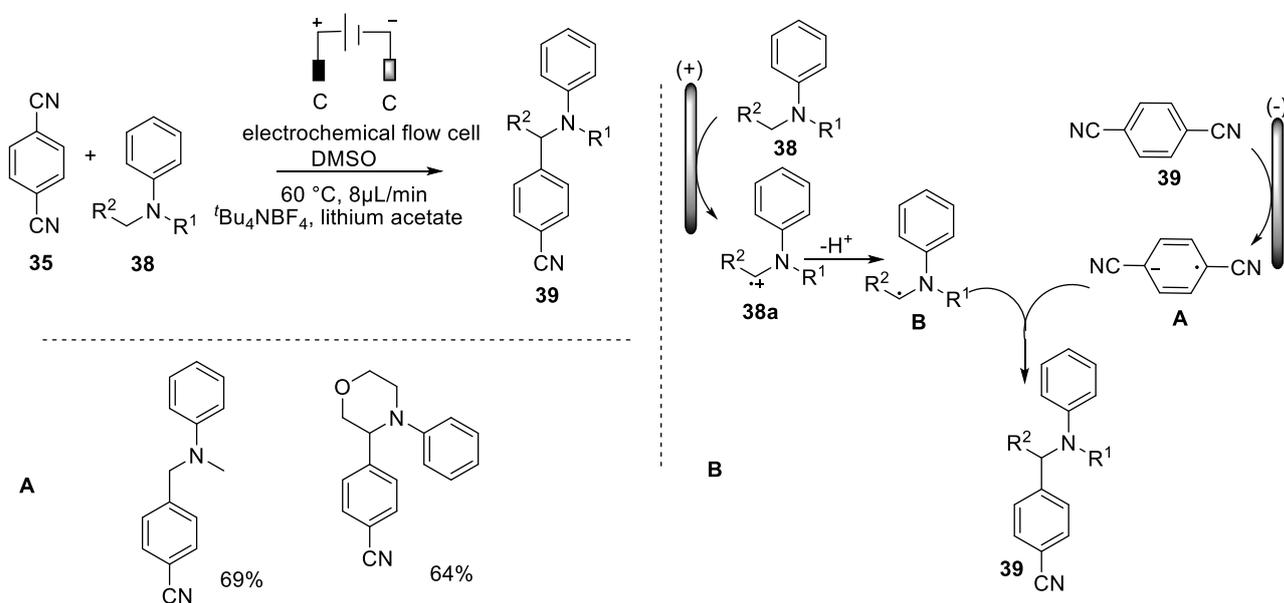


Scheme 25. Plausible mechanism for convergent paired synthesis of phenylcarbonimidoyl dicyanide dyes **34**.

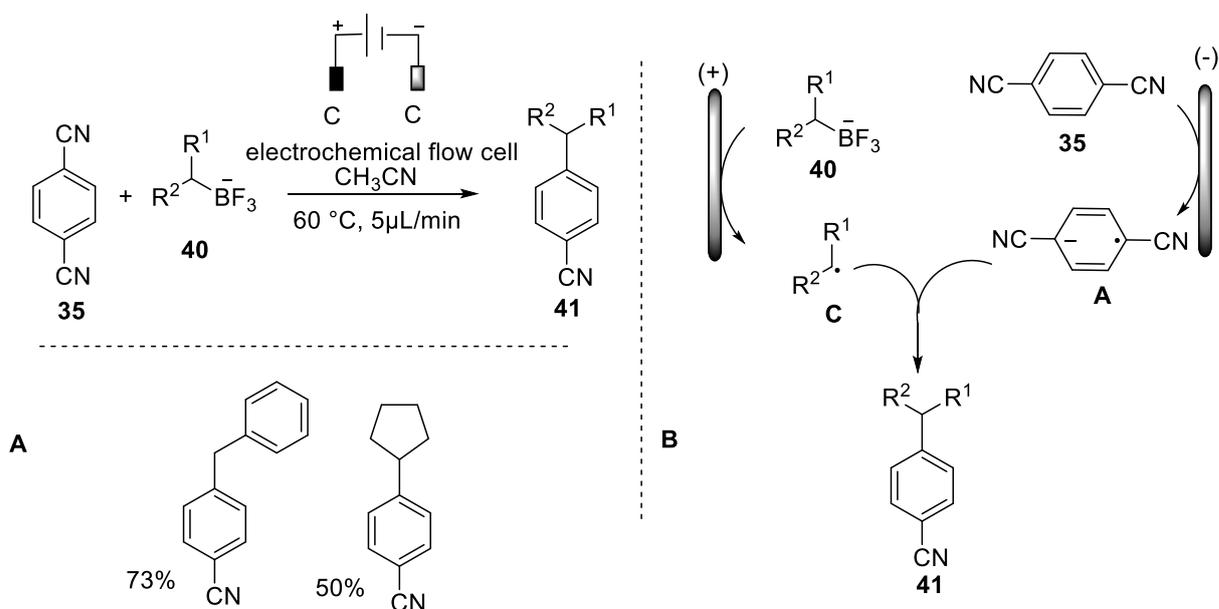
More recently, Jensen and co-workers achieved an elegant method for catalysis-free convergent paired reactions to synthesise a different family of benzonitrile derivatives **37** by decarboxylative arylation, by α -amino C-H arylation or by deboronative arylation.⁵⁹ For decarboxylative arylation reaction (**Scheme 26 A**), the reaction proceeded between aryl nitrile derivatives **35** and carboxylic acid derivatives **36** in CH_3CN at $60^\circ C$, α -amino C-H arylation reaction (**Scheme 27 A**) progressed between 1,4-dicyanobenzene **35** and aniline derivatives **38** in DMSO using tetrabutylammonium tetrafluoroborate as an electrolyte, and for deboronative arylation (**Scheme 28 A**), the reaction took place between trifluoroborate tetrabutylammonium salt **40** and 1,4-dicyanobenzene **35** in CH_3CN at $60^\circ C$. The electrolysis was performed in an electrochemical flow cell using glassy carbon as both electrodes. In addition, this transformation occurs without an additional supporting electrolyte because of the excellent conductivity in the microfluidic reactor. In the microfluidic cell, the interelectrode radical transport is primarily controlled by molecular diffusion. However, the carboxylic acid should be used in excess of 6 equiv. Nevertheless, different substrates such as aniline, nitriles derivatives, and trifluoroborate tetrabutylammonium were well tolerated in this transformation with high yields. The convergent paired mechanism of these transformations (**Scheme 26 B**, **27 B** and **28 B**) shows that the cathode and anode simultaneously generated the corresponding reactive persistent intermediates radicals, which reacted together, yielding the desired products **37**, **39**, **41**. This selective transformation is explained by the rapid molecular diffusion through a microfluidic channel that outpaces the decomposition of the intermediates radicals.



Scheme 26. A. Convergent paired reactions for decarboxylative arylation, **B.** Plausible mechanism for decarboxylative arylation.

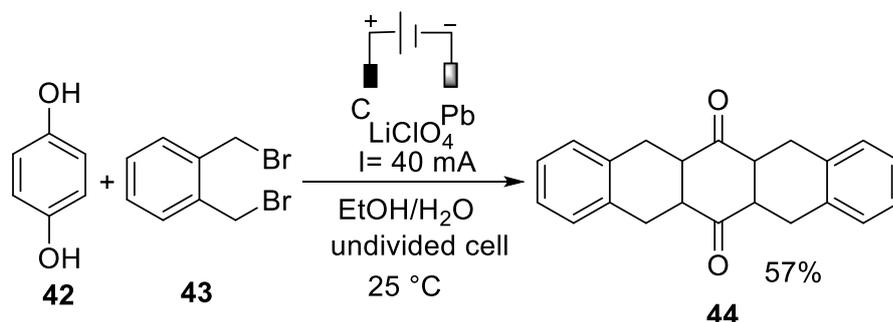


Scheme 27. A. Convergent paired reactions for α -amino C-H arylation, **B.** Plausible mechanism for α -amino C-H arylation.

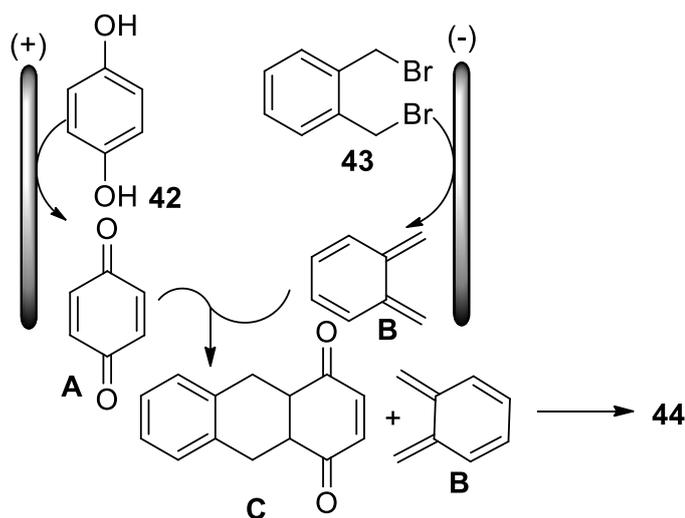


Scheme 28. **A.** Convergent paired reactions for deboronative arylation. **B.** Plausible mechanism for deboronative arylation

Habibi *et al.* reported, in 2010, a new green synthetic approach to achieve the convergent paired electrosynthesis of octahydropentacene-6,13-dione **44**.⁶⁰ The cathodic reduction of 1,2-bis(bromomethyl)benzene **43** with the anodic oxidation of 1,4-hydroquinone **42** provided the final product **44** in 57% yield (**Scheme 29**). The reaction proceeded in an undivided cell equipped with a graphite electrode as an anode and Pb as the cathode, using ethanol/water as a solvent under a constant current. A limited scope of Diels-Alder transformation was noticed, only one example of which was reported. Nevertheless, a catalyst was not required for this transformation, and the final product was formed with high yield and good selectivity. A mechanistic elucidation for this methodology in **Scheme 30** shows that the anodic oxidation of phenol **42** gave hydroquinone **A**. Meanwhile, on the cathode, the substrate **43** was reduced to form dimethylenecyclohexa-1,3-diene **B**. Then, the coordination between intermediate **B** and **A** gave **C**. Finally, **C** reacted with other molecules of **B** to provide the final product **44**.

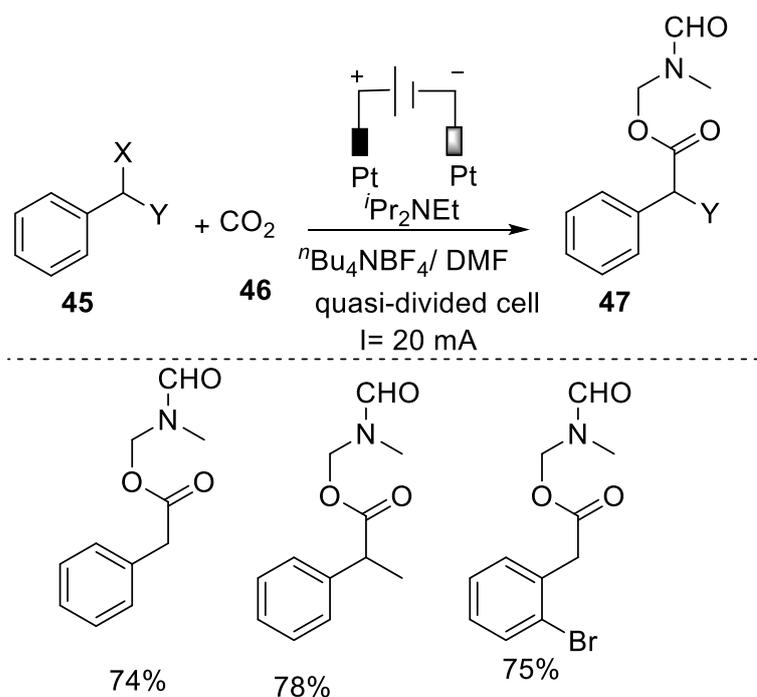


Scheme 29. The convergent paired green electrosynthesis of octahydropentacene-6,13-dione.

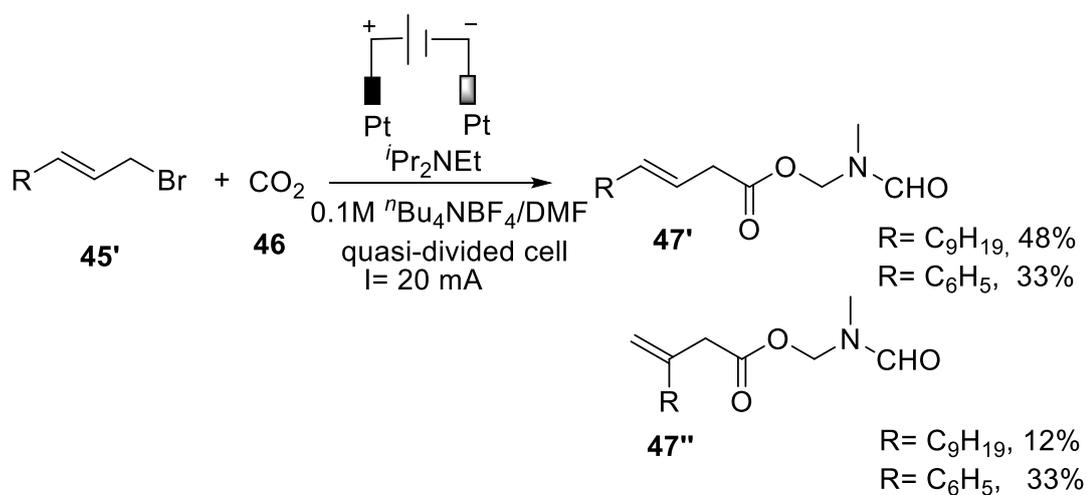


Scheme 30. Plausible mechanism for the convergent paired green electrosynthesis of octahydropentacene-6,13-dione.

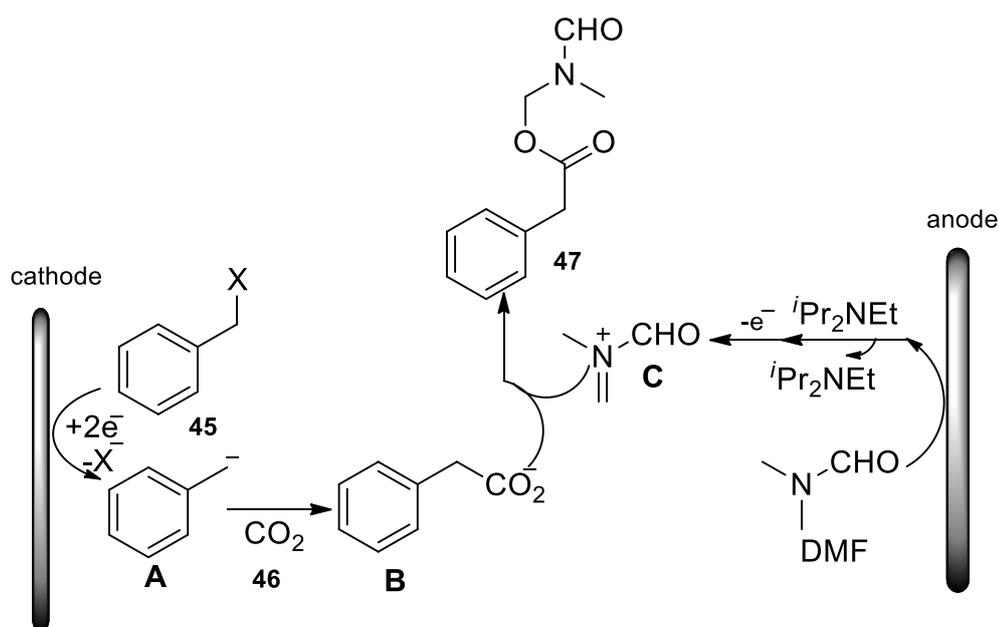
In 2015, Senboku and co-workers reported an efficient convergent electrosynthesis of (*N*-methylformamido) methyl 2-phenylacetate derivatives **47** (**Scheme 31**),⁶¹ Electrolysing benzylic halides **45**, carbon dioxide **46**, and DMF at a controlled potential led to the desired products **47** in yields of up to 78%. Allylic bromides can also be applied to this transformation, although the electrochemical carboxylation of allylic bromides **45'** gave an inseparable isomeric mixture of β,γ -unsaturated carboxylic acids **47'** and **47''** (**Scheme 32**). Nevertheless, the electrolysis was successfully applied for the synthesis of an ibuprofen derivative, which is well known as a non-steroidal anti-inflammatory agent. The reaction was performed in a quasi-divided cell equipped with platinum electrodes both as a cathode and anode. The plausible convergent mechanism in **Scheme 33** shows that the cathodic reduction of benzyl halides results a benzylic anion **A**. This later attacked carbon dioxide to provide the carboxylate ion **B**. Concurrently, the anodic oxidation of DMF followed by deprotonation and further oxidation gave *N*-acyliminium ion **C**. Finally, the combination of intermediate **B** with **C** gave the final products **47**.



Scheme 31. The convergent electrosynthesis of (*N*-methylformamido) methyl 2-phenylacetate derivatives.

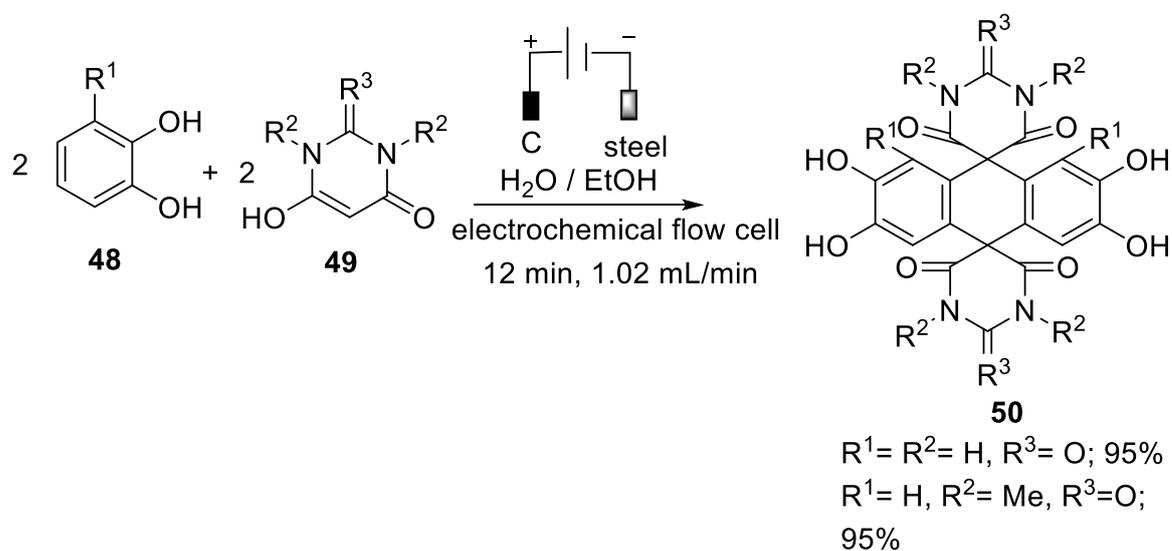


Scheme 32: The convergent synthesis of inseparable isomeric mixture of β,γ -unsaturated carboxylic acids.

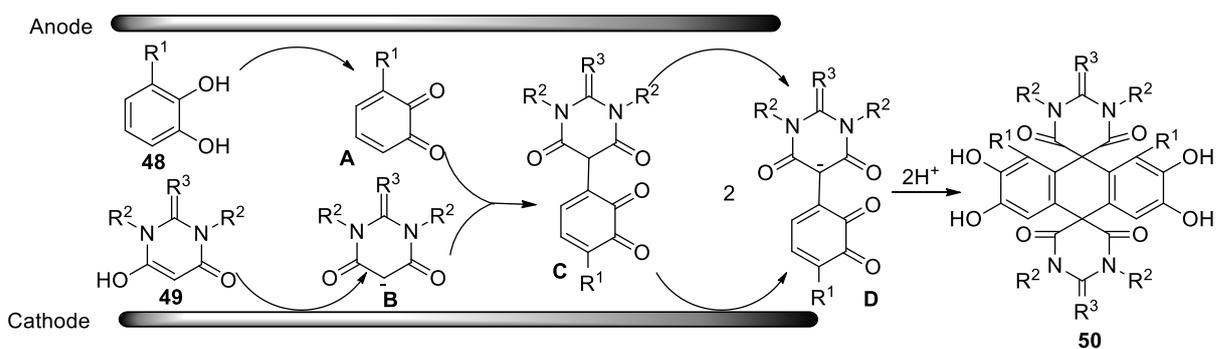


Scheme 33. Plausible mechanism for the convergent electrosynthesis of (*N*-methylformamido) methyl 2-phenylacetate derivatives.

Recently in 2020, Nematollahi *et al.* reported a new synthetic strategy for the convergent electrosynthesis of pyrimidines derivatives **50** (**Scheme 34**).⁶² A wide range of catechol derivatives **48** with barbituric acid **49** could afford the desired products **50** in excellent yields of up to 95%. The reaction proceeded in an electrochemical flow cell under a constant current; a steel electrode was used as a cathode and a carbon rod as the anode using H₂O/EtOH as a solvent. Moreover, this reaction was performed in the absence of any electrolytes and occurred within a short time window of 8-12 min. The convergent mechanism took place at the anode and the cathode (**Scheme 35**). Firstly, the anodic oxidation of catechol derivatives **48** gave diones intermediate **A**, and the reduction of barbituric acid **49** afforded the intermediate **B**, which then combined with intermediate **A** to provide intermediate **C**. This later, after further oxidation or reduction, gave intermediate anion **D**. Finally, the protonation of **D** gave the desired product **50**.



Scheme 34. The convergent electrosynthesis of pyrimidines derivatives.

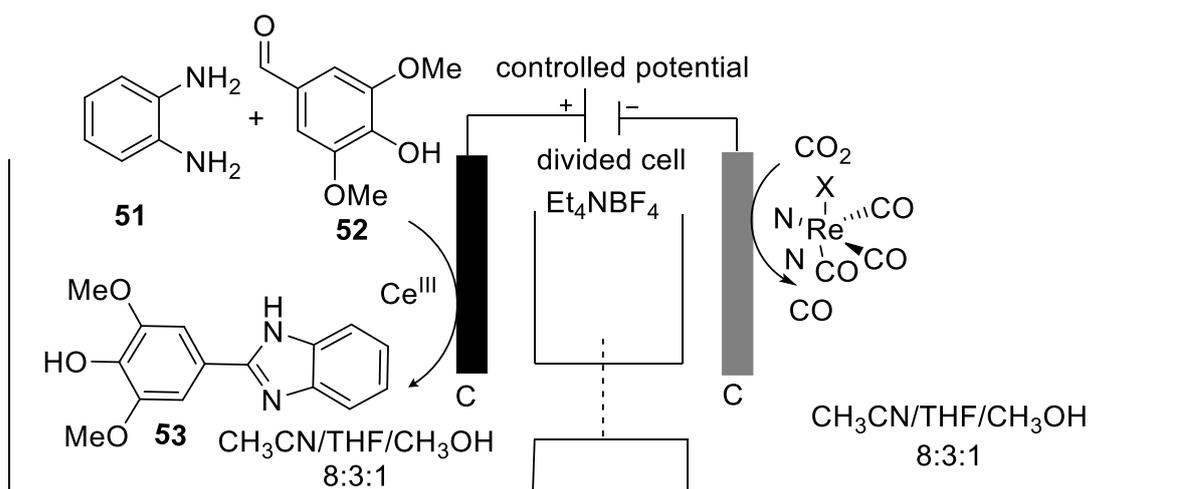


Scheme 35. Plausible mechanism for the convergent electrocatalytic synthesis of pyrimidines derivatives.

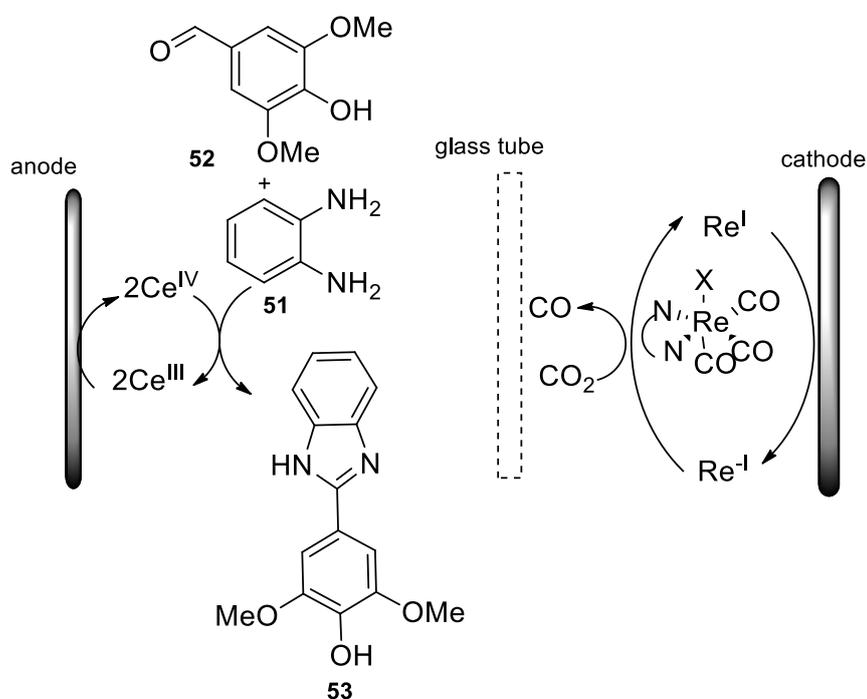
Parallel paired electrolysis

Mediated electrolysis

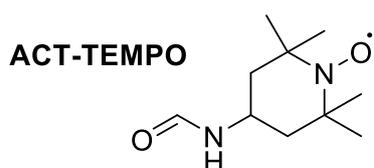
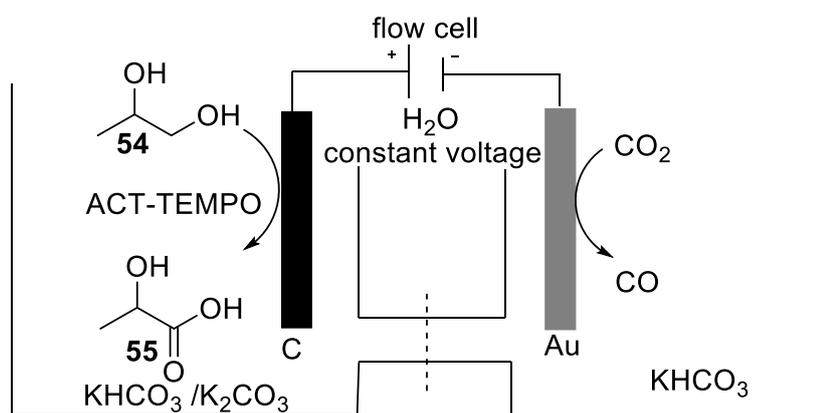
Nowadays, parallel paired electrochemical synthesis has proved useful for industrial application, especially for interesting chemical reactions that convert CO₂ gas into a valuable chemicals and fuels, e.g. CO reagent.⁶³ In 2016, Moeller and co-workers²⁶ reported a parallel paired electroreduction of CO₂ to CO catalysed by (Re(4,4'-di-tert-butyl-2,2'-bipyridine)(CO)₃Cl. The paired synthesis is combined with the electrocatalytic synthesis of 2-(3,5-dimethoxy-4-hydroxyphenyl)-benzimidazole **53** from the oxidation of syringaldehyde **52** and *o*-phenylenediamine **51** by employing Ceric ammonium nitrate as a catalyst (**Scheme 36**). The reaction proceeded in a divided cell equipped with a glassy carbon working electrode for both the cathode and anode in a mixture of CH₃CN: THF: CH₃OH/Et₄NBF₄ as a solvent/electrolyte, under a controlled potential. For this type of paired synthesis, focus should be put onto compatibilities and complementarities of the two half reactions, which should be selected carefully, taking care with the amount of voltage used. As an improvement, the authors suggested a plausible mechanism for this transformation (**Scheme 37**). The reaction at the anode started with the oxidation of Ce^{III} to Ce^{IV}. Then, the coordination of syringaldehyde **52** and *o*-phenylenediamine **51** with Ce^{IV} led to the desired product **53**. Meanwhile at the cathode, the reaction started by the reduction of Re^I to Re^I⁻, which catalysed the transformation of CO₂ to CO. Independently of Moeller's group, Goetheer and co-workers developed an excellent approach for a parallel paired electrocatalytic synthesis of Lactic acid **55** from the oxidation of 1,2-propanediol **54** using 4-acetamido-(2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (ACT-TEMPO) as a catalyst in parallel with the reduction of CO₂ to CO.⁶⁴ The reaction proceeded in a flow cell with two compartments, divided by an anionic exchange membrane, equipped with a gold plate as a cathode and carbon felt as the anode in a solution of KHCO₃ for the cathode compartment and a solution of KHCO₃/K₂CO₃ for the anode compartment, under a constant voltage (**Scheme 38**). The authors demonstrated that when the anodic half-reaction of oxygen evolution was replaced by alcohol oxidation, a lower energy consumption of ~35% and an increase in the total product value of the process would occur. Moreover, this resulted in a faradaic efficiency, for the combined cathodic and anodic processes, of up to 160% compared to the reduction of CO₂ in which oxygen is formed at the anode. As an improvement, the authors suggested a plausible mechanism for this transformation (**Scheme 39**). The cathodic reduction of CO₂ on the Au cathode provided CO. Concurrently, 4-acetamido-(2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (ACT-TEMPO) underwent anodic oxidation to form an oxoammonium ion ACT-TEMPO⁺ whose further interaction with the substrate **54** provided the desired product **55**.



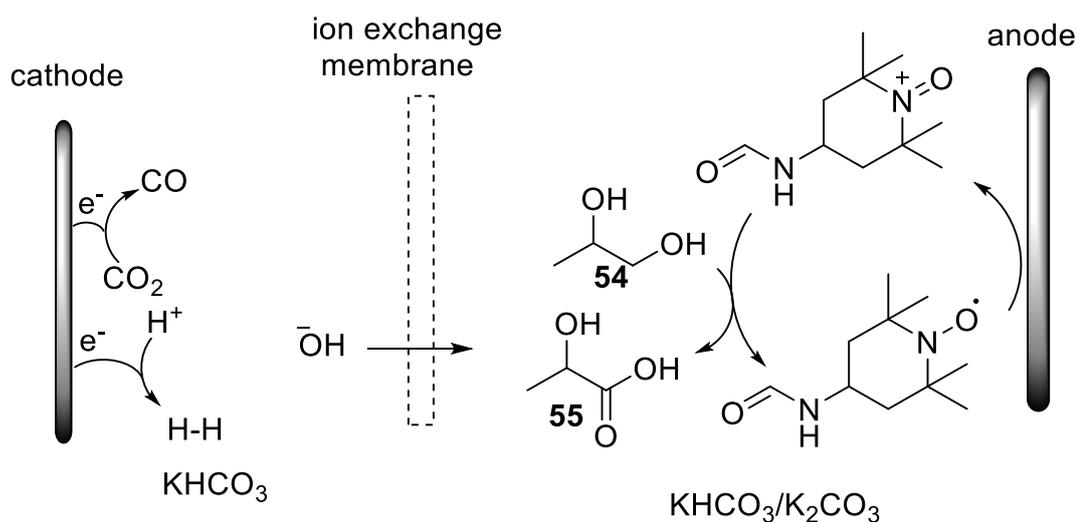
Scheme 36. Parallel paired electrolysis for the formation of 2-(3,5-dimethoxy-4-hydroxyphenyl)-benzimidazole and CO.



Scheme 37. Plausible mechanism for the parallel paired electrolysis for the formation of 2-(3,5-dimethoxy-4-hydroxyphenyl)-benzimidazole and CO.



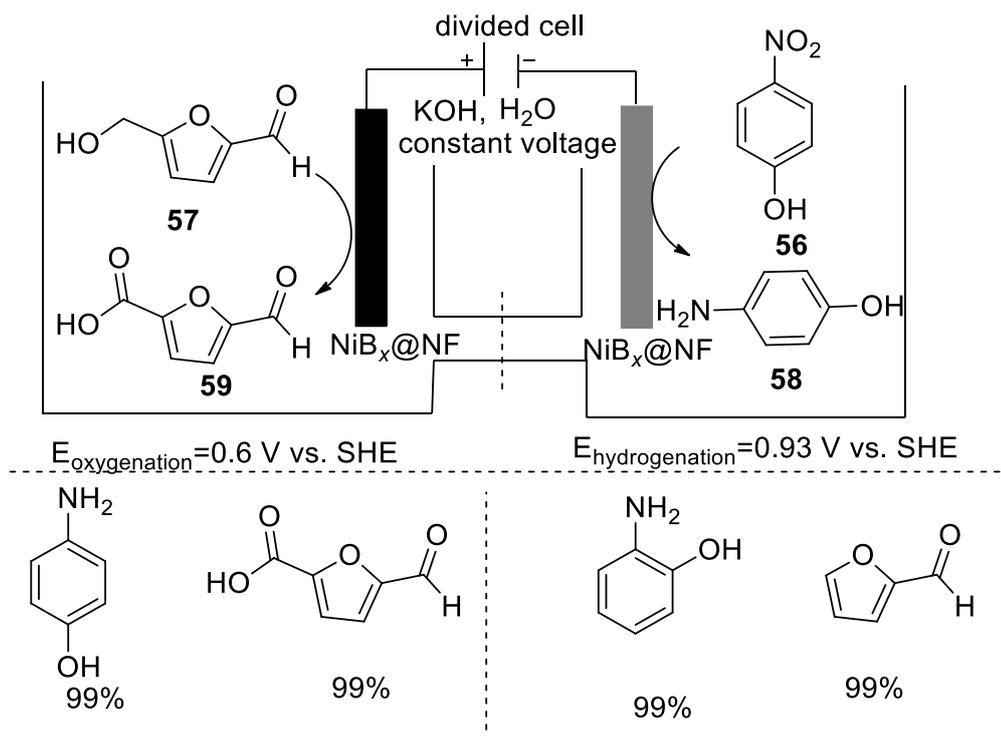
Scheme 38. A parallel paired electrocatalytic synthesis of Lactic acid and CO.



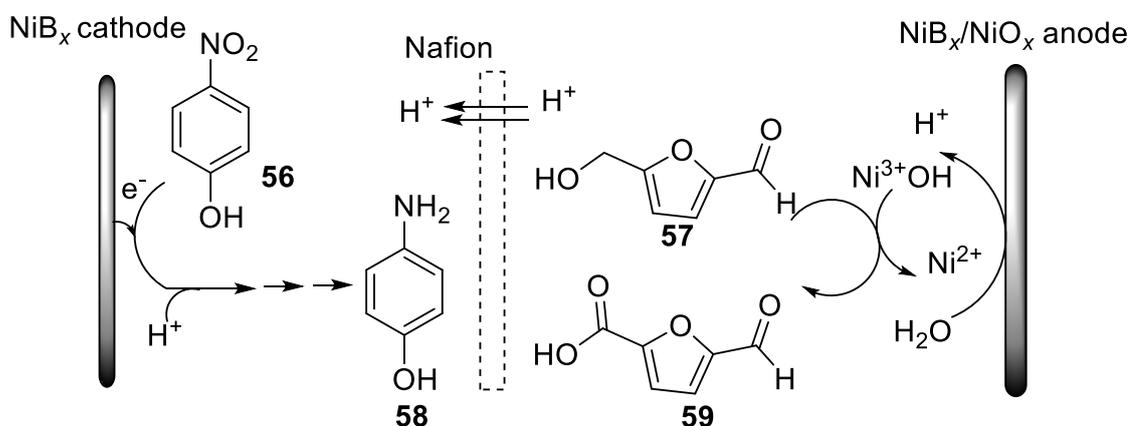
Scheme 39. Plausible mechanism for the parallel paired electrocatalytic synthesis of Lactic acid and CO.

In 2019 Sun and co-workers reported an excellent green method for parallel paired reactions to form 2,5-furandicarboxylic acid derivatives **59** and *p*-aminophenol derivatives **58**.⁶⁵ The reaction was conducted in a photoelectrocatalytic cell equipped with NiB_x@NF as a both electrodes, at a controlled potential, in water as the solvent (**Scheme 40**). Under mild conditions, using water as an oxygen and hydrogen source, a family of hydroxy-methylfural derivatives **57** and nitrophenol derivatives **56** were tolerated, affording the desired products **58** and **59** in excellent yields of up to 99%. The reaction combines two desirable half-reactions for the oxygenation of 5-hydroxy-methylfural **57** to 2,5-furandicarboxylic acid **59** in parallel with the hydrogenation of *p*-nitrophenol **56** to *p*-aminophenol **58** using NiB_x as a catalyst. In this case, the theoretical maximum electron efficiency is 200%, twice that for conventional unpaired cells. Moreover, this paired synthetic process may lower operation costs by reducing the number of reactors or processing steps required. The newly designed electrochemical cell exhibited high conversions, selectivities, and Faradaic efficiencies at

both the anode and cathode, simultaneously, without the involvement of oxygen and hydrogen. High conversions and selectivities were also observed when using furan-2-carbaldehyde, furan-2-ylmethanol, pyridin-4-ylmethanol, and 4-(hydroxymethyl) phenol, as the compounds undergoing oxygenation, and when *p*-NP was replaced with *m*-NP, *o*-NP, 4-nitrobenzonitrile, and 1-ethynyl-4-nitrobenzene. A mechanistic elucidation in **Scheme 41** showed that firstly, Ni^{2+} was electrooxidised with water to form the complex Ni^{3+}OH , accompanied by the liberation of a proton. Then the resulting Ni^{3+} species reacted with 5-hydroxy-methylfural **57** to provide 2,5-furandicarboxylic acid **59** and regenerate Ni^{2+} . Furthermore, the proton penetrated through to the cathode compartment to ensure the hydrogenation of *p*-nitrophenol **56** to *p*-aminophenol **58**.



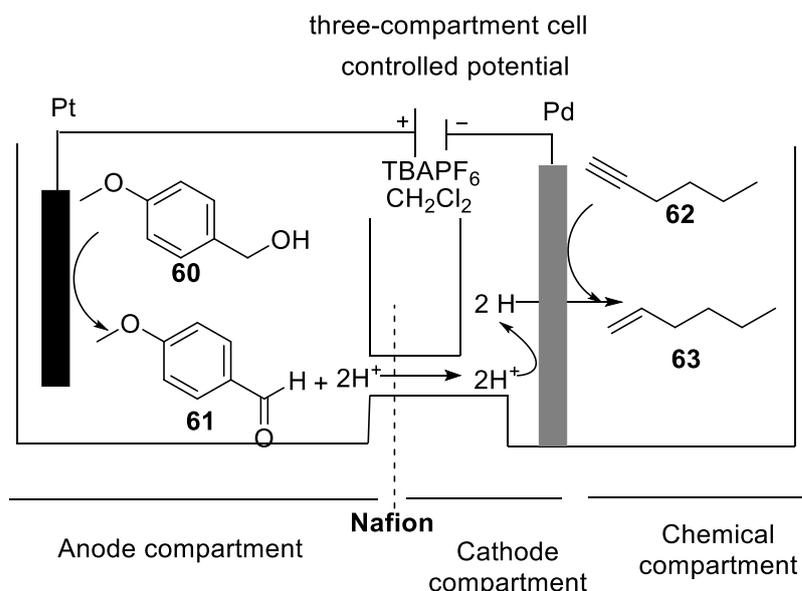
Scheme 40. Parallel paired electrosynthesis of 2,5-furandicarboxylic acid and *p*-aminophenol by using $\text{NiB}_x\text{@NF}$ as both electrodes.



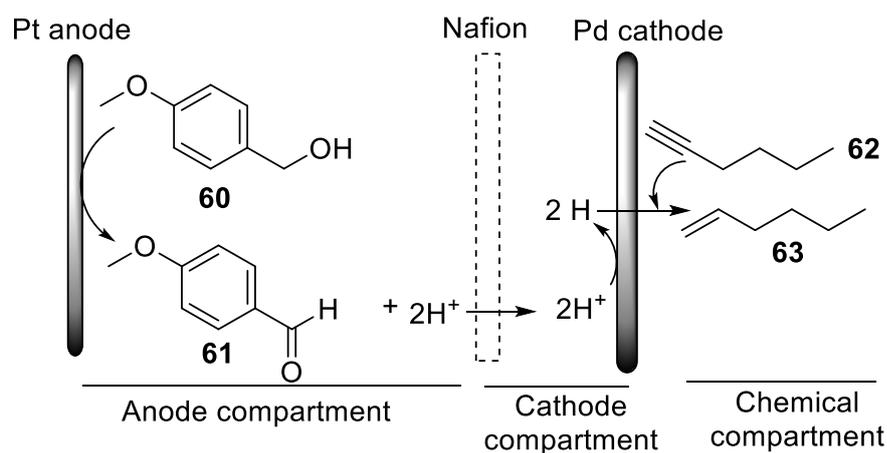
Scheme 41. Plausible mechanism for parallel paired electrosynthesis of 2,5-furandicarboxylic acid and *p*-aminophenol.

Non-mediated electrolysis

In 2018, Berlinguette and co-workers reported a good strategy, described by a paired parallel reaction, for the formation of 4-methoxy benzaldehyde **61** from the anodic oxidation of 4-methoxyalcohols **60** and the electro-formation of 1-hexene **63** from 1-hexyne **62** via an electrolytic palladium membrane reactor (**Scheme 42**).⁶⁶ The reaction proceeds in a three-compartment cell, using Pt plates as the anode and Pd as the cathode in a system of CH₂Cl₂/tetrabutylammonium hexafluorophosphate (TBAPF₆) as the solvent/electrolyte. The anode and cathode sides of the electrochemical compartment were separated by a Nafion membrane. The fundamental success of this device is the selectivity of the palladium foil which acts as a cathode for proton reduction and a hydrogen diffusion membrane. The authors reported that the adsorbed hydrogen must transition into the bulk of the palladium lattice, diffuse through the lattice and transition to the surface on the other side of the cell to react with the organic substrate. If the kinetics of hydrogen gas evolution on the electrochemical side of the palladium are faster than the competing absorption and diffusion steps, hydrogen would evolve only on the electrochemical side of the foil and would not hydrogenate the substrate on the chemical side. It was found that the majority of the total evolved hydrogen was detected on the chemical compartment of the foil at every applied current. Even at an applied current of 50 mA it was found that 90% of the hydrogen was detected on the chemical side of the foil, indicating that almost all the protons being reduced at the cathode are diffusing and recombining on the opposite side of the foil. These results confirm that palladium is acting effectively as a selectively permeable membrane for hydrogen atoms. A mechanistic elucidation in **Scheme 43** shows that firstly, alcohol **60** was oxidised at the anode to provide the corresponding aldehyde **61** with the liberation of a proton. Then, the protons cross a Nafion proton exchange membrane. These protons were reduced at the palladium foil cathode to form the adsorbed hydrogen atom, which easily reacted with alkyne **62** yielding the corresponding alkene **63**.

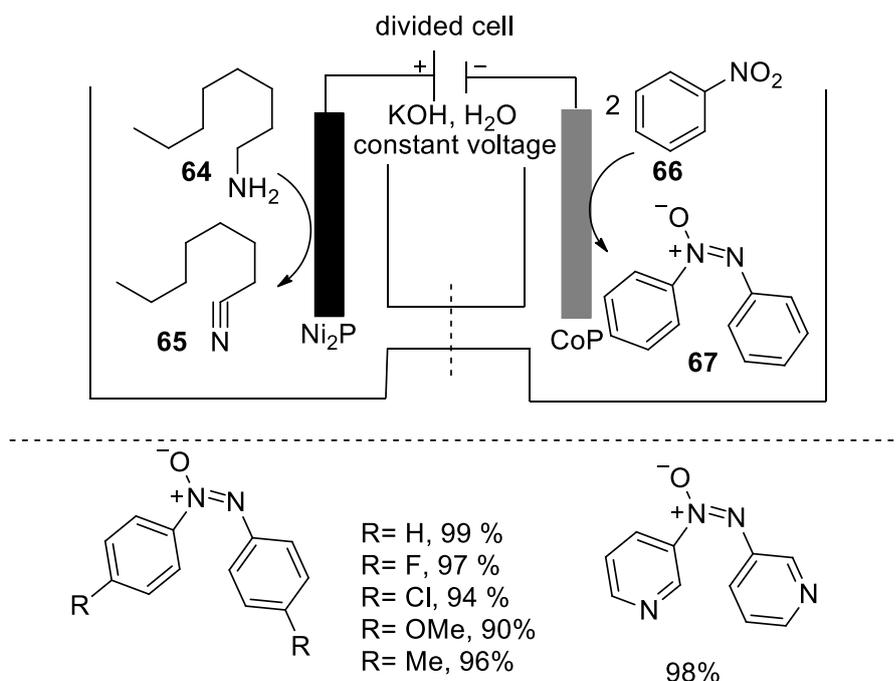


Scheme 42. Paired parallel reactions for the formation of 4-methoxy benzaldehyde and 1-hexene.

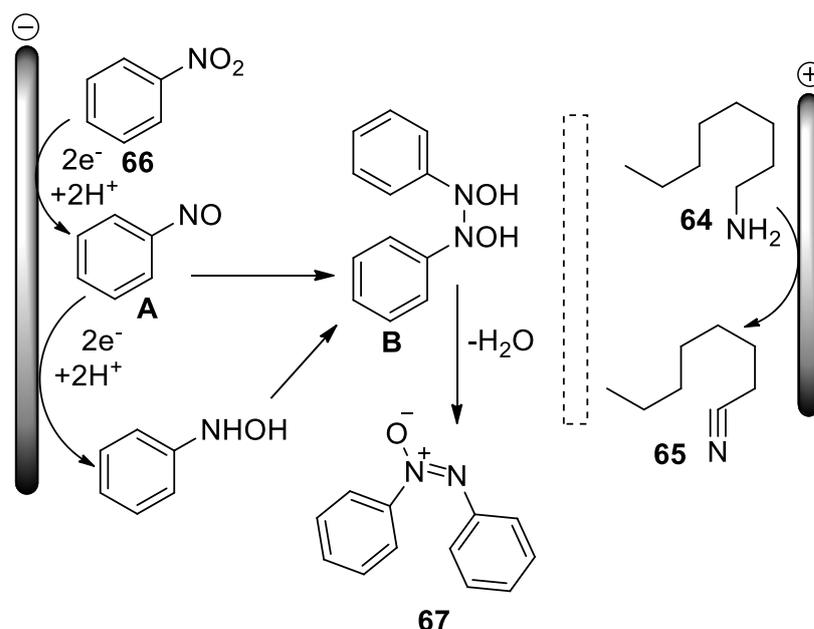


Scheme 43. Plausible mechanism for paired parallel reactions for the formation of 4-methoxy benzaldehyde and 1-hexene.

Very recently, Zhang and co-workers reported an excellent paired parallel reaction for the electroformation of azoxy-aromatics derivatives **67** from the cathodic reduction of nitrobenzene **66** and the electro-formation of nitriles **65** by the anodic oxidation of amine derivatives **64** (**Scheme 44**).⁶⁷ Different nitrobenzene derivatives **66** provide a broad scope of desired compounds in good to excellent yields of up to 99%. Substrates with electron-rich substituents such as Me, MeO, and electron-deficient groups such as F, Cl and Br have a good tolerance in this transformation. The reaction was performed in divided cell equipped with a Ni₂P electrode at the anode and CoP at the cathode, in water (solvent) and KOH as an electrolyte, under a constant voltage for 6 h. The authors found that the required potential is only 1.25 V to achieve a current density of 20 mA cm⁻², which is lower than the potential 1.70 V of overall water splitting. Furthermore, these paired reactions can also be driven by 1.5 V batteries to synthesise nitrile and azoxybenzene with high selectivity. Additionally, the amount of KOH should be essentially 1.0 M because it will prevent unwanted hydrogenation of the two intermediates due to the trace amount of protons at low potentials. A higher reductive potential results in more active *H which will be generated at the surface of CoP via water splitting, trapping phenylhydroxylamine to form aniline and inhibiting the condensation of nitrosobenzene and phenylhydroxylamine. A mechanistic elucidation in **Scheme 45** shows that the cathodic reduction of nitrobenzene gave nitrosobenzene **A**. After further reduction, the latter could provide intermediate **B** (or **B** can be formed directly from **A**). Finally, **B** led to the final product after losing one molecule of H₂O. Concurrently at the anode, amine **64** was directly oxidised to nitrile derivatives **65**.



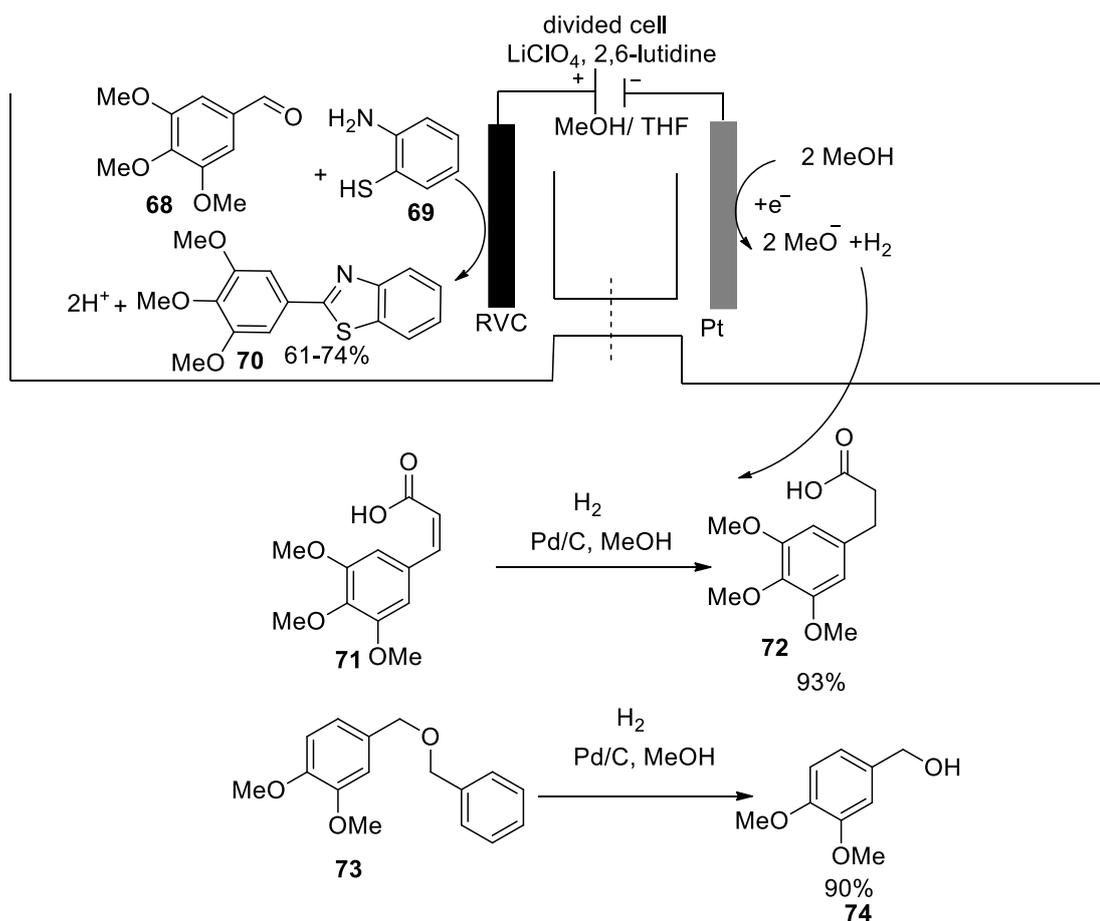
Scheme 44. Electroformation of azoxy-aromatics and nitriles derivatives.



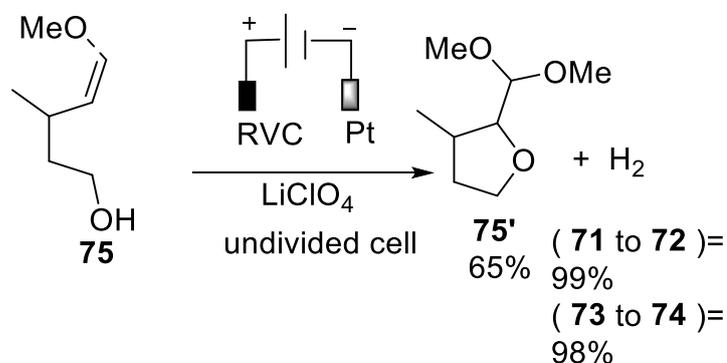
Scheme 45. Plausible mechanism for the electroformation of azoxy-aromatics and nitriles derivatives.

In 2019, Moeller and co-workers reported an important paired parallel reaction for the electroformation of 2-(3,4,5-trimethoxyphenyl) benzothiazole derivatives **70** from the anodic oxidation of 3,4,5-trimethoxybenzaldehyde derivatives **68** and 2-aminobenzenethiol **69**.²⁷ The paired synthesis is combined with a hydrogenation reaction of trimethoxyphenyl-acrylic acid derivatives **71** (**Scheme 46**). The 4-((benzyloxy)methyl)-1,2-dimethoxybenzene derivative **73** were also tested for this transformation, and the hydrogenated product **74** was formed with a good yield of 90%. Here, the authors proved the environmental and financial cost benefit of producing H₂ gas during the oxidation reactions; the hydrogen gas can be

synthesised easily by the cathodic reduction of MeOH. The key advantage of this technology is to transfer the gas, which was formed in the cathodic compartment, to a flask containing the unsaturated acid in the presence of Pd catalyst by the insertion of a cannula into the headspace of the cell. In a divided cell, equipped with a Pt plate as a cathode and an RVC anode in the system MeOH: THF (1:1)/LiClO₄ as solvent/electrolyte. It was found that the use of different substrates for the oxidation reaction did not have any influence on the reduction reaction. This advantage allowed the authors to test the electrolysis in an undivided cell, for the main objective was a cyclisation reaction by anodic oxidation of **75** to form the cyclic product **75'** (Scheme 47).



Scheme 46: A paired oxidative condensation with hydrogen generation in a divided cell.

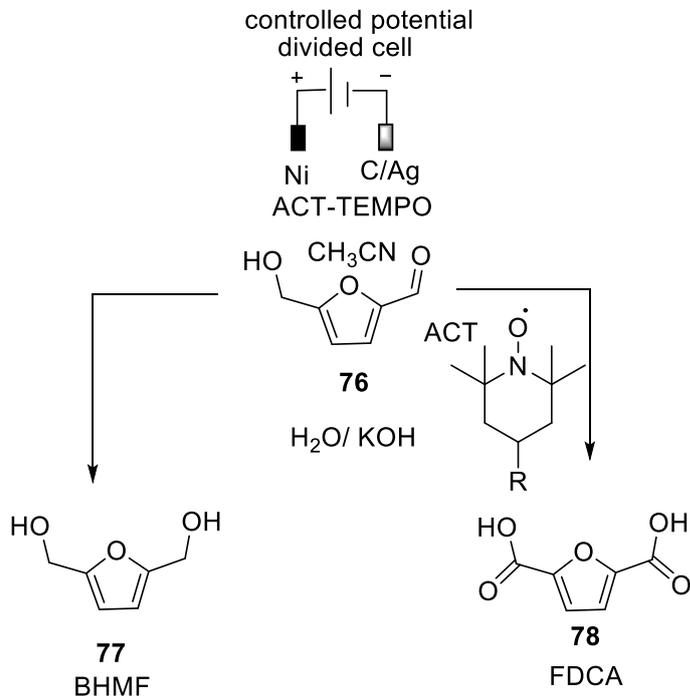


Scheme 47: Paired anodic cyclisation in an undivided cell.

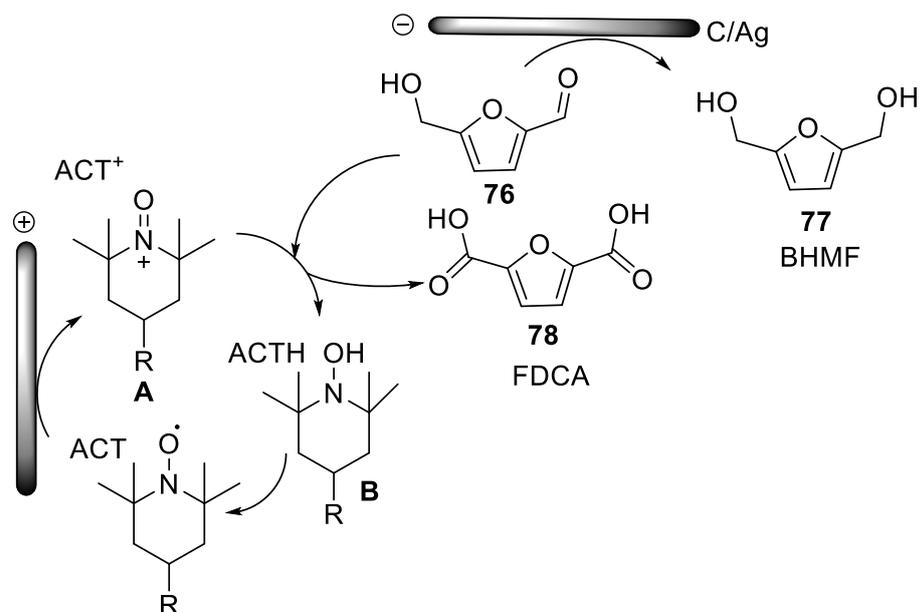
Divergent paired electrolysis

Mediated electrolysis

In 2019 Li and co-workers reported an efficient approach for divergent paired production of biomass-derived 2,5-bis(hydroxymethyl) furan (BHMf) **77** and 2,5-furandicarboxylic acid (FDCA) **78** using ACT-TEMPO as a redox catalyst (**Scheme 48**) from 5-(hydroxymethyl) furfural (HMF) **76**.⁶⁸ The results showed that the conversion was achieved in high yields of BHMf in 85% and FDCA in 98%. The electrolysis proceeded in a divided cell equipped with C/Ni as the cathode/anode system separated by an anion exchange membrane, at a controlled potential in H₂O/KOH as a solvent/electrolyte system. For the electrocatalytic hydrogenation of HMF to BHMf, the authors used self-prepared Ag/C as the cathode. The studies show that the selectivity and efficiency for BHMf formation were dependent on cathode potential and bulk HMF concentration. Additionally, they proved that the reduction of HMF on the carbon support material in Ag/C at cathodic potentials is more negative by about -1.2 V, resulting in hydrodimerisation with low formation and selectivity of BHMf. **Scheme 49** illustrates a proposed mechanism for the cascade. At the anode, 4-acetamido-TEMPO underwent oxidation to give intermediate **A**. This was then catalysed by the oxidation of HMF to FDCA **78**. Meanwhile, the cathodic reduction of HMF provided the desired product BHMf **77**.



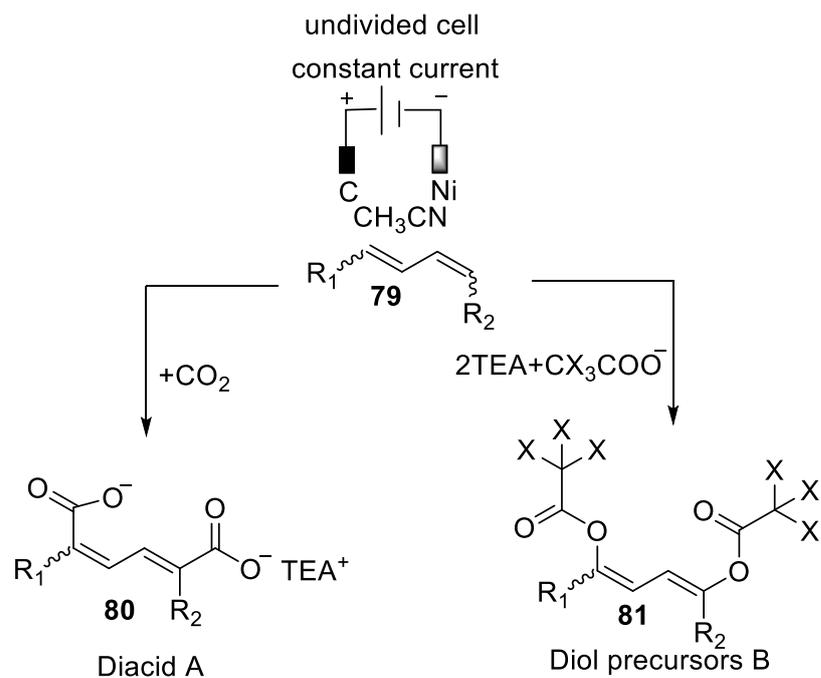
Scheme 48. The divergent paired production of BHMf and FDCA.



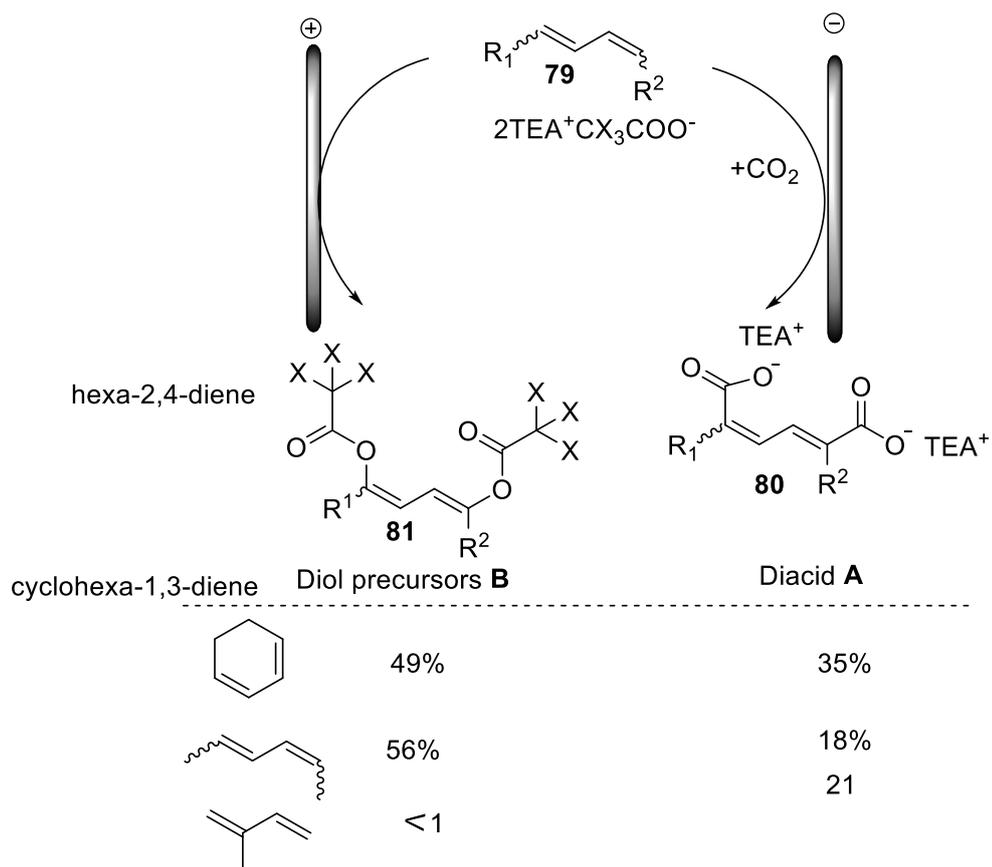
Scheme 49. Plausible mechanism for the divergent paired production of BHMf and FDCA.

Non-mediated electrolysis

In 2015, Vos and co-workers reported an efficient method describing the divergent paired electrolysis to synthesise diol precursors **81** and diacid **80** from diene derivatives **79** under CO₂ pressure (**Scheme 50**).⁶⁹ The reaction proceeded in an undivided cell equipped with a Ni cathode and a carbon anode in CH₃CN at a constant current using a mixture of TEA⁺/TFA⁻ (tetraethyl ammonium/tetrafluoroacetic acid) as an electrolyte. The cathodic carboxylation and anodic acetoxylation of 1,3-cyclohexa-diene **79** provided a moderate yield of desired products **80** and **81** (**B**: 49%, **A**: 35%). However, when hexa-2,4-diene was used, the desired product **A** was formed with a yield of 56%, but the electrodicarboxylation yield decreased to 18%. Lower yields for both reactions (**B**: <1%, **A**: 21%) were obtained when isoprene was used as a substrate; the authors explained these unsuccessful results by a radical polymerisation of the reactive primary radicals, formed by isoprene or 1,3-butadiene oxidation, which suppresses the 1,4-incorporation of trifluoroacetate. Moreover, high substrate dependence was observed, complicating extension to other conjugated dienes. In any case, this innovative transformation shows that paired reactions can provide an energy-efficient alternative to current electrocarboxylation processes. A plausible mechanism implies that the transformation began with the cathodic reduction of 1,3-cyclohexa-diene in the presence of CO₂ to form the diacid **A**. Meanwhile, 1,3-cyclohexa-diene was oxidised with TEA⁺ to provide the compound **81** (**Scheme 51**).



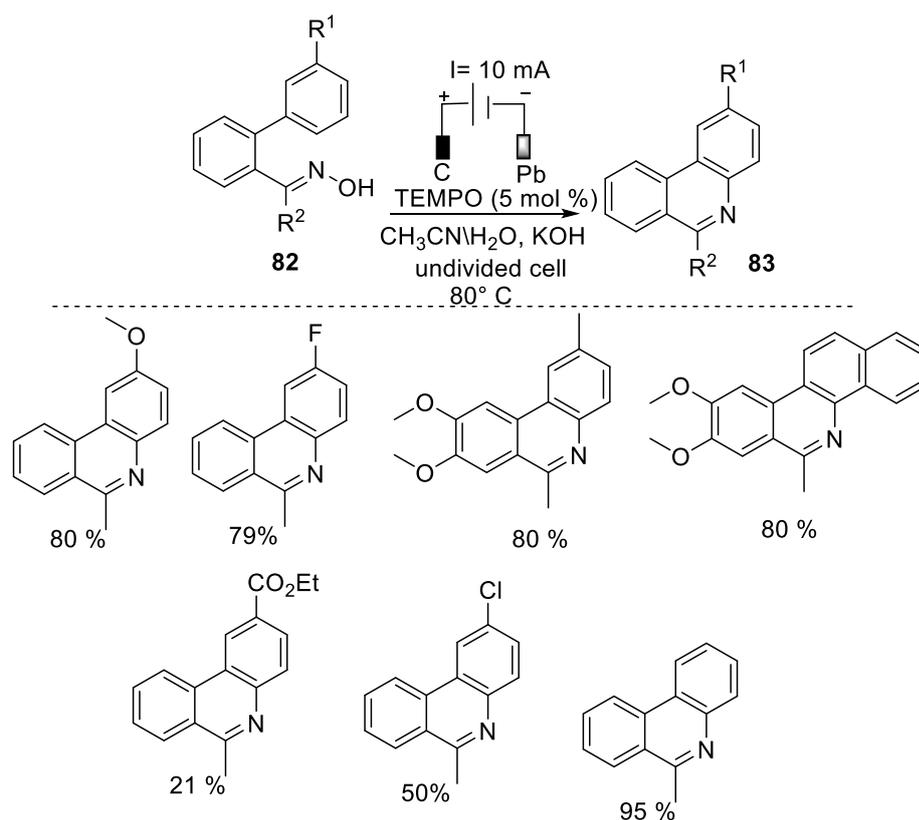
Scheme 50. Divergent paired electrolysis to synthesise diol precursors and diacid.



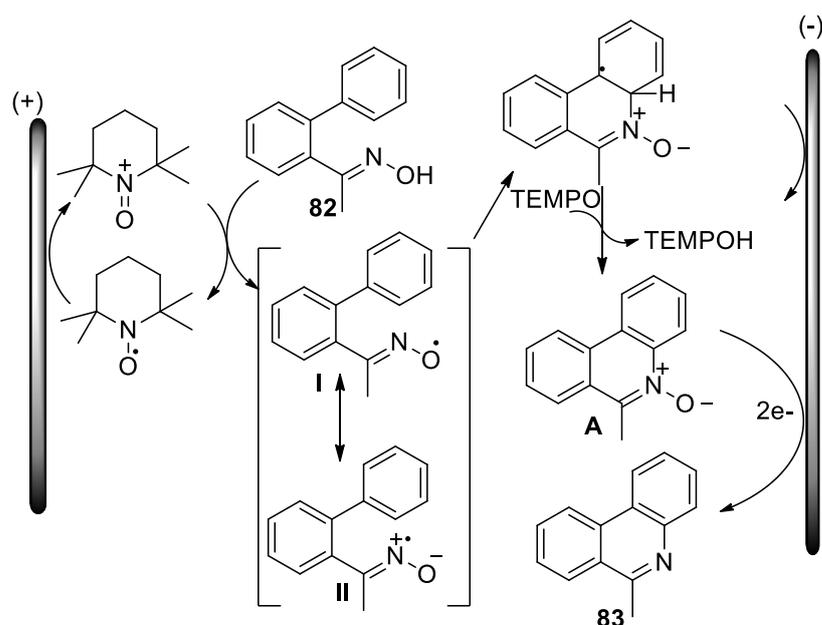
Scheme 51. Plausible mechanism for the divergent paired electrolysis to synthesise diol precursors and diacid.

Linear paired electrolysis

In 2018, Xu *et al.* reported an efficient linear electrochemical C-H functionalisation of biaryl ketoximes reactions. Different [1,1'-biphenyl]-2-carbaldehyde-oximes **82** could afford a wide range of desired compounds **83** in excellent yields of up to 95% (**Scheme 52**).⁷⁰ The experimental study shows an interesting result; the cathode material played a key role in the reaction's outcome. Investigations revealed that the platinum electrode results in the formation of *N*-heteroaromatic *N*-oxide, whereas in contrast, sequential hydrogenative cyclisation occurred using a Pb cathode. The key advantage of this method is utilised with the Pd electrode, which could replace some chemical reductants. It was found that the heating condition worked well, giving yields of up to 95%. The reaction was performed in an undivided cell, at a constant current of 10 mA with a carbon anode and a Pb cathode, in CH₃CN/H₂O, in the presence of KOH as an electrolyte. The products attached to electron-donating substituents such as Me, MeO, or electron-withdrawing groups such as Cl, and F had a good tolerance in this transformation. Lower yields of 21% were obtained when CO₂Et was used as a substituted group. The electrolysis commenced with the anodic oxidation of TEMPO into TEMPO⁺, which then reacts with **82** to provide an iminoxyl radical (resonance structures **I** and **II**) (**Scheme 53**). The cyclisation of the iminoxyl radical onto the phenyl ring, followed by rearomatisation, gave the *N*-oxide **A**. Finally, the reduction of *N*-oxide **A** on the Pb cathode provided the desired product **83**.

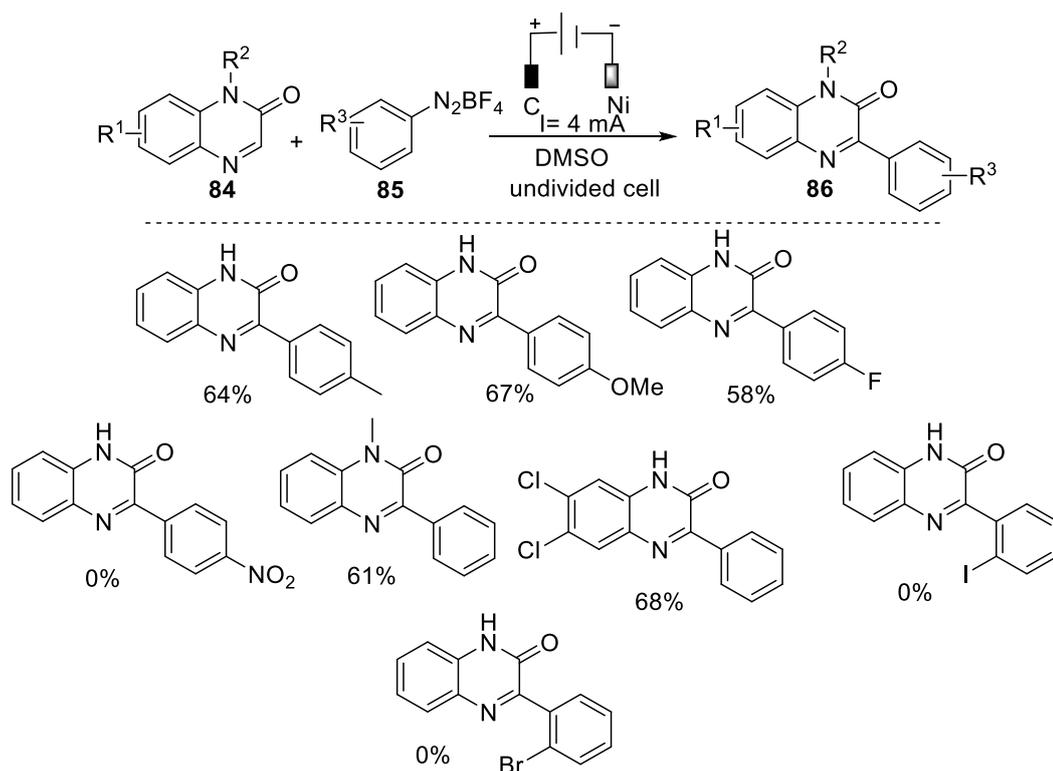


Scheme 52. The linear dehydrative cyclisation.

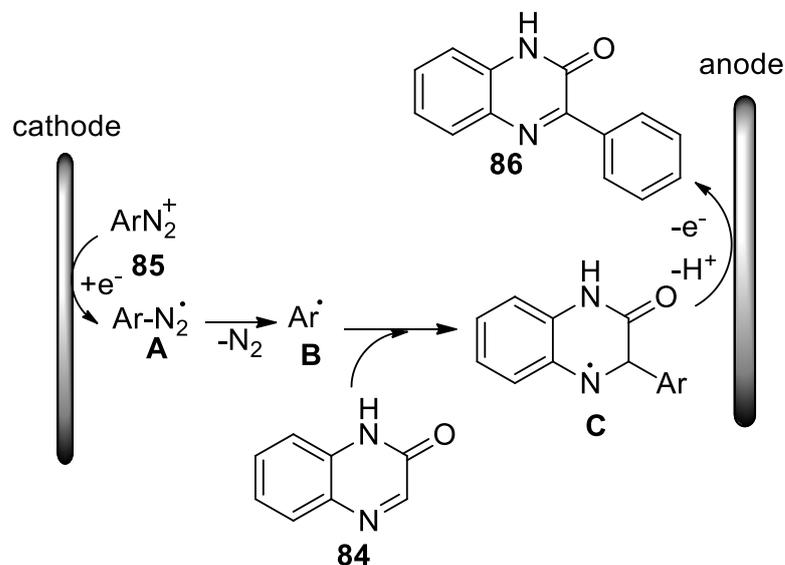


Scheme 53. Plausible mechanism for the dehydrative cyclisation.

More recently, Zeng and co-workers reported efficient linear C(sp²)-H electrochemical cross-coupling reactions.⁷¹ Different quinoxalin-2(1*H*)-ones **84** and phenyldiazonium salts **85** could afford a wide range of desired compounds **86** in moderate to good yields (**Scheme 54**). The reaction was performed in an undivided cell, under a constant current with a carbon anode and a Ni plate cathode, in DMSO, without an external electrolyte. The products attached to electron-donating moieties such as Me, MeO, or electron-withdrawing substituents such as Cl, Br, F had a good tolerance in this transformation. However, when the strong electron-withdrawing nitro group was appended to C4 of the aryl ring, the desired product was not formed and the starting substrate was recovered. Notably, when the 2-Br- or 2-I-substituted phenyldiazonium salts were employed the desired products were not detected. The authors attributed these unsuccessful results to the possible reduction reaction of aryl bromides or aryl iodides under these conditions. The linear paired mechanism for the electrochemical arylation in **Scheme 55** shows that initially, aryl diazonium salts **85** are reduced on the cathode to provide the phenyl diazo radical **A**, which released N₂ to afford the radical intermediate **B**. Then, the combination of quinoxalin-2(1*H*)-one **84** with **B** gave intermediate radical **C**. This is then oxidised at the anode to provide the corresponding product **86**.



Scheme 54. Linear C(sp²)-H electrochemical cross-coupling reactions.



Scheme 55. Plausible mechanism for the linear C(sp²)-H electrochemical cross-coupling reactions.

Conclusion & Perspective

This review highlighted the recent advances of paired electrolysis, specifically concerning convergent, parallel, divergent, and linear paired reactions. All of these were presented with advantageous energy and atom economies, cost-efficiency, and done so in an environmentally friendly manner. Paired electrochemical reactions not only avoid the generation of toxic waste by-products but also allow a more efficient use of electrical

current at both electrodes to achieve specific products. These examples illustrate the diversity, as well as the common features, of a paired electrocatalysis that are performed mainly under mild conditions with good selectivities. Some paired syntheses required the presence of a catalyst such as iodide, Ni, Mn, Br, TEMPO, Ag, Au, and Sn, which could be regenerated at the anode or cathode by the end of electrolysis, and some reactions were carried out in the absence of a catalyst. Paired reactions can start with one or two substrates to generate one or two products. Also, both types of cells under batch and continuous flow conditions (undivided or divided cell) can be employed in paired electrocatalysis. Paired electrocatalysis allows, theoretically, a current efficiency of 200%. However, this can be quite difficult to realise, and therefore, more attention is needed to expand organic transformations under ideal paired electrolysis to access value-added compounds. Industrial scale applications of paired electrolysis are rare; as such a much greater emphasis needs to be given to such developments. The first commercial process using paired electrocatalysis by BASF allowed the simultaneous generation of phthalide and *tert*-butylbenzaldehyde dimethylacetal with 100% atom efficiency and 180% current efficiency. Paired electrocatalysis prevents unwanted side reactions and protects the electrodes from corrosion by reactive species. Increased work will be required to perform paired electrocatalysis with more systematic and rational approaches to achieve optimum products under paired conditions. New computational tools could be applied in this field.⁴⁷ Such an approach can be effective to improve atom economies at the possible expense of energy economy.

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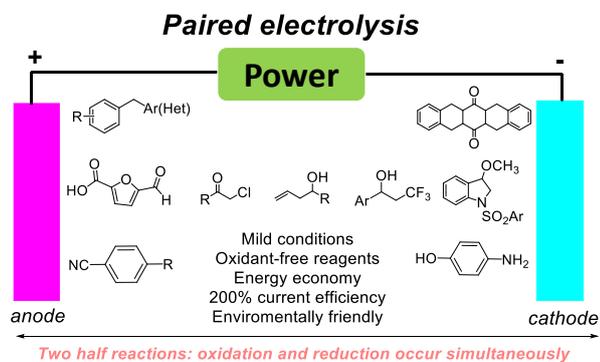
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Synopsis for Table of Contents:

Herein, paired electrosynthesis to provide energy-efficient chemical transformations involving mainly convergent, parallel, divergent, and linear type, have been discussed.