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Transition-Metal Catalyzed Electroreductive Cross-Couplings for C-C Bond Formation

Meng-Yu Gao,^[a] Corinne Gosmini*^[b]*Dedicated to Professor Jacques Périchon*

Abstract: This mini review provides an overview of a range of Ni-, Co- and Pd-catalyzed electroreductive cross-coupling reactions. The combination of homogeneous transition-metal catalysis and electrochemistry are green alternatives to traditional reductive cross-coupling reactions to form Csp²-Csp², Csp²-Csp³ and some Csp³-Csp³ bonds in one step. Most of these reactions use the sacrificial anode process

Keywords: electroreduction • cobalt • nickel • cross-coupling • C-C bond

1. Introduction

Cross-coupling reactions have revolutionized techniques to form carbon-carbon bonds.¹ They are now widely employed in various synthetic ways, from the total synthesis of natural products² to the preparation of new materials. They have also been recognized by the Nobel Prize in 2010 with palladium catalysis.³ Moreover, these reactions are increasingly applied in industrial protocols emphasizing the importance of the methodology. They take place with a transition-metal complex and involve a mechanism following an oxidative addition, a transmetalation and a reductive elimination. First reported cross-coupling reactions implied an organometallic species as a nucleophile and an electrophile. However, more recently, different cross-electrophile-coupling reactions were developed in one step between two electrophiles via chemical or electrochemical processes avoiding the preliminary formation of an organometallic species allowing the direct activation of organic precursors.⁴ Although these reactions are performed in one step, classical chemical methods imply a large amount of powdered metal reductant to reduce catalyst and intermediate species. Some alternative processes were developed to overcome this disadvantage such as photochemistry⁵ and electro synthesis⁶ and can sometimes provide complementary reactivity. Among these methods, electrosynthesis is an interesting method to form bonds in a sustainable manner using electron as **reductant** or oxidant. Compared to conventional chemical synthesis, the electrochemical process avoids wastes and generally the conditions are mild and many functional groups can be tolerated. Moreover, the possibility to control the reaction, by tuning the potential, is an enormous advantage. However, although electrosynthesis was developed in the last century, organic chemists were reluctant to use this method. They considered that it was not easy to handle

and needed specific equipment of high cost. In spite of this, these last years, practical experimental electrochemical setups were simplified using only 2 electrodes in an undivided cell to work at constant intensity. In this mini review, we focused on transition metals-catalyzed electroreductive cross-coupling reactions, which have seen a resurgence of interest these recent years. In these electroreductive cross-coupling reactions, the working electrode is the cathode (negative pole) where the reduction of transition metal, especially a first-row one, occurs and in the major cases, the anode is consumable

2. Electroreductive cross-coupling of Csp²-Csp² bond formation

2.1. Ni-catalyzed electroreductive cross-coupling of Csp²-Csp² bond formation

First, non-noble metal catalyzed electroreductive cross-coupling reactions were developed by Périchon with Nickel as catalyst using the sacrificial anode process in order to form C-C bonds. Nickel-2-2'-bipyridine complexes are useful catalysts to prepare both Csp²-Csp³ and Cp²-Csp² bonds. Before heterocoupling of two different aryl halides by electroreductive cross-coupling, electrochemical homocouplings of aryl compounds were already described

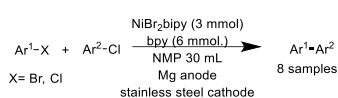
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using Ni⁷ or Pd⁸ catalyst. Poly(pyridine-2,5-diyl) were also obtained by dehalogenation polycondensation of 2,5-dibromopyridine, under electrochemical reductive conditions mediated by various nickel(II) and palladium(II) complexes (nickel-2,2'-bipyridine (bpy) and -phosphine complexes and palladium-bpy complexes).⁹ Nickel-catalyzed electroreduction of dibromomonomers also allowed to several poly(N-alkyl-3,6-carbazole-diyl)s.¹⁰ Thus, the first preparation of unsymmetrical biaryls was reported using a Ni-catalysis by electroreduction of a mixture of two aryl halides, one para-substituted with electron acceptors and the other by electron donors. The syntheses were carried out in N-methylpyrrolidone by constant current electrolysis in an undivided cell fitted with a sacrificial magnesium anode. However, this process was not easy to carry out because the more reactive aryl halide had to be added with a syringe pump.¹¹ (Figure 1)

Figure 1: Synthesis of dissymmetrical biaryls by electroreduction of aromatic halides catalyzed by Ni complexes



Mengyu Gao obtained her BS in chemistry at Yantai University under the supervision of Prof. Peiqing. Zhang. In 2016, she joined the research group of Prof. Hegui Gong at Shanghai University and focused on the development of Ni-catalyzed reductive cross-coupling via C-O bond activation. Then in 2019, she moved to Ecole Polytechnique, Institut Polytechnique de Paris, and is currently a PhD candidate focusing on the Co-catalyzed reductive cross-coupling between C- Heteroatom (S, N, O, X) electrophiles to build C-C bonds under the supervision of Dr. Corinne Gosmini.

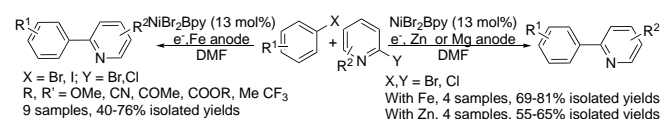


Corinne Gosmini was born near Paris in France. She obtained her PhD in chemistry at Université Pierre et Marie Curie (Paris, France) under the guidance of Prof. Jean F. Normant and Dr Raymond Sauvêtre. In 1993, she was appointed by the CNRS as « Chargée de Recherches » in the laboratory of Prof. Jacques Périchon. She is currently CNRS Director of Research at the « Laboratoire de Chimie Moléculaire » and Associate Professor at the Ecole Polytechnique (Palaiseau – France). From 2013 to 2020, she was the head of the « Laboratoire de Chimie Moléculaire ». Her early interests were devoted toward the development of new electrochemical reactions catalyzed by nickel and mainly cobalt complexes. Since 2003, her main research activities have been concerned with the development of new chemical coupling reactions, and the preparation of organometallic compounds catalyzed by cobalt complexes under versatile conditions in order to form C-C and C-heteroatom bonds first from C-halide bonds and now from non-activated bond such as C-O, C-N and C-C bonds.



In 1998, the Ni-catalyzed electro-reductive cross-coupling was extended to couplings between Nitrogen heteroaryl halides and aryl halides. Firstly, a mixture of 1/1 halogeno pyridines and aryl (or heteroaryl) halides were coupled in order to obtain 2-arylpiperidines in good to high yields. This reaction was performed with a Mg or Zinc sacrificial anode depending on the nature of the substituent on the aryl moiety and the aryl (or heteroaryl) compound had to be more reactive than halogeno pyridines to observe the cross-coupling product in good yields.¹² Two years later, this electro-synthesis of functionalized 2-arylpiperidines was improved using an iron anode. In these conditions, various functional groups both on the aryl and pyridine moieties can be tolerated and led to better yields.¹³ (Figure 2)

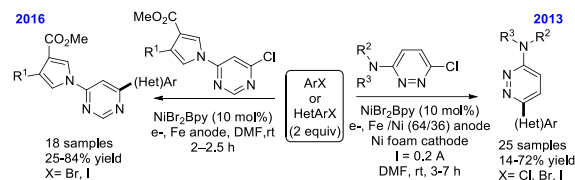
Figure 2. Electro-synthesis of functionalized 2-arylpiperidines by Ni-catalyzed



The same year, the same group extended this reaction to other N-heteroaromatic halides such as 2-chloropyrimidine or 2-chloropyrazine in order to form 2-arylpiperidines and 2-arylpiperazines modifying some parameters in the experimental protocol.¹⁴

Indeed, the latter process developed for synthesis of 2-arylpiperidines was not suitable due to the probably strong linkage of pyrimidine or pyrazine to nickel catalyst. However, the presence of iron salts at the beginning of the electrolysis and adding pyridine as cosolvent circumvented this problem. In 2016, the electroreductive cross-coupling of 4-chloro-6-pyrrolypyrimidine and aryl or heteroaryl halides was reported in DMF in similar conditions involving a pre-electrolysis of iron ions.¹⁵(Figure 3) It was also shown that nickel-catalyzed electrochemical arylation of 3-amino-6-chloropyridazines was possible to obtain 3-amino-6-arylpiperidazines in good yields using an iron/nickel (64/36) sacrificial anode at room temperature in DMF.¹⁶ (Figure 3)

Figure 3. Electroreductive synthesis of 4-aryl- or 4-heteroaryl-6-pyrrolypiperidines and arylation of 3-amino-6-chloropyridazines.

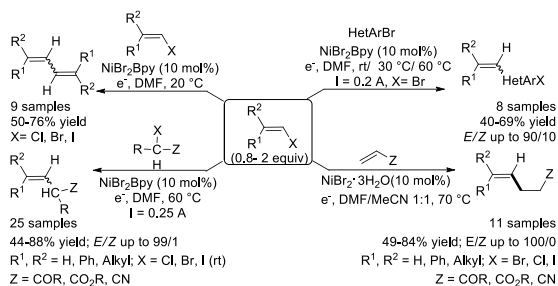


Thiophene derivatives such as 2- or 3-bromothiophene were also coupled in good yields with alkenyl halides by electrochemical reduction in the presence of NiBr₂-2,2'-bipyridine complex as catalyst.¹⁷

The cross-coupling involving other Csp² bonds such as bromo styrenes, and heteroaryl halides has also been performed efficiently using an electro-assisted nickel-complex catalysis to generate alkenylated aryl compounds with 40-69% yields and high stereoselectivity if the more reactive bromostyrene was added with a syringe pump. The (*E*)-β-bromostyrene

gives the (*E*)-product and (*Z*)- β -bromostyrene gives 85% to 95% of the (*Z*)-product.¹⁸ (Figure 4)

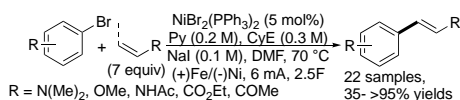
Figure 4. Nickel-catalyzed electrochemical couplings of vinyl halides.



In the same manner, another possibility to form Csp²-Csp² by cross-coupling reaction between organohalides and alkenes is the Heck reaction previously discovered by Mizoroki¹⁹ and Heck²⁰ in 1972 in the presence of a palladium catalyst and a base. The resulting alkenylated aryl compounds could also be synthesized by electrochemistry using the nickel-catalyzed Heck cross-coupling but it remained challenging even on conventional chemistry. In 2002, the Gosmini group developed the first electrochemical Heck reaction using a consumable iron anode permitting the cross-coupling of aromatic or vinylic halides and acrylate esters using CoBr₂(bpy) as catalyst in a mixture of acetonitrile/triethylamine/pyridine as solvent²¹. However, although they demonstrated that Heck reaction is possible, a mixture of Heck and addition products was always obtained depending on the nature of the functional group on the aryl moiety. Aryl bromides bearing an electro-donating group and vinyl chlorides gave the best selectivity in favor of the Heck product.

Recently, Sevov reported a new electrochemical Ni-catalyzed Heck coupling between aryl halides and a broad range of activated and unactivated alkenes under mild conditions²² (Figure 5). The key point of this reaction is the addition of cyclohexenone, which promoted by ligation the reduction of Ni(II)aryl complexes intermediates and in consequence, the coupling of various alkenes.

Figure 5. Electrochemical nickel-catalyzed Mizoroki-Heck reaction.

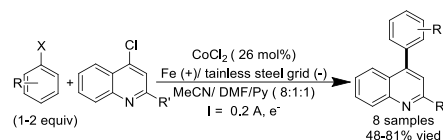


2.2. Co-catalyzed electroreductive cross-coupling of Csp²-Csp² bond formation

Although elegant works and first results were published using nickel as catalyst for different electroreductive cross-couplings, this catalyst has the disadvantage to be not eco-compatible and controversial due to its allergenic and cancerogenic toxicity. Fortunately, inexpensive and more eco-compatible alternative catalysts are available such as iron and cobalt. However, the cobalt presents a higher reactivity and could be used in electroreductive cross-coupling in mild conditions compared to iron. This catalyst has also an excellent tolerance of functional groups. Moreover, sometimes its reactivity is complementary to nickel. As reported previously, Ni-catalyzed electroreductive cross-coupling between either aryl halides and N-heteroaryl halides

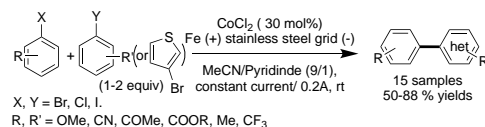
or two different biaryl halides was performed. Nevertheless, the last electroreductive synthesis of unsymmetrical biaryls was limited to one bearing an electron-donating group and the other with an electron-withdrawing group. However, the hetero-electro-cross-coupling between two different aromatic halides bearing one electron withdrawing group on each aromatic moiety was not possible in these conditions. Previously, Gosmini showed that Co(I) formed by electroreduction of CoX₂ (X=Cl or Br) in DMF or acetonitrile as solvent containing pyridine underwent reaction with aryl bromides and chlorides to form arylzinc species in an undivided cell fitted with a consumable Zinc anode.²³ Taking into account these results, this group developed the first Co-catalyzed electroreductive cross-coupling between functionalized aryl halides (X= I or Br) and 4-chloroquinoline derivatives in an undivided cell fitted with a sacrificial Fe anode in a mixture of MeCN, DMF and pyridine as solvent at room temperature. Both electron donating and withdrawing groups on the aryl moiety allowed 4-phenylquinoline derivative in 48-81% isolated yields. With an electron-donating group on the aryl halide, better yields were observed starting from an Aryl iodide whereas an aryl bromide could be used with an aryl ring bearing an electron-withdrawing.²⁴ (Figure 6)

Figure 6. Cobalt-catalyzed electrochemical cross-coupling of functionalized phenyl halides with 4-chloroquinoline derivatives.



One year later, the same group demonstrated that the consumable anode process allowed the Co-catalyzed electroreductive synthesis of biaryls starting from two different functionalized aromatic halides either iodides, bromides or chlorides. On the contrary to nickel, the reaction was carried out in a mixture of acetonitrile/pyridine as solvent starting from two aryl halides, not having a big difference of reactivity, and the more reactive aryl halide was in excess. When this reaction was extended to the coupling of an aryl bromide and the 3-bromothiophene, it was necessary to introduce at the beginning of the electrolysis iron salts to prevent catalyst poisoning by the coordination of cobalt to thiophene. In this manner, the cross-coupling became more efficient but yields were moderate.²⁵ (Figure 7)

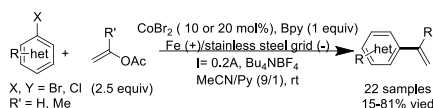
Figure 7. Synthesis of unsymmetrical biaryls by electroreductive cobalt-catalyzed cross-coupling of aryl halides.



Styrene derivatives which are useful chemical intermediates could also be formed from (hetero)aryl halides and vinyl acetates in the presence of catalytic amounts of cobalt bromide with 2,2'-bipyridine as ligand. This electrochemical method led to α -substituted styrenes which are normally difficult to synthesize. Moreover, vinyl acetates were not classical partners for cross-couplings when this electrochemical method was developed. Thus, a series of

substituted styrenes were prepared in good yields from various functionalized aromatic or heteroaromatic halides (chlorides or bromides) and different vinylic acetates. Although it was the first direct vinylation using vinyl acetates, this electroreductive cross-coupling needed a stoichiometric amount of 2,2'-bipyridine²⁶ (Figure 8) in contrast to the more recent chemical Co-catalyzed reductive cross-coupling that used a catalytic amount of bipyridine.²⁷ This excess of bipyridine was due to the competitive complexation of electrogenerated Fe(II) ions with 2,2'-bipyridine instead of cobalt catalyst. From a regioselective point of view, the cross-coupling occurred at the carbon attached to the acetate group and a six centers transition state was proposed to explain that the aryl group is well positioned to be added on this carbon.

Figure 8. Cobalt-catalyzed electrochemical vinylation of aryl halides.



3. Electroreductive cross-coupling of Csp²-Csp³ bond formation

3.1. Ni-catalyzed electroreductive cross-coupling of Csp²-Csp³ bond formation

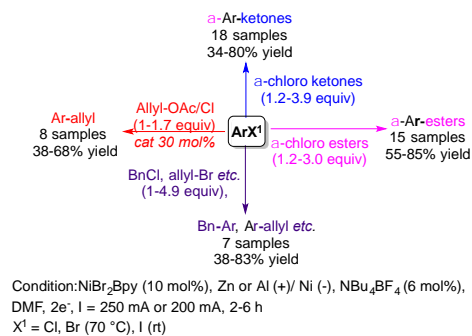
The presence of Csp²-Csp³ linkages is an essential motif in countless active pharmaceutical ingredients alkyl halides are easily accessible and stable compounds. They can be employed in C-C bond formation but the faster β -hydride elimination than the oxidative addition of transition metal hampers the cross-coupling reaction. However, this β -hydride elimination tends to be slower with first-row metals relative to second-row such as palladium.

So, α -aryl esters and β , γ -unsaturated esters were obtained in moderate to good yields by a one-step electrochemical procedure from α -chloroesters and respectively aryl or vinyl halides in a dimethylformamide as solvent, using a sacrificial aluminium anode, and a catalytic amount of nickel bromide-2,2'-bipyridine complex.²⁸

Later, this reaction was extended to electroreductive couplings of α -chloroketones and aryl halides to obtain α -arylated ketones in moderate to good yields using an Al- or Zn-sacrificial anode and a catalytic amount of a nickel complex.²⁹

Since these preliminary results, the process has been both optimized on the basis of a better understanding of the reaction mechanism and extended to the cross-coupling reactions between aromatic halides and allylic derivatives were performed with allylic compounds such as allylic chloride and allylic acetate.³⁰ (Figure 9)

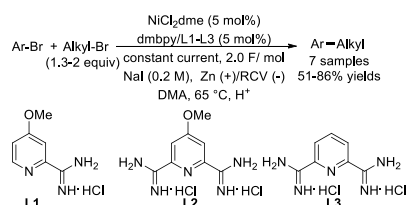
Figure 9. Nickel-catalyzed direct electrochemical cross-coupling between aryl halides and activated alkyl halides.



Budnikova also reported a one-step catalytic method for aromatic perfluoroalkylation under mild conditions from aryl halides (X= Br, I) and perfluoroalkyl iodides using a nickel complex and the sacrificial anode process.³¹

In all these previous reactions, the alkyl compound was activated. However, Hansen developed later an electrochemical method using another nickel catalytic complex to form Csp²-Csp³ bonds by cross-couplings between aryl and non-activated alkyl bromides in DMA at constant current in an undivided cell fitted with a reticulated vitreous carbon (RVC) cathode and a sacrificial zinc rod anode. The electrochemical conditions were compatible not only with the commercially available 4-4'-dimethoxy-2,2'-bipyridine ligand (dmbpy) but also with other amidine-based ligands. This electrochemical reaction gave moderate to excellent yields (51–86%) of wide substrate scope with high selectivity (Figure 10).³² Two years later, in collaboration with Weix, Hansen modified the previous conditions to avoid the use of a sacrificial anode and an amide solvent. Thus, this nickel-catalyzed reductive cross-coupling of aryl bromides with alkyl bromides was conducted in a divided electrochemical cell using acetonitrile as the solvent and diisopropylamine as the sacrificial reductant to afford coupling products in good yields.³³ More recently, they developed a simple electrochemical approach to scale-up this Csp²-Csp³ cross-electrophile coupling. They showed that a broad range of aryl-alkyl compounds was obtained in a simple undivided cell [graphite (+)/nickel foam (-)]. Moreover, a combination of two ligands, 4,4'-di-tert-butyl-2,2'-bipyridine and 4,4',4''-trtert-butyl-2,2':6',2''-terpyridine with nickel, had to be used to avoid byproducts. These optimized batch conditions were applied in flow setup and were demonstrated on a gram scale increasing catalyst concentration and flow rate.³⁴

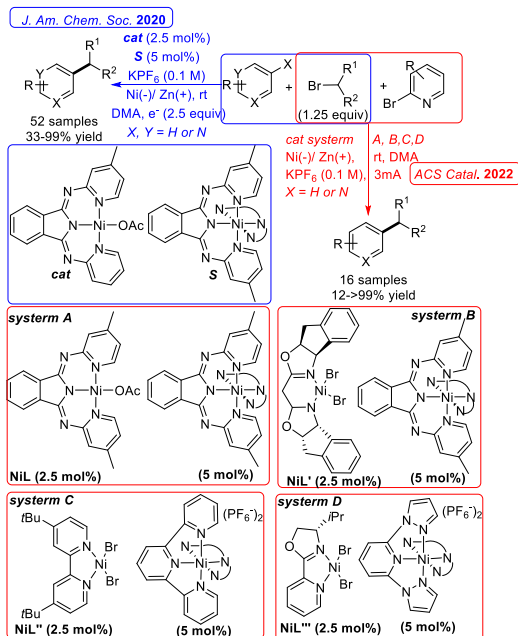
Figure 10. Electrochemical Ni-catalyzed cross-electrophile coupling reactions of unactivated alkyl halides.



Electroreductive cross-coupling of two electrophiles is an attractive approach for the direct C-C bond formation but generally with challenging substrates, the scope was limited compared to reductive cross-coupling using a chemical reductant. However, Sevov reported that nickel complexes were able to generate near quantitative yields when a redox-

matched mediator assisted the system as a redox shuttle.³⁵ (Figure 11) This redox active mediator protected the catalysts from over-reduction. This dramatic influence of overcharge protection on coupling reactions is particularly striking in the case of secondary alkyl electrophiles³⁶ (Figure 3) increasing the cross-coupling yield from 20 to 80%.

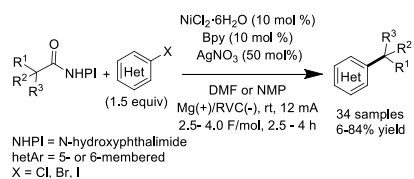
Figure 3. Electroreductive Csp²-Csp³ cross-electrophile coupling reactions.



Although electroreductive cross-coupling reactions of aryl bromides and primary or secondary alkyl bromides are often quantitative, generally those with tertiary alkyl bromides failed to form any cross-products or even rare with reductant metal. However, Sevov showed that an unusual mechanism involving dynamic ligand exchange can control the redox states of Ni and extend the electroreductive cross-coupling of tertiary alkyl bromides with not only aryl bromides but also with aryl chlorides, aryl or vinyl triflates.³⁷

Recently, the electroreductive formation of Csp²-Csp³ was also developed by decarboxylative cross-coupling of redox-active esters and halo(hetero)arenes.³⁸ (Figure 12) This protocol allowed to use more sustainable carboxylic acids in medicinal chemistry³⁹ as starting materials and a radical source instead of halides.

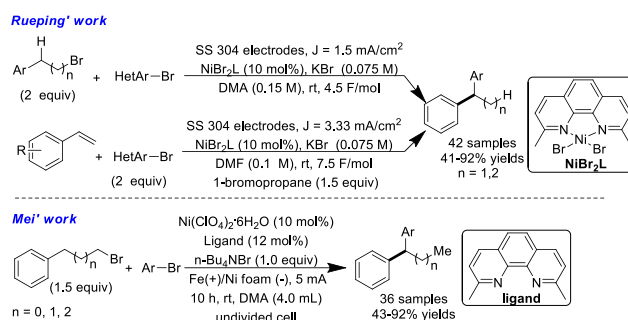
Figure 12. Electrochemical Ni-catalyzed cross-electrophile coupling reactions of redox-active esters and halo(hetero)arenes.



This Ag-Ni electrocatalytic protocol featured high simplicity, robustness, short reaction times and can be applied to a wide range of substrates. In order to scale up, a simple recirculating-flow setup for more than decagram scale was proposed. This electrode modification previously reported

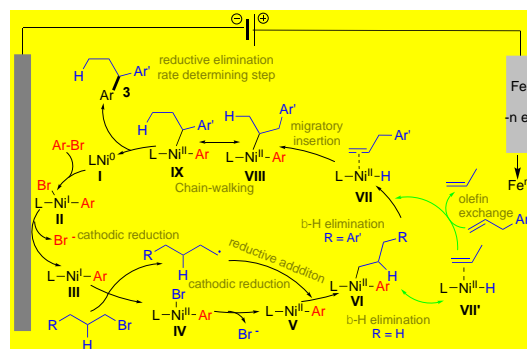
was also beneficial for the synthesis of terpenes.⁴⁰ The silver-NP layer on the electrode has several effects on the reaction components such as for instance to lower the overpotential preventing catalyst overreduction and electrode passivation. The disadvantage of the faster β-hydride elimination than the oxidative addition of transition metal with alkyl halides was taking advantage for selective Ni-catalyzed C-H functionalization through migration insertion/β hydrogen elimination. Recently, Rueping⁴¹ and Mei⁴² (Figure 13) demonstrated at the same time that a highly regioselective Ni-catalyzed electrochemical reductive relay cross-coupling between an aryl bromide and an alkyl bromide allowed to synthesize 1,1-diarylalkanes in good yields and excellent regioselectivity under mild conditions by chain-walking of an alkyl-nickel species.

Figure 4. Nickel-catalyzed cross-electrophile coupling of alkyl and aryl halides.

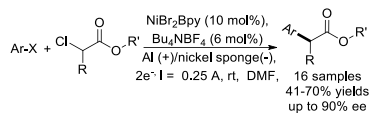


Cyclic voltammetry measurements and DFT calculations were conducted by Rueping to propose a mechanistic pathway for the migratory Ni-catalyzed electro-reductive cross-coupling reaction. (Figure 14) This mechanism is similar to Mei's one but it is more detailed.

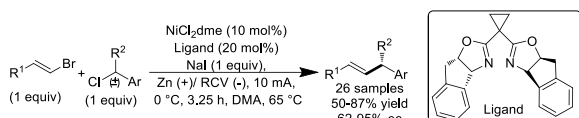
Figure 5. Proposed mechanism for the remote C-H functionalization by Rueping.



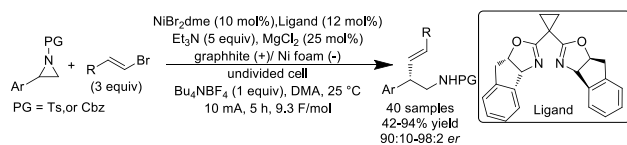
Some nickel-catalyzed enantioselective electroreductive cross-coupling were also reported at constant current in an undivided cell either with a sacrificial anode or not. The pioneered one was reported by Durandetti and Périchon between aryl iodides and α-chloropropionic acids bearing chiral auxiliaries. This last reactive compound had to be added constantly to the reaction mixture using a syringe pump and a stoichiometric chiral auxiliary was necessary⁴³ (Figure 15). This reaction was applied to the preparation of two drugs such as (S)-naproxen and (S)-flurbiprofen in good yields and enantiomeric excess after conversion of the product into the corresponding acid.

Figure 6. Asymmetric induction in the electrochemical Ni-catalyzed cross-coupling of aryl halides with α -chloropropionic acid derivatives.

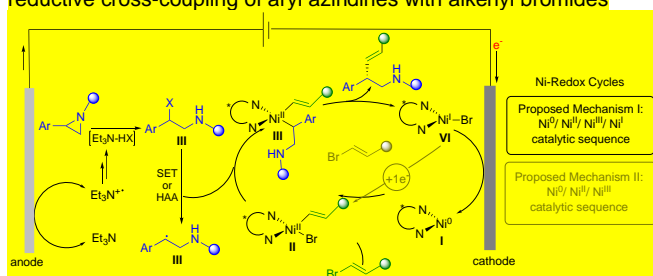
More recently, Reisman extended the nickel-catalyzed enantioselective reductive cross-coupling between various functionalized alkyl bromides and secondary benzyl chlorides to an electrochemical version to avoid the excess of Mn as reductant.⁴⁴ Similar yields and enantioselectivities were obtained in an undivided cell fitted with a zinc sacrificial anode and a bis(oxazoline) as chiral ligand. In this reaction, sodium iodide was used as additive and electrolyte.⁴⁵ (Figure 16)

Figure 7. Enantioselective electroreductive coupling of alkenyl and benzyl halides via nickel catalysis.

Very recently, a Ni-catalyzed enantioselective electroreductive cross-coupling was also reported by Nevado between aryl aziridines and alkenyl bromides to afford enantioenriched functionalized α -aryl homoallylic amines with high enantioselectivities and excellent *E*-stereoselectivity. Contrary to previous cases, herein triethylamine was the terminal reductant instead of a sacrificial anode. The same chiral indanyl-substituted bis(oxazoline) with a cyclopropyl as the central linker used by Reisman was also the best chiral ligand in this reaction (Figure 17). This efficient methodology allowed to access after late-stage functionalization to different pharmacological substrates such as Estrone, Fenofibrate, and gemfibrozil derivatives.⁴⁶

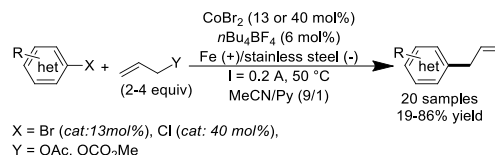
Figure 8. Nickel-catalyzed enantioselective electro-chemical reductive cross-coupling of aryl aziridines with alkenyl bromides.

Two plausible mechanisms for this nickel-catalyzed electrochemical reductive cross-coupling were proposed involving either a $\text{Ni}^0/\text{Ni}^{\text{II}}/\text{Ni}^{\text{III}}/\text{Ni}^{\text{I}}$ or a $\text{Ni}^{\text{I}}/\text{Ni}^{\text{II}}/\text{Ni}^{\text{III}}$ catalytic sequence as shown in Figure 18.

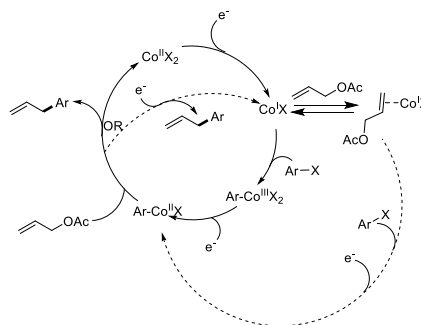
Figure 9. Nickel-catalyzed enantioselective electro-chemical reductive cross-coupling of aryl aziridines with alkenyl bromides

3.2. Co-catalyzed electroreductive cross-coupling of $\text{Csp}^2\text{-Csp}^3$ bond formation

Although several Co-catalyzed reductive cross-coupling involving alkyl compounds were studied,⁴⁷ only one electroreductive cross-coupling was performed with a Csp^3 . The Co-catalyzed electroreduction of various functionalized (hetero)aromatic halides and allylic compounds such as acetates or carbonates afforded arylallyl skeletons which are found in many natural products.⁴⁸ Depending on both the nature of the functional group on the aromatic ring and the halide, the choice of the allylic compound varied. Considering the reactivity of allylic compounds decreasing from allylic halide, allylic carbonate to allylic acetate, aryl bromides bearing an electron-withdrawing or-donating group reacted with allylic acetate or allylic carbonate to lead in acetonitrile or DMF to the corresponding coupling product in good yields in an electrochemical cell fitted with a sacrificial iron anode in the presence of cobalt halide associated with pyridine as ligand. (Figure 19)

Figure 10: Co-catalyzed electroreductive cross-coupling of Aryl halides and allylic acetate.

This reaction could be applied to heteroaromatic halides by coupling with allylic acetates. On the other hand, the less reactive aryl chloride reacted with allylic acetates if they were substituted by an electron-withdrawing group. Low yields were obtained from allylic carbonates. A substituent on the double bond of the allylic compound furnished as the major or sole product the linear one. Allylic halides for all substrates are too reactive. The mechanism of this reaction was studied both by cyclic voltammetry and preparative-scale electrolysis (Figure 20).

Figure 20. Proposed mechanism for Co-catalyzed cross-coupling of aryl halides and allylic acetate.

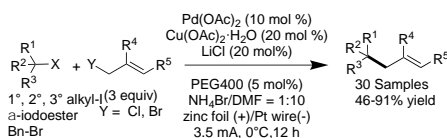
After the reduction of Co(II) to Co(I), a fast complexation with the allyl acetate occurred. This species reacted with aryl halide to form an σ -arylcobalt(III) with different rates depending strongly on the nature of both the halide and the substituent on the aromatic ring which is reduced at the same potential as the original Co-II/Co-I couple. The ultimate steps leading to the coupling product were not elucidated.⁴⁹

4. Electroreductive cross-coupling of Csp³-Csp³ bond formation.

4.1. Pd-catalyzed electroreductive cross-coupling of Csp³-Csp³ bond formation

Except for the cross-coupling of various alkyl organometallic reagents with allylic electrophiles, up to date, there are only a few reports involving direct reductive cross-coupling between two different Csp³ electrophiles and these couplings were carried out in aprotic media using Co, Ni or Cu.⁵⁰ The construction of Csp³-Csp³ bonds between an alkyl halide and an allylic halide was also accomplished by a Pd-catalyzed aqueous Barbier-Negishi-type reaction by a Zn-mediated electroreduction using Pd(OAc)₂ as catalyst under air.⁵¹ This reaction was efficient for the coupling reaction of substituted allylic halides with various alkyl halides, including unactivated primary, secondary, and tertiary halides as well as activated halides. The reaction worked with only Pd as catalyst but a Cu(OAc)₂ as cocatalyst led to 20% yield increased. (Figure 21)

Figure 21. Pd-catalyzed electrochemical allylic alkylation between alkyl and allylic halides in aqueous solution.

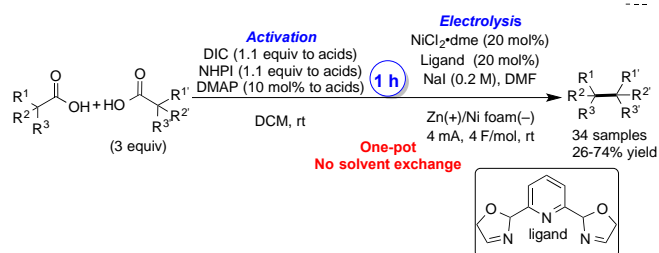


4.2. Ni-catalyzed electroreductive cross-coupling of Csp³-Csp³ bond formation

The oldest Kolbe reaction allowed the Csp³-Csp³ bond formation by oxidative electrochemical decarboxylation of alkyl carboxylic acids generating radical species and the subsequent Csp³-Csp³ bond creation.⁵² This reaction was limited to stabilized radicals obtained from primary alkyl carboxylic acids. Very recently, Baran showed that a Ni catalyst system could be used to cross-couple two different

primary, secondary or tertiary carboxylates by double decarboxylation using electroreduction. The corresponding redox-active esters were in situ generated by acid activation before electrolysis.⁵³ (Figure 22)

Figure 22. Ni-electrocatalytic Csp³-Csp³ doubly decarboxylative coupling.



5. Summary (or Outlook)

This mini review presents an overview of electroreductive cross-coupling reactions which involve mainly first row transition metals catalysts such as Ni or Co. In most cases, these reactions allow the formation of Csp²-Csp² or Csp²-Csp³ bonds and generally use the consumable anode process except in some cases. The formation of Csp³-Csp³ bonds by electroreductive reactions is more recent, rarer and is performed electrochemically either using Pd catalyst or by decarboxylation of alkyl carboxylic acids. All these reactions can present an exceptional functional group compatibility and are easy to handle using inexpensive catalysts.

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