

Electrochemistry

Organic Electrochemistry: Expanding the Scope of Paired Reactions

Tiandi Wu and Kevin D. Moeller*

Abstract: Paired electrochemical reactions allow the optimization of both atom and energy economy of oxidation and reduction reactions. While many paired electrochemical reactions take advantage of perfectly matched reactions at the anode and cathode, this matching of substrates is not necessary. In constant current electrolysis, the potential at both electrodes adjusts to the substrates in solution. In principle, any oxidation reaction can be paired with any reduction reaction. Various oxidation reactions conducted on the anodic side of the electrolysis were paired with the generation and use of hydrogen gas at the cathode, showing the generality of the anodic process in a paired electrolysis and how the auxiliary reaction required for the oxidation could be used to generate a substrate for a non-electrolysis reaction. This is combined with variations on the cathodic side of the electrolysis to complete the picture and illustrate how oxidation and reduction reactions can be combined.

Introduction

Paired electrochemical reactions that produce desirable products at both the anode and cathode have long held promise as a means to maximize both the atom and energy economy of oxidation and reduction reactions.^[1–3] A series of truly impressive paired electrolyses have been reported,^[5–25] including reactions that have been performed on a massive scale.^[4] Yet in spite of these successes, the use of paired electrochemical reactions still remains primarily a technique employed and developed by electrochemists who target systems that produce perfectly matched sets of products. These reactions run with optimized cell voltages and generate products at the two electrodes that are matched in terms of the scale required for their production.

One of the consequences of illustrating the technique with these ideal cases is that they tend to paint the overall technique as one of limited scope. Most synthetic chemists are focused on the construction of molecules for a specific purpose. In such efforts, the synthetic reactions performed are each chosen to accomplish a step within that larger objective. In that context it can be nearly impossible to find a perfectly matched pair of oxidation and reduction reactions. However, paired electrochemical processes do not require a perfectly matched pair of reactions.^[26] In a constant current

electrolysis reaction, the working potential at both electrodes automatically adjusts to match that of the substrate in solution that is easiest to oxidize (anode) and easiest to reduce (cathode).^[27] In a similar manner, for a constant potential electrolysis the potential at the working electrode is set relative to a reference electrode and then the potential at the auxiliary electrode allowed to adjust to the substrates at its surface. In both cases, the electrolysis reaction will adjust to any two half reactions as long as there is a sufficient energy to run the cell. This energy must accommodate the potential difference between the working potential at the anode and the working potential at the cathode and any cell resistance encountered (Figure 1). For most synthetic reactions, the energy required to meet these criteria is small relative to the

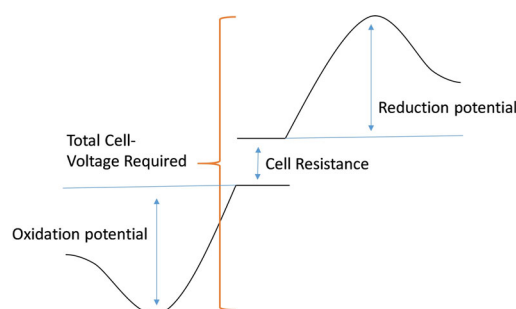


Figure 1. The total energy (potential/Y-axis) required to drive an electrochemical reaction.

total cell voltage available. Typical oxidation potentials for organic reactions vary from about +0.5 to +2.3 V relative to a Ag/AgCl reference electrode, while typical reduction potentials vary from about –0.5 to –2.3 V relative to the same reference electrode. This leads to a difference in the working potentials that is on the order of one to four volts. Even the use of a 6 V lantern-battery as a power supply easily has sufficient energy to overcome this difference plus any reasonable cell resistance encountered.

Furthermore, the scale of the two reactions being paired does not have to be identical. Since current can be split, a larger oxidation reaction can be used to run multiple smaller reduction reactions or vice versa.

Initial Studies, the Hydrogen Evolution Reaction, and Varying Reactions at the Anode

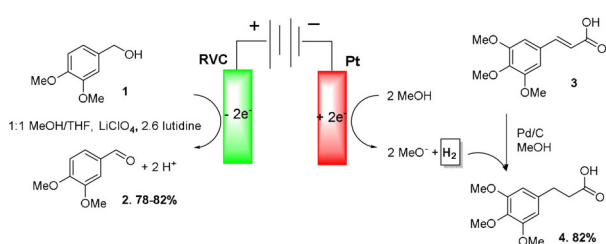
Given this flexibility, paired electrochemical reactions can in principle be used to improve the sustainability of any number of transformations. For our part, we have been exploring the use of paired electrochemical reactions within

*] T. Wu, K. D. Moeller

Department of Chemistry, Washington University
St. Louis, MO 63130 (USA)
E-mail: moeller@wustl.edu

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under:
<https://doi.org/10.1002/anie.202100193>.

a synthetic effort to not only improve the sustainability of a targeted oxidation or reduction, but also to improve the sustainability of other reactions within that larger effort. While paired electrochemical reactions all optimize the energy consumption in a reaction, the need for a divided cell or the increase separation costs associated with the mixture of products generated in a paired electrolysis reaction can overwhelm the cost of the energy consumed in the unpaired systems. Hence, we sought to take advantage of the energy at the counter electrode in an electrolysis to reduce the costs of a second reaction by removing the need to purchase and ship reagents and/or dispose of unwanted byproducts. In our previously published efforts, this concept was demonstrated by pairing a series of electrochemical oxidation reactions with both hydrogenation and hydrogenolysis reactions that take advantage of the hydrogen evolution reaction that occurred at the cathode.^[25] The work grew out of efforts to convert lignin derived materials into synthetic building blocks.^[28] In those efforts, there was a need to accomplish both oxidation and hydrogenation reactions. Rather than buy the hydrogen gas needed for the hydrogenation, having it shipped to us in a cylinder, and then returning the cylinder when the hydrogen was consumed, we inserted a cannula into the headspace above an electrolysis reaction that was already being used to oxidize a lignin derived synthetic building block (Scheme 1). In the case shown, the oxidation reaction converted an

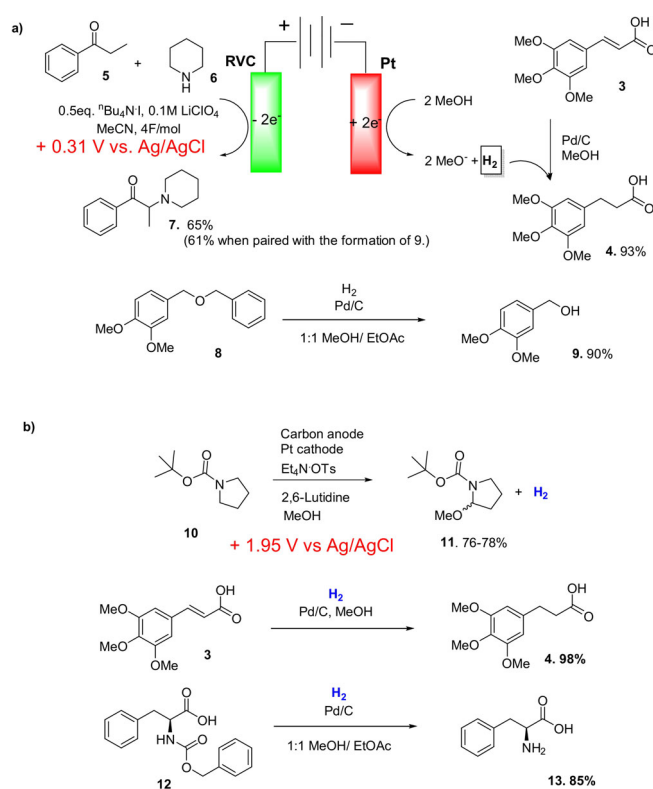


Scheme 1. A paired oxidation and hydrogenation reaction.^[28]

electron-rich benzylic alcohol into its corresponding aldehyde while the hydrogenation removed a double bond from an electron-rich cinnamate derivative derived from lignin. The yields obtained for both reactions were competitive with the corresponding unpaired reactions. In this way, the electrochemical oxidation reaction was used to improve the sustainability of a hydrogenation reaction that would not typically be thought of in the context of electrochemistry.

Changes in the oxidation reaction were also made to see if they altered the efficiency of the paired electrolysis. Two examples from this effort are illustrated in Scheme 2. In the first reaction (equation a), two different reduction reactions were paired with the anodic amination of a carbon α - to a ketone.^[29] The reaction is mediated by iodide with a working potential at the anode of +0.31 V vs. Ag/AgCl. The two reduction reactions, a hydrogenation of a double bond and a hydrogenolysis of a benzylic C–O bond, were both accomplished in excellent yield.

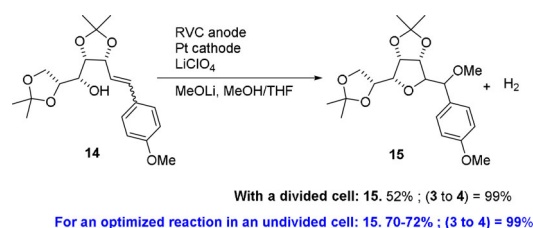
In the second reaction, an amide oxidation at a working anode potential of +1.95 V vs. Ag/AgCl was paired with both a hydrogenation of substrate **3** and the removal of a Cbz



Scheme 2. Varying the oxidation potential of the anodic substrate in a paired electrochemical reaction.^[29]

group from a phenylalanine derivative.^[30] The amide oxidation proceeded smoothly in both cases as did the cathodic process. When taken together, the paired electrolyses illustrated in Scheme 2 varied the oxidation potential of the anode substrate by over 1.5 V without any change in the cathodic processes.

It is also instructive to examine the previously published anodic oxidation of substrate **14** to form C-glycoside derivative **15** in the context of a paired electrochemical reaction (Scheme 3).^[31] In this case, the reaction was run in both a divided cell and an undivided cell even though it is known that the use of the divide cell leads to lower yields of the C-glycoside product. Making this change did not alter the cathodic process in any measurable way, an observation that indicated that the two reactions in a paired electrolysis can be optimized independently of each other.

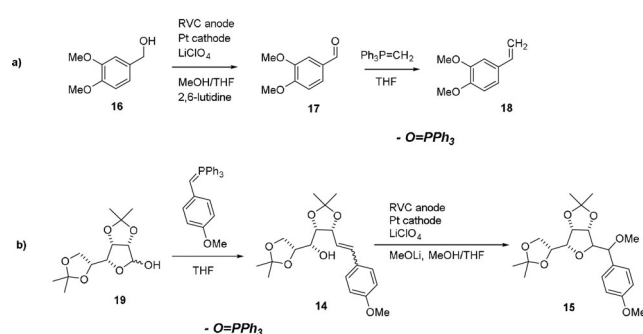


Scheme 3. The effect of an unoptimized anodic oxidation.^[29]



Varying the Reaction at the Cathode

While the work outlined above proceeded nicely, the paired electrolysis reactions conducted were ideal cases. The hydrogen evolution reaction is the auxiliary reaction of choice for the majority of anodic oxidation reactions because it is the most efficient cathodic process available. A much larger challenge moving forward is varying the reduction reaction for a paired electrolysis reaction, especially since many cathodic reactions are paired with the use of a sacrificial anode to avoid the protons generated from the majority of organic oxidation reactions and the competitive hydrogen evolution reaction that follows. Overcoming this challenge is intriguing since cathodic reactions can be used to generate bases, produce reactive anions and radical anions, synthesize syngas from carbon dioxide, reduce halogenated waste products, recycle transition metals, trigger reductive coupling reactions, etc.^[1,3,32] It is tempting to suggest that an oxidation reaction in a synthetic sequence might be used to improve the sustainability of a wide variety of reactions if one could capitalize on these cathodic transformations. Consider the two reactions shown in Scheme 4. In both cases, the synthetic



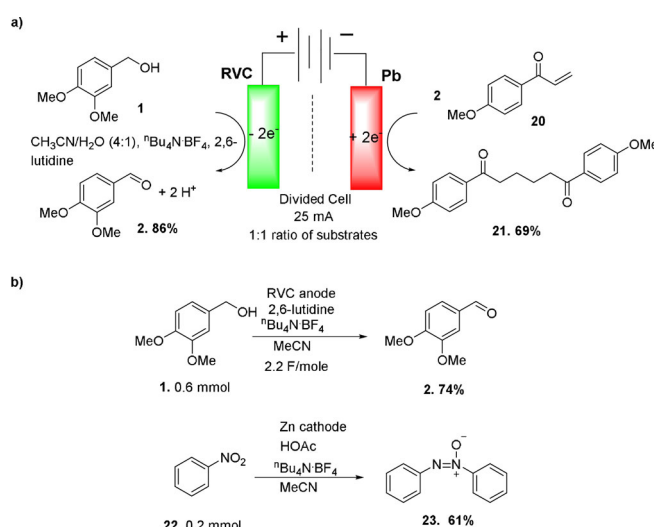
Scheme 4. Two-step sequences involving an anodic oxidation reaction.

sequence shown involves an oxidation reaction and a Wittig reaction. Both oxidation reactions have been accomplished at an anode and paired with the hydrogen evolution reaction. The anodic oxidation of the alcohol has also been paired with the reduction of carbon dioxide.^[33] In both examples, the two-step sequence shown generates triphenylphosphine oxide as a waste product, a situation that raises the question of whether it is possible to use the energy required at the cathode for the anodic oxidations to recycle that waste product.

While this suggestion is easy to make, the electrochemical reduction of $\text{Ph}_3\text{P}=\text{O}$ is not so readily paired with the oxidation of an organic molecule.^[34,35] The reactions typically use a sacrificial anode, avoid the use of a protic solvent, and take advantage of an activating group that lowers the reduction potential of the $\text{Ph}_3\text{P}=\text{O}$. All three aspects of the reaction are used to avoid the hydrogen evolution reaction that competes with the reduction of $\text{Ph}_3\text{P}=\text{O}$. The reactions can be optimized beautifully.^[35] The Sevov group has illustrated how the cathodic reduction of $\text{Ph}_3\text{P}=\text{O}$ can be paired with the use of a sacrificial aluminum anode. The anodic

reaction generates a Lewis acid that then serves to activate the $\text{Ph}_3\text{P}=\text{O}$ for reduction. This allows the reaction to be initiated with sub-stoichiometric amounts of activating group and leads to a process that is both efficient and scalable. The beautiful interplay between the anodic and cathodic processes in this reaction also illustrates the issues surrounding an effort that seeks to combine the reduction of $\text{Ph}_3\text{P}=\text{O}$ with the oxidation of an organic molecule. If the electrochemical reduction of $\text{Ph}_3\text{P}=\text{O}$ is optimized by taking full advantage of a sacrificial anode, then how easy is it to replace that sacrificial anode?

Answering this question began with an effort to overcoming the individual aspects of the challenge. Namely, we hoped to explore removal of the sacrificial anode and the use of protic solvents in cases that did not require special activation of the groups to be reduced. With this in mind, a pair of anodic oxidations were chosen to replace the sacrificial anode; an alcohol oxidation and an anodic cyclization reaction that required the use of an alcohol solvent. The reactions were paired with two reductive dimerization reactions (Scheme 5). The first of these reactions was an electrohydrodimerization reaction (Scheme 5 reaction a).^[36] It was selected because it proceeds through a radical anion intermediate that requires control of pH. Protons are needed for the final product, but the hydrogen evolution reaction needs to be avoided as a competitive cathodic process. The paired electrolysis reaction between the alcohol oxidation and the electrohydrodimerization was conducted in a mixture of acetonitrile and water (4:1) with tetrabutylammonium tetrafluoroborate (0.12 M) as the electrolyte. The reaction utilized a lead cathode along with the RVC anode employed for oxidation of the alcohol. Both the lead cathode and the hydrophobic electrolyte were used to reduce the rate of the hydrogen evolution reaction and favor the electroreductive coupling reaction. Lead cathodes have a higher over-potential for the reduction of protons,^[37] and the tetrabutylammonium tetrafluoroborate electrolyte was used to form a hydrophobic double layer at the cathode surface that lowered the local concentration of water (the substrate for the hydrogen



Scheme 5. Initial efforts to vary the cathodic reduction reaction.

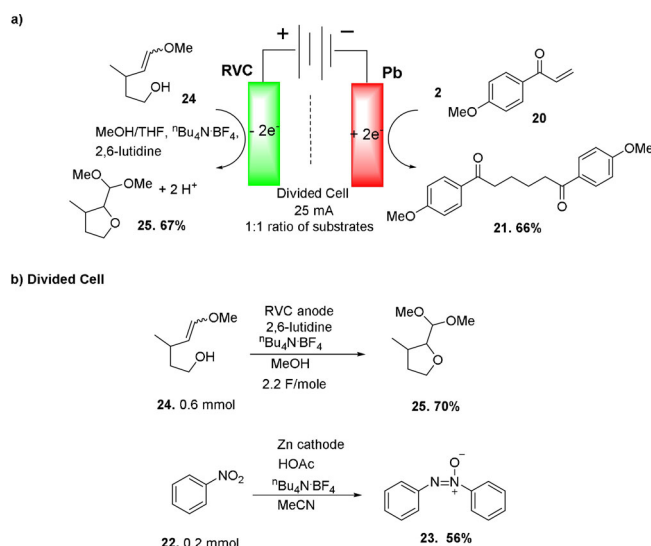
evolution reaction).^[27,32] The reaction was carried out in a divided cell using a medium porosity glass frit that was permeable to protons, a situation that allowed for protonation of the dimerization product while maintaining a low concentration of protons in order to avoid hydrogen evolution. A 1:1 ratio of the two substrates was used. After 2.2 F mol^{-1} of charge was passed through the cell, an 86 % yield of aldehyde **2** was generated at the anode and a 69 % yield of the desired dimer **21** was generated at the cathode. The oxidation reaction proceeded in a manner directly analogous to the early reactions paired with the hydrogen evolution reaction and the reduction of carbon dioxide.

The second reaction highlighted in Scheme 5 paired the alcohol oxidation reaction with the dimerization of a nitro group. This reaction was selected because it represents a particularly difficult challenge. The oxidation of an electron-rich alcohol is a two-electron process that benefits from basic conditions while the reductive dimerization of the nitro group is a six-electron process that benefits from acidic conditions. To achieve this compromise, the reaction was setup in a divided cell using acetonitrile as solvent and tetrabutylammonium tetrafluoroborate as the electrolyte. The ratio of substrate in the anodic chamber to substrate in the cathodic chamber was 3:1 to accommodate the different stoichiometry of charge needed for the two reactions. Acetic acid was then added to the cathodic chamber to provide protons for the reduction, and 2,6-lutidine was added to the anodic chamber to maintain the basic environment needed for the oxidation. A constant current of 25 mA was then passed through the cell until 2.2 F mol^{-1} of electricity was consumed relative to the veratryl alcohol oxidation substrate. The reaction afforded a 74 % yield of the aldehyde oxidation product and a 61 % yield of dimer at the cathode. Once again, the success of both transformations illustrated that the cathodic process in the paired electrolysis could be varied without significantly altering the alcohol oxidation, even when that cathodic process was significantly more complex requiring multiple steps and a different pH.

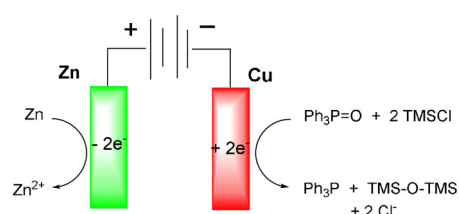
Once the cathodic reactions shown in Scheme 5 were established, varying the oxidation chemistry could be done easily. When the alcohol oxidation was replaced with an anodic cyclization reaction (Scheme 6),^[38] the working potential at the anode simply adjusted to the new substrate without changing the chemistry at the cathode.

Pairing Oxidations with the Reduction of $\text{Ph}_3\text{P}=\text{O}$

With that background, attention was turned to the reactions illustrated in Scheme 4. As a starting point, we selected a method developed by the Tanaka group (Scheme 7).^[34] This reaction utilizes TMSCl as the activating agent for the reduction of $\text{Ph}_3\text{P}=\text{O}$ along with a sacrificial Zn-anode. The reduction reaction is not directly coupled to the anodic oxidation, a situation that implied that the sacrificial Zn-anode might not be needed. This suggestion was confirmed with a series of control experiments (for details see the supporting information) that replaced the Zn-anode with an RVC anode and an alternative oxidation reaction. For

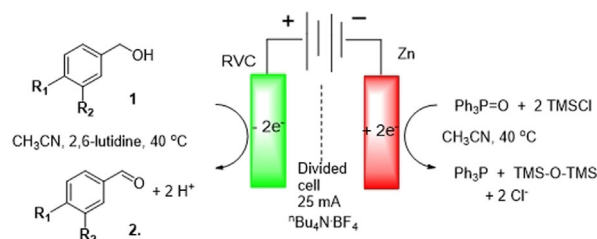


Scheme 6. Varying the oxidation paired with the new cathodic processes.



Scheme 7. Previous $\text{Ph}_3\text{P}=\text{O}$ reduction.

example, the sacrificial electrode can be replaced with veratryl alcohol as the anodic substrate for the paired electrolysis (Scheme 8/ entry 1). In these experiments, tetrabutylammonium tetrafluoroborate was used as the electrolyte along with a zinc cathode.^[39] As in the reaction highlighted earlier, the tetrabutylammonium ion was used to lower the



Entry	R ₁	R ₂	Yield 2 ^a	Yield Ph_3P
1	OMe	OMe	83%	79%
2	OMe	H	73%	70%
3	CH ₃	CH ₃	61%	72%
4	CH ₃	H	72%	66%
5	H	H	62%	70%
6	NO ₂	H	0%	--

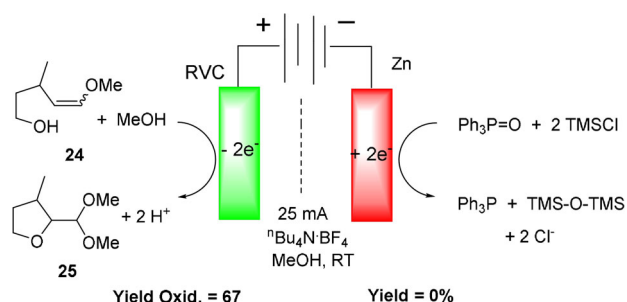
Scheme 8. Pairing alcohol oxidations with the reduction of $\text{Ph}_3\text{P}=\text{O}$. a) Isolated yield. b) Ph_3P was isolated along with about 10% of the TMSOTMS ether. The yield reported in the Table reflects the Ph_3P portion of this mixture as determined by phosphorous NMR.



concentration of water at the surface of the cathode in combination with a cathode having a higher hydrogen overpotential to minimize the hydrogen evolution reaction and optimize the reduction of $\text{Ph}_3\text{P}=\text{O}$ in the presence of protons. The reaction provided an 83% yield of the aldehyde product at the anode and a 79% isolated yield of triphenylphosphine at the cathode. The yield of the oxidation reaction was for all practical purposes the same as that obtained in all of the other paired electrochemical reactions using veratryl alcohol as the oxidation substrate. Clearly, the scope of the reduction reactions paired with the oxidation of veratryl alcohol could be expanded to include the reduction of $\text{Ph}_3\text{P}=\text{O}$.

Having established that we could pair veratryl alcohol oxidation with the reduction of $\text{Ph}_3\text{P}=\text{O}$, we examined the scope of the reactions with less electron-rich alcohols (Scheme 8). With the exception of the electrolysis using the electron-poor 4-nitrobenzyl alcohol, the reactions proceeded well with the cathodic reaction undergoing little to no change as the oxidation potential of the alcohol substrate was varied. The failure of the oxidation with 4-nitrobenzyl alcohol was not a surprise since the direct oxidation reaction conducted involves the generation of a radical cation from the aryl ring.

Next we turned our attention to pairing the reduction of $\text{Ph}_3\text{P}=\text{O}$ with the anodic cyclization. Unfortunately, all attempts to accomplish this pairing met with failure (Scheme 9). While the cyclization reaction proceeded well,



Scheme 9. Pairing an anodic cyclization with $\text{Ph}_3\text{P}=\text{O}$ reduction in the presence of methanol.

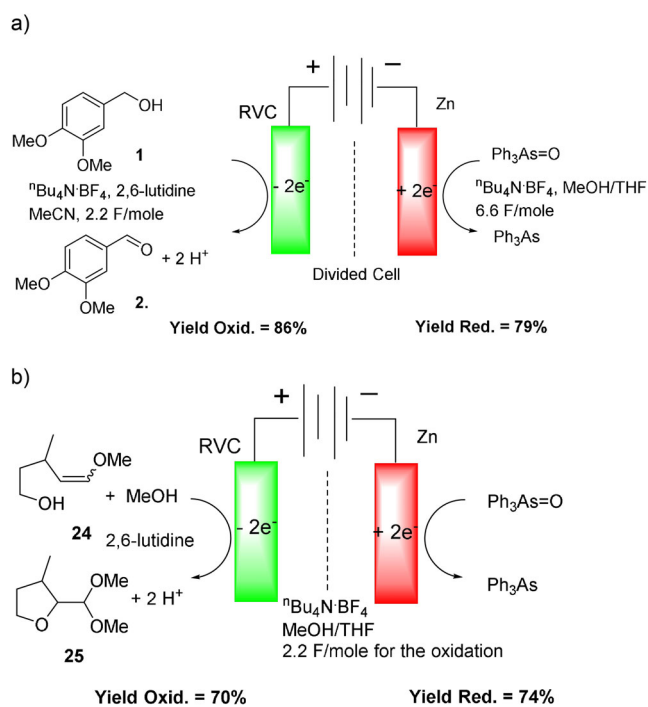
anodic cyclization reactions require a significant concentration of methanol in order to trap the cations generated by the net two-electron oxidation.^[38] The use of the methanol solvent is not compatible with the TMSCl used to activate the $\text{Ph}_3\text{P}=\text{O}$. We had hoped to avoid this problem by only adding the methanol to the anodic chamber of the reaction. However, enough of this methanol migrated through the glass frit dividing the anodic chamber to the cathodic chamber of the cell to destroy the TMSCl in the cathodic chamber. The hydrogen evolution reaction dominated the cathodic process and no more than a trace of the reduced triphenylphosphine product could be observed. In each case, $\text{Ph}_3\text{P}=\text{O}$ was recovered in high yield, an observation that indicated that the initial reduction of the $\text{P}=\text{O}$ bond was not accomplished.

While the electrolysis cell could be engineered to prevent the migration of methanol to the cathode or the activating group changed to one compatible with methanol, it is

important to point out that the overall process itself is not ideal. While the reactions in Scheme 8 do allow for the recycling of $\text{Ph}_3\text{P}=\text{O}$, they do so by using an activating group that leads to a stoichiometric amount of a different waste product. A better solution would be the development of a triphenylphosphine oxide reduction that did not require a stoichiometric activating group or the generation of any stoichiometric waste product.

One approach to accomplish this goal would be the use of an electrocatalyst for the reduction that would operate at a potential lower than that required for the hydrogen evolution reaction and selectively reduce phosphine-oxygen bonds in the presence of protons. Such a catalyst would operate in a manner directly analogous to the mediated reduction of carbon dioxide in water.^[33] Insight into the potential at which a catalyst of this type would need to operate was gained by examining the reduction of triphenylarsine oxide in the presence of methanol. The reduction of $\text{Ph}_3\text{As}=\text{O}$ can be accomplished chemically,^[40] and $\text{Ph}_3\text{As}=\text{O}$ is known to be a better oxygen donor than $\text{Ph}_3\text{P}=\text{O}$.^[41] This increased reactivity is presumably due to the arsine oxygen bond being weaker than the phosphine oxygen bond.^[42] We hoped that the increased reactivity of the $\text{Ph}_3\text{As}=\text{O}$ might make its reduction compatible with an anodic cyclization in the presence of the required methanol solvent and thereby provide information on the reduction potential needed for such a process. This alternative for $\text{Ph}_3\text{P}=\text{O}$ was intriguing because Geary and co-workers have demonstrated that Wittig reactions can be conducted with the use of Ph_3As in place of the Ph_3P .^[43,44]

The reduction of $\text{Ph}_3\text{As}=\text{O}$ was initially paired with the oxidation of veratryl alcohol [Scheme 10, Eq. (a)]. In this



Scheme 10. Reactions using triphenylarsine oxide in place of triphenylphosphine oxide.

case, the reaction tolerated the presence of methanol solvent even when methanol was added directly to the cathodic chamber. As in the earlier reactions, a Zn-cathode was employed to minimize the competing hydrogen evolution reaction, and a divided cell was used to avoid re-oxidation of the Ph_3As product generated at the cathode. The reaction did benefit from the oxidation reaction being conducted on a scale about three times that of the reduction, presumably because of a background hydrogen evolution reaction consuming some of the current at the cathode. With this caveat, both reactions proceeded in good yield. With the observation that the reduction of $\text{Ph}_3\text{As}=\text{O}$ could tolerate the presence of methanol, the reaction highlighted in Scheme 10b was conducted. Both reactions proceeded well.

Insight into the success of this reaction was gained by cyclic voltammetry (see the Supporting Information for the CV data). As a baseline, the reduction potential of $\text{Ph}_3\text{P}=\text{O}$ was measured in acetonitrile at a glassy carbon electrode and found to be $E_{p/2} = -2.50$ V vs. Ag/AgCl . The reduction wave was found in the same place as the reduction wave for methanol which has an onset potential of around -2.2 V vs. Ag/AgCl , an observation that showed why the reduction of $\text{Ph}_3\text{P}=\text{O}$ fails in the presence of methanol. The addition of TMSCl to the reduction of $\text{Ph}_3\text{P}=\text{O}$ in acetonitrile led to a shift in the reduction potential for $\text{Ph}_3\text{P}=\text{O}$ of approximately 800 mV ($E_{p/2} = -1.70$ V vs. Ag/AgCl), presumably due to either silylation of the $\text{Ph}_3\text{P}=\text{O}$ prior to the reduction or rapid trapping of the radical anion derived from $\text{Ph}_3\text{P}=\text{O}$ reduction. This shift made the reduction of $\text{Ph}_3\text{P}=\text{O}$ significantly more favorable than the hydrogen evolution reaction, a change that enabled the success of the reactions shown in Scheme 8. Of course, the presence of the methanol solvent in the reaction shown in Scheme 9 destroyed the TMSCl and stopped the desired reduction.

When the cyclic voltammetry experiment was repeated with the use of $\text{Ph}_3\text{As}=\text{O}$ in acetonitrile, the potential measured for the $\text{Ph}_3\text{As}=\text{O}$ was $E_{p/2} = -2.45$ V vs. Ag/AgCl . This result was a surprise given the success of the reaction shown in Scheme 10b relative to the same reaction using $\text{Ph}_3\text{P}=\text{O}$ (Scheme 9). Since the reduction of $\text{Ph}_3\text{As}=\text{O}$ did not require the presence of the TMSCl , we had assumed it was easier to reduce than $\text{Ph}_3\text{P}=\text{O}$. However, the 50 mV difference in reduction potential for the two substrates was far too small for such an explanation, especially with a methanol onset potential of $E_{p/2} = -2.2$ V vs. Ag/AgCl .

The key issue turned out to be a difference between the CV and preparative electrolyses. The CV data reported above was obtained in the absence of methanol solvent while the preparative reactions shown in Scheme 9 and Scheme 10b required methanol. When the CV experiment utilizing $\text{Ph}_3\text{P}=\text{O}$ was repeated in the presence of methanol, a small shift in the reduction potential to $E_{p/2} = -2.35$ V vs. Ag/AgCl was observed along with a significant increase in current. It appeared that the reduction of the triphenylphosphine might help catalyze a reaction with the methanol, an observation that was consistent with the preparative reaction leading to a complete recovery of the $\text{Ph}_3\text{P}=\text{O}$ starting material.

When the CV experiment utilizing $\text{Ph}_3\text{As}=\text{O}$ was repeated in the presence of methanol, a different conclusion was

reached. In this case, the presence of the methanol solvent led to a shift in the reduction potential for the $\text{Ph}_3\text{As}=\text{O}$ of approximately 350 mV to an $E_{p/2}$ value of -2.10 V vs. Ag/AgCl . This potential is significantly more positive than the onset potential needed for the reduction of methanol, a scenario that enabled the paired electrolysis reaction shown in Scheme 10b.

The result obtained for the reduction of $\text{Ph}_3\text{As}=\text{O}$ indicated that a successful pairing of an anodic cyclization in methanol solvent with the reduction of $\text{Ph}_3\text{P}=\text{O}$ will require an electrocatalyst that operates at a potential that is only 250 mV more positive than the reduction potential of triphenylphosphine oxide (in methanol), a difference in potential that is consistent with the energy difference commonly seen between an electrocatalyst and its targeted substrate.^[45]

Recycling Sacrificial Anodes

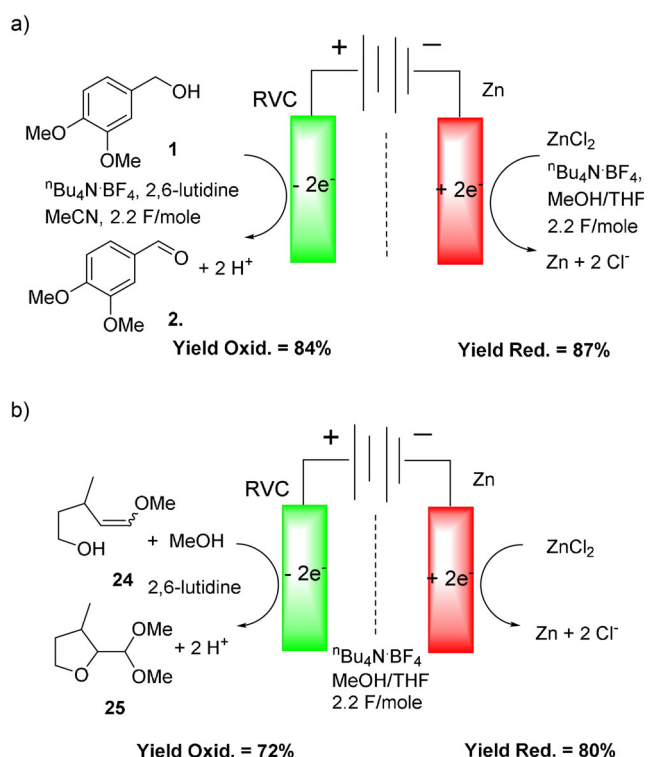
While the chemistry discussed above targeted reduction reactions that do not require the use of a sacrificial anode, a large number of reduction reactions (the generation of an anionic nucleophiles, the use of electrogenerated bases, etc.) do require such an electrode. In those cases, the direct pairing of the cathodic reaction with the oxidation of an organic molecule can be ruled out. However, an oxidation can still be utilized to make the corresponding reduction more sustainable. Reduction reactions paired with a sacrificial anode still produce a stoichiometric waste product that can be recycled with the energy used at the auxiliary electrode of an anodic reaction.

Consider the reactions shown in Scheme 11. For each oxidation reaction, a Zn-electrode was employed as the cathode and a Zn^{2+} -salt was added to cathodic chamber. The cathode was weighed before and after the reaction to determine the weight of Zn^0 that was deposited on the electrode. Both reactions proceeded smoothly leading to good yields of the anodic products and over 80% recovery of Zn on the cathode.^[46] The reactions were run using equal molar amounts of substrate for both the anodic and cathodic reactions indicating that the hydrogen evolution reaction was not competitive with the desired reduction.

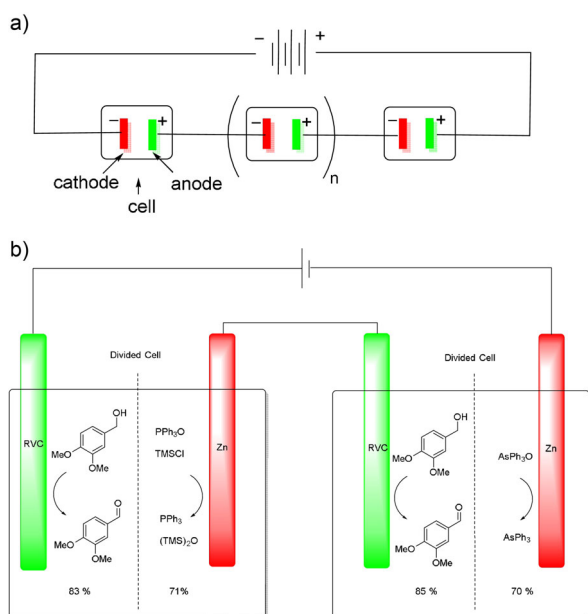
Pairing Reactions on Different Scales

In the introduction, we mentioned that since current can be split, paired electrochemical reactions do not have to be conducted using reactions that are required on the same scale. One can engineer an electrolysis cell to demonstrate this capability, but there are simpler ways to achieve that demonstration. Take for example the chemistry illustrated in Scheme 12. The reactions shown were run in electrochemical cells linked together in a series format. In this format, the cathode of the first cell was wired to the anode of the second cell, the cathode of the second cell was wired to the anode of the third cell, etc. A constant current was then passed through each of the cells and all of the electrodes





Scheme 11. Regeneration of a sacrificial anode.



Scheme 12. Pairing reactions on different scales. a) Organization of electrochemical cells in a series format. b) An example of using a series electrolysis for paired synthesis.

allowed to adjust their working potentials to match the substrate present.^[47] An application of this approach to paired electrochemical reactions is highlighted in Scheme 12. In these reactions, the anodic oxidation of veratryl alcohol was paired with both a $\text{Ph}_3\text{P}=\text{O}$ reduction in the presence of TMSCl and a $\text{Ph}_3\text{As}=\text{O}$ reduction in the presence of

methanol. The two reduction reactions were chosen because they are not compatible with each other. The oxidation reaction was conducted on roughly twice the scale of either reduction (0.5 mmol of alcohol in each cell along with 0.25 mmol of $\text{Ph}_3\text{P}=\text{O}$ in one cell and 0.17 mmol of $\text{Ph}_3\text{As}=\text{O}$ in the other; the reduction in both cases was a four-electron process). Of course, there was no need for this stoichiometry. If one wanted to run a much larger oxidation reaction without increasing the scale of the reduction reactions, then a third cell could have been added to the series pairing the oxidation with a hydrogen evolution reaction or another reduction. One could either take advantage of the cathodic product from that cell or not. The point is that some of the current used at the counter electrode of a large-scale oxidation reaction can be put to a productive use without any need for a reduction reaction of matching scale.

It is also important to point out that this is the approach that would be taken to scaling the reactions. While one always has an option of scaling-up or scaling-out a chemical process, the compatibility of the reactions with a series format suggests that scaling-out the current reactions is an attractive approach.

Conclusion

While the utility of paired electrochemical reactions has been known for quite some time and there are numerous examples of how the energy efficiency of such processes can be optimized in the context of perfectly matched sets of oxidation and reduction reactions, the reactions have found limited use by the larger synthetic community that is motivated by the need to synthesize molecules for a specific purpose. With that in mind, paired electrochemical reactions that do not involve perfectly matched pairs of substrates have been examined. The work described here illustrates that the chemistry at the cathode in a paired electrolysis can also be used to drive a variety of processes without altering the anodic oxidation, even when those processes are less than optimal. Furthermore, it was shown that the scale of the paired reactions does not have to be matched. The result is an expanded opportunity to use paired electrochemical reactions in a manner that is driven entirely by synthetic need.

Acknowledgements

We thank the National Science Foundation (CHE-1764449) for their generous support of our program. We also thank Professor Laina M. Geary (UN Reno) for helpful conversations.

Conflict of interest


The authors declare no conflict of interest.

Keywords: organic synthesis · paired electrolysis · sustainability

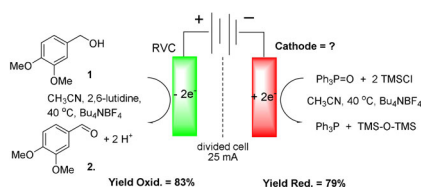
Research Articles



Electrochemistry

T. Wu, K. D. Moeller* 

Organic Electrochemistry: Expanding the Scope of Paired Reactions



Many paired electrochemical reactions use perfectly matched reactions at the anode and cathode, but this matching is not necessary. In constant current electrolysis, the potential at both electrodes adjusts to the substrates in solution. Oxidation reactions were paired with H₂ generation, showing the generality of the anodic process. This effort was followed by pairing multiple cathodic reactions with a pair of established oxidation reactions.

