Organic Electrochemistry as a Tool for Synthesis

Umpolung Reactions, Reactive Intermediates, and the Design of New Synthetic Methods

by R. Daniel Little and Kevin D. Moeller

Because electrochemistry allows for the selective introduction and removal of electrons from organic molecules, it is an ideal tool for reversing the polarity of known functional groups and triggering umpolung reactions. For example, electrons can be added to electron-poor functional groups in order to convert them from electrophiles into nucleophiles or removed from electron-rich functional groups in order to convert them from nucleophiles into electrophiles (Fig. 1). The ensuing reactive intermediates can then be trapped in order to complete reactions that involve the net coupling of either two electrophiles or two nucleophiles in ways that would be otherwise impossible. Such reactions are intriguing because their availability creates the potential for developing entirely new synthetic strategies for the construction of complex molecules. What follows is a short (non-comprehensive) review of recent developments that point the way to what can be accomplished using synthetic electrochemistry in the future.

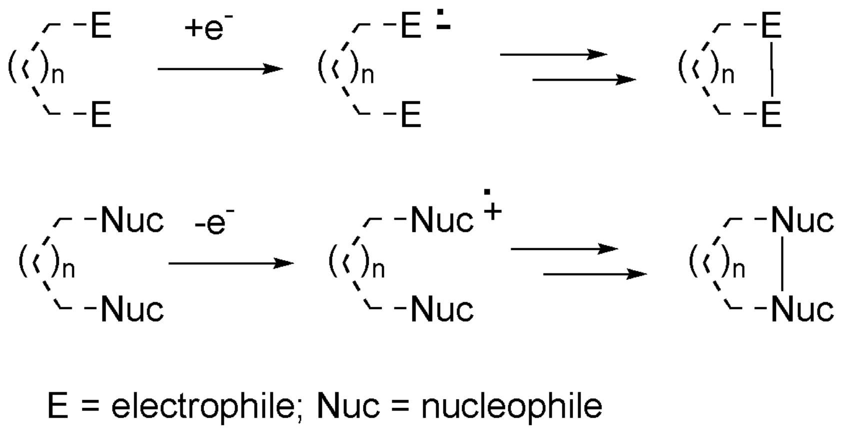

FIG. 1. Electrons can be added to electron-poor functional groups in order to convert them from electrophiles into nucleophiles or removed from electron-rich functional groups in order to convert them from nucleophiles into electrophiles.

Cathodic Reductions

It can be argued that the carbonyl is the most versatile and important functional group in organic chemistry. Its polarization renders the carbonyl carbon susceptible to nucleophilic attack. As indicated in the introduction, reduction reverses the polarity so that the carbonyl carbon becomes nucleophilic. Electron deficient alkenes display similar characteristics. Both the carbonyl carbon and that positioned β to an α,β-unsaturated carbonyl compound, for example, display electrophilic character. Once reduced, both sites assume nucleophilic characteristics.

Figure 2 illustrates a number of bond constructions and functional group arrays that are accessible using the carbonyl (left) or the electron deficient alkene (right) radical anion building blocks. Each scheme is organized with the radical anion at the center, while the array of accessible functionality is displayed around the perimeter. The coupling partner is indicated in parenthesis. New bonds are highlighted in blue. A few of the many specific examples that exist are portrayed in Fig. 3. Notice that even aryl groups,[2] esters,[3] and nitriles[4] can participate (Reactions (a), (b), and (f)); that four membered rings can be constructed (Reaction (d));[5] and that hindered quaternary centers can be assembled in high yield (Reaction (e)).[6] Thus, the chemistry provides a convenient means to synthesize a variety of building blocks, some of which have proven useful in the total synthesis of natural products (Reactions (e) and (f)).[7]

We do not mean to imply that only carbonyl containing substrates are useful. This is by no means the case. Many other functional groups can, and do participate in reductive coupling reactions.[8] Imines, for example, undergo electrohydrocyclization.[9] A particularly interesting example from Shono's group illustrates the utility of the process as a route to C_2 symmetric diamine ligands that have been used to activate normally unreactive dialkyl zinc reagents toward nucleophilic addition to a carbonyl group, and to achieve asymmetric induction (Fig. 3, example (g)).[10] Nitroalkenes can also serve as substrates.[11] When reduced, the radical anion participates in two different reaction pathways, depending upon whether a divided cell, or a single cell at high current density, is utilized (Fig. 3, example (h)). Given the functional group equivalence of a nitro group to a carbonyl adds interest to these transformations.

It is difficult to imagine a method better suited to the recycling of reagents than is electrochemistry. A recent review entitled "Environmental Protection and Economization of Resources by Electroorganic and Electroenzymatic Syntheses" elaborates upon this notion.[12] The authors highlight the electrochemical generation of redox reagents (mediators) and their regeneration at the electrode for reuse, the utility of paired electrosynthesis and the design and utility of electroenzymatic syntheses.

While many researchers have used mediators in creative and useful ways, we site but two examples, both from Utley's laboratory. The first example is particularly intriguing in that the mediator, maleic anhydride, also serves as the dienophile in a Diels-Alder reaction with *in situ* generated *o*-xylylene (Fig. 4, example (a)).[13] *p*-Xylylenes are also accessible via indirect electrolysis. As illustrated, nickel salen can serve as a mediator of a process that leads to *p*-xylylene, its further reduction to a radical anion, and ultimately to the controlled formation of poly(*p*-xylylenes) (Fig. 4, example (b)).[14]

Sigma bond formation between sp^2 hybridized carbon with preservation of the hybridization (aryl-aryl, vinyl-vinyl, aryl-vinyl, vinyl-alkyne) has become commonplace. This was not the case, even a comparatively short time ago. Thus, the development of the Heck and Stille reactions,[15,16] as well as the Sonogashira and Suzuki coupling processes[17,18] have rendered this bond construction relatively routine. Detailed electroanalytical studies by Amatore and Jutand have provided significant insight into the mechanism of palladium-catalyzed Heck and cross-coupling reactions.[19] Nedelec and coworkers have made notable contributions to the development of electrochemical alternatives to some of these reactions, and have uncovered several exceptionally useful variations.[20] The Nozaki-Hiyama-Kishi coupling between allyl, vinyl, or aryl halides and aldehydes, for example, is traditionally achieved using an excess of $CrCl_2$ in the presence of catalytic amounts of nickel chloride. Given the well-established toxicity of chromium salts, the chemistry is not environmentally friendly. Nedelec's group has found it possible to generate catalytic amounts of chromium and nickel from a preelectrolysis of a stainless steel rod. That material, used in the presence of 3% 2,2'-bipyridine and a sacrificial iron anode make it possible to achieve coupling in moderate to good yield (Fig. 5, Reaction (a)).[21]

While the utility of cyclic voltammetry is clear to an electrochemist, it is not obvious to others. Recently, voltammetric studies were used to gain mechanistic insight into the nickel-catalyzed homocoupling of halopyridines. Significant improvements resulted. It was discovered, for example, that the use of a sacrificial iron anode produced iron ions at a rate that allowed them, rather than nickel, to preferentially complex with the product thereby freeing the nickel to re-enter the catalytic cycle (Fig. 5, Reaction (b)). Another example of how an appropriate choice of a sacrificial anode can have a positive influence, this time upon the stereochemical outcome of an electroreductive cyclization that leads to a useful

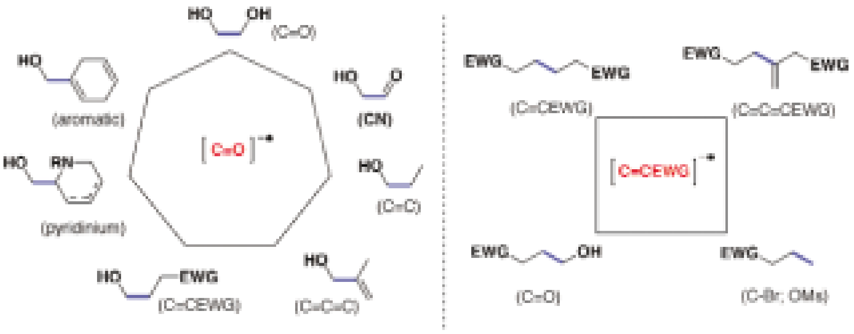

Fig. 2. This figure illustrates a number of bond constructions and functional group arrays that are accessible using the carbonyl (left) or the electron deficient alkene (right) radical anion building blocks. Each scheme is organized with the radical anion at the center, while the array of accessible functionality is displayed around the perimeter. The coupling partner is indicated in parenthesis. New bonds are highlighted in blue.

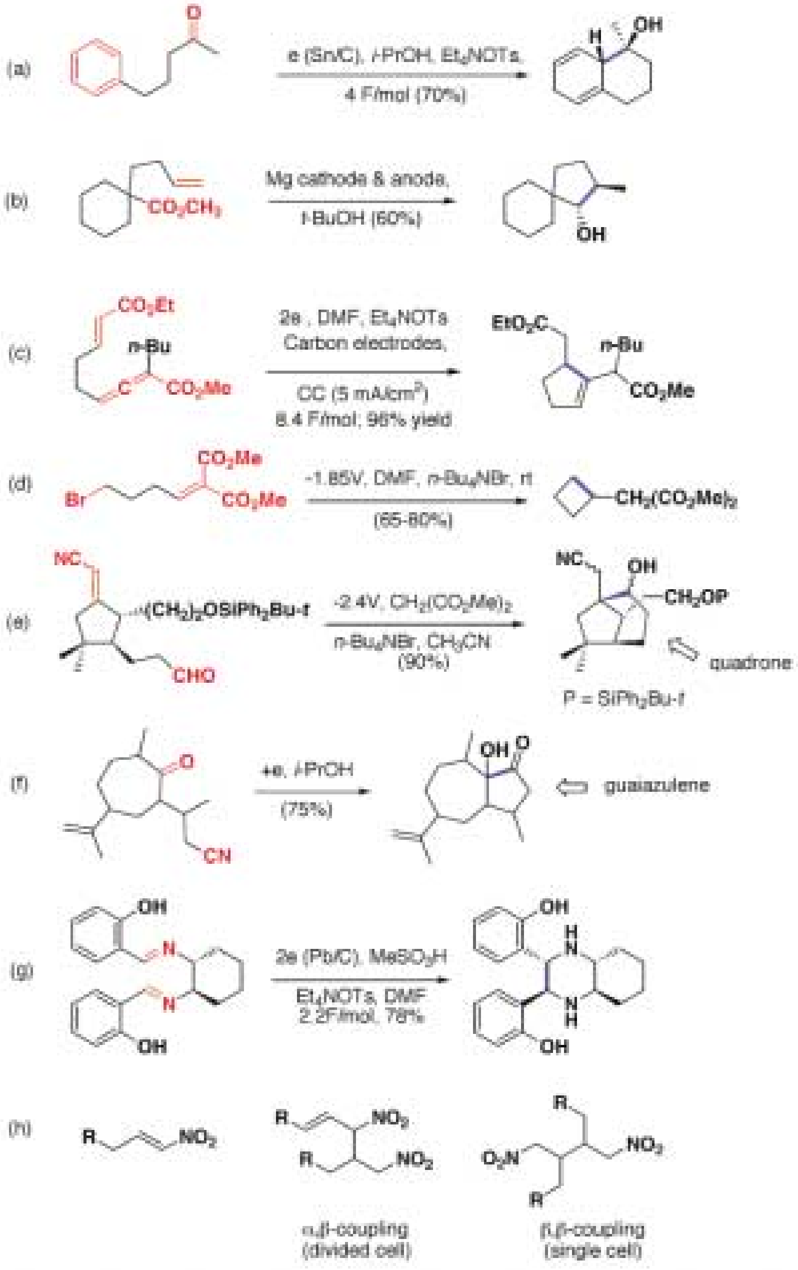

Fig. 3. A few of the many examples of the generalized scheme in Fig. 2.

building block,[22] is illustrated as Reaction (c) in Fig. 5. Presumably, the magnesium ions formed at the electrode complex with the ester and aldehyde units in a manner that favors cyclization to afford the trans substituted product. When a platinum anode is used, no stereoselectivity is observed.

Simple voltammetric experiments were also instrumental in the development of an electrochemical route to one electron lanthanide reducing agents.[23] Voltammetry provided a simple and systematic means to screen the properties of redox active species. The data provided mechanistic insight and assisted in determining which reagents were best suited for further investigation, and fine-tuning of the properties of the metal to fit the redox needs of the problem at hand. In the case of samarium(II) diiodide, CV was used to determine that ligand exchange occurs between triflate and iodide when samarium(III) triflate is mixed with the TBAI being used as the supporting electrolyte (Fig. 5, Reaction (d)). Because samarium triflate is available in large quantities, is easy to handle, and is inexpensive, the electrochemical protocol provides a convenient alternative to existing routes to SmI_2. Of added interest is that fact that one can operate at a potential less reducing than that required for the direct reductive coupling of the substrate. This suggests that it should be possible to use more elaborate substrates whose functionality would normally be reduced. A similar protocol was used to electrochemically generate ytterbium (II) reagents whose reducing properties differed from those of samarium (Fig. 5, Reaction (e)).

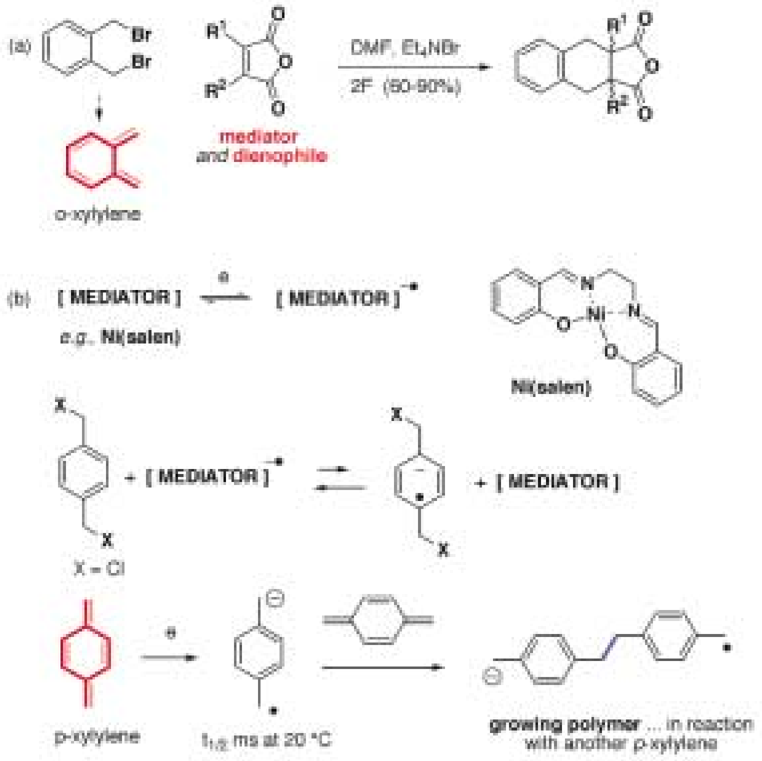

Fig. 4. Nickel salen can serve as a mediator of a process that leads to p-*xylylene, its further reduction to a radical anion, and ultimately to the controlled formation of poly(*p-*xylylenes).*

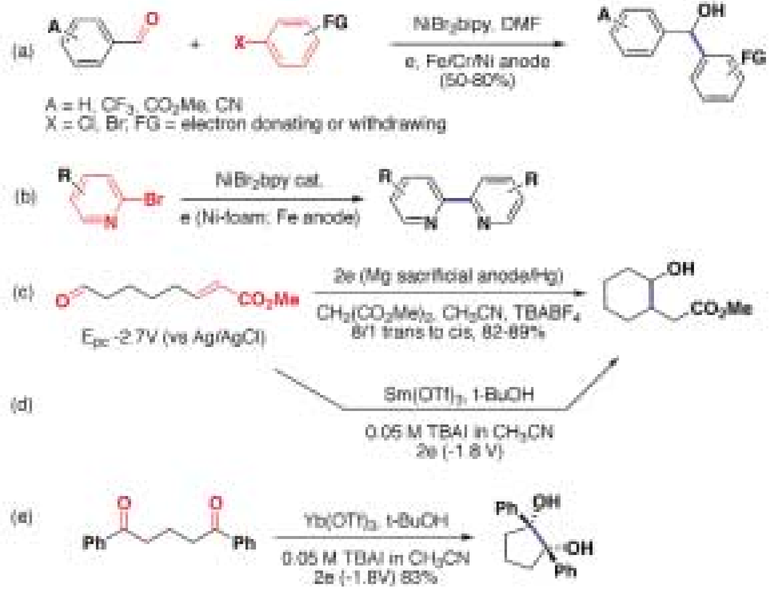

Fig. 5. Stainless steel, used in the presence of 3% 2,2'-bipyridine and a sacrificial iron anode, make it possible to achieve sp^2-sp^2 *coupling in moderate to good yield. Ligand exchange occurs between triflate and iodide when samarium (III) triflate is mixed with the TBAI supporting electrolyte. Reduction provides a convenient alternative to existing routes to* SmI_2.

Anodic Oxidations

Anodic electrochemistry offers a unique opportunity for initiating reactions that construct new bonds while either increasing or preserving the functionality needed to further manipulate the product generated. For this reason, a number of groups have focused on the development of anodically initiated synthetic methods. Much of this work has been recently reviewed.[24] For that reason, we will focus this abbreviated summary on recent examples that illustrate the potential synthetic utility of anodically generated umpolung reactions. In so doing we hope to entice interested readers to probe the broader area in more detail on their own. In particular, we would call readers attention to the fine work done utilizing the Kolbe electrolysis reaction[25] as well as the synthetic utility of mediated electrochemical processes.[26]

Elimination Reactions

The anodic oxidation reaction of a neutral substrate leads to a reactive radical cation intermediate that can then undergo either an elimination or fragmentation reaction, a trapping reaction, or an electron transfer reaction to form a second reactive intermediate. Elimination reactions most often lead to reactive cation species that subsequently

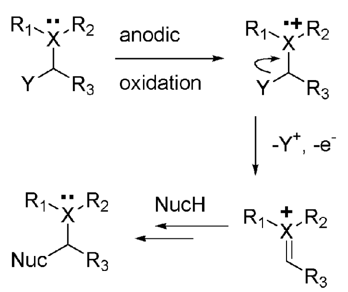

Fig. 6. The anodic oxidation reaction of a neutral substrate leads to a reactive radical cation intermediate that can then undergo either an elimination or fragmentation reaction, a trapping reaction, or an electron transfer reaction to form a second reactive intermediate. Elimination reactions most often lead to reactive cation species that subsequently trap nucleophiles.

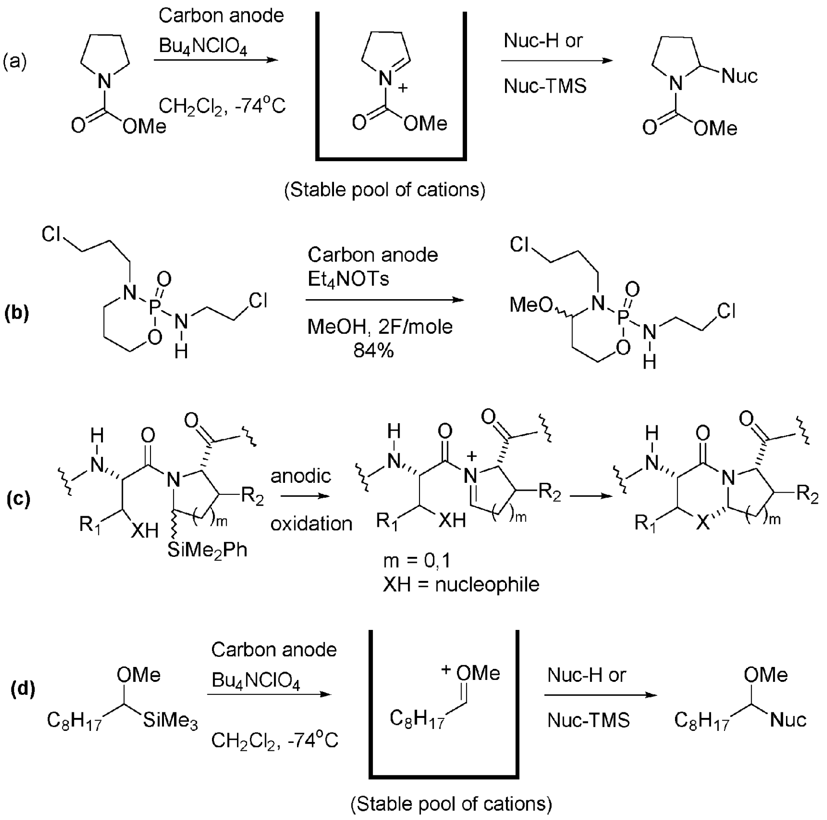

Fig. 7. Examples of the generalized Scheme in Fig. 6.

trap nucleophiles (Fig. 6). Such transformations are frequently used to selectively introduce functionality into a substrate and are notable because they reverse the flow of electrons normally used to generate the cationic intermediate. For example, cationic intermediates are typically generated from general substrates like the one illustrated in Fig. 6 by treatment of the substrate with acid. This protonates Y and converts it into a leaving group. The lone pair on X then assists in the departure of the leaving group. In the case of an oxidation reaction, the opposite scenario occurs. In this case the C-Y bond donates electron density to the radical cation that is formed by the initial oxidation. Hence Y is not a leaving group but rather a hydrogen, silyl group, etc.

To date, the most common application of this chemistry has been the oxidative generation of N-acyliminium ions from amides and carbamates. While this area has been extensively reviewed,[27] several recent examples deserve comment here. Yudin and coworkers have developed electrochemical techniques for effecting the parallel synthesis of N-acyliminium ions from pyrrolidine (R_1= $-CO_2Me$ or -COR, R_2=R_3 = $-(CH_2)_3$-, Y=H) and piperidine (R_1= $-CO_2Me$ or -COR, R_2=R_3 = $-(CH_2)_4$, Y=H) based carbamates.[28] The N-acyliminium ions generated were used to build a small library of alkylated amines. Taking an alternative approach, Yoshida and coworkers utilized low temperature anodic oxidation reactions to generate "cation pools" of N-acyliminium ions in the absence of a nucleophile (Fig. 7, example (a)).[29] Under such conditions, the cations are stable and can be used to build combinatorial libraries of molecules using split-pool synthesis techniques. The cation-pool method has also been used to establish cation-flows for use in microflow synthesis systems,[30] as well as to provide substrates for initiating the formation of α-N-alkyl radicals.[31]

Amide oxidation reactions have not been restricted to model systems or the construction of simple alkylated building blocks. Hudlicky and coworkers have used an anodic amide oxidation in the construction of both octahydroisoquinoline[32] and azathymine derivatives.[33] Royer and coworkers utilized an anodic amide oxidation in order to build metabolites of the anticancer drugs ifosfamide and cyclophophamide (Fig. 7, example (b)).[34] Anodic amide oxidations have also proven useful for the construction of constrained peptide mimetics.[35] In a recent variation on these efforts, the use of a silyl group as an electroauxiliary[36] was employed so that an N-acyliminium ion could be inserted into a polypeptide (Fig. 7, example (c)).[37] This work clearly illustrated the synthetic utility of reversing the polarity in which the N-acyliminium ion was formed by showing how the electroauxiliary could be added to an amino acid starting material and then the resulting building block incorporated into preselected sites within the peptide. An analogous strategy that masked the N-acyliminium ion with a leaving group on the carbon alpha to nitrogen would fail due to the instability of the initial functionalized amino acid building block.

Electroauxiliaries have also been used in the synthesis of oxonium ions.[38] As in the iminium ion case, this chemistry can be employed to make cation-pools (Fig. 7, example (d)).[39] When generated in this fashion the oxonium ions are stable and can be used in a split pool synthesis.

Interestingly, when both a stannyl and a silyl electroauxiliary are placed on the carbon alpha to an oxygen, the electroauxiliaries can be removed one at a time. This enables the sequential addition of nucleophiles to the carbon bearing the oxygen.[40]

In addition to nitrogen and oxygen heteroatoms, the oxidation of sulfur compounds has been used to trigger synthetically useful reactions.[41] For example, Chiba and coworkers have taken advantage of the oxidation and then elimination of sulfur groups in order to generate highly reactive o-quinodimethane dienes for use in novel Diels-Alder reactions.[42]

Trapping Reactions

While elimination reactions have been employed in a number of successful syntheses, it is perhaps the trapping of a radical cation intermediate that most clearly illustrates the utility of anodic electrochemistry for initiating umpolung reactions. Consider the second of the two generalized reactions outlined earlier in Fig. 1. In this reaction, the oxidation of a substrate having two nucleophiles leads to the formation of a radical cation followed by a coupling of the two nucleophiles. Such transformations open up the possibility of developing new methods for the construction of ring systems.

Initially, reactions of this nature were demonstrated by the coupling of electron-rich aromatic rings.[43] More recently, the oxidation of an enol ether was shown to afford a radical cation that can be trapped by a host of nucleophiles.[44] As illustrated in Fig. 8, example (a), the anodic coupling of an enol ether and an allylsilane can be used to form fused bicyclic ring skeletons while generating a quaternary carbon.[45] This example illustrates the uniqueness of the anodic oxidation approach. On one hand, the radical cation intermediate generated is reactive enough to generate the quaternary carbon in high yield. On the other hand, the reaction conditions are gentle enough to be compatible with an alkoxy-leaving group on the allylic carbon of an allylsilane. Such reactions are not restricted to simple olefinic terminating groups. Wright and coworkers have used the anodic coupling of an enol ether to a furan ring in order to build the tetracyclic core of the cyathin ring skeleton (Fig. 8, example (b)).[46] Anodic coupling reactions of this nature can also be initiated by the oxidation of ketene acetal equivalents.[47] In related reactions, Yamamura and coworkers have used the intramolecular coupling of phenols and electron-rich olefins in order to synthesize a variety of natural products. Since this work has been recently reviewed,[48] a single example leading to the synthesis of acourtia-isocedrene (Fig. 8, example (c)) is illustrated here.[49] Intermolecular examples of these reactions have also been used in synthesis. For example, Chiba and coworkers have demonstrated that intermolecular coupling reactions between phenols and electron-rich olefins can provide a nice [3+2]-cycloaddition route to furan rings (Fig. 8, example (d)).[50] This work was analogous to earlier efforts published by the Swenton group.[51]

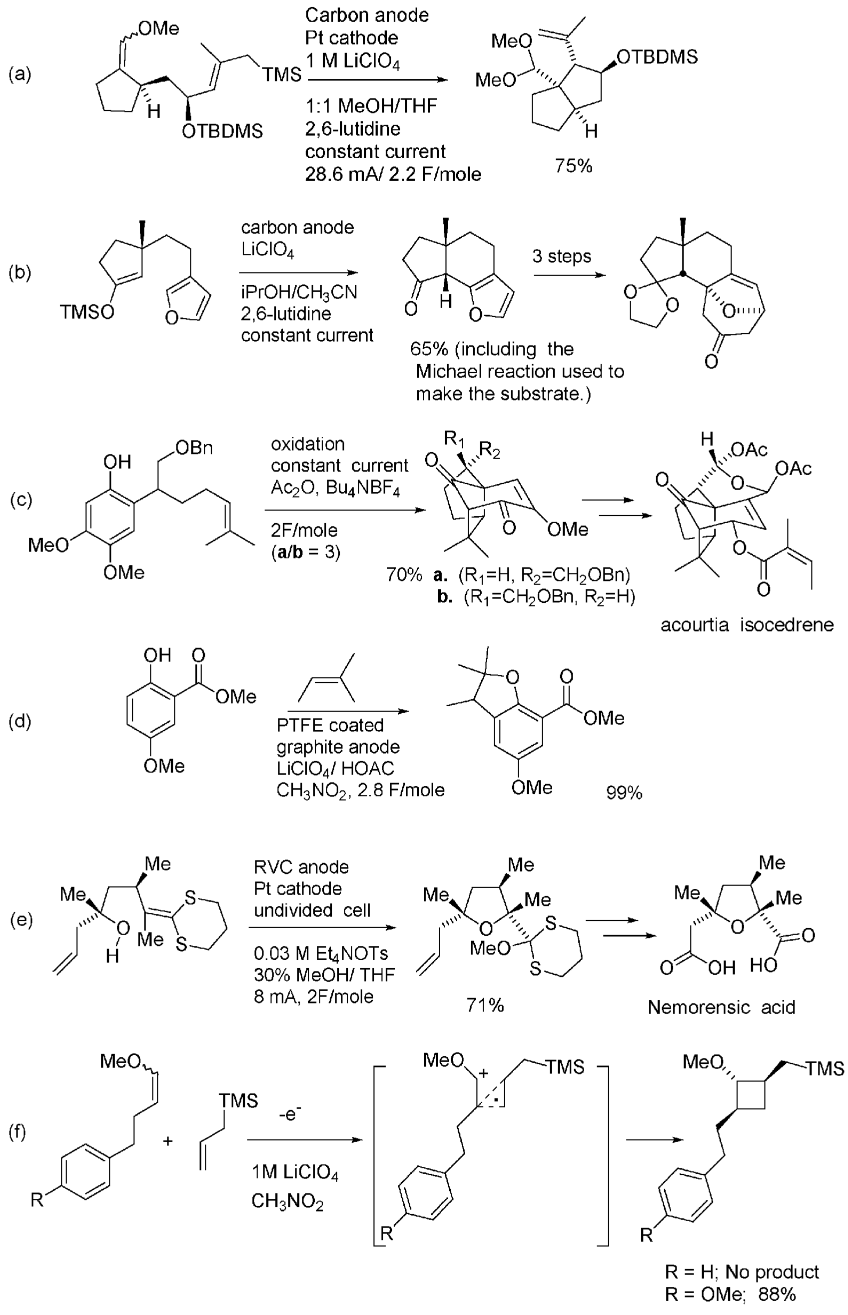

FIG. 8. *Trapping reactions where the insipient radical cation intermediate is coupled to a nucleophile can also provide a powerful method for constructing new bonds and synthesizing new ring skeletons.*

Oxygen nucleophiles have been used to terminate anodic cyclization reactions originating from the oxidation of both enol ethers and ketene dithioacetals in order to form tetrahydrofuran and tetrahydropyran rings.[52] For example, the anodic oxidation of a ketene dithioacetal has been used to trigger the formation of a tetrahydrofuran derivative used in the synthesis of (+)-nemorensic acid (Fig. 8, example (e)).[53] Note how in a retrosynthetic sense the availability of this reaction allowed for the disconnection of an oxygen nucleophile from the normally nucleophilic carbon alpha to a carbonyl.

In an interesting twist on these reactions, a pair of recent anodic couplings benefited from an internal electron transfer reaction. In the first example, an anodic coupling between an enol ether and an alcohol nucleophile was accomplished in the presence of a more easily oxidized dithioacetal.[54] In this case, the initial oxidation took place on sulfur. An intramolecular electron transfer then led to formation of the enol ether radical cation that was trapped by the oxygen. In the second example, an intermolecular [2+2] cycloaddition reaction was aided by the presence of a remote aryl ring (Fig. 8, example (f)).[55] In this case, the initial coupling led to a radical cation intermediate that accepted an electron from the electron rich aromatic ring. The resulting aryl radical cation oxidized another molecule of the substrate leading to an electrocatalytic reaction. In the absence of the electron rich aryl ring, the initial reaction led to none of the cyclized product.

As a final note, the reactions illustrated in Figures 5 and 6 combine to further demonstrate the versatility of the electrochemical method. The nature, stability, and oxidation potentials of the substrates vary widely. Yet the same technique is used to accomplish each of the reactions. In order to study the same set of reactions using either chemical or photochemical oxidation methods, a host of stoichiometric oxidants would have been required. Hence, it is easy to see why electrochemistry provides such a powerful tool for investigating new radical cation based synthetic methodology.

Conclusions

The discussion among chemists about the true synthetic utility of organic electrochemistry was initiated long before many of us started to do science. What is known is that electrochemistry can provide a neutral, tunable method for generating and studying a wide variety of reactive intermediates in a systematic way. This can be accomplished with readily available equipment and well-defined synthetic protocols.[56] Recent efforts have discovered a host of new transformations that open up novel synthetic routes to many complex molecules.

But with the development of these new synthetic methods, will electrochemistry finally take its place among the tools commonly used by synthetic chemists in the future? The success, ease, and uniqueness of current electrochemical methods suggest that the answer to this question may no longer lie in demonstrating that electrochemistry can serve as a useful alternative to existing chemical methods, but rather in demonstrating that there is no need to develop new, stoichiometric chemical methods to serve as alternatives to existing electrochemical methods. ■

References

1. (a) M. F. Nielsen and J. H. P. Utley, in *Organic Electrochemistry, 4th ed.*, p. 795, H. Lund and O. Hammerich, Eds., Marcel Dekker, New York (2001); (b) R. D. Little and M. K. Schwaebe, in *Topics in Current Chemistry,* 185, 1-48, E. Steckhan, Ed., Springer, Berlin (1996).
2. (a) T. Shono, N, Kise, T. Suzumoto, and T. Morimoto, *J. Am. Chem. Soc.*, **108,** 4676 (1986); (b) N. Kise, T. Suzumoto, and T. Shono, *J. Org. Chem.*, **59,** 1407 (1994).
3. S. Kashimura, Y. Murai, M. Ishifune, H. Masuda, M. Shimomura, H. Murase, and T. Shono, *Acta Chem. Scand.*, **53**, 949 (1999).
4. T. Shono, N. Kise, T. Fujimoto, N. Tominaga, and H. J. Morita, *Org. Chem.*, **57**, 7175 (1992).
5. S. T. Nugent, M. M. Baizer, and R. D. Little, *Tetrahedron Lett.*, **23**, 1339 (1982).
6. C. G. Sowell, R. L. Wolin, and R. D. Little, *Tetrahedron Lett.*, **31**, 485 (1990).
7. R. D. Little and P. Mikesell in *Organic Electrochemistry, 4th ed,* p. 725, H. Lund and O. Hammerich, Eds., Marcel Dekker, New York, (2001).
8. (a) R. E. Sioda, B. Terem, J. H. P. Utley, B. C. L. Weedon, *J. Chem. Soc. Perkin Trans. 1,* **5**, 561 (1976); (b) T. Shono, I. Nishiguchi, H. Ohmizu, and M. Mitani, *J. Am. Chem. Soc.*, **100**, 545 (1978); (c) R. Gorny, H. J. Schaefer, and R. Froehlich, *Angew. Chem., Int. Ed. Eng.*, **34**, 2007 (1995); (c) S. Torii, H. Okumoto, M. Abdur Rashid, and M. Mohri, *Synlett,* **9**, 721 (1992).
9. T. Shono, N. Kise, E. Shirakawa, H. Matsumoto, and E. Okazaki, *J. Org. Chem.*, **56**, 3063 (1991).
10. M. Kitamura, S. Okada, S. Suga, and R. Noyori, *J. Am. Chem. Soc.*, **111**, 4028 (1989).
11. P. Mikesell, M. Schwaebe, M. DiMare, and R. D. Little, *Acta Chem. Scand.*, **53**, 792 (1999).
12. E. Steckhan, T. Arns, W. R. Heineman, G. Hilt, D. Hoormann, J. Jorissen, L. Kroner, B. Lewall, and H. Putter, *Chemosphere*, **43**, 63 (2001).
13. E. Oguntoye, S. Szunerits, J. H. P. Utley, and P. B. Wyatt, *Tetrahedron Lett.*, **52**, 7771 (1996); (b) E. Eru, G. E. Hawkes, J. H. P. Utley, and P. B. Wyatt, *Tetrahedron*, **51**, 3033 (1995).
14. J. H. P. Utley and J. Gruber, *J. Materials Chem.*, **12**, 1613 (2002).
15. J. G. de Vries, *Can. J. Chem.*, **79**, 1086 (2001).
16. G. Pattenden and D. J. Sinclair, *J. Organomet. Chem.*, **653**, 261 (2002).
17. M. Sonoda, A. Inaba, and K. Itahashi, *Org. Lett.*, **3**, 2419 (2001).
18. R. Franzen, *Can. J. Chem.*, **78**, 957 (2000).
19. C. Amatore and A. Jutand, *Acc. Chem. Research,* **33**, 314 (2000).
20. (a) K. W. R. de Franca, M. Navarro, E. Leonel, M. Durandetti, and J.-Y. Nedelec, *J. Org. Chem.*, 67, 1838 (2002); (b) C. Cannes, S. Condon, M. Durandetti, J. Perichon, and J.-Y. Nedelec, *J. Org. Chem.*, **65**, 4575 (2000); (c) C. Gosmini, Y. Rollin, J.-Y. Nedelec, and J. Perichon, *J. Org. Chem.*, **65**, 6024 (2000).
21. M. Durandetti, J.-Y. Nedelec, and J. Perichon, *Org. Lett.*, **3**, 2073 (2001).
22. G. L. Carroll and R. D. Little, *Org. Lett.*, **2**, 2873 (2000).
23. (a) J. D. Parrish and R. D. Little, *Tetrahedron Lett.*, **42**, 7767 (2001); (b) R. J. Enemaerke, K. Daasbjerg, and T. Skrydstrup, *Chem. Commun.*, **4,** 343 (1999); (c) E. Prasad and R. A. Flowers, *J. Am. Chem. Soc.*, **124**, 6357 (2002).
24. (a) For a series of reviews on anodic oxidation reactions see *Organic Electrochemistry: 4th ed.*, H. Lund, and O. Hemmerich, O. Ed.; Marcel Dekker, Inc., New York (2001); (b) For a recent review focusing on synthetic applications of anodic electrochemistry see K. D. Moeller, *Tetrahedron*, **56**, 9527 (2000).
25. (a) For a review see H. J. Schäfer, in *Topics in Current Chemistry*, **152**, 91 (1990); (b) For a summary of recent examples see Ref. 24 and in particular Ref. 7-14 therein.
26. For recent examples see Ref. 24 and Ref. 91-103 therein.
27. For a review see T. Shono, in *Topics in Current Chemistry*, **148**, 131 (1988) as well as Ref. 24.
28. (a) T. Siu, W. Li, and A. Yudin, *J. Comb. Chem.*, **2**, 545 (2000); (b) For a review see A. Yudin and T. Siu, in *Current Opinion in Chemical Biology*, **5**, 269 (2001).
29. (a) J. Yoshida, S. Suga, S. Uzuki, N. Kinomura, A. Yamamoto, and K. Fujiwara, *J. Am. Chem. Soc.*, **121**, 9546 (1999); (b) S. Suga, M. Okajima, and J. Yoshida, *Tetrahedron Lett.*, **42**, 2173 (2001).
30. S. Suga, M. Okajima, K. Fujiwara, and J. Yoshida, *J. Am. Chem. Soc.*, **123**, 7941 (2001).
31. S. Suga, S. Suzuki, and J. Yoshida, *J. Am. Chem. Soc.*, 124, 30 (2002).
32. M. A. Endoma, G. Butora C. D. Claeboe, T. Hudlicky, and K. A. Abboud, *Tetrahedron Lett.*, **38**, 8833 (1997).
33. G. Butora, J. W. Reed. T. Hudicky, L. E. Brammer Jr., P. I. Higgs, D. P. Simmons, and N. E. Heard, *J. Am. Chem. Soc.*, 119, 7694 (1997).
34. A. Paci, T. Martens, and J. Royer, *Biorg. Med. Chem. Lett.*, **11**, 1347 (2001).
35. For a review see Ref. 24.

(continued on next page)

36. For a review describing electroauxiliaries see J. Yoshida in *Topics in Current Chemistry*, **170**, 39 (1994).
37. H. Sun and K. D. Moeller, *Org. Lett.*, **4**, 1547 (2002).
38. For a summary of recent examples see Ref. 24.
39. J. Yoshida, Presented at the 197th Meeting of the Electrochemical Society, May 14-19, 2000, Toronto, Canada; Abstract 1035.
40. J. Yoshida, M. Watanabe, H. Toshioka, M. Imagawa, and S. Suga, *Chem. Lett.*, 1011 (1998).
41. See Ref. 24 and Ref. 32-37 therein.
42. M. Jinno, Y. Kitano, M. Tada, and K. Chiba, Org. Lett., **1,** 435 (1999).
43. K. Yoshida, in Electrooxidation in *Organic Chemistry: The Role of Cation Radicals as Synthetic Intermediates,* John Wiley and Sons, New York (1984).
44. For a recent review see Ref. 24.
45. D. A. Frey, S. H. K. Reddy, and K. D. Moeller, *J. Org. Chem.*, **64**, 2805 (1999).
46. D. L. Wright, C. R. Whitehead, E. H. Sessions, I. Ghiviriga, and D. A. Frey, *Org. Lett.*, **1**, 1535 (1999).
47. Y. Sun, B. Liu, J. Kao, D. A. d'Avignon, and K. D. Moeller, *Org. Lett.*, **3**, 1729 (2001).
48. S. Yamamura and S. Nishiyama, *Synlett*, **4**, 533 (2002).
49. H. Takakura and S. Yamamura, *Tetrahedron Lett.*, **40**, 299 (1999).
50. K. Chiba, M. Fukuda, S. Kim, Y. Kitano, and M. Tada, *J. Org. Chem.*, **64**, 7654 (1999).
51. (a) B. D. Gates, P. Dalidowicz, A. Tebben, S. Wang, and J. S. Swenton, *J. Org. Chem.*, **57**, 2135 (1992); (b) S. Wang,B. D. Gates, and J. S. Swenton, *J. Org. Chem.*, **56**, 1979 (1991).
52. (a) A. Sutterer and K. D. Moeller, *J. Am. Chem. Soc.*, **122**, 5636 (2000); (b) S. Duan and K. D. Moeller, *Org. Lett.*, **3**, 2685 (2001).
53. B. Liu, S. Duan, A. C. Sutterer, and K. D. Moeller, *J. Am. Chem. Soc.*, **124**, 10101 (2002).
54. S. Duan and K. D. Moeller, *J. Am. Chem. Soc.*, **124**, 9368 (2002).
55. K. Chiba, T. Miura, S. Kim, Y. Kitano, and M. Tada, *J. Am. Chem. Soc.*, **123**, 11314 (2001).
56. For a simple setup see D. A. Frey, N. Wu, and K. D. Moeller, *Tetrahedron Lett.*, **37**, 8317 (1996).

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