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EC-backward-E electrochemistry supported by an alkoxyphenyl group

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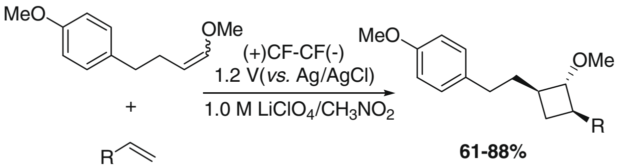
ABSTRACT

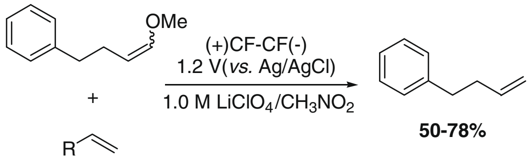
EC-backward-E electrochemistry through electrocatalytic formal [2+2] cycloaddition reaction between anodically activated aliphatic enol ethers and unactivated olefins possessing an alkoxyphenyl group was clearly described by using cyclic voltammetric studies and spin density observation with B3LYP/6-31G(d) calculations. The alkoxyphenyl group was found to regulate the electron transfer, which operates as an electron donor during the formation of the cyclobutane ring and as an electron acceptor from the anode to give the final product (EC-backward-E).

Electrochemical reactions have proven to be an effective way of generating radical anions or cations and causing both inter- and intramolecular cyclization reactions.[1] Anodic oxidation of electron-rich olefins provides radical cations, which can be used in carbon–carbon bond formation reactions to build up varied carbon frameworks. For electrocatalytic reactions in particular, targeted organic reactions proceed with very low energy consumption.[2] In addition, the progress of these chemical reactions can be externally regulated simply by controlling the application of potential. These electrochemical reactions offer new and efficient pathways for the production of organic compounds. Furthermore, electrochemical reactions provide a platform in which mechanistic studies would be carried out on reaction intermediates, including ions, radicals, and radical ions, which support to optimize reaction conditions.[3]

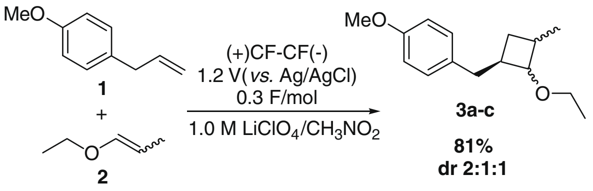
We previously reported electrocatalytic formal [2+2] cycloaddition reactions between anodically activated enol ethers possessing an alkoxyphenyl group and unactivated aliphatic olefins.[4] For example, anodic oxidation of 1-methoxy-4-(4-methoxybut-3-enyl)benzene in the presence of unactivated aliphatic olefins in lithium perchlorate/nitromethane electrolyte solution gave the corresponding [2+2] cycloadducts in moderate to high yield (Scheme 1). However, anodic oxidation of enol ethers without an alkoxyphenyl group did not give the corresponding [2+2] cycloadduct, with anodically induced olefin metathesis taking place instead (Scheme 2).[5] These results indicated that the alkoxyphenyl group played an important role in the formation of the cyclobutane ring. On the basis of these hypotheses, we also reported electrocatalytic formal [2+2] cycloaddition reactions between anodically activated aliphatic enol ethers and unactivated olefins possessing an alkoxyphenyl group.[6] For example, anodic oxidation of 1-ethoxyprop-1-ene **1** in the presence of 4-allylanisole **2** in lithium perchlorate/nitromethane electrolyte solution gave the corresponding [2+2] cycloadduct **3a–c** in high yield (Scheme 3).



Scheme 1. Electrocatalytic formal [2+2] cycloaddition reactions between anodically activated enol ethers possessing an alkoxyphenyl group and unactivated aliphatic olefins.



Scheme 2. Anodically induced olefin metathesis.



Scheme 3. Electrocatalytic formal [2+2] cycloaddition reaction between anodically activated aliphatic enol ethers and unactivated olefins possessing an alkoxyphenyl group.

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A radical cation generated from the enol ether is trapped by the olefin to give the corresponding cyclobutyl radical cation intermediate, followed by intramolecular electron transfer from the alkoxyphenyl group. As the oxidation potential of the alkoxyphenyl group is higher than that of the enol ether, intermolecular electron transfer occurs between the starting enol ether and the alkoxyphenyl radical cation, which completes the formation of [2+2] cycloadduct with a catalytic amount of electric input.

In these sequential reactions, anodic backward discharge is also possible, which reduces alkoxyphenyl radical cation at the anode to complete the overall electrocatalytic pathway of the electrochemical reactions (Fig. 1). The electron transfer from the anode is a key process in the EC-backward-E electrochemistry, which consists of the initial electron transfer from **1** to anode, oxidation of **1**, its reaction with **2**, and then the electron transfer from anode to alkoxyphenyl radical cation, reduction of alkoxyphenyl radical cation, to give **3a–c** (vide infra).

Herein we wish to report that the EC-backward-E electrochemistry is actually observed, which supports the observed electrocatalytic results. We also provide pieces of evidence from molecular orbital calculations that uncovers the role of the alkoxyphenyl group that regulates the electron transfers required for the formation of cyclobutane ring.

First, we measured the oxidation potential of the substrates. 1 showed peak oxidation potential at 1.18 V (vs Ag/AgCl), while the oxidation potential of **2** and **3a**–**c** was 1.57 V and 1.52 V (vs Ag/AgCl), respectively. These potentials show that **1** is preferentially oxidized on the anode to generate the corresponding radical cation **1**$^{+\cdot}$, even in the presence of nucleophiles. **1**$^{+\cdot}$ is then trapped by **2** to form a cyclobutyl radical cation intermediate **3a–c**$^{+\cdot}$. To complete the formation of the cyclobutane ring, intramolecular electron transfer must take place from the alkoxyphenyl group to the cyclobutyl moiety. As the oxidation potential of **3a–c** is relatively high compared to that of **1**, the intermediate ring-closed radical cation can repeatedly oxidize other starting enol ether molecules. However, if the intermolecular carbon–carbon bond formation and the subsequent electron transfer from the alkoxyphenyl group to the cyclobutyl moiety take place, it should also be possible that the radical cation intermediate—which corresponds to the one-electron oxidized species of the desired cycloadduct, with an oxidation potential of 1.52 V (vs Ag/AgCl)—is directly reduced on the anode by backward electron transfer.

We then monitored the electrochemical process by cyclic voltammetry (CV). Figure 2 shows the cyclic voltammograms of **1** (8 mM) and of **1** in the presence of **2** (160 mM) in 0.1 M lithium perchlorate/nitromethane electrolyte solution using a glassy carbon working electrode, a platinum counter electrode, and an Ag/AgCl reference electrode.

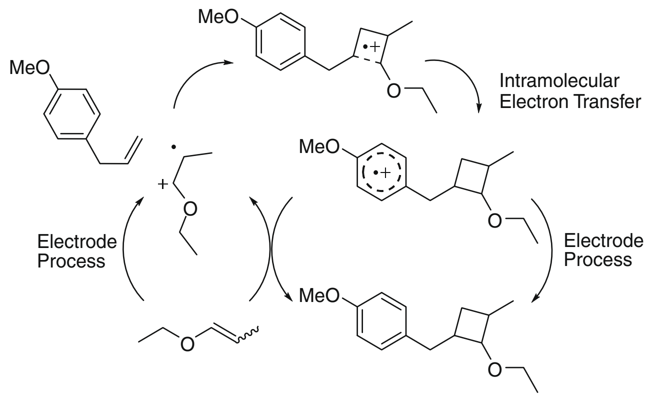


Figure 1. The cyclic voltammograms of 1-ethoxyprop-1-ene (8 mM) and of 1-ethoxyprop-1-ene (8 mM) in the presence of 4-allyanisole (160 mM) in 0.1 M lithium perchlorate/nitromethane.

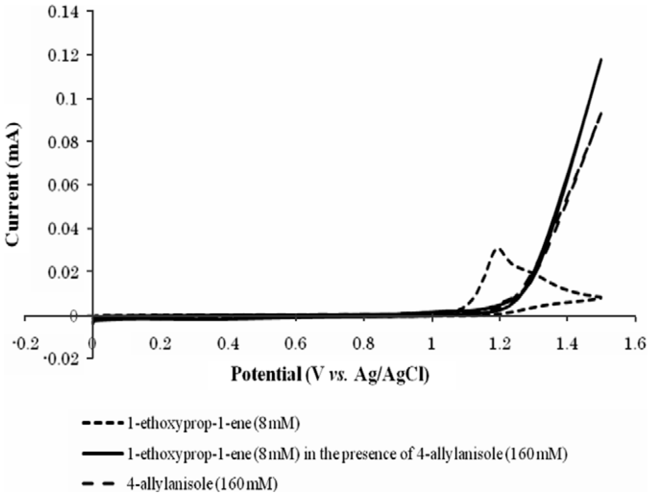


Figure 2. The cyclic voltammograms of 1-ethoxyprop-1-ene (8 mM) and of 1-ethoxyprop-1-ene (8 mM) in the presence of 4-allyanisole (160 mM) in 0.1 M lithium perchlorate/nitromethane.

The oxidation peak of **1**, at around 1.18 V versus Ag/AgCl, was hardly visible in the presence of **2**. In sharp contrast, in the presence of allylbenzene, which did not give a cycloadduct in the anodic oxidation of **1** in lithium perchlorate/nitromethane, the oxidation peak of **1** was clearly observed, as shown in Figure 3. These results indicate that intermolecular carbon–carbon bond formation between anodically activated aliphatic enol ethers and unactivated olefins possessing an alkoxyphenyl group was based on EC-backward-E electrochemistry on the anode. Furthermore, in these cyclic voltammograms for **1** and **2**, an increase in the oxidation current was observed at the potential where **3a–c** is oxidized. This oxidation peak enhancement is consistent with in-situ generation of **3a–c** via the EC-backward-E process on the anode. Intermolecular electron transfer between **3a–c**$^{+\cdot}$ and another **1** can also take place in a bulk solution.

We propose the following mechanism consistent with the observed EC-backward-E electrochemistry (Scheme 4). **1**$^{+\cdot}$ reacts with **2** to give a ring-opened radical cation **A**$^{+\cdot}$ which is rapidly converted to a ring-closed radical cation **B**$^{+\cdot}$. **B**$^{+\cdot}$ thus formed is rapidly

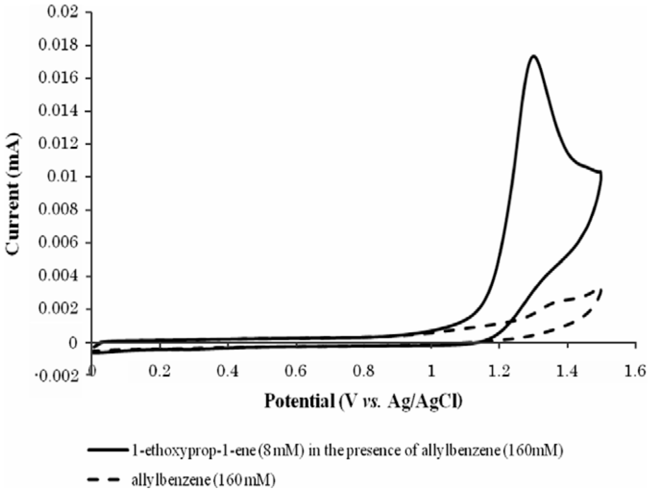
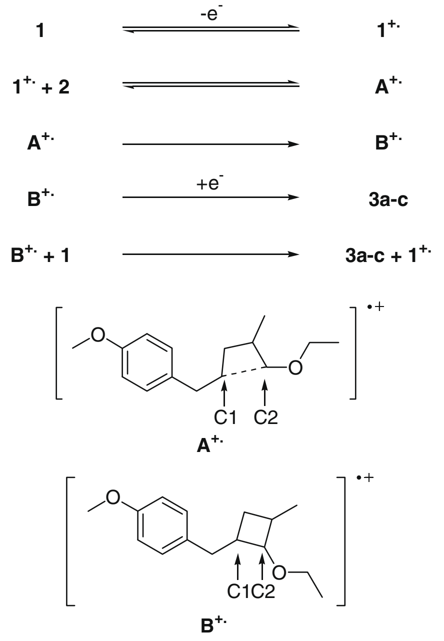


Figure 3. The cyclic voltammograms of 1-ethoxyprop-1-ene (8 mM) in the presence of allybenzene (160 mM) in 0.1 M lithium perchlorate/nitromethane.



Scheme 4. Summarization of the EC-backward-E reactions.

reduced at the anode to give **3a–c** since the electron transfer from the anode to a substrate radical cation can only be possible when its neutral form has an oxidation potential that is relatively high compared to that of anode. In this case, the oxidation potential of **3a–c** is 1.52 V (vs Ag/AgCl), which can be reduced at the anode under these reaction conditions (vide supra). The EC-backward-E electrochemistry seems to be rare, but Feldberg and Jeftic described it fully, both theoretically and experimentally.[7] Our case is the first one in which electrochemical oxidation triggers the [2+2] cycloaddition reaction between olefins to give a cyclobutane ring though such electrochemical behavior has been reported for the oxygenations of olefin radical cations.[8]

Molecular orbital calculations support the observed EC-backward-E electrochemistry. The calculations with B3LYP/6-31G(d) level of theory show that, although the spin density is almost localized in the cyclobutyl moiety in **A**$^{+\cdot}$ (the bond distance between C1 and C2 is 2.90 A), it is localized in the alkoxyphenyl group in **B**$^{+\cdot}$ (the bond distance between C1 and C2 is 1.54 A), as shown in Figure 4.[9] The Mulliken positive charges on the alkoxyphenyl group were also found to undergo large shift from 0.12 to 0.84 during the ring closure of **A**$^{+\cdot}$ to **B**$^{+\cdot}$. These results clearly indicate that the alkoxyphenyl group acts as an electron donor to give the ring-closed radical cation **B**$^{+\cdot}$ which is then reduced at the anode.

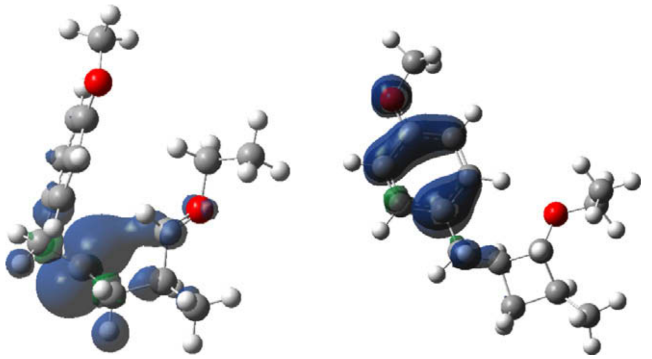


Figure 4. Spin density distribution of the intermediate calculated with B3LYP/6-31G(d). The left is the structure of **A**$^{+\cdot}$ and the right is the structure of **B**$^{+\cdot}$. The isovalue of spin density is 0.002.

It is of interest to note that the ring-closed **B**$^{+\cdot}$ would have a lifetime long enough to be reduced at the anode and to oxidize **1**. Lifetime of cyclobutyl radical cations reported so far seems to be very short, and could not be detected even by the nanosecond time-resolved laser flash photolysis studies.[10]

In conclusion, we described EC-backward-E electrochemistry through electrocatalytic formal [2+2] cycloaddition reactions between anodically activated aliphatic enol ethers and unactivated olefins possessing an alkoxyphenyl group by cyclic voltammetric and computational studies. The results demonstrated the role of the alkoxyphenyl group that regulates the electron transfer, which operates as an electron donor during the formation of the cyclobutane ring and as an electron acceptor from the anode to give the final product. The first intramolecular electron transfer from the alkoxyphenyl group is thought to be triggered by the formation of the cyclobutyl radical cation via intermolecular carbon–carbon bond formation. The unique intermolecular reaction that generates the unstable cyclobutyl radical cation intermediate is assisted by a lithium perchlorate/nitromethane electrolyte solution, which effectively stabilizes the cationic intermediates and promotes intermolecular carbon–carbon bond formation. This type of electrocatalytic reaction is expected to open the door to more efficient electro-organic reactions. It is also emphasized that EC-backward-E electrochemistry should be more frequently observed and may conveniently be utilized as a diagnostic tool to find electrocatalytic reactions in general. Further efforts in the development of electrocatalytic reactions are underway in our laboratory.

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