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Electrocatalytic Formal [2+2] Cycloaddition Reactions between Anodically Activated Aliphatic Enol Ethers and Unactivated Olefins Possessing an Alkoxyphenyl Group

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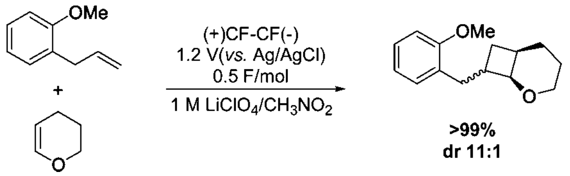
ABSTRACT



Electrocatalytic formal [2+2] cycloadditions between anodically activated aliphatic enol ethers and unactivated olefins possessing an alkoxyphenyl group have been accomplished in a lithium perchlorate/nitromethane electrolyte solution. The alkoxyphenyl group was revealed to play an important role in the reaction intermediates to complete formation of the cyclobutane ring through intramolecular electron transfer between the cyclobutane radical cation and the alkoxyphenyl group.

Electrochemical reactions have proven to be effective for generating nucleophilic or electrophilic carbons and forming carbon−carbon bonds in unique ways.[1] In particular, anodic oxidation of electron-rich olefins can set up olefin cross-coupling through which intra- and intermolecular cyclization reactions are achieved.[2]

We have previously reported novel electrocatalytic formal [2+2] cycloaddition reactions between anodically activated enol ethers possessing an alkoxyphenyl group and unactivated aliphatic olefins.[3] For example, anodic oxidation of 1-methoxy-4-(4-methoxybut-3-enyl)benzene in the presence of an excess amount (20 mol equiv) of aliphatic olefins in a lithium perchlorate/nitromethane (LPC/NM) electrolyte solution afforded the corresponding [2+2] cycloadducts in

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(1) (a) Moeller, K. D. *Tetrahedron* **2000**, *56*, 9527. (b) Sperry, J. B.; Whitehead, C. R.; Ghiviriga, I.; Walczak, R. M.; Wright, D. L. *J. Org. Chem.* **2004**, *69*, 3726. (c) Mihelcic, J.; Moeller, K. D. *J. Am. Chem. Soc.* **2004**, *126*, 9106. (d) For a review of electrolytic reductive couplings, see: Nielsen, M. F.; Utley, J. H. P. In *Organic Electrochemistry*, 4th ed.; Lund, H., Hammerich, O., Eds.; Marcel Dekker: New York, 2001; p 795. (e) Little, D. R. *Electrochem. Soc. Interface* **2002**, *11*, 36. (f) Little, D. R. In *Electrochemistry VI: Electroorganic Synthesis: Bond Formation at Anode and Cathode*; Topics in Current Chemistry No. 185; Steckhan, E., Ed.; Springer : Berlin, Germany, 1997; p 1. (g) Anderson, J. D.; Baizer, M. M.; Petrovich, J. P. *J. Org. Chem.* **1966**, *31*, 3890.

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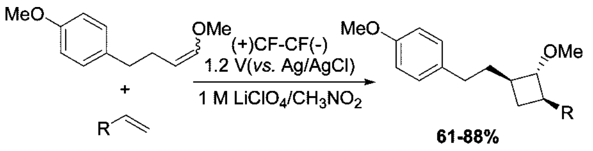
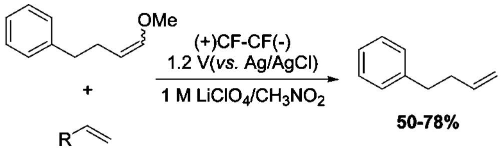
Scheme 1



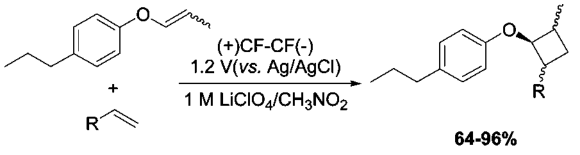
moderate to high yield (Scheme 1). However, anodic oxidation of (4-methoxybut-3-enyl)benzene in the presence of an excess amount (20 mol equiv) of aliphatic olefins in LPC/NM electrolyte solution resulted in olefin metathesis instead (Scheme 2).[4]

Scheme 2



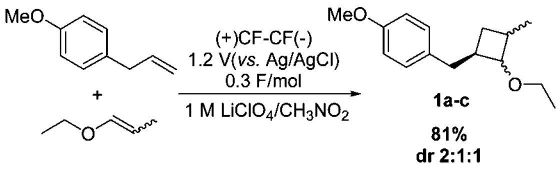
On the other hand, we also reported electrocatalytic formal [2+2] cycloaddtion reactions between anodically activated enyloxybenzenes and unactivated aliphatic olefins.[5] For example, anodic oxidation of 1-propenyloxy-4-propylbenzene in the presence of an excess amount (20 mol equiv) of aliphatic olefins in LPC/NM solution produced the corresponding [2+2] cycloadducts in moderate to excellent yield (Scheme 3). These results suggest that an alkoxyphenyl group derived from the enol ether is necessary for the reaction intermediate to complete the formation of a cyclobutane through intramolecular electron transfer from the alkoxyphenyl group to the cyclobutane radical cation. On the basis of this plausible mechanism, the alkoxyphenyl group of a reaction intermediate derived from the olefin could also complete formation of the cyclobutane ring through the same intramolecular electron transfer.

Scheme 3



Herein, we report novel electrocatalytic formal [2+2] cycloaddition reactions between anodically activated aliphatic enol ethers and unactivated olefins possessing an alkoxyphenyl group. All reactions were conducted in 1 M LPC/NM electrolyte solution with carbon felt anodes and cathodes.

Scheme 4



Initially, anodic oxidation of 1-ethoxyprop-1-ene was attempted in the presence of an excess amount (20 mol equiv) of 4-allylanisole. After application of 0.3 F/mol, the desired cycloadduct **1a**−**c** was obtained in high yield as a mixture of diastereomers (Scheme 4). However, it is notable that the anodic oxidation of 1-ethoxyprop-1-ene in the presence of an excess amount (20 mol equiv) of allylbenzene did not afford the corresponding cycloadduct, even in the presence of an excess amount (20 mol equiv) of anisole. This suggests that an intramolecular electron transfer from the alkoxyphenol group to the radical cation of the cyclobutane is necessary to provide the desired cycloadducts (Figure 1).

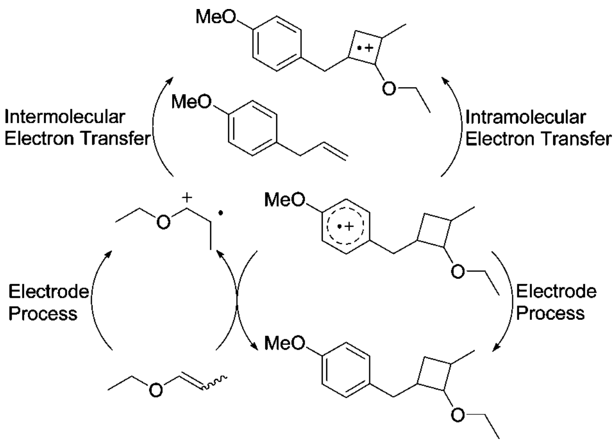


Figure 1. A plausible reaction mechanism of electrocatalytic formal [2+2] cycloaddition reactions with 1-ethoxyprop-1-ene and 4-allylanisole.

Similarly, anodic oxidation of 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran in the presence of an excess amount (20 mol equiv) of 4-allylanisole afforded the desired cycloadducts **2a**,**b** and **3a**,**b** in moderate to excellent yield as a mixture of diastereomers, respectively (Scheme 5). Furthermore, anodic oxidation of 3,4-dihydro-2*H*-pyran in the presence of an excess amount (20 mol equiv) of 2-allylanisole also produced the desired cycloadduct **4a**,**b** in excellent yield as a mixture of diastereomers (Scheme 6). The configurations of these cycloadducts were confirmed by nuclear Overhauser effect spectroscopy (NOES).

These results indicate that the reaction is driven by an electrocatalytic process and that an intramolecular alkoxy-

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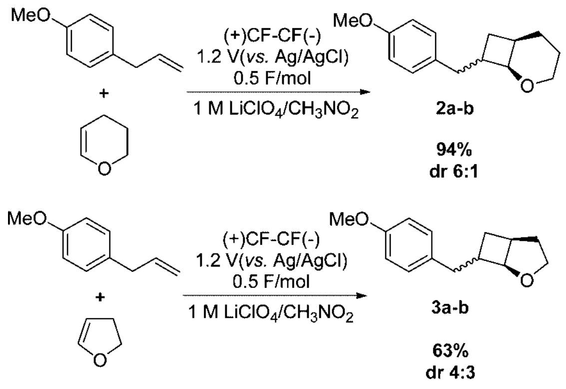
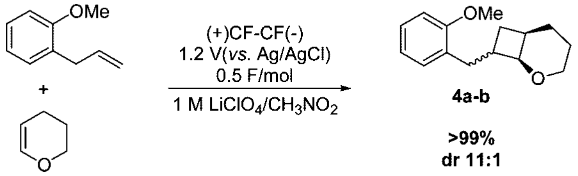
Scheme 5

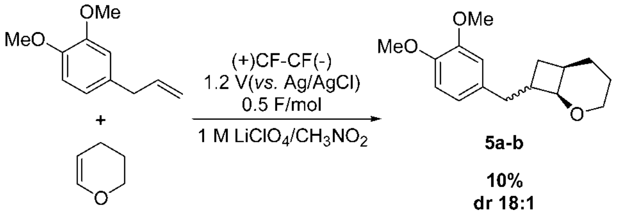


phenyl group is necessary for the completion of the cyclobutane ring formation by the electron transfer after the nucleophilic attack of olefins. However, the anodic oxidation of 3,4-dihydro-2*H*-pyran in the presence of an excess amount (20 mol equiv) of 4-allylveratrole gave the desired cycloadduct **5a**,**b** in 10% yield as a mixture of diastereomers (Scheme 7). This suggests that there is an appropriate value for the electron density of the alkoxyphenyl group for the reaction to proceed. The anodic oxidation of 3,4-dihydro-2*H*-pyran in the presence of an excess amount (20 mol equiv) of 5-allyl-1,2,3-trimethoxybenzene yielded only a trace amount of the desired cycloadduct, which strongly supports this hypothesis.

Scheme 6



Scheme 7



The oxidation potentials of the substrates used in these reactions, measured by cyclic voltammetry, also support this hypothesis; the oxidation potentials of 4-allylveratrole ($E_{\mathrm{p}}^{\mathrm{ox}}$ = 1.33 V vs Ag/AgCl) and 5-allyl-1,2,3-trimethoxybenzene ($E_{\mathrm{p}}^{\mathrm{ox}}$ = 1.18 V vs Ag/AgCl) are lower than that of 3,4-dihydro-2*H*-pyran ($E_{\mathrm{p}}^{\mathrm{ox}}$ = 1.41 V vs Ag/AgCl). Probably, the anodic oxidation of 3,4-dihydro-2*H*-pyran does not preferentially occur in the presence of an excess amount (20 mol equiv) of 4-allylveratrole or 5-allyl-1,2,3-trimethoxybenzene. In contrast, the oxidation potentials of 4-allylanisole ($E_{\mathrm{p}}^{\mathrm{ox}}$ = 1.57 V vs Ag/AgCl) and 2-allylanisole ($E_{\mathrm{p}}^{\mathrm{ox}}$ = 1.52 V vs Ag/AgCl) are higher than that of 3,4-dihydro-2*H*-pyran. These oxidation potentials of 4- and 2-allyanisoles should be important to effectively provide selective anodic oxidation of 3,4-dihydro-2*H*-pyran, followed by electron transfer from the closely located intramolecular aromatic rings to the cyclobutyl radical cation of higher oxidation potential in comparison with those of anisoles.

In conclusion, we have established novel electrocatalytic formal [2+2] cycloaddition reactions between anodically activated aliphatic enol ethers and olefins possessing an alkoxyphenol group. The alkoxyphenyl group is necessary for the reaction intermediates to complete formation of the cyclobutane ring through intramolecular electron transfer between the cyclobutane radical cation and the alkoxyphenyl group. This reaction should be applicable to the formation of various [2+2] cycloadducts. Further applications of such reactions are presently under investigation.

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Supporting Information Available: Experimental procedures and characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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