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Electron-Transfer-Induced Intermolecular [2 + 2] Cycloaddition Reactions Assisted by Aromatic “Redox Tag”

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1. Introduction

Electron transfer is a fundamental and ubiquitous process in chemical and biological reactions and thus has been extensively studied. A wide variety of unique molecular systems have been developed that connect electron donor and electron acceptor using different types of bridges to investigate electron-transfer reactions. Typically, laser flash photolysis techniques are used in combination with photo-excitabile electron donors to provide insights into the chemical and physical properties of electron-transfer reactions. Electron donors are photochemically activated to induce electron transfer toward the electron acceptor, which is then detected spectroscopically. One recent achievement in this field is the discovery of long-range photo-induced electron transfer through a DNA helix, which offers interesting applications as novel conductive materials.

In organic synthesis, electron-transfer-induced reactions have been used extensively to achieve various chemical transformations and construct a wide variety of organic compounds, including natural products, pharmaceutical products, and functional materials. To trigger these electron-transfer-induced reactions, photochemical processes are widely employed. One-electron oxidants and reductants also can be used to initiate electron-transfer-induced reactions. In this context, electrochemical approaches have been utilized to trigger either one- or two-electron transfers through electrode processes that afford electron-transfer-induced reactions. Based on electrochemical processes, various functional group transformations and a wide variety of carbon-carbon bond formation reactions can be accomplished in a controlled manner. For example, Kolbe electrolysis is a well-established process for forming carbon-carbon bonds (Fig. 1). In this reaction, decarboxylation is anodically induced to generate carbon free radicals, which are then homocoupled to make a new carbon-carbon bond.

In addition to free radicals, electrochemical processes also are efficient for the generation of several reactive organic species, including ions and radical ions that can be introduced into organic syntheses as intermediates. In this chapter, we describe electron-transfer-induced carbon-carbon bond formation reactions based on the generation of carbon radical cations as reactive intermediates through electrode processes. Electrochemical studies of the reaction mechanisms have led to the development of new intermolecular [2 + 2] cycloaddition reactions.

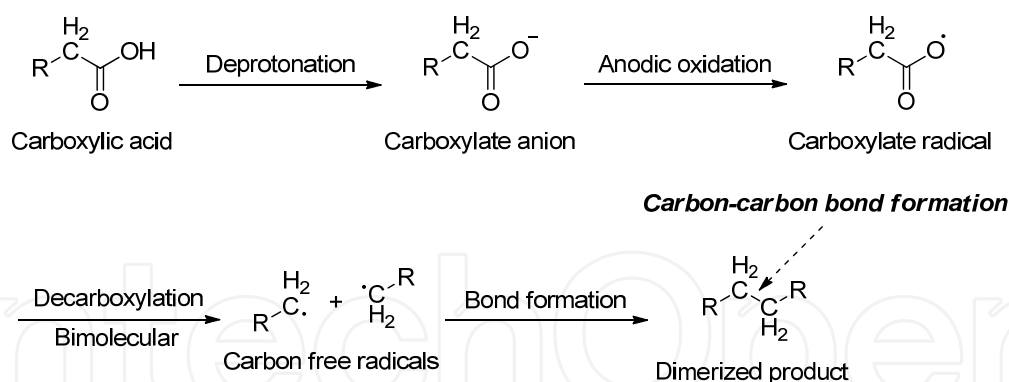


Fig. 1. Reaction mechanism of Kolbe electrolysis

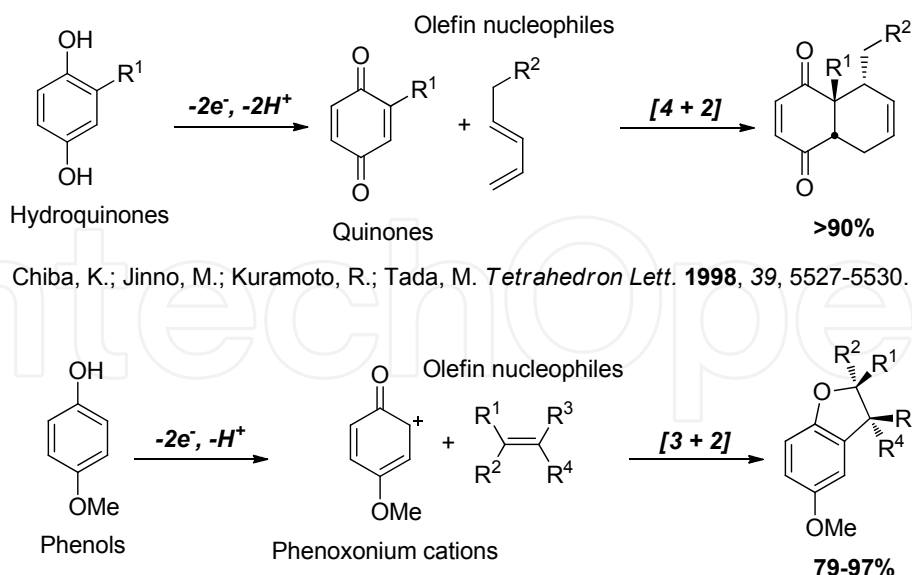
2. Electron-transfer-induced cycloaddition reactions

Cycloaddition reactions play important roles in organic synthesis, allowing complicated ring systems to be synthesized in one step. Numerous synthetic strategies based on cycloaddition reactions have been established to construct various frameworks. As an example, Diels-Alder reactions have been studied from not only synthetic but also mechanistic aspects. Recently, several types of enzymatic Diels-Alder-like reactions also have been reported, leading to the recognition that they are critical in biological systems. In this field, electron-transfer-induced cycloaddition reactions are one of the most intriguing research subjects, both practically and theoretically. To generate radical ions as reactive intermediates for such electron-transfer-induced cycloaddition reactions, photochemical processes are commonly used with photosensitizers. In addition, one-electron oxidants and reductants also are effective for triggering electron-transfer-induced cycloaddition reactions.

In this context, electrochemical approaches can afford reactive organic species, including radicals, ions, and radical ions, at electrodes, which can accomplish various types of electron-transfer-induced cycloaddition reactions without oxidants or reductants. Oxidation or reduction potentials can be controlled easily and the reaction conditions can be simply designed using a combination of supporting electrolytes and typical polar organic solvents, initiating both electron-transfer-induced intra- and intermolecular cycloaddition reactions. We have been developing a series of electron-transfer-induced cycloaddition reactions initiated by anodic oxidation using lithium perchlorate (LPC)/nitromethane (NM) electrolyte solution. An LPC/NM electrolyte solution can stabilize anodically generated carbocation intermediates, facilitating carbon-carbon bond formation reactions. Previously, we have reported electron-transfer-induced intermolecular [4 + 2] and [3 + 2] cycloaddition reactions using an LPC/NM electrolyte solution (Fig. 2). These reactions were conducted under constant potential conditions using carbon felt (CF) working electrodes, platinum counter electrodes, and Ag/AgCl reference electrodes. Hydroquinones and phenols were anodically oxidized to generate corresponding quinones and phenoxonium cations as reactive intermediates, which were then trapped by olefin nucleophiles to construct various substituted [4 + 2] and [3 + 2] cycloadducts.

3. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions

Among reported electron-transfer-induced cycloaddition reactions, the [2 + 2] reactions have received attention because they appear to be involved in DNA lesions and repair.

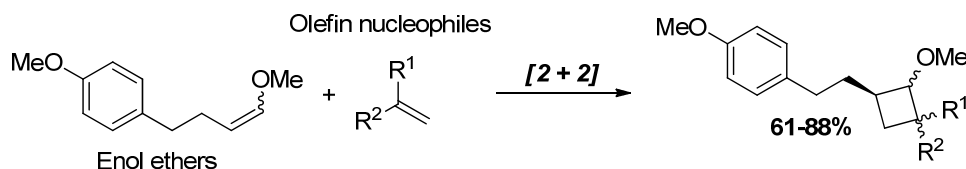


Chiba, K.; Fukuda, M.; Kim, S.; Kitano, Y.; Tada, M. *J. Org. Chem.* **1999**, *64*, 7654-7656.

Fig. 2. Electron-transfer-induced intermolecular [4 + 2] and [3 + 2] cycloaddition reactions

Electron-transfer-induced cycloreversion reactions of four-membered rings also have been represented through radical ion intermediates. Many mechanistic studies on these electron-transfer-induced [2 + 2] cycloaddition reactions and cycloreversion reactions of four-membered ring have been reported.

Enol ethers were then introduced into a LPC/NM electrolyte solution. Enol ethers can generate corresponding radical cations through anodic oxidation, which are then employed as reactive intermediates for cycloaddition reactions. We found that intermolecular [2 + 2] cycloaddition reactions proceeded to construct cyclobutane rings when anodic oxidation of enol ethers were conducted in the presence of olefin nucleophiles in LPC/NM electrolyte solution using CF electrodes as both working and counter, and Ag/AgCl electrodes as reference under constant potential conditions (Fig. 3). These reactions were completed with a catalytic amount of electricity, and starting materials were recovered quantitatively when no potentials were applied. In addition, no cyclobutane ring formation was observed through the anodic oxidation of enol ethers in the absence of olefin nucleophiles followed by their addition, even under radiation conditions. Thus, the intermolecular [2 + 2] cycloaddition reactions clearly responded to the application of electricity, and the corresponding radical cations of enol ethers did not accumulate, indicating that their immediate trapping by olefin nucleophiles was required for the reactions.



Chiba, K.; Miura, T.; Kim, S.; Kitano, Y.; Tada, M. *J. Am. Chem. Soc.* **2001**, *123*, 11314-11315.

Fig. 3. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions

As described above, examples of electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions utilized the enol ether that possessed an alkoxyphenyl group. When similar enol ethers that did not possess an alkoxyphenyl group were prepared and used, [2 + 2] cycloaddition reactions did not occur; instead, olefin cross-metathesis reactions were induced through anodic oxidation in the presence of olefin nucleophiles (Fig. 4).

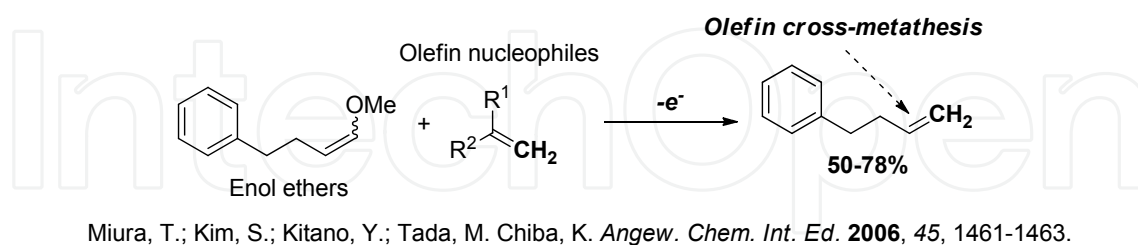


Fig. 4. Electron-transfer-induced olefin cross-metathesis reactions

These results indicate that the alkoxyphenyl group was essential for the formation of the cyclobutane ring. This can be explained by electron-transfer-induced [2 + 2] cycloaddition reactions beginning with the anodic oxidation of enol ethers to generate their radical cations, which were then trapped by olefin nucleophiles, resulting in the corresponding cyclobutyl radical cations as electron acceptor. The electron-rich alkoxyphenyl group was expected to function as an effective electron donor to complete the formation of the cyclobutane ring through intramolecular electron transfer from the alkoxyphenyl group to the cyclobutyl moiety. In contrast, the phenyl group was not an effective electron donor for the reactions, leading not to the [2 + 2] cycloaddition reaction but to the olefin cross-metathesis reaction (Fig. 5).

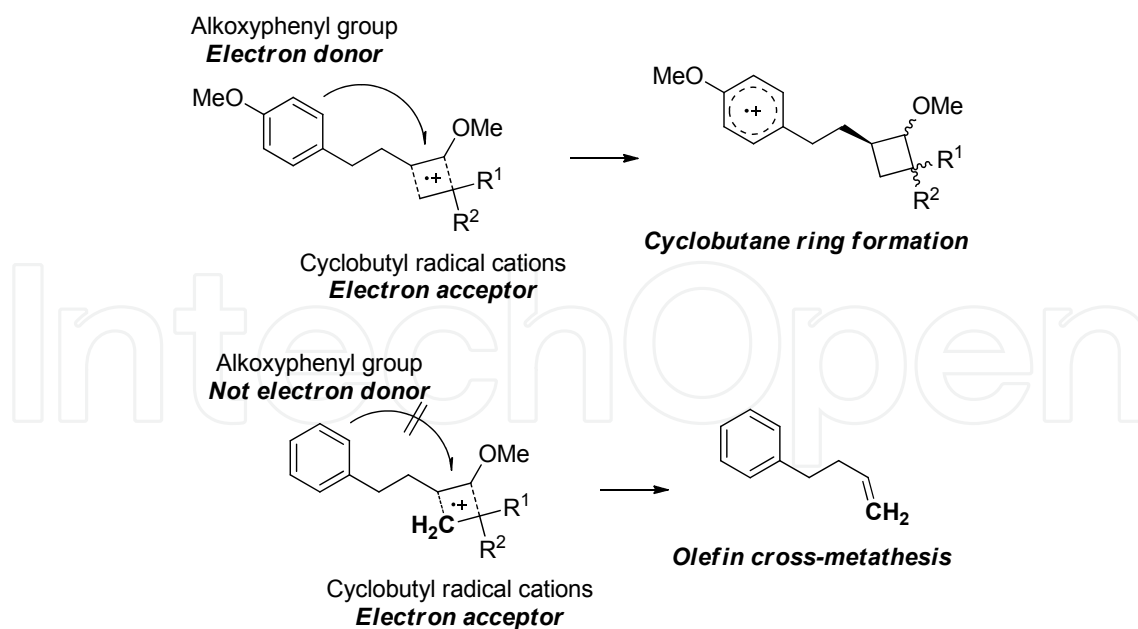


Fig. 5. Plausible reaction mechanisms of electron-transfer-induced [2 + 2] cycloaddition reactions and olefin cross-metathesis.

On the basis of these plausible reaction mechanisms, we envisioned that the alkoxyphenyl group of radical cation intermediates derived from olefin nucleophiles also could function

as an effective electron donor for completion of the formation of the cyclobutane ring through similar intramolecular electron transfer. Therefore, 4-allylanisole (**1**) and 1-ethoxyprop-1-ene (**2**) were chosen as olefin nucleophiles that possessed an alkoxyphenyl group and aliphatic enol ether. The anodic oxidation of 1-ethoxyprop-1-ene (**2**) in the presence of an excess of 4-allylanisole (**1**) gave the corresponding cyclobutane ring-containing product (**3**) in high yield (Fig. 6). An excess of olefin nucleophile was essential for effective trapping of transient enol ether radical cations. When similar olefin nucleophiles not possessing an alkoxyphenyl group, such as allylbenzene (**4**), were used in place of 4-allylanisole (**1**), no [2 + 2] cycloaddition reaction occurred, even in the presence of the electron-rich alkoxyphenyl compound, anisole (**5**). These results support the plausible reaction mechanisms. Thus, the anodic oxidation of 1-ethoxyprop-1-ene (**2**) triggered the reaction to generate a radical cation, which then reacted with 4-allylanisole (**1**) to form the corresponding cyclobutyl radical cation as the electron acceptor. Electron transfer from the intramolecular electron donor, the alkoxyphenyl group of the radical cation intermediate, to the cyclobutyl moiety, completed the formation of the cyclobutane ring. In contrast, the intermolecular electron donor, anisole (**5**), was not effective in the reaction even when the corresponding cyclobutyl radical cation formed between the radical cation of 1-ethoxyprop-1-ene (**2**) and allylbenzene (**4**). Thus, since the radical cation remained on the alkoxyphenyl group, and the reaction completed with a catalytic amount of electricity, the alkoxyphenyl radical cation could act as an electron acceptor to oxidize the starting enol ether, completing the overall reaction (Fig. 7).

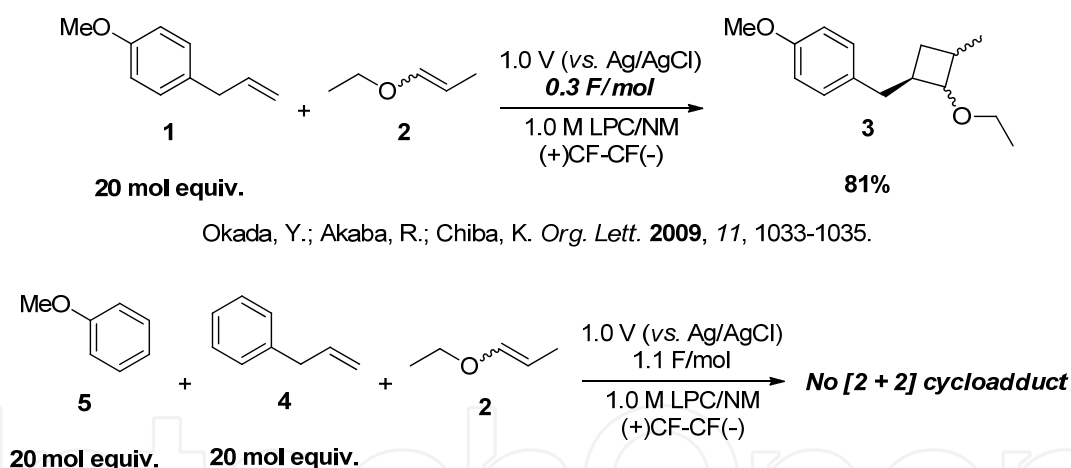


Fig. 6. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 4-allylanisole (**1**) and 1-ethoxyprop-1-ene (**2**).

Moreover, 3,4-dihydro-2H-pyran (**6**), the cyclic version of 1-ethoxyprop-1-ene (**2**), can be introduced into the reaction to afford the corresponding bicyclic cyclobutane ring-containing product (**7**) in excellent yield through intermolecular reaction with 4-allylanisole (**1**) (Fig. 8). As described, the bicyclic framework can be efficiently prepared in one step.

4. Cyclic voltammetric studies on electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions

These synthetic results prompted cyclic voltammetric studies on electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions with the goal of understanding the details of

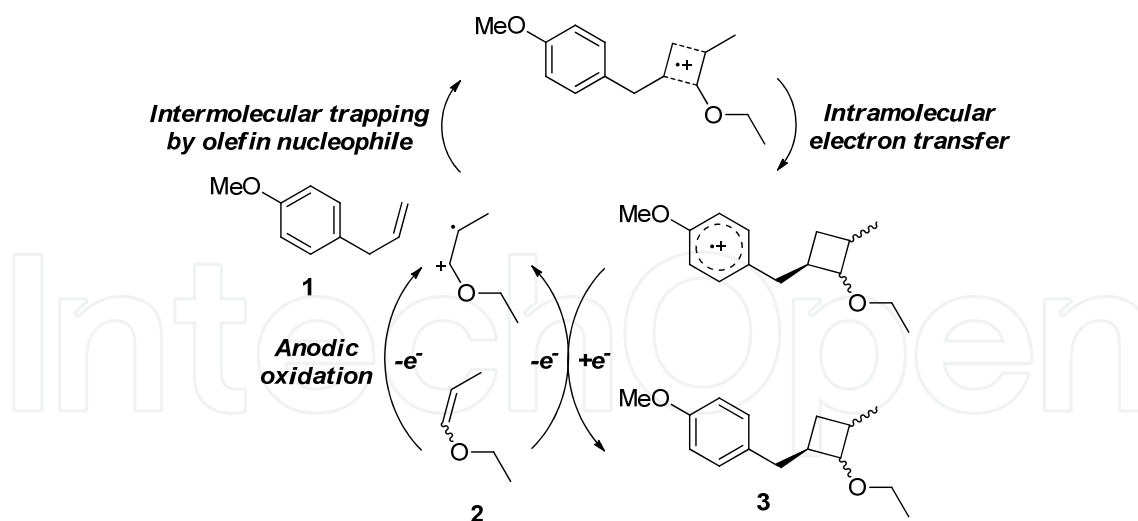
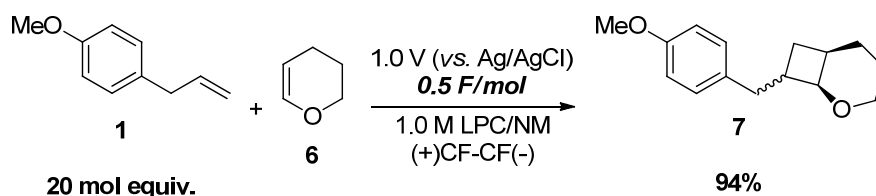


Fig. 7. Plausible reaction mechanism of the electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 4-allylanisole (1) and 1-ethoxyprop-1-ene (2).



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Fig. 8. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 4-allylanisole (1) and 3,4-dihydro-2H-pyran (6).

their reaction mechanisms. For this purpose, electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 4-allylanisole (1) and 1-ethoxyprop-1-ene (2) was chosen as a model, because the electrocatalytic nature is prominent. Cyclic voltammograms were recorded using a glassy carbon working electrode, platinum counter electrode, and Ag/AgCl reference electrode in an LPC/NM electrolyte solution. Peak oxidation potentials of 4-allylanisole (1), 1-ethoxyprop-1-ene (2), and the cyclobutane ring-containing product (3) were shown at 1.51 V, 1.18 V, and 1.50 V, respectively. The oxidation potential of 1-ethoxyprop-1-ene (2) was significantly lower than that of 4-allylanisole (1), enabling the selective anodic oxidation of 1-ethoxyprop-1-ene (2), even in the presence of an excess of 4-allylanisole (1). In addition, the oxidation potential of the cyclobutane ring-containing product (3) was similar to that of 4-allylanisole (1), indicating that anodic oxidations of both 4-allylanisole (1) and the cyclobutane ring-containing product (3) could occur on their electron-rich alkoxyphenyl groups to give the corresponding alkoxyphenyl radical cations. Thus, based on their oxidation potentials, the alkoxyphenyl radical cation of the cyclobutane ring-containing product (3) could oxidize 1-ethoxyprop-1-ene (1) to generate the neutral cyclobutane ring-containing product (3) and the radical cation of 1-ethoxyprop-1-ene (1). Furthermore, in these sequential reactions, anodic backward discharge also was possible; thus, the alkoxyphenyl radical cation of the cyclobutane ring-containing product (3) also might be reduced at the anode to complete the overall electrocatalytic pathway of the reactions, when lower constant potential conditions were employed for the reaction (Fig. 9).

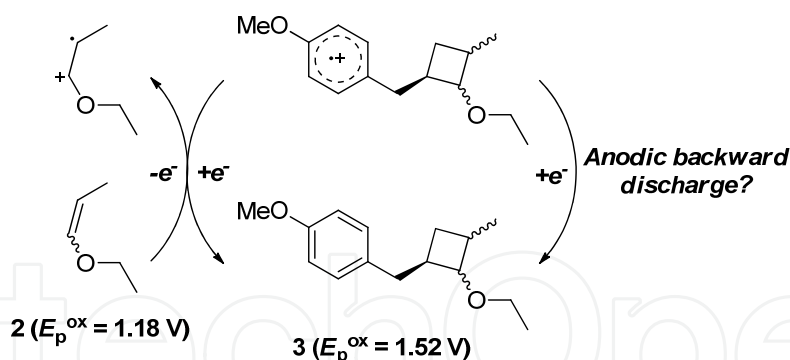


Fig. 9. Plausible reduction mechanism of the alkoxyphenyl radical cation of the cyclobutane ring-containing product (3).

Such anodic backward discharge would be a key process in the EC-backward-E electrochemistry. EC-backward-E electrochemistry can be defined as sequential reactions involving interactive electron transfers through a certain chemical transformation. Initial electron transfer (E) occurred between the starting substrate and the electrode to trigger a certain chemical transformation (C), and the resulting product induced subsequent backward electron transfer (bE) at the electrode. To address the reduction mechanism of the alkoxyphenyl radical cation of the cyclobutane ring-containing product (3), the reaction was monitored by cyclic voltammetry. The cyclic voltammogram of 1-ethoxyprop-1-ene (2) showed an oxidation peak clearly *ca.* 1.18 V (Fig. 10). However, when the cyclic voltammogram of 1-ethoxyprop-1-ene (2) was recorded in the presence of an excess of 4-allylanisole (1), its oxidation peak was hardly visible. This observation indicated that the alkoxyphenyl radical cation of the cyclobutane ring-containing product (3) significantly decreased the oxidation current of 1-ethoxyprop-1-ene (2) because of the anodic backward discharge. In contrast, a clear oxidation peak was observed, even when the cyclic voltammogram of 1-ethoxyprop-1-ene (2) was recorded in the presence of an excess of allylbenzene (4) (Fig. 11). In this case,

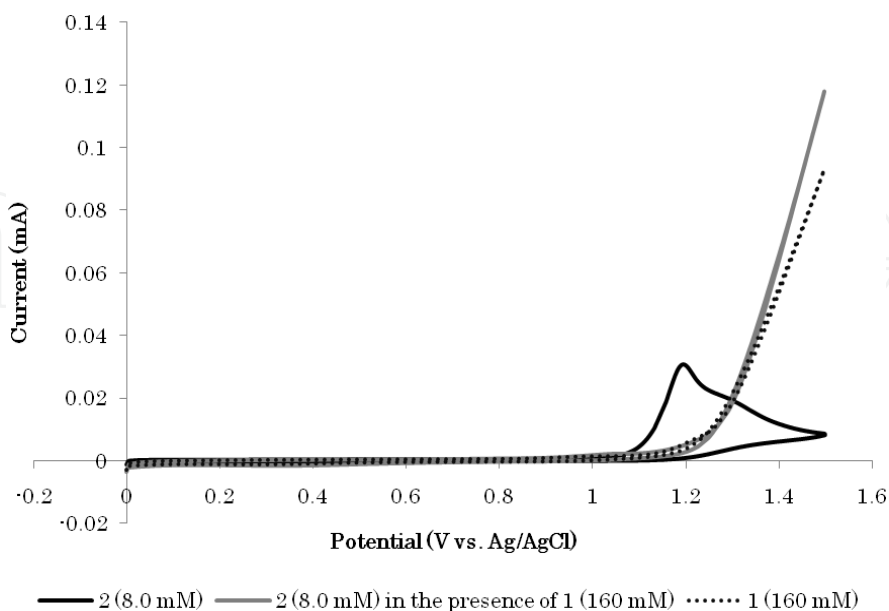


Fig. 10. Cyclic voltammogram of 1-ethoxyprop-1-ene (2) with and without the presence of 4-allylanisole (1).

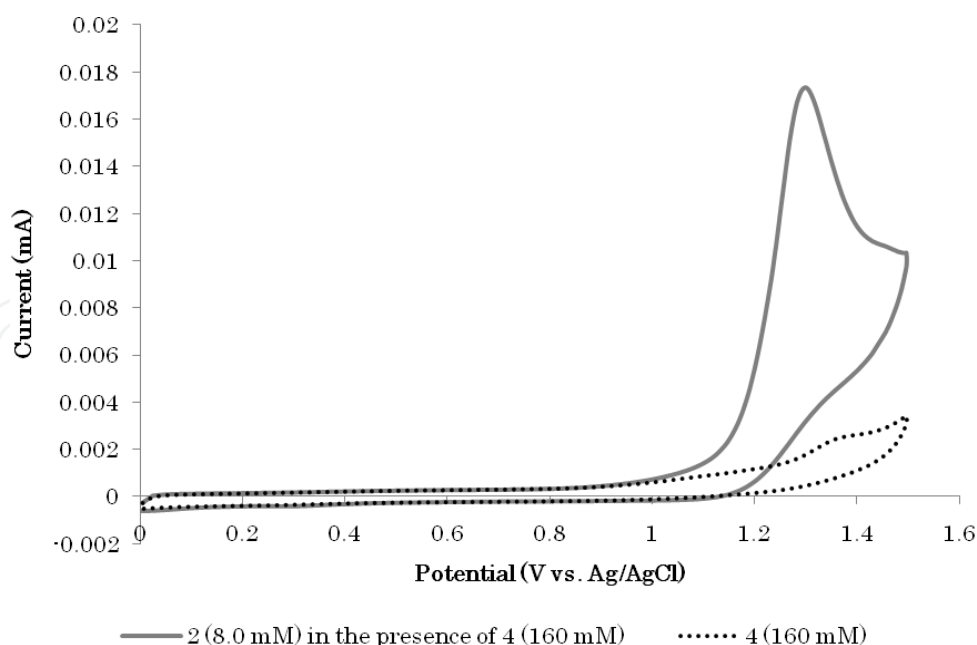
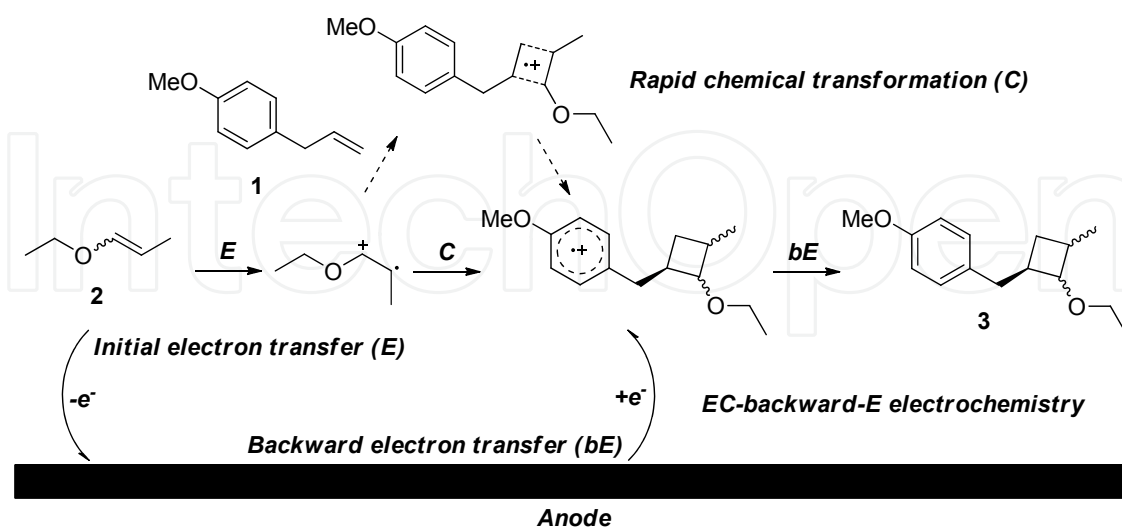


Fig. 11. Cyclic voltammogram of 1-ethoxyprop-1-ene (**2**) in the presence of allylbenzene (**4**).

allylbenzene (**4**) was not able to form the corresponding cyclobutane ring-containing product through reaction with the radical cation of 1-ethoxyprop-1-ene (**2**). Therefore, EC-backward-E electrochemistry at the anode was conjugated to the formation of the cyclobutane ring between the anodically generated radical cation of 1-ethoxyprop-1-ene (**2**) and 4-allylanisole (**1**).

To observe this EC-backward-E electrochemistry, the chemical transformation (C) needed to occur relatively faster than diffusion from the electrode, indicating that intermolecular trapping of the anodically generated radical cation of 1-ethoxyprop-1-ene (**2**) by 4-allylanisole (**1**) was a rapid process (Fig. 12). Moreover, the conversion of the cyclobutyl



Okada, Y.; Akaba, R.; Chiba, K. *Tetrahedron Lett.* **2009**, *50*, 5413-5416.

Fig. 12. EC-backward-E electrochemistry observed through the electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 4-allylanisole (**1**) and 1-ethoxyprop-1-ene (**2**).

radical cation intermediate to the alkoxyphenyl radical cation intermediate could be rationalized as extremely rapid intramolecular electron transfer, since the lifetime of cyclobutyl radical cations previously reported was very short and could not be detected even by nanosecond time-resolved laser flash photolysis studies.

The alkoxyphenyl group was confirmed to be crucial for the reactions and its role could be defined as a "redox tag" (Fig. 13). During sequential electron-transfer processes, the alkoxyphenyl "redox tag" initially functioned as an electron donor that induced intramolecular electron transfer to form the cyclobutane ring. As described above, the intramolecular electron transfer from the alkoxyphenyl group to the cyclobutyl radical cation has been demonstrated as a key step for the formation of cyclobutane ring and the alkoxyphenyl radical cation intermediate generated. The subsequent role of the alkoxyphenyl "redox tag" was as an electron acceptor to complete the overall reactions. As the oxidation potential of the alkoxyphenyl group was relatively high, it must be reduced either through the oxidation of 1-ethoxyprop-1-ene (**2**) or through anodic backward discharge.

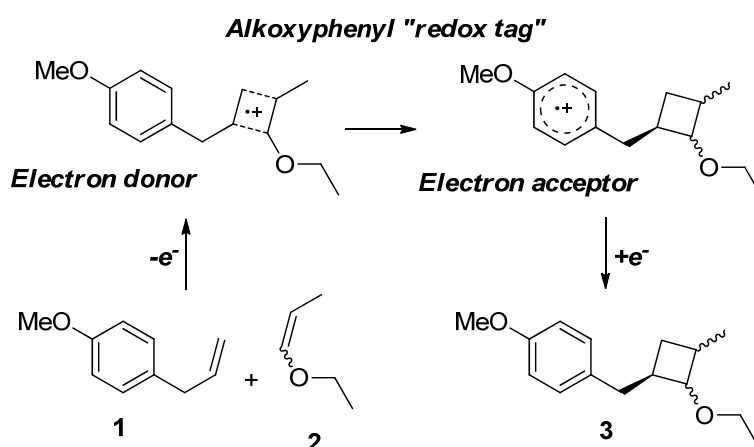


Fig. 13. Plausible function of alkoxyphenyl "redox tag."

5. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions assisted by aromatic "redox tag"

These mechanistic results prompted a search for new electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions based on the aromatic "redox tag" strategy. For this purpose, electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction of 3,4-dihydro-2H-pyran (**6**) was chosen as a model, because of its relatively simple stereochemistry. Initially, both 3-allylanisole (**8**) and 2-allylanisole (**9**) could effectively trap the anodically generated radical cation of 3,4-dihydro-2H-pyran (**6**) to construct the corresponding bicyclic cyclobutane ring-containing products (**10,11**) in excellent yields (Fig. 14). These results indicate minimal positional effects of the substituent on the aromatic ring, and that the "redox tag" function might be dependent on the electron-density of the aromatic ring. Several functional groups were introduced into the aromatic ring to control its electron density, which led to new electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions (Fig. 15).

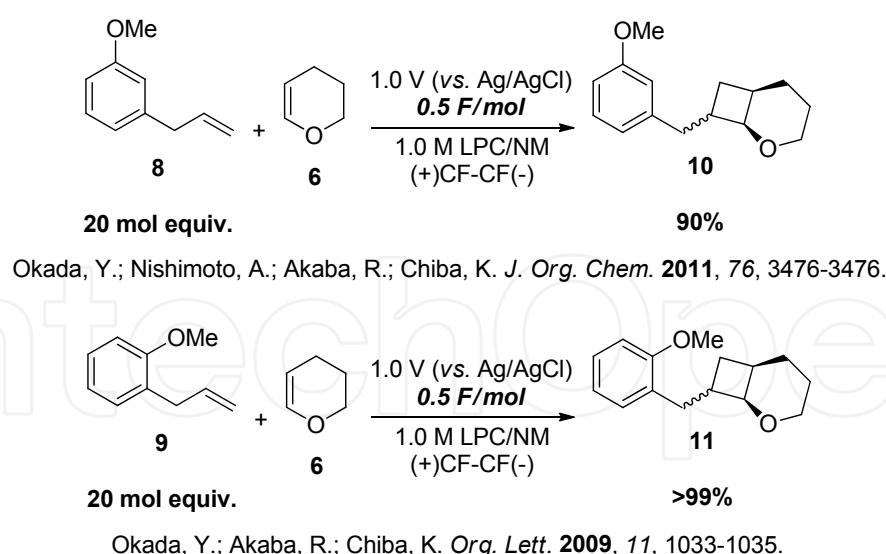


Fig. 14. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 3-allylanisole (**8**) or 2-allylanisole (**9**) and 3,4-dihydro-2H-pyran (**6**).

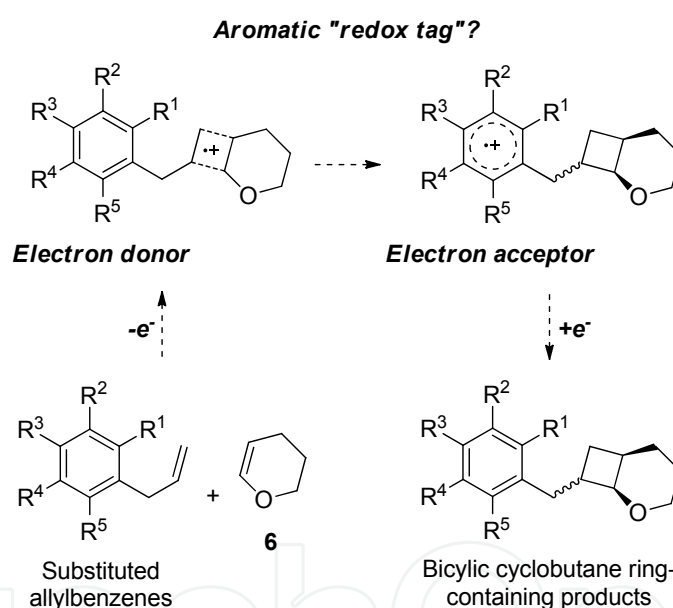
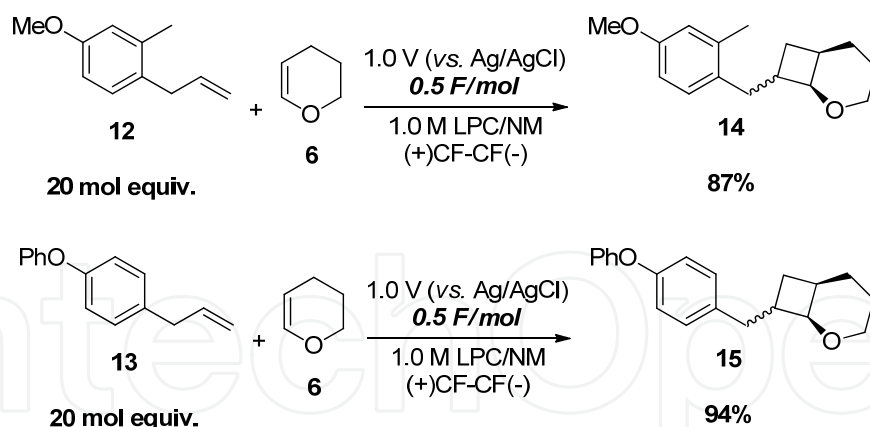


Fig. 15. New electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions based on aromatic "redox tag" strategy.

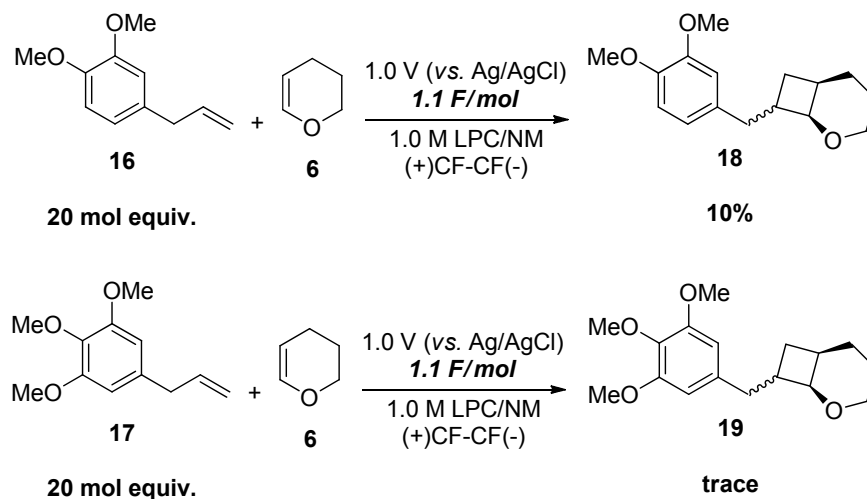
For this purpose, various substituted allylbenzenes as olefin nucleophiles were prepared to test their function as an aromatic "redox tag." The anodic oxidations of 3,4-dihydro-2H-pyran (**6**) were attempted in the presence of an excess of these substituted allylbenzenes.

Results indicated that both 4-allyl-2-methylanisole (**12**) and 1-allyl-4-phenoxybenzene (**13**) functioned as effective olefin nucleophiles in the reaction to afford the corresponding bicyclic cyclobutane ring-containing products (**14**, **15**) in excellent yields (Fig. 16); however, 4-allyl-1,2-dimethoxybenzene (**16**) and 5-allyl-1,2,3-trimethoxybenzene (**17**) were less efficient for the reaction and resulted in production of only small amounts of the corresponding bicyclic cyclobutane ring-containing products (**18**,**19**), even with stoichiometric amounts of electricity



Okada, Y.; Nishimoto, A.; Akaba, R.; Chiba, K. *J. Org. Chem.* **2011**, 76, 3476-3476.

Fig. 16. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 4-allyl-2-methylanisole (**12**) or 1-allyl-4-phenoxybenzene (**13**) and 3,4-dihydro-2H-pyran (**6**).

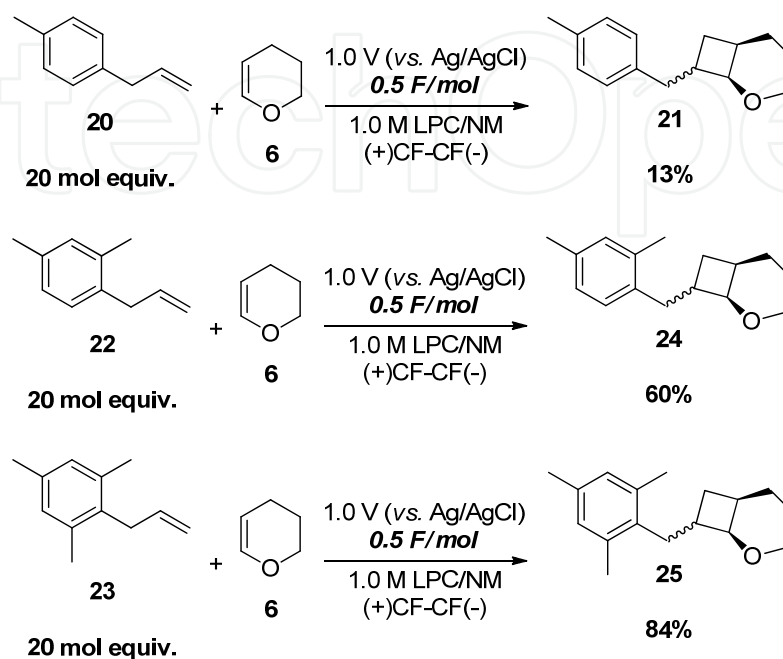


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Fig. 17. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 4-allyl-1,2-dimethoxybenzene (**16**) or 5-allyl-1,2,3-trimethoxybenzene (**17**) and 3,4-dihydro-2H-pyran (**6**).

(Fig. 17). Moreover, 1-allyl-4-methylbenzene (**20**) also functioned as an aromatic "redox tag" to induce the corresponding [2 + 2] cycloaddition reaction, which was in sharp contrast with non-substituted allylbenzene (**4**) (as described above), and the efficiencies of the alkylphenyl "redox tag" relied significantly on the number of alkyl substituent (Fig. 18). Thus, 1-allyl-2,4-dimethylbenzene (**22**) and 2-allyl-1,3,5-trimethylbenzene (**23**) could react with 3,4-dihydro-2H-pyran (**6**) effectively to give the corresponding bicyclic cyclobutane ring-containing products (**24**, **25**). These observations clearly indicated that the aromatic "redox tag" function was closely related to electron density, which could be quantified as an oxidation potential. Then, the oxidation potentials of several substituted allylbenzenes were measured to represent an appropriate value of oxidation potential for the aromatic ring to function as a "redox tag;" namely, the lower oxidation potentials were favorable, as long as they were greater than that of 3,4-dihydro-2H-pyran (**6**) (Table 1). The electron densities of both 4-allyl-1,2-dimethoxybenzene (**16**) and 5-allyl-1,2,3-trimethoxybenzene (**17**) were significantly increased

because of the strong electron-donating nature of the alkoxy group, precluding selective anodic oxidation of 3,4-dihydro-2H-pyran (**6**) in the presence of 4-allyl-1,2-dimethoxybenzene (**16**) or 5-allyl-1,2,3-trimethoxybenzene (**17**). In contrast, the electron densities of the aromatic rings also could be adjusted to an appropriate value even with relatively low electron-donating alkyl groups (Fig. 19).



Okada, Y.; Nishimoto, A.; Akaba, R.; Chiba, K. *J. Org. Chem.* **2011**, 76, 3476-3476.

Fig. 18. Electron-transfer-induced intermolecular [2 + 2] cycloaddition reaction between 1-allyl-4-methylbenzene (**20**), 1-allyl-2,4-dimethylbenzene (**22**), or 2-allyl-1,3,5-trimethylbenzene (**23**) and 3,4-dihydro-2H-pyran (**6**).

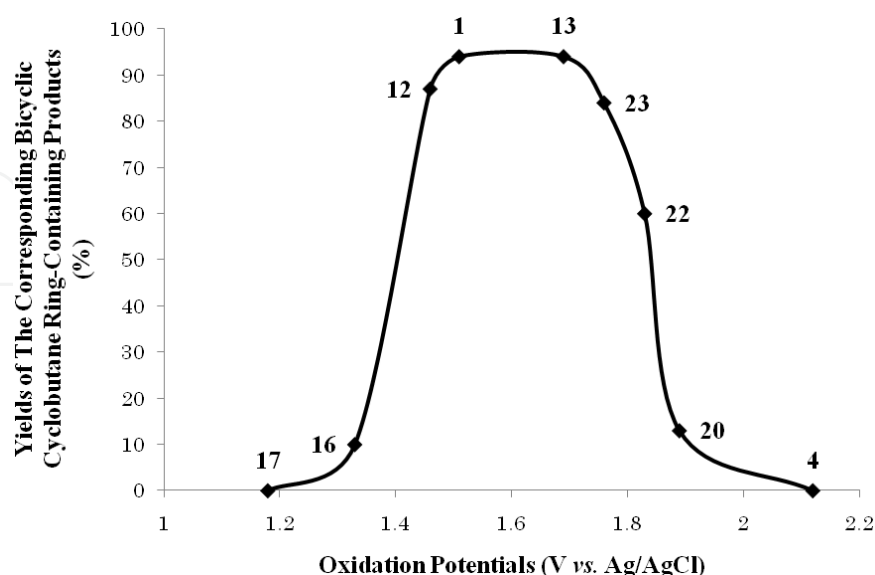
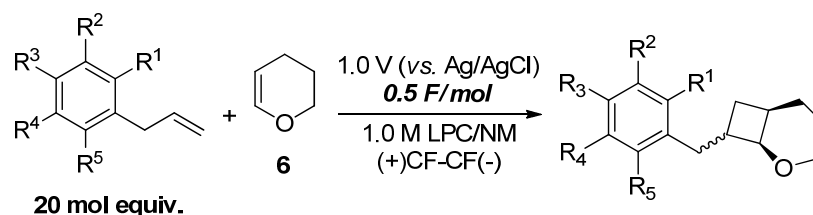


Fig. 19. Relation between oxidation potentials of various substituted allylbenzenes and yields of the corresponding bicyclic cyclobutane ring-containing products.



Substrates	Oxidation Potentials (vs. Ag/AgCl)	Yields ^a (%)
17 (R ¹ = H, R ² = MeO, R ³ = MeO, R ⁴ = MeO, R ⁵ = H)	$E_p^{ox} = 1.18 \text{ V}$	trace
16 (R ¹ = H, R ² = MeO, R ³ = MeO, R ⁴ = H, R ⁵ = H)	$E_p^{ox} = 1.33 \text{ V}$	10
6	$E_p^{ox} = 1.41 \text{ V}$	-
12 (R ¹ = Me, R ² = H, R ³ = MeO, R ⁴ = H, R ⁵ = H)	$E_p^{ox} = 1.46 \text{ V}$	87
1 (R ¹ = H, R ² = H, R ³ = MeO, R ⁴ = H, R ⁵ = H)	$E_p^{ox} = 1.51 \text{ V}$	94
13 (R ¹ = H, R ² = H, R ³ = PhO, R ⁴ = H, R ⁵ = H)	$E_p^{ox} = 1.69 \text{ V}$	94
23 (R ¹ = Me, R ² = H, R ³ = Me, R ⁴ = H, R ⁵ = Me)	$E_p^{ox} = 1.76 \text{ V}$	84
22 (R ¹ = Me, R ² = H, R ³ = Me, R ⁴ = H, R ⁵ = H)	$E_p^{ox} = 1.83 \text{ V}$	60
20 (R ¹ = Me, R ² = H, R ³ = H, R ⁴ = H, R ⁵ = H)	$E_p^{ox} = 1.89 \text{ V}$	13
4 (R ¹ = H, R ² = H, R ³ = H, R ⁴ = H, R ⁵ = H)	$E_p^{ox} = 2.12 \text{ V}$	n.d.

^aYields of the corresponding bicyclic cyclobutane ring-containing products determined by NMR

Table 1. Oxidation potentials of various substituted allylbenzenes.

6. Electron-transfer-induced cycloreversion reactions of cyclobutane rings assisted by aromatic “redox tags”

The electron impact mass spectrum of the *trans*-bicyclic cyclobutane ring-containing product (7) possessed a fragmentation pattern that contained a base peak at m/z 148, which was assigned to the radical cation of 4-allylanisole (1). This result suggests that the high-energy radical cation of the *trans*-bicyclic cyclobutane ring-containing product (7) produced in the mass spectrometer participated in the cycloreversion reaction of the cyclobutane ring. Based on this observation, the electron-transfer-induced cycloreversion reactions could be initiated through electrode processes.

The cyclic voltammogram of the *trans*-bicyclic cyclobutane ring-containing product (7) was then recorded under same conditions as described above to measure its peak oxidation potential at 1.54 V, which was similar to that of 4-allylanisole (1). Based on these values, the anodic oxidation of the *trans*-bicyclic cyclobutane ring-containing product (7) also was expected to occur on the electron-rich alkoxyphenyl group to give the corresponding alkoxyphenyl radical cation, which might induce cycloreversion reaction of the cyclobutane ring. Indeed, anodic oxidation of the *trans*-bicyclic cyclobutane ring-containing product (7) was attempted to give the cycloreversion product, 4-allylanisole (1), in moderate yield (Fig. 20). Analysis of the reaction mixture revealed that this reaction was accompanied by formation of a small amount of *cis*-bicyclic cyclobutane ring-containing product (7), verifying that the radical cation generated on the alkoxyphenyl group contributed to cleavage of the carbon-carbon bond that constitutes the cyclobutane ring. Intramolecular electron transfer between the alkoxyphenyl group and the cyclobutyl moiety was reversible; therefore, the cycloreversion reaction required an excess amount of electricity (Fig. 21). In this case, the amount of 4-allylanisole (1), derived from the cycloreversion reaction, was not sufficient to trap the radical cation of 3,4-dihydro-2H-pyran (6); thus, the reaction was irreversible. Although the

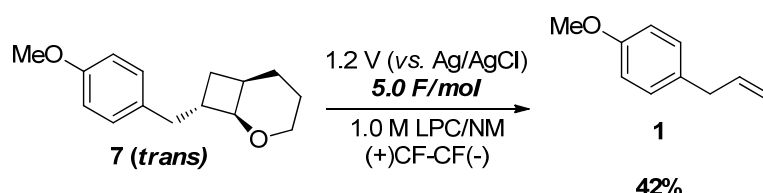


Fig. 20. Electron-transfer-induced cycloreversion reaction of the *trans*-bicyclic cyclobutane ring-containing product (**7**).

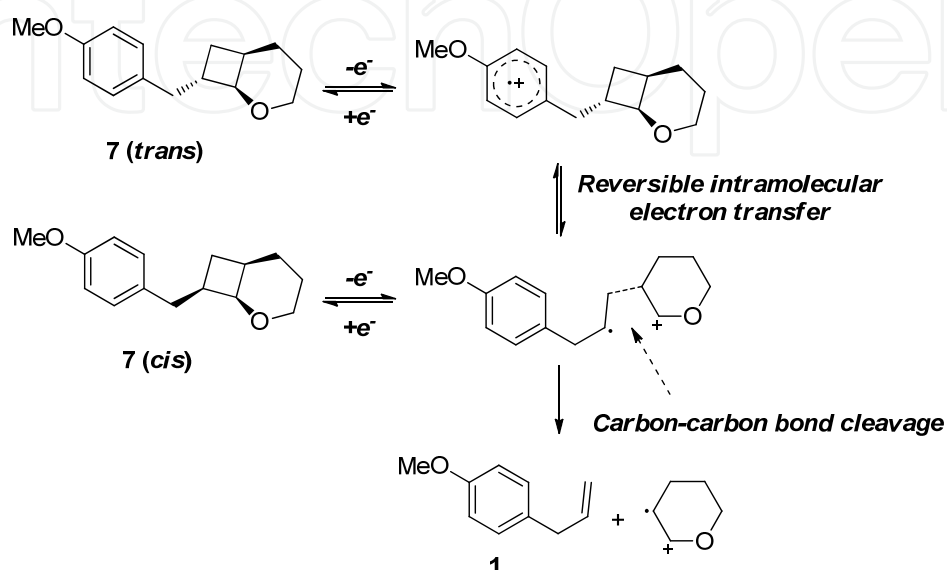


Fig. 21. Reaction mechanism of the electron-transfer-induced cycloreversion reaction of the *trans*-bicyclic cyclobutane ring-containing product (**7**).

cycloreversion reaction was highly chemoselective, the isolated yield was moderate because the cycloreversion product, 4-allylanisole (**1**), also was anodically oxidized under the reaction conditions, leading to its decomposition. Moreover, anodic oxidation of the *trans*-bicyclic cyclobutane ring-containing product (**25**) was attempted to give the cycloreversion product, 2-allyl-1,3,5-trimethylbenzene (**23**), in moderate yield. These results suggest that the aromatic “redox tag” also could facilitate the cycloreversion reaction of cyclobutane rings through the production of the corresponding aromatic radical cations (Fig. 22).

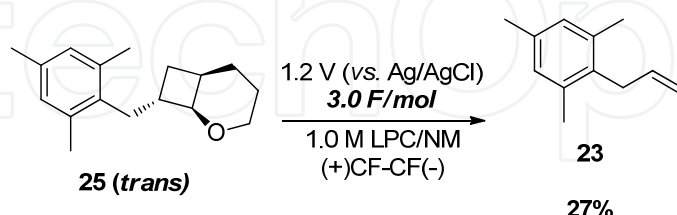


Fig. 22. Electron-transfer-induced cycloreversion reaction of the *trans*-bicyclic cyclobutane ring-containing product (**25**).

In contrast with the electron-transfer-induced cycloreversion of the *trans*-bicyclic cyclobutane ring-containing product (**7**), that of the all *trans*-cyclobutane ring-containing product (**3**) was less efficient; its peak oxidation potential was measured at 1.52 V (Fig. 23). Based on this value, the anodic oxidation of the all *trans*-cyclobutane ring-containing product (**3**) also was expected to occur on its electron-rich alkoxyphenyl group, producing

the corresponding radical cation. However, it could not facilitate the cycloreversion reaction of the cyclobutane ring efficiently. Apparently, the ring strain of the bicyclic structure was responsible for driving the cycloreversion reactions. Thus, the following mechanisms were proposed for the electron-transfer-induced cycloreversion reactions assisted by the aromatic “redox tag” (Fig. 24). The initial oxidation of the bicyclic cyclobutane ring-containing products occurred on the aromatic ring. Through reversible intramolecular electron transfer between the aromatic ring and cyclobutyl moiety, the corresponding cyclobutyl radical cations formed, leading to their cycloreversion reactions.

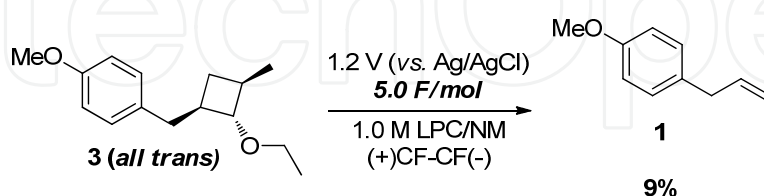


Fig. 23. Electron-transfer-induced cycloreversion reaction of the all *trans*-cyclobutane ring-containing product (**3**).

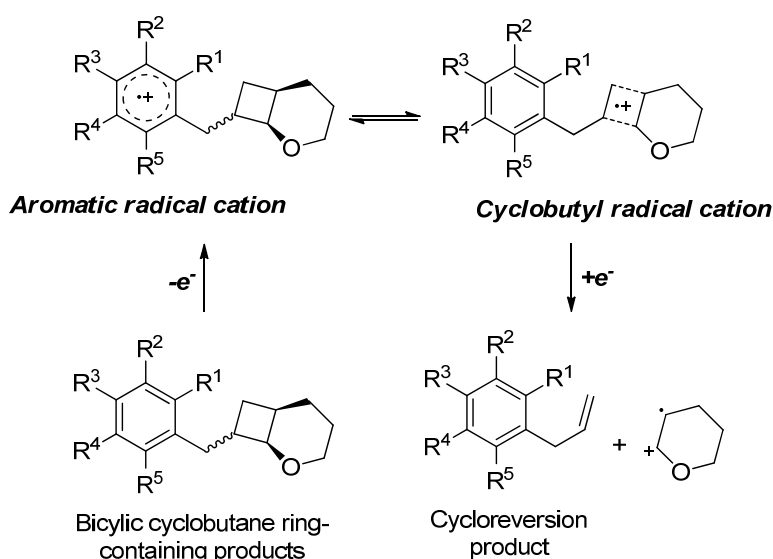


Fig. 24. Plausible reaction mechanism of electron-transfer-induced cycloreversion reaction of bicyclic cyclobutane ring-containing products.

7. Conclusion

The electrochemistry of electron transfer at the electrodes was key for generating reactive intermediates, leading to both carbon-carbon bond formation reactions and cleavage reactions. In particular, new electron-transfer-induced intermolecular [2 + 2] cycloaddition reactions between anodically generated enol ether radical cations and olefin nucleophiles were discovered to produce cyclobutane rings. Through mechanistic studies based on an electrochemical approach, these carbon-carbon bond formation reactions were found to be assisted by the aromatic “redox tag,” which could also facilitate several carbon-carbon bond cleavage reactions leading to the cycloreversion of cyclobutane rings. The aromatic “redox tag” functioned as both electron-donor and electron-acceptor in the sequential electron-transfer processes.

Electron-transfer-induced reactions play an important role in organic synthesis. In particular, electrochemical approaches that involve electron transfer at the electrode can regulate organic transformations in a highly controlled manner, which should lead to additional applications in both academic and industrial fields.

8. Acknowledgments

This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology. In addition, we thank Professor Dr. Ryoichi Akaba at Gunma National College of Technology for his valuable suggestions and comments regarding the reaction mechanisms.

9. References

- Arata, M.; Miura, T. & Chiba, K. (2007). Electrocatalytic Formal [2+2] Cycloaddition Reactions between Anodically Activated Enyloxy Benzene and Alkenes. *Organic Letters*, Vol. 9, No. 21, pp. 4347-4350, ISSN 1523-7052
- Chiba, K.; Jinno, M.; Kuramoto, R. & Tada, M. (1998). Stereoselective Diels-Alder reaction of electrogenerated quinones on a PTFE-fiber coated electrode in lithium perchlorate / nitromethane. *Tetrahedron Letters*, Vol. 39, No. 31, pp. 5527-5530, ISSN 0040-4039
- Chiba, K.; Fukuda, M.; Kim, S.; Kitano, Y. & Tada, M. (1999). Dihydrobenzofuran Synthesis by an Anodic [3 + 2] Cycloaddition of Phenols and Unactivated Alkenes. *The Journal of Organic Chemistry*, Vol. 64, No. 20, pp. 7654-7656, ISSN 0022-3263
- Chiba, K.; Miura, T.; Kim, S.; Kitano, Y. & Tada, M. (2001). Electrocatalytic Intermolecular Olefin Cross-Coupling by Anodically Induced Formal [2+2] Cycloaddition between Enol Ethers and Alkenes. *Journal of the American Chemical Society*, Vol. 123, No. 45, pp. 11314-11315, ISSN 0002-7863
- Fry, A. J. & Britton, W. E. (Eds.). (April 30, 1986). *Topics in Organic Electrochemistry*, Springer, ISBN 978-0306420580, New York, New York, USA
- Little, R. D. & Weinberg, N. L. (Eds.). (August 30, 1991). *Electroorganic Synthesis*, CRC Press, ISBN 978-0824785840, New York, New York, USA
- Lund, H. & Hammerich, O. (Eds.). (December 14, 2000). *Organic Electrochemistry* (Fourth Edition), CRC Press, ISBN 978-0824704308, New York, New York, USA
- Miura, T.; Kim, S.; Kitano, Y.; Tada, M. & Chiba, K. (2006). Electrochemical Enol Ether/Olefin Cross-Metathesis in a Lithium Perchlorate/Nitromethane Electrolyte Solution. *Angewandte Chemie International Edition*, Vol. 45, No. 9, pp. 1461-1463, 1521-3773
- Okada, Y.; Akaba, R. & Chiba, K. (2009). Electrocatalytic Formal [2+2] Cycloaddition Reactions between Anodically Activated Aliphatic Enol Ethers and Unactivated Olefins Possessing an Alkoxyphenyl Group. *Organic Letters*, Vol. 11, No. 4, pp. 1033-1035, 1523-7052
- Okada, Y.; Akaba, R. & Chiba, K. (2009). EC-backward-E electrochemistry supported by an alkoxyphenyl group. *Tetrahedron Letters*, Vol. 50, No. 38, pp. 5413-5416, 0040-4039
- Okada, Y. & Chiba, K. (2010). Continuous electrochemical synthetic system using a multiphase electrolyte solution. *Electrochimica Acta*, Vol. 55, No. 13, pp. 4112-4119, 0013-4686
- Okada, Y. & Chiba, K. (2010). Electron transfer-induced four-membered cyclic intermediate formation: Olefin cross-coupling vs. olefin cross-metathesis. *Electrochimica Acta*, Vol. 56, No. 3, pp. 1037-1042, 0013-4686
- Okada, Y.; Nishimoto, A.; Akaba, R. & Chiba, K. (2011). Electron-Transfer-Induced Intermolecular [2 + 2] Cycloaddition Reactions Based on the Aromatic "Redox Tag" Strategy. *The Journal of Organic Chemistry*, Vol. 76, No. 9, pp. 3470-3476, 0022-3263



Recent Trend in Electrochemical Science and Technology

Edited by Dr. Ujjal Kumar Sur

ISBN 978-953-307-830-4

Hard cover, 306 pages

Publisher InTech

Published online 27, January, 2012

Published in print edition January, 2012

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How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Kazuhiro Chiba and Yohei Okada (2012). Electron-Transfer-Induced Intermolecular [2 + 2] Cycloaddition Reactions Assisted by Aromatic "Redox Tag", Recent Trend in Electrochemical Science and Technology, Dr. Ujjal Kumar Sur (Ed.), ISBN: 978-953-307-830-4, InTech, Available from:
<http://www.intechopen.com/books/recent-trend-in-electrochemical-science-and-technology/electron-transfer-induced-intermolecular-2-2-cycloaddition-reactions-assisted-by-aromatic-redox-tag->

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