

[2+2] Cycloaddition Reaction for Probing the Electron Transfer Pathways

Yusuke YAMAGUCHI, Yohei OKADA, Kazuhiro CHIBA*

Tokyo University of Agriculture and Technology

3-5-8 Saiwai-cho, Fuchu, Tokyo 183-8509, Japan

Tel: (+81)-42-367-5667

E-mail: chiba@cc.tuat.ac.jp

Several types of bis-enol ether substrates that are tethered through various hydrocarbon linkers have been designed and prepared to investigate the reactivity of the radical cation, which are generated by anodic oxidation. The enol ether radical cations are effectively trapped by unactivated olefin as carbon nucleophile in lithium perchlorate/nitromethane electrolyte solution, enabling efficient intermolecular carbon-carbon bond formations to construct four-membered rings. When the bis-enol ether substrates are used for the reactions, a more detailed about mechanisms is obtained in unique way.

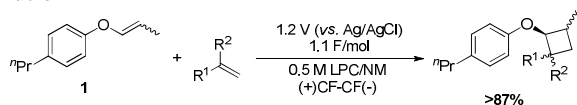
Anodic oxidation of electron-rich olefins is powerful methods in modern organic synthesis to generate the corresponding radical cations that can be employed as reactive intermediates for various chemical reactions. Such electrochemical processes are intriguing from both synthetic and mechanistic aspects because the reactions are easily controlled and several electrochemical analyses can also be combined to study electron transfer pathways.

We have been developing the electrochemical carbon-carbon bond formations in lithium perchlorate/nitromethane electrolyte solution, which was found to enhance the nucleophilicity of unactivated olefins, realizing various intermolecular cycloadditions.¹ For example, the anodic oxidation of enol ether (**1**) in the presence of olefin nucleophiles gave carbon four-membered ring products in high yields (Scheme 1).²

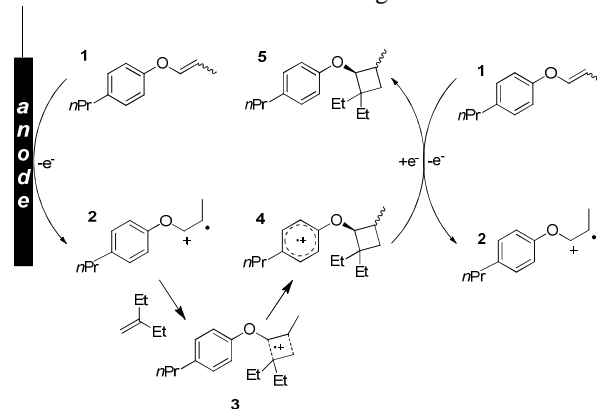
As shown in Scheme 2, the radical cation (**2**), which was generated by anodic oxidation from starting enol ether (**1**), reacted with olefin nucleophiles to form transient cyclobutyl radical cations (**3**). In order for cyclobutane ring formation to be successful, an intramolecular alkoxyphenyl ring intermediate was essential as an electron donor to reduce the cyclobutyl radical cation, affording the relatively long-lived alkoxyphenyl radical cation (**4**). This radical cation was expected to be reduced by the starting enol ether, affording cycloadduct (**5**) and completing the reaction with a catalytic amount of electricity.

Based on the reaction mechanism described in Scheme 2, we envisioned that the electron transfer from the intramolecular "second" enol ether would also be possible when bis-enol ether (**6**) was used instead of normal enol ether (**1**) (Scheme 3).

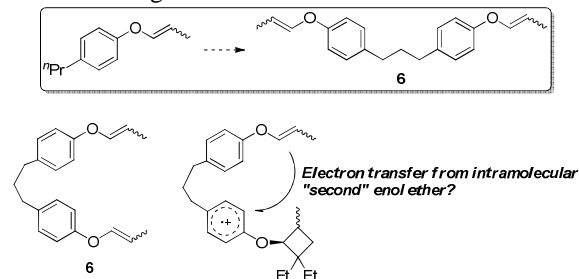
Scheme 1. Electrochemical four-membered ring formations in lithium perchlorate/nitromethane electrolyte solution



Scheme 2. Proposed reaction mechanism of the electrochemical four-membered ring formations

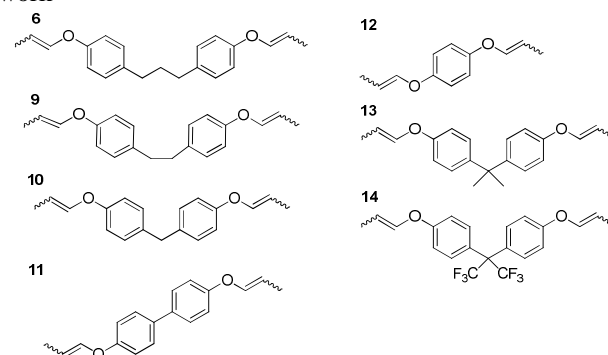


Scheme 3. Design of the bis-enol ether substrate



For this purpose, we designed and synthesized several types of bis-enol ether substrates, whose enol ethers were tethered via various hydrocarbon linkers, including the enol ether (**6**) (Scheme 4). These bis-enol ethers were then used for the electrochemical four-membered ring formations to show unique electron transfer mechanisms that largely depend on the structure of the linkers. Synthetic and mechanistic details would be discussed in the presentation.

Scheme 4. Structures of the bis-enol ethers used in this work



References

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