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Electrocatalytic Intermolecular Olefin Cross-Coupling by Anodically Induced Formal [2+2] Cycloaddition between Enol Ethers and Alkenes

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Electrochemical reactions have proven to be a valuable means for reversing the polarity of alkenes and triggering radical anion-based or radical cation-based cyclizing reactions.[1] Anodic olefin coupling initiated by oxidation of electron-rich olefins can provide powerful tools for achieving intramolecular cyclization reactions and building new ring systems.[2] In this case, several combinations of olefins can be introduced in the intramolecular cyclizing system, securing diverse functional groups in the newly cyclized skeletons (Figure 1). Electrocatalytic intermolecular cyclodimerization of olefins activated by carbazole,[3] aryl sulfonyl,[4] pyridyl, and quinolyl[5] groups has been achieved for four-membered-ring formation. On the other hand, it has unfortunately been difficult to achieve electrolytic intermolecular selective cross-coupling of two different olefins to provide the [2+2] cycloadduct. This was disappointing because the electrochemical method might allow for the selective polarity inversion of electron-rich olefins and open the door for the construction of four-membered rings by new combinations of olefins even in neutral conditions. This gave us the incentive to try to determine whether such an electrochemical approach might provide a unique pathway to their selective intermolecular olefin cross-coupling to construct [2+2] cycloadducts between the in situ generated electron-deficient olefins and nonactivated ones under the regulation of oxidation potentials and intra- and intermolecular electron transfers. We report herein our initial efforts to develop the novel electrocatalytic intermolecular formal [2+2] cross-coupling of electron-rich olefins.

Initially, the electrolytic cycloaddition between enol ethers **1**−**3** and allyltrimethylsilane **4** was studied (Figure 2). Anodic oxidation of enol ethers was accomplished by using a carbon felt anode, a constant current of 2.5 mA, a carbon felt counter electrode, and a 1.0 M lithium perchlorate/nitromethane electrolyte solution[6] in an undivided cell. Electrolytic substrates **1** or **2** gave no major cyclized product with **4** in the anodic reaction condition. On the other hand, it was surprising that the anodic activation of the enol ether **3** in the presence of 3 mol equiv of **4** selectively led to their intermolecular cross-coupling to form corresponding [2+2] cycloadduct **5** in 88% yield (Scheme 2). The reaction was complete after the passage of ca. 0.5 F/mol of charge, and the product **5** was also obtained even under dark electrolytic conditions. The product **5** had all trans stereochemistry, which was established by an nOe experiment. In the current case, no desired product was obtained from a mixture of **3** and **4** in 1.0 M lithium perchlorate/nitromethane left to stand for more than 4 h without

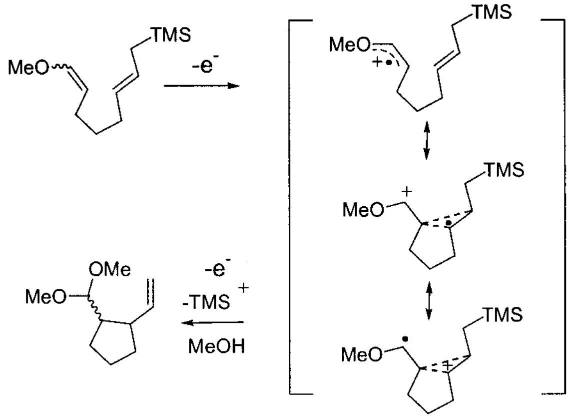


Figure 1. An example of an anodic intramolecular olefin coupling reaction.[2a−c]

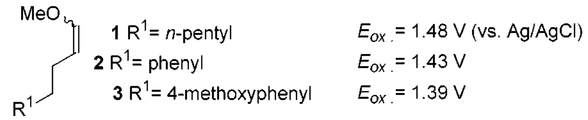
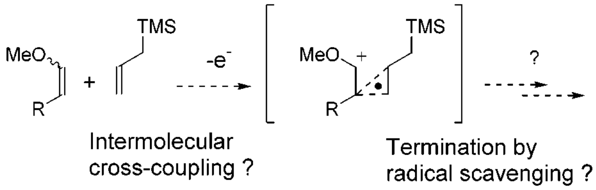
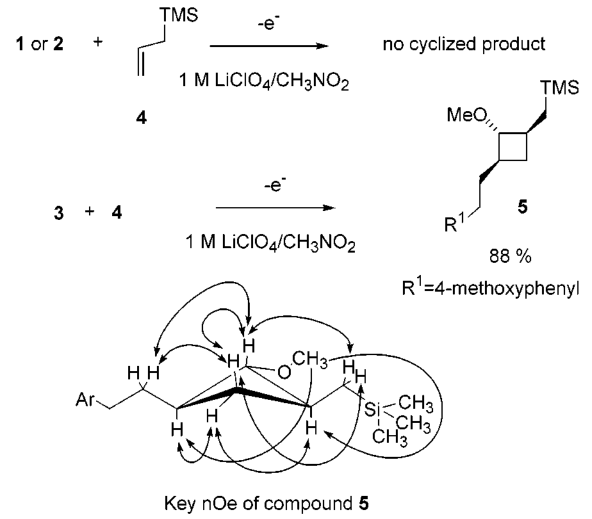


Figure 2. Structures and oxidation potentials of electrolytic substrates.

Scheme 1



Scheme 2



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[1] (a) Shono, T.; Nishiguchi, I.; Kashimura, S.; Okawa, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2181. (b) Swenton, J. S.; Morrow, G. W. *Tetrahedron Lett.* **1987**, *28*, 5445. (c) Schaefer, H. J.; Becking, L. *Tetrahedron Lett.* **1988**, *29*, 2797. (d) Yamamura, S.; Shizuri, Y.; Okuno, Y.; Shigemori, H. *Tetrahedron Lett.* **1987**, *28*, 6661. (e) Swenton, J. S.; Callinan A.; Chen, Y.; Rohde, J. J.; Kerns, M. L.; Morrow, G. W. *J. Org. Chem.* **1996**, *61*, 1267. Gao, J.

[2] (a) Moeller, K. D.; Marzabadi, M. R.; New, D. G.; Chiang, Michael Y.; Keith, S. *J. Am. Chem. Soc.* **1990**, *112*, 6123. (b) Moeller, K. D.; Tinao, L. V. *J. Am. Chem. Soc.* **1992**, *114*, 1033. (c) Hudson, C. M.; Moeller, K. D. *J. Am. Chem. Soc.* **1994**, *116*, 3347. (d) Little, D. R. *Chem. Rev.* **1996**, *96*, 93.

[3] Ledwith, A. *Acc. Chem. Res.* **1972**, *5*, 133.

[4] (a) Delaunay, J.; Mabon, G.; Orliac, A.; Simonet, J. *Tetrahedron Lett.* **1990**, *31* (5), 667. (b) Delaunary, J.; Orliac, A.; Simonet, J. *Tetrahedron Lett.* **1995**, *36* (12), 2083. (c) Fourets, O.; Cauliez, P.; Simonet, J. *Tetrahedron Lett.* **1998**, *39*, 565.

[5] Janssen, R. G.; Motevalli, M.; Utley, J. H. P. *Chem. Commun.* **1998**, 539.

[6] (a) Chiba, K.; Tada, M. *J. Chem. Soc., Chem. Commun.* **1994**, 2485. (b) Ayerbe, M.; Cossio, F. P.; Kim. F.; Euskal H. U.; San Sebastian D. *Tetrahedron Lett.* **1995**, *36*, 4447. (c) Chapuis, C.; Kucharska, A.; Rzepecki, P.; Jurczak, J. *Helv. Chim. Acta* **1998**, *81*, 2314. (d) Kumareswaran, R.; Vankar, P. S.; Reddy, M. V. R.; Pitre, S. V.; Roy, R.; Vankar, Y. D. *Tetrahedron* **1999**, *55*, 1099. (e) Sankararaman, S.; Sudha. R. *J. Org. Chem.* **1999**, *64*, 2155.

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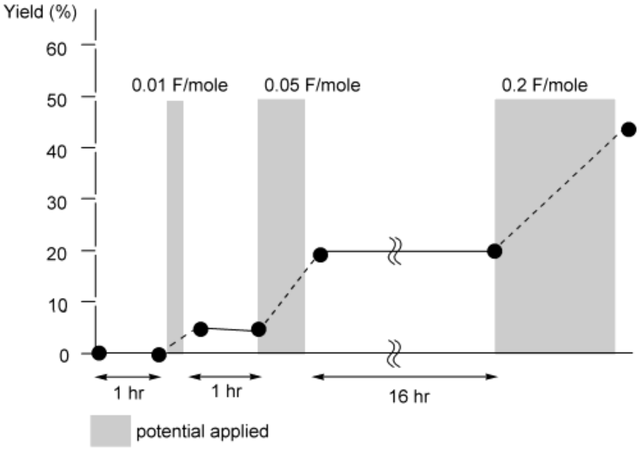
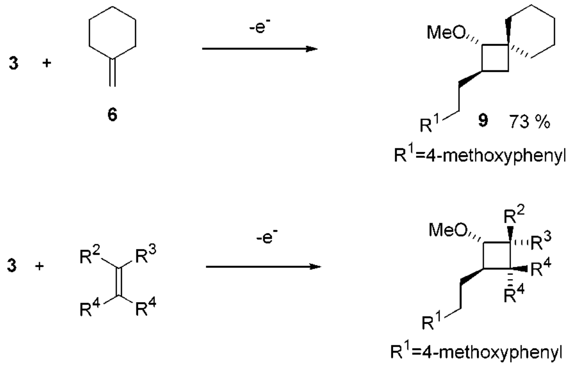


Figure 3. An interval electrolysis for the mixture of **3** and **4** in 1.0 M lithium perchlorate/nitromethane.

Scheme 3

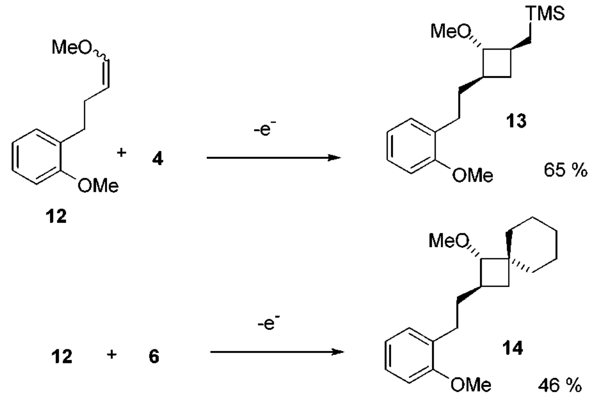


7 R^2=*n*-butyl, R^3, R^4=H **10** R^2=*n*-butyl, R^3, R^4=H 61 %

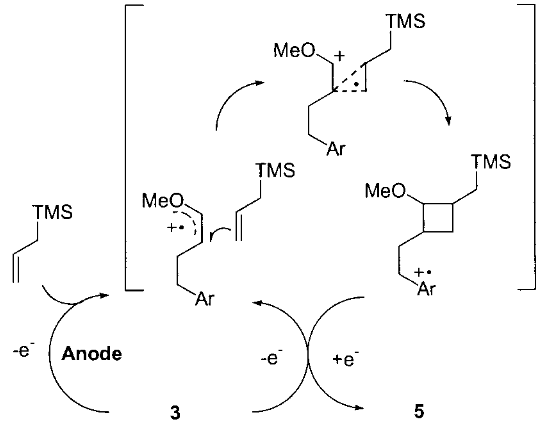
8 R^2, R^3=Me, R^4=H **11** R^2, R^3=Me, R^4=H 76 %

applying any potential. Pre-electrolyzed solution in the absence of the substrates followed by the addition of **3** and **4** also gave no product. In addition, yields of the generated product clearly responded to the stair-step application of electricity. The amount of product at each stage scarcely changed during the time when no potential was applied (Figure 3). The cyclization reaction also worked with **3** and nonactivated aliphatic alkenes. For compound **3** and methylene cyclohexane **6**, a single spiro product was obtained that had trans stereochemistry. Even a one-alkyl-substituted alkene **7** gave the corresponding cycloadduct **10** with **3** (Scheme 3). Anodic oxidation of *o*-methoxyphenyl derivative **12** in the presence of **4** also gave the desired cycloadduct **13** (Scheme 4). These reactions clearly show that a methoxyphenyl group in enol ether molecules plays an important role in those electrocatalytic cycloadditions. The cycloaddition reaction should be initiated by the anodic oxidation of the enol ether, followed by intermolecular carbon−carbon bond formation. To this end, intramolecular disproportionation between the radical cation and the methoxyphenyl group must have taken place to complete the formation of the four-membered ring. The in situ generated methoxyphenyl radical cation regenerates the radical cation of the enol ether by intermolecular disproportionation (Scheme 5).

Scheme 4



Scheme 5. A Proposed Reaction Mechanism of the Electrocatalytic Intermolecular Olefin Coupling



In conclusion, anodic oxidation of the enol ethers can be used to trigger the formation of intermolecular formal [2+2] cycloaddition with a variety of alkenes. The intermolecular reactions allow the formation of cyclobutanes between the enol ethers and alkenes of choice, leading to the construction of a wide variety of substituted cyclobutane rings. The methodology further complements the existing photochemical, thermal, and Lewis acid-catalyzed means to construct [2+2] cycloadducts. Efforts to utilize this methodology for the synthesis of various substituted cyclobutanes and to extend the work to intramolecular cyclizations are underway.

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Supporting Information Available: Experimental procedures and spectroscopic data for compounds **5**, **9**−**11**, **13**, and **14** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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