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Cycloaddition Reactions of Unactivated Olefins Catalyzed by an Organorhenium Electron-Transfer Mediator

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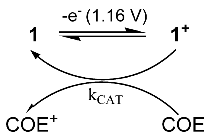
There is growing awareness of the efficacy of oxidative electron-transfer (ET) processes in inducing cycloaddition reactions[1] and intramolecular cyclizations[2] through either a direct anodic process[2] or one involving an ET mediator.[1,3,4] A restraint on this synthetic strategy arises from the requirement that removal of an electron from the intended coupling group must be facile. Thus, the ET-induced coupling of olefins, which are inherently hard to oxidize,[5] has been carried out successfully only on those which are activated (i.e., given lower oxidation potentials) either by delocalization (e.g., stilbenes) or by substitution with one or more electron-donating (e.g., methoxy) groups.[1a,2a,4,6] We now report an electrocatalytic method that allows, apparently for the first time, ET-induced cycloaddition reactions of unactivated cyclic olefins. These experiments take advantage of *in situ* generation of the strong one-electron oxidant $[\mathrm{ReCp(CO)_3}]^+$ ($\mathbf{1}^+$, Cp = η^5-C_5H_5)[7] as an ET mediator and provide a synthetic entry to cycloaddition products that is superior to previously reported methods, which generally require a week-long photolysis in the presence of Cu(I) catalysts.[8]

Previous literature reports on the anodic oxidation of unactivated cyclic olefins have been carried out in electrolyte media containing solvents or electrolyte anions that are sufficiently nucleophilic to attack the putative radical cation and account for substituted electrolysis products.[5a,9] The same difficulty was addressed for organometallic radical cations by using a more benign electrolyte medium, for example, dichloromethane/$[\mathrm{NBu_4}][\mathrm{TFAB}]$ (TFAB = $[\mathrm{B(C_6F_5)_4}]^-$), based on a weakly coordinating anion (WCA).[10] This direct oxidation approach is not possible for cyclic olefins from cyclopentene to *cis*-cyclooctene (COE), C_nH_{2n-2}, $n = 5-8$, owing to the fact that these compounds show no voltammetric response prior to the anodic background.[11] However, when a 25 mM solution of *cis*-COE containing a catalytic amount (1 mM) of **1** was electrolyzed at a potential sufficient to form the radical $\mathbf{1}^+$ ($E_{1/2}$ = 1.16 V vs $\mathrm{FeCp_2}^{0/+}$),[7] complete conversion of COE to *uncharged* organic products occurred within a time frame of several minutes. Similar results were found for the C_5 through C_7 analogues, albeit over somewhat longer electrolysis times.

The voltammetric response of the system COE/**1** is consistent with classic ET catalysis[12] (Scheme 1), wherein $\mathbf{1}^+$, produced at the electrode, receives an electron from the olefin, thereby returning the organorhenium complex to its reduced state, **1**, for reoxidation. The increase in anodic current observed at a 1 mm glassy carbon electrode for the oxidation of **1** upon addition of cis-COE permitted estimation[13] of the catalytic rate constant, k_{CAT}, as 0.02 $\mathrm{M^{-1}\ s^{-1}}$.

Scheme 1



When the 25:1 (*cis*-COE:**1**) solution was bulk electrolyzed at E_{appl} = 1.25 V at a Pt basket, the concentration of COE (monitored by sampling for gc analysis) fell to nearly zero after ~10 min (Figure 1), with a total coulomb count of ~0.1 F/equiv of COE. Separation[14] and characterization of the organic products by elemental analysis, GC-MS,[15] NMR, and IR showed that the major product (70−80% based on COE) is a mixture of four diastereoisomers of the 2 + 2 cyclobutyl derivative tricyclohexadecane, $C_{16}H_{28}$ (**2**), with the major isomer having the *cis-anti-cis* structure shown below [^{1}H, ^{13}C, and 2D NMR (HMQC, HMBC, ^{1}H−^{1}H HOMOCOSY and TOCSY; see Supporting Information)].

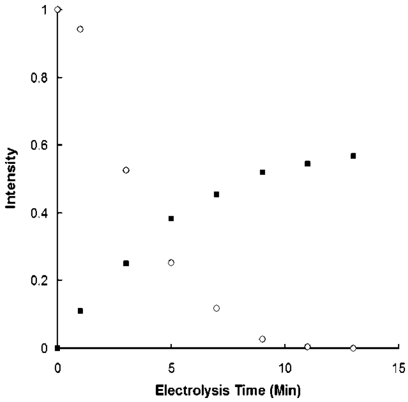
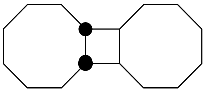
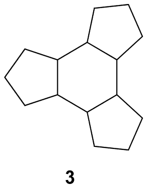


Figure 1. Plot of GC intensities (FID detector), summed for the four major $C_{16}H_{28}$ isomers, relative to initial intensity of *cis*-COE as a function of bulk electrolysis time. Legend: ○ = COE; ■ = sum of four major cycloaddition isomers.



2



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Voltammograms taken after the mediated electrolysis of *cis*-COE (as well as the other cyclic olefins) showed irreversible cathodic features in the potential range −0.6 to −0.9 V due to *ca.* 10% unidentified organic side products, most likely containing reducible groups formed by reaction of the organic radical cations with adventitious agents such as trace water. The rhenium catalyst is recovered almost quantitatively.[16]

The major products of identical electrolyses of the C_5 through C_7 cyclic olefins were shown by GC-MS to be, for C_6 and C_7, the appropriate 2+2 cyclobutyl derivatives and, for C_5, the 2+2+2 cyclohexyl product **3**, the geometries of which have not been investigated. The reaction times progressively increased for the

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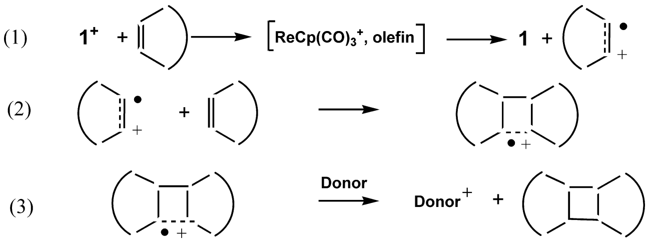
smaller, less easily oxidized, olefins, but even for cyclopentene, the reaction was complete within 1 h.

The very low coulomb counts suggest that, after initial formation of $\mathbf{1}^+$, radical chain processes are involved in the net conversion of olefins to cycloaddition products. The initiating ET step (eq 1 in Scheme 2) is energetically highly unfavorable, based on the fact that $E_{1/2}$ values for the olefins[11] are 700−900 mV positive of that of **1**. The ET reaction must be kinetically driven either by lowering of its transition state by an inner-sphere process[17] or by a fast radical-substrate reaction (eq 2), which would serve to rapidly remove the olefin cation radical from the unfavorable ET equilibrium. The overall cyclization would be completed by back-electron-transfer (eq 3) to the cyclized radical cation from a donor which could be either **1** or the neutral olefin, both of which are energetically facile one-electron donors compared to the neutral cycloaddition product.[18]

Scheme 2



Preliminary experiments have shown that *trans*-COE gives the same family of cyclobutyl addition compounds as seen for the *cis* isomer, but in different isomeric ratios. Although we cannot rule out the possibility of a stereoscopic role played by a Re(II)-olefin intermediate in these reactions, we consider it likely that the geometries of the organic products are determined largely by the radical/substrate reaction of eq 2. Progress on this and other mechanistic questions will be aided by investigations of the *direct* anodic oxidation of olefins under WCA-electrolyte conditions, and we are pursuing this with the more easily oxidized *trans*-COE system (E_{pa} = 1.5 V) as well as with other olefins.

Clearly, under Re(II)-based ET-mediator conditions, an unactivated olefin may act as an electroauxiliary, thereby providing a starting point for simple olefin-based C−C coupling reactions. Future work will focus on broadening the scope of these coupling reactions to include olefins with electron-withdrawing groups that would allow further functionalization of the cyclized products. The potential synthetic impact of the electrochemical method is substantial, considering that relatively high product yields may be obtained under time and energy requirements that are minimal compared to those necessary[8] for the thermally or photolytically induced coupling of unactivated olefins.

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Supporting Information Available: A set of cyclic voltammograms showing the effects of addition of *cis*-COE on the anodic current of **1** (Figure S1); a sample gas chromatogram for COE electrolysis products (Figure S2); NMR data used to assign *cis-anti-cis* structure to major product of **2** (Figures S3 and S4). This information is available free of charge via the Internet at http://pubs.acs.org.

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(11) Versus ferrocene, onset of the anodic background in CH_2Cl_2 occurs at ~1.8 V. The $E_{1/2}$ potentials for one-electron oxidation of the cyclic olefins C_5H_8, C_6H_{10}, C_7H_{12}, and *cis*-C_8H_{14} are estimated to be 2.06, 2.04, 1.96, and 1.85 V, respectively, based on the increase in their reported ionization potentials compared to that of naphthalene, for which $E_{1/2}$ = 1.35 V under these conditions. The potential of 1.65 V computed thusly for *trans*-COE is slightly positive of the E_{pa} value of 1.5 V measured in our medium. See: (a) Robinson, J.; Osteryoung, R. A. *J. Am. Chem. Soc.* **1979**, *101*, 323. for details about the relationship between I.P. and $E_{1/2}$ for hydrocarbons.
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(13) The rate constant was measured from steady-state voltammograms using the treatment in Denuault, G.; Pletcher, D. *J. Electroanal. Chem.* **1991**, *305*, 131. Increases in the cyclic voltammetry anodic peak currents were also seen (see Supporting Information Figure S1).
(14) Typical conditions: 6.7 mg (20 μmol) of **1** and 54 mg (500 μmol) of COE in 10 mL of 0.1 M $[NBu_4][TFAB]/CH_2Cl_2$ under nitrogen; electrolyze at 293 K for 15 min; add 30 mL of hexanes to precipitate supporting electrolyte; filter, evaporate, extract, and elute with hexane through activated alumina, affording 43 mg of an oil shown to be a mixture of **2** and its diastereomers.
(15) Saturn 2100T with CP8944 column, methanol chemical ionization.
(16) Longer electrolysis times result in some conversion of the rhenium catalyst to 18-electron addition products $[ReCp(CO)_3X]^+$ (X = H, Cl),[7a] but the original complex **1** may be regenerated by cathodic reduction of those side products.
(17) The bracketed intermediate in Scheme 2 is meant to convey that the ET step may follow either an inner- or outer-sphere pathway. Although the former would be consistent with the ability of the Re complex to adopt seven-coordination,[7] the latter is supported by the fact that some oxidation of *cis*-COE was found to be catalyzed by the aminium ET mediator[1,3,4] $[N(C_6H_3Br_2)_3]^+$. Although the aminium ion is also a strong one-electron oxidant ($E_{1/2}$ = 1.1 V in this medium), it lacks a metal center capable of expanding its coordination sphere. Compared to the Re-catalyzed process, the aminium-catalyzed reaction proceeds at a slower rate and gives greater product diversity. Detailed comparisons are under investigation.
(18) The cyclized radical cation formed in eq 2 is a stronger oxidant than the radical cation of the olefin substrate. See ref 1a, pp 163−165.

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