Intramolecular Anodic Olefin Coupling Reactions: The Use of Bis Enol Ether Substrates

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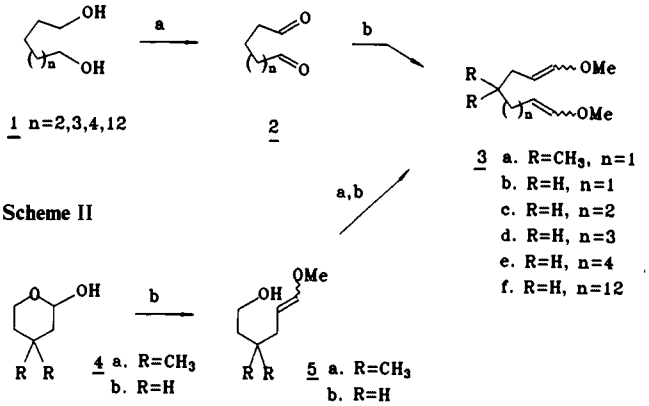
Abstract: In an effort to develop electrochemical methods for directly initiating oxidative cyclization reactions, the anodic oxidation of bis enol ether substrates has been examined. The reactions were found to lead to the formation of five-, six-, and seven-membered-ring 1,4-dicarbonyl equivalents. The reactions were not found to be useful for generating larger ring sizes. Both alkyl and silyl enol ether substrates were found to be compatible with the conditions required for carbon–carbon bond formation. Cyclic voltammetry studies indicated that the cyclizations were fast and that the reactions happened at or near the electrode surface. Finally, the cyclization reactions were shown to be compatible with the formation of quaternary carbons, even when carbon–carbon bond formation involved the generation of two vicinal quaternary carbons.

Introduction

In recent years, oxidative cyclization reactions have been receiving considerable attention.[1,2] These reactions, which most often originate from the generation of a radical cation, offer advantages over corresponding reductive and free radical cyclization pathways because they lead to more highly functionalized products. The increased level of functionality in these products can greatly simplify further synthetic transformations. Although a number of chemical methods exist for accomplishing these transformations, chemical methods are often limited by the acidic nature of the oxidizing agent or the inability of the reagent to oxidize functional groups having a wide range of oxidation potentials. For example, one of the most common reagents for initiating oxidative C–C bond-forming reactions is $Mn(OAc)_3$. This reagent has been shown to be compatible with the use of alkyl enol ether substrates.[1k,l] However, to date $Mn(OAc)_3$ reactions using silyl enol ether substrates have not been successful, presumably due to the acid lability of the silyl enol ether group. Recently, Snider and co-workers have demonstrated that the oxidation of silyl enol ethers derived from phenyl ketones can lead to efficient cyclization reactions using either Cu(II) or Ce(IV) salts.[3] However, cyclization reactions starting with silyl enol ethers derived from dialkyl ketones, which are more difficult to oxidize, currently proceed in much lower yields.

It is tempting to suggest that electrochemistry can provide a general means for initiating oxidative cyclization reactions because it can be used to oxidize a variety of functional groups under neutral conditions.[4] Indeed several anodic reactions have proven useful for constructing carbon–carbon bonds,[5] and a handful of these reactions have been applied to the construction of rings.[6,7] Yet in spite of the success of these reactions and the apparent utility of electrochemistry as a synthetic tool, anodic electrochemistry has failed to play a major role in the design and de-

Scheme I[a]



[a] Reagents: (a) i. $(COCl)_2$, DMSO, CH_2Cl_2, −78 °C; ii. Et_3N. (b) Ph_3PCH_2OMe, THF, 0 °C to room temperature.

(1) For reactions using $Mn(OAc)_3$, see: (a) Snider, B. B.; Merritt, J. E.; Dombroski, M. A.; Buckman, B. O. *J. Org. Chem.* **1991**, *56*, 5544. (b) Curran, D. P.; Morgan, T. M.; Schwartz, C. E.; Snider, B. B.; Dombroski, M. A. *J. Am. Chem. Soc.* **1991**, *113*, 6607. (c) Dombroski, M. A.; Kates, S. A.; Snider, B. B. *J. Am. Chem. Soc.* **1990**, *112*, 2759. (d) Kates, S. A.; Dombroski, M. A.; Snider, B. B. *J. Org. Chem.* **1990**, *55*, 2427. (e) Snider, B. B.; Patricia, J. J. *J. Org. Chem.* **1989**, *54*, 38. (f) Snider, B. B.; Patricia, J. J.; Kates, S. A. *J. Org. Chem.* **1988**, *53*, 2137. (g) Snider, B. B.; Dombroski, M. A. *J. Org. Chem.* **1987**, *52*, 5487. (h) Mohan, R.; Kates, S. A.; Dombroski, M. A.; Snider, B. B. *Tetrahedron Lett.* **1987**, *28*, 845. (i) Snider, B. B.; Mohan, R.; Kates, S. A. *Tetrahedron Lett.* **1987**, *28*, 841. (j) Snider, B. B.; Mohan, R.; Kates, S. A. *J. Org. Chem.* **1985**, *50*, 3659. (k) Corey, E. J.; Ghosh, A. K. *Tetrahedron Lett.* **1987**, *28*, 175. (l) Corey, E. J.; Ghosh, A. K. *Chem. Lett.* **1987**, 223. (m) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1985**, *26*, 4291. (n) Corey, E. J.; Kang, M. *J. Am. Chem. Soc.* **1984**, *106*, 5384. (o) Fristad, W. E.; Peterson, J. R.; Ernst, A. B.; Urbi, G. B. *Tetrahedron* **1986**, *42*, 3429. (p) Fristad, W. E.; Hershberger, S. S. *J. Org. Chem.* **1985**, *50*, 1026. (q) Fristad, W. E.; Peterson, J. R.; Ernst, A. B. *J. Org. Chem.* **1985**, *50*, 3143. (r) Fristad, W. E.; Peterson, J. R. *J. Org. Chem.* **1985**, *50*, 10. (s) Fristad, W. E.; Ernst, A. B. *Tetrahedron Lett.* **1985**, *26*, 3761.

(2) For reactions using other metals, see: (a) Pattenden, G.; Bhandal, H.; Russell, J. J. *Tetrahedron Lett.* **1986**, *27*, 2299. (b) Pattenden, G.; Patel, V. F.; Russell, J. J. *Tetrahedron Lett.* **1986**, *27*, 2303. (c) Breslow, R.; Olin, S. S.; Groves, J. T. *Tetrahedron Lett.* **1968**, *15*, 1837. (d) Kraus, G. A.; Landgrebe, K. *Tetrahedron Lett.* **1984**, *25*, 3939. (e) Baldwin, J. E.; Li, C. S. *J. Chem. Soc., Chem. Commun.* **1987**, 166. (f) For an alternative route, see: Curran, D. P.; Chang, C. T. *J. Org. Chem.* **1989**, *54*, 3140 and references therein.

(3) Snider, B. B.; Kwon, T. *J. Org. Chem.* **1990**, *55*, 4786.

(4) For a general overview, see: (a) Baizer, M. M. *Organic Electrochemistry: An Introduction and a Guide*, 2nd ed.; Baizer, M. M., Lund, H., Eds.; Marcel Dekker: New York, 1983. For overviews of anodic electrochemistry, see: (b) Torii, S. *Electroorganic Synthesis: Methods and Applications: Part I-Oxidations*; VCH: Deerfield Beach, FL, 1985. (c) Yoshida, K. *Electrooxidation in Organic Chemistry: The Role of Cation Radicals as Synthetic Intermediates*; John Wiley and Sons: New York, 1984. (d) Ross, S. D.; Finkelstein, M.; Rudd, E. J. *Anodic Oxidation*; Academic Press: New York, 1975. (e) Schaefer, H. J. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 911.

(5) (a) For a review, see refs 4b–e (especially ref 4b Appendix 1.1, ref 4c Chapter 4, and ref 4e). For several recent examples, see: (b) Yamamura, S.; Shizuri, Y.; Nakamura, K. *J. Chem. Soc., Chem. Commun.* **1985**, 530. (c) Yoshida, J.; Sakaguchi, K.; Isoe, S. *J. Org. Chem.* **1988**, *53*, 2525 as well as Yoshida, J.; Sakaguchi, K.; Isoe, S. *Tetrahedron Lett.* **1986**, *27*, 6075. (d) Holze, R.; Hamann, C. H. *Tetrahedron* **1991**, *47*, 737. (e) Amatore, C.; Moustafid, T. E.; Rolando, C.; Verpeaux, J. N. *Tetrahedron* **1991**, *47*, 777 and (f) Chapuzet, J. M.; Simonet, J. *Tetrahedron* **1991**, *47*, 791.

(6) For a review, se ref 4c, section 4-3 and references therein.

(7) For some recent examples, see: (a) Swenton, J. S.; Morrow, G. W. *Tetrahedron Lett.* **1987**, *28*, 5445. (b) Morrow, G. W.; Chen, Y.; Swenton, J. S. *Tetrahedron* **1991**, *47*, 655. (c) Becking, L.; Schaefer, H. J. *Tetrahedron Lett.* **1988**, *29*, 2797. (d) Yamamura, S.; Shizuri, Y.; Okuno, Y.; Shigemori, H. *Tetrahedron Lett.* **1987**, *28*, 6661. (e) Yamamura, S.; Shizuri, Y.; Shigemori, H.; Okuno, Y.; Ohkubo, M. *Tetrahedron* **1991**, *47*, 635. (f) Swanson, K. L.; Snow, K. M.; Jeyakumar, D.; Smith, K. M. *Tetrahedron* **1991**, *47*, 685.

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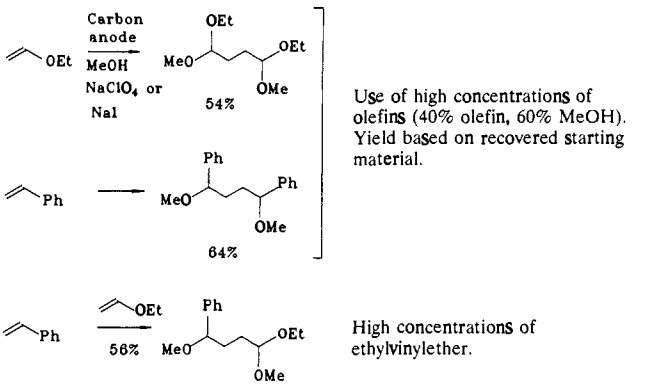


Figure 1.

velopment of new reaction strategies for the construction of complex organic molecules. With these things in mind, we have begun a search for anodic carbon–carbon bond-forming reactions that can be developed into generally useful tools for initiating oxidative cyclization reactions.

One family of reactions that appears ideal for development along these lines is the anodic coupling of electron-rich olefins. Intermolecular anodic olefin coupling reactions have been known for years.[8] Several examples taken from ref 4e are illustrated in Figure 1. It was reasoned that these reactions could be used to initiate oxidative cyclizations by tethering together two of the electron-rich olefins. Initially, the intramolecular coupling of an enol ether with a styrene and the intramolecular coupling of two enol ethers were selected for study.

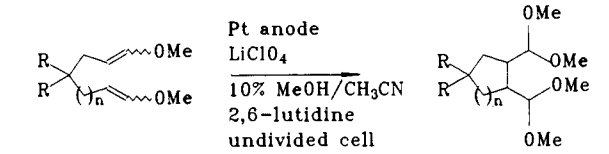
Anodic oxidation of a substrate containing an enol ether and a styrene moiety illustrated that oxidative cyclization reactions could be efficiently initiated at anode surfaces.[9] This work led to the discovery that electron-rich olefins could be coupled at anode surfaces to simple alkyl olefins, that radical cations generated from enol ethers more readily led to intramolecular carbon–carbon bond formation than did radical cations generated from styrenes, and that allylsilanes could be used as terminators for controlling the regiochemical outcome of the reactions.

Herein, we report our initial efforts concerning the intramolecular coupling of two enol ethers.[10,11]

Initial Studies

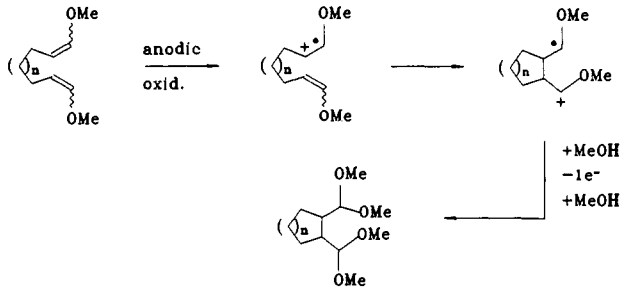
The intramolecular anodic coupling reactions of enol ethers were appealing because a successful cyclization would lead to the formation of potentially useful cyclic 1,4-dialdehyde equivalents. In order to address the utility of these reactions, substrates **3a–f** were synthesized. Initially, the route outlined in Scheme I was

Scheme III



3a. R=Me, n=1	6a. 68%
3b. R=H, n=1	6b. 70%
3c. R=H, n=2	6c. 65%
3d. R=H, n=3	6d. 50%
3e. R=H, n=4	6e. --
3f. R=H, n=12	6f. --

Scheme IV



followed. In this route, the desired substrates were made via a two-step procedure starting from the appropriate diol. This route allowed for the rapid construction of substrates **3c–f** (the yield for the two-step procedure ranged from 60 to 77%), but did not allow for the construction of substrates **3a** and **3b**.

The synthesis of **3a** and **3b** was accomplished using a second route as outlined in Scheme II. In this route, 4,4-dimethyl-2-hydroxytetrahydropyran was converted to compound **5a** in a 77% isolated yield (yield of **5b** = 70%), and then compound **5a** was treated with a tandem Swern oxidation–Wittig sequence in order to form the desired bis enol ether **3a** in a combined 55% yield (yield of **3b** = 52% over the two steps). It should be noted that the intermediate aldehydes in this sequence could not be isolated from the normal aqueous Swern oxidation workup; instead, the oxidation reaction was carried out in THF solvent, the crude reaction product filtered to remove the triethylamine hydrochloride, and the resulting THF filtrate cooled to 0 °C and treated directly with 3 equiv of the Wittig reagent. This modification of the procedure reported by Ireland[12] allowed for the direct treatment of the *highly sensitive* aldehyde with the unstabilized Wittig reagent without loss of a significant portion of the reagent to quenching by triethylamine hydrochloride.

The preparative electrolyses of substrates **3a–f** were conducted in an undivided cell using constant current conditions, a platinum anode, a 1 M lithium perchlorate in 10% methanol/acetonitrile electrolyte solution, 2,6-lutidine as a proton scavenger, and a carbon auxiliary electrode (Scheme III). Electrolysis of substrates **3a–c** demonstrated that the intramolecular coupling of enol ether substrates could cleanly lead to the formation of five- and six-membered rings. In all three cases an ca. 1:1 ratio of cis and trans isomers was obtained. The yields of these cyclizations were not optimized due to the propensity of the products to form aldehydes. For convenience, the reactions in Scheme III were all run on a scale ranging from 0.6 to 0.9 mmol. The reaction could be readily scaled up. For example, a single run using 4 mmol (675 mg) of **3c** led to a 56% (520 mg) isolated yield of **6c**.

A possible mechanism for the cyclization reactions is outlined in Scheme IV. This mechanism is directly analogous to the mechanism forwarded for the corresponding intermolecular coupling reactions.[13] This mechanism involves oxidation of one

(8) For reviews, see ref 5a. See also: (a) Belleau, B.; Au-Young, Y. K. *Can. J. Chem.* **1969**, *47*, 2117. (b) Fritsch, J. M.; Weingarten, H. *J. Am. Chem. Soc.* **1968**, *90*, 793. (c) Fritsch, J. M.; Weingarten, H.; Wilson, J. D. *J. Am. Chem. Soc.* **1970**, *92*, 4038. (d) Le Moing, M. A.; Le Guillanton, G.; Simonet, J. *Electrochim. Acta* **1981**, *26*, 139. (e) Engels, R.; Schaefer, H. J.; Steckhan, E. *Liebigs Ann. Chem.* **1977**, *204*. (f) Schaefer, H. J.; Steckhan, E. *Tetrahedron Lett.* **1970**, *44*, 3835. (g) Schaefer, H. J.; Steckhan, E. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 472. (h) Koch, D.; Schaefer, H. J.; Steckhan, E. *Chem. Ber.* **1974**, *107*, 3640. (i) Fox, M. A.; Akaba, R. *J. Am. Chem. Soc.* **1983**, *103*, 3460.

(9) (a) Moeller, K. D.; Marzabadi, M. R.; New, D. G.; Chiang, M. Y.; Keith, S. *J. Am. Chem. Soc.* **1990**, *112*, 6123. (b) Moeller, K. D.; Hudson, C. M. *Tetrahedron Lett.* **1991**, *32*, 2307. (c) Hudson, C. M.; Marzabadi, M. R.; Moeller, K. D.; New, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 7372.

(10) For a preliminary account of this work, see: Moeller, K. D.; Tinao, L. V. In *Electroorganic Synthesis-Festschrift in Honor of Manuel M. Baizer*; Little, R. D., Weinberg, N. L., Eds.; Marcel Dekker: New York, 1991; pp 153–160.

(11) (a) For a related intermolecular chemical coupling of silyl enol ethers with Ag_2O, see: Ito, Y.; Konoike, T.; Saegusa, T. *J. Am. Chem. Soc.* **1975**, *97*, 649. (b) For the intermolecular coupling of enolates to form 1,3-dicarbonyl compounds, see: Tokuda, M.; Shigei, T.; Itoh, M. *Chem. Lett.* **1975**, 621 and Ito, Y.; Konoike, T.; Harada, T.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 1487. (c) For related intramolecular couplings of enolates, see: Kobayashi, Y.; Taguchi, T.; Morikawa, T.; Tokuno, E.; Sekiguchi, S. *Chem. Pharm. Bull.* **1980**, *28*, 262. Paquette, L. A.; Snow, R. A.; Muthard, J. L.; Cynkowski, T. *J. Am. Chem. Soc.* **1979**, *101*, 6991. Hiyama, T.; Sumi, K.; Kwawbata, T. *J. Am. Chem. Soc.* **1989**, *111*, 6843.

(12) Ireland, R. E.; Norbeck, D. W. *J. Org. Chem.* **1985**, *50*, 2198–2200.

(13) Burgbacher, G.; Schaefer, H. J. *J. Am. Chem. Soc.* **1979**, *101*, 7590.

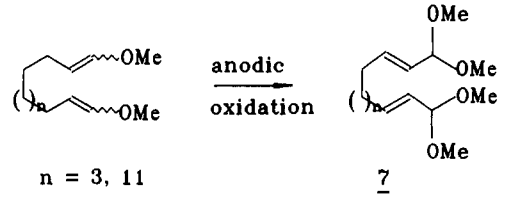


Figure 2.

of the enol ethers to form a radical cation intermediate that would then undergo addition to the second enol ether to form a second, cyclized radical cation intermediate. The cyclized radical cation intermediate would lead to product formation through a series of steps involving the loss of the second electron and the net addition of 2 equiv of methoxide. It is important to note that the sequence of reactions following the initial anodic oxidation is not known and that a mechanism involving the intramolecular coupling of two radical cation intermediates has not been ruled out.

In addition to the formation of five- and six-membered rings, the electrolysis could be used to generate seven-membered-ring compounds. In this case, preparative electrolysis of **3d** led to the formation of a 50% isolated yield of the cyclized product along with 14% of the recovered starting material. Again, a 1:1 mixture of cis and trans isomers was obtained. In addition to the cyclized products, a small amount (ca. 5%) of uncyclized unsaturated acetal product (analogous to **7**) was observed in the crude proton NMR spectrum, although none of this product was isolated after silica gel chromatography. The use of acetonitrile as a cosolvent was essential for seven-membered-ring formation. Only a small amount of seven-membered-ring product was formed when pure methanol was used as the solvent. In this case, the major product obtained was a bis α-methoxy acetal that apparently arose from methanol trapping of the initial radical cation intermediate prior to cyclization. For comparison, both **3a** and **3c** cleanly led to cyclized products when methanol was used as the solvent.

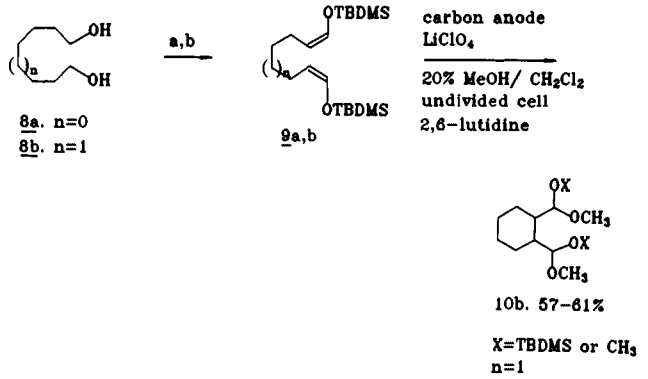
The use of the coupling reactions to generate larger ring sizes was not successful, even with the use of acetonitrile as a cosolvent. For example, oxidation of substrates **3e** and **3f** led to the formation of unsaturated acetal products (Figure 2). Removal of the 2,6-lutidine in an effort to slow down the elimination reaction led to the formation of saturated acetal products that apparently arose from acid decomposition of the initial substrates. Reexamination of the anodic oxidation of substrate **3a** without the use of 2,6-lutidine confirmed that the presence of the 2,6-lutidine was essential for obtaining cyclized products.

Use of Silyl Enol Ethers

The intramolecular couplings of silyl enol ethers were also examined. To this end, compounds **9a** and **9b** were synthesized from **8a** and **8b** by oxidation of the diol using Swern conditions followed by treatment with *tert*-butyldimethylsilyl triflate and triethylamine.[14] The conversion of **8a** to **9a** led to the desired five-membered-ring cyclization substrate in an overall 40% yield. The conversion of **8b** to **9b** led to the desired six-membered-ring cyclization substrate in an overall 74% yield. The lower overall yield in the synthesis of **8a** was apparently due to the instability of the intermediate bisaldehyde. In this case, it was best not to isolate the aldehyde. Instead, the crude bisaldehyde was treated immediately with the reagents needed for silyl enol ether formation (Scheme V).

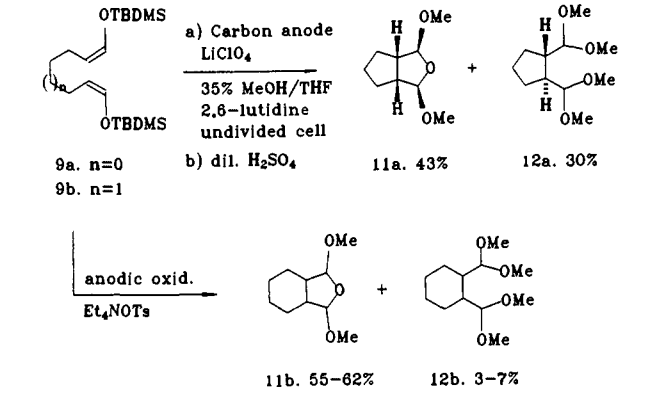
In the initially attempted electrolysis, **9b** was oxidized in a undivided cell using a reticulated vitreous carbon (carbon foam)[15] anode, 2,6-lutidine as a proton scavenger, and a 1 M lithium perchlorate in 20% methanol/dichloromethane electrolyte solution. These conditions led to the formation of cyclized product in a 57–61% isolated yield. The products were formed as a mixture of dimethoxy and *tert*-butyldimethylsiloxy, methoxy acetals. The

Scheme V[a]



[a] Reagents: (a) i. DMSO, $(COCl)_2$, CH_2Cl_2, −78 °C; ii. Et_3N. (b) Et_3N, $CF_3SO_3Si(CH_3)_2C(CH_3)_3$.

Scheme VI



yields were not optimized due to the instability of the *tert*-butyldimethylsiloxy, methoxy acetals.

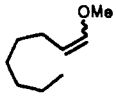
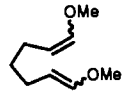
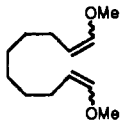
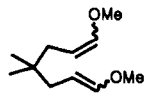
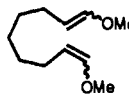
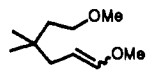
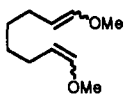
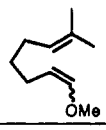
The cyclized products were more easily isolated when the electrolyses were run in a 0.1 M lithium perchlorate in 35% methanol/tetrahydrofuran electrolyte solution and then the reaction mixture treated with dilute sulfuric acid before workup (please see the Experimental Section for details). For example, when the five-membered-ring precursor **9a** was cyclized under these conditions, a 43% isolated yield of **11a** was obtained along with a 30% isolated yield of **12a** (Scheme VI). The cyclizations worked best when they were run under dilute conditions (0.01 M substrate) and not oxidized past 2 faradays of current. Compound **11a** was isolated as predominantly one isomer. The stereochemistry of **11a** was assumed to be cis across the ring fusion. The methoxy groups were assigned as being cis to each other because the acetal protons combined to give rise to a single proton NMR resonance at 4.80 ppm. A single methoxy resonance was observed at 3.42 ppm. The acetal protons gave rise to a singlet, indicating that the methoxy groups were on the convex face of the 2-oxabicyclo[3.3.0]octane ring skeleton (the dihedral angle between the acetal protons and the bridgehead protons was ca. 90° for this isomer). Product **11a** was contaminated by a minor isomer (about 10% of the total by ^1H NMR integration). Product **12a** was isolated as a single isomer that gave rise to a ^1H NMR resonance for the acetal protons at 4.21 ppm (d, J = 5.8 Hz) and a single methoxy resonance at 3.38 ppm. Product **12a** was tentatively assigned as being the trans isomer for the following reasons: (1) all of the intramolecular bis enol ether reactions have led to cis/trans mixtures, (2) products **11a** and **12a** were formed in a 1.4:1 ratio and were each found to be predominantly a single isomer, and (3) the trans isomer would not be expected to cyclize to the 2-oxabicyclo[3.3.0]octane ring skeleton.

When the six-membered-ring precursor, **9b**, was cyclized, a 55–62% isolated yield of **11b** was isolated along with a 3–7% isolated yield of **12b**. Both products were isolated as a mixture of stereoisomers. The low yield of **12b** compared to **12a** was

(14) Corey, E. J.; Cho, H.; Ruecker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.

(15) This electrode material was purchased from The Electrosynthesis Co., Inc.

Table I

	substrate	potential, V ($E_p/2$)		substrate	potential, V ($E_p/2$)
1		+1.40	5		+1.20
2		+1.42	6		+1.10
3		+1.40	7		+1.40
4		+1.30	8		+1.32

attributed to the ability of both cis and trans **12b** to form bicyclic derivatives.

In both cases, the reactions were found to be compatible with the use of silyl enol ethers, and little difference was found between the anodic oxidation of bis alkyl enol ethers and the anodic oxidation of bis silyl enol ethers.

Cyclic Voltammetry Studies

Additional information about the enol ether coupling reactions was obtained by cyclic voltammetry. The potential at one-half the peak height was measured for several substrates. The data is recorded in Table I. All of the waves were irreversible. The potentials measured (Ag/AgCl reference electrode, Pt anode, 0.1 N $LiClO_4$ in CH_3CN) for the eight- and seven-membered-ring substrates (cases 2 and 3 in Table I) were within experimental error of the half-wave obtained for a simple enol ether (case 1, +1.40 V). However, the potential measured for the six-membered-ring precursor (**3c**, case 4) was 100 mV lower than that of the parent enol ether. Measurement of the potential for the five-membered-ring precursor (**3b**, case 5) led to another 100-mV drop, while the placement of geminal methyls on the chain (**3a**, case 6) dropped the potential by an additional 100 mV. At this point, the cyclization substrate was showing an oxidation wave *300 mV lower than that of the parent enol ether.*

There are two possible explanations for the lowering of the observed potential as the cyclization substrate was changed. First, it is possible that cyclization and loss of the first electron occur in a concerted fashion. Second, and more likely, it is possible that the five- and six-membered-ring cyclizations proceed fast enough to "drain off" the radical cation from the equilibrium established at the anode surface and alter the observed reduction potential. For example, if the rate of the cyclization reaction is roughly equal to the rate of electron transfer at the anode surface, then the reaction can best be described by steady-state kinetics.

$$\text{SM} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\text{radical cation}] \xrightarrow{k_2} \text{Product}$$

The concentration of the radical cation at any time would be

$$[\text{radical cation}] = \frac{k_1[\text{SM}]}{(k_{-1} + k_2)}$$

and the Nernst equation would become

$$E_{obsd} = E^\circ - RT/nF \ln \frac{[\text{SM}]}{[\text{radical cation}]}$$

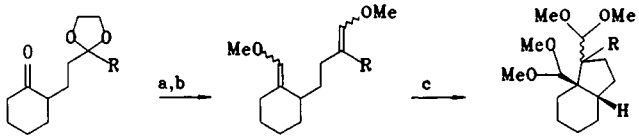
$$= E^\circ - RT/nF \ln \frac{(k_{-1} + k_2)}{k_1}$$

From this equation, it is clear that as the rate of the cyclization increases (larger value of k_2), the magnitude of the observed reduction potential will decrease (both E_{obsd} and E° are positive values).

If the above relationship is general, then *the relative magnitude of the measured potential can give us a qualitative feel for the rates of the corresponding cyclization reactions.* The relative ordering of the potentials in Table I would fit with what would be expected for the rates of five-, six-, and seven-membered-ring cyclizations. Using these criteria, the 100-mV drop in potential when going from case 5 to case 6 would indicate the ability of geminal substituents to accelerate the cyclization reactions. Case 7 was examined and compared with case 1 in order to show that this drop in potential was not due to an electronic effect caused by the geminal methyls. Although the *gem*-dialkyl effect is well-known for a variety of cyclizations,[16] to the best of our knowledge this represents the first evidence of such an effect on an electrochemically initiated cyclization reaction.

At the present time, we do not know the generality of these observations. Case 8, which has a measured potential 80 mV below that of the parent enol ether, seems to indicate that similar observations can be made for some of our previously described cyclizations.[9]

Scheme VII[a]



13a. R=H **14a.** R=H **15a.** 65%
13b. R=CH_3 **14b.** R=CH_3 **15b.** 44%

[a] Reagents: (a) When R = H, i. TsOH, MeOH, 43 h; ii. PPTs, acetone, 36 h, 72% over two steps. When R = CH_3, $HOAc/H_2O$ (4:1), 15 min, 65 °C, 97%. (b) Ph_3PCH_2OMe, THF, when R = H, 35%, when R = CH_3, 59%. (c) When R = H, constant current, Pt anode, undivided cell, 2,6-lutidine, 0.1 N $LiClO_4$ in 10% MeOH/CH_3CN. When R = CH_3, constant current, Pt anode, undivided cell, 2,6-lutidine, 0.5 N $LiClO_4$ in 20% $MeOH/CH_2Cl_2$.

Formation of Quaternary Carbons

The relationship between the observed reduction potential and the nature of the substrate suggests that the radical cation intermediates are very reactive and that the cyclization reactions occur at or near the electrode surface. With this in mind, cyclization substrates **14a** and **14b** were synthesized in order to probe the overall reactivity of the radical cation intermediates by testing the ability of the coupling reactions to form quaternary carbons (Scheme VII).

Preparative electrolysis of **14a** using an undivided cell, constant current conditions, a platinum anode, 2,6-lutidine as a proton scavenger, and a 0.1 M lithium perchlorate in 10% methanol/acetonitrile electrolyte solution led to the formation of a 65% isolated yield of the bicyclic products **15a**. The yield was unoptimized due to the propensity of the acetals to form aldehydes. An approximately 2:1 ratio of diastereomers was obtained. NOE experiments indicated that both diastereomers were cis with respect to the ring junction and that the major diastereomer had the two dimethoxy acetals cis to each other with respect to the five-membered ring. As in the earlier cases, cyclic voltammetry data proved to be interesting. In this case, the potential at one-half the peak height for compound **14a** was determined to be +1.01 V vs a Ag/AgCl reference electrode (same conditions as earlier). The potential measured for the parent 1-(methoxymethylidene)cyclohexane was found to be +1.16 V. When compared to the 200-mV drop in potential associated with five-membered-ring formation (case 5, Table I), the 150-mV drop in potential for compound **14a** vs the parent enol ether suggested

(16) See for example: (a) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Wiley-Interscience: New York, 1967; p 191. (b) Allinger, N. L.; Zalkow, V. *J. Org. Chem.* **1960**, *25*, 701.

that the formation of a quaternary carbon did not substantially hinder the anodic carbon–carbon bond-forming reaction.

In addition, preparative electrolysis of **14b** using an undivided cell, constant current conditions, a platinum anode, 2,6-lutidine as a proton scavenger, and a 0.5 M lithium perchlorate in 20% methanol/dichloromethane electrolyte solution led to the formation of a 44% unoptimized yield of the desired bicyclic product. An approximately 2:1 ratio of diastereomers was formed. As in the earlier example, NOE experiments indicated that both diastereomers were cis with respect to the ring junction and that the dimethoxy acetal groups were cis to each other in the major product. In this example, the steric constraints associated with the generation of *two vicinal quaternary carbons* did not stop the anodic carbon–carbon bond-forming reaction!

Conclusion

In summary, we have found that the anodic oxidation of bis enol ethers can effectively lead to the formation of five-, six-, and seven-membered-ring products. These reactions represent a new method for electrochemically initiating oxidative cyclization reactions and lead to potentially useful 1,4-dicarbonyl equivalents. The cyclization reactions were found to occur at or near the anode surface and were found to be compatible with the formation of quaternary carbons.

The anodic cyclization reactions did not lead to stereoselectivity in the carbon–carbon bond-forming step. In all cases, cis/trans mixtures were obtained. At the present time, it appears that the stereochemistry of the reactions will need to be controlled either by stereochemical constraints built into the starting substrates or by thermochemically setting the stereochemistry in a subsequent step (for example, hydrolysis of the acetal followed by epimerization). Studies aimed at identifying factors that influence the stereochemical outcome of the reactions and examining the overall synthetic potential of the reactions are currently underway.

Experimental Section[17]

3,3-Dimethyl-6-methoxy-(*E*,*Z*)-5-hexen-1-ol (5a). To a stirred suspension of 5.77 g (16.8 mmol) of (methoxymethyl)triphenylphosphonium chloride in 40 mL of tetrahydrofuran at 0 °C was added 6.72 mL (16.8 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The dark red mixture was allowed to stir for 30 min at 0 °C. A solution of 0.91 g (7.0 mmol) of 2-hydroxy-4,4-dimethyltetrahydropyran in 10 mL of tetrahydrofuran was added over a period of 5 min. The reaction mixture was allowed to warm to room temperature. After 20 h, the reaction was quenched with saturated brine solution (2 × 50 mL), and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed using a 40% ether/pentane solution containing 1% triethylamine. Elution with 40% ether/pentane afforded 0.85 g (77%) of the alcohol enol ether **5a**. The spectral data for the 1.6:1 mixture of trans and cis isomers were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.22 (d, J = 13.1 Hz, 0.62 H, vinyl proton at C_6), 5.88 (d, J = 6.6 Hz, 0.38 H, vinyl proton at C_6), 4.66 (dt, J_d = 12.8 Hz, J_t = 6.3 Hz, 0.62 H, vinyl proton at C_5), 4.29 (q, J = 7.0 Hz, 0.38 H, vinyl proton at C_5), 3.68 (t, J = 7.0 Hz, 2 H, methylene proton at C_1), 3.58, 3.52 (two s, 3 H, methoxy protons), 2.78 (br s, 1 H, OH), 1.97 (d, J = 7.5 Hz, 0.7 H), 1.81 (d, J = 7.2 Hz, 1.3 H), 1.50 (t, J = 7.5 Hz, 2 H), 0.90, 0.86 (two s, 6 H, geminal methyl protons); ^{13}C NMR ($CDCl_3$/75 MHz) δ 148.6, 147.3, 103.2, 99.0, 59.7, 59.5, 55.8, 43.8, 43.5, 40.5, 35.9, 32.4, 27.1, 26.8; IR (neat/NaCl) 3311, 3059, 3040, 2955, 2936, 2904, 2871, 1664, 1655, 1467, 1386, 1261, 1177, 1131, 1110, 1054, 1028, 936, 914 cm^{-1}; GCMS (PCI)[18] m/e (rel intensity) 159 (M^+ + H, 5), 158 (M^+, 0.8), 128 (18), 127 ($M^+ - OCH_3$, 100), 113 (25), 111 (11), 109 (27), 85 (18), 83 (28), 71 (25), 69 (9), 61 (9), 57 (16); HRMS (EI) m/e calcd for $C_9H_{18}O_2$ 158.1307, found 158.1293. Anal. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.46. Found: C, 68.02; H, 11.33.

4,4-Dimethyl-1,7-dimethoxy-1,6-heptadiene (3a). To a 0 °C solution of 10.97 g (31.8 mmol) of (methoxymethyl)triphenylphosphonium chloride in 60 mL of tetrahydrofuran was added 12.8 mL (32.0 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The resulting dark red solution was allowed to stir for 1 h. In a separate flask, a solution of 1.27 g (8.0 mmol) of the alcohol enol ether **5a** and 0.69 mL (9.7 mmol) of dimethyl sulfoxide in 20 mL of tetrahydrofuran at −70 °C was treated with 0.77 mL (8.9 mmol) of oxalyl chloride. The resulting mixture turned cloudy. After 20 min, 3.37 mL (24.2 mmol) of triethylamine was added and the reaction allowed to stir for an additional 5 min at −70 °C. The reaction was diluted with 10 mL of tetrahydrofuran and filtered under suction. The residue was washed with 2 10-mL portions of tetrahydrofuran. The filtrate was then concentrated to about 20 mL and cannulated into a 0 °C solution of the ylide generated above over a period of 10 min. The reaction mixture was allowed to warm to room temperature. After 20 h, the reaction was quenched with 75 mL of water. The organic layer was separated and washed with saturated brine solution (2 × 75 mL). The aqueous layers were combined and extracted with ether (2 × 75 mL). The combined organic fractions were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed with a 1% triethylamine/pentane solution. This column separated the desired enol ether and the triphenylphosphine oxide byproduct, both of which move faster than the rest of the crude reaction products. The enol ether and triphenylphosphine oxide had the same R_f values by TLC when the solvent system described above was used. Most of the triphenylphosphine oxide was separated from the enol ether by concentrating the solution in vacuo, diluting with 5 mL of pentane, and storing the solution in the freezer. The triphenylphosphine oxide precipitated out of the solution. The supernatant was then decanted and the precipitate washed with pentane. The washings and the supernatant were combined and concentrated in vacuo, diluted with 3 mL of pentane, and again stored in the freezer. This procedure was repeated until most of the triphenylphosphine oxide was separated. The resulting crude product was chromatographed through silica gel that was slurry-packed with a 1% triethylamine in pentane solution, and elution with pentane afforded 0.81 g (55%) of the desired bis enol ether **3a**. The spectral data for the trans and cis isomers (2:1 ratio) were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.24 (d, J = 12.5 Hz, 1.34 H, vinyl proton at C_1 or C_7), 5.95 (ddd, J = 6.5, 1.5, 1.4 Hz, 0.66 H, vinyl proton at C_1 or C_7), 4.74 (m, 1.34 H, vinyl proton at C_2 or C_6), 4.38 (tq, J_t = 1.5 Hz, J_q = 7.8 Hz, 0.66 H, vinyl proton at C_2 or C_6), 3.57, 3.56, 3.53, 3.52 (four s, 6 H, methoxy protons), 1.96 (dt, J_d = 1.4 Hz, J_t = 7.8 Hz, 1.32 H), 1.79 (ddd, J = 7.7, 3.8, 1.4 Hz, 2.68 H), 0.85, 0.83, 0.81 (three s, 6 H, geminal methyl protons); ^{13}C NMR ($CDCl_3$/75 MHz) δ 148.5, 148.4, 147.3, 103.8, 103.5, 99.6, 99.4, 59.3, 55.9, 55.8, 39.5, 35.4, 35.3, 33.7, 29.5, 26.3, 26.2; IR (neat/NaCl) 3064, 3038, 3000, 2868, 2832, 1664, 1657, 1465, 1453, 1440, 1391, 1383, 1364, 1261, 1210, 1177, 1162, 1129, 1109, 1008, 936 cm^{-1}; GCMS (EI) m/e (rel intensity) 184 (M^+, 0.6), 152 ($M^+ - CH_3OH$, 7), 137 (5), 113 (47), 112 (6), 109 (9), 97 (10), 82 (8), 81 (100), 79 (25), 75 ($(CH_3O)_2CH^+$, 46), 71 (37), 55 (11); HRMS (EI) m/e calcd for $C_{11}H_{23}O_2$ (M^+ + H) 185.1541, found 185.1505. Anal. Calcd for $C_{11}H_{22}O_2$: C, 71.69; H, 10.93. Found: C, 71.66; H, 10.94.

4,4-Dimethyl-1,2-bis(dimethoxymethyl)cyclopentane (6a). A 25-mL, three-neck, round-bottom flask equipped with a platinum gauze anode, a carbon rod cathode, and a nitrogen inlet was charged with a solution of 0.131 g (0.72 mmol) of the bis enol ether **3a** in 10 mL of a 1:9 mixture of methanol/acetonitrile. To this solution were added 1.064 g (10.0 mmol) of $LiClO_4$ and 0.51 mL (7.2 mmol) of 2,6-lutidine. The reaction was degassed by bubbling nitrogen through the solution and then electrolyzed at a constant current of 9 mA until only a trace amount of starting material remained as monitored by TLC (259 C or 3.75 faradays). The reaction mixture was worked up with water and ether. The aqueous layer was extracted with ether, and the combined organic extracts were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed with 10% ether/pentane containing 1% triethylamine. Gradient elution from 10% ether/pentane to 40% ether/pentane gave 0.120 g (68%) of the desired cyclized products, which was contaminated with a small amount of aldehyde products arising from the hydrolysis of the acetals. The spectral data for the 1.8:1 mixture of diastereoisomers (cis and trans about the five-membered ring) were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.44 (d, J = 6.0 Hz, 0.7 H, acetal proton), 4.32 (d, J = 5.4 Hz, 1.3 H, acetal proton), 3.40, 3.39, 3.36, 3.34 (four s, 12 H, methoxy protons), 2.53–2.41 (m, 1 H), 2.30–2.17 (m, 1 H), 1.62–1.36 (m, 4 H), 1.06, 1.00, 0.96 (three s, 6 H, geminal methyls); ^{13}C NMR ($CDCl_3$/75 MHz) δ 108.6, 105.9, 54.8, 54.7, 53.9, 53.0, 44.0, 41.6, 41.5, 41.3, 37.3, 36.9, 29.7, 29.5, 29.4, 28.8; IR (neat/NaCl) 2953, 2937, 2898, 1466, 1447, 1384, 1366, 1190, 1140, 1124, 1060, 971 cm^{-1}; GCMS (EI) m/e (rel intensity) 215 ($M^+ - OCH_3$, 0.5), 183 (12), 107 (26), 101 (29), 91 (13), 79 (12), 77 (9), 76 (29), 75 ($(CH_3O)_2CH^+$, 100), 74 (12), 73 (7), 59 (11), 55 (9); HRMS (EI) m/e calcd for $C_{12}H_{23}O_3$ ($M^+ - OCH_3$) 215.1648, found 215.1670.

6-Methoxy-(*E*,*Z*)-5-hexen-1-ol (5b). The alcohol enol ether was prepared using the procedure described above for the synthesis of 3,3-dimethyl-6-methoxy-(*E*,*Z*)-5-hexen-1-ol (**5a**). In this experiment, 0.306 g (3.0 mmol) of 2-hydroxytetrahydropyran was treated under Wittig

(17) For a description of general experimental details, see: Moeller, K. D.; Wang, P. W.; Tarazi, S.; Marzabadi, M. R.; Wong, P. L. *J. Org. Chem.* **1991**, *56*, 1058.

(18) PCI = positive chemical ionization. Methane was used as the carrier gas.

conditions to give 0.275 g (71%) of compound **5b**. The spectral data for the mixture of olefin isomers were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.30 (d, J = 12.5 Hz, 0.74 H, vinyl proton at C_6), 5.90 (dt, J_d = 6.1 Hz, J_t = 1.3 Hz, 0.26 H, vinyl proton at C_6), 4.72 (dt, J_d = 12.6 Hz, J_t = 7.3 Hz, 0.76 H, vinyl proton at C_5), 4.35 (q, J = 7.4 Hz, 0.24 H, vinyl proton at C_5), 3.64 (q, J = 6.0 Hz, 2 H, methylene protons at C_1), 3.58, 3.50 (two s, 3 H methoxy protons), 2.10 (q, J = 8.0 Hz, 0.43 H), 1.96 (dq, J_d = 1.4 Hz, J_q = 7.3 Hz, 1.57 H), 1.64–1.53 (m, 3 H), 1.47–1.36 (m, 2 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.4, 146.5, 106.6, 102.8, 62.7, 55.8, 31.9, 27.2, 26.6; IR (neat/NaCl) 3400 (br), 3056, 3034, 2998, 2846, 1658, 1454, 1210, 1182, 1111, 1066, 1040, 995 cm^{-1}; GCMS (PCI) m/e (rel intensity) 130 (M^+, 44), 112 ($M^+ - H_2O$, 8), 98 (14), 97 (13), 85 (7), 84 (29), 72 (10), 71 (100), 70 (18), 69 (10), 58 (7), 55 (7); HRMS (EI) m/e calcd for $C_7H_{14}O_2$ 130.0994, found 130.1003. Anal. Calcd for $C_7H_{14}O_2$: C, 64.58; H, 10.84. Found: C, 64.65; H, 10.88.

1,7-Dimethoxy-1,6-heptadiene (3b). Bis enol ether **3b** was prepared in a fashion identical to the procedure described above for the synthesis of compound **3a**, except for the substitution of *tert*-butyllithium for *n*-butyllithium as the base. The desired compound was obtained in 52% yield over the tandem Swern–Wittig sequence. The spectral data for the mixture of olefin isomers were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.29 (d, J = 12.7 Hz, 1.4 H, vinyl proton at C_1 or C_7), 5.88 (d, J = 8.0 Hz, 0.6 H, vinyl proton at C_1 or C_7), 4.71 (dt, J_d = 12.6 Hz, J_t = 7.1 Hz, 1.4 H, vinyl proton at C_2 or C_6), 4.33 (dt, J_d = 7.2 Hz, J_t = 6.4 Hz, 0.6 H, vinyl proton at C_2 or C_6), 3.58, 3.50 (two s, 6 H, methoxy protons), 2.06 (dtd, J_d = 1.4 Hz, J_t = 6.4 Hz, J_d = 7.5 Hz, 1.3 H, C_3 or C_5 protons), 1.93 (app q, J = 7.4 Hz, 2.7 H, C_3 or C_5 protons), 1.38 (p, J = 7.4 Hz, 2 H, C_4 protons); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.3, 146.4, 106.7, 102.9, 102.8, 59.3, 55.7, 31.5, 30.7, 27.0, 26.7, 23.3, 23.0; IR (neat/NaCl) 3056, 3034, 2999, 2928, 2854, 1657, 1457, 1260, 1210, 1132, 1111, 933 cm^{-1}; GCMS (EI) m/e (rel intensity) 156 (M^+, 0.8), 124 ($M^+ - CH_3OH$, 7), 123 (5), 109 (14), 97 (30), 85 (18), 81 (14), 79 (14), 75 (100), 71 (92), 69 (18), 67 (23), 56 (15), 55 (59), 53 (21); HRMS (EI) m/e calcd for $C_9H_{15}O_2$ ($M^+ - H$) 155.1072, found 155.1081. Anal. Calcd for $C_9H_{16}O_2$: C, 69.23; H, 10.26. Found: C, 69.28; H, 10.42.

1,2-Bis(dimethoxymethyl)cyclopentane (6b). The electrolysis of compound **3b** was done in a fashion identical to the above procedure for compound **6a**. In this experiment, 0.141 g (0.90 mmol) of the bis enol ether **3b** was electrolyzed at a constant current of 10 mA until 175 C (2.0 faradays) of charge had been passed. The reaction led to the formation of 0.317 g (70%) of the desired cyclized products containing a small amount of the aldehyde due to the hydrolysis of the acetals. The spectral data for the 1.3:1 mixture of diastereomers (cis and trans about the five-membered ring) were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.39 (d, J = 6.5 Hz, 0.86 H, acetal proton), 4.20 (d, J = 7.0 Hz, 1.14 H, acetal proton), 3.362, 3.358, 3.35, 3.34 (four s, 12 H, methoxy protons), 2.29 (m, 1 H), 2.14 (m, 1 H), 1.70–1.50 (m, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 108.4, 105.9, 54.7, 54.3, 54.1, 53.0, 43.8, 43.2, 27.5, 26.8, 25.3, 23.2; IR (neat/NaCl) 2972, 2965, 1449, 1368, 1190, 1060, 968 cm^{-1}; GCMS (PCI) m/e (rel intensity) 218 (M^+, 0.4), 217 ($M^+ - H$, 3), 188 (10), 187 ($M^+ - OCH_3$, 84), 185 (9), 156 (24), 155 (100), 154 (9), 153 (14), 141 (14), 125 (9), 123 (17), 75 ($(CH_3O)_2CH^+$, 52), 55 (14); HRMS (EI) m/e calcd for $C_{11}H_{21}O_4$ ($M^+ - H$) 217.1440, found 217.1451.

1,8-Dimethoxy-(*E*,*Z*)-1,7-octadiene (3c). To a stirred solution of 20.57 g (60.0 mmol) of (methoxymethyl)triphenylphosphonium chloride in 100 mL of tetrahydrofuran at 0 °C was added dropwise 35.3 mL (60.0 mmol) of a 1.7 M *tert*-butyllithium in hexane solution. The resulting dark red solution was allowed to stir for 1 h. In a separate reaction flask, a −50 °C solution of 1.182 g (10.0 mmol) of 1,6-hexanediol, 25 mL of dimethyl sulfoxide, and 67 mL of dichloromethane was treated with 2.62 mL (30.0 mmol) of oxalyl chloride. The Swern oxidation was done using an excess amount of DMSO to prevent the 1,6-diol from precipitating out of the solution. The resulting mixture was stirred for 30 min and then quenched with 8.36 mL (60.0 mmol) of triethylamine. The reaction mixture was allowed to warm to room temperature and then diluted with 100 mL of ether. The reaction was suction-filtered from the ammonium salts and the filtrate then filtered a second time into an additional funnel. The crude Swern product was then added dropwise (over 15 min) to the 0 °C solution of the ylide generated above. The resulting mixture was allowed to warm to room temperature. After 16 h, the reaction was worked up with water and ether. The bis enol ether product was separated in a fashion similar to the one described for compound **3a**. The reaction afforded 1.306 g (77%) of the desired enol ether **3c**. The spectral data for the 1.5:1 mixture of the trans and cis isomers were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.28 (dd, J = 12.6, 1.1 Hz, 1.2 H, vinyl proton at C_1 or C_8), 5.87 (dm, J_d = 6.3 Hz, 0.8 H, vinyl proton at C_1 or C_8), 4.72 (dt, J_d = 12.6 Hz, J_t = 7.1 Hz, 1.2 H, vinyl proton at C_2 or C_7), 4.33 (dq, J_d = 7.5 Hz, J_q = 1.6 Hz, 0.8 H, vinyl proton at C_2 or C_7), 3.57, 3.50 (two s, 6 H, methoxy protons), 2.15–2.05 (m, 1.6 H), 1.97–1.87 (m, 2.4 H), 1.40–1.29 (m, 4 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.2, 147.1, 146.2, 146.1, 107.1, 106.9, 103.1, 103.0, 59.3, 55.6, 30.1, 29.9, 29.2, 28.9, 27.3, 23.4; IR (neat/NaCl) 3063, 3031, 2988, 2928, 2853, 2830, 1664, 1654, 1464, 1457, 1437, 1391, 1261, 1208, 1179, 1132, 1110, 934 cm^{-1}; GCMS (PCI) m/e (rel intensity) 171 (M^+ + H, 10), 170 (M^+, 4), 139 ($M^+ - OCH_3$, 46), 137 (25), 111 (17), 109 (14), 107 (59), 97 (14), 79 (18), 75 ($(CH_3O)_2CH^+$, 100), 71 (92), 57 (26), 55 (53); HRMS (EI) m/e calcd for $C_{10}H_{18}O_2$ 170.1307, found 170.1303.

1,2-Bis(dimethoxymethyl)cyclohexane (6c). The electrolysis of bis enol ether **3c** was performed in a fashion identical to the above procedure for compound **6a**. In this experiment, 0.106 g (0.62 mmol) of compound **3c** was electrolyzed at a constant current of 10 mA until 130 C (2.1 faradays) of charge had been passed and only a small amount of the starting material remained by TLC. The reaction afforded 0.906 g (65%) of the desired six-membered-ring products. The mixture of bis acetal products was contaminated with a small amount of the carboxaldehyde due to the hydrolysis of the dimethoxy acetals. The spectral data for the 1:1 mixture of diastereoisomers (cis and trans about the six-membered ring) were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.51 (d, J = 8.1 Hz, 1 H, acetal proton), 4.38 (d, J = 3.6 Hz, 1 H, acetal proton), 3.39, 3.34, 3.31 (three s, 12 H, methoxy protons), 1.95 (m, 1 H), 1.78–1.10 (m, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 107.3, 104.7, 55.2, 54.9, 53.3, 52.0, 39.3, 29.5, 25.1, 24.7, 24.4, 23.7; IR (neat/NaCl) 2924, 2854, 2829, 1465, 1451, 1382, 1369, 1187, 1152, 1135, 1112, 1082, 1069, 966 cm^{-1}; GCMS (PCI) m/e (rel intensity) 201 ($M^+ - OCH_3$, 51), 200 (2), 199 (7), 170 (20), 169 ($M^+ - OCH_3 - HOCH_3$, 100), 168 (5), 167 (15), 137 (3), 76 (10), 75 ($(CH_3O)_2CH^+$, 82), 57 (3); HRMS (EI) m/e calcd for $C_{11}H_{21}O_3$ ($M^+ - OCH_3$) 201.1491, found 201.1505. The reaction was also run on a 4-mmol (678 mg) scale using the same conditions. This experiment afforded a 56% (520 mg) isolated yield of **6c**.

1,9-Dimethoxy-(*E*,*Z*)-1,8-nonadiene (3d). This compound was prepared in a fashion identical to the one described above for compound **3c**. In this example, the tandem Swern–Wittig procedure led to the formation of a 61% isolated yield of compound **3d**. The spectral data for the mixture of olefin isomers were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.29 (dq, J_d = 12.6 Hz, J_q = 1.2 Hz, 1.3 H, vinyl proton at C_1 or C_9), 5.86 (dq, J_d = 6.4 Hz, J_q = 1.6 Hz, 0.7 H, vinyl proton at C_1 or C_9), 4.72 (td, J_t = 12.6 Hz, J_d = 3.1 Hz, 1.3 H, vinyl proton at C_2 or C_8), 4.33 (q, J = 7.4 Hz, 0.7 H, vinyl proton at C_2 or C_8), 3.58, 3.57, 3.50 (three s, 6 H, methoxy protons), 2.09–2.00 (m, 1.6 H), 1.95–1.85 (m, 2.4 H), 1.39–1.22 (m, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.1, 146.2, 146.1, 107.2, 107.1, 103.2, 103.1, 59.3, 55.6, 30.4, 29.4, 28.7, 28.4, 28.1, 27.4, 23.6; IR (neat/NaCl) 3046, 3012, 2998, 2880, 2836, 1671, 1667, 1664, 1660, 1658, 1652, 1463, 1455, 1391, 1209, 1177, 1159, 1132, 1111, 933 cm^{-1}; GCMS (PCI) m/e (rel intensity) 185 (M^+ + H, 31), 153 ($M^+ - OCH_3$, 40), 151 (32), 123 (24), 121 (100), 109 (19), 95 (34), 93 (20), 81 (28), 75 (56), 71 (88), 61 (21); HRMS (EI) m/e calcd for $C_{11}H_{20}O_2$ 184.1464, found 184.1428. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.69; H, 11.04.

1,2-Bis(dimethoxymethyl)cycloheptane (6d). The electrolysis of compound **3d** was done using a procedure similar to the one used for the synthesis of **6a**. In this example, 0.132 g (0.72 mmol) of the bis enol ether **3d** was electrolyzed at a constant current of 12 mA. Although some starting material remained by TLC after 276 C (4.0 faradays) had been passed, the reaction was stopped and worked up. The reaction led to the formation of 0.090 g (51%) of the desired cyclized products, which were contaminated with a small amount of the carboxaldehyde products due to the hydrolysis of the acetals. The starting material was recovered (14%), and a small amount (ca. 5%) of the uncyclized unsaturated acetal product (compound **7** in the text) was observed in the proton NMR spectrum of the crude material. The uncyclized product was not isolated after the chromatography. The spectral data for the 1:1 mixture of diastereoisomers (cis and trans about the seven-membered ring) were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.45 (d, J = 8.4 Hz, 1 H, acetal proton), 4.33 (d, J = 5.5 Hz, 1 H, acetal proton), 3.39, 3.37, 3.34, 3.32 (four s, 12 H, methoxy protons), 2.16–2.10 (m, 1 H), 1.92–1.84 (m, 1 H), 1.78–1.35 (m, 10 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 109.1, 108.9, 106.2, 53.5, 52.2, 51.8, 41.0, 39.9, 33.5, 30.7, 29.1, 27.0, 26.9, 26.3, 25.8, 24.2; IR (neat/NaCl) 2980, 2925, 2857, 1462, 1453, 1446, 1380, 1370, 1212, 1191, 1148, 1119, 1112, 1074, 972 cm^{-1}; GCMS (PCI) m/e (rel intensity) 246 (M^+, 2), 245 ($M^+ - H$, 11), 215 ($M^+ - OCH_3$, 38), 213 (39), 184 (90), 183 ($M^+ - OCH_3 - HOCH_3$, 100), 182 (67), 181 (92), 155 (46), 152 (35), 151 (82), 137 (64), 75 ($(CH_3O)_2CH^+$, 94), 61 (36); HRMS (EI) m/e calcd for $C_{12}H_{23}O_3$ ($M^+ - OCH_3$) 215.1647, found 215.1669.

1,7-Bis[(*tert*-butyldimethylsilyl)oxy]-1,6-heptadiene (9a). To a solution of 2.508 g (19.0 mmol) of 1,7-heptanediol in 130 mL of dichloromethane and 50 mL of dimethyl sulfoxide at −60 °C was slowly added

5.2 mL (60.0 mmol) of $(COCl)_2$. The reaction was allowed to stir at −60 °C for 30 min, after which 15.9 mL (114 mmol) of triethylamine was added. After 10 min, the reaction was allowed to warm to room temperature. The triethylamine hydrochloride salts that precipitated out of the crude reaction mixture were removed by vacuum filtration, and the residue was washed with ether (2 × 50 mL). The filtrate was then washed with a saturated brine solution (2 × 100 mL), dried over $MgSO_4$, and concentrated in vacuo. Upon concentration, more ammonium salts precipitated out. The salts were again removed by filtration, and the residue was washed with ether. The filtrate was concentrated in vacuo. Due to the instability of the 1,7-dialdehyde, the crude Swern product was taken to the next step for the formation of the bis silyl enol ether. The crude product was diluted with 40 mL of benzene and 7.9 mL (57.0 mmol) of triethylamine. The resulting mixture was cooled down to 0 °C and 10.5 mL (45.6 mmol) of *tert*-butyldimethylsilyl triflate added. The reaction was allowed to warm to room temperature and stirred for 1 h. The reaction was worked up with a saturated brine solution and ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed with 1% triethylamine/pentane. Gradient elution from pure pentane to 5% ether/pentane afforded 2.701 g (40%) of the desired bis silyl enol ether **9a**, which was mainly the cis isomer. The spectral data for the cis olefin were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.15 (d, J = 5.7 Hz, 2 H, vinyl protons on C_1 and C_7), 4.45 (dt, J_d = 5.7 Hz, J_t = 7.2 Hz, 2 H, vinyl protons on C_2 and C_6), 2.08 (dt, J_d = 6.6 Hz, J_t = 7.2 Hz, 4 H, C_3 and C_5 methylene protons), 1.36 (p, J = 7.5 Hz, 2 H, C_4 methylene protons), 0.91 (s, 18 H, *tert*-butyl protons), 0.098 (s, 12 H, methyl protons); ^{13}C NMR ($CDCl_3$/75 MHz) δ 138.6, 110.9, 29.6, 26.3, 23.2, 18.1, −5.6; IR (neat/NaCl) 3032, 2957, 2932, 2858, 1656, 1473, 1464, 1400, 1362, 1255, 1189, 1177, 1159, 1118, 1085, 1062, 1036, 1019, 1004, 980, 834, 780 cm^{-1}; GCMS (PCI) *m/e* (rel intensity) 357 (M^+ + 1, 2), 299 (M^+ − *tert*-butyl group, 17), 275 (14), 225 (66), 209 (16), 173 (15), 171 (18), 147 (19), 115 (23), 93 (24), 89 (100), 75 (17), 73 (94); HRMS (EI) *m/e* calcd for $C_{19}H_{40}O_2Si_2$ 356.2566, found 356.2559. Anal. Calcd for $C_{19}H_{40}O_2Si_2$: C, 64.04; H, 11.24; Si, 15.73. Found: C, 64.24; H, 11.57; Si, 15.75.

1,3-Dimethoxyhexahydro-1*H*-cyclopenta[*c*]furan (11a) and 1,2-Bis(dimethoxymethyl)cyclopentane (12a). A solution of 0.454 g (1.3 mmol) of compound **9a** in 100 mL of methanol/tetrahydrofuran (35:65) was placed in a 250-mL, three-neck, round-bottom flask equipped with a reticulated vitreous carbon anode (suspended from a sharpened carbon rod), a carbon rod cathode, and a nitrogen inlet. To this solution were added 6 g (20 mmol) of tetraethylammonium tosylate and 0.456 mL (6.4 mmol) of 2,6-lutidine. The resulting mixture was degassed by bubbling nitrogen through the solution and then electrolyzed with a constant current of 15 mA. The reaction was monitored by TLC and stopped after 4.6 faradays of electricity had been passed. The crude reaction mixture was then treated with 33 mL of a 0.4 N sulfuric acid in tetrahydrofuran solution and was allowed to stir for 1 h. The reaction was concentrated in vacuo and chromatographed through silica gel that was slurry-packed with 3% triethylamine in 10% ether/pentane. Elution with 10% ether/pentane afforded two major products: 0.094 g (43%) of the bicyclic acetal **11a** and 0.072 g (30.7%) of the dimethoxy acetal **12a**. The spectral data for the impure compound **11a** were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.79 (s, 2 H, cyclic acetal protons), 3.42 (s, 6 H, methoxy protons), 2.78–2.68 (m, 2 H), 1.90–1.72 (m, 2 H), 1.60–1.45 (m, 2 H) (in addition, the ^{1}H NMR showed a second methoxy peak at 3.52 ppm that integrated for ca. one-tenth the area of the methoxy signal for **11a**); ^{13}C NMR ($CDCl_3$/75 MHz) δ 113.7, 55.1, 49.6, 31.2, 25.9; IR (neat/NaCl) 2954, 2910, 2894, 2871, 2831, 1471, 1448, 1376, 1363, 1268, 1252, 1200, 1102, 1065, 1007, 986 cm^{-1}; GCMS (PCI) *m/e* (rel intensity) 171 (M^+ − H, 2), 142 (9), 141 (M^+ − OCH_3, 100), 140 (5), 139 (4), 125 (3), 113 (9), 112 (8), 111 (11), 109 (16), 107 (3), 81 (34), 79 (6); HRMS (EI) *m/e* calcd for $C_9H_{15}O_3$ (M^+ − H) 171.1021, found 171.1009. The spectral data for compound **12a** were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.21 (d, J = 5.8 Hz, 2 H, acetal proton), 3.57 (s, 12 H, methoxy protons), 2.18–2.08 (m, 2 H), 1.72–1.48 (m, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 108.1, 54.3, 54.0, 43.5, 27.1, 25.0.

1,7a-Bis(dimethoxymethyl)-1-methyloctahydro-1*H*-indene (9b). To a solution of 2.19 g (15.0 mmol) of 1,8-octanediol in 150 mL of dichloromethane and 50 mL of dimethyl sulfoxide at −45 °C was slowly added 3.93 mL (45.0 mmol) of oxalyl chloride. The reaction mixture was allowed to stir for 30 min at −45 °C, and 12.5 mL (90.0 mmol) of triethylamine was then added. After 15 min, the reaction was allowed to warm to room temperature. The triethylamine hydrochloride salts that fell out of solution were filtered under suction, and the residue was washed with ether. The filtrate was then washed with saturated brine solution, dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed with 1% triethylamine in ether. Elution with ether gave 1.8 g (85%) of the dialdehyde:[19] ^{1}H NMR ($CDCl_3$/300 MHz) δ 9.78 (t, J = 2.0 Hz, 2 H, CHO), 2.46 (dt, J_d = 2.1 Hz, J_t = 7.3 Hz, 4 H, methylene protons at C_2 and C_7), 1.72–1.60 (m, 4 H), 1.45–1.32 (m, 4 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 202.9, 43.4, 28.5, 21.4.

To a 0 °C solution of 0.284 g (2.0 mmol) of the 1,8-octanedial in 4 mL of benzene were added 0.84 mL of triethylamine and 1.15 mL (4.4 mmol) of *tert*-butyldimethylsilyl triflate. The reaction was allowed to warm up to room temperature and stirred for 1 h. The reaction was worked up with a saturated brine solution and ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed with 1% triethylamine/pentane. Elution with 5% ether/pentane afforded 0.745 g (82%) of the desired enol ether **9b**, which was mainly the cis isomer. The spectral data for the cis olefin were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.14 (d, J = 6.0 Hz, 2 H, vinyl proton at C_1 and C_8), 4.43 (q, J = 6.0 Hz, 2 H, vinyl protons on C_2 and C_7), 2.11–2.00 (m, 4 H, C_3 and C_6 methylene protons), 1.40–1.26 (m, 4 H, C_4 and C_5 methylene protons), 0.92 (s, 18 H, *tert*-butyl protons), 0.09 (s, 12 H, methyl protons); ^{13}C NMR ($CDCl_3$/75 MHz) δ 138.5, 111.0, 29.3, 25.5, 23.3, 18.1, −5.7; IR (neat/NaCl) 3031, 2960, 2858, 1657, 1472, 1463, 1400, 1363, 1257, 1166, 1103, 1073, 1006, 838 cm^{-1}; GCMS (PCI) *m/e* (rel intensity) 371 (M^+ + 1, 20), 355 (M^+ − CH_3, 30), 314 (18), 313 (M^+ − *tert*-butyl, 63), 240 (21), 239 (M^+ − (*tert*-butyldimethylsilyl)oxy, 100), 211 (50), 115 (*tert*-butyldimethylsilyl$^+$, 21), 107 (16), 89 (37), 75 (14), 73 (83); HRMS (EI) *m/e* calcd for $C_{19}H_{39}O_2Si_2$ (M^+ − CH_3) 355.2488, found 355.2460. Anal. Calcd for $C_{20}H_{42}O_2Si_2$: C, 64.86; H, 11.35; Si, 15.14. Found: C, 64.82; H, 11.52; Si, 15.05.

1,3-Dimethoxyoctahydroisobenzofuran (11b) and 1,2-Bis(dimethoxymethyl)cyclohexane (12b). The conditions used for the electrolysis of compound **9b** were similar to those used for the electrolysis of compound **9a**. In this example, 0.31 g (0.84 mmol) of compound **9b** that was 0.01 M in $LiClO_4$ in 100 mL of methanol/tetrahydrofuran (35:65) was electrolyzed at a constant current of 13 mA. The reaction was monitored by TLC. After 2 faradays of electricity had been passed, the reaction was disconnected from the electrochemical apparatus and 30 mL of 0.4 N H_2SO_4 in tetrahydrofuran added. After 30 min, the reaction was worked up with water and ether. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed using 1% triethylamine/20% ether/pentane. Gradient elution from 20% ether/pentane to 50% ether/pentane afforded 0.086 g (55%) of the bicyclic acetal **11b** and 0.006 g (3%) of the dimethoxy acetal **12b**. The spectral data for **11b** were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.01 (d, J = 5.5 Hz, 0.5 H, acetal proton), 4.79 (d, J = 2 Hz, 0.5 H, acetal proton), 4.78 (d, J = 4 Hz, 1 H, acetal proton), 3.42, 3.38 (two s, 6 H, methoxy protons), 2.39–2.28 (m, 1 H), 2.07–1.96 (m, 1 H), 1.85–1.72 (m, 3 H), 1.70–1.48 (m, 2 H), 1.37–1.20 (m, 3 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 109.0, 108.6, 105.5, 56.2, 55.3, 55.2, 44.7, 43.2, 38.3, 25.5, 25.0, 24.9, 23.4, 22.9, 22.0; IR (neat/NaCl) 2929, 2857, 1448, 1239, 1192, 1182, 1145, 1128, 1106, 1067, 1053, 995, 972, 906 cm^{-1}; GCMS (PCI) *m/e* (rel intensity) 185 (M^+ − H, 2), 156 (10), 155 (M^+ − OCH_3, 100), 154 (7), 153 (4), 127 (14), 126 (16), 125 (24), 123 (25), 96 (4), 95 (53), 94 (7), 93 (12); HRMS (EI) *m/e* calcd for $C_{10}H_{17}O_3$ (M^+ − H), 185.1178, found 185.1171. The spectral data for the compound **12b** were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.45 (d, J = 8.0 Hz, 1.3 H, acetal proton), 4.32 (d, J = 4.3 Hz, 0.7 H, acetal proton), 3.34, 3.32, 3.28, 3.25 (four s, 12 H, methoxy protons), 1.98 (m, 1 H), 1.75–1.12 (m, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 107.3, 104.6, 55.2, 55.0, 53.3, 52.2, 39.0, 29.5, 25.1, 24.6, 24.5, 23.6.

2-[2-(1,3-Dioxolan-2-yl)ethyl]cyclohexanone (13a). To a −74 °C solution of 1.44 mL (11.0 mmol) of diisopropylamine in 30 mL of THF was added 4 mL (10 mmol) of a 2.5 M *n*-butyllithium in hexane solution. When the addition was complete, the solution was warmed to 0 °C and allowed to stir for 30 min, after which it was cooled back down to −74 °C, and 1.04 mL (10.0 mmol) of cyclohexane diluted to 10 mL with THF was transferred into the reaction flask using a syringe pump over a period of 10 min. The solution was allowed to stir at −74 °C for another 15 min before 6.837 g (30.0 mmol) of 2-(2-iodoethyl)-1,3-dioxolane[20] was added neat. The reaction was allowed to warm to room temperature. After 24 h, the reaction was quenched by adding 50 mL of water. The organic layer was separated and washed with water (2 × 50 mL). The combined aqueous layers were washed with ether, and all

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of the organic layers were combined, dried over $MgSO_4$, and concentrated in vacuo. The crude product was chromatographed through silica gel using a 30% ether/hexane eluent to afford 0.87 g (54%) of the desired product. The spectral data for the alkylated cyclohexanone **13a** were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 4.85 (t, J = 4.7 Hz, 1 H, acetal H on dioxolane), 3.99–3.82 (m, 4 H, OCH_2CH_2O), 2.43–2.24 (m, 3 H), 2.18–1.95 (m, 2 H), 1.92–1.80 (m, 2 H), 1.76–1.57 (m, 4 H), 1.46–1.24 (m, 2 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 213.5, 104.6, 64.7, 50.2, 41.9, 33.8, 31.1, 27.8, 24.7, 23.5; IR (neat/NaCl) 2936, 2862, 2769, 1709, 1449, 1432, 1411, 1226, 1144, 1131, 1116, 1079, 1053, 1036, 992, 974, 911 cm^{-1}; GCMS (PCI) m/e (rel intensity) 198 (M^+, 0.3), 136 (3), 99 (14), 86 (5), 74 (19), 73 (100), 67 (5), 58 (3), 57 (10), 56 (6), 55 (29), 54 (5), 53 (6); HRMS (EI) m/e calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.1272. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.57; H, 9.12.

2-(3-Oxopropyl)cyclohexanone. To a solution of 3.15 g (15.9 mmol) of compound **13a** in 150 mL of MeOH was added 0.75 g (4.0 mmol) of toluenesulfonic acid monohydrate. After 36 h, the reaction was worked up with a saturated brine solution and ether. The organic layer was separated, and the aqueous layer was washed with ether. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The crude product was then treated with 150 mL of acetone, 10 mL of water, and 0.75 g (3.0 mmol) of pyridinium *p*-toluenesulfonate and was allowed to stir for 40 h. The reaction was worked up with a saturated brine solution and ether. The aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel using a gradient elution from 20% ether/pentane to 50% ether/pentane to give 1.852 g (76%) of the deprotected product. The spectral data for the deprotected acetal were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 9.77 (t, J = 1.5 Hz, 1 H, CHO), 2.63–2.46 (m, 2 H), 2.44–2.24 (m, 3 H), 2.16–1.96 (m, 3 H), 1.94–1.80 (m, 1 H), 1.78–1.50 (m, 3 H), 1.48–1.33 (m, 1 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 213.1, 202.8, 49.6, 42.0, 41.6, 34.2, 27.8, 24.9, 21.8; IR (neat/NaCl) 2934, 2861, 2722, 1711, 1449, 1431, 1412, 1391, 1375, 1312, 1227, 1132, 1054, 917, 733 cm^{-1}; GCMS (EI) m/e (rel intensity) 154 (M^+, 3), 98 (100), 97 (24), 83 (56), 82 (20), 79 (19), 70 (33), 69 (18), 68 (15), 67 (49), 57 (18), 55 (94), 54 (29); HRMS (EI) m/e calcd for $C_9H_{14}O_2$ 154.0994, found 154.1004. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.95; H, 9.27.

1-(Methoxy-(*E*,*Z*)-methylidene)-2-(4-methoxy-3-(*E*,*Z*)-butenyl)cyclohexane (14a). To a 0 °C solution of 3.74 g (10.9 mmol) of (methoxymethyl)triphenylphosphonium chloride in 20 mL of tetrahydrofuran was added 4.36 mL (10.9 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The reaction was stirred for 30 min, and then a solution of 0.42 g (2.7 mmol) of the aldehyde–ketone made above in 5 mL of tetrahydrofuran was added over a period of 30 min. The reaction was allowed to warm to room temperature and stirred for 18 h. The reaction was worked up with ether and water. The layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The bis enol ether product was isolated in a fashion similar to the one described for compound **3a**. The reaction afforded 0.192 g (35%) of the desired bis enol ether **14a**. The spectral data for the mixture of cis and trans isomers were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.30 (dd, J = 12.6, 3.2 Hz, 0.5 H, vinyl proton at C_4 of the butenyl substituent), 5.87 (tt, J = 5.9, 1.5 Hz, 0.5 H, vinyl proton on C_1 of the methylidene), 5.78 (t, J = 2.1 Hz, 0.5 H, vinyl proton on C_1 of the methylidene), 5.73 (d, J = 4.9 Hz, 0.5 H, vinyl proton at C_4 of the butenyl substituent), 4.84–4.68 (m, 0.5 H, vinyl proton on C_3 of the butenyl substituent), 4.43–4.40 (m, 0.5 H, vinyl proton at C_3 of the butenyl substituent), 3.58, 3.55, 3.54, 3.51, 3.50 (five s, 6 H, methoxy protons), 2.9–2.8 (m, 0.5 H, 2.25–1.15 (m, 12.5 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.2, 147.0, 146.2, 145.9, 139.9, 139.8, 139.3, 120.9, 120.6, 120.4, 107.5, 107.1, 103.6, 103.3, 38.5, 38.0, 33.3, 33.2, 32.7, 32.5, 32.4, 32.2, 31.7, 31.3, 30.9, 28.3, 27.2, 26.4, 25.5, 23.2, 23.1, 22.8, 22.7, 21.7, 21.4; IR (neat/NaCl) 3063, 3027, 2996, 2941, 2853, 1666, 1657, 1460, 1390, 1378, 1263, 1251, 1233, 1209, 1129, 1112, 933 cm^{-1}; GCMS (PCI) m/e (rel intensity) 211 (M^+ + 1, 31), 210 (M^+, 16), 180 (15), 179 ($M^+ - OCH_3$, 41), 178 (14), 177 (22), 149 (20), 148 ($M^+ - 2OCH_3$, 40), 147 (100), 146 (13), 125 (21), 75 (48); HRMS (EI) m/e calcd for $C_{13}H_{22}O_2$ 210.1620, found 210.1658. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.29; H, 10.48. Found: C, 74.46; H, 10.70.

1,7a-Bis(dimethoxymethyl)octahydro-1*H*-indene (15a). The electrolysis of compound **14a** was done in a fashion similar to the procedure used for compound **6a**. In this experiment, 0.226 g (1.1 mmol) of the bis enol ether **14a** was electrolyzed using a platinum foil anode and a carbon rod cathode at a constant current of 11 mA until 2.3 faradays of electricity had been passed and only a small amount of the starting material was visible by TLC. The reaction led to the formation of 0.16 g (65%) of the fused-ring products contaminated with a small amount of the carboxaldehyde due to the hydrolysis of the acetals. Two diastereoisomers (cis and trans about the five-membered ring) were isolated in a 2:1 ratio. The stereochemistry of the product was determined after the dimethoxymethyl acetal attached to C_1 was hydrolyzed to the aldehyde. The minor isomer was found to be the α isomer, which showed a 2% NOE enhancement of the C_1 methine proton when the acetal proton of the dimethoxymethyl substituent at C_{7a} was irradiated. The major isomer showed a 1% NOE enhancement of the aldehyde proton when the same proton (as above) was irradiated. Both diastereoisomers were found to be cis-fused from the experiment since, in both isomers, the methine proton at C_{3a} was enhanced by 2% when the acetal proton of the C_{7a} substituent was irradiated. The spectral data for the two diastereoisomers (cis and trans about the five-membered ring) were as follows: ^1H NMR ($CDCl_3$/300 MHz) α isomer δ 4.43 (d, J = 7.02 Hz, 1 H, acetal H of C attached to C_1), 4.08 (s, 1 H, acetal H of C attached to C_{7a}), 3.52, 3.50, 3.32 (three s, 12 H, methoxy protons), 2.38–2.26 (m, 1 H), 2.08–1.94 (m, 1 H), 1.84–1.02 (m, 12 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 112.5, 106.5, 59.0, 54.3, 53.1, 48.9, 46.7, 38.4, 26.4, 25.8, 24.7, 22.7, 22.1, 20.2; IR (neat/NaCl) 2933, 2925, 2873, 2860, 2829, 1463, 1450, 1372, 1189, 1139, 1099, 1075, 976 cm^{-1}; β isomer ^1H NMR ($CDCl_3$/300 MHz) δ 4.44 (d, J = 5.6 Hz, 1 H, acetal H of C attached to C_1), 4.43 (s, 1 H, acetal H of C attached to C_{7a}), 3.55, 3.53, 3.32, 3.317 (four s, 12 H, methoxy protons), 2.45–2.36 (m, 1 H), 2.24–2.12 (m, 1 H), 1.72–1.53 (m, 6 H), 1.53–1.30 (m, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 111.9, 106.9, 59.0, 58.6, 54.0, 52.5, 51.9, 43.4, 40.3, 30.0, 29.4, 26.7, 24.4, 24.3, 21.3; IR (neat/NaCl) 2931, 2873, 2860, 2828, 1457, 1447, 1189, 1121, 1102, 1069; GCMS (PCI) m/e (rel intensity for the α and β isomers) 272 (M^+, 0.4), 241 (3), 240 (3), 239 (9), 211 (4), 210 (32), 209 (100), 208 (10), 207 (15), 178 (3), 177 (11), 76 (7), 75 (50); HRMS (EI) m/e calcd for $C_{15}H_{27}O_4$ (M^+ - 1) 271.1909, found 271.1892.

2-[2-(2-Methyl-1,3-dioxolan-2-yl)ethyl]cyclohexanone (13b). To a solution of 4.84 g (20.0 mmol) of 2-(2-iodoethyl)-2-methyl-1,3-dioxolane[20] in 10 mL of toluene was added 1.6 mL (10.0 mmol) of 1-pyrrolidino-1-cyclohexene, and the resulting solution was refluxed for 18 h. The reaction was worked up with a saturated brine solution and ether. The layers were separated, and the aqueous layer was extracted with ether (2 × 20 mL). The organic layers were combined and concentrated under vacuo. The crude product was chromatographed through silica gel using a gradient elution from 10% ether/pentane to 50% ether/pentane to afford 0.662 g (31%) of the desired alkylated product **13b**. Spectral data for compound **13b**: ^1H NMR ($CDCl_3$/300 MHz) δ 3.94 (m, 4 H, methylene protons on the dioxolane), 2.43–2.24 (m, 3 H), 2.17–1.98 (m, 2 H), 1.96–1.80 (m, 2 H), 1.78–1.53 (m, 4 H), 1.65–1.20 (m, with an s at 1.32 (methyl protons), 5 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 214.0, 110.4, 64.9, 50.9, 42.2, 36.6, 34.2, 28.2, 25.0, 24.0, 23.8; IR (neat/NaCl) 2980, 2920, 1710, 1449, 1431, 1377, 1312, 1252, 1223, 1150, 1127, 1077, 1065, 1051, 948 861 cm^{-1}; GCMS (PCI) m/e (rel intensity) 212 (M^+, 2), 211 (M^+ - H, 8), 195 (78), 177 (53), 152 (22), 151 (100), 150 (19), 149 (41), 139 (38), 133 (21), 115 (38), 111 (28), 99 (60), 95 (78), 87 (50); HRMS (EI) m/e calcd for $C_{12}H_{20}O_3$ 212.1412, found 212.1424. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43. Found: C, 68.15; H, 9.63.

2-(3-Oxobutyl)cyclohexanone. A solution of 1.06 g (5.0 mmol) of **13b** in 5 mL of water and 20 mL of glacial acetic acid was warmed to 65 °C and allowed to stir for 15 min. The reaction was then cooled down to room temperature and slowly added to 375 mL of a cold, saturated sodium bicarbonate solution contained in a 1-L beaker to prevent loss of product due to foaming and evolution of CO_2. The neutralized reaction was then transferred to a separatory funnel and the diketone was extracted with ether (5 × 150 mL). The combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry-packed with 2% triethylamine in ether. Elution with ether afforded 0.806 g (96%) of the desired diketone. The spectral data for the diketone matched the literature[21] and were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 2.64–2.18 (m, 5 H), 2.14 (s, 3 H), 2.10–1.80 (m, 5 H), 1.76–1.34 (m, 3 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 213.9, 209.7, 50.0, 42.3, 41.5, 34.5, 30.0, 28.2, 25.1, 23.8; GCMS (PCI) m/e (rel intensity) 169 (M^+ + 1, 32), 168 (M^+, 4), 152 (12), 151 (100), 150 (6), 139 (9), 133 (12), 123 (9), 111 (68), 99 (43), 71 (17), 55 (6); HRMS (EI) m/e calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1141.

1-(Methoxy-(*E*,*Z*)-methylidene)-2-(3-methyl-4-methoxy-3-(*E*,*Z*)-butenyl)cyclohexane (14b). This compound was prepared in a fashion identical to the procedure used above for compound **14a**. In this experiment, 0.84 g (5.0 mmol) of 2-(3-oxobutyl)-1-cyclohexanone was treated under Wittig conditions for 20 h. After workup, precipitation of the triphenylphosphine oxide byproduct and chromatography through silica gel led to the formation of 0.659 g (59%) of the desired bis enol ether. The spectral data for compound **14b** were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 5.79, 5.76, 5.75, 5.73 (four s, 2 H, vinyl protons), 3.55, 3.52, 3.51, 3.50 (four s, 6 H, methoxy protons), 2.85–2.76 (m, 0.5

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H), 2.28-1.28 (m, 12.5 H), 1.60, 1.52 (two s, 3 H, methyl); ^{13}C NMR ($CDCl_3$/75 MHz) δ 141.8, 141.5, 139.9, 139.7, 120.9, 120.6, 115.3, 114.6, 59.1, 38.8, 32.9, 32.6, 31.8, 31.2, 30.8, 29.9, 28.9, 28.4, 26.9, 26.8, 26.4, 23.4, 21.4, 17.1, 12.7; IR (neat/NaCl) 3002, 2931, 2854, 1682, 1456, 1447, 1380, 1234, 1209, 1173, 1136, 1092, 991 cm^{-1}; GCMS (PCI) *m/e* (rel intensity) 224 (M^+, 1), 162 (7), 161 (25), 125 (9), 121 (6), 105 (6), 93 (6), 85 (22), 81 (4), 76 (14), 75 (100), 73 (4), 59 (28); HRMS (EI) *m/e* calcd for $C_{14}H_{24}O_2$ 224.1776, found 224.1751. Anal. Calcd for $C_{14}H_{24}O_2$: C, 75.00; H, 10.78. Found: C, 75.37; H, 11.04.

1,7a-Bis(dimethoxymethyl)-1-methyloctahydro-1*H*-indene (15b). A 50-mL, three-neck, round-bottom flask equipped with a platinum gauze anode, carbon rod cathode, and a nitrogen inlet was charged with a solution of 0.198 g (0.88 mmol) of bis enol ether **14b** in 35 mL of a 2:8 mixture of methanol/dichloromethane. To this solution was added 1.862 g of lithium perchlorate and 0.316 mL (4.4 mmol) of 2,6-lutidine. The reaction was degassed by passing a stream of nitrogen through the solution and electrolyzed at a constant current of 13 mA until 175 C (2.2 faradays) of charge had been passed and only a small amount of the starting material remained by TLC. The reaction was diluted with water and ether, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through 20 g of silica gel that was slurry-packed with 10% ether/pentane containing 1% triethylamine. Gradient elution from 10% ether/pentane to 40% ether/pentane afforded 0.112 g (44%) of the desired cyclized products. The desired products were contaminated with a small amount of aldehyde products arising from the hydrolysis of the acetals. Two diastereoisomers were separated. The major diastereoisomer was found to be the β isomer (cis isomer with respect to the carboxaldehyde dimethoxy acetal substituents), which gave a 3% NOE enhancement of the acetal proton on the carbon attached to C_1 when the acetal proton on the carbon attached to the bridgehead (C_{7a}) was irradiated. The other isomer did not exhibit this enhancement. The product was cis-fused across the bridgehead as suggested by the 1% enhancement on the methine proton attached to C_{3a} when the same proton (as the one above) was irradiated in both isomers. The spectral data of the mixture of diastereoisomers (cis and trans about the five-membered ring) were as follows: α isomer ^1H NMR ($CDCl_3$/300 MHz) δ 4.43 (s, 1 H, acetal proton), 4.27 (s, 1 H, acetal proton), 3.52, 3.49, 3.47, 3.46 (four s, 12 H, methoxy protons), 2.57-2.45 (m, 1 H, methine proton), 1.99-1.20 (m, 12 H), 0.96 (s, 3 H, methyl protons); ^{13}C NMR ($CDCl_3$/75 MHz) δ 112.8, 111.4, 58.7, 58.4, 57.8, 56.6, 54.6, 51.8, 35.6, 32.6, 25.9, 25.7, 24.1, 22.8, 19.6, 17.3; β isomer ^1H NMR ($CDCl_3$/300 MHz) δ 4.30 (s, 1 H, acetal proton), 4.12 (s, 1 H, acetal proton), 3.53, 3.52, 3.49, 3.44 (four s, 12 H, methoxy protons), 2.60-2.49 (m, 1 H, methine protn at C3a), 1.95-1.20 (m, 12 H), 0.93 (s, 3 H, methyl protons); ^{13}C NMR ($CDCl_3$/75 MHz) δ 113.0, 59.5, 59.4, 57.1, 56.6, 56.1, 51.2, 38.7, 31.2, 27.2, 26.6, 26.3, 23.0, 20.3, 18.6; IR (neat/NaCl) α and β isomers 2928, 2876, 1465, 1440, 1375, 1188, 1103, 1072, 969, 915 cm^{-1}; GCMS (PCI) *m/e* (rel intensity) 285 (M^+ - 1, 1), 253 (5), 224 (8), 223 (54), 221 (9), 191 (12), 159 (9), 149 (9), 89 (7), 76 (11), 75 ($(CH_3O)_2CH^+$, 100), 74 (10), 61 (11); HRMS (EI) *m/e* calcd for $C_{15}H_{27}O_3$ (M^+ - OCH_3) 255.1960, found 255.1958.

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Molecular Structure and Intramolecular Motion of (*E*)-Stilbenes in Crystals. An Interpretation of the Unusually Short Ethylene Bond

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Abstract: Crystal structures of (*E*)-2,2′-dimethylstilbene (**2**), (*E*)-2,2′,4,4′-tetramethylstilbene (**3**), (*E*)-2,2′,5,5′-tetramethylstilbene (**4**), (*E*)-2,2′,4,4′,5,5′-hexamethylstilbene (**5**), and (*E*)-2,2′,3,3′-tetramethylstilbene (**6**) were determined at several temperatures by X-ray diffraction. Analyses of these results and also of those reported for (*E*)-stilbene (**1**) and its related compounds revealed that the X-ray structures of compounds having the (*E*)-stilbene skeleton commonly show an unusually short bond length for the ethylene bond and a strong temperature dependence for the molecular structure. No sign confirming these anomalies could be detected in solution by NMR or UV spectroscopy. It is concluded that the short ethylene bond in the X-ray structures of these compounds is an artifact caused by dynamic averaging originating from the torsional vibration of the C–Ph bonds, during which the movement of the benzene rings is restrained to be a minimum. The observed temperature dependence of the ethylene bond length and angles and of the torsion angles of the C–Ph bonds is ascribed to the slight energy difference between the conformers, which interconvert by the torsional vibration. It has also been revealed that the rotational vibration of the benzene rings around the normal axes through C1 and C1′ is a characteristic motion of (*E*)-stilbenes in the crystalline state.

Introduction

(*E*)-Stilbene (**1**) is a well-known compound which has been extensively studied for a long time in various areas of chemistry, and much effort has been devoted to understanding its ground- and excited-state properties.[1] The molecular geometry is, however, still not unambiguously established, because the ethylene bond was observed to be unusually short by X-ray diffraction.[2-6]

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