Preparation of (1S*,4R*,13R*)-2,12-Dioxo-3-oxatricyclo-[8.2.1.0^{4,13}]tridec-10-ene (29). Ozone was bubbled into a solution of **24** (8.0 mg, 0.023 mmol) in 1.2 mL of methanol at -78 °C until a blue color persisted. Excess ozone was removed by bubbling nitrogen gas through the mixture, and the ozonide was reduced at room temperature by the addition of 0.5 mL of dimethyl sulfide in 0.5 mL of methanol. The solvent was removed under a stream of nitrogen, and the residue was treated with a solution of triethylamine (100 μL) in 500 μL of methylene chloride. After 10 min of stirring at room temperature, the solvent was removed in vacuo and the residue purified via flash chromatography (silica gel, 1:1 hexane/ether) to give 1.1 mg of starting material and 2.7 mg (66%, based on 86% conversion) of **29**, which solidified to a white solid upon trituration with ether: mp 128-130 °C (ether/pentane); IR ($CDCl_3$) 1783, 1712, 1611, 1457, 1429 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (s, 1 H), 4.44 (ddd, J = 11.1, 7.1, 3.8 Hz, 1 H), 3.63 (t, J = 7.3 Hz, 1 H), 3.58 (d, J = 7.5 Hz, 1 H), 2.96 (dd, J = 15.0, 7.0 Hz, 1 H), 2.40 (dd, J = 14.7, 10.1 Hz, 1 H), 2.23 (ddt, J = 16.9, 7.7, 3.6 Hz, 1 H), 2.15 (m, 1 H), 1.3-2.0 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 180.7, 168.3, 128.2, 83.9, 54.1, 50.7, 34.7, 32.4, 26.4, 26.3, 25.1; exact mass calcd for $C_{12}H_{14}O_3$ (M^+) 206.0943, found 206.0950.

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Supplementary Material Available: Experimental procedures for **3**, **6** (R = CH_2CF_3), **1b**, (*E*)-1-(phenylsulfonyl)-1-buten-4-ol, **11b** (R = CH_2CF_3), 3-hydroxy-1-(phenylsulfonyl)-1-cyclododecene, **9**, **13a**, and **16**, and equilibrations of **19**, **21**, and **27** (6 pages). Ordering information is given on any current masthead page.

Intramolecular Anodic Olefin Coupling Reactions: A Useful Method for Carbon-Carbon Bond Formation

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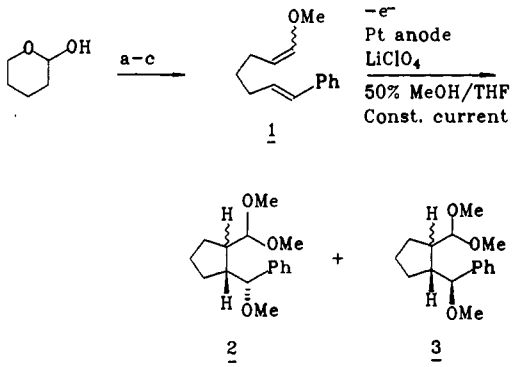
Abstract: The utility of intramolecular anodic olefin coupling reactions for effecting carbon-carbon bond formation has been examined. All of the successful cyclizations studied utilized either an alkyl or silyl enol ether as one of the participating olefins. The enol ethers could be coupled to simple alkyl olefins, styrenes, and allylsilanes in isolated yields ranging from 57 to 84%. The reactions were found to be effective for generating both five- and six-membered rings. The best conditions for cyclization utilized a reticulated vitreous carbon anode, constant-current conditions in an undivided cell, and a lithium perchlorate in either 50% methanol/tetrahydrofuran or 20% methanol/dichloromethane electrolyte solution. The use of an allylsilane as one of the participating olefins allowed for the regiospecific formation of olefinic products. In addition to the olefinic products, these reactions produced a small amount of a cyclized ether product in which the silyl group had not been eliminated. Deuterium-labeling studies showed that at least half of this ether byproduct arose from intramolecular migration of the methoxy group that was initially part of the starting enol ether to the carbon β to the silyl group. Intramolecular migration reactions of this type were found to participate in a number of the reported cyclization reactions.

The discovery of new, useful means for constructing carbon-carbon bonds is essential for the continued growth of synthetic organic chemistry. These reactions are important because they allow not only for the accomplishment of specific transformations within a synthetic sequence but also for the development of entirely new synthetic strategies. One method that appears ideal for initiating new carbon-carbon bond-forming reactions is oxidative organic electrochemistry. Oxidative organic electrochemistry would appear to have the ability to selectively generate highly reactive radical cation intermediates and initiate carbon-carbon bond formation under neutral conditions and at preset potentials.[1] This technique appears particularly attractive when one considers the growing importance of oxidative cyclization reactions.[2,3] It is tempting to suggest that anodic electrochemistry might provide a mild, generally useful method for initiating oxidative cyclization

Scheme I[a]



Yield = 65-73% (Ratio 2/3=5.3)

(a) Ph_3PCHPh, THF, 0 °C-RT. (b) Swern oxidation; styrene isomers were separated by silica gel chromatography. (c) $Ph_3PCHOMe$, THF, 0 °C-RT.

(1) For a general overview, see: (a) Baizer, M. M. *Organic Electrochemistry: An Introduction and a Guide*, 2nd ed.; Baizer, M. M., Lund, H., Eds.; M. Dekker: New York, 1983. For overviews of anodic electrochemistry, see: (b) Torii, S. *Electroorganic Synthesis: Methods and Applications: Part 1 - 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.

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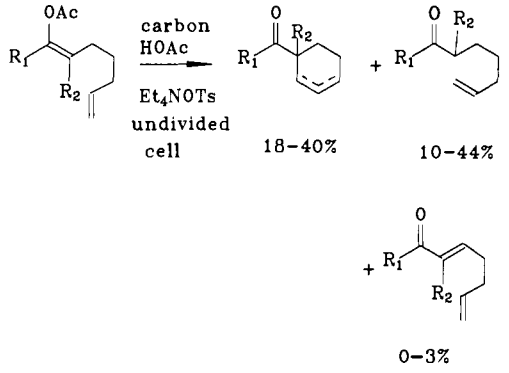
reactions from a host of electron-rich functional groups. Yet, in spite of this potential, anodic electrochemistry has not played a major role in designing new synthetic strategies and remains a vastly underutilized tool. In practice there exists few anodic carbon–carbon bond-forming reactions,[4] and only a handful of these have been used to initiate cyclization reactions.[5] In this paper, we report our initial efforts to develop the intramolecular anodic coupling of electron-rich olefins for such a purpose.

Our interest in this area was sparked by a 1978 report of a cyclization reaction that was initiated by the anodic oxiation of an enol acetate.[6] In this report, six-membered ring products were obtained in moderate-to-low yields. The major side product



formed was the saturated ketone that arose from hydrolysis of the starting enol acetate. Some of the α,β-unsaturated ketone derived from acetic acid trapping of the radical cation was also obtained.

The low yield of cyclized product in this reaction appeared to be due to the conditions used for the reaction. The reactions were carried out in an undivided cell with carbon electrodes, glacial acetic acid as the solvent, and tetrabutylammonium tosylate as the electrolyte. For comparison, intermolecular anodic olefin coupling reactions, which had been used for a number of years,[7] were most successful when either methanol[7e] or acetonitrile[7d] was used as the solvent and when either sodium perchlorate or sodium iodide was used as the electrolyte. In addition, the intermolecular reactions were at times buffered with 2,6-lutidine or sodium carbonate to prevent acidic decomposition of the initial enol ethers.[7d] Several examples taken from ref 1e are illustrated in Figure 1.

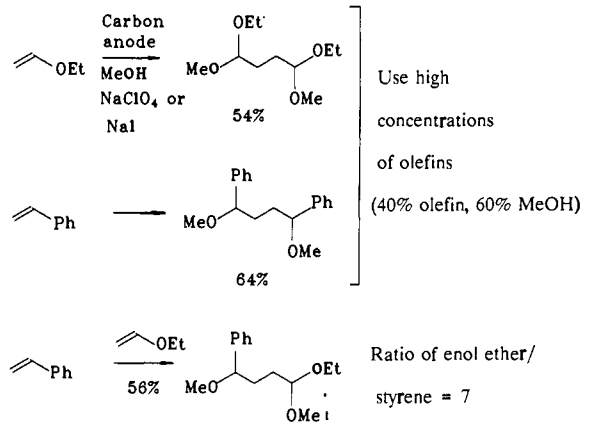
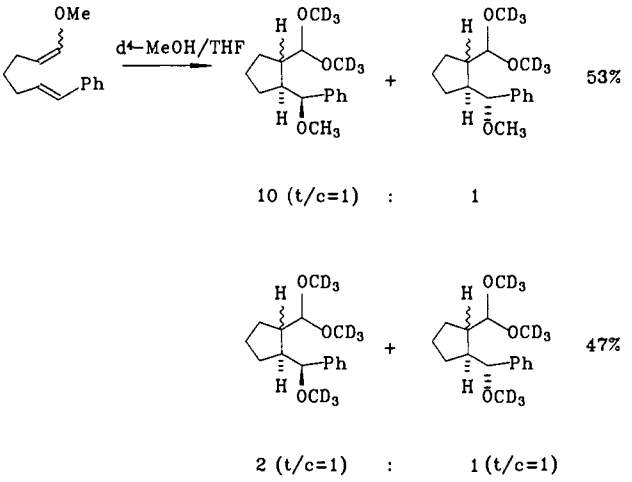


Figure 1.

Scheme II



With this in mind, we hoped to develop the intramolecular coupling reactions of electron-rich olefins into a useful synthetic tool by utilizing the electrochemical conditions normally used for intermolecular olefin coupling reactions. Initially, this work focused on studying the intramolecular coupling of bis enol ether substrates[8] and the intramolecular coupling reactions of enol ethers and styrenes. Intramolecular enol ether–styrene coupling reactions appeared to be ideal candidates for development because the intermolecular reactions did not require the use of one of the olefins as a cosolvent and because both olefins were known to be successful dimerization substrates. It was hoped that either olefin could function as the initiator (both styrenes and enol ethers have similar oxidation potentials)[9] or the terminator for a cyclization reaction.

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

(3) 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.

(4) (a) For a review, see ref 1b–e (especially ref 1b Appendix 1.1, ref 1c Chapter 4, and ref 1e). 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. (f) Chapuzet, J. M.; Simonet, J. *Tetrahedron* **1991**, *47*, 791.

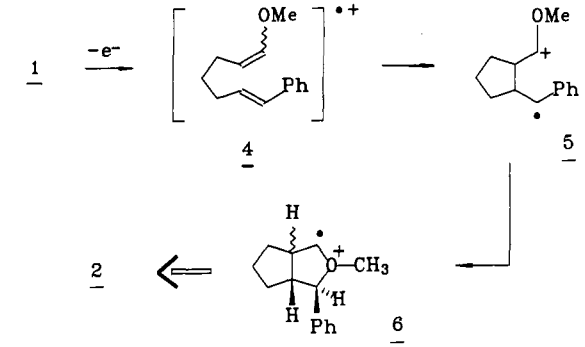
(5) For a review, see ref 1c, section 4-3 and references therein. For some recent examples, see: (a) Swenton. J. S.; Morrow, G. W. *Tetrahedron Lett.* **1987**. *28*, 5445. (b) Morrow, G. W.; Chen, Y.; Swenton, J. S. *Tetrahedron* **1991**, *47*, 655. (c) Becking, L.; Schaefer, H. J. *Tetrahedron Lett.* **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.

(6) Shono, T.; Nishiguchi, I.; Kashimura, S.; Okawa, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*. 2181.

(7) For reviews, see ref 4a. 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.

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

Scheme III

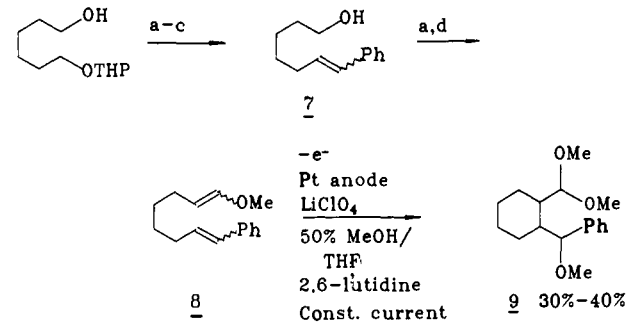


To test this hypothesis, compound **1** was synthesized and oxidized (Scheme I). Anodic oxidation of compound **1** using an undivided cell, constant-current conditions, a platinum foil anode, and a 1 M lithium perchlorate in 50% methanol/tetrahydrofuran electrolyte solution led to the formation of cyclized products in 68–73% isolated yields. Electrolysis conditions using an undivided cell and electrolysis conditions using a divided cell with 2,6-lutidine as a proton scavenger could be used interchangeably. The reaction led to a 5.3:1 ratio of diastereomers at the benzylic carbon (compounds **2** and **3**). Cis and trans isomers about the five-membered ring were formed. The cis and trans isomers having the same stereochemstry at the benzylic carbon were identified by hydrolysis of the acetals and epimerization of the products to a single aldehyde isomer. The stereochemistry at the benzylic carbon was determined by a single-crystal X-ray analysis of the 2,4-DNP derivative derived from the trans major aldehyde.[10]

Initially, we were surprised by the diastereoselectivity obtained at the benzylic carbon of the product. Since it was felt that formation of the benzylic ether arose from solvent trapping of an incipient benzylic carbocation, we hoped to influence the diastereoselectivity of the reaction by changing both the reaction medium and the solvent nucleophile. Most of these studies were not fruitful; however, one alteration proved to be very informative. When the solvent for the reaction was changed to 40% water/acetonitrile, the reaction led directly to the formation of aldehyde products as expected, although the yield of the reaction was disappointingly low (ca. 30%). Surprisingly, *a 6:1 ratio of methyl ethers was formed at the benzylic position even in the complete absence of methanol.* These methyl ether products could only be formed by an intramolecular migration of the methoxy group originally at C_1 of the starting enol ether to the benzylic carbon. In order to determine if this mechanism also operated in the original 50% methanol/tetrahydrofuran experiment, the cyclization was repeated with 50% methanol-d_4/tetrahydrofuran as the solvent (Scheme II). In this experiment, a 68% yield of cyclized products was obtained. Compounds **2** and **3** were isolated as the OCD_3 acetals and were again formed in a 5.3:1 ratio. Approximately half (53%) of the cyclized products still had an OCH_3 group at the benzylic position. This material was predominately (greater than 10:1) the cis and trans major products, **2**, and had to be derived from intramolecular transfer of the methoxy group originally at C_1 of the starting enol ether. The remainder of the material (47%) had an OCD_3 group at the benzylic position and was formed in an ca. 2:1 ratio of cyclized products **2** and **3**. These products were assumed to arise from solvent trapping of an incipient benzylic carbocation.

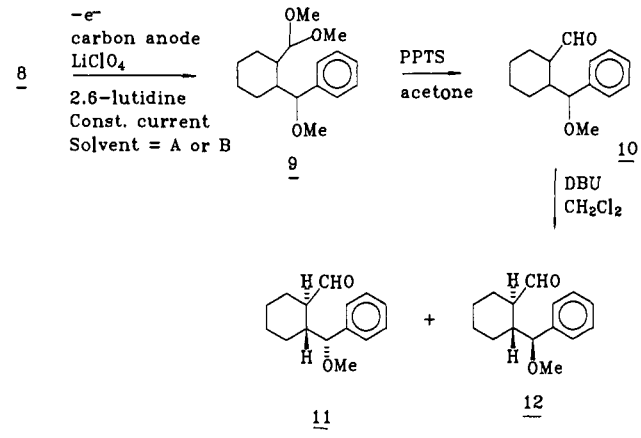
The methanol-d_4 experiment suggested that the bulk of the diastereoselectivity was derived from the intramolecular transfer of the enol ether methoxy group to the benzylic carbon, and that at one point, half of the material had to pass through a bicyclic intermediate like **6** (Scheme III). The stereochemistry of the major products can be explained by suggesting that the phenyl ring occupies the sterically least hindered position in this intermediate. The suggestion of a possible trans-fused bicyclic intermediate is bothersome. However, both cis and trans products about the five-membered ring having an OCH_3 ether at the benzylic carbon are formed in a 1:1 ratio. The possibility for the trans material being formed by epimerization of a cis product was ruled out because no deuterium incorporation at the bridgehead positions was observed by either proton or deuterium NMR. A mechanism wherein either **4** or **5** is trapped by solvent to form a mixed OCH_3–OCD_3 acetal prior to migration seems unlikely in view of the difference in diastereomer ratios obtained for the OCH_3 and OCD_3 benzyl ether products. At this point, no evidence has been obtained to indicate when the second electron is removed.[11]

Scheme IV[a]



[a] Conditions: (a) Swern oxidation. (b) Ph_3PCHPh, THF, 0 °C to room temperature. (c) PPTS, EtOH, 50 °C. (d) $Ph_3PCHOMe$, THF, 0 °C to room temperature.

Scheme V



Solvent A = 15% MeOH/CH_3CN: Yield = 58% (11/12=2.8/1)
Solvent B = 20% MeOH/CH_2Cl_2: Yield = 65% (11/12=2/1)

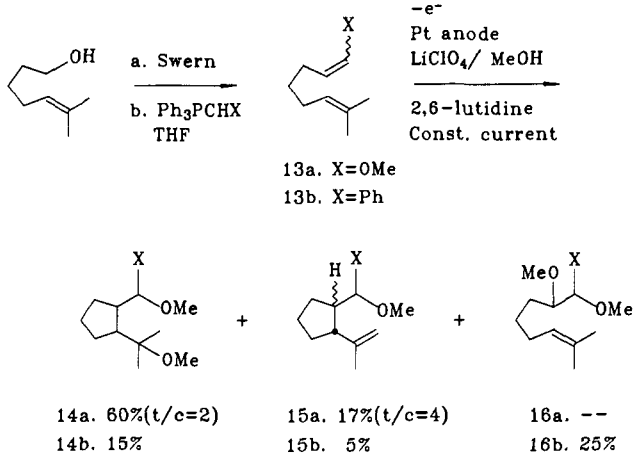
The intramolecular coupling of an enol ether to a styrene to form six-membered ring products was not as efficient. As illustrated in Scheme IV, the electrochemical oxidation of compound **8** under similar reaction conditions to those used for the cyclization of compound **1** led to only a 30–40% isolated yield of cyclized product. The yield of the cyclized product varied because of its tendency to form aldehydes upon purification. The 300-MHz ^1H NMR spectrum of the crude product indicated the presence of a large excess of methoxy signals. Unfortunately, the products that gave rise to the extra methoxy signals could not be isolated or characterized. Efforts to increase the yield of the cyclization

(9) For example, cyclic voltammetry of both **13a** and **13b** give rise to an initial oxidation wave at +1.4 V vs a Ag/AgCl reference electrode (Pt anode/1 N $LiClO_4$ in CH_3CN electrolyte solution).

(10) For a preliminary account of this work, see: Moeller, K. D.; Marzabadi, M. R.; New, D. G.; Chiang, M. Y.; Keith, S. *J. Am. Chem. Soc.* **1990**, *112*, 6123. Details of the X-ray analysis are included in the supplementary material of this manuscript.

(11) For example, as a possible alternative to a mechanism involving loss of the second electron followed by subsequent trapping with methanol, the trapping of electrochemically generated radical cations with methoxy radicals is well-precedented: Dolson, M. G.; Swenton, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 2361 and Nilsson, A.; Palmquist, U.; Pettersson, T.; Ronlan, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, *7*, 708.

Scheme VI



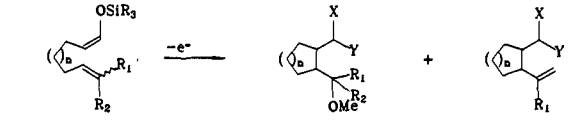
14a. 60%(t/c=2) 15a. 17%(t/c=4) 16a. --
14b. 15% 15b. 5% 16b. 25%

by changing the anode material (carbon vs platinum), cell type (divided vs undivided), current density, substrate concentration, and reaction temperature did not improve either the spectral data obtained for the crude reaction or the isolated yield of cyclized product.

Fortunately, the yield of six-membered ring formation could be improved by changing the cosolvent and lowering the amount of methanol used. When the cyclization was attempted with constant-current conditions, a carbon rod anode, an undivided cell, 5 equiv of 2,6-lutidine as a proton scavenger, and a 0.1 M lithium perchlorate in 10% methanol/acetonitrile electrolyte solution, the yield of the reaction improved markedly (Scheme V). In this example, the products were isolated after deprotection of the acetal by using pyridinium *p*-toluenesulfonate in acetone and epimerization of the resulting aldehydes with diazabicyclo[5.4.0]undec-7-ene in dichloromethane. The isolated yield of products **11** and **12** obtained from the three-step sequence was 58%. The two diastereomers were obtained in a 2.8:1 ratio. Compound **11** was tentatively assigned as the major product by analogy to the five-membered ring cyclization product. The use of dichloromethane as a cosolvent, which has been reported to stabilize radical cations,[12] led to further improvement of six-membered ring formation. In this case, the use of 20% methanol/dichloromethane as solvent and a reticulated vitreous carbon anode[13] for the electrolysis led to a 65% isolated yield of products **11** and **12** from the three-step sequence. The two diastereomers were obtained in a 2:1 ratio. The nature of the carbon anode (reticulated vitreous carbon vs a carbon rod) was found to make little difference in the overall yield of the three-step sequence. The switch from tetrahydrofuran as a cosolvent to acetonitrile or dichloromethane was initially made because these solvents allowed for the use of lower methanol concentrations. For comparison, methanol concentrations lower than 30% methanol in tetrahydrofuran led to severe fluctuations in current flow and drastic decreases in the yield of the cyclized products.

Two additional points about this cyclization reaction deserve comment. First, the stereochemistry of the products did not depend upon the initial geometry of the styrene double bond. The cyclization (using 10% methanol/acetonitrile as solvent) of a substrate having 90% trans geometry about the styrene double bond (compound **8** was a 1:1 mixture of cis and trans isomers about the styrene double bond) led to the two diastereomeric five-membered ring products in a 2.7:1 ratio. Second, the cyclization to form six-membered rings also gave rise to an intramolecular migration of the enol ether methoxy group of the starting material to the benzylic position of the product. In this case, cyclization utilizing 10% methanol-d_4/acetonitrile followed by deprotection and epimerization led to aldehyde products having

Scheme VII[a]



17a. $R_1=R_2=CH_3$,n=1;R=i-Pr[a] 14. 48%(X=Y=OMe) 15. 19%(X=Y=OMe)

17b. R_1=Ph,R_2=H,n=1;R=t-Pr[b] 2/3. 57%(X=Y=OMe; 2/3=1.8) --
16b. 10%(X=OSiR₃,Y=OMe)

17c. R_1=Ph,R_2=H,n=2; R_3Si=TBDMS[c] 11/12. 63%(X=Y=O;[d] 11/12=0.91) --

[a] Conditions: (a) Pt anode, MeOH, $LiClO_4$, undivided cell. (b) Pt anode, 50% MeOH/THF, $LiClO_4$, undivided cell. (c) Carbon anode, 20% MeOH/CH_2Cl_2, $LiClO_4$, 2,6-lutidine, undivided cell. (d) The products were isolated after treatment with PPTS in acetone, followed by DBU in CH_2Cl_2.

a 1.4:1 ratio of OCH_3 to OCD_3 ethers at the benzylic position. The products having an OCH_3 benzylic ether were obtained as 3.7:1 ratio of compounds **11** to **12**. The products having an OCD_3 benzylic ether were obtained as a 2:1 ratio of compounds **11** to **12**.

Having established that the intramolecular coupling of enol ethers and styrenes could lead to carbon–carbon bond formation, we set out to determine whether the enol ether, the styrene, or both activated olefins were necessary for effective cyclization. To this end, compounds **13a** and **13b** were synthesized and oxidized (Scheme VI). Anodic oxidation of **13a** using constant-current conditions, a platinum anode, a divided cell, 2,6-lutidine as a proton scavenger, and a 1 M lithium perchlorate in methanol electrolyte solution led to the formation of a 77% isolated yield of cyclization products **14a** and **15a** (the ratio of **14a** to **15a** was 3.5:1). No cosolvent was needed for this cyclization. As in the earlier cyclization of compound **1**, electrolysis conditions using an undivided cell could be used interchangeably with the use of a divided cell and 2,6-lutidine as a proton scavenger. The anodic oxidation of **13b** under identical conditions led to a complex mixture of products. Only a 20% yield of cyclized products was isolated from the mixture along with 25% of the uncyclized compound, **16b**. From these results, it was clear that the enol ether group could serve as a more effective initiator for the cyclization reaction than the styrene group, and that enol ethers could effectively initiate carbon–carbon bond-forming reactions with simple alkyl-substituted olefins.

In addition to alkyl enol ethers, silyl enol ethers were found to be effective initiators for the cyclization reactions (Scheme VII).[14] Anodic oxidation of **17a** led to the formation of a 67% isolated yield of cyclized products. During the reaction, the siloxy group of the acetal product was exchanged for methanol. Anodic oxidation of **17b** also led to a 67% yield of cyclized products. The diastereoselectivity of the reaction at the benzylic carbon was only 1.8:1 (**2**/**3**), reflecting the lack of any possible intramolecular methoxy group migration. Anodic oxidation of **17c** led to the formation of a 63% isolated yield of six-membered ring products after deprotection of the acetal and epimerization. The conditions used for the electrolysis were identical with those found to be optimal for the earlier six-membered ring-forming reactions. Curiously, approximately 16% of the cyclized product has a *tert*-butyldimethylsiloxy group at the benzylic carbon. In all of the cyclizations, little difference was found between the use of alkyl and silyl enol ethers.

At this point, the majority of the cyclization reactions had led to mixtures of products. This problem was particularly acute when a disubstituted olefin was used as the terminating group. When compound **19** was oxidized at a platinum anode in a divided cell with 2,6-lutidine as a proton scavenger and a 1 M lithium perchlorate in 50% methanol/tetrahydrofuran electrolyte solution, a mixture of cyclized products was obtained in a 35–60% isolated

(12) Phelps, J.; Santhanam. K. S. V.; Bard, A. J. *J. Am. Chem. Soc.* **1967**, *89*, 1752.

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

(14) For a related chemical oxidation of phenyl-substituted silyl enol ether, see: Snider, B. B.; Kwon, T. *J. Org. Chem.* **1990**, *55*, 4786.

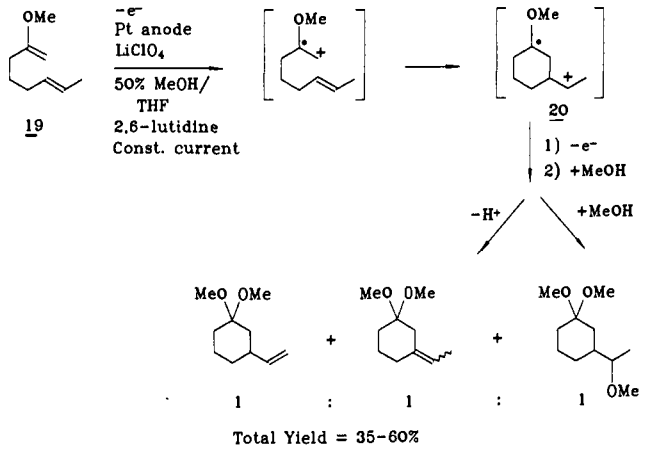
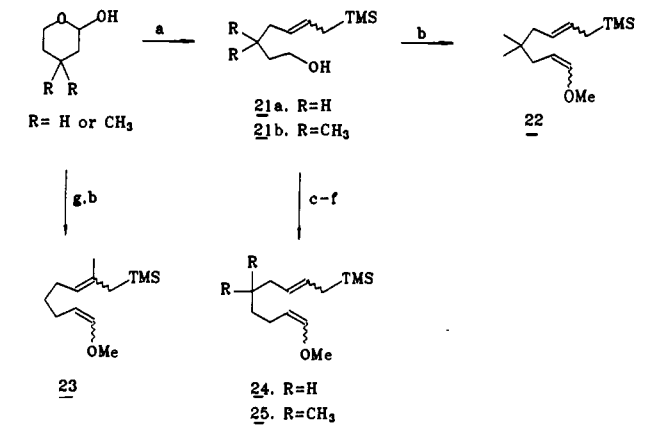


Figure 2.

Scheme VIII[a]



[a] Conditions: (a) Ph_3PCHCH_2TMS, THF, -78 °C. (b) i. $(COCl)_2$, DMSO, THF; ii. Et_3N; iii. filter; iv. $Ph_3PCHOMe$, 0 °C. (c) *n*-BuLi, TsCl, DMSO, THF, -15 °C. (d) NaCN, DMSO. (e) DIBAL-H, benzene, 0 °C. (f) $Ph_3PCHOMe$, THF, 0 °C. (g) $Ph_3PC(CH_3)$-CH_2TMS, THF, -78 °C.

yield. The yield of the cyclized products was not optimized due to the propensity of the products to deketalize and the volatility of the resulting ketones. The mixture of products obtained could best be explained by suggesting that the initially formed radical cation cyclized to form either a secondary carbocation, as illustrated in Figure 2, or a secondary radical that was subsequently oxidized to a secondary carbocation. The product mixtures would then arise from the nonselective decomposition of the secondary radical cation. If this were the case, then it seemed reasonable to employ an allylsilane as the terminating olefin in order to control product formation.[15] The choice of an allylsilane group was ideal because competitive oxidation of the allylsilane group might be expected to give rise to the same desired product.[16]

In order to test the effectiveness of allylsilanes for the cyclization reactions, substrates **22–25** were synthesized as outlined in Scheme VIII.[17] It is important to note that enol ethers **22** and **23** were made by using a simple modification of the Swern oxidation procedure recently reported by Ireland.[18] In this procedure, tetrahydrofuran is used as the solvent for the Swern oxidations,

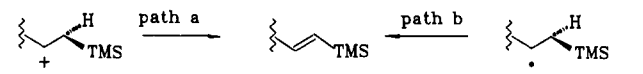


Figure 3.

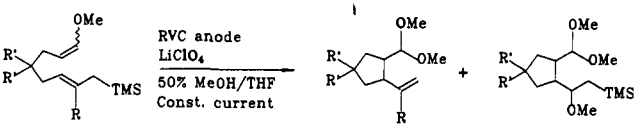


Figure 4.

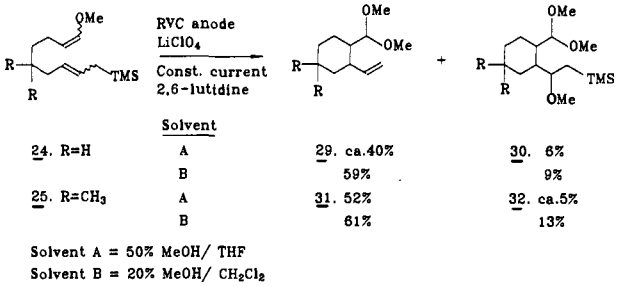
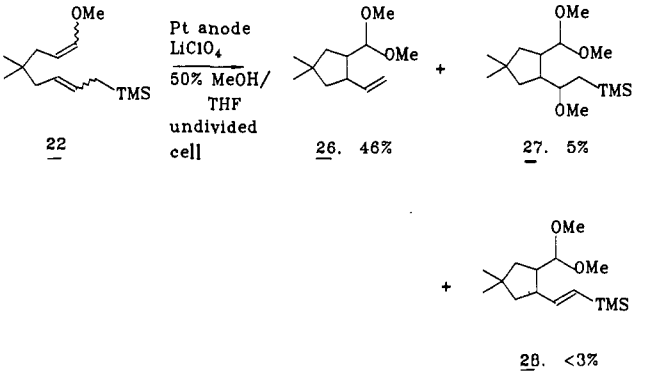


Figure 5.

and then a nucleophile (e.g. stabilized ylides and Grinard reagents) added directly to the crude reaction mixture. In this way, very unstable aldehydes can be utilized as intermediates without the need for isolation. We have found that this procedure can be readily extended to the use of unstabilized ylides by filtering the crude Swern reaction mixture before adding the ylide.

Compound **22** was initially selected for study. Anodic oxidation of **22** at a platinum anode using constant-current conditions, an undivided cell, and a 1 M lithium perchlorate in 50% methanol/tetrahydrofuran electrolyte solution led to the formation of a 46% isolated yield of the desired olefinic product, **26**. In addition, a 5% yield of **27** was obtained along with a small amount of impure vinylsilane **28**. Although only isolated in minor quantities, the



presence of a vinylsilane product was very surprising. It seemed unlikely that a vinylsilane product would be formed by competitive loss of a proton from a conformationally unrestricted β-silyl carbocation, as illustrated in Figure 3 (path a). It seemd more likely than a vinylsilane product would be formed by competitive loss of a hydrogen atom from a β-silyl radical (Figure 3, path b). This mechanism would arise if the radical cation cyclization led to the formation of the β-silyl radical, and then elimination occurred either faster than or competitively with the loss of a second electron. If this mechanism operated to a large extent, then it seemed reasonable that the reaction might benefit from the use of a carbon anode. Carbon anodes have been reported to be much more efficient than platinum anodes at removing a second electron from a radical cation.[19]

(15) For a review of reactions involving allylsilanes, see: (a) Schinzer, D. *Synthesis* **1988**, 263 and (b) Fleming, I. In *Comprehensive Organic Chemistry*; Jones, D. N., Ed.; Pergamon Press: Oxford, 1979; Vol. 3, p 541 and references therein.

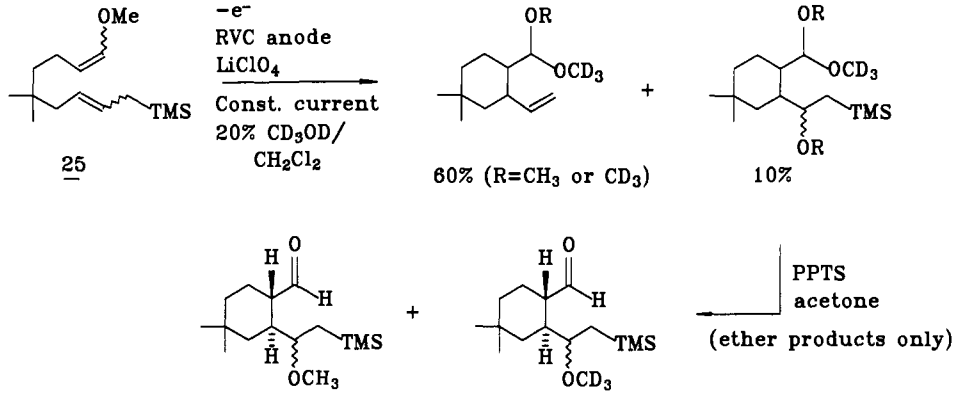
(16) For electrochemical oxidations of allylsilanes, see: (a) Yoshida, J.; Murata, T.; Isoe, S. *Tetrahedron Lett.* **1986**, *27*, 3373. (b) Koizumi, T.; Fuchigami, T.; Nonaka, T. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 219. For photochemical oxidations of allylsilanes, see: (a) Tu, C. L.; Mariano, P. S. *J. Am. Chem. Soc.* **1987**, *109*, 5287 and references therein. (b) Mizuno, K.; Yasueda, M.; Otsuji, Y. *Chem. Lett.* **1988**, 229.

(17) For a preliminary account of this work, see: Moeller, K. D.; Hudson, C. M. *Tetrahedron Lett.* **1991**, *32*, 2307.

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

(19) (a) See ref 1a p 183. (b) Brennan, M. P. J.; Brettle, R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 257.

Scheme IX



In practice, the anodic oxidation of **22** using a reticulated vitreous carbon anode led to an *84% isolated yield of compound* ***26***. A 7% isolated yield of compound **27** was obtained. None of the vinylsilane product was observed (Figure 4). In a similar fashion, compound **23** was cyclized to afford a 66% isolated yield of the desired olefinic product along with a 15% yield of recovered starting material.

As with the enol ether–styrene coupling reactions, enol ether–allylsilane coupling reactions leading to six-membered rings were not as efficient as their five-membered ring counterparts. For example, the anodic oxidation of compound **24** using the conditions that were successful above led to only a 40% yield of slightly impure olefin **29** along with 6% of the ether product **30** and 7% of uncyclized material. Anodic oxidation of compound **25** afforded a 52% yield of the desired olefinic compound **31** along with an ca. 5% yield of **32** (Figure 5). Fortunately, the use of a cosolvent and lower concentrations of methanol also served to improve these reactions. A change in solvent from 50% methanol/tetrahydrofuran to 20% methanol/dichloromethane afforded a 59% isolated yield of **29** along with a 9% isolated yield of **30** from the anodic oxidation of **24**. The cyclization reaction originating from the anodic oxidation of **25** led to a 61% isolated yield of olefinic product **31** along with a 13% isolated yield of compound **32** when 20% methanol/dichloromethane was used as the solvent. Unlike earlier enol ether–styrene coupling reactions, in these examples the use of acetonitrile as the cosolvent led to complex mixtures of products.

As in earlier examples, the origins of the cyclized ether products (like compound **32**) were examined. The anodic oxidation of **25** was repeated with 20% methanol-d_4/dichloromethane as the solvent. A 60% isolated yield of olefinic product was obtained along with 10% of the cyclized ether. The ether product was treated with pyridinium toluenesulfonate in acetone to remove the acetal methoxy groups, and then the product mixture was examined by 300-MHz ^{1}H NMR (Scheme IX). Fifty-six percent of the cyclized ether products contained in an OCH_3 ether and clearly arose from intramolecular migration of the methoxy group that was originally part of the starting enol ether. The remaining 44% of the ether products contained an OCD_3 group. This product was formed either from solvent trapping of an incipient β-silyl carbocation or from intramolecular migration of an OCD_3 group from a mixed OCH_3–OCD_3 acetal formed during the oxidation reaction. At this time, neither mechanism can be ruled out.

On a final note, the cyclized ether side products could be readily converted to the desired olefinic products under acidic conditions. For example, treatment of compound **32** with acetic acid in methanol led to the formation of **31** in a 74% isolated yield.

In conclusion, it has been found that the intramolecular anodic coupling of electron-rich olefins can serve as a useful method for the generation of carbon–carbon bonds and the construction of five- and six-membered rings. The reactions can be efficiently initiated by the oxidation of both alkyl and silyl enol ethers and terminated with the use of styrenes, simple alkyl olefins, and allylsilanes. From a synthetic standpoint, the reactions are most useful when allylsilanes are employed because they allow for the selective generation of olefinic products. Studies aimed at exploring the utility of the coupling reactions for total synthesis are currently underway and will be reported in due course.

Experimental Section[20]

(*E* and *Z*)-6-Phenyl-5-hexenal. Sodium hydride (3.63 g, 80% emulsion in oil, 0.12 mol) was placed in a round-bottom flask and washed three times (5 mL) with hexane. Anhydrous dimethyl sulfoxide (110 mL) was added and the mixture heated to 75 °C until no further bubbling was observed (30 min, deep blue solution). The mixture was cooled to room temperature, 52.4 g (0.12 mol) of benzyltriphenylphosphonium bromide added, and the reaction reheated to 75 °C for 30 min. A maroon solution was formed. To this mixture was added a solution of 4.4 g (43 mmol) of 2-hydroxytetrahydropyran in 10 mL of dry dimethyl sulfoxide over a period of 45 min. The reaction was stirred at 75 °C for 1 h, cooled to room temperature, and quenched with water and ether. The layers were separated, and the aqueous layer was extracted two times with ether. The combined organic layers were washed three times with water, dried over $MgSO_4$, and concentrated in vacuo. The crude product was chromatographed through 250 g of silica gel with a gradient elution from ca. 5% ether/hexane as eluant to 33% ether/hexane in order to afford 6.34 g (84%) of the desired styrene alcohol. The product was isolated as a 1:1 mixture of stereoisomers and was carried on to the next reaction without further purification.

To a stirred solution of 2.36 g (13.4 mmol) of the alcohol made above and 2.09 g (26.8 mmol) of dimethyl sulfoxide in 150 mL of dichloromethane at −78 °C was added 1.87 g (26.8 mmol) of oxalyl chloride. The resulting mixture was warmed to −60 °C, stirred for 30 min, and then quenched with 6.79 g (67.0 mmol) of triethylamine. The reaction mixture was then allowed to warm to room temperature. The reaction was diluted with water and ether, and the layers were separated. The organic layer was washed with water, dried over $MgSO_4$, and concentrated in vacuo. The crude product was chromatographed through 150 g of silica gel with a gradient elution from 0.5% ether/pentane to 2.5% ether/pentane as eluant to afford a combined yield of 1.63 g (70%) of the desired cis and trans products (0.70 g of pure cis product, 0.61 g of pure trans product, and 0.32 g of a mixture of the two isomers). The spectral data for the cis isomer are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 9.77 (t, 1 H, J = 1.7 Hz), 7.37–7.22 (m, 5 H), 6.48 (br d, 1 H, J = 11.6 Hz), 5.63 (dt, 1 H, J_d = 11.6 Hz, J_t = 7.3 Hz), 2.46 (td, 2 H, J_t = 7.3 Hz, J_d = 1.6 Hz), 2.36 (app qd, 2 H, J_q = 7.5 Hz, J_d = 1.7 Hz), 2.38 (p, 2 H, J = 7.4 Hz) ppm; IR (neat/NaCl) 3078, 3050, 3000, 2930, 2820, 2715, 1724, 1492, 1443, 1406, 1387, 1070, 915, 764, 695 cm^{-1}; GC/MS (EI) *m/e* (rel intensity) 174 (M^+, 1), 146 (M^+ − CO, 1), 131 (M^+ − CH_2CHO, 13), 130 (M^+ − CH_3CHO, 100), 129 (51), 117 (58), 115 (63), 104 (20), 77 (13). The spectral data for the trans isomer are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 9.79 (t, 1 H, J = 1.7 Hz), 7.40–7.18 (m, 5 H). 6.40 (d, 1 H, J = 15.8 Hz), 6.17 (dt, 1 H, J_d = 15.8 Hz, J_t = 7.0 Hz), 2.49 (td, 2 H, J_t = 7.3 Hz, J_d = 1.6 Hz), 2.26 (app qd, 2 H, J_q = 7.1 Hz, J_d = 1.4 Hz), 1.82 (p, 2 H, J = 7.3 Hz) ppm; IR (neat/NaCl) 3078, 3055, 3020, 2925, 2820, 2715, 1724, 1480, 1446, 1408, 1388, 915, 839, 688 cm^{-1}; GC/MS (EI) *m/e* (rel intensity) 175 (M^+ + 1, 1), 174 (M^+, 6), 146 (1), 131 (19), 130 (100), 129 (74), 117 (58), 116 (21), 115 (99), 104 (20), 77 (13). Analysis was conducted on the (2,4-dinitrophenyl)hydrazone derivative of the trans product: mp

(20) 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.

112.8–113.3 °C (EtOH). Anal. Calcd for $C_{18}H_{18}N_4$: C, 61.01; H, 5.12; N, 15.81. Found: C, 60.35; H, 5.03; N, 15.83.

(*E*)-6-Phenyl-(*E* and *Z*)-1-methoxy-1,6-heptadiene (1). To a 0 °C solution of 3.09 g (9.0 mmol) of (methoxymethyl)triphenylphosphonium chloride in 30 mL of tetrahydrofuran was added 3.6 mL (9.0 mmol) of 2.5 M *n*-butyllithium in hexane solution. The resulting red solution was stirred for 30 min, and then a solution of 0.504 g (2.9 mmol) of the aldehyde made above in 13 mL of dry tetrahydrofuran was added. The reaction was allowed to warm to room temperature and then stirred for 36 h. The reaction was quenched with 50 mL of 40% sodium bisulfite solution and 50 mL of ether. The layers were separated, and the organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude product was distilled (Kugelrohr) at 125 °C (0.5 mm) in order to remove the triphenylphosphine oxide, and the resulting oil was chromatographed through 30 g of silica gel. The column was packed with hexane containing 1% triethylamine and gradient eluted with 1% ether/hexane to 1.5% ether/hexane to afford 0.34 g (58%) of the desired diene **1**. The product was obtained as an ca. 53:47 mixture of trans and cis enol ether isomers. The spectral data for the mixture are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.45–7.18 (m, 5 H), 6.39 (br d, 1 H, J = 15.9 Hz), 6.39–6.17 (m, 1.53 H, styrene proton plus the proton at C_1 of the trans enol ether), 5.90 (dt, 0.47 H, J_d = 6.2 Hz, J_t ca. 1 Hz, proton at C_1 of the cis isomer), 4.74 (dt, 0.53 H, J_d = 12.6 Hz, J_t = 7.3 Hz, proton at C_2 of the trans isomer), 4.36 (q, 0.47 H, J = 7.0 Hz, proton at C_2 of the cis isomer), 3.59 (s, 1.41 H, methoxy protons of the cis isomer), 3.52 (s, 1.59 H, methoxy protons of the trans isomer), 2.23 (app q, 2 H, J = 7.2 Hz), 2.12 (qd, 0.94 H, J_q = 7.5 Hz, J_d = 1.3 Hz, allylic methylene protons for the cis isomer), 1.99 (q with some fine structure, 1.06 H, J_{av} = 7.1 Hz, allylic methylene protons for the trans isomer), 1.52 (p, 2 H, J = 7.5 Hz) ppm; IR (neat/NaCl) 3025, 2929, 2854, 1663, 1457, 1209, 1110, 964, 742, 692 cm^{-1}; GC/MS (35 eV) *m/e* (rel intensity) first peak 202 (M^+, 4), 171 ($M^+ - OCH_3$, 2), 170 ($M^+ - CH_3OH$, 15), 157 (5), 155 (17), 134 (60), 129 (56), 115 (70), 98 (47), 91 (PhCH, 89), 71 (MeOCH=$CHCH_2$, 100), second peak 202 (1), 171 (2), 170 (15), 157 (5), 155 (17), 134 (58), 129 (58), 117 (35), 115 (71), 104 (19), 91 (91), 71 (100); HRMS (EI) *m/e* calcd for $C_{14}H_{18}O$ 202.1358, found 202.1391.

Electrolysis of Compound 1: Synthesis of 2-(Methoxyphenylmethyl)-cyclopentane-1-carboxaldehyde Dimethyl Acetal (2a,b and 3a,b). A solution of 1.60 g of $LiClO_4$ in 5 mL of MeOH/THF (1:1) containing 0.134 g (0.66 mmol) of enol ether **1** was placed in a vial equipped with platinum electrodes and a nitrogen inlet. The reaction was electrolyzed at a constant current of 10.2 mA until only a trace of starting material remained by TLC (3.4 faradays). The reaction mixture was diluted with ether (30 mL containing 10 drops of triethylamine) and water (20 mL). The layers were separated, and the organic layer was washed with water (5 mL) and brine (5 mL), dried over sodium sulfate, and concentrated in vacuo. The crude product was immediately chromatographed through 30 g of silica gel with gradient elution (5% ether/hexane to 20% ether/hexane) to afford 127 mg (73%) of a mixture of acetals **2** and **3**. All four diastereomers of **2** (cis and trans about the five-membered ring) and **3** (cis and trans about the five-membered ring) could be separated by careful chromatography with a gradient 1% to 10% ether/hexane elution. The spectral data for the four isomers are as follows. **2a** cis major: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.45–7.25 (m, 5 H), 4.52 (d, 1 H, J = 5.0 Hz, acetal methine proton), 4.04 (d, 1 H, J = 10.4 Hz, benzylic methine proton), 3.45 (s, 3 H), 3.44 (s, 3 H), 3.14 (s, 3 H), 2.52 (app ddt, 1 H, J_d = 10.1 Hz, J_d = 7.7 Hz, J_t = 5.0 Hz, bridgehead methine proton α to the acetal), 2.23 (app tt, 1 H, J_t = 10.6 Hz, J_t = 7.4 Hz, bridgehead methine proton), 1.93–1.45 (m, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 142.0, 128.0, 127.3, 127.1, 106.0, 84.7, 55.8, 54.5, 54.1, 49.3, 42.4, 28.9, 25.5, 23.5; IR (neat/NaCl) 3059, 3020, 2942, 2924, 2920, 2865, 2819, 1491, 1452, 1358, 1187, 1152–1055, 965, 761, 696, 626 cm^{-1}; GC/MS (35 eV) *m/e* (rel intensity) 232 (1), 201 (1), 200 (1), 169 (2), 122 (10), 91 (18), 77 (20), 75 (100); HRMS (EI) *m/e* calcd for $C_{15}H_{20}O_2$ (M^+ – MeOH) 232.1464; found 232.1470. **2b** trans major: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.45–7.28 (m, 5 H), 4.23 (d, 1 H, J = 5.0 Hz, methine proton of the acetal), 3.96 (d, 1 H, J = 7.7 Hz, benzylic methine proton), 3.39 (s, 3 H), 3.38 (s, 3 H), 3.19 (s, 3 H), 2.31–2.18 (m, 2 H, bridgehead methine protons), 1.75–1.18 (m, 6 H): IR (CH_2Cl_2) 3025, 2955, 2923, 2865, 1491, 1450, 1118, 1090, 1067, 965, 680 cm^{-1}; GC/MS (35 eV) *m/e* (rel intensity) 232 (1), 201 (1), 169 (3), 168 (1), 122 (10), 121 (12), 111 (16), 91 (15), 77 (17), 70 (100); HRMS (EI) *m/e* calcd for $C_{15}H_{20}O_2$ (M^+ – MeOH) 232.1464, found 232.1464. The stereochemistry of the product was determined by single-crystal X-ray analysis of the (2,4-dinitrophenyl)hydrazone derivative (mp 149.8–151.5 °C) obtained from the acetal.[10] **3a** cis minor: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.39–7.24 (m, 5 H), 4.54 (d, 1 H, J = 6.4 Hz, acetal methine proton), 4.53 (d, 1 H, J = 4.8 Hz, benzylic methine proton), 3.37 (s, 3 H), 3.35 (s, 3 H), 3.21 (s, 3 H), 2.34–2.16 (m, 2 H, bridgehead methine protons), 1.85–1.30 (m, 6 H); IR (neat/NaCl) 3088, 3068, 2929, 2871, 2827, 1454, 1191, 1135, 1108, 1062, 956, 745, 703 cm^{-1}; GC/MS (35 eV) *m/e* (rel intensity) 233 (M^+ – OMe, <1), 232 (M^+ – MeOH, 2), 201 (1), 200 (1), 121 (100), 111 (16), 91 (15), 75 (65); HRMS (EI) *m/e* calcd for $C_{15}H_{20}O_2$ (M^+ – MeOH) 232.1464, found 232.1467. **3b** trans minor: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.41–7.27 (m, 5 H), 4.15 (d, 1 H, J = 5.6 Hz, acetal methine proton), 3.78 (d, 1 H, J = 6.2 Hz, benzylic methine proton), 3.28 (s, 3 H), 3.24 (s, 3 H), 3.19 (s, 3 H), 2.13 (m, 1 H, bridgehead methine), 2.03 (app p, 1 H, J_{av} ca. 6.6 Hz, bridgehead methine proton), 1.77–1.45 (m, 6 H); IR (neat/NaCl) 3084, 3062, 3025, 2952, 2932, 2872, 2828, 1452, 1374, 1190, 1126–1072, 966, 910, 763, 705 cm^{-1}; GC/MS (35 eV) *m/e* (rel intensity) 232 (1), 201 (1), 200 (1), 169 (3), 168 (1), 121 (100), 91 (12), 77 (11), 75 (65); HRMS (EI) *m/e* calcd for $C_{15}H_{20}O_2$ (M^+ – MeOH) 232.1464, found 232.1473. Analysis was obtained for the (2,4-dinitrophenyl)hydrazone derivative obtained from the acetal; mp 149.4–149.9 °C. Anal. Calcd for $C_{20}H_{22}N_4O_5$: C 60.29; H, 5.57; N, 14.06. Found: C, 60.23; H, 5.58; N, 13.90. It is important to note that all of the stereochemical assignments hinge on the X-ray obtained for the trans major product **2b**. The cis major product **2a** was assigned by conversion to the corresponding aldehyde with pyridinium *p*-toluenesulfonate (3 equiv) in acetone (concentration of substrate 0.015 M) and then epimerization to form the same aldehyde as derived from the trans major product **2b**. In the same manner, the cis minor product **3a** was converted to the same aldehyde as derived from the trans minor product **3b**. Both of the trans aldehydes obtained could be converted back to the original acetals.

(*E* and *Z*)-7-Phenyl-6-hepten-1-ol (7). The product was derived from the mono THP-protected 1,6-hexanediol after three steps. The intermediates were not isolated. A solution of 19.85 g (98.1 mmol) of alcohol and 15.32 g (196.2 mmol) of dimethyl sulfoxide in 500 mL of dichloromethane was cooled to −78 °C. To this mixture was added 13.69 g (107.9 mmol) of oxalyl chloride. The reaction was stirred for 15 min, and then the temperature was raised to −50 to −60 °C. After an additional 15 min, 49.64 g (490.5 mmol) of triethylamine was added and the reaction allowed to warm to room temperature. Water (100 mL) was added to the crude reaction mixture and the dichloromethane removed in vacuo. The remaining aqueous phase was extracted three times (100 mL each) with ether. The combined ether layers were washed with saturated sodium chloride, dried over sodium sulfate, and concentrated in vacuo. The resulting aldehyde was used in the following reaction without further purification.

To a 0 °C solution of 106.2 g (245.6 mmol) of benzyltriphenylphosphonium bromide in 200 mL of tetrahydrofuran was slowly added 98.1 mL (245.6 mmol) of a 2.5 N *n*-butyllithium in hexane solution. The solution was stirred for 30 min, a solution of the aldehyde made above in 400 mL of tetrahydrofuran added, the temperature allowed to warm to room temperature, and the reaction stirred for an additional 40.5 h. When complete, the crude reaction was washed three times with saturated sodium bisulfate followed by three washings with water. The combined aqueous layers were extracted with ether. The combined ether layers were then washed three times with saturated sodium chloride, dried over $MgSO_4$, and concentrated in vacuo. The crude product was taken up in pentane in order to precipitate the triphenylphosphine oxide formed during the reaction, filtered, and concentrated a second time in vacuo. The pentane precipitation procedure was repreated to remove more of the triphenylphosphine solid. This product was again carried on without further purification.

A solution of the protected alcohol from the last step and 2.46 g (9.8 mmol) of pyridinium *p*-toluenesulfonate in 250 mL of 95% ethanol was heated to 50 °C for 4 h. cooled to room temperature, and stirred overnight. To the crude reaction mixture was added 50 mL of water, and then the ethanol was removed in vacuo. The remaining aqueous layer was extracted three times with ether. The combined ether washings were washed three times with saturated sodium chloride, dried over $MgSO_4$, and concentrated in vacuo. The crude product was chromatographed through ca. 500 g of silica gel with a gradient elution from 10% ether/pentane to 50% ether/pentane to afford 12.61 g (67% over the three steps) of the desired alcohol product **7**. The spectral data for the mixture of cis and trans isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.36–7.17 (m, 5 H), 6.38 (d, 0.66 H, J = 15.8 Hz, C_7 vinyl protons in the trans isomer), 6.42 (d, 0.33 H, J = 11.7 Hz, C_7 vinyl proton in the cis isomer). 6.22 (dt, 0.66 H, J_d = 15.8 Hz, J_t = 6.9 Hz, C_6 vinyl proton in the trans isomer), 5.68 (dt, 0.33 H, J_d = 11.7 Hz, J_t = 7.3 Hz, C_6 vinyl proton in the cis isomer), 3.64 (t, 2 H, J = 6.7 Hz, protons for the cis isomer are buried underneath the trans), 2.35 (app qd, 0.67 H, J_q = 7.2 Hz, J_s = 1.8 Hz, C_5 methylene protons in the cis isomer), 2.22 (app q, 1.33 H, J = 6.7 Hz, C_5 methylene protons in the trans isomer), 1.64–1.35 (m. 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 138.3, 133.3, 131.3, 130.4, 129.4, 129.2, 129.0, 128.6, 127.3, 126.9, 126.4, 63.2, 33.1, 32.8, 32.7, 29.9, 29.3, 28.6, 25.5, 25.4; IR (neat/NaCl) 3346 br, 3081, 3056, 3024, 2930, 2856, 1598, 1494, 1473, 1410, 1379, 1351, 1071, 1054, 1029, 1004

cm^{-1}; GC/MS (30 eV) *m/e* (rel intensity) peak 1 190 (M^+, 4), 130 ($M^+ - C_3H_7O$, 16), 129 (20), 117 ($M^+ - C_4H_9O$, 58), 115 (39), 104 ($M^+ - C_5H_{10}O$, 100), 92 (22), 91 (61), 85 (28), 81 (32), 55 (22), peak 2 190 (4), 130 (16), 129 (21), 117 (58), 115 (40), 104 (100), 92 (22), 91 (6), 85 (27), 81 (32), 55 (17); HRMS (EI) *m/e* calcd for $C_{13}H_{18}O$ 190.1358, found 190.1335. Anal. Calcd for $C_{13}H_{18}O$: C, 82.04; H, 9.55. Found: C, 82.15; H, 9.57.

(*E* and *Z*)-7-Phenyl-6-heptenal. To a −78 °C solution of 5.18 g (30.6 mmol) of alcohol **7** and 4.77 g (61.1 mmol) of dimethyl sulfoxide in 300 mL of dichloromethane was added 4.26 g (33.6 mmol) of oxalyl chloride. The reaction was stirred for 15 min and then warmed to −50 to −60 °C for 15 min before 15.46 g (152.8 mmol) of triethylamine was added. The reaction was allowed to warm to room temperature, 100 mL of water added, and the dichloromethane removed with the use of a rotary evaporator. The aqueous layer was extracted three times with ether, and then the combined ether layers were washed with saturated sodium chloride, dried over sodium sulfate, and concentrated in vacuo. The aldehyde was chromatographed through ca. 200 g of silica gel with 10% ether/pentane as eluant to afford 5.08 g (88%) of the desired aldehyde. The spectral data for the mixture of olefin isomers are as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 9.69 (t, 0.65 H, J = 0.9 Hz, aldehyde proton in the trans isomer), 9.65 (t, 0.35 H, J = 0.9 Hz, aldehyde proton in the cis isomer), 7.36–7.12 (m, 5 H), 6.36 (d, 0.35 H, J = 12.1 Hz, C_7 vinyl proton in the cis isomer), 6.31 (d, 0.65 H, J = 16.1 Hz, C_7 vinyl proton in the trans isomer), 6.12 (dt, 0.65 H, J_d = 15.9 Hz, J_t = 6.9 Hz, C_6 vinyl proton in the trans isomer), 5.56 (dt, 0.35 H, J_d = 11.6 Hz, J_t = 7.3 Hz, C_6 vinyl proton in the cis isomer), 2.40–2.23 (m, 0.7 H, C_5 methylene protons in the cis isomer), 2.12 (app q, 1.3 H, J = 6.9 Hz, C_5 methylene protons in the trans isomer), 1.66–1.38 (m, 4 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 203.3, 138.2, 132.6, 130.8, 130.6, 129.8, 129.2, 129.0, 128.6, 127.4, 126.4, 43.9, 43.8, 32.8, 29.4, 28.9, 28.3, 21.7, 21.6; IR (neat/NaCl) 3081, 3057, 3025, 2932, 2858, 2720, 1725, 1493, 1459, 1448, 1408, 1389 cm^{-1}; GC/MS (EI) *m/e* (rel intensity) peak 1 188 (M^+, 5), 129 ($M^+ - C_3H_5O$, 29), 117 ($M^+ - C_4H_7O$, 80), 115 (56), 104 ($M^+ - C_5H_8O$, 53), 97 (30), 91 (C_7H_7, 100), 84 (94), 83 (24), 57 (25), 55 (22), peak 2 188 (4), 129 (25), 117 (62), 115 (47), 105 (32), 104 (41), 91 (100), 85 (89), 84 (27), 79 (26), 67 (25); HRMS (EI) *m/e* calcd for $C_{13}H_{16}O$ 188.1201, found, 188.1214.

1-Methoxy-8-phenyl-1,7-octadiene (8). To a 0 °C solution of 22.28 g (62.3 mmol) of (methoxymethyl)triphenylphosphonium chloride in 30 mL of tetrahydrofuran was added 25.6 mL (64.0 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The reaction was stirred for 30 min, and then 4.08 g (21.7 mmol) of aldehyde in 300 mL of tetrahydrofuran was added over a period of 4 h. The reaction was allowed to warm to room temperature and stirred for 16 h. When complete, the reaction was diluted with ether and water. The layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were washed two times with saturated sodium chloride, dried over sodium sulfate, and concentrated in vacuo. The crude product was chromatographed through 150 g of silica gel with 1% ether/hexane as eluant and then distilled with the use of a Kugelrohr apparatus to afford 2.96 g (63%) of the desired enol ether. The spectral data for the mixture of four olefin isomers are as follows: ^1H NMR ($CDCl_3$/300 MHz) 7.35–7.16 (m, 5 H), 6.42–6.12 (m, 2 H), 5.87 (m, 0.5 H), 5.66 (app dtd, 0.5 H, J_d = 11.7 Hz, J_t = 7.3 Hz, J_d = 1.7 Hz), 4.77–4.65 (m, 0.5 H), 4.37–4.29 (m, 0.5 H), 3.57, 3.55, 3.50, 3.48 (four s, 3 H), 2.37–1.87 (four m, total 4 H), 1.57–1.31 (m, 4 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.6, 146.6, 138.4, 138.3, 138.2, 133.7, 133.5, 131.6, 131.4, 130.3, 130.2, 129.2, 129.1, 128.9, 128.8, 128.6, 127.2, 127.18, 126.9, 126.4, 107.2, 103.2, 59.6, 56.0, 33.0, 30.5, 30.4, 29.7, 29.6, 29.5, 29.4, 29.0, 28.8, 28.6, 28.5, 27.7, 27.6, 23.8; IR (neat/NaCl) 3080, 3056, 3025, 3006, 2928, 2854, 1664, 1655, 1494, 1459, 1448, 1390, 1261, 1209, 1132 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 217 ($M^+ + 1$, 7), 216 (M^+, 4), 185 ($M^+ - CH_3O$, 48), 143 ($M^+ - C_4H_9O$, 30), 135 (21), 129 (29), 121 (23), 117 (100), 91 (55), 81 (32), 71 (87); HRMS (EI) *m/e* calcd for $C_{15}H_{20}O$ 216.1514, found 216.1519. Anal. Calcd for $C_{15}H_{20}O$: C, 83.27; H, 9.34. Found: C, 83.27; H, 9.30.

Electrolysis of Compound 8: Synthesis of 2-(Methoxyphenylmethyl)-cyclohexane-1-carboxaldehyde (11 and 12). To a 100-mL round-bottom flask (24/40 joint) were added 0.271 g (1.25 mmol) of compound **8**, 0.73 mL (6.26 mmol) of 2,6-lutidine, and 50 mL of a 1 M lithium perchlorate in 15% methanol/acetonitrile electrolyte solution. The flask was fitted with a two-holed rubber stopper with a needle "pushed through it" as a nitrogen inlet. Two carbon rod electrodes were placed into the reaction solution through the two-holed rubber stopper. The reaction was degassed by bubbling nitrogen through the solution and then electrolyzed at a constant current of 11.6 mA. After 30 C of charge had been passed, the cathode was replaced with a new carbon rod due to deposits on the original electrode. A total of 270.5 C (2.25 faradays) of charge was passed through the cell. When complete, the reaction was diluted with ether and water. The layers were separated, and the ether layer was washed once with 30 mL of a 0.2 M hydrochloric acid in water solution. The combined aqueous layers were extracted three times with ether. The combined ether layers were then washed with brine, dried over $MgSO_4$, concentrated in vacuo, and carried on to the next step.

The crude cyclic acetals were placed in a 25-mL round-bottom flask. To the flask were added 1.63 g (6.5 mmol) of pyridinium *p*-toluenesulfonate and 25 mL of acetone. The reaction was stirred at room temperature for 16 h and diluted with ether and water, and then the layers were separated. The aqueous layer was extracted three times with ether, and then the combined organic layers were washed with brine, dried over $MgSO_4$, concentrated in vacuo, and carried on to the next step.

The crude cyclic aldehydes were placed in a 25-mL round-bottom flask along with 0.57 g (3.75 mmol) of diazabicyclo[5.4.0]undec-7-ene and 10 mL of dichloromethane. The reaction was stirred for 16 h and then diluted with water and ether, the layers were separated, and the organic layer was washed with a 0.2 M hydrochloric acid in water solution. The aqueous layer was extracted three times with ether. The combined organic layers were then washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was chromatographed through silica gel and a gradient elution from pentane to 20% ether/pentane as eluant to afford 0.168 g (58% over the three steps) of the cyclized products **11** and **12** in a 2.8:1 ratio. In addition, 3% of the cyclized acetal product was recovered. Upon more careful chromatography, isomers **11** and **12** could be separated. The spectral data for compound **11** are as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 9.50 (d, 1 H, J = 5.4 Hz), 7.39–7.23 (m, 5 H), 3.69 (d, 1 H, J = 9.0 Hz), 3.04 (s, 3 H), 2.12 (m, 1 H), 1.98 (m, 1 H), 1.81–1.58 (m, 3 H), 1.44–1.03 (m, 4 H), 0.90–0.77 (m, 1 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 203.5, 140.6, 128.8, 128.4, 128.1, 88.9, 56.1, 55.6, 44.9, 27.4, 26.4, 25.1, 24.8; IR (neat/NaCl) 2930, 2856, 2822, 2716, 1721, 1693, 1493, 1449, 1232, 1137, 1110, 1094, 1085, 1070 cm^{-1}; GC/MS (70 eV) *m/e* (rel intensity) 232 (M^+, 1), 129 (14), 122 (42), 121 (100), 118 (14), 115 (15), 91 (69), 81 (21), 77 (60); HRMS (EI) *m/e* calcd for $C_{15}H_{20}O_2$ 232.1457, found 232.1463. Anal. Calcd for $C_{15}H_{20}O_2$: C 77.53; H, 8.69. Found: C, 77.26; H, 8.92. The spectral data for compound **12** are as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 9.55 (d, 1 H, J = 4.0 Hz), 7.38–7.21 (m, 5 H), 4.22 (d, 1 H, J = 4.2 Hz), 3.20 (s, 3 H), 2.34–2.24 (m, 1 H), 2.13–2.03 (m, 1 H), 1.73–1.55 (m, 4 H), 1.37–1.05 (m, 4 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 205.2, 139.7, 128.6, 128.0, 85.7, 57.3, 51.2, 43.7, 26.2, 25.4, 25.2, 24.8; IR (neat/NaCl) 2930, 2856, 2824, 2803, 1722, 1451, 1374, 1362, 1195, 1190, 1125, 1105, 1074, 1029 cm^{-1}; GC/MS (70 eV) *m/e* (rel intensity) 232 (M^+, 1), 129 (9), 122 (27), 121 (100), 115 (10), 105 (16), 104 (15), 96 (10), 91 (49), 81 (13), 77 (42); HRMS (EI) *m/e* calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1460. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.53; H, 8.69. Found: C, 77.64, H, 8.64.

The cyclization of **8** could also be accomplished with a reticulated vitreous carbon anode and a 0.4 M lithium perchlorate in 20% methanol/dichloromethane electrolyte solution. All other conditions were the same. In this way, 0.231 g (1.07 mmol) of enol ether was electrolyzed (12.4 mA/210.6 C/2.04 faradays) and then treated with PPTS in acetone followed by DBU in dichloromethane to afford 0.161 g (65% over the three steps) of the desired cyclic aldehydes **11** and **12**. The ratio of **11**:**12** was ca. 2:1.

(*E*,*Z*)-1-Methoxy-7-methyl-1,6-octadiene (13a). To a −78 °C solution of 4.03 g (51.6 mmol) of dimethyl sulfoxide and 3.30 g (25.8 mmol) of 6-methyl-5-hepten-1-ol[21] was added 4.91 g (38.7 mmol) of oxalyl chloride. The reaction was stirred at −78 °C for 15 min, 13.0 g (128.9 mmol) of triethylamine added, and then the reaction stirred at −78 °C for an additional 5 min. The reaction was allowed to warm to room temperature, quenched with ether and water, and the layers were separated. The aqueous layer was extracted with ether, and the combined organic layers were washed with water, dried over $MgSO_4$, and concentrated in vacuo. The crude reaction product was carried on directly to the next reaction.

To a 0 °C solution of 26.5 g (77.3 mmol) of (methoxymethyl)triphenylphosphonium chloride in 180 mL of tetrahydrofuran was added 31 mL (77.3 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The reaction was stirred at 0 °C for 40 min, and then a solution of the crude aldehyde synthesized above in 50 mL of tetrahydrofuran was added. The reaction was warmed to room temperature and allowed to stir overnight. The reaction was quenched with ether and water, the layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated in vacuo. The material was chromatographed through silica gel with hexane as eluant to afford 3.07 g (77%) of the purified enol ether. The spectral data for the mixture of olefin isomers are as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.29 (dt, 0.5 H, J_d = 12.6 Hz, J_t = 1.2 Hz,

(21) Kinney, R. J.; Jones, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 7902.

vinyl proton at C_1 for the trans isomer), 5.88 (dt, 0.5 H, J_d = 6.3 Hz, J_t = 1.5 Hz, vinyl proton at C_1 for the cis isomer), 5.12 (m, 1 H, vinyl proton at C_6 for both isomers), 4.73 (dt, 0.5 H, J_d = 12.6 Hz, vinyl proton at C_2 of the trans isomer), 4.34 (dt, 0.5 H, J_d = 6.6 Hz, J_t = 7.2 Hz, vinyl proton at C_2 of the cis isomer), 3.58 (s, 1.5 H, methoxy of the cis isomer), 3.51 (s, 1.5 H, methoxy of the trans isomer), 1.99 (m, 4 H), 1.69 (s, 3 H), 1.60 (s, 3 H), 1.37 (app p, 2 H, J = 7.5 Hz); IR (neat/NaCl) 3056, 3032, 2926, 2855, 1657, 1452, 1390, 1377, 1262, 1210, 1134, 1112, 934, 738 cm^{-1}; GC/MS (35 eV) m/e (rel intensity) for the cis isomer, 154 (M^+, 2), 139 (M^+ - Me, 1), 122 (M^+ - MeOH, 30), 111 (139 - CO, 23), 107 (122 - Me, 81), 97 (59), 86 (69), 84 (53), 81 (42), 79 (35), 71 (100), 69 (47), 67 (45), 55 (74); for the trans isomer, 154 (1), 139 (<1), 122 (18), 111 (14), 107 (51), 97 (43), 86 (52), 84 (40), 81 (35), 79 (28), 71 (100), 69 (41), 67 (40), 55 (69); HRMS (EI) m/e calcd for $C_{10}H_{18}O$ 154.1357, found 154.1358. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87: H, 11.76. Found: C, 77.74; H, 11.85.

Electrolysis of Compound 13a: Synthesis of 2-(1-Methoxy-1-methylethyl)cyclopentane-1-carboxaldehyde Dimethyl Acetal (14a) and 2-(1-Methyldeneethyl)cyclopentane-1-carboxaldehyde Dimethyl Acetal (15a). To the cathodic chamber of a standard "H" cell was added 6.5 mL of a 1 M lithium perchlorate in methanol electrolyte solution. The anodic chamber was charged with 5 mL of the electrolyte solution, 1.05 g (9.81 mmol) of 2,6-lutidine, and 0.151 g (0.98 mmol) of the starting enol ether. The chambers were degassed with a stream of nitrogen, and then the anode was equipped with a platinum foil (1 cm × 0.5 cm) electrode and the cathode equipped with a platinum wire electrode. The reaction was electrolyzed at a constant current of 12.3 mA until no starting material remained by TLC analysis (236 C/2.5 faradays). When complete, the anolyte was transferred to a separatory funnel, diluted with 30 mL of ether, and washed with saturated ammonium chloride, water, and brine. The organic layer was dried over $MgSO_4$ and carefully concentrated in vacuo. The solvent was removed on a rotary evaporator equipped with a manometer. At no time was the pressure in the system allowed to fall below 150 mm. When the pressure fell to 150 mm, nitrogen or air was let into the system and then the pressure reduced again. All of the solvent in the reaction could be removed by repeating this process several times. The crude product was chromatographed through silica gel with 10% ether/30–60 petroleum ether as the eluant to afford 0.128 g (60%) of the ether product **14a** and 0.030 g (17%) of the olefinic product **15a**. The spectral data for **14a** are as follows (a 2:1 mixture of trans to cis acetals was obtained): ^1H NMR ($CDCl_3$/300 MHz) δ 4.61 (d, 0.33 H, J = 4.5 Hz, acetal methine proton in the cis isomer), 4.21 (d, 0.66 H, J = 5.0 Hz, acetal methine proton in the trans isomer), 3.39 (s, 4 H, acetal methoxy protons in the trans isomer), 3.37 (s, 1 H, acetal methoxy protons in the cis isomer), 3.36 (s, 1 H, acetal methoxy protons in the cis isomer), 3.22 (s, 1 H, methoxy ether in the cis isomer), 3.19 (s, 2 H, methoxy ether in the trans isomer), 2.27 (m, 0.33 H, bridgehead methine in the cis isomer), 2.14 (m, 0.66 H, bridgehead methine in the trans isomer), 2.07 (m, 0.66 H, bridgehead methine in the trans isomer), 1.91 (m, 0.33 H, bridgehead methine in the cis isomer), 1.75–1.45 (m, 6 H), 1.24 (s, 1 H, methyl group in the cis isomer), 1.19 (s, 1 H, methyl group in the cis isomer), 1.11 (s, 4 H, methyls of the trans isomer); IR (neat/NaCl) 2948 br, 2827, 1466, 1381, 1364, 1241, 1190, 1117, 1078, 939, 924, 910 cm^{-1}. The acetals quickly "fell apart" to give rise to a cis/trans mixture of aldehydes. The spectral data of the aldehydes are as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 9.61 (d, 0.66 H, J = 2.9 Hz, aldehyde proton in the trans isomer), 9.58 (d, 0.33 H, J = 5.7 Hz, aldehyde proton in the cis isomer), 3.17 (s, 2 H, methoxy protons of the trans isomer), 3.12 (s, 1 H, methoxy protons of the cis isomer), 2.73 (m, 1 H, bridgehead methine for both the cis and trans isomers), 2.42 (app. q, 0.66 H, bridgehead methine proton in the trans isomer), 2.15 (m, 0.33 H, bridgehead methine proton in the cis isomer), 1.95–1.45 (m, 6 H), 1.25 (s, 1 H, methyl group in the cis isomer), 1.16 (s, 1 H, methyl group in the cis isomer), 1.13 (s, 2 H, methyl group in the trans isomer), 1.11 (s, 2 H, methyl group in the cis isomer); IR (neat/NaCl) 2958 br, 2872, 2828, 1722, 1450, 1380, 1370. 1124, 1075 cm^{-1}. Mass spectral data were taken on the 2,4-DNP derivative of the aldehyde: LRMS (PCI) m/e (rel intensity) 351 (M^+ + 1, 100), 350 (M^+, 2), 319 (M^+ - OMe, 54), 318 (M^+ - MeOH, 6), 255 (57), 184 (16), 139 (21), 121 (23), 109 (53), 73 (60), 57 (39). 55 (39); HRMS (EI) m/e calcd for $C_{16}H_{22}N_4O_5$ 350.1585, found 350.1589. The spectral data for **15a** were as follows (a 4:1 mixture of trans to cis acetals was formed): ^1H NMR ($CDCl_3$/300 MHz) δ 4.81 (narrow m, 0.2 H, vinyl proton in the minor isomer), 4.74 (narrow m, 0.8 H, vinyl proton in the major isomer), 4.72 (narrow m, 1 H, vinyl protons in both isomers), 4.15 (d, 0.8 H, J = 6.1 Hz, acetal methine proton in the major isomer), 4.10 (d, 0.2 H, J = 7.6 Hz, acetal methine proton in the minor isomer). 3.37 (s, 2.4 H, methoxy protons in the major isomer), 3.32 (s, 2.4 H, methoxy protons in the major isomer), 3.30 (s, 0.6 H, methoxy protons in the minor isomer), 3.29 (s, 0.6 H, methoxy protons in the minor isomer), 2.36 (m, 1 H, bridgehead methine protons in both isomers), 2.12 (m, 1 H, bridgehead methine protons in both isomers), 1.78 (s, 0.6 H, allylic methyl in the minor isomer), 1.72 (s, 2.4 H, allylic methyl in the major isomer), 1.80–1.55 (m, 6 H); IR (neat/NaCl) 3086, 2988 br, 2875, 2847, 1455, 1377, 1195, 1124, 1061, 977, 885 cm^{-1}; GC/MS (35 eV) m/e (rel intensity) for the first isomer 152 (M^+ - MeOH, 10), 137 (152 - CH_3, 16), 121 (12), 101 (10), 95 (13), 93 (12), 79 (15), 75 (100), 71 (10), for the second isomer 152 (1), 137 (3), 127 (1), 121 (3), 101 (10), 95 (9), 84 (7), 79 (9), 75 (100), 71 (9), 69 (12); HRMS (EI) m/e calcd for $C_{11}H_{20}O_2$ 184.1463, found 184.1463.

(*E*,*Z*)-1-Phenyl-7-methyl-1,6-octadiene (13b). To a stirred −78 °C solution of 1.22 g (15.6 mmol) of dimethyl sulfoxide and 1.00 g (7.8 mmol) of 6-methyl-5-hepten-1-ol in 27 mL of dichloromethane was added 1.49 (11.7 mmol) of oxalyl chloride. The reaction was stirred at −78 °C for 20 min, and then 3.95 g (39.0 mmol) of triethylamine was added. The reaction was stirred for an additional 5 min at −78 °C before being allowed to warm to room temperature. The reaction was diluted with ether and water, the layers were separated, and the aqueous phase was extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The aldehyde product was used in the Wittig reaction without further purification.

Sodium hydride (0.52 g of 80% dispersion in oil, 17.2 mmol) was placed in a round-bottom flask and washed with hexane. The flask was charged with 20 mL of dimethyl sulfoxide. The mixture was heated until no solid sodium hydride was visible and the evolution of hydrogen stopped. The resulting dark blue solution was cooled to room temperature and added to 5.27 g (15.6 mmol) of benzyltriphenylphosphonium bromide in 30 mL of dimethyl sulfoxide. The mixture was stirred for 30 min, and then 0.98 g (7.8 mmol, assuming all of the product from the previous reaction was aldehyde) of aldehyde in 8 mL of dimethyl sulfoxide was added. After 2 h at room temperature, the reaction was quenched with water and ether, the layers were separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with saturated sodium chloride, dried over $MgSO_4$, and concentrated in vacuo. The crude material was chromatographed through silica gel with 100% 30/60 petroleum ether as the eluant to afford 0.93 g (60%) of the desired diene product. An inseparable mixture of cis and trans isomers was obtained. The spectral data for the mixture are as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 7.35–7.16 (m, 5 H), 6.41 (d, 0.5 H, J = 11.7 Hz, vinyl proton at C_1 of the cis isomer), 6.38 (d, 0.5 H, J_d = 16 Hz, vinyl proton of C_1 of the trans compound), 6.22 (dt, 0.5 H, J_d = 16 Hz, J_t = 7.0 Hz, vinyl proton at C_2 of the trans compound), 5.66 (dt, 0.5 H, J_d = 11.7 Hz, J_t = 7.2 Hz, vinyl proton at C_2 of the cis compound), 5.13 (br q, 1 H, J = 5.1 Hz, vinyl proton at C_6 in both isomers), 2.33 (app qd, 1 H, J_q = 7.2 Hz, J_d = 1.8 Hz, methylene protons at C_3 of the cis isomer), 2.20 (app q, 1 H, J = 6.9 Hz, methylene protons at C_3 of the trans isomer), 2.02 (app p, 2 H, methylene protons at C_5 for both isomers), 1.70 and 1.60 (two s, total 3 H, allylic methyls of the cis isomer), 1.67 and 1.58 (two s, total 3 H, allylic methyls of the trans isomer), 1.49 (m, 2 H, methylene protons at C_4 in both isomers); IR (neat/NaCl) 3102, 3082, 3057, 3025, 3009, 2965, 2923, 2856, 1599, 1494, 1447, 1376, 980, 963, 743, 730, 694 cm^{-1}; GC/MS (35 eV) m/e (rel intensity) trans isomer 201 (M^+ + 1, 1), 200 (M^+, 6), 157 (84), 131 (20), 130 (54), 129 (100), 117 (57), 115 (78), 109 (20), 96 (53), 91 (74), cis isomer 200 (M^+, 2), 157 (29), 130 (41), 129 (79), 117 (50), 115 (63), 109 (17), 96 (64), 91 (100), 81 (62), 67 (82), 55 (79); HRMS (EI) m/e calcd for $C_{15}H_{20}$ 200.1565, found 200.1556.

Electrolysis of Compound 13b: Synthesis of 1-(Methoxyphenylmethyl)-2-(1-methoxy-1-methylethyl)cyclopentene (14b), 1-(Methoxyphenylmethyl)-2-(1-methylideneethyl)cyclopentane (15b), and 1,2-Dimethoxy-7-methyl-1-phenyl-6-octene (16b). The electrolysis of compound **13b** was conducted under conditions identical with those used for the electrolysis of compound **13a** described above. Under these conditions, 0.19 g (0.97 mmol) of the starting styrene compound was electrolyzed. The crude product was chromatographed through silica gel with a gradient elution from hexane to 3% ether/hexane to afford 0.038 g (15%) of compound **14b**, 0.012 g (5%) of **15b**, and 0.065 g (25%) of **16b**. The spectral data are as follows. **14b** (the material was obtained as a mixture of two inseparable isomers): ^1H NMR ($CDCl_3$/300 MHz) δ 7.36–7.22 (m, 5 H, phenyl protons), 4.25 (d. 0.5 H, J = 4.5 Hz, benzylic methine proton of one isomer), 3.90 (d, 0.5 H, J = 7.5 Hz, benzylic methine proton of the second isomer), 3.26, 3.21, 3.16, 3.14 (four s, 6 H), 2.21 (m, 2.5 H), 2.02 (m, 0.5 H), 1.9–1.3 (br m, 6 H), 1.16, 1.09, 1.06, 0.99 (four s, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz), 142.7, 141.6, 128.4, 128.3, 128.2, 128.1, 127.5, 127.1, 87.6, 85.8, 77.3, 77.2, 65.8, 57.3, 56.8, 49.6, 48.9, 48.7. 48.5, 48.4, 47.1, 29.4, 28.6, 27.9, 26.9, 25.4, 25.3, 23.1, 22.8, 22.0, 15.0: IR (neat/NaCl) 3085, 3062, 3027, 2945 br, 2823, 1240, 1205, 1189, 1125, 1100, 1092, 1071, 762 cm^{-1}; HRMS (EI) m/e calcd for $C_{16}H_{22}O$ (M^+ - MeOH) 230.1671, found 230.1669. **15b** (the reaction led to a very small amount of a mixture of olefinic products; three of the

isomers were isolated as a mixture in the experiment described): ^{1}H NMR ($CDCl_3$/300 MHz) (for the mixture of isomers) δ 4.9–4.6 (series of br s, 2 H, vinyl protons), 4.11, 4.06, 4.01 (three d, total of 1 H, J = 5.4 Hz, J = 4.5 Hz, J = 6.3 Hz, respectively), 3.23, 3.17, 3.12 (three s, 3 H), 2.5 (app q, 0.5 H, J = 9 Hz, bridgehead methine proton for one of the isomers), 2.4–2.2 (m, 1.5 H), 2.02 (m, 0.5 H), 1.9–1.45 (br m) 1.75, 1.73, 1.61 (three s, total 3 H); IR (neat/NaCl) (for the mixture) 3080, 3020, 2950, 2928, 2868, 2822, 1452, 1104, 1088, 701 cm^{-1}; GC/MS (30 eV) *m/e* (rel intensity) for isomer one 230 (M^+, 1), 198 (M^+ – MeOH, 2), 183 (1.5), 155 (2), 147 (2), 122 (18), 121 (100), 91 (13), 77 (9), for isomer 2 230 (1), 198 (1.5), 187 (1), 183 (1), 155 (2), 147 (5), 122 (8), 121 (100), 91 (11), 77 (6), for isomer 3 230 (22), 198 (21), 183 (100), 162 (36), 155 (48), 147 (57), 141 (32), 130 (49), 129 (60), 121 (4), 91 (40), 86 (22), 55 (20). **16b** (two isomers were obtained; data for isomer 1 are as follows): ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.39–7.27 (m, 5 H), 5.09 (m, 1 H), 3.26 and 3.23 (two s plus m, 7 H, methine proton at C_2 underneath the methoxy protons), 1.95 (app q, 2 H, J_{av} = 6.8 Hz), 1.66 and 1.57 (two s, 6 H), 1.6–1.3 (br m); IR (neat/NaCl) 3087, 3063, 3029, 2927 br, 2877, 2860, 2824, 1494, 1454, 1376, 1186, 1154, 1111, 1077, 761, 701, 601 cm^{-1}; GC/MS (30 eV) *m/e* (rel intensity) 230 (M^+ – MeOH, 0.5), 198 (230 – MeOH, 4), 165 (2), 159 (1), 155 (4), 141 (77), 122 (44), 121 (99), 111 (34), 110 (34), 109 (100), 99 (21), 91 (32), 81 (46), 71 (91), 67 (99), 55 (80); HRMS (EI) *m/e* calcd for $C_{16}H_{22}O$ (M^+ – MeOH) 230.1671, found 230.1668. The spectra for isomer 2 are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.38–7.27 (m, 5 H), 5.03 (m, 1 H), 4.16 (d 1 H, J = 6 Hz), 3.42 (s, 3 H), 3.32 (m, 1 H), 3.25 (s, 3 H), 1.88 (m, 2 H), 1.64 and 1.54 (two s, 6 H), 1.45–1.15 (m, 4 H); IR (neat/NaCl) 3100, 3060, 3020, 2927, 2876, 2862, 2823, 1453, 1153, 1123, 1101, 1066, 760, 702, 635 cm^{-1}.

7-Methyl-(*Z*)-1-(triisopropylsiloxy)-1,6-octadiene (17a). To a solution of 0.293 g (2.04 mmol) of 7-methyl-6-octenal and 0.317 (3.12 mmol) of triethylamine in 4 mL of benzene was added 0.705 g (2.3 mmol) of triisopropylsilyl triflate. The reaction was stirred for 16 h and then diluted with ether and water. The layers were separated, and the aqueous layer was extracted three times with ether. The combined organic layers were dried over sodium sulfate, concentrated in vacuo, and chromatographed through 75 g of silica gel packed with a 3% triethylamine in pentane solution. A gradient of pentane to 10% ether/pentane was used as eluant to afford 0.333 g (54%) of the desired triisopropylsilyl enol ether **17a**. The spectral data are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.28 (dt, 1 H, J_d = 5.7 Hz, J_t = 1.5 Hz), 5.14 (m, 1 H), 4.41 (app q, 1 H, J_q = 5.7 Hz). 2.10 (d, app q, 2 H, J_d = 1.4 Hz, $J_{q\,av}$ = 6 Hz), 1.99 (app q, 2 H, J_{av} = 7.3 Hz), 1.69 (s, 3 H), 1.60 (s, 3 H), 1.37 (app p, 2 H, J_{av} = 7.5 Hz), 1.13 (m, 3 H), 1.08 (d, 18 H, J = 5.4 Hz); IR (neat/NaCl) 3032, 2944 br, 2867, 1655, 1464, 1400, 1363, 1257, 1160, 1118, 1103, 1062, 1014, 996, 883, 685 cm^{-1}. Due to instability, the silyl enol ether product was cyclized without further characterization.

Electrolysis of Compound 17a. The electrolysis was conducted under conditions identical with those described above for the electrolysis of enol ether **13a**. In this manner, 0.084 g (0.29 mmol) of **17a** was electrolyzed by using a constant current of 10.2 mA until 75.8 C (2.7 faradays) of charge had been passed. After purification, the electrolysis afforded 0.030 g (48%) of the cyclized ether product **14** and 0.010 g (19%) of the cyclized olefinic product **15**. The spectral data for the products matched that obtained previously.

(*E* and *Z*)-7-Phenyl-(*Z*)-1-(triisopropylsiloxy)-1,6-heptadiene (17b). Compound **17b** was prepared in a fashion identical with that described above for the formation of enol ether **17a**. In this manner, 1.004 g (5.33 mmol) of (*E* and *Z*)-7-phenyl-6-heptenal was converted into 1.61 (87%) of the desired silyl enol ether. The material was obtained as a 2:1 mixture of *E*/*Z* isomers about the styrene. The spectral data for the mixture of styrene isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.38–7.20 (m, 5 H), 6.44–6.22 (m, 2.66 H, vinyl proton at C_6 of the trans isomer along with the vinyl protons at C_7 and C_1 in both isomers), 5.71 (dt, 0.33 H, J_d = 11.4 Hz, J_t = 7.5 Hz, vinyl proton at C_6 of the cis isomer), 4.40 (m, 1 H), 2.38 (app qd, 0.66 H, J_q = 7.2 Hz, J_d = 1.8 Hz, allylic methylene protons in the cis isomer), 2.24 (m, 3.33 H, allylic methylene protons in the trans isomer), 1.55 (m, 2 H), 1.11 (m, 3 H), 1.07 (d, 18 H, J_d = 5.5 Hz); IR (neat/NaCl) 3090, 3075, 3027, 2943 br, 2866, 1654, 1462, 1256, 1117, 1085, 1066, 1014, 996, 962, 883, 691 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 345 (M^+ + 1, 7), 301 (M^+ – C_3H_7, 8), 199 ($C_{11}H_{23}OSi$, 22), 171 ($C_{13}H_{15}$, 100), 157 ($C_9H_{21}Si$, 36), 145 ($C_{11}H_{13}$, 60), 131 (16), 117 (15), 91 (10), 57 (33), 56 (10), 55 (43); HRMS (EI) *m/e* calcd for $C_{22}H_{36}OSi$ 344.2535, found 344.2537.

Electrolysis of Compound 17b. A solution of 0.236 g (0.68 mmol) of enol ether **17b** in 15 mL of a 1 M lithium perchlorate in 50% methanol/tetrahydrofuran electrolyte solution was placed in an oven-dried three-neck flask and degassed by sonication. The flask was fitted with an nitrogen inlet, a platinum foil anode (1 cm × 0.5 cm), and a platinum wire cathode. The reaction mixture was electroyzed at a constant current of 13.5 mA until 232 C (3.5 faradays) of charge had been passed. When complete, the reaction was diluted with ether and water, the layers were separated, and the aqueous layer was extracted two times with ether. The combined organic layers were then washed with brine, dried over sodium sulfate, concentrated in vacuo, and chromatographed through 75 g of silica gel with a gradient elution from pentane to 20% ether/pentane. The reaction led to the formation of 0.090 g (57%) of the cyclized dimethyl acetal products **2** and **3** and 0.028 g (10%) of the methyl triisopropylsilyl acetal product **18b**. In addition, 9% of the starting material was recovered. Product **18b** could not be isolated in pure form; it was always contaminated with a small amount of a second isomer (about 10–20% based on the ^{1}H NMR integration of the triisopropylsilyl groups), as well as small amounts of some unidentified products. The major product was characterized by hydrolysis to the aldehyde, purification, and then comparison with the spectral data of the aldehyde derived from the trans major product **2b** (which was in turn characterized by X-ray crystallography on its 2,4-DNP derivative). The proton NMR data for the major triisopropylsilyl acetal obtained are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.40–7.20 (m, 5 H), 4.85 (d, 1 H, J = 7.5 Hz), 4.71 (d, 1 H, J = 5.07 Hz), 3.43 (s, 3 H), 3.42 (s, 3 H), 2.41 (m, 2 H), 1.60–1.33 (m, 6 H), 0.96 (m buried under a br s, 21 H).

(*E* and *Z*)-8-Phenyl-7-octen-1-ol. This compound was prepared in a three-step sequence that was identical with the one described previously for the preparation of compound **7**. After the three steps, 7.82 g (78%) of the desired alcohol was obtained. The spectral data for the mixture of olefin isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.35–7.15 (m, 5 H), 6.41 (d, 0.35 H, J = 11.7 Hz, C_8 vinyl proton in the cis isomer), 6.37 (d, 0.65 H, J = 15.6 Hz, C_8 vinyl proton in the trans isomer), 6.21 (dt, 0.65 H, J_d = 15.8 Hz, J_t = 6.7 Hz, C_7 vinyl proton in the trans isomer), 5.65 (dt, 0.35 H, J_d = 11.7 Hz, J_t = 7.3 Hz, C_7 vinyl proton in the cis isomer), 3.61 (t, 1.3 H, J = 6.6 Hz, C_1 methylene protons in the trans isomer), 3.58 (t, 0.7 H, J = 6.9 Hz, C_1 methylene protons in the cis isomer), 2.33 (app qd, 0.7 H, J_q = 7.4 Hz, J_d = 1.7 Hz, C_6 methylene protons in the cis isomer), 2.20 (app q, 1.3 H, J = 6.7 Hz, C_6 methylene protons in the trans isomer), 1.84 (br s, 1 H, OH proton), 1.60–1.30 (m, 8 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 138.3, 133.5, 131.4, 130.3, 129.3, 129.2, 128.9, 128.6, 126.9, 126.3, 63.1, 33.1, 32.8, 30.0, 29.4, 29.2, 29.1, 28.6, 25.72, 25.68; IR (neat/NaCl) 3353 br, 3081, 3058, 3024, 2930, 2923, 2855, 1598, 1493, 1462, 1447, 1072, 1055, 1038, 1028; GC/MS (PCI) *m/e* (rel intensity) peak 1 204 (M^+, 6), 203 (M^+ – 1, 6), 187 (M^+ – OH, 39), 159 (M^+ – C_2H_5O, 9), 145 (M^+ – C_3H_7O, 20), 132 (11), 131 (M^+ – C_4H_9O, 100), 119 (15), 117 (70), 105 (12), 104 (9), 91 (36), peak 2 204 (9), 203 (9), 187 (42), 1150 (10), 145 (19), 132 (12), 131 (100), 119 (15), 117 (69), 105 (12), 91 (35); HRMS (EI) *m/e* calcd for $C_{14}H_{20}O$ 204.1514, found 204.1511. Anal. Calcd for $C_{14}H_{20}O$: C, 82.28; H, 9.89. Found: C, 82.38; H, 9.97.

(*E* and *Z*)-8-Phenyl-7-octenal. The aldehyde was prepared by Swern oxidation of the corresponding alcohol using the procedure described above for the synthesis of (*E* and *Z*)-7-phenyl-6-heptenal. In this example, the 5.63 g (92%) of the aldehyde was obtained. The spectral data for the mixture of olefin isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 9.75 (t, 0.68 H, J = 1.8 Hz, aldehyde proton in the trans isomer), 9.72 (t, 0.32 H, J = 1.8 Hz, aldehyde proton in the cis isomer), 7.36–7.15 (m, 5 H), 6.42 (d, 0.32 H, J = 11.2 Hz, C_8 vinyl proton in the cis isomer), 6.38 (d, 0.68 H, J = 15.5 Hz, C_8 vinyl proton in the trans isomer), 6.20 (dt, 0.68 H, J_d = 15.8 Hz, J_t = 6.8 Hz, C_7 vinyl proton in the trans isomer), 5.64 (dt, 0.32 H, J_d = 11.6 Hz, J_t = 7.2 Hz, C_7 vinyl proton in the cis isomer), 2.44–2.28 (m, 2.64 H), 2.21 (app q, 1.36 H, J = 6.6 Hz), 1.70–1.29 (m, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 203.4, 138.2, 138.1, 133.1, 131.0, 130.5, 129.5, 129.2, 128.9, 128.6, 127.3, 126.9, 126.3, 44.0, 43.9, 32.9, 29.7, 29.2, 28.8, 28.7, 28.4, 22.0; IR (neat/NaCl) 3081, 3057, 3024, 2930, 2856, 2719, 1723, 1598, 1493, 1461, 1448, 1409, 1390 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) peak 2 203 (M^+ + 1, 11), 185 (M^+ + 1 – H_2O, 41), 143 (M^+ – C_3H_7O, 29), 131 (15), 129 (29), 119 (20), 117 (M^+ – C_5H_9O, 100), 107 (14), 98 (14), 91 (83), 81 (20), peak 2 203 (16), 185 (48), 143 (27), 131 (18), 129 (27), 123 (24), 119 (21), 117 (100), 105 (18), 91 (93), 81 (21); HRMS (EI) *m/e* calcd for $C_{14}H_{18}O$ 202.1358, found 202.1361.

(*Z*)-1-(*tert*-Butyldimethylsiloxy)-(*E* and *Z*)-8-phenyl-1,7-octadiene (17c). To a 0 °C solution of 3.53 g (17.4 mmol) of 8-phenyl-7-octenal and 2.64 g (26.1 mmol) of triethylamine in 35.7 mL of distilled benzene was added 5.04 g (19.2 mmol) of *tert*-butyldimethylsilyl triflate in a dropwise fashion. When complete by TLC, the reaction was diluted with 25 mL of ether and 50 mL of water. The layers were separated, and the aqueous layer was extracted three times with ether. The combined organic layers were washed with saturated sodium chloride, dried over sodium sulfate, and concentrated in vacuo. The crude product was chromatographed through 100 g of silica gel with a gradient elution from 100% pentane to 20% ether/pentane to afford 2.91 g (55%) of the desired silyl enol ether. Only the cis isomer was obtained for the enol ether. The

spectral data for the mixture of isomers (cis and trans about the styrene double bond) are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.34–7.13 (m, 5 H), 6.40–6.34 (m, 1 H), 6.23–6.14 (m, 1.5 H), 5.65 (dt, 0.5 H, J_d = 11.6 Hz, J_t = 7.3 Hz), 4.46–4.39 (m, 1 H), 2.38–2.06 (three m, total 4 H), 1.53–1.31 (m, 4 H), 0.93 and 0.92 (two s, 9 H), 0.12 and 0.11 (two s, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 139.0, 138.5, 138.4, 133.7, 131.6, 130.2, 129.2, 129.1, 128.9, 128.6, 127.2, 126.8, 126.4, 110.9, 33.0, 29.8, 29.5, 29.4, 29.1, 28.7, 25.8, 23.5, 18.4, −2.9, −5.4; IR (neat/NaCl) 3027, 2954, 2929, 2857, 1656, 1494, 1471, 1462, 1447, 1401, 1361, 1255, 1115, 1082, 1071, 963 cm^{-1}; LRMS (PCI) *m/e* (rel intensity) peak 1 317 (M^+ + 1, 68), 301 ($M^+ - CH_3$, 28), 259 ($M^+ - C_4H_9$, 57), 185 ($M^+ - C_6H_{15}OSi$, 86), 183 (19), 117 (58), 91 (20), 89 (100), 75 (35), 73 (39), peak 2 317 (26), 259 (35), 213 (14), 185 (80), 143 (14), 117 (54), 91 (18), 89 (100), 75 (29), 73 (31); HRMS (EI) *m/e* calcd for $C_{20}H_{32}OSi$ 316.2222, found 316.2221. Anal. Calcd for $C_{20}H_{32}OSi$: C, 75.87; H, 10.21. Found: C, 75.85; H, 10.33.

Electrolysis of Compound 17c. The electrolysis of **17c** was accomplished in a fashion identical with that described above for the conversion of enol ether **8** into cyclized products **11** and **12**. The conditions using a reticulated vitreous carbon anode and 20% methanol/dichloromethane as the solvent were employed. In this fashion, 0.644 g (2.03 mmol) of the enol ether was electrolyzed and then treated with PPTS in acetone followed by DBU in dichloromethane to afford 0.104 g (22% over the three steps) of compound **11** and 0.118 (25% over the three steps) of compound **12**. In addition, 0.105 g (16% over the three steps) of the cyclized product having a *tert*-butyldimethylsiloxy group at the benzylic carbon was obtained.

3,3-Dimethyl-7-(trimethylsilyl)-(*E* and *Z*)-5-hepten-1-ol (21b).[22] To a stirred suspension of 46.2 g (130 mmol) of methyltriphenylphosphonium bromide in 200 mL of tetrahydrofuran at 0 °C was added 58.0 mL (145 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The mixture was raised to room temperature, allowed to stir for 1 h, and then recooled to 0 °C. To this mixture was added (dropwise over 10 min) 27.7 g (130 mmol) of (iodomethyl)trimethylsilane. The mixture was again allowed to warm to room temperature. After 1 h, the reaction was cooled to −78 °C and treated with an additional 58 mL (145 mmol) of the 2.5 M *n*-butyllithium in hexane solution. The dark red solution was allowed to warm to room temperature and then stirred for 1.5 h. The solution was cooled to 0 °C and 7.5 g (58 mmol) of 2-hydroxy-4,4-dimethyltetrahydropyran in 50 mL of tetrahydrofuran added over a 20 min period. The mixture was allowed to slowly warm to room temperature and then stirred for 64 h. The reaction was quenched with 300 mL of saturated aqueous ammonium chloride and the aqueous layer extracted with ether (3 × 100 mL). The combined organic layers were washed with 100 mL of brine, dried over potassium carbonate, and concentrated in vacuo. The crude reaction product was taken up in 100 mL of hexane to precipitate the triphenylphosphine oxide and then filtered. The hexane was removed in vacuo. The material was chromatographed through 200 g of silica gel that was slurry-packed with a 10% ether/pentane solution containing 1% triethylamine. Gradient elution from 10% ether/pentane to 30% ether/pentane afforded 8.4 g (70%) of compound **21b** as a clear colorless oil. The spectral data for the 2.6:1 mixture of trans and cis isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.40–5.12 (m, 2 H), 3.69–3.64 (m, 2 H, C_1 methylene protons for both isomers), 1.89–1.84 (m, 2 H, C_4 methylene protons for both isomers), 1.53–1.39 (m, 4 H), 1.22, 1.20 (two br s, 1 H, OH proton for both isomers), 0.88 (s, 4.33 H, geminal methyl protons for the major isomer), 0.84 (s, 1.67 H, geminal methyl protons for the minor isomer), 0.03 (s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 129.1, 127.4, 125.0, 123.7, 59.8, 59.6, 45.7, 44.1, 39.2, 32.7, 32.6, 27.1, 22.6, 18.2, −2.0, −2.2; IR (neat/NaCl) 3346, 3012, 2929, 1645, 1469, 1418, 1384, 1365, 1248, 1152, 1054, 1028, 985, 853 cm^{-1}; GC/MS (EI) *m/e* (rel intensity) 214 (M^+, 1.6), 199 ($M^+ - CH_3$, 1.2), 181 (1.8), 157 (6.8), 127 ($M^+ - CH_2TMS$, 48), 109 (41), 101 (17), 95 (34), 81 (67), 75 (100), 73 (99); HRMS (EI) *m/e* calcd for $C_{12}H_{26}OSi$ 214.1753, found 214.1750. Anal. Calcd for $C_{12}H_{26}OSi$: C, 67.3; H, 12.2. Found: C, 67.3; H, 12.4.

7-(Trimethylsilyl)-(*E* and *Z*)-5-hepten-1-ol (21a). Compound **21a** was prepared from 2-hydroxytetrahydropyran in a fashion similar to that described above for the preparation of compound **21b**. In this experiment, the final reaction mixture was allowed to stir for 16 h. A 62% yield (13.8 g) of **21b** was obtained as a mixture of cis and trans isomers. In addition, the product was contaminated with approximately 12% of the desilated material. This impurity was separated after the next step in the synthetic sequence. The spectral data are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.45–5.20 (m, 2 H), 3.63 and 3.61 (two t, 2 H, *J* = 6.5 Hz, C_1 methylene protons for both isomers), 2.08–1.97 (m, 2 H, C_4 methylene protons for both isomers), 1.64–1.34 (m, 6 H), −0.04 and −0.06 (two s, 9 H); ^{13}C ($CDCl_3$/75 MHz) δ 128.6, 127.3, 126.6, 125.8, 62.7, 32.3, 32.2, 32.0, 26.5, 25.8, 25.6, 22.3, 18.2, −2.1, −2.4; IR (neat/NaCl) 3325, 3009, 2931, 1637, 1462, 1250, 1152, 1080, 851 cm^{-1}; GC/MS (EI) *m/e* (rel intensity) 186 (M^+, 0.3), 171 ($M^+ - CH_3$, 0.5), 129 (3), 113 ($M^+ - C_3H_9Si$, 0.4), 101 (1.2) 99 ($M^+ - C_4H_{11}Si$, 0.6), 81 (14), 73 (100), 67 (50); HRMS (EI) *m/e* calcd for $C_{10}H_{22}OSi$ 186.1440, found 186.1440.

3,3-Dimethyl-1-methoxy-8-(trimethylsilyl)-(*E*,*Z*)-1,6-octadiene (22). To a stirred solution of 8.2 g (24 mmol) of (methoxymethyl)triphenylphosphonium chloride in 50 mL of tetrahydrofuran at 0 °C was added dropwise 9.6 mL (24 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The resulting dark red solution was allowed to warm to room temperature and then stirred for 1.5 h. In a separate reaction flask, a stirred solution of 1.71 g (8.0 mmol) of alcohol **21b** and 1.28 g (16.6 mmol) of dimethyl sulfoxide in 80 mL of dichloromethane at −60 °C was treated with 2.21 g (17.4 mmol) of oxalyl chloride. The resulting mixture was stirred for 15 min and then quenched with 16.3 g (161 mmol) of triethylamine. The reaction mixture was allowed to warm to room temperature and then diluted with 100 mL of ether. The reaction was washed with water (2 × 100 mL), dried over potassium carbonate, and concentrated in vacuo. The crude Swern product was filtered through 10 g of silica gel with ether as the mobile phase. The product was concentrated a second time in vacuo, diluted with 8 mL of tetrahydrofuran, and added dropwise to a 0 °C solution of the ylide generated above. The resulting reaction mixture was allowed to warm to room temperature. After 16 h, the mixture was diluted with 100 mL of ether and washed with a saturated brine solution (3 × 100 mL). The aqueous fractions were combined and extracted two times (100 mL) with ether. The combined organic fractions were dried over potassium carbonate and concentrated in vacuo. The crude reaction mixture was diluted with pentane to precipitate the triphenylphosphine oxide, filtered, and concentrated in vacuo. The product was chromatographed through 150 g of silica gel that was slurry-packed with a 1% triethylamine in pentane solution. The column was eluted with pentane to afford 1.04 g (54%) of the desired enol ether **22**. The spectral data for the mixture of olefin isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.21 (d, 0.4 H, *J* = 13.0 Hz, vinyl proton at C_1), 5.92 (d, 0.6 H, *J* = 7.0 Hz, vinyl proton at C_1), 5.47–5.27 (m, 2 H, vinyl protons at C_6 and C_7), 4.70 (dt, 0.4 H, J_d = 12.6 Hz, J_t = 7.9 Hz, vinyl proton at C_2), 4.35 (app q, 0.6 H, *J* ca. 7 Hz, vinyl proton at C_2), 3.54 and 3.50 (two s, 3 H), 1.96–1.73 (m, 4 H), 1.44 (d, 1.5 H, *J* = 8.2 Hz, methylene protons at C_8), 1.40 (d, 0.5 H, *J* = 7.1 Hz, methylene protons at C_8), 0.83, 0.81, 0.79, 0.77 (four s, 6 H), −0.03 (s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 148.5, 147.3, 128.7, 128.5, 127.0, 126.8, 125.7, 125.4, 124.4, 124.1, 103.7, 99.5, 59.3, 55.9, 45.0, 44.9, 39.7, 38.5, 38.4, 35.7, 35.6, 34.0, 33.9, 26.4, 22.6, 18.2, 18.1, −2.0, −2.2; IR (neat/NaCl) 3011, 2965, 2899, 2870, 2833, 1664, 1653, 1465, 1436, 1418, 1390, 1382, 1363, 1248, 1211, 1152, 1135, 1110, 949, 936, 851, 716, 700 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 240 (M^+, 1), 225 ($M^+ - CH_3$, 42), 209 ($M^+ - CH_3O$, 9), 167 ($M^+ - C_3H_9Si$, 29), 137 (100), 135 ($M^+ - C_4H_{13}OSi$, 75), 105 (20), 95 (85), 89 (68), 73 (91); HRMS (EI) *m/e* calcd for $C_{14}H_{28}OSi$ 240.1909, found 240.1914.

6-Methyl-7-(trimethylsilyl)-(*E* and *Z*)-5-hepten-1-ol. This product was prepared in a fashion similar to that for **21b** by treating 2-hydroxytetrahydropyran with the ylide derived from ethyltriphenylphosphonium bromide. The reaction was allowed to stir for 16 h at room temperature. A vacuum distillation (91–94 °C, 0.1 Torr) using a 6-in. Vigreaux column afforded 10.4 g (52%) of the desired alcohol. The spectral data for the mixture of cis and trans products are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.98–4.88 (m, 1 H), 3.64–3.58 (m, 2 H), 2.01–1.86 (m, 2 H, allylic methylene protons at C_4), 1.63 (s, 1.5 H, allylic methyl protons for one isomer), 1.60–1.50 (m, 3.5 H, allylic methyl protons for one isomer plus a total of two methylene protons), 1.46 and 1.42 (two s, 2 H, methylene protons at C_7 for both isomers), 1.40–1.30 (m, 3 H, OH proton plus a total of two methylene protons), −0.01 and −0.04 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 133.4, 133.2, 122.4, 122.1, 62.9, 32.3, 32.2, 29.6, 28.0, 27.7, 26.0, 25.8, 23.0, 18.4, −1.0, −1.6; IR (neat/NaCl) 3329, 2935, 1652, 1436, 1248, 1069, 856 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 200 (M^+, 1.1), 185 ($M^+ - CH_3$, 9.3), 165 ($M^+ - CH_5O$, 1.6), 149 (3.9), 141 ($M^+ - C_3H_7O$, 3.1), 127 ($M^+ - C_3H_9Si$, 3.7), 113 ($M^+ - C_4H_{11}Si$, 3.6), 111 (25), 83 (14), 73 (37), 55 (100); HRMS (EI) *m/e* calcd for $C_{11}H_{24}OSi$ 200.1590, found 200.1594. Anal. Calcd for $C_{11}H_{24}OSi$: C, 66.00; H, 12.00. Found: C, 66.25; H, 12.14.

1-Methoxy-6-methyl-8-(trimethylsilyl)-(*E*,*Z*)-1,6-octadiene (23). To a 0 °C solution of 11.4 g (33.4 mmol) of (methoxymethyl)triphenylphosphonium chloride in 6.7 mL of tetrahydrofuran was added 13.4 mL (33.4 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The dark red reaction mixture was allowed to warm to room temperature and then stirred for 1 h. In a separate reaction flask, 1.16 g (9.2 mmol) of oxalyl chloride was added to a stirred solution of 1.67 g (8.4 mmol) of 6-

(22) The silyl-containing Wittig reagents were made by using the known procedure. (a) Seyfreth, D.; Worsthorn, K. R.; Mammarella, R. E. *J. Org. Chem.* **1977**, *42*, 3104. (b) Flemming, I.; Paterson, I. *Synthesis* **1979**, 445.

methyl-7-(trimethylsilyl)-5-hepten-1-ol and 0.78 g (10.0 mmol) of dimethyl sulfoxide in 3.5 mL of tetrahydrofuran at −40 °C. The reaction temperature was lowered to −60 °C and the reaction allowed to stir for 15 min. The reaction was quenched with 2.54 g (25 mmol) of triethylamine, warmed to room temperature, and stirred for an additional 5 min. The reaction mixture was diluted with 10 mL of tetrahydrofuran and filtered to remove the insoluble salts. The salts were washed with an additional 10 mL of tetrahydrofuran. The clear filtrate was then added to the ylide formed above at 0 °C. The reaction mixture was warmed to room temperature and stirred for 16 h. After this period, the reaction was diluted with 150 mL of ether, washed with saturated aqueous ammonium chloride (2 × 150 mL) and brine (100 mL), and concentrated in vacuo. The crude reaction mixture was taken up in hexane to precipitate triphenylphosphine oxide, filtered, concentrated in vacuo, and chromatographed through 100 g of silica gel packed with 1% triethylamine in hexane. The column was eluted with 100% hexane to afford 0.83 g (44%) of the desired cyclization substrate. The spectral data for the mixture of isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.26 (app dd, 0.6 H, J = 12.6 and 1.5 Hz, vinyl proton at C_1), 5.85 (m, 0.4 H, vinyl proton at C_1), 5.00–4.90 (m, 1 H, vinyl proton at C_6), 4.74–4.65 (m, 0.6 H, vinyl proton at C_2), 4.35–4.28 (m, 0.4 H, vinyl proton at C_2), 3.55 and 3.48 (two s, 3 H), 2.07–1.85 (m, 4 H), 1.63 and 1.56 (two s, 3 H), 1.47 and 1.43 (two s, 2 H, methylene protons at C_8), 1.33 (p, 2 H, J = 7.2 Hz, methylene protons at C_4), −0.01 and −0.03 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.2, 146.2, 133.2, 133.0, 132.9, 132.8, 122.7, 122.6, 122.4, 122.2, 107.1, 103.1, 59.4, 55.7, 31.1, 30.9, 30.2, 29.9, 29.6, 29.0, 27.7, 27.3, 27.1, 26.1, 23.5, 23.3, 22.9, 18.4, −0.99, −1.55; IR (neat/NaCl) 3027, 2952, 2854, 1664, 1656, 1456, 1439, 1259, 1248, 1210, 1112, 855 cm^{-1}; GC/MS (PCI) m/e (rel intensity) 226 (M^+, 24), 211 ($M^+ - CH_3$, 40), 179 ($M^+ - C_2H_7O$, 55), 123 (94), 122 ($M^+ - C_4H_{12}OSi$, 29), 109 (27), 95 (35), 89 (99.9), 73 (100); HRMS (PCI) m/e calcd for $C_{13}H_{26}OSi$ 226.1753, found 226.1747.

1-Tosyl-7-(trimethylsilyl)-(*E* and *Z*)-5-heptene. To a −15 °C solution of 7.1 g (38 mmol) of 7-(trimethylsilyl)-5-hepten-1-ol and 38 mL of dimethyl sulfoxide in 150 mL of tetrahydrofuran was added 16 mL (40 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The ice bath was removed and the reaction allowed to stir for 20 min at room temperature. The reaction temperature was lowered to 0 °C and 7.3 g (38 mmol) of *p*-toluenesulfonyl chloride in 75 mL of tetrahydrofuran added. The ice bath was removed and the reaction allowed to stir for 50 min at room temperature. The reaction mixture was diluted with 150 mL of ether and washed three times with 100 mL of water. The organic fraction was dried over potassium carbonate, concentrated in vacuo, and chromatographed through 100 g of silica gel packed with a 5% ether/pentane solution containing 1% triethylamine. After elution with 5% ether/pentane as the eluant, 8.0 g (62%) of the desired tosylate was isolated. (A 73% yield of tosylate was obtained when the reaction was done with 1 mmol of the starting alcohol.) The spectral data for the mixture of cis and trans isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.76 (d, 2 H, J = 8.4 Hz), 7.32 (d, 2 H, J = 7.9 Hz), 5.41–5.08 (m, 2 H), 3.99 (t, 2 H, J = 6.6 Hz), 2.41 (s, 3 H), 1.90 (app q, 2 H), 1.67–1.57 (m, 2 H), 1.39–1.30 (m, 4 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 144.8, 133.3, 129.9, 128.0, 127.8, 127.1, 126.5, 126.4, 70.5, 31.7, 28.2, 27.9, 25.9, 25.3, 25.1, 22.3, 21.4, 18.2, −2.2, −2.4; IR (neat/NaCl) 3014, 2954, 1598, 1362, 1245, 1188, 1175, 1097, 841 cm^{-1}.

8-(Trimethylsilyl)-(*E* and *Z*)-6-octenenitrile. This product was prepared from 1-tosyl-7-(trimethylsilyl)-5-heptene in a fashion similar to that reported below for the synthesis of 4,4-dimethyl-8-(trimethylsilyl)-(*E* and *Z*)-6-octenenitrile. In this example, 8.4 g (92%) of the desired product was obtained. The spectral data for the mixture of olefin isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.46–5.15 (m, 2 H), 2.31 and 2.30 (two t, 2 H, $J_1 = J_2$ = 7.0 Hz), 2.00 (app q, 2 H, J = 7.2 Hz), 1.70–1.36 (m, 6 H), −0.03 and −0.05 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 127.5, 126.8, 126.2, 119.9, 31.6, 28.6, 28.5, 25.9, 24.8, 24.5, 22.4, 18.3, 16.9, 16.7, −2.1, −2.3; IR (neat/NaCl) 3007, 2953, 2248, 1425, 1248, 1151, 856 cm^{-1}; GC/MS (EI) m/e (rel intensity) 195 (M^+, 0.2), 180 ($M^+ - CH_3$, 3.6), 154 ($M^+ - C_2H_3N$, 0.6), 140 ($M^+ - C_3H_5N$, 1.1), 127 ($M^+ - C_4H_7N$, 1.8), 113 ($M^+ - C_5H_8N$, 63), 100 (4.0), 73 (100); HRMS (EI) m/e calcd for $C_{10}H_{18}NSi$ ($M^+ - CH_3$) 180.1208, found 180.1190. Anal. Calcd for $C_{11}H_{21}NSi$: C, 67.69; H, 10.77; N, 7.18. Found: C, 67.58; H, 10.84; N, 7.15.

1-Methoxy-9-(trimethylsilyl)-(*E*,*Z*)-1,7-nonadiene (24). To a 0 °C solution of 2.95 g (15 mmol) of 8-(trimethylsilyl)-6-octenenitrile in 33 mL of benzene was added 37 mL (37 mmol) of a 1 M diisobutylaluminum hydride in hexane solution. The resulting solution was allowed to warm to room temperature and then stirred for 17 h. The reaction temperature was decreased to 0 °C and the reaction quenched with 15 mL of a 1:1 mixture of methanol and benzene. The reaction mixture was allowed to warm to room temperature, diluted with 50 mL of 30% sodium potassium tartrate (Rochelle's salt) and 150 mL of ether, and allowed to stir until two clear layers separated (ca. 1 h). The layers were separated, and the organic phase was washed three times with 30% sodium potassium tartrate (50 mL). The combined aqueous layers were extracted twice with ether (100 mL) and then the combined organic layers dried over potassium carbonate and concentrated in vacuo. The crude product was flash chromatographed through 75 g of silica gel packed with a 5% ether/pentane solution containing 1% triethylamine. The column was eluted with 5% ether/pentane to afford 2.44 g (82%) of the desired aldehyde. The aldehyde was *immediately* carried on to the enol ether formation step.

To a 0 °C solution of 13.0 g (38 mmol) of (methoxymethyl)triphenylphosphonium chloride in 75 mL of tetrahydrofuran was added 15.5 mL (39 mmol) of a 2.5 M *n*-butyllithium in hexane solution. The resulting red solution was warmed to room temperature and stirred for 1 h. The reaction temperature was again decreased to 0 °C and the aldehyde made above added in 12 mL of tetrahydrofuran. The reaction was warmed to room temperture and stirred for 64 h. The reaction was then quenched with 100 mL of a 40% sodium bisulfite solution and 250 mL of ether. The layers were separated, and the organic layer was then washed with 100 mL of 40% sodium bisulfite solution, washed with brine, and dried over potassium carbonate. The reaction mixture was concentrated in vacuo, the crude product vacuum distilled (70–72 °C, 0.1 Torr) through a 6-in. Vigreaux column to remove the triphenylphosphine oxide, and chromatographed through 50 g of silica gel packed with 1% triethylamine in pentane. The column was eluted with pentane to afford 1.53 g (55%) of the desired product as a clear, colorless oil. The spectral data for the mixture of olefin isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.26 (d, 0.45 H, J = 12.6 Hz, vinyl proton at C_1), 5.84 (d, 0.55 H, J = 6.1 Hz, vinyl proton at C_1), 5.41–5.15 (m, 2 H, vinyl protons at C_7 and C_8), 4.70 (dt, 0.45 H, J_d = 12.6 Hz, J_t = 7.3 Hz, vinyl proton at C_2), 4.31 (m, 0.55 H, vinyl proton at C_2), 3.55 and 3.47 (two s, 3 H), 2.05–1.88 (m, 4 H, methylene protons at C_3 and C_6), 1.43 (d, 2 H, J = 8.6 Hz, methylene protons at C_9), 1.38–1.30 (m, 4 H), −0.03, −0.05 (two s, 9 H); ^{13}C NMR ($CDCl_3$/300 MHz) δ 147.2, 146.2, 129.2, 129.0, 127.7, 126.1, 125.5, 125.4, 107.1, 103.2, 59.3, 55.7, 32.4, 30.3, 30.0, 29.4, 29.2, 29.1, 29.0, 27.4, 26.7, 23.5, 22.4, 18.2, −2.1, −2.3; IR (neat/NaCl) 3004, 2928, 2854, 1655, 1457, 1390, 1248, 1209, 1181, 1151, 1131, 1111, 933, 860 cm^{-1}; GC/MS (PCI) m/e (rel intensity) 226 (M^+, 0.8), 211 ($M^+ - CH_3$, 10), 153 ($M^+ - C_3H_9Si$, 2), 121 ($M^+ - C_4H_{13}OSi$, 17), 105 (5), 89 (49), 73 (100); HRMS (EI) m/e calcd for $C_{12}H_{23}OSi$ ($M^+ - CH_3$) 211.1518, found 211.1516.

3,3-Dimethyl-1-tosyl-7-(trimethylsilyl)-(*E* and *Z*)-5-heptene. To a solution of 4.20 g (19.6 mmol) of 3,3-dimethyl-7-(trimethylsilyl)-5-hepten-1-ol in 20 mL of pyridine was added 4.20 g (22.0 mmol) of *p*-toluenesulfonyl chloride. The reaction was allowed to stir at room temperature for 16 h and then diluted with ether (50 mL) and water (100 mL). The layers were separated, and the organic fraction was washed twice with water (100 mL), dried over potassium carbonate, concentrated in vacuo, and chromatographed through 150 g of silica gel packed with a 5% ether/hexane solution containing 1% triethylamine. The column was eluted with 5% ether/hexane to afford 5.2 g (72%) of the desired product. The spectral data for the mixture of cis and trans isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 7.77 (d, 2 H, J = 8.3 Hz), 7.32 (d, 2 H, J = 8.0 Hz), 5.46–5.14 (m, 2 H), 4.05 (t, 2 H, J = 7.5 Hz), 2.42 (s, 3 H), 1.82–1.77 (m, 2 H), 1.59–1.51 (m, 2 H), 1.37 (d, 1 H, J = 7.6 Hz, C_7 methylene protons for one isomer), 1.36 (d, 1 H, J = 8.4 Hz, C_7 methylene protons for the second isomer), 0.82, 0.78 (two s, 6 H), −0.05 and −0.06 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 144.8, 133.4, 129.9, 129.7, 128.0, 124.2, 122.9, 68.2, 45.4, 39.5, 32.7, 26.8, 22.7, 21.4, 18.2, −2.1, −2.2; IR (neat/NaCl) 3018, 2954, 1599, 1470, 1365, 1247, 1188, 962 cm^{-1}.

4,4-Dimethyl-8-(trimethylsilyl)-(*E* and *Z*)-6-octenenitrile. A solution of 2.45 g (50.0 mmol) of sodium cyanide and 10.8 g (29.3 mmol) of 3,3-dimethyl-1-tosyl-7-(trimethylsilyl)-5-heptene in 30 mL of dimethyl sulfoxide was allowed to stir for 16 h under nitrogen at room temperature. The reaction was diluted with 300 mL of ether, washed three times with water (150 mL), dried over potassium carbonate, and concentrated in vacuo. The crude material was chromatographed through 150 g of silica gel that was packed with a 7% ether/hexane solution containing 1% triethylamine. The column was eluted with 7% ether/hexane to afford 6.42 g (98%) of the desired nitrile product as a clear colorless oil. The spectral data for the mixture of olefin isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.55–5.15 (m, 2 H), 2.26–2.21 (m, 2 H), 1.86 (d, 1 H, J = 6.0 Hz, C_5 methylene protons for one isomer), 1.84 (d, 1 H, C_5 methylene protons for the second isomer), 1.62–1.44 (m, 2 H), 1.42 (d, 2 H, J = 8.8 Hz), 0.87 and 0.84 (two s, 6 H), −0.03 and −0.04 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 130.0, 128.2, 123.8, 122.5, 120.7, 44.6, 38.1, 36.7, 33.2, 26.1, 22.7, 18.3, 12.1, 12.0, −2.1, −2.2; IR (neat/NaCl) 3012, 2955, 2247, 1643, 1471, 1248, 1151, 855 cm^{-1}; GC/MS (70 eV) m/e (rel intensity) 223 (M^+, 0.4), 208 ($M^+ - CH_3$,

4.2), 180 (3.8), 167 ($M^+ - C_3H_6N$, 4.1), 152 ($M^+ - C_4H_9N$, 11.2), 127 ($M^+ - C_6H_{10}N$, 24.0), 126 (100), 113 ($M^+ - C_7H_{12}N$, 99.9), 95 (15.2), 73 (98.9), 59 (40.5); HRMS (EI) *m/e* calcd for $C_{12}H_{22}NSi$ ($M^+ - CH_3$) 208.1521, found 208.1483. Anal. Calcd for $C_{13}H_{25}NSi$: C, 69.96; H, 11.21; N, 6.28. Found: C, 69.99; H, 11.28; N, 6.29.

5,5-Dimethyl-1-methoxy-9-(trimethylsilyl)-(*E*,*Z*)-1,7-nonadiene (25). This compound was prepared in a manner similar to that for compound **24**. The intermediate aldehyde was obtained in a 70% yield (1.58 g). The Wittig reaction was allowed to stir for 16 h at room temperature. The crude product was vacuum distilled (110–121 °C at 5 mmHg) through a 6-in. Vigreaux column and then chromatographed through 50 g of silica gel packed with pentane containing 1% triethylamine. The column was eluted with 1% ether/pentane to afford 0.601 g (31% over the two steps) of the desired product **25** as a clear colorless oil. The spectral data for the mixture of olefins are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.27 (d, 0.5 H, J = 12.6 Hz, vinyl proton at C_1), 5.82 (dt, 0.5 H, J_d = 6.0 Hz, J_t = 1.5 Hz, vinyl proton at C_1), 5.51–5.19 (m, 2 H, vinyl protons at C_7 and C_8), 4.74–4.64 (m, 0.5 H, vinyl proton at C_2), 4.31–4.25 (m, 0.5 H, vinyl proton at C_2), 3.56 and 3.47 (two s, 3 H), 2.04–1.95 (m, 1 H, methylene protons at C_3 and C_6), 1.87–1.80 (m, 3 H, methylene protons at C_3 and C_6), 1.43 (d, 1.5 H, J = 9.3 Hz, methylene protons at C_9), 1.40 (d, 0.5 H, J = 6.3 Hz, methylene protons at C_9), 1.25–1.15 (m, 2 H, methylene protons at C_4), 0.84, 0.83, 0.81, 0.80 (four s, 6 H), –0.033 and –0.039 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 146.8, 145.8, 128.6, 128.5, 126.9, 126.8, 125.6, 125.4, 124.3, 124.1, 107.9, 103.9, 59.4, 55.7, 45.1, 43.1, 41.9, 38.7, 33.4, 26.7, 22.6, 22.3, 22.2, 18.6, 18.4, 18.2, –2.0, –2.2; IR (neat/NaCl) 3012, 2952, 2930, 2905, 2869, 2853, 1655, 1637, 1466, 1384, 1364, 1249, 1209, 1151, 1133, 1110, 967, 932, 855, 717, 700, 667 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 254 (M^+, 0.1), 239 ($M^+ - CH_3$, 4), 225 (1), 181 ($M^+ - C_3H_9Si$, 1), 163 (2), 150 ($M^+ - C_4H_{12}OSi$, 4), 135 (7), 109 (21), 95 (45), 89 (37), 73 (100); HRMS (EI) *m/e* calcd for $C_{15}H_{30}OSi$ 254.2066, found 254.2066.

Electrolysis of Compound 22: Synthesis of 2-Ethenyl-4,4-dimethylcyclopentane-1-carboxaldehyde Dimethyl Acetal (26) and 2-(1-Methoxy-2-(trimethylsilyl)ethyl)-4,4-dimethylcyclopentane-1-carboxaldehyde Dimethyl Acetal (27). A mixture of 0.224 g (0.93 mmol) of enol ether **22**, 1.3 g (9 mmol) of potassium carbonate, and 2.64 g of lithium perchlorate in 25 mL of a 1:1 methanol/tetrahydrofuran solution was placed in a vial equipped with a reticulated vitreous carbon anode (suspended from a stainless steel spatula), a platinum wire cathode, and a nitrogen inlet. The reaction mixture was degassed by bubbling nitrogen through the solution, cooled to 0 °C, and electrolyzed at a constant current of 50.4 mA until 180 C (2.0 faradays) of charge had been passed. When complete, the reaction was diluted with 25 mL of ether and 10 mL of water, the layers were separated, and the organic layer was washed twice with water (10 mL). The aqueous fractions were combined, washed twice with ether (10 mL), and then the combined organic layers dried over potassium carbonate and concentrated in vacuo. The crude product was immediately chromatographed through 50 g of silica gel packed with a pentane solution containing 1% triethylamine. Gradient elution with 100% pentane to 2% ether/pentane as eluant led to the isolation of 0.155 g (84%) of the olefinic product **26** and 0.019 g (7%) of the ether product **27**. The spectral data for **26** (mixture of cis and trans isomers) are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.90–5.73 (m, 1 H), 4.98–4.86 (m, 2 H), 4.18 (d, 1 H, J = 6.2 Hz, methine proton of the acetal), 3.33, 3.30, 3.29, 3.27 (four s, 6 H, methyl groups of the acetal), 2.77 (p, 0.7 H, J = 7.7 Hz, methine proton), 2.53–2.39 (m, 1 H, methine proton), 2.16–2.05 (m, 0.3 H, methine proton), 1.62–1.16 (m, 4 H, methylene protons at C_2 and C_4), 1.06, 0.99, 0.98, 0.97 (four s, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 143.3, 140.4, 113.9, 113.0, 108.2, 106.0, 54.0, 53.9, 53.5, 52.1, 47.8, 47.7, 46.8, 45.9, 44.6, 41.9, 37.4, 30.4, 30.2, 29.9, 29.7; IR (neat/NaCl) 3078, 2980, 2965, 2924, 2907, 2895, 2865, 2830, 1639, 1464, 1448, 1384, 1365, 1190, 1139, 1127, 1081, 992, 964, 907, 734 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 198 (M^+, 2), 195 (99), 175 (61), 167 ($M^+ - CH_3O$, 89), 164 (100), 152 ($M^+ - C_2H_6O$, 99), 136 ($M^+ - C_2H_6O_2$, 99), 123 ($M^+ - C_3H_7O_2$, 96), 108 (99), 97 (95), 85 (95), 73 (89); HRMS (EI) *m/e* calcd for $C_{11}H_{19}O$ ($M^+ - CH_3O$) 167.1436, found 167.1430. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.7; H, 11.1. Found: C, 72.1; H, 11.3. The spectral data for **27** (a mixture of diastereomers was obtained) are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.42 (d, 0.2 H, J = 9.0 Hz, acetal methine proton), 4.25 (d, 0.35 H, J = 6.3 Hz, acetal methine proton), 4.20 (d, 0.45 H, J = 7.6 Hz, acetal methine proton), 3.65–3.44 (m, 1 H, C*H*OMe), 3.33, 3.31, 3.30, 3.27, 3.26, 3.25, 3.18 (seven s, 9 H, methyl ether and acetal protons), 2.48–2.28 (m, 1 H), 2.11–1.88 (m, 1 H), 1.66–1.30 (m, 6 H), 1.02, 0.98, 0.97, 0.94, 0.91 (five s, 6 H), 0.01, 0.00, –0.01 (three s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 109.3, 81.1, 78.8, 56.4, 55.9, 54.7, 54.2, 53.8, 52.0, 47.3, 44.6, 44.2, 42.4, 42.2, 41.9, 41.3, 40.0, 37.1, 36.9, 30.3, 30.0, 29.71, 29.68, 29.5, 20.0, 17.3, –0.86, –1.14; IR (CCl_4 film) 2952, 2869, 1458, 1378, 1249. 1060, 1094, 1129, 861 cm^{-1}; GC/MS (70 eV) *m/e* (rel intensity) 270 (M^+ – MeOH, 0.3) 239 ($M^+ - C_2H_7O_2$, 1.1), 223 (3), 197 ($M^+ - C_4H_{13}OSi$, 0.4), 183 (6), 165 (197 – MeOH, 2), 151 (197 – C_2H_6O, 4), 135 (20), 131 (98), 107 (32), 101 (24), 93 (33), 89 (100), 73 (78); HRMS (EI) *m/e* calcd for $C_{15}H_{30}O_2Si$ ($M^+ - CH_4O$) 270.2015, found 270.1999.

Electrolysis of Compound 23: Synthesis of 2-(1-Methylideneethyl)-cyclopentane-1-carboxaldehyde Dimethyl Acetal (15a). The electrolysis of compound **23** was done in a fashion similar to the electrolysis of **22**. In this reaction, a constant current of 27 mA was passed until 199 C (2.3 faradays) of charge had been passed. The reaction led to the formation of 0.124 g (66%) of product **15a** along with 0.035 g (15%) of recovered starting material. Product **15a** was obtained as a 3:1 mixture of trans and cis isomers. Interestingly, the major and minor isomers were reversed when compared with the material obtained earlier from the oxidation of **13a**. The ^{1}H NMR spectral data for the current mixture is as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.81 (narrow m, 0.75 H, vinyl proton), 4.74 (narrow m, 0.25 H, vinyl proton), 4.72 (narrow m, 1 H, vinyl protons in both isomers), 4.15 (d, 0.25 H, J = 6.1 Hz, acetal methine proton), 4.10 (d, 0.75 H, J = 7.6 Hz, acetal methine proton), 3.37, 3.32, 3.30, 3.29 (four s, 6 H), 2.36 (m, 1 H), 2.12 (m, 1 H), 1.78 and 1.72 (two s, 3 H), 1.80–1.55 (m, 6 H).

Electrolysis of Compound 24: Synthesis of 2-Ethenylcyclohexane-1-carboxaldehyde Dimethyl Acetal (29) and 2-(1-Methoxy-2-(trimethylsilyl)ethyl)cyclohexane-1-carboxaldehyde Dimethyl Acetal (30). The electrolysis was conducted in a fashion similar to that described below for compound **25**. In this experiment, the reaction mixture was electrolyzed at a constant current of 27 mA until 205 C (2.0 faradays) of charge had been passed. The reaction led to the formation of 0.115 g (59%) of **29** and 0.028 g (9%) of **30**. Over four runs the yield of compound **29** ranged from 55 to 65%. The spectral data for **29** as a mixture of cis and trans isomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.04 (dt, 0.33 H, J_d = 16.9 Hz, J_t = 9.8 Hz, vinyl proton), 5.64 (dt, 0.67 H, J_d = 17.0 Hz, J_t = 9.2 Hz, vinyl proton), 5.09–4.91 (m, 2 H, vinyl protons), 4.20 (d, 0.60 H, J = 2.9 Hz, acetal methine proton), 4.01 (d, 0.40 H, J = 8.9 Hz, acetal methine proton), 3.40, 3.34, 3.28, 3.25, (four s, 6 H), 2.55–2.51 (m, 0.4 H), 2.04–1.92 (m, 0.6 H), 1.82–1.10 (m, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 143.5, 138.3, 116.0, 114.0, 107.9, 106.2, 56.8, 55.7, 53.3, 52.1, 45.2, 44.0, 42.1, 39.2, 33.4, 32.1, 31.7, 29.5, 25.8, 25.5, 23.2, 22.7, 20.8; IR (neat/NaCl) 3075, 2930, 2854, 1638, 1449, 1376, 1245, 1211, 1189, 1166, 1135, 1113, 1077, 1056, 971, 914, 851 cm^{-1}; GC/MS (EI) *m/e* (rel intensity) 184 (M^+, 0.7), 153 ($M^+ - CH_3O$, 10), 137 ($M^+ - C_2H_7O$, 2), 121 ($M^+ - C_2H_7O_2$, 37), 101 (22), 93 (24), 79 (39), 75 (100); HRMS (EI) *m/e* calcd for $C_{10}H_{17}O$ (M – CH_3O) 153.1279, found 153.1310. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.7; H, 10.9. Found: C, 71.3; H, 10.8. The spectral data for **30** as a mixture of diastereomers are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.48 (d, 0.44 H, J = 7.6 Hz, acetal methine proton), 4.36 (d, 0.56 H, J = 2.5 Hz, acetal methine proton), 3.58–3.52 (m, 0.5 H, methine proton α to the ether), 3.37, 3.36, 3.31, 3.28, 3.25, 3.21 (six s + buried m, 9.5 H, methoxy protons + methine proton α to the ether), 2.02–1.96 (m, 0.5 H), 1.83–0.68 (m, 11.5 H), 0.015 and 0.00 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 107.7, 105.7, 80.4, 79.7, 56.0, 55.8, 55.1, 54.0, 52.3, 41.7, 41.0, 40.7, 39.1, 26.4, 26.1, 25.8, 25.2, 24.3, 24.0, 23.8, 18.8, 17.2, –0.41, –1.22; IR (neat/NaCl) 2927, 2854, 2818, 1572, 1566, 1461, 1451, 1247, 1190, 1119, 1093, 860, 838 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 288 (M^+, 0.16), 273 ($M^+ - CH_3$, 0.3), 257 ($M^+ - CH_3O$, 1), 241 ($M^+ - C_2H_7O$, 3), 225 ($M^+ - C_2H_7O_2$, 4), 168 (1), 153 (5), 139 (10), 122 (20), 121 (100), 109 (5), 103 (12), 93 (12), 89 (40), 73 (77); HRMS (EI) *m/e* calcd for $C_{14}H_{28}O_2Si$ ($M^+ - CH_4O$) 256.1858, found 256.1859.

Electrolysis of Compound 25: Synthesis of 2-Ethenyl-4,4-dimethylcyclohexane-1-carboxaldehyde Dimethyl Acetal (31) and 2-(1-Methoxy-2-(trimethylsilyl)ethyl)-4,4-dimethylcyclohexane-1-carboxaldehyde Dimethyl Acetal (32). A solution of 0.134 g (0.53 mmol) of enol ether **25**, 0.16 g (1.5 mmol) of 2,6-lutidine, and 2.12 g of lithium perchlorate in 50 mL of a 20% methanol/dichloromethane solution was placed in a three-neck round-bottom flask equipped with a reticulated vitreous carbon anode (suspended from a pencil-sharpened carbon rod), a carbon rod cathode, and a nitrogen inlet. The solution was electrolyzed at a constant current of 13.6 mA until 102 C (2.0 faradays) of charge had been passed. When complete, the reaction was diluted with 25 mL of water and 25 mL of dichloromethane. The layers were separated, and the organic layer was washed twice with water (25 mL). The combined aqueous layers were extracted twice with dichloromethane (25 mL), and then the combined organic layers were dried over potassium carbonate and concentrated in vacuo. The crude product was chromatographed through 50 g of silica gel packed with a pentane solution containing 1% triethylamine. Gradient elution of the column with 100% pentane to 2.5% ether/pentane led to the isolation of 0.068 g (61%) of **31** and 0.022 g (13%) of **32**. The spectral data for **31** (as a mixture of cis and trans isomers) are as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.08–5.96 (m,

0.45 H, vinyl proton), 5.63-5.51 (m, 0.55 H, vinyl proton), 4.99-4.89 (m, 2 H, terminal vinyl protons), 4.22-4.18 (m, 1 H, acetal methine proton), 3.40, 3.33, 3.26, 3.25 (four s, 6 H), 2.52-2.46 (m, 0.5 H, methine proton at C_2), 2.21-2.09 (m, 0.5 H, methine proton at C_2), 1.8-0.93 (m, 7 H), 0.90, 0.88, 0.86, 0.85 (four s, 6 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 143.7, 141.7, 113.9, 113.8, 108.0, 105.2, 57.0, 55.8, 53.5, 52.4, 46.5, 45.5, 43.5, 41.2, 40.1, 39.7, 38.4, 37.2, 32.9, 30.4, 30.3, 30.1, 29.9, 24.5, 21.0, 19.2; IR (neat/NaCl) 2950, 2899, 2840, 1637, 1457, 1384, 1375, 1364, 1209, 1190, 1165, 1128, 1072, 1059, 995, 961, 911, 858, 840 cm^{-1}; GC/MS for isomer one (PCI) *m/e* (rel intensity) 212 (M^+, 0.6), 182 (24), 181 ($M^+ - CH_3O$, 100), 165 ($M^+ - C_2H_7O$, 13), 149 ($M^+ - C_2H_7O_2$, 90), 133 (20), 109 (8), 75 (64); GC/MS for isomer two (PCI) *m/e* (rel intensity) 212 (M^+, 0.4), 181 ($M^+ - CH_3O$, 100), 165 ($M^+ - C_2H_7O$, 10), 149 ($M^+ - C_2H_7O$, 34), 133 (12), 109 (5), 75 (22); HRMS (EI) *m/e* calcd for $C_{12}H_{20}O$ ($M^+ - CH_4O$) 180.1514, found 180.1514. Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.58; H, 11.32. Found: C, 73.47; H, 11.48. The spectral data for compound **32** (obtained as a mixture of diastereomers) are as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 4.53 (d, 0.23 H, J = 8.1 Hz, acetal methine proton), 4.46 (d, 0.46 H, J = 6.4 Hz, acetal methine proton), 4.35 (d, 0.31 H, J = 2.0 Hz, acetal methine proton), 3.37-3.19 (m, 10 H, methoxy protons and the methine proton α to the OCH_3), 2.11 (m, 0.5 H), 1.92-0.95 (m, 0.5 H), 0.90, 0.88, 0.87, 0.85 (four s, 6 H), 0.01 and 0.00 (two s, 9 H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 107.9, 105.0, 103.8, 80.9, 80.4, 80.3, 56.0, 55.9, 55.2, 54.3, 52.8, 51.4, 42.1, 40.7, 40.2, 39.0, 38.7, 37.8, 37.5, 36.5, 36.2, 35.5, 35.0, 34.7, 33.3, 33.1, 30.5, 25.2, 24.7, 22.9, 20.2, 19.2, 18.7, 17.0, -0.53, -0.78, -1.1; IR (neat/NaCl) 2950, 2824, 1456, 1364, 1248, 1080, 1096, 1117, 960, 946, 861, 837 cm^{-1}; GC/MS (PCI) *m/e* (rel intensity) 316 (M^+, 1), 301 ($M^+ - CH_3$, 2.6), 285 ($M^+ - CH_3O$, 4), 269 ($M^+ - C_2H_7O$, 19), 253 ($M^+ - C_2H_7O_2$, 35), 237 (17), 181 (22), 149 (96), 131 (22), 89 (11), 75 (100), 73 (12); HRMS (EI) *m/e* calcd for $C_{16}H_{33}O_2Si$ ($M^+ - CH_4O$) 284.2171, found 284.2164.

Conversion of **Compound 32 to 31.** Compound **32** (0.037 g/0.12 mmol) was taken up in 4 mL of methanol and 1 mL of acetic acid. The reaction was stirred at room temperature for 16 h. After this period, there was still evidence of starting material by TLC so the reaction was refluxed for an additional 3 h. The reaction was then cooled to room temperature, diluted with ether (10 mL), and washed with saturated sodium bicarbonate (2 × 50 mL). The organic layer was dried over potassium carbonate, concentrated in vacuo, and chromatographed through 10 g of silica gel that had been packed with a 2% ether/hexane solution containing 1% triethylamine. The column was eluted with 2% ether/hexane to afford 0.018 g (74%) of the desired compound **31**.

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Stereochemistry and Mechanism of Aldol Reactions Catalyzed by Kynureninase

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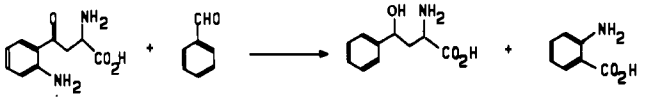
Abstract: Kynureninase from *Pseudomonas* has been reported to catalyze aldol and retro-aldol reactions, in addition to the physiological hydrolytic cleavage of L-kynurenine to anthranilic acid and L-alanine. However, the stereochemistry of these novel aldol reactions has not been previously determined. We have determined that the reaction of L-kynurenine and benzaldehyde catalyzed by kynureninase results in (2*S*,4*R*)-2-amino-4-hydroxy-4-phenylbutanoic acid. Similarly, the 4*R* isomer of dihydro-L-kynurenine readily undergoes retro-aldol cleavage, while the 4*S* isomer is unreactive as a substrate. Both isomers of dihydro-L-kynurenine are competitive inhibitors of kynureninase from *Pseudomonas*. However, the 4*S* isomer of dihydro-L-kynurenine is the most potent inhibitor, with a K_i of 0.3 μM. These results provide additional support for a general base mechanism for kynureninase, and suggest that the hydration occurs on the *re* face of the carbonyl group of kynurenine to give an (*S*)-*gem*-diolate intermediate.

Introduction

Kynureninase (L-kynurenine hydrolase, EC 3.7.1.3) is a pyridoxal-5'-phosphate-dependent enzyme that catalyzes the hydrolytic cleavage of L-kynurenine to give L-alanine and anthranilic acid (eq 1). This enzyme plays a central role in the catabolism

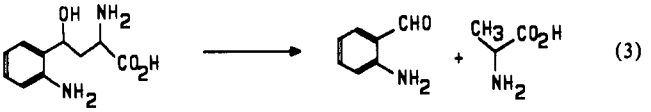
(1)

of L-tryptophan in some bacteria, including *Pseudomonas fluorescens*.[1] A similar enzyme, 3-hydroxykynureninase, is involved in L-tryptophan metabolism to NAD in animals and plants.[1] Kynureninase has also been found to catalyze an aldol-type condensation of benzaldehyde with incipient L-alanine formed from L-kynurenine to give 2-amino-4-hydroxy-4-phenylbutanoic acid[2] (eq 2). However, the stereochemistry of the aldol product at the



(2)

4-position was not determined, although Bild and Morris believed that only a single isomer was formed.[2] Furthermore, Tanizawa and Soda have reported that dihydro-L-kynurenine (2-amino-4-hydroxy-4-(2'-aminophenyl)butanoic acid) is a substrate for kynureninase, yielding 2-aminobenzaldehyde and L-alanine[3] in a retro-aldol cleavage reaction (eq 3). However, the diastereo-



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