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Anodic oxidations of electron-rich olefins: radical cation based approaches to the synthesis of bridged bicyclic ring skeletons

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Dedicated to Professor Barry M. Trost on the occasion of his 60th birthday

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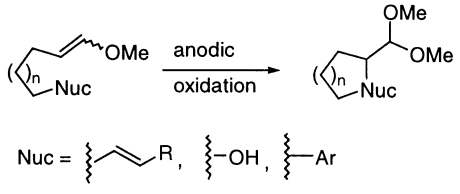
Abstract—The use of intramolecular anodic olefin coupling reactions for building bicyclo[3.2.1]octane ring skeletons has been examined. While simple model systems using bis enol ether substrates readily led to the formation of bicyclic products, application of the reactions to total synthesis efforts were hindered by reactions forming dimethoxy acetal groups at both the terminating and initiating ends of the cyclization reactions. In an effort to solve this problem, ketene acetal based initiating groups have been studied. The use of a ketene dithioacetal group proved especially useful for this purpose.

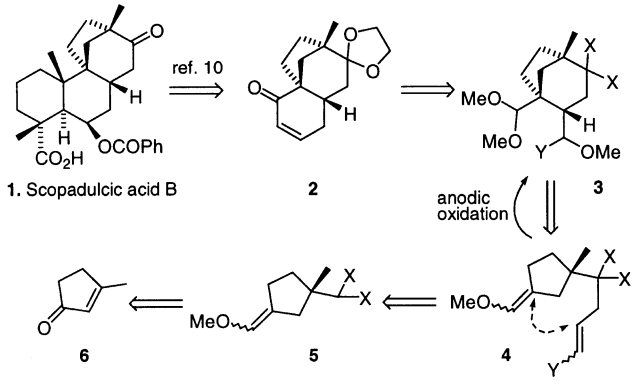
1. Introduction

The anodic oxidation of electron-rich olefins can provide a powerful means for triggering oxidative cyclization reactions and building new ring systems.[1] These reactions are intriguing because they reverse the polarity of enolate equivalents and lead to the formation of new bonds without giving up the functionality used to initiate the reaction, and generate highly reactive radical cation intermediates (Scheme 1). To date, the reactions have been terminated with the use of simple alkyl olefins, styrenes, allylsilanes,[2] vinylsilanes,[3] electron-rich aromatic rings,[4] enol ethers,[5] and alcohols.[6] The reactions have proven to be compatible with the use of very acid sensitive substrates[3,7] and the formation of quaternary carbons.[5,7,8]

Having established the potential for the reactions in model systems, efforts were begun to examine the utility of the reactions for building natural products. As part of these efforts, we became curious as to whether anodic cyclization reactions might prove useful as tools for constructing the bicyclo[3.2.1]octane ring skeletons found in many natural products.[9,10] For example, consider the retrosynthetic analysis of (+)-scopadulcic acid B[11,12] outlined in Scheme 2. In this proposed synthesis, an anodic cyclization reaction would appear useful for generating the bridged bicyclic ring skeleton, as well as one of the critical quaternary carbons found in the natural product. This transformation looked particularly ideal because it would convert the enol ether used to initiate the reaction into an acetal group that could then be used to further elaborate the product. Similar cyclization reactions had been used to construct quaternary carbons with control of relative stereochemistry, and the resulting acetals had been used in the synthesis of angularly fused tricyclic ring skeletons.[8] However, these reactions had struggled to make six-membered rings and quaternary carbons at the same time. While enol ether–enol ether based cyclization reactions had been successful, the corresponding reactions using less reactive radical trapping



Scheme 1.



Scheme 2.

Keywords: olefins; anodic oxidation; cyclization.

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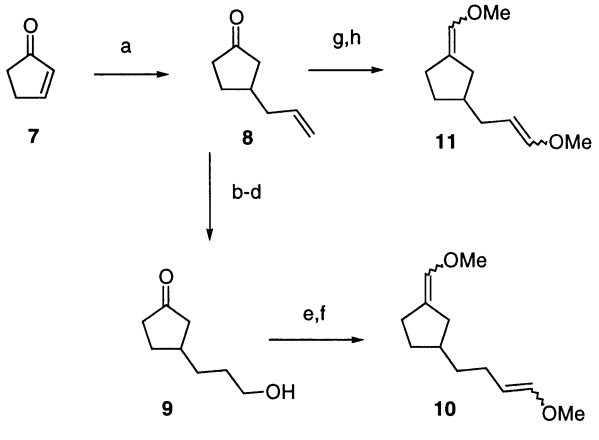
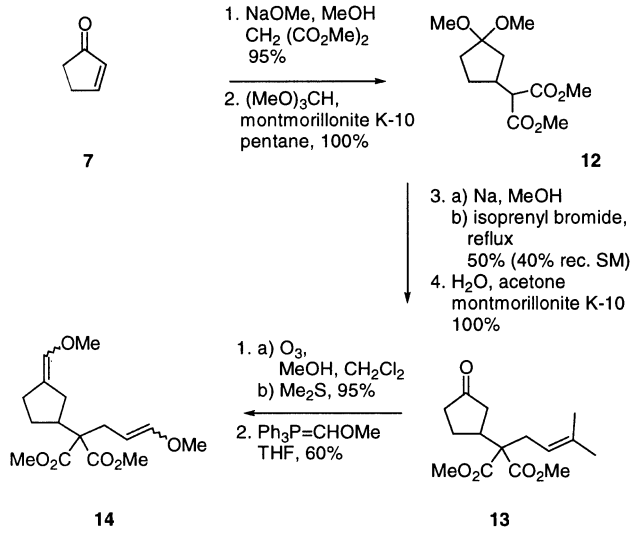
groups like allylsilanes had not been.[8] These observations raised questions about how the extra strain associated with building a bicyclic ring skeleton would influence the reactions and if a terminating group could be found that would both allow for an effective cyclization and provide a convenient handle in the product for completing the synthesis. With these questions in mind, a study aimed at determining the utility of intramolecular anodic olefin coupling reactions for the synthesis of bridged bicyclic ring skeletons was undertaken.

2. Initial studies

Work in this area began by examining the oxidation of three bis enol ether substrates.[13] The bis enol ether substrates were selected as starting points because enol ether trapping groups have been among the best radical cation trapping groups studied to date. In this way, it was hoped that the cyclization reactions would have the best possible chance for success. The first two substrates **10** and **11** were synthesized from 3-allylcyclopentanone **8** (Scheme 3). The allylcyclopentanone was synthesized by the cuprate-mediated addition of allylmagnesium bromide to cyclopentenone.[14] For the synthesis of **10**, compound **8** was converted into keto alcohol **9**. Attempts to effect this conversion in a single step were not successful. Hence, the transformation was completed by first protecting the carbonyl as a dimethoxy ketal, then converting the double bond into an alcohol with a hydroboration reaction, and finally deprotecting the ketone. This three-step sequence could be run without purifying the intermediates. As a sidenote, formation of the dimethoxy ketal benefited greatly from premixing the trimethylorthoformate and montmorillonite clay and then allowing the mixture to stir for at least 30 min prior to the addition of the ketone. Without this premixing step, the yield of the reaction was greatly reduced. In cases where the reaction did not go to completion (as monitored by TLC), the equilibrium was pushed toward product by adding more of the premixed trimethylorthoformate and montmorillonite clay.



Scheme 3. *Reagents*: (a) $CuBr/Me_2S$, LiCl, allylMgBr, TMSCl, THF, −78°C, 80%; (b) $(MeO)_3CH$, montmorillonite K-10, room temp.; (c) (i) disiamylborane, THF, 0°C to room temp, (ii) NaOH, H_2O_2; (d) H_2O, acetone, montmorillonite K-10, 60% over three steps; (e) (i) $(COCl)_2$, DMSO, THF, −78 to −50°C, (ii) Et_3N, −78°C to room temp.; (f) Ph_3P=CHOMe, THF, room temp., 50% over two steps; (g) (i) O_3, $MeOH/CH_2Cl_2$ (1:1), (ii) Me_2S, (iii) H_2O, acetone, montmorillonite K-10, 60%; (h) Ph_3P=CHOMe, THF, room temp., 60%.



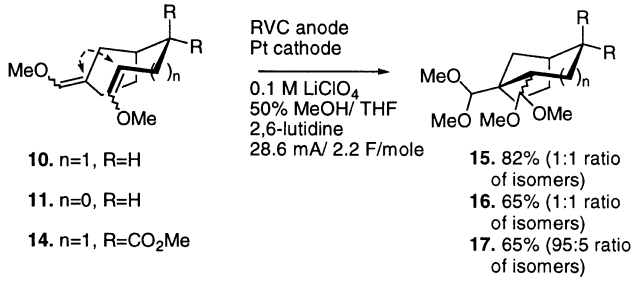
Scheme 4.

The addition of the independent reagents without premixing was not successful. Following formation of **9**, the alcohol was oxidized with the use of DMSO and oxalyl chloride and the resulting keto aldehyde treated under Wittig conditions in order to introduce the enol ethers needed for the electrochemical coupling reaction. For the synthesis of **11**, the olefin in **8** was cleaved by ozonolysis and then the Wittig reaction used to introduce the enol ethers.

The third substrate **14** was synthesized by first adding dimethylmalonate to cyclopentene (Scheme 4). The ketone was protected as a dimethoxy acetal, the malonate moiety alkylated with isoprenyl bromide, and the ketone deprotected to form **13**. Ozonolysis of the olefin followed by a Wittig reaction to introduce the desired enol ethers then completed the synthesis.

Each of the substrates was oxidized[15] at a reticulated vitreous carbon (RVC) anode[16] using a platinum wire cathode, an undivided cell (a three neck round bottom flask), a 0.1 M lithium perchlorate in 50% MeOH/THF electrolyte solution, 2,6-lutidine as a proton scavenger, and a constant current of 28.6 mA (Scheme 5). All three reactions were run until a total of 2.2 F/mol of electricity had been passed. The electrolyses were typically run with a substrate concentration of 0.03 M and a scale ranging from 100 to 400 mg.

In the case of **10**, an 82% isolated yield of the bicyclo[3.2.1]octane product **15** was obtained as a 1:1



Scheme 5.

mixture of isomers. As with earlier anodic cyclization reactions, it was found that this cyclization reaction could be initiated with the use of a 6-volt lantern battery as a power supply.[17] In this case, a 70% isolated yield of product **15** was obtained. All of the other conditions for the oxidation remained the same as described above. While the yield of the cyclization was not quite as high as the yield obtained when the current passed through the reaction was more carefully controlled, the reaction did indicate that the viability of such an electrolysis reaction can be readily tested without the need for specialized equipment.

Substrate **11** was studied in order to determine what effect the additional strain of forming a bicyclo[2.2.1]heptane ring skeleton would have on the cyclization reaction. In this case, the anodic oxidation afforded a 65% isolated yield of product **16** as a 1:1 mixture of stereoisomers. Interestingly, this reaction did not fare very well when a 6-volt lantern battery was used as the power supply. Using the battery only a 33% yield of product **16** could be obtained. Clearly, either the reaction or the product was sensitive to the much harsher reaction conditions associated with the use of the battery.

It was tempting to suggest that the lower yield obtained for the oxidation of **11** relative to **10** was the result of a slower cyclization reaction. If the strain associated with forming the bicyclo[2.2.1]heptane ring skeleton slowed the cyclization, then the very reactive radical cation intermediate would have more time to decompose prior to intramolecular trapping by the second enol ether. However, cyclic voltammetry data did not support such a conclusion. For a reaction that involves an electrochemical oxidation followed by a very fast chemical reaction, the potential measured for the substrate depends on the rate of the chemical reaction. The faster the chemical reaction, the lower the potential measured. Intramolecular anodic olefin coupling reactions between enol ethers have typically shown this behavior.[5] For example, the oxidation potential measured for **18a** (Fig. 1) was 200 mV lower than that measured for the parent enol ether **19**. The potential measured for **18b** was 100 mV lower than that measured for **19**. These data indicated that the formation of the six-membered ring from **18b** was slower that the formation of the five-membered ring from **18a** as would be expected. Even the formation of a quaternary carbon showed this shift in potential.[5] The $E_{p/2}$ value for **20** was 150 mV lower than that measured for its parent enol ether **21a**. In the current study, no such potential drops were observed. The $E_{p/2}$ values[18] (vs. Ag/AgCl) obtained for **10** and **11** were +1.13 and +1.10 V. The $E_{p/2}$ value measured for the parent enol ether (**21b**) was +1.14 V. Evidently, none of the cyclizations to form bridged bicyclic reactions occurred at a rate equivalent to that observed for the earlier cyclization to form a quaternary carbon. Presumably, this was due to the formation of a six-membered ring in the case of **10** and **14** and the formation of a strained ring system in the case of **11**. Finally, the very small difference in $E_{p/2}$ measured for **10** and **11** indicated that the cyclization reactions resulting from these two substrates were not substantially different in rate. Therefore, the lower yield obtained for the oxidation of **11** could not be attributed to a rate difference and was most likely a result of product instability.

Substrate **14** was studied in order to determine if placing substituents on the chain connecting the olefins (as required for an approach to scopadulcic acid B) would allow for control over product stereochemistry. It was hoped that the presence of an axial ester group in the transition state of the cyclization would force the disubstituted enol ether into an equatorial position (Fig. 2). From an electrochemical standpoint the presence of the methyl esters had little influence on the reaction. The $E_{p/2}$ value measured for **14** was +1.15 V vs. Ag/AgCl while the value measured for the parent enol ether in a substrate that did not cyclize (**22**, Fig. 1) was +1.17 V. Once again the rate of the cyclization reaction was not as rapid as earlier cyclizations generating fused bicyclic ring skeletons. With respect to the preparative electrolysis of **14**, a 65% isolated yield of the desired bicyclo[3.2.1]octane product **17** was formed (Scheme 5). Because of the problems encountered using such products for the synthesis of scopadulcic acid B (see below), the yield of this reaction was not optimized. However, the cyclization reaction did indicate that the presence of the *gem* substituents dramatically influenced the stereochemistry of the cyclization. In this experiment, a 19:1 ratio of stereoisomers about the newly formed carbon–carbon bond was obtained. The major isomer had the C_2-dimethoxyacetal substituent in an equatorial position. This assignment was made by examining the NMR coupling pattern observed for the C_2-methine proton. This proton gave rise to a doublet of triplets with J_d=12.7 Hz and J_t=4.0 Hz. The 12.7 Hz coupling constant was indicative of a *trans* diaxial coupling indicating that the methine proton was in the axial position.

3. Working toward scopadulcic acid B; differentiating the ends of the cyclization

While studying these initial substrates taught us a great deal about the anodic cyclization reactions, they did not afford a useful approach to building scopadulcic acid B. Because an enol ether group was used as the trapping group for the enol ether radical cation reactions, the products generated had a pair of dimethoxy acetal groups. Initial plans called for

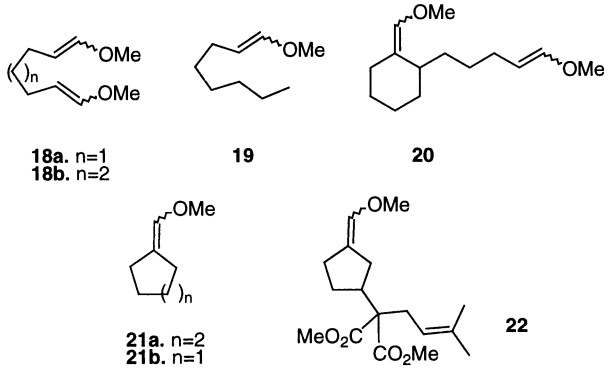


Figure 1.

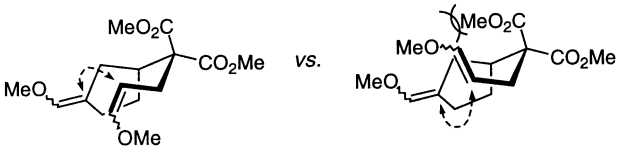


Figure 2.

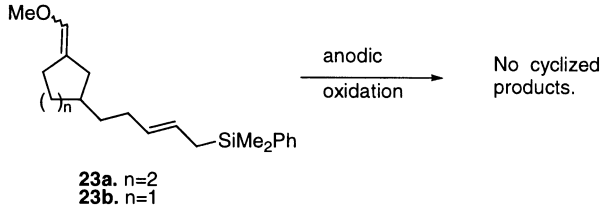
deprotecting the acetals and then capitalizing on the steric hindrance associated with the neopentyl aldehyde in order to differentiate between these two groups. Unfortunately, such efforts were never successful. While the acetals in **15** could be readily cleaved, the subsequent reactions studied either failed to differentiate between the aldehydes or led to the formation of tetrahydrofuran type products. Typically, the reactions led to a bad mixture of products.

Struggling to differentiate the ends of the cyclization reaction was particularly bothersome because it pointed to a limitation associated with the anodic reactions themselves. Instead of searching to find ways to manipulate the products, would it not be better if the coupling reactions could be used to generate products with the ends already differentiated? While potentially ideal, such a suggestion was worrisome. As mentioned earlier, the bis enol ether substrates were selected because enol ethers had proven to be among the most reactive groups found for trapping the radical cation intermediates generated at the anode. It was clear from the CV data discussed above that the cyclization reactions were not fast. Would the use of a less reactive radical cation trapping group still allow for the cyclization reaction to occur?

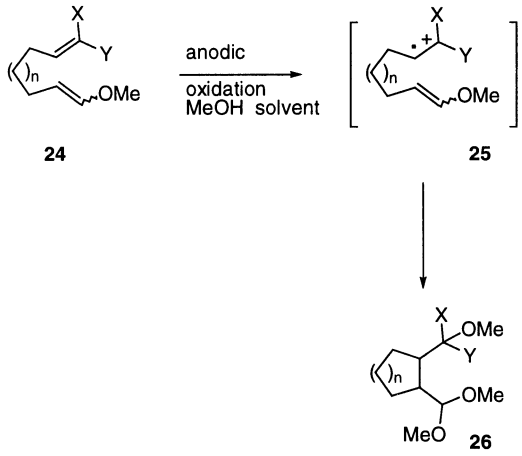
Attempts to address this question were not promising. For example, two cyclization substrates having an allylsilane terminating group (**23a** and **23b**) were synthesized[19] and oxidized (Scheme 6). In neither case was a cyclized product obtained. Only products resulting from the elimination of a proton from the initially formed radical cation were observed. In all of the products obtained, the allylsilane group remained unchanged. In a similar fashion, the anodic oxidation of a substrate having a trisubstituted olefin trapping group (**22**, Fig. 1)[20] generated a similar mixture of products. Hence, it appeared that the reactive enol ether trapping group was required for the cyclization.

What was needed was a change in strategy. If the ends of the cyclization could not be differentiated by altering the terminating group for the cyclization, then maybe they could be differentiated by making a change in the initiating group. For instance, if an anodic olefin coupling reaction could be initiated by oxidizing an even more electron-rich ketene acetal group, then the reaction would lead to the formation of a product having an ortho ester equivalent and an acetal (Scheme 7).

A related oxidative cyclization reaction had proven useful for the synthesis of a tetrahydrofuran ring (Scheme 8).[6] In this example, a trimethylsilyl substituted enol ether was oxidized in order to generate a cyclic product having a silyl substituted acetal. Further oxidation led to replacement



Scheme 6.

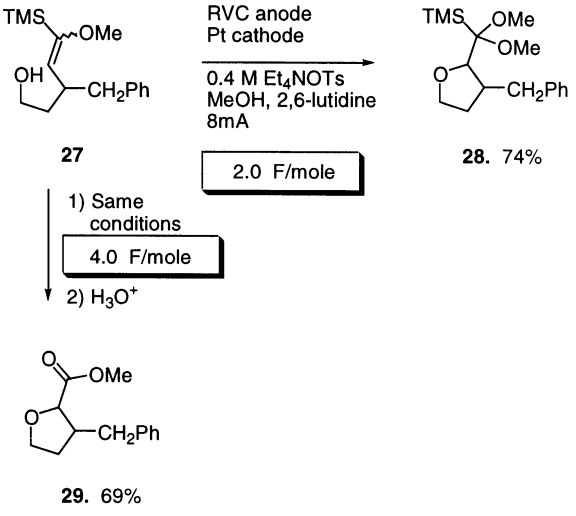


Scheme 7.

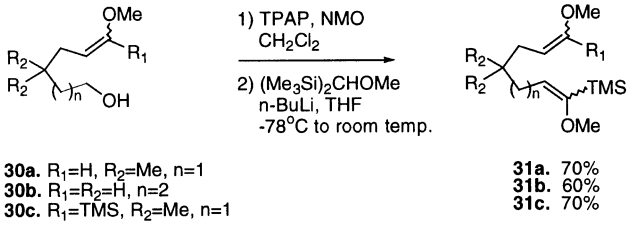
of the silyl group with a methoxy substituent.[21] A hydrolysis reaction then led to the formation of methyl ester **29**.

With this in mind, three substrates (**31a–c**) were built in order to determine if the oxidation of a silylated enol ether would also trigger the formation of new carbon–carbon bonds. In each of these examples, the substrate was built starting from an unsaturated alcohol[22] using a two-step TPAP oxidation–Peterson olefination strategy (Scheme 9).[23]

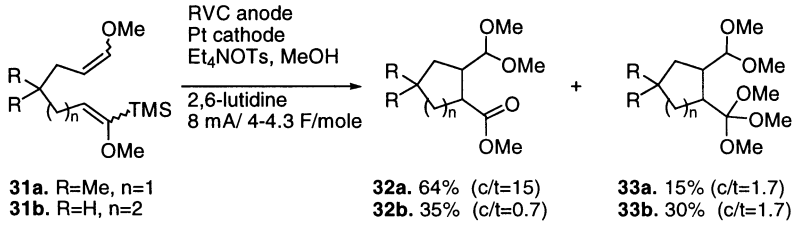
The substrates were then oxidized using conditions similar



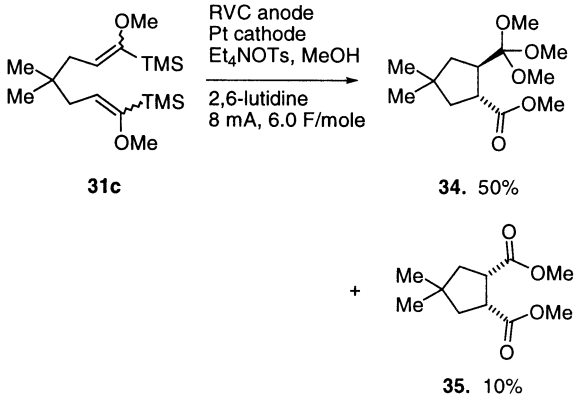
Scheme 8.



Scheme 9.



Scheme 10.



Scheme 11.

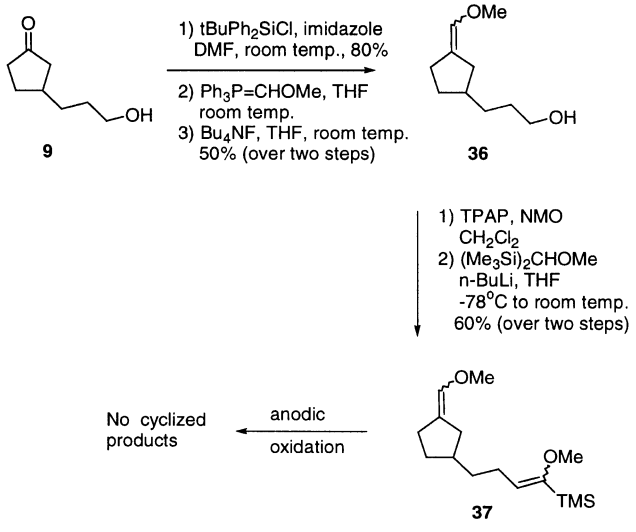
to those described above. Two main changes were made. First, the reactions were run in pure methanol solvent. Second, the reactions were allowed to proceed until at least 4.0 F/mol of charge had passed for cases **31a** and **31b** (Scheme 10) and at least 6.0 F/mol had been passed for the case of **31c** (Scheme 11). The extra electricity was passed in order to ensure cleavage of the initially formed silated acetal to either an ortho ester or methyl ester product. In the case of **31c** enough current was passed to ensure cyclization (2 F/mol) and removal of both silyl groups (2 F/mol each).

The anodic oxidation of **31a** led to the formation of a 79% isolated yield of cyclized product (Scheme 10). A 64% yield of the methyl ester product (**32a**) was obtained (presumably by hydrolysis of an ortho ester upon aqueous workup) along with approximately 15% (*cis*/*trans*=1.7) of a product tentatively assigned as the ortho ester (**33a**). The presumed ortho ester could not be unambiguously assigned because it was contaminated with the methyl ester products. The ester product **32a** was obtained as a 15:1 ratio of *cis* to *trans* isomers. This assignment was made based on the chemical shift difference between the *gem* methyl groups on the five-membered ring. Normally, for a five-membered ring product of this type the difference in chemical shifts for the *gem* methyl groups is significantly larger for the *cis*-isomer than for the *trans*-isomer. In this case, the chemical shift difference between the *gem* methyl was approximately 10 times greater in the major product than in the minor product. The assignment of the major product as the *cis*-isomer was supported by hydrolysis of the dimethoxy acetal which slowly converted the aldehyde ester obtained from the major isomer into the aldehyde ester obtained from the minor isomer.

Substrate **31b** was oxidized in order to determine if the reactions were compatible with six-membered ring formation. In this example, a 65% yield of the cyclized products was obtained. A 35% yield of the methyl ester products was obtained as a 1.5:1 ratio of *cis* to *trans* isomers. A 30% yield of the ortho ester product was obtained as a 1.7:1 ratio of *cis* to *trans* isomers. For both molecules, the stereochemistry of the isomer could be readily assigned by the coupling pattern of the methine proton alpha to either the ester or the ortho ester. For the *trans* compound, this proton gave rise to a clean triplet of doublets in the proton NMR spectrum with two large *trans*-diaxial couplings (11.8 Hz) and one smaller axial–equatorial coupling (3.7 Hz). The same methine proton in the *cis* product led to an apparent quartet with a coupling constant of approximately 4.5 Hz.

The success of the two previous cyclizations caused us to wonder if the ketene acetal groups could be coupled to directly generate bis-ester products. To this end, substrate **31c** was electrolyzed to form a 60% isolated yield of cyclized product (Scheme 11). In this case, the major product obtained was the *trans*-isomer which was initially obtained as the ortho ester. The *cis*-isomer hydrolyzed upon workup and was isolated as the ester.

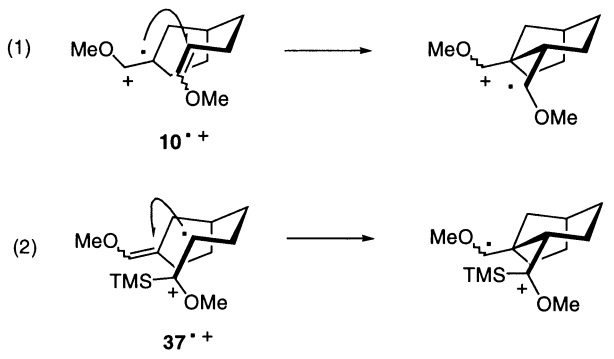
Having established the ability of the silated enol ether to participate in anodic carbon–carbon bond forming reactions, attention was turned toward seeing if the ketene acetal equivalent could be used to construct a bridged bicyclic ring skeleton. Because of the difficulties associated with doing Peterson olefination reactions on ketones, the initial



Scheme 12.

substrate designed (**37**) placed the ketene acetal on the side chain and the enol ether group on the ring (Scheme 12). To synthesize this substrate, the side chain hydroxyl group in **9** was protected with a *t*-butyldiphenylsilyl group, the ketone converted to an enol ether using a Wittig reaction, and then the silyl group removed. Oxidation of the alcohol using TPAP followed by the Peterson olefination afforded the desired electrolysis substrate.

Unfortunately, all attempts to cyclize **37** met with failure. In no case was the desired bicyclo[3.2.1]octane ring skeleton observed. This result was puzzling because the presence of the trimethylsilyl substituent had not interfered with the cyclization in any of the model systems. While the formation of the quaternary carbon would slow the cyclization, why would the presence of the trimethylsilyl substituent lower the efficiency of the cyclization relative to substrate **10**? One possible explanation for this observation was that the presence of the silicon group caused the olefin on the side chain to be oxidized and hence changed the site of initial radical cation formation. This suggestion was consistent with cyclic voltammetry data that gave rise to an $E_{p/2}$ of +1.0 V vs. Ag/AgCl for substrate **37**. Recall that the oxidation potential measured for **10** was +1.13 V vs. Ag/AgCl. If the oxidation of **37** did take place on the side chain, then the resulting cyclization reaction would run in the opposite direction to one that originated from **10**. Previous olefin coupling reactions had demonstrated that the cyclization reactions were 'radical-like' in their behavior.[3] What this meant was that the radical cation attacked the olefin in a fashion that led to the formation of a radical intermediate at the terminating end of the cyclization. It was possible that the problems associated with the cyclization resulting from **37** simply represented further evidence for this mechanism. For **10**, such a mechanism would involve initial formation of a radical cation from the ring enol ether and then a subsequent 6-*exo-trig* type cyclization onto the disubstituted olefin of the side chain (Scheme 13 (1)). If the presence of the silyl group in **37** were to reverse the direction of this cyclization reaction, then the radical cation would be generated on the side chain (Scheme 13 (2)). The ensuing radical-like cyclization would then require a 6-*exo-trig* cyclization onto the trisubstituted ring enol ether. For radical cyclization reactions, it is known that substituents at the radical center (R_1 in Fig. 3) have little effect on the cyclization.[24] However, substituents on the internal carbon of the olefin being attacked (R_2 in Fig. 3) dramatically slow the cyclization.



Scheme 13.

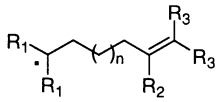


Figure 3.

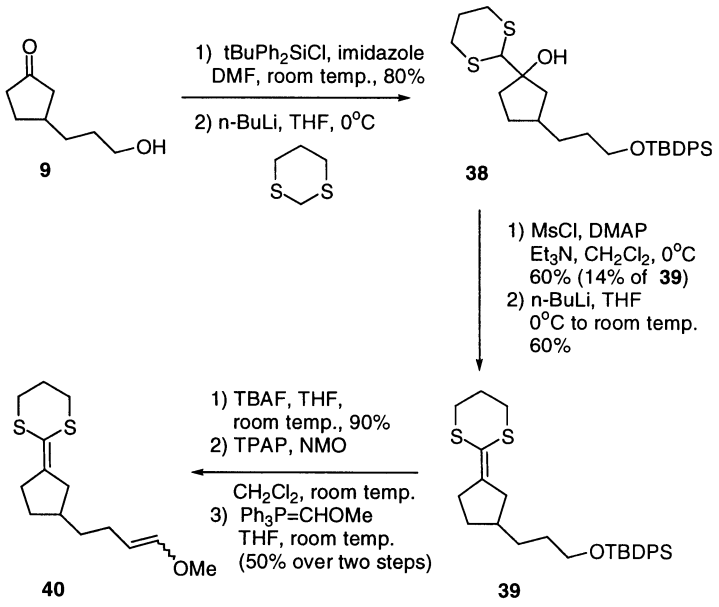
This is exactly the scenario outlined in Scheme 13. For the cyclization resulting from the oxidation of **10** the extra substituents would be on the carbon bearing the 'radical'. For the cyclization resulting from **37** the extra substituent would be on the internal carbon of the olefin to be attacked.

If such a scenario were the case, then moving the ketene acetal equivalent to the position on the ring should lead to a successful cyclization. Unfortunately, Peterson olefination reactions often do not work well with ketone substrates. In the current case, all attempts to build a substrate with a silyl substituent on the ring enol ether of **10** met with failure and a direct test of the theory above was not possible. It became clear that an alternative ketene acetal equivalent was needed.

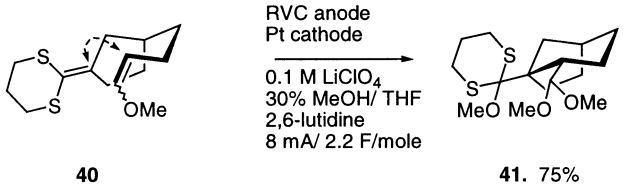
4. The use of a ketene dithioacetal initiating group

What was required was a ketene acetal equivalent that could be readily generated from a ketone, could be isolated and purified, and could be introduced into an electrolysis cell. To this end, a ketene dithioacetal seemed ideal.[25] While oxidative cyclization reactions using this substrate were rare,[26] the combination of hydrolytic stability and the low oxidation potential of the sulfur groups suggested that such an initiating group would be very effective for the anodic reactions. To investigate this idea, substrate **40** was built from alcohol **9** as outlined in Scheme 14. This was accomplished by first protecting the alcohol as the *t*-butyldiphenylsiloxy ether and then adding a dithiane anion to the ketone. The tertiary alcohol was converted to a chloride and followed by an elimination reaction to complete formation of the ketene dithioacetal group.[27] The synthesis of the substrate was completed by cleaving the silyl ether, oxidizing the resulting alcohol, and introducing the enol ether terminating group with a Wittig reaction.

The anodic oxidation of **40** proceeded smoothly to the desired bridged bicyclic product in a 75% isolated yield (Scheme 15). One major product was isolated along with 5% of what looked to be a minor isomer. The structure of the minor isomer could not be unequivocally assigned because the majority of its signals in the proton NMR were buried underneath those observed for the major isomer. The stereochemistry of the major product also proved to be difficult to assign in an unambiguous fashion because the proton NMR signal for the methine proton on the carbon bearing the dimethoxy acetal group was obscured by other signals. A hydrolysis reaction of the major product moved this proton to a position where it could be observed by converting the acetal to an aldehyde (see Section 6 for details). In this case, the methine proton alpha to the aldehyde appeared as a doublet of doublets with 11.3 and 4.8 Hz coupling



Scheme 14.



Scheme 15.

constants. Clearly, the methine proton was in an axial position and the aldehyde was in the equatorial position. A second aldehyde isomer was not observed. At this point, we believe that the major product from the cyclization reaction had the dimethoxy acetal group in the equatorial position as well.

5. Conclusions

While the anodic cyclization resulting from **40** did not directly address what went wrong with the planned cyclization of **37**, it did clearly indicate that the use of a ketene acetal initiating group on the ring could be employed to build bicyclo[3.2.1]octane products having the ends differentiated for further synthetic transformations. Of course, the success of this cyclization reaction immediately led to a number of questions. Can the ketene dithioacetal group be used to directly probe the mechanistic suggestion made in connection with Scheme 13? Can a cyclization reaction utilizing a ketene dithioacetal be used to complete the synthesis of scopadulcic acid B? How general are anodic cyclization reactions using initiating groups of this nature? What other ketene acetal groups can be used to trigger anodic cyclization reactions? Efforts to address these questions and exploit the reactions for use in total synthesis are currently underway.

6. Experimental[28]

6.1. Data for compounds

6.1.1. 3-(3′-Hydroxypropyl)cyclopentan-1-one (9). Initially, 3-(2′-propenyl)cyclopentanone (**8**) was synthesized as follows.[14] CuBr/Me_2S (20.6 g, 20 mmol) and dry LiCl (4.32 g, 20 mmol) were placed in a two-necked 100 mL round-bottom flask equipped with a stir bar and sealed with two septa. The flask was evacuated with a vacuum pump and then purged with Ar while drying with a heat gun. Heating was continued for several hours until the solid became a pale green or blue. This process was repeated three times. At that point, THF (150 mL) was added and the resulting mixture stirred for 3 min to yield a dark yellow, homogeneous solution which was then cooled to −78°C. Next, 90 mL of a 1.0 M solution of allyl magnesium bromide in THF was added in a dropwise fashion. TMSCl (12.7 mL, 100 mmol) was then added followed immediately by the neat addition of cyclopentenone (3.70 mL, 45 mmol). The reaction was allowed to proceed for 5 min before being quenched at −78°C with a saturated aqueous NH_4OH/NH_4Cl solution (1:9). The mixture was extracted four times with 100 mL of ether. The combined organic layers were then dried over $MgSO_4$ and then concentrated in vacuo. The resulting liquid was treated with THF (150 mL) and tetrabutylammonium fluoride (100 mL, 100 mmol, 1.0 M sol. in THF) for 10 min.

The solution was again concentrated in vacuo and the oil was subjected to flash chromatography (hexane/ether 8:1) to yield the known 3-(2′-propenyl)cyclopentanone (80%). As an important sidenote the product is volatile. In our hands, it was best to dissolve the crude product in THF, add silica gel to the solution, and then remove the THF in vacuo. The coated silica gel was then added to the top of the chromatography column.

Once the allyl substituted cyclopentanone was generated, it

was converted into **9** using a three-step procedure as follows. A slurry of 2.15 g (20.0 mmol) of trimethylorthoformate and 1.4 g of montmorillonite K-10 clay (dried in an oven at 120°C for 16 h) was allowed to stir for 30 min at room temp. under N_2. Following this step, a solution of 0.5 g (4.0 mmol) of 3-(2′-propenyl)cyclopentanone in 5.0 mL of pentane was added and the reaction mixture allowed to stir for 6 h. The reaction was monitored by TLC. If starting material remained, then additional premixed trimethylorthoformate and MK-10 was added until the reaction was forced to completion. The reaction mixture was then suction filtered through a glass filter, dried over $MgSO_4$, and concentrated in vacuo in order to obtain the corresponding acetal.

The acetal was directly used for the next step without purification. To a stirred 0°C mixture of 7.2 mL (72.0 mmol) of a 10 M borane dimethysulfide complex in THF solution with 20 mL of THF was added 15 mL (144 mmol) of 2-methyl-2-butene over 10 min. The reaction was warmed to room temperature and stirred for 2 h. The reaction mixture was then cooled back to 0°C and a solution of 7.92 g (48.0 mmol) of 3-(2′-propenyl)cyclopentanone dimethylacetal in 20 mL of THF was added dropwise. The reaction mixture was warmed to room temperature and stirred for an additional 2 h. The reaction mixture was cooled back to 0°C. A mixture of 84 mL of 30% H_2O_2 and 48 mL of 3 M NaOH solution was slowly added. The reaction was allowed to stir at room temperature for 16 h, diluted with ether, washed with sat. Na_2SO_3 and aq. K_2CO_3. The aqueous fractions were combined and extracted with ether. The combined organic fractions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo.

The acetal was then removed by dissolving the crude alcohol in wet acetone and adding 16.8 g of montmorillonite K-10 clay. The resulting suspension was stirred at room temperature for 12 h, filtered through $MgSO_4$, concentrated in vacuo, and the residue chromatographed through a silica gel column. Elution with ether furnished 3-(3′-hydroxypropyl)cyclopentan-1-one (4.12 g, 60% over three steps). IR (NaCl, neat) 3424, 2931, 1734, 1163, 1057, 731 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 3.483 (td, J_t=6.0 Hz, J_d=3.0 Hz, 2H), 3.03–3.00 (br s, 1H), 2.35–1.90 (series of m, 5H), 1.68 (dd, J_1=18.2 Hz, J_2=9.0 Hz, 1H), 1.60–1.25 (series of m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) 220.3, 62.1, 45.0, 38.3, 36.8, 31.6, 30.6, 29.2; HRMS (EI) *m/e* calcd for $C_8H_{15}O_2$ (M^++H) 143.1072, found 143.1071.

6.1.2. 1-(1′-Methoxymethylene)-3-(4′-methoxy-3′-butenyl)cyclopentane (10). In a flame dried flask, under argon blanket, to a stirred suspension of 34.9 g (101.9 mmol) of methoxymethyltriphenylphosphonium chloride in 100 mL of tetrahydrofuran at 0°C was added dropwise 78.4 mL (101.9 mmol) of 1.3 M *sec*-butyllithium in cyclohexane. The dark red mixture was allowed to warm to room temperature, stirred for 1 h, and then cooled to 0°C. In a second flask, 2.895 g (20.4 mmol) of 3-(3′-hydroxypropyl)cyclopentane and 1.88 mL (26.5 mmol) of dimethyl sulfoxide in 40.0 mL of abs. tetrahydrofuran were cooled to −78°C under nitrogen atmosphere. Oxalyl chloride (2.13 mL, 24.5 mmol) was added dropwise and the resulting mixture warmed slowly with stirring over 30 min until the temperature was −50°C. The reaction was then stirred for 10 min before being cooled back down to −78°C and quenched with triethylamine (8.55 mL, 61.2 mmol). The resulting solution was stirred for another 10 min, diluted with 100 mL of tetrahydrofuran, and allowed to warm to room temperature. The white solids were removed by filtration and then washed with tetrahydrofuran. The combined washings were concentrated in vacuo. The crude aldehyde generated in this step was diluted with 50 mL of tetrahydrofuran and then cannulated into the stirred 0°C solution of methoxymethyltriphenylphosphonium ylide generated above. The reaction mixture was allowed to warm to room temperature. After 48 h, the reaction was diluted with ether and quenched with brine. The layers were separated and the aqueous layer was extracted with ether. The combined organic extracts were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through silica gel that was slurry packed using 1% triethylamine/hexane solution. Gradient elution with hexane followed by 5% ether/hexane afforded 1-(1′-methoxymethylene)-3-(4′-methoxy-3′-butenyl)cyclopentane (2.0 g, 50%, over two steps). IR (NaCl, neat) 2929, 2848, 1694, 1654, 1456, 1221, 1119 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 6.27 (d, J=12.6 Hz, 0.5H), 5.85 (m, 1.5H), 4.70 (td J_t=12.5 Hz, J_d=7.5 Hz, 0.5H,), 4.32 (dt, J_d=J_t=6.0 Hz, 0.25H), 4.31 (dt, J_d=J_t=6.0 Hz, 0.25H), 3.55, 3.53, 3.47 (three singlets, 6H), 2.25–1.65 (series of m, 6H), 1.45–1.25 (m, 3H), 1.25–1.05 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) 146.9, 146.00, 138.7, 138.6, 120.5, 120.2, 107.0, 103.0, 59.4, 59.3, 55.8, 40.2, 39.8, 39.4, 36.8, 36.3, 35.7, 35.2, 33.6, 33.5, 33.00, 32.4, 28.4, 28.4, 26.6, 26.3, 22.9; HRMS (EI) *m/e* calcd for $C_{11}H_{17}O$ (M^+−OMe) 165.1279, found 165.1278.

6.1.3. 3-Formylmethylcyclopentan-1-one. 3-(2′-Propenyl)-cyclopentanone (1.0 g) was dissolved in 100 mL of a 1:1 mixture of methanol/methylene chloride and cooled to −78°C. Ozone gas was bubbled through the solution until a pale blue color persisted. Nitrogen was then bubbled through the reaction until no blue color remained. Dimethyl sulfide (4.0 equiv.) was added and the reaction warmed to room temperature. After 12 h, the solvent was removed in vacuo and the crude product directly subjected to hydrolysis reaction by dissolving it in a mixture of 1.5% water/acetone. Excess montmorillonite K-10 was added and the mixture stirred for 2 h at room temperature. The reaction mixture was then filtered through $MgSO_4$, concentrated in vacuo, and the residue chromatographed through a silica gel column. Elution with 50% ether/hexane furnished 3-formylmethylcyclopentan-1-one in a 60% yield (0.61 g). Due to volatility the product was not fully characterized until after the subsequent Wittig reaction. IR (neat/NaCl) 2959, 2897, 1739, 1718, 1406, 1158 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 9.67 (s, 1H, C*H*O), 2.65–2.45 (m, 3H), 2.37 (dd, J_d=18.0, 6.9 Hz, 1H), 2.25–1.95 (m, 3H), 1.72 (dd, J_d=18.0, 8.5 Hz, 1H), 1.55–1.35 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 218.1, 200.7, 49.2, 44.4, 38.1, 30.9, 29.2.

6.1.4. 1-(1′-Methoxymethylene)-3-(3′-methoxy-2′-propenyl)cyclopentane (11). The keto aldehyde generated in the preceding reaction was converted into substrate **11** using a Wittig reaction that was identical to the reaction used to build substrate **10** above. In this case, a 60% yield (scale=1.73 g of product) of the desired substrate **11** was

obtained. IR (NaCl, neat) 2932, 2832, 1653, 1457, 1222, 1119 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 6.25 (d, J_d=12.6 Hz, 0.3H), 6.24 (d, J_d=12.6 Hz, 0.3H), 5.84 (m, 1.4H), 4.75–4.60 (m, 0.6H), 4.33 (m, 0.4H), 3.53 (s), 3.51 (s), 3.50 (s), 3.46 (s), 2.52–1.68 (series of m, 8H), 1.35–1.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 147.4, 146.4, 138.8, 138.7, 120.3, 120.1, 105.6, 101.8, 101.7, 59.3, 59.2, 55.7, 55.7, 41.3, 41.0, 40.6, 40.2, 35.3, 35.0, 33.3, 33.2, 33.1, 32.8, 32.5, 32.4, 31.9, 31.7, 29.2, 28.8, 28.2, 28.2, 26.2, 26.0; HRMS (EI) *m/e* calcd for $C_{11}H_{19}O_2$ (M^++H) 183.1385, found 183.1384.

6.1.5. 3-(Bis-carbomethoxymethyl)-1-cyclopentanone. In a flame-dried flask under nitrogen atmosphere, to a suspension of 9.9 g (180 mmol) of sodium methoxide in 50 mL of methanol was slowly added dimethyl malonate (20.9 mL, 183 mmol). The mixture was stirred for 1 h at room temperature. Cyclopentenone (10.2 mL, 122 mmol) was then added very slowly and the reaction stirred for an additional 18 h at room temperature. The reaction mixture was quenched with brine, the methanol removed under reduced pressure, and the remaining material diluted with water and extracted with ether. The combined organic layers were then washed with brine, dried over magnesium sulfate, and concentrated in vacuo. The crude product was chromatographed through a silica gel column. Elution with ether furnished 3-(bis-carbomethoxymethyl)-1-cyclopentanone in a 95% yield (24.8 g). IR (NaCl, neat) 2959, 1738, 1433, 1157, 1021, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 3.73 (s, 3H), 3.70 (s, 3H), 3.35 (d, J=9.6 Hz, 1H), 2.92–2.73 (m, 1H), 2.54–2.40 (dd, J_d=18.3, 8.1 Hz, 1H), 2.40–2.07 (series of m, 3H), 2.05–1.90 (dd, J_d=18.6, 11.1 Hz, 1H), 1.72–1.50 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 216.9, 216.8, 168.5, 168.4, 56.0, 55.9, 52.5, 42.8, 42.7, 38.1, 38.0, 36.3, 36.2, 27.4, 27.3; HRMS (EI) *m/e* calcd for $C_{10}H_{15}O_5$ (M^++H) 215.0919, found 215.0910.

6.1.6. 1,1-Dimethoxy-3-(bis-carbomethoxymethyl)cyclopentane (12). To a stirred suspension of 4.99 g (47.0 mmol) of trimethyl orthoformate and 3.3 g of montmorillinite K-10 clay was added a solution of 2.0 g (9.4 mmol) of the keto diester made above in 20 mL of pentane at room temperature. The mixture was stirred for 1 h. The dark reaction was then filtered, dried over $MgSO_4$, concentrated in vacuo, and the residue chromatographed through a silica gel column (packed with 1% triethylamine). Elution with 50% ether/hexane furnished 1,1-dimethoxy-3-(bis-carbomethoxymethyl)cyclopentane in near quantitative yield (2.43 g, 100%). IR (NaCl, neat) 2953, 2832, 1738, 1436, 1140, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 3.63 (s, 6H), 3.21 (d, J=10.2 Hz, 1H), 3.08 (s, 6H), 2.66–2.48 (m, 1H), 1.99 (dd, J_1=13.3 Hz, J_2=7.8 Hz, 1H), 1.88–1.58 (series of m, 3H), 1.48–1.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) 168.9, 168.9, 110.7, 56.7, 52.2, 52.2, 49.1, 49.0, 38.7, 36.5, 33.5, 27.8; HRMS (EI) *m/e* calcd for $C_{12}H_{21}O_6$ (M^++H) 261.1338, found 261.1358.

6.1.7. 1,1-Dimethoxy-3-(1,1′-bis-carbomethoxy-4′-methyl-3′-pentenyl)cyclopentane. To 5 mL of dry methanol in a flame-dried flask under nitrogen atmosphere was slowly added 426 mg (18.5 mmol) of sodium metal. After the sodium completely reacted, 1,1-dimethoxy-3-(bis-carbomethoxymethyl)cyclopentane (4.80 g, 18.4 mmol) in 5 mL of methanol followed by isoprenyl bromide (2.15 mL, 18.5 mmol) was added to the flask. The reaction mixture was refluxed for 16 h and then cooled in an ice-bath, quenched with water, and diluted with ether. The organic layer was separated and then washed with saturated NaCl. The combined aqueous layers were extracted with ether. The combined organic layers were then washed with brine, dried over magnesium sulfate, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (packed with 1% triethylamine). Elution with 10% ether/hexane afforded a 50% yield of 1,1-dimethoxy-3-(1,1′-bis-carbomethoxy-4′-methyl-3′-pentenyl)-cyclopentane (3.02 g, 50%) along with 40% of the recovered starting material. IR (NaCl, neat) 2965, 2832, 1737, 1433, 1240, 1048, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 4.96 (t, J=7.3 Hz, 1H), 3.69 (s, 6H), 3.17 (s, 3H), 3.16 (s, 3H), 2.72–2.55 (m, 1H), 2.53 (d, J=7.2 Hz, 2H), 2.06 (dd, J_d=13.2, 8.13 Hz, 1H), 1.90–1.45 (series of m, 5H), 1.67 (s, 3H), 1.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 171.2, 171.0, 134.9, 117.9, 110.1, 60.3, 51.8, 48.9, 48.6, 39.39, 36.0, 33.2, 32.4, 25.8, 24.9, 17.5; HRMS (EI) *m/e* calcd for $C_{16}H_{25}O_5$ (M^+−OMe) 297.1702, found 297.1692.

6.1.8. 3-(1′,1′-Bis-carbomethoxy-4′-methyl-3′-pentenyl)-cyclopentanone (13). The dimethoxy ketal in the product formed during the previous step was removed using the same procedure employed in the synthesis of **9**. In this case, a near quantitative yield of product was obtained (scale=1.18 g of product). IR (NaCl, neat) 2943, 1728, 1654, 1232, 908, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 4.93 (t, J=7.3 Hz, 1H), 3.69 (s, 6H), 2.86–2.69 (m, 1H), 2.69–2.56 (m, 2H), 2.43 (dd, J_1=18.5 Hz, J_2=7.8 Hz, 1H), 2.34–2.04 (series of m, 5H), 1.66 (s, 3H), 1.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 217.2, 170.7, 170.7, 135.6, 117.3, 59.9, 52.0, 40.9, 39.5, 38.2, 32.2, 25.8, 24.8, 17.6; HRMS (EI) *m/e* calcd for $C_{15}H_{23}O_5$ (M^++H) 283.1545, found 283.1546.

6.1.9. 3-(1′,1′-Bis-carbomethoxy-3′-oxo-propyl)cyclopentanone. The olefin in **13** was cleaved using an ozonolysis in a fashion identical to that described above for the synthesis of 3-formylmethylcyclopentan-1-one. In this case, a 95% yield (0.95 g of product) of the desired keto aldehyde was obtained. IR (NaCl, neat) 3470, 2960, 2848, 1736, 1432, 1272, 1167, 916, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 9.66 (br s, 1H), 3.71 (s, 6H), 2.96 (s, 2H), 2.94–2.80 (m, 1H), 2.50–2.00 (series of m, 5H), 1.76–1.58 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 216.1, 198.1, 169.8, 169.7, 72.6, 56.4, 52.7, 45.7, 40.8, 40.7, 38.1, 24.9; HRMS (EI) *m/e* calcd for $C_{12}H_{17}O_6$ (M^++H) 257.1025, found 257.1028.

6.1.10. 1-(1′-Methoxymethylene)-3-(1′,1′-bis-carbomethoxy-4′-methoxy-3′-butenyl)cyclopentanone (14). The synthesis of substrate **14** was completed in a fashion identical to that reported for the synthesis of substrate **10**. In this case, the bis-Wittig reaction led to the formation of a 60% yield (0.73 g) of the desired bis enol ether substrate. IR (NaCl, neat) 2948, 2835, 1736, 1656, 1438, 1286, 1219, 1120 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 6.29 (d, J=12.6 Hz, 0.5H), 5.92 (d with fine coupling, J=6.3 Hz, 0.5H), 5.84 (br s, 1H), 4.66–4.48 (m, 0.5H), 4.26–4.13 (m, 0.5H), 3.68 (s, 3H), 3.67 (s, 3H), 3.54 (s, 1.5H), 3.51

(s, 1.5H), 3.50 (s, 1.5H), 3.45 (s, 1.5H), 2.78–1.84 (series of m, 7H), 1.48–1.28 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) 171.4, 171.2, 149.6, 148.6, 139.1, 138.9, 102.3, 100.4, 100.2, 96.5, 96.4, 61.3, 61.1, 60.1, 59.6, 59.4, 55.8, 52.0, 43.1, 43.0, 42.9, 42.8, 33.2, 31.0, 29.1, 29.0, 28.6, 28.5, 28.2, 27.7, 26.0, 25.9; HRMS (EI) *m/e* calcd for $C_{16}H_{25}O_6$ (M^++H) 313.1651, found 313.1653.

6.2. General procedure for the preparative electrolysis reactions

6.2.1. Synthesis of 1,2-(bis-carboxaldehydedimethylacetal)bicyclo[3.2.1]heptane (15). To a dry three neck round bottom flask equipped with a nitrogen inlet, a reticulated vitreous carbon anode, and a Pt cathode were added 364 mg (1.86 mmol) of 1-(1′-methoxymethylene)-3-(4′-methoxy-3′-butenyl)cyclopentane, 62 mL of a 50% methanol/tetrahydrofuran solvent mixture, 660 mg of lithium perchlorate (1 M solution), and 1.194 g (11.14 mmol) of 2,6-lutidine. The resulting solution was degassed under nitrogen atmosphere with the aid of a sonicator for 30 min. The electrolysis was then carried out at constant current of 28.6 mA until 395.4 C (2.2 F/mol) of electricity had been passed. Following the passage of current, the reaction mixture was diluted with ether and then washed with brine. The aqueous layers were extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed through a silica gel column that was slurry packed using a 1% triethylamine/hexane solution. Elution with 30% ether/hexane solution afforded product **15** in an 82% yield as a 1:1 mixture of stereoisomers (392 mg). IR (NaCl, neat) 2928, 1454, 1076 cm^{-1}; ^{1}H NMR for a 4:1 ratio of isomers ($CDCl_3$, 300 MHz) 4.57 (d, *J*=6.0 Hz, 0.5H), 4.36 (d, *J*=3.0 Hz, 0.5H), 4.07 (s, 1H), 3.51 (s), 3.47 (s), 3.44 (s), 3.42 (s), 3.37 (s), 3.34 (s), 3.33 (s, 7 's', 12H), 2.16 (m, 1H), 2.00–1.78 (m, 2H), 1.78–1.55 (m, 3H), 1.55–1.10 (series of m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 112.1, 110.9, 107.2, 106.4, 59.2, 58.9, 57.0, 56.8, 55.7, 55.1, 54.2, 53.8, 51.1, 50.8, 44.0, 41.5, 41.0, 35.3, 35.3, 34.8, 31.9, 30.9, 29.8, 29.0, 28.7, 27.0, 19.4, 18.3; HRMS (EI) *m/e* calcd for $C_{13}H_{23}O_3$ (M^+−OMe) 227.1647, found 227.1647.

6.2.2. 1,2-(Bis-carboxaldehydedimethylacetal)bicyclo-[2.2.1]hexane (16). Substrate **11** was electrolyzed using the general procedure described for the oxidation of substrate **10**. In this example, 100 mg of the starting material was electrolyzed in order to form 87 mg (65%) of the isolated product as a 1:1 mixture of isomers. IR (NaCl, neat) 2925, 1460, 1077, 733 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 4.48 (s, 0.5H), 4.38 (s, 0.5H), 4.29 (d, *J*=9.0 Hz, 0.5H), 4.27 (d, *J*=6.1 Hz, 0.5H), 3.52 (s), 3.49 (s), 3.48 (s), 3.44 (s), 3.34 (s), 3.33 (s), 3.31 (s), 3.28 (s, 8 's', 12H), 2.35–2.08 (series of m, 3H), 1.92–1.00 (series of m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) 108.9, 108.8, 106.7, 105.7, 58.4, 56.5, 54.0, 53.8, 53.3, 45.0, 41.0, 39.3, 37.6, 36.0, 35.7, 33.9, 32.8, 32.0, 30.0, 29.8, 29.7, 29.5, 29.3; HRMS (EI) *m/e* calcd for $C_{12}H_{21}O_3$ (M^+−OMe) 213.1491, found 213.1489.

6.2.3. 1,2-(Bis-carboxaldehydedimethylacetal)-4,4-bis-carbomethoxy-bicyclo[3.2.1]heptane (17). The electrolysis of substrate **14** was conducted in a fashion identical to the general procedure described for the oxidation of **10**. In this example, 45 mg of the substrate was oxidized in order to obtain 35 mg (65%) of the cyclized product. IR (NaCl, neat) 2954, 2835, 1736, 1438, 1240, 1193, 1081 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 4.38 (d, *J*=3.3 Hz, 1H), 4.08 (s, 1H), 3.70 (s, 3H), 3.65 (s, 3H), 3.50 (s, 3H), 3.44 (s, 3H), 3.39 (s, 3H), 3.36 (s, 3H), 2.85 (t, J_t=6.0 Hz, 1H), 2.43 (dd with fine coupling, J_d=15.4, 4.4 Hz, 1H), 2.25 (dt, J_d=15.4 Hz, J_t=4.4 Hz, 1H), 2.02–1.73 (series of m, 2H), 1.71–1.52 (m, 3H), 1.43–1.29 (m, 1H), 1.27–1.16 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 171.7, 171.7, 111.3, 106.4, 59.1, 58.7, 57.2, 55.4, 54.8, 52.6, 52.4, 50.7, 40.3, 40.3, 37.3, 27.3, 26.0, 23.8; HRMS (EI) *m/e* calcd for $C_{17}H_{27}O_7$ (M^+−OMe) 343.1757, found 343.1760.

6.2.4. 1-(Trimethylsilyl)-1,7-dimethoxy-4,4-dimethylhepta-1,6-diene (31a). To a solution of bis(trimethylsilyl)-methoxymethane[29] (2.27 g, 12.0 mmol) in 10 mL of abs. tetrahydrofuran at −78°C was added dropwise 4.78 mL (12.0 mmol) of 2.5 M *n*-butyllithium in hexanes. The mixture was warmed slowly to room temperature and then stirred for 45 min. In a second flask, 1-(methoxy)-4,4-dimethyl-1-en-hexan-6-ol[17] (755 mg, 4.78 mmol) was dissolved in 10.0 mL of methylene chloride. *N*-Methylmorpholine oxide (842 mg, 7.17 mmol) and molecular sieves (4 Å) powder (1.51 g, 2.0 equiv. by wt.) were added and cooled to 0°C. Tetrapropylammonium perruthinate (84 mg, 0.239 mmol) was added very slowly, warmed to room temperature and stirred for 90 min. The reaction mixture was filtered through small silica gel pad packed with 1% triethylamine, and then the solvent removed in vacuo. The crude aldehyde was dissolved in 10 mL of tetrahydrofuran and transferred via cannulae into a stirred −78°C solution of the anion generated above. The reaction mixture was allowed to warm to room temperature. After 20 h, the reaction mixture was diluted with ether and quenched with brine. The layers were separated and the aqueous layer was extracted with ether. The combined organic extracts were dried over $MgSO_4$, concentrated in vacuo, and chromatographed through a silica gel column that was slurry packed using 1% triethylamine/hexane solution. Elution with 10% ether/hexane afforded 1-(trimethylsilyl)-1,7-dimethoxy-4,4-dimethylhepta-1,6-diene **31a** (856 mg, 70%, over two steps). IR (NaCl, neat) 2954, 2900, 2828, 1655, 1462, 1249, 1116, 837 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 6.24 (d, *J*=12.5 Hz, 0.2H), 5.95 (d, *J*=6.2 Hz, 0.8H), 5.22 (t, *J*=7.8 Hz, 0.8H), 5.20–5.04 (m, 0.2H), 4.72 (td, J_d=12.6 Hz, J_t=7.8 Hz, 0.2H), 4.48–4.28 (m, 0.8H), 3.55 (s, 2.4H), 3.51 (s, 0.6H), 3.46 (s, 3H), 2.10–1.85 (m, 4H), 0.85 (s, 4.8H), 0.83 (s, 1.2H), 0.16 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 148.4, 147.2, 109.7, 109.2, 103.5, 99.3, 59.4, 55.9, 54.4, 40.4, 38.7, 36.2, 34.2, 26.8, 26.6, 26.5, −0.4; HRMS calcd for $C_{14}H_{29}O_2Si$ (M^++H) 257.1937, found 257.1935.

6.2.5. 1-(Trimethylsilyl)-1,8-dimethoxyocta-1,7-diene (31b). In a fashion identical to that described for the synthesis of **31a** 1-(methoxy)heptan-1-en-7-ol (1.0 g, 6.94 mmol) was converted into substrate **31b** in a 60% isolated yield. IR (NaCl, neat) 2936, 2856, 1659, 1459, 1251, 1104, 842, 762 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 6.26 (d, *J*=12.6 Hz, 0.5H), 5.84 (d, *J*=6.2 Hz, 0.5H), 5.11 (t, *J*=7.8 Hz, 1H), 4.70 (td, J_d=12.6 Hz, J_t=7.3 Hz, 0.5H),

4.30 (q, J=7.3 Hz, 0.5H), 3.54 (s, 1.5H), 3.47 (s, 1.5H), 3.41 (s, 3H), 2.20–1.82 (m, 4H), 1.50–1.20 (m, 4H), 0.14 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 147.0, 146.0, 112.8, 112.6, 106.9, 102.9, 59.3, 58.2, 55.7, 54.2, 31.1, 30.9, 30.4, 29.4, 27.6, 27.3, 23.8, −0.7; HRMS (EI) *m/e* calcd for $C_{10}H_{17}O_2$ (M^+-SiMe_3) 169.1228, found 169.1074.

6.2.6. 1-(Trimethylsilyl)-1-methoxy-4,4-dimethylhexan-1-en-6-ol. To a solution of bis(trimethylsilyl)methoxymethane (10.13 g, 53.3 mmol) in 30.0 mL of abs. tetrahydrofuran at −78°C was added dropwise 21.31 mL (53.3 mmol) of 2.5 M *n*-butyllithium in hexanes. The mixture was warmed slowly to room temperature and stirred for 45 min. The solution was cooled to −78°C and then 2-hydroxy-4,4-dimethyltetrahydropyran (2.31 g, 17.76 mmol) in 20.0 mL of abs. tetrahydrofuran added with the use of a cannula. The reaction was allowed to warm to room temperature and stirred for 20 h. The reaction mixture was then diluted with ether, quenched with brine, the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed through a silica gel column that was slurry packed using 1% triethylamine/hexane solution. Elution with 50% ether/hexane furnished 1-(trimethylsilyl)-1-methoxy-4,4-dimethylhexan-1-en-6-ol (2.45 g, 60%, over two steps). IR (NaCl, neat) 3346, 2956, 2896, 1470, 1245, 1120, 836 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 5.18, (t, J=7.7 Hz, 0.7H), 5.12 (t, J=7.7 Hz, 0.3H), 3.73–3.64 (m, 2H), 3.57 (s, 0.9H), 3.47 (s, 2.1H), 2.40–2.10 (br s, 1H), 2.08 (d, J=7.5 Hz, 0.6H), 1.99 (d, J=7.7 Hz, 1.4H), 1.55 (t, J=8.5 Hz, 1.4H), 1.49 (t, J=7.2 Hz, 0.6H), 0.91 (s, 6H), 0.17 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 162.9, 161.8, 122.7, 108.7, 59.1, 58.5, 54.3, 44.3, 43.8, 38.6, 36.9, 32.7, 32.6, 27.4, 26.9, −0.5; HRMS (EI) *m/e* calcd for $C_{11}H_{23}OSi$ (M^+-OMe) 199.1518, found 199.1508.

6.2.7. 1,7-(Bis-trimethylsilyl)-1,7-dimethoxy-4,4-dimethylhepta-1,6-diene (31c). In a fashion identical to that described for the synthesis of **31a** 1-(trimethylsilyl)-1-(methoxy)-4,4-dimethyl-1-en-hexan-6-ol (888 mg, 3.86 mmol) was converted into substrate **31c** in a 70% isolated yield. IR (NaCl, neat) 3025, 2958, 2898, 2825, 1605, 1465, 1253, 1114, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 5.22 (t, J=7.8 Hz, 1.6H), 5.12 (t, J=7.4 Hz, 0.4H), 3.57 (s, 1.2H), 3.47 (s, 4.8H), 2.09 (d, J=7.4 Hz, 0.4H), 2.00 (d, J=7.9 Hz, 1.6H), 0.87 (s, 6H), 0.17 (s, 18H); ^{13}C NMR ($CDCl_3$, 75 MHz) 163.7, 161.8, 161.6, 122.8, 109.4, 108.9, 58.6, 54.3, 39.4, 38.9, 37.3, 34.2, 34.1, 26.7, 26.5, 2.5, −0.3; HRMS (EI) *m/e* calcd for $C_{16}H_{33}O_2Si_2$ (M^+-Me) 313.2019, found 313.2020.

6.2.8. Preparative electrolysis of 31a. Using the setup described for the oxidation of substrate **10**, compound **31a** (110 mg) was electrolyzed. In this case, pure methanol solvent and a constant current of 8 mA were used. The reaction was stopped after 4.0 F/mol of electricity was passed. All other conditions were the same. The cyclization reaction produced 14.3 mg (15%) of the ortho ester product **33a** along with 50.9 mg (64%) of the methyl ester product **32a**. The spectral data for **32a** were as follows: IR (NaCl, neat) 2952, 2868, 1733, 1436, 1369, 1178, 1062 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 4.39 (d, J=8.7 Hz, 0.94H), 4.16 (d, J=6.8 Hz, 0.06H), 3.65 (s, 0.18H), 3.64 (s, 2.82H), 3.30 (s, 0.18H), 3.28 (s, 0.18H), 3.26 (s, 2.82H), 3.23 (s, 2.82H), 3.05–2.92 (m, 1H), 2.74–2.58 (m, 1H), 1.80–1.45 (series of m, 4H), 1.08 (s, 2.82H), 1.02 (s, 0.18H), 0.99 (s, 0.18H), 0.93 (s, 2.82H); ^{13}C NMR ($CDCl_3$, 75 MHz) 176.0, 107.8, 105.4, 53.5, 52.4, 51.4, 46.2, 45.5, 44.9, 43.9, 43.7, 43.1, 42.3, 39.0, 29.8, 29.5, 29.2, 28.0; HRMS (EI) *m/e* calcd for $C_{11}H_{19}O_3$ (M^+-OMe) 199.1334, found 199.1331.

6.2.9. Preparative electrolysis of 31b. Using the setup described for the oxidation of substrate **10**, compound **31a** (106 mg) was electrolyzed. In this case, pure methanol solvent and a constant current of 8 mA were used. The reaction was stopped after 4.3 F/mol of electricity was passed. All other conditions were the same. The cyclization reaction produced 34.4 mg (30%) of the ortho ester product **33b** along with 33.1 mg (35%) of the methyl ester product **32b**. The spectral data for the relatively unstable **33b** were as follows: ^{1}H NMR ($CDCl_3$, 300 MHz) 4.49 (d, J=8.6 Hz, 0.6H), 4.03 (d, J=6.1 Hz, 0.4H), 3.65 (s), 3.64 (s), 3.47 (s, three S's, 9H)), 3.33 (s), 3.30 (s), 3.29 (s, three S's, 6H), 2.73 (q, J=4.7 Hz, 1H), 2.24–2.13 (m, 1H), 2.30–1.00 (series of m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz) 111.4, 107.8, 105.5, 55.4, 54.4, 53.7, 53.3, 51.4, 51.2, 45.5, 41.7, 41.2, 40.9, 29.9, 27.7, 25.9, 25.2, 25.0, 24.6, 24.5, 23.1. The spectral data for **32b** were as follows: IR (NaCl, neat) 2829, 2754, 2728, 1663, 1134, 1110, 1079, 1059, 1016, 998 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 4.48 (d, J=8.6 Hz, 0.4H), 4.02 (d, J=5.8 Hz, 0.6H), 3.64 (s), 3.63 (s, two S's, 3H)), 3.32 (s), 3.29 (s), 3.28 (s, three S's, 6H), 2.72 (q, J=4.7 Hz, 0.6H), 2.45–2.25 (m, 0.4H), 2.18 (dt, J_t=11.8 Hz, J_d=3.7 Hz, 1H), 2.05–0.95 (series of m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz) 176.7, 107.8, 105.5, 55.3, 54.4, 53.7, 53.3, 51.4, 51.2, 45.4, 41.7, 41.2, 40.9, 29.9, 27.7, 25.9, 25.2, 24.9, 24.6, 24.5, 23.0; HRMS (EI) *m/e* calcd for $C_{10}H_{17}O_3$ (M^+-OMe) 185.1178, found 185.1180.

6.2.10. Preparative electrolysis of 31c. Using the setup described for the oxidation of substrate **10**, compound **31c** (110 mg) was electrolyzed. In this case, pure methanol solvent and a constant current of 8 mA were used. The reaction was stopped after 6.0 F/mol of electricity was passed. All other conditions were the same. The cyclization led to the formation of 43.6 mg (50%) of the *trans*-isomer as the ortho ester **34** and 7.2 mg (10%) of the *cis*-isomer as the methyl ester **35**. The ortho ester **34** was not stabilized and was therefore hydrolyzed (water, montmorillonite K-10) to the corresponding methyl ester prior to characterization. The spectral data for the methyl ester obtained from **34** were as follows: IR (NaCl, neat) 2954, 2869, 1735, 1436, 1174, 1029, 733 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 3.68 (s, 6H), 3.36–3.23 (m, 2H), 1.94–1.60 (m, 4H), 1.03 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 175.5, 52.0, 46.5, 44.5, 39.4, 29.0; HRMS (EI) *m/e* calcd for $C_{10}H_{15}O_3$ (M^+-OMe) 183.1021, found 183.1019. The spectral data for **35** were as follows: IR (NaCl, neat) 2958, 2872, 1744, 1433, 1207, 1041, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) 3.65 (s, 6H), 3.30–3.16 (m, 2H), 2.00–1.70 (m, 4H), 1.13 (s, 3H), 0.98 (s, 3H); HRMS calcd for $C_{10}H_{15}O_3$ (M^+-OMe) 183.1021, found 183.1019.

6.2.11. 3-(3′-*t*-Butyldiphenylsilyloxypropyl)cyclopentan-1-one. To a stirred solution of 3-(3′-hydroxypropyl)cyclo-

pentane (2.84 g, 20 mmol) and imidazole (2.95 g, 44 mmol) in 40 mL of DMF was slowly added *t*-butyldiphenylsilyl chloride (6.1 g, 22 mmol). The reaction mixture was stirred for 12 h at room temperature, diluted with ether, and then washed with water. The aqueous layers were combined and extracted with ether. The combined ether fractions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was chromatographed through a silica gel column using 25% ether/hexane as eluant in order to afford 6.08 g (80%) of the protected alcohol 3-(3′-*t*-butyldiphenylsilyloxypropyl)cyclopentan-1-one. IR (NaCl, neat) 3071, 2931, 2853, 1741, 1111, 703 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 7.74–7.64 (m, 4H), 7.50–7.35 (m, 6H), 3.68 (t, J=6.2 Hz, 2H, CH_2OH), 2.32 (dt, J_t=18.0 Hz, J_d=7.2 Hz, 2H), 2.22–2.02 (m, 3H), 1.88–1.70 (m, 1H), 1.70–1.40 (series of m, 6H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 219.8, 135.6, 134.0, 129.7, 127.7, 63.8, 45.3, 38.6, 36.9, 31.9, 30.8, 29.6, 27.0, 19.3; HRMS (EI) *m/e* calcd for $C_{24}H_{31}O_2Si$ (M^++H−H_2) 379.2093, found 379.2094.

6.2.12. 1-(1′-Methoxymethylene)-3-(3′-hydroxypropyl)-cyclopentane (36). To a stirred suspension of 8.57 g (25 mmol) of methoxymethyltriphenylphosphonium chloride in 25 mL of tetrahydrofuran at 0°C was added dropwise 19.3 mL (25 mmol) of 1.3 M *sec*-butyllithium in cyclohexane. The dark red mixture was allowed to warm to room temperature and stirred for 1 h. After cooling the solution back to 0°C, 3-(3′-*t*-butyldiphenylsilyloxypropyl)-cyclopentan-1-one (3.8 g, 10 mmol) in 20 mL of tetrahydrofuran was added via a cannula. The reaction was allowed to warm to room temperature. After 16 h, the reaction mixture was diluted with ether and quenched with brine. The layers were separated and the aqueous layer was extracted with ether. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The crude silyl protected enol ether was then dissolved in tetrahydrofuran (20 mL) and 1 M tetrabutylammonium fluoride (20.0 mL, 20 mmol) was added. After 12 h, the reaction was diluted with ether and washed with water and brine. The aqueous fractions were combined, saturated with sodium chloride, and extracted with ether. The combined organic fractions were dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed through a silica gel column that was slurry packed using 1% triethylamine/hexane solution. Elution with 50% ether/hexane afforded 1-(1′-methoxymethylene)-3-(3′-hydroxypropyl)cyclopentane (0.85 g, 50%, over two steps). IR (NaCl, neat) 3263, 2826, 2760, 1625, 1373, 1064 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 5.82 (br s, 1H), 3.55 (t, J=6.6 Hz, 2H), 3.49 (s, 3H), 2.52–2.00 (series of m, 3H), 1.90–1.65 (m, 3H), 1.65–1.45 (m, 3H), 1.45–1.25 (m, 2H), 1.25–1.02 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) 138.6, 138.6, 120.3, 62.9, 59.3, 40.3, 39.9, 35.6, 33.6, 33.0, 32.4, 31.6, 31.5, 31.1, 28.3, 26.2; HRMS calcd for $C_{10}H_{18}O_2Li$ (M^++Li) 177.1467, found 177.1461.

6.2.13. 1-(1′-Methoxymethylene)-3-(4′-methoxy-4′-trimethylsilyl-3′-butenyl)cyclopentane (37). Using the procedure described above for the synthesis of substrate **31a**, 100 mg of 1-(2′-methoxymethylene)-3-(3′-hydroxypropyl)cyclopentane was converted into 94.6 mg (60% over two steps) of the desired substrate **37**. IR (NaCl, neat) 2826, 2795, 2744, 2728, 1190, 1064, 789 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 5.92–5.83 (m, 1H), 5.14 (dt J_d=7.8 Hz, J_t=1.77 Hz, 1H), 3.54 (s, 3H), 3.43 (s, 3H), 2.62–1.98 (series of m, 7H), 1.50–1.08 (series of m, 4H), 0.16 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 160.8, 138.8, 120.3, 112.8, 59.4, 54.4, 40.4, 40.0, 37.6, 37.1, 35.8, 33.7, 33.1, 32.5, 28.4, 26.6, 26.3, 14.2, −0.6; HRMS (EI) *m/e* calcd for $C_{15}H_{29}O_2Si$ (M^++H) 269.1937, found 269.1945.

6.2.14. 1-Hydroxy-1-(2′,6′-dithiocyclohexyl)-3-(3′-*t*-butyldiphenylsilyloxypropyl)cyclopentane (38). In a flame-dried flask, dithiane (320 mg, 2.7 mmol) was placed under argon atmosphere. Tetrahydrofuran was added and the mixture cooled to 0°C. A 2.5 M solution of *n*-BuLi in hexanes (1.36 mL, 3.4 mmol) was added, and then the reaction raised to room temperature and stirred for one hour. The reaction was then cooled back down to 0°C and 3-(3′-*t*-butyldiphenylsilyloxypropyl)cyclopentan-1-one (380 mg, 1.0 mmol) in 5 mL of THF added. The reaction was allowed to warm to room temperature and stirred for 1 h. The reaction was then diluted with ether and washed with brine. The aqueous layer was extracted with ether. The combined organic layers were then dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed through a silica gel column using 20% ether/hexane as eluant to afford 400 mg (80%) of the desired product. IR (NaCl, neat) 3463, 3066, 2934, 2862, 1432, 1108, 710 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 7.70–7.63 (m, 4H), 7.46–7.34 (m, 6H), 4.30 (br s, 1H), 4.26 (s, 1H), 3.64 (t, J=6.3 Hz, 2H), 2.96–2.84 (m, 4H), 2.30–1.65 (series of m, 8H), 1.64–1.12 (series of m, 5H), 1.04 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 135.6, 134.2, 129.6, 127.6, 84.2, 74.8, 64.1, 59.3, 47.5, 45.5, 37.9, 37.5, 32.0, 31.5, 30.8, 30.5, 27.9, 27.2, 27.0, 25.8, 25.5, 19.3; HRMS (EI) *m/e* calcd for $C_{24}H_{31}S_2O_2Si$ (M^+−CMe_3) 443.1535, found 443.1543.

6.2.15. 1-Chloro-1-(2′,6′-dithiocyclohexyl)-3-(3′-*t*-butyldiphenylsilyloxypropyl)cyclopentane. In a flame-dried flask, 1-hydroxy-(2′,6′-dithiacyclohexyl)-3-(3′-*t*-butyldiphenylsilyloxypropyl)cyclopentane **38** (150 mg, 0.3 mmol) was dissolved in CH_2Cl_2 (10 mL). 1.5 equiv. of *N*,*N*-dimethylaminopyridine (58.6 mg, 0.45 mmol) and 3.0 equiv. of triethylamine (0.13 mL, 0.9 mmol) were added and cooled to 0°C. 2.0 equiv. of MsCl (0.6 mmol) was added very slowly and stirred for 3 h at room temperature. When complete, the reaction was poured into the ice water. The aqueous layer was extracted with ether. The organic layer was then washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed through a silica gel column using 20% ether/hexane as eluant to afford 93 mg (60%) of the chlorinated product along with 20 mg (14%) of the ketene dithioacetal product from elimination of the chloride. This reaction afforded a 40% yield of the chloride when done on a large scale (5.27 g of product). The spectral data for the chlorinated product were as follows: IR (NaCl, neat) 3067, 2927, 2861, 1396, 1109, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 7.76–7.60 (m, 4H), 7.50–7.40 (m, 6H), 4.32 (d, J=12.0 Hz, 1H), 3.65 (t, J=6.0 Hz, 2H), 3.00–2.86 (m, 4H), 2.65–1.75 (series of m, 8H), 1.75–1.20 (series of m, 5H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$,

75 MHz) 135.6, 134.1, 134.1, 129.6, 127.7, 82.6, 81.6, 63.9, 60.8, 60.5, 48.7, 47.5, 42.4, 40.9, 38.6, 37.5, 32.9, 32.1, 31.7, 31.5, 31.4, 31.0, 30.1, 27.0, 25.7, 19.3; HRMS (EI) *m/e* calcd for $C_{28}H_{40}S_2OSi^{35}Cl$ (M^+) 519.1978, found 519.1939.

6.2.16. 1-(2′,6′-Dithiocyclohexylidene)-3-(3′-*t*-butyldiphenylsilyloxypropyl)cyclopentane (39). In a flame-dried flask, 1-chloro-1-(2′,6′-dithiacyclohexyl)-3-(3′-*t*-butyldiphenylsilyloxypropyl)cyclopentane (6.3 g, 12.2 mmol) was dissolved in tetrahydrofuran under argon atmosphere and cooled to 0°C. A 2.5 M solution of *n*-BuLi in hexanes (5.8 mL, 14.6 mmol) was added and then the reaction warmed to room temperature. The resulting mixture was stirred for 1 h, diluted with ether and quenched with brine. The aqueous layer was then extracted with ether. The combined organic layers were washed with water and brine before being dried over magnesium sulfate and concentrated in vacuo. The crude product was chromatographed through a silica gel column using 10% ether/hexane as eluant to afford 3.51 g (60%) of the desired ketene dithioacetal. IR (NaCl, neat) 3064, 2932, 2859, 1465, 1426, 1114, 696 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 7.72–7.63 (m, 4H), 7.47–7.34 (m, 6H), 3.66 (t, J=6.3 Hz, 2H), 2.92–2.76 (m, 4H), 2.72–2.45 (m, 2H), 2.34–2.19 (m, 1H), 2.19–2.06 (m, 2H), 1.96–1.78 (m, 3H), 1.66–1.52 (m, 2H), 1.48–1.33 (m, 2H), 1.33–1.18 (m, 1H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) 147.8, 135.6, 134.1, 129.6, 127.6, 113.5, 64.1, 40.1, 39.7, 32.7, 32.5, 31.4, 30.0, 30.0, 26.9, 25.3, 19.3; HRMS (EI) *m/e* calcd for $C_{28}H_{39}S_2OSi$ (M^++H) 483.2212, found 483.2199.

6.2.17. 1-(2′,6′-Dithiacyclohexylidene)-3-(3′-hydroxypropyl)cyclopentane. In a dry flask, compound **39** (4.3 g, 8.9 mmol) was dissolved in tetrahydrofuran and treated with tetrabutylammonium fluoride (18.0 mL, 18.0 mmol) at room temperature. The resulting mixture was stirred for 4 h, diluted with ether and quenched with brine. The aqueous layer was extracted with ether, and then the combined organic layers dried over magnesium sulfate and concentrated in vacuo. The crude product was chromatographed through a silica gel column using 75% ether/hexane as eluant to afford 1.96 g (90%) of the deprotected alcohol. IR (NaCl, neat) 3354, 2921, 1424, 1270, 1053, 914 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 3.64 (t, J=6.6 Hz, 2H), 2.90–2.78 (m, 4H), 2.75–2.45 (m, 2H), 2.36–2.19 (m, 1H), 2.19–2.06 (m, 2H), 2.00–1.82 (m, 3H), 1.66–1.53 (m, 2H), 1.48 (br s, 1H), 1.46–1.18 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 147.3, 113.6, 62.9, 40.1, 39.5, 32.6, 32.4, 31.5, 31.3, 29.9, 29.9, 25.2; HRMS (EI) *m/e* calcd for $C_{12}H_{21}S_2O$ (M^++H) 245.1034, found 245.1025.

6.2.18. 1-(2′,6′-Dithiacyclohexylidene)-3-(4′-methoxy-3′-butenyl)cyclopentane (40). Using the two step oxidation–Wittig reaction sequence outlined above for the synthesis of substrate **10**, 427 mg (1.75 mmol) of the alcohol synthesized in the previous step was converted into 236 mg (50%) of substrate **40**. The procedure only differed from the one reported above in that 2.5 equiv. of the ylide were used for the Wittig reaction instead of the five equivalents used to make the bis enol ether substrate **10**. IR (NaCl, neat) 2923, 2850, 1654, 1424, 1206, 1100, 921 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 6.29 (d, J=12.6 Hz, 0.4H), 5.86 (dt, J_d=6.3 Hz, J_t=1.5 Hz, 0.6H), 4.71 (dt, J_d=12.6 Hz, J_t=7.2 Hz, 0.4H), 4.32 (q, J=7.2 Hz, 0.6H), 3.58 (s, 1.8H), 3.50 (s, 1.2H), 2.89–2.76 (m, 4H), 2.74–2.43 (m, 2H), 2.35–2.18 (m, 1H), 2.18–2.02 (m, 3H), 2.02–1.81 (m, 4H), 1.46–1.18 (series of m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 148.1, 147.7, 147.1, 146.2, 113.3, 106.9, 103.0, 59.6, 56.0, 40.1, 39.6, 39.6, 36.5, 35.4, 32.6, 32.6, 30.1, 26.6, 25.4, 22.8; HRMS (EI) *m/e* calcd for $C_{14}H_{23}S_2O$ (M^++H) 271.1190, found 271.1188.

6.2.19. Preparative electrolysis of 40: 1-(1′-methoxy-2′,6′-dithiacyclohexyl)-2-(carboxaldehyde dimethoxy acetal)bicyclo[3.2.1]heptane (44). Using the setup described for the oxidation of substrate **10**, compound **40** (299 mg, 1.11 mmol) was electrolyzed. In this case, 30% methanol/THF was used as solvent. A current of 8 mA was applied until 2.2 F/mol of electricity was passed. All other conditions were the same. The cyclization led to the formation of 276 mg (75%) of the desired bicyclic product was obtained. The product was predominately one isomer. IR (NaCl, neat) 2821, 1385, 1049, 1042, 1012, 994 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 4.85 (br s, 1H), 3.53 (s, 3H), 3.42 (s, 3H), 3.39 (s, 3H), 3.30–3.10 (m, 1H), 2.80–2.55 (m, 3H), 2.25–1.20 (series of m, 14H); ^{13}C NMR ($CDCl_3$, 75 MHz) 107.5, 56.6, 56.3, 56.1, 52.6, 46.2, 45.6, 44.1, 36.2, 35.0, 30.7, 30.2, 28.7, 28.0, 27.6, 27.4, 27.3, 24.0, 23.2, 22.7, 18.8, 11.2; HRMS (EI) *m/e* calcd for $C_{16}H_{28}O_3S_2Li$ (M^++Li) 339.1640, found, 339.1653.

6.2.20. Hydrolysis of 41: 1-(1′-oxo-2′-thia-5′-thiol-pentyl)-2-(carboxaldehyde)bicyclo[3.2.1]heptane. In a round bottom flask, 1-(1′-methoxy-2′,6′-dithiacyclohexyl)-2-(carboxaldehyde-dimethylacetal)bicyclo[3.2.1]heptane (100 mg, 0.3 mmol) was dissolved in 1.5% water/acetone. Amberlyst-15 (200 mg, 2.0 equiv. by weight) was added and the mixture stirred for 1 h at room temperature. When complete the reaction mixture was filtered through $MgSO_4$, concentrated in vacuo and the residue chromatographed through a silica gel column. Elution with 20% ether/hexane furnished 1-(1′-oxo-2′-thia-5′-thiol-pentyl)-2-(carboxaldehyde)bicyclo[3.2.1]heptane (74 mg, 90%). IR (NaCl, neat) 2832, 2765, 1700, 1155 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 9.59 (s, 0.1H), 9.57 (d, J=1.5 Hz, 0.9H), 2.98 (t, J=6.9 Hz, 2H), 2.88 (dd, J_d=11.3, 4.8 Hz, 1H), 2.57 (q, J_1=14.5 Hz, J_2=7.5 Hz, 2H), 2.42–2.34 (m, 1H), 2.32–2.16 (m, 1H), 2.02–1.78 (series of m, 6H), 1.70–1.36 (series of m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 204.0, 202.3, 59.7, 55.3, 44.7, 35.3, 33.6, 30.8, 29.4, 28.8, 27.1, 23.5, 20.0; HRMS (EI) *m/e* calcd for $C_{13}H_{20}O_2S_2Li$ (M^++Li) 279.1065, found 279.1061.

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