Tetrahedron 65 (2009) 10863–10875

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Anodic oxidations and polarity: exploring the chemistry of olefinic radical cations

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ARTICLE INFO

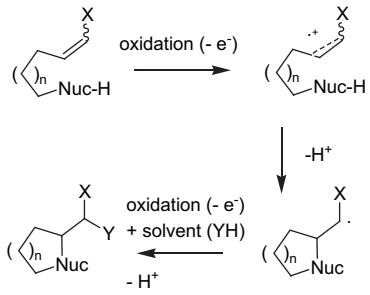
Article history:
Received 23 July 2009
Received in revised form 15 August 2009
Accepted 7 September 2009
Available online 11 September 2009

ABSTRACT

The cyclization chemistry of radical cations derived from electron-rich olefins has been examined and the relationship between the polarization of the radical cation and the chemoselectivity of the reaction probed. It was found that more polarized radical cations favor carbon–carbon bond formation while less polarized radical cations favor carbon–heteroatom bond formation. A new approach to the synthesis of quaternary carbons was uncovered and the compatibility of ene diol ethers with anodic olefin coupling reactions examined.

1. Introduction

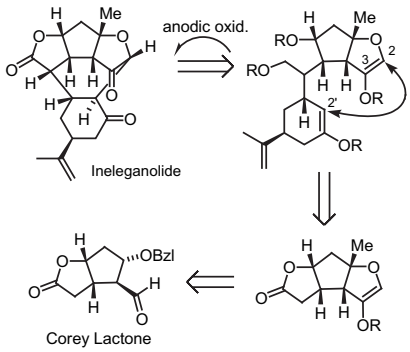
Anodic electrochemistry has proven to be an effective tool for removing electrons from electron-rich functional groups and triggering interesting new umpolung reactions.[1] As part of an ongoing effort to develop the synthetic utility of such reactions, we have been studying transformations having the overall format illustrated in Scheme 1.[2] In the reactions, the one electron oxidation of an electron-rich olefin forms a radical cation that is then trapped with a nucleophile. After the addition of solvent and a second oxidation step, the transformation affords a cyclic product that retains the initial functionality used to trigger the cyclization. Both the umpolung nature of the reactions that provides new opportunities for generating bonds from existing functional groups and the preservation of functionality that can be employed in subsequent synthetic transformations suggest that the reactions have significant potential for constructing complex molecules.



Scheme 1.

To date, the reactions have been initiated by the oxidation of enol ethers, ketene acetals, and electron-rich aromatic rings and terminated with the use of simple olefins, enol ethers, allyl- and vinylsilanes, electron-rich aryl rings, alcohols, amides, and sulfonamides.[2,3] The reactions are compatible with the formation of fused and bridged ring skeletons, the generation of quaternary carbons, and the use of simple reaction setups.[4] They have been used as key reactions in total synthesis efforts.[5]

It was with this in mind that we turned our attention toward a potential use of the reactions for the synthesis of the natural product ineleganolide (Scheme 2).[6] The plan called for an oxidative cyclization reaction to form the final ring and join carbons C2 and C2′. This coupling reaction was intriguing because it involved the oxidation of an electron-rich ene diol ether moiety to form a new type of radical cation intermediate. Previous studies of more electron-rich ketene acetal derived radical cations led to very efficient carbon–carbon bond forming reactions.[7] Would the same be true here? If the reactions were successful, then a second question would be important. The proposed cyclization could lead to either



Scheme 2.

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doi:10.1016/j.tet.2009.09.028

the formation of a six- or a seven-membered ring. Would the conformational requirements imposed on the cyclization by the bicyclic nature of the substrate dictate this regiochemistry?

Support for the suggestion that the reaction might lead to seven-membered ring formation was obtained from molecular modeling studies using a simplified radical cation structure (Fig. 1). The modeling study was conducted using Spartan© 02 on an SGI workstation.[8] Geometry optimization of the initial radical cation was performed using the PM3 and HF/3-21G force fields with the single point energy of the optimized structure calculated using B3LYP/6-31G. The energy profile for the cyclization reaction was performed using a semi-empirical method (PM3) in order to provide a rough approximation of the transition state for the cyclization. For the seven-membered ring, the drive distance for the calculation was set from the initial distance in the optimized radical cation to 1.5 Å with 25 points chosen within this distance. The energy maximum point in the energy profile was taken as the initial transition state structure. This structure was then optimized using both the PM3 and HF/3-21G force fields. The resulting transition state was confirmed with one and only one imaginary frequency that indicates stretching along the reaction coordinate of the forming bond. The single point energy of the transition state was then calculated by B3LYP/6-31G. For the six-membered ring cyclization, the same approach led to an energy maximum that when followed again led to the seven-membered ring product. Hence, for the six-membered ring cyclization the transition state was found by modeling the reverse reaction with a drive distance varying from 1.5 Å to 3.0 Å. The optimized transition state energy was then calculated as described for the seven-membered ring cyclization. A large difference in energy was found for the two pathways (6.4 kcal/mol using HF/3-21G and 11.9 kcal/mol using B3LYP/6-31G to calculate the energy of the transition state) favoring formation of the seven-membered ring. It appeared that the conformation constraints of the bicyclic ring system would indeed impose seven-membered ring formation on the cyclization. That is, of course, if the new radical cation led to any cyclization at all.

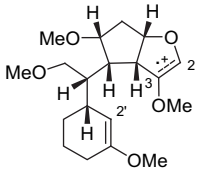
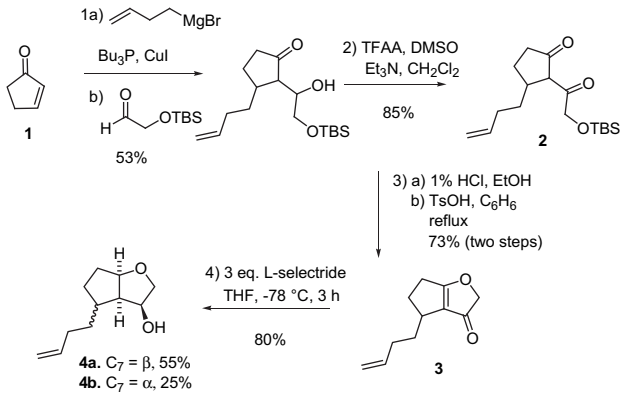


Figure 1.

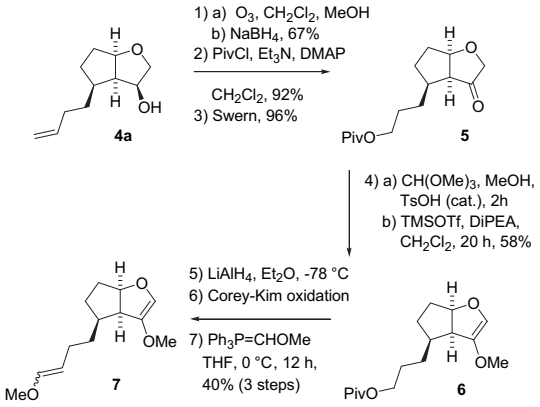
2. Initial studies

With this in mind, a model substrate for the electrolysis was designed and synthesized. The synthesis began with the construction of compound **4a** (Scheme 3), an effort that started with the conversion of cyclopentenone to compound **2**[9] followed by deprotection of the alcohol and then an acid catalyzed cyclization to form tetrahydrofuranone **3**.[10] The resulting enone was reduced with an excess of L-Selectride to afford a mixture of two alcohols (**4a**,**b**).[11] The stereochemistry of the isomers was assigned using an NOE experiment after oxidation of the alcohols to ketones. For isomer a, the methine proton at C_3 showed roughly equal NOE couplings to both the methine at C_4 and the methine at C_7. For isomer b, no interaction was observed for the methine at C_3 with the methine at C_7.



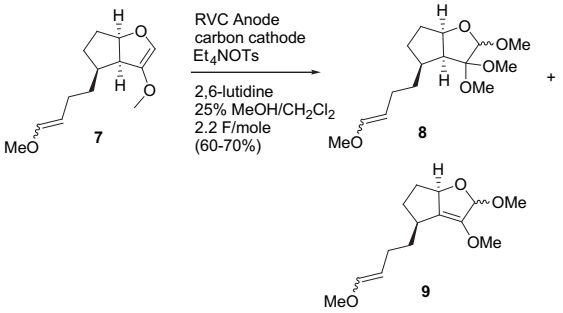
Scheme 3.

With **4a** in hand, the bicyclic oxidation substrate (**7**) was synthesized as outlined in Scheme 4. To this end, **4a** was converted to **5** using an ozonolysis reaction followed by reduction of the secondary ozonide with sodium borohydride, selective protection of the primary alcohol, and then a Swern oxidation to form the ketone. Conversion of the ketone to a dimethoxy ketal followed by an elimination led to formation of the ene diol ether needed for the electrolyis.[12] Deprotection of the primary alcohol, oxidation to form an aldehyde, and a Wittig reaction installed the necessary trapping group for the anodic cyclization.



Scheme 4.

The oxidation of **7** was conducted at a reticulated vitreous carbon (RVC) anode using an electrolyte solution containing 0.05 M tetraethylammonium tosylate in 25% methanol/dichloromethane, 2,6-lutidine as a proton scavenger, a carbon cathode, and a constant current of 8 mA. A total of 2.0–2.2 F/mol of charge was passed through the cell (Scheme 5). To our surprise, no cyclized product was observed. Instead, a 60–70 % yield of product resulting from solvent trapping was obtained.[13] Initially, two products (**8** and **9**) were observed. However, with a careful workup the formation of the methanol elimination product **9** could be avoided and a 59% yield of the pure methanol trapping product **8** isolated. A proton NMR of the crude reaction indicated that **8** was the only product formed in the reaction. The methyl enol ether trapping group was

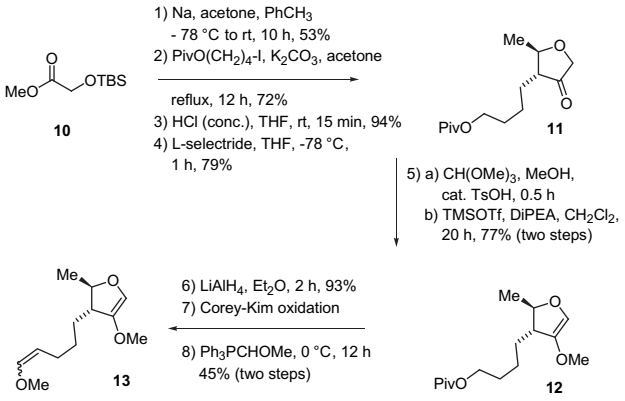


Scheme 5.

completely intact. Clearly, either the presence of the bicyclic ring skeleton or the use of the ene diol ether completely stopped the cyclization.

3. Removing the conformational constraint

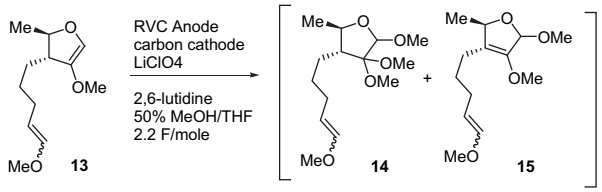
In order to separate the effect of the bicyclic ring skeleton on the cyclization from that of the ene diol ether, monocyclic substrate **13** was synthesized (Scheme 6). While we understood that removing the conformational constraint from the substrate would lead to six-membered ring formation, we wanted to know if the ene diol ether derived radical cation was compatible with carbon–carbon bond formation. How would this electron-rich radical cation compare with the one generated from the oxidation of a ketene acetal?[7]



Scheme 6.

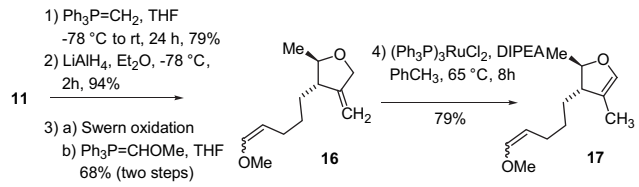
The synthesis began with the conversion of **10** into a 1,3-dicarbonyl[14] that was then alkylated,[15] cyclized using the acid catalyzed conditions employed in the synthesis of the bicyclic substrate,[10b] and the resulting enone reduced with L-Selectride to form furanone **11**. Compound **11** was converted into the electrolysis substrate using the chemistry described previously for the synthesis of **7**.

The electrolysis of **13** was conducted using nearly identical conditions to those employed for the earlier oxidation of substrate **7** (Scheme 7).[13a] Once again, no cyclic product resulting from carbon–carbon bond formation was obtained, and the only observable products resulted from either methanol trapping of, or elimination of a proton from, the radical cation. In this case, the products could not be readily separable from the crude reaction mixture. However, the conclusion of the experiment was obvious. Either the use of the ene diol ether derived radical cation was preventing cyclization or there was some undetermined reason that formation of the tetrasubstituted carbon was in this case preventing the cyclization. The compatibility of the cyclization with forming the tetrasubstituted carbon was quickly demonstrated by replacing the methoxy group of the ene diol ether with a methyl substituent. To this end, a substrate (**17**) was synthesized (Scheme 8). The synthesis took advantage of the previously synthesized furanone ring by converting the ketone into an olefin that was subsequently migrated into the ring.[16] The

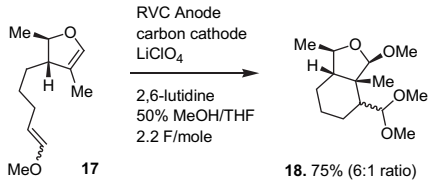


Scheme 7.

anodic oxidation of **17** smoothly led to the formation of a new carbon–carbon bond, a quaternary center, and a bicyclic ring skeleton (Scheme 9).[13a]



Scheme 8.



Scheme 9.

A 75% isolated yield of the cyclic product was obtained as a 6:1 ratio of diastereomers. The major diastereomer had the dimethoxy acetal group on the convex face of the bicyclic ring skeleton. From a synthetic standpoint, the reaction was intriguing because it formed a functionalized bicyclic product having four contiguous stereogenic atoms one of which was the central quaternary carbon. Clearly, the formation of the quaternary carbon was not a problem for the electrolysis reaction. The lack of cyclization resulting from substrate **13** must have been due to the ene diol ether derived radical cation.

4. Polarization and carbon–carbon bond formation

So why did the use of an ene diol ether derived radical cation stop the cyclization reaction when the earlier use of an electron-rich olefin had favored carbon–carbon bond formation?[7] Two suggestions arose from looking at trends associated with the radical cations studied to date (Fig. 2). Our studies started with the examination of enol ether derived radical cations. These intermediates proved adept at forming both carbon–carbon and carbon–oxygen bonds.[2] Two types of ketene acetal derived radical cations were then studied. Ketene dithioacetal derived radical cations were shown to be less effective than the enol ether derived radical cations for generating carbon–carbon bonds but very effective for use in generating carbon–oxygen bonds.[17] *N,O*-Ketene acetal derived radical cations behaved in the opposite fashion and proved to be more efficient at generating carbon–carbon bonds than their enol ether derived counterparts.[5a,7b] Cyclic voltammetry studies showed that this later

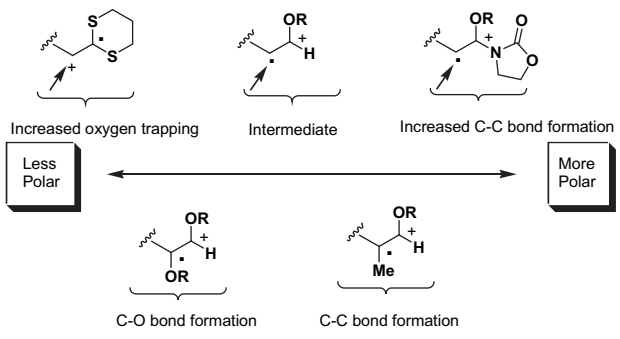
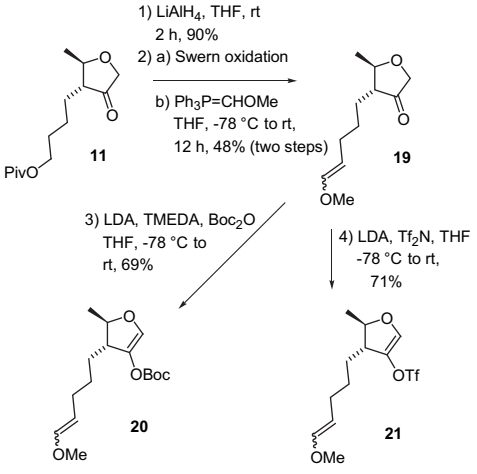


Figure 2.

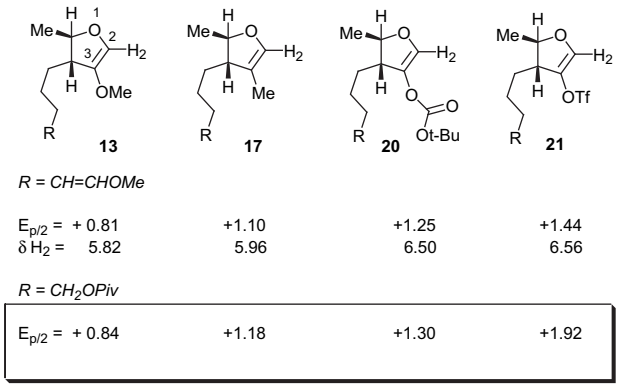
observation was a result of the *N*,*O*-ketene acetal derived radical cations being more stable to methanol solvent trapping.[7b]

At the time, it was thought that the tendency toward carbon–carbon bond formation might be dependent on the 'electron-richness' of the radical cation. It was suggested that the more the groups on the initial double bond stabilized a cation, the more the radical cation would behave as a radical and favor carbon–carbon bond formation.[7b,18] This description of the reactions is not consistent with the oxidation chemistry of substrates **7**, **13**, and **17**. In these cases, the more electron-rich double bond did not lead to carbon–carbon bond formation, but instead favored carbon–oxygen bond formation. The reactions were more consistent with a second possibility suggesting that more polarized radical cations favor carbon–carbon bond formation and less polarized radical cations favor carbon–heteroatom formation. This view of the reactions was consistent with all five radical cations shown in Figure 2.

In order to probe this idea in more detail, two new substrates were constructed (Scheme 10). The first (**20**) replaced the OMe substituent in substrate **13** with a *t*-butylcarbonate group. Since acyloxy type substituents are known to be 'neutral' from an electron-donation perspective,[19] substrate **20** should be less electron-rich but more polar than either the previously studied **13** or **17**. In the second substrate (**21**) the OMe substituent in substrate **13** was replaced with an electron-withdrawing triflate group. Again, the plan was to build a less electron-rich but more polar substrate. The 'electron-richness' versus polarity of all the substrates in the series was examined using a combination of cyclic voltammetry and proton NMR chemical shift data (Scheme 11).[13a] The cyclic voltammetry data was used to gauge the 'electron-richness' of the substrates. The lower the oxidation potential (easier to oxidize) measured for the substrate, the more electron-rich the substrate. The trend established for the initial olefin was assumed to be the same as that for the radical cation intermediate following the oxidation. In other words, a more electron-rich olefin was assumed to give rise to a more electron-rich radical cation intermediate. Two sets of data are presented, one for the preparative electrolysis substrates themselves (R═CH═CHOMe) and a second for a model cyclic voltammetry substrate containing the five-membered ring functional group but lacking the side chain enol ether (R═CH_2O-Piv). All of the CV data reported was measured relative to a Ag/AgCl reference electrode using identical conditions.[20] The 'electron-richness' of the double bond used to generate the radical cation can be best assessed with the model substrate. For this series, the oxidation potential depends directly on the electron-donating ability of the substituent at C_3 of the substrates. From left to right in the Scheme, the substrates go from being more electron-rich to less



Scheme 10.



Scheme 11.

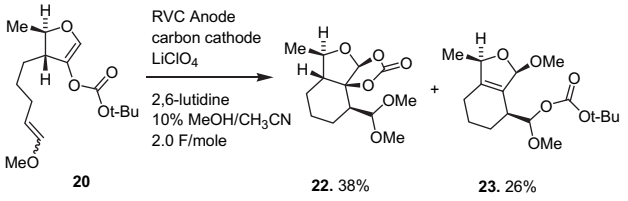
electron-rich. When the enol ether trapping group is added to the side chain of the substrates two changes can be noticed. First, for substrates **13**, **17**, and **20**, a slight drop in potential is observed. This drop in potential is consistent with a rapid cyclization of the radical cation.[21] For substrate **13**, the cyclic voltammogram was run in the absence of methanol solvent. Hence, there was no chance for competitive solvent trapping of the radical cation as observed in the preparative electrolysis. The drop in potential for **13** suggests the possibility for a preparative cyclization from **13** if the methanol solvent could be removed from the reaction. Second, for substrate **21** a dramatic drop in potential is observed relative to the model substrate. In this case, the oxidation potential measured is for the methoxy enol ether group, an observation that suggests that a preparative oxidation of this substrate will not lead a radical cation derived from the five-membered ring double bond.

The polarity of the five-membered ring double bond was gauged by looking at the proton NMR chemical shift observed for H_2 in each of the substrates. The chemical shift of this proton reflects the ability of the group at C_3 to donate electron density to the double bond. The better the electron–donor at C_3 the more upfield the chemical shift of the proton at C_2. Since the donation of electron density to the double bond by the group at C_3 opposes the donation of electron density to the double bond by the oxygen in the ring, the more electron density donated by the group at C_3 the less polar the π-system. Hence, the lower the chemical shift observed for the proton at C_2 the less polar the double bond. The more polar the double bond, the more downfield the chemical shift for H_2. As in the case of electron-richness, it was assumed that the trends observed for the π-system in the starting material would remain the same for the radical cation intermediates generated by the oxidation reaction.

For the substrates in Scheme 11, the polarity of the five-membered ring double bond increased from lowest polarity to highest polarity from left to right in the Scheme. Hence, an oxidation of substrate **13** would be expected to lead to the least polarized radical cation while an oxidation of substrate **21** would be expected lead to the most polarized radical cation (if the five-membered ring double bond was oxidized in this case instead of the side chain enol ether).

When taken in context with the earlier ketene acetal studies,[7] the series of substrates highlighted in Scheme 11 provide a nice test of whether the 'electron-richness' or polarization of a radical cation favors carbon–carbon bond formation. The preparative oxidation of substrates **13** and **17** clearly supports the idea of polarization favoring carbon–carbon bond formation (Fig. 2).[13a] If this trend is general, then the preparative oxidation of substrate **20** should also lead to carbon–carbon formation. This turned out to be the case (Scheme 12). The anodic oxidation of substrate **20** at an RVC anode led to a 64% unoptimized yield of two cyclized products. No uncyclized material was observed in the proton NMR of the crude reaction mixture. This was easy to determine because no signal

remained for either the five-membered ring double bond or the side chain enol ether. The two cyclic products formed arose from the expected initial cyclization followed by a subsequent reaction involving the carbonate group. The products were not stable (the reason for the unoptimized yields) and had a tendency to form furan products derived from elimination. The use of 10% MeOH/CH_3CN as the solvent for the reaction reduced these side reactions. A closely related reaction using an electrolysis substrate having a pivaloyl group in place of the carbonate led almost exclusively to furan products. As in the case of **20**, no uncyclized products were observed following oxidation of the pivaloyl-containing substrate.



Scheme 12.

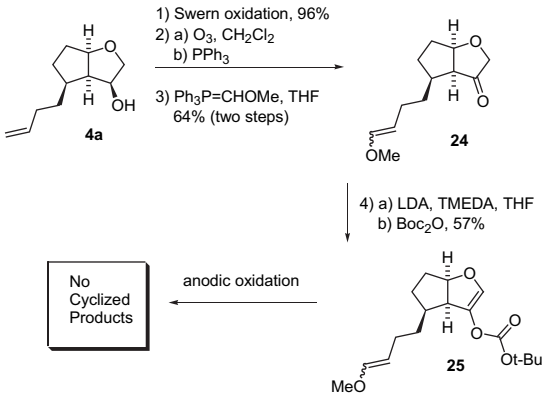
An attempt to probe the chemistry of an even more electron-poor but highly polarized radical cation using substrate **21** met with failure when the preparative reaction did indeed lead to side chain oxidation. In this reaction, the only products observed were derived from methoxylation of the methoxy enol ether. During the reaction, the vinyl triflate group remained intact. The lack of cyclized products in this oxidation is consistent with both the cyclic voltammetry data shown above and earlier cyclization attempts demonstrating that like radical intermediates, radical cations are sensitive to sterics at the terminating end of a cyclization.[17c]

From these studies, two things were clear. First, one cannot simply improve the yield of carbon–carbon bond formation in an anodic olefin coupling reaction by adding a heteroatom to the enol ether starting material. In the case of a ketene acetal, such a change does help the cyclization, but in the case of an ene diol ether the change hurts the cyclization. In other words, it matters where the heteroatom is added to the substrate with the success of a cyclization tracking the polarity of the resulting double bond rather than how electron-rich it is. Second, ene diol ether type substrates can be compatible with the anodic olefin coupling reaction as long as they are substituted in a manner that leads to a polarized radical cation.

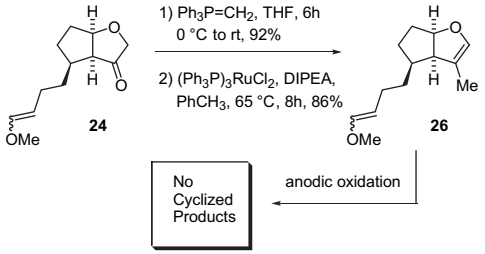
5. A return to bicyclic substrates

Having determined the substituent pattern necessary for triggering cyclizations with ene diol ether type substrates, attention was returned to the bicyclic substrate, the synthesis of ineleganolide, and the key question of whether or not the ring skeleton can be used to channel the anodic cyclization toward the formation of a seven-membered ring. To this end, the methoxy group on the five-membered ring of **7** was replaced with a *t*-butylcarbonyloxy group (**25**) using the synthesis illustrated in Scheme 13. The synthesis started from **4a** and capitalized on the chemistry developed previously.

Unfortunately, the anodic oxidation of **25** did not lead to either a six- or a seven-membered ring product. In this case, evidence for polymerization of the radical cation was obtained. While the reaction led to an inseparable mixture of products, the side chain enol ether appeared to be unchanged in all of them. Clearly, the constraints associated with the bicyclic ring skeleton stopped the cyclization. The same observation was made for a bicyclic substrate based upon the earlier successful cyclization of **17** (Scheme 14). Once again, no cyclized products were observed from the anodic oxidation reaction.

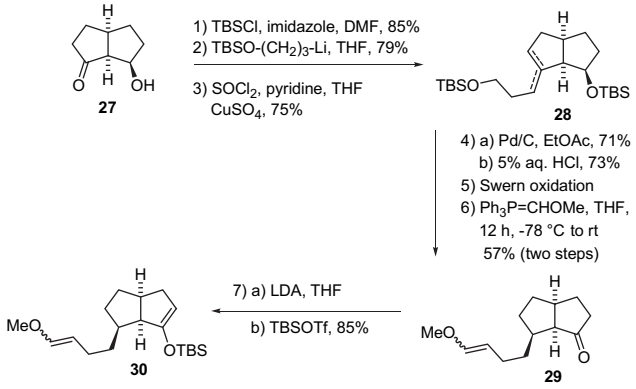


Scheme 13.



Scheme 14.

The failure the anodic oxidation arising from substrate **26** was not that surprising. From our earlier calculations, we knew that the formation of a six-membered ring product from the bicyclic substrate was unlikely. We hoped that the result would be initial trapping of the radical cation by methanol at C_3 followed by a radical cyclization that would form a seven-membered ring at C_2 (the alpha carbon of the radical cation). However, to date no anodic cyclization has led to the formation of a carbon–carbon bond to the alpha carbon of an enol ether derived radical cation. With this in mind, one final test of the anodic cyclization was attempted. In this case, a substrate was built that would enable seven-membered ring formation from an enol ether–enol ether coupling reaction at the beta carbons of the two enol ethers. Similar anodic cyclizations have been used to generate seven-membered ring products.[21a,22] The synthesis of the substrate for the cyclization is shown in Scheme 15.[23] Once again, the anodic oxidation of **30** failed to afford any cyclized product. A variety of conditions were utilized.



Scheme 15.

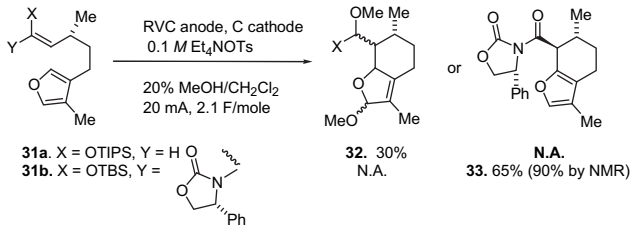
In the end, it was clear that the bicyclic ring skeleton would not allow the cyclization reaction to occur. Evidently, it is simply too difficult for the enol ether to approach the radical cation in a fashion

that allows an intramolecular trapping reaction to compete with decomposition or polymerization of the radical cation.

6. Long range implications and conclusions

While the work reported above indicates that the approach to ineleganolide is fatally flawed, the successful cyclization of **17** suggests a new method for the construction of functionalized quaternary carbons,[24] and the mechanistic insight gained has had an immediate impact on our continuing studies. Two recent examples are particularly useful for highlighting this later point.

The first capitalized on the observation that polarized radical cations lead to more efficient carbon–carbon bond forming reactions (Scheme 16). During efforts to synthesize the arteannuin ring skeleton,[5a] we examined the coupling of electron-rich olefins with substituted furan rings. Two cyclization reactions are shown in Scheme 16. In the first, the coupling reaction was attempted utilizing a silyl enol ether substrate. In the second, an *N*,*O*-ketene acetal was used. Of the two oxidation reactions, the one utilizing the *N*,*O*-ketene acetal (**31b**) led to a far superior yield. A yield for the reaction obtained by NMR using an internal standard showed that this reaction proceeded very cleanly. The lower isolated yield was due to the instability of the furan product. Once again, the use of a more polarized radical cation led to more efficient carbon–carbon bond formation. The total synthesis is being pursued using the ketene acetal-based strategy.



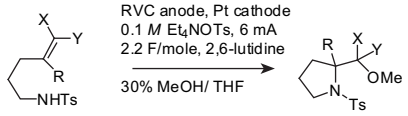
31a. X = OTIPS, Y = H
31b. X = OTBS, Y =

32. 30%
N.A.

N.A.
33. 65% (90% by NMR)

Scheme 16.

The second example capitalized on the relationship between radical cation polarization and chemoselectivity in the opposite direction (Scheme 17). In this case, the trapping of a radical cation by a sulfonamide group was examined.[3] When the reaction was initiated by oxidation of an enol ether, a very low yield of cyclic product was obtained (Scheme 17, substrate **34a**). A switch to a less polar thioenol ether substrate fixed this problem and led to a significantly higher yield of cyclic product. The yield of both reactions could be dramatically improved by using LiOMe as a base to deprotonate the sulfonamide group. Still, the use of the less polarized radical cation led to a higher yield of the desired cyclic product.



34a. X = H, Y = OMe, R = H
34b. X = H, Y = SMe, R = H

35a. 20% (82% with *n*-BuLi/MeOH)
35b. 54% (90% with *n*-BuLi/MeOH)

Scheme 17.

The chemistry outlined in Schemes 16 and 17 demonstrate how important it is to account for the nature of the radical cation intermediate when planning an anodic cyclization reaction. The key is to match the nature of the radical cation intermediate with the type of trapping group being used, an idea that will be implemented in all future anodic olefin coupling reactions.

7. Experimental

7.1. General

7.1.1. 3-(But-3-enyl)-2-(2-(tert-butyldimethylsilyloxy)-1-hydroxyethyl) cyclopentanone. A flame-dried 250 mL three-neck flask under argon was charged with magnesium turnings (2.12 g, 87 mmol) in anhydrous ether (50 mL). A solution of 4-bromobut-1-ene (10.0 g, 74 mmol) in anhydrous ether (50 mL) was placed in the additional funnel and a small portion of the solution was added to the flask. The mixture was heated to reflux and the remaining solution added dropwise at a rate to maintain reflux. After complete addition, the mixture was refluxed for another 30 min and then cooled to rt.

A flame-dried 500 mL three-neck flask under argon was charged with CuI (14.1 g, 74 mmol) in anhydrous ether (200 mL). To the suspension was added Bu_3P (18.3 mL, 74 mmol) and the mixture stirred for 30 min. The resulting slightly yellow solution was added to the Grignard reagent made above at −78 °C and the resulting solution stirred for 30 min. A solution of 2-cyclopenten-1-one (4.2 mL, 50 mmol) in anhydrous ether (30 mL) was then added dropwise. The reaction was stirred for 1.5 h at −78 °C. A solution of 2-dimethyl-*t*-butylsiloxyacetaldehyde (17.2 g, 99 mmol) in anhydrous ether (30 mL) was added over 30 min. The resulting solution was warmed to room temperature for 3 h and then quenched by satd NH_4Cl (200 mL). The aqueous layer was extracted with ether (2×200 mL). The combine organic phase was washed with brine (300 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution from 5% to 35% EtOAc in hexane) to afford desired product in 53% yield (8.30 g, 27 mmol) as a yellow oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.85–5.70 (m, 1H), 5.03, 4.97 (d plus d with fine coupling, J=17.1 Hz, 10.2 Hz, 2H), 3.94 (p, J=5.1 Hz, 0.35H), 3.87 (dd, J=9.6 Hz, 7.5 Hz, 0.65H), 3.78 (p, J=3.6 Hz, 0.65H), 3.70–3.58 (m, 1.35H), 3.47 (d, J=6.6 Hz, 0.35H), 2.74 (d, J=3.6 Hz, 0.65H), 2.30–1.90 (m, 6H), 1.86–1.71 (m, 2H), 1.41–1.27 (m, 2H), 0.85, 0.84 (s plus s, 9H), 0.03, 0.01 (s plus s, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 220.9, 219.5, 138.2, 138.1, 114.8, 114.7, 71.7, 71.4, 65.2, 64.8, 55.8, 55.7, 39.0, 38.7, 38.5, 37.2, 34.6, 34.0, 31.2, 27.0, 25.8, 18.2, 18.1, −5.4, −5.5, −5.6; IR (neat/KBr) 3459, 2928, 2856, 1738, 1640, 1471, 1254, 1105, 837, 777 cm^{-1}; HRMS (ESI) m/z calculated for $C_{17}H_{32}O_3NaSi$ $[M+Na]^+$ 335.2018, found 335.2000.

*7.1.2. 3-(But-3-enyl)-2-(2-(tert-butyldimethylsilyloxy)-acetyl)cyclopentanone (**2**).* To a −78 °C solution of DMSO (15 mL, 0.21 mol) in dry CH_2Cl_2 (150 mL) was added TFAA (115 mL, 0.11 mol). The reaction was stirred for 40 min at this temperature, a solution of the alcohol made above (8.3 g, 27 mmol) in dry CH_2Cl_2 (50 mL) added at −78 °C, and the mixture stirred for 40 min (at −78 °C). Triethylamine (59 mL, 0.43 mol) was then added to the solution and the reaction stirred for 0.5 h. The reaction was warmed to 0 °C, stirred for 40 min, and quenched with satd NH_4Cl (200 mL). HCl (0.5 N) was added until the mixture reached pH=4. The aqueous layer was extracted by ether (3×40 mL), and then the combined organic phase washed with brine (200 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 5% to 10% EtOAc in hexane) to afford the desired product in 85% yield (7.0 g, 22 mmol, 85%) as a pale reddish oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.82–5.67 (m, 1H), 5.07–4.92 (m, 2H), 4.51 (d, J=18 Hz, 1H), 4.28 (d, J=18 Hz, 1H), 3.24 (d, J=10.8 Hz, 1H), 2.80 (m, 1H), 2.41–2.19 (m, 3H), 2.13–1.95 (m, 2H), 1.60–1.42 (m, 3H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 212.1, 204.6, 137.8, 114.9, 69.9, 64.6, 38.9, 38.6, 34.2, 31.5, 27.2, 25.8, 25.7, 18.3, −5.5, −5.6; IR (neat/KBr) 2954, 2929, 2856, 1747, 1723, 1641,

1471, 1254, 1151, 838, 780 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{17}H_{31}O_3Si$ $[M+H]^+$ 311.2042, found 311.2038.

*7.1.3. 4-(But-3-enyl)-5,6-dihydro-2H-cyclopenta[b]furan-3(4H)-one (**3**).* To a 25-mL round-bottom flask was added the ketone made above (1.0 g, 3.22 mmol) and a solution of 5% HCl in THF (20 mL). The reaction was stirred for 3 h and then neutralized by $NaHCO_3$. The aqueous phase was extracted with ether (3×40 mL), and the combined organic layer dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was used in next step without further purification.

To this end, the crude product was taken up in benzene (80 mL) and tosylic acid monohydrate (0.80 g, 4.2 mmol) added. The resulting solution was refluxed using a Dean Stark trap for 20 min. Ether (200 mL) was added and the crude product washed with satd Na_2CO_3 (2×20 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo to give a crude product that was chromatographed through a silica gel column (gradient elution from 10% to 25% EtOAc in hexane) to afford the desired product **3** in 73% yield (0.42 g, 2.4 mmol) as a pale reddish oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.89–5.76 (ddt, *J*=17.1 Hz, 10.2 Hz, 6.6 Hz, 1H), 5.07 (dq, *J*=17.1 Hz, 1H), 4.97 (d with fine coupling, *J*=10.2 Hz, 1H), 4.90 (d with fine coupling, *J*=1.2 Hz, 2H), 2.88 (m, 1H), 2.63–2.53 (m, 3H), 2.22–2.14 (q with fine coupling, *J*=8.1 Hz, 2H), 2.05–1.94 (m, 1H), 1.79–1.73 (m, 1H), 1.54–1.41 (m, 1H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 200.8, 194.6, 138.3, 122.9, 114.4, 84.0, 35.1, 34.5, 32.9, 31.7, 26.5; IR (neat/KBr) 3075, 2920, 2852, 1693, 1613, 1435, 1200, 997, 912 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{11}H_{15}O_2$ $[M+H]^+$ 179.1072, found 179.1067.

7.1.4. (3S,3aR*,4S*,6aR*)-4-(But-3-enyl)-hexahydro-2H-cyclopenta[b]-furan-3-ol (4a) and (3R*,3aS*,4S*,6aS*)-4-(but-3-enyl)hexahydro-2H-cyclopenta[b]furan-3-ol (**4b**).* To a flame-dried 100 mL round-bottom flask under an argon atmosphere was added a solution of compound **3** (1.0 g, 5.6 mmol) in anhydrous THF (20 mL). The reaction was cooled to −78 °C and a 1 M L-Selectride solution in THF (17 mL, 17 mmol) added dropwise. The resulting solution was stirred for 6 h and quenched with 30% H_2O_2 (10 mL), followed by satd $NaHCO_3$ (10 mL). The mixture was stirred for 1 h at rt. Ethyl acetate (50 mL) was added and washed by satd $Na_2S_2O_3$. The aqueous layer was extracted with ethyl acetate (3×20 mL) and the combined organic layer dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 10% to 25% EtOAc in hexane) to afford the desired product **4a** in 55% yield (0.57 g, 3.1 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.62–5.78 (m, 1H), 5.06 (d with fine coupling, *J*=17.1 Hz, 1H), 4.93 (d with fine coupling, *J*=10.2 Hz, 1H), 4.41 (t, *J*=7.2 Hz, 1H), 4.34 (t with fine coupling, *J*=5.7 Hz, 1H), 3.78 (d, *J*=9.6 Hz, 1H), 3.51 (dd, *J*=2.1 Hz, 9.6 Hz, 1H), 2.52 (q, *J*=7.2 Hz, 1H), 2.16 (q, *J*=6.6 Hz, 2H), 1.97–1.80 (m, 4H), 1.71–1.51 (m, 3H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 139.1, 114.2, 84.8, 76.8, 75.0, 50.8, 42.8, 33.5, 32.1, 31.4, 29.0; IR (neat/KBr) 3399, 3078, 2924, 2856, 1639, 1453, 1227, 1048, 998 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{11}H_{18}NaO_2$ $[M+Na]^+$ 205.1204, found 205.1208.

Diastereomer **4b** was isolated in a 25% yield (0.25 g, 1.4 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.90–5.76 (m, 1H), 5.06–4.94 (dq, *J*=1.8 Hz, 17.1 Hz and d with fine coupling, *J*=10.2 Hz, 2H), 4.44 (m, 1H), 4.32 (septet, *J*=3.9 Hz, 1H), 3.73 (dq, *J*=4.2 Hz, 9.6 Hz, 2H), 2.27–2.06 (m, 5H), 1.93–1.86 (m, 2H), 1.69 (m, 1H), 1.49–1.34 (m, 3H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 138.8, 114.3, 85.8, 75.4, 72.7, 54.0, 37.1, 34.7, 32.4, 32.3, 32.2; IR (neat/KBr) 3399, 3078, 2924, 2856, 1639, 1453, 1227, 1048, 998 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{11}H_{18}NaO_2$ $[M+Na]^+$ 205.1204, found 205.1199.

7.1.5. (3S,3aR*,4S*,6aR*)-4-(3-Hydroxypropyl)-hexahydro-2H-cyclopenta[b]furan-3-ol.* Ozone was bubbled through a −78 °C solution of compound **4a** (0.56 g, 3.1 mmol) in CH_2Cl_2 (20 mL) until the solution turned a persistent pale blue. The excess ozone was removed by flushing the solution with Ar. $NaBH_4$ (0.72 g, 19 mmol) and MeOH (20 mL) were added and the mixture stirred for 0.5 h at −78 °C. The reaction was warmed to 0 °C and stirred for 1 h. The solution was quenched by H_2O (10 mL). The aqueous layer was extracted by CH_2Cl_2 (3×40 mL) and then the combined organic layers dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 0% to 2% methanol in EtOAc) to afford the desired product in 67% yield (0.38 g, 2.0 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.41 (t, *J*=7.5 Hz, 1H), 4.37 (dd, *J*=2.4 Hz, 5.7 Hz, 1H), 3.82 (d, *J*=9.6 Hz, 1H), 3.67 (q, *J*=6.3 Hz, 2H), 3.52 (dd, *J*=2.7 Hz, 9.6 Hz, 1H), 2.50 (m, 3H), 1.96–1.86 (m, 3H), 1.78–1.57 (m, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 84.9, 76.8, 74.9, 62.9, 50.7, 43.4, 32.4, 32.2, 31.6, 26.1; IR (neat/KBr) 3400, 2931, 2865, 1653, 1059, 997 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{10}H_{18}NaO_3$ $[M+Na]^+$ 209.1154, found 209.1154.

7.1.6. 3-((3S,3aR*,4S*,6aR*)-3-Hydroxy-hexahydro-2H-cyclopenta[b]-furan-4-yl)propyl pivalate.* To a solution of the diol synthesized above (0.30 g, 1.6 mmol), Et_3N (270 μL, 1.9 mmol), and DMAP (20 mg, 0.16 mmol) in anhydrous CH_2Cl_2 (10 mL) was added in a dropwise fashion a solution of trimethylacetic chloride (194 mg, 1.61 mmol) in anhydrous CH_2Cl_2 (3 mL). The reaction was stirred overnight. Ethyl acetate (20 mL) was added and the mixture washed with satd NH_4Cl (20 mL), H_2O (20 mL), and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 10% to 25% EtOAc in hexane) to afford the desired product in 92% yield (0.40 g, 1.48 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.38 (t, *J*=6.9 Hz, 1H), 4.31 (t with fine coupling, *J*=6 Hz, 1H), 4.05 (t with fine coupling, *J*=6.6 Hz, 2H), 3.78 (d, *J*=9.6 Hz, 1H), 3.48 (dd, *J*=2.1 Hz, 9.6 Hz, 1H), 2.48 (q, *J*=7.2 Hz, 1H), 1.91–1.60 (m, 9H), 1.17 (s, 9H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 178.6, 84.8, 76.9, 74.9, 64.5, 50.8, 43.1, 38.7, 32.2, 31.5, 28.5, 27.1, 26.0; IR (neat/KBr) 3445, 2959, 1726, 1480, 1285, 1162 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{15}H_{27}O_4$ $[M+H]^+$ 271.1909, found 271.1903.

7.1.7. 3-((3aS,4S*,6aR*)-3-Oxo-hexahydro-2H-cyclopenta[b] furan-4-yl) propyl pivalate (**5**).* To a flame-dried 50-mL round-bottom flask under argon was added a solution of oxalyl chloride (508 μL, 6 mol) in anhydrous CH_2Cl_2 (15 mL). The reaction was cooled to −78 °C and DMSO (840 μL, 12 mmol) added dropwise over 5 min. The reaction was stirred 10 min and then a solution of the alcohol synthesized above (0.40 g, 1.5 mmol) in anhydrous CH_2Cl_2 (5 mL) added. The reaction was stirred for 0.5 h before triethylamine (2.1 mL, 15 mmol) was added, the reaction allowed to warm to room temperature, and then the mixture stirred for 0.5 h. EtOAc (100 mL) was added and the reaction washed with satd NH_4Cl (30 mL), H_2O (30 mL), and brine (30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 10% to 20% EtOAc in hexane) to afford the desired product **5** in 96% yield (0.38 g, 1.4 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.85 (t, *J*=5.1 Hz, 1H), 4.06 (t, *J*=6.3 Hz, 2H), 3.89 (AB, *J*=17.1 Hz, 2H), 2.75 (dd, *J*=5.7 Hz, 10.8 Hz, 1H), 2.20–2.09 (m, 2H), 1.93 (dt, *J*=11.7 Hz, 6.6 Hz, 1H), 1.79–1.62 (m, 4H), 1.48–1.35 (m, 1H), 1.22–1.18 (m buried s at 1.20, 10H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 216.9, 178.4, 85.2, 72.4, 64.1, 52.6, 43.7, 38.6, 34.0, 30.9, 27.8, 27.7, 27.0; IR (neat/KBr)

2958, 1750, 1726, 1480, 1285, 1158, 1072 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{15}H_{24}NaO_4$ $[M+Na]^+$ 291.1572, found 291.1567.

7.1.8. 3-((3aS,4S*,6aR*)-3-Methoxy-4,5,6,6a-tetrahydro-3aH-cyclopenta[b] furan-4-yl)propyl pivalate (**6**).* To a solution of compound **5** (0.36 g, 1.3 mmol) in anhydrous MeOH (5 mL) was added trimethyl orthoformate (5 mL), followed by *p*-toluenesulfonic acid monohydrate (25 mg, 0.13 mmol). The reaction was heated at reflux for 2 h, and then quenched with satd Na_2CO_3 (20 mL). The aqueous layer was extracted with ether (4×30 mL) and then the combined organic layers dried over K_2CO_3, filtered, and concentrated in vacuo. The crude product was used in next step.

To a 0 °C solution of the crude dimethyl ketal in anhydrous dichloromethane (5 mL) was added diisopropylethylamine (0.89 mL, 3.5 mmol), followed by TMSOTf (0.92 mL, 3.5 mmol). The reaction was stirred for 12 h at ambient temperature and quenched by saturated Na_2CO_3 (20 mL). To the reaction mixture was added 50 mL of ether and then the reaction washed with water (2×30 mL) and brine (30 mL). The organic layer was dried over K_2CO_3, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column packed with 1% Et_3N in hexane (5% EtOAc in hexane) to afford the desired product **6** in 58% yield over two steps (0.21 g, 0.74 mmol) as a colorless oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 5.93 (s, 1H), 4.97 (dd, *J*=5.1 Hz, 8.4 Hz, 1H), 4.05 (dt, *J*=3.3 Hz, 6.3 Hz, 2H), 3.49 (s, 3H), 3.29 (t, *J*=7.8 Hz, 1H), 1.97–2.88 (m, 2H), 1.79–1.56 (m, 5H), 1.46–1.34 (m, 2H), 1.20 (s, 9H); ^{13}C NMR (C_6D_6/75 MHz) δ 177.6, 143.0, 122.9, 86.2, 64.6, 56.7, 49.5, 45.1, 38.6, 34.9, 29.9, 28.4, 27.2, 27.1; IR (neat/KBr) 2956, 1727, 1480, 1285, 1159, 1095 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{16}H_{26}NaO_4$ $[M+Na]^+$ 305.1729, found 305.1726.

7.1.9. (3aS,4S*,6aR*)-3-Methoxy-4-(4-methoxybut-3-enyl)-4,5,6,6a-tetra-hydro-3aH-cyclopenta[b]furan (**7**).* To a solution of compound **6** (0.21 g, 0.74 mmol) in anhydrous ether (3 mL) was added a 1 M lithium aluminum hydride solution in ether (2 mL, 2 mmol) at −78 °C. The reaction was stirred for 2 h at this temperature and then quenched by the addition of ethyl acetate (2 mL). To the resulting solution was added ether (100 mL) followed by saturated sodium potassium tartrate (100 mL). The solution was stirred for 1 h, the layers separated, and the aqueous layer extracted with ether (30 mL×2). The combined organic layers were dried over Na_2SO_4, filtered through a short silica plug, and concentrated in vacuo. The crude product was used in the next step without further purification.

To a stirred suspension of *N*-chlorosuccinimide (0.20 g, 1.5 mmol) in dry toluene (4 mL) was added dimethyl sulfide (0.13 mL, 1.8 mmol) at 0 °C. The reaction was stirred for 20 min at this temperature, a solution of crude product made above in dry toluene (4 mL) added, and then the reaction stirred for an additional 30 min. Triethylamine (0.42 mL, 3.0 mmol) was added and the mixture stirred further for 0.5 h at ambient temperature. At this point hexane (20 mL) was added, the resulting mixture filtered, and the filtrate used in next step.

A flame-dried 50 mL round-bottom flask under argon was charged with a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (0.72 g, 2.1 mmol) in anhydrous THF (10 mL) at 0 °C. A 1 M NaHMDS solution in THF (2.0 mL, 2.0 mmol) was added dropwise and stirred for 1 h. The crude aldehyde synthesized above was added via cannula. The mixture was allowed to warm to rt and stirred overnight. The reaction was quenched by the addition of satd NH_4Cl (25 mL). The aqueous layer was extracted with ether (3×30 mL) and the combined organic layers dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution using 5% EtOAc in hexane) to afford the desired product **7** in 40% yield over three steps (67 mg, 0.3 mmol) as a colorless oil. The spectral data were as follows: ^1H NMR (C_6D_6/300 MHz) δ 6.42 (d, *J*=12.6 Hz, 0.7H), 5.85 (s, 1H), 5.73 (d with fine coupling, *J*=6.0 Hz, 0.3H), 4.84 (m, 1H), 4.75 (dt, *J*=7.2 Hz, 12.6 Hz, 0.7H), 4.45 (q, *J*=7.2 Hz, 0.3H), 3.20–3.08 (s at 3.20; s at 3.15; s at 3.09; s at 3.08; m, 7H), 2.46–2.35 (m, 0.7H), 2.07–1.97 (m, 2.3H), 1.89–1.68 (m, 2.3H), 1.61–1.43 (m, 2.7H), 1.40–1.27 (m, 1H); ^{13}C NMR (C_6D_6/75 MHz) δ 147.5, 146.4, 143.3, 122.9, 122.8, 107.2, 102.9, 86.3, 58.8, 56.7, 55.2, 49.7, 49.6, 45.3, 44.9, 35.0, 34.9, 32.2, 31.1, 29.8, 29.7, 27.5, 23.8; IR (neat/KBr) 2931, 2855, 1654, 1451, 1254, 1209, 1095, 1026, 933 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{13}H_{20}NaO_3$ $[M+Na]^+$ 247.1310, found 247.1308.

7.1.10. (3aS,4S*,6aR*)-2,3,3-Trimethoxy-4-(4-methoxybut-3-enyl)-hexahydro-2H-cyclopenta[b]furan (**8**).* A solution of **7** (38 mg, 0.17 mmol), 2,6-lutidine (0.18 g, 1.7 mmol), and Et_4NOTs (0.23 g, 0.75 mmol) in 25% MeOH/CH_2Cl_2 (15 mL) was placed in a flame-dried 25 mL three-necked round-bottom flask equipped with a reticulated vitreous carbon (RVC) anode and a carbon rod cathode. The reaction was electrolyzed at a constant current of 8 mA until 2.0 F/mol of charge was passed. The solution was diluted with 50 mL ether and then washed with water (3×20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered and, concentrated in vacuo. The residue was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution with 2.5%–5% EtOAc in hexane) to afford product **8** (28 mg, 0.10 mmol, 59%) as a colorless oil. The spectral data were as follows: ^1H NMR (C_6D_6/300 MHz) δ 6.35 (d, *J*=12.6 Hz, 0.6H), 5.69 (d with fine coupling, *J*=6.3 Hz, 0.4H), 4.76–4.63 (m, 2.6H), 4.42–4.35 (m, 0.4H), 3.22–2.97 (s at 3.22, s at 3.21, s at 3.17, s at 3.16, s at 3.15, s at 3.09, s at 2.99, s at 2.97, 12H), 2.57 (t, *J*=7.8 Hz, 1H), 2.39–1.50 (m, 8H), 1.37–1.24 (m, 1H); ^{13}C NMR (C_6D_6/75 MHz) δ 147.5, 146.4, 111.4, 107.1, 103.4, 103.3, 102.9, 84.1, 83.9, 58.8, 55.3, 54.0, 52.0, 50.5, 49.2, 49.1, 44.2, 43.9, 32.3, 32.2, 32.1, 31.0, 29.5, 28.4, 24.7; IR (neat/KBr) 2941, 1654, 1453, 1210, 1147 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{15}H_{26}NaO_5$ $[M+Na]^+$ 309.1678, found 309.1672.

7.1.11. 1-(tert-Butyldimethylsilyloxy) pentane-2,4-dione. A flame-dried 250 mL round-bottom flask under argon was charged with freshly cut sodium (4.71 g, 200 mmol) in anhydrous toluene (100 mL). A solution of 3.3 (20.8 g, 100 mmol) in anhydrous toluene (25 mL) was added at room temperature. The resulting solution was cooled to −78 °C, followed by a solution of **10** (20.8 g, 100 mmol) and anhydrous acetone (15 mL, 200 mmol) in anhydrous toluene (25 mL). The mixture was stirred overnight at ambient temperature. The reaction was quenched with satd NH_4Cl (200 mL). The layers were separated and the aqueous layer acidified with 0.5 M HCl until pH=4–5. The aqueous layer was extracted with ether (2×100 mL) and then the combined organic layers were washed with brine (200 mL), dried by Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 0% to 10% EtOAc in hexane) afford the desired product in 51% yield (24 g, 100 mmol) as a pale reddish oil. The NMR spectrum met spectral data reported in literature.[14]

7.1.12. 5-Acetyl-7-(tert-butyldimethylsilyloxy)-6-oxoheptyl pivalate. A solution of the 1,3-dicarbonyl made above (30 g, 0.13 mol), 4-iodo-1-pivoyloxybutane (37 g, 0.13 mol), and K_2CO_3 (19.8 g, 0.14 mol) in acetone (200 mL) was refluxed overnight. The reaction was filtered and concentrated in vacuo. The residue was dissolved in ether (400 mL) and washed with satd NH_4Cl (3×100 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column in 1:8 EtOAc/hexane to afford the desired product in 72% yield (36.2 g, 0.094 mol) as a yellow oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 4.11 (s with shoulder, 2H), 3.96 (t, *J*=6.6 Hz, 2H), 3.87–3.82 (dd, *J*=7.5 Hz, 7.7 Hz, 1H), 2.12 (s, 3H), 1.85–1.51 (m, 4H), 1.30–1.22 (m, 2H), 1.09 (s, 9H), 0.83 (s, 9H), 0.01 (s, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 206.3, 203.1, 178.1, 68.7, 63.5, 61.9, 38.4, 28.9, 28.3,

26.9, 25.6, 23.9, 18.1, −5.8, −5.9; IR (neat/KBr) 3430, 2956, 2858, 1730, 1606, 1480, 1462, 1361, 1284, 1156, 839, 781 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{20}H_{38}O_5NaSi$ $[M+Na]^+$ 409.2381, found 409.2386.

7.1.13. 4-(2-Methyl-4-oxo-4,5-dihydrofuran-3-yl)butyl pivalate. Concentrated hydrochloric acid (10 mL, 12 M) was added dropwise to a 250 mL round-bottom flask containing the alkylated product made above (36 g, 93 mmol) in THF (100 mL) until the reactant was completely converted to product by TLC. The reaction was quenched by satd Na_2CO_3 (50 mL). The aqueous layer was extracted with ether (3×200 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column in 1:3 EtOAc/hexane to afford the desired product in 94% yield (22.2 g, 88 mmol) as a yellow oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 4.43 (d, *J*=0.9 Hz, 2H), 4.06 (t, *J*=6.3 Hz, 2H), 2.20–2.15 (t, *J*=7.2 Hz, buried with s at 2.20, 5H), 1.68–1.59 (m, 2H), 1.55–1.45 (m, 2H), 1.19 (s, 9H); ^{13}C NMR ($CDCl_3$/300 MHz) δ 202.7, 186.3, 178.5, 115.6, 73.7, 63.9, 38.7, 28.3, 27.1, 24.9, 20.642, 14.9; IR (neat/KBr) 2958, 1725, 1698, 1630, 1480, 1409, 1284, 1161, 1028, 934 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{14}H_{22}O_4$ $[M]^+$ 254.1518, found 254.1516.

7.1.14. 4-((2R,3R*)-2-Methyl-4-oxo-tetrahydrofuran-3-yl)butyl pivalate (**11**).* To a flame-dried 250 mL round-bottom flask under argon were added a solution of the product made above (4.0 g, 16 mmol) in anhydrous THF (50 mL). The reaction was cooled to −78 °C and a 1 M L-Selectride solution in THF (17 mL, 17 mmol) was added dropwise. The resulting solution was stirred for 1 h and quenched by satd NH_4Cl (100 mL). The aqueous layer was extracted with ether (3×100 mL) and then the combined organic layer dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column in 1:8 EtOAc/hexane to afford the desired product **11** in 79% yield (3.18 g, 12 mmol) as a slightly yellow oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 4.14 (d with fine coupling, *J*=16.8 Hz, 1H), 4.04 (t, *J*=6.3 Hz, 2H), 3.92–3.87 (m, 1H), 3.80 (d, *J*=16.8 Hz, 1H), 1.96–1.92 (m, 1H), 1.69–1.58 (m, 3H), 1.55–1.37 (m buried with d at 1.41, *J*=6 Hz, 6H); 1.17 (s, 9H); ^{13}C NMR ($CDCl_3$/300 MHz) δ 216.9, 178.5, 79.3, 71.3, 63.7, 53.8, 38.7, 28.7, 27.1, 26.4, 23.5, 20.4; IR (neat/KBr) 2972, 2935, 1761, 1726, 1480, 1459, 1387, 1284, 1158, 1070, 848 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{14}H_{24}O_4$ $[M]^+$ 256.1675, found 256.1675.

7.1.15. 4-((2R,3R*)-4-Methoxy-2-methyl-2,3-dihydrofuran-3-yl)butyl pivalate (**12**).* To a solution of **11** (0.53 g, 2.1 mmol) in anhydrous MeOH (5 mL) was added trimethyl orthoformate (5 mL) followed by *p*-toluenesulfonic acid monohydrate (50 mg, 0.26 mmol). The reaction was heated at reflux for 0.5 h and then quenched by saturated Na_2CO_3 (20 mL). The aqueous layer was extracted with ether (3×20 mL) and the combined organic layers dried over K_2CO_3, filtered, and concentrated in vacuo to afford a residue (0.59 g) that was used in next step without further purification.

To a 0 °C solution of crude dimethyl ketal (0.59 g) in anhydrous dichloromethane (2.5 mL) was added diisopropylethylamine (0.89 mL, 5.1 mmol) followed by TMSOTf (0.92 mL, 5.1 mmol). The reaction was stirred for 12 h at ambient temperature and then quenched by saturated 20 mL of Na_2CO_3. To the reaction mixture was added 50 mL ether and the resulting mixture washed with water (2×30 mL) and brine (40 mL). The organic layer was dried over K_2CO_3, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column packed with 1% Et_3N in hexane (10% EtOAc in hexane) to afford product **12** in 77% yield over 2 steps (0.43 g, 1.6 mmol) as a yellow oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 5.83 (d, *J*=2.1 Hz, 1H), 4.15 (p, *J*=6.6 Hz, 1H), 4.06 (t, *J*=6.6 Hz, 2H), 3.53 (s, 3H), 2.54 (m, 1H), 1.67–1.60 (m, 3H), 1.45–1.38 (m, 3H), 1.33 (d, *J*=6.3 Hz, 3H), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 178.6, 145.6, 119.5, 81.6, 64.1, 57.4, 49.4, 38.7, 32.1, 28.8, 27.2, 22.9, 21.8; IR (neat/KBr) 2970, 2935, 2869, 1727, 1666, 1480, 1460, 1285, 1157, 1098, 1031 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{15}H_{26}O_4$ $[M]^+$ 270.1831, found 270.1831.

7.1.16. (2R,3R*)-4-Methoxy-3-(5-methoxypent-4-enyl)-2-methyl-2,3-dihydrofuran (**13**).* Compound **12** was converted into **13** using the same sequence used to convert **6**–**7**. In this case, a 42% yield was obtained for the three step sequence. ^1H NMR ($CDCl_3$/300 MHz) δ 6.31 (dt, *J*=12.6 Hz, 0.9 Hz, 0.6H), 5.89 (dt, *J*=6.3 Hz, 1.2 Hz, 0.4H), 5.82 (m, 1H) 4.73 (dt, *J*=12.3 Hz, 7.5 Hz, 0.6H), 4.34 (m, 0.4H), 4.16 (m, 1H), 3.57 (s, 1.2H), 3.54, 3.52 (two s, 3H), 3.50 (s, 1.8H), 2.53 (m, 1H), 2.06 (m, 0.6H), 1.92 (m, 1.4H), 1.44–1.34 (m, 3H), 1.32 (d, *J*=6 Hz, 3H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.2, 146.2, 145.8, 145.7, 119.3, 119.2, 106.5, 102.6, 81.7, 81.6, 59.4, 57.4, 55.8, 49.4, 49.3, 32.0, 31.8, 27.8, 27.7, 26.7, 23.9, 21.8; IR (neat/KBr) 2931, 2857, 1655, 1450, 1310, 1258, 1209, 1102, 1031, 935 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{12}H_{20}O_3[M]^+$ 212.1412, found 212.1409.

7.1.17. 4-((2R,3S*)-2-Methyl-4-methylene-tetrahydrofuran-3-yl)butyl pivaloate and 4-((2R*,3S*)-2-methyl-4-methylene-tetrahydrofuran-3-yl)butan-1-ol.* A flame-dried 50 mL round-bottom flask under argon was charged with a stirred suspension of methyltriphenylphosphonium bromide (2.79 g, 7.8 mmol) in anhydrous THF (25 mL) at 0 °C. A 1.6 M solution of *n*-butyllithium in hexane (4.6 mL, 7.4 mol) was added dropwise and stirred for 1 h. The reaction was cooled to −78 °C, followed by a solution of **11** (1.00 g, 3.9 mmol) in anhydrous THF (5 mL). The mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched by addition of satd NH_4Cl (50 mL), the layers separated, and the aqueous layer was extracted with ether (3×100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 5% to 40% EtOAc in hexane) to afford the desired product in a 49% yield (0.48 g, 1.9 mmol) as a colorless oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 4.92 (q, *J*=2.4 Hz, 1H), 4.89 (q, *J*=2.4 Hz, 1H), 4.37 (dt, *J*=13.2 Hz, 1.8 Hz, 1H), 4.22 (dq, *J*=13.2 Hz, 2.1 Hz, 1H), 4.07 (t, *J*=6.3 Hz, 2H), 3.72 (p, *J*=6.9 Hz, 1H), 2.16 (m, 1H), 1.68–1.56 (m, 3H), 1.53–1.41 (m, 3H), 1.28 (d, *J*=6 Hz, 3H), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 178.5, 152.5, 103.5, 80.6, 70.6, 64.0, 50.1, 38.7, 31.1, 28.9, 27.2, 23.4, 20.1; IR (neat/KBr) 2969, 1726, 1479, 1383, 1283, 1152, 1036, 882 cm^{-1}; HRMS (EI) *m/z* calculated for $C_{15}H_{26}O_3$ $[M]^+$ 254.1882, found 254.1868. In addition, the alcohol product having lost the pivaloyl protecting group (the desired product for the next reaction) was obtained in a 30% yield (0.20 g, 1.2 mmol) as a slightly yellow oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 4.86 (m, 2H), 4.31 (dt, *J*=13.2 Hz, 2.1 Hz, 1H), 4.16 (dq, *J*=13.2 Hz, 2.1 Hz, 1H), 3.68 (p, *J*=6.6 Hz, 1H), 3.57 (t, *J*=6.6 Hz, 2H), 2.37 (br, 1H), 2.12 (m, 1H), 1.55–1.35 (m, 6H), 1.21 (d, *J*=6 Hz, 3H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 152.4, 103.5, 80.6, 70.4, 62.3, 50.1, 32.9, 31.4, 23.2, 20.1; IR (neat/KBr) 3400, 2933, 2861, 1666, 1459, 1384, 1037, 884 cm^{-1}; HRMS (ESI) *m/z* calculated for $C_{10}H_{19}O_2$ $[M+H]^+$ 170.1380, found 170.1379.

7.1.18. (2R,3S*)-3-(5-Methoxypent-4-enyl)-2-methyl-4-methyl-enetetrahydrofuran (**16**).* Compound **16** was synthesized using the same three step sequence employed in the conversion of **6**–7. In this case a Swern oxidation (procedure described for the synthesis of **5**) was used in place of the Corey Kim oxidation. The yield for the three step sequence was 64%. The spectral data for **16** were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.32 (d, *J*=12.6 Hz, 0.7H), 5.89 (dt, *J*=6.3 Hz, 1.2 Hz, 0.3H), 4.91 (m, 2H), 4.71 (dt, *J*=12.6 Hz, 7.5 Hz, 0.7H), 4.406–4.205 (m, 2.3H), 3.71 (p, *J*=6.6 Hz, 1H), 3.575 (s, 0.9H), 3.50 (s, 2.1H), 2.15–2.04 (m, 1.7H), 1.98–1.91 (m, 1.3H), 1.61–1.63 (m, 4H), 1.26 (d, *J*=6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 152.8, 152.7, 147.2, 146.2, 106.3, 103.3, 103.2, 102.4, 80.7, 80.6, 70.5, 59.3, 55.8, 50.0, 49.9, 31.0, 30.9, 28.1, 27.9, 27.1, 23.9, 20.1; IR (neat/KBr) 2929.

1651, 1455, 1384, 1209, 1106, 934, 883, 737, 665, 542 cm^{-1}; HRMS (EI) *m*/*z* calculated for $C_{12}H_{20}O_2$ $[M]^+$ 196.1463, found 196.1455.

7.1.19. (2R,3S*)-3-(5-Methoxypent-4-enyl)-2,4-dimethyl-2,3-dihydrofuran (**17**).* To a stirred solution of **16** (0.14 g, 0.71 mmol) in dry toluene (4 mL) was added diisopropylethylamine (123 μL, 0.71 mmol) and dichlorotris(triphenylphosphine) ruthenium (II) (134 mg, 0.14 mmol). The reaction was heated at 65 °C for 8 h and then concentrated. The residue was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution from 10% to 50% dichloromethane in hexane) to afford the desired product **17** in 79% yield (0.11 g, 0.56 mmol) as a colorless oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.30 (dt, *J*=12.6 Hz, 1.2 Hz, 0.64H), 5.66 (m, 1H), 5.86 (dt, *J*=6.3 Hz, 1.5 Hz, 0.36H), 4.69 (dt, *J*=12.3 Hz, 7.5 Hz, 0.64H), 4.357–4.287 (m, 0.36H), 4.24–4.17 (m, 1H), 3.57 (s, 1.08H), 3.50 (s, 1.92H), 2.31–2.27 (m, 1H), 2.11–2.02 (m, 0.64H), 1.97–1.89 (m, 1.36H), 1.62–1.55 (m, buried with s at 1.57, 4H), 1.36–1.24 (m, buried with d at 1.26, *J*=6.3 Hz, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.2, 146.3, 138.7, 138.6, 112.3, 112.2, 106.5, 102.7, 83.0, 82.9, 59.4, 55.9, 52.7, 52.6, 32.1, 31.9, 27.9, 27.7, 26.7, 23.9, 22.1, 9.7; IR (neat/KBr) 2925, 2855, 1668, 1655, 1454, 1374, 1259, 1209, 1107, 934, 841 cm^{-1}; HRMS (EI) *m*/*z* calculated for $C_{12}H_{20}O_2$ $[M]^+$ 196.1463, found 196.1473.

7.1.20. (1R,3R*,3aS*,4S*,7aS*)-4-(Dimethoxymethyl)-3-methoxy-1,3a-dimethyl-octahydroisobenzofuran (**18**).* A solution of **17** (80 mg, 0.41 mmol), 2,6-lutidine (0.43 g, 4.1 mmol), and $LiClO_4$ (0.65 g, 6 mmol) in 50% MeOH–THF (20 mL) was placed in a flame-dried, 25-mL three-necked round-bottom flask equipped with a reticulated vitreous carbon (RVC) anode and a carbon rod cathode. The reaction was electrolyzed at a constant current of 10 mA until 2.2 F/mol charge was passed. The solution was diluted with Et_2O (80 mL) and washed with H_2O (3×20 mL) and brine (40 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was column chromatographed (silica gel, packed with 1% Et_3N in CH_2Cl_2, gradient elution from 2% to 10% EtOAc–CH_2Cl_2) to afford **18** in 75% yield (79 mg, 0.31 mmol) as a colorless oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/500 MHz) δ 4.96 (s, 0.86H), 4.90 (s, 0.14H), 4.44 (d, *J*=4 Hz, 0.14H), 4.14 (d, *J*=7 Hz), 4.07 (m, 0.86H), 3.81 (m, 0.14H), 3.40 (s, 0.42H), 3.37–3.33 (s plus s, 6H), 3.26 (s, 2.58H), 1.78–1.65 (m, 3H), 1.60–1.48 (m, 3H), 1.42–1.35 (m, 1H), 1.31 (d, *J*=6 Hz, 0.42H), 1.24 (d, *J*=6 Hz, 2.58H), 1.18–1.09 (m, buried with s at 1.147, 1.42H), 0.98 (s, 2.58H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 109.9, 107.7, 106.9, 105.5, 78.2, 76.3, 55.9, 55.1, 54.6, 54.3, 53.5, 51.4, 50.6, 50.4, 47.0, 45.3, 44.6, 39.1, 25.5, 23.1, 22.7, 22.3, 21.5 21.2, 20.5, 20.1, 14.0; IR (neat/KBr) 2925, 2855, 1668, 1655, 1454, 1374, 1259, 1209, 1107, 934, 841 cm^{-1}; HRMS (EI) *m*/*z* calculated for $C_{13}H_{23}O_3$ $[M\text{-}OMe]^+$ 227.1647, found 227.1644.

7.1.21. (4R,5R*)-4-(5-Methoxypent-4-enyl)-5-methyl-dihydrofuran-3(2H)-one (**19**).* Compound **19** was made from **11** using the same three step procedure used to convert **6** into **7**. In this case, the Swern oxidation (see the synthesis of **5**) was used in place of the Corey Kim oxidation. The overall yield for the three step sequence was 43%. The spectral data for **19** were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.31 (dt, *J*=12.3 Hz, 1.2 Hz, 0.7H), 5.90 (dt, *J*=6.3 Hz, 1.5 Hz, 0.3H), 4.71 (dt, *J*=12.6 Hz, 5.1 Hz, 0.7H), 4.32 (m, 0.3H), 4.15 (d with fine coupling, *J*=17.1 Hz, 1H), 3.94 (m, 1H), 3.83 (d with fine coupling, *J*=17.1 Hz, 1H), 3.57 (s, 0.9H), 3.50 (s, 2.1H), 2.11–1.88 (m, 3H), 1.72–1.62 (m, 1H), 1.55–1.37 (m, buried with d at 1.46, *J*=5.7 Hz, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 217.3, 217.2, 147.4, 146.5, 105.7, 102.0, 79.4, 79.3, 71.2, 59.3, 55.8, 53.7, 53.6, 28.0, 27.7, 26.9, 26.2, 26.0, 23.6, 20.4; IR (neat/KBr) 2971, 2933, 2859, 1759, 1655, 1459, 1388, 1209, 1132, 1108, 935, 852 cm^{-1}; HRMS (EI) *m*/*z* calculated for $C_{11}H_{18}O_3$ $[M]^+$ 198.1256, found 198.1256.

7.1.22. tert-Butyl (4R,5R*)-4-(5-methoxypent-4-enyl)-5-methyl-4,5-dihydro-furan-3-yl carbonate (**20**).* Into a flamed-dried 25 mL round-bottom flask under argon was placed freshly distilled diisopropylamine (0.87 mL, 6.2 mmol) and anhydrous THF (15 mL). The mixture was cooled to −78 °C, a 1.6 M solution of *n*-butyllithium in hexane (3.4 mL, 5.4 mmol) added, and then allowed to warm to 0 °C over 30 min. The reaction was re-cooled to −78 °C, a solution of **19** (0.47 g, 2.4 mmol) in anhydrous THF (10 mL) added via cannula, and the mixture stirred for 0.5 h. While the reaction was still at −78 °C, TMEDA (4.1 mL, 28 mmol) was added, the resulting solution stirred further for 30 min, and then a solution of 1 M ditertbutyldicarbonate in THF (23 mL, 23 mmol) added. The reaction was allowed to slowly warm to rt over 2 h and quenched by saturated NH_4Cl (15 mL). The aqueous phase was extracted with ether (2×30 mL) and then the combined organic layers were washed with brine (2×40 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution from 10% to 50% methylene chloride in hexane) to afford product **20** in 69% yield (0.49 g, 1.6 mmol) as a yellow oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.50 (m, 1H), 6.30 (d, *J*=12.6 Hz, 0.7H), 5.88 (d, *J*=6.3 Hz, 0.3H), 4.72 (dt, *J*=12.9 Hz, 7.2 Hz, 0.7H), 4.26 (m, 1.3H), 3.57 (s, 0.9H), 3.50 (s, 2.1H), 2.27 (m, 1H), 2.09 (m, 0.7H), 1.95 (q, *J*=6.9 Hz, 1.3H), 1.70–1.55 (m, 1H), 1.51 (s, 9H), 1.43–1.30 (m, buried with d at 1.36, *J*=6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 151.1, 147.2, 146.3, 134.8, 134.7, 132.1, 132.0, 106.2, 102.4, 83.2, 83.1, 82.5, 82.4, 55.8, 48.1, 31.9, 31.7, 27.9, 27.7, 27.6, 27.5, 27.5, 26.5, 23.8, 21.9; IR (neat/KBr) 2978, 2931, 2857, 1756, 1655, 1456, 1370, 1254, 1153, 935, 872, 780 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{12}H_{19}O_5$ $[M\text{-isobutylene}+H]^+$ 243.1227, found 243.1229.

7.1.23. (4R,5R*)-4-(5-Methoxypent-4-enyl)-5-methyl-4,5-dihydrofuran-3-yl trifluoromethanesulfonate (21).* Into a flamed-dried, 25 mL round-bottom flask under argon was placed freshly distilled diisopropylamine (0.12 mL, 1.2 mmol) and anhydrous THF (4 mL). The reaction was cooled to −78 °C, a 1.6 M solution of *n*-butyllithium in hexane (0.68 mL, 1.1 mmol) added, and then allowed to warm to 0 °C over 30 min. The reaction was cooled to −78 °C, a solution of **19** (0.10 g, 0.39 mmol) in anhydrous THF (2 mL) added via cannula, and stirred for 0.5 h. While the reaction was stirred at −78 °C, a solution of *N*-phenyltrifluoromethanesulfonimide (0.28 g, 0.78 mmol) in THF (3 mL) was added. The reaction was allowed to slowly warm to room temperature over 2 h before being quenched with satd $NaHCO_3$ (10 mL). The aqueous phase was extracted with ether (30 mL×2) and then the combined organic layers washed with brine (2×20 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution from 20% to 50% dichloromethane in hexane) to afford the desired product **21** in 71% yield (91 mg, 0.28 mmol) as a slightly yellow oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.56 (m, 1H), 6.32 (d, *J*=12.9 Hz, 0.7H), 5.91 (d with fine coupling, *J*=6.3 Hz, 0.3H), 4.71 (dt, *J*=12.6 Hz, 7.5 Hz, 0.7H), 4.41 (m, 1.3H), 3.58 (s, 0.9H), 3.51 (s, 2.1H), 2.74 (m, 1H), 2.08 (m, 0.7H), 1.97 (m, 1.3H), 1.68 (m, 1H), 1.48–1.32 (m, buried with d at 1.36, *J*=6.3 Hz, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 147.6, 146.7, 137.2, 137.1, 134.6, 134.5, 120.7 (q, *J*=319 Hz), 105.7, 102.0, 84.4, 59.4, 55.9, 48.1, 48.0, 31.4, 31.3, 27.5, 27.2, 26.1, 23.5, 21.7; IR (neat/KBr) 2977, 2934, 1656, 1423, 1245, 1211, 1140, 935, 908, 845 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{12}H_{18}O_5F_3S$ $[M+H]^+$ 331.0822, found 331.0821.

*7.1.24. tert-Butyl methoxy(3-methoxy-1-methyl-1,3,4,5,6,7-hexahydroiso-benzofuran-4-yl)methyl carbonate (**22**) and 9-(dimethoxymethyl)octahydroindeno[1-d][1,3]dioxol-2-one (**23**).* The electrolysis was conducted using the same procedure reported above or the oxidation of **17**. The only change was in the electrolyte solution used. In this case, the electrolyte solution was made by dissolving $LiClO_4$ (0.65 g, 6 mmol) in 10% MeOH/CH_3CN (20 mL). The reaction led to product **22** in 38% yield (36 mg, 0.13 mmol) and **23** in 26%

yield (29 mg, 0.09 mmol), both as colorless oils. The spectral data were as follows: For **22**: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.17 (s, 0.6H), 5.99 (s, 1H), 4.40 (d, J=8.1 Hz, 1H), 4.28 (d, J=4.2 Hz, 0.6H), 4.15–4.00 (q plus p, J=7.2 Hz, 6.6 Hz, 1.6H), 3.41 (s, s, 4.8H), 3.40 (s, 1.8H), 3.36 (s, 3H), 2.26 (m, 1.2H), 2.14–1.92 (m, 3.2H), 1.85–1.68 (m, 3.6H), 1.55–1.45 (m, 2H), 1.43–1.15 (m, buried with d at 1.42, J=6.9 Hz, and d at 1.37, J=6.6 Hz, 7H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 153.9, 153.5 108.1, 105.3, 104.8, 104.1, 93.8, 90.9, 85.0, 80.6, 56.0, 55.9, 55.2, 52.8, 49.7, 48.6, 43.5, 40.2, 30.8, 22.8, 22.5, 21.9, 21.7, 21.0, 19.1; IR (neat/KBr) 2930, 1795, 1533, 1449, 1367, 1282, 1209, 1023, 972, 859, 765 cm^{-1}; HRMS (EI) m/z calculated for $C_{12}H_{17}O_5$ [M-OMe]$^+$ 241.1076, found 241.1076. For **22**: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.69 (d with fine coupling, J=3.6 Hz, 1H), 5.61 (d with fine coupling, J=3.6 Hz, 1.2H), 5.58 (d, J=5.7 Hz, 1.2H), 5.51 (d, J=5.7 Hz, 1H), 4.78 (m, 2.2H), 3.46 (s, 3.2H), 3.45 (s, 3H), 3.42 (s, 6.2H), 2.67 (m, 2.2H), 1.96 (m, 4.4H), 1.83–1.54 (m, 8.8H, water peak at 1.62), 1.50, 1.49 (s, s, 19.8H), 1.26 (d, d, J=6.6 Hz, 6.6 Hz, 6.6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 153.3, 153.2, 144.3, 144.2, 129.2, 128.3, 109.3, 108.9, 103.3, 102.6, 82.3, 82.1, 81.8, 81.7, 77.4, 56.8, 56.7, 54.9, 54.7, 36.7, 27.7, 23.5, 23.1, 21.4, 20.4, 20.2; IR (neat/KBr) 2933, 1739, 1449, 1369, 1287, 1254, 1162, 1060, 940, 850 cm^{-1}; HRMS (EI) m/z calculated for $C_{16}H_{25}O_5$ [M-OMe]$^+$ 297.1702, found 297.1701.

7.1.25. (3aS,4S*,6aR*)-4-(But-3-enyl)-tetrahydro-2H-cyclopenta[b]-furan-3(3aH)-one (from **4a**).* To a flame-dried 25 mL round-bottom flask under an argon atmosphere was added a solution of oxalyl chloride (0.38 mL, 4.5 mmol) in anhydrous dichloromethane (12 mL). The reaction was cooled to −78 °C and then DMSO (0.91 mL, 13 mmol) added dropwise over 5 min. The reaction was stirred 10 min, a solution of compound **4a** (0.20 g, 1.1 mmol) in anhydrous dichloromethane (8 mL) added, and the reaction stirred for 0.5 h. Triethylamine (2.7 mL, 19 mmol) was added and stirred further for 0.5 h at 0 °C. The reaction was quenched by H_2O (20 mL). The aqueous layer was extracted with EtOAc (3×20 mL) and then the combined organic phase washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 5% to 10% EtOAc in hexane) to afford the desired ketone in 96% yield (0.19 g, 1.1 mmol) as a yellow solid. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/500 MHz) δ 5.83–5.75 (ddt, J=17 Hz, 10 Hz, 7 Hz, 1H), 5.04 (dq, J=17 Hz, 1.5 Hz, 1H), 4.96 (d with fine coupling, J=10 Hz, 1H), 4.84 (t, J=5.5 Hz, 1H), 3.95 (d, J=17.5 Hz, 1H), 3.87 (d, J=17.5 Hz, 1H), 2.75 (dd, J=11 Hz, 5.5 Hz, 1H), 2.21–2.07 (m, 4H), 1.93 (dt, J=12.5 Hz, 6.5 Hz, 1H), 1.83–1.76 (m, 1H), 1.71–1.63 (m, 1H), 1.44–1.35 (dq, J=5.5 Hz, 12 Hz, 1H), 1.25–1.18 (m, 1H); ^{13}C NMR ($CDCl_3$/125 MHz) δ 217.3, 183.2, 114.7, 85.3, 72.5, 52.8, 43.4, 34.1, 32.8, 30.8, 30.6; IR (neat/KBr) 3075, 2930, 1749, 1639, 1437, 1175, 1071, 911 cm^{-1}; HRMS (ESI) m/z calculated for $C_{11}H_{17}O_2$ [M+H]$^+$ 181.1229, found 181.1223.

7.1.26. (3aS,4S*,6aR*)-4-(4-Methoxybut-3-enyl)-tetrahydro-2H-cyclopenta-[b]furan-3(3aH)-one (**24**).* Ozone was bubbled through a −78 °C solution of the compound made above (0.47 g, 2.6 mmol) in CH_2Cl_2 (10 mL) until the solution turned a persistent blue color. The excess ozone was removed by flushing the solution with Ar. To the reaction was added PPh_3 (1.37 g, 5.2 mmol) and the reaction then stirred for 1 h at ambient temperature. The solution was dried over $MgSO_4$, filtered and concentrated in vacuo. To the residue was added THF (20 mL). This solution was used in the next step without further purification.

A flame-dried 100 mL round-bottom flask under an argon atmosphere was charged with a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (1.52 g, 4.4 mmol) in anhydrous THF (20 mL) at 0 °C. To this mixture was added a 1 M NaHMDS solution in THF (3.9 mL, 3.9 mmol) in a dropwise fashion. The resulting solution was stirred for 1 h. The Wittig reagent made in this fashion was added to the crude aldehyde generated above in a dropwise fashion at −78 °C. The reaction was stirred until the aldehyde was consumed completely by TLC. The mixture was allowed to warm to room temperature and stirred for 2 h before being quenched by the addition of saturated NH_4Cl (50 mL). The aqueous layer was extracted with EtOAc (4×40 mL) and the combined organic layers were washed by brine (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution from 5 to 10% EtOAc in hexane) to afford product **24** in a 64% yield (0.35 g, 1.7 mmol) as a slightly yellow oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.33 (d, 12.6 Hz, 0.7H), 5.89 (dt, J=6 Hz, 1.2 Hz, 0.3H), 4.83 (t, J=5.1 Hz, 1H), 4.71 (dt, J=12.3 Hz, 7.5 Hz, 0.7H), 4.32 (q, J=6.3 Hz, 0.3H), 3.91 (d, J=17.1 Hz, 1H), 3.88 (d, J=17.1 Hz, 1H), 3.57 (s, 0.9H), 3.49 (s, 2.1H), 2.76 (dd, J=11.1 Hz, 6 Hz, 1H), 2.23–1.87 (m, 5H), 1.78–1.60 (m, 2H), 1.46–1.31 (dq, J=6 Hz, 12 Hz, 1H), 1.26–1.11 (m, 1H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 217.3, 147.2, 146.4, 106.1, 102.2, 85.4, 85.3, 72.5, 59.4, 55.7, 52.9, 52.8, 43.5, 43.2, 34.1, 34.0, 32.5, 31.4, 30.7, 30.6, 26.7, 23.0; IR (neat/KBr) 2931, 2854, 1749, 1654, 1452, 1438, 1268, 1209, 1071, 934 cm^{-1}; HRMS (ESI) m/z calculated for $C_{12}H_{18}NaO_3$ [M+Na]$^+$ 233.1154, found 233.1162.

7.1.27. tert-Butyl (3aS,4S*,6aR*)-4-(4-methoxybut-3-enyl)-4,5,6,6a-tetra-hydro-3aH-cyclopenta[b]furan-3-yl carbonate (**25**).* Compound **25** was synthesized from **24** using the same conditions used to construct substrate **20**. In this case, a 57% yield (0.10 g, 0.32 mmol) of the product was obtained as a slightly yellow oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.58 (d, 1.2 Hz, 0.7H), 6.56 (d, J=0.9 Hz, 0.3H), 6.34 (d, J=12.6 Hz, 0.7H), 5.88 (d with fine coupling, J=6.3 Hz, 0.3H), 5.10 (dd, J=8.4 Hz, 5.4 Hz, 1H), 4.74 (dt, J=12.9 Hz, 6.9 Hz, 0.7H), 4.34 (q, J=6.9 Hz, 0.3H), 3.58–3.49 (m buried s at 3.57 and s at 3.49, 4H), 2.16–1.89 (m, 4H), 1.79–1.40 (m buried with s at 1.48, 14H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 151.3, 151.2, 147.0, 146.1, 135.6, 135.5, 132.1, 106.8, 102.8, 87.6, 87.5, 83.0, 82.9, 59.3, 55.7, 47.8, 47.7, 45.0, 44.7, 34.7, 34.6, 31.5, 30.2, 29.3, 29.3, 27.6, 27.0, 23.2; IR (neat/KBr) 2931, 2858, 1756, 1654, 1456, 1370, 1278, 1256, 1155, 1112, 876 cm^{-1}; HRMS (ESI) m/z calculated for $C_{17}H_{26}NaO_5$ [M+Na]$^+$ 333.1678, found 333.1675.

7.1.28. (3aR,4S*,6aR*)-4-(4-Methoxybut-3-enyl)-3-methylene-hexahydro-2H-cyclopenta[b]furan.* A Wittig reaction was used to convert the ketone in **24** into an exocyclic methylene using the same chemistry described above for the monocyclic substrate. The yield of the methylene product was 92% yield (92 mg, 0.44 mmol of a colorless oil). The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.32 (d with fine coupling, d=12.6 Hz, 0.7H), 5.89 (dt, J=6 Hz, 1.5 Hz, 0.3H), 4.99 (m, 1H), 4.94 (m, 1H), 4.76 (dt, J=12.6 Hz, 7.2 Hz, 0.7H), 4.61 (t, J=5.1 Hz, 1H), 4.34 (q, J=7.2 Hz, 0.3H), 4.22 (m, 2H), 3.57 (s, 0.9H), 3.50 (s, 2.1H), 3.05 (dd, J=9 Hz, 6 Hz, 1H), 2.11–1.88 (m, 4H), 1.84–1.74 (m, 1H), 1.63–1.50 (m, 2H), 1.27–1.11 (m, 2H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 149.8, 149.7, 146.9, 146.0, 106.7, 106.1, 102.8, 86.5, 86.4, 73.0, 72.9, 59.3, 55.8, 50.8, 50.7, 42.6, 42.2, 34.1, 34.0, 32.6, 31.5, 30.9, 30.8, 26.9, 23.1; IR (neat/KBr) 2929, 1851, 1654, 1451, 1209, 1109, 1054, 932 cm^{-1}; HRMS (ESI) m/z calculated for $C_{13}H_{21}O_2$ [M+H]$^+$ 209.1542, found 209.1536.

7.1.29. (3aR,4S*,6aR*)-4-(4-Methoxybut-3-enyl)-3-methyl-4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan (**26**).* Compound **26** was synthesized using the same procedure described for the synthesis of substrate **17**. An 86% yield of the rearranged olefin (79 mg, 0.38 mmol) was obtained as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.30 (d, J=12.3 Hz, 0.6H), 6.06 (s, 1H), 5.87 (d, J=6.3 Hz, 0.4H), 5.01 (dd, J=8.1 Hz, 5.4 Hz, 1H), 4.73 (dt, J=12.3 Hz, 7.5 Hz, 0.6H), 4.33 (q, J=6.6 Hz, 0.4H), 3.56 (s, 1.2H), 3.49 (s, 1.8H), 3.07 (t, J=8.1 Hz, 1H), 2.12–1.86 (m, 4H), 1.74–1.52 (m buried with s at 1.65, 6H), 1.41–1.24 (m, 2H); ^{13}C NMR

($CDCl_3$/75 MHz) δ 146.9, 146.0, 142.5, 142.4, 109.5, 106.8, 102.9, 88.5, 88.4, 59.4, 55.8, 52.8, 52.7, 46.0, 45.6, 34.3, 34.3, 32.3, 31.3, 29.2, 29.1, 27.3, 23.5, 12.2, 12.1; IR (neat/KBr) 2929, 1855, 1656, 1454, 1436, 1209, 1106, 933 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{13}H_{21}O_2$ $[M+H]^+$ 209.1542, found 209.1537.

7.1.30. (3aS,6S*,6aR*)-6-(tert-Butyldimethylsilyloxy)-hexahydropentalen-1(2H)-one.* To a 0 °C solution of compound **27** (2.70 g, 19 mmol) in DMF (40 mL) was added imidazole (1.97 g, 29 mmol) and TBS-Cl (4.05 g, 27 mmol). The reaction was stirred for 12 h at ambient temperature and then EtOAc (250 mL) added. The solution was washed with H_2O (3×50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 5% to 10% EtOAc in hexane) to afford the protected alcohol in 85% yield (4.20 g, 16.5 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.40 (t with fine coupling, *J*=3.9 Hz, 1H), 2.71 (p, *J*=7.5 Hz, 1H), 2.54 (dd, *J*=9.6 Hz, 6 Hz, 1H), 2.31–2.20 (m, 1H), 2.12–1.93 (m, 3H), 1.78–1.65 (m, 3H), 1.61–1.53 (m, 1H), 0.77 (s, 9H), −0.3, −0.4 (s, s, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 218.5, 75.7, 58.2, 40.6, 40.3, 37.9, 31.4, 28.4, 25.6, 17.7, −5.0, −5.4; IR (neat/KBr) 2953, 2856, 1741, 1471, 1253, 1051, 1034, 836, 777 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{14}H_{27}O_2Si$ $[M+H]^+$ 255.1780, found 255.1775.

7.1.31. (1S,3aS*,6S*,6aR*)-6-(tert-Butyldimethylsilyloxy)-1-(3-(tert-butyldimethylsilyloxy)propyl)-octahydropentalen-1-ol.* To a −78 °C solution of (3-bromopropoxy)(tertbutyl)-dimethylsilane (4.48 g, 17.7 mmol) in anhydrous ether (50 mL) was added a 1.7 M solution of *tert*-butyllithium in pentane (20.8 mL, 35 mmol). The reaction was stirred at −78 °C for 0.5 h and then warmed to 0 °C for 1 h. A flame-dried 250 mL round-bottom flask under argon was charged with a −78 °C solution of starting ketone (1.50 g, 5.9 mmol) in anhydrous ether (50 mL). The alkyl lithium solution above was added to this solution via cannula. The reaction was stirred for 1 h and then warmed to 0 °C for 2 h. The reaction was quenched by satd NH_4Cl (40 mL), the layers separated, and the aqueous layer extracted with CH_2Cl_2 (3×30 mL). The combined organic layer was washed with brine (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 0% to 3% EtOAc in hexane) to afford the desired addition product in 79% yield (2.00 g, 4.7 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.31–4.23 (m, 2H), 3.63–3.50 (m, 2H), 2.40 (t with fine coupling, *J*=9 Hz, 1H), 2.13 (t, *J*=9.3 Hz, 1H), 1.97–1.61 (m, 6H), 1.58–1.40 (m, 5H), 1.28 (dtd, *J*=6.6 Hz, 12.3 Hz, 2.1 Hz, 1H), 0.88, 0.86 (s, s, 18H), 0.08, 0.07 (s, s, 6H), 0.01 (s, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 84.6, 78.1, 64.0, 52.8, 42.5, 39.8, 39.3, 34.1, 32.4, 28.3, 27.5, 26.0, 25.8, 18.3, 17.8, −4.8, −5.2, −5.28, −5.32; IR (neat/KBr) 3507, 2953, 2858, 1471, 1361, 1253, 1090, 836, 776 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{23}H_{49}O_3Si_2$ $[M+H]^+$ 429.3220, found 429.3216.

7.1.32. tert-Butyl(3-((6S)-6-(tert-butyldimethylsilyloxy)3,3a,4,5,6,6a-hexa-hydropentalen-1-yl)propoxy)dimethylsilane (**28**).* To a −40 °C solution of the alcohol made in the previous step (1.00 g, 2.3 mmol) in THF (50 mL) was added pyridine (5 mL, 60 mmol) and $SOCl_2$ (5 mL, 70 mmol). The reaction was stirred at this temperature for 0.5 h and then poured into satd aqueous solution of $CuSO_4$ (150 mL) at 0 °C. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were washed with satd $NaHCO_3$ (2×30 mL) and brine (30 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 0% to 2.5% EtOAc in hexane) to afford product **28** in 75% yield (0.72 g, 1.8 mmol) as a colorless oil. The spectral data of major isomer were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 5.31 (m, 1H), 4.21 (q, *J*=5.4 Hz, 1H), 3.59 (dt, *J*=3.6 Hz, 6.9 Hz, 2H), 2.91 (t with fine coupling, *J*=7.2 Hz, 1H), 2.68–2.49 (m, 2H), 2.56–1.94 (m, 3H), 1.81–1.37 (m, 6H), 0.89 (s, 9H), 0.86 (s, 9H), 0.05, 0.03 (s, s, 12H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 143.1, 124.8, 75.6, 63.4, 57.6, 41.2, 40.3, 35.5, 31.2, 31.0, 27.2, 26.0, 25.9, 18.4, 18.1, −4.4, −5.0, −5.3; IR (neat/KBr) 2953, 2938, 2889, 1471, 1387, 1253, 1102, 1060, 834, 773 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{23}H_{47}O_2Si_2$ $[M+H]^+$ 411.3115, found 411.3118.

7.1.33. tert-Butyl(3-((1S,3aR*,6S*,6aR*)-6-(tert-butyldimethyl-silyloxy)-octahydropentalen-1-yl)propoxy)dimethylsilane and (3aR*,6S*,6aR*)-6-(3-(tert-butyldimethylsilyloxy)propyl)octa hydropentalen-1-ol.* To a solution of compound **28** (1.10 g, 2.7 mmol) in EtOAc (7 mL) was added Pd/C (0.30 g). After three vacuum/H_2 cycles, the reaction was charged with atmosphere H_2 and stirred for 24 h. The reaction was filtered through Celite and the filtrate concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 2.5% to 12.5% EtOAc in hexane) to afford the hydrogenated product in 47% yield (0.52 g, 1.3 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.26 (m, 1H), 3.64 (t, *J*=6.6 Hz, 2H), 2.43 (p, *J*=6.9 Hz, 1H), 2.17 (m, 1H), 1.92 (m, 1H), 1.77–1.57 (m, 9H), 1.42 (m, 3H), 0.91, 0.88 (s+s, 18H), 0.09, 0.05 (s+s, 12H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 75.9, 63.4, 52.6, 43.6, 42.2, 37.7, 32.9, 32.8, 32.0, 31.8, 26.0, 25.9, 25.6, 17.8, −3.6, −3.9, −4.8; IR (neat/KBr) 2953, 2930, 2858, 1471, 1252, 1099, 1043, 912, 833 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{23}H_{49}O_2Si_2$ $[M+H]^+$ 413.3271, found 413.3268.

In addition, a monodeprotected product was obtained in 24% yield (0.19 g, 0.64 mmol) as a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.28 (m, 1H), 3.66 (t, *J*=6.6 Hz, 2H), 2.46 (m, 1H), 2.19 (m, 1H), 1.95 (m, 1H), 1.85–1.55 (m, 9H), 1.53–1.37 (m, 3H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 75.9, 63.4, 52.5, 43.6, 42.2, 37.7, 32.9, 32.8, 32.0, 31.8, 26.0, 25.9, 17.8, −3.9, −4.8; IR (neat/KBr) 3338, 2930, 2857, 1471, 1360, 1253, 1044, 912, 833, 773 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{17}H_{35}O_2Si$ $[M+H]^+$ 299. 2401, found 299.2408.

7.1.34. (1S,3aR*,6S*,6aR*)-6-(3-Hydroxypropyl)-octahydropentalen-1-ol.* The products above were deprotected to form the diol using aqueous HCl. For example, to a solution of the disilated material (0.2 g, 0.5 mmol) in THF (6 mL) was added concentrated HCl (1 mL) at 0 °C. The reaction was stirred at ambient temperature for 12 h and then quenched carefully with satd $NaHCO_3$ (5 mL). The reaction was then neutralized with K_2CO_3 until pH>7. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (5×20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was chromatographed through a silica gel column (gradient elution from 20% to 35% EtOAc in hexane) to afford the diol in 73% yield (64 mg, 0.35 mmol) as a white solid. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 4.30 (m, 1H), 3.66 (q with fine coupling, *J*=6 Hz, 2H), 2.46 (p, *J*=8.7 Hz, 1H), 2.24–2.17 (m buried with br, 2H), 2.00–1.91 (m, 1H), 1.83–1.76 (m, 1H), 1.71–1.40 (m, 10H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 75.8, 63.2, 51.8, 43.8, 42.1, 37.9, 32.7, 32.6, 32.4, 31.9, 26.8; IR (neat/KBr) 3368, 2936, 2863, 1458, 1057, 1000, 979 cm^{-1}; HRMS (ESI) *m*/*z* calculated for $C_{11}H_{21}O_2$ $[M+H]^+$ 185.1536, found 185.1525.

7.1.35. (3aR,6R*,6aR*)-6-(4-Methoxybut-3-enyl)-hexahydropentalen-1(2H)-one (**29**).* Product **29** was generated from the diol using the two step Swern oxidation–Wittig sequence described above in 57% yield (123 mg, 0.59 mmol) as a pale yellow oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$/300 MHz) δ 6.27 (d, *J*=12.6 Hz, 0.7H), 5.82 (d, *J*=3.3 Hz, 0.3H), 4.68 (dt, *J*=12.6 Hz, 7.5 Hz, 0.7H), 4.29 (q, *J*=7.2 Hz, 0.3H), 3.52 (s, 0.9H), 3.44 (s, 2.1H), 2.78 (m, 1H), 2.45 (t, *J*=9 Hz, 1H), 2.15–1.89 (m, 6H), 1.89–1.52 (m, 5H), 1.21–1.06 (m, 2H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 221.9, 146.8, 146.0, 106.6, 102.3, 59.3, 55.6, 54.3, 54.1, 44.4, 44.1, 40.7, 40.6, 39.9, 32.9, 32.8, 32.4, 32.3,

32.0, 30.9, 29.8, 28.1, 26.9, 23.1; IR (neat/KBr) 2941, 2863, 1731, 1654, 1452, 1410, 1390, 1265, 1207, 1145, 1107, 933, 741 cm^{-1}; HRMS (ESI) m/z calculated for $C_{13}H_{21}O_2$ $[M+H]^+$ 209.1536, found 209.1529.

7.1.36. tert-Butyl((3aR,6R*,6aR*)-6-(4-methoxybut-3-enyl)-3,3a,4,5,6,6a-hexahydropentalen-1-yloxy)dimethylsilane (**30**).* Into a flamed-dried 25 mL round-bottom flask under an argon atmosphere was introduced freshly distilled diisopropylamine (0.20 mL, 1.43 mmol) and anhydrous THF (5 mL). To this mixture was added a 1.6 M solution of *n*-butyllithium in hexane (0.73 mL, 1.2 mmol) at −78 °C. The reaction was allowed to warm to 0 °C over 30 min and then it was recooled to −78 °C before adding a solution of compound **29** (0.12 g, 0.59 mmol) in anhydrous THF (5 mL) via cannula. The mixture was stirred for 0.5 h. While the reaction was still at −78 °C, TBS-OTf (270 μL, 1.2 mmol) was added. The resulting solution was stirred for 1 h at −78 °C and 1 h at 0 °C. The reaction was quenched with saturated $NaHCO_3$ (20 mL). The aqueous phase was extracted with ether (4×20 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was chromatographed through a silica gel column packed with 1% Et_3N in hexane (gradient elution from 0% to 5% methylene chloride in hexane) to afford product **30** in 85% yield (0.16 g, 0.50 mmol) as a colorless oil. The spectral data were as follows: ^1H NMR ($CDCl_3$/300 MHz) δ 6.30 (d, J=12.6 Hz, 0.7H), 5.84 (d, J=3.3 Hz, 0.3H), 4.74 (dt, J=12.6 Hz, 6.3 Hz, 0.7H), 4.53 (s, 1H), 4.33 (q, J=7.2 Hz, 0.3H), 3.56 (s, 0.9H), 3.48 (s, 2.1H), 2.83 (m, 2H), 2.54 (dd, J=9.3 Hz, 15.6 Hz, 1H), 2.21–1.75 (m, 5H), 1.66–1.56 (m, 2H), 1.42–1.08 (m, 3H), 0.92 (s, 9H), 0.15 (s, 6H); ^{13}C NMR ($CDCl_3$/75 MHz) δ 154.9, 154.8, 146.6, 145.6, 107.6, 103.5, 102.8, 102.7, 59.3, 55.6, 52.4, 52.3, 44.7, 44.3, 39.4, 39.3, 37.0, 34.3, 32.4, 31.3, 30.4, 27.5, 25.8, 23.8, 18.0, −2.7, −4.7, −4.8; IR (neat/KBr) 2932, 2856, 1643, 1471, 1462, 1252, 1228, 1208, 1110, 933, 839, 780 cm^{-1}; HRMS (ESI) m/z calculated for $C_{19}H_{35}O_2Si$ $[M+H]^+$ 323.2401, found 323.2398.

Acknowledgments

We thank the National Science Foundation (CHE-0809142) for their generous support of our work. We also gratefully acknowledge the Washington University High Resolution NMR facility, partially supported by NIH grants RR02004, RR05018, and RR07155, and the Washington University Mass Spectrometry Resource Center, partially supported by NIHRR00954, for their assistance.

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