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The Remarkable Effect of Cosolvent on a Samarium(II)-Mediated 4-*exo-trig* Cyclization: Further Synthetic Studies on Pestalotiopsin A

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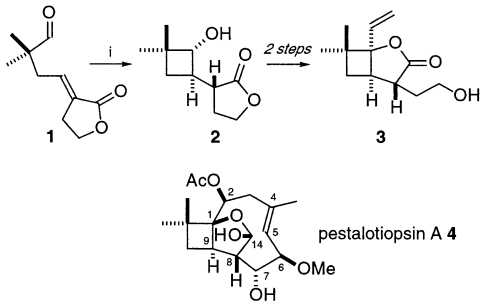
A samarium(II)-mediated 4-*exo-trig* cyclization in which a remote stereocenter serves to control the facial selectivity of the cyclization is described. The apparent coordination of a *tert*-butyldimethylsilyl ether to the samarium center appears to give rise to the selectivity. The remarkable effect of the cosolvent, 2,2,2-trifluoroethanol, on the cyclization of this substrate, is also discussed. A stereoselective synthesis of the general class of γ,δ-unsaturated aldehyde cyclization substrate is reported, and the utility of the cyclization is demonstrated in an approach to the fully functionalized core of pestalotiopsin A.

Introduction

Samarium(II) iodide continues to be used widely throughout organic synthesis. This mild, single-electron reductant has been used to mediate a broad range of radical and anionic transformations.[1] We have recently developed a stereoselective approach to functionalized cyclobutanols via the samarium(II)-mediated 4-*exo-trig* cyclizations of γ,δ-unsaturated aldehydes.[2,3] This cyclization proceeds under mild conditions and allows the generation of up to three contiguous stereocenters with excellent stereocontrol. We have recently applied this cyclization in the first synthetic studies on the structurally intriguing natural product, pestalotiopsin A **4** (Scheme 1).[4,5] The pestalotiopsins are an interesting class of caryophyllene-type sesquiterpenes, isolated from *Pestalotiopsis sp.*, an endophytic fungus of *Taxus brevifolia*.[5] Pestalotiopsin A is of particular interest, possessing a unique oxa-tricyclic structure.[6] In our preliminary approach, cyclization of aldehyde **1** proceeded in high yield to give *anti*-cyclobutanol **2**. Cyclobutanol **2** could then be readily converted to bicyclic lactones, such as **3**, which are precursors of the core of the natural product.

SCHEME 1[a]



[a] Reagents and conditions: (i) SmI_2, THF−MeOH (4:1), 0 °C, 79%.

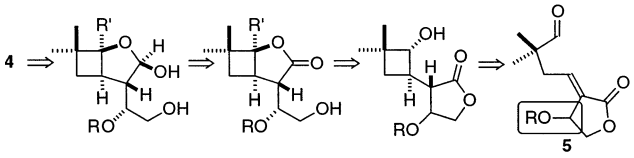


FIGURE 1. Synthetic approach to pestalotiopsin A.

In this paper, we will describe the incorporation of a stereocontrol element into substrates such as **1** to control the facial selectivity of the cyclization thus leading to enantiomerically pure cyclobutanol products. Enantiomerically pure aldehydes **5** (Figure 1) were selected as ideal cyclization substrates. We envisaged the derivatized hydroxyl substituent on the lactone ring would control the facial selectivity of the 4-*exo-trig* cyclization, despite its remote position relative to the reacting centers. According to our synthetic strategy, Figure 1, the directing hydroxyl substituent will be incorporated into the target compound, becoming the C7-OH of pestalotiopsin

(1) For reviews on the use of samarium(II) iodide in organic synthesis, see: (a) Soderquist, J. A. *Aldrichim. Acta* **1991**, *24*, 15. (b) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29−68. (c) Molander, G. A. *Org. React.* **1994**, *46*, 211. (d) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307. (e) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321. (f) Krief, A.; Laval, A.-M. *Chem. Rev.* **1999**, *99*, 745. (g) Steel, P. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727.

(2) (a) Johnston, D.; McCusker, C. M.; Procter, D. J. *Tetrahedron Lett.* **1999**, *40*, 4913. (b) Johnston, D.; McCusker, C. F.; Muir, K.; Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 681.

(3) Prior to our work, a single example of such a cyclization had been described by Weinges: Weinges, K.; Schmidbauer, S. B.; Schick, H. *Chem. Ber.* **1994**, *127*, 1305.

(4) Johnston, D.; Francon, N.; Edmonds, D. J.; Procter, D. J. *Org. Lett.* **2001**, *3*, 2001.

(5) (a) Pulici, M.; Sugawara, F.; Koshino, H.; Uzawa, J.; Yoshida, S.; Lobkovsky, E.; Clardy, J. *J. Org. Chem.* **1996**, *61*, 2122. (b) Pulici, M.; Sugawara, F.; Koshino, H.; Okada, G.; Esumi, Y.; Uzawa, J.; Yoshida, S. *Phytochemistry* **1997**, *46*, 313.

(6) Kende has reported a synthetic intermediate having a related structure in his approach to Punctaporin B. See ref 13a.

10.1021/jo026827o CCC: $25.00
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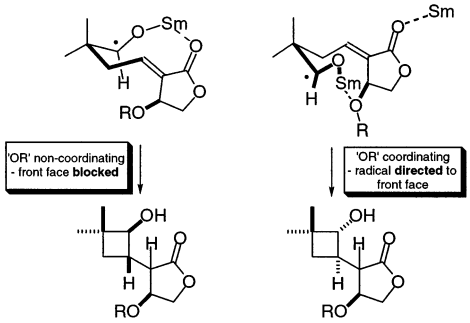


FIGURE 2. Possible origins of remote stereocontrol in the samarium(II)-mediated 4-*exo-trig* cyclization.

A. Our studies have resulted in the first synthesis of the fully functionalized core of pestalotiopsin A.

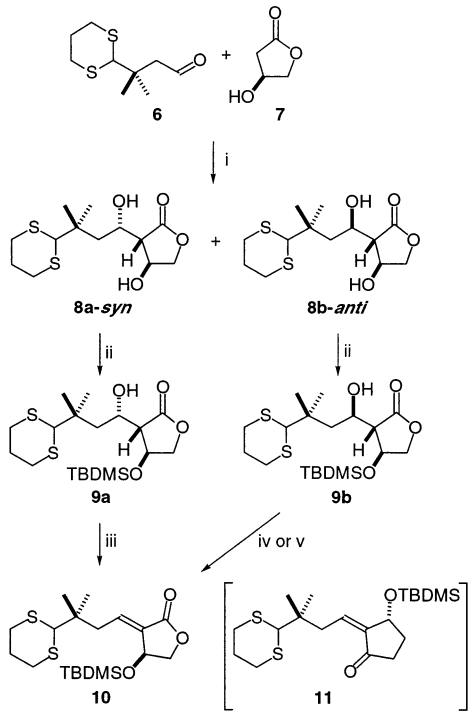
Results and Discussion

We envisaged two possible roles for the derivatized hydroxyl stereocontrol element in generic substrates **5**. First, if the lactone substituent is bulky and noncoordinating (Figure 2), we envisaged a steric blocking effect, forcing radical attack on the opposite face of the olefin. Alternatively, with a coordinating group in this position, the samarium(III) radical anion might be delivered to the same face of the alkene (Figure 2) via a nine-membered chelate.[7] We expected the nature of stereocontrol in the cyclization would depend markedly on the nature of the "R" substituent in the substrates.

In the synthesis of aldehydes **5**, it was crucial that the double-bond could be formed stereoselectively. In previous studies, we have shown that the anti selectivity of the 4-*exo-trig* cyclization is dependent upon the initial double-bond stereochemistry.[4] We chose to proceed via the aldol reaction of readily available (*S*)-*β*-hydroxy-*γ*-butyrolactone **7**[8] with aldehyde **6**,[2a] followed by a regio- and stereocontrolled dehydration to introduce the olefin moiety.

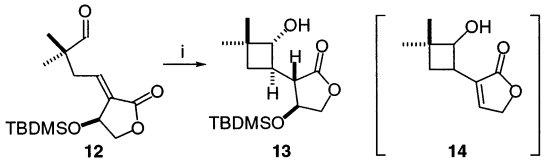
Reaction of lactone **7** with aldehyde **6** proceeded in excellent yield, giving a 1:1 mixture of the aldol products **8a-*syn*** and **8b-*anti***. The stereochemistry of **8b-*anti*** was confirmed by single-crystal X-ray analysis,[9] and that of **8a-*syn*** was inferred from literature observations.[8] The ring hydroxyl in both **8a-*syn*** and **8b-*anti*** could be protected with complete selectivity to give the monosilylated aldols **9a** and **9b**. Dehydration of syn adduct **9a** (MsCl, NEt_3, −5 °C) proceeded smoothly and rapidly to give the *E*-alkene **10** as the only product, and in excellent yield (Scheme 2). The stereochemistry of the double bond in **10** was confirmed by single-crystal X-ray analysis.[9] The reaction of **9b** under similar conditions

SCHEME 2[a]



[a] Reagents and conditions: (i) LDA, THF−HMPA (4:1), −78 to −30 °C, 86%, dr 1:1; (ii) TBDMSCl, imidazole, DMF, rt, 92% for **9a** and 84% for **9b**; (iii) MsCl, NEt_3, CH_2Cl_2, −5 °C, 89%, *E*-only; (iv) MsCl, NEt_3, CH_2Cl_2, −5 °C to rt, 37% of **10** and 46% of **11**; (v) MsCl, 2,6-lutidine, CH_2Cl_2, 40 °C, 80%, *E* only.

SCHEME 3[a]



[a] Reagents and conditions: (i) SmI_2, THF−MeOH (4:1), 0 °C, 25%.

proceeded very slowly to give a mixture of **10** and the corresponding *Z*-alkene **11** in 83% overall yield. Pleasingly, the use of 2,6-lutidine in place of triethylamine in the dehydration of **9b** resulted in the formation of the *E*-alkene **10** as the only detectable product in high yield. Thus, both **8a** and **8b** can be efficiently converted to the *E*-alkene **10**. Deprotection of **10** under standard conditions (MeI, $CaCO_3$, aq MeCN, 60 °C, 99%) gave cyclization substrate **12**.

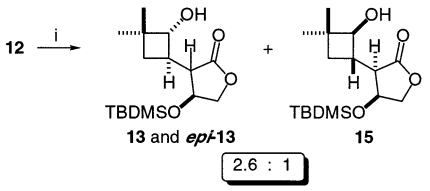
With an efficient route to the TBDMS-protected substrate **12** in place, we began to investigate the samarium(II)-mediated cyclization. On treatment with SmI_2 in THF−MeOH, **12** underwent rapid reaction to give a complex mixture of products from which only cyclobutanol **13** could be isolated in low yield (Scheme 3). The stereochemistry of **13** was determined by single-crystal X-ray analysis.[9] Further studies on the cyclization in MeOH allowed us to identify the elimination product **14** as one byproduct. Cyclobutanol **14** is presumably formed by the elimination of the *tert*-butyldimethylsilyloxy substituent from the intermediate samarium(III) enolate. The elimination of the OTBDMS moiety appears

(7) Large chelates are not uncommon in SmI_2-mediated transformations. Eight-membered chelates in particular have been invoked to rationalize stereoselectivity in a number of reactions; see: (a) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447. (b) Molander, G. A.; Etter, J. B.; Harring, L. S.; Thorel, P.-J. *J. Am. Chem. Soc.* **1991**, *113*, 8036. (c) Molander, G. A.; McKie, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 5821. (d) Keck, G. E.; Truong, A. P. *Org. Lett.* **2002**, *4*, 3131.

(8) Prestwich has shown that aldol reactions of the dianion derived from this lactone proceed with approach of the aldehyde from the opposite face to the ring alkoxide; see: Shieh, H.-M.; Prestwich, G. D. *J. Org. Chem.* **1981**, *46*, 4319.

(9) See the Supporting Information for details of X-ray analyses of compounds **8b**, **10**, **13**, ***epi*-13**, and **15**.

SCHEME 4[a]



[a] Reagents and conditions: (i) SmI_2, THF, CF_3CH_2OH−MeOH (3:1), 0 °C, 80% (**13**, 52%; *epi*-**13**, 6%; **15**, 22%).

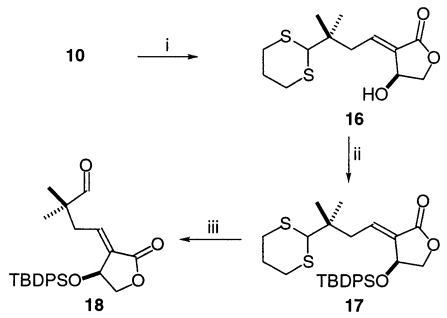
to be responsible for the low mass recovery in this reaction. Additional byproducts can be envisaged, arising from the further reduction of **14**.

We believe the stereochemistry of cyclobutanol **13** suggests a cyclization directed by *coordination* of the incoming samarium(III)-radical anion to the *tert*-butyldimethylsilyloxy group (Figure 2). This was unexpected, as it has been observed that TBDMS ethers appear not to coordinate to samarium(III).[10] In an attempt to disrupt any possible chelation, the cyclization was carried out in the presence of HMPA.[11] However, HMPA is well-known to dramatically increase the reduction potential of SmI_2,[12] thus changing the very nature of the reagent system. No products could be isolated from this reaction. Studies using MeOD gave complete deuterium incorporation α- to the lactone carbonyl in **13**, confirming that the reaction concludes by protonation of an intermediate samarium(III) enolate. In the formation of **13**, this protonation appears to occur from the more hindered face, possibly due to protonation by a methanol molecule coordinated to a samarium(III) center.

To improve the cyclization process, we investigated the use of a less activating, more acidic alcohol cosolvent, capable of tempering the reduction potential of SmI_2 while ensuring rapid protonation of the intermediate samarium(III) enolate, thus preventing elimination. With these properties in mind, we felt fluorous alcohols might prove suitable alternative cosolvents for the cyclization. Pleasingly, cyclization using 2,2,2-trifluoroethanol as cosolvent gave cyclobutanol products, **13**/***epi*-13** and **15**, now in an excellent overall yield of 80%, with only a trace of elimination (Scheme 4). Thus, the judicial choice of cosolvent clearly has a remarkable effect on the efficiency of the transformation. The stereochemistry of ***epi*-13** and **15** was determined by single-crystal X-ray analysis.[9] The stereochemistry of cyclobutanol **15** suggests it arises from a cyclization where the controlling group blocks one face of the olefin acceptor, forcing the radical to approach from the opposite face (see Figure 2). The ratio of "directed" to "blocked" products was 2.6:1 (Scheme 4).

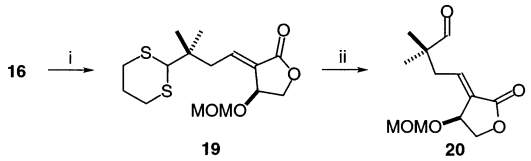
In an attempt to investigate the role of the derivatized hydroxyl in the cyclization, we prepared the bulky

SCHEME 5[a]



[a] Reagents and conditions: (i) HF (40% aq), pyridine, MeCN, 0 °C to rt, 97%; (ii) TBDPSCl, imidazole, DMF, rt, 54%; (iii) MeI, $CaCO_3$, MeCN−H_2O 4:1, 60 °C, 83%.

SCHEME 6[a]



[a] Reagents and conditions: (i) MOMCl, $^iPr_2NEt$, CH_2Cl_2, 0 °C to rt, 98%; (ii) MeI, $CaCO_3$, MeCN−H_2O 2:1, rt, 82%.

TBDPS ether **18** and the potentially more coordinating MOM ether **20**. We chose to access these substrates from alkene **10**. Removal of the TBDMS protecting group from alkene **10** was best achieved using aqueous HF in acetonitrile−pyridine, giving alcohol **16** in excellent yield. Protection as the TBDPS ether **17** and cleavage of the thioacetal protecting group gave substrate **18** in good yield (Scheme 5).

The MOM cyclization substrate **20** was prepared in a similar manner. Protection of alcohol **16** under standard conditions proceeded efficiently to give MOM ether **19**. Removal of the thioacetal protecting group proved troublesome in this case. After investigation of a number of alternative methods, our original procedure was modified. Using lower temperatures and a prolonged reaction time, a good yield of the desired aldehyde **20** was obtained (Scheme 6).

Treatment of aldehyde **18** with SmI_2 in THF−methanol led to complex mixtures of products. This could not be improved using our trifluoroethanol conditions. The major product observable in the crude NMR, and the only isolable product, was the cyclobutanol **14**. Attempts to cyclize the MOM ether **20** with SmI_2, using either methanol or trifluoroethanol as cosolvent similarly led to complex product mixtures, which in this case also contained acyclic aldehyde byproducts. The study of substrates **18** and **20** therefore failed to provide further insight into the cyclization process. The TBDMS cyclization substrate **12** provides the most efficient progress toward pestalotiopsin A.

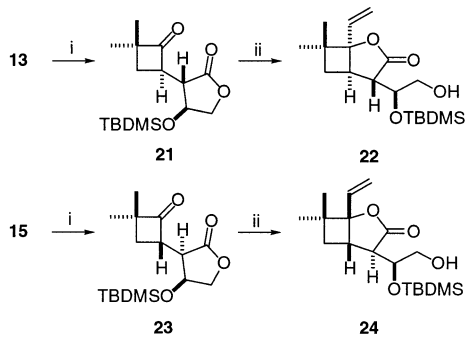
With an efficient route to cyclobutanols **13** and **15** in hand, we continued our synthetic approach. Crucially, **13** and **15** are potential precursors to *either* enantiomer of the pestalotiopsin core. This is desirable as the absolute stereochemistry of the natural product is not known. Our approach should allow synthetic studies to be carried out in either enantiomeric series starting from

(10) For the role of an OTBDMS group in a samarium(II)-mediated reduction, see: Keck, G. E.; Wager, C. A. *Org. Lett.* **2000**, *2*, 2307.

(11) HMPA is known to disrupt chelation in SmI_2-mediated transformations, leading to a loss of stereoselectivity. For an illustrative example, see: Fukazawa, S.-I.; Seki, K.; Tatsuzawa, M.; Mutoh, K. *J. Am. Chem. Soc.* **1997**, *119*, 1482.

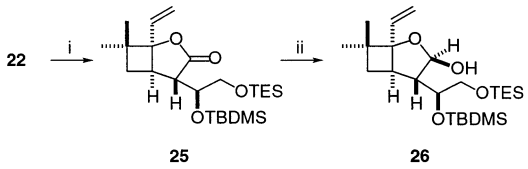
(12) Shabangi, M.; Flowers, R. A. *Tetrahedron Lett.* **1997**, *38*, 1137. (b) Shabangi, M.; Sealy, J. M.; Fuchs, J. R.; Flowers, R. A. *Tetrahedron Lett.* **1998**, *39*, 4429. (c) Enemaerke, R. J.; Hertz, T.; Skrydstrup, T.; Daasbjerg, K. *Chem. Eur. J.* **2000**, *6*, 3747. (d) Miller, R. S.; Sealy, J. M.; Shabangi, M.; Kuhlman, M. L.; Fuchs, J. R.; Flowers, R. A. *J. Am. Chem. Soc.* **2000**, *122*, 7718.

SCHEME 7[a]



[a] Reagents and conditions: (i) TPAP, NMO, CH_2Cl_2, rt, 95% for **21**, 90% for **23**; (ii) vinyl ytterbium triflate, THF, −78 °C, 68% for **22**, 81% for **24**.

SCHEME 8[a]



[a] Reagents and conditions: (i) TESCl, imidazole, DMF, rt, 81%; (ii) DIBAL-H, CH_2Cl_2, −78 °C, 97%, dr 3.4:1 (major isomer shown).

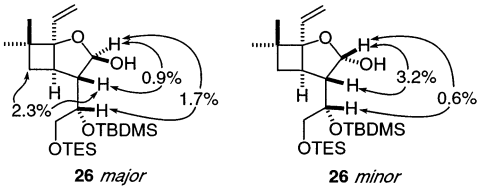


FIGURE 3. Key NOE observations for lactol **26**.

a single enantiomer of starting material. For example, cyclobutanol **13** was oxidized to cyclobutanone **21**, which was then treated with vinylytterbium triflate, according to our previously described addition/trans-lactonization sequence,[4,13] giving bicyclic lactone **22** in good yield (Scheme 7).

Cyclobutanol **15** was also subjected to oxidation and the addition/trans-lactonization sequence. Oxidation gave cyclobutanone **23**, which reacted smoothly with vinylytterbium triflate to give bicyclic lactone **24** in excellent yield (Scheme 7). Lactones **22** and **24** can be considered as pseudoenantiomers, lactone **22** simply requiring inversion of the stereochemistry at C-7 to allow access to the opposite enantiomer of the target.

Continuing our approach, the pendant primary alcohol of lactone **22** was protected as the triethylsilyl ether **25** before reduction of the lactone carbonyl. Treatment of the lactone with DIBAL-H at −78 °C gave lactol **26**, which was initially isolated as a 3.4:1 mixture of diastereoisomers (Scheme 8). This mixture was found to equilibrate on standing in $CDCl_3$ solution, and as such, no attempt was made to separate the diastereoisomers.

We envisaged that the major product would arise from hydride attack from the convex face of the bicyclic system. This was confirmed by NOE studies on the diastereomeric mixture. Key NOE observations are shown in Figure 3. The reduction to lactol **26** constitutes the first synthesis of the fully functionalized core of pestalotiopsin A.

(13) For a similar addition/trans-lactonization sequence on a cyclobutanone substrate, see: (a) Kende, A. S.; Kaldor, I.; Aslanian, R. *J. Am. Chem. Soc.* **1988**, *110*, 6265. (b) Kende, A. S.; Kaldor, I. *Tetrahedron Lett.* **1989**, *30*, 7329.

Conclusions

In summary, we have developed an efficient stereoselective route to generic cyclization substrates **5** from (*S*)-*β*-hydroxy-*γ*-butyrolactone, featuring an aldol reaction and convergent, selective dehydration. The cyclization of one such substrate proceeds efficiently in the presence of 2,2,2-trifluoroethanol as cosolvent. We have shown that the remote stereocontrol element in this substrate is capable of modest control of facial selectivity in the samarium(II)-mediated 4-*exo-trig* cyclization. The nature of stereocontrol appears to involve the unexpected coordination of an OTBDMS ether to a samarium center. We have applied this methodology to the stereoselective synthesis of the fully functionalized core of pestalotiopsin A.

Experimental Section

General Considerations. THF was freshly distilled from sodium−benzophenone ketyl radical under a nitrogen atmosphere and CH_2Cl_2 from calcium hydride. DMF was distilled under vacuum from calcium hydride and stored over 3 Å sieves. Triethylamine and 2,6-lutidine were distilled from calcium hydride and stored over KOH pellets. HMPA was distilled and stored over 3 Å sieves. Reactions were carried out using oven-dried glassware. NMR spectra were obtained using a Fourier transform spectrometer, operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C spectra. NMR signals were assigned using DEPT-135, HMQC, and COSY spectra. Proton spectra are referenced to residual $CHCl_3$ at 7.270 ppm, and carbon spectra to $CDCl_3$ at 77.4 ppm. IR spectra were recorded using a Fourier transform spectrometer. Mass spectra and microanalyses were recorded at the University of Glasgow.

Samarium(II) iodide was prepared by the method of Imamoto and Ono, with the modification that the samarium−iodine−THF mixture was heated at 60 °C rather than at reflux.[14]

Crystal Structure Analyses of 8b, 10, 13, *epi*-13, and 15. All measurements were made at 100 K using a Nonius KappaCCD diffractometer and Mo Kα X-rays, $\lambda = 0.710\ 73$ Å. Except for **13**, the expected absolute structures were confirmed experimentally from the X-ray data. This was not possible for **13** because the crystals were of poor quality, displaying twinning and high mosaicity. However, our proposed molecular structure for **13** has been confirmed by two independent analyses. Only the better of these two analyses is described here.

(3*S*,4*S*)-3-[(1*S*)-3-([1,3]Dithian-2-yl)-1-hydroxy-3-methylbutyl]-4-hydroxy-4,5-dihydrofuran-2(3*H*)-one 8a and (3*S*,4*S*)-3-[(1*R*)-3-([1,3]Dithian-2-yl)-1-hydroxy-3-methylbutyl]-4-hydroxy-4,5-dihydrofuran-2(3*H*)-one 8b. To a stirred solution of diisopropylamine [3.16 mL, 22.5 mmol, 3.8 equiv (2.3 equiv with respect to lactone)] in dry THF (25 mL) at −78 °C under argon was added *n*-butyllithium (10.7 mL, 2.10 M in hexanes, 22.5 mmol, 3.8 equiv) dropwise, and the mixture was stirred for 50 min. To the resulting LDA solution was added *β*-hydroxy-*γ*-butyrolactone **7** (1.00 g, 9.80 mmol, 1.65 equiv) in THF (1.5 mL) dropwise, via cannula at −78 °C. After a further 90 min, a solution of aldehyde **6** (1.21 g, 5.92 mmol, 1 equiv) in dry THF (6 mL) and HMPA (7 mL) was

(14) Imamoto, T.; Ono, M. *Chem. Lett.* **1987**, 501.

added dropwise via cannula at −78 °C and the solution allowed to warm to −30 °C over 3 h. After 1 h, the reaction was quenched with 10 mL of aq satd NH_4Cl and the aqueous layer extracted with 60% EtOAc in petroleum ether (40−60 °C). The combined organic layers were washed with aq satd $NaHCO_3$ and dried over $MgSO_4$. Concentration followed by column chromatography (silica gel, 60% EtOAc in petroleum ether (40−60 °C)) gave the aldols **8a/b** (1.33 g mg, 4.33 mmol, 73%) as a 1:1 mixture of diastereomers, along with aldehyde **6** (185 mg, 0.91 mmol, 15%). Overall yield of the adducts was 86% based on recovered starting material. Repeated chromatography allowed separation of the **8a-*syn*** and **8b-*anti*** as a colorless oil and a colorless solid, respectively. The *anti*-aldol **8b** crystallized from hexane/$CHCl_3$ to give colorless needles (mp 90−93 °C), from which an X-ray crystal structure was obtained (see the Supporting Information): MS *m*/*z* (EI mode) 306.1 (8) $[M]^+$, 199.1 (5), 160.0 (7), 119.0 (100), 82.9 (15); HRMS calcd for $C_{13}H_{22}O_4S_2$ 306.0960, found 306.0963. Anal. Calcd for $C_{13}H_{22}O_4S_2$: C, 50.95; H, 7.24. Found: C, 50.86; H, 7.23.

8a: ν_{max} (film)/cm^{-1} 3434br,m (OH), 2960m, 2931m, 2900m (C−H), 1751s (C═O), 1176m; $[\alpha]_D = +7.10$ (*c* = 1.24, $CHCl_3$); ^1H NMR δ 1.19 (3H, s, 3H from $C(CH_3)_2$), 1.23 (3H, s, 3H from $C(CH_3)_2$), 1.79−1.88 (1H, m, 1H from CH_2CH_2S), 1.97 (2H, d, *J* = 5.2 Hz, CMe_2CH_2), 2.09−2.16 (1H, m, 1H from CH_2CH_2S), 2.52 (1H, t, *J* = 6.3 Hz, CHC(O)O), 2.69 (1H, d, *J* = 3.5 Hz, OH), 2.88−2.93 (4H, m, 2 × CH_2S), 3.46 (1H, d, *J* = 4.3 Hz, OH), 4.03 (1H, dd, *J* = 6.3, 9.2 Hz, 1H from $CH(OH)CH_2O$), 4.24 (1H, s, CHS_2), 4.28 (1H, apparent quintet, *J* = 5.4 Hz, $CMe_2CH_2CH(OH)$), 4.48 (1H, dd, *J* = 6.9, 9.2 Hz, 1H from $CH(OH)CH_2O$), 4.77 (1H, apparent dq, *J* = 3.1, 6.6 Hz, $CH(OH)CH_2O$); ^{13}C NMR δ 26.2 (CH_2CH_2S), 26.6 (CH_3), 27.3 (CH_3), 31.6 (CH_2S), 31.7 (CH_2S), 39.0 (CMe_2), 45.8 (CMe_2CH_2), 55.5 (CHC(O)O), 60.3 (CHS_2), 67.9 ($CMe_2CH_2CH(OH)$), 69.8 ($CH(OH)CH_2O$), 72.8 (CH_2O), 176.0 (C═O).

8b: ν_{max} (golden gate)/cm^{-1} 3255m (OH), 2966m, 2898m (CH), 1757s (C═O), 1168m, 1078m, 997m; $[\alpha]_D = -50.8$ (*c* = 1.03, $CHCl_3$); ^1H NMR δ 1.18 (3H, s, 3H from $C(CH_3)_2$), 1.20 (3H, s, 3H from $C(CH_3)_2$), 1.64 (1H, dd, *J* = 1.2, 15.4 Hz, AB system, 1H from CMe_2CH_2), 1.74−1.86 (1H, m, 1H from CH_2CH_2S), 2.03−2.14 (2H, m, 1H from CH_2CH_2S and 1H, AB system, from CMe_2CH_2), 2.59 (1H, t, *J* = 5.6 Hz, CHC(O)O), 2.84−2.92 (4H, m, 2 × CH_2S), 3.08 (1H, broad s, OH), 3.69 (1H, broad s, OH), 4.06 (1H, dd, *J* = 5.5, 9.4 Hz, 1H from $CH(OH)CH_2O$), 4.09−4.46 (2H, m, CHS_2 and $CMe_2CH_2CH(OH)$), 4.49 (1H, dd, *J* = 6.6, 9.4 Hz, 1H from $CH(OH)CH_2O$), 4.77 (1H, apparent q, *J* = 6.0 Hz, $CH(OH)CH_2O$); ^{13}C NMR δ 26.3 (CH_2CH_2S), 26.8 (CH_3), 27.0 (CH_3), 31.6 (CH_2S), 31.7 (CH_2S), 38.8 (CMe_2), 45.2 (CMe_2CH_2), 55.4 (CHC(O)O), 60.4 (CHS_2), 68.1 ($CMe_2CH_2CH(OH)$), 70.6 ($CH(OH)CH_2O$), 73.5 (CH_2O), 176.5 (C═O). X-ray analysis of **8b**: $C_{13}H_{22}O_4S_2$, *M* = 306.43, space group $P2_12_12_1$, *a* = 8.3999(1) Å, *b* = 12.2442(2) Å, *c* = 29.2148(4) Å, *Z* = 8, $D_c = 1.355$ Mg/m^3, $\theta_{max} = 32.6°$. Intensity measurements: N_{meas}, = 15664; unique reflections, N_{unique}, = 5864 [R_{int} = 0.039]; least-squares observations including Friedel pairs, N_{ref}, = 9906; no. of parameters, N_p, = 351, $R(F)$ = 0.050, wR(F^2) = 0.091, Flack parameter = −0.06(4), $|\Delta\rho| <$ 0.39 e·$Å^{-3}$.

(3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[(1*S*)-3-([1,3]-dithian-2-yl)-1-hydroxy-3-methylbutyl]-4,5-dihydrofuran-2(3*H*)-one 9a. To a stirred solution of the *syn*-aldol **8a** (660 mg, 2.15 mmol) in dry DMF (1.6 mL) under argon were added imidazole (733 mg, 10.8 mmol, 5 equiv) and TBDMSCl (974 mg, 6.46 mmol, 3 equiv), and the reaction mixture was stirred for 2 h at room temperature. The reaction was quenched with 4 mL of aq satd $NaHCO_3$, and the aqueous layer was extracted into 50% EtOAc in petroleum ether (40−60 °C). The combined organic layers were washed with water and dried over Na_2SO_4. Concentration followed by column chromatography (silica gel, 30% EtOAc in petroleum ether (40−60 °C)) gave the monoprotected *syn*-aldol **9a** (831 mg, 1.98 mmol, 92%) as a viscous oil: MS *m*/*z* (EI mode) 420.1 (5) $[M]^+$, 363.0 (3), 313.1 (8), 160.0 (11), 119.1 (100), 75.0 (33); HRMS calcd for $C_{19}H_{36}O_4S_2Si$ 420.1825, found 420.1827; ν_{max} (film)/cm^{-1} 3473m (OH), 2956s, 2929s, 2898m, 2857m (CH), 1771s (C═O), 1471m, 1256m; $[\alpha]_D = -8.51$ (*c* = 1.01, $CHCl_3$); ^1H NMR δ 0.10 (3H, s, 3H from $Si(CH_3)_2$), 0.15 (3H, s, 3H from $Si(CH_3)_2$), 0.90 (9H, s, $Si(CH_3)_3$), 1.16 (3H, s, 3H from $C(CH_3)_2$), 1.21 (3H, s, 3H from $C(CH_3)_2$), 1.70 (1H, dd, AB system, *J* = 1.4, 15.2 Hz, 1H from CMe_2CH_2), 1.78−1.85 (1H, m, 1H from CH_2CH_2S), 1.98 (1H, dd, AB system, *J* = 9.5, 15.2 Hz, 1H from CMe_2CH_2), 2.08−2.14 (1H, m, 1H from CH_2CH_2S), 2.53 (1H, dd, *J* = 3.3, 5.6 Hz, CHC(O)O), 2.86−2.92 (4H, m, 2 × CH_2S), 3.06 (1H, d, *J* = 4.9 Hz, OH), 3.97 (1H, dd, *J* = 5.2, 9.0 Hz, 1H from $CH(OTBDMS)CH_2O$), 4.28 (1H, s, CHS_2), 4.38−4.43 (2H, m, 1H from $CH(OTBDMS)CH_2O$ and CH(OH)), 4.75 (1H, apparent q, *J* = 5.6 Hz, CH(OTBDMS)). ^{13}C NMR δ −4.4 ($Si(CH_3)$), −3.9 ($Si(CH_3)$), 18.1 ($SiC(CH_3)_3$) 26.0 ($SiC(CH_3)_3$) 26.3 (CH_2CH_2S), 26.6 (CH_3), 26.9 (CH_3), 31.6 (CH_2S), 31.7 (CH_2S), 38.8 (CMe_2), 45.6 (CMe_2CH_2), 56.9 (CHC(O)O), 60.2 (CHS_2), 66.8 (CH(OH)), 68.8 (CH(OTBDMS)), 74.4 (CH_2O), 176.8 (C═O).

(3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[(1*R*)-3-([1,3]-dithian-2-yl)-1-hydroxy-3-methylbutyl]-4,5-dihydrofuran-2(3*H*)-one 9b. Similarly, a solution of the *anti*-aldol **8b** (340 mg, 1.11 mmol), imidazole (378 mg, 5.55 mmol), and TBDMSCl (502 mg 3.32 mmol) in dry DMF (1.0 mL) was stirred at room temperature for 19 h to give, after column chromatography (silica gel, 30% EtOAc/petroleum ether (40−60 °C)), the monoprotected *anti*-aldol **9b** (393 mg, 0.935 mmol, 84%) as a waxy white solid (mp 67−68 °C): ν_{max} (golden gate)/cm^{-1} 3490br,w (OH), 2927m, 2856m, (CH), 1761 (C═O), 1462m, 1105m, 998s; $[\alpha]_D = -74.2$ (*c* = 1.00, $CHCl_3$); ^1H NMR δ 0.10 (3H, s, 3H from $Si(CH_3)_2$), 0.13 (3H, s, 3H from $Si(CH_3)_2$), 0.90 (9H, s, $Si(CH_3)_3$), 1.20 (6H, s, $C(CH_3)_2$), 1.70 (1H, dd, AB system, *J* = 1.5, 15.4 Hz, 1H from CMe_2CH_2), 1.79−1.85 (1H, m, 1H from CH_2CH_2S), 2.07−2.12 (1H, m, 1H from CH_2CH_2S), 2.21 (1H, dd, AB system, *J* = 9.9, 15.5 Hz, 1H from CMe_2CH_2), 2.46 (1H, dd, *J* = 4.5, 5.7 Hz, CHC(O)O), 2.86−2.91 (4H, m, 2 × CH_2S), 3.28 (1H, d, *J* = 3.3 Hz, OH), 3.97 (1H, dd, *J* = 5.3, 9.0 Hz, 1H from CH_2O), 4.11−4.18 (1H, m, CH(OH)), 4.27 (1H, s, CHS_2), 4.41 (1H, dd, *J* = 6.4, 9.0 Hz, 1H from CH_2O), 4.55 (1H, apparent q, *J* = 5.9 Hz, CH(OTBDMS)); ^{13}C NMR δ −4.3 ($Si(CH_3)$), −4.1 ($Si(CH_3)$), 18.2 ($SiC(CH_3)_3$), 26.0 ($SiC(CH_3)_3$) 26.3 (CH_2CH_2S), 26.7 (CH_3), 27.1 (CH_3), 31.6 (CH_2S), 31.7 (CH_2S), 38.7 (CMe_2), 45.7 (CMe_2CH_2), 56.3 (CHC(O)O), 60.2 (CHS_2), 67.9 (CH(OH)), 71.6 (CH(OTBDMS)), 74.2 (CH_2O), 176.3 (C═O).

(4*S*)-(*E*)-4-(*tert*-Butyldimethylsilyloxy)-3-[3-([1,3]dithian-2-yl)-3-methylbutylidene]-4,5-dihydrofuran-2-one 10 and (4*S*)-(*Z*)-4-(*tert*-Butyldimethylsilyloxy)-3-[3-([1,3]dithian-2-yl)-3-methylbutylidene]-4,5-dihydrofuran-2-one 11. Method A: From 9a. To a stirred solution of **9a** (185 mg, 0.440 mmol) in dry CH_2Cl_2 (4.4 mL) at −5 °C under argon were added triethylamine (0.91 mL, 6.53 mmol, 15 equiv) and methanesulfonyl chloride (0.17 mL, 2.20 mmol, 5 equiv). The reaction mixture was maintained between −5 and −10 °C for 2.5 h. The reaction was quenched with 3 mL of aq satd $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration followed by column chromatography (silica gel, 40% EtOAc in petroleum ether (40−60 °C)) gave the *E*-olefin **10** (158 mg, 0.392 mmol, 89%) as a white solid.

Method B: From 9b. To a stirred solution of **9b** (40 mg, 0.0951 mmol) in dry CH_2Cl_2 (1 mL) at −10 °C under argon were added triethylamine (0.20 mL, 1.93 mmol, 20 equiv) and methanesulfonyl chloride (35 μL, 0.475 mmol, 5 equiv). The reaction mixture was maintained between −15 and −5 °C for 42 h before warming to room temperature for 5 h. The reaction was quenched with 2 mL of aq satd $NaHCO_3$ and the aqueous layer extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated to give a crude mixture of the *E*- and *Z*-olefins. ^1H NMR showed *E*/*Z* = 1:1.5. The olefins were easily separated by column chromatography (silica gel, 20% EtOAc in petroleum ether (40−60 °C)) to give the

E-olefin **10** (14.0 mg, 0.0347 mmol, 37%) and the *Z*-olefin **11** (17.7 mg, 0.0440 mmol, 46%) as a white solid (mp 62−63 °C).

Method C: From 9b. To a stirred solution of **9b** (150 mg, 0.357 mmol) in dry CH_2Cl_2 (3.5 mL) at room temperature under argon were added 2,6-lutidine (0.71 mL, 6.06 mmol, 17 equiv) and methanesulfonyl chloride (0.14 mL, 1.78 mmol, 5 equiv). The reaction mixture was then heated at 40 °C for 22 h. The reaction was quenched with 5 mL of aq satd $NaHCO_3$ and the aqueous layer extracted with CH_2Cl_2. The combined extracts were washed with 0.5 M $CuSO_4$ and dried over $MgSO_4$. Concentration followed by column chromatography (silica gel, 20% EtOAc/petroleum ether (40−60 °C)) gave *E*-olefin **10** (115 mg, 0.286 mmol, 80%). ^{1}H NMR of the crude showed the *E*-olefin as the only detectable product.

The *E*-olefin **10** crystallized from petroleum ether (40−60 °C) to give colorless crystals (mp 109−112 °C) from which a crystal structure was obtained (see the Supporting Information): MS *m*/*z* (EI mode) 402.2 (3) $[M]^+$, 345.0 (4), 283.1 (10), 161.0 (54), 119.0 (100), 75.0 (20); HRMS calcd for $C_{19}H_{34}O_3S_2Si$ 402.1719, found 402.1720. Anal. Calcd for $C_{19}H_{34}O_3S_2Si$: C, 56.67; H, 8.51. Found: C, 56.51; H, 8.57.

10: ν_{max} (golden gate)/cm^{-1} 2929m, 2900m, 2856m (CH), 1741s (C═O), 1681m, 1209s, 1097s, 993s; $[\alpha]_D = -125.2$ (c = 1.00, $CHCl_3$); ^{1}H NMR δ 0.12 (3H, s, 3H from Si(CH_3)$_2$), 0.18 (3H, s, 3H from Si(CH_3)$_2$), 0.90 (9H, s, Si(CH_3)$_3$), 1.16 (3H, s, 3H from C(CH_3)$_2$), 1.19 (3H, s, 3H from C(CH_3)$_2$), 1.78−1.83 (1H, m, 1H from CH_2CH$_2$S), 2.07−2.12 (1H, m, 1H from CH_2-CH$_2$S), 2.43 (1H, ddd, J = 1.2, 5.4, 15.4 Hz, 1H from CMe$_2$CH_2), 2.69 (1H, dd, J = 9.9, 15.4 Hz, 1H from CMe$_2$CH_2), 2.84−2.92 (4H, m, 2 × CH_2S), 4.02 (1H, s, CHS$_2$), 4.12 (1H, dd, J = 2.6, 9.8 Hz, 1H from CH_2O), 4.41 (1H, dd, J = 6.1, 9.8 Hz, 1H from CH_2O), 5.12−5.14 (1H, m, CH(OTBDMS)), 7.00 (1H, ddd, J = 1.8, 5.4, 9.8 Hz, CH═C); ^{13}C NMR δ −4.2 (Si(*C*H$_3$)), −3.7 (Si-(*C*H$_3$)), 18.3 (Si*C*(CH$_3$)$_3$), 25.8 (*C*H$_3$), 25.9 (*C*H$_3$), 26.0 (SiC-(*C*H$_3$)$_3$), 26.3 (*C*H$_2$CH$_2$S), 31.6 (2 × *C*H$_2$S), 39.4 (*C*Me$_2$), 40.4 (*C*H$_2$CH═C), 60.3 (*C*HS$_2$), 67.2 (*C*H(OTBDMS)), 74.7 (*C*H$_2$O), 131.0 (CH═*C*), 142.9 (*C*H═C), 170.4 (*C*═O). X-ray analysis of **10**: $C_{19}H_{34}O_3S_2Si$, M = 402.67, space group $P2_12_12_1$, a = 6.3021(1) Å, b = 11.8532(6) Å, c = 28.975(2) Å, Z = 4, D_c = 1.236 Mg/m^3, θ_{max} = 27.6°. N_{meas} = 9003; N_{unique}, = 2775 [R_{int} = 0.067]; N_{ref} = 4525; N_p, = 233, $R(F)$ = 0.044, wR(F^2) = 0.090, Flack parameter = −0.05(7), $|\Delta\rho| < 0.34$ e·Å^{-3}.

11: ν_{max} (golden gate)/cm^{-1} 2958m, 2925m, 2887m, 2852m (CH), 1738s (C═O), 1674m, 1384m, 1105m, 991s; $[\alpha]_D = -51.4$ (c = 1.01, $CHCl_3$); ^{1}H NMR δ 0.11 (3H, s, 3H from Si(CH_3)$_2$), 0.15 (3H, s, 3H from Si(CH_3)$_2$), 0.93 (9H, s, Si(CH_3)$_3$), 1.15 (6H, s, C(CH_3)$_2$), 1.81−1.87 (1H, m, 1H from CH_2CH$_2$S), 2.07−2.12 (1H, m, 1H from CH_2CH$_2$S), 2.82−2.93 (5H, m, 2 × CH_2S and 1H from CMe$_2$CH_2), 3.02−3.07 (1H, m, 1H from CMe$_2$CH_2), 3.98 (1H, dd, J = 5.2, 9.2 Hz, 1H from CH_2O), 4.04 (1H, s, CHS$_2$), 4.40 (1H, dd, J = 6.6, 9.0 Hz, 1H from CH_2O), 4.87−4.90 (1H, m, CH(OTBDMS)), 6.52−6.56 (1H, apparent t, J = 9.2, CH×C); ^{13}C NMR δ −4.2 (Si(*C*H$_3$)), −4.1 (Si(*C*H$_3$)), 18.4 (Si*C*(CH$_3$)$_3$), 25.5 (*C*H$_3$), 25.6 (*C*H$_3$), 26.1 (SiC(*C*H$_3$)$_3$) 26.4 (*C*H$_2$-CH$_2$S), 31.8 (2 × *C*H$_2$S), 37.7 (*C*H$_2$CH═C), 40.0 (*C*Me$_2$), 60.9 (*C*HS$_2$), 70.3 (*C*H(OTBDMS)), 73.2 (*C*H$_2$O), 130.7 (CH═*C*), 143.7 (*C*H═C), 168.8 (*C*═O).

(*E*)-4-[(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-oxo-4,5-dihydrofuran-3-ylidene]-2,2-dimethylbutanal 12. To a stirred solution of **10** (150 mg, 0.373 mmol) in MeCN (2.2 mL) and water (1.1 mL) at room temperature were added $CaCO_3$ (112 mg, 1.12 mmol, 3 equiv) and MeI (0.70 mL, 11.2 mmol, 30 equiv). The solution was heated to 60 °C and stirred for 18 h. After this time, the solution was cooled and passed through a short plug column (silica gel) eluted with 40% EtOAc in petroleum ether (40−60 °C). Concentration gave the aldehyde **12** (115 mg, 0.368 mmol, 99%) as a white solid (mp 92 °C), which was used without further purification: MS *m*/*z* (FAB+ mode) 313.2 (84) $[M + H]^+$, 283.2 (9), 255.1 (34), 181.1 (63), 139.1 (17), 117.2 (9), 73.8 (100), 60.0 (14); HRMS calcd for $C_{16}H_{29}O_4Si$ 313.1835, found 313.1837; ν_{max} (golden gate)/cm^{-1} 2929m, 2856m (C−H), 1745s, 1725s (C═O), 1685w, 1463m, 995s; $[\alpha]_D = -125.2$ (c = 0.98, $CHCl_3$); ^{1}H NMR δ 0.12 (3H, s, 3H from Si(CH_3)$_2$), 0.17 (3H, s, 3H from Si(CH_3)$_2$), 0.91 (9H, s, Si(CH_3)$_3$), 1.15 (3H, s, 3H from C(CH_3)$_2$), 1.17 (3H, s, 3H from C(CH_3)$_2$), 2.51 (1H, ddd, J = 1.0, 7.1, 15.2 Hz, 1H from CMe$_2$CH_2), 2.58 (1H, dd, J = 8.5, 15.2 Hz, 1H from CMe$_2$CH_2), 4.10 (1H, dd, J = 3.1, 9.8 Hz, 1H from CH_2O), 4.44 (1H, dd, J = 6.3, 9.8 Hz, 1H from CH_2O), 5.08−5.10 (1H, m, CH(OTB-DMS)), 6.89 (1H, ddd, J = 2.0, 7.1, 8.8 Hz, CH═C), 9.50 (1H, s, CHO); ^{13}C NMR δ −4.3 (Si(*C*H$_3$)), −3.8 (Si(*C*H$_3$)), 18.2 (Si*C*(CH$_3$)$_3$), 21.6 (*C*H$_3$), 22.3 (*C*H$_3$), 26.0 (SiC(*C*H$_3$)$_3$), 36.0 (*C*H$_2$-CH═C), 46.2 (*C*Me$_2$), 67.2 (*C*H(OTBDMS)), 74.3 (*C*H$_2$O), 131.3 (CH═*C*), 141.6 (*C*H═C), 169.9 (*C*(O)O), 204.6 (*C*HO).

(3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[(1*R*,2*R*)-2-hydroxy-3,3-dimethylcyclobutyl]-4,5-dihydrofuran-2(3*H*)-one 13, (3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[(1*R*,2*R*)-2-hydroxy-3,3-dimethylcyclobutyl)-4,5-dihydrofuran-2(3*H*)-one *epi*-13, and (3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[(1*S*,2*S*)-2-hydroxy-3,3-dimethylcyclobutyl)-4,5-dihydrofuran-2(3*H*)-one 15. To a solution of SmI_2 (3.52 mL, 0.1 M in THF, 0.352 mmol, 2.2 equiv), CF_3CH_2OH (0.85 mL), and MeOH (0.29 mL) at 0 °C under argon was added aldehyde **12** (50 mg, 0.160 mmol) in THF solution (1 mL), via cannula. After 30 min, the reaction was quenched with aq satd NaCl (5 mL) and water (15 mL). The aqueous layer was extracted with 60% EtOAc in petroleum ether (40−60 °C), and the combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography (silica gel, 30% EtOAc in petroleum ether (40−60 °C)) gave cyclobutanols **13** (26.1 mg, 0.0830 mmol, 52%), ***epi*-13** (2.9 mg, 0.0092 mmol, 6%), and **15** (11.1 mg, 0.0353 mmol, 22%), all as white crystalline solids.

13. Cyclobutanol **13** crystallized from $CHCl_3$/petroleum ether (40−60 °C) to give colorless needles (mp 127 °C), from which an X-ray crystal structure was obtained (see the Supporting Information): MS *m*/*z* (EI+ mode) 314.2 (4) $[M]^+$, 257.1 (13), 243.1 (42), 201.1 (18), 173.1 (12), 117.0 (100), 73.1 (59), 59.0 (16); HRMS calcd for $C_{16}H_{30}O_4Si$ 314.1913, found 314.1913; ν_{max} (golden gate)/cm^{-1} 3436m (OH), 2952m, 2929m, 2858m (CH), 1739s (C═O), 1461m, 1419w, 1394w, 1361w, 1245w, 1110m, 1082s, 993s; $[\alpha]_D = -26.6$ (c = 1.47, $CHCl_3$); ^{1}H NMR δ 0.07 (3H, s, 3H from Si(CH_3)$_2$), 0.09 (3H, s, 3H from Si(CH_3)$_2$), 0.85 (9H, s, Si(CH_3)$_3$), 1.13 (6H, s, C(CH_3)$_2$), 1.30 (1H, apparent t, J = 10.0 Hz, 1H from CMe$_2$CH_2), 1.74 (1H, apparent t, J = 10.0 Hz, 1H from CMe$_2$CH_2), 2.12−2.21 (1H, m, CH(OH)CH), 2.53 (1H, dd, J = 5.9, 9.9 Hz, CHC═O), 2.62 (1H, d, J = 3.4 Hz, OH), 3.80 (1H, dd, J = 3.4, 7.6 Hz, CH(OH)), 3.98 (1H, dd, J = 5.4, 9.2 Hz, 1H from CH_2O), 4.25 (1H, apparent q, J = 5.8 Hz, CH(OTBDMS)), 4.41 (1H, dd, J = 6.0, 9.2 Hz, 1H from CH_2O); ^{13}C NMR δ −4.5 (Si(*C*H$_3$)), −4.2 (Si(*C*H$_3$)), 18.2 (Si*C*(CH$_3$)$_3$), 21.2 (*C*H$_3$), 26.0 (SiC(*C*H$_3$)$_3$), 28.9 (*C*H$_3$), 33.0 (CMe$_2$*C*H$_2$), 39.6 (*C*Me$_2$), 40.3 (CH(OH)*C*H), 53.1 (*C*HC(O)O), 73.1 (*C*H(OTBDMS)), 74.2 (*C*H$_2$O), 78.0 (*C*H(OH)), 178.1 (*C*═O). X-ray analysis of **13**: $C_{16}H_{30}O_4Si$, M = 314.49, space group $P2_1$, a = 6.4174(2) Å, b = 25.1035(7) Å, c = 11.5090(3) Å, β = 91.53(1)°, Z = 4, D_c = 1.127 Mg/m^3 , θ_{max} = 27.6°. N_{meas} = 14055; N_{unique} = 4142 [R_{int} = 0.098]; N_{ref} = 7535; N_p = 380, $R(F)$ = 0.12, wR(F^2) = 0.30, absolute structure not determined, $|\Delta\rho| < 1.3$ e·Å^{-3}.

***epi*-13.** Cyclobutanol ***epi*-13** crystallized from petroleum ether (40−60 °C) to give colorless needles (mp 106−107 °C) from which an X-ray crystal structure was obtained (see the Supporting Information): ν_{max} (golden gate)/cm^{-1} 3479w (OH), 2950m, 2929m, 2856m (CH), 1741s (C═O), 1462m, 1385w, 1360w, 1323m, 1097m, 993s; $[\alpha]_D = -4.1$ (c = 1.00, $CHCl_3$); ^{1}H NMR δ 0.11 (3H, s, 3H from Si(CH_3)$_2$), 0.13 (3H, s, 3H from Si(CH_3)$_2$), 0.91 (9H, s, Si(CH_3)$_3$), 1.09 (3H, s, 3H from C(CH_3)$_2$), 1.11 (3H, s, 3H from C(CH_3)$_2$), 1.36 (1H, apparent t, J = 10.2 Hz, 1H from CMe$_2$CH_2), 1.78 (1H, apparent t, J = 10.2 Hz, 1H from CMe$_2$CH_2), 1.87 (1H, d, J = 6.9 Hz, OH), 2.39−2.47 (1H, m, CH(OH)CH), 2.64 (1H, apparent t, J = 6.4 Hz, CHC═O), 3.90 (1H, apparent t, J = 6.9 Hz, CH(OH)), 4.04 (1H, dd, J = 3.4, 9.6 Hz, 1H from CH_2O), 4.25 (1H, dd, J = 4.7, 9.6 Hz, 1H from CH_2O), 4.62 (1H, ddd, J = 3.4, 4.7, 5.9 Hz,

C*H*(OTBDMS)); ^{13}C NMR δ −4.4 (Si(*C*H$_3$)), −4.3 (Si(*C*H$_3$)), 18.4 (Si*C*(CH$_3$)$_3$), 21.0 (*C*H$_3$), 26.1 (SiC(*C*H$_3$)$_3$), 28.4 (*C*H$_3$), 32.4 (CMe$_2$*C*H$_2$), 37.2 (CH(OH)*C*H), 39.6 (*C*Me$_2$), 47.9 (*C*HC(O)O), 71.1 (*C*H(OTBDMS)), 73.7 (*C*H$_2$O), 77.0 (*C*H(OH)), 176.5 (*C*=O). X-ray analysis of ***epi*-13**: $C_{16}H_{30}O_4Si$, M = 314.49, space group $P2_1$, a = 6.5054(1) Å, b = 10.3069(1) Å, c = 27.6367(4) Å, β = 95.565(1)°, Z = 4, D_c = 1.133 Mg/m^3 , θ_{max} = 30.0°. N_{meas} = 18910; N_{unique} = 5552 [R_{int} = 0.031]; N_{ref} = 10290; N_p = 395, $R(F)$ = 0.048, wR(F^2) = 0.087, Flack parameter 0.01-(6), $|\Delta\rho|$ < 0.34 e·Å^{-3}.

15. Cyclobutanol **15** crystallized from petroleum ether (40−60 °C) to give colorless needles (mp 105 °C) from which an X-ray crystal structure was obtained (see the Supporting Information): ν_{max} (golden gate)/cm^{-1} 3452br,w (OH), 2952m, 2929m, 2858m (CH), 1749s (C=O), 1462m, 1361w, 1245m, 1095m, 993s; [α]$_D$ = −61.8 (*c* = 1.05, CHCl$_3$); ^{1}H NMR δ 0.09 (6H, s, Si(C*H*$_3$)$_2$), 0.91 (9H, s, Si(C*H*$_3$)$_3$), 1.06−1.11 (1H, m, 1H from CMe$_2$C*H*$_2$), 1.13 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.15 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.73 (1H, apparent t, *J* = 9.0 Hz, 1H from CMe$_2$C*H*$_2$), 2.40−2.46 (1H, m, CH(OH)C*H*), 2.50 (1H, dd, *J* = 4.7, 10.7 Hz, C*H*C(O)O), 3.24 (1H, broad s, O*H*), 3.82 (1H, d, *J* = 7.7 Hz, C*H*(OH)), 4.20 (1H, d, *J* = 10.0 Hz, 1H from C*H*$_2$O), 4.30 (1H, dd, *J* = 3.2, 10.0 Hz, 1H from C*H*$_2$O), 4.62 (1H, dd, *J* = 3.2, 4.7 Hz, C*H*(OTBDMS)); ^{13}C NMR δ −4.8 (Si(*C*H$_3$)), −4.2 (Si(*C*H$_3$)), 18.3 (Si*C*(CH$_3$)$_3$), 21.3 (*C*H$_3$), 25.9 (SiC(*C*H$_3$)$_3$), 29.2 (*C*H$_3$), 33.4 (CMe$_2$*C*H$_2$), 35.7 (CH(OH)*C*H), 39.2 (*C*Me$_2$), 51.8 (*C*HC(O)O), 70.0 (*C*H(OTBDMS)), 76.0 (*C*H$_2$O), 78.2 (*C*H-(OH)), 179.1 (*C*=O). X-ray analysis of **15**: $C_{16}H_{30}O_4Si$, M = 314.49, space group $P2_12_12_1$, a = 6.3837(1) Å, b = 14.1709(3) Å, c = 20.0712(5) Å, Z = 4, D_c = 1.150 Mg/m^3 , θ_{max} = 27.5°. N_{meas} = 28522; N_{unique} = 2397 [R_{int} = 0.075]; N_{ref} = 4150; N_p = 198, $R(F)$ = 0.045, wR(F^2) = 0.085, Flack parameter −0.03-(10), $|\Delta\rho|$ < 0.23 e·Å^{-3}.

(4*S*)-(*E*)-3-[3-([1,3]Dithian-2-yl)-3-methylbutylidene]-4-hydroxy-4,5-dihydrofuran-2-one 16. To a stirred solution of the TBDMS ether **10** (150 mg, 0.373 mmol) in MeCN (13.0 mL) and pyridine (6.50 mL) at 0 °C was added HF (1.65 mL, 40% aq soln) dropwise, and the solution was allowed to warm slowly to room temperature. After 43 h, the reaction was quenched by the careful addition of aq satd NaHCO$_3$ (approximately 40 mL) and the aqueous layer extracted with 70% EtOAc in petroleum ether (40−60 °C). The organic extracts were washed with 0.1 M CuSO$_4$ solution, combined, and dried over Na$_2$SO$_4$. Concentration gave the alcohol **16** (104 mg, 0.362 mmol, 97%) as a colorless oil: MS *m*/*z* (EI+ mode) 288.1 [M]$^+$, 160.0, 119.0; HRMS calcd for $C_{13}H_{20}O_3S_2$ 288.0854, found 288.0852; ν_{max} (film)/cm^{-1} 3421 (OH), 2964, 2931, 2900 (CH), 1745 (C=O), 1675; [α]$_D$ = −53.3 (*c* = 1.21, CHCl$_3$); ^{1}H NMR δ 1.22 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.29 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.73−1.84 (1H, m, 1H from C*H*$_2$CH$_2$S), 2.06−2.13 (1H, m, 1H from C*H*$_2$CH$_2$S), 2.32 (1H, dd, *J* = 5.3, 14.9 Hz, 1H from CMe$_2$C*H*$_2$), 2.80 (1H, dd, *J* = 10.8, 14.9 Hz, 1H from CMe$_2$C*H*$_2$), 2.81−2.94 (4H, m, 2 × C*H*$_2$S), 3.57 (1H, broad s, O*H*), 3.95 (1H, s, C*H*S$_2$), 4.31 (1H, dd, *J* = 1.3, 10.2 Hz, 1H from C*H*$_2$O), 4.38 (1H, dd, *J* = 5.3, 10.2 Hz, 1H from C*H*$_2$O), 5.05 (1H, apparent d, *J* = 4.2 Hz, C*H*(OH)), 6.97 (1H, ddd, *J* = 1.3, 5.3, 10.8 Hz, CH=C); ^{13}C NMR δ 25.9 (*C*H$_2$CH$_2$S), 26.1 (*C*H$_3$), 26.2 (*C*H$_3$), 31.3 (*C*H$_2$S), 31.4 (*C*H$_2$S), 39.6 (*C*Me$_2$), 41.4 (*C*H$_2$CH=C), 59.3 (*C*HS$_2$), 65.6 (*C*H(OH)), 74.1 (*C*H$_2$O), 132.5 (CH=*C*), 141.4 (*C*H=C), 170.4 (*C*=O).

(4*S*)-(*E*)-4-(*tert*-Butyldiphenylsilyloxy)-3-[3-([1,3]dithian-2-yl)-3-methylbutylidene]-4,5-dihydrofuran-2-one 17. To a stirred solution of alcohol **16** (28 mg, 0.0971 mmol) in dry DMF (0.1 mL) at room temperature under argon were added TBDPSCl (75 μL, 0.291 mmol, 3 equiv) and imidazole (33 mg, 0.485 mmol, 5 equiv). The reaction mixture was then stirred overnight before quenching with aq satd NaHCO$_3$ (1 mL) and water (1 mL). The aqueous layer was extracted with 50% EtOAc in petroleum ether (40−60 °C), and the extracts were combined and dried (Na$_2$SO$_4$). Concentration followed by column chromatography (silica gel, 20% EtOAc in petroleum ether (40−60 °C)) gave the TBDPS ether **17** (27.6 mg, 0.0524 mmol, 54%) as a colorless oil: MS *m*/*z* (FAB+ mode) 527.1 [M + H]$^+$, 526.1 [M]$^+$, 469.1, 407.1, 352.1, 271.1, 199.1, 161.1, 119.2, 73.8; HRMS calcd for $C_{29}H_{39}O_3S_2Si$ [M + H]$^+$ 527.21102, found 527.2108; ν_{max} (golden gate)/cm^{-1} 2929, 2856 (CH), 1759 (C=O), 1675, 1461, 1427, 1388, 1105, 995; [α]$_D$ = −53.3, (*c* = 0.92, CHCl$_3$); ^{1}H NMR δ 0.96 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.06 (9H, s, Si(C*H*$_3$)$_3$), 1.08 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.73−1.78 (1H, m, 1H from C*H*$_2$CH$_2$S), 2.03−2.07 (1H, m, 1H from C*H*$_2$CH$_2$S), 2.16 (1H, dd, *J* = 4.7, 15.2 Hz, 1H from CMe$_2$C*H*$_2$), 2.32 (1H, dd, *J* = 10.7, 15.2 Hz, 1H from CMe$_2$C*H*$_2$), 2.68−2.91 (4H, m, 2 × C*H*$_2$S), 3.82 (1H, s, C*H*S$_2$), 3.99 (1H, dd, *J* = 5.3, 10.5 Hz, 1H from C*H*$_2$O), 4.23 (1H, dd, *J* = 1.4, 10.5 Hz, 1H from C*H*$_2$O), 5.10 (1H, apparent d, *J* = 5.0 Hz, C*H*(OTBDPS)), 6.93 (1H, dd, *J* = 3.6, 10.8 Hz, C*H*=C), 7.37−7.49 (6H, m, 6H from Ar*H*), 7.68−7.74 (4H, m, 4H from Ar*H*); ^{13}C NMR δ 19.7 (Si*C*(CH$_3$)$_3$), 25.6 (*C*H$_3$), 25.7 (*C*H$_3$), 26.3 (*C*H$_2$CH$_2$S), 27.2 (SiC(*C*H$_3$)$_3$), 31.6 (CH$_2$(*C*H$_2$S)$_2$), 39.3 (*C*Me$_2$), 41.1 (*C*H$_2$CH=C), 60.0 (*C*HS$_2$), 68.3 (*C*H(OTBDPS)), 74.5 (*C*H$_2$O), 128.1 (Ar*C*H), 128.4 (2C from Ar*C*H), 130.0 (Ar*C*H), 130.6 (Ar*C*H), 131.3 (CH=*C*), 132.9 (Ar*C*Si), 133.5 (Ar*C*Si), 135.2 (Ar*C*H), 136.3 (2C from Ar*C*H), 142.5 (*C*H=C), 170.7 (*C*=O).

(*E*)-4-[(4*S*)-4-(*tert*-Butyldimethylsilyloxy)-2-oxo-4,5-dihydrofuran-3-ylidene]-2,2-dimethylbutanal 18. To a stirred solution of thioacetal **17** (60 mg, 0.114 mmol) in MeCN (2 mL) and water (0.5 mL) at room temperature were added CaCO$_3$ (34 mg, 0.342 mmol, 3 equiv) and MeI (0.21 mL, 3.42 mmol, 30 equiv). The solution was heated to 60 °C and stirred for 24 h. After this time, the solution was cooled and passed through a plug column (silica gel) eluted with 30% EtOAc in petroleum ether (40−60 °C). Concentration gave the aldehyde **18** (41.3 mg, 0.0946 mmol, 83%) as a white solid (mp 71−74 °C): MS *m*/*z* (FAB+ mode) 437.2 (40) [M + H]$^+$, 410.3 (25), 379.1 (33), 199.0 (35), 181.0 (45), 136.0 (42), 73.7 (100; HRMS calcd for $C_{26}H_{33}O_4Si$ 437.2148, found 437.2148; ν_{max} (golden gate)/cm^{-1} 2962w, 2859w (CH), 1752s (C=O), 1714m (C=O), 1681m, 1464m, 1425s, 1194s, 1105s, 991s; [α]$_D$ = −67.7 (*c* = 0.90, CHCl$_3$); ^{1}H NMR δ 0.957 (3H, s, 3H from C(C*H*$_3$)$_2$), 0.964 (3H, s, C(C*H*$_3$)$_2$), 1.06 (9H, s, Si(C*H*$_3$)$_3$), 2.14−2.25 (2H, m, CMe$_2$C*H*$_2$), 3.96 (1H, dd, *J* = 5.5, 10.2 Hz, 1H from C*H*$_2$O), 4.23 (1H, dd, *J* = 1.9, 10.2 Hz, 1H from C*H*$_2$O), 5.38 (1H, apparent d, *J* = 5.4 Hz, C*H*(OTBDPS)), 6.80 (1H, ddd, *J* = 1.6, 6.5, 8.9 Hz, CH=C), 7.36−7.50 (6H, m, 6H from Ar*H*), 7.66−7.74 (4H, m, 4H from Ar*H*), 9.28 (1H, s, C*H*O); ^{13}C NMR δ 19.7 (Si*C*(CH$_3$)$_3$), 21.4 (*C*H$_3$), 21.9 (*C*H$_3$), 27.1 (SiC(*C*H$_3$)$_3$), 36.5 (*C*H$_2$CH=C), 46.1 (*C*Me$_2$), 68.1 (*C*H(OTBDPS)), 74.2 (*C*H$_2$O), 128.3 (4 × Ar*C*H), 128.4 (2 × Ar*C*H), 130.6 (Ar*C*H), 130.7 (Ar*C*H), 131.5 (CH=*C*), 132.8 (Ar*C*Si), 133.2 (Ar*C*Si), 136.2 (4 × Ar*C*H), 141.3 (*C*H=C), 170.2 (*C*(O)O), 204.3 (*C*HO).

(4*S*)-(*E*)-3-[3-([1,3]Dithian-2-yl)-3-methylbutylidene]-4-methoxymethoxy-4,5-dihydrofuran-2-one 19. To a stirred solution of alcohol **16** (90 mg, 0.312 mmol) in dry CH$_2$Cl$_2$ (0.5 mL) and ^{i}Pr$_2$NEt (0.5 mL) under argon at 0 °C was added MOMCl (140 μL, approximately 1.25 mmol, 4 equiv) and the solution allowed to warm slowly to rt over 24 h. A further approximately 4 equiv of MOMCl was then added and the solution stirred for a further 17 h. The reaction was quenched by the addition of water (5 mL). The aqueous layer was extracted with 60% EtOAc in petroleum ether (40−60 °C), and the combined extracts were washed with aq satd NaHCO$_3$ and dried (Na$_2$SO$_4$). Concentration gave the MOM ether **19** (102 mg, 0.307 mmol, 98%) as a pale yellow oil. This was used without further purification: MS *m*/*z* (FAB+ mode) 333.1 [M + H]$^+$, 332.1 [M$^+$], 271.1 160.1, 119.2, 89.6, 77.7; HRMS calcd for $C_{15}H_{24}O_4S_2$ 332.1194, found 332.1193; υ_{max} (film)/cm^{-1} 2961, 2897 (CH), 1761 (C=O), 1678; [α]$_D$ −49.9 (*c* = 1.61, CHCl$_3$); ^{1}H NMR δ 1.16 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.20 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.74−1.85 (1H, m, 1H from C*H*$_2$CH$_2$S), 2.04−2.13 (1H, m, 1H from C*H*$_2$CH$_2$S), 2.47 (1H, dd, *J* = 6.0, 15.0 Hz, 1H from CMe$_2$C*H*$_2$), 2.68 (1H, dd, *J* = 9.7, 15.0 Hz, 1H from CMe$_2$C*H*$_2$), 2.81−2.95 (4H, m, 2 × C*H*$_2$S), 3.43 (3H, s, C*H*$_3$O), 4.00 (1H, s, C*H*S$_2$), 4.36 (1H, dd, *J* = 2.3, 10.4 Hz, 1H from C*H*$_2$O), 4.41 (1H, dd, *J* = 5.4, 10.4 Hz, 1H from C*H*$_2$O), 4.70

(1H, AB system, d, J = 7.1, 1H from CH_2O_2), 4.75 (1H, AB system, d, J = 7.1, 1H from CH_2O_2), 5.00−5.01 (1H, m, C*H*(OMOM)), 7.09 (1H, ddd, J = 1.7, 6.1, 9.7 Hz, C*H*=C); ^{13}C NMR δ 26.0 (2 × *C*H$_3$), 26.3 (*C*H$_2$CH$_2$S), 31.6 (2 × *C*H$_2$S), 39.6 (*C*Me$_2$), 40.5 (*C*H$_2$CH=C), 56.6 (*C*H$_3$O), 60.5 (*C*HS$_2$), 71.6 (*C*H(OMOM)), 72.6 (*C*H$_2$O), 96.1 (*C*H$_2$O$_2$), 128.9 (CH=*C*), 144.4 (*C*H=C), 170.2 (*C*=O).

(*E*)-4-[(4*S*)-4-Methoxymethoxy-2-oxo-4,5-dihydrofuran-3-ylidene]-2,2-dimethylbutanal 20. To a solution of thioacetal **19** (102 mg, 0.307 mmol) in acetonitrile (1.2 mL) and water (0.6 mL) at rt under argon were added $CaCO_3$ (92 mg, 0.920 mmol, 3 equiv) and MeI (0.57 mL, 9.20 mmol, 30 equiv), and the solution was stirred for 44 h. The solution was then passed through a plug column (silica gel, 60% EtOAc in petroleum ether (40−60 °C)). Concentration gave the aldehyde **20** (60.8 mg, 0.251 mmol, 82%) as a colorless oil: MS m/z (FAB+ mode) 243.2 [M + H]$^+$, 181.1, 137.1, 136.1, 107.3, 77.7, 63.9, 52.1; HRMS calcd for $C_{12}H_{19}O_5$ 243.1232, found 243.1230; ν_{max} (film)/cm^{-1} 2960m (CH), 1755s, (C=O), 1720s (C=O), 1682m, 1468m, 1381w, 1207m, 1147s, 1009s, 916m; $[\alpha]_D$ −56.9 (c = 0.98, $CHCl_3$); ^{1}H NMR δ 1.16 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.18 (3H, s, 3H from C(C*H*$_3$)$_2$), 2.51 (1H, dd, J = 7.1, 15.0 Hz, 1H from CMe$_2$C*H*$_2$), 2.58 (1H, dd, J = 8.7, 15.0 Hz, 1H from CMe$_2$C*H*$_2$), 3.43 (3H, s, C*H*$_3$O), 4.37 (1H, dd, J = 2.2, 10.4 Hz, 1H from C*H*$_2$O), 4.43 (1H, dd, J = 5.6, 10.4 Hz, 1H from C*H*$_2$O), 4.69 (1H, AB system, d, J = 7.1, 1H from C*H*$_2$O$_2$), 4.73 (1H, AB system, d, J = 7.2, 1H from C*H*$_2$O$_2$), 4.95 (1H, apparent d, J = 5.5 Hz, C*H*(OMOM)), 6.98 (1H, ddd, J = 1.7, 7.2, 8.7 Hz, CH=C), 9.41 (1H, s, C*H*O); ^{13}C NMR δ 21.7 (*C*H$_3$), 22.3 (*C*H$_3$), 36.5 (*C*H$_2$CH=C), 46.3 (*C*Me$_2$), 56.3 (*C*H$_3$O), 71.1 (*C*H(OMOM)), 72.4 (*C*H$_2$O), 95.8 (*C*H$_2$O$_2$), 129.1 (CH=*C*), 143.0 (*C*H=C), 169.7 (*C*(O)O), 204.5 (*C*HO).

(3*S*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[(1*R*)-3,3-dimethyl-2-oxocyclobutyl]-4,5-dihydrofuran-2(3*H*)-one 21. To a stirred solution of **13** (15 mg, 0.048 mmol) in dry CH_2Cl_2 (0.9 mL) under argon at room temperature was added 4 Å molecular sieves followed by NMO (23 mg, 0.190 mmol, 4 equiv) and a catalytic quantity of TPAP (few crystals). The solution was stirred for 2 h before passing the mixture through a short plug column eluting with 20% EtOAc in petroleum ether (40−60 °C). Concentration gave the cyclobutanone **21** (15 mg, 0.048 mmol, 100%) and as a white crystalline solid (mp 67−69 °C): MS m/z (CI$^+$ mode) 313.2 (27) [M + H]$^+$, 83.0 (7), 57.1 (100); HRMS calcd for $C_{16}H_{29}O_4Si$ 313.1835, found 313.1836; ν_{max} (golden gate)/cm^{-1} 2960m, 2929m, 2857m (CH), 1772s, 1755s (C=O), 1460m, 1385w, 1361w, 1255m, 1169m, 1005s; $[\alpha]_D$ = −62.2 (c = 0.77, $CHCl_3$); ^{1}H NMR δ 0.08 (3H, s, 3H from Si(C*H*$_3$)$_2$), 0.10 (3H, s, 3H from Si(C*H*$_3$)$_2$), 0.90 (9H, s, SiC(C*H*$_3$)$_3$), 1.20 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.29 (3H, s, 3H from C(C*H*$_3$)$_2$), 2.04 (1H, apparent t, J = 10.9 Hz, 1H from CMe$_2$C*H*$_2$), 2.27 (1H, dd, J = 8.9, 10.7 Hz, 1H from CMe$_2$C*H*$_2$), 2.69 (1H, dd, J = 4.1, 7.2 Hz, C*H*C(O)O), 3.71 (1H, ddd, J = 4.1, 8.8, 11.1 Hz, C*H*C(O)CMe$_2$), 3.91 (1H, dd, J = 6.3, 8.9 Hz, 1H from C*H*$_2$O), 4.46 (1H, dd, J = 6.5, 8.9 Hz, 1H from C*H*$_2$O), 4.57 (1H, apparent q, J = 6.5 Hz, C*H*(OTBDMS)); ^{13}C NMR δ −4.5 (Si(*C*H$_3$)), −4.2 (Si(*C*H$_3$)), 18.2 (Si*C*(CH$_3$)$_3$), 21.4 (*C*H$_3$), 24.4 (*C*H$_3$), 26.0 (SiC(*C*H$_3$)$_3$), 29.8 (CMe$_2$*C*H$_2$), 47.6 (*C*HC(O)O), 51.7 (*C*HC(O)CMe$_2$), 58.3 (*C*Me$_2$), 72.3 (*C*H(OTBDMS)), 73.2 (*C*H$_2$O), 175.4 (*C*(O)O), 214.9 (CMe$_2$*C*(O)).

(1*S*,4*S*,5*R*)-4-[(1*S*)-1-(*tert*-Butyldimethylsilyloxy)-2-hydroxyethyl]-7,7-dimethyl-1-vinyl-2-oxabicyclo[3.2.0]-heptan-3-one 22. To a stirred solution of Yb(OTf)$_3$ (480 mg, 0.774 mmol, 5.9 equiv) in THF (19.5 mL) at −78 °C under argon was added vinylmagnesium bromide (0.82 mL, 1.0 M in THF, 6.2 equiv) and the solution stirred for 15 min. After this time, a portion of the resulting bright orange vinylytterbium triflate solution (6.9 mL, ∼2 equiv) was added via syringe to a stirred solution of cyclobutanone **21** (41 mg, 0.131 mmol) in THF (0.8 mL) at −78 °C. This solution was stirred for 20 min before the reaction mixture was quenched by the addition of aq satd NH_4Cl (4.0 mL) and aq satd potassium sodium tartrate (4.0 mL). The aqueous layer was extracted with 60% EtOAc in petroleum ether (40−60 °C), and the combined organic portions were dried over $MgSO_4$ and concentrated. Column chromatography of the residue (silica gel, 20% EtOAc in petroleum ether (40−60 °C)) gave the bicyclic lactone **22** (30.7 mg, 0.090 mmol, 68%) as a colorless oil: MS m/z (FAB$^+$ mode) 341.2 (42) [M + H]$^+$, 283.1 (18), 165.1 (27), 117.1 (24), 73.7 (100); HRMS calcd for $C_{18}H_{33}O_4Si$ 341.2148, found 341.2143; ν_{max} (golden gate)/cm^{-1} 3325w,br (OH), 2927m, 2856m (CH), 1751s (C=O), 1462m, 1247m, 1039m, 926m, 835s, 777s; $[\alpha]_D$ = +31.9 (c = 1.13, $CHCl_3$); ^{1}H NMR δ 0.05 (3H, s, 3H from Si(C*H*$_3$)$_2$), 0.09 (3H, s, 3H from Si(C*H*$_3$)$_2$), 0.88 (9H, s, SiC(C*H*$_3$)$_3$), 1.09 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.13 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.56 (1H, dd, J = 6.4, 12.1 Hz, 1H from CMe$_2$C*H*$_2$), 1.94 (1H, br s, O*H*), 2.06 (1H, dd, J = 9.1, 12.1 Hz, 1H from CMe$_2$C*H*$_2$), 2.83 (1H, dd, J = 2.0, 5.4 Hz, C*H*C(O)O), 3.11 (1H, ddd, J = 2.0, 6.4, 8.8 Hz, C*H*CH$_2$CMe$_2$), 3.58 (1H, dd, J = 5.6, 11.4 Hz, 1H from C*H*$_2$O), 3.71 (1H, dd, J = 3.6, 11.4 Hz, 1H from C*H*$_2$O), 3.96−4.00 (1H, m, C*H*(OTBDMS)), 5.22 (1H, dd, J = 1.4, 11.1 Hz, 1H from CH=C*H*$_2$), 5.33 (1H, dd, J = 1.4, 17.4 Hz, 1H from CH=C*H*$_2$), 5.99 (1H, dd, J = 11.1, 17.4 Hz, CH=CH$_2$); ^{13}C NMR δ −4.3 (Si(*C*H$_3$)), −4.0 (Si(*C*H$_3$)), 18.4 (Si*C*(CH$_3$)$_3$), 23.3 (*C*H$_3$), 26.3 (SiC(*C*H$_3$)$_3$), 26.7 (*C*H$_3$), 35.1 (CMe$_2$CH$_2$CH), 38.2 (CMe$_2$*C*H$_2$), 42.9 (*C*Me$_2$), 53.5 (*C*HC(O)O), 65.6 (*C*H$_2$OH), 72.1 (*C*H(OTBDMS)), 92.3 (CMe$_2$*C*), 116.5 (CH=*C*H$_2$), 134.8 (*C*H=CH$_2$), 179.2 (C=O).

(3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-[(1*S*)-3,3-dimethyl-2-oxocyclobutyl]-4,5-dihydrofuran-2(3*H*)-one 23. As for the preparation of **21**, cyclobutanol **15** (56 mg, 0.178 mmol), NMO (83 mg, 0.712 mmol, 4 equiv), and a catalytic quantity of TPAP (few crystals) were stirred with 4 Å molecular sieves in dry CH_2Cl_2 (2.5 mL) to give, after column chromatography (silica gel, 20% EtOAc in petroleum ether (40−60 °C)), the cyclobutanone **23** (50 mg, 0.160 mmol, 90%) as a white solid (mp 84−85 °C): MS m/z (FAB$^+$ mode) 313.1 (100) [M + H]$^+$, 255.0 (38), 119.0 (9), 73.7 (70); HRMS calcd for $C_{16}H_{29}O_4Si$ 313.1835, found 313.1833; ν_{max} (golden gate)/cm^{-1} 2954m, 2929m, 2858m (C−H), 1774s, 1755s (C=O), 1462m, 1363m, 1107m, 995s; $[\alpha]_D$ = −30.7 (c = 0.62, $CHCl_3$); ^{1}H NMR δ 0.10 (3H, s, 3H from Si(C*H*$_3$)$_2$), 0.11 (3H, s, 3H from Si(C*H*$_3$)$_2$), 0.91 (9H, s, SiC(C*H*$_3$)$_3$), 1.19 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.30 (3H, s, 3H from C(C*H*$_3$)$_2$), 1.90 (1H, apparent t, J = 9.7 Hz, 1H from CMe$_2$C*H*$_2$), 2.10 (1H, apparent t, J = 10.7 Hz, 1H from CMe$_2$C*H*$_2$), 2.81 (1H, apparent t, J = 6.1 Hz, C*H*C(O)O), 3.84 (1H, ddd, J = 6.3, 9.3, 11.0 Hz, C*H*C(O)CMe$_2$), 4.23 (1H, dd, J = 2.6, 9.7 Hz, 1H from C*H*$_2$O), 4.31 (1H, dd, J = 4.3, 9.7 Hz, 1H from C*H*$_2$O), 4.57−4.60 (1H, m, C*H*(OTBDMS)); ^{13}C NMR δ −4.4 (Si(*C*H$_3$)), −4.2 (Si(*C*H$_3$)), 18.3 (Si*C*(CH$_3$)$_3$), 22.2 (*C*H$_3$), 24.4 (*C*H$_3$), 26.0 (SiC(*C*H$_3$)$_3$), 31.2 (CMe$_2$*C*H$_2$), 45.1 (*C*HC(O)O), 50.7 (*C*HC(O)CMe$_2$), 57.8 (*C*Me$_2$), 70.2 (*C*H(OTBDMS)), 74.5 (*C*H$_2$O), 176.1 (*C*(O)O), 212.5 (CMe$_2$*C*(O)).

(1*R*,4*R*,5*S*)-4-[(1*S*)-1-(*tert*-Butyldimethylsilyloxy)-2-hydroxyethyl]-7,7-dimethyl-1-vinyl-2-oxabicyclo[3.2.0]-heptan-3-one 24. To a stirred solution of Yb(OTf)$_3$ (190 mg, 0.306 mmol, 3.8 equiv) in THF (7.7 mL) at −78 °C under argon was added vinylmagnesium bromide (0.32 mL, 1.0 M in THF, 4.0 equiv) and the solution stirred for 15 min. After this time, a portion of the resulting bright orange vinylytterbium triflate solution (4.2 mL, ∼2.0 equiv) was added via syringe to a stirred solution of cyclobutanone **23** (25 mg, 0.0800 mmol) in THF (0.5 mL) at −78 °C. This solution was stirred for 1 h at −78 °C, before the reaction mixture was quenched by the addition of aq satd NH_4Cl (2.5 mL) and aq satd potassium sodium tartrate (2.5 mL). The aqueous layer was extracted with 60% EtOAc in petroleum ether (40−60 °C), and the combined organic portions were dried over $MgSO_4$ and concentrated. Column chromatography of the residue (silica gel, 20% EtOAc in petroleum ether (40−60 °C)) gave the bicyclic lactone **24** (22.1 mg, 0.0649 mmol, 81%) as a white crystalline solid (mp 75−76 °C): MS m/z (FAB$^+$ mode) 341.2 (72) [M + H]$^+$, 323.2 (16), 283.1 (23), 245.1 (11), 175.1 (13), 117.2 (26), 107.3 (18), 73.7 (100), 69.7 (15); HRMS calcd for $C_{18}H_{33}O_4Si$ 341.2148, found 341.2147; ν_{max} (golden gate)/cm^{-1} 3176m (OH), 2929m, 2856m

(CH), 1759s (C=O), 1464m, 1250m, 1190m, 1105m, 1043s, 835s; $[\alpha]_D = -59.5$ ($c = 1.10$, $CHCl_3$); ^{1}H NMR δ 0.09 (3H, s, 3H from Si(CH_3)$_2$), 0.10 (3H, s, 3H from Si(CH_3)$_2$), 0.89 (9H, s, SiC(CH_3)$_3$), 1.06 (3H, s, 3H from C(CH_3)$_2$), 1.16 (3H, s, 3H from C(CH_3)$_2$), 1.54 (1H, dd, $J = 6.9$, 12.2 Hz, 1H from CMe$_2$CH_2), 1.95 (1H, br s, O*H*), 2.09 (1H, dd, $J = 9.1$, 12.2 Hz, 1H from CMe$_2$CH_2), 2.85 (1H, dd, $J = 1.2$, 5.7 Hz, C*H*C(O)O), 2.98 (1H, ddd, $J = 1.2$, 6.9, 9.1 Hz, C*H*CH$_2$CMe$_2$), 3.41−3.50 (2H, m, 2H from CH_2O), 4.02 (1H, apparent q, $J = 5.6$ Hz, C*H*(OTBDMS)), 5.24 (1H, dd, $J = 1.3$, 11.1 Hz, 1H from CH=CH_2), 5.36 (1H, dd, $J = 1.3$, 17.3 Hz, 1H from CH=CH_2), 6.01 (1H, dd, $J = 11.1$, 17.3 Hz, CH=CH$_2$); ^{13}C NMR δ −4.4 (Si(*C*H$_3$)), −4.2 (Si(*C*H$_3$)), 18.4 (Si*C*(CH$_3$)$_3$), 23.0 (*C*H$_3$), 26.1 (SiC(*C*H$_3$)$_3$), 26.7 (*C*H$_3$), 36.0 (CMe$_2$CH$_2$*C*H), 38.7 (CMe$_2$*C*H$_2$), 43.1 (*C*Me$_2$), 53.5 (*C*HC(O)O), 64.5 (*C*H$_2$OH), 72.0 (*C*H(OTBDMS)), 92.3 (CMe$_2$*C*), 116.5 (CH=*C*H$_2$), 134.8 (*C*H=CH$_2$), 177.5 (C=O).

(1*S*,4*S*,5*R*)-4-[(1*S*)-1-(*tert*-Butyldimethylsilyloxy)-2-(triethylsilyloxy)ethyl]-7,7-dimethyl-1-vinyl-2-oxabicyclo-[3.2.0]heptan-3-one 25. To a stirred solution of **22** (20 mg, 0.0587 mmol) in DMF (0.1 mL) at rt was added imidazole (28 mg, 0.411 mmol,7 equiv) followed by triethylchlorosilane (49 μL, 0.294 mmol, 5 equiv). The solution was stirred for 2.5 h before the addition of aq satd $NaHCO_3$ (2 mL). The aqueous mixture was extracted with 20% EtOAc in petroleum ether (40−60 °C), dried over Na_2SO_4, and concentrated. Purification of the residue by column chromatography (silica gel, 3% EtOAc in petroleum ether (40−60 °C)) gave the TES ether **25** (20 mg, 0.0440 mmol, 75%) as a colorless oil, along with starting material (2.6 mg, 0.0076 mmol, 13%): MS *m*/*z* (FAB$^+$ mode) 455.2 (38) [M + H]$^+$, 425.2 (25), 397.1 (43), 289.1 (37), 251.1 (14), 161.1 (20), 115.2 (57), 73.7 (100), 59.9 (26); HRMS calcd for $C_{24}H_{47}O_4Si_2$ 455.3013, found 455.3014; ν_{max} (golden gate)/cm^{-1} 2954m, 2929m, 2877m (CH), 1770s (C=O), 1461w, 1252m, 1082s, 1005m; $[\alpha]_D = +15.0$ ($c = 1.39$, $CHCl_3$); ^{1}H NMR δ −0.01 (3H, s, 3H from Si(CH_3)$_2$), 0.05 (3H, s, 3H from Si-(CH_3)$_2$), 0.62 (6H, q, $J = 7.8$ Hz, 6H from Si(CH_2CH$_3$)$_3$), 0.83 (9H, s, SiC(CH_3)$_3$), 0.96 (9H, t, $J = 7.9$ Hz, 9H from Si-(CH$_2$CH_3)$_3$), 1.09 (3H, s, 3H from C(CH_3)$_2$), 1.10 (3H, s, 3H from C(CH_3)$_2$), 1.54 (1H, dd, $J = 5.8$, 12.2 Hz, 1H from CMe$_2$CH_2), 2.06 (1H, dd, $J = 9.2$, 12.2 Hz, 1H from CMe$_2$CH_2), 2.93 (1H, apparent t, $J = 2.6$ Hz, C*H*C(O)O), 3.05 (1H, ddd, $J = 2.6$, 5.8, 9.2 Hz, C*H*CH$_2$CMe$_2$), 3.37 (1H, dd, $J = 8.6$, 9.9 Hz, 1H from CH_2OTES), 3.58 (1H, dd, $J = 5.2$, 9.9 Hz, 1H from CH_2-OTES), 4.17 (1H, ddd, $J = 2.6$, 5.2, 8.6 Hz, C*H*(OTBDMS)), 5.20 (1H, dd, $J = 1.3$, 11.0 Hz, 1H from CH=CH_2), 5.31 (1H, dd, $J = 1.3$, 17.3 Hz, 1H from CH=CH_2), 5.97 (1H, dd, $J = 11.0$, 17.3 Hz, CH=CH$_2$); ^{13}C NMR δ −4.6 (Si(*C*H$_3$)), −4.0 (Si-(*C*H$_3$)), 4.7 (Si(*C*H$_2$CH$_3$)$_3$), 7.1 (Si(CH$_2$*C*H$_3$)$_3$), 18.4 (Si*C*(CH$_3$)$_3$), 23.8 (*C*H$_3$), 26.3 (SiC(*C*H$_3$)$_3$), 27.0 (*C*H$_3$), 33.3 (CMe$_2$CH$_2$*C*H), 38.3 (CMe$_2$*C*H$_2$), 43.0 (*C*Me$_2$), 53.3 (*C*HC(O)O), 64.8 (*C*H$_2$-(OTES)), 72.4 (*C*H(OTBDMS)), 91.6 (CMe$_2$*C*), 116.3 (CH=*C*H$_2$), 135.0 (*C*H=CH$_2$), 180.3 (C=O).

(1*S*,3*R*,4*S*,5*R*)-4-[(1*S*)-1-(*tert*-Butyldimethylsilyloxy)-2-triethylsilyloxyethyl]-7,7-dimethyl-1-vinyl-2-oxabicyclo-[3.2.0]heptan-3-ol 26. To a stirred solution of **25** (19 mg, 0.0418 mmol) in CH_2Cl_2 (0.4 mL) at −78 °C was added DIBAL-H (33 μL, 1.5 M in toluene, 0.0501 mmol, 1.2 equiv). The solution was stirred at −78 °C for 2 h before quenching with potassium sodium tartrate (35 mg, 0.124 mmol, 3 equiv) in water (2 mL). The aqueous layer was separated and extracted with CH_2Cl_2, and the combined organic portion was dried over $MgSO_4$. Concentration gave the lactol **26** (18.5 mg, 0.0404 mmol, 97%) as a 3.4:1 mixture of diastereomers. This mixture was found to equilibrate on standing in $CDCl_3$ solution, and no attempt was made to separate the diastereomers. The stereochemistry of the two diastereomers was assigned using NOE studies conducted on the crude product mixture (see Figure 3): MS *m*/*z* (FAB$^+$ mode, sodium) 479.1 (13) [M + Na]$^+$, 439.1 (10), 307.1 (11), 289.1 (42), 175.0 (30), 115.2 (51), 73.7 (100), 59.9 (24); HRMS calcd for $C_{24}H_{48}O_4Si_2$-Na 479.2989, found 479.2986; ν_{max} (golden gate)/cm^{-1} 3409w (OH), 2952m, 2931m, 2875w, 2856w (CH), 1462w, 1250w, 1091s, 1003s, 833s, 775s; ^{1}H NMR δ 0.04 (3H, s, 3H from Si-(CH_3)$_2$ of major), 0.06 (3H, s, 3H from Si(CH_3)$_2$ of major), 0.08 (3H, s, 3H from Si(CH_3)$_2$ of minor), 0.09 (3H, s, 3H from Si-(CH_3)$_2$ of minor), 0.56−0.64 (12H, m, 6H from Si(CH_2CH$_3$)$_3$ of major and 6H from Si(CH_2CH$_3$)$_3$ of minor), 0.88 (18H, s, 9H from SiC(CH_3)$_3$ of major and 9H from SiC(CH_3)$_3$ of minor), 0.93−0.98 (18H, m, 9H from Si(CH$_2$CH_3)$_3$ of major and 9H from Si(CH$_2$CH_3)$_3$ of minor), 1.02 (3H, s, 3H from C(CH_3) of minor), 1.05 (3H, s, 3H from C(CH_3) of minor), 1.07 (3H, s, 3H from C(CH_3) of major), 1.08 (3H, s, 3H from C(CH_3) of major), 1.47 (1H, dd, $J = 4.9$, 11.8 Hz, 1H from CMe$_2$CH_2 of minor), 1.78−1.93 (3H, m, 2H from CMe$_2$CH_2 of major and 1H from CMe$_2$CH_2 of minor), 2.18−2.21 (1H, m, C*H*CH(OH) of major), 2.48 (1H, apparent q, $J = 5.7$ Hz, C*H*CH(OH) of minor), 2.76−2.82 (2H, m, CMe$_2$CH$_2$C*H* of major and minor), 3.04 (1H, d, $J = 5.3$ Hz, O*H* of major), 3.34 (1H, d, $J = 6.6$ Hz, O*H* of minor), 3.41−3.51 (3H, m, 2H from CH_2(OTES) of major and 1H from CH_2(OTES) of minor), 3.61 (1H, dd, $J = 4.8$, 9.8 Hz, 1H from CH_2(OTES) of minor), 3.65 (1H, apparent q, $J = 5.8$ Hz, C*H*(OTBDMS) of major), 3.87−3.90 (1H, m, C*H*(OTBDMS) of minor), 5.05 (1H, dd, $J = 2.1$, 10.8 Hz, 1H from CH=CH_2 of major), 5.12 (1H, dd, $J = 2.0$, 10.8 Hz, 1H from CH=CH_2 of minor), 5.24 (1H, dd, $J = 2.1$, 17.2 Hz, 1H from CH=CH_2 of major), 5.31 (1H, dd, $J = 2.0$, 17.2 Hz, 1H from CH=CH_2 of minor), 5.45 (1H, dd, $J = 4.2$, 5.2 Hz, C*H*(OH) of major), 5.63 (1H, dd, $J = 5.3$, 6.4 Hz, C*H*(OH) of minor), 5.94 (1H, dd, $J = 10.8$, 17.2 Hz, CH=CH$_2$ of major), 6.14 (1H, dd, $J = 10.8$, 17.2 Hz, CH=CH$_2$ of minor); ^{13}C NMR δ −4.3 (Si(*C*H$_3$) of major and minor), −3.7 (Si(*C*H$_3$) of major), −3.5 (Si(*C*H$_3$) of minor), 4.6 (Si(*C*H$_2$CH$_3$)$_3$ of minor), 4.7 (Si(*C*H$_2$CH$_3$)$_3$ of major), 7.1 (Si-(CH$_2$*C*H$_3$)$_3$ of minor), 7.2 (Si(CH$_2$*C*H$_3$)$_3$ of major), 18.4 (Si*C*(CH$_3$)$_3$ of minor), 18.5 (Si*C*(CH$_3$)$_3$ of major), 23.5 (CH$_3$ of major), 24.3 (CH$_3$ of minor), 26.2 (SiC(*C*H$_3$)$_3$ of minor), 26.4 (SiC(*C*H$_3$)$_3$ of major), 27.3 (*C*H$_3$ of minor), 27.5 (*C*H$_3$ of major), 37.8 (CMe$_2$-CH$_2$*C*H of major), 37.9 (CMe$_2$CH$_2$*C*H of minor), 38.9 (CMe$_2$CH$_2$ of major), 39.0 (CMe$_2$*C*H$_2$ of minor), 39.5 (*C*Me$_2$ of major), 40.3 (*C*Me$_2$ of minor), 57.9 (*C*HCH(OH) of minor), 59.5 (*C*HCH(OH) of major), 66.8 (*C*H$_2$(OTES) of major), 66.9 (*C*H$_2$(OTES) of minor), 72.5 (*C*H(OTBDMS) of major), 73.5 (*C*H(OTBDMS) of minor), 91.4 (CMe$_2$*C* of minor), 92.2 (CMe$_2$*C* of major), 102.4 (*C*H(OH) of minor), 104.1 (*C*H(OH) of major), 113.7 (CH=*C*H$_2$ of minor), 113.9 (CH=*C*H$_2$ of major), 138.2 (*C*H=CH$_2$ of major), 139.9 (*C*H=CH$_2$ of minor).

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Supporting Information Available: Additional experimental procedures and characterization data for compound **14**. Full details of the crystal structure analyses and ORTEP diagrams of compounds **8b**, **10**, **13**, *epi*-**13**, and **15**. This material is available free of charge via the Internet at http://pubs.acs.org.

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