JOC Article

Diastereoselective Dihydroxylation and Regioselective Deoxygenation of Dihydropyranones: A Novel Protocol for the Stereoselective Synthesis of C_1-C_8 and $C_{15}-C_{21}$ Subunits of (+)-Discodermolide

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Diastereoselective dihydroxylation of dihydropyranones and subsequent regioselective α-deoxygenation provides 1,3-*trans*-*β*-hydroxy-*δ*-lactones stereoselectively. This protocol has been applied for the synthesis of C_1-C_8 and $C_{15}-C_{21}$ subunits of (+)-discodermolide.

Introduction

The α-pyranone moiety is an important structural feature found in many biologically active natural products.[1] They also act as versatile synthetic intermediates in organic synthesis.[2] For the past few years, we have been developing various α-pinene-based chiral allylboranes and applying them to the stereoselective synthesis of α-pyranone-containing molecules.[3] As a part of this program we undertook a project involving the dihydroxylation of dihydropyranones since this method would lead to a simple synthesis of pyranose carbohydrate units. We also envisaged that the dihydroxylated products should provide *β*-hydroxy-*δ*-lactones upon selective deoxygenation at the position α- to the carbonyl group. With these goals in mind, we carried out a systematic examination on the diastereoselectivity in dihydroxylation and regioselectivity in the deoxygenation of dihydropyranones. Our interesting results are presented here.

Results and Discussion

For the present study, we chose various C_4- and C_5-substituted optically active dihydropyranones.[3] Accordingly α-pyrones **7a**–**l** were prepared via allylboration of aldehydes **1**–**3** with our α-pinene-based allylboranes **4a**–**d**[4] (Figure 1). As expected, all of the homoallylic alcohols **5a**–**l** were obtained in excellent de and ee, which upon treatment with acryloyl chloride and subsequent ring-closing metathesis[5] with Grubbs's second-generation ruthenium catalyst afforded the corresponding dihydropyranones **7a**–**l** (Scheme 1 and Table 1).

We observed that the dihydroxylation of the dihydropyranones **7a**–**l** under standard conditions using OsO_4/NMO is highly diastereoselective leading to the exclusive formation of the trans isomers **8a**–**l**. The relative stereochemistry is with respect to the substituent at C-5 regardless of the stereochemistry at C-4 (Scheme 1). The intermediate osmate ester formation takes place from the side opposite to the substituent at C-5 due to the favorable stereoelectronic factors.[6] In fact, a similar kind of diastereoselectivity has been reported by O'Doherty[7] and also by Nicolaou[2] during the synthesis of everninomicin. We then converted these diols into *β*-hydroxy-*δ*-lactones regioselectively. Several biologically active molecules contain a *β*-hydroxy-*δ*-lactone moiety as an important constituent[8a–c] or as a key pharmacophore.[8d]

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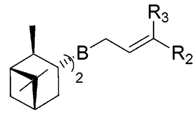
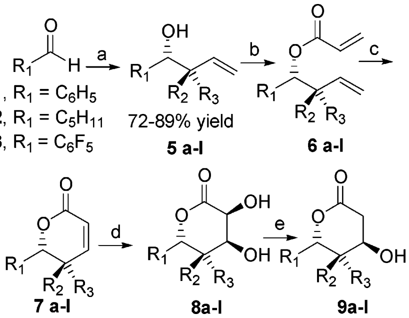


4a, R_2 = H, R_3 = H
4b, R_2 = H, R_3 = Me
4c, R_2= Me, R_3 = H
4d, R_2 = H, R_3 = OMEM

FIGURE 1. *B*-"Allyl"-diisopinocampheylboranes.

SCHEME 1[a]



[a] Key: (a) **4a**−**d**, NaOH, H_2O_2; (b) $CH_2{=}CHCOCl$, Py; (c) Grubbs II generation catalyst; (d) OsO_4, NMO; (e) (i) PhOC(S)Cl, Py; (ii) Bu_3SnH, AIBN.

Because of its proximity to the carbonyl group, α-hydroxyl group at C-3 is more acidic and hence more reactive than the *β*-hydroxyl group at C-4.[9] Treatment of diols **8a**−**l** with 1 equiv of phenylchlorothionoformate selectively transformed the α-hydroxyl group to the thionocarbonate, which upon reaction with tributyltin hydride and AIBN under Barton−McCombie conditions[10] provided 1,3-*trans*-*β*-hydroxy-*δ*-lactones **9a**−**l** regioselectively (Scheme 1 and Table 1).

We applied this methodology for the synthesis of C_1−C_8 and C_{15}−C_{21} subunits of (+)-discodermolide (**10**), a complex natural product isolated by Gunasekara and co-workers from deepwater Caribbean sponge *Discodermia dissolute*.[11] It exhibits excellent microtubule-stabilizing capabilities with an IC_{50} value of <2.5 nM toward paclitaxel (Taxol)[12]-resistant ovarian and colon cancer cell lines.[13a,b] Collaborative efforts by Smith and Horwitz[13c] reveal that a combination of discodermolide and Taxol is 20-fold more active on the Taxol-dependent cell lines. This highly encouraging biological profile makes **10** a promising candidate for the synergistic cancer treatment therapy[13c] and for clinical development as a chemotherapeutic agent for Taxol-resistant breast, ovarian, colon, and several other multidrug-resistant cancers. However, the supply of this molecule from natural sources (0.002% w/w from the frozen sponge) severely limits its potential. Laboratory synthesis seems to be the only feasible alternative to obtain useful quantities of this cytotoxic polyketide.

Several groups have reported the total synthesis of **10**,[14] and many other groups have reported the syntheses of subunits of **10**.[15,16] Our retrosynthetic strategy for the synthesis of discodermolide is outlined in Scheme 2. Examination of the subunits **11** and **12** illustrates that both of them contain 1,2-*syn*- and 1,2-*anti*-polypropionate units and a 1,3-*syn*-diol unit. The presence of this stereoregular array prompted us to develop a common synthetic strategy for both of these subunits. We envis-

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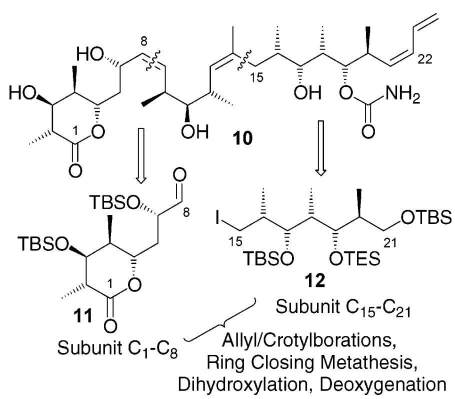
TABLE 1. Preparation of Dihydropyranones, Dihydroxylactones, and β-Hydroxylactones

dihydropyranone							dihydroxylactone		β-hydroxylactone	
no.	R_1	R_2	R_3	% yield[a]	de[b]	ee[b]	no.	% yield	no.	% yield
7a	C_6H_5	H	H	76		98	**8a**	72	**9a**	79
7b	C_6H_5	H	Me	60	>98	96	**8b**	75	**9b**	70
7c	C_6H_5	Me	H	59	>98	96	**8c**	78	**9c**	71
7d	C_6H_5	H	OMEM	60	>98	98	**8d**	86	**9d**	75
7e	C_6F_5	H	H	86		97	**8e**	80	**9e**	60
7f	C_6F_5	H	Me	77	>98	97	**8f**	80	**9f**	55
7g	C_6F_5	Me	H	84	>98	97	**8g**	85	**9g**	50
7h	C_6F_5	H	OMEM	59	>98	97	**8h**	75	**9h**	60
7i	C_5H_{11}	H	H	63		96	**8i**	81	**9i**	80
7j	C_5H_{11}	H	Me	56	>98	95	**8j**	79	**9j**	80
7k	C_5H_{11}	Me	H	67	>98	95	**8k**	88	**9k**	90
7l	C_5H_{11}	H	OMEM	59	>98	97	**8l**	87	**9l**	80

[a] Combined yields for the two steps (conversion of **5a−l** to **7a−l**). [b] de and ee on the basis of homoallylic alcohol **5**.

SCHEME 2

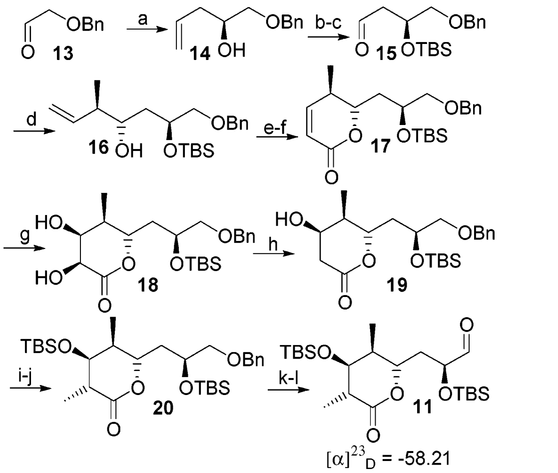


aged that diastereoselective 1,3-trans dihydroxylation of dihydropyranones that can be readily prepared via a tandem asymmetric "allyl"-boration and ring-closing metathesis protocol, followed by a regioselective deoxygenation of the more reactive α-hydroxyl group under Barton−McCombie conditions,[10] should furnish the β-hydroxy-δ-lactone with a 1,3-syn configuration. α-Methylation of β-hydroxy-δ-lactone should take place in a trans orientation to provide the 1,2-*syn*-polypropionate moiety.

The synthesis of subunit C_1−C_8 (**11**) was initiated with the allylboration of benzyloxyacetaldehyde **13** with (−)-diisopinocampheylallylborane.[4a] Silyl protection of the resulting homoallylic alcohol **14** and ozonolysis of the olefin afforded the aldehyde **15**. Crotylboration of **15** with (*E*)-*B*-crotyldiisopinocampheylborane[4b,c] furnished the homoallylic alcohol **16**.

Acryloylation, followed by ring-closing metathesis using Grubbs's second-generation ruthenium catalyst,[5] provided the dihydropyranone derivative **17**. Dihydroxylation under standard conditions with OsO_4 and NMO proved to be highly diastereoselective, and the diol **18** was obtained as a single diastereomer. Selective conversion of the more reactive α-hydroxy group to the phenylchlorothionoformate ester, followed by reduction with Bu_3SnH in the presence of AIBN, led to the regioselective deoxygenation of the α-hydroxy group and yielded the β-hydroxy-δ-lactone **19**. The relative stereochemistry in **19** was confirmed by single-crystal X-ray analysis. The hydroxy-directed methylation at the α- position provided the anti product,[17] and protection of the alcohol as its silyl ether using TBS triflate and 2,6-lutidine afforded

SCHEME 3[a]



[a] Key: (a) (−)-Ipc_2BAll; (b) TBSCl, Im, 80% overall; (c) O_3, Me_2S, 76%; (d) (*E*)-2-butene, *n*-BuLi, KO^tBu, (+)-Ipc_2BOMe, 82%; (e) CH_2=CHCOCl, NEt_3, 85%; (f) Grubbs' II generation catalyst, 96%; (g) OsO_4, NMO, 87%; (h) (i) PhOC(S)Cl, Py; (ii) Bu_3SnH, AIBN, 93%; (i) LDA, HMPA, MeI, 78%; (j) TBSOTf, 2,6-lutidine, 92%; (k) H_2, Pd, 90%; (l) DMP, 93%.

the lactone **20**. Cleavage of the benzyl group via hydrogenolysis and oxidation of the resulting primary alcohol using Dess−Martin periodinane[18] provided the required subunit **11** (Scheme 3).

The synthesis of C_{15}−C_{21} segment **12** began with the protection of commercially available hydroxy methyl ester **21** as its silyl ether, followed by the reduction of the ester to the alcohol **22**. Oxidation of the alcohol to the corresponding aldehyde and subsequent crotylboration with *B*-(*Z*)-crotyldiisopinocampheylborane furnished the homoallylic alcohol **23** in >90% diastereoselectivity. Acryloylation and ring-closing metathesis afforded the dihydropyranone **24** in good yield. As expected, dihydroxylation using OsO_4 and NMO provided the dihydroxylactone **25** as a single diastereomer. Regioselective α-deoxygenation under Barton−McCombie conditions yielded the β-hydroxy lactone **26**. Treatment with LDA

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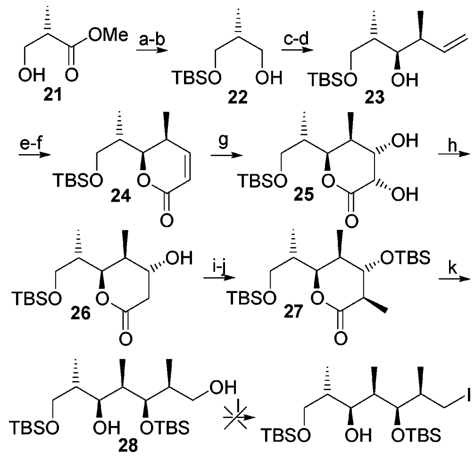
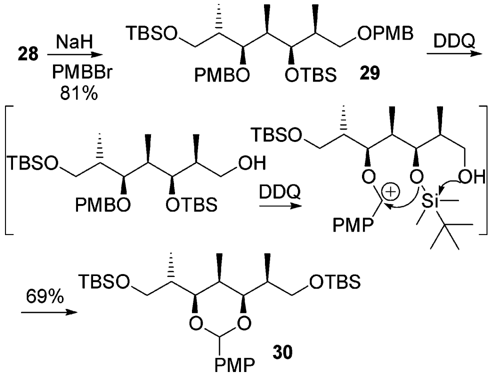
(19) Contribution no. 34 from the Herbert C. Brown Center for Borane Research.

SCHEME 4[a]



[a] Key: (a) TBSCl, Im, 90%; (b) $BH_3{\cdot}Me_2S$, MeOH, NEt_3, 78%; (c) DMP, 87%; (d) (*Z*)-2-butene, *n*-BuLi, KO^tBu, (+)-Ipc_2BOMe, 75%; (e) $CH_2{=}CHCOCl$, DIEA, 79%; (f) Grubbs' II generation catalyst, 86%; (g) OsO_4, NMO, 72%; (h) (i) PhOC(S)Cl, Py; (ii) Bu_3SnH, AIBN, 68%; (i) LDA, HMPA, MeI, 75%; (j) TBSOTf, 2,6-di-*tert*-butyl-4-methylpyridine, 78%; (k) $LiBH_4$, 76%; (l) I_2, PPh_3, imidazole.

SCHEME 5

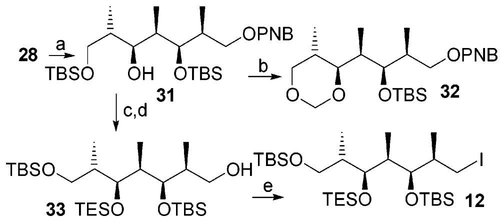


and MeI,[17] followed by silylation of the resulting α-methylated alcohol with TBS triflate and 2,6-di-*tert*-butyl-4-methylpyridine, afforded **27**. Utilization of conventional amines such as Hunig's base and 2,6-lutidine resulted in the *β*-elimination to afford the corresponding α-methylated dihydropyranone. After establishing all of the necessary chiral centers by reagent- and substrate-controlled reactions, the lactone **27** was reduced with $LiBH_4$ to the acyclic diol **28** in good yield. Our initial strategy was to selectively iodinate the primary alcohol in **28** and then protect the secondary alcohol as the PMB ether. However, the conversion of **28** to the primary iodide posed some unexpected problems. Treatment of **28** with I_2 and PPh_3 in the presence of imidazole resulted in a complex mixture of products as indicated by TLC (Scheme 4).

Conversion of the diol **28** as its di-PMB ether **29** followed by attempts to selectively deprotect the primary PMB ether using 1.2 equiv of DDQ did not materialize and resulted in the formation of 1,3-dioxane unit **30** (Scheme 5).

Selectively converting the primary alcohol in **28** to the *p*-nitrobenzoate ester **31** and protection of the secondary alcohol as its PMB ether under different conditions also proved futile. This compelled us to change the protecting group to MEM ether (Scheme 6). However, treatment of the hydroxy ester **31** with MEM chloride and Hunig's base resulted in the deprotection of the primary TBS group and subsequent *trans*-acetalization furnished the 1,3-dioxane unit **32**. Finally, protection of the secondary alcohol in **31** as its triethylsilyl ether, which can be selectively deprotected in the presence of a secondary TBS group at C_{17} at a later stage of the synthesis, followed by the hydrolysis of PNB group under basic conditions led to the formation of the primary alcohol **33**. Iodination of **33** with I_2 and PPh_3 furnished the required subunit **12** (Scheme 6).

SCHEME 6[a]



[a] Key: (a) PNBCl, Py, DMAP, 93%; (b) MEMCl, DIPEA, 56%; (c) TESOTf, 2,6-lutidine, 97%; (d) K_2CO_3, MeOH, 83%; (e) I_2, PPh_3, imidazole, 72%.

Conclusion

In summary, we have developed a novel protocol for the preparation of *trans*-*β*-hydroxy-*δ*-lactones via diastereoselective dihydroxylation and regioselective deoxygenation of dihydropyranones. Application of this methodology has been demonstrated by the synthesis two subunits of potent anti cancer agent (+)-discodermolide. The key steps in the synthesis involve the utilization of inexpensive α-pinene-based chiral "allyl"-borane reagents to introduce the initial chirality and ring-closing metathesis reaction to obtain α-pyranones. We believe that this protocol will find further applications for the synthesis of various other complex molecules.

Experimental Section

Preparation of (6*S*)-6-Phenyl-5,6-dihydropyran-2-one, $C_{11}H_{10}O_2$, 7a. Acrylate **6a** (8.0 g, 19.1 mmol) was refluxed in toluene (200.0 mL) at 100 °C. Grubbs' second-generation catalyst (0.81 g, 0.95 mmol) was added and the solution refluxed for 3 h. After completion of the reaction (TLC), solvent was evaporated under vacuum and the crude product was purified by column chromatography (silica gel, 3:2, hexane/ethyl acetate) to obtain 7.2 g (96%) of the lactenone **7a**: ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (ppm) 7.26−7.40 (m, 5H), 6.95−6.99 (m, 1H), 6.12 (d, J = 9.3 Hz, 1H), 5.45 (dd, J = 6.4, 8.9 Hz, 1H), 2.62−2.64 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) *δ* (ppm) 164.2, 145.4, 138.5, 128.7, 128.6, 126.1, 121.6, 79.3, 31.8.

(5*S*,6*R*)-5-Methyl-6-phenyl-5,6-dihydropyran-2-one, $C_{12}H_{12}O_2$, 7b. Same procedure as for **7a**: ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (ppm) 7.30−7.42 (m, 5H), 7.10 (dd, J = 6.2, 9.7 Hz, 1H), 6.08 (d, J = 9.6 Hz, 1H), 5.59 (d, J = 3.4 Hz, 1H), 2.59−2.69 (m, 1H), 0.81 (d, J = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) *δ* (ppm) 164.5, 151.8, 137.0, 128.5, 128.0, 125.6, 120.0, 81.0, 34.8, 11.8.

(5*R*,6*R*)-5-Methyl-6-phenyl-5,6-dihydropyran-2-one, $C_{12}H_{12}O_2$, 7c. Same procedure as for **7a**: ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (ppm) 7.20−7.33 (m, 5H), 6.70 (dd, J = 2.1, 9.7 Hz, 1H), 6.01 (dd, J = 2.5, 9.8 Hz, 1H), 4.91 (d, J = 10.6 Hz, 1H), 2.71−2.80 (m, 1H), 0.94 (d, J = 7.3 Hz, 3H); ^{13}C NMR (75.5

MHz, $CDCl_3$) δ (ppm) 164.0, 151.5, 137.4, 129.0, 128.6, 127.5, 120.3, 86.0, 35.2, 15.8.

(5*S*,6*S*)-5-Methoxyethoxymethoxy-6-phenyl-5,6-dihydropyran-2-one, $C_{15}H_{18}O_5$, 7d. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.32−7.46 (m, 5H), 7.12 (dd, *J* = 5.8, 9.7 Hz, 1H), 6.24 (d, *J* = 9.7 Hz, 1H), 5.49 (d, *J* = 2.5 Hz, 1H), 4.49 (d, *J* = 7.2 Hz, 1H), 4.27 (dd, *J* = 2.8, 5.7 Hz, 1H), 4.09−4.18 (m, 1H), 3.46−3.51 (m, 1H), 3.26−3.38 (m, 5H), 3.10−3.16 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 143.3, 128.5, 128.3, 126.8, 123.5, 94.8, 81.2, 71.5, 67.6, 67.0, 59.0.

(6*S*)-6-Pentyl-5,6-dihydropyran-2-one, $C_{10}H_{16}O_2$, 7e. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.83 (ddd, *J* = 3.1, 5.5, 9.7 Hz, 1H), 5.93 (ddd, *J* = 1.2, 2.4, 9.7 Hz, 1H), 4.31−4.41 (m, 1H), 2.24−2.31 (m, 2H), 1.20−1.80 (m, 8H), 0.83 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 164.6, 145.3, 121.3, 78.0, 34.8, 31.5, 29.4, 24.5, 22.5, 14.0.

(5*R*,6*S*)-5-Methyl-6-pentyl-5,6-dihydropyran-2-one, $C_{11}H_{18}O_2$, 7g. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.60 (dd, *J* = 2.6, 9.7 Hz, 1H), 5.89 (dd, *J* = 2.4, 9.7 Hz, 1H), 3.98−4.08 (m, 1H), 2.38−2.48 (m, 1H), 1.21−1.79 (m, 8H), 1.10 (d, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 164.4, 151.7, 120.0, 83.7, 33.1, 32.7, 31.6, 25.7, 24.4, 22.5, 16.5, 14.0.

(5*S*,6*S*)-5-Methoxyethoxymethoxy-6-pentyl-5,6-dihydropyran-2-one, $C_{14}H_{24}O_5$, 7h. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.04 (dd, *J* = 5.4, 9.7 Hz, 1H), 6.09 (d, *J* = 9.7 Hz, 1H), 4.79 (d, *J* = 7.1 Hz, 1H), 4.31−4.35 (m, 1H), 4.00−4.02 (m, 1H), 3.50−3.72 (m, 4H), 3.36 (s, 3H), 1.30−1.91 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 163.6, 143.8, 123.3, 95.2, 80.2, 71.6, 67.4, 67.2, 59.1, 31.6, 30.0, 24.8, 22.5, 14.0.

(6*R*)-6-Pentafluorophenyl-5,6-dihydropyran-2-one, $C_{11}H_5O_2F_5$, 7i. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.99−7.05 (m, 1H), 6.17 (d, *J* = 9.1 Hz, 1H), 5.81 (dd, *J* = 3.8, 13.0 Hz, 1H), 3.01−3.11 (m, 1H), 2.47−2.57 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 162.7, 144.8, 121.4, 69.7, 28.6; $[\alpha]^{25}$ = +118.6 (*c* 1.25, $CHCl_3$); EI-MS *m/z* 264 (M^+), 195, 194, 117, 68 [$CH_2CH{=}CHCO^+$, 100]; CI-MS *m/z* 265 [$(M + H)^+$, 100], 81; HRMS-CI 264.0207 (actual), 264.0210 (calcd).

(5*S*,6*R*)-5-Methyl-6-pentafluorophenyl-5,6-dihydropyran-2-one, $C_{12}H_7O_2F_5$, 7j. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.06 (dd, *J* = 6.1, 9.9 Hz, 1H), 6.10 (d, *J* = 8.8 Hz, 1H), 5.93 (d, *J* = 4.0 Hz, 1H), 2.61−2.68 (m, 1H), 1.13 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 162.7, 150.8, 119.9, 74.5, 33.9, 12.7; EI-MS *m/z* 195, 82 [$C_5H_6O^+$, 100], 54; CI-MS *m/z* 279 [$(M + H)^+$, 100]; HRMS-CI 279.0435 (actual), 279.0445 (calcd).

(5*R*,6*R*)-5-Methyl-6-pentafluorophenyl-5,6-dihydropyran-2-one, $C_{12}H_7O_2F_5$, 7k. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.79 (dd, *J* = 1.9, 9.8 Hz, 1H), 6.12 (dd, *J* = 2.6, 9.8 Hz, 1H), 5.40 (d, *J* = 11.8 Hz, 1H), 3.12−3.24 (m, 1H), 1.07 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 162.6, 151.2, 120.3, 75.5, 32.7, 15.3; EI-MS *m/z* 195, 82 [$C_5H_6O^+$, 100], 54; CI-MS *m/z* 279 [$(M + H)^+$, 100]; HRMS-CI 279.0435 (actual), 279.0445 (calcd).

(5*S*,6*S*)-5-Methoxyethoxymethoxy-6-pentafluorophenyl-5,6-dihydropyran-2-one, $C_{15}H_{13}O_5$ F_5, 7l. Same procedure as for **7a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.16 (dd, *J* = 5.5, 9.9 Hz, 1H), 6.27 (d, *J* = 9.9 Hz, 1H), 5.90 (d, *J* = 3.5 Hz, 1H), 4.72 (d, *J* = 7.2 Hz, 1H), 4.52 (d, *J* = 7.2 Hz, 1H), 4.26 (dd, *J* = 3.6, 5.4 Hz, 1H), 3.60−3.66 (m, 1H), 3.42−3.46 (m, 2H), 3.52 (s, 3H), 3.31−3.38 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 161.4, 142.9, 123.2, 94.9, 74.1, 71.3, 67.3, 66.7, 59.0; EI-MS *m/z* 323 ($M - CH_2OCH_3$), 263, 195, 89, 59 [$CH_3OCH_2CH_2^+$, 100]; CI-MS *m/z* 369 [$(M + H)^+$, 100], 281, 263, 195, 172, 165, 105; HRMS-CI 369.0753 (actual), 369.0761 (calcd).

Preparation of (3*S*,4*S*,6*R*)-3,4-Dihydroxy-6-phenyltetrahydropyran-2-one, $C_{11}H_{12}O_4$, 8a. NMO (1.4 g, 11.5 mmol) was added to the dihydropyranone **7a** (3.0 g, 7.7 mmol) dissolved in acetone/water (4:1, 15 mL) at 0 °C. OsO_4 (156 mg, 0.6 mmol) was added to the above solution and stirred for 6 h at room temperature, the product was extracted with Et_2O (3 × 20 mL) and washed, and the organic layers were concentrated under aspirator vacuum. The crude product was purified by column chromatography (silica gel, hexane/ethyl acetate (1:4)) to obtain 2.8 g (87%) of **8a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.35−7.40 (m, 5H), 5.81 (dd, *J* = 3.4, 12.0 Hz, 1H), 4.45 (m, 1H), 4.26 (d, *J* = 2.4 Hz, 1H), 3.70 (bs, 1H), 3.10 (bs, 1H), 2.49 (ddd, *J* = 3.5, 4.5, 14.9 Hz, 1H), 2.18 (t, *J* = 13.4, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.1, 138.7, 128.8, 128.7, 125.8, 79.4, 70.5, 66.3, 36.3; CI-MS 209 $(M + H)^+$, 191 [$(M + H - H_2O)^+$, 100], 173, 145; HRMS-CI 209.0817 (actual), 209.0814 (calcd).

(3*S*,4*S*,5*S*,6*R*)-3,4-Dihydroxy-5-methyl-6-phenyltetrahydropyran-2-one, $C_{12}H_{14}O_4$, 8b. Same procedure as for **8a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.28−7.41 (m, 5H), 6.04 (d, *J* = 3.2 Hz, 1H), 4.39 (d, *J* = 3.1 Hz, 1H), 4.31 (t, *J* = 3.5 Hz, 1H), 2.53−2.63 (m, 1H), 3.66 (bs, 1H), 3.31 (bs, 1H), 0.81 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.7, 137.1, 128.5, 127.8, 125.1, 80.9, 71.4, 67.6, 39.1, 10.3; EI-MS *m/z* 222 (M^+), 176, 147, 134, 118, 107 (100), 91, 79, 70, 51; CI-MS *m/z* 223 [$(M + H)^+$, 100], 187, 119; HRMS-CI 222.0887 (actual), 222.0892 (calcd).

(3*S*,4*S*,5*R*,6*R*)-3,4-Dihydroxy-5-methyl-6-phenyltetrahydropyran-2-one, $C_{12}H_{14}O_4$, 8c. Same procedure as for **8a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.29−7.40 (m, 5H), 5.35 (d, *J* = 10.8 Hz, 1H), 4.32−4.33 (m, 1H), 4.21 (bs, 1H), 3.64 (bs, 1H), 2.94 (bs, 1H), 2.24−2.35 (m, 1H), 0.99 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.1, 137.4, 129.1, 128.7, 127.4, 85.4, 71.4, 71.0, 39.0, 13.6; EI-MS *m/z* 222 (M^+), 118 [$C_9H_{10}^+$, 100], 107, 91, 77; CI-MS *m/z* 223 $(M + H)^+$, 205 $(M + H - H_2O)^+$, 187 [$(M + H - 2H_2O)^+$, 100], 159, 119; HRMS-CI 222.0889 (actual), 222.0892 (calcd).

(3*S*,4*R*,5*S*,6*S*)-3,4-Dihydroxy-5-methoxyethoxymethoxy-6-phenyltetrahydropyran-2-one, $C_{15}H_{20}O_7$, 8d. Same procedure as for **8a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.30−7.36 (m, 5H), 5.89 (bs, 1H), 4.61 (d, *J* = 3.0 Hz, 1H), 4.47−4.50 (m, 2H), 4.22−4.24 (m, 1H), 4.10 (d, *J* = 7.1 Hz, 1H), 3.60 (bs, 1H), 3.33−3.42 (m, 1H), 3.26−3.31 (m, 6H), 2.95−3.01 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.2, 135.5, 128.4, 128.3, 126.5, 95.2, 80.9, 75.5, 71.5, 69.1, 68.0, 67.3, 59.0.

(3*S*,4*S*,6*S*)-3,4-Dihydroxy-6-pentyltetrahydropyran-2-one, $C_{10}H_{18}0_4$, 8e. Same procedure as for **8a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.73−4.80 (m, 1H), 4.33 (m, 1H), 4.10 (m, 1H), 3.86 (bs, 1H), 3.20 (bs, 1H), 2.21 (dt, *J* = 14.6, 3.5 Hz, 1H), 1.30−1.86 (m, 9H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.4, 78.4, 70.6, 66.1, 35.6, 34.0, 31.5, 24.5, 22.5, 14.0; EI-MS *m/z* 139, 60 (100%), 57; CI-MS 203 [$(M + H)^+$, 100], 157, 113; HRMS-CI 203.1285 (actual), 203.1283 (calcd).

(3*S*,4*S*,5*S*,6*S*)-3,4-Dihydroxy-5-methyl-6-pentyltetrahydropyran-2-one, $C_{11}H_{20}O_4$, 8f. Same procedure as for **8a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.78−4.80 (m, 1H), 4.24 (d, *J* = 3.4 Hz, 1H), 4.14 (t, *J* = 3.4 Hz, 1H), 3.50 (bs, 1H), 2.20−2.25 (m, 1H), 1.28−1.72 (m, 8H), 1.00 (d, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 6.3 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.9, 80.6, 71.6, 67.6, 36.4, 31.6(2 carbons), 25.1, 22.5, 14.0, 10.0; EI-MS *m/z* 199 $(M - OH)^+$, 60 [$(C_2H_4O_2)^+$, 100], 55; CI-MS *m/z* 217 [$(M + H)^+$, 100], 199 $(M + H - H_2O)^+$, 181, 153; HRMS-CI 217.1440 (actual), 217.1440 (calcd).

(3*S*,4*S*,5*R*,6*S*)-3,4-Dihydroxy-5-methyl-6-pentyltetrahydropyran-2-one, $C_{11}H_{20}O_4$, 8g. Same procedure as for **8a**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.45 (ddd, *J* = 2.8, 7.8, 10.5 Hz, 1H), 4.10 (d, *J* = 3.0 Hz, 1H), 4.06 (m, 1H), 3.52 (bs, 1H), 2.74 (bs, 1H), 1.93−2.03 (m, 1H), 1.70−1.80 (m, 1H), 1.50−1.63 (m, 2H), 1.25−1.43 (m, 5H), 1.14 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.3, 83.5, 71.1, 71.1, 36.7, 33.0, 31.6, 24.1, 22.6, 14.2, 14.0; EI-MS *m/z* 160, 60 [$(C_2H_4O_2)^+$, 100], 55; CI-MS *m/z* 217 [$(M + H)^+$, 100], 199 $(M + H - H_2O)^+$, 181, 153; HRMS-CI 217.1445 (actual), 217.1440 (calcd).

(3*S*,4*R*,5*S*,6*S*)-3,4-Dihydroxy-5-methoxyethoxymethoxy-6-pentyltetrahydropyran-2-one, $C_{14}H_{26}O_7$, 8h. Same procedure as for **8a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.86 (d, J = 7.1 Hz, 1H), 4.77 (d, J = 7.1 Hz, 1H), 4.70−4.75 (m, 1H), 4.42−4.44 (m, 2H), 3.93−3.96 (m, 1H), 3.66−3.75 (m, 3H), 3.56 (t, J = 4.6 Hz, 2H), 3.39 (s, 3H), 3.33 (bs, 1H), 1.22−1.91 (m, 8H), 0.89 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.2, 96.2, 80.2, 75.4, 71.6, 68.7, 68.0 (2 carbons), 59.1, 31.6, 30.3, 25.0, 22.5, 14.0; EI-MS *m*/*z* 200, 89, 59 [$(CH_3OCH_2CH_2)^+$, 100]; CI-MS *m*/*z* 307 [$(M + H)^+$, 100], 231, 89; HRMS-CI 307.1753 (actual), 307.1757 (calcd).

(3*S*,4*S*,6*R*)-3,4-Dihydroxy-6-pentafluorophenyltetrahydropyran-2-one, $C_{11}H_7O_4F_5$, 8i. Same procedure as for **8a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.16 (dd, J = 4.6, 11.9 Hz, 1H), 4.47−4.48 (m, 1H), 4.32 (d, J = 2.7 Hz, 1H), 3.51 (bs, 1H), 2.87 (bs, 1H), 2.47−2.52 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 172.6, 70.4, 69.8, 66.2, 33.0; ^{19}F NMR (280 MHz, $CDCl_3$) δ (ppm) −79.9, −89.2, −98.1; $[\alpha]^{25}$ = −5.6 (*c* 0.5, CH_3OH); EI-MS *m*/*z* 223; CI-MS *m*/*z* 299 [$(M + H)^+$, 100]; HRMS-CI 299.0342 (actual), 299.0343 (calcd).

(3*S*,4*S*,5*S*,6*R*)-3,4-Dihydroxy-5-methyl-6-pentafluorophenyltetrahydropyran-2-one, $C_{12}H_9O_4F_5$, 8j. Same procedure as for **8a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.33 (d, J = 3.8 Hz, 1H), 4.45 (d, J = 3.0 Hz, 1H), 4.32 (t, J = 3.4 Hz, 1H), 2.55 (dqu, J = 3.8, 15.1 Hz, 1H), 3.40 (bs, 1H), 3.13 (bs, 1H), 1.12 (d, J = 7.6 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 172.8, 74.6, 71.1, 67.4, 38.1, 11.0; EI-MS *m*/*z* 312 (M^+), 197, 181, 76, 60 (100), 43; CI-MS *m*/*z* 313 [$(M + H)^+$, 100], 267, 105; HRMS-CI 312.0421 (actual), 312.0421 (calcd).

(3*S*,4*S*,5*R*,6*R*)-3,4-Dihydroxy-5-methyl-6-pentafluorophenyltetrahydropyran-2-one, $C_{12}H_9O_4F_5$, 8k. Same procedure as for **8a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.77 (d, J = 11.3 Hz, 1H), 4.33 (d, J = 2.7 Hz, 1H), 4.20−4.24 (m, 1H), 3.50 (bs, 1H), 2.90 (bs, 1H); 2.53−2.64 (m, 1H), 1.09 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 172.7, 75.0, 71.1, 70.6, 36.5, 13.2; EI-MS *m*/*z* 312 (M^+), 197, 181, 76, 60 (100%), 43; CI-MS *m*/*z* 313 [$(M + H)^+$, 100], 267, 105; HRMS-CI 312.0421 (actual), 312.0421 (calcd).

(3*S*,4*R*,5*S*,6*S*)-3,4-Dihydroxy-5-methoxyethoxymethoxy-6-pentafluorophenyl-tetrahydropyran-2-one, $C_{15}H_{15}O_7F_5$, 8l. Same procedure as for **8a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.22 (d, J = 3.2 Hz, 1H), 4.70 (d, J = 7.1 Hz, 2H), 4.55−4.56 (m, 1H), 4.47 (d, J = 7.2 Hz, 1H), 4.19−4.22 (m, 1H), 3.94 (bs, 1H), 3.78 (bs, 1H), 3.52−3.59 (m, 1H), 3.38−3.43 (m, 1H), 3.33 (s, 3H), 3.22−3.29 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 172.4, 95.5, 75.0, 74.5, 71.3, 69.4, 67.9, 67.8, 59.1.

Preparation of (4*S*, 6*R*)-4-Hydroxy-6-phenyltetrahydropyran-2-one, $C_{11}H_{12}O_3$, 9a. Diol **8a** (2.0 g, 4.7 mmol) was dissolved in 10.0 mL of CH_2Cl_2 and cooled to 0 °C. Phenylchlorothionoformate (0.75 mL, 5.4 mmol) was added followed by the addition of pyridine (0.76 mL, 9.4 mmol). After completion of the reaction as indicated by TLC, the reaction mixture was worked up with ether and water. The crude thionoformate ester was dissolved in benzene (50.0 mL) and refluxed at 85 °C. Tributyltin hydride (3.2 mL, 11.8 mmol) was added followed by the addition of AIBN (77 mg, 0.47 mmol) and the mixture refluxed for 5 h. The reaction mixture was concentrated under vacuum and purified by column chromatography (silica gel, hexanes/ethyl acetate, 2:3) to obtain 1.8 g (93%) of pure β-hydroxylactone **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.33−7.40 (m, 5H), 5.76 (dd, J = 3.0, 11.0 Hz, 1H), 4.45 (qu, J = 3.9 Hz, 1H), 2.86 (dd, J = 4.9, 17.8 Hz, 1H), 2.74 (ddd, J = 1.6, 3.6, 17.7 Hz, 1H), 2.01−2.29 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 170.1, 139.3, 128.7, 128.4, 125.9, 77.1, 62.8, 38.7, 38.4.

(4*R*,5*S*,6*R*)-4-Hydroxy-5-methyl-6-phenyltetrahydropyran-2-one, $C_{12}H_{14}O_3$, 9b. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26−7.38 (m, 5H), 5.92 (m, 1H), 4.15−4.19 (m, 1H), 3.10 (bs, 1H), 2.92 (dd, J = 5.2, 18.6 Hz, 1H), 2.65−2.72 (m, 1H), 2.18−2.25 (m, 1H), 0.71 (d, J = 7.4 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 170.9, 137.7, 128.4, 127.7, 125.5, 78.9, 68.2, 40.0, 35.7, 10.3; EI-MS *m*/*z* 206 (M^+), 188 ($M - H_2O$), 178, 164, 117, 107 [$(C_6H_5CH_2O^+$, 100], 79, 58; CI-MS *m*/*z* 207 $(M + H)^+$, 189 [$(M + H - H_2O)^+$, 100], 171, 119; HRMS-CI 206.0950 (actual), 206.0943 (calcd).

(4*R*,5*R*,6*R*)-4-Hydroxy-5-methyl-6-phenyltetrahydropyran-2-one, $C_{12}H_{14}O_3$, 9c. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.04−7.12 (m, 5H), 5.06 (d, J = 10.7 Hz, 1H), 4.82 (bs, 1H), 3.81 (bs, 1H), 2.54−2.55 (m, 2H), 1.73−1.82 (m, 1H), 0.60 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 170.2, 138.6, 128.4, 128.3, 127.2, 83.0, 66.5, 39.8, 39.0, 13.4; EI-MS *m*/*z* 206 (M^+), 188 ($M - H_2O$), 178, 164, 117, 107 [$(C_6H_5CH_2O^+$, 100], 79, 58; CI-MS *m*/*z* 207 $(M + H)^+$, 189 [$(M + H - H_2O)^+$, 100], 171, 119; HRMS-CI 206.0950 (actual), 206.0943 (calcd).

(4*S*,6*S*)-4-Hydroxy-6-pentyltetrahydropyran-2-one, $C_{10}H_{18}O_3$, 9e. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.63−4.72 (m, 1H), 4.31−4.37 (m, 1H), 2.98 (bs, 1H), 2.68 (dd, J = 17.9, 4.8 Hz, 1H), 2.59 (ddd, J = 17.9, 3.8, 1.4 Hz, 1H), 1.92−1.99 (m, 1H), 1.23−1.73 (m, 9H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 171.4, 76.3, 62.5, 38.6, 35.8, 35.5, 31.6, 24.6, 22.5, 14.0; EI-MS *m*/*z* 168 $(M - H_2O)^+$, 115 (100), 97, 73, 55; CI-MS *m*/*z* 187 [$(M + H)^+$, 100], 169 $(M + H - H_2O)^+$, 127; HRMS-CI 187.1335 (actual), 187.1334 (calcd).

(4*R*,5*S*,6*S*)-4-Hydroxy-5-methyl-6-pentyltetrahydropyran-2-one, $C_{11}H_{20}0_3$, 9f. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.70 (ddd, J = 2.7, 4.7, 8.0 Hz, 1H), 4.01−4.05 (m, 1H), 2.78 (dd, J = 5.4, 18.3 Hz, 1H), 2.53 (dd, J = 3.1, 18.3 Hz, 1H), 2.52 (bs, 1H), 1.91−1.96 (m, 1H), 1.24−1.78 (m, 8H), 0.92 (d, J = 7.3 Hz, 3H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 171.0, 78.3, 68.6, 37.3, 35.8, 31.8, 31.6, 25.2, 22.6, 14.0, 10.3; EI-MS *m*/*z* 182 $(M - H_2O)^+$, 158, 129, 111, 87, 82, 71, 58 [$(C_4H_{10})^+$, 100]; CI-MS *m*/*z* 201 [$(M + H)^+$, 100], 183 $(M + H - H_2O)^+$, 141; HRMS-CI 201.1492 (actual), 201.1491 (calcd).

(4*R*,5*R*,6*S*)-4-Hydroxy-5-methyl-6-pentyltetrahydropyran-2-one, $C_{11}H_{20}O_3$, 9g. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.38−4.44 (m, 1H), 4.05 (m, 1H), 2.59−2.74 (m, 3H), 1.65−1.79 (m, 2H), 1.48−1.59 (m, 2H), 1.24−1.41 (m, 5H), 1.05 (d, J = 6.9 Hz, 3H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 170.9, 80.8, 67.7, 39.4, 36.8, 33.1, 31.7, 24.0, 22.5, 14.1, 13.7; EI-MS *m*/*z* 182 $(M - H_2O)^+$, 158, 129, 111, 87, 82, 71, 58 [$(C_4H_{10})^+$, 100]; CI-MS *m*/*z* 201 [$(M + H)^+$, 100], 183 $(M + H - H_2O)^+$, 141; HRMS-CI 201.1492 (actual), 201.1491 (calcd).

(4*R*,5*S*,6*S*)-4-Hydroxy-5-methoxyethoxymethoxy-6-pentyltetrahydropyran-2-one, $C_{14}H_{26}O_6$, 9h. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.83 (d, J = 7.1 Hz, 1H), 4.74 (d, J = 7.1 Hz, 1H), 4.54 (ddd, J = 2.4, 4.7, 7.6 Hz, 1H), 4.19−4.25 (m, 1H), 3.81 (ddd, J = 3.2, 6.8, 9.9 Hz, 1H), 3.46−3.69 (m, 5H), 3.39 (s, 3H), 2.90 (dd, J = 5.4, 17.2 Hz, 1H), 2.56 (dd, J = 5.8, 17.1 Hz, 1H), 1.22−1.82 (m, 8H), 0.89 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 170.5, 96.1, 78.2, 77.6, 71.6, 67.5, 66.9, 59.1, 35.6, 31.6, 30.3, 25.0, 22.5, 14.0.

(4*S*,6*R*)-4-Hydroxy-6-pentafluorophenyltetrahydropyran-2-one, $C_{11}H_7O_3F_5$, 9i. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ(ppm) 6.16 (dd, J = 4.8, 12.0 Hz, 1H), 4.47−4.48 (m, 1H), 2.80−2.85 (m, 2H), 2.33−2.42 (m, 1H), 2.23−2.44 (m, 1H), 2.1 (bs, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 172.6, 70.4, 69.8, 66.2, 33.0; ^{19}F NMR (280 MHz, $CDCl_3$) δ (ppm) −79.87, −89.20, −98.15; $[\alpha]^{25}$ = −5.6 (*c* 0.5, CH_3OH); EI-MS *m*/*z* 223; CI-MS *m*/*z* 283 $(M + H)^+$, 265 [$(M + H - H_2O)^+$, 100].

(4*R*,5*S*,6*R*)-4-Hydroxy-5-methyl-6-pentafluorophenyltetrahydropyran-2-one, $C_{12}H_9O_3F_5$, 9j. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.19 (d, J = 4.2 Hz, 1H), 4.11 (q, J = 4.9 Hz, 1H), 3.00 (dd, J = 5.0, 18.5 Hz, 1H), 2.66 (dd, J = 4.4, 18.7 Hz, 2H), 2.21−2.27 (m, 1H), 1.01 (d, J = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 168.8, 73.3, 67.5, 38.8, 36.3, 11.2.

(4*R*,5*R*,6*R*)-4-Hydroxy-5-methyl-6-pentafluorophenyltetrahydropyran-2-one, $C_{12}H_9O_3F_5$, 9k. Same procedure as for **9a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.79 (d, J = 11.3 Hz, 1H), 4.21−4.24 (m, 1H), 2.86−2.88 (m, 2H), 2.37−2.48 (m, 1H), 2.12 (d, J = 3.0 Hz, 1H), 1.00 (d, J = 6.9 Hz, 3H).

Preparation of (*S*)-1-Benzyloxypent-4-en-2-ol, $C_{12}H_{16}O_2$, 14. Aldehyde **13** (50.0 g, 333.3 mmol) dissolved in 200 mL of CH_2Cl_2 was added to a stirred solution of (−)-*B*-allyldiisopinocampheylborane (Ipc_2BAll) (800 mL of 0.5 M solution in Et_2O−pentane) at −100 °C and maintained at that temperature for 2 h. The reaction was followed by ^{11}B NMR spectroscopy (δ 56). Upon completion, the mixture was oxidized with 160.0 mL of 3.0 M NaOH and 160.0 mL of 30% H_2O_2, stirred for 4 h at room temperature, and extracted with Et_2O. Alcohol **14** and isopinocampheol (byproduct) have a similar R_f, and hence, it was not possible to purify the alcohol by column chromatography. (The alcohol was injected on the HPLC and the ee was found to be 96%.)

Preparation of (2*S*)-1-Benzyloxy-2-*tert*-butyldimethylsilyloxypent-4-ene, $C_{18}H_{30}O_2Si$, TBS-14. Crude alcohol **14** (30.0 g, 156.2 mmol) was dissolved in 1000 mL of dimethylformamide. *tert*-Butyldimethylsilyl chloride (117.2 g, 781.2 mmol) and imidazole (79.7 g, 1171.9 mmol) were added at 25 °C, and the mixture was stirred for 8 h. After the completion of the reaction as indicated by TLC, the reaction mixture was worked up with ether and water. The organic layer was dried over $MgSO_4$, concentrated under aspirator vacuum, and purified by column chromatography (silica gel, hexanes/ethyl acetate, 9:1) to obtain 42.9 g (80% overall) of pure silyl ether **TBS-14**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.24−7.36 (m, 5H), 5.77−5.91 (m, 1H), 5.02−5.11 (m, 2H), 4.53 (s, 2H), 3.90 (qu, J = 5.5 Hz, 1H), 3.41 (d, J = 5.6 Hz, 2H), 2.32−2.42 (m, 1H), 2.19−2.29 (m, 1H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 138.5, 135.0, 128.4, 127.6, 127.5, 117.1, 74.3, 73.4, 71.2, 39.4, 25.9, 18.2, −4.4, −4.6.

Preparation of (3*S*)-4-Benzyloxy-3-*tert*-butyldimethylsilyloxybutanal, $C_{17}H_{28}O_3Si$, 15. Olefin **TBS-14** (31.9 g, 104.2 mmol) was dissolved in 200 mL of methanol and cooled to −78 °C. Ozone gas was bubbled through the reaction mixture until a persistent blue color was observed. The resultant ozonide was quenched with methyl sulfide (38.2 mL, 521.0 mmol) and stirred for 1 h at room temperature. Methanol was concentrated under vacuum and filtered over $MgSO_4$. The crude product was purified by column chromatography (silica gel, hexanes/ethyl acetate, 7:3) to obtain 24.4 g (76%) of pure aldehyde **15**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.80 (m, 1H), 7.25−7.36 (m, 5H), 4.54 (s, 2H), 4.33−4.41 (m, 1H), 3.51 (dd, J = 5.1, 9.5 Hz, 1H), 3.40 (dd, J = 6.2, 9.5 Hz, 1H), 2.67 (ddd, J = 2.1, 5.2, 15.9 Hz, 1H), 2.58 (ddd, J = 2.7, 6.5, 15.9 Hz, 1H), 0.87 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 201.5, 138.0, 128.4, 127.8, 127.1, 74.0, 73.4, 67.4, 49.0, 25.8, 18.1, −4.4, −4.9.

Preparation of (2*S*,4*S*,5*R*)-1-Benzyloxy-2-*tert*-butyldimethylsilyloxy-5-methyl-6-hepten-4-ol, $C_{21}H_{36}O_3Si$, 16. Potassium *tert*-butoxide (56.7 mL, 1.0 M solution, 56.7 mmol) was dissolved in 100 mL THF at −78 °C, and *trans*-2-butene (12.0 mL, 128.9 mmol) was added. *n*-Butyllithium (22.7 mL, 2.5 M solution, 56.7 mmol) was added and the mixture stirred for 20 min at −45 °C. The reaction mixture was cooled to −78 °C, (+)-*B*-methoxydiisopinocampheylborane [(+)-Ipc_2BOMe] (22.0 g, 69.6 mmol) dissolved in 50.0 mL of THF was added, and the mixture was stirred for 1 h. Aldehyde **15** (15.9 g, 51.6 mmol) was dissolved in 20.0 mL of THF precooled to −78 °C, and the reaction mixture was transferred via cannula at −78 °C and stirred for 3 h. The reaction mixture was oxidized with 27.8 mL of 3 M NaOH and 27.7 mL 30% H_2O_2 and stirred overnight. The reaction mixture was worked up with ether and water. The organic layer was dried over $MgSO_4$, concentrated under vacuum, and purified by column chromatography (silica gel, 3:2, hexane/ethyl ether) to obtain 15.4 g (82%) of pure alcohol **16**. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26−7.36 (m, 5H), 5.75−5.88 (m, 1H), 5.04−5.10 (m, 2H), 4.48−4.58 (m, 2H), 4.11−4.18 (m, 1H), 3.70−3.76 (m, 1H), 3.40−3.50 (m, 2H), 3.00 (bs, 1H), 2.16−2.23 (m, 1H), 1.57−1.74 (m, 2H), 1.03 (d, J = 6.9 Hz, 3H), 0.89 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 140.7, 138.2, 128.4, 127.8, 127.7, 115.4, 73.7, 73.4, 71.4, 70.2, 44.3, 37.7, 25.9, 18.1, 15.8, −4.5, −5.0; EI-MS *m/z* 201, 91 (100), 75, 55; CI-MS *m/z* 365 [(M + H)$^+$, 100], 347 [(M + H) − H_2O]$^+$; HRMS-CI 365.2510 (actual), 365.2512 (calcd).

Preparation of (1*S*,3*S*)-1-((1*R*)-1-Methyl-2-propenyl)-4-benzyloxy-3-*tert*-butyldimethylsilyloxybutyl Prop-2-enoate, $C_{24}H_{38}O_4Si$, Acr-16. Alcohol **16** (10.0 g, 27.5 mmol) was dissolved in CH_2Cl_2 (60.0 mL) and cooled to 0 °C. Acryloyl chloride (3.4 mL, 41.2 mmol) and triethylamine (9.6 mL, 68.7 mmol) were added at 0 °C and the mixture stirred for 1 h at room temperature. After completion of the reaction as indicated by TLC, the reaction mixture was filtered over magnesium sulfate pad and purified by column chromatography (silica gel, 9:1, hexane/ethyl acetate) to obtain 9.8 g (85%) of pure acrylate ester **Acr-16**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.24−7.36 (m, 5H), 6.38 (dd, J = 1.6, 17.3 Hz, 1H), 6.11 (dd, J = 10.3, 17.3 Hz, 1H), 5.70−5.82 (m, 2H), 5.04−5.15, (m, 3H), 4.51 (s, 2H), 3.81−3.89 (m, 1H), 3.41 (dd, J = 5.3, 9.6 Hz, 1H), 3.33 (dd, J = 5.7, 9.6 Hz, 1H), 2.51−2.60 (m, 1H), 1.82 (ddd, J = 3.0, 9.7, 14.5 Hz, 1H), 1.62 (ddd, J = 2.6, 9.0, 14.5 Hz, 1H), 1.10 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 165.8, 139.4, 138.3, 130.4, 129.0, 128.4, 127.7, 127.6, 115.6, 75.0, 74.2, 73.3, 68.5, 41.5, 36.1, 26.0, 18.1, 14.8, −4.1, −5.0; EI-MS *m/z* 289, 91 [($C_6H_5CH_2$)$^+$, 100], 73, 55; CI-MS *m/z* 419 [(M + H)$^+$, 100], 347 [(M + H) − (CH_2=CHCOOH)]$^+$, 287, 255, 215, 201; HRMS-CI 419.2607 (actual), 419.2618 (calcd).

Preparation of (5*R*,6*S*)-(6-((2*S*)-3-benzyloxy-2-*tert*-butyldimethylsilyloxypropyl)-6-methyldihydropyran-2-one, $C_{22}H_{34}O_4Si$, 17. Acrylate **Acr-16** (8.0 g, 19.1 mmol) was refluxed in toluene (200.0 mL) at 120 °C. Grubbs' second-generation catalyst (0.81 g, 0.95 mmol) was added and the mixture refluxed for 3 h. After completion of the reaction (TLC), solvent was evaporated under vacuum and the crude product was purified by column chromatography (silica gel, 3:2, hexane/ethyl acetate) to obtain 7.2 g (96%) of the lactenone **17**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26−7.34 (m, 5H), 6.64 (dd, J = 2.4, 9.8 Hz, 1H), 5.95 (dd, J = 2.4, 9.8 Hz, 1H), 4.53 (s, 2H), 4.20−4.30 (m, 2H), 3.44 (dd, J = 4.9, 9.8 Hz, 1H), 3.38 (dd, J = 5.4, 9.8 Hz, 1H), 2.42−2.47 (m, 1H), 1.61−1.92 (m, 2H), 1.12 (d, J = 7.4 Hz, 3H), 0.86 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 163.9, 151.8, 138.3, 128.4, 127.7, 127.6, 120.2, 80.0, 74.8, 73.3, 66.8, 38.2, 33.8, 25.9, 18.1, 16.5, −4.2, −4.9; EI-MS *m/z* 333 (M − $C(CH_3)_3$)$^+$, 91 [($C_6H_5CH_2$)$^+$, 100], 73, 57; CI-MS *m/z* 391 [(M + H)$^+$, 100]; HRMS-CI 391.2304 (actual), 391.2305 (calcd).

Preparation of (3*S*,4*S*,5*R*,6*S*)-(6-((2S)-3-benzyloxy-2-*tert*-butyldimethylsilyloxypropyl)-3,4-dihydroxy-6-methyltetrahydropyran-2-one, $C_{22}H_{36}O_6Si$, 18. NMO (1.4 g, 11.5 mmol) was added to the dihydropyranone **17** (3.0 g, 7.7 mmol) dissolved in acetone/water (4:1, 15 mL) at 0 °C. OsO_4 (156 mg, 0.6 mmol) was added to the above solution and stirred for 6 h at room temperature, the product was extracted with Et_2O (3 × 20 mL) and washed, and the organic layers were concentrated under aspirator vacuum. The crude product was purified by column chromatography (silica gel, hexane/ethyl acetate (1:4)) to obtain 2.8 g (87%) of **18**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26−7.38 (m, 5H), 4.60−4.67 (m, 1H), 4.54 (s, 2H), 4.15−4.21 (m, 1H), 4.07 (d, J = 9.3 Hz, 2H), 3.33−3.52 (m, 3H), 2.73 (s, 1H), 1.91−1.96 (m, 1H), 1.78 (t, J = 6.2 Hz, 2H), 1.14 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 173.7, 138.3, 128.4, 127.7, 127.6, 79.9, 74.8, 73.3, 71.2, 71.0, 67.0, 39.0, 37.4, 25.9, 18.1, 14.2, −4.3, −4.9; EI-MS *m/z* 275, 91 [($C_6H_5CH_2$)$^+$, 100], 81, 69, 57; CI-MS *m/z* 425 [(M + H)$^+$, 100], 407 [(M + H) − H_2O]$^+$; HRMS-CI 425.2351 (actual), 425.2359 (calcd).

Preparation of (4*S*,5*R*,6*S*)-(6-((2*S*)-3-Benzyloxy-2-*tert*-butyldimethylsilyloxypropyl)-4-hydroxy-6-methyltetrahydropyran-2-one, $C_{22}H_{36}O_5Si$, 19. Diol **18** (2.0 g, 4.7 mmol) was dissolved in 10.0 mL of CH_2Cl_2 and cooled to 0 °C.

Phenylchlorothionoformate (0.75 mL, 5.4 mmol) was added followed by the addition of pyridine (0.76 mL, 9.4 mmol). After completion of the reaction as indicated by TLC, the reaction mixture was worked up with ether and water. The crude thionoformate ester was dissolved in benzene (50.0 mL) and refluxed at 85 °C. Tributyltin hydride (3.2 mL, 11.8 mmol) was added followed by addition of AIBN (77 mg, 0.47 mmol) and refluxed for 5 h. The reaction mixture was concentrated under vacuum and purified by column chromatography (silica gel, hexanes/ethyl acetate, 2:3) to obtain 1.8 g (93%) of pure β-hydroxylactone **19**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26−7.35 (m, 5H), 4.53 (s, 2H), 4.61 (dt, J = 2.5, 10.3 Hz, 1H), 4.65 (m, 3H), 4.19−4.27 (m, 1H), 4.03−4.07 (m, 1H), 3.44 (dd, J = 5.0, 9.7 Hz, 1H), 3.38 (dd, J = 5.4, 9.8 Hz, 1H), 2.58−2.73 (m, 2H), 2.45 (bs, 1H), 1.66−1.82 (m, 3H), 1.05 (d, J = 6.8 Hz, 3H), 0.88 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 170.2, 138.3, 128.4, 127.7, 127.6, 127.5, 77.2, 75.0, 73.3, 67.6, 67.0, 39.4, 38.9, 37.6, 26.0, 18.1, 13.8, −4.2, −4.8; EI-MS m/z 351 (M − $C(CH_3)_3)^+$, 91 [$(C_6H_5CH_2)^+$, 100], 81, 69, 57; CI-MS m/z 409 [$(M + H)^+$, 100], 391 [$(M + H) - H_2O]^+$, 107, 91 $(C_6H_5CH_2)^+$, 81, 69; HRMS-CI 409.2415 (actual), 409.2410 (calcd).

Preparation of (3*R*,4*S*,5*R*,6*S*)-(6-((2*S*)-3-Benzyloxy-2-*tert*-butyldimethylsilyloxypropyl)-4-hydroxy-3,6-dimethyltetrahydropyran-2-one, $C_{23}H_{38}O_5Si$, Me-19. A solution of lithium diisopropylamide (LDA) in hexanes (3.5 mL, 1.7 M solution, 6.0 mmol) was cooled to −60 °C, and a solution of the hydroxylactone **19** (1.0 g, 2.45 mmol) and hexamethylphosphoramide (3.0 mL, 0.017 mmol) in THF was added dropwise over 40 min and stirred at −60 °C for 2 h. The reaction mixture was cooled to −78 °C, *n*-butyllithium (1.9 mL, 2.5M solution, 4.9 mmol) was added dropwise over 30 min, and the mixture was stirred for 45 min at −78 °C. Iodomethane (0.92 mL, 14.7 mmol) was added in one portion and stirred for 16 h. The reaction mixture was quenched with water and worked up with ether. The organic layer was dried over $MgSO_4$, concentrated under aspirator vacuum, and purified by column chromatography (silica gel, 3:2, hexane/ethyl acetate) to obtain 0.81 g (78%) of the α-methyl-β-hydroxylactone **Me-19**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26−7.35 (m, 5H), 4.49−4.57 (m, 3H), 4.17−4.24 (m, 1H), 3.72 (t, J = 4.0 Hz, 1H), 3.43 (dd, J = 5.0, 9.7 Hz, 1H), 3.37 (dd, J = 5.3, 9.7 Hz, 1H), 2.62 (dq, J = 4.4, 7.3 Hz, 1H), 2.22 (bs, 1H), 1.81−1.94 (m, 1H), 1.65−1.77 (m, 2H), 1.30 (d, J = 7.3 Hz, 3H), 1.03 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.0, 138.3, 128.4, 127.7, 127.6, 76.6, 75.0, 73.3, 73.2, 67.1, 43.3, 38.6, 36.0, 25.9, 18.1, 15.6, 12.6, −4.3, −4.9; EI-MS m/z 365 (M − $C(CH_3)_3)^+$, 91 [$(C_6H_5CH_2)^+$, 100], 81, 69, 57; CI-MS m/z 423 [$(M + H)^+$, 100], 405 [$(M + H) - H_2O]^+$; HRMS-CI 423.2561 (actual), 423.2567 (calcd).

Preparation of (3*R*,4*S*,5*R*,6*S*)-(6-((2*S*)-3-Benzyloxy-2-*tert*-butyldimethylsilyloxypropyl)-4-*tert*-butyldimethylsilyloxy-3,6-dimethyltetra hydropyran-2-one, $C_{29}H_{52}O_5Si_2$, 20. Alcohol Me-19 (0.5 g, 1.2 mmol) was dissolved in CH_2Cl_2 (2.0 mL) and cooled to −78 °C. *tert*-Butyldimethylsilyltrifluoromethanesulfonate (0.33 mL, 1.42 mmol) was added dropwise followed by the addition of 2,6-lutidine (0.21 mL, 1.8 mmol) and the mixture stirred for 2 h at −78 °C. The reaction mixture was worked up with ether and water. The organic layer was dried ($MgSO_4$) and concentrated under vacuum to obtain the crude silyl ether 20, which was purified by column chromatography (silica gel, hexanes/ethyl acetate (5:1)) to obtain 0.59 g (92%) of 20: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26−7.34 (m, 5H), 4.49−4.57 (m, 3H), 4.21−4.28 (m, 1H), 3.66 (m, 1H), 3.42 (dd, J = 4.9, 9.7 Hz, 1H), δ 3.36 (dd, J = 5.4, 9.8 Hz, 1H), 2.64 (dq, J = 2.6, 7.6 Hz, 1H), 1.63−1.90 (m, 3H), 1.26 (d, J = 7.6 Hz, 3H), 0.99 (d, J = 6.8 Hz, 3H), 0.87−0.89 (m, 18H), 0.06−0.09 (m, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 173.7, 138.4, 128.4, 127.7, 127.6, 77.1, 75.0, 74.8, 73.3, 66.9, 44.1, 39.1, 34.6, 26.0, 25.8, 18.1, 18.0, 16.5, 14.1, −4.3, −4.5, −4.8, −4.9; EI-MS m/z 479 (M − $C(CH_3)_3)^+$, 117, 91 [$(C_6H_5CH_2)^+$, 100], 73; CI-MS m/z 537 [$(M + H)^+$, 100]; HRMS-CI 537.3429 (actual), 537.3432 (calcd).

Preparation of (3*R*,4*S*,5*R*,6*S*)-(6-((2*S*)-2-*tert*-Butyldimethylsilyloxy-3-hydroxypropyl)-4-*tert*-butyldimethylsilyloxy-3,6-dimethyltetrahydropyran-2-one, $C_{22}H_{46}O_5Si_2$, OH-20. Benzyl ether 20 (0.5 g, 0.93 mmol) was dissolved in ethyl acetate (2.0 mL). 0.1 g (10%, 0.09 mmol) of 10% palladium over charcoal was added, and hydrogen gas was bubbled through the reaction mixture for 6 h. The reaction mixture was filtered over silica gel and purified by column chromatography (silica gel, hexanes/ethyl acetate, (3:1)) to obtain 0.37 g (90%) of pure alcohol OH-20: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.46 (t, J = 9.93 Hz, 1H), 4.13−4.20 (m, 1H), 3.62−3.68 (m, 2H), 3.44 (dd, J = 2.6, 11.2 Hz, 1H), 2.64 (dq, J = 2.6, 7.6 Hz, 1H), 1.79−2.01 (m, 3H), 1.49−1.58 (m, 1H), 1.26 (d, J = 7.5 Hz, 3H), 0.98 (d, J = 6.5 Hz, 3H), 0.88−0.89 (m, 18H), 0.11 (m, 6H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 173.7, 77.4, 74.7, 68.1, 67.1, 44.1, 38.4, 34.4, 25.9, 25.7, 18.0 (two carbons), 16.5, 14.1, −4.5, −4.6, −4.8, −4.9; EI-MS m/z 415 (M − $CH_2OH)^+$, 217, 115, 73 [$(SiCH_3)_3^+$, 100]; CI-MS m/z 447 [$(M + H)^+$, 100], 429 [$(M + H) - H_2O]^+$; HRMS-CI 447.2971 (actual), 447.2962 (calcd).

Preparation of (3*R*,4*S*,5*R*,6*S*)-6-((2*S*)-2-*tert*-Butyldimethylsilyloxy-3-oxopropyl)-4-*tert*-butyldimethylsilyloxy-3,6-dimethyltetrahydropyran-2-one, $C_{22}H_{44}O_5Si_2$, 11. Dess−Martin periodinane (285 mg, 0.67 mmol) was suspended in 1 mL of CH_2Cl_2, and alcohol **OH-20** (0.2 g, 0.45 mmol) was added at 25 °C. The reaction mixture was stirred for 2 h and filtered over a sodium sulfate pad. The crude product was concentrated under vacuum and purified by column chromatography (silica gel, hexanes/ethyl acetate, (4:1)) to obtain 185 mg (93%) of pure aldehyde **11**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.66 (d, J = 0.8 Hz, 1H), 4.54 (dd, J = 2.4, 10.3 Hz, 1H), 4.44−4.49 (m, 1H), 3.67 (t, J = 2.3 Hz, 1H), 2.66 (dq, J = 2.5, 7.7 Hz, 1H), 1.71−1.98 (m, 3H), 1.27 (d, J = 7.6 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 203.4, 173.2, 76.1, 74.7, 73.7, 42.2, 36.2, 34.2, 25.8, 25.7, 18.1, 18.0, 16.6, 14.1, −4.5, −4.6, −4.8, −5.1; EI-MS m/z 415, 159, 115, 73 [$(SiCH_3)_3^+$, 100]; CI-MS m/z 445 [$(M + H)^+$, 100], 313, 217, 133; HRMS-CI 445.2804 (actual), 445.2806 (calcd).

Preparation of Methyl (2*S*)-3-*tert*-Butyldimethylsilyloxy-2-methylpropionate, $C_{11}H_{24}O_3Si$, TBS-21. Alcohol **21** (50.0 g, 423.7 mmol) was dissolved in 800 mL of dimethylformamide. *tert*-Butyldimethylsilyl chloride (69.9 g, 466.1 mmol) and imidazole (43.2 g, 635.6 mmol) were added at 0 °C, and the mixture was stirred for 3 h. After completion of the reaction as indicated by TLC, the reaction mixture was worked up with ether and water. The organic layer was dried over $MgSO_4$ and concentrated under aspirator vacuum to obtain 88.5 g (90%) of silyl ether **TBS-21**, which was used for the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.76 (dd, J = 6.86, 9.66 Hz, 1H), 3.60−3.85 (m, 4H), 2.57−2.69 (m, 1H), 1.12 (d, J = 7.1 Hz, 3H), 0.85 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 175.5, 65.3, 51.5, 42.5, 25.8, 18.2, 13.5, −5.5.

Preparation of (2*R*)-3-*tert*-Butyldimethylsilyloxy-2-methyl-1-propanol, $C_{10}H_{24}O_2Si$, 22. Silyl ether **TBS-21** (70.0 g, 301.7 mmol) was dissolved in 600 mL of diethyl ether, borane−methyl sulfide (50.9 mL, 10 M solution, 509.9 mmol) was added at 0 °C, and the mixture was stirred overnight at room temperature. The excess borane methyl sulfide was quenched with triethylamine and methanol (1:5, 200.0 mL). The reaction mixture was worked up with ether and water. The organic layer was dried over $MgSO_4$ and evaporated under aspirator vacuum to obtain 48.0 g (78%) of alcohol **22**, which was used for the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.66−3.70 (m, 1H), 3.48−3.59 (m, 3H), 3.02 (bs, 1H), 1.86−1.94 (m, 1H), 0.9 (s, 9H), 0.84

(d, $J = 8.7$ Hz, 3H), 0.08 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 68.4, 67.9, 37.2, 25.9, 18.2, 13.1, −5.5, −5.6.

Preparation of (2S)-3-*tert*-Butyldimethylsilyloxy-2-methyl-1-propanal, $C_{10}H_{22}O_2Si$, Ald-22. Dess−Martin periodinane (197.5 g, 465.7 mmol) was suspended in 100 mL of CH_2Cl_2, and alcohol **22** (50.0 g, 245.1 mmol) was added at 0 °C. The reaction mixture was stirred for 1 h and filtered over a sodium sulfate pad to obtain 43.1 g (87%) of aldehyde **Ald-22**, which was used for the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.71 (s, 1H), 3.74−3.86 (m, 2H), 2.48−2.52 (m, 1H), 1.05 (d, $J = 7.0$ Hz, 3H), 0.85 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 204.7, 63.4, 48.8, 25.8, 18.2, 10.2, −5.6.

Preparation of (2*S*,3*R*,4*S*)-1-*tert*-Butyldimethysilyloxy-2,4-dimethyl-5-hexen-3-ol, $C_{14}H_{30}O_2Si$, 23. Potassium *tert*-butoxide (237.6 mL, 1.0 M solution, 237.6 mmol) was dissolved in 200 mL THF at −78 °C, and *cis*-2-butene (38.3 mL, 396.0 mmol) was added. *n*-Butyllithium (95.0 mL, 2.5 M solution, 237.6 mmol) was added and the mixture stirred for 20 min at −45 °C. The reaction mixture was cooled to −78 °C, and (+)-*B*-methoxydiisopinocampheylborane [(+)-Ipc_2BOMe] (112.7 g, 356.4 mmol) dissolved in 100.0 mL of THF was added and stirred for 1 h. Aldehyde **Ald-22** (40.0 g, 198.0 mmol) was dissolved in 20.0 mL of THF precooled to −78 °C and transferred to the reaction mixture via a cannula at −78 °C and the mixture stirred for 3 h. The reaction mixture was oxidized with 142.6 mL of 3 M NaOH and 142.6 mL of 30% H_2O_2 and stirred overnight. The reaction mixture was worked up with ether and water. The organic layer was dried over $MgSO_4$, concentrated under vacuum, and purified by column chromatography (silica gel, 19:1 hexane/ethyl ether) to obtain 38.3 g (75%) of pure alcohol **23**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.81−5.93 (m, 1H), 4.97−5.09 (m, 2H), 3.82−3.88 (m, 1H), 4.04−4.12 (m, 2H), 3.35−3.45 (bs, 1H), 2.29−2.31 (m, 1H), 1.74−1.83 (m, 1H), 1.06 (d, $J = 5.4$ Hz, 3H), 0.84−0.96 (m, 12H), 0.08 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 142.5, 113.9, 79.6, 68.0, 41.3, 36.7, 25.9, 18.2, 14.1, 13.5, −5.5, −5.6; EI-MS *m/z* 203 (M − C_4H_7)$^+$, 145, 109, 75 [$(CH_3)_2SiOH^+$, 100], 55, 43; CI-MS *m/z* 259 (M + H), 241 (M + H − H_2O)$^+$, 145, 127, 109 (100), 89.

Preparation of (1*R*,2*S*)-1-((1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl)-2-methyl-3-butenyl Prop-2-enoate, $C_{17}H_{32}O_3Si$, Acr-23. Alcohol **23** (4.0 g, 15.5 mmol) was dissolved in CH_2Cl_2 (30.0 mL) and cooled to −15 °C. Acryloyl chloride (10.1 mL, 124.0 mmol) and diisopropylethylamine (43.1 mL, 248.0 mmol) were added at −15 °C and the mixture stirred for 1 h at room temperature. After completion of the reaction as indicated by TLC, the reaction mixture was filtered over a magnesium sulfate pad and then purified by column chromatography (silica gel, 19:1, hexane/ethyl acetate) to obtain 3.8 g (79%) of pure acrylate ester **Acr-23**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.38 (dd, $J = 1.4$, 17.3 Hz, 1H), 6.11 (dd, $J = 10.3$, 17.3 Hz, 1H), 5.70−5.83 (m, 2H), 5.00−5.09 (m, 2H), 4.91 (t, $J = 6.3$ Hz, 1H), 3.66 (dd, $J = 4.4$, 9.5 Hz, 1H), 3.37 (dd, $J = 7.8$, 9.7 Hz, 1H), 2.54−2.62 (m, 1H), 1.97−2.07 (m, 1H), 0.99 (d, $J = 6.9$ Hz, 3H), 0.95 (d, $J = 6.7$ Hz, 3H), 0.88 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 165.9, 140.6, 130.5, 128.6, 115.0, 78.1, 64.2, 39.3, 37.6, 26.0, 18.3, 14.4, 14.3, −5.4; EI-MS *m/z* 257 (M − C_4H_9)$^+$, 227, 129 (100), 109, 89, 75, 55; CI-MS *m/z* 313 [(M + H)$^+$, 100], 241, 181, 127, 109; HRMS-CI 313.2193 (actual), 313.2199 (calcd).

Preparation of (5*S*,6*R*)-6-((1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl)-5-methyl-5,6-dihydropyran-2-one, $C_{15}H_{28}O_3Si$, 24. Acrylate **Acr-23** (2.5 g, 8.0 mmol) was refluxed in toluene (80.0 mL). Grubbs' second-generation catalyst (0.7 g, 0.8 mmol) was added and the mixture refluxed for 3 h. After completion of the reaction (TLC), solvent was evaporated under vacuum and the crude product was purified by column chromatography (silica gel, 2:3, hexane/ethyl acetate) to obtain 2.0 g (86%) of the dihydropyranone **24**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.99 (dd, $J = 6.5$, 9.6 Hz, 1H), 5.96 (d, $J = 9.6$ Hz, 1H), 4.25 (dd, $J = 3.0$, 10.6 Hz, 1H), 3.83 (dd, $J = 5.0$, 9.8 Hz, 1H), 3.72 (dd, $J = 2.8$, 9.7 Hz, 1H), 2.36−2.45 (m, 1H), 1.90−1.99 (m, 1H), 1.03 (d, $J = 7.0$ Hz, 3H), 0.96 (d, $J = 6.9$ Hz, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 164.7, 152.0, 120.0, 80.1, 63.5, 36.4, 30.1, 25.9, 18.3, 12.6, 10.8, −5.4; EI-MS *m/z* 227 (M − C_4H_9)$^+$, 145, 75 [$(CH_3)_2SiOH^+$, 100], 59; CI-MS *m/z* 285 [(M + H)$^+$, 100], 271, 153, 69; HRMS-CI 285.1889 (actual), 285.1886 (calcd).

Preparation of (3*S*,4*S*,5*S*,6*S*)-6-((1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl)-3,4-dihydroxy-5-methyltetrahydropyran-2-one, $C_{15}H_{30}O_5Si$, 25. NMO (0.8 g, 13.8 mmol) was added to the dihydropyranone **24** (1.9 g, 6.9 mmol) dissolved in acetone/water (4:1, 15 mL) at 0 °C. OsO_4 (0.18 g, 0.7 mmol) was added to the above solution and stirred for 6 h at room temperature, and the product was extracted with Et_2O (3 × 10 mL), washed with saturated solution of sodium sulfite, and dried over $MgSO_4$. The solvent was removed under aspirator vacuum. The crude product was purified by column chromatography (silica gel, hexane/ethyl acetate (3:2)) to obtain 1.6 g (72%) of **25**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.64 (dd, $J = 2.7$, 10.8 Hz, 1H), 4.21 (d, $J = 3.5$ Hz, 1H), 4.14 (t, $J = 3.7$ Hz, 1H), 3.77 (dd, $J = 2.9$, 9.7 Hz, 1H), 3.63 (dd, $J = 6.0$, 9.8 Hz, 1H), 2.27−2.34 (m, 1H), 1.85−1.94 (m, 1H), 1.02 (d, $J = 7.3$ Hz, 3H), 0.92 (d, $J = 6.8$ Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.6, 80.6, 71.4, 67.6, 64.2, 36.7, 34.5, 25.9, 18.3, 12.6, 9.7, −5.40; EI-MS *m/z* 285, 243, 215, 199, 143, 75 [$(CH_3)_2SiOH^+$, 100], 55, 43; CI-MS *m/z* 319 [(M + H)$^+$, 100], 301, 261, 187; HRMS-CI 319.1941 (actual), 319.1941 (calcd).

Preparation of (4*S*,5*S*,6*S*)-6-((1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl)-4-hydroxy-5-methyltetrahydropyran-2-one, $C_{15}H_{30}O_4Si$, 26. Diol **25** (1.5 g, 4.7 mmol) was dissolved in 10.0 mL of CH_2Cl_2 and cooled to 0 °C. Phenylchlorothionoformate (0.71 mL, 5.2 mmol) was added followed by the addition of pyridine (0.83 mL, 10.24 mmol). After completion of the reaction as indicated by TLC, the reaction mixture was worked up with ether and water. The crude thionoformate ester was dissolved in benzene (10.0 mL) and refluxed at 80 °C. Tributyltin hydride (5.06 mL, 18.8 mmol) was added followed by the addition of AIBN (0.08 g, 0.5 mmol) and refluxed for 5 h. The reaction mixture was concentrated under vacuum and purified by column chromatography (silica gel, hexanes/ethyl acetate, 4:1) to obtain 0.96 g (67% overall) of pure β-hydroxylactone **26**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.57 (dd, $J = 2.3$, 10.6 Hz, 1H), 4.04 (dt, $J = 2.9$, 5.7 Hz, 1H), 3.76 (dd, $J = 3.1$, 9.7 Hz, 1H) 3.70 (dd, $J = 5.4$, 9.7 Hz, 1H), 2.77 (dd, $J = 5.6$, 18.1 Hz, 1H), 2.51 (dd, $J = 3.0$, 18.1 Hz, 1H), 1.98−2.07 (m, 1H), 1.83−1.95 (m, 1H), 0.94, (d, $J = 7.8$ Hz, 3H), 0.88−0.90 (m, 12H), 0.03 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 170.8, 78.2, 68.7, 64.0, 36.7, 35.7, 35.3, 25.9, 18.3, 12.7, 10.0, −5.3, −5.4; EI-MS *m/z* 245 (M − C_4H_9)$^+$, 227, 203, 185, 153, 145, 115, 83, 75 [$(CH_3)_2SiOH^+$, 100], 55, 43; CI-MS *m/z* 303 [(M + H)$^+$, 100], 285 (M + H−H_2O)$^+$, 245, 227, 171, 153, 133, 113; HRMS-CI 303.1999 (actual) 303.1992 (calcd).

Preparation of (3*R*,4*S*,5*S*,6*S*)-6-((1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl)-4-hydroxy-3,5-dimethyltetrahydropyran-2-one, $C_{16}H_{32}O_4Si$, Me-26. A solution of LDA in hexanes (4.3 mL, 1.7 M solution, 7.3 mmol) was cooled to −60 °C, a solution of the hydroxylactone **26** (1.0 g, 3.3 mmol) and hexamethylphosphoramide (4.0 mL, 22.3 mmol) in THF was added dropwise over 40 min, and the mixture was stirred at −60 °C for 2 h. The reaction mixture was cooled to −78 °C, and *n*-butyllithium (2.8 mL, 2.5M solution, 6.9 mmol) was added dropwise over 30 min and stirred for 45 min at −78 °C. Iodomethane (1.2 mL, 19.8 mmol) was added in one portion and stirred for 16 h. The reaction mixture was quenched with water and worked up with ether. The organic layer was dried over $MgSO_4$, concentrated under aspirator vacuum, and purified by column chromatography (silica gel, 1:3, hexane/ethyl acetate) to obtain 0.8 g (75%) of the α-methyl-β-hydroxylactone **Me-26**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.40 (d, $J = 10.2$ Hz, 1H), 3.74 (dd, $J = 4.8$, 9.8 Hz, 1H), 3.66 (dd, $J = 2.5$, 9.6

Hz, 1H), 3.36 (d, $J = 5.8$ Hz, 1H), 2.72 (bs, 1H), 2.50 (qu, $J = 6.8$, 1H), 1.99−2.07 (m, 1H), 1.83−1.90 (m, 1H), 1.30 (d, $J = 6.9$, 3H), 0.93 (d, $J = 6.9$ Hz, 3H), 0.90 (d, $J = 7.7$ Hz, 3H), 0.86 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.6, 78.1, 77.5, 63.9, 41.9, 39.3, 36.1, 25.9, 18.3, 13.9, 12.7, 11.9, −5.4, −5.5; EI-MS *m/z* 259 $(M - C_4H_9)^+$, 203, 185, 167, 145, 115, 75 [$(CH_3)_2SiOH^+$, 100], 55, 43; CI-MS 317 $(M + H)^+$, 299 $(M + H - H_2O)^+$, 259, 185, 167; HRMS-CI 317.2158 (actual), 317.2148 (calcd).

Preparation of (3*R*,4*S*,5*R*,6*S*)-6-((1*S*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl)-4-*tert*-butyldimethylsilyloxy-3,5-dimethyltetrahydropyran-2-one, $C_{22}H_{46}O_4Si_2$, 27. Alcohol **Me-26** (0.5 g, 1.6 mmol) was dissolved in CH_2Cl_2 (3.0 mL) and cooled to −78 °C. *tert*-Butyldimethyl silyltrifluoromethanesulfonate (0.4 mL, 1.7 mmol) was added dropwise followed by the addition of 2,6-di-*tert*-butyl-4-methylpyridine (0.6 g, 3.2 mmol) and stirred for 1 h at −78 °C. The reaction mixture was filtered with ether over silica gel and purified by column chromatography (silica gel, hexanes/ethyl acetate, 5:1) to obtain 0.54 g (78%) of **27**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.44 (d, $J = 10.5$ Hz, 1H), 3.76 (dd, $J = 4.6, 9.6$ Hz, 1H), 3.67 (dd, $J = 2.8, 9.7$ Hz, 1H), 3.32 (d, $J = 5.9$ Hz, 1H), 2.47 (qu, $J = 6.7$ Hz, 1H), 1.82−1.96 (m, 2H), 1.27 (d, $J = 6.9$ Hz, 3H), 0.91 (d, $J = 7.1$ Hz, 3H), 0.89 (s, 9H), 0.88 (s, 9H), 0.84 (d, $J = 7.4$ Hz, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.03 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 174.6, 78.5, 77.2, 63.9, 43.0, 39.4, 36.2, 25.9, 25.7, 18.3, 17.8, 14.6, 12.7, 11.0, −4.4, −4.7, −5.4, −5.5; EI-MS *m/z* 373 $(M - C_4H_9)^+$, 115, 89, 73 [$(CH_3)_3Si^+$, 100], 57, 47; CI-MS 431 $(M + H)^+$, 133, 81, 69; HRMS-CI 431.3000 (actual), 431.3013 (calcd).

Preparation of (2*S*,3*R*,4*R*,5*S*,6*S*)-3,7-Bis(*tert*-butyldimethylsilyloxy)-2,4,6-trimethylheptane-1,5-diol, $C_{22}H_{50}O_4Si_2$, 28. Silyl ether **27** (0.4 g, 0.9 mmol) was dissolved in THF (2.0 mL) and cooled to 0 °C. $LiBH_4$ (30 mg, 1.4 mmol) was added and the mixture stirred for 2 h. After completion of the reaction, the reaction mixture was quenched with water and worked up with ether. The organic layer was dried, concentrated under vacuum, and purified by column chromatography (silica gel, hexanes/ethyl acetate, 1:4) to obtain 0.25 g (65%) of pure diol **28**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.82−3.86 (m, 1H), 3.75 (dd, $J = 3.9, 9.8$ Hz, 1H), 3.45−3.65 (m, 4H), 2.04−2.11 (m, 1H), 1.68−1.86 (m, 2H), 0.95 (d, $J = 6.9$ Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.86 (d, $J = 7.1$ Hz, 3H), 0.76 (d, $J = 7.1$ Hz, 3H), 0.09 (s, 6H), 0.08 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 77.3, 75.2, 69.6, 66.3, 39.0, 38.6, 37.6, 26.2, 25.9, 18.5, 18.2, 13.1, 11.3, 9.8, −3.7, −3.8, −5.5, −5.6; EI-MS *m/z* 377 $(M - C_4H_9)^+$, 203, 145, 89, 75 [$(CH_3)_2SiOH^+$, 100], 57; CI-MS *m/z* 435 [$(M + H)^+$ 100], 303 $(M + H - HOSi(CH_3)_2)^+$, 203, 153, 133, 83, 69; HRMS-CI 435.3327 (actual), 435.3326 (calcd).

Preparation of (2*S*,3*S*,4*R*,5*R*,6*S*)-1,5-Bis(*tert*-butyldimethylsilyloxy)-3,7-bis(*p*-methoxybenzyloxy)-2,4,6-trimethylheptane, $C_{36}H_{62}O_6Si_2$, 29. Diol 28 (0.2 g, 0.5 mmol) was dissolved in 2 mL of THF/DMF (10:1) and added slowly to a precooled suspension of NaH (58 mg, 1.2 mmol) in 2 mL of THF at 0 °C. After the mixture was stirred for 2 h at 0 °C, *p*-methoxybenzyl bromide (0.4 g, 1.8 mmol) was added and the mixture stirred for 12 h. After completion of the reaction (TLC), the mixture was worked up with ether and water. The organic layer was dried over $MgSO_4$ and concentrated under vacuum and purified by column chromatography (silica gel, hexanes/ethyl acetate, 2:3) to obtain 0.26 g (81%) of 29.

Preparation of (4*R*,5*S*,6*S*)-4,6-Bis((1*S*)-2-*tert*-butyldimethylsilyloxy-1-methylethyl)-2-*p*-methoxyphenyl-5-methyl-1,3-dioxane, $C_{30}H_{56}O_5Si_2$, 30. Ether **29** (0.2 g, 0.3 mmol) was dissolved in 1 mL of CH_2Cl_2/water (20:1) mixture and cooled to 0 °C. DDQ (77 mg, 0.34 mmol) was added and the mixture stirred for 5 min. The reaction mixture was filtered over silica gel and washed with CH_2Cl_2. The organic layer was dried, concentrated under vacuum, and purified by column chromatography (silica gel, hexanes: ethyl acetate, 4:1) to obtain 117 mg (69%) of **30**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.42 (d, $J = 8.8$ Hz, 2H), 6.88 (d, $J = 8.5$ Hz, 2H), 5.44 (s, 1H), 3.80 (s, 3H), 3.50−3.84 (m, 6H), 1.70−1.94 (m, 3H), 1.08 (d, $J = 6.6$ Hz, 3H), 0.86−0.97 (m, 24H), 0.03−0.08 (m, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 132.1, 127.2, 113.5, 101.3, 84.0, 81.2, 64.3, 64.2, 55.3, 36.8, 36.6, 26.0, 25.9, 18.4, 18.2, 14.5, 12.1, 6.3, −5.3, −5.4, −5.5, −5.6.

Preparation of (2*S*,3*R*,4*R*,5*S*,6*S*)-3,7-Bis(*tert*-butyldimethylsilyloxy)-5-hydroxy-2,4,6-trimethylheptyl-*p*-nitrobenzoate, $C_{29}H_{53}NO_7Si_2$, 31. Diol **28** (0.2 g, 0.5 mmol) was dissolved in CH_2Cl_2 (1.0 mL). 4-Nitrobenzoyl chloride (0.1 g, 0.6 mmol), pyridine (1.0 mL, 1.0 mmol), and catalytic amounts of DMAP (5 mg, 0.04 mmol) were added at 25 °C and the mixture stirred for 3 h at room temperature. After completion of the reaction as indicated by TLC, the reaction mixture was filtered over magnesium sulfate pad and purified by column chromatography (silica gel, 19:1, hexane/ethyl acetate) to obtain 271 mg (93%) of pure acrylate ester **31**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.26 (d, $J = 9.0$, 2H), 8.22 (d, $J = 9.0$ Hz, 2H), 4.32 (dd, $J = 7.1, 10.5$ Hz, 1H), 4.22 (dd, $J = 7.8, 10.6$ Hz, 1H), 3.96 (d, $J = 8.1$ Hz, 1H), 3.89 (bs, 1H), 3.77 (dd, $J = 3.9, 10.0$ Hz, 1H), 3.53−3.60 (m, 2H), 2.36−2.43 (m, 1H), 1.70−1.85 (m, 2H), 0.85−0.99 (m, 24H), 0.74 (d, $J = 6.9$ Hz, 3H), 0.06−0.09 (m, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 164.7, 150.5, 136.0, 130.7, 123.6, 77.0, 73.8, 69.9, 69.1, 39.0, 37.7, 35.1, 26.3, 25.9, 18.6, 18.1, 12.9, 10.3, 9.9, −3.3, −3.9, −5.5, −5.6; EI-MS *m/z* 364, 185, 150, 145, 135, 115, 75 [$(CH_3)_2SiOH^+$, 100], 69, 57; CI-MS *m/z* 584 $(M + H)^+$, 452 $(M + H - HOSi(CH_3)_2)^+$, 422 [100], 417; HRMS-CI 584.3442 (actual), 584.3439 (calcd).

Preparation of (2*S*,3*R*,4*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-methyl-4-((4*S*,5*S*)-5-methyl-1,3-dioxan-4-yl)pentyl *p*-Nitrobenzoate, $C_{24}H_{39}NO_7Si$, 32. Alcohol **31** (0.2 g, 0.34 mmol)) was dissolved in CH_2Cl_2 and MEM chloride (0.05 mL, 0.41 mmol) and *N*,*N*-diisopropylethylamine (0.08 mL, 0.51 mmol) and the mixture stirred for 2 h. The reaction mixture was worked up with dilute acid, and the combined organic layers were dried, concentrated under vacuum, and purified by column chromatography (silica gel, hexanes/ethyl acetate, 5:1) to yield 91 mg (56%) of **32**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.30 (d, $J = 8.9$ Hz, 2H), 8.19 (d, $J = 8.9$ Hz, 2H), 4.95 (d, $J = 5.8$ Hz, 1H), 4.56 (d, $J = 6.0$ Hz, 1H), 4.31 (dd, $J = 6.8, 10.7$ Hz, 1H), 4.18 (dd, $J = 8.4, 10.6$ Hz, 1H), 3.97 (dd, $J = 4.5, 11.1$ Hz, 1H), 3.86 (dd, $J = 1.2, 7.5$ Hz, 1H), 3.19−3.30 (m, 2H), 2.25−2.32 (m, 1H), 1.96−2.08 (m, 1H), 1.82−1.92 (m, 1H), 0.93−1.00 (m, 15H), 0.69 (d, $J = 6.6$ Hz, 3H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 164.6, 150.6, 135.8, 130.6, 123.7, 93.7, 82.8, 77.3, 73.0, 72.9, 69.0, 37.6, 34.9, 31.5, 26.2, 18.5, 12.3, 10.7, 10.2, −3.5, −4.0; EI-MS *m/z* 436, 394 [100], 185, 73; CI-MS *m/z* 482 $(M + H)^+$, 350 $[(M + H) - HOSi(CH_3)_3]^+$, 320; HRMS-CI 482.2576 (actual), 482.2574 (calcd).

Preparation of (2*S*,3*R*,4*R*,5*S*,6*S*)-3,7-Bis(*tert*-butyldimethylsilyloxy)-5-triethylsilyloxy-2,4,6-trimethylheptyl *p*-Nitrobenzoate, $C_{35}H_{67}NO_7Si_3$, TES-31. Alcohol **31** (0.2 g, 0.34 mmol) was dissolved in CH_2Cl_2 (1.0 mL) and cooled to −78 °C. Triethylsilyltrifluoromethanesulfonate (0.09 mL, 0.41 mmol) was added dropwise followed by the addition of 2,6-lutidine (0.08 mL, 0.68 mmol) and the mixture stirred for h at −78 °C. The reaction mixture was worked up with ether and water. The organic layer was dried ($MgSO_4$) and concentrated under vacuum to obtain the crude silyl ether, which was purified by column chromatography (silica gel, hexanes/ethyl acetate, (5:1)) to obtain 229 mg (97%) of **TES-31**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.29 (d, $J = 9.0$ Hz, 2H), 8.21 (d, $J = 9.0$ Hz, 2H), 4.32 (dd, $J = 7.6, 10.9$ Hz, 1H), 4.25 (dd, $J = 7.1, 10.7$ Hz, 1H), 3.74 (dd, $J = 1.7, 8.0$ Hz, 1H), 3.66 (dd, $J = 2.8, 5.5$ Hz, 1H), 3.62 (dd, $J = 5.5, 9.8$ Hz, 1H), 3.43 (dd, $J = 6.5, 9.8$ Hz, 1H), 2.22−2.29 (m, 1H), 1.78−1.89 (m, 2H), 0.88−0.99 (m, 36H), 0.58 (q, $J = 8.2$ Hz, 6H), 0.09 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 164.7, 150.5, 135.8, 130.7, 123.6, 74.2, 73.4, 69.3, 65.1, 40.9, 38.7, 36.6, 26.3, 25.9, 18.6, 18.3, 14.3, 12.0, 10.5, 7.2, 5.7,

−3.1, −3.9, −5.3, −5.4; EI-MS *m/z* 224, 185, 115, 89, 73 [$(CH_3)_3$-Si^+, 100], 59, 47; CI-MS *m/z* 698 $(M + H)^+$, 434, 399, 185 (100), 135; HRMS-CI 698.4302 (actual), 698.4304 (calcd).

Preparation of (2*S*,3*R*,4*R*,5*S*,6*S*)-3,7-Bis(*tert*-butyldimethylsilyloxy)-2,4,6-trimethyl-5-triethylsilyloxyheptan-1-ol, $C_{28}H_{64}O_4Si_3$, 33. K_2CO_3 (78 mg, 0.57 mmol) was added to the ester **TES-31** (0.2 g, 0.28 mmol) dissolved in 1 mL of methanol and stirred for 1 h. Solvent was removed under aspirator vacuum, extracted with ether, washed with water, dried ($MgSO_4$), and purified by silica gel column chromatography to obtain 127 mg (83%) of alcohol **33**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.72 (dd, J = 2.4, 6.4 Hz, 1H), 3.67 (dd, J = 5.1, 9.9 Hz, 1H), 3.49−3.61 (m, 2H), 3.39 (dd, J = 7.0, 9.8 Hz, 1H), 1.80−1.96 (m, 2H), 1.71−1.73 (m, 1H), 1.57 (bs, 1H), 0.84−1.00 (m, 36H), 0.63 (q, J = 8.0 Hz, 6H), 0.04−0.08 (m, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 75.3, 74.0, 66.3, 65.0, 40.2, 39.8, 38.4, 26.2, 26.0, 18.5, 18.4, 15.0, 11.8, 11.2, 7.2, 5.7, −3.4, −3.9, −5.3, −5.4; CI-MS *m/z* 549 $(M + H)^+$, 417, 317, 285, 259, 203 [100]; HRMS-CI 549.4188 (actual), 549.4191 (calcd).

Preparation of (2*S*,3*S*,4*R*,5*S*,6*R*)-1,5-Bis(*tert*-butyldimethylsilyloxy)-7-iodo-2,4,6-trimethyl-3-triethylsilyloxyheptane, $C_{28}H_{63}IO_3Si_2$, 12. Alcohol **33** (0.1 g, 0.18 mmol) was dissolved in CH_2Cl_2. Iodine (81 mg, 0.32 mmol), triphenylphosphine (83 mg, 0.32 mmol), and imidazole (40 mg, 0.59 mmol) were added, and the mixture was stirred for 6 h. After completion of the reaction as indicated by TLC, the reaction mixture was worked up with ether and water. The organic layers were dried, concentrated under vacuum, and purified by column chromatography (silica gel, hexanes/ethyl acetate, 50:1) to afford 85 mg (72%) of **12**: ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.57−3.66 (m, 3H), 3.40 (dd, J = 6.8, 9.8 Hz, 1H), 3.26 (dd, J = 5.1, 9.5 Hz, 1H), 3.05−3.11 (m, 1H), 2.03−2.05 (m, 1H), 1.73−1.84 (m, 2H), 0.82−1.00 (m, 36H), 0.64 (q, J = 7.9 Hz, 6H), 0.08 (s, 6H), 0.04 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm) 76.0, 74.5, 65.0, 40.9, 40.6, 39.2, 26.2, 26.0, 18.6, 18.4, 14.5, 14.2, 14.1, 11.9, 7.2, 5.7, −3.4 (2 carbons), −5.2, −5.3; ESI-MS 681 (Na adduct), 658.7, 624.9, 608.9, 582.8, 567, 554 [100], 544; HRMS-ESI 681.3023 (actual), 681.3028 (calcd).

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Supporting Information Available: Experimental and spectral data along with ^1H and ^{13}C NMR spectra for various compounds and an X-ray structure of compound **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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