A New Route for the Preparation of Succinates

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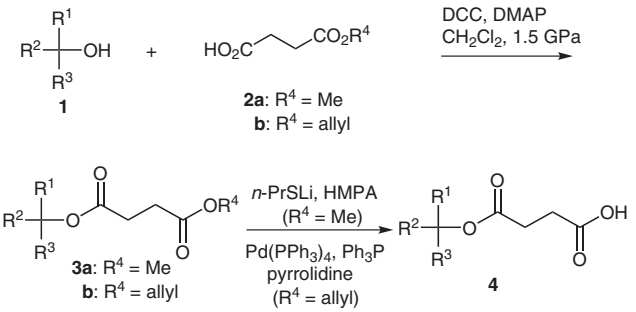
Abstract: Succinates of the tertiary hydroxy group having a formyl group in the structure were conveniently synthesized by oxidative cleavage of dihydropyrans prepared from lactones via coupling of ketene acetal triflates and zinc homoenolates.

Key words: succinates, dihydropyrans, esters, lactones, dihydroxylations

Butanedioic acid monoesters, namely the hemisuccinates, are found in several biologically active natural products such as punctatin C,[1] (–)-A26771B,[2] gamahonolide B,[3] and reveromycins.[4] It was reported that the hemisuccinyl group of reveromycin A, a selective isoleucyl-tRNS synthetase inhibitor, is important for its strong activity.[5] In addition, hemisuccinates attract much attention as the prodrugs of steroids,[6] anthracyclins,[7,8] and taxol[9–11] because of their water-soluble properties. Several methods for their preparation with succinic anhydride, succinic acid monoester, succinyl chloride, and the carboxylate anion have been reported.[6–11] However, few methods are known for the acylation of sterically hindered alcohols.[12,13] We have already reported an efficient preparation of the succinates **3** of hindered tertiary alcohols **1** with succinic acid monoesters **2** in dichloromethane in the presence of *N*,*N*′-dicyclohexylcarbodiimide or 1,3-diisopropylcarbodiimide and 4-(dimethylamino)pyridine under high pressure (1.5 GPa) and the conversion of the succinates **3** into the hemisuccinates **4** (Scheme 1).[14]

This procedure was successfully applied as a key step in the first asymmetric total synthesis of reveromycin A.[15] In this paper, we report a new general methodology for the preparation of succinates of tertiary alcohols without using high pressure (Scheme 2).



Scheme 1 Succinylation of tertiary alcohols **1** under high pressure

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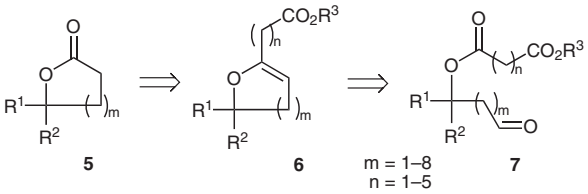
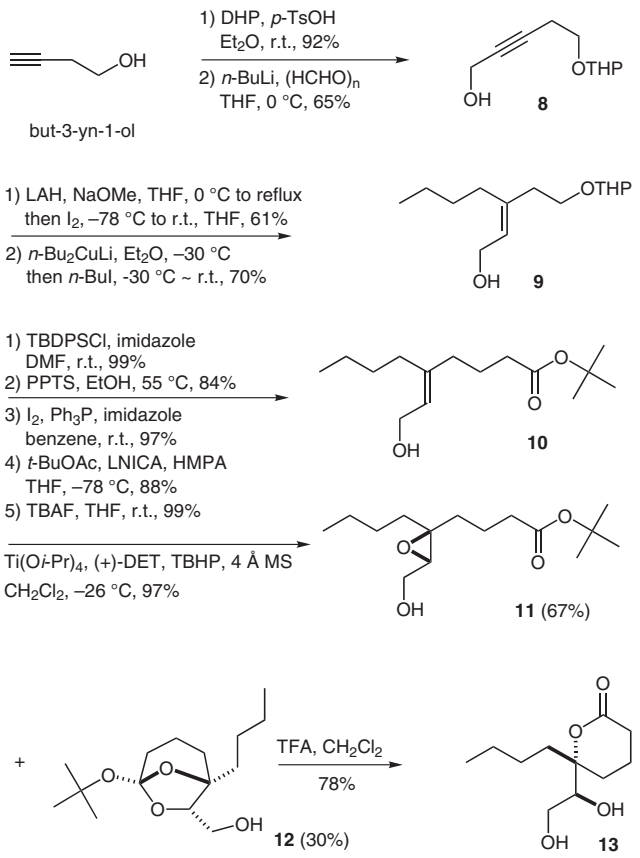


Scheme 2 Synthetic plan for dicarboxylic acid diesters **7**

Oxidative cleavage of olefinic double bonds to give dicarbonyl compounds is one of the most useful chemical conversions. It was expected that the cyclic vinyl ethers **6** having an α-substituent with a terminal ester group might be converted into the dicarboxylic acid diesters **7** that include a formyl group in their structure by oxidative cleavage of the double bond (Scheme 2). The cyclic vinyl ethers **6** could be prepared by palladium-catalyzed coupling of the ketene acetal triflate derived from the lactone **5** and ω-(ethoxycarbonyl)alkylzinc bromide. For confirmation of the hypothesis, δ-lactones **5** (m = 2) were converted into the succinates **7** (m = 2, n = 2) via the dihydropyrans **6** (m = 2, n = 2). The succinate **18** was selected as a model compound, which could be the key compounds for the synthesis of reveromycin A (Scheme 4).[15]

Lactone **13** was prepared as the model compound from but-3-yn-1-ol in 14% overall yield in eleven steps (Scheme 3). Namely, the propargyl alcohol **8**, prepared from but-3-yn-1-ol, was successively treated with lithium aluminum hydride/sodium methoxide and iodine to furnish the (*Z*)-vinyl iodide (61%), which was alkylated by treatment with lithium dibutylcuprate and then butyl iodide[16] to give the allyl alcohol **9** (70%). After protection of the hydroxy group in **9** by the *tert*-butyldiphenylsilyl group, the tetrahydropyran group was hydrolyzed with pyridinium 4-toluenesulfonate in ethanol at 55 °C to give the alcohol (84%, two steps), which was then converted into the iodide (97%). Alkylation of the iodide with *tert*-butyl acetate/lithium *N*-isopropylcyclohexylamide (LNICA) followed by deprotection of the *tert*-butyldiphenylsilyl group with tetrabutylammonium fluoride gave the *tert*-butyl ester **10** (88%, two steps). The Sharpless asymmetric epoxidation[17] of the allyl alcohol **10** with *tert*-butyl hydroperoxide in the presence of (+)-diethyl tartrate and titanium(IV) isopropoxide afforded the epoxide **11** (67%, 92% ee) and the bicyclo derivative **12** (30%, 92% ee). The enantiomeric excess of both **11** and **12** were determined on the basis of the ^{1}H NMR spectra of the corresponding MTPA esters. Hydrolysis of the *tert*-butyl ester group in **11** with trifluoroacetic acid resulted in simultaneous cy-

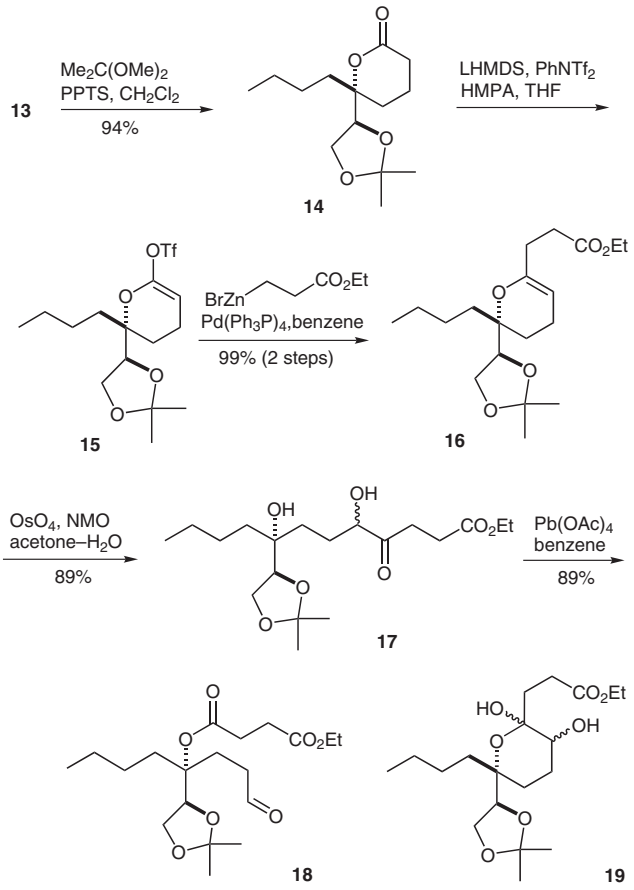


Scheme 3 Synthesis of lactone **13**

clization to give the lactone **13**. The bicyclo derivative **12** was also treated with trifluoroacetic acid to afford **13** as the sole product. Practically, the mixture of **11** and **12** directly produced the lactone diol **13** (78%) by treatment with trifluoroacetic acid.

Next, the lactone **13** was converted into the succinate **18** of the tertiary hydroxy group, which includes a formyl group in the structure, in 74% overall yield in five steps (Scheme 4). The hydroxy groups in **13** were protected as an acetonide to afford **14** (94%). The acetonide **14** was then treated with lithium hexamethyldisilazanide/*N*-phenylbis(trifluoromethanesulfonimide)[18] to give the ketene acetal triflate **15**, which was coupled with zinc homoenolate, 3-ethoxy-3-oxopropylzinc bromide, in the presence of tetrakis(triphenylphosphine)palladium[19] to afford the cyclic enol ether **16** (99%, two steps). Ozonolysis of **16** followed by reduction with dimethyl sulfide or triphenylphosphine afforded a mixture of the succinate **18** (10~51%) and the ketone diol **17** (~50%). The Lemieux–Johnson oxidation[20] of **16** with osmium tetroxide/sodium periodate also afforded a mixture of **17** and **18**. The succinate **18** might be a useful intermediate for the synthesis of reveromycin A. However, these oxidations were not reproducible. On the other hand, the oxidation of **16** with osmium tetroxide (0.1 equiv)/*N*-methylmorpholine *N*-oxide (14 equiv) in acetone–water (4:1) constantly gave **17** in good yield (89%), which is the ring-opened derivative of the desired dihydroxytetrahydropyran **19**. We anticipated that if **17** and **19** are in a state of equilibrium, the treatment of **17** with lead(IV) acetate might afford the succinate **18** via the oxidative cleavage of **19**. In fact, the treatment of **17** with lead(IV) acetate in benzene at room temperature promptly gave **18** in good yield (89%).

This new procedure for the preparation of the succinate of a tertiary alcohol was applied to the synthesis of derivatives having other protecting groups such as benzylidene acetal or silyl groups (Scheme 5). The treatment of the lactone diol **13** with benzaldehyde dimethyl acetal in the presence of 4-toluenesulfonic acid gave the benzylidene acetal **20** as a 1:1 mixture (90%). The ketene acetal triflate prepared from **20** by treatment with potassium hexamethyldisilazanide and *N*-phenylbis(trifluoromethanesulfonimide) in the presence of hexamethylphosphoramide was converted into the cyclic enol ether **21** via palladium-catalyzed coupling with the zinc homoenolate. The oxidation of dihydropyran **21** with osmium tetroxide/*N*-methylmorpholine *N*-oxide in acetone and water (78%, three steps) followed by treatment with lead(IV) acetate afforded the succinate **22** (84%), which also included the formyl group. The lactone diol **13** was then silylated with *tert*-butylchlorodiphenylsilane followed by the addition of chlorotriethylsilane in the presence of imidazole in *N*,*N*-dimethylformamide to give the silyl ether **23** (88%) in a one-pot procedure. Then, **23** was reacted with potassium hexamethyldisilazanide and *N*-phenylbis(trifluoro-

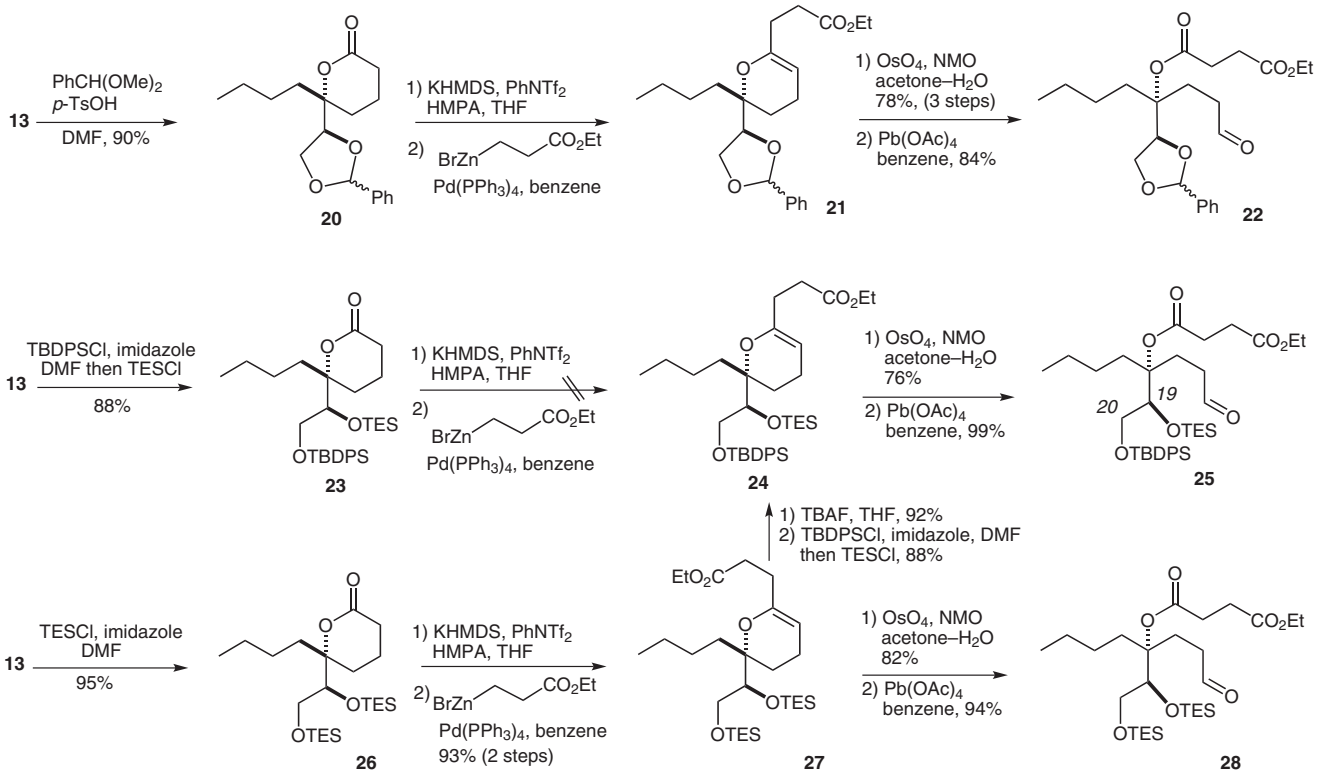


Scheme 4 Synthesis of succinate **18**

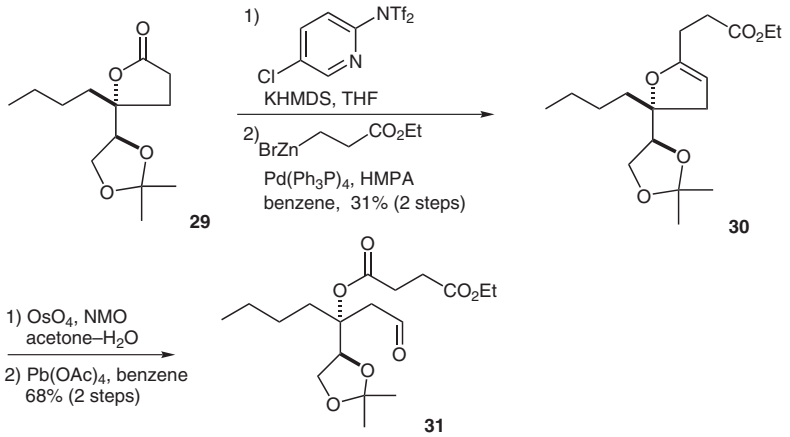
methanesulfonimide) in the presence of hexamethylphosphoramide to afford the triflate (99%), while no reaction occurred when lithium hexamethyldisilazanide was used in place of potassium hexamethyldisilazanide. The palladium-catalyzed coupling reactions of the triflate and zinc homoenolate in the presence of $Pd(PPh_3)_4$, $Pd(dppf)Cl_2$, or $PdCl_2(PPh_3)_2$ did not take place and the dihydropyran **24** was not obtained. It was assumed that the reason for no reaction is due to the steric hindrance resulting from both silyl groups. Next, another attempt to prepare the succinate **25** was made, because the Weinreb amide corresponding to the aldehyde **25** was conveniently used in the total synthesis of **1**.[15] The lactone diol **13** was protected with chlorotriethylsilane to afford the bis(triethylsilyl) ethers **26**. The triflate prepared from **26** using potassium hexamethyldisilazanide and *N*-phenylbis(trifluoromethanesulfonimide) reacted with zinc homoenolate to afford the dihydropyran **27** unlike the triflate of **23**. Deprotection of the silyl groups in **27** with tetrabutylammonium fluoride followed by silylation with *tert*-butylchlorodiphenylsilane and successive treatment with chlorotriethylsilane afforded the dihydropyran **24** (81%, two steps) having the triethylsilyl and *tert*-butyldiphenylsilyl groups. The treatment of **24** with osmium tetroxide/*N*-methylmorpholine *N*-oxide followed by oxidation with lead(IV) acetate formed the succinate **25** (75%, two steps). The dihydropyran **27** having bis(triethylsilyl) groups was also oxidatively cleaved by successive treatment with osmium tetroxide/*N*-methylmorpholine and lead(IV) acetate to afford the succinate **28** (77%, two steps). As a result, four succinates **18**, **22**, **25**, and **28** having a different protecting group were conveniently prepared via the oxidative cleavage of the corresponding dihydropyrans.

Next, this new procedure for the preparation of the succinate of the tertiary alcohol was applied to a γ-lactone **29**,[2,1] (**5**, m = 1) (Scheme 6). The acetonide **29** was treated with lithium hexamethyldisilazanide and *N*-phenylbis(trifluoromethanesulfonimide) in the presence of hexamethylphosphoramide to recover **29**, although the acetonide **14** was quantitatively converted into the triflate **15**. However, treatment of **29** with potassium hexamethyldisilazanide and *N*-phenylbis(trifluoromethanesulfonimide) afforded a labile triflate,[18] which was directly converted into the cyclic enol ether **30** via palladium-catalyzed coupling with the zinc homoenolate in low yield (16%, two steps). On the other hand, the use of the Commins' reagent in place of *N*-phenylbis(trifluoromethanesulfonimide) increased the yield (31%, two steps). The oxidation of the dihydrofuran **30** with osmium tetroxide/*N*-methylmorpholine in acetone and water followed by treatment with lead(IV) acetate afforded the succinate **31** (68%, two steps), which also include the formyl group.

In conclusion, the succinates **18**, **22**, **25**, **28** (**7**, m = 2, n = 2), and **31** (**7**, m = 1, n = 2) of the tertiary hydroxy group having a formyl group in the structures were generally synthesized by oxidative cleavage of the dihydropyrans **16**, **21**, **24**, and **27** and the dihydrofuran **30**, prepared from the lactones **13** and **29**, respectively, via coupling of the ketene acetal triflates and ω-(ethoxycarbonyl)alkylzinc bromide. This protocol would be applicable to the preparation of the dicarboxylic acid diesters **7** (m = 3–8,



Scheme 5 Synthesis of succinates **22**, **25**, and **28**



Scheme 6 Synthesis of succinate **31**

n = 1, 3–5) because zinc reagents [$EtO_2C(CH_2)_nZnBr$: n = 1–5] are commercially available or known.

All reactions were carried out under N_2 with anhydrous solvents under anhydrous conditions, unless otherwise noted. Anhyd Et_2O, CH_2Cl_2, THF, and DMF were purchased from Kanto Chemical Co., Ltd, and purified with the GlassContour solvent dispensing system. Kanto chemical silica gel 60 N (spherical, neutral) (40–100 μm) was used for flash chromatography. NMR spectra were recorded on a Jeol JNM-ECP-500 or a JNM-AL-400 spectrometer in $CDCl_3$ with TMS δ = 0 (^{1}H NMR) or $CDCl_3$ δ = 77.1 (^{13}C NMR) as internal standard. IR spectra were recorded on a Jasco VALOR-III FT-IR spectrophotometer. Optical rotations were recorded on a Jasco DIP-370 digital polarimeter. HRMS were recorded on a Jeol MStation JMS-700 mass spectrometer under FAB conditions.

5-(Tetrahydro-2*H*-pyran-2-yloxy)pent-2-yn-1-ol (8)
4-(Tetrahydro-2*H*-pyran-2-yloxy)but-1-yne
To a stirred soln of but-3-yn-1-ol (10.0 g, 143 mmol) and 3,4-dihydro-2*H*-pyran (14.4 g, 171 mmol) in Et_2O (200 mL) at r.t. was added *p*-TsOH (0.400 g, 2.10 mmol). The mixture was stirred for 1 d, quenched with aq $NaHCO_3$ (40 mL), and diluted with Et_2O. The organic layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 20:1) to provide the product (20.3 g, 92%) as a colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.5–1.9 (m, 6 H), 1.98 (t, *J* = 2.6 Hz, 1 H), 2.50 (dt, *J* = 6.9, 2.6 Hz, 2 H), 3.52 (m, 1 H), 3.57 (dt, *J* = 9.6, 6.9 Hz, 1 H), 3.84 (dt, *J* = 9.6, 6.9 Hz, 1 H), 3.89 (m, 1 H), 4.66 (dd, *J* = 4.0, 3.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.4, 19.9, 25.4, 30.5, 62.2, 65.5, 69.2, 81.4, 98.8.

5-(Tetrahydro-2*H*-pyran-2-yloxy)pent-2-yn-1-ol (8)
To a soln of 4-(tetrahydro-2*H*-pyran-2-yloxy)but-1-yne (4.30 g, 27.9 mmol) in THF (100 mL) at 0 °C was added 1.52 M *n*-BuLi in *n*-hexane (22.0 mL, 33.5 mmol). The mixture was stirred at this temperature for 30 min. To the mixture was added $(HCHO)_n$ (1.10 g, 36.3 mmol) in one portion, and the mixture was allowed to warm to r.t. After 2.5 h, the mixture was added to aq NH_4Cl (10 mL) and diluted with Et_2O. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to provide **8** (3.32 g, 65%) as a yellow oil.

IR (neat): 3415, 2940, 2870, 1440, 1352, 1134, 1118, 1018, 969 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.5–2.1 (m, 6 H), 2.53 (m, 2 H), 3.52 (m, 1 H), 3.57 (dt, *J* = 9.6, 7.3 Hz, 1 H), 3.82 (dt, *J* = 9.6, 7.3 Hz, 1 H), 3.88 (m, 1 H), 4.24 (br s, 2 H), 4.64 (dd, *J* = 4.1, 3.2 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.5, 20.3, 25.4, 30.6, 51.3, 62.4, 65.7, 79.5, 83.2, 98.9.

(*E*)-3-[2-(Tetrahydro-2*H*-pyran-2-yloxy)ethyl]hept-2-en-1-ol (9)
(*Z*)-3-Iodo-5-(tetrahydro-2*H*-pyran-2-yloxy)pent-2-en-1-ol
To a stirred soln of **8** (7.18 g, 39.0 mmol) in THF (325 mL) at 0 °C was added NaOMe (5.05 g, 93.6 mmol) and suspension of $LiAlH_4$ (1.78 g, 46.8 mmol) in THF (40 mL) over 20 min. The mixture was heated under reflux for 3 h and then cooled to 0 °C. EtOAc (1.52 mL) was added and the mixture was stirred for 20 min. The mixture was cooled to –78 °C and I_2 (14.8 g, 58.5 mmol) in THF (65 mL) was added. The mixture was allowed to warm to r.t., quenched with aq $Na_2S_2O_3$, and diluted with Et_2O. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to provide the vinyl iodide (7.42 g, 61%) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.5–1.9 (m, 7 H), 2.80 (t, *J* = 6.6 Hz, 2 H), 3.54 (m, 1 H), 3.57 (dt, *J* = 10.2, 6.6 Hz, 1 H), 3.86 (m, 1 H), 3.87 (dt, *J* = 10.2, 6.6 Hz, 1 H), 4.18 (d, *J* = 5.6 Hz, 2 H), 4.61 (dd, *J* = 3.3, 2.6 Hz, 1 H), 5.95 (tt, *J* = 5.6, 1.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.4, 25.3, 30.5, 45.2, 62.4, 65.9, 67.2, 98.9, 104.7, 135.8.

(*E*)-3-[2-(Tetrahydro-2*H*-pyran-2-yloxy)ethyl]hept-2-en-1-ol (9)
To a suspension of CuI (9.27 g, 48.7 mmol) in Et_2O (100 mL) at –20 °C was added 1.52 M *n*-BuLi in hexane (64.1 mL, 97.4 mmol) over 20 min, and then the mixture was stirred for 30 min at this temperature. To the cooled mixture at –30 °C was added the vinyl iodide (3.04 g, 9.74 mmol) in Et_2O (30 mL) over 20 min. After 5 h, *n*-BuI (2.21 mL, 19.4 mmol) was added and the mixture was stirred at r.t. for 1 d. The mixture was diluted with Et_2O and H_2O and filtered through a pad of Celite. The organic layer was washed with H_2O and brine, dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to provide **9** (1.65 g, 70%) as a yellow oil.

IR (neat): 3407, 2933, 2867, 1662, 1025, 498 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.9 Hz, 3 H), 1.2–1.9 (m, 10 H), 2.08 (t, *J* = 7.3 Hz, 2 H), 2.33 (t, *J* = 7.3 Hz, 2 H), 3.49 (dt, *J* = 9.9, 7.3 Hz, 1 H), 3.50 (m, 1 H), 3.82 (dt, *J* = 9.9, 7.3 Hz, 1

H), 3.85 (m, 1 H), 4.15 (d, *J* = 6.6 Hz, 2 H), 4.59 (dd, *J* = 5.1, 2.8 Hz, 1 H), 5.45 (t, *J* = 6.6 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 19.6, 22.7, 25.4, 30.5, 30.7, 30.9, 36.7, 59.1, 62.4, 66.4, 98.8, 125.2, 140.9.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{26}NaO_3$: 265.1780; found: 265.1775.

tert-Butyl (*E*)-5-(2-Hydroxyethylidene)nonanoate (10)

(*E*)-3-[2-(*tert*-Butyldiphenylsiloxy)ethylidene]-1-(tetrahydro-2*H*-pyran-2-yloxy)heptane

To a mixture of **9** (2.95 g, 12.2 mmol) and imidazole (1.82 g, 26.8 mmol) in DMF (12 mL) at r.t. was added TBDPSCl (3.43 mL, 13.4 mmol). The mixture was stirred for 2 h and then diluted with Et_2O. The organic layer was washed with H_2O, 1 M HCl, aq $NaHCO_3$, and then brine, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 10:1) to provide the silyl ether (5.80 g, 99%) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 7.0 Hz, 3 H), 1.03 (s, 9 H), 1.1–1.9 (m, 10 H), 1.85 (t, *J* = 7.6 Hz, 2 H), 2.29 (t, *J* = 7.3 Hz, 2 H), 3.45 (dt, *J* = 9.8, 7.3 Hz, 1 H), 3.51 (m, 1 H), 3.79 (dt, *J* = 9.8, 7.3 Hz, 1 H), 3.88 (m, 1 H), 4.21 (d, *J* = 6.1 Hz, 2 H), 4.60 (dd, *J* = 4.0, 3.1 Hz, 1 H), 5.42 (t, *J* = 6.1 Hz, 1 H), 7.39 (m, 6 H), 7.68 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 19.2, 19.7, 22.7, 25.6, 26.9, 30.7, 30.8, 36.7, 60.8, 62.4, 66.6, 98.8, 125.9, 127.7, 129.6, 134.1, 135.6, 135.7, 138.6.

(*E*)-3-[2-(*tert*-Butyldiphenylsiloxy)ethylidene]heptan-1-ol

To a stirred soln of the silyl ether (4.81 g, 10.0 mmol) in EtOH (100 mL) was added PPTS (251 mg, 1.00 mmol). After heating at 55 °C for 2 h, the mixture was cooled. Et_3N (202.4 μL, 2.0 mmol) was added to the mixture and the solvent was evaporated. The residue was diluted with Et_2O and the organic layer was washed with H_2O, 1 M HCl, 1 M $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 10:1) to provide the alcohol (3.33 g, 84%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7.3 Hz, 3 H), 1.04 (s, 9 H), 1.1–1.4 (m, 4 H), 1.81 (br t, *J* = 7.3 Hz, 2 H), 2.24 (br t, *J* = 6.0 Hz, 2 H), 3.63 (br t, *J* = 6.0 Hz, 2 H), 4.23 (d, *J* = 6.6 Hz, 2 H), 5.44 (br t, *J* = 6.6 Hz, 1 H), 7.40 (m, 6 H), 7.69 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 19.1, 22.6, 30.0, 30.7, 39.6, 60.4, 60.5, 127.2, 127.6, 129.6, 133.8, 135.6, 137.8.

(*E*)-3-[2-(*tert*-Butyldiphenylsiloxy)ethylidene]-1-iodoheptane

To a stirred soln of the alcohol (4.11 g, 10.4 mmol) in benzene (30 mL) at r.t. was added imidazole (1.06 g, 15.6 mmol), Ph_3P (4.09 g, 15.6 mmol), and I_2 (3.96 g, 15.6 mmol). The mixture was stirred for 15 min then it was diluted with Et_2O. The organic layer was washed with H_2O, aq $Na_2S_2O_3$, and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 10:1) to provide the iodide (5.11 g, 97%) as a colorless oil.

IR (neat): 2958, 2931, 2858, 1428, 1112 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 6.9 Hz, 3 H), 1.04 (s, 9 H), 1.18 (m, 4 H), 1.80 (t, *J* = 7.3 Hz, 2 H), 2.53 (t, *J* = 7.6 Hz, 2 H), 3.16 (t, *J* = 7.6 Hz, 2 H), 4.21 (d, *J* = 6.3 Hz, 2 H), 5.41 (br t, *J* = 6.3 Hz, 1 H), 7.40 (m, 6 H), 7.69 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 4.1, 13.9, 19.1, 22.6, 26.8, 29.8, 30.6, 41.0, 60.6, 126.8, 127.6, 129.5, 133.9, 135.6, 140.0.

tert-Butyl (*E*)-5-[2-(*tert*-Butyldiphenylsiloxy)ethylidene]nonanoate

To a soln of *i*-PrNHCy (602 μL, 3.30 mmol) in THF (5 mL) at 0 °C was added 1.53 M *n*-BuLi in hexane (1.96 mL, 3.00 mmol). The mixture was stirred at this temperature for 15 min. The mixture was cooled to –78 °C, and *t*-BuOAc (445 μL, 3.30 mmol) was added. The mixture was stirred for 10 min and then HMPA (555 μL, 3.00 mmol) and the iodide (506 mg, 1.00 mmol) were added. The mixture was stirred for 1 h and then slowly warmed to r.t. The mixture was quenched with aq NH_4Cl and diluted with Et_2O. The organic layer was washed with 1 M HCl, 1 M $NaHCO_3$, and brine, dried ($MgSO_4$), and the solvent evaporated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 50:1) to provide the *tert*-butyl ester (435 mg, 88%) as a colorless oil.

IR (neat): 2932, 2859, 1731, 1147, 1112, 702 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7.0 Hz, 3 H), 1.05 (s, 9 H), 1.18 (m, 4 H), 1.46 (s, 9 H), 1.67 (m, 2 H), 1.80 (t, *J* = 7.5 Hz, 2 H), 1.99 (t, *J* = 7.7 Hz, 2 H), 2.20 (t, *J* = 7.7 Hz, 2 H), 4.21 (d, *J* = 6.2 Hz, 2 H), 5.37 (t, *J* = 6.3 Hz, 1 H), 7.39 (m, 6 H), 7.69 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.9, 19.1, 22.6, 23.3, 26.8, 28.1, 29.9, 30.6, 35.0, 35.8, 60.7, 79.9, 124.9, 127.6, 129.5, 134.0, 135.5, 140.7, 173.1.

tert-Butyl (*E*)-5-(2-Hydroxyethylidene)nonanoate (10)

To a soln of the *tert*-butyl ester (864 mg, 1.75 mmol) in THF (15 mL) was added TBAF (915 mg, 3.50 mmol) at r.t. and the mixture was stirred for 1 h. The mixture was diluted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 5:1) to provide **10** (443 mg, 99%) as a colorless oil.

IR (neat): 3386, 2958, 2933, 2873, 1731, 1457, 1368, 1256, 1147, 1001, 847 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.0 Hz, 3 H), 1.2–1.4 (m, 5 H), 1.45 (s, 9 H), 1.71 (m, 2 H), 2.03 (t, *J* = 6.9 Hz, 2 H), 2.05 (t, *J* = 6.9 Hz, 2 H), 2.21 (t, *J* = 7.3 Hz, 2 H), 4.15 (dd, *J* = 6.9, 5.0 Hz, 2 H), 5.40 (t, *J* = 6.9 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 22.8, 23.4, 28.2, 30.0, 31.0, 35.2, 36.0, 59.2, 80.2, 124.3, 143.2, 173.0.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{28}NaO_3$: 279.1936; found: 279.1937.

tert-Butyl 4-[(2*S*,3*S*)-2-Butyl-3-(hydroxymethyl)oxiran-2-yl]butanoate (11) and [(1*R*,5*S*,7*S*)-5-*tert*-Butoxy-1-butyl-6,8-dioxabicyclo[3.2.1]octan-7-yl]methanol (12)

To a stirred suspension of MS4A (523 mg) in CH_2Cl_2 (10 mL) at –26 °C was added Ti(O*i*-Pr)$_4$ (387 μL, 1.32 mmol) and (+)-DET (282 μL, 1.65 mmol). After 15 min, allyl alcohol **10** (843 mg, 3.29 mmol) in CH_2Cl_2 (5 mL) was added and the mixture was stirred for 20 min. 5 M TBHP in decane (0.99 mL, 4.94 mmol) was added and the mixture was kept at –26 °C for 1 d. The mixture was quenched with aq Na_2SO_4 (16.5 mL) and diluted with EtOAc. The mixture was filtered through a pad of Celite and the solvent was evaporated. The residue was purified by flash chromatography (*n*-hexane–EtOAc, 5:1) to provide epoxide **11** (600 mg, 67%) as a colorless oil and bicyclo derivative **12** (269 mg, 30%) as a colorless oil:

Epoxide 11

$[\alpha]_D^{27}$ –7.7 (*c* 1.58, $CHCl_3$).

IR (neat): 3436, 2957, 2932, 2871, 1727, 1367, 1146, 1034 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.9 Hz, 3 H), 1.2–1.7 (m, 10 H), 1.45 (s, 9 H), 2.24 (m, 2 H), 2.96 (dd, *J* = 6.9, 4.6 Hz, 1 H), 3.69 (ddd, *J* = 11.9, 6.9, 3.2 Hz, 1 H), 3.84 (ddd, *J* = 11.9, 6.0. 4.6 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 20.4, 23.0, 27.5, 28.2, 30.1, 34.4, 35.4, 61.2, 62.9, 63.9, 80.4, 172.8.

HRMS (FAB): *m/z* [M + H]$^+$ calcd for $C_{15}H_{29}O_4$: 273.2066; found: 273.2062.

Bicyclo Derivative 12

$[\alpha]_D^{27}$ +26.0 (*c* 3.80, $CHCl_3$).

IR (neat): 3433, 2933, 2873, 1730, 1389, 1236, 1101, 1026 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.8 Hz, 3 H), 1.3–2.0 (m, 12 H), 1.40 (s, 9 H), 3.61 (br, 1 H), 3.96 (dd, *J* = 11.0, 8.7 Hz, 1 H), 4.01 (ddd, *J* = 8.7, 3.2, 1.4 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 18.9, 23.2, 25.9, 28.6, 30.6, 34.2, 36.3, 61.4, 77.0, 82.0, 83.4, 121.4.

HRMS (FAB): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{28}NaO_4$: 295.1885; found: 295.1887.

(*R*)-6-Butyl-6-[(*S*)-1,2-dihydroxyethyl]tetrahydro-2*H*-pyran-2-one (13)

To a stirred soln of **11** and **12** (272 mg, 1.00 mmol) in CH_2Cl_2 (6 mL) was added TFA (7.7 μL, 0.10 mmol) at r.t. and the mixture was stirred at this temperature for 1 d. To the mixture was added Et_3N (27.9 μL, 0.2 mmol) and then it was diluted with Et_2O. The organic layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 1:1) to provide **13** (169 mg, 78%) as a colorless oil.

$[\alpha]_D^{27}$ +18.3 (*c* 1.00, $CHCl_3$).

IR (neat): 3401, 2958, 2873, 1706, 1256, 1042 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.2 Hz, 3 H), 1.2–2.1 (m, 10 H), 2.32 (br, 1 H), 2.48 (m, 2 H), 3.10 (br, 1 H), 3.56 (dd, *J* = 11.2, 3.0 Hz, 1 H), 3.72 (dd, *J* = 11.2, 3.0 Hz, 1 H), 3.88 (dd, *J* = 8.4, 3.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 16.9, 23.1, 25.1, 26.0, 29.9, 36.9, 62.1, 75.5, 87.4, 172.9.

HRMS (FAB): *m/z* [M + H]$^+$ calcd for $C_{11}H_{21}O_4$: 217.1440; found: 217.1434.

(*R*)-6-Butyl-6-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]tetrahydro-2*H*-pyran-2-one (14)

To a mixture of **13** (108 mg, 0.50 mmol) and acetone dimethyl acetal (306 μL, 2.50 mmol) in CH_2Cl_2 (7 mL) was added PPTS (12.6 mg, 0.05 mmol) at r.t. The mixture was stirred for 3 h and quenched with Et_3N (13.9 μL, 0.10 mmol). The mixture was diluted with Et_2O and the organic layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to provide **14** (120 mg, 94%) as a colorless oil.

$[\alpha]_D^{27}$ +6.0 (*c* 1.00, $CHCl_3$).

IR (neat): 2958, 2933, 1735, 1255, 1065, 756 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.6 Hz, 3 H), 1.2–2.0 (m, 10 H), 1.33 (s, 3 H), 1.45 (s, 3 H), 2.45 (m, 2 H), 3.81 (dd, *J* = 8.8, 6.4 Hz, 1 H), 4.02 (dd, *J* = 8.8, 7.1 Hz, 1 H), 4.25 (dd, *J* = 7.1, 6.4 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 17.1, 23.1, 24.7, 25.1, 25.9, 26.1, 30.1, 36.3, 64.8, 79.3, 85.2, 109.7, 171.3.

HRMS (FAB): *m/z* [M + H]$^+$ calcd for $C_{14}H_{25}O_4$: 257.1753; found: 257.1751.

(*R*)-6-Butyl-6-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-5,6-dihydro-4*H*-pyran-2-yl Trifluoromethanesulfonate (15)

To a soln of **14** (20.0 mg, 78 μmol) in THF (1 mL) was added 1.0 M LHMDS in THF (234 μL, 234 μmol) and HMPA (20.3 μL, 117 μmol) at –78 °C and the mixture was stirred at this temperature for 2 h. A soln of $PhNTf_2$ (33.2 mg, 93 μmol) in THF (1 mL) was added, and the mixture was stirred for 7 h, and then slowly warmed to r.t. To the mixture was added Et_3N (221 μL, 1.59 mmol) and it was then diluted with hexane. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 10:1, 1% Et_3N) to provide **15** (30.3 mg) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 6.8 Hz, 3 H), 1.2–1.8 (m, 8 H), 1.35 (2 s, 3 H), 1.43 (s, 3 H), 2.11 (m, 2 H), 3.93 (dd, *J* = 8.7, 6.3 Hz, 1 H), 4.02 (dd, *J* = 8.7, 6.9 Hz, 1 H), 4.29 (dd, *J* = 6.9, 6.3 Hz, 1 H), 4.68 (dd, *J* = 4.0, 3.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 17.8, 23.7, 24.7, 25.5, 25.5, 26.5, 31.6, 65.0, 76.5, 84.8, 86.9, 110.0, 118.8, 149.3.

Ethyl 3-{(*R*)-6-Butyl-6-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-5,6-dihydro-4*H*-pyran-2-yl}propanoate (16); Typical Procedure

To a soln of the enol triflate **15** (30.3 mg, 78 μmol) in benzene (1 mL) was successively added $Pd(PPh_3)_4$ (4.6 mg, 4 μmol) and 0.5 M 3-ethoxy-3-oxopropylzinc bromide in THF (312 μL, 156 μmol) at r.t. The mixture was stirred for 2 h and Et_3N (174 μL, 1.25 mmol) was added. The mixture was filtered through a pad of silica gel and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 10:1) to provide **16** (26.3 mg, 99%) as a colorless oil.

$[\alpha]_D^{27}$ –3.9 (*c* 1.00, $CHCl_3$).

IR (neat): 2956, 2932, 2873, 1736, 1678, 1456, 1370, 1250, 1210, 1155, 1069, 1044, 855 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.3 Hz, 3 H), 1.2–1.7 (m, 8 H), 1.25 (t, *J* = 7.3 Hz, 3 H), 1.35 (s, 3 H), 1.43 (s, 3 H), 1.99 (m, 2 H), 2.32 (t, *J* = 7.8 Hz, 2 H), 2.43 (m, 2 H), 3.91 (dd, *J* = 8.2, 6.4 Hz, 1 H), 3.96 (dd, *J* = 8.2, 6.8 Hz, 1 H), 4.12 (q, *J* = 7.3 Hz, 2 H), 4.25 (t, *J* = 6.4 Hz, 1 H), 4.49 (dd, *J* = 3.7 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 14.5, 17.5, 23.6, 25.3, 25.5, 25.5, 26.3, 30.1, 31.8, 32.4, 60.4, 64.8, 77.1, 77.4, 94.6, 109.2, 150.7, 173.0.

HRMS (FAB): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{32}NaO_5$: 363.2147; found: 363.2150.

Ethyl (*R*)-8-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-5,8-dihydroxy-4-oxododecanoate (17); Typical Procedure

To a soln of **16** (30.0 mg, 88 μmol) in acetone–H_2O (4:1, 1 mL) was added 2.5 wt% OsO_4 in *t*-BuOH (2.9 μL, 0.2 μmol) and NMO (15.5 mg, 130 μmol) at r.t. The mixture was stirred for 1 d and diluted with Et_2O. To the mixture was added aq $Na_2S_2O_3$ and it was stirred for 10 min. After the addition of H_2O, the mixture was stirred for 40 min and diluted with EtOAc. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to afford **17** (29.0 mg, 89%) as a colorless oil.

IR (neat): 3469, 2956, 2935, 1716, 1371, 1209, 1069, 859 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (m, 3 H), 1.2–2.1 (m, 10 H), 1.25 (m, 3 H), 1.35 (m, 3 H), 1.42 (m, 3 H), 2.18 (br, 1 H), 2.64 (m, 2 H), 2.80 (m, 2 H), 3.70 (br, 1 H), 3.86 (m, 1 H), 3.94 (m, 1 H), 4.03 (m, 1 H), 4.13 (m, 2 H), 4.22 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.2, 23.5, 25.6, 25.6, 26.1, 26.6, 27.5, 28.0, 32.7, 36.5, 60.9, 64.7, 73.0, 76.7, 79.5, 108.9, 172.3, 210.5.

HRMS (FAB): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{34}NaO_7$: 397.2202; found: 397.2206.

(*R*)-1-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-1-(3-oxopropyl)pentyl Ethyl Succinate (18); Typical Procedure

To a soln of **17** (29 mg, 77 μmol) in benzene (1 mL) was added $Pb(OAc)_4$ (51 mg, 0.166 mmol) at r.t. The mixture was stirred for 30 min, diluted with Et_2O, and filtered through Celite. After evapo-

ration of the solvents, the resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to afford **18** (25.4 mg, 89%) as a colorless oil.

$[\alpha]_D^{27}$ –1.4 (*c* 0.80, $CHCl_3$).

IR (neat): 2959, 2931, 1729, 1460, 1371, 1270, 1160, 1071, 859 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, 3 H), 1.2–1.6 (m, 4 H), 1.26 (t, *J* = 7.3 Hz, 3 H), 1.32 (s, 3 H), 1.41 (s, 3 H), 1.84 (t, 2 H), 2.13 (m, 1 H), 2.35 (m, 1 H), 2.57 (s, 4 H), 2.62 (m, 2 H), 3.88 (dd, *J* = 8.5, 7.0 Hz, 1 H), 3.96 (dd, *J* = 8.5, 7.0 Hz, 1 H), 4.14 (q, *J* = 7.3 Hz, 2 H), 4.55 (t, *J* = 7.0 Hz, 1 H), 9.76 (t, *J* = 1.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 14.4, 23.5, 24.9, 25.6, 26.3, 27.2, 29.3, 30.1, 33.0, 39.0, 60.9, 65.4, 78.5, 85.6, 109.3, 172.1, 172.3, 201.6.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{32}NaO_7$: 395.2046; found: 395.2049.

(*R*)-6-Butyl-6-[(*S*)-2-phenyl-1,3-dioxolan-4-yl]tetrahydro-2*H*-pyran-2-one (20)

To a mixture of **13** (46.0 mg, 210 μmol) and benzaldehyde dimethyl acetal (64.0 μL, 430 μmol) in DMF (1 mL) was added *p*-TsOH (4.0 mg, 21 μmol) at r.t. The mixture was stirred for 3 h and quenched with Et_3N (7.0 μL, 0.05 mmol). The mixture was diluted with Et_2O and the organic layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to provide **20** (58.3 mg, 90%) as a colorless oil as a 1:1 mixture of diastereomers.

IR (neat): 2995, 2872, 1729, 1458, 1401, 1329, 1251 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.3 Hz, 3 H), 0.92 (t, *J* = 6.8 Hz, 3 H), 1.2–2.1 (m, 20 H), 2.42 (m, 2 H), 2.50 (m, 2 H), 3.97 (dd, *J* = 8.1, 6.9 Hz, 1 H), 4.09 (m, 2 H), 4.18 (dd, *J* = 8.7, 6.9 Hz, 1 H), 4.33 (dd, *J* = 6.9, 6.9 Hz, 1 H), 4.37 (dd, *J* = 7.3, 5.9 Hz, 1 H), 5.76 (s, 1 H), 6.05 (s, 1 H), 7.3–7.5 (m, 10 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 16.7, 17.0, 23.1, 23.1, 25.0, 25.4, 26.0, 26.1, 30.0, 30.0, 35.9, 36.1, 65.9, 66.1, 79.3, 79.8, 85.4, 86.1, 104.3, 104.7, 125.7, 126.1, 128.4, 129.3, 129.5, 136.4, 137.9, 171.1, 171.4.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{24}NaO_4$: 327.1572; found: 327.1565.

Ethyl 3-{(*R*)-6-Butyl-6-[(*S*)-2-phenyl-1,3-dioxolan-4-yl]-5,6-dihydro-4*H*-pyran-2-yl}propanoate (21)

(*R*)-6-Butyl-6-[(*S*)-2-phenyl-1,3-dioxolan-4-yl]-5,6-dihydro-4*H*-pyran-2-yl Trifluoromethanesulfonate

To a soln of **20** (16.1 mg, 53 μmol) in THF (1 mL) was added 0.5 M KHMDS in THF (528 μL, 264 μmol) and HMPA (45.0 μL, 264 μmol) at –78 °C and the mixture was stirred at this temperature for 30 min. A soln of $PhNTf_2$ (94.0 mg, 264 μmol) in THF (1 mL) was added and the mixture was stirred for 30 min. To the mixture was added Et_3N (336 μL, 2.64 mmol) and the mixture was diluted with hexane. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 2:1, 1% Et_3N) to provide crude enol triflate (169 mg) as a colorless oil as a 1:1 mixture of diastereomers.

^1H NMR (500 MHz, $CDCl_3$) (both diastereomers): δ = 0.88 (t, *J* = 7.3 Hz, 3 H), 0.88 (t, *J* = 7.3 Hz, 3 H), 1.2–2.3 (m, 20 H), 4.05 (dd, *J* = 8.7, 6.9 Hz, 1 H), 4.07 (dd, *J* = 7.8, 7.8 Hz, 1 H), 4.17–4.28 (m, 2 H), 4.37 (dd, *J* = 6.9, 6.9 Hz, 1 H), 4.44 (dd, *J* = 7.8, 5.0 Hz, 1 H), 4.71 (m, 1 H), 4.72 (m, 1 H), 5.75 (s, 1 H), 5.93 (s, 1 H), 7.3–7.5 (m, 10 H).

Ethyl 3-{(*R*)-6-Butyl-6-[(*S*)-2-phenyl-1,3-dioxolan-4-yl]-5,6-dihydro-4*H*-pyran-2-yl}propanoate (21)

Following the typical procedure for **16** using enol triflate (169 mg, <53 μmol) in benzene (1 mL), $Pd(PPh_3)_4$ (4.6 mg, 4 μmol), and 0.5 M 3-ethoxy-3-oxopropylzinc bromide in THF (212 μL, 106 μmol). Work up used Et_3N (105 μL, 0.85 mmol) to give crude dihydropyran **21** (46 mg) as a colorless oil as a 1:1 mixture of diastereomers.

IR (neat): 2956, 2930, 2871, 1734, 1678, 1458, 1373, 1293 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) (both diastereomers): δ = 0.89 (t, *J* = 7.3 Hz, 3 H), 0.91 (t, *J* = 7.3 Hz, 3 H), 1.2–2.1 (m, 20 H), 1.24 (t, *J* = 7.3 Hz, 3 H), 1.25 (t, *J* = 7.3 Hz, 3 H), 2.3–2.5 (m, 8 H), 4.00 (dd, *J* = 8.2, 7.8 Hz, 1 H), 4.05 (dd, *J* = 8.7, 6.8 Hz, 1 H), 4.13 (m, 6 H), 4.32 (dd, *J* = 6.8, 6.8 Hz, 1 H), 4.37 (dd, *J* = 7.8, 6.0 Hz, 1 H), 4.51 (m, 2 H), 5.80 (s, 1 H), 5.96 (s, 1 H), 7.3–7.5 (m, 10 H).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{32}NaO_5$: 411.2147; found: 411.2144.

Ethyl (*R*)-1-(3-Oxopropyl)-1-[(*S*)-2-phenyl-1,3-dioxolan-4-yl]pentyl Succinate (22)

Ethyl (*R*)-5,8-Dihydroxy-4-oxo-8-[(*S*)-2-phenyl-1,3-dioxolan-4-yl]dodecanoate

To a soln of the crude **21** (46.0 mg, <53 μmol) in acetone–H_2O (4:1, 1 mL) was added 2.5 wt% OsO_4 in *t*-BuOH (107 μL, 5.3 μmol) and NMO (9.3 mg, 80 μmol) at r.t. The mixture was stirred for 2 h and diluted with EtOAc. To the mixture was added aq $Na_2S_2O_3$ and it was stirred for 10 min. After the addition of H_2O, the mixture was stirred for 40 min and diluted with EtOAc. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 2:1) to afford dihydroxy ketone (17.5 mg, 78%, 3 steps from **20**) as a colorless oil as a 2:2:1:1 mixture of diastereomers.

IR (neat): 3476, 2956, 2933, 2872, 1715, 1459, 1399, 1376, 1206, 1090 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) (both diastereomers): δ = 0.91 (m, 18 H), 1.2–2.1 (m, 60 H), 1.25 (m, 18 H), 2.18 (br, 2 H), 2.22 (br, 2 H), 2.29 (br, 2 H), 2.65 (m, 12 H), 2.80 (m, 12 H), 3.64 (br s, 2 H), 3.69 (br s, 4 H), 4.02 (m, 6 H), 4.12 (m, 12 H), 4.17 (m, 12 H), 4.18 (m, 6 H), 4.23 (m, 3 H), 4.28 (m, 3 H), 5.79 (s, 2 H), 5.80 (s, 1 H), 5.97 (s, 2 H), 5.98 (s, 1 H), 7.3–7.5 (m, 30 H).

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{34}NaO_7$: 445.2202; found: 445.2200.

Ethyl (*R*)-1-(3-Oxopropyl)-1-[(*S*)-2-phenyl-1,3-dioxolan-4-yl]pentyl Succinate (22)

Following the typical procedure for **18** using dihydroxy ketone (14.6 mg, 35 μmol) in benzene (1 mL) and $Pb(OAc)_4$ (23.0 mg, 52 μmol) with stirring for 10 min. Flash chromatography (*n*-hexane–EtOAc, 3:1) afforded succinate **22** (12.2 mg, 84%) as a colorless oil as a 1:1 mixture of diastereomers.

IR (neat): 2958, 2929, 2873, 1725, 1460, 1376, 1270, 1158, 1069 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) (both diastereomers): δ = 0.89 (t, *J* = 6.9 Hz, 3 H), 0.92 (t, *J* = 6.9 Hz, 3 H), 1.2–2.7 (m, 20 H), 1.25 (t, *J* = 7.3 Hz, 6 H), 2.58 (m, 8 H), 4.03 (m, 2 H), 4.13 (m, 6 H), 4.61 (dd, *J* = 6.9, 6.9 Hz, 1 H), 4.72 (dd, *J* = 6.8, 6.8 Hz, 1 H), 5.72 (s, 1 H), 5.74 (s, 1 H), 7.3–7.5 (m, 10 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 14.1, 14.3, 23.2, 23.3, 25.5, 25.6, 26.9, 27.1, 29.2, 29.2, 29.8, 30.0, 33.0, 33.1, 38.8, 39.1, 60.8, 60.9, 66.4, 66.5, 79.2, 79.5, 85.7, 86.0, 104.1, 104.3, 126.3, 126.7, 128.4, 128.5, 129.2, 129.6, 136.6, 138.2, 171.4, 171.5, 172.3, 201.6, 201.7.

HRMS (FAB): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{32}NaO_7$: 443.2046; found: 443.2048.

(*R*)-6-Butyl-6-[(*S*)-2-(*tert*-butyldiphenylsiloxy)-1-(triethylsiloxy)ethyl]tetrahydro-2*H*-pyran-2-one (23)

To a mixture of **13** (250 mg, 1.16 mmol) and imidazole (236 mg, 3.47 mmol) in DMF (500 μL) was added TBDPSCl (296 μL, 1.16 mmol) at 0 °C. After the mixture was stirred for 15 min, TESCl (290 μL, 1.73 mmol) was added and the mixture was stirred for 30 min. The mixture was diluted with Et_2O and the organic layer was washed with H_2O, brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 10:1) to provide **23** (577 mg, 88%) as a colorless oil.

$[\alpha]_D^{27}$ +13.5 (*c* 0.7, $CHCl_3$).

IR (neat): 3447, 2954, 2932, 2857, 1735, 1428, 1242, 1106, 793, 701 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.57 (q, *J* = 8.0 Hz, 6 H), 0.86 (t, *J* = 7.2 Hz, 3 H), 0.89 (t, *J* = 8.0 Hz, 9 H), 1.06 (s, 9 H), 1.2–2.1 (m, 10 H), 2.36 (m, 2 H), 3.57 (dd, *J* = 10.9, 5.1 Hz, 1 H), 3.64 (dd, *J* = 10.9, 5.1 Hz, 1 H), 3.87 (t, *J* = 5.1 Hz, 1 H), 7.42 (m, 6 H), 7.66 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 5.0, 6.1, 6.8, 7.1, 14.2, 17.7, 19.3, 23.4, 25.2, 26.4, 27.0, 30.4, 38.4, 65.6, 77.4, 87.1, 127.7, 127.7, 129.8, 129.8, 132.9, 132.9, 135.7, 135.7, 171.7.

HRMS (FAB): *m/z* $[M + Na]^+$ calcd for $C_{33}H_{52}NaO_4Si_2$: 591.3302; found: 591.3301.

(*R*)-6-Butyl-6-[(*S*)-2-(*tert*-butyldiphenylsiloxy)-1-(triethylsiloxy)ethyl]-5,6-dihydro-4*H*-pyran-2-yl Trifluoromethanesulfonate

To a soln of **23** (10.0 mg, 18 μmol) in THF (200 μL) was added 0.5 M KHMDS in THF (48 μL, 24 μmol) and HMPA (4.7 μL, 27 μmol) at –78 °C and the mixture was stirred at this temperature for 30 min. A soln of $PhNTf_2$ (7.9 mg, 22 μmol) in THF (200 μL) was added and the mixture was allowed to increase to r.t. and it was stirred for 6 h. To a mixture was added Et_3N (46.8 μL, 0.36 mmol) and the mixture was diluted with hexane. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane, 1% Et_3N) to provide crude enol triflate (33 mg) as a colorless oil.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.63 (q, *J* = 7.9, 6 H), 0.90 (t, *J* = 6.9 Hz, 3 H), 0.94 (t, *J* = 7.9 Hz, 9 H), 1.06 (s, 9 H), 1.2–2.1 (m, 8 H), 2.21 (m, 2 H), 3.58 (dd, *J* = 10.6, 6.0 Hz, 1 H), 3.71 (dd, *J* = 10.6, 3.1 Hz, 1 H), 4.00 (dd, *J* = 6.0, 3.1, 1 H), 4.62 (t, *J* = 4.1, 3 H), 7.40 (m, 6 H), 7.66 (m, 4 H).

(*R*)-6-[(*S*)-1,2-Bis(triethylsiloxy)ethyl]-6-butyltetrahydro-2*H*-pyran-2-one (26)

To a mixture of **13** (490 mg, 2.27 mmol) and imidazole (516 mg, 7.49 mmol) in DMF (980 μL) was added TESCl (1.14 mL, 6.81 mmol) at 0 °C. The mixture was stirred for 1.5 h and then diluted with Et_2O. The organic layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 10:1) to provide silyl ether **26** (934 mg, 95%) as a colorless oil.

$[\alpha]_D^{27}$ +9.9 (*c* 1.00, $CHCl_3$).

IR (neat): 3460, 2956, 2913, 2877, 1738, 1459, 1415, 1379, 1330, 1194, 975, 960, 815 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.62 (m, 12 H), 0.90 (t, *J* = 7.3 Hz, 3 H), 0.95 (m, 18 H), 1.2–2.1 (m, 10 H), 2.39 (m, 2 H), 3.81 (m, 1 H), 3.54 (dd, *J* = 10.6, 6.0 Hz, 1 H), 3.67 (dd, *J* = 10.6, 3.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 4.5, 5.2, 7.0, 7.1, 14.2, 17.4, 23.4, 25.3, 26.5, 30.0, 37.9, 64.2, 77.6, 87.0, 171.7.

HRMS (FAB): *m/z* $[M + Na]^+$ calcd for $C_{23}H_{48}NaO_4Si_2$: 467.2989; found: 467.2971.

Ethyl 3-{(*R*)-6-[(*S*)-1,2-Bis(triethylsiloxy)ethyl]-6-butyl-5,6-dihydro-4*H*-pyran-2-yl}propanoate (27)
(*R*)-6-[(*S*)-1,2-Bis(triethylsiloxy)ethyl]-6-butyl-5,6-dihydro-4*H*-pyran-2-yl Trifluoromethanesulfonate

To a soln of **26** (200.0 mg, 0.45 mmol) in THF (5 mL) was added 0.5 M KHMDS in THF (2.70 mL, 1.35 mmol) and HMPA (234 μL, 1.35 mmol) at –78 °C and the mixture was stirred at this temperature for 30 min. A soln of $PhNTf_2$ (560 mg, 1.57 mmol) in THF (1 mL) was added and the mixture was allowed to increase to r.t. and stirred for 1 h. To a mixture was added Et_3N (1.11 mL, 9.0 mmol) and the mixture was diluted with hexane. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane, 1% Et_3N) to provide crude enol triflate (423 mg) as a colorless oil.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.61 (m, 12 H), 0.90 (t, *J* = 7.3 Hz, 3 H), 0.95 (m, 18 H), 1.2–2.0 (m, 8 H), 2.13 (m, 2 H), 3.52 (dd, *J* = 10.5, 6.9 Hz, 1 H), 3.75 (dd, *J* = 10.5, 3.2 Hz, 1 H), 3.86 (dd, *J* = 6.9, 3.2 Hz, 1 H), 4.64 (t, *J* = 4.1 Hz, 1 H).

Ethyl 3-{(*R*)-6-[(*S*)-1,2-Bis(triethylsiloxy)ethyl]-6-butyl-5,6-dihydro-4*H*-pyran-2-yl}propanoate (27)

Following the typical procedure for **16** using enol triflate (423 mg, <0.45 mmol) in benzene (5 mL), $Pd(PPh_3)_4$ (4.6 mg, 4 μmol), and 0.5 M 3-ethoxy-3-oxopropylzinc bromide in THF (1.80 mL, 0.90 mmol) with stirring for 12 h; workup used Et_3N (808 mL, 1.56 mmol). Flash chromatography (*n*-hexane–EtOAc, 10:1) provided **27** (221 mg, 93%, 2 steps) as a colorless oil.

$[\alpha]_D^{24}$ –12.3 (*c* 1.00, $CHCl_3$).

IR (neat): 2954, 2875, 1739, 1678, 1237, 1133, 1064, 1009, 727 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.61 (m, 12 H), 0.89 (t, *J* = 7.2 Hz, 3 H), 0.95 (m, 18 H), 1.2–1.9 (m, 8 H), 1.25 (t, *J* = 7.0, 3 H), 1.92 (m, 2 H), 2.29 (m, 2 H), 2.44 (m, 2 H), 3.50 (dd, *J* = 10.4, 8.0 Hz, 1 H), 3.79 (m, 2 H), 4.12 (q, *J* = 7.0 Hz, 2 H), 4.46 (dd, *J* = 3.6, 3.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.4, 5.6, 7.0, 7.3, 14.3, 14.5, 17.5, 23.7, 25.0, 25.4, 25.5, 30.1, 32.5, 32.6, 60.3, 64.7, 76.3, 79.0, 94.4, 150.6, 173.1.

HRMS (FAB): *m/z* $[M + Na]^+$ calcd for $C_{28}H_{56}NaO_5Si_2$: 551.3564; found: 551.3560.

Ethyl 3-{(*R*)-6-Butyl-6-[(*S*)-2-(*tert*-butyldiphenylsiloxy)-1-(triethylsiloxy)ethyl]-5,6-dihydro-4*H*-pyran-2-yl}propanoate (24)
3-{(*R*)-6-Butyl-6-[(*S*)-1,2-dihydroxyethyl]-5,6-dihydro-4*H*-pyran-2-yl}propanoate

To a soln of **27** (40.0 mg, 76 μmol) in THF (2 mL) was added 1 M TBAF in THF (224 μL, 224 μmol) at r.t. and the mixture was stirred at this temperature for 30 min. The mixture was diluted with Et_2O. The organic layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 1:1) to provide the diol (20.0 mg, 92%) as a colorless oil.

$[\alpha]_D^{22}$ +7.0 (*c* 1.00, $CHCl_3$).

IR (neat): 3431, 2957, 2872, 1737, 1679, 1249, 967, 950 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.3 Hz, 3 H), 1.2–2.5 (m, 14 H), 1.25 (t, *J* = 7.0, 3 H), 2.25 (br, 1 H), 2.66 (br, 1 H), 3.64 (m, 1 H), 3.71 (m, 1 H), 3.81 (m, 1 H), 4.13 (q, *J* = 7.0 Hz, 2 H), 4.51 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 14.5, 17.4, 23.2, 24.1, 25.3, 31.9, 32.9, 60.6, 63.6, 74.0, 79.4, 94.3, 150.0, 173.5.

HRMS (FAB): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{28}NaO_5Si_2$: 323.1834; found: 323.1835.

Ethyl 3-{(*R*)-6-Butyl-6-[(*S*)-2-(*tert*-butyldiphenylsiloxy)-1-(triethylsiloxy)ethyl]-5,6-dihydro-4*H*-pyran-2-yl}propanoate (24)
To a mixture of the diol (16.7 mg, 57 μmol) and imidazole (11 mg, 0.17 mmol) in DMF (50 μL) was added TBDPSCl (16 μL, 62 μmol) at 0 °C. The mixture was stirred for 15 min and then TESCl (14.4 μL, 85 μmol) was added and it was stirred for 30 min. The mixture was diluted with Et_2O and the organic layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 20:1) to provide silyl ether **24** (31.9 mg, 88%) as a colorless oil.

$[\alpha]_D^{26}$ –0.4 (*c* 1.00, $CHCl_3$).

IR (neat): 2956, 2934, 2874, 2860, 1737, 1678, 1428, 1112, 740, 700 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.69 (m, 6 H), 0.82 (t, *J* = 6.8 Hz, 3 H), 0.96 (m, 9 H), 1.0–2.0 (m, 10 H), 1.05 (s, 9 H), 1.24 (t, *J* = 6.8, 3 H), 2.17 (m, 2 H), 2.30 (m, 2 H), 3.59 (m, 1 H), 3.79 (m, 1 H), 3.94 (m, 1 H), 4.11 (q, *J* = 6.8 Hz, 2 H), 4.41 (m, 1 H), 7.38 (m, 6 H), 7.67 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.6, 7.3, 14.2, 14.7, 17.4, 19.3, 23.6, 25.0, 25.3, 25.8, 30.1, 32.2, 32.4, 60.3, 66.3, 76.6, 79.0, 94.2, 127.6, 127.6, 129.5, 132.5, 135.6, 135.7, 150.5, 173.1.

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{38}H_{60}NaO_5Si_2$: 675.3877; found: 675.3859.

(*R*)-1-[(*S*)-2-(*tert*-Butyldiphenylsiloxy)-1-(triethylsiloxy)ethyl]-1-(3-oxopropyl)pentyl Ethyl Succinate (25)
Ethyl (*R*)-8-[(*S*)-2-(*tert*-Butyldiphenylsiloxy)-1-(triethylsiloxy)ethyl]-5,8-dihydroxy-4-oxododecanoate
Following the typical procedure for **17** using **24** (21 mg, 32 μmol) in acetone–H_2O (4:1, 1 mL), 2.5 wt% OsO_4 in *t*-BuOH (38μL, 3 μmol), and NMO (5.9 mg, 45 μmol). Flash chromatography (*n*-hexane–EtOAc, 5:1) afforded the dihydroxy ketone (16 mg, 76%) as a colorless oil .

IR (neat): 3456, 2957, 2932, 2875, 2859, 1734, 1157, 1112, 740, 702 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.47 (m, 6 H), 0.85 (m, 9 H), 0.89 (m, 3 H), 1.06 (s, 9 H), 1.2–2.1 (m, 10 H), 1.25 (m, 3 H), 2.63 (m, 2 H), 2.80 (m, 2 H), 3.33 (br, 1 H), 3.57 (m, 1 H), 3.72 (m, 1 H), 3.73 (m, 1 H), 3.95 (br, 1 H), 4.12 (m, 2 H), 4.17 (m, 1 H), 7.43 (m, 6 H), 7.66 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.2, 5.2, 7.0, 14.3, 14.4, 19.2, 23.7, 25.8, 25.9, 27.0, 27.5, 27.6, 31.1, 32.9, 35.6, 35.7, 60.8, 65.7, 75.6, 75.6, 75.9, 77.3, 77.4, 127.8, 129.9, 135.6, 135.6, 172.3, 211.0, 211.1.

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{38}H_{62}NaO_7Si_2$: 709.3932; found: 709.3933.

(*R*)-1-[(*S*)-2-(*tert*-Butyldiphenylsiloxy)-1-(triethylsiloxy)ethyl]-1-(3-oxopropyl)pentyl Ethyl Succinate (25)
Following the typical procedure for **18** using dihydroxy ketone (27 mg, 40 μmol) in benzene (2 mL) and $Pb(OAc)_4$ (27 mg, 60 μmol) with stirring for 10 min. Flash chromatography (*n*-hexane–EtOAc, 10:1) afforded **25** (27 mg, 99%) as a colorless oil.

$[\alpha]_D^{27}$ +0.7 (*c* 0.30, $CHCl_3$).

IR (neat): 2956, 2933, 2875, 1731, 1427, 1160, 1112, 740, 703 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.62 (m, 6 H), 0.82 (t, *J* = 6.9 Hz, 3 H), 0.92 (t, *J* = 8.0 Hz, 9 H), 1.05 (s, 9 H), 1.1–1.9 (m, 6 H), 1.25 (t, *J* = 7.3 Hz, 3 H), 2.07 (m, 1 H), 2.25 (m, 1 H), 2.48 (s, 4 H), 2.60 (m, 2 H), 3.58 (dd, *J* = 11.2, 6.0 Hz, 1 H), 3.67 (dd, *J* = 11.2, 4.0 Hz, 1 H), 4.13 (q, *J* = 7.3 Hz, 2 H), 4.37 (dd, *J* = 6.0, 4.0 Hz, 1 H), 7.41 (m, 6 H), 7.66 (m, 4 H), 9.70 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.3, 7.2, 14.1, 14.4, 19.3, 23.3, 26.0, 26.6, 27.1, 29.2, 30.0, 34.7, 39.2, 60.8, 66.4, 77.0, 87.0, 127.7, 127.7, 129.8, 129.8, 132.9, 133.0, 135.6, 135.7, 171.0, 172.1, 202.2.

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{38}H_{60}NaO_7Si_2$: 707.3775; found: 707.3775.

(*R*)-1-[(*S*)-1,2-Bis(triethylsiloxy)ethyl]-1-(3-oxopropyl)pentyl Ethyl Succinate (28)
Ethyl (*R*)-8-[(*S*)-1,2-Bis(triethylsiloxy)ethyl]-5,8-dihydroxy-4-oxododecanoate
Following the typical procedure for **17** using **27** (145 mg, 0.274 mmol) in acetone–H_2O (4:1, 2 mL), 2.5 wt% OsO_4 in *t*-BuOH (376 μL, 30 μmol) and NMO (48 mg, 0.411 mmol) and dilution with Et_2O. Flash chromatography (*n*-hexane–EtOAc, 5:1) to afford the dihydroxy ketone (126 mg, 82%) as a colorless oil.

IR (neat): 3491, 2954, 2876, 1737, 1716, 1069, 1005, 727 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.63 (m, 12 H), 0.90 (m, 3 H), 0.97 (m, 18 H), 1.2–2.1 (m, 10 H), 1.25 (t, *J* = 7.3 Hz, 3 H), 2.64 (m, 2 H), 2.84 (m, 2 H), 3.40 (br, 0.6 H), 3.48 (br, 0.4 H), 3.59 (m, 1 H), 3.72 (m, 1 H), 3.72 (m, 1 H), 3.90 (br, 0.6 H), 4.04 (br, 0.4 H), 4.13 (m, 2 H), 4.19 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 4.2, 5.2, 5.3, 6.8, 7.0, 14.1, 14.2, 23.6, 25.7, 27.4, 27.5, 28.0, 28.0, 31.0, 31.1, 32.9, 35.4, 35.5, 60.8, 64.4, 64.5, 75.5, 75.5, 76.0, 76.2, 77.3, 77.4, 172.5, 211.3, 211.4.

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{58}NaO_7Si_2$: 585.3619; found: 585.3618.

(*R*)-1-[(*S*)-1,2-Bis(triethylsiloxy)ethyl]-1-(3-oxopropyl)pentyl Ethyl Succinate (28)
Following the typical procedure for **18** using dihydroxy ketone (9.3 mg, 17 μmol) in benzene (1 mL) and $Pb(OAc)_4$ (11.0 mg, 25 μmol). Flash chromatography (*n*-hexane–EtOAc, 10:1) afforded **28** (8.7 mg, 94%) as a colorless oil.

$[\alpha]_D^{27}$ –3.0 (*c* 0.60, $CHCl_3$).

IR (neat): 2955, 2876, 1731, 1413, 1159, 1005, 963, 740 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.51 (m, 12 H), 0.80 (m, 3 H), 0.96 (m, 18 H), 1.1–1.4 (m, 4 H), 1.26 (t, *J* = 7.3 Hz, 3 H), 1.84 (m, 2 H), 2.13 (m, 1 H), 2.35 (m, 1 H), 2.57 (m, 4 H), 2.62 (m, 2 H), 3.52 (dd, *J* = 10.5, 6.4 Hz, 1 H), 3.70 (dd, *J* = 10.5, 3.2 Hz, 1 H), 4.14 (q, *J* = 7.3 Hz, 2 H), 4.22 (dd, *J* = 6.3, 3.2 Hz, 1 H), 9.74 (t, *J* = 1.4 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 4.3, 5.2, 6.8, 7.1, 14.0, 14.3, 23.3, 26.0, 26.5, 29.2, 30.0, 34.6, 39.3, 60.4, 64.7, 77.3, 87.0, 171.4, 172.2, 202.5.

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{56}NaO_7Si_2$: 583.3462; found: 583.3461.

Ethyl 3-{(*R*)-5-Butyl-4,5-dihydro-5-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]furan-2-yl}propanoate (30)
(*R*)-5-Butyl-5-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4,5-dihydrofuran-2-yl Trifluoromethanesulfonate
To a stirred soln of **29** (20.3 mg, 83 μmol) and *N*-(5-chloro-2-pyridyl)triflimide (181 mg, 460 μmol) in THF (1 mL) was dropwise added 0.5 M KHMDS in toluene (840 μL, 420 μmol) over 30 min at –78 °C. The mixture was stirred at this temperature for 30 min and then allowed to warm to r.t. and stirred for 15 min. Et_3N (234 μL, 1.68 mmol) was added and the mixture was diluted with hexane. The organic layer was washed with H_2O and brine and dried ($MgSO_4$). To the mixture was added HMPA (73 μL, 150 μmol), which was concentrated to give crude enol triflate and HMPA as a yellow oil.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.0 Hz, 3 H), 1.2–1.8 (m, 6 H), 1.36 (s, 3 H), 1.43 (s, 3 H), 2.62 (m, 2 H), 3.79 (dd, *J* = 8.4,

6.6 Hz, 1 H), 4.03 (dd, *J* = 8.4, 6.6 Hz, 1 H), 4.22 (dd, *J* = 6.6, 6.6 Hz, 1 H), 4.59 (t, *J* = 2.6 Hz, 1 H).

Ethyl 3-{(*R*)-5-Butyl-4,5-dihydro-5-[(*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]furan-2-yl}propanoate (30)

To the crude triflate in benzene (2 mL) was successively added $Pd(PPh_3)_4$ (4.8 mg, 4.2 μmol) and 0.5 M 3-ethoxy-3-oxopropylzinc bromide in THF (670 μL, 335 μmol) at 0 °C and allowed to warm to r.t. The mixture was stirred for 2.5 h and then Et_3N (234 μL, 1.68 mmol) was added. The mixture was filtered through a pad of silica gel and concentrated. The resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 10:1, 1% Et_3N) to provide **30** (8.6 mg, 31%, 2 steps) as a colorless oil.

$[\alpha]_D^{27}$ –176.05 (*c* 1.17, $CHCl_3$).

IR (neat): 2982, 2956, 2872, 1737, 1674, 1370, 1256, 1212, 1184, 1158, 1073, 857 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.9 Hz, 3 H), 1.2–1.6 (m, 5 H), 1.25 (t, *J* = 7.3 Hz, 3 H), 1.36 (s, 3 H), 1.44 (s, 3 H), 1.69 (m, 1 H), 2.42 (m, 4 H), 2.50 (m, 2 H), 3.75 (dd, *J* = 8.3, 6.9 Hz, 1 H), 3.97 (dd, *J* = 8.3, 6.9 Hz, 1 H), 4.12 (q, *J* = 7.3 Hz, 2 H), 4.14 (dd, *J* = 6.9, 6.9 Hz, 1 H), 4.45 (br dd, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 14.3, 23.3, 23.6, 24.8, 25.4, 26.3, 31.7, 36.1, 36.3, 60.5, 65.1, 80.1, 87.7, 93.6, 109.5, 156.5, 172.8.

HRMS (FAB): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{31}O_5$: 327.2171; found: 327.2163.

Ethyl (*R*)-1-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-1-(2-oxoethyl)pentyl Succinate (31)

To a soln of dihydrofuran **30** (8.6 mg, 26 μmol) in acetone–H_2O (4:1, 1 mL) was added 2.5 wt% OsO_4 in *t*-BuOH (17 μL, 1.32 μmol) and NMO (4.6 mg, 39.5 μmol) at r.t. The mixture was stirred for 2 h. To the mixture was added aq $Na_2S_2O_3$ and the mixture was stirred for 10 min. After the addition of H_2O, the mixture was stirred for 40 min and diluted with EtOAc. The aqueous layer was extracted with EtOAc (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated to afford a colorless oil. To a stirred soln of the colorless oil in benzene (500 μL) was added $Pb(OAc)_4$ (23.3 mg, 52.6 μmol) at 0 °C and allowed to warm to r.t. The mixture was stirred for 1.5 h, diluted with Et_2O, and filtered through Celite. After evaporation of the solvents, the resulting oil was purified by flash chromatography (*n*-hexane–EtOAc, 10:1) to afford **31** (6.6 mg, 68%, 2 steps) as a colorless oil.

$[\alpha]_D^{27}$ –6.9 (*c* 0.55, $CHCl_3$).

IR: 2983, 2960, 2935, 2873, 1733, 1458, 1372, 1212, 1162, 1072, 858 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.9 Hz, 3 H), 1.2–1.4 (m, 3 H), 1.26 (t, *J* = 7.3 Hz, 3 H), 1.33 (s, 3 H), 1.38 (s, 3 H), 1.88 (m, 2 H), 2.61 (m, 3 H), 2.66 (m, 3 H), 3.00 (dd, *J* = 16.0, 1.4 Hz, 1 H), 3.73 (dd, *J* = 8.7, 6.9 Hz, 1 H), 4.01 (dd, *J* = 8.7, 6.9 Hz, 1 H), 4.15 (q, *J* = 7.3 Hz, 2 H), 4.73 (dd, *J* = 6.9, 6.9 Hz, 1 H), 9.79 (dd, *J* = 3.2, 1.4 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.9, 14.3, 23.0, 24.9, 25.2, 25.7, 29.2, 30.0, 33.6, 46.8, 60.9, 65.2, 78.3, 84.9, 110.3, 171.7, 172.2, 199.8.

HRMS (FAB): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{31}O_7$: 359.2070; found: 359.2176.

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