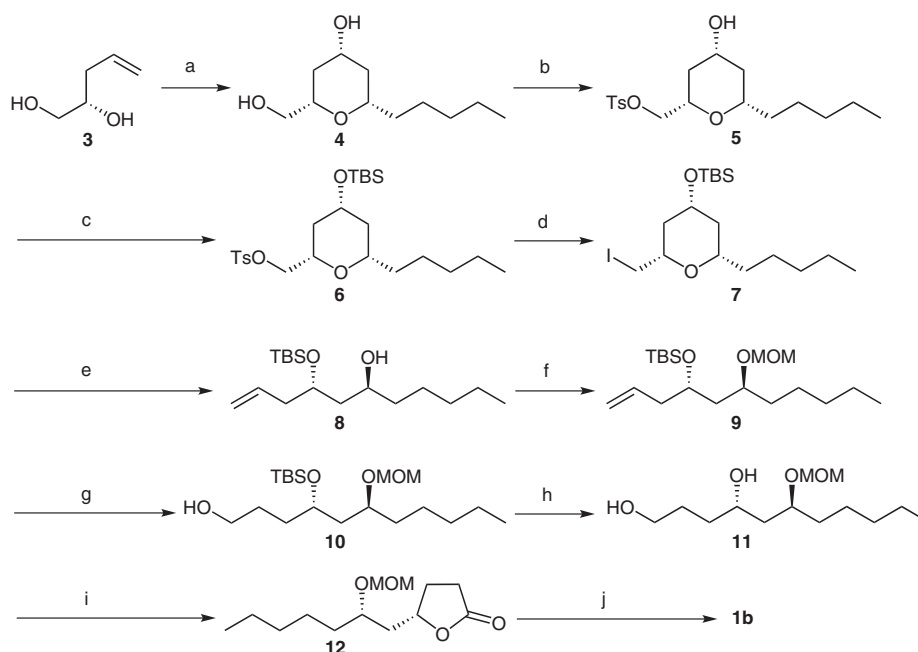


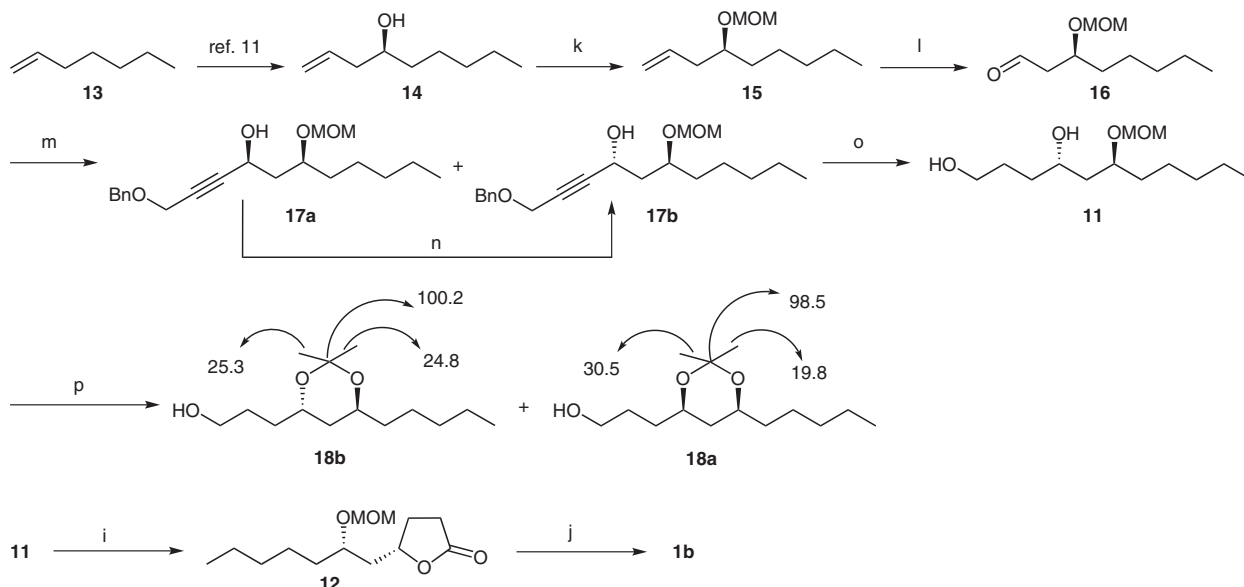
(52%).⁶ The stereochemistry was assumed to be in accordance with the literature as it was well examined and established previously.⁷ Moreover, the assumption was confirmed when compound **4** was elaborated to synthesize the target molecule **1b** (overall yield 15%), which in all respects was identical with the reported data.³ Tosylation of the compound **4** with 1.2 equivalents of tosyl chloride in the presence of triethylamine in dichloromethane gave the corresponding primary tosylate **5** (95%). Protection of the secondary alcohol as a silyl ether in the presence of *tert*-butyldimethylsilyl chloride and imidazole in dichloromethane gave the compound **6** (97%). Treatment of tosylate **6** with sodium iodide in refluxing acetone gave the corresponding iodo derivative **7** (95%). Reductive opening of the iodo derivative **7** with activated zinc in refluxing ethanol furnished the compound **8** (92%).⁸ The secondary alcohol of compound **8** was protected as its methoxymethyl ether **9** (98%) in the presence of *N*-diisopropylethylamine and methoxymethyl chloride in dichloromethane. Upon exposure of compound **9** to dicyclohexylborane and 30% hydrogen peroxide afforded the primary alcohol **10** (77%).⁹ Subsequent removal of the silyl group from compound **10** using tetra-*n*-butylammonium fluoride in tetrahydrofuran furnished the 1,4-diol **11** (97%), which was readily converted into lactone **12** (87%) by chemoselective oxidation using TEMPO and (diacetoxyiodo)benzene in dichloromethane.¹⁰ Deprotection of methoxymethyl ether **12** using trifluoroacetic acid in dichloromethane (1:4) gave the final product **1b** (97%), which in all respects was identical to the reported structure.³

The alternative synthetic approach (route B, Scheme 3) commenced from **13**, which was converted into **14** ac-

cording to a reported procedure¹¹ in three steps (overall yield 30%). Compound **14** was protected as its methoxymethyl ether gave **15** (98%). Ozonolytic oxidative cleavage of **15** gave the aldehyde **16** (85%), which was then treated with *O*-benzylpropargyl alcohol in the presence of *n*-butyllithium in tetrahydrofuran at -78°C . The resulting propargylic alcohol was obtained as a mixture of *syn*-**17a** and *anti*-**17b** in a 1:1 ratio. To assign the stereochemistry, both the isomers were converted into the corresponding acetonides **18a** and **18b** in a three-step sequence. Upon exposure of both the isomers **17a/17b** to 10% Pd/C in methanol resulted in the reduction of triple bond with concomitant removal of benzyl group to furnish the diols, which were then treated with aqueous 3 M hydrochloric acid in tetrahydrofuran to give the triols (structures not shown). Upon treatment of the triols with 2,2-DMP in acetone the acetonides **18a** and **18b** were obtained. The stereochemistry of the diastereomers could be established by ^{13}C NMR analysis. In **18a**, the two methyl groups resonate at $\delta = 19.8$ and 30.5 ppm and quaternary carbon shows a peak at $\delta = 98.5$ ppm representing the 1,3-*syn* orientation of two hydroxy groups. However, the two methyl groups and quaternary carbon resonate at $\delta = 24.7$, 24.9, and 100.3 ppm, respectively, indicating the 1,3-*anti*-orientation of the two hydroxy groups in **18b**.¹² The undesired isomer **17a** was converted into **17b** (overall yield 70%) under standard Mitsunobu condition.¹³ Reduction of the triple bond with a concomitant debenzylation of compound **17b** was achieved using Pd/C in methanol to give the key fragment 1,4-diol **11** (97%). The chemoselective oxidation of 1,4-diol **11** using TEMPO and (diacetoxyiodo)benzene in dichloromethane gave the lactone **12** (87%).¹⁰ Deprotection of the methoxymethyl ether **12** us-



Scheme 2 Route A. Reagents and conditions: (a) *n*-hexanal, TFA, CH_2Cl_2 , 3 h; then K_2CO_3 , MeOH, 25°C , 0.5 h, 52%; (b) Et_3N , TsCl, CH_2Cl_2 , $0-25^{\circ}\text{C}$, 3 h, 95%; (c) TBSCl, imidazole, DMAP, CH_2Cl_2 , 0 to 25°C , 3 h, 97%; (d) NaI, acetone, reflux, 24 h, 95%; (e) Zn, EtOH, reflux, 2 h, 92%; (f) MOMCl, DIPEA, DMAP, CH_2Cl_2 , $0-25^{\circ}\text{C}$, 3 h, 98%; (g) Cy_2BH , THF, 30% H_2O_2 , NaOH, 77%; (h) TBAF, THF, $0-25^{\circ}\text{C}$, 4 h, 97%; (i) TEMPO, $\text{PhI}(\text{OAc})_2$, CH_2Cl_2 , 25°C , 4 h, 87%; (j) TFA, CH_2Cl_2 (1:4), $0-25^{\circ}\text{C}$, 2 h, 97%.



Scheme 3 Route B. *Reagents and conditions:* (a) MOMCl, DIPEA, DMAP, CH₂Cl₂, 0 °C to r.t., 3 h, 98%; (b) O₃, TPP, CH₂Cl₂, –78 °C to r.t.; (c) BnOCH₂C≡CH, *n*-BuLi, THF, –78 °C, 2 h, 85%; (d) DEAD, TPP, *p*-nitrobenzoic acid, THF, 0 °C to r.t., 88%; (e) Pd/C, MeOH, r.t., 4 h, 97%; (f) 1. aq 3 M HCl, THF, 0 °C to r.t., 4 h, 2. 2,2-DMP, acetone, PTSA, r.t., 2 h; (g) TEMPO, PhI(OAc)₂, CH₂Cl₂, 25 °C, 4 h, 87%; (h) TFA–CH₂Cl₂ (1:4), 0–25 °C, 2 h, 97%.

ing trifluoroacetic acid in dichloromethane (1:4) gave the final product **1b** in 97% yield (overall yield 17%) (Scheme 3), which in all respects was identical to the reported one.³

Using the above two synthetic approaches, optically active **1a** and **1c** should be accessed readily.

In summary, we have described a stereoselective formal total synthesis of (4*S*,6*S*)-6-hydroxy-4-undecanolide (**1b**) employing two alternative strategies. These methods would be very useful to generate a wide variety of five-membered-ring lactones.

All reactions were carried out under inert atmosphere. Solvents were dried and purified by conventional methods prior to use. The progress of the reaction was monitored by TLC using glass plates precoated with silica gel 60 F254 to a thickness of 0.5 mm (Merck). Column chromatography was performed on silica gel (60–120 mesh) and neutral alumina using Et₂O, EtOAc, and hexanes as eluents. Optical rotation values were measured on PerkinElmer P241 polarimeter and JASCO DIP-360 digital polarimeter at 25 °C. IR spectra were recorded on PerkinElmer FT-IR spectrophotometer. ¹H and ¹³C NMR spectra were recorded on Varian Gemini 200 MHz, Bruker Avance 300 MHz, Varian Unity 400 MHz, or Varian Inova 500 MHz spectrometer using TMS as an internal standard in CDCl₃. Mass spectra were recorded on Micromass VG-7070H for EI and VG Autospec M for FAB-MS.

(2*S*,4*R*,6*S*)-2-(Hydroxymethyl)-6-pentyltetrahydro-2*H*-pyran-4-ol (**4**)

TFA (48.34 mL) was added slowly to a solution of **3** (3 g, 29.40 mmol) and *n*-hexanal (8.82 g, 88.23 mmol) in anhyd CH₂Cl₂ (95 mL) at 25 °C under N₂ atmosphere. The reaction mixture was stirred at r.t. for 3 h and then diluted with sat. aq NaHCO₃ (150 mL). The pH was then adjusted to >7 by the addition of Et₃N. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 70 mL) and the organic layers were combined and the solvent

was removed under reduced pressure. The trifluoroacetate obtained in this reaction was directly used in the next step without purification. The residue was dissolved in MeOH (40 mL) and stirred with K₂CO₃ (6.0 g) for 0.5 h. The mixture was extracted with CH₂Cl₂ (3 × 30 mL) and the combined organic layers were dried (Na₂SO₄) and the solvent was removed under reduced pressure. Purification of the crude by column chromatography on silica gel gave **4** (3.08 g, 52%) as a colorless gummy liquid; *R*_f = 0.3 (silica gel, 60% EtOAc in hexane); [α]_D²⁰ +2.4 (c 2.8, CHCl₃).

IR (neat): 3380, 2930, 2859, 1722, 1651, 1458, 1373, 1025 cm^{–1}.

¹H NMR (300 MHz, CDCl₃): δ = 0.89 (t, *J* = 6.7 Hz, 3 H), 1.05–1.64 (m, 10 H), 1.78–1.84 (m, 1 H), 1.88–1.94 (m, 1 H), 3.26–3.60 (m, 4 H), 3.73–3.81 (m, 1 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 22.4, 25.0, 31.6, 35.8, 36.7, 40.9, 65.6, 67.7, 75.2, 75.89.

HRMS (ESI): *m/z* calcd for C₁₁H₂₂O₃ + Na: 225.1466; found: 225.1471.

[(2*S*,4*R*,6*S*)-4-6-Pentyltetrahydro-2*H*-pyran-2-yl]methyl 4-Methylbenzenesulfonate (**5**)

To stirred solution of diol **4** (2.5 g, 12.3 mmol) in anhyd CH₂Cl₂ (25 mL) was added Et₃N (8.68 mL, 61.88 mmol) at 0 °C, and then TsCl (2.82 g, 14.8 mmol) was added over 2 h. The reaction mixture was allowed to warm to 25 °C and then allowed to stir for 3 h. The mixture was then treated with aq 1 M HCl (10 mL) and extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were washed with sat. aq NaHCO₃ (15 mL), followed by H₂O (15 mL). The combined organic phases were dried (Na₂SO₄) and concentrated under reduced pressure. Flash chromatography of the crude product afforded tosylate **5** (4.18 g, 95%) as a gummy liquid; *R*_f = 0.6 (silica gel, 40% EtOAc in hexane); [α]_D²⁰ –3.0 (c 1.0, CHCl₃).

IR (neat): 3410, 2930, 2860, 1598, 1454, 1360, 1176, 1097, 1030, 979, 816, 668 cm^{–1}.

¹H NMR (300 MHz, CDCl₃): δ = 0.89 (t, *J* = 6.6 Hz, 3 H), 1.03–1.49 (m, 10 H), 1.87–1.93 (m, 2 H), 2.44 (s, 3 H), 3.18–3.26 (m, 1 H), 3.50–3.58 (m, 1 H), 3.71–3.82 (m, 1 H), 3.94–4.05 (m, 2 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 7.80 (d, *J* = 8.3 Hz, 2 H).

^{13}C NMR (75 MHz, CDCl_3): δ = 13.9, 21.5, 22.4, 24.9, 31.6, 35.6, 36.7, 40.5, 67.4, 72.0, 72.6, 75.7, 127.8, 129.6, 132.7, 132.7, 144.6.

HRMS (ESI): m/z calcd for $\text{C}_{18}\text{H}_{28}\text{O}_3\text{S} + \text{Na}$: 379.1555; found: 379.156.

[(2*S*,4*R*,6*S*)-4-(*tert*-Butyldimethylsilyloxy)-6-pentyltetrahydro-2*H*-pyran-2-yl]methyl 4-Methylbenzenesulfonate (6)

To a stirred solution of alcohol **5** (3.8 g, 10.67 mmol) in anhyd CH_2Cl_2 (30 mL) at 0 °C were added TBSCl (1.93 g, 12.8 mmol), DMAP (cat.), and imidazole (2.9 g, 42.6 mmol) successively. The mixture was stirred for 3 h at 25 °C, quenched with H_2O (10 mL), and extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with brine (10 mL) and dried (Na_2SO_4). Removal of the solvent followed by purification by column chromatography afforded the pure product **6** (4.86 g, 97%) as a colorless liquid; R_f = 0.7 (silica gel, 10% EtOAc in hexane); $[\alpha]_{\text{D}}^{20}$ –1.6 (c 2.0, CHCl_3).

IR (neat): 2931, 2857, 1598, 1463, 1364, 1254, 1178, 1122, 1079, 982, 837 cm^{-1} .

^1H NMR (300 MHz, CDCl_3): δ = 0.03 (s, 6 H), 0.85–0.9 (m, 12 H), 1.06–1.45 (m, 10 H), 1.69–1.77 (m, 2 H), 2.43 (s, 3 H), 3.16–3.23 (m, 1 H), 3.48–3.56 (s, 1 H), 3.65–3.76 (m, 1 H), 3.92–4.02 (m, 2 H), 7.32 (d, J = 7.9 Hz, 2 H), 7.80 (d, J = 8.3 Hz, 2 H).

^{13}C NMR (75 MHz, CDCl_3): δ = –4.5, 14.0, 18.0, 21.6, 22.5, 25.0, 25.7, 31.8, 35.7, 37.4, 41.2, 68.2, 72.2, 72.7, 75.8, 127.9, 129.7, 132.9, 144.6.

MS (ESI): m/z = 493 [$\text{M} + \text{Na}$].

***tert*-Butyl[(2*S*,4*R*,6*S*)-2-(iodomethyl)-6-pentyltetrahydro-2*H*-pyran-4-yloxy]dimethylsilane (7)**

To a solution of **6** (3.8 g, 8.08 mmol) in acetone (70 mL) was added NaI (6.06 g, 40.43 mmol) and the mixture was heated to reflux for 24 h. After completion, the solvent was removed under reduced pressure. The residue was quenched with H_2O (20 mL) and extracted with CH_2Cl_2 (2×20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification of the crude product by column chromatography gave **7** (3.27 g, 95%) as a colorless liquid; R_f = 0.8 (silica gel, 10% EtOAc in hexane); $[\alpha]_{\text{D}}^{20}$ +10.8 (c 1.65, CHCl_3).

IR (neat): 2930, 2856, 1465, 1378, 1254, 1148, 1125, 1076, 893, 839, 774 cm^{-1} .

^1H NMR (200 MHz, CDCl_3): δ = 0.05 (s, 6 H), 0.88–0.93 (m, 12 H), 1.06–1.57 (m, 10 H), 1.66–1.74 (m, 1 H), 1.97–2.06 (m, 1 H), 3.08–3.16 (m, 2 H), 3.21–3.38 (m, 2 H), 3.63–3.81 (m, 1 H).

^{13}C NMR (75 MHz, CDCl_3): δ = –4.5, 9.0, 14.0, 18.0, 22.6, 25.2, 25.8, 31.7, 35.8, 41.3, 41.2, 68.5, 75.1, 75.9.

HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{35}\text{IO}_2\text{Si} + \text{Na}$: 449.1348; found: 449.1365.

(4*S*,6*S*)-4-(*tert*-Butyldimethylsilyloxy)undec-1-en-6-ol (8)

To a solution of iodide **7** (3.0 g, 7.04 mmol) in EtOH (90 mL) was added activated Zn dust (4.6 g, 70.36 mmol). The resulting mixture was stirred under reflux for 2 h and then cooled to 25 °C. Addition of solid NH_4Cl (7.55 g) and Et_2O (110 mL) followed by stirring for 5 min gave a gray suspension, which was filtered through Celite and the filtrate was concentrated in vacuo. Purification of the residue by flash chromatography gave **8** (1.94 g, 92%) as a colorless liquid; R_f = 0.5 (silica gel, 10% EtOAc in hexane); $[\alpha]_{\text{D}}^{20}$ –0.7 (c 1.1, CHCl_3).

IR (neat): 3379, 2931, 2858, 1641, 1465, 1254, 1073, 999, 913, 835 cm^{-1} .

^1H NMR (200 MHz, CDCl_3): δ = 0.08 (s, 6 H), 0.83–0.97 (m, 12 H), 1.21–1.57 (m, 10 H), 2.33 (t, J = 7.3 Hz, 2 H), 2.82 (br, OH), 3.85–

4.07 (m, 2 H), 4.97–5.09 (m, 2 H), 5.01–5.08 (m, 2 H), 5.61–5.82 (m, 1 H).

^{13}C NMR (75 MHz, CDCl_3): δ = –4.5, –4.8, 14.0, 17.9, 22.6, 25.2, 25.7, 31.8, 37.9, 41.0, 41.2, 68.1, 71.2, 117.3, 134.6.

HRMS (ESI): m/z calcd for $\text{C}_{17}\text{H}_{36}\text{O}_2\text{Si} + \text{Na}$: 323.2382; found: 323.2389.

(5*S*,7*S*)-7-Allyl-9,9,10,10-tetramethyl-5-pentyl-2,4,8-trioxa-9-silaundecane (9)

To a solution of alcohol **8** (1.8 g, 6 mmol) in anhyd CH_2Cl_2 (15 mL) at 0 °C were added successively DIPEA (3.10 mL, 17.95 mmol), DMAP (cat.), and MOMCl (0.96 g, 11.99 mmol). The mixture was stirred for 3 h at 25 °C, quenched with H_2O (10 mL), and extracted with CH_2Cl_2 (2×20 mL). The combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The resulting residue was purified by column chromatography to afford the pure product **9** (2.02 g, 98%) as a colorless liquid; R_f = 0.7 (silica gel, 10% EtOAc in hexane); $[\alpha]_{\text{D}}^{20}$ +19.0 (c 1.5, CHCl_3).

IR (neat): 3076, 2953, 2930, 1640, 1466, 1379, 1253, 1150, 1044, 1001, 916, 834 cm^{-1} .

^1H NMR (300 MHz, CDCl_3): δ = 0.06 (s, 6 H), 0.88–0.92 (m, 12 H), 1.25–1.63 (m, 10 H), 2.20–2.24 (t, J = 6.4 Hz, 2 H), 3.34 (s, 3 H), 3.55–3.63 (m, 1 H), 3.81–3.89 (m, 1 H), 4.59 (s, 2 H), 5.01–5.05 (m, 2 H), 5.71–5.85 (m, 1 H).

^{13}C NMR (75 MHz, CDCl_3): δ = –4.5, –4.0, 14.0, 18.0, 22.6, 24.7, 25.8, 31.9, 35.2, 42.3, 42.6, 55.4, 69.2, 75.7, 95.8, 116.9, 134.7.

HRMS (ESI): m/z calcd for $\text{C}_{19}\text{H}_{40}\text{O}_3\text{Si} + \text{Na}$: 367.2644; found: 367.2631.

(4*S*,6*S*)-4-(*tert*-Butyldimethylsilyloxy)-6-(methoxymethoxy)undecan-1-ol (10)

To a stirred solution of cyclohexene (2.64 mL, 26 mmol) in anhyd THF (2 mL) was added $\text{Me}_2\text{S} \cdot \text{BH}_3$ (1.22 mL, 13 mmol) at 0 °C. The mixture was stirred for 1 h at 0 °C, and then a solution of **9** (1.50 g, 4 mmol) in anhyd THF (15 mL) was added slowly over 10–15 min at 0 °C. The resulting solution was allowed to warm to 25 °C and then allowed to stir for 6 h. Upon completion, the mixture was quenched at 0 °C with EtOH (5 mL), and treated with 1 M aq NaOH (21.8 mL, 21.8 mmol) and 30% H_2O_2 (10 mL, 87 mmol). After stirring at r.t. for 1 h, the resulting mixture was quenched with 1 M aq $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL). The aqueous phase was extracted with EtOAc (2×30 mL). The combined organic extracts were washed with 1 M aq $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL) followed by brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography to afford the alcohol **10** (1.21 g, 77%) as a colorless liquid; R_f = 0.3 (silica gel, 20% EtOAc in hexane); $[\alpha]_{\text{D}}^{20}$ +15.8 (c 1.2, CHCl_3).

IR (neat): 3417, 2931, 2858, 1466, 1380, 1253, 1212, 1150, 1041, 919, 835 cm^{-1} .

^1H NMR (300 MHz, CDCl_3): δ = 0.07 (s, 6 H), 0.88–0.89 (m, 12 H), 1.29–1.88 (m, 15 H), 3.34 (s, 3 H), 3.53–3.61 (m, 3 H), 3.83–3.90 (m, 1 H), 4.59 (s, 2 H).

^{13}C NMR (75 MHz, CDCl_3): δ = –4.6, –4.1, 13.9, 18.0, 22.5, 24.0, 24.5, 25.4, 25.8, 27.7, 31.9, 41.9, 55.4, 69.3, 70.2, 75.6, 95.6.

MS (ESI): m/z = 385 [$\text{M} + \text{Na}$].

(4*S*,6*S*)-6-(Methoxymethoxy)undecan-1,4-diol (11)

To an ice cold solution of silyl ether **10** (0.75 g, 2.07 mmol) in anhyd THF (10 mL) was added TBAF (2.48 mL, M in THF, 2.48 mmol). After stirring for 15 min, the reaction mixture was brought to 25 °C and the stirring was continued for 4 h. The mixture was then cooled to 0 °C and quenched with sat. aq NH_4Cl (10 mL) and

extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by column chromatography to afford the alcohol **11** (0.49 mg, 97%) as a colorless gummy liquid; *R*_f = 0.2 (silica gel, 20% EtOAc in hexane); [α]_D²⁰ –17.1 (*c* 1.2, CHCl₃).

IR (neat): 3413, 2931, 1639, 1456, 1377, 1214, 1148, 1097, 1036, 914 cm^{–1}.

¹H NMR (300 MHz, CDCl₃): δ = 0.83 (t, *J* = 6.7 Hz, 3 H), 1.12–1.28 (m, 6 H), 1.43–1.71 (m, 8 H), 2.74 (br, OH), 3.35 (s, 3 H), 3.56–3.66 (m, 2 H), 3.70–3.91 (m, 2 H), 4.58–4.68 (m, 2 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 22.4, 25.0, 29.2, 31.8, 34.5, 34.7, 41.2, 55.7, 62.7, 67.7, 76.1, 96.2.

HRMS (ESI): *m/z* calcd for C₁₃H₂₈O₄ + Na: 271.1909; found: 271.1894.

(4*S*)-4-(Methoxymethoxy)non-1-ene (**15**)

To a solution of alcohol **14** (5.0 g, 35.2 mmol) in anhyd CH₂Cl₂ (25 mL) at 0 °C were added successively DIPEA (12.13 mL, 70.4 mmol), DMAP (20 mg, cat.), and MOMCl (8.02 mL, 105.5 mmol). The mixture was stirred for 3 h at 25 °C, quenched with H₂O (25 mL), and extracted with CH₂Cl₂ (3 × 20 mL). The combined organic extracts were washed with brine (25 mL), dried (Na₂SO₄), and concentrated under reduced pressure. The residue was purified by column chromatography to afford the pure product **15** (6.35 g, 97%) as a colorless liquid; *R*_f = 0.8 (silica gel, 10% EtOAc in hexane); [α]_D²⁰ –17.8 (*c* 1.5, CHCl₃).

IR (neat): 3367, 3019, 1215, 1096, 1038 cm^{–1}.

¹H NMR (400 MHz, CDCl₃): δ = 0.89 (t, *J* = 6.7 Hz, 3 H), 1.26–1.47 (m, 8 H), 2.23–2.27 (m, 2 H), 3.33 (s, 3 H), 3.52–3.58 (m, 1 H), 4.57–4.63 (m, 2 H), 5.00–5.06 (m, 2 H), 5.72–5.83 (m, 1 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 22.5, 24.9, 31.8, 34.0, 38.8, 55.3, 76.7, 95.2, 116.8, 134.7.

MS (ESI): *m/z* = 209 [M + Na].

(3*S*)-3-(Methoxymethoxy)octanal (**16**)

O₃ was bubbled through a solution of **15** (4.5 g, 24.19 mmol) in CH₂Cl₂ (35 mL) at –78 °C until no unreacted starting material was observed on TLC (eluent: 10% EtOAc in hexanes). The reaction mixture was then purged with N₂ to remove the excess O₃ and cooled to 0 °C. Ph₃P (7.6 g, 29.0 mmol) was added and the mixture was stirred for 2 h and concentrated in vacuo. After adding hexane (10 mL), the mixture was filtered through a Celite pad and the residue was washed with hexane (30 mL). The filtrate was dried (Na₂SO₄) and concentrated under reduced pressure. The resulting residue was purified by column chromatography to afford the pure product **16** (3.64 g, 80%) as a colorless liquid; *R*_f = 0.6 (silica gel, 10% EtOAc in hexane); [α]_D²⁰ +20.1 (*c* 1.5, CHCl₃).

IR (neat): 3019, 2932, 1724, 1215, 1036, 758 cm^{–1}.

¹H NMR (300 MHz, CDCl₃): δ = 0.82 (t, *J* = 6.7 Hz, 3 H), 1.16–1.60 (m, 8 H), 2.50–2.56 (m, 2 H), 3.28 (s, 3 H), 3.97–4.06 (m, 1 H), 4.57–4.63 (m, 2 H), 9.73 (m, 1 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 22.5, 24.8, 31.7, 34.8, 48.7, 55.5, 73.1, 95.7, 201.4.

MS (ESI): *m/z* = 209 [M + Na].

(4*S*,6*S*)-1-(Benzyloxy)-6-(methoxymethoxy)undec-2-yn-4-ol (**17b**)

A solution of *n*-BuLi in hexane (14.73 mL, 19.14 mmol, 1.3 M solution in hexane) was added to a solution (10 mL) of *O*-benzylpropargyl alcohol (2.79 g, 19.11 mmol) in THF at –78 °C under N₂ atmosphere and the mixture was allowed to stir for 20 min. To this mixture, a solution of aldehyde **16** (3.0 g, 15.95 mmol) in anhyd THF (15 mL) was added. After stirring the mixture for 2 h at

–78 °C, the reaction was quenched by sat. aq NH₄Cl (15 mL), extracted with EtOAc (2 × 30 mL), and the combined organic layers were dried (Na₂SO₄). Evaporation of the solvent followed by purification on column chromatography afforded alcohols **17b** (2.76 g, 43%) and **17a** (2.70 g, 42%). Unwanted **17a** was converted into **17b** by Mitsunobu inversion; **17b** (total yield: 4.53 g, 70%) was obtained as a viscous liquid; *R*_f = 0.4 (SiO₂, 30% EtOAc in hexane); [α]_D²⁰ +23.5 (*c* 0.9, CHCl₃).

IR (neat): 3399, 3019, 2930, 1215, 1095, 757 cm^{–1}.

¹H NMR (300 MHz, CDCl₃): δ = 0.81 (t, *J* = 6.7 Hz, 3 H), 1.26–1.30 (m, 6 H), 1.45–1.50 (m, 2 H), 1.79–1.84 (m, 2 H), 3.31 (s, 3 H), 3.36–3.41 (m, 1 H), 3.71–3.76 (m, 1 H), 4.14 (s, 2 H), 4.51 (s, 2 H), 4.55–4.63 (m, 2 H), 7.27 (m, 5 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 22.5, 24.4, 31.8, 34.3, 42.4, 53.5, 55.7, 57.3, 71.5, 76.0, 80.6, 87.3, 95.3, 127.7, 127.9, 128.3, 137.3.

MS (ESI): *m/z* = 357 [M + Na].

(4*S*,6*S*)-6-(Methoxymethoxy)undecan-1,4-diol (**11**)

To a solution of **17b** (2.0 g) in anhyd MeOH (15 mL) was added a catalytic amount of 10% Pd/C and the resulting mixture was stirred under H₂ atmosphere at r.t. for 4 h. After completion, the catalyst was filtered and then washed with EtOAc (3 × 10 mL). The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography to afford the alcohol **11** (1.44 g, 97%) as a colorless gummy liquid; *R*_f = 0.2 (silica gel, 20% EtOAc in hexane); [α]_D²⁰ –17.1 (*c* 1.2, CHCl₃).

IR (neat): 3413, 2931, 1639, 1456, 1377, 1214, 1148, 1097, 1036, 914 cm^{–1}.

¹H NMR (300 MHz, CDCl₃): δ = 0.83 (t, *J* = 6.7 Hz, 3 H), 1.12–1.28 (m, 6 H), 1.43–1.71 (m, 8 H), 2.74 (br, OH), 3.35 (s, 3 H), 3.56–3.66 (m, 2 H), 3.70–3.91 (m, 2 H), 4.58–4.68 (m, 2 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 22.4, 25.0, 29.2, 31.8, 34.5, 34.7, 41.2, 55.7, 62.7, 67.7, 76.1, 96.2.

HRMS (ESI): *m/z* calcd for C₁₃H₂₈O₄ + Na: 271.1909; found: 271.1894.

(*S*)-5-[(*S*)-2-(Methoxymethoxy)heptyl]dihydrofuran-2(3*H*)-one (**12**)

To a stirred solution of diol **11** (0.23 g, 0.92 mmol) in anhyd CH₂Cl₂ (5 mL) were added sequentially PhI(OAc)₂ (943 mg, 2.93 mmol) and TEMPO (33 mg, 0.21 mmol). After stirring the reaction mixture at 25 °C for 3.5 h, sat. aq Na₂S₂O₃ (10 mL) was added, and the mixture was extracted with Et₂O (2 × 10 mL). The combined organic extracts were washed with sat. aq NaHCO₃ (10 mL) and brine (6 mL), and concentrated in vacuo. The residue was subjected to column chromatography to afford the lactone **12** (0.196 g, 87%) as a colorless liquid; *R*_f = 0.5 (silica gel, 40% EtOAc in hexane); [α]_D²⁰ +48.5 (*c* 1.9, CHCl₃).

IR (neat): 2933, 1773, 1730, 1455, 1333, 1278, 1181, 1102, 1035, 918, 798, 737, 651 cm^{–1}.

¹H NMR (300 MHz, CDCl₃): δ = 0.90 (t, *J* = 6.7 Hz, 3 H), 1.30–1.61 (m, 8 H), 1.71–1.91 (m, 3 H), 2.28–2.39 (m, 1 H), 2.46–2.53 (m, 2 H), 3.35 (s, 3 H), 3.71–3.79 (m, 1 H), 4.57–4.71 (m, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.7, 22.3, 24.2, 28.3, 29.6, 31.7, 34.7, 41.1, 55.4, 74.6, 77.7, 95.8, 176.8.

MS (ESI): *m/z* = 245 [M + 1].

(*S*)-5-[(*S*)-2-Hydroxyheptyl]dihydrofuran-2(3*H*)-one (**1b**)

To a solution of **12** (0.13 g, 0.53 mmol) in anhyd CH₂Cl₂ (0.92 mL) was added TFA (0.23 mL, 2.13 mmol) dropwise at 25 °C. After stirring the mixture at the same temperature for 2 h, it was quenched with sat. aq NaHCO₃ (6 mL) and extracted with CH₂Cl₂ (2 × 6 mL).

The combined organic extracts were washed with brine (6 mL) and concentrated in vacuo. The residue was purified by column chromatography to afford the pure alcohol **1b** (0.103 g, 97%) as a colorless oil; R_f = 0.3 (silica gel, 40% EtOAc in hexane); $[\alpha]_D^{20}$ +59.6 (c 1.2, Et₂O).

IR (neat): 3445, 2929, 2859, 1767, 1460, 1420, 1359, 1185, 1036, 917, 766, 653 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ = 0.83 (t, J = 6.6 Hz, 3 H), 1.18–1.46 (m, 8 H), 1.69 (ddd, J = 3.5, 9.8, 14.3 Hz, 1 H), 1.78 (ddd, J = 2.8, 9.2 Hz, 1 H), 1.90 (ddt, J = 8.4, 9.4, 12.6 Hz, 1 H), 2.13 (br, OH), 2.25–2.36 (m, 1 H), 2.45–2.51 (m, 2 H), 3.76–3.85 (m, 1 H), 4.70–4.78 (m, 1 H).

¹³C NMR (75 MHz, CDCl₃): δ = 13.9, 22.5, 25.0, 28.4, 28.8, 31.6, 37.9, 43.1, 68.3, 78.1, 177.2.

HRMS (ESI): m/z calcd for C₁₁H₂₀O₃ + Na: 223.1310; found: 223.1336.

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