Supplementary Information A

The synthesis of single enantiomers of α-mycolic acids of Mycobacterium tuberculosis and related organisms, with alternative cyclopropane stereochemistries

C. Don Lawson, M. Maza–Iglesias, M. M. Sirhan, J. R. Al Dulayymi, and M. S. Baird*
Department of Chemistry, Bangor University, Gwynedd LL 57 2 UW, UK

5–(Nonadecyl–1–sulphonyl)–1–phenyl–1H–tetrazole 4

(i) 1–Phenyl–1H–tetrazole–5–thiol (14.6 g, 0.082 mol.), 1–bromononadecane (28 g, 0.081 mol.) and K₂CO₃ (21.9 g, 0.159 mol.) were dissolved in acetone (300 mL) and refluxed at 80 °C for 2.5 hours. Whilst the mixture was still hot, the inorganic salts were filtered off and washed with hot acetone. The filtrate was evaporated, and the residue was dissolved in hot dichloromethane (200 mL) and then washed with water (350 mL). The aqueous layer was re-extracted with dichloromethane (2 × 30 mL), and the combined organic layers were washed with water (350 mL), dried and evaporated. The product was recrystallized from methanol/acetonitrile (2:1) to give a white solid, 5–(nonadecyl–1–sulphonyl)–1–phenyl–1H–tetrazole (35 g, 96%), m.p. 64 – 66 °C. [Found (M+Na)⁺ 467.3170. C₂₃H₄₆N₅SNa requires: 467.3184], which showed δH (500 MHz, CDCl₃): 7.58 – 7.52 (5H, m), 3.38 (2H, t, J 7.7 Hz), 1.82 (2H, pent, J 7.6 Hz), 1.43 (2H, pent, J 6.5 Hz), 1.33 – 1.24 (30H, m), 0.88 (3H, t, J 6.9 Hz); δC (126 MHz, CDCl₃): 154.5, 133.8, 130.0, 129.7, 123.8, 33.4, 31.9, 29.64, 29.62, 29.6, 29.55, 29.5, 29.4, 29.3, 29.1, 20.0, 22.6, 14.0; νmax : 2919, 1502, 759 cm⁻¹.

(ii) Sodium hydrogen carbonate (14.5 g, 0.34 mol.) was added to a stirred solution of the tetrazole (17.0 g, 0.038 mol.) in dichloromethane (250 mL), followed by the addition of dry 3–chloroperoxybenzoic acid (17.6 g, 0.077 mol.) in dichloromethane (250 mL). The mixture was stirred for 18 h then quenched with sodium hydroxide (5%; 200 mL) and diluted with dichloromethane (500 mL). After shaking vigorously, the organic layer was separated and the aqueous layer was re-extracted with dichloromethane (300 mL). The combined organic layers were washed with water (2 × 200 mL), dried and evaporated. The product was re-crystallized from methanol/acetonitrile (1:1) to obtain a white solid, compound 4 (17 g; 92%), m.p. 60 – 68 °C [Found (M+Na)⁺ 499.3045. C₂₃H₄₆N₅SNa requires: 499.3082], which showed δH (500 MHz, CDCl₃): 7.71 – 7.69 (2H, m), 7.63 – 7.57 (3H, m), 3.74 (2H, t, J 7.8 Hz), 1.96 (2H, pent, J 7.0 Hz), 1.50 (2H, pent, J 7.0 Hz), 1.35 – 1.25 (30H, br.m), 0.89 (3H, t, J 6.6 Hz); δC (125 MHz, CDCl₃): 153.5, 133.1, 131.5, 129.7, 125.1, 57.0, 31.9, 29.73, 29.7, 29.64, 29.6, 29.5, 29.4, 29.2, 28.9, 22.7, 22.0, 14.1; νmax : 2919, 1470, 1342, 1154, 771 cm⁻¹.

5–[13–((1S,2R)–2–Eicosylecyclopropyl)tridecyl–1–sulfonyl]–phenyl–1H–tetrazole 15

(i) Diethyl azodicarboxylate (1.6 mL, 10 mmol.) in dry THF (5 mL) was added to a stirred mixture of 13–((1S,2R)–2–eicosylecyclopropyl)tridecan–1–ol (4.0 g, 7.7 mmol.), triphenylphosphine (2.6 g, 10 mmol.) and 1–phenyl–1H–tetrazole–5–thiol (1.8 g, 10 mmol.) in dry THF (50 mL) at 0 °C. After that the mixture was allowed to reach room temperature and stirred overnight. The solvent was evaporated and the residue was refluxed with petrol/ether (5:2) and filtered. The filtrate was evaporated; column chromatography, eluting with dichloromethane gave 5–[13–((1S,2R)–2–eicosylecyclopropyl)tridecyl–sulfanyl]–phenyl–1H–tetrazole (5.2 g; 96%), m.p. 53 – 55 °C, [α]D²₁₅ +1.5 (c 1.5, CHCl₃) [Found (M+Na)⁺ 703.5643. C₃₅H₅₂N₅SNa requires: 703.5683]. which showed δH (500 MHz, CDCl₃): 7.62 – 7.56 (5H, m), 3.42 (2H, t, J 7.4 Hz), 1.85 (2H, pent, J 7.5 Hz), 1.48 (2H, pent, J 7.5 Hz), 1.45 – 1.14 (58 H, m), 0.92 (3H, t, J 6.9 Hz), 0.71 – 0.65 (2H, m), 0.59 (1H, dt, J 4.2, 8.5 Hz), – 0.34 (1H, q, J 4.9 Hz); δC (126 MHz, CDCl₃): 154.8, 139.9 133.2, 130.2, 33.9, 30.2, 29.7, 29.65, 29.6, 29.5, 29.4, 29.1, 28.73, 28.7, 22.7, 16.1, 14.5, 11.3; νmax : 1600, 1461, 1377, 1239, 1168, 1011, 690 cm⁻¹.

(ii) Sodium hydrogen carbonate (2.8 g, 33.1 mmol.) was added to a stirred solution of tetrazole (5.0 g, 7.4 mmol.) in dichloromethane (50 mL), followed by the addition of dry 3–chloroperoxybenzoic acid (3.4 g, 14.7 mmol.) in dichloromethane (50 mL). The reaction was stirred at r.t. for 18 h to give a whitish precipitate. It was quenched with sodium hydroxide (5%; 100 mL) and diluted with dichloromethane (200 mL) and stirred for 2h. The aqueous layer was re-extracted with dichloromethane (2 × 150 mL). The combined organic layers were washed with water (2 × 200 mL), dried and evaporated. The product was purified by recrystallizing from methanol/acetonitrile (1:1) which gave compound 15 as a whitish solid (3.5 g; 67 %), m.p. 51 – 53°C, [α]D²₁₅ –1.9 (c 1.3, CHCl₃) [Found (M+Na)⁺ 735.5613. C₃₃H₃₄N₂SO₃Na requires: 735.5581], which showed δH (500 MHz, CDCl₃): 7.75 – 7.60 (5H, m), 3.74 (2H, t, J 8.0 Hz), 1.97 (2H, pent, J 7.8 Hz), 1.52
(2H, pent, J 7.5 Hz), 1.45 – 1.10 (57 H, m), 0.91 (3H, t, J 6.8 Hz), 0.70 – 0.62 (2H, m), 0.58 (1H, dt, J 4.2, 8.5 Hz), – 0.34 (1H, q, J 4.8 Hz); δc (125 MHz, CDCl3): 155.0, 135.1, 133.5, 129.9, 125.8, 56.5, 31.9, 30.3, 29.7, 29.5, 29.48, 29.4, 29.2, 28.9, 28.7, 28.2, 22.8, 16.3, 14.3, 11.1; νmax: 1760, 1595, 1461, 1372, 1352, 1218, 1143, 1013, 681 cm⁻¹.

Scheme S1: (i) BrMg(CH₂)₆CH₃, dilithiumtetrachlorocuprate (33%); (ii) N-Bromosuccinimide, PPh₃, CH₂Cl₂ (71%); (iii) 1-Phenyl-1H-tetrazole-5-thiol, K₂CO₃, acetone (69%); (iv) H₂O₂, MoO₇O₂₄(NH₄)₆.4H₂O, IMS (51%); (v) LiHMDS, THF (91%); (vi) LiAlH₄, THF (91%); (vii) N₂H₄, NaIO₄, AcOH, CuSO₄, i-PrOH (92%); (viii) PCC, CH₂Cl₂ (86%).

Scheme S2: (i) NaCN, DMSO (90%); (ii) NaOH (25%), MeOH, reflux then H⁺ (67%); (iii) LiAlH₄, THF (83%); (iv) Pivaloyl chloride, Et₃N, DMAP (88%); (v) pTSA, MeOH, H₂O, THF (93%); (vi) N-Bromosuccinimide, Ph₃P, CH₂Cl₂ (76%); (vii) 1-Phenyl-1H-tetrazole-5-thiol, K₂CO₃ (88%); (viii) H₂O₂, MoO₇O₂₄(NH₄)₆.4H₂O, IMS (93%); (ix) LiHMDS, THF (87%); (x) LiAlH₄, THF (95%); (xi) NaOAc, CuSO₄, AcOH, i-PrOH, N₂H₄ (97%); (xii) PCC, CH₂Cl₂ (62%).

Scheme S3: (i) LiHMDS, THF (51%); (ii) Pd/C 10%, H₂ (95%); (iii) 1-phenyl-1H-tetrazole-5-thiol, K₂CO₃, acetone (67%); (iv) H₂O₂, MoO₇O₂₄(NH₄)₆.4H₂O, IMS (91%).
Heptadecan–1–ol 40
Magnesium turnings (11.3 g, 470 mmol) in dry THF (120 mL) was stirred at ambient temperature. 1–Bromohexane (56.7 g, 317 mmol) in dry THF (80 mL) and gradually added to the suspension at a steady rate that was enough to maintain a reflux. An exothermic reaction occurred, and then the mixture was refluxed at 80 °C for 1 h. This was cooled to room temperature, and then added to a stirred solution of dilithiumtetrachlorocuprate (24 mL, 0.1 M) at –30 °C for 30 min, followed by the addition of 10-bromodecan–1–ol (25.0 g, 105 mmol) in dry THF (120 mL). The mixture was allowed to warm to r.t., stirred overnight, then quenched with sat. aq. NH₄Cl (200 mL) at 0 °C, followed by ethyl acetate (200 mL). The bluish aqueous layer and solid precipitate were re-extracted with ethyl acetate (2 × 200 mL). The organic layer was washed with sat. brine (200 mL), dried and evaporated to give a pale yellow residue which was crystallized to yield a white solid. The product was filtered, washed with cold petroleum and dried to give a white crystalline solid, heptadecan–1–ol (9.1 g, 33%); δH (500 MHz, CDCl₃), δC (126 MHz, CDCl₃) and νmax were identical to the literature.₂⁶

1–Bromo–heptadecane 41
N–Bromosuccinimide (24.5 g, 138 mmol) was added in portions to a stirred solution of heptadecan–1–ol (23.5 g, 91.6 mmol) and triphenyl phosphate (28.8 g, 110 mmol) in CH₂Cl₂ (300 mL) at 0 °C. Sodium bicarbonate (0.20 g, 2.4 mmol) was added to a stirred solution of 1–bromohexadecane (24.5 g, 138 mmol) in dry THF (120 mL). The reaction was stirred at r.t. for 16 h, then quenched with aq. sodium hydroxide (200 mL, 5%), stirred for 2h, then extracted with CH₂Cl₂ (3 × 200 mL). The combined organic layers were washed with brine (300 mL), dried and evaporated to give the crude product which was crystallized from petroleum. The product was filtered, washed with cold petroleum and dried to give a white precipitate 5–heptadecylsulfanyl–1–phenyl–1H–tetrazole–5–thiol (12.9 g, 72.3 mmol) and anhydrous potassium carbonate (18.2 g, 131 mmol) in acetone (165 mL), then vigorously stirred and refluxed for 2.5 h. The solvent was evaporated and the residue was diluted with water and extracted with CH₂Cl₂ (3 × 200 mL). The combined organic layers were washed with brine (300 mL), dried and evaporated to give crude product which was identical to the literature.

5–(Heptadecane–1–sulfonfonyl)–1–phenyl–1H–tetrazole 42
(i) 1–Bromohexadecane (21.0 g, 65.7 mmol) was added to a stirred solution of 1–phenyl–1H–tetrazole–5–thiol (12.9 g, 72.3 mmol) and anhydrous potassium carbonate (18.2 g, 131 mmol) in acetone (165 mL) then vigorously stirred and refluxed for 2.5 h. The solvent was evaporated and the residue was diluted with water and extracted with CH₂Cl₂ (3 × 200 mL). The combined organic layers were washed with brine (300 mL), dried and evaporated to give the crude product which was crystallized from petroleum. The product was filtered, washed with cold petroleum and dried to give a white precipitate 5–heptadecylsulfanyl–1–phenyl–1H–tetrazole (19 g, 69%), m.p 60–62 °C {Found (M+Na)⁺: 439.3170; C₂₅H₃₅N₄O₂Na requires: 439.3184}, which showed δH (500 MHz, CDCl₃): 7.60 – 7.52 (5H, m), 3.40 (2H, t, J 7.3 Hz), 1.82 (2H, pent, J 7.3 Hz), 1.47 – 1.41 (4H, m), 1.34 – 1.22 (24H, m), 0.88 (3H, t, J 6.9 Hz); δC (126 MHz, CDCl₃): 154.5, 133.8, 130.0, 129.7, 123.8, 33.4, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 28.7, 28.1, 22.6, 22.1, 14.1; νmax: 2922 , 2812.55, 1465, 1377, 1252, 721, 647 cm⁻¹.

(ii) 3–Chloroperoxybenzoic acid (13.7 g, 55.3 mmol) in CH₂Cl₂ (100 mL) was added to a stirred solution of the tetrazole (9.1 g, 22 mmol) and NaHCO₃ (7.3 g, 87 mmol) in CH₂Cl₂ (100 mL) at 0 °C. The reaction was stirred at r.t. for 16 h, then quenched with aq. sodium hydroxide (200 mL, 5%), stirred for 2h, then extracted with CH₂Cl₂ (3 × 200 mL). The combined organic layers were dried, filtered and evaporated. The product was re–crystallised from methanol/acetone (1:1), to give the title compound as a white solid, (5.0 g, 51%), m.p 64 – 65 °C {Found (M+Na)⁺: 471.3045; C₂₅H₃₅N₄O₂Na requires: 471.3082}, which showed δH (500 MHz, CDCl₃): 7.71–7.69 (2H, m), 7.65 – 7.59 (3H, m), 3.73 (2H, t, J 7.9 Hz), 1.99 – 1.92 (2H, m), 1.53 – 1.47 (4H, m), 1.36 – 1.22 (24H, m), 0.88 (3H, t, J 6.6 Hz); δC (126 MHz, CDCl₃): 153.5, 133.0, 131.4, 129.7, 125.0, 56.0, 31.9, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 28.8, 28.1, 22.6, 21.9, 14.1; νmax: 2949, 2810, 1497, 1473, 1419, 1390, 1250, 1073, 1091, 758, 694 cm⁻¹.

((1R,2S)–2–Octadecyclopropyl)methanol
A solution of ((1R,2S)−2−(hydroxymethyl)cyclopropyl)methyl butyrate\(^{0,31}\) (5.0 g, 29 mmol) in CH\(_2\)Cl\(_2\) (50 mL) was added to a stirred solution of PCC (13.8 g, 64.0 mmol) in CH\(_2\)Cl\(_2\) (350 mL). The mixture was stirred for 2 h at r.t. then diluted with petroleum/ethyl acetate (5:1, 500 mL), filtered through a bed of silica and the solvent was evaporated. The product was purified by column chromatography eluting with petroleum/ethyl acetate (5:2) to give a colourless oil, ((1R,2S)−2−formylcyclopropyl)−methyl butyrate (3.6 g, 73%). Lithium bis(trimethylsilyl)amide (30.6 mL, 32.5 mmol, 1.06 M) was added dropwise to a stirred solution of the above aldehyde and 42 (11.4 g, 25.0 mmol) in dry THF (150 mL) under nitrogen at −10 °C. The mixture was allowed to reach room temperature, stirred for 2 h, then ethyl acetate (75 mL) and sat.aq. NH\(_4\)Cl (25 mL) were added. The aqueous layer was extracted with ethyl acetate (2 × 200 mL). The combined organic layers were dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (20:1) gave ((E/Z)−(1R,2R)−2−(octadec−1−eny1)cyclopropyl)methyl butyrate (8.0 g, 86%) in ratio 2.5:1. The mixture (7.5 g, 19.10 mmol) in THF (60 mL) was added dropwise over 15 min to a suspension of LAH (1.1 g, 28.6 mmol) in THF (120 mL) at r.t., refluxed for 1 h, then cooled to room temperature and quenched carefully with freshly prepared sat.aq. sodium sulphate decahydrate (40 mL) until a white precipitate formed, followed by addition of MgSO\(_4\) (10 g). The mixture was stirred vigorously for 10 min, filtered through a pad of Celite and washed well with THF (2 × 50 mL). The combined organic layers were dried and evaporated to give a colourless oil, ((E/Z)−(1R,2R)−2−(octadec−1−eny1)cyclopropyl)methyl butyrate (5.5 g, 90%), which was used without purification. Sodium metaperiodate (36.5 g, 171 mmol) in hot water (90 mL) was added over 90 min at 70–80 °C to a stirred solution of the alcohol (5.5 g, 17 mmol) in isopropanol (250 mL), acetic acid (2 mL), sat.aq. copper sulphate (2 mL) and hydrazine hydrate (20 mL), then stirred for 2 h to reach r.t. and worked up with ethyl acetate (250 mL); sat.aq. sodium thiosulphate decahydrate was added to bleach the brown colour. The aqueous layer was re−extracted with petroleum/ethyl acetate (1:1, 3 × 100 mL). The combined organic layers were dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (5:1) gave the title compound as a white precipitate (5.2 g, 94%), m.p. 54−55 °C, \([\alpha]\)\(^D\)\(^{23}+12.5 (c 1.41, CHCl\(_3\)) \{Found (M+Na): 347.3217; C\(_{22}\)H\(_{43}\)ONa requires: 347.3284\}, which showed \(\delta\)\(_{\text{H}}\) (500 MHz, CDCl\(_3\)): 3.65 (1H, dd, J 6.9, 11.4 Hz), 3.58 (1H, br.dd, J 8.2, 11.4 Hz), 1.45 − 1.40 (4H, m), 1.30 − 1.20 (3H, m), 1.14 − 1.07 (2H, m), 0.88 (3H, br.t, J 6.6 Hz), 0.73 (1H, dt, J 4.7, 8.2 Hz), −0.02 (1H, br.q, J 5.4 Hz); \(\delta\)\(_C\) (126 MHz, CDCl\(_3\)): 63.3, 31.9, 30.1, 29.64, 29.6, 29.57, 29.5, 29.3, 28.5, 28.5, 22.6, 18.1, 16.1, 14.1, 9.4; \(\nu_{\text{max}}\): 3351, 2953, 2921, 2811, 1463, 1377, 1008, 719, 459 cm\(^{-1}\).

((1R,2S)−2−Octadecyclopropanecarbaldehyde 45

((1R,2S)−2−Octadecyclopropyl)methanol (5.2 g, 16.2 mmol) in CH\(_2\)Cl\(_2\) (25 mL) was added to a stirred suspension of PCC (8.7 g, 40.3 mmol) in CH\(_2\)Cl\(_2\) (150 mL). The mixture was stirred for 2 h at r.t. then diluted with petroleum/ethyl acetate (10:1, 500 mL) and filtered through a pad of silica then washed well with ethyl acetate (2 × 75 mL). The filtrate was evaporated; column chromatography eluting with petroleum/ethyl acetate (5:2) gave compound 5 as a white solid (5.0 g, 95%), m.p. 40 − 42 °C \([\alpha]\)\(^D\)\(^{23}+7.0 (c 1.5 , CHCl\(_3\)) \{Found (M+Na): 345.3132; C\(_{22}\)H\(_{42}\)ONa requires: 345.3133\}, which showed \(\delta\)\(_{\text{H}}\) (500 MHz, CDCl\(_3\)): 9.35 (1H, d, J 5.7 Hz), 1.89 − 1.84 (2H, m), 1.62 − 1.56 (2H, m), 1.53 − 1.46 (2H, m), 1.43 − 1.18 (33H, br.m), 0.88 (3H, t, J 6.9 Hz); \(\delta\)\(_C\) (126 MHz, CDCl\(_3\)): 201.8, 31.9, 29.9, 29.6, 29.6, 29.5, 29.3, 29.2, 28.2, 27.8, 24.7, 22.6, 14.7, 14.1; \(\nu_{\text{max}}\): 3295, 2504, 1965, 1465, 1364, 981, 722 cm\(^{-1}\).

((1S,2R)−2−Octadecyclopropyl)methanol 43

Lithium bis(trimethylsilyl)amide (60.0 mL, 63.6 mmol, 1.06 M) was added dropwise to a stirred solution of ((1S,2R)−2−((1−phenyl−1H−tetrazol−5−ylsulfonyl)methyl)−cyclopropyl)methyl butyrate\(^{29}\) (17.9 g, 49.1 mmol) and heptadecanal (10.4 g, 40.8 mmol) in dry THF (120 mL) under nitrogen at −10 °C. The mixture was allowed to reach r.t. and stirred for 2 h, then worked up as above to give ((E/Z)−((1S,2S)−2−(octadec−1−eny1)cyclopropyl)methyl butyrate (13.6 g, 85%) in ratio 2.3:1. The mixture (13.5 g, 34.4 mmol) in THF (60 mL) was added dropwise over 15 min to a suspension of LAH (2.0 g,
51.6 mmol) in THF (150 mL) at r.t., then refluxed for 1 h. Work up as above gave a colourless oil, (E/Z)-(15,2S)-2−(octadec−1-ethyl)cyclopropylmethanol (10.0 g, 91%), which was used without purification. Sodium metaperiodate (33.2 g, 155.2 mmol) in hot water (100 mL) was added over 90 min at 70−80 °C to a stirred solution of the mixture of alcohols (10.0 g, 31.0 mmol) in isopropanol (250 mL), acetic acid (2 mL), sat. aq. copper sulphate (2 mL) and hydrazine hydrate (20 mL). The mixture was stirred for 2 h at r.t and worked up as above to give compound 43 as a white precipitate (9.3 g, 92%), m.p. 54−55 °C, [α]D 20 +11.2 (c 1.15, CHCl3) [Found (M+Na)+: 347.3219; C22H32ONa requires: 347.3284], which showed δH (500 MHz, CDCl3): 3.66 (1H, dd, J 6.9, 11.4 Hz), 3.58 (1H, dd, J 7.9, 11.4 Hz), 1.47−1.37 (4H, m), 1.35−1.20 (31H, m), 1.15−1.07 (2H, m), 0.88 (3H, br.t, J 6.9 Hz), 0.71 (1H, dt, J 4.7, 8.2 Hz), δC (126 MHz, CDCl3): 63.3, 31.9, 30.1, 29.64, 29.6, 29.57, 29.5, 29.3, 28.5, 22.6, 18.1, 16.1, 14.1, 9.4; νmax: 3350, 2918, 2849, 1377, 1008, 719 cm−1.

(1S,2R)-2-Octadecyclopropopropanecarbaldehyde 44

The above alcohol (9.3 g, 28.7 mmol) in CH2Cl2 (50 mL) was added to a stirred suspension of PCC (15.7 g, 72.8 mmol) in CH2Cl2 (200 mL). The mixture was stirred for 2 h at r.t, then worked up as above to give the title compound as a white solid (7.9 g, 86%), m.p 39−40 °C, [α]D 20−7.7 (c 1.41, CHCl3) [Found (M+Na)+: 345.3139; C22H32NaO requires: 345.3133], which showed δH (500 MHz, CDCl3): 2.35−2.17 (16H, m), 1.89−1.84 (1H, m), 1.62−1.56 (2H, m), 1.53−1.46 (2H, m), 1.43−1.18 (33H, br.m), 0.88 (3H, t, J 6.9 Hz); δC (126 MHz, CDCl3): 201.8, 31.9, 29.9, 29.64, 29.6, 29.5, 29.3, 29.2, 28.2, 27.8, 24.7, 22.6, 14.7, 14.1; νmax: 2920, 2849, 1698, 1465, 1364, 1252, 981, 722, 693 cm−1.

11-Hydroxyundecyl pivalate 48

(i) Sodium cyanide (10.0 g, 204 mmol) was added to a stirred solution of 2−(10-bromodecyl)−tetrahydropyran 46 (22.1 g, 68.8 mmol) in DMSO (300 mL) and the mixture was heated to 60 °C for 3 h. Water (500 mL) was added and the product was extracted with ethyl acetate (3 × 300 mL). The combined organic layers were dried, evaporated and the crude product was purified by column chromatography eluting with 5:2 petroleum/ethyl acetate to give a colourless oil, 11−(tetrahydropyran−2−yloxy)undecanenitrile (16g, 90%) [Found (M+Na)+: 290.2094; C16H30O2Na requires: 290.2091], which showed δH (500 MHz, CDCl3): 4.58 (1H, t, J 2.9 Hz), 3.90−3.86 (1H, m), 3.74 (1H, td, J 6.9, 9.7 Hz), 3.53−3.49 (1H, m), 3.39 (1H, td, J 6.6, 9.5 Hz), 2.33 (2H, t, J 7.3 Hz), 1.86−1.79 (1H, m), 1.73−1.50 (8H, m), 1.45−1.41 (2H, m), 1.35−1.29 (11H, m); δC (126 MHz, CDCl3): 119.8, 98.8, 67.6, 62.3, 30.7, 29.7, 29.3, 29.1, 28.7, 28.6, 26.1, 25.4, 25.3, 19.6, 17.0; νmax: 2938, 2815, 2245, 1465, 1078, 904, 813, 722 cm−1.

(ii) A solution of the nitrile (11.0 g, 41.1 mmol) and 25% aqueous NaOH (180 mL) in methanol (92 mL) was stirred with reflux for 3 days at 100 °C, then the solvent was evaporated, followed by the addition of water (150 mL) and the solution was acidified to pH 4−5 with conc. HCl. The product was extracted with CH2Cl2 (3 × 200 mL). The combined organic layers were washed with brine and dried, evaporated and the product was purified by column chromatography eluting with petroleum/ethyl acetate (5:2) to give a colourless oil, 11−(tetrahydropyran−2−yloxy)undecanoic acid (8.1 g, 67%) [Found (M+Na)+: 309.2030; C16H30O2Na requires: 309.2036], which showed δH (500 MHz, CDCl3): 4.58 (1H, t, J 3.2 Hz), 3.89−3.84 (1H, m), 3.72 (1H, td, J 6.9, 9.5 Hz), 3.52−3.48 (1H, m), 3.8 (1H, td, J 4.7, 7.5 Hz), 2.33 (2H, br.t, J 7.2 Hz), 1.85−1.79 (1H, m), 1.74−1.68 (1H, m), 1.65−1.52 (8H, m), 1.51−1.27 (13H, m); δC (126 MHz, CDCl3): 179.6, 98.7, 67.6, 62.2, 34.0, 30.7, 29.6, 29.4, 29.3, 29.3, 29.1, 28.9, 26.1, 25.4, 24.6, 19.5; νmax: 2928, 1712, 1455, 1120, 814 cm−1.

(iii) The acid (8.1 g, 28 mmol) in THF (50 mL) was added over 15 min to a suspension of LAH (1.70 g, 42.4 mmol) in THF (250 mL) at 0 °C. The mixture was allowed to reach r.t and refluxed for 1 h, then cooled to 0 °C and sat. aq. sodium sulphate decahydrate (30 mL) was added dropwise and stirring continued until a white precipitate formed. THF (200 mL) was added and the mixture was stirred at r.t overnight followed by the addition of MgSO4 (30 g), and then filtered through a bed of celite and the
solvent was evaporated. The crude product was purified by column chromatography, eluting with (5:2) petroleum/ethyl acetate to give a colourless oil, 11–(tetrahydropyran–2–yloxy)undecan–1–ol 47 (6.4 g, 83%) {Found (M+Na)+: 295.2238; C_{19}H_{32}O_{2}Na requires: 295.2244}, which showed $\delta_H$ (500 MHz, CDCl$_3$): 4.55 (1H, br.t, J 3.7 Hz), 3.86–3.83 (1H, m), 3.70 (1H, td, J 7.0, 9.8 Hz), 3.60 (2H, t, J 6.6 Hz), 3.50 – 3.45 (1H, m), 3.35 (1H, td, J 6.6, 9.5 Hz), 1.88 (1H, s), 1.83 – 1.8 (1H, m), 1.71 – 1.67 (1H, m), 1.58 – 1.51 (8H, m), 1.26 (14H, br. s); $\delta_C$ (126 MHz, CDCl$_3$): 98.7, 67.6, 62.8, 62.2, 32.7, 30.7, 29.6, 29.5, 29.47, 29.4, 29.37, 29.3, 29.3, 26.1, 25.6, 25.4; v$_{max}$: 3401, 2926, 2813, 1465, 1441, 1353, 1137, 1121, 1076 cm$^{-1}$.

(iv) Trimethylacetyl chloride (19.3 mL, 158.2 mmol) in CH$_2$Cl$_2$ (80 mL) was added to a stirred solution of alcohol 47 (33.0 g, 121.1 mmol), triethylamine (24.5 g, 24.2 mmol) and DMAP (1.50 g, 12.2 mmol) in CH$_2$Cl$_2$ (250 mL) at 0 °C. The mixture was stirred for 3 h, then quenched with water (200 mL). The aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 150 mL) and the combined organic layers were dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (10:1) gave a colourless oil, 11–(tetrahydro–2H–pyran–2–yloxy)undecyl pivalate (38 g, 88%), which showed $\delta_H$ (500 MHz, CDCl$_3$), $\delta_C$ (126 MHz, CDCl$_3$) and v$_{max}$ were identical to the literature.$^{33}$

(v) p-Toluen sulfonic acid monohydrate (0.80 g, 4.14 mmol) was added to a stirred solution of the above pivalate (29.5 g, 82.8 mmol) in THF (250 mL), methanol (25 mL) and water (5 mL) at room temperature. The mixture was stirred for 16 h. Sat.aq. NaHCO$_3$ (10 mL) and water (25 mL) were added and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were dried and the solvent was evaporated. The crude product was purified by column chromatography eluting with petroleum/ethyl acetate (10:1), then: 1) to give a colourless oil, the title compound 48 (21 g, 93%), which showed $\delta_H$ (500 MHz, CDCl$_3$), $\delta_C$ (126 MHz, CDCl$_3$) and v$_{max}$ identical to the literature.$^{33}$

11–(1–Phenyl–1H–tetrazol–5–ylsulfonyl)undecyl pivalate 49

(i) N-Bromosuccinimide (17.7 g, 99.0 mmol) was added in portions to a stirred solution of pivalate 48 (20.9 g, 76.7 mmol) and triphenylphosphine (26.1 g, 99.5 mmol) in CH$_2$Cl$_2$ (300 mL) at 10 °C. Sodium bicarbonate (0.2 g, 2.4 mmol) was then added. The mixture was allowed to reach room temperature and stirred for 2 h, then the solvent was evaporated. The residue was treated with petrol/ethyl acetate (20:1, 3 × 200 mL) and refluxed for 30 min. The precipitate was filtered off and the filtrate was evaporated to give a crude product which was purified with column chromatography eluting with petroleum/ethyl acetate (10:1) to give 11–bromoundecylic pivalate as a colourless oil (20g, 76%), {Found (M+Na)$^+$: 357.1388; C$_{16}$H$_{31}$O$_2$BrNa requires: 357.1400}, which showed $\delta_H$ (500 MHz, CDCl$_3$): 4.02 (2H, t, J 6.6 Hz), 3.38 (2H, t, J 6.6 Hz), 1.83 (2H, pent, J 6.9 Hz), 1.60 (2H, br. pent, J 6.6 Hz), 1.42 – 1.37 (2H, m), 1.34 – 1.21 (12H, m), 1.17 (9H, s); $\delta_C$ (126 MHz, CDCl$_3$): 178.6, 64.3, 38.6, 33.8, 32.7, 29.4, 29.3, 28.6, 28.5, 28.0, 27.1, 25.8; v$_{max}$: 2929, 2815, 1729, 1729, 1480, 1398, 1309, 1281, 1158 cm$^{-1}$.

(ii) 1–Phenyl–1H–tetrazole–5–thiol (11.5 g, 64.5 mmol), the above pivalate (19.7 g, 58.7 mmol) and anhydrous potassium carbonate (16.2 g, 117.2 mmol) were mixed in acetone (200 mL). The mixture was vigorously stirred for 18 h at r.t, then the solvent was evaporated and the residue was diluted with water (1.5 L) and the product was extracted with CH$_2$Cl$_2$ (3 × 200 mL). The combined organic layers were washed with brine (2 × 200 mL), dried and the solvent was evaporated. The product was purified by column chromatography eluting with petroleum/ethyl acetate (5:1 and then 1:1) to give a colourless oil, 11–(1–phenyl–1H–tetrazol–5–ylthio)undecyl pivalate (22.5 g, 88%) {Found (M+Na)$^+$: 455.2425; C$_{23}$H$_{35}$N$_2$O$_3$S requires: 455.2451}, which showed $\delta_H$ (500 MHz, CDCl$_3$): 7.58 – 7.51 (5H, m), 4.03 (2H, t, J 6.6 Hz), 3.38 (2H, t, J 7.4 Hz), 1.82 (2H, pent, J 7.4 Hz), 1.62 (2H, pent, J 6.9 Hz), 1.45 – 1.40 (2H, m), 1.33 – 1.21 (12H, m), 1.18 (9H, s); $\delta_C$ (126 MHz, CDCl$_3$): 178.6, 154.5, 133.8, 130.0, 129.9, 129.7, 123.8, 64.4, 38.7, 33.3, 29.4, 29.3, 29.2, 29.1, 29.0, 28.6, 28.5, 27.2, 25.9; v$_{max}$: 2928, 2815, 1726, 1500, 1460, 1387, 1284, 1159 cm$^{-1}$.

(iii) A solution of ammonium molybdate (VI) tetrahydrate (32.0 g, 25.9 mmol) in 35 % H$_2$O$_2$ (40 mL), prepared and cooled in an ice bath, was added dropwise to a stirred solution of the above tetrazole (22.5 g, 51.9 mmol) in THF (140 mL) and IMS (350 mL) at 10 °C and stirred at r.t. for 2 h. A further solution of ammonium molybdate (VI) tetrahydrate (16.0 g, 12.9 mmol) in 35% H$_2$O$_2$ (20 mL) was added stirred at r.t. for 18 h. The mixture was poured into water (1.5 L) and extracted with CH$_2$Cl$_2$ (1 ×
200 mL, 3 x 100 mL). The combined organic layers were washed with water (500 mL), dried and the solvent was evaporated. The crude product was purified by column chromatography eluting with petroleum/ethyl acetate (5:1 and then 1:1) to give a yellow oil, the title compound 49 (22.6 g, 93%) (Found (M+Na)$^+$: 487.2344; $C_{32}H_{52}N_2NaO_2S$ requires: 487.2349), which showed $\delta_H$ (500 MHz, CDCl$_3$): 7.70 – 7.68 (2H, m), 7.63 – 7.58 (3H, m), 4.04 (2H, t, $J$ 6.6 Hz), 3.73 (2H, br.t, $J$ 7.9 Hz), 1.98 (2H, br. pent, $J$ 7.9 Hz), 1.61 (2H, pent, $J$ 6.9 Hz), 1.49 (2H, pent, $J$ 7.4 Hz), 1.33 – 1.23 (12H, m), 1.19 (9H, s); $\delta_C$ (126 MHz, CDCl$_3$): 178.6, 153.4, 133.0, 131.4, 129.7, 125.0, 64.3, 55.9, 38.7, 29.4, 29.3, 29.1, 29.0, 28.8, 28.5, 28.1, 27.2, 25.8, 21.9; $v_{max}$: 2929, 2817, 1725, 1498, 1480, 1462, 1398, 1342, 1282, 1154 cm$^{-1}$.

12-((1R,2S)-2-Octadecycyclopropyl)dodecan-1-ol

Lithium bis(trimethylsilyl)amide (22.6 mL, 24.0 mmol, 1.06M) was added dropwise to a stirred solution of (1R,2S)-2-octadecyclopropoxyacylcarboxylic acid 45 (5.0 g, 15.5 mmol) and the sulphone 49 (8.7 g, 18.6 mmol) in dry THF (80 mL) under nitrogen at –10 ºC. The mixture was allowed to reach room temperature and stirred for 2 h, cooled to 0 ºC, then worked up and purified as before to give a yellow oil, (E/Z)-12-((1R,2S)-2-octadecycyclopropyl)-dodec-11-enyl pivalate (7.0 g, 80%) in ratio 3.5:1. The above mixture (6.5 g, 11.6 mmol) in dry THF (30 mL) was added dropwise over 10 min to a suspension of lithium aluminium hydride (0.7 g, 18.4 mmol) in dry THF (70 mL) under nitrogen at –10 ºC. The mixture was refluxed for 1 h, then allowed to reach room temperature and worked up and purified as before to give (E/Z)-12-((1R,2S)-2-octadecycyclopropyl)dodec-11-en-1-ol as a white precipitate (4.9 g, 89%). Sodium metaperiodate (22.0 g, 102 mmol) in hot water (90 mL) was added over a 90 min at 70 – 80 ºC to a stirred solution of the mixture of alcohol (4.9 g, 10.2 mmol) in isopropanol (200 mL), acetic acid (2 mL), sat.aq. copper sulphate (2 mL) and hydrazine hydrate (20 mL). The mixture was stirred for 2 h to reach r.t. and then worked up and purified as before to give a solid; re-crystallisation from petrol gave the title compound as a white solid (4.0 g, 82%), m.p. 58 – 59 ºC, $[\alpha]_D^{20}$ +0.5 (c 1.4 , CHCl$_3$) (Found (M+Na)$^+$: 510.5007; $C_{32}H_{54}NaO$ requires: 510.5011), which showed $\delta_H$ (500 MHz, CDCl$_3$): 3.64 (2H, t, $J$ 6.6 Hz), 1.70 (2H, pent, $J$ 6.0 Hz), 1.57 (2H, pent, $J$ 6.6 Hz), 1.37 – 1.20 (53H, m), 0.88 (3H, t, $J$ 6.6 Hz), 0.67 – 0.61 (2H, m), 0.56 (1H, dt, $J$ 3.8, 7.8 Hz), – 0.32 (1H, q, $J$ 5.4 Hz); $\delta_C$ (126 MHz, CDCl$_3$): 63.1, 32.8, 31.9, 30.2, 29.7, 29.6, 29.4, 29.3, 28.7, 25.7, 22.6, 15.7, 14.1, 10.9; $v_{max}$: 3348, 2992, 2812, 1469, 1379, 1056, 719 cm$^{-1}$.

12-((1S,2R)-2-Octadecycyclopropyl)dodecan-1-ol 50

Lithium bis(trimethylsilyl)amide (25.5 mL, 27.0 mmol, 1.06 M) was added dropwise to a stirred solution of (1S,2R)-2-octadecyclopropanecarbaldehyde 44 (6.10 g, 18.9 mmol) and the sulphone 49 (9.70 g, 20.8 mmol) in dry THF (80 mL) under nitrogen at –10 ºC. The mixture was allowed to reach room temperature and stirred for 2 h, cooled to 0 ºC, quenched with sat.aq. NH$_4$Cl (25 mL), then worked up as above to give a yellow oil, (E/Z)-12-((1S,2R)-2-octadecycyclopropyl)dodec-11-enyl pivalate (9.2 g, 87%) in ratio 2.5:1. The above mixture (9.2 g, 16.4 mmol) in dry THF (40 mL) was added dropwise over 10 min to a suspension of lithium aluminium hydride (0.97 g, 25.52 mmol) in dry THF (80 mL) under nitrogen at –10 ºC. The mixture was refluxed for 1 h, then allowed to reach room temperature and worked up as above to give (E/Z)-12-((1S,2R)-2-octadecycyclopropyl)dodec-11-en-1-ol as a white precipitate (7.4 g, 95%). Sodium metaperiodate (32.8 g, 153.3 mmol) in hot water (90 mL) was added over a 90 min at 70 – 80 ºC to a stirred solution of the mixture of alcohol (7.3 g, 15.3 mmol) in isopropanol (200 mL), acetic acid (2 mL), sat.aq. copper sulphate (2 mL) and hydrazine hydrate (20 mL). The mixture was allowed to reach r.t and stirred for 2 h, then worked up as above to give the title compound as a white solid 50 (7.1 g, 97%), m.p. 59 – 61 ºC, $[\alpha]_D^{22}$ –0.7 (c 1.2 , CHCl$_3$) (Found (M+Na)$^+$: 510.5001; $C_{32}H_{56}ONa$ requires: 510.5011), which showed $\delta_H$ (500 MHz, CDCl$_3$): 3.64 (2H, t, $J$ 6.6 Hz), 1.70 (2H, pent, $J$ 6.0 Hz) 1.57 (2H, pent, $J$ 6.6 Hz), 1.30 – 120 (51H, m), 1.17 – 1.07 (2H, m), 0.88 (3H, t, $J$ 6.6 Hz), 0.67 – 0.61 (2H, m), 0.56 (1H, dt, $J$ 3.8, 7.8 Hz), –0.32 (1H, br. q, $J$ 5.4 Hz); $\delta_C$ (126 MHz, CDCl$_3$): 63.1, 32.8, 31.9, 30.2, 29.7, 29.6, 29.4, 29.3, 28.7, 25.7, 22.6, 15.7, 14.1, 10.9; $v_{max}$: 3360, 2992, 2848, 1469, 1379, 1056, 719 cm$^{-1}$. 
12-((1R,2S)—2-Octadecyclopropyl)dodecanal 51

A solution of 12-((1R,2S)—2-octadecyclopropyl)dodecan-1-ol (8.0 g, 43.9 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (30 mL) was added to a stirred suspension solution of PCC (9.0 g, 42.2 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (160 mL). The mixture was stirred for 2 h at r.t. then diluted with petroleum/ethyl acetate (10:1, 250 mL), filtered through a bed of silica and the solvent was evaporated. The crude product was purified by column chromatography eluting with petroleum/ethyl acetate (5:2) to give a white solid, compound 51 (4.8 g, 61%), m.p. 58 – 60°C, [\(\alpha\)]\textsubscript{D} \textsuperscript{20} +0.13 (c 1.2, CHCl\textsubscript{3}) {Found (M+Na): 499.4865; \(C_{33}H_{64}ONa\) requires: 499.4849}, which showed \(\delta\)\textsubscript{H} (500 MHz, CDCl\textsubscript{3}): 9.77 (1H, t, \(J\) 1.9 Hz), 2.42 (2H, br.d.t, \(J\) 1.9, 7.3 Hz), 1.63 (2H, pent, \(J\) 6.9 Hz), 1.38 – 1.13 (52H, br. m), 0.88 (3H, t, \(J\) 6.9 Hz), 0.67 – 0.61 (2H, m), 0.56 (1H, dt, \(J\) 3.7, 7.8 Hz), – 0.32 (1H, br. q, \(J\) 5.4 Hz); \(\delta\)\textsubscript{C} (126 MHz, CDCl\textsubscript{3}): 203.0, 43.9, 31.9, 30.2, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 28.7, 22.6, 22.0, 15.7, 14.1, 10.8; \(\nu\)\textsubscript{max}: 2991, 2848, 1715, 1469, 1391, 1018, 720 cm\textsuperscript{-1}.

12-((1S,2R)—2-Octadecyclopropyl)dodecanal 25

A solution of 12-((1S,2R)—2-octadecyclopropyl)dodecan-1-ol 50 (7.0 g, 14 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (30 mL) was added to a stirred suspension solution of PCC (9.5 g, 43.9 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (150 mL). The mixture was stirred for 2 h at r.t. Work up as above gave a white solid, compound 25 (4.3 g, 62%), m.p. 57 – 60°C, [\(\alpha\)]\textsubscript{D} \textsuperscript{20} –0.12 (c 1.10, CHCl\textsubscript{3}) {Found (M+Na): 499.4860; \(C_{33}H_{64}ONa\) requires: 499.4849}, which showed \(\delta\)\textsubscript{H} (500 MHz, CDCl\textsubscript{3}): 9.77 (1H, t, \(J\) 1.9 Hz), 2.42 (2H, br.d.t, \(J\) 1.9, 7.2 Hz), 1.63 (2H, pent, \(J\) 6.9 Hz), 1.38 – 1.22 (52H, br. m), 0.88 (3H, t, \(J\) 6.9 Hz), 0.67 – 0.61 (2H, m), 0.56 (1H, dt, \(J\) 3.7, 7.8 Hz), – 0.32 (1H, br. q, \(J\) 5.4 Hz); \(\delta\)\textsubscript{C} (126 MHz, CDCl\textsubscript{3}): 203.0, 43.9, 31.9, 30.2, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 28.7, 22.6, 22.0, 15.7, 14.1, 10.8; \(\nu\)\textsubscript{max}: 2991, 2848, 1715, 1469, 1391, 1018, 720 cm\textsuperscript{-1}.

15-Bromopentadecyl pivalate 54

Lithium bis(trimethylsilyl)amide (53.7 mL, 56.9 mmol, 1.06 M) was added to a stirred solution of ester 53 (19.2 g, 43.7 mmol)12 and 6-bromohexanal 52 (7.50 g, 41.8 mmol) in dry THF (150 mL) under nitrogen at –10°C. The mixture was allowed to reach r.t and stirred for 2 h, then quenched with sat.aq. NH\textsubscript{4}Cl (25 mL). The organic layer was separated and aqueous layer was extracted with ethyl acetate (2 x 100 mL). The combined organic layers were dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (10:1) gave a colourless oil (\(E/Z\))—15-bromopentadecy–9-ethyl pivalate (8.3 g, 51%). Palladium on charcoal (10 %, 1.5 g) was added to a stirred solution of the pivalate (8.30 g, 21.3 mmol) in ethanol (40 mL) and THF (30 mL). The mixture was stirred while being hydrogenated at atmospheric pressure, and when hydrogen absorption was complete the mixture was quenched with few drops of water and filtered through a pad of celite and washed with ethyl acetate (100 mL). The filtrate was evaporated. Column chromatography eluting with petroleum/ethyl acetate (5:1 and then 1:1) gave a colourless oil, the title compound (7.9 g, 95%) {Found (M+Na): 413.2046; \(C_{15}H_{28}O_2NaBr\) requires: 413.2066}, which showed \(\delta\)\textsubscript{H} (500 MHz, CDCl\textsubscript{3}): 4.05 (2H, t, \(J\) 6.6 Hz), 3.40 (2H, t, \(J\) 6.9 Hz), 1.83 (2H, br.pent, \(J\) 6.6 Hz), 1.61 (2H, pent, \(J\) 6.6 Hz), 1.43 – 1.38 (2H, m), 1.31 – 1.21 (20H, m), 1.19 (9H, s); \(\delta\)\textsubscript{C} (126 MHz, CDCl\textsubscript{3}): 178.4, 64.4, 38.6, 33.8, 32.7, 31.8, 30.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 28.5, 28.5, 28.1, 27.1, 25.8, 22.6; \(\nu\)\textsubscript{max}: 2925, 2814, 1731, 1463, 1284, 1156 cm\textsuperscript{-1}.

15—(1-Phenyl-1H—tetrazole–5–thio)pentadecyl pivalate

15—Bromopentadecyl pivalate 54 (7.9 g, 20 mmol) was added to a stirred solution of 1—phenyl—1H—tetrazole–5–thiol (3.90 g, 22.2 mmol) and anhydrous potassium carbonate (5.90 g, 42.7 mmol) in acetone (160 mL) at r.t. The mixture was vigorously stirred for 18 h at r.t. then the solvent was evaporated and the residue diluted with water (300 mL) and CH\textsubscript{2}Cl\textsubscript{2} (200 mL). The organic layer was separated and the aqueous layer was re—extracted with CH\textsubscript{2}Cl\textsubscript{2} (2 x 50 mL). The combined organic layers were washed with brine (2 x 200 mL) and evaporated. Column chromatography eluting with petroleum/ethyl acetate (5:2 and then 1:1) gave a colourless oil, the title compound (6.6 g, 67%) {Found (M+Na): 511.3055;
C$_{27}$H$_{32}$N$_2$NaO$_2$S requires: 511.3077, which showed $\delta_{II}$ (500 MHz, CDCl$_3$): 7.61 – 7.54 (5H, m), 4.04 (2H, t, J 6.6 Hz), 3.40 (2H, t, J 7.4 Hz), 1.82 (2H, pent, J 7.4 Hz), 1.62 (2H, pent, J 6.9 Hz), 1.48 – 1.42 (2H, m), 1.33 – 1.28 (20H, m), 1.20 (9H, s); $\delta_c$ (126 MHz, CDCl$_3$): 178.6, 154.5, 133.8, 130.0, 129.7, 123.8, 64.4, 38.7, 33.3, 29.4, 29.3, 29.2, 29.1, 29.0, 28.6, 28.5, 27.2, 25.9; $\nu_{max}$: 2925, 2814, 1727, 1500, 1463, 1387, 1284, 1158, 760, 694 cm$^{-1}$.

**15-((1-Phenyl-1H--tetrazol-5-ylsulfonyl)--pentadecy l pivalate 32**

A solution of ammonium molybdate (VI) tetrahydrate (8.2 g, 6.6 mmol) in THF (100 mL) and IMS (200 mL) at 10 °C. The mixture was stirred at r.t. for 2 h, then further solution of ammonium molybdate (VI) tetrahydrate (4.1 g, 3.3 mmol) in 35% H$_2$O$_2$ (20 mL) was added. The mixture was stirred at r.t. for 18 h, then poured into water (1.5 L) and extracted with CH$_2$Cl$_2$ (1 $\times$ 200 mL, 2 $\times$ 50 mL). The combined organic layers were washed with water (300 mL), dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (5:1 and then 1:1) gave a yellow oil, the title compound (6.2 g, 91%) $\{\text{Found (M+Na}$)$: 543.2973; C$_{27}$H$_{32}$N$_2$NaO$_2$S requires: 543.2975$, which showed $\delta_{II}$ (500 MHz, CDCl$_3$): 7.64 – 7.61 (2H, m), 7.59 – 7.56 (3H, m), 4.04 (2H, t, J 6.6 Hz), 3.72 (2H, t, J 7.8 Hz), 2.03 – 1.91 (2H, m), 1.62 (2H, pent, J 6.6 Hz), 1.50 (2H, pent, J 6.9 Hz), 1.35 – 1.25 (20H, m), 1.19 (9H, s); $\delta_c$ (126 MHz, CDCl$_3$): 178.5, 153.4, 133.0, 131.3, 129.6, 125.0, 64.4, 55.9, 38.6, 29.4, 29.3, 29.14, 29.1, 28.5, 28.5, 28.0, 27.1, 25.8, 21.8; $\nu_{max}$: 2917, 2812, 1725, 1593, 1474, 1284, 1154, 1149, 764, 543 cm$^{-1}$. 

(S)-2,2-Dimethyl-4-((1R,2R)-2-((S)-16-((1R,2S)-2-octadecylo cyclopropyl)hexadecan-2-yl)cyclo-propyl)-1,3-dioxolane

Lithium bis(trimethylsilyl)amide (16.0 mL, 14.4 mmol, 1.06 M) was added dropwise to a stirred solution of 12-((1R,2S)-2-octadecylo cyclopropyl)dodecanol 51 (4.8 g, 10.0 mmol) and sulphone 27 (4.70 g, 11.6 mmol) in dry THF (50 mL) under nitrogen at –10 °C. The reaction was exothermic and the temperature rose to 0 °C, resulting in a dark orange solution. The mixture was allowed to reach r.t., stirred for 2 h, then quenched with sat.aq. NH$_4$Cl (15 mL), and diluted with petroleum/ethyl acetate (10:1, 50 mL). The aqueous layer was re-extracted with petroleum/ethyl acetate (10:1, 2 $\times$ 100 mL). The combined organic layers were washed with brine (50 mL), dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (20:1) gave a colourless oil, (S)-2,2-dimethyl-4-((1R,2R)-2-[(E/Z)-((S)-16-((1R,2S)-2-octadecylo cyclopropyl)hexadec-3-en-2-yl)cyclopropyl])-1,3-dioxolane (5.6 g, 86%). Dipotassium azodicarboxylate (4.50 g, 23.2 mmol) was added to a stirred solution of the dioxolane (5.5 g, 8.4 mmol) in THF (40 mL) and methanol (15 mL) under nitrogen at 10 °C. A solution of glacial acetic acid (6 mL) and THF (6 mL) was added dropwise for 24 h then additional dipotassium azodicarboxylate (2.30 g, 11.8 mmol) and a solution of glacial acetic acid (3 mL) and THF (3 mL) were added and stirred for a further 24 h; a white precipitate was formed and the mixture was poured slowly into sat.aq. NaHCO$_3$ (25 mL) and the product was extracted with petroleum/ethyl acetate (10:1, 3 $\times$ 50 mL). The combined organic extracts were washed with water (50 mL), dried and evaporated to give a residue. The residue was then purified by column chromatography eluting with petroleum/ethyl acetate (50:1) to give a thick oil which solidified later, the title compound (4.6 g, 83%), $[\alpha]_D^{20} = -12 (c 1.1, CHCl_3)$ $\{\text{Found (M+Na}$)$: 681.6560; C$_{51}$H$_{80}$O$_2$Na$_2$ requires: 681.6526$, which showed $\delta_{II}$ (500 MHz, CDCl$_3$): 4.14 – 4.08 (1H, m), 3.76 – 3.68 (2H, m), 1.45 (3H, s), 1.37 – 1.13 (67H, br. m, including s integrating to 3H at $\delta$ 1.36), 0.99 (3H, br.s), 0.88 (3H, t, J 6.3 Hz), 0.83 (1H, dt, J 4.5, 8.0 Hz), 0.71 – 0.64 (3H, m), 0.56 (1H, dt, J 4.1, 8.2 Hz), 0.24 (1H, br.q, J 5.3 Hz), – 0.33 (1H, br.q, J 5.1 Hz); $\delta_c$ (126 MHz, CDCl$_3$): 108.2, 77.9, 79.0, 37.4, 33.2, 31.9, 30.0, 29.6, 29.3, 28.7, 27.1, 26.8, 25.7, 23.8, 22.6, 20.0, 19.2, 15.7, 14.1, 10.9, 9.0; $\nu_{max}$: 2932, 2813, 1609, 1455, 1368, 1063, 824, 687 cm$^{-1}$. 

cis-(1R,2R)-2-((S)-16-((1R,2S)-2-Octadecylo cyclopropyl)hexadecan-2-yl)cyclopropane-carbaldehyde
Periodic acid (4.0 g, 21 mmol) was added to a stirred solution of the above dioxolane (4.6 g, 7.0 mmol) in dry ether (60 mL) under nitrogen at r.t. The mixture was stirred for 16 h, then filtered and the solvent evaporated to give a residue which was purified by column chromatography eluting with petroleum/ethyl acetate (10:1) to give the title aldehyde as a white solid (3.4 g, 83%), m.p. 36 – 38 °C, \([\alpha]_D^20 = -0.08 \) (c 1.06, CHCl₃) \{Found (M+Na)^+: 609.5940; C₂₇H₅₅O₃Na requires: 609.5950\}, which showed \(\delta_H\) (500 MHz, CDCl₃): 9.33 (1H, d, J 6.0 Hz), 1.94 – 1.87 (1H, m), 1.41 – 1.10 (66H, br m), 1.05 (3H, d, J 6.5 Hz), 0.89 (3H, t, J 6.5 Hz), 0.64 – 0.58 (2H, m), 0.56 (1H, dt, J 4.1, 8.2 Hz), – 0.33 (1H, br.q, J 5.1 Hz); \(\delta_C\) (126 MHz, CDCl₃): 201.7, 37.4, 32.5, 32.2, 31.9, 30.2, 29.8, 29.6, 29.5, 29.4, 29.3, 29.1, 28.8, 28.7, 28.5, 26.7, 22.6, 20.0, 15.7, 14.1, 13.6, 10.9; \(v_{max}\): 2924, 2849, 1694, 1471, 1399, 825, 718 cm⁻¹.

**trans-\((1S,2R)\)–2–\((S)\)–16–\((1R,2S)\)–2–Octadeccyclopropyl)hexadecan–2–yl)cyclopropane-carbaldehyde 31**

Sodium methoxide (0.60 g, 11 mmol) was added to a stirred solution of \(cis\)–\((1R,2R)\)–2–\((S)\)–16–\((1R,2S)\)–2–octadecyclopropyl)hexadecan–2–yl)cyclopropane-carbaldehyde (3.30 g, 5.63 mmol) in methanol (20 mL) and THF (30 mL) and refluxed for 56 h. The mixture was cooled to r.t, quenched with sat.aq. NH₄Cl (15 mL), and then extracted with petroleum/ethyl acetate (1:1, 50 mL). The aqueous layer was re-extracted with 1:1 petroleum/ethyl acetate (2 × 40 mL). The combined organic layers were dried and evaporated to yield a thick oil which solidified later. Column chromatography eluting with petroleum/ethyl acetate (10:1) gave the title compound as a semi–solid (2.9 g, 88%), \([\alpha]_D^20 = +9.8\) (c 1.2, CHCl₃) \{Found (M+Na)^+: 609.5942; C₂₇H₅₅O₃Na requires: 609.5950\}, which showed \(\delta_H\) (500 MHz, CDCl₃): 8.99 (1H, d, J 5.7 Hz), 1.71 – 1.66 (1H, m), 1.37 – 1.13 (65H, br.m), 0.98 (3H, d, J 6.6 Hz), 0.94 – 0.91 (1H, m), 0.89 (3H, t, J 6.5 Hz), 0.64 (2H, br.m), 0.56 (1H, dt, J 3.8, 8.2 Hz), – 0.33 (1H, br.q, J 5.1 Hz); \(\delta_C\) (126 MHz, CDCl₃): 200.9, 36.8, 31.9, 30.6, 30.4, 30.2, 30.0, 29.9, 29.8, 29.3, 29.2, 28.7, 27.0, 22.6, 19.6, 15.7, 14.7, 13.2, 10.9; \(v_{max}\): 2920, 2818, 1690, 1468, 1002, 922, 720 cm⁻¹.

**16–\((1S,2R)\)–2–\((S)\)–16–\((1R,2S)\)–2–Octadeccyclo-propyl)hexadecan–2–yl)cyclopropyl)hexadec-15-ynyl pivalate**

Lithium \(\text{(trimethylsilyl)amide (7.2 mL, 7.6 mmol, 1.06M) was added dropwise to a stirred solution of \((E/Z)\)–16–\((1S,2R)\)–2–\((S)\)–16–\((1R,2S)\)–2–octadecyclopropyl)–hexadecan–2–yl)cyclopropyl)hexadec–15–enyl pivalate (2.9 g, 67%). Dipotassium azodicarboxylate (4.5 g, 23.2 mmol) was added to a stirred solution of the above alkene (2.9 g, 3.3 mmol) in THF (50 mL) and methanol (15 mL) at 10 °C under nitrogen. A solution of glacial acetic acid (6 mL) and THF (6 mL) was added dropwise for 24 h then additional dipotassium azodicarboxylate (2.20 g, 11.6 mmol) and a solution of glacial acetic acid (3 mL) and THF (3 mL) were added and stirred for a further 24 h. A white precipitate had formed. The mixture was poured slowly into sat.aq. NaHCO₃ (25 mL) and the product was extracted with petroleum/ethyl acetate (1:1, 2 × 100 mL). The combined organic layers were washed with water (50 mL), dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (20:1) gave a colourless oil, the title compound (2.7 g, 93%), \([\alpha]_D^20 = +3.55\) (c 1.07, CHCl₃) \{Found (M+Na)^+: 905.9038; C₄₀H₇₁O₂Na requires: 905.9030\}, which showed \(\delta_H\) (500 MHz, CDCl₃): 4.05 (2H, br.t, J 6.6 Hz), 1.62 (2H, br.pent, J 6.3 Hz), 1.38 – 1.21 (90H, br.m), 1.20 (9H, s), 0.90 (3H, d, J 6.6 Hz), 0.89 (3H, t, J 7.2 Hz), 0.70 – 0.64 (3H, m), 0.47 (1H, dt, J 4.7, 6.9 Hz), 0.45 – 0.42 (1H, m), 0.21 – 0.09 (3H, m), – 0.32 (1H, br.q, J 5.4); \(\delta_C\) (126 MHz, CDCl₃): 178.5, 64.4, 38.7, 38.1, 37.4, 34.5, 31.9, 30.2, 30.0, 29.7, 29.6, 29.5, 29.3, 29.2, 28.7, 28.6, 27.2, 26.1, 25.9, 22.6, 19.6, 18.6, 15.8, 14.0, 10.9, 10.4; \(v_{max}\): 2917, 2810, 1728, 1471, 1153 cm⁻¹.
16-((1S,2R)-2-((S)-16-((1R,2S)-2-Octadecycyclopropyl)hexadecan-2-yl)cyclopropyl)hexadecan-1-ol

The above pivalate (2.7 g, 2.9 mmol) was added to a stirred solution of potassium hydroxide (0.70 g, 12.5 mmol) dissolved in a mixture of THF: MeOH: water (30: 20: 5 mL). The mixture was stirred at 70 °C, then quenched with water (50 mL) and extracted with petroleum/ethyl acetate (1:1, 3 x 100 mL), dried and the solvent was evaporated. Column chromatography eluting with petroleum/ethyl acetate (5:1 and then 1:1) gave a white solid, the title compound (2.4 g, 98%), m.p. 50 – 52 °C, [α]25D +4.1 (c 0.7, CHCl3) {Found (M+Na)+: 821.8460; C36H58O3Na requires: 821.8454}, which showed δH (500 MHz, CDCl3): 3.64 (2H, br.t, J 6.6 Hz), 1.62 – 1.54 (4H, pent, J 6.6 Hz, and 1H, br.s, for the hydroxyl group), 1.37 – 1.17 (88H, br.m), 0.97 (1H, d, J 5.1 Hz), 0.68 – 0.63 (3H, m), 0.57 (1H, dt, J 3.8, 7.9 Hz), 0.48 – 0.42 (1H, m), 0.22 – 0.09 (3H, m), –0.32 (1H, br.q, J 5.1 Hz); δc (126 MHz, CDCl3): 63.1, 43.9, 38.1, 37.4, 34.4, 32.8, 31.9, 30.2, 29.7, 29.6, 29.4, 29.3, 28.7, 27.2, 26.1, 25.7, 22.6, 19.6, 18.6, 15.8, 14.1, 10.9, 10.4; νmax: 3419, 2918, 2845, 1471, 1366, 1057, 898, 719 cm−1.

16-((1S,2R)-2-((S)-16-((1R,2S)-2-Octadecycyclo–propyl)hexadecan–2–yl)cyclopropyl)hexadecan–34

The above alcohol (1.40 g, 1.75 mmol) was dissolved in hot CH2Cl2 (20 mL) and added to a refluxing stirred suspension of PCC (0.87 g, 4.03 mmol) in CH2Cl2 (30 mL). The mixture was stirred vigorously for 2 h, then diluted with warm petroleum/ethyl acetate (5:2) and filtered over a bed of silica/celite and washed well with ethyl acetate (200 mL). The filtrate was evaporated to give a residue which was purified by column chromatography eluting with petroleum/ethyl acetate (10:1) to give a white solid, the title compound (1.2 g, 86%), m.p. 41 – 42 °C, [α]25D +6.1 (c 1.1, CHCl3) {Found(M+Na)+: 819.8205; C36H58O3Na requires: 819.8298}, which showed δH (500 MHz, CDCl3): 9.77 (1H, t, J 1.9 Hz), 2.42 (2H, dt, J 1.9, 7.2 Hz), 1.63 (2H, br.pent, J 7.3 Hz), 1.38 – 1.14 (88H, br. m), 0.90 (3H, d, J 6.6 Hz), 0.89 (3H, t, J 6.6 Hz), 0.68 – 0.62 (3H, m), 0.57 (1H, dt, J 3.8, 7.9 Hz), 0.48 – 0.42 (1H, m), 0.22 – 0.09 (3H, m), –0.32 (1H, br.q, J 5.1 Hz); δc (126 MHz, CDCl3): 202.8, 43.9, 38.1, 37.4, 34.4, 31.9, 30.2, 30.0, 29.7, 29.6, 29.4, 29.3, 29.1, 29.0, 28.7, 27.2, 26.1, 22.6, 22.6, 20.3, 22.1, 19.6, 18.6, 15.7, 14.2, 14.0, 10.9, 10.5; νmax: 2917, 2810, 1721, 1471, 1019, 845, 718 cm−1.

Methyl (R)-2-((E/Z) methyl (R)-2-((S)-16-((1R,2S)-2–octadecycyclopropyl)hexadecan–2–yl)cyclopropyl)nonadecyl)-tetracosanoate

Lithium bis(trimethylsilyl)amide (1.90 mL, 2.07 mmol, 1.06 M) was added dropwise to a stirred solution of aldehyde 34 (1.00 g, 1.25 mmol) and sulphone 35 (1.05 g, 1.38 mmol) in dry THF (25 mL) under nitrogen at –10 °C. The mixture was allowed to reach room temperature and stirred for 2 h, then quenched with sat.aq. NH4Cl (20 mL) at r.t. and the product was extracted with petroleum/ethyl acetate (5:2, 3 x 100 mL). The combined organic layers were dried and evaporated, the crude product was purified by column chromatography eluting with petroleum/ethyl acetate (30:1) to give a colourless oil as a mixture of (E/Z) methyl (R)-2-((E/Z)-1-((tert–butyldimethylsilyloxy)-19-((1S,2R)-2-((S)-16-((1R,2S)-2–octadecycyclopropyl)hexadecan–2–yl)cyclopropyl)nonadec-4–enyl)tetrasonoate (0.85 g, 65%). Dipotassium azodicarboxylate (2.0 g, 10 mmol) was added to a stirred solution of the above alkene (0.85 g, 0.64 mmol) in THF (25 mL) and methanol (15 mL) at 5 °C. A solution of glacial acetic acid (3 mL) and THF (3 mL) was added dropwise for 24 h then additional dipotassium azodicarboxylate (1.5 g, 7.7 mmol) and a solution of glacial acetic acid (2 mL) and THF (2 mL) were added and stirred for a further 24 h. The mixture was poured slowly to sat.aq. NH4Cl (20 mL) and extracted with petroleum/ethyl acetate (1:1, 3 x 100 mL) and the combined organic layers were washed with water (50 mL), dried and evaporated. Column chromatography eluting with petroleum/ethyl acetate (20:1) gave a colourless oil methyl (R)-2-((E/Z)-1-((tert–butyldimethylsilyloxy)-19-((1S,2R)-2-((S)-16-((1R,2S)-2–octadecycyclopropyl)hexadecan–2–yl)cyclopropyl)nonadec–4–enyl)tetrasonoate (0.80 g, 94%), [α]25D +4.3 (c 1.2, CHCl3) {Found (M+Na)+: 1358.3227; C49H76O5SiNa requires: 1358.3443}, which showed δH (500 MHz, CDCl3): 3.93 – 3.89 (1H, m), 3.66 (3H, s), 2.53 (1H, ddd, J 3.7, 6.9, 1.0 Hz), 1.37 – 1.15 (140H, br m), 0.91 – 0.81 (18H, m, including 3H d integrating to 3H, t integrating to 6H and s integrating to 9H), 0.68 – 0.63 (3H, m), 0.57 (1H, dt, J 4.1, 7.9 Hz), 0.48 – 0.42
(1H, m), 0.21 – 0.09 (3H, m), 0.052 (3H, s), 0.027 (3H, s), – 0.32 (1H, br.q, J 5.4 Hz); δC (126 MHz, CDCl₃): 175.1, 73.2, 51.5, 51.1, 38.1, 37.4, 36.3, 34.5, 34.1, 33.7, 31.9, 30.2, 30.0, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.8, 27.8, 27.6, 27.5, 26.1, 25.8, 25.7, 23.7, 22.6, 22.3, 20.4, 19.6, 19.4, 18.6, 17.9, 15.7, 14.1, 10.9, 10.4, 8.8 – 4.3, – 4.9; νmax: 2923, 2813, 1741, 1465, 1361, 1254, 1166, 836, 775 cm⁻¹.
30

\[
\text{CH}_3(\text{CH}_2)_3\text{CH} = (\text{CH}_2)_{14}\text{CH}_3
\]
$\text{CH}_2(\text{CH}_2)_7\gamma(\text{CH}_3)_6 \quad \text{OH} \quad \text{O}$

$\text{CH}_2(\text{CH}_3)_2 \cdot \text{CH}_2$
Supplementary Information B

The synthesis of single enantiomers of α-mycolic acids of *Mycobacterium tuberculosis* and related organisms, with alternative cyclopropane stereochemistries

C. Don Lawson, M. Maza–Iglesias, M. M. Sirhan, J. R. Al Dulayymi, and M. S.Baird*
Department of Chemistry, Bangor University, Gwynedd LL 57 2 UW, UK

S2 Preparation of sugar esters

\[
\text{Scheme S4: (i) EDCI, DMAP, CH}_2\text{Cl}_2, 4\Delta \text{ molecular sieves, rt, 6 days; (ii) TBAF, THF, 5 °C, then 1 hr at rt; (iii) Pyridine, THF, HF–pyridine complex, 43 °C, 17 hrs.}
\]

(R)–2–((R)–1–(tert–Butyldimethylsilyloxy)–19–((1S,2R)–2–((S)–16–((1S,2R)–2–octadecylocyclopropyl)hexaadecan–2–yl)cyclopropyl)nona–deyl)tetracosanic acid 55
Imidazole (0.180 g, 2.64 mmol) was added to a stirred solution of the acid 37 (0.31 g, 0.26 mmol) in anhydrous DMF (3 mL) and dry toluene (6 mL) at r.t. followed by tert–butyldimethylsilylchloride (0.40 g, 2.7 mmol) and 4-dimethylaminopyridine (0.03 g, 0.25 mmol). The mixture was stirred at 70 °C for 24 h and at r.t. for another 18 h, the solvent was removed under high vacuum and the residue was diluted with petrol/ethyl acetate (10:2, 2 × 30 mL). The combined organic layers were washed with water, dried and evaporated to give a residue, which was purified by column chromatography eluting with petroleum/ethyl acetate (5:2, 40 mL) then water (2 mL), then acidified with potassium hydrogen sulphate to pH 2. The organic layer was separated and the aqueous layer was re-extracted with petrol/ethyl acetate (2 × 30 mL). The combined organic layers were dried and evaporated to give a residue, which was purified by column chromatography eluting with petroleum/ethyl acetate (10:1) to give the title compound (0.281 g, 80%), [α]_D22 +15 (c 0.9, CHCl₃) (Found (M+Na)⁺: 1344.3270; C₂₉H₇₀O₅SiNa requires: 1344.3282), which showed δ_H (500 MHz, CDCl₃ + few drops of CD₂OD): 3.85 – 3.82 (1H, m), 2.53 (1H, ddd, J 3.2, 5.7, 9.2 Hz), 1.70 – 1.51 (8H, m), 1.37 – 1.15 (133H, m), 0.93 (9H, s), 0.90 (3H, d, J 6.9 Hz), 0.89 (6H, t, J 6.6 Hz), 0.67 – 0.63 (3H, m), 0.57 (1H, dt, J 4.1, 7.9 Hz), 0.46 – 0.42 (1H, m), 0.21 – 0.10 (9H, m, including two s at δ 0.15, 0.14), – 0.33 (1H, br.q, J 5.4 Hz); δ_C (126 MHz, CDCl₃): 175.8, 73.6, 50.2, 38.1, 37.4, 35.5, 34.5, 31.9, 30.2, 30.0, 29.7, 29.6, 29.5, 29.4, 29.3, 28.7, 27.4, 27.2, 26.1, 25.7, 25.6, 24.9, 22.6, 19.6, 18.6, 18.1, 17.9, 15.7, 14.1, 10.9, 10.4, – 4.2, – 4.8; ν_max: 3416, 2923, 2814, 1709, 1463, 1388, 1254, 1073, 1004, 939, 836, 720, 670 cm⁻¹.

(R)–2–((S)–1–(tert–Butyldimethylsilyloxy)–19–((1S,2R)–2–((S)–16–((1R,2S)–2–octadecylcyclo–propyl)hexadecan–2–yl)cyclopropyl)nonadecyl)tetracosanoic acid 56

Imidazole (0.27 g, 3.96 mmol) was added to a stirred solution of (R)–2–((R)–1–hydroxy–19–((1S,2R)–2–((S)–16–((1R,2S)–2–octadecylcyclopropyl)hexadecane–2–yl)cyclopropyl)nonadecyl)tetracosanoic acid (0.48 g, 0.40 mmol) in anhydrous DMF (4 mL) and dry toluene (6 mL) at r.t. followed by tert–butyldimethylsilylchloride (0.60 g, 3.98 mmol) and 4-dimethylaminopyridine (0.05 g, 0.40 mmol). The mixture was stirred at 70 °C for 24 h and at r.t. for another 18 h. The solvent was removed under high vacuum and the residue was diluted with petrol/ethyl acetate (10:2, 50 mL) and water (30 mL). The organic layer was separated and the aqueous layer was re–extracted with petrol/ethyl acetate (10:2, 2 × 50 mL). The combined organic layers were washed with water, dried and evaporated to give a colourless oil. The residue was dissolved in THF (15 mL), water (1.5 mL), and methanol (1.5 mL), to this was added potassium carbonate (0.26 g). The mixture was stirred at 45 °C for 18 h, then evaporated to 1/4 of the volume and diluted with petrol/ethyl acetate (5:1, 50 mL) then acidified with potassium hydrogen sulphate to pH 2. The organic layer was separated and the aqueous layer was re–extracted with petrol/ethyl acetate (3 × 20 mL). The combined organic layers were washed with water, dried and evaporated to give a residue, which was purified by column chromatography on silica eluting with petroleum/ethyl acetate (10:1) to give the title compound (0.45 g, 85%), [α]_D22 +14 (c 0.10, CHCl₃) (Found [M+Na]⁺: 1344.3248; C₂₉H₇₀O₅SiNa requires: 1344.3282), which showed δ_H (400 MHz, CDCl₃ + few drops of CD₂OD): 3.86 – 3.82 (1H, m), 2.53 (1H, ddd, J 3.2, 5.7, 9.2 Hz), 1.37 – 1.15 (141H, m), 0.93 (9H, s), 0.89 (3H, d, J 6.9 Hz), 0.88 (6H, t, J 6.6 Hz), 0.66 – 0.62 (3H, m), 0.57 (1H, dt, J 4.1, 7.9 Hz), 0.46 – 0.42 (1H, m), 0.21 – 0.10 (9H, m, including two s at δ 0.17, 0.14), – 0.33 (1H, br.q, J 5.3 Hz); δ_C (100 MHz, CDCl₃): 171.1, 73.5, 50.5, 38.1, 37.4, 35.1, 34.5, 31.9, 30.2, 29.7, 29.6, 29.5, 29.4, 29.3, 28.7, 27.4, 27.2, 26.1, 25.7, 25.6, 24.9, 22.6, 19.6, 18.6, 18.1, 17.9, 15.7, 14.1, 10.9, 10.4, – 4.2, – 4.8; ν_max: 3416, 2923, 2814, 1709, 1463, 1388, 1254, 1073, 1004, 939, 836, 720, 670 cm⁻¹.
30.0, 29.7, 29.5, 29.4, 29.2, 28.7, 27.5, 27.2, 26.1, 25.7, 22.7, 19.7, 18.6, 15.7, 14.1, 10.9, 10.5, – 4.2, – 4.9; \( \nu_{\text{max}} \): 3148, 2923, 2813, 1708, 1465, 1372, 1255, 1100, 836, 720, 665 cm\(^{-1}\).

6,6'-Bis-O-(2-((1R)-1-(tert-butylidimethylsilyloxy)-19-((1S)-2-((1S)-16-((1S,2R)-2-octadecylcyclopropyl)hexadecan-2-yl)cyclo propyl)nonadecyl)tetracosanoate-2,3,4,2',3',4'-hexakis-O-(trimethylsilyl)-a,a'-trehalose (58a) and 6,6'-Bis-O-(2-((1R)-1-(tert-butylidimethylsilyloxy)-19-((1S)-2-((1S)-16-((1S,2R)-2-octadecylcyclopropyl)hexadecan-2-yl)cyclo propyl)nonadecyl)tetracosanoate-2,3,4,2',3',4'-hexakis-O-(trimethylsilyl)-a,a'-trehalose (58c)

1-(3-Dimethylaminopropyl)-3-ethylcarbodiimidehydrochloride (EDCI) (0.16 g, 0.82 mmol) and 4-dimethylaminopyridine (0.088 g, 0.720 mmol) were added to a stirred solution of acid 55 (0.281 g, 0.216 mmol), protected α,α'-trehalose 57 (0.08 g, 0.10 mmol) and powdered 4 Å molecular sieves in dry dichloromethane (3 mL) under nitrogen at r.t. The mixture was stirred for 6 days at r.t. then diluted with CH\(_2\)Cl\(_2\) (10 mL) and filtered. The filtrate was evaporated under reduced pressure to give a residue, which was purified by column chromatography on silica eluting with petroleum/ethyl acetate (50:1) and then (20:1) to give the first fraction, \( 58a \) (0.185 g, 54%), as a colourless thick oil, [\( \alpha \)]\( D \)\(^{+41} (c 0.72, \text{CHCl}_3)\), \{Found-MALDI (M+Na)\}\(^{+}: 3407.2; \text{C}_{209}\text{H}_{419}\text{O}_{51}\text{Si}_{8}\text{Na} \text{requires: 3407.2} \}, which showed \( \delta_t \) (500 MHz, CDCl\(_3\) + few drops of CD\(_2\)OD): 4.86 (2H, d, J 3.2 Hz), 4.37 (2H, br. d, J 10.1 Hz), 4.04 – 3.98 (4H, m), 3.94 (2H, br. q, J 5.1 Hz), 3.90 (2H, t, J 8.8 Hz), 3.52 (2H, t, J 9.2 Hz), 3.38 (2H, dd, J 3.2, 9.4 Hz); 2.57 – 2.53 (2H, m), 1.36 – 1.12 (28H, m), 0.90 – 0.85 (36H, including a 2 x tert-butyl groups, 2 x α-methyl groups and 4 x terminal CH\(_2\) groups), 0.64 – 0.57 (6H, m), 0.55 (2H, dt, J 3.8, 8.0 Hz), 0.47 – 0.42 (2H, m), 0.21 – 0.09 (60H, m, including 3 x s for (CH\(_3\))\(_3\)Si groups at δ 0.16, 0.14, 0.13), 0.061 (12H, s), – 0.32 (2H, br. q, J 5.4 Hz); \( \delta_c \) (126 MHz, CDCl\(_3\)): 173.8, 94.8, 73.5, 73.4, 72.8, 71.8, 70.7, 62.3, 51.8, 38.1, 37.4, 34.1, 33.4, 31.9, 30.2, 30.0, 29.8, 29.73, 29.7, 29.6, 29.5, 29.3, 28.7, 28.1, 27.2, 26.1, 25.9, 25.8, 25.18, 22.6, 22.6, 22.3, 19.6, 18.6, 18.0, 15.7, 14.1, 10.9, 10.4, 1.0, 0.9, 0.1, – 4.5, – 4.6; \( \nu_{\text{max}} \): 2924, 2813, 1743, 1638, 1464, 1469, 1251, 1163, 1077, 899, 720, 665 cm\(^{-1}\). The second fraction was \( 58a \) (0.085 g, 46%), [\( \alpha \)]\( D \)\(^{2+4} (c 0.70, \text{CHCl}_3)\) [Found-MALDI (M+Na)\}\(^{+}: 2101.60; \text{C}_{115}\text{H}_{224}\text{O}_{31}\text{Si}_{8}\text{Na} \text{requires: 2101.67} \}, which showed \( \delta_t \) (500 MHz, CDCl\(_3\) + few drops of CD\(_2\)OD): 4.91 (1H, d, J 3.2 Hz), 4.84 (1H, d, J 3.2 Hz), 4.35 (1H, dd, J 2.6, 12.0 Hz), 4.08 (1H, dd, J 7.9, 12.0 Hz), 3.97 (1H, br. d, J 11.4 Hz), 3.94 – 3.85 (2H, br. m), 3.82 (2H, br. t, J 2.9, 9.2 Hz), 3.71 – 3.65 (2H, m), 3.47 (2H, dt, J 5.9, 8.8 Hz), 3.40 (2H, dd, J 3.2, 9.2, 12.3 Hz), 2.57 – 2.53 (1H, m), 1.71 – 1.15 (141H, m, including s at δ1.56), 0.89 – 0.83 (18H, including s for tert-butyl group at δ 0.84 and br t at δ 0.86 with J 6.65 Hz), 0.71 – 0.65 (3H, m), 0.56 (1H, dt, J 4.1, 7.9 Hz), 0.46 – 0.42 (1H, m), 0.28 – 0.10 (57H, br. m, including six s for (CH\(_3\))\(_3\)Si groups), 0.06 (3H, s), 0.05 (3H, s), – 0.32 (1H, br. q, J 5.4 Hz); \( \delta_c \) (126 MHz, CDCl\(_3\)): 174.0, 94.5, 94.4, 73.4, 73.3, 72.8, 72.8, 72.7, 72.0, 71.4, 70.7, 68.1, 62.4, 61.6, 51.8, 38.7, 38.1, 37.44, 34.4, 33.37, 31.9, 30.3, 30.2, 30.0, 29.8, 29.76, 29.7, 29.6, 29.5, 29.3, 28.9, 28.7, 28.1, 27.2, 26.4, 26.1, 25.8, 24.8, 23.7, 22.9, 22.6, 19.6, 18.6, 18.0, 15.7, 14.1, 10.9, 10.9, 10.4, 1.0, 0.9, 0.8, 0.1, 0.04, – 4.4, – 4.7; \( \nu_{\text{max}} \): 2923, 2813, 1741, 1464, 1251, 1165, 1076, 1007, 843, 720 cm\(^{-1}\).
(i) Tetrabutylammonium fluoride (0.16 mL, 0.16 mmol, 1M) was added to a stirred solution of compound 58a (0.187 g, 0.055 mmol) in dry THF (12 mL) at 5 °C under nitrogen. The mixture was allowed to reach r.t. and then it was stirred for 1 h, then the solvent was evaporated and the residue was purified by column chromatography eluting with CHCl₃/MeOH (10:1) to give 58b (0.159 g, 99%) as a colourless thick oil, [α]D²⁵ +41 (c 0.5, CHCl₃) {Found-MALDI (M+Na)⁺: 2974.15; C₁₉₈H₃₇O₁₅Si₂Na requires: 2974.12}, which showed δH (500 MHz, CDCl₃ + few drops of CD₂OD): 5.07 (2H, d, J 3.5 Hz), 4.34 (2H, dd, J 4.4, 12.3 Hz), 4.1 (2H, d, J 10.4 Hz), 3.93 – 3.86 (4H, m), 3.78 (2H, t, J 9.1 Hz), 3.46 (2H, dd, J 3.5, 9.8 Hz), 3.30 (2H, t, J 9.5 Hz), 2.64 – 2.43 (2H, m), 1.41 – 1.10 (282H, m), 0.86 (6H, d, J 6.9 Hz), 0.85 – 0.82 (30H, including a 2 × tert–butyl groups and 4 × CH₃ groups), 0.67 – 0.61 (6H, m), 0.52 (2H, dt, J 4.1, 7.9 Hz), 0.44 – 0.39 (2H, m), 0.18 – 0.07 (6H, m), 0.051 (6H, s), 0.041 (6H, s), – 0.36 (2H, br.q, J 5.1 Hz); δC (126 MHz, CDCl₃): 175.0, 93.3, 73.1, 71.5, 70.2, 69.8, 62.8, 51.5, 37.9, 37.2, 34.2, 33.4, 31.7, 30.0, 29.8, 29.7, 29.6, 29.5, 29.43, 29.4, 29.3, 29.1, 28.5, 27.5, 27.0, 26.8, 25.9, 25.6, 25.5, 24.0, 22.4, 19.4, 18.4, 17.7, 15.5, 13.8, 10.6, 10.2, –4.7, –5.1; v+w: 3391, 2923, 2813, 1738, 1465, 1372, 1254, 1146, 1105, 1078, 992, 836, 775, 720 cm⁻¹.

(ii) A dry polyethylene vial equipped with a rubber septum was charged with compound 58b (0.15 g, 0.05 mmol) and pyridine (0.1 mL) in dry THF (10 mL) and stirred under nitrogen at r.t. Hydrogen fluoride (0.05 mmol) and pyridine (0.1 mL) in dry THF (10 mL) were added to a stirred solution of compound (i) (0.085 g, 0.040 mmol) in dry THF (8 mL) under nitrogen at 5 °C. The mixture was allowed to reach r.t. and then it was stirred for 1 h, then the solvent was evaporated and the residue was purified by column chromatography eluting with CHCl₃/MeOH (10:1) to give 58c (0.104 g, 75%) as a syrup, [α]D²⁵ +43 (c 0.52, CHCl₃) {Found-MALDI (M+Na)⁺: 2745.5; C₁₇₅H₃₄O₁₃SiNa requires: 2745.6; (M+Na)⁺: 3390, 2917, 2849, 1729, 1468, 1050, 993, 807, 720 cm⁻¹}.

6-O-[1(2-(R))-1-Hydroxy-19-(1S,2R)-2-(5S)-16-((1S,2R)-2-octadecyl-cyclopropyl)hexadecan-2-yl)(cyclopropyl)nonadecyl)-a,a'-trehalose 59c

(i) Tetrabutylammonium fluoride (0.12 mL, 0.12 mmol, 1M) was added to a stirred solution of compound 59a (0.085 g, 0.040 mmol) in dry THF (8 mL) under nitrogen at 5 °C. The mixture was allowed to reach r.t. and then it was stirred for 1 h then worked up and purified as above to give 59b (0.06 g, 88%) as a colourless syrup, [α]D²⁵ +53 (c 0.7, CHCl₃) {Found-MALDI (M+Na)⁺: 1669.3; C₁₅₀H₂₉₆O₁₅SiNa requires: 1669.4}, which showed δH (500 MHz, CDCl₃ + few drops of CD₂OD): 5.07 (2H, d, J 2.2 Hz), 4.31 (1H, br.d, J 7.6 Hz), 4.24 (1H, br.d, J 10.4 Hz), 3.93 (1H, br.d, J 6.0, 8.5 Hz), 3.88 – 3.83 (4H, m), 3.67 (2H, br.d, J 8.0, 11.3 Hz), 3.50 (2H, dd, J 3.5, 9.7 Hz), 3.37 – 3.33 (2H, m), 2.55 – 2.46 (1H, m), 1.43 – 1.10 (147H, m), 0.87 – 0.82 (18H, including s for the tert–butyl group at δ 0.82 and br t at δ 0.84 with J 6.6 Hz), 0.68 – 0.57 (3H, m), 0.53 (1H, dt, J 3.8, 7.9 Hz), 0.44 – 0.38 (1H,
m), 0.18 – 0.05 (3H, m), 0.014 (3H, s), – 0.007 (3H, s), – 0.36 (1H, br q, J 5.4 Hz); δc (126 MHz, CDCl3): 175.1, 93.2, 73.2, 73.0, 72.6, 72.1, 70.6, 70.2, 69.9, 68.1, 67.8, 62.6, 61.9, 51.6, 38.6, 38.0, 37.3, 34.4, 33.5, 31.8, 30.1, 29.9, 29.7, 29.6, 29.6, 29.5, 29.4, 29.2, 28.8, 28.6, 27.6, 27.1, 26.9, 26.0, 25.73, 25.7, 25.5, 24.2, 23.6, 22.8, 22.6, 19.5, 18.5, 17.8, 15.7, 14.0, 10.8, 10.3, – 4.5, – 4.9; νmax: 3391, 2918, 2810, 1722, 1467, 1254, 1077, 991, 836, 720 cm⁻¹.

(ii) A dry polyethylene vial equipped with a rubber septum was charged with compound 59b (0.055 g, 0.033 mmol) and pyridine (0.1 mL) in dry dichloromethane (7 mL) and stirred under nitrogen at r.t. Hydrogen fluoride–pyridine complex as ~70 % hydrogen fluoride (0.5 mL) was then added at 5 °C. The mixture was stirred at 43 °C for 17 h. The mixture was worked up and purified as above to give 59c (0.024 g, 47%) as a syrup, [α]D +52 (c 0.61, CHCl3) [Found-MALDI (M+Na)+]: 1555.31; C39H128O13Na requires: 1555.35], which showed δ0 (500 MHz, CDCl3 + few drops of CD2OD): 5.05 (1H, d, J 3.4 Hz), 4.98 (1H, d, J 3.5 Hz), 4.64 (1H, br d, J 11.4 Hz), 4.20 (1H, br t, J 8.2 Hz), 3.95 (1H, br d.d, J 8.8, 12.6 Hz), 3.93 – 3.74 (4H, m), 3.72 – 3.56 (2H, m), 3.51 (1H, dd, J 3.3, 9.7 Hz), 3.44 (1H, dd, J 3.8, 10.1 Hz), 3.26 – 3.16 (2H, m), 2.39 – 2.34 (1H, m), 1.51 – 1.08 (14H, m), 0.84 (3H, d, J 6.6 Hz), 0.83 (6H, t, J 7.2 Hz), 0.70 – 0.59 (3H, m), 0.51 (1H, dt, J 4.1, 7.9 Hz), 0.43 – 0.37 (1H, m), 0.15 – 0.03 (3H, m), – 0.38 (1H, br q, J 5.4 Hz); δc (126 MHz, CDCl3): 175.4, 94.3, 72.5, 72.3, 72.2, 71.3, 71.2, 70.9, 70.7, 69.9, 64.1, 61.9, 52.3, 37.9, 37.2, 34.5, 34.3, 31.7, 30.0, 29.8, 29.5, 29.3, 29.2, 29.1, 28.5, 27.1, 27.0, 25.9, 25.0, 22.5, 19.4, 18.4, 15.6, 13.8, 10.7, 10.2; νmax: 3369, 2925, 2813, 1723, 1466, 1215, 1047, 756 cm⁻¹.

6,6'-Bis-O-2-((1R)–1-(tert–butyldimethyl–silyloxy)-19-(15S)–2-((1R,2S)–2-oc Hendeka-2-yl)cyclopropyl)hexadecan-2-yl)cyclopropyl)nonadecyl)tetracosanaotae-2,3,4,2',3',4'-hexakis-O-(trimethylsilyl)-α,α'-trehalose (60a) and 6-O-2-((1R)–1-(tert–butyldimethylsilyloxy)-19-(15S)–2-((1R,2S)–2-oc Hendeka-2-yl)cyclopropyl)nonadecyl)tetracosa-2,3,4,2',3',4'-hexakis-O-(trimethylsilyl)-α,α'-trehalose (61a)

EDCI (0.16 g, 0.82 mmol) and 4–dimethylaminopyridine (0.088 g, 0.720 mmol) were added to a stirred solution of acid 56 (0.281 g, 0.216 mmol), protected α,α'-trehalose 57 (0.08 g, 0.10 mmol) and powdered 4 A° molecular sieves in dry dichloromethane (3 mL) at r.t under nitrogen. The mixture was stirred for 6 days, then diluted with CH2Cl2 (10 mL) and filtered. The reaction was worked up and purified as before to give the first fraction 60a (0.235 g, 69%), as a colourless thick oil, [α]D +43 (c 1.1, CHCl3) [Found-MALDI (M+Na)+]: 3407.24; C29H66O5Si4Na requires: 3407.20], which showed δ0 (400 MHz, CDCl3 + few drops of CD2OD): 4.85 (2H, d, J 2.9 Hz), 4.37 (2H, br d, J 10.0 Hz), 4.04 (2H, d, J 2.9 Hz), 3.99 (2H, d, J 10.4 Hz), 3.96 (2H, br q, J 4.9 Hz), 3.89 (2H, d, J 8.9 Hz), 3.53 (2H, br t, J 8.7 Hz), 3.38 (2H, dd, J 2.9, 9.4 Hz), 2.56 – 2.53 (2H, m), 1.36 – 1.12 (280H, m), 0.91 – 0.87 (36H, including a 2 × tert–butyl groups, 2 × α–methyl groups and 4 × terminal CH₃ groups), 0.71 – 0.64 (6H, m), 0.57 (2H, dt, J 3.97 Hz, 1.2 Hz), 0.47 – 0.42 (2H, m), 0.21 – 0.09 (60H, m, including three s for (CH3)2Si groups at δ 0.17, 0.15, 0.14), 0.061 (12H, s), – 0.32 (2H, br q, J 5.2 Hz); δc (101 MHz, CDCl3): 173.8, 94.7, 73.5, 73.4, 72.8, 71.8, 70.7, 62.3, 51.8, 38.1, 37.4, 34.5, 33.4, 31.9, 30.2, 30.1, 29.8, 29.7, 29.6, 29.5, 28.7, 28.1, 27.2, 26.1, 25.9, 25.8, 22.7, 19.7, 18.6, 18.0, 15.7, 14.1, 10.9, 10.5, 1.0, 0.9, 0.1, – 4.5, – 4.6; νmax: 2924, 2813, 1744, 1465, 1251, 1164, 1077, 899, 720, 665 cm⁻¹. The second fraction was 61a (0.107 g, 47%), [α]D +53 (c 0.70, CHCl3) [Found-MALDI (M+Na)+]: 2101.60; C195H358O53Si4Na requires: 2101.67], which showed δ0 (400 MHz, CDCl3 + few drops of CD2OD): 4.91 (1H, d, J 3.0 Hz), 4.84 (1H, d, J 3.1 Hz), 4.37 (1H, br dd, J 2.0, 11.7 Hz), 4.09 (1H, dd, J 4.0, 11.7 Hz), 3.98 (1H, br d, J 9.9 Hz), 3.95 – 3.88 (2H, m), 3.85 (2H, br dd, J 3.5, 9.2 Hz), 3.71 – 3.65 (2H, m), 3.49 (2H, d, J 6.2, 8.9 Hz), 3.41 (2H, d, d, J 3.2, 9.4, 12.8 Hz), 2.60 – 2.55 (1H, m), 1.72
– 1.12 (141H, m, including s at δ1.55), 0.91 – 0.85 (18H, including s for the tert–butyl group at δ 0.87 and br t at δ 0.89 with J 6.65 Hz), 0.71 – 0.62 (3H, m), 0.57 (1H, dt, J 3.9, 7.9 Hz), 0.46 – 0.42 (1H, m), 0.28 – 0.10 (57H, br. m, including six singlets for (CH3)3Si groups), 0.06 (3H, s), 0.05 (3H, s), – 0.32 (1H, br. q, J 5.1 Hz); δc (101 MHz, CDCl3): 174.0, 94.4, 94.3, 73.4, 73.3, 72.8, 72.7, 71.9, 71.3, 70.7, 62.4, 61.6, 51.7, 38.1, 37.4, 34.43, 33.4, 31.9, 30.2, 30.0, 29.8, 29.7, 29.6, 29.5, 29.4, 28.7, 28.1, 27.2, 26.4, 26.1, 25.8, 25.7, 24.8, 22.7, 19.7, 18.6, 18.0, 15.7, 14.1, 10.9, 10.5, 1.0, 0.9, 0.8, 0.1, 0.04, – 4.4, –4.7; νmax: 3447, 2924, 2814, 1743, 1464, 1251, 1166, 1077, 1007, 843, 720 cm⁻¹.

6,6'-Bis-O-(2-((R)–1−hydroxy–19–((1S,2R)−2-((S)–16–((1R,2S)−2–octadecylcyclopropyl)hexadecan–2–yl)cyclopropyl)nonadecyl)tetracosanoate-o,a'-trehalose 60c

(i) Tetrabutylammonium fluoride (0.20 mL, 0.20 mmol, 1M) was added to a stirred solution of compound 60a (0.235 g, 0.070 mmol) in dry THF (12 mL) under nitrogen at 5 °C. The mixture was allowed to reach r.t. and then it was stirred for 1 h then worked up and purified as before to give 60b (0.18 g, 88%) as a colourless thick oil, [α]D370 +40 (c 0.89, CHCl3) [Found-MALDI (M+Na)+: 2974.10; C198H170O15Si2Na requires: 2974.12], which showed δ31 (400MHz, CDCl3 + few drops of CD3OD): 5.07 (2H, d, J 3.5 Hz), 4.32 (2H, dd, J 3.9, 12.0 Hz), 4.1 (2H, d, J 10.8 Hz), 3.91 – 3.84 (4H, m), 3.75 (2H, br.t, J 9.3 Hz), 3.45 (2H, dd, J 3.3, 9.6 Hz), 3.29 (2H, br. t, J 9.4 Hz), 2.54 – 2.47 (2H, m), 1.49 – 1.11 (282H, m), 0.86 (6H, d, J 6.9 Hz), 0.85 – 0.78 (30H, including a 2 × tert–butyl groups and 4 × CH3 groups), 0.65 – 0.60 (6H, m), 0.51 (2H, dt, J 4.0, 7.9 Hz), 0.47 – 0.33 (2H, m), 0.17 – 0.06 (6H, m), 0.04 (6H, s), 0.03 (6H, s), – 0.37 (2H, br.q, J 5.1 Hz); δc (101 MHz, CDCl3): 175.2, 93.4, 73.1, 71.6, 70.2, 69.9, 62.8, 51.5, 38.0, 37.3, 34.3, 33.5, 31.4, 29.7, 29.5, 27.6, 26.8, 25.9, 25.6, 25.5, 24.1, 22.4, 19.5, 18.5, 15.6, 13.9, 10.7, 10.3, –4.7, –5.0; νmax: 3437, 2923, 2812, 1734, 1493, 1360, 1251, 1050, 992, 836, 720 cm⁻¹.

(ii) A dry polyethylene vial equipped with a rubber septum was charged with compound 60b (0.175 g, 0.059 mmol) and pyridine (0.1 mL) in dry THF (10 mL) and stirred under nitrogen at r.t. Hydrogen fluoride–pyridine complex as ~70 % hydrogen fluoride (0.75 mL) was then added at 5 °C. The mixture was stirred at 43 °C for 17 h, then worked up and purified as before to give 60c (0.11g, 72%) as a syrup, [α]D370 +44 (c 1.2, CHCl3) [Found (MALDI) (M+Na)+: 2745.61; C179H142O9Si2Na requires: 2745.60], which showed δ31 (400 MHz, CDCl3 + few drops of CD3OD): 4.97 (2H, d, J 3.0 Hz), 4.73 (2H, br.d, J 11.2 Hz), 4.38 (2H, br.t, J 8.6 Hz), 3.89 (2H, br.d.d, J 7.9, 10.5 Hz), 3.74 (2H, br.t, J 9.3 Hz), 3.65 – 3.61 (2H, m), 3.49 (2H, d, J 2.9, 9.8 Hz), 3.20 (2H, t, J 9.6 Hz), 2.41 – 2.36 (2H, m), 1.54 – 1.09 (288H, m), 0.86 (6H, d, J 6.5 Hz), 0.84 (12H, t, J 6.9 Hz), 0.65 – 0.60 (6H, m), 0.52 (2H, dt, J 3.9, 8.0 Hz), 0.49 – 0.37 (2H, m), 0.18 – 0.04 (6H, m), – 0.36 (2H, br.q, J 5.1 Hz); δc (100 MHz, CDCl3): 175.4, 94.8, 72.4, 72.3, 71.2, 69.7, 64.3, 52.2, 38.0, 37.2, 34.3, 31.8, 30.0, 29.9, 29.5, 29.3, 29.2, 28.5, 27.1, 26.0, 25.0, 22.5, 19.5, 18.5, 15.6, 14.0, 10.7, 10.3; νmax: 3436, 2920, 2810, 1732, 1466, 1050, 991, 824, 720 cm⁻¹.

6-O-(2-((R)–1−hydroxy–19–((1S,2R)−2-((S)–16–((1R,2S)−2–octadecylcyclopropyl)hexadecan–2–yl)cyclopropyl)nonadecyl)tetracosanoate-o,a'-trehalose 61c
(i) Tetrabutylammonium fluoride (0.14 mL, 0.14 mmol, 1M) was added to a stirred solution of compound 61a (0.10 g, 0.05 mmol) in dry THF (8 mL) under nitrogen at 5 °C. The mixture was allowed to reach r.t. and then it was stirred for 1 h. Work up as before gave 61b (0.55 g, 73%) as a colourless syrup, [α]_D^22 +52 (c 0.6, CHCl₃) [Found-MALDI (M+Na)^+]: 1669.40; C₁₀₁H₁₉₆O₁₃SiNa requires: 1669.43, which showed δ_H (400 MHz, CDCl₃ + few drops of CD₃OD): 5.05 (2H, d, J = 2.7 Hz), 4.30 (1H, br d, J = 9.2 Hz), 4.23 (1H, br dd, J = 5.7, 11.9 Hz), 3.48 (2H, td, J = 3.6, 9.8 Hz), 3.37 – 3.25 (2H, m), 2.55 – 2.47 (1H, m), 1.42 – 1.12 (147H, br m), 0.86 – 0.72 (18H, including s for the tert-butyl group at δ 0.82 and br t at δ 0.84 with J 6.6 Hz), 0.66 – 0.58 (3H, m), 0.53 (1H, dt, J = 3.6, 7.5 Hz), 0.44 – 0.37 (1H, m), 0.16 – 0.04 (3H, m), 0.014 (3H, s), – 0.007 (3H, s), – 0.36 (1H, br q, J = 4.7 Hz); δ_C (100 MHz, CDCl₃): 175.1, 93.4, 73.1, 72.9, 72.5, 72.1, 71.5, 70.6, 70.2, 70.1, 69.9, 62.6, 61.9, 51.6, 38.0, 37.3, 34.3, 31.8, 30.1, 29.9, 29.6, 29.5, 29.2, 28.6, 27.6, 27.1, 26.0, 25.6, 22.5, 19.5, 18.5, 17.8, 15.6, 13.9, 10.7, 10.3, –4.6, –4.9; ν_max: 3436, 2919, 2810, 1733, 1452, 1250, 1077, 991, 825, 720 cm⁻¹.

(ii) A dry polyethylene vial equipped with a rubber septum was charged with compound 61b (0.05 g, 0.03 mmol) and pyridine (0.05 mL) in dry THF (10 mL) and stirred under nitrogen at r.t. Hydrogen fluoride–pyridine complex as ~70 % hydrogen fluoride (0.75 mL) was then added at 5 °C. The mixture was stirred at 43 °C for 17 h, then worked up and purified as before to give 61c (0.02 g, 42%) as a syrup, [α]_D^22 +52 (c 0.50, CHCl₃) [Found-MALDI (M+Na)^+]: 1555.2; C₉₅H₁₈₂O₁₃Na requires: 1555.3, which showed δ_H (400 MHz, CDCl₃ + few drops of CD₃OD): 5.04 (1H, d, J = 3.3 Hz), 4.98 (1H, d, J = 3.5 Hz), 4.62 (1H, br.d, J = 10.5 Hz), 4.17 (1H, br.t, J = 8.6 Hz), 3.95 (1H, br.dd, J = 8.8, 11.9 Hz), 3.86 – 3.72 (4H, m), 3.60 – 3.56 (2H, m), 3.50 (1H, dd, J = 3.2, 9.7 Hz), 3.43 (1H, dd, J = 3.5, 9.7 Hz), 3.28 – 3.21 (2H, m), 2.39 – 2.33 (1H, m), 1.39 – 1.05 (148H, br.m), 0.84 (3H, d, J = 6.6 Hz), 0.83 (6H, t, J = 6.4 Hz), 0.65 – 0.58 (3H, m), 0.50 (1H, dt, J = 4.1, 7.9 Hz), 0.47 – 0.34 (1H, m), 0.16 – 0.03 (3H, m), –0.38 (1H, br.q, J = 5.3 Hz); δ_C (101 MHz, CDCl₃): 175.4, 94.4, 72.5, 72.3, 71.4, 71.1, 71.0, 70.7, 69.9, 69.2, 64.2, 62.0, 52.3, 37.9, 37.2, 34.3, 31.7, 30.0, 29.9, 29.5, 29.3, 29.2, 28.5, 27.1, 25.9, 22.5, 19.5, 18.4, 15.6, 13.9, 10.7, 10.3; ν_max: 3369, 2925, 2813, 1723, 1466, 1215, 1047, 758, 669 cm⁻¹.
60a