Supporting Information

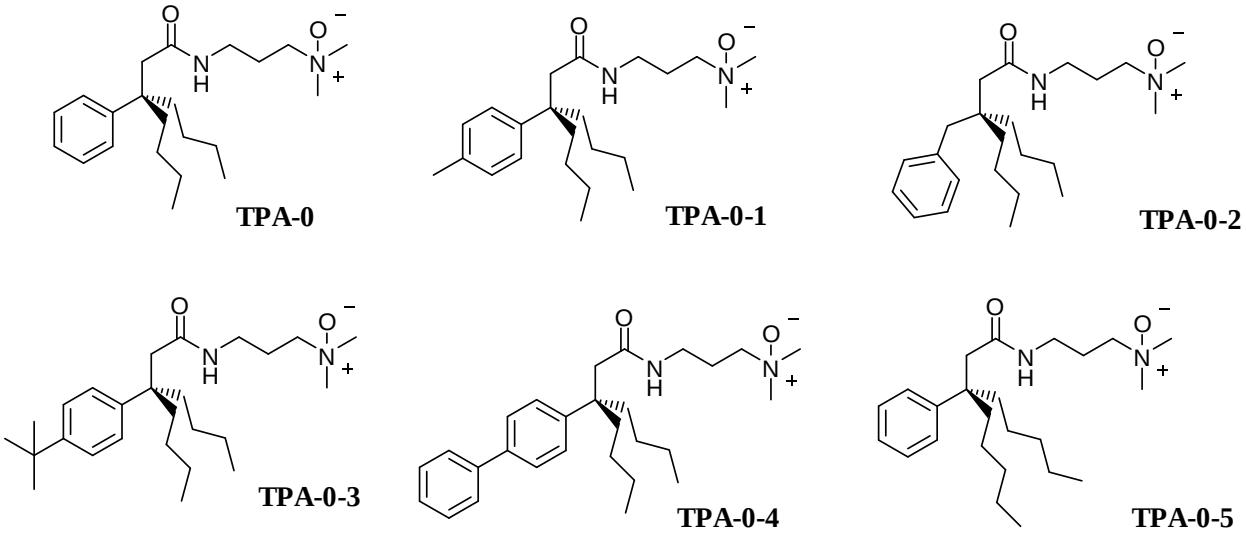
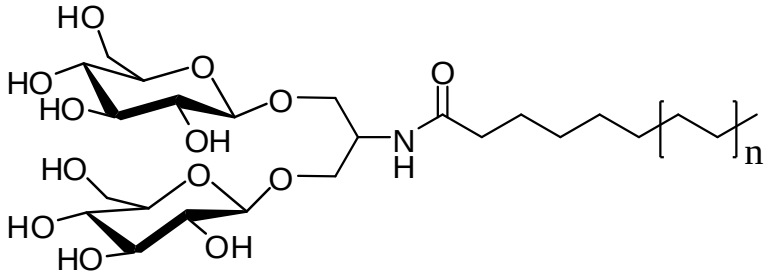


Figure S1. Chemical structures of the hydrophobic variations of TPA-0 with an *N*-oxide headgroup. TPA-0 and TPA-0-1 are only water-soluble when dissolved in sufficiently high concentration (> 5%) while others have limited solubility (<1%). On the other hand, all TPA-2 analogs with similar hydrophobic variations are exceedingly water-soluble, due to the favorable solubility characteristics of the branched diglucoside headgroup (see main text for details)



n = 1 : MPA-2 (C8)
n = 2 : MPA-2 (C10)
n = 3 : MPA-2 (C12)
n = 4 : MPA-2 (C14)
n = 5 : MPA-2 (C16)

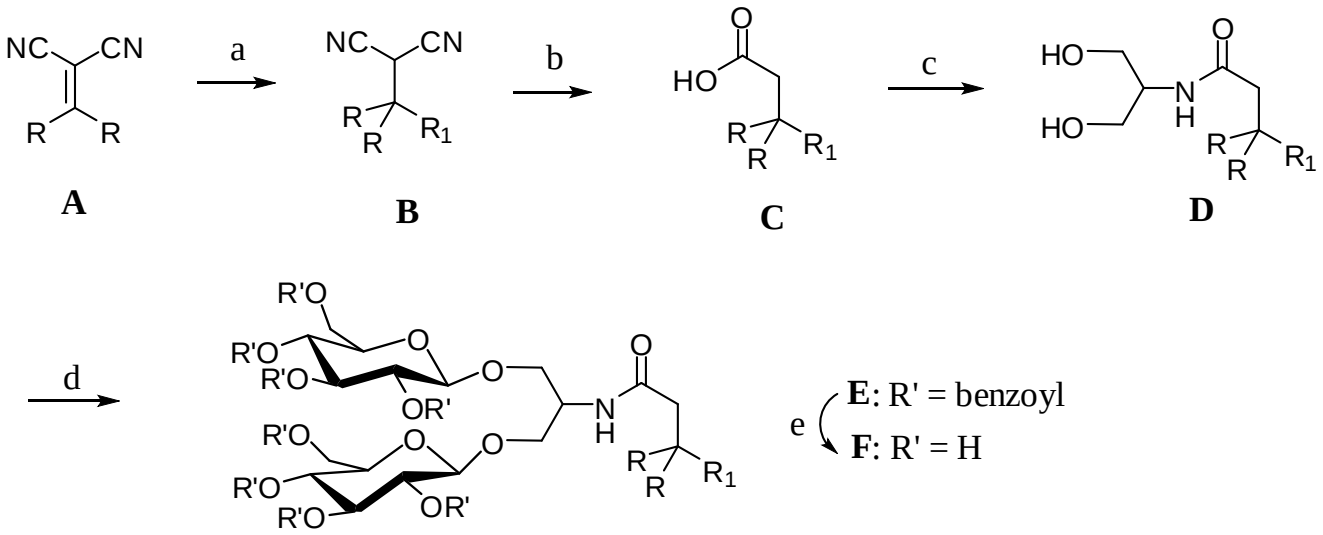
Figure S2. Chemical structures of previously-described monopod amphiphiles (MPAs) bearing the branched diglucoside headgroup, the "MPA-2 series." MPA-2 (C12) was the most efficient (~ 30%) at extracting the LHI–RC superassembly from *R. capsulatus* membranes and MPA-2 (C16) was water-insoluble. In contrast, tripod amphiphiles with the same headgroup generally gave good solubilization yield up to 80% (see main text for details).

Protein solubilization and purification

The solubilization and purification of the *R. capsulatus* superassembly were conducted according to previously published protocols.[1, 2] First, specialized photosynthetic membranes known as intracytoplasmic membranes (ICM) were isolated from an engineered strain of *Rhodobacter (R.) capsulatus*, U43[pUHTM86Bgl], lacking the peripheral light-harvesting complex II (LHII). Solubilization experiments were commenced by quickly thawing and homogenizing frozen aliquots of *R. capsulatus* ICM at room temperature. These membranes are highly enriched in LHI-RC complexes and had an initial OD_{875} = 10. Solutions were pre-incubated with mild agitation at 32˚C for 30 min. Subsequently, membrane protein solubilization was initiated by adding individual detergents at 1.0 wt % to 1.0 mL solutions and incubating for another 30 min at 32˚C. The solubilized slurry was then ultracentrifugated at 310,000 x *g* at 4℃ for 30 min to remove membrane debris and to pellet those LHI-RC superassemblies that were not removed from the ICM by incubation in the presence of the amphiphile. The spectra of solubilized supernatant and homogenized pellet were taken in a spectral range from 650 nm to 950 nm. For purification of the protein, detergent-solubilized samples were transferred into a fresh microcentrifuge tube containing Ni-NTA resin pre-equilibriated and stored in an equal volume of buffer containing 10 mM Tris, pH 7.8, and 100 mM NaCl. Following protein binding for one-hour at 4℃, the resin was collected and washed twice with 0.5 mL of binding buffer (10 mM Tris, pH 7.8 containing respective detergent 1xCMC). Protein that had been purified by this process was collected by eluting three times with 0.20 mL binding buffer solution containing 1 M imidazole (the pH of each solution was readjusted to pH = 7.8 due to the buffering capacity of high concentrations of imidazole) and diluted with 0.4 mL of the binding buffer for a final purified protein volume of 1.0 mL. UV-Vis spectra of the purified samples (containing intact superassemblies or combinations or natured and denatured LHI and/or RCs) in individual detergents were taken to assess whether or not the new amphiphiles and the micelles they form proved stabilizing or destabilizing to this pigment-protein complex in an aqueous environment.

Amphiphile synthesis and characterization

Supplementary scheme 1



(a) ArMgBr, Cu(I)CN, THF, 0°C; (b) KOH, ethylene glycol, 200°C; (c) serinol, EDC • HCl, HOBt, DMF, room temperature; (d) perbenzoylated glucosylbromide, AgOTf, CH_2Cl_2, -45°C → room temperature; (e) NaOMe, MeOH, room temperature.

General procedures for conjugate addition reaction (step a; **A→ B***)*

This procedure followed a literature method[3] with slight modifications. To the Grignard reagent (ArMgBr, 0.1 mol), Cu(I)CN (0.05 mol) was added at 0 ℃ under N_2, and the mixture was stirred for 1 h. A solution of the alkylidene, 1,1-dicyano-2,2-dialkylethylene (**A**, 0.045 mol), in THF was added to the reaction mixture. After 2 h of stirring, the reaction mixture was poured into an ice-cold saturated NH_4Cl solution (100 mL). The mixture was then extracted with diethyl ether (2 x 80 mL). The combined organic layer was washed with brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated by rotary evaporation. Column chromatography (EtOAc/hexane) afforded the desired dinitrile compound **(B)** as yellowish oil.

General procedures for solvolysis reactions (step b; **B→ C***)*

This procedure followed a literature method[3] with slight modifications. The dinitrile (10 mmol; **B**) was dissolved in ethylene glycol (50 mL) and potassium hydroxide (50 mmol) was then added to the solution. The mixture was refluxed for 3 days at 200 ℃. The reaction mixture was then cooled to room temperature and diluted with 50 mL of water. The solution was poured into ice-cold aqueous 6 M HCl (100 mL), and the resulting solution was extracted with ether (3 x 50 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated by rotary evaporation. Column

chromatography (EtOAc/hexane) afforded a desired carboxyl acid derivative (**C**) as a solid.

General procedures for amide coupling reactions (step c; **C→ D***)*

The carboxylic acid derivative (**C**) (3.8 mmol), serinol (7.6 mmol), 1-hydroxybenzotriazole monohydrate (HOBt) (1.2 g, 9.1 mmol) were dissolved in anhydrous DMF (30 mL). 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochloride (EDC • HC1) (1.7 g, 9.1 mmol) was then added in small portions at 0°C, and the resulting solution was stirred at room temperature for 20 h. The solution was taken up with EtOAc (100 mL) and washed successively with a 1 M aqueous $NaHCO_3$ solution (100 mL), a 0.1 M aqueous HCl solution (100 mL) and brine (2 x 100 mL). Then the organic layer was dried with anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation. Column chromatography (EtOAc/hexane) afforded a desired carboxyl acid derivative (**D**) as a solid.

General procedures for glycosylation reactions (step d; **D→ E***)*

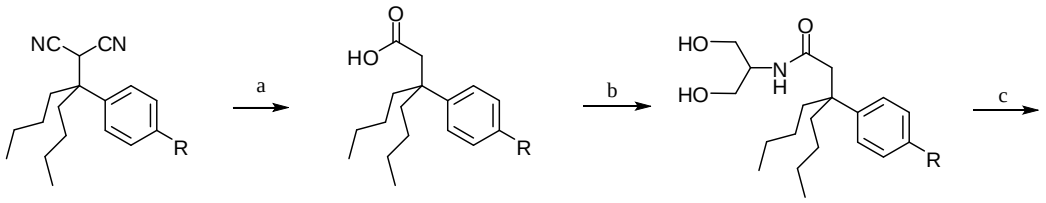
This procedure followed a literature method[4] with slight modification. A mixture of alcohol derivative (**D**), AgOTf (2.4 equiv.) and 2,4,6-collidine (2.0 equiv.) in anhydrous CH_2Cl_2 (40 mL) was stirred at -45°C. A solution of perbenzoylated glucosylbromide (2.4 equiv.) in CH_2Cl_2 (40 mL) was added dropwise over 0.5 h to this suspension. Stirring was continued for 0.5 h at -45°C, and then the reaction mixture was allowed to warm to 0 °C and left stirring for 1.5 h. After completion of the reaction (as detected by TLC), pyridine was added to the reaction mixture, and it was diluted with CH_2Cl_2 (40 mL) before being filtered through celite. The filtrate was washed successively with a 1 M aqueous $Na_2S_2O_3$ solution (40 mL), a 0.1 M aqueous HCl solution (40 mL), and brine (2 x 40 mL). Then the organic layer was dried with anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation. The residue was purified by silica gel column chromatography (EtOAc/hexane), which provided the desired product (**E**) as a glassy solid.

General procedures for deprotection reactions (step e; **E→ F***)*

This procedure followed the de-*O*-benzoylation or de-*O*-acetylation under Zemplén's conditions.[4] The *O*-pretected compounds (**E**) were dissolved in MeOH and then treated with the catalytic amount of NaOMe such that the final concentration of NaOMe was about 0.05 M. The reaction mixture was stirred for 6 h at room temperature, and then neutralized with Amberlite IR-120 (H^+ form) resin. The resin was removed by filtration and washed with MeOH, and solvent was removed from the combined filtrate *in vacuo*. The residue was purified by silica gel column chromatography (MeOH/CH_2Cl_2).

Further purification, by recrystallization using CH_2Cl_2/MeOH/diethyl ether, afforded fully deprotected product (**F**) as a white solid.

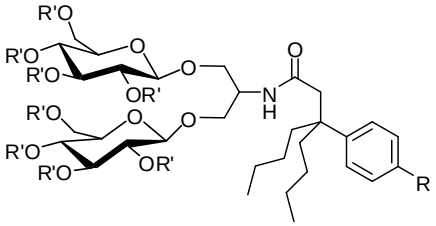
Supplementary scheme 2



1 : R = CH_3
2 : R = $CH(CH_3)_2$
3 : R = $C(CH_3)_3$
4 : R = C_6H_5

5 : R = CH_3
6 : R = $CH(CH_3)_2$
7 : R = $C(CH_3)_3$
8 : R = C_6H_5

9 : R = CH_3
10 : R = $CH(CH_3)_2$
11 : R = $C(CH_3)_3$
12 : R = C_6H_5



TPA-6a : R = CH_3, R' = benzoyl
TPA-7a : R = $CH(CH_3)_2$, R' = benzoyl
TPA-8a : R = $C(CH_3)_3$, R' = benzoyl
TPA-9a : R = C_6H_5, R' = benzoyl

d →

TPA-6 : R = CH_3, R' = H
TPA-7 : R = $CH(CH_3)_2$, R' = H
TPA-8 : R = $C(CH_3)_3$, R' = H
TPA-9 : R = C_6H_5, R' = H

(a) KOH, ethylene glycol, 200°C; (b) serinol, EDC • HCl, HOBt, DMF, room temperature; (c) perbenzoylated glucosylbromide, AgOTf, CH_2Cl_2, -45°C → room temperature; (d) NaOMe, MeOH, room temperature.

2-(5-*p*-tolyl)nonan-5-yl)malononitrile (**1**) was prepared in 88% yield according to the general procedure for conjugate addition reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.35-7.28 (m, 2H), 7.25-7.18 (m, 2H), 3.96 (s, 1H), 2.36 (s, 3H), 2.06-1.94 (m, 4H), 1.45-1.31 (m, 4H), 1.28-1.14 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 138.0, 136.5, 129.8, 126.6, 112.3, 46.9, 35.3, 34.4, 26.1, 23.3, 21.1, 14.1; **HRMS (ESI)**: calcd. for $C_{19}H_{26}N_2$ $[M-H]^+$ 281.2023, found 281.2023.

2-(5-(4-isopropylphenyl)nonan-5-yl)malononitrile (**2**) was prepared in 89% yield according to the general procedure for conjugate addition reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.37-7.30 (m, 2H), 7.29-7.28 (m, 2H), 3.96 (s, 1H), 2.91 (sept, *J* = 7.3 Hz, 1H), 2.07-1.96 (m, 4H), 1.46-1.31 (m, 4H), 1.30-1.16 (m, 10H), 0.93 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 148.8, 136.7, 127.1, 126.7, 112.3, 46.9, 35.3, 34.4, 33.7, 26.1, 24.0, 23.3, 14.1; **HRMS (ESI)**: calcd. for $C_{21}H_{30}N_2$ $[M-H]^+$ 309.2336, found 309.2333.

2-(5-(4-*tert*-butylphenyl)nonan-5-yl)malononitrile (**3**) was prepared in 89% yield according to the general procedure for conjugate addition reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): 7.41 (d, *J* = 8.4 Hz , 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 3.97 (s, 1H), 2.06-1.96 (m, 4H), 1.46-1.30 (m, 13H), 1.28-120 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): 151.0, 136.3, 126.4, 125.9, 112.3, 46.8, 35.3,

34.6, 34.3, 31.4, 26.0, 23.3, 14.0; **HRMS (ESI)**: calcd. for $C_{22}H_{32}N_2$ $[M-H]^+$ 323.2492, found 323.2492.

2-(5-(biphenyl-4-yl)nonan-5-yl)malononitrile (**4**) was prepared in 88% yield according to the general procedure for conjugate addition reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.68-7.58 (m, 5H), 7.54-7.32 (m, 5H), 4.01 (s, 1H), 2.12-2.01 (m, 4H), 1.48-1.34 (m, 4H), 1.34-1.19 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 140.9, 140.2, 138.5, 129.0, 127.8, 127.6, 127.5, 127.2, 126.8, 112.2, 60.5, 53.6, 47.0, 35.3, 34.3, 26.1, 23.3, 21.2, 14.7, 14.0; **HRMS (ESI)**: calcd. for $C_{24}H_{28}N_2$ $[M-H]^+$ 343.2169, found 343.2166.

3-butyl-3-*p*-tolylheptanoic acid (**5**) was prepared in 92% yield according to the general procedure for solvolysis reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.17-7.07 (m, 4H), 2.72 (s, 2H), 2.32 (s, 3H), 1.82-1.68 (m, 4H), 1.31-1.15 (m, 4H), 1.15-0.88 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 178.4, 143.0, 135.3, 129.0, 126.3, 43.1, 41.3, 38.7, 26.1, 23.4, 21.1, 14.2; **HRMS (ESI)**: calcd. for $C_{18}H_{28}O_2Na$ $[M+Na]^+$ 299.1982, found 299.1978.

3-butyl-3-(4-isopropylphenyl)heptanoic acid (**6**) was prepared in 91% yield according to the general procedure for solvolysis reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.15 (s, 4H), 2.88 (sept, *J* = 7.1 Hz, 1H), 2.72 (s, 2H), 1.84-1.69 (m, 4H), 1.32-1.07 (m, 4H), 1.07-0.90 (m, 4H), 0.83 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 178.4, 146.2, 143.2, 126.3, 126.2, 43.2, 41.3, 38.8, 33.6, 26.7, 24.1, 23.4, 14.2; **HRMS (ESI)**: calcd. for $C_{20}H_{32}O_2Na$ $[M+Na]^+$ 327.2295, found 327.2293.

3-butyl-3-(4-*tert*-butylphenyl)heptanoic acid (**7**) was prepared in 90% yield according to the general procedure for solvolysis reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): 7.41 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 2.74 (s, 2H), 1.78 (m, 4H), 1.31 (s, 9H), 1.23 (quin, 4H), 1.20-1.06 (m, 2H), 1.05-0.90 (m, 2H), 0.83 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): 178.3, 148.5, 142.8, 125.8, 126.0, 125.1, 43.1, 41.2, 38.8, 34.5, 31.6, 26.1,23.5, 14.2; **HRMS (ESI)**: calcd. for $C_{21}H_{34}O_2$ $[M-H]^+$ 317.2486, found 317.2476.

3-(biphenyl-4-yl)-3-butylheptanoic acid (**8**) was prepared in 90% yield according to the general procedure for solvolysis reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.65-7.59 (m, 4H), 7.47-7.38 (m, 2H), 7.37-7.28 (m, 3H), 2.79 (s, 2H), 1.82 (t, *J* = 8.0 Hz, 4H), 1.34-1.10 (m, 6H), 1.10-0.93 (m, 2H) 0.84 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 178.4, 144.8, 144.2, 140.6, 129.8, 128.6, 128.4, 128.2, 127.2, 43.2, 41.3, 38.6, 26.1, 23.2, 21.2, 14.3; **HRMS (ESI)**: calcd. for $C_{23}H_{30}O_2Na$ $[M+Na]^+$ 361.2138, found 361.2145.

3-butyl-*N*-(1,3-dihydroxypropan-2-yl)-3-p-tolylheptanamide (**9**) was prepared in 91% yield according to the general procedure for amide coupling reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.40 (d, *J* = 7.6 Hz, 1H), 3.70-3.58 (m, 1H), 3.58-3.46 (m, 2H), 3.46-3.31 (m, 2H), 2.57 (br s, 2H), 2.50 (s, 2H), 2.32 (s, 3H), 1.88-1.66 (m, 4H), 1.40-1.12 (m, 6H), 1.12-0.96 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 172.0, 143.8, 135.9, 129.4, 126.6, 63.4, 52.3, 47.4, 43.3, 36.5, 25.9, 23.5, 21.0, 14.3; **HRMS (ESI)**: calcd. for $C_{21}H_{35}NO_3Na$ $[M+Na]^+$ 372.2510, found 372.2512.

3-butyl-*N*-(1,3-dihydroxypropan-2-yl)-3-(4-isopropylphenyl)heptanamide (**10**) was prepared in 90% yield according to the general procedure for amide coupling reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.30-7.13 (m, 4H), 5.66 (d, *J* = 7.8 Hz, 1H), 4.03-3.93 (m, 1H), 3.63-3.52 (m, 1H), 3.50-3.33 (m, 4H), 3.32-3.16 (m, 2H), 2.89 (sept, *J* = 7.1 Hz, 1H), 2.50 (s, 2H), 1.78 (t, *J* = 8.1 Hz, 4H), 1.41-0.98 (m, 14H), 0.88 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 172.3, 146.7, 143.6, 126.5, 126.4, 61.3, 52.1, 46.8, 43.1, 41.3, 36.6, 33.6, 25.8, 24.0, 23.4, 14.1; **HRMS (ESI)**: calcd. for $C_{23}H_{39}NO_3Na$ $[M+Na]^+$ 400.2823, found 400.2827.

3-butyl-3-(4-*tert*-butylphenyl)-*N*-(1,3-dihydroxypropan-2-yl)heptanamide (**11**) was prepared in 92% yield according to the general procedure for amide coupling reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 5.37 (d, *J* = 7.6 Hz, 1H), 3.68-3.53 (m, 1H), 3.52-3.37 (m, 4H), 3.37-3.21 (m, 2H), 3.05-2.97 (br s, 2H), 2.49 (s, 2H), 1.88-1.68 (m, 4H), 1.43-1.14 (m, 14H), 1.14-0.97 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 172.0, 149.0, 143.4, 126.2, 125.4, 62.3, 52.3, 47.3, 43.1, 36.5, 34.4, 31.5, 25.8, 24.0, 23.5, 14.2; **HRMS (ESI)**: calcd. for $C_{24}H_{41}NO_3$ $[M+H]^+$ 392.3160, found 392.3146.

3-(biphenyl-4-yl)-3-butyl-*N*-(1,3-dihydroxypropan-2-yl)heptanamide (**12**) was prepared in 89% yield according to the general procedure for amide coupling reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.64-7.54 (m, 4H), 7.50-7.39 (m, 2H), 7.39-7.30 (m, 3H), 5.44 (d, *J* = 7.8 Hz, 1H), 3.71-3.61 (m, 1H), 3.60-3.50 (m, 4H), 3.50-3.37 (m, 2H), 2.56 (s, 2H), 1.95-1.75 (m, 4H), 1.41-1.21 (m, 6H), 1.16-1.00 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 172.0, 145.8, 140.6, 139.0, 129.0, 127.5, 127.2, 127.1, 127.0, 62.6, 52.3, 46.9, 43.4, 36.7, 25.9, 23.5, 14.2; **HRMS (ESI)**: calcd. for $C_{26}H_{37}NO_3Na$ $[M+Na]^+$ 434.2666, found 434.2657.

TPA-6a was prepared in 90% yield according to the general procedure for glycosylation reactions**.** **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.19-8.08 (m, 4H), 8.05-7.98 (m, 4H), 7.96-7.88 (m, 4H), 7.88-7.79 (m, 4H), 7.74-7.61 (m, 6H), 7.60-7.47 (m, 4H), 7.47-7.34 (m, 10H), 7.34-7.22 (m, 4H), 7.12 (s, 4H),

5.64-5.44 (m, 4H), 5.38-5.17 (m, 3H), 4.56-4.41 (m, 2H), 4.39-4.27 (m, 2H), 4.14-4.02 (br s, 1H), 3.77 (dd, *J* = 11.0, 8.0 Hz, 2H), 3.60-3.48 (m, 2H), 3.36-3.20 (m, 3H), 2.74 (t, *J* = 9.5 Hz, 1H), 2.49-2.24 (m, 5H), 1.79-1.59 (m, 4H), 1.33-1.15 (m, 4H), 1.15-0.92 (m, 4H), 0.84 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.6, 166.2, 166.0, 165.9, 165.3, 165.2, 164.9, 164.8, 143.3, 135.2, 133.9, 133.8, 133.7, 133.6, 133.4, 133.3, 130.2, 129.9, 129.8, 129.7, 129.6, 129.3, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 126.3, 101.5, 101.4, 77.6, 72.1, 71.9, 69.6, 67.8, 66.7, 63.1, 63.0, 60.5, 47.0, 45.8, 43.0, 37.3, 26.0, 23.4, 21.2, 21.1, 14.3, 14.2; **MS (MALDI-TOF)**: calcd. for $C_{89}H_{87}NO_{21}Na[M+Na]^+$ 1528.6, found 1528.7.

TPA-7a was prepared in 88% yield according to the general procedure for glycosylation reactions**.** **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.17-8.06 (m, 4H), 8.05-7.96 (m, 4H), 7.95-7.87 (m, 4H), 7.87-7.78 (m, 4H), 7.73-7.60 (m, 6H), 7.60-7.47 (m, 4H), 7.47-7.33 (m, 10H), 7.33-7.22 (m, 4H), 7.13 (s, 4H), 5.66-5.43 (m, 4H), 5.39-5.16 (m, 3H), 4.55-4.40 (m, 2H), 4.38-4.26 (m, 2H), 4.14-4.00 (br s, 1H), 3.85 (dd, *J* = 10.6, 7.8 Hz, 2H), 3.60-3.50 (m, 2H), 3.40-3.24 (m, 3H), 2.92-2.72 (m, 2H), 2.45-2.32 (m, 2H), 1.77-1.62 (m, 4H), 1.32-1.14 (m, 10H), 1.14-0.96 (m, 4H), 0.90-0.77 (m, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.8, 166.2, 166.0, 165.9, 165.3, 165.2, 165.0, 164.9, 164.8, 146.2, 143.6, 133.9, 133.8, 133.7, 133.6, 133.4, 133.3, 130.2, 129.9, 129.8, 129.7, 129.3, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 126.4, 126.3, 101.5, 101.4, 72.6, 72.1, 72.0, 69.6, 67.9, 66.8, 63.1, 63.0, 60.5, 47.2, 45.7, 43.3, 37.4, 33.6, 26.0, 24.3, 24.1, 23.5, 21.2, 14.4, 14.3, 14.2; **MS (MALDI-TOF)**: calcd. for $C_{91}H_{91}NO_{21}Na[M+Na]^+$ 1556.6, found 1556.9.

TPA-8a was prepared in 93% yield according to the general procedure for glycosylation reactions**.** **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.18-8.07 (m, 4H), 8.06-7.98 (m, 4H), 7.96-7.87 (m, 4H), 7.87-7.80 (m, 4H), 7.73-7.59 (m, 6H), 7.59-7.47 (m, 4H), 7.47-7.33 (m, 10H), 7.33-7.23 (m, 6H), 7.18-7.08 (m, 2H), 5.68-5.45 (m, 4H), 5.40-5.22 (m, 3H), 4.55-4.41 (m, 2H), 4.39-4.26 (m, 2H), 4.08 (br s, 1H), 3.88 (dd, *J* = 13.0, 7.2 Hz, 2H), 3.65-3.54 (m, 2H), 3.42-3.26 (m, 3H), 2.84 (t, *J* = 8.9 Hz, 1H), 2.40 (s, 2H), 1.78-1.66 (m, 4H), 1.34-1.14 (m, 13H), 1.14-0.95 (m, 4H), 0.91-0.78 (m, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.8, 166.2, 166.0, 165.9, 165.3, 165.2, 165.0, 164.9, 148.5, 143.2, 133.9, 133.7, 133.6, 133.4, 133.3, 133.2, 130.2, 129.9, 129.8, 129.7, 129.6, 129.3, 128.9, 128.6, 128.5, 126.1, 125.2, 101.5, 101.4, 72.6, 72.1, 72.0, 71.9, 69.6, 69.5, 67.9, 66.8, 63.1, 62.9, 47.2, 45.6, 42.9, 37.6, 37.3, 34.4, 31.5, 29.9, 26.1, 26.0, 23.5, 23.4, 14.4, 14.3, 14.2; **MS (MALDI-TOF)**: calcd. for $C_{92}H_{93}NO_{21}Na[M+Na]^+$ 1570.6, found 1570.5.

TPA-9a was prepared in 92% yield according to the general procedure for glycosylation reactions**.** **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.13-8.04 (m, 4H), 8.04-7.97 (m, 4H), 7.95-7.86 (m, 4H), 7.86-7.78 (m, 4H), 7.73-7.49 (m, 14H), 7.44-7.35 (m, 12H), 7.35-7.23 (m, 6H), 5.59-5.40 (m, 3H), 5.40-5.13 (m,

3H), 4.46-4.18 (m, 4H), 4.05 (br s, 1H), 3.79 (d, *J* = 7.5 Hz, 1H), 3.67 (d, *J* = 8.0 Hz, 1H), 3.60-3.50 (m, 2H), 3.30-3.20 (m, 2H), 3.11-3.02 (m, 1H), 2.65 (t, *J* = 9.0 Hz, 1H), 2.45 (d, *J* = 13.3 Hz, 1H), 2.30 (d, *J* = 13.7 Hz, 1H), 1.84-1.64 (m, 5H), 1.35-1.19 (m, 5H), 1.19-0.97 (m, 4H), 0.87 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.5, 166.2, 166.0, 165.9, 165.3, 165.2, 165.0, 145.7, 140.8, 138.3, 133.9, 133.7, 133.6, 133.5, 133.3, 130.2, 130.0, 129.9, 129.8, 129.7, 129.6, 129.3, 129.1, 129.0, 128.7, 128.6, 128.5, 128.4, 128.0, 112.3, 101.5, 101.4, 72.6, 72.2, 72.0, 71.9, 71.8, 69.7, 69.5, 67.9, 66.7, 63.2, 62.9, 60.6, 53.6, 47.1, 46.0, 43.3, 37.4, 36.8, 33.6, 26.0, 23.5, 21.2, 14.4, 14.3; **MS (MALDI-TOF)**: calcd. for $C_{94}H_{89}NO_{21}Na[M+Na]^+$ 1590.6, found 1590.6.

TPA-6 was prepared in 95% yield according to the general procedure for deprotecting reactions**.** **^{1}H NMR** (300 MHz, CD_3OD): δ 7.24 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 4.23 (dd, *J* = 7.7, 6.8 Hz, 2H), 4.10-4.05 (m, 1H), 3.95-3.85 (m, 2H), 3.80 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.74-3.63 (m, 4H), 3.43-3.25 (m, 6H), 3.24-3.12 (m, 2H), 2.59 (s, 2H), 2.35 (s, 3H), 1.94-1.79 (m, 4H), 1.40-1.22 (m, 4H), 1.22-1.02 (m, 4H), 0.95-0.84 (m, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 174.0, 144.7, 136.3, 130.0, 127.7, 105.1, 104.8, 78.2, 78.1, 75.2, 71.8, 69.6, 62.9, 45.0, 44.4, 39.1, 38.5, 27.2, 24.6, 24.5, 21.2, 14.6; **HRMS (ESI)**: calcd. for $C_{33}H_{55}NO_{13}Na$ $[M+Na]^+$ 696.3566, found 696.3566.

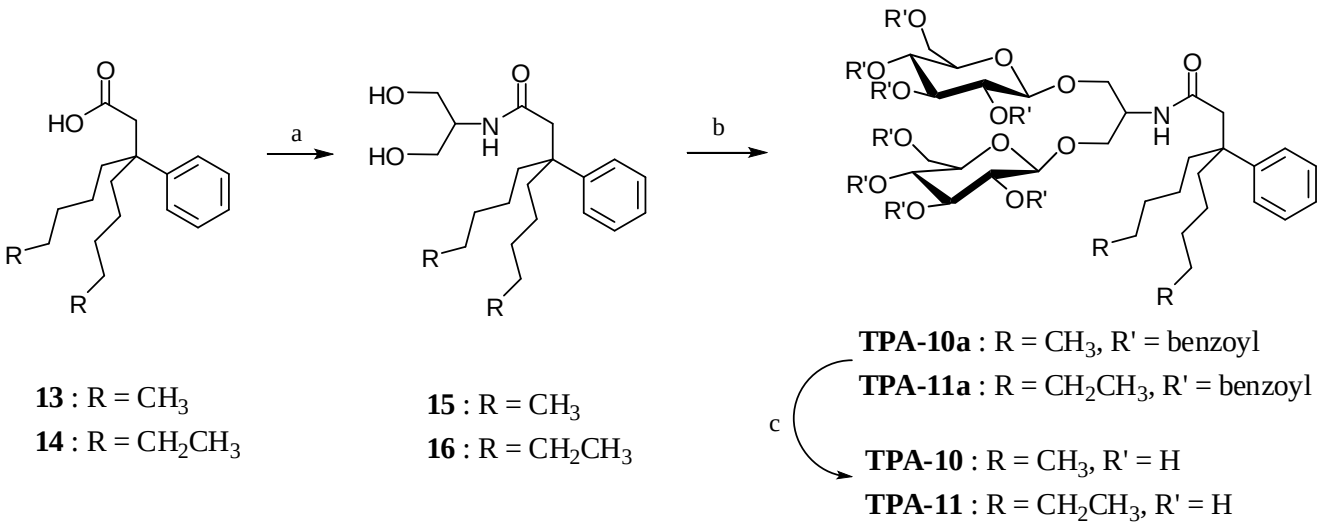
TPA-7 was prepared in 94% yield according to the general procedure for deprotecting reactions. **^{1}H NMR** (300 MHz, CD_3OD): δ 7.28 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.25 (dd, *J* = 7.7, 6.4 Hz, 2H), 4.16-4.05 (m, 1H), 3.95-3.85 (m, 2H), 3.84-3.76 (m, 1H), 3.74-3.62 (m, 4H), 3.42-3.22 (m, 6H), 3.24-3.14 (m, 2H), 2.99-2.82 (m, 1H), 2.59 (s, 2H), 1.96-1.76 (m, 4H), 1.41-1.22 (m, 10H), 1.22-1.03 (m, 4H), 0.97-0.83 (m, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 174.0, 147.4, 145.1, 127.7, 127.2, 105.0, 104.8, 78.1, 75.2, 71.8, 71.7, 69.6, 62.9, 45.0, 44.4, 39.1, 38.6, 34.9, 27.2, 24.8, 24.7, 24.6, 24.5, 14.6; **HRMS (ESI)**: calcd. for $C_{35}H_{59}NO_{13}Na$ $[M+Na]^+$ 724.3879, found 724.3867.

TPA-8 was prepared in 94% yield according to the general procedure for deprotecting reactions. **^{1}H NMR** (300 MHz, CD_3OD): δ 7.38 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 8.6 Hz, 2H), 4.25 (dd, *J* = 7.6, 4.6 Hz, 2H), 4.16-4.04 (m, 1H), 3.94-3.84 (m, 2H), 3.84-3.75 (m, 1H), 3.73-3.64 (m, 4H), 3.43-3.26 (m, 6H), 3.25-3.14 (m, 2H), 2.60 (s, 2H), 1.93-1.79 (m, 4H), 1.38-1.24 (m, 13H), 1.24-1.05 (m, 4H), 0.90 (td, *J* = 7.0, 4.0 Hz, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 174.1, 149.6, 144.7, 127.4, 126.1, 105.0, 104.8, 78.1, 75.2, 71.8, 71.7, 69.7, 69.6, 62.9, 44.9, 44.3, 39.1, 38.6, 35.3, 32.1, 27.2, 24.6, 24.5, 14.6; **HRMS (ESI)**: calcd. for $C_{36}H_{61}NO_{13}Na$ $[M+Na]^+$ 738.4041, found 738.4032.

TPA-9 was prepared in 92% yield according to the general procedure for deprotecting reactions. **^{1}H NMR** (300 MHz, CD_3OD): δ 7.72-7.59 (m, 4H), 7.50-7.40 (m, 4H), 7.38-7.30 (m, 1H), 4.24 (d, *J* = 7.8 Hz, 1H), 4.11 (d, *J* = 7.6 Hz, 1H), 4.07 (quin, *J* = 5.6 Hz, 1H), 3.91-3.57 (m, 7H), 3.38-3.04 (m,

6H), 2.63 (s, 2H), 2.07-1.83 (m, 4H), 1.45-1.23 (m, 4H), 1.23-1.09 (m, 4H), 0.90 (quart, *J* = 7.5 Hz, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 173.8, 147.0, 142.2, 139.7, 130.0, 128.3, 128.0, 127.8, 104.8, 104.7, 78.0, 75.2, 71.7, 71.5, 69.5, 69.4, 62.9, 62.7, 44.6, 39.0, 38.0, 27.2, 24.5, 14.6; **HRMS (ESI)**: calcd. for $C_{38}H_{57}NO_{13}Na$ $[M+Na]^+$ 758.3728, found 758.3732.

Supplementary scheme 3



13 : R = CH_3
14 : R = CH_2CH_3

15 : R = CH_3
16 : R = CH_2CH_3

TPA-10a : R = CH_3, R' = benzoyl
TPA-11a : R = CH_2CH_3, R' = benzoyl

TPA-10 : R = CH_3, R' = H
TPA-11 : R = CH_2CH_3, R' = H

(a) serinol, EDC • HCl, HOBt, DMF, room temperature; (b) perbenzoylated glucosylbromide, AgOTf, CH_2Cl_2, -45°C → room temperature; (c) NaOMe, MeOH, room temperature.

3-pentyl-3-phenyloctanoic acid (**13**) was prepared in 92% yield according to the general procedure for solvolysis reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.36-7.23 (m, 4H), 7.23-7.16 (m, 1H), 2.74 (s, 2H), 1.82-1.72 (m, 4H), 1.30-1.05 (m, 10H), 1.05-0.92 (m, 2H), 0.82 (t, *J* = 6.9 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): 178.2, 146.0, 128.3, 126,4, 126.0, 43.5, 41.2, 38.9, 32.6, 23.5, 22.7, 14.2; **HRMS (ESI)**: calcd. for $C_{19}H_{30}O_2Na$ $[M+Na]^+$ 313.2138, found 313.2141.

3-hexyl-3-phenylnonanoic acid (**14**) was prepared in 88% yield according to the general procedure for solvolysis reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.39-7.22 (m, 4H), 7.22-7.13 (m, 1H), 2.74 (s, 2H), 1.85-1.68 (m, 4H), 1.34-1.06 (m, 14H), 1.06-0.91 (m, 2H), 0.84 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 177.5, 146.1, 128.3, 126.4, 126.0, 43.5, 41.2, 38.9, 31.9, 30.1, 23.8, 22.8, 14.3. **MS (MALDI-TOF)**: calcd. for $C_{21}H_{34}O_2$ $[M+Na]^+$ 341.2458, found 341.2452.

N-(1,3-dihydroxypropan-2-yl)-3-pentyl-3-phenyloctanamide (**15**) was prepared in 92% yield according to the general procedure for amide coupling reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.40-7.30 (m, 4H), 7.26-7.16 (m, 1H), 5.40 (d, *J* = 7.6 Hz, 1H), 3.68-3.58 (m, 1H), 3.56-3.42 (m, 2H), 3.42-3.28 (m, 2H), 2.66 (t, *J* = 7.0 Hz, 2H), 2.52 (s, 2H), 1.92-1.69 (m, 4H), 1.40-1.18 (m, 6H), 1.16-0.98 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.8, 146.9, 128.7, 126.7, 126.3, 63.3, 63.2, 52.2, 47.4, 43.7, 36.7, 32.7, 23.3, 22.7, 14.3; **HRMS (ESI)**: calcd. for $C_{22}H_{37}NO_3Na$ $[M+Na]^+$ 386.2666, found 386.2671.

N-(1,3-dihydroxypropan-2-yl)-3-hexyl-3-phenylnonanamide (**16**) was prepared in 90% yield according to the general procedure for amide coupling reactions. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.41-7.29 (m, 4H), 7.26-7.16 (m, 1H), 5.41 (d, *J* = 7.6 Hz, 1H), 3.68-3.57 (m, 1H), 3.56-3.43 (m, 2H), 3.42-3.27 (m, 2H), 2.65 (t, *J* = 7.0 Hz, 2H), 2.52 (s, 2H), 1.90-1.68 (m, 4H), 1.39-1.15 (m, 10H), 1.14-0.97 (m, 2H), 0.86 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.8, 147.0, 128.7, 126.8, 126.3, 63.6, 52.2, 47.5, 43.7, 36.7, 31.9, 30.1, 23.6, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{24}H_{41}NO_3Na$ $[M+Na]^+$ 414.2979, found 414.2978.

TPA-10a was prepared in 91% yield according to the general procedure for glycosylation reactions**.** **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.20-8.07 (m, 4H), 8.06-7.98 (m, 4H), 7.96-7.88 (m, 4H), 7.88-7.79 (m, 4H), 7.75-7.61 (m, 6H), 7.60-7.48 (m, 4H), 7.48-7.34 (m, 10H), 7.34-7.18 (m, 8H), 7.16-7.07 (m, 1H), 5.62-5.44 (m, 4H), 5.37-5.25 (m, 2H), 5.06 (d, *J* = 8.8 Hz, 1H), 4.56-4.40 (m, 2H), 4.33 (td, *J* = 11.6, 4.5 Hz, 2H), 4.01 (br s, 1H), 3.71 (dd, *J* = 12.6, 8.0 Hz, 2H), 3.51-3.40 (m, 2H), 3.31-3.16 (m, 3H), 2.59 (t, *J* = 9.5 Hz, 1H), 2.39 (quin, *J* = 9.7 Hz, 2H), 1.84-1.63 (m, 4H), 1.38-0.94 (m, 12H), 0.84 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.4, 166.2, 166.0, 165.9, 165.3, 165.2, 164.9, 164.8, 146.4, 133.9, 133.7, 133.6, 133.4, 133.3, 130.2, 129.9, 129.8, 129.7, 129.4, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 126.4, 126.1, 101.5, 101.4, 72.6, 72.1, 72.0, 71.9, 69.7, 69.6, 67.8, 66.6, 63.1, 46.9, 46.4, 43.4, 37.3, 36.6, 32.6, 23.4, 22.7, 14.3, 14.2; **MS (MALDI-TOF)**: calcd. for $C_{90}H_{89}NO_{21}Na[M+Na]^+$ 1542.6, found 1542.9.

TPA-11a was prepared in 92% yield according to the general procedure for glycosylation reactions**.** **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.20-8.06 (m, 4H), 8.06-7.98 (m, 4H), 7.96-7.88 (m, 4H), 7.88-7.78 (m, 4H), 7.75-7.61 (m, 6H), 7.61-7.48 (m, 4H), 7.48-7.34 (m, 10H), 7.34-7.18 (m, 8H), 7.17-7.07 (m, 1H), 5.63-5.42 (m, 4H), 5.37-5.25 (m, 2H), 5.02 (d, *J* = 8.8 Hz, 1H), 5.55-5.40 (m, 2H), 4.33 (td, *J* = 11.6, 4.5 Hz, 2H), 4.00 (br s, 1H), 3.70 (dd, *J* = 12.6, 8.0 Hz, 2H), 3.50-3.37 (m, 2H), 3.31-3.14 (m, 3H), 2.57 (t, *J* = 9.5 Hz, 1H), 2.37 (quin, *J* = 9.7 Hz, 2H), 1.85-1.62 (m, 4H), 1.33-0.94 (m, 16H), 0.85 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.4, 166.3, 166.2, 166.0, 165.9, 165.3, 165.2, 164.9, 164.8, 146.4, 133.9, 133.7, 133.6, 133.5, 133.3, 130.2, 129.9, 129.8, 129.7, 129.4, 129.2, 129.0,

128.7, 128.6, 126.5, 126.1, 101.5, 101.4, 72.6, 72.1, 72.0, 71.9, 69.7, 67.9, 66.6, 63.1, 46.9, 46.6, 43.5, 37.5, 36.6, 31.9, 30.1, 23.7, 22.9, 14.3, 14.2; **MS (MALDI-TOF)**: calcd. for $C_{92}H_{93}NO_{21}Na[M+Na]^+$ 1570.6, found 1570.7.

TPA-10 was prepared in 94% yield according to the general procedure for deprotecting reactions**.** **^{1}H NMR** (300 MHz, CD_3OD): δ 7.41-7.29 (m, 4H), 7.25-7.15 (m, 1H), 4.24 (t, *J* = 7.6 Hz, 2H), 4.17-4.06 (m, 1H), 3.96-3.85 (m, 2H), 3.85-3.76 (m, 1H), 3.76-3.62 (m, 4H), 3.45-3.24 (m, 6H), 3.24-3.14 (m, 2H), 2.62 (s, 2H), 1.98-1.78 (m, 4H), 1.40-1.05 (m, 12H), 0.95-0.81 (m, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 174.0, 147.9, 129.4, 127.8, 126.9, 105.1, 104.8, 78.1, 75.2, 71.8, 69.6, 63.0, 44.8, 39.4, 39.0, 38.9, 33.8, 24.6, 23.8, 14.6; **HRMS (ESI)**: calcd. for $C_{34}H_{57}NO_{13}Na$ $[M+Na]^+$ 710.3723, found 710.3719.

TPA-11 was prepared in 93% yield according to the general procedure for deprotection reactions**.** **^{1}H NMR** (300 MHz, CD_3OD):): δ 7.41-7.30 (m, 4H), 7.25-7.16 (m, 1H), 4.24 (t, *J* = 7.5 Hz, 2H), 4.16-4.06 (m, 1H), 3.95-3.85 (m, 2H), 3.84-3.76 (m, 1H), 3.75-3.62 (m, 4H), 3.45-3.25 (m, 6H), 3.24-3.14 (m, 2H), 2.62 (s, 2H), 1.95-1.79 (m, 4H), 1.39-1.04 (m, 16H), 0.97-0.85 (m, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 173.9, 147.9, 129.3, 127.8, 126.9, 105.0, 104.8, 78.1, 75.1, 71.8, 71.7, 69.6, 62.9, 44.8, 39.4, 38.8, 33.1, 31.2, 24.8, 23.8, 14.6; **HRMS (ESI)**: calcd. for $C_{36}H_{61}NO_{13}Na$ $[M+Na]^+$ 738.4041, found 738.4012.

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