Supplementary Information

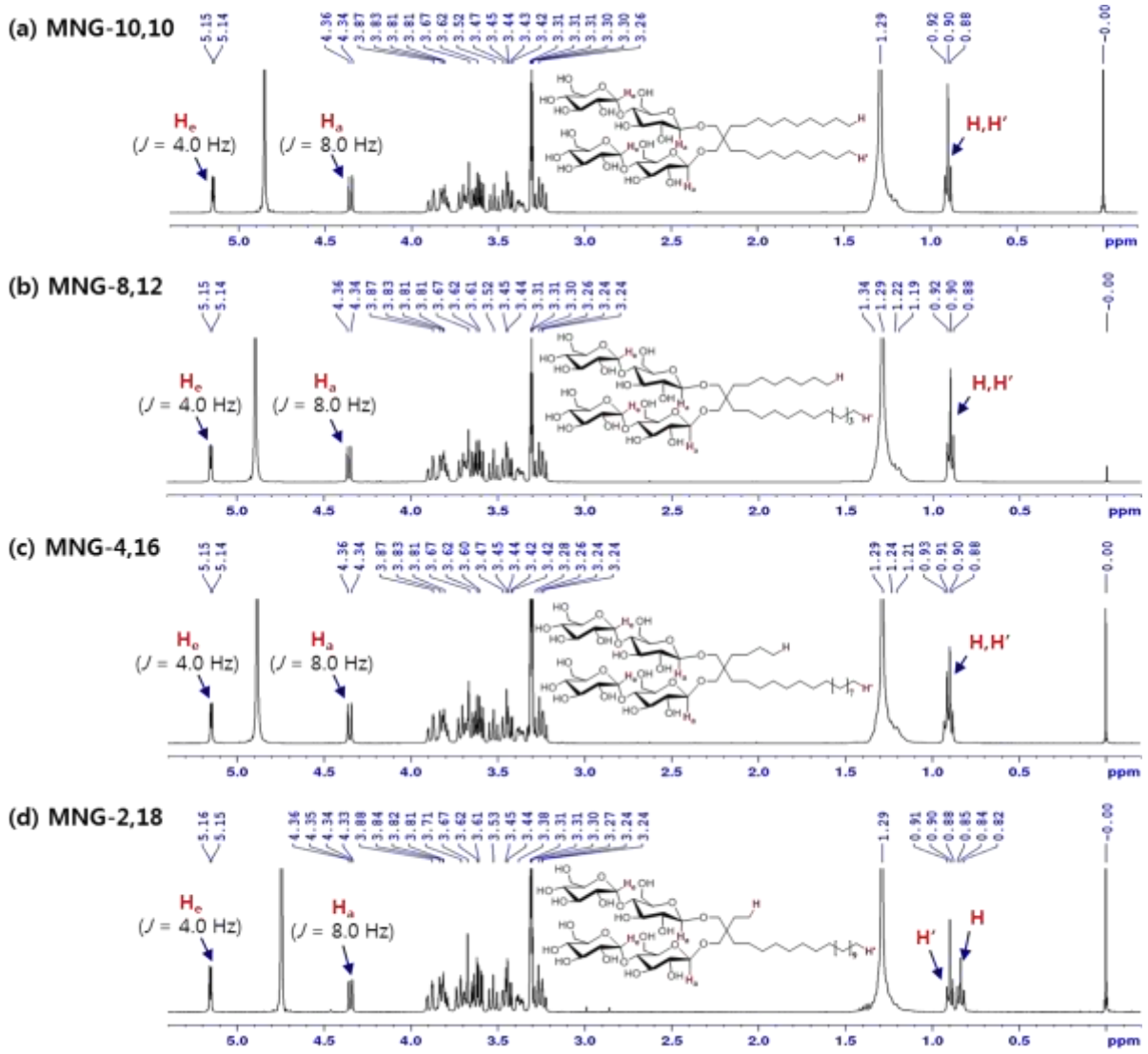


Figure S1. ^{1}H NMR spectra of representative MNGs along with the chemical structures of corresponding amphiphiles (MNG-10,10 (a) MNG-8,12 (b), MNG-4,16 (c) and MNG-2,18 (d)). Anomeric protons (H_a and H_e) as well as methyl protons (H and H') at each alkyl chain tip were indicated in the chemical structures and the corresponding NMR peaks were assigned in the individual spectra. The NMR peaks for α and β-anomeric protons of all the MNGs (H_e and H_a, respectively) appeared as two individual doublets at 5.15 and 4.35 ppm, with vicinal coupling constants (J) of 4.0 and 8.0 Hz, respectively. The NMR peaks for the methyl protons (H and H') appeared as a single triplet at 0.90 ppm for MNG-10,10 and MNG-8,12, while the counterparts for MNG-4,16 and MNG-2,18 appeared separately as two triplet peaks. The differences in the chemical shift for these A-MNGs with high asymmetricity were 0.01 and 0.06 ppm, respectively.

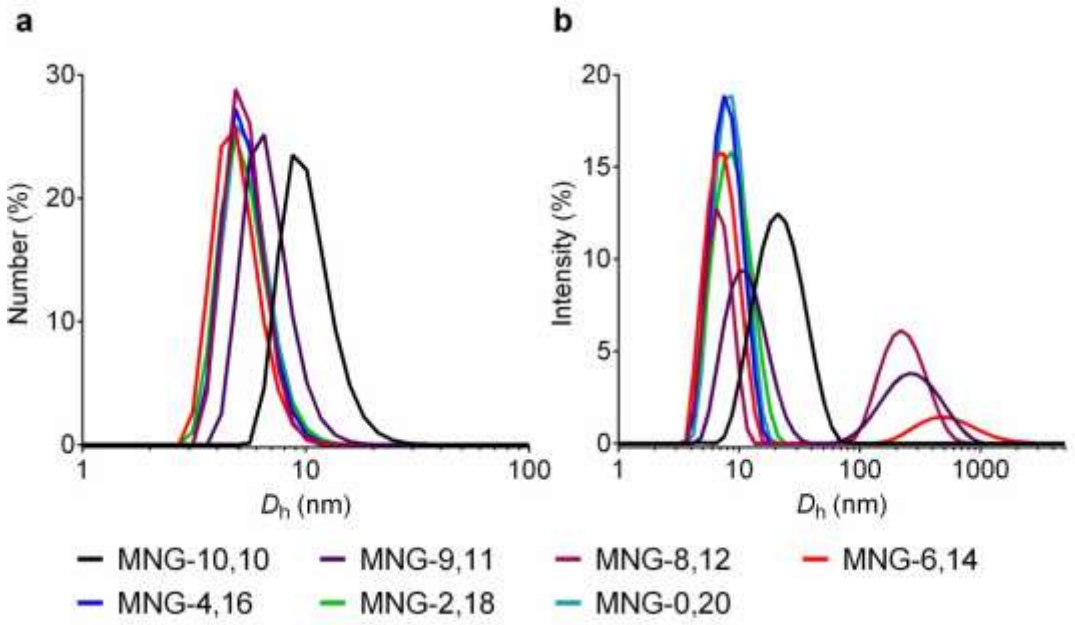


Figure S2. (a) Number- and (b) intensity-weighted dynamic light scattering (DLS) profiles of asymmetric MNG micelles and MNG-10,10. All the MNGs were tested at 1.0 wt% at room temperature. Detergent micelle size was represented by hydrodynamic diameter (D_h). Time-dependent fluctuation in the scattered light intensity was analyzed by autocorrelation, giving translational diffusion coefficient (D). The hydrodynamic diameters (D_h) of detergent micelles were obtained from the diffusion constant using the Stokes-Einstein equation.

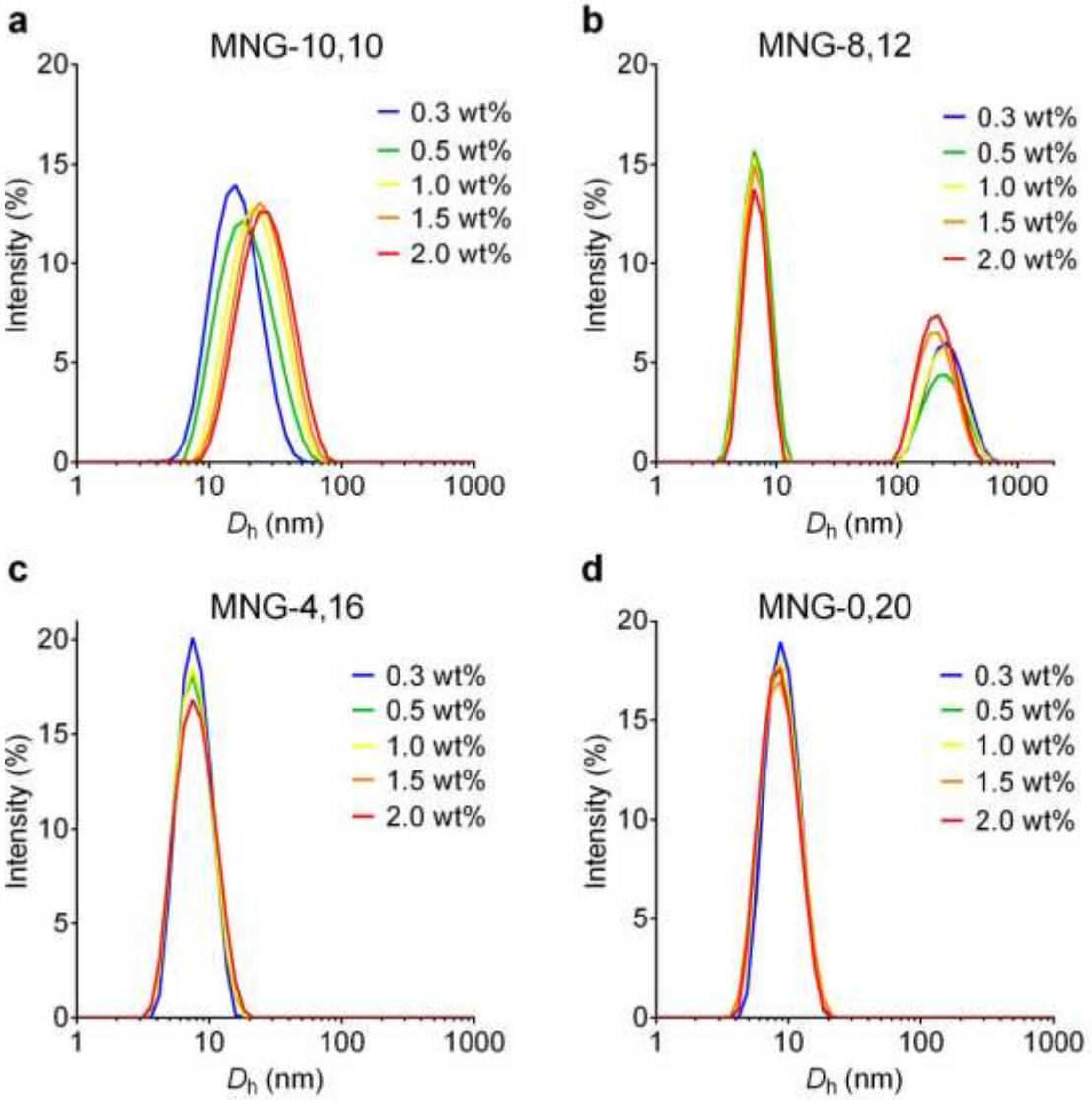


Figure S3. Concentration-dependent DLS profiles of selected asymmetric MNG micelles (MNG-10,10, MNG-8,12, MNG-4,16 and MNG-0,20). Micelle size was obtained from intensity-weighted analysis, with detergent concentration varying from 0.3 wt% to 2.0 wt%. The experiment was carried out at 25 ° C. In this range of detergent concentration, MNG-10,10 showed a gradual increase in micelle size while the other three (MNG-8,12, MNG-4,16 and MNG-0,20) were more or less invariable in this regard. All tested asymmetric MNGs except MNG-8,12 showed a single set of populations in their micelle size. Time-dependent fluctuation in the scattered light intensity was analyzed by autocorrelation, giving translational diffusion coefficient. The hydrodynamic diameter (D_h) of detergent micelles were correlated with the diffusion constant *via* the Stokes-Einstein equation.

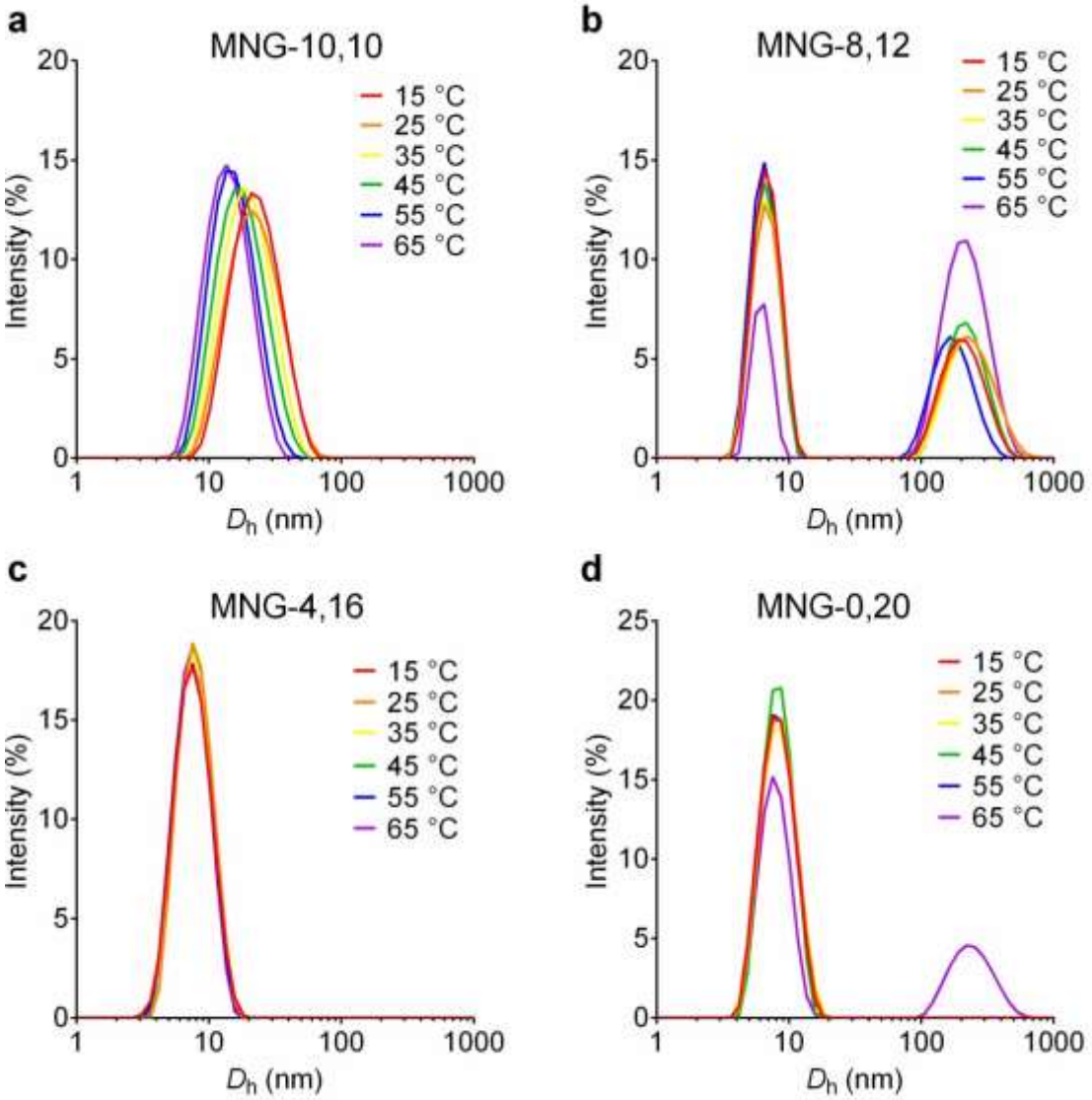


Figure S4. Temperature-dependent DLS profiles of selected asymmetric MNG micelles (MNG-10,10, MNG-8,12, MNG-4,16 and MNG-0,20). Micelle size was obtained from intensity-weighted analysis, with solution temperature varying from 15 °C to 65 °C. Detergent concentration was kept at 1.0 wt%. In this range of solution temperature, MNG-10,10 showed a gradual decrease in micelle size while the other three (MNG-8,12, MNG-4,16 and MNG-0,20) were more or less invariable in this regard. All tested asymmetric MNGs except MNG-8,12 showed a single set of populations in their micelle size under the conditions. At 65 °C, MNG-8,12 showed an abrupt increase in the proportion of large aggregates while MNG-0,20 showed a sudden appearance of large aggregates. Time-dependent fluctuation in the scattered light intensity was analyzed by autocorrelation, giving translational diffusion coefficient. The hydrodynamic diameter (D_h) of detergent micelles were calculated from the diffusion constant using the Stokes-Einstein equation.

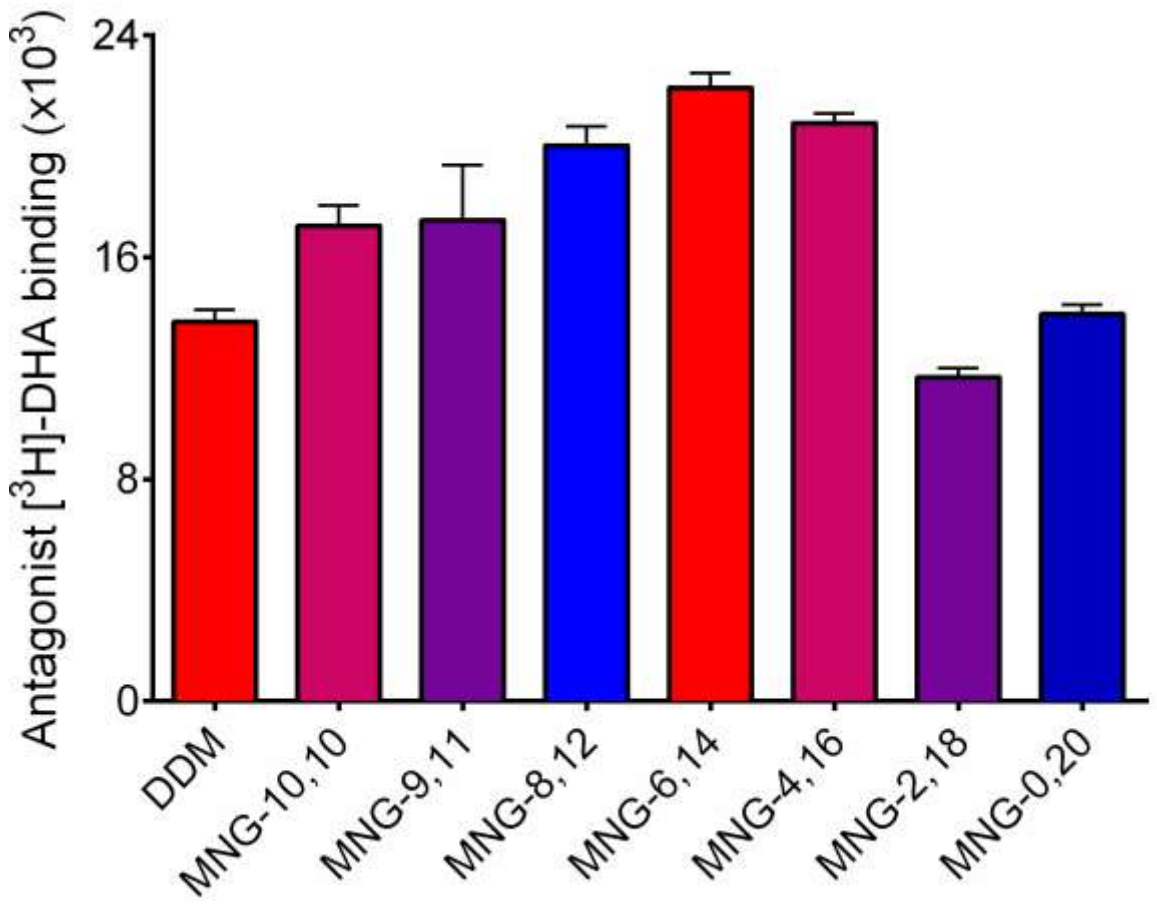


Figure S5. Ligand binding ability of the β_2AR solubilized in DDM, MNG-10,10, or a respective A-MNG (MNG-9,11, MNG-8,12, MNG-6,14, MNG-4,16, MNG-2,18 and MNG-0,20). DDM-purified β_2AR was mixed with individual detergent-containing solution to give a final detergent concentration of CMC + 0.2 wt%. The radiolabeled antagonist ([^{3}H]-dihydroalprenolol (DHA)) was used to measure he ligand biding ability of the receptor. Error bars, SEM, n = 3.

Table S1. Melting temperatures (T_m; mean ± SD) of MOR solubilized in MNGs (MNG-10,10, MNG-9,11, MNG-8,12, MNG-6,14, MNG-4,16, MNG-2,18, and MNG-0,20) and a conventional detergent (DDM).

Detergent	T_m (mean ± SD)	*n*, number of repeats
DDM	21.9 ± 1.0	*n* = 3
MNG-10,10	30.8 ± 0.2	*n* = 3
MNG-9,11	38.0 ± 1.0	*n* = 4
MNG-8,12	41.1 ± 2.0	*n* = 4
MNG-6,14	37.6 ± 1.6	*n* = 3
MNG-4,16	35.8 ± 1.8	*n* = 4
MNG-2,18	30.4 ± 1.2	*n* = 4
MNG-0,20	22.9 ± 1.1	*n* = 2

Protein stability evaluation

R. capsulatus superassembly stability assay

The superassembly was solubilized and purified according to a reported protocol.[1] Specialized photosynthetic membranes were first obtained from an engineered strain of *Rhodobacter capsulatus* used for the experiment. A 10 mL aliquot of the frozen membranes was slowly warmed for melting at room temperature and homogenized using a glass tissue homogenizer. The protein solution was incubated with mild agitation at 32 ºC for 30 mins. The resulting homogenized membranes were treated with DDM at 1.0 wt% and incubated for 30 min at 32 ºC. Following ultracentrifugation, the supernatant containing the solubilized LHI-RC complexes was transferred into a buffer solution containing Ni^{2+}-NTA resins and incubated at 4 ºC for one hour. The resin-containing protein solution was filtered onto 10 His-SpinTrap columns and washed the resins two times with 500 μL binding buffer (10 mM Tris (pH 7.8), 100 mL NaCl, 1×CMC DDM). For protein elution from the column, the elution buffer containing 1 M imidazole (3×200 μl) was used, leading to collection of DDM-purified LHI-RC complexes. 80 μL of this protein sample was mixed into 920 μL buffer solutions supplemented with individual detergents (MNG-10,10, MNG-9,11, MNG-8,12, MNG-6,14, MNG-4,16, MNG-2,18, MNG-0,20, DDM and OG). A final detergent concentration was CMC+0.04 wt% or CMC+0.2 wt%. The resulting LHI-RC complex solubilized in each detergent was incubated at room temperature over 15 days. Protein integrity was assessed by monitoring 875 nm absorbance (A_{875}) at regular intervals during the incubation.

LeuT stability assay

The wild-type of the leucine transporter (LeuT) from *Aquifex aeolicus* was purified according to a protocol described previously.[2] LeuT was expressed in *E. Coli* C41(DE3) transformed with pET16b (kindly provided by Dr. E. Gouaux, Vollum Institute, Portland, Oregon, USA) encoding C-terminally 8xHis-tagged transporter. Bacterial membranes were isolated using a high pressure homogenizer (Constant Systems, Daventry, UK) and the protein was extracted from the membranes by treating with 1.0 wt% DDM. The DDM-solubilized protein was immobilized on Ni^{2+}-NTA resin (Life Technologies, Denmark) and eluted from a gravity column in buffer A (20 mM Tris-HCl (pH 8.0), 1 mM NaCl, 199 mM KCl, 0.05% DDM and 300 mM imidazole). Subsequently, approx. 1.5 mg/mL protein stock was diluted ten-fold in the identical buffer without DDM and imidazole but supplemented with an individual A-MNGs (MNG-9,11, MNG-8,12, MNG-6,14, MNG-4,16, MNG-2,18, and MNG-0,20), MNG-10,10 or DDM (control). To allow for the detergent exchange, we incubated the samples for 16 hours before the first measurement. The final detergent concentrations were CMC + 0.04 wt% or CMC + 0.2 wt%. Protein samples were incubated at room temperature for 12 days and, at the indicated time points, the samples were centrifuged and the ligand binding ability of the transporter was determined *via*

scintillation proximity assay (SPA) using [^{3}H]-leucine (Leu).[3] The assay was performed with a buffer containing 450 mM NaCl and the respective A-MNGs at the concentrations indicated above. SPA binding experiment was carried out using 20 nM [^{3}H]-Leu and 1.25 mg/ml copper chelate (His-Tag) YSi beads (both PerkinElmer, Denmark). Total [^{3}H]-Leu binding for the respective samples was obtained using a MicroBeta liquid scintillation counter (PerkinElmer).

MelB solubilization and thermal stability

For production of the target protein, *E. coli* DW2 strain (Δ*melB* and Δ*lacZY*) harboring pK95ΔAHB/WT $MelB_{St}$/CH10 plasmid were used.[4] The plasmid encodes the wild-type melibiose permease of *Salmonella typhimurium* ($MelB_{St}$) including a 10xHis tag at the C-terminus. Cell growth and membrane preparation were carried out as described.[5] Protein assay was carried out using a Micro BCA kit (Thermo Scientific, Rockford, IL). The membrane samples containing $MelB_{St}$ (a final total membrane protein concentration was 10 mg/mL) dispersed in a solubilization buffer (20 mM sodium phosphate, pH 7.5, 200 mM NaCl, 10% glycerol and 20 mM melibiose) were mixed with 1.5% (w/v) individual detergents (DDM, MNG-10,10, A-MNGs (MNG-9,11, MNG-8,12, MNG-6,14, MNG-4,16, MNG-2,18, and MNG-0,20)). The protein extractions were carried out at four different temperatures (0, 45, 55, and 65 ℃) for 90 min. Following the extraction, insoluble fractions were removed by ultracentrifugation at 355,590 *g* in a Beckman OptimaTM MAX ultracentrifuge using a TLA-100 rotor for 45 min at 4 °C. 20 μg membrane proteins were applied for the untreated membrane (Memb) or detergent extracts before ultracentrifugation, and equal volume of solutions were loaded for samples that the ultracentrifugation were applied. All $MelB_{St}$ samples were analyzed by SDS-15% PAGE, and the transporter was visualized by immunoblotting with a Penta-His- HRP antibody (Qiagen, Germantown, MD) as described.[6]

Trp→D^2G FRET assay

D^2G was obtained from Drs. Gerard Leblanc and H. Ronald Kaback. The right-side out (RSO) membrane vesicles containing either $MelB_{St}$[6] or $MelB_{Ec}$[4] in a buffer containing 100 mM KPi (pH 7.5) and 100 mM NaCl at a protein concentration of 1 mg/ml were solubilized with 1.0 % of a given detergent at 23 °C for 30 min and subjected to ultracentrifugation using TLA 120.2 rotor at >300,000 g for 45 min at 4 ℃. The supernatants were used for Trp→D^2G FRET experiments using an Amico-Bowman Series 2 (AB2) Spectrofluorometer. Excitation wavelength was set at 290 nm, Trp→D^2G FRET was recorded at 465 nm and 490 nm for $MelB_{Ec}$ and $MelB_{St}$, respectively. On a time trace, 10 μM D^2G and excess melibiose or equal volume of water were added at 1-min and 2-min time points, respectively.

Long-term stability of β_2AR

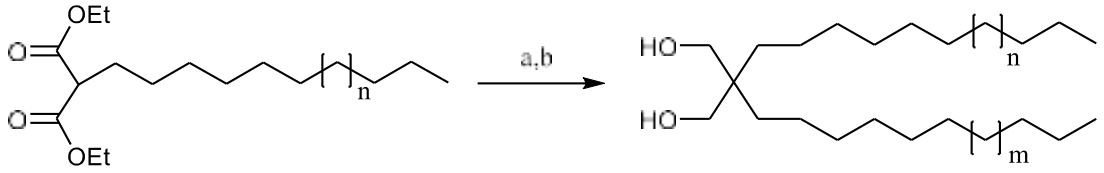
The receptor was first purified 0.1% DDM and then diluted into buffer solutions supplemented with DDM, MNG-10,10, or individual A-MNGs (MNG-9,11, MNG-8,12, MNG-6,14, MNG-4,16, MNG-2,18, and MNG-0,20) to give a final detergent concentration of CMC + 0.2 wt%. β_2AR in each detergent was incubated for 5 days at room temperature and its ligand binding capacity was measured at regular intervals during the incubation by incubating with 10 nM of radioactive [^{3}H]-dihydroalprenolol (DHA). The [^{3}H]-DHA-containing mixture was loaded onto a G-50 column and the flow-through was collected with a certain amount of binding buffer (20 mM HEPES pH 7.5, 100 mM NaCl, supplemented with 0.5 mg/ml BSA) where 15 ml scintillation fluid was added into. Receptor-bound [^{3}H]-DHA was measured with a scintillation counter (Beckman).

MOR thermostability (CPM assay)

N-[4-(7-diethylamino-4-methyl-3-coumarinyl)phenyl] maleimide (CPM) dye in DMSO (3 mg/ml stock) was diluted 40x in buffer containing 20 mM HEPES pH 7.5 and 150 mM NaCl.[7] The μ-opioid receptor (~ 4 μM) in DDM was incubated with 250 μL of 1.0 % solutions of the different detergents. After 40 min, the receptor solution was diluted 2x in 20 mM HEPES pH 7.5, 150 mM NaCl to reach the final detergent concentration of 0.5 wt%. Receptor stability in the different detergents was measured by adding 5 μL of the diluted CPM dye and then recording the fluorescence spectra (excitation 387 nm) from 20 °C to 60 °C at every 5 °C with 2-min incubation at each temperature. The melting temperature (T_m) was computed by plotting the reading at 370 nm and fitting a non-linear regression curve using GraphPad Prism.

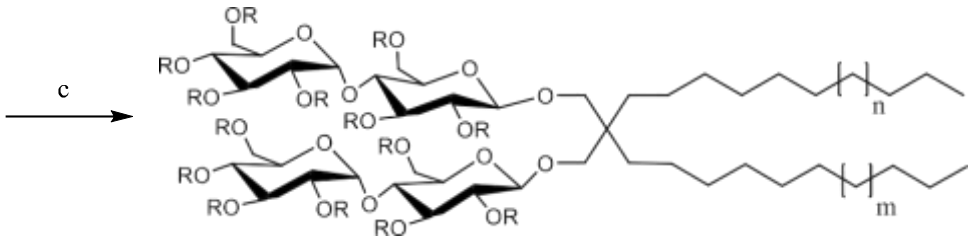
Supplemental Experimental Procedure

Synthetic scheme of A-MNGs



1: n = 2 **4**: n = 7
2: n = 3 **5**: n = 9
3: n = 5 **6**: n = 11

7: n = 2, m = 0 **10**: n = 7, m = -5
8: n = 3, m = -1 **11**: n = 9, m = -7
9: n = 5, m = -3 **12**: n = 11, m = -9



MNG-9,11a: n = 2, m = 0, R = benzoyl
MNG-8,12a: n = 3, m = -1, R = benzoyl
MNG-6,14a: n = 5, m = -3, R = benzoyl
MNG-4,16a: n = 7, m = -5, R = benzoyl
MNG-2,18a: n = 9, m = -7, R = benzoyl
MNG-0,20a: n = 11, m = -9, R = benzoyl

d

MNG-9,11: n = 2, m = 0, R = H
MNG-8,12: n = 3, m = -1, R = H
MNG-6,14: n = 5, m = -3, R = H
MNG-4,16: n = 7, m = -5, R = H
MNG-2,18: n = 9, m = -7, R = H
MNG-0,20: n = 11, m = -9, R = H

a) NaH, RI, DMF, THF, 100 °C; b) $LiAlH_4$, THF, R.T.; c) perbenzoylated maltosylbromide, AgOTf, CH_2Cl_2, R.T.; d) NaOMe, MeOH, R.T.

*General procedure for preparation of monoalkylated diethylmalonate **(A)***[8]

K_2CO_3 (5.0 equiv.) was added to diethylmalonate (5.0 equiv.) in a 1:1 mixture of THF (20 mL) and DMF (20 mL) at 0 °C. The mixture was stirred until evolution of gas ceases. To this solution was added 1-bromoalkane (1.0 equiv.) and the mixture was heated 100 °C for 18 hrs. The resulting solution was extracted with diethyl ether and washed with 1.0 M aqueous HCl (100 mL) and brine (100 mL). The combined organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation. The residue was purified by silica gel column chromatography (EtOAc/hexane), providing the desired product as an oily liquid (86 to 91%).

*General procedure for alkylation and reduction of monoalkylated diethylmalonate **(step a,b)***[8]

NaH (1.5 equiv.) and monoalkylated diethylmalonate (**A**, 1.0 equiv.) were dissolved in a 1:2 mixture of THF (15 mL) and DMF (30 mL) at 0 °C. 1-Iodoalkane (1.5 equiv.) was added in small portions, and the resulting solution was heated at 80 °C for 6 hrs. After completion of the reaction (as detected by

TLC), the solution was diluted with diethyl ether (50 mL) and washed successively with 1.0 M aqueous HCl (20 mL) and brine (100 mL). The organic layer was dried with anhydrous Na_2SO_4. After complete evaporation of solvent, $LiAlH_4$ (3.0 equiv.) was added slowly to the residue dissolved in THF (20 mL) at 0 °C. The mixture was stirred at room temperature for 24 hrs, quenched with MeOH, water, 1.0 M aqueous HCl solution successively at 0 °C and then extracted with diethyl ether (2x30 mL). The combined organic layer was washed with brine and dried with anhydrous Na_2SO_4. The residue was purified by silica gel column chromatography (EtOAc/hexane), providing a desired product as a white solid (85 to 93% (two steps)).

*General procedure for glycosylation reaction **(step c)***[9]

Under N_2 atmosphere, a mixture of a di-ol derivative (1.0 equiv.), AgOTf (3.5 equiv.), 2,4,6-collidine (1.0 equiv.) in anhydrous CH_2Cl_2 was stirred at room temperature. A solution of perbenzoylated maltosylbromide (3.0 equiv.) in CH_2Cl_2 was added dropwise to this suspension. Stirring was continued for 10 min at room temperature. After completion of reaction (as detected by TLC), pyridine was added to the reaction mixture, and the resulting solution was diluted with CH_2Cl_2 before being filtered over celite. The filtrate was washed successively with 1.0 M aqueous $Na_2S_2O_3$ solution, 0.1 M aqueous HCl solution, and brine. The organic layer was collected and dried over anhydrous Na_2SO_4 and followed by rotary evaporation. The resulting residue was purified by silica gel column chromatography (EtOAc/hexane), providing the glycosylated product as a white solid (88 to 92%).

*General procedure for the de-O-benzoylations under Zemplén's condition **(step d)***[9]

The *O*-benzoylated compounds were dissolved in MeOH and then treated with required amount of a methanolic solution of 0.5 M NaOMe such that the final concentration of NaOMe was 0.05 M. The reaction mixture was left stirring for 6 hrs 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), providing the fully deprotected compounds as a white solid (90 to 95%).

Diethyl 2-undecylmalonate (**1**) was prepared in 90% yield according to the general procedure for preparation of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.23-4.16 (m, 4H), 3.31 (t, *J* = 7.6Hz, 1H), 1.89-1.87 (m, 2H), 1.31-1.25 (m, 24H), 0.88 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.8, 61.5, 52.3, 32.1, 29.8, 29.7, 29.6, 29.4, 28.9, 27.5, 22.9, 14.3.

Diethyl 2-dodecylmalonate (**2**) was prepared in 91% yield according to the general procedure for preparation of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.22-4.16 (m, 4H), 3.31 (t, *J* = 7.6 Hz, 1H), 1.90-1.87 (m, 2H), 1.30-1.25 (m, 26H), 0.87 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.9, 61.5, 52.3, 32.1, 29.9, 29.7, 29.6, 29.5, 29.4, 28.9, 27.5, 22.9, 14.4.

Diethyl 2-tetradecylmalonate (**3**) was prepared in 89% yield according to the general procedure for preparation of monoalkylated diethyl malonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.22-4.16 (m, 4H), 3.31 (t, *J* = 7.6 Hz, 1H), 1.90-1.87 (m, 2H), 1.30-1.25 (m, 30H), 0.87 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.9, 61.5, 52.3, 32.1, 29.9, 29.7, 29.6, 29.5, 29.4, 28.9, 27.5, 22.9, 14.4.

Diethyl 2-hexadecylmalonate (**4**) was prepared in 86% yield according to the general procedure for preparation of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.22-4.16 (m, 4H), 3.31 (t, *J* = 7.6 Hz, 1H), 1.90-1.87 (m, 2H), 1.30-1.25 (m, 34H), 0.87 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.9, 61.5, 52.3, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 28.9, 27.5, 22.9, 14.4, 14.3.

Diethyl 2-octadecylmalonate (**5**) was prepared in 88% yield according to the general procedure for preparation of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.22-4.16 (m, 4H), 3.31 (t, *J* = 7.6 Hz, 1H), 1.90-1.87 (m, 2H), 1.30-1.25 (m, 38H), 0.87 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.9, 61.6, 52.3, 32.1, 29.9, 29.8, 29.7, 29.6, 29.4, 28.9, 27.5, 22.9, 14.4, 14.3.

Diethyl 2- eicosanylmalonate (**6**) was prepared in 90% yield according to the general procedure for preparation of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.22-4.16 (m, 4H), 3.31 (t, *J* = 7.6 Hz, 1H), 1.90-1.87 (m, 2H), 1.30-1.25 (m, 42H), 0.87 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.9, 61.5, 52.3, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 28.9, 27.5, 22.9, 14.4, 14.3.

2-nonyl-2-undecylpropane-1,3-diol (**7**) was prepared in 90% yield according to the general procedure for alkylation and reduction of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.60 (s, 4H), 2.65 (s, 2H), 1.42-1.08 (m, 36H), 0.89 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ66.6, 42.6, 33.1, 31.8, 31.5, 30.9, 30.7, 30.5, 26.2, 24.8, 23.8, 14.6, 14.5.

2-octyl-2-dodecylpropane-1,3-diol (**8**) was prepared in 93% yield according to the general procedure for alkylation and reduction of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.60 (s, 4H), 2.60 (s, 2H), 1.42-1.08 (m, 36H), 0.89 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ66.5, 42.5, 33.2, 31.8, 31.5, 30.8, 30.7, 30.5, 26.1, 24.8, 23.8, 14.5.

2-hexyl-2-tetradecylpropane-1,3-diol (**9**) was prepared in 85% yield according to the general procedure for alkylation and reduction of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.65 (s, 4H), 2.55 (s, 2H), 1.42-1.08 (m, 36H), 0.88 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ66.4, 42.4, 33.1, 31.7, 31.5, 30.8, 30.7, 30.5, 26.1, 24.8, 23.8, 14.5.

2-butyl-2-tetradecylpropane-1,3-diol (**10**) was prepared in 88% yield according to the general procedure for alkylation and reduction of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.65 (s, 4H), 2.55 (s, 2H), 1.42-1.08 (m, 36H), 0.88 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ66.1, 42.6, 33.1, 31.9, 31.7, 31.3, 30.8, 30.5, 26.0, 24.8, 23.8, 14.5.

2-ethyl-2-octadecylpropane-1,3-diol (**11**) was prepared in 90% yield according to the general procedure for alkylations and reduction of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.63 (s, 4H), 2.65 (s, 2H), 1.42-1.08 (m, 36H), 0.88 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ 66.0, 42.5, 33.1, 31.8, 31.3, 30.8, 30.5, 26.1, 23.9, 23.8, 14.5.

2-eicosylpropane-1,3-diol (**12**) was prepared in 88% yield according to the general procedure for alkylations and reduction of monoalkylated diethylmalonate. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.63 (s, 4H), 2.50 (s, 2H), 1.95 (s, 1H)1.42-1.08 (m, 38H), 0.88 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3OD): δ 62.4, 38.8, 33.1, 31.8, 31.3, 30.8, 30.7, 26.1, 23.9, 23.7, 14.4.

MNG-9,11a was prepared in 90% yield according to the general procedure for glycosylation reaction.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.4 Hz, 4H), 8.02-7.95 (m, 8H), 7.92 (d, *J* = 8.4 Hz, 4H), 7.86 (d, *J* = 8.4 Hz, 4H), 7.85 (d, *J* = 8.4 Hz, 4H), 7.80 (d, *J* = 8.4 Hz, 4H), 7.75-7.18 (m, 42H), 6.13 (t, *J* = 9.8 Hz, 2H), 5.68–5.58 (m, 4H), 5.34 (t, *J* = 10.2 Hz, 2H), 5.18-5.08 (m, 4H), 4.68-4.52 (m, 4H), 4.38-4.16 (m, 8H), 3.32 (d, *J* = 7.6 Hz, 2H), 2.92-2.86 (m, 2H), 2.72 (d, *J* = 8.6 Hz, 2H), 1.35-0.98 (m, 34H), 0.87 (t, *J* = 6.9 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.3, 166.0, 165.7, 165.3, 165.2, 165.0, 133.9, 133.7, 133.6, 133.4, 130.3, 130.1, 130.0, 129.9, 129.8, 129.7, 129.6, 129.4, 129.2, 129.0, 128.9, 128.8, 128.6, 128.5, 95.9, 72.3, 72.2, 71.5, 69.2, 62.8, 40.4, 32.1, 30.6, 30.3, 29.9, 29.8, 29.7, 29.6, 22.9, 14.3.

MNG-8,12a was prepared in 89% yield according to the general procedure for glycosylation reaction. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.4 Hz, 4H), 8.02-7.95 (m, 8H), 7.92 (d, *J* = 8.4 Hz, 4H), 7.76 (d, *J* = 8.4 Hz, 4H), 7.64 (d, *J* = 8.4 Hz, 4H), 7.61 (d, *J* = 8.4 Hz, 4H), 7.56 -7.16 (m, 42H), 6.18 (t, *J* = 9.8 Hz, 2H), 5.71–5.58 (m, 4H), 5.35 (t, *J* = 10.2 Hz, 2H), 5.18-5.08 (m, 4H), 4.68-4.52 (m, 4H), 4.38-4.16 (m, 8H), 3.32 (d, *J* = 7.6 Hz, 2H), 2.92-2.86 (m, 2H), 2.72 (d, *J* = 8.6 Hz, 2H), 1.35-0.98 (m, 34H), 0.87 (t, *J* = 6.9 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.3, 166.0, 165.7, 165.3, 165.2, 165.0, 133.9, 133.7, 133.6, 133.4, 130.3, 130.1, 130.0, 129.9, 129.8, 129.7, 129.6, 129.4, 129.2, 129., 128.7, 128.6, 128.5, 128.3, 95.9, 72.3, 72.2, 71.5, 69.2, 62.8, 40.4, 32.1, 30.6, 30.3, 29.9, 29.8, 29.7, 29.6, 22.9, 14.3.

MNG-6,14a was prepared in 91% yield according to the general procedure for glycosylation reaction. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.4 Hz, 4H), 8.03-7.95 (m, 8H), 7.89 (d, *J* = 8.4 Hz, 4H), 7.76 (d, *J* = 8.4 Hz, 4H), 7.64 (d, *J* = 8.4 Hz, 4H), 7.61 (d, *J* = 8.4 Hz, 4H), 7.56 -7.16 (m, 42H), 6.22 (t, *J* = 9.8 Hz, 2H), 5.79–5.74 (m, 4H), 5.45 (t, *J* = 10.2 Hz, 2H), 5.18-5.08 (m, 4H), 4.63-4.52 (m, 4H), 4.38-4.16 (m, 8H), 3.35 (d, *J* = 7.6 Hz, 2H), 2.92-2.86 (m, 2H), 2.72 (d, *J* = 8.6 Hz, 2H), 1.35-0.98 (m, 34H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.75 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.2, 166.0, 165.6, 165.2, 165.0, 133.6, 130.2, 130.1, 129.9, 129.8, 129.7, 129.0, 128.7, 128.6, 128.5, 128.3, 72.2, 71.4, 69.9, 69.1, 32.1, 29.9, 22.9, 14.3.

MNG-4,16a was prepared in 88% yield according to the general procedure for glycosylation reaction. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.4 Hz, 4H), 8.03-7.95 (m, 8H), 7.89 (d, *J* = 8.4 Hz, 4H), 7.76 (d, *J* = 8.4 Hz, 4H), 7.64 (d, *J* = 8.4 Hz, 4H), 7.61 (d, *J* = 8.4 Hz, 4H), 7.56 -7.16 (m, 42H), 6.22 (t, *J* = 9.8 Hz, 2H), 5.79–5.74 (m, 4H), 5.45 (t, *J* = 10.2 Hz, 2H), 5.18-5.08 (m, 4H), 4.63-4.52 (m, 4H), 4.38-4.16 (m, 8H), 3.35 (d, *J* = 7.6 Hz, 2H), 2.92-2.86 (m, 2H), 2.72 (d, *J* = 8.6 Hz, 2H), 1.35-0.98 (m, 34H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.78 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.2, 166.0, 165.6, 165.2, 165.0, 133.6, 130.2, 130.1, 129.9, 129.8, 129.7, 129.0, 128.7, 128.6, 128.5, 128.3, 72.2, 71.4, 69.9, 69.1, 32.1, 29.9, 29.8, 29.5, 22.9, 14.3.

MNG-2,18a was prepared in 90% yield according to the general procedure for glycosylation reaction. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.4 Hz, 4H), 8.03-7.96 (m, 8H), 7.92 (d, *J* = 8.4 Hz, 4H), 7.86 (d, *J* = 8.4 Hz, 4H), 7.86 (d, *J* = 8.4 Hz, 4H), 7.80 (d, *J* = 8.4 Hz, 4H), 7.75-7.18 (m, 42H), 6.12 (t, *J* = 9.8 Hz, 2H), 5.67–5.58 (m, 4H), 5.33 (t, *J* = 10.2 Hz, 2H), 5.18-5.06 (m, 4H), 4.68-4.52 (m, 4H), 4.38-4.16 (m, 8H), 3.34-3.28 (m, 4H), 2.92-2.87 (m, 2H), 2.70 (d, *J* = 8.6 Hz, 2H), 1.61 (s, 2H), 1.35-0.98 (m, 34H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.61 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.2, 166.0, 165.6, 165.2, 165.0, 133.6, 133.3, 130.2, 130.1, 129.9, 129.8, 129.6, 129.3, 129.1, 128.8, 128.6, 128.4, 72.2, 71.4, 69.9, 69.1, 32.1, 29.9, 29.8, 29.5, 22.9, 14.3.

MNG-0,20a was prepared in 92% yield according to the general procedure for glycosylation reaction. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.4 Hz, 4H), 8.04-7.98 (m, 8H), 7.92 (d, *J* = 8.4 Hz, 4H), 7.86 (d, *J* = 8.4 Hz, 4H), 7.86 (d, *J* = 8.4 Hz, 4H), 7.80 (d, *J* = 8.4 Hz, 4H), 7.75-7.22 (m, 42H), 6.11 (t, *J* = 9.8 Hz, 2H), 5.69–5.58 (m, 4H), 5.38 (t, *J* = 10.2 Hz, 2H), 5.18-5.06 (m, 4H), 4.68-4.52 (m, 4H), 4.38-4.16 (m, 8H), 3.62-3.57 (m, 2H), 3.31-3.27 (m, 2H), 3.04-2.94 (m, 2H), 2.77 (t, *J* = 9.8 Hz, 1H), 1.57 (s, 4H), 1.35-0.98 (m, 36H), 0.87 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 166.2, 166.0, 165.6, 165.2, 133.6, 133.3, 130.2, 130.1, 129.9, 129.8, 129.6, 129.3, 129.1, 129.0, 128.8, 128.6, 128.4, 72.2, 69.2, 69.1, 32.1, 29.9, 29.8, 29.5, 22.9, 14.3.

MNG-9,11 was prepared in 92% yield according to the general procedure for the de-*O*-benzoylation under Zemplén's condition. **^{1}H NMR** (400 MHz, CD_3OD): δ 5.15 (d, *J* = 4.0 Hz, 2H), 4.36 (d, *J* = 8.0 Hz, 2H), 3.90 (d, *J* = 10.0 Hz, 2H), 3.84-3.78 (m, 4H), 3.72-3.58 (m, 10H), 3.54-3.20 (m, 18H), 1.34-1.21 (m, 36H), 0.89 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ 105.0, 103.0, 81.6, 78.0, 76.6, 75.2, 74.9, 74.3, 71.6, 62.8, 42.2, 33.2, 31.7, 30.9, 30.6, 23.9, 14.6; **HRMS (EI)**: calcd. for $C_{47}H_{88}O_{22}$ $[M+Na]^+$ 1027.5665, found 1027.5663.

MNG-8,12 was prepared in 95% yield according to the general procedure for the de-*O*-benzoylation under Zemplén's condition. **^{1}H NMR** (400 MHz, CD_3OD): δ 5.15 (d, *J* = 4.0 Hz, 2H), 4.36 (d, *J* = 8.0 Hz, 2H), 3.90 (d, *J* = 10.0 Hz, 2H), 3.84-3.78 (m, 4H), 3.72-3.58 (m, 10H), 3.54-3.22 (m, 18H), 1.34-1.21 (m, 36H), 0.89 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ 105.0, 102.9, 81.5, 77.9, 76.5, 75.1, 74.8, 74.2, 73.1, 71.5, 62.7, 62.2, 40.7, 33.1, 33.0, 31.6, 31.3, 30.8, 30.6, 30.5, 23.7, 14.5, 14.4; **HRMS (EI)**: calcd. for $C_{47}H_{88}O_{22}$ $[M+Na]^+$ 1027.5665, found 1027.5643.

MNG-6,14 was prepared in 95% yield according to the general procedure for the de-*O*-benzoylation under Zemplén's condition. **^{1}H NMR** (400 MHz, CD_3OD): δ 5.15 (d, *J* = 4.0 Hz, 2H), 4.36 (d, *J* = 8.0 Hz, 2H), 3.90 (d, *J* = 10.0 Hz, 2H), 3.84-3.78 (m, 4H), 3.72-3.58 (m, 10H), 3.54-3.22 (m, 18H), 1.34-1.21 (m, 36H), 0.89 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ 104.9, 102.9, 81.5, 77.9, 76.5, 75.1, 74.8, 74.2, 73.1, 71.5, 62.7, 62.2, 40.7, 33.1, 31.6, 31.3, 30.8, 30.6, 30.5, 23.7, 14.5, 14.4; **HRMS (EI)**: calcd. for $C_{47}H_{88}O_{22}$ $[M+Na]^+$ 1027.5665, found 1027.5661.

MNG-4,16 was prepared in 90% yield according to the general procedure for the de-*O*-benzoylation under Zemplén's condition. **^{1}H NMR** (400 MHz, CD_3OD): δ 5.15 (d, *J* = 4.0 Hz, 2H), 4.36 (d, *J* = 8.0 Hz, 2H), 3.90 (d, *J* = 10.0 Hz, 2H), 3.84-3.78 (m, 4H), 3.72-3.58 (m, 10H), 3.54-3.21 (m, 18H), 1.34-1.21 (m, 36H), 0.88-0.92 (m, 6H); **^{13}C NMR** (100 MHz, CD_3OD): δ 104.8, 102.9, 81.4, 77.9, 76.5, 75.1, 74.8, 74.2, 71.5, 62.7, 62.5, 40.7, 33.1, 31.1, 30.7, 30.5, 28.2, 23.7, 14.4; **HRMS (EI)**: calcd. for $C_{47}H_{88}O_{22}$ $[M+Na]^+$ 1027.5665, found 1027.5663.

MNG-2,18 was prepared in 93% yield according to the general procedure for the de-*O*-benzoylation under Zemplén's condition. **^{1}H NMR** (400 MHz, CD_3OD): δ 5.15 (d, *J* = 4.0 Hz, 2H), 4.36 (d, *J* = 8.0 Hz, 2H), 3.90 (d, *J* = 10.0 Hz, 2H), 3.84-3.78 (m, 4H), 3.72-3.58 (m, 10H), 3.54-3.20 (m, 18H), 1.34-1.21 (m, 36H), 0.89 (t, *J* = 7.2 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3OD): δ 104.8, 102.9, 81.4, 77.9, 76.5, 75.1, 74.8, 74.2, 71.5, 62.7, 62.5, 40.7, 33.1, 31.1, 30.7, 30.5, 28.2, 23.7, 14.4; **HRMS (EI)**: calcd. for $C_{47}H_{88}O_{22}$ $[M+Na]^+$ 1027.5665, found 1027.5668.

MNG-0,20 was prepared in 94% yield according to the general procedure for the de-*O*-benzoylation under Zemplén's condition. **^{1}H NMR** (400 MHz, CD_3OD): δ 5.16 (d, *J* = 4.0 Hz, 2H), 4.36 (d, *J* = 8.0

Hz, 2H), 3.90 (d, *J* = 10.0 Hz, 2H), 3.84-3.78 (m, 4H), 3.72-3.58 (m, 10H), 3.54-3.20 (m, 18H), 1.87 (s, 1H), 1.34-1.21 (m, 38H), 0.90 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, CD_3OD): δ 105.0, 102.9, 81.4, 77.9, 76.5, 75.1, 74.8, 74.2, 72.9, 71.5, 62.8, 62.2, 42.1, 33.1, 31.7, 30.8, 30.5, 23.7, 23.5, 14.4; **HRMS (EI)**: calcd. for $C_{47}H_{88}O_{22}$ $[M+Na]^+$ 1027.5665, found 1027.5661.

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