Supporting Information

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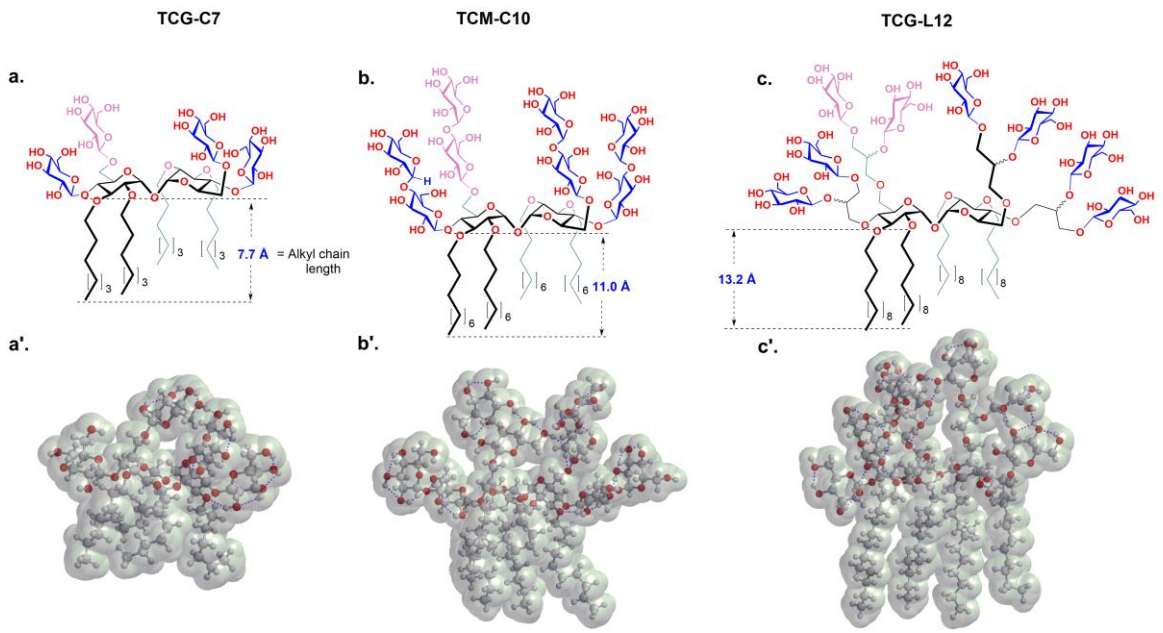


Figure S1. Chemical structures of TCG-C7 (a), TCM-C10 (b), TCG-L12 (c) and their energy-minimized conformation (a', b' and c', respectively). The lengths of the alkyl chain regions of TCG-C7, TCM-C10, and TCG-L12 were estimated using energy-minimized conformations obtained *via* density functional theory (DFT) calculation at the level of B3LYP/6-31G*. Atoms are indicated by different colors and size in the energy minimized conformations (gray-large for carbon atoms, gray-small for hydrogen atoms and red for oxygen atoms).

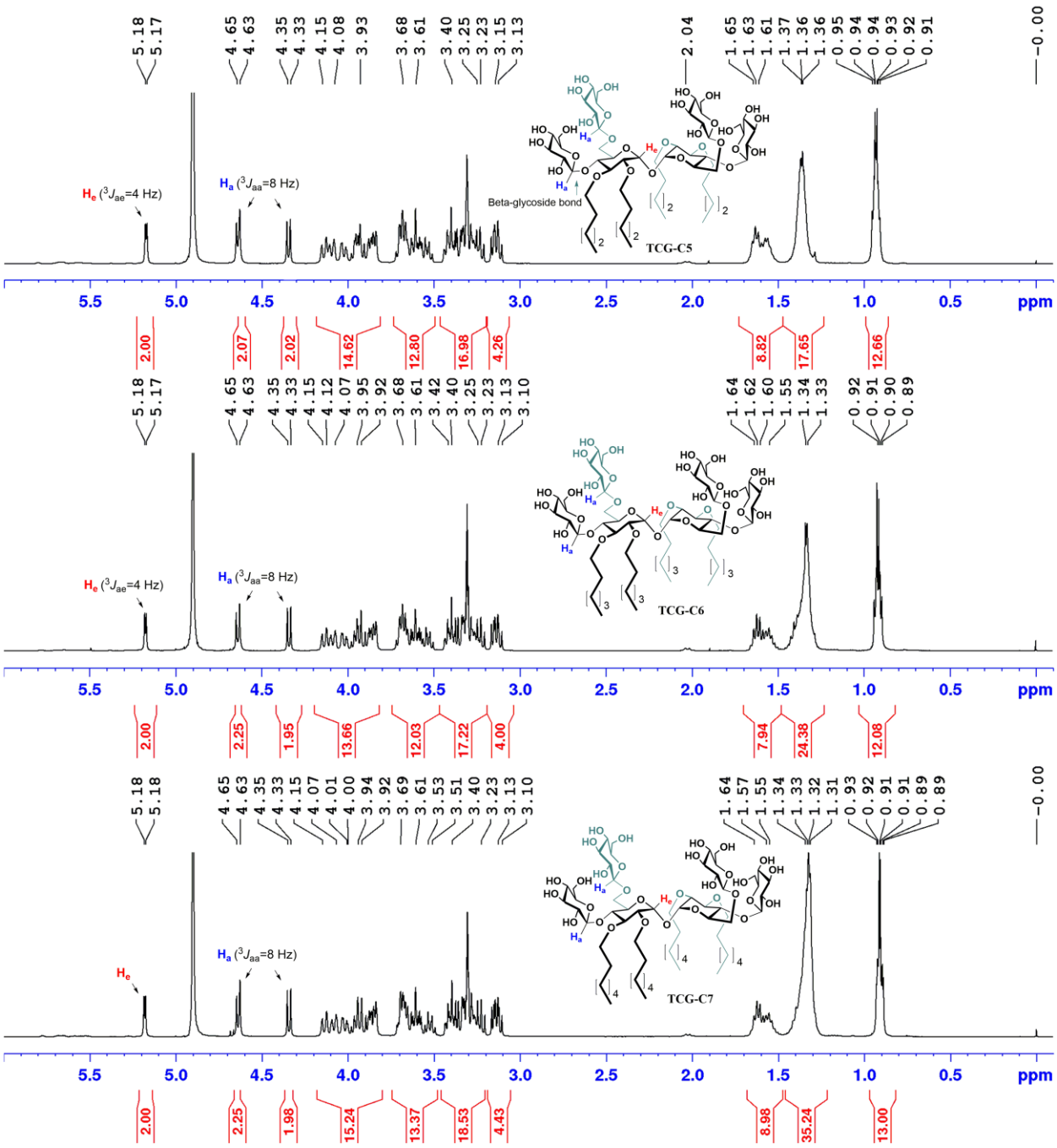


Figure S2. ^{1}H NMR spectra of TCG agents (TCG-C5 (*top*), TCG-C6 (*middle*) and TCG-C7 (*bottom*)) dissolved in CD_3OD at room temperature. High anomeric purity of each detergent was confirmed by the respective ^{1}H NMR spectrum. The peaks for α-anomeric protons (*i.e.*, H_e in trehalose unit) appeared at ~5.18 ppm as doublets with a vicinal axial-equatorial coupling constant ($^{3}J_{ae}$) of ~4.0 Hz, whereas the peaks for β-anomeric protons (*i.e.*, H_a in glucose unit) appeared as two separated doublets individually centered at 4.64 and 4.34 ppm, with a vicinal axial-axial

coupling ($^3J_{aa}$) of 8.0 Hz in all cases. The chemical sthifts and coupling constants observed here are typical for anomeric protons with α- and β-glycosidic bonds (H_e and H_a), respectively.

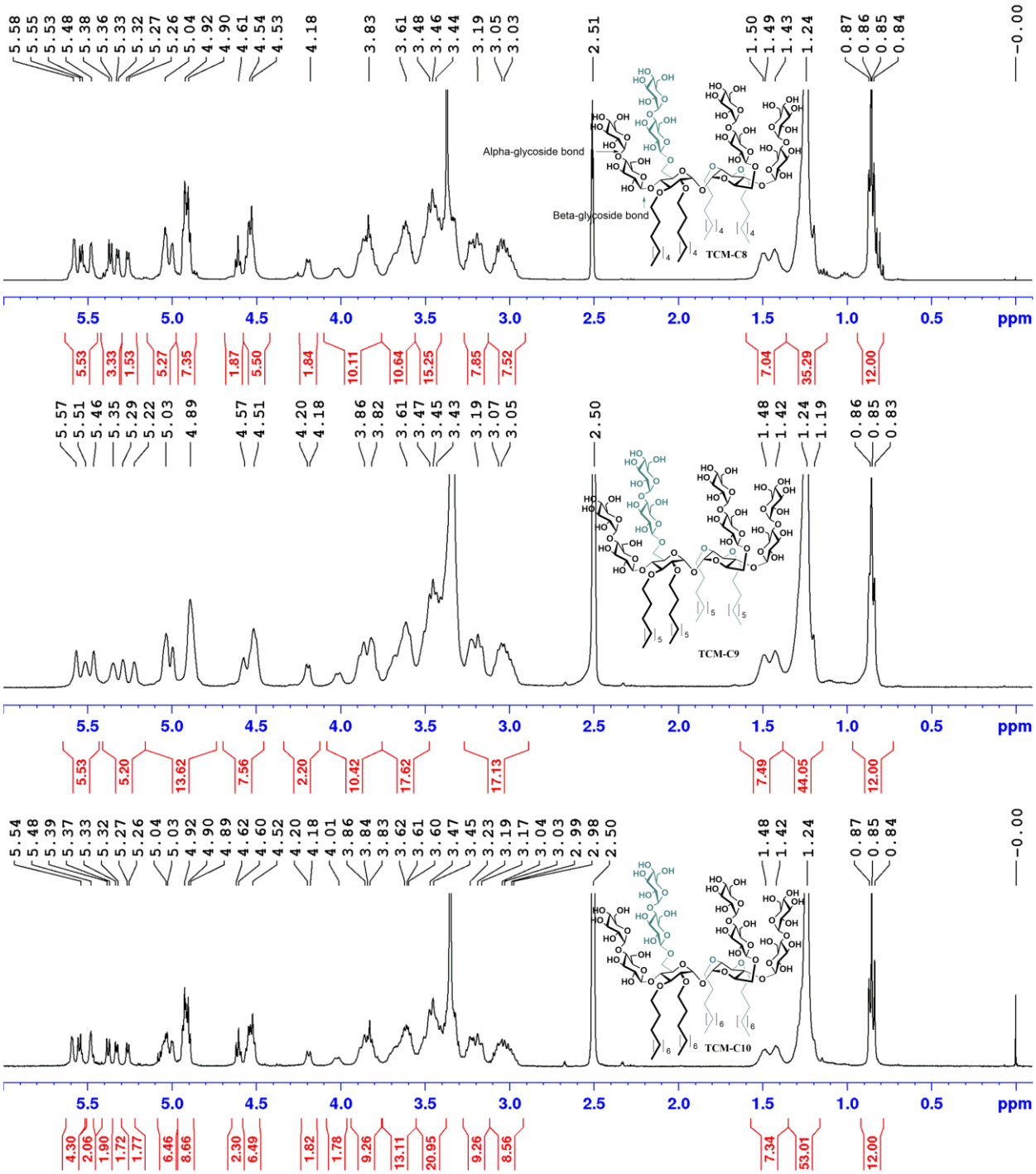


Figure S3. Full range of ^{1}H NMR spectra of TCMs (TCM-C8, TCM-C9 and TCM-C10) dissolved in DMSO-d_6 at room temperature. We used DMSO-d_6 as an NMR solvent as these detergents showed limited solubility in CD_3OD.

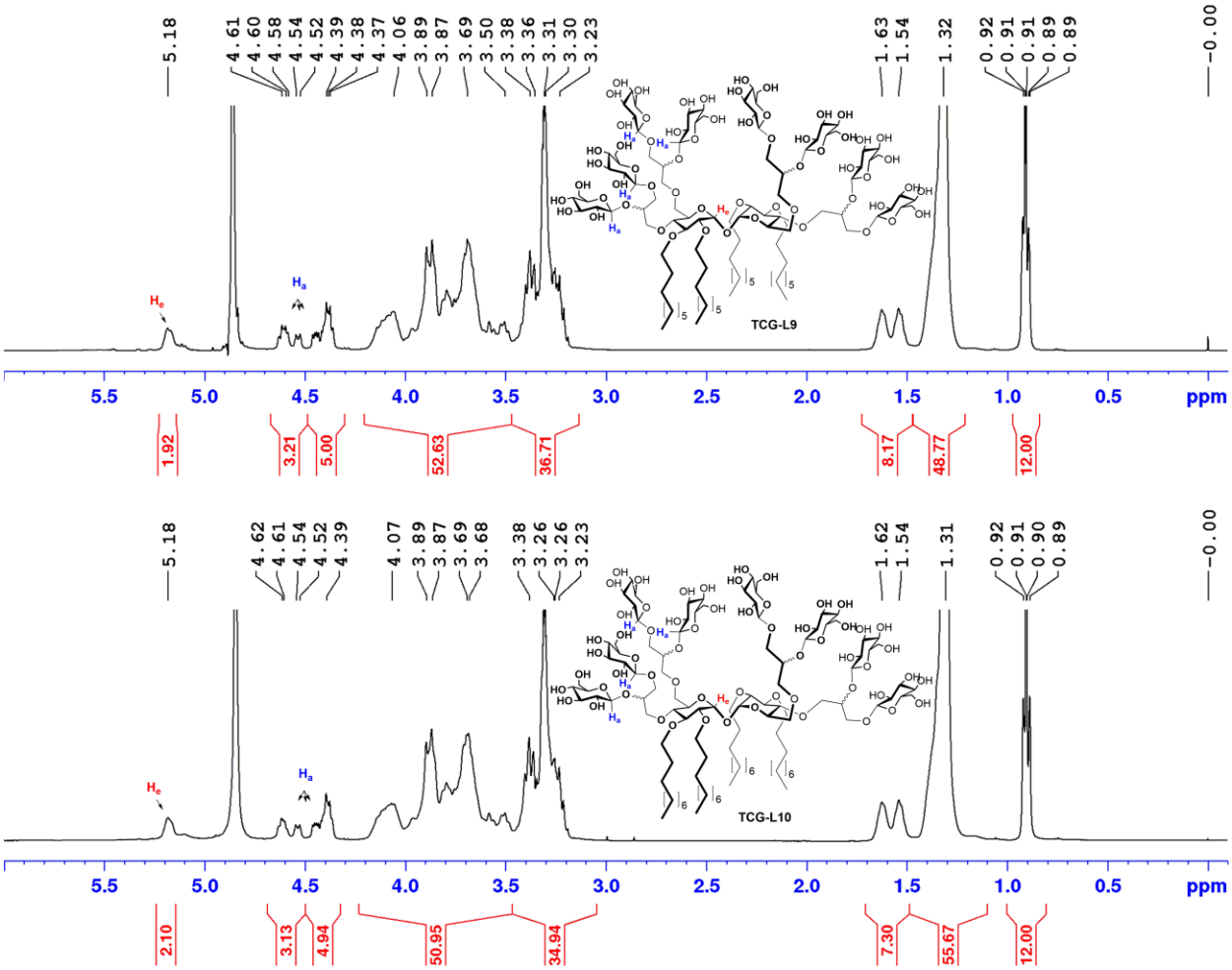


Figure S4. ^{1}H NMR spectra of TCG-L9 (*top*) and TCG-L10 (*bottom*) dissolved in CD_3OD at room temperature. Two sets of anomeric protons within the detergents, labeled H_a and H_e, are different in terms of their chemical shifts. Peak assignments for the anomeric protons are given above the peaks in the individual NMR spectra. The chemical shifts observed here are typical for anomeric protons with α- and β-glycosidic bonds (H_e and H_a), respectively.

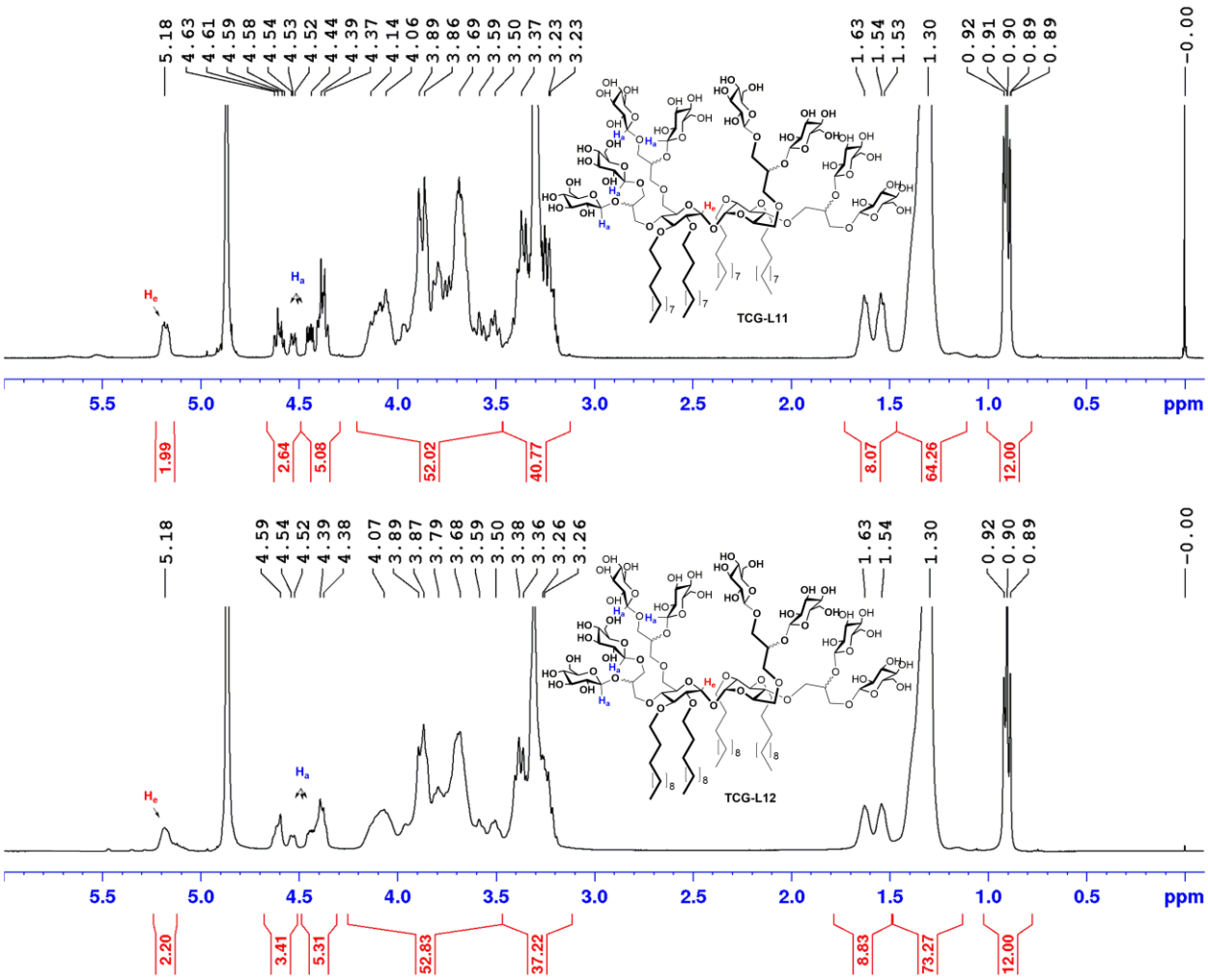


Figure S5. ^{1}H NMR spectra of TCG-L11 (*top*) and TCG-L12 (*bottom*) dissolved in CD_3OD at room temperature. Peak assignments for anomeric protons are given above the peaks in individual NMR spectra.

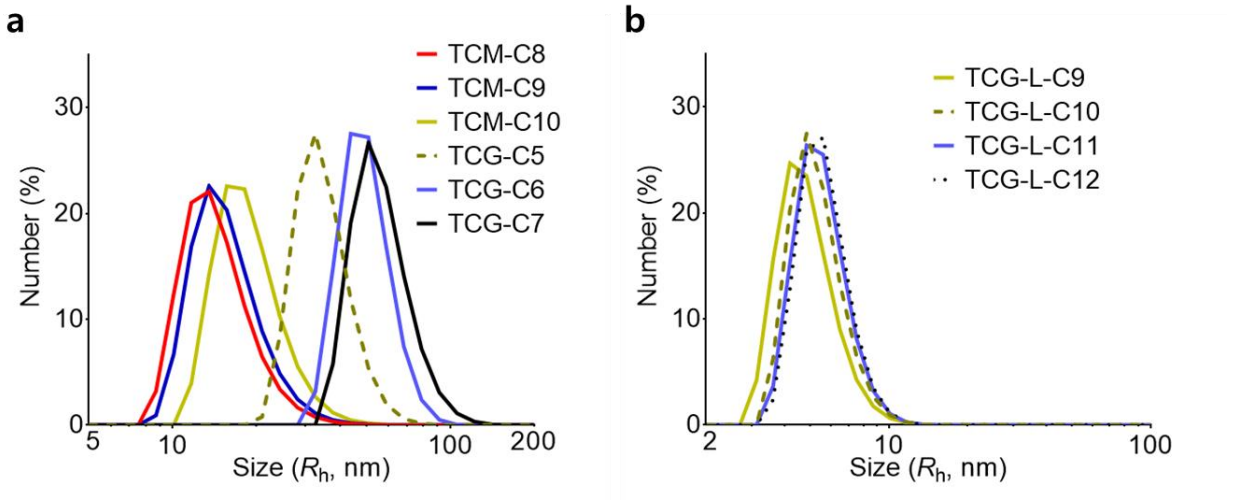


Figure S6. Dynamic light scattering (DLS) profiles for micelles formed by TCGs/ TCMs (a) or TCG-Ls (b). These agents were used at 1.0 wt% at 25 °C and showed a single set of micelle size populations. Time-dependent fluctuation in the scattered light intensity was analyzed by autocorrelation. The Stokes-Einstein equation was used to calculate the hydrodynamic radii (R_h) of detergent micelles.

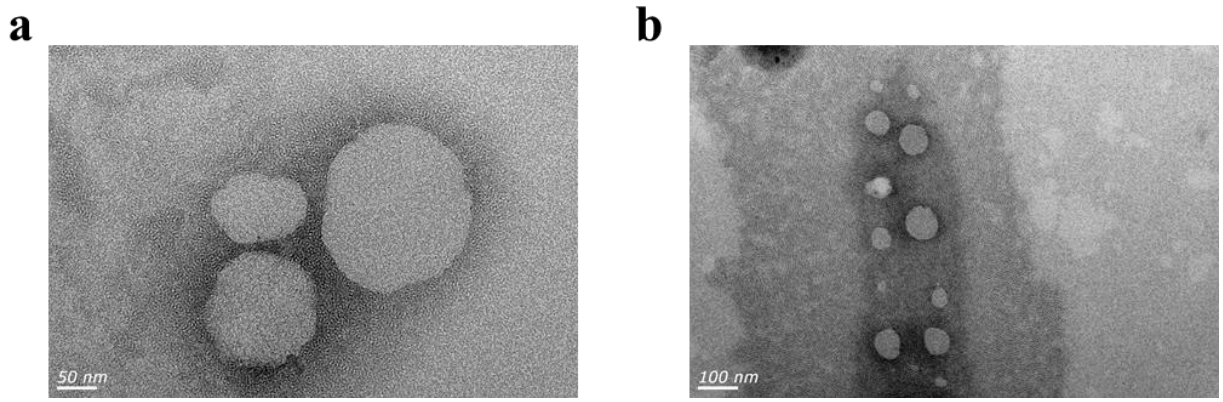


Figure S7. TEM images of (a) TCG-C7 and (b) TCM-C10. The detergents were used at 1.0 wt%. Aggregate sizes of TCG-C7 and TCM-C10 observed here were more or less comparable to those detected in their DLS profiles. TEM: transmission electron microscope.

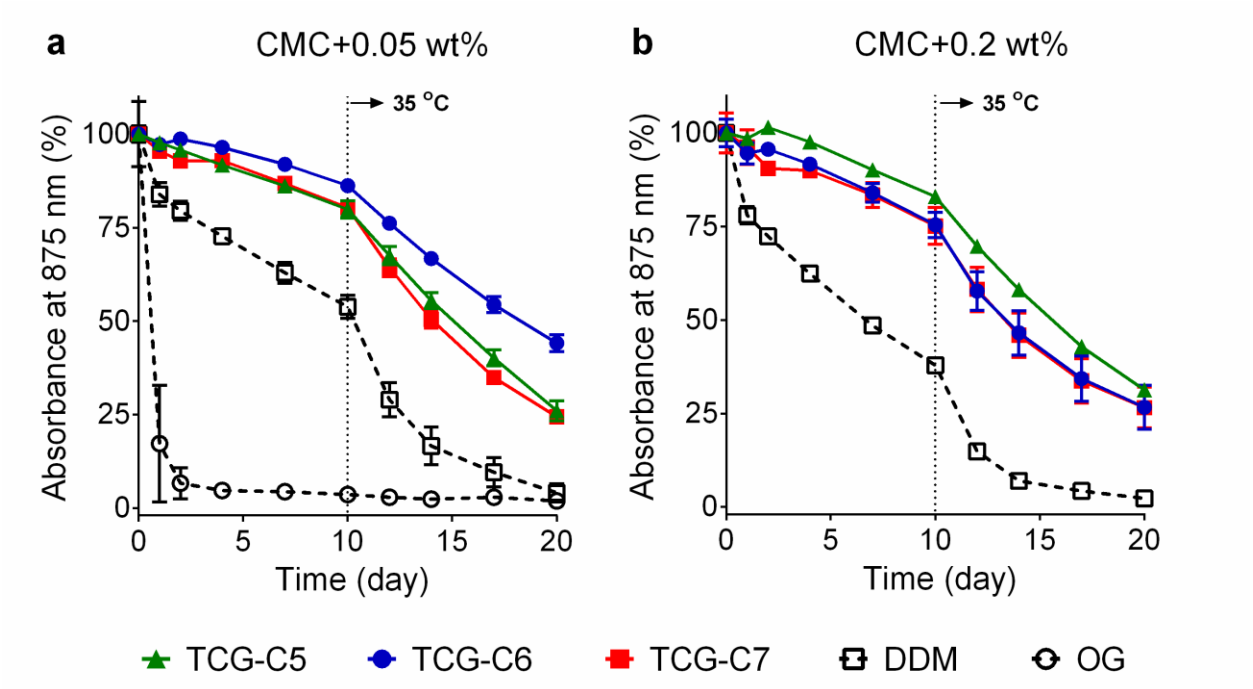


Figure S8. Long-term stability of the *R. capsulatus* superassembly, comprising light harvesting complex I and reaction centre (LHI-RC), solubilized in individual detergents (DDM, OG, TCG-C5, TCG-C6 and TCG-C7). Detergents were used at two different concentrations (CMC+0.05 wt% (a) and CMC+0.2 wt% (b)). DDM-purified LHI-RC complex was diluted into buffer solutions containing the individual detergents. UV-Visible spectra of the individual samples were collected at regular intervals over the course of a 10-day incubation at room temperature, followed by a further 10-day incubation at 35 °C. The complex integrity was monitored using absorbance value at 875 nm (A_{875}). Error bars, SEM, n = 2.

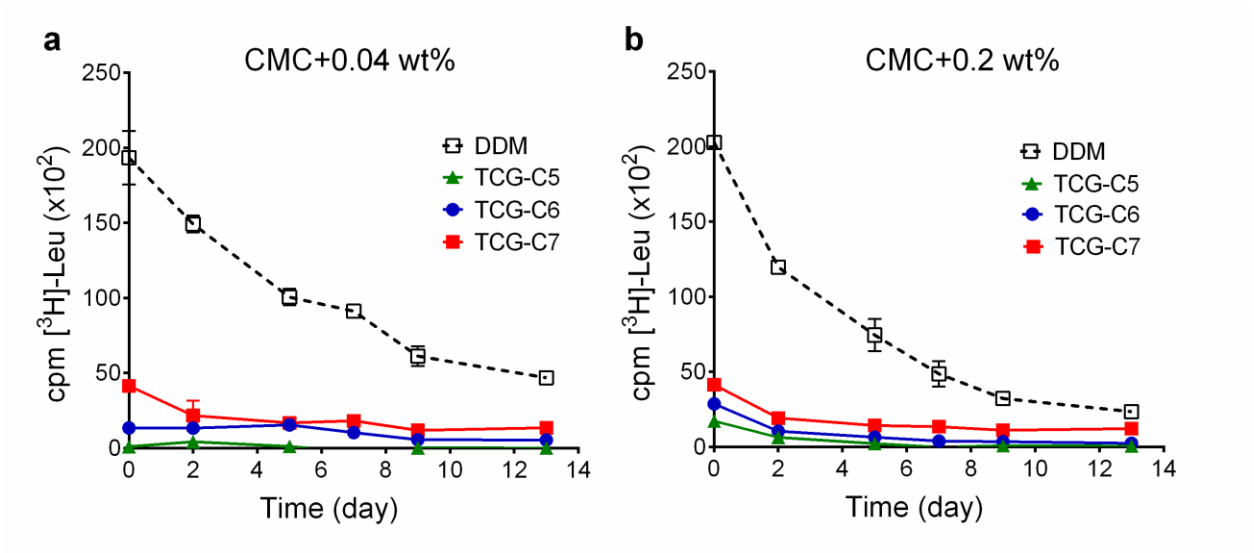


Figure S9. Long-term stability of LeuT solubilized in TCG-C5, TCG-C6, TCG-C7 or DDM at two different detergent concentrations: (a) CMC+0.04 wt% and (b) CMC+0.2 wt%. Substrate binding activity of the transporter was measured using the radio-labeled substrate ([^{3}H]-Leu) *via* scintillation proximity assay (SPA) at regular intervals during a 13-day incubation at room temperature. Error bars, SEM, n = 2-3.

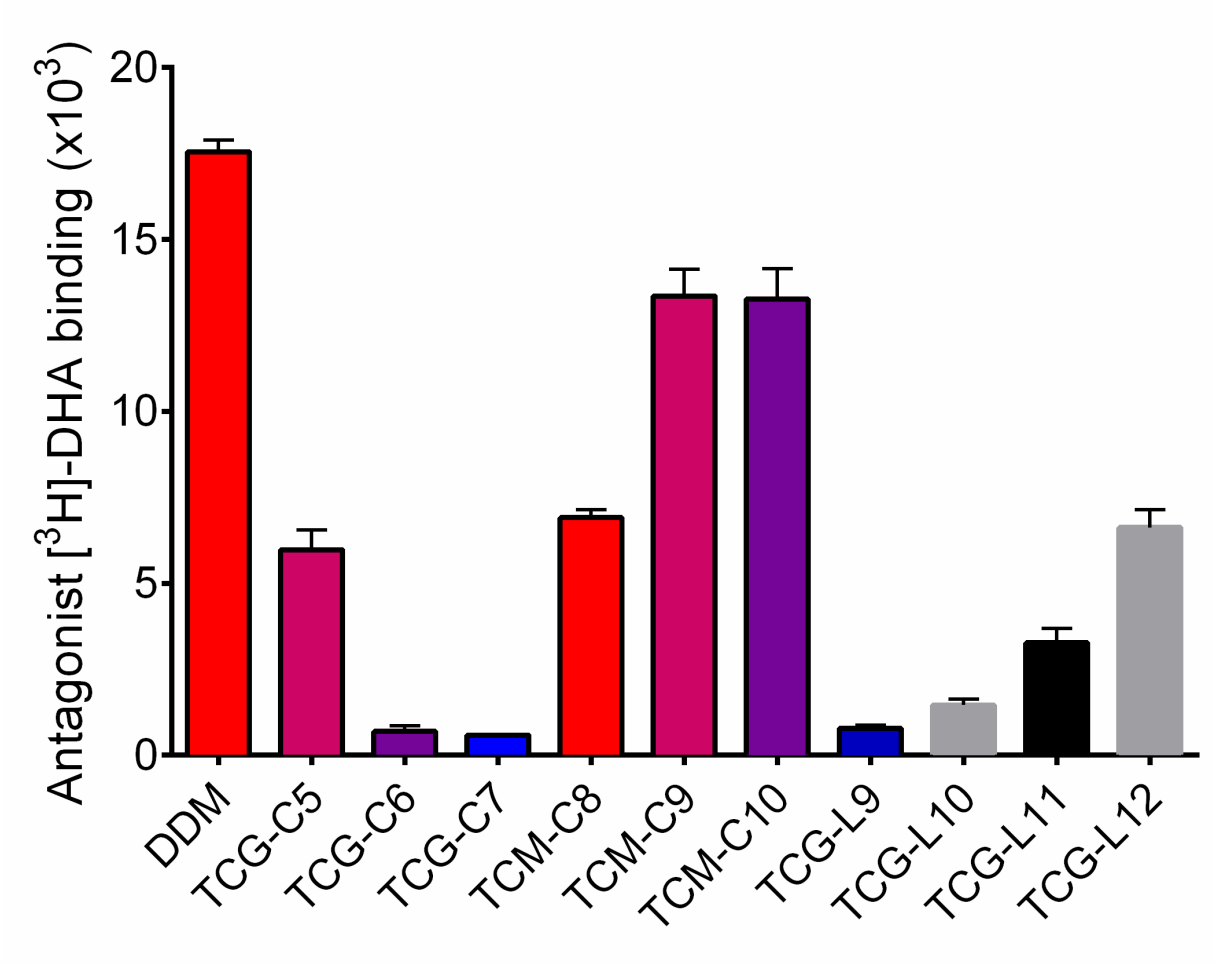


Figure S10. Initial ligand binding activity of β_2AR solubilized in new detergents (TCGs, TCMs and TCG-Ls). DDM was used as a positive control. Each detergent was used at CMC+0.2 wt%. Ligand binding activity of the receptor was measured using a radio-labelled ligand ([^{3}H]-dihydroalprenolol (DHA)) after a 30-min dilution. Error bars, SEM, n = 3.

Detergent micelle size measurement by dynamic light scattering (DLS) experiment

The new agents (TCGs/ TCMs/ TCG-Ls) were dissolved individually in distilled and deionized water to give a detergent concentration of 1.0 wt. %. These detergent solutions were filtered by a syringe filter with a pore size of 0.22 μm. Hydrodynamic radii of the micelles produced by the new agents were measured using a Malvern Zeta Sizer Nano ZS90 particle analyzer. With a maximum power of 5 Mw, a He-Ne laser set at 633 nm was used as the light source. The scattered light was collected at an angle of 90°. Temperature was kept constant at 25 °C throughout all experiments. The translational diffusion coefficient and hydrodynamic radius (R_h) of detergent micelles was calculated by autocorrelation analysis on time-dependent scattered light intensity. Hydrodynamic radius (R_h) values for micelles formed by the individual detergents were expressed as mean ± SD (n = 4).

Detergent CMC determination by diphenylhexatriene (DPH) encapsulation

5.0 mM new agent (TCGs/TCMs/TCG-Ls) stock solutions were prepared in deionized and distilled water. A series of detergent solutions were prepared with a range of concentrations from the stock solutions. 200 μL of each detergent sample was transferred to a 96-well plate in duplicate. A DPH stock solution was prepared by dissolving 3.0 mg DPH in 5.0 mL THF. 50 μL of the stock solution was added to 950 μL of distilled water to prepare a DPH working solution and then 2.0 μL DPH work solution was added into each well containing a detergent solution for dye encapsulation. After 15 ~ 20 min incubation at room temperature, fluorescence intensities were measured at 430 nm upon excitation at 358 nm using a Synergy Mx Monochromator Based Multi-Mode Microplate reader. Detergent CMC values were determined by plotting florescence intensities as a function of detergent concentrations

Protein stability evaluation

R. capsulatus superassembly stability assay

The superassembly was solubilized and purified according to the reported protocol.[1] Specialized photosynthetic membranes obtained from an engineered strain of *Rhodobacter capsulatus* were used for protein extraction. A 10 mL aliquot of the frozen membranes was completely thawed and then homogenized using a glass tissue homogenizer. The homogenate was incubated with mild agitation at 32 °C for 30 mins. The resulting homogenate was mixed with 1.0 wt% DDM and incubated at 32 °C for an additional 30 mins to allow the complex solubilization. Following ultracentrifugation, the supernatant containing the solubilized LHI-RC complexes was incubated with Ni^{2+}-NTA resins at 4 °C for one hour. The resin-containing solution was filtered using 10 HisSpinTrap columns and the individual columns were washed two times with 500 μL binding buffer containing 10 mM Tris (pH 7.8), 100 mL NaCl and 1×CMC DDM. Buffer containing 1 M imidazole (2×300 μL) was used to elute the DDM-purified LHI-RC complexes. 80 μL of the protein sample was diluted into 920 μL of individual detergent solutions ((TCGs, TCMs, TCG-Ls, DDM and OG) so that the final detergent concentration was CMC+0.05 wt% or CMC+0.2 wt%. The resulting LHI-RC complex in each detergent was first incubated for 10 days at 25 °C, followed by another 10-day incubation at 35 °C. Protein stability was measured at regular intervals during the incubation by measuring the UV-Visible spectra of the samples in the range of 650 nm to 950 nm. Protein integrity was assessed by monitoring 875 nm absorbance (A_{875}).

LeuT stability assay

Purification of the wild type leucine transporter (LeuT) from *Aquifex aeolicus* was performed according to the protocol described previously.[2] LeuT was expressed in *E. coli* C41(DE3) transformed with pET16b encoding C-terminally 8xHis-tagged transporter. After isolation of bacterial membranes, the protein was solubilized by treatment of 1.0 wt% of DDM. The DDM-solubilized protein was bound to Ni^{2+}-NTA resin (Life Technologies, Denmark) and further eluted in 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 identical bufferwithout DDM and imidazole, but supplemented with individual detergents TCGs or TCMs or TCG-Ls or DDM (control). The final detergent concentration was made either CMC + 0.04 wt% or CMC + 0.2 wt%. Protein samples were stored for 13 days at room temperature and, at the indicated time points, were centrifuged and the substrate binding activity of the transporter was determined via scintillation proximity assay (SPA) using [^{3}H]-Leucine.[3] The assay was performed with buffer containing 450 mM NaCl and the respective detergents at the concentrations specified above. The SPA reaction was carried out in the presence of 20 nM [^{3}H]-Leu and 1.25 mg/ml copper chelate (His-Tag) YSi beads (from PerkinElmer,

Denmark). Total [^{3}H]-Leu binding for the respective samples was measured using a MicroBeta liquid scintillation counter (PerkinElmer).

β_2AR stability assay

Soluble radioligand binding assay

The β_2AR in 0.1% DDM was purified based on the protocol as reported before[4] and finally concentrated to around 10 mg/ml (approximately 200 μM).[5] The DDM-purified β_2AR was used to prepare a master binding mixture containing 10 nM [^{3}H] dihydroalprenolol (DHA) supplemented with 0.5 mg/ml BSA, in 0.2% DDM/TCGs/TCMs/TCG-Ls, respectively. The activity of the detergent-purified receptor at 0.2 pmol was monitored at the regular intervals during three-day of incubation at room temperature. The receptor activity was measured by the soluble radioligand binding assay described below. The receptor purified in DDM or individual TCGs/TCMs/TCG-Ls was incubated with 10 nM of [^{3}H]-DHA for 30 min at room temperature. The mixture was loaded on a G-50 column and collected the follow-through with 1 ml binding buffer (20 mM HEPES pH 7.5, 100 mM NaCl, supplemented with 0.5 mg/ml BSA and 20 × CMC individual detergents), and further filled with 15 ml scintillation fluid. Receptor-bound [^{3}H]-DHA was measured with a scintillation counter (Beckman). Non-specific binding of [^{3}H]-DHA was calculated by adding 2 μM alprenolol (Sigma) in the same binding reaction. The binding capacity of [^{3}H]-DHA was measured as column graph. Each experiment was performed in triplicate.

MelB$_{St}$ solubilization assay

The plasmid pK95ΔAHB/WT MelB$_{St}$/CH10) was used to express *Salmonella typhimurium* melibiose permease (MelB$_{st}$) with a 10-His tag at the C-terminus in *E. coli* DW2 cells (Δ*melB* and Δ*lacZY*). Cell growth and membrane preparation were carried out as described in a previous report.[1a] Protein assay was performed with a Micro BCA kit (Thermo Scientific, Rockford, IL). The reported protocol was used to evaluate the trehalose-cored amphiphiles (TCGs, TCMs and TCG-Ls) and DDM for MelB$_{St}$ solubility.[1b] Membrane samples containing MelB$_{St}$ (the final protein concentration was 10 mg/mL) were incubated with a solubilization buffer (20 mM sodium phosphate, pH 7.5, 200 mM NaCl, 10% glycerol, 20 mM melibiose) containing 1.5 % (w/v) DDM or a new agent (TCGs, TCMs or TCG-Ls) at three different temperatures (0, 45 and 55 °C) for 90 min. In order to remove insoluble material, ultracentrifugation was carried out at 355,590 g in a Beckman Optima^{TM} MAX Ultracentrifuge with a TLA-100 rotor for 45 min at 4 °C. The soluble portions were separated by SDS-16% PAGE, followed by immunoblotting with a Penta-His-HRP antibody (Qiagen, Germantown, MD). A membrane fraction containing 20 μg of proteins without treatment was used to present the total MelB$_{St}$; the treated sample was loaded onto each well at equal volume. MelB$_{St}$

was detected using SuperSignal West Pico chemiluminescent substrate by the ImageQuant LAS 4000 Biomolecular Imager (GE Health Care Life Science).

Amphiphiles Synthesis

General procedure for tetra-O-alkylation and followed by benzylidene deprotection

NaH (6.0 equiv.) and 4,6,4′,6′-dibenzylidenated trehalose (**A**)[6] (1 equiv., 550 mg) were dissolved in DMF (15 mL) at 0 °C. Alkyl iodide (6.5 equiv.) was added dropwise, and the resulting solution was stirred at 80 °C for 4 days. After completion of the reaction (as detected by TLC), the solution was diluted with diethyl ether (170 mL) and the washed successively with 1 M aqueous HCl (2 x 20 mL) and brine (150 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation. The residue (~500 mg) was dissolved in a mixture of methanol and DCM (50 mL of a 1:1 mixture) and treated with *p*-toluene sulfonic acid (~50 mg) with stirring for 11 h at room temperature. Upon completion by TLC examination, solvent was evaporated in *vacuo*. The crude product was mixed with dry silica gel powder and further dried under vacuum. The resulting preabsorbed silica gel was loaded to silica column (eluent: DCM/MeOH), by which tetra-ol (**B**) was purified.

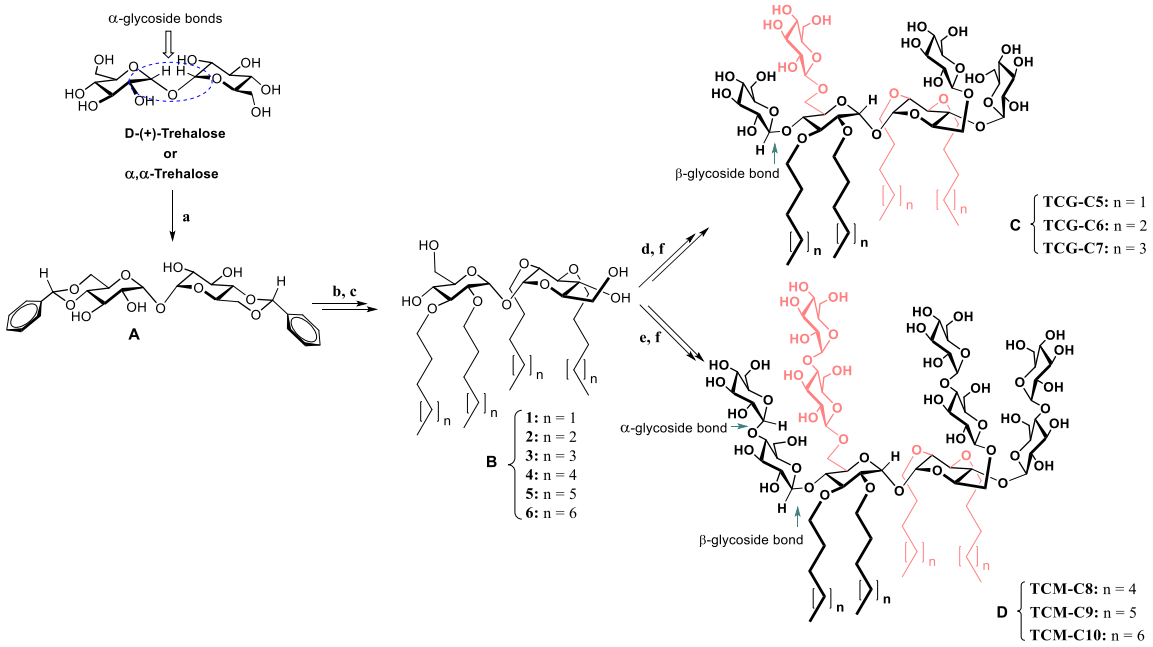
General procedures for β-glycosylation reaction

This procedure followed a literature method[7] with slight modification. A mixture of alcohol (**B** or **E**, 1 equiv.), AgOTf and 2,4,5-collidine (1.1 equiv.) in anhydrous CH_2Cl_2 was stirred at -45 °C. A solution of perbenzoylated glucosylbromide or perbenzoylated maltosylbromide in CH_2Cl_2 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 h. After completion of the reaction, pyridine was added to the reaction mixture, and it was diluted with CH_2Cl_2 before being filtered through celite. The filtrate was washed successively with a 1 M aqueous $Na_2S_2O_3$, a 0.1 M aqueous HCl solution, and brine. The organic layer was dried with anhydrous Na_2SO_4, and the solvent was removed by rotary evaporation. The glossy white solid residue was passed through silica gel bed with ~50% EtOAc/hexane, concentrate and directly taken to the next step without further purification.

General procedures for deprotection reaction

This procedure followed the de-*O*-benzoylation under Zemplén's conditions.[7] The *O*-protected crude glycosylated compound was dissolved in MeOH and treated with the 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 stirred for 12 h at room temperature, and then neutralized with Amberlite IR-120 resin (H^+ form). The resin was removed by filtration and washed with MeOH, and the solvent was removed from the combined filtrate *in vacuo*. The residue was purified by silica gel column chromatography (eluting with MeOH/CH_2Cl_2). Further purification, by recrystallization using CH_2Cl_2/MeOH/diethyl ether, afforded fully deprotected product (**TCGs**, **TCMs** or **TCG-Ls**) as a white solid.

Supplementary scheme S1



(a) $PhCH(OMe)_2$, *p*-TsOH, 88%; (b) alkyl iodide, NaH; (c) *p*-TsOH, MeOH, DCM, room temperature; (d) perbenzoylated glucosylbromide (4.2 equiv.), AgOTf (4.2 equiv.), DCM, -45°C → 0 °C; (e) perbenzoylated malotsylbromide (4.2 equiv.), AgOTf (4.2 equiv.), DCM, -45 °C → 0 °C; (f) NaOMe, MeOH, 12 hr.

Synthesis of 4,6,4′,6′-dibenzylidenated trehalose (compound A) (step a): Compound **A** was prepared in 88% yield according to the literature procedure[6] with slight modification. *p*-Toluenesulfonic acid monohydrate (0.12 g, 0.7 mmol) was dehydrated by rotary evaporation of a suspension in toluene (30 mL). Commercially available *α,α*-trehalose dihydrate (5.00 g, 13.25 mmol) was dried by refluxing in ethanol (30 mL) for 4 h and drying overnight at 60 °C in high vacuum to remove crystalline water molecules. To a suspension of the residual anhydrous trehalose in dried DMF (20 mL) was added a solution of *p*-toluenesulfonic acid (catalytic amount) and (dimethoxymethyl)benzene (2 mL, 13.25 mmol) in dry DMF (20 mL). The mixture was heated at 100 °C for 30 min and concentrated at 50 °C. More (dimethoxymethyl)benzene (2 mL, 13.25 mmol) was added and the heating procedure repeated. A further amount of (dimethoxymethyl)benzene (0.5 mL, 3.3 mmol) was added, and the mixture was heated on a steam bath for 10 min to give a colorless solution. The reaction was quenched by addition of Et_3N (pH > 7) dropwise. Solvents were evaporated on rotary evaporator and the thick glassy liquid was purified by column chromatography to obtain 4,6,4′,6′-dibenzylidenated trehalose (compound **A**) as a white solid; **^{1}H NMR** (400 MHz, $CDCl_3$: CD_3OD = 1:2): δ 7.49-7.34 (m, 5H), 5.56 (s, 1H), 5.16 (d, 1H, *J* = 4.0 Hz), 4.27-4.02 (m, 3H), 3.76-3.65 (m, 2H), 3.50 (t, 1H, *J* = 8.0 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 138.2, 129.7, 128.8, 127.0, 102.6, 95.6, 82.3, 73.2, 71.0, 69.6, 63.7.

Compound **1** was prepared using 1-iodopentane in 81% yield (two steps) according to the general procedure for tetra-*O*-alkylation and followed by benzylidene deprotection. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.16 (d,

1H, *J* = 4.0 Hz), 3.99-3.27 (m, 10H), 2.81 (s, 1H), 2.26 (app. t, *J* = 4.0 Hz, 1H), 1.62-1.53 (m, 4H), 1.35-1.25 (m, 8H), 0.87 (app. t, *J* = 4.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.8, 80.9, 80.5, 73.6, 71.4 (2C), 70.2, 62.3, 30.3, 30.0, 28.5, 28.4, 22.8 (2C), 14.3, 14.2; **HRMS (FAB)**: calcd. for $C_{32}H_{62}O_{11}Na^+$ $[M+Na]^+$ 645.4190, found 645.4187.

Compound **2** was prepared using 1-iodohexane in 80% yield (two steps) according to the general procedure for tetra-*O*-alkylation and followed by benzylidene deprotection. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.16 (d, 1H, *J* = 4.0 Hz), 3.98-3.27 (m, 10H), 3.01 (s, 1H), 2.51 (app. t, *J* = 4.0 Hz, 1H), 1.62-1.50 (m, 4H), 1.35-1.24 (m, 12H), 0.87 (app. t, *J* = 4.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.8, 80.9, 80.4, 73.6, 71.5, 71.4, 70.0, 62.1, 31.9 (2C), 30.6, 30.3, 25.9, 22.8 (2C), 14.2; **HRMS (FAB)**: calcd. for $C_{36}H_{70}O_{11}Na^+$ $[M+Na]^+$ 701.4816, found 701.4814.

Compound **3** was prepared using 1-iodoheptane in 79% d yield (two steps) according to the general procedure for tetra-*O*-alkylation and followed by benzylidene deprotection. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.16 (d, 1H, *J* = 4.0 Hz), 3.92-3.27 (m, 10H), 2.94 (s, 1H), 2.43 (br s, 1H), 1.60-1.52 (m, 4H), 1.33-1.28 (m, 16H), 0.88 (app. t, *J* = 4.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.9, 80.9, 80.5, 73.7, 71.5, 71.4, 70.1, 62.2, 32.1, 32.0, 30.7, 30.3, 25.9, 29.4, 26.3 (2C), 22.8, 14.3; **HRMS (FAB)**: calcd. for $C_{40}H_{78}O_{11}Na^+$ $[M+Na]^+$ 757.5442, found 757.5445.

Compound **4** was prepared using 1-iodooctane in 78% yield (two steps) according to the general procedure for tetra-*O*-alkylation and followed by benzylidene deprotection. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.16 (d, 1H, *J* = 4.0 Hz), 4.00-3.28 (m, 10H), 2.61 (s, 1H), 2.02 (app. t, *J* = 2.0 Hz, 1H), 1.60-1.53 (m, 4H), 1.33-1.28 (m, 20H), 0.88 (app. t, *J* = 4.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.9, 80.9, 80.5, 73.6, 71.4 (2C), 70.4, 62.5, 32.1, 30.7, 30.3, 29.8, 29.7, 29.6, 29.5 (2C), 26.4, 26.3, 22.9, 14.3; **HRMS (FAB)**: calcd. for $C_{44}H_{86}O_{11}Na^+$ $[M+Na]^+$ 813.6068, found 813.6066.

Compound **5** was prepared using 1-iodononane in 79% yield (two steps) according to the general procedure for tetra-*O*-alkylation and followed by benzylidene deprotection. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.16 (d, 1H, *J* = 4.0 Hz), 3.97-3.27 (m, 10H), 2.58 (s, 1H), 2.41 (br s, 1H), 1.60-1.52 (m, 4H), 1.33-1.26 (m, 24H), 0.88 (app. t, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.8, 80.9, 80.4, 73.7, 71.6, 71.4, 70.0, 62.0, 32.1, 32.0, 30.6, 30.3, 29.8 (3C), 29.5, 26.3, 22.9, 14.3; **HRMS (FAB)**: calcd. for $C_{48}H_{94}O_{11}Na^+$ $[M+Na]^+$ 869.6694, found 869.6690.

Compound **6** was prepared using 1-iododecane in 78% yield (two steps) according to the general procedure for tetra-*O*-alkylation and followed by benzylidene deprotection. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.16 (d, 1H, *J* = 4.0 Hz), 3.97-3.26 (m, 10H), 2.56 (s, 1H), 2.41 (br s, 1H), 1.60-1.50 (m, 4H), 1.33-1.26 (m, 28H), 0.88 (app. t, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.8, 80.9, 80.4, 73.7, 71.6, 71.4, 69.9, 62.0, 32.1, 30.7, 30.3, 29.9 (2C), 29.8 (2C), 29.6, 26.3, 22.9, 14.3 **HRMS (FAB)**: calcd. for $C_{52}H_{102}O_{11}Na^+$ $[M+Na]^+$ 925.7320, found 925.7321.

TCG-C5 was prepared from compound **1** in 75% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reactions. **^{1}H NMR** (400MHz, CD_3OD): δ 5.18 (d, *J* =4.0 Hz, 2H), 4.64 (d, *J* = 8.0 Hz, 2H), 4.34 (d, *J* = 8.0 Hz, 2H), 4.15-3.84 (m, 14H), 3.70-3.10 (m, 33H), 1.65-1.57 (m, 8H), 1.37-1.31 (m, 17H), 0.94-0.92 (m, 12H); **^{13}C NMR** (100MHz, CD_3OD): δ 104.5, 103.5, 94.9, 81.6, 81.0, 78.3, 78.0, 77.0, 75.7, 75.2, 75.0, 73.0, 72.4, 71.9, 71.6, 68.2, 63.7, 62.8, 31.1, 31.0, 29.6, 29.5, 23.9, 23.8, 14.7 (2C); **HRMS (EI)**: calcd. for $C_{56}H_{102}O_{31}Na^+$ $[M+Na]^+$ 1293.6303, found 1293.6300.

TCG-C6 was prepared from compound **2** in 75% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reactions. **^{1}H NMR** (400MHz, CD_3OD): δ 5.18 (d, *J* =4.0 Hz, 2H), 4.64 (d, *J* = 8.0 Hz, 2H), 4.34 (d, *J* = 8.0 Hz, 2H), 4.15-3.84 (m, 14H), 3.70-3.10 (m, 33H), 1.64-1.55 (m, 8H), 1.40-1.31 (m, 24H), 0.94-0.92 (m, 12H); **^{13}C NMR** (100MHz, CD_3OD): δ 104.5, 103.5, 94.8, 81.6, 81.0, 78.4, 78.1, 77.1, 75.8, 75.2, 75.1, 73.0, 72.5, 71.9, 71.6, 68.2, 63.7, 62.8, 33.2, 33.1, 31.4, 31.3, 27.1, 27.0, 23.9, 14.6 (2C); **HRMS (EI)**: calcd. for $C_{60}H_{110}O_{31}Na^+$ $[M+Na]^+$ 1349.6929, found 1349.6935.

TCG-C7 was prepared from compound **3** in 74% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reactions. **^{1}H NMR** (400MHz, CD_3OD): δ 5.18 (d, *J* =4.0 Hz, 2H), 4.64 (d, *J* = 8.0 Hz, 2H), 4.34 (d, *J* = 8.0 Hz, 2H), 4.15-3.84 (m, 17H), 3.67-3.10 (m, 36H), 1.64-1.55 (m, 9H), 1.34-1.31 (m, 36H), 0.93-0.89 (m, 12H); **^{13}C NMR** (100MHz, CD_3OD): δ 104.5, 103.6, 94.8, 81.6, 81.0, 78.4, 78.2, 78.1, 78.0, 77.1, 75.8, 75.2, 75.1, 72.9, 72.4, 71.9, 71.6, 68.2, 63.7, 62.9, 33.3 (2C), 31.4, 30.7, 30.5, 27.4, 27.3, 23.9, 14.7 (2C); **HRMS (EI)**: calcd. for $C_{64}H_{118}O_{31}Na^+$ $[M+Na]^+$ 1405.7555, found 1405.7560.

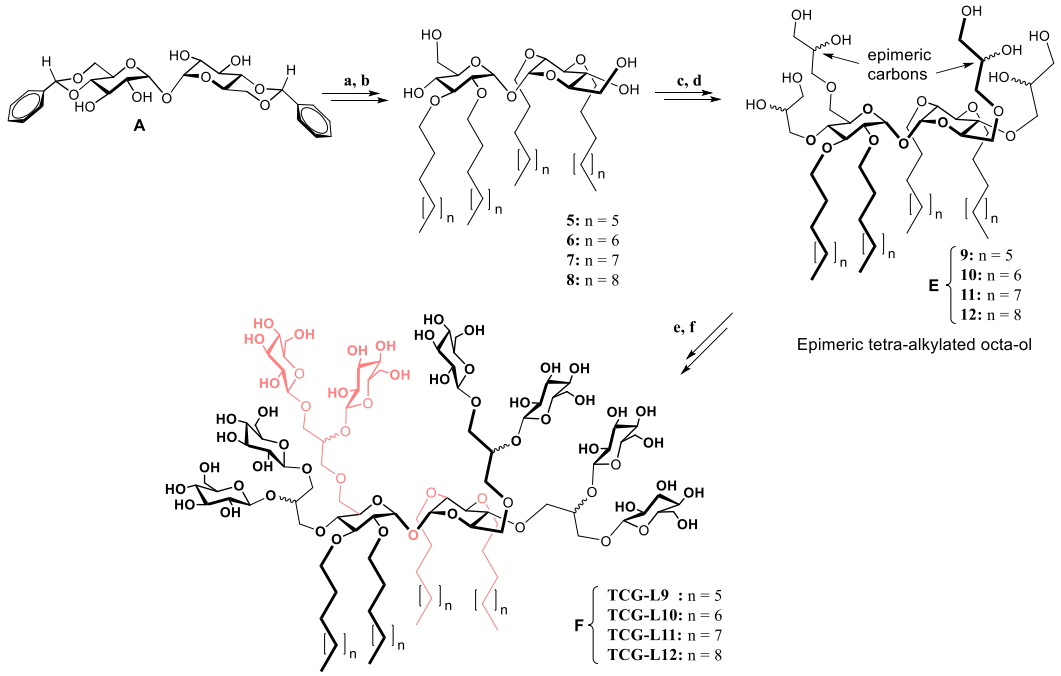
TCM-C8 was prepared from compound **4** in 80% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reactions. **^{1}H NMR** (400MHz, DMSO-d6): δ 5.58-5.26 (m, 10H), 5.04-4.90 (m, 12H), 4.61-4.53 (m, 7H), 4.18-3.03 (m, 51H), 1.50-1.43 (m, 7H), 1.40-1.10 (m, 36H), 0.87-0.84 (m, 12H); **^{13}C NMR** (100MHz, DMSO-d6): δ 102.9, 101.2, 100.6, 80.3, 76.4, 75.2, 73.5, 73.3, 72.5, 70.3, 69.9, 60.8, 31.4, 29.8, 29.6, 29.3, 29.2, 29.1, 29.0, 28.8, 25.8, 25.6, 22.1, 14.0; **MS (MALDI-TOF)**: calcd. for $C_{92}H_{166}O_{51}Na^+$ $[M+Na]^+$ 2110.0294, found 2110.5188.

TCM-C9 was prepared from compound **5** in 81% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reactions. **^{1}H NMR** (400MHz, DMSO-d6): δ 5.57-5.22 (m, 10H), 5.03-4.89 (m, 13H), 4.57-4.51 (m, 7H), 4.20-3.05 (m, 46H), 1.48-1.42 (m, 7H), 1.40-1.19 (m, 44H), 0.86-0.83 (m, 12H); **^{13}C NMR** (100MHz, DMSO-d6): δ 102.9, 101.2, 100.6, 80.4, 76.5, 75.2, 73.5, 73.3, 72.5, 70.2, 69.9, 60.8, 31.4, 29.8, 29.6, 29.3, 29.2 (2C), 29.1, 29.0, 28.8, 25.8, 25.7, 22.2, 14.2; **MS (MALDI-TOF)**: calcd. for $C_{96}H_{174}O_{51}Na^+$ $[M+Na]^+$ 2167.0953, found 2167.5685.

TCM-C10 was prepared from compound **6** in 75% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reactions. **^{1}H NMR** (400MHz, DMSO-d6): δ 5.54-5.26 (m, 10H), 5.04-4.89 (m, 14H), 4.62-4.52 (m, 8H), 4.20-2.98 (m, 65H), 1.48-1.42 (m, 7H), 1.40-1.19 (m, 53H), 0.87-0.84 (m, 12H); **^{13}C NMR** (100MHz, DMSO-d6): δ 102.9, 101.2, 100.6, 80.4, 76.4, 75.2, 73.4, 73.3, 72.5,

70.2, 69.9, 60.7, 31.4, 29.8, 29.6, 29.3, 29.2 (2C), 29.1, 29.0, 28.7, 25.8, 25.7, 25.6, 22.2, 14.1; **MS (MALDI-TOF)**: calcd. for $C_{100}H_{182}O_{51}Na^+$ $[M+Na]^+$ 2223.1579, found 2223.1655.

Supplementary scheme S2



(a) alkyl iodide, NaH; (b) *p*-TsOH, MeOH, DCM, room temperature, 11 hr; (c) allyl iodide, NaH; (d) OsO_4, NMO, THF, H_2O, 0 °C → room temperature, 24 h; (e) perbenzoylated glucosylbromide (8.4 equiv.), AgOTf (8.4 equiv.), DCM, -45 °C → 0 °C; (f) NaOMe, MeOH, 12 hr.

Compounds **7** and **8** were prepared according to the general procedure for tetra-*O*-alkylation and followed by benzylidene deprotection.

Compound **7** was prepared using 1-iodoundecane in 78% yield (two steps). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.14 (d, 1H, *J* = 4.0 Hz), 3.96-3.26 (m, 10H), 2.56 (s, 1H), 2.41 (br s, 1H), 1.58-1.50 (m, 4H), 1.33-1.26 (m, 32H), 0.86 (app. t, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.9, 80.9, 80.5, 73.7, 71.5, 71.3, 70.1, 62.2, 32.1, 30.7, 30.3, 29.9 (2C), 29.8, 29.6, 26.4, 26.3, 22.9, 14.3; **HRMS (FAB)**: calcd. for $C_{56}H_{110}O_{11}Na^+$ $[M+Na]^+$ 981.7946, found 981.7951.

Compound **8** was prepared using 1-iodododecane in 80% yield (two steps). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.16 (d, 1H, *J* = 4.0 Hz), 3.97-3.26 (m, 10H), 2.56 (s, 1H), 2.41 (br s, 1H), 1.59-1.52 (m, 4H), 1.33-1.26 (m, 36H), 0.88 (app. t, *J* = 8.0 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 93.9, 80.9, 80.5, 73.6, 71.4, 70.2, 62.3, 32.1, 30.7, 30.3, 29.9 (2C), 29.8 (2C), 29.6, 26.4, 26.3, 22.9, 14.3; **HRMS (FAB)**: calcd. for $C_{60}H_{118}O_{11}Na^+$ $[M+Na]^+$ 1037.8572, found 1037.8566.

Preparation of compound E (step c & d in supplementary scheme 2): To a solution of **5**, **6**, **7** or **8** (1 g, 1.0 equiv.) in dry tetrahydrofuran (THF, 20 mL), NaH (60% in mineral oil, 5.0 equiv.) at 0 °C was added. The mixture was slowly warmed to room temperature and stirred for 1 h, and then, allyl iodide was added (5.0 equiv.). After overnight reaction, saturated NH_4Cl solution was added. The organic phase was extracted with EtOAc, washed with brine, and dried over Na_2SO_4. After filtration and removal of solvent in vacuo, the residue was passed through silica gel bed with ~20% EtOAc/hexane, concentrate to dryness and directly taken to the next step without further purification. Separately, a solution of NMO (5.0 equiv.) in water (50 wt%) was added to a mixture of THF and water (15 mL of a 9:1 mixture) at 0 °C. The crude reaction mixture (~500 mg, 1 equiv.) was then added in one portion, the mixture allowed to stir for 15 minutes and then OsO_4 (1.4 mL of a 2.5 wt% solution in ^{t}BuOH) was added dropwise by syringe over 20 minutes. The mixture was stirred at room temperature for 24 h. The reaction was quenched by the addition of sodium sulfite (8 g) and diluted with water (30 mL). The solution was then extracted with EtOAc (2 × 70 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo and the residue was purified by silica gel column chromatography (EtOAc/hexane) providing a desired octa-ol (**E**) as an orange gum.

Compound **9** was prepared from compound **5** in 89% yield (two steps) (*i.e.* allylation followed by dihydroxylation). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.10 (broad s, 2H), 4.07 (broad s, 10H), 3.85-3.31 (m, 42H), 1.62-1.27 (m, 56H), 0.88 (t, *J* = 8.0 Hz, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 94.2, 81.2, 81.1, 81.1, 80.6, 74.1, 73.9, 73.0, 72.3, 71.8, 71.8, 71.5, 71.3, 71.0, 70.9, 70.6, 69.8, 69.7, 64.1, 63.3, 63.0, 53.7, 32.1, 30.7, 30.6, 30.4, 29.8, 26.2, 22.7, 14.1; **HRMS (FAB)**: calcd. for $C_{60}H_{118}O_{19}Na^+$ $[M+Na]^+$ 1165.8165, found 1165.8169.

Compound **10** was prepared from compound **6** in 91% yield (two steps) (*i.e.* allylation followed by dihydroxylation). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.11 (broad s, 2H), 4.13 (broad s, 10H), 3.85-3.29 (m, 42H), 1.62-1.27 (m, 64H), 0.87 (t, *J* = 8.0 Hz, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 94.1, 81.3, 81.1, 81.1, 80.7, 74.1, 73.9, 73.0, 72.3, 71.9, 71.8, 71.5, 71.3, 71.0, 70.9, 70.6, 69.8, 69.7, 64.1, 63.3, 63.0, 53.7, 32.1, 30.7, 30.6, 30.4, 29.9, 29.8, 26.2, 22.8, 14.1; **HRMS (FAB)**: calcd. for $C_{64}H_{126}O_{19}Na^+$ $[M+Na]^+$ 1221.8791, found 1221.8797.

Compound **11** was prepared from compound **7** in 89% yield (two steps) (*i.e.* allylation followed by dihydroxylation). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.10 (broad s, 2H), 4.08 (broad s, 10H), 3.84-3.29 (m, 42H), 1.62-1.27 (m, 72H), 0.88 (t, *J* = 8.0 Hz, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 94.1, 81.3, 81.2, 81.1, 80.7, 74.0, 73.9, 73.0, 72.3, 71.9, 71.8, 71.5, 71.3, 71.0, 70.9, 70.6, 69.8, 69.7, 64.1, 63.3, 63.0, 53.7, 32.1, 30.7, 30.6, 30.4, 29.9 (2C), 29.8, 26.3, 22.8, 14.2; **HRMS (FAB)**: calcd. for $C_{68}H_{134}O_{19}Na^+$ $[M+Na]^+$ 1277.9417, found 1277.9420.

Compound **12** was prepared from compound **8** in 90% yield (two steps) (*i.e.* allylation followed by dihydroxylation). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.11 (broad s, 2H), 4.14 (broad s, 10H), 3.84-3.29 (m, 42H), 1.63-1.27 (m, 80H), 0.88 (t, *J* = 8.0 Hz, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 94.2, 81.3, 81.2, 81.1, 80.8, 74.0, 73.9, 73.0, 72.3, 71.9, 71.8, 71.5, 71.3, 71.0, 70.9, 70.6, 69.8, 69.7, 64.1, 63.3, 63.0, 53.8, 32.1,

30.7, 30.6, 30.4, 29.9 (2C), 29.8, 26.4, 26.3, 22.8, 14.2; **HRMS (FAB)**: calcd. for $C_{72}H_{142}O_{19}Na^+$ $[M+Na]^+$ 1334.0043, found 1334.0049.

TCG-L9 was prepared from compound **9** in 78% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reaction. **^{1}H NMR** (400MHz, CD_3OD): δ 5.18 (broad s, 2H), 4.61-4.38 (m, 8H), 4.07-3.21 (m, 60H), 1.62-1.32 (m, 56H), 0.92-0.89 (m, 12H); **^{13}C NMR** (100MHz, CD_3OD): δ 104.8, 104.6, 104.5, 104.4, 104.2, 82.6, 81.5, 79.2, 78.9, 78.4, 78.0, 75.4, 75.2, 75.0, 74.7, 72.9, 72.8, 72.3, 72.1, 71.6 (2C), 62.9, 62.8, 33.3, 33.2, 31.9, 31.4, 31.0 (2C), 30.9, 30.7, 27.6, 27.5, 23.9, 14.7 (2C); **MS (MALDI-TOF)**: calcd. for $C_{108}H_{198}O_{59}Na^+$ $[M+Na]^+$ 2463.2424, found 2463.1799.

TCG-L10 was prepared from compound **10** in 75% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reaction. **^{1}H NMR** (400MHz, CD_3OD): δ 5.18 (broad s, 2H), 4.62-4.39 (m, 8H), 4.07-3.21 (m, 60H), 1.62-1.31 (m, 60H), 0.92-0.89 (m, 12H); **^{13}C NMR** (100MHz, CD_3OD): δ 104.8 (2C), 104.6, 104.5, 104.2, 82.9, 82.6, 81.5, 79.4, 79.2, 78.9, 78.4, 78.0, 75.4, 75.2, 75.0, 74.7, 72.9, 72.8, 72.3, 72.1, 71.6 (2C), 62.9, 62.8, 33.3, 33.2, 31.4, 31.1, 31.0 (2C), 30.7, 27.6, 27.5, 23.9, 14.7 (2C); **MS (MALDI-TOF)**: calcd. for $C_{112}H_{206}O_{59}Na^+$ $[M+Na]^+$ 2519.3050, found 2519.2441.

TCG-L11 was prepared from compound **11** in 76% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reaction. **^{1}H NMR** (400MHz, CD_3OD): δ 5.18 (broad s, 2H), 4.61-4.37 (m, 8H), 4.14-3.20 (m, 60H), 1.63-1.30 (m, 72H), 0.92-0.89 (m, 12H); **^{13}C NMR** (100MHz, CD_3OD): δ 104.9 (2C), 104.7, 104.6, 104.5, 104.3, 104.1, 82.7, 81.5, 78.9, 78.1, 75.5, 75.2, 75.1, 74.7, 72.9, 72.5, 72.4, 72.2, 71.7 (2C), 71.6, 71.0, 70.4, 63.0, 62.8, 33.3 (2C), 32.0, 31.5, 31.2, 31.1, 31.0 (2C), 30.8, 30.7, 27.7, 27.0, 24.0; **MS (MALDI-TOF)**: calcd. for $C_{116}H_{214}O_{59}Na^+$ $[M+Na]^+$ 2575.3676, found 2575.3853.

TCG-L12 was prepared from compound **12** in 72% yield (two steps) according to the general procedure for β-glycosylation followed by deprotection reaction. **^{1}H NMR** (400MHz, CD_3OD): δ 5.18 (broad s, 2H), 4.59-4.38 (m, 8H), 4.07-3.26 (m, 60H), 1.63-1.30 (m, 80H), 0.92-0.89 (m, 12H); **^{13}C NMR** (100MHz, CD_3OD): δ 104.9, 104.6, 104.5, 104.2, 104.1, 94.0, 82.6, 81.4, 79.4, 78.9, 78.5, 78.0, 75.4, 75.2, 75.0, 74.7, 72.9, 72.7, 72.3, 71.6, 70.5, 62.9, 62.8, 33.3, 33.2, 31.9, 31.5, 31.2, 31.1, 31.0, 30.7, 27.6, 23.9, 14.7; **MS (MALDI-TOF)**: calcd. for $C_{120}H_{222}O_{59}Na^+$ $[M+Na]^+$ 2631.4302, found 2631.3655.

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