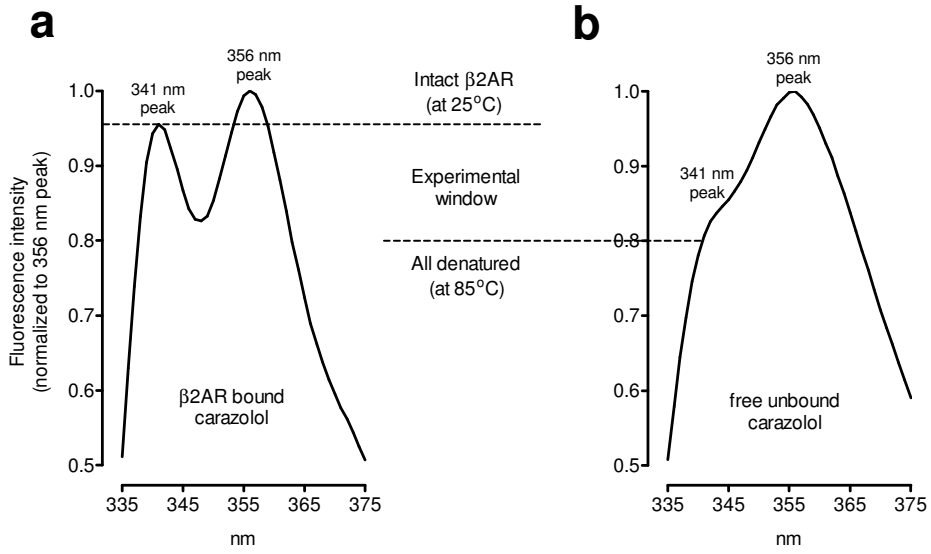
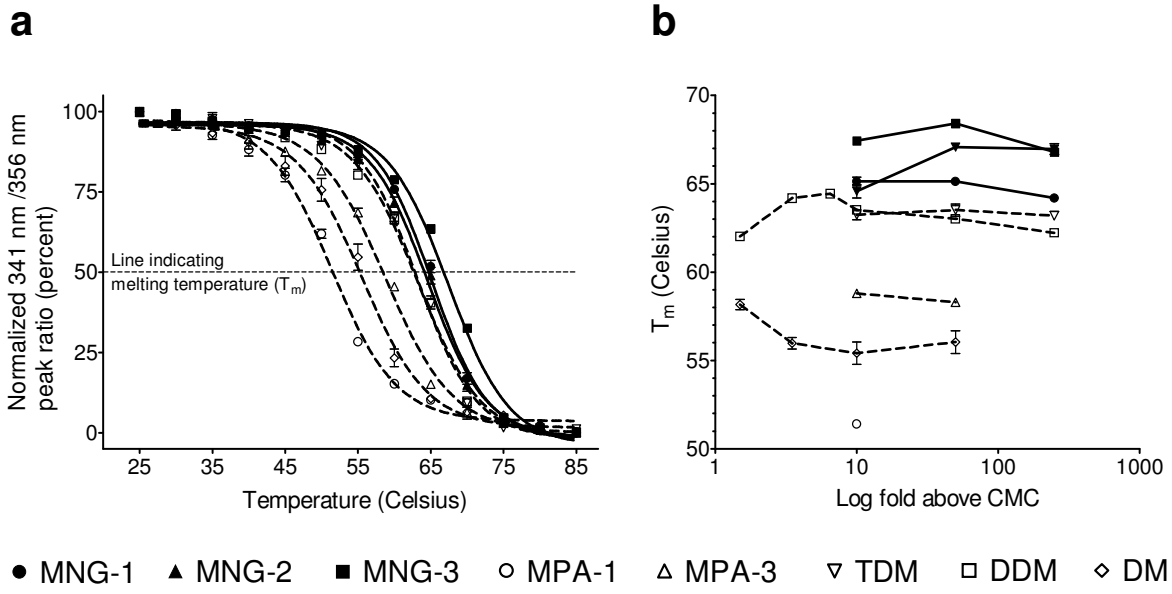
Supplementary Figure 1 Emission spectra of carazolol bound to β_2AR-T4L.



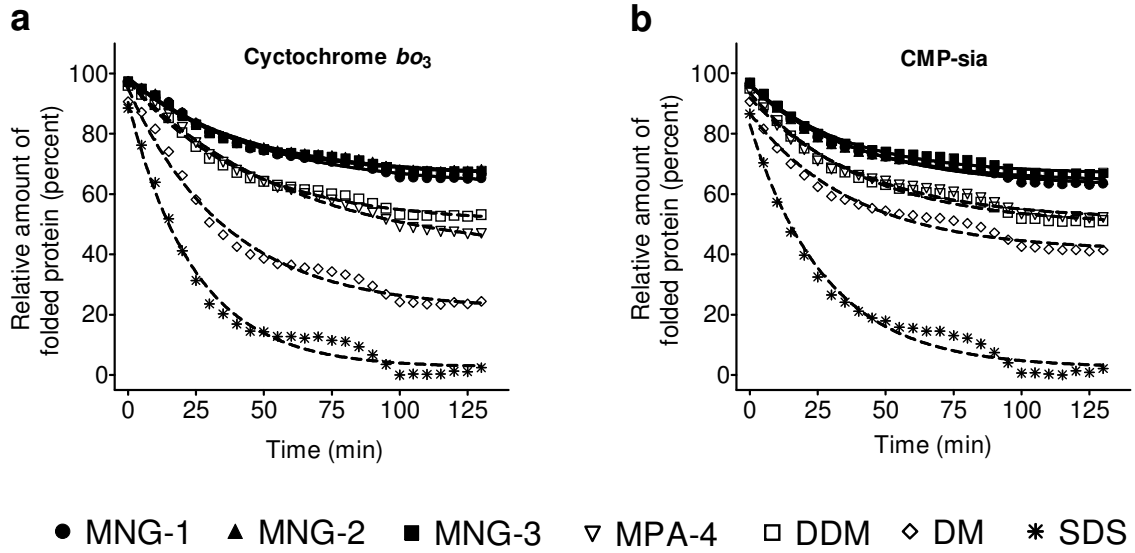
(**a**) Emission spectra of bound carazolol to the β_2AR-T4L and (**b**) spectra of free carazolol in solution following complete receptor denaturation. Thirteen continuous emission spectra were obtained following 5 min incubations at temperatures ranging from 25 to 85 °C in 5 °C intervals. The 356 nm peaks were all normalized and the height of the 341 nm peaks (indicated by the dotted lines) were plotted as a function of temperature and normalized as illustrated in **Supplementary figure 2a**.

Supplementary Figure 2 Melting temperatures (T_m) of the β_2AR-T4L in MNG ampihphiles or conventional detergents.



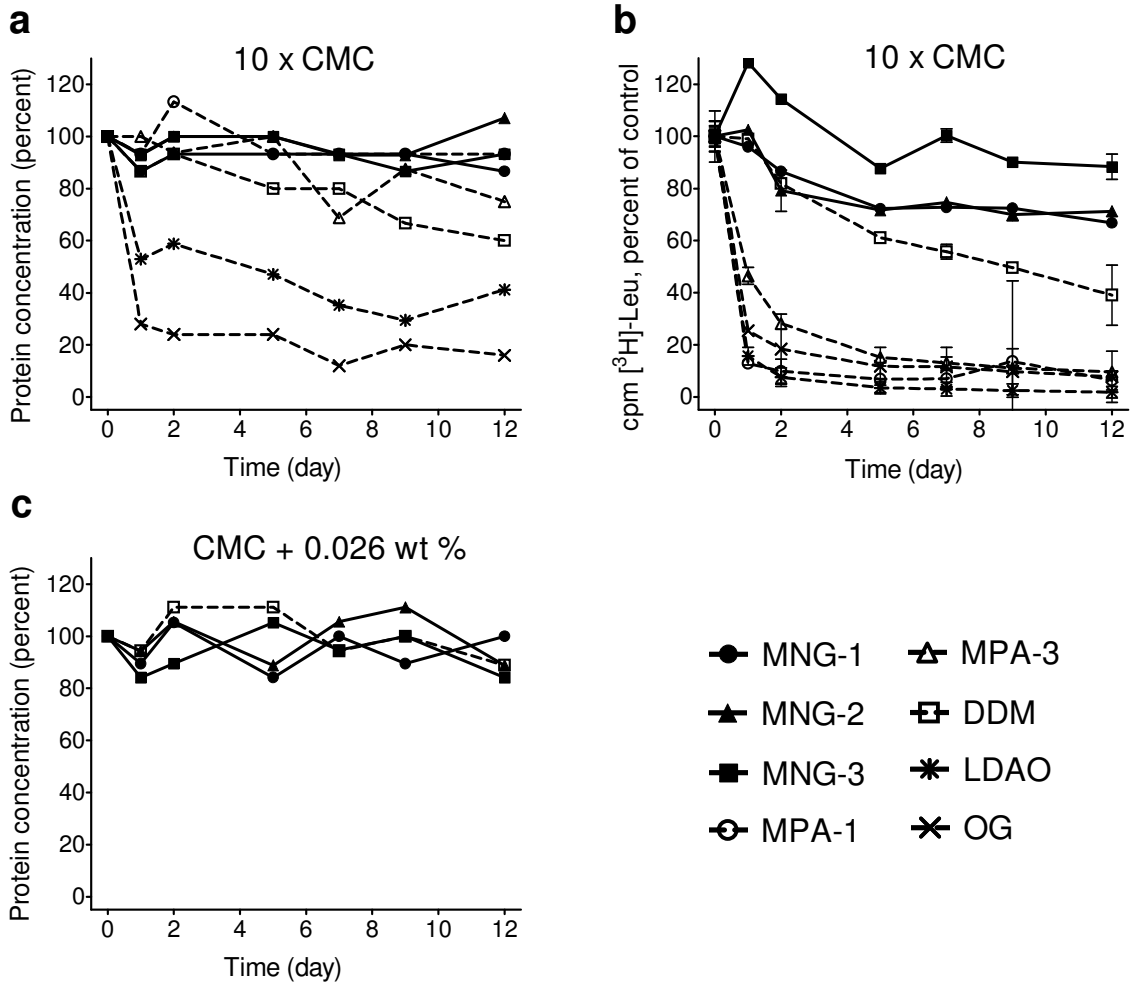
(**a**) Temperature dependence of fluorescence peak ratio (341 nm/356 nm) of β_2AR-T4L in the presence of detergents or amphiphiles at 10 × CMC. (**b**) T_m values of the receptor were plotted in terms of CMC of the MNG amphiphiles (MNG-1, MNG-2, and MNG-3) or conventional detergents (MPA-1, MPA-3, DM, DDM, and TDM). β_2AR-T4L with bound carazolol (an inverse agonist) was incubated with various agents at the various concentrations at indicated temperatures for 5 min prior to fluorescence emission measurement as described in the Online Methods and in **Supplementary Figure 1**. Normalized results are expressed as mean ± s.e.m. (n = 3, 4, or 5).

Supplementary Figure 3 Thermal stability of Cytochrome bo_3 and CMP-Sia in MNG amphiphiles or conventional detergents using CPM assay.



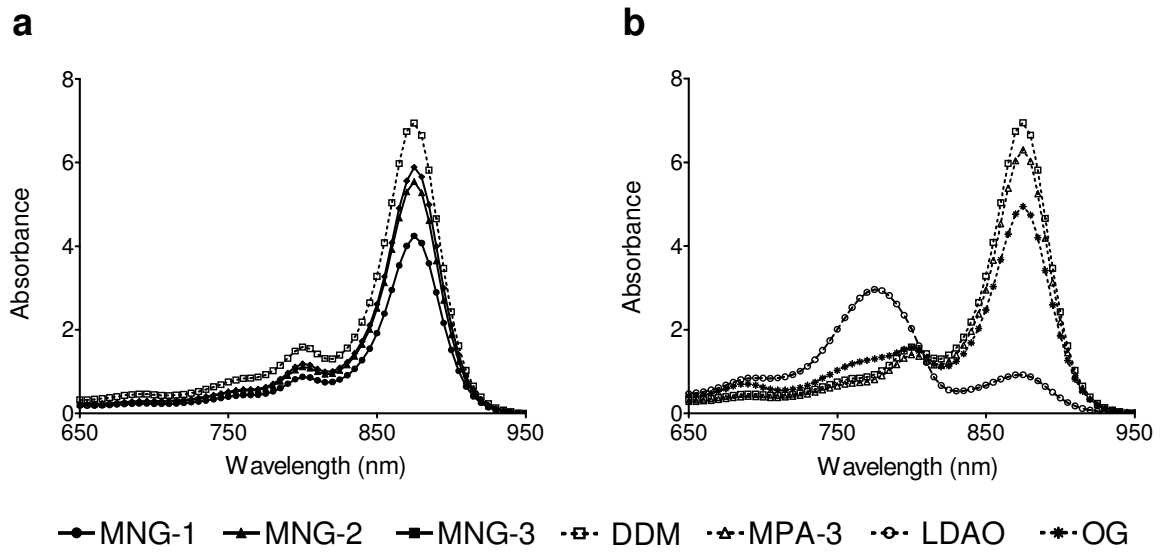
CPM assays for (**a**) Cytochrome bo_3, and (**b**) CMP-Sia with MNG amphiphiles (MNG-1, MNG-2, and MNG-3) or conventional detergents (MPA-4, DDM, DM and SDS). All agents were used at 10 × CMC. The unfolding of the each protein in various amphiphiles was monitored at 40 °C for 130 min using a microplate spectrofluorometer set at an excitation wavelength of 387 nm and an emission wavelength of 463 nm. Measurements were taken every 5 min after automatic agitation of the plate.

Supplementary Figure 4 Long-term solubility and activity of LeuT in MNG amphiphiles or conventional detergents.



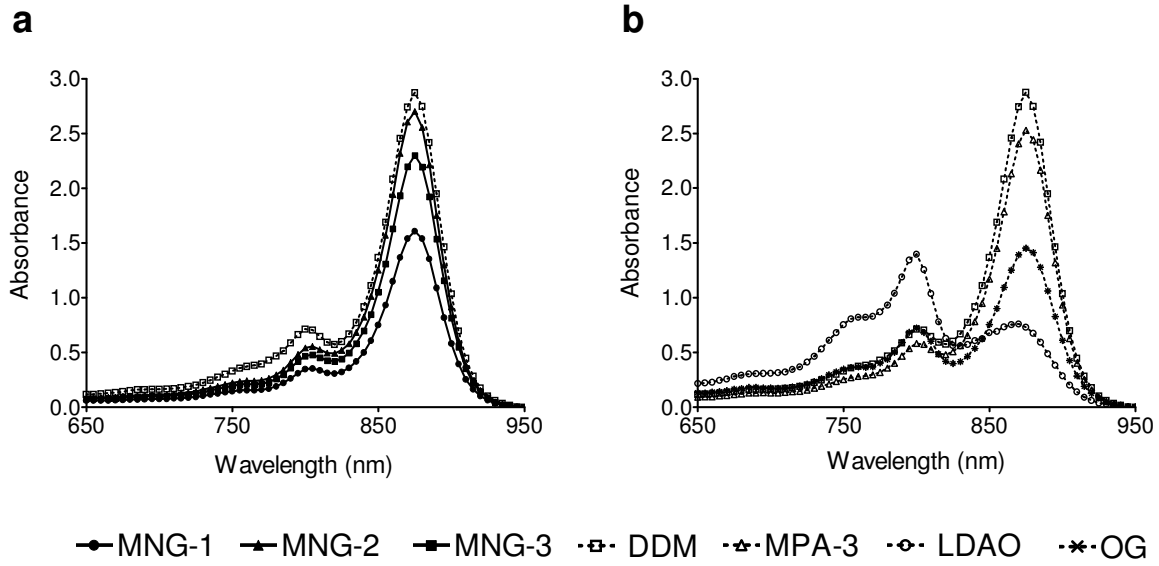
Long-term (**a**) solubility and (**b**) activity ([^{3}H]-Leu binding) assay for LeuT solubilized with MNG amphiphiles (MNG-1, MNG-2, and MNG-3) and conventional detergents (MPA-1, MPA-3, DDM, laurydimethylamine-N-oxide (LDAO) and *n*-octyl-β-D-glucopyranoside (OG)) at 10 × CMC except OG, which was tested at 2 × CMC. (**c**) LeuT solubility in MNG amphiphiles or DDM at 0.026 wt % above each CMC. LeuT concentrations and activities were monitored at indicated time points for protein stored at the room temperature. Protein concentration was measured by UV-visible spectroscopy and activity was evaluated using a scintillation proximity assay (SPA). Results are expressed as % concentration or % activity relative to the appropriate day 0 measurement. Normalized results are expressed as mean ± s.e.m. (n = 2).

Supplementary Figure 5 Absorption spectra of LHI-RC complex solubilized with MNG amphiphiles or conventional detergents.



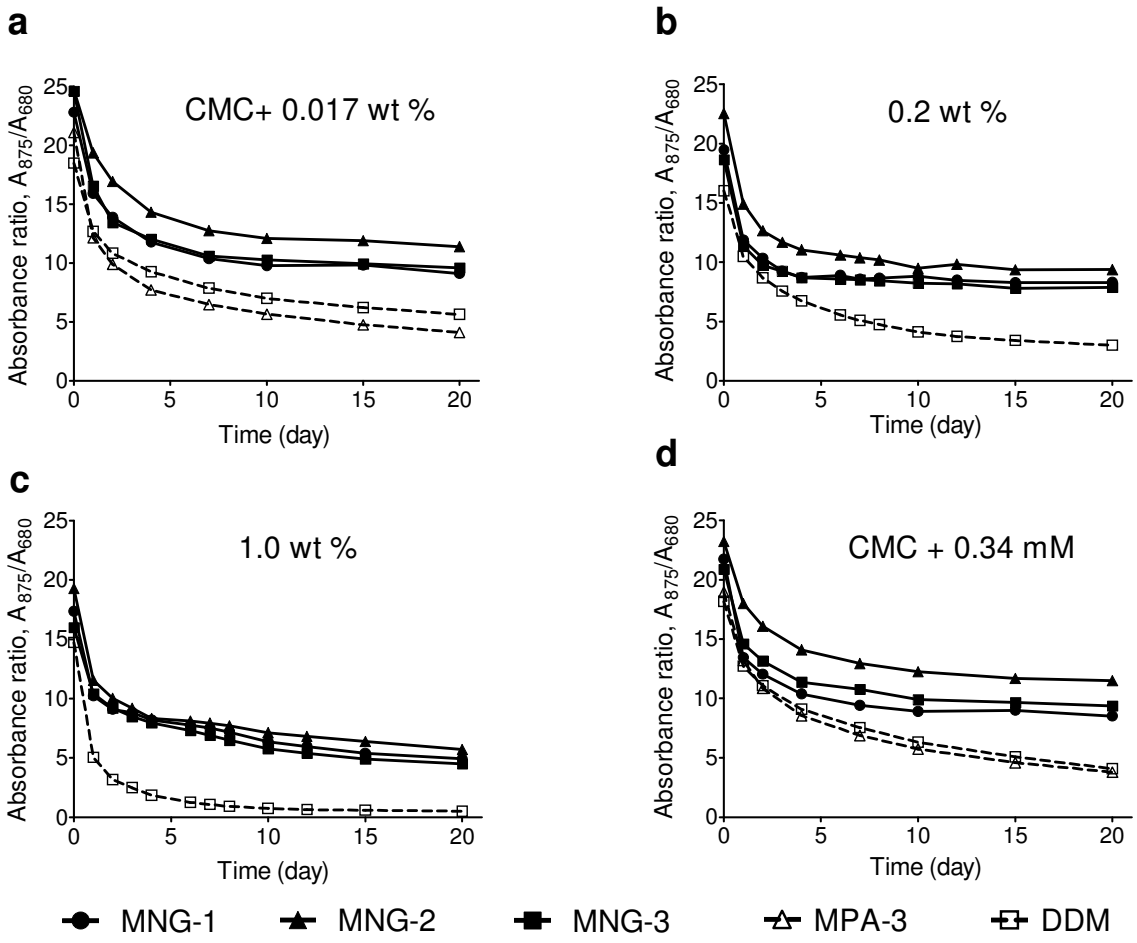
Spectroscopic comparison of LHI-RC complex from *Rhodobacter Capsulatus* solubilized with (**a**) MNG amphiphiles (MNG-1, MNG-2, and MNG-3) and (**b**) conventional detergents (MPA-3, DDM, laurydimethylamine-N-oxide (LDAO), and *n*-octyl-β-D-glucopyranoside (OG)). All amphiphiles or detergents were used at 1.0 wt % except OG, which was tested at 2.0 wt %.

Supplementary Figure 6 Absorption spectra of LHI-RC complex purified with MNG amphiphiles or conventional detergents.



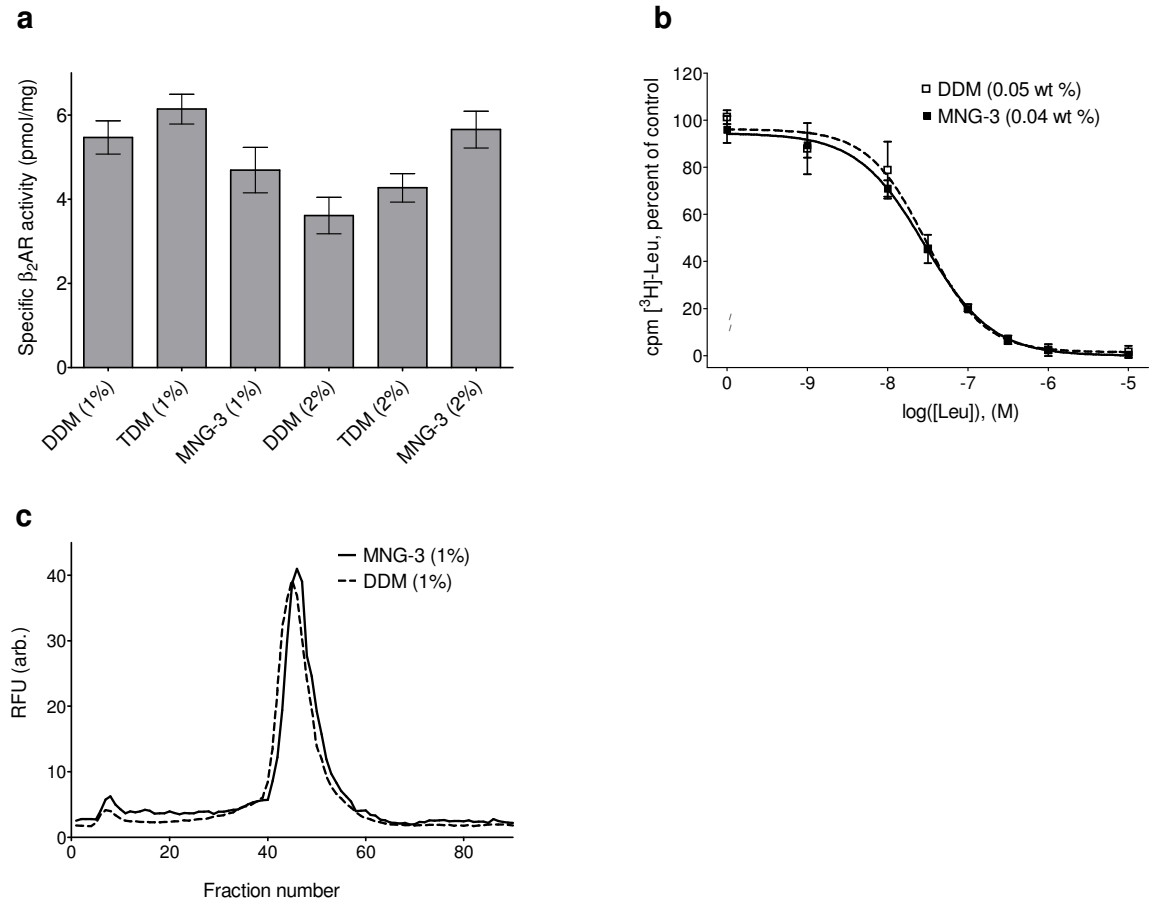
Spectroscopic comparison of LHI-RC complex from *Rhodobacter Capsulatus* purified with (**a**) MNG amphiphiles (MNG-1, MNG-2, and MNG-3) and (**b**) conventional detergents (MPA-3, DDM, LDAO, and OG). The complex was purified with the amphiphiles or detergents at 1 × CMC at room temperature.

Supplementary Figure 7 Long-term stability of LHI-RC complex in MNG amphiphiles or conventional detergents.



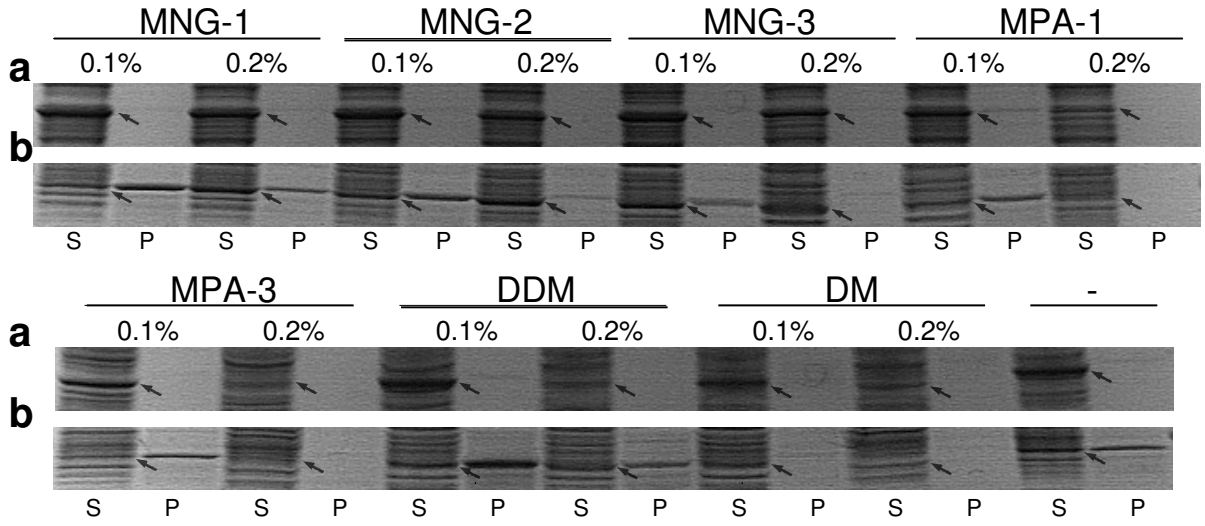
All agents were tested at (**a**) CMC + 0.017 wt %, (**b**) 0.2 wt %, (**c**) 1.0 wt % and (**d**) CMC + 0.34 mM. The absorption ratios (A_{875}/A_{680}) of the protein samples were followed as a function of time at room temperature.

Supplementary Figure 8 Biochemical characterization of membrane proteins extracted with amphiphilic agents from the native membranes.



(**a**) Activity of wild-type β_2AR extracted with MNG-3, DDM, or TDM at 1% or 2% from an insect cell membrane. Results are expressed as mean ± s.d. (n = 3). (**b**) Competition [^{3}H]-Leu/Leu binding curves for LeuT extracted and purified with MNG-3 and DDM from a bacterial membrane. Normalized results are expressed as mean ± s.e.m. (n = 2). (**c**) Fluorescent size exclusion chromatography (FSEC) analysis of CMP-Sia-GFP fusion protein after solubilization with 1% MNG-3 or 1% DDM from a yeast membrane.

Supplementary Figure 9 SDS-PAGE of wheat germ CF translation of the proteins in the presence of MNG amphiphiles or conventional detergents.



SDS-PAGE of wheat germ CF translation of (**a**) green fluorescent protein (GFP) and (**b**) bacterio-opsin (BO) in the presence of MNG amphiphiles (MNG-1, MNG-2, and MNG-3) and conventional detergents (MPA-1, MPA-3, DDM, and DM). The agents were used at 0.1 wt % or 0.2 wt %. Arrows indicate the location of GFP and BO protein bands in SDS-PAGE. "S" and "P" represent supernatant and pellet fractions of protein samples after centrifugation. GFP study showed that CF expression is not inhibited by any of the conventional detergents at 0.1 wt %, but significant inhibition is observed at 0.2 wt % of each detergent. The three MNG amphiphiles did not inhibit GFP expression even at 0.2 wt %. CF expression of a membrane protein, BO, showed that expression of the protein was inhibited in the presence of the conventional detergents at 0.2 wt % (DDM is the best of the conventional detergents). These detergents at 0.1 wt % did not effectively solubilize the BO, most of which was found in an aggregated form. In contrast, 0.2 wt % MNG-1 or MNG-2 did not cause any inhibition of BO expression, as seen with GFP, and these amphiphiles efficiently solubilized the BO that was produced. The behavior of MNG-3 was slightly different. Even at 0.1 wt %, this MNG amphiphile was reasonably effective at solubilizing the BO produced, but 0.2 wt % MNG-3 seemed to reduce BO expression slightly (all expressed protein was soluble).

Supplementary Table 1 Melting Temperatures (T_m) of carazolol bound β_2 adrenergic receptor (β_2AR-T4L) at various critical micelle concentrations (CMC) measured in °C.

Melting temperatures (T_m) of carazolol bound β_2AR-T4L at various critical micelle concentrations (CMC) measured in °C

	1.5x CMC T_m ± SEM	3.5x CMC T_m ± SEM	6.5x CMC T_m ± SEM	10x CMC T_m ± SEM	50x CMC T_m ± SEM	250x CMC T_m ± SEM	ΔT_m
DDM	62.0 ± 0.23 (n=5)	64.2 ± 0.06 (n=4)	**64.4** ± 0.14 (n=4)	63.5 ± 0.16 (n=4)	63.0 ± 0.08 (n=4)	62.2 ± 0.22 (n=4)	
TDM	n.d.	n.d.	n.d.	63.2 ± 0.28 (n=3)	**63.5** ± 0.34 (n=3)	63.2 ± 0.24 (n=3)	-0.9
DM	**58.2** ± 0.29 (n=3)	56.0 ± 0.33 (n=3)	n.d.	55.4 ± 0.63 (n=4)	56.0 ± 0.64 (n=3)	n.d.	-6.2
MPA-1	n.d.	n.d.	n.d.	**51.4** ± 0.21 (n=3)	n.d.	n.d.	-13.0
MPA-3	n.d.	n.d.	n.d.	**58.8** ± 0.14 (n=3)	58.3 ± 0.10 (n=3)	n.d.	-5.6
MNG-1	n.d.	n.d.	n.d.	**65.1** ± 0.25 (n=3)	**65.1** ± 0.14 (n=3)	64.2 ± 0.21 (n=3)	+0.7
MNG-2	n.d.	n.d.	n.d.	64.6 ± 0.37 (n=3)	**67.1** ± 0.10 (n=3)	67.0 ± 0.31 (n=3)	+2.7
MNG-3	n.d.	n.d.	n.d.	67.4 ± 0.06 (n=3)	**68.4** ± 0.09 (n=3)	66.8 ± 0.15 (n=3)	+4.0

The highest T_m value obtained for each amphiphiles is shown in bold and used to calculate ΔT_m relative to DDM.

The highest T_m value obtained for each amphiphile is shown in bold and used to calculated ΔT_m relative to DDM. n.d. = not determined; n = number of replicates.

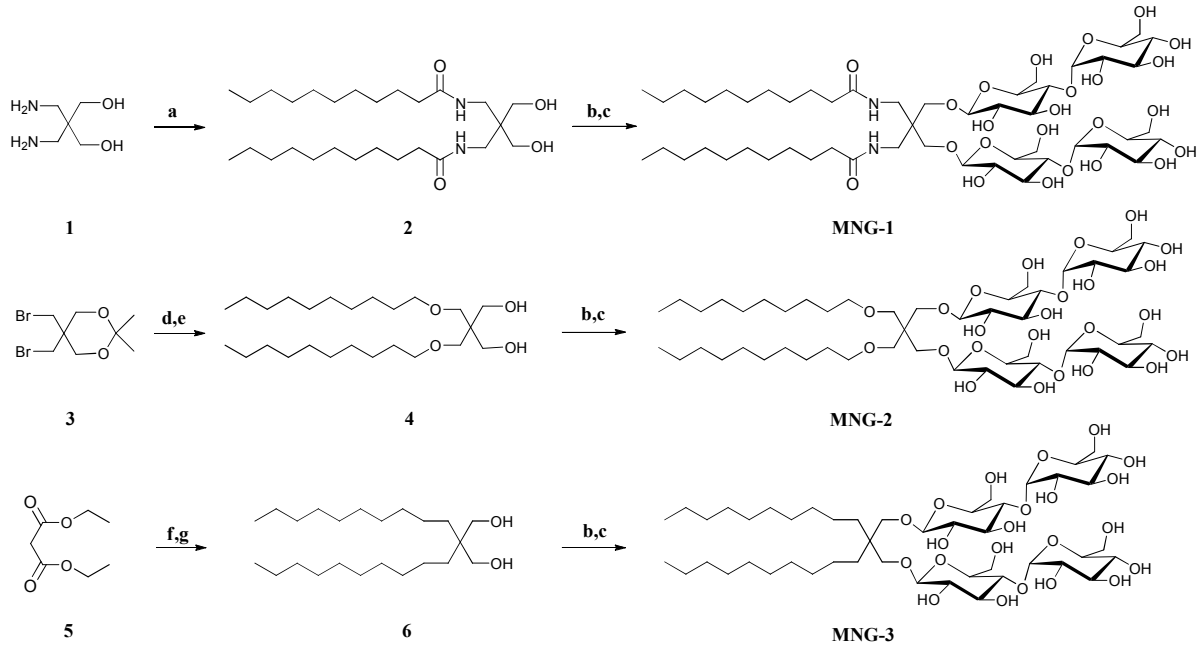
Supplementary Table 2 Crystal data collection statistics for cytochrome b_6f/MNG-3 complex.

Space group	I222
Unit cell dimension (Å)	102.1 169.3 352.6
Number of reflections	195299
Number of unique reflections	39941
Resolution limits (Å)	44.03 - 3.47
Higher resolution shell (Å)	(3.68 - 3.47)
Completness	99.6% (99.2%)
Redundancy	4.9
R_{merged}	8.69% (59.9%)
$R_{measured}$	9.7% (67.1%)
I/σ(I)	13.8 (2.6)

Crystallographic refinement statistics

Resolution range (Å)	39.97 - 3.47
Number of reflections	39850
R / FreeR	0.1937 / 0.2334
Number of atoms (total)	7821
Mean B value ($Å^2$)	112.60
rms deviation from ideal values:	
bond length (Å)	0.010
bond angle (degree)	1.20

Supplementary Note Synthetic scheme and detailed protocol for preparation of MNG amphiphiles and monopod amphiphiles (MPAs), and their physical characterization.



Synthetic route for MNG amphiphiles (MNG-1, MNG-2, and MNG-3): (a) undecanoic acid, EDC • HCl, HOBt, room temperature; (b) perbenzoylated maltosylbromide (2.1 equiv.), AgOTf, CH_2Cl_2, – 45 °C → room temperature; (c) NaOMe, MeOH, room temperature; (d) decanol, NaH, DMF, 120 °C; (e) *p*-TSA, MeOH, room temperature; (f) NaH, decyl iodide, THF, room temperature; (g) $LiAlH_4$, THF, room temperature.

General procedure for glycosylation reactions

This reaction was performed according to a literature method[1] with slight modification. A mixture of alcohol derivative, AgOTf (2.4 equiv.), 2,4,6-collidine (1.8 equiv.) in anhydrous CH_2Cl_2 (40 mL) was stirred at − 45 °C. A solution of perbenzoylated maltosylbromide (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 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 over 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 × 40 mL). Then the organic layer was dried with anhydrous Na_2SO_4 and the solvents were removed by rotary evaporation.

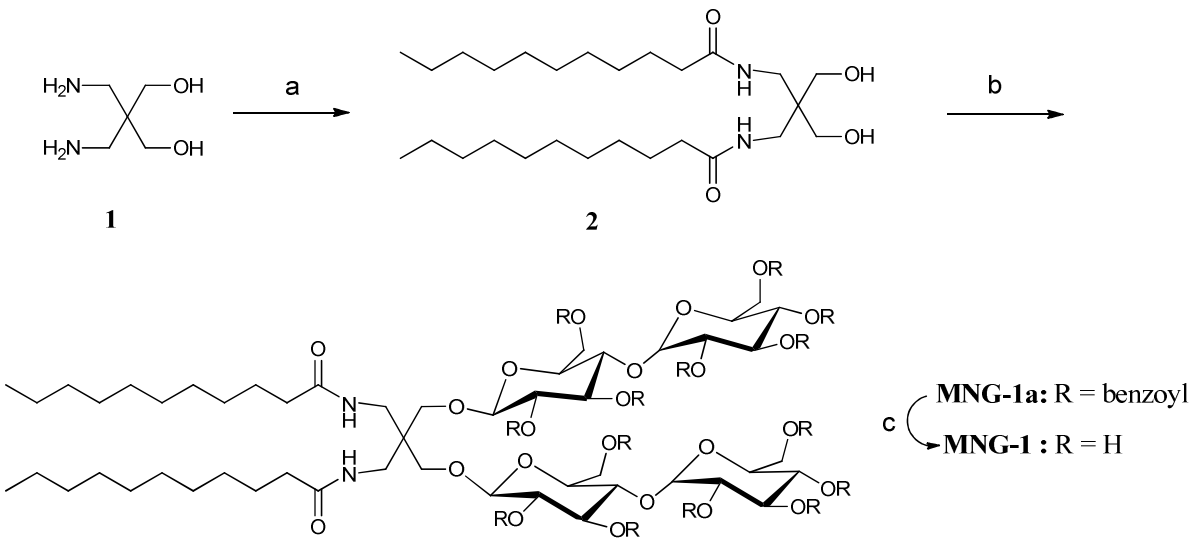
The residue was purified by silica gel column chromatography (EtOAc/hexane) providing desired product as a glassy solid.

General Procedure for the de-*O*-benzoylations under Zemplén's conditions[1]

The *O*-benzoylated compounds were dissolved in MeOH and then 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 left stirring 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 carried out by recrystallization using CH_2Cl_2/MeOH/diethyl ether afforded fully de-*O*-benzoylated product as a white solid.

Synthesis and characterization of MNG amphiphiles

Scheme 1



(a) undecanoic acid, EDC • HCl, HOBt, room temperature, 91%; (b) (g) perbenzoylated maltosylbromide (2.4 equiv.), AgOTf, CH_2Cl_2, – 45 °C → room temperature, 92% ; (c) NaOMe, MeOH, room temperature, 95%.

Undecanoic acid (2,2-bis-hydroxymethyl-3-undecanolylamino-propyl)-amide (2)

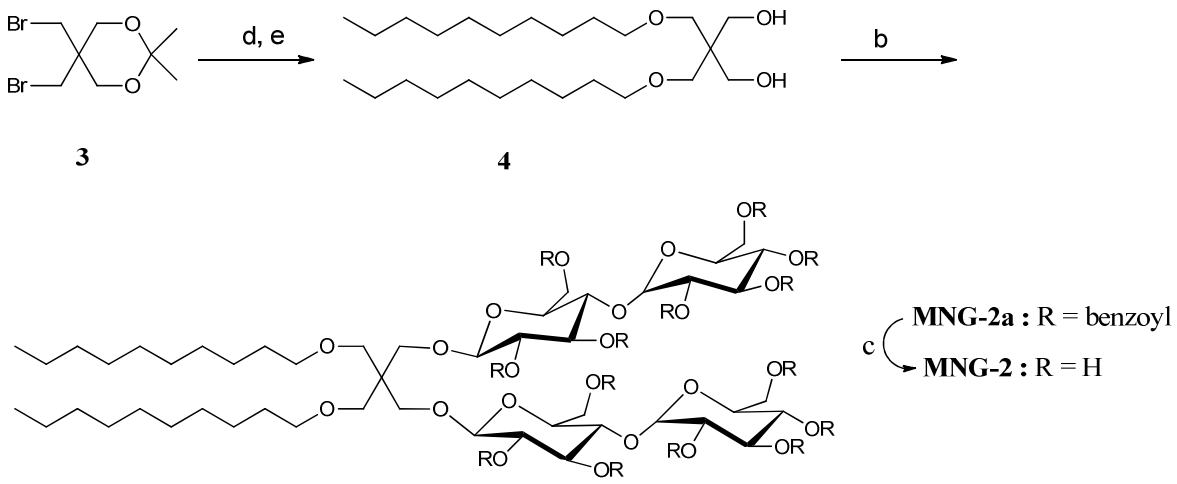
This compound was synthesized according to **scheme 1**. 2,2-bis-aminomethyl-propane-1,3-diol (**1**)[2] (0.51 g, 3.8 mmol), undecanoic acid (1.42 g, 7.6 mmol), 1-hydroxybenzotriazole monohydrate (HOBt) (1.2 g, 9.1 mmol) was dissolved in anhydrous DMF (30 mL). 1-(3-(dimethylamino)propyl)-3-ethylcarbodiimide hydrochoride (EDC • HC1) (1.7 g, 0.91 mmol) was added in small portions at 0 °C and the resulting solution left stirring at room temperature for 20 hr. The solution was taken up with

EtOAc (100 mL) and was washed successively with a 1 M aqueous $NaHCO_3$ solution (100 mL), a 0.1 M aqueous HCl solution (100 mL) and brine (2 × 100 mL). Then the organic layer was dried with anhydrous Na_2SO_4 and the solvent was removed by rotary evaporation. The reaction mixture was precipitated with ether (100 mL) and the resulting solid was collected and dried *in vacuo* to afford amide-containing diol (**2**) as a white solid (1.63 g, 91%). This product was used for next reaction without further purification. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 6.97 (t, *J* = 6.8 Hz, 2H), 4.65 (t, *J* = 6.6 Hz, 2H), 3.27 (d, *J* = 7.0 Hz, 4H), 3.01 (d, *J* = 7.0 Hz, 4H), 2.25 (t, *J* = 7.4 Hz, 2H), 1.64 (quin, 4H), 1.30-1.23 (m, 28H), 1.38-1.21 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 176.1, 61.0, 46.6, 38.3, 36.9, 32.1, 29.8, 29.7, 29.5, 26.2, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{27}H_{54}N_2O_4$ $[M]^+$ 471.4157, found 471.4154.

MNG-1a was synthesized according to the general procedure for glycosylation. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.4 Hz, 4H), 8.02-7.85 (m, 12H), 7.87 (d, *J* = 8.4 Hz, 4H), 7.80 (d, *J* = 8.4 Hz, 4H), 7.74 (d, *J* = 8.4 Hz, 4H), 7.65-7.20 (m, 42H), 6.22-6.15 (m, 2H), 6.12 (t, *J* = 10.0 Hz, 2H), 5.70 (d, *J* = 4.1 Hz, 2H), 5.66 (t, *J* = 10.0 Hz, 2H), 5.32 (t, *J* = 9.4 Hz, 2H), 5.17 (dd, *J* = 10.0, 3.5 Hz, 2H), 5.06 (dd, *J* = 10.0, 8.0 Hz, 2H), 4.75 (d, *J* = 10.0 Hz, 2H), 4.57 (dd, *J* = 12.7, 3.2 Hz, 2H), 4.40-4.27 (m, 5H), 4.18 (dd, *J* = 13.1, 4.4 Hz, 2H), 3.53 (d, *J* = 9.6 Hz, 2H), 3.39 (m, 2H), 3.21 (d, *J* = 8.0 Hz, 2H), 3.06 (m, 4H), 2.91 (dd, *J* = 13.6, 3.0 Hz, 2H), 2.26 (t, *J* = 7.5 Hz, 4H), 1.6 (br s, 4H), 1.35-1.15 (br s, 28H), 0.86 (t, *J* = 6.9 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 174.1, 166.2, 166.0, 165.9, 165.6, 165.4, 165.2, 165.1, 134.3, 133.8, 133.6, 133.5, 133.4, 133.3, 130.2, 130.1, 129.9, 129.8, 129.7, 129.5, 129.4, 129.2, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 101.3, 95.9, 74.3, 72.8, 72.1, 71.4, 69.9, 69.3, 69.1, 62.7, 42.2, 42.0, 36.6, 32.0, 29.8, 29.7, 29.5, 26.0, 22.9, 14.3; **MS (MALDI-TOF)**: calcd. for $C_{149}H_{150}N_2O_{38}Na$ $[M+Na]^+$ 2597.9759, found 2597.9653.

MNG-1 was synthesized according to the general procedure for de-*O*-benzoylation. **^{1}H NMR** (300 MHz, CD_3OD): δ 5.20 (d, *J* = 3.8 Hz, 2H), 4.34 (d, *J* = 7.9 Hz, 2H), 3.96-3.80 (m, 8H), 3.73-3.63 (m, 9H), 3.60-3.39 (m, 10H), 3.38-3.22 (m, 7H), 2.27 (t, *J* = 6.6 Hz, 4H), 1.65 (br t, 4H), 1.42-1.25 (br s, 28H), 0.93 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 177.1, 104.8, 103.1, 81.4, 77.9, 76.8, 75.2, 74.9, 74.8, 74.3, 71.7, 71.3, 62.9, 62.2, 45.9, 41.0, 37.5, 33.2, 30.9, 30.8, 30.6, 30.5, 27.2, 23.9, 14.6; **HRMS (ESI)**: calcd. for $C_{51}H_{94}N_2O_{24}Na$ $[M+Na]^+$ 1141.6089, found 1141.6071.

Scheme 2



(d) decanol, NaH, DMF, 120 °C; (e) *p*-TSA, MeOH, room temperature, 92% (in two steps); (b) perbenzoylated maltosylbromide (2.4 equiv.), AgOTf, CH_2Cl_2, – 45 °C → room temperature, 93%; (c) NaOMe, MeOH, room temperature, 96%.

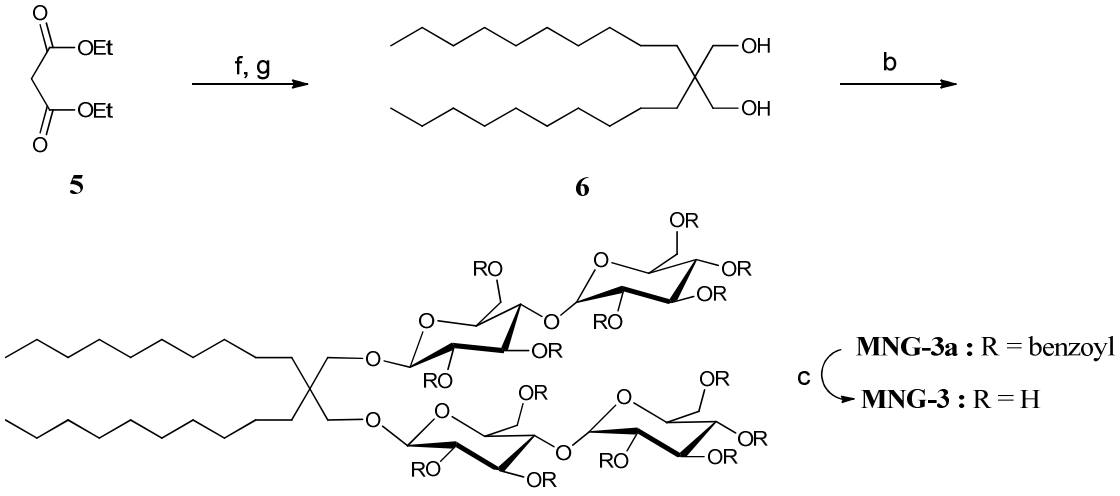
2,2-Bis-decyloxymethyl-propane-1,3-diol (4)

This compound was synthesized according to **scheme 2**. To a solution of decanol (3.3 g, 17 mmol) in DMF (40 mL) was added NaH (0.69 g, 0.17 mmol, 60%) at 0 °C. The mixture was stirred at room temperature under N_2 atmosphere for 0.5 h. After addition of 5,5-bis-bromomethyl-2,2-dimethyl-[1,3]dioxane (**3**)[3] (1.3 g, 4.3 mmol), the reaction mixture was warmed to 120 °C and stirred further for 15 hr. After cooling to room temperature, the reaction was quenched with ice-cold H_2O (100 mL) and extracted with ether (3 × 80 mL). The combined organic layer washed with brine (2 × 100 mL), dried with anhydrous Na_2SO_4 and then concentrated by rotary evaporation. To the residue dissolved in 1:1 mixture of CH_2Cl_2 and MeOH (120 mL) was added *p*-toluenesulfonic acid (*p*-TSA) monohydrate (300 mg) and left stirring at room temperature for 2 hr. After the neutralization of the reaction mixture with a saturated aqueous $NaHCO_3$ solution, the volume of solvent was reduced by rotary evaporation. The residue was partitioned between CH_2Cl_2 and water. The separated organic layer was washed with brine, dried with anhydrous Na_2SO_4, and then concentrated *in vacuo*. Flash column chromatography (EtOAc/hexane) affords ether-containing diol (**4**) as a white solid (1.89 g, 92% (two steps)). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 3.64 (d, *J* = 6.4 Hz, 4H), 3.51 (s, 4H), 3.42 (t, *J* = 6.3 Hz, 4H), 2.87 (t, *J* = 6.3 Hz, 2H), 1.56 (quin, *J* = 6.7 Hz, 4H), 1.26 (br s, 28H), 1.38-1.21 (m, 28H), 0.88 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 73.4, 72.3, 71.1, 65.7, 44.7, 32.1, 29.8, 29.7, 29.6, 29.5, 26.4, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{25}H_{52}O_4Na$ $[M+Na]^+$ 439.3758, found 439.3778.

MNG-2a was synthesized according to the general procedure for glycosylation. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.4 Hz, 4H), 8.02-7.95 (m, 8H), 7.91 (d, *J* = 8.4 Hz, 4H), 7.87 (d, *J* = 8.4 Hz, 4H), 7.80 (d, *J* = 8.4 Hz, 4H), 7.74 (d *J* = 8.4 Hz, 4H), 7.65-7.20 (m, 42H), 6.12 (t, *J* = 9.8 Hz, 2H), 5.68 (d, *J* = 4.5 Hz, 2H), 5.65 (t, *J* = 9.4 Hz, 2H), 5.40 (t, *J* = 9.8 Hz, 2H), 5.22-5.10 (m, 4H), 4.65-4.55 (m, 4H), 4.38-4.13 (m, 8H), 3.70 (d, *J* = 9.2 Hz, 2H), 3.46 (d, *J* = 8.0 Hz, 2H), 3.35-3.15 (m, 8H), 2.97 (t, *J* = 9.4 Hz, 4H), 1.40 (br s, 4H), 1.33-1.12 (br s, 30H), 0.87 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 166.3, 166.0, 165.9, 165.7, 165.2, 165.0, 133.9, 133.6, 133.5, 133.4, 133.3, 130.3, 130.2, 130.1, 130.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 101.1, 95.9, 74.8, 72.4, 72.3, 71.7, 71.5, 69.9, 69.2, 69.1, 68.9, 68.6, 63.5, 62.7, 45.0, 32.1, 29.8, 29.7, 29.5, 26.2, 22.9, 14.3; **MS (MALDI-TOF)**: calcd. for $C_{147}H_{148}O_{38}Na$ $[M+Na]^+$ 2543.9541, found 2543.9468.

MNG-2 was synthesized according to the general procedure for de-*O*-benzoylation. **^{1}H NMR** (300 MHz, CD_3OD): δ 5.19 (d, *J* = 3.8 Hz, 2H), 4.36 (d, *J* = 7.9 Hz, 2H), 3.98-3.80 (m, 8H), 3.77-3.67 (m, 12H), 3.55-3.23 (m, 20H), 1.58 (br m, 4H), 1.45-1.30 (br s, 28H), 0.94 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 105.2, 103.1, 81.5, 78.0, 76.7, 75.2, 75.0, 74.9, 74.3, 72.8, 71.6, 62.9, 46.7, 33.2, 31.0, 30.9, 30.8, 30.7, 27.6, 23.9, 14.6; **HRMS (ESI)**: calcd. for $C_{49}H_{92}O_{24}Na$ $[M+Na]^+$ 1087.5871, found 1087.5876.

Scheme 3



(f) NaH, decyl iodide, THF, room temperature; (g) $LiAlH_4$, THF, room temperature, 93% (in two steps); (b) perbenzoylated maltosylbromide (2.4 equiv.), AgOTf, 2,4,6-Collidine, CH_2Cl_2, – 45 °C → room temperature, 90%; (c) NaOMe, MeOH, room temperature, 94%.

2,2-Bis-decyl-propane-1,3-diol (6)

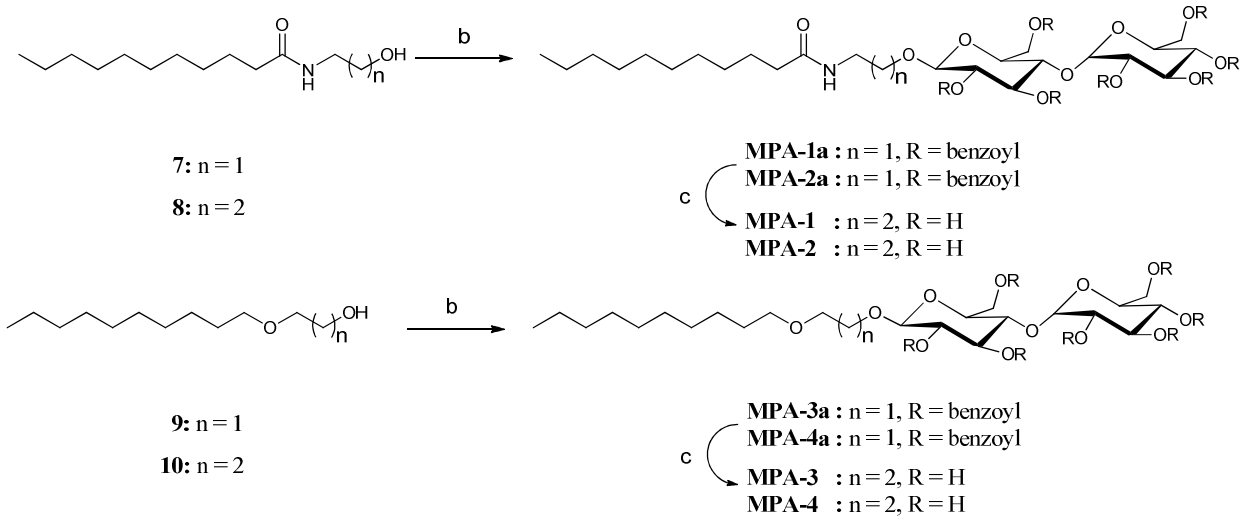
This compound was synthesized according to a literature method[4] (**scheme 3**) with slight modification. To a solution of diethyl malonate (**5**) (1.04 mL, 6.9 mmol) in THF (40 mL) was added dropwise a solution of NaH (0.82g, 21 mmol) in THF at 0 °C and left stirring for 20 min. After addition of iododecane (3.8 mL, 18 mmol), the reaction mixture was stirred at room temperature for 24 hr, quenched by adding ice-cold saturated NH_4Cl (100 mL) and then extracted with diethyl ether (2 × 50 mL). The organic layer was washed with brine and dried with anhydrous Na_2SO_4. After complete evaporation of solvent, $LiAlH_4$ (0.52 g, 14.0 mmol) was added slowly to the residue dissolved in THF (50 mL) at 0 °C. The mixture was stirred at room temperature for 4 hr, quenched with MeOH, water, a 1 N aqueous HCl solution successively at 0 °C and then extracted with diethyl ether (2 × 50 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 alkyl-containing diol (**6**) as a white solid (2.3 g, 93% (two steps)). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 3.55 (s, 4H), 2.55 (s, 2H), 1.38-1.08 (m, 36H), 0.88 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 69.6, 41.2, 32.1, 31.0, 30.8, 29.9, 29.8, 29.6, 23.1, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{23}H_{48}O_2Na$ $[M+Na]^+$ 379.3547, found 379.3546.

MNG-3a was synthesized according to the general procedure for glycosylation. **^{1}H NMR** (300 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), 7.86 (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), 5.68–5.58 (m, 4H), 5.34 (t, *J* = 10.2 Hz, 2H), 5.18-5.06 (m, 4H), 4.68-4.52 (m, 4H), 4.38-4.16 (m, 8H), 3.32 (d, *J* = 7.6 Hz, 2H), 2.94-2.86 (m, 2H), 2.70 (d, *J* = 8.6 Hz, 2H), 1.35-0.98 (m, 34H), 0.87 (t, *J* = 6.9 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 166.3, 166.0, 165.7, 165.3, 165.2, 165.0, 133.9, 133.7, 133.6, 133.4, 133.3, 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, 74.5, 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, 22.3, 14.3; **MS (MALDI-TOF)**: calcd. for $C_{145}H_{144}O_{36}Na$ $[M+Na]^+$ 2483.9330, found 2483.928.

MNG-3 was synthesized according to the general procedure for de-*O*-benzoylation. **^{1}H NMR** (300 MHz, CD_3OD): δ 5.18 (d, *J* = 3.8 Hz, 2H), 4.39 (d, *J* = 7.9 Hz, 2H), 3.98-3.78 (m, 4H), 3.77-3.60 (m, 6H), 3.58-3.23 (m, 20H), 1.58 (br m, 6H), 1.42-1.16 (br s, 34H), 0.93 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (75 MHz, CD_3OD): δ 105.1, 103.0, 78.0, 76.6, 74.9, 74.8, 71.6, 42.2, 33.2, 31.7, 30.9, 30.8, 30.6, 23.9, 14.6; **HRMS (ESI)**: calcd. for $C_{47}H_{88}O_{22}Na$ $[M+Na]^+$ 1027.5660, found 1027.5653.

Synthesis and characterization of monopod amphiphiles (MPAs)

Scheme 4



(b) perbenzoylated maltosylbromide (1.2 equiv.), AgOTf, CH_2Cl_2, – 45 °C → room temperature, 95% (MPA-1a), 95% (MPA-2a), 94% (MPA-3a), 93% (MPA-4a); (c) NaOMe, MeOH, room temperature, 96% (MPA-1 and MPA-2), 95 % (MPA-3 and MPA-4).

Undecanonic acid (2-hydroxy-ethyl)-amide (7) & **undecanonic acid (2-hydroxy-propyl)-amide (8)**
These compounds were synthesized according to the synthetic protocol for the preparation of amide-containing diol (**2**) using 1.1 equivalent of 2-aminoethanol and 3-amino-propan-1-ol with undecanoic acid, respectively.

Undecanonic acid (2-hydroxy-ethyl)-amide (7), Yield: 95%; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 6.14 (br s, 1H), 3.72 (q, *J* = 5.0 Hz, 2H), 3.42 (q, *J* = 5.4 Hz, 2H), 3.16 (t, *J* = 5.1 Hz, 1H), 2.21 (t, *J* = 7.6 Hz, 2H), 1.63 (quin, *J* = 7.0 Hz, 2H), 1.38-1.20 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 174.8, 62.7, 42.6, 36.9, 32.1, 29.8, 29.7, 29.5, 25.9, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{13}H_{27}NO_2$ $[M]^+$ 229.2037, found 229.2043.

Undecanonic acid (2-hydroxy-propyl)-amide (8), Yield: 93%; **^{1}H NMR** (300 MHz, $CDCl_3$): δ 6.25 (br s, 1H), 3.67 (quin, *J* = 6.0 Hz, 4H), 3.62 (q, *J* = 5.6 Hz, 2H), 3.40 (q, *J* = 6.2 Hz, 2H), 2.19 (t, *J* = 7.4 Hz, 2H), 1.72-1.56 (m, 4H), 1.36-1.20 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 174.9, 59.3, 36.9, 36.3, 32.5, 32.1, 29.7, 29.6, 29.5, 29.4, 26.0, 22.8, 14.3; **HRMS (ESI)**: calcd. for $C_{14}H_{29}NO_2$ $[M]^+$ 243.2193, found 243.2188.

MPA-1a was synthesized according to the general procedure for glycosylation. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.3 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.92-7.83 (m, 4H), 7.78-7.67 (m, 4H), 7.65-7.17 (m, 23H), 6.10 (t, *J* = 10.2 Hz, 1H), 5.85-5.73 (m, 3H), 5.67 (t, *J* = 9.8 Hz, 1H), 5.35-5.22 (m, 2H), 4.97 (dd, *J* = 12.3, 2.5 Hz, 1H), 4.79 (dd, *J* = 12.2, 3.2 Hz, 2H), 4.55-4.45 (m, 3H), 4.34-4.25 (dd, *J* = 12.9, 3.8 Hz, 1H), 4.15-4.07 (m, 1H), 3.92-3.83 (m, 1H), 3.66 (td, *J* = 10.4, 4.0 Hz, 1H), 3.55-3.43 (m, 1H), 3.36-3.23 (m, 1H), 1.91-1.81 (m, 2H), 1.42 (quin, *J* = 7.2 Hz, 2H), 1.35-1.05 (m, 14H), 0.88 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 173.3, 166.3, 166.0, 165.8, 165.6, 165.5, 165.3, 165.2, 133.8, 133.6, 133.5, 133.3, 130.2, 130.1, 130.0, 129.9, 129.8, 129.7, 129.5, 129.2, 128.9, 128.8, 128.6, 128.4, 128.3, 101.2, 96.7, 74.8, 73.4, 72.6, 71.1, 69.6, 69.4, 69.3, 63.5, 62.7, 39.1, 36.6, 32.1, 29.8, 29.7, 29.5, 29.4, 29.3, 25.7, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{74}H_{75}NO_{19}Na$ $[M+Na]^+$ 1304.4826, found 1304.4805.

MPA-2a was synthesized according to the general procedure for glycosylation. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.3 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.92-7.83 (m, 4H), 7.78-7.67 (m, 4H), 7.65-7.17 (m, 23H), 6.11 (t, *J* = 10.2 Hz, 1H), 5.95 (t, *J* = 5.6 Hz, 1H), 5.85-5.75 (m, 2H), 5.68 (t, *J* = 9.8 Hz, 1H), 5.34-5.24 (m, 2H), 5.00 (dd, *J* = 12.3, 2.5 Hz, 1H), 4.80-4.71 (m, 2H), 4.56-4.45 (m, 3H), 4.31 (dd, *J* = 12.9, 3.8 Hz, 1H), 4.15-4.05 (m, 1H), 4.01-3.90 (m, 1H), 3.62-3.53 (m, 1H), 3.35-3.23 (m, 1H), 3.21-3.08 (m, 1H), 2.10 (t, *J* = 7.0 Hz, 2H), 1.82-1.63 (m, 2H), 1.62-1.50 (m, 2H), 1.35-1.18 (m, 14H), 0.86 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 173.4, 166.3, 166.0, 165.8, 165.6, 165.5, 165.2, 165.1, 133.7, 133.6, 133.5, 133.4, 133.2, 130.1, 130.0, 129.9, 129.8, 129.7, 129.6, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 101.0, 96.7, 74.8, 73.5, 72.6, 71.1, 69.4, 69.3, 68.8, 63.4, 62.7, 37.1, 36.7, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 26.0, 22.8, 14.3; **HRMS (ESI)**: calcd. for $C_{75}H_{77}NO_{19}Na$ $[M+H]^+$ 1296.5163, found 1296.5222.

MPA-1 was synthesized according to the general procedure for de-*O*-benzoylation. **^{1}H NMR** (300 MHz, CD_3OD): δ 5.15 (d, *J* = 3.4 Hz, 1H), 4.29 (d, *J* = 7.8 Hz, 1H), 3.97-3.75 (m, 4H), 3.73-3.54 (m,

5H), 3.54-3.20 (m, 7H), 2.19 (t, *J* = 7.5 Hz, 2H), 1.59 (br quin, 2H), 1.29 (br s, 14H), 0.89 (t, *J* = 6.8 Hz, 3H); **^{13}C NMR** (75 MHz, CD_3OD): δ 176.6, 104.6, 103.1, 81.5, 77.9, 76.8, 75.2, 74.9, 74.8, 74.3, 71.6, 69.9, 62.9, 40.7, 37.3, 33.2, 30.9, 30.8, 30.6, 30.5, 27.2, 23.9, 14.6; **HRMS (ESI)**: calcd. for $C_{25}H_{47}NO_{12}Na$ $[M+Na]^+$ 576.2991, found 576.2964.

MPA-2 was synthesized according to the general procedure for de-*O*-benzoylation. **^{1}H NMR** (300 MHz, CD_3OD): δ 5.21 (d, *J* = 3.8 Hz, 1H), 4.32 (d, *J* = 7.7 Hz, 1H), 3.99-3.76 (m, 4H), 3.75-3.56 (m, 5H), 3.56-3.23 (m, 7H), 2.22 (t, *J* = 7.0 Hz, 2H), 1.83 (quin, *J* = 6.2 Hz, 2H), 1.64 (br quin, 2H), 1.33 (br s, 14H), 0.94 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, CD_3OD): δ 176.5, 104.4, 103.0, 81.5, 77.9, 76.7, 75.2, 74.9, 74.9, 74.8, 74.3, 71.6, 68.5, 62.9, 62.3, 37.6, 37.3, 33.2, 30.8, 30.7, 30.6, 30.5, 30.4, 27.2, 23.9, 14.6; **HRMS (ESI)**: calcd. for $C_{26}H_{49}NO_{12}Na$ $[M+Na]^+$ 568.3328, found 568.3345.

2-decyloxy-ethanol (9) & 3-decyloxy-propan-1-ol (10)

These were synthesized according to a literature method[5].

2-decyloxy-ethanol (9); ^{1}H and ^{13}C NMR spectra of **9** are in good agreement with the previously reported spectra; **HRMS (ESI)**: calcd. for $C_{12}H_{26}O_2Na$ $[M+H]^+$ 203.2007, found 203.2011.

3-decyloxy-propan-1-ol (10); ^{1}H and ^{13}C NMR spectra of **10** are in good agreement with the previously reported spectra; **HRMS (ESI)**: calcd. for $C_{13}H_{28}O_2Na$ $[M+H]^+$ 217.2163, found 217.2171.

MPA-3a was synthesized according to the general procedure for glycosylation. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.90-7.83 (m, 4H), 7.74 (d, *J* = 8.4 Hz, 4H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.61-7.10 (m, 2H), 6.10 (t, *J* = 10.0 Hz, 1H), 5.82-5.70 (m, 2H), 5.66 (t, *J* = 9.9 Hz, 1H), 5.36-5.23 (m, 2H), 5.00-4.88 (m, 2H), 4.75 (dd, *J* = 12.0, 4.1 Hz, 1H), 4.55-4.37 (m, 3H), 4.28 (dd, *J* = 12.4, 3.6 Hz, 1H), 4.15-4.07 (m, 1H), 4.00-3.89 (m, 1H), 3.56-3.42 (m, 2H), 3.25 (t, *J* = 6.8 Hz, 2H), 1.42-1.06 (m, 14H), 0.87 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 166.3, 166.0, 165.8, 165.6, 165.5, 165.4, 165.2, 133.7, 133.6, 133.5, 133.4, 133.3, 133.2, 130.1, 130.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.1, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 101.0, 96.6, 75.2, 73.5, 73.1, 72.5, 71.8, 71.1, 70.1, 69.9, 69.4, 69.3, 63.8, 62.7, 32.1, 29.8, 29.7, 29.6, 29.5, 26.1, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{73}H_{74}O_{19}Na$ $[M+Na]^+$ 1277.4717, found 1277.4775.

MPA-4a was synthesized according to the general procedure for glycosylation. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.90-7.83 (m, 4H), 7.74 (d, *J* = 8.4 Hz,

4H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.61-7.10 (m, 2H), 6.10 (t, *J* = 10.0 Hz, 1H), 5.82-5.70 (m, 2H), 5.66 (t, *J* = 9.9 Hz, 1H), 5.36-5.23 (m, 2H), 4.92 (dd, *J* = 12.0, 2.6 Hz, 1H), 4.81-4.70 (m, 2H), 4.55-4.37 (m, 3H), 4.27 (dd, *J* = 12.4, 3.6 Hz, 1H), 4.15-4.05 (m, 1H), 4.00-3.92 (m, 1H), 3.67-3.56 (m, 1H), 3.27 (t, *J* = 6.0 Hz, 2H), 3.18-3.03 (m, 2H), 1.82-1.68 (m, 2H), 1.39 (quin, *J* = 6.8 Hz, 2H), 1.34-1.10 (m, 12H), 0.88 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 166.4, 166.0, 165.8, 165.6, 165.3, 165.2, 133.7, 133.6, 133.5, 133.4, 133.3, 133.2, 130.2, 130.1, 130.0, 129.9, 129.7, 129.6, 129. 5, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 101.0, 96.6, 75.1, 73.4, 73.1, 72.5, 71.2, 71.1, 70.1, 69.3, 67.4, 67.1, 63.7, 62.7, 32.1, 30.0, 29.8, 29.7, 29.6, 29.5, 26.2, 22.9, 14.3; **HRMS (ESI)**: calcd. for $C_{74}H_{76}O_{19}Na$ $[M+Na]^+$ 1291.4874, found 1291.4838.

MPA-3 was synthesized according to the general procedure for de-*O*-benzoylation. **^{1}H NMR** (300 MHz, CD_3OD): δ 5.20 (d, *J* = 3.7 Hz, 1H), 4.36 (d, *J* = 8.0 Hz, 1H), 4.18-4.00 (m, 1H), 3.97-3.82 (m, 3H), 3.82-3.60 (m, 8H), 3.58-3.47 (m, 4H), 3.45-3.38 (m, 1H), 3.37-3.26 (m, 2H), 1.62 (br quin, 2H), 1.34 (br s, 14H), 0.94 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (75 MHz, CD_3OD): δ 104.5, 103.1, 81.4, 77.8, 76.8, 75.2, 74.9, 74.8, 74.3, 72.6, 71.6, 71.2, 69.8, 62.9, 62.3, 40.7, 33.2, 30.9, 30.8, 30.7, 30.6, 27.3, 23.9, 14.6; **HRMS (ESI)**: calcd. for $C_{21}H_{41}NO_7Na$ $[M+Na]^+$ 442.2781, found 442.2776.

MPA-4 was synthesized according to the general procedure for de-*O*-benzoylation. **^{1}H NMR** (300 MHz, CD_3OD): δ 5.20 (d, *J* = 3.7 Hz, 1H), 4.31 (d, *J* = 7.5 Hz, 1H), 4.04-3.94 (m, 1H), 3.93-3.81 (m, 3H), 3.76-3.54 (m, 9H), 3.52-3.43 (m, 3H), 3.43-3.37 (m, 1H), 3.36-3.23 (m, 2H), 1.91 (quin, *J* = 6.4 Hz, 2H), 1.60 (br quin, 2H), 1.34 (br s, 14H), 0.94 (t, *J* = 6.9 Hz, 3H); **^{13}C NMR** (75 MHz, CD_3OD): δ 104.6, 103.1, 81.4, 77.9, 76.7, 75.2, 74.9, 74.8, 74.3, 72.2, 71.6, 68.9, 68.1, 62.9, 62.3, 33.2, 31.2, 30.9, 30.8, 30.7, 30.6, 27.4, 23.9, 14.6; **HRMS (ESI)**: calcd. for $C_{24}H_{46}O_{12}Na$ $[M+Na]^+$ 549.2882, found 549.2874.

SUPPLEMENTARY REFERENCES

1 Ashton, P.R., Boyd, S.E., Brown, C.L., Jayaraman, N., Nepogodiev, S.A. & Stoddart, J.F. A convergent synthesis of carbohydrate-containing dendrimers. *Chem. Eur. J*. **2**, 1115-1128 (1996).

2 Virta, P., Leppaenen, M. & Loennberg, H. Pentaerythrityltetramine scaffolds for solid-phase combinatorial chemistry. *J. Org. Chem*. **69**, 2008-2016 (2004).

3 Nishizono, N., Sugo, M., Machida, M. & Oda, K. Synthesis of thietane nucleosides by glycosidation of thietanose derivatives with nucleobases *Tetrahedron* **63**, 11622-11625 (2007).

4 Kim, Y.S., Kane, R.R., Beno, C.L., Ropmano, S., Mendez, G. & Hawthorne, M.F. Synthesis of new building blocks for boron-rich oligomers in boron neutroncapture therapy (BNCT). II: monomers derived from 2,2-disubstituted-1,3-diols. *Tetrahedron Lett*. **36**, 5147-5150 (1995).

5 Mihai, C., Kravchuk, A.V., Tsai, M.-D. & Bruzik, K.S. Application of brønstead-type LFER in the study of the phopolipase C mechanism. *J. Am. Chem. Soc*. **125**, 3236-3242 (2003).