Supplementary Information

Specific surface modification of the acetylene-linked glycolipid vesicle by click chemistry

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Experimental Section

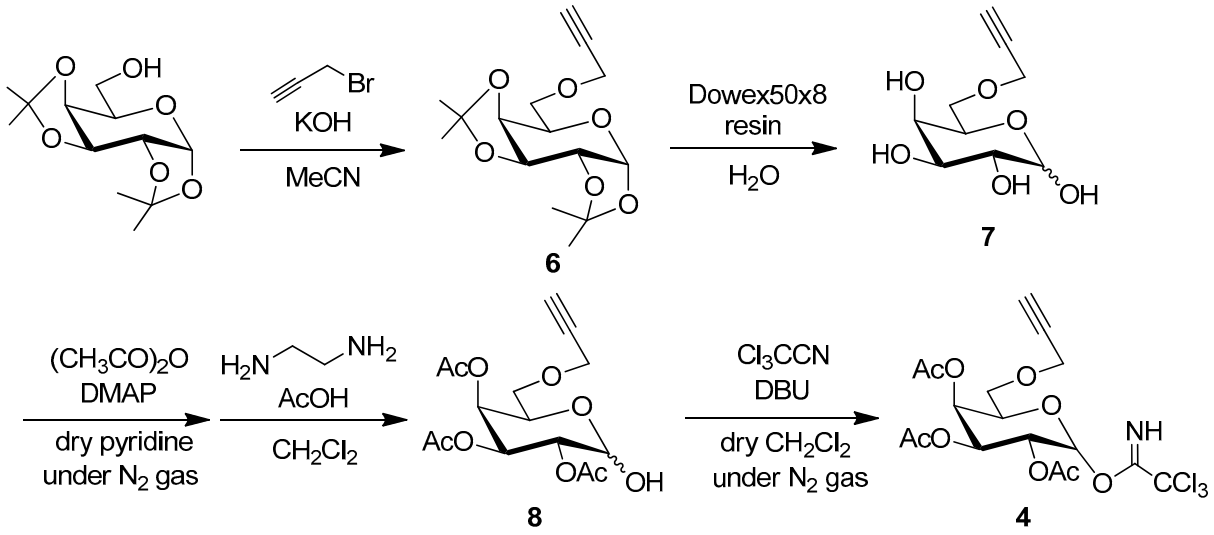
Material

Anhydrous dichloromethane (CH_2Cl_2), ethanol (EtOH), methanol (MeOH), chloroform ($CHCl_3$), dimethylformamide (DMF), acetonitrile (CH_3CN), acetic acid (AcOH), pyridine, triethylamine (NEt_3), acetic anhydride, ethylenediamine, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), potassium hydroxide (KOH), ammonium acetate ($AcONH_4$), cesium carbonate, boron trifluoride etherate, sodium methoxide, triethylene glycol, 3-bromo-1-propyne, sodium hydroxide and sodium L-ascorbate were purchased from Wako (Osaka, Japan). Dowex 50 x 8-resine, Amberlite IR-120H ion-exchange resin, 4-dimethylaminopyridine (DMAP) and 2-decyl-1-tetradecanol were from Sigma-Aldrich (St. Louis, USA) and sodium azide (NaN_3), *p*-toluene sulfonyl chloride and copper (II) sulfate pentahydrate ($CuSO_4 \cdot 5H_2O$) were obtained from Kishida (Osaka, Japan). 1,2:3,4-Di-*O*-isopropylidine-D-galactopyranose, trichloroacetonitrile, *a,a*-dimethoxytoluene, *p*-toluenesulfonic acid monohydrate and benzoyl chloride (PhCOCl) were purchased from Tokyo Kasei (TCI, Tokyo, Japan).

Instruments

The IR spectra were recorded using a JASCO Fourier Transform IR-620 spectrophotometer (Hachioji, Japan). The NMR spectra were taken on a Varian VXR-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometer with a solvent residual peak or tetramethylsilane (TMS) as the internal standard. The absorption spectra were measured in a 10 mm quartz cell using a JASCO V-560 or V-570 spectrophotometer. The electro-spray ionization mass (ESI-MS) spectra were recorded on a JEOL JMS-T100CS mass spectrometer or a Mariner (PE Biosystems) mass spectrometer. The transmission electron microscope (TEM) measurements were performed on a HITACHI H-7500 (100 kV). The dynamic light scattering (DLS) measurements were performed on a DLS-7000HK (Otsuka Electronics Co. Ltd., Japan) equipped with a 10 mW He-Ne Laser (632.8 nm) in water at 25 ˚C. Solvent separations were performed with an AKTA purifier using a HiTrap Desalting column (Sephadex G-25) using degassed H_2O as the eluent at a flow rate of 0.5 mL/min.

Synthetic Procedures



Scheme S1

1, 2:3, 4-Di-*O*-isopropylidine-6-*O*-prop-2-yn-1-yl-α-D-galactopyranose (6).

1, 2:3, 4-Di-*O*-isopropylidine-D-galactopyranose (2.25 g, 8.64 mmol), KOH (1.14 g, 20.1 mmol) and propargyl bromide (2.39 g, 20.1 mmol) in dry CH_3CN (10 mL) were stirred at rt for 21 h under nitrogen. After the solvent was evaporated *in vacuo*, the residue was dissolved in CH_2Cl_2 (25 mL) and the solution was washed with water (25 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic layers were dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (*n*-hexane: ethyl acetate = 3:1 (v/v)) to give **6** (2.39 g, 93% yield) as a colorless syrup. δ_H(500 MHz, $CDCl_3$, rt) 1.33 (s, 3H, -CH_3), 1.35 (s, 3H, -CH_3), 1.46 (s, 3H, -CH_3), 1.55 (s, 3H, -CH_3), 2.42 (t, 1H, H$CCCH_2$, *J*= 2.4 Hz), 3.67 (dd, 1H, H-6, *J* = 7.1. 10.1 Hz), 3.78 (dd, 1H, H-6', *J* = 5.3, 10.1 Hz), 4.01 (ddd, 1H, H-5, *J* = 1.8, 5.2, 7.0 Hz), 4.22 (dd, 2H, -OCH_2CCH, *J* = 2.4 Hz), 4.27 (dd, 1H, H-4, *J* = 1.9, 7.9 Hz), 4.32 (dd, 1H, H-2, *J* = 2.4, 5.1 Hz), 4.61 (dd, 1H, H-3, *J* = 2.4, 7.9 Hz), 5.54 (dd, 1H, H-1, *J* = 5.0 Hz).

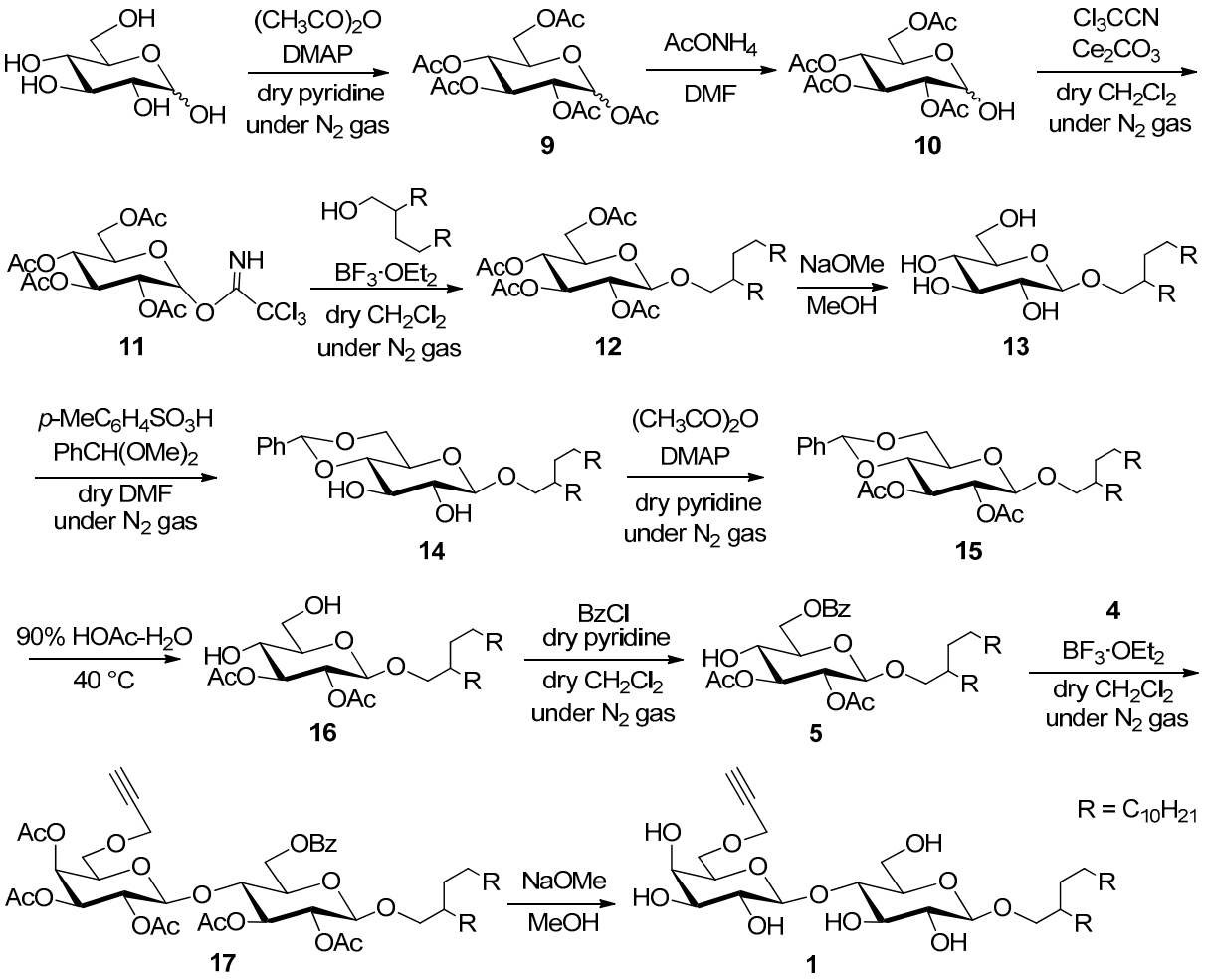
6-*O*-Prop-2-yn-1-yl-D-galactopyranose (7).

The compound **6** (2.39 g, 8.02 mmol) was suspended in water (100 mL) in the presence of Dowex 50 x 8-resine (2.88 g) and the mixture was heated to 80 °C overnight. After cooling, followed by filtration, the mixture was freeze-dried to give **7** as a colorless oil (1.71 g, 92% yield).

2,3,4-Tri-*O*-acetyl-6-*O*-prop-2-yn-1-yl-D-galactopyranose (8).

The compound **7** (1.20 g, 5.50 mmol) was acetylated in pyridine (15 mL) by dropwise addition of acetic anhydride (10.5 mL, 137 mmol) over 10 min at 0 °C under nitrogen, followed by stirring at rt overnight in the presence of DMAP (66.8 mg, 0.55 mmol). After the reaction mixture was diluted with ethyl acetate, the organic layer was washed with 1 N HCl, sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure, affording 1, 2:3, 4-tetra-*O*-acetyl-6-*O*-(prop-2-ynyloxy)-D-galactopyranose in quantitative yield. The obtained compound (2.32 g, 6.0 mmol) was then added to a solution of ethylenediamine (450 mg, 7.50 mmol) and glacial acetic acid (496 mg, 8.26 mmol) in CH_2Cl_2, and the mixture was stirred overnight. The reaction mixture was then diluted with water and extracted with CH_2Cl_2. The combined organic layer was washed with 1 N HCl, sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure, giving **8** as a white oil (1.48 g, 72% yield). δ_H (500 MHz, $CDCl_3$, rt, α/β mixture) 2.00 (s, 3H, -CH_3), 2.10 (s, 3H, -CH_3), 2.16 (s, 3H, -CH_3), 2.42 (m, 1H, H$CCCH_2$), 3.58 (m, 2H, H-6, 6'), 4.16 (dd, 2H, -OCH_2CCH, J = 2.4, 16.0 Hz), 4.47 (t, 1H, H-5, J = 6.0 Hz), 5.09 (m, 1H, H-4), 5.18 (dd, 1H, H-2, J = 3.6, 10.8 Hz), 5.41 (dd, 1H, H-3, J = 3.4, 10.8 Hz), 5.50 (m, 1H, H-1 (α and β)). MS (ESI) *m/z* calcd for $C_{15}H_{20}O_9$ $[M+Na]^+$ 367.10, found 367.10.

2,3,4-Tri-*O*-acetyl-6-*O*-prop-2-yn-1-yl-α-D-galactopyranosyl trichloroacetimidate (4).
To a solution of **8** (1.07 g, 3.11 mmol) in dry CH_2Cl_2 (30 mL), trichloroacetonitrile (0.63 mL, 6.22 mmol) and DBU (0.10 mL, 0.67 mmol) were added dropwise at 0 °C and the mixture was stirred at 0 °C overnight under nitrogen. After the reaction was completed, the solvent was evaporated *in vacuo* and the residue was purified by silica gel column chromatography (*n*-hexane: ethyl acetate = 1:2 (v/v)) to give **4** (1.03 g, 68% yield) as a yellowish solid. δ_H(500 MHz, $CDCl_3$, rt) 2.02 (s, 3H, -CH_3), 2.03 (s, 3H, -CH_3), 2.17 (s, 3H, -CH_3), 2.42 (t, 1H, H$CCCH_2$, J = 2.4 Hz), 3.60 (d, 2H, H-6, 6', J = 6.9 Hz), 4.12 (dd, 2H, -OCH_2CCH, J = 2.4, 16.1 Hz), 4.41 (t, 1H, H-5, J = 6.9 Hz), 5.37 (dd, 1H, H-4, J = 3.5, 10.9 Hz), 5.43 (dd, 1H, H-2, J = 3.2, 10.9 Hz), 5.60 (dd, 1H, H-3), 6.60 (d, 1H, H-1, J = 3.4 Hz), 8.64 (s, 1H, NH). δ_C (125 MHz, $CDCl_3$, rt) 170.1, 170.0, 169.9, 161.0, 90.8, 70.4, 69.5, 68.3, 67.5, 67.4, 67.1, 66.6, 58.4, 21.1, 20.2 (2C). FT-IR (KBr, cm^{-1}) 3300, 2120 (C≡C-H), 1750 (C=O), 798 (C-Cl). Anal. Calcd for $C_{17}H_{20}Cl_3NO_9$: C, 41.78; H, 4.12; N, 2.87. Found: C, 41.62; H, 3.89; N, 2.75.



Scheme S2

Penta-*O*-acetyl-D-glucopyranose (9).

D-glucose (18.0 g, 100 mmol) was acetylated in 150 mL of pyridine by dropwise addition of acetic anhydride (95 mL, 1000 mmol) over 20 min at 0 °C under nitrogen, followed by stirring at rt overnight in the presence of DMAP (1.22 g, 10 mmol). After the reaction mixture was diluted with ethyl acetate, the organic layer was washed with 1 N HCl, sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure, affording **9** in quantitative yield. δ_H(500 MHz, $CDCl_3$, rt,) 2.02 (s, 3H, -CH_3), 2.03 (s, 3H, -CH_3), 2.05 (s, 3H, -CH_3), 2.10 (s, 3H, -CH_3), 2.19 (s, 3H, -CH_3), 4.08-4.11 (m, 2H, H-6, 6'), 4.27 (dd, 1H, H-5, J = 12.5 Hz), 5.10 (dd, 1H, H-2, J = 3.8, 10.5 Hz), 5.15 (t, 1H, H-3, J = 10.5 Hz), 5.48 (t, 1H, H-4, J = 10.0, 12.4 Hz), 6.33 (d, 1H, H-1, J = 3.7).

2,3,4,6-Tetra-*O*-acetyl-D-glucopyranose (10).

The compound **9** (24.3 g, 62.2 mmol) and ammonium acetate (9.63 g, 124 mmol) in dry DMF (100 mL) were stirred at rt overnight under nitrogen and the solvent was evaporated *in vacuo*. The residue was then purified by silica gel column chromatography (*n*-hexane: ethyl acetate =

1:1 (v/v)) to give **10** (13.0 g, 60% yield) as a white solid.

2,3,4,6-Tetra-*O*-acetyl-*α*-D-glucopyranosyl trichloroacetimidate (11).

To a suspension solution of **10** (7.54 g, 21.7 mmol) and cesium carbonate (14.1 g, 43.4 mmol) in dry CH_2Cl_2 (100 mL) was added dropwise trichloroacetonitrile (4.40 mL, 43.4 mmol) at 0 °C and the mixture was stirred at 0 °C overnight under nitrogen. After the reaction was completed, the reaction mixture was filtered with Celite and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (*n*-hexane: ethyl acetate = 3:2 (v/v)) to give **11** (3.61 g, 34% yield) as a yellowish solid. δ_H (500 MHz, $CDCl_3$, rt) 2.02 (s, 3H, -CH_3), 2.04 (s, 3H, -CH_3), 2.05 (s, 3H, -CH_3), 2.08 (s, 3H, -CH_3), 4.14 (dd, 1H, H-6, *J* = 2.2, 12.4 Hz), 4.22 (m, 1H, H-5, *J* = 2.2, 4.1 Hz), 4.28 (dd, 1H, H-6', *J* = 4.1, 12.4 Hz), 5.14 (dd, 1H, H-2, *J* = 3.7, 10.2 Hz), 5.18 (t, 1H, H-3, *J* = 9.7, 10.2 Hz), 5.57 (dd, 1H, H-4, *J* = 9.7 Hz), 6.60 (d, 1H, H-1, *J* = 3.7 Hz), 8.70 (s, 1H, NH). δ_C(125 MHz, $CDCl_3$, rt) 170.7, 170.2, 170.0, 169.7, 160.9, 93.0, 90.8, 70.1, 70.0, 69.9, 67.9, 61.5, 20.8 (2C), 20.7, 20.6.

Tricosan-11-ylmethyl 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (12).

The compound **11** (3.06 g, 6.21 mmol), 2-decyl-1-tetradecanol (2.88 mL, 6.83 mmol) and molecular sieve 4A were charged in a 200 mL round bottom flask and dried under vacuum overnight. To this was added dry CH_2Cl_2 (60 mL) at 0 °C under nitrogen, followed by $BF_3{\cdot}OEt_2$ (2.49 mL, 19.8 mmol) dropwise and the mixture was stirred at rt for 2 h. After the reaction was completed, the reaction mixture was diluted with ethyl acetate (50 mL) and the organic layer was washed with 1 N HCl, sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (*n*-hexane: ethyl acetate = 4:1 to 3:1 (v/v)), giving **12** (960 mg, 23% yield) as a colorless syrup. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$), 1.25 (m, 41H, -CH_2-, β-H), 2.01 (s, 3H, -CH_3), 2.02 (s, 3H, -CH_3), 2.03 (s, 3H, -CH_3), 2.09 (s, 3H, -CH_3), 3.29 (dd, 1H, α-H, *J* = 6.4, 9.4 Hz), 3.68 (dq, 1H, H-5, *J* = 2.5, 4.7, 10.0 Hz), 3.81 (dd, 1H, α'-H, *J* = 5.1, 9.4 Hz), 4.13 (dd, 1H, H-6, *J* = 2.5, 12.3 Hz), 4.27 (dd, 1H, H-6', *J* = 4.7, 12.3 Hz), 4.45 (d, 1H, H-1, *J* = 8.0 Hz), 5.00 (dd, 1H, H-2, *J* = 8.0, 9.7 Hz), 5.09 (t, 1H, H-3, *J* = 9.7 Hz), 5.20 (t, 1H, H-4, *J* = 9.5 Hz).

Tricosan-11-ylmethyl *β*-D-glucopyranoside (13).

To a solution of **12** (935 mg, 1.37 mmol) in MeOH (30 mL) was added sodium methoxide (148 mg, 2.74 mmol). After the reaction was completed, the reaction mixture was neutralized using Amberlite IR-120H ion-exchange resin, and the solvent was evaporated *in vacuo,* affording **13** in quantitative yield as a white solid. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$, *J* = 7.0 Hz), 1.25 (m, 40H, -CH_2-), 1.60 (s, 1H, β-H), 3.25-3.85 (m, 8H, H-2, 3, 4, 5,

6, 6', α-H, H'), 4.25 (d, 1H, H-1, J = 7.6 Hz). MS (ESI) *m/z* calcd for $C_{30}H_{60}O_6$ $[M+Na]^+$ 539.43, found 539.43.

Tricosan-11-ylmethyl 4,6-*O*-benzylidene-*β*-D-glucopyranoside (14).

The compound **13** (710 mg, 1.37 mmol) was dissolved in dry DMF (20 mL) under nitrogen and to this were added *α,α*-dimethoxytoluene (417 mg, 2.74 mmol) and *p*-toluenesulfonic acid monohydrate (24.1 mg, 0.14 mmol). After 4 h, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (*n*-hexane: ethyl acetate = 2:1 (v/v)) to give **14** (792 mg, 96% yield) as a colorless solid. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$, J = 6.9 Hz), 1.25 (m, 40H, -CH_2-), 1.56 (s, 1H, β-H), 3.40 (dd, 1H, α-H, J = 6.2, 9.5 Hz), 3.45 (ddd, 1H, H-5, J = 5.0 Hz), 3.51 (dd, 1H, H-2, J = 7.8, 8.4 Hz), 3.58 (t, 1H, H-4, J = 9.4 Hz), 3.77-3.86 (m, 3H, H-3, 6, α-H'), 4.34 (dd, 1H, H-6', J = 5.0, 10.5 Hz), 4.36 (d, 1H, H-1, J = 7.7 Hz), 5.54 (s, 1H, -C<u>H</u>(Ph)-), 7.35-7.40 (m, 3H, Ar-H), 7.49-7.51 (m, 2H, Ar-H). δ_C(125 MHz, $CDCl_3$, rt) 137.1, 129.4, 128.5, 126.4, 103.6, 103.1, 102.1, 80.8, 75.3, 74.1, 73.2, 68.9, 66.6, 38.4, 32.1, 31.4, 31.3, 30.2, 29.8, 29.5, 26.9, 22.8, 14.3. FT-IR (NaCl, cm^{-1}) 3400 (-OH), 697 (Ph-H). HRMS (ESI) *m/z* calcd for $C_{37}H_{64}O_6$ $[M+Na]^+$ 627.4585, found 627.4601.

Tricosan-11-ylmethyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-*β*-D-glucopyranoside (15).

The compound **14** (790 mg, 1.30 mmol) was acetylated in 20 mL of pyridine by dropwise addition of acetic anhydride (1.0 mL, 10.5 mmol) over 5 min at 0 °C under nitrogen, followed by stirring at rt overnight in the presence of DMAP (15.9 mg, 0.13 mmol). After the reaction mixture was diluted with ethyl acetate, the organic layer was washed with 1 N HCl, sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure, affording **15** (840 mg, 94% yield) as a colorless solid. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$, J = 6.9 Hz), 1.25 (m, 40H, -CH_2-), 1.55 (s, 1H, β-H), 2.04 (s, 3H, -CH_3), 2.05 (s, 3H, -CH_3), 3.31 (dd, 1H, α-H, J = 6.3, 9.4 Hz), 3.53 (ddd, 1H, H-5, J = 4.9 Hz), 3.70 (t, 1H, H-4, J = 9.5 Hz), 3.78-3.83 (m, 2H, H-6, α-H'), 4.37 (dd, 1H, H-6', J = 4.9, 10.6 Hz), 4.54 (d, 1H, H-1, J = 7.9 Hz), 5.00 (dd, 1H, H-2, J = 7.9, 9.4 Hz), 5.31 (t, 1H, H-3, J = 9.5 Hz), 5.50 (s, 1H, -C<u>H</u>(Ph)-), 7.35-7.38 (m, 3H, Ar-H), 7.43-7.45 (m, 2H, Ar-H). δ_C(125 MHz, $CDCl_3$, rt) 170.4, 169.6, 137.0, 129.3, 128.4, 126.3, 101.9, 101.6, 73.5, 72.5, 72.0, 68.8, 66.5, 38.2, 32.1, 31.3, 31.0, 30.2, 29.8-29.9, 29.5, 27.0, 26.8, 22.8, 21.0, 20.8, 14.3. FT-IR (NaCl, cm^{-1}) 1756 (C=O), 697 (Ph-H). HRMS (ESI) *m/z* calcd for $C_{41}H_{68}O_8$ $[M+Na]^+$ 711.4807, found 711.4812.

Tricosan-11-ylmethyl 2,3-di-*O*-acetyl-*β*-D-glucopyranoside (16).

The compound **15** (820 mg, 1.20 mmol) was stirred in 90% HOAc–H_2O (30 mL) at 40 °C. After 15 h, the mixture was diluted with CH_2Cl_2 (50 mL) and the solution was washed with

sat. $NaHCO_3$ (50 mL). The aqueous phase was then extracted with CH_2Cl_2 (2 x 10 mL) and the combined organic layers were dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (*n*-hexane: ethyl acetate = 3:2 (v/v)) to provide a product **16** (634 mg, 88% yield) as a colorless syrup. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$, *J* = 6.9 Hz), 1.25 (m, 40H, -CH_2-), 1.53 (s, 1H, β-H), 2.04 (s, 3H, -CH_3), 2.09 (s, 3H, -CH_3), 3.29 (dd, 1H, α-H, *J* = 6.4, 9.4 Hz), 3.53 (ddd, 1H, H-5, *J* = 3.6, 4.5 Hz), 3.74-3.81 (m, 2H, H-4, α-H'), 3.84 (dd, 1H, H-6, *J* = 4.5,11.9 Hz), 3.93 (dd, 1H, H-6', *J* = 3.5, 12.0 Hz), 4.47 (d, 1H, H-1, *J* = 7.9 Hz), 4.92 (dd, 1H, H-2, *J* = 7.9, 9.8 Hz), 5.03 (t, 1H, H-3, *J* = 9.6 Hz). δ_C(125 MHz, $CDCl_3$, rt) 172.0, 169.5, 101.4, 76.4, 75.5, 703.4, 71.4, 69.8, 62.4, 38.2, 32.1, 31.2, 31.0, 30.2, 29.8-29.9, 29.5, 27.0, 26.8, 22.8, 21.0, 20.8, 14.3. FT-IR (NaCl, cm^{-1}) 3445 (-OH), 1756 (C=O). HRMS (ESI) *m/z* calcd for $C_{34}H_{64}O_8$ $[M+Na]^+$ 623.4499, found 623.4487.

Tricosan-11-ylmethyl 2,3-di-*O*-acetyl-6-*O*-benzoyl-*β*-D-glucopyranoside (5).

The compound **16** (630 mg, 1.04 mmol) was dissolved in dry CH_2Cl_2 (10 mL) containing pyridine (540 μL, 6.69 mmol) under nitrogen, and to this was added PhCOCl (120 μL, 1.04 mmol) dropwise at 0 °C. The reaction mixture was slowly warmed to rt and further stirred for 12 h. The solvent was then evaporated under reduced pressure and the residue was purified by silica gel column chromatography (*n*-hexane: ethyl acetate = 3:2 (v/v)) to provide a product **5** (636 mg, 87% yield) as a colorless syrup. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$, *J* = 6.9 Hz), 1.25 (m, 40H, -CH_2-), 1.54 (s, 1H, β-H), 2.04 (s, 3H, -CH_3), 2.08 (s, 3H, -CH_3), 3.29 (dd, 1H, α-H, *J* = 6.5, 9.4 Hz), 3.61 (m, 1H, H-5), 3.66 (dd, 1H, H-4, *J* = 9.8 Hz), 3.81 (dd, 1H, α-H', *J* = 5.2, 9.4 Hz), 4.46 (d, 1H, H-1, *J* = 8.0 Hz), 4.55 (dd, 1H, H-6, *J* = 2.2, 12.5 Hz), 4.55 (dd, 1H, H-6', *J* = 4.0,12.2 Hz), 4.94 (dd, 1H, H-2, *J* = 8.0, 9.7 Hz), 5.07 (t, 1H, H-3, *J* = 9.7 Hz), 7.46 (t, 2H, (*m*-)Ph-H, *J* = 7.8 Hz), 7.60 (m, 1H, (*p*-)Ph-H, *J* = 1.3, 7.4 Hz), 8.07 (dd, 2H, (*o*-)Ph-H, *J* = 1.2, 7.8 Hz). δ_C(125 MHz, $CDCl_3$, rt) 171.6, 169.5, 167.3, 133.6, 130.1, 129.6, 128.6, 101.4, 75.6, 74.4, 73.1, 71.5, 69.3, 63.5, 38.1, 32.1(2C), 31.2, 31.0, 29.8-29.9, 29.5, 26.9, 26.8, 22.8, 21.0, 20.8, 14.3. FT-IR (NaCl, cm^{-1}) 3445 (-OH), 1756, 1726 (C=O), 712 (Ph-H). HRMS (ESI) *m/z* calcd for $C_{41}H_{68}O_9$ $[M+Na]^+$ 727.4761, found 727.4754.

(2-Decyl-tetradeceyl)
2,3,4-Tri-*O*-acetyl-6-*O*-(prop-2-ynyloxy)-*β*-D-galactpyranosyl-(1→4)-
2,3-di-*O*-acetyl-6-*O*-benzoyl-*β*-D-lactopyranoside (17).

The compounds **4** (441 mg, 0.90 mmol), **5** (636 mg, 0.90 mmol) and molecular sieve 4A were charged in a 100 mL round bottom flask and dried under vacuum for 1 h.

To this was added dry CH_2Cl_2 (10 mL) at 0 °C under nitrogen, followed by $BF_3{\cdot}OEt_2$ (400 μL, 3.17 mmol) dropwise and the mixture was stirred at rt for 10 h. The solvent was then evaporated under reduced pressure and the residue was purified by silica gel column

chromatography (*n*-hexane: ethyl acetate = 3:2 (v/v)) and recycle SEC chromatography (CH_3Cl), affording **17** (93 mg, 10% yield) as a colorless syrup. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$, *J* = 7.0 Hz), 1.25 (m, 40H, -CH_2-), 1.52 (s, 1H, β-H), 1.94 (s, 3H, -CH_3), 2.03 (s, 3H, -CH_3), 2.04 (s, 3H, -CH_3), 2.07 (s, 3H, -CH_3), 2.14 (s, 3H, -CH_3), 2.44 (t, 1H, $\underline{H}CCCH_2$, *J* = 2.4 Hz), 3.27 (dd, 1H, α-H, *J* = 6.4, 9.5 Hz), 3.52, 3.58 (dd, 2H, H-(6, 6')', *J* = 5.8, 10.5 Hz), 3.69-3.76 (m, 3H, α-H, H-5, 5'), 3.96 (t, 1H, H-4', *J* = 9.5 Hz), 4.15 (t, 2H, -$OC\underline{H}_2CCH$, *J* = 2.5 Hz), 4.34 (dd, 1H, H-6, *J* = 4.9, 11.9 Hz), 4.45 (d, 1H, H-1', *J* = 7.9 Hz), 4.52 (d, 1H, H-1, *J* = 7.9 Hz), 4.72 (dd, 1H, H-(6'), *J* = 1.9, 11.9 Hz), 4.88 (dd, 1H, H-3, *J* = 3.5, 10.5 Hz), 4.94 (dd, 1H, H-2', *J* = 7.9, 9.6 Hz), 5.10 (dd, 1H, H-2, *J* = 7.9, 10.5 Hz), 5.23 (t, 1H, H-3', *J* = 9.4 Hz), 5.36 (d, 1H, H-4, *J* = 2.6 Hz), 7.49 (t, 2H, (*m*-)Ph-H, *J* = 7.8 Hz), 7.60 (m, 1H, (*p*-)Ph-H, *J* = 1.3, 7.4 Hz), 8.06 (dd, 2H, (*o*-)Ph-H, *J* = 1.2, 7.1 Hz). δ_C(125 MHz, $CDCl_3$, rt) 171.0, 170.5, 170.1, 170.0, 169.8, 166.1, 133.4, 130.0, 129.9, 128.6, 100.7, 96.2, 79.1, 76.0, 74.9, 73.1, 72.5, 72.4, 68.4, 67.5, 67.3, 67.1, 63.4, 58.4, 38.0, 32.1, 31.2, 31.0, 30.2, 29.8, 29.5(m), 29.5(3), 26.9, 26.7, 22.8, 21.1, 20.9, 20.8(3C), 14.3. FT-IR (NaCl, cm^{-1}) 1751 (C=O), 712 (Ph-H). HRMS (ESI) *m/z* calcd for $C_{56}H_{86}O_{17}$ $[M+Na]^+$ 1053.5763, found 1053.5749.

Tricosan-11-ylmethyl
6-*O*-(prop-2-ynyloxy)-*β*-D-galactpyranosyl-(1→4)-*β*-D-lactopyranoside (1).

To a solution of the compound **17** (40 mg, 0.039 mmol) in MeOH (2 mL) was added sodium methoxide (5.4 mg, 0.10 mmol). After the reaction was completed, the reaction mixture was neutralized using Amberlite IR-120H ion-exchange resin, and the solvent was evaporated *in vacuo,* affording **1** in quantitative yield as a white solid. Mp: 75.2-75.4 °C. δ_H(500 MHz, $CDCl_3$, rt) 0.88 (t, 6H, -$CH_2C\underline{H}_3$, *J* = 7.0 Hz), 1.25 (m, 40H, -CH_2-), 1.60 (s, 1H, β-H), 2.53 (t, 1H, $\underline{H}CCCH_2$, *J* = 2.4 Hz), 3.36 (dd, 1H, α-H, *J* = 6.4, 9.5 Hz), 3.40-4.00 (m, 13H), 4.19, 4.25 (dd, 2H, -$OC\underline{H}_2CCH$, *J* = 2.5, 16.0 Hz), 4.28 (d, 1H, H-1', *J* = 7.8 Hz), 4.43 (d, 1H, H-1, *J* = 7.8 Hz). δ_C(125 MHz, $CDCl_3$, rt) 103.2, 103.1, 80.2, 79.4, 77.4, 75.6, 74.9, 74.5, 73.9, 73.8, 73.6, 69.1, 68.9, 62.4, 58.9, 38.3, 32.1, 31.2, 30.3, 29.9, 29.8, 29.5, 26.9, 22.8, 14.3. FT-IR (NaCl, cm^{-1}) 3422 (-OH). MS (ESI) *m/z* calcd for $C_{39}H_{72}O_{11}$ $[M+Na]^+$ 739.50, found 739.47. Anal. Calcd for $C_{39}H_{72}O_{11}$: C, 65.33; H, 10.12. Found: C, 65.32; H, 10.07.

1, 8-Di-azido-3, 6-dioxaundecane (2)

Triethylene glycol (0.8 mL, 6.0 mmol), KOH (2.00 g, 35.7 mmol) and *p*-toluene sulfonyl chloride (2.29 g, 12.0 mmol) in dry CH_2Cl_2 (6.0 mL) were stirred at 0 °C for 9 h under nitrogen. After the solvent was evaporated *in vacuo*, the residue was dissolved in CH_2Cl_2 (10 mL) and the solution was washed with water (20 mL). The aqueous phase was extracted with CH_2Cl_2 (2 x 6.0 mL) and the combined organic layers were dried over $MgSO_4$. After filtration,

the solvent was evaporated under reduced pressure, giving 1, 8-ditosyl-3, 6-dioxaundecane (2.37 g) in 86% yield as a white solid. δ_H(500 MHz, $CDCl_3$, rt) 2.45 (s, 6H, -CH_3), 3.53 (s, 4H, -O-C$\underline{H_2}$-C$\underline{H_2}$-O-), 3.64-3.67 (m, 4H, -C$\underline{H_2}$-OTs), 4.13-4.16 (m, 4H, -O-C$\underline{H_2}$-), 7.34 (d, 4H, Ar-H, J = 8.5 Hz), 7.79 (d, 4H, Ar-H, J = 8.4 Hz). MS (ESI) *m/z* calcd for $C_{20}H_{26}O_8S_2$ $[M+Na]^+$ 481.10, found 481.30.

The obtained 1, 8-ditosyl-3,6-dioxaundecane (0.92 g, 2.0 mmol) was allowed to react with NaN_3 (0.52 g, 8.0 mmol) in DMF (5 mL) at 80 °C for 18 h under stirring. After cooling to room temperature, water (15 mL) was added. The resulting mixture was extracted with ethyl acetate (3 x 20 mL) and the combined organic layers were washed with brine (20 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure, giving **2** (0.367 g, 92% yield) as a colorless oil. δ_H(500 MHz, $CDCl_3$, rt) 3.38-3.41 (m, 4H, -C$\underline{H_2}$-N_3), 3.68-3.71 (m, 8H, -C$\underline{H_2}$-O-C$\underline{H_2}$-). FT-IR (NaCl): 2109 cm^{-1} (N_3).

1, 11-Di-azido-3, 6, 9-trioxaundecane (3)

The azido compound **3** was synthesized from tetraethylene glycol via 1, 11-ditosyl-3, 6, 9-trioxaundecane in the same way for the synthesis of **2**, affording **3** in 92% yield as a colorless oil.

1, 11-Ditosyl-3, 6, 9-trioxaundecane. δ_H(500 MHz, $CDCl_3$, rt) 2.44 (s, 6H, -CH_3), 3.56 (m, 8H), 3.68 (t, 4H), 4.15 (t, 4H), 7.34 (d, 4H, Ar-H, J = 8.5 Hz), 7.79 (d, 4H, Ar-H, J = 8.4 Hz).

3. δ_H(500 MHz, $CDCl_3$, rt) 3.38-3.40 (m, 4H, -C$\underline{H_2}$-N_3), 3.66-3.70 (m, 12H, -C$\underline{H_2}$-O-C$\underline{H_2}$-). FT-IR (NaCl): 2104 cm^{-1} (N_3).

Transmission Electron Microscope Measurements

The sample solution were 0.1 mM glycolipid **1** vesicle solution and the resulting mixture of 0.1 mM glycolipid **1** vesicle solution reacted with 0.1 mM azido compound **2** in the presence of 0.02 mM copper sulfate, 0.05 mM sodium ascorbate in water. A 400-mesh collodion membrane-coated copper grid (Nisshin EM Co., JAPAN) hydrophilized by a glow discharge process using Ion coater IB-2 (EIKO Engineering Co. Ltd., JAPAN) was placed on a drop of a water-diluted suspension of the glycolipid **1** vesicle, allowed to adsorb for 1 min and the surplus was removed by filter paper. A drop of 2% (w/v) aqueous solution of uranyl acetate was added and left in contact with the sample for 5 minutes. The surplus water was removed by filter paper and the sample was dried in a desiccator for overnight. The vesicles imaged with a TEM operating at an acceleration voltage of 100 KV.

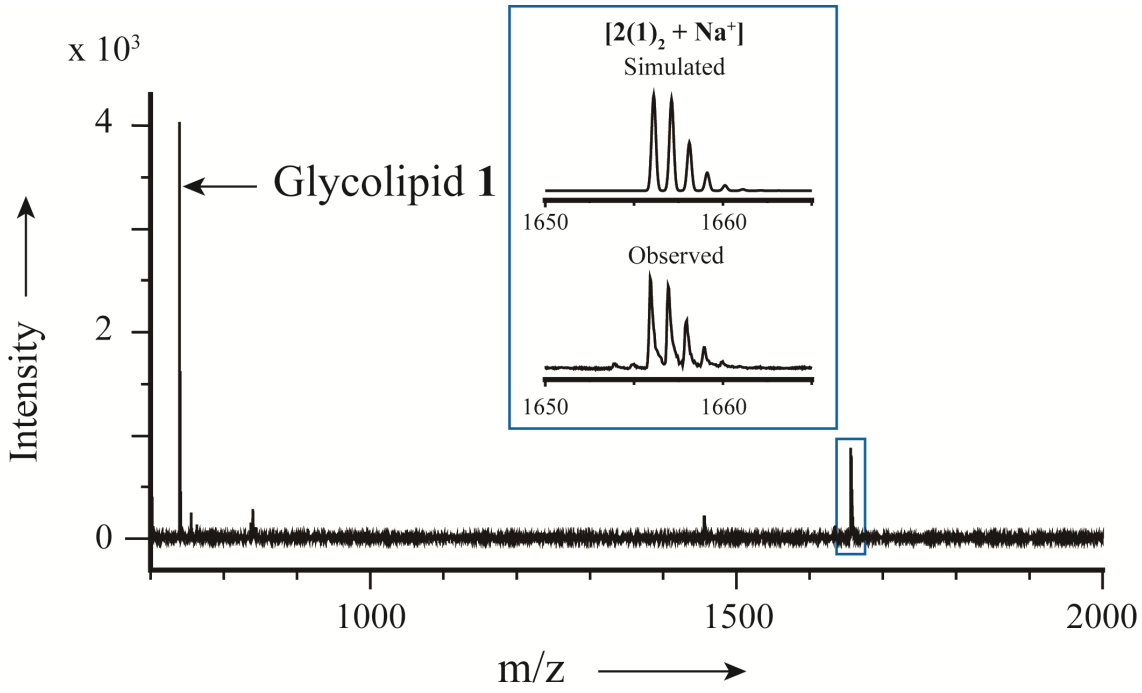


Fig. S1 ESI-MS spectra of the glycolipid **1** vesicle (0.1 mM) after addition of azido compound **2** (0.1 mM), $CuSO_4$•$5H_2O$ (0.02 mM) and sodium ascorbate (0.05 mM) overnight at room temperature.

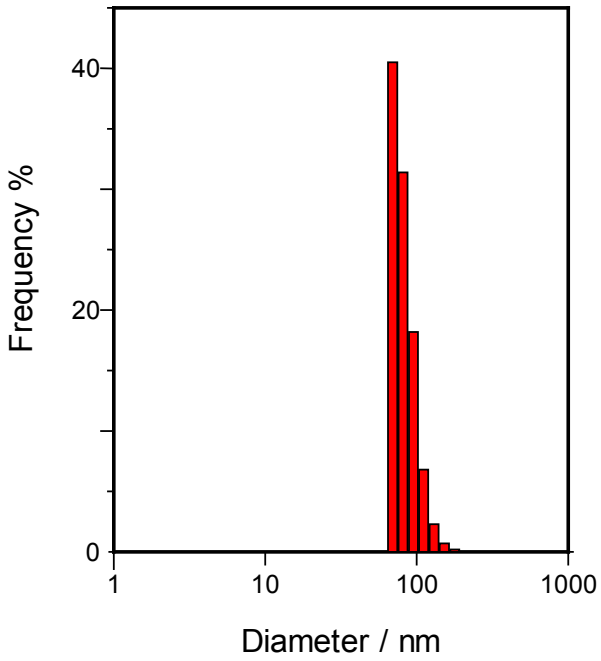


Fig. S2 The number average histogram of the glycolipid 1 vesicles (0.1 mM) after addition of azido compound **2** (0.1 mM), $CuSO_4$•$5H_2O$ (0.02 mM) and sodium ascorbate (0.05 mM) overnight in water. The solution was filtered through a 0.45 μm syringe filter (Toyo Roshi, Japan) prior to use, and then the DLS measurement of the sample was performed at a fixed scattering angle of 90° at 25 ^{o}C.

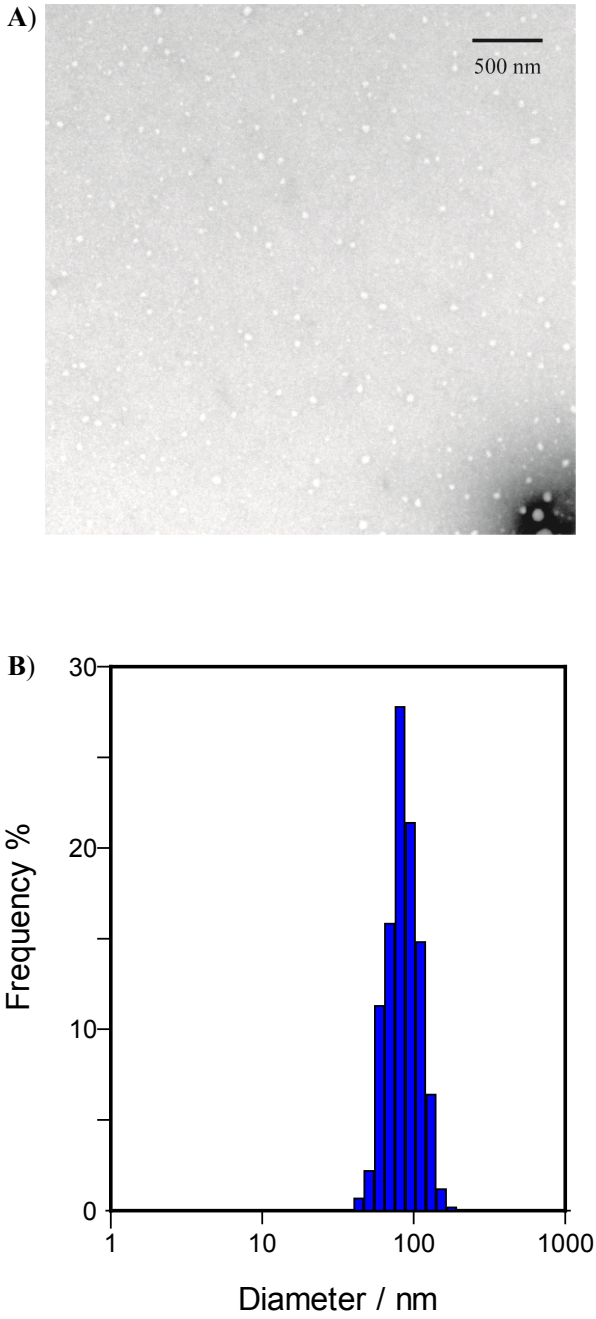


Fig. S3 A) TEM image of the glycolipid **1** vesicles (0.1 mM) after addition of azido compound **2** (0.1 mM), $CuSO_4 \cdot 5H_2O$ (0.02 mM) and sodium ascorbate (0.05 mM) overnight stained with uranyl acetate. **B**) Histogram of a diameter of the glycolipid **1** vesicles after addition of azido compound **2**, $CuSO_4 \cdot 5H_2O$ and sodium ascorbate by TEM.