Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supplementary Information

Synthesis and biological activity of phosphoglycolipids from *Thermus thermophilus*

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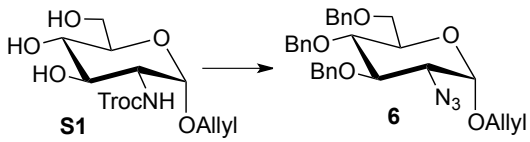
1. General Procedures

^{1}H-NMR spectra were measured at 30 °C in an indicated solvent with a JEOL Lambda 500 NMR spectrometer and a Delta ECA 500 NMR spectrometer and analyzed using Alice2® program version 5.2 (JOEL). The proton chemical shifts in $CDCl_3$ are given in δ values from tetramethylsilane as an internal standard, and the chemical shifts in other solvents or conditions are given in δ values from the residual proton signal of solvent. Mass spectra were obtained on an ESI-TOF mass spectrometer (Mariner^{TM}, Applied Biosystems). High resolution mass spectra (HR-MS) were obtained on the quadrupole time of flight (QTOF) mass spectrometer (QTOF-micro, Micromass). Silica-gel column chromatography was performed using Kieselgel 60 (Merck, 0.040-0.063mm) or Silica Gel 60N [spherical neutral (Kanto Chemical Co., 40-50 μm)] at medium pressure (2-4 kgcm-2) using the indicated solvent system. Analytical thin layer chromatographies (TLC) were performed on Kieselgel 60F254 Plates (Merck, 0.25 mm thickness). Specific rotations were measured on a Perkin Elmer model 241 polarimeter. Unless otherwise noted, non-aqueous reactions were carried out under argon atmosphere. Anhydrous dichloromethane were prepared by distillation from calcium hydride. Anhydrous THF, DMF, $CHCl_3$ were purchased from Kanto Chemicals Co. Distilled water was purchased from Otsuka Pharmaceutical Factory, Inc (Tokushima, Japan). Molecular sieves 4A were activated in vacuo at 250 °C for 3 h before use. $[Ir(cod)(PMe(C_6H_5)_2)_2]PF_6$ was activated with H_2 previously as follows; $[Ir(cod)(PMe(C_6H_5)_2)_2]PF_6$ was suspended in dry THF (7.5 times (wt)) under Ar at room temperature, and Ar in the system was replaced with H_2 to activate the complex. The color of the solution was changed from red to yellow, and then filled again with Ar.

All other commercially obtained materials were used as received.

2. Preparation of compound **2a** and **2b** (in Scheme 2)



Allyl 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranoside (6):

To a solution of **Allyl 2-*N*-Troc-2-deoxy-α-D-glucopyranoside S1** [*Tetrahedron Lett*. **2001**,

42, 7613; *Synlett* **2010**, (18), 2711.] (5.0 g, 12.7 mmol) in AcOH (100 mL) was added Zn-Cu couple (11.5 g) at room temperature. After the suspension was stirred vigorously for 4 h, insoluble materials were filtered off, and the filtrate was concentrated *in vacuo*. The residual AcOH was removed by co-evaporation with Toluene. The residue was dissolved in MeOH, and saturated aqueous $NaHCO_3$ was added. The resulted precipitates were filtered off, and the filtrate was concentrated *in vacuo* to give Allyl 2-amino-2-deoxy-α-D-glucopyranoside as a crude product as a white solid, and it was used for following reaction without further purification.

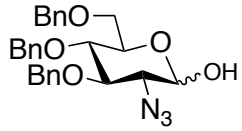
(TfN_3 was prepared before use of the next reaction as follows; To a solution of NaN_3 (8.3 g, 127 mmol) in H_2O (24 mL) was added CH_2Cl_2 (16 mL) and then added Tf_2O (5.2 mL, 31.7 mmol) at 0 °C. After the reaction mixture was stirred vigorously for 3 h at 0 °C, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (8 mL ×2). The organic layers were combined and washed with saturated aqueous $NaHCO_3$ and used immediately.)

To a suspension of Allyl 2-amino-2-deoxy-α-D-glucopyranoside (crude 7.7 g from **S1** 12.7 mmol) in MeOH (81 mL) was added a solution of TfN_3 in CH_2Cl_2 (32 mL) and DMAP (5.4 g, 44.5 mmol) at room temperature. After being stirred vigorously overnight, the reaction mixture was concentrated in vacuo. The residue was dissolved in EtOAc, and insoluble materials were filtered off. The filtrate was then concentrated *in vacuo*. The residue was purified by silica-gel column chromatography ($CHCl_3$: MeOH = 15 : 1 → 5 : 1) to give crude Allyl 2-azido-2-deoxy-α-D-glucopyranoside as a major product.

To a solution of Allyl 2-azido-2-deoxy-α-D-glucopyranoside (crude 6.1 g, from **S1** 12.7 mmol) in dry DMF (121 mL) was added NaH (60%, 2.5 g, 62.5 mmol) at 0 °C under Ar. After the reaction was stirred for 45 min, BnBr (7.5 mL, 63.5 mmol) was added to the reaction at 0 °C. The reaction mixture was stirred overnight at room temperature and quenched with saturated aqueous $NaHCO_3$, and then extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and the aqueous layer was extracted with EtOAc. The organic layers were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica-gel column chromatography (Toluene : EtOAc = 30 : 1) to give **6** (5.5 g, 84% from **S1**) as yellow oil.

ESI-MS (positive) *m/z* = 516.25 $[M+H]^+$, 533.28 $[M+NH_4]^+$, 538.22 $[M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.38-7.14 (m, 15H, $C_6\underline{H_5}$-CH_2-O-×3), 5.96-5.88 (m, 1H,

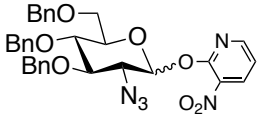
-CH_2-C<u>H</u>=CH_2), 5.35-5.31 (m, 1H, -CH_2-CH=C<u>H_2</u>), 5.23-5.20 (m, 1H, -CH_2-CH=C<u>H_2</u>), 4.98 (d, *J* =3.5 Hz, 1H, H-1), 4.90-4.48 (m, 6H, C_6H_5-C<u>H_2</u>-O-×3), 4.22-4.17 (m, 1H, -C<u>H_2</u>-CH=CH_2), 4.07-4.03 (m, 1H, -C<u>H_2</u>-CH=CH_2), 4.01 (dd, 1H, *J* = 10.2 Hz, 8.9 Hz, H-3), 3.84 (ddd, *J* = 10.1 Hz, 3.5 Hz, 2.15 Hz, 1H, H-5), 3.77-3.64 (m, 3H, H-4 and H-6), 3.40 (dd, *J* = 10.2 Hz, 3.5 Hz, 1H, H-2).



2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranose (7)

To a solution of **6** (995.2 mg, 1.93 mmol) in dry THF (7.5 mL) was added a solution of activated iridium complex [Ir(cod)(PMe(C_6H_5)$_2$)$_2$]PF_6 in dry THF under Ar. The mixture was stirred under Ar at room temperature for 4 h. Water (5 mL) and iodine (1.47 g, 5.79 mmol) were then added at room temperature, and the reaction mixture was stirred for 30 min. After excess of iodine was quenched with 5% aqueous $Na_2S_2O_3$, the reaction mixture was extracted with EtOAc. The organic layer was washed with 5% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$ and brine. The solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (Toluene : EtOAc = 10 : 1) to give **7** of α / β mixture (731 mg, 80%) as a yellow solid.

^{1}H-NMR (500 MHz, $CDCl_3$) **7-α form:** δ (ppm) = 7.38-7.13 (m, 15H, C_6<u>H_5</u>-CH_2-O-×3), 5.33 (d, *J* = 3.4 Hz, 1H, H-1), 4.90-4.78 and 4.60-4.49 (m, 6H, C_6H_5-C<u>H_2</u>-O-×3), 4.04 (ddd, *J* = 10.1 Hz, 4.3 Hz, 2.0 Hz, 1H, H-5), 4.01 (dd, *J* = 10.0, 9.0 Hz, 1H, H-3), 3.71-3.57 (m, 3H, H-4 and H-6), 3.45 (dd, *J* = 10.2, 3.5 Hz, 1H, H-2); ESI-MS (positive) *m/z* = 493.28 $[M+NH_4]^+$, 498.23 $[M+Na]^+$, 514.20 $[M+K]^+$; HR-MS (*m/z*): Calcd. for $C_{27}H_{29}N_3O_5Na$ $[M+Na]^+$, 498.2005: Found, 498.2008.

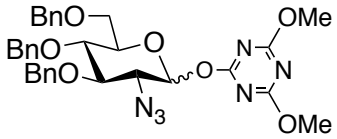


3-Nitro-2-pyridyl 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranoside (2a)

Azide sugar **7** was dehydrated by lyophilization of the benzene solution before the reaction. To a mixture of **46** (943.9 mg, 1.98 mmol) and 2-bromonitropyridine (483.7 mg, 2.38 mmol) in dry

THF (20 mL) was added NaH (60%, 283 mg, 7.08 mmol) at 0 °C under Ar. After the reaction mixture was stirred for 6 h, the mixture was allowed to warm up gradually to 10 °C and then 2-bromonitropyridine (120.8 mg, 0.595 mmol) was added again. The reaction mixture was stirred for 2 h and quenched with brine, and then extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and the aqueous layer was extracted with EtOAc. The organic layers were combined, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (Toluene : EtOAc = 40 : 1 → 5 : 1) to give **2a** of α / β (= 15 / 85) mixture (876.5 mg, 74%) as a yellow solid.

ESI-MS (positive) *m/z* = 615.25 $[M+NH_4]^+$, 620.21 $[M+Na]^+$, 636.23 $[M+K]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) **2a-β form:** δ (ppm) = 8.39-7.13 (m, 19H, Ph-×3 and NPy), 6.02 (d, *J* = 8.5 Hz, 1H, H-1), 4.94-4.81 and 4.58-4.44 (m, 6H, C_6H_5-CH_2-O-×3), 3.83 (dd, *J* = 9.8 Hz, 8.4 Hz, 1H, H-2), 3.77 (dd, *J* = 9.6 Hz, 9.0 Hz, 1H, H-4), 3.72 (d, *J* = 3.1 Hz, 2H, H-6), 3.66 (dt, *J* = 9.6 Hz, 3.1 Hz, 1H, H-5), 3.59 (dd, *J* = 9.8 Hz, 9.0 Hz, 1 H, H-3).

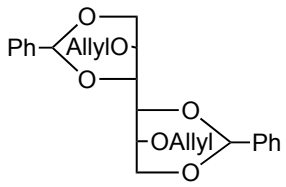


4,6-dimethoxy-1,3,5-triazine-2-yl-2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranoside (2b)

To a mixture of **7** (144.0 mg, 0.30mmol) and DMT-MM (165.4 mg, 0.60mmol) in dry THF (3.0 mL) was added DBU (53.7 μ L, 0.36 mmol) at 0˚C under Ar. After the addition of DBU, the reaction mixture was allowed to warm up gradually to room temperature and stirred for 8 h. The reaction mixture was quenched with brine, and then extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and was then dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (Toluene : EtOAc = 25 : 1→ 10 : 1→ 5 : 1) to give **2b** (189.2 mg, 93%) as colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$) **2b-β form**: δ (ppm) = 7.35-7.17 (m, 15H, Ph-×3), 5.81 (d, *J* = 8.5 Hz, 1H, H-1), 4.90-4.80 and 4.60-4.45 (m, 6H, C_6H_5-CH_2-O-×3), 4.02 (s, 6H, CH_3-O-×2) 3.76 (dd, *J* = 9.5 Hz, 9.3 Hz, 1H, H-2), 3.73 (d, *J* = 3.9 Hz, 2H, H-6), 3.72 (dd, *J* = 6.1 Hz, 8.6 Hz, 1H, H-4), 3.63 (dt, *J* = 12 Hz, 3.0 Hz, 1H, H-5), 3.60 (dd, *J* = 9.0 Hz, 9.8 Hz, 1 H, H-3); ESI-MS (positive) *m/z* = 637.2474 $[M+Na]^+$

3. Preparation of **3a** (in Scheme 2)



1,3:4,6-Di-*O*-benzylidene-2,5-di-*O*-allyl-D-mannitol (9)

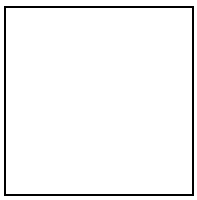
To a solution of D-mannitol (50 g, 0.27 mol) in DMF (200 mL) was added benzaldehyde (60 mL, 0.69 mol) at room temperature under Ar. To the mixture was added concentrated sulfuric acid (10 mL) dropwisely at 0 ˚C. After being allowed to warm up gradually to the room temperature, the mixture was stirred for 5 d. Then the mixture was poured into 1.2 L of ice water containing 20 g of $NaHCO_3$ and 200mL of *n*-hexane under vigorous stirring. After the mixture was allowed to warm up gradually to the room temperature, the precipitate was filtered and washed with *n*-hexane. The precipitate was suspended in chloroform and heated under reflux for 15 min under vigorous stirring. When the mixture reached room temperature, the undissolved precipitate was collected. Recrystallization from MeOH gave **1,3:4,6-Di-*O*-benzylidene-D-mannitol** (19 g, 20%) as a colorless needle crystal.

ESI-MS (positive) *m/z* = 381.11 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.46-7.25 (m, 10H, $C_6\underline{H}_5$-), 5.50 (s, 2H, acetal-H), 4.38 (dd, *J* = 10.5, 5.3 Hz, 2H, H-1eq and H-6eq), 4.21 (m, 2H, H-2 and H-5), 4.16 (m, 2H, H-1ax and H-6ax), 3.65 (t, *J* = 10.3 Hz, 2H, H-3 and H-4), 2.94 (s, 2H, -O<u>H</u>); Anal. Calcd. for $C_{20}H_{22}O_6$: C, 67.03; H, 6.19%. Found: C, 66.82; H, 6.10%.

To a suspension of NaH (60%, 1.3 g, 31.8 mmol) in dry DMF (30 mL) was added **1,3:4,6-Di-*O*-benzylidene-D-mannitol** in dry DMF (70 mL) dropwise at 0 ˚C under Ar and the mixture was stirred for 10 min. Then allyl bromide (3.4 mL, 39.8 mmol) was added dropwise to the reaction mixture at 0 ˚C. After the mixture was allowed to warm up gradually to the room temperature, the mixture was stirred for 15 min. Then the mixture was poured into ice water containing diethyl ether under vigorous stirring. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (mobile phase: $CHCl_3$) to

give **9** (5.3 g, 76%) as a colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.45-7.25 (m, 10H, $C_6\underline{H}_5$-), 5.91-5.81 (m, 2H, -CH_2-C$\underline{H}$=CH_2), 5.49 (s, 2H, acetal-H), 5.23 (ddd, *J* = 17.0, 3.17, 1.47 Hz, 2H, -CH_2-CH=C$\underline{H}_2$ cis), 5.15 (ddd, *J* = 10.2, 2.68, 1.22 Hz, 2H, -CH_2-CH=C$\underline{H}_2$ trans), 4.40 (dd, *J* = 10.5, 5.1 Hz, 2H, H-1eq and H-6eq), 4.05-4.10 (m, 2H, -C$\underline{H}_2$-CH=CH_2), 4.01 (dd, *J* = 10.2, 1.3 Hz, 2H, H-1ax and H-6ax), 3.95-3.90 (m, 2H, H-2 and H-5), 3.65 (t, *J* = 10.3 Hz, 2H, H-3 and H-4); Anal. Calcd. for $C_{26}H_{30}O_6$: C, 71.21; H, 6.90%. Found: C, 71.22; H, 6.91%.



2,5-Di-*O*-allyl-1,6-di-*O*-*tert*-butyldimethylsilyl-D-mannitol (10)

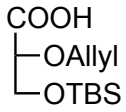
To a suspension of **9** (7.5 g, 17.1 mmol) in 16.5 mL of EtOH and 3.5 mL of water was added 1N HCl aq. (1.2 mL). The mixture was heated at 70 ˚C and stirred for 3 h. Being cooled at 0 ˚C, the reaction was quenched by addition of $NaHCO_3$. Insoluble materials were filtered off and the filtrate was concentrated in vacuo. The residue was recrystallized from EtOAc-hexane to give pure **2,5-Di-*O*-allyl-D-mannitol** (0.46g, 77%) as colorless crystal.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 5.95-5.85 (m, 2H, -CH_2-C$\underline{H}$=CH_2), 5.28 (ddd, *J* = 17.3, 3.17, 1.46 Hz, 2H, -CH_2-CH=C$\underline{H}_2$ cis), 5.21 (ddd, *J* = 10.2, 2.93, 1.22 Hz, 2H, -CH_2-CH=C$\underline{H}_2$ trans), 4.20-4.16 (m, 4H, -C$\underline{H}_2$-CH=CH_2), 3.93 (t, *J* = 4.76, 2H, H-3 and H-4), 3.88-3.77 (m, 4H, H-1 and H-6), 3.58-3.53 (m, 2H, H-2 and H-5), 3.08 (d, *J* = 4.40, 2H, 3-O$\underline{H}$ and 4-O$\underline{H}$), 2.49 (s, 2H, 1-O$\underline{H}$ and 6-O$\underline{H}$); Anal. Calcd. for $C_{12}H_{22}O_6$: C, 54.95; H, 8.45%. Found: C, 54.59; H, 8.36%.

To a mixture of **2,5-Di-*O*-allyl-D-mannitol** (1.95 g, 7.4 mmol) and imidazole (2.01 g, 29.6 mmol) in dry CH_2Cl_2 (50 mL) was added TBSCl (2.45 g, 16.2 mmol) at room temperature and the mixture was stirred for 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ and the mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (toluene: EtOAc = 20: 1) to give **10** (3.56 g, 97% from **2,5-Di-*O*-allyl-D-mannitol**) as colorless oil.

ESI-MS (positive) *m/z* = 491.34 $[M+H]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.91 (ddt, *J* = 18.7, 9.5, 4.0 Hz, 2H, -CH_2-C$\underline{H}$=CH_2), 5.25 (dq, *J* = 17.2, 1.6 Hz, 2H, -CH_2-CH=C$\underline{H}_2$ cis), 5.15 (ddd, *J* = 10.4, 2.9, 1.2 Hz, 2H, -CH_2-CH=C$\underline{H}_2$ trans), 4.23-4.00 (m, 4H, -C$\underline{H}_2$-CH=CH_2),

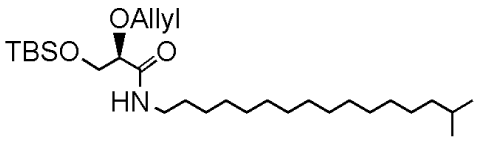
3.88-3.80 (m, 4H, H-1a, H-6a, H-3 and H-4), 3.79-3.75 (m, 2H, H-1b and H-6b), 3.54 (dd, J = 11.6, 5.2 Hz, 2H, H-2 and H-5), 3.26 (d, J = 5.3 Hz, 2H, -OH×2), 0.90 (s, 18H, *t*-butyl-H), 0.08 (s,12H, -Si-($C\underline{H}_3$)$_2$); Anal. Calcd. for $C_{24}H_{50}O_6Si$: C, 58.73; H, 10.27%. Found: C, 58.61; H, 10.32%.



(*R*)-2-Allyloxy-3-*t*-butyldimethylsilyloxy-propanoic acid (13)

To a solution of **10** (1.74 g, 3.5 mmol) in dry THF (35 mL) was added $Pb(OAc)_4$ (2.2 g, 5.0 mmol) and the mixture was stirred for 30 min at room temperature. Insoluble materials were filtered off by Celite® and the filtrate was concentrated in vacuo to give crude compound **11**. The residue was dissolved in THF: *t*-BuOH: H_2O (=3: 4: 1) (70 mL). To the solution were added NaH_2PO_4 (0.83 g, 7.0 mmol) and 2-methyl-2-butene (3.7 mL, 35.0 mmol). Then 80% $NaClO_4$ (1.58 g, 14.0 mmol) was added and the mixture was stirred for 20 min at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography ($CHCl_3$: MeOH: AcOH = 30: 1: 1) to give **11** (1.27 g, 70% for 2 steps) as colorless oil.

ESI-MS (negative) m/z = 259.13 $[M-H]^-$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.94-5.91 (m, 1H, -CH_2-C$\underline{H}$=CH_2), 5.35-5.25 (m, 2H, -CH_2-CH=C$\underline{H}_2$), 4.28-4.01 (m, 4H, -C$\underline{H}_2$-CH=CH_2, -C$\underline{H}_2$OTBS), 3.96-3.90 (m, 1H, -C$\underline{H}$(OAllyl)-COOH), 0.88 (s, 6H, -C($C\underline{H}_3$)$_3$), 0.09 (s, 6H, Si-($C\underline{H}_3$)$_2$).

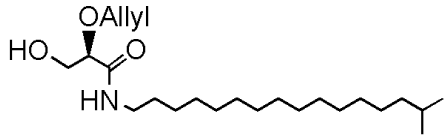


(*R*)-1-Allyloxy-2-*t*-butyldimethylsilyloxy-1-(15-methylhexadecanylcarbamoyl)ethane (15)

To a mixture of amine **14a** (34 mg, 0.13 mmol) and the appropriately protected glyceric acid **8** (51 mg, 0.20 mmol) in dry $CHCl_3$ (1.3 mL) were added -hydroxy-7-azabenzotriazole (HOAt) (27 mg, 0.20 mmol) and *N*,*N*′-diisopropylcarbodiimide (DIC) (41 μL, 0.26 mmol, 2.0 eq.) at room temperature. After the mixture was stirred for 10 h, the reaction was quenched with

saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (toluene: EtOAc: HFIP = 30: 1: 0.3) to give **15** (50.8 mg, 79%) as colorless oil.

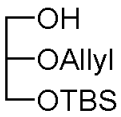
ESI-MS (positive) *m/z* = 498.43 $[M+H]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 6.63 (s, 1H, -CONH-) 5.94-5.88 (m, 1H, $-CH_2-CH=CH_2$), 5.30 (d, *J* = 17.2, 1.5 Hz, 1H, $-CH_2-CH=CH_2$ cis), 5.21 (dd, *J* = 10.4, 1.2 Hz, 1H, $-CH_2-CH=CH_2$ trans), 4.15-4.11 (m, 2H, $-CH_2-CH=CH_2$), 3.97 (dd, *J* = 10.8, 2.4 Hz, 1H, -CH(OAllyl)-CONHR), 3.88-3.80 (m, 2H, $-CH_2$OTBS), 3.29-3.20 (m, 2H, -NH-CH_2-), 1.55-1.48 (m, 3H, $-NH-CH_2-CH_2-$ and $-CH(CH_3)_2$), 1.30-1.12 (m, 24H, $-(CH_2)-\times12$), 0.88 (s, 9H, $-C(CH_3)_3$), 0.86 (d, *J* = 6.6 Hz, 6H, $-CH(CH_3)_2$), 0.06 (s, 6H, Si-$(CH_3)_2$); Anal. Calcd. For $C_{29}H_{59}NO_3Si\bullet0.25H_2O$: C, 69.33; H, 11.94; N, 2.79%. Found: C, 69.35; H, 11.95; N; 2.98%.



(*R*)-1-Allyloxy-2-hydroxy-1-(15-methylhexadecanylcarbamoyl)ethane (3a)

To a solution of **15** (0.12 g, 0.24 mmol) in dry THF (4.2 mL) was added TBAF 1M THF solution (0.72 mL, 0.72 mmol) and the mixture was stirred for 30 min at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ and the mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (toluene: EtOAc: HFIP = 1: 1: 0.02) to give **3a** (78 mg, 85%) as a colorless solid.

ESI-MS (positive) *m/z* = 384.35 $[M+H]^+$, 406.33 $[M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 6.59 (s, 1H, -CONH-) 5.88-5.82 (m, 1H, $-CH_2-CH=CH_2$), 5.28-5.13 (m, 2H, $-CH_2-CH=CH_2$), 4.10-4.00 (m, 2H, $-CH_2-CH=CH_2$), 3.83 (t, *J* = 5.1 Hz, 1H, -CH(OAllyl)-CONHR), 3.78-3.70 (m, 2H, $-CH_2$OH), 3.24-3.18 (m, 2H, -NH-CH_2-), 1.49-1.42 (m, 3H, $-NH-CH_2-CH_2-$ and $-CH(CH_3)_2$), 1.23-1.06 (m,24H, $-(CH_2)-\times12$), 0.79 (d, *J* = 6.7 Hz, 6H, $-CH(CH_3)_2$); Anal. Calcd. for $C_{23}H_{45}NO_3$: C, 72.01; H, 11.82; N, 3.70%. Found: C, 71.74; H, 11.81; N; 3.70%.



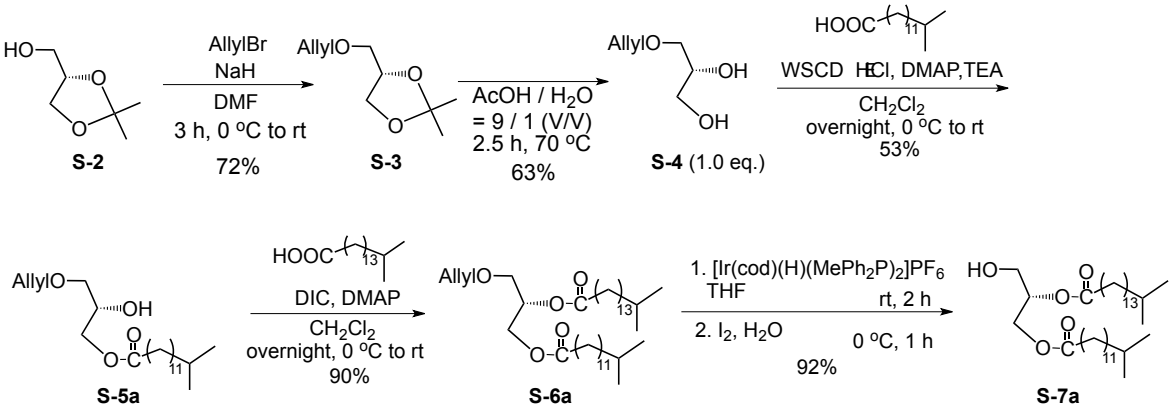
2-*O*-allyl-1-*O*-*t*-butyldimethylsilyl-*sn*-glycerol (12)

To a solution of **10** (3.73 g, 7.62 mmol) in dry THF (50 mL) was added $Pb(OAc)_4$ (4.74 g, 10.7 mmol) and the mixture was stirred for 1 h at room temperature. Insoluble materials were filtered off by Celite® to give a solution of crude compound **11**. To the filtrate was added $NaBH_4$ (0.58 g, 15.2 mmol) in 30 mL of water dropwise at 0 ˚C. After the mixture was allowed to warm up gradually to the room temperature, the mixture was stirred for 15 h. The reaction was diluted with 30 mL of water and the mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (toluene: EtOAc = 20: 1) to give **12** (2.4 g, 65% for 2 steps from **10**) as colorless oil.

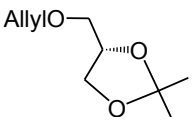
ESI-MS (positive) *m/z* = 269.16 $[(M+Na)^+]$; ^{1}H-NMR (270 MHz, $CDCl_3$) δ (ppm) = 5.92 (ddt, *J* = 18.7, 9.5, 4.1, 1H, -CH_2-C<u>H</u>=CH_2), 5.28 (dq, *J* = 17.2, 1.6 Hz, 1H, -CH_2-CH=C<u>H_2</u> cis), 5.15 (m, 1H, -CH_2-CH=C<u>H_2</u>trans), 4.20-4.00 (m, 2H, -C<u>H_2</u>-CH=CH_2), 3.79-3.50 (m, 4H, H-1 and H-3), 3.79-3.75 (m, 2H,H-2), 2.11 (t, *J*= 6.3 Hz, 1H, -OH), 0.90 (s, 9H, *t*-butyl-H), 0.08 (s, 6H, -Si-(C<u>H_3</u>)$_2$); Anal. Calcd. for $C_{12}H_{26}O_3Si$: C, 58.49; H, 10.63%. Found: C, 58.60; H, 10.66%.

4. Preparation of diacylglycerol moieties for **5a (5c**, **5d**, and **5e**)/**5b**

3-1. Diacylglycerol moieties for **5a (5c**, **5d**, and **5e**)



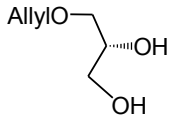
Scheme S1



3-allyl-1,2-isopropylidene-*sn*-glycerol (S-3)

To a suspension of NaH (60%, 1.82 g, 45.5 mmol) in dry DMF (43 mL) was added (*S*)-(+)-2,2-dimethyl-1,3-dioxolane-4-methanol **S-2** (3.00 g, 22.7 mmol) in dry DMF (100 mL) dropwise for 15 min at 0 °C under Ar. After the mixture was stirred for 20 min, ally bromide (4.80 mL, 56.7 mmol) was added dropwise to the reaction mixture at 0 °C. After the mixture was allowed to warm up gradually to the room temperature, the mixture was stirred for 15 min. Then the mixture was poured into ice water (100 mL) containing Et_2O (100 mL) under vigorous stirring. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography ($CHCl_3$ only) to give **S-3** (2.8 g, 72%) as colorless oil.

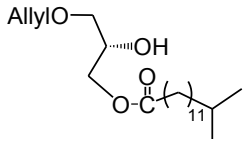
ESI-MS (positive) *m/z* = 173.14 $[M+H]^+$, 195.13 $[M+Na]^+$, 367.24 $[2M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.94-5.87 (m, 1H, -O-CH_2-C<u>H</u>=CH_2), 5.30-5.18 (m, 2H, -O-CH_2-CH=C<u>H_2</u>), 4.31-4.26 (m, 1H, Gro H-2), 4.06 (dd, *J* = 8.2 Hz, 6.4 Hz, 1H, Gro H-1a), 4.07-4.00 (m, 2H, -O-C<u>H_2</u>-CH=CH_2), 3.74 (dd, *J* = 8.2, 6.4 Hz, 1H, Gro H-1b), 3.53 (dd, *J* = 9.8 Hz, 5.7 Hz, 1H, Gro H-3a), 3.45 (dd, *J* = 9.9 Hz, 5.5 Hz, 1H, Gro H-3b), 1.43 (s, 3H, -CC<u>H_3</u>), 1.37 (s, 3H, -CC<u>H_3</u>).



3-allyl-*sn*-glycerol (S-4)

A solution of **S-3** (0.8 g, 11.6 mmol) in AcOH (20 mL) and H_2O (2.2 mL) was heated at 70 °C and stirred for 2.5 h. Being cooled at room temperature, the reaction mixture was concentrated in vacuo. The residue was purified by silica-gel column chromatography (Hexane : EtOAc =1 : 1) to give **S-4** (387 mg, 63%) as colorless oil.

ESI-MS (positive) *m/z* = 155.06 $[M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.94-5.87 (m, 1H, -O-CH_2-C<u>H</u>=CH_2), 5.32-5.20 (m, 2H, -O-CH_2-CH=C<u>H_2</u>), 4.04-4.02 (m, 2H, -O-C<u>H_2</u>-CH=CH_2), 3.91-3.87 (m, 1H, Gro H-2), 3.73 (dd, *J* = 11 Hz, 4.0 Hz, 1H, Gro H-1a), 3.65 (dd, *J* = 11 Hz, 5.3 Hz, 1H, Gro H-1b), 3.56 (dd, *J* = 9.7 Hz, 4.0 Hz, 1H, Gro H-3a), 3.52 (dd, *J* = 9.8, 6.3 Hz, 1H, Gro H-3b), 1.62 (brs, 2H, -O<u>H</u>×2).



3-Allyl-1-(13-methyltetradecanoyl)-*sn*-glycerol (S-5a)

To a mixture of **S-4** (35.0 mg, 0.265 mmol) and **13-methyltetradecanoic acid** (25.7 mg, 0.106 mmol) in dry CH_2Cl_2 (2.6 mL) was added WSCD·HCl (55.8 mg, 0.291 mmol), DMAP (25.9 mg, 0.212 mmol) and TEA (74.4 μg, 0.530 mmol) at 0 °C under Ar. After the mixture was stirred for 1 h, the reaction mixture was stirred overnight at room temperature. The reaction mixture was quenched with MeOH (420 μL), then a small amount of AcOH and extracted with CH_2Cl_2. The solution was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (1st $CHCl_3$ only; 2nd Hexane : EtOAc = 15 : 1) to give **S-5a** (24.8 mg, 66%) as colorless oil.

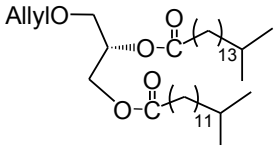
ESI-MS (positive) *m/z* = 357.35 $[M+H]^+$, 374.37 $[M+NH_4]^+$, 379.32 $[M+Na]^+$, 735.67 $[2M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.94-5.86 (m, 1H, -O-CH_2-C<u>H</u>=CH_2), 5.30-5.19 (m, 2H, -O-CH_2-CH=C<u>H$_2$</u>), 4.18 (dd, *J* = 11.6 Hz, 4.4 Hz, 1H, Gro H-1a), 4.13 (dd, *J* = 11.5, 6.1 Hz, 1H, Gro H-1b), 4.04-4.00 (m, 3H, -O-C<u>H$_2$</u>-CH=CH_2 and Gro H-2), 3.52 (dd, *J* = 9.6, 4.3 Hz, 1H, Gro H-3a), 3.46 (dd, *J* = 9.6, 6.3 Hz, 1H, Gro H-3b), 2.34 (t, *J* = 7.5 Hz, 2H, -OCOC<u>H$_2$</u>-), 1.66-1.60 (m, 2H, -OCOCH_2-C<u>H$_2$</u>-), 1.55-1.48 (m, 1H, -C<u>H</u>$(CH_3)_2$), 1.29-1.26 (m, 16H, -OCO-CH_2-CH_2-(C<u>H$_2$</u>)$_8$-), 1.17-1.13 (m, 2H, -C<u>H$_2$</u>-CH$(CH_3)_2$), 0.86 (d, *J* = 6.8 Hz, 6H, -CH(C<u>H$_3$</u>)$_2$).

3-Allyl-1-myristoyl-*sn*-glycerol (S-5b)

In a manner similar to the synthesis of **S-5a**, it condensed a primary alcohol of **S-4** (136.2 mg, 1.03 mmol) and myristic acid (95.0 mg, 0.412 mmol) to give **S-5b** (80.6 mg, 57%) as colorless oil.

ESI-MS (positive) *m/z* = 343.27 $[M+H]^+$, 365.26 $[M+Na]^+$, 381.25 $[M+K]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.93-5.87 (m, 1H, -O-CH_2-C<u>H</u>=CH_2), 5.30-5.19 (m, 2H, -O-CH_2-CH=C<u>H$_2$</u>), 4.19 (dd, *J* = 11.5 Hz, 4.3 Hz, 1H, Gro H-1a), 4.13 (dd, *J* = 11.6 Hz, 6.2 Hz, 1H, Gro H-1b), 4.04-4.01 (m, 3H, -O-C<u>H$_2$</u>-CH=CH_2 and Gro H-2), 3.52 (dd, *J* = 9.7 Hz, 4.3 Hz, 1H, Gro H-3a), 3.46 (dd, *J* = 9.8 Hz, 6.3 Hz, 1H, Gro H-3b), 2.34 (t, *J* = 7.6 Hz, 2H, -OCOC<u>H$_2$</u>-), 1.66-1.60 (m, 2H, OCOCH_2-C<u>H$_2$</u>-), 1.33-1.26 (m, 20H,

-OCO-CH_2-CH_2-(CH_2)$_{10}$-CH_3), 0.88 (t, J = 6.9 Hz, 3H, -CH_2-CH_3).



3-Allyl-1-(13-methyltetradecanoyl)-2-(15-methylhexadecanoyl)-*sn*-glycerol (S-6a)

To a mixture of **S-5a** (152.6 mg, 0.428 mmol) and **15-methylhexadecanoic acid** (139.0 mg, 0.514 mmol) in dry CH_2Cl_2 (7.5 mL) was added DMAP (10.5 mg, 0.0856 mmol) and DIC (132 μL, 0.856 mmol) at 0 °C under Ar. Ar. After the mixture was stirred for 10 min, the reaction mixture was stirred overnight at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (Hexane : EtOAc = 30 : 1) to give **S-6a** (233.9 mg, 90%) as colorless oil.

ESI-MS (positive) m/z = 626.56 $[M+NH_4]^+$, 631.51 $[M+Na]^+$, 1240.00 $[2M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.90-5.83 (m, 1H, -O-CH_2-C$\underline{H}$=CH_2), 5.28-5.18 (m, 3H, -O-CH_2-CH=C$\underline{H_2}$ and Gro H-2), 4.34 (dd, J = 12 Hz, 3.7 Hz, 1H, Gro H-1a), 4.17 (dd, J = 12 Hz, 6.4 Hz, 1H, Gro H-1b), 4.03-3.96 (m, 2H, -O-C$\underline{H_2}$-CH=CH_2), 3.56 (d, J = 5.2 Hz, 2H, Gro H-3), 2.32 (t, J = 7.5 Hz, 2H, -OCOC$\underline{H_2}$-), 2.30 (t, J = 7.5 Hz, 2H, -OCOC$\underline{H_2}$-), 1.63-1.59 (m, 4H, -OCOCH_2-C$\underline{H_2}$-×2), 1.54-1.49 (m, 2H, -C$\underline{H}$(CH_3)$_2$×2), 1.28-1.26 (m, 36H, -(C$\underline{H_2}$)-×18), 1.16-1.14 (m, 4H, -C$\underline{H_2}$-CH(CH_3)$_2$×2), 0.86 (d, J = 6.8 Hz, 12H, -CH(C$\underline{H_3}$)$_2$×2).

3-Allyl-1,2-di-(15-methylhexadecanoyl)-*sn*-glycerol (S-6c)

To a mixture of **S-4** (77.7 mg, 0.588 mmol) and **15-methylhexadecanoic acid** (381.6 mg, 1.41 mmol) in dry CH_2Cl_2 (15 mL) was added DMAP (28.7 mg, 0.235 mmol) and DIC (364 μL, 2.35 mmol) at 0 °C under Ar. Ar. After the mixture was stirred for 30 min, the reaction mixture was stirred overnight at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (Hexane : EtOAc = 30 : 1) to give **S-6c** (338.8 mg, 90%) as colorless oil.

ESI-MS (positive) m/z = 637.54 $[M+H]^+$, 654.59 $[M+NH_4]^+$, 659.53 $[M+Na]^+$, 1297.19 $[2M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.90-5.83 (m, 1H, -O-CH_2-C$\underline{H}$=CH_2),

5.28-5.18 (m, 3H, -O-CH_2-CH=CH_2 and Gro H-2), 4.34 (dd, J = 12 Hz, 3.7 Hz, 1H, Gro H-1a), 4.17 (dd, J = 12 Hz, 6.4 Hz, 1H, Gro H-1b), 4.01-3.99 (m, 2H, -O-CH_2-CH=CH_2), 3.56 (d, J = 5.2 Hz, 2H, Gro H-3), 2.32 (t, J = 7.5 Hz, 2H, -OCOCH_2-), 2.30 (t, J = 7.5 Hz, 2H, -OCOCH_2-), 1.63-1.59 (m, 4H, -OCOCH_2-CH_2-×2), 1.54-1.49 (m, 2H, -CH(CH_3)$_2$×2), 1.28-1.26 (m, 40H, -(CH_2)-×20), 1.17-1.13 (m, 4H, -CH_2-CH(CH_3)$_2$×2), 0.86 (d, J = 6.8 Hz, 12H, -CH(CH_3)$_2$×2).

3-Allyl-1-myristoyl-2-palmitoyl-*sn*-glycerol (S-6d)

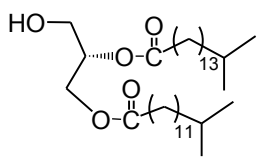
In a manner similar to the synthesis of **S-6a**, it condensed a secondary alcohol of **S-4** (68.1 mg, 0.228 mmol) and palmitic acid (76.0 mg, 0.296 mmol) to give **S-6d** (120.9 mg, 91%) as colorless oil.

ESI-MS (positive) m/z = 581.55 $[M+H]^+$, 598.52 $[M+NH_4]^+$, 603.47 $[M+Na]^+$, 1183.95 $[2M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.90-5.83 (m, 1H, -O-CH_2-CH=CH_2), 5.28-5.17 (m, 3H, -O-CH_2-CH=CH_2 and Gro H-2), 4.34 (dd, J = 12 Hz, 3.9 Hz, 1H, Gro H-1a), 4.17 (dd, J = 12 Hz, 6.4 Hz, 1H, Gro H-1b), 4.01-3.99 (m, 2H, -O-CH_2-CH=CH_2), 3.56 (d, J = 5.4 Hz, 2H, Gro H-3), 2.32 (t, J = 7.6 Hz, 2H, -OCOCH_2-), 2.30 (t, J = 7.6 Hz, 2H, OCOCH_2-), 1.65-1.58 (m, 4H, OCOCH_2-CH_2-×2), 1.31-1.26 (m, 44H, -(CH_2)-×22), 0.88 (d, J = 6.7 Hz, 6H, -CH_2CH_3×2).

3-Allyl-1,2-di-palmitoyl-*sn*-glycerol (S-6e)

In a manner similar to the synthesis of **S-6a**, it condensed alcohols of **S-4a** (64.8 mg, 0.490 mmol) and palmitic acid (301.7 mg, 1.18 mmol) to give **S-6e** (201.3 mg, 71%) as a white solid.

ESI-MS (positive) m/z = 609.47 $[M+H]^+$, 626.54 $[M+NH_4]^+$, 631.53 $[M+Na]^+$, 1240.02 $[2M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.90-5.83 (m, 1H, -O-CH_2-CH=CH_2), 5.28-5.17 (m, 3H, -O-CH_2-CH=CH_2 and Gro H-2), 4.34 (dd, J = 12 Hz, 3.9 Hz, 1H, Gro H-1a), 4.17 (dd, J = 12 Hz, 6.4 Hz, 1H, Gro H-1b), 4.01-3.98 (m, 2H, -O-CH_2-CH=CH_2), 3.56 (d, J = 5.4 Hz, 2H, Gro H-3), 2.32 (t, J = 7.6 Hz, 2H, -OCOCH_2-), 2.30 (t, J = 7.6 Hz, 2H, -OCOCH_2-), 1.63-1.56 (m, 4H, -OCOCH_2-CH_2-×2), 1.30-1.26 (m, 48H, -(CH_2)-×24), 0.88 (d, J = 6.7 Hz, 6H, -CH_2CH_3×2).



1-(13-Methyltetradecanoyl)-2-(15-methylhexadecanoyl)-*sn*-glycerol (S-7a)

To a solution of **S-6a** (217.8 mg, 0.358 mmol) in dry THF (5 mL) was added a solution of activated iridium complex $[Ir(cod)(PMe(C_6H_5)_2)_2]PF_6$ in dry THF under Ar. The mixture was stirred under Ar at room temperature for 2 h. Water (4 mL) and iodine (271.5 mg, 1.07 mmol) were then added at 0 °C, and the reaction mixture was stirred for 1 h. After excess of iodine was quenched with 5% aqueous $Na_2S_2O_3$, the reaction mixture was extracted with EtOAc. The organic layer was washed with 5% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$ and brine. The solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by rapid silica-gel (Neutral) column chromatography (Toluene : EtOAc : HFIP = 20 : 1 : 0.1) to give **S-7a** (188.2 mg, 92%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.10-5.06 (m, 1H, Gro H-2), 4.32 (dd, J = 12 Hz, 4.5 Hz, 1H, Gro H-1a), 4.24 (dd, J = 12 Hz, 5.7 Hz, 1H, Gro H-1b), 3.76-3.70 (m, 2H, Gro H-3), 2.34 (t, J = 7.5 Hz, 2H, -OCOC$\underline{H}_2$-), 2.32 (t, J = 7.5 Hz, 2H, -OCOC$\underline{H}_2$-), 2.01 (brs, 1H, -OH), 1.66-1.60 (m, 4H, -OCOCH$_2$-C$\underline{H}_2$-×2), 1.59-1.48 (m, 2H, -C$\underline{H}$(CH$_3$)$_2$×2), 1.29-1.26 (m, 36H, -(C$\underline{H}_2$)-×18), 1.16-1.14 (m, 4H, -C$\underline{H}_2$-CH(CH$_3$)$_2$×2), 0.86 (d, J = 6.6 Hz, 12H, -CH(C$\underline{H}_3$)$_2$×2); m.p. 30.5-31.5 °C; ESI-MS (positive) m/z = 551.49 $[M-H_2O+H]^+$, 586.52 $[M+NH_4]^+$, 591.49 $[M+Na]^+$; HR-MS (m/z): Calcd. for $C_{35}H_{68}O_5Na$ $[M+Na]^+$, 591.4964: Found, 591.4954;

1,2-Di-(15-methylhexadecanoyl)-*sn*-glycerol (S-7c)

In a manner similar to the synthesis of **S-7a**, Allyl group of **S-6c** (320.8 mg, 0.504 mmol) was deprotected to give **S-7c** (238.2 mg, 79%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.10-5.06 (m, 1H, Gro H-2), 4.32 (dd, J = 12 Hz, 4.5 Hz, 1H, Gro H-1a), 4.24 (dd, J = 12 Hz, 5.7 Hz, 1H, Gro H-1b), 3.76-3.70 (m, 2H, Gro H-3), 2.34 (t, J = 7.5 Hz, 2H, -OCOC$\underline{H}_2$-), 2.32 (t, J = 7.5 Hz, 2H, -OCOC$\underline{H}_2$-), 2.01 (brs, 1H, -OH), 1.66-1.59 (m, 4H, -OCOCH$_2$-C$\underline{H}_2$-×2), 1.56-1.48 (m, 2H, -C$\underline{H}$(CH$_3$)$_2$×2), 1.30-1.21 (m, 40H, -(C$\underline{H}_2$)-×24), 1.17-1.13 (m, 4H, -C$\underline{H}_2$-CH(CH$_3$)$_2$×2), 0.86 (d, J = 6.6 Hz, 12H, -CH(C$\underline{H}_3$)$_2$×2); Anal. Calcd. for $C_{37}H_{72}O_5$; C, 74.44; H, 12.16%, Found: C, 73.73; H, 11.86%.m.p. 40-41 °C; ESI-MS (positive) m/z = 579.52 $[M-H_2O+H]^+$, 614.56 $[M+NH_4]^+$, 619.46 $[M+Na]^+$; HR-MS (m/z): Calcd. for $C_{37}H_{72}O_5Na$ $[M+Na]^+$, 619.5277: Found, 619.5281.

1-Myristoyl-2-palmitoyl-*sn*-glycerol (S-7d)

In a manner similar to the synthesis of **S-7a**, Allyl group of **S-6d** (125.3 mg, 0.216 mmol) was deprotected to give **S-7d** (98.7 mg, 85%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.10-5.06 (m, 1H, Gro H-2), 4.32 (dd, J = 12 Hz, 4.6

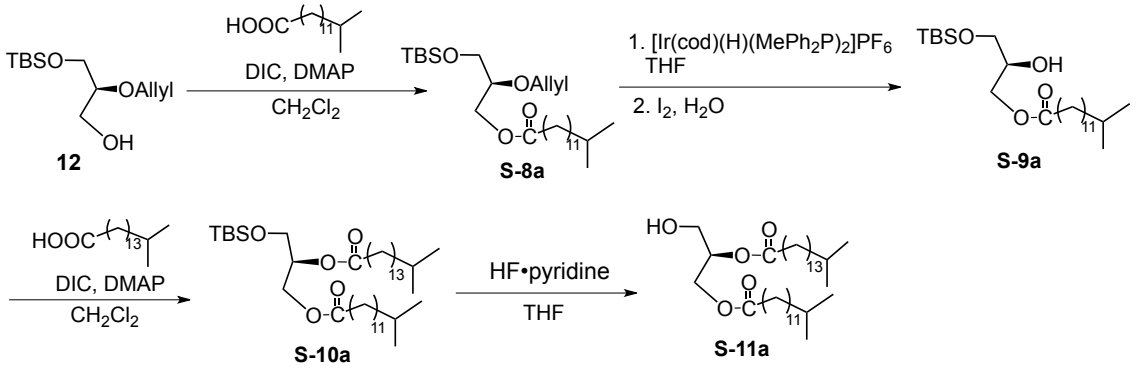
Hz, 1H, Gro H-1a), 4.24 (dd, *J* = 12 Hz, 5.7 Hz, 1H, Gro H-1b), 3.74-3.72 (m, 2H, Gro H-3), 2.34 (t, *J* = 7.5 Hz, 2H, -OCOC$\underline{H_2}$-), 2.32 (t, *J* = 7.5 Hz, 2H, -OCOC$\underline{H_2}$-), 1.99 (t, *J* = 6.2 Hz, 1H, -O$\underline{H}$), 1.66-1.59 (m, 4H, -OCOCH$_2$-C$\underline{H_2}$-×2), 1.29-1.26 (m, 44H, -(C$\underline{H_2}$)-×22), 0.88 (d, *J* = 6.9 Hz, 6H, -CH$_2$C$\underline{H_3}$×2); m.p. 59-60 °C; ESI-MS (positive) *m/z* = 523.46 $[M-H_2O+H]^+$, 558.51 $[M+NH_4]^+$; HR-MS (*m/z*): Calcd. for $C_{33}H_{64}O_5Na$ $[M+Na]^+$, 563.4651: Found, 563.4651.

1,2-Di-palmitoyl-*sn*-glycerol (S-7e)

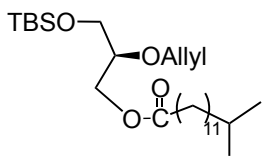
In a manner similar to the synthesis of **S-7a**, Allyl group of **S-6a** (194.2 mg, 0.319 mmol) was deprotected to give **S-7e** (143.1 mg, 79%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.10-5.06 (m, 1H, Gro H-2), 4.32 (dd, *J* = 12 Hz, 4.6 Hz, 1H, Gro H-1a), 4.24 (dd, *J* = 12 Hz, 5.7 Hz, 1H, Gro H-1b), 3.74-3.72 (m, 2H, Gro H-3), 2.34 (t, *J* = 7.5 Hz, 2H, OCOC$\underline{H_2}$-), 2.30 (t, *J* = 7.6 Hz, 2H, OCOC$\underline{H_2}$-), 1.99 (brs, 1H, -O$\underline{H}$), 1.66-1.59 (m, 4H, -OCOCH$_2$-C$\underline{H_2}$-×2), 1.31-1.26 (m, 48H, -(C$\underline{H_2}$)-×24), 0.88 (d, *J* = 6.9 Hz, 6H, -CH$_2$C$\underline{H_3}$×2); Anal. Calcd. for $C_{35}H_{68}O_5$; C, 73.89; H, 12.05%, Found: C, 73.59; H, 11.84%.m.p. 64-65 °C; ESI-MS (positive) *m/z* = 551.49 $[M-H_2O+H]^+$, 586.51 $[M+NH_4]^+$, 591.46 $[M+Na]^+$; HR-MS (*m/z*): Calcd. for $C_{35}H_{68}O_5Na$ $[M+Na]^+$, 591.4964: Found, 591.4966.

3-2. Preparation of diacylglycerol moiety for **5b**



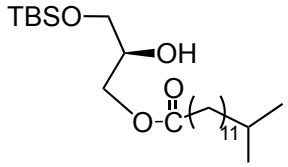
Scheme S2



2-*O*-Allyl-1-*O*-*t*-butyldimethylsilyl-3-(13-methyltetradecanoyl)-*sn*-glycerol (S-8a)

To a mixture of **12** (0.42 g, 1.7 mmol) and 1-methyltetradecanoic acid (0.50 g, 2.0 mmol) in dry CH_2Cl_2 (17 mL) were added DMAP (42 mg, 0.3 mmol) and DIC (0.40 mL, 2.6 mmol) at room temperature. After the mixture was stirred for 12 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane: EtOAc = 25/ 1) to give **S-8a** (0.40 g, 50%) as colorless oil.

ESI-MS (positive) *m/z* = 493.38 $[M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.93-5.88 (m, 1H, -CH_2-C<u>H</u>=CH_2), 5.30-5.18 (m, 1H, -CH_2-CH=C<u>H</u>$_2$ cis), 5.18-5.16 (m, 1H, -CH_2-CH=C<u>H</u>$_2$ trans), 4.29-4.26 (m, 1H, -C<u>H</u>$_2$a-CH=CH_2), 4.13-4.08 (m, 3H, -C<u>H</u>$_2$b-CH=CH_2 and Gro H-3), 3.71-3.53 (m, 3H, Gro H-2 and H-1), 2.33 (t, *J* = 7.6 Hz, 2H, OCOC<u>H</u>$_2$-), 1.66-1.60 (m, 2H, OCOCH_2-C<u>H</u>$_2$-), 1.56-1.40 (m, 1H, -C<u>H</u>$(CH_3)_2$), 1.29-1.10 (m, 18H, -(C<u>H</u>$_2$)-×9), 0.90 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 0.87 (d, *J* = 6.7 Hz, 6H, -CH(C<u>H</u>$_3$)$_2$), 0.07 (s, 6H, Si-(C<u>H</u>$_3$)$_2$); Anal. Calcd. for $C_{27}H_{54}O_4Si$: C, 68.88; H, 11.56%. Found: C, 68.77; H, 11.56%.

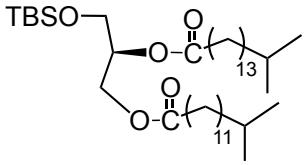


1-*O*-*t*-butyldimethylsilyl-3-(13-methyltetradecanoyl)-*sn*-glycerol (S-9a)

To a solution of **S-8a** (50 mg, 0.10 mmol) in dry THF (1 mL) was added a solution of activated iridium complex $[Ir(cod)(PMe(C_6H_5)_2)_2]PF_6$ in dry THF under Ar. The mixture was stirred under Ar at room temperature for 30 min. Water (0.5 mL) and iodine (76 mg, 0.30 mmol) were then added and the reaction mixture was stirred for 5 min. After excess of iodine was quenched with 10% aqueous $Na_2S_2O_3$, the mixture was extracted with EtOAc. The organic layer was washed with 10% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$ and brine. The solution was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane: EtOAc = 7: 1) to give **S-9a** (35 mg, 81%) as colorless oil.

ESI-MS (positive) *m/z* = 453.35 $[M+Na]^+$, 883.72 $[2M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 4.14-4.06 (m, 2H, Gro H-3), 3.86-3.82 (m, 1H, Gro H-2), 3.65 (dd, *J* = 16.1, 4.6 Hz, 1H, Gro H-1a), 3.58 (dd, *J* = 10.1, 5.6 Hz, 1H, Gro H-1b), 2.45 (s, 1H, -O<u>H</u>), 2.31 (t, *J* = 7.6 Hz, 2H, OCOC<u>H</u>$_2$-), 1.63-1.57 (m, 2H, OCOCH_2-C<u>H</u>$_2$-), 1.53-1.45 (m, 1H, -C<u>H</u>$(CH_3)_2$), 1.26-1.10 (m, 18H, -(C<u>H</u>$_2$)-×9), 0.88 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 0.83 (d, *J* = 6.6 Hz, 6H, -CH(C<u>H</u>$_3$)$_2$), 0.05 (s, 6H,

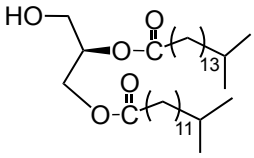
Si-(C<u>H</u>$_3$)$_2$); Anal. Calcd. for $C_{24}H_{50}O_4Si$: C, 66.92; H, 11.70%. Found: C, 66.58; H, 11.78%.



1-*O*-*t*-butyldimethylsilyl-3-(13-methyltetradecanoyl)-2-(15-methylhexadecanoyl)-*sn*-glycerol (S-10a)

To a mixture of **S-9a** (0.27 g, 0.62 mmol) and **1-methylhexadecanoic acid** (0.20 g, 0.75 mmol) in dry CH_2Cl_2 (6 mL) were added DMAP (15 mg, 0.12 mmol) and DIC (0.19 mL, 1.24 mmol) at room temperature. After the mixture was stirred for 20 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica-gel column chromatography (hexane: EtOAc: 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) = 15/ 1/ 0.3) to give **S-10a** (0.31 g, 74%) as colorless oil.

ESI-MS (positive) *m/z* = 683.61 $[M+H]^+$, 705.59 $[(M+Na)^+]$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.09-5.05 (m, 1H, Gro H-2), 4.34 (dd, *J* = 11.8, 3.7 Hz, 1H, Gro H-3a), 4.16 (dd, *J* = 11.8, 6.3 Hz, 1H, Gro H-3b), 3.77-3.71 (dd, m, 2H, Gro H-1), 2.30 (m, 4H, OCOC<u>H</u>$_2$-×2), 1.63-1.58 (m, 4H, OCOCH$_2$-C<u>H</u>$_2$-×2), 1.55-1.48 (m, 2H, -C<u>H</u>(CH$_3$)$_2$×2), 1.28-1.14 (m, 40H, -(C<u>H</u>$_2$)-×15), 0.88 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 0.86 (d, *J* = 6.7 Hz, 12H, -CH(C<u>H</u>$_3$)$_2$×2), 0.05 (s, 6H, Si-(C<u>H</u>$_3$)$_2$); Anal. Calcd. for $C_{41}H_{82}O_5Si$: C, 72.08; H, 12.10%. Found: C, 72.01; H, 12.34%.



3-(13-methyltetradecanoyl)-2-(15-methylhexadecanoyl)-*sn*-glycerol (S-11a)

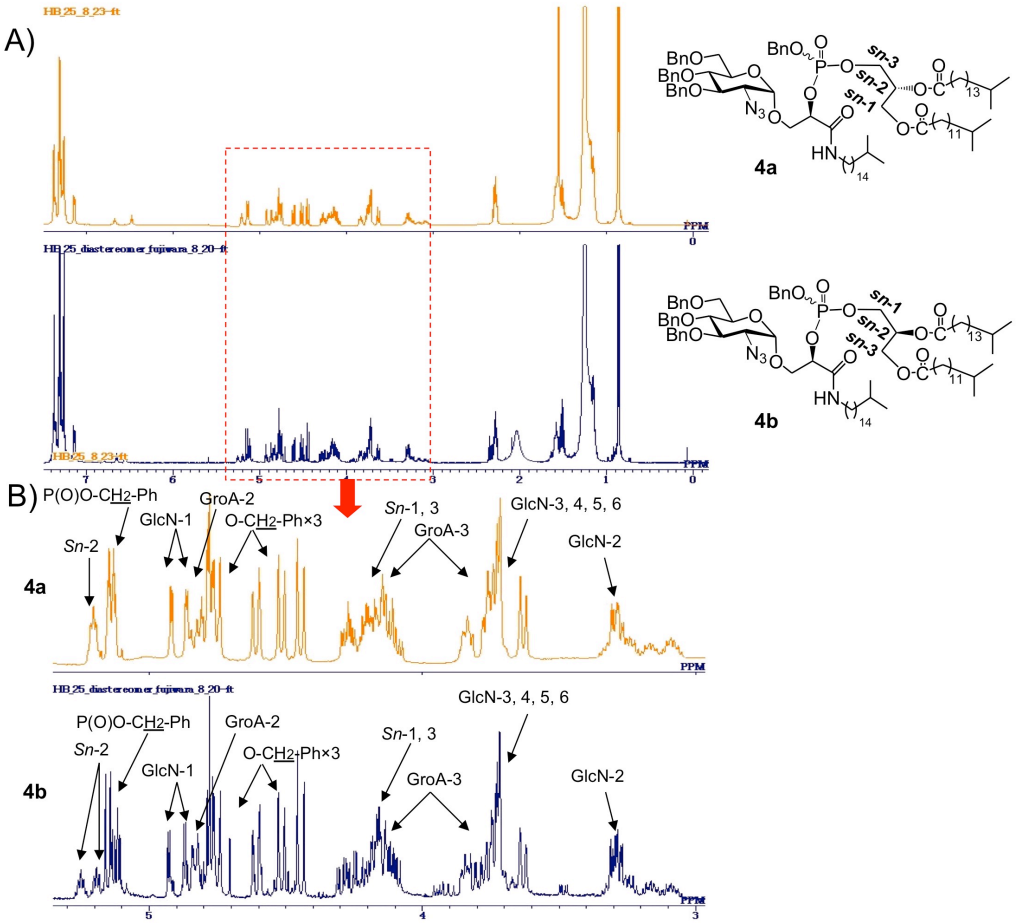
To a solution of **S-10a** (100 mg, 0.15 mmol) in dry THF (1.5 mL) was added pyridine (0.15 mL). HF·pyridine (75 µL) was added to the mixture, and stirred for 2 h at room temperature. Additional HF·pyridine (75 µL) was added and the mixture was stirred for 3 h. The reaction was quenched with saturated aqueous $NaHCO_3$ and the mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4 and

concentrated in vacuo. The residue was purified by silica-gel column chromatography (toluene: EtOAc: 1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) = 20: 1: 0.2) to give **S-11a** (73 mg, 86%) as a colorless solid.

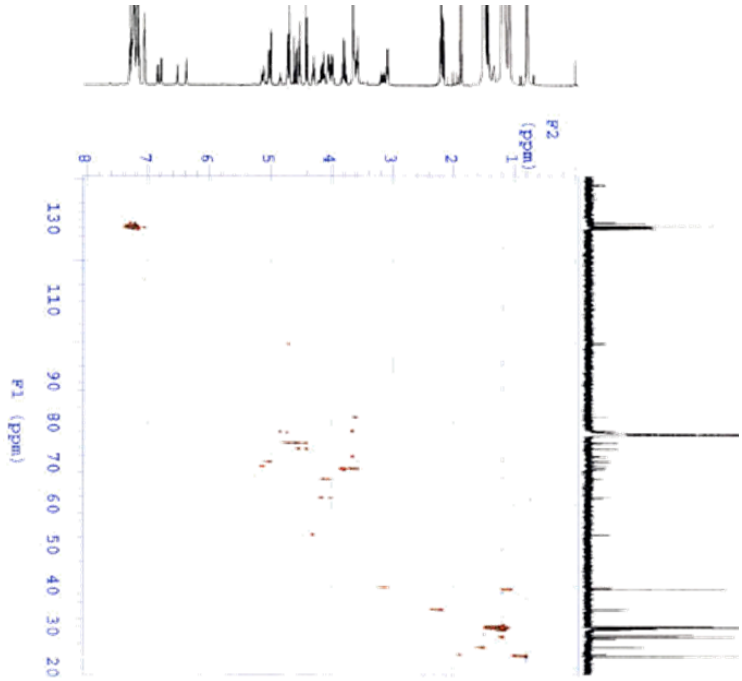
ESI-MS (positive) *m/z* = 591.47 $[M+Na]^+$; ^{1}H-NMR (500 MHz, $CDCl_3$) δ (ppm) = 5.10-5.06 (m, 1H, Gro H-2), 4.32 (dd, *J* = 12.0, 4.5 Hz, 1H, Gro H-3a), 4.24 (dd, *J* = 12.1, 5.6 Hz, 1H, Gro H-3b), 3.73 (dd, *J* = 5.0, 1.6 Hz, 2H, Gro H-1), 2.33 (t, *J* = 7.5 Hz, 4H, $OCOCH_2$-×2), 1.66-1.59 (m, 4H, $OCOCH_2$-CH_2-×2), 1.56-1.48 (m, 2H, -$CH(CH_3)_2$×2), 1.29-1.14 (m, 40H, -(CH_2)-×15), 0.86 (d, *J* = 6.6 Hz, 12H, -$CH(CH_3)_2$×2); Anal. Calcd. for $C_{35}H_{68}O_5$: C, 73.89; H, 12.05%. Found: C, 72.75; H, 11.78%.

5. NMR spectra of later stage of compounds

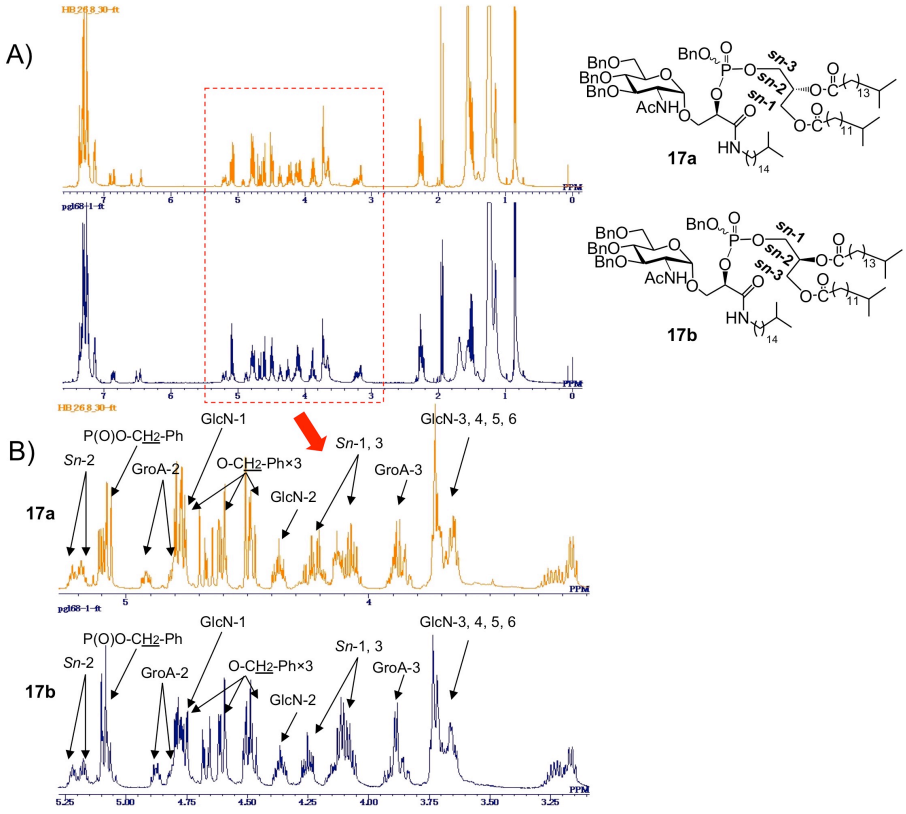
1) NMR spectra of compound **4a** and **4b**



2) $^{1}H^{13}C$ HMQC of compound **4a**



3) NMR spectra of compound **17a** and **17b**



4) $^{1}H^{13}C$ HMQC of compound **1a**