Supplementary Information

Key entity of DCAR agonist, phosphatidylinositol mannoside Ac_1PIM_1; Synthesis and its immunomodulatory function

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Figure S1. TLR2-specific NF-κB induction by synthesized compounds in A) HEK-Blue mouse TLR2 cells and B) humanTLR2 cells.

Figure S2. Antigen presenting cell (APC)-free assay for compounds binding to mCD1d.

Figure S3. Binding assay based on AlphaScreen™, applied to the synthesized compounds **1**, and **2a**–**c** in comparison with the known ligands.

Figure S4. Proinflammatory cytokine inductions by synthesized compounds in BMDCs. (A) MCP-1 induction. (B) TNF-α induction.

Experimental Section

1. Synthesis
2. Biology
3. NMR spectra

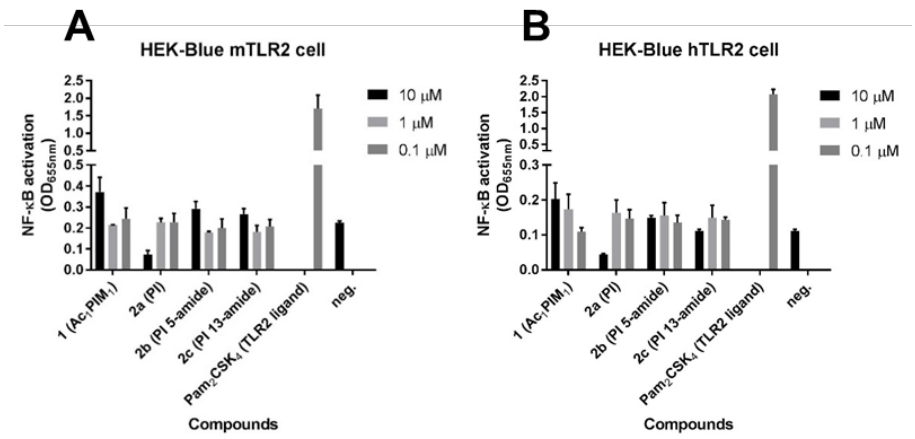


Figure S1. TLR2-specific NF-κB induction by synthesized compounds in A) HEK-Blue mouse and B) human TLR2 cells.

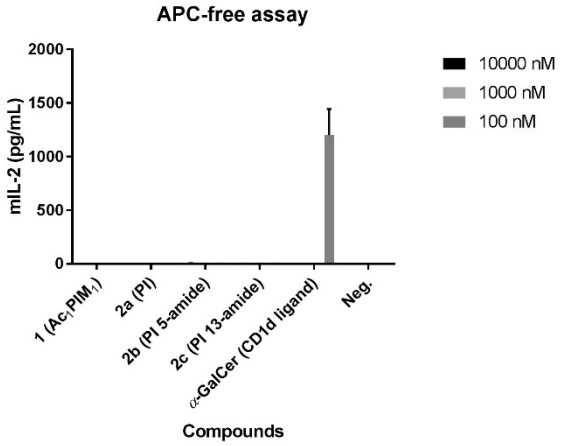


Figure S2. Antigen presenting cell (APC)-free assay[1, 2] for compounds binding to mCD1d.

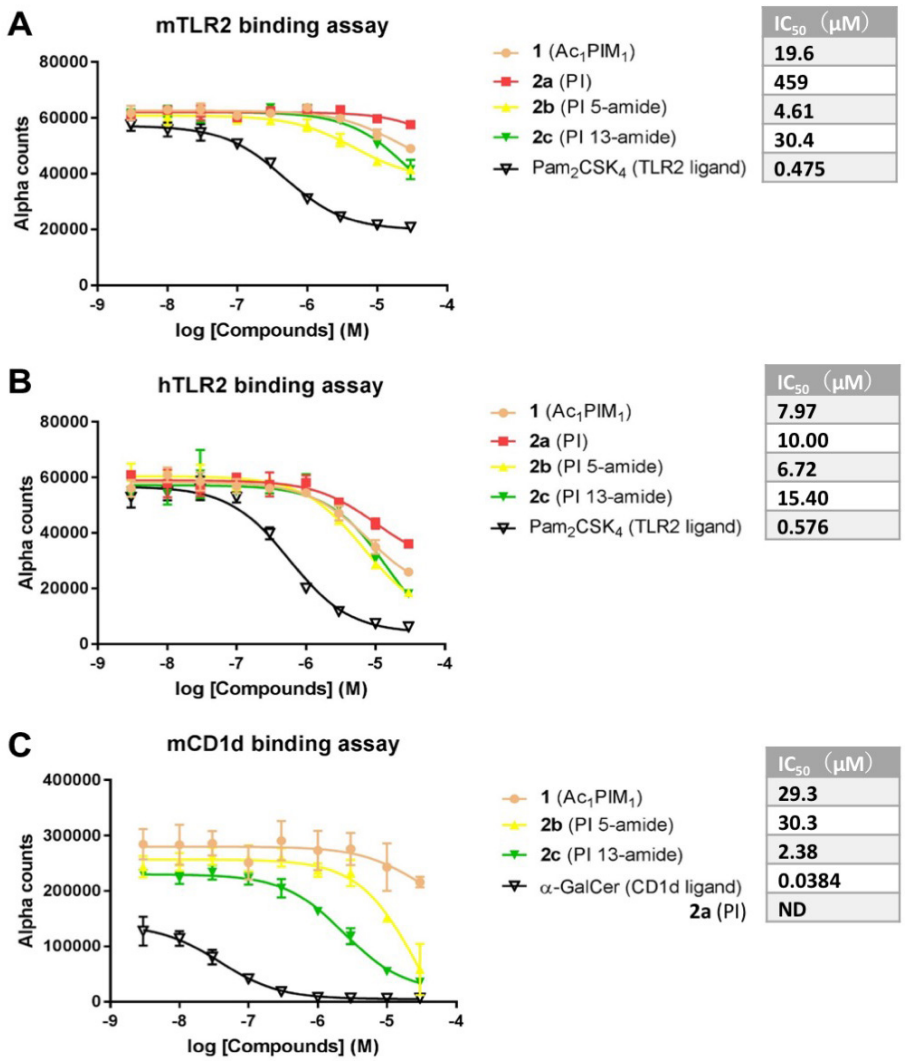


Figure S3. Binding assay based on AlphaScreen™, applied to the synthesized compounds **1**, and **2a**–**c** in comparison with the known ligands.[3, 4]

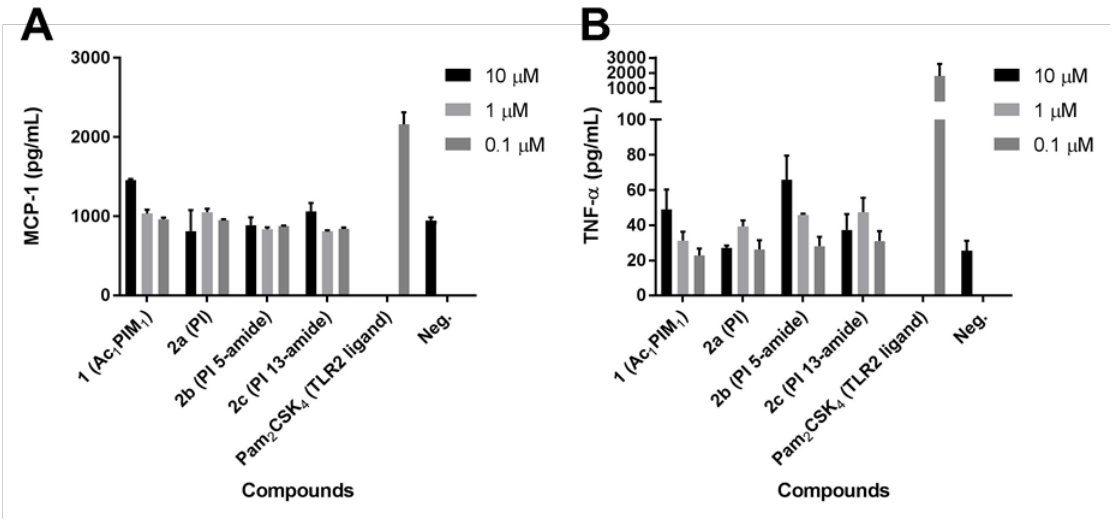


Figure S4. Proinflammatory cytokine inductions by synthesized compounds in BMDCs.

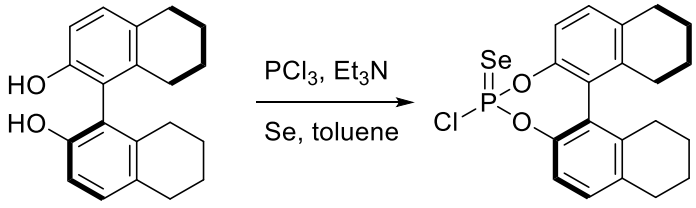
(A) MCP-1 induction. (B) TNF-α induction.

1. Synthesis

General procedure:

Nuclear magnetic resonance (^{1}H NMR, ^{13}C NMR, ^{31}P NMR) spectra were measured at 25 °C in an indicated solvent with either JEOL ECX 400, ECS 400, JNM-ECZ800R or Bruker AVANCE 800US and analyzed Delta 5.0.5 (JEOL). The proton chemical shifts in $CDCl_3$ or in mixture solvent ($CDCl_3$, CD_3OD and D_2O) are reported in parts per million (δ) from tetramethylsilane as an internal standard and coupling constants are in Heltz (Hz). The chemical shifts in other solvent are reported in ppm from the residual proton signal of solvent. The chemical shits for ^{13}C NMR are reported in ppm from the internal solvent signal ($CDCl_3$, δ 77.0). The chemical shits for ^{31}P NMR are reported in ppm from the external standard signal (H_3PO_4, δ 0.0). High-resolution mass spectra (HRMS) of synthetic compounds were obtained on an electron spray ionization quadrupole time of flight (ESI-QTOF) mass spectrometer (micrOTOF-QII-HC; BRUKER). Analytical thin layer chromatography (TLC) was performed on Silica gel 60 F_{254} Plates (Merck, 0.25 mm thickness). Silica gel column chromatography was performed using Silica gel 60 N [spherical neutral (Kanto Chemical Co., Inc., 40 – 50 μm)] at medium pressure (2 – 4 $kgcm^{-2}$) using indicated solvent systems. Reagents were purchased from commercial supplier (TCI, nacalai tesque, Wako pure chemical industry, Ltd., Kanto Chemical Co., Inc., Watanabe Chemical ndustries, Ltd.) and were used without further purification. Unless otherwise noted, Non-aqueous reactions were carried out under argon atmosphere. Anhydrous dichloromethane, tetrahydrofuran, *N, N*-dimethylformamide, methanol and toluene were purchased from Kanto Chemical Co., Inc. Chiral HPLC was performed on a Prominence system (Shimadzu Corporation). Chiral HPLC was carried out by using a CHIRALPAK® AD-H packed column (5 μm, 4.6 x 250 mm) at a flow rate of 1 ml/min.

Synthesis of phosphoryl reagent 9b



(R)-(+)-5,5',6,6',7,7',8,8'
-octahydro-1,1'-bi-2-naphthol

9b

To a solution of PCl_3 (148 μL, 1.70 mmol) and Et_3N (477 μL, 3.40 mmol) in toluene (3 mL) at 0 ˚C was added (*R*)-(+)-5,5',6,6',7,7',8,8'-octahydro-1,1'-bi-2-naphthol (500 mg, 1.70 mmol) under Ar. After stirring for 3 min, to the resulting solution was added Se (148 mg, 1.87 mmol). The mixture was warmed to 110 ˚C and stirred for 6 h. The reaction was concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-CH_2Cl_2 (3:2) to give **9b** (335 mg, 45%) as a pink solid.

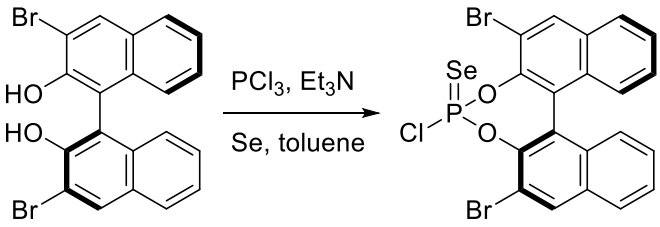
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.18 (d, *J* = 4.3 Hz, 1H), 7.16 (d, *J* = 4.1 Hz, 1H), 7.12 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.06 (dd, *J* = 8.4, 2.3 Hz, 1H), 2.89-2.78 (m, 4H), 2.73-2.64 (m, 2H), 2.33-2.25 (m, 2H), 1.85-1.74 (m, 6H), 1.65-1.54 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 147.17, 145.36, 138.90, 138.78, 136.85, 136.51, 130.21, 129.98, 126.66, 126.47, 119.12, 118.26, 29.19 (2C), 27.83 (2C), 22.36, 22.34, 22.22, 22.17.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: 71.16.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}ClNaO_2PSe$ $[M+Na]^+$ 460.9945, found 460.9944.

Synthesis of phosphoryl reagent 9c



(R)-3,3'-dibromo -1,1'-bi-2-naphthol

9c

The title compound was synthesized following the procedure for **9b**. (*R*)-3,3'-dibromo-1,1'-bi-2-naphthol (500 mg, 1.13 mmol) was used as starting materials. **9c** (458 mg, 69%) was obtained as a pink solid.

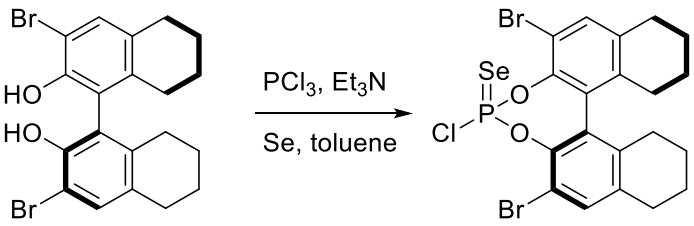
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.36 (s, 2H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 134.47, 134.30, 132.40, 132.23, 131.41, 131.30, 129.01, 128.20, 127.66, 127.65, 127.41, 127.37, 127.27, 127.00, 126.93, 125.27, 124.04, 123.83, 114.26, 113.60.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: 64.35.

HRMS (ESI-TOF) calcd for $C_{20}H_{10}Br_2ClNaO_2PSe$ $[M+Na]^+$ 608.7530, found 608.7524.

Synthesis of phosphoryl reagent 9d



(R)-(+)-3,3'-dibromo-5,5',6,6',7,7',8,8'-octahydro-1,1'-bi-2-naphthol

9d

The title compound was synthesized following the procedure for **9b**. (*R*)-(+)-3,3'-dibromo-5,5',6,6',7,7',8,8'-octahydro-1,1'-bi-2-naphthol (500 mg, 1.106 mmol) was used as starting materials. Compound **9d** (584 mg, 89%) was obtained as a pink solid.

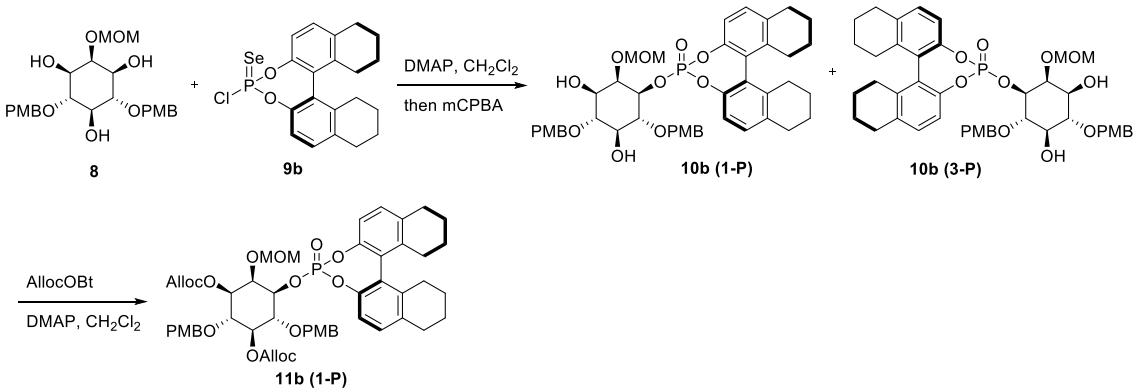
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.43 (s, 2H), 2.84-2.79 (m, 4H), 2.59-2.50 (m, 2H), 2.25-2.16 (m, 2H), 1.82-1.75 (m, 6H), 1.63-1.54 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 138.03 (2C), 137.86 (2C), 134.17 (2C), 133.90 (2C), 112.40, 112.36, 111.61 (2C), 28.96 (2C), 27.59, 27.55, 22.14, 22.11, 22.02, 21.99.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: 65.01.

HRMS (ESI-TOF) calcd for $C_{20}H_{18}Br_2ClNaO_2PSe$ $[M+Na]^+$ 616.8156, found 616.8153.

Synthesis of inositol phosphate derivative 11b



To a stirred solution of **8** (100 mg, 215 μmol) and DMAP (52.6 mg, 431 μmol) in CH_2Cl_2 (3 mL) at 0 ºC was added **9b** (189 mg, 431 μmol). After stirring for overnight at the same temperature, *m*CPBA (70%) (106 mg, 431 μmol) was added to the reaction mixture. The reaction was extracted with EtOAc

and the extract was washed with H_2O and brine. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude mixture was purified by column chromatography of SiO_2 with toluene-EtOAc (2:1 = in vol. ratio) to afford the mixture of **10b (1-P)** and **(3-P)** (32.5 mg, 19%) as a white foam.

To a solution of AllocOBt (83.8 mg, 383 μmol) and DMAP (46.7 mg, 383 μmol) in CH_2Cl_2 (1 mL) was added **10b (1-P)** and **(3-P)** (32.5 mg, 40.5 μmol). The reaction mixture was stirred for overnight and quenched by an addition of 10% aqueous citric acid. The reaction was extracted with CH_2Cl_2 and washed with brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. Part of the mixture was analyzed by HPLC [COSMOSIL 5SL-II Packed column, 254 nm, linear gradient of 5–20% (v/v) of IPA in *n*-hexane over 15 min, 1 mL/min] to determine ratio of **11b (1-P)**:**(3-P)** (77:23). The crude mixture was purified by column chromatography of SiO_2 with toluene-EtOAc (6:1) to give the **11b (1-P)** (28.4 mg, 72%) as a white solid.

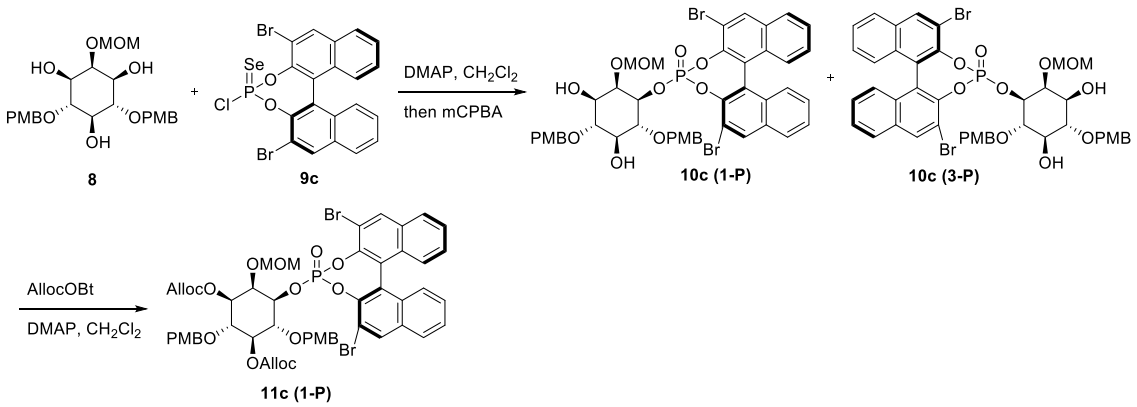
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.17 (d, *J* = 8.5 Hz, 2H), 7.12-7.05 (m, 4H), 7.00-6.85 (m, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 8.5 Hz, 2H), 5.98-5.79 (m, 2H), 5.37 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.31 (dd, *J* = 17.3, 1.2 Hz, 1H), 5.28 (dd, *J* = 10.3, 1.1 Hz, 1H), 5.21 (dd, *J* = 10.3, 1.1 Hz, 1H), 4.92-4.76 (m, 2H), 4.71 (d, *J* = 6.5 Hz, 1H), 4.65-4.49 (m, 9H), 4.39 (d, *J* = 10.5 Hz, 1H), 4.24 (d, *J* = 10.5 Hz, 1H), 3.97 (t, *J* = 10.0 Hz, 1H), 3.91 (t, *J* = 9.8 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.45 (s, 3H), 2.85-2.58 (m, 6H), 2.27-2.20 (m, 2H), 1.81-1.68 (m, 6H), 1.56-1.46 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.16 (2C), 154.05, 153.92, 146.82 (2C), 138.46, 136.01, 131.40, 131.36, 130.39, 130.21, 130.01, 129.72, 129.43 (2C), 129.35 (2C), 125.72 (2C), 119.12, 119.02, 113.59 (4C), 113.45 (2C), 98.02, 77.98, 75.85, 75.66, 74.93, 74.80, 74.52, 68.81 (2C), 68.69 (2C), 56.11, 55.22 (2C), 29.06, 29.04, 27.84, 27.79, 22.38, 22.33, 22.25, 22.23.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -0.83.

HRMS (ESI-TOF) calcd for $C_{52}H_{59}NaO_{16}P$ $[M+Na]^+$ 993.3433, found 993.3442.

Synthesis of inositol phosphate derivative 11c



8 9c 10c (1-P) 10c (3-P) 11c (1-P)

The title compound was synthesized following the procedure for **11b**. **8** (100 mg, 215 μmol) and **9c** (253 mg, 431 μmol) were used as starting materials. Compound **10c (1-P)** and **(3-P)** (53.0 mg, 26%) was obtained as a white form. The ratio of **11c (1-P)**:**(3-P)** (81:19) was analyzed by HPLC [COSMOSIL 5SL-II Packed column, 254 nm, linear gradient of 5–20% (v/v) of IPA in *n*-hexane over 15 min, 1 mL/min]. Compound **11c (1-P)** (51.6 mg, 83%) was obtained as a white solid.

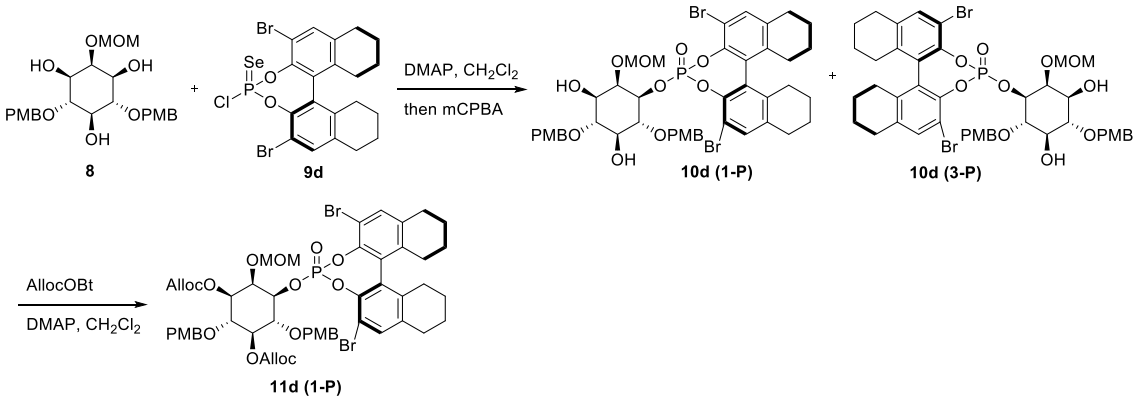
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.31 (s, 1H), 8.26 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 7.35-7.10 (m, 6H), 6.83-6.79 (m, 2H), 6.59 (d, *J* = 8.5 Hz, 2H), 6.42 (d, *J* = 8.5 Hz, 2H), 6.00-5.73 (m, 2H), 5.39 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.33-5.23 (m, 2H), 5.18 (dd, *J* = 10.3, 1.1 Hz, 1H), 4.96 (d, *J* = 6.7 Hz, 1H), 4.89-4.84 (m, 2H), 4.76 (d, *J* = 6.5 Hz, 1H), 4.74-4.61 (m, 4H), 4.56-4.37 (m, 4H), 4.29 (d, *J* = 11.0 Hz, 1H), 4.19 (d, *J* = 11.0 Hz, 1H), 4.09-3.96 (m, 2H), 3.77 (s, 3H), 3.65 (s, 3H), 3.40 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.15, 158.65, 154.01, 153.96, 143.86, 143.00, 134.44, 133.92, 132.30, 131.99, 131.43, 131.39, 131.28, 131.15, 130.01, 129.86, 129.44 (2C), 128.77 (2C), 127.68, 127.62, 127.37, 127.22, 127.14, 126.98, 126.95, 126.77, 122.78, 122.71, 119.06, 118.90, 114.41, 113.73, 113.58 (2C), 113.16 (2C), 98.37, 79.85, 77.87, 77.78, 76.59, 75.80, 75.04, 74.84, 74.64, 68.83, 68.64, 56.16, 55.21, 55.08.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: 0.19.

HRMS (ESI-TOF) calcd for $C_{52}H_{49}Br_2NaO_{16}P$ $[M+Na]^+$ 1141.1017, found 1141.1009.

Synthesis of inositol phosphate derivative 11d



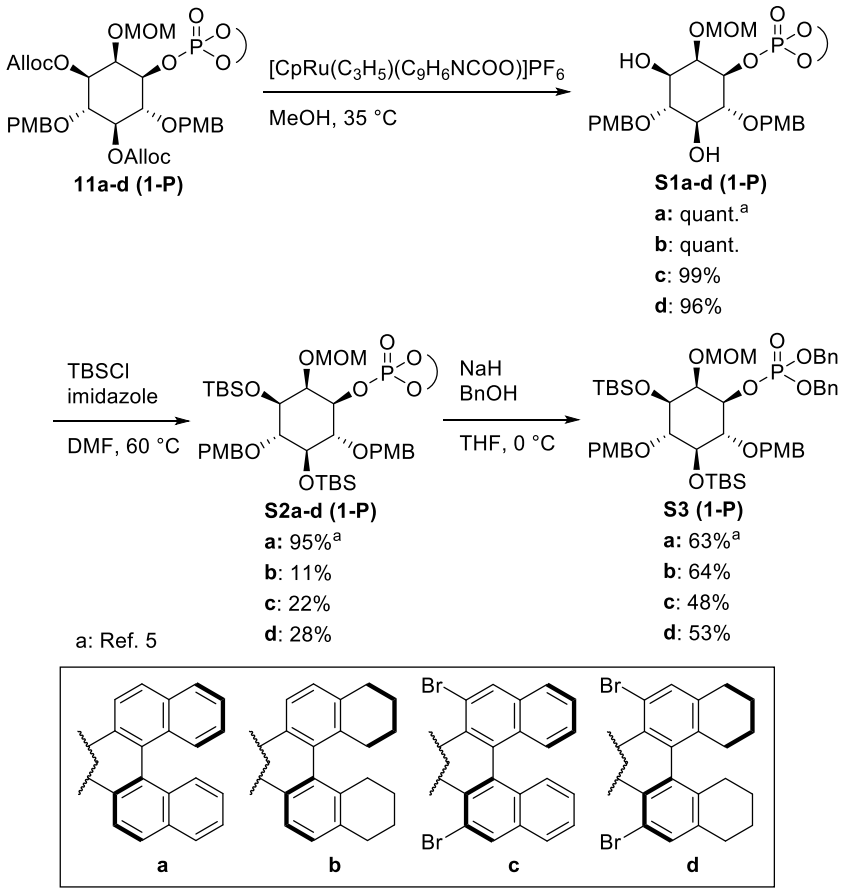
The title compound was synthesized following the procedure for **11b**. **8** (100 mg, 215 μmol) and **9d** (257 mg, 431 μmol) were used as starting materials. Compound **10d (1-P)** and **(3-P)** (55.7 mg, 27%) was obtained as a white form. The ratio of **11d (1-P)**:**(3-P)** (>99:1) was analyzed by HPLC [COSMOSIL 5SL-II Packed column, 254 nm, linear gradient of 5–20% (v/v) of IPA in *n*-hexane over 15 min, 1 mL/min]. Compound **11d (1-P)** (45.6 mg, 70%) was obtained as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.40 (s, 1H), 7.32 (s, 1H), 7.23-7.14 (m, 3H), 6.97 (d, *J* = 8.5 Hz, 1H), 6.82-6.72 (m, 4H), 5.98-5.74 (m, 2H), 5.39-5.23 (m, 3H), 5.19 (d, *J* = 10.5 Hz, 1H), 4.95-4.76 (m, 4H), 4.68-4.34 (m, 9H), 4.29 (d, *J* = 11.2 Hz, 1H), 4.08-3.95 (m, 2H), 3.77 (s, 3H), 3.75 (s, 3H), 3.41 (s, 3H), 2.82-2.68 (m, 4H), 2.58-2.44 (m, 2H), 2.23-2.07 (m, 2H), 1.80-1.66 (m, 6H), 1.63-1.39 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.09, 158.86, 153.98, 153.89, 143.47, 142.17, 137.78, 137.51, 134.02, 133.42, 131.40 (2C), 130.33, 130.01, 129.37 (2C), 129.11 (2C), 127.28, 127.10, 125.23, 120.27, 118.96, 118.76, 113.53 (2C), 113.36 (2C), 112.30, 111.38, 98.41, 79.74, 77.94, 77.58, 76.49, 75.69, 74.77, 74.64, 68.74, 68.65, 68.54, 56.08, 55.69, 55.18, 28.83, 28.71, 27.55 (2C), 22.09 (2C), 21.96 (2C).

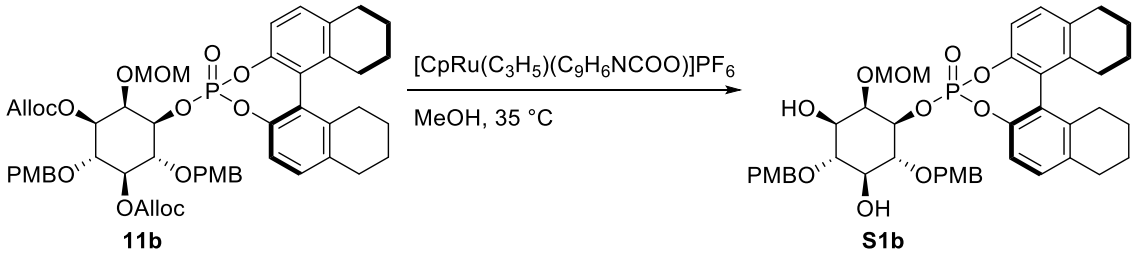
^{31}P-NMR (160 MHz, $CDCl_3$) δ: -2.49.

HRMS (ESI-TOF) calcd for $C_{52}H_{57}Br_2NaO_{16}P$ $[M+Na]^+$ 1149.1643, found 1149.1647.



Scheme S1. Synthesis of inositol phosphate **29**

Synthesis of inositol phosphate derivative S1b



The solution of **11b** (16.0 mg, 16.5 μmol), and $[CpRu(C_3H_5)(C_9H_6NCOO)]PF_6$ (173 μg, 0.33 μmol) in MeOH (1 mL) was stirred at 35 ˚C. After stirring for 3 h, the reaction mixture was concentrated under reduced pressure. The crude residue was purified by column chromatography of SiO_2 with toluene-EtOAc (1:1) to give the **S1b** (16.6 mg, quant.) as a colorless oil.

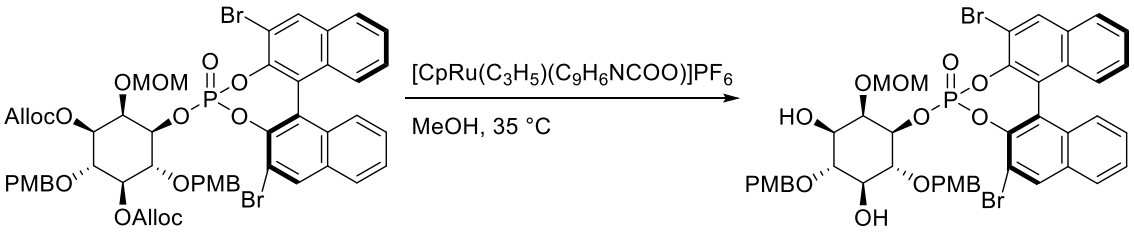
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37-7.28 (m, 2H), 7.18-7.00 (m, 6H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.78 (d, *J* = 8.1 Hz, 2H), 4.92-4.73 (m, 4H), 4.68-4.33 (m, 3H), 4.28 (d, *J* = 10.5 Hz, 1H), 3.79-3.71 (m,

8H), 3.57-3.42 (m, 5H), 3.30-3.22 (m, 2H), 2.89-2.57 (m, 6H), 2.27-2.17 (m, 2H), 1.83-1.63 (m, 6H), 1.56-1.40 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.30, 159.18, 146.93, 146.81, 138.43 (2C), 136.05, 135.66, 130.64, 130.46, 129.76 (2C), 129.70, 129.55 (2C), 129.36, 125.82, 125.78, 118.44, 117.75, 113.87 (2C), 113.75 (2C), 98.78, 80.68, 80.49, 79.80, 79.24, 77.20, 74.74, 74.53, 74.17, 70.84, 70.81 (2C), 56.13, 55.74, 55.25, 29.68, 29.07, 29.03, 27.82, 22.38, 22.30, 22.24, 22.22.

HRMS (ESI-TOF) calcd for $C_{44}H_{51}NaO_{12}P$ $[M+Na]^+$ 825.3010, found 825.3011.

Synthesis of inositol phosphate derivative S1c



11c **S1c**

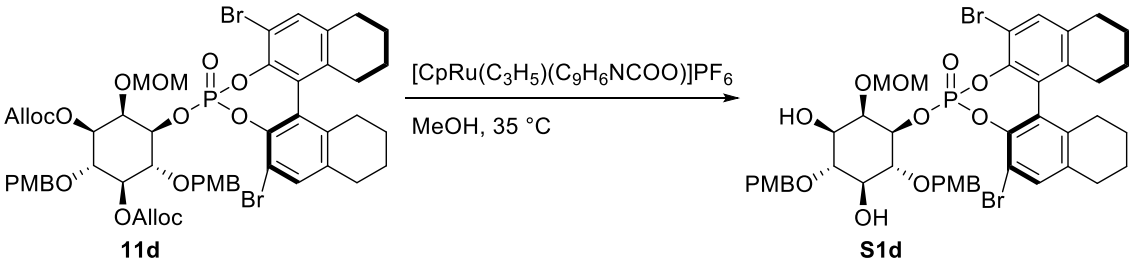
The title compound was synthesized following the procedure for **S1b**. **11c** (32.5 mg, 29.0 μmol) was used as starting materials. Compound **S1c** (27.4 mg, 99%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.33 (s, 1H), 8.25 (s, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.38-7.14 (m, 6H), 6.87 (d, *J* = 8.5 Hz, 2H), 6.71 (d, *J* = 8.5 Hz, 2H), 6.43 (d, *J* = 8.5 Hz, 2H), 4.93 (dd, *J* = 11.7, 6.5 Hz, 2H), 4.86 (d, *J* = 11.2 Hz, 1H), 4.74 (d, *J* = 11.0 Hz, 1H), 4.68-4.60 (m, 2H), 4.41 (d, *J* = 10.8 Hz, 1H), 4.33 (d, *J* = 11.0 Hz, 1H), 3.84 (t, *J* = 9.2 Hz, 1H), 3.79 (s, 3H), 3.65 (s, 3H), 3.56-3.47 (m, 3H), 3.43 (s, 3H), 2.36-2.34 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.26, 158.85, 143.99, 143.05, 134.41, 133.89, 132.28, 131.99, 131.24, 131.17, 130.69, 130.19, 129.74, 129.16, 129.01, 128.99, 128.20, 127.67, 127.62, 127.35, 127.26, 127.09, 126.97, 126.80, 125.27, 122.82, 114.34, 113.84, 113.79, 113.75, 113.71, 113.48, 99.06, 81.33, 80.77, 80.29, 80.04, 74.96, 74.42, 74.11, 70.85, 56.13, 55.25, 55.10.

HRMS (ESI-TOF) calcd for $C_{44}H_{41}Br_2NaO_{12}P$ $[M+Na]^+$ 973.0595, found 973.0587.

Synthesis of inositol phosphate derivative S1d



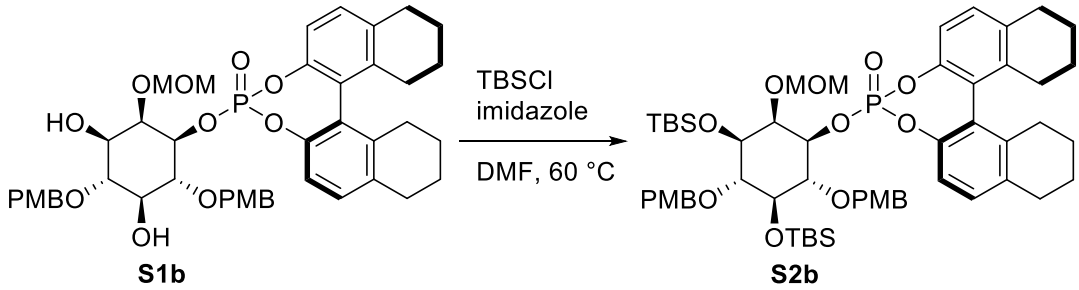
The title compound was synthesized following the procedure for **S1b**. **11d** (33.2 mg, 29.4 μmol) was used as starting materials. Compound **S1d** (29.4 mg, 96%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.41 (s, 1H), 7.34-7.29 (m, 3H), 7.28-7.14 (m, 2H), 7.06 (d, *J* = 8.8 Hz, 1H), 6.90-6.84 (m, 2H), 6.77 (d, *J* = 8.8 Hz, 1H), 4.90 (s, 2H), 4.82 (t, *J* = 10.7 Hz, 1H), 4.76 (t, *J* = 11.0 Hz, 1H), 4.63-4.52 (m, 2H), 4.48-4.38 (m, 1H), 4.22 (d, *J* = 11.2 Hz, 1H), 3.85-3.80 (m, 2H), 3.79 (s, 3H), 3.76 (s, 3H), 3.60-3.51 (m, 3H), 3.42 (s, 3H), 3.24 (s, 1H), 2.84-2.69 (m, 3H), 2.58-2.47 (m, 3H), 2.22-2.08 (m, 2H), 1.81-1.39 (m, 8H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.23, 159.15, 137.77, 137.56, 137.12, 134.01, 133.43, 130.75, 130.63, 129.73, 129.71, 129.34, 129.32, 129.02, 128.21, 127.31, 127.26, 125.27, 113.84, 113.81, 113.78, 112.21, 111.48, 99.11, 81.23, 80.62, 80.22, 80.16, 74.67, 74.38, 73.89, 70.74, 56.10, 55.25, 28.86, 28.76, 27.57, 22.12, 22.01.

HRMS (ESI-TOF) calcd for $C_{44}H_{49}Br_2NaO_{12}P$ $[M+Na]^+$ 981.1221, found 981.1215.

Synthesis of inositol phosphate derivative S2b



To a solution of **S1b** (16.6 mg, 20.7 μmol) in DMF (1 mL) at room temperature were added TBSCl (31.2 mg, 207 μmol) and imidazole (16.9 mg, 248 μmol). The mixture was warmed up to 60 ˚C. After stirring for 1 d, methanol was added to the reaction, and then extracted with Et_2O and washed with brine. The organic phase was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (10:1) to give **S2b** (2.73 mg, 11%)

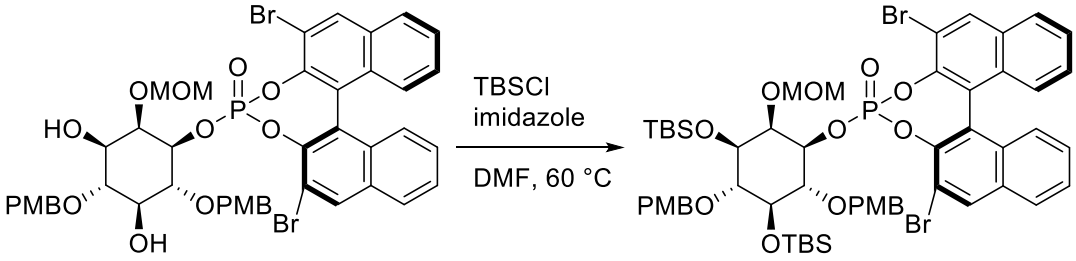
as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.42-7.36 (m, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.04-6.97 (m, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.5 Hz, 2H), 5.39-5.30 (m, 2H), 5.04-4.82 (m, 3H), 4.75-4.61 (m, 1H), 4.44-4.28 (m, 3H), 3.79 (s, 3H), 3.74 (s, 3H), 3.64 (t, *J* = 9.0 Hz, 2H), 3.50 (s, 3H), 3.43 (t, *J* = 8.9 Hz, 1H), 2.96-2.51 (m, 4H), 2.06-1.94 (m, 2H), 1.77-1.60 (m, 10H), 0.82 (s, 9H), 0.78 (s, 9H), 0.10 (s, 3H), -0.03 (s, 3H), -0.17 (s, 3H), -0.18 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 158.49, 158.13, 146.80 (2C), 138.21, 138.14, 131.28, 130.96, 130.22, 130.01, 129.56, 128.84 (3C), 127.37 (3C), 125.85, 118.44, 118.40, 113.18 (2C), 113.07 (2C), 97.90, 81.59, 80.06, 77.84, 77.20, 74.80, 74.66, 74.61, 73.20, 56.06, 55.20, 55.13, 31.92, 29.68, 29.51, 29.31, 29.06, 27.77, 25.95 (2C), 25.89 (2C), 22.68, 22.41, 22.25, 22.10, -0.01, -3.98, -4.33, -4.90.

HRMS (ESI-TOF) calcd for $C_{56}H_{79}NaO_{12}PSi_2$ $[M+Na]^+$ 1053.4740, found 1053.4736.

Synthesis of inositol phosphate derivative S2c



S1c **S2c**

The title compound was synthesized following the procedure for **S2b**. **S1c** (27.4 mg, 28.8 μmol) was used as starting materials. Compound **S2c** (7.46 mg, 22%) was obtained as a colorless oil.

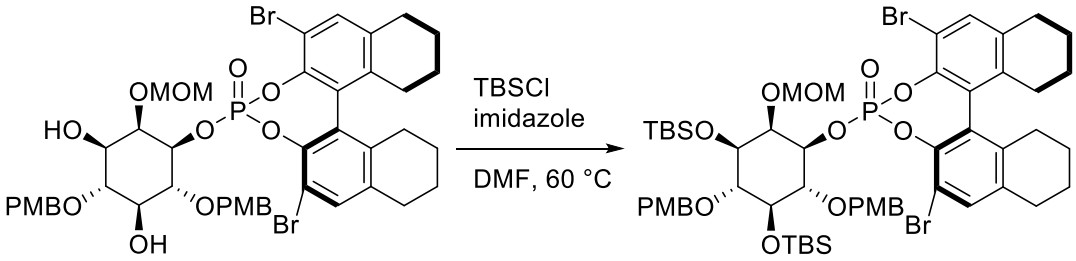
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.23 (s, 1H), 8.14 (s, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.0 Hz, 1H), 7.28-7.23 (m, 8H), 7.13 (t, *J* = 7.0 Hz, 1H), 6.94 (d, *J* = 7.7 Hz, 2H), 6.85 (d, *J* = 8.2 Hz, 2H), 4.72-4.69 (m, 1H), 4.58-4.45 (m, 4H), 4.34-4.28 (m, 3H), 3.89-3.83 (m, 4H), 3.80 (s, 3H), 3.75-3.70 (m, 1H), 3.56-3.50 (m, 1H), 3.41 (s, 3H), 3.28-3.21 (m, 1H), 0.74 (s, 9H), 0.70 (s, 9H), -0.09 (s, 3H), -0.17 (s, 3H), -0.21 (s, 3H), -0.81 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.47, 159.30, 148.73, 147.63, 133.81, 132.81, 132.60, 129.82 (3C), 129.67 (3C), 129.46, 129.28, 127.11, 126.99, 126.82, 126.78, 126.68, 126.48, 126.10, 125.98, 124.87, 122.98, 122.25, 116.78, 113.91 (2C), 113.77 (2C), 111.37, 95.01, 81.79, 80.97, 80.79, 79.85, 75.38, 72.14, 71.49, 70.94, 55.90, 55.35, 55.26, 26.11 (3C), 25.76 (3C), 18.69, 18.00, -3.12, -3.72, -4.78, -

4.86.

HRMS (ESI-TOF) calcd for $C_{56}H_{69}Br_2NaO_{12}PSI_2$ $[M+Na]^+$ 1201.2324, found 1201.2325.

Synthesis of inositol phosphate derivative S2d



S1d **S2d**

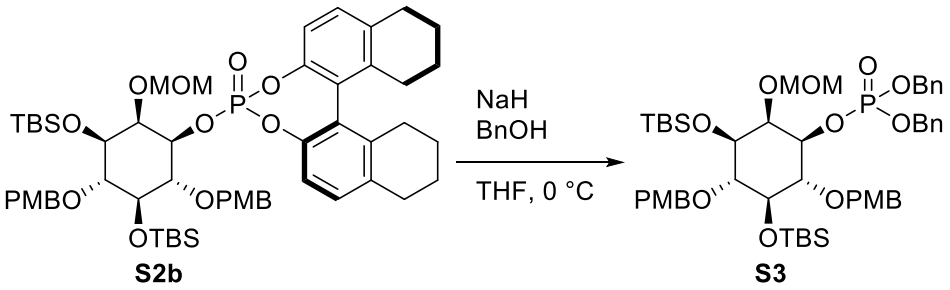
The title compound was synthesized following the procedure for **S2b**. **S1d** (29.4 mg, 30.6 μmol) was used as starting materials. Compound **S2d** (10.01 mg, 28%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.40 (s, 1H), 7.23-7.11 (m, 3H), 6.96 (d, *J* = 7.9 Hz, 2H), 6.83 (d, *J* = 7.7 Hz, 2H), 6.64 (d, *J* = 8.4 Hz, 2H), 5.06-4.93 (m, 2H), 4.87 (t, *J* = 10.5 Hz, 1H), 4.69 (t, *J* = 11.2 Hz, 1H), 4.56 (d, *J* = 8.6 Hz, 2H), 4.30 (dt, *J* = 37.5, 12.5 Hz, 2H), 3.87-3.78 (m, 5H), 3.74 (s, 3H), 3.66-3.56 (m, 2H), 3.50 (s, 3H), 2.84-1.68 (m, 16H), 0.85 (s, 9H), 0.75 (s, 9H), 0.14 (s, 3H), 0.00 (s, 3H), -0.18 (s, 3H), -0.27 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 158.26, 158.10, 137.62, 137.35 (2C), 136.82, 133.79 (2C), 133.28 (2C), 131.32, 131.07, 128.45 (3C), 127.45 (3C), 113.24, 113.06 (2C), 113.00 (2C), 111.14, 98.35, 81.27, 80.44, 77.67, 77.20, 74.79, 74.55, 74.37, 73.17, 56.24, 55.13 (2C), 29.65, 28.88, 28.61, 27.52, 27.26, 26.01, 25.90 (6C), 22.16, 21.98, 18.07, 17.91, -4.05, -4.09, -4.40, -4.76.

HRMS (ESI-TOF) calcd for $C_{56}H_{77}Br_2NaO_{12}PSI_2$ $[M+Na]^+$ 1209.2950, found 1209.2955.

Synthesis of inositol phosphate derivative S3 from S2b

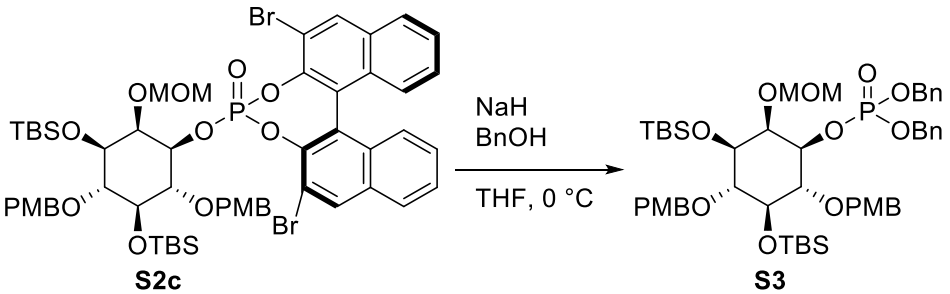


S2b **S3**

To a suspension of NaH (60% oil dispersion) (0.275 mg, 6.90 μmol) in THF (0.5 mL) at 0 °C was added benzyl alcohol (0.785 μL, 7.59 μmol). After stirring for 30 min, the reaction was added to the solution of **S2b** (2.37 mg, 2.30 μmol) in THF (0.5 mL) at 0 °C. The reaction mixture was warmed up to room temperature, and stirred for 1.5 h. The reaction was cooled to 0 °C, and then quenched with 10% aqueous citric acid. The mixture was extracted with ethyl acetate. The organic solution was washed with sat. $NaHCO_3$ aq. and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (15:1) to give the compound **S3** (1.40 mg, 64%) as a colorless oil.

^{1}H NMR spectra was consistent with literature data.[5]

Synthesis of inositol phosphate derivative S3 from S2c

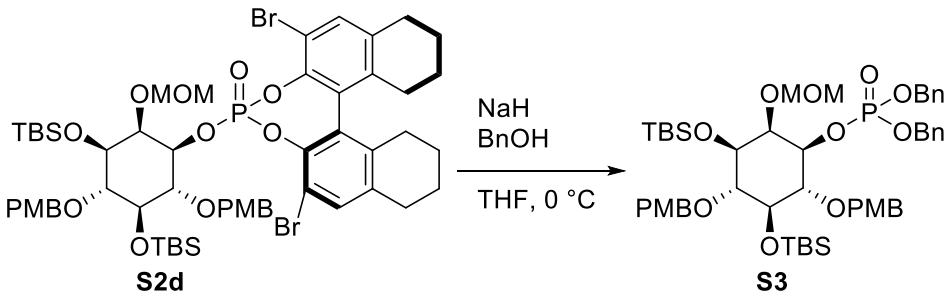


S2c **S3**

The title compound was synthesized following the procedure for **S3** from **S2b**. **S2c** (5.95 mg, 5.04 μmol) was used as starting materials. Compound **S3** (2.31 mg, 48%) was obtained as a colorless oil.

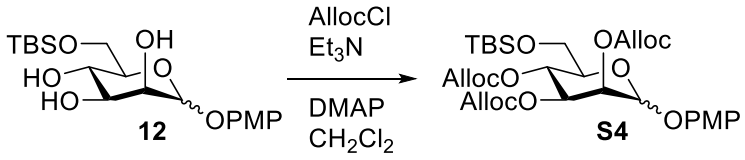
^{1}H NMR spectra was consistent with literature data.[5]

Synthesis of inositol phosphate derivative S3 from S2d



The title compound was synthesized following the procedure for **S3** from **S2b**. **S2d** (4.61 mg, 3.88 μmol) was used as starting materials. Compound **S3** (1.96 mg, 53%) was obtained as a colorless oil. ^{1}H NMR spectra was consistent with literature data.[5]

Synthesis of mannose derivative S4



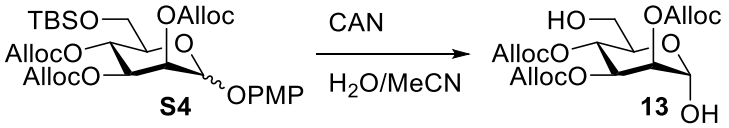
To a solution of **12**[6] (3.37 g, 8.41 mmol), Et_3N (5.91 mL, 42.1 mmol) and DMAP (514 mg, 4.21 mmol) in CH_2Cl_2 (20 mL) was added AllocCl (4.47 mL, 42.1 mmol). The resulting mixture was stirred at room temperature for overnight. The reaction was quenched by an addition of sat. $NaHCO_3$ aq. and extracted with $CHCl_3$. Organic layer was washed with 10% citric acid aq. and brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-EtOAc (5:1) to give **S4** (3.06 g, 56%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.04 (td, *J* = 6.3, 4.0 Hz, 2H), 6.81 (td, *J* = 6.3, 4.0 Hz, 2H), 5.98-5.85 (m, 3H), 5.47 (d, *J* = 1.8 Hz, 1H), 5.43-5.20 (m, 9H), 4.67-4.62 (m, 6H), 4.02 (ddd, *J* = 10.1, 5.2, 2.7 Hz, 1H), 3.80-3.71 (m, 5H), 0.87-0.85 (m, 9H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 155.39, 154.22, 153.91, 149.87 (2C), 131.31, 131.22, 131.05, 119.19, 118.96, 118.89, 118.18 (2C), 114.59 (2C), 96.41, 73.15, 72.74, 71.65, 70.31, 69.06, 68.93, 68.81, 62.20, 55.61, 25.77 (3C), 18.19, -5.49 (2C).

HRMS (ESI-TOF) calcd for $C_{31}H_{44}NaO_{13}Si$ $[M+Na]^+$ 675.2443, found 675.2451.

Synthesis of mannose derivative 13



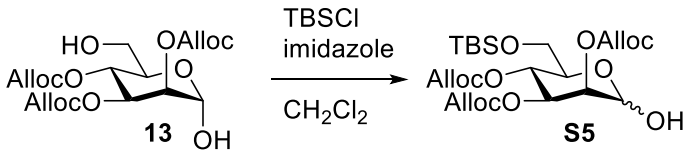
To a solution of **S4** (2.25 g, 3.45 mmol) in MeCN/H_2O (4:1) (30 mL) at 0 ˚C was added CAN (5.67 g, 10.3 mmol) and stirred for overnight. The reaction was poured into water and extracted with EtOAc. Organic layer was washed with brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (1:1) to give **13** (640 mg, 43%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.99-5.87 (m, 3H), 5.41-5.23 (m, 9H), 5.14 (t, *J* = 10.1 Hz, 1H), 4.66-4.62 (m, 6H), 4.09 (ddd, *J* = 9.9, 4.3, 2.5 Hz, 1H), 3.85 (d, *J* = 3.8 Hz, 1H), 3.80-3.70 (m, 2H), 2.64 (t, *J* = 6.5 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 154.26 (2C), 153.79, 131.24, 131.02, 130.96, 119.44, 119.36, 118.96, 91.93, 73.19, 72.51, 70.43, 70.07, 69.17 (2C), 68.96, 61.23.

HRMS (ESI-TOF) calcd for $C_{18}H_{24}NaO_{12}$ $[M+Na]^+$ 455.1160, found 455.1169.

Synthesis of mannose derivative S5



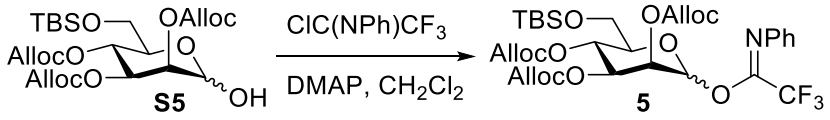
To a solution of **13** (1.70 g, 3.93 mmol) and TBSCl (652 mg, 4.33 mmol) in CH_2Cl_2 (50 mL) was added imidazole (293 mg, 4.33 mmol). The resulting mixture was stirred at room temperature for overnight. The reaction was quenched by an addition of water and extracted with EtOAc. Organic layer was washed with brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (3:1) to give **S5** (1.69 g, 79%) as white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.97-5.86 (m, 3H), 5.40-5.23 (m, 8H), 5.20 (dd, *J* = 3.3, 1.9 Hz, 1H), 5.10 (t, *J* = 10.1 Hz, 1H), 4.64-4.61 (m, 6H), 4.12-4.08 (m, 1H), 4.05 (d, *J* = 4.3 Hz, 1H), 3.84-3.72 (m, 2H), 0.90-0.87 (m, 9H), 0.07 (s, 3H), 0.06 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 154.24, 153.97, 153.79, 131.31, 131.17, 131.10, 119.11, 119.01, 118.77, 91.76, 73.23, 72.93, 71.16, 70.52, 68.95, 68.83, 68.78, 62.72, 25.87 (3C), 18.41, -5.41, -5.49.

HRMS (ESI-TOF) calcd for $C_{24}H_{38}NaO_{12}Si$ $[M+Na]^+$ 569.2025, found 569.2033.

Synthesis of mannose derivative 5



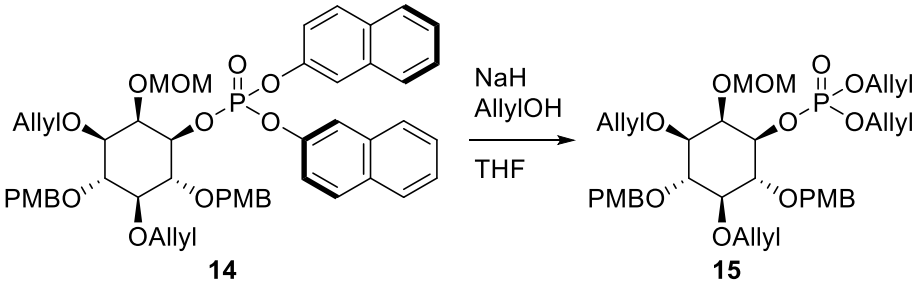
To the solution of the **S5** (356 mg, 651 μmol) and $ClC(NPh)CF_3$ (87.9 μL, 542 μmol) in CH_2Cl_2 (5 mL) was added DMAP (66.2 mg, 542 μmol). After stirring for 6 h, the reaction mixture was purified by column chromatography of SiO_2 with toluene-EtOAc (9:1) to give **5** (419 mg, quant.) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.34-7.28 (m, 2H), 7.14-7.10 (m, 1H), 6.83 (d, *J* = 7.6 Hz, 2H), 6.38 (s, 1H), 5.97-5.87 (m, 3H), 5.40-5.26 (m, 9H), 4.66-4.62 (m, 6H), 4.02-3.95 (m, 1H), 3.81 (d, *J* = 3.6 Hz, 2H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 154.00, 153.78, 153.72, 142.89, 131.20, 131.11, 130.89, 128.80 (2C), 124.62, 119.31 (3C), 119.12, 118.97, 73.69, 72.82, 71.16, 69.47 (2C), 69.23 (2C), 69.04, 68.95 (2C), 61.96, 25.76, 18.21 (3C), -5.41, -5.45.

HRMS (ESI-TOF) calcd for $C_{32}H_{42}F_3NNaO_{12}Si$ $[M+Na]^+$ 740.2321, found 740.2327.

Synthesis of inositol phosphate derivative 15



To a suspension of NaH (60% oil dispersion) (229 mg, 5.71 mmol) in THF (15 mL) at 0 °C was added allyl alcohol (435 μL, 6.40 mmol). After stirring for 30 min, the reaction was added to the solution of **14**[7] (2.00 g, 2.29 mmol) in THF (35 mL) at 0 °C. The reaction mixture was warmed up to room temperature, and stirred for 1.5 h. The reaction was cooled to 0 °C, and then quenched with 10%

aqueous citric acid. The mixture was extracted with ethyl acetate. The organic solution was washed with sat. $NaHCO_3$ aq. and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-EtOAc (5:1) to give the compound **15** (1.10 g, 68%) as a colorless oil.

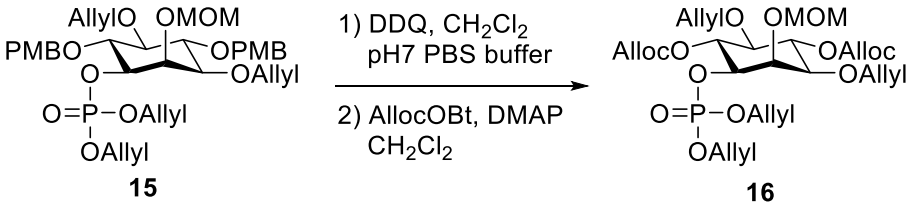
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.32-7.26 (m, 4H), 6.85 (t, *J* = 8.6 Hz, 4H), 6.01-5.77 (m, 4H), 5.35-5.14 (m, 8H), 4.83-4.75 (m, 4H), 4.70 (t, *J* = 10.1 Hz, 2H), 4.55-4.44 (m, 4H), 4.36 (dd, *J* = 12.3, 5.4 Hz, 1H), 4.32-4.27 (m, 2H), 4.19 (dd, *J* = 12.6, 5.4 Hz, 1H), 4.15-4.11 (m, 1H), 4.07 (dd, *J* = 12.6, 5.4 Hz, 1H), 3.90 (t, *J* = 9.6 Hz, 1H), 3.84 (t, *J* = 9.5 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.44 (s, 3H), 3.29-3.23 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.18, 159.04, 135.16, 134.57, 132.47, 132.39, 130.87, 130.69, 129.85 (2C), 129.49 (2C), 118.12, 118.00, 116.82, 116.39, 113.73 (2C), 113.57 (2C), 97.48, 82.70, 80.92, 79.58, 79.28, 77.83, 75.59, 75.25, 74.53, 73.73, 71.35, 68.20, 68.10, 55.81, 55.25, 55.23.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -1.02.

HRMS (ESI-TOF) calcd for $C_{36}H_{49}NaO_{12}P$ $[M+Na]^+$ 727.2854, found 727.2861.

Synthesis of inositol phosphate derivative 16



To a stirred mixture of **15** (900 mg, 1.28 mmol) in CH_2Cl_2 (34.5 mL) and pH 7 phosphate buffer (3.83 mL) was added DDQ (870 mg, 3.83 mmol). After stirring for 4 h, the reaction mixture was extracted with $CHCl_3$ and washed with sat. $NaHCO_3$ aq. and brine, dried over Na_2SO_4, filtrated and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (1:1) to give PMB group deprotected compound (560 mg, 94 %) as a colorless oil. To a PMB group deprotected compound (560 mg, 1.20 mmol) and AllocOBt (1.31 g, 6.00 mmol) in CH_2Cl_2 (15 mL) was added DMAP (733 mg, 6.00 mmol) and the mixture was stirred for 4 h. The reaction was quenched by addition of 10% citric acid aq. and extracted with $CHCl_3$. The organic layer was washed with brine, dried over Na_2SO_4, filtrated and concentrated *in vacuo*. The crude mixture was purified by column chromatography of SiO_2 with toluene-EtOAc (3:1) to give **16** (422 mg, 56 %) as

a colorless oil.

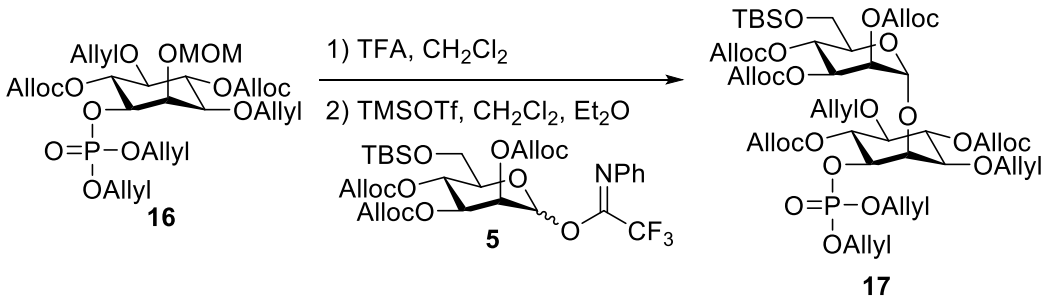
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.98-5.74 (m, 6H), 5.40-5.15 (m, 13H), 5.12 (dd, *J* = 10.4, 1.5 Hz, 1H), 4.78 (s, 2H), 4.67-4.63 (m, 3H), 4.61 (dt, *J* = 5.8, 1.3 Hz, 1H), 4.58-4.50 (m, 4H), 4.37-4.31 (m, 2H), 4.19-4.11 (m, 3H), 3.94 (ddt, *J* = 12.9, 5.5, 1.4 Hz, 1H), 3.45 (t, *J* = 9.5 Hz, 1H), 3.40 (s, 3H), 3.34 (dd, *J* = 10.2, 2.1 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 154.27, 154.21, 134.16, 133.80, 132.17, 132.09, 131.45, 131.33, 119.02, 118.94, 118.36, 118.25, 117.30, 117.06, 97.35, 78.08, 76.53, 76.17, 75.22, 73.62, 72.65, 72.62, 70.97, 68.73, 68.61, 68.38, 68.31, 55.92.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -1.04.

HRMS (ESI-TOF) calcd for $C_{28}H_{41}NaO_{14}P$ $[M+Na]^+$ 655.2126, found 655.2135.

Synthesis of 17



The solution of **16** (775 mg, 1.23 mmol) in CH_2Cl_2 (15 mL) was cooled to 0 °C. To the solution was added TFA (15 mL) at 0 ºC and stirred for 1h. The solvent removed under reduced pressure and added toluene then concentrated *in vacuo* to give the de-2-*O*-MOM compound (629 mg, 87%). The de-2-*O*-MOM compound (124 mg, 211 μmol) and **5** (313 mg, 435 μmol) were co-evaporated with toluene three times and dried highly under vacuum. The residue was dissolved with Et_2O (0.5 mL) and CH_2Cl_2 (0.5 mL) under Ar. To the mixture was added MS4A (100 mg) and then TMSOTf (19.1 μL, 106 μmol). The mixture was stirred at room temperature for 13 h. The reaction was quenched with Et_3N (400 μL) and then the mixture was concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (3:1) to give **17** (112 mg, 48%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.00-5.74 (m, 9H), 5.38-5.10 (m, 22H), 4.67-4.58 (m, 12H), 4.54-4.50 (m, 4H), 4.45-4.40 (m, 2H), 4.27-4.23 (m, 1H), 4.20-4.15 (m, 1H), 4.14-4.12 (m, 2H), 3.96-3.90

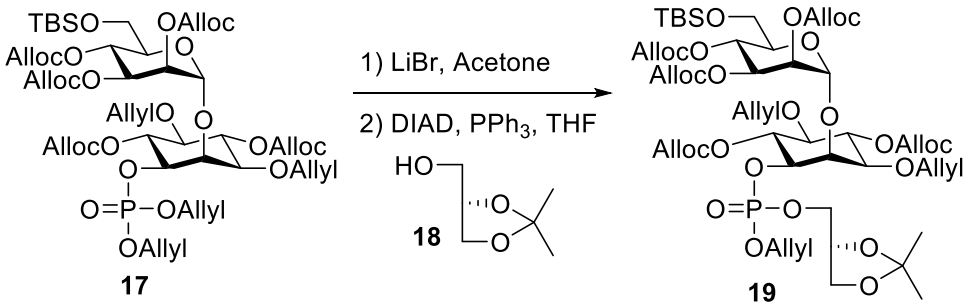
(m, 1H), 3.73 (dd, *J* = 11.6, 3.7 Hz, 1H), 3.67 (dd, *J* = 11.4, 2.0 Hz, 1H), 3.48 (t, *J* = 9.5 Hz, 1H), 3.36 (dd, *J* = 10.1, 2.2 Hz, 1H), 0.88 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 153.89, 153.85, 153.78, 153.73, 153.38, 134.11, 133.63, 132.20, 132.13, 132.02, 131.95, 131.46, 131.39, 131.21, 128.97, 128.17, 125.24, 118.99, 118.69, 118.48, 118.23, 117.49, 117.14, 98.36, 77.72, 76.41, 75.96, 75.69, 75.46, 74.01, 73.49, 73.30, 72.59, 71.46, 70.98, 69.58, 68.76, 68.73, 68.71, 68.69, 68.65, 68.56, 68.43, 61.72, 25.81, 18.25 (3C), -5.51, -5.56.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -1.50.

HRMS (ESI-TOF) calcd for $C_{50}H_{73}NaO_{24}PSi$ $[M+Na]^+$ 1139.3891, found 1139.3888.

Synthesis of 19



To the solution of **17** (127 mg, 114 μmol) in acetone (4 mL) was added LiBr (29.7 mg, 342 μmol) and refluxed for overnight. After the removal of solvent, the crude mixture was purified by column chromatography of SiO_2 with toluene:EtOAc (5:1) to $CHCl_3$:MeOH (6:1) to give lithium salt. The desire product was diluted with EtOAc and washed with sat. $KHSO_4$ aq. and brine. The organic layer was dried over Na_2SO_4, filtrated and concentrated *in vacuo* to obtain proton form. The resulting phosphoric acid, (S)-(+)-2,2-Dimethyl-1,3-dioxolane-4-methanol **18** (42.2 μL, 342 μmol) and PPh_3 (89.7 mg, 342 μmol) were dissolved with THF (1 mL) under Ar. To the mixture was added DIAD (62.5 μL, 342 μmol) and stirred for overnight. The reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (3:1) to give **19** (69.9 mg, 51%) as white solid.

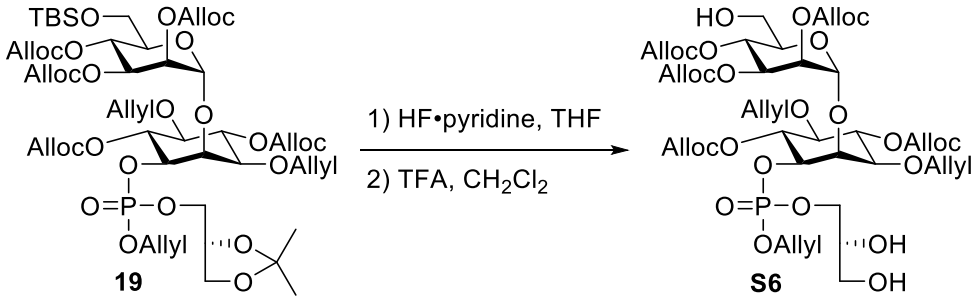
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.00-5.74 (m, 8H), 5.39-5.33 (m, 7H), 5.30-5.21 (m, 11H), 5.20-5.11 (m, 4H), 4.74-4.53 (m, 12H), 4.46-4.38 (m, 2H), 4.29-3.90 (m, 9H), 3.83-3.71 (m, 2H), 3.67 (dd, *J* = 11.6, 1.9 Hz, 1H), 3.48 (td, *J* = 9.6, 2.9 Hz, 1H), 3.37-3.35 (m, 1H), 1.41 (s, 3H), 1.34-1.33 (m, 3H), 0.88 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 153.97, 153.92, 153.82, 153.76, 153.43, 134.10, 133.65, 132.16, 132.00, 131.50, 131.45, 131.41, 131.20, 119.06, 119.04, 118.74, 118.72, 118.66, 118.43, 117.42, 117.19, 109.84, 98.63, 77.66, 76.39, 75.94, 75.61, 75.48, 74.66, 73.86, 73.51, 73.37, 72.62, 71.40, 71.01, 69.55, 68.86, 68.81, 68.74, 68.71, 68.58, 68.01, 65.97, 65.73, 61.64, 26.70, 25.82 (3C), 25.20, 18.26, -5.52, -5.58.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -1.68.

HRMS (ESI-TOF) calcd for $C_{53}H_{79}Na_2O_{26}PSi$ $[M+2Na]^{2+}$ 618.2075, found 618.2076.

Synthesis of S6



To the solution of **19** (69.9 mg, 58.7 μmol) in THF (6 mL) was added the mixture of pyridine (94.5 μL, 1.17 mmol) and HF·pyridine (70% HF) (145 μL) and stirred for 2 d. After an addition of EtOAc, the mixture was quenched by addition of sat. $NaHCO_3$ aq. and extracted with EtOAc. The organic layer was dried over Na_2SO_4, filtrated and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (1:1) to give de-TBS compound (34.1 mg, 54%) as a colorless oil. The solution of de-TBS compound (34.1 mg, 31.7 μmol) in CH_2Cl_2 (5 mL) was cooled to 0 °C. To the solution was added TFA (382 μL) at 0 ºC and stirred for 4 h. The reaction was quenched by addition of sat. $NaHCO_3$ aq. and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, filtrated and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with $CHCl_3$-MeOH (30:1) to give **S6** (30.0 mg, 91%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.00-5.74 (m, 8H), 5.38-5.11 (m, 22H), 4.70-4.41 (m, 14H), 4.24-3.86 (m, 8H), 3.71-3.58 (m, 4H), 3.50 (t, J = 9.6 Hz, 1H), 3.39 (td, J = 10.2, 2.2 Hz, 1H).

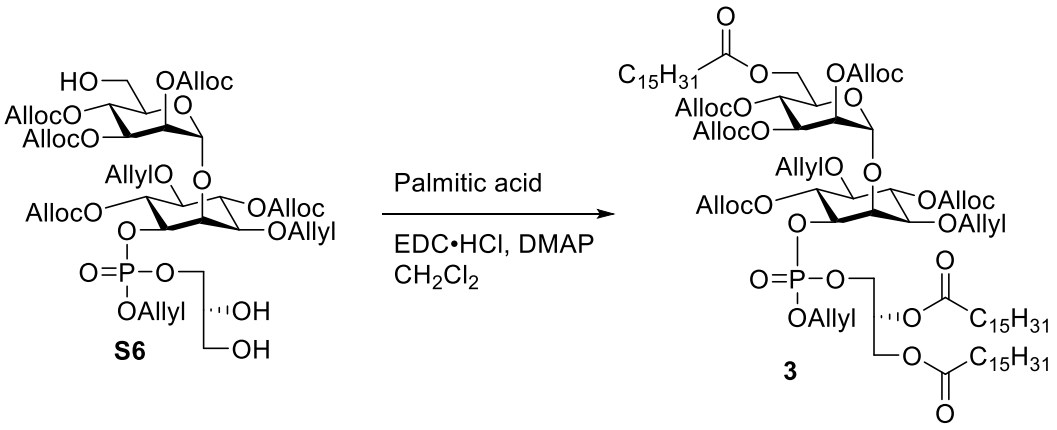
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 154.11, 154.04, 154.00, 153.92, 153.40, 134.01, 133.53, 131.95, 131.42, 131.29, 131.24, 131.01, 130.94, 119.42, 119.36, 119.22, 119.10, 119.01, 118.77, 117.71,

117.25, 97.91, 77.20, 76.89, 75.47, 73.77, 72.65, 72.57, 71.76, 71.10, 70.37, 70.33, 69.65, 69.23, 69.16, 69.09 (2C), 68.99, 68.95 (2C), 68.89, 68.76, 62.76, 60.94.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -0.88.

HRMS (ESI-TOF) calcd for $C_{44}H_{61}Na_2O_{26}P$ $[M+2Na]^{2+}$ 541.1487, found 541.1493.

Synthesis of 3



To a solution of **S6** (13.6 mg, 13.1 μmol), palmitic acid (16.8 mg, 65.7 μmol) and EDC•HCl (12.6 mg, 65.7 μmol) in CH_2Cl_2 (1 mL) was added DMAP (8.02 mg, 65.7 μmol). The resulting mixture was stirred at room temperature for overnight. The reaction was quenched by an addition of sat. $KHSO_4$ aq. and extracted with $CHCl_3$. Organic layer was washed with brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (10:1) to give **3** (11.7 mg, 51%) as white solid.

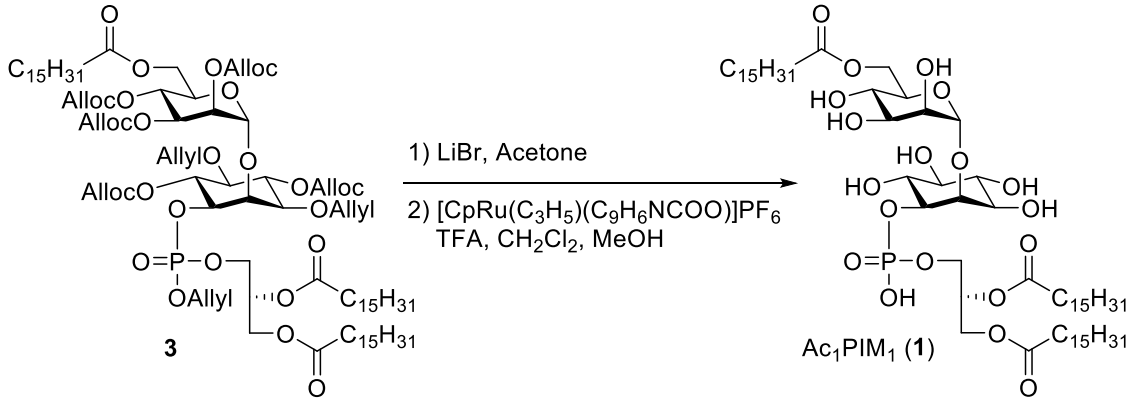
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.99-5.75 (m, 8H), 5.39-5.11 (m, 23H), 4.66-4.07 (m, 24H), 3.98 (dd, *J* = 12.9, 5.3 Hz, 1H), 3.53-3.46 (m, 1H), 3.43-3.37 (m, 1H), 2.41-2.28 (m, 6H), 1.62-1.59 (m, 6H), 1.33-1.23 (m, 72H), 0.88 (t, *J* = 6.8 Hz, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.55, 173.20, 172.86, 154.01, 153.89, 153.85, 153.33, 153.31, 134.13, 133.54, 132.11, 132.05, 131.45, 131.29, 131.22, 119.17, 119.13, 119.05, 118.86, 118.72, 118.61, 117.80, 117.26, 98.73, 77.62, 77.23, 76.36, 75.95, 75.57, 75.41, 73.66, 72.86, 72.50, 71.62, 69.37 (2C), 69.06, 68.99, 68.88, 68.80 (3C), 68.71 (2C), 65.94, 61.68, 34.18, 34.10, 34.01, 31.93 (3C), 29.72 (12C), 29.67 (6C), 29.54 (3C), 29.38 (3C), 29.33 (3C), 29.17 (3C), 24.85 (2C), 24.70, 22.70 (3C), 14.13 (3C).

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -1.87.

HRMS (ESI-TOF) calcd for $C_{92}H_{151}Na_2O_{29}P$ $[M+2Na]^{2+}$ 898.4932, found 898.4940.

Synthesis of Ac_1PIM_1 1



To a stirred solution of **3** (21.8 mg, 12.5 μmol) in acetone (1 mL) was added LiBr (10.8 mg, 125 μmol) and refluxed for 6 h. After the removal of solvent, the crude mixture was purified by column chromatography of SiO_2 (toluene:EtOAc = 1:1 to $CHCl_3$:MeOH = 6:1) to give a lithium salt. The salt was dissolved in CH_2Cl_2:MeOH = 1:1 containing 1% TFA (vol/vol) (1 mL). $[CpRu(C_3H_5)(C_9H_6NCOO)]PF_6$ (6.53 mg, 12.5 μmol) was added to the reaction mixture. After stirring for 1 h, the solvent was removed *in vacuo*. The crude mixture was purified by column chromatography of SiO_2 with $CHCl_3$-MeOH (10:1 to 1:1) and metal scavenger SiliaMetS® DMT with $CHCl_3$-MeOH (10:1 to 1:1) and SiO_2 with $CHCl_3$-MeOH (10:1 to 1:1) to give **1** (2.15 mg, 14%) as a white solid. The purity of **1** was 99% (measured by quantitative NMR using CHBr3 as an internal standard).

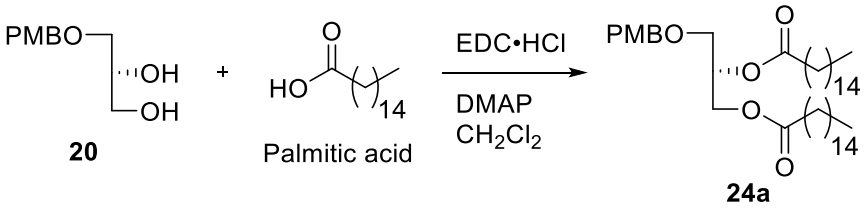
^{1}H-NMR (800 MHz, $CDCl_3$:CD_3OD:D_2O = 65:35:8) δ: 5.25 (d, *J* = 4.7 Hz, 1H), 5.10-5.09 (m, 1H), 4.42 (dd, *J* = 12.1, 2.7 Hz, 1H), 4.34 (dd, *J* = 11.7, 1.6 Hz, 1H), 4.26-4.24 (m, 1H), 4.22-4.21 (m, 1H), 4.18 (dd, *J* = 12.1, 7.4 Hz, 1H), 4.15-4.13 (m, 1H), 4.06-4.02 (m, 1H), 4.02-4.00 (m, 1H), 3.99-3.94 (m, 2H), 3.74 (dd, *J* = 9.4, 3.9 Hz, 1H), 3.72 (t, *J* = 9.4 Hz, 1H), 3.65 (t, *J* = 9.8 Hz, 1H), 3.57 (t, *J* = 9.8 Hz, 1H), 3.47 (dd, *J* = 10.2, 2.3 Hz, 1H), 3.26 (t, *J* = 9.0 Hz, 1H), 2.36 (t, *J* = 7.8 Hz, 2H), 2.34 (t, *J* = 7.4 Hz, 2H), 2.30 (td, *J* = 7.8, 1.8 Hz, 2H), 1.63-1.56 (m, 6H), 1.33-1.22 (m, 72H), 0.88 (t, *J* = 7.0 Hz, 9H).

^{13}C-NMR (200 MHz, $CDCl_3$:CD_3OD:D_2O = 65:35:8) δ: 175.15, 174.29, 173.97, 101.75, 78.99, 76.51, 74.55, 72.60, 72.29, 70.73, 70.59, 70.48, 70.44, 70.11, 67.09, 63.62, 63.54, 62.90, 34.18, 34.06, 33.86, 31.86 (3C), 29.67 (3C), 29.64 (6C), 29.58 (3C), 29.55 (3C), 29.52 (3C), 29.36 (3C), 29.28 (3C), 29.17 (3C), 29.10 (3C), 24.89, 24.80, 24.73, 22.58 (3C), 13.86 (3C).

^{31}P-NMR (160 MHz, $CDCl_3$:CD_3OD:D_2O = 65:35:8) δ: -0.16.

HRMS (ESI-TOF) calcd for $C_{63}H_{118}O_{19}P$ $[M-H]^-$ 1209.8019, found 1209.8010.

Synthesis of glycerolipid derivative 24a



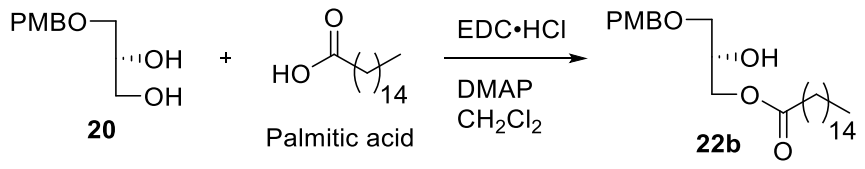
To a solution of (R)-3-(4-methoxybenzyloxy)propane-1,2-diol **20**[8] (108 mg, 500 μmol), palmitic acid (385 mg, 1.50 mmol) and EDC•HCl (288 mg, 1.50 mmol) in CH_2Cl_2 (3 mL) was added DMAP (18.3 mg, 150 μmol). The resulting mixture was stirred at room temperature for overnight. The reaction was quenched by an addition of sat. $KHSO_4$ aq. and extracted with $CHCl_3$. Organic layer was washed with brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-EtOAc (6:1) to give **24a** (345 mg, 95%) as white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.26-5.19 (m, 1H), 4.47 (dd, *J* = 19.1, 11.8 Hz, 2H), 4.33 (dd, *J* = 12.1, 3.8 Hz, 1H), 4.17 (dd, *J* = 12.0, 6.3 Hz, 1H), 3.81 (s, 3H), 3.55 (d, *J* = 5.1 Hz, 2H), 2.33-2.25 (m, 4H), 1.64-1.51 (m, 4H), 1.33-1.18 (m, 48H), 0.88 (t, *J* = 6.8 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.25, 172.97, 159.23, 129.64, 129.19 (2C), 113.68 (2C), 72.84, 69.92, 67.77, 62.59, 55.07, 34.22, 34.01, 31.87 (2C), 29.64 (3C), 29.61 (3C), 29.58 (2C), 29.53, 29.43 (2C), 29.40, 29.31 (2C), 29.23 (2C), 29.20, 29.05 (2C), 29.01, 24.88, 24.81, 22.62 (2C), 14.04 (2C).

HRMS (ESI-TOF) calcd for $C_{43}H_{76}NaO_6$ $[M+Na]^+$ 711.5534, found 711.5538.

Synthesis of glycerolipid derivative 22b



To a solution of (R)-3-(4-methoxybenzyloxy)propane-1,2-diol **20**[8] (425 mg, 2.00 mmol), palmitic acid (513 mg, 2.00 mmol) and EDC•HCl (383 mg, 2.00 mmol) in CH_2Cl_2 (10 mL) was added DMAP (24.4 mg, 200 μmol). The resulting mixture was stirred at room temperature for overnight. The reaction was quenched by an addition of sat. $KHSO_4$ aq. and extracted with $CHCl_3$. Organic layer was washed with

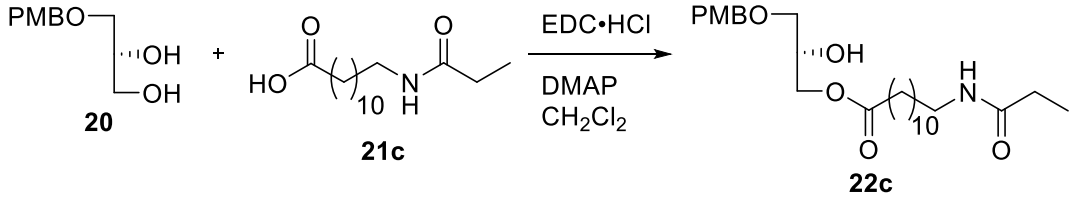
brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-EtOAc (2:1 to EtOAc only) to give **22b** (83.0 mg, 35%) as white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.25 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 5.29 (s, 1H), 4.48 (s, 2H), 4.20-4.09 (m, 2H), 4.05-3.98 (m, 1H), 3.80 (s, 3H), 3.52 (dd, *J* = 9.3, 4.4 Hz, 1H), 3.45 (dd, *J* = 9.5, 6.1 Hz, 1H), 2.56 (d, *J* = 4.4 Hz, 1H), 2.32 (t, *J* = 7.6 Hz, 2H), 1.65-1.57 (m, 2H), 1.25-1.25 (m, 22H), 0.88 (t, *J* = 6.6 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.91, 159.33, 129.71, 129.38 (2C), 113.82 (2C), 73.12, 70.52, 68.87, 65.32, 55.22, 34.11, 31.89, 29.65 (2C), 29.63, 29.61 (2C), 29.57, 29.43, 29.32, 29.22, 29.09, 24.87, 22.65, 14.08.

HRMS (ESI-TOF) calcd for $C_{27}H_{46}NaO_5$ $[M+Na]^+$ 473.3237, found 473.3241.

Synthesis of glycerolipid derivative 22c



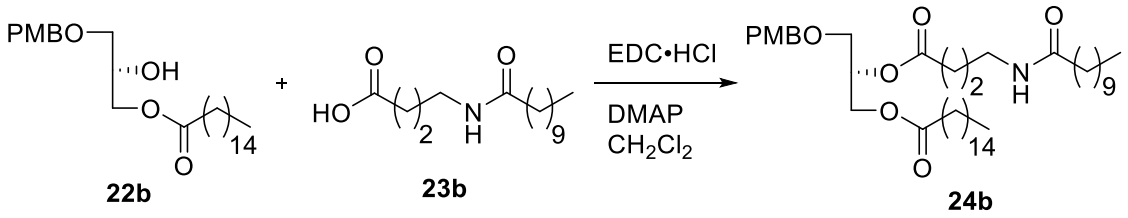
The title compound was synthesized following the procedure for **22b**. (R)-3-(4-methoxybenzyloxy)propane-1,2-diol **20**[8] (106 mg, 500 μmol) and compound **21c**[3] (136 mg, 500 μmol) were used as starting materials. Compound **22c** (97.8 mg, 33%) was obtained as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.25 (d, *J* = 8.8 Hz, 2H), 6.89 (dd, *J* = 6.6, 2.2 Hz, 2H), 4.49 (s, 2H), 4.20-4.09 (m, 2H), 4.02 (td, *J* = 9.6, 5.0 Hz, 1H), 3.81 (s, 3H), 3.53 (dd, *J* = 9.5, 4.1 Hz, 1H), 3.46 (dd, *J* = 9.5, 6.1 Hz, 1H), 3.24 (q, *J* = 6.8 Hz, 2H), 2.52 (d, *J* = 4.4 Hz, 1H), 2.39-2.25 (m, 2H), 2.19 (q, *J* = 7.6 Hz, 2H), 1.51-1.44 (m, 2H), 1.34-1.22 (m, 16H), 1.15 (t, *J* = 7.6 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.77, 159.11, 129.64, 129.21 (2C), 129.11, 113.62 (2C), 72.92, 70.47, 68.55, 65.26, 55.06, 39.33, 33.94, 29.50, 29.42, 29.27, 29.26, 29.18, 29.08, 29.01, 28.88, 26.72, 24.68, 9.83.

HRMS (ESI-TOF) calcd for $C_{26}H_{43}NNaO_6$ $[M+Na]^+$ 488.2983, found 488.2992.

Synthesis of glycerolipid derivative 24b



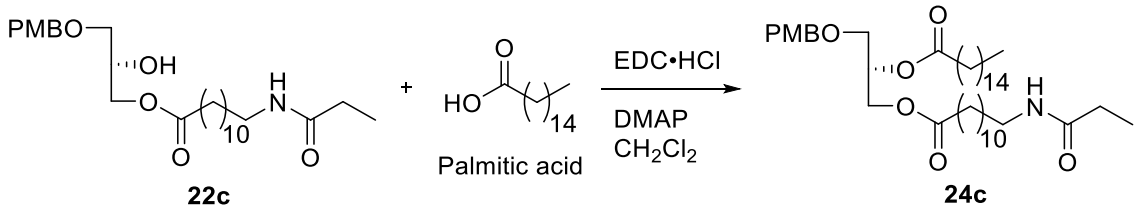
To a solution of **22b** (83.0 mg, 184 μmol), **23b**[3] (100 mg, 368 μmol) and EDC•HCl (70.6 mg, 368 μmol) in CH_2Cl_2 (3 mL) was added DMAP (4.50 mg, 36.8 μmol). The resulting mixture was stirred at room temperature for overnight. The reaction was quenched by an addition of sat. $KHSO_4$ aq. and extracted with $CHCl_3$. Organic layer was washed with brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-EtOAc (2:1) to give **24b** (112 mg, 87%) as white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.92-5.82 (m, 1H), 5.21 (dt, *J* = 10.3, 4.6 Hz, 1H), 4.46 (dd, *J* = 15.7, 11.6 Hz, 2H), 4.38 (dd, *J* = 12.0, 3.7 Hz, 1H), 4.15 (dd, *J* = 11.9, 5.9 Hz, 1H), 3.80 (s, 3H), 3.56 (d, *J* = 5.3 Hz, 2H), 3.35-3.19 (m, 2H), 2.36 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 2.12 (t, *J* = 7.6 Hz, 2H), 1.86-1.79 (m, 2H), 1.65-1.52 (m, 4H), 1.35-1.19 (m, 38H), 0.88 (t, *J* = 6.7 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.43, 173.24, 172.57, 159.29, 129.51, 129.28 (2C), 113.76 (2C), 72.93, 70.41, 67.73, 62.36, 55.17, 38.50, 36.68, 34.02, 31.85, 31.82, 31.52, 29.62 (2C), 29.58 (2C), 29.55, 29.51, 29.44, 29.42, 29.31, 29.28 (3C), 29.25, 29.21, 29.05, 25.68, 24.81, 24.51, 22.62, 14.04.

HRMS (ESI-TOF) calcd for $C_{42}H_{73}NNaO_7$ $[M+Na]^+$ 726.5279, found 726.5287.

Synthesis of glycerolipid derivative 24c



The title compound was synthesized following the procedure for **24b**. **22c** (177 mg, 380 μmol) and palmitic acid (292 mg, 1.14 mmol) were used as starting materials. Compound **24c** (230 mg, 86%) was obtained as a white solid.

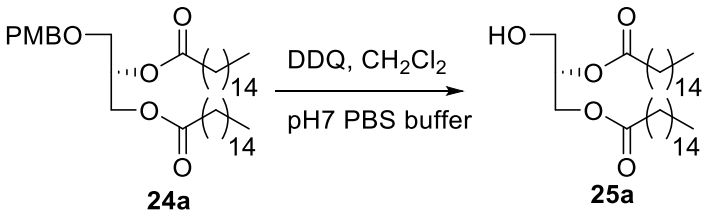
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.41 (s, 1H), 5.26-5.19 (m, 1H), 4.47 (dd, *J* = 18.6, 11.7 Hz, 2H), 4.32 (dd, *J* = 11.8, 3.8 Hz, 1H), 4.17 (dd, *J* = 11.8, 6.5

Hz, 1H), 3.81 (s, 3H), 3.55 (dd, *J* = 5.2, 1.0 Hz, 2H), 3.24 (dd, *J* = 13.1, 7.0 Hz, 2H), 2.37-2.24 (m, 4H), 2.19 (q, *J* = 7.6 Hz, 2H), 1.64-1.56 (m, 4H), 1.51-1.45 (m, 2H), 1.33-1.20 (m, 38H), 1.16 (t, *J* = 7.6 Hz, 3H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.64, 173.42, 173.14, 159.28, 129.73, 129.28 (2C), 113.79 (2C), 72.94, 69.99, 67.88, 62.69, 55.25, 39.51, 34.32, 34.08, 31.91, 29.80, 29.68 (2C), 29.65 (3C), 29.63, 29.47 (3C), 29.40, 29.35 (2C), 29.28, 29.27, 29.23, 29.07 (2C), 26.89, 24.94, 24.84, 22.67, 14.12, 9.94.

HRMS (ESI-TOF) calcd for $C_{42}H_{73}NNaO_7$ $[M+Na]^+$ 726.5279, found 726.5287.

Synthesis of glycerolipid derivative 25a



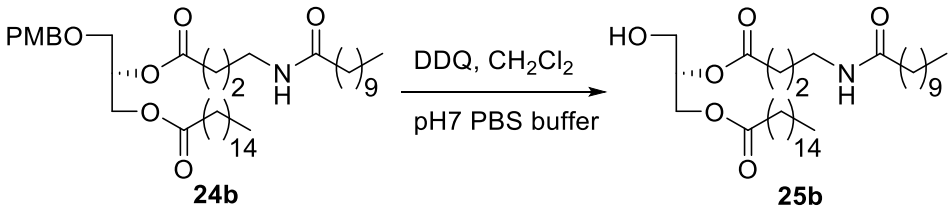
To a solution of **24a** (46.7 mg, 67.8 μmol) in CH_2Cl_2 (2 mL) and pH 7 phosphate buffer (220 μL) was added DDQ (30.8 mg, 136 μmol). The resulting mixture was stirred at room temperature for overnight. The reaction was quenched by an addition of sat. $NaHCO_3$ aq. and extracted with $CHCl_3$. Organic layer was washed with brine and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with toluene-EtOAc (6:1) to give **25a** (29.4 mg, 76%) as white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.04-4.99 (m, 1H), 4.25 (dd, *J* = 12.0, 4.4 Hz, 1H), 4.16 (dd, *J* = 12.0, 5.7 Hz, 1H), 3.66 (d, *J* = 5.2 Hz, 2H), 2.26 (q, *J* = 7.9 Hz, 4H), 1.60-1.51 (m, 4H), 1.27-1.14 (m, 48H), 0.81 (t, *J* = 6.7 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.80, 173.44, 72.08, 61.99, 61.51, 34.27, 34.09, 31.91 (2C), 29.68 (4C), 29.67 (2C), 29.64 (4C), 29.61 (2C), 29.46 (2C), 29.34 (2C), 29.26 (2C), 29.10, 29.07, 24.93, 24.87, 22.67 (2C), 14.10 (2C).

HRMS (ESI-TOF) calcd for $C_{35}H_{68}NaO_5$ $[M+Na]^+$ 591.4959, found 591.4963.

Synthesis of glycerolipid derivative 25b



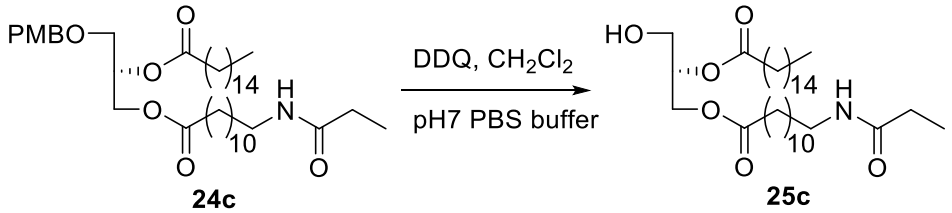
The title compound was synthesized following the procedure for **25a**. **24b** (30.0 mg, 42.6 μmol) and DDQ (19.3 mg, 85.2 μmol) were used as starting materials. Compound **25b** (23.3 mg, 94%) was obtained as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.72-5.68 (m, 1H), 5.10-5.05 (m, 1H), 4.32-4.05 (m, 2H), 3.84-3.80 (m, 1H), 3.69 (dd, *J* = 12.5, 5.4 Hz, 1H), 3.51-3.09 (m, 2H), 2.39-2.26 (m, 4H), 2.16-2.11 (m, 2H), 1.91-1.69 (m, 2H), 1.61-1.54 (m, 4H), 1.31-1.18 (m, 38H), 0.85 (t, *J* = 6.8 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.84, 173.66, 172.50, 72.94, 62.16, 61.22, 38.04, 36.75, 34.10, 31.91, 31.87, 31.07, 29.68 (3C), 29.64 (3C), 29.60, 29.55, 29.48, 29.46, 29.34, 29.31, 29.28, 29.27, 29.10, 25.68, 25.09, 24.87, 22.67, 22.66, 14.11 (2C).

HRMS (ESI-TOF) calcd for $C_{34}H_{65}NNaO_6$ $[M+Na]^+$ 606.4704, found 606.4708.

Synthesis of glycerolipid derivative 25c



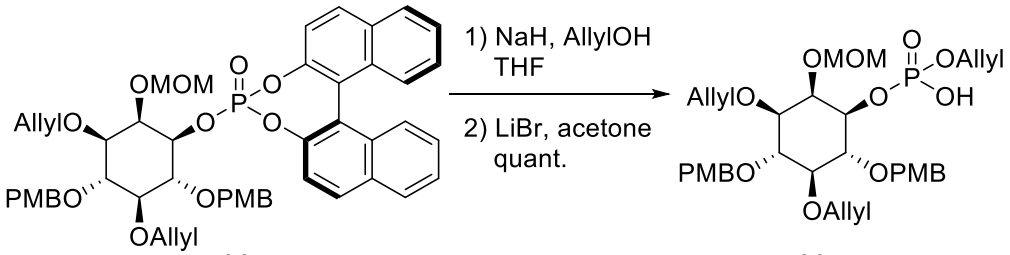
The title compound was synthesized following the procedure for **25a**. **24c** (193 mg, 274 μmol) and DDQ (125 mg, 549 μmol) were used as starting materials. Compound **25c** (145 mg, 90%) was obtained as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.47-5.35 (m, 1H), 5.11-5.06 (m, 1H), 4.32 (dd, *J* = 12.0, 4.6 Hz, 1H), 4.24 (dd, *J* = 12.0, 5.6 Hz, 1H), 3.76-3.70 (m, 2H), 3.24 (td, *J* = 6.8, 6.1 Hz, 2H), 2.34 (q, *J* = 7.9 Hz, 4H), 2.19 (q, *J* = 7.6 Hz, 2H), 1.66-1.58 (m, 4H), 1.52-1.46 (m, 2H), 1.33-1.21 (m, 38H), 1.16 (t, *J* = 7.6 Hz, 3H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.77, 173.65, 173.41, 72.07, 62.00, 61.49, 39.49, 34.27, 34.07, 31.91, 29.80, 29.68 (3C), 29.64 (3C), 29.60, 29.46, 29.42, 29.39, 29.34, 29.31, 29.26, 29.21, 29.14, 29.07, 29.02, 26.84, 24.93, 24.83, 22.67, 14.11, 9.93.

HRMS (ESI-TOF) calcd for $C_{34}H_{65}NNaO_6$ $[M+Na]^+$ 606.4704, found 606.4713.

Synthesis of inositol phosphate derivative 26



14 **26**

To a suspension of NaH (60% oil dispersion) (27.6 mg, 689 μmol) in THF (7 mL) at 0 °C was added allyl alcohol (52.6 μL, 773 μmol). After stirring for 30 min, the reaction was added to the solution of **14**[7] (241 mg, 276 μmol) in THF (3 mL) at 0 °C. The reaction mixture was warmed up to room temperature, and stirred for 1.5 h. The reaction was cooled to 0 °C, and then quenched with 10% aqueous citric acid. The mixture was extracted with ethyl acetate. The organic solution was washed with sat. $NaHCO_3$ aq. and brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-EtOAc (5:1). The resulting product was dissolved with acetone (3 mL). To the solution was added LiBr (120 mg, 1.38 mmol) and refluxed for 6 h. After the removal of solvent, the crude mixture was purified by column chromatography of SiO_2 with toluene-EtOAc (5:1), then CH_2Cl_2-MeOH (6:1) to give lithium salt. The desire product was diluted with EtOAc and washed with sat. $KHSO_4$ aq. and brine. The organic layer was dried over Na_2SO_4, filtrated and concentrated *in vacuo* to obtain proton form **26** (138 mg, 75%) as a colorless oil.

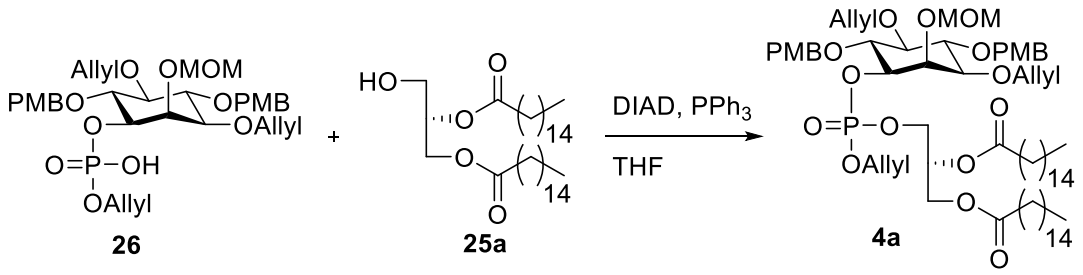
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 9.82 (s, 1H), 7.33-7.27 (m, 4H), 6.87-6.82 (m, 4H), 6.01-5.78 (m, 3H), 5.34-5.30 (m, 1H), 5.29-5.22 (m, 2H), 5.19-5.14 (m, 3H), 4.83-4.66 (m, 6H), 4.48-4.45 (m, 2H), 4.34-4.28 (m, 3H), 4.19-4.15 (m, 1H), 4.11-4.04 (m, 2H), 3.89 (t, J = 9.6 Hz, 1H), 3.83 (t, J = 9.5 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.44 (s, 3H), 3.27-3.20 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 159.12, 159.08, 135.16, 134.52, 132.37, 132.30, 130.87, 130.49, 129.83, 129.75, 117.86, 116.74, 116.27, 113.65, 113.56, 97.47, 82.50, 80.82, 79.68, 79.61, 79.17, 77.88, 77.82, 75.49, 75.39, 74.49, 73.80, 71.31, 68.00, 67.94, 55.71, 55.19, 55.14.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: 0.69.

HRMS (ESI-TOF) calcd for $C_{33}H_{44}NaO_{12}P$ $[M+Na]^+$ 663.2576, found 663.2584.

Synthesis of inositol phospholipid derivative 4a



To the solution of **26** (50.1 mg, 75.4 μmol), **25a** (85.9 mg, 151 μmol) and PPh_3 (39.6 mg, 151 mmol) in THF (750 μL) was added DIAD (27.6 μL, 151 μmol) and stirred for overnight. The reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with *n*-hexane-EtOAc (1:3) to give **4a** (60.5 mg, 66%) as white solid.

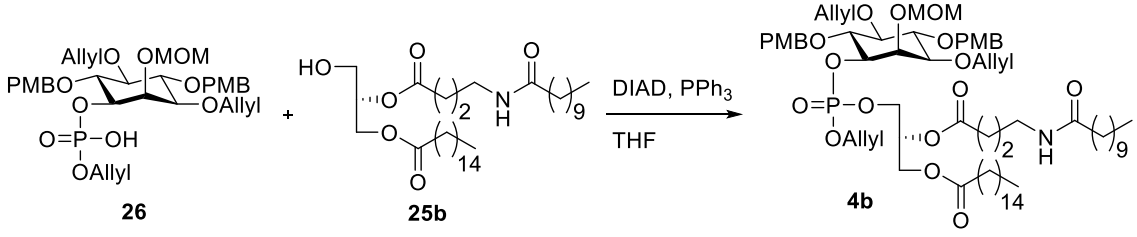
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.32-7.26 (m, 4H), 6.87-6.83 (m, 4H), 6.00-5.77 (m, 3H), 5.35-5.14 (m, 6H), 5.10-4.94 (m, 1H), 4.81-4.76 (m, 4H), 4.68 (dd, *J* = 10.3, 3.4 Hz, 2H), 4.55-4.41 (m, 2H), 4.37 (dd, *J* = 13.0, 4.9 Hz, 1H), 4.31-3.92 (m, 9H), 3.88 (t, *J* = 8.5 Hz, 1H), 3.83 (t, *J* = 8.5 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.45-3.39 (m, 3H), 3.30-3.23 (m, 2H), 2.32-2.23 (m, 4H), 1.62-1.52 (m, 4H), 1.33-1.19 (m, 48H), 0.88 (t, *J* = 6.7 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.08, 172.74, 159.17, 159.06, 135.11, 134.56, 132.28, 132.22, 130.85, 130.59, 129.81, 129.45, 129.32, 118.28, 118.16, 116.77, 116.39, 113.71, 113.60, 113.56, 97.46, 82.68, 80.91, 79.28, 77.96, 75.56, 75.15, 74.50, 73.67, 71.38, 69.23, 68.41, 65.56, 65.23, 61.61, 55.78, 55.22, 55.19, 34.06, 33.92, 31.89 (2C), 29.67 (6C), 29.63 (6C), 29.47 (2C), 29.33 (2C), 29.27 (2C), 29.09, 29.06, 24.78 (2C), 22.66 (2C), 14.09 (2C).

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -0.59.

HRMS (ESI-TOF) calcd for $C_{68}H_{111}NaO_{16}P$ $[M+Na]^+$ 1273.7502, found 1273.7496.

Synthesis of inositol phospholipid derivative 4b



The title compound was synthesized following the procedure for **4a**. compounds **26** (65.0 mg, 97.8 μmol) and **25b** (114 mg, 196 μmol) were used as starting materials. Compound **4b** (70.6 mg, 59%) was obtained as a white solid.

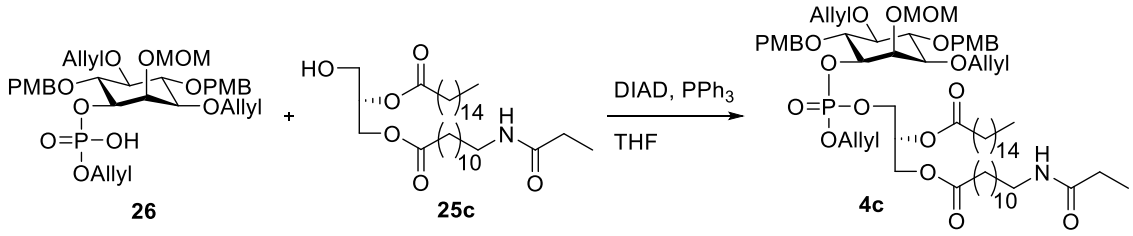
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.30-7.27 (m, 4H), 6.88-6.84 (m, 4H), 6.27-6.04 (m, 1H), 5.93-5.84 (m, 3H), 5.34-5.05 (m, 7H), 4.82-4.76 (m, 4H), 4.70-4.64 (m, 2H), 4.53-4.46 (m, 2H), 4.39-4.00 (m, 10H), 3.98-3.77 (m, 8H), 3.43 (s, 3H), 3.40-3.13 (m, 4H), 2.41-2.24 (m, 4H), 2.18-2.10 (m, 2H), 1.86-1.76 (m, 2H), 1.64-1.56 (m, 4H), 1.33-1.21 (m, 38H), 0.88 (t, J = 6.5 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.31, 173.27, 172.24, 159.19, 159.12, 135.06, 134.51, 130.81, 130.57, 130.53, 129.82, 129.79, 129.47, 129.34, 118.42, 118.26, 116.86, 116.80, 116.41, 113.72, 113.61, 97.42, 82.74, 80.90, 79.26, 78.04, 75.58, 74.50, 73.65, 71.39, 68.39, 67.70, 65.62, 64.81, 61.43, 61.43, 55.74, 55.23, 55.20, 38.22, 36.69, 33.94, 31.88, 31.84, 31.06, 29.65 (2C), 29.61, 29.58, 29.55, 29.53, 29.49, 29.45, 29.42, 29.36, 29.31, 29.28, 29.25, 29.10, 29.08, 25.74, 24.78, 24.21, 22.65, 22.63, 14.08 (2C).

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -0.64.

HRMS (ESI-TOF) calcd for $C_{67}H_{108}NNaO_{17}P$ $[M+Na]^+$ 1252.7247, found 1252.7253.

Synthesis of inositol phospholipid derivative 4c



The title compound was synthesized following the procedure for **4a**. Compounds **26** (65.0 mg, 97.8 μmol) and **25c** (114 mg, 196 μmol) were used as starting materials. Compound **4c** (115 mg, 95%) was obtained as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.31-7.28 (m, 4H), 6.87-6.83 (m, 4H), 6.00-5.77 (m, 3H), 5.35-5.24 (m, 3H), 5.22-5.14 (m, 3H), 5.12-5.07 (m, 1H), 4.80-4.77 (m, 4H), 4.68 (dd, J = 10.3, 4.4 Hz, 2H), 4.52-4.42 (m, 2H), 4.39-4.01 (m, 10H), 3.97-3.71 (m, 8H), 3.45-3.40 (m, 3H), 3.29-3.20 (m, 5H), 2.36-2.12 (m, 6H), 1.63-1.56 (m, 4H), 1.50-1.46 (m, 2H), 1.30-1.23 (m, 38H), 1.15 (t, J = 7.6 Hz, 3H), 0.88 (t, J = 6.7 Hz, 3H).

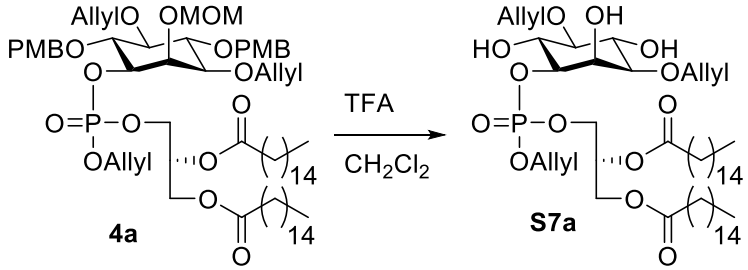
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.63, 173.28, 172.67, 159.11, 159.02, 135.05, 134.49, 132.21,

132.13, 130.80, 130.52, 129.72, 129.38, 129.26, 118.21, 116.72, 116.29, 113.64 (2C), 113.53, 113.50, 97.37, 82.63, 80.85, 79.22, 75.47, 75.08, 74.42, 73.61, 71.98, 71.33, 69.27, 68.22, 62.09, 61.47, 61.17, 55.70, 55.15, 55.10, 39.41, 34.19, 33.98, 31.81, 29.64, 29.58 (3C), 29.54 (3C), 29.40 (2C), 29.31, 29.25 (2C), 29.19 (2C), 29.13, 29.06, 28.98, 28.93, 26.81, 24.74, 24.69, 22.57, 14.02, 9.87.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -0.67.

HRMS (ESI-TOF) calcd for $C_{67}H_{108}NNaO_{17}P$ $[M+Na]^+$ 1252.7247, found 1252.7255.

Synthesis of inositol phospholipid derivative S7a



The solution of **4a** (60.5 mg, 49.8 μmol) in CH_2Cl_2 (1 mL) was cooled to 0 ˚C. To the solution was added trifluoroacetic acid (1 mL) and stirred for 1h. The solvent removed under reduced pressure and added toluene then concentrated *in vacuo*. The residue was purified by column chromatography of SiO_2 with $CHCl_3$-MeOH (9:1) to give **S7a** (55.5 mg, quant.) as a colorless oil.

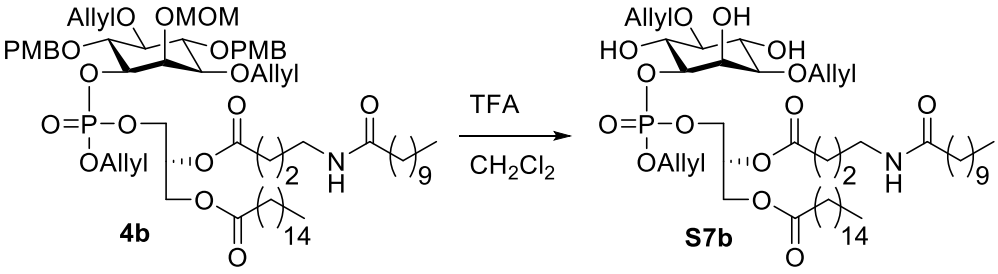
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.02-5.89 (m, 3H), 5.40-5.16 (m, 7H), 4.65-4.57 (m, 2H), 4.39-4.12 (m, 10H), 4.07-4.01 (m, 1H), 3.93 (td, *J* = 9.5, 4.6 Hz, 1H), 3.29-3.25 (m, 1H), 3.19 (td, *J* = 9.3, 4.2 Hz, 1H), 2.35-2.28 (m, 4H), 1.62-1.57 (m, 4H), 1.29-1.23 (m, 48H), 0.88 (t, *J* = 6.8 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.50, 173.25, 134.95, 134.05 (2C), 118.83, 118.27, 117.30, 81.51, 81.47, 78.27, 78.23, 73.92, 73.90, 71.60, 71.58, 71.48, 71.36, 61.83, 61.78, 34.12, 33.99, 31.90 (2C), 29.68 (6C), 29.66 (2C), 29.64 (4C), 29.48 (2C), 29.34 (2C), 29.28 (2C), 29.11, 29.07, 24.79 (2C), 22.67 (2C), 14.09 (2C).

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -1.44.

HRMS (ESI-TOF) calcd for $C_{50}H_{91}NaO_{13}P$ $[M+Na]^+$ 953.6090, found 953.6082.

Synthesis of inositol phospholipid derivative S7b



The title compound was synthesized following the procedure for **S7a**. Compound **4b** (70.6 mg, 57.4 μmol) was used as starting materials. Compound **S7b** (41.3 mg, 76%) was obtained as a colorless oil.

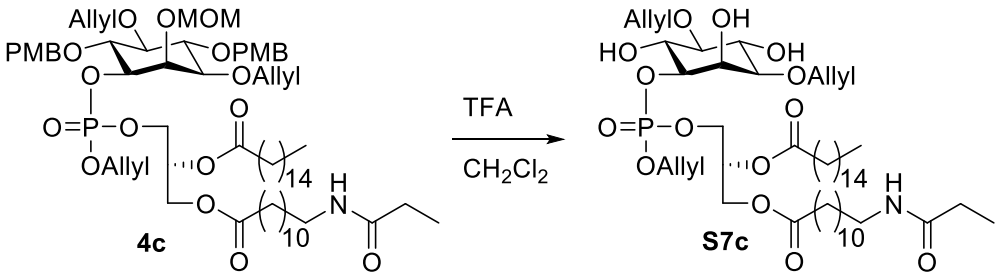
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.02-5.89 (m, 3H), 5.41-5.17 (m, 7H), 4.66-4.57 (m, 2H), 4.39-4.10 (m, 10H), 4.03 (t, *J* = 9.5 Hz, 1H), 3.93 (td, *J* = 9.5, 6.6 Hz, 1H), 3.33-3.23 (m, 3H), 3.16 (td, *J* = 9.3, 4.2 Hz, 1H), 2.44-2.37 (m, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.15 (t, *J* = 7.7 Hz, 2H), 1.87-1.79 (m, 2H), 1.62-1.58 (m, 4H), 1.25-1.25 (m, 38H), 0.88 (t, *J* = 6.7 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.70, 173.43, 172.49, 135.02, 134.11, 132.12, 118.70, 118.14, 117.22, 81.73, 79.10, 78.46, 73.98, 71.67, 71.26, 70.91, 69.79, 68.90, 68.09, 65.71, 61.55, 38.34, 36.73, 33.97, 31.89, 31.85, 31.15, 29.66 (3C), 29.62 (2C), 29.59, 29.55, 29.49, 29.45, 29.35, 29.32 (2C), 29.28, 29.25, 29.09, 25.75, 24.79, 24.59, 22.65 (2C), 14.08 (2C).

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -0.80.

HRMS (ESI-TOF) calcd for $C_{49}H_{88}NNaO_{14}P$ $[M+Na]^+$ 968.5835, found 968.5842.

Synthesis of inositol phospholipid derivative S7c



The title compound was synthesized following the procedure for **S7a**. **4c** (115 mg, 93.3 μmol) were used as starting materials. Compound **S7c** (59.9 mg, 68%) was obtained as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.01-5.90 (m, 3H), 5.40-5.17 (m, 7H), 4.65-4.58 (m, 2H), 4.38-4.32 (m, 5H), 4.26-4.11 (m, 5H), 4.06-4.01 (m, 1H), 3.93 (td, *J* = 9.5, 5.0 Hz, 1H), 3.28-3.14 (m, 4H), 2.35-2.29 (m, 4H), 2.20 (q, *J* = 7.6 Hz, 2H), 1.63-1.57 (m, 4H), 1.50-1.46 (m, 2H), 1.30-1.24 (m, 38H),

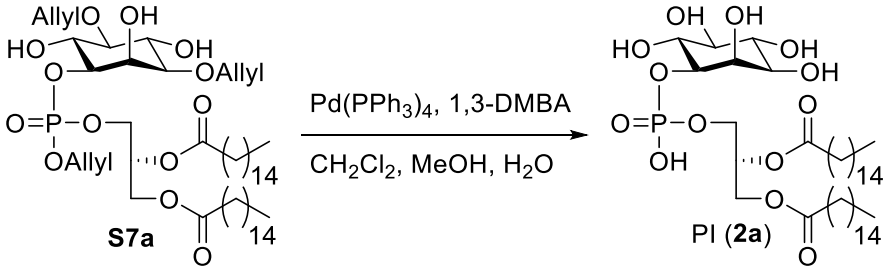
1.15 (t, *J* = 7.6 Hz, 3H), 0.88 (t, *J* = 6.8 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ: 173.78, 173.40, 173.06, 134.99 (2C), 134.10, 118.70, 118.14, 117.20, 81.64, 79.11, 78.39, 73.93, 71.61, 71.38, 71.23, 69.34, 68.95, 68.27, 65.72, 61.73, 39.49, 34.10, 33.95, 31.87, 29.72, 29.65 (3C), 29.62, 29.60, 29.56, 29.45, 29.40, 29.38, 29.30 (3C), 29.25, 29.20, 29.13, 29.04, 28.99, 26.82, 24.77, 24.73, 22.64, 14.07, 9.90.

^{31}P-NMR (160 MHz, $CDCl_3$) δ: -0.96.

HRMS (ESI-TOF) calcd for $C_{49}H_{88}NNaO_{14}P$ $[M+Na]^+$ 968.5835, found 968.5839.

Synthesis of PI 2a



To a solution of **S7a** (55.5 mg, 59.6 μmol) and 1,3-dimethylbarbituric acid (55.8 mg, 358 μmol) in CH_2Cl_2/MeOH/H_2O (10/10/3) (5 mL) was added $Pd(PPh_3)_4$ (68.9 mg, 59.6 μmol). The resulting mixture was stirred at room temperature for 4 h. The reaction was concentrated under reduced pressure. The crude mixture was purified by column chromatography of SiO_2 with $CHCl_3$-MeOH (10:1 to 1:1) and metal scavenger SiliaMetS® DMT with $CHCl_3$-MeOH (10:1 to 1:1) and SiO_2 with $CHCl_3$-MeOH (10:1 to 1:1) to give PI **2a** (13.5 mg, 28%) as white solid. The purity of **2a** was 99% (measured by quantitative NMR using CHBr3 as an internal standard).

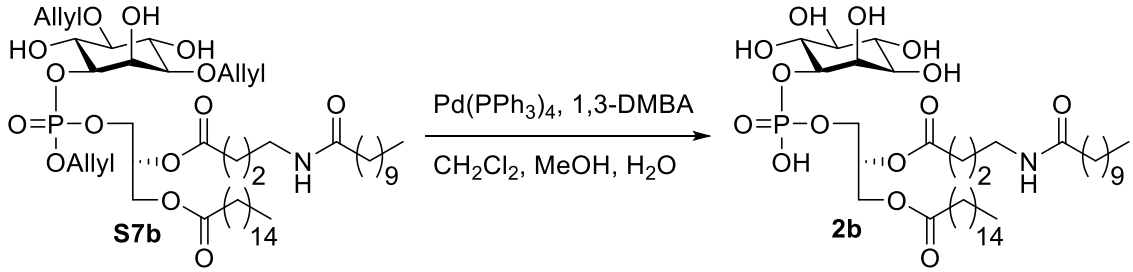
^{1}H-NMR (800 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 5.25-5.24 (m, 1H), 4.42 (dd, *J* = 11.9, 2.8 Hz, 2H), 4.20-4.16 (m, 1H), 4.08-3.99 (m, 2H), 3.89-3.85 (m, 1H), 3.74 (t, *J* = 9.6 Hz, 1H), 3.62 (t, *J* = 9.6 Hz, 1H), 3.42 (dd, *J* = 10.1, 2.8 Hz, 1H), 3.24 (t, *J* = 9.2 Hz, 1H), 2.33 (t, *J* = 7.3 Hz, 2H), 2.30 (t, *J* = 7.8 Hz, 2H), 1.61-1.56 (m, 4H), 1.31-1.22 (m, 48H), 0.87 (t, *J* = 6.9 Hz, 6H).

^{13}C-NMR (200 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 173.88, 173.57, 76.19, 74.02, 72.06, 71.30, 71.08, 70.81, 70.15, 63.21, 62.49, 33.77, 33.64, 31.45 (2C), 29.22 (4C), 29.19 (2C), 29.17 (2C), 29.11 (2C), 29.07 (2C), 28.92 (2C), 28.87 (2C), 28.69 (2C), 28.66 (2C), 24.46, 24.40, 22.18 (2C), 13.44 (2C).

^{31}P-NMR (160 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 0.03.

HRMS (ESI-TOF) calcd for $C_{41}H_{78}O_{13}P$ $[M-H]^-$ 809.5195, found 809.5186.

Synthesis of PI derivative 2b



The title compound was synthesized following the procedure for **2a**. **S7b** (41.3 mg, 43.7 μmol) were used as starting materials. Compound **2b** (13.0 mg, 34%) was obtained as a colorless oil. The purity of **2b** was 98% (measured by quantitative NMR using CHBr3 as an internal standard).

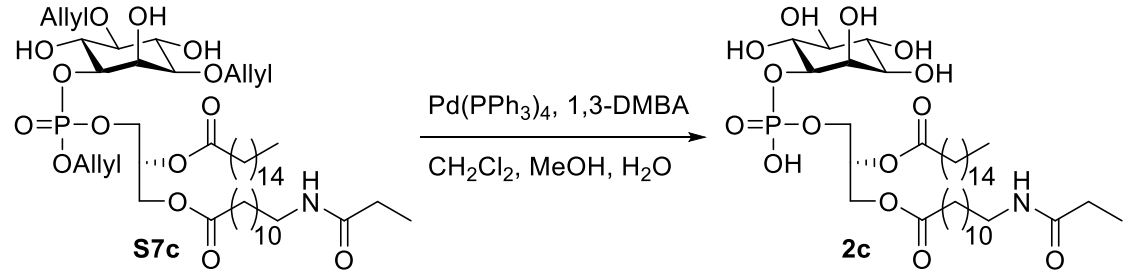
^{1}H-NMR (800 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 5.26-5.23 (m, 1H), 4.40 (dd, *J* = 12.2, 3.0 Hz, 1H), 4.20-4.17 (m, 2H), 4.05 (t, *J* = 5.5 Hz, 2H), 3.92-3.88 (m, 1H), 3.75 (t, *J* = 9.4 Hz, 1H), 3.63 (t, *J* = 9.6 Hz, 1H), 3.43 (dd, *J* = 9.9, 3.0 Hz, 1H), 3.25 (t, *J* = 9.4 Hz, 1H), 3.21 (td, *J* = 7.1, 2.8 Hz, 2H), 2.46-2.33 (m, 2H), 2.31 (t, *J* = 7.6 Hz, 2H), 2.17 (t, *J* = 7.8 Hz, 2H), 1.83-1.78 (m, 2H), 1.61-1.56 (m, 4H), 1.30-1.24 (m, 38H), 0.89-0.86 (m, 6H).

^{13}C-NMR (200 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 175.68, 174.93, 174.02, 77.02, 74.93, 73.02, 72.30, 72.01, 71.79, 71.51, 64.35, 63.21, 38.95, 36.88, 34.50, 32.41, 32.39, 31.89, 30.18 (3C), 30.13 (3C), 30.09, 30.04, 30.02, 29.89, 29.83 (2C), 29.81 (2C), 29.63, 26.44, 25.31, 24.86, 23.13 (2C), 14.39 (2C).

^{31}P-NMR (240 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 0.06.

HRMS (ESI-TOF) calcd for $C_{40}H_{75}O_{14}P$ $[M-H]^-$ 824.4931, found 824.4935.

Synthesis of PI derivative 2c



The title compound was synthesized following the procedure for **2a**. **S7c** (59.9 mg, 63.3 μmol) were

used as starting materials. Compound **2c** (16.2 mg, 31%) was obtained as a colorless oil. The purity of **2c** was 98% (measured by quantitative NMR using CHBr3 as an internal standard).

^{1}H-NMR (800 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 5.27-5.21 (m, 1H), 4.47-4.39 (m, 1H), 4.20-4.14 (m, 2H), 4.07-3.97 (m, 2H), 3.93-3.86 (m, 1H), 3.74 (t, *J* = 9.5 Hz, 1H), 3.62 (t, *J* = 9.7 Hz, 1H), 3.43 (dd, *J* = 9.6, 2.3 Hz, 1H), 3.24 (t, *J* = 9.3 Hz, 1H), 3.15 (t, *J* = 7.2 Hz, 2H), 2.35-2.27 (m, 4H), 2.18 (q, *J* = 7.6 Hz, 2H), 1.61-1.55 (m, 4H), 1.50-1.43 (m, 2H), 1.33-1.21 (m, 38H), 1.12 (t, *J* = 7.6 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H).

^{13}C-NMR (200 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 176.21, 174.92, 174.62, 77.03, 74.91, 73.00, 72.27, 72.05, 71.77, 71.09, 64.30, 63.48, 40.04, 34.75, 34.60, 32.45, 30.21 (2C), 30.17 (2C), 30.08, 30.05, 30.00 (2C), 29.92 (2C), 29.88 (2C), 29.82, 29.64 (2C), 27.47, 25.44, 25.34, 23.18, 14.44, 10.43.

^{31}P-NMR (160 MHz, $CDCl_3$:CD_3OD:D_2O = 70:40:6) δ: 2.09.

HRMS (ESI-TOF) calcd for $C_{40}H_{75}O_{14}P$ $[M-H]^-$ 824.4931, found 824.4940.

2. Biology

DCAR Reporter Assay

2B4-NFAT-GFP reporter cells expressing DCAR + FcRγ were prepared as previously described[9]. For stimulation of reporter cells, compounds were diluted in isopropanol (Nakalai tesque) and added on 96-well plates (Corning) at 20 μL/well.[10] After evaporation of the solvent, the cells were stimulated with plate-coated lipids. Anti-flag tag antibody (Wako) was dissolved in $NaHCO_3$ buffer (10 μg/ml) and 50 μl of the antibody solution were incubated in DOTAP (Avanti) coated 96-well plate wells for 2 h at 37 ºC.

Ac_1PIM_2

Ac_1PIM_2 was purified from *M. bovis* BCG as previous described.[11]

HEK- Blue Reporter Assay

The induction of NF-κB in a reporter gene assay was quantified using HEK-Blue mTLR2 and hTLR2 cells (Invivogen). HEK-Blue cells were cultured in DMEM (Nacalai tesque) supplemented with 10% fetal bovine serum (FBS; Biowest), 1% penicillin–streptomycin (Gibco) and 100 μg/mL Normocin. The cells were seeded into 96-well plates (1.0 $x10^5$ cells/well), and ligands were added with the indicated concentrations before incubation at 37 °C for 24 h. SEAP was measured using a HEK-Blue Detection (Invivogen).

APC (Antigen Presenting Cell)-free Assay for CD1d-Lipid Binding [1, 2]

Initially, 96-well microplates (multiwell plate 96F, Sumitomo Bakelite Co., Ltd.) were coated with mouse CD1d:Ig fusion protein (0.25 μg/well, BD Biosciences) in PBS (100 μL) at 37 °C for 24 h. After washing with PBS, various concentrations of compounds in PBS containing 1% DMSO and 0.005% TritonX-100 were added and incubated at 37 °C for 24 h. After washing with PBS, 2E10 NKT hybridoma cells[12] (2.5×10^5 cells/well) were added and cultured at 37 °C for 48 h. IL-2 in the supernatant were measured by ELISA kit (Affymetrix). 2E10 NKT hybridoma cells were a kind gift of Prof. Kazuya Iwabuchi (Kitasato University).

Binding Studies

The AlphaScreen assay (PerkinElmer Life Science) was used to determine receptor (mouse TLR2, human TLR2 and mouse CD1d) -ligand interactions.[3,4] For analysis of mouse TLR2-ligand interaction, mouse TLR2-Fc (R&D systems, final concentration 10 nM) was mixed with Pam2CSK4-biotin (InvivoGen, final concentration 10 nM), in PBS containing 0.05 % human serum albumin. After 45 min, compounds (concentration range 3 nM-30 μM) was added and incubation was continued for another 45 min. Next, 10 μg/mL streptavidin donor beads and 10 μg/mL Protein-A acceptor beads were added and incubated for 45 min. Samples were measured at 680 nm in EnSpire™ Alpha (PerkinElmer) or Spark 10M (Tecan Ltd.). Data were analyzed using Graphpad Prism (GraphPad Software Inc.).

For analysis of human TLR2-ligand interaction, human TLR2-His tag (R&D systems, final concentration 15 nM) was mixed with Pam2CSK4-biotin (InvivoGen, final concentration 15 nM), in PBS containing 0.05 % human serum albumin. After 45 min, compounds (concentration range 3 nM-30 μM) was added and incubation was continued for another 45 min. Next, 10 μg/mL streptavidin donor beads and 10 μg/mL Ni chelate acceptor beads were added and incubated for 45 min. Samples were measured at 680 nm in EnSpire™ Alpha (PerkinElmer) or Spark 10M (Tecan Ltd.). Data were analyzed using Graphpad Prism (GraphPad Software Inc.).

For analysis of mouse CD1d-ligand interaction, mouse CD1d-IgG (BD Biosciences, final concentration 5 nM) was mixed with 10 μg/mL anti-mouse IgG acceptor beads in PBS containing 0.005% Tween 20. After 1 h, Biotinyl-PE (Avanti, final concentration 2 mM) and compounds (concentration range 3 nM-30 μM) was added to the plate. After incubation at 37 °C for 18 h, 10 μg/mL streptavidin donor beads was added and incubation was continued for another 1 h. Samples were measured at 680 nm in EnSpire™ Alpha (PerkinElmer) or Spark 10M (Tecan Ltd.). Data were analyzed using Graphpad Prism (GraphPad Software Inc.).

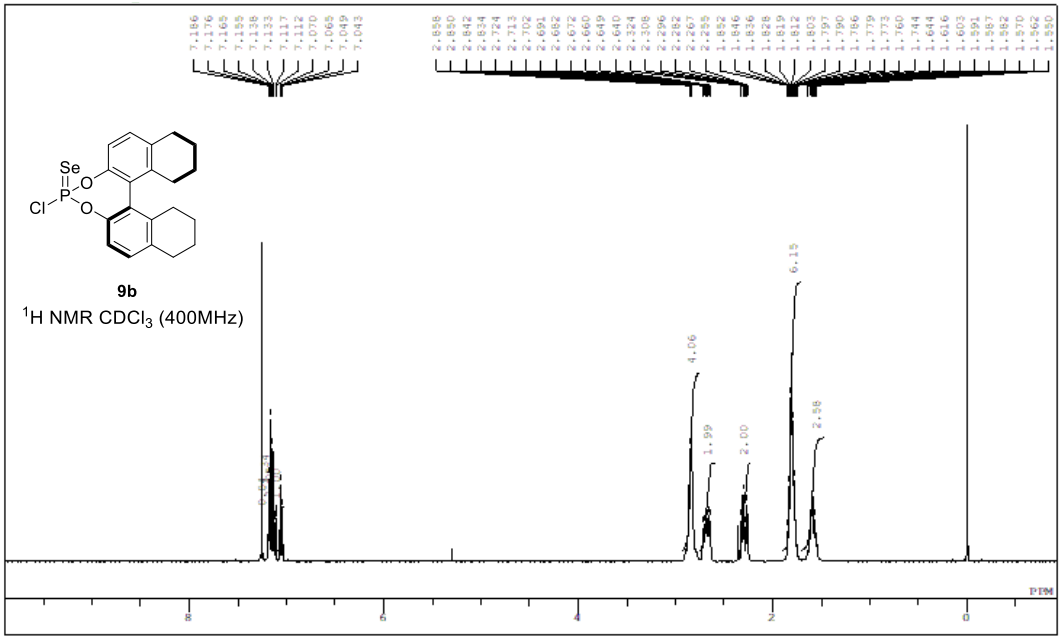
Inflammatory cytokine induction assay

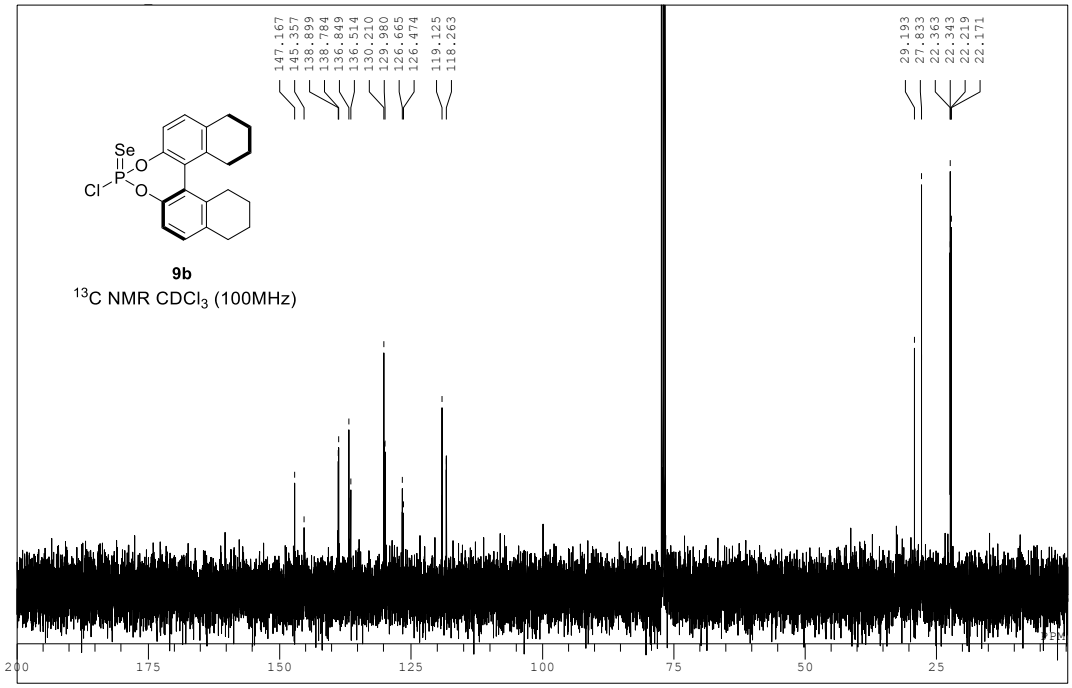
Mouse macrophages (RAW264.7 cells) were purchased from ATCC (TIB-71). These cells were

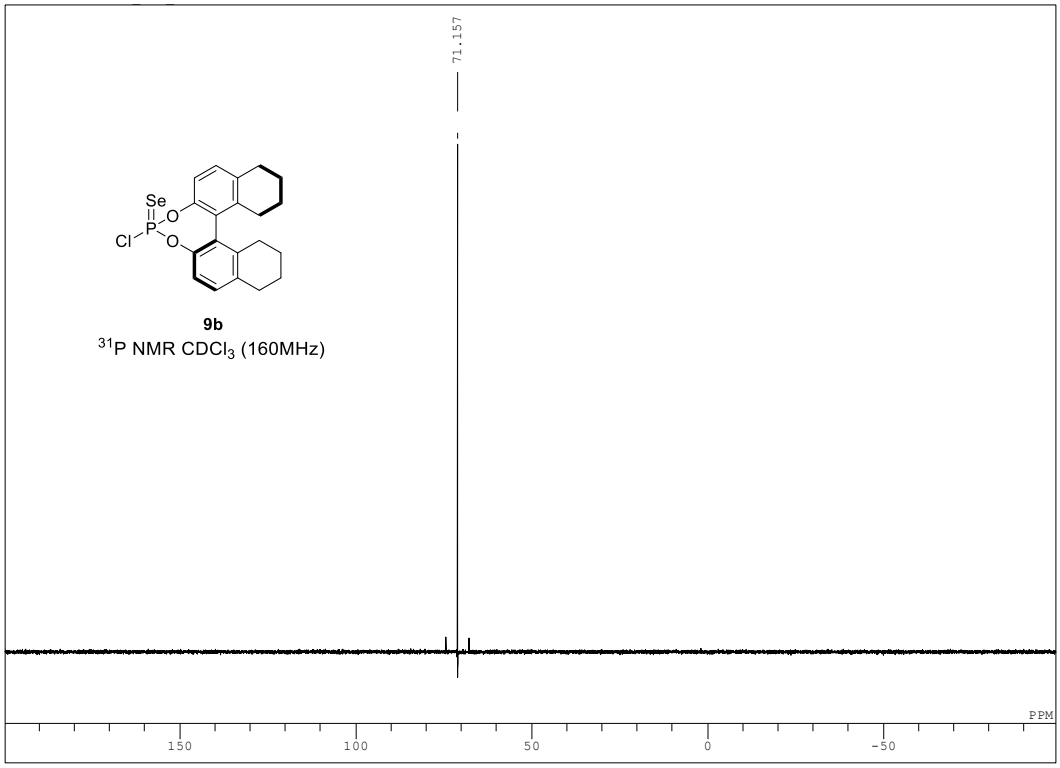
cultured as monolayers in RPMI-1640 (Nacalai Tesque) supplemented with 10% fetal bovine serum (FBS; Biowest), and 1% penicillin–streptomycin (Gibco). The cells were seeded into 96-well plates (5.0 x10^4 cells/well), and ligands were added with the indicated concentrations before incubation at 37 °C for 24 h. Cytokine release was measured using an ELISA kit (Affymetrix).

Bone marrow cells were flushed from the tibias and femurs of C57BL/6J mice (Charles River) with PBS. For BMDCs differentiation, the cell suspension was cultured at a density of 1.0 x 10^6 cells/mL in RPMI-1640 (Nacalai Tesque) supplemented with 10% fetal bovine serum (FBS; Biowest), 1% penicillin–streptomycin (Gibco) and 20 ng/mL GM-CSF. On day 3, fresh medium containing GM-CSF was added and on day 5 one half of the medium was renewed. BMDCs were harvested on day 8 and seeded into 96-well plates (2.0 x10^5 cells/well), and ligands were added with the indicated concentrations before incubation at 37 °C for 24 h. Cytokine release was measured using an ELISA kit (Affymetrix).

3. NMR spectra

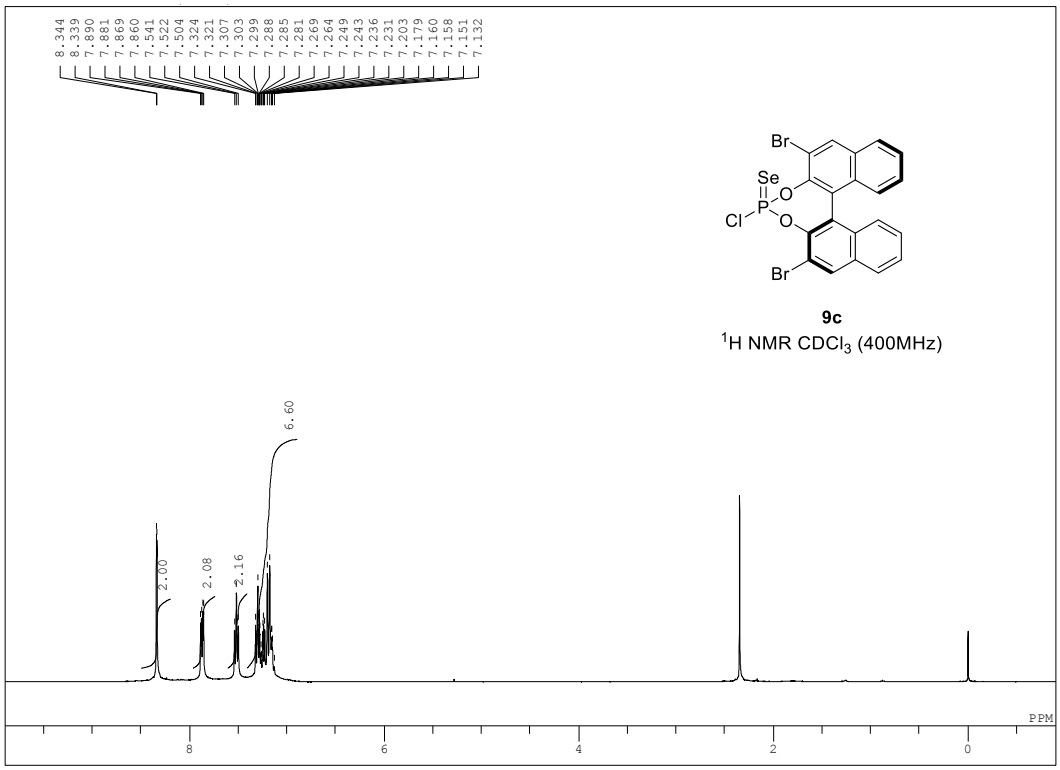






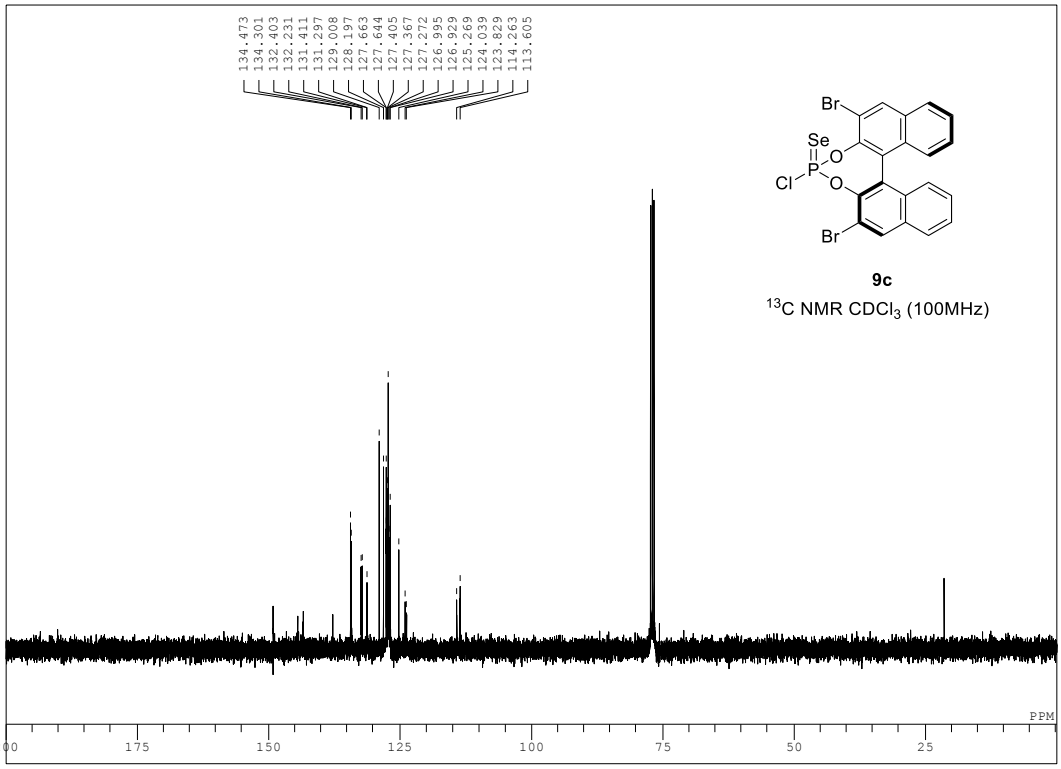
9b

^{31}P NMR $CDCl_3$ (160MHz)



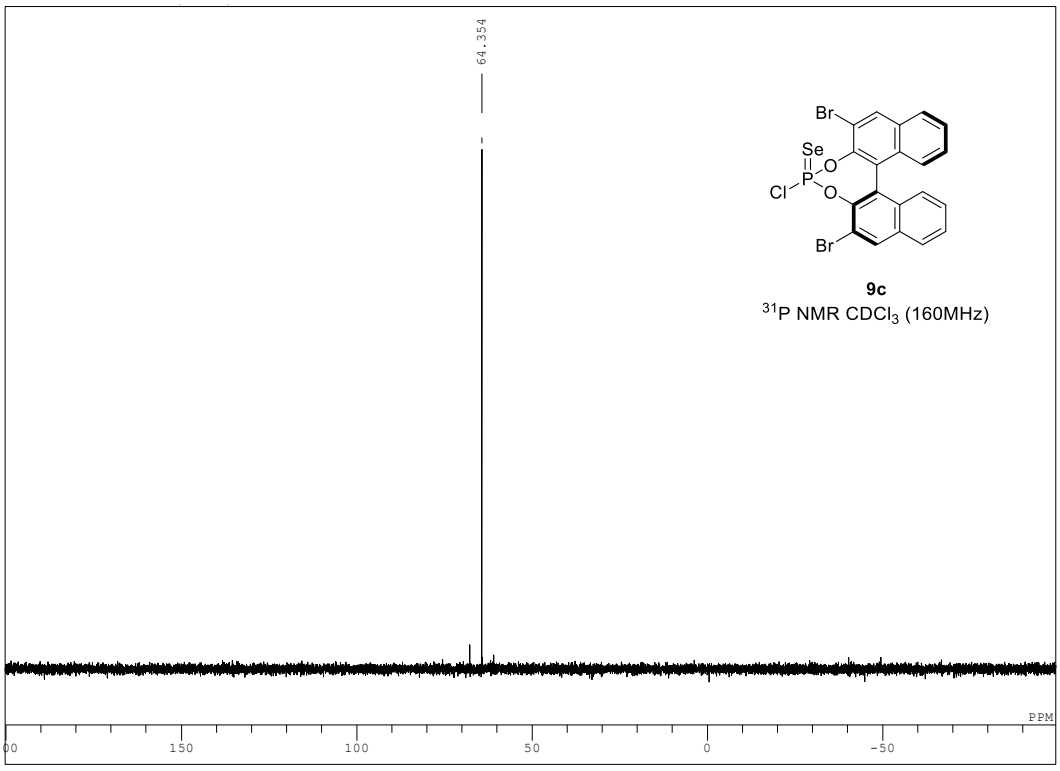
9c

^{1}H NMR $CDCl_3$ (400MHz)



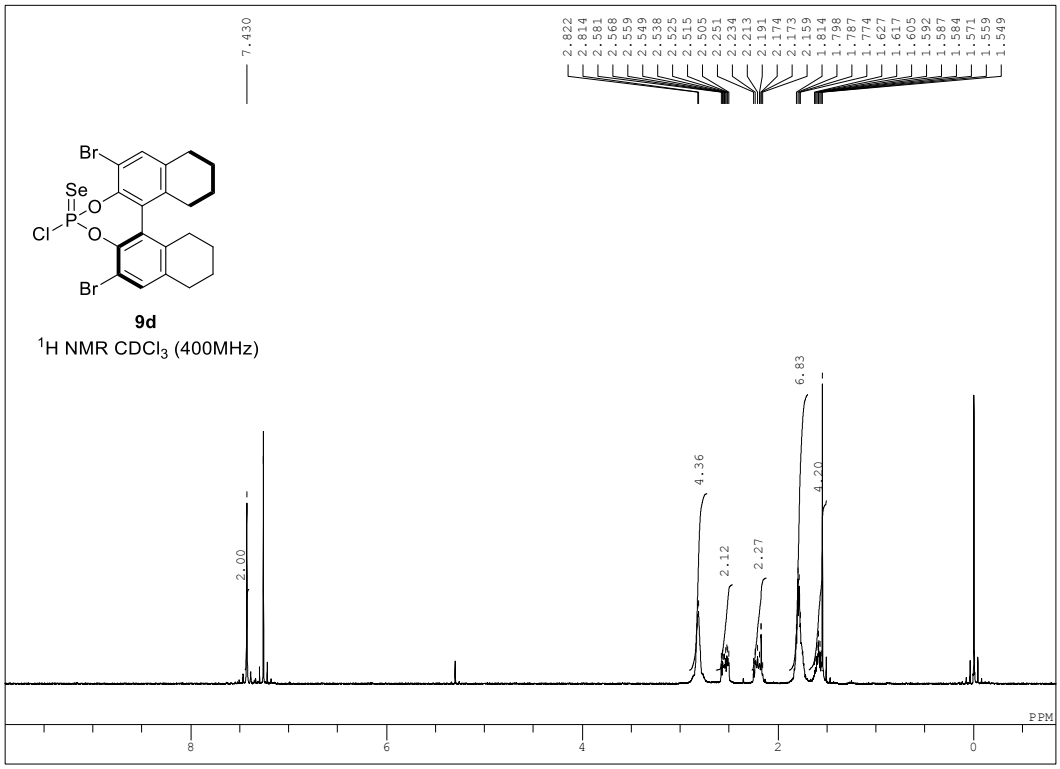
9c

^{13}C NMR $CDCl_3$ (100MHz)



9c

^{31}P NMR $CDCl_3$ (160MHz)



9d

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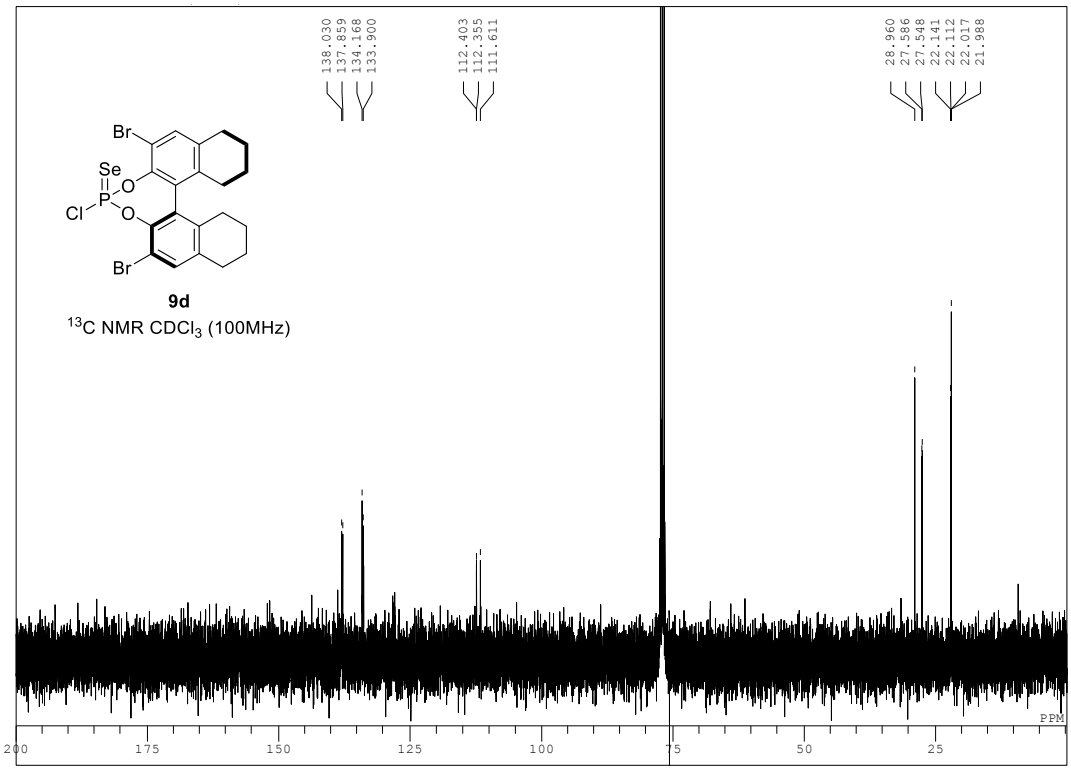

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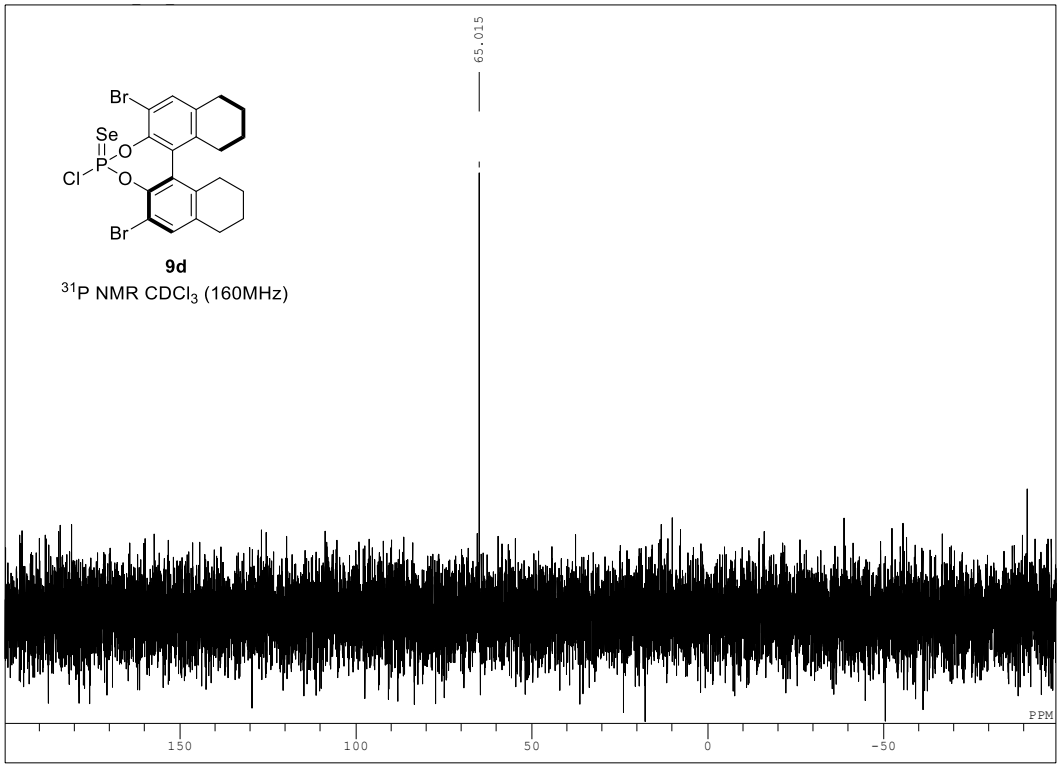
^{13}C NMR $CDCl_3$ (100MHz)



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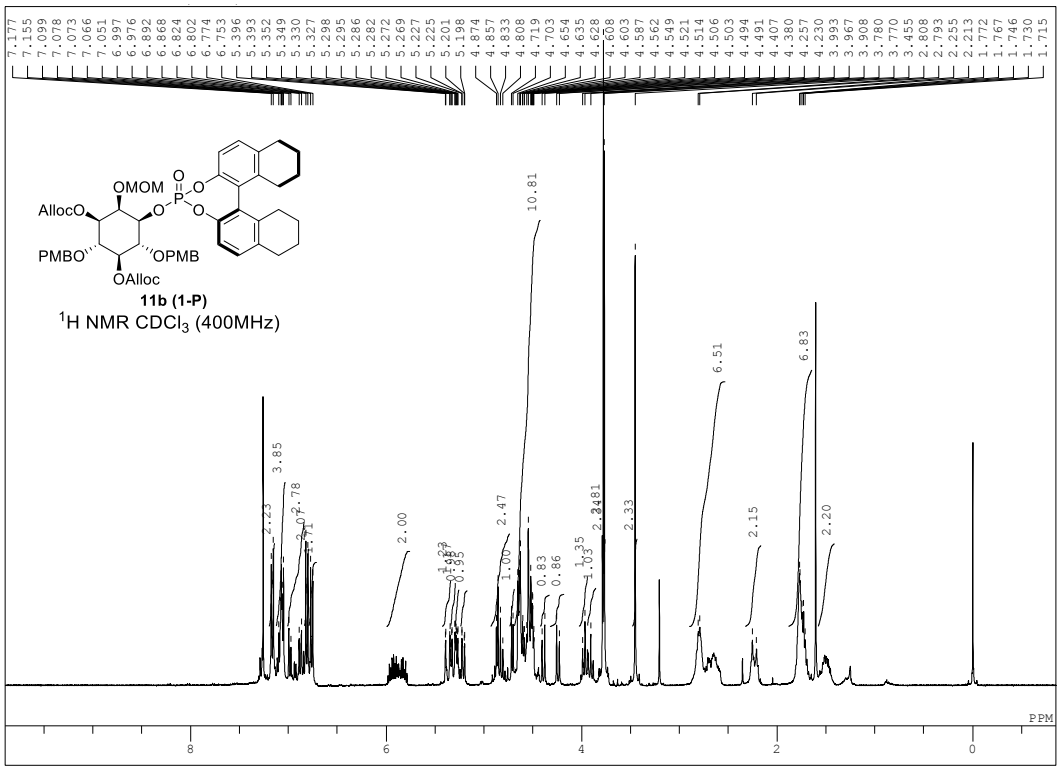
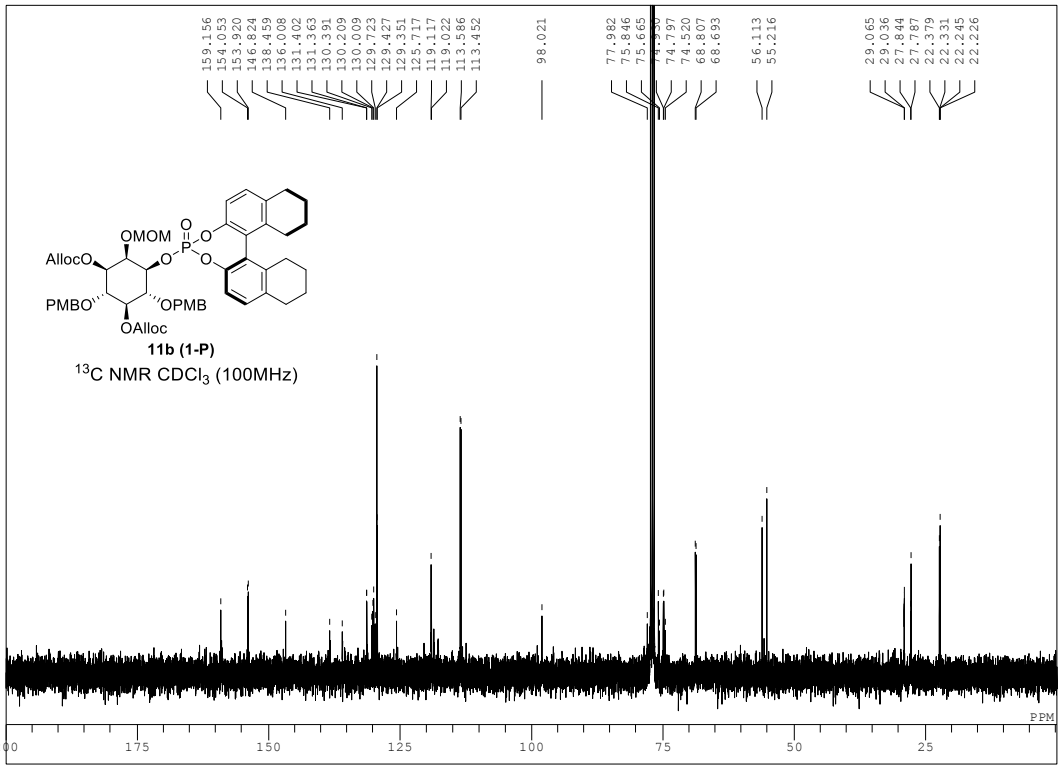
^{31}P NMR $CDCl_3$ (160MHz)



11b (1-P)

^{1}H NMR $CDCl_3$ (400MHz)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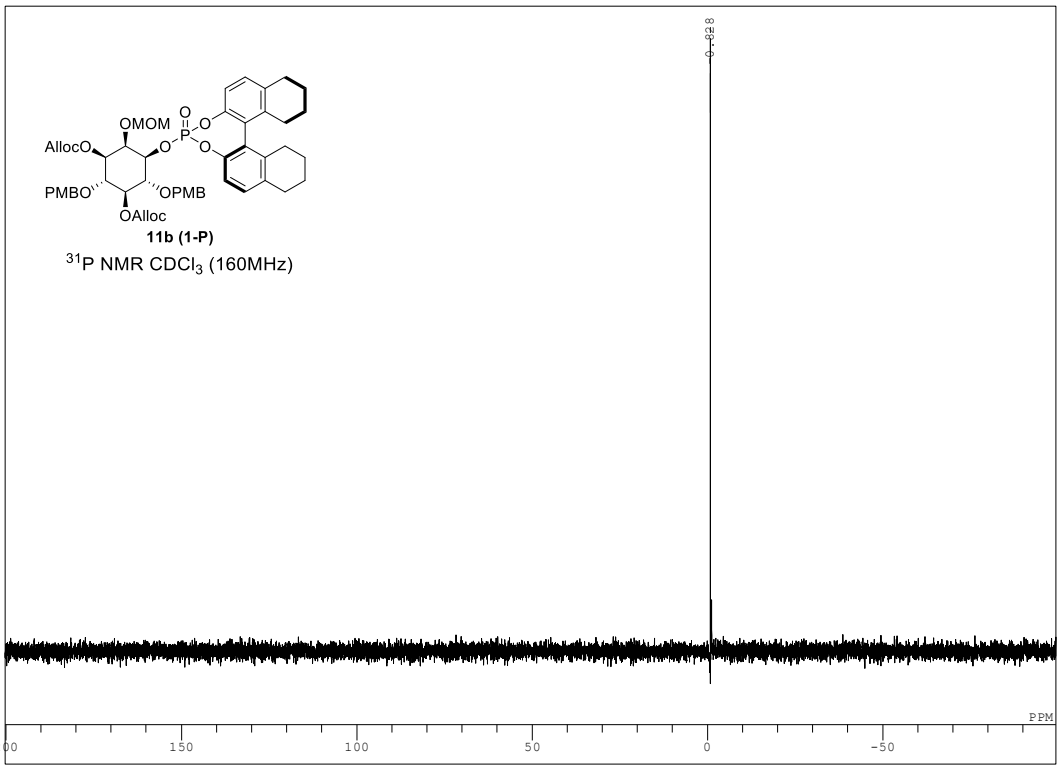
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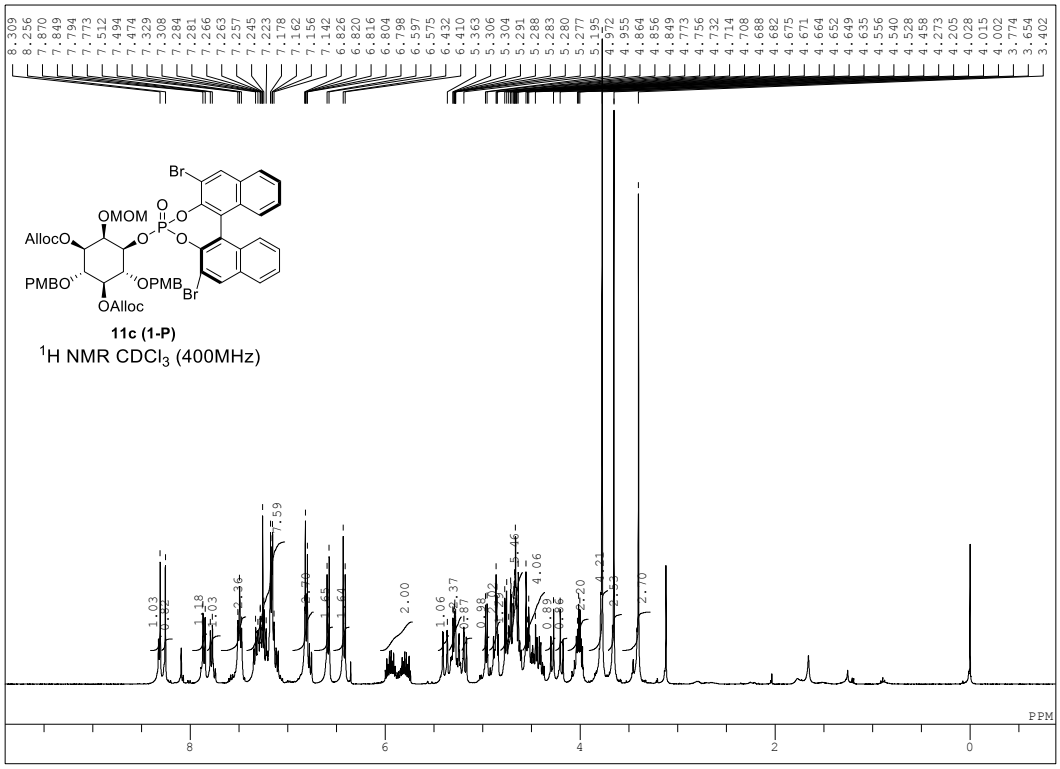
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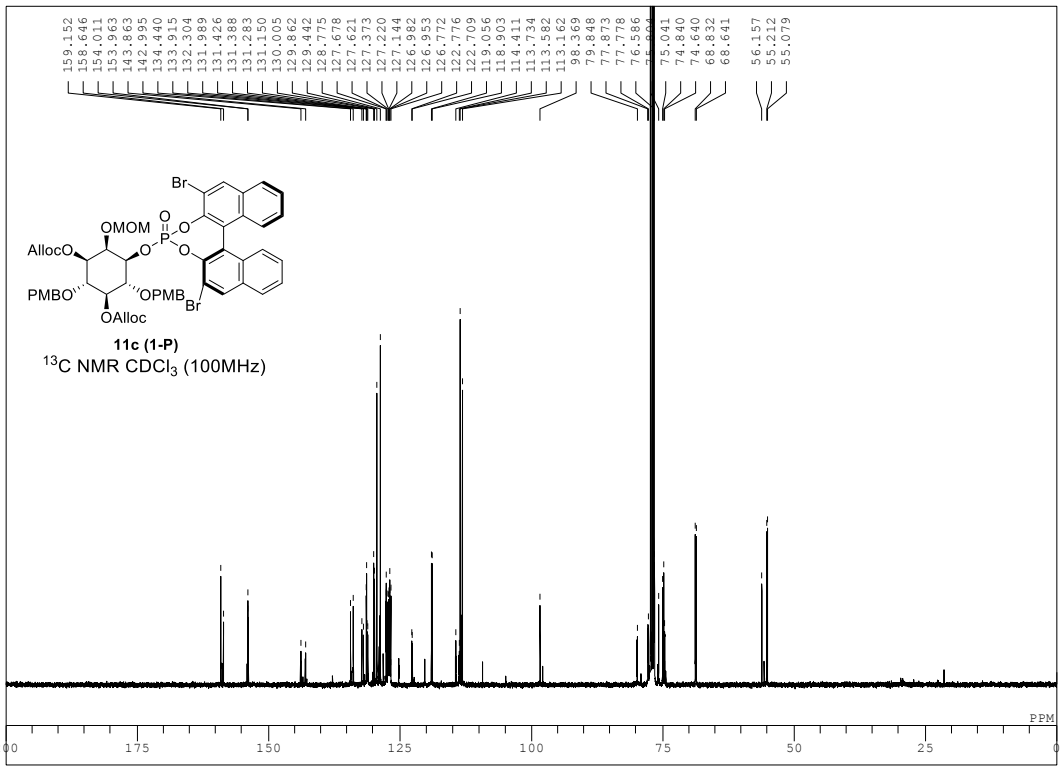
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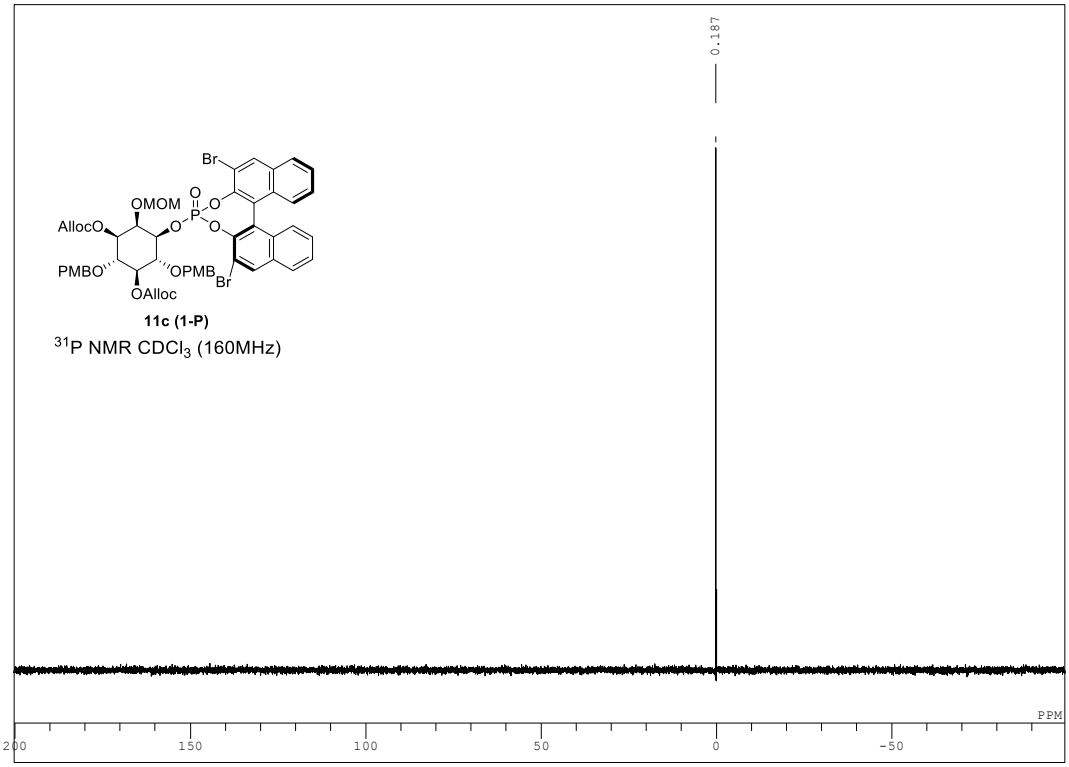
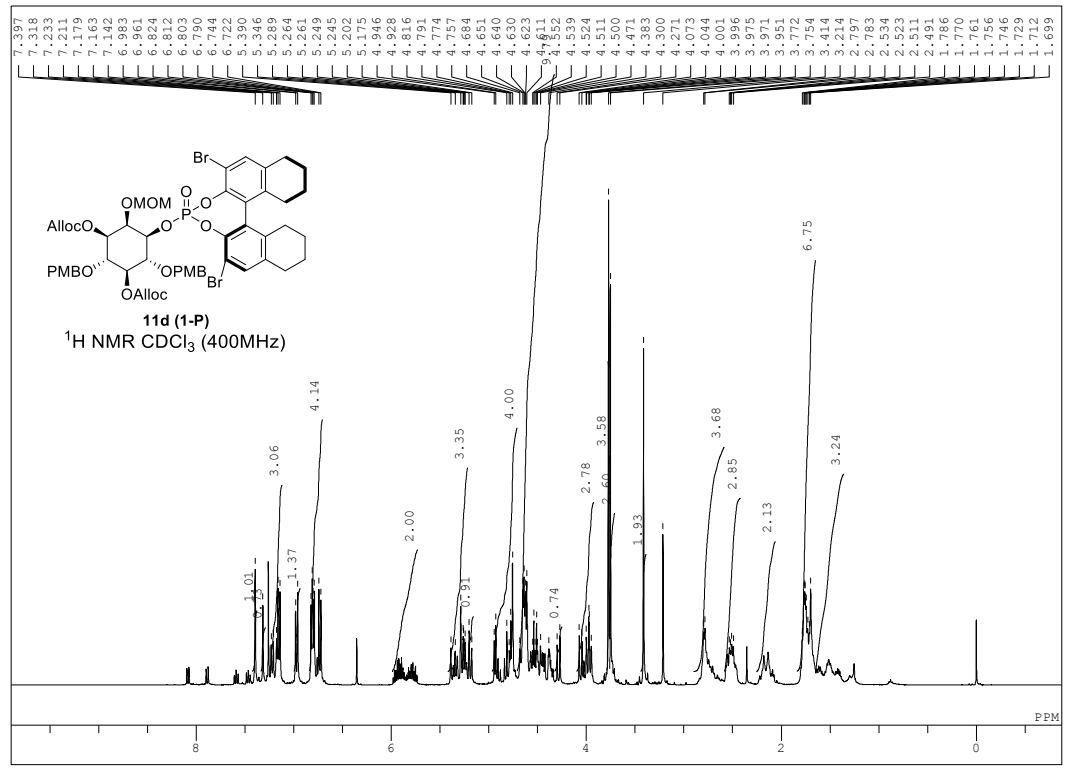


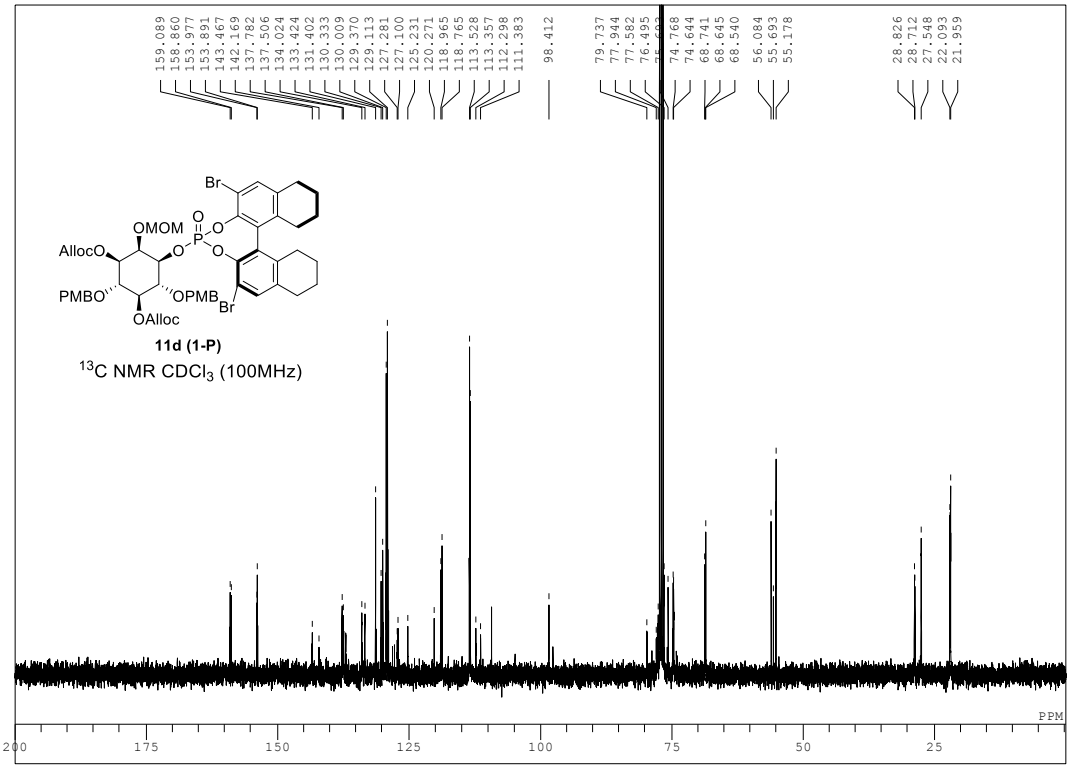
11c (1-P)

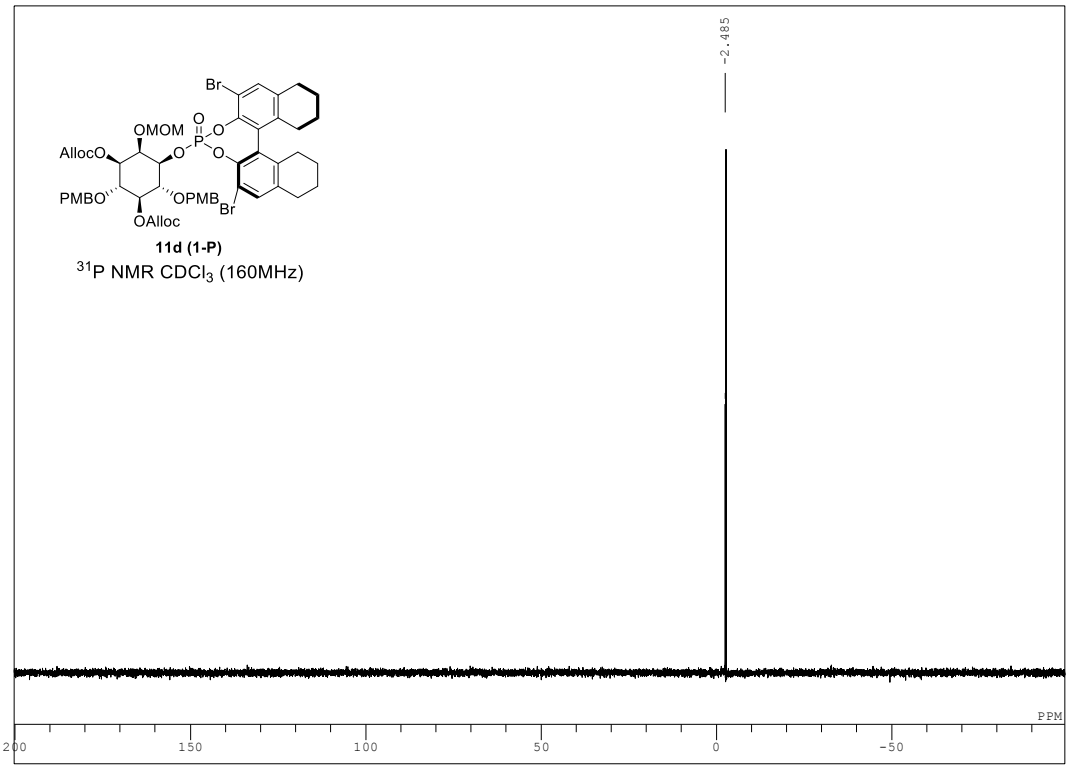
^{31}P NMR $CDCl_3$ (160MHz)

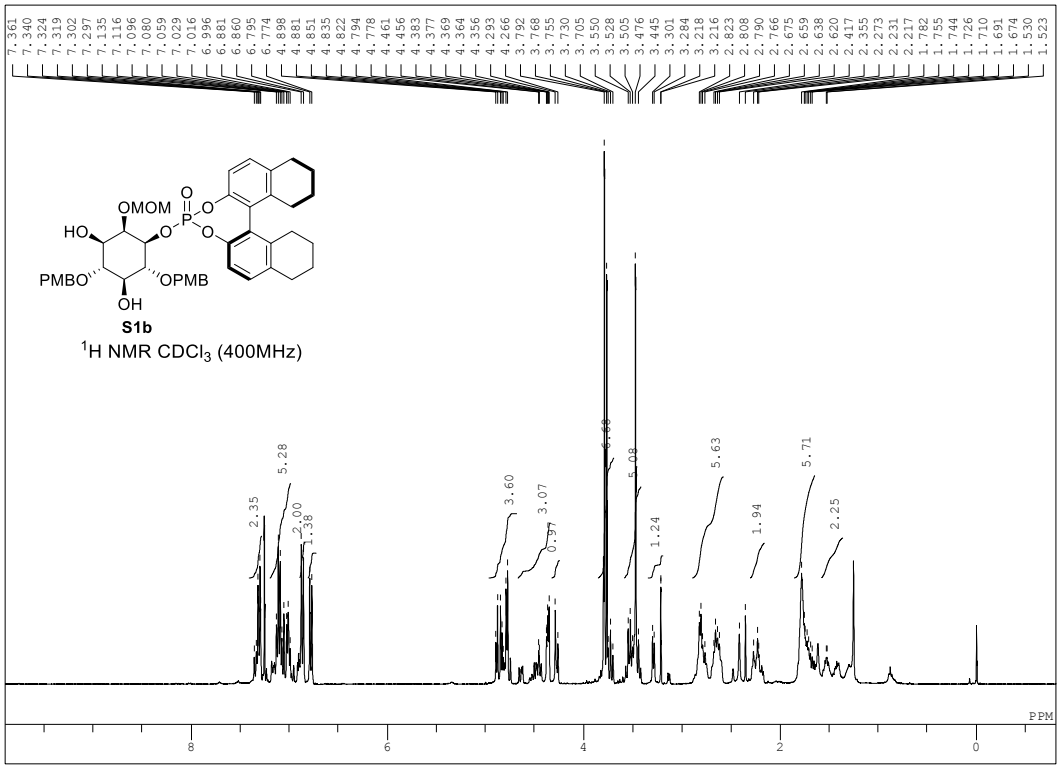


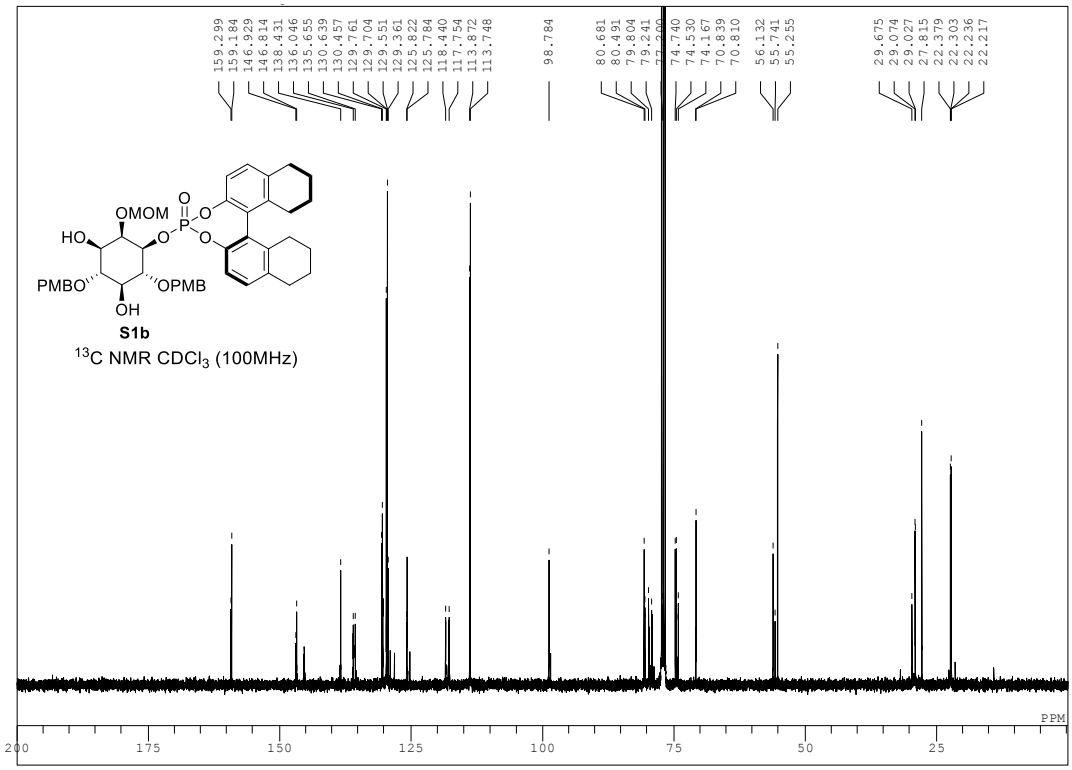
11d (1-P)

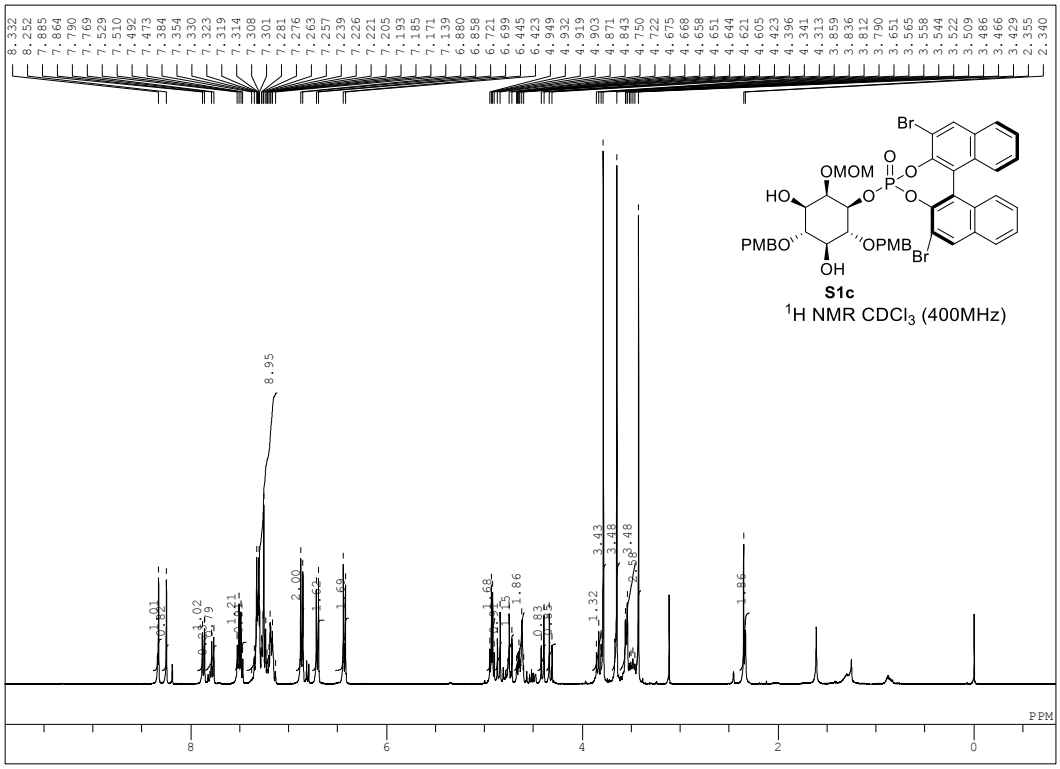
^{1}H NMR $CDCl_3$ (400MHz)

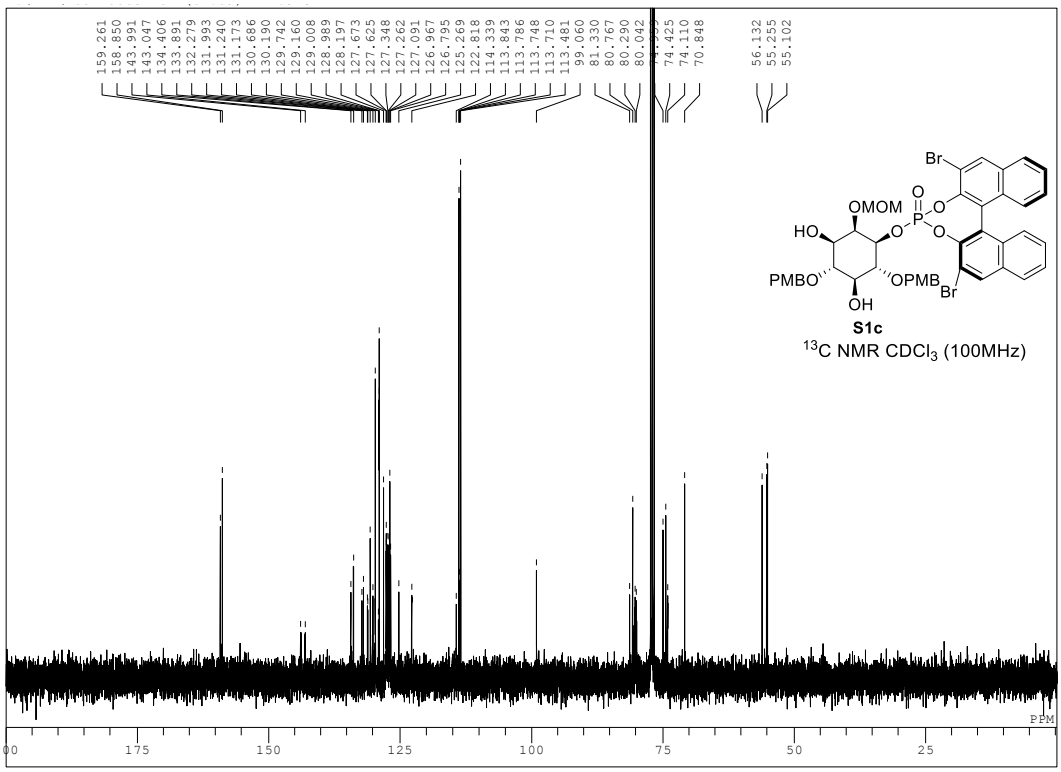

159.089
158.860
153.977
153.891
143.467
142.169
137.782
137.506
134.024
133.424
131.402
130.333
130.009
129.370
129.113
127.281
127.100
125.231
120.271
118.965
118.765
113.528
113.357
112.298
111.383
98.412
79.737
77.944
77.582
76.495
74.768
74.644
68.741
68.645
68.540
56.084
55.693
55.178
28.826
28.712
27.548
22.093
21.959
Br
OMOM
AllocO
PMBO
OPMB
Br
OAlloc
11d (1-P)
13C NMR CDCl3 (100MHz)
PPM
200
175
150
125
100
75
50
25

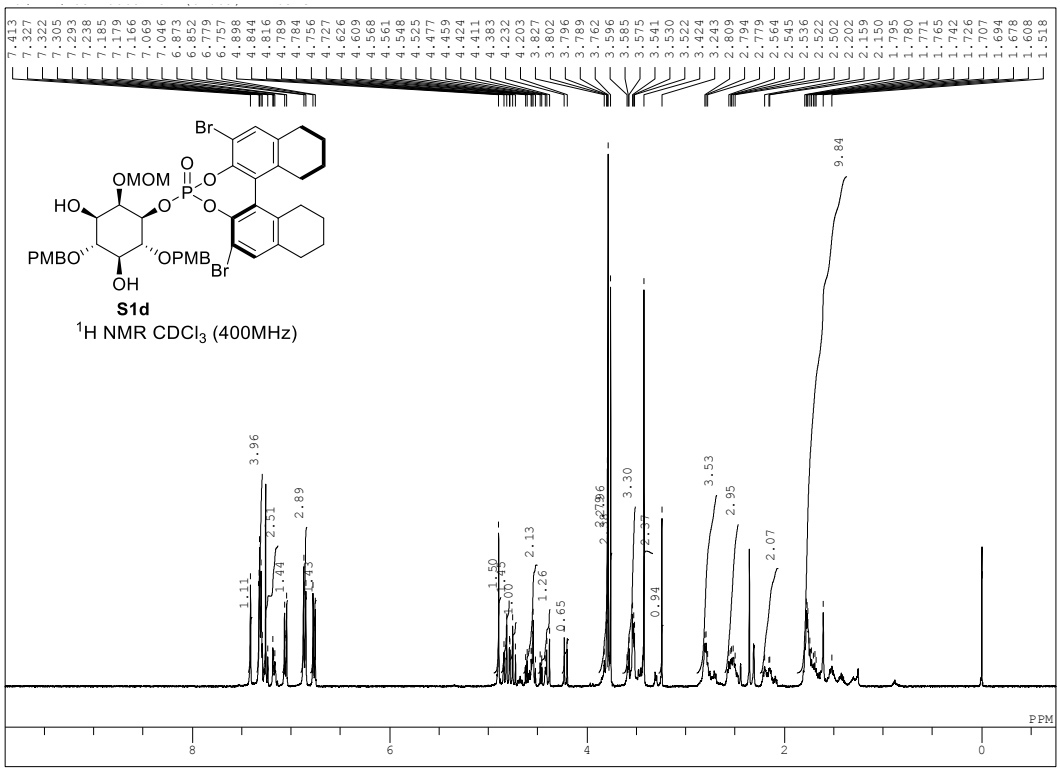

-2.485
Br
OMOM
AllocO
PMBO
OPMB
Br
OAlloc
11d (1-P)
31P NMR CDCl3 (160MHz)
PPM
200
150
100
50
0
-50

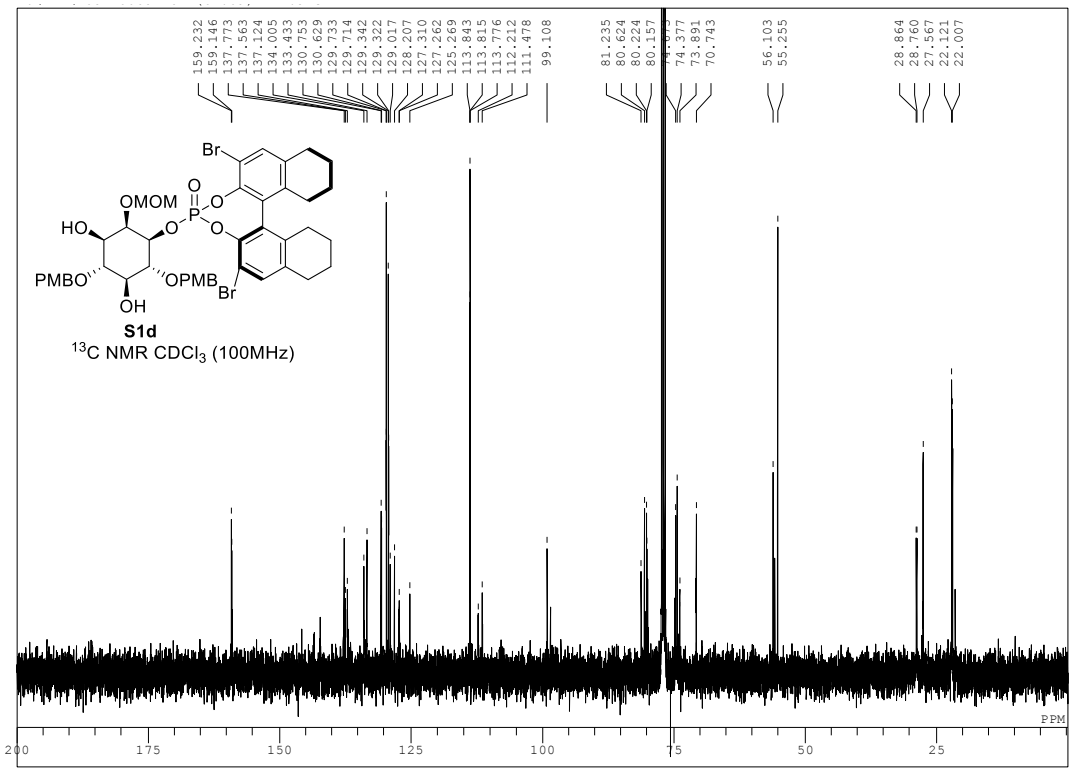

OMOM
HO
PMBO
OPMB
OH
S1b
1H NMR CDCl3 (400MHz)
PPM

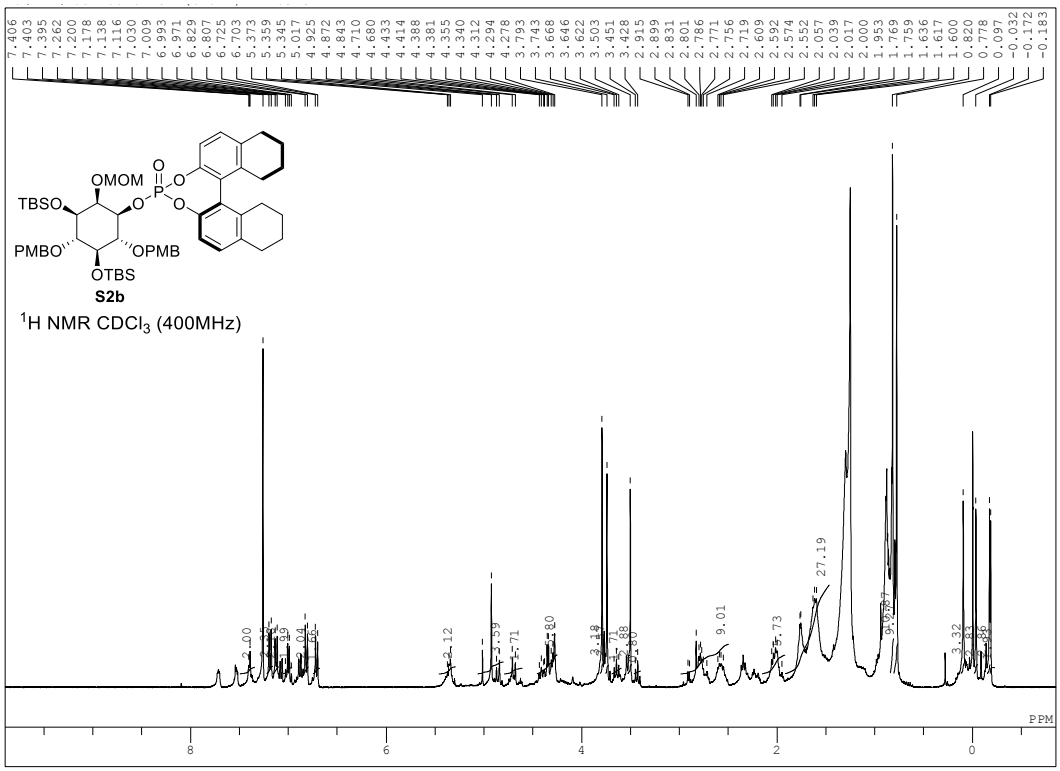

OMOM
HO
PMBO
OPMB
OH
S1b
13C NMR CDCl3 (100MHz)
PPM

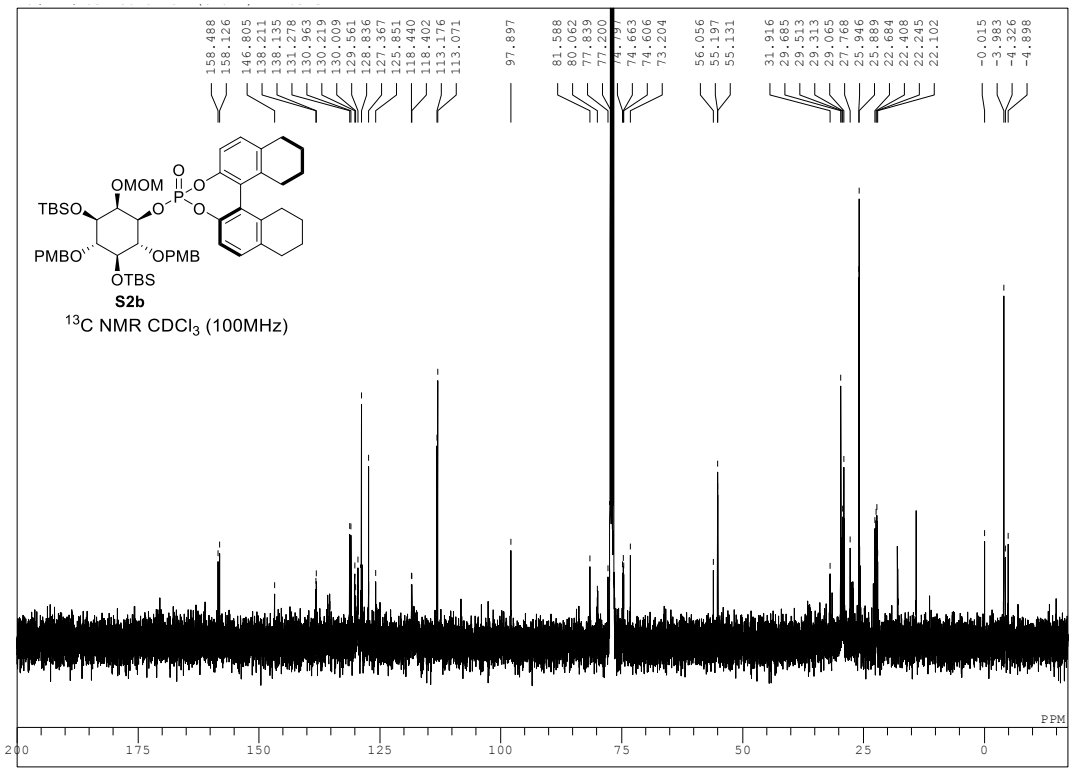

Br
OMOM
O
P
O
HO
PMBO
OPMB
Br
OH
S1c
^{1}H NMR CDCl$_3$ (400MHz)
PPM

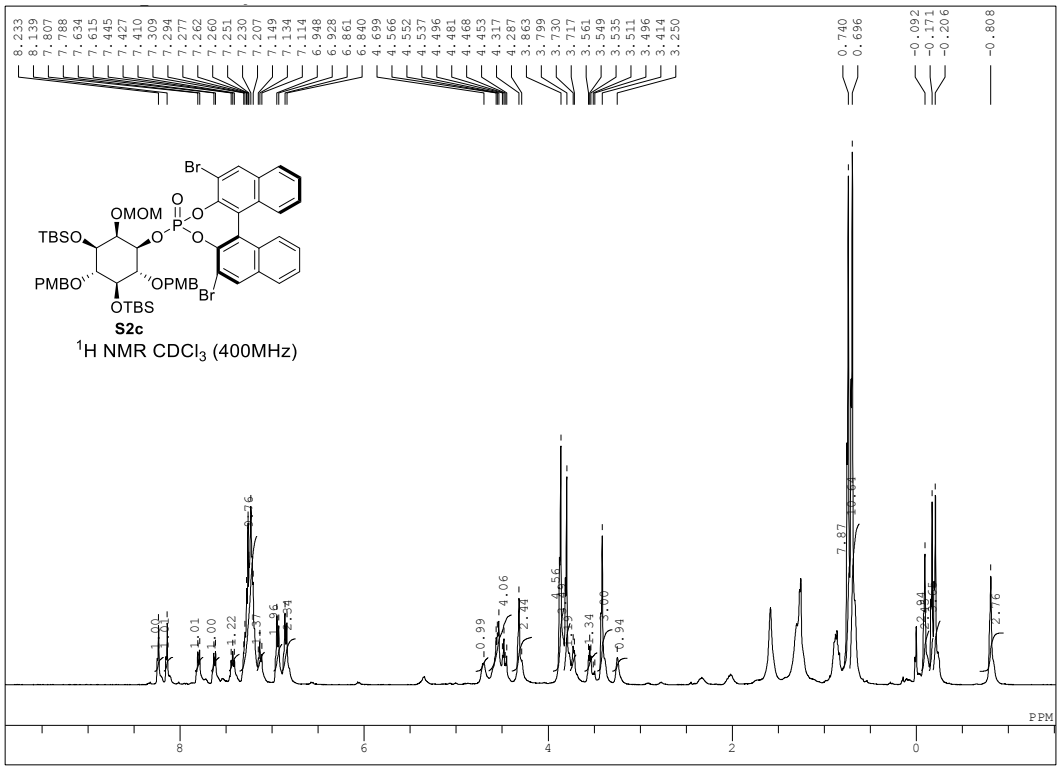

Br
OMOM
O
P
O
HO
PMBO
OPMB
Br
OH
S1c
^{13}C NMR CDCl$_3$ (100MHz)
PPM

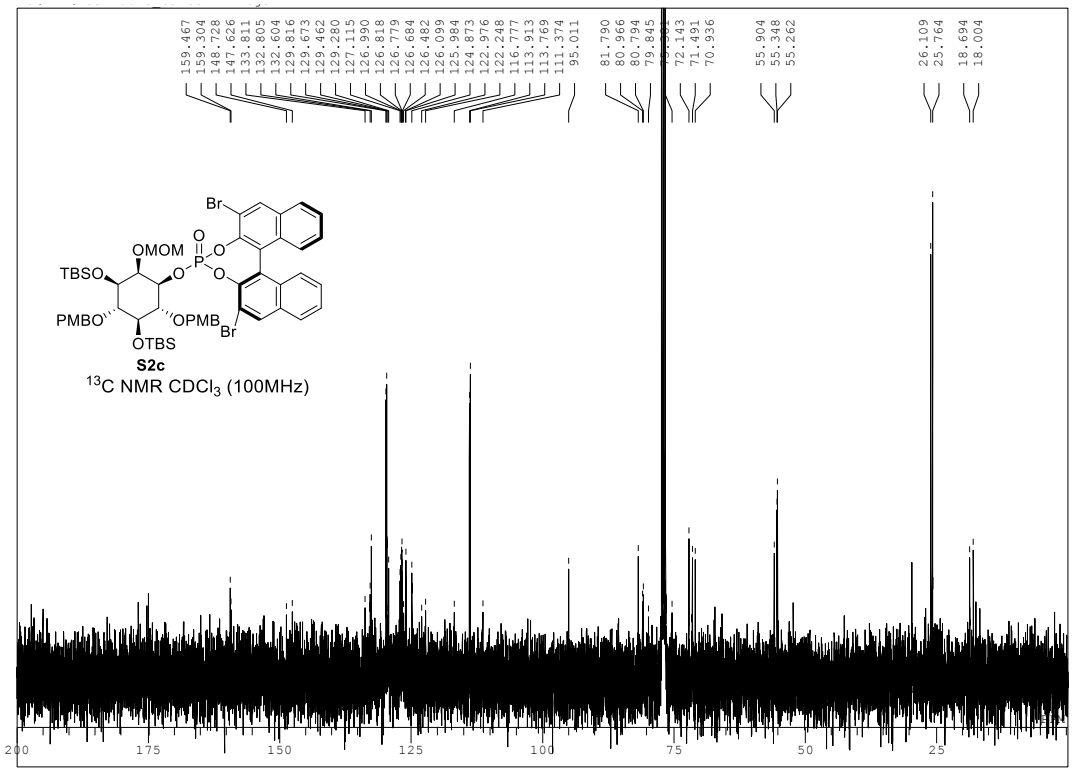

Br
OMOM
O
P
HO
PMBO
OPMB
Br
OH
S1d
^{1}H NMR CDCl$_3$ (400MHz)
PPM

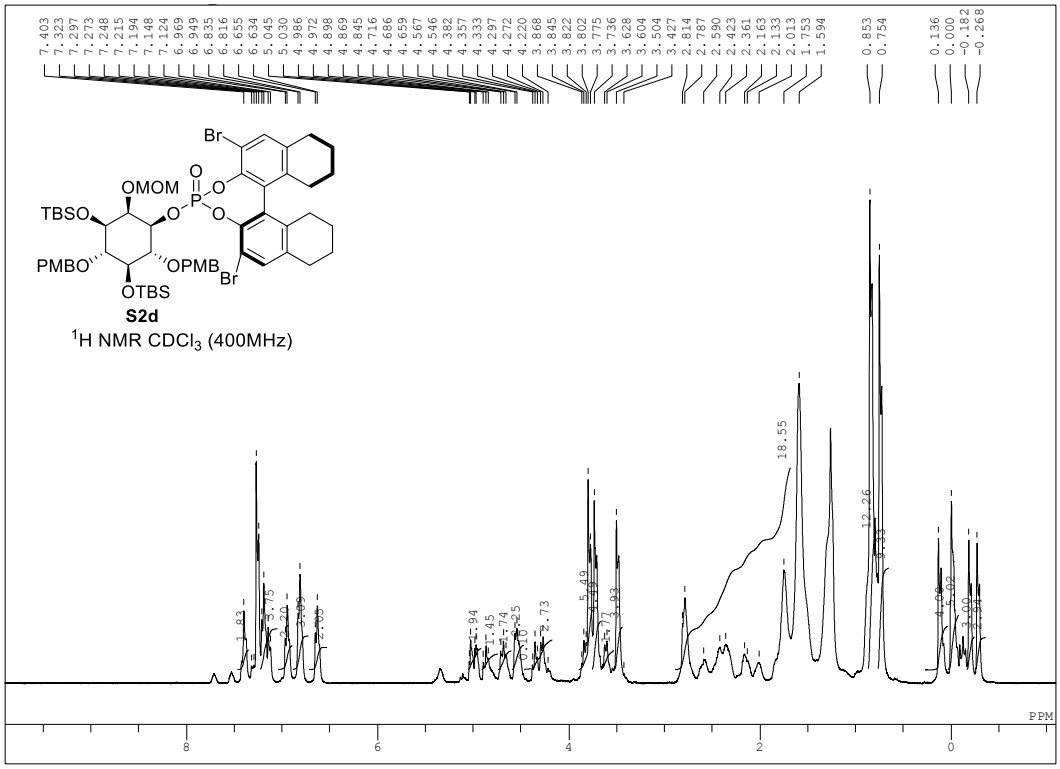

Br
OMOM
O
P
HO
PMBO
OPMB
Br
OH
S1d
^{13}C NMR CDCl$_3$ (100MHz)
PPM

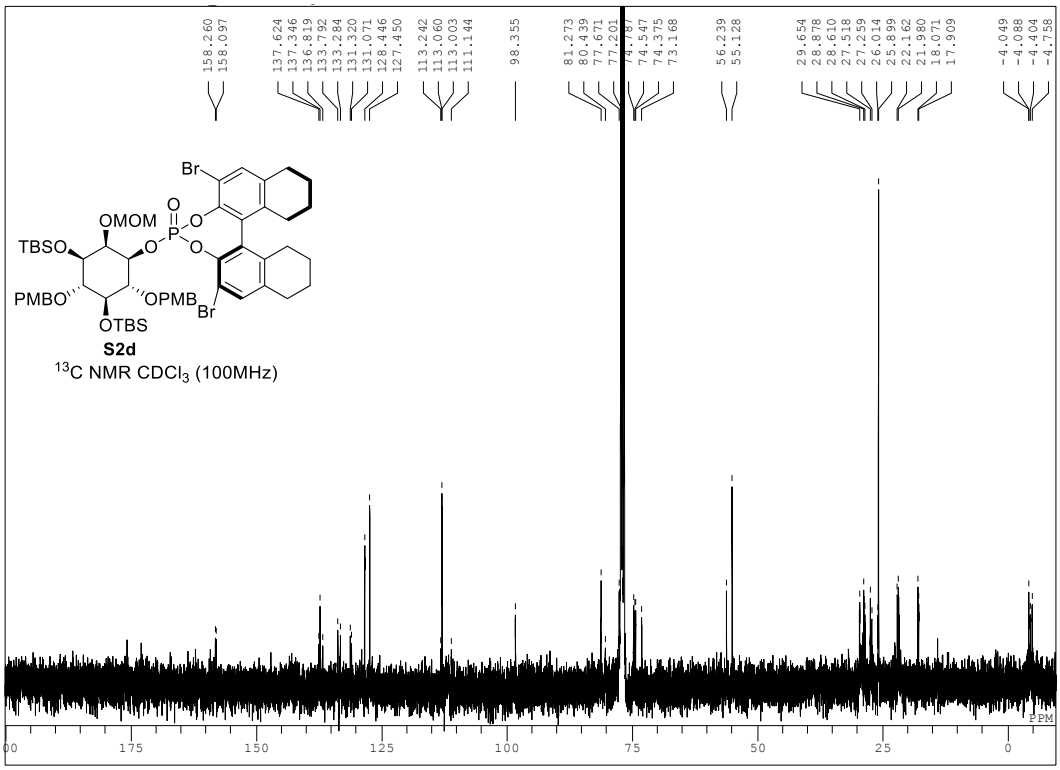

OMOM
TBSO
PMBO
OPMB
OTBS
S2b
1H NMR CDCl3 (400MHz)
PPM

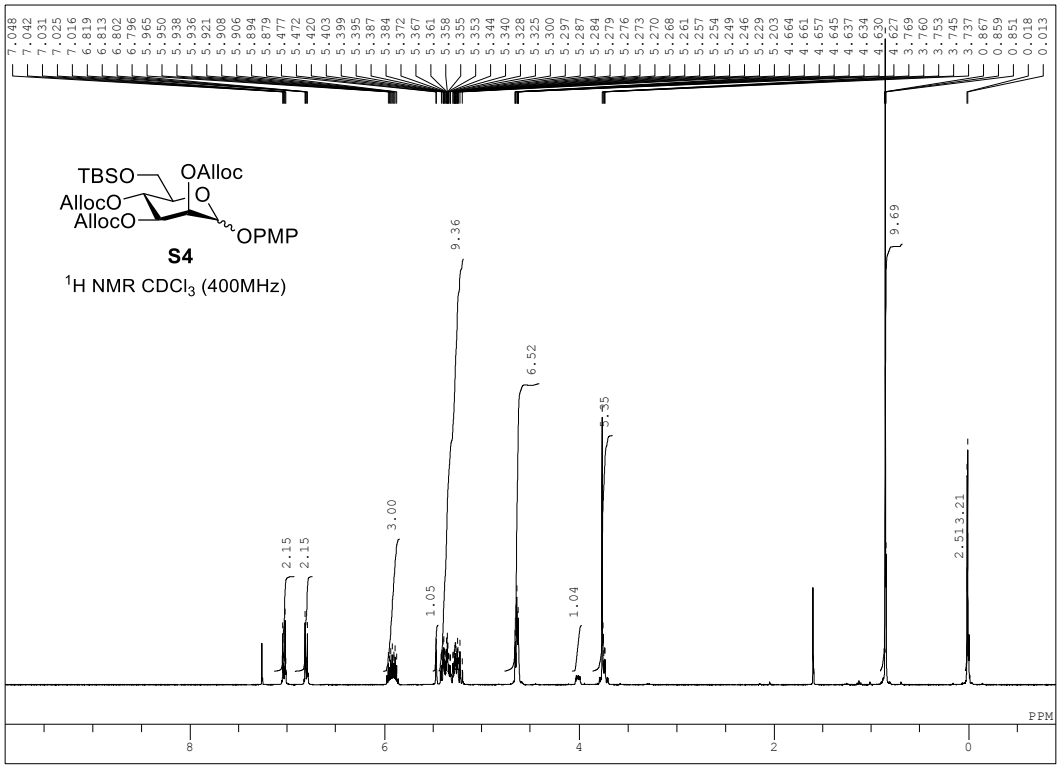

OMOM
TBSO
PMBO
OPMB
OTBS
S2b
13C NMR CDCl3 (100MHz)
PPM

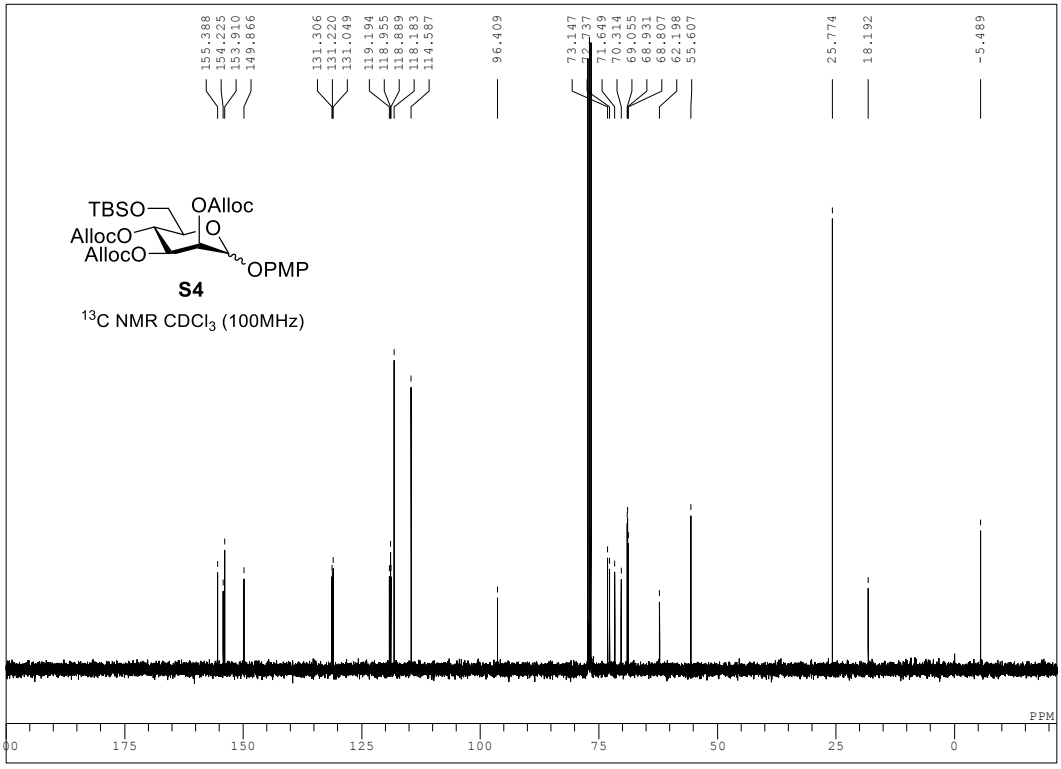

Br
OMOM
TBSO
PMBO
OPMB
Br
OTBS
S2c
^{1}H NMR CDCl$_3$ (400MHz)
PPM

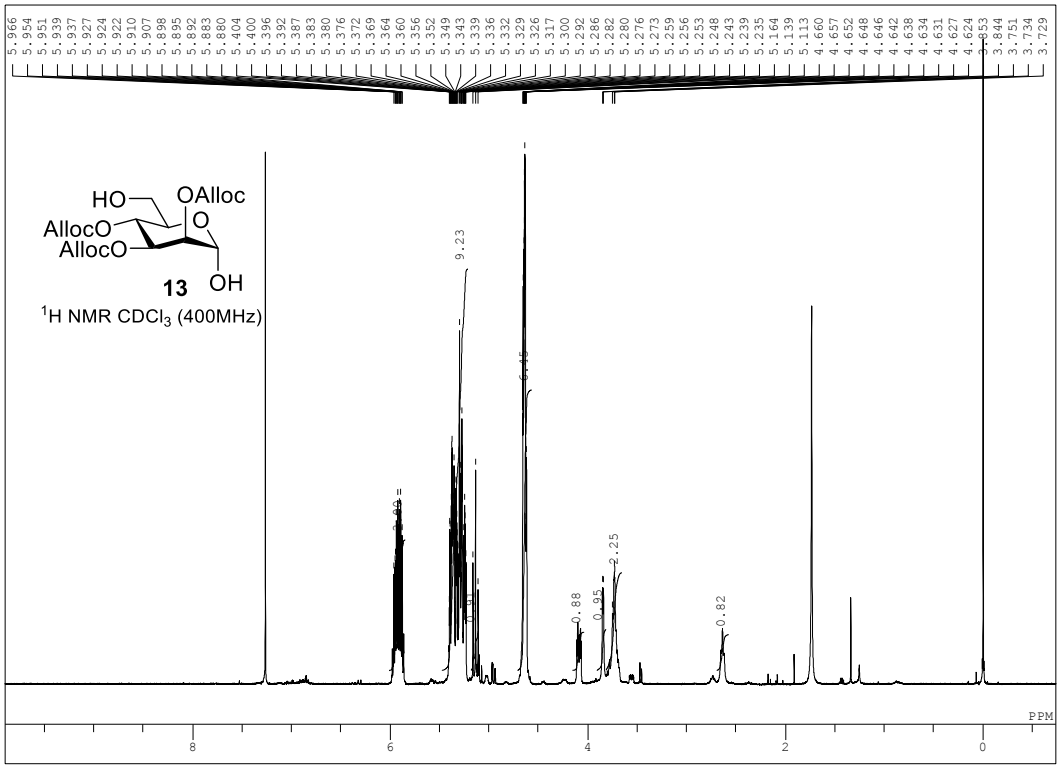

Br
OMOM
TBSO
PMBO
OPMB
Br
OTBS
S2c
^{13}C NMR CDCl$_3$ (100MHz)

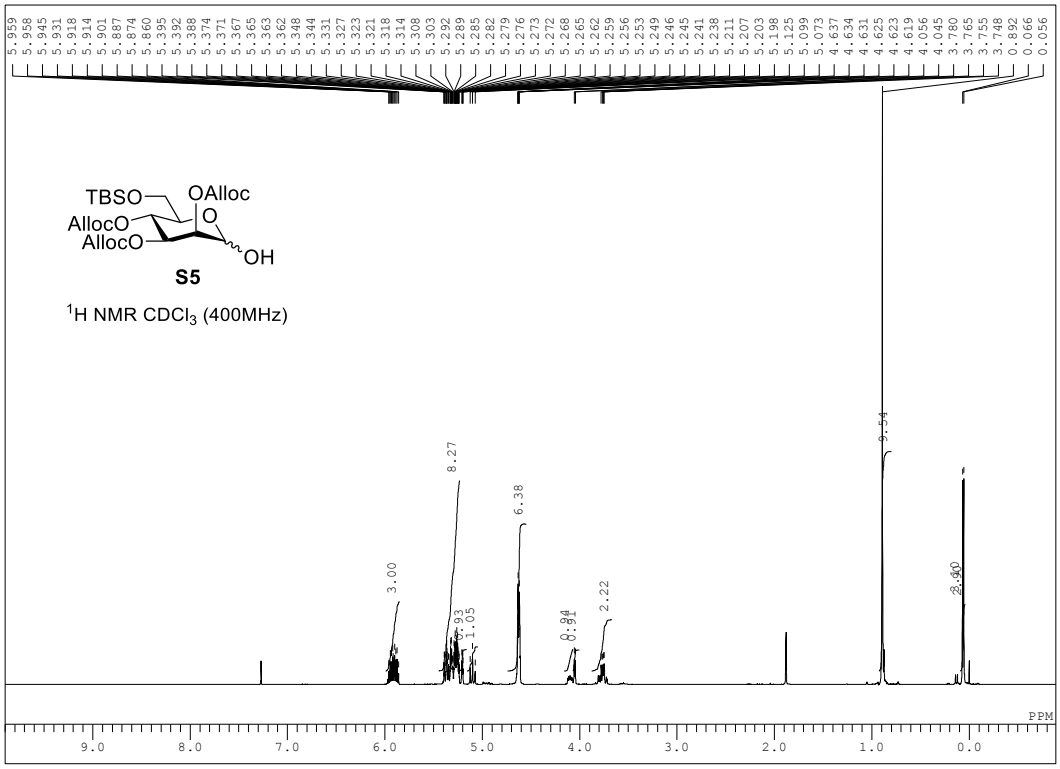

Br
OMOM
TBSO
PMBO
OPMB
Br
OTBS
S2d
1H NMR CDCl3 (400MHz)
PPM

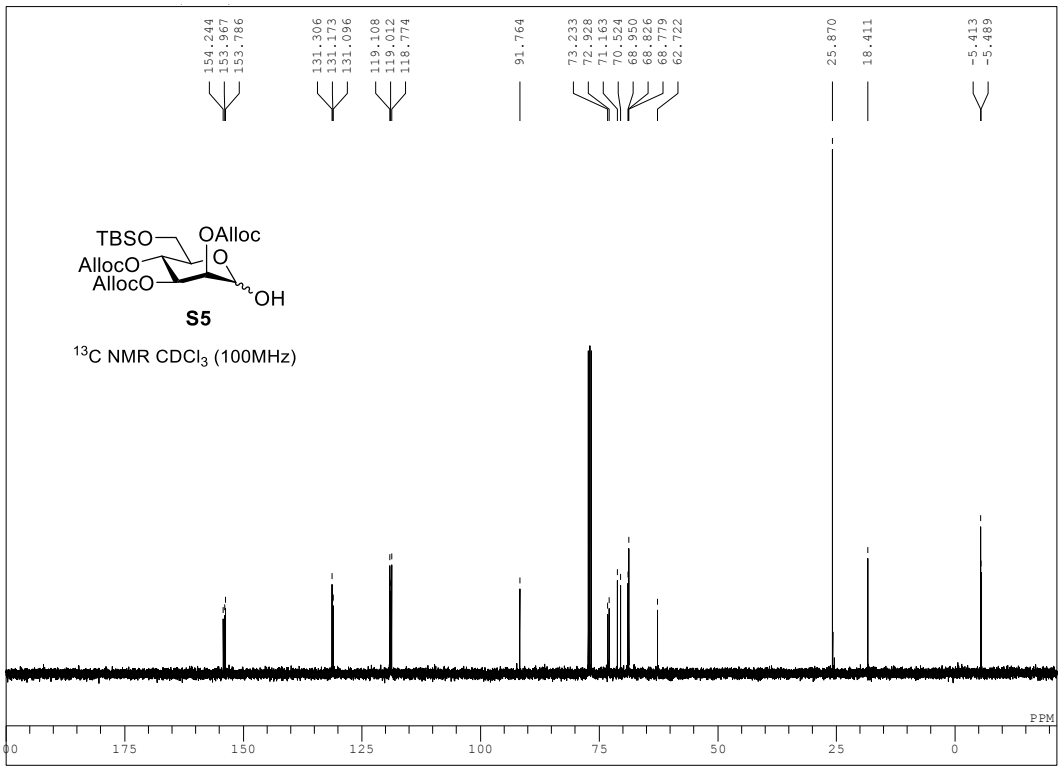

Br
OMOM
TBSO
PMBO
OPMB
Br
OTBS
S2d
13C NMR CDCl3 (100MHz)
PPM

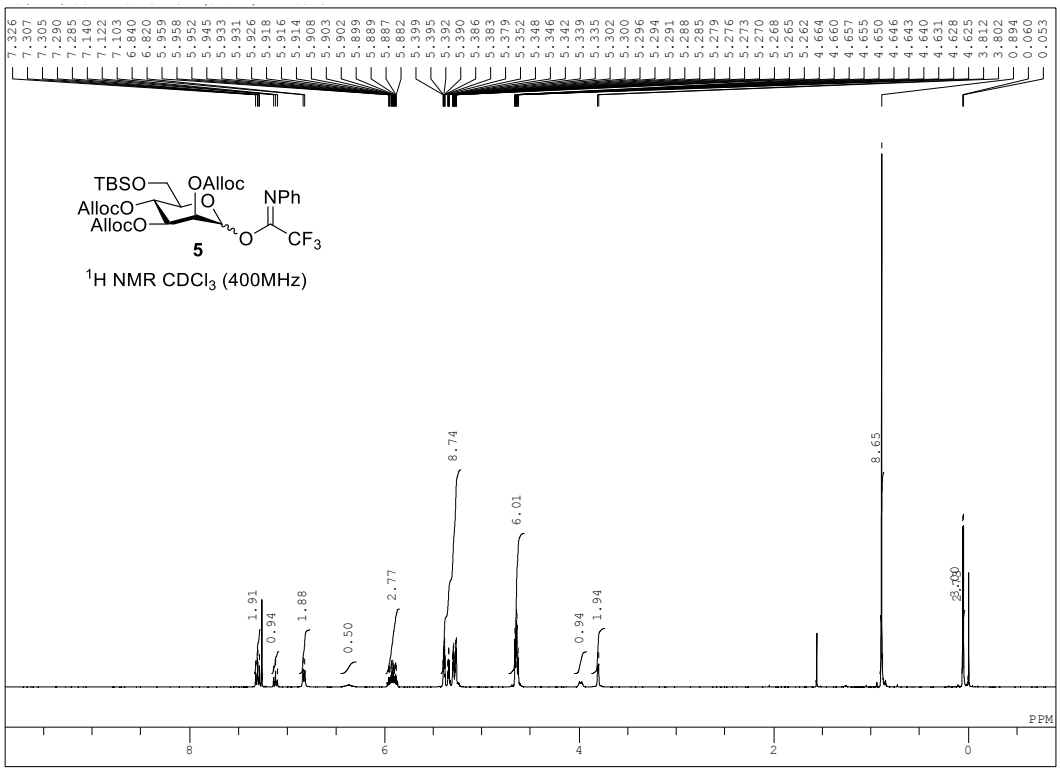

TBSO
OAlloc
O
AllocO
AllocO
OPMP
S4
1H NMR CDCl3 (400MHz)
9.36
9.69
6.52
3.00
2.15
2.15
1.05
1.04
2.51
3.21
PPM

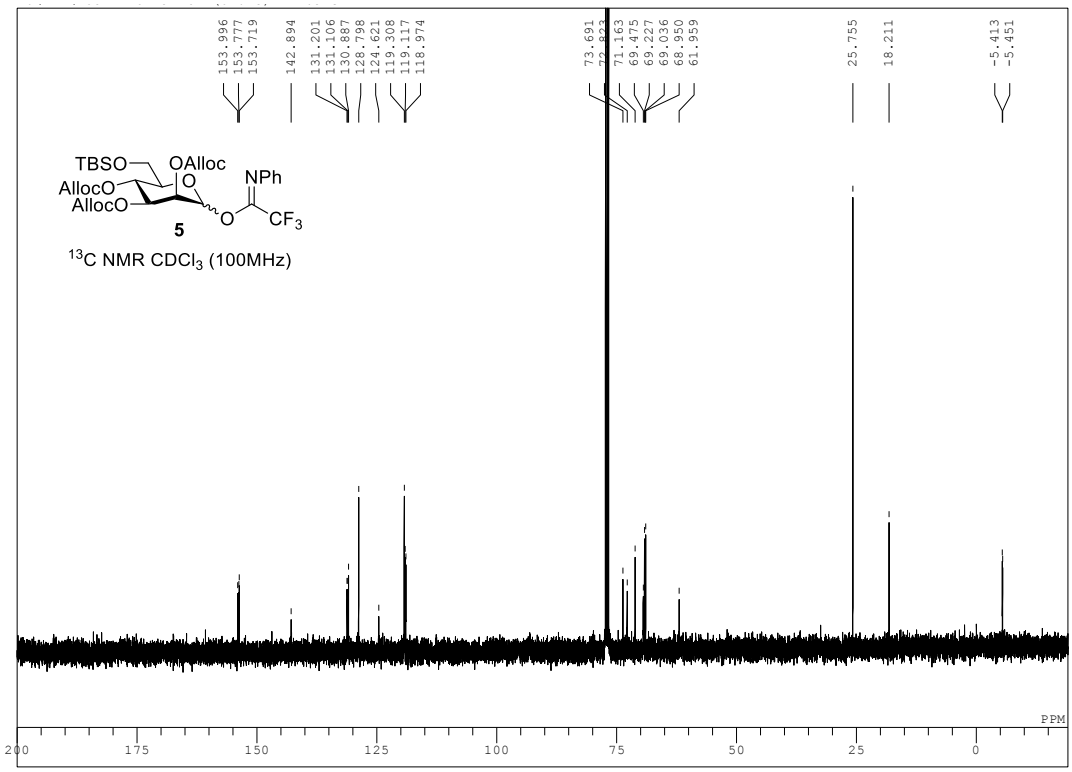

TBSO
OAlloc
O
AllocO
AllocO
OPMP
S4
13C NMR CDCl3 (100MHz)
155.388
154.225
153.910
149.866
131.306
131.220
131.049
119.194
118.955
118.889
118.183
114.587
96.409
73.147
71.649
70.314
69.055
68.931
68.807
62.198
55.607
25.774
18.192
-5.489
PPM

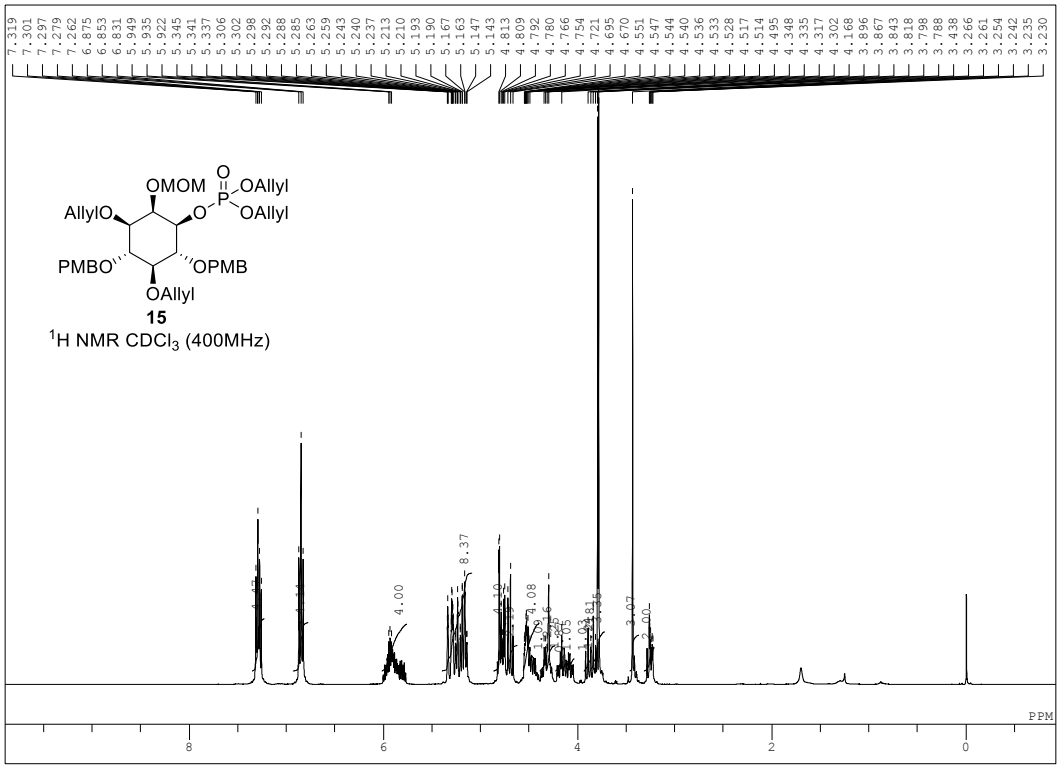

HO
OAlloc
O
AllocO
AllocO
OH
13
^{1}H NMR CDCl$_3$ (400MHz)
9.23
6.45
2.25
0.88
0.95
0.82
PPM
8
6
4
2
0
^{13}C NMR CDCl$_3$ (100MHz)
154.263
153.786
131.240
131.020
130.963
119.442
119.356
118.955
91.926
73.195
72.508
70.429
70.066
69.170
68.960
61.225
200
175
150
125
100
75
50
25

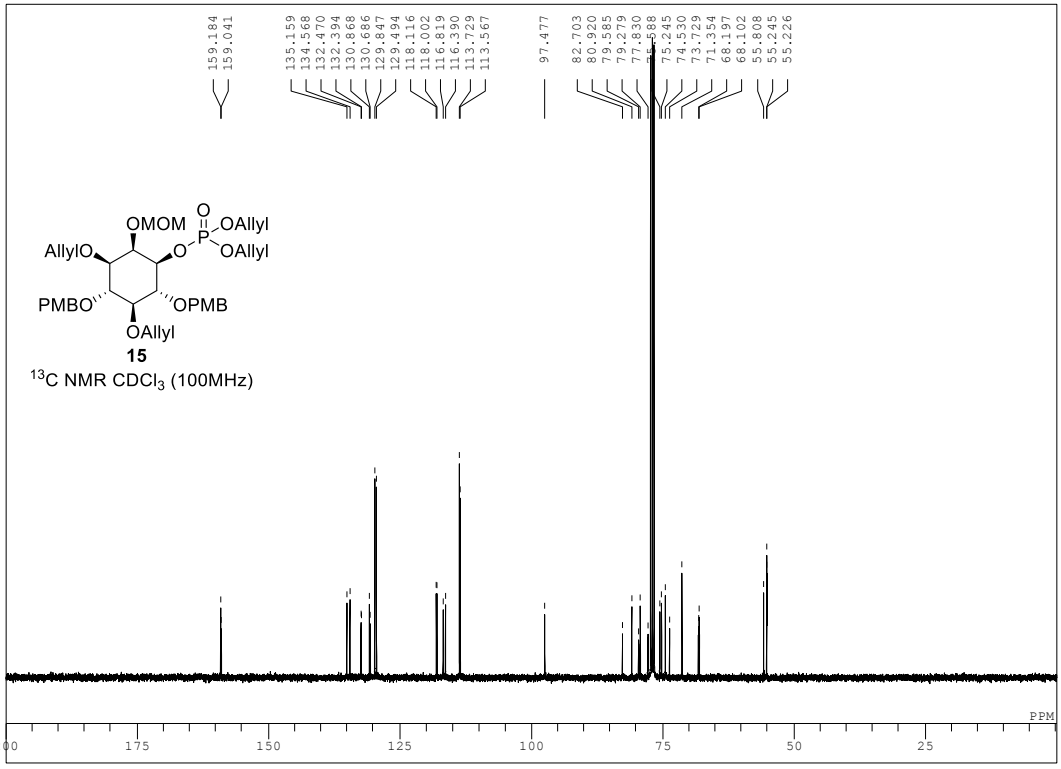

TBSO
OAlloc
AllocO
AllocO
OH
S5
1H NMR CDCl3 (400MHz)
PPM

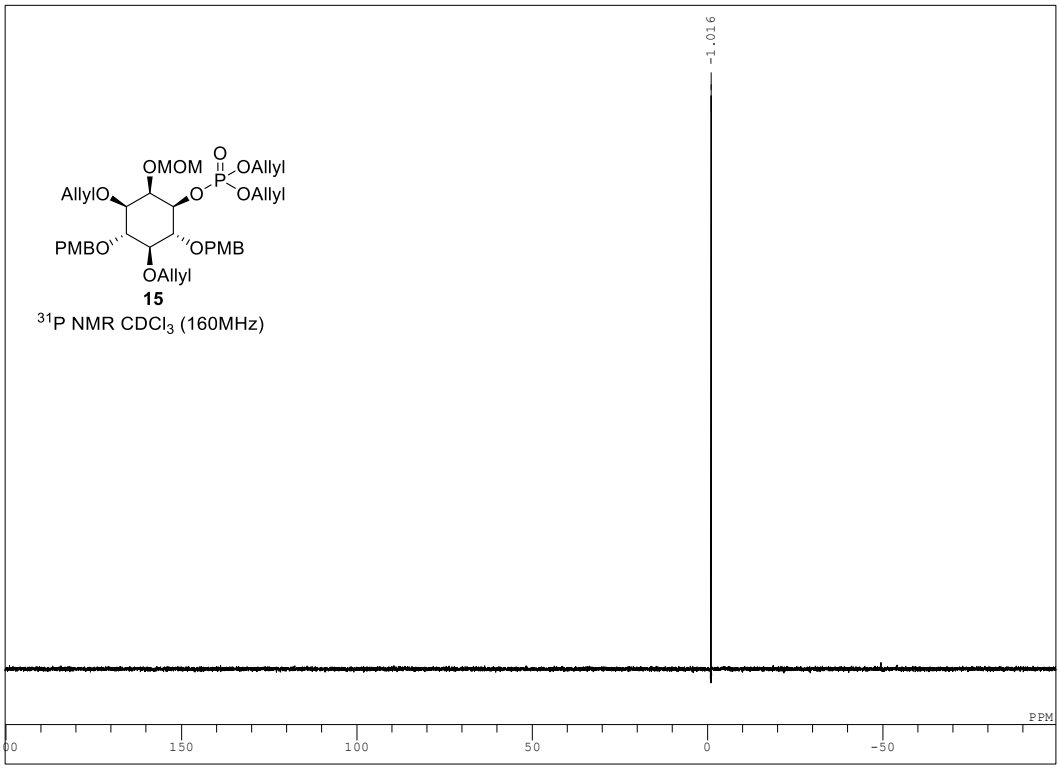

TBSO
OAlloc
AllocO
AllocO
OH
S5
13C NMR CDCl3 (100MHz)
PPM


TBSO
OAlloc
AllocO
AllocO
O
NPh
O
CF3
5
1H NMR CDCl3 (400MHz)
PPM


TBSO
OAlloc
AllocO
AllocO
O
NPh
O
CF3
5
13C NMR CDCl3 (100MHz)
PPM

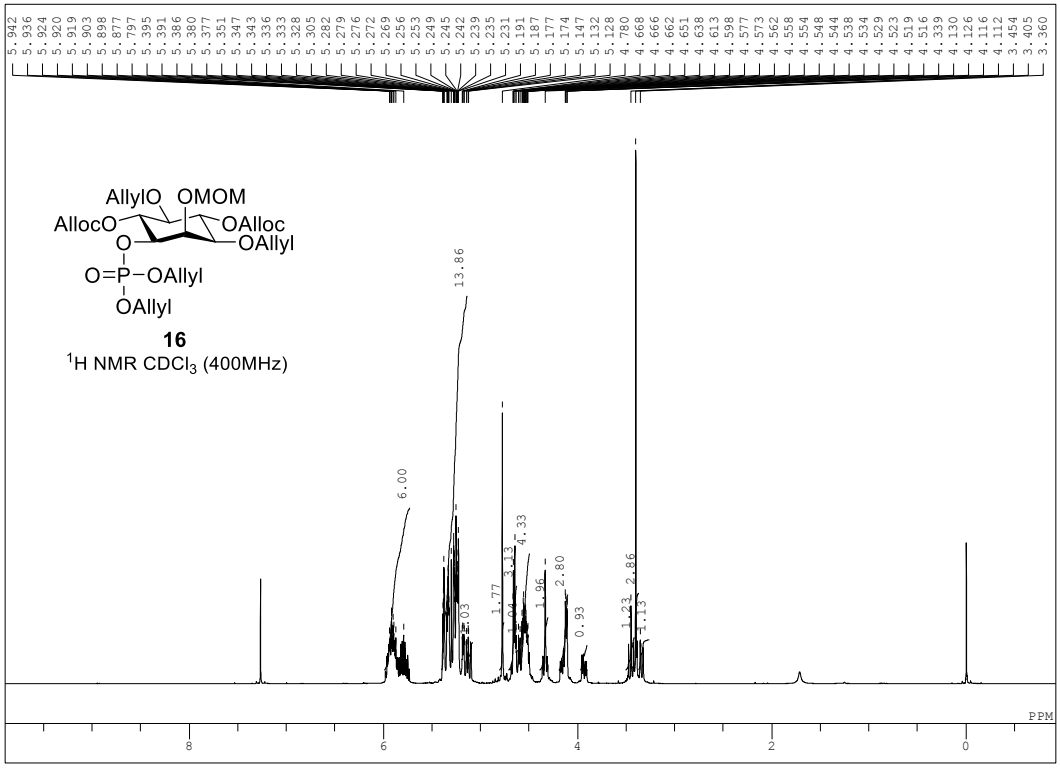

OMOM
O
OAllyl
AllylO
O
P
OAllyl
PMBO
OPMB
OAllyl
15
1H NMR CDCl3 (400MHz)
PPM


OMOM
O
OAllyl
AllylO
O
P
OAllyl
PMBO
OPMB
OAllyl
15
13C NMR CDCl3 (100MHz)
PPM



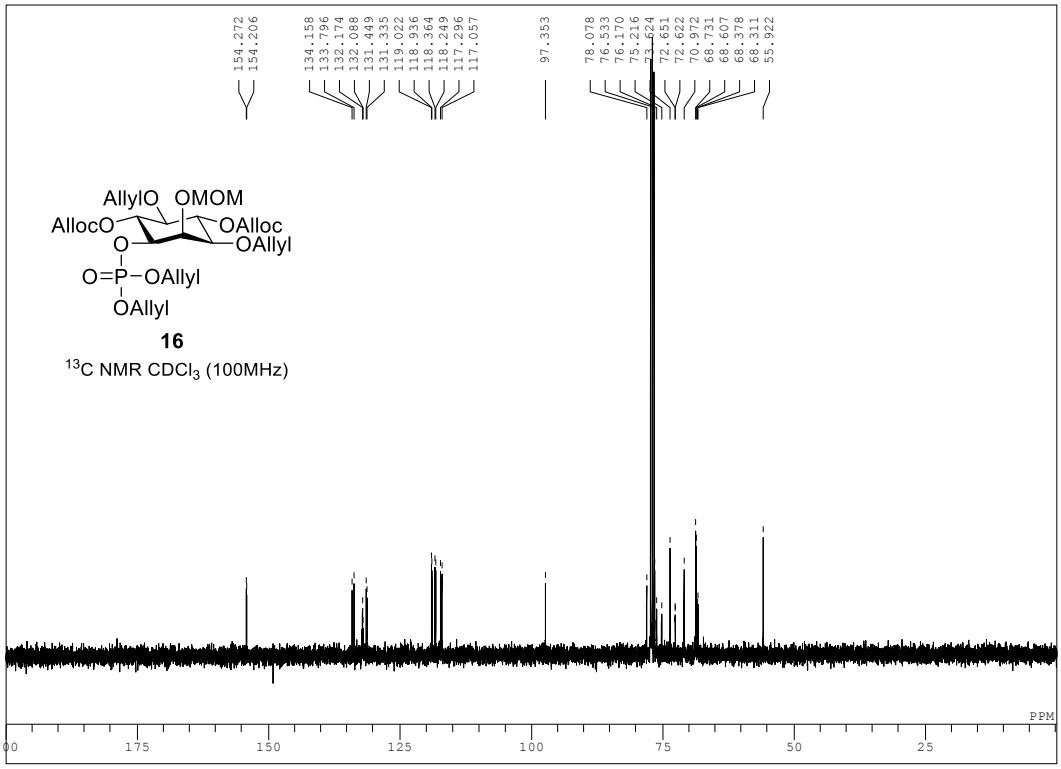
15

^{31}P NMR $CDCl_3$ (160MHz)



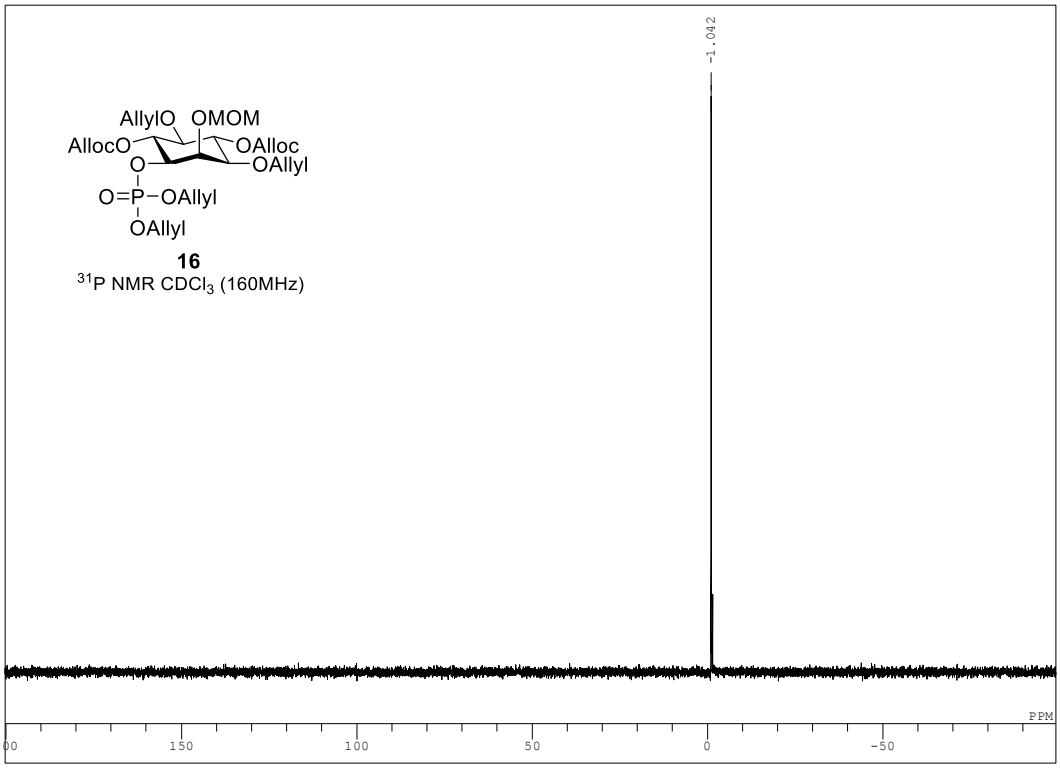
16

^{1}H NMR $CDCl_3$ (400MHz)



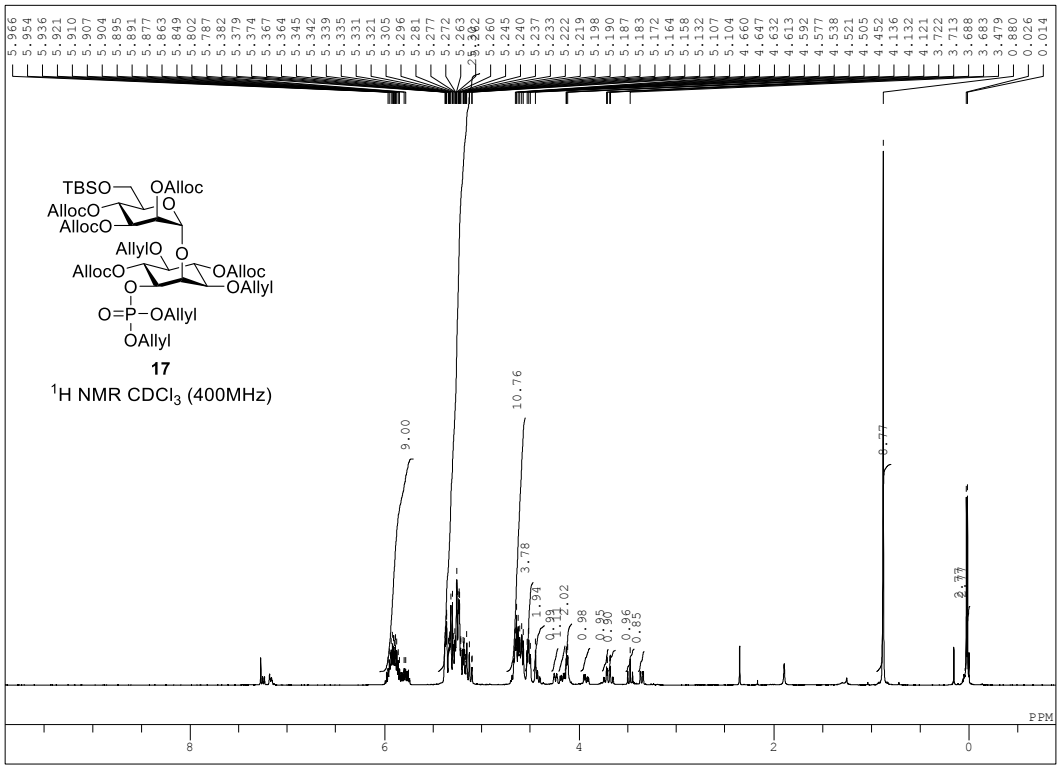
16

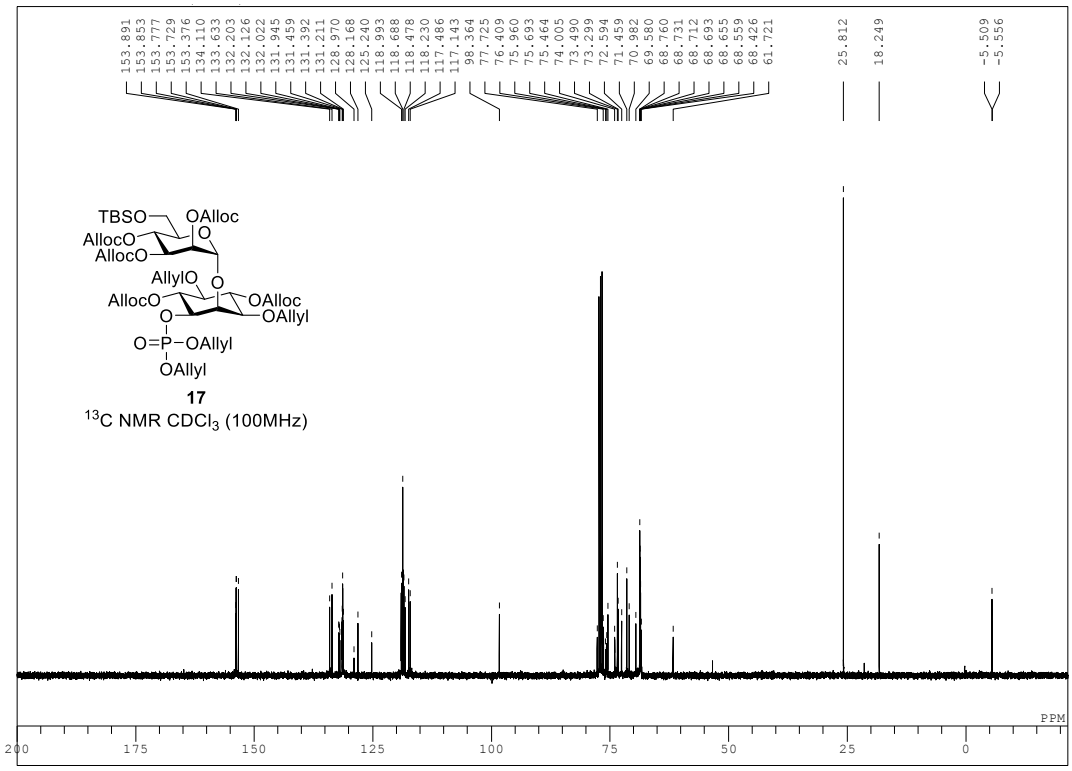
^{13}C NMR $CDCl_3$ (100MHz)

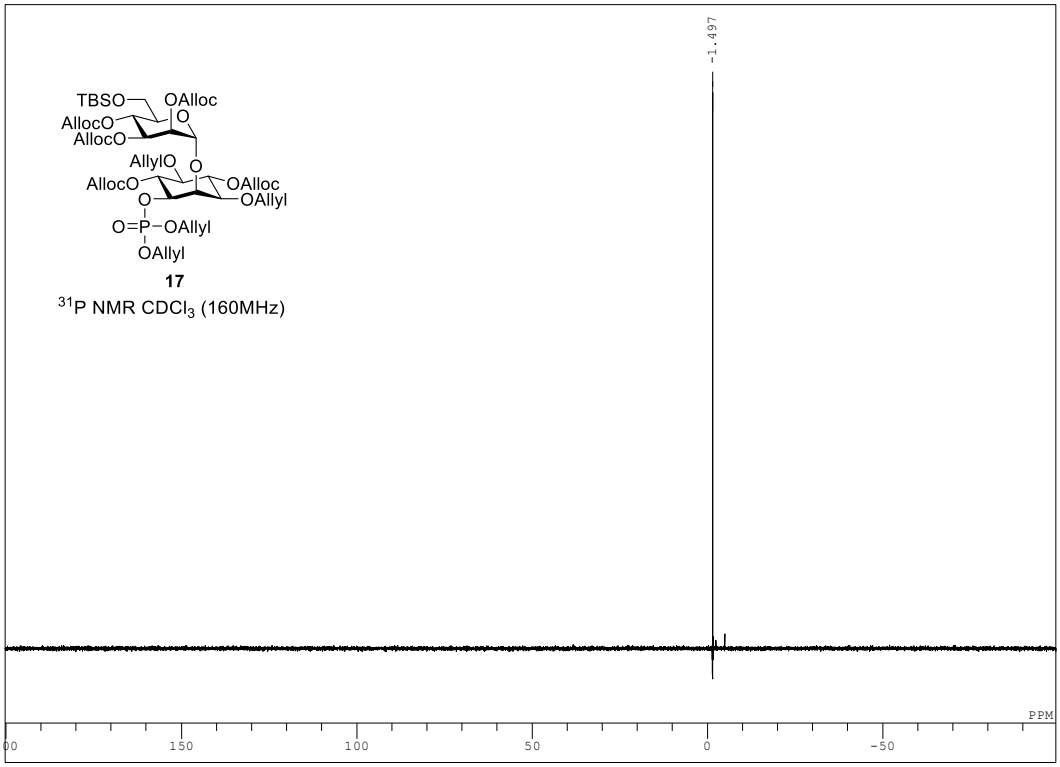


16

^{31}P NMR $CDCl_3$ (160MHz)

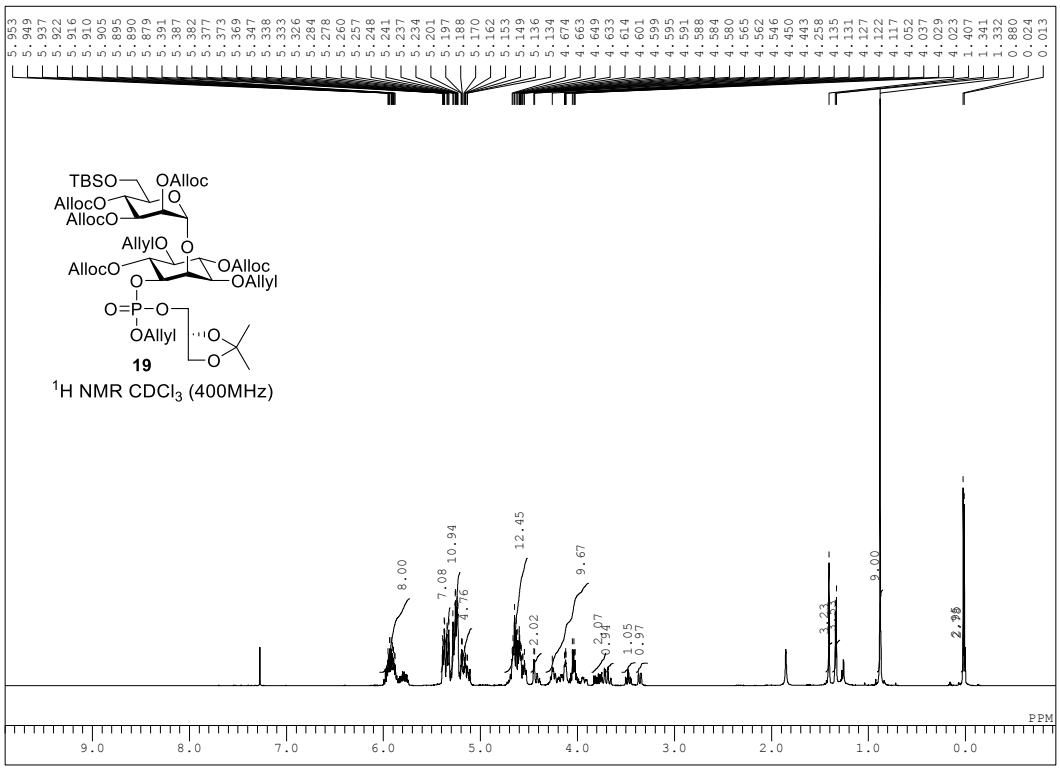

TBSO
OAlloc
AllocO
AllocO
AllylO
AllocO
OAlloc
OAllyl
O=P–OAllyl
OAllyl
17
1H NMR CDCl3 (400MHz)
9.00
10.76
8.77
3.78
1.94
1.91
2.02
0.98
0.95
0.90
0.96
0.85
PPM


TBSO
OAlloc
AllocO
AllocO
AllylO
AllocO
OAlloc
OAllyl
O=P–OAllyl
OAllyl
17
13C NMR CDCl3 (100MHz)
PPM



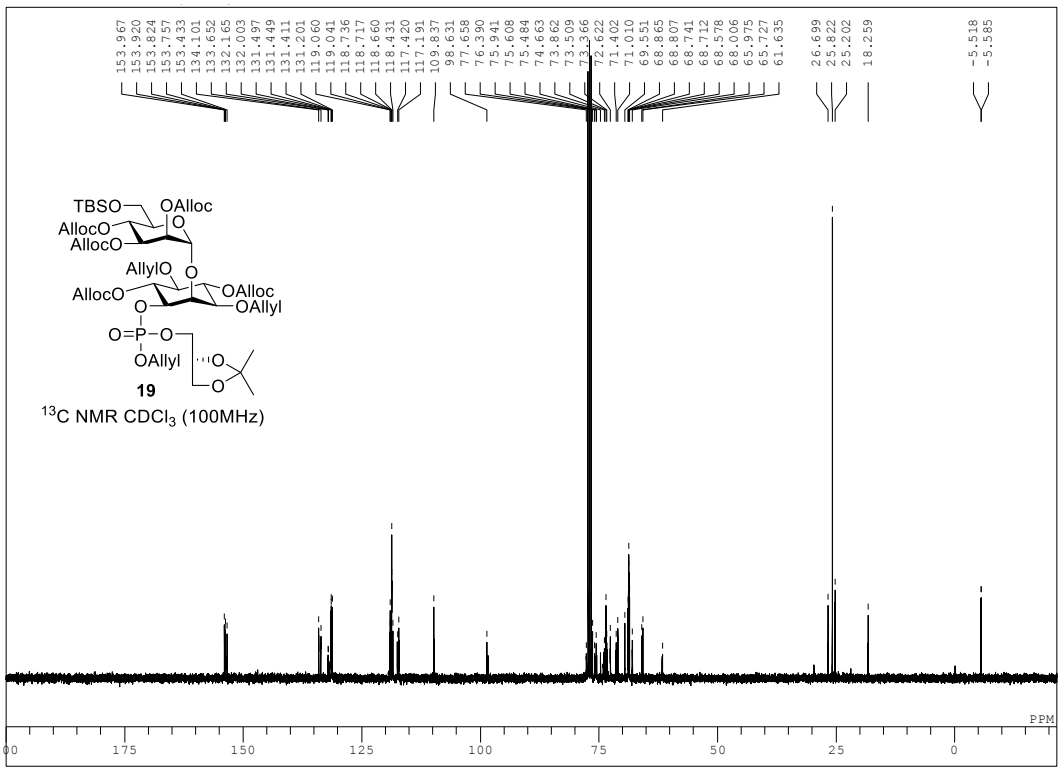
17

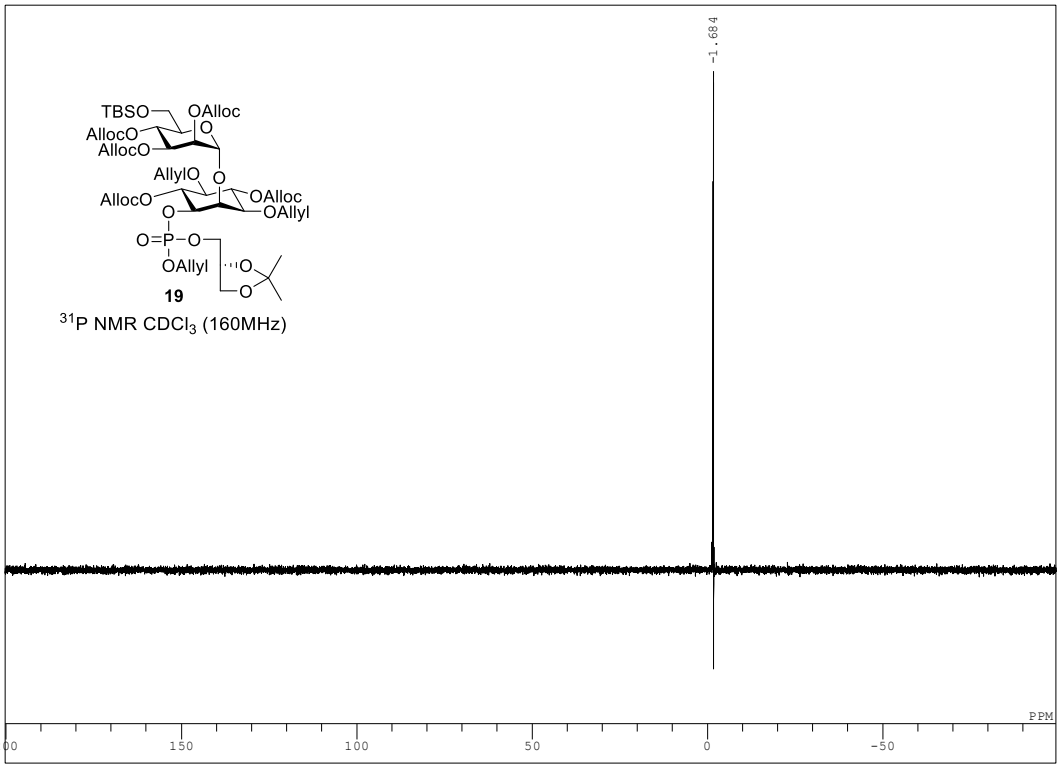
^{31}P NMR $CDCl_3$ (160MHz)

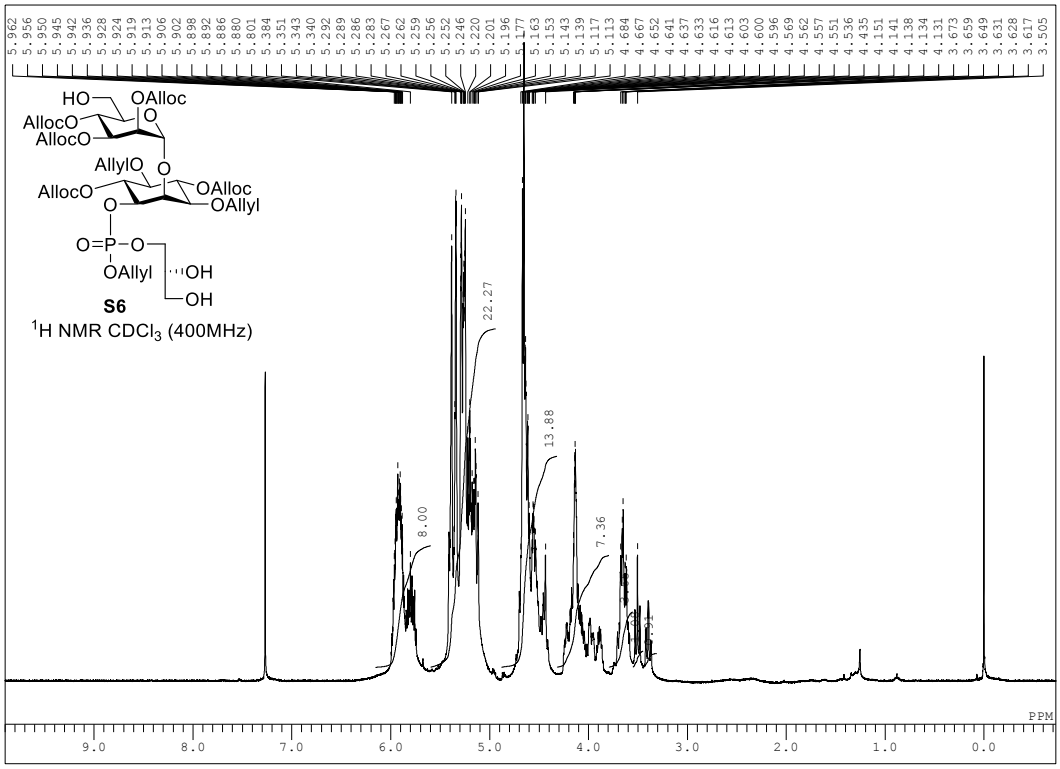


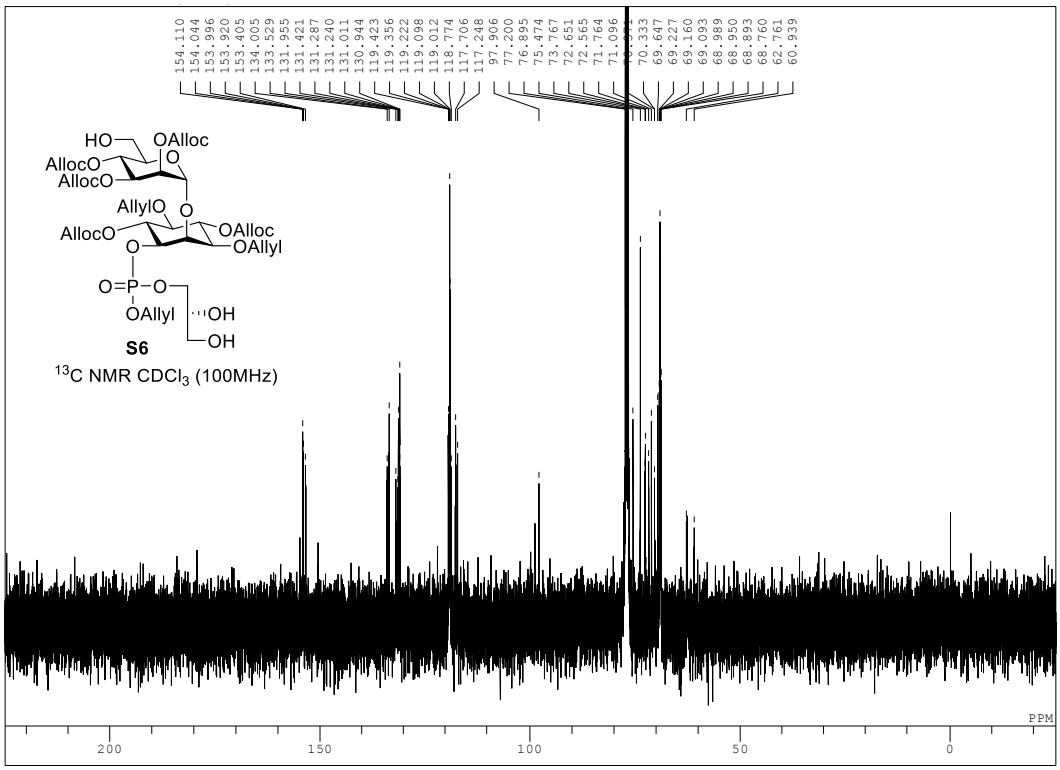
19

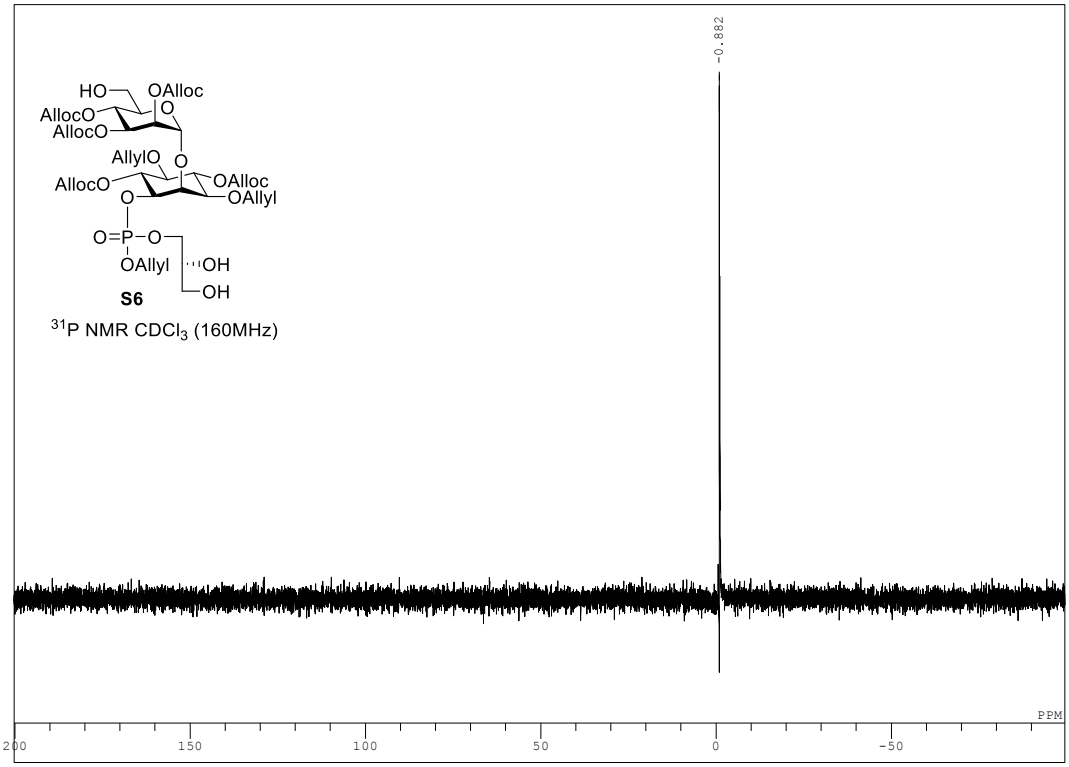
^{1}H NMR $CDCl_3$ (400MHz)

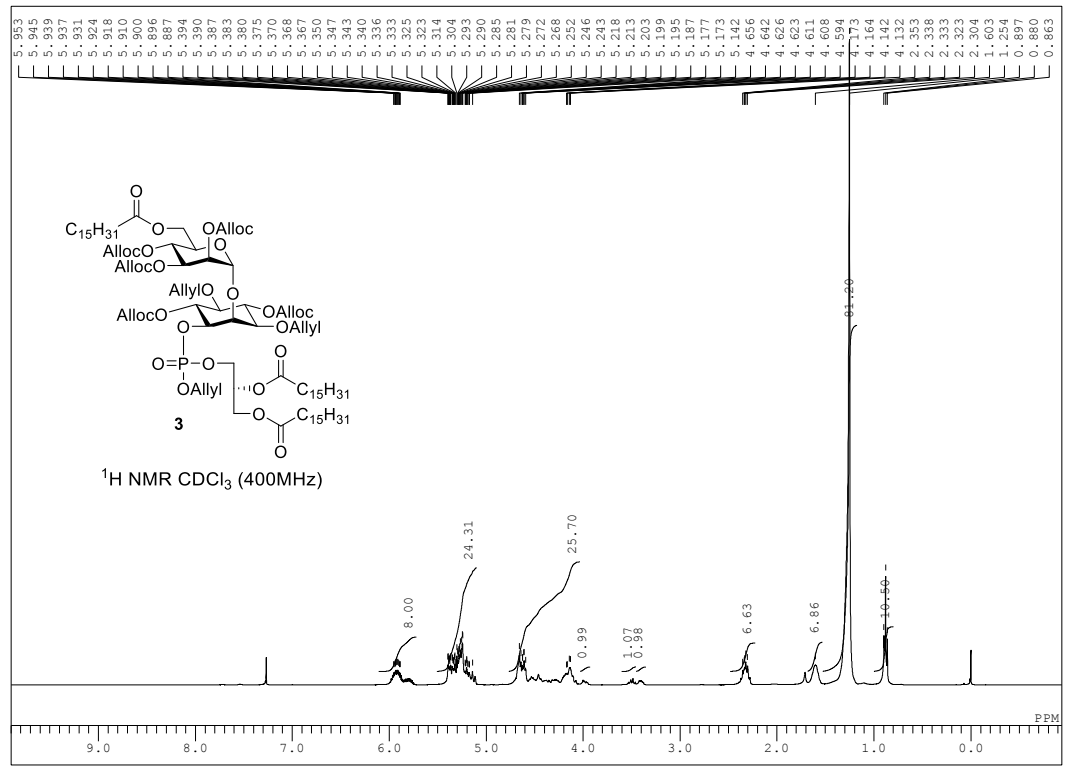

153.967
153.920
153.824
153.757
153.433
134.101
133.652
132.165
132.003
131.497
131.449
131.411
131.201
119.060
119.041
118.736
118.717
118.660
118.431
117.420
117.191
109.837
98.631
77.658
76.390
75.941
75.608
75.484
74.663
73.862
73.509
73.366
72.622
71.402
71.010
69.551
68.865
68.807
68.741
68.712
68.578
68.096
65.975
65.727
61.635
26.699
25.822
25.202
18.259
-5.518
-5.585
TBSO
OAlloc
AllocO
AllocO
AllylO
AllocO
OAlloc
OAllyl
O=P-O
OAllyl
19
^{13}C NMR CDCl$_3$ (100MHz)
PPM
200
175
150
125
100
75
50
25
0

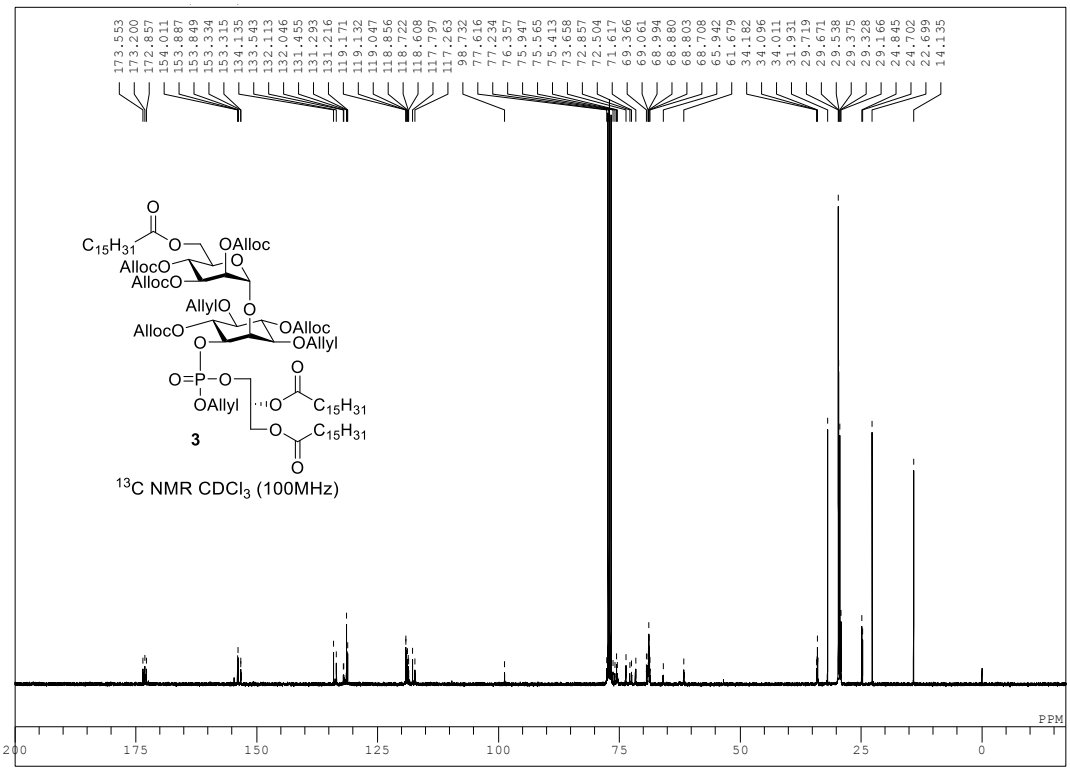

-1.684
TBSO
OAlloc
AllocO
AllocO
AllylO
AllocO
OAlloc
OAllyl
O=P-O
OAllyl
19
^{31}P NMR CDCl$_3$ (160MHz)
PPM
200
150
100
50
0
-50

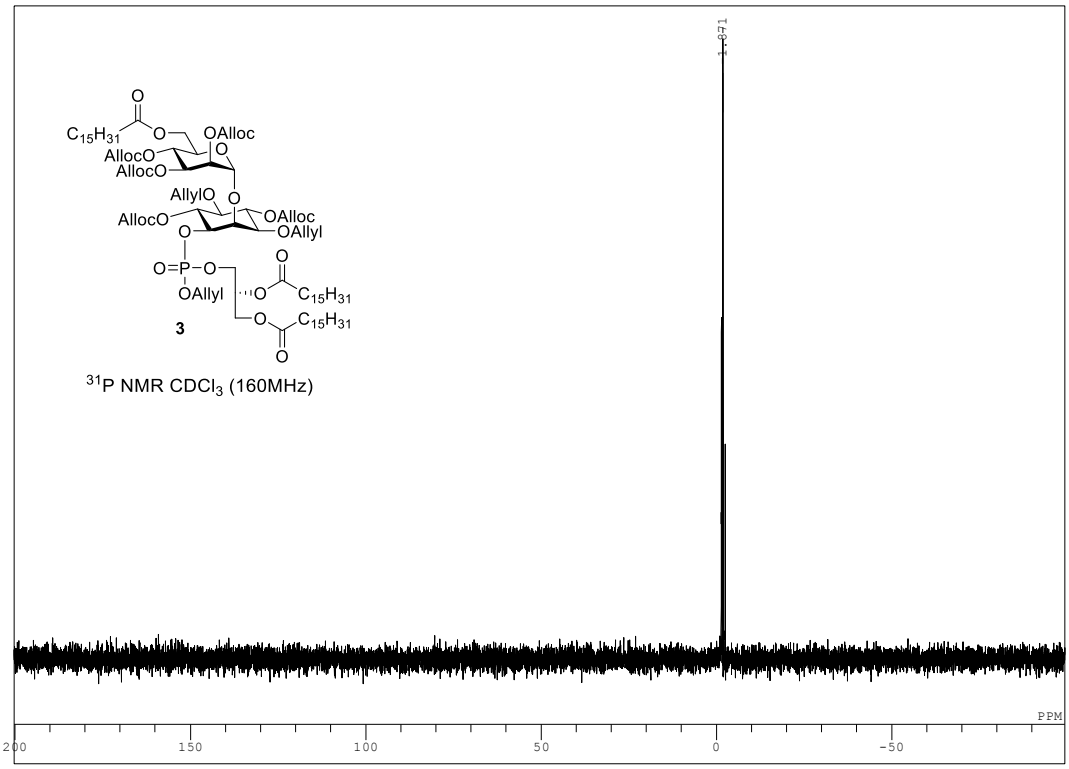

HO
OAlloc
AllocO
AllocO
AllylO
AllocO
OAlloc
OAllyl
O=P–O
OAllyl
OH
OH
S6
^{1}H NMR CDCl$_3$ (400MHz)
8.00
22.27
13.88
7.36
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

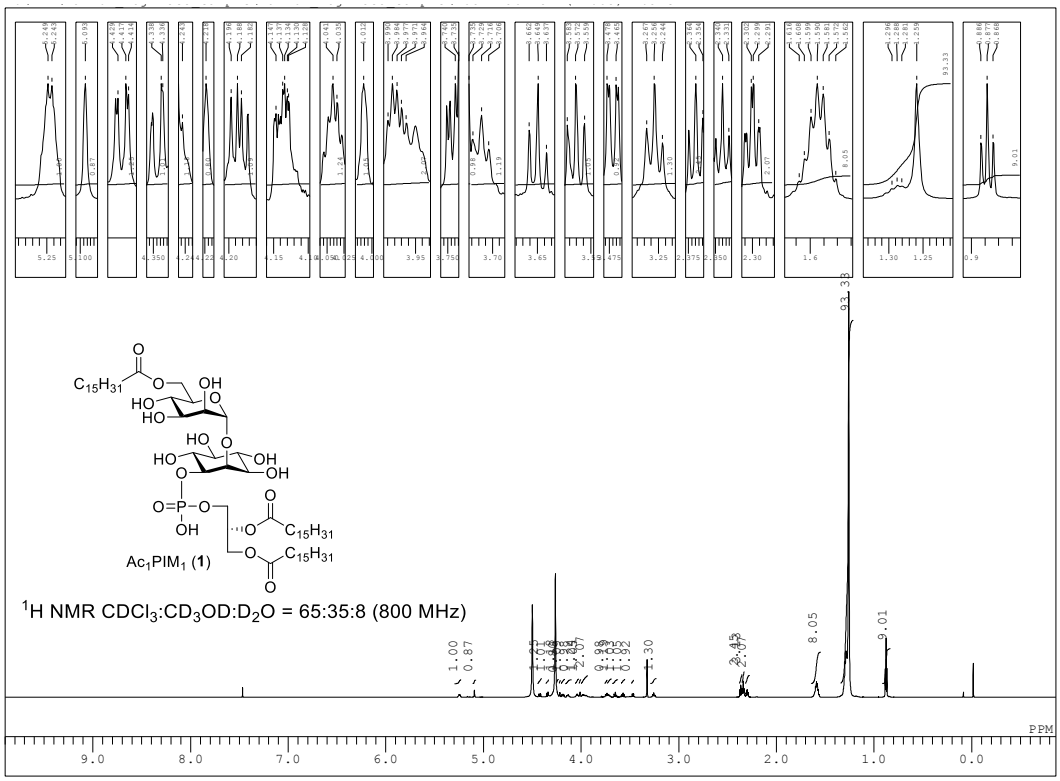

HO
OAlloc
AllocO
AllocO
AllylO
AllocO
OAlloc
OAllyl
O=P–O
OAllyl
OH
OH
S6
^{13}C NMR CDCl$_3$ (100MHz)
PPM
200
150
100
50
0

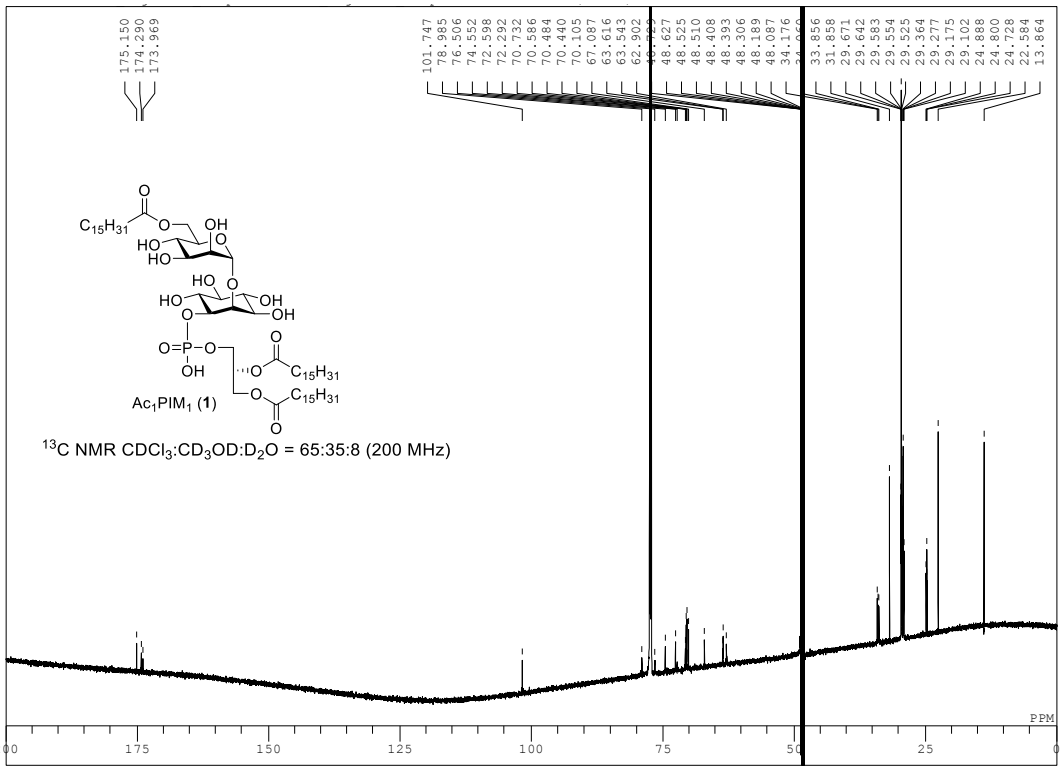

HO
OAlloc
AllocO
AllocO
AllylO
O
AllocO
OAlloc
OAllyl
O=P–O
OAllyl
OH
OH
S6
31P NMR CDCl3 (160MHz)
-0.882
PPM
200
150
100
50
0
-50

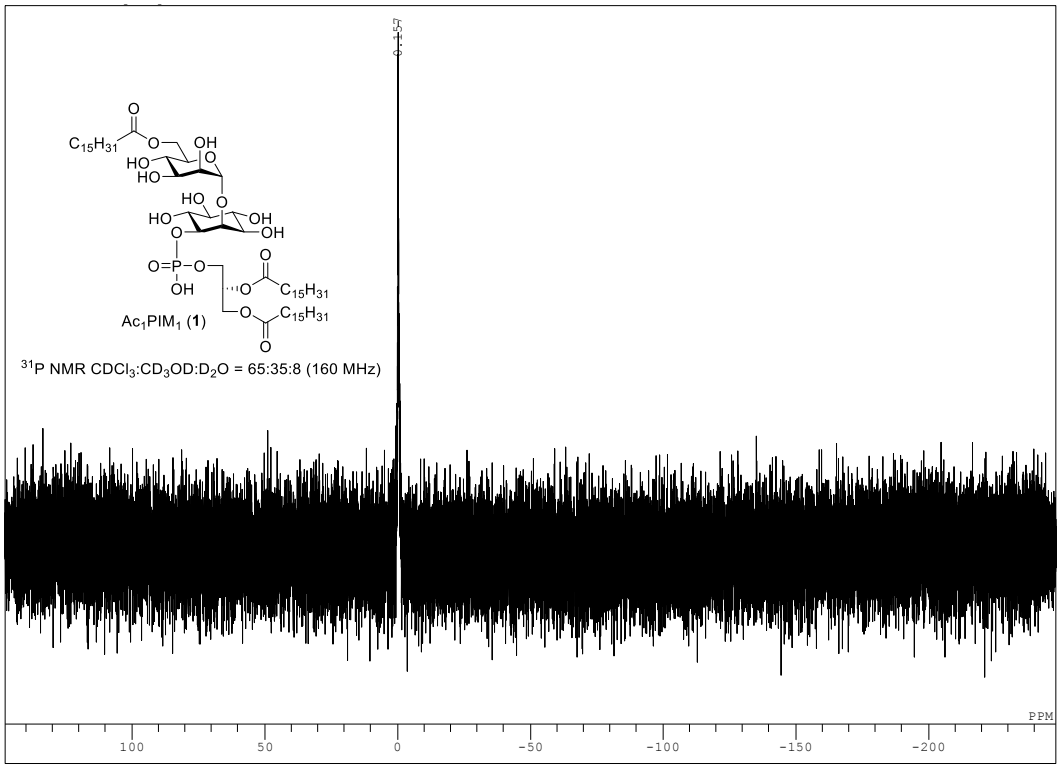

5.953
5.945
5.939
5.937
5.931
5.924
5.918
5.910
5.900
5.896
5.887
5.394
5.390
5.387
5.383
5.380
5.375
5.370
5.368
5.367
5.350
5.347
5.343
5.340
5.336
5.333
5.325
5.323
5.314
5.304
5.293
5.290
5.285
5.281
5.279
5.272
5.268
5.252
5.246
5.243
5.218
5.213
5.203
5.199
5.195
5.187
5.177
5.173
5.142
4.656
4.642
4.626
4.623
4.611
4.608
4.594
4.173
4.164
4.142
4.132
2.353
2.338
2.333
2.323
2.304
1.603
1.254
0.897
0.880
0.863
C15H31
O
OAlloc
AllocO
AllocO
AllylO
AllocO
OAlloc
OAllyl
O=P–O
OAllyl
C15H31
C15H31
3
1H NMR CDCl3 (400MHz)
8.00
24.31
25.70
0.99
1.07
0.98
6.63
6.86
61.20
10.60
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

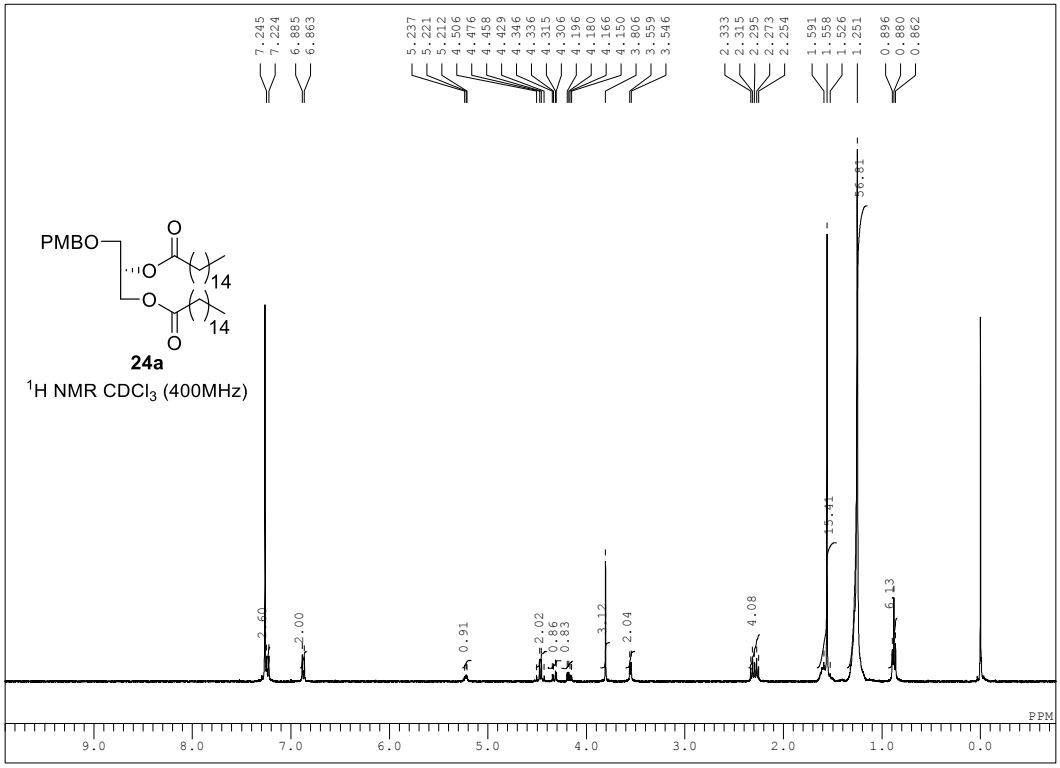

173.553
173.200
172.857
154.011
153.887
153.849
153.334
153.315
134.135
133.543
132.113
132.046
131.455
131.293
131.216
119.171
119.132
119.047
118.856
118.722
118.608
117.797
117.263
98.732
77.616
77.234
76.357
75.947
75.565
75.413
73.658
72.857
72.504
71.617
69.366
69.061
68.994
68.880
68.803
68.708
65.942
61.679
34.182
34.096
34.011
31.931
29.719
29.671
29.538
29.375
29.328
29.166
24.845
24.702
22.699
14.135
3
13C NMR CDCl3 (100MHz)
PPM
200
175
150
125
100
75
50
25
0

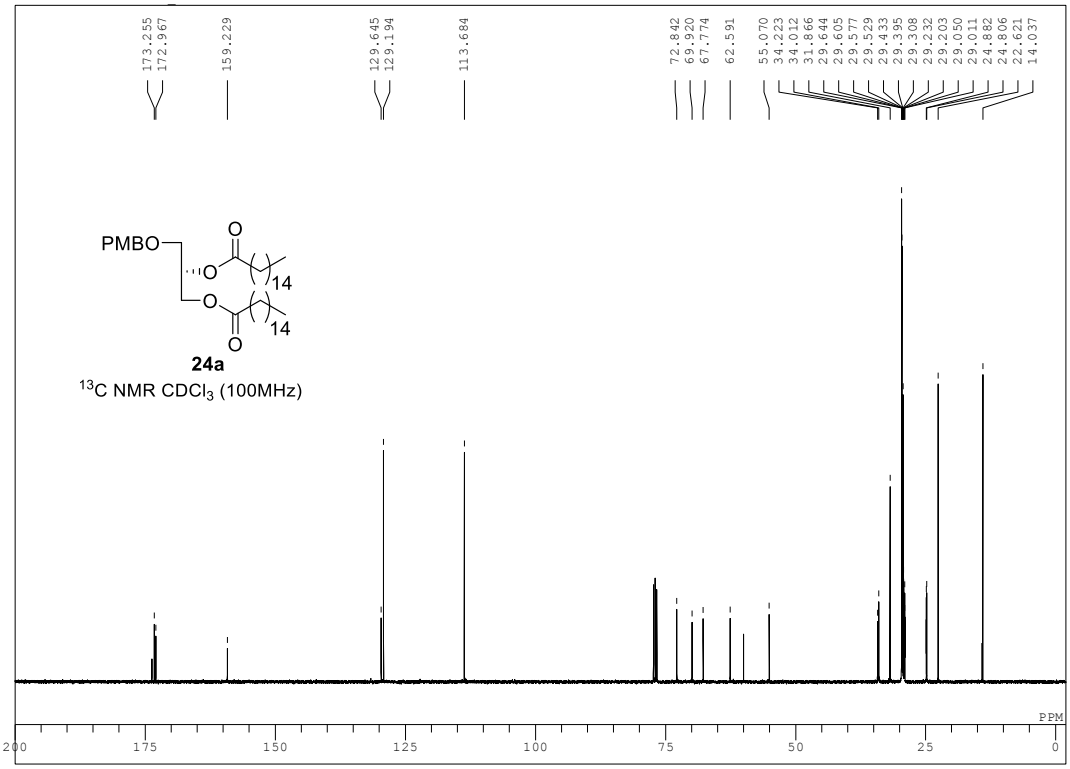

1.671
3
31P NMR CDCl3 (160MHz)
PPM
200
150
100
50
0
-50

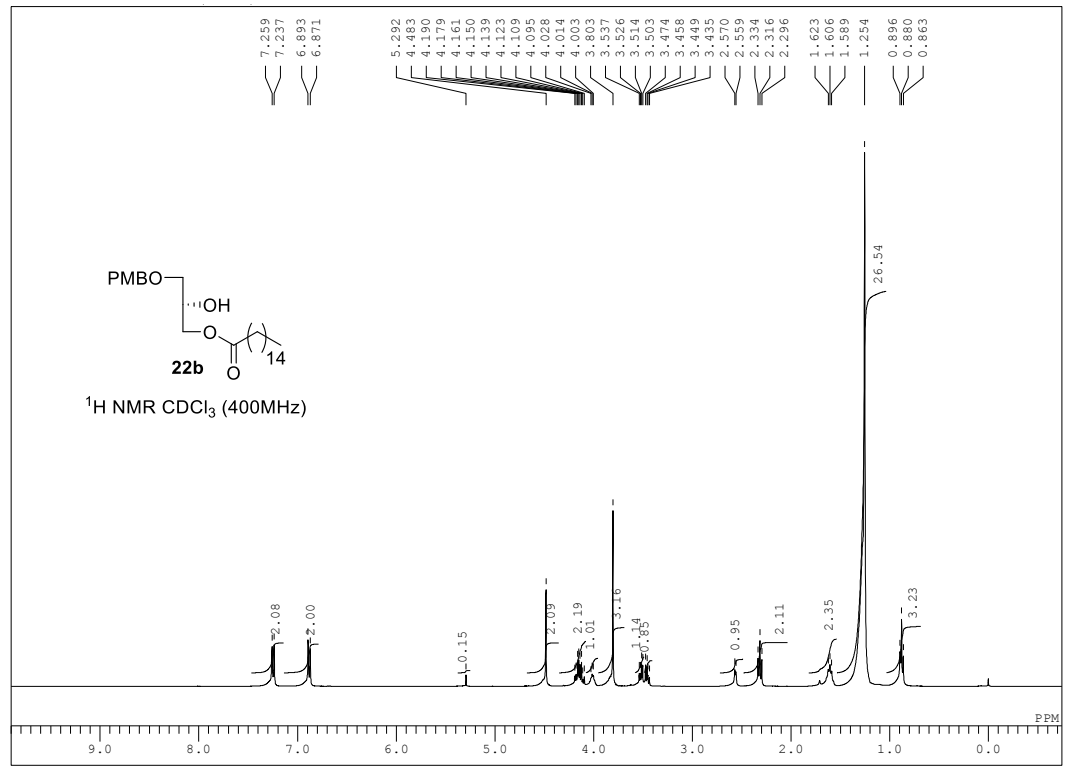

Ac1PIM1 (1)
1H NMR CDCl3:CD3OD:D2O = 65:35:8 (800 MHz)
PPM

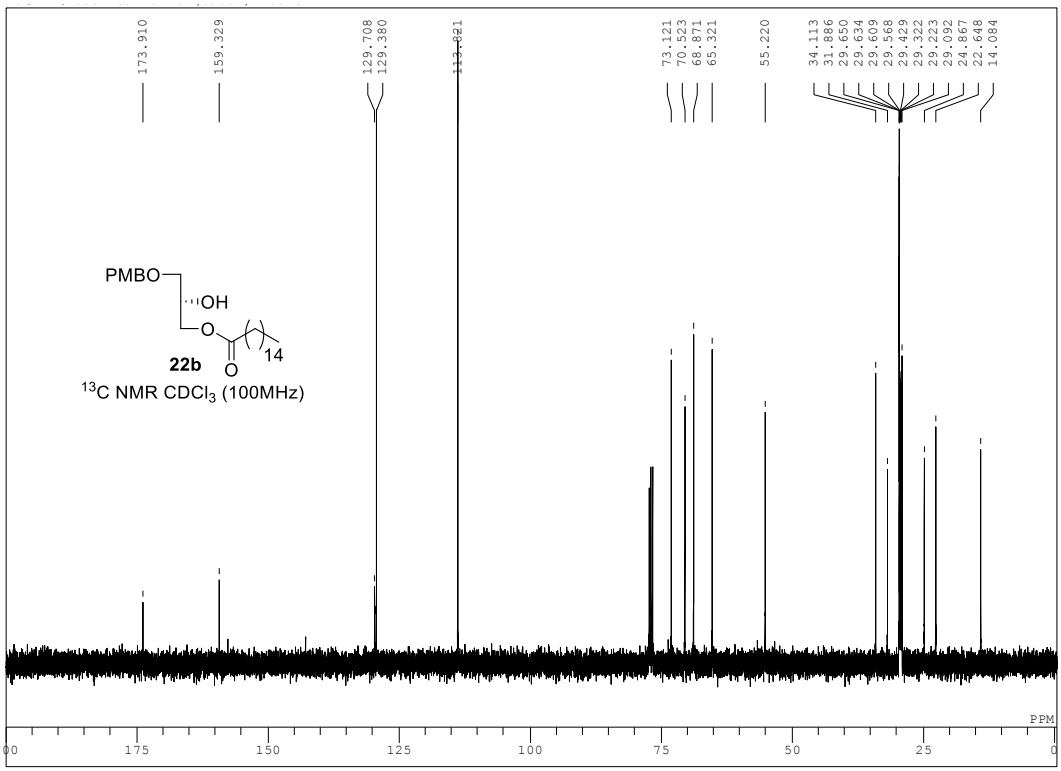

Ac1PIM1 (1)
13C NMR CDCl3:CD3OD:D2O = 65:35:8 (200 MHz)
PPM

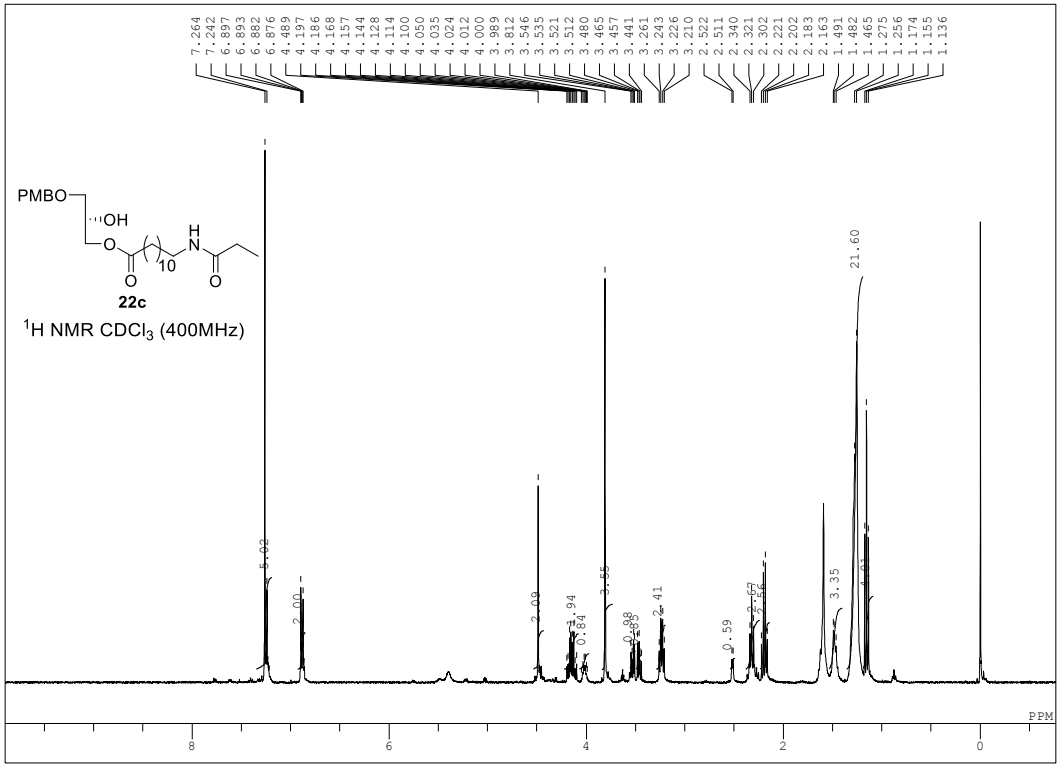

0.157
Ac1PIM1 (1)
31P NMR CDCl3:CD3OD:D2O = 65:35:8 (160 MHz)
PPM
100
50
0
-50
-100
-150
-200

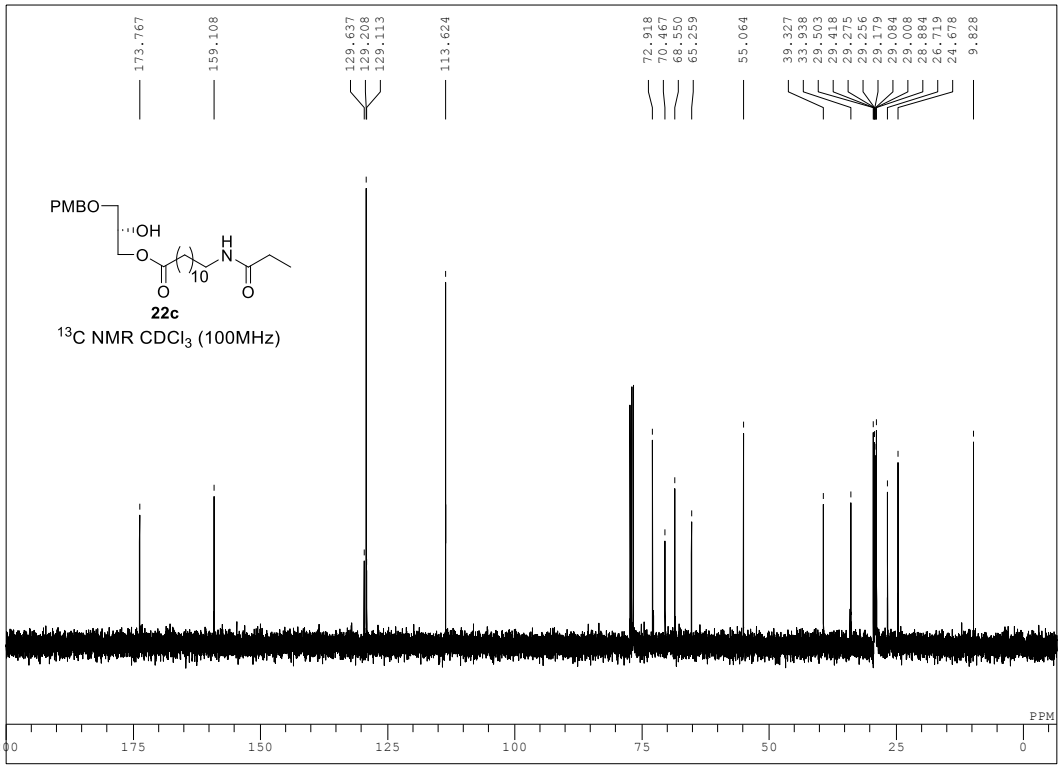

7.245
7.224
6.885
6.863
5.237
5.221
5.212
4.506
4.476
4.458
4.429
4.346
4.336
4.315
4.306
4.196
4.180
4.166
4.150
3.806
3.559
3.546
2.333
2.315
2.295
2.273
2.254
1.591
1.558
1.526
1.251
0.896
0.880
0.862
PMBO
24a
1H NMR CDCl3 (400MHz)
2.60
2.00
0.91
2.02
0.86
0.83
3.12
2.04
4.08
15.41
56.81
6.13
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

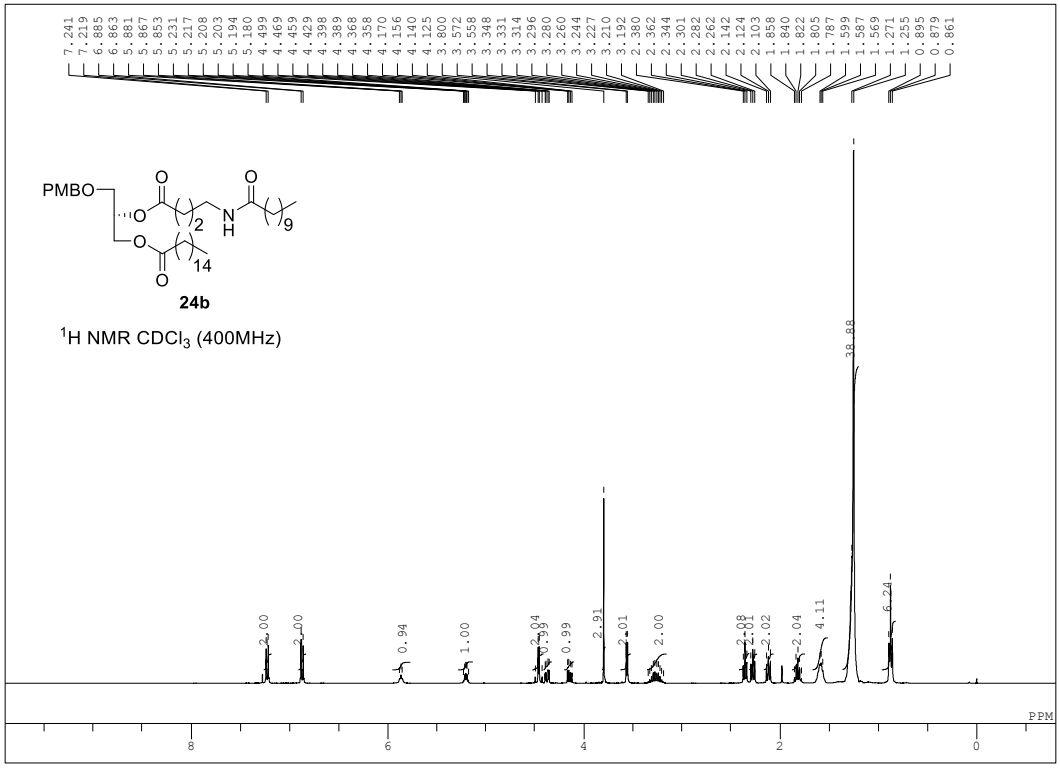

173.255
172.967
159.229
129.645
129.194
113.684
72.842
69.920
67.774
62.591
55.070
34.223
34.012
31.866
29.644
29.605
29.577
29.529
29.433
29.395
29.308
29.232
29.203
29.050
29.011
24.882
24.806
22.621
14.037
PMBO
O
O
14
O
O
14
24a
13C NMR CDCl3 (100MHz)
PPM
200
175
150
125
100
75
50
25
0

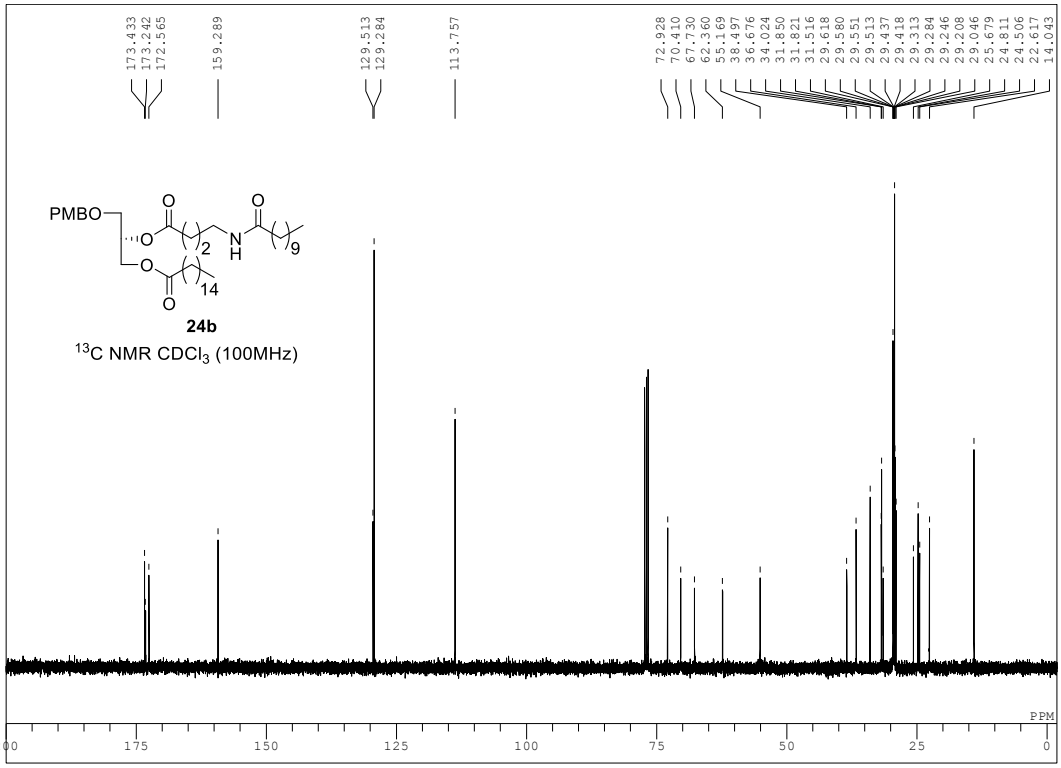

7.259
7.237
6.893
6.871
5.292
4.483
4.190
4.179
4.161
4.150
4.139
4.123
4.109
4.095
4.028
4.014
4.003
3.803
3.537
3.526
3.514
3.503
3.474
3.458
3.449
3.435
2.570
2.559
2.334
2.316
2.296
1.623
1.606
1.589
1.254
0.896
0.880
0.863
PMBO
OH
O
14
O
22b
1H NMR CDCl3 (400MHz)
2.08
2.00
0.15
2.09
2.19
1.01
3.16
1.14
0.85
0.95
2.11
2.35
26.54
3.23
PPM
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


173.910
159.329
129.708
129.380
113.921
73.121
70.523
68.871
65.321
55.220
34.113
31.886
29.650
29.634
29.609
29.568
29.429
29.322
29.223
29.092
24.867
22.648
14.084
PMBO
OH
O
14
O
22b
13C NMR CDCl3 (100MHz)
PPM
200
175
150
125
100
75
50
25
0


7.264
7.242
6.897
6.893
6.882
6.876
4.489
4.197
4.186
4.168
4.157
4.144
4.128
4.114
4.100
4.050
4.035
4.024
4.012
4.000
3.989
3.812
3.546
3.535
3.521
3.512
3.480
3.465
3.457
3.441
3.261
3.243
3.226
3.210
2.522
2.511
2.340
2.321
2.302
2.221
2.202
2.183
2.163
1.491
1.482
1.465
1.275
1.256
1.174
1.155
1.136
PMBO
OH
O
H
N
10
O
O
22c
1H NMR CDCl3 (400MHz)
5.62
2.00
2.09
3.94
0.84
3.55
0.98
0.95
2.41
0.59
2.67
2.66
3.35
21.60
PPM
8
6
4
2
0

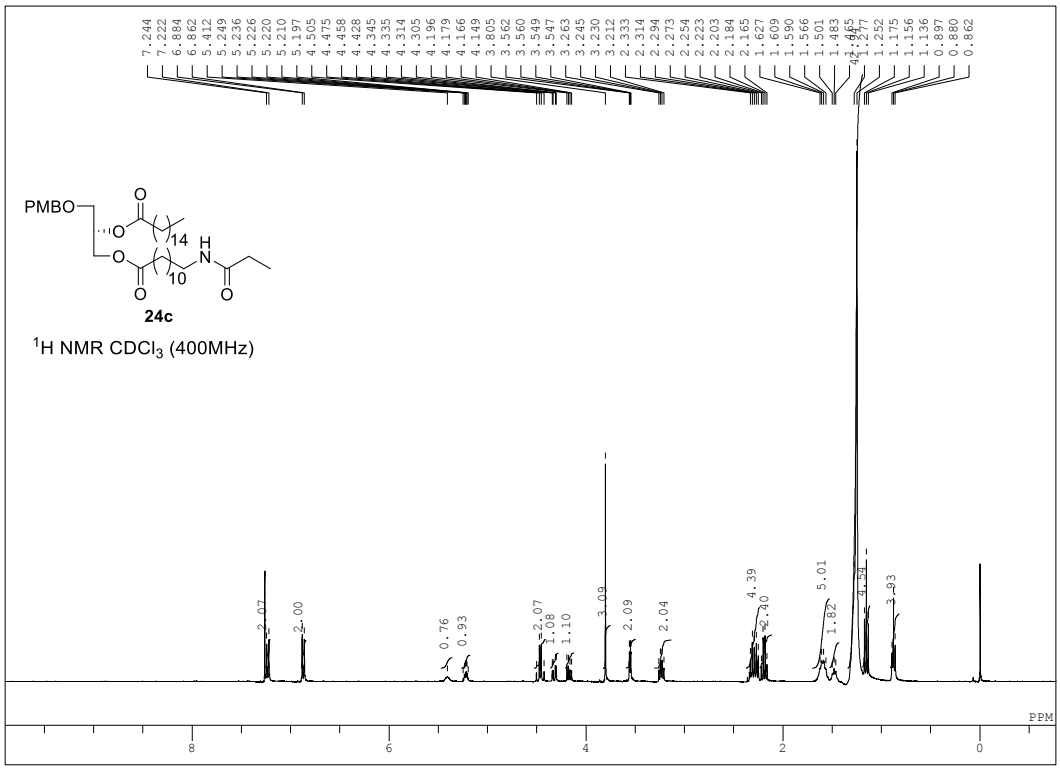

173.767
159.108
129.637
129.208
129.113
113.624
72.918
70.467
68.550
65.259
55.064
39.327
33.938
29.503
29.418
29.275
29.256
29.179
29.084
29.008
28.884
26.719
24.678
9.828
PMBO
OH
O
10
H
N
O
O
22c
13C NMR CDCl3 (100MHz)
PPM
200
175
150
125
100
75
50
25
0


7.241
7.219
6.885
6.863
5.881
5.867
5.853
5.231
5.217
5.208
5.203
5.194
5.180
4.499
4.469
4.459
4.429
4.398
4.389
4.368
4.358
4.170
4.156
4.140
4.125
3.800
3.572
3.558
3.348
3.331
3.314
3.296
3.280
3.260
3.244
3.227
3.210
3.192
2.380
2.362
2.344
2.301
2.282
2.262
2.142
2.124
2.103
1.858
1.840
1.822
1.805
1.787
1.599
1.587
1.569
1.271
1.255
0.895
0.879
0.861
PMBO
O
O
2
N
H
O
9
O
O
14
24b
1H NMR CDCl3 (400MHz)
38.88
6.24
4.11
2.91
2.04
2.02
2.01
2.00
2.00
1.00
0.99
0.94
PPM
8
6
4
2
0



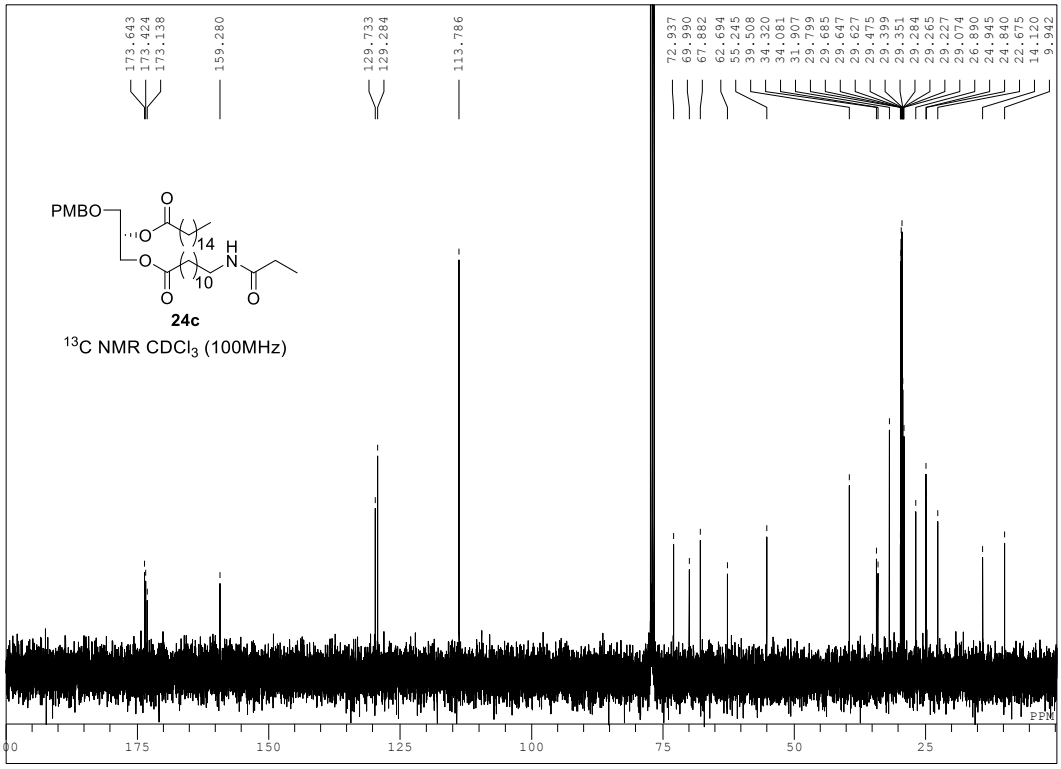
24b

^{13}C NMR $CDCl_3$ (100MHz)



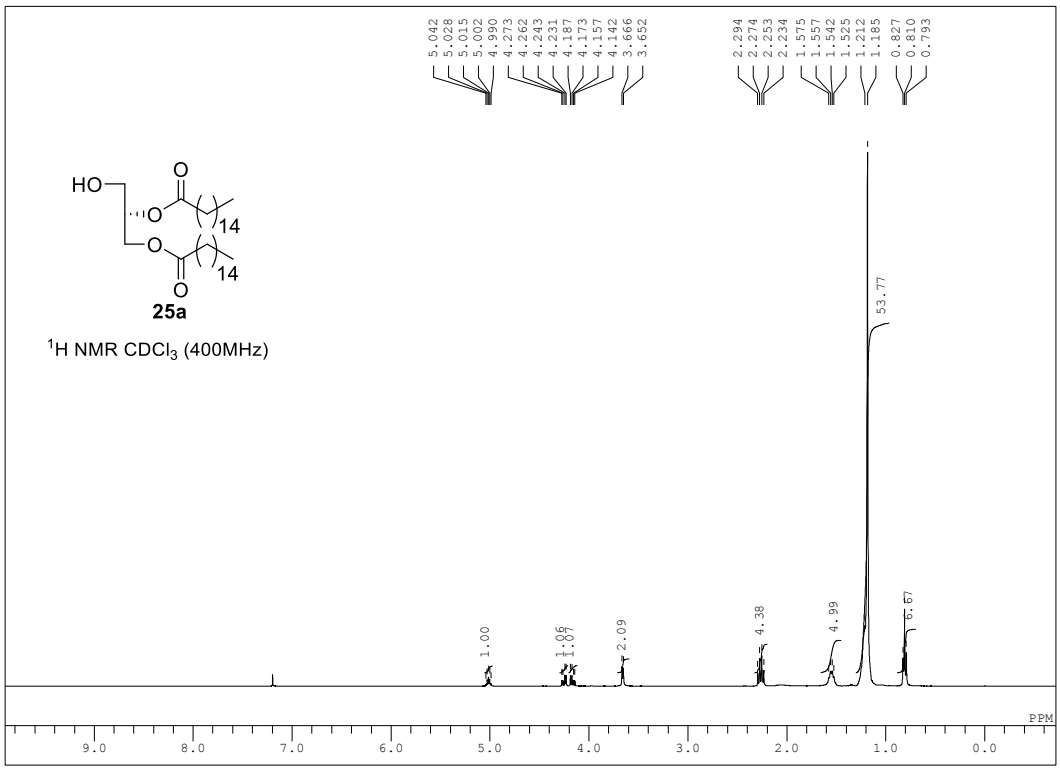
24c

^{1}H NMR $CDCl_3$ (400MHz)



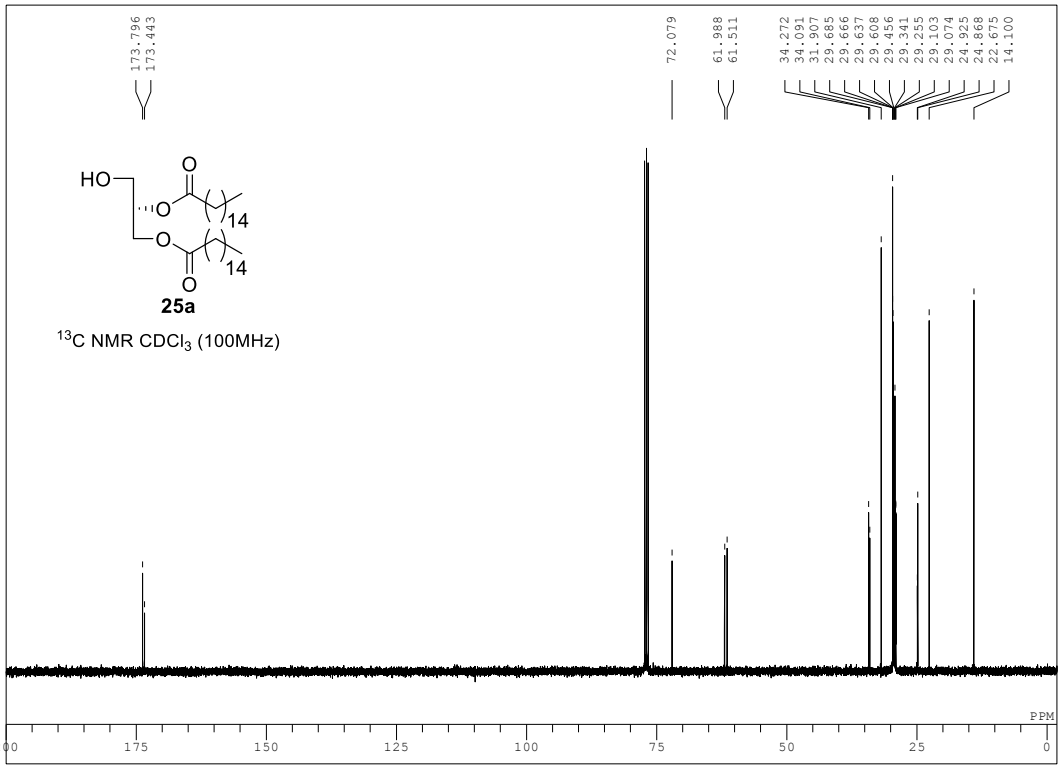
24c

^{13}C NMR $CDCl_3$ (100MHz)



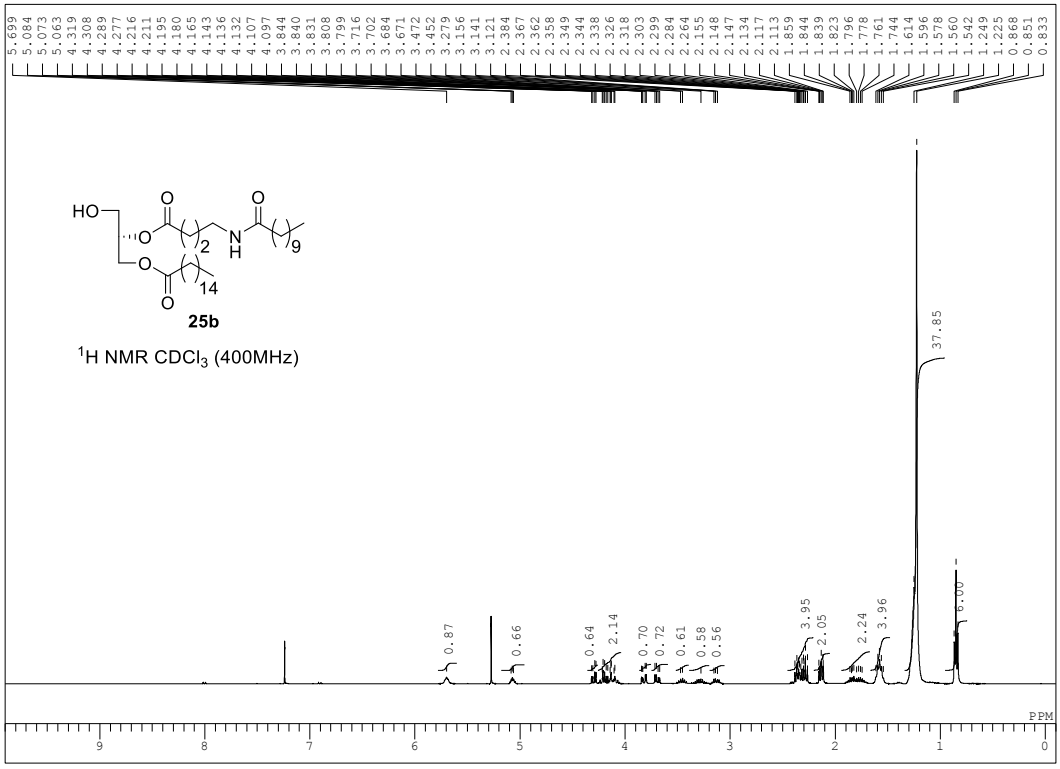
25a

^{1}H NMR $CDCl_3$ (400MHz)



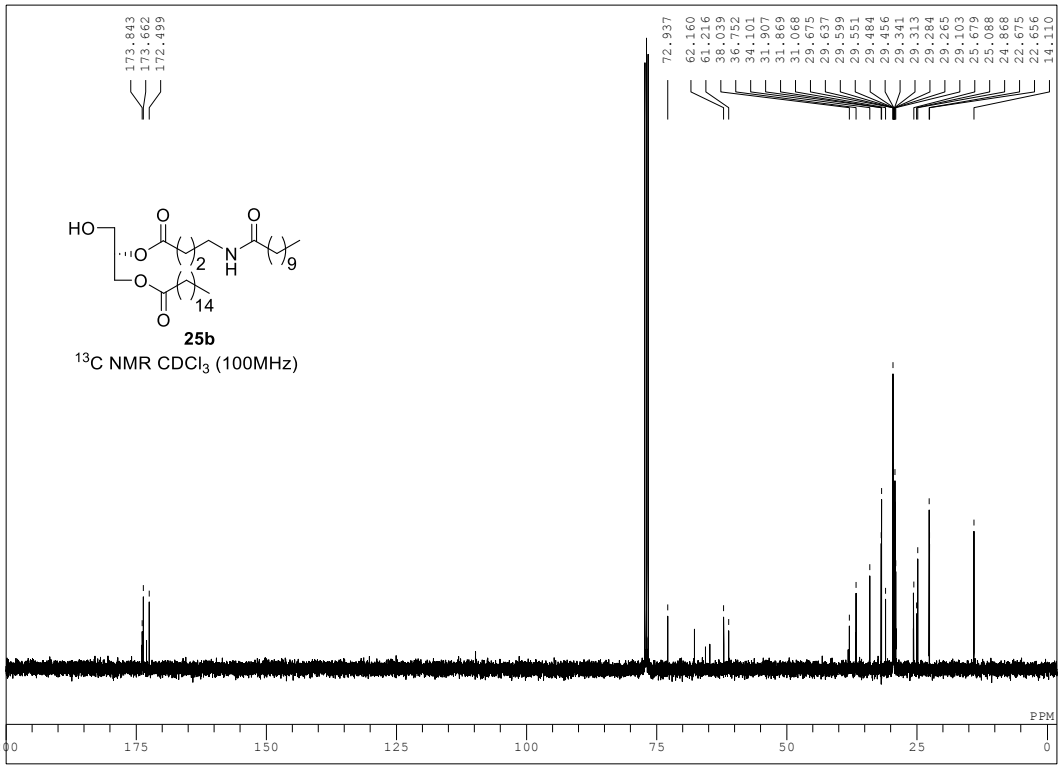
25a

^{13}C NMR $CDCl_3$ (100MHz)



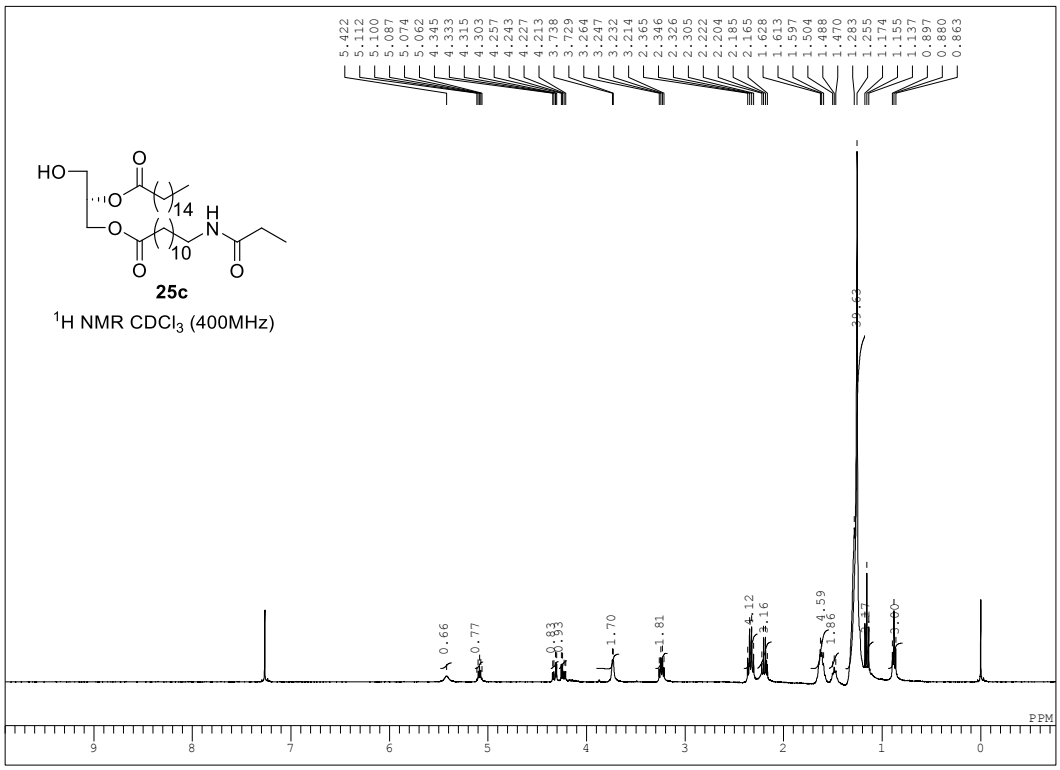
25b

^{1}H NMR $CDCl_3$ (400MHz)



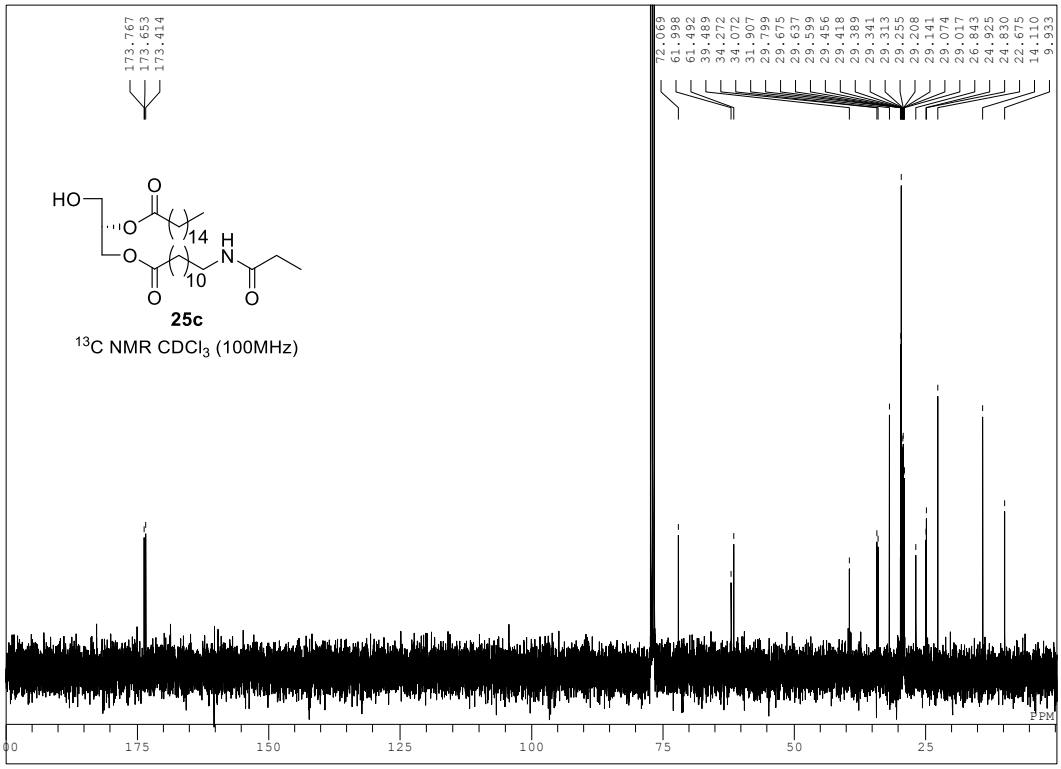
25b

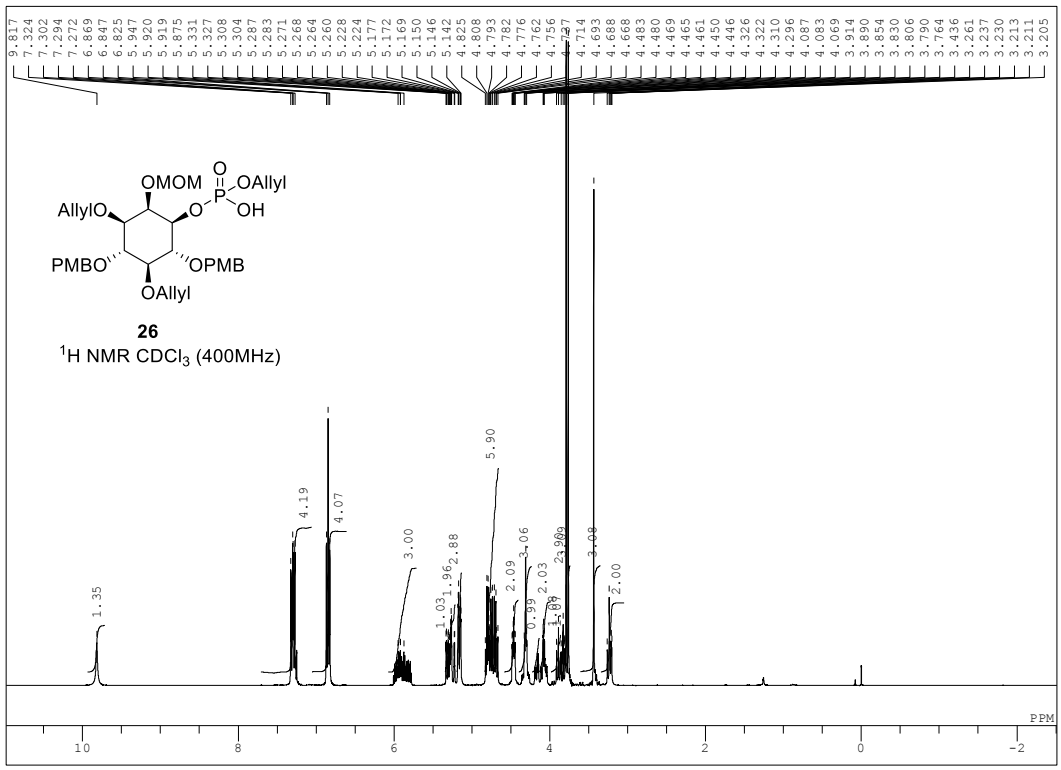
^{13}C NMR $CDCl_3$ (100MHz)

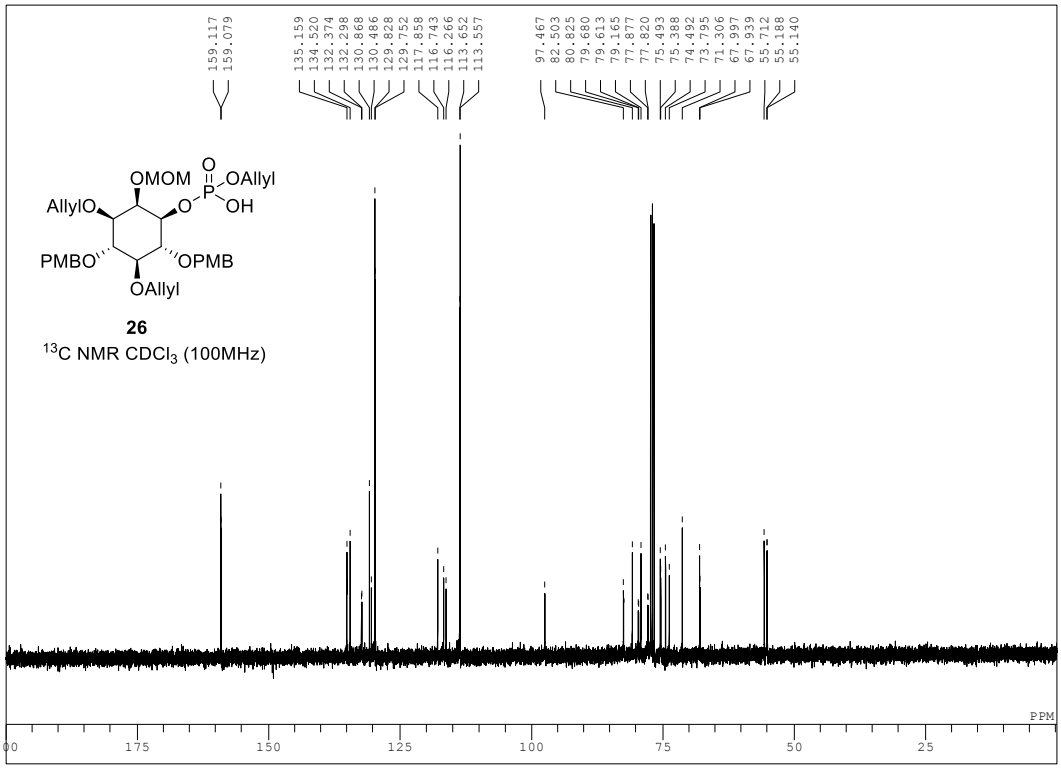


25c

^{1}H NMR $CDCl_3$ (400MHz)

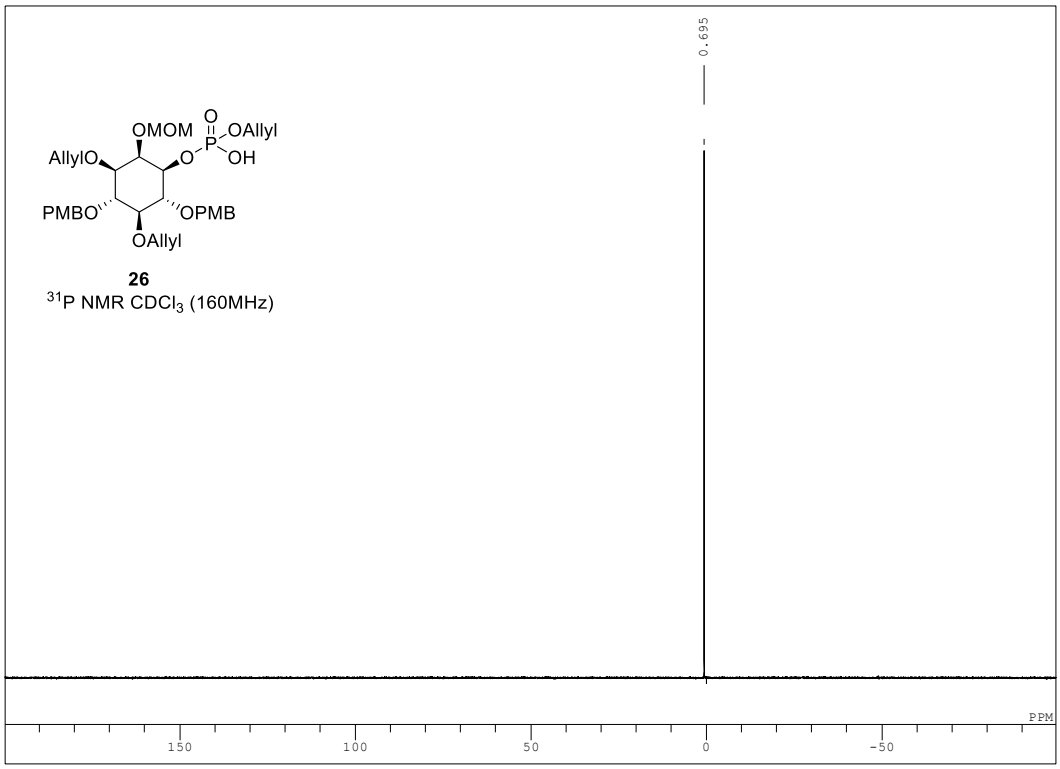

173.767
173.653
173.414
72.069
61.998
61.492
39.489
34.272
34.072
31.907
29.799
29.675
29.637
29.599
29.456
29.418
29.389
29.341
29.313
29.255
29.208
29.141
29.074
29.017
26.843
24.925
24.830
22.675
14.110
9.933
HO
O
O
14
H
N
O
O
10
O
25c
13C NMR CDCl3 (100MHz)
PPM
200
175
150
125
100
75
50
25


9.817
7.324
7.302
7.294
7.272
6.869
6.847
6.825
5.947
5.920
5.919
5.875
5.331
5.327
5.308
5.304
5.287
5.283
5.271
5.268
5.264
5.260
5.228
5.224
5.177
5.172
5.169
5.150
5.146
5.142
4.825
4.808
4.793
4.782
4.776
4.762
4.756
4.747
4.714
4.693
4.688
4.668
4.483
4.480
4.469
4.465
4.461
4.450
4.446
4.326
4.322
4.310
4.296
4.087
4.083
4.069
3.914
3.890
3.854
3.830
3.806
3.790
3.764
3.436
3.261
3.237
3.230
3.213
3.211
3.205
OMOM
O
P
OAllyl
AllylO
O
OH
PMBO
OPMB
OAllyl
26
1H NMR CDCl3 (400MHz)
1.35
4.19
4.07
3.00
1.03
1.96
2.88
5.90
2.09
3.06
0.99
2.03
1.89
3.08
2.00
PPM
10
8
6
4
2
0
-2



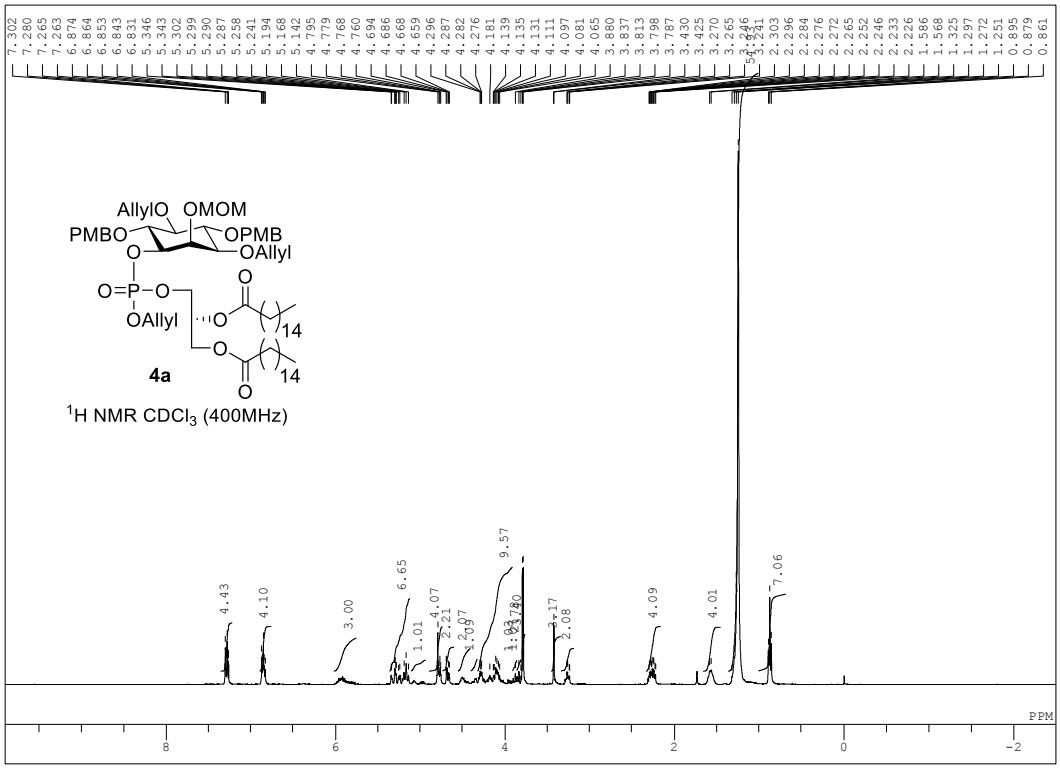
26

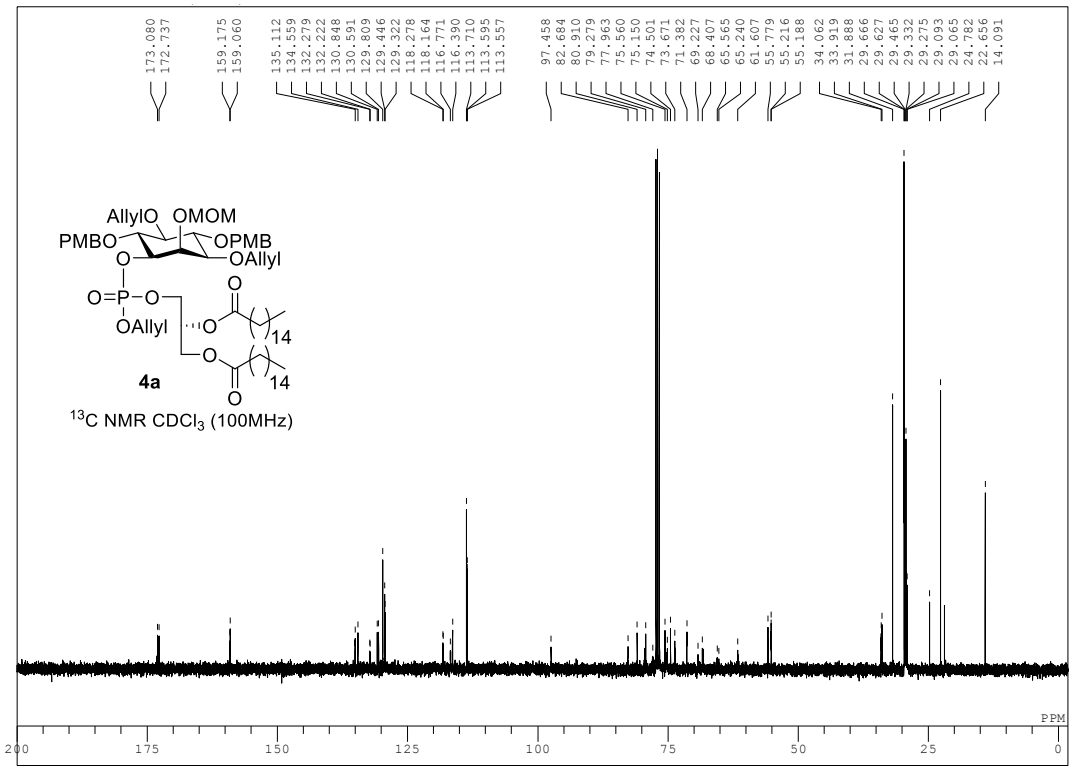
^{13}C NMR $CDCl_3$ (100MHz)

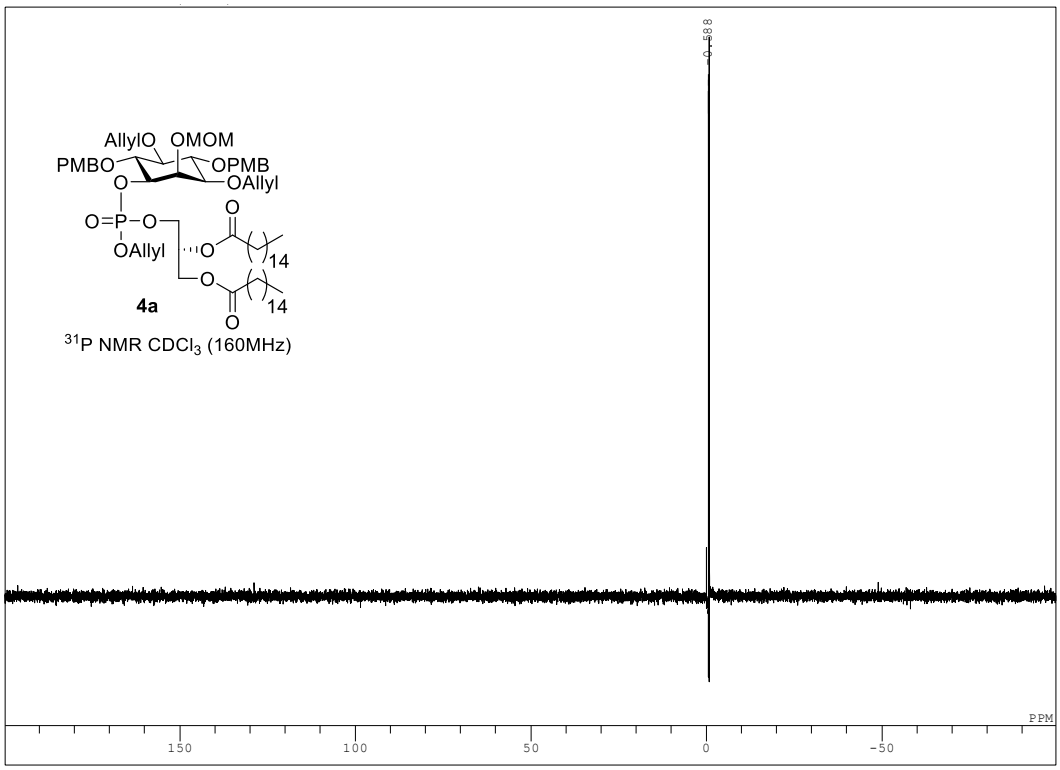


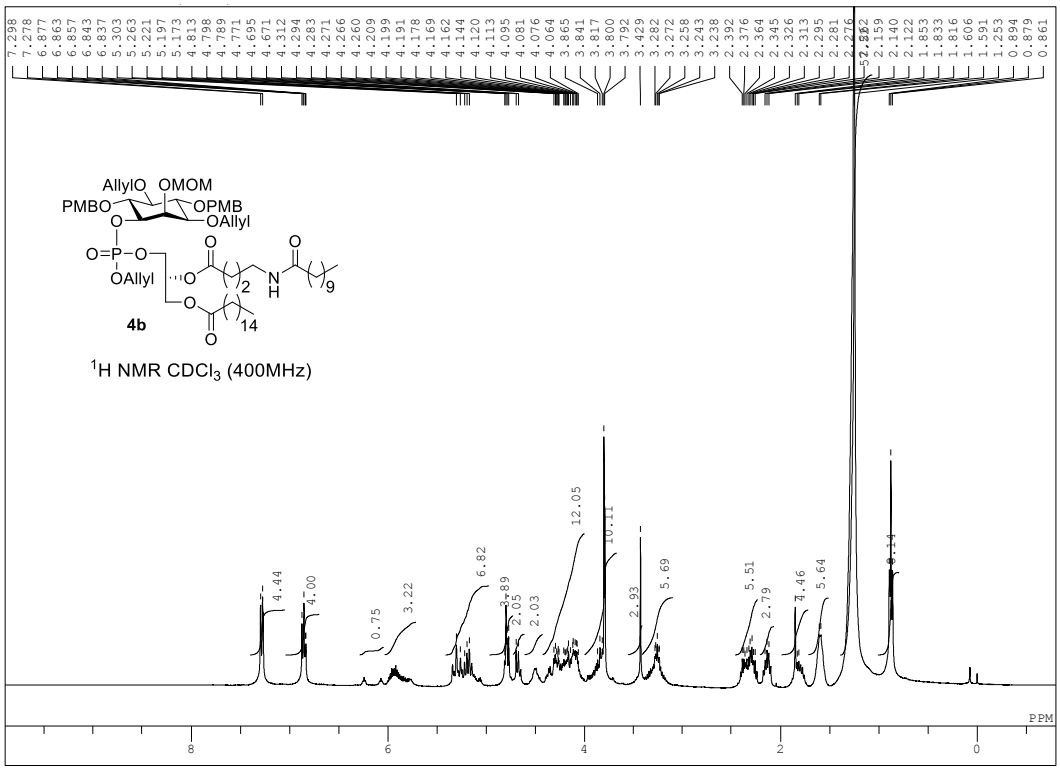
26

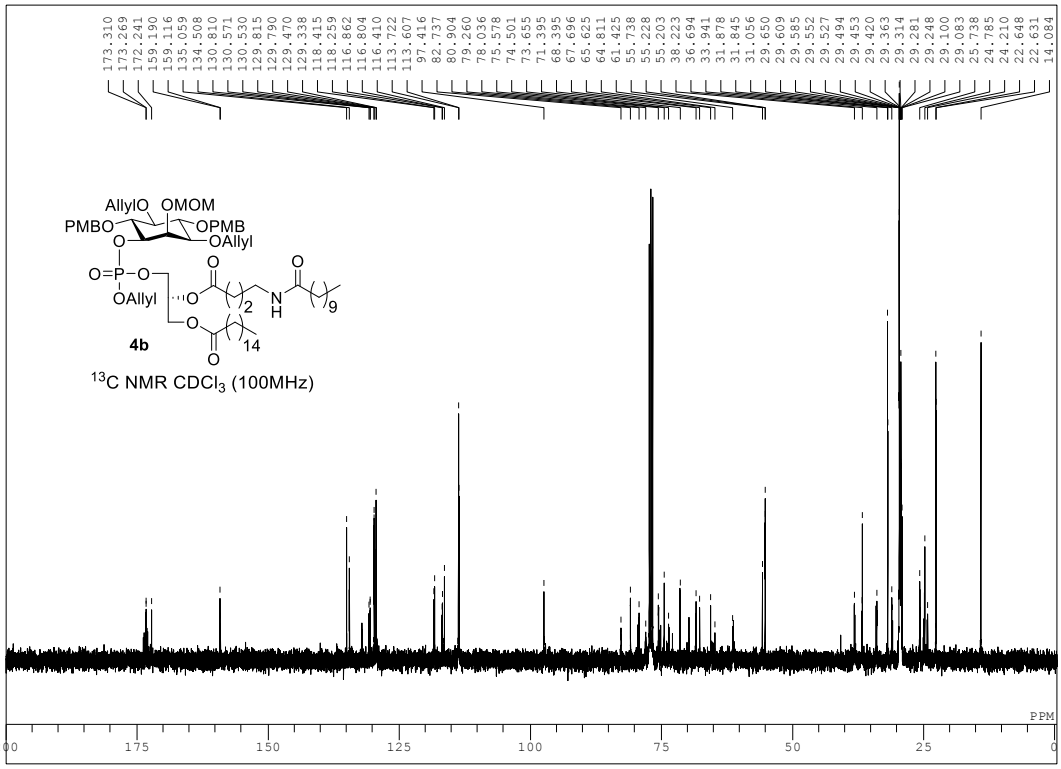
^{31}P NMR $CDCl_3$ (160MHz)

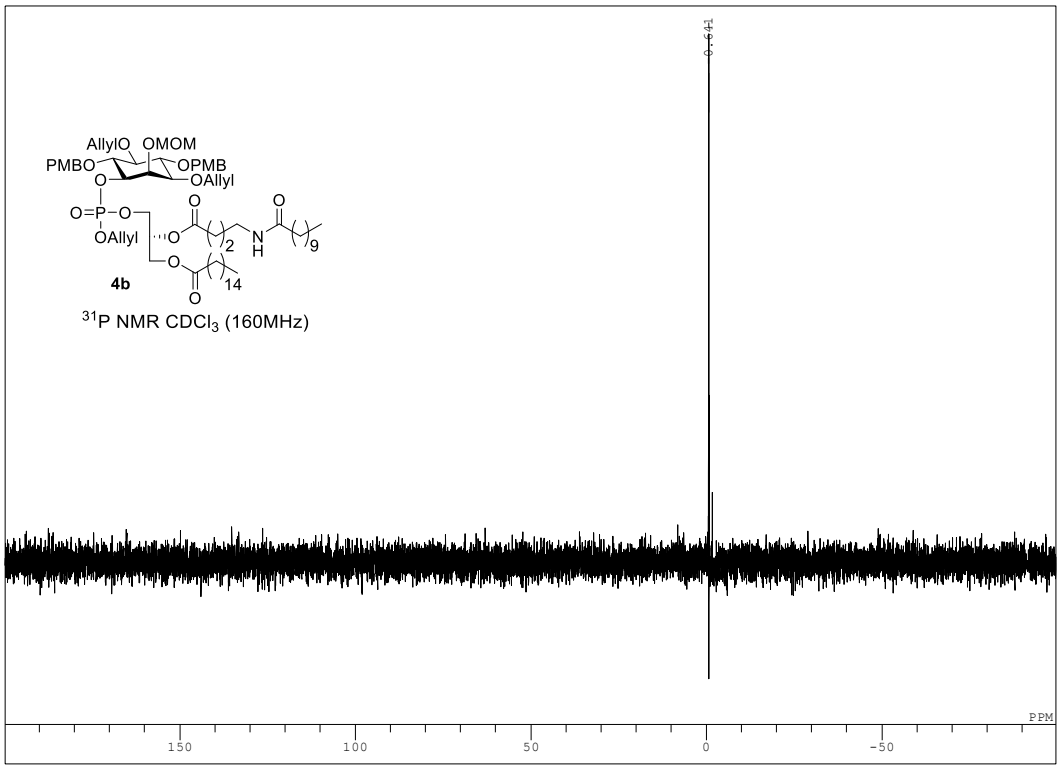

AllylO OMOM
PMBO OPMB
OAllyl
O=P–O
OAllyl
14
14
4a
^{1}H NMR CDCl$_3$ (400MHz)
PPM

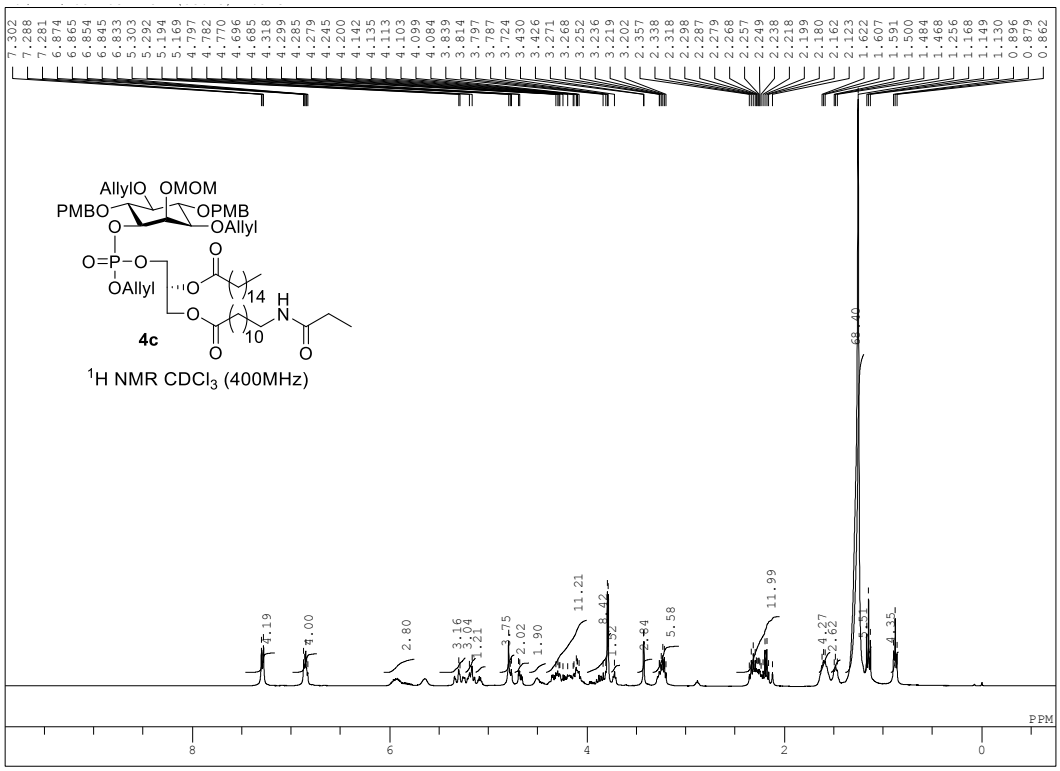

AllylO OMOM
PMBO OPMB
OAllyl
O=P–O
OAllyl
14
14
4a
^{13}C NMR CDCl$_3$ (100MHz)
PPM

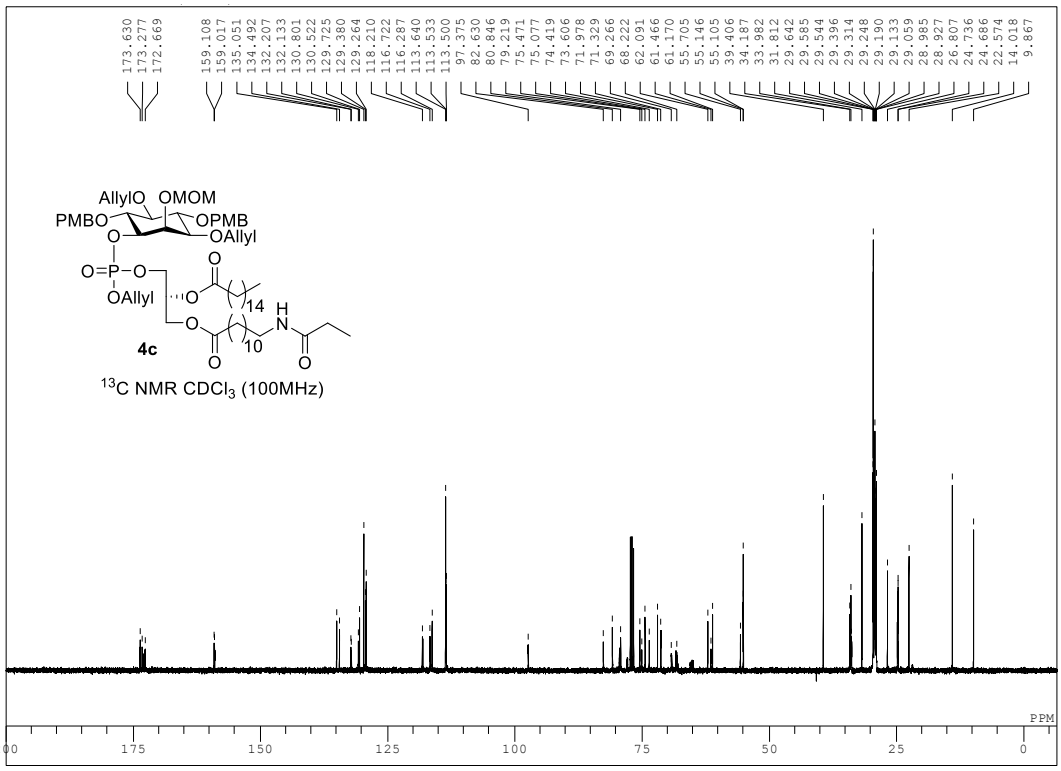

AllylO OMOM
PMBO OPMB
OAllyl
O=P-O
OAllyl
14
14
4a
31P NMR CDCl3 (160MHz)
-0.888
PPM
150
100
50
0
-50

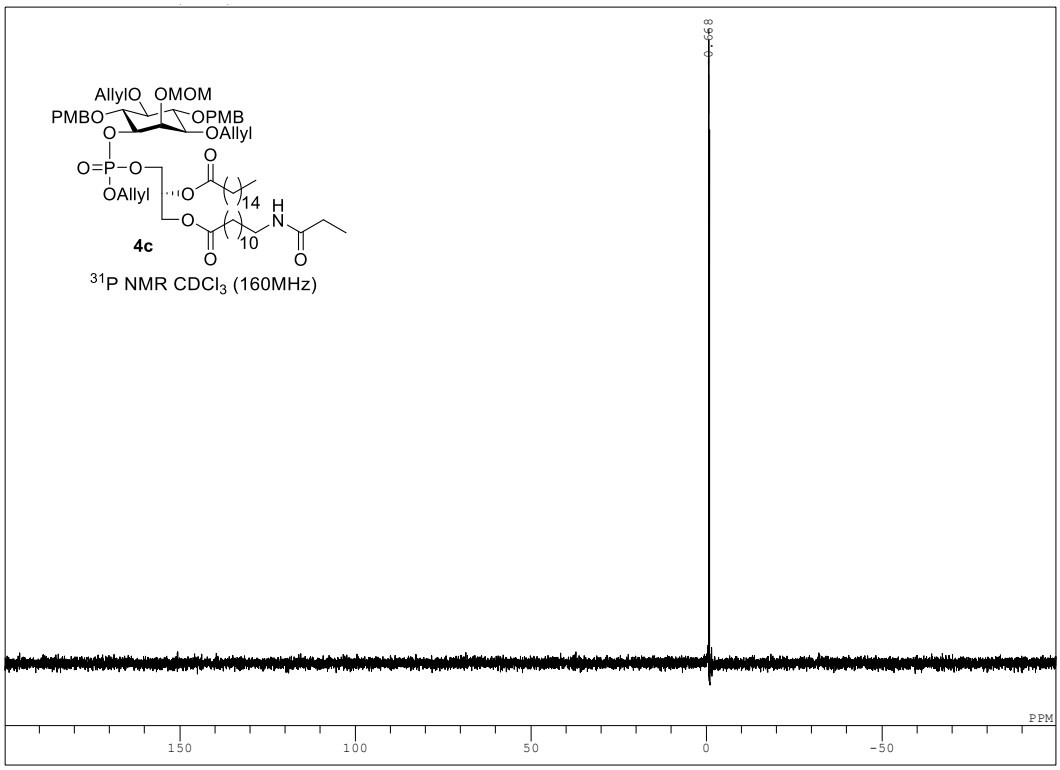

AllylO OMOM
PMBO OPMB
OAllyl
O=P-O
OAllyl
2
N
H
9
14
4b
1H NMR CDCl3 (400MHz)
4.44
4.00
0.75
3.22
6.82
3.89
2.05
2.03
12.05
10.11
2.93
5.69
5.51
2.79
7.46
5.64
8.14
PPM
8
6
4
2
0


173.310
173.269
172.241
159.190
159.116
135.059
134.508
130.810
130.571
130.530
129.815
129.790
129.470
129.338
118.415
118.259
116.862
116.804
116.410
113.722
113.607
97.416
82.737
80.904
79.260
78.036
75.578
74.501
73.655
71.395
68.395
67.696
65.625
64.811
61.425
55.738
55.228
55.203
38.223
36.694
33.941
31.878
31.845
31.056
29.650
29.609
29.585
29.552
29.527
29.494
29.453
29.420
29.363
29.314
29.281
29.248
29.100
29.083
25.738
24.785
24.210
22.648
22.631
14.084
AllylO
OMOM
PMBO
OPMB
OAllyl
O=P–O
OAllyl
4b
^{13}C NMR CDCl$_3$ (100MHz)
PPM
200
175
150
125
100
75
50
25
0

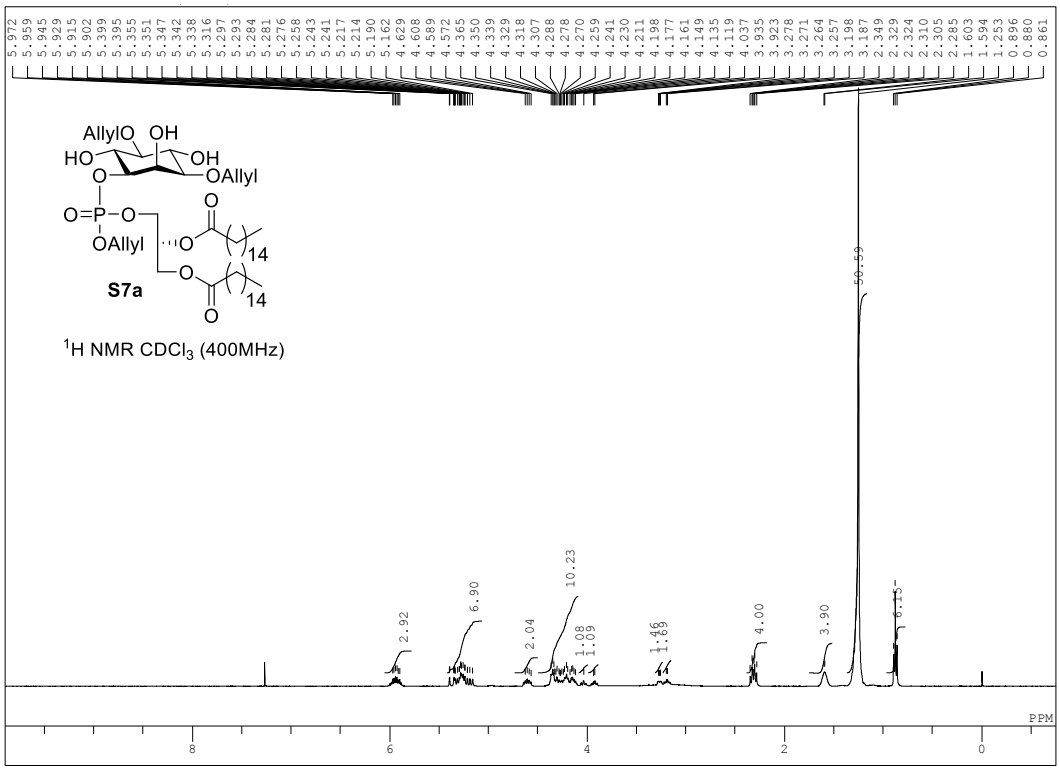

0.641
AllylO
OMOM
PMBO
OPMB
OAllyl
O=P–O
OAllyl
4b
^{31}P NMR CDCl$_3$ (160MHz)
PPM
150
100
50
0
-50


AllylO OMOM
PMBO
OPMB
OAllyl
O=P–O
OAllyl
14
10
H
N
4c
^{1}H NMR CDCl$_3$ (400MHz)
PPM

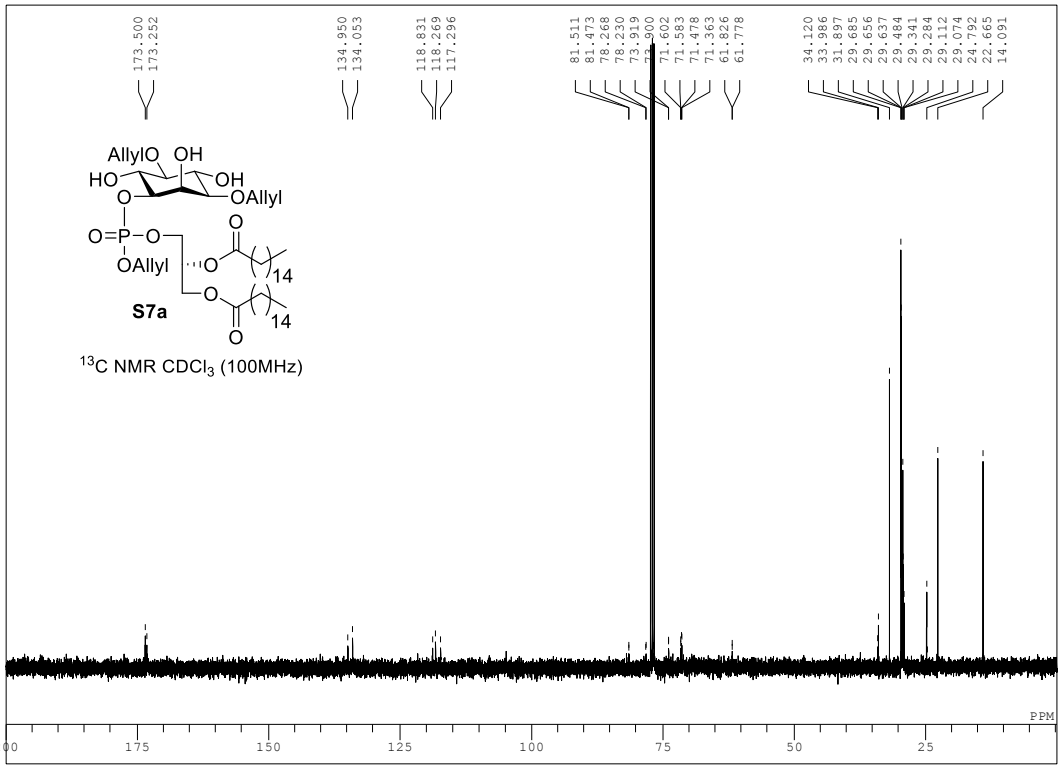

AllylO OMOM
PMBO
OPMB
OAllyl
O=P–O
OAllyl
14
10
H
N
4c
^{13}C NMR CDCl$_3$ (100MHz)
PPM



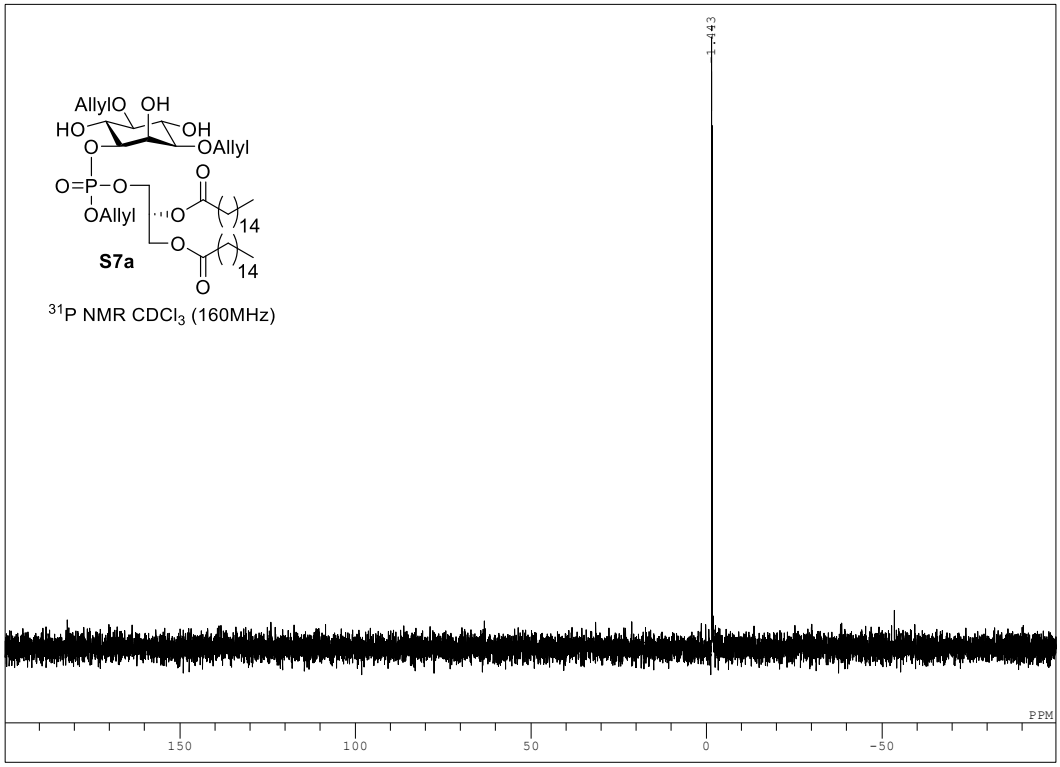
^{31}P NMR $CDCl_3$ (160MHz)



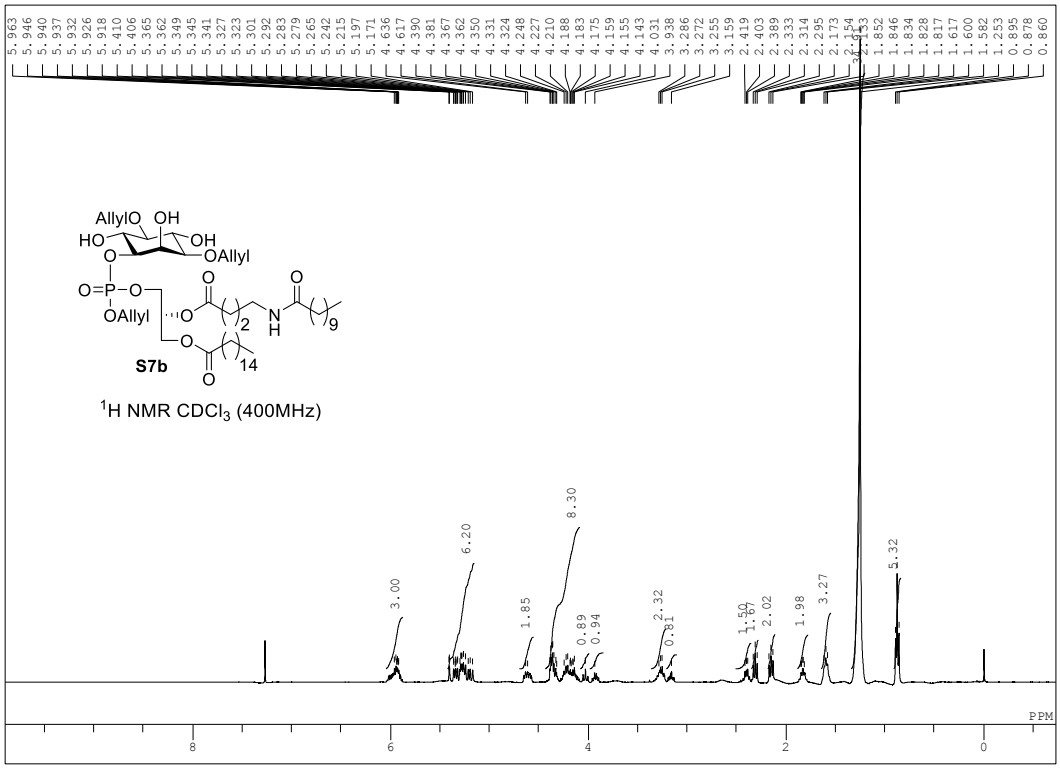
^{1}H NMR $CDCl_3$ (400MHz)

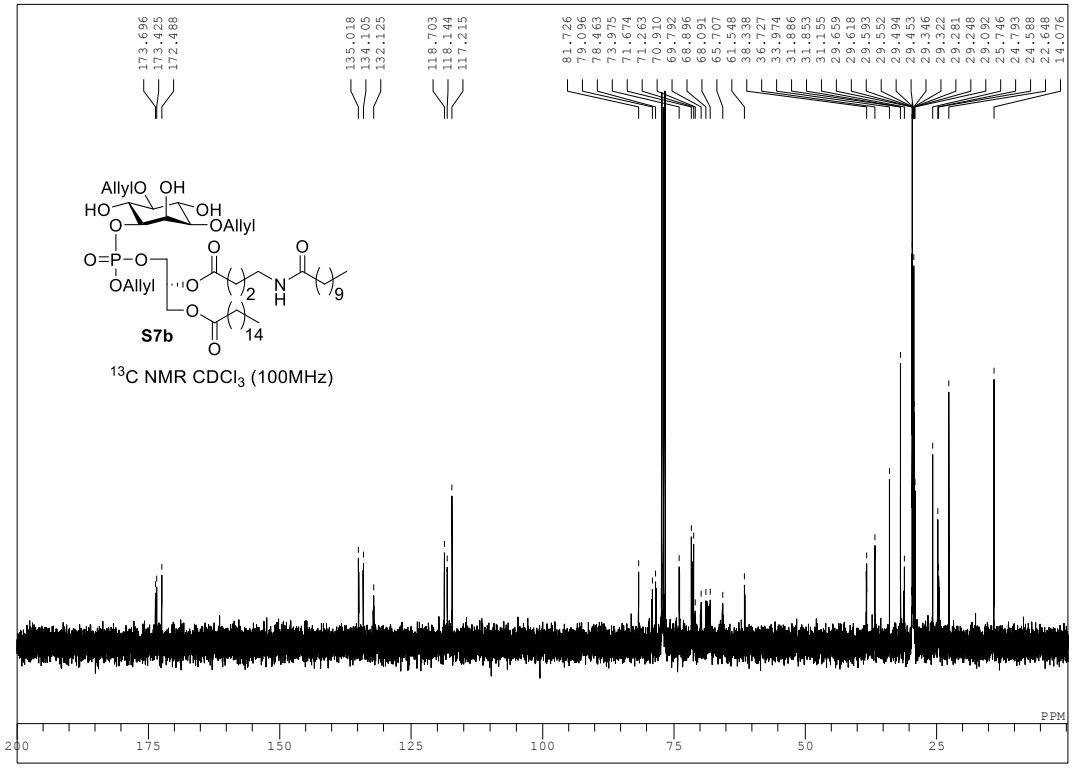


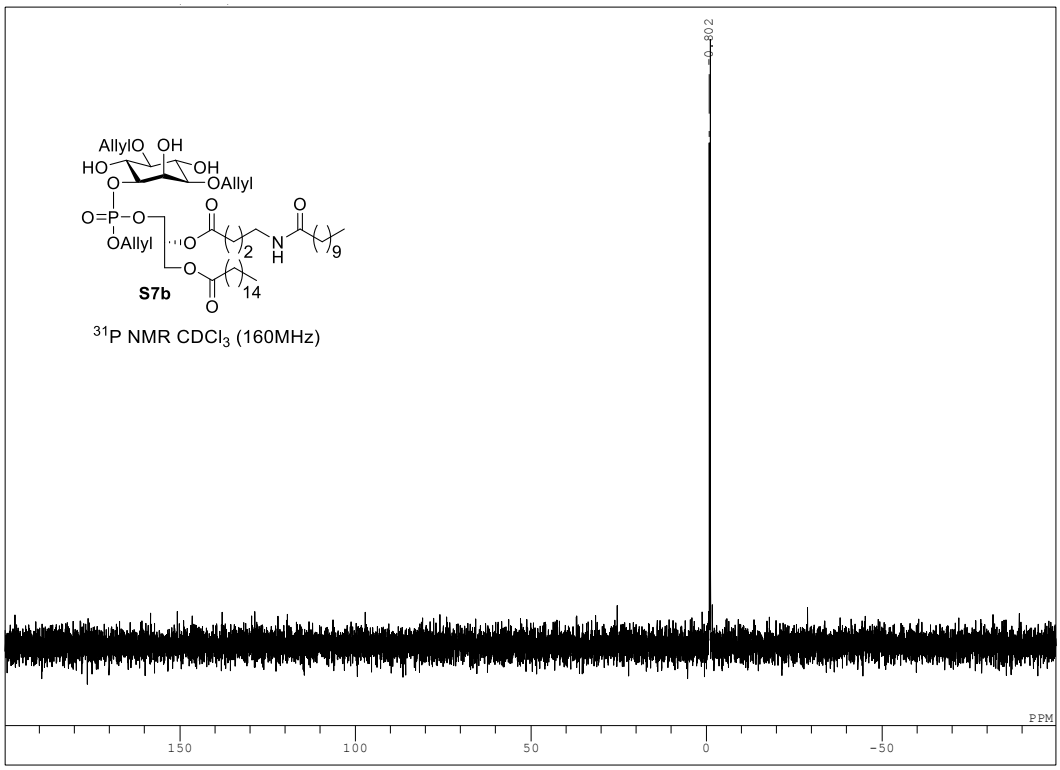
^{13}C NMR $CDCl_3$ (100MHz)

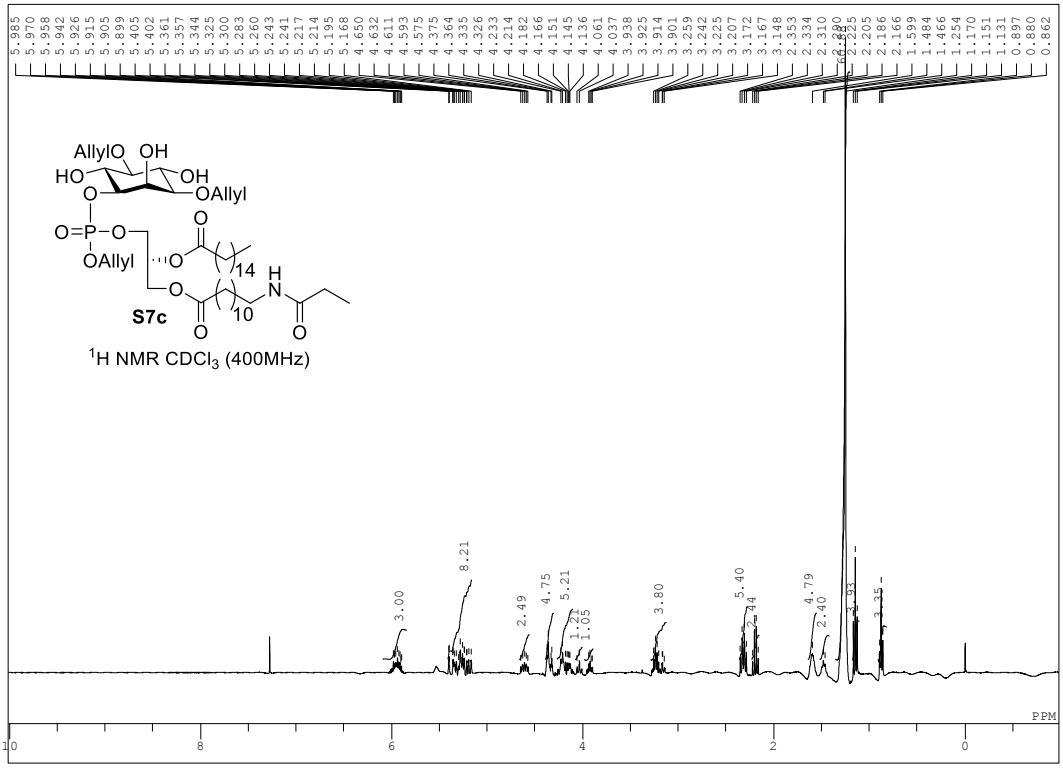


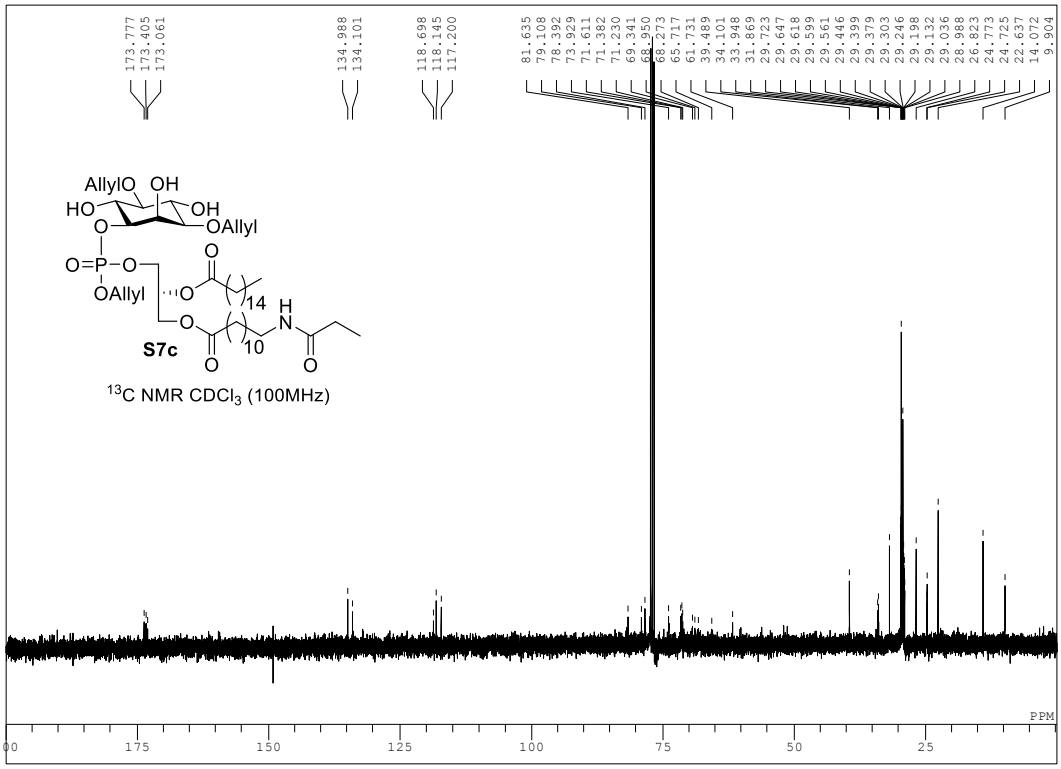
^{31}P NMR $CDCl_3$ (160MHz)


S7b
^{1}H NMR CDCl$_3$ (400MHz)
PPM

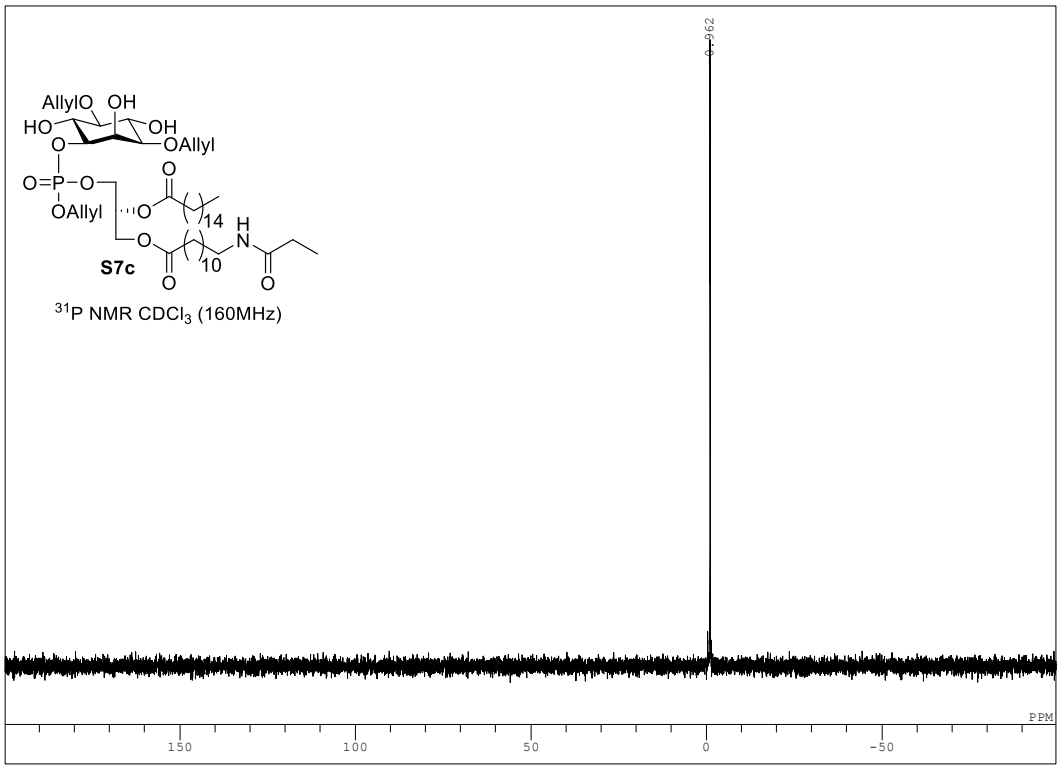

S7b
^{13}C NMR CDCl$_3$ (100MHz)
PPM


AllylO OH
HO
OH
O
OAllyl
O=P–O
OAllyl
O
O
2
N
H
O
9
O
O
14
O
S7b
31P NMR CDCl3 (160MHz)
-0.802
PPM
150
100
50
0
-50

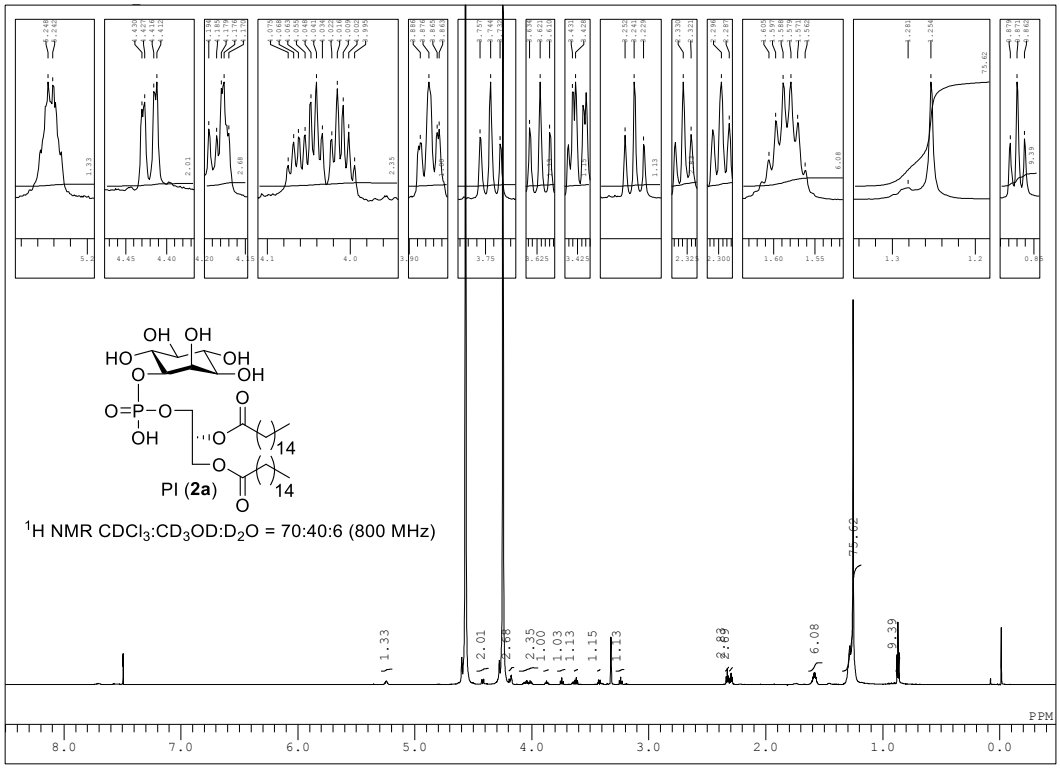

5.985
5.970
5.958
5.942
5.926
5.915
5.905
5.899
5.405
5.402
5.361
5.357
5.344
5.325
5.300
5.283
5.260
5.243
5.241
5.217
5.214
5.195
5.168
4.650
4.632
4.611
4.593
4.575
4.375
4.364
4.335
4.326
4.233
4.214
4.182
4.166
4.151
4.145
4.136
4.061
4.037
3.938
3.925
3.914
3.901
3.259
3.242
3.225
3.207
3.172
3.167
3.148
2.353
2.334
2.310
2.288
2.225
2.205
2.186
2.166
1.599
1.484
1.466
1.254
1.170
1.151
1.131
0.897
0.880
0.862
AllylO OH
HO
OH
O
OAllyl
O=P–O
OAllyl
O
O
14
H
N
O
O
10
O
S7c
1H NMR CDCl3 (400MHz)
3.00
8.21
2.49
4.75
5.21
1.22
1.05
3.80
5.40
2.44
4.79
2.40
2.93
3.35
PPM
10
8
6
4
2
0

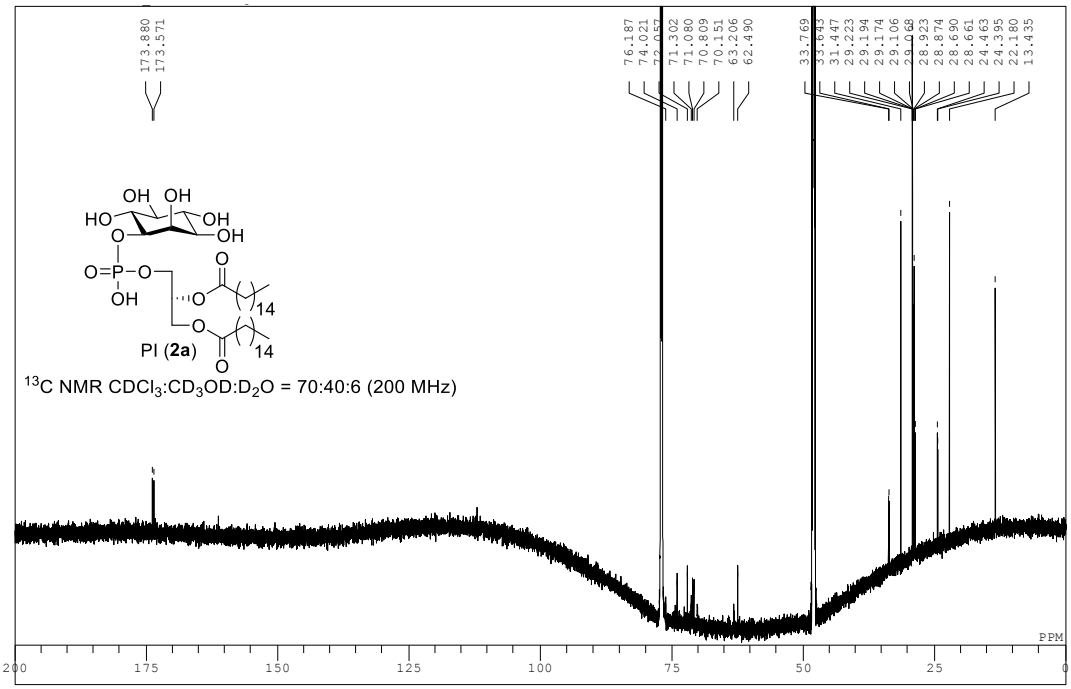


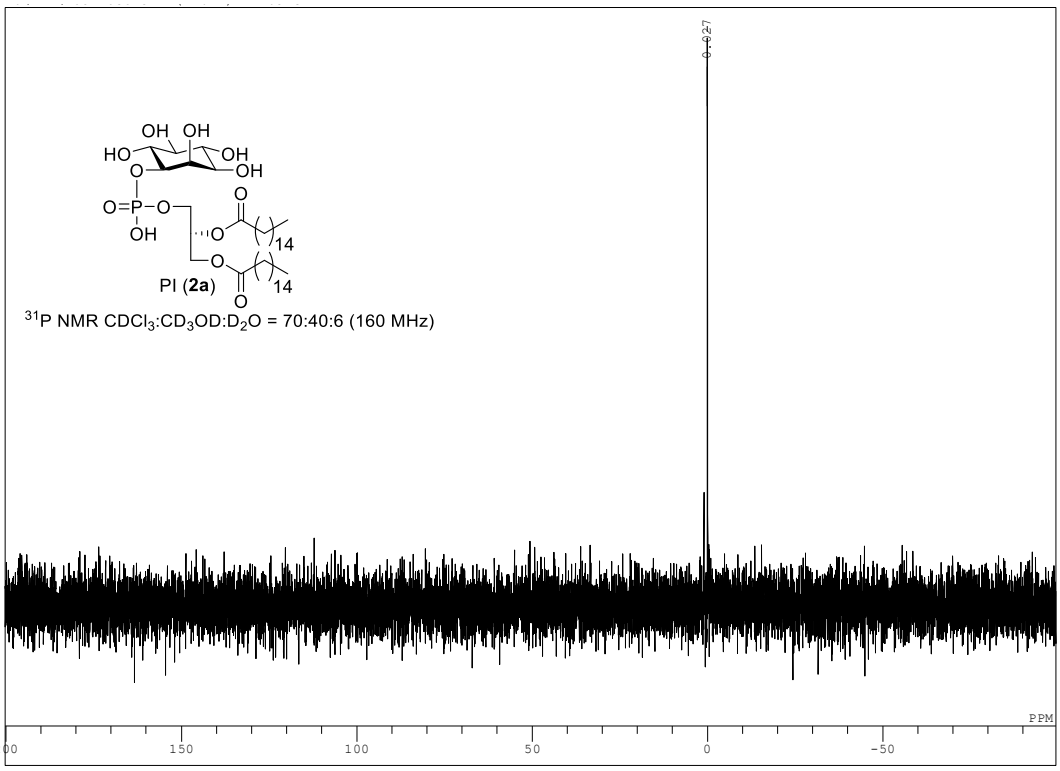
^{13}C NMR $CDCl_3$ (100MHz)



^{31}P NMR $CDCl_3$ (160MHz)

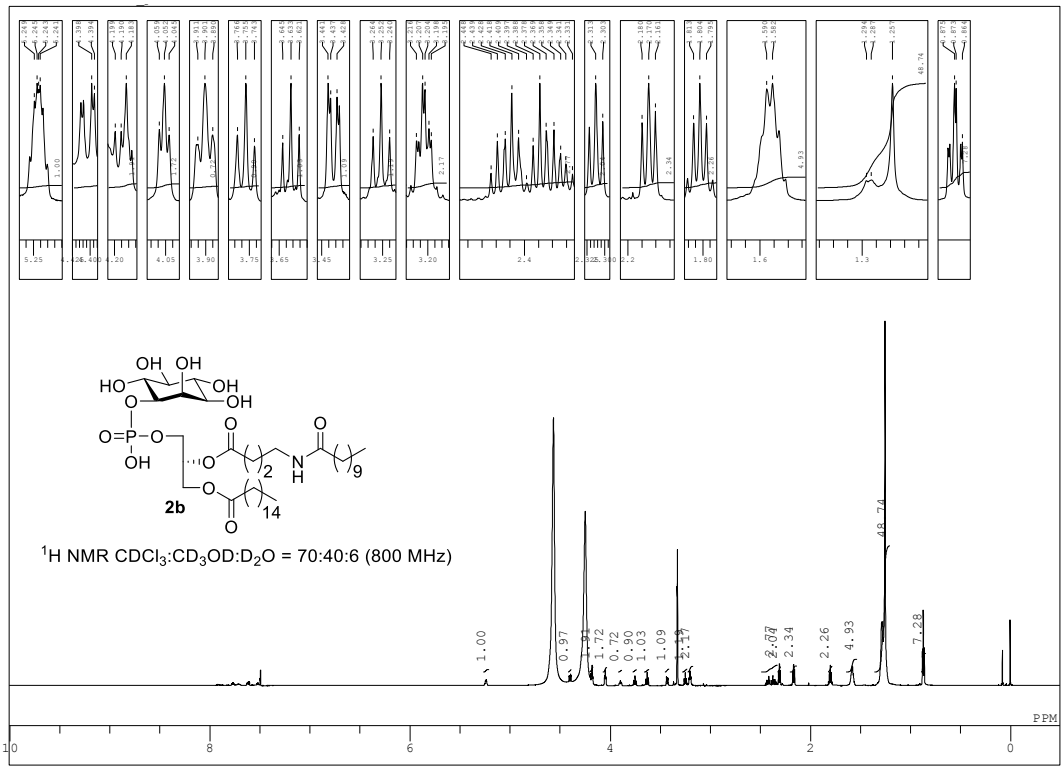

PI (2a)
1H NMR CDCl3:CD3OD:D2O = 70:40:6 (800 MHz)
1.33
2.01
2.68
2.35
1.00
1.03
1.13
1.15
1.13
2.83
2.89
6.08
75.62
9.39
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


PI (2a)
13C NMR CDCl3:CD3OD:D2O = 70:40:6 (200 MHz)
173.880
173.571
76.187
74.021
72.057
71.302
71.080
70.809
70.151
63.206
62.490
33.769
33.643
31.447
29.223
29.194
29.174
29.106
29.068
28.923
28.874
28.690
28.661
24.463
24.395
22.180
13.435
PPM
200
175
150
125
100
75
50
25
0



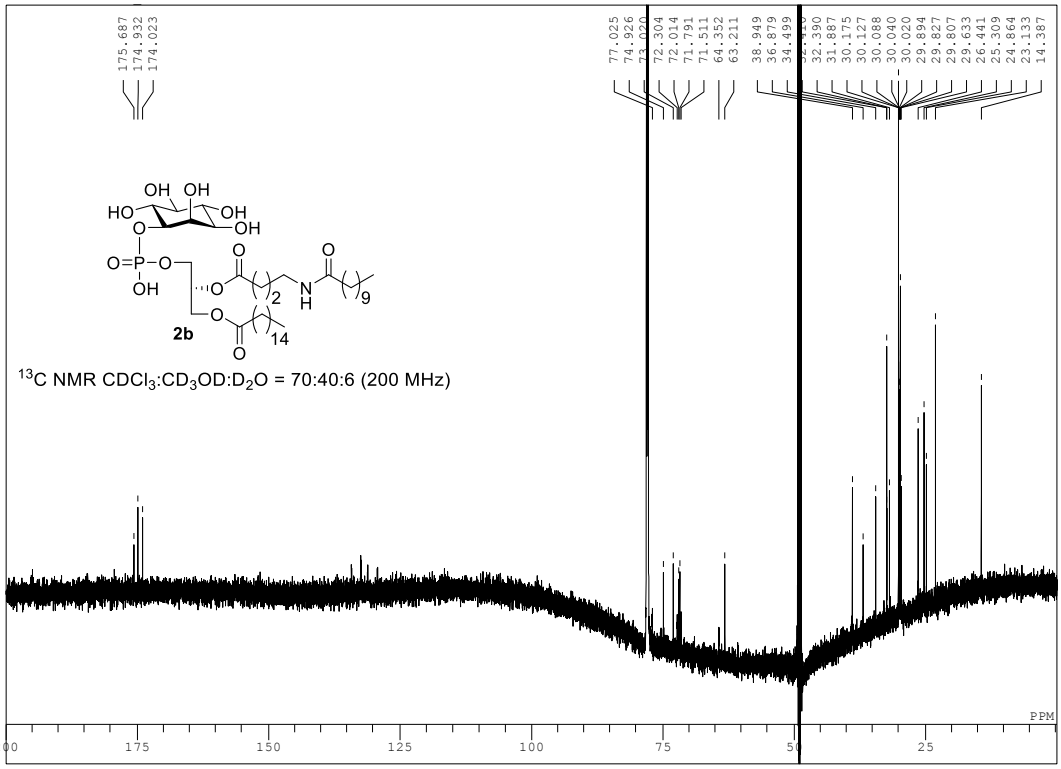
PI (**2a**)

^{31}P NMR $CDCl_3$:CD_3OD:D_2O = 70:40:6 (160 MHz)

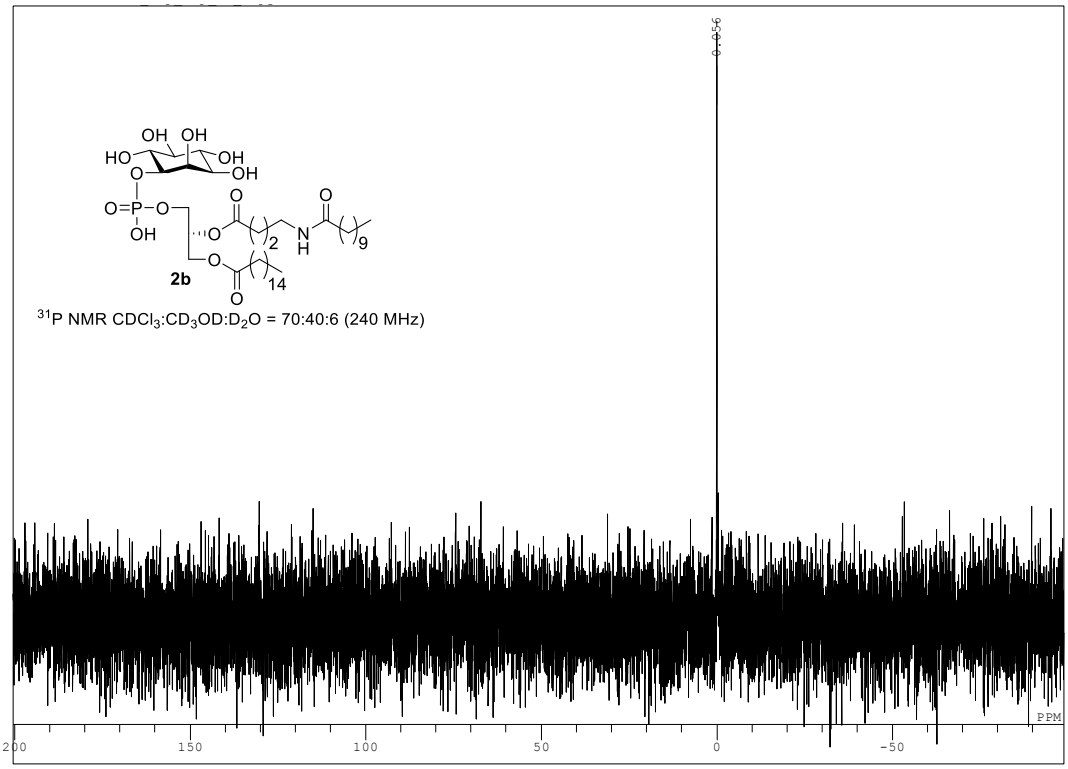


2b

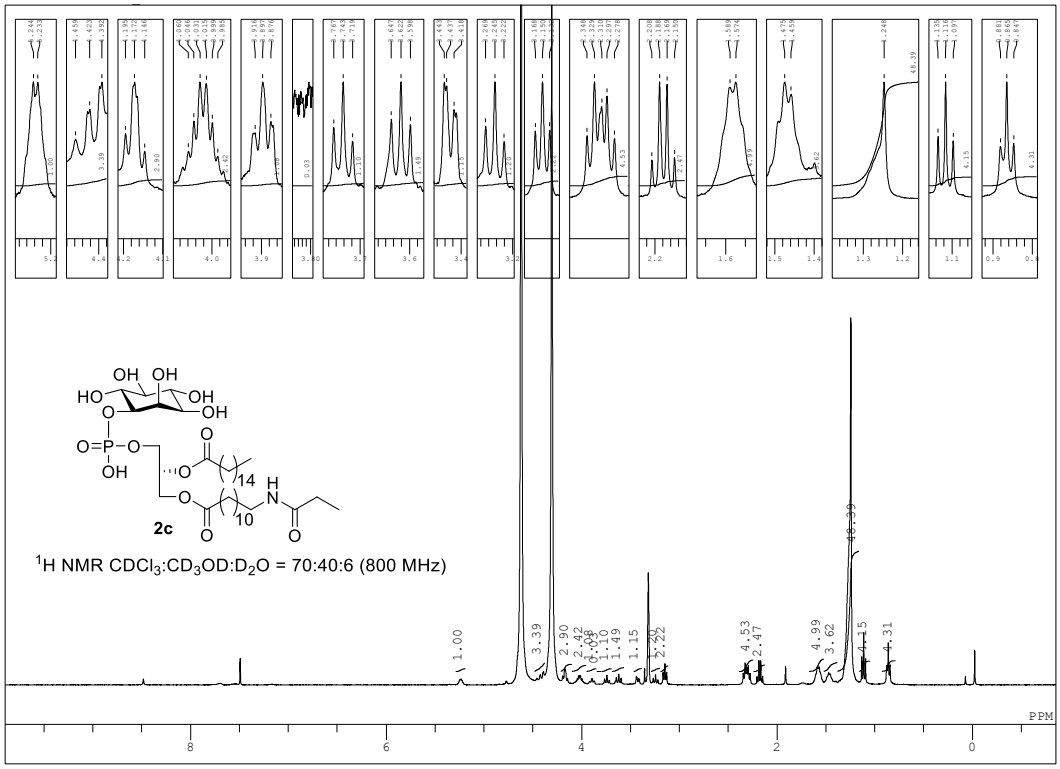
^{1}H NMR $CDCl_3$:CD_3OD:D_2O = 70:40:6 (800 MHz)



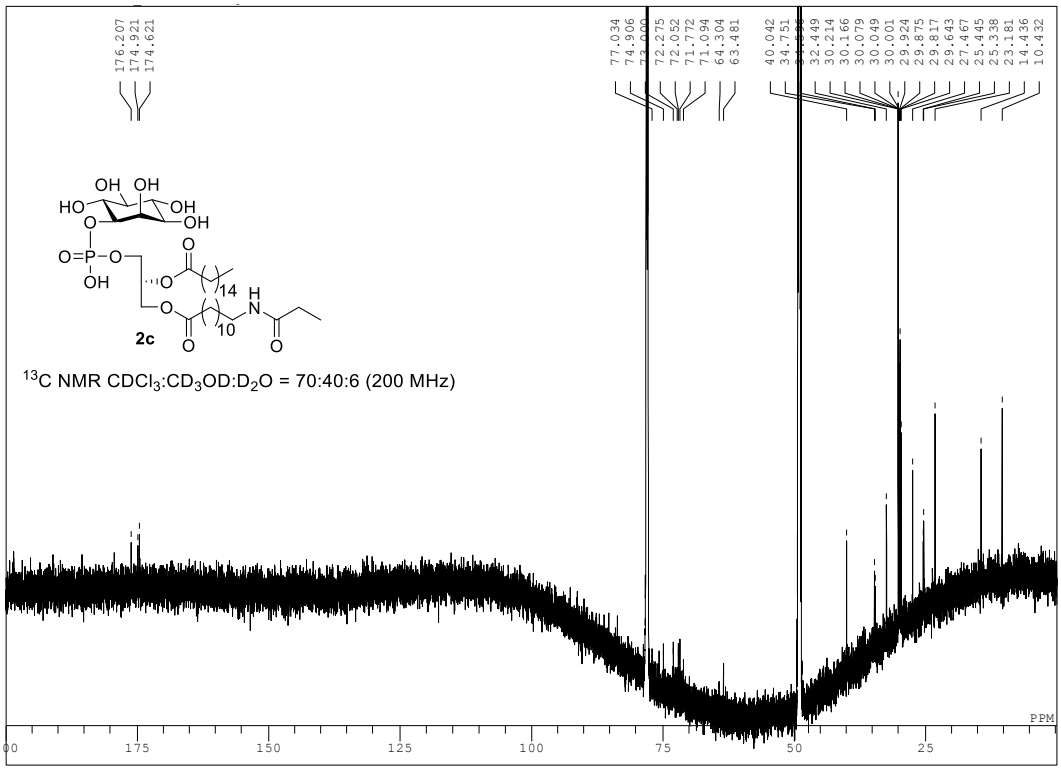
^{13}C NMR $CDCl_3$:CD_3OD:D_2O = 70:40:6 (200 MHz)



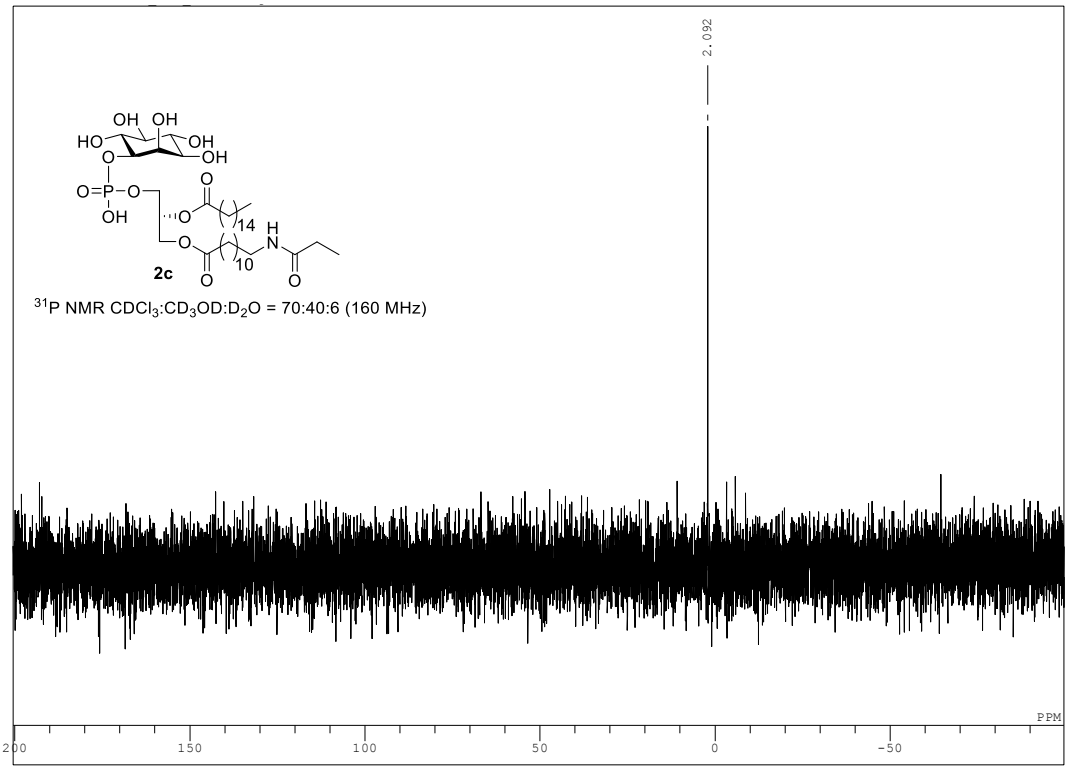
^{31}P NMR $CDCl_3$:CD_3OD:D_2O = 70:40:6 (240 MHz)



^{1}H NMR $CDCl_3$:CD_3OD:D_2O = 70:40:6 (800 MHz)



^{13}C NMR $CDCl_3$:CD_3OD:D_2O = 70:40:6 (200 MHz)



^{31}P NMR $CDCl_3$:CD_3OD:D_2O = 70:40:6 (160 MHz)

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