Supporting Information

Manuscript for: *J. Am. Chem. Soc (Communication)*
Submitted: July 24, 2006
Revised: Nov 15, 2006

Synthesis and Biological Activity of PTEN-Resistant Analogues of Phosphatidylinositol 3,4,5-trisphosphate

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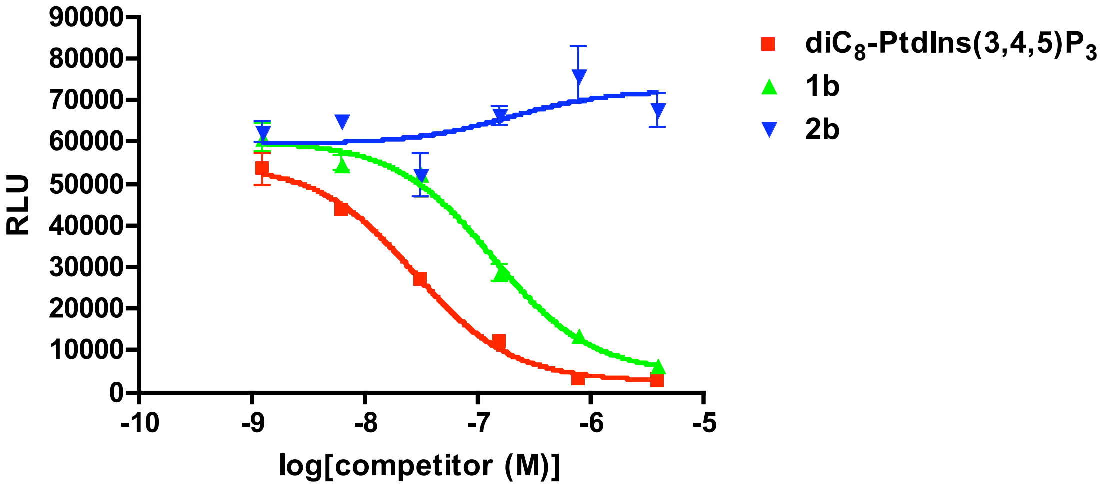
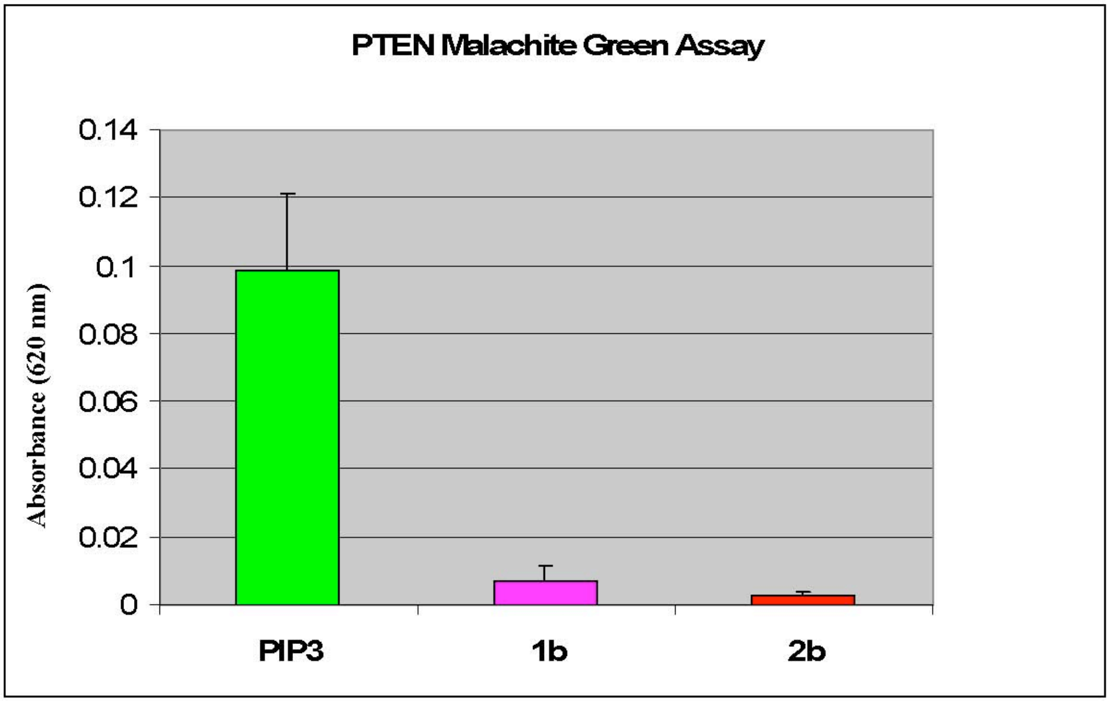
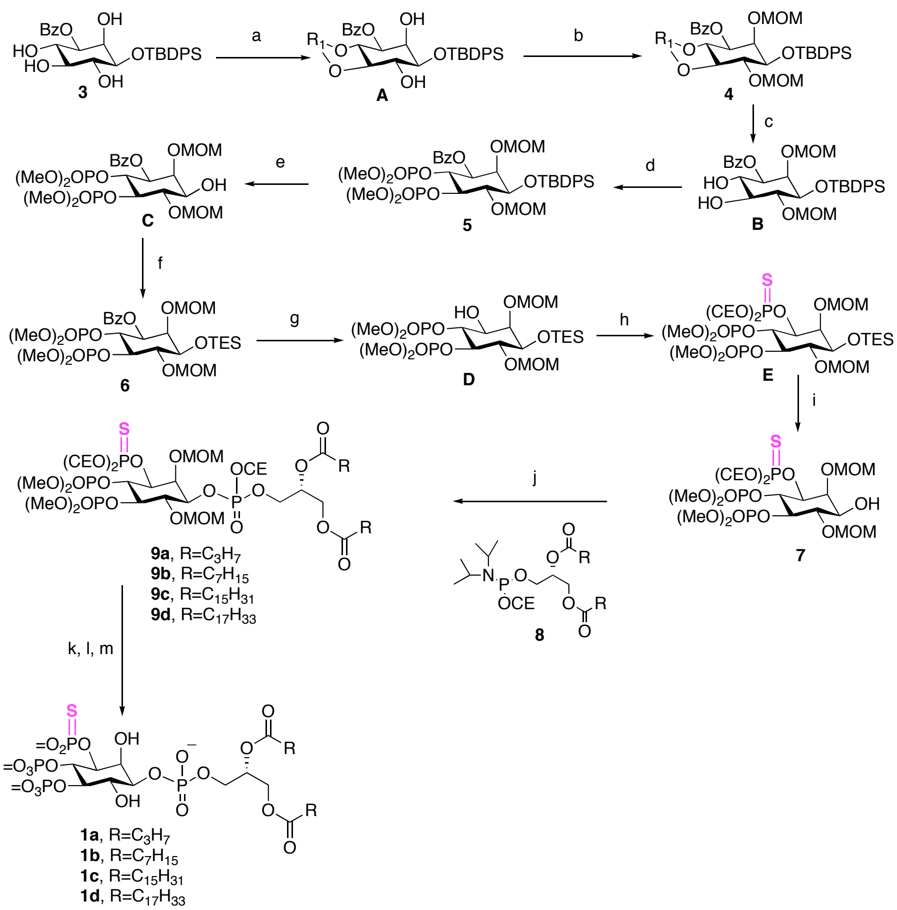


Supplementary Figure 2. Competitive displacement of biotinylated-PtdIns(3,4,5)P_3 (10 nM) from Grp1 (10 nM) binding by diC_8-PtdIns(3,4,5)P_3 and analogues **1b** and **2b.**



Supplementary Figure 3. Detection of free phosphate produced in the PTEN reactions with **diC$_8$-PI(3,4,5)P$_3$**,**1b** and **2b.**

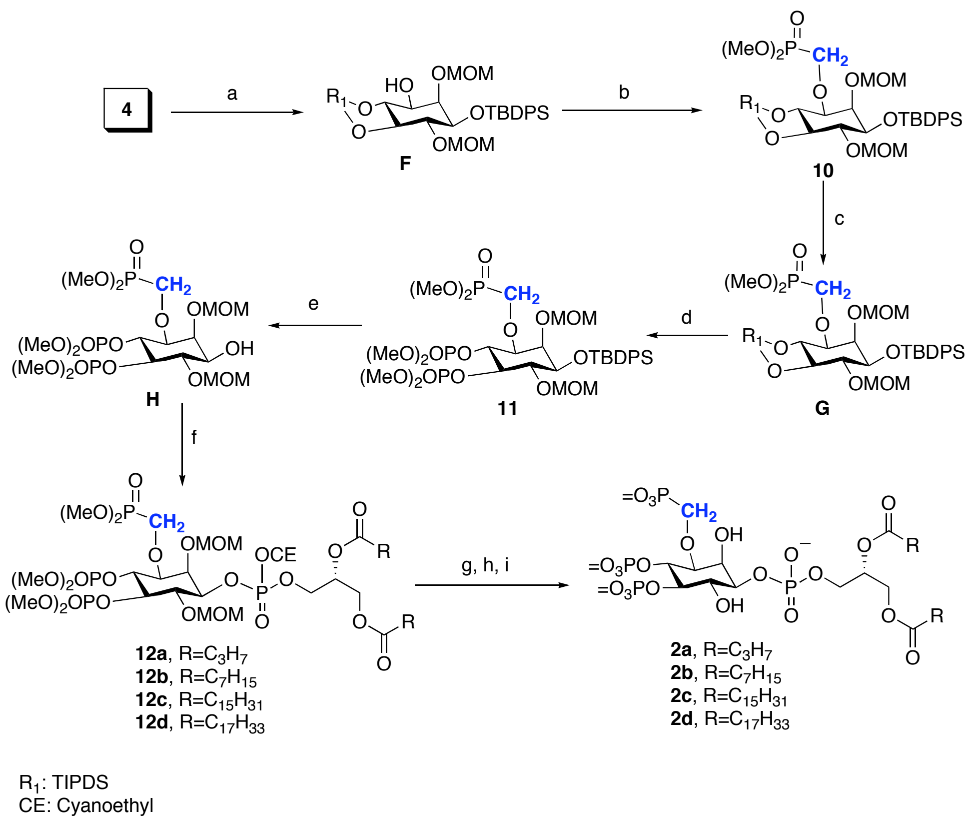
Scheme 1. Synthesis of Phosphorothioates **1**[a]



R1: TIPDS
CE: Cyanoethyl

[a] Conditions: (a) $TIPDSCl_2$, imidazole, Py, 12 h, 88%; (b) MOMCl, DIPEA, DMF, 65 ºC, 24 h, 63%; (c) TBAF, THF, 1 h, 77%; (d) *N*,*N*-dimethylphosphoramidite, 1*H*-tetrazole, 12 h; *m*-CPBA, 81%; (e) TBAF•$3H_2O$, DMF, 3 h, 91%; (f) TESCl, imidazole, CH_2Cl_2, 12 h, 88%; (g) Dibal-H, CH_2Cl_2, -78 ºC, 1.5 h, 84%; (h) Bis(2-cyanoethoxy)(diisopropylamino)phosphine, 1*H*-tetrazole, 12 h; phenylacetyl disulfide, 30 min, 72%; (i) NH_4F, MeOH, 85%; (j) 1*H*-tetrazole, CH_2Cl_2, rt, 12 h; *t*-BuOOH; (k) TEA, BSTFA, CH_3CN; (l) TMSBr/CH_2Cl_2 (2:3), rt, 40 min; (m) MeOH, 1 h.

Scheme 2. Synthesis of Methylenephosphonates **2**[a]



[a] Conditions: (a) Dibal-H, CH_2Cl_2, -78 °C, 1.5 h, 88%; (b) *n*-BuLi, HMPA, dimethyl phosphonomethyltriflate, THF, -78 °C to rt, 80%; (c) TBAF, THF, 1 h, 90%; (d) *N*,*N*-dimethylphosphoramidite, 1*H*-tetrazole, 12 h; *m*-CPBA, 95%; (e) TBAF•3H_2O, DMF, 3 h, 75%; (f) **8**, 1*H*-tetrazole, CH_2Cl_2, rt, 12 h; *t*-BuOOH; (g) TEA, BSTFA, CH_3CN; (h) TMSBr/CH_2Cl_2 (2:3), rt, 40 min; (i) MeOH, 1 h.

Experimental details for chemical synthesis.

General. Chemicals were purchased from Aldrich and Acros Chemical Corporation and used without prior purification. Solvents were reagent-grade and distilled before use: CH_2Cl_2 was distilled from CaH_2 and THF was distilled from sodium wire. TLC used precoated silica gel glass sheets (EM SCIENCE silica gel $60F_{254}$). Flash chromatography (FC) employed Whatman 230~400 mesh ASTM silica gel. NMR spectra were recorded on a Varian INOVA 400 at 400 MHz (^{1}H), 101 MHz (^{13}C), 162 MHz (^{31}P) and 376 MHz (^{19}F) at 25 °C. Chemical shifts are reported in ppm with TMS as internal standard (δ = 0.00); ^{31}P, 85% H_3PO_4 (δ = 0.00); ^{19}F, $CFCl_3$ (δ = 0.00). Low- and high-resolution mass spectra were obtained on HP5971A MSD and Finnigan MAT95 double focusing mass spectrometer (MS) instruments, respectively.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3-*O*-benzoyl-3,4-*O*-(1,1,3,3-tetraisopropyldisil-oxanedi-1,3-yl)-*myo*-inositol (A). A solution of tetrol **3** (900 mg, 1.72 mmol) and imidazole (250 mg, 3.44 mmol) in pyridine (10 mL) was treated with TIPDS-$C1_2$ (597.8 mg, 1.9 mmol) at - 5 °C and then slowly warmed to rt. The progress of the reaction was monitored by TLC. After 12 h the mixture was concentrated and subjected to the aqueous workup. The organic phase was concentrated, and the residue was chromatographed on silica gel (hexanes/EtOAc, 10 :1) giving pure product **A** (720 mg, 88%) as a colorless glassy solid. $[\alpha]^{20}_{D}$ = + 13.4 (*c* 0.85, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.0 Hz, 2H), 7.79-7.74 (m, 4H), 7.56-7.38 (m, 9H), 4.99 (dd, *J* = 10.4, 2.0 Hz, 1H), 4.30 (t, *J* = 9.2 Hz, 1H), 4.04 (t, *J* = 9.2 Hz, 1H), 3.98 (t, *J* = 2.8 Hz, 1H), 3.80 (dd, *J* = 9.2, 2.8 Hz, 1H), 3.48 (t, *J* = 9.2 Hz, 1H), 2.67 (s, 1H), 2.33 (s, 1H), 1.13 (s, 9H), 1.08-0.81 (m, 28H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 136.2, 136.2, 133.4, 133.2, 133.2, 130.3, 130.1, 130.1, 128.5, 128.1, 127.9, 78.4, 74.0, 73.9, 73.3, 73.2, 71.5, 27.3, 19.7, 17.7, 17.6, 17.6, 17.5, 17.3, 17.2, 13.1, 13.0, 12.3, 12.3; MALDI-HRMS $[M + Na]^+$ calcd for $C_{41}H_{60}O_8Si_3Na$ 787.3488, found 787.3488.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3-*O*-benzoyl-2,6-*O*-bis(methoxymethylene)-4,5-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (4). To a solution of the diol **A** (700 mg, 0.92 mmol) and DIPEA (1.4 mL, 8.27 mmol) in DMF (8 mL), was added MOMCl (0.5 mL, 6.59 mmol). After 24 h at 65 °C, the solvents were removed and the residue after aqueous work-up was loaded on a silica gel column. Purification (hexanes/EtOAc, 20:1) afforded **4** (1.8 g, 63%) as a colorless glass. $[\alpha]^{20}_D = +40.1$ (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.2 Hz, 2H), 7.84 (d, *J* = 6.8 Hz, 2H), 7.76 (m, 2H), 7.54-7.37 (m, 9H), 5.03 (d, *J* = 6.0 Hz, 1H), 4.85 (d, *J* = 6.4 Hz, 1H), 4.79 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.56 (d, *J* = 2.8 Hz, 2H), 4.19 (t, *J* = 8.8 Hz, 1 H), 4.08 (t, *J* = 9.6 Hz, 1H), 4.06 (s, 1H), 3.64 (t, *J* = 8.4 Hz, 1H), 3.47 (s, 3H), 3.21 (s, 3H), 1.16 (s, 9H), 1.11-0.82 (m, 28H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 136.5, 136.2, 134.1, 133.2, 133.0, 130.3, 130.3, 130.1, 129.9, 128.4, 128.2, 127.9, 98.8, 98.1, 78.5, 77.0, 74.6, 73.9, 73.2, 56.8, 55.9, 27.5, 19.5, 17.7, 17.6, 17.5, 17.5, 17.4, 17.3, 17.2, 13.1, 13.1, 12.2, 12.2; MALDI-HRMS $[M + Na]^+$ calcd for $C_{45}H_{68}O_{10}Si_3Na$ 875.4013, found 875.4037.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3-*O*-benzoyl-2,6-*O*-bis(methoxymethylene)-*myo*-inositol (B). At 0 °C TBAF (1 M in THF, 2 mL, 2 mmol) was added to inositol **4** (780 mg, 0.92 mmol) in 2 mL THF, then warmed to rt. The reaction mixture was stirred at rt for 1 h, TLC showed the end of the reaction. The reaction system was diluted with EtOAc, and washed with water, 1 N HCl, then saturated aqueous NaCl solution. The organic solvents were dried with Na_2SO_4, then concentrated and flash chromatographed (hexanes/EtOAc, 1:1) to afford diol **B** (430 mg, 77%). $[\alpha]^{20}_D$ = + 18.7 (*c* 0.97, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.72 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.67 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.55- 7.35 (m, 9H), 4.84 (d, *J* = 6.8 Hz, 1H), 4.79 (dd, *J* = 10.4, 2.4 Hz, 1H), 4.71 (d, *J* = 6.4 Hz, 1H), 4.34 (d, *J* = 7.2 Hz, 1H), 4.19-3.98 (m, 3H), 3.91 (d, *J* = 7.2 Hz, 1H), 3.86 (dd, *J* = 9.2, 2.4 Hz, 1H), 3.71 (t, *J* = 9.2 Hz, 1H), 3.34 (s, 1H), 3.21 (s, 3H), 3.18 (s, 3H), 2.99 (s, 1H), 1.04 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ; 166.4, 136.2, 135.8, 134.6, 133.3, 133.2, 130.2, 130.1, 129.7, 128.5, 128.2, 128.0, 127.7, 98.3, 98.2, 85.6, 74.6, 73.5, 73.1, 71.1, 56.1, 55.7, 27.3, 19.6. MALDI-HRMS $[M + Na]^+$ calcd for $C_{33}H_{42}O_9SiNa$ 633.2490, found 633.2498.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3-*O*-benzoyl-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (5). A solution of diol **B** (103 mg, 0.17 mmol) and 1-*H* tetrazole (40 mg, 0.55 mmol) in CH_2Cl_2 (2 mL) was treated with dimethyl *N*,*N*-diisopropylphosphoramidite (0.16 mL, 0.68 mmol) under Ar. After 12 h the result mixture was cooled to – 20 °C and treated with *m*-CPBA (230 mg, 1mmol). After warm-up to rt, saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$ were added and stirred for 30 min. The reaction mixture was extracted with CH_2Cl_2 and dried with Na_2SO_4. The organic phase was concentrated, and the residue was chromatographed on silica gel (hexanes/acetone, 1:1) giving pure product **5** (113 mg, 81%) as an oil. $[\alpha]^{20}_D$ = + 39.3 (*c* 0.70, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.72 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.60 (dd, *J* = 8.0, 2.4 Hz, 2H), 4.99 (d, *J* = 6.0 Hz, 1H), 4.97 (t, *J* = 8.4 Hz, 1H), 4.74 (d, *J* = 5.6 Hz, 1H), 4.72 (dd, *J* = 10.4, 2.8 Hz, 1H), 4.43-4.34 (m, 3H), 4.17 (t, *J* = 9.6 Hz, 1H), 3.98 (dd, *J* = 9.6, 1.8 Hz, 1H), 3.81 (d, *J* = 5.6 Hz, 3H), 3.78 (d, *J* = 5.2 Hz, 3H), 3.68 (d, *J* = 11.6 Hz, 3H), 3.46 (s, 3H), 3.44 (t, *J* = 2.2 Hz, 1H), 3.15 (d, *J* = 11.2 Hz, 3H), 3.08 (s, 3H), 1.09 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 136.2, 136.0, 133.5, 133.3, 132.5, 130.4, 130.3, 130.2, 129.6, 128.4, 128.3, 128.1, 99.0, 98.0, 78.9, 76.5, 76.2, 73.6, 71.5, 57.1, 56.1, 54.8, 54.8, 54.7, 53.8, 53.7, 27.4, 19.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 1.71 (s, 1P), 0.86 (s, 1P). MALDI-HRMS $[M + Na]^+$ calcd for $C_{37}H_{52}O_{15}P_2SiNa$ 849.2443, found 849.2445.

1D-3-*O*-Benzoyl-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (C): Diphosphate **5** (180 mg, 0.22 mmol) was dissolved in 2.4 mL DMF, to the mixture was added TBAF•3H_2O (110 mg, 0.35 mmol), stirred at room temperature for 3 h. The mixture was concentrated, diluted with EtOAc, and then washed with water, 1 N HCl, saturated aqueous NaCl solution. The organic phase dried with Na_2SO_4. The crude product was chromatographed on silica gel (hexanes/acetone, 1:2) to give bisphosphate **C** (118 mg, 91%) as colorless oil. $[\alpha]^{D}_{20}$ = + 6.0 (*c* 0.65, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 8.15 – 8.13 (m, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 5.08 – 5.04 (m, 2H), 4.78 (d, *J* = 6.8 Hz, 2H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.58 (d, *J* = 6.8Hz, 1H), 4.48-4.42 (m, 1H), 4.26 (t, *J* = 3.0 Hz, 2H), 3.80 (s, 6H), 3.77 (s, 6H), 3.74 (s, 1H), 3.71 (s, 1H), 3.68 (s, 1H), 3.65-3.61 (m, 2H), 3.44 (s, 3H), 3.24 (s, 1H), 3.22 (s, 1H), 3.20 (s, 3H), 3.17 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 133.6, 130.4, 130.1, 129.4, 128.6, 128.5, 99.1, 99.2, 83.3, 79.1, 79.1, 76.8, 75.5, 71.9, 70.4, 56.5, 56.2, 54.9, 54.7, 54.5, 53.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 1.51 (1P), 1.21 (1P); MALDI-HRMS [M + Na]$^+$ calcd for $C_{21}H_{34}O_{15}P_2Na$ 611.1271, found 611.1306.

1D-1-*O*-triethylsilyl-3-*O*-Benzoyl-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (6). A solution of alcohol obtained above **C** (60 mg, 0.10 mmol) and imidazole (68 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was treated with TESC1 (0.10 mL, 0.6 mmol) at rt. After 12 h the mixture was concentrated and subjected to the aqueous workup. The organic phase was concentrated, and the residue was chromatographed on silica gel (hexanes/acetone, 2:3) giving pure product **6** (63 mg, 88%) as a colorless oil. $[\alpha]^D_{20}$ = + 27.9 (*c* 0.68, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 8.15 – 8.12 (m, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 5.05 – 4.94 (m, 2H), 4.85 (d, *J* = 6.4 Hz, 2H), 4.73 (dd, *J* =10.4, 6.8 Hz, 2H), 4.54 (d, *J* = 6.8Hz, 1H), 4.39 (q, *J* = 9.2 Hz, 1H), 4.06 (s, 1H), 3.99 (t, *J* = 9.6 Hz, 1H), 3.77 (d, *J* = 1.2 Hz, 3H), 3.75 (d, *J* = 1.6 Hz, 3H), 3.67 (d, *J* = 11.6 Hz, 4H), 3.41 (s, 3H), 3.17 (d, *J* = 11.6 Hz, 3 H), 3.14 (s, 3H), 0.91 (t, *J* = 7.6 Hz, 9 H), 0.60 (q, *J* = 7.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 133.5, 130.4, 129.5, 128.5, 98.6, 97.5, 79.0, 76.1, 75.9, 73.0, 72.0, 57.0, 56.1, 54.1, 54.8, 54.8, 54.7, 54.6, 54.6, 53.8, 53.7, 7.0, 5.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 1.79 (1P), 1.02 (1P); MALDI-HRMS [M + Na]$^+$ calcd for $C_{27}H_{48}O_{15}P_2Na$ 725.2135, found 725.2148.

1D-1-*O*-triethylsilyl-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (D). A solution of diisobutylaluminium hydride (0.5 mL, 1 M in Hexanes, 0.5 mmol) was added dropwise at – 78 ºC to a solution of **6** (63 mg, 0.09 mmol) in dry

CH_2Cl_2 (3 mL). After stirring for 1.5 h at – 78 °C, methanol (5 mL) was added slowly to quench the reaction and allowed to warm to rt. The reaction mixture was poured to wet Na_2SO_4 and stirred for a wile. The solid Na_2SO_4 was filtered off and washed with EtOAc. The filtrate was concentrated and the residue was chromatographed on silica gel (hexanes/acetone, 1:2) giving pure product **D** (45 mg, 84%) as a colorless oil. $[\alpha]^{D}_{20}$ = + 9.7 (*c* 0.50, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 4.82 (d, *J* = 6.0 Hz, 1H), 4.75 (d, *J* = 6.8 Hz, 2H), 4.70 (t, *J* = 6.8Hz, 2H), 4.46 (q, *J* = 6.8 Hz, 2H), 4.26 (q, *J* = 9.2 Hz, 1H), 3.89 (t, *J* = 9.6 Hz, 1H), 3.82 (t, *J* = 2.0 Hz, 1H), 3.79 (d, *J* = 3.6 Hz, 3H), 3.77 (d, *J* = 3.6 Hz, 3H), 3.75 (d, *J* = 6.8 Hz, 3H), 3.72 (d, *J* = 6.4 Hz, 3H), 3.55 (m, 2H), 3.40 (s, 3H), 3.39 (s, 3H), 0.91 (t, *J* = 8.0 Hz, 9 H), 0.60 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 98.5, 98.3, 80.6, 80.5, 80.2, 78.7, 76.4, 72.9, 70.8, 56.9, 56.3, 55.2, 55.1, 55.1, 54.7, 54.6, 54.6, 7.0, 5.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 3.05 (1P), 2.04 (1P); CI-HRMS $[M + H]^+$ calcd for $C_{20}H_{45}O_{14}P_2Si$ 599.2053, found 599.2040.

1D-1-*O*-triethylsilyl-3-(bis(cyanoethyl)phosphothionate)-2,6-*O*-bis (methoxy-methylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (E). Bis(2-cyanoethoxy) (diisopropylamino)phosphine (38.5 mg, 0.16 mmol) was added to a solution of inositol **D** (40 mg, 0.067 mmol) and 1*H*-tetrazole (11 mg, 0.16 mmol) in 0.5 mL mixture solvents of CH_2Cl_2/CH_3CN (1:1). The mixture was stirred at rt under Ar for overnight. Then the phenylacetyl disulfide (140 mg, 0.4 mmol) was added and stirred for 30 min. The result mixture was diluted with 50 mL EtOAc and washed with water. After dried with Na_2SO_4, The organic phase was concentrated, and the residue was chromatographed on silica gel (hexanes/acetone, 1:2) to afford pure product **E** (41 mg, 72%) as a colorless oil. $[\alpha]^{D}_{20}$ =

+ 5.8 (*c* 0.40, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 4.81 (d, *J* = 6.4 Hz, 1H), 4.76 (d, *J* = 6.8 Hz, 1H), 4.74-4.66 (m, 3H), 4.36-4.22 (m, 6H), 4.13 (s, 1H), 3.91 (t, *J* = 9.6 Hz, 1H), 3.78-3.75 (m, 12H), 3.54 (dd, *J* = 9.6, 1.6 Hz, 1H), 3.39 (s, 3H), 3.35 (s, 3H), 0.91 (t, *J* = 8.0 Hz, 9 H), 0.61 (q, *J* = 8.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 116.9, 116.7, 98.6, 97.7, 78.2, 76.7, 76.6, 75.9, 72.6, 63.3, 63.2, 63.1, 63.0, 57.0, 56.3, 55.3, 55.2, 55.1, 55.0, 55.0, 55.0, 54.9, 54.9, 19.6, 19.6, 7.0, 4.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 67.63 (1P), 1.77 (1P), 1.74 (1P); CI-HRMS $[M + H]^+$ calcd for $C_{26}H_{52}N_2O_{16}P_3SSi$ 801.2019, found 801.1970.

1D-3-(bis(cyanoethyl)phosphothionate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (7). To a solution of **E** (10 mg, 0.012 mmol) in methanol (0.5 mL) was added NH_4F (4.5 mg, 0.12 mmol). The resulting mixture was stirred at rt for 3 h, concentrated and chromatographed on silica gel (hexanes/acetone, 1: 3) to afford pure product **7** (7.5 mg, 85%) as a colorless oil. $[\alpha]^D_{20}$ = - 16.7 (*c* 0.75, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 4.81 (d, *J* = 6.4 Hz, 1H), 4.78 (d, *J* = 6.8 Hz, 1H), 4.72 (q, *J* = 7.2 Hz, 2H), 4.64 (d, *J* =7.2 Hz, 1H), 4.40-4.26 (m, 1H), 3.91 (t, *J* = 9.6 Hz, 1H), 3.78-3.75 (m, 12H), 3.54 (dd, *J* = 9.6, 1.6 Hz, 1H), 3.39 (s, 8H), 3.78-3.67 (m, 12H), 3.48 (dd, *J* = 9.2, 2.0 Hz, 1H), 3.40 (s, 3H), 3.39 (s, 3H), 2.75 (q, *J* = 6.0 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 117.0, 116.8, 99.1, 98.3, 83.2, 78.6, 76.5, 76.3, 70.1, 63.3, 63.23, 63.1, 63.0, 56.5, 56.3, 55.3, 55.2, 55.0, 54.94, 54.9, 54.6, 54.6, 29.3, 19.7, 19.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 67.59 (1P), 1.79 (1P), 1.54 (1P); MALDI-HRMS $[M + Na]^+$ calcd for $C_{20}H_{37}N_2NaO_{16}P_3S$ 709.0974, found 709.1033.

1D-*O*-(1,2-Di-*O*-butanoyl-*sn*-(2*S*)-glycerol-3-*O*-cyanoethylphospho)-3-(bis(cyano ethyl)phosphothionate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (9a). To a solution of alcohol **7** (20 mg, 0.029 mmol) in dry CH_2Cl_2 (0.5 mL) was added *N*,*N*-diisopropyl-*O*-cyanoethyl-*O*-(di-butanoyl-*sn*-(2*S*)-glycerol)phosphonamidite **8a** (20 mg, 0.047 mmol) and 1*H*-tetrazole (6 mg, 0.085 mmol). The mixture was stirred at rt for 12 h. Oxidation was then performed with *t*-BuOOH (25 μL, 5.5 M in decane, 0.14 mmol) at rt for 1 h. The solution was diluted with CH_2Cl_2 (20 mL) and washed with saturated aqueous $Na_2S_2O_4$. The organic layer was concentrated and the residue purified by chromatograph (acetone/hexanes, 2:1) to give **9a** (28 mg, 93%) as a yellow oil. $[\alpha]^{D}_{20}$ = - 13.8 (*c* 1.07, $CHCl_3$); ^1H NMR(400 MHz, $CDCl_3$) δ 5.22 (m, 1H), 4.77-4.69 (m, 5H), 4.50 (d, *J* = 10.0 Hz, 1H), 4.41-4.06 (m, 13H), 4.00 (td, *J* = 9.6, 2.4 Hz, 1H), 3.79-3.74 (m, 12H), 3.38 (s, 3H), 3.37 (s, 3H), 2.80-2.72 (m, 6H), 2.29-2.23 (m, 4H), 1.62-1.55 (m, 4H), 0.91-0.86 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 173.0, 172.9, 117.1, 117.0, 116.8, 99.0, 98.3, 98.3, 77.9, 75.8, 75.2, 75.0, 69.5, 69.5, 66.5, 66.4, 63.3, 63.2, 62.7, 62.7, 62.7, 62.6, 61.7, 56.9, 56.5, 56.4, 55.3, 55.2, 55.1, 55.0, 54.99, 54.9, 54.8, 36.5, 36.2, 19.0, 19.7, 19.6, 19.5, 18.5, 13.8, 13.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 67.45 and 67.28 (1P), 1.94 and 1.92 (1P), 1.86 and 1.83 (1P), -1.02 and –1.34 (1P); MALDI-HRMS $[M + H]^+$ calcd for $C_{34}H_{60}N_3O_{23}P_4S$ 1034.2288, found 1034.2270.

1D-*O*-(1,2-Di-*O*-octanoyl-*sn*-(2*S*)-glycerol-3-*O*-cyanoethylphospho)-3-(bis(cyano ethyl)phosphothionate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (9b) was obtained from **7** in 72% yield analogously as described for compound **9a**. $[\alpha]^{D}_{20}$ = - 13.0 (*c* 0.75, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.20 (m, 1H), 4.77-4.68 (m, 5H), 4.50 (d, *J* = 13.2 Hz, 1H), 4.40-4.05 (m, 13H), 3.99 (td, *J* = 9.6, 2.4 Hz, 1H), 3.78-3.73 (m, 12H), 3.37 (s, 3H), 3.36 (s, 3H), 2.77-2.71 (m, 6H), 2.29-2.22 (m, 4H), 1.55-1.51 (m, 4H), 1.21 (m, 16H), 0.81 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 173.1, 173.1, 117.1, 117.09, 117.0, 116.99, 116.8, 116.8, 99.0, 98.3, 98.27, 77.9, 75.9, 75.8, 75.8, 75.2, 75.0, 69.6, 69.5, 66.5, 66.4, 66.4, 63.3, 63.3, 63.2, 63.2, 62.8, 62.7, 62.6, 62.6, 61.8, 56.9, 56.4, 56.4, 55.3, 55.2, 55.1, 55.0, 54.9, 54.8, 54.81, 34.3, 34.2, 31.8, 29.2, 29.2, 29.12, 29.1, 25.0, 22.8, 19.9, 19.88, 19.8, 19.8, 19.7, 19.6, 19.5, 14.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 67.47 and 67.29 (1P), 1.95 and 1.93 (1P), 1.86 and 1.83 (1P), -1.02 and –1.31 (1P); MALDI-HRMS $[M + H]^+$ calcd for $C_{42}H_{76}N_3O_{23}P_4S$ 1146.3540, found 1146.3556.

1D-*O*-(1,2-Di-*O*-palmitoyl-*sn*-(2*S*)-glycerol-3-*O*-cyanoethylphospho)-3-(bis(cyano ethyl)phosphothionate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (9c) was obtained from **7** in 87% yield analogously as described for compound **9a**. $[\alpha]^{D}_{20}$ = - 11.3 (*c* 0.80, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.21 (m, 1H), 4.78-4.69 (m, 5H), 4.50 (d, *J* = 13.6 Hz, 1H), 4.40-4.05 (m, 13H), 3.99 (td, *J* = 9.6, 2.4 Hz, 1H), 3.79-3.74 (m, 12H), 3.37 (s, 6H), 2.80-2.72 (m, 6H), 2.29-2.22 (m, 4H), 1.55-1.51 (m, 4H), 1.19 (m, 48H), 0.81 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 173.1, 173.0, 117.1, 117.0, 116.81, 116.8, 98.9, 98.3, 98.2, 77.9, 75.8, 75.6, 75.2, 75.0, 69.5, 69.46, 66.4, 63.3, 63.27, 63.2, 62.8, 62.7, 62.66, 62.6, 61.8, 56.9, 56.4, 55.2, 55.19, 55.1, 55.0, 54.97, 54.8, 54.76, 34.3, 34.2, 32.1, 29.9, 29.8, 29.7, 29.5, 29.49, 29.3, 29.27, 25.0, 22.8, 19.9, 19.8, 19.7, 19.6, 19.5, 14.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 67.43

and 67.23 (1P), 1.94 and 1.91 (1P), 1.84 and 1.81 (1P), -1.04 and –1.35 (1P); MALDI-HRMS $[M + Na]^+$ calcd for $C_{58}H_{107}N_3O_{23}P_4SNa$ 1392.5864, found 1392.5876.

1D-*O*-(1,2-Di-*O*-oleoyl-*sn*-(2*S*)-glycerol-3-*O*-cyanoethylphospho)-3-(bis(cyano ethyl)phosphothionate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (9d) was obtained from **7** in 70% yield analogously as described for compound **9a**. $[\alpha]^D_{20}$ = - 9.8 (*c* 0.77, $CHCl_3$); ^{1}H NMR(400 MHz, $CDCl_3$) δ 5.31-5.20 (m, 5H), 4.78-4.69 (m, 5H), 4.50 (d, *J* = 13.2 Hz, 1H), 4.48-3.95 (m, 14H), 3.79-3.74 (m, 12H), 3.37 (s, 6H), 2.78-2.72 (m, 6H), 2.29-2.23 (m, 4H), 1.94 (m, 7H), 1.73 (m, 1H), 1.55 (m, 4H), 1.19 (m, 40H), 0.81 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 173.0, 130.2, 129.9, 117.1, 117.0, 116.8, 98.9, 98.3, 98.2, 77.9, 75.8, 75.5, 75.2, 75.0, 69.6, 69.5, 66.4, 63.3, 63.28, 63.2, 62.8, 62.7, 62.66, 62.6, 61.8, 56.9, 56.4, 55.3, 55.2, 55.1, 55.0, 54.97, 54.8, 54.77, 34.3, 34.2, 32.1, 29.9, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.37, 29.3, 29.2, 27.8, 27.4, 27.35, 25.0, 22.9, 19.9, 19.86, 19.8, 19.79, 19.6, 19.6, 19.5, 14.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 67.43 and 67.24 (1P), 1.94 and 1.91 (1P), 1.84 and 1.82 (1P), -1.04 and –1.34 (1P); MALDI-HRMS $[M + H]^+$ calcd for $C_{62}H_{112}N_3O_{23}P_4S$ 1422.6357, found 1422.6363.

1D-*O*-(1,2-Di-*O*-butanoyl-*sn*-(2*S*)-glycerol-3-phospho)-3-phosphothionate-4,5-bisphosphate-*myo*-inositol (1a). To a solution of **9a** (16 mg, 0.015 mmol) in CH_3CN (0.5 mL) under Ar was added triethylamine (0.25 mL) followed by the addition of bis(trimethylsilyl)trifluoroacetamide (0.25 mL). After 24 h, the reaction mixture was concentrated and the residue was completely dried and dissolved in CH_2Cl_2 (0.3 mL). At

0 °C, TMSBr (0.2 mL) was added to the mixture and then warmed to rt for 40 min. The solvents were removed by evaporation and then dried completely to remove the excess TMSBr. The residue was stirred with methanol (1 mL) for 1 h. After concentration, the residue was washed with $CHCl_3$ at low temperature to give **1a** (10 mg, 89%) as white solid. $[\alpha]^{D}_{20}$ = + 4.1 (*c* 1.1, CH_3OH); ^{1}H NMR(400 MHz, CD_3OD) δ 5.16 (m, 1H), 4.61 (q, *J* = 9.2 Hz, 1H), 4.47 (s, 1H), 4.41-4.28 (m, 2H), 4.15-3.99 (m, 5H), 3.89 (t, *J* =9.6 Hz, 1H), 2.27-2.19 (m, 4H), 1.57-1.50 (m, 4H), 0.88-0.83 (m, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 173.7, 173.3, 79.8, 77.2, 77.1, 75.7, 70.2, 70.1, 70.0, 69.5, 65.2, 62.0, 35.7, 35.5, 18.2, 12.7; ^{31}P NMR (162 MHz, CD_3OD) δ 63.77 (1P), 1.07 (1P), 0.89 (1P), -0.64 (1P); MALDI-HRMS $[M - H]^-$ calcd for $C_{17}H_{33}O_{21}P_4S$ 729.0185, found 729.0162.

1D-*O*-(1,2-Di-*O*-octanoyl-*sn*-(2*S*)-glycerol-3-phospho)-3-phosphothionate-4,5-bisphosphate-*myo*-inositol (1b) was obtained from **9b** in 90% yield analogously as described for compound **1a.** $[\alpha]^{D}_{20}$ = + 4.9 (*c* 0.77, CH_3OH); ^{1}H NMR(400 MHz, CD_3OD) δ 5.17 (m, 1H), 4.62 (q, *J* = 8.8 Hz, 1H), 4.48 (s, 1H), 4.41-4.28 (m, 2H), 4.15-4.00 (m, 5H), 3.92 (m, 1H), 2.28-2.22 (m, 4H), 1.54-1.50 (m, 4H), 1.22 (m, 16H), 0.81 (t, *J* = 6.4 Hz, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 173.8, 173.4, 79.6, 77.0, 75.7, 70.2, 69.7, 65.1, 62.1, 33.9, 33.7, 31.7, 28.9, 24.8, 22.5, 13.3; ^{31}P NMR (162 MHz, CD_3OD) δ 63.20 (1P), 0.69 (1P), 0.51 (1P), -0.67 (1P); MALDI-HRMS $[M - H]^-$ calcd for $C_{25}H_{49}O_{21}P_4S$ 841.1438, found 841.1443.

1D-*O*-(1,2-Di-*O*-palmitoyl-*sn*-(2S)-glycerol-3-phospho)-3-phosphothionate-4,5-bisphosphate-*myo*-inositol (1c) was obtained from **9c** in 95% yield analogously as described for compound **1a.** $[\alpha]^{D}_{20}$ = + 4.7 (*c* 0.92, CH_3OH); ^{1}H NMR(400 MHz, $CD_3OD/CDCl_3$ 5:1) δ 5.18 (m, 1H), 4.63 (q, *J* = 8.8 Hz, 1H), 4.47 (s, 1H), 4.41-4.27 (m, 2H), 4.18-3.95 (m, 5H), 3.82 (m, 1H), 2.30-2.20 (m, 4H), 1.58-1.50 (m, 4H), 1.19 (m, 48H), 0.78 (t, *J* = 6.4 Hz, 6H); ^{13}C NMR (101 MHz, $CD_3OD/CDCl_3$ 5:1) δ 177.8, 177.5, 83.7, 81.1, 79.6, 76.2, 74.5, 74.2, 74.0, 73.9, 73.88, 73.5, 69.2, 67.2, 66.2, 38.0, 37.9, 37.83, 37.8, 35.9, 35.89, 33.66, 33.6, 33.52, 33.5, 33.46, 33.4, 33.3, 33.31, 33.24, 33.2, 33.1, 33.0, 28.9, 28.8, 26.6, 17.52, 17.5; ^{31}P NMR (162 MHz, $CD_3OD/CDCl_3$ 5:1) δ 63.66 (1P), 0.92 (1P), 0.75 (1P), -0.66 (1P); MALDI-HRMS $[M - H]^-$ calcd for $C_{41}H_{81}O_{21}P_4S$ 1065.3947, found 1065.3918.

1D-*O*-(1,2-Di-*O*-oleoyl-*sn*-(2S)-glycerol-3-phospho)-3-phosphothionate-4,5-bisphosphate-*myo*-inositol (1d) was obtained from **9d** in 91% yield analogously as described for compound **1a.** $[\alpha]^{D}_{20}$ = + 6.0 (*c* 0.86, CH_3OH); ^{1}H NMR(400 MHz, CD_3OD) δ 5.24 (m, 5H), 4.59 (m, 1H), 4.47 (s, 1H), 4.41-4.31 (m, 2H), 4.18-3.95 (m, 5H), 3.90 (m, 1H), 2.26-2.20 (m, 4H), 1.93 (m, 7H), 1.69 (m, 1H), 1.51 (m, 4H), 1.20 (m, 40H), 0.78 (s, br, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 177.7, 177.5, 133.7, 133.6, 83.5, 80.8, 79.6, 74.2, 73.6, 69.1, 66.4, 43.3, 38.0, 37.8, 37.7, 36.0, 35,9, 33.8, 33.7, 33.7, 33.6, 33.5, 33.4, 33.37, 33.34, 33.3, 33.26, 33.2, 33.17, 33.1, 33.08, 31.2, 31.1, 28.9, 26.7, 17.7; ^{31}P NMR (162 MHz, CD_3OD) δ 62.62 (1P), 0.89 (2P), -0.60 (1P); MALDI-HRMS $[M - H]^-$ calcd for $C_{45}H_{85}O_{21}P_4S$ 1117.4260, found 1117.4249.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-2,6-*O*-bis(methoxymethylene)-4,5-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (F) was obtained from **4** in 88% yield analogously as described for compound **D**. $[\alpha]^{20}_{D}$ = + 11.7 (*c* 0.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.63 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.36-7.26 (m, 6H), 4.94 (d, *J* = 6.4 Hz, 1H), 4.78 (d, *J* = 6.0 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 4.17 (d, *J* = 6.4 Hz, 1H), 3.86 (t, *J* = 9.6 Hz, 1H), 3.75 (dd, *J* = 9.6, 2.4 Hz, 1H), 3.60 (t, *J* = 9.2 Hz, 1H), 3.41 (t, *J* = 8.4 Hz, 1H), 3.37 (s, 3H), 3.22 (s, 3H), 3.04 (s, 1H), 2.90 (dd, *J* = 9.2, 2.0 Hz, 2H), 1.02 (s, 9H), 1.01-0.84 (m, 28H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3, 136.0, 134.5, 133.3, 130.4, 130.1, 128.1, 127.9, 98.9, 98.8, 82.3, 78.9, 78.5, 77.7, 73.67, 71.3, 56.8, 56.1, 27.4, 19.5, 17.7, 17.66, 17.65, 17.5, 17.52, 17.4, 17.3, 13.2, 12.9, 12.3, 12.2; MALDI-HRMS $[M + Na]^+$ calcd for $C_{38}H_{64}O_9Si_3Na$ 771.3755, found 771.3761.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3-(dimethyl methylenephosphonate)-2,6-*O*-bis(methoxymethylene)-4,5-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol (10). *n*-BuLi (1.6 M in THF, 0.55 mL, 0.88 mmol) was added under Ar atmosphere to a solution of **F** (540 mg, 0.72 mmol) at – 78 °C. The reaction mixture was stirred for 30 min at – 78 °C and then added 1 mL HMPA. After 15 min, dimethyl methylenephosphonate (272 mg, 1.11 mmol) was added. The reaction was stirred at – 78 °C for 2 h and then allowed to warm to rt and then stirred at rt for 5 h. The reaction was diluted with 200 mL EtOAc and washed with Brine and water. The organic layer was dried with Na_2SO_4, concentrated and purified by flash chromatograph (hexanes/EtOAc, 3:2) to give **10** (500 mg, 80%) as an oil. $[\alpha]^{20}_{D}$ = + 14.8 (*c* 1.0 , $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.65 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.39-7.29 (m, 6H), 4.93 (d, *J* = 6.0 Hz, 1H), 4.79 (d, *J* = 6.4 Hz, 1H), 4.50 (d, *J* = 6.4 Hz, 1H), 4.45 (d, *J* = 6.0 Hz, 1H), 3.89 (t, *J* = 9.6 Hz, 1H), 3.81 (dd, *J* = 11.6, 9.2 Hz, 1H), 3.68 (dd, *J* =

10.0, 1.6 Hz, 1H), 3.60 (d, *J* = 10.8 Hz, 3H), 3.57 (d, *J* = 10.8 Hz, 3.48-3.41 (m, 2H), 3.40 (s, 3H), 3.33-3.27 (m, 1H), 3.19 (s, 3H), 3.12 (s, 1H), 2.70 (dd, *J* = 9.6, 2.0 Hz, 2H), 1.04 (s, 9H), 1.02-0.90 (m, 28H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.73 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.5, 136.2, 134.7, 130.3, 128.2, 127.9, 98.7, 97.6, 82.1, 82.0, 78.6, 78.4, 76.3, 75.1, 73.7, 64.7, 62.5, 56.8, 55.6, 52.9, 52.8, 27.4, 19.4, 17.6, 17.6, 17.5, 17.4, 13.2, 17.0, 13.1, 12.8, 12.2, 12.1; MALDI-HRMS $[M + H]^+$ calcd for $C_{41}H_{72}O_{12}Si_3P$ 871.4069, found 871.4064.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3-(dimethyl methylenephosphonate)-2,6-*O*-bis(methoxymethylene)-*myo*-inositol (G). At 0 ºC TBAF (1 M in THF, 1.2 mL, 1.2 mmol) was added to inositol **10** (430 mg, 0.49 mmol) in 4 mL THF, then warmed to rt. The reaction mixture was stirred at rt for 1 h, TLC showed the end of the reaction. The reaction system was diluted with EtOAc, and washed with water, 1 N HCl, then saturated aqueous NaCl solution. The organic solvents were dried with Na_2SO_4, then concentrated and flash chromatographed (hexanes/acetone, 1:4) to afford diol **G** (280 mg, 90%). $[\alpha]^{20}_{D}$ = + 42.9 (*c* 1.2 , $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (td, *J* = 8.0, 1.6 Hz, 4H), 7.42-7.32 (m, 6H), 4.75 (d, *J* = 6.4 Hz, 1H), 4.62 (d, *J* = 6.4 Hz, 1H), 4.50 (d, *J* = 6.4 Hz, 1H), 4.19 (d, *J* = 7.2 Hz, 1H), 3.87-3.57 (m, 15H), 3.32 (s, 3H), 3.25 (s, 3H), 3.11 (t, *J* = 8.4 Hz, 1H), 3.00 (dd, *J* = 10.0, 2.4 Hz, 1H), 1.04 (s, 9H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.10 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 135.9, 134.1, 133.7, 130.2, 129.8, 127.9, 127.7, 98.4, 97.7, 84.5, 82.0, 81.9, 75.1, 74.2, 73.2, 72.7, 64.3, 62.7, 55.8, 55.79, 53.4, 53.36, 53.2, 53.1, 27.2, 19.5; MALDI-HRMS $[M + Na]^+$ calcd for $C_{29}H_{45}O_{11}PSiNa$ 651.2361, found 651.2343.

1D-1-*O*-(*tert*-Butyldiphenylsilyl)-3-(dimethylmethylenephosphonate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (11). A solution of diol **G** (210 mg, 0.33 mmol) and 1-*H* tetrazole (80 mg, 1.0 mmol) in CH_2Cl_2 (4 mL) was treated with dimethyl *N*,*N*-diisopropylphosphoramidite (0.3 mL, 1.38 mmol) under Ar. After 12 h the result mixture was cooled to – 20 °C and treated with *m*-CPBA (460 mg). After warm-up to rt, saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$ were added and stirred for 30 min. The reaction mixture was extracted with CH_2Cl_2 and dried with Na_2SO_4. The organic phase was concentrated, and the residue was chromatographed on silica gel (MeOH/acetone, 1:2) giving pure product **11** (270 mg, 95%) as a liquid. $[\alpha]^{20}_{D}$ = + 13.8 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.62 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.38-7.28 (m, 6H), 4.97 (d, *J* = 6.0 Hz, 1H), 4.76 (d, *J* = 6.4 Hz, 1H), 4.55 (t, *J* = 9.2 Hz, 1H), 4.50 (d, *J* = 6.4 Hz, 1H), 4.40 (d, *J* = 6.8 Hz, 1H), 4.22-4.16 (m, 1H), 4.04 (t, *J* = 9.6 Hz, 1H), 3.77-3.57 (m, 18H), 3.42 (s, 3H), 3.21-3.14 (m, 5H), 3.10 (s, 1H), 2.84 (dd, *J* = 10.0, 2.0 Hz, 1H), 1.04 (s, 9H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.27 (1P), 1.67 (1P), 1.09 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.2, 136.1, 134.2, 132.5, 130.5, 130.2, 128.3, 128.0, 98.9, 97.6, 80.0, 79.8, 79.0, 78.9, 78.89, 78.0, 76.1, 73.5, 73.2, 63.6, 62.0, 57.2, 55.9, 54.8, 54.7, 54.6, 54.5, 54.46, 54.4, 53.43, 53.36, 53.0, 52.9, 27.4, 19.3; MALDI-HRMS $[M + Na]^+$ calcd for $C_{33}H_{55}O_{17}P_3SiNa$ 867.2314, found 867.2324.

1D-3-(dimethylmethylenephosphonate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (H). Phosphonate **11** (270 mg, 0.32 mmol) was dissolved in 3 mL DMF, to the mixture was added TBAF•3H_2O (168 mg, 0.53 mmol), stirred at room temperature for 3 h. The mixture was concentrated, the crude product was chromatographed on silica gel (MeOH/acetone, 1:2) to give phosphonate **H** (145 mg, 75%) as colorless oil. $[\alpha]^{20}_{D}$ = - 18.7 (*c* 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.78 (d, *J* = 6.8 Hz, 1H), 4.75-4.70 (m, 3H), 4.65 (d, *J* = 7.2 Hz, 1H), 4.30 (t, *J* = 8.8 Hz, 1H), 4.23 (s, 1H), 4.01-3.87 (m, 2H), 3.79-3.67 (m, 19H), 3.45 (dd, *J* = 9.2, 2.4 Hz, 2H), 3.41 (s, 3H), 3.38 (s, 3H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 24.01 (1P), 1.65 (1P), 1.53 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 99.1, 98.0, 83.2, 80.4, 80.3, 79.2, 79.15, 79.1, 78.0, 77.99, 77.9, 74.4, 70.3, 65.1, 63.4, 56.4, 56.0, 54.9, 54.87, 54.86, 54.8, 54.6, 54.59, 54.5, 54.4, 53.3, 53.2, 53.16; MALDI-HRMS $[M + Na]^+$ calcd for $C_{17}H_{37}O_{17}P_3Na$ 629.1136, found 629.1144.

1D-*O*-(1,2-Di-*O*-butanoyl-*sn*-(2*S*)-glycerol-3-*O*-cyanoethylphospho)-3-(dimethylmethylenephosphonate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (12a) was obtained from **H** in 68% yield analogously as described for compound **9a**. $[\alpha]^{20}_{D}$ = - 28.0 (*c* 0.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.27 (m, 1H), 4.85 (d, *J* = 7.2 Hz, 1H), 4.79-4.67 (m, 4H), 4.47 (m, 1H), 4.37-4.25 (m, 5H), 4.24-3.96 (m, 5H), 3.94-3.87 (m, 1H), 3.82-3.74 (m, 18 H), 3.44 (t, *J* = 2.4 Hz, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 2.80 (q, *J* = 5.6 Hz, 2H), 2.33-2.26 (m, 4H), 1.66-1.58 (m, 4H), 0.92 (m, 6H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.86 (d, 1P), 1.83 (d, 1P), 1.71 (d, 1P), -1.05 and –1.36 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 172.9, 116.9, 116.8, 99.0, 98.97, 98.1, 98.0, 80.6, 80.5, 78.8, 76.5, 76.3, 75.9, 75.7, 73.8, 73.7, 69.58, 69.56, 69.51, 69.47, 66.45, 66.40, 66.28, 66.22, 65.82, 64.17, 62.58, 62.53, 62.51, 62.46, 61.68, 57.03, 57.00, 56.92, 56.16, 56.13, 55.04, 55.02, 54.97, 54.96, 54.72, 54.65, 54.60, 53.28, 53.22, 36.18, 36.03, 19.86, 19.83, 19.79, 19.75, 18.50, 13.82, 13.78; MALDI-HRMS $[M + Na]^+$ calcd for $C_{31}H_{59}O_{24}NP_4Na$ 976.2270, found 976.2293.

1D-*O*-(1,2-Di-*O*-octanoyl-*sn*-(2S)-glycerol-3-*O*-cyanoethylphospho)-3-(dimethylmethylenephosphonate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (12b) was obtained from **H** in 66% yield analogously as described for compound **9a**.$[\alpha]^{20}_D$ = - 19.9 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.26 (m, 1H), 4.84 (d, *J* = 7.2 Hz, 1H), 4.79-4.66 (m, 4H), 4.46 (s, 1H), 4.35-4.25 (m, 5H), 4.24-3.96 (m, 5H), 3.90 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.81-3.75 (m, 18 H), 3.44 (m, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 2.80 (q, *J* = 5.6 Hz, 2H), 2.33-2.26 (m, 4H), 1.57 (q, *J* = 6.8 Hz, 4H), 1.25 (m, 16H), 0.84 (t, *J* = 6.8 Hz, 6H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.88 (d, 1P), 1.81 (d, 1P), 1.69 (d, 1P), -1.04 and –1.33 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 173.1, 116.9, 116.8, 99.0, 98.9, 98.1, 98.0, 80.5, 80.4, 78.7, 76.5, 76.4, 76.3, 76.2, 76.0, 75.7, 73.9, 73.8, 69.55, 69.50, 69.47, 66.4, 66.38, 66.3, 66.2, 65.8, 64.2, 62.6, 62.6, 62.55, 62.50, 61.7, 57.0, 56.99, 56.2, 56.1, 55.0, 55.02, 54.97, 54.96, 54.7, 54.67, 54.6, 53.3, 53.2, 34.3, 34.2, 31.8, 29.2, 29.22, 29.1, 29.11, 25.03, 25.01, 22.8, 19.86, 19.8, 19.78, 19.7, 14.3; MALDI-HRMS $[M + Na]^+$ calcd for $C_{39}H_{75}O_{24}NP_4Na$ 1088.3522, found 1088.3499.

1D-*O*-(1,2-Di-*O*-palmitoyl-*sn*-(2*S*)-glycerol-3-*O*-cyanoethylphospho)-3-(dimethylmethylenephosphonate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (12c) was obtained from **H** in 78% yield analogously as described for compound **9a**. $[\alpha]^{20}_D$ = - 14.1 (*c* 0.5, $CHCl_3$); ^1H NMR (400

MHz, $CDCl_3$) δ 5.25 (m, 1H), 4.84 (d, *J* = 6.8 Hz, 1H), 4.77-4.66 (m, 4H), 4.46 (m, 1H), 4.35-3.97 (m, 10H), 3.91 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.78 (m, 18 H), 3.44 (m, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 2.80 (q, *J* = 6.0 Hz, 2H), 2.33-2.26 (m, 4H), 1.57 (q, *J* = 6.8 Hz, 4H), 1.23 (m, 48H), 0.84 (t, *J* = 6.8 Hz, 6H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.92 (d, 1P), 1.76 (d, 1P), 1.66 (s, 1P), -1.08 and -1.39 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 173.1, 116.85, 116.8, 99.0, 98.96, 98.1, 98.0, 80.5, 80.4, 78.8, 76.3, 75.9, 75.7, 73.8, 73.7, 69.5, 66.4, 66.3, 65.7, 64.1, 62.6, 62.5, 62.49, 61.7, 57.0, 56.99, 56.2, 56.1, 55.0, 54.98, 54.96, 54.7, 54.67, 54.6, 53.3, 53.2, 34.3, 34.2, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.49, 29.3, 29.31, 25.0, 22.9, 19.8, 19.78, 14.3; MALDI-HRMS $[M + Na]^+$ calcd for $C_{55}H_{107}O_{24}NP_4Na$ 1312.6026, found 1312.6058.

1D-*O*-(1,2-Di-*O*-oleoyl-*sn*-(2*S*)-glycerol-3-*O*-cyanoethylphospho)-3-(dimethylmethylenephosphonate)-2,6-*O*-bis(methoxymethylene)-4,5-bis(dimethylphosphate)-*myo*-inositol (12d) was obtained from **H** in 72% yield analogously as described for compound **9a**. $[\alpha]^{20}_D$ = - 15.0 (*c* 0.3 , $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36-5.30 (m, 4H), 5.27 (m, 1H), 4.85 (d, *J* = 6.8 Hz, 1H), 4.78-4.67 (m, 4H), 4.49 (m, 1H), 4.36-3.98 (m, 10H), 3.92 (dd, *J* = 14.0, 7.6 Hz, 1H), 3.79 (m, 18 H), 3.47 (m, 1H), 3.42 (s, 3H), 3.39 (s, 3H), 2.81 (q, *J* = 6.4 Hz, 2H), 2.30 (q, *J* = 7.6 Hz, 4H), 1.98 (m, 6H), 1,78 (m, 1H), 1.58 (m, 5H), 1.24 (m, 40H), 0.86 (t, *J* = 7.2 Hz, 6H); ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.91 (d, 1P), 1.79 (s, 1P), 1.59 (s, 1P), -1.04 and –1.39 (1P); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4, 173.1, 130.2, 129.9, 129.89, 116.9, 116.8, 99.0, 98.97, 98.1, 98.0, 80.5, 80.4, 78.8, 76.5, 76.4, 76.3, 76.0, 75.8, 73.9, 69.6, 69.5, 66.4, 65.8, 64.1, 62.5, 61.8, 59.2, 57.0, 57.0, 56.2, 56.1, 55.1, 55.0, 54.8, 54.7, 54.6, 53.4, 39.4, 39.37, 34.3, 34.2, 32.8, 32.79, 32.1, 32.06, 30.0, 29.9, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.43, 29.36, 29.3, 29.29, 29.2, 27.8, 27.4, 27.39, 25.0, 22.9, 19.9, 19.85, 19.80, 19.77, 14.3; MALDI-HRMS $[M + Na]^+$ calcd for $C_{59}H_{111}O_{24}NP_4Na$ 1364.6339, found 1364.6318.

1D-*O*-(1,2-Di-*O*-butanoyl-*sn*-(2*S*)-glycerol)-3-methylenephosphonate-4,5-bisphosphate-*myo*-inositol (2a) was obtained from **12a** in 92% yield analogously as described for compound **1a.** $[\alpha]^{20}_{D}$ = + 3.6 (*c* 0.5, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ 5.18 (m, 1H), 4.54 (q, *J* = 9.6 Hz, 1H), 4.37-4.28 (m, 2H), 4.15-4.01 (m, 5H), 3.91 (m, 2H), 3.75 (t, *J* = 11.2 Hz, 1H), 3.46 (d, *J* = 10.0 Hz, 1H), 2.27-2.20 (m, 4H), 1.58-1.51 (m, 4H), 0.86 (m, 6H); ^{31}P NMR (162 MHz, CD_3OD) δ 20.58 (s, 1P), 0.62 (s, 1P), 0.28 (s, 1P), -0.50 (s, 1P); ^{13}C NMR (101 MHz, CD_3OD) δ 178.6, 84.6, 84.5, 83.7, 81.7, 81.1, 76.6, 75,7, 74,9, 74.6, 74.1, 72.5, 71.9, 71.3, 70.0, 69.2, 68.4, 67.1, 65.5, 65.2, 39.4, 22.2, 16.6; MALDI-HRMS $[M - H]^-$ calcd for $C_{18}H_{35}O_{22}P_4$ 727.0570, found 727.0605.

1D-*O*-(1,2-Di-*O*-octanoyl-*sn*-(2*S*)-glycerol)-3-methylenephosphonate-4,5-bisphosphate-*myo*-inositol (2b) was obtained from **12b** in 96% yield analogously as described for compound **1a.** $[\alpha]^{20}_{D}$ = + 3.4 (*c* 0.5, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ 5.17 (m, 1H), 4.52 (q, *J* = 9.2 Hz, 1H), 4.36-4.28 (m, 2H), 4.14-4.00 (m, 5H), 3.92 (m, 2H), 3.72 (dd, *J* = 12.8, 10.4 Hz, 1H), 3.43 (dd, *J* = 10.0, 2.4 Hz, 1H), 2.28-2.21 (m, 4H), 1.51 (m, 4H), 1.22 (m, 16H), 0.80 (t, *J* = 6.8 Hz, 6H); ^{31}P NMR (162 MHz, CD_3OD) δ 21.06 (s, 1P), 0.90 (s, 1P), 0.88 (s, 1P), -0.54 (s, 1P); ^{13}C NMR (101 MHz,

CD_3OD) δ 177.7, 177.3, 84.7, 84.6, 83.8, 81.7, 81.4, 81.3, 74.0, 73.9, 71.2, 70.0, 69.2, 69.1, 68.3, 66.0, 37.8, 37.6, 37.5, 35.6, 32.9, 32.9, 32.8, 28.8, 28.7, 26.4, 26.41, 17.2; MALDI-HRMS $[M - H]^-$ calcd for $C_{26}H_{51}O_{22}P_4$ 839.1822, found 839.1819.

1D-*O*-(1,2-Di-*O*-palmitoyl-*sn*-(2*S*)-glycerol)-3-methylenephosphonate-4,5-bisphosphate-*myo*-inositol (2c) was obtained from **12c** in 90% yield analogously as described for compound **1a.** $[\alpha]^{20}_D$ = + 2.2 (*c* 0.95, $CH_3OH/CHCl_3$ 1:1); ^1H NMR (400 MHz, $CD_3OD/CDCl_3$ 3:1) δ 5.20-5.17 (m, 1H), 4.52 (q, *J* = 9.2 Hz, 1H), 4.34-4.28 (m, 2H), 4.14-4.00 (m, 5H), 3.90 (m, 2H), 3.77-3.67 (m, 1H), 3.56-3.38 (m, 2H), 2.27-2.18 (m, 4H), 1.51 (m, 4H), 1.17 (m, 48H), 0.78 (t, *J* = 6.8 Hz, 6H); ^{31}P NMR (162 MHz, $CD_3OD/CDCl_3$ 3:1) δ 20.29 (s, 1P), 0.42 (br, 2P), -0.61 (s, 1P); ^{13}C NMR (101 MHz, $CD_3OD/CDCl_3$ 3:1) δ 177.9, 177.5, 84.6, 84.4, 83.6, 81.1, 74.4, 74.2, 74.0, 73.9, 71.3, 70.1, 69.2, 68.5, 67.2, 66.2, 38.0, 37.9, 37.8, 35.91, 35.9, 33.7, 33.6, 33.6, 33.58, 33.5, 33.46, 33.4, 33.3, 33.31, 33.2, 33.21, 33.1, 33.07, 33.0, 28.9, 26.6, 17.6; MALDI-HRMS $[M - H]^-$ calcd for $C_{42}H_{83}O_{22}P_4$ 1063.4332, found 1063.4382.

1D-*O*-(1,2-Di-*O*-oleoyl-*sn*-(2*S*)-glycerol)-3-methylenephosphonate-4,5-bisphosphate-*myo*-inositol (2d) was obtained from **12d** in 95% yield analogously as described for compound **1a.** $[\alpha]^{20}_D$ = + 1.7 (*c* 0.4, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ 5.29-5.12 (m, 5H), 4.53 (q, *J* = 9.2 Hz, 1H), 4.36-4.29 (m, 2H), 4.17-3.99 (m, 5H), 3.96-3.88 (m, 2H), 3.72 (t, *J* = 10.8 Hz, 1H), 3.43 (dd, *J* = 9.6, 2.4Hz, 1H), 2.27-2.19 (m, 4H), 1.94-1.93 (m, 6H), 1.70 (m, 1H), 1.50 (m, 5H), 1.20 (m, 40H), 0.80 (t, *J* = 6.0 Hz, 6H); ^{31}P NMR (162 MHz, CD_3OD) δ 21.05 (s, 1P), 0.92 (s, 1P), 0.90 (s, 1P), -0.53 (s, 1P); ^{13}C

NMR (101 MHz, CD_3OD) δ 177.6, 177.3, 133.7, 133.5, 84.8, 84.6, 83.8, 81.7, 81.3, 74.0, 71.2, 70.0, 68.3, 67.1, 66.0, 62.4, 43.1, 37.8, 37.6, 37.6, 35.8, 35.8, 33.6, 33.6, 33.5, 33.4, 33.37, 33.3, 33.2, 33.19, 33.1, 33.0, 32.98, 32.94, 32.9, 31.4, 30.9, 30.88, 30.8, 28.8, 17.3; MALDI-HRMS $[M - H]^-$ calcd for $C_{46}H_{88}O_{22}P_4$ 1115.4645, found 1115.4646.

Experimental determination and evaluation of sodium transport (I_{Na^+}, $\mu A/cm^2$).[1] Briefly, A6 cells were subcultured onto 24-mm Millicell inserts (Millipore, Bedford, MA) for 10 days and the day before the experiment, incubated overnight in a serum-free 260 mosmol/kg H_2O amphibian Ringer solution. DiC$_{16}$-PtdIns(3,4,5)P$_3$, analogue **1c** and analogue **2c** (50 μM) were complexed by histone H1 carrier (50 μM) and then added to the apical side of the monolayer. Results were compared with insulin basolateral stimulation (100 nM) and control (histone H1 alone). This experiment is representative of three independent experiments.

Binding of analogues 1b and 2b to Grp1.[2] Competitive displacement of biotinylated-PtdIns(3,4,5)P$_3$ (10 nM) from Grp1 (10 nM) binding by diC$_8$-PtdIns(3,4,5)P$_3$ and analogues **1b** and **2b** (4000, 800, 160, 32, 6.4, 1.28 nM) in 50 mM Tris pH 7.5, 150 mM NaCl, 0.1% Tween-20, 0.1% BSA. Alphascreen® assays were performed on a Fusion instrument (Perkin Elmer, Inc.) using standard settings and the recommended buffer (50 mM Tris pH 7.5, 150 mM NaCl, 0.1% Tween-20, 0.1% BSA). In a 384-well microplate was added 5 μL buffer followed by 5 μL each of the Grp1 PH domain (50 nM), biotinylated PtdIns(3,4,5)P$_3$ (50 nM), and the respective competitor (20, 4, 0.8, 0.16, 0.032, 0.0064 μM). A solution of anti-GST acceptor beads and streptavidin donor beads

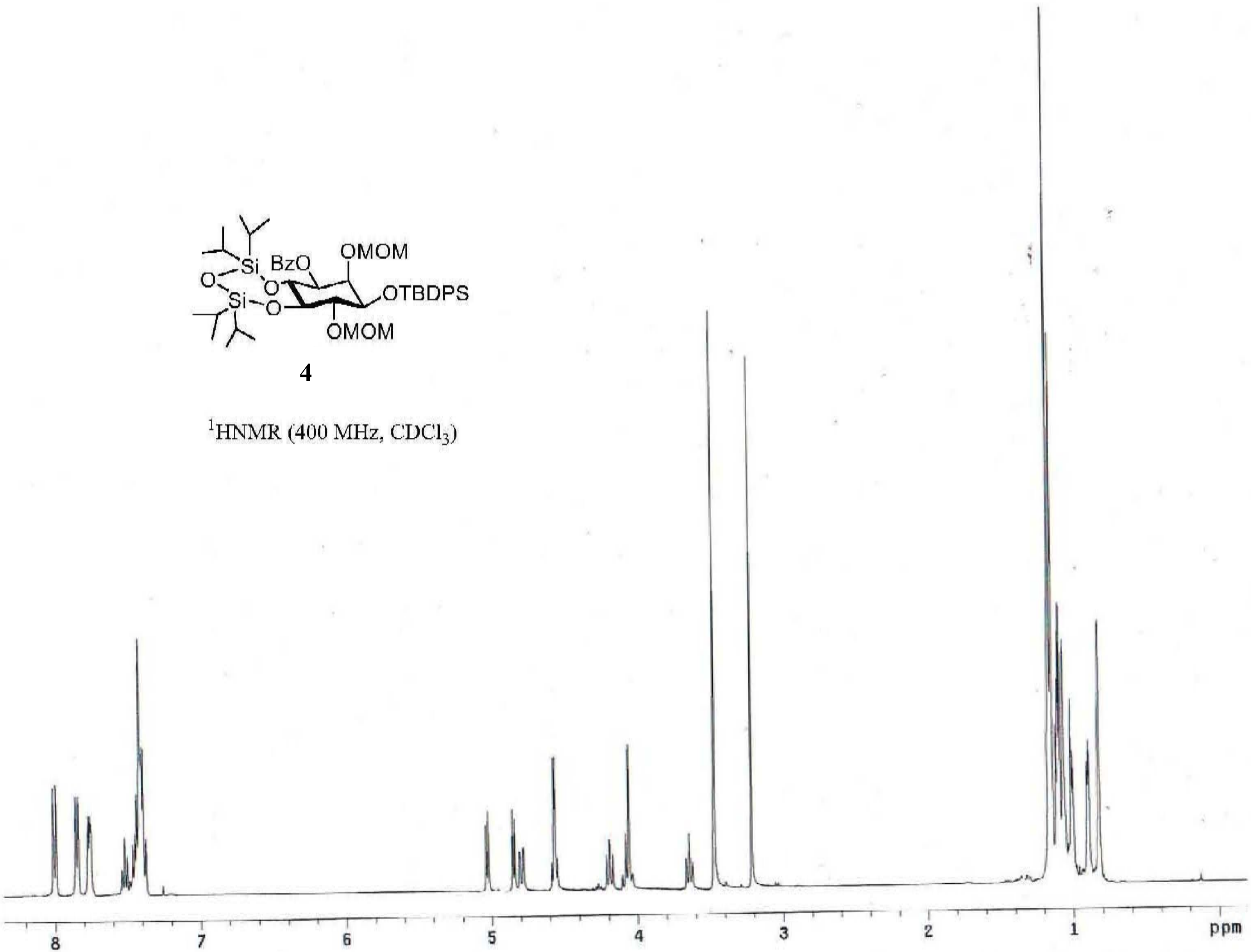
(5 μL, 100 μg/mL) was added, the plate gently shaken and stored for 2 hours in the dark, and read on the Fusion instrument.

(1) Markadieu, N.; Blero, D.; Boom, A.; Erneux, C.; Beauwens, R. *Am. J. Physiol. Renal. Physiol.* **2004**, *287*, F319-328.

(2) Drees, B. E.; Weipert, A.; Hudson, H.; Ferguson, C. G.; Chakravarty, L.; Prestwich, G. D. *Comb. Chem. High Throughput Screen* **2003**, *6*, 321-330.

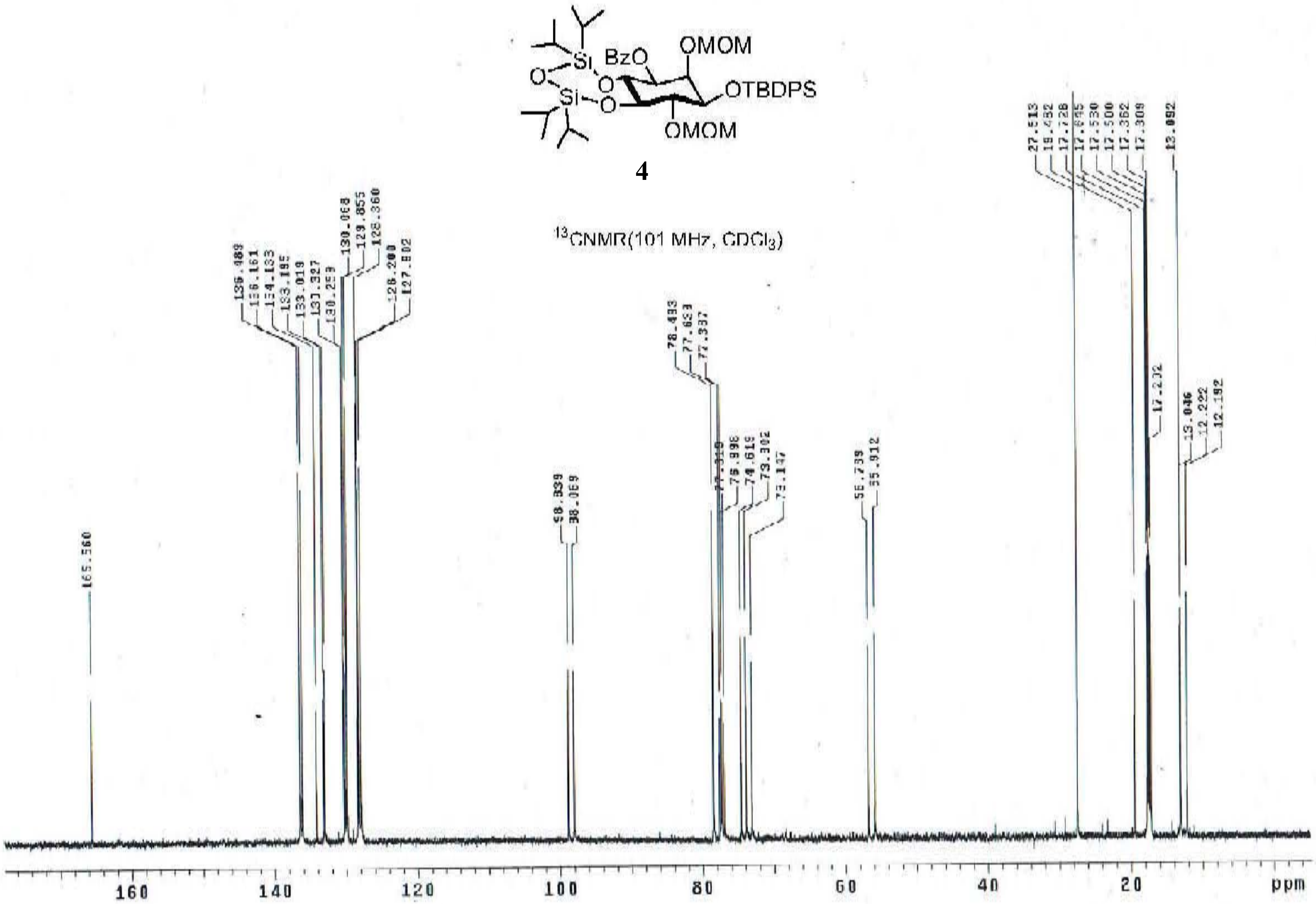
PTEN Malachite Green Assay Protocol. This experimental procedure was adapted from the PTEN Malachite Green assay protocol (Echelon Biosciences, Inc.), and the reaction buffer was also prepared according to this protocol. The PTEN enzyme reactions were performed in triplicate wells using the amounts in the table below. The buffer and enzyme were added first, and then the addition of the substrate solution (diC$_8$-PI(3,4,5)P$_3$, **1b** or **2b)** initiated the reaction. The plates were sealed to prevent evaporation, mixed on plate shaker for 30 sec, and then incubated at 37 ºC for 15 min. The enzyme reaction was quenched by addition of 100 μl/well of Malachite Green solution to each well of reactions of the table above. The plate was re-sealed, covered with Al foil to protect from light, and then incubated on a plate shaker for 15 min at rt to develop color. The absorbance was read at 620 nm, and the relative absorbances are shown in Supplementary Figure 3 (Page S4).

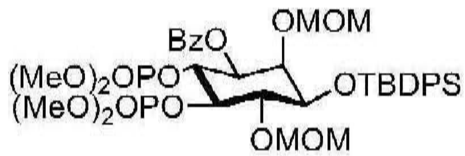
Sample	**Reaction buffer, μl**	**PTEN (20 ng/μl), μl**	**Substrate (1 mM), μl**	**Reaction volume, μl**
PTEN+PIP$_3$	17	5	3	25
PTEN+1b	17	5	3	25
PTEN+2b	17	5	3	25
Background 1	25	0	0	25
Background 2	20	5	0	25
Background 3	22	0	3 (**PIP$_3$**)	25
Background 4	22	0	3 (**1b**)	25
Background 5	22	0	3 (**2b**)	25



4

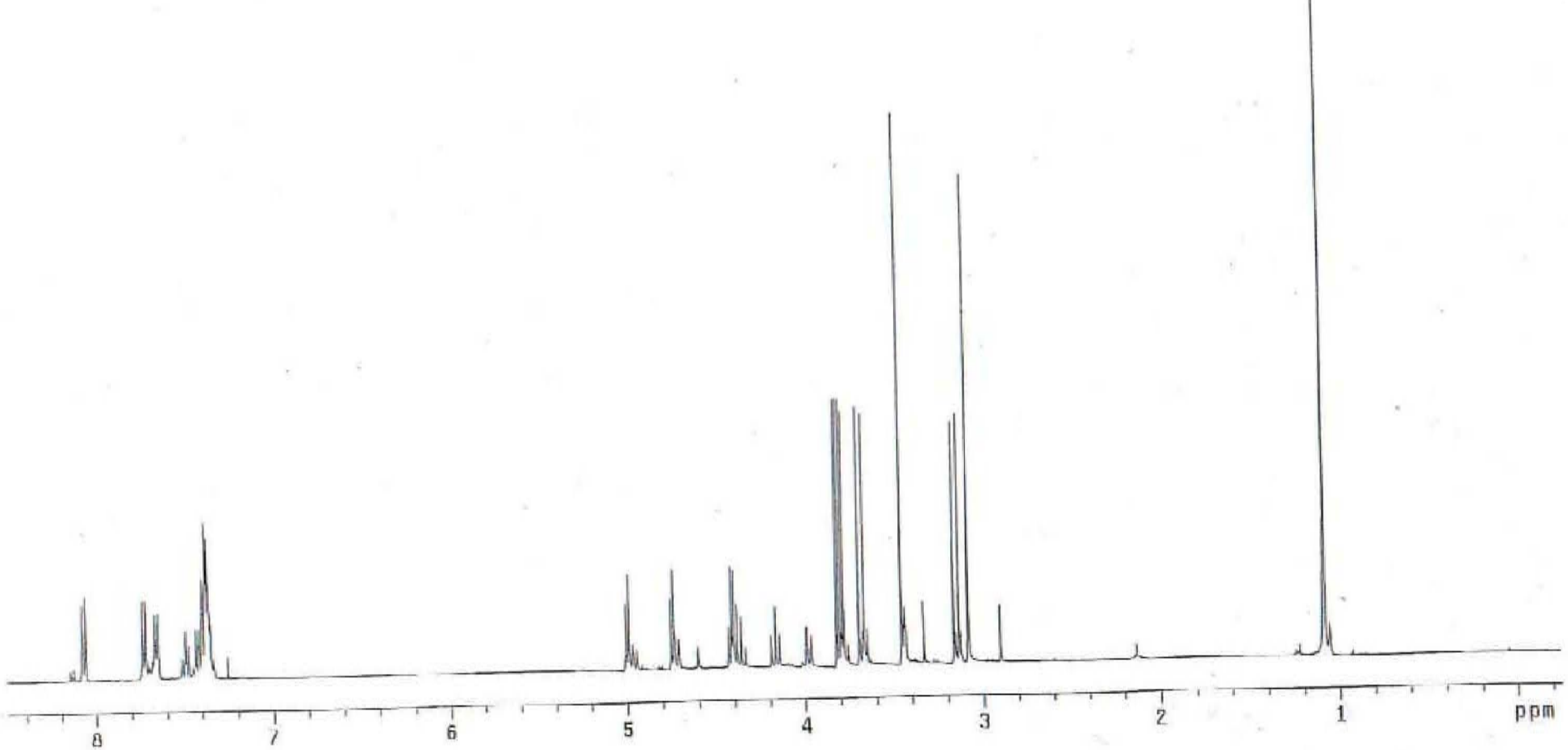
^{1}HNMR (400 MHz, $CDCl_3$)

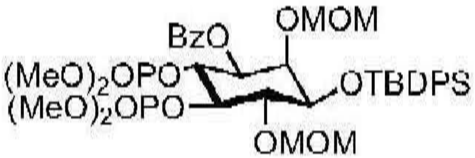

BzO
OMOM
OTBDPS
OMOM
Si
Si
O
4
13CNMR(101 MHz, CDCl3)
165.560
136.489
136.161
134.133
133.195
133.019
131.327
130.259
130.068
129.855
128.360
128.200
127.802
98.839
98.069
78.493
77.633
77.337
76.998
74.619
73.302
73.147
56.739
55.912
27.513
19.482
17.728
17.695
17.530
17.500
17.362
17.309
17.232
13.092
13.046
12.222
12.192
160
140
120
100
80
60
40
20
ppm



5

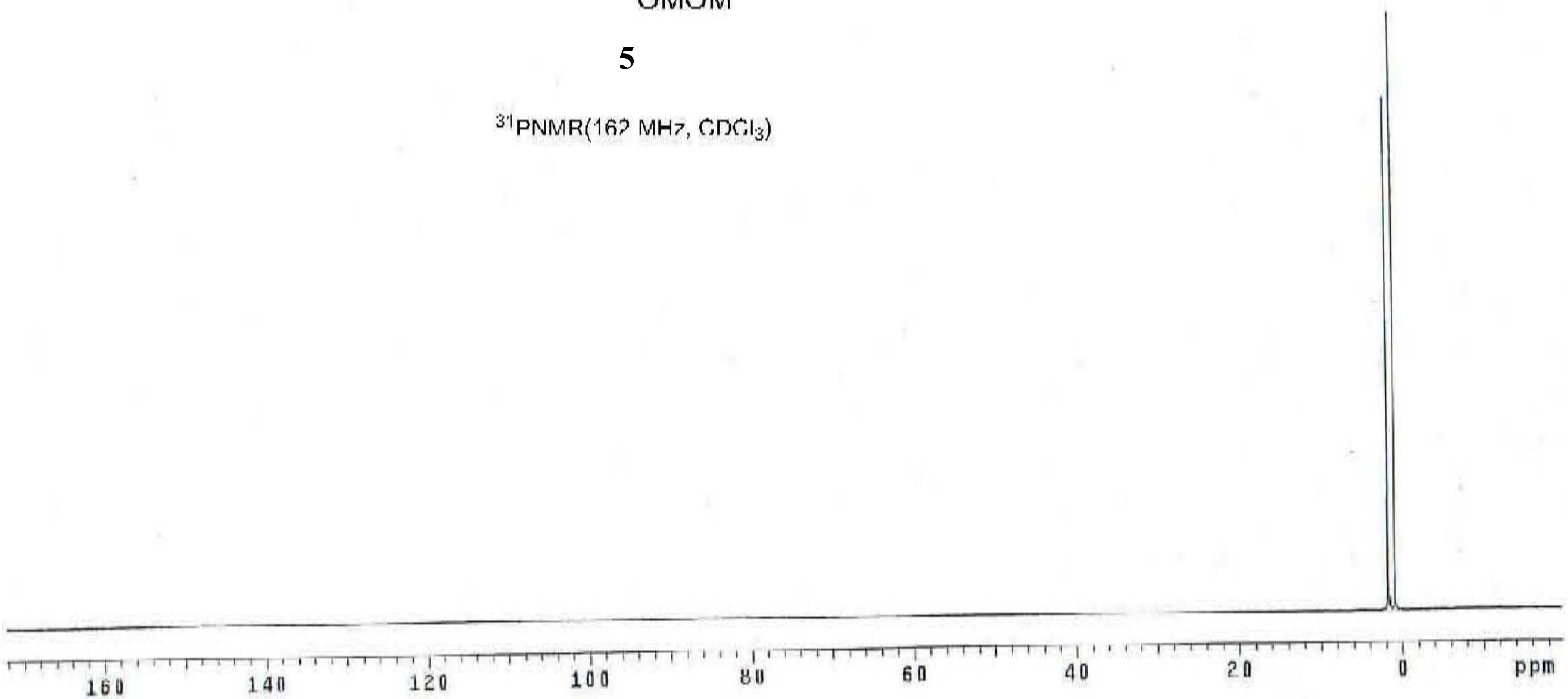
^{1}HNMR (400 MHz, $CDCl_3$)

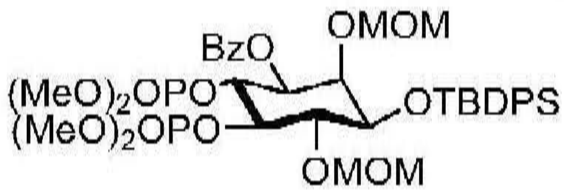




5

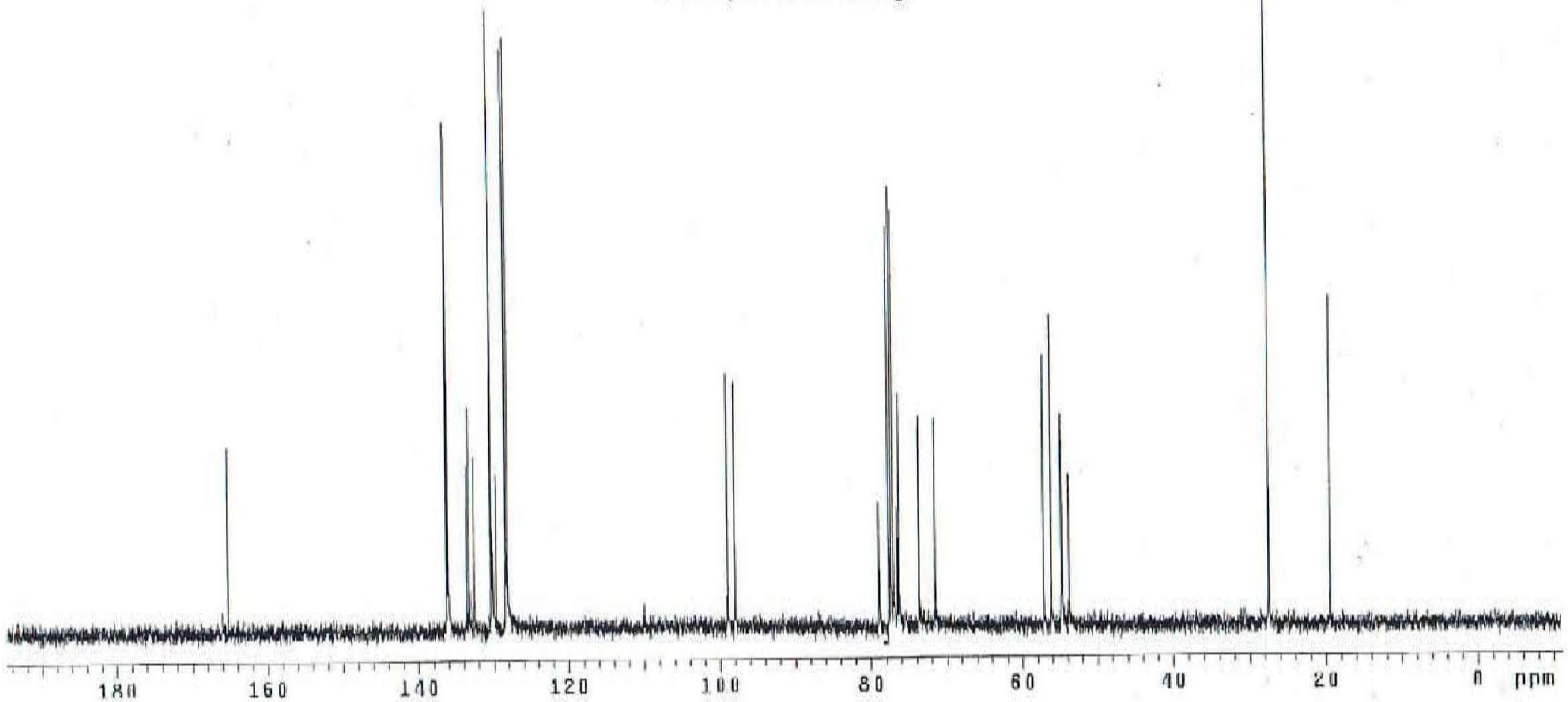
^{31}PNMR(162 MHz, CDCl$_3$)

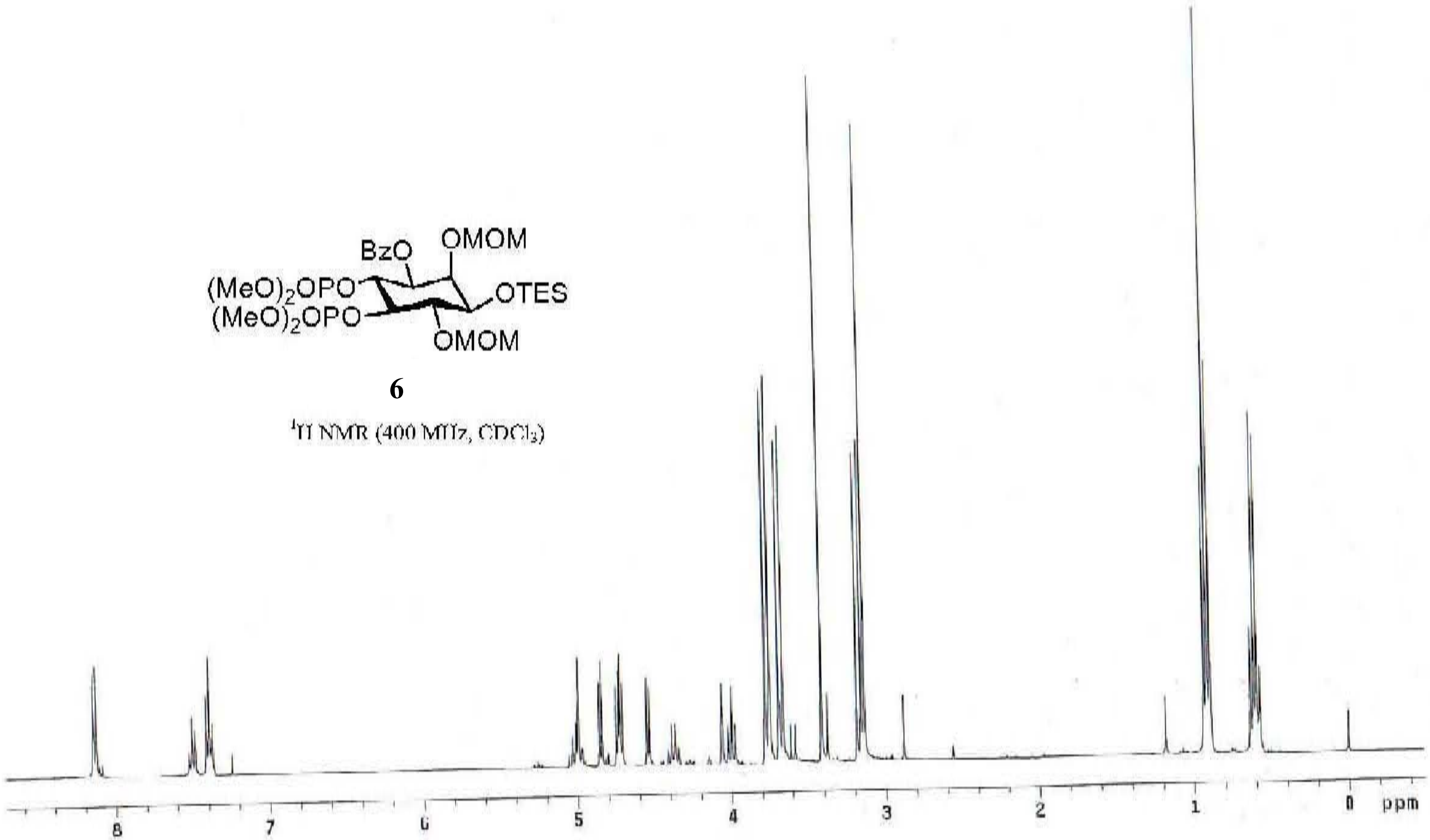




5

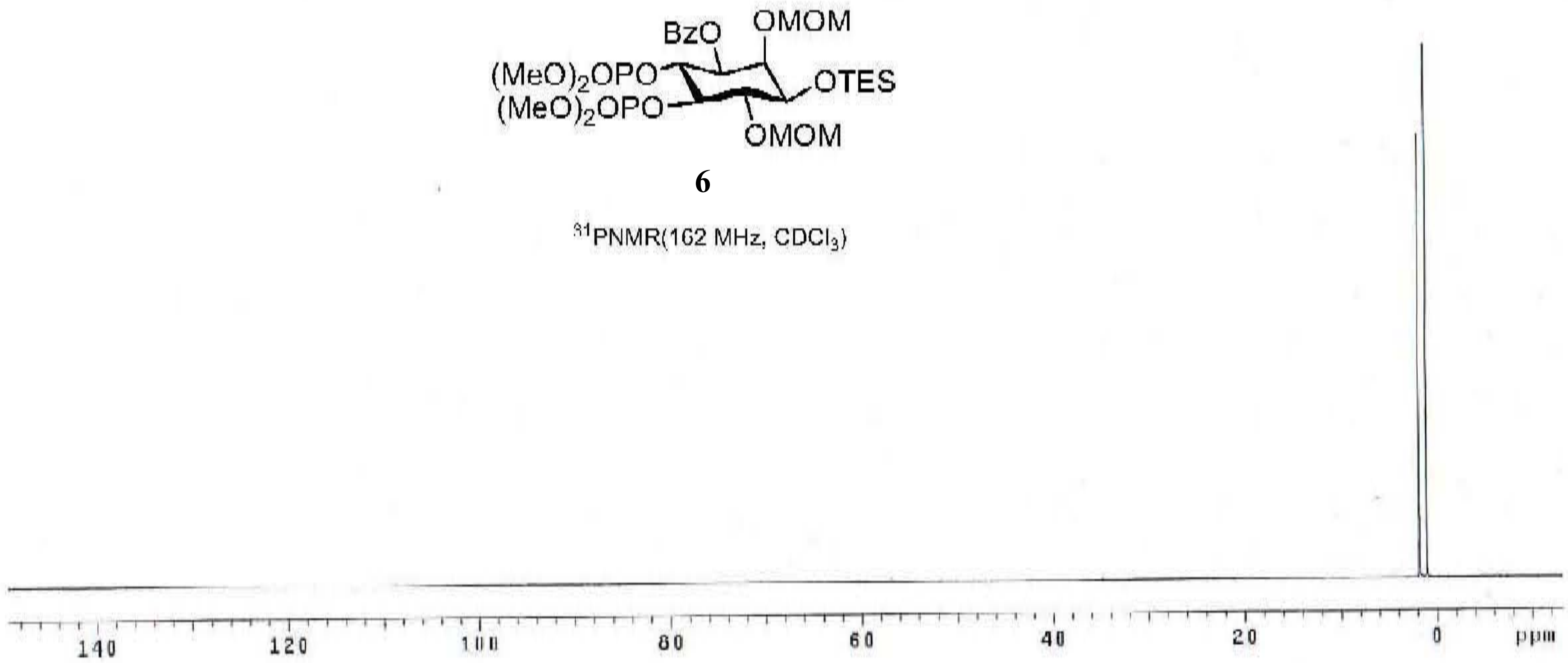
^{13}CNMR(101 MHz, $CDCl_3$)





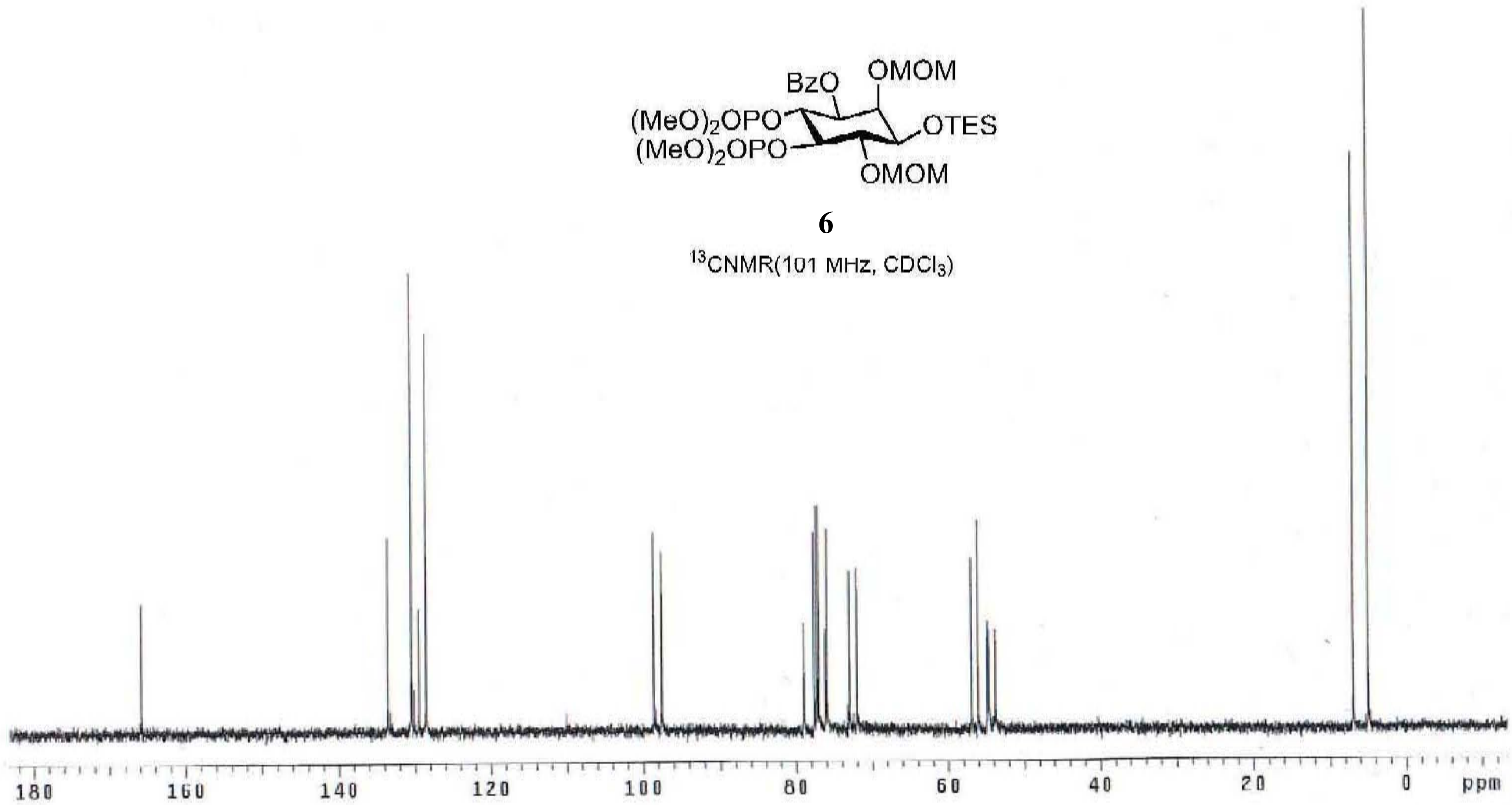
6

^1H NMR (400 MHz, $CDCl_3$)



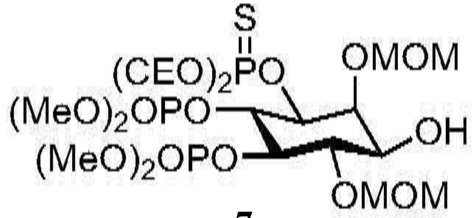
6

^{31}PNMR(162 MHz, $CDCl_3$)



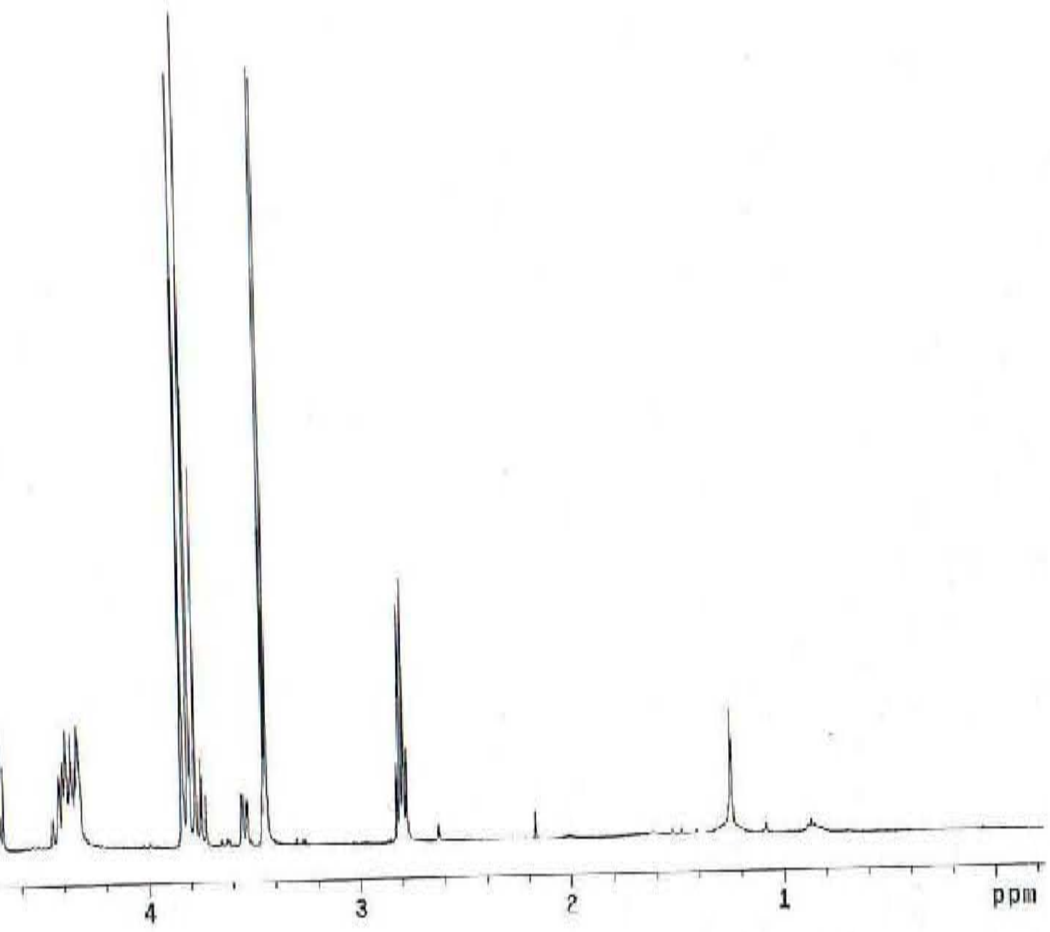
6

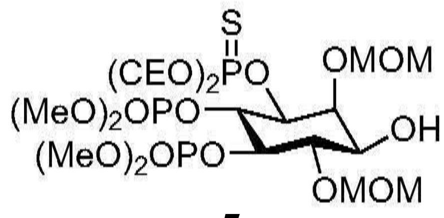
^{13}CNMR(101 MHz, $CDCl_3$)



7

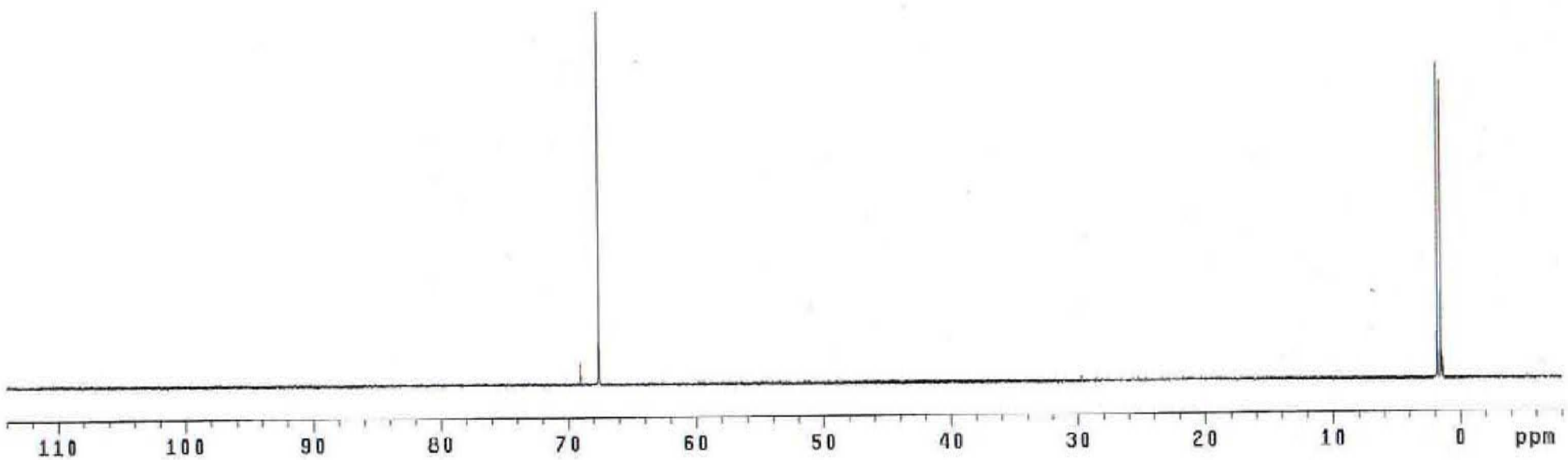
^{1}HNMR (400 MHz, $CDCl_3$)

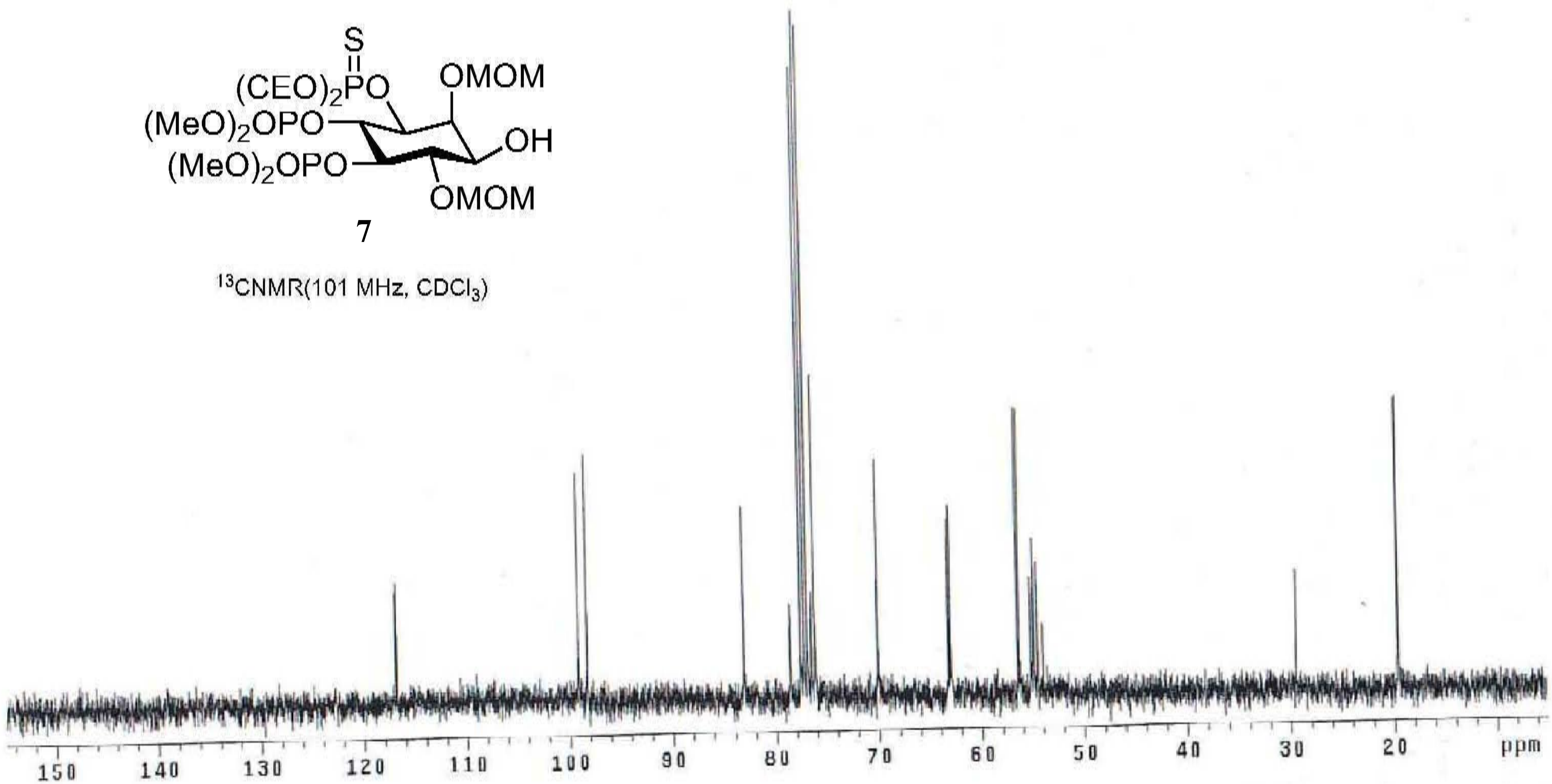




7

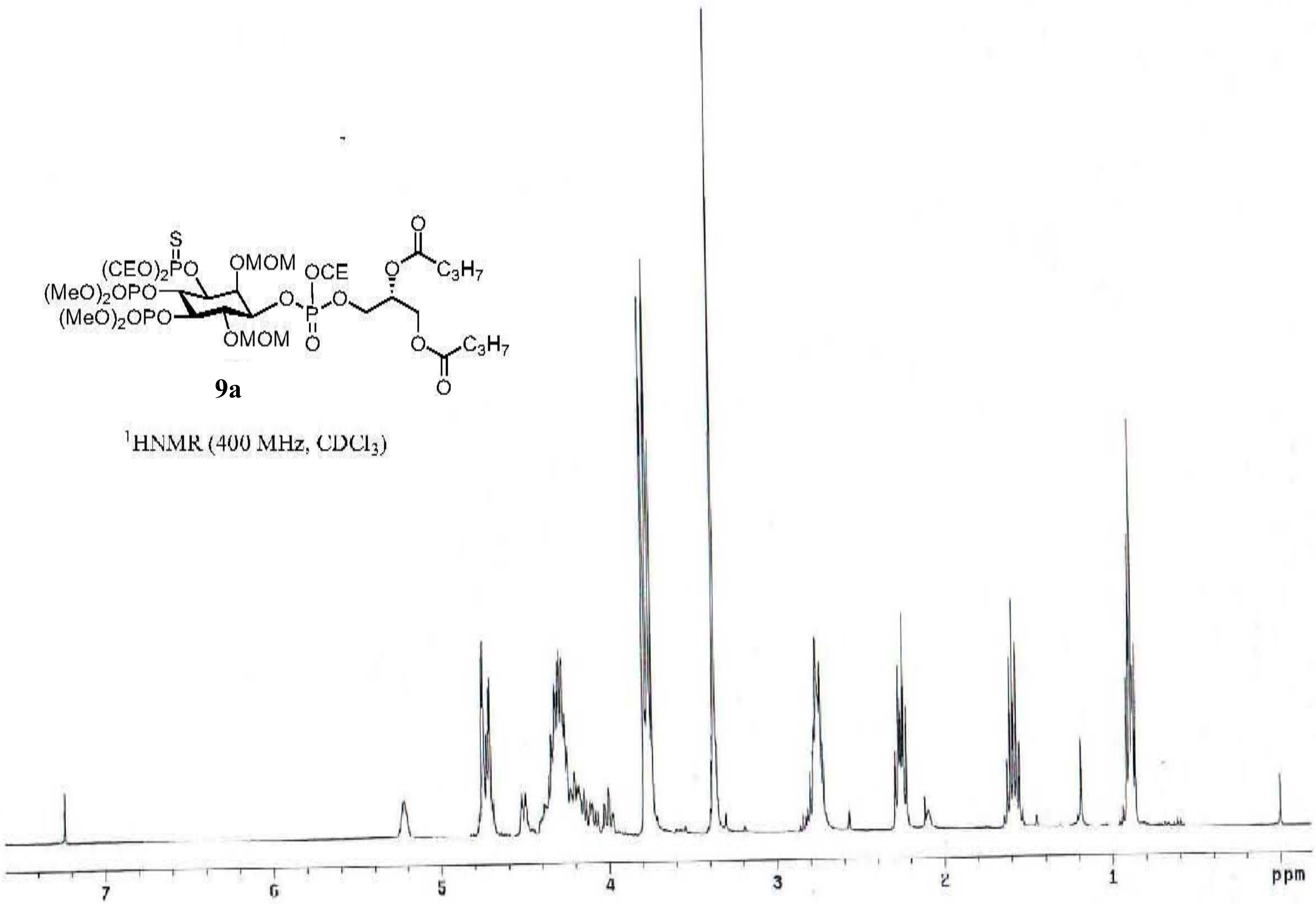
^{31}PNMR(162 MHz, $CDCl_3$)





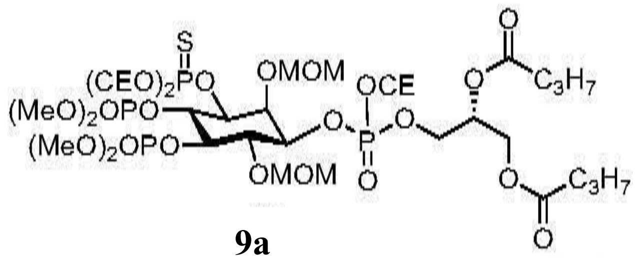
7

^{13}CNMR(101 MHz, $CDCl_3$)



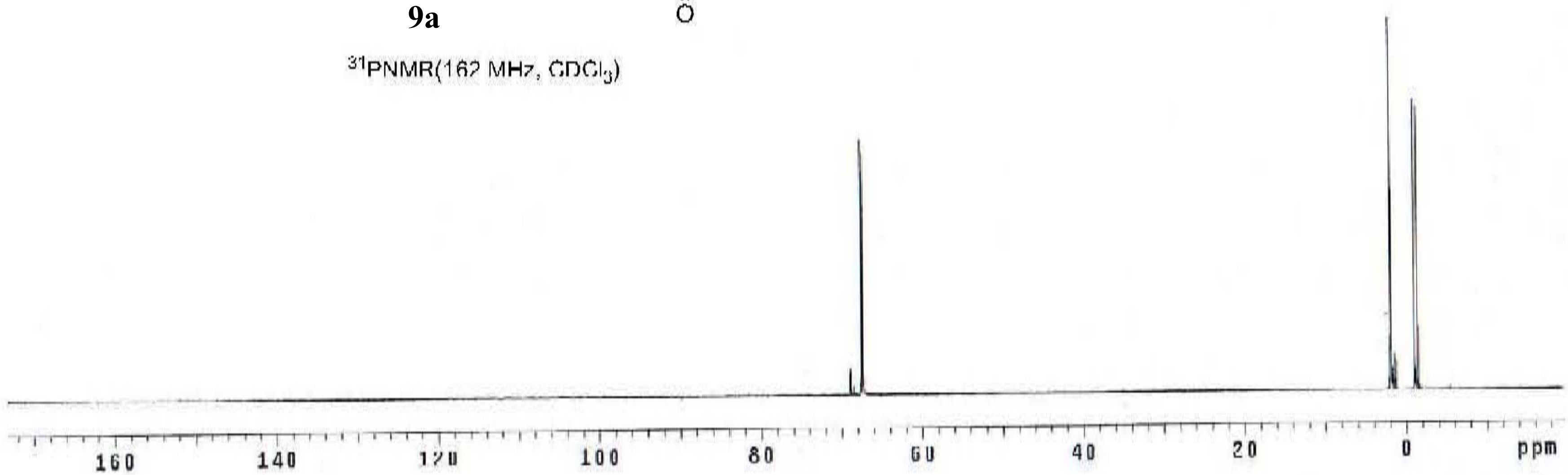
9a

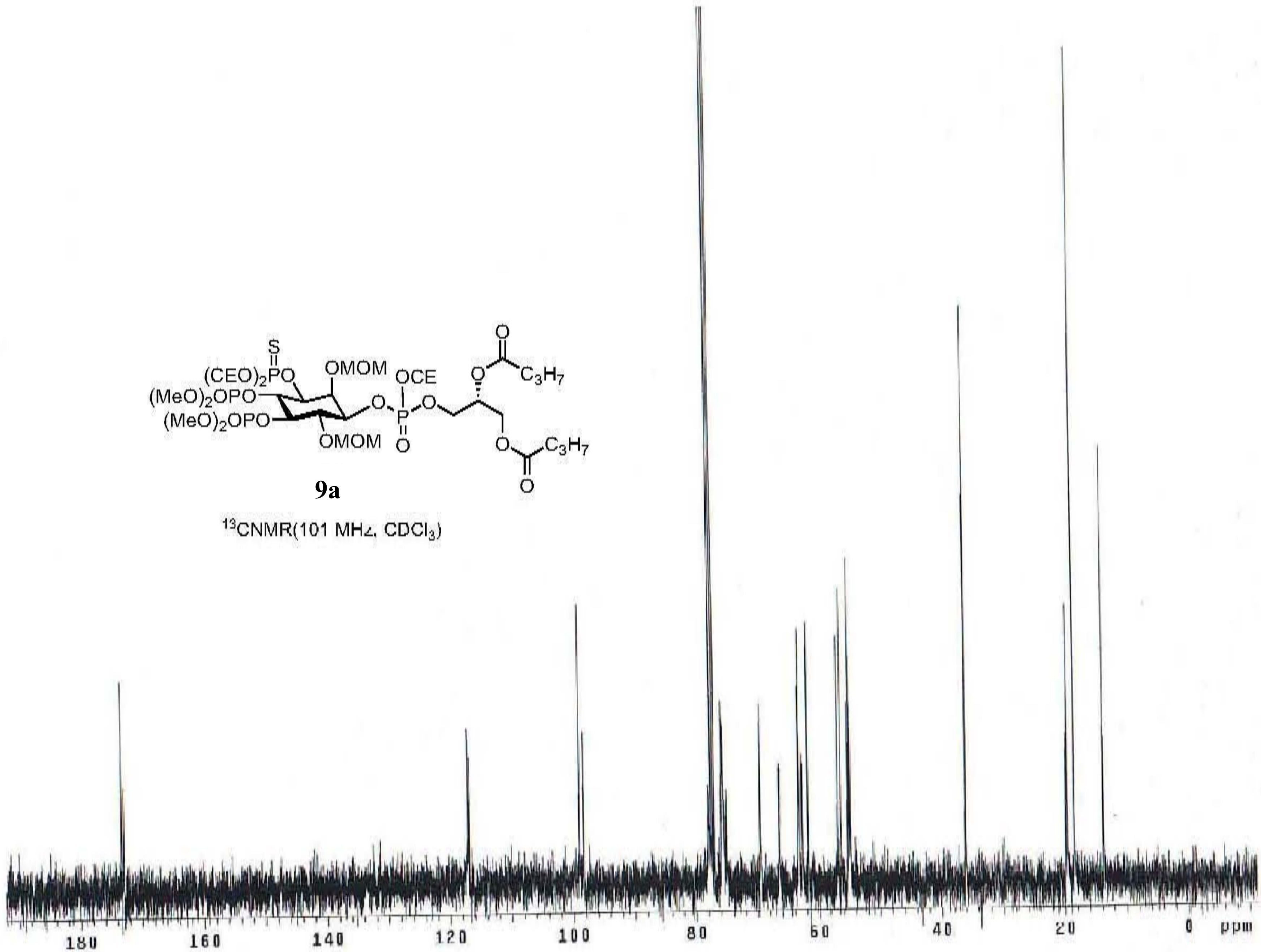
[1]HNMR (400 MHz, $CDCl_3$)



9a

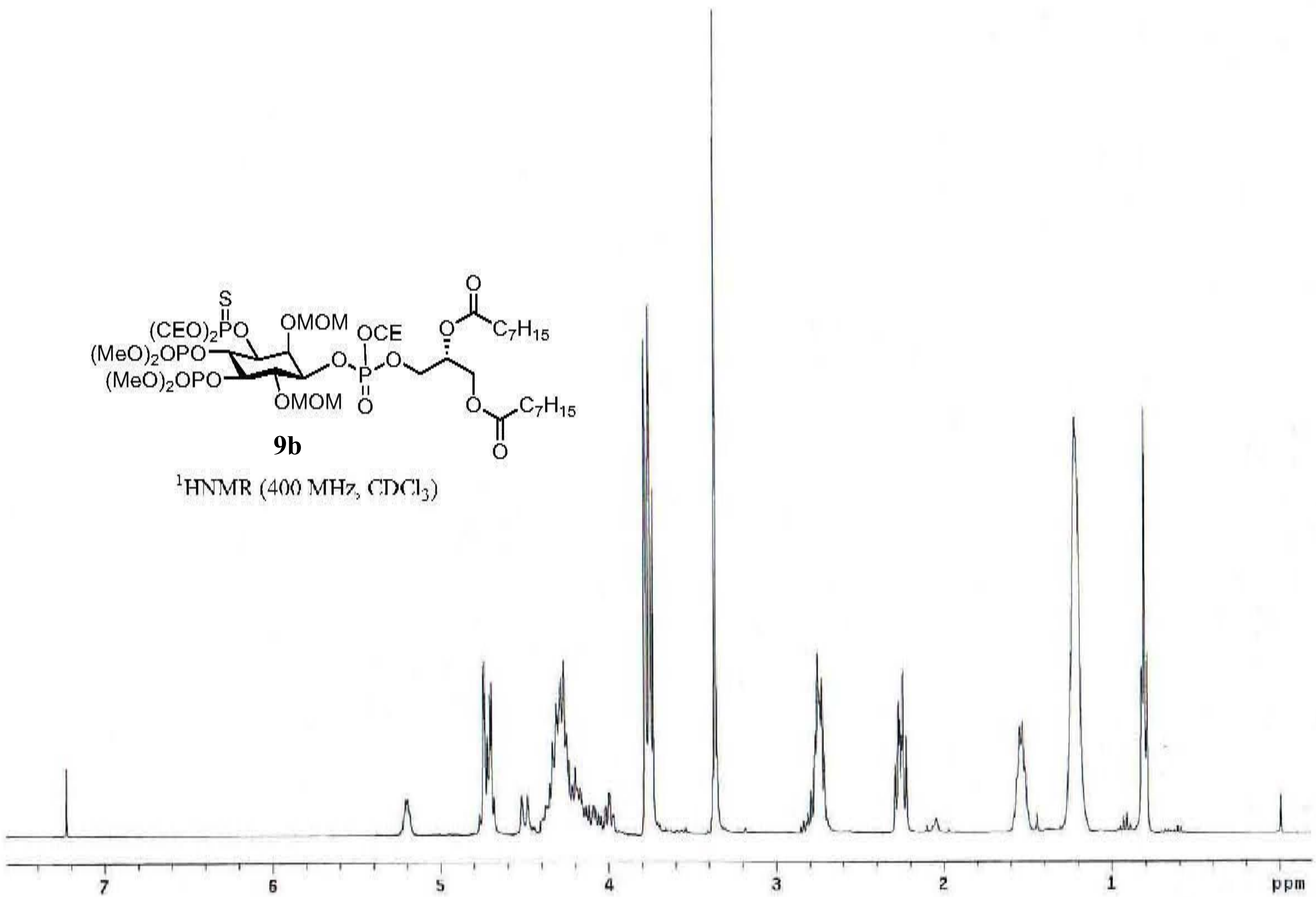
^{31}PNMR(162 MHz, CDCl$_3$)





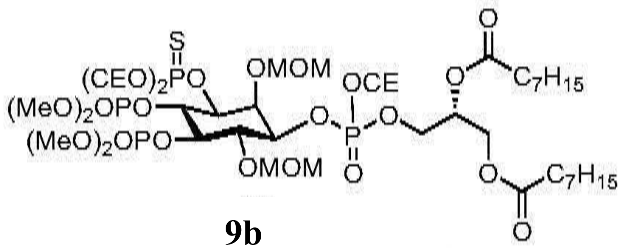
9a

^{13}CNMR(101 MHz, $CDCl_3$)



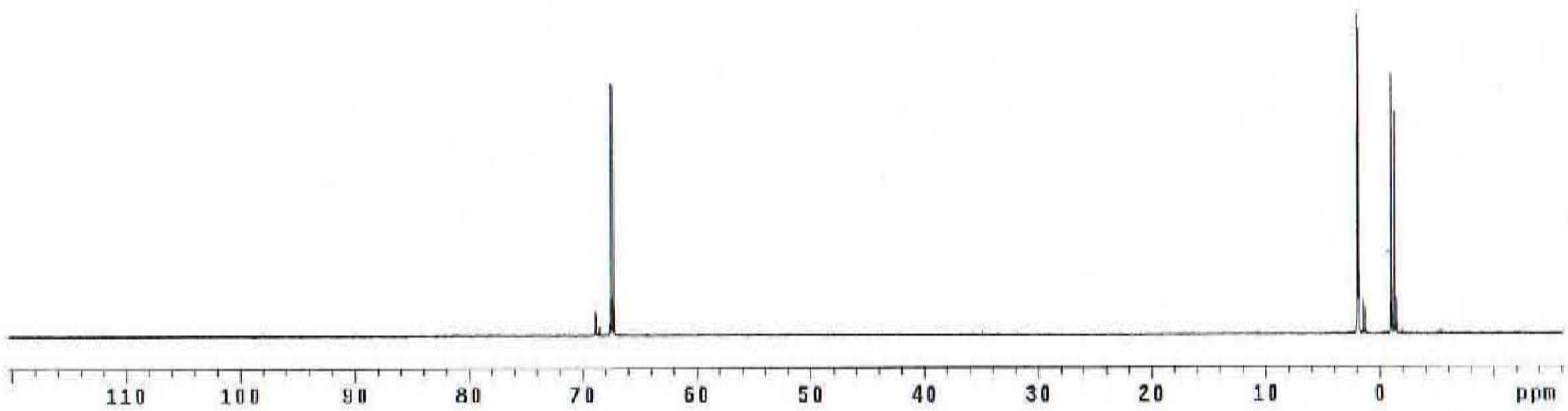
9b

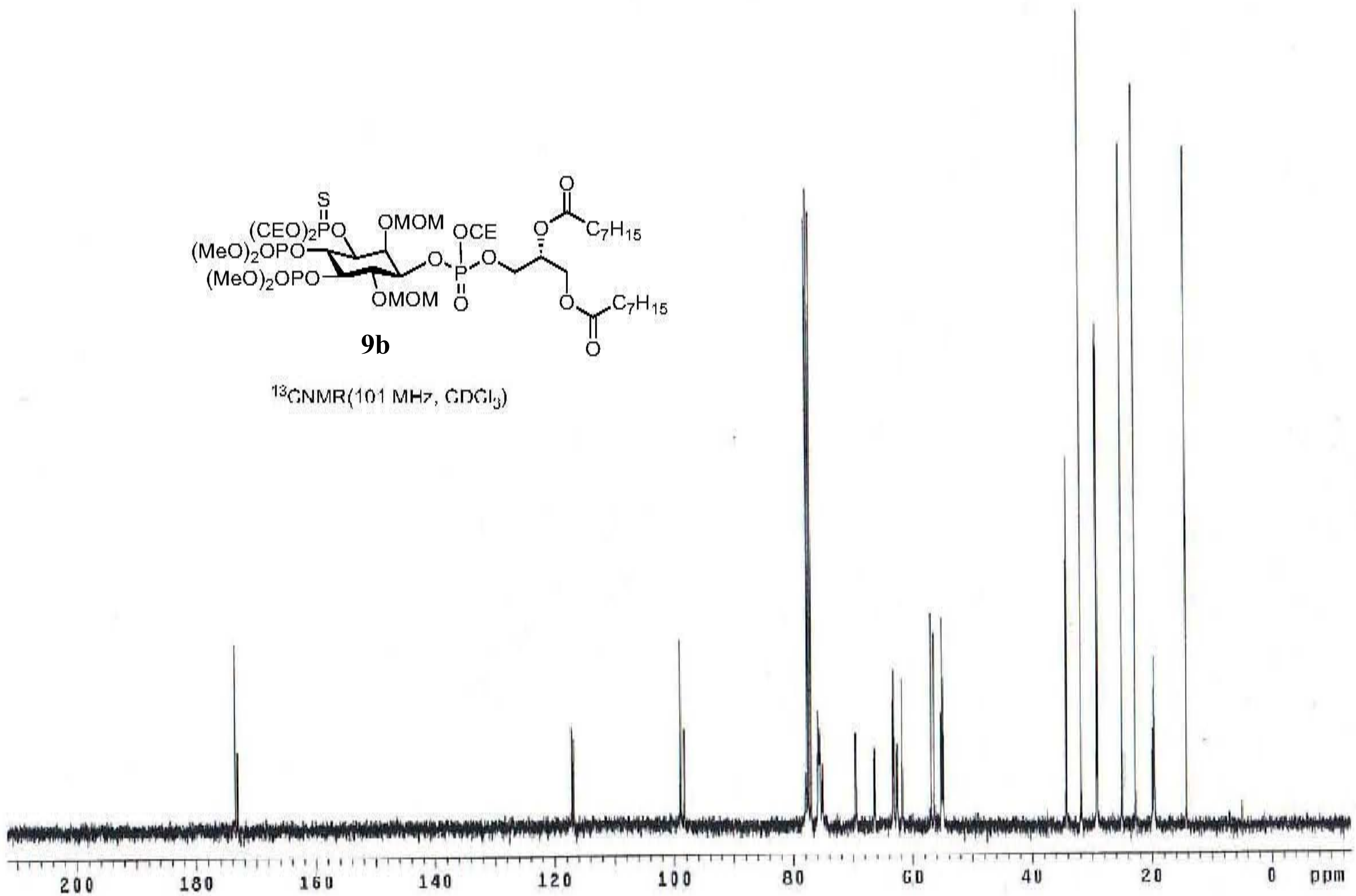
^{1}HNMR (400 MHz, CDCl$_3$)



9b

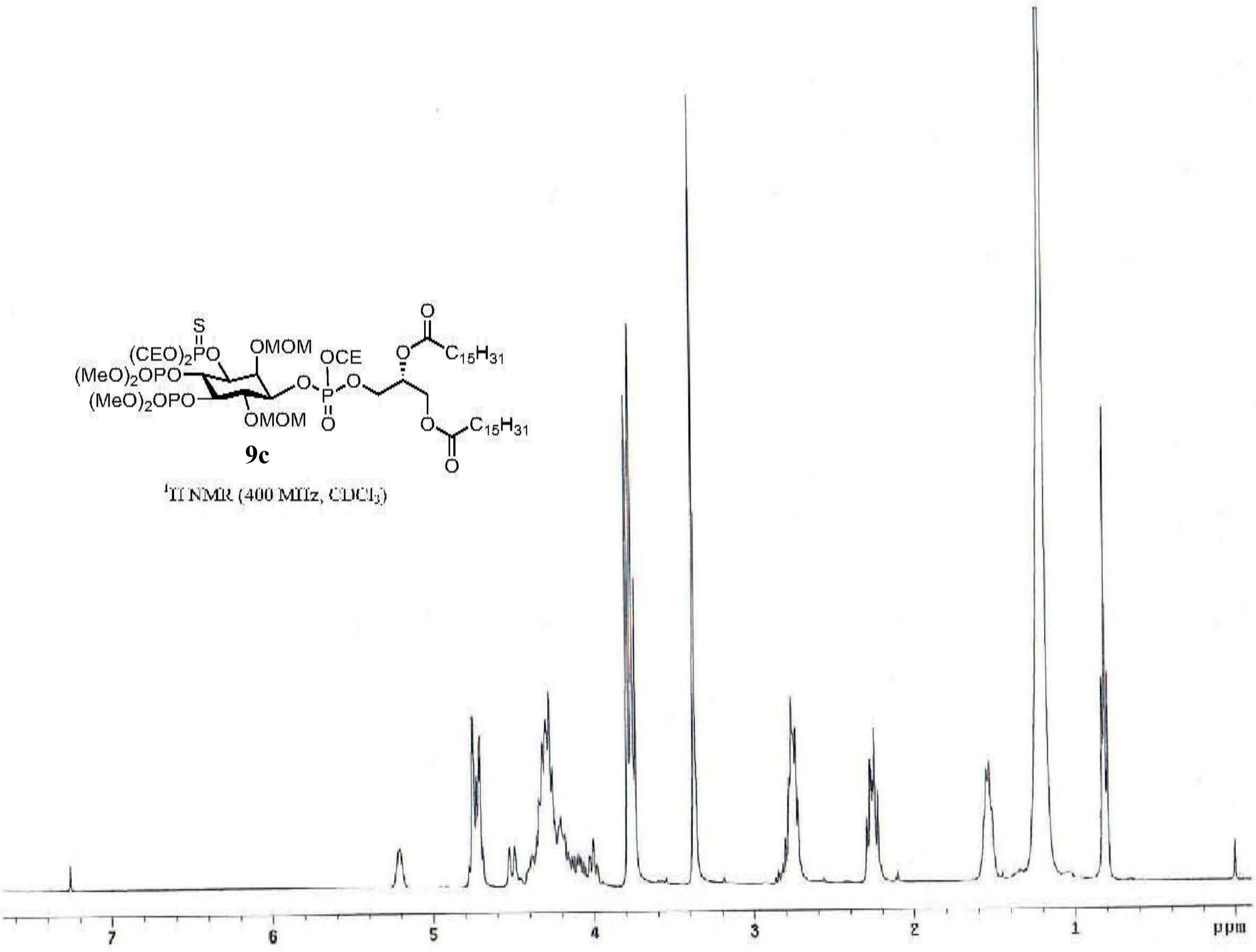
^{31}PNMR(162 MHz, $CDCl_3$)





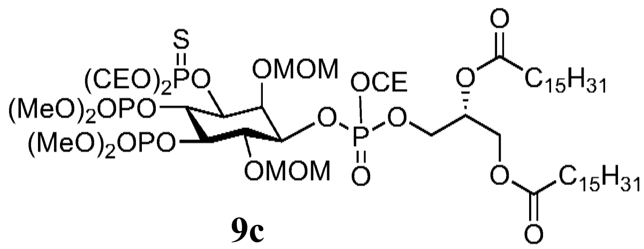
9b

^{13}CNMR(101 MHz, CDCl$_3$)



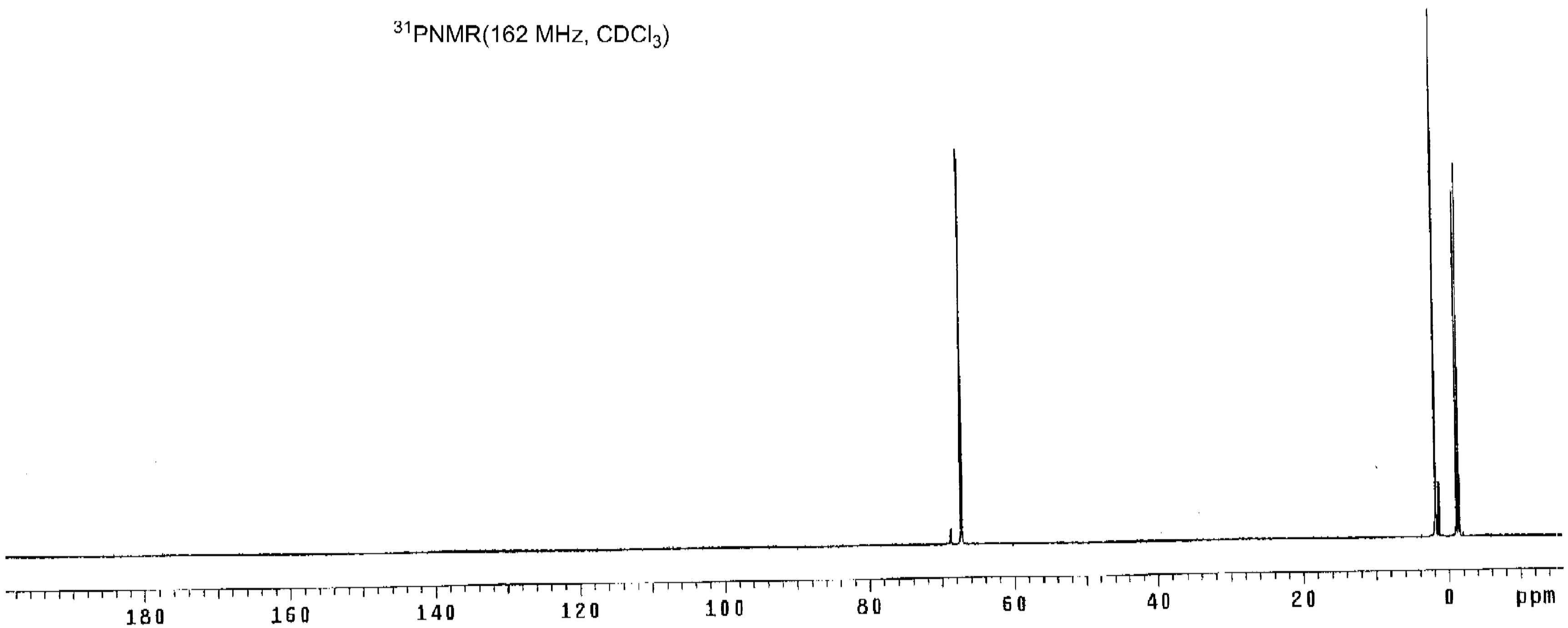
9c

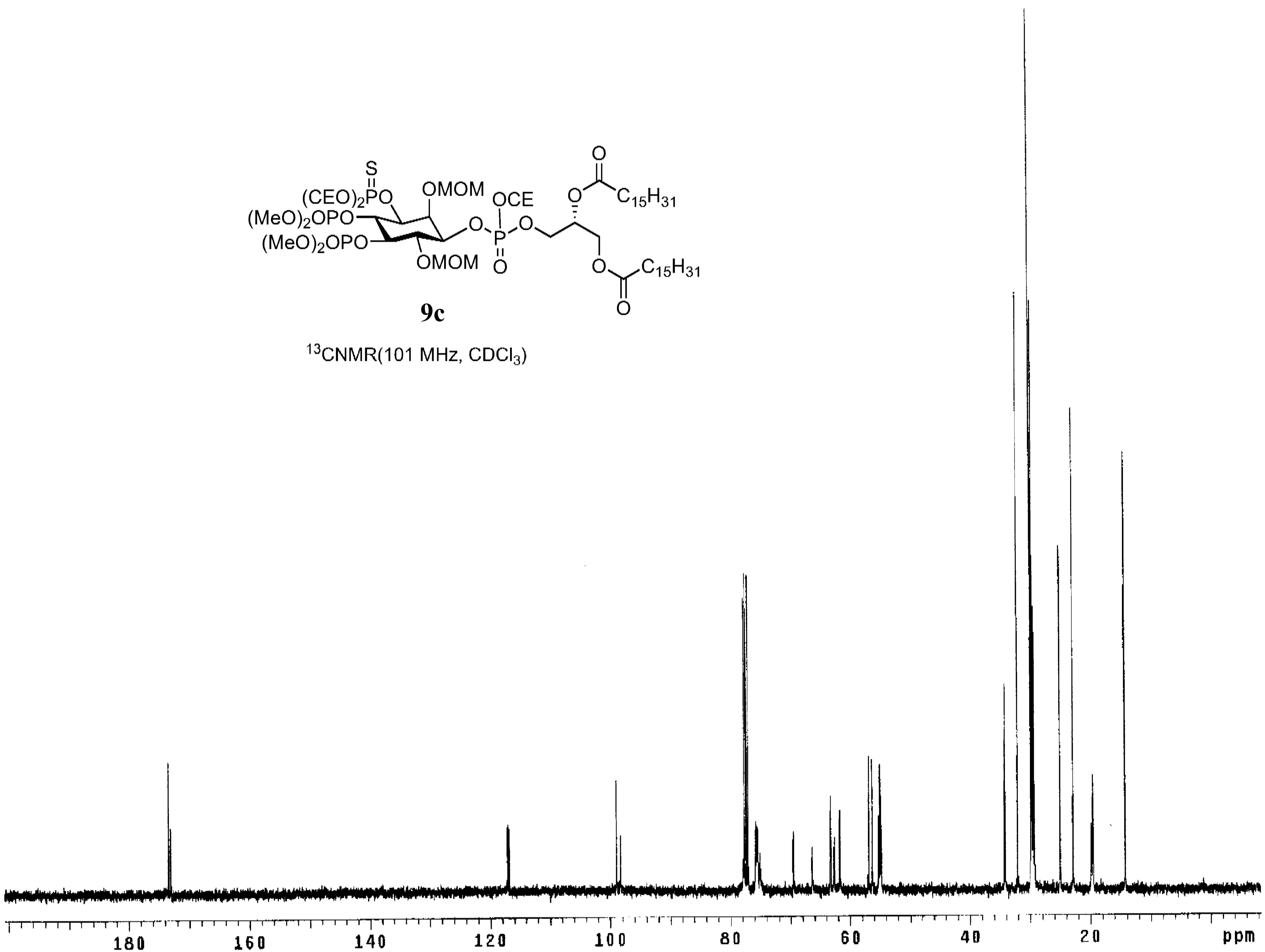
^{1}H NMR (400 MHz, $CDCl_3$)



9c

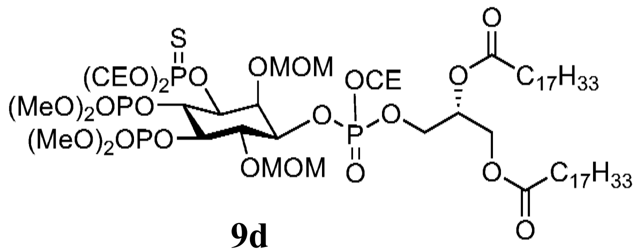
^{31}PNMR(162 MHz, $CDCl_3$)





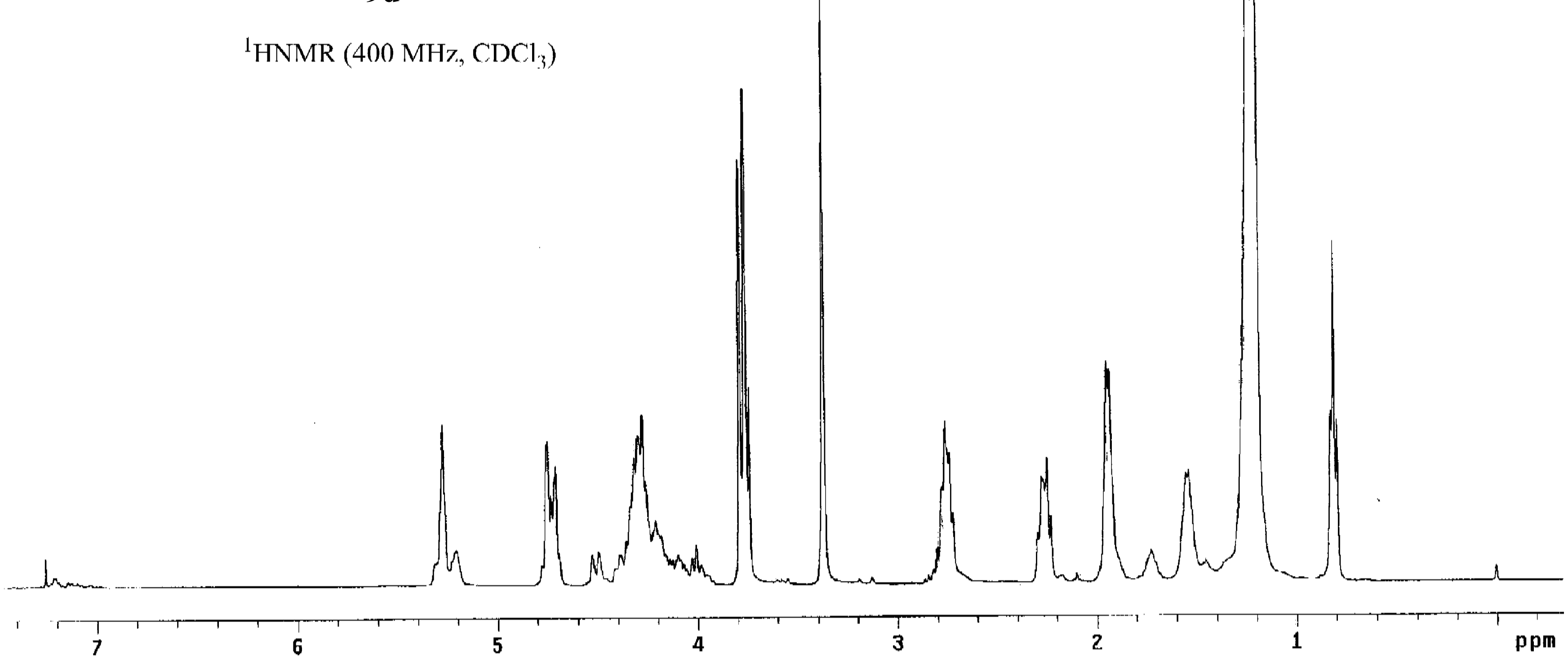
9c

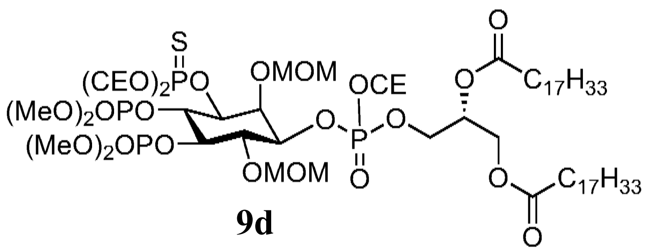
^{13}CNMR(101 MHz, $CDCl_3$)



9d

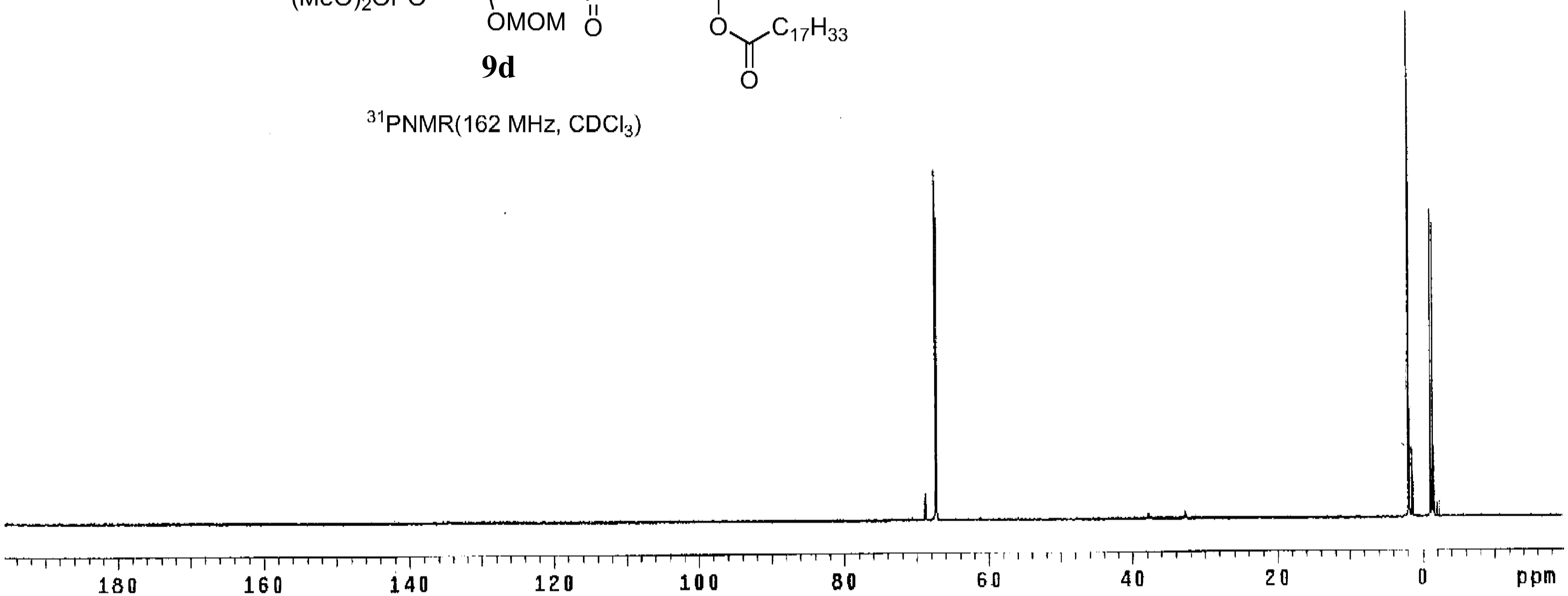
^{1}HNMR (400 MHz, $CDCl_3$)

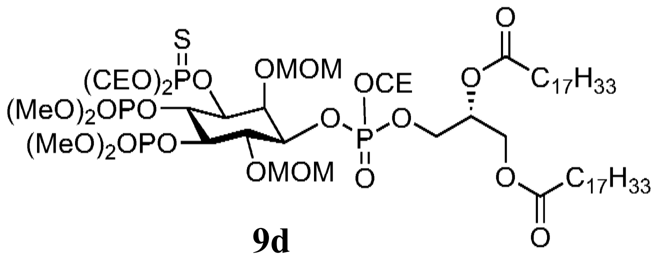




9d

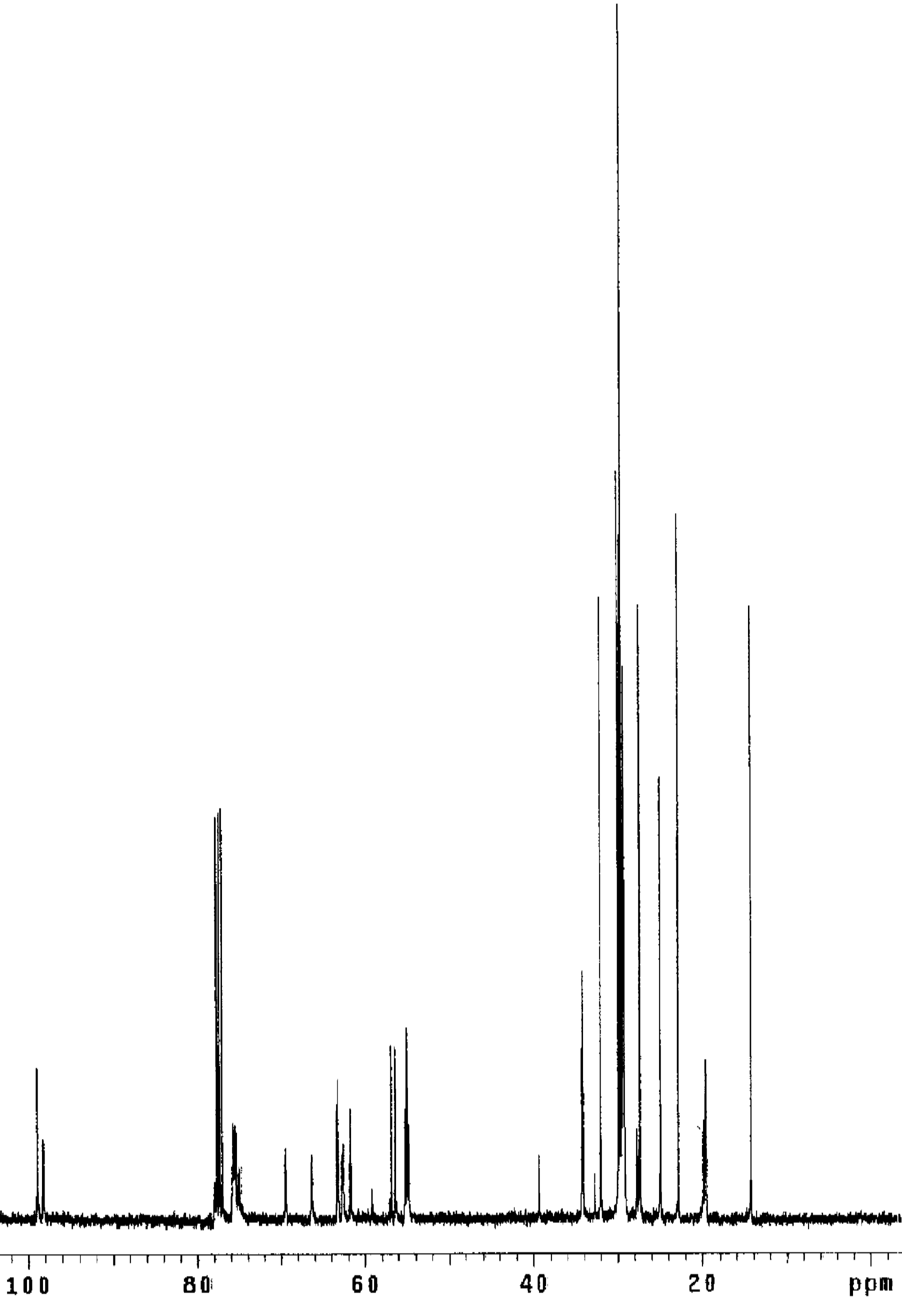
^{31}PNMR(162 MHz, $CDCl_3$)

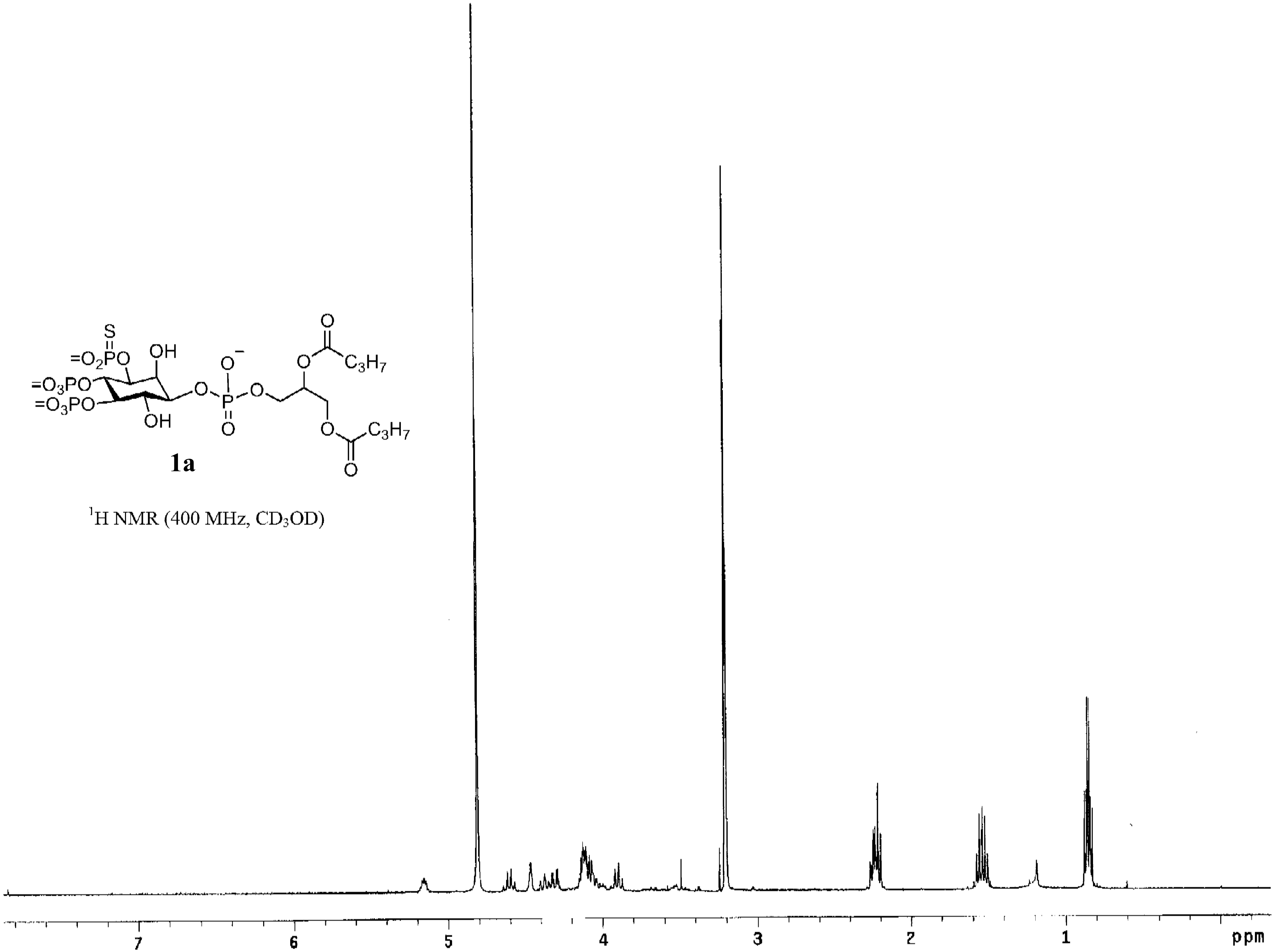




9d

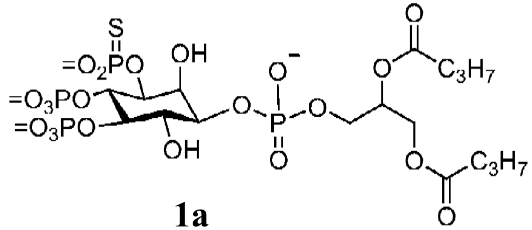
^{13}CNMR(101 MHz, $CDCl_3$)





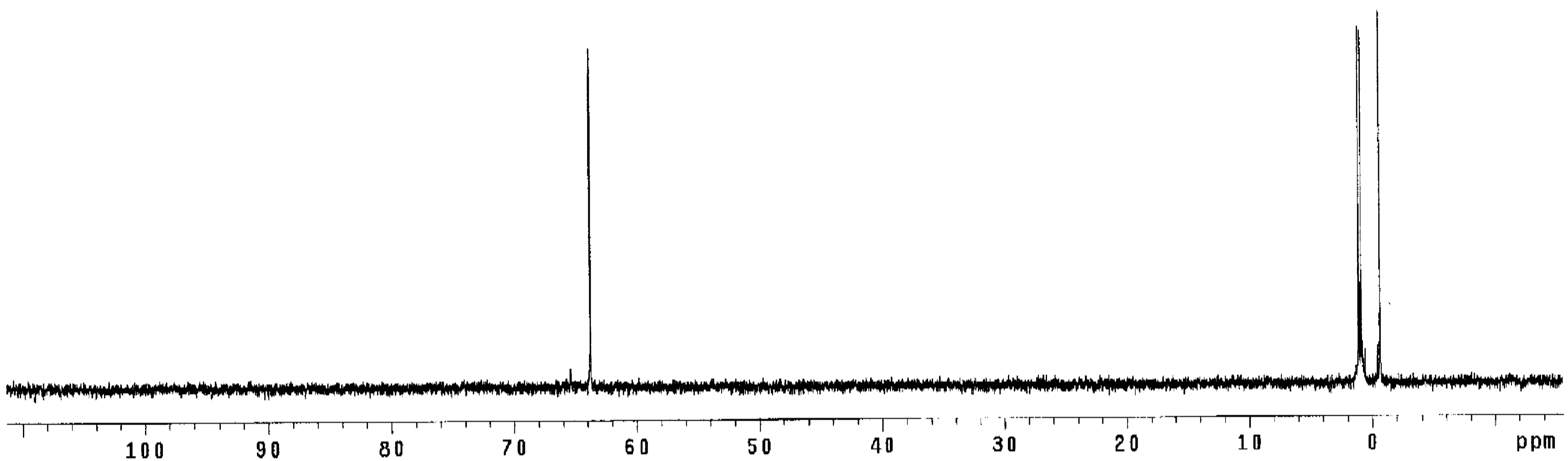
1a

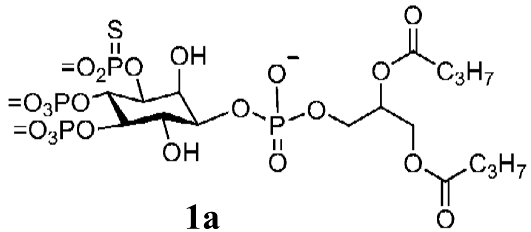
^{1}H NMR (400 MHz, CD_3OD)



1a

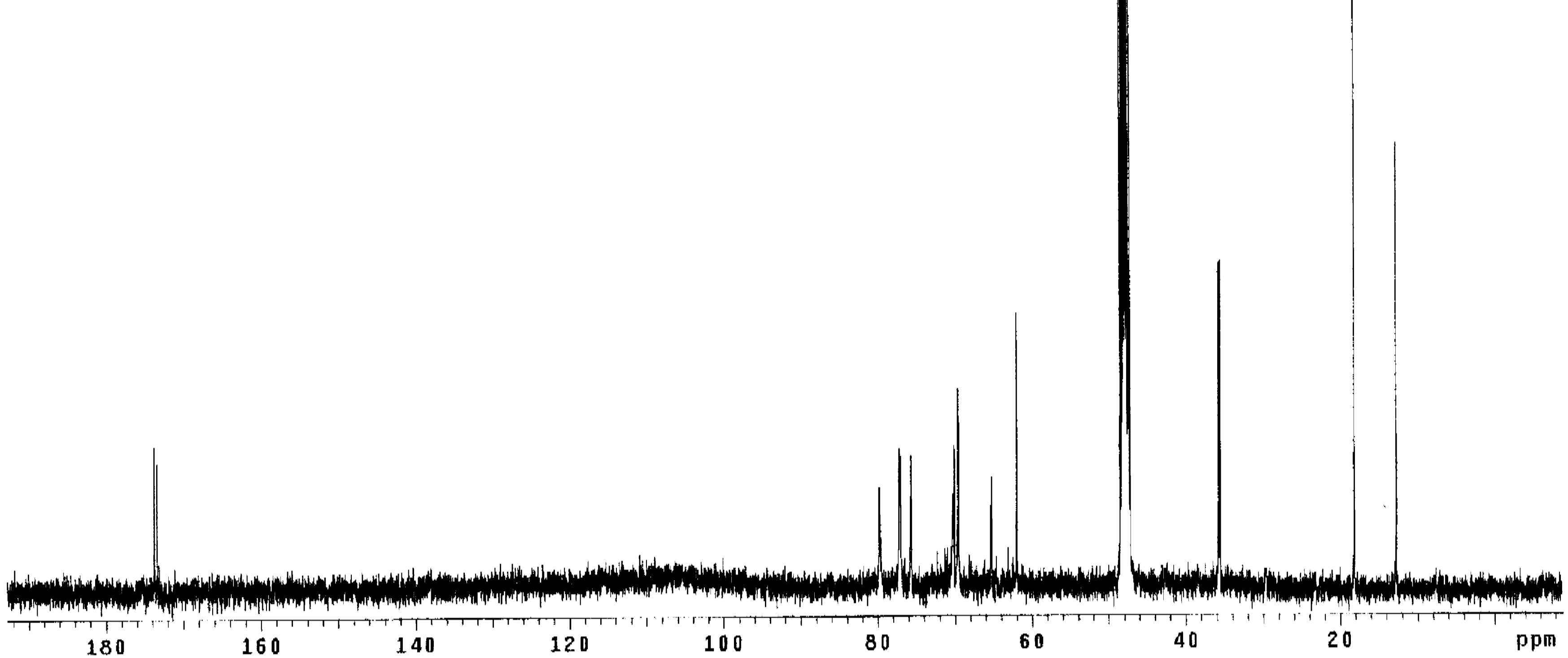
^{31}P NMR (162 MHz, CD_3OD)

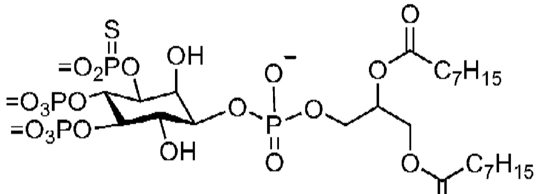




1a

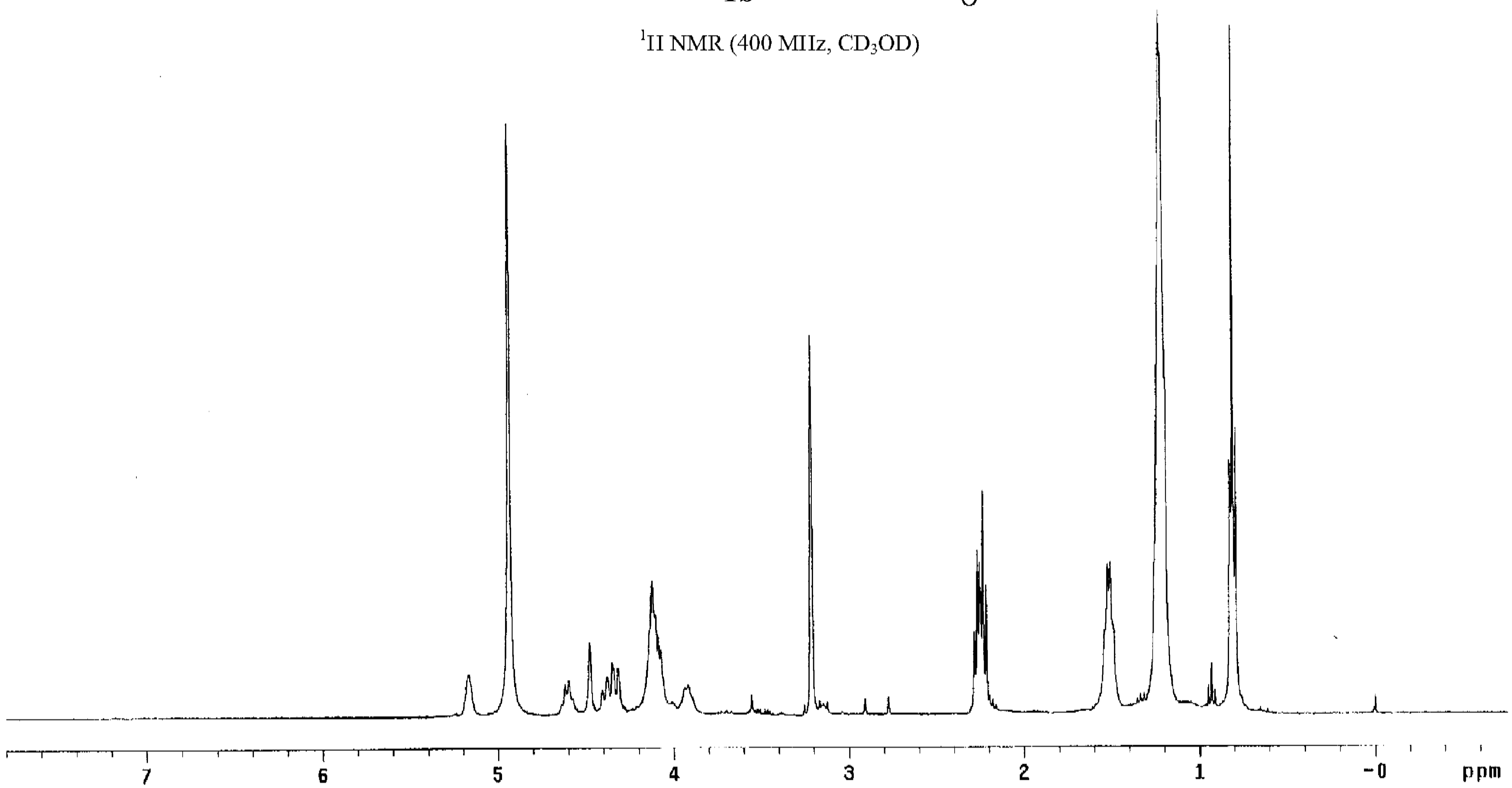
^{13}C NMR (400 MHz, CD_3OD)

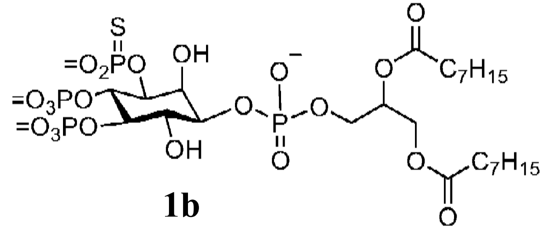




1b

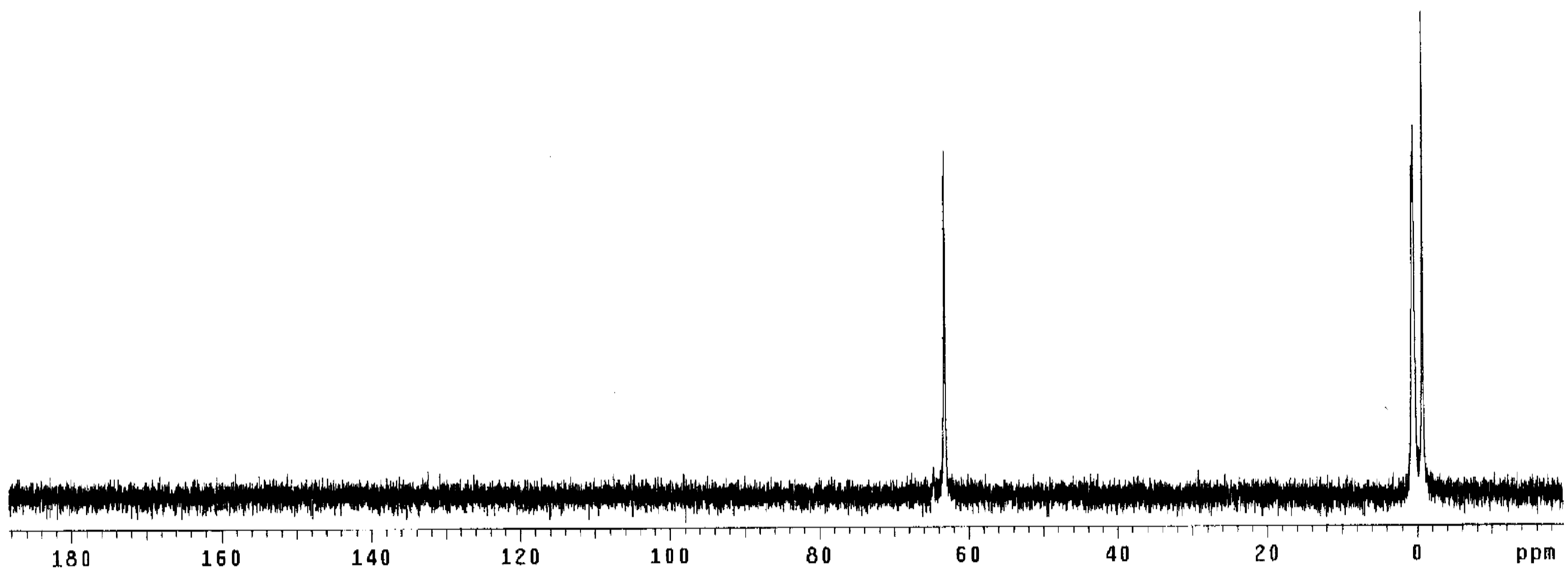
^{1}H NMR (400 MHz, CD_3OD)

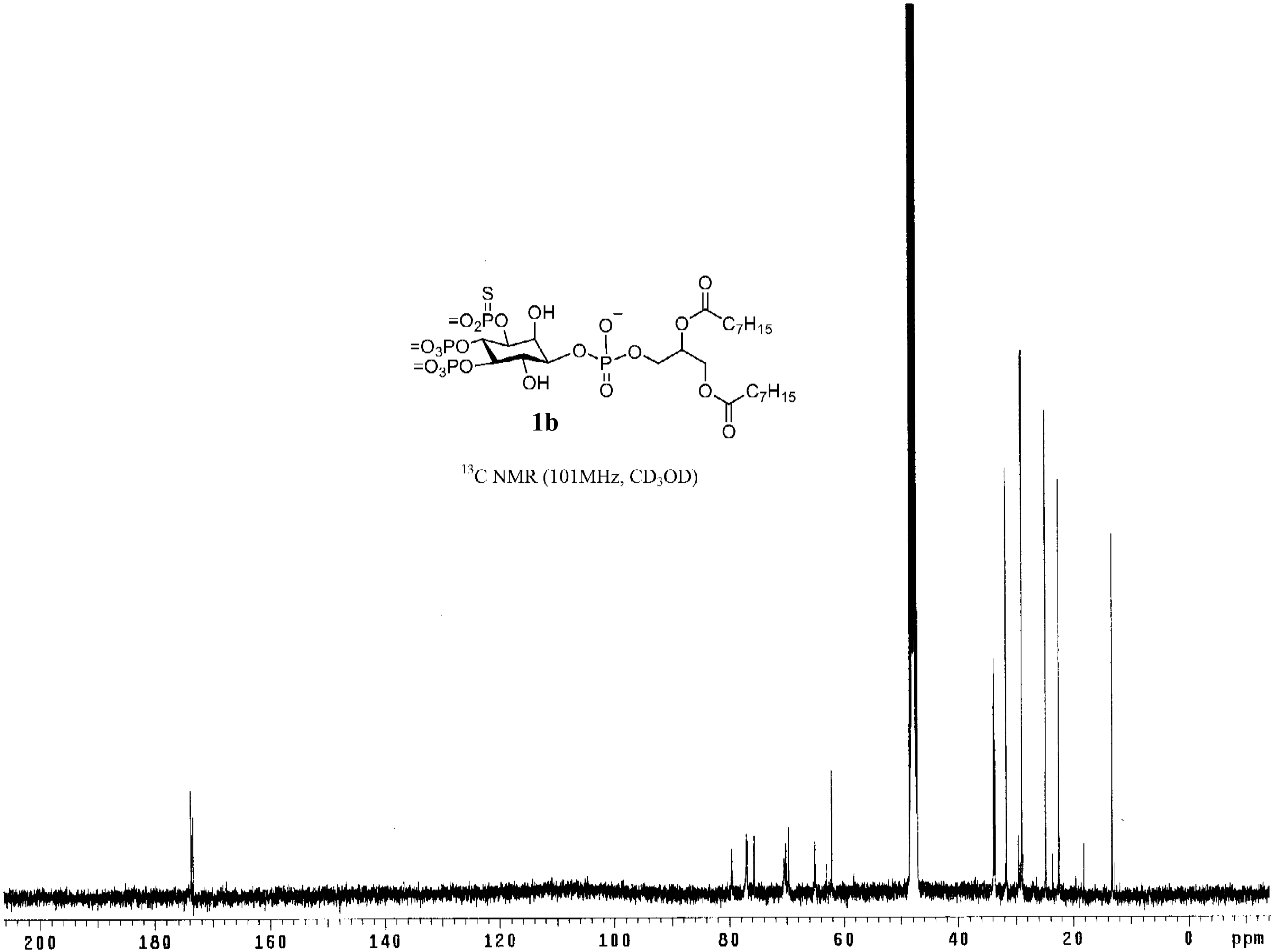




1b

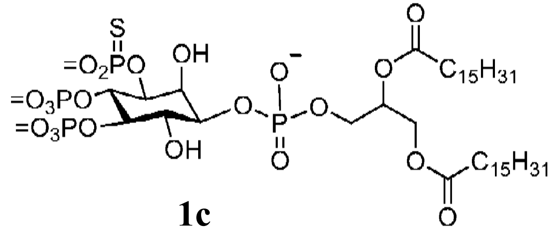
^{31}P NMR (162 MHz, CD_3OD)





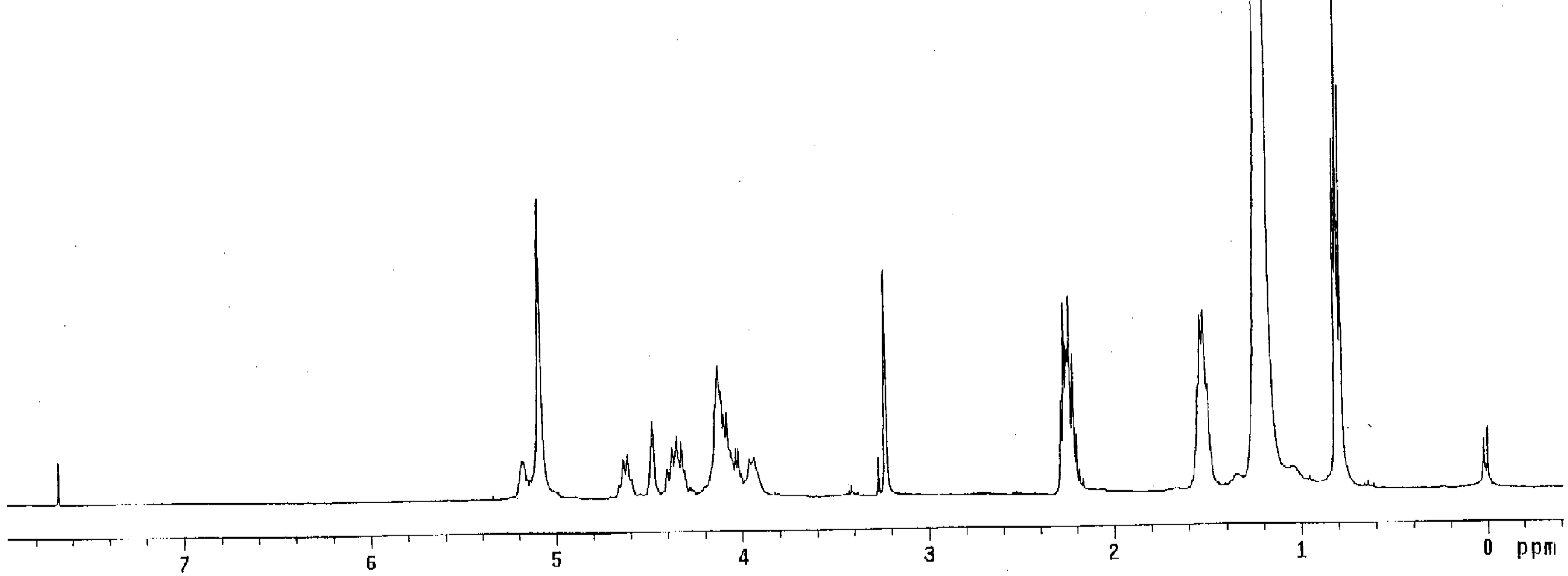
1b

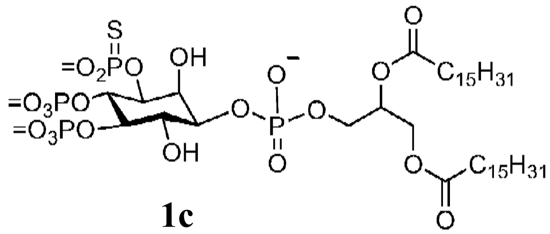
^{13}C NMR (101MHz, CD_3OD)



1c

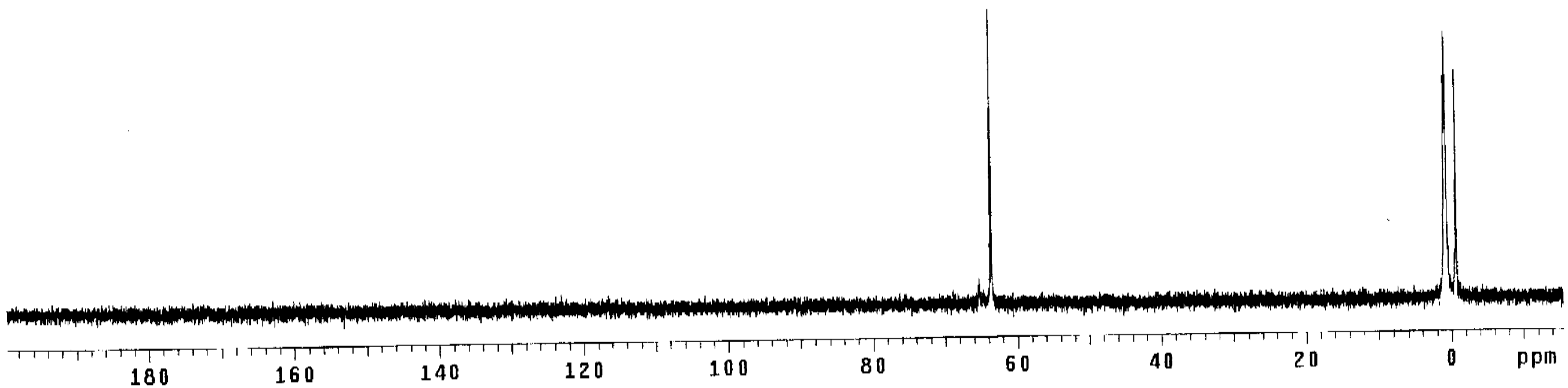
[1]H NMR (400 MHz, $CD_3OD/CDCl_3$ – 3:1)

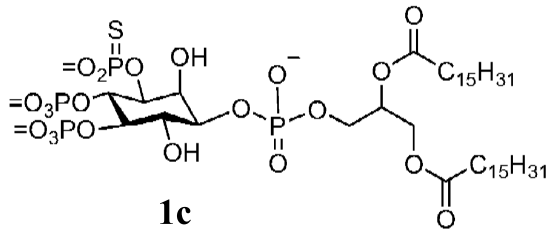




1c

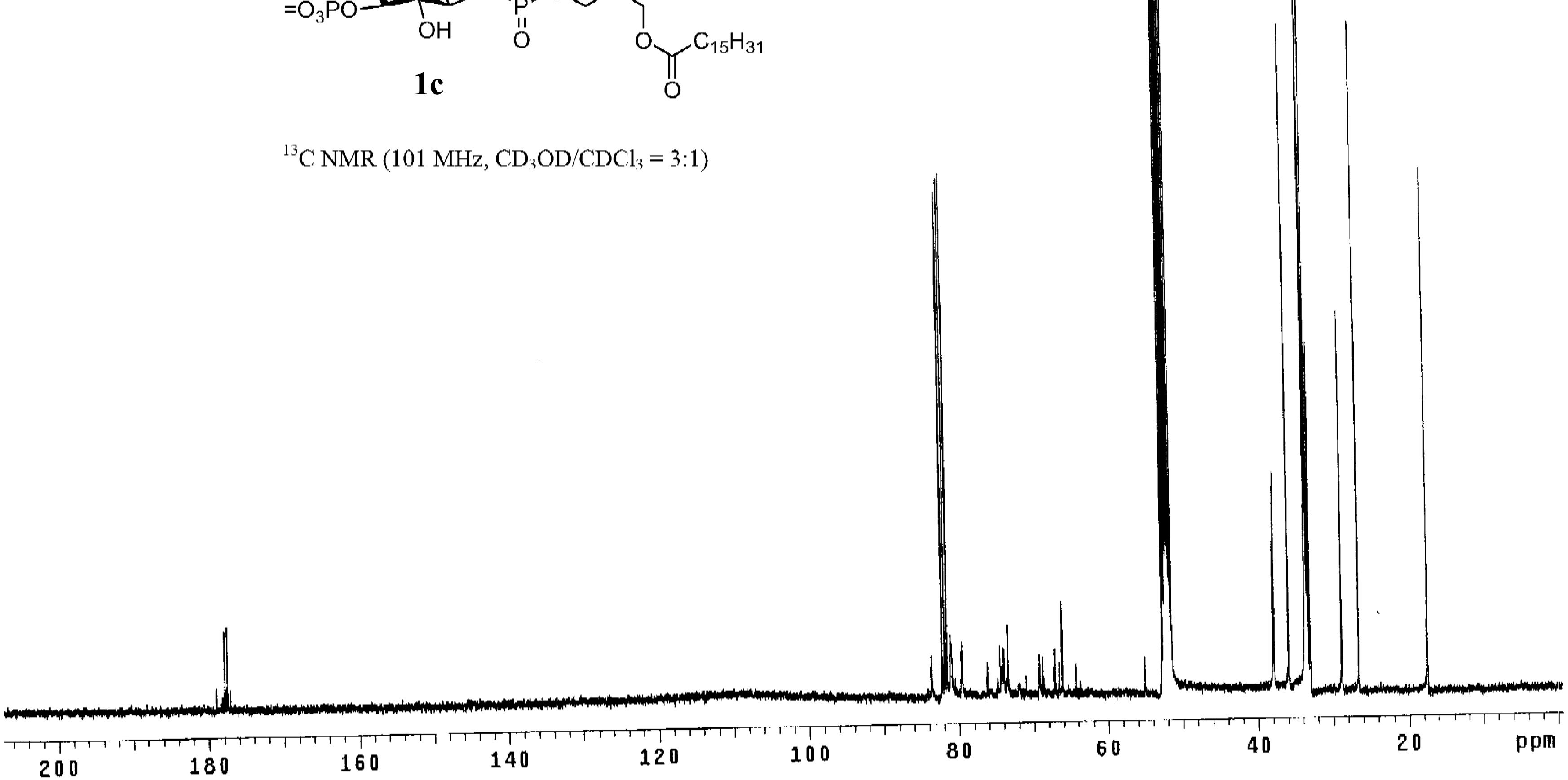
^{31}P NMR (162 MHz, $CD_3OD/CDCl_3$= 3:1)

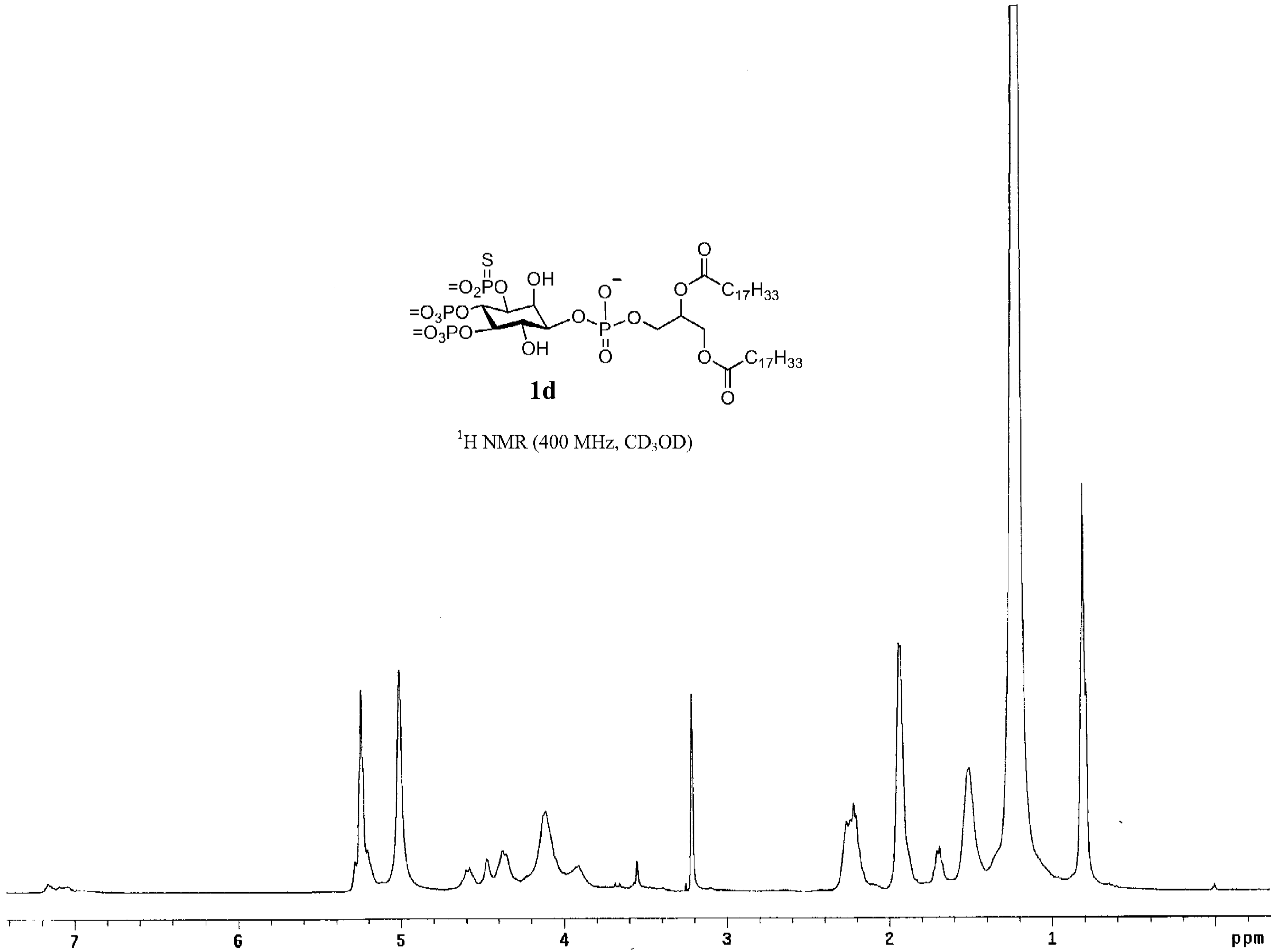




1c

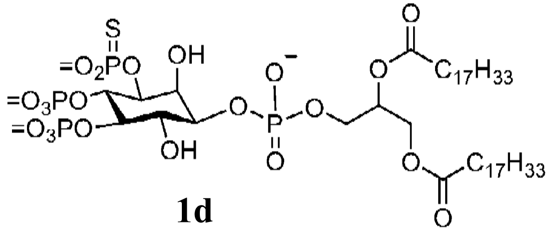
^{13}C NMR (101 MHz, $CD_3OD/CDCl_3 = 3:1$)





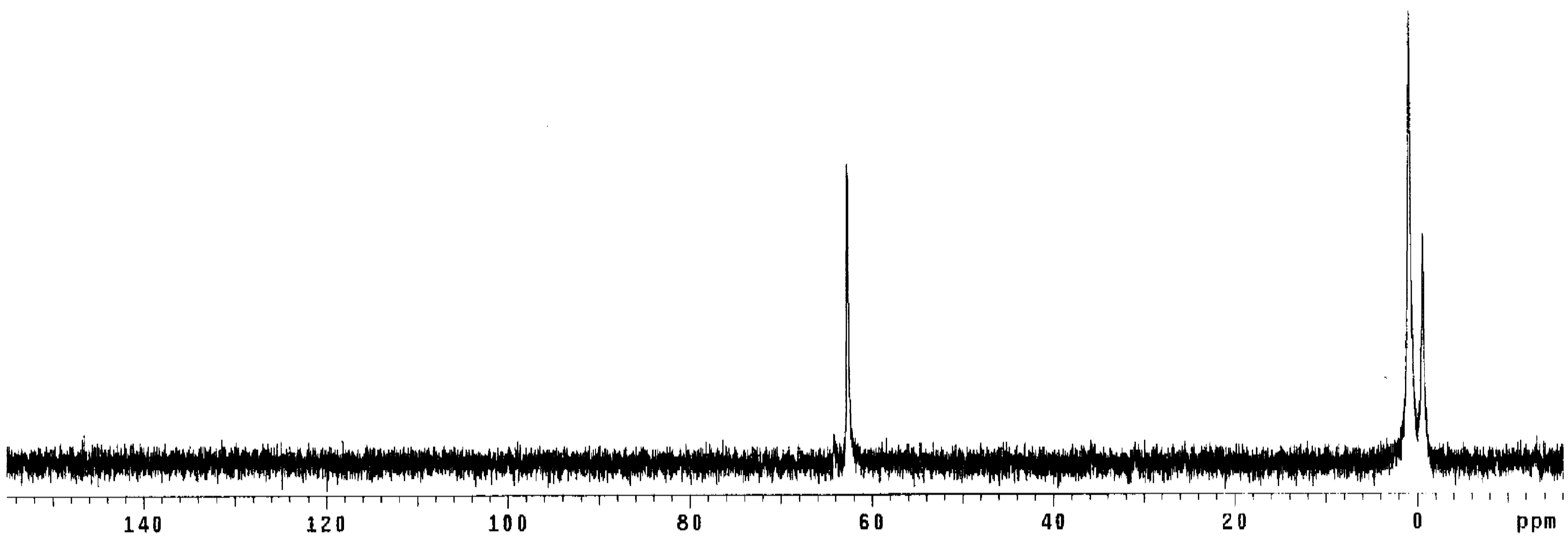
1d

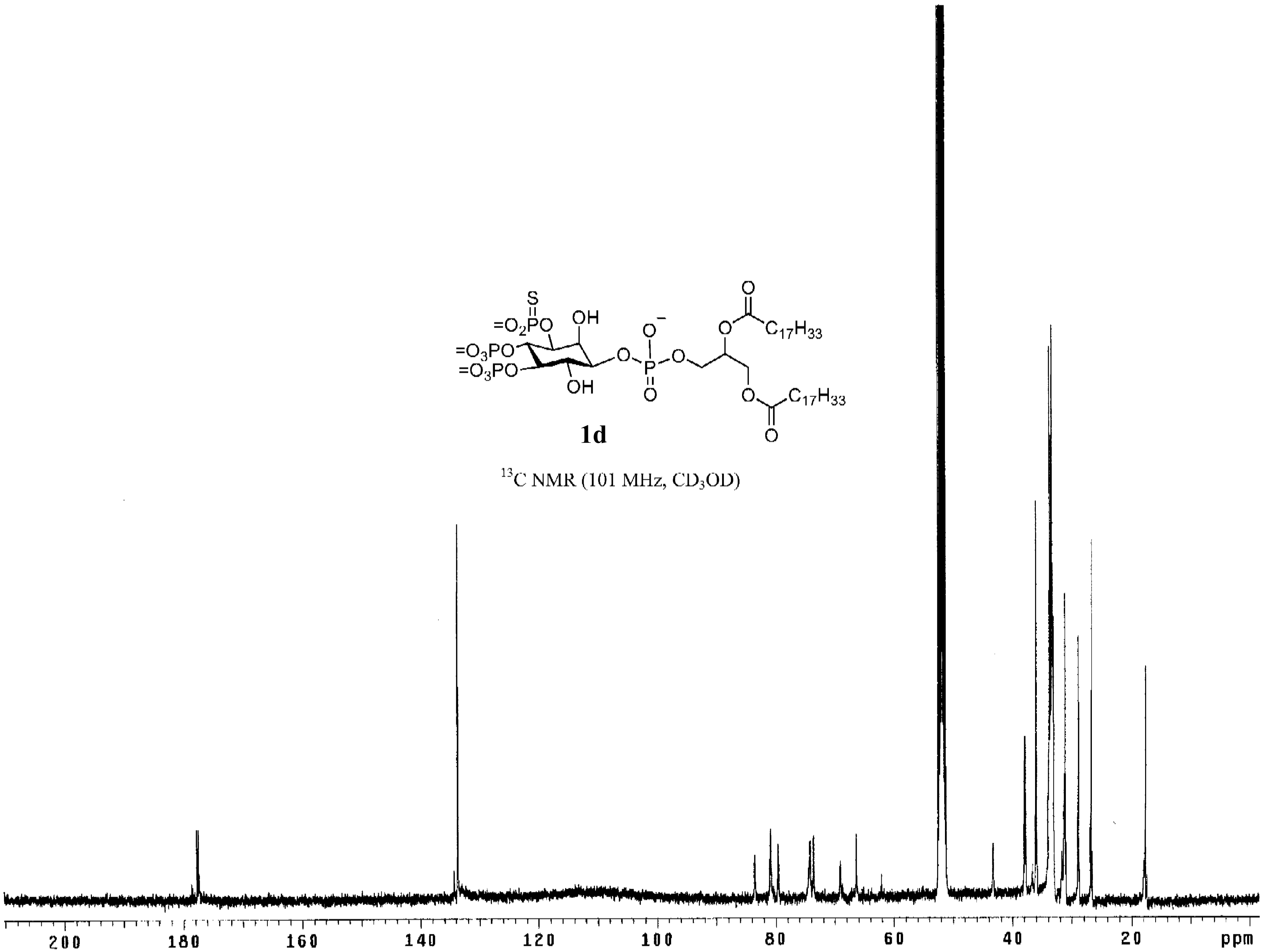
^{1}H NMR (400 MHz, CD_3OD)



1d

^{31}P NMR (162 MHz, CD_3OD)

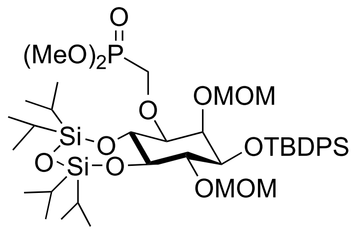




1d

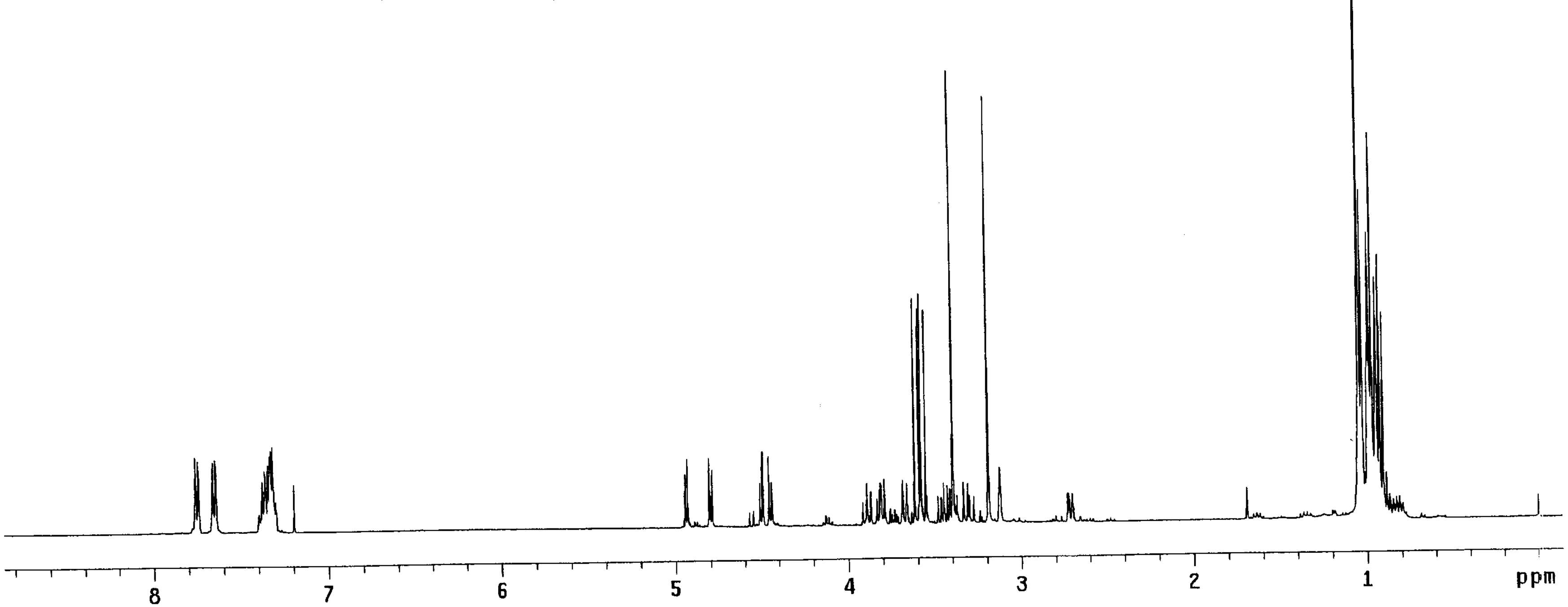
^{13}C NMR (101 MHz, CD_3OD)

zh22611 10H



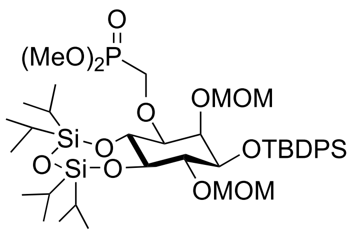
10

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



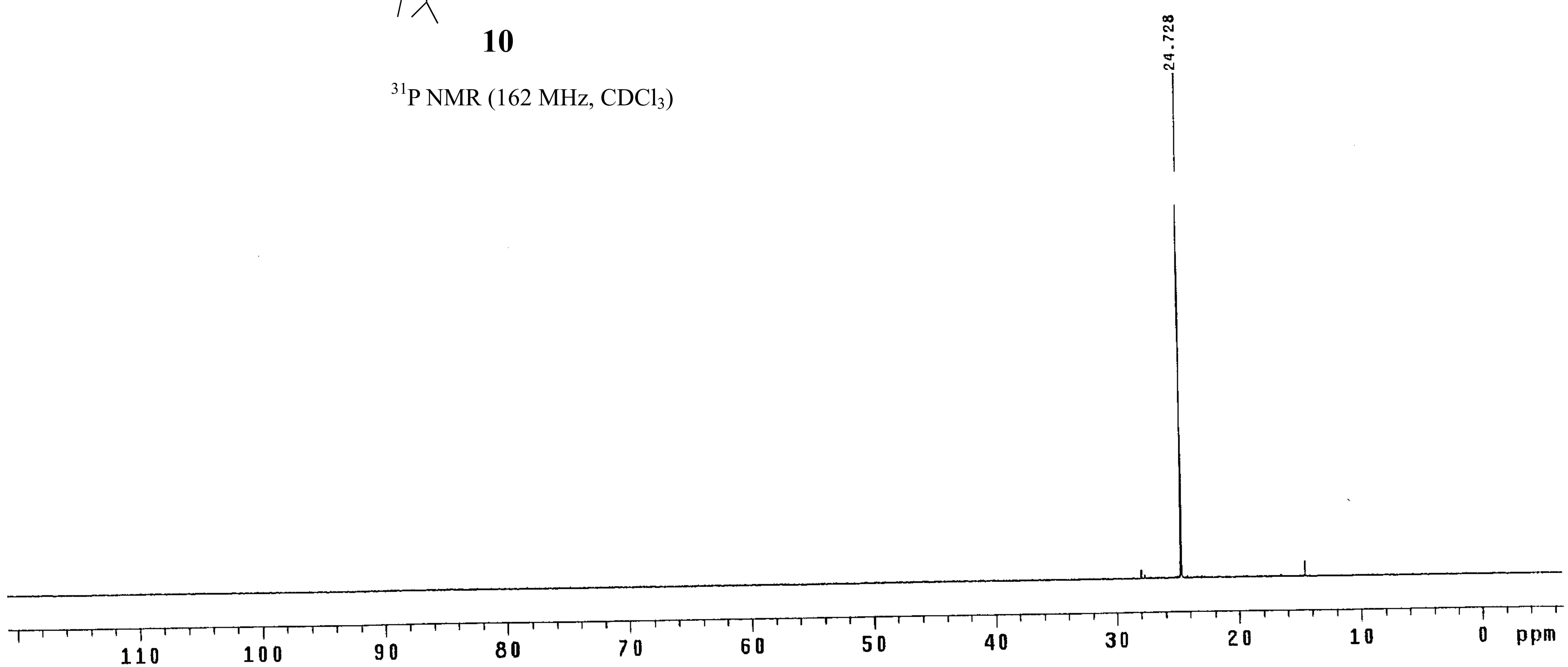
pP

zh22611P



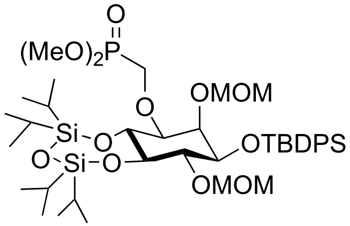
10

^{31}P NMR (162 MHz, $CDCl_3$)



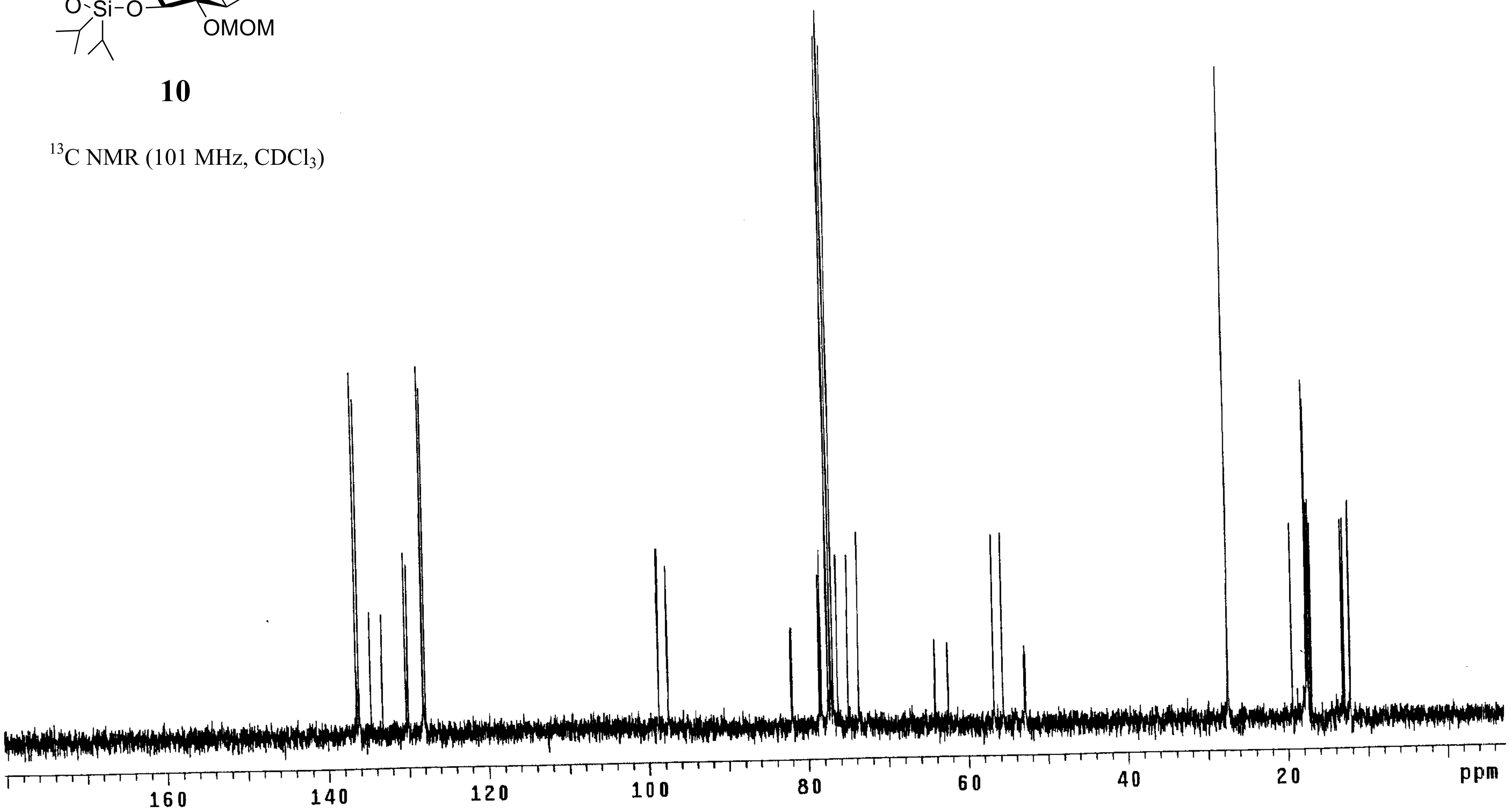
10C

zh22611C



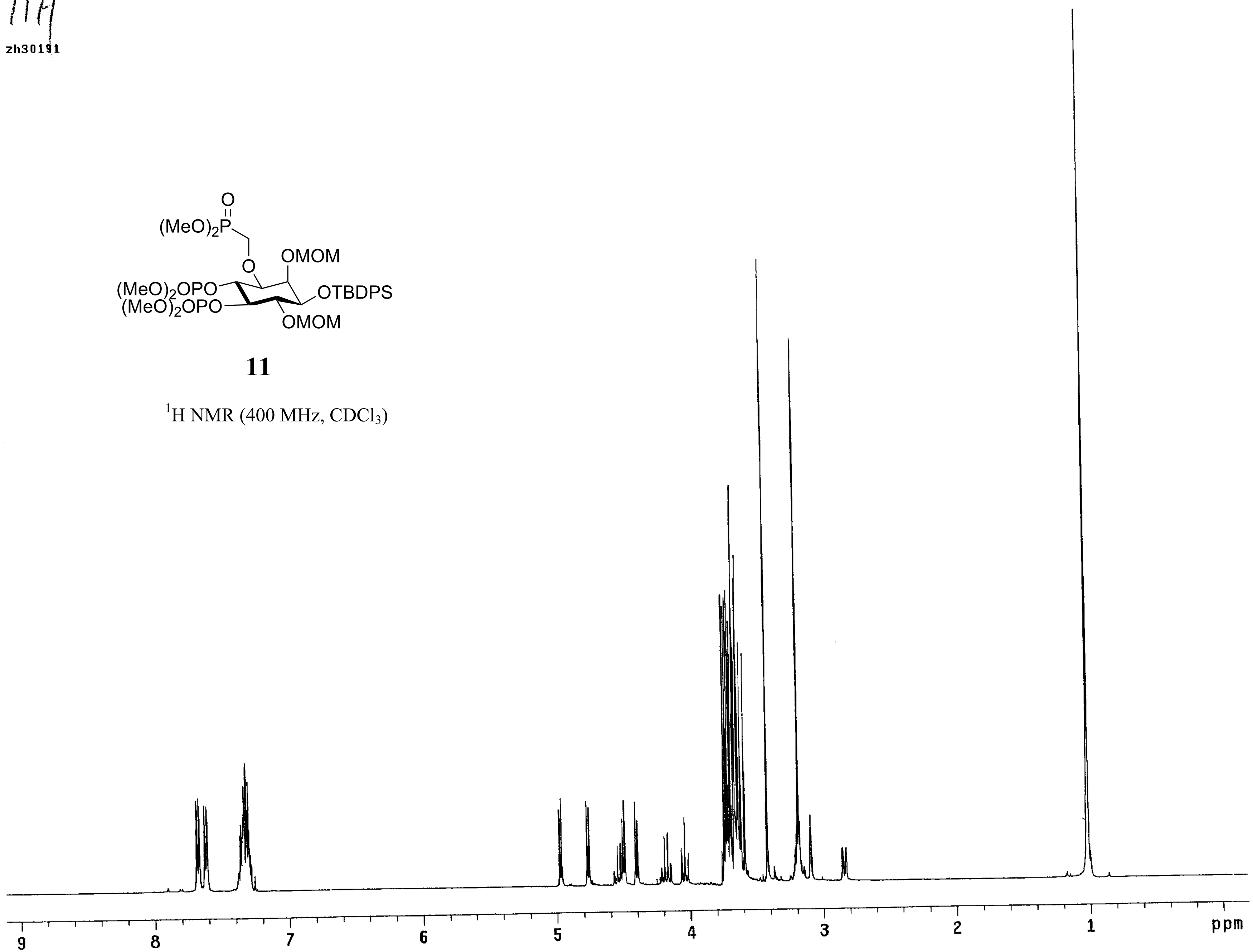
10

^{13}C NMR (101 MHz, $CDCl_3$)



11H

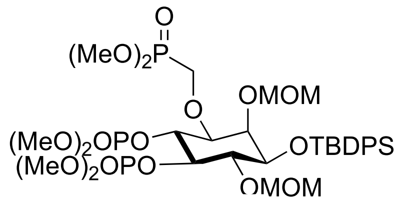
zh30191



11

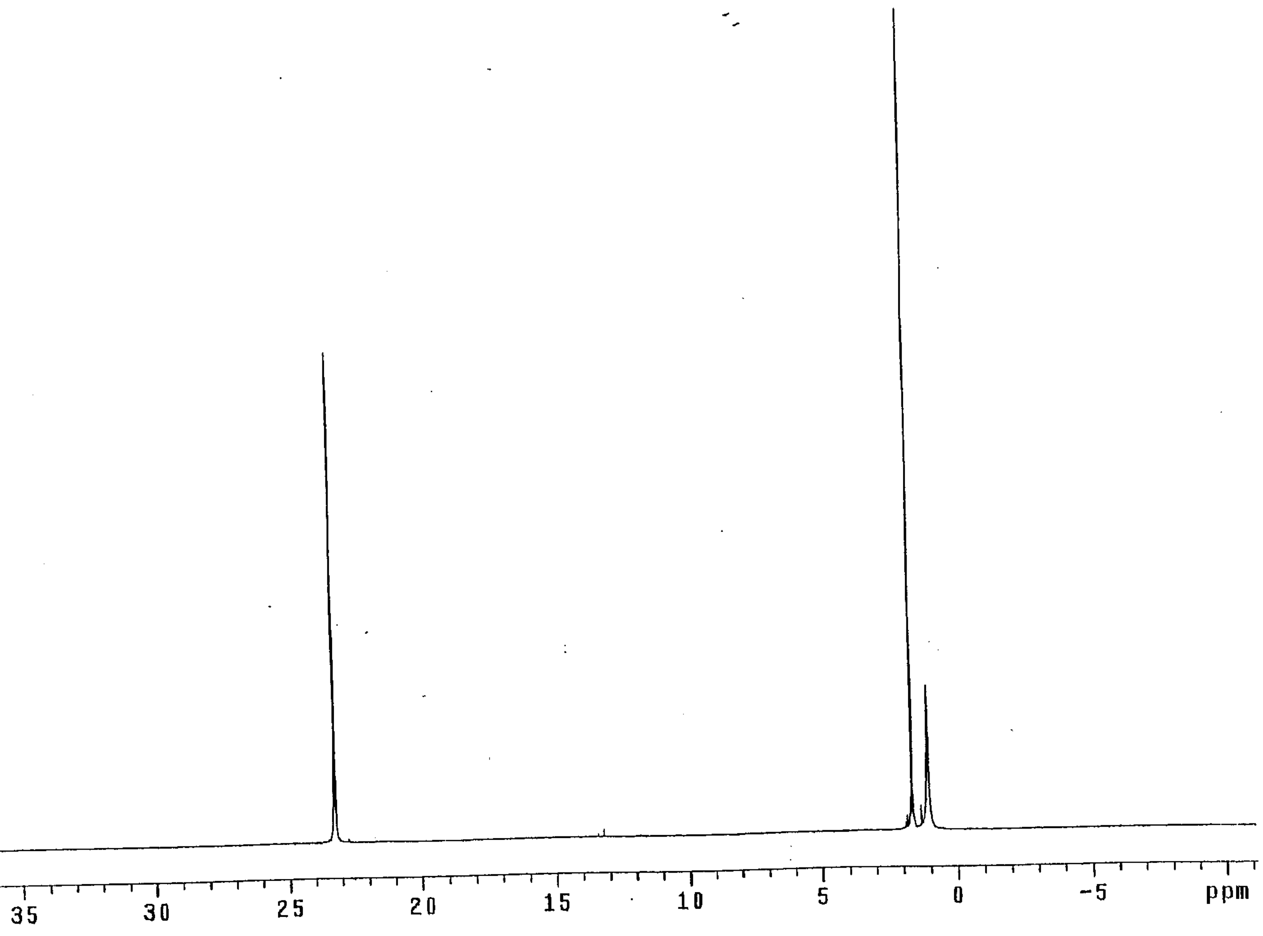
^{1}H NMR (400 MHz, $CDCl_3$)

zh30191P

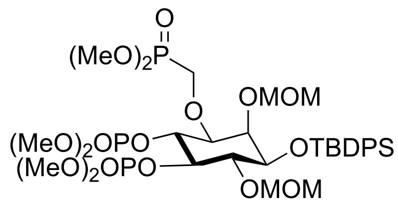


11

^{31}P NMR (162 MHz, $CDCl_3$)

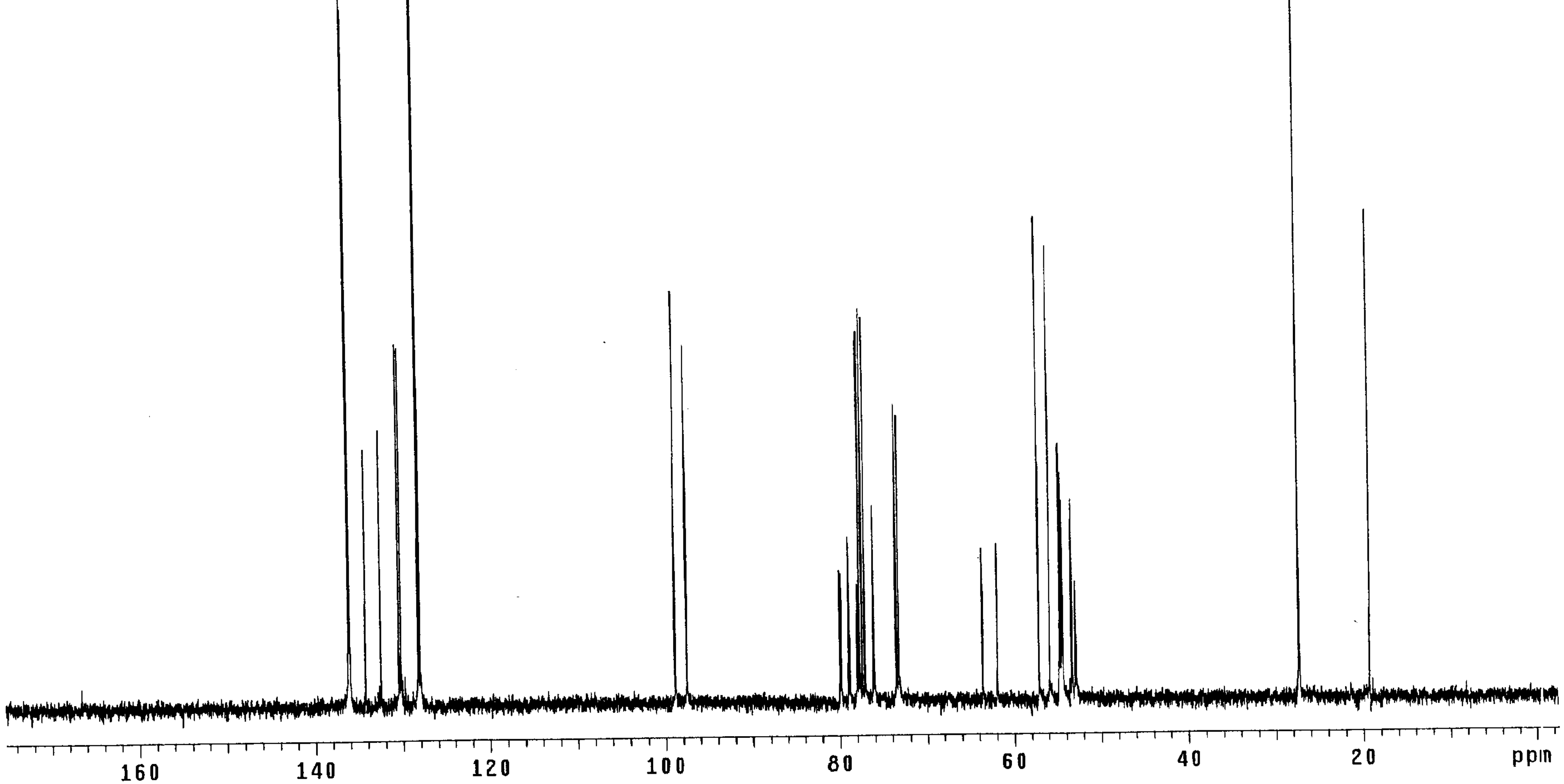


11C



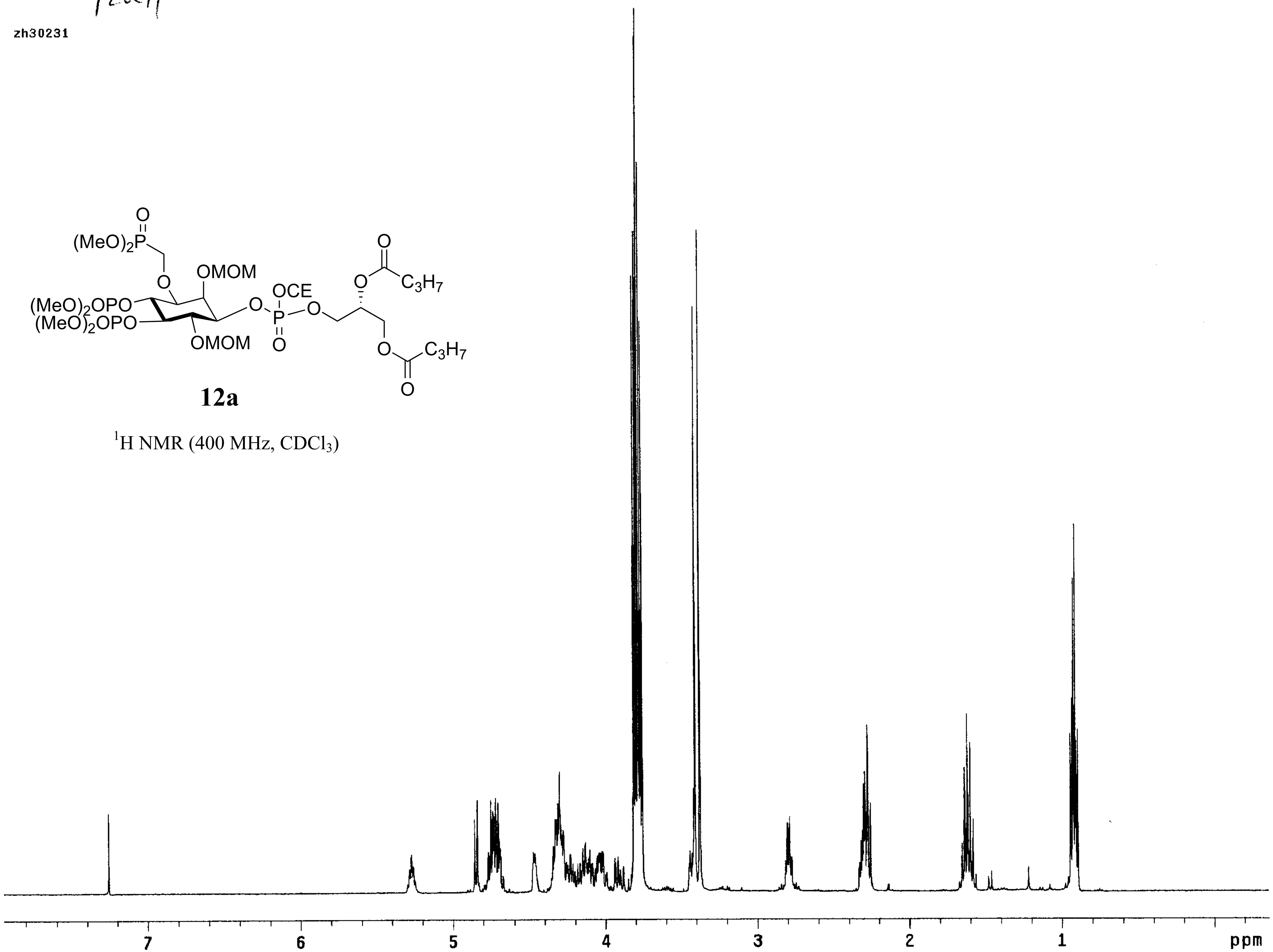
11

^{13}C NMR (101 MHz, $CDCl_3$)



zh30231

12aH

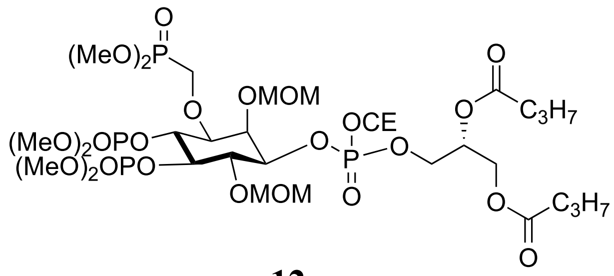


12a

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

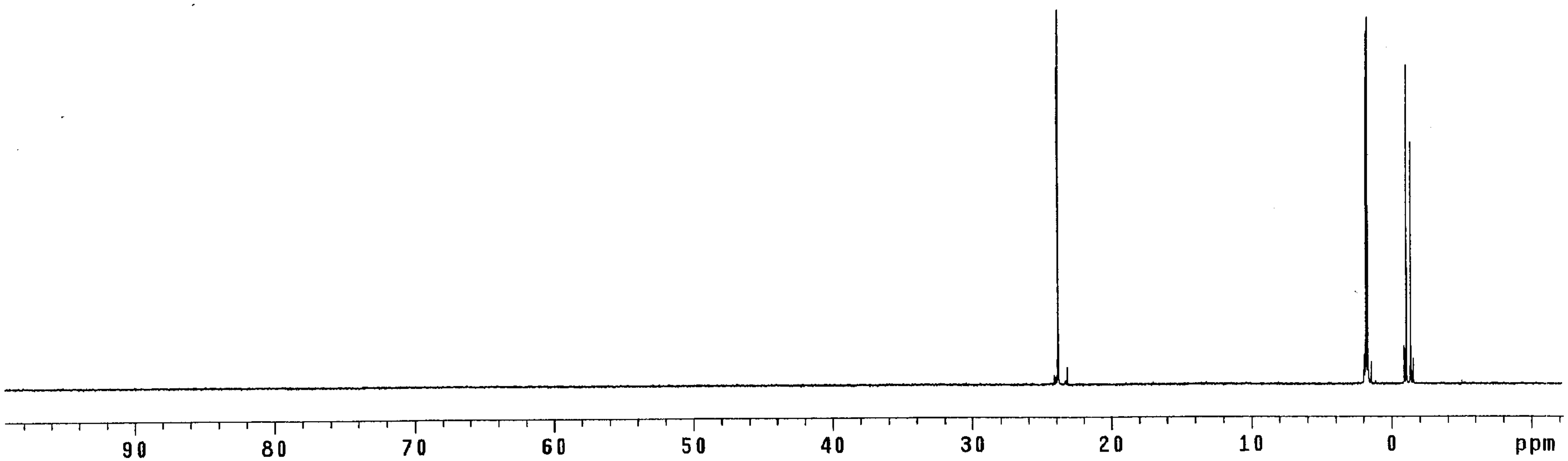
12a P

zh30231P

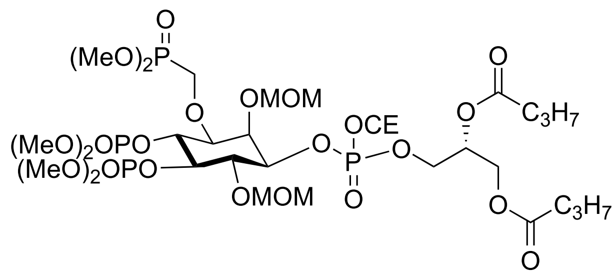


12a

^{31}P NMR (162 MHz, $CDCl_3$)

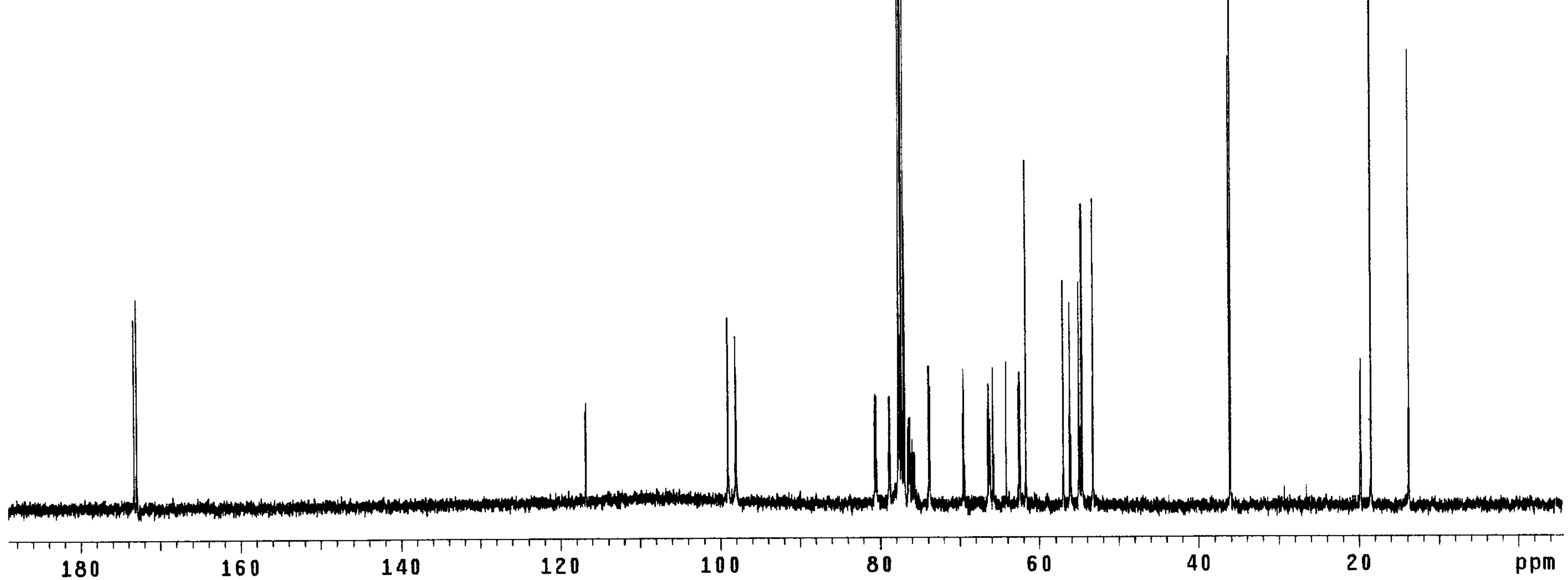


12ac

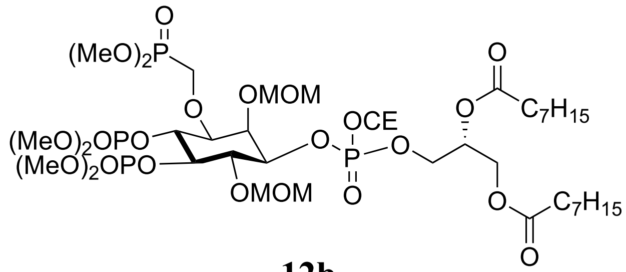


12a

^{13}C NMR (101 MHz, $CDCl_3$)

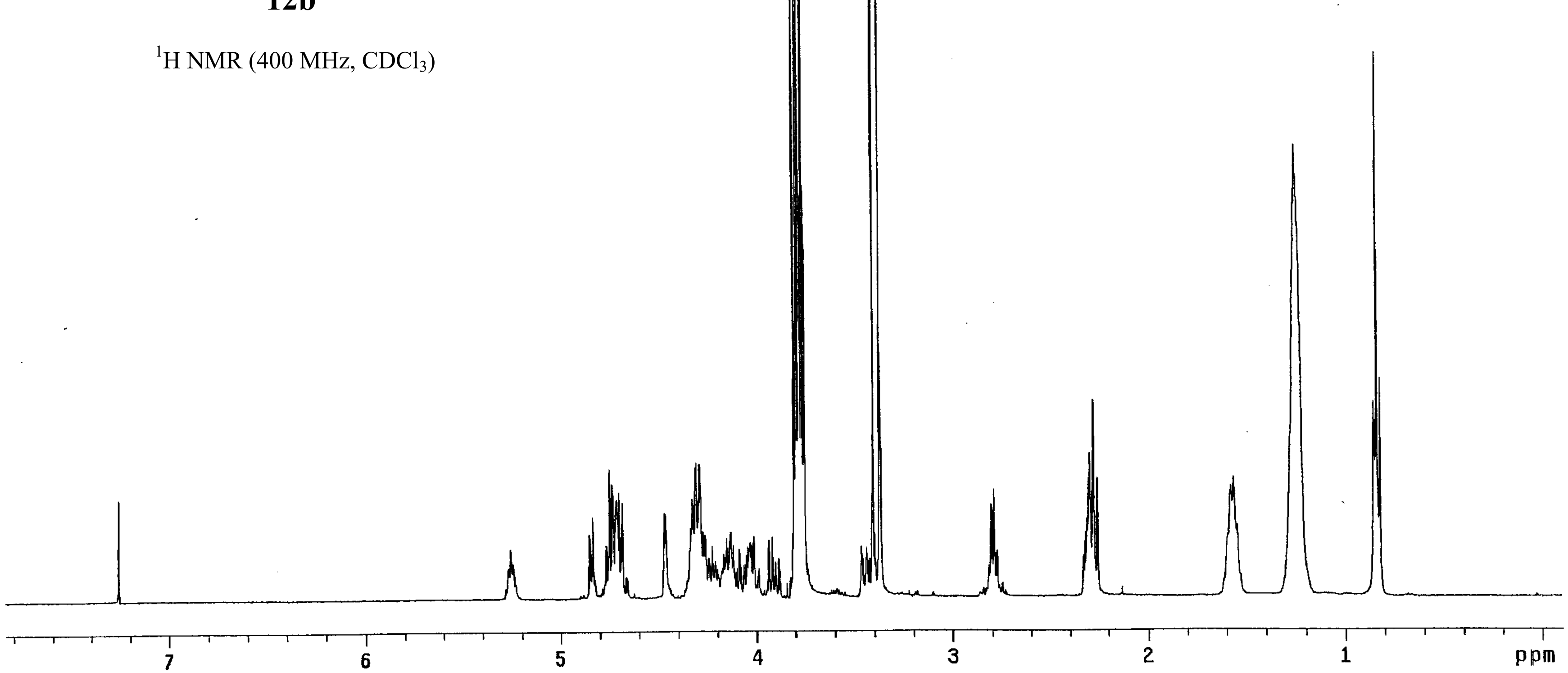


zh30251 12bH



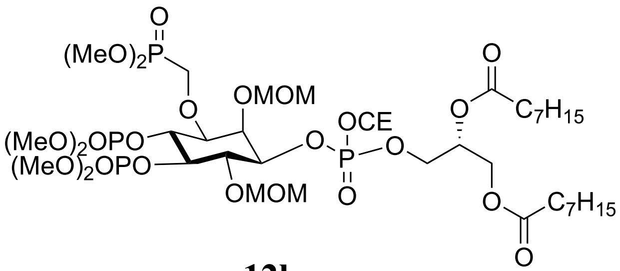
12b

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



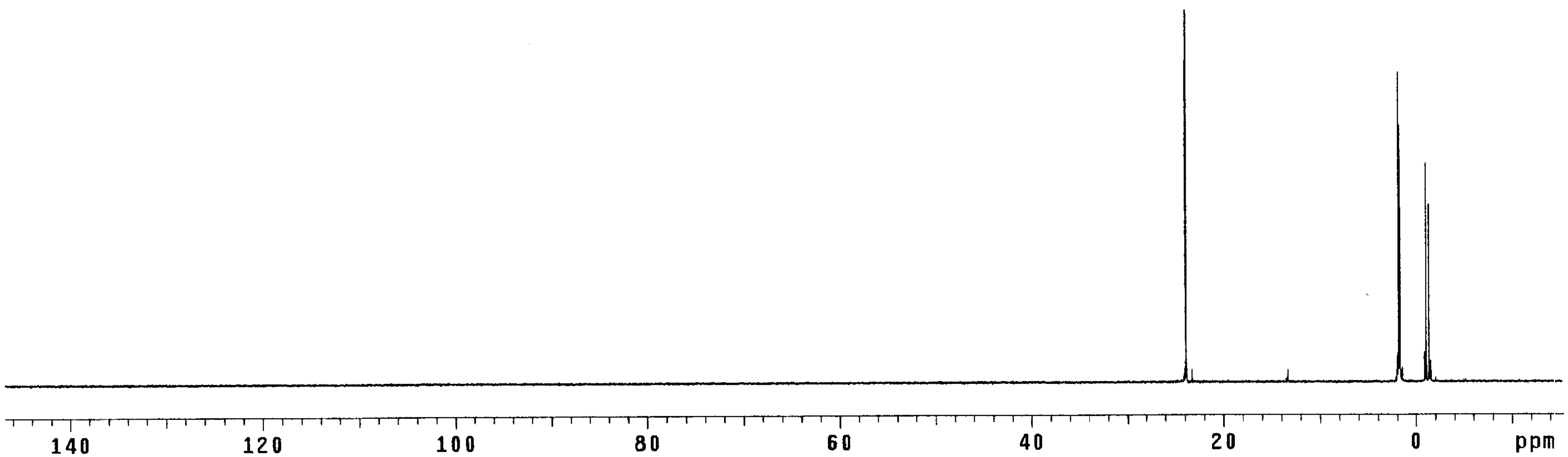
nbP

zh30251P

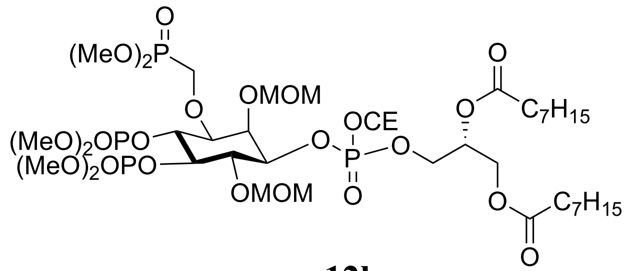


12b

^{31}P NMR (162 MHz, $CDCl_3$)

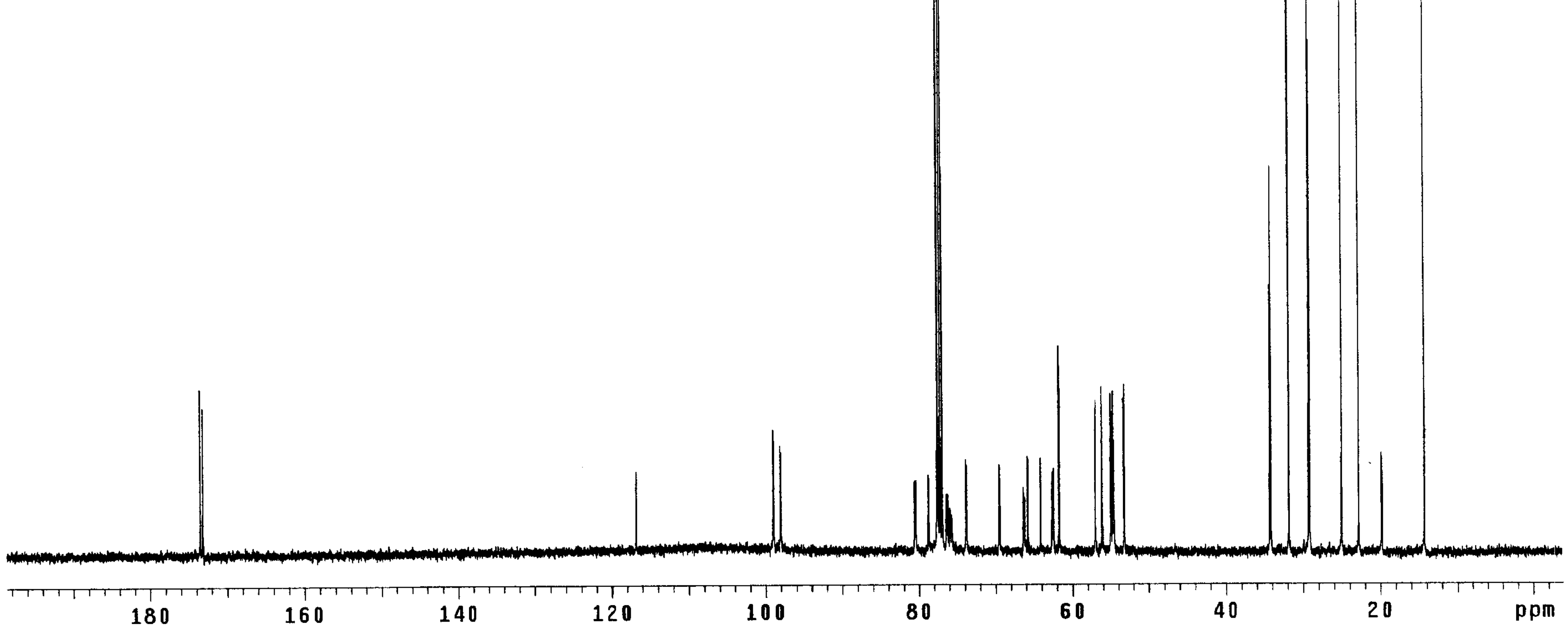


12bC



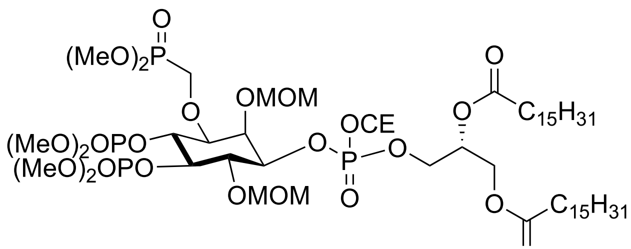
12b

^{13}C NMR (101 MHz, $CDCl_3$)



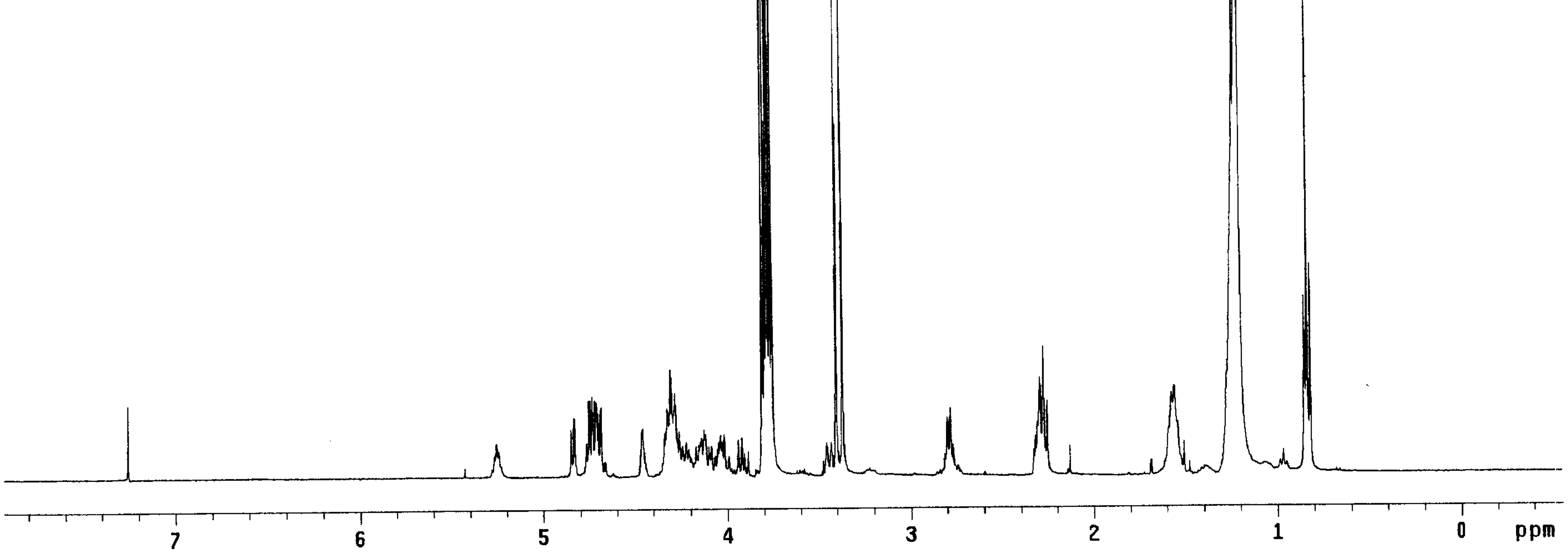
12cH

zh30271



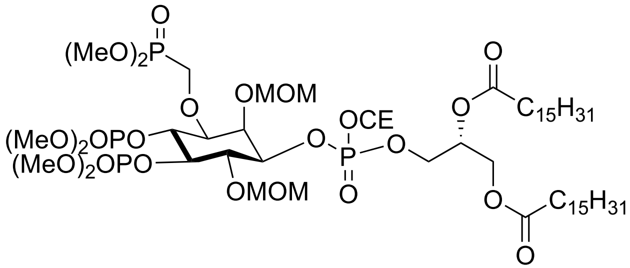
12c

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



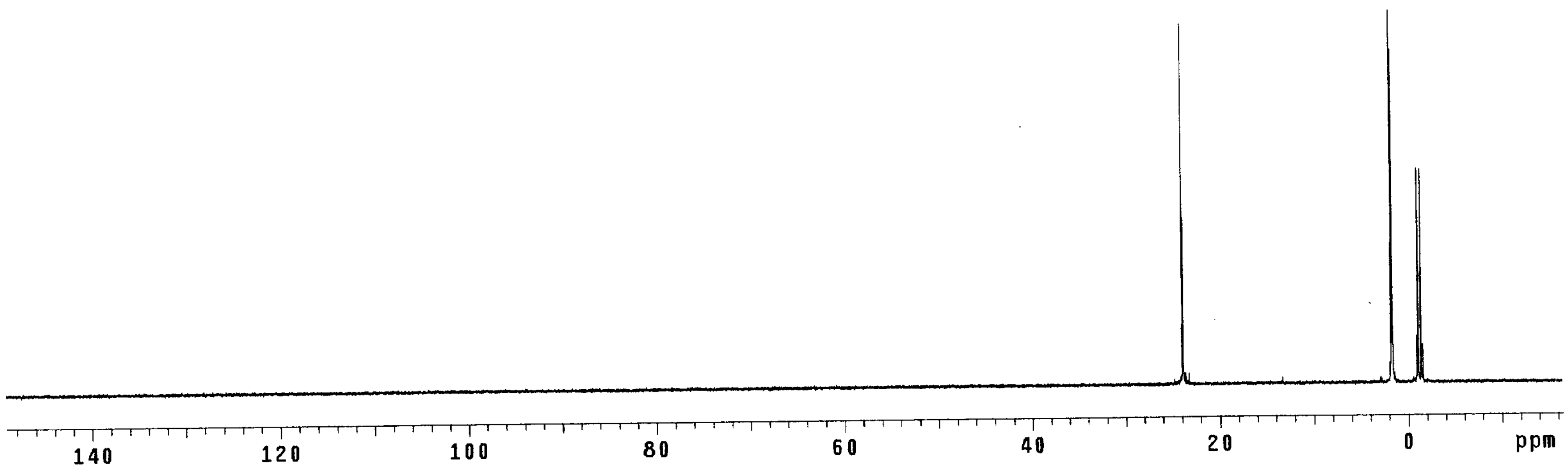
12cP

zh30271P

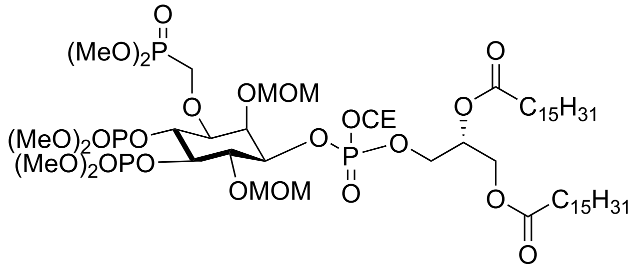


12c

^{31}P NMR (162 MHz, $CDCl_3$)

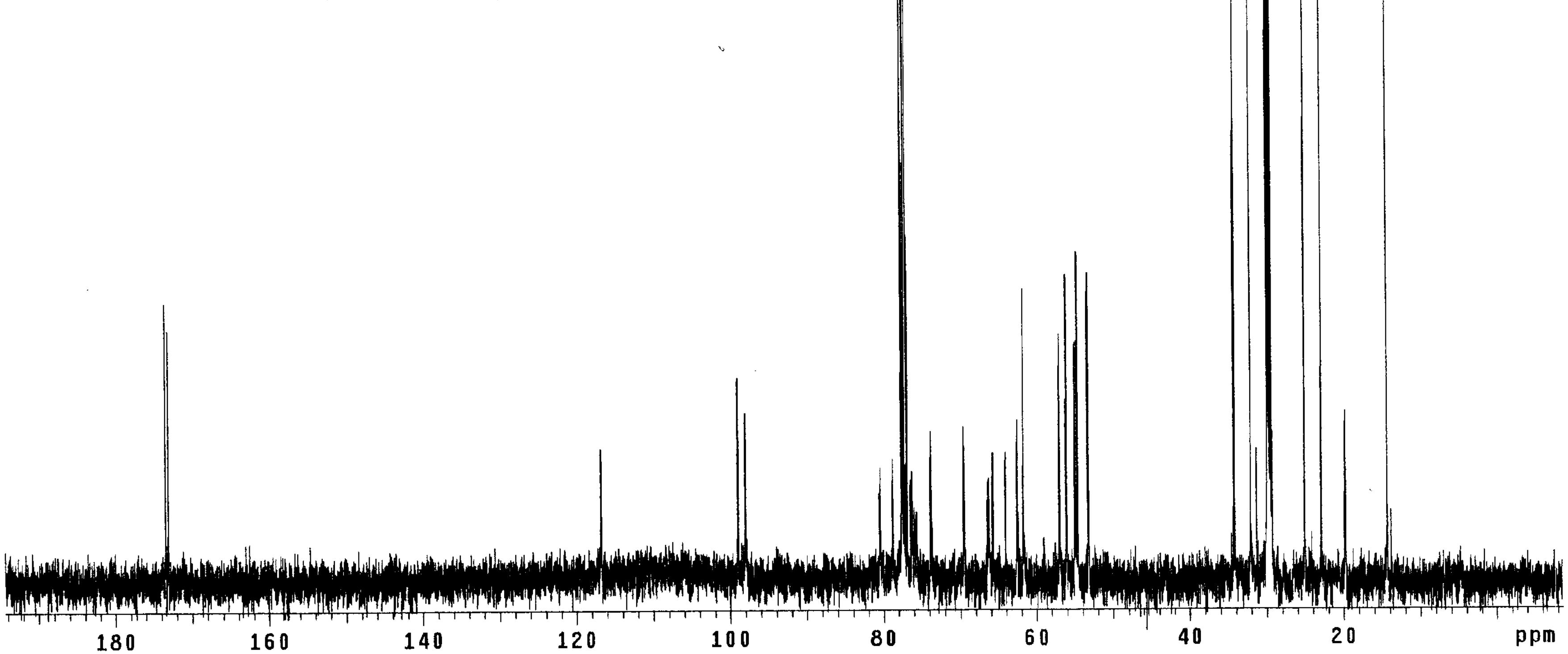


12cc



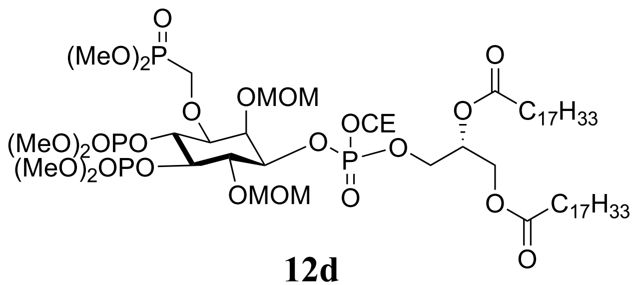
12c

^{13}C NMR (101 MHz, $CDCl_3$)



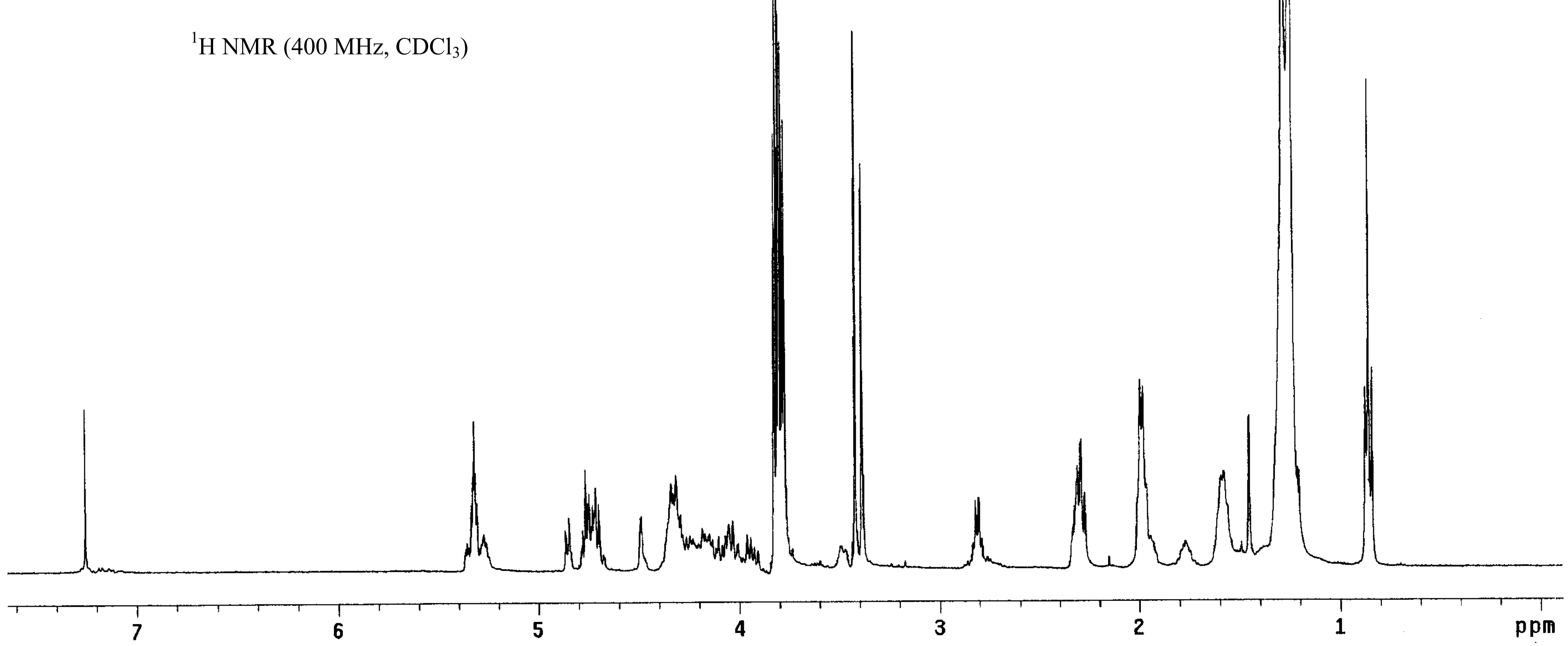
ndH

zh30291



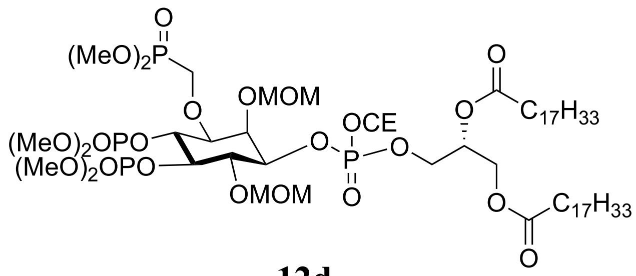
12d

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



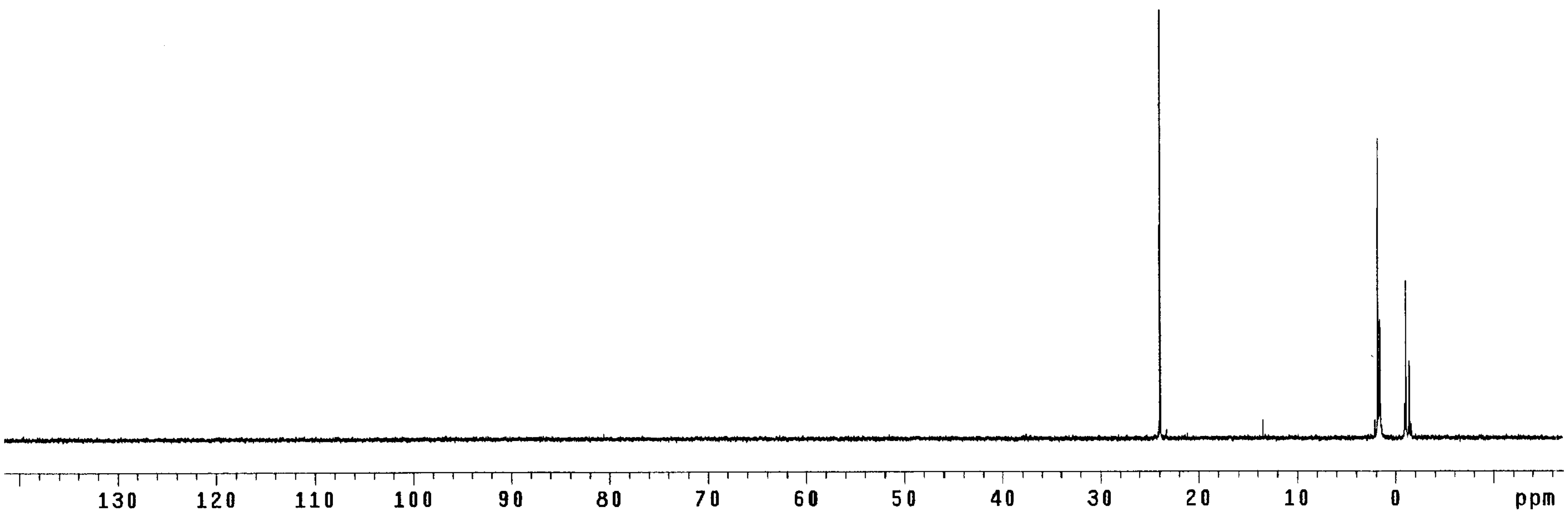
12d P

zh30291P

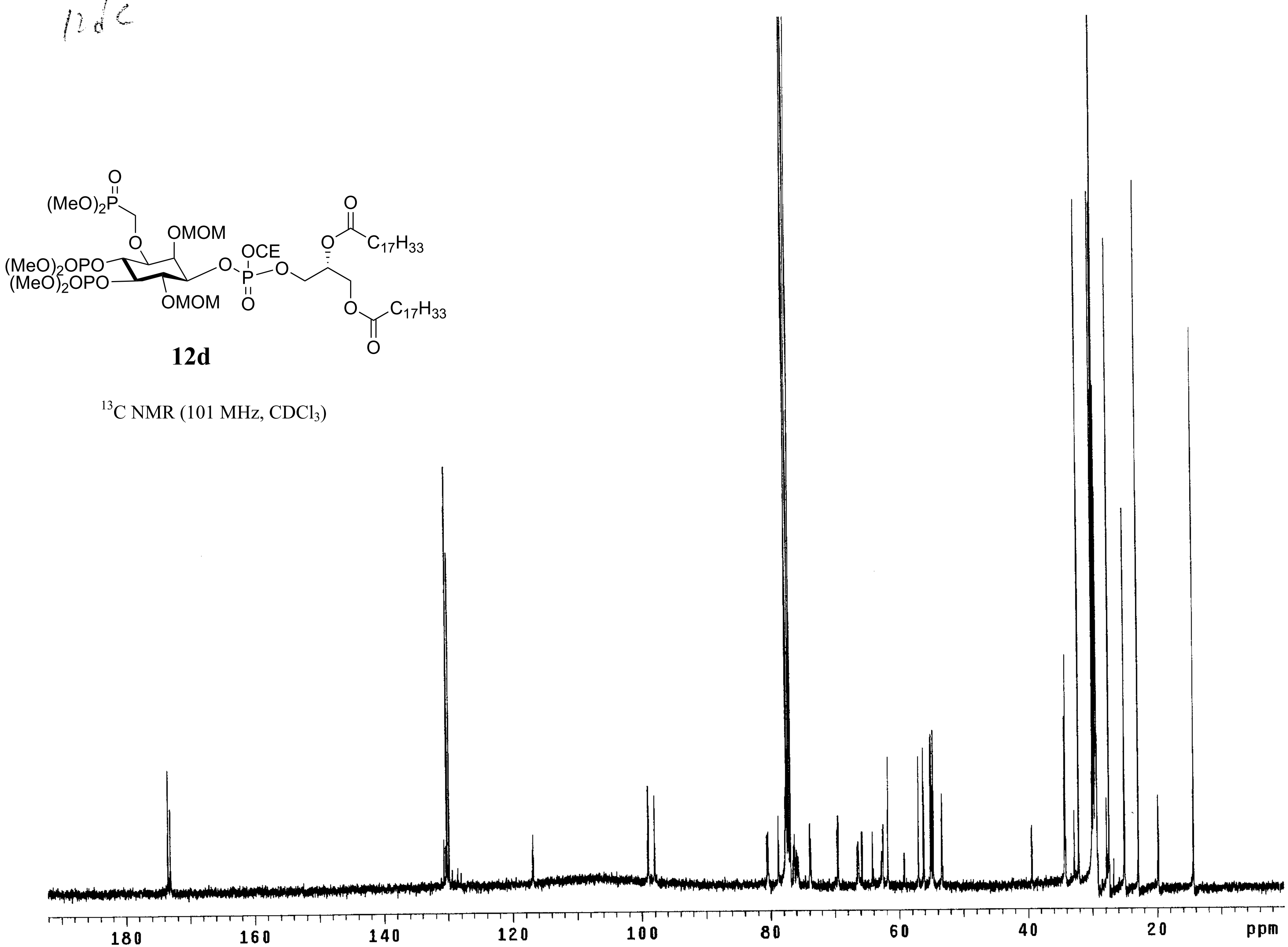


12d

^{31}P NMR (162 MHz, $CDCl_3$)



12dC

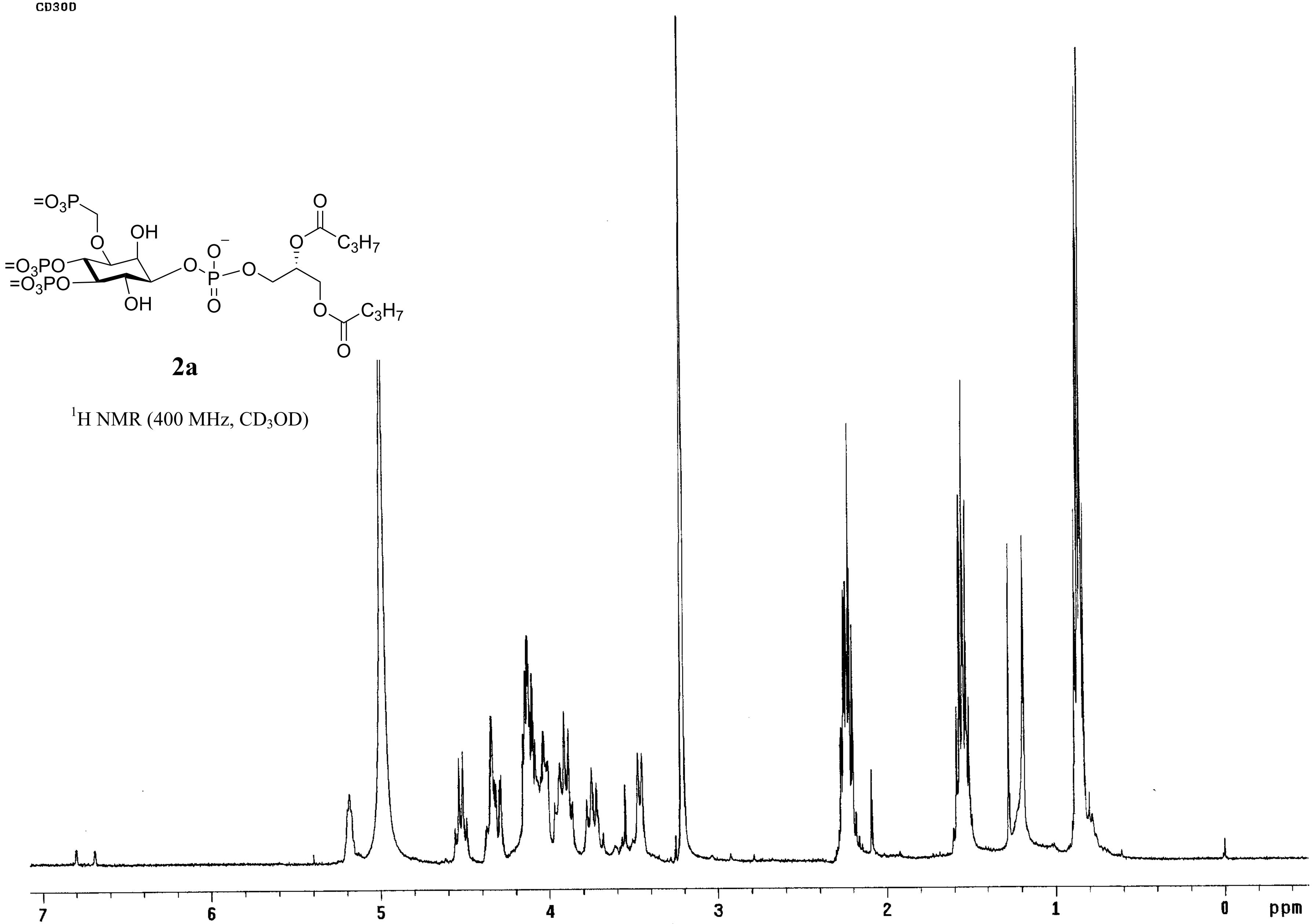


12d

^{13}C NMR (101 MHz, $CDCl_3$)

2a H

zh30241
CD3OD

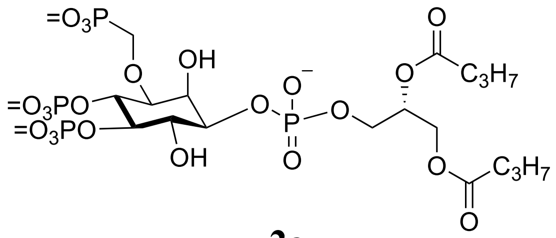


2a

^{1}H NMR (400 MHz, CD_3OD)

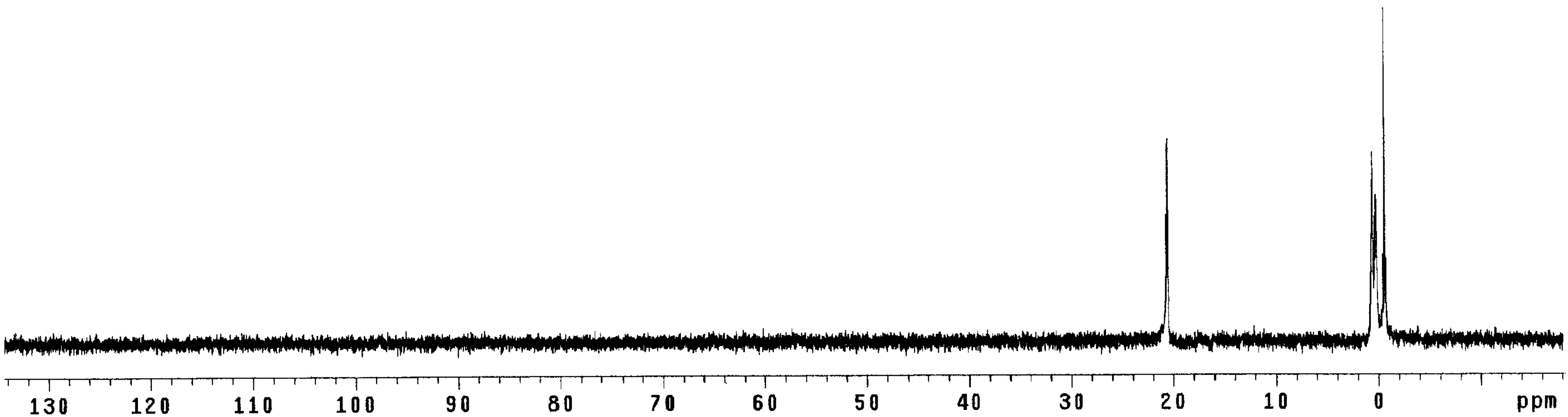
zap

zh30241P
CD3OD

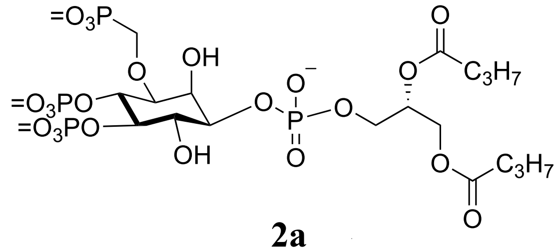


2a

^{31}P NMR (162 MHz, CD_3OD)

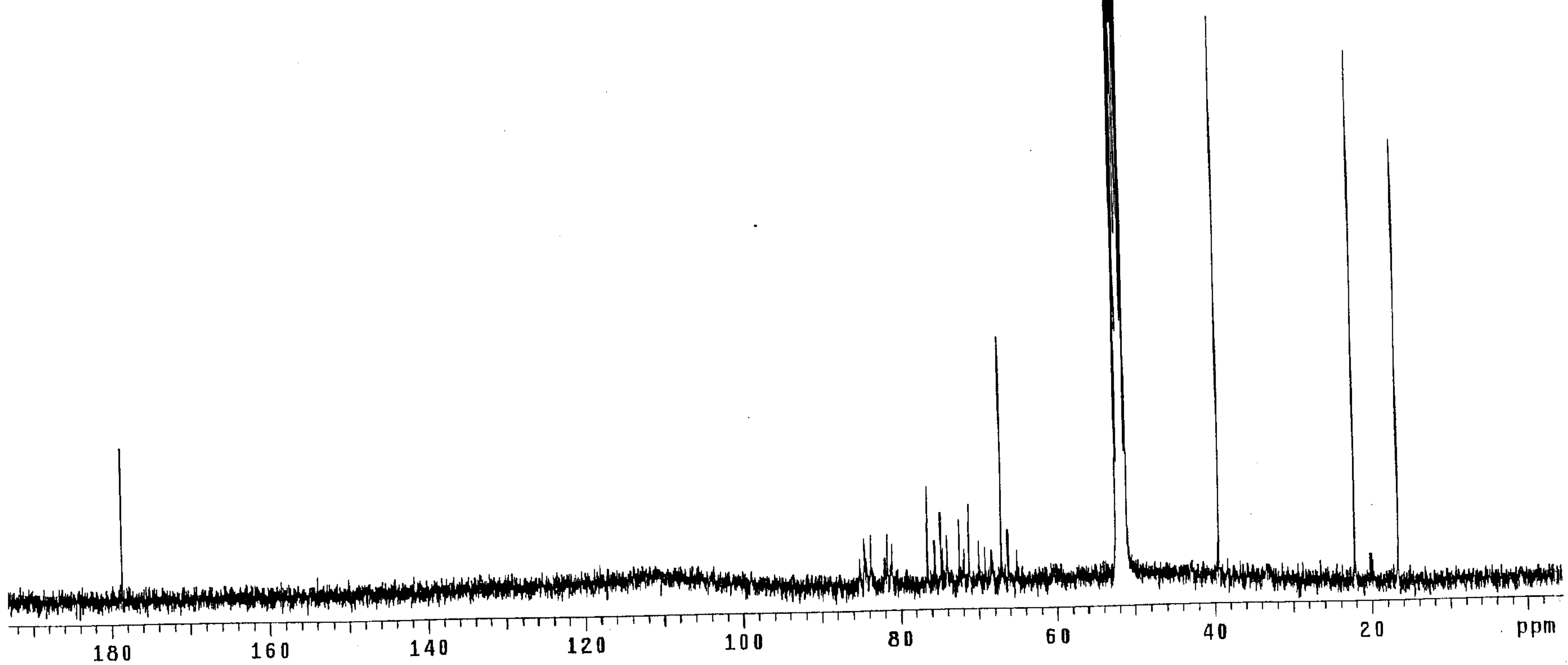


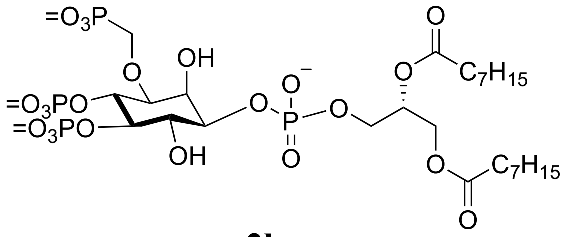
2aC



2a

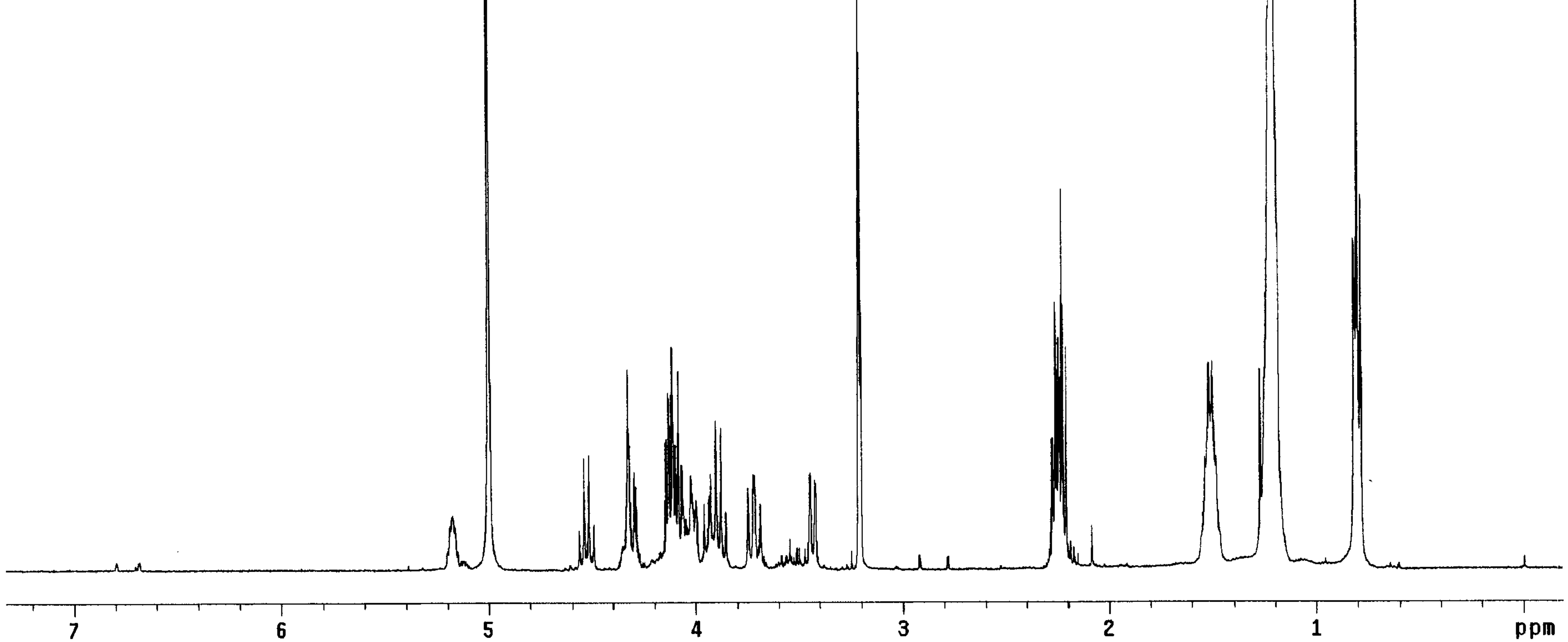
^{13}C NMR (101 MHz, CD_3OD)





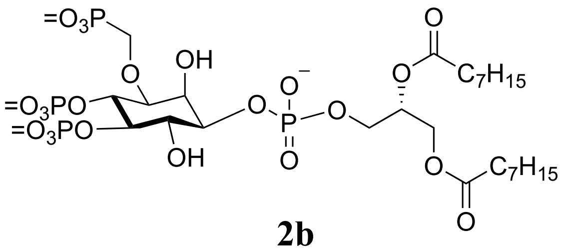
2b

^1H NMR (400 MHz, CD_3OD)



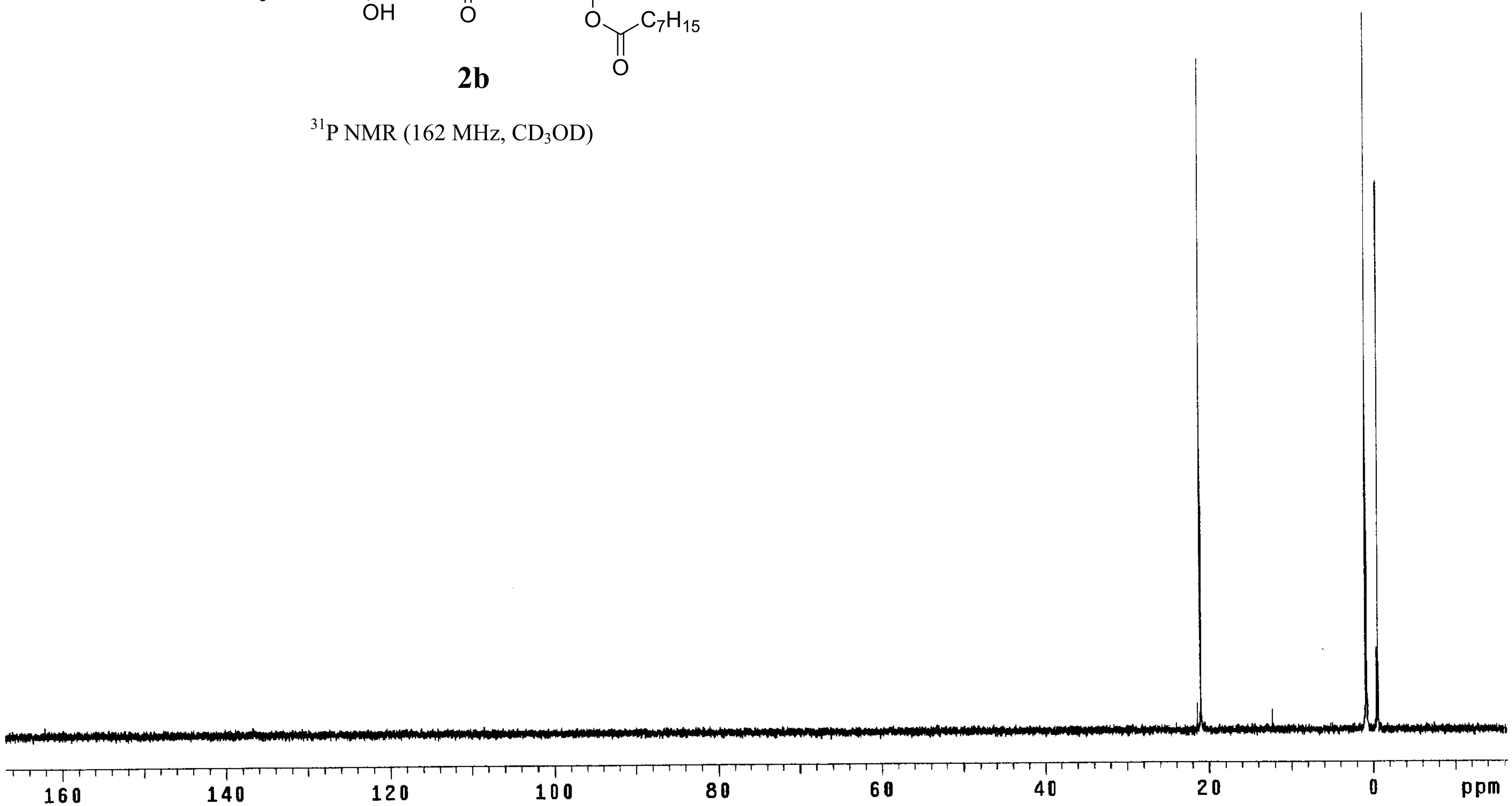
2bP

zh30261P

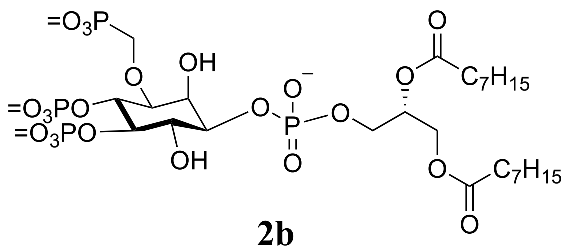


2b

^{31}P NMR (162 MHz, CD_3OD)

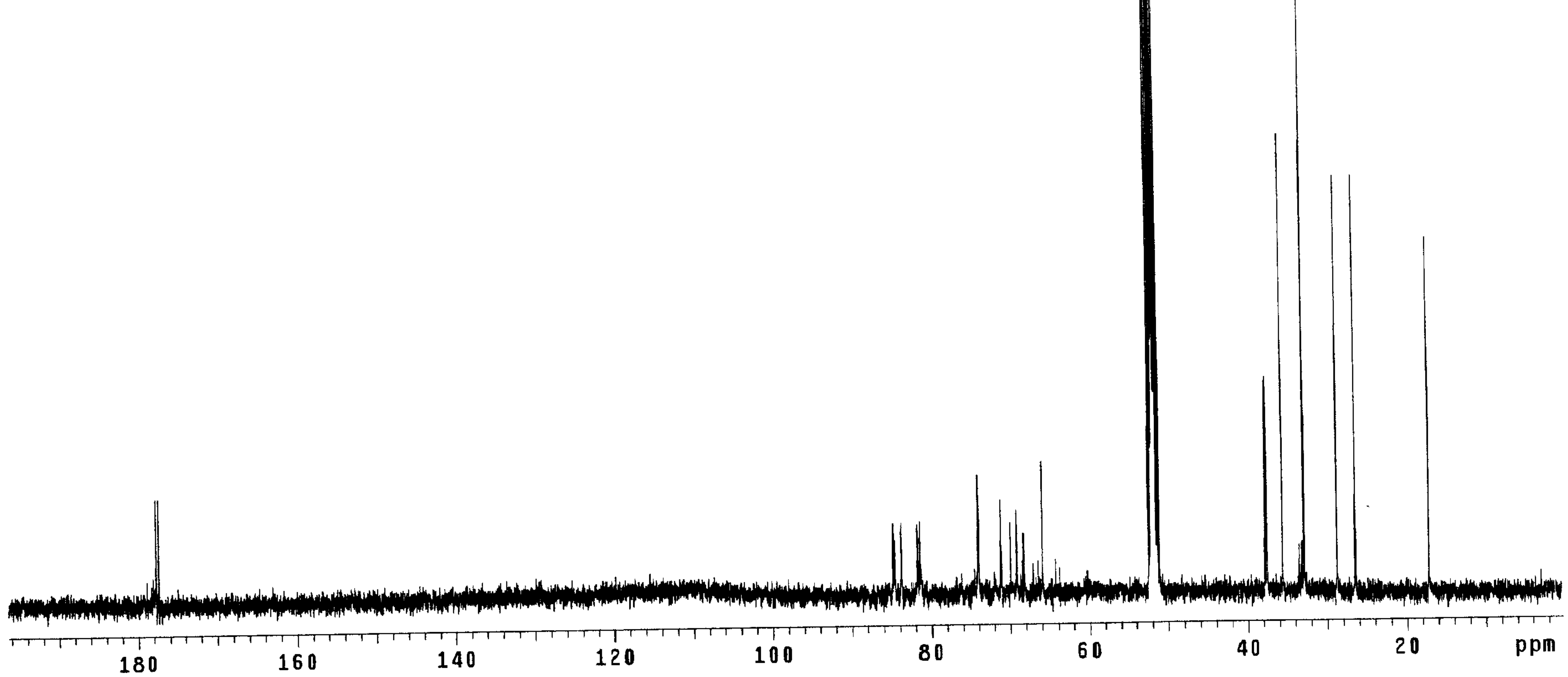


2bC



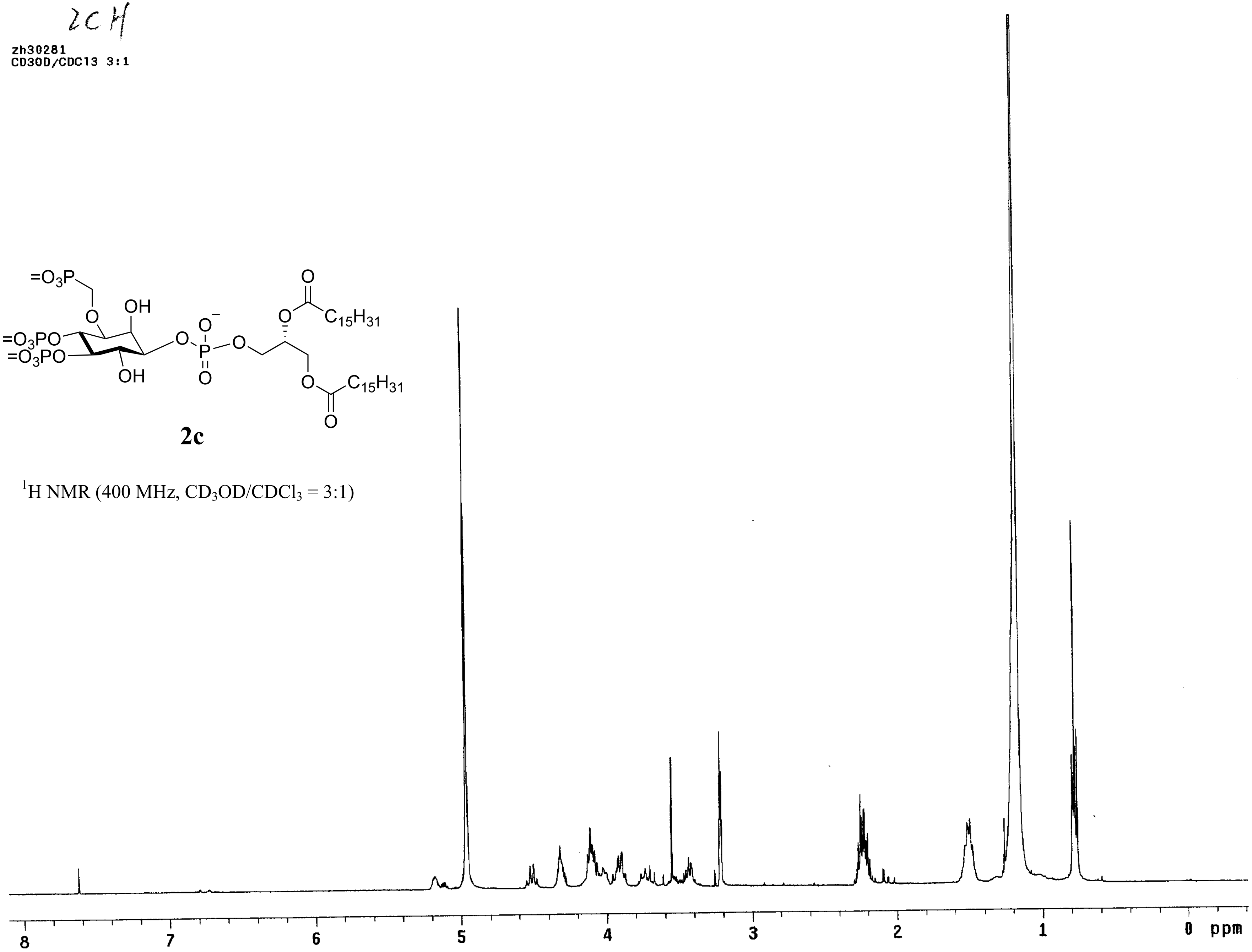
2b

^{13}C NMR (101 MHz, CD_3OD)



2C H

zh30281
CD3OD/CDC13 3:1

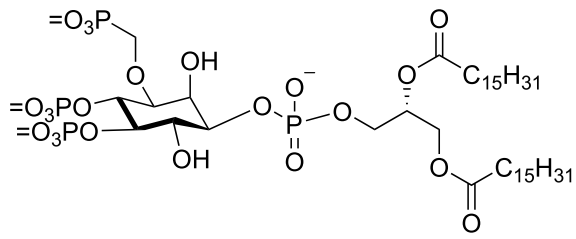


2c

^{1}H NMR (400 MHz, $CD_3OD/CDCl_3$ = 3:1)

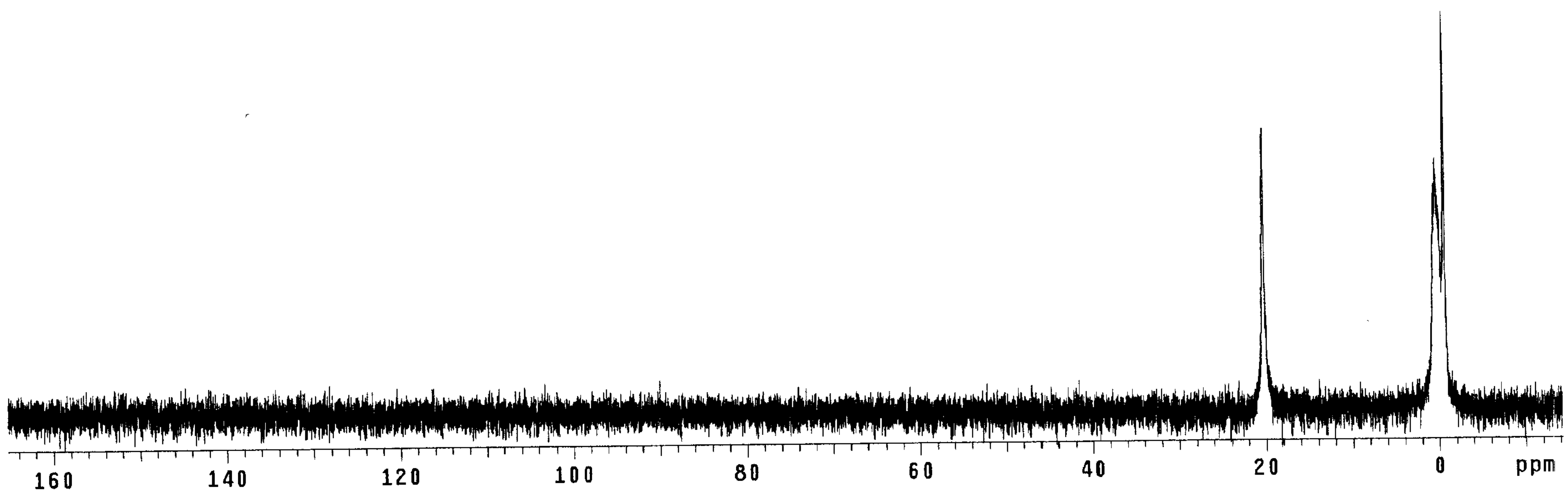
zh30281P
CD3OD/CDCl3 3:1

2cP

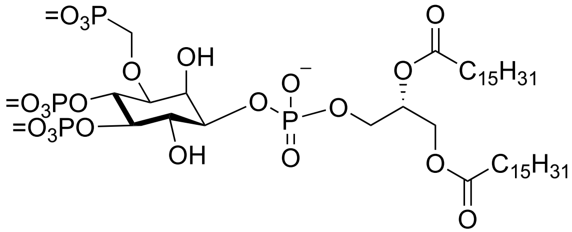


2c

^{13}C NMR (101 MHz, $CD_3OD/CDCl_3$ = 3:1)

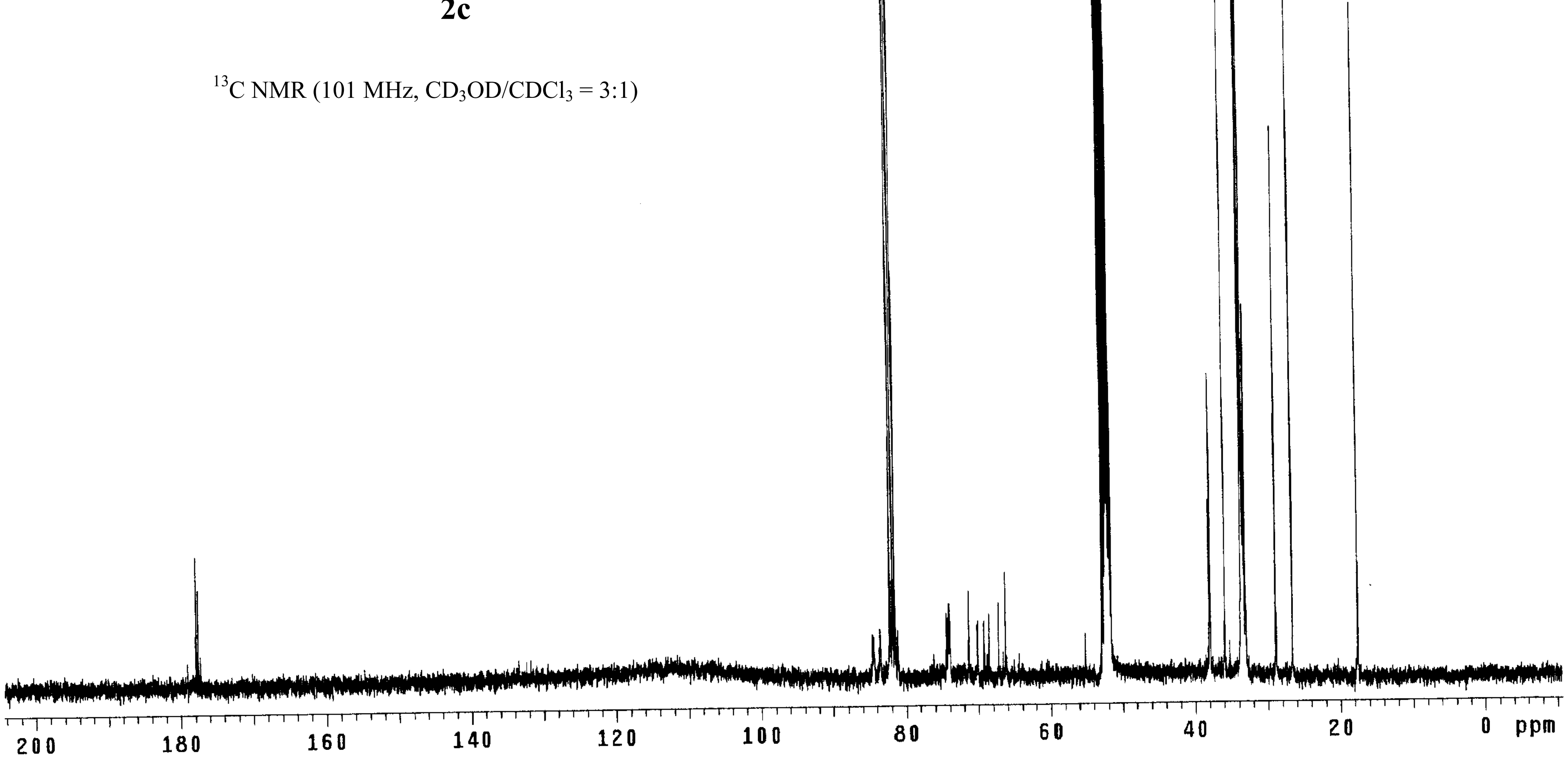


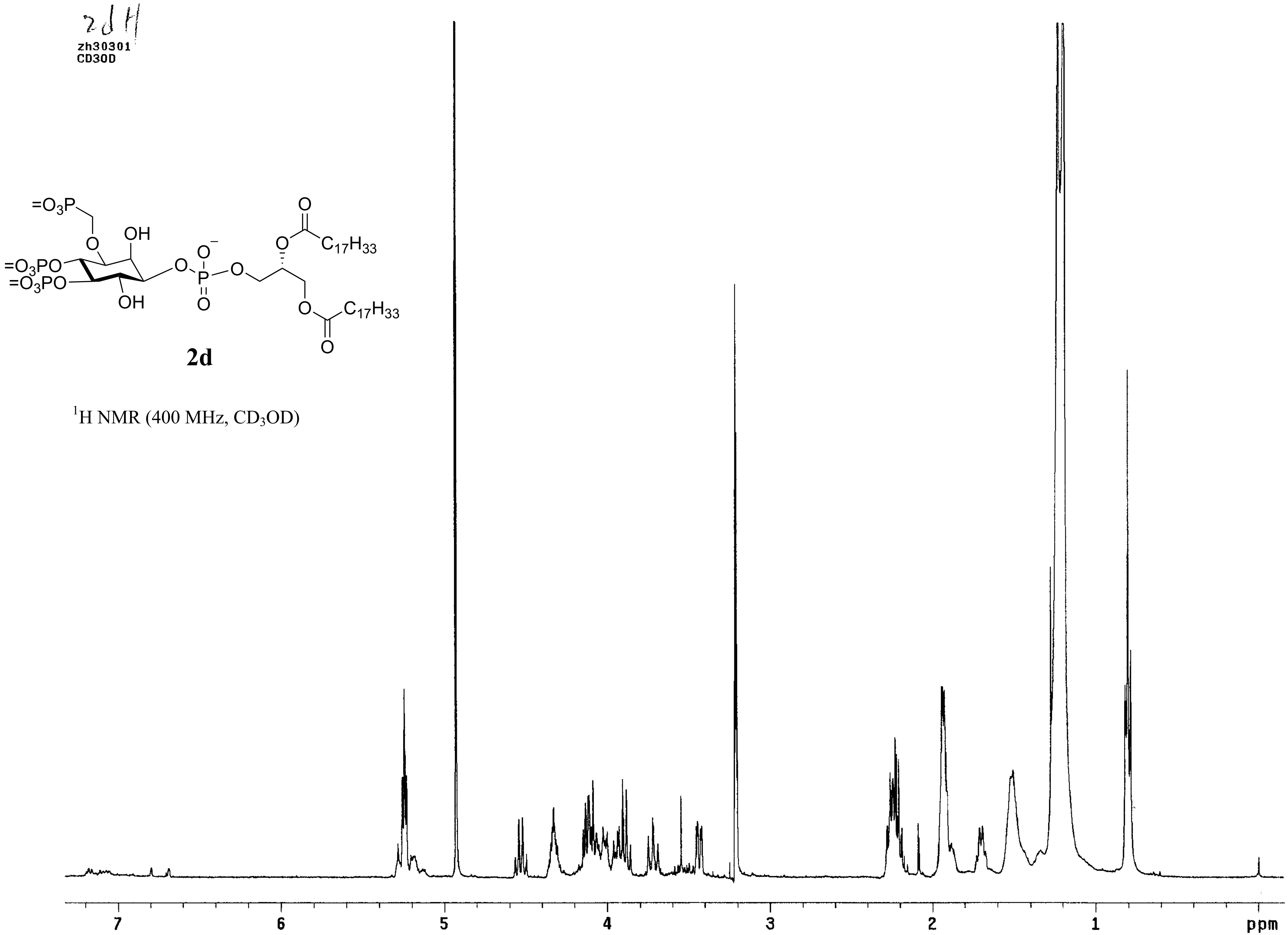
2cc



2c

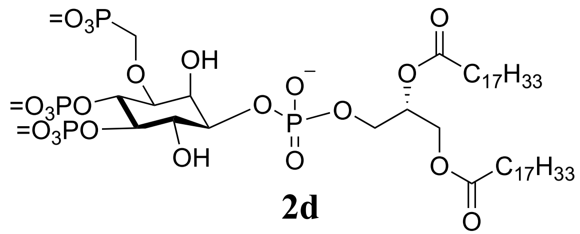
[13]C NMR (101 MHz, $CD_3OD/CDCl_3 = 3:1$)




2d
^{1}H NMR (400 MHz, CD_3OD)
2d H
zh30301
CD3OD
7
6
5
4
3
2
1
ppm

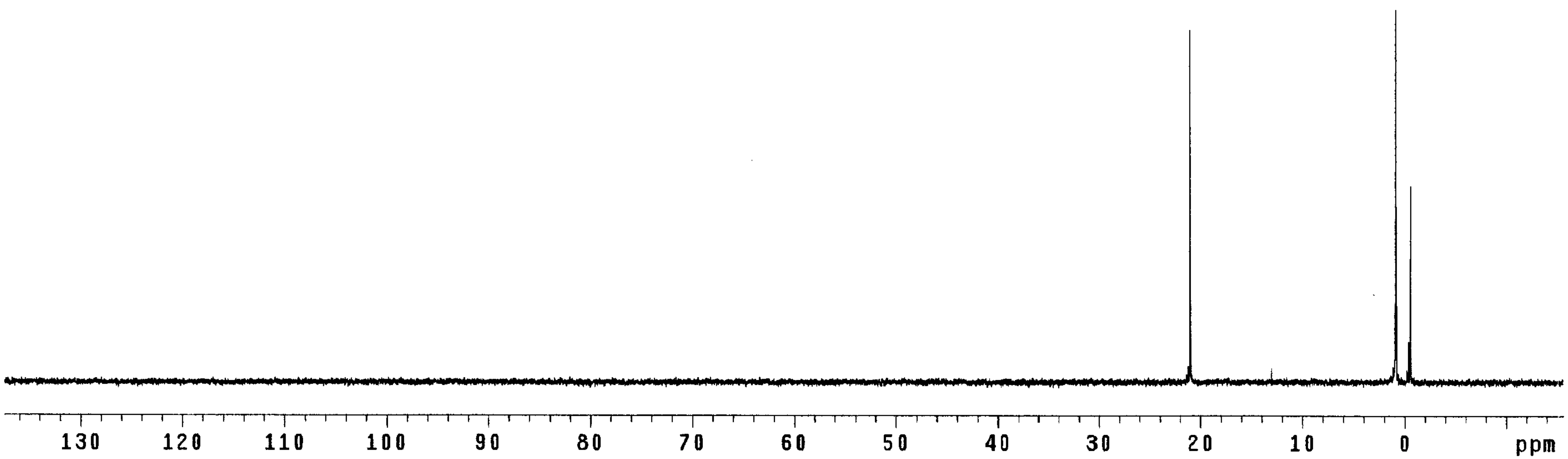
2d P

zh30301P
CD3OD

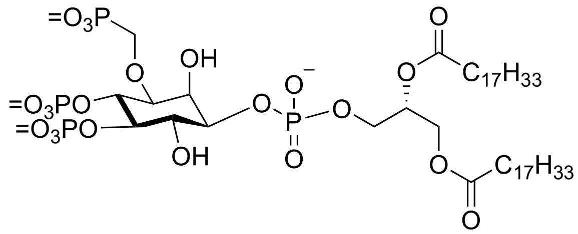


2d

^{31}P NMR (162 MHz, CD_3OD)



2dC



2d

^{13}C NMR (101 MHz, CD_3OD)