Synthesis and Use of Glycosyl Phosphates as Powerful Glycosyl Donors

Obadiah J. Plante, Rodrigo B. Andrade, and Peter H. Seeberger*

Department of Chemistry, Massachusetts Institute of Technology

Cambridge, Massachusetts 02139

Supplementary Material

Supporting Information Available. Detailed experimental procedures and compound characterization data including ^{1}H, ^{13}C and ^{31}P NMR spectra for all compounds in this study (61 pages).

Experimental Section

General Methods. All chemicals used were reagent grade and used as supplied except where noted. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride under N_2. Analytical thin-layer chromatography was performed on E. Merck silicagel 60 F_{254} plates (0.25 mm). Compounds were visualized by dipping the plates in a cerium sulfate-ammonium molybdate solution followed by heating. Liquid column chromatography was performed using forced flow of the indicated solvent on Sigma H-type silica (10-40 μm). ^{1}H NMR spectra were obtained on a Varian VXR-500 (500 MHz) or (300 MHz) and are reported in parts per million (δ) relative to tetramethylsilane (0.00 ppm), $CHCl_3$

(7.24 ppm). Coupling constants (*J*) are reported in Hertz. ^{13}C NMR spectra were obtained on a VXR-500 (125 MHz) and are reported in δ relative to $CDCl_3$ (77.0 ppm) as an internal reference. ^{31}P NMR spectra were obtained on a VXR-500 (200 MHz) and are reported in δ relative to H_3PO_4 (0.0 ppm) as an external reference.

Synthesis of β-Enriched Glycosyl Phosphates. General Procedure A. Suitably protected glycal (0.30 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0°C. A 0.08M solution of dimethyldioxirane in acetone (6 mL, 0.45 mmol) was added and the reaction was stirred for 15 min. After the solvent was removed in a stream of N_2 and the remaining residue dried in vacuo for 15 min at 0°C, 5 mL CH_2Cl_2 were added. The solution was cooled to -78°C for 15 min. A solution of dialkylphosphate (0.33 mmol) in 5 mL CH_2Cl_2 was added dropwise over 5 min. After complete addition, DMAP (0.15 mg, 1.2 mmol) and pivaloyl chloride (75 μL, 0.60 mmol) were added. The solution was warmed to room temperature over 1 h. The solvent was removed in a stream of N_2 and the residue chromatographed over silica gel to afford glycosyl phosphates as clear oils.

Synthesis of α-Enriched Glycosyl Phosphates. General Procedure B. Suitably protected glycal (0.30 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0°C. A 0.08M solution of dimethyldioxirane in acetone (6 mL, 0.45 mmol) was added and the reaction was stirred for 15 min. After the solvent was removed in a stream of N_2 and the remaining residue dried in vacuo for 15 min at 0°C, 5 mL THF were added. The solution was cooled to -78°C for 15 min. A solution of dialkylphosphate (0.33 mmol) in 5 mL THF was added dropwise over 5 min. After complete addition, DMAP (0.15 mg, 1.2

mmol) and pivaloyl chloride (75 μL, 0.60 mmol) were added. The solution was warmed to room temperature over 1 h. The solvent was removed in a stream of N_2 and the residue chromatographed over silica gel to afford the glycosyl phosphates as clear oils.

Dibenzyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside phosphate 1β. General Procedure A (74%, 10:1 β:α) $[\alpha]^{24}_D$: +45.4° (c 1.16, CH_2Cl_2); IR (thin film) 3010, 2941, 1740, 1455, 1016 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.37-7.25 (m, 23H), 7.18-7.16 (m, 2H), 5.35 (t, *J* = 7.25 Hz, 1H), 5.24 (t, *J* = 8.50 Hz, 1H), 5.11-5.09 (m, 2H), 5.03 (d, *J* = 7.00 Hz, 2H), 4.82-4.77 (m, 2H), 4.72 (d, *J* = 11.0 Hz, 1H), 4.58-4.52 (m, 2H), 4.44 (d, *J* = 12.0 Hz, 1H), 3.85 (t, *J* = 9.50 Hz, 1H), 3.77-3.64 (m, 4H), 1.15 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 177.7, 138.3, 138.2, 138.0, 135.9, 135.8, 128.8, 128.7, 128.6, 128.0, 127.9, 127.6, 95.2, 95.1, 79.5, 76.8, 75.6, 75.3, 73.7, 72.7, 72.6, 69.7, 69.6, 69.5, 68.0, 38.9, 27.3; ^{31}P-NMR ($CDCl_3$) δ -3.1; FAB MS *m/z* (M^+) calcd 794.3219, obsd 794.3224.

Dibenzyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside phosphate 1α. General Procedure B (71%, 1:10 β:α) $[\alpha]^{24}_D$: +53.3° (c 1.44, CH_2Cl_2); IR (thin film) 2941, 2866, 1740, 1454, 1282 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.37-7.25 (m, 23H), 7.18-7.16 (m, 2H), 5.95 (dd, *J* = 3.50, 6.00 Hz, 1H), 5.09-5.05 (m, 4H), 4.97 (dt, *J* = 3.50, 10.0 Hz, 1H), 4.82-4.79 (m, 3H), 4.58 (d, *J* = 11.5 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 1H), 4.44 (d, *J* = 11.0 Hz, 1H), 4.02 (t, *J* = 9.25 Hz, 2H), 3.81 (t, *J* = 9.50 Hz, 1H), 3.69 (dd, *J* = 3.50, 12.5 Hz, 1H), 3.50 (dd, *J* = 1.50, 11.0 Hz, 1H), 1.18 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 177.7, 138.3, 138.2, 138.0, 135.9, 135.8, 128.8, 128.7, 128.6, 128.0, 127.9, 127.6, 95.2, 95.1, 79.5, 76.8, 75.6, 75.3, 73.7, 72.7, 72.6, 69.7, 69.6, 69.5, 68.0, 38.9, 27.3; ^{31}P-NMR ($CDCl_3$) δ -1.8; FAB MS *m/z* (M^+) calcd 794.3219, obsd 794.3216.

Dibutyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside phosphate 2β. General Procedure A (65%, 11:1 β:α) $[\alpha]^{24}_{D}$: -1.9° (c 1.50, CH_2Cl_2); IR (thin film) 2946, 1740, 1454, 1282, 1016 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.33-7.25 (m, 13H), 7.16-7.14 (m, 2H), 5.24 (t, *J* = 7.25 Hz, 1H), 5.17 (t, *J* = 8.50 Hz, 1H), 4.80-4.75 (m, 2H), 4.70 (d, *J* = 11.0 Hz, 1H), 4.69-4.54 (m, 2H), 4.51 (d, *J* = 11.0 Hz, 1H), 4.08-4.00 (m, 4H), 3.82 (t, *J* = 9.50 Hz, 1H), 3.78-3.70 (m, 3H), 3.64-3.61 (m, 1H), 1.64-1.59 (m, 4H), 1.40-1.34 (m, 4H), 1.20 (s, 9H), 0.96-0.88 (m, 6H); ^{13}C-NMR ($CDCl_3$) δ 177.2, 138.2, 138.1, 128.7, 128.3, 128.2, 128.1, 128.0, 127.6, 97.0, 96.5, 83.1, 76.2, 75.9, 73.9, 73.3, 68.4, 68.2, 68.1, 39.2, 32.7, 26.9, 19.1, 14.0; ^{31}P-NMR ($CDCl_3$) δ -2.2; FAB MS *m/z* (M^+) calcd 726.3532, obsd 726.3537.

Dibutyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranoside phosphate 2α. General Procedure B (59%, 1:4 β:α) $[\alpha]^{24}_{D}$: +50.5° (c 0.63, CH_2Cl_2); IR (thin film) 2960, 2872, 1736, 1454, 1282 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.35-7.27 (m, 13 H), 7.18-7.15 (m, 2H), 5.85 (dd, *J* = 1.75, 6.35 Hz, 1H), 4.99-4.97 (m, 1H), 4.83-4.80 (m, 3H), 4.63 (d, *J* = 11.5 Hz, 1H), 4.56-4.50 (m, 3H), 4.10-4.02 (m, 5H), 3.86-3.79 (m, 2H), 3.68 (d, *J* = 11.0 Hz, 1H), 1.86-1.61 (m, 4H), 1.44-1.36 (m, 4H), 1.24 (s, 9H), 0.97-0.91 (m, 6H); ^{13}C-NMR ($CDCl_3$) δ 177.7, 138.3, 138.1, 138.0, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 94.7, 94.6, 79.5, 75.6, 75.4, 73.7, 72.7, 72.6, 68.2, 68.0, 67.9, 67.8, 39.0, 32.5, 32.4, 27.3, 18.8, 13.8; ^{31}P-NMR ($CDCl_3$) δ -2.5; FAB MS *m/z* (M^+) calcd 726.3532, obsd 726.3537.

Dibutyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranoside phosphate 3β. General Procedure A (57%, 4:1 β:α) $[\alpha]^{24}_{D}$: +7.7° (c 0.64,

CH_2Cl_2); IR (thin film) 2960, 2872, 1740, 1454, 1277 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.36-7.25 (m, 15H), 5.49 (dd, *J* = 8.00, 10.0 Hz, 1H), 5.20 (t, *J* = 7.50 Hz, 1H), 4.92 (d, *J* = 11.5 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 11.5 Hz, 1H), 4.47-4.41 (m, 2H), 4.05-3.96 (m, 5H), 3.73 (t, *J* = 6.50 Hz, 1H), 3.64 (t, *J* = 7.00 Hz, 1H), 3.60-3.57 (m, 3H), 1.64-1.56 (m, 4H), 1.41-1.32 (m, 4H), 1.20 (s, 9H), 0.93-0.87 (m, 6H); ^{13}C-NMR ($CDCl_3$) δ 177.3, 138.6, 138.0, 137.8, 128.8, 128.7, 128.5, 128.2, 128.1, 128.0, 127.6, 97.4, 80.7, 74.9, 74.4, 73.8, 72.8, 72.6, 71.2, 71.1, 68.3, 68.1, 68.0, 39.2, 32.4, 32.3, 27.5, 18.9, 13.9; ^{31}P-NMR ($CDCl_3$) δ -2.2; FAB MS *m/z* (M^+) calcd 726.3532, obsd 726.3531.

Dibutyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-α-D-galactopyranoside phosphate 3α. General Procedure A (57%, 4:1 β:α) $[\alpha]^{24}_D$: +65.4° (c 2.41, CH_2Cl_2); IR (thin film) 2960, 2872, 1734, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.36-7.25 (m, 15H), 5.84 (dd, *J* = 3.60, 6.00 Hz, 1H), 5.41 (dt, *J* = 3.30, 7.20 Hz, 1H), 4.96 (d, *J* = 11.40 Hz, 1H), 4.70 (s, 2H), 4.56 (d, *J* = 11.40 Hz, 1H), 4.43 (d, *J* = 1.80 Hz, 2H), 4.19 (t, *J* = 6.30, 1H), 4.09-3.97 (m, 6H), 3.63-3.51 (m, 2H), 1.66-1.57 (m, 4H), 1.43-1.29 (m, 4H), 1.24 (s, 9H), 0.94-0.88 (m, 6H); ^{13}C-NMR ($CDCl_3$) δ 177.8, 138.4, 138.1, 137.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.5, 95.4, 95.3, 76.4, 75.0, 74.2, 73.7, 72.9, 71.5, 70.0, 69.9, 68.5, 68.0, 67.9, 67.8, 39.0, 32.5, 32.4, 27.4, 18.8, 13.8; ^{31}P-NMR ($CDCl_3$) δ -2.3; FAB MS *m/z* (M^+) calcd 726.3532, obsd 726.3536.

Dibenzyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-6-*O*-triisopropylsilyl-β-D-glucopyranoside phosphate 4. General Procedure A (65%, 1:0 β:α) $[\alpha]^{24}_D$: +32.9° (c 1.12, CH_2Cl_2); IR (thin film) 2941, 2866, 1740, 1455, 1127 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.36-7.26 (m, 20H), 5.33 (t, *J* = 7.75 Hz, 1H), 5.16 (t, *J* = 8.75 Hz, 1H), 5.07 (d, *J* = 7.50 Hz, 2H), 4.99 (d, *J* = 7.00 Hz, 2H), 4.81 (d, *J* = 10.5 Hz,

2H), 4.75-4.69 (m, 2H), 4.02-3.95 (m, 2H), 3.90 (t, J = 9.25 Hz, 1H), 3.75 (t, J = 9.00 Hz, 1H), 3.51-3.49 (m, 1H), 1.14 (s, 9H), 1.03 (s, 21H); ^{13}C-NMR ($CDCl_3$) δ 177.2, 138.2, 138.1, 128.1, 128.0, 127.8, 127.6, 97.2, 83.0, 75.4, 75.2, 73.2, 73.1, 69.7, 69.5, 67.3, 62.2, 39.0, 18.2, 12.1; ^{31}P-NMR ($CDCl_3$) δ -2.8; FAB MS *m/z* (M^+) calcd 860.4084, obsd 860.4080.

Dibutyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-6-*O*-triisopropylsilyl-β-D-glucopyranoside phosphate 5β. General Procedure B (70%, 1:1 β:α) $[\alpha]^{24}_D$: -9.1° (c 2.79, CH_2Cl_2); IR (thin film) 2960, 2866, 1742, 1462, 1396 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.38-7.21 (m, 10H), 5.24 (t, J = 6.90 Hz, 1H), 5.10 (t, J = 9.00, 1H), 4.78 (t, J = 12.00 Hz, 2H), 4.71 (t, J = 10.8 Hz, 2H), 4.12-3.94 (m, 6H), 3.87 (t, J = 9.30 Hz, 1H), 3.72 (t, J = 9.30 Hz, 1H), 3.48 (d, J = 9.90 Hz, 1H), 1.65-1.56 (m, 4H), 1.20 (s, 9H), 1.07 (s, 21H); ^{13}C-NMR ($CDCl_3$) δ 177.0, 138.2, 128.6, 128.4, 128.2, 128.0, 127.8, 127.5, 96.8, 83.0, 75.1, 73.2, 68.0, 62.3, 39.0, 32.4, 27.3, 18.8, 13.8, 12.1; ^{31}P-NMR ($CDCl_3$) δ -2.56; FAB MS *m/z* (M^+) calcd 792.4397, obsd 792.4392.

Dibutyl 3,4-di-*O*-benzyl-2-*O*-pivaloyl-6-*O*-triisopropylsilyl-α-D-glucopyranoside phosphate 5α. General Procedure B (70%, 1:1 β:α) $[\alpha]^{24}_D$: +10.8° (c 1.00, CH_2Cl_2); IR (thin film) 2959, 2866, 1737, 1460, 1363 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.38-7.19 (m, 10H), 5.78 (dd, J = 6.25, 3.00 Hz, 1H), 4.86 (t, J = 10.0 Hz, 1H), 4.80 (t, J = 12.0 Hz, 2H), 4.74 (t, J = 10.0 Hz, 1H), 4.11-3.92 (m, 6H), 3.92-3.82 (m, 3H), 1.70-1.58 (m, 4H), 1.44-1.32 (m, 4H), 1.21 (s, 9H), 1.05 (m, 21H), 0.95-0.88 (m, 6H); ^{13}C-NMR ($CDCl_3$) δ 177.8, 138.4, 128.6, 127.9, 94.8, 79.3, 75.4, 72.7, 67.8, 61.8, 38.9, 32.5, 27.3, 18.8, 18.5, 18.2, 13.7, 13.1; ^{31}P-NMR ($CDCl_3$) δ -2.45; FAB MS *m/z* (M^+) calcd 792.4397, obsd 792.4394.

Dibutyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-tri-*O*-pivaloyl-β-D-glucopyranoside phosphate 6. General Procedure A (75%, 1:0 β:α) $[\alpha]^{24}_{D}$: +13.1° (c 1.00, CH_2Cl_2); IR (thin film) 2961, 2874, 1746, 1479, 1397 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.29 (t, *J* = 9.50 Hz, 1H), 5.18 (t, *J* = 9.50 Hz, 1H), 5.09 (t, *J* = 8.50 Hz, 1H), 4.14-3.94 (m, 5H), 3.74-3.62 (m, 4H), 1.64-1.57 (m, 4H), 1.42-1.31 (m, 4H), 1.14 (s, 9H), 1.13 (s, 9H), 1.11 (s, 9H), 0.96-0.84 (m, 6H), 0.86 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 177.2, 176.7, 176.2, 96.6, 75.6, 72.5, 68.1, 31.7, 38.9, 32.3, 27.3, 25.9, 18.4, 13.7, -5.2; ^{31}P-NMR ($CDCl_3$) δ -3.21; FAB MS *m/z* (M^+) calcd 754.4452, obsd 754.4455.

Synthesis of 2-O-Triethylsilyl Glycosyl Phosphates. General Procedure C. Suitably protected glycal (0.30 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0°C. A 0.08M solution of dimethyldioxirane in acetone (6 mL, 0.45 mmol) was added and the reaction was stirred for 15 min. After the solvent was removed in a stream of N_2 and the remaining residue dried in vacuo for 15 min at 0°C, 5 mL THF were added. To the reaction vessel was added a solution of dialkylphosphate (0.33 mmol) in 5 mL THF dropwise over 5 min. at 0°C. After stirring for 10 min, imidazole (71 mg, 1.05 mmol) and triethylsilylchloride (126 μL, 0.75 mmol) were added. The solution was warmed to room temperature for 2 h. The reaction mixture was diluted with EtOAc (50 mL) and washed with a saturated $NaHCO_3$ solution, brine and water. After back extraction of the aqueous layers with 2 x 50 mL EtOAc, the organics were dried over Na_2SO_4 and concentrated. The crude product was purified by flash silica column chromatography to afford 2-O-triethylsilylglycosyl phosphates.

Dibutyl 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside-(1→4)-3,6-di-*O*-benzyl-2-*O*-triethylsilyl-β-D-glucopyranoside phosphate 7. General Procedure C (71%, 1:0 β:α) $[\alpha]^{24}_{D}$: +5.4° (c 1.06, CH_2Cl_2); IR (thin film) 2957, 2874, 1454, 1362, 1279 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.33-7.15 (m, 30H), 5.17 (d, *J* = 18.0 Hz, 1H), 5.00 (dd, *J* = 5.85, 6.00 Hz, 1H), 4.90 (d, *J* = 12.0 Hz, 1H), 4.80-4.60 (m, 5H), 4.50-4.28 (m, 5H), 4.19 (d, *J* = 12.0 Hz, 1H), 4.11-3.98 (m, 6H), 3.86-3.82 (m, 2H), 3.74-3.56 (m, 3H), 3.49-3.25 (m, 5H), 1.66-1.56 (m, 4H), 1.43-1.31 (m, 4H), 0.97-0.85 (m, 15H), 0.64-0.56 (m, 6H); ^{13}C-NMR ($CDCl_3$) δ 139.6, 139.3, 138.9, 138.8, 138.4, 138.3, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 126.9, 102.9, 99.6, 99.5, 83.5, 82.7, 80.1, 76.3, 75.7, 75.6, 74.9, 74.8, 73.8, 73.6, 73.4, 73.3, 72.8, 68.3, 68.1, 67.8, 67.7, 32.5, 32.4, 18.9, 13.9, 7.1, 5.2; ^{31}P-NMR ($CDCl_3$) δ -2.0; FAB MS *m/z* (M^+) calcd 1188.5759, obsd 1188.5756.

Dibutyl 3,4,6-tri-*O*-benzyl-2-*O*-triethylsilyl-β-D-glucopyranoside phosphate 8β. General Procedure C (79%, 2:1 β:α) $[\alpha]^{24}_{D}$: -8.3° (c 4.39, CH_2Cl_2); IR (thin film) 2976, 2870, 1460, 1130 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.37-7.25 (m, 13H), 7.12-7.09 (m, 2H), 5.02 (dd, *J* = 6.00, 7.50 Hz, 1H), 4.93-4.86 (m, 2H), 4.75 (d, *J* = 11.0 Hz, 1H), 4.61-4.50 (m, 3H), 4.13-4.08 (m, 4H), 3.75-3.67 (m, 4H), 3.61-3.58 (m, 1H), 3.55 (t, *J* = 8.57 Hz, 1H), 1.69-1.60 (m, 4H), 1.45-1.38 (m, 4H), 1.00-0.89 (m, 15H), 0.68 (q, *J* = 8.00 Hz, 6H); ^{13}C-NMR ($CDCl_3$) δ 139.0, 138.3, 138.2, 128.7, 128.6, 128.2, 128.1, 128.0, 127.6, 127.5, 99.5, 85.8, 77.9, 75.8, 75.6, 75.5, 75.4, 75.2, 73.8, 68.8, 68.0, 67.9, 32.6, 32.5, 19.0, 14.0, 13.9, 7.2, 5.3; ^{31}P-NMR ($CDCl_3$) δ -1.4; FAB MS *m/z* (M^+) calcd 756.3822, obsd 756.3822.

Dibutyl 3,4,6-tri-*O*-benzyl-2-*O*-triethylsilyl-α-D-glucopyranoside phosphate 8α. General Procedure C (79%, 2:1 β:α) $[\alpha]^{24}_{D}$: +44.1° (c 1.50, CH_2Cl_2); IR (thin film) 2976, 2870, 1460, 1130 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.37-7.26 (m, 13H), 7.10-7.09 (m, 2H), 5.65 (dd, *J* = 2.50, 6.25 Hz, 1H), 4.93 (d, *J* = 11.5 Hz, 1H), 4.83-4.79 (m, 2H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.51-4.47 (m, 2H), 4.12-3.98 (m, 5H), 3.84-3.70 (m, 4H), 3.65 (d, *J* = 10.0 Hz, 1H), 1.70-1.60 (m, 4H), 1.45-1.34 (m, 4H), 1.02-0.89 (m, 15H), 0.67 (q, *J* = 8.00 Hz, 6H); ^{13}C-NMR ($CDCl_3$) δ 138.9, 138.3, 138.0, 128.6, 128.5, 128.2, 128.0, 127.9, 127.7, 127.6, 97.9, 97.8, 82.2, 75.8, 75.3, 73.8, 73.4, 73.3, 72.5, 68.3, 67.8, 67.6, 67.5, 32.5, 32.4, 18.9, 18.8, 13.8, 7.0, 5.1; ^{31}P-NMR ($CDCl_3$) δ -2.3; FAB MS *m/z* (M^+) calcd 756.3822, obsd 756.3823.

Synthesis of Disaccharides and Thioglycosides. General Procedure D. β–Phosphate glycosyl donor (0.12 mmol) and glycosyl acceptor (0.10 mmol) were combined and azeotropically dried with toluene (3 x 5 mL) followed by 1h under vacuum. The mixture was dissolved in anh. CH_2Cl_2 and cooled to -78°C for 15 min. Trimethylsilyltriflate (22 μL, 0.12 mmol) was added dropwise. After stirring for 10 min at -78°C, triethylamine (30 μL) was added. The solution was warmed to room temperature and the solvent was removed in a stream of N_2. The resulting crude product was purified by flash silica column chromatography to afford fully protected disaccharides and thioglycosides.

Synthesis of Disaccharides and Thioglycosides. General Procedure E. α–Phosphate glycosyl donor (0.12 mmol) and glycosyl acceptor (0.10 mmol) were combined and azeotropically dried with toluene (3 x 5 mL) followed by 1h under vacuum. The mixture was dissolved in anh. CH_2Cl_2

and cooled to -20°C for 15 min. Trimethylsilyltriflate (22 μL, 0.13 mmol) was added dropwise. After stirring for 10 min at -20°C, triethylamine (30 μL) was added. The solution was warmed to room temperature and the solvent was removed in a stream of N_2. The resulting crude product was purified by flash silica column chromatography to afford fully protected disaccharides and thioglycosides.

3,4,6-Tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside 13. General Procedure D (94%). All spectral data matched that described in reference 13, Plante and Seeberger *J. Org. Chem.* in press.

Methyl 2-*O*-Pivaloyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside-(1→2)-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside 14. General Procedure D (83%) $[\alpha]^{24}_D$: -14.3° (c 1.65, CH_2Cl_2); IR (thin film) 2868, 1740, 1456, 1054 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.42-7.26 (m, 28 H), 7.20-7.17 (m, 2H), 5.18 (t, *J* = 8.50 Hz, 1H), 5.03 (d, *J* = 8.00 Hz, 1H), 4.97 (d, *J* = 11.5 Hz, 1H), 4.84-4.75 (m, 4H), 4.71-4.64 (m, 3H), 4.61-4.54 (m, 4H), 4.40 (d, *J* = 14.0 Hz, 1H), 3.81-3.62 (m, 9H), 3.53 (s, 4H), 3.51-3.46 (m, 1H), 1.13 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 177.0, 139.0, 138.5, 138.3, 128.7, 128.6, 128.3, 128.1, 128.0, 127.8, 127.7, 127.5, 103.3, 99.8, 85.4, 84.0, 80.0, 78.2, 75.8, 75.3, 75.2, 75.0, 73.9, 73.8, 69.1, 69.0, 57.3, 39.1, 27.5; FAB MS *m/z* (M^+) calcd 980.4710, obsd 980.4708.

3,4-Di-*O*-benzyl-2-*O*-pivaloyl-6-*O*-triisopropylsilyl-β-D-glucopyranoside-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside 15. General Procedure D (82%) $[\alpha]^{24}_D$: -37.7° (c 1.37, CH_2Cl_2); IR (thin film) 2964, 2868, 1740, 1650, 1037 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.34-7.26 (m, 10H), 5.49 (d, *J*

= 5.00 Hz, 1H), 5.04 (t, *J* = 8.75 Hz, 1H), 4.79 (t, *J* = 9.00 Hz, 2H), 4.70 (t, *J* = 9.00 Hz, 2H), 4.57 (d, *J* = 8.00 Hz, 1H), 4.45 (d, *J* = 8.00 Hz, 1H), 4.28-4.27 (m, 1H), 4.26 (t, *J* = 15.0 Hz, 1H), 4.04-3.98 (m, 3H), 3.90 (t, *J* = 5.75 Hz, 1H), 3.81 (t, *J* = 9.25 Hz, 1H), 3.71 (t, *J* = 9.25 Hz, 1H), 3.56 (dd, *J* = 6.00 10.0 Hz, 1H), 3.34 (d, *J* = 9.50 Hz, 1H), 1.50 (s, 3H), 1.44 (s, 3H), 1.33 (s, 3H), 1.31 (s, 3H), 1.20 (s, 9H), 1.14-1.09 (m, 21H); ^{13}C-NMR ($CDCl_3$) δ 177.1, 138.5, 128.6, 128.5, 128.1, 127.9, 127.8, 127.7, 109.2, 108.6, 101.4, 96.4, 83.5, 77.5, 76.4, 75.2, 75.1, 73.3, 71.2, 70.8, 70.7, 68.1, 67.1, 62.4, 39.0, 27.4, 26.3, 26.2, 25.2, 24.5, 18.2, 12.2; FAB MS *m/z* (M^+) calcd 842.4636, obsd 842.4639.

3,4,6-Tri-*O*-benzyl-β-D-glucopyranoside-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside 16. General Procedure D (71%) $[\alpha]^{24}_D$: -45.9° (c 0.61, CH_2Cl_2); IR (thin film) 3474, 2916, 1453, 1381, 1068 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.42-7.25 (m, 13H), 7.17-7.13 (m, 2H), 5.57 (d, *J* = 5.29 Hz, 1H), 5.03 (d, *J* = 11.2 Hz, 1H), 4.83 (t, *J* = 10.9 Hz, 2H), 4.64-4.60 (m, 2H), 4.55-4.49 (m, 2H), 4.37-4.32 (m, 2H), 4.23 (dd, *J* = 1.87, 7.79 Hz, 1H), 4.12 (dd, *J* = 3.43, 10.9 Hz, 1H), 4.06-4.01 (m, 1H), 3.78-3.70 (m, 3H), 3.63-3.61 (m, 3H), 3.52-3.47 (m, 1H), 3.04 (bs, 1H), 1.55 (s, 3H), 1.46 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 138.9, 138.2, 128.5, 128.0, 127.8, 127.7, 109.7, 109.0, 104.2, 96.4, 84.8, 77.5, 75.3, 75.0, 73.7, 71.4, 70.9, 70.6, 69.7, 69.0, 68.1, 26.3, 26.2, 25.3, 24.7; FAB MS *m/z* (M^+) calcd 692.3196, obsd 692.3192.

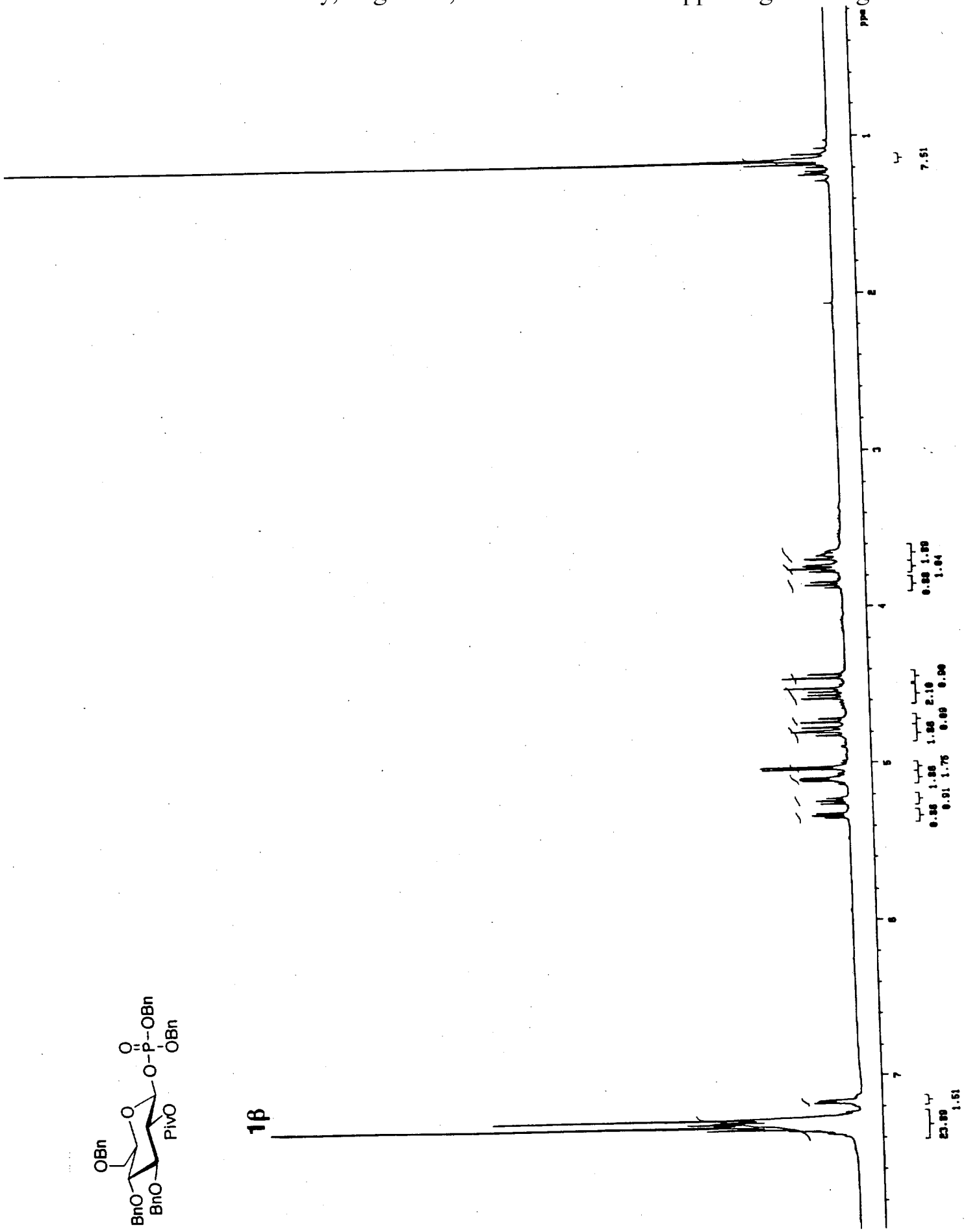
Thioethyl 3,4,6-Tri-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 17. General Procedure D (90%) All spectral data matched that described in reference 18, Seeberger et al. *J. Am. Chem. Soc.* **1997**, *119*, 10064.

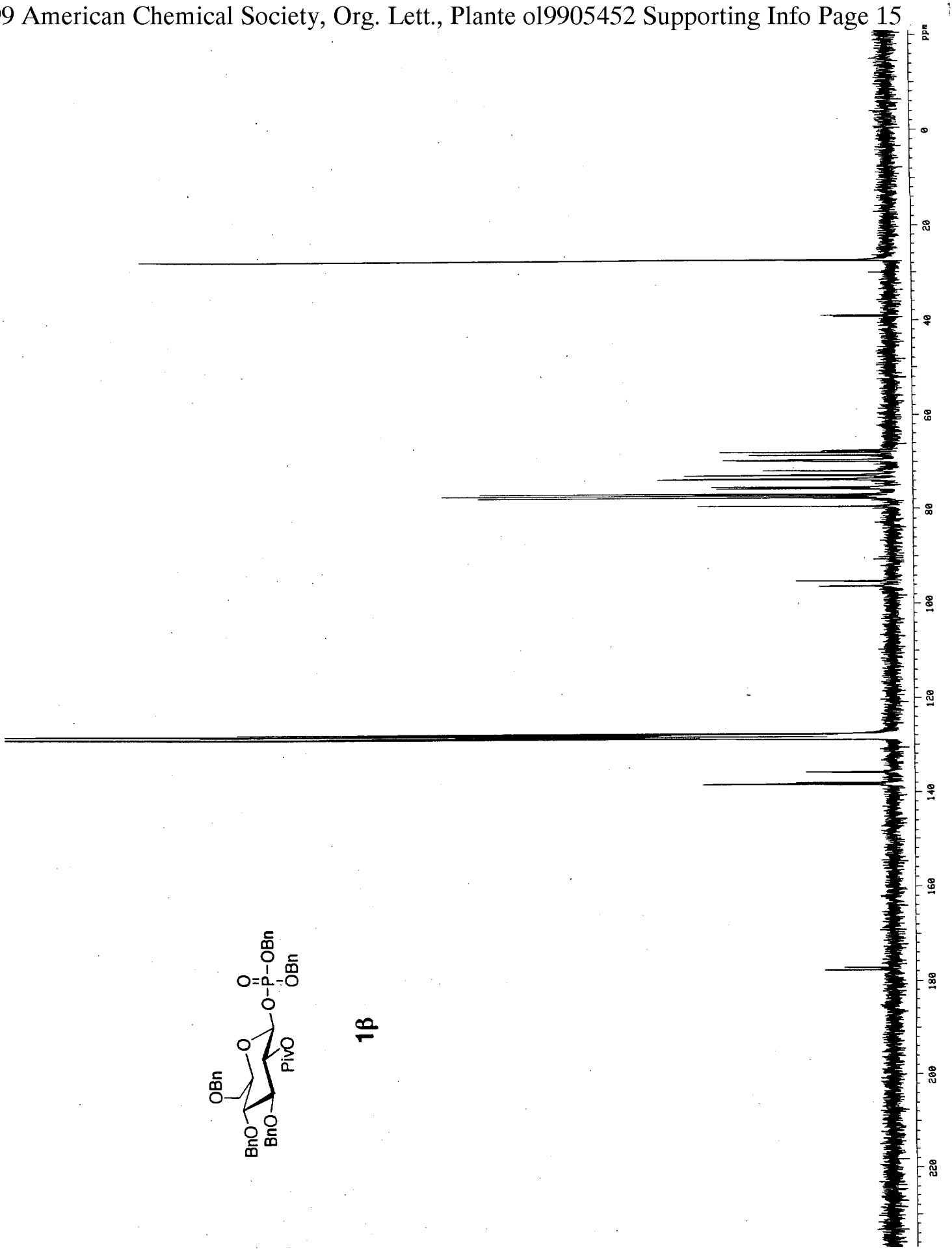
Thioethyl 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-β-D-mannopyranoside 18.

General Procedure D (83%) $[\alpha]^{24}_{D}$: -38.3° (c 1.14, CH_2Cl_2); IR (thin film) 2968, 2869, 1734, 1453, 1364 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.35-7.24 (m, 23H), 7.18-7.16 (m, 2H), 5.56 (d, *J* = 2.50 Hz, 1H), 5.10 (t, *J* = 8.50 Hz, 1H), 4.84 (d, *J* = 11.0 Hz, 1H), 4.79-4.74 (m, 2H), 4.72-4.68 (m, 2H), 4.62-4.50 (m, 6H), 4.43 (d, *J* = 11.0 Hz, 1H), 4.06 (d, *J* = 11.0 Hz, 1H), 3.75-3.66 (m, 5H), 3.61-3.56 (m, 3H), 3.41 (t, *J* = 9.50 Hz, 1H), 2.73 (q, *J* = 7.50 Hz, 2H), 1.30 (t, *J* = 7.50 Hz, 3H), 1.26 (s, 9H), 1.20 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 177.9, 176.9, 138.4, 138.3, 138.1, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 101.4, 83.7, 82.4, 82.0, 79.8, 78.2, 75.4, 75.3, 75.1, 74.7, 73.9, 73.2, 71.8, 69.5, 69.4, 69.1, 39.4, 39.1, 27.6, 27.5, 25.9, 15.4; FAB MS *m/z* (M^+) calcd 1004.4744, obsd 1004.4741.

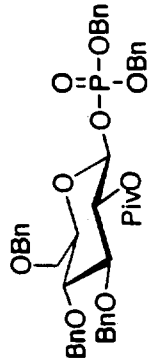
Synthesis of 2-*O*-pivaloyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside-(1→6)-3,4-di-*O*-benzyl-2-*O*-pivaloyl-α-D-mannopyranoside (1→4)-3,6-di-*O*-benzyl-D-*arabino*-hex-1-enitol 20. A mixture of thioethyl glycosyl donor **18** (55.3 mg, 0.055 mmol) and 3,6-di-*O*-benzylglucal **19** (16.3 mg, 0.050 mmol) was azeotroped with toluene (3 x 3 mL) and dried under vacuum for 1 h. CH_2Cl_2 (1 mL) was added to the mixture along with 60 mg freshly dried 4Å molecular sieves. The solution was cooled to 0°C and di-tert-butylpyridine (45 μL, 0.20 mmol) was added. After stirring at 0°C for 30 min, methyl triflate (22 μL, 0.20 mmol) was added. Stirring was continued for 16 h at 0°C followed by gradual warming to room temperature over 1 h. Triethylamine (50 μL) was added and stirring continued for 30 min. The solvent was removed in a stream of N_2 and the residue purified by flash silica column chromatography to afford trisaccharide **20** (44 mg, 68% yield). $[\alpha]^{24}_{D}$: -6.1° (c 0.89, CH_2Cl_2); IR (thin film) 2967, 2870, 1734, 1649, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.35-7.24 (m, 33H), 7.16-7.13 (m, 2H), 6.44 (d, *J* = 6.50 Hz, 1H), 5.36-5.34 (m, 1H), 5.19 (d, *J* =

1.50 Hz, 1H), 5.14 (t, J = 8.25 Hz, 1H), 4.89-4.87 (m, 1H), 4.83 (d, J = 11.0 Hz, 1H), 4.77 (d, J = 11.5 Hz, 1H), 4.73-4.67 (m, 2H), 4.64-4.42 (m, 11H), 4.26-4.22 (m, 1H), 4.11-4.08 (m, 1H), 4.05-4.03 (m, 2H), 3.92-3.88 (m, 2H), 3.84-3.78 (m, 2H), 3.71-3.62 (m, 6H), 3.54-3.30 (m, 1H), 1.19 (s, 9H), 1.15 (s, 9H); ^{13}C-NMR ($CDCl_3$) δ 177.7, 176.6, 144.9, 138.6, 138.5, 138.4, 138.3, 138.2, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 127.5, 101.2, 99.0, 97.8, 83.5, 78.3, 78.1, 76.5, 75.6, 75.1, 74.9, 74.6, 73.8, 73.7, 73.5, 72.9, 72.2, 71.8, 71.5, 70.0, 69.2, 69.0, 68.5, 68.0, 67.0, 39.1, 38.9, 27.4; FAB MS *m/z* (M^+) calcd 1268.6072, obsd 1268.6075.





1β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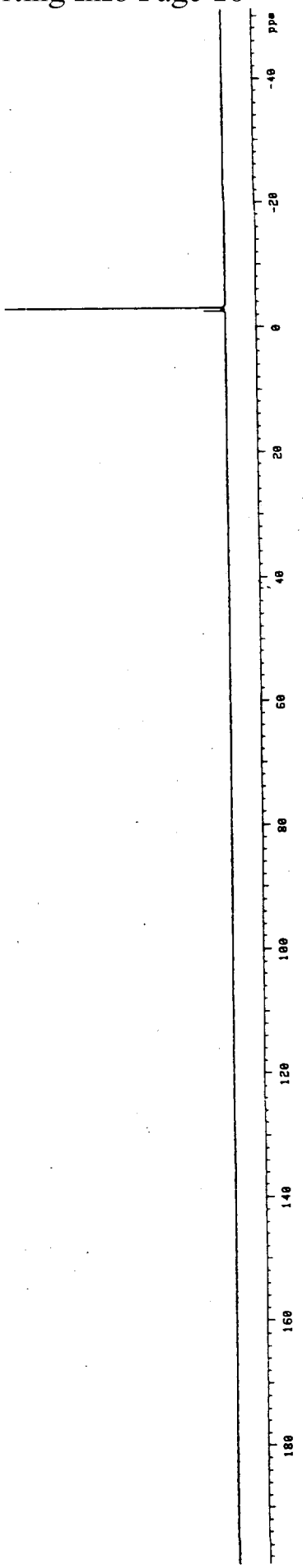
O-P-OBn
OBn
O
PivO
OBn
BnO
BnO

1β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40
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80
100
120
140
160
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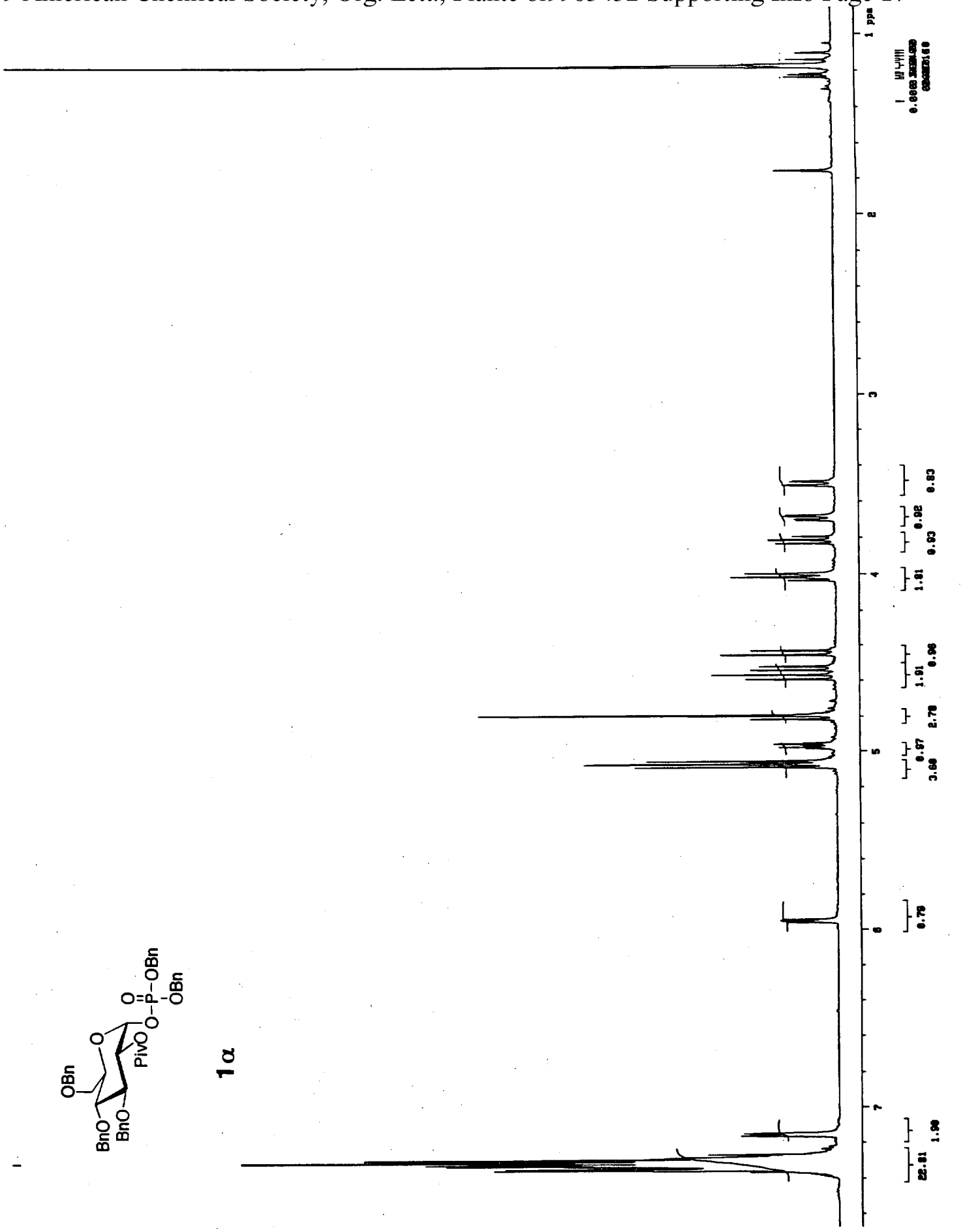

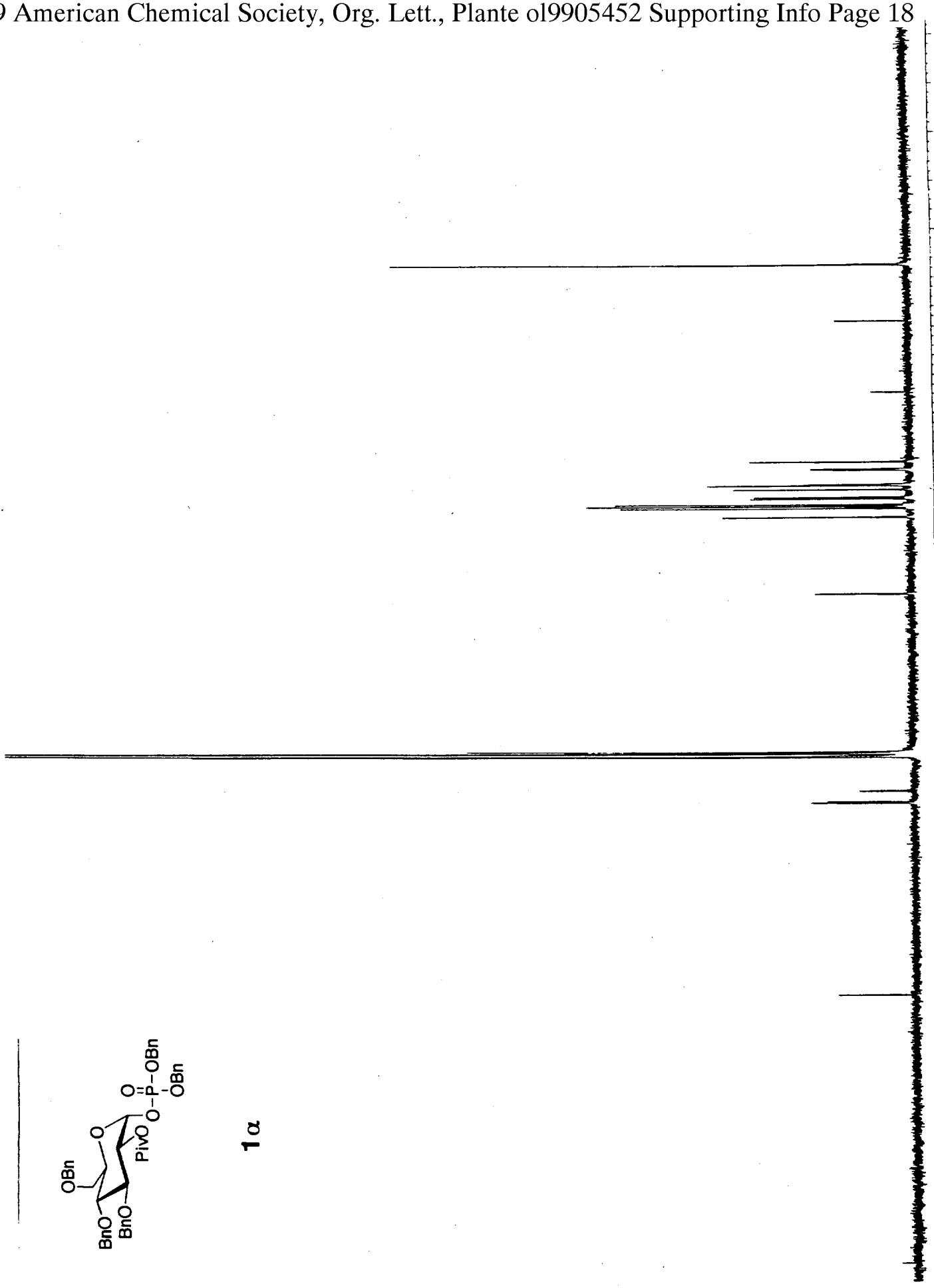

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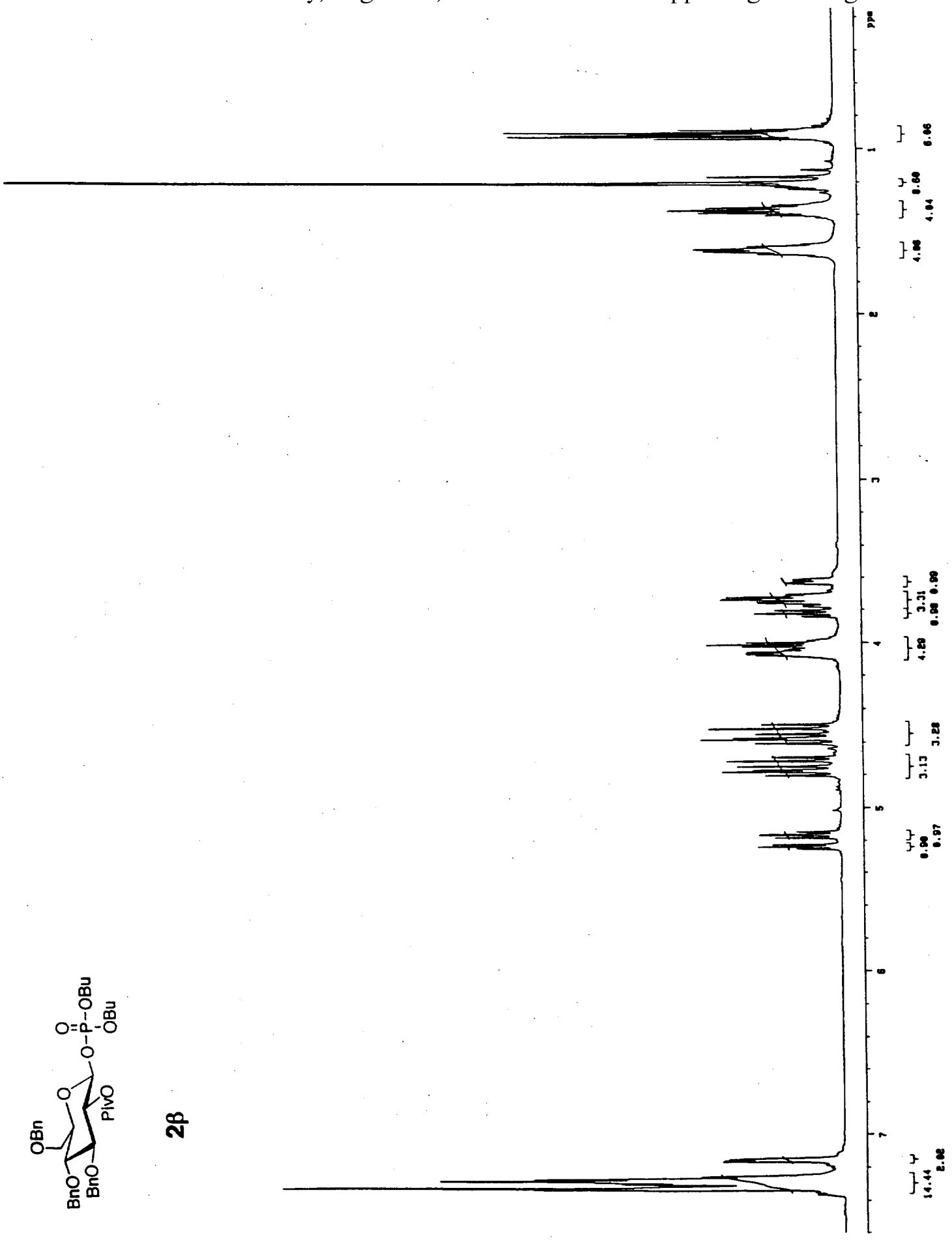

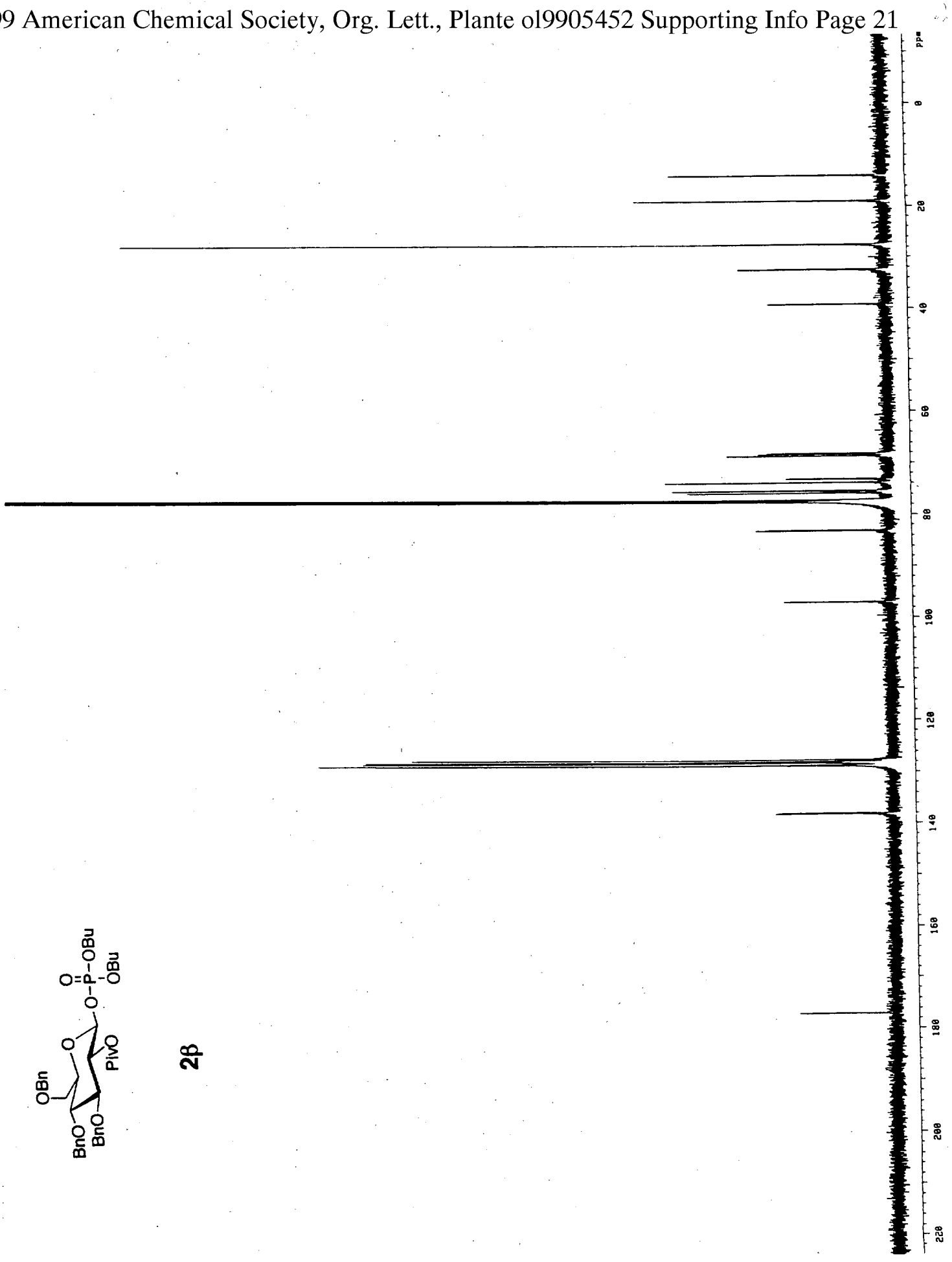
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80
100
120
140
160
180
200
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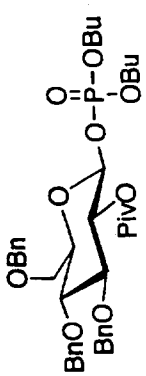
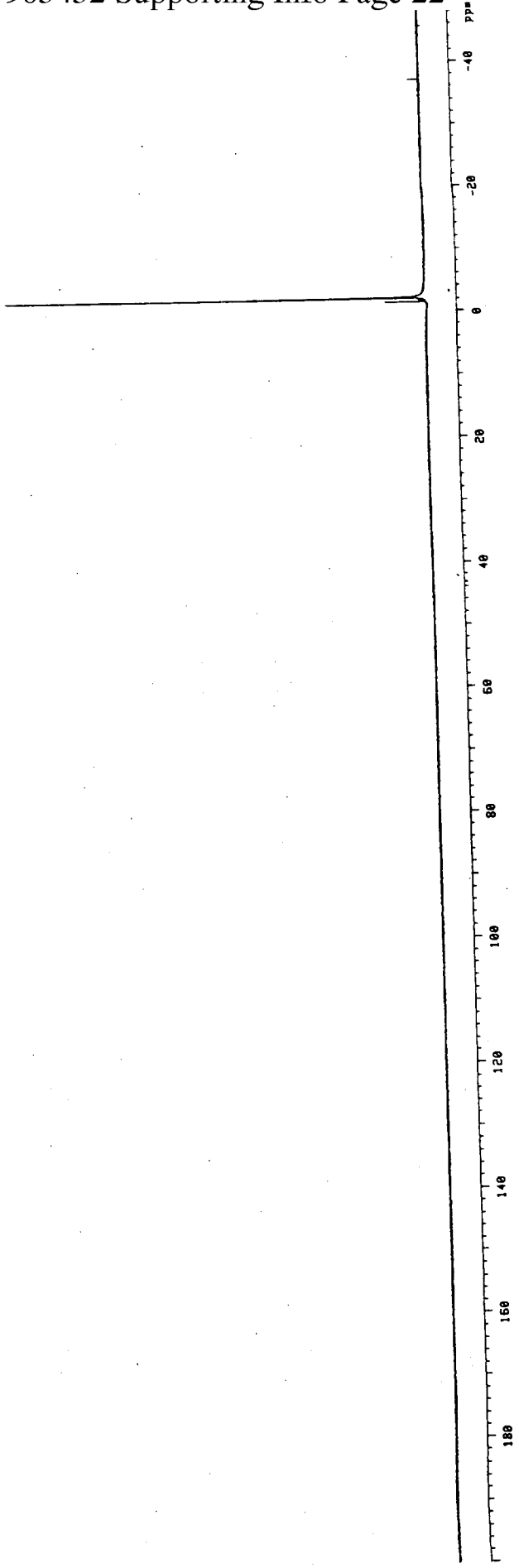
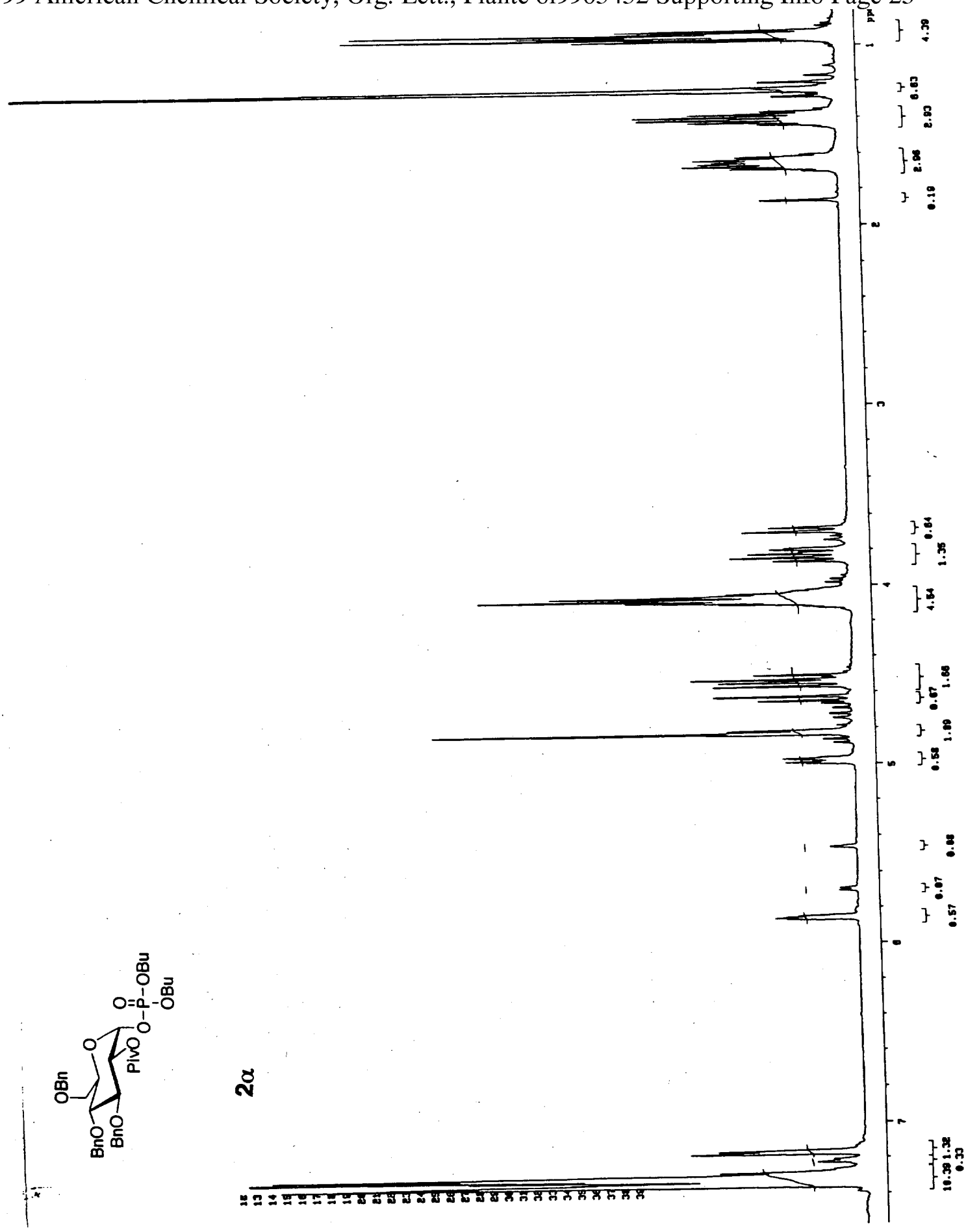
OBn
BnO
BnO
O
PivO
O
O=P-OBu
OBu

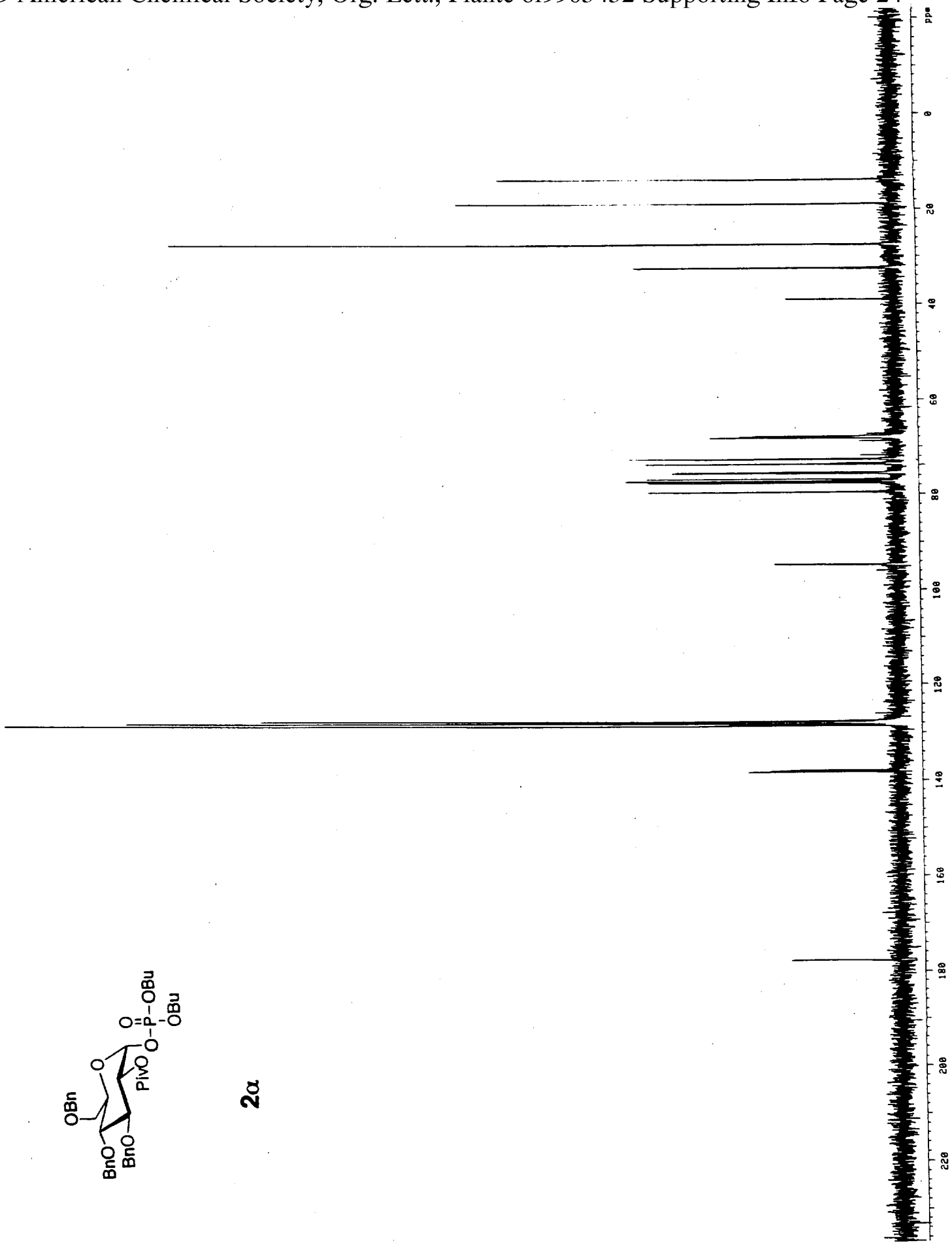
2β



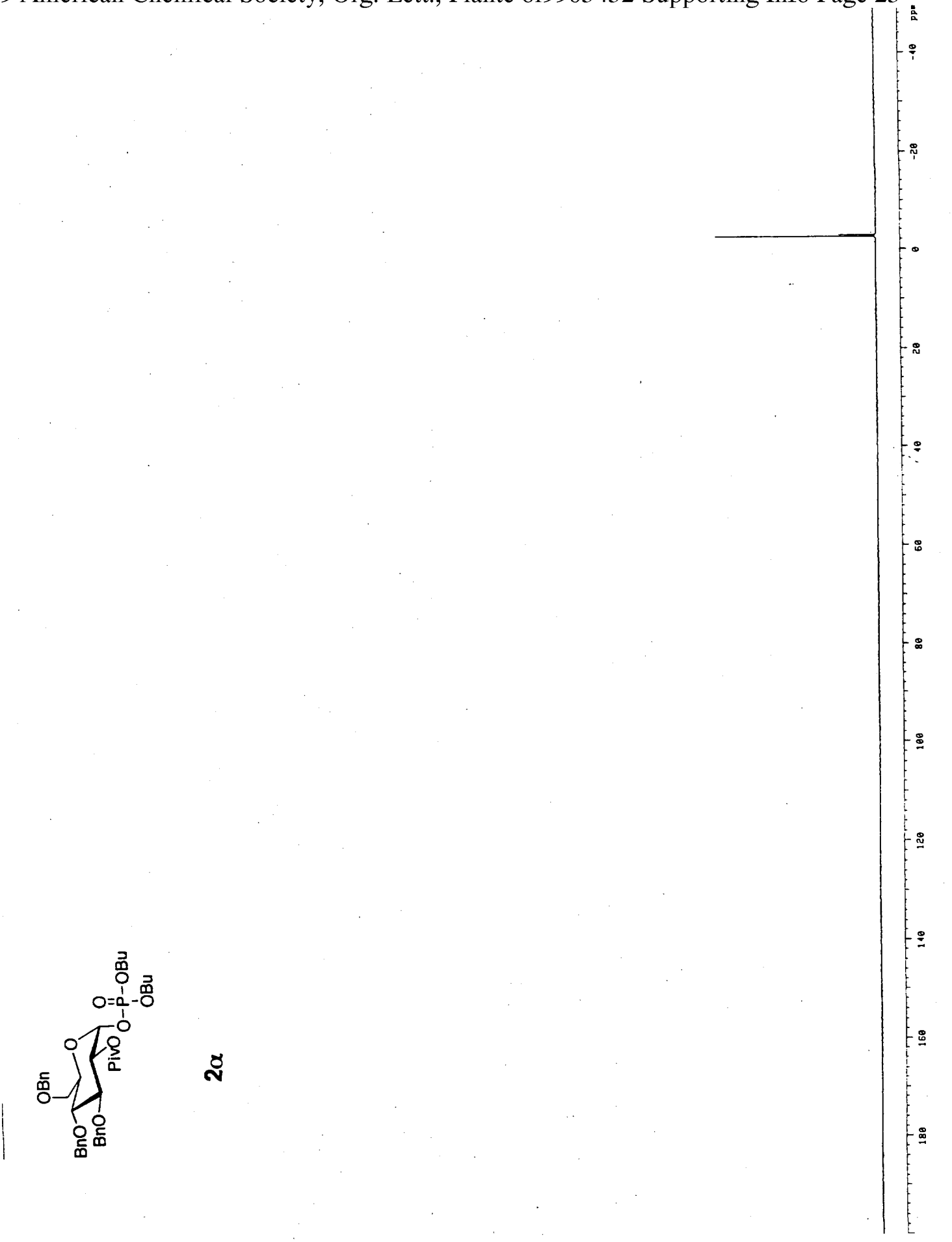
2β







2α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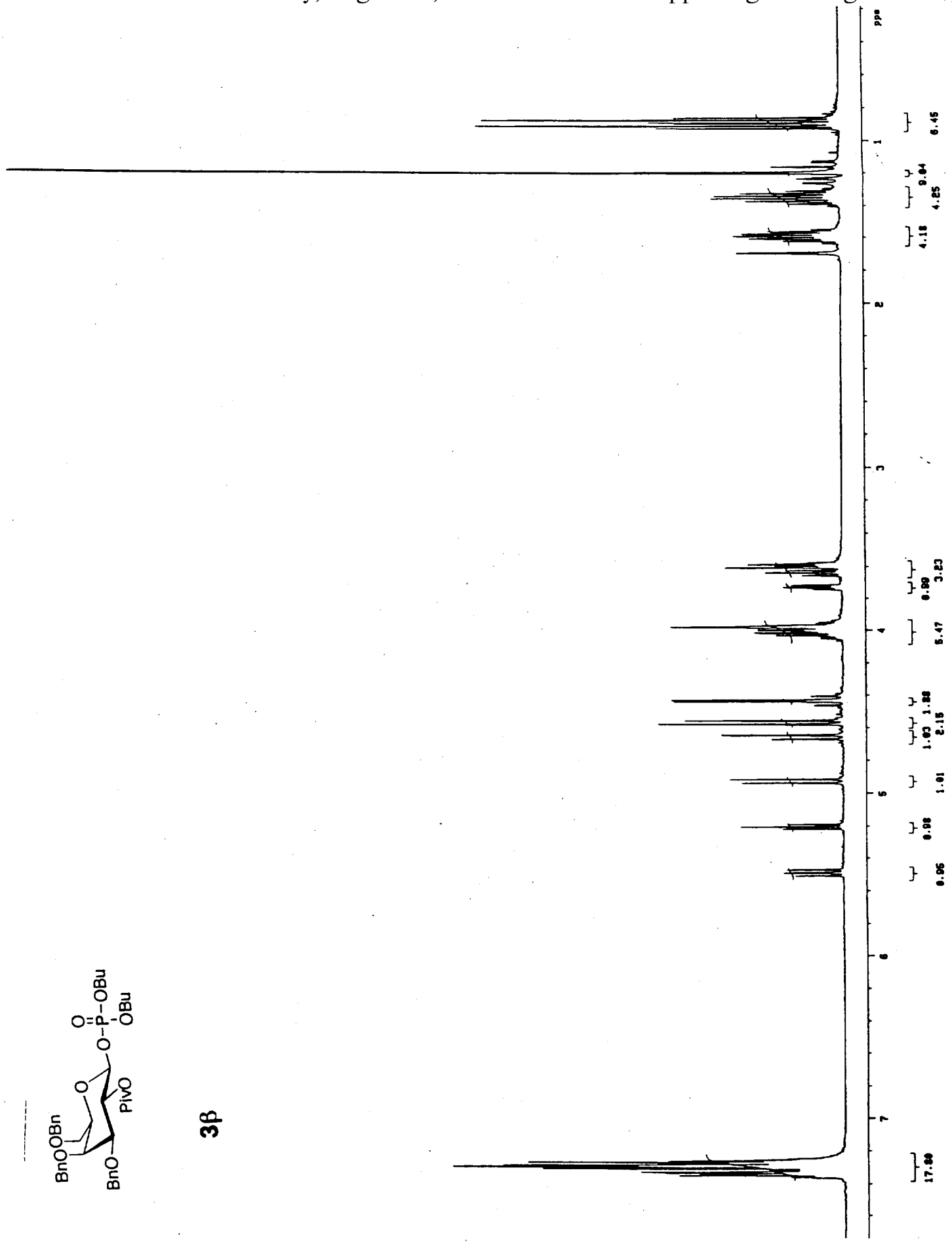
BnO
BnO
PivO
O
O
P
OBu
OBu

2α



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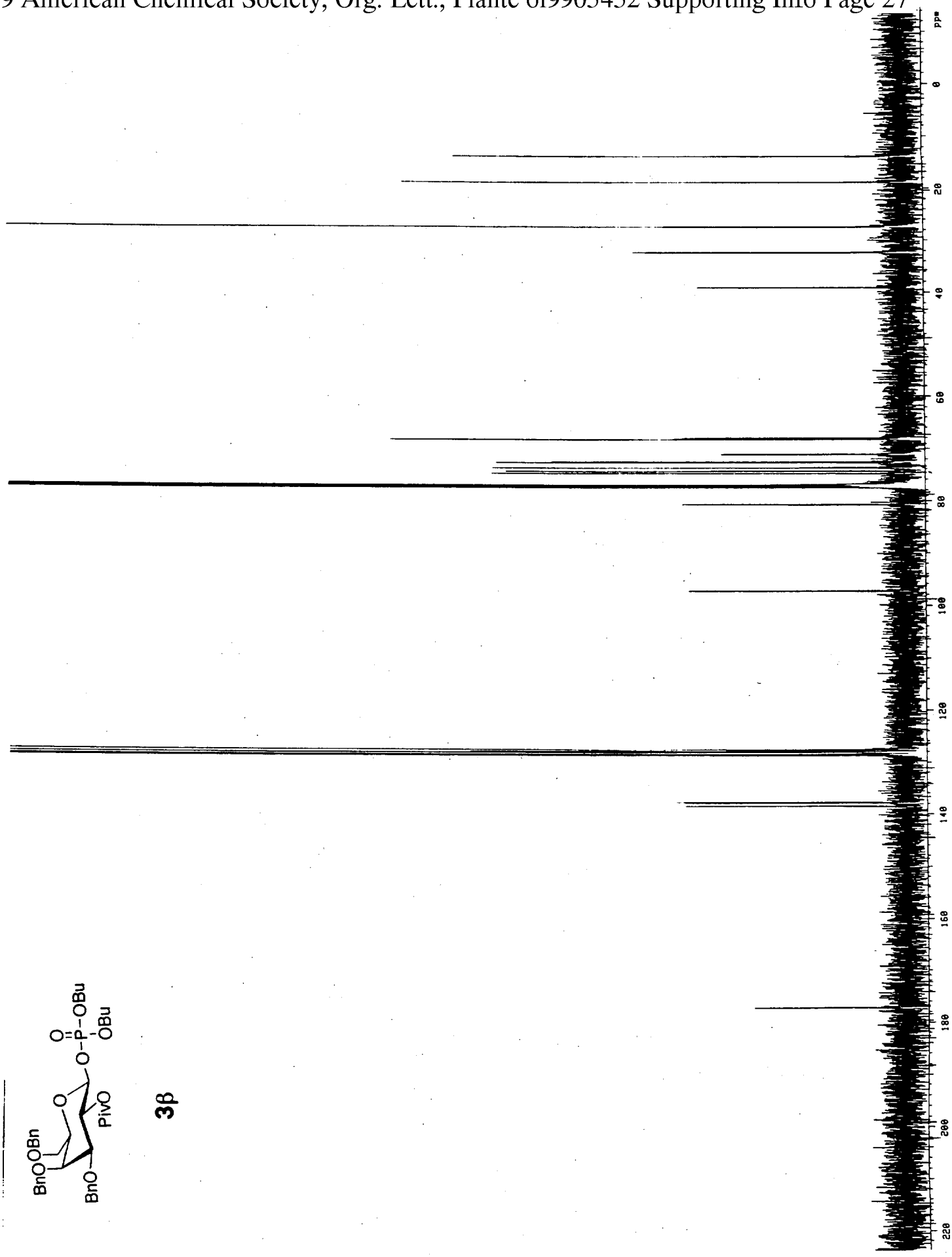
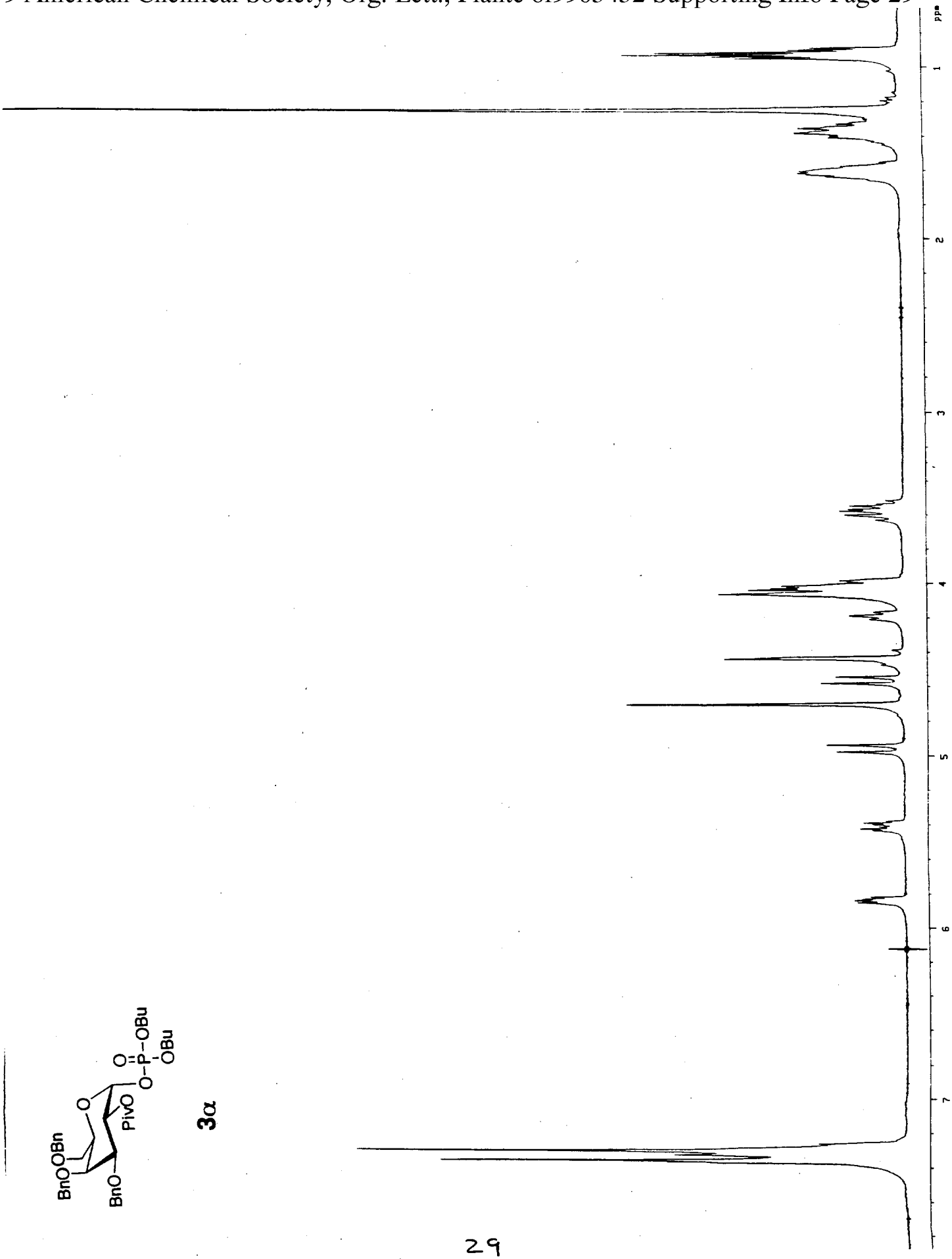
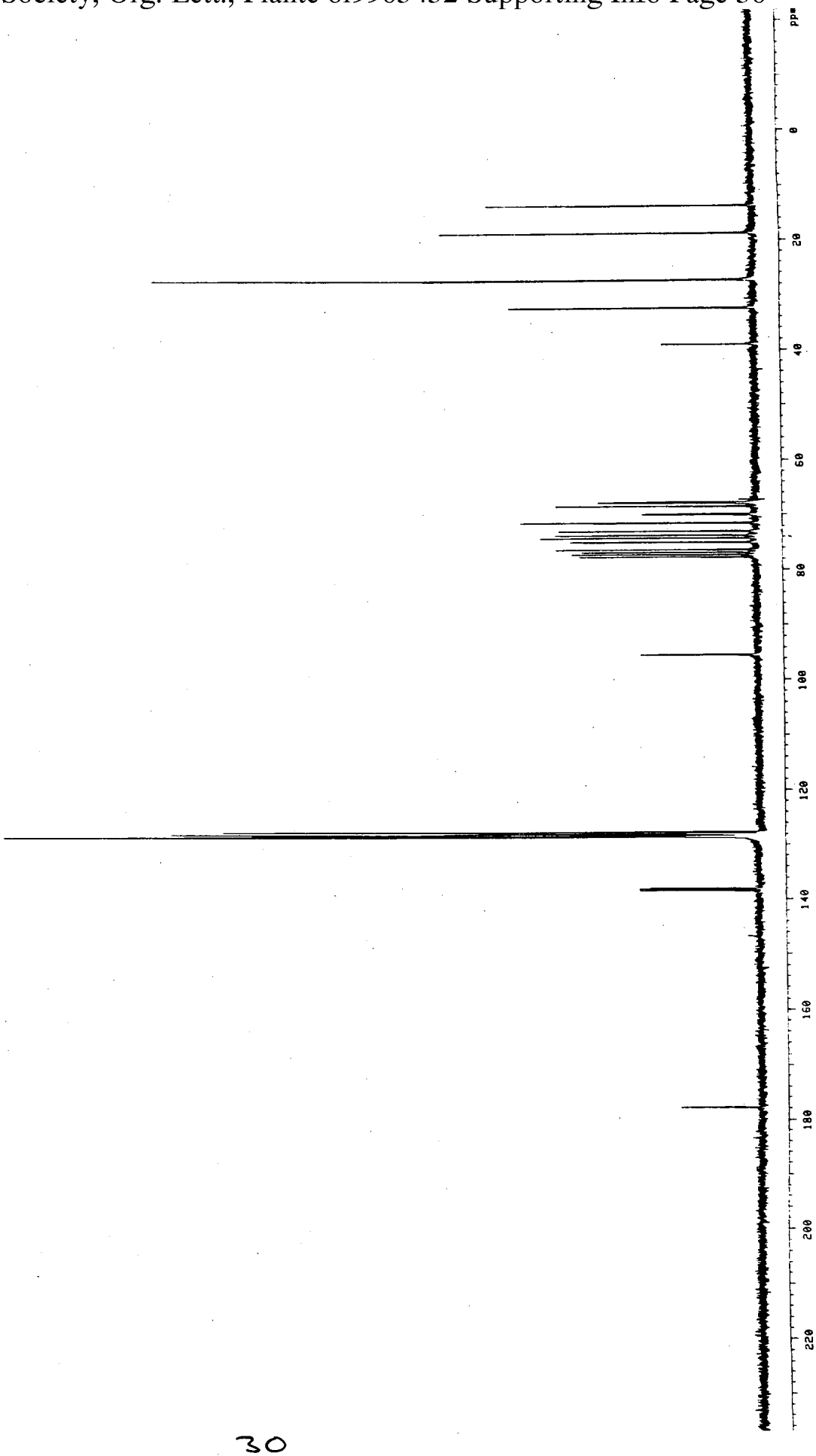
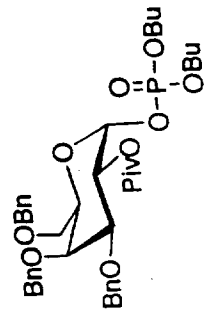


3β

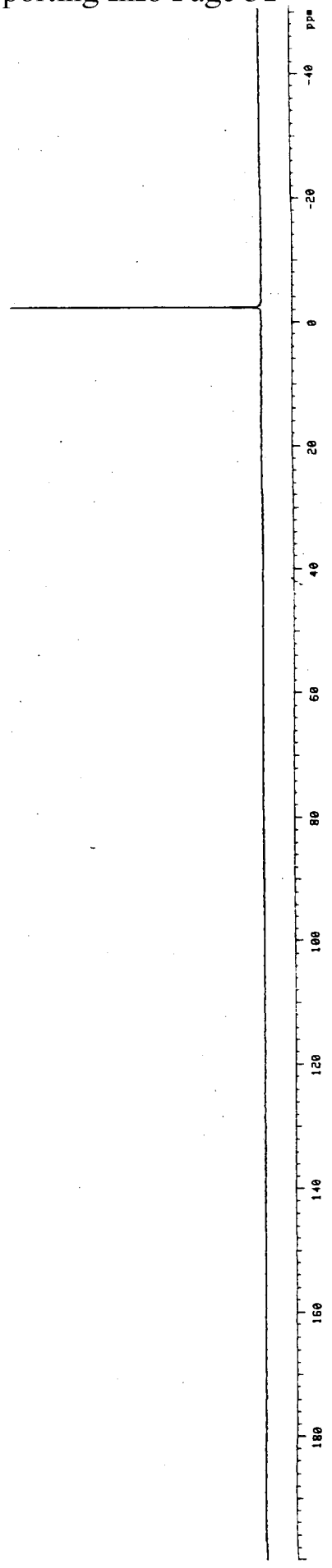


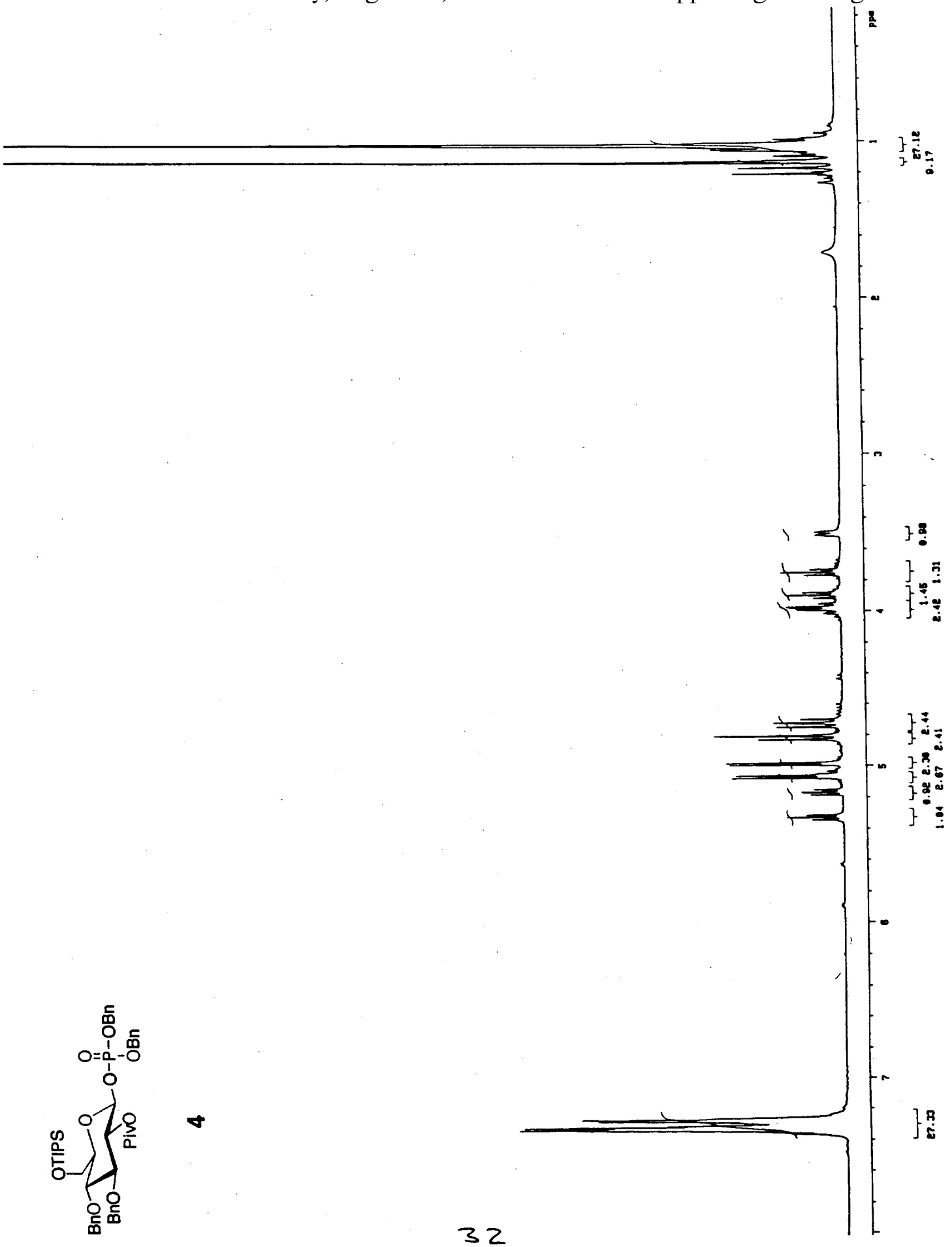
3α





3α





4

INDEX	FREQUENCY (PPM)	HEIGHT
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3	138.113	0.6
4	128.658	6.5
5	128.583	4.1
6	128.083	2.6
7	128.047	4.4
8	127.876	1.6
9	127.591	2.5
10	97.151	0.6
11	82.975	0.7
12	77.643	4.1
13	77.222	4.3
14	76.921	1.2
15	76.798	4.3
16	75.413	0.8
17	75.175	0.8
18	73.187	0.6
19	73.072	0.5
20	69.715	0.6
21	69.513	0.6
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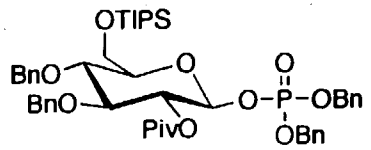

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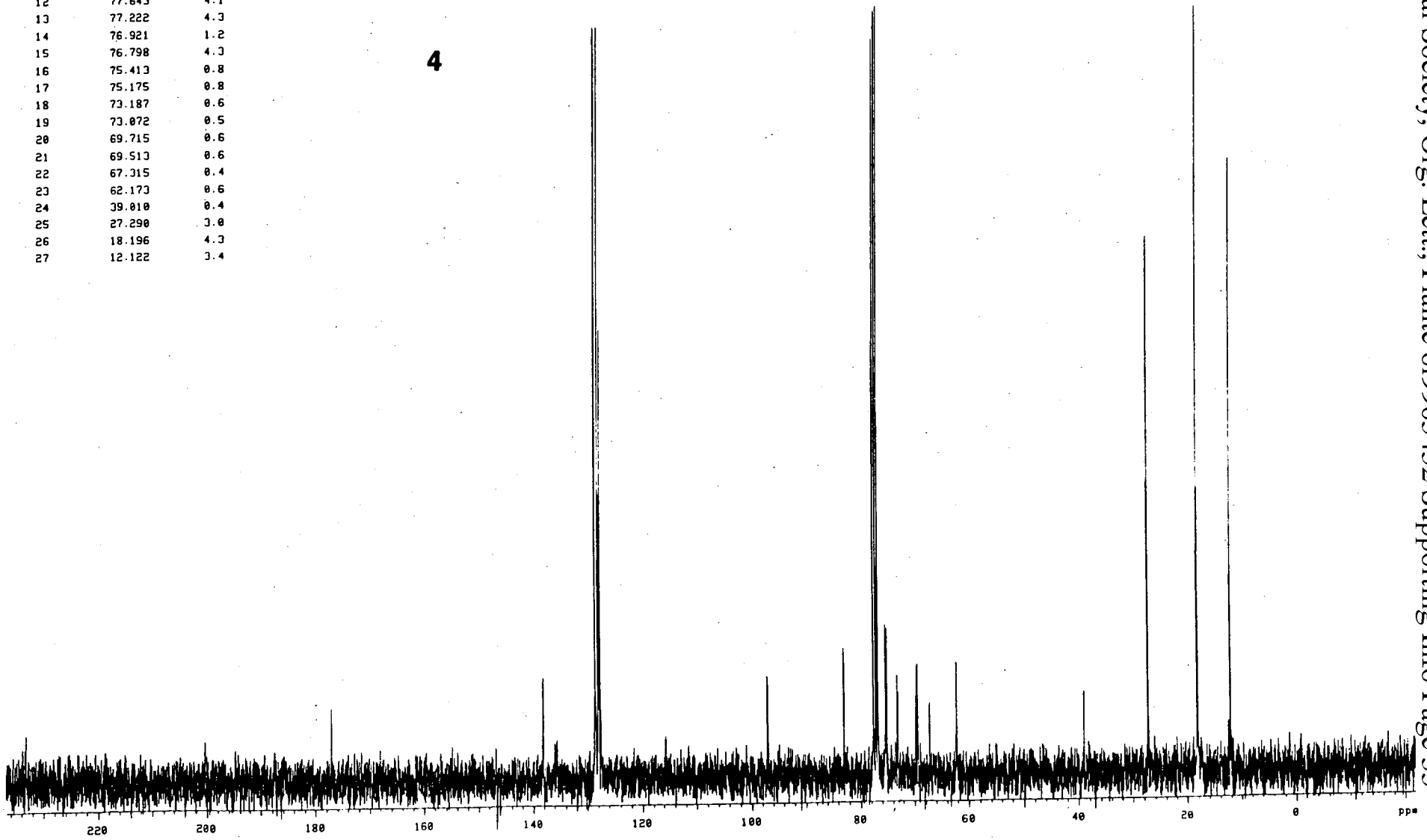

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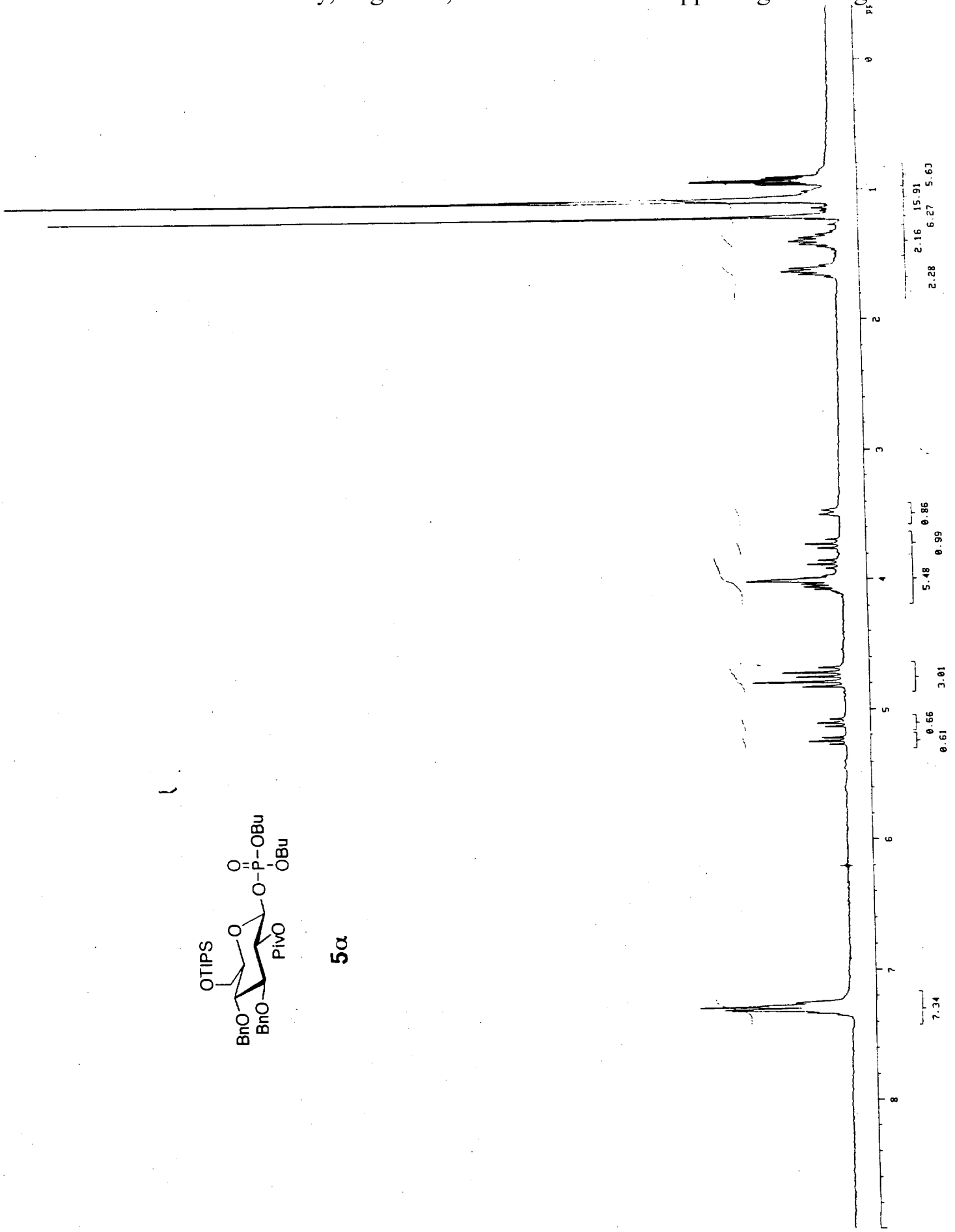
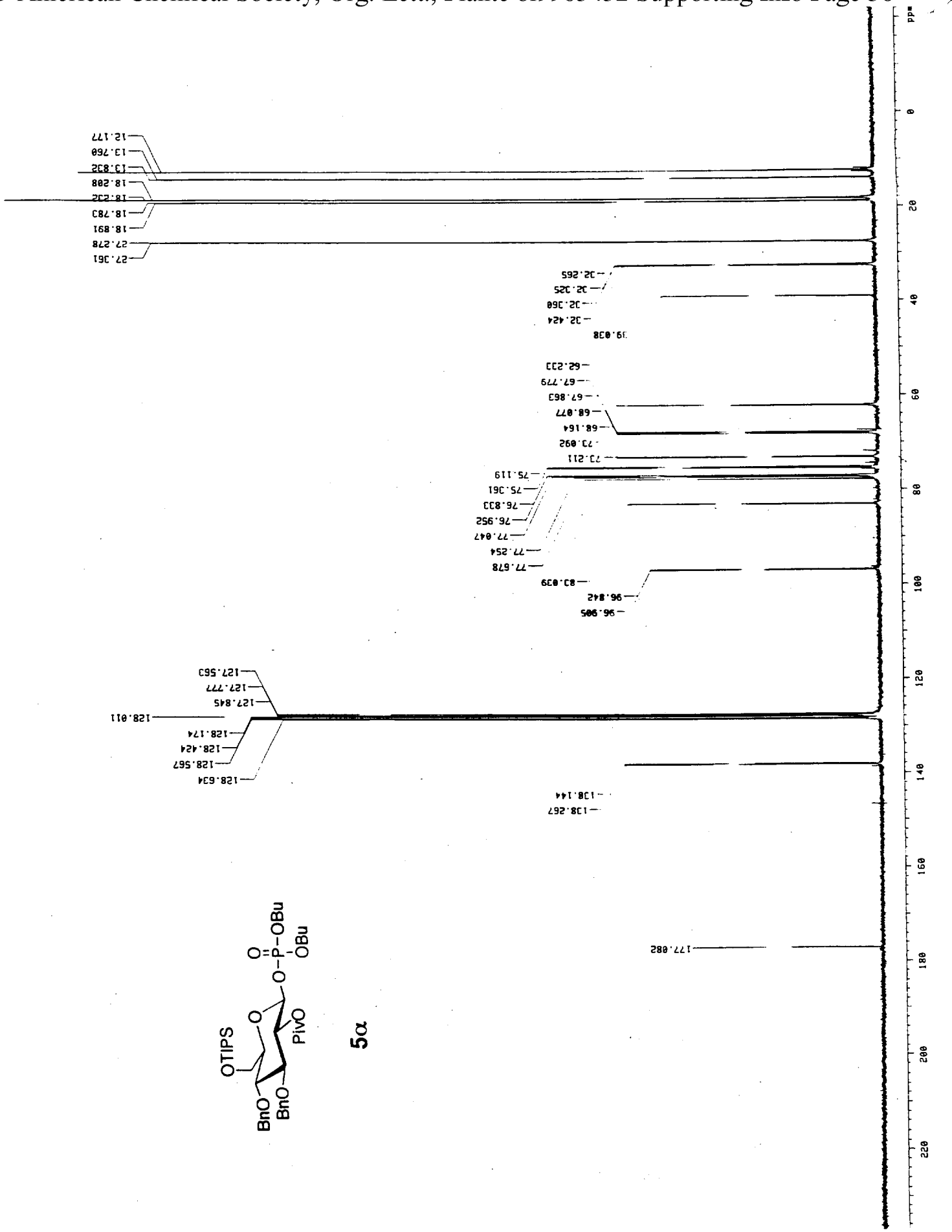


5α



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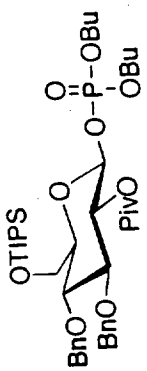
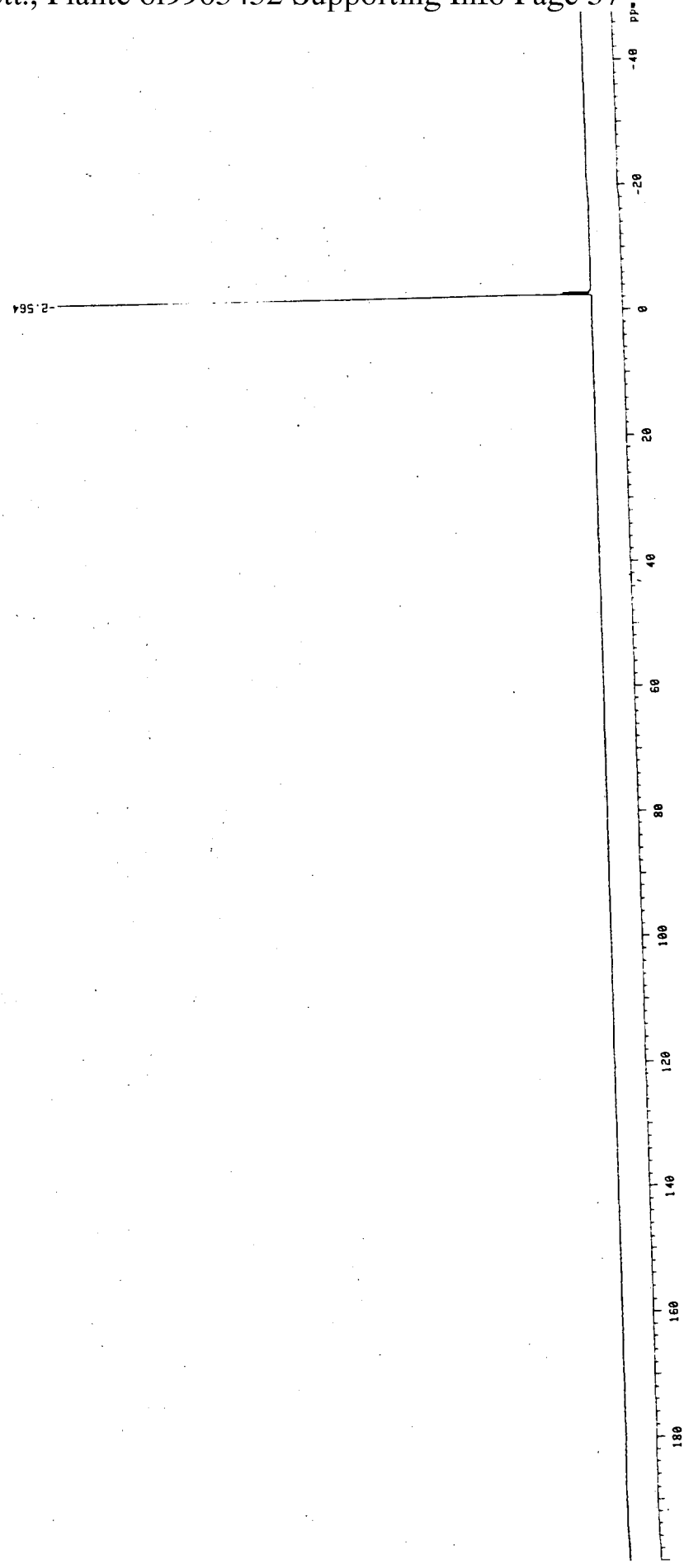
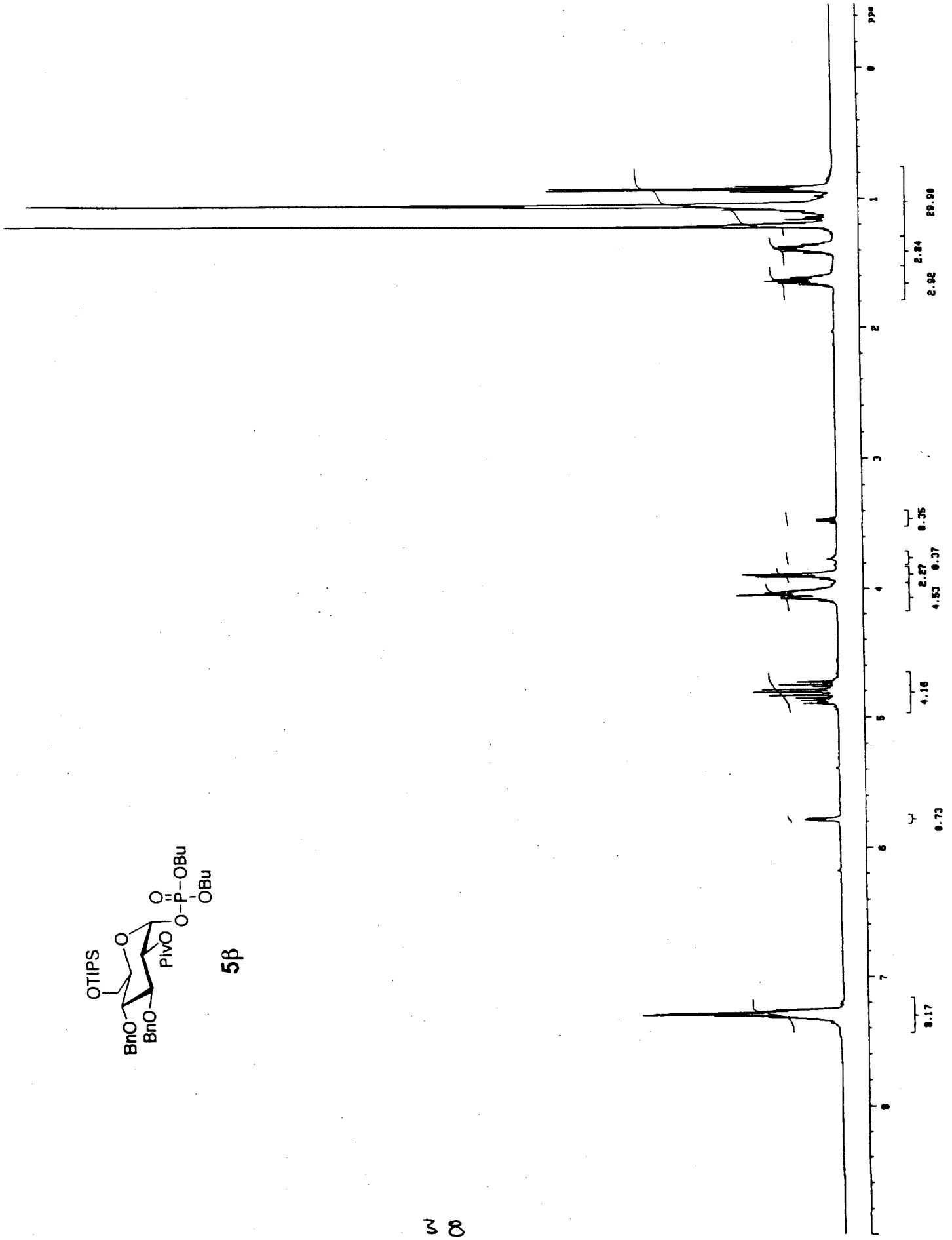


5α

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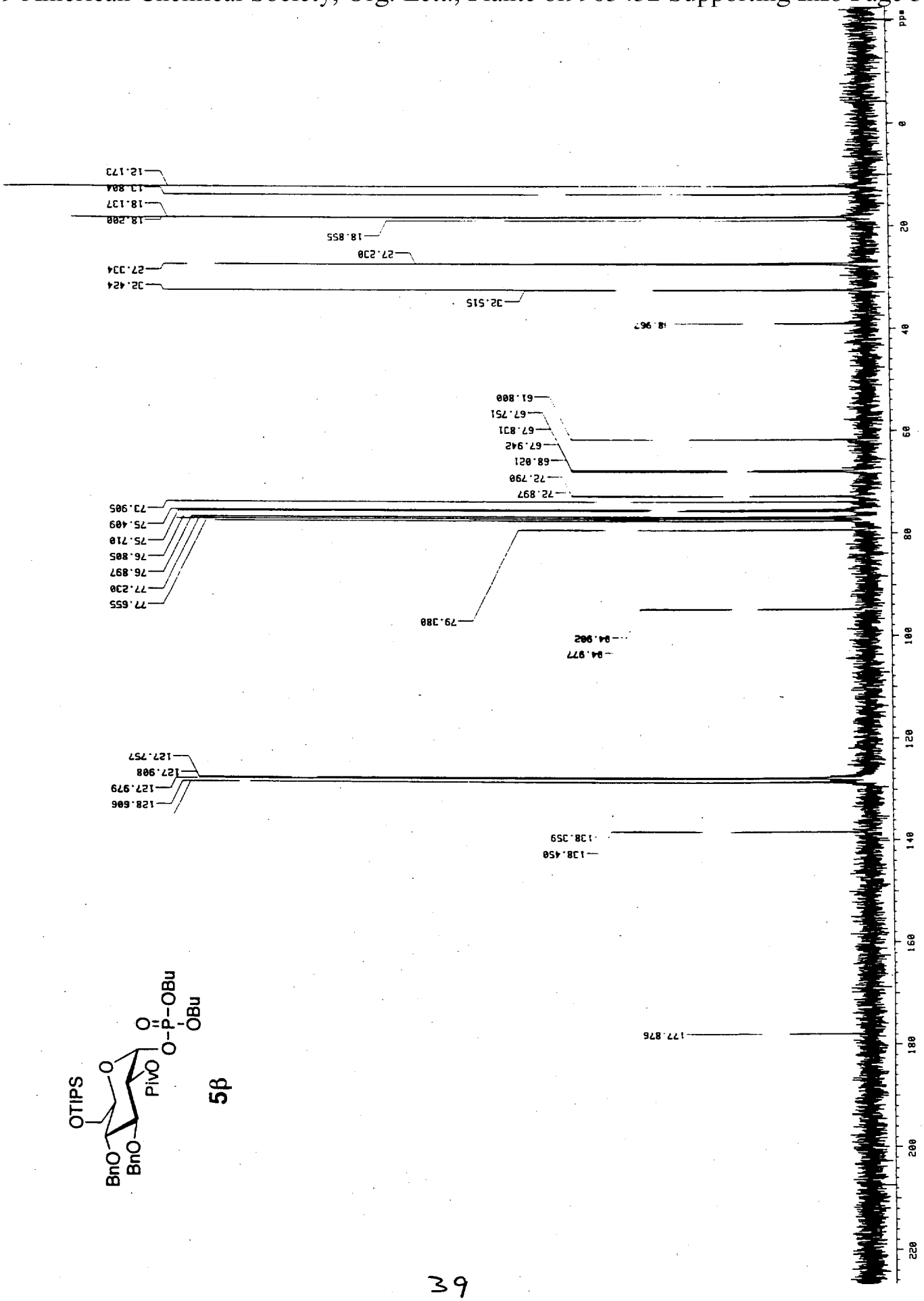
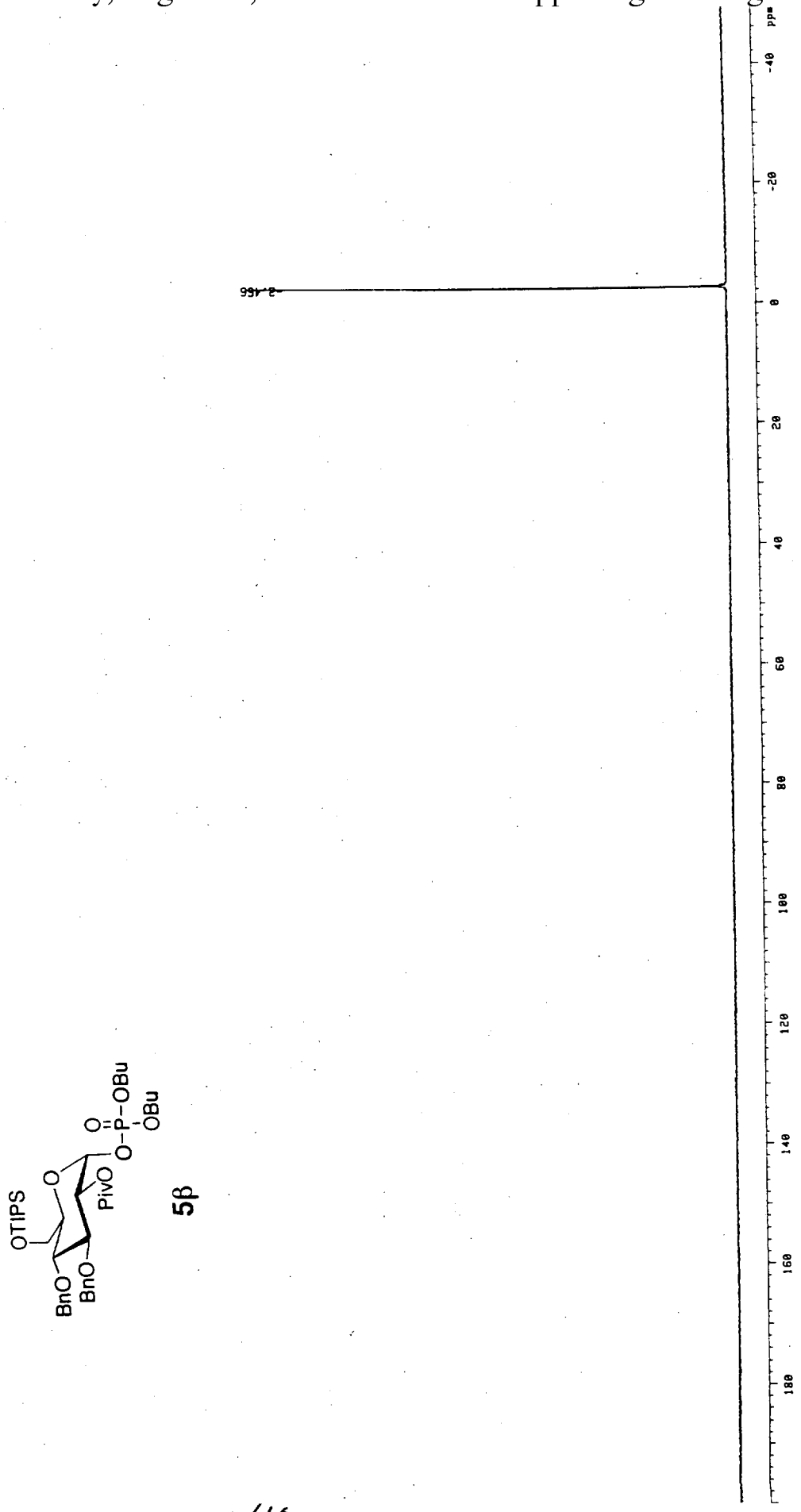
4.16
0.73
0.17

OTIPS
O
PivO
O
O-P-OBu
OBu
BnO
BnO

5β





5β