

Synthesis of the ABCDEFG Ring System of Maitotoxin

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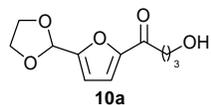
Supporting Information

Experimental Data for Compounds

General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, benzene, diethyl ether (Et₂O), acetonitrile (MeCN), ethylene glycol dimethyl ether (DME), and methylene chloride (CH₂Cl₂) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further

purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker DRX-600, DRX-500, AMX-500 or AMX-400 instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, quin = quintuplet, sext = sextet, sep = septet, br = broad. IR spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. Electrospray ionization (ESI) mass spectrometry (MS) experiments were performed on an API 100 Perkin Elmer SCIEX single quadrupole mass spectrometer at 4000V emitter voltage. High-resolution mass spectra (HR-MS) were recorded on a VG ZAB-ZSE mass spectrometer using MALDI (matrix-assisted laser-desorption ionization) or ESI (electrospray ionization).

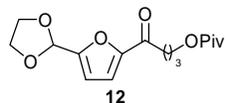
Alcohol 10a. To a stirred solution of furan **10**¹ (55.1 g, 393 mmol, 1.0 equiv) in THF (400 mL)



at $-78\text{ }^{\circ}\text{C}$ was added *n*-BuLi (2.5 M in hexanes, 157 mL, 393 mmol, 1.0 equiv). The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 15 min, at which point a solution of butyrolactone (**11**, 29.6 mL, 393 mmol, 1.0 equiv) in THF (400 mL) at $-78\text{ }^{\circ}\text{C}$ was added by cannula. The reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 2.5 h, and then quenched with sat. aq. NH_4Cl (800 mL). The biphasic mixture was extracted with EtOAc ($3 \times 300\text{ mL}$), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 to 1:4) yielded alcohol **10a** (55.1 g, 243 mmol, 62% yield) as a yellow foam and recovered furanal **10** (10.87 g, 78 mmol, 20% yield). **10a**: $R_f = 0.15$ (silica gel, hexanes:EtOAc 2:3); IR (film) ν_{max} 3422, 2955, 2892, 1671, 1603, 1520, 1402, 1338, 1263, 1199, 1105, 1026, 939, 805 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.15$ (d, $J = 3.6\text{ Hz}$, 1 H),

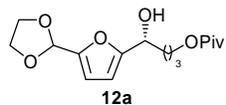
6.55 (d, $J = 3.6$ Hz, 1 H), 5.97 (s, 1 H), 4.14–4.10 (m, 2 H), 4.07–4.03 (m, 2 H), 3.71 (t, $J = 6.0$ Hz, 2 H), 1.98 (quin, $J = 6.6$ Hz, 2 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 189.7, 155.4, 152.6, 117.2, 110.3, 65.3, 62.2, 35.1, 26.7$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{11}\text{H}_{14}\text{O}_5$ [$\text{M} + \text{H}^+$]: 227.0914, found 227.0916.

Pivaloate 12. To a stirred solution of alcohol **10a** (64.7 g, 286 mmol, 1.0 equiv) in CH_2Cl_2 (1.0



L) at 25 °C were added PivCl (42.3 mL, 343 mmol, 1.2 equiv), Et_3N (119.1 mL, 857 mmol, 3.0 equiv), and DMAP (3.49 g, 28.6 mmol, 0.1 equiv), and the reaction mixture was stirred at 25 °C for 20 min. The reaction mixture was then quenched with sat. aq. NaHCO_3 (750 mL), the biphasic mixture was extracted with CH_2Cl_2 (3×200 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 7:3) yielded pivaloate **12** (83.4 g, 269 mmol, 94% yield) as a yellow oil. **12**: $R_f = 0.37$ (silica gel, hexanes:EtOAc 3:2); IR (film) ν_{max} 2971, 2900, 1724, 1678, 1588, 1522, 1480, 1399, 1366, 1284, 1199, 1155, 1107, 1033, 940, 891, 805, 771 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.13$ (d, $J = 3.6$ Hz, 1 H), 6.55 (d, $J = 3.0$ Hz, 1 H), 5.97 (s, 1 H), 4.15–4.09 (m, 4 H), 4.07–4.03 (m, 2 H), 2.91 (t, $J = 7.2$ Hz, 2 H), 2.06 (quin, $J = 7.2$ Hz, 2 H), 1.19 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 188.5, 178.4, 155.4, 152.6, 117.0, 110.3, 97.3, 65.3, 63.5, 38.7, 34.7, 27.2, 23.0$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{16}\text{H}_{22}\text{O}_6$ [$\text{M} + \text{H}^+$]: 311.1489, found 311.1491.

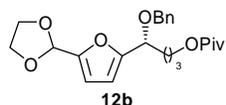
Secondary alcohol 12a. To a vigorously stirred solution of pivaloate **12** (61.0 g, 197 mmol, 1.0



equiv) in $\text{CH}_2\text{Cl}_2:\text{H}_2\text{O}$ (1:1, 400 mL) at 25 °C were added $n\text{-Bu}_4\text{NCl}$ (16.4 g, 59 mmol, 0.3 equiv), HCO_2Na (133.7 g, 1.97 mol, 10 equiv) and cat. **13** (1.23 g, 1.97 mmol, 0.01 equiv), and the reaction mixture was stirred vigorously for 48 h at 25 °C. The reaction mixture was diluted in H_2O (600 mL), and the biphasic mixture was extracted with EtOAc (3×400 mL), dried (MgSO_4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) gave secondary alcohol **12a** [59.5 g, 190 mmol, 97% yield, 94% *ee* (as measured by ^1H NMR analysis of the corresponding Naproxen[®] spectroscopic ester)] as a pale

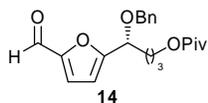
yellow oil. **12a**: $R_f = 0.23$ (silica gel, hexanes:EtOAc 3:2); $[\alpha]_D^{32} = +7.5$ (CH_2Cl_2 , $c = 1.15$); IR (film) ν_{max} 3473, 2961, 2891, 1724, 1480, 1399, 1366, 1286, 1159, 1102, 1014, 942, 796 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 6.39$ (d, $J = 3.0$ Hz, 1 H), 6.21 (d, $J = 3.6$ Hz, 1 H), 5.89 (s, 1 H), 4.71 (t, $J = 6$ Hz, 1 H), 4.17–4.08 (m, 4 H), 4.03–3.99 (m, 2 H), 2.06 (bs, 1 H), 1.95–1.89 (m, 2 H), 1.87–1.79 (m, 1 H), 1.73–1.67 (m, 1 H), 1.19 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.6, 157.3, 150.5, 109.3, 106.4, 97.7, 67.3, 65.1, 63.9, 38.7, 31.8, 27.2, 24.8$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{16}\text{H}_{24}\text{O}_6$ $[\text{M} + \text{H}^+]$: 313.1646, found 313.1648.

Benzyl ether 12b. To a stirred solution of secondary alcohol **12a** (59.0 g, 189 mmol, 1.0 equiv)



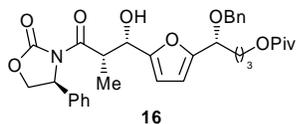
in THF (1.0 L) at 0 °C were added BnBr (56.2 mL, 472 mmol, 2.5 equiv) and $n\text{-Bu}_4\text{NI}$ (34.9 g, 94.5 mmol, 0.5 equiv) followed by portionwise addition of NaH (60% in mineral oil, 30.1 g, 756 mmol, 4.0 equiv), and the reaction mixture was warmed to 25 °C and stirred for 16 h. The reaction mixture was slowly quenched with H_2O (700 mL), the biphasic mixture was extracted with EtOAc (3×500 mL), and the combined organic layers were washed with H_2O (750 mL) and brine (750 mL), and then dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1 to 3:1) yielded benzyl ether **12b** (75.9 g, 189 mmol, quant. yield) as a pale yellow oil. **12b**: $R_f = 0.28$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{32} = +61.7$ (CH_2Cl_2 , $c = 1.02$); IR (film) ν_{max} 2959, 2870, 1724, 1480, 1455, 1397, 1365, 1284, 1155, 1101, 1028, 940, 796, 771, 737, 698 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.34$ –7.27 (m, 5 H), 6.42 (d, $J = 3.6$ Hz, 1 H), 6.26 (d, $J = 3.6$ Hz, 1 H), 5.92 (s, 1 H), 4.54 (d, $J = 12.0$ Hz, 1 H), 4.38 (dd, $J = 7.2, 5.4$ Hz, 1 H), 4.35 (d, $J = 11.4$ Hz, 1 H), 4.16–4.10 (m, 2 H), 4.07–3.99 (m, 4 H), 2.02–1.96 (m, 1 H), 1.92–1.86 (m, 1 H), 1.81–1.74 (m, 1 H), 1.66–1.60 (m, 1 H), 1.18 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.5, 155.2, 150.9, 138.1, 128.3, 127.8, 127.6, 109.0, 108.2, 97.8, 73.7, 70.6, 65.13, 65.08, 63.4, 38.7, 30.9, 27.2, 24.9$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{23}\text{H}_{30}\text{O}_6$ $[\text{M} + \text{Na}^+]$: 425.1934, found 425.1927.

Aldehyde 14. To a stirred solution of benzyl ether **12b** (73.9 g, 183.5 mmol, 1.0 equiv) in THF (1.2 L) at 25 °C was added 2.0 M aq. HCl (600 mL), and the reaction mixture was stirred at 25



°C for 1 h. The reaction mixture was slowly quenched with sat. aq. NaHCO₃ (1.0 L), the biphasic mixture was extracted with EtOAc (3 × 600 mL), and the combined organic layers were dried (MgSO₄) and concentrated, providing pure aldehyde **14** (66.5 g, 183.5 mmol, quant.) as a yellow oil. **14**: *R*_f = 0.39 (silica gel, hexanes:EtOAc 7:3); [α]_D³² = +73.5 (CH₂Cl₂, *c* = 1.18); IR (film) *v*_{max} 2961, 2871, 1724, 1681, 1517, 1480, 1455, 1328, 1283, 1156, 1023, 768, 754 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 9.62 (s, 1 H), 7.36–7.28 (m, 5 H), 7.23 (s, 1 H), 6.52 (s, 1 H), 4.58 (d, *J* = 12.0 Hz, 1 H), 4.50 (t, *J* = 6.0 Hz, 1 H), 4.42 (d, *J* = 11.4 Hz, 1 H), 4.07–4.01 (m, 2 H), 2.02–1.90 (m, 2 H), 1.82–1.76 (m, 1 H), 1.75–1.61 (m, 1 H), 1.18 (s, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 178.5, 177.6, 161.8, 152.4, 137.5, 128.5, 127.9, 127.8, 121.9, 109.9, 74.0, 71.5, 63.7, 38.7, 31.2, 27.2, 24.6 ppm; HRMS (ESI-TOF); calcd for C₂₁H₂₆O₅ [M + H⁺]: 359.1853, found 359.1858.

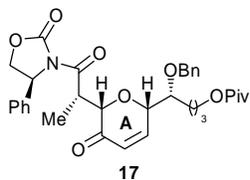
Oxazolidinone 16. To a stirred solution of oxazolidinone **15**² (38.1 g, 173.8 mmol, 1.0 equiv) in



CH₂Cl₂ (900 mL) at –78 °C was added *n*-Bu₂BOTf (1.0 M in CH₂Cl₂, 209 mL, 209 mmol, 1.2 equiv) followed by Et₃N (31.4 mL, 226 mmol, 1.3 equiv). The reaction mixture was warmed to 0 °C, stirred for 45 min, and re-cooled to –78 °C. A cold (–78 °C) solution of aldehyde **14** (62.3 g, 173.8 mmol, 1.0 equiv) in CH₂Cl₂ (800 mL) was added *via* cannula to the stirred reaction mixture and then the solution was allowed to warm up to 0 °C and stirred at that temperature for 4.5 h. The reaction mixture was quenched by slow sequential addition of 0.05 M phosphate buffer (pH = 7, 175 mL), MeOH (350 mL), and MeOH:30% H₂O₂ (1:1, 350 mL), and the resulting biphasic mixture was vigorously stirred at 0 °C for 1 h. After warming to 25 °C, the biphasic mixture was diluted with H₂O (1.0 L) and then extracted with CH₂Cl₂ (3 × 600 mL). The combined organic layers were washed with sat. aq. Na₂S₂O₃ (600 mL) and brine (600 mL), and then dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 3:1 to 3:2) gave oxazolidinone **16** (98.4 g, 170 mmol, 98% yield) as a viscous pale yellow oil. **16**: *R*_f = 0.18 (silica gel, hexanes:EtOAc 7:3); [α]_D³² = +78.6 (CH₂Cl₂, *c* = 1.25); IR (film) *v*_{max} 3490, 2970,

2870, 1780, 1719, 1706, 1480, 1455, 1382, 1318, 1285, 1197, 1159, 1106, 1042, 980, 949, 797, 738, 700 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.41–7.27 (m, 10 H), 6.28 (d, J = 3.6 Hz, 1 H), 6.25 (d, J = 3.6 Hz, 1 H), 5.40 (dd, J = 8.4, 3.6 Hz, 1 H), 5.07 (s, 1 H), 4.64 (t, J = 9.0 Hz, 1 H), 4.52 (d, J = 12.0 Hz, 1 H), 4.37–4.33 (m, 2 H), 4.26–4.22 (m, 2 H), 4.07–4.01 (m, 2 H), 2.92 (d, J = 4.2 Hz, 1 H), 2.02–1.96 (m, 1 H), 1.90–1.84 (m, 1 H), 1.79–1.73 (m, 1 H), 1.64–1.60 (m, 1 H), 1.25 (d, J = 7.2 Hz, 3 H), 1.18 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): δ = 178.6, 175.7, 153.9, 153.8, 153.0, 138.7, 138.2, 129.3, 128.8, 128.4, 127.9, 127.6, 125.5, 108.7, 107.3, 73.6, 70.4, 69.9, 68.4, 64.0, 57.5, 42.5, 38.7, 30.7, 27.2, 24.9, 11.8 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{33}\text{H}_{39}\text{NO}_8$ [$\text{M} + \text{Na}^+$]: 600.2568, found 600.2569.

A Ring enone 17. To a mechanically stirred solution of oxazolidinone **16** (86.0 g, 149 mmol,



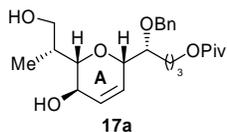
1.0 equiv) in CH_2Cl_2 (1.1 L) at 0 $^\circ\text{C}$ was added dry *m*-CPBA (47.7 g, 193.7 mmol, 1.2 equiv), and the reaction mixture was allowed to warm up to 25 $^\circ\text{C}$ and stirred for 2.5 h. After cooling to -50 $^\circ\text{C}$, Et_3SiH (47.6 mL, 298

mmol, 2.0 equiv) and $\text{BF}_3 \cdot \text{OEt}_2$ (37.4 mL, 298 mmol, 2.0 equiv) were added to the reaction mixture, which was subsequently warmed to -10 $^\circ\text{C}$ and stirred for 20 min. The reaction mixture was quenched with sat. aq. NaHCO_3 (700 mL), the biphasic mixture was extracted with CH_2Cl_2 (3×500 mL), and the combined organic layers were dried (MgSO_4) and concentrated.

Flash column chromatography (silica gel, hexanes:EtOAc 3:2) yielded A ring enone **17** (64.5 g, 112 mmol, 75% yield) as a white solid. **17**: R_f = 0.42 (silica gel, hexanes:EtOAc 3:2); mp = 32–33 $^\circ\text{C}$; $[\alpha]_D^{32}$ = +30.7 (CH_2Cl_2 , c = 0.98); IR (film) ν_{max} 2971, 2870, 1780, 1721, 1693, 1480, 1456, 1383, 1285, 1201, 1160, 1112, 984, 759, 705 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.40–7.28 (m, 10 H), 7.13 (d, J = 10.8 Hz, 1 H), 6.13 (dd, J = 10.2, 2.4 Hz, 1 H), 5.49 (dd, J = 9.0, 3.6 Hz, 1 H), 4.78 (t, J = 9.0 Hz, 1 H), 4.61 (d, J = 11.4 Hz, 1 H), 4.58 (d, J = 11.4 Hz, 1 H), 4.34–4.31 (m, 2 H), 4.27 (dd, J = 9.0, 3.6 Hz, 1 H), 4.22–4.17 (m, 1 H), 4.12–4.02 (m, 2 H), 3.60–3.57 (m, 1 H), 1.83–1.78 (m, 1 H), 1.76–1.71 (m, 3 H), 1.24 (d, J = 6.6 Hz, 3 H), 1.19 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): δ = 194.9, 178.5, 173.9, 153.5, 148.9, 139.4, 137.8, 129.2, 128.6,

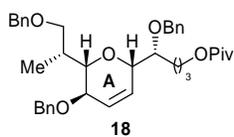
128.5, 127.9, 127.2, 125.6, 81.0, 79.2, 77.0, 72.5, 70.0, 64.1, 57.8, 38.7, 38.2, 27.2, 27.1, 23.9, 13.6 ppm; HRMS (ESI-TOF); calcd for C₃₃H₃₉NO₈ [M + H⁺]: 578.2748, found 500.2743.

A Ring diol 17a. To a stirred solution of A ring enone **17** (49.2 g, 85.2 mmol, 1.0 equiv) in CH₂Cl₂:MeOH (1:1, 1.0 L) at -30 °C were added dry CeCl₃ (63.5 g, 170.4 mmol, 2.0 equiv) and NaBH₄ (12.9 g, 340.8 mmol, 4.0 equiv), and the reaction mixture was warmed to -10 °C and stirred for 15 min. The reaction



mixture was quenched with sat. aq. NH₄Cl (600 mL), and the aqueous layer was acidified with 1.0 M HCl to pH = 5. The biphasic mixture was extracted with EtOAc (3 × 400 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 11:9 to 3:7) gave A ring diol **17a** (28.7 g, 68.2 mmol, 80% yield) as a white solid. **17a**: *R*_f = 0.21 (silica gel, hexanes:EtOAc 2:3); mp = 77–80 °C; [α]_D³² = -60.2 (CH₂Cl₂, *c* = 1.28); IR (film) ν_{max} 3356, 2962, 2931, 2873, 1725, 1480, 1455, 1398, 1285, 1158, 1038, 993, 966, 737, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.35–7.27 (m, 5 H), 5.90 (dt, *J* = 10.2, 1.2 Hz, 1 H), 5.86 (dt, *J* = 10.2, 1.8 Hz, 1 H), 4.62 (d, *J* = 11.4 Hz, 1 H), 4.54 (d, *J* = 11.4 Hz, 1 H), 4.18–4.14 (m, 2 H), 4.07–3.99 (m, 2 H), 3.76 (dd, *J* = 11.4, 4.2 Hz, 1 H), 3.65 (dd, *J* = 10.8, 7.2 Hz, 1 H), 3.42–3.40 (m, 1 H), 3.27 (dd, *J* = 8.4, 4.8 Hz, 1 H), 2.84 (bs, 1 H), 2.71 (bs, 1 H), 2.04–2.01 (m, 1 H), 1.83–1.78 (m, 1 H), 1.72–1.60 (m, 3 H), 1.19 (s, 9 H), 1.02 (d, *J* = 7.2 Hz, 3 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 178.6, 138.3, 130.4, 128.4, 128.3, 127.8, 127.6, 81.5, 80.2, 76.3, 72.3, 66.3, 65.5, 64.3, 38.7, 37.7, 27.2, 26.7, 24.3, 11.8 ppm; HRMS (ESI-TOF); calcd for C₂₄H₃₆O₆ [M + H⁺]: 421.2585, found 421.2590.

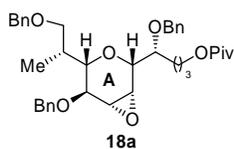
A Ring tri-benzyl ether 18. To a vigorously stirred solution of A ring diol **17a** (4.80 g, 11.4 mmol, 1.0 equiv) in 25% aq. NaOH:PhMe (1:1, 300 mmol) at 25 °C were added BnBr (33.9 mL, 285 mmol, 25.0 equiv) and *n*-Bu₄NI (3.16 g, 8.9 mmol, 0.75 equiv), and the reaction mixture was stirred vigorously at 25 °C



for 48 h. The reaction mixture was then diluted in H₂O (300 mL), and the resulting biphasic mixture was extracted with EtOAc (3 × 200 mL). The combined organic layers were washed

with H₂O (300 mL) and brine (300 mL), and then dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1 to 17:3) yielded A ring tri-benzyl ether **18** (6.2 g, 10.4 mmol, 91% yield) as a pale yellow oil. **18**: $R_f = 0.34$ (silica gel, hexanes:EtOAc 17:3); $[\alpha]_D^{32} = -55.0$ (CH₂Cl₂, $c = 0.65$); IR (film) ν_{\max} 2963, 2926, 2865, 1726, 1454, 1284, 1159, 1095, 735, 697 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): $\delta = 7.35\text{--}7.28$ (m, 15 H), 6.04 (dt, $J = 10.8, 1.8$ Hz, 1 H), 5.92 (dt, $J = 10.2, 1.2$ Hz, 1 H), 4.67 (d, $J = 11.4$ Hz, 1 H), 4.60 (d, $J = 11.4$ Hz, 1 H), 4.56–4.50 (m, 3 H), 4.57 (d, $J = 12.0$ Hz, 1 H), 4.08–4.07 (m, 1 H), 4.02–3.99 (m, 3 H), 3.63 (dd, $J = 9.0, 1.8$ Hz, 1 H), 3.54 (t, $J = 8.4$ Hz, 1 H), 3.39–3.36 (m, 2 H), 2.36–2.29 (m, 1 H), 1.78–1.70 (m, 2 H), 1.69–1.59 (m, 2 H), 1.19 (s, 9 H), 0.83 (d, $J = 7.2$ Hz, 3 H) ppm; ¹³C NMR (150 MHz, CDCl₃): $\delta = 179.4, 139.6, 139.4, 139.1, 129.6, 129.3, 129.20, 129.16, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 81.2, 77.8, 77.0, 73.71, 73.69, 73.2, 71.5, 71.4, 65.2, 39.6, 34.5, 28.1, 27.9, 25.4, 11.1$ ppm; HRMS (ESI-TOF); calcd for C₃₈H₄₈O₆ [M + Na⁺]: 623.3343, found 623.3337.

A Ring epoxide 18a. To a stirred solution of A ring tri-benzyl ether (6.0 g, 10 mmol, 1.0 equiv)

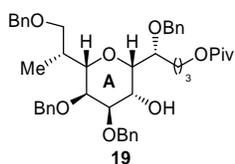


in CH₂Cl₂ (75 mL) at 25 °C was added *m*-CPBA (70%, 7.1 g, 30 mmol, 3.0 equiv), and the reaction mixture was stirred at 25 °C for 48 h. The reaction mixture was then quenched sequentially with Me₂S (2.2 mL, 30 mmol, 3.0

equiv) and sat. aq. NaHCO₃ (100 mL). The biphasic mixture was extracted with CH₂Cl₂ (3 × 50 mL), dried (MgSO₄), and concentrated. Silica gel chromatography (hexanes:EtOAc 17:3) gave A ring epoxide **18a** (5.6 g, 9.1 mmol, 91%) as a pale yellow oil (ca. 4.5:1 mix of diastereomers). Repeated preparative-plate chromatography (silica gel, hexanes:EtOAc 17:3) provided a sample of pure **18a** for characterization. **18a**: $R_f = 0.39$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{32} = -58.4$ (CH₂Cl₂, $c = 0.58$); IR (film) ν_{\max} 2965, 2921, 2865, 1725, 1455, 1284, 1156, 1112, 1094, 735, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): $\delta = 7.36\text{--}7.28$ (m, 15 H), 4.78 (d, $J = 11.4$ Hz, 1 H), 4.60 (s, 2 H), 4.57 (d, $J = 12.0$ Hz, 1 H), 4.50 (d, $J = 12.0$ Hz, 1 H), 4.41 (d, $J = 12.0$ Hz, 1 H), 4.04–3.97 (m, 2 H), 3.61 (d, $J = 8.4$ Hz, 1 H), 3.57–3.54 (m, 1 H), 3.51 (d, $J = 9.6$ Hz, 1 H), 3.42–3.37

(m, 3 H), 3.32 (dd, $J = 9.6, 2.4$ Hz, 1 H), 3.27 (dd, $J = 9.0, 6.0$ Hz, 1 H), 2.17–2.13 (m, 1 H), 1.75–1.67 (m, 3 H), 1.59–1.55 (m, 1 H), 1.17 (s, 9 H), 0.66 (d, $J = 7.2$ Hz, 3 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.5, 138.5, 138.2, 137.3, 128.5, 128.4, 128.33, 128.28, 128.1, 127.9, 127.8, 127.54, 127.50, 78.0, 76.0, 75.3, 72.9, 72.7, 72.4, 71.8, 69.4, 64.5, 64.5, 54.5, 50.6, 38.7, 33.9, 27.3, 27.2, 23.5, 10.1$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{38}\text{H}_{48}\text{O}_7$ [$\text{M} + \text{H}^+$]: 617.3473, found 617.4365.

A Ring secondary alcohol 19. To a stirred solution of A ring epoxide **18a** (ca. 4.5:1

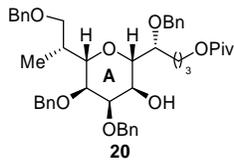


diastereomeric mix, 5.6 g, 9.1 mmol, 1.0 equiv) in CH_2Cl_2 (100 mL) at 25 °C were added BnOH (1.13 mL, 10.9 mmol, 2.5 equiv) and $\text{BF}_3 \cdot \text{OEt}_2$ (1.14 mL, 9.1 mmol, 1.0 equiv), and the reaction mixture was stirred at 25 °C for 18 h.

The reaction mixture was then quenched with sat. aq. NaHCO_3 (100 mL), the biphasic mixture was extracted with CH_2Cl_2 (3×50 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 7:3) yielded A ring secondary alcohol **19** (6.0 g, 8.3 mmol, 91% yield) as a colorless oil [ca. inseparable 5:1 mix of isomers corresponding to the epoxide (**18a**) diastereomeric ratio]. A sample of pure **19** was obtained for characterization by subjection of a small amount of isomerically pure epoxide (**18a**) to the reaction conditions described above. **19**: $R_f = 0.30$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{32} = -15.6$ (CH_2Cl_2 , $c = 0.23$); IR (film) ν_{max} 3453, 2962, 2925, 2870, 1726, 1454, 1284, 1155, 1100, 1024, 736, 698 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.35\text{--}7.27$ (m, 20 H), 4.78 (t, $J = 11.4$ Hz, 2 H), 4.61–4.59 (m, 2 H), 4.56 (d, $J = 12.6$ Hz, 1 H), 4.50 (d, $J = 11.4$ Hz, 1 H), 4.48 (d, $J = 12.0$ Hz, 1 H), 4.45 (d, $J = 11.4$ Hz, 1 H), 4.05 (bs, 1 H), 4.00–3.97 (m, 4 H), 3.93 (d, $J = 1.8$ Hz, 1 H), 3.85 (dd, $J = 10.2, 2.4$ Hz, 1 H), 3.66 (quin, $J = 3.6$ Hz, 1 H), 3.63–3.62 (m, 1 H), 3.56 (dd, $J = 9.0, 7.2$ Hz, 1 H), 3.39 (dd, $J = 9.0, 7.8$ Hz, 1 H), 2.43–2.37 (m, 1 H), 1.76–1.70 (m, 1 H), 1.57–1.51 (m, 2 H), 1.52–1.43 (m, 1 H), 1.19 (s, 9 H), 0.88 (d, $J = 7.2$ Hz, 3 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.5, 138.81, 138.76, 138.2, 137.8, 128.4, 128.34, 128.32, 128.27, 128.22, 127.93, 127.86, 127.7, 127.65, 127.58, 127.4, 80.3, 77.1, 75.6, 74.6, 74.3, 74.1,$

73.2, 73.1, 72.8, 71.0, 68.5, 64.0, 38.7, 32.9, 28.2, 27.2, 25.0, 10.1 ppm; HRMS (ESI-TOF); calcd for C₄₅H₅₆O₈ [M + H⁺]: 725.4048, found 725.4037.

A Ring inverted secondary alcohol 20. To a stirred solution of DMSO (628 μ L, 8.84 mmol,

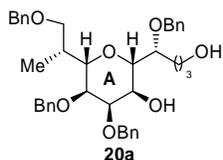


4.0 equiv) in CH₂Cl₂ (20 mL) at -78 °C was added (COCl)₂ (286 μ L, 4.42 mmol, 2.0 equiv). The reaction mixture was stirred for 15 min at -78 °C, at which point a -78 °C solution of A ring secondary alcohol **19** (ca. 5:1

isomeric mix, 1.60 g, 2.21 mmol, 1.0 equiv) in CH₂Cl₂ (20 mL) was added *via* cannula. The reaction mixture was stirred for 2 h at -78 °C, and Et₃N (1.84 mL, 13.3 mmol, 6.0 equiv) was added. The reaction mixture was warmed to 0 °C and stirred for 45 min, and then quenched with brine (50 mL). The biphasic mixture was extracted with CH₂Cl₂ (3 \times 20 mL), and the combined organic layers were dried (MgSO₄) and concentrated. The so obtained crude ketone was carried forward without further purification. To a solution of the crude ketone in MeOH (50 mL) at -78 °C was added NaBH₄ (159 mg, 4.42 mmol, 2.0 equiv), and the resulting mixture was stirred at -78 °C for 45 min. The reaction mixture was then quenched with H₂O (2 mL), warmed to 25 °C, and concentrated. The residue was partitioned between EtOAc (50 mL) and sat. aq. NH₄Cl (50 mL), the aqueous layer was extracted with EtOAc (2 \times 30 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1 to 4:1) gave the desired inverted A ring secondary alcohol **20** (1.02 g, 1.41 mmol, 64% yield over the two steps) as a pale yellow oil (The region- and stereoisomeric secondary alcohol derived from the minor isomer present in starting material **19** was removed at this stage). **20**: R_f = 0.22 (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{32}$ = -14.7 (CH₂Cl₂, c = 1.09); IR (film) ν_{max} 3483, 3030, 2962, 2926, 2871, 1724, 1496, 1479, 1454, 1364, 1284, 1207, 1156, 1110, 1065, 1028, 735, 697 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.38–7.27 (m, 20 H), 5.00 (d, J = 11.4 Hz, 1 H), 4.71 (d, J = 11.4 Hz, 1 H), 4.67 (d, J = 11.4 Hz, 1 H), 4.56 (d, J = 11.4 Hz, 1 H), 4.53–4.47 (m, 4 H), 4.18 (t, J = 2.4 Hz, 1 H), 4.05–3.96 (m, 3 H), 3.64–3.60 (m, 2 H), 3.53–3.51 (m, 2 H), 3.38 (dd, J = 9.0, 7.2 Hz, 1 H), 3.34 (dd, J = 10.2, 2.4 Hz, 1 H), 2.95 (d, J = 5.4

Hz, 1 H), 2.35–2.30 (m, 1 H), 1.80–1.73 (m, 2 H), 1.66–1.57 (m, 2 H), 1.19 (s, 9 H), 0.75 (d, $J = 7.2$ Hz, 3 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.6, 138.9, 138.8, 138.2, 137.7, 128.44, 128.39, 128.37, 128.28, 127.93, 127.91, 127.86, 127.82, 127.7, 127.6, 127.5, 127.4, 80.2, 76.3, 75.9, 74.7, 73.3, 73.2, 72.9, 71.6, 71.2, 70.6, 64.4, 38.7, 32.9, 27.2, 26.2, 24.5, 9.9$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{45}\text{H}_{56}\text{O}_8$ [$\text{M} + \text{H}^+$]: 725.4048, found 725.4043.

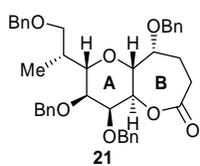
A Ring diol 20a. To a stirred solution of A ring inverted secondary alcohol **20** (2.16 g, 2.98



mmol, 1.0 equiv) in CH_2Cl_2 (25 mL) at -78 °C was added Dibal-H (1.0 M in CH_2Cl_2 , 7.45 mL, 7.45 mmol, 2.5 equiv), and the reaction mixture was stirred at -78 °C for 1 h. The reaction mixture was then diluted in EtOAc (30 mL)

and quenched with sat. aq. Rochelle's salt (50 mL). The resulting biphasic mixture was stirred vigorously for 16 h. The mixture was then extracted with EtOAc (3×30 mL), dried (MgSO_4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 3:2) yielded A ring diol **20a** (1.58 g, 2.47 mmol, 83% yield) as a pale yellow oil. **20**: $R_f = 0.29$ (silica gel, hexanes:EtOAc 2:3); $[\alpha]_D^{32} = -17.3$ (CH_2Cl_2 , $c = 0.99$); IR (film) ν_{max} 3434, 3030, 2922, 2870, 1496, 1454, 1363, 1207, 1105, 1062, 1027, 735, 697 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.38\text{--}7.27$ (m, 20 H), 5.00 (d, $J = 11.4$ Hz, 1 H), 4.71 (d, $J = 11.4$ Hz, 1 H), 4.67 (d, $J = 11.4$ Hz, 1 H), 4.56 (d, $J = 11.4$ Hz, 1 H), 4.53–4.47 (m, 4 H), 4.18 (t, $J = 2.4$ Hz, 1 H), 4.05–3.96 (m, 3 H), 3.64–3.60 (m, 2 H), 3.53–3.51 (m, 2 H), 3.38 (dd, $J = 9.0, 7.2$ Hz, 1 H), 3.34 (dd, $J = 10.2, 2.4$ Hz, 1 H), 2.95 (d, $J = 5.4$ Hz, 1 H), 2.35–2.30 (m, 1 H), 1.80–1.73 (m, 2 H), 1.66–1.57 (m, 2 H), 1.19 (s, 9 H), 0.75 (d, $J = 7.2$ Hz, 3 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 138.9, 138.8, 138.1, 137.7, 128.5, 128.41, 128.38, 128.3, 127.98, 127.95, 127.87, 127.81, 127.7, 127.59, 127.56, 127.4, 80.6, 76.3, 75.8, 75.6, 74.7, 73.24, 73.19, 72.9, 71.6, 71.1, 70.6, 62.9, 32.7, 28.5, 26.2, 9.9$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{40}\text{H}_{48}\text{O}_7$ [$\text{M} + \text{H}^+$]: 641.3473, found 641.3468.

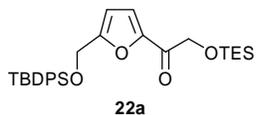
AB Lactone 21. To a stirred solution of A ring diol **20a** (1.00 g, 1.56 mmol, 1.0 equiv) in CH_2Cl_2 (150 mL) at 25 °C were added TEMPO (49 mg, 0.31 mmol, 0.2 equiv) and $\text{PhI}(\text{OAc})_2$ (2.59 g, 7.80 mmol, 5 equiv). After stirring at that temperature for 48 h, the reaction mixture was



quenched with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ (75 mL), extracted with CH_2Cl_2 (3×50 mL), dried (MgSO_4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1 to 4:1) yielded AB lactone **21** (914 mg, 1.44 mmol, 92%

yield) as a pale yellow oil. **21**: $R_f = 0.33$ (silica gel, hexanes:EtOAc 1:3); $[\alpha]_D^{32} = -61.1$ (CH_2Cl_2 , $c = 0.95$); IR (film) ν_{max} 3030, 2926, 2865, 1736, 1496, 1453, 1347, 1260, 1208, 1101, 1059, 1027, 736, 697 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.46\text{--}7.24$ (m, 20 H), 4.99 (d, $J = 11.4$ Hz, 1 H), 4.81 (d, $J = 11.4$ Hz, 1 H), 4.71 (d, $J = 12.0$ Hz, 1 H), 4.57–4.51 (m, 3 H), 4.50 (dd, $J = 12.0, 1.2$ Hz, 1 H), 4.46 (d, $J = 12.0$ Hz, 1 H), 4.40 (d, $J = 12.0$ Hz, 1 H), 4.30 (t, $J = 2.4$ Hz, 1 H), 4.13 (dd, $J = 9.6, 1.8$ Hz, 1 H), 3.78–3.76 (m, 2 H), 3.53 (dd, $J = 9.0, 7.2$ Hz, 1 H), 3.39 (dd, $J = 9.0, 7.2$ Hz, 1 H), 3.32 (dd, $J = 9.6, 1.8$ Hz, 1 H), 3.11 (dt, $J = 7.2, 1.2$ Hz, 1 H), 2.42 (dd, $J = 15.0, 6.6$ Hz, 1 H), 2.37 (dq, $J = 6.6, 1.6$ Hz, 1 H), 1.98 (m, 1 H), 1.69 (t, $J = 7.8$ Hz, 1 H), 0.81 (d, $J = 6.6$ Hz, 3 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 174.5, 138.9, 138.69, 138.66, 137.7, 128.4, 128.30, 128.28, 128.1, 127.94, 127.87, 127.85, 127.7, 127.6, 127.5, 127.4, 127.3, 75.7, 75.4, 75.2, 74.9, 74.7, 73.5, 73.3, 72.9, 72.8, 71.84, 71.82, 70.9, 32.6, 27.4, 25.7, 9.9$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{40}\text{H}_{44}\text{O}_7$ [$\text{M} + \text{H}^+$]: 637.3160, found 637.3157.

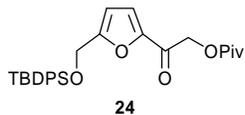
Keto furan 22a. To a stirred solution of freshly distilled furfuryl alcohol (52.2 mL, 600 mmol, 1.0 equiv) in CH_2Cl_2 (1.2 L) at 25 °C were added imidazole (61.3 g, 900 mmol, 1.5 equiv) and TBDPSCI (156 mL, 600 mmol, 1.0 equiv), and the



reaction mixture was stirred at 25 °C for 30 min. The resulting mixture was then quenched with sat. aq. NH_4Cl (1.0 L) and extracted with CH_2Cl_2 (3×500 mL). The combined organic layers were washed with brine (1.0 L), dried (MgSO_4), and concentrated to afford TBDPS-protected furfuryl alcohol **22** (202 g, 600 mmol, quant. yield) of sufficient purity to carry on to the next step. To a stirred solution of furan derivative **22** (193 g, 573 mmol, 1.2 equiv) in THF (1.0 L) at -78 °C was added *n*-BuLi (2.5 M in hexanes, 230 mL, 573 mmol, 1.2 equiv), and the reaction mixture was allowed to warm to 0 °C, stirred for 1 h, then re-cooled to -78 °C. To this mixture was added amide **23**³ (116 g, 477 mmol, 1.0 equiv), and the mixture was warmed to 0 °C and

stirred for 1 h. The reaction mixture was quenched with sat. aq. NH₄Cl (500 mL), and the, extracted with EtOAc (3 × 500 mL). The combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1) gave keto furan **20a** (203 g, 400 mmol, 84% yield) as a colorless oil. **20a**: *R*_f = 0.67 (silica gel, hexanes:EtOAc 4:1); IR (film) ν_{\max} 2926, 1711, 1362, 1265, 1221, 910, 732 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 7.69–7.65 (m, 4 H), 7.43 (s, 1 H), 7.42–7.35 (m, 6 H), 6.37 (d, *J* = 3.5 Hz, 1 H), 4.72 (s, 2 H), 4.66 (s, 2 H), 1.08 (s, 9 H), 0.99 (t, *J* = 7.9 Hz, 9 H), 0.68 (d, *J* = 8.0 Hz, 6 H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ = 187.15, 159.21, 150.59, 135.93, 135.20, 133.26, 130.33, 130.03, 128.22, 128.20, 128.19, 128.11, 119.35, 109.71, 77.67, 77.41, 77.16, 67.00, 59.66, 31.99, 27.12, 26.97, 23.05, 19.65, 14.51, 7.09, 7.08, 4.83, 4.82 ppm; HRMS (ESI-TOF); calcd for C₂₉H₄₀O₄Si₂ [M + Na⁺]: 531.2363, found 531.2361.

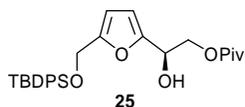
Pivaloate 24. To a stirred solution of keto furan **22a** (203 g, 400 mmol, 1.0 equiv) in CH₂Cl₂:MeOH (5:1, 1.2 L) at 25 °C was added CSA (9.3 g, 40 mmol, 0.1 equiv), and the reaction mixture was stirred at 25 °C for 1 h. The resulting



mixture was quenched with sat. aq. NaHCO₃ (400 mL) and extracted with CH₂Cl₂ (3 × 500 mL). The combined organic layers were dried (MgSO₄) and concentrated. To the resulting crude primary alcohol in CH₂Cl₂ (1.0 L) at 25 °C were added Et₃N (184 mL, 1320 mmol, 2.0 equiv) and PivCl (98 mL, 792 mmol, 1.2 equiv), and the reaction mixture was stirred at that temperature for 12 h. The reaction mixture was quenched with sat. aq. NaHCO₃ (500 mL), the biphasic mixture was extracted with CH₂Cl₂ (3 × 500 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1) gave pivaloate **24** (293 g, 613 mmol, 93% yield) as a light yellow oil. **24**: *R*_f = 0.65 (silica gel, hexanes:EtOAc 4:1); IR (film) ν_{\max} 2932, 1735, 1428, 1112, 821, 741, 701, 607, 519, 526 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.68 (dt, *J* = 8.4, 1.2 Hz, 4 H), 7.51–7.35 (m, 6 H), 7.18 (dd, *J* = 3.6, 1.8 Hz, 1H), 6.41–6.32 (m, 1 H), 5.06 (d, *J* = 1.8 Hz, 2 H), 4.74–4.67 (m, 2 H), 1.30 (d, *J* = 1.8 Hz, 9 H), 1.08 (d, *J* = 1.8 Hz, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 182.44, 178.63,

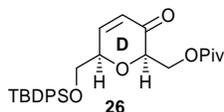
159.81, 150.58, 136.20, 133.42, 130.64, 128.52, 119.13, 110.38, 65.79, 59.81, 39.48, 27.90, 27.38, 19.91 ppm; HRMS (ESI-TOF); calcd for C₂₈H₃₄O₅Si [M + Na⁺]: 501.2068, found 501.2070.

Secondary alcohol 25. To a vigorously stirred solution of pivaloate **24** (146 g, 305 mmol, 1.0 equiv) in CH₂Cl₂:H₂O (1:1, 1.5 L) at 25 °C were added *n*-Bu₄NCl (25 g, 92 mmol, 0.3 equiv), HCO₂Na (207 g, 3050 mmol, 10.0 equiv), and cat. *ent*-**13**



(3.8 g, 6.1 mmol, 0.02 equiv), and the reaction mixture was vigorously stirred at that temperature for 24 h. The reaction mixture was then diluted with H₂O (500 mL), the biphasic mixture was extracted with CH₂Cl₂ (3 × 500 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) provided secondary alcohol **25** [137 g, 286 mmol, 94% yield, ≥95% *ee* (as measured by ¹H NMR spectroscopic analysis of the corresponding Naproxen[®] ester)] as a colorless oil. **25**: *R*_f = 0.34 (silica gel, hexanes:EtOAc 4:1); [α]_D³² = +8.7 (CHCl₃, *c* = 1.0); IR (film) ν_{max} 3450, 2959, 2859, 1731, 1480, 1428, 1364, 1283, 1155, 1112, 1069, 940, 823, 740 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 7.68 (dt, *J* = 8.4, 1.2 Hz, 4 H), 7.40 (dt, *J* = 14.4, 7.2 Hz, 6 H), 6.22 (d, *J* = 3.0 Hz, 1 H), 6.10 (d, *J* = 3.0 Hz, 1 H), 4.87 (dd, *J* = 6.6, 4.8 Hz, 1 H), 4.63 (s, 2 H), 4.33 (t, *J* = 5.4 Hz, 2 H), 1.19 (s, 9 H), 1.05 (s, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 178.80, 157.54, 154.57, 152.58, 145.45, 135.94, 134.92, 134.61, 133.36, 130.39, 126.45, 126.15, 108.46, 108.27, 103.34, 81.97, 77.58, 77.37, 77.16, 74.24, 66.89, 66.75, 63.88, 59.18, 58.55, 39.12, 27.50, 27.44, 27.10, 19.60, 18.38 ppm; HRMS (ESI-TOF); calcd for C₂₈H₃₆O₅Si [M + Na⁺]: 503.2224, found 503.2227.

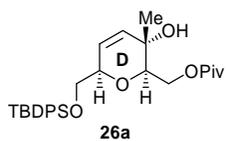
D Ring enone 26. To a stirred solution of secondary alcohol **25** (128 g, 266 mmol, 1.0 equiv) in



CH₂Cl₂ (1.2 L) at 0 °C was added dry *m*-CPBA (92 g, 532 mmol, 1.2 equiv), and the reaction mixture was warmed to 25 °C and stirred for 2 h. Me₂S (24 mL, 320 mmol, 1.2 equiv) was then added to the reaction mixture, which was subsequently quenched with sat. aq. NaHCO₃ (400 mL). The biphasic mixture was extracted with CH₂Cl₂ (3 × 400 mL), and the combined organic layers were dried (MgSO₄) and concentrated. The resulting

crude hemiacetal was carried on to the next step without further purification. To a stirred solution of the crude hemiacetal in CH₂Cl₂ (1.2 L) at -78 °C were added Et₃SiH (130 mL, 792 mmol, 3.0 equiv) and BF₃•OEt₂ (67 mL, 532 mmol, 2.0 equiv), and the reaction mixture was warmed to -20 °C and stirred for 3 h. The reaction mixture was then quenched with sat. aq. NaHCO₃ (500 mL), the biphasic mixture was extracted with CH₂Cl₂ (3 × 400 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1) gave D ring enone **26** (94 g, 196 mmol, 74% yield over the two steps) as a colorless oil. **26**: *R*_f = 0.55 (silica gel, hexanes:EtOAc 1:1); [α]_D³² = +36.0 (C₆H₆, *c* = 1.0); IR (film) *v*_{max} 2930, 1732, 1698, 1462, 1428, 1279, 1155, 1113, 823, 747, 702 cm⁻¹; ¹H NMR (500 MHz, C₆D₆): δ = 7.71 (ddd, *J* = 5.4, 3.6, 1.8 Hz, 4 H), 7.25–7.21 (m, 6 H), 6.47 (dd, *J* = 10.4, 1.2 Hz, 1 H), 5.90 (dd, *J* = 10.4, 2.4 Hz, 1 H), 4.65 (dd, *J* = 12.0, 2.4 Hz, 1 H), 4.52 (dd, *J* = 12.0, 5.6 Hz, 1 H), 3.93 (d, *J* = 1.8 Hz, 1 H), 3.82–3.74 (m, 1 H), 3.67 (dd, *J* = 10.4, 5.4 Hz, 1 H), 3.56 (dd, *J* = 10.4, 5.4 Hz, 1 H), 1.13 (d, *J* = 4.8 Hz, 18 H) ppm; ¹³C NMR (125 MHz, C₆D₆): δ = 192.59, 177.56, 148.51, 135.92, 133.40, 133.35, 130.17, 130.16, 128.26, 128.16, 128.11, 128.09, 127.97, 127.78, 127.50, 78.71, 74.79, 65.59, 63.08, 38.77, 27.21, 26.96, 26.94, 26.93, 19.39 ppm; HRMS (ESI-TOF); calcd for C₂₈H₃₆O₅Si [M + Na⁺]: 503.2224, found 503.2228.

D Ring tertiary alcohol 26a. To a stirred solution of D ring enone **26** (77 g, 160 mmol, 1.0

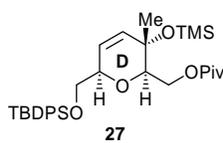


equiv) in THF (800 mL) at -78 °C was added MeMgBr (3.0 M in Et₂O, 107 mL, 320 mmol, 2.0 equiv), and the reaction mixture was stirred at -78 °C for 2 h. The reaction mixture was then quenched with sat. aq. NH₄Cl (400 mL),

the biphasic mixture was extracted with EtOAc (3 × 400 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) gave D ring tertiary alcohol **26a** (63 g, 128 mmol, 80% yield) as a colorless oil. **26a**: *R*_f = 0.19 (silica gel, hexanes:EtOAc 4:1); [α]_D³² = +43.0 (CHCl₃, *c* = 1.0); IR (film) *v*_{max} 3681, 3452, 2966, 2935, 1729, 1480, 1461, 1428, 1392, 1362, 1286, 1159, 1107, 1056, 1033, 914, 823, 800, 739, 702 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ = 7.76–7.66 (m, 4 H), 7.50–

7.37 (m, 6 H), 5.77 (dd, $J = 10.4, 1.8$ Hz, 2 H), 4.39 (d, $J = 3.6$ Hz, 1 H), 4.28 (ddd, $J = 7.2, 3.6, 1.8$ Hz, 1 H), 4.19 (s, 1 H), 3.71 (d, $J = 5.4$ Hz, 1 H), 3.70–3.63 (m, 2 H), 1.26 (s, 3 H), 1.23 (s, 9 H), 1.08 (s, 10 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.89, 136.04, 135.95, 134.98, 133.85, 133.73, 130.02, 130.00, 127.98, 127.96, 127.95, 127.12, 79.32, 77.58, 77.37, 77.16, 76.46, 68.61, 66.61, 63.75, 60.77, 39.11, 27.51, 27.13, 22.53, 19.60$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{29}\text{H}_{40}\text{O}_5\text{Si}$ [$\text{M} + \text{Na}^+$]: 519.2537, found 519.2537.

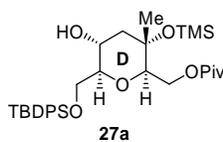
D Ring TMS ether 27. To a stirred solution of D ring tertiary alcohol **26a** (63 g, 128 mmol, 1.0



equiv) in CH_2Cl_2 (600 mL) at -78 °C were added Et_3N (45 mL, 320 mmol, 2.5 equiv) and TMSOTf (35 mL, 192 mmol, 1.5 equiv), and the reaction mixture was stirred at -78 °C for 1 h. The reaction mixture was then

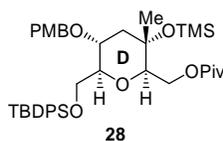
quenched with sat. aq. NaHCO_3 (300 mL), the biphasic mixture was extracted with CH_2Cl_2 (3×300 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1) gave D ring TMS ether **27** (71 g, 125 mmol, 98% yield) as a colorless oil. **27**: $R_f = 0.69$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{32} = +32.6$ ($\text{CHCl}_3, c = 1.0$); IR (film) ν_{max} 2959, 1731, 1480, 1428, 1366, 1284, 1252, 1216, 1162, 1112, 1033, 867, 841, 756, 702 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.68$ (ddd, $J = 8.4, 6.0, 1.2$ Hz, 4 H), 7.37 (dd, $J = 6.6, 1.2$ Hz, 6 H), 5.82 (dd, $J = 10.4, 2.4$ Hz, 1 H), 5.69 (dd, $J = 10.4, 1.2$ Hz, 1 H), 4.35 (dd, $J = 11.4, 1.8$ Hz, 1 H), 4.25 (s, 1 H), 4.10 (dd, $J = 11.4, 9.0$ Hz, 1 H), 3.69 (dd, $J = 11.4, 6.0$ Hz, 1 H), 3.66 (dd, $J = 8.4, 1.8$ Hz, 1 H), 3.61 (dd, $J = 10.2, 5.4$ Hz, 1 H), 1.20 (s, 9 H), 1.16 (s, 3 H), 1.05 (s, 9 H), 0.15 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 179.05, 136.05, 135.96, 135.56, 133.90, 130.00, 129.98, 127.98, 127.95, 126.36, 79.89, 77.58, 77.37, 77.16, 76.43, 71.15, 66.70, 63.74, 39.10, 27.54, 27.14, 24.14, 19.61, 2.86$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{32}\text{H}_{48}\text{O}_5\text{Si}_2$ [$\text{M} + \text{Na}^+$]: 591.2932, found 591.2929.

D Ring secondary alcohol 27a. To a stirred solution of D ring TMS ether **27** (57 g, 100 mmol, 1.0 equiv) in THF (400 mL) at -78 °C was added diisoamylborane (1.0 M in THF, 400 mL, 400 mmol, 4.0 equiv), and the reaction mixture was warmed to 0 °C and stirred for 72 h. The



reaction mixture was quenched by the slow addition of 1.0 M aq. NaOH (400 mL) and 35% H₂O₂ (120 mL), and the biphasic mixture was warmed to 25 °C and vigorously stirred for 5 h. The mixture was diluted with EtOAc (800 mL), the layers were separated, and the organic layer was washed with sat. aq. Na₂SO₃ (800 mL) and brine (800 mL), and then dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) gave D ring secondary alcohol **27a** (44 g, 75 mmol, 75% yield) as a colorless oil. **27a**: *R*_f = 0.45 (silica gel, hexanes:EtOAc 4:1); [α]_D³² = +23.6 (CHCl₃, *c* = 1.0); IR (film) ν_{max} 2959, 2859, 1729, 1480, 1428, 1280, 1214, 1167, 1052, 1007, 866, 841, 753, 702, 668 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.68 (ddd, *J* = 7.8, 2.4, 1.2 Hz, 4 H), 7.48–7.35 (m, 6 H), 4.29 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.98 (dd, *J* = 11.4, 8.4 Hz, 1 H), 3.90 (dd, *J* = 10.4, 4.2 Hz, 1 H), 3.84–2.76 (m, 2 H), 3.38 (dd, *J* = 8.4, 1.8 Hz, 1 H), 3.33–3.22 (m, 1 H), 3.11 (d, *J* = 2.4 Hz, 1 H), 2.25 (dd, *J* = 11.4, 4.8 Hz, 1 H), 1.71 (t, *J* = 11.4 Hz, 1 H), 1.22 (s, 3 H), 1.14 (s, 9 H), 1.06 (s, 9 H), 0.85 (s, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 178.98, 135.93, 135.89, 132.90, 132.83, 130.34, 130.32, 128.20, 82.59, 80.36, 77.58, 77.37, 77.16, 72.75, 68.95, 66.59, 63.50, 48.55, 39.05, 27.48, 27.14, 22.63, 19.48, 2.92 ppm; HRMS (ESI-TOF); calcd for C₃₂H₅₀O₆Si₂ [M + Na⁺] 609.3038, found 609.3036.

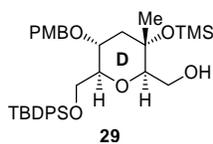
D Ring PMB ether 28. To a stirred solution of D ring secondary alcohol **27a** (28 g, 47 mmol,



1.0 equiv) in PhMe (300 mL) at 25 °C were added PMBOC(NH)CCl₃ (26 g, 94 mmol, 2.0 equiv) and La(OTf)₃ (1.4 g, 2.4 mmol, 0.05 equiv), and the reaction mixture was stirred at 25 °C for 3 h. The reaction mixture was then concentrated and purified by flash column chromatography (silica gel, hexanes:EtOAc 9:1) to give D ring PMB ether **28** (30 g, 43 mmol, 96% yield) as a colorless oil. **28**: *R*_f = 0.37 (silica gel, hexanes:EtOAc 9:1); [α]_D³² = +6.0 (CH₂Cl₂, *c* = 1.44); IR (film) ν_{max} 2957, 2931, 2858, 1728, 1612, 1587, 1513, 1462, 1428, 1283, 1250, 1170, 1138, 1111, 1085, 1036, 1008, 864, 840, 823, 742, 702 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.75–7.71 (m, 4 H), 7.43–7.35 (m, 6 H), 7.19–7.17 (m, 2 H), 6.84–6.83 (m, 2 H), 4.54 (d, *J* = 10.8 Hz, 1 H), 4.46 (d, *J* = 10.8 Hz, 1 H), 4.34 (d,

$J = 10.8$ Hz, 1 H), 4.08 (dd, $J = 11.4, 8.4$ Hz, 1 H), 3.90 (m, 2 H), 3.80 (s, 3 H), 3.71–3.66 (m, 1 H), 3.43 (d, $J = 7.8$ Hz, 1 H), 3.28 (d, $J = 9.0$ Hz, 1 H), 2.24 (dd, $J = 11.4, 4.8$ Hz, 1 H), 1.65 (t, $J = 11.4$ Hz, 1 H), 1.25 (s, 3 H), 1.18 (s, 9 H), 1.05 (s, 9 H), 0.13 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.8, 159.2, 135.8, 135.6, 133.9, 133.3, 130.4, 129.50, 129.47, 129.38, 127.6, 127.5, 113.8, 80.1, 81.5, 72.7, 71.4, 71.2, 63.7, 63.0, 55.3, 46.2, 38.7, 27.2, 26.7, 22.2, 19.3, 2.6$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{40}\text{H}_{58}\text{O}_7\text{Si}_2$ [$\text{M} + \text{Na}^+$]: 729.3613, found 729.3602.

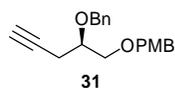
D Ring primary alcohol 29. To a stirred solution of D ring PMB ether **29** (53 g, 76 mmol, 1.0



equiv) in CH_2Cl_2 (380 mL) at -78 °C was added Dibal-H (1.0 M in CH_2Cl_2 , 168 mL, 168 mmol, 2.2 equiv), and the reaction mixture was stirred at the same temperature for 1 h. The reaction mixture was diluted in EtOAc (400

mL), then quenched with sat. aq. Rochelle's salt (600 mL) and stirred vigorously for 16 h. The biphasic mixture was extracted with EtOAc (3×400 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) yielded D ring primary alcohol **29** (40 g, 64 mmol, 84% yield) as a colorless oil. **29**: $R_f = 0.44$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{32} = -7.7$ (CH_2Cl_2 , $c = 1.13$); IR (film) ν_{max} 3503, 2951, 2939, 2857, 1612, 1513, 1463, 1428, 1250, 1173, 1137, 1112, 1077, 1035, 999, 873, 840, 822, 742, 702 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.74\text{--}7.70$ (m, 4 H), 7.45–7.36 (m, 6 H), 7.23–7.22 (m, 2 H), 6.87–6.86 (m, 2 H), 4.56 (d, $J = 10.8$ Hz, 1 H), 4.49 (d, $J = 10.8$ Hz, 1 H), 3.97 (dd, $J = 11.4, 3.6$ Hz, 1 H), 3.89 (d, $J = 11.4$ Hz, 1 H), 3.80 (s, 3 H), 3.80–3.76 (m, 1 H), 3.72–3.68 (m, 1 H), 3.57–3.53 (m, 1 H), 3.29 (dd, $J = 7.8, 4.2$ Hz, 1 H), 3.26 (dt, $J = 9.0, 1.8$ Hz, 1 H), 2.22 (dd, $J = 11.4, 4.8$ Hz, 1 H), 2.07 (dd, $J = 8.4, 4.2$ Hz, 1 H), 1.65 (t, $J = 11.4$ Hz, 1 H), 1.22 (s, 3 H), 1.07 (s, 9 H), 0.13 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 159.3, 135.8, 135.6, 133.8, 133.4, 130.4, 129.64, 129.62, 129.4, 127.6, 127.5, 113.8, 83.2, 81.3, 73.4, 71.4, 71.1, 62.8, 61.7, 55.3, 46.0, 26.8, 22.1, 19.3, 2.5$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{35}\text{H}_{50}\text{O}_6\text{Si}_2$ [$\text{M} + \text{Na}^+$]: 645.3038, found 645.3035.

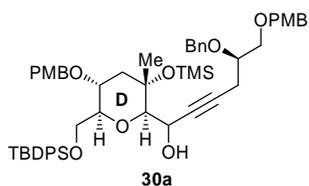
Alkyne 31. To a stirred solution of (*R*)-1-((4-methoxybenzyl)oxy)-5-(trimethylsilyl)pent-4-yn-



2-ol⁴ (42 g, 142 mmol, 1.0 equiv) in THF (500 mL) at 0 °C were added BnBr (34 mL, 284 mmol, 2.0 equiv), *n*-Bu₄NI (5.3 g, 14 mmol, 0.1 equiv), and NaH (60% in mineral oil, 11.4 g, 284 mmol, 2.0 equiv), and the reaction mixture was

warmed to 25 °C and stirred for 24 h. The resulting mixture was then quenched slowly with H₂O (300 mL), the biphasic mixture was extracted with EtOAc (3 × 500 mL), and the combined organic layers were dried (MgSO₄) and concentrated. The crude benzyl ether was taken on to the next step without further purification. To a stirred solution of the crude benzyl ether in THF (500 mL) at 25 °C was added TBAF (1.0 M in THF, 284 mL, 284 mmol, 2.0 equiv), and the resulting mixture was stirred at the same temperature for 2 h before it was quenched with sat. aq. NH₄Cl (300 mL) and extracted with EtOAc (3 × 500 mL). The combined organic layers were dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) gave alkyne **31** (40 g, 130 mmol, 92% yield over the two steps) as a yellow oil. **31**: *R*_f = 0.35 (silica gel, hexanes:EtOAc 17:3); [α]_D³² = -4.3 (CH₂Cl₂, *c* = 1.04); IR (film) ν_{max} 3291, 3027, 2906, 2863, 1612, 1586, 1513, 1454, 1350, 1302, 1247, 1173, 1092, 1034, 820, 738, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.37–7.32 (m, 4 H), 7.29–7.26 (m, 3 H), 6.89–6.87 (m, 2 H), 4.69 (d, *J* = 12.0 Hz, 1 H), 4.66 (d, *J* = 12.0 Hz, 1 H), 4.50 (s, 2 H), 3.81 (s, 3 H), 3.75 (quin, *J* = 5.4 Hz, 1 H), 3.64–3.59 (m, 2 H), 2.55 (ddd, *J* = 16.8, 6.0, 2.4 Hz, 1 H), 2.49 (ddd, *J* = 16.8, 5.4, 3.0 Hz, 1 H), 1.99 (t, *J* = 3.6 Hz, 1 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 159.1, 138.3, 130.3, 129.2, 128.3, 127.7, 127.6, 113.7, 80.8, 76.2, 73.1, 71.9, 70.9, 69.9, 55.2, 21.6 ppm; HRMS (ESI-TOF); calcd for C₂₀H₂₂O₃ [*M* + Na⁺]: 333.1461, found 333.1451.

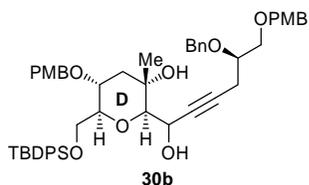
D Ring propargylic alcohol 30a. To a stirred solution of D ring primary alcohol **29** (35 g, 57



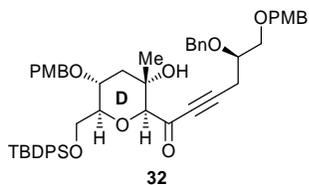
mmol, 1.0 equiv) in CH₂Cl₂ (600 mL) at 25 °C were added NaHCO₃ (24 g, 285 mmol, 5.0 equiv) and DMP (36 g, 85 mmol, 1.5 equiv), and the reaction mixture was stirred at 25 °C for 1 h. The resulting mixture was then quenched with sat. aq. NaHCO₃/sat. aq. Na₂S₂O₃ (1:1, 200

mL), the biphasic mixture was extracted with CH₂Cl₂ (3 × 200 mL), the combined organic extracts were washed with NaHCO₃ (200 mL) and brine (200 mL), and then dried (MgSO₄) and concentrated. The crude aldehyde so obtained (**30**) was carried on to the next step without further purification. To a stirred solution of alkyne **31** (44 g, 142 mmol, 2.5 equiv) in THF (500 mL) at -78 °C was added *n*-BuLi (2.5 M in hexanes, 22.8 mL, 57 mmol, 2.5 equiv), and the reaction mixture was warmed to -40 °C and stirred at 10 min. The reaction mixture was then cooled to -78 °C, and a cold (-78 °C) solution of the crude aldehyde **30** in THF (90 mL) was added *via* cannula with stirring. The reaction mixture was warmed to -50 °C and stirred for 1.5 h before it was quenched with sat. aq. NH₄Cl (300 mL). The resulting biphasic mixture was extracted with EtOAc (3 × 300 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) gave D ring propargylic alcohol **30a** (45 g, 49 mmol, 86% yield over the two steps, ca. 7:1 *dr*) as a colorless oil. **30a** (major diastereomer): *R*_f = 0.39 (silica gel, hexanes:EtOAc 4:1); [α]_D³² = -11.7 (CH₂Cl₂, *c* = 0.99); IR (film) ν_{max} 3564, 2946, 2933, 2858, 1612, 1587, 1513, 1463, 1428, 1389, 1302, 1249, 1173, 1112, 1037, 995, 840, 742, 702 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.74–7.69 (m, 4 H), 7.42–7.28 (m, 10 H), 7.25–7.20 (m, 5 H), 6.86–6.84 (m, 4 H), 4.65 (d, *J* = 11.4 Hz, 1 H), 4.61 (d, *J* = 12.0 Hz, 1 H), 4.58–4.55 (m, 1 H), 4.54 (d, *J* = 11.4 Hz, 1 H), 4.47 (d, *J* = 10.8 Hz, 1 H), 4.44 (s, 2 H), 3.95–3.90 (m, 2 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.74–3.68 (m, 2 H), 3.62 (dd, *J* = 10.2, 4.2 Hz, 1 H), 3.55 (dd, *J* = 10.2, 6.0 Hz, 1 H), 3.33 (d, *J* = 9.6 Hz, 1 H), 3.25 (d, *J* = 3.6 Hz, 1 H), 2.58 (d, *J* = 9.0 Hz, 1 H), 2.50 (d, *J* = 6.0 Hz, 1 H), 2.21 (dd, *J* = 11.4, 4.2 Hz, 1 H), 1.63–1.59 (m, 2 H), 1.33 (s, 3 H), 1.06 (s, 9 H), 0.13 (s, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 159.3, 159.1, 138.4, 135.6, 135.5, 133.7, 133.3, 130.4, 130.3, 129.71, 129.66, 129.4, 129.2, 128.3, 127.7, 127.5, 113.8, 113.7, 84.6, 82.2, 81.9, 80.7, 76.7, 73.4, 73.0, 71.9, 71.4, 70.9, 62.6, 60.4, 55.3, 55.2, 46.4, 26.8, 23.1, 22.1, 19.3, 2.6 ppm; HRMS (ESI-TOF); calcd for C₅₅H₇₀O₉Si₂ [M + Na⁺]: 953.4450, found 953.4439.

D Ring diol 30b. To a stirred solution of D ring propargylic alcohol **30a** (ca. 7:1 mix of diastereomers, 45 g, 49 mmol, 1.0 equiv) in MeOH (500 mL) at 25 °C was added K₂CO₃ (34 g, 245 mmol, 5.0 equiv), and the reaction mixture was stirred at 25 °C for 30 min. The reaction mixture was then concentrated, and the resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc 2:1) to provide D ring diol **30b** (41 g, 48.5 mmol, 99% yield, ca. 7:1 *dr*) as a pale yellow oil. **30b** (major diastereomer): *R*_f = 0.32 (silica gel, hexanes:EtOAc 3:2); [α]_D³² = -8.4 (CH₂Cl₂, *c* = 1.14); IR (film) *v*_{max} 3531, 2931, 2857, 1612, 1586, 1513, 1463, 1427, 1359, 1302, 1247, 1173, 1111, 1074, 1035, 822, 742, 702 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.71–7.68 (m, 4 H), 7.45–7.28 (m, 12 H), 7.25–7.22 (m, 3 H), 6.89–6.85 (m, 4 H), 4.64 (d, *J* = 12.0 Hz, 1 H), 4.60 (d, *J* = 12.0 Hz, 1 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.47 (s, 2 H), 4.46 (d, *J* = 10.8 Hz, 1 H), 4.28 (dq, *J* = 7.8, 1.8 Hz, 1 H), 3.98 (dd, *J* = 11.4, 3.6 Hz, 1 H), 3.87 (dd, *J* = 11.4, 1.8 Hz, 1 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.72–3.68 (m, 2 H), 3.59–3.54 (m, 2 H), 3.27–3.26 (m, 2 H), 3.10 (s, 1 H), 2.61 (ddd, *J* = 10.2, 6.0, 1.8 Hz, 1 H), 2.55 (ddd, *J* = 10.2, 4.8, 1.8 Hz, 1 H), 2.50 (d, *J* = 1.8 Hz, 1 H), 2.22 (dd, *J* = 12.0, 4.2 Hz, 1 H), 1.68 (s, 1 H), 1.61 (t, *J* = 11.4 Hz, 1 H), 1.23 (s, 3 H), 1.07 (s, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 159.21, 159.18, 138.0, 135.7, 135.5, 133.6, 133.4, 130.2, 130.1, 129.8, 129.7, 129.4, 129.3, 128.3, 127.9, 127.69, 127.67, 127.58, 113.8, 113.7, 85.6, 85.3, 81.4, 78.9, 75.2, 73.0, 71.6, 71.0, 70.7, 70.5, 69.9, 62.5, 61.9, 55.2, 44.2, 31.6, 26.8, 22.6, 19.3, 14.1 ppm; HRMS (ESI-TOF); calcd for C₅₂H₆₂O₉Si [M + Na⁺]: 881.4055, found 881.4047.

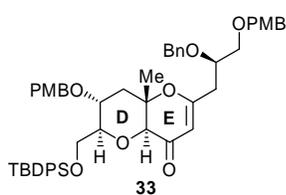


D Ring ynone 32. To a stirred solution of D ring diol **30b** (41 g, 48.5 mmol, 1.0 equiv) in CH₂Cl₂ (500 mL) at 25 °C was added DMP (30 g, 72 mmol, 1.5 equiv), and the reaction mixture was stirred at 25 °C for 1 h. The reaction mixture was then quenched with sat. aq. NaHCO₃:sat. aq. Na₂S₂O₃ (1:1, 200 mL) and stirred vigorously for 30 min. The biphasic mixture was then extracted with CH₂Cl₂ (3 × 200 mL), dried (MgSO₄), and concentrated. Flash column chromatography (silica



gel, hexanes:EtOAc 4:1) yielded D ring ynone **32** (38 g, 44 mmol, 91%) as a pale yellow oil. **32**: $R_f = 0.26$ (silica gel, hexanes:EtOAc 15:7); $[\alpha]_D^{32} = -32.8$ (CH_2Cl_2 , $c = 0.89$); IR (film) ν_{max} 3508, 2932, 2857, 2212, 1737, 1664, 1612, 1513, 1462, 1427, 1361, 1302, 1247, 1173, 1111, 1087, 1034, 822, 742, 703 cm^{-1} ; $^1\text{H NMR}$ (600 MHz, C_6D_6): $\delta = 7.99\text{--}7.87$ (m, 4 H), 7.33–7.21 (m, 8 H), 7.18–7.14 (m, 6 H), 7.09–7.06 (m, 1 H), 6.81–6.78 (m, 4 H), 4.39 (d, $J = 10.8$ Hz, 1 H), 4.38 (s, 2 H), 4.26 (s, 2 H), 4.22 (d, $J = 11.4$ Hz, 1 H), 4.06 (d, $J = 2.4$ Hz, 1 H), 3.77–3.72 (m, 1 H), 3.64 (s, 1 H), 3.57 (quin, $J = 5.4$ Hz, 1 H), 3.43 (dd, $J = 10.2, 5.4$ Hz, 1 H), 3.41–3.38 (m, 2 H), 3.30 (s, 3 H), 3.29 (s, 3 H), 3.21 (dt, $J = 9.0, 2.4$ Hz, 1 H), 2.57 (dd, $J = 11.4, 5.4$ Hz, 1 H), 2.49 (dd, $J = 11.4, 6.0$ Hz, 1 H), 2.33 (dd, $J = 12.0, 4.8$ Hz, 1 H), 1.71 (t, $J = 12.0$ Hz, 1 H), 1.36 (s, 3 H), 1.19 (s, 9 H) ppm; $^{13}\text{C NMR}$ (150 MHz, C_6D_6): $\delta = 188.1, 159.8, 159.7, 138.8, 136.3, 136.0, 134.2, 133.8, 131.0, 130.6, 130.1, 130.0, 129.6, 129.5, 128.6, 128.4, 128.1, 128.02, 127.98, 127.86, 114.1, 114.0, 96.2, 87.3, 82.4, 82.2, 76.1, 73.2, 72.1, 71.5, 70.9, 70.8, 70.7, 63.2, 54.80, 54.77, 44.4, 27.0, 23.1, 22.8, 19.7$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{52}\text{H}_{60}\text{O}_9\text{Si}$ [$\text{M} + \text{Na}^+$]: 879.3899, found 879.3897.

DE Pyranone 33. To a stirred solution of D ring ynone **32** (38 g, 44 mmol, 1.0 equiv) in CH_2Cl_2

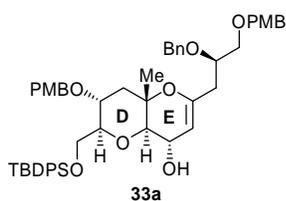


(880 mL) at -45 °C was added AgOTf (10 g, 40 mmol, 0.9 equiv), and the reaction mixture was stirred at -45 °C for 20 h. The reaction mixture was then quenched with sat. aq. NaHCO_3 (400 mL), the biphasic mixture was warmed to 25 °C and extracted with CH_2Cl_2 (3×400 mL). The

combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) gave DE pyranone **32** (28 g, 33 mmol, 76% yield) as a yellow oil. **32**: $R_f = 0.46$ (silica gel, hexanes:EtOAc 3:2); $[\alpha]_D^{32} = -7.9$ (CH_2Cl_2 , $c = 1.14$); IR (film) ν_{max} 2932, 2856, 1692, 1611, 1513, 1463, 1427, 1360, 1302, 1248, 1112, 1082, 1033, 904, 822, 742, 703 cm^{-1} ; $^1\text{H NMR}$ (600 MHz, C_6D_6): $\delta = 8.14\text{--}8.13$ (m, 2 H), 7.99–7.95 (m, 2 H), 7.52–7.50 (m, 2 H), 7.35–7.16 (m, 12 H), 7.09–7.07 (m, 1 H), 6.82–6.79 (m, 4 H), 5.35 (s, 1 H), 4.50 (d, $J = 11.4$ Hz, 1 H), 4.46 (d, $J = 10.8$ Hz, 1 H), 4.41 (d, $J = 12.0$ Hz, 1 H), 4.37 (d, $J = 11.4$ Hz,

1 H), 4.29 (s, 2 H), 4.10 (dd, $J = 12.0, 1.8$ Hz, 1 H), 4.05 (dd, $J = 11.4, 3.0$ Hz, 1 H), 3.89 (ddd, $J = 11.4, 9.6, 5.4$ Hz, 1 H), 3.80 (quin, $J = 5.4$ Hz, 1 H), 3.76 (s, 1 H), 3.42 (dd, $J = 10.2, 5.4$ Hz, 1 H), 3.33–3.30 (m, 7 H), 3.16–3.14 (m, 1 H), 2.32–2.30 (m, 3 H), 1.76 (t, $J = 5.4$ Hz, 1 H), 1.27 (s, 3 H), 1.20 (s, 9 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 187.7, 169.1, 159.94, 159.90, 139.1, 136.7, 136.2, 134.3, 133.3, 130.9, 130.6, 130.1, 130.0, 129.7, 129.6, 128.6, 128.4, 128.0, 127.81, 127.76, 114.21, 114.20, 104.7, 82.3, 80.7, 80.5, 76.0, 73.3, 72.1, 71.7, 71.5, 70.6, 62.8, 54.85, 54.80, 42.8, 38.0, 27.1, 19.6, 16.0$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{52}\text{H}_{60}\text{O}_9\text{Si}$ [$\text{M} + \text{H}^+$]: 857.4079, found 857.4085.

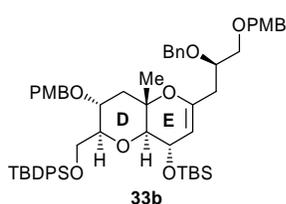
DE Allylic alcohol 33a. To a stirred solution of DE pyranone **33** (27 g, 32 mmol, 1.0 equiv) in



PhMe (320 mL) at -50 °C was added (*R*)-CBS (1.0 M in PhMe, 48 mL, 48 mmol, 1.5 equiv) followed by $\text{BH}_3 \cdot \text{THF}$ (1.0 M in THF, 48 mL, 48 mmol, 1.5 equiv), and the reaction mixture was warmed to -20 °C and stirred for 1 h. The reaction mixture was then quenched with MeOH (160 mL) followed by 1.0 M aq. NaOH (160 mL), and the biphasic mixture was warmed to 25 °C and stirred vigorously for 30 min. The biphasic mixture was extracted with EtOAc (3×300 mL), and the combined organic layers were washed with H_2O (300 mL) and brine (300 mL), and then dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) yielded DE allylic alcohol **33a** (25 g, 29 mmol, 93% yield) as a colorless oil. **33a**: $R_f = 0.35$ (silica gel, hexanes:EtOAc 15:7); $[\alpha]_D^{32} = +3.0$ (CH_2Cl_2 , $c = 0.89$); IR (film) ν_{max} 3463, 2932, 2857, 1669, 1612, 1586, 1512, 1463, 1427, 1301, 1247, 1174, 1111, 1078, 1035, 980, 822, 740, 702 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6): $\delta = 7.88\text{--}7.81$ (m, 4 H), 7.40–7.39 (m, 2 H), 7.26–7.17 (m, 12 H), 6.81–6.79 (m, 4 H), 4.76 (d, $J = 1.8$ Hz, 1 H), 4.68 (d, $J = 11.4$ Hz, 1 H), 4.58 (d, $J = 12.0$ Hz, 1 H), 4.46 (d, $J = 11.4$ Hz, 1 H), 4.38 (d, $J = 12.0$ Hz, 1 H), 4.35 (d, $J = 12.0$ Hz, 1 H), 4.32 (d, $J = 11.4$ Hz, 1 H), 4.12 (d, $J = 8.4$ Hz, 1 H), 4.05 (dd, $J = 11.4, 3.6$ Hz, 1 H), 3.98–3.96 (m, 2 H), 3.81 (ddd, $J = 10.8, 9.0, 3.6$ Hz, 1 H), 3.55–3.50 (m, 2 H), 3.31–3.29 (m, 7 H), 3.25–3.22 (m, 2 H), 2.40 (d, $J = 6.0$ Hz, 2 H), 2.33 (dd, $J = 11.4, 4.8$ Hz, 1 H), 1.71 (t, $J = 5.4$ Hz, 1

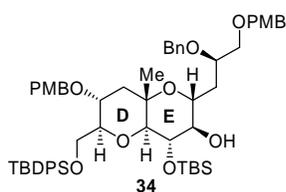
H), 1.18 (s, 9 H), 1.17 (s, 3 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 159.82, 159.76, 150.1, 139.8, 136.4, 136.1, 134.3, 134.0, 131.1, 131.0, 130.05, 130.03, 129.6, 129.5, 128.5, 128.1, 128.0, 127.7, 127.5, 114.15, 114.14, 100.7, 82.8, 82.2, 76.7, 75.4, 73.2, 72.6, 72.1, 71.0, 70.9, 66.2, 63.3, 54.81, 54.80, 43.1, 37.2, 27.2, 19.6, 17.3 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{52}\text{H}_{62}\text{O}_9\text{Si}$ [$\text{M} + \text{Na}^+$]: 881.4055, found 881.4045.

DE TBS-Protected allylic alcohol 33b. To a stirred solution of DE allylic alcohol **33a** (25 g, 29



mmol, 1.0 equiv) in CH_2Cl_2 (300 mL) at 25 °C were added TBSCl (26 g, 174 mmol, 6.0 equiv) and imidazole (20 g, 290 mmol 11 equiv), and the reaction mixture was stirred at 25°C for 1 h. The reaction mixture was then quenched with sat. aq. NH_4Cl (300 mL), the biphasic mixture was extracted with CH_2Cl_2 (3 \times 300 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) gave DE TBS-protected allylic alcohol **33b** (27 g, 28 mmol, 98% yield) as a pale yellow oil. **33b**: R_f = 0.28 (silica gel, hexanes:EtOAc 17:3); $[\alpha]_D^{32} = +24.6$ (CH_2Cl_2 , $c = 0.81$); IR (film) ν_{max} 2931, 2856, 1671, 1613, 1513, 1463, 1428, 1302, 1248, 1173, 1082, 1036, 988, 836, 779, 739, 702 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6): δ = 7.87–7.79 (m, 4 H), 7.42–7.41 (m, 2 H), 7.29–7.14 (m, 12 H), 7.11–7.08 (m, 1 H), 6.81–6.80 (m, 4 H), 4.78 (d, $J = 1.8$ Hz, 1 H), 4.71 (d, $J = 12.0$ Hz, 1 H), 4.59 (d, $J = 12.0$ Hz, 1 H), 4.43 (d, $J = 10.8$ Hz, 1 H), 4.40–4.34 (m, 3 H), 4.27 (d, $J = 10.8$ Hz, 1 H), 4.05 (dd, $J = 11.4, 3.0$ Hz, 1 H), 4.02–3.99 (m, 2 H), 3.92 (ddd, $J = 11.4, 9.6, 5.4$ Hz, 1 H), 3.56–3.51 (m, 2 H), 3.45 (d, $J = 7.8$ Hz, 1 H), 3.32 (s, 3 H), 3.30 (s, 3 H), 3.29–3.27 (m, 1 H), 2.44 (d, $J = 6.0$ Hz, 2 H), 2.38 (dd, $J = 11.4, 4.8$ Hz, 1 H), 1.74 (t, $J = 5.4$ Hz, 1 H), 1.31 (s, 3 H), 1.22 (s, 9 H), 1.06 (s, 9 H), 0.25 (s, 3 H), 0.23 (s, 3 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 159.8, 159.7, 149.5, 139.9, 136.3, 136.1, 134.2, 133.9, 131.12, 131.10, 130.03, 129.99, 129.5, 129.3, 128.5, 128.13, 128.11, 127.7, 127.5, 114.13, 114.07, 102.2, 82.7, 82.3, 76.8, 75.8, 73.2, 72.6, 72.3, 71.2, 70.7, 67.5, 63.4, 54.82, 54.80, 43.2, 37.3, 27.2, 26.3, 19.7, 18.6, 17.3, –3.7, –4.3 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{58}\text{H}_{76}\text{O}_9\text{Si}_2$ [$\text{M} + \text{Na}^+$]: 995.4920, found 995.4907.

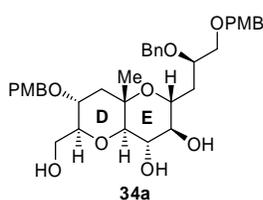
DE Secondary alcohol 34. To a stirred solution of DE TBS-protected allylic alcohol **33b** (24 g,



25 mmol, 1.0 equiv) in THF (250 mL) at 0 °C was added $\text{BH}_3 \cdot \text{THF}$ (1.0 M in THF, 250 mL, 250 mmol, 10.0 equiv), and the reaction mixture was stirred at 0 °C for 18 h. The reaction mixture was then quenched by the slow addition of 1.0 M NaOH (500 mL) and 35% H_2O_2 (120 mL), and

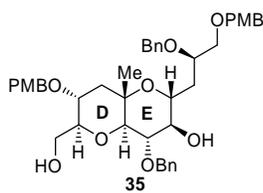
the biphasic mixture was warmed to 25 °C and stirred vigorously for 5 h. The biphasic mixture was then diluted with EtOAc (1000 mL), the layers were separated, and the organic layer was washed with sat. aq. Na_2SO_3 (600 mL) and brine (600 mL), and then dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1 to 7:3) gave DE secondary alcohol **34** (13.3 g, 13.5 mmol, 54% yield) as a colorless oil. **34**: $R_f = 0.41$ (silica gel, hexanes:EtOAc 7:3); $[\alpha]_D^{32} = +23.6$ (CH_2Cl_2 , $c = 0.81$); IR (film) ν_{max} 3468, 2930, 2856, 1612, 1514, 1463, 1360, 1302, 1248, 1172, 1094, 837, 780, 740, 702 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.69\text{--}7.66$ (m, 4 H), 7.42–7.26 (m, 12 H), 7.09–7.07 (m, 2 H), 6.83–6.81 (m, 4 H), 4.75 (d, $J = 11.4$ Hz, 1 H), 4.59 (d, $J = 11.4$ Hz, 1 H), 4.51–4.47 (m, 3 H), 4.28 (d, $J = 10.2$ Hz, 1 H), 4.04–3.98 (m, 2 H), 3.92–3.90 (m, 2 H), 3.86–3.85 (m, 1 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.63 (dd, $J = 9.6, 8.4$ Hz, 1 H), 3.56–3.54 (m, 2 H), 3.26 (dd, $J = 9.6, 1.2$ Hz, 1 H), 3.17 (dd, $J = 9.6, 8.4$ Hz, 1 H), 2.93 (d, $J = 9.6$ Hz, 1 H), 2.29 (dd, $J = 11.4, 5.4$ Hz, 1 H), 2.14–2.10 (m, 1 H), 1.59–1.55 (m, 1 H), 1.49 (t, $J = 5.4$ Hz, 1 H), 1.22 (s, 3 H), 1.09 (s, 9 H), 0.86 (s, 9 H), 0.14 (s, 3 H), 0.05 (s, 3 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 159.1, 139.0, 135.8, 135.7, 133.5, 133.3, 130.5, 130.3, 129.61, 129.59, 129.2, 129.1, 128.2, 127.8, 127.6, 127.5, 127.4, 113.73, 113.71, 82.9, 81.8, 74.7, 74.0, 73.2, 72.98, 72.97, 72.3, 70.8, 70.7, 68.8, 62.3, 55.27, 55.25, 43.6, 36.0, 26.9, 25.9, 19.3, 18.3, 16.6, -3.9, -4.8$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{58}\text{H}_{78}\text{O}_{10}\text{Si}_2$ [$\text{M} + \text{Na}^+$]: 1013.5025, found 1013.5023.

DE Triol 34a. To a stirred solution of DE secondary alcohol (557 mg, 0.58 mmol, 1.0 equiv) in THF (10 mL) at 25 °C was added TBAF (1.0 M in THF, 2.9 mL, 2.9 mmol, 5.0 equiv), and the reaction mixture was stirred at the same temperature for 16 h. The reaction mixture was then



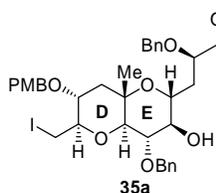
quenched with sat. aq. NH_4Cl (10 mL), the biphasic mixture was extracted with EtOAc (3×10 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, EtOAc:MeOH 100:0 to 19:1) gave DE triol **34a** (370 mg, 0.58 mmol, quant. yield) as a white foam. **34a**: $R_f = 0.30$ (silica gel, EtOAc:MeOH 19:1); $[\alpha]_D^{32} = +14.2$ (CH_2Cl_2 , $c = 1.1$); IR (film) ν_{max} 3681, 3396, 2937, 2866, 2844, 1612, 1513, 1455, 1355, 1302, 1247, 1173, 1057, 1033, 819, 739, 698 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.33\text{--}7.29$ (m, 4 H), 7.26–7.24 (m, 3 H), 7.21–7.20 (m, 2 H), 6.87–6.86 (m, 4 H), 4.71 (d, $J = 11.4$ Hz, 1 H), 4.53 (d, $J = 11.4$ Hz, 1 H), 4.49 (d, $J = 11.4$ Hz, 1 H), 4.46 (s, 2 H), 4.30 (d, $J = 10.8$ Hz, 1 H), 3.88–3.83 (m, 3 H), 3.79–3.78 (m, 7 H), 3.68 (dt, $J = 9.0, 1.8$ Hz, 1 H), 3.62 (t, $J = 9.0$ Hz, 1 H), 3.56 (dd, $J = 10.8, 3.0$ Hz, 1 H), 3.51 (d, $J = 4.8$ Hz, 1 H), 3.38 (bs, 2 H), 3.14 (t, $J = 9.0$ Hz, 1 H), 2.97 (d, $J = 9.6$ Hz, 1 H), 2.19–2.17 (m, 1 H), 2.09–2.05 (m, 1 H), 1.56–1.52 (m, 1 H), 1.45–1.44 (m, 1 H), 1.05 (s, 3 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 159.3, 159.1, 138.6, 130.3, 129.8, 129.4, 129.3, 128.3, 127.9, 127.5, 113.8, 113.7, 82.3, 82.1, 76.8, 76.3, 74.7, 73.0, 72.9, 72.4, 72.2, 71.9, 70.6, 69.5, 62.7, 55.2, 43.3, 36.1, 16.8$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{36}\text{H}_{46}\text{O}_{10}$ $[\text{M} + \text{Na}^+]$: 661.2983, found 661.2979.

DE Diol 35. To a stirred solution of DE diol **34a** (340 mg, 0.53 mmol, 1.0 equiv) in PhMe (7 mL) at 25 °C was added $n\text{-Bu}_2\text{SnO}$ (132 mg, 0.53 mmol, 1.0 equiv), and the reaction mixture was equipped with a condenser and Dean–Stark apparatus, heated to 110 °C, and stirred for 12 h. The reaction mixture was then cooled to 25 °C, at which point BnBr (95 μL , 0.80 mmol, 1.5 equiv) and $n\text{-Bu}_4\text{NI}$ (196 mg, 0.53 mmol, 1.0 equiv) were added, and the reaction mixture was heated to 100 °C for 4.5 h. After cooling to 25 °C, the reaction mixture was diluted with EtOAc (25 mL) and washed with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL), H_2O (mL), and brine (10 mL), and then dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 to 1:1) yielded DE diol **35** (330 mg, 0.45 mmol, 85% yield) as a pale yellow oil. **35**: $R_f = 0.28$



(silica gel, hexanes:EtOAc 1:1); $[\alpha]_D^{32} = -3.3$ (CH_2Cl_2 , $c = 0.81$); IR (film) ν_{max} 3456, 2926, 2869, 1612, 1513, 1455, 1357, 1302, 1247, 1173, 1075, 1033, 820, 738, 698 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6): $\delta = 7.43\text{--}7.34$ (m, 4 H), 7.23–7.18 (m, 6 H), 7.13–7.09 (m, 4 H), 6.80–6.76 (m, 4 H), 4.90 (d, $J = 11.4$ Hz, 1 H), 4.86 (d, $J = 12.0$ Hz, 1 H), 4.66 (d, $J = 12.0$ Hz, 1 H), 4.63 (d, $J = 12.0$ Hz, 1 H), 4.35–4.33 (m, 3 H), 4.15 (d, $J = 11.4$ Hz, 1 H), 4.14–4.10 (m, 1 H), 4.00 (dt, $J = 9.6, 1.8$ Hz, 1 H), 3.82 (d, $J = 11.4$ Hz, 1 H), 3.71–3.68 (m, 1 H), 3.57–3.51 (m, 2 H), 3.48–3.45 (m, 2 H), 3.32–3.29 (m, 2 H), 3.29 (s, 3 H), 3.27 (s, 3 H), 3.20 (d, $J = 10.2$ Hz, 1 H), 2.40–2.35 (m, 2 H), 2.23 (dd, $J = 11.4, 4.8$ Hz, 1 H), 1.73–1.68 (m, 1 H), 1.65 (t, $J = 6.0$ Hz, 1 H), 1.57 (t, $J = 5.4$ Hz, 1 H), 1.02 (s, 3 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 159.9, 159.8, 140.0, 139.7, 131.1, 130.7, 129.6, 129.5, 128.7, 128.6, 128.1, 128.0, 127.8, 127.5, 114.2, 114.1, 84.1, 82.4, 80.6, 76.1, 75.2, 74.6, 73.9, 73.2, 73.1, 72.6, 71.8, 70.6, 69.7, 62.9, 54.80, 54.78, 44.1, 36.8, 17.0$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{43}\text{H}_{52}\text{O}_{10}$ $[\text{M} + \text{Na}^+]$: 751.3452, found 751.3442.

DE Iodide 35a. To a stirred solution of DE diol **35** (178 mg, 0.244 mmol, 1.0 equiv) in CH_2Cl_2

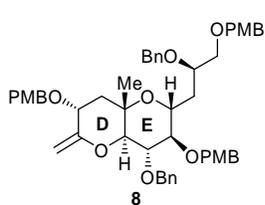


(7 mL) at 25 °C were added TsCl (140 mg, 0.73 mmol, 3.0 equiv), Et_3N (203 μL , 1.46 mmol, 6.0 equiv), and DMAP (3 mg, 0.024 mmol, 0.1 equiv), and the reaction mixture was heated to 45 °C and stirred for 20 h.

After cooling to 25 °C, the reaction mixture was quenched with sat. aq. NaHCO_3 , (10 mL), the resulting biphasic mixture was extracted with CH_2Cl_2 (3×5 mL), and the combined organic layers were dried (MgSO_4) and concentrated. The mixture was passed through a plug of silica gel, eluting with 3:2 hexanes:EtOAc to yield the partially pure primary tosylate, which was carried forward without further purification. To a stirred solution of the so obtained primary tosylate in DME (10 mL) at 25 °C was added NaI (366 mg, 2.44 mmol, 10.0 equiv), and the reaction mixture was heated to 85 °C and stirred in the dark for 7 h. After cooling to 25 °C, the reaction mixture was diluted in EtOAc (30 mL), washed with brine (15 mL), dried (MgSO_4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 7:3) gave DE iodide **35a** (182 mg, 0.217 mmol, 89% yield over the two steps) as

a colorless oil. **35a**: $R_f = 0.26$ (silica gel, hexanes:EtOAc 7:3); $[\alpha]_D^{32} = -11.6$ (C_6H_6 , $c = 0.93$); IR (film) ν_{max} 3443, 2931, 2906, 2868, 1612, 1513, 1454, 1357, 1302, 1247, 1210, 1173, 1075, 1029, 820, 737, 698 cm^{-1} ; 1H NMR (600 MHz, C_6D_6): $\delta = 7.45\text{--}7.41$ (m, 4 H), 7.22–7.18 (m, 6 H), 7.12–7.09 (m, 4 H), 6.79–6.77 (m, 4 H), 5.20 (d, $J = 12.0$ Hz, 1 H), 4.86 (d, $J = 11.4$ Hz, 1 H), 4.71 (d, $J = 12.0$ Hz, 1 H), 4.65 (d, $J = 12.0$ Hz, 1 H), 4.35 (d, $J = 12.0$ Hz, 1 H), 4.33 (d, $J = 12.0$ Hz, 1 H), 4.30 (d, $J = 10.8$ Hz, 1 H), 4.13–4.10 (m, 1 H), 4.09 (d, $J = 11.4$ Hz, 1 H), 4.01 (dt, $J = 9.6, 1.8$ Hz, 1 H), 3.56 (dd, $J = 10.2, 6.0$ Hz, 1 H), 3.50 (dd, $J = 9.6, 9.0$ Hz, 1 H), 3.45 (dd, $J = 9.6, 4.2$ Hz, 1 H), 3.32–3.27 (m, 9 H), 3.19 (d, $J = 10.2$ Hz, 1 H), 3.12 (dd, $J = 10.8, 6.0$ Hz, 1 H), 2.88 (ddd, $J = 8.4, 5.4, 2.4$ Hz, 1 H), 2.40 (ddd, $J = 14.4, 10.2, 2.4$ Hz, 1 H), 2.32 (d, $J = 3$ Hz, 1 H), 2.17 (dd, $J = 11.4, 5.4$ Hz, 1 H), 1.70 (ddd, $J = 13.8, 9.6, 2.4$ Hz, 1 H), 1.52 (t, $J = 5.4$ Hz, 1 H), 1.07 (s, 3 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 160.0, 159.7, 140.0, 139.9, 131.1, 130.4, 129.7, 129.5, 128.7, 128.5, 128.4, 128.2, 127.84, 127.77, 127.5, 114.2, 114.1, 84.5, 80.3, 79.8, 75.9, 75.3, 75.1, 74.6, 73.9, 73.2, 73.1, 72.6, 70.6, 69.6, 54.82, 54.80, 43.7, 36.8, 17.2, 8.2$ ppm; HRMS (ESI-TOF); calcd for $C_{43}H_{51}IO_9$ [$M + Cl^-$]: 873.2272, found 873.2236.

DE Enol ether 8. To a solution of DE iodide **35a** (163 mg, 0.194 mmol, 1.0 equiv) in THF (15

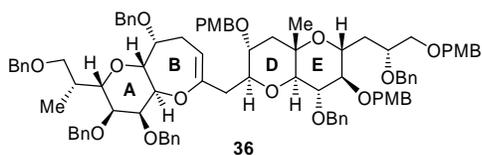


mL) at 0 °C was added KO t -Bu (261 mg, 2.33 mmol, 12 equiv), and the reaction mixture was stirred at 0 °C for 16 h. NaH (60% suspension in mineral oil, 77 mg, 1.94 mmol, 10.0 equiv), PMBCl (99 μ L, 0.97 mmol, 5.0 equiv), and n -Bu $_4$ Ni (36 mg, 0.097 mmol, 0.5 equiv) were sequentially

added to the reaction mixture, and the reaction mixture was warmed to 25 °C and stirred for 36 h. The reaction mixture was quenched by slow sequential addition of MeOH (400 μ L) and H $_2$ O (20 mL), the biphasic mixture was extracted with EtOAc (3 \times 15 mL), and the combined organic layers were washed with brine (20 mL), dried (MgSO $_4$), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1 to 17:3) gave DE enol ether **8** (140 mg, 0.168 mmol, 88% yield) as a colorless oil. **8**: $R_f = 0.33$ (silica gel, hexanes:EtOAc 3:1); $[\alpha]_D^{32} = +15.2$ (C_6H_6 , $c = 0.91$); IR (film) ν_{max} 2933, 2906, 2865, 1612, 1513, 1455, 1302, 1247, 1173, 1082,

1035, 821, 737, 698 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6): δ = 7.51–7.49 (m, 2 H), 7.41–7.40 (m, 2 H), 7.23–7.17 (m, 10 H), 7.12–7.07 (m, 2 H), 6.79–6.72 (m, 6 H), 5.18 (d, J = 11.4 Hz, 1 H), 4.89 (d, J = 10.8 Hz, 1 H), 4.86 (d, J = 11.4 Hz, 1 H), 4.84 (d, J = 12.0 Hz, 1 H), 4.71 (s, 1 H), 4.63 (d, J = 12.0 Hz, 1 H), 4.54–4.52 (m, 2 H), 4.39 (d, J = 10.2 Hz, 1 H), 4.36 (s, 3 H), 4.26 (d, J = 12.0 Hz, 1 H), 4.11–4.07 (m, 1 H), 4.05 (dt, J = 10.8, 1.2 Hz, 1 H), 3.89 (dd, J = 9.6, 9.0 Hz, 1 H), 3.82 (dd, J = 7.2, 4.8 Hz, 1 H), 3.53 (dd, J = 10.2, 6.0 Hz, 1 H), 3.46 (dd, J = 9.6, 4.2 Hz, 1 H), 3.29 (s, 3 H), 3.28 (s, 3 H), 3.28–3.27 (m, 1 H), 3.27 (s, 3 H), 3.21 (dd, J = 9.6, 8.4 Hz, 1 H), 2.28 (ddd, J = 13.8, 10.2, 1.8 Hz, 1 H), 2.11 (dd, J = 13.2, 4.2 Hz, 1 H), 1.99 (dd, J = 13.2, 7.2 Hz, 1 H), 1.55 (ddd, J = 13.2, 10.2, 1.2 Hz, 1 H), 1.11 (s, 3 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 159.8, 159.73, 159.68, 140.1, 139.9, 131.4, 131.2, 130.8, 129.8, 129.7, 129.4, 128.55, 128.52, 128.2, 127.8, 127.6, 127.5, 114.2, 114.1, 114.0, 92.6, 82.8, 81.8, 81.2, 75.20, 75.15, 75.0, 73.9, 73.8, 73.2, 73.0, 72.6, 69.8, 69.5, 54.79, 54.75, 44.9, 36.3, 18.7 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{51}\text{H}_{58}\text{O}_{10}$ [$\text{M} + \text{Na}^+$]: 853.3922, found 853.3929.

ABDE Enol ether 36. To a stirred solution of AB lactone **21** (410 mg, 0.65 mmol, 1.0 equiv) in



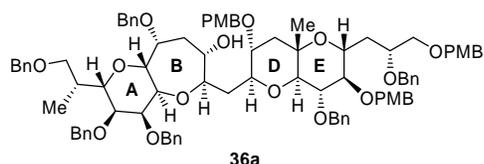
THF:HMPA (10:1, 66 mL) at -78 $^{\circ}\text{C}$ was added $(\text{PhO})_2\text{P}(\text{O})\text{Cl}$ (1.35 mL, 6.48 mmol, 10.0 equiv) followed by KHMDS (0.5 M in PhMe, 3.86 mL, 1.93 mmol, 3.0

equiv), and the reaction mixture was stirred at -78 $^{\circ}\text{C}$ for 30 min. The reaction mixture was then quenched with 10% aq. NH_4OH (50 mL), warmed to 25 $^{\circ}\text{C}$, and stirred vigorously for 30 min. The biphasic mixture was diluted in EtOAc (125 mL), the layers were separated, and the organic layer was washed with brine (75 mL), dried (MgSO_4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc:Et₃N 85:15:2) gave ketene acetal phosphate **7** (546 mg, 0.63 mmol, 97% yield), which was immediately carried on to the next step. To a stirred solution of enol ether **8** (647 mg, 0.78 mmol, 1.5 equiv) in THF (8 mL) at 25 $^{\circ}\text{C}$ was added 9-BBN (0.5 M in THF, 4.67 mL, 2.34 mmol, 4.5 equiv) and the reaction mixture was stirred at 25 $^{\circ}\text{C}$ for 4 h. 0.5 M aq. KHCO_3 (14.0 mL, 7.02 mmol, 13.5 equiv) was added to the reaction

mixture, and the biphasic mixture was stirred vigorously at 25 °C for 20 min. After a solution of ketene acetal phosphate **7** (451 mg, 0.52 mmol, 1.0 equiv) in THF (10 mL) was added to this mixture *via* cannula, SPhos (64 mg, 0.16 mmol, 0.3 equiv) and Pd(OAc)₂ (17 mg, 0.08 mmol, 0.15 equiv) were added, and the biphasic mixture was stirred vigorously at 25 °C for 72 h. The resulting mixture was then diluted with brine (20 mL), extracted with EtOAc (3 × 15 mL), and the combined organic extracts were dried (MgSO₄) and concentrated. The resulting residue was taken up in THF (65 mL) and cooled to 0 °C before 3.0 M aq. NaOH (9 mL) and 35% H₂O₂ (4.5 mL) were added. The biphasic mixture was stirred vigorously at 0 °C for 30 min and then diluted in EtOAc (125 mL). The layers were separated, and the organic phase was washed with sat. aq. Na₂SO₃ (50 mL) and brine (50 mL), dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc:Et₃N 45:5:1 to 40:10:1) yielded ABDE enol ether **36** (675 mg, 0.47 mmol, 90% yield) as a colorless oil. **36**: *R*_f = 0.21 (silica gel, hexanes:EtOAc 3:1); [α]_D³² = -56.1 (C₆H₆, *c* = 0.57); IR (film) *v*_{max} 3032, 2936, 2911, 2868, 1612, 1513, 1454, 1350, 1302, 1247, 1172, 1077, 1029, 819, 735, 697, 680 cm⁻¹; ¹H NMR (600 MHz, C₆D₆): δ = 7.79–7.59 (m, 4 H), 7.45–7.44 (m, 2 H), 7.36–7.34 (m, 2 H), 7.29–7.27 (m, 6 H), 7.24–7.16 (m, 13 H), 7.13–7.05 (m, 9 H), 6.78–6.75 (m, 6 H), 5.34 (d, *J* = 10.8 Hz, 1 H), 5.20 (d, *J* = 12.0 Hz, 1 H), 5.04 (d, *J* = 10.8 Hz, 1 H), 4.93 (dd, *J* = 7.8, 4.8 Hz, 1 H), 4.91 (d, *J* = 12.0 Hz, 1 H), 4.90 (d, *J* = 11.4 Hz, 1 H), 4.78 (d, *J* = 10.8 Hz, 1 H), 4.72 (d, *J* = 12.0 Hz, 1 H), 4.64 (d, *J* = 11.4 Hz, 1 H), 4.56 (d, *J* = 12.0 Hz, 1 H), 4.42–4.33 (m, 7 H), 4.28 (t, *J* = 1.8 Hz, 1 H), 4.24 (d, *J* = 11.4 Hz, 1 H), 4.18–4.15 (m, 3 H), 4.09–4.05 (m, 2 H), 3.99 (d, *J* = 11.4 Hz, 1 H), 3.96 (dd, *J* = 9.6, 2.4 Hz, 1 H), 3.90 (d, *J* = 9.0 Hz, 1 H), 3.60–3.54 (m, 3 H), 3.50 (d, *J* = 10.2 Hz, 1 H), 3.48 (dd, *J* = 10.2, 4.2 Hz, 1 H), 3.44 (t, *J* = 7.8 Hz, 1 H), 3.35–3.29 (m, 2 H), 3.28 (s, 3 H), 3.27 (s, 3 H), 3.26 (s, 3 H), 3.16 (dd, *J* = 9.6, 2.4 Hz, 1 H), 3.05 (d, *J* = 13.8 Hz, 1 H), 2.64–2.59 (m, 1 H), 2.38–2.33 (m, 2 H), 2.28 (dd, *J* = 14.4, 10.2 Hz, 1 H), 2.12 (quin, *J* = 7.8 Hz, 1 H), 2.00 (d, *J* = 14.4 Hz, 1 H), 1.76 (t, *J* = 11.4 Hz, 1 H), 1.59 (ddd, *J* = 13.2, 10.2, 2.4 Hz, 1 H), 1.15 (s, 3 H), 0.99 (d, *J* = 7.2 Hz, 3 H) ppm; ¹³C NMR (150 MHz, C₆D₆): δ = 159.9, 159.71, 159.69, 155.8, 140.18, 140.15, 140.11, 139.9, 139.7, 139.0, 131.5, 131.2, 130.7, 129.9, 129.8, 129.4, 129.0, 128.8,

128.7, 128.6, 128.54, 128.52, 128.4, 128.1, 128.0, 127.9, 127.80, 127.75, 127.68, 127.6, 127.5, 127.43, 127.42, 114.2, 114.1, 114.0, 106.4, 85.9, 82.9, 80.9, 79.5, 78.5, 76.7, 76.3, 76.2, 75.6, 75.5, 75.4, 75.13, 75.11, 75.9, 74.1, 73.6, 73.5, 73.2, 73.0, 72.9, 72.7, 72.0, 70.7, 70.5, 69.2, 54.78, 54.76, 44.6, 39.7, 36.6, 33.5, 27.1, 17.3, 10.4 ppm; HRMS (ESI-TOF); calcd for C₉₁H₁₀₂O₁₆ [M + Na⁺]: 1473.7060, found 1473.7052.

ABDE Secondary alcohol 36a. To a stirred solution of ABDE enol ether **36** (675 mg, 0.47

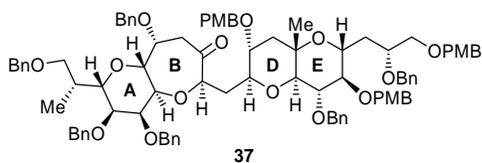


mmol, 1.0 equiv) in THF (30 mL) at 0 °C was added BH₃•THF (1.0 M in THF, 4.7 mL, 4.7 mmol, 10.0 equiv), and the reaction mixture was stirred at 0 °C for 18 h. The

reaction mixture was then quenched by slow addition of 1.0 M aq. NaOH (15 mL) and 35% H₂O₂ (2.5 mL), and the resulting biphasic mixture was warmed to 25 °C and stirred vigorously for 6 h. The resulting mixture was then diluted with EtOAc (60 mL), the layers were separated, and the organic layer was washed with sat. aq. Na₂SO₃ (30 mL) and brine (30 mL), dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexane:EtOAc 4:1 to 3:2) gave ABDE secondary alcohol **36a** (476 mg, 0.32 mmol, 70% yield) as a white foam and its diastereomer **36b** (105 mg, 0.07 mmol, 15% yield). **36a**: *R*_f = 0.29 (silica gel, hexanes:EtOAc 17:3); [α]_D³² = -10.9 (CH₂Cl₂, *c* = 0.82); IR (film) ν_{max} 3529, 2930, 2906, 2875, 1612, 1513, 1454, 1302, 1248, 1075, 1030, 821, 736, 698 cm⁻¹; ¹H NMR (600 MHz, C₆D₆): δ = 7.59–7.44 (m, 6 H), 7.31–7.18 (m, 20 H), 7.13–7.04 (m, 10 H), 6.79–6.73 (m, 6 H), 5.19 (d, *J* = 11.4 Hz, 1 H), 5.10 (d, *J* = 12.0 Hz, 1 H), 4.98 (d, *J* = 10.8 Hz, 1 H), 4.91–4.85 (m, 3 H), 4.72 (d, *J* = 10.8 Hz, 1 H), 4.70 (d, *J* = 12.0 Hz, 1 H), 4.62 (d, *J* = 10.8 Hz, 1 H), 4.47 (d, *J* = 12.6 Hz, 1 H), 4.43 (d, *J* = 12.6 Hz, 1 H), 4.38–4.34 (m, 5 H), 4.28 (s, 1 H), 4.23 (dd, *J* = 10.8, 1.8 Hz, 1 H), 4.19–4.14 (m, 3 H), 4.09–4.06 (m, 2 H), 3.95 (dt, *J* = 9.6, 6.0 Hz, 1 H), 3.91–3.87 (m, 1 H), 3.85 (dd, *J* = 9.6, 9.0 Hz, 1 H), 3.76 (d, *J* = 7.8 Hz, 1 H), 3.69–3.65 (m, 2 H), 3.58–3.54 (m, 2 H), 3.50–3.47 (m, 2 H), 3.44–3.38 (m, 2 H), 3.33 (t, *J* = 9.0 Hz, 1 H), 3.28 (s, 3 H), 3.27 (s, 3 H), 3.26 (s, 3 H), 3.19 (d, *J* = 10.8 Hz, 1 H), 3.06 (dd, *J* = 9.6, 2.4 Hz, 1 H), 2.64–2.58 (m, 1 H), 2.45 (dt, *J* = 13.8,

4.8 Hz, 1 H), 2.37–2.34 (m, 2 H), 2.26 (quin, $J = 6.0$ Hz, 1 H), 2.00 (ddd, $J = 15.0, 7.8, 1.2$ Hz, 1 H), 1.71 (t, $J = 11.4$ Hz, 1 H), 1.68–1.61 (m, 2 H), 1.13 (s, 3 H), 0.97 (d, $J = 6.6$ Hz, 1 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 159.8, 159.72, 159.71, 140.2, 140.1, 139.9, 139.6, 139.4, 139.0, 131.3, 131.2, 130.8, 129.95, 129.87, 129.4, 128.8, 128.65, 128.60, 128.55, 128.53, 128.18, 128.17, 128.14, 128.01, 127.98, 127.87, 127.85, 127.80, 127.6, 127.53, 127.51, 127.49, 114.15, 114.12, 114.0, 85.1, 84.8, 81.3, 80.6, 79.3, 79.0, 78.9, 77.3, 76.5, 75.5, 75.4, 75.3, 75.1, 74.8, 74.4, 74.3, 74.1, 74.0, 73.5, 73.2, 73.0, 72.9, 72.7, 70.7, 70.4, 69.3, 54.78, 54.75, 44.7, 40.9, 36.7, 34.6, 33.4, 17.2, 10.5$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{91}\text{H}_{104}\text{O}_{17}$ [$\text{M} + \text{Na}^+$]: 1491.7165, found 1491.7161.

ABDE Ketone 37 from oxidation of alcohol 36a. To a stirred solution of ABDE secondary



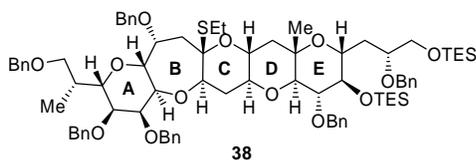
alcohol **36a** (476 mg, 0.32 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at 0°C was added DMP (551 mg, 1.30 mmol, 4.0 equiv), and the reaction mixture was warmed to 25°C

and stirred for 2 h. The reaction mixture was quenched with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$:sat. aq. NaHCO_3 (1:1, 20 mL), the resulting biphasic mixture was stirred vigorously for 30 min and extracted with CH_2Cl_2 (3×10 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 7:3) gave ABDE ketone **37** (461 mg, 0.31 mmol, 97% yield) as a colorless oil. **37**: $R_f = 0.34$ (silica gel, hexanes:EtOAc 7:3); $[\alpha]_D^{32} = -2.9$ (CH_2Cl_2 , $c = 0.47$); IR (film) ν_{max} 2932, 2865, 1715, 1612, 1513, 1454, 1302, 1248, 1078, 1033, 820, 736, 698 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6): $\delta = 7.61\text{--}7.60$ (m, 2 H), 7.48–7.44 (m, 4 H), 7.37–7.30 (m, 6 H), 7.25–7.16 (m, 13 H), 7.15–7.02 (m, 11 H), 6.79–6.70 (m, 6 H), 5.06 (d, $J = 12.0$ Hz, 1 H), 5.03 (d, $J = 12.0$ Hz, 1 H), 4.92–4.84 (m, 4 H), 4.71 (d, $J = 12.0$ Hz, 1 H), 4.61 (d, $J = 10.8$ Hz, 1 H), 4.55 (d, $J = 12.6$ Hz, 1 H), 4.50 (d, $J = 12.6$ Hz, 1 H), 4.44 (d, $J = 12.0$ Hz, 1 H), 4.40 (d, $J = 12.6$ Hz, 1 H), 4.38 (s, 2 H), 4.34–4.28 (m, 3 H), 4.25 (dd, $J = 10.2, 1.8$ Hz, 1 H), 4.19–4.14 (m, 2 H), 4.11–4.08 (m, 2 H), 4.01 (d, $J = 10.8$ Hz, 1 H), 3.94 (dt, $J = 9.0, 6.6$ Hz, 1 H), 3.82 (t, $J = 9.0$ Hz, 1 H), 3.77 (dd, $J = 10.2, 2.4$ Hz, 1 H), 3.60–3.57 (m, 2 H), 3.55 (dd, $J =$

9.6, 1.8 Hz, 1 H), 3.51 (dd, $J = 10.2, 4.2$ Hz, 1 H), 3.45 (t, $J = 7.8$ Hz, 1 H), 3.36–3.34 (m, 2 H), 3.32–3.27 (m, 2 H), 3.28 (s, 3 H), 3.27 (s, 3 H), 3.25 (s, 3 H), 2.98 (dd, $J = 10.2, 2.4$ Hz, 1 H), 2.79 (d, $J = 10.8$ Hz, 1 H), 2.67–2.58 (m, 3 H), 2.39–2.28 (m, 3 H), 1.70–1.64 (m, 2 H), 1.11 (s, 3 H), 1.03 (d, $J = 7.2$ Hz, 3 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 211.6, 159.9, 159.75, 159.74, 140.2, 140.1, 140.0, 139.6, 139.3, 139.0, 131.2, 131.1, 130.5, 130.2, 129.9, 129.4, 128.7, 128.61, 128.58, 128.57, 128.56, 128.55, 128.19, 128.18, 128.14, 128.0, 127.9, 127.84, 127.77, 127.7, 127.6, 127.5, 127.4, 114.2, 114.1, 114.0, 84.5, 84.2, 83.6, 81.0, 78.6, 78.4, 78.0, 77.3, 76.5, 75.4, 75.3, 75.1, 74.8, 74.3, 74.1, 73.9, 73.8, 73.6, 73.2, 73.04, 72.95, 72.7, 72.3, 70.8, 70.5, 69.3, 54.8, 54.7, 44.6, 43.4, 37.9, 36.7, 33.4, 17.2, 10.4$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{91}\text{H}_{102}\text{O}_{17} [\text{M} + \text{Na}^+]$: 1489.7009, found 1489.6981.

ABDE Ketone 37 from oxidation/isomerization of alcohol 36b. To a stirred solution of ABDE secondary alcohol diastereomer **36b** (105 mg, 0.071 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) at 0 °C was added DMP (121 mg, 0.29 mmol, 4.0 equiv), and the reaction mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched with sat. aq. $\text{Na}_2\text{S}_2\text{O}_3$:sat. aq. NaHCO_3 (1:1, 5 mL), the resulting biphasic mixture was stirred vigorously for 30 min and extracted with CH_2Cl_2 (3×5 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) gave ABDE ketone diastereomer C_{23} -*ent*-**37** (88 mg, 0.06 mmol, 84% yield). To a stirred solution of ABDE ketone diastereomer C_{23} -*ent*-**37** (88 mg, 0.06 mmol, 1.0 equiv) in PhMe (20 mL) at 25 °C was added imidazole (817 mg, 12 mmol, 200 equiv), and the reaction mixture was heated to 105 °C and stirred for 120 h. The reaction mixture was then cooled to 25 °C, diluted with CH_2Cl_2 (40 mL), washed with brine (30 mL), dried (MgSO_4), and concentrated. Preparative-plate chromatography (silica gel, hexanes:EtOAc 3:1) yielded ABDE ketone **37** (59 mg, 0.04 mmol, 67% yield) along with recovered ketone diastereomer C_{23} -*ent*-**37** (21 mg, 0.014 mmol, 24% yield).

ABCDE *S,O*-Acetal 38. To a stirred solution of ABDE ketone **37** (427 mg, 0.29 mmol, 1.0



equiv) in CH₂Cl₂:EtSH (5:1, 30 mL) at 25 °C was added Zn(OTf)₂ (529 mg, 1.45 mmol, 5.0 equiv), and the reaction mixture was stirred at 25 °C for 20 h. The resulting mixture was quenched by the addition of Et₃N (2

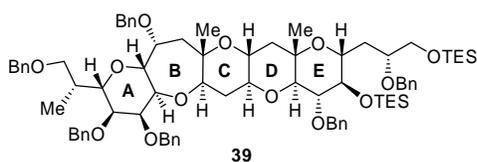
mL), and concentrated to afford the corresponding *S,O*-acetal diol, which was carried on crude.

To a stirred solution of the crude diol in CH₂Cl₂ (15 mL) 25 °C were added imidazole (396 mg, 5.82 mmol, 20 equiv) and TESCOI (488 μL, 2.91 mmol, 10.0 equiv), and the reaction mixture was stirred at 25 °C for 1 h. The reaction mixture was quenched with sat. aq. NH₄Cl (20 mL), the resulting biphasic mixture was extracted with CH₂Cl₂ (3 × 15 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 97:3 to 9:1)

gave ABCDE *S,O*-acetal **38** (367 mg, 0.27 mmol, 91% yield over the two steps) as a pale yellow oil. **38**: *R*_f = 0.35 (silica gel, hexanes:EtOAc 9:1); [α]_D³² = +40.4 (CH₂Cl₂, *c* = 0.74); IR (film) *v*_{max} 2946, 2911, 2875, 1454, 1249, 1085, 1028, 840, 734, 697 cm⁻¹; ¹H NMR (600 MHz, C₆D₆): δ = 7.66–7.65 (m, 2 H), 7.51–7.50 (m, 2 H), 7.43–7.38 (m, 4 H), 7.28–7.27 (m, 4 H), 7.24–7.17 (m, 10 H), 7.13–7.02 (m, 8 H), 5.30 (d, *J* = 12.0 Hz, 1 H), 5.24 (d, *J* = 12.0 Hz, 1 H), 4.84 (d, *J* = 12.0 Hz, 1 H), 4.81 (d, *J* = 12.0 Hz, 1 H), 4.66 (d, *J* = 12.0 Hz, 1 H), 4.62 (d, *J* = 12.0 Hz, 1 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.48 (d, *J* = 9.6 Hz, 1 H), 4.43–4.34 (m, 4 H), 4.32 (dd, *J* = 9.6, 1.8 Hz, 1 H), 4.19 (t, *J* = 1.2 Hz, 1 H), 4.14 (d, *J* = 11.4 Hz, 1 H), 4.10 (dt, *J* = 9.6, 1.2 Hz, 1 H), 4.02–3.97 (m, 2 H), 3.83 (dd, *J* = 9.6, 1.8 Hz, 1 H), 3.77–3.74 (m, 3 H), 3.64 (dd, *J* = 9.6, 7.8 Hz, 1 H), 3.55 (q, *J* = 9.0 Hz, 2 H), 3.46 (t, *J* = 7.8 Hz, 1 H), 3.26 (dd, *J* = 7.2, 1.8 Hz, 1 H), 3.20 (d, *J* = 10.2 Hz, 1 H), 2.94 (ddd, *J* = 12.0, 9.6, 4.2 Hz, 1 H), 2.65–2.59 (m, 1 H), 2.47–2.40 (m, 2 H), 2.37 (dd, *J* = 15.6, 2.4 Hz, 1 H), 2.28–2.24 (m, 3 H), 2.15 (dt, *J* = 9.0, 4.8 Hz, 1 H), 2.11 (dd, *J* = 11.4, 4.8 Hz, 1 H), 1.79–1.75 (m, 2 H), 1.23 (s, 3 H), 1.11 (t, *J* = 7.8 Hz, 3 H), 1.07 (t, *J* = 7.8 Hz, 9 H), 1.04 (d, *J* = 6.6 Hz, 3 H), 1.02 (t, *J* = 7.8 Hz, 9 H), 0.80–0.73 (m, 6 H), 0.62 (q, *J* = 7.8 Hz, 6 H) ppm; ¹³C NMR (150 MHz, C₆D₆): δ = 140.3, 140.2, 140.04, 140.01, 140.00, 139.6, 139.5, 138.8, 128.69, 128.65, 128.54, 128.50, 128.48, 128.45,

128.2, 128.1, 128.01, 127.98, 127.9, 127.8, 127.54, 127.52, 127.50, 127.4, 93.5, 85.6, 80.6, 78.6, 78.3, 77.4, 76.83, 76.76, 76.6, 76.2, 76.0, 75.0, 74.8, 74.7, 74.6, 73.8, 73.6, 73.5, 73.3, 73.0, 72.7, 70.8, 70.55, 70.47, 69.0, 66.2, 44.9, 43.91, 43.88, 35.1, 33.4, 19.8, 17.4, 14.5, 10.4, 7.4, 7.17, 7.15, 5.8, 4.88, 4.87, 1.0 ppm; HRMS (ESI-TOF); calcd for C₈₁H₁₁₀O₁₃Si₂ [M + Na⁺]: 1401.7097, found 1407.7089.

ABCDE Pentacycle 39. To a stirred solution of ABCDE *S,O*-acetal **38** (361 mg, 0.26 mmol, 1.0

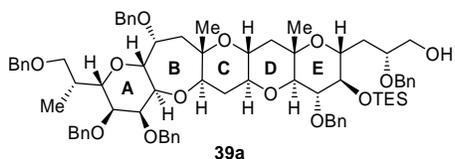


equiv) in CH₂Cl₂ (18 mL) at 0 °C was added dry *m*-CPBA (180 mg, 0.73 mmol, 2.5 equiv) as a solution in CH₂Cl₂ (1.5 mL), and the reaction mixture was stirred at 0 °C for

30 min. AlMe₃ (2.0 M in hexanes, 729 μL, 1.46 mmol, 5.0 equiv) was subsequently added, and the reaction mixture was stirred at 0 °C for an additional 30 min. The reaction mixture was quenched with sat. aq. NaHCO₃ (20 mL), the resulting biphasic mixture was extracted with Et₂O (3 × 25 mL), and the combined organic layers were washed with sat. aq. Na₂S₂O₃ (30 mL), sat. aq. NaHCO₃ (30 mL) and brine (30 mL), and then dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1) yielded ABCDE pentacycle **39** (327 mg, 0.25 mmol, 94% yield) as a white foam. **39**: *R*_f = 0.24 (silica gel, hexanes:EtOAc 9:1); [α]_D³² = +24.7 (CH₂Cl₂, *c* = 0.79); IR (film) ν_{max} 3030, 2952, 2906, 2875, 1496, 1454, 1083, 1028, 733, 696 cm⁻¹; ¹H NMR (600 MHz, C₆D₆): δ = 7.52–7.51 (m, 4 H), 7.44–7.43 (m, 2 H), 7.40–7.39 (m, 2 H), 7.29–7.27 (m, 4 H), 7.24–7.18 (m, 9 H), 7.13–7.02 (m, 9 H), 5.28 (d, *J* = 10.8 Hz, 1 H), 4.95 (d, *J* = 10.8 Hz, 1 H), 4.81 (d, *J* = 11.4 Hz, 1 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 4.73 (d, *J* = 10.8 Hz, 1 H), 4.58 (d, *J* = 12.0 Hz, 1 H), 4.54 (d, *J* = 11.4 Hz, 1 H), 4.43 (d, *J* = 12.0 Hz, 1 H), 4.39 (d, *J* = 11.4 Hz, 1 H), 4.37 (d, *J* = 12.6 Hz, 1 H), 4.34 (dd, *J* = 11.4, 4.8 Hz, 1 H), 4.27 (dd, *J* = 9.6, 1.8 Hz, 1 H), 4.17–4.14 (m, 2 H), 4.10 (dt, *J* = 10.2, 1.8 Hz, 1 H), 3.99–3.94 (m, 1 H), 3.77–3.71 (m, 4 H), 3.65–3.61 (m, 2 H), 3.60 (dd, *J* = 8.4, 7.2 Hz, 1 H), 3.54 (dd, *J* = 9.0, 8.4 Hz, 1 H), 3.44 (dd, *J* = 9.0, 7.2 Hz, 1 H), 3.38 (ddd, *J* = 11.4, 9.6, 4.8 Hz, 1 H), 3.24 (dd, *J* = 9.6, 2.4 Hz, 1 H), 3.21 (d, *J* = 10.2 Hz, 1 H), 2.95 (ddd, *J* = 12.0, 9.6, 4.2 Hz, 1 H), 2.64–

2.58 (m, 1 H), 2.41 (ddd, $J = 13.8, 10.2, 1.8$ Hz, 1 H), 2.36 (dd, $J = 15.6, 3.6$ Hz, 1 H), 2.18–2.12 (m, 2 H), 1.80–1.70 (m, 3 H), 1.59 (dd, $J = 15.6, 4.2$ Hz, 1 H), 1.22 (s, 3 H), 1.17 (s, 3 H), 1.07 (t, $J = 7.8$ Hz, 9 H), 1.02 (t, $J = 7.8$ Hz, 1 H), 1.00 (d, $J = 7.2$ Hz, 3 H), 0.81–0.71 (m, 6 H), 0.63 (q, $J = 7.8$ Hz, 6 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 140.17, 140.16, 140.1, 139.7, 139.5, 138.8, 128.7, 128.6, 128.54, 128.51, 128.48, 128.46, 128.14, 128.10, 128.02, 128.01, 127.98, 127.84, 127.78, 127.7, 127.59, 127.56, 127.52, 127.4, 86.0, 80.9, 79.7, 79.1, 78.6, 77.5, 77.1, 76.9, 76.6, 79.2, 75.72, 75.67, 74.9, 74.6, 73.6, 73.49, 73.48, 73.47, 73.0, 72.8, 72.6, 70.7, 69.0, 66.1, 44.7, 44.6, 36.8, 34.2, 33.4, 21.0, 17.5, 10.3, 7.4, 7.2, 5.8, 4.9$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{80}\text{H}_{108}\text{O}_{13}\text{Si}_2$ [$\text{M} + \text{Na}^+$]: 1355.7220, found 1355.7216.

ABCDE Primary alcohol 39a. To a stirred solution of ABCDE pentacycle **39** (159 mg, 0.119

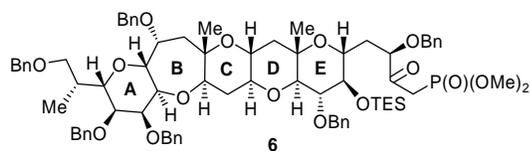


mmol, 1.0 equiv) in CH_2Cl_2 :MeOH (10:1, 6 mL) at 0°C was added PPTS (15 mg, 0.060 mmol, 0.5 equiv), and the reaction mixture was stirred at 0°C for 1 h. The reaction

mixture was quenched with Et_3N (500 μL), concentrated, and purified by flash column chromatography (silica gel, hexanes:EtOAc 9:1 to 3:1) to yield ABCDE primary alcohol **39a** (128 mg, 0.105 mmol, 88% yield) as a white foam. **39a**: $R_f = 0.31$ (silica gel, hexanes:EtOAc 3:1); $[\alpha]_D^{32} = +15.1$ (C_6H_6 , $c = 0.88$); IR (film) ν_{max} 3463, 2946, 2916, 2875, 1496, 1454, 1375, 1346, 1084, 1067, 1032, 828, 734, 697 cm^{-1} ; ^1H NMR (600 MHz, C_6D_6): $\delta = 7.53$ – 7.49 (m, 4 H), 7.41–7.39 (m, 2 H), 7.33–7.32 (m, 2 H), 7.33–7.27 (m, 4 H), 7.24–7.17 (m, 9 H), 7.13–7.02 (m, 9 H), 5.27 (d, $J = 10.8$ Hz, 1 H), 4.95 (d, $J = 11.4$ Hz, 1 H), 4.82 (d, $J = 12.0$ Hz, 1 H), 4.71 (d, $J = 10.8$ Hz, 1 H), 4.59 (d, $J = 12.0$ Hz, 1 H), 4.55 (d, $J = 12.0$ Hz, 1 H), 4.51 (s, 2 H), 4.43 (d, $J = 12.0$ Hz, 1 H), 4.40 (d, $J = 11.4$ Hz, 1 H), 4.37 (d, $J = 12.0$ Hz, 1 H), 4.35 (dd, $J = 11.4, 4.8$ Hz, 1 H), 4.27 (d, $J = 10.2$ Hz, 1 H), 4.17–4.15 (m, 2 H), 3.93 (t, $J = 7.8$ Hz, 1 H), 3.78 (s, 2 H), 3.27 (sext, $J = 4.2$ Hz, 1 H), 3.71–3.65 (m, 2 H), 3.62–3.58 (m, 2 H), 3.48–3.43 (m, 3 H), 3.35 (ddd, $J = 13.8, 10.8, 4.2$ Hz, 1 H), 3.25 (dd, $J = 9.0, 1.8$ Hz, 1 H), 3.16 (d, $J = 10.2$ Hz, 1 H), 2.94 (ddd, $J = 12.6, 7.8, 3.6$ Hz, 1 H), 2.65–2.59 (m, 1 H), 2.46 (dd, $J = 13.8, 9.0$ Hz, 1 H), 2.37

(dd, $J = 16.2, 3.0$ Hz, 1 H), 2.17 (dt $J = 11.4, 4.2$ Hz, 1 H), 2.10 (dd, $J = 11.4, 4.2$ Hz, 1 H), 1.79–1.72 (m, 2 H), 1.67 (t, $J = 12.0$ Hz, 1 H), 1.61 (dd, $J = 16.8, 4.8$ Hz, 1 H), 1.57 (ddd, $J = 14.4, 10.2, 4.2$ Hz, 1 H), 1.23 (s, 3 H), 1.13 (s, 3 H), 1.04 (t, $J = 8.4$ Hz, 9 H), 1.00 (d, $J = 6.6$ Hz, 1 H), 0.78–0.68 (m, 6 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 140.2, 140.1, 139.7, 139.6, 139.5, 138.8, 128.69, 128.66, 128.61, 128.59, 128.52, 128.49, 128.48, 128.1, 128.03, 127.98, 127.84, 127.77, 127.74, 127.43, 127.60, 127.56, 127.53, 127.50, 85.7, 80.7, 79.6, 79.0, 78.6, 77.2, 77.1, 76.9, 76.2, 75.7, 74.9, 74.6, 73.7, 73.6, 73.5, 73.0, 72.9, 71.9, 71.2, 70.7, 69.0, 64.9, 44.7, 44.6, 36.2, 34.2, 33.4, 21.1, 17.4, 10.3, 7.4, 5.8$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{74}\text{H}_{94}\text{O}_{13}\text{Si}$ [$\text{M} + \text{H}^+$]: 1219.6536, found 1219.6538.

ABCDE Ketophosphonate 6. To a stirred solution of ABCDE primary alcohol **40a** (127 mg,



0.104 mmol, 1.0 equiv) in CH_2Cl_2 :MeCN (9:1, 5 mL)

at 25 °C were added flame-dried 4 Å molecular sieves

(300 mg), NMO (37 mg, 0.312 mmol, 3 equiv), and

TPAP (3.7 mg, 0.01 mmol, 0.1 equiv), and the reaction mixture was stirred at 25 °C for 30 min.

The reaction mixture was then diluted in hexanes (4 mL), and Celite™ (500 mg) was added.

This homogenous mixture was loaded directly onto a short plug of silica gel eluted with hexanes:Et₂O (1:1) to afford the partially purified aldehyde **41** (99 mg, 0.0813 mmol, 78%

yield), which was carried on to the next step without further purification. To a stirred mixture of

(PhO)₂P(O)CH₃ (43 μL, 0.407 mmol, 5.0 equiv) in THF (2 mL) at –78 °C was added *n*-BuLi

(2.5 M in hexanes, 163 μL, 0.407 mmol, 5.0 equiv), and the resulting mixture was stirred at –78

°C for 1 h. To this reaction mixture was added a solution of aldehyde **41** in THF (2 mL) at –78

°C *via* cannula, and the resulting mixture was stirred at –78 °C for an additional 2.5 h. The

mixture was quenched with sat. aq. NH₄Cl (5 mL), the resulting biphasic mixture was extracted

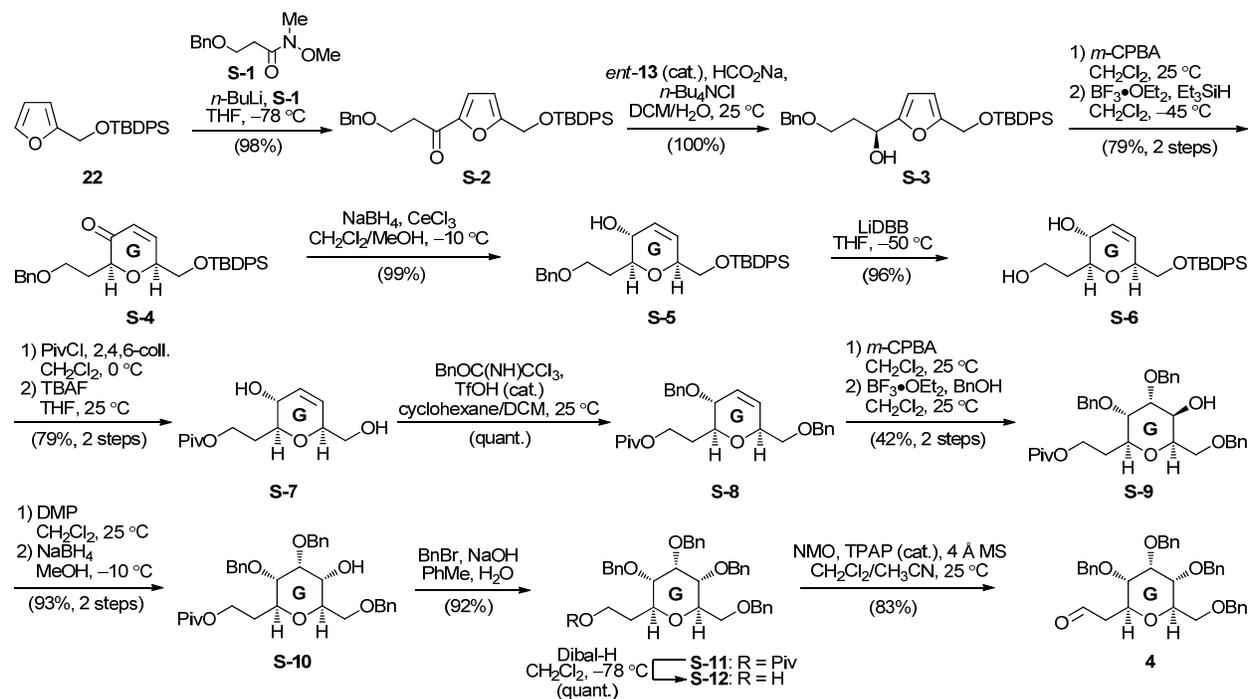
with EtOAc (3 × 5 mL), and the combined organic extracts were dried (MgSO₄), and

concentrated. The crude secondary alcohol was carried on to the next step without further

purification. To a stirred solution of the crude secondary alcohol in CH_2Cl_2 (4 mL) at 25 °C was

added DMP (103 mg, 0.244 mmol, 3.0 equiv), and the reaction mixture was stirred at 25 °C for 30 min. The resulting mixture was quenched with sat. aq. Na₂S₂O₃:sat. aq. NaHCO₃ (1:1, 5 mL), and the biphasic mixture was stirred vigorously at 25 °C for 30 min. The mixture was extracted with CH₂Cl₂ (3 × 5 mL), and the combined organic extracts were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 17:3 to 1:1) gave ABCDE ketophosphonate **6** (72 mg, 0.054 mmol, 66% yield) as a white foam along with recovered aldehyde **41** (17 mg, 0.014 mmol, 17% yield). **6**: *R*_f = 0.35 (silica gel, hexanes:EtOAc 1:1); [α]_D³² = +23.2 (C₆H₆, c = 0.73); IR (film) ν_{max} 2946, 2901, 2875, 1723, 1496, 1454, 1378, 1340, 1261, 1082, 1069, 1028, 828, 736, 697 cm⁻¹; ¹H NMR (600 MHz, C₆D₆): δ = 7.52–7.49 (m, 4 H), 7.41–7.38 (m, 4 H), 7.29–7.27 (m, 4 H), 7.23–7.18 (m, 8 H), 7.15–7.05 (m, 10 H), 5.25 (d, *J* = 11.4 Hz, 1 H), 4.95 (d, *J* = 12.0 Hz, 1 H), 4.83 (d, *J* = 12.0 Hz, 1 H), 4.75 (d, *J* = 12.0 Hz, 1 H), 4.69 (d, *J* = 10.8 Hz, 1 H), 4.60 (d, *J* = 12.0 Hz, 1 H), 4.55 (d, *J* = 12.0 Hz, 1 H), 4.44–4.41 (m, 2 H), 4.40–4.36 (m, 3 H), 4.35 (dd, *J* = 12.0, 4.8 Hz, 1 H), 4.27 (dd, *J* = 9.6, 1.2 Hz, 1 H), 4.17–4.14 (m, 2 H), 3.93 (d, *J* = 9.6 Hz, 1 H), 3.78 (d, 2 H), 3.66 (t, *J* = 3.6 Hz, 1 H), 3.60 (t, *J* = 7.8 Hz, 1 H), 3.57 (dd, *J* = 9.6, 8.4 Hz, 1 H), 3.49–3.45 (m, 1 H), 3.45 (d, *J* = 11.4 Hz, 3 H), 3.41 (d, *J* = 11.4 Hz, 3 H), 3.36–3.32 (m, 1 H), 3.24 (dd, *J* = 9.6, 2.4 Hz, 1 H), 3.20 (d, *J* = 7.2 Hz, 1 H), 3.16 (d, *J* = 7.2 Hz, 1 H), 3.12 (d, *J* = 9.6 Hz, 1 H), 2.92 (ddd, *J* = 12.6, 8.4, 4.2 Hz, 1 H), 2.64–2.58 (m, 1 H), 2.46 (dd, *J* = 12.6, 10.2 Hz, 1 H), 2.36 (dd, *J* = 15.6, 3.0 Hz, 1 H), 2.16 (dt, *J* = 11.4, 4.2 Hz, 1 H), 2.07 (dd, *J* = 11.4, 4.2 Hz, 1 H), 1.88 (ddd, *J* = 13.8, 10.2, 3.6 Hz, 1 H), 1.75 (q, *J* = 12.0 Hz, 1 H), 1.64–1.58 (m, 2 H), 1.22 (s, 3 H), 1.10 (s, 3 H), 1.02 (t, *J* = 7.8 Hz, 9 H), 1.00 (d, *J* = 6.6 Hz, 3 H), 0.77–0.66 (m, 6 H) ppm; ¹³C NMR (150 MHz, C₆D₆): δ = 203.9, 203.8, 140.2, 140.0, 139.7, 139.5, 138.8, 138.4, 128.69, 128.66, 128.62, 128.52, 128.48, 128.47, 128.45, 128.14, 128.10, 128.02, 127.99, 127.93, 127.84, 127.75, 127.60, 127.54, 127.53, 127.50, 85.6, 82.2, 82.1, 80.7, 79.7, 79.1, 78.6, 77.1, 76.9, 76.2, 75.7, 74.9, 74.5, 73.7, 73.6, 73.5, 73.0, 72.91, 72.86, 70.7, 70.3, 69.0, 52.50, 52.46, 42.43, 42.39, 44.7, 44.3, 36.8, 35.93, 35.89, 35.0, 34.1, 33.4, 32.0, 21.1, 17.2, 10.3, 7.4, 5.7 ppm; HRMS (ESI-TOF); calcd for C₇₇H₉₉O₁₆PSi [M + H⁺]: 1339.6512, found 1339.6481.

Scheme S1. Furan-based Synthesis of G Ring Aldehyde **5**.

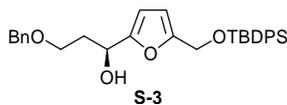


Furyl ketone S-2. To a stirred solution of TBDPS-protected furfuryl alcohol **22** (942 mg, 2.78

mmol, 2.5 equiv) in THF (10 mL) at 0 °C was added *n*-BuLi (2.5 M in hexanes, 1.74 mL, 2.78 mmol, 2.5 equiv), and the resulting mixture was stirred at 0 °C for 30 min and then cooled to -78 °C. A solution of Weinreb's amide **S-1**⁵ (250 mg, 1.12 mmol, 1.0 equiv) in THF (5 mL) was subsequently added, and the mixture was stirred at -78 °C for 75 min. The resulting mixture was then quenched with sat. aq. NH₄Cl (20 mL), the biphasic mixture was extracted with EtOAc (3 × 15 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 17:3) gave furyl ketone **S-2** (547 mg, 1.10 mmol, 98% yield) as a yellow oil. **S-2**: *R*_f = 0.20 (silica gel, hexanes:EtOAc 9:1); IR (film) ν_{max} 3070, 2930, 2858, 1674, 1588, 1520, 1472, 1428, 1364, 1200, 1111, 1026, 1015, 823, 737, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.79–7.68 (m, 4 H), 7.45–7.31 (m, 11 H), 7.14 (d, *J* = 3.6 Hz, 1 H), 6.36 (d, *J* = 3.0 Hz, 1 H), 4.71 (s, 2 H), 4.54 (s, 2 H), 3.88 (t, *J* = 6.6 Hz, 2 H), 3.08 (t, *J* = 6.6 Hz, 2 H), 1.08 (s, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 187.0, 159.0, 152.0, 138.1, 135.5, 132.8, 129.9, 128.3, 127.8, 127.63,

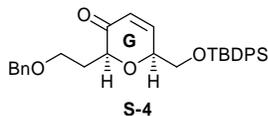
127.57, 118.4, 109.4, 73.2, 65.3, 59.2, 38.7, 26.7, 19.2 ppm; HRMS (ESI-TOF); calcd for C₃₁H₃₄O₄Si [M + H⁺]: 499.2299, found 499.2296.

Secondary alcohol S-3. To a solution of ketone **S-2** (10.4 g, 20.9 mmol, 1.0 equiv) in



CH₂Cl₂:H₂O (1:1, 50 mL) at 25 °C were added HCO₂Na (14.2 g, 209 mmol, 10.0 equiv), *n*-Bu₄NCl (1.74 g, 6.27 mmol, 0.3 equiv) and cat. *ent*-**13** (262 mg, 0.42 mmol, 0.02 equiv), and the biphasic mixture was stirred vigorously at 25 °C for 24 h. The mixture was then diluted with H₂O (150 mL), extracted with CH₂Cl₂ (3 × 50 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 7:3) provided secondary alcohol **S-3** [10.5 g, 20.9 mmol, quant. yield, ≥95% *ee* (based on ¹H NMR spectroscopic analysis of the corresponding Naproxen[®] ester)] as a pale yellow oil. **S-2**: *R*_f = 0.31 (silica gel, hexanes:EtOAc 4:1); [α]_D³² = –10.1 (CH₂Cl₂, *c* = 0.88); IR (film) *v*_{max} 3428, 3070, 2930, 2858, 1472, 1454, 1427, 1362, 1110, 1073, 1016, 941, 823, 791, 738, 700 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ = 7.70–7.68 (m, 4 H), 7.44–7.28 (m, 11 H), 6.15 (d, *J* = 3.0 Hz, 1 H), 6.08 (d, *J* = 3.0 Hz, 1 H), 4.87 (q, *J* = 5.5 Hz, 1 H), 4.63 (s, 2 H), 4.53 (d, *J* = 7.0 Hz, 1 H), 4.51 (d, *J* = 7.0 Hz, 1 H), 3.71–3.68 (m, 1 H), 3.66–3.61 (m, 1 H), 2.91 (d, *J* = 4.5 Hz, 1 H), 2.12 (q, *J* = 5.5 Hz, 2 H), 1.05 (s, 9 H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ = 155.9, 153.3, 137.9, 135.6, 133.4, 129.7, 128.4, 127.73, 127.67, 127.63, 107.9, 106.3, 73.3, 68.0, 66.9, 58.9, 35.1, 26.8, 19.2 ppm; HRMS (ESI-TOF); calcd for C₃₁H₃₆O₄Si [M + Na⁺]: 523.2275, found 523.2280.

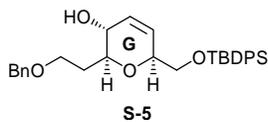
G Ring enone S-4. To a stirred solution of secondary alcohol **S-3** (1.50 g, 3.00 mmol 1.0 equiv)



in CH₂Cl₂ (40 mL) at 25 °C was added dry *m*-CPBA (671 mg, 3.89 mmol, 1.3 equiv), and the reaction mixture was stirred at 25 °C for 1.5 h. The reaction mixture was then quenched with Me₂S (290 μL, 3.89 mmol, 1.3 equiv) followed by sat. aq. NaHCO₃ (75 mL), the biphasic mixture was extracted with CH₂Cl₂ (3 × 30 mL), and the combined organic layers were washed with sat. aq. NaHCO₃ (50 mL) and brine (50 mL), and then dried (MgSO₄) and concentrated. The resulting hemiketal was taken on to the next step

without further purification. To a stirred solution of the crude hemiketal in CH₂Cl₂ (30 mL) at –78 °C were added Et₃SiH (958 μL, 6.0 mmol, 2 equiv) and BF₃•OEt₂ (942 μL, 7.5 mmol, 2.5 equiv), and the resulting mixture was warmed to –45 °C and stirred for 2.5 h. The reaction mixture was then quenched with sat. aq. NaHCO₃ (50 mL), the biphasic mixture was extracted with CH₂Cl₂ (3 × 25 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 17:3) gave G ring enone **S-4** (1.19 g, 2.38 mmol, 79% yield) as a pale yellow oil. **S-4**: *R*_f = 0.35 (silica gel, hexanes:EtOAc 17:3); [α]_D³² = –50.1 (CH₂Cl₂, *c* = 1.20); IR (film) *v*_{max} 3070, 2930, 2857, 1693, 1472, 1428, 1390, 1361, 1315, 1202, 1112, 823, 739, 701 cm^{–1}; ¹H NMR (600 MHz, CDCl₃): δ = 7.69–7.67 (m, 4 H), 7.45–7.38 (m, 6 H), 7.31–7.24 (m, 5 H), 7.18 (d, *J* = 10.2 Hz, 1 H), 6.17 (dd, *J* = 10.2, 2.4 Hz, 1 H), 4.51 (d, *J* = 12.0 Hz, 1 H), 4.46 (d, *J* = 12.0 Hz, 1 H), 4.43 (t, *J* = 6.0 Hz, 1 H), 4.18 (dt, *J* = 8.4, 1.8 Hz, 1 H), 3.88 (dd, *J* = 10.2, 6.0 Hz, 1 H), 3.71 (dd, *J* = 11.4, 6.0 Hz, 1 H), 3.66–3.59 (m, 2 H), 2.42–2.36 (m, 1 H), 1.88–1.82 (m, 1 H), 1.08 (m, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 196.5, 148.9, 138.5, 135.6, 135.5, 133.1, 133.0, 129.84, 129.83, 128.3, 127.75, 127.72, 127.6, 127.5, 127.4, 77.1, 74.7, 72.7, 65.7, 65.2, 30.0, 26.8, 19.3 ppm; HRMS (ESI-TOF); calcd for C₃₁H₃₆O₄Si [M + H⁺]: 501.2455, found 501.2456.

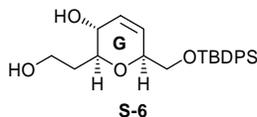
G Ring allylic alcohol S-5. To a stirred solution of G ring enone **S-4** (1.48 g, 2.96 mmol, 1.0



equiv) in MeOH:CH₂Cl₂ (1:1, 6 mL) at –10 °C were sequentially added CeCl₃•7H₂O (551 mg, 1.48 mmol, 0.5 equiv) and NaBH₄ (112 mg, 2.96 mmol, 1.0 equiv), and the reaction mixture was stirred at –10 °C for 10 min. The mixture was then quenched with sat. aq. NH₄Cl (10 mL), and the biphasic mixture was acidified to pH = 5 with 1.0 M aq. HCl and then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with sat. aq. NaHCO₃ (15 mL) and brine (15 mL), and then dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) gave G ring allylic alcohol **S-5** (1.47 g, 2.92 mmol, 99% yield) as a colorless oil. **S-5**: *R*_f = 0.36 (silica gel, hexanes:EtOAc 4:1); [α]_D³² = –50.0 (CHCl₃, *c* = 1.00); IR (film) *v*_{max} 3410, 2930, 2858, 1472,

1428, 1362, 1216, 1112, 823, 754, 701 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.74–7.62 (m, 4 H), 7.47–7.28 (m, 11 H), 5.88 (d, J = 10.4 Hz, 1 H), 5.84 (d, J = 10.4 Hz, 1 H), 4.53 (t, J = 8.4 Hz, 2 H), 4.22 (dd, J = 2.4, 1.2 Hz, 1 H), 4.02–3.91 (m, 1 H), 3.78–3.51 (m, 4 H), 3.34 (dd, J = 7.8, 3.6 Hz, 2 H), 2.08 (ddd, J = 14.4, 8.4, 4.2 Hz, 1 H), 1.94–1.85 (m, 1 H), 1.06 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): δ = 137.9, 136.0, 133.96, 133.94, 130.2, 130.0, 128.87, 128.85, 128.24, 128.20, 127.96, 127.96, 127.95, 78.2, 77.6, 77.4, 77.2, 75.8, 73.6, 68.6, 67.9, 66.7, 34.8, 27.2, 19.7 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{31}\text{H}_{38}\text{O}_4\text{Si}$ [$\text{M} + \text{Na}^+$]: 525.2431, found 525.2436.

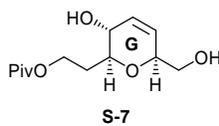
G Ring diol S-6. To a stirred solution of G ring allylic alcohol **S-5** (12.0 g, 23.8 mmol, 1.0



equiv) in THF (170 mL) at -78 $^\circ\text{C}$ was added LiDBB (1.0 M in THF, 47.6 mL, 47.6 mmol, 2.0 equiv), and the reaction mixture was warmed to -50

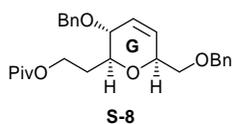
$^\circ\text{C}$ and stirred for 2.5 h. The reaction mixture was then quenched with sat. aq NH_4Cl (200 mL), the biphasic mixture was extracted with EtOAc (3×100 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 4:1 to 1:4) gave G ring diol **S-6** (9.4 g, 22.7 mmol, 96%) as a colorless oil. **S-6**: R_f = 0.36 (silica gel, hexanes:EtOAc 1:3); $[\alpha]_D^{32} = -19.8$ (CHCl_3 , c = 1.00); IR (film) ν_{max} 3341, 3071, 2929, 2857, 1589, 1472, 1427, 1390, 1361, 1262, 1183, 1111, 1063, 939, 823, 739, 701 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.67 (ddd, J = 5.4, 2.4, 1.2 Hz, 4 H), 7.46–7.32 (m, 6 H), 5.83 (d, J = 1.2 Hz, 2 H), 4.27 (dd, J = 3.6, 2.4 Hz, 1 H), 4.05–3.94 (m, 1 H), 3.94–3.79 (m, 2 H), 3.68 (ddd, J = 10.4, 6.6, 1.2 Hz, 1 H), 3.58 (ddd, J = 10.4, 5.4, 1.2 Hz, 1 H), 3.44 (d, J = 4.2 Hz, 1 H), 2.12–2.02 (m, 1 H), 1.92–1.83 (m, 1 H), 1.05 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): δ = 136.0, 130.2, 130.06, 130.05, 129.0, 128.0, 80.1, 77.6, 77.4, 77.2, 75.8, 68.3, 66.61, 61.62, 35.6, 27.1, 19.6 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{24}\text{H}_{32}\text{O}_4\text{Si}$ [$\text{M} + \text{Na}^+$]: 435.1962, found 435.1960.

G Ring pivaloate S-7. To a stirred solution of G ring diol **S-6** (2.0 g, 4.85 mmol, 1.0 equiv) in CH_2Cl_2 (30 mL) at 0 $^\circ\text{C}$ were added 2,4,6-collidine (2.15 mL, 19.0 mmol, 4.0 equiv) and PivCl (1.41 mL, 12.0 mmol, 2.5 equiv), and the resulting mixture was stirred at 0 $^\circ\text{C}$ for 40 h. The



mixture was then quenched with sat. aq. NaHCO₃ (50 mL), the resulting biphasic mixture was extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with sat. aq. CuSO₄ (2 × 30 mL), H₂O (50 mL), and brine (50 mL), and then dried (MgSO₄) and concentrated. The resulting crude primary pivaloate was carried on to the next step without further purification. To a solution of crude pivaloate in THF (75 mL) at 25 °C was added TBAF (1.0 M in THF, 19.0 mL, 19.0 mmol, 4.0 equiv), and the reaction mixture was stirred at 25 °C for 1 h. The mixture was then quenched with sat. aq. NH₄Cl (75 mL), the resulting biphasic mixture was extracted with EtOAc (3 × 40 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 1:3) gave pivaloate G ring **S-7** (990 mg, 3.83 mmol, 79% over the two steps) as a colorless oil. **S-7**: *R*_f = 0.21 (silica gel, hexanes:EtOAc 2:3); [α]_D³² = -64.0 (CHCl₃, *c* = 1.00); IR (film) *v*_{max} 3311, 2960, 1728, 1480, 1428, 1286, 1162, 1112, 757, 702 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 5.89 (d, *J* = 10.2 Hz, 1 H), 5.72 (d, *J* = 10.2 Hz, 1 H), 4.33–4.18 (m, 3 H), 3.98 (s, 1 H), 3.69 (d, *J* = 4.2 Hz, 1 H), 3.57–3.49 (m, 1 H), 3.40–3.33 (m, 1 H), 2.30–2.19 (m, 1 H), 1.99 (t, *J* = 5.4 Hz, 1 H), 1.88–1.79 (m, 1 H), 1.75 (d, *J* = 7.2 Hz, 1 H), 1.65 (s, 1 H), 1.20 (s, 9 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 179.0, 131.6, 128.5, 77.6, 77.4, 77.2, 76.5, 75.9, 68.1, 65.5, 61.3, 39.1, 32.2, 27.6 ppm; HRMS (ESI-TOF); calcd for C₁₃H₂₂O₅ [M + Na⁺]: 281.1359, found 281.1359.

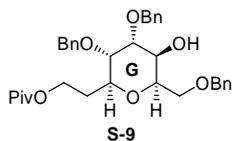
G Ring bis-benzyl ether S-8. To a stirred solution of pivaloate **S-7** (600 mg, 2.55 mmol, 1.0 equiv) in cyclohexane:CH₂Cl₂ (2:1, 75 mL) at 0 °C were added



BnOC(NH)CCl₃ (5.15 g, 20.4 mmol, 8.0 equiv) and TfOH (45 μL, 0.51 mmol, 0.2 equiv), and the resulting mixture was warmed to 25 °C and stirred for 1.5 h. The mixture was then filtered through a cotton plug and subsequently quenched with NaHCO₃ (100 mL), the biphasic mixture was extracted with Et₂O (3 × 50 mL), and the combined organic layers were washed with brine (75 mL), dried (MgSO₄), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 19:1 to 17:3) provided G ring bis-benzyl ether **S-8**

(1.12 g, 2.55 mmol, quant. yield) as a colorless oil. **S-8**: $R_f = 0.27$ (silica gel, hexanes:EtOAc 9:1); $[\alpha]_D^{32} = -64.0$ (CHCl_3 , $c = 1.00$); IR (film) ν_{max} 2959, 1726, 1480, 1428, 1364, 1283, 1160, 1112, 1069, 723 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.44\text{--}7.32$ (m, 10 H), 6.00 (d, $J = 10.2$ Hz, 1 H), 5.85 (d, $J = 10.2$ Hz, 1 H), 4.67 (d, $J = 11.4$ Hz, 1 H), 4.64–4.49 (m, 3 H), 4.32–4.16 (m, 3 H), 3.86–3.78 (m, 1 H), 3.61–3.40 (m, 3 H), 1.29–1.14 (m, 11 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.8, 138.5, 138.4, 129.7, 128.8, 128.7, 128.3, 128.2, 128.1, 128.0, 127.6, 77.6, 77.4, 77.2, 75.0, 74.8, 74.4, 73.8, 72.6, 71.3, 61.4, 39.1, 32.2, 30.7, 27.6$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{27}\text{H}_{34}\text{O}_5$ $[\text{M} + \text{Na}^+]$: 461.2304, found 461.2307.

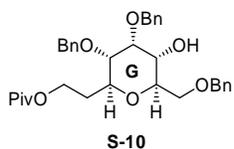
G Ring secondary alcohol S-9. To a stirred solution of G ring bis-benzyl ether **S-8** (804 mg, 1.77 mmol, 1.0 equiv) in CH_2Cl_2 (50 mL) at 25 °C was added *m*-CPBA (70%, 2.51 g, 10.2 mmol, 4.0 equiv), and the reaction mixture was stirred at 25 °C for 36 h. The reaction mixture was then quenched with Me_2S (775 μL ,



10.2 mmol, 4.0 equiv) followed by sat. aq. NaHCO_3 (75 mL), the biphasic mixture was extracted with CH_2Cl_2 (3×30 mL), and the combined organic layers were washed with sat. aq. NaHCO_3 (50 mL) and brine (50 mL), and then dried (MgSO_4) and concentrated. The residue was filtered through a short plug of silica gel, eluting with hexanes:EtOAc (4:1) to provide 834 mg of the corresponding epoxide as an inseparable ca. 4:1 mix of diastereomers, which was taken on to the next step without further purification. To a stirred solution of the partially purified epoxide obtained above (834 mg, 1.84 mmol, 1.0 equiv) in CH_2Cl_2 (35 mL) at 25 °C was added BnOH (956 μL , 9.2 mmol, 5.0 equiv) followed by $\text{BF}_3 \cdot \text{OEt}_2$ (231 μL , 1.84 mmol, 1.0 equiv), and the reaction mixture was stirred at 25 °C for 6 h. The resulting mixture was then quenched with sat. aq. NaHCO_3 (50 mL), the biphasic mixture was extracted with CH_2Cl_2 (3×25 mL), and the combined organic layers were dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 9:1 to 3:2) gave G ring secondary alcohol **S-9** (610 mg, 1.09 mmol, 42% yield over the two steps) as a colorless oil. **S-9**: $R_f = 0.10$ (silica gel, hexanes:EtOAc 4:1); $[\alpha]_D^{32} = -44.7$ (CH_2Cl_2 , $c = 1.07$); IR (film) ν_{max} 3482, 3030, 2969, 2906, 2871, 1724, 1496,

1479, 1454, 1365, 1285, 1207, 1156, 1100, 1073, 1028, 736, 697 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ = 7.31–7.20 (m, 15 H), 4.67 (d, J = 12.0 Hz, 1 H), 4.57 (d, J = 12.0 Hz, 2 H), 4.52 (d, J = 12.0 Hz, 1 H), 4.45 (d, J = 12.0 Hz, 1 H), 4.39 (d, J = 11.4 Hz, 1 H), 4.14 (dd, J = 7.8, 5.4 Hz, 2 H), 3.95 (d, J = 3.6 Hz, 1 H), 3.88 (t, J = 3.6 Hz, 1 H), 3.86–3.82 (m, 2 H), 3.69 (dd, J = 10.2, 4.2 Hz, 1 H), 3.64 (dd, J = 10.2, 3.6 Hz, 1 H), 3.57 (dd, J = 9.6, 3.0 Hz, 1 H), 2.18 (ddt, J = 13.8, 7.8, 3.0 Hz, 1 H), 1.66 (ddt, J = 13.8, 11.4, 5.4 Hz, 1 H), 1.13 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): δ = 178.6, 138.5, 138.0, 137.4, 128.5, 128.4, 128.3, 127.9, 127.83, 127.77, 127.71, 127.63, 127.60, 76.5, 73.9, 73.7, 72.9, 72.7, 72.5, 71.4, 71.3, 70.5, 61.2, 38.7, 31.1, 27.2 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{34}\text{H}_{42}\text{O}_7$ [$\text{M} + \text{H}^+$]: 563.3003, found 563.3002.

G Ring inverted secondary alcohol S-10. To a stirred solution of G ring secondary alcohol **S-9**

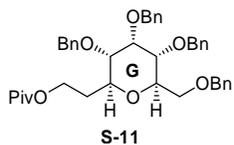


(509 mg, 0.91 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) was added DMP (575 mg, 1.34 mmol, 1.5 equiv), and the reaction mixture was stirred at 25 °C for 45 min. The resulting mixture was then quenched with sat. aq. NaHCO_3 :sat.

aq. $\text{Na}_2\text{S}_2\text{O}_3$ (1:1, 30 mL), and the biphasic mixture was stirred vigorously for 15 min. The mixture was extracted with CH_2Cl_2 (3×15 mL), and the combined organic layers were washed with sat. aq. NaHCO_3 (20 mL) and brine (20 mL), and then dried (MgSO_4) and concentrated. The crude ketone was taken on to the next step without further purification. To a solution of the crude ketone obtained above in MeOH (20 mL) at -78 °C was added NaBH_4 (171 mg, 4.54 mmol, 5.0 equiv), and the reaction mixture was warmed to -10 °C and stirred for 15 min. The resulting mixture was then quenched with sat. aq. NH_4Cl (50 mL), the biphasic mixture was extracted with EtOAc (3×25 mL), and the combined organic layers were washed with brine (40 mL), dried (MgSO_4), and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 3:1) provided G ring inverted secondary alcohol **S-10** (473 mg, 0.85 mmol, 93% yield over the two steps) as a colorless oil. **S-10**: R_f = 0.22 (silica gel, hexanes:EtOAc 3:1); $[\alpha]_D^{32} = -36.3$ (CH_2Cl_2 , c = 0.49); IR (film) ν_{max} 3480, 3030, 2959, 2906, 2871, 1724, 1479, 1454, 1365, 1284, 1160, 1101, 1057, 1028, 735, 697 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ =

7.37–7.27 (m, 15 H), 5.02 (d, $J = 11.4$ Hz, 1 H), 4.70 (d, $J = 12.0$ Hz, 1 H), 4.60 (d, $J = 11.4$ Hz, 1 H), 4.57–4.54 (m, 3 H), 4.25–4.21 (m, 1 H), 4.19 (dd, $J = 8.4, 7.2$ Hz, 1 H), 4.15 (t, $J = 2.4$ Hz, 1 H), 3.86 (dt, $J = 9.6, 2.4$ Hz, 1 H), 3.70 (dd, $J = 13.2, 4.8$ Hz, 1 H), 3.60 (dd, $J = 13.2, 4.2$ Hz, 2 H), 3.56 (t, $J = 6.6$ Hz, 1 H), 3.22 (dd, $J = 9.6, 1.8$ Hz, 1 H), 2.43 (d, $J = 9.6$ Hz, 1 H), 2.21 (ddt, $J = 16.2, 7.8, 2.4$ Hz, 1 H), 1.68–1.62 (m, 1 H), 1.19 (s, 9 H) ppm; ^{13}C NMR (150 MHz, CDCl_3): $\delta = 178.5, 138.5, 138.2, 137.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.7, 127.6, 127.5, 80.1, 75.8, 75.6, 74.7, 73.5, 71.8, 71.2, 70.0, 68.5, 61.2, 38.7, 30.8, 27.2$ ppm; HRMS (ESI-TOF); calcd for $\text{C}_{34}\text{H}_{42}\text{O}_7$ [$\text{M} + \text{H}^+$]: 563.3003, found 563.3005.

G Ring tetra-benzyl ether S-11. To a vigorously stirred solution of G ring inverted secondary

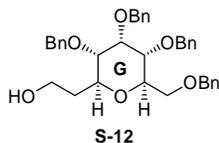


alcohol **S-10** (405 mg, 0.72 mmol, 1.0 equiv) in PhMe (10 mL) at 25 °C were added BnBr (855 μL , 7.2 mmol, 10.0 equiv), $n\text{-Bu}_4\text{NI}$ (133 mg, 0.36 mmol, 0.5 equiv) and 25% aq. NaOH (10 mL), and the resulting biphasic mixture

was vigorously stirred at 25 °C for 20 h. The mixture was then diluted with H_2O (20 mL) and extracted with EtOAc (3×15 mL), and the combined organic layers were washed with H_2O (15 mL) and brine (15 mL), and then dried (MgSO_4) and concentrated. Flash column chromatography (silica gel, 19:1 to 17:3) gave G ring tetra-benzyl ether **S-11** (434 mg, 0.67 mmol, 92% yield) as a colorless oil. **S-11**: $R_f = 0.27$ (silica gel, hexanes:EtOAc 17:3); $[\alpha]_D^{32} = -6.2$ (CH_2Cl_2 , $c = 0.75$); IR (film) ν_{max} 3030, 2959, 2900, 2871, 1725, 1496, 1479, 1454, 1364, 1284, 1207, 1160, 1099, 1073, 1028, 735, 697 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): $\delta = 7.36\text{--}7.30$ (m, 14 H), 7.27–7.23 (m, 6 H), 4.81 (d, $J = 12.0$ Hz, 1 H), 4.78 (d, $J = 11.5$ Hz, 1 H), 4.62 (d, $J = 12.5$ Hz, 1 H), 4.58 (d, $J = 12.0$ Hz, 1 H), 4.56 (d, $J = 11.5$ Hz, 1 H), 4.51 (d, $J = 12.0$ Hz, 1 H), 4.46 (d, $J = 11.5$ Hz, 1 H), 4.41 (d, $J = 12.0$ Hz, 1 H), 4.25–4.15 (m, 3 H), 3.95–3.89 (m, 2 H), 3.71 (d, $J = 2.5$ Hz, 2 H), 3.51 (dd, $J = 9.5, 2.0$ Hz, 1 H), 3.12 (dd, $J = 9.5, 2.0$ Hz, 1 H), 2.20 (ddt, $J = 16.5, 8.0, 2.0$ Hz, 1 H), 1.69–1.62 (m, 1 H), 1.18 (s, 9 H) ppm; ^{13}C NMR (125 MHz, CDCl_3): $\delta = 178.5, 139.1, 138.4, 138.1, 137.8, 128.4, 128.35, 128.27, 128.1, 127.81, 127.80, 127.74, 127.67, 127.60, 127.5, 127.2, 79.6, 76.1, 74.3, 73.9, 73.5, 72.1, 71.6, 71.4, 71.2, 69.2,$

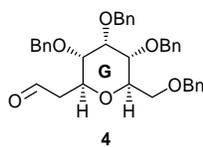
61.4, 38.7, 30.9, 27.2 ppm; HRMS (ESI-TOF); calcd for C₄₁H₄₈O₇ [M + H⁺]: 653.3473, found 653.3471.

G Ring primary alcohol S-12. To a stirred solution of G ring tetra-benzyl ether **S-11** (423 mg, 0.65 mmol, 1.0 equiv) in CH₂Cl₂ (10 mL) at -78 °C was added Dibal-H (1.0 M in CH₂Cl₂, 2.59 mL, 2.59 mmol, 4.0 equiv), and the reaction mixture was stirred at -78 °C for 1.5 h. The resulting mixture was then diluted with EtOAc



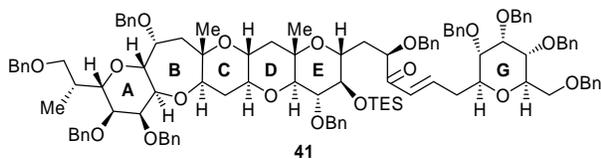
(10 mL) and quenched with sat. aq. Rochelle's salt (20 mL), and the biphasic mixture was stirred vigorously at 25 °C for 16 h. The mixture was then extracted with EtOAc (3 × 15 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 1:1) gave G ring primary alcohol **S-12** (369 mg, 0.65 mmol, quant. yield) as a colorless oil. **S-11**: *R*_f = 0.26 (silica gel, hexanes:EtOAc 3:2); [α]_D³² = -2.3 (CH₂Cl₂, *c* = 0.94); IR (film) ν_{max} 3493, 3030, 2872, 1496, 1454, 1364, 1332, 1307, 1207, 1089, 1072, 1027, 736, 697 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ = 7.37–7.31 (m, 12 H), 7.29–7.25 (m, 8 H), 4.84 (d, *J* = 12.0 Hz, 1 H), 4.80 (d, *J* = 12.0 Hz, 1 H), 4.58–4.55 (m, 3 H), 4.50 (d, *J* = 12.6 Hz, 1 H), 4.44 (d, *J* = 11.4 Hz, 1 H), 4.39 (d, *J* = 12.0 Hz, 1 H), 4.20 (t, *J* = 1.8 Hz, 1 H), 4.06 (dt, *J* = 9.0, 3.0 Hz, 1 H), 4.03 (ddd, *J* = 9.6, 4.8, 1.8 Hz, 1 H), 3.84–3.72 (m, 2 H), 3.69 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.61 (dd, *J* = 10.2, 4.8 Hz, 1 H), 3.45 (dd, *J* = 10.2, 2.4 Hz, 1 H), 3.18 (dd, *J* = 9.6, 2.4 Hz, 1 H), 2.90 (bs, 1 H), 2.08 (dq, *J* = 14.4, 3.0 Hz, 1 H), 1.69 (ddt, *J* = 14.4, 8.4, 3.6 Hz, 1 H) ppm; ¹³C NMR (150 MHz, CDCl₃): δ = 138.9, 138.1, 137.9, 137.6, 128.5, 128.41, 128.36, 128.2, 127.93, 127.90, 127.80, 127.77, 127.72, 127.6, 127.4, 79.0, 76.2, 75.5, 74.0, 73.8, 73.5, 71.7, 71.6, 71.2, 69.4, 61.8, 36.6 ppm; HRMS (ESI-TOF); calcd for C₃₆H₄₀O₆ [M + H⁺]: 569.2898, found 569.2896.

G Ring aldehyde 4. To a stirred solution of G ring primary alcohol **S-12** (64 mg, 0.113 mmol, 1.0 equiv) in CH₂Cl₂:MeCN (9:1, 5 mL) at 25 °C were added flame-dried 4 Å MS (85 mg), NMO (26 mg, 0.225 mmol, 2.0 equiv), and TPAP (4 mg, 0.011 mmol, 0.1 equiv), and the reaction mixture was stirred at 25 °C for 30 min.



The resulting mixture was then diluted in hexanes (7 mL), and Celite™ (150 mg) was added. This homogenous mixture was directly subjected to flash column chromatography (silica gel, hexanes:EtOAc 7:3) to provided G ring aldehyde **5** (53 mg, 0.094 mmol, 83% yield) as a colorless oil. **5**: $R_f = 0.34$ (silica gel, hexanes:EtOAc 3:1); $[\alpha]_D^{32} = +1.2$ (CH₂Cl₂, $c = 1.00$); IR (film) ν_{\max} 3030, 2869, 1725, 1496, 1454, 1364, 1314, 1206, 1091, 1027, 735, 697 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): $\delta = 9.74$ (t, $J = 2.4$ Hz, 1 H), 7.37–7.30 (m, 12 H), 7.28–7.25 (m, 8 H), 4.83 (d, $J = 12.0$ Hz, 1 H), 4.79 (d, $J = 12.0$ Hz, 1 H), 4.59 (d, $J = 12.6$ Hz, 1 H), 4.56 (d, $J = 10.8$ Hz, 1 H), 4.54 (d, $J = 11.4$ Hz, 1 H), 4.51 (d, $J = 12.6$ Hz, 1 H), 4.47 (d, $J = 12.0$ Hz, 1 H), 4.40 (sext, $J = 4.2$ Hz, 1 H), 4.34 (d, $J = 12.0$ Hz, 1 H), 4.20 (t, $J = 1.8$ Hz, 1 H), 4.02 (dt, $J = 9.6, 2.4$ Hz, 1 H), 3.69 (d, $J = 2.4$ Hz, 2 H), 3.51 (dd, $J = 10.0, 2.4$ Hz, 1 H), 3.16 (dd, $J = 9.6, 1.8$ Hz, 1 H), 2.75 (ddd, $J = 16.2, 4.8, 2.4$ Hz, 1 H), 2.49 (ddd, $J = 16.2, 8.4, 2.0$ Hz, 1 H) ppm; ¹³C NMR (150 MHz, CDCl₃): $\delta = 201.2, 138.9, 138.2, 137.9, 137.2, 128.5, 128.4, 128.3, 128.2, 128.0, 127.79, 127.77, 127.76, 127.72, 127.5, 127.4, 78.9, 75.9, 74.4, 74.0, 73.5, 71.74, 71.68, 71.0, 70.1, 69.0, 46.2$ ppm; HRMS (ESI-TOF); calcd for C₃₆H₃₈O₆ [M + H⁺]: 567.2741, found 567.2731.

ABCDEG Enone 41. To a stirred solution of ABCDE ketophosphonate **6** (75 mg, 0.056 mmol,

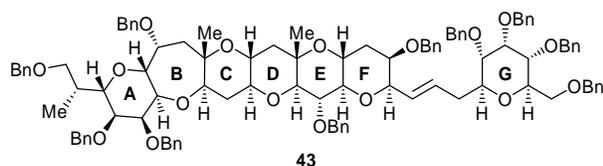


1.0 equiv) in MeCN (1 mL) at 25 °C were added flame-dried LiCl (7 mg, 0.168 mmol, 3.0 equiv) and *i*-Pr₂NEt (29 μ L, 0.168 mmol, 3.0 equiv)

followed by dropwise addition of a solution of aldehyde **4** (44 mg, 0.078 mmol, 1.4 equiv) in 2 mL MeCN *via* cannula, and the reaction mixture was stirred at the same temperature for 72 h. The resulting mixture was then quenched with sat. aq. NH₄Cl (4 mL), the biphasic mixture was extracted with Et₂O (3 \times 3 mL), and the combined organic extracts were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 17:3 to 2:3) yielded ABCDEG enone **41** (91 mg, 0.051 mmol, 91% yield) as a white foam along with recovered ABCDE ketophosphonate **6** (3 mg, 0.002 mmol, 4% yield). **41**: $R_f = 0.33$ (silica gel,

hexanes:EtOAc 4:1); $[\alpha]_D^{32} = +11.8$ (C_6H_6 , $c = 0.80$); IR (film) ν_{max} 3027, 2951, 2875, 1691, 1623, 1496, 1454, 1345, 1203, 1083, 1028, 734, 697 cm^{-1} ; 1H NMR (600 MHz, C_6D_6): $\delta = 7.56$ – 7.48 (m, 5 H), 7.45 – 7.37 (m, 6 H), 7.30 – 7.25 (m, 10 H), 7.24 – 7.16 (m, 13 H), 7.13 – 7.02 (m, 17 H), 6.75 (d, $J = 16.2$ Hz, 1 H), 5.26 (d, $J = 10.8$ Hz, 1 H), 4.95 (d, $J = 11.4$ Hz, 1 H), 4.86 (d, $J = 12.0$ Hz, 1 H), 4.81 (d, $J = 11.4$ Hz, 1 H), 4.79 (d, $J = 11.4$ Hz, 1 H), 4.71 (d, $J = 11.4$ Hz, 1 H), 4.61 – 4.54 (m, 3 H), 4.53 – 4.47 (m, 3 H), 4.43 – 4.32 (m, 8 H), 4.29 (d, $J = 12.0$ Hz, 1 H), 4.27 (dd, $J = 9.6, 1.8$ Hz, 1 H), 4.17 – 4.13 (m, 4 H), 4.12 – 4.08 (m, 3 H), 3.78 – 3.75 (m, 3 H), 3.68 – 3.64 (m, 2 H), 3.62 – 3.58 (m, 2 H), 3.55 (dd, $J = 9.6, 1.8$ Hz, 1 H), 3.42 (m, 2 H), 3.36 (ddd, $J = 11.4, 7.2, 4.2$ Hz, 1 H), 3.24 (dd, $J = 10.2, 2.4$ Hz, 1 H), 3.16 (d, $J = 10.2$ Hz, 1 H), 2.99 (dd, $J = 9.0, 1.8$ Hz, 1 H), 2.94 (ddd, $J = 12.0, 8.4, 3.6$ Hz, 1 H), 2.72 – 2.67 (m, 1 H), 2.64 – 2.58 (m, 1 H), 2.54 (t, $J = 11.4$ Hz, 1 H), 2.41 – 2.34 (m, 2 H), 2.16 (dt, $J = 11.4, 4.2$ Hz, 1 H), 2.10 (dd, $J = 11.4, 4.8$ Hz, 1 H), 1.94 (ddd, $J = 13.2, 10.2, 3.0$ Hz, 1 H), 1.76 (q, $J = 12.0$ Hz, 1 H), 1.69 (t, $J = 11.4$ Hz, 1 H), 1.60 (dd, $J = 16.2, 4.2$ Hz, 1 H), 1.22 (s, 3 H), 1.16 (s, 3 H), 1.00 (d, $J = 6.6$ Hz, 3 H), 0.99 (t, $J = 8.4$ Hz, 9 H), 0.72 – 0.60 (m, 6 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): $\delta = 200.1, 145.3, 140.2, 140.1, 139.8, 139.7, 139.5, 139.4, 139.0, 138.8, 138.7, 138.6, 128.8, 128.69, 128.68, 128.63, 128.62, 128.60, 128.52, 128.50, 128.48, 128.45, 128.27, 128.26, 128.18, 128.17, 128.14, 128.10, 128.03, 128.02, 127.98, 127.94, 127.84, 127.83, 127.75, 127.7, 127.68, 127.64, 127.58, 127.54, 127.53, 127.49, 127.45, 85.8, 80.9, 80.8, 79.9, 79.7, 76.1, 78.59, 78.57, 77.1, 77.0, 76.9, 76.6, 76.2, 75.71, 75.67, 75.1, 74.9, 74.7, 74.5, 73.7, 73.64, 73.60, 73.5, 73.1, 73.0, 72.9, 72.3, 71.8, 71.2, 70.7, 70.0, 69.8, 69.0, 44.7, 44.6, 36.7, 35.4, 34.1, 33.4, 21.1, 17.4, 10.3, 7.4, 5.8$ ppm; HRMS (ESI-TOF); calcd for $C_{111}H_{130}O_{18}Si$ $[M + H]^+$: 1779.9099, found 1779.9063.

ABCDEFGH Alkene 43. To a stirred solution of ABCDEGH enone **41** (34 mg, 0.019 mmol, 1.0



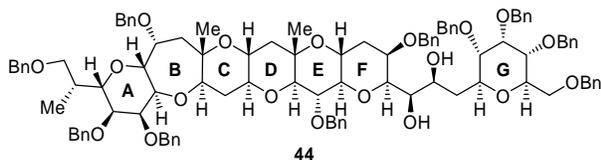
equiv) in MeOH:CH₂Cl₂ (3:1, 3 mL) at 25 °C was added TsOH (11 mg, 0.057 mmol, 3.0 equiv), and the reaction mixture was stirred at

25 °C for 2.5 h. The resulting mixture was then quenched with sat. aq. NaHCO₃ (5 mL), the

biphasic mixture was extracted with EtOAc (3 × 3 mL), and the combined organic layers were dried (MgSO₄) and concentrated. The crude methyl acetal **42** was carried on to the next step without further purification. To a solution of crude acetal **42** in MeCN (2.5 mL) at -40 °C were added Et₃SiH (30 μL, 0.19 mmol, 10.0 equiv) and TMSOTf (12 μL, 0.012 mmol, 5 equiv), and the reaction mixture was warmed to -25 °C and stirred for 30 min. The resulting mixture was quenched with sat. aq. NaHCO₃ (3 mL), the biphasic mixture was extracted with Et₂O (3 × 3 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Flash column chromatography (silica gel, hexanes:EtOAc 4:1) gave ABCDEFG alkene **43** (22 mg, 0.013 mmol, 69% yield over the two steps) as a white foam. **43**: *R*_f = 0.19 (silica gel, hexanes:EtOAc 4:1); [α]_D³² = -7.8 (CH₂Cl₂, *c* = 0.79); IR (film) *v*_{max} 3022, 2923, 2865, 1496, 1454, 1347, 1206, 1084, 1068, 1027, 735, 697 cm⁻¹; ¹H NMR (600 MHz, C₆D₆): δ = 7.61–7.60 (m, 2 H), 7.53–7.52 (m, 2 H), 7.46–7.44 (m, 2 H), 7.40–7.39 (m, 2 H), 7.35–7.23 (m, 14 H), 7.20–7.16 (m, 13 H), 7.14–7.05 (m, 15 H), 6.18 (dt, *J* = 15.0, 6.6 Hz, 1 H), 6.02 (dd, *J* = 15.6, 6.6 Hz, 1 H), 5.13 (d, *J* = 12.0 Hz, 1 H), 5.07 (d, *J* = 12.0 Hz, 1 H), 4.95 (d, *J* = 11.4 Hz, 1 H), 4.86 (d, *J* = 12.0 Hz, 1 H), 4.83 (d, *J* = 12.0 Hz, 1 H), 4.81 (d, *J* = 12.0 Hz, 1 H), 4.57 (d, *J* = 12.0 Hz, 1 H), 4.53 (d, *J* = 12.0 Hz, 1 H), 4.51 (d, *J* = 12.6 Hz, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.43–4.36 (m, 8 H), 4.31 (d, *J* = 11.4 Hz, 1 H), 4.27 (d, *J* = 10.2 Hz, 1 H), 4.24–4.12 (m, 7 H), 3.85–3.78 (m, 5 H), 3.74 (d, *J* = 10.8 Hz, 1 H), 3.65–3.59 (m, 3 H), 3.44 (t, *J* = 8.4 Hz, 1 H), 3.39 (dt, *J* = 10.8, 4.2 Hz, 1 H), 3.35–3.31 (m, 2 H), 3.25 (dd, *J* = 10.2, 1.8 Hz, 1 H), 3.21–3.17 (m, 2 H), 3.05 (ddd, *J* = 12.0, 8.4, 3.6 Hz, 1 H), 2.75 (ddd, *J* = 13.2, 3.6, 1.8 Hz, 1 H), 2.61 (sext, *J* = 7.2 Hz, 1 H), 2.52 (quin, *J* = 7.2 Hz, 1 H), 2.35 (dd, *J* = 9.6, 2.4 Hz, 1 H), 2.32–2.26 (m, 2 H), 2.21 (dd, *J* = 10.8, 4.2 Hz, 1 H), 1.81 (q, *J* = 11.4 Hz, 2 H), 1.59 (dd, *J* = 16.2, 4.2 Hz, 1 H), 1.20 (s, 3 H), 1.13 (s, 3 H), 1.00 (d, *J* = 7.2 Hz, 3 H) ppm; ¹³C NMR (150 MHz, C₆D₆): δ = 140.4, 140.2, 140.0, 139.7, 139.5, 139.4, 139.1, 139.0, 138.9, 138.8, 131.0, 129.2, 128.72, 128.67, 128.58, 128.57, 128.51, 128.47, 128.3, 128.2, 128.14, 128.12, 128.10, 127.98, 127.97, 127.86, 127.85, 127.79, 127.68, 127.64, 127.58, 127.57, 127.51, 127.46, 85.5, 85.0, 81.6, 80.0, 79.9, 78.6, 77.3, 77.2, 76.92, 76.89, 76.8, 76.2, 75.8, 75.5, 75.1, 74.9, 74.8, 74.68, 74.66, 74.63, 73.67, 73.65, 73.5, 73.2, 73.0, 72.8, 72.0,

71.7, 71.5, 70.6, 70.1, 69.1, 65.5, 44.7, 44.6, 35.2, 34.5, 34.2, 33.4, 21.2, 17.7, 10.3 ppm; HRMS (ESI-TOF); calcd for C₁₀₅H₁₁₆O₁₇ [M + Na⁺]: 1671.8104, found 1671.8130.

ABCDEFGH Diol 44. To a stirred solution of ABCDEFGH alkene **43** (23.0 mg, 0.014 mmol, 1.0

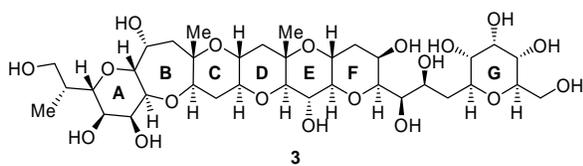


equiv) in acetone/H₂O (4:1, 5 mL) at 25 °C were added OsO₄ (2.5 wt% in *t*-BuOH, 7 μL, 0.0007 mmol, 0.05 equiv) and NMO (5 mg, 0.042

mmol, 3.0 equiv), and the reaction mixture was stirred at 25 °C for 72 h. The resulting mixture was quenched with sat. aq. Na₂SO₃ (5 mL), and the biphasic mixture was stirred vigorously at 25 °C for 30 min. The biphasic mixture was then extracted with EtOAc (3 × 5 mL), and the combined organic layers were dried (MgSO₄) and concentrated. Preparative-plate chromatography (silica gel, hexanes:EtOAc 3:2) gave ABCDEFGH diol **44** (14.3 mg, 0.008 mmol, 61% yield) as a colorless oil, along with its opposite diastereomer (6 mg, 0.004 mmol, 26% yield). **44**: *R*_f = 0.25 (silica gel, hexanes:EtOAc 3:2); [α]_D³² = +7.4 (CH₂Cl₂, *c* = 0.62); IR (film) *v*_{max} 3463, 3029, 2923, 2855, 1496, 1453, 1362, 1346, 1207, 1085, 1067, 1027, 734, 697 cm⁻¹; ¹H NMR (600 MHz, C₆D₆): δ = 7.63–7.61 (m, 2 H), 7.51–7.52 (m, 2 H), 7.41–7.36 (m, 6 H), 7.31–7.24 (m, 12 H), 7.19–7.17 (m, 10 H), 7.13–7.02 (m, 12 H), 5.00 (d, *J* = 11.4 Hz, 1 H), 4.95 (d, *J* = 11.4 Hz, 1 H), 4.94 (d, *J* = 11.4 Hz, 1 H), 4.80 (d, *J* = 11.4 Hz, 1 H), 4.77 (s, 2 H), 4.69 (dd, *J* = 10.2, 3.0 Hz, 1 H), 4.56 (d, *J* = 11.4 Hz, 1 H), 4.53 (d, *J* = 12.0 Hz, 1 H), 4.51 (d, *J* = 11.4 Hz, 1 H), 4.50 (d, *J* = 12.0 Hz, 1 H), 4.48–4.35 (m, 8 H), 4.28 (dd, *J* = 9.6, 1.2 Hz, 1 H), 4.24 (d, *J* = 12.0 Hz, 2 H), 4.19–4.11 (m, 5 H), 4.08 (ddd, *J* = 9.6, 4.2, 1.8 Hz, 1 H), 4.04 (bs, 1 H), 3.90 (bs, 1 H), 3.84 (dd, *J* = 9.6, 1.8 Hz, 1 H), 3.78 (d, *J* = 10.2 Hz, 1 H), 3.74 (t, *J* = 9.0 Hz, 1 H), 3.65–3.59 (m, 4 H), 3.57–3.54 (m, 2 H), 3.44 (dd, *J* = 9.0, 7.2 Hz, 1 H), 3.40 (dt, *J* = 10.8, 4.8 Hz, 1 H), 3.29–3.24 (m, 3 H), 3.15 (dd, *J* = 9.6, 1.8 Hz, 1 H), 3.01 (ddd, *J* = 12.6, 9.6, 3.6 Hz, 1 H), 2.71 (bs, 1 H), 2.61 (dq, *J* = 7.2, 3.0 Hz, 1 H), 2.55 (ddd, *J* = 14.4, 10.2, 3.0 Hz, 1 H), 2.38–2.33 (m, 2 H), 2.24–2.19 (m, 2 H), 1.99 (ddd, *J* = 15.0, 6.0, 3.6 Hz, 1 H), 1.82–1.76 (m, 2 H), 1.59 (dd, *J* = 15.6, 3.0 Hz, 1 H), 1.43 (t, *J* = 12.0 Hz, 1 H), 1.19 (s, 3 H), 1.18 (s, 3 H), 1.00 (d, *J*

= 6.6 Hz, 3 H) ppm; ^{13}C NMR (150 MHz, C_6D_6): δ = 140.3, 140.2, 139.8, 139.7, 139.5, 139.4, 139.0, 139.9, 138.8, 138.7, 128.8, 128.70, 128.67, 128.66, 128.58, 128.51, 128.47, 128.17, 128.14, 128.02, 127.98, 127.83, 127.82, 127.70, 127.69, 127.64, 127.60, 127.58, 127.52, 85.4, 84.8, 80.5, 80.0, 79.4, 79.0, 78.6, 77.4, 77.2, 76.9, 76.4, 76.2, 75.7, 75.5, 74.81, 74.78, 74.6, 74.54, 74.50, 73.9, 73.6, 73.54, 73.50, 73.47, 73.0, 72.9, 72.8, 72.5, 72.3, 71.6, 71.5, 70.6, 69.6, 69.1, 67.9, 66.0, 44.6, 44.5, 35.3, 34.6, 34.2, 33.4, 21.1, 17.6, 10.3 ppm; HRMS (ESI-TOF); calcd for $\text{C}_{105}\text{H}_{118}\text{O}_{19}$ [$\text{M} + \text{H}^+$]: 1683.8340, found 1683.8328.

ABCDEFGF Model system 3. To a stirred solution of ABCDEFG diol **45** (21.3 mg, 0.0126



mmol, 1.0 equiv) in EtOH (2.5 mL) at 25 °C was added 20% $\text{Pd}(\text{OH})_2/\text{C}$ (6 mg, 30% w/w), and the solution was purged with Ar, then H_2 , and then

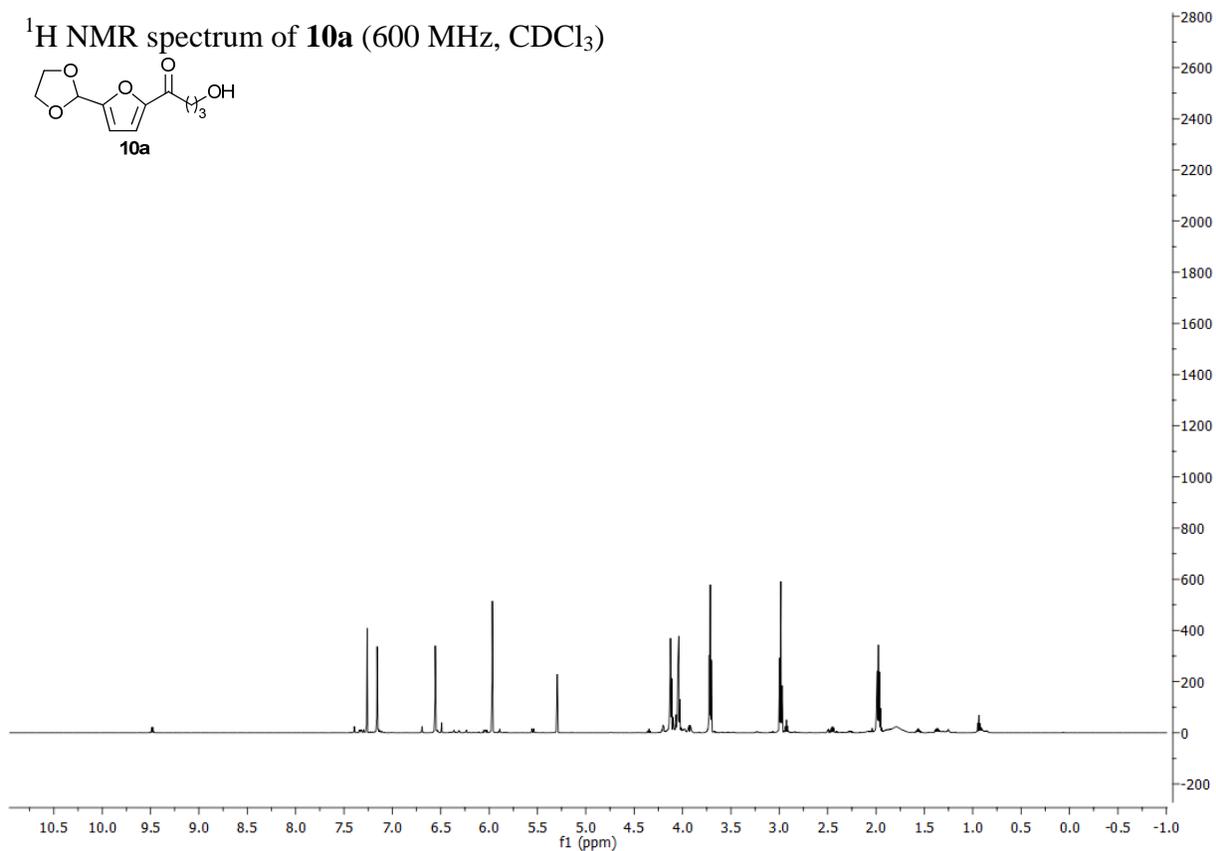
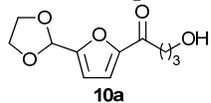
stirred at 25 °C for 6 d under an atmosphere of H_2 (balloon). The reaction mixture was then filtered through a short pad of Celite™, washed with MeOH, and concentrated. Trituration of the resulting residue with EtOAc (3 × 1.5 mL) and removal of the solvent provided pure heptacyclic ABCDEFG model system **3** (9.6 mg, 0.012 mmol, 97% yield) as a white foam. **3**: R_f = 0.00 (silica gel, EtOAc:MeOH 17:3); $[\alpha]_D^{32} = +18.3$ (MeOH, $c = 0.48$); IR (film) ν_{max} 3362, 2919, 1593, 1413, 1384, 1350, 1264, 1079, 1064, 1034 cm^{-1} ; ^1H NMR (600 MHz, $\text{CD}_3\text{OD}:\text{C}_5\text{D}_5\text{N}$ 1:1): δ = 4.52 (d, $J = 9.0$ Hz, 1 H), 4.46–4.44 (m, 2 H), 4.35 (bs, 1 H), 4.27 (bs, 1 H), 4.17–4.11 (m, 3 H), 4.04–3.99 (m, 3 H), 3.88 (d, $J = 9.6$ Hz, 1 H), 3.83–3.80 (m, 2 H), 3.79–3.71 (m, 3 H), 3.68–3.59 (m, 4 H), 3.40–3.38 (m, 2 H), 3.10 (t, $J = 9.6$ Hz, 1 H), 3.06 (d, $J = 9.6$ Hz, 1 H), 3.00 (ddd, $J = 12.0, 8.4, 1.8$ Hz, 1 H), 2.59 (t, $J = 12.0$ Hz, 1 H), 2.30–2.25 (m, 1 H), 2.21–2.14 (m, 3 H), 1.95 (dd, $J = 10.8, 2.4$ Hz, 1 H), 1.90 (dd, $J = 15.6, 2.4$ Hz, 1 H), 1.71 (q, $J = 11.4$ Hz, 1 H), 1.67–1.62 (m, 2 H), 1.49 (t, $J = 11.4$ Hz, 1 H), 1.27 (s, 3 H), 1.17 (s, 3 H), 0.94 (d, $J = 6.6$ Hz, 3 H) ppm; ^{13}C NMR (150 MHz, $\text{CD}_3\text{OD}:\text{C}_5\text{D}_5\text{N}$ 1:1): δ = 86.0, 85.3, 81.0, 80.7, 79.6, 77.2, 76.7, 76.53, 76.49, 75.3, 75.1, 73.5, 73.4, 73.1, 72.8, 72.4, 71.5, 69.72, 69.66, 69.44, 69.42,

67.5, 66.3, 66.2, 65.9, 63.4, 48.3, 44.9, 38.8, 37.8, 36.9, 34.4, 21.6, 17.9, 10.5 ppm; HRMS (ESI-TOF); calcd for C₃₅H₅₈O₁₉ [M + H⁺]: 783.3645, found 783.3649.

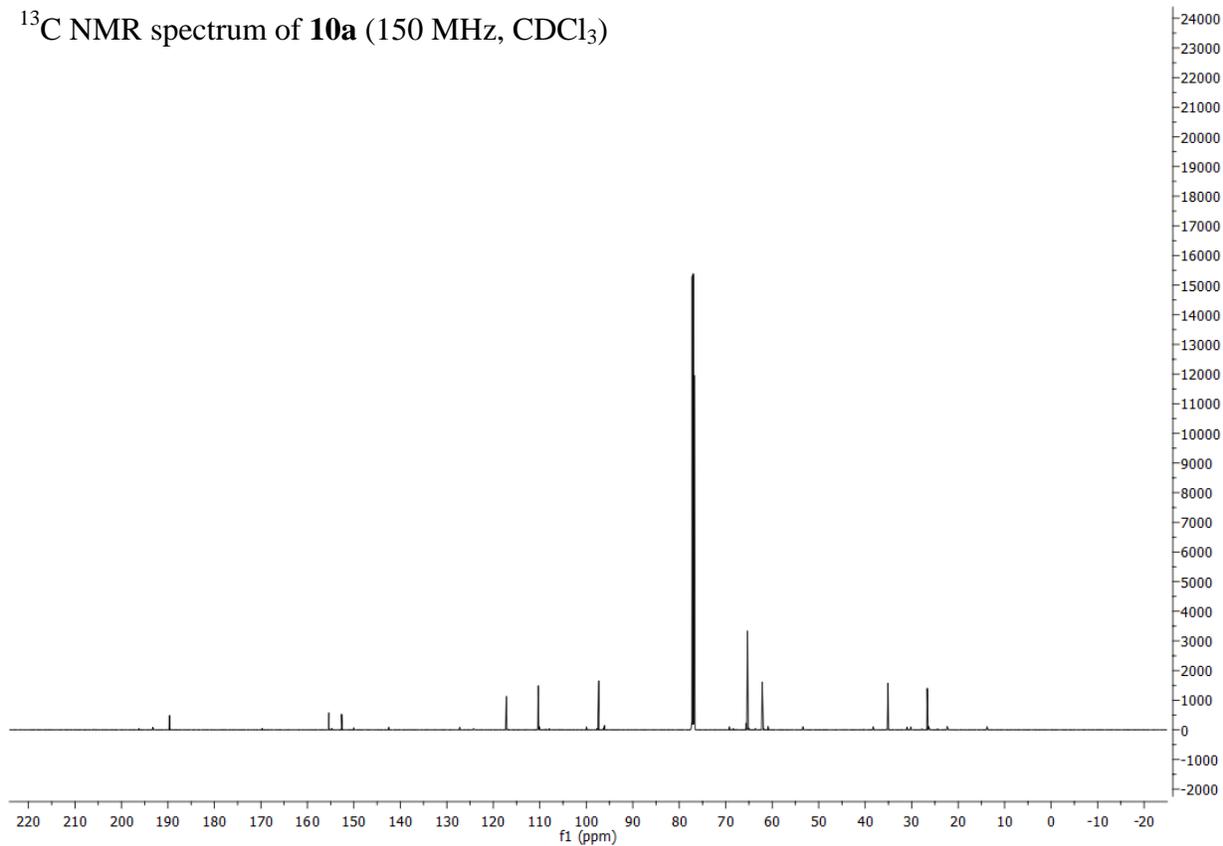
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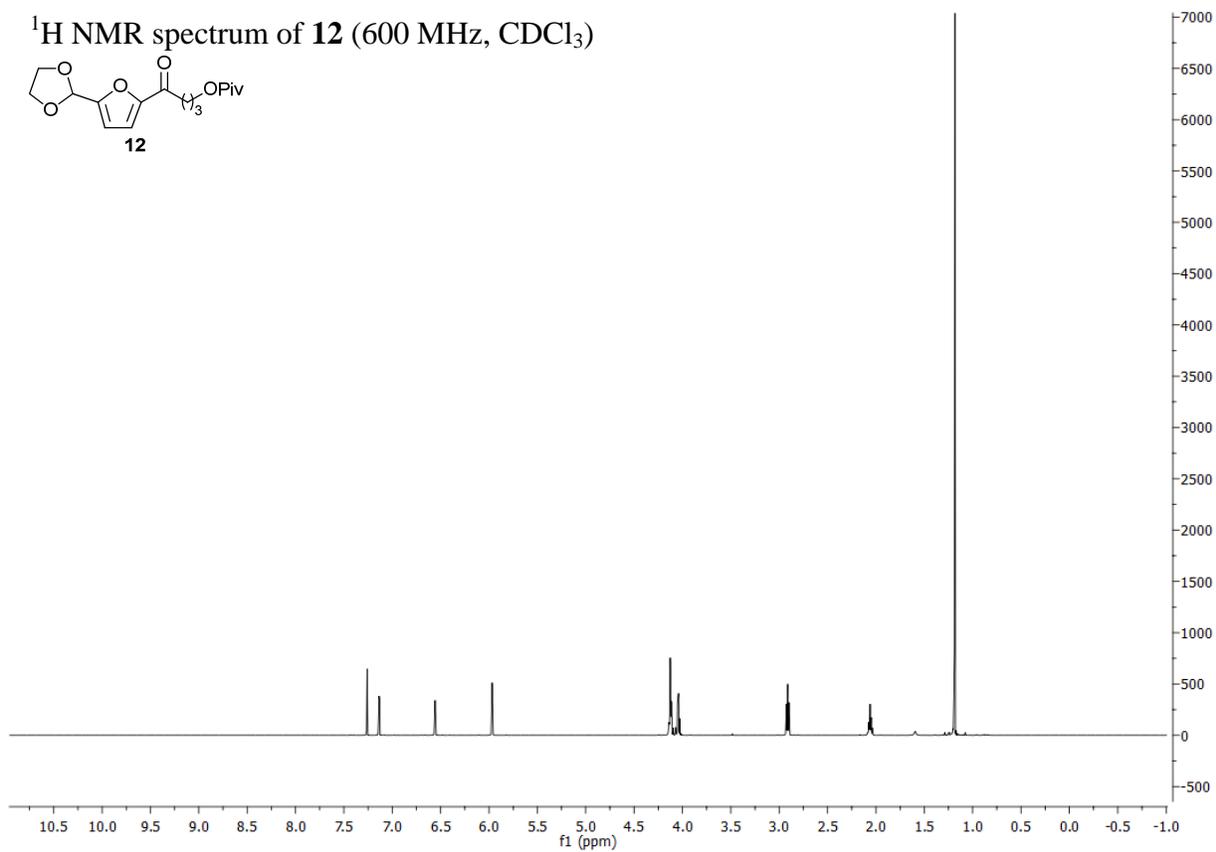
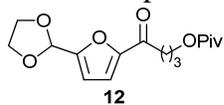
^1H NMR spectrum of **10a** (600 MHz, CDCl_3)



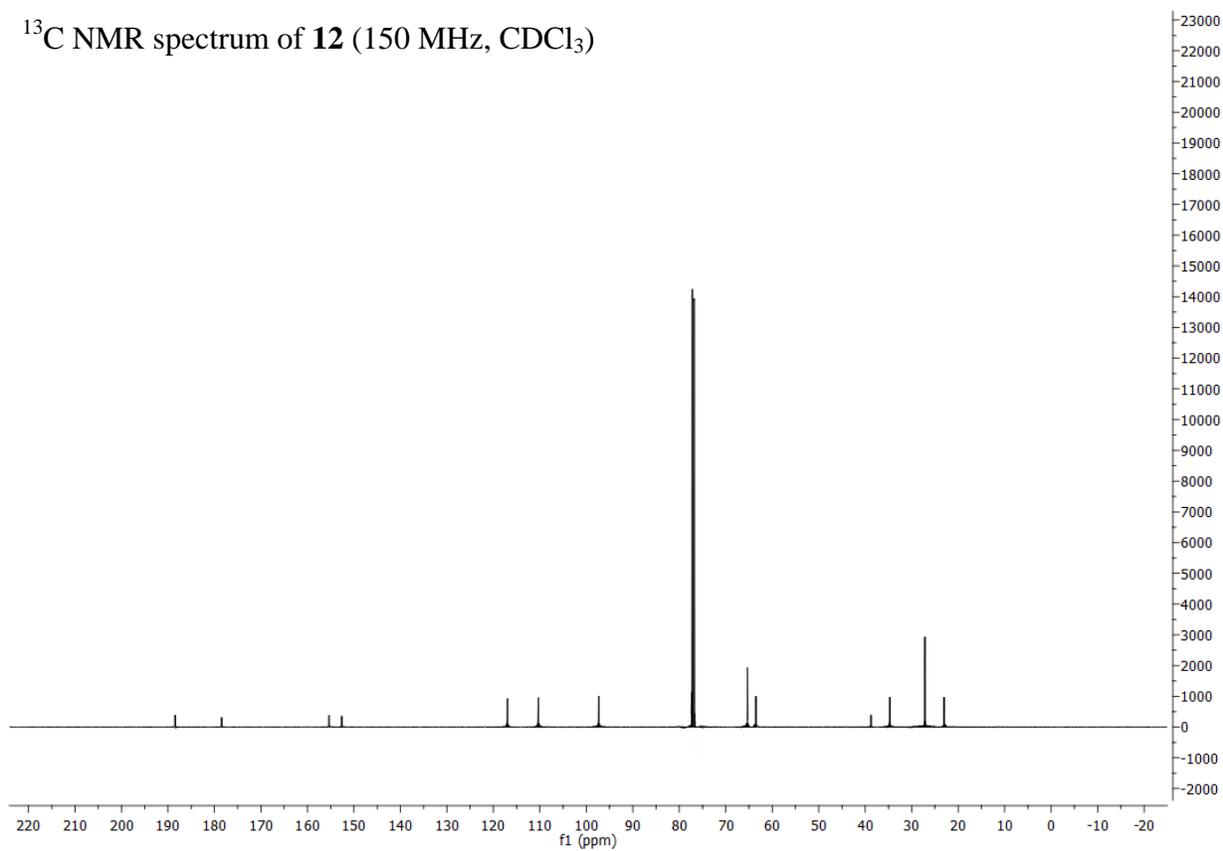
^{13}C NMR spectrum of **10a** (150 MHz, CDCl_3)



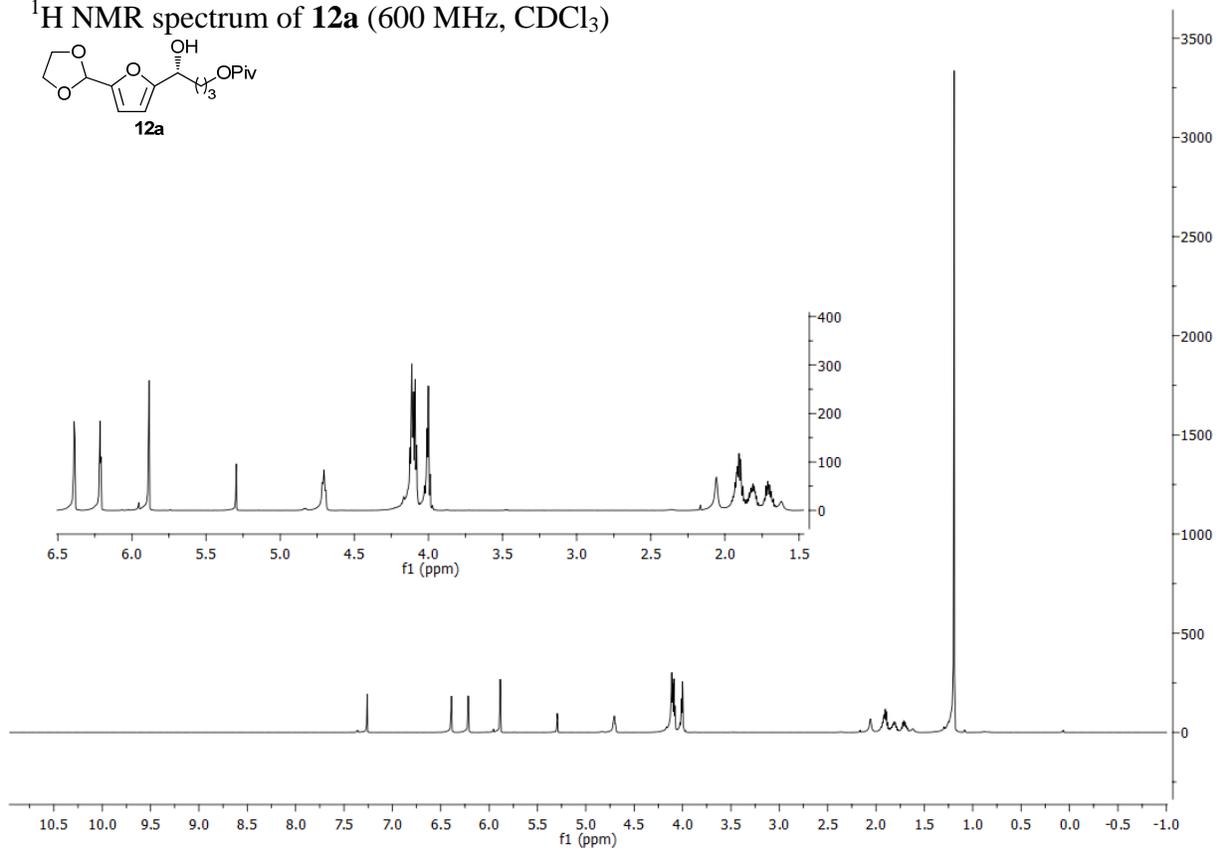
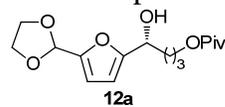
¹H NMR spectrum of **12** (600 MHz, CDCl₃)



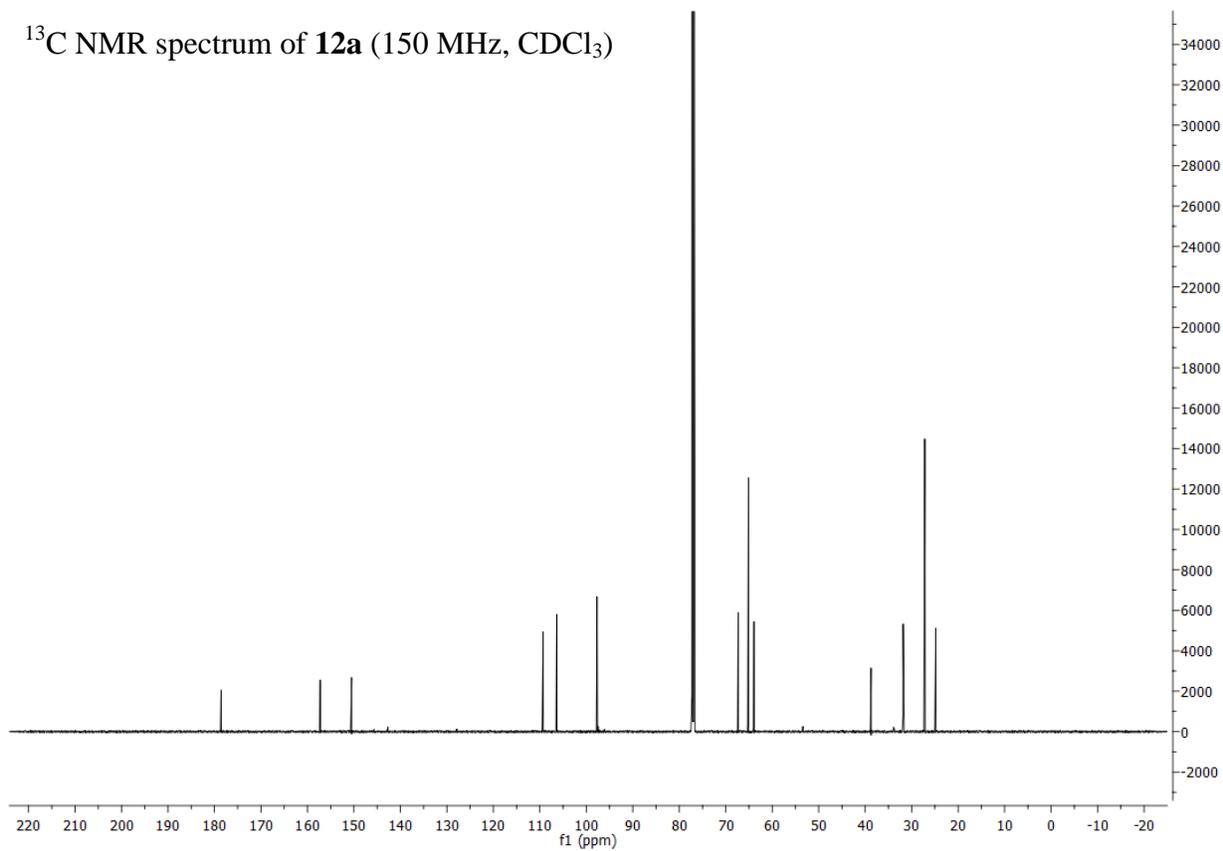
¹³C NMR spectrum of **12** (150 MHz, CDCl₃)



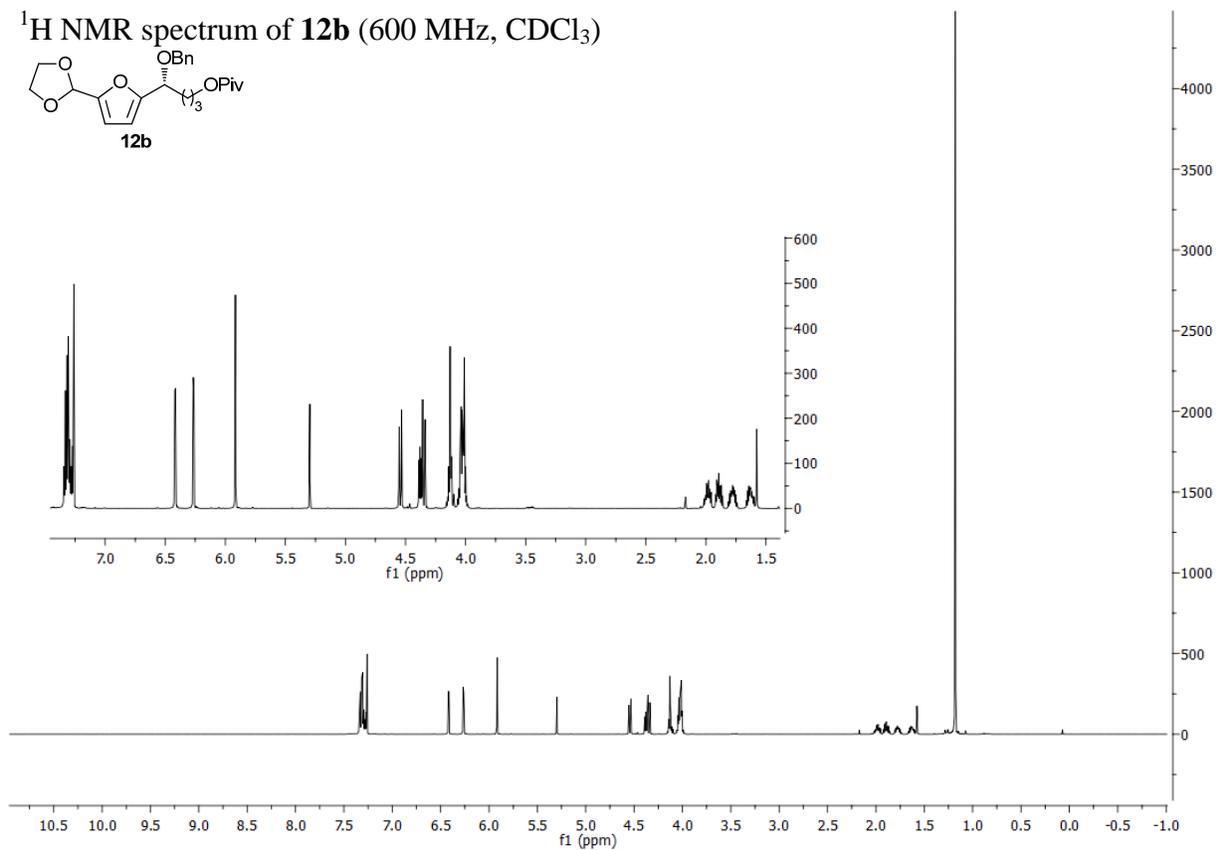
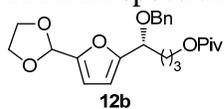
¹H NMR spectrum of **12a** (600 MHz, CDCl₃)



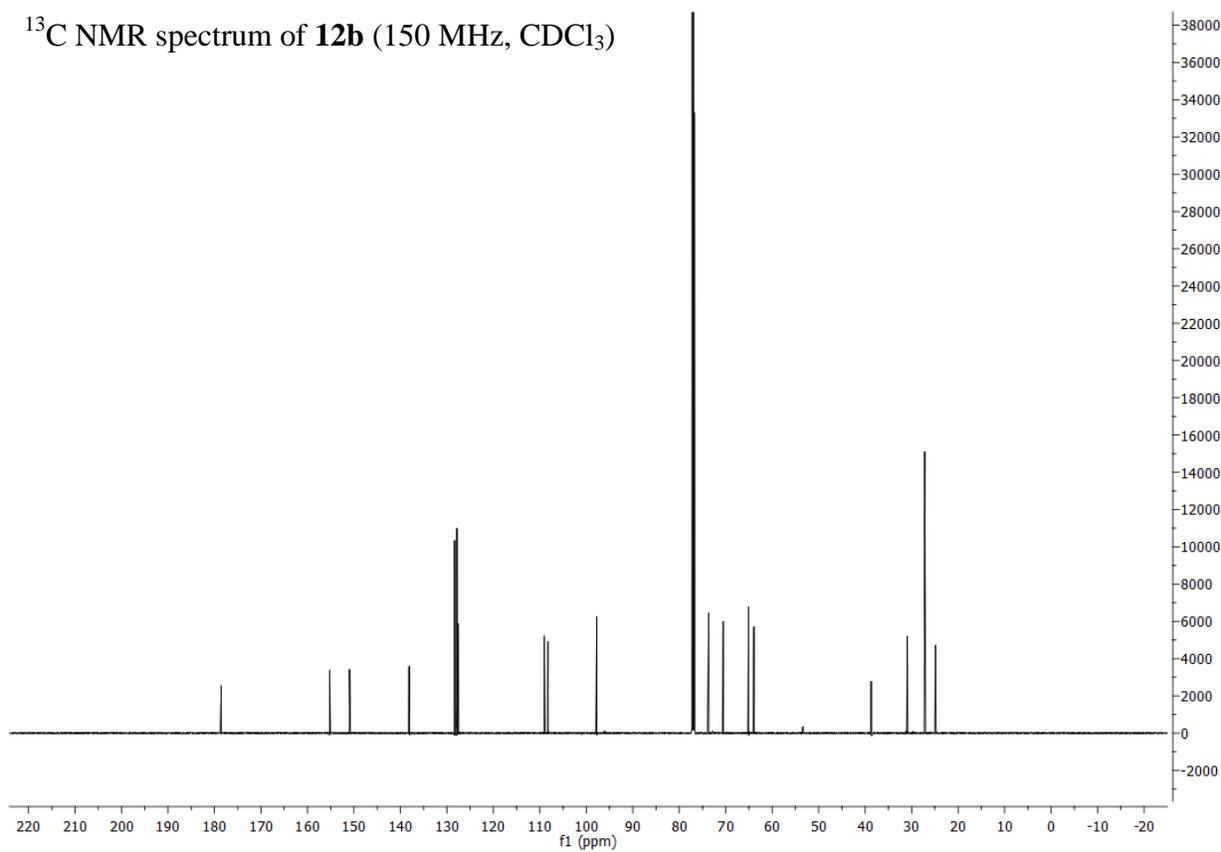
¹³C NMR spectrum of **12a** (150 MHz, CDCl₃)



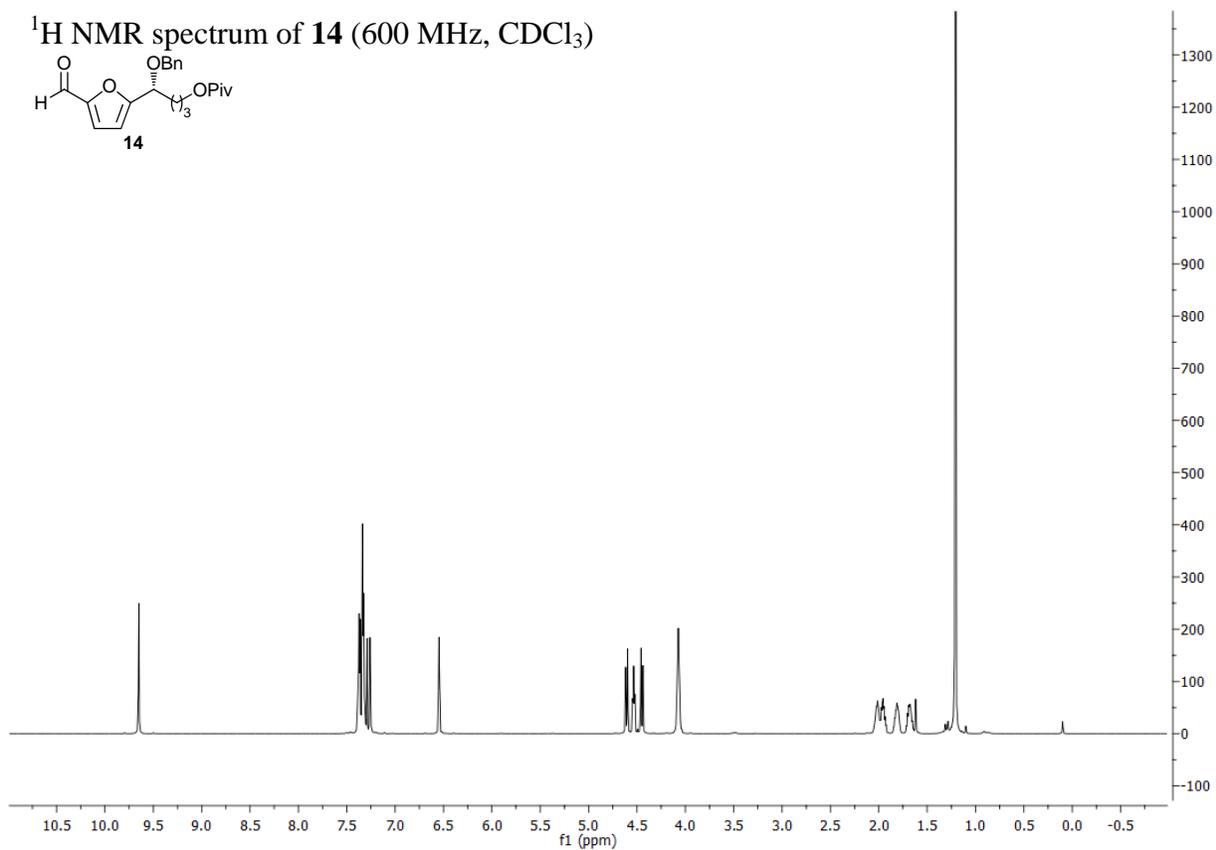
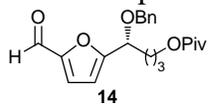
^1H NMR spectrum of **12b** (600 MHz, CDCl_3)



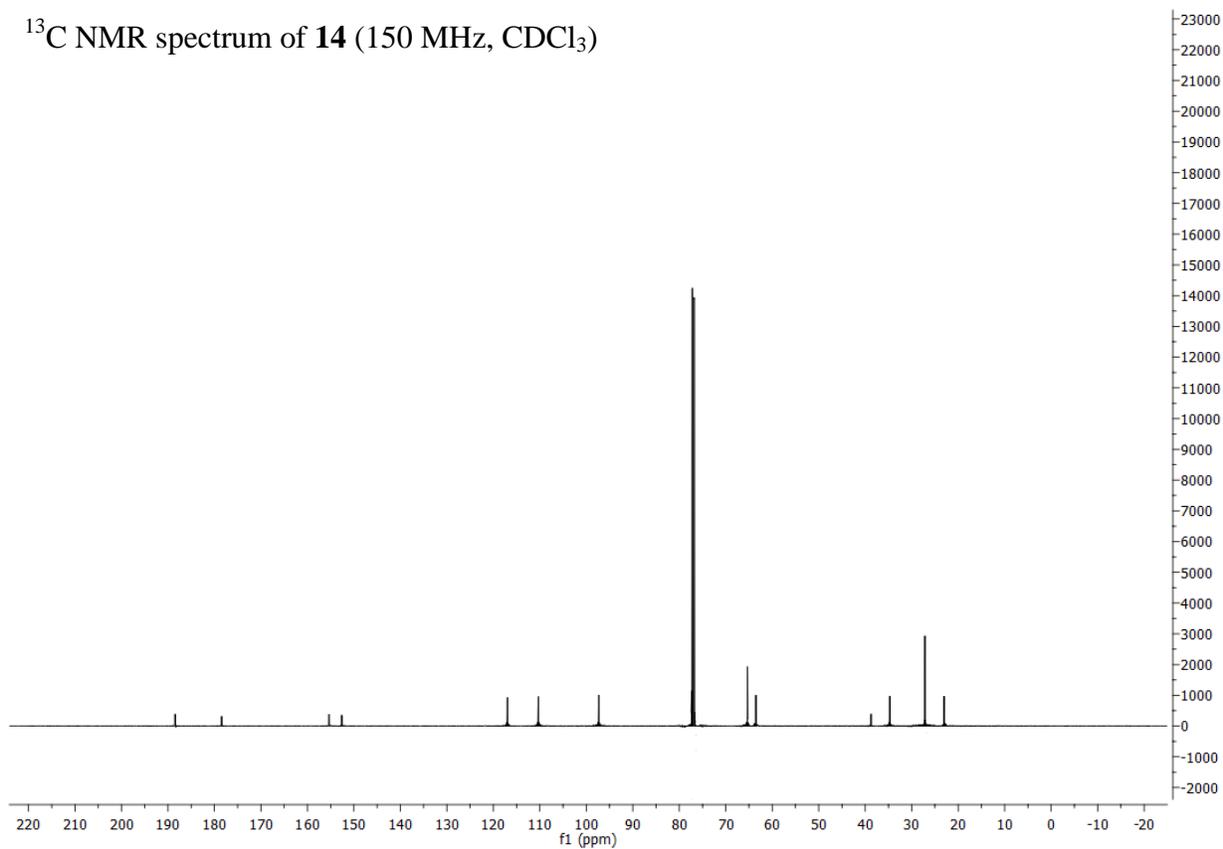
^{13}C NMR spectrum of **12b** (150 MHz, CDCl_3)



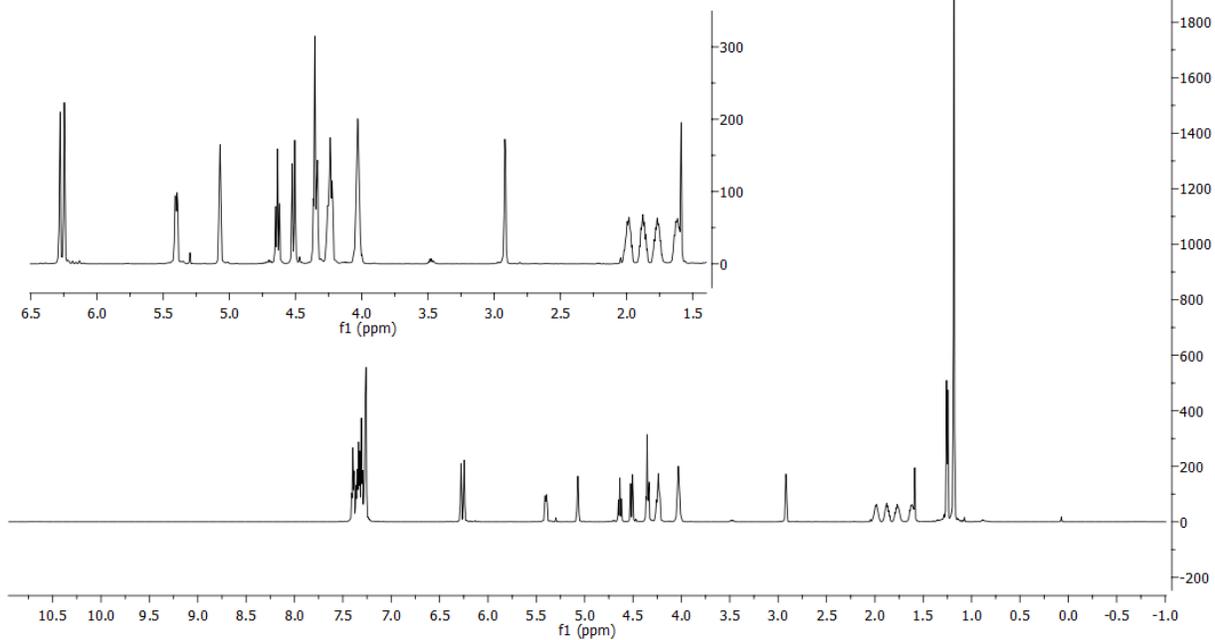
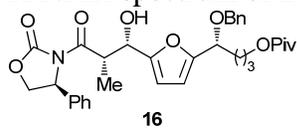
^1H NMR spectrum of **14** (600 MHz, CDCl_3)



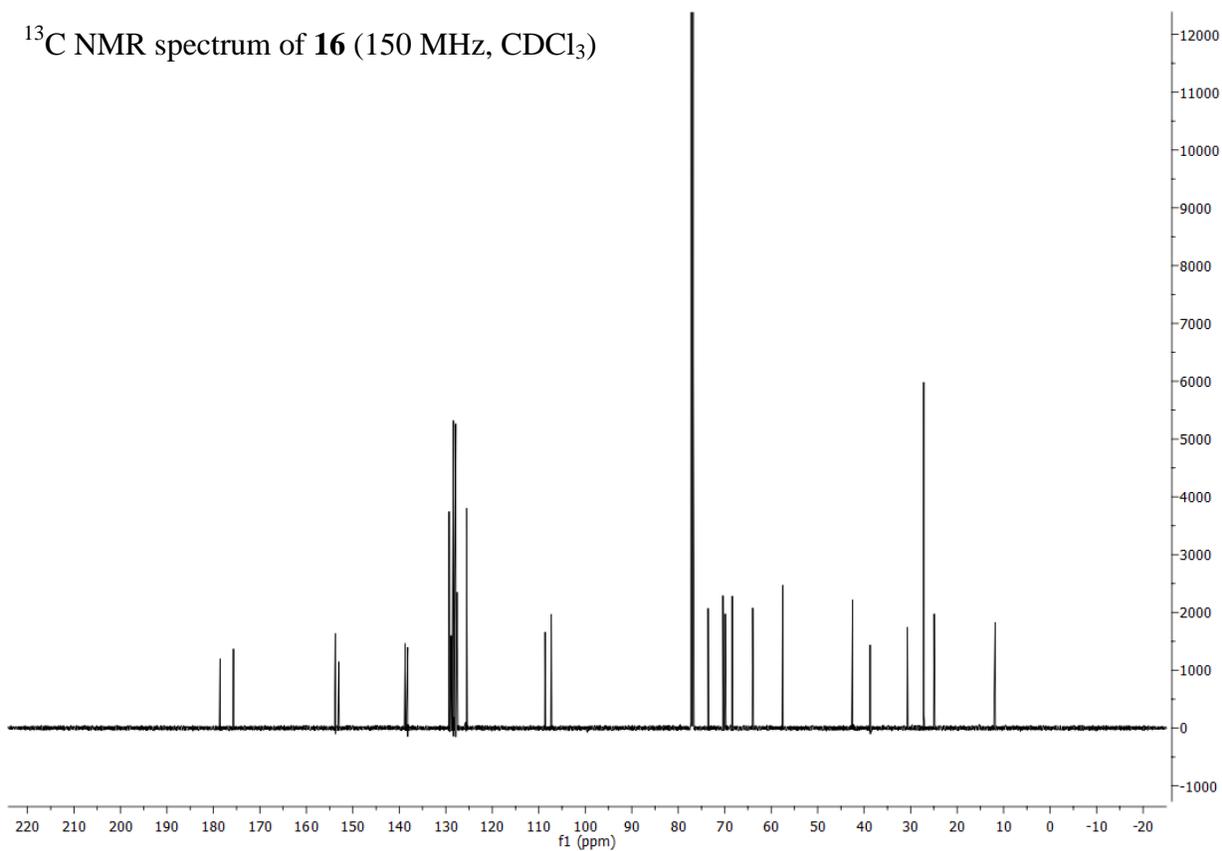
^{13}C NMR spectrum of **14** (150 MHz, CDCl_3)



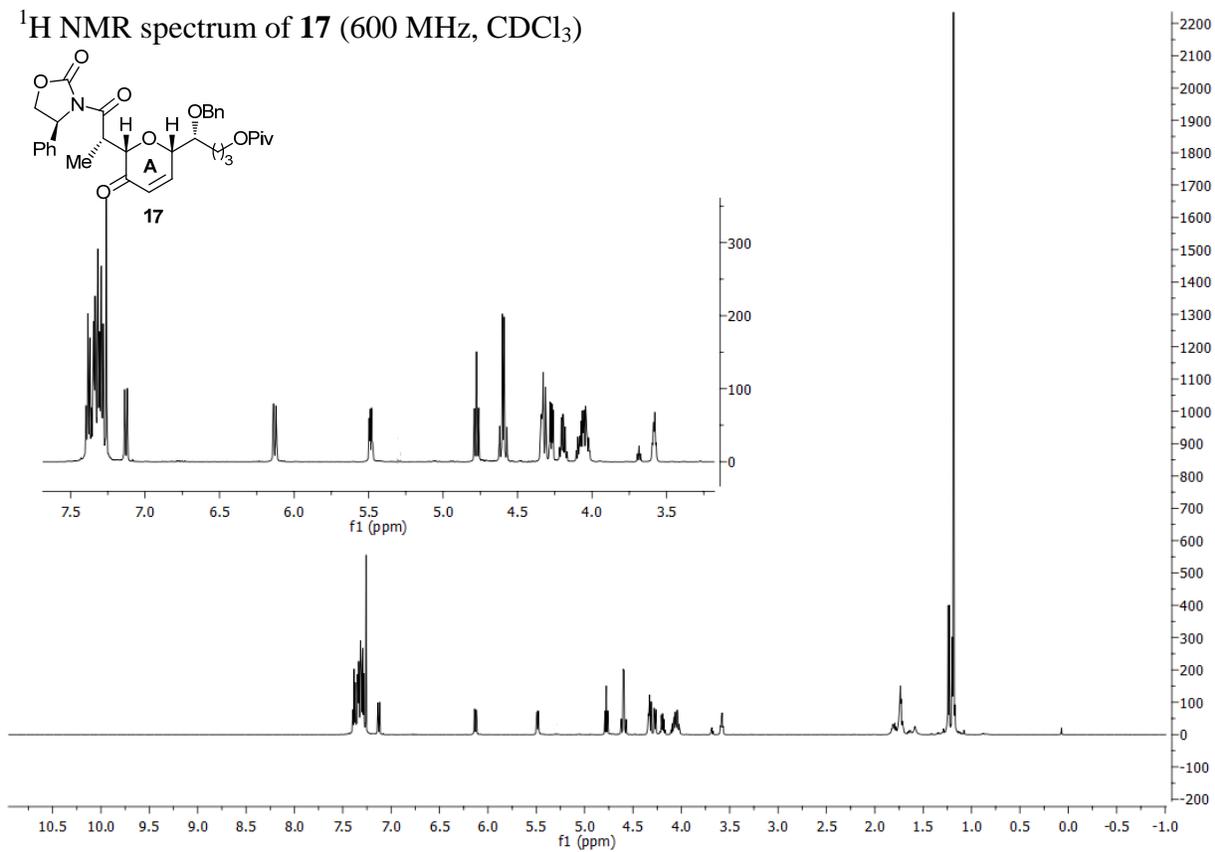
¹H NMR spectrum of **16** (600 MHz, CDCl₃)



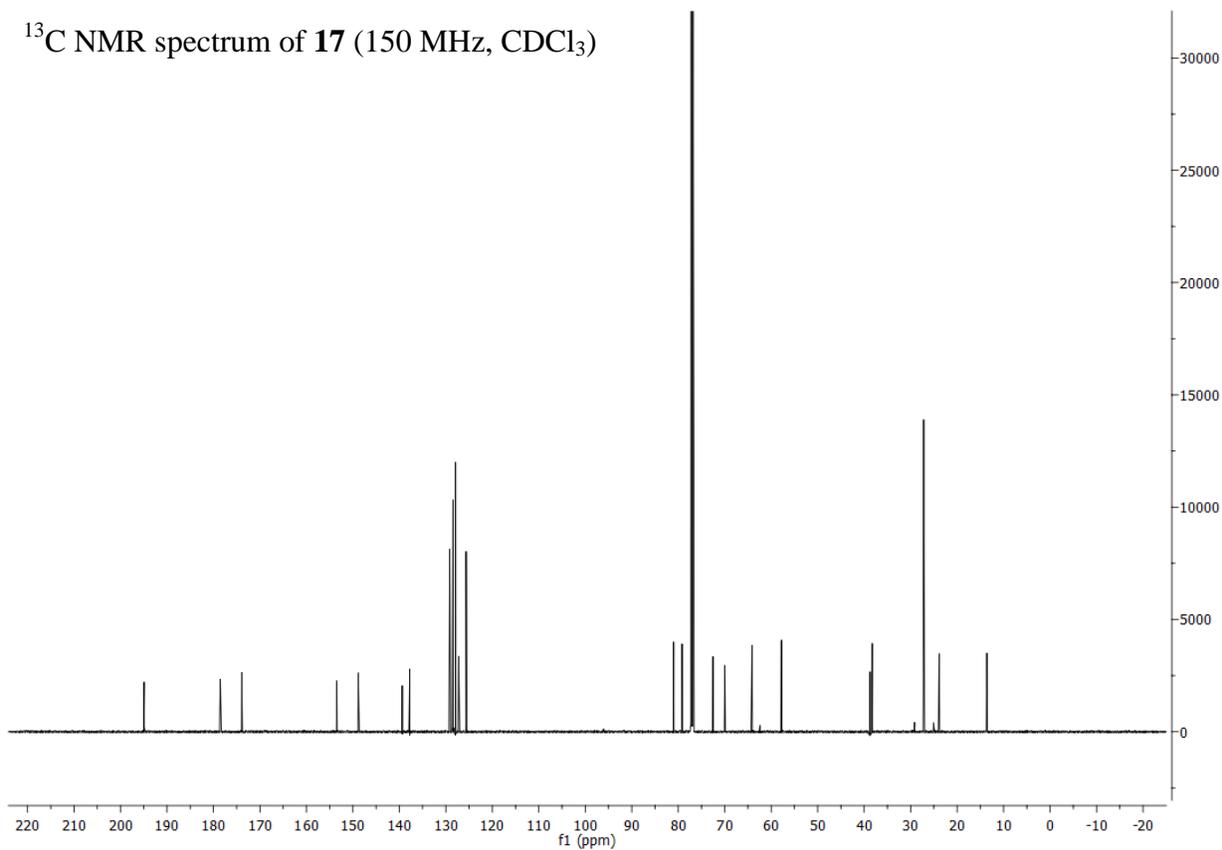
¹³C NMR spectrum of **16** (150 MHz, CDCl₃)



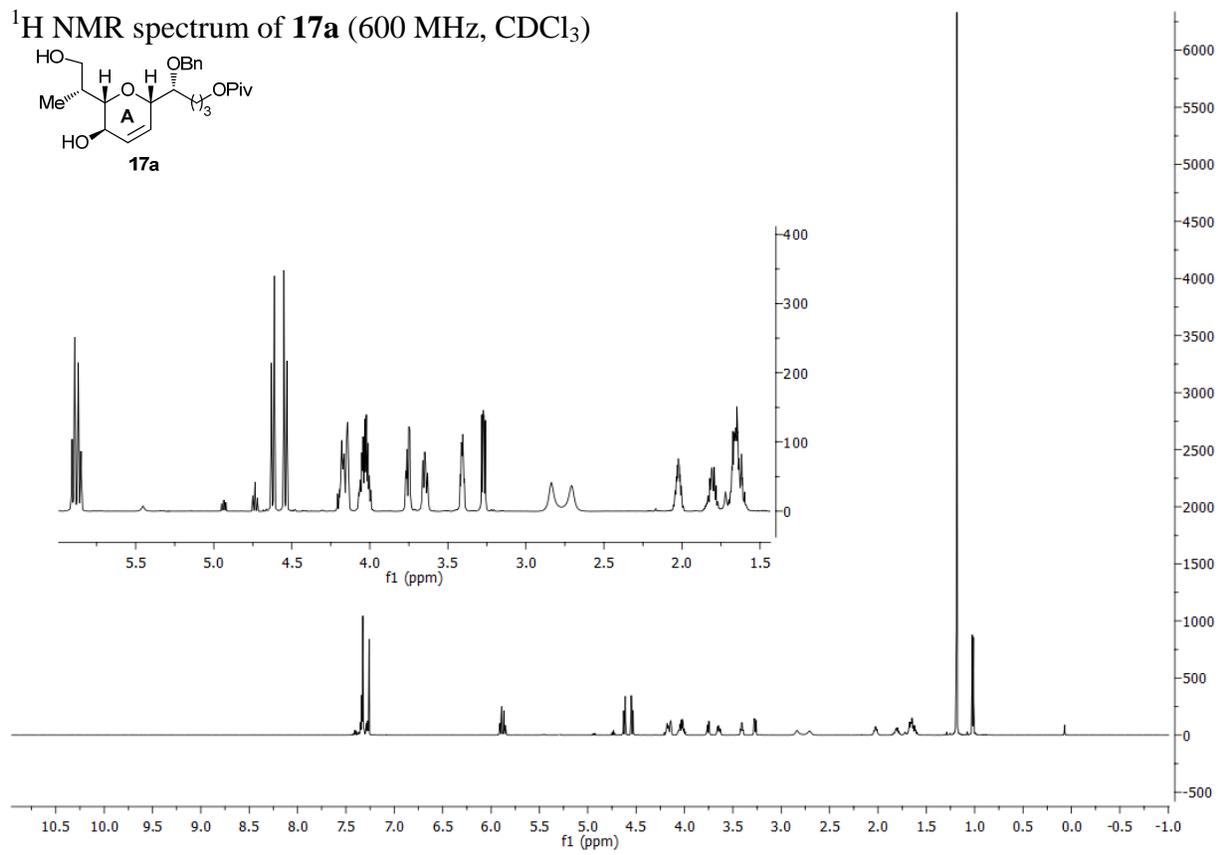
^1H NMR spectrum of **17** (600 MHz, CDCl_3)



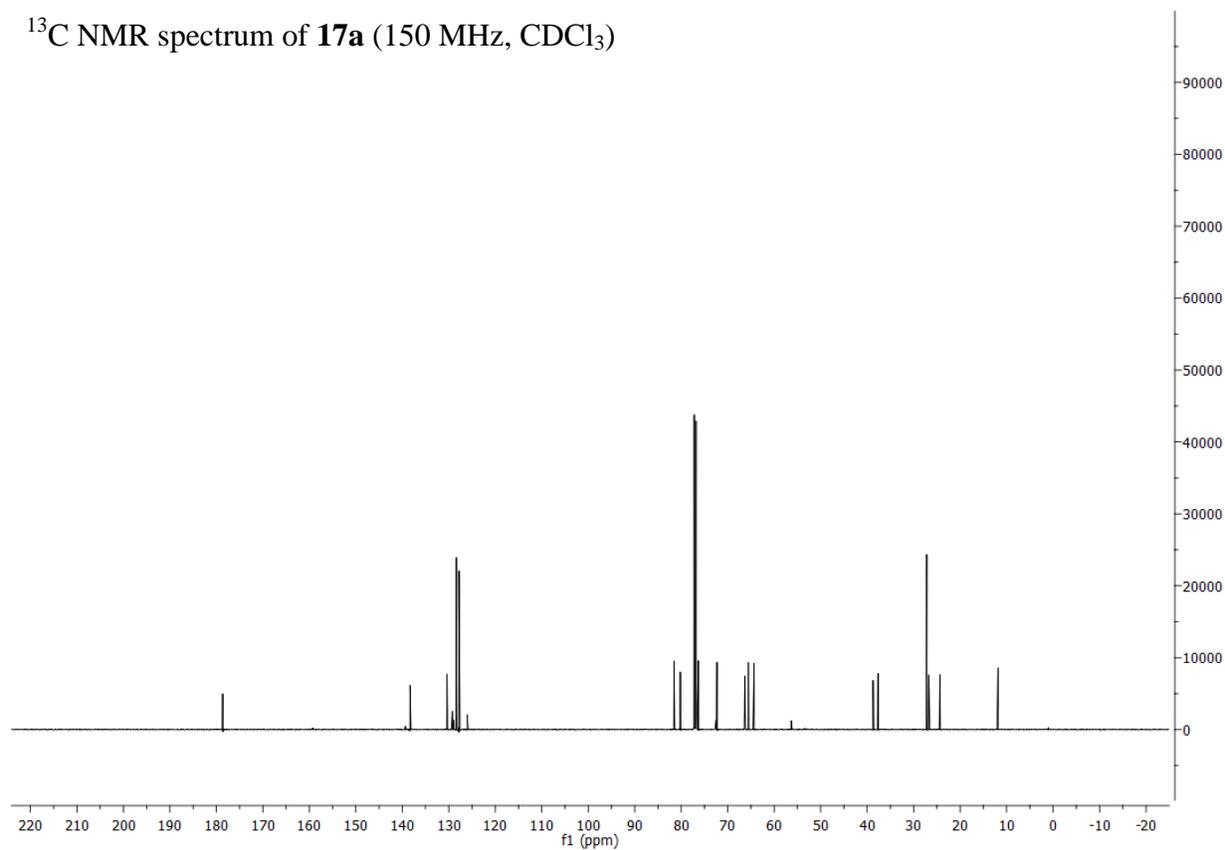
^{13}C NMR spectrum of **17** (150 MHz, CDCl_3)



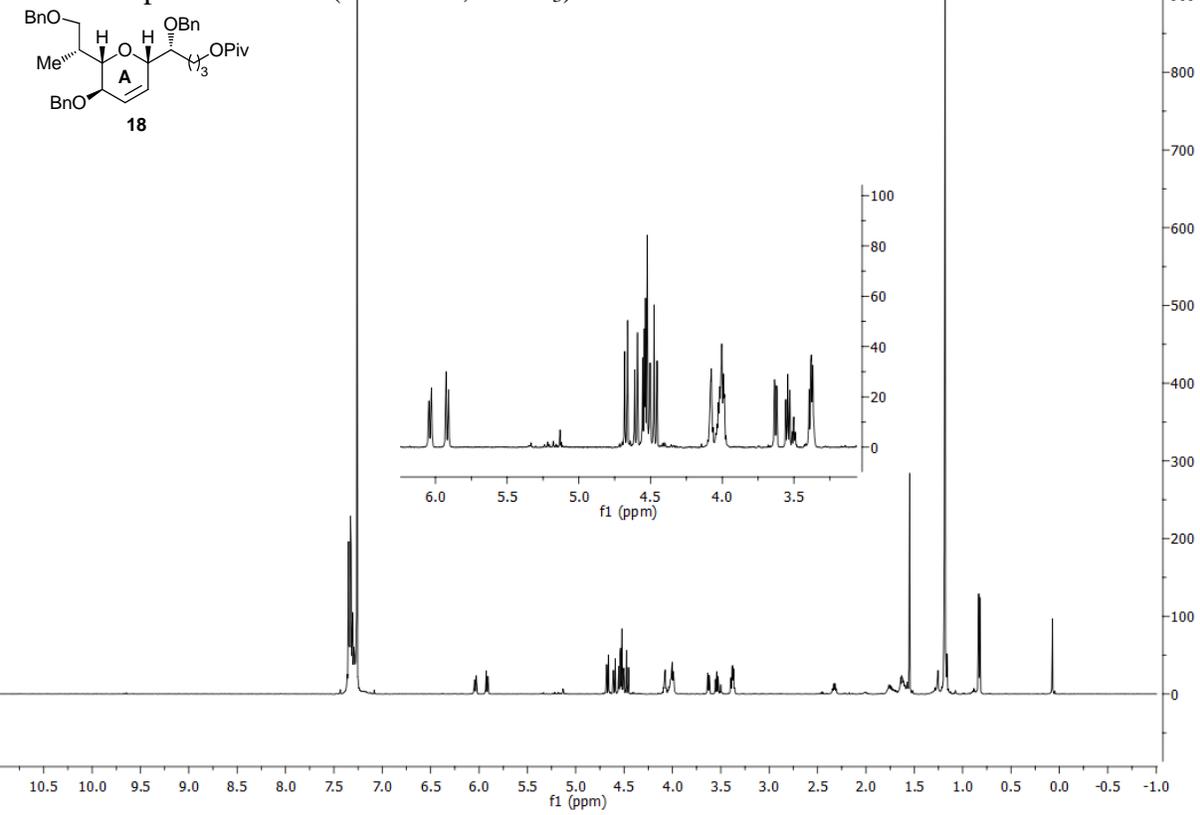
^1H NMR spectrum of **17a** (600 MHz, CDCl_3)



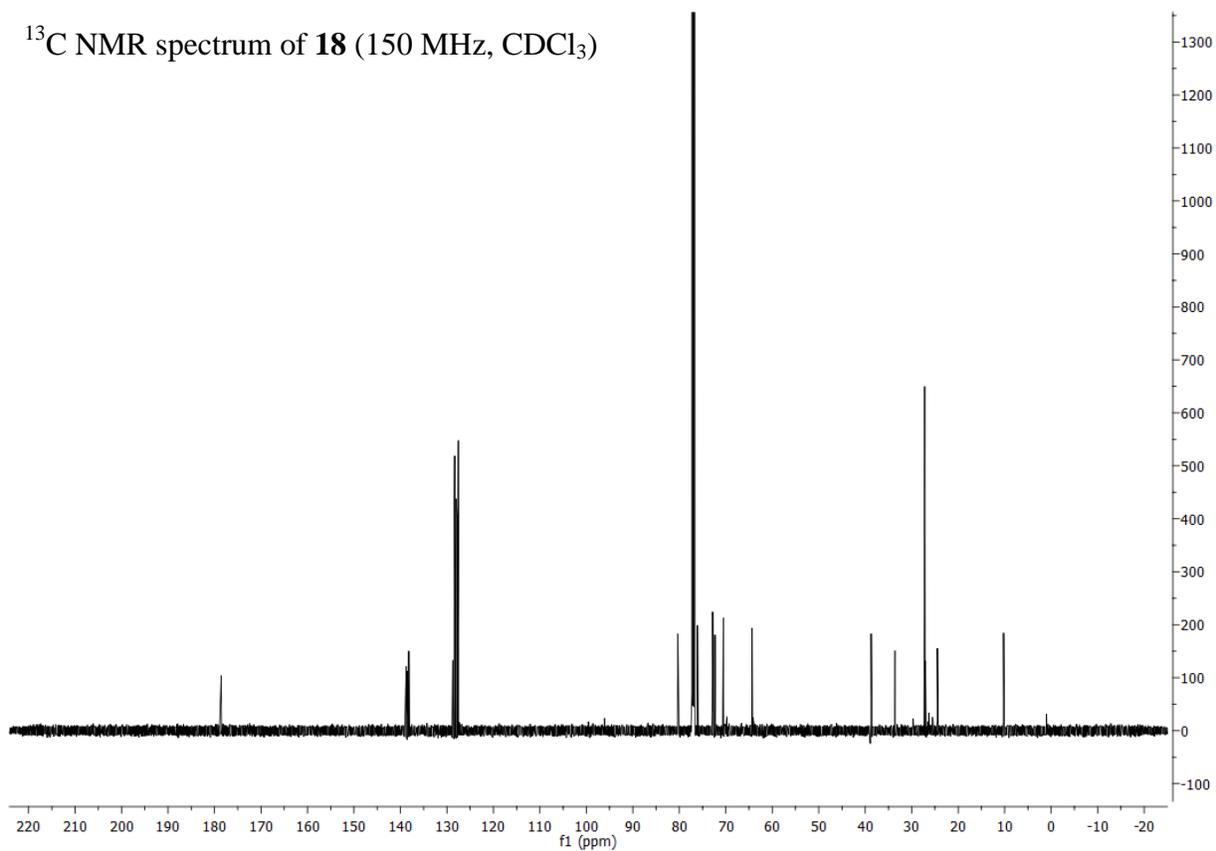
^{13}C NMR spectrum of **17a** (150 MHz, CDCl_3)



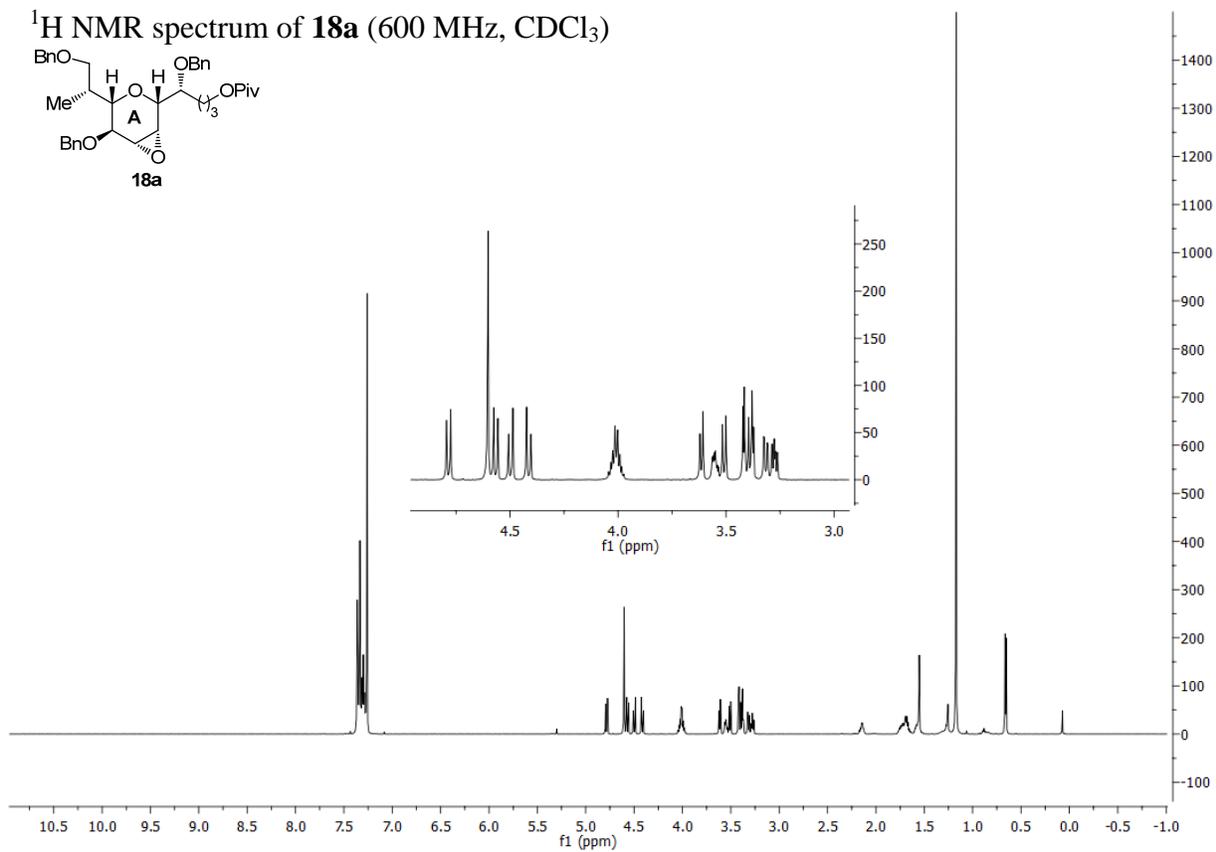
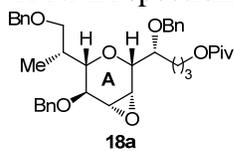
^1H NMR spectrum of **18** (600 MHz, CDCl_3)



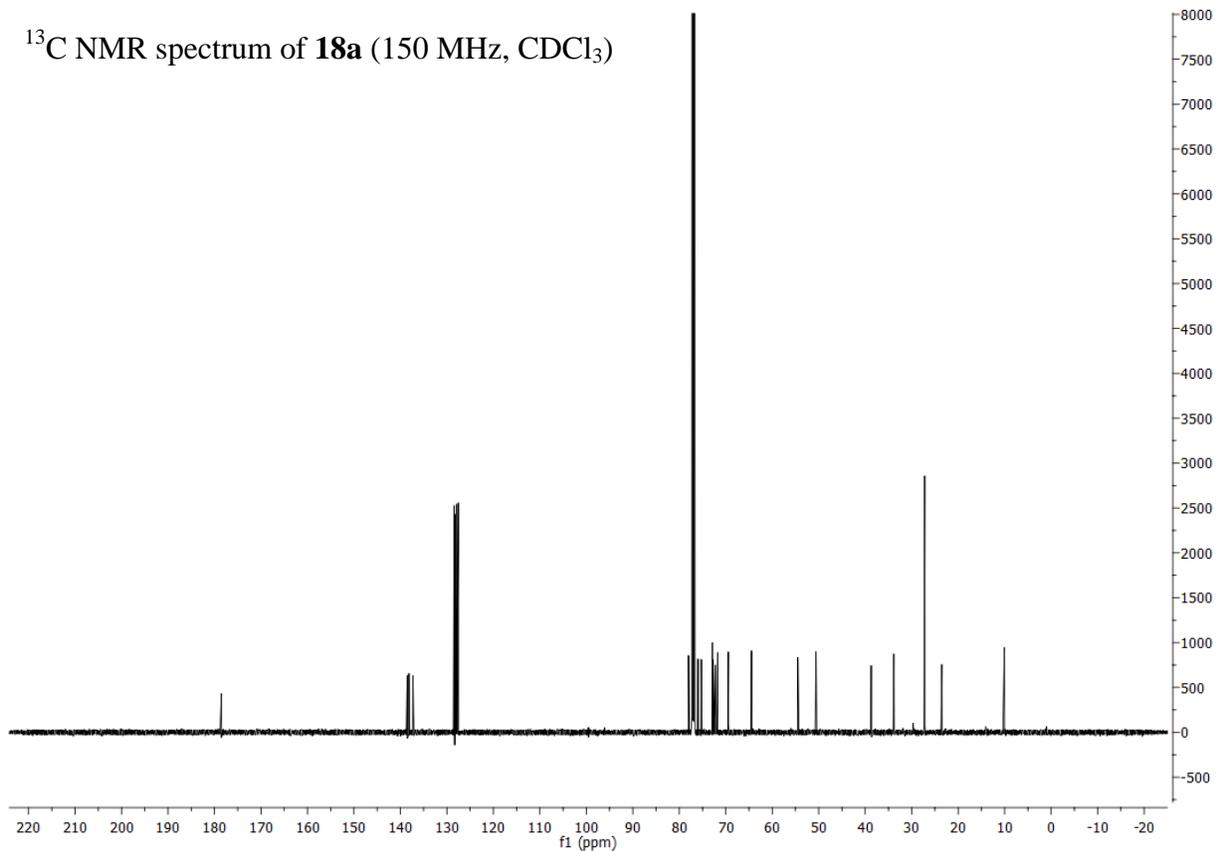
^{13}C NMR spectrum of **18** (150 MHz, CDCl_3)



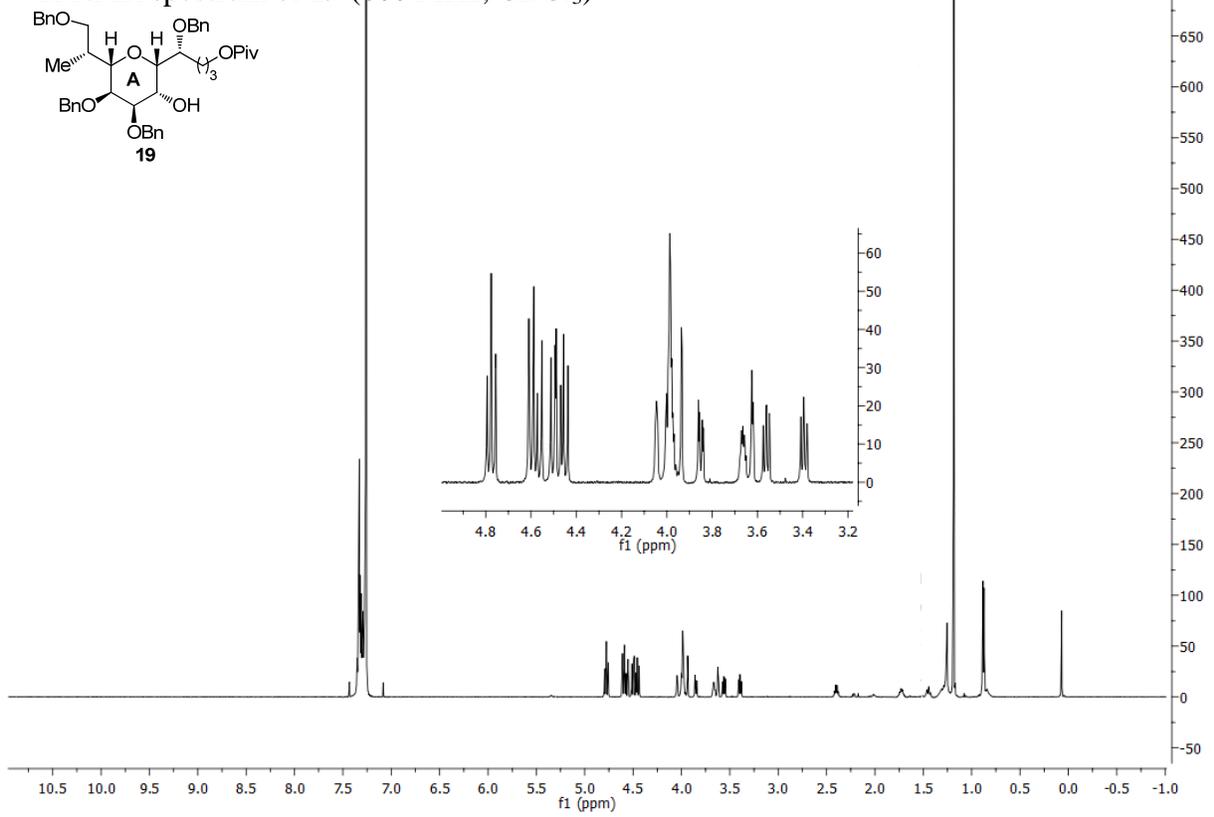
^1H NMR spectrum of **18a** (600 MHz, CDCl_3)



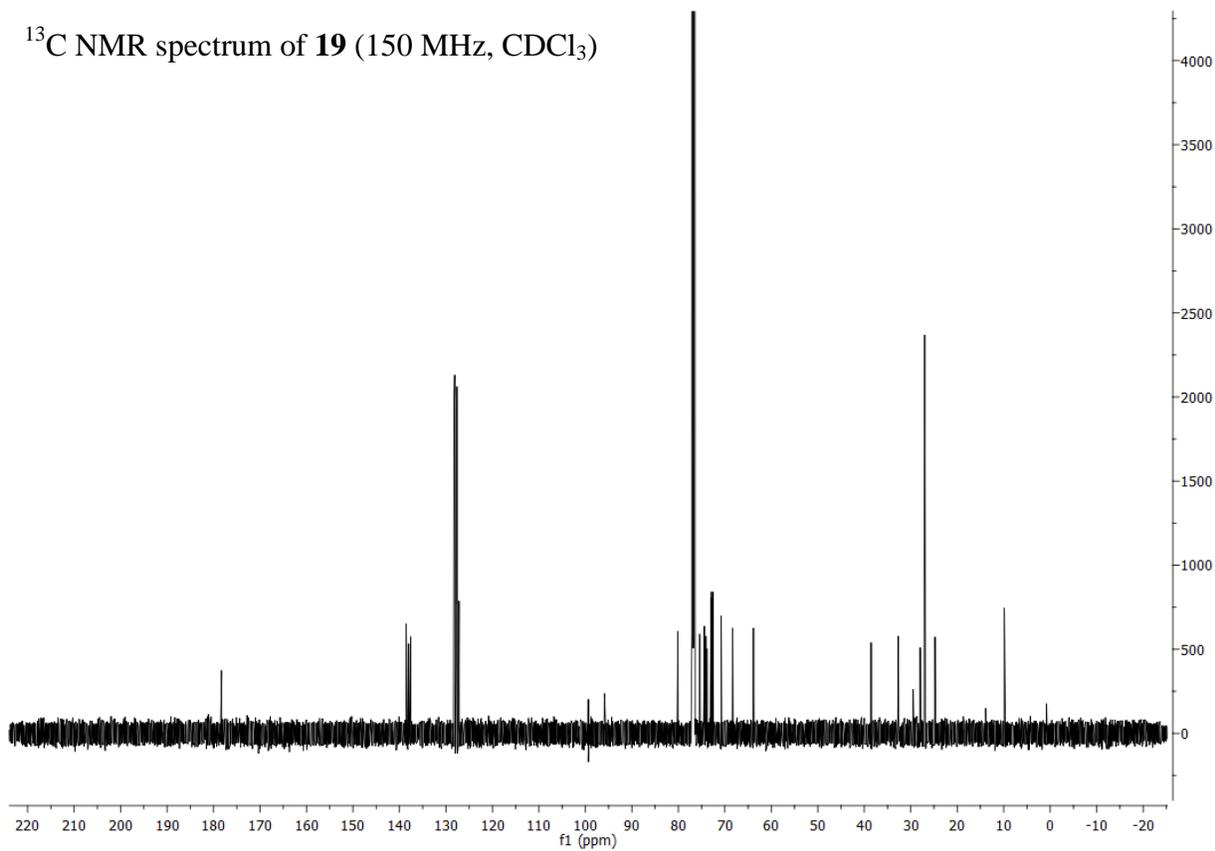
^{13}C NMR spectrum of **18a** (150 MHz, CDCl_3)



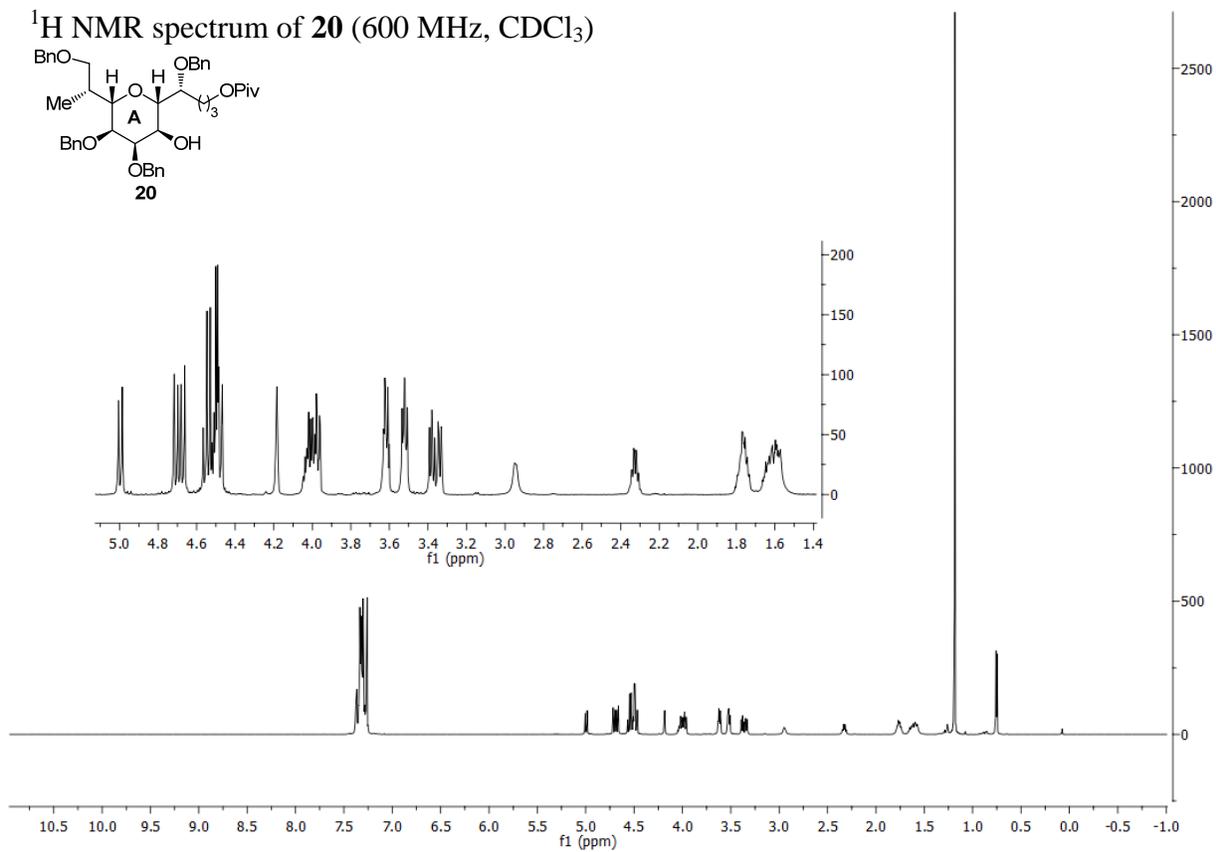
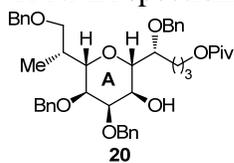
^1H NMR spectrum of **19** (600 MHz, CDCl_3)



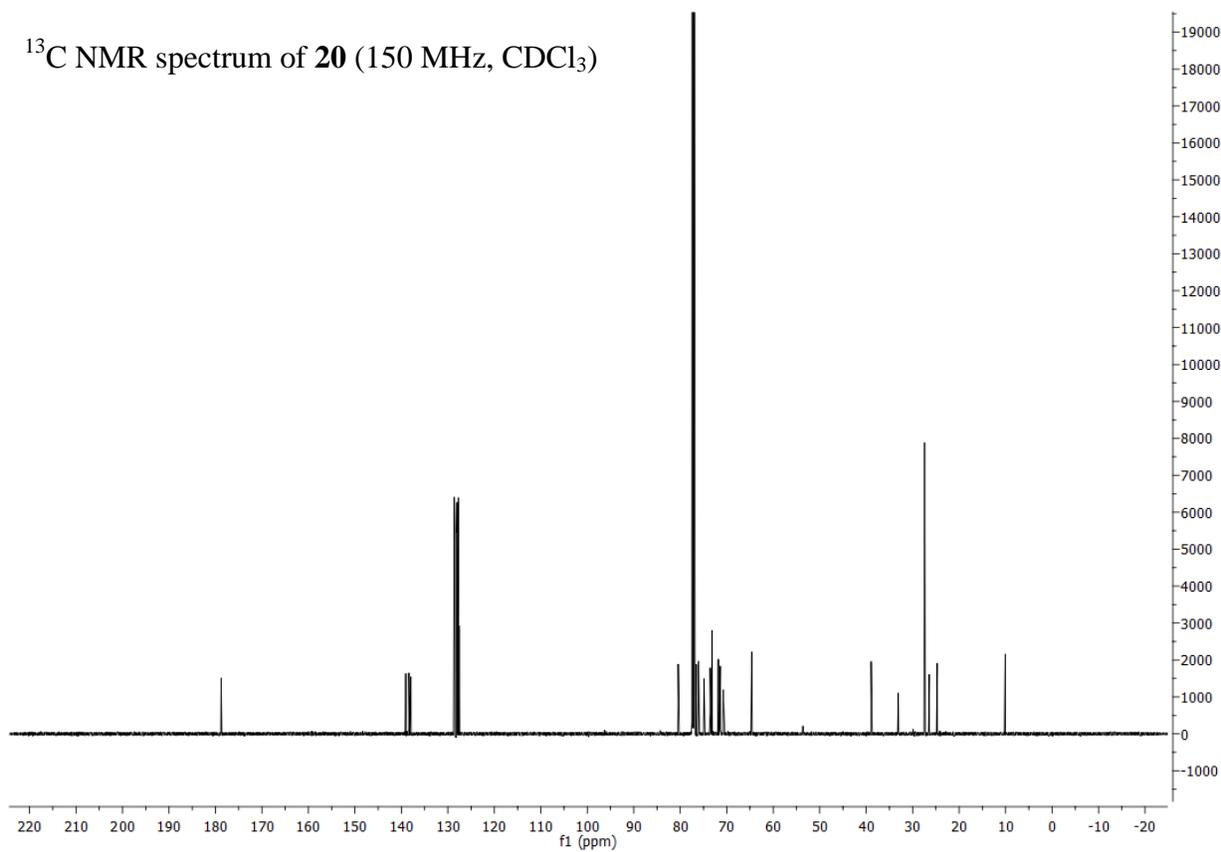
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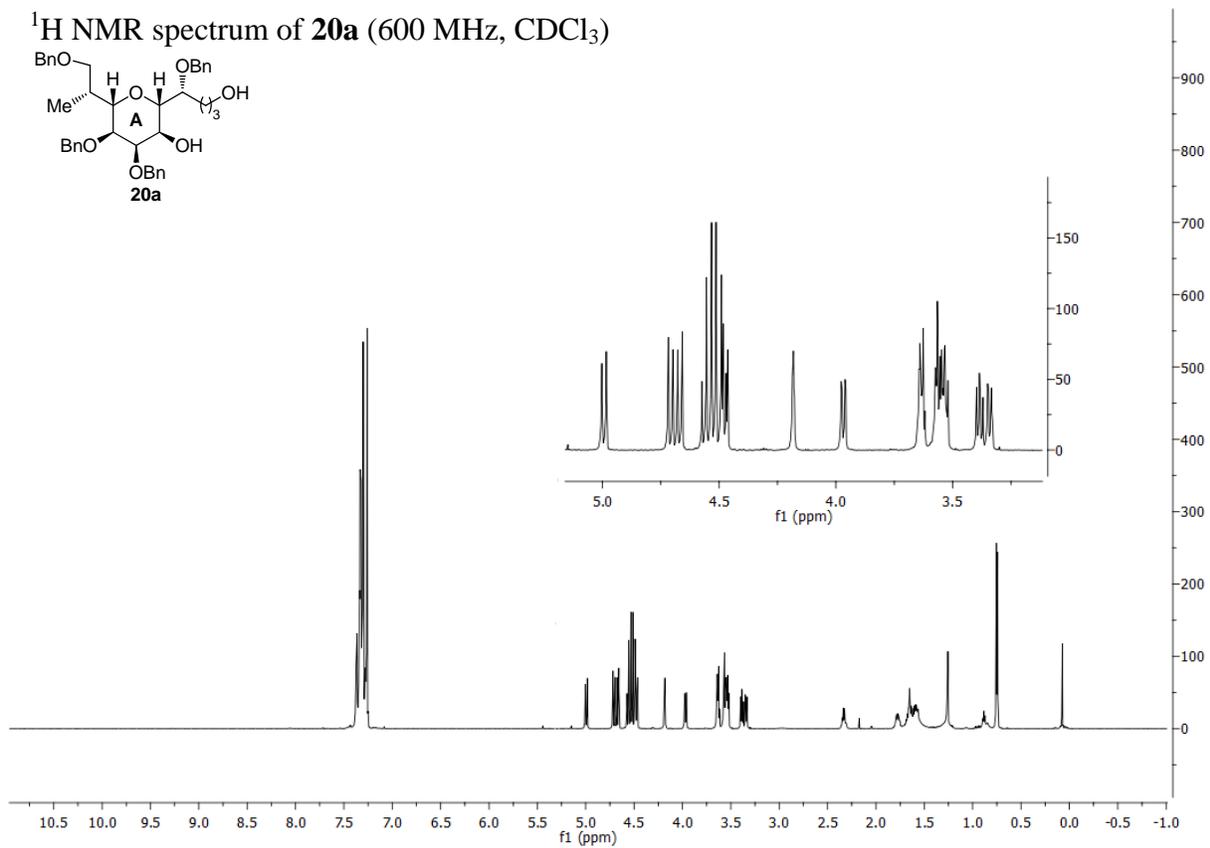
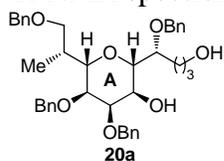
^1H NMR spectrum of **20** (600 MHz, CDCl_3)



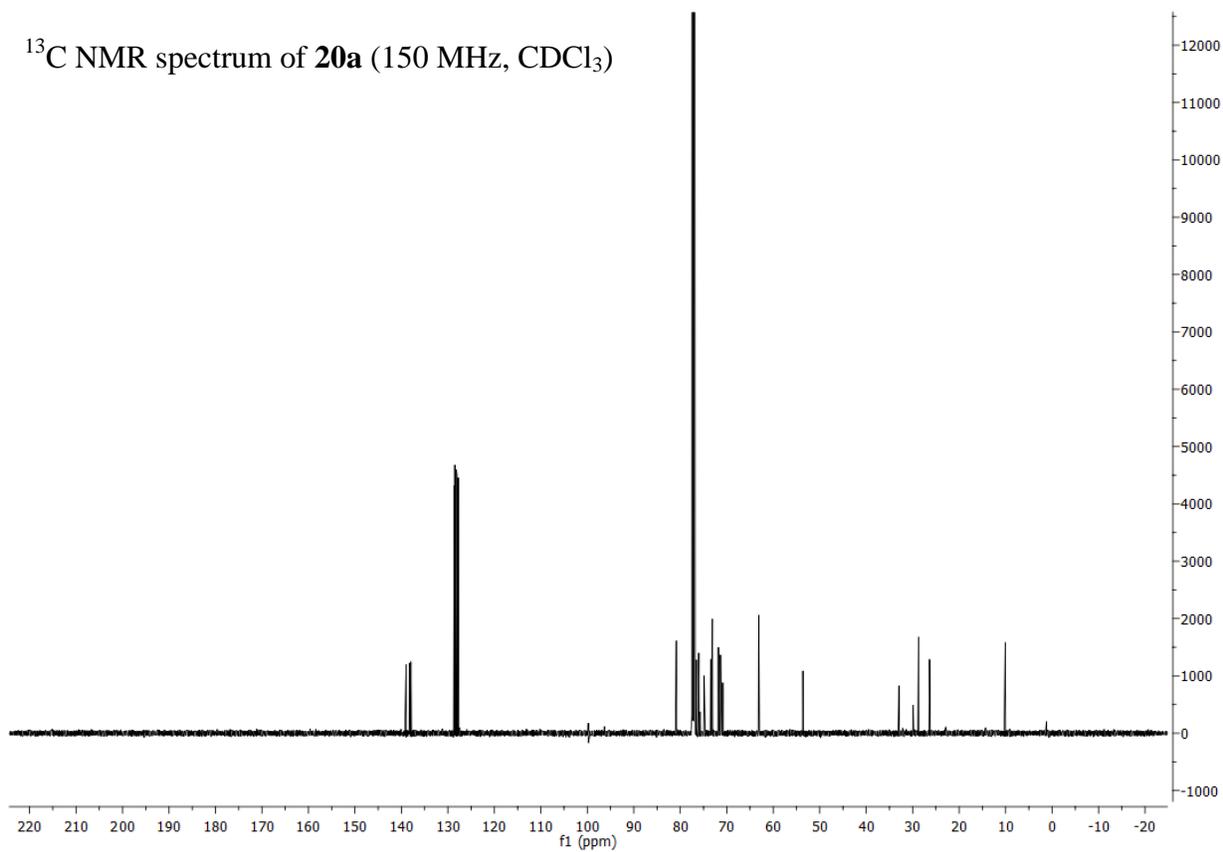
^{13}C NMR spectrum of **20** (150 MHz, CDCl_3)



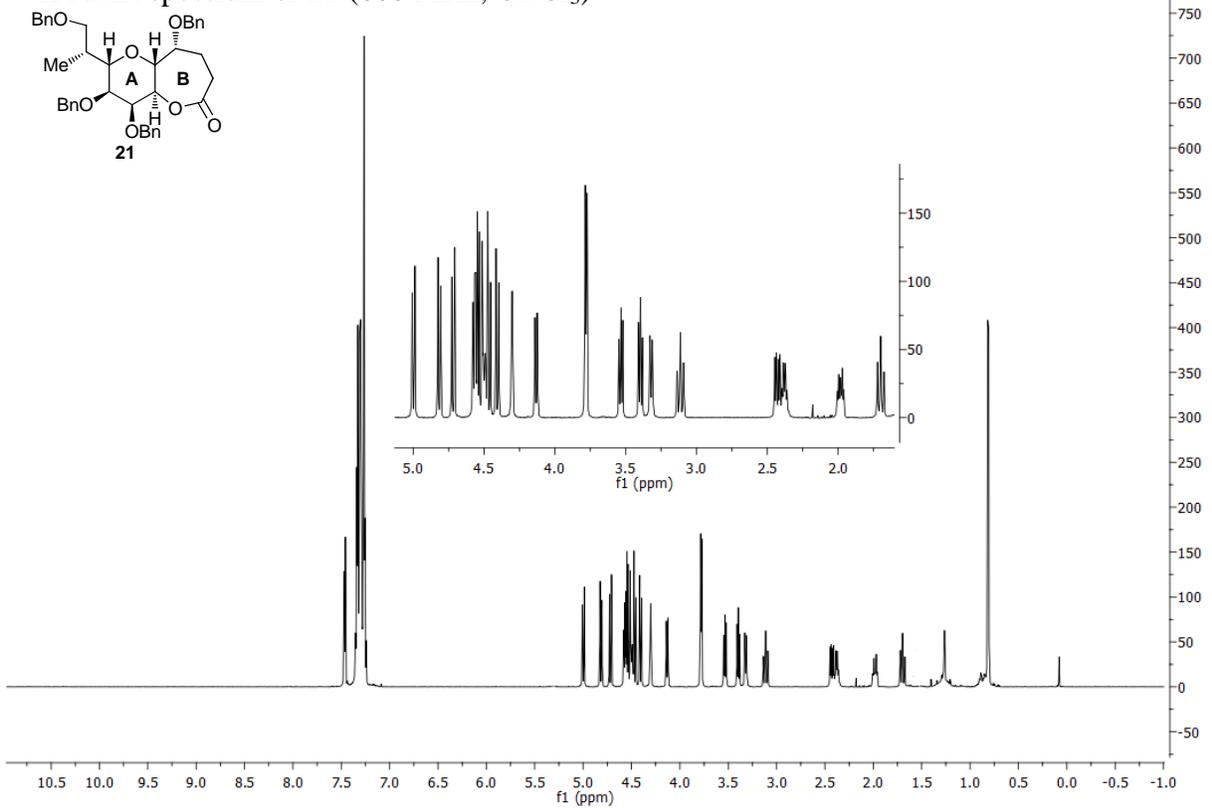
^1H NMR spectrum of **20a** (600 MHz, CDCl_3)



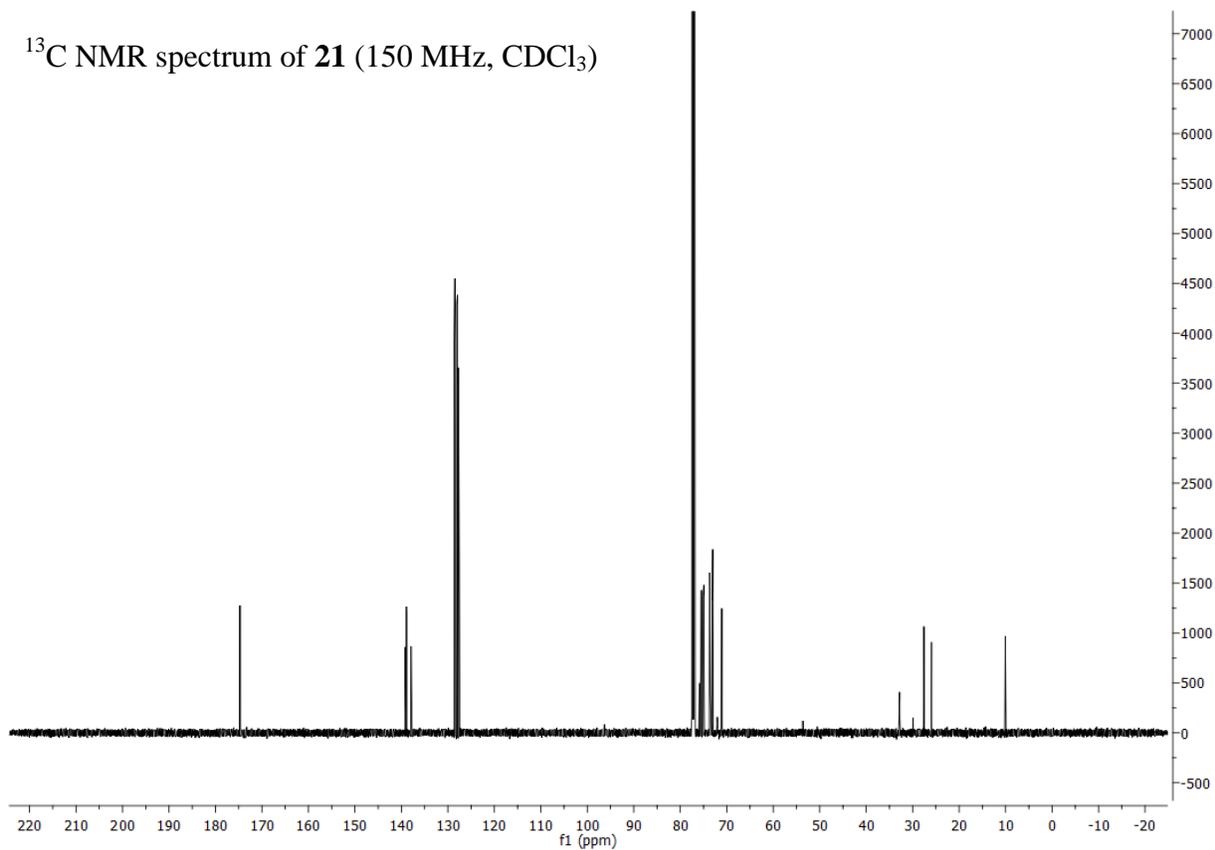
^{13}C NMR spectrum of **20a** (150 MHz, CDCl_3)



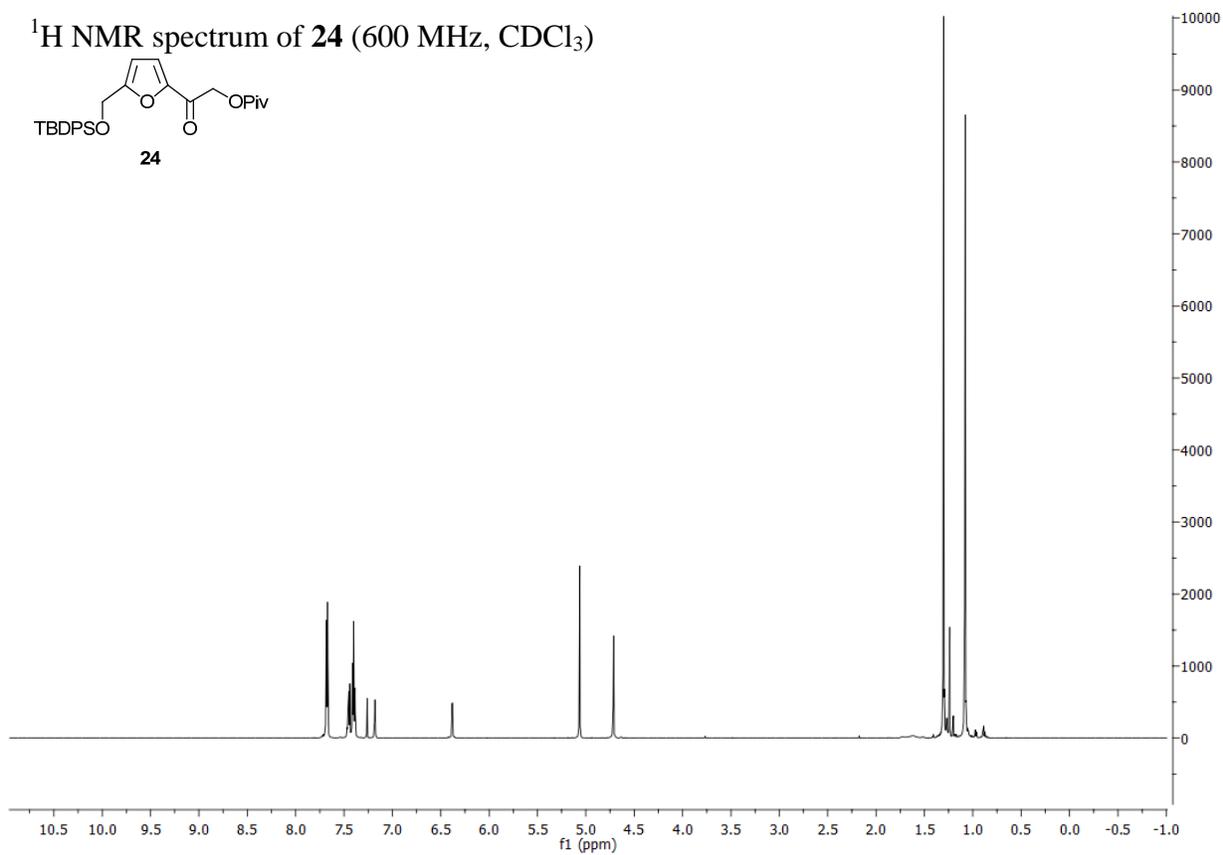
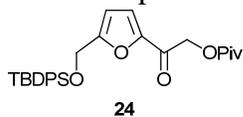
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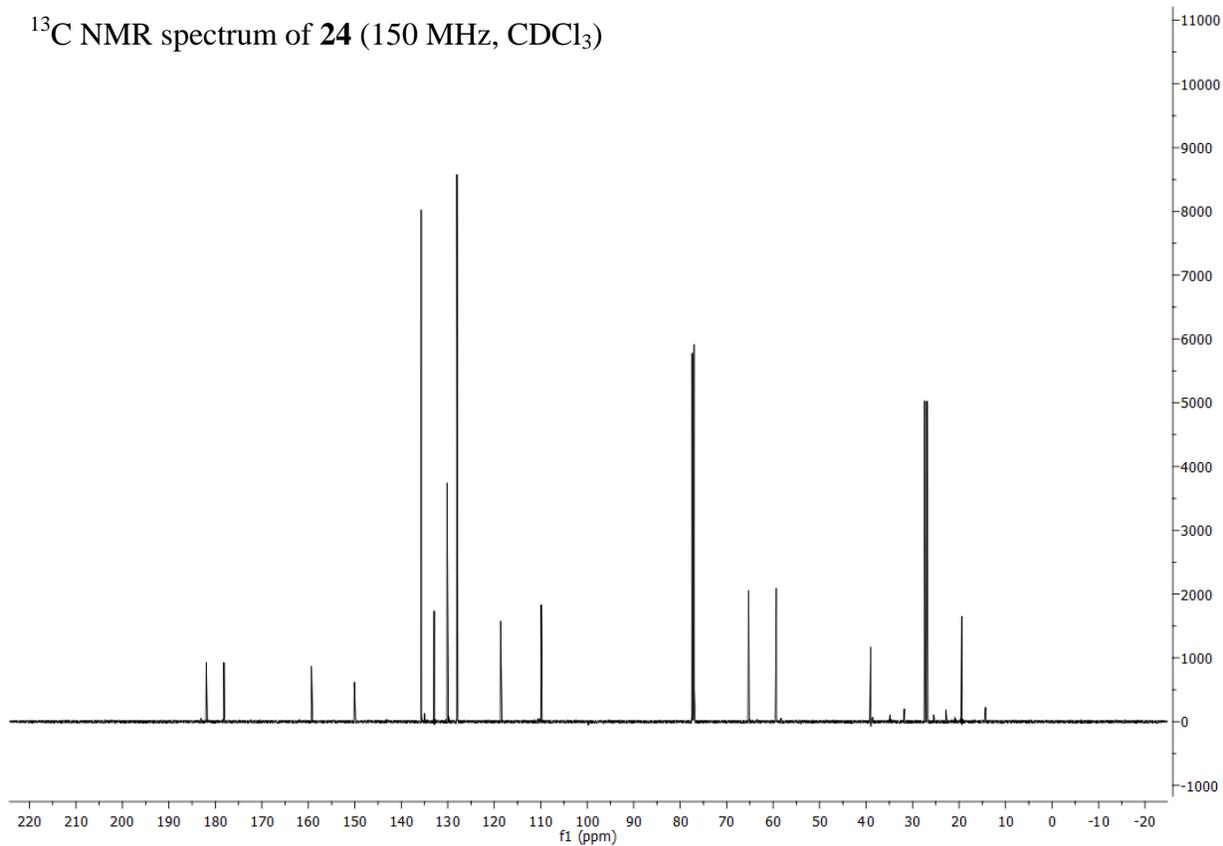
^{13}C NMR spectrum of **21** (150 MHz, CDCl_3)



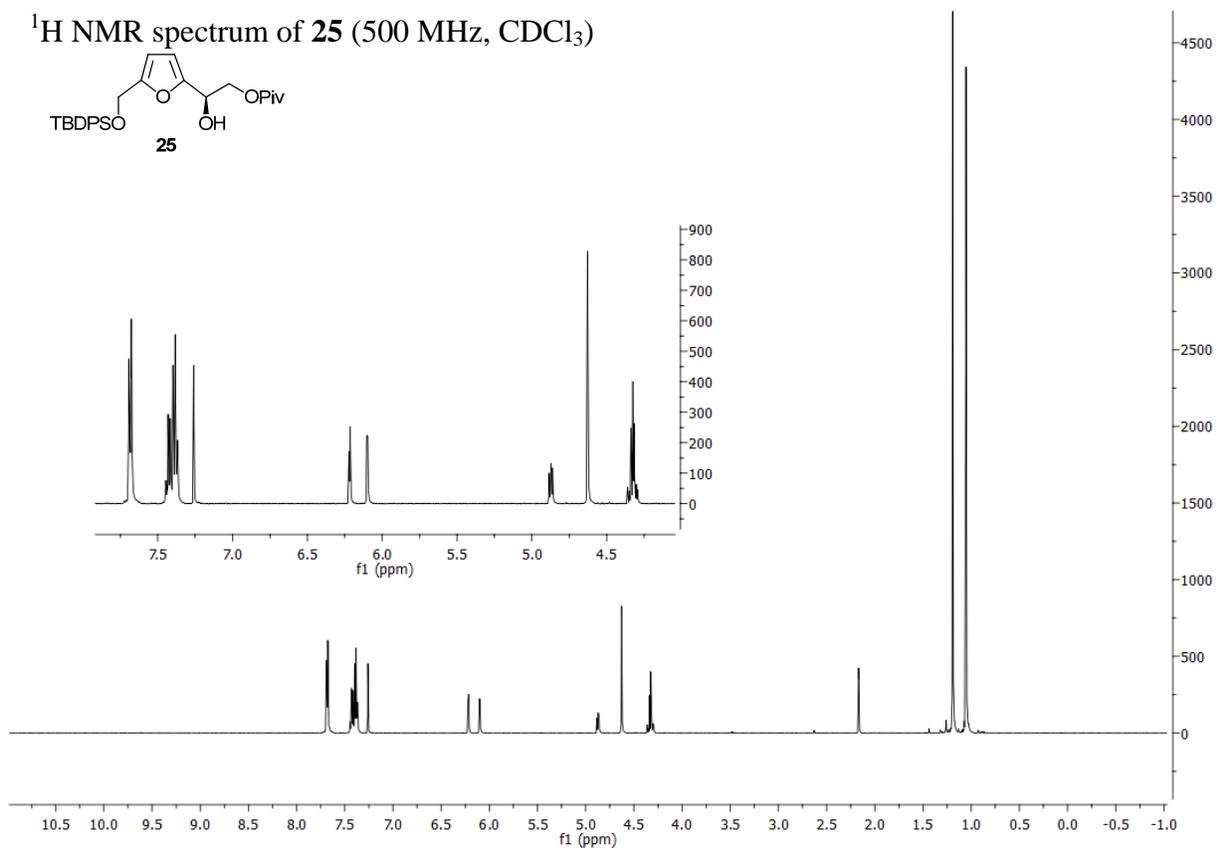
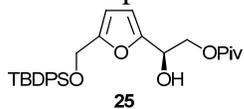
^1H NMR spectrum of **24** (600 MHz, CDCl_3)



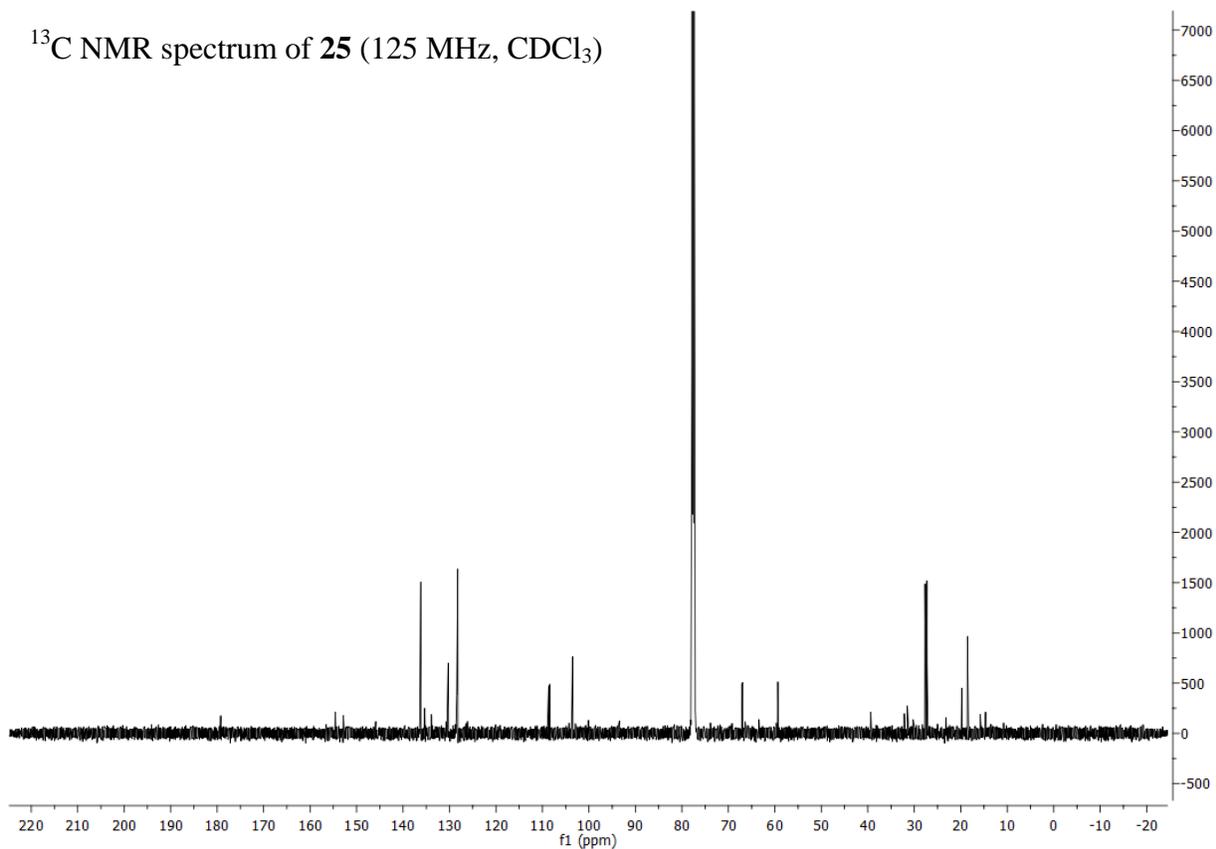
^{13}C NMR spectrum of **24** (150 MHz, CDCl_3)



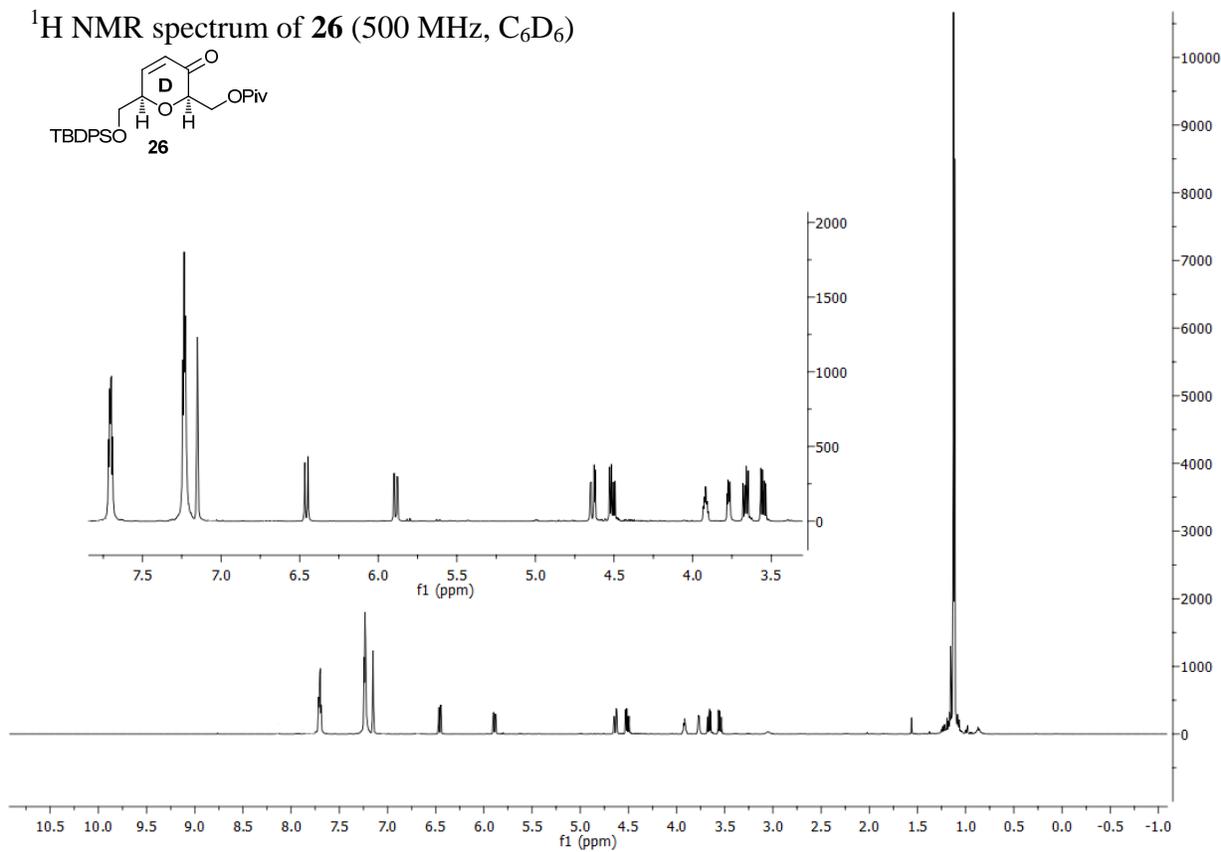
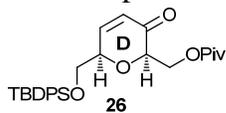
^1H NMR spectrum of **25** (500 MHz, CDCl_3)



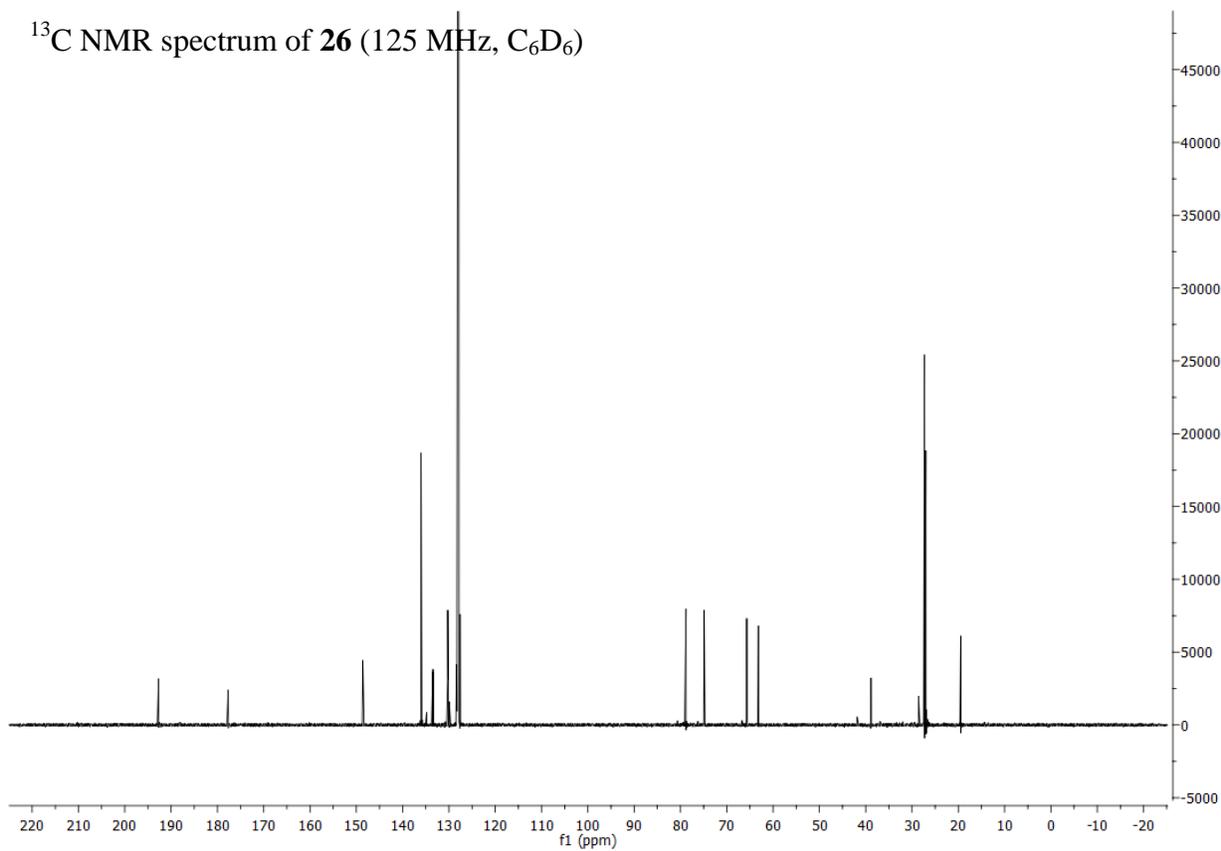
^{13}C NMR spectrum of **25** (125 MHz, CDCl_3)



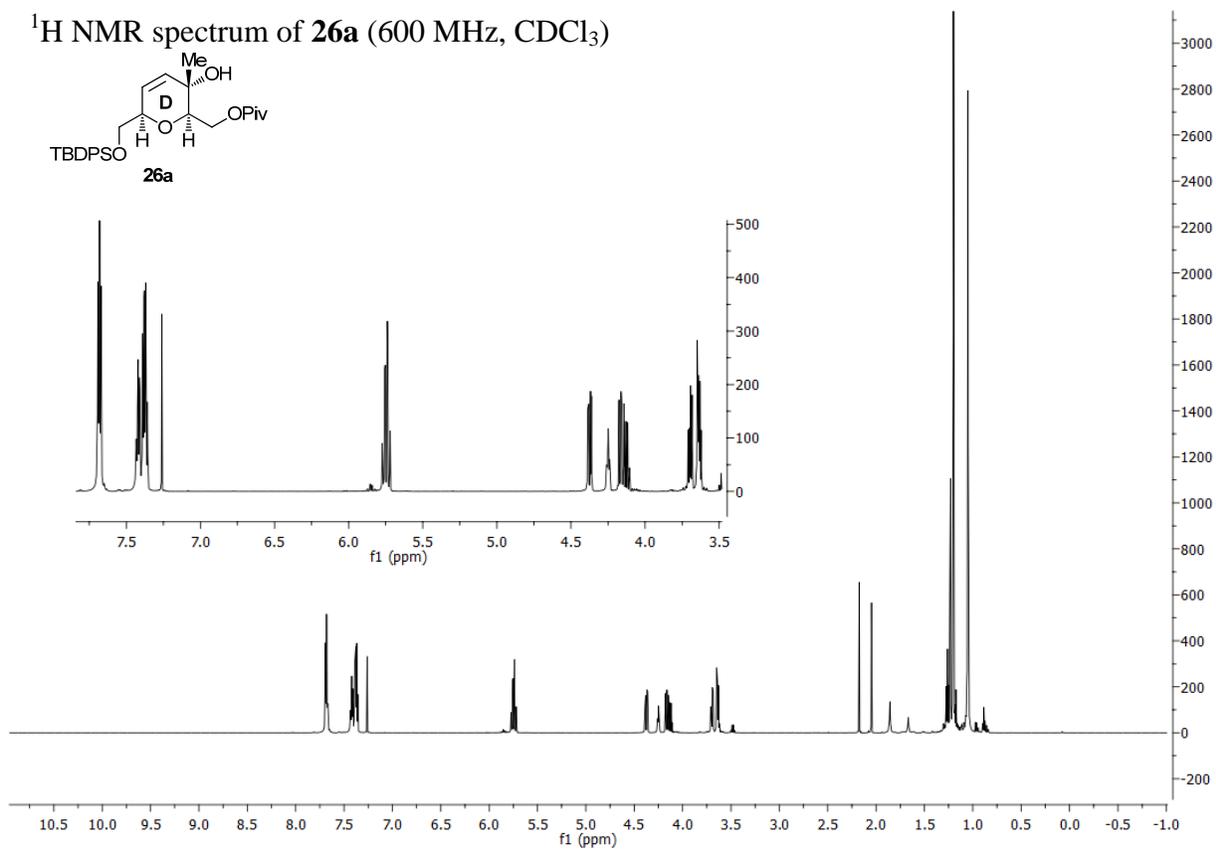
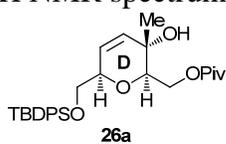
^1H NMR spectrum of **26** (500 MHz, C_6D_6)



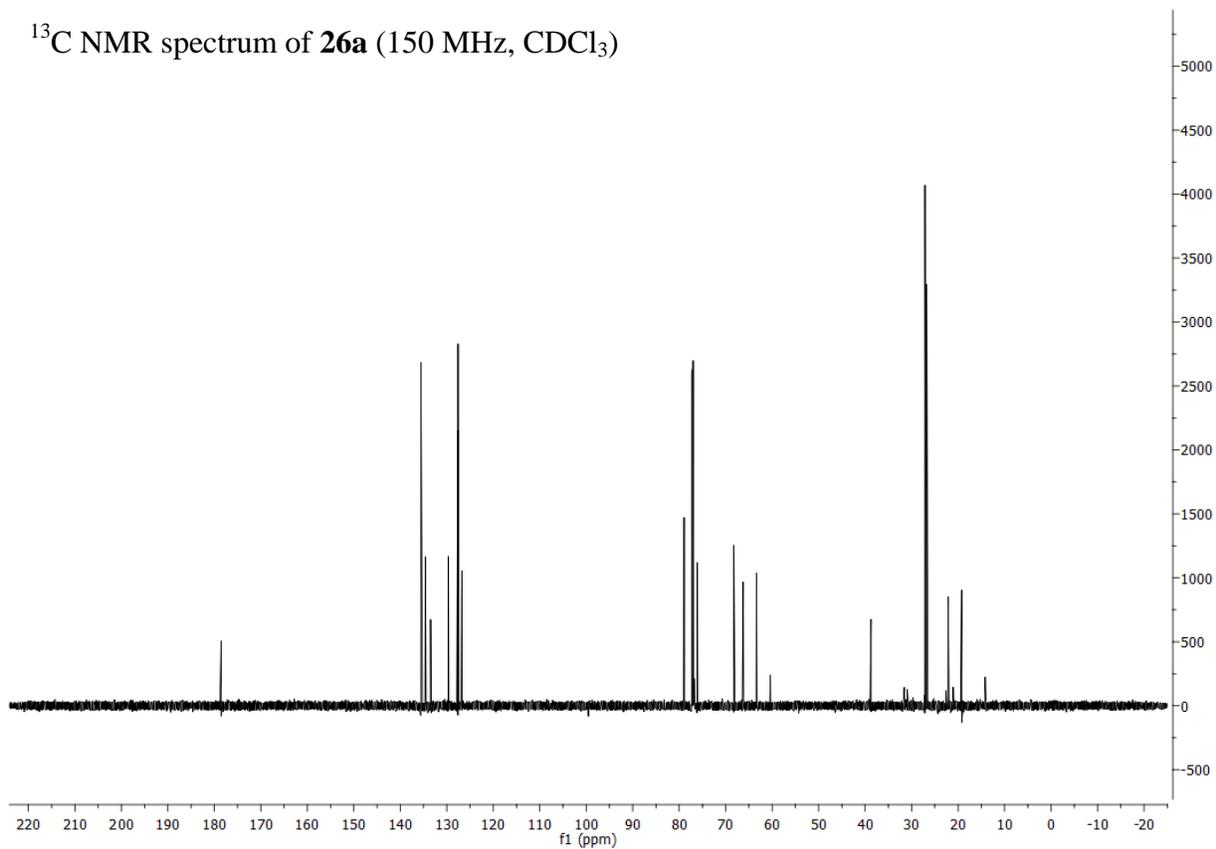
^{13}C NMR spectrum of **26** (125 MHz, C_6D_6)



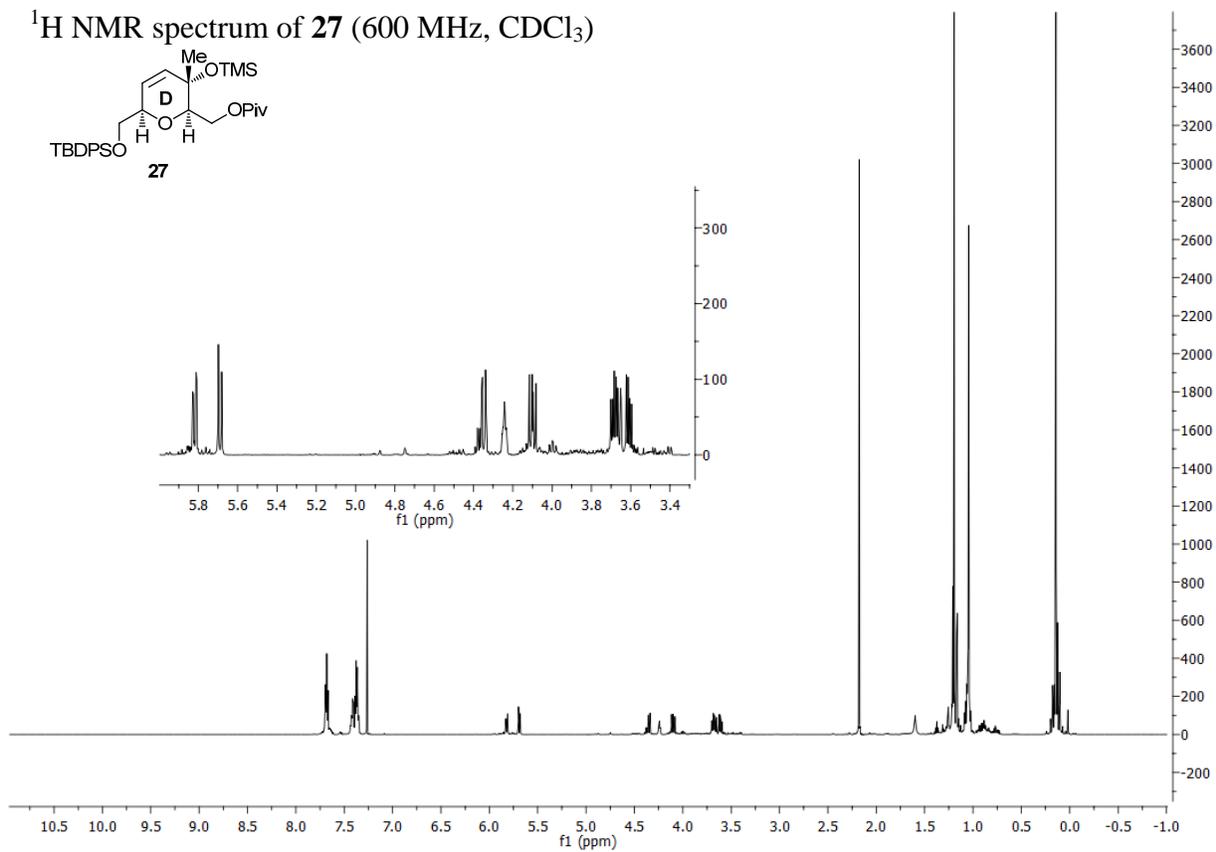
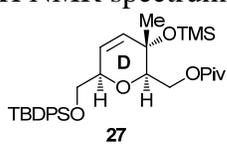
^1H NMR spectrum of **26a** (600 MHz, CDCl_3)



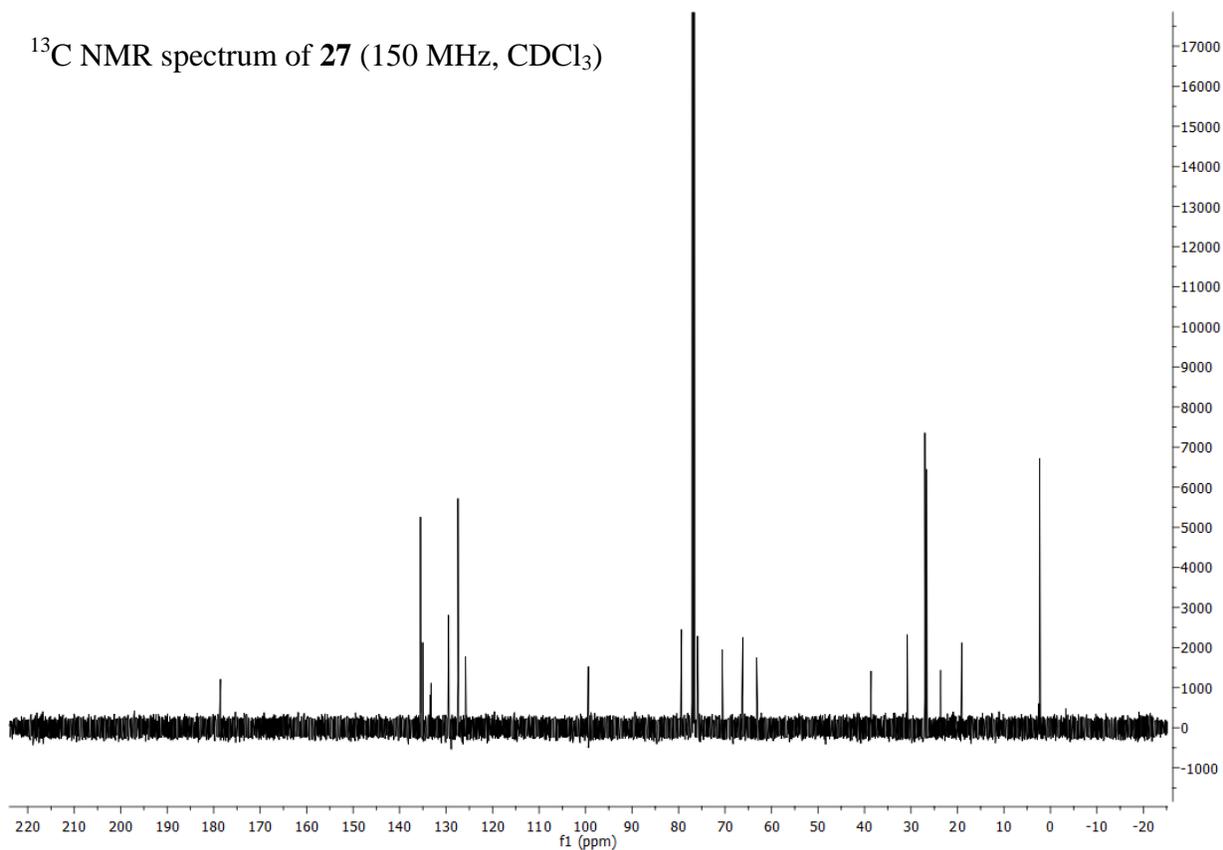
^{13}C NMR spectrum of **26a** (150 MHz, CDCl_3)



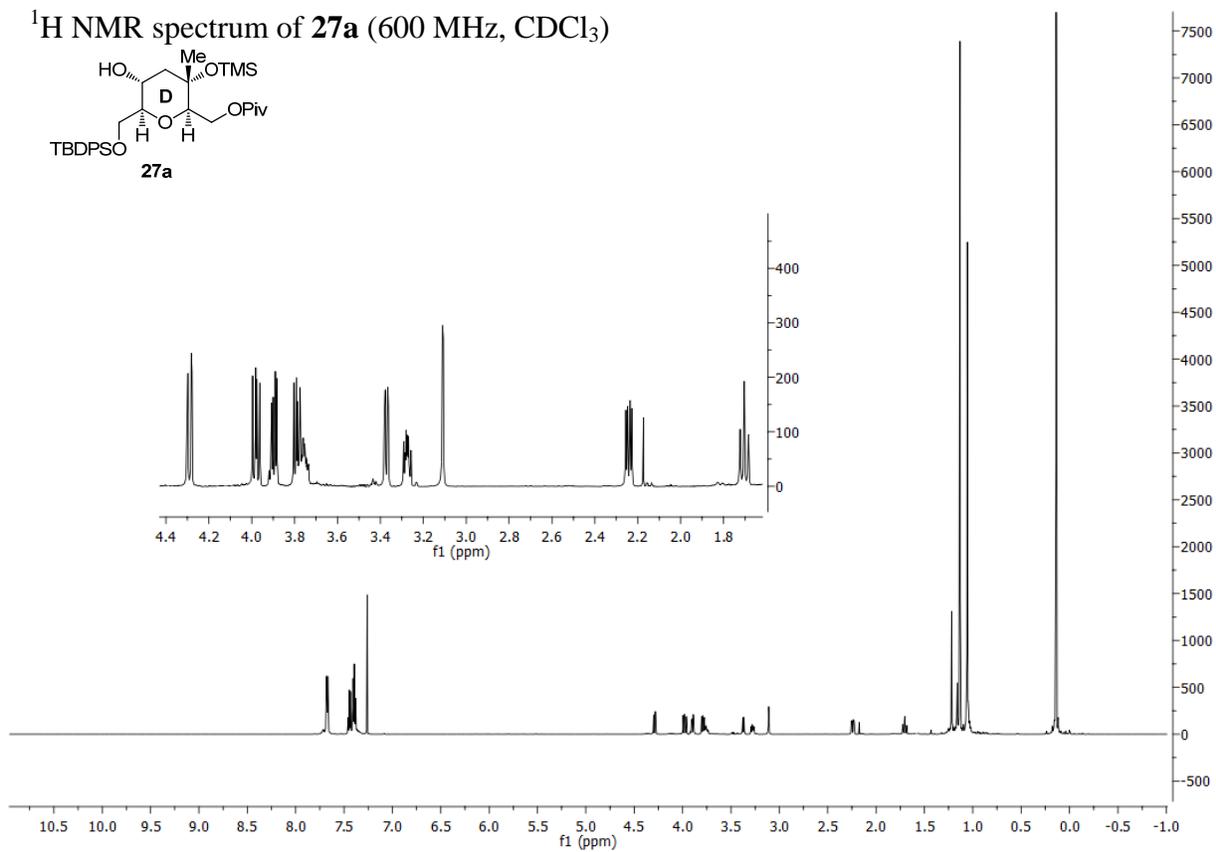
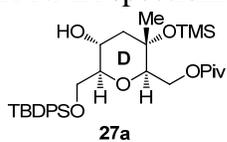
^1H NMR spectrum of **27** (600 MHz, CDCl_3)



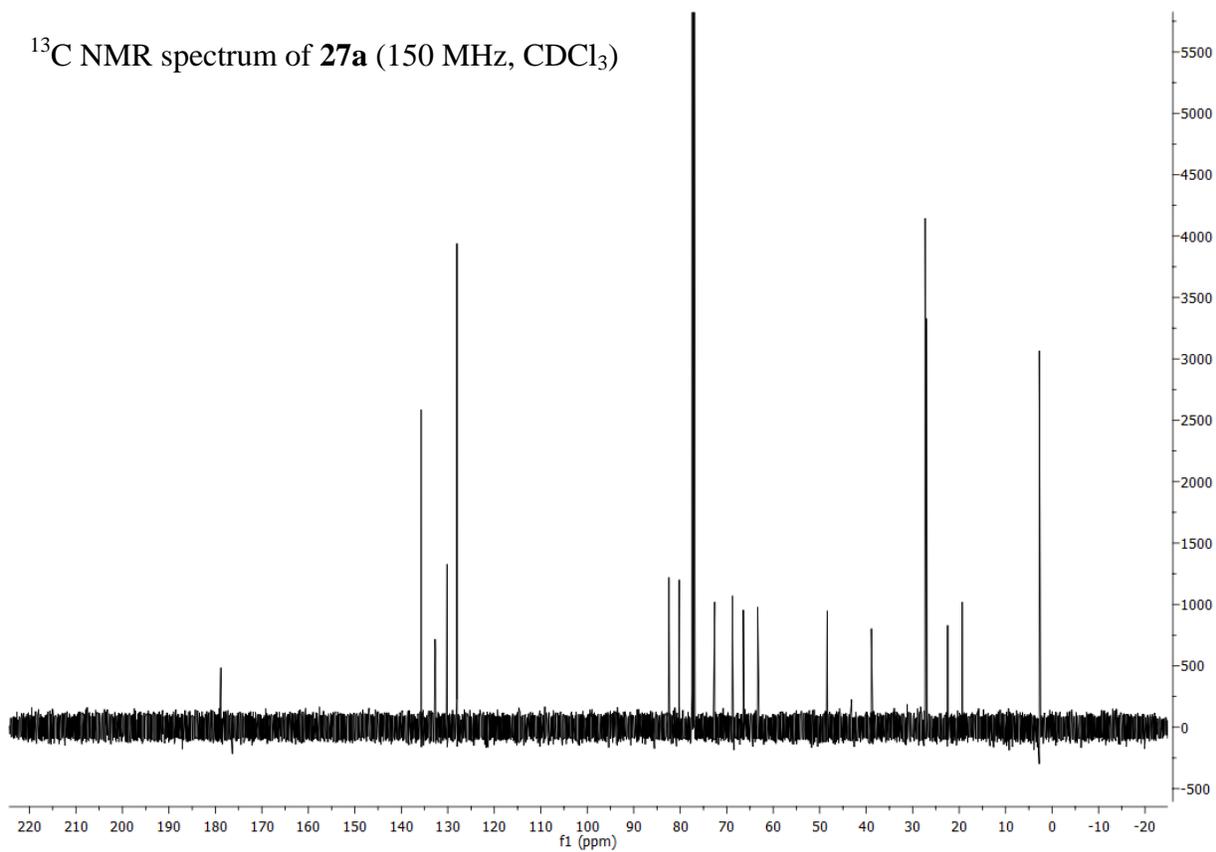
^{13}C NMR spectrum of **27** (150 MHz, CDCl_3)



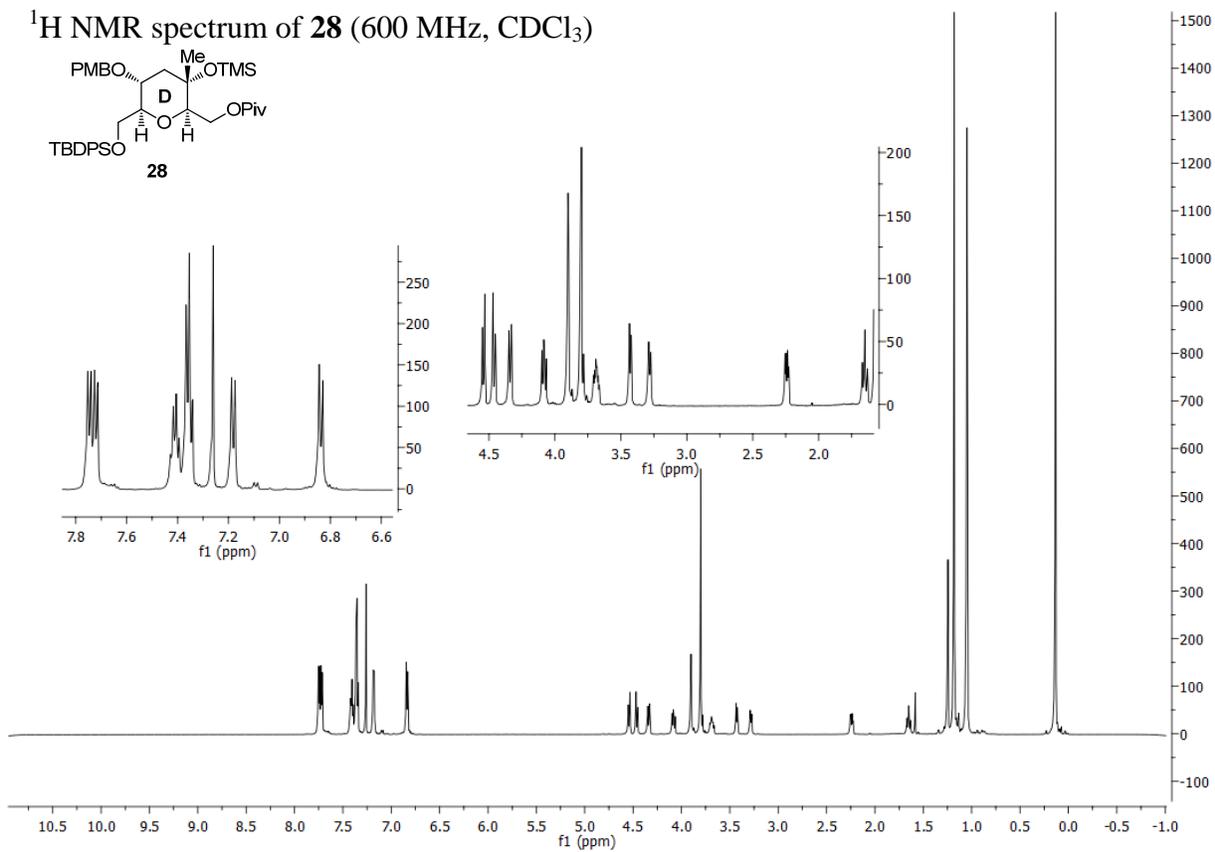
^1H NMR spectrum of **27a** (600 MHz, CDCl_3)



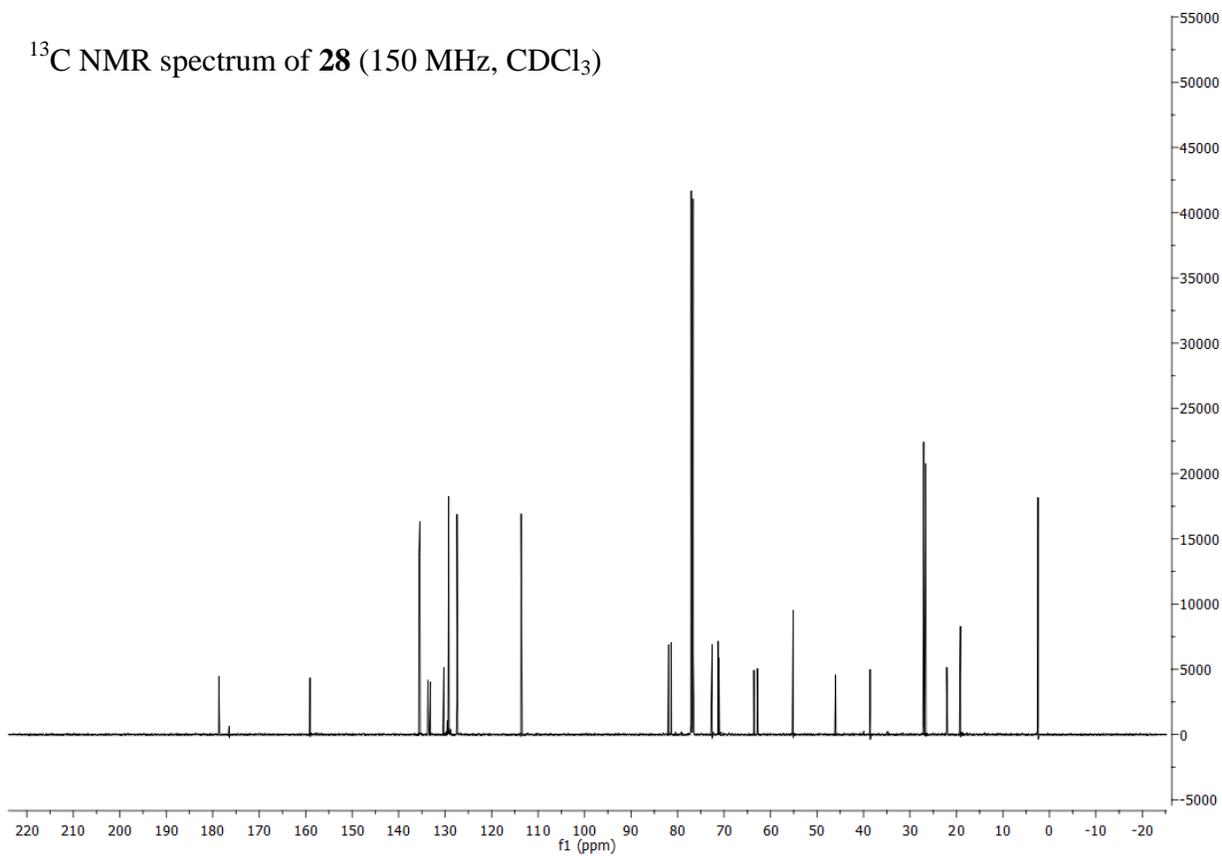
^{13}C NMR spectrum of **27a** (150 MHz, CDCl_3)



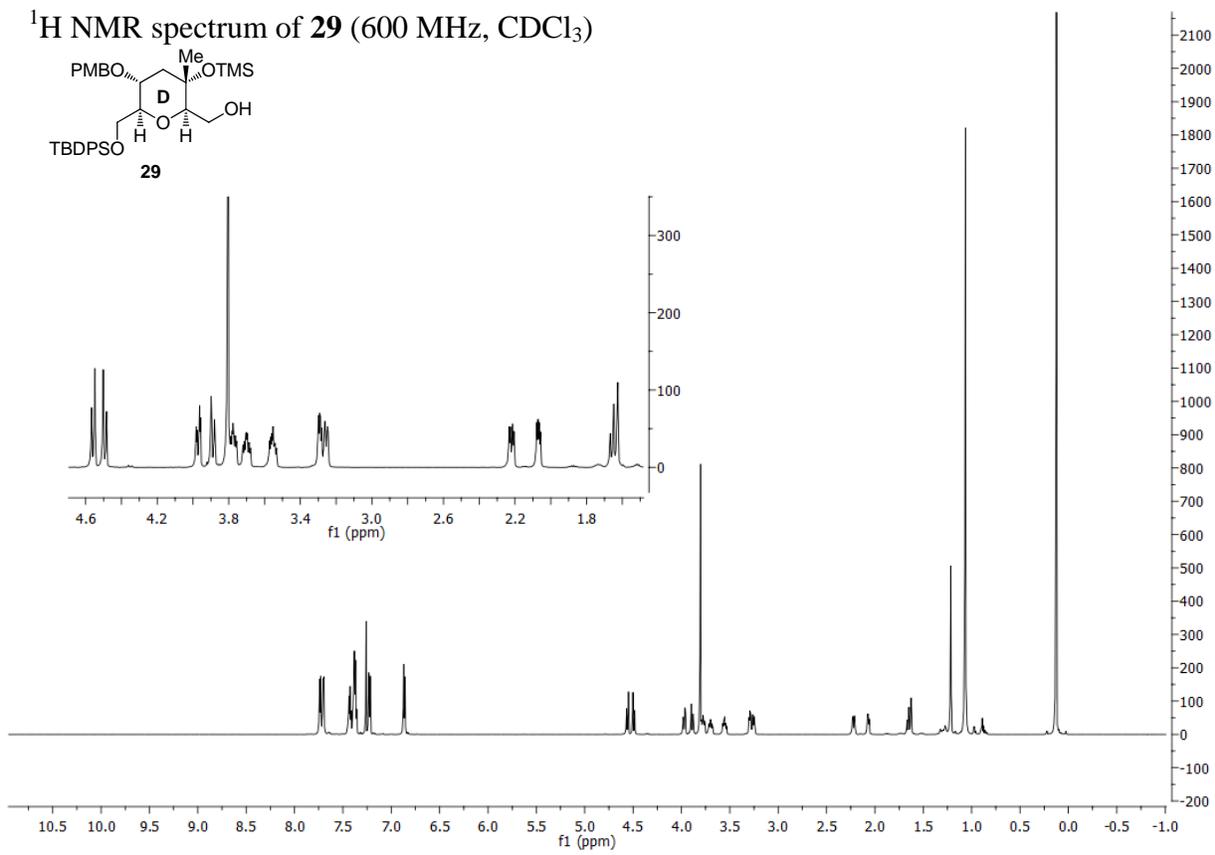
^1H NMR spectrum of **28** (600 MHz, CDCl_3)



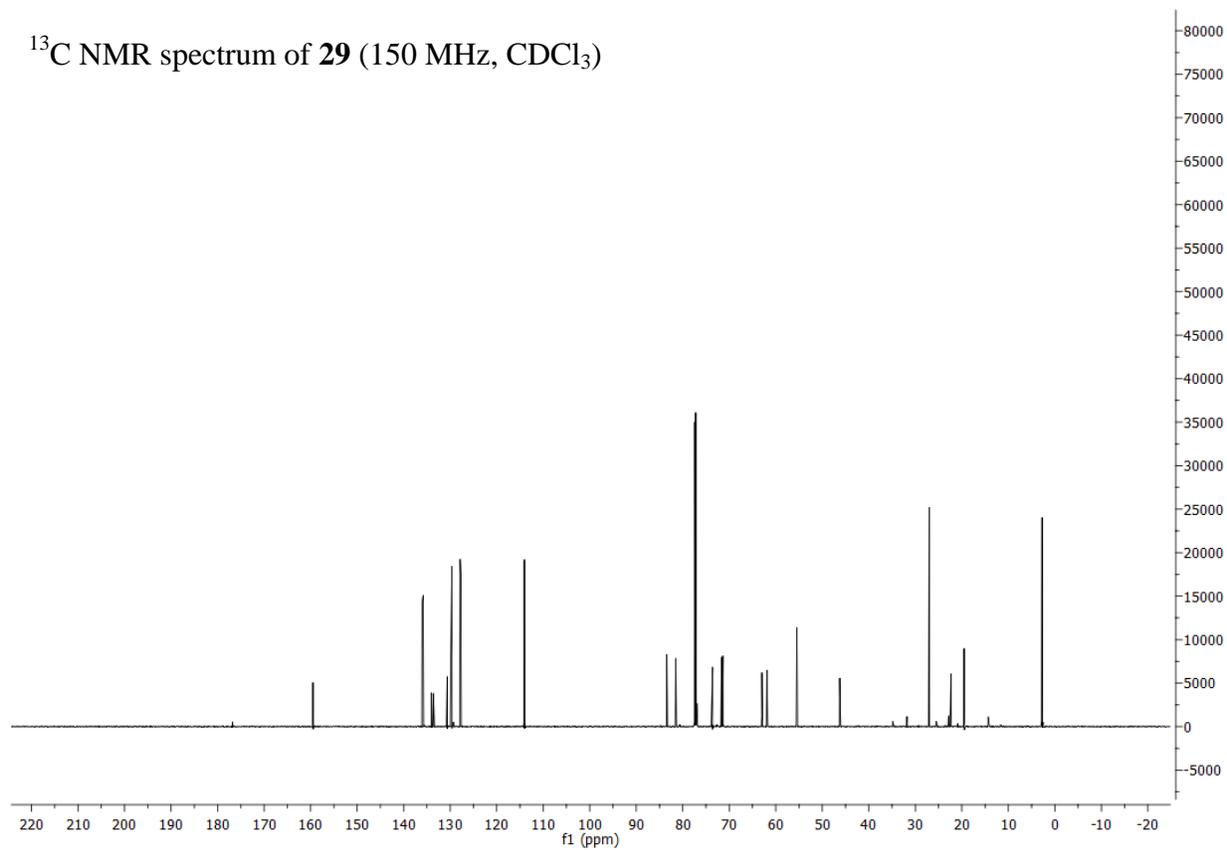
^{13}C NMR spectrum of **28** (150 MHz, CDCl_3)



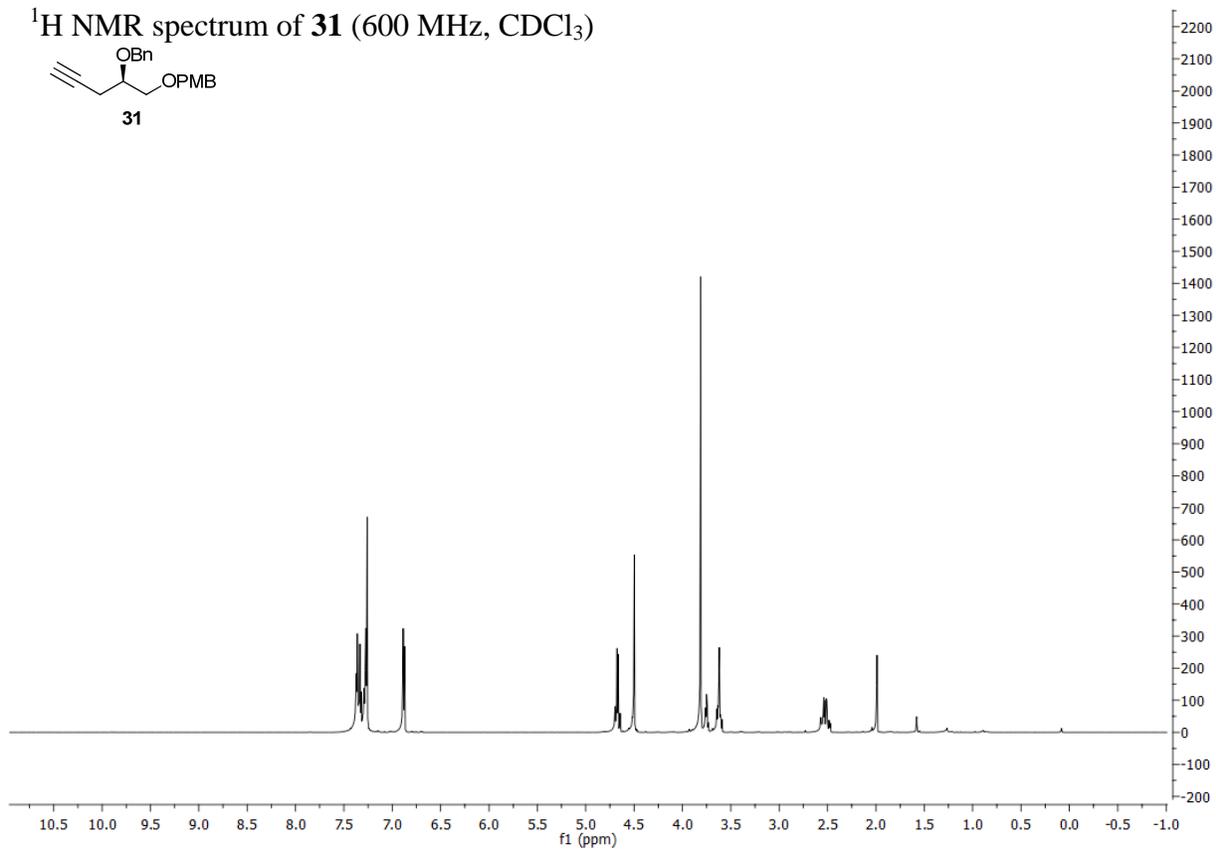
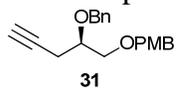
^1H NMR spectrum of **29** (600 MHz, CDCl_3)



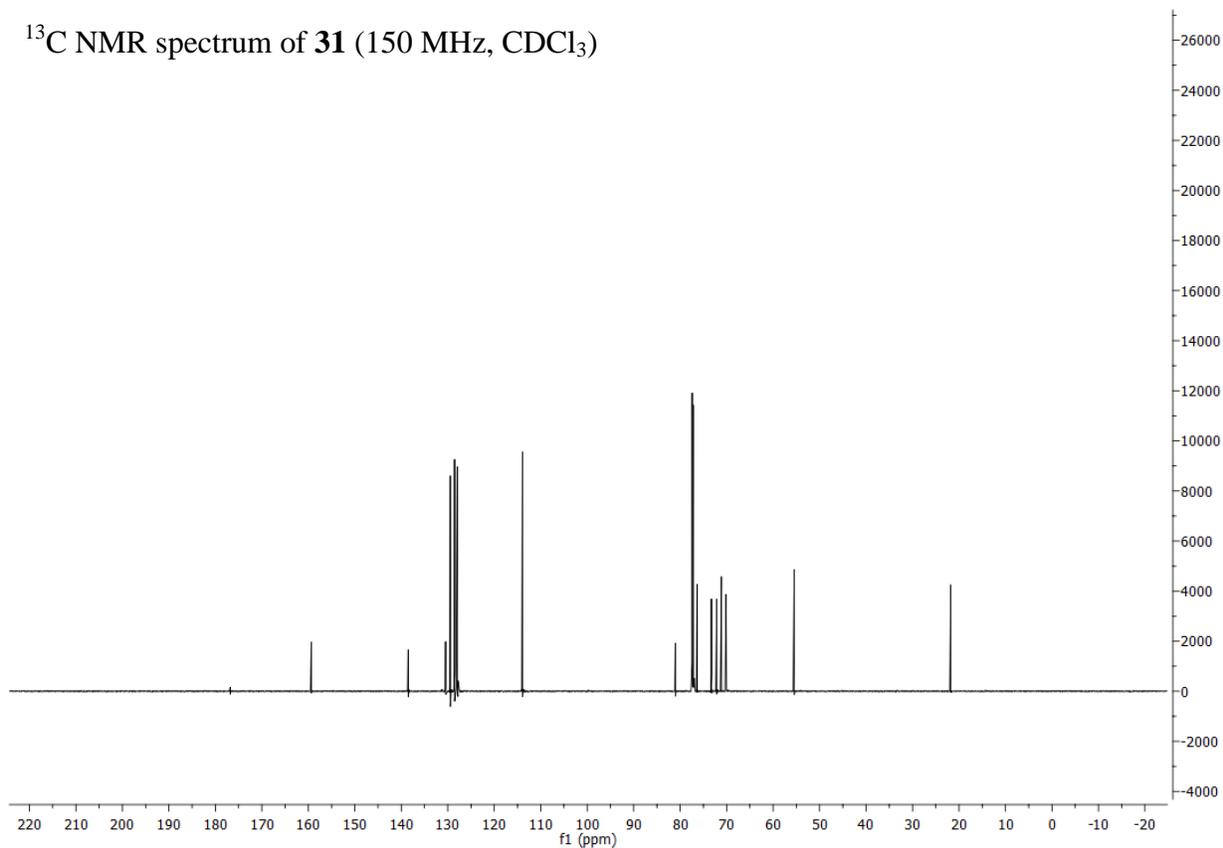
^{13}C NMR spectrum of **29** (150 MHz, CDCl_3)



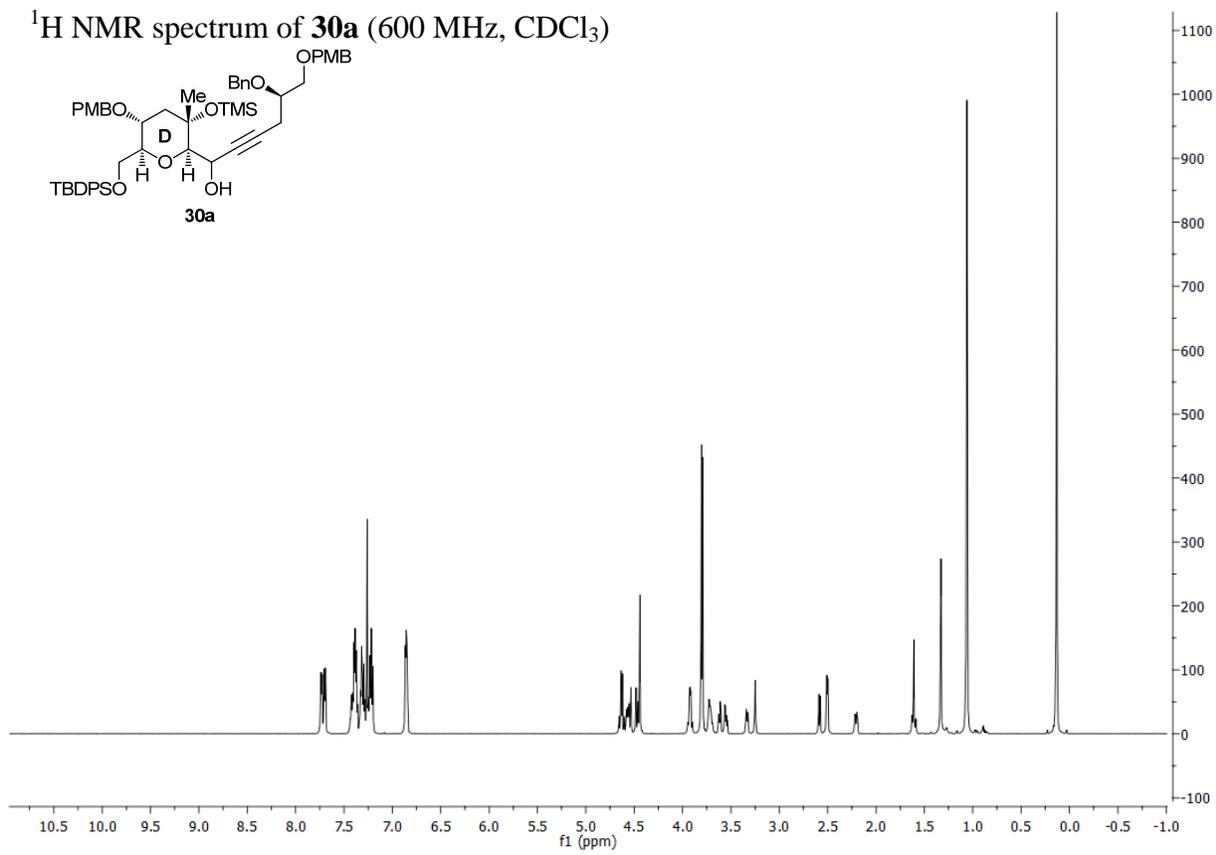
^1H NMR spectrum of **31** (600 MHz, CDCl_3)



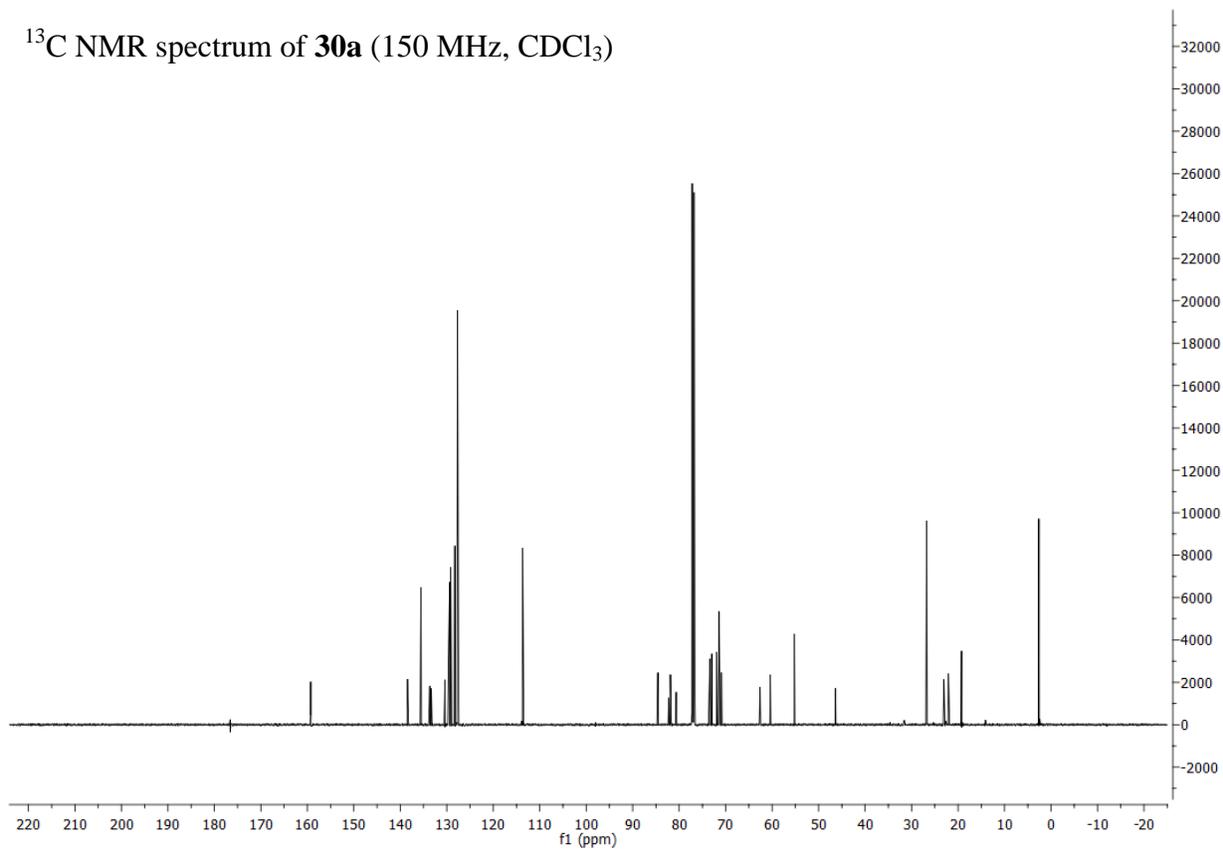
^{13}C NMR spectrum of **31** (150 MHz, CDCl_3)



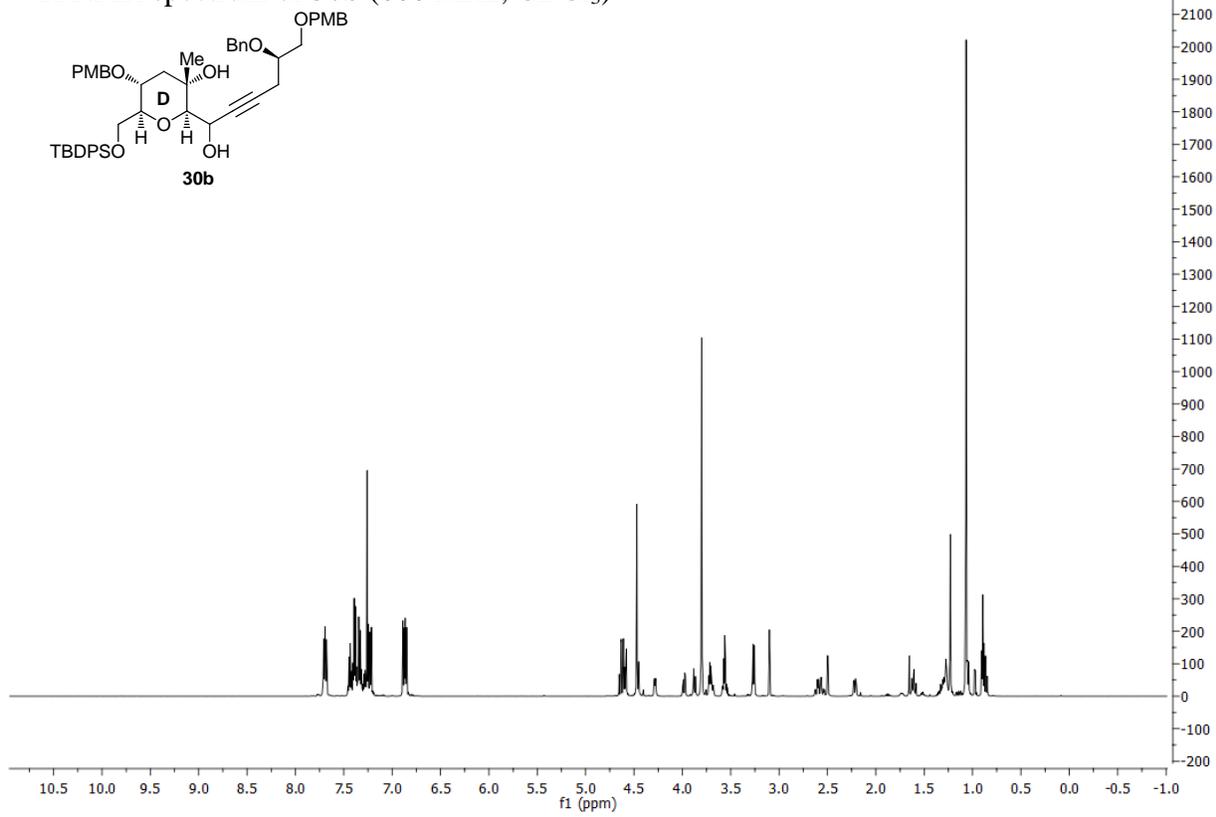
^1H NMR spectrum of **30a** (600 MHz, CDCl_3)



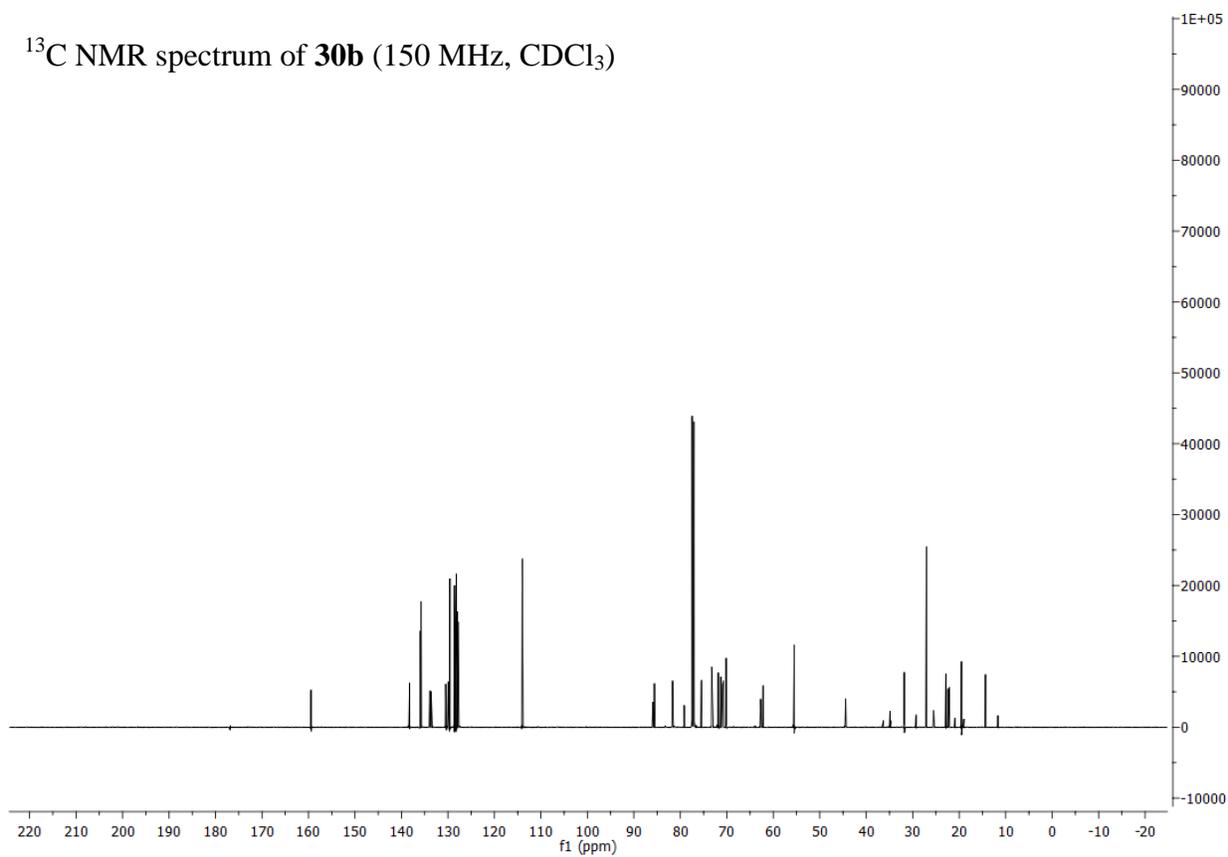
^{13}C NMR spectrum of **30a** (150 MHz, CDCl_3)



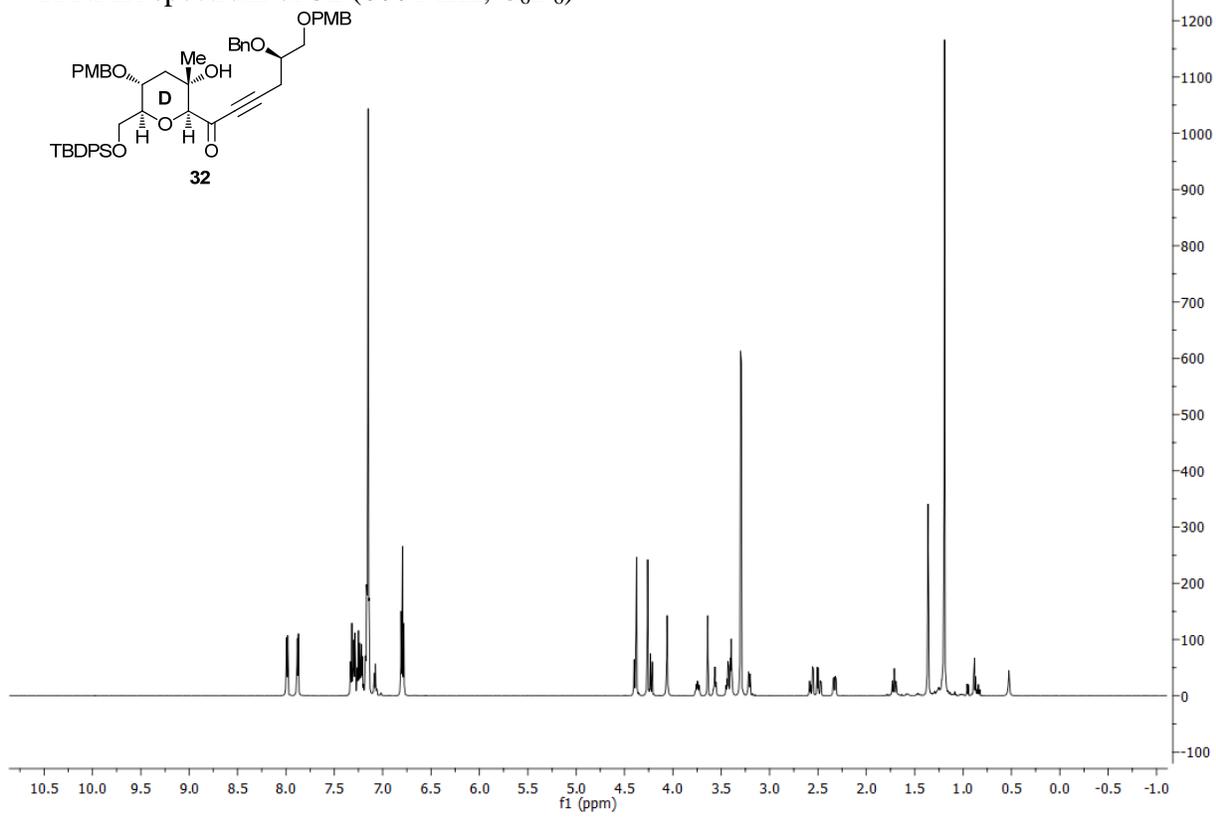
^1H NMR spectrum of **30b** (600 MHz, CDCl_3)



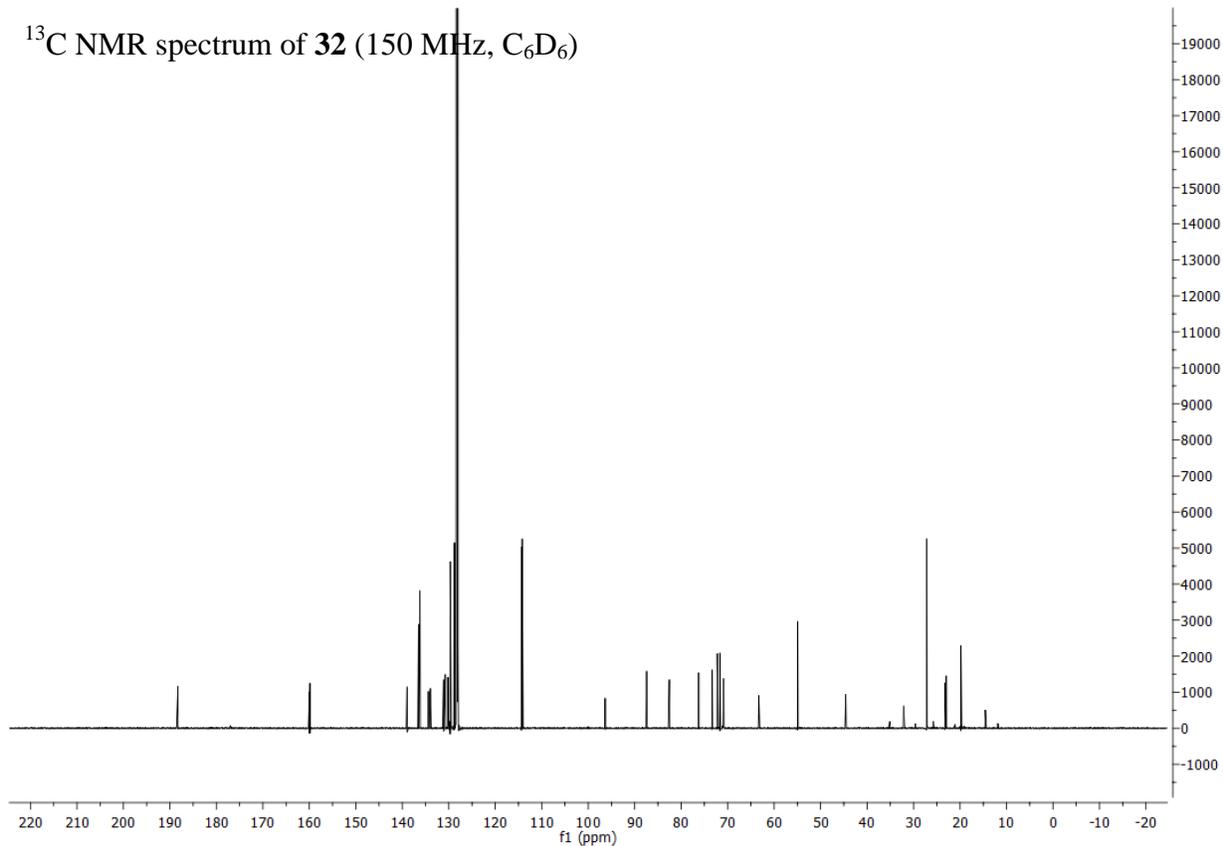
^{13}C NMR spectrum of **30b** (150 MHz, CDCl_3)



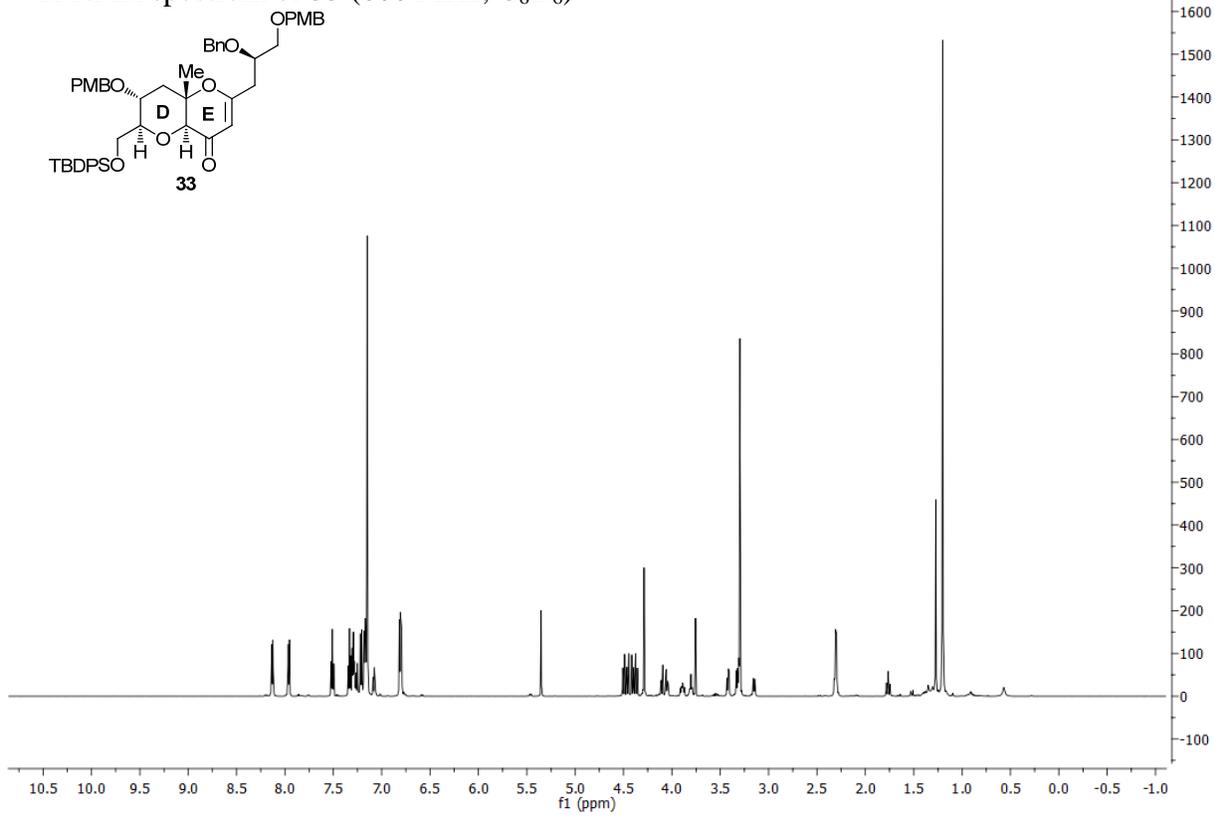
^1H NMR spectrum of **32** (600 MHz, C_6D_6)



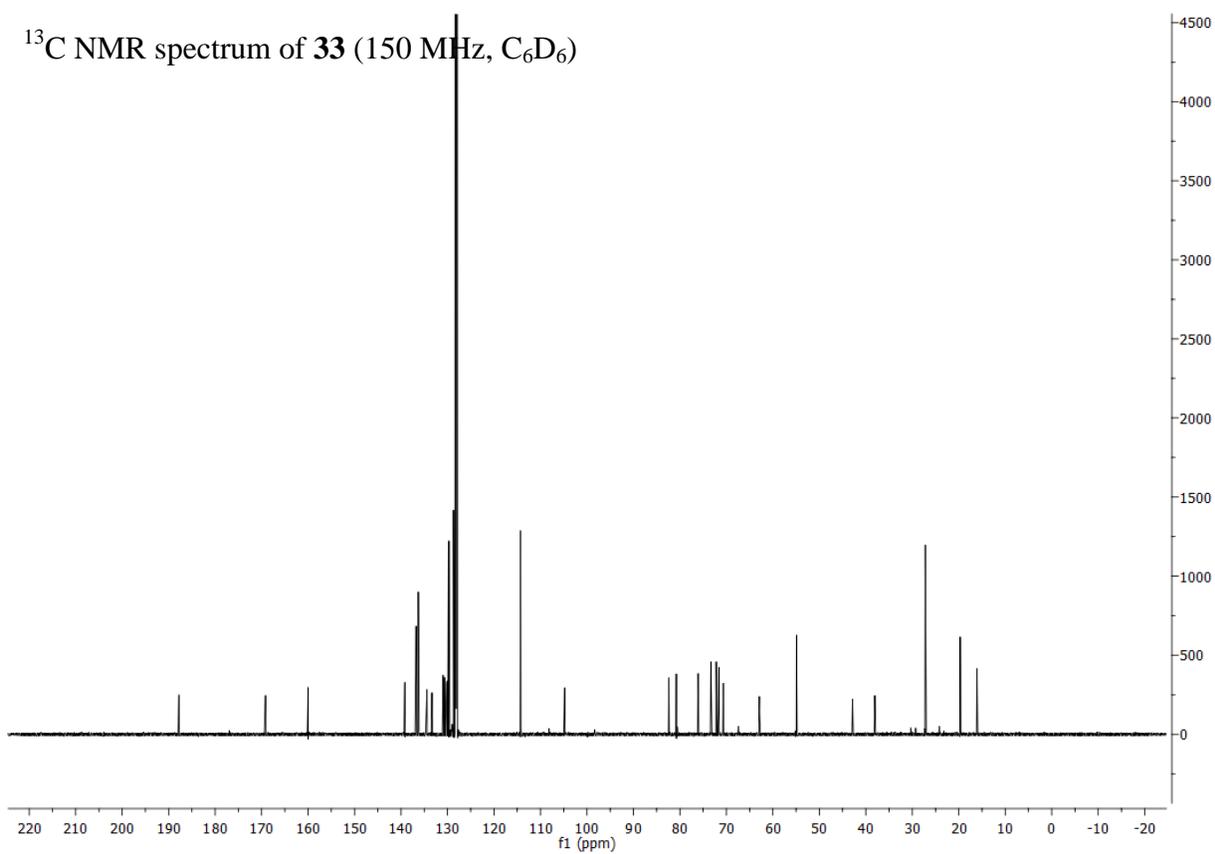
^{13}C NMR spectrum of **32** (150 MHz, C_6D_6)



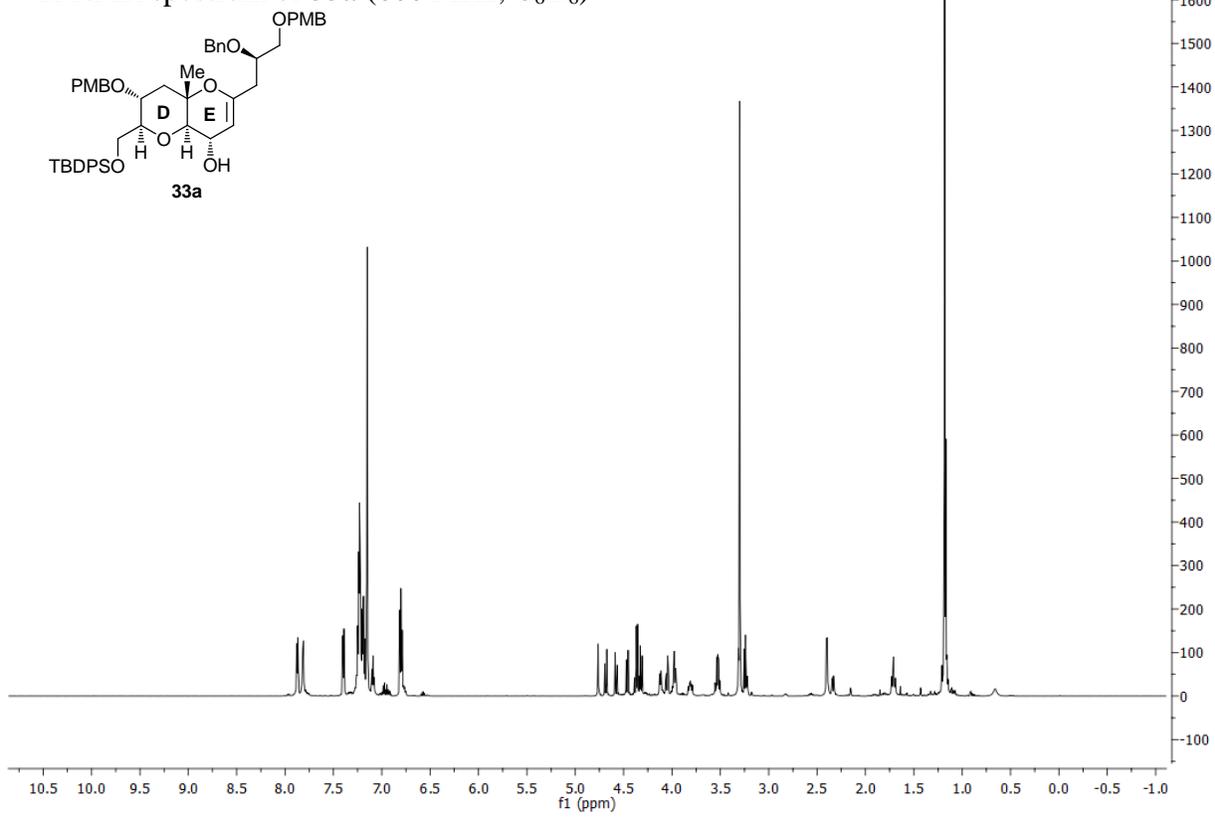
^1H NMR spectrum of **33** (600 MHz, C_6D_6)



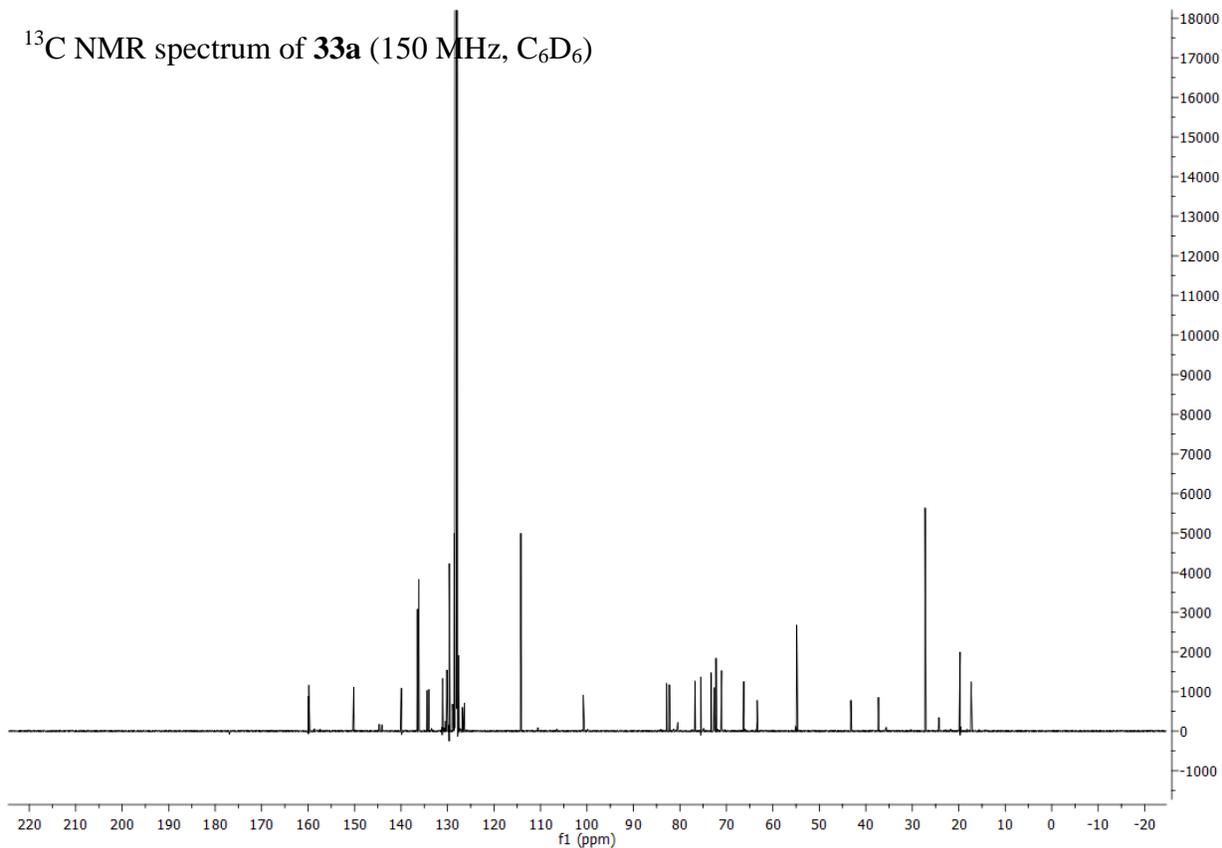
^{13}C NMR spectrum of **33** (150 MHz, C_6D_6)



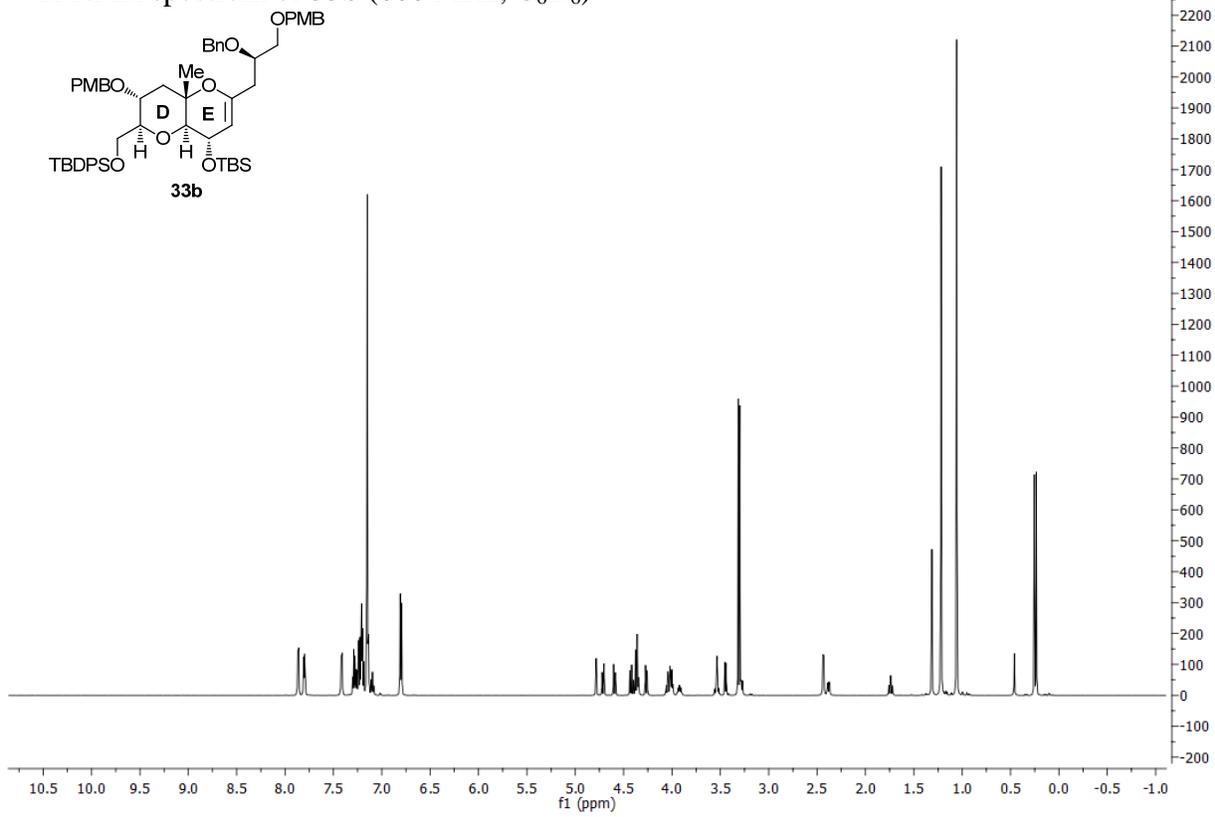
^1H NMR spectrum of **33a** (600 MHz, C_6D_6)



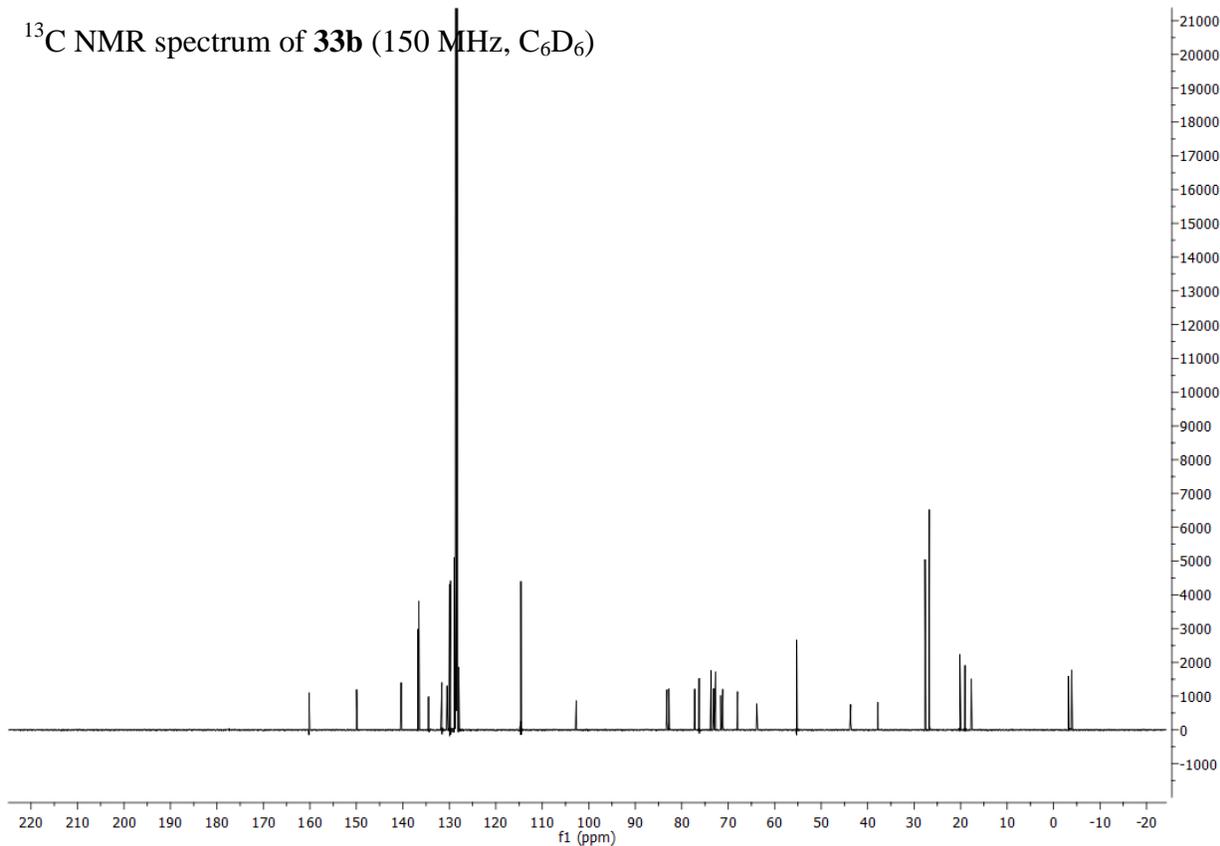
^{13}C NMR spectrum of **33a** (150 MHz, C_6D_6)



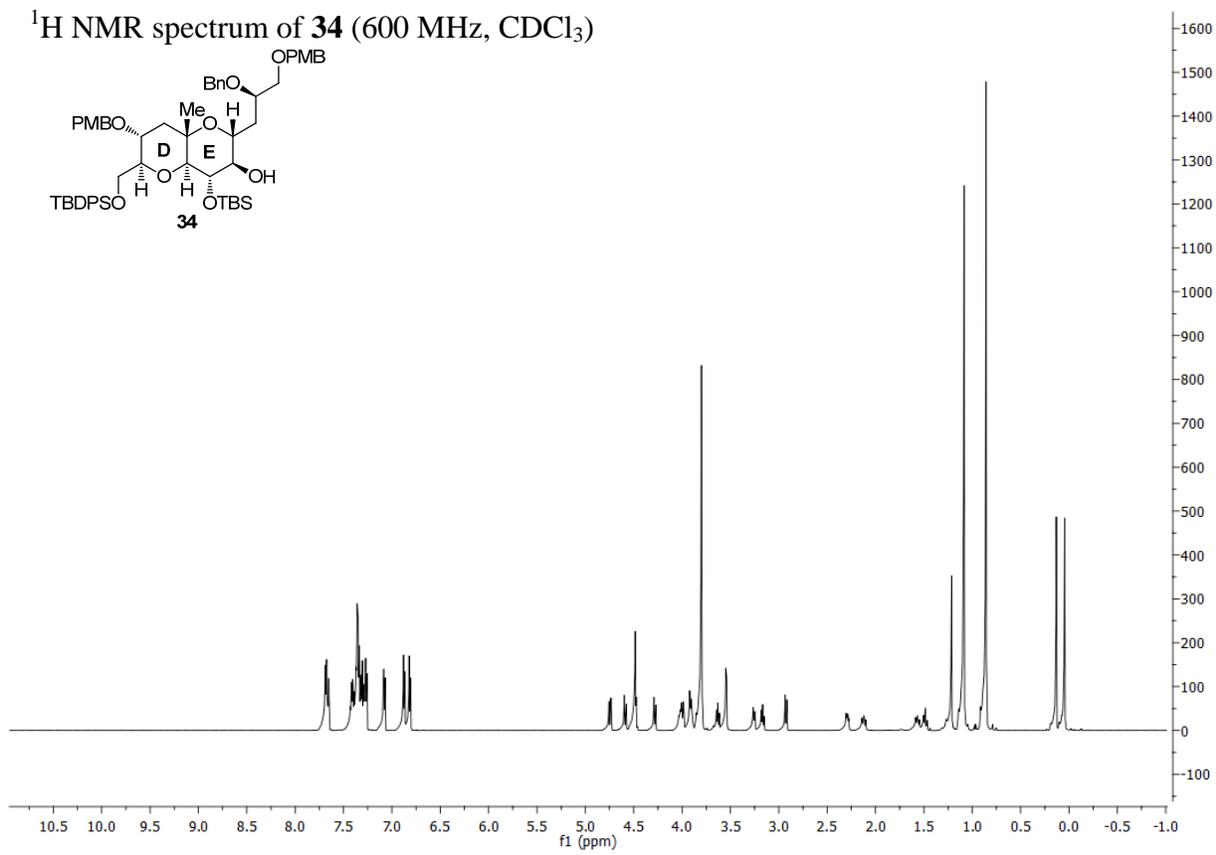
^1H NMR spectrum of **33b** (600 MHz, C_6D_6)



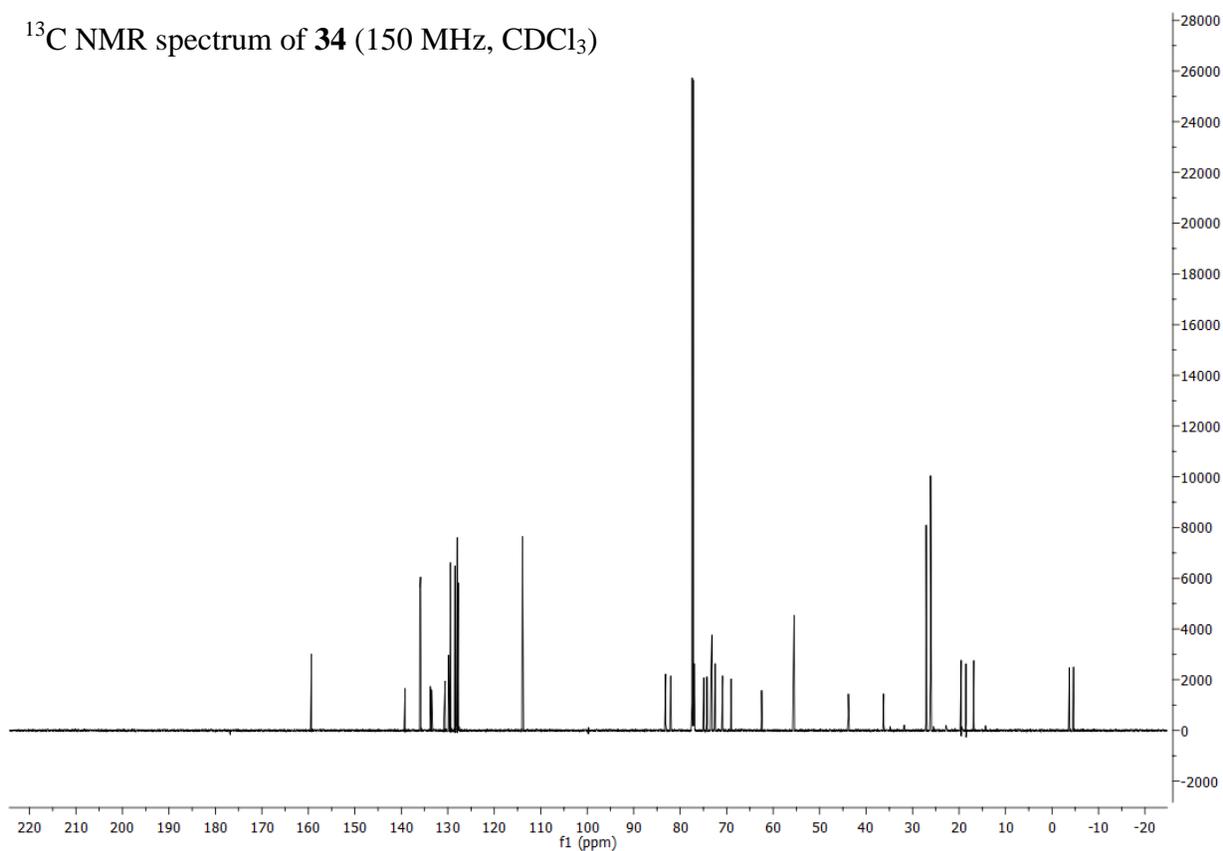
^{13}C NMR spectrum of **33b** (150 MHz, C_6D_6)



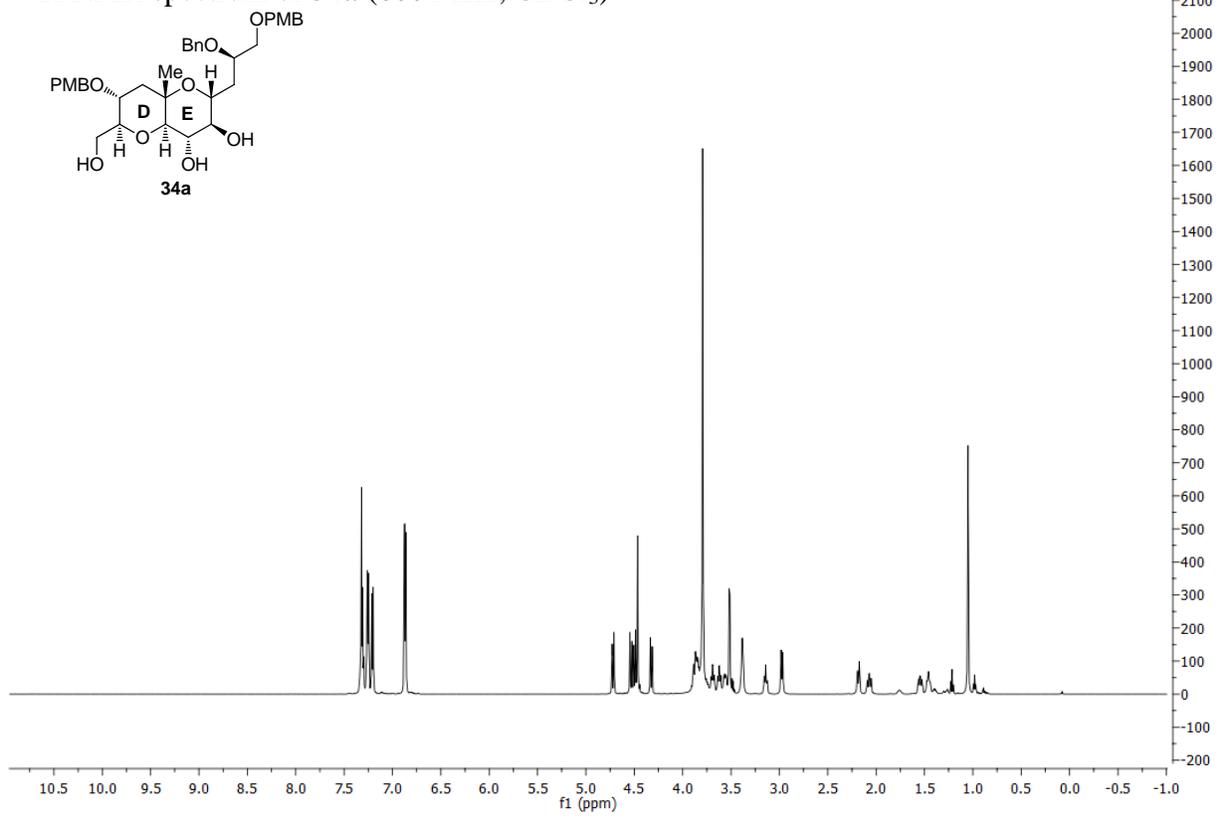
^1H NMR spectrum of **34** (600 MHz, CDCl_3)



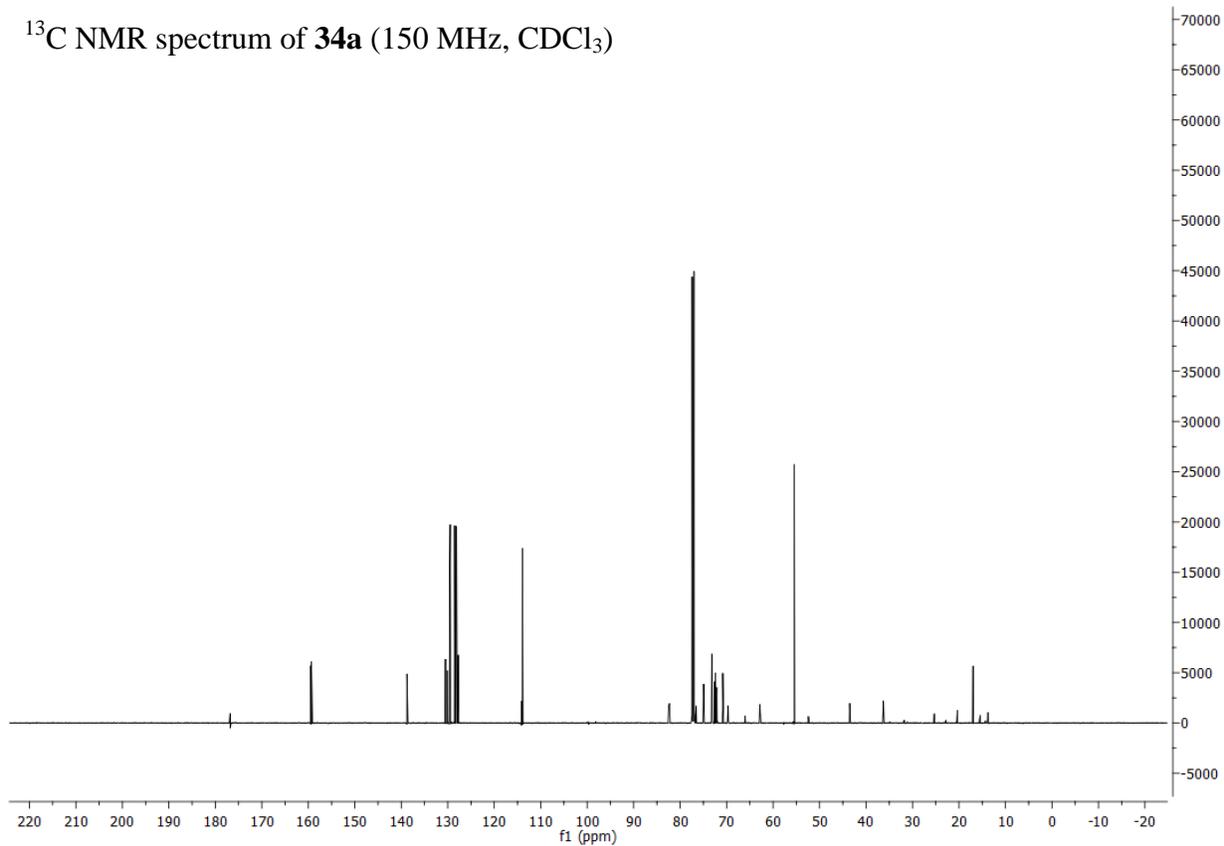
^{13}C NMR spectrum of **34** (150 MHz, CDCl_3)



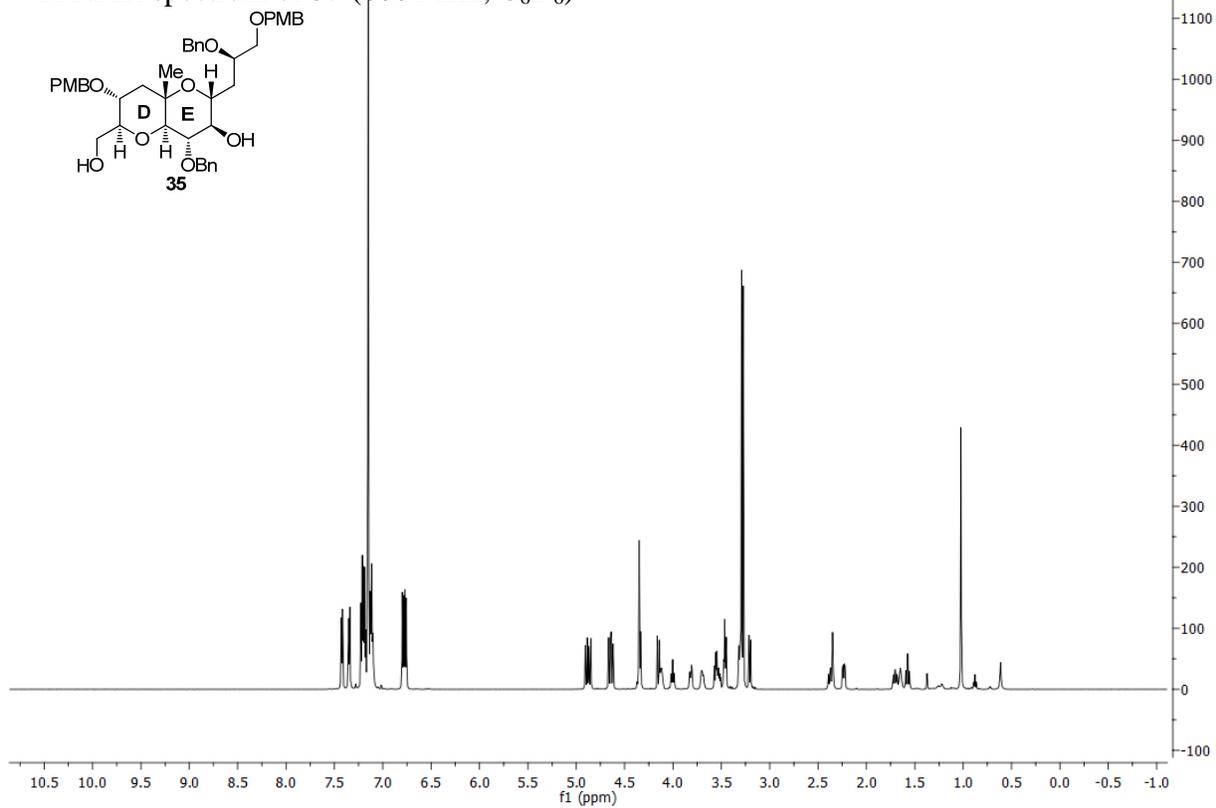
^1H NMR spectrum of **34a** (600 MHz, CDCl_3)



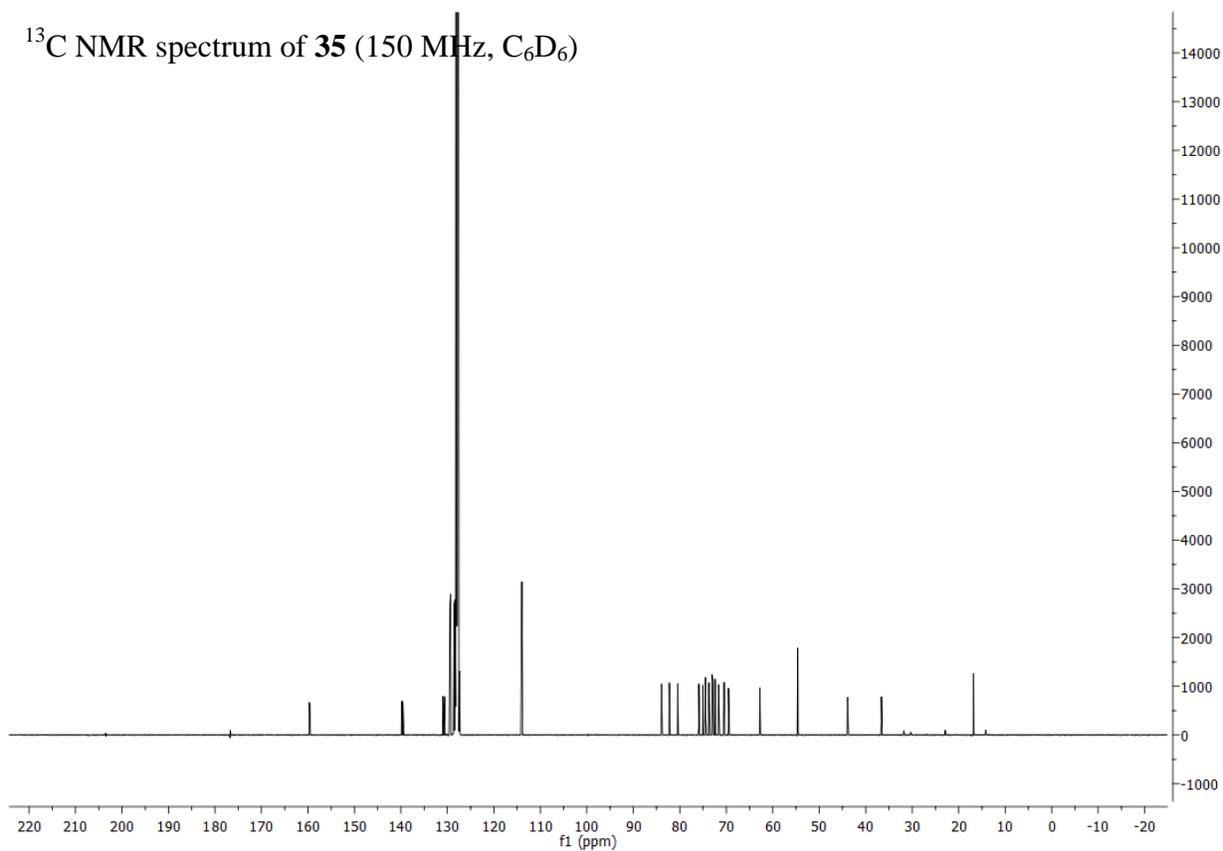
^{13}C NMR spectrum of **34a** (150 MHz, CDCl_3)



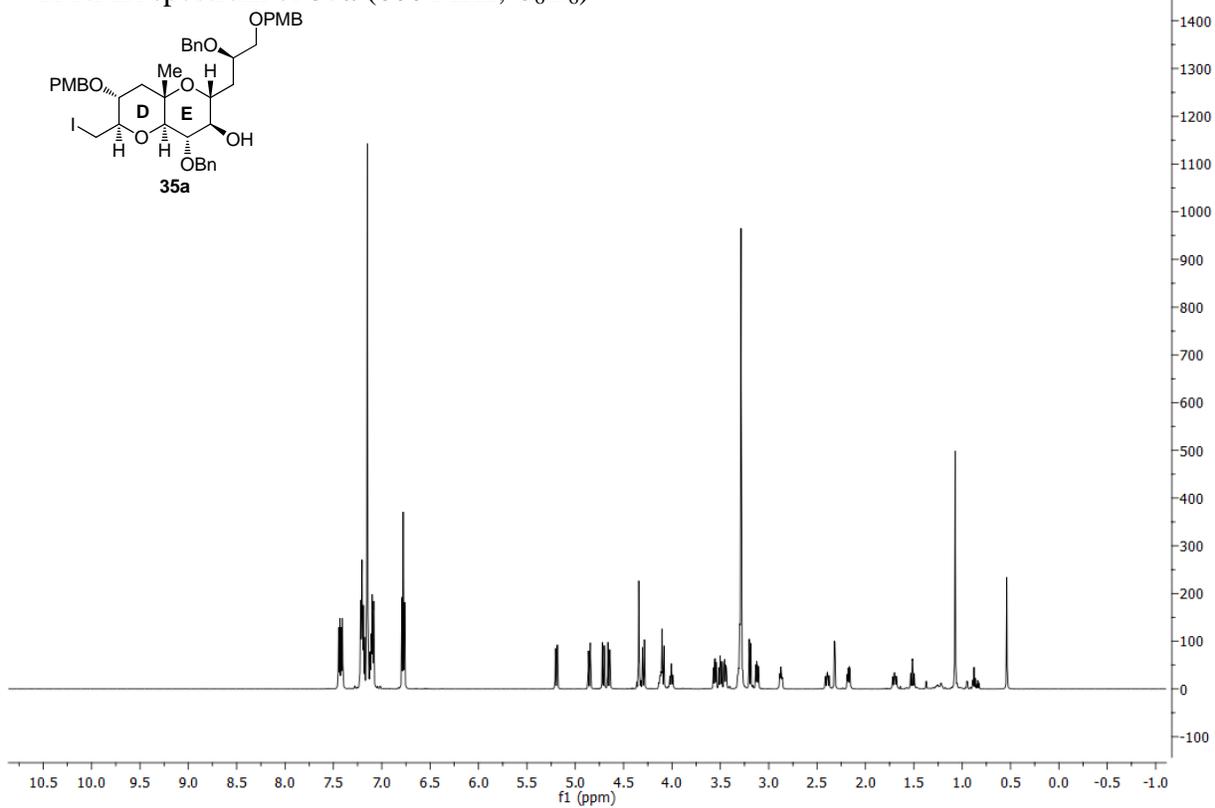
^1H NMR spectrum of **35** (600 MHz, C_6D_6)



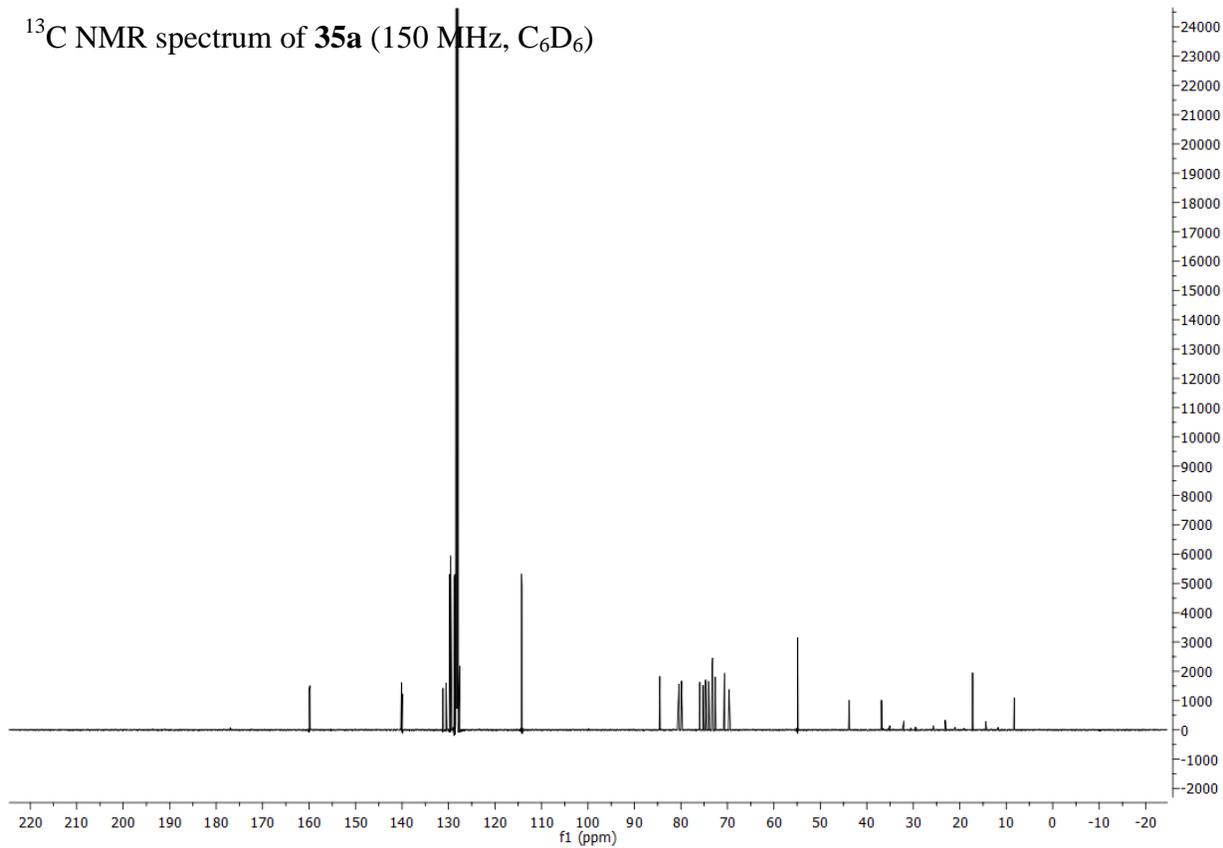
^{13}C NMR spectrum of **35** (150 MHz, C_6D_6)



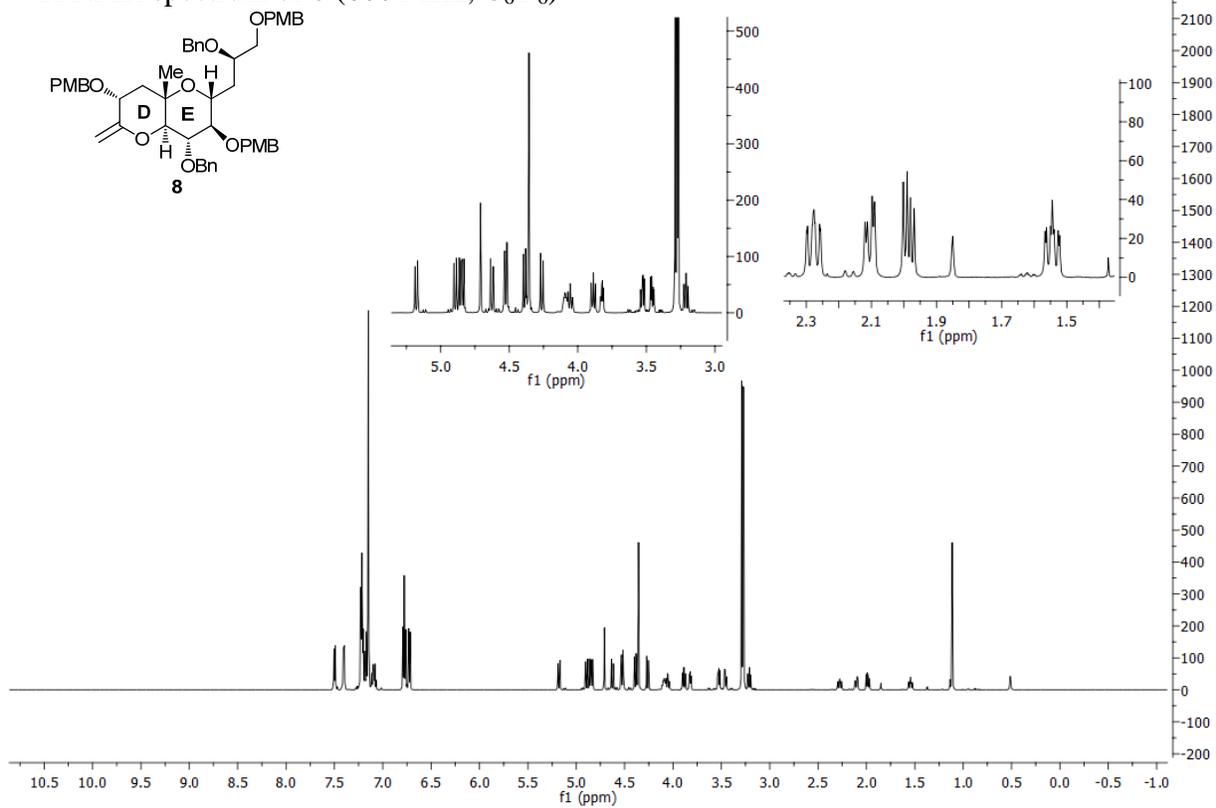
^1H NMR spectrum of **35a** (600 MHz, C_6D_6)



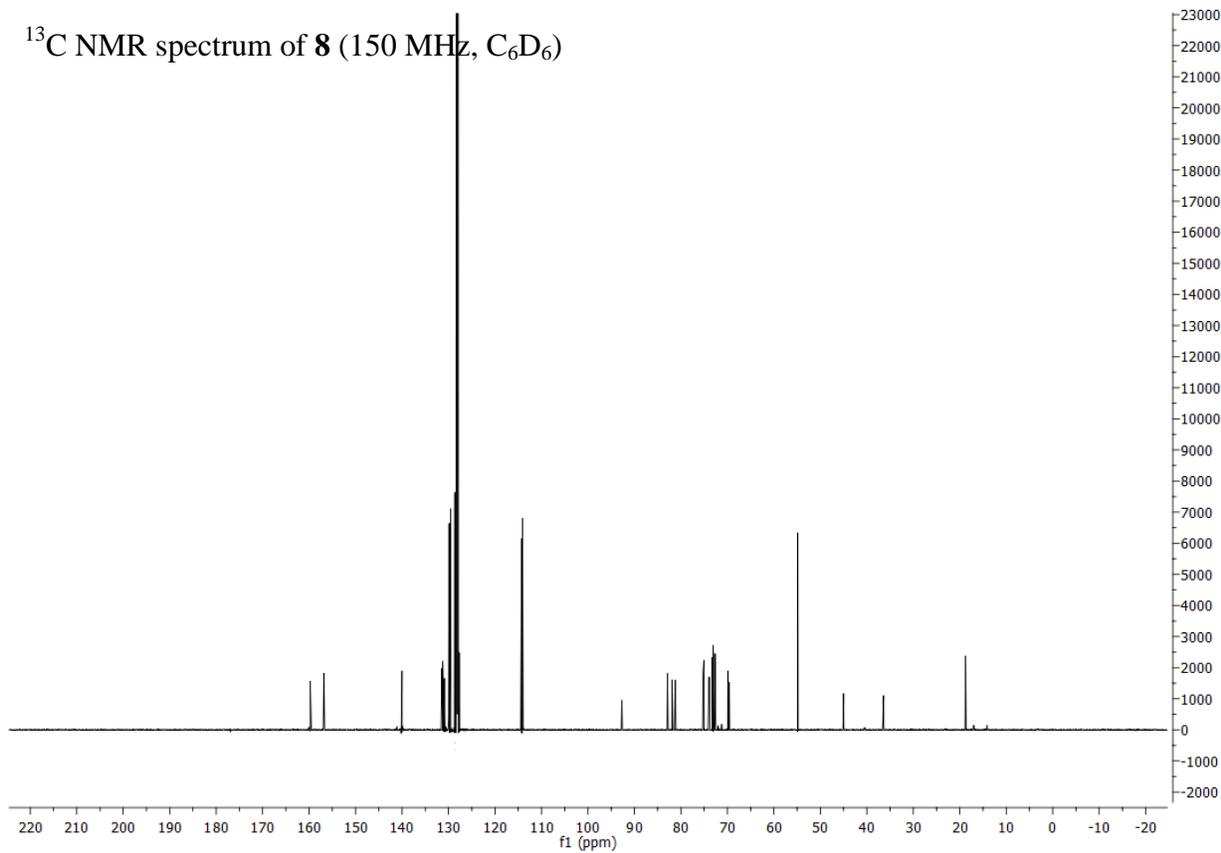
^{13}C NMR spectrum of **35a** (150 MHz, C_6D_6)



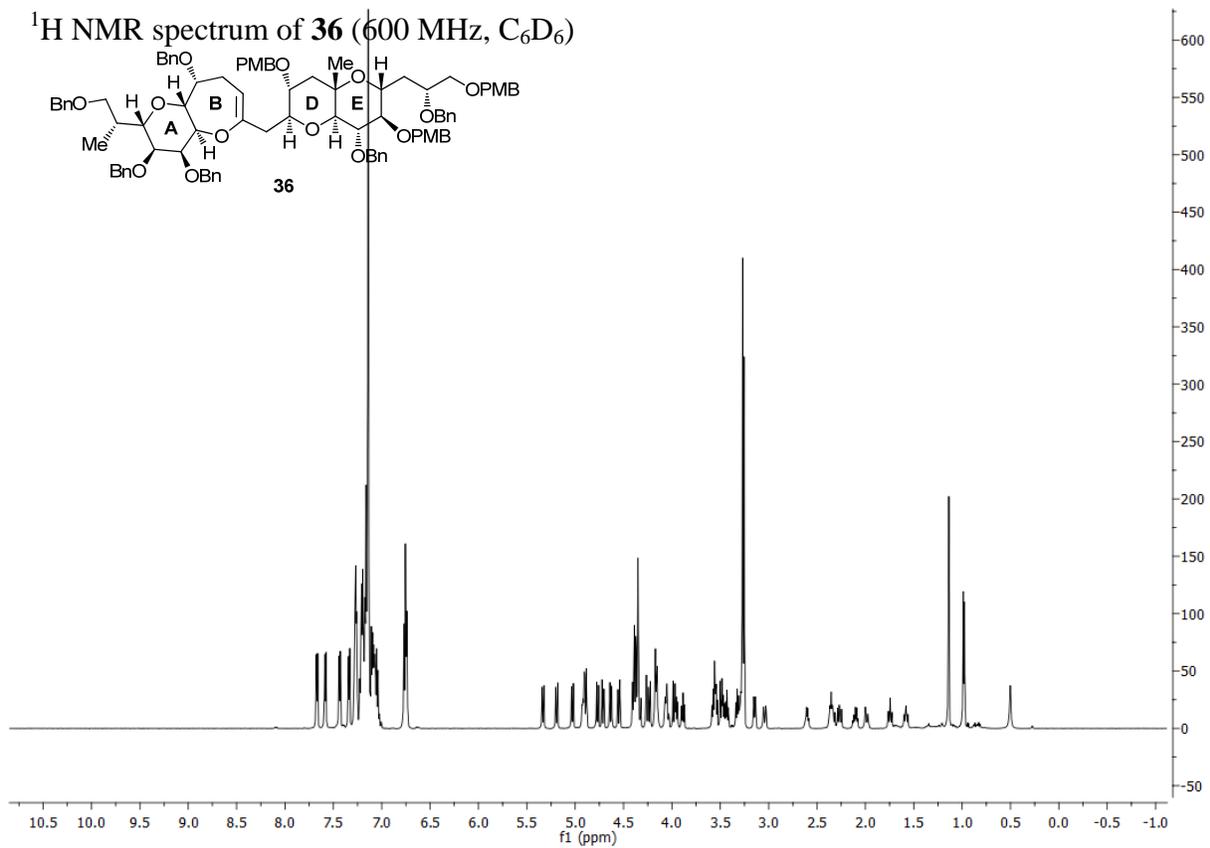
^1H NMR spectrum of **8** (600 MHz, C_6D_6)



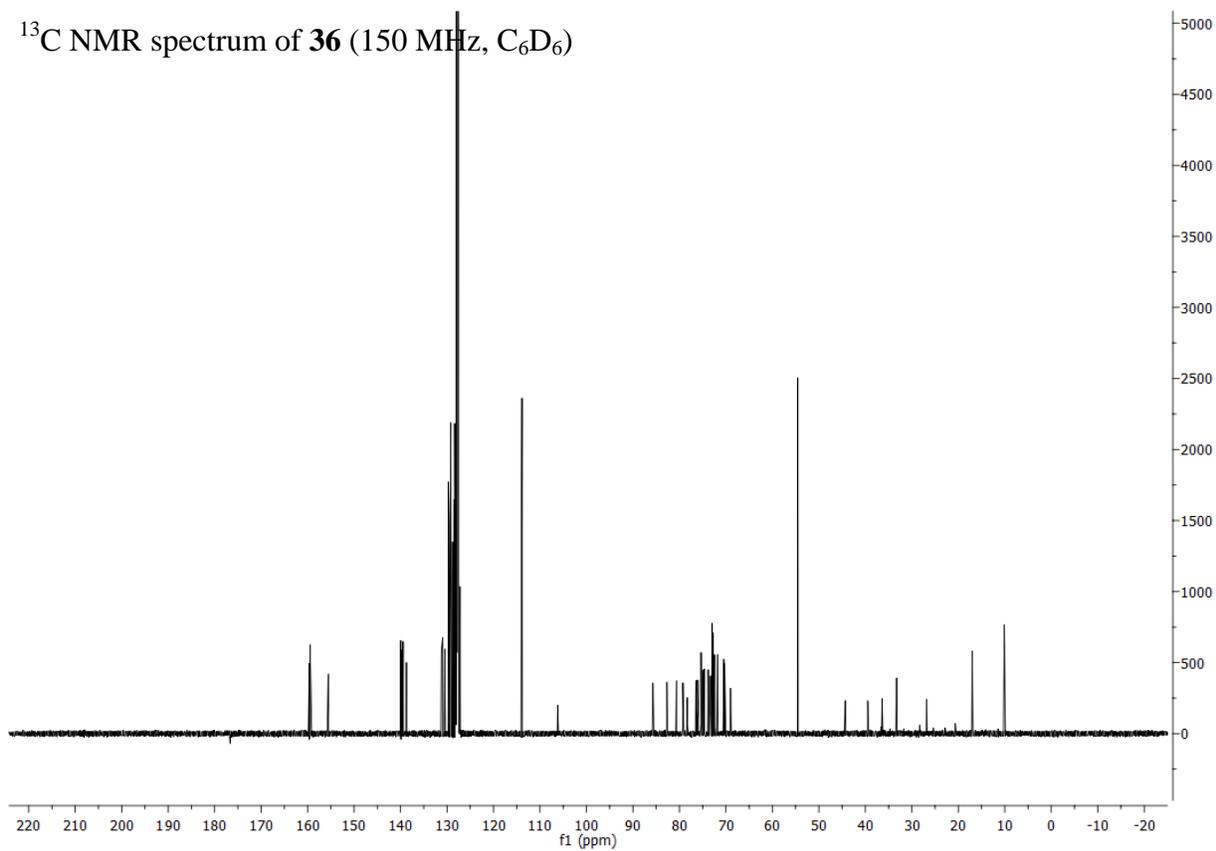
^{13}C NMR spectrum of **8** (150 MHz, C_6D_6)



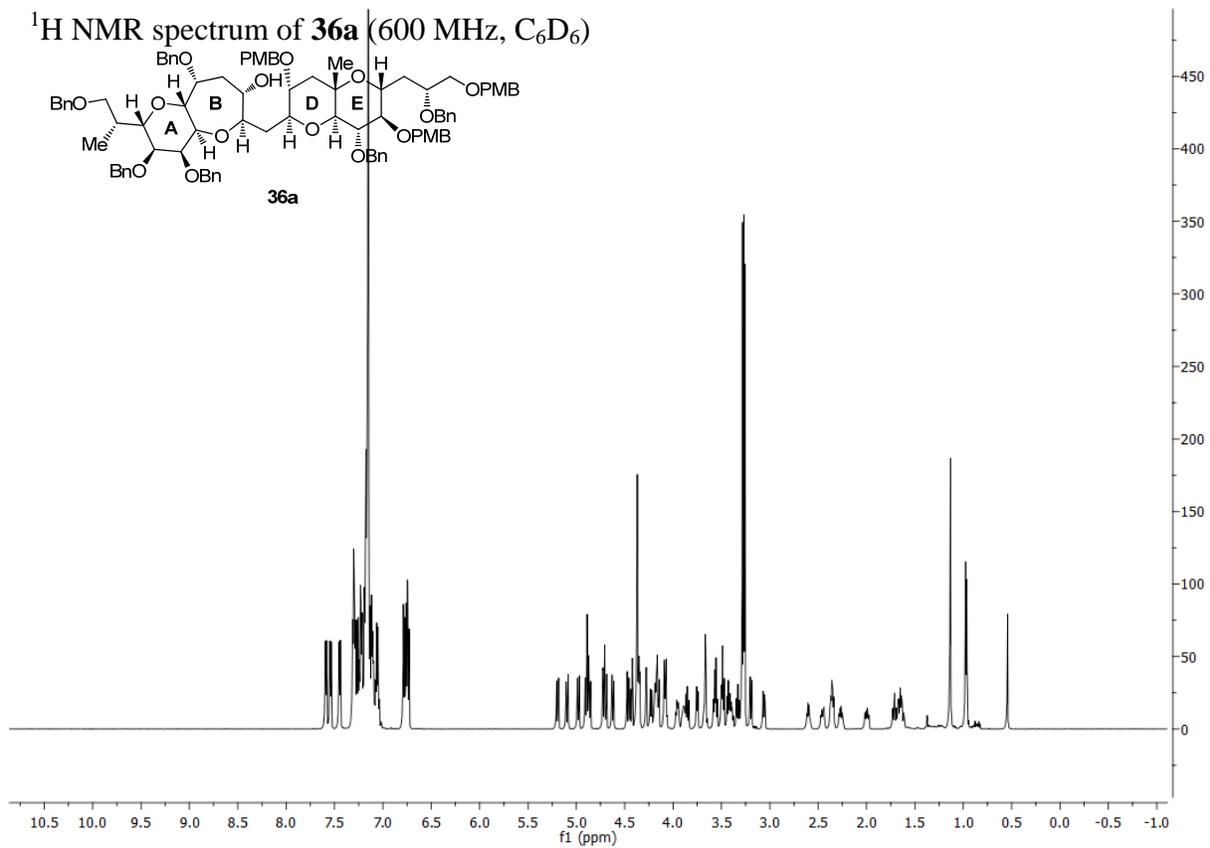
^1H NMR spectrum of **36** (600 MHz, C_6D_6)



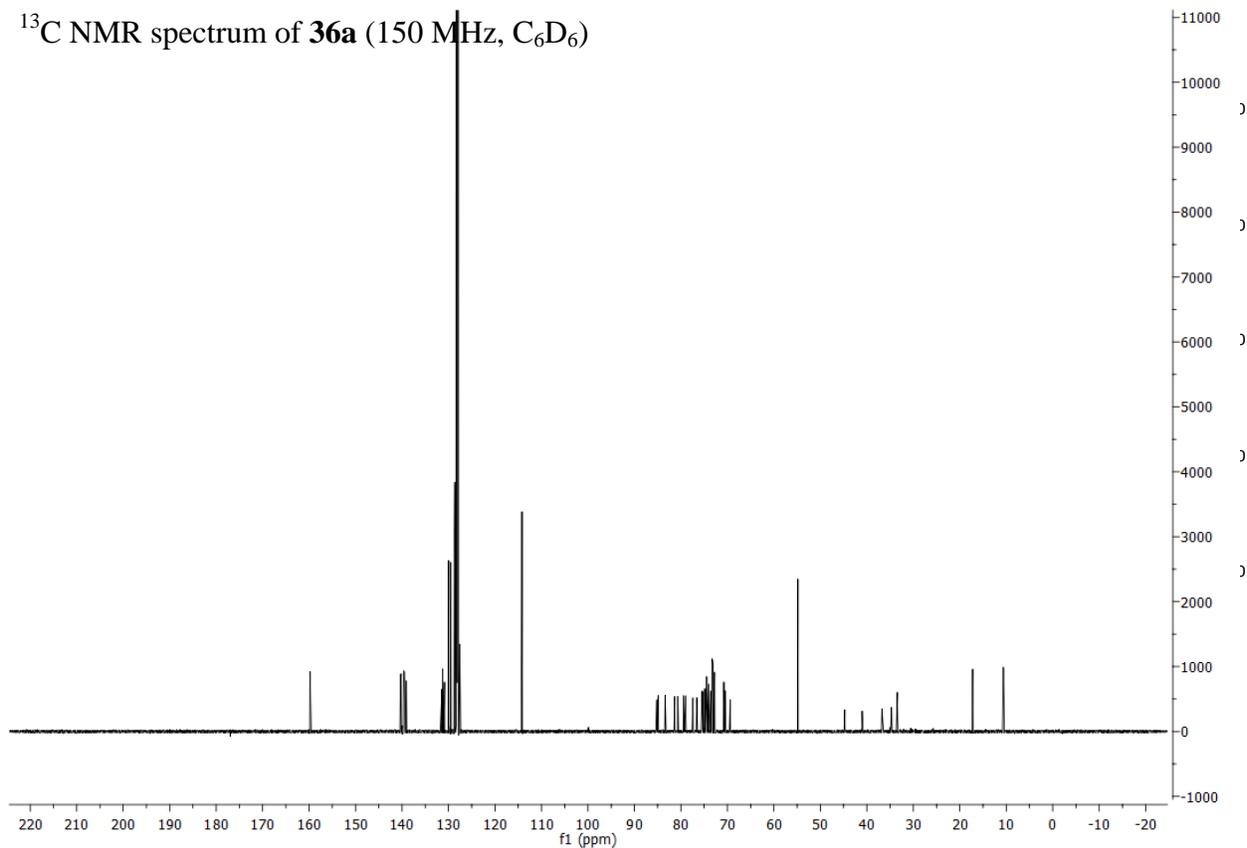
^{13}C NMR spectrum of **36** (150 MHz, C_6D_6)



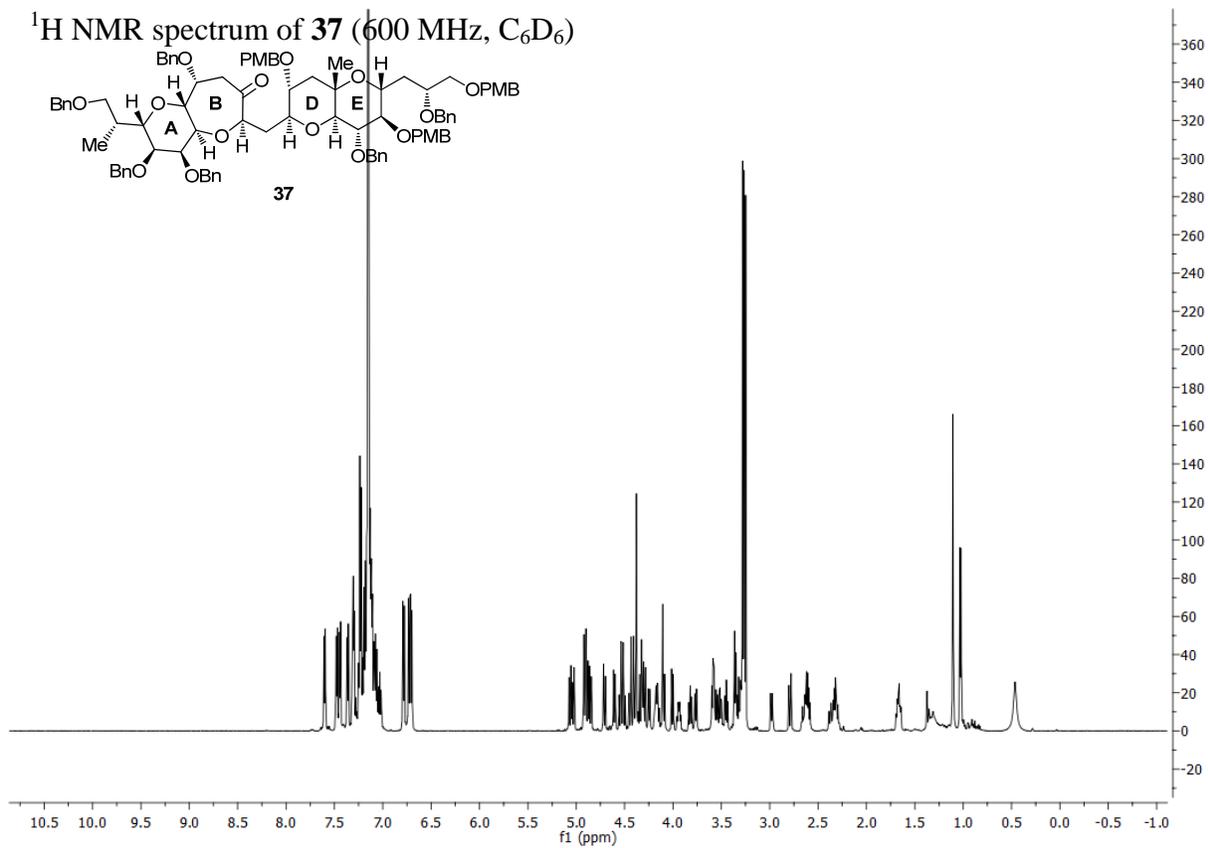
^1H NMR spectrum of **36a** (600 MHz, C_6D_6)



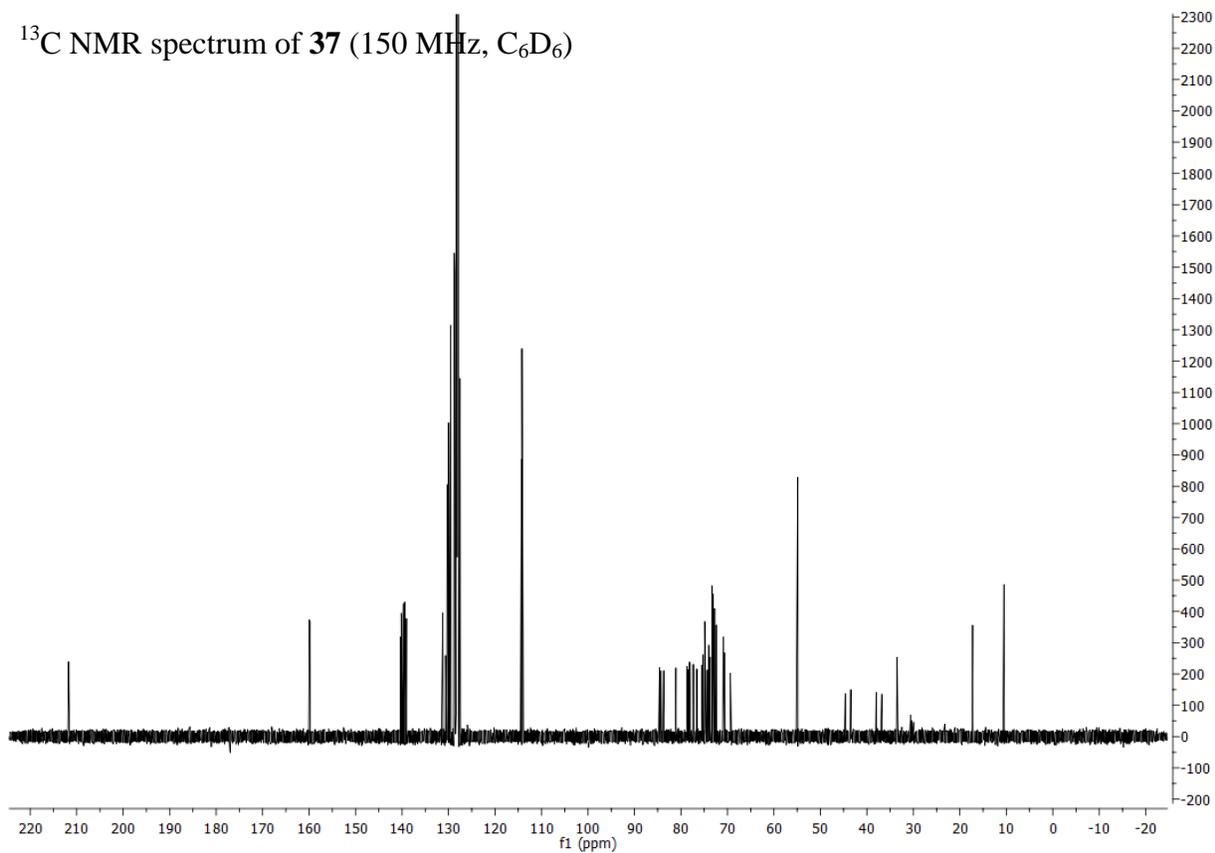
^{13}C NMR spectrum of **36a** (150 MHz, C_6D_6)



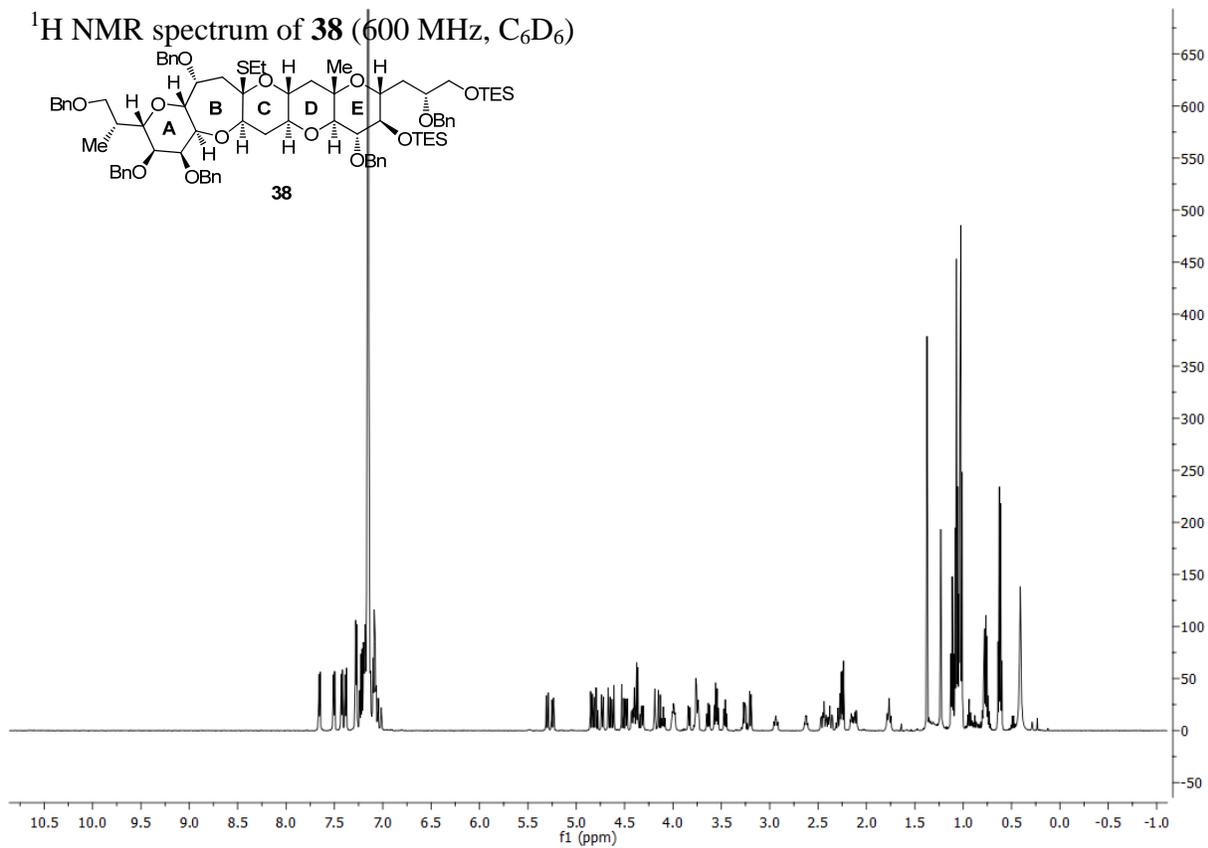
^1H NMR spectrum of **37** (600 MHz, C_6D_6)



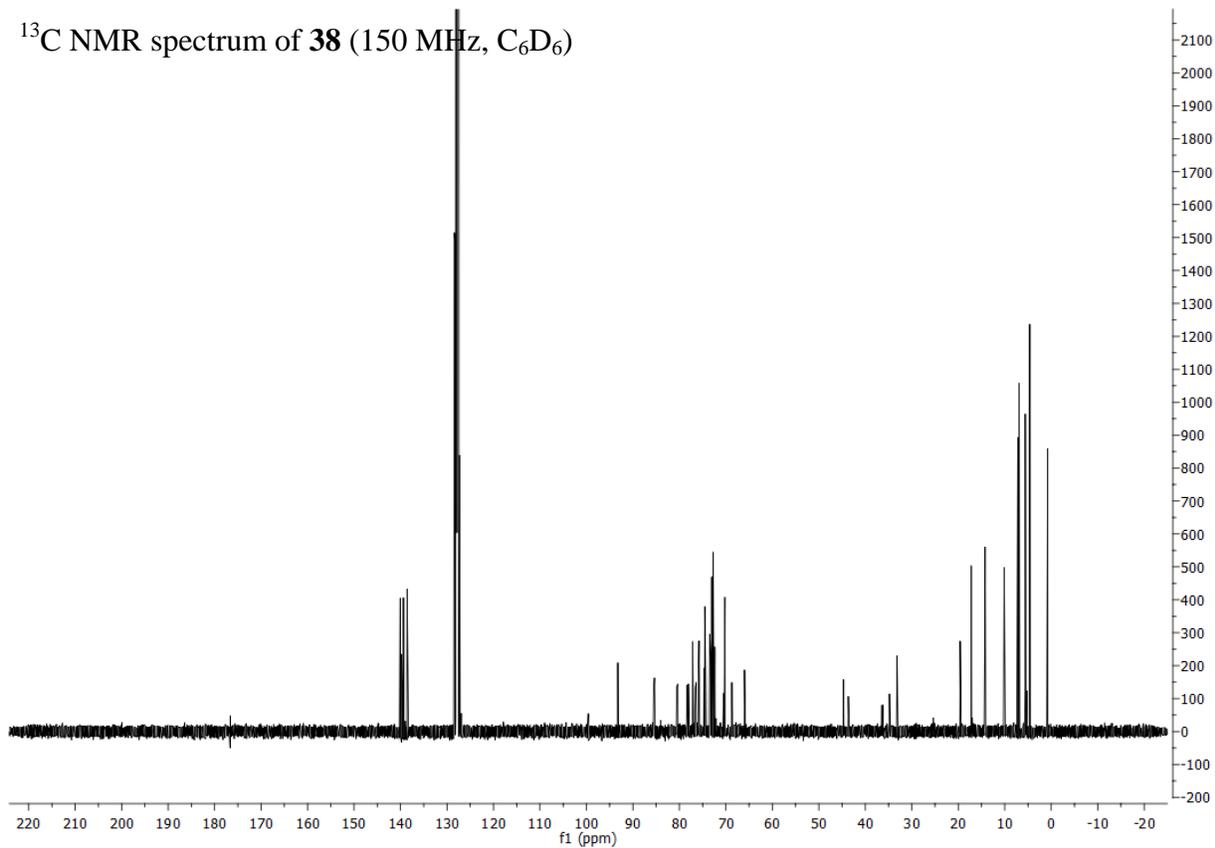
^{13}C NMR spectrum of **37** (150 MHz, C_6D_6)



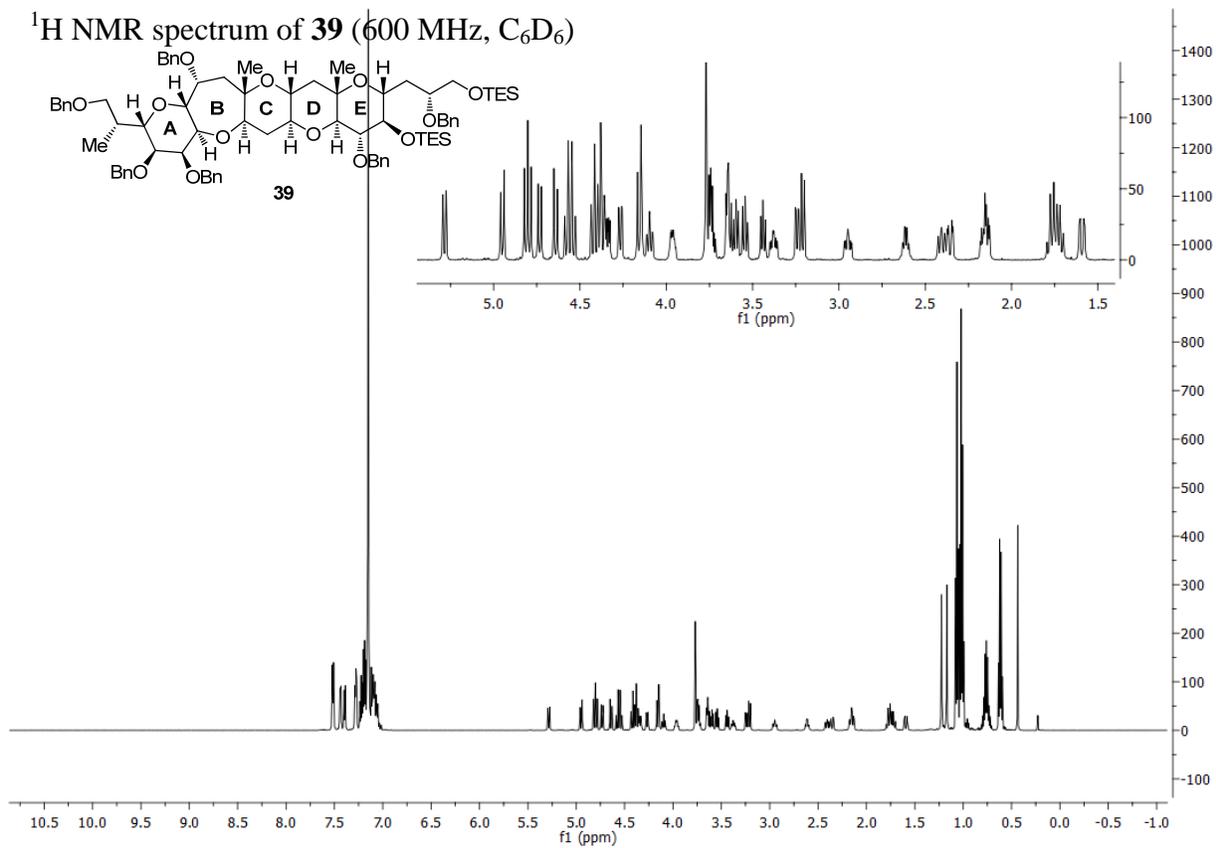
^1H NMR spectrum of **38** (600 MHz, C_6D_6)



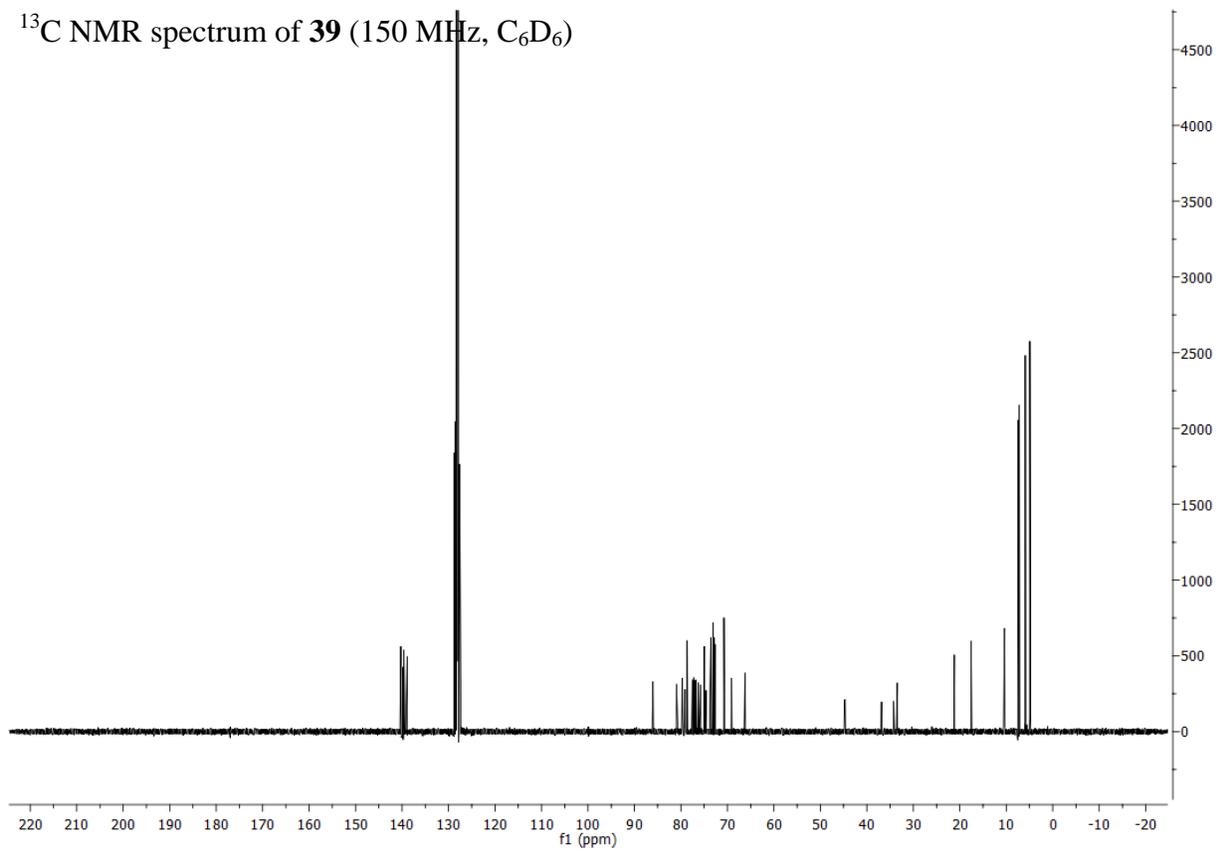
^{13}C NMR spectrum of **38** (150 MHz, C_6D_6)



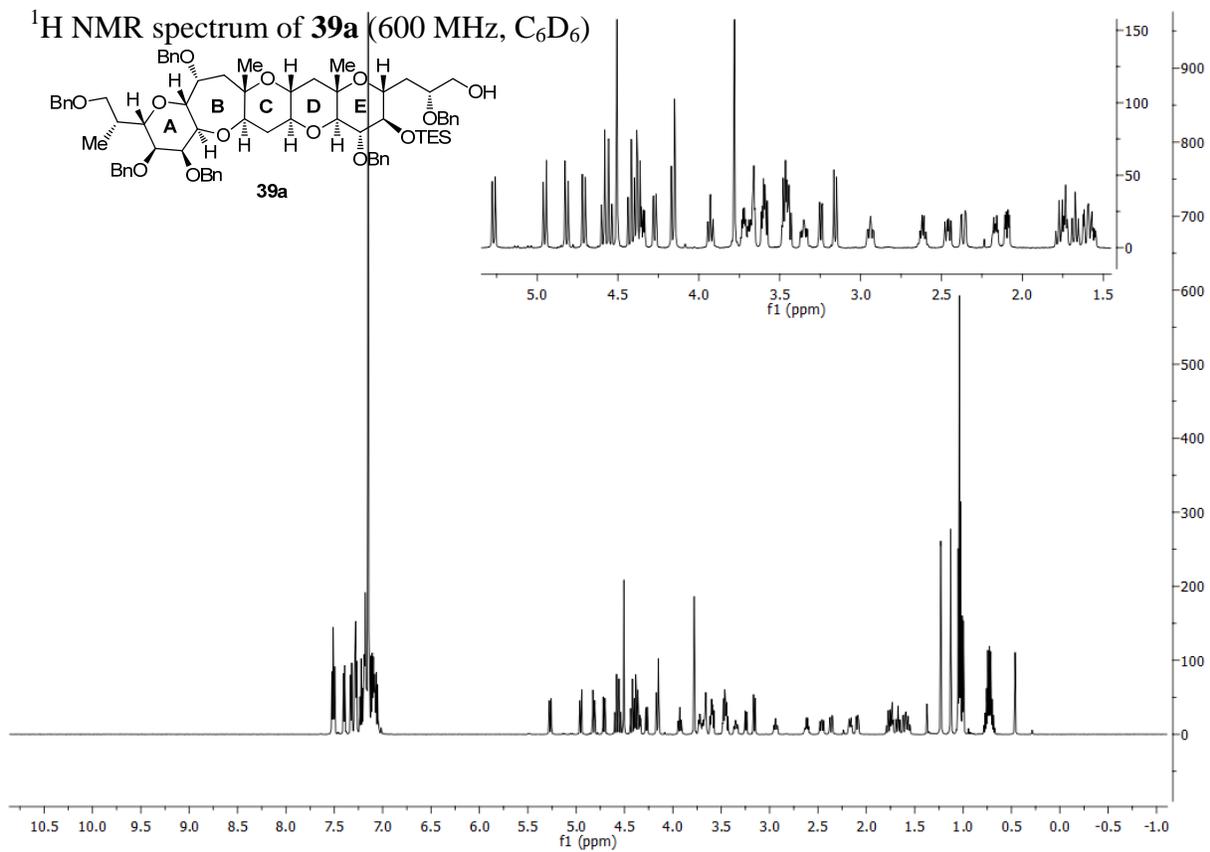
^1H NMR spectrum of **39** (600 MHz, C_6D_6)



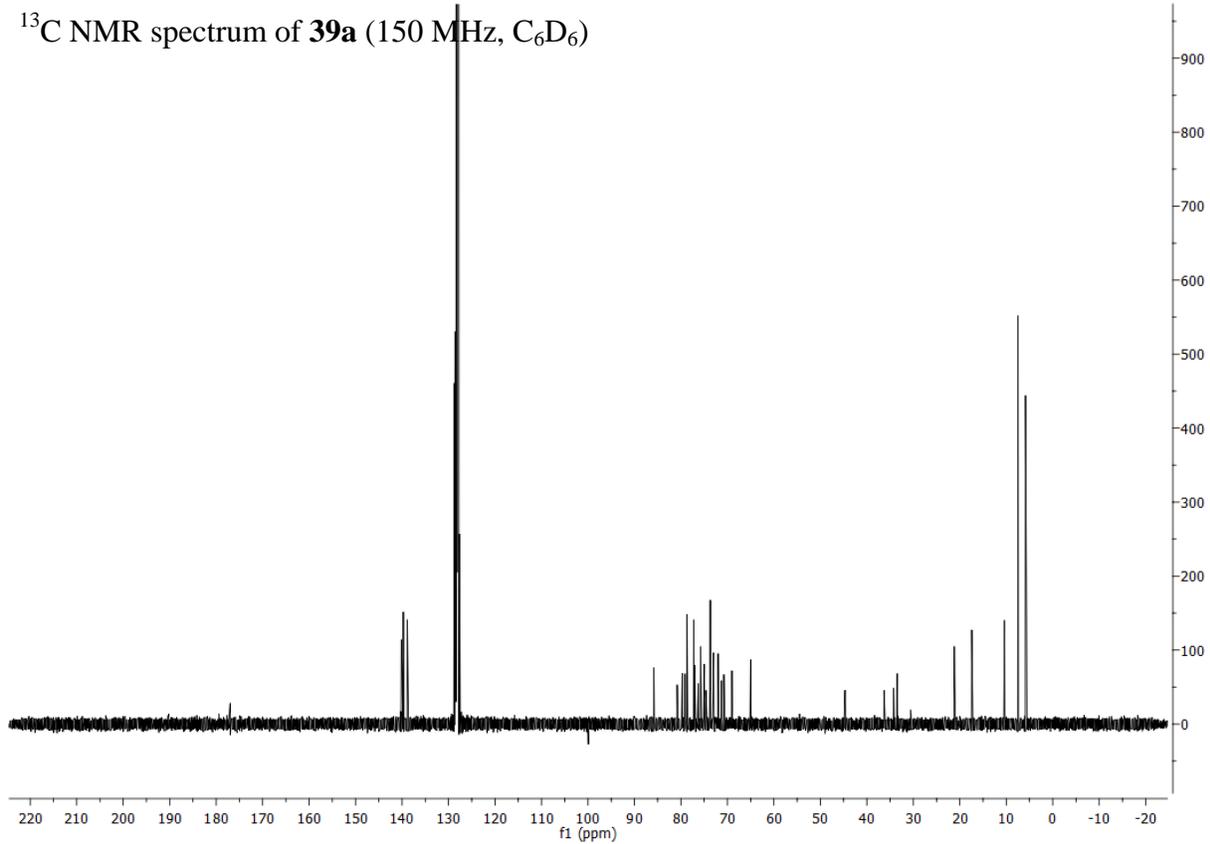
^{13}C NMR spectrum of **39** (150 MHz, C_6D_6)



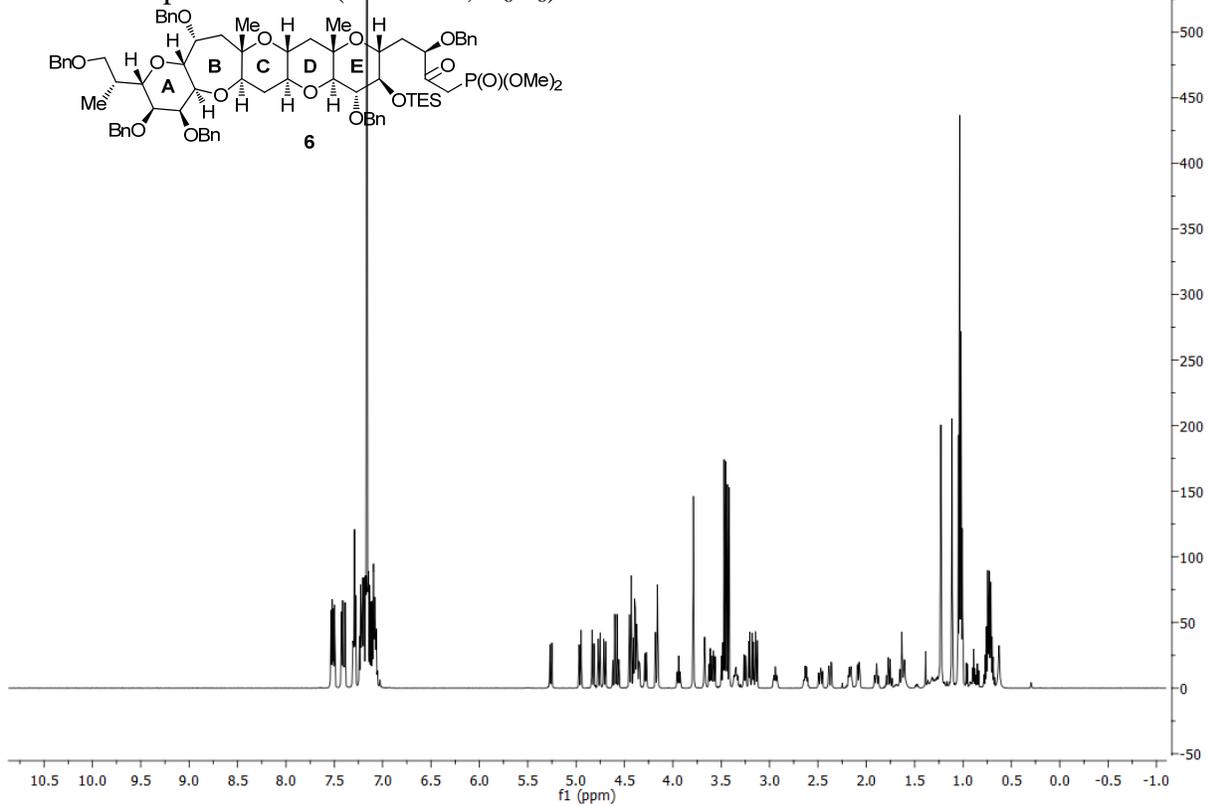
^1H NMR spectrum of **39a** (600 MHz, C_6D_6)



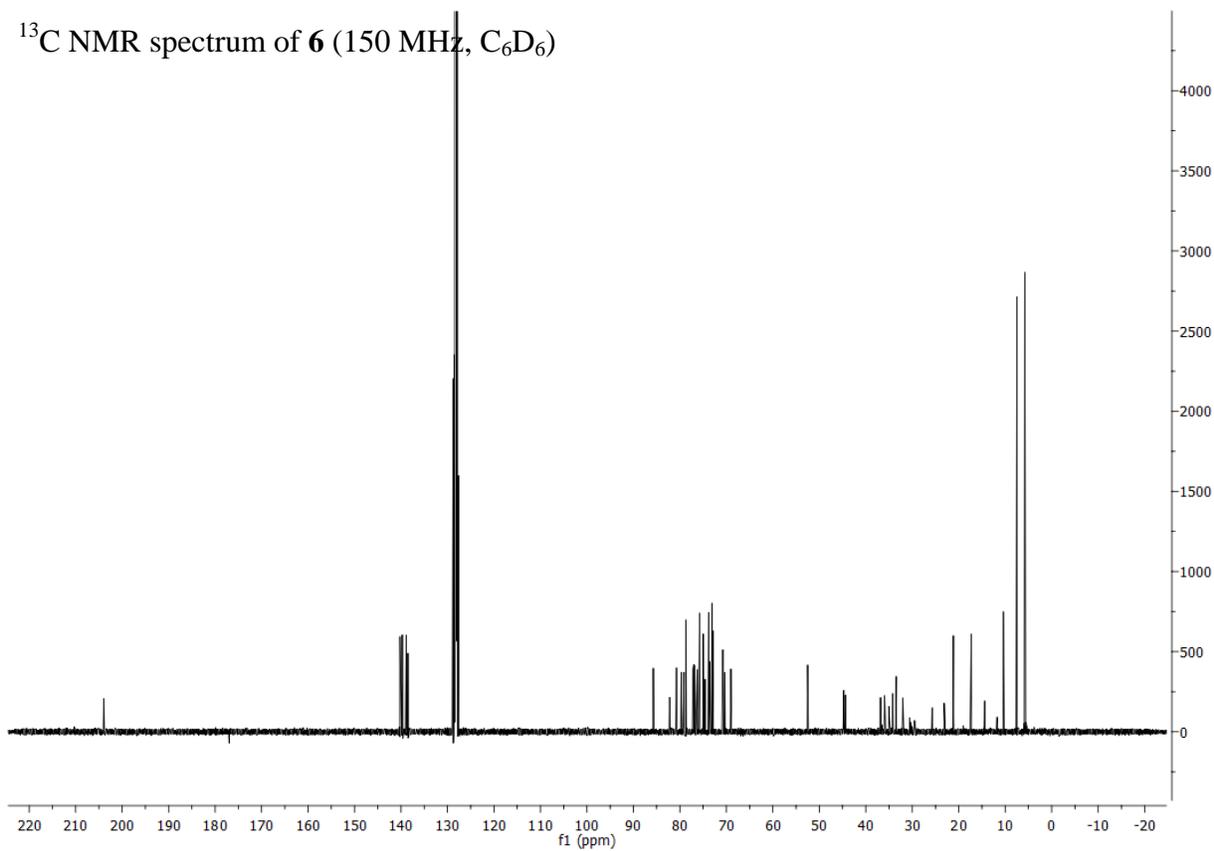
^{13}C NMR spectrum of **39a** (150 MHz, C_6D_6)



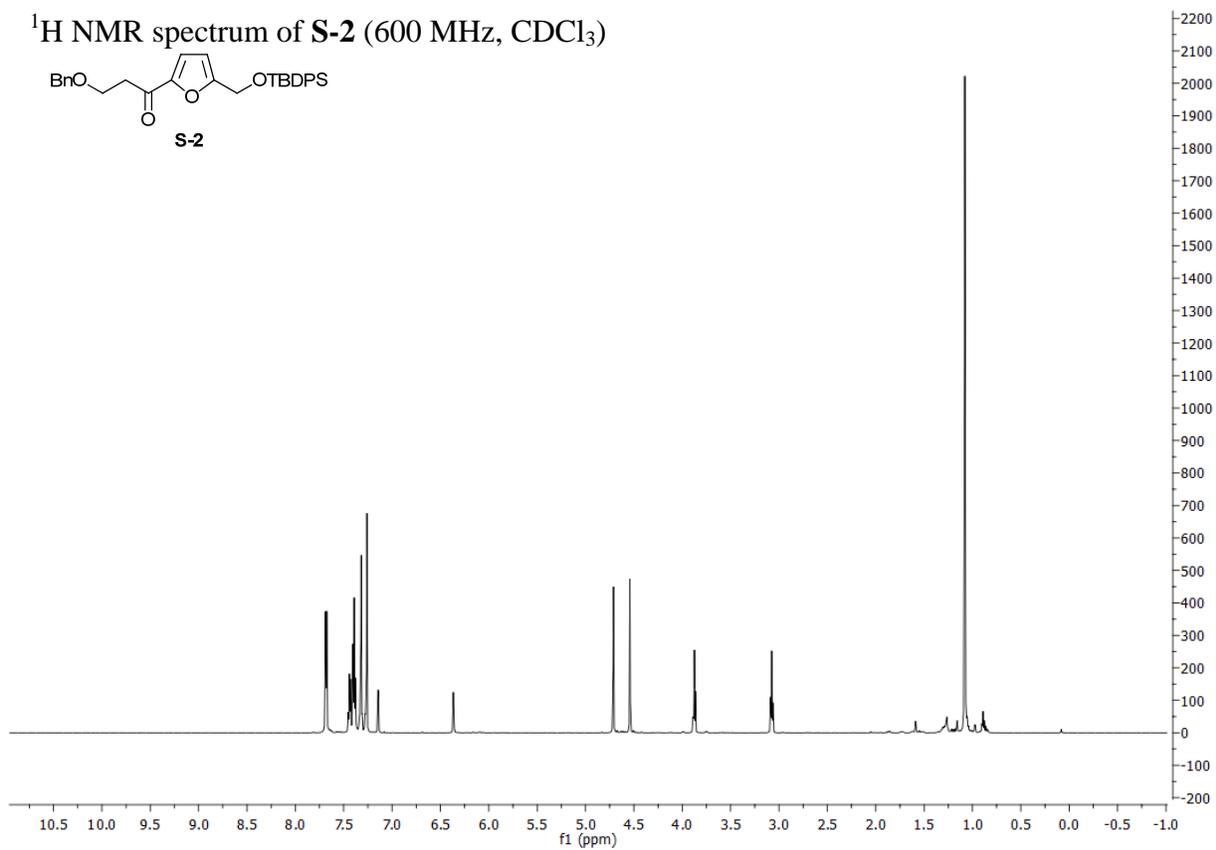
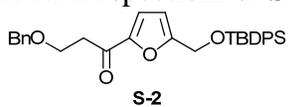
^1H NMR spectrum of **6** (600 MHz, C_6D_6)



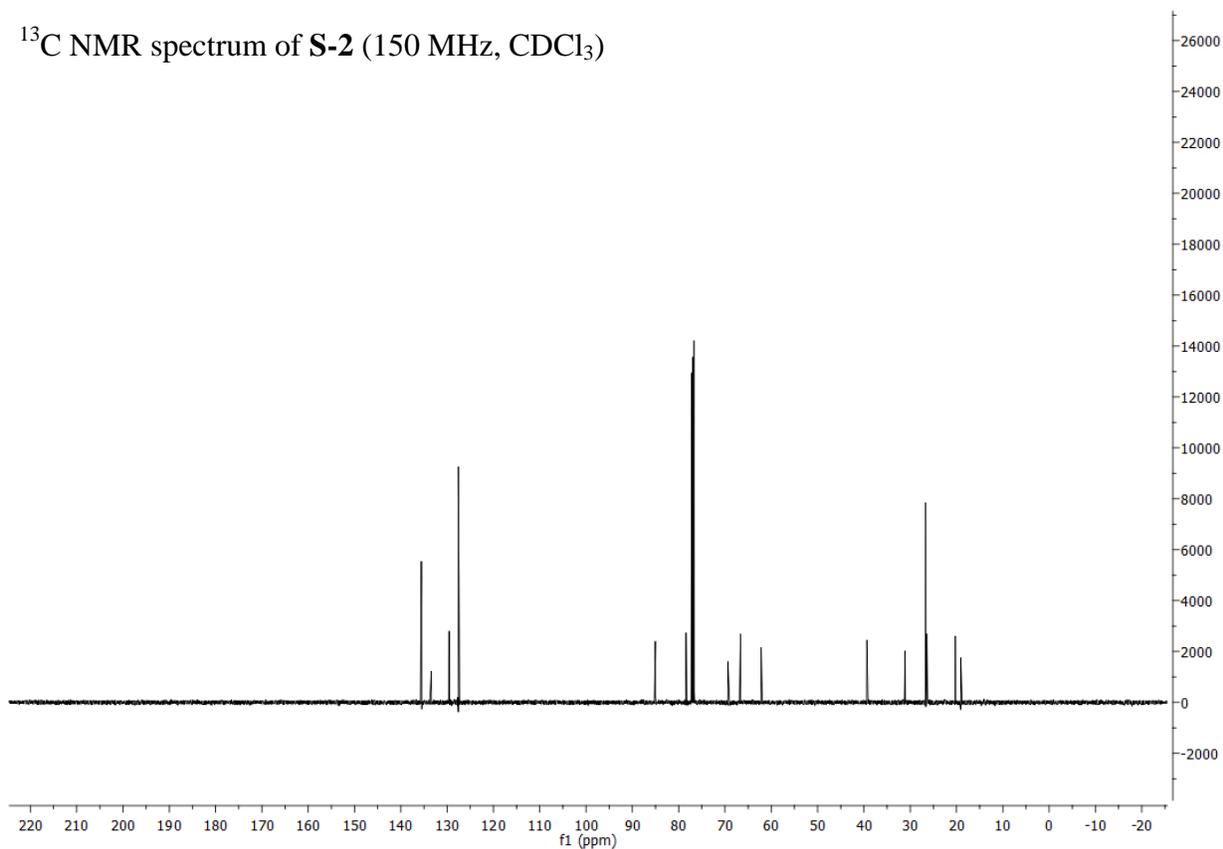
^{13}C NMR spectrum of **6** (150 MHz, C_6D_6)



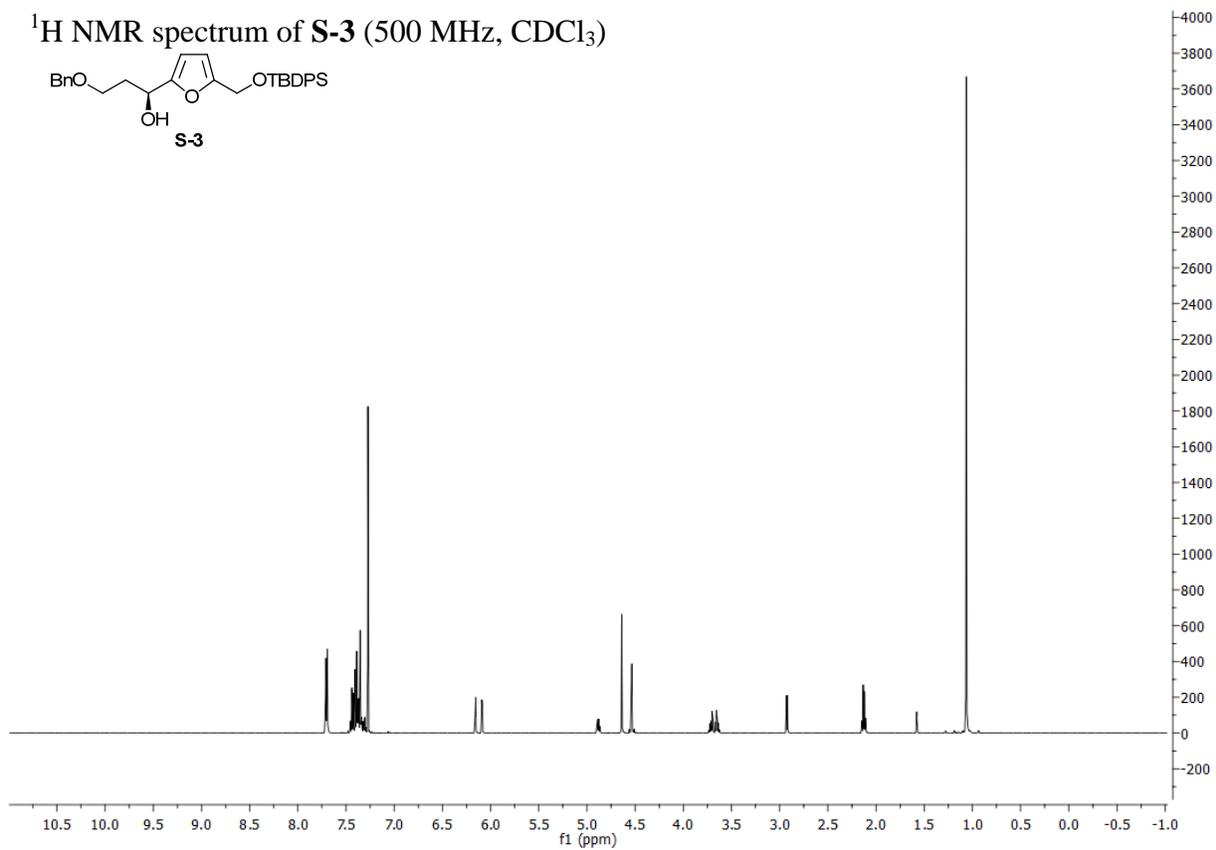
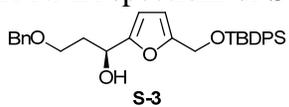
¹H NMR spectrum of **S-2** (600 MHz, CDCl₃)



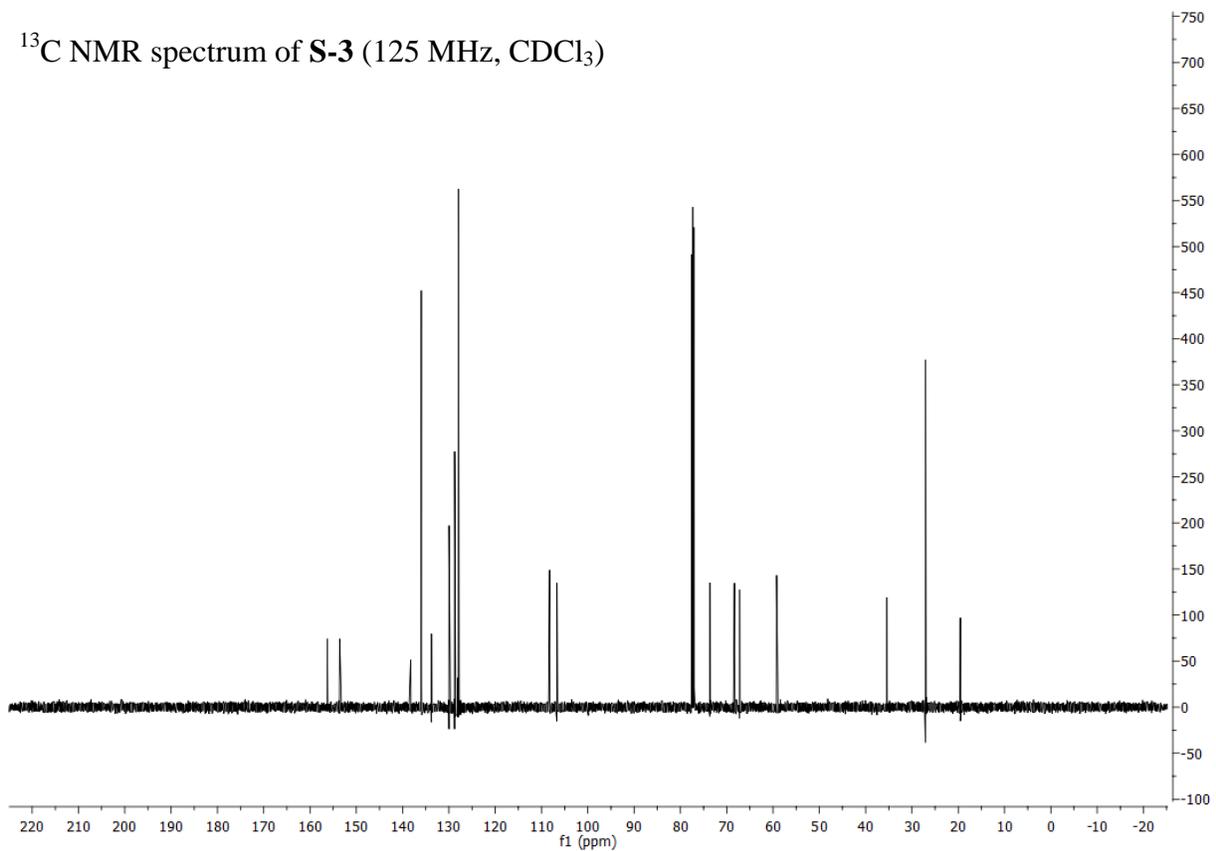
¹³C NMR spectrum of **S-2** (150 MHz, CDCl₃)



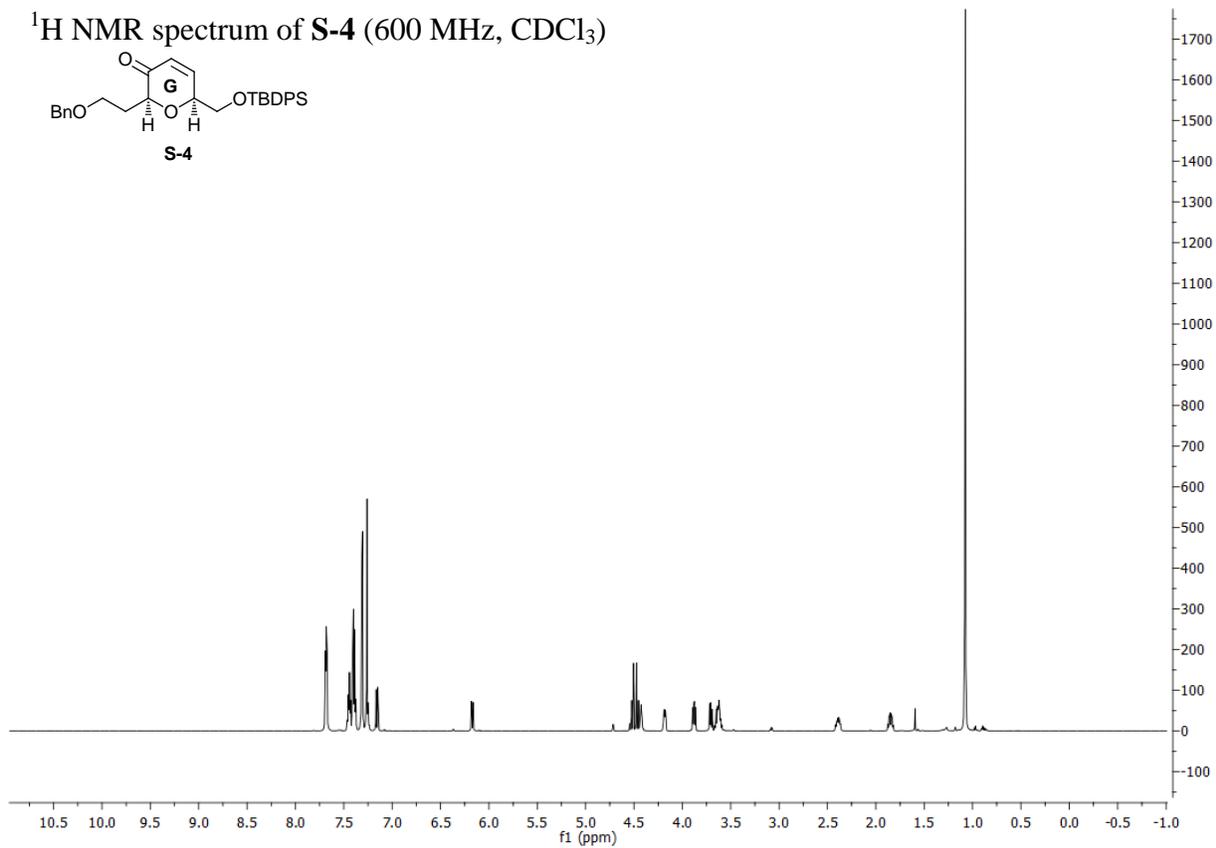
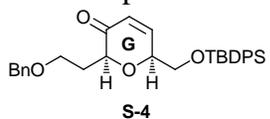
¹H NMR spectrum of **S-3** (500 MHz, CDCl₃)



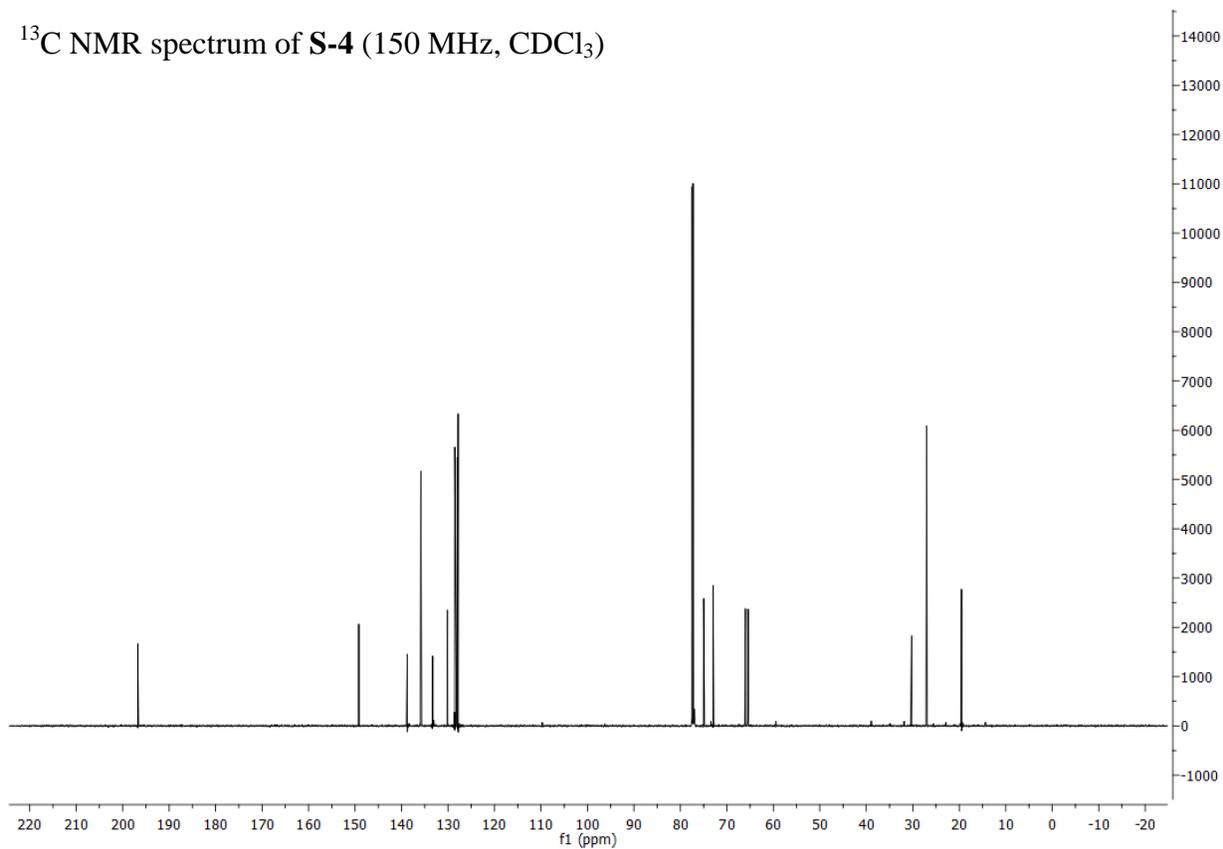
¹³C NMR spectrum of **S-3** (125 MHz, CDCl₃)



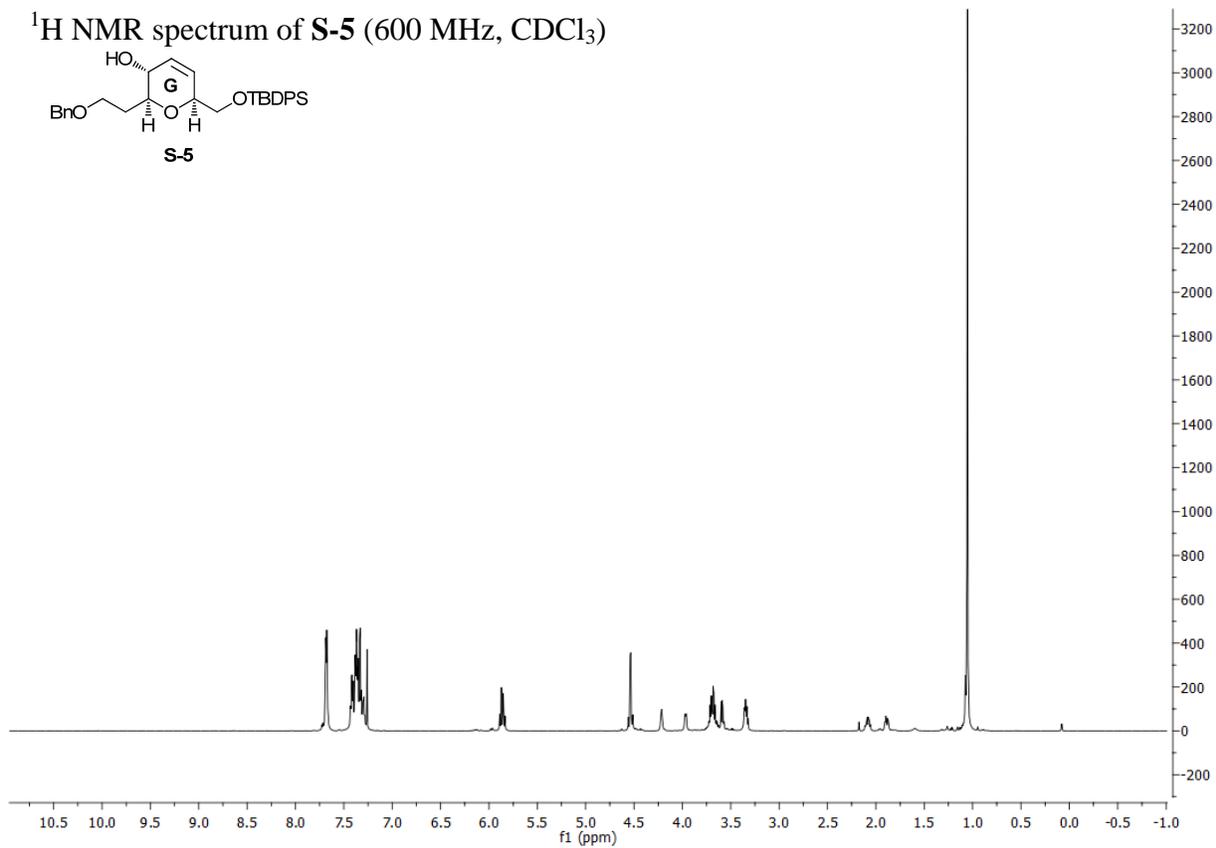
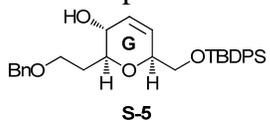
¹H NMR spectrum of **S-4** (600 MHz, CDCl₃)



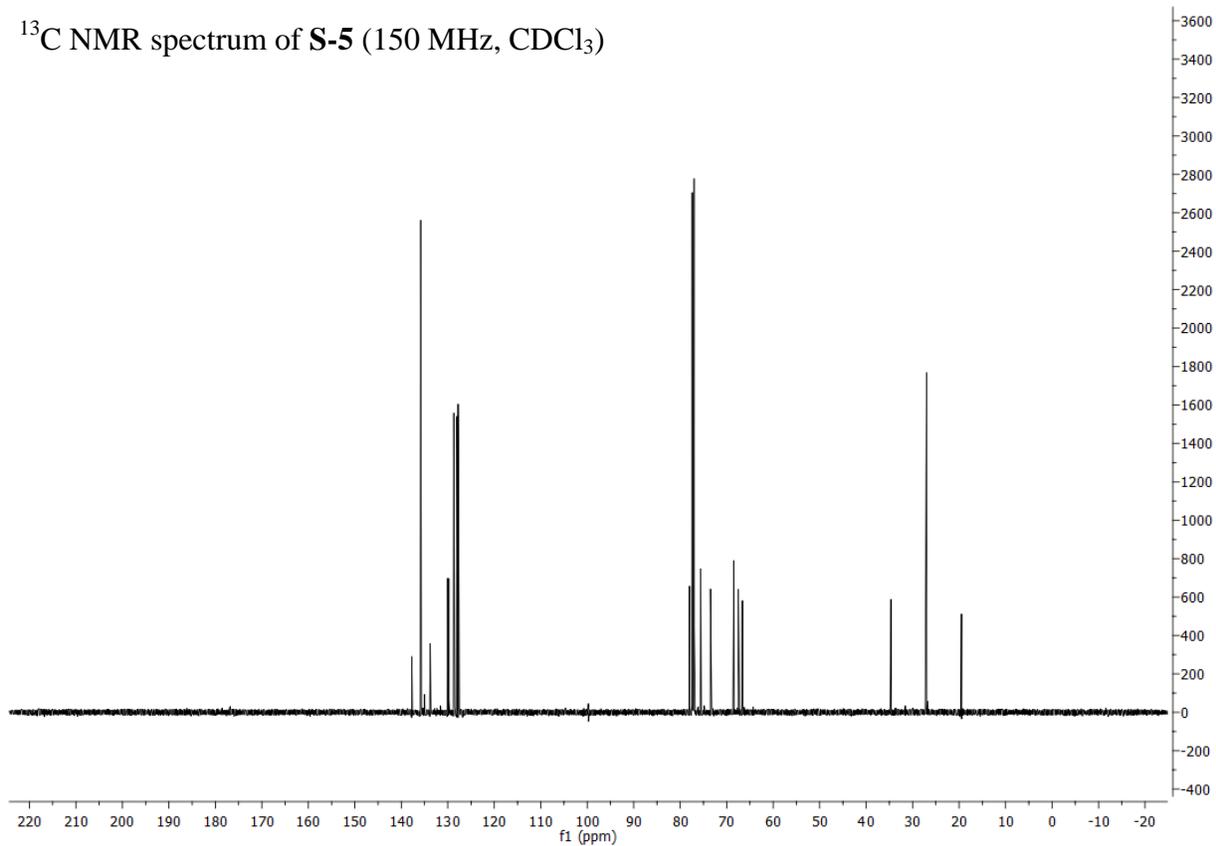
¹³C NMR spectrum of **S-4** (150 MHz, CDCl₃)



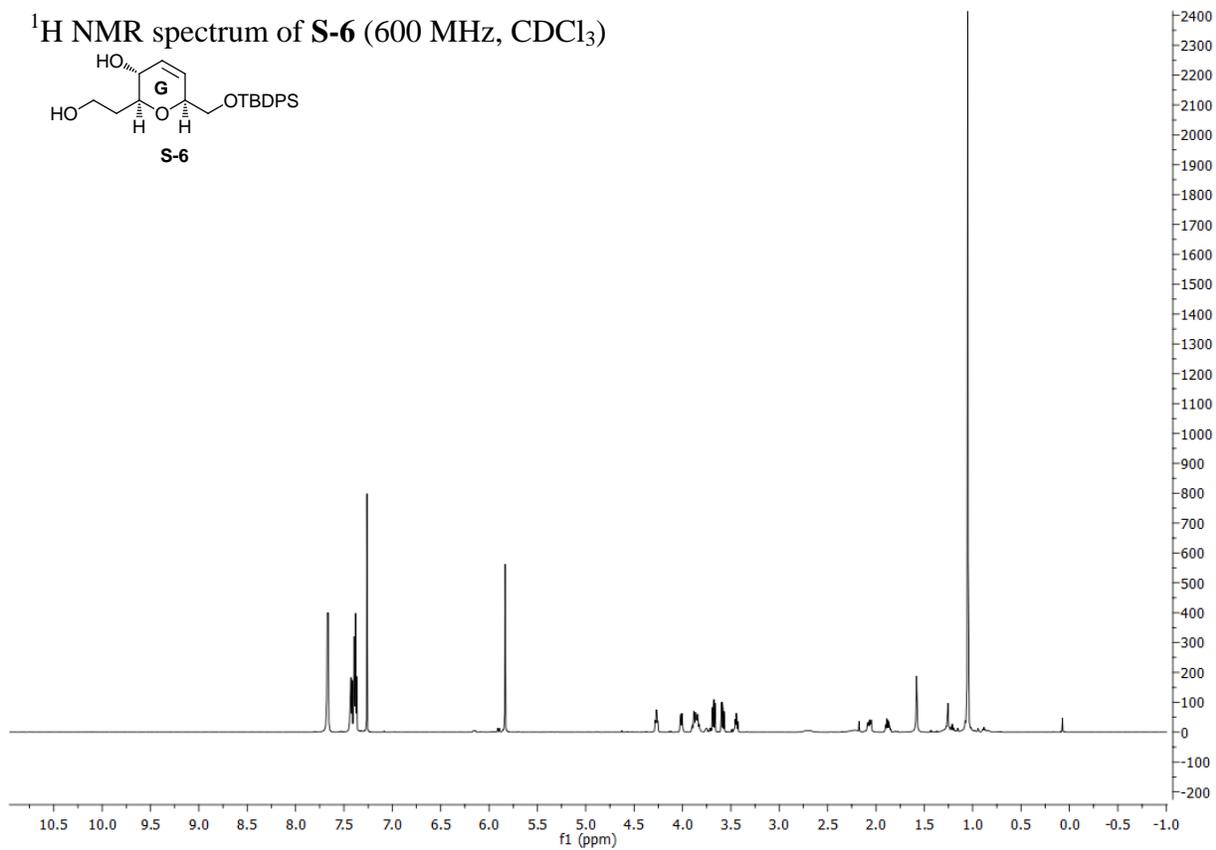
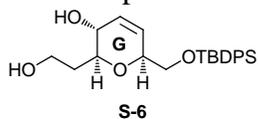
¹H NMR spectrum of **S-5** (600 MHz, CDCl₃)



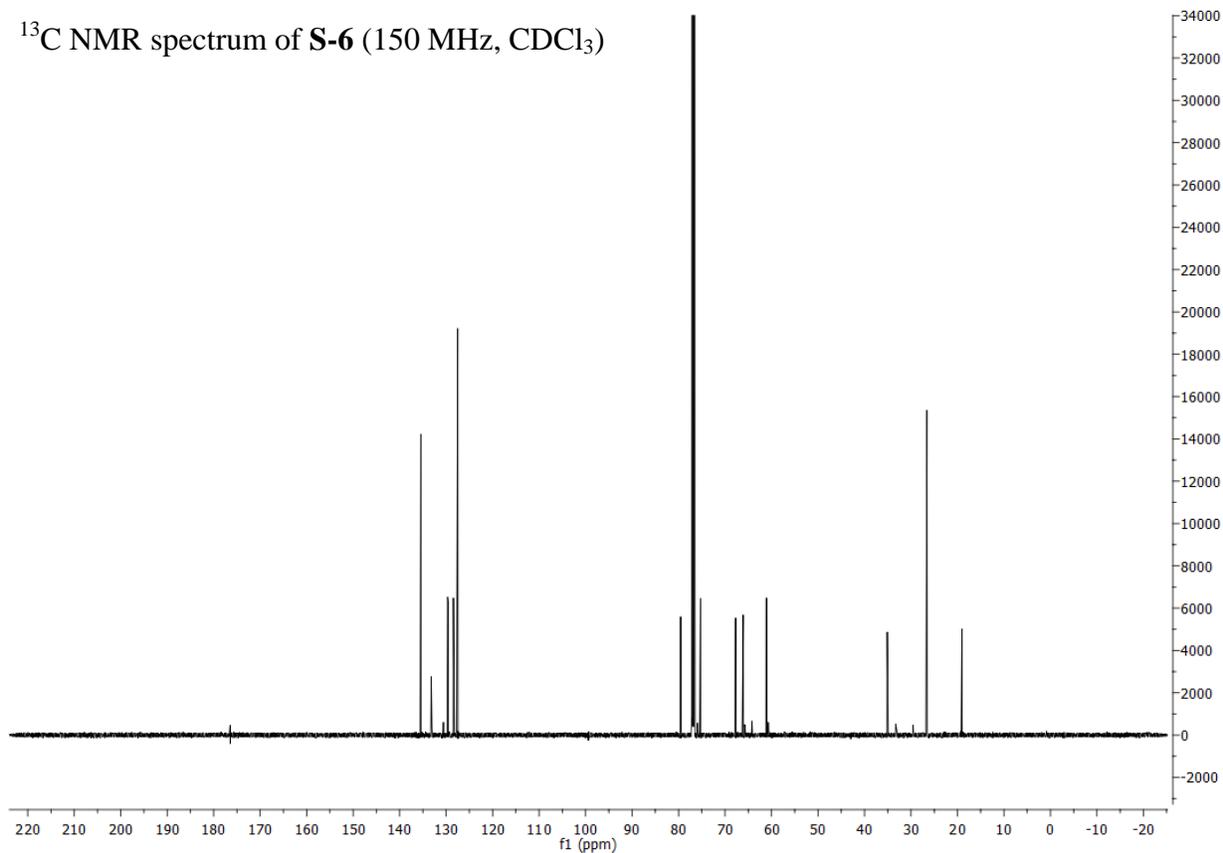
¹³C NMR spectrum of **S-5** (150 MHz, CDCl₃)



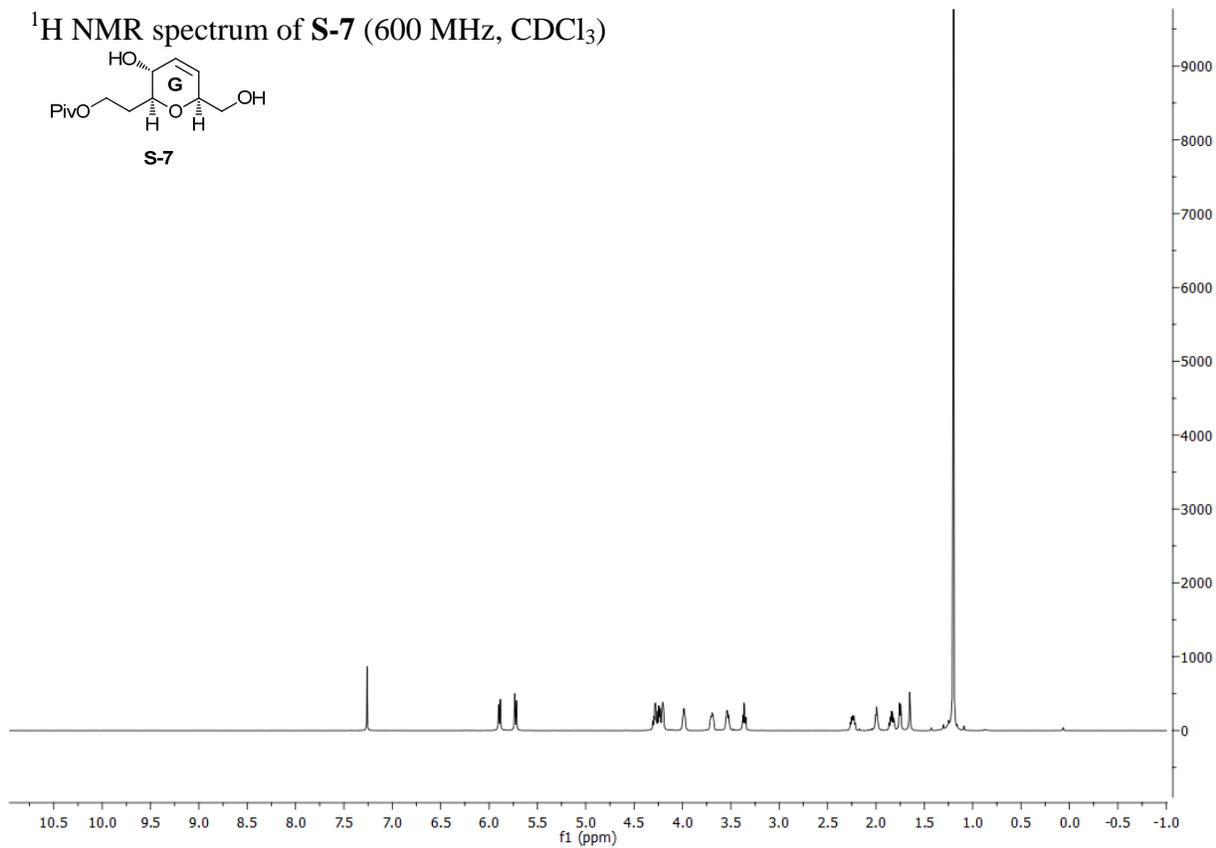
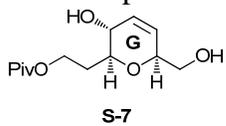
¹H NMR spectrum of **S-6** (600 MHz, CDCl₃)



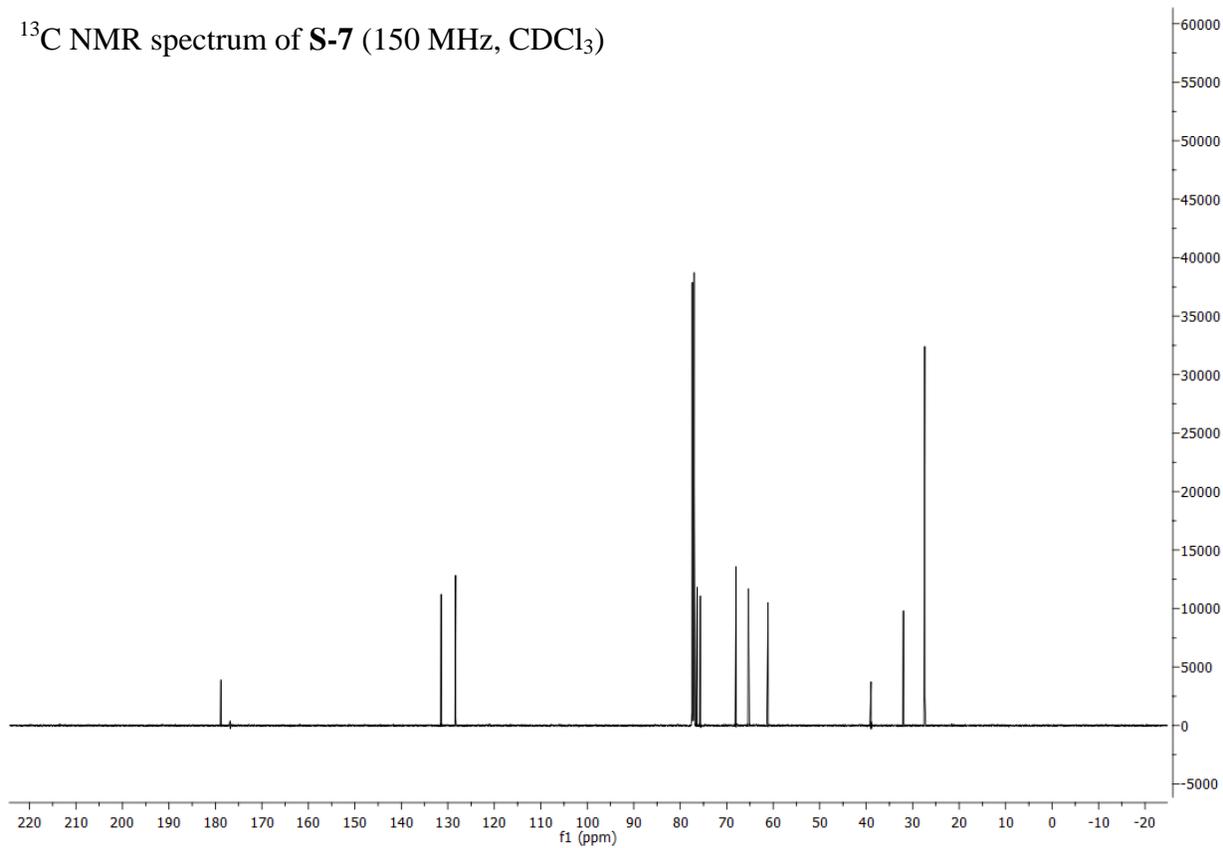
¹³C NMR spectrum of **S-6** (150 MHz, CDCl₃)



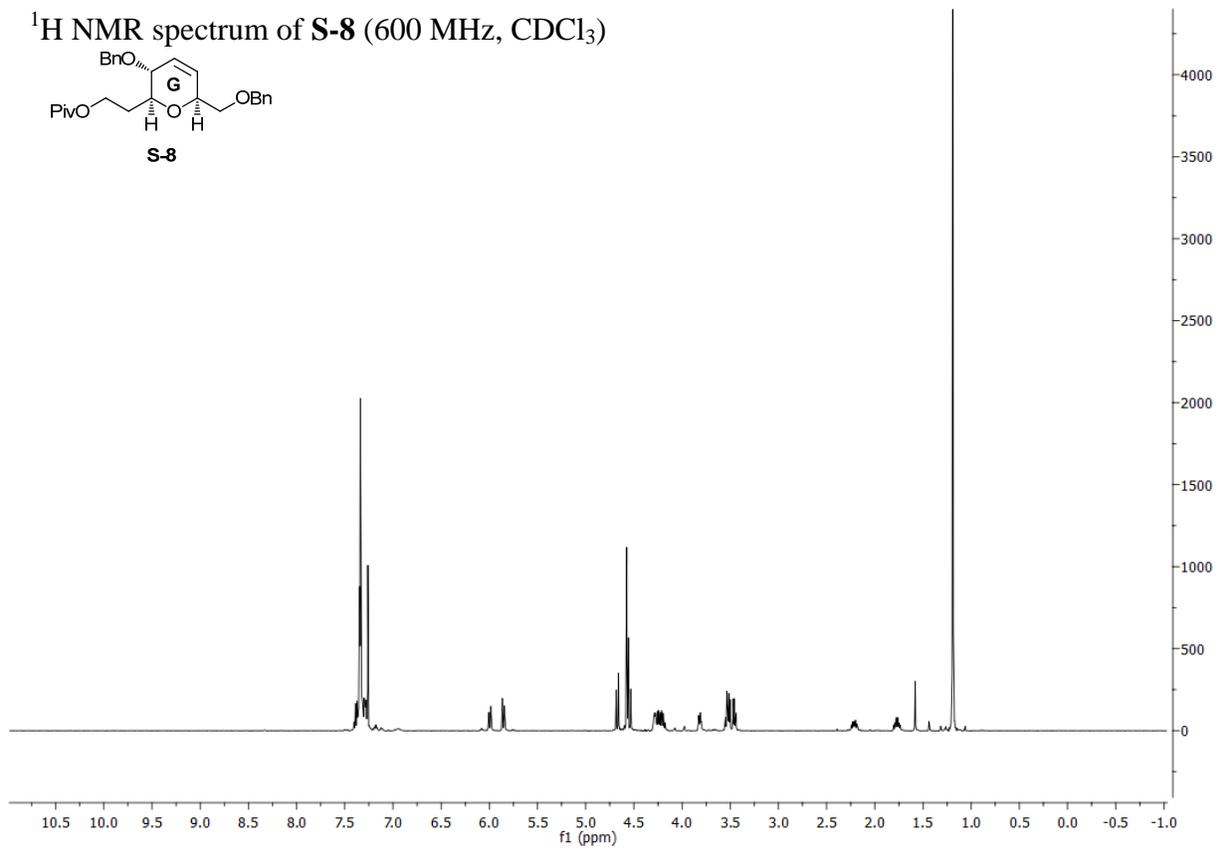
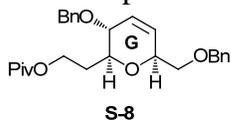
¹H NMR spectrum of **S-7** (600 MHz, CDCl₃)



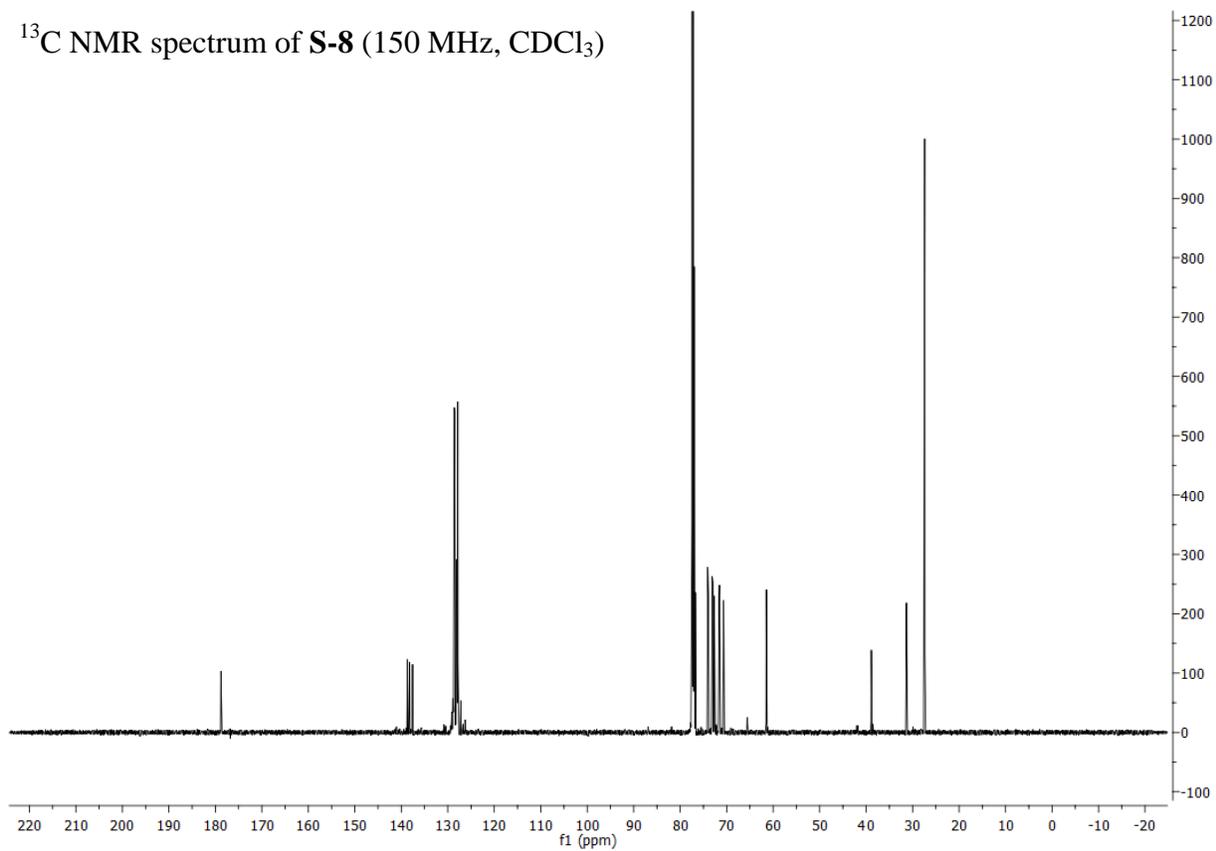
¹³C NMR spectrum of **S-7** (150 MHz, CDCl₃)



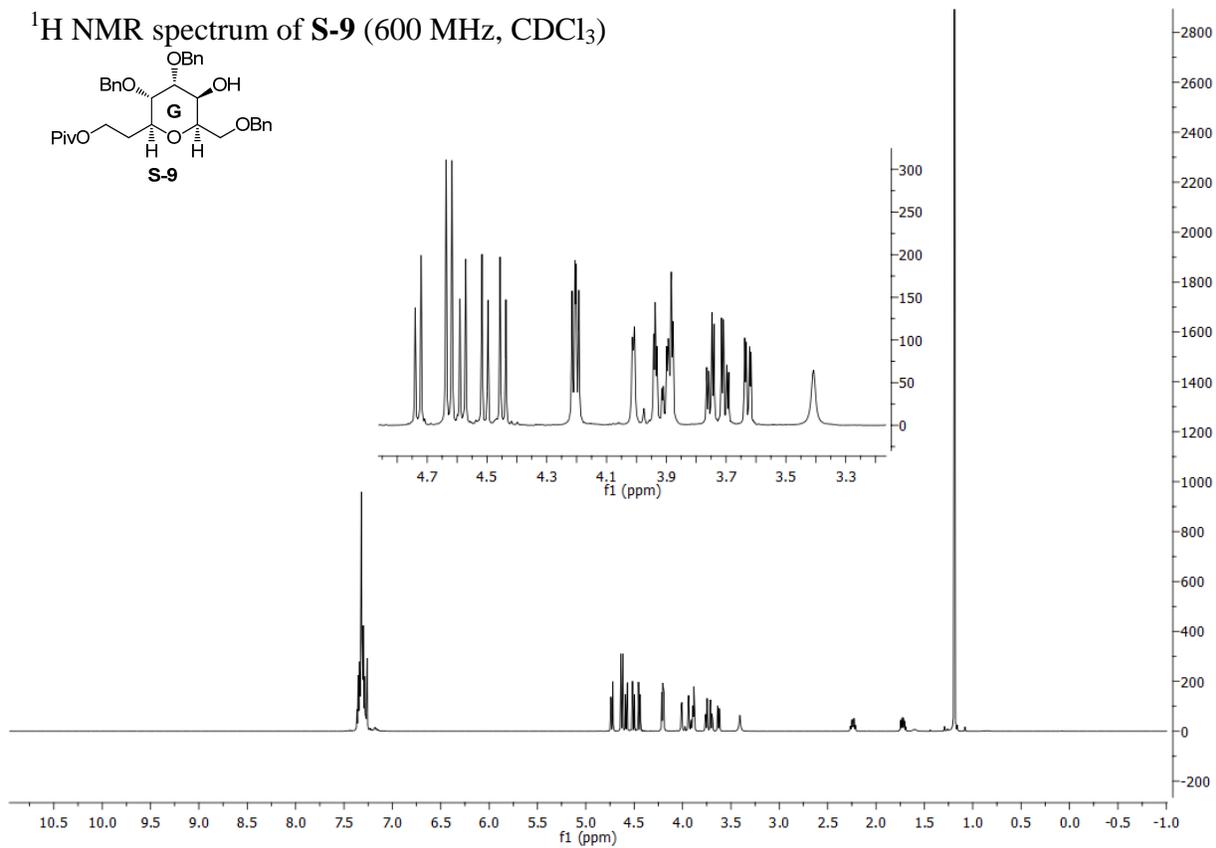
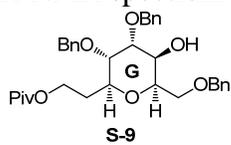
¹H NMR spectrum of **S-8** (600 MHz, CDCl₃)



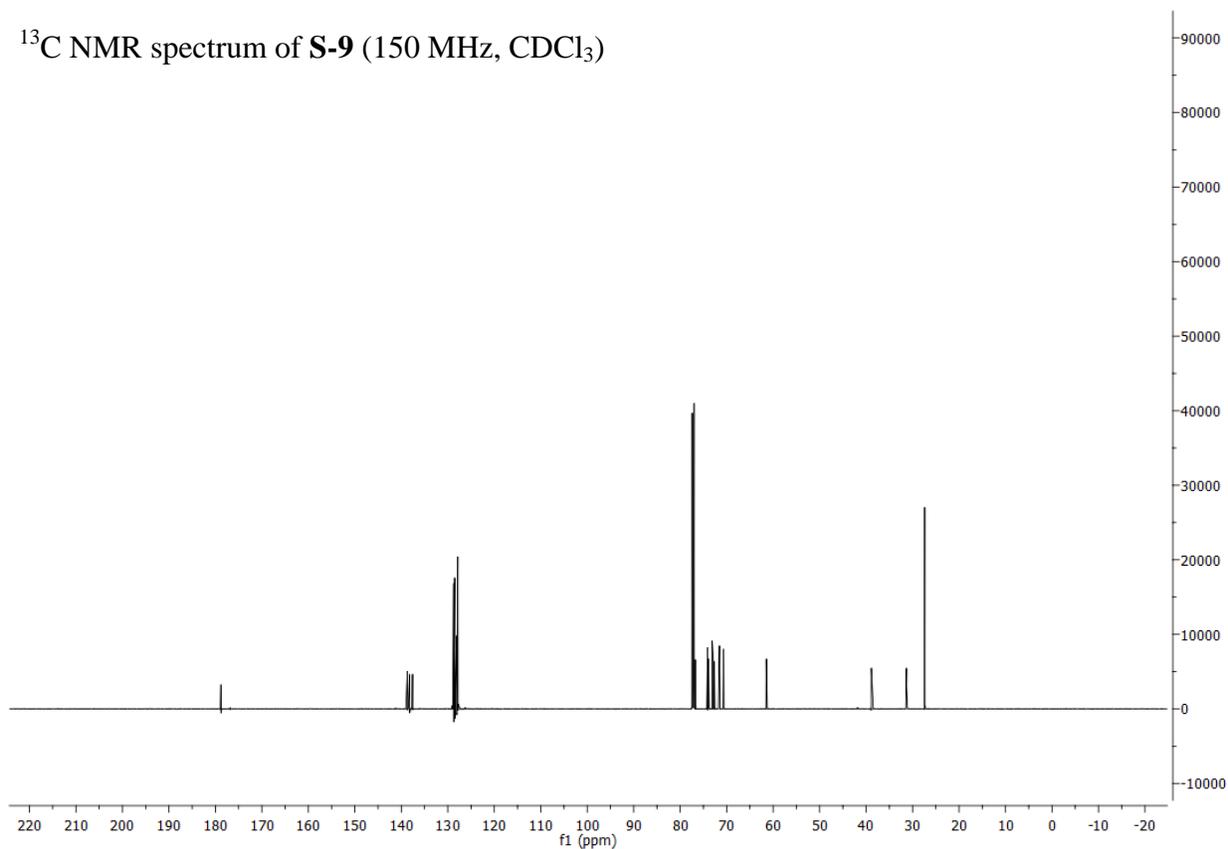
¹³C NMR spectrum of **S-8** (150 MHz, CDCl₃)



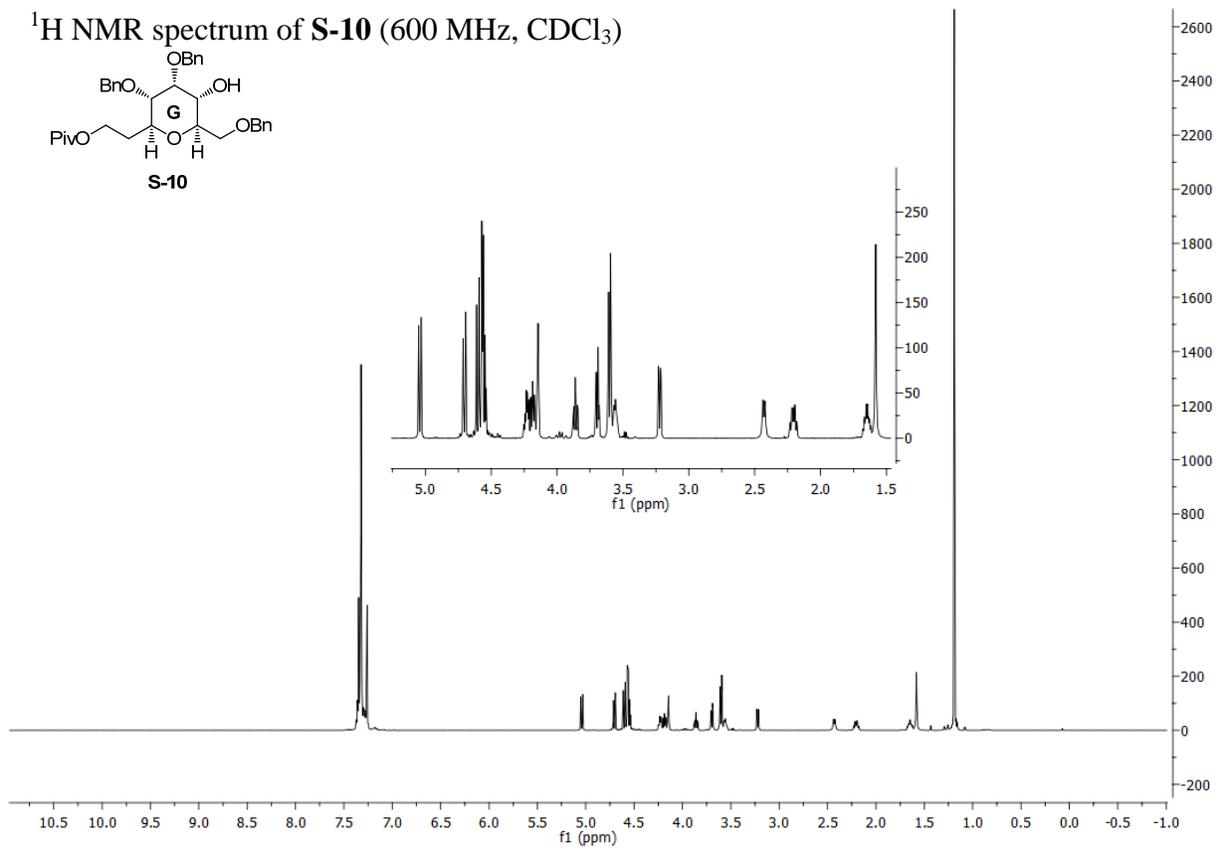
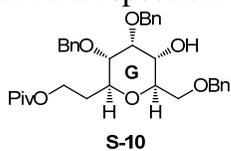
¹H NMR spectrum of **S-9** (600 MHz, CDCl₃)



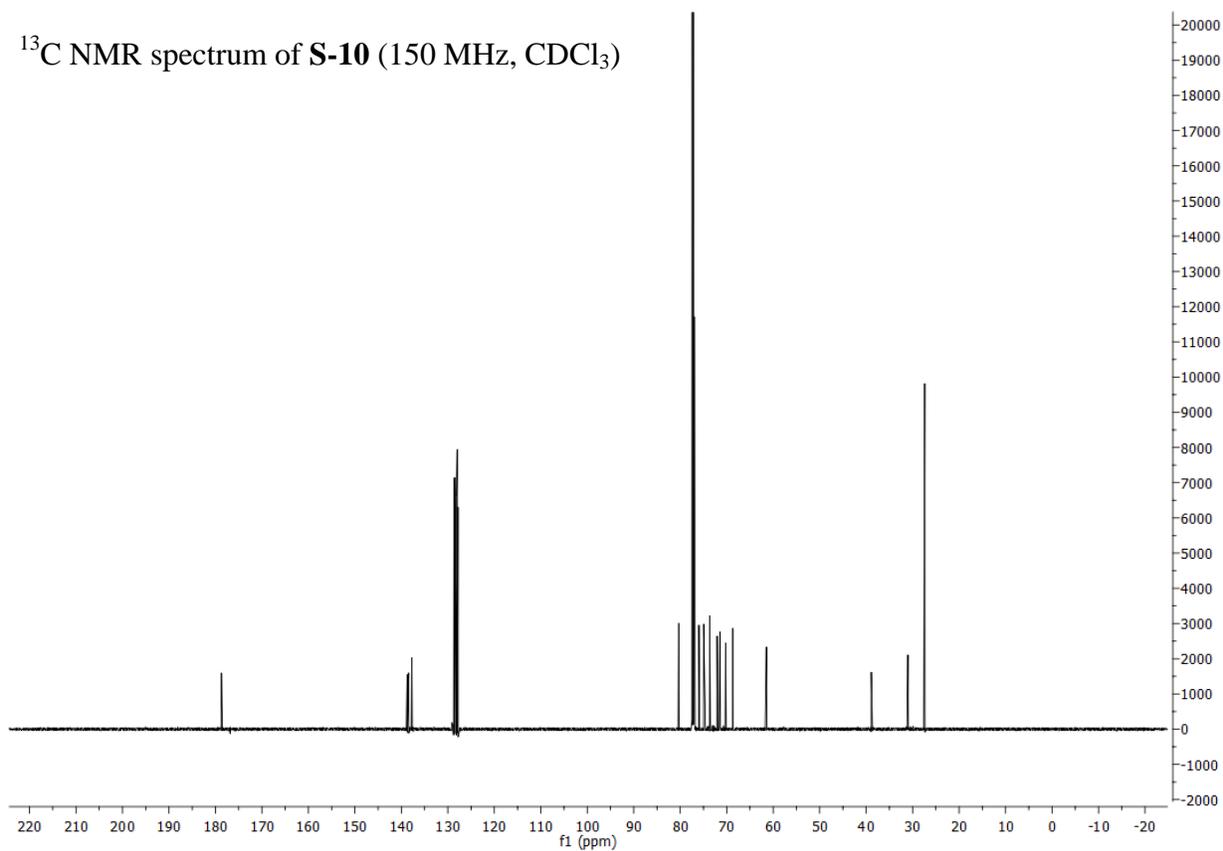
¹³C NMR spectrum of **S-9** (150 MHz, CDCl₃)



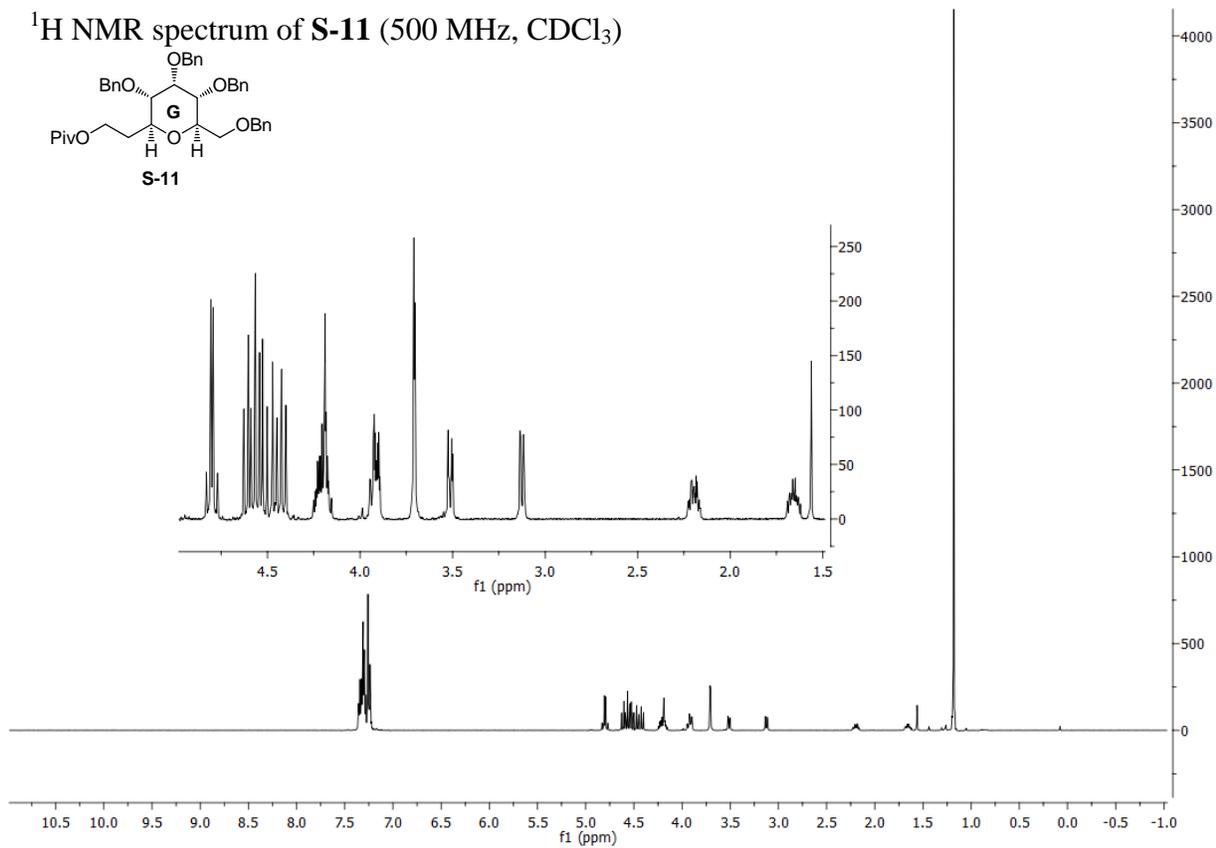
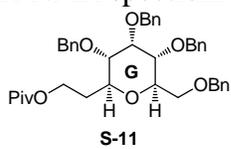
¹H NMR spectrum of **S-10** (600 MHz, CDCl₃)



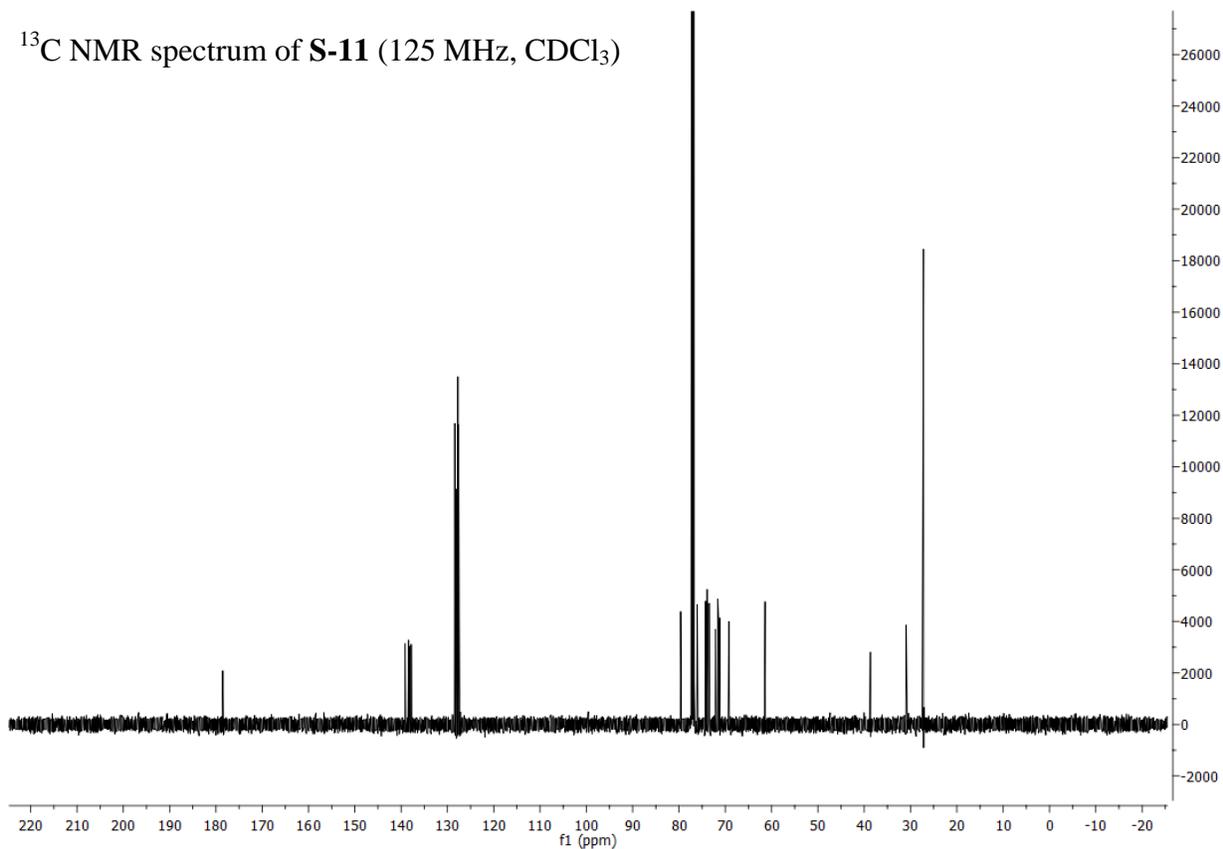
¹³C NMR spectrum of **S-10** (150 MHz, CDCl₃)



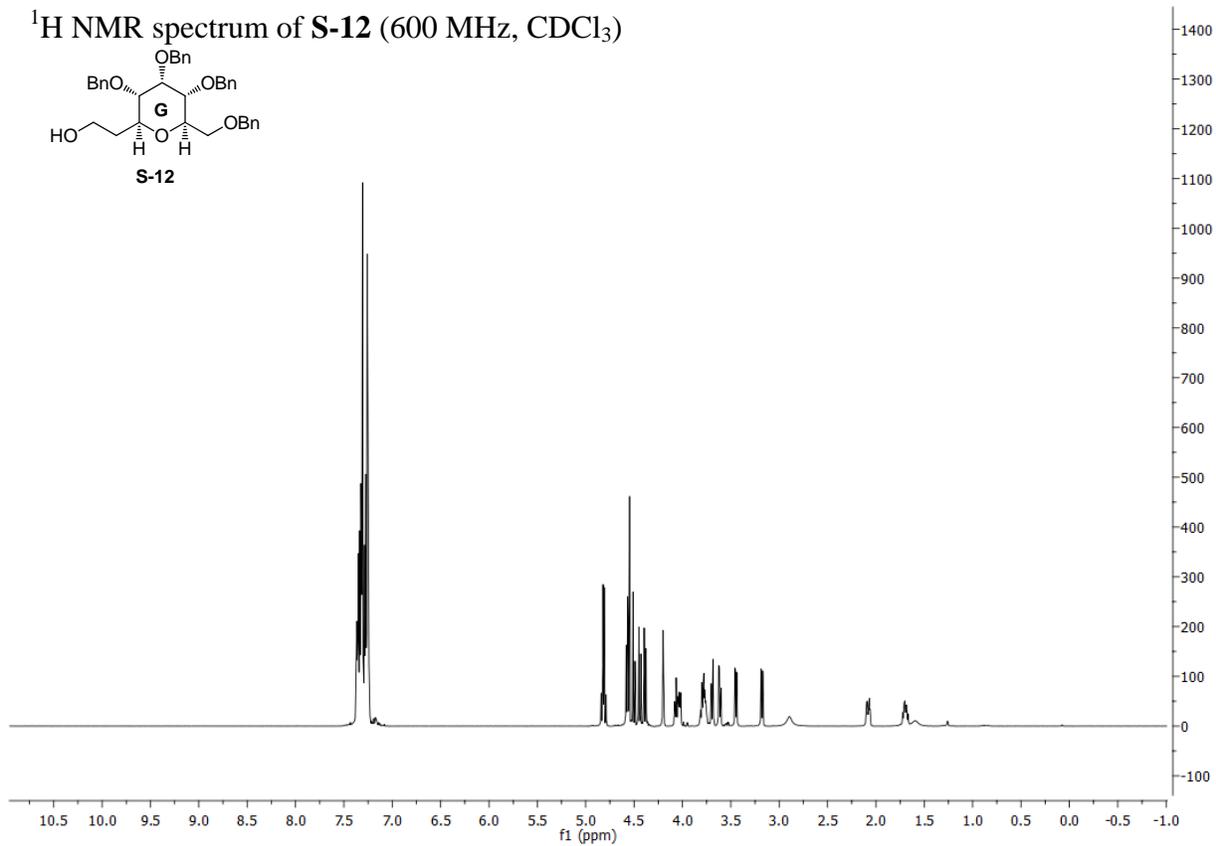
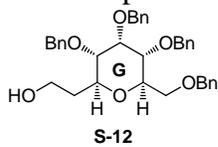
^1H NMR spectrum of **S-11** (500 MHz, CDCl_3)



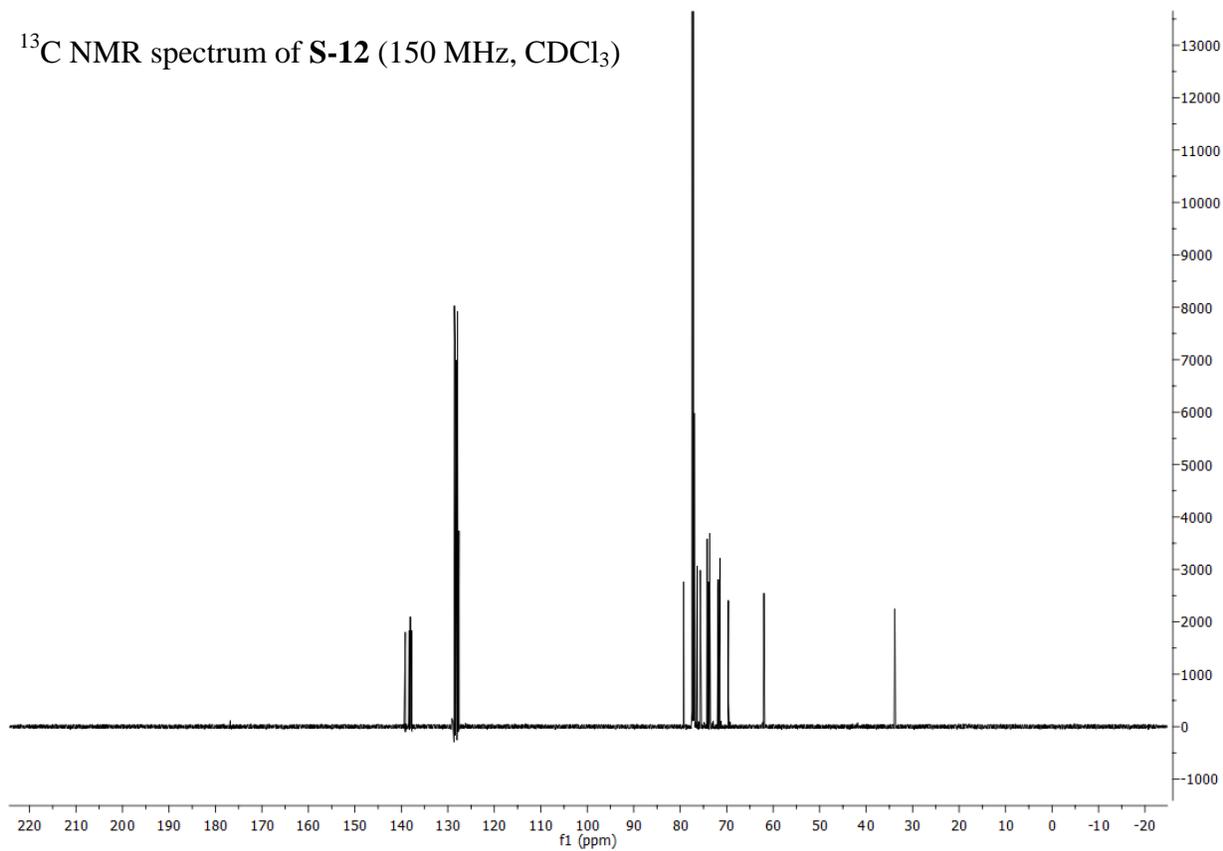
^{13}C NMR spectrum of **S-11** (125 MHz, CDCl_3)



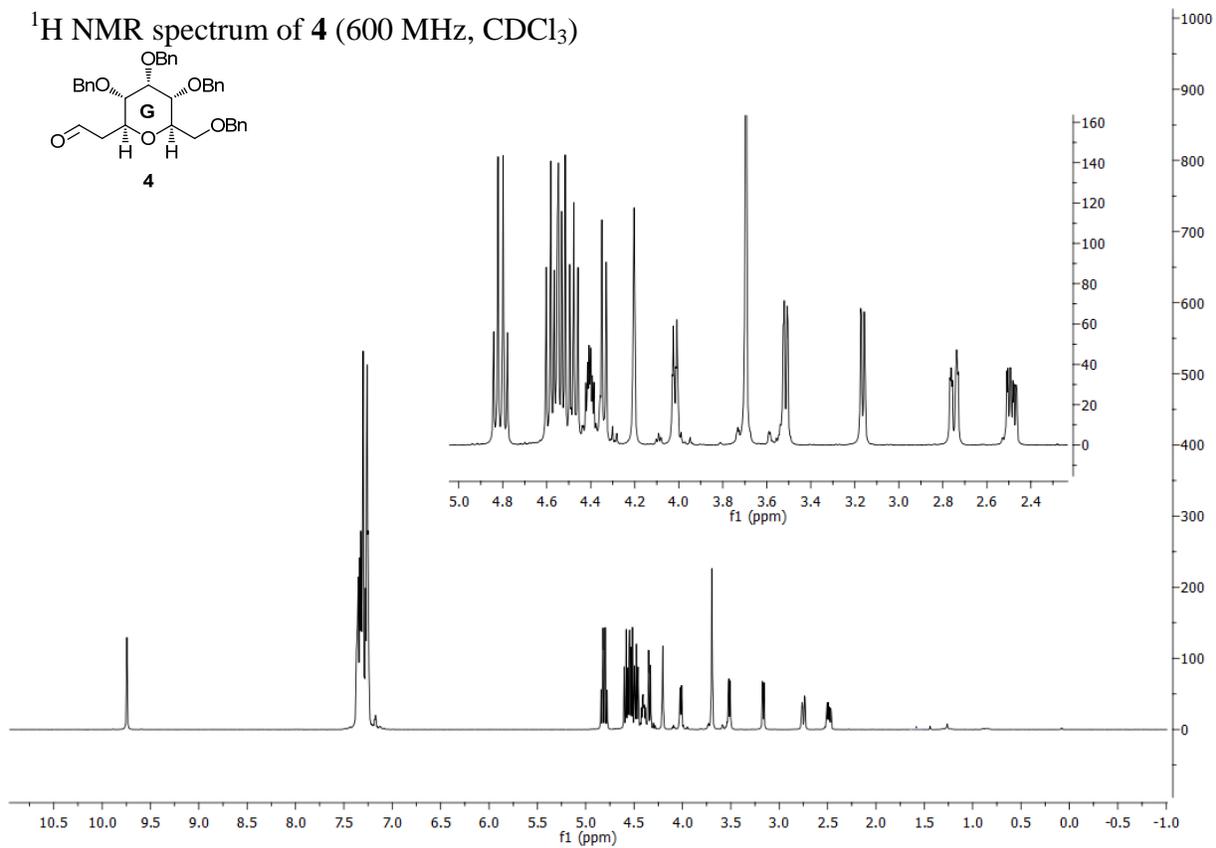
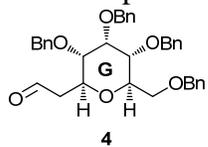
¹H NMR spectrum of **S-12** (600 MHz, CDCl₃)



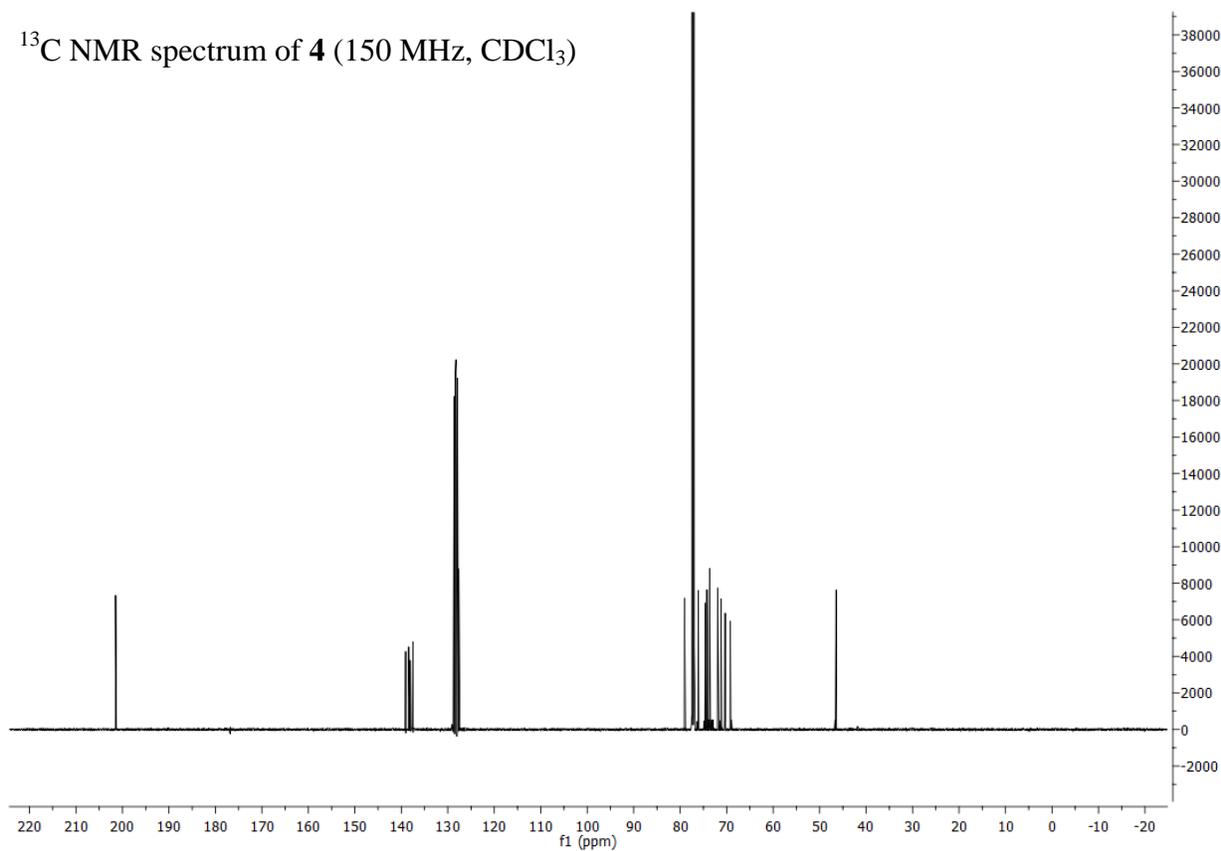
¹³C NMR spectrum of **S-12** (150 MHz, CDCl₃)



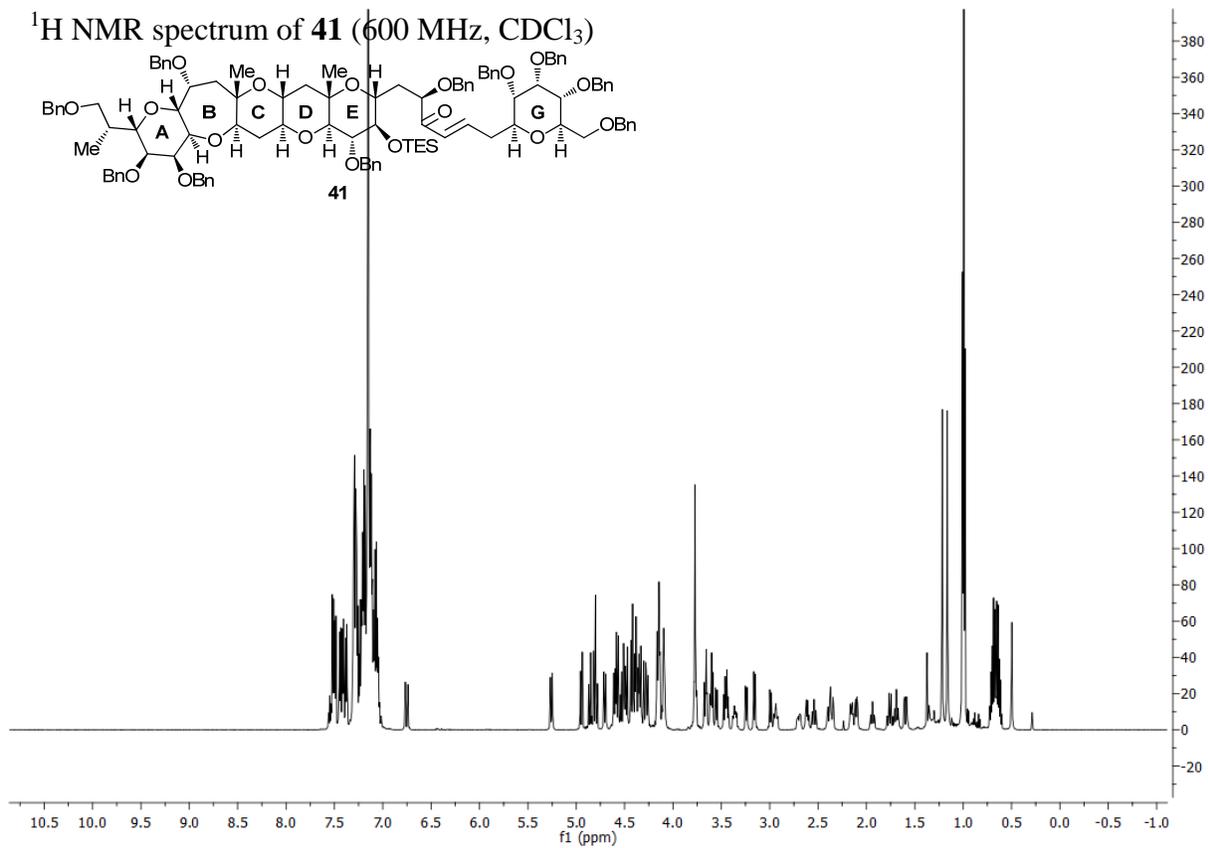
^1H NMR spectrum of **4** (600 MHz, CDCl_3)



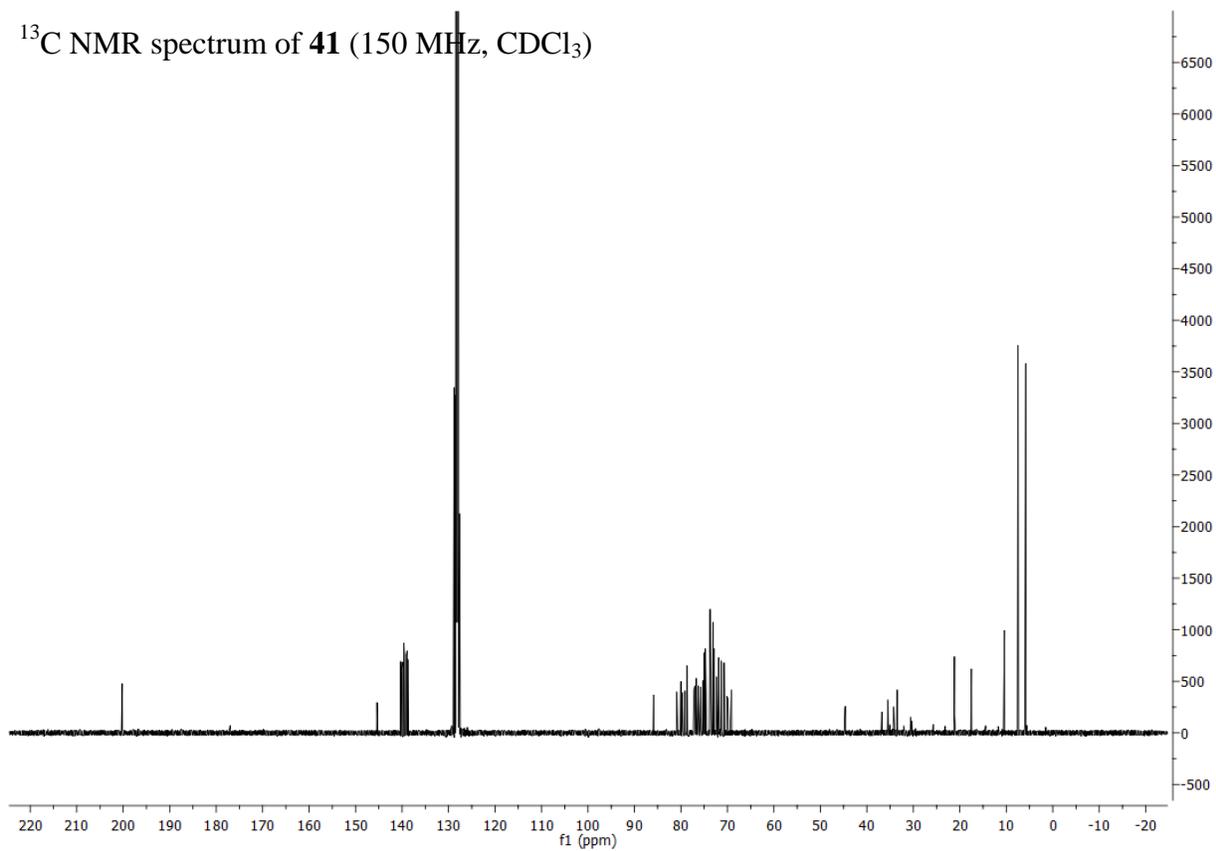
^{13}C NMR spectrum of **4** (150 MHz, CDCl_3)



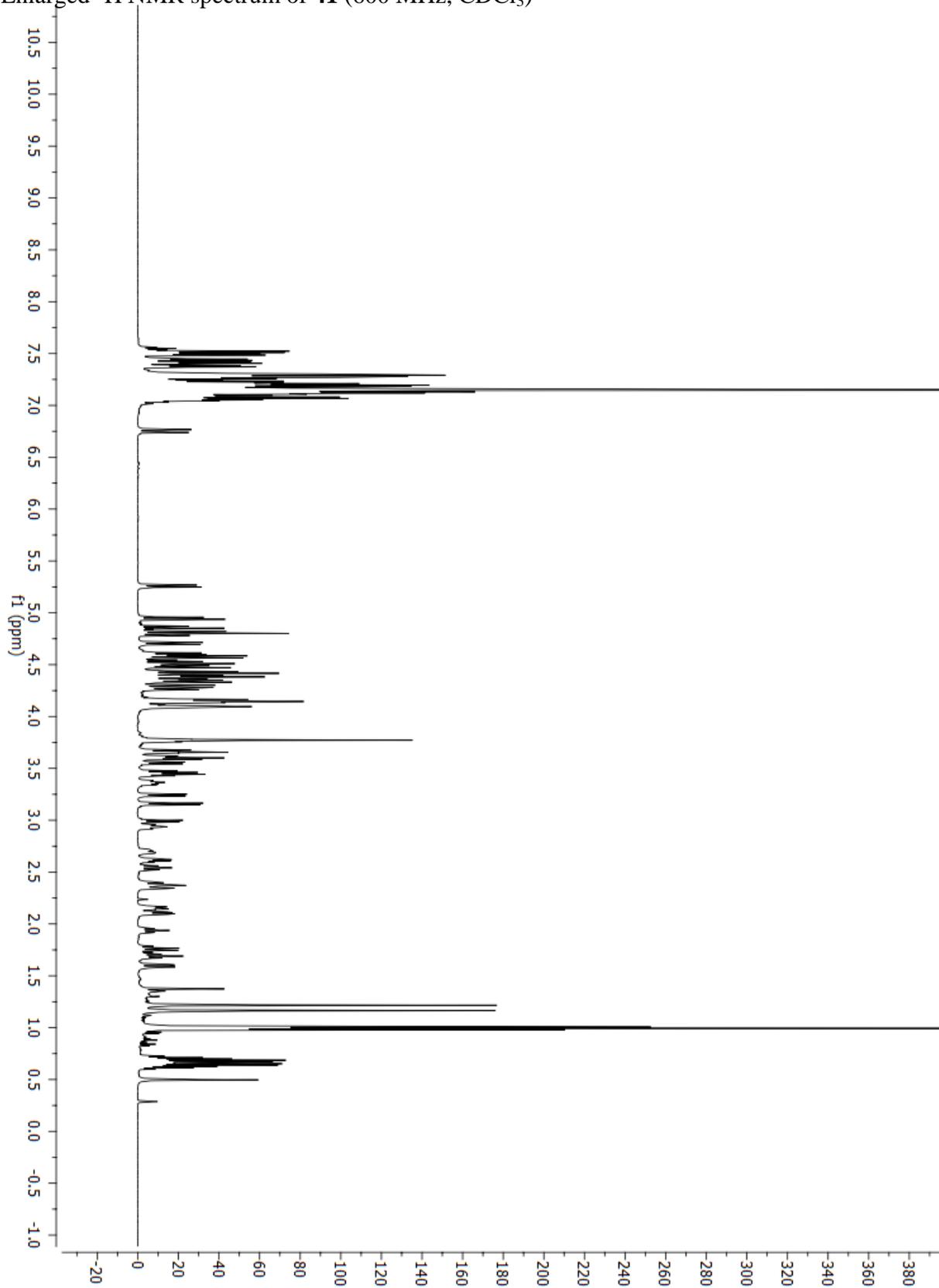
^1H NMR spectrum of **41** (600 MHz, CDCl_3)



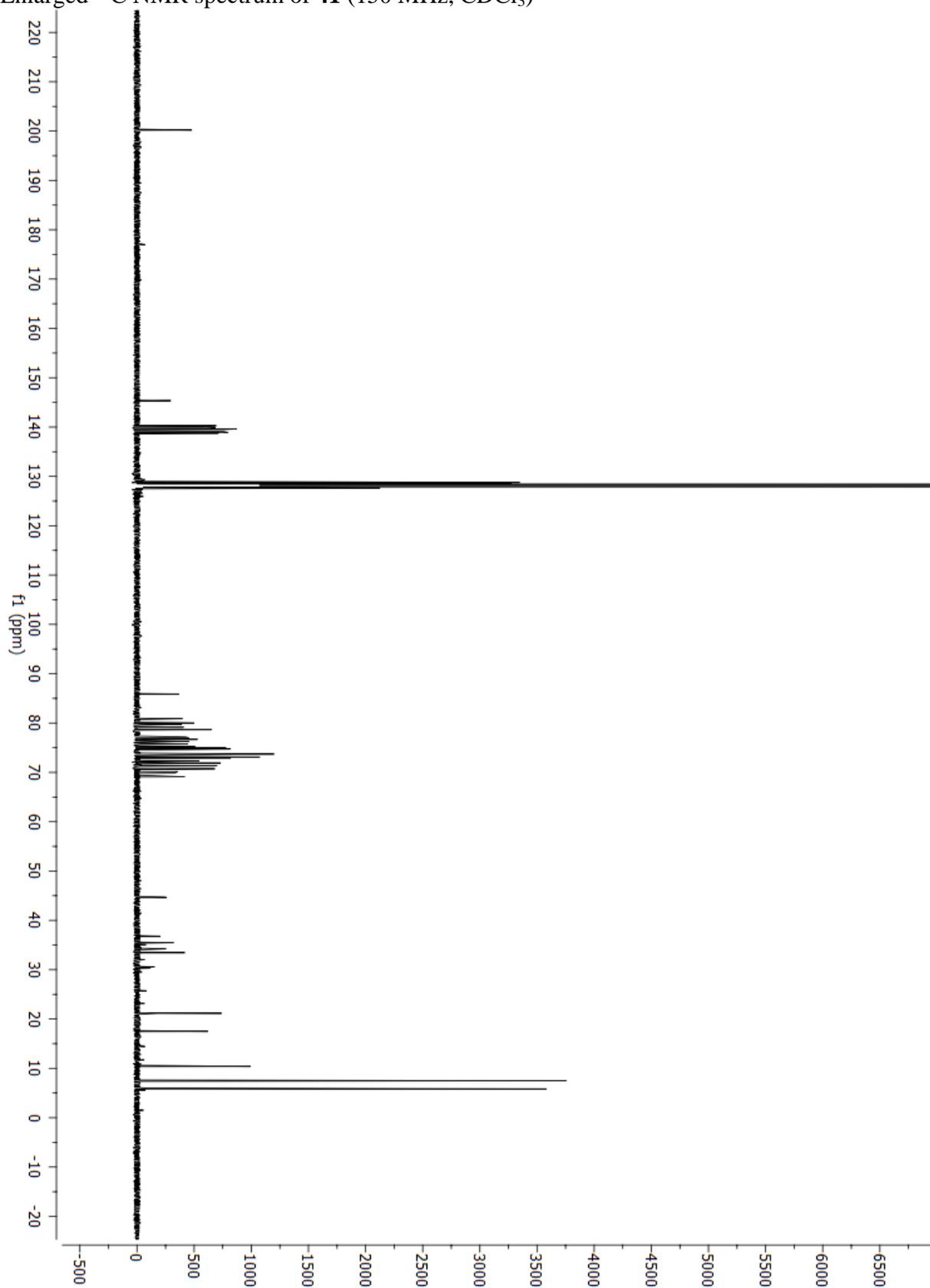
^{13}C NMR spectrum of **41** (150 MHz, CDCl_3)



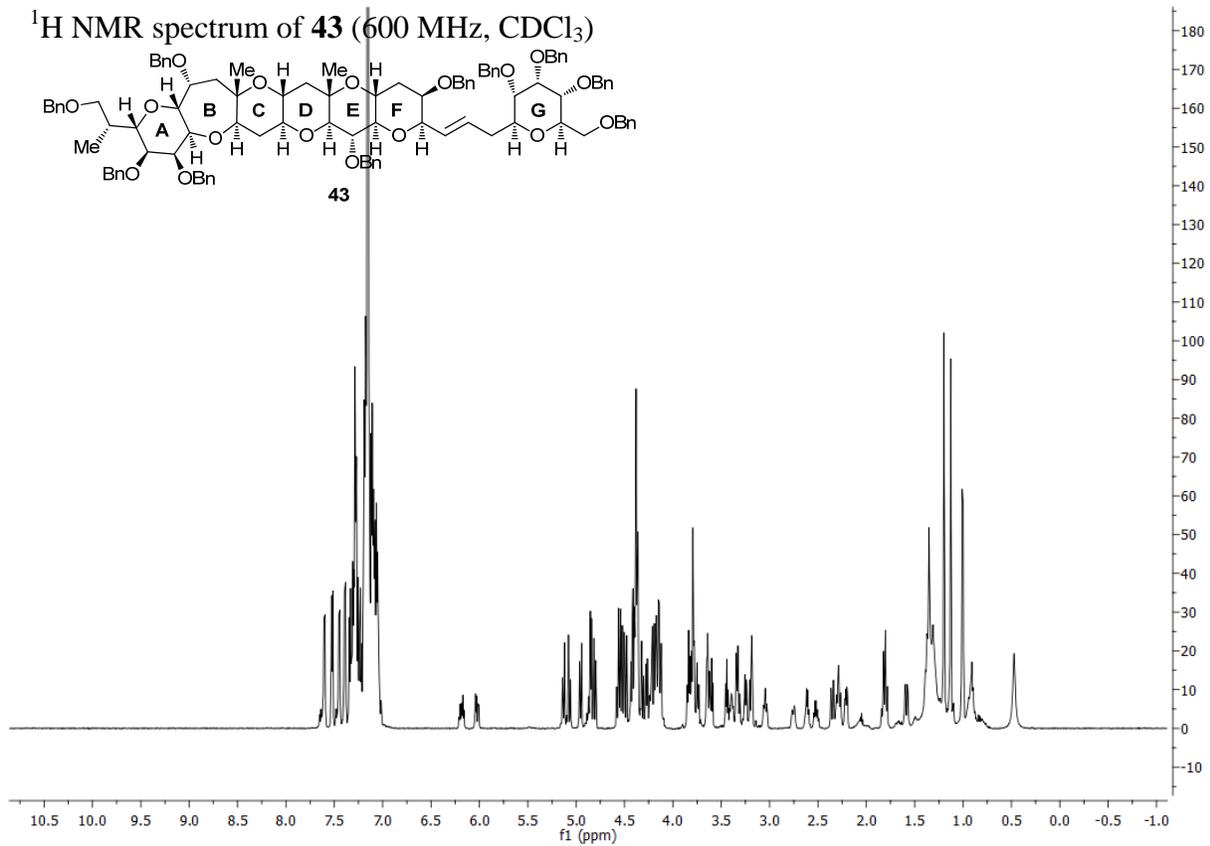
Enlarged ^1H NMR spectrum of **41** (600 MHz, CDCl_3)



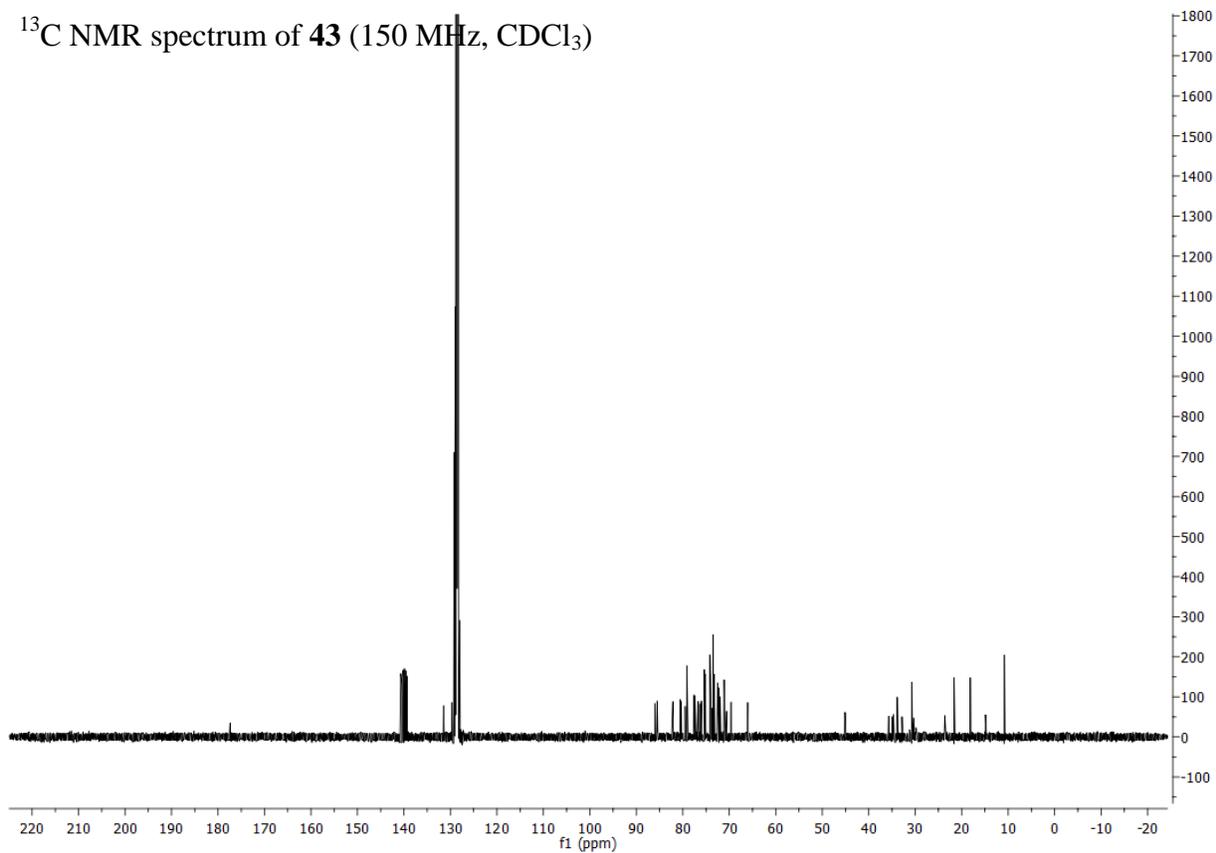
Enlarged ^{13}C NMR spectrum of **41** (150 MHz, CDCl_3)



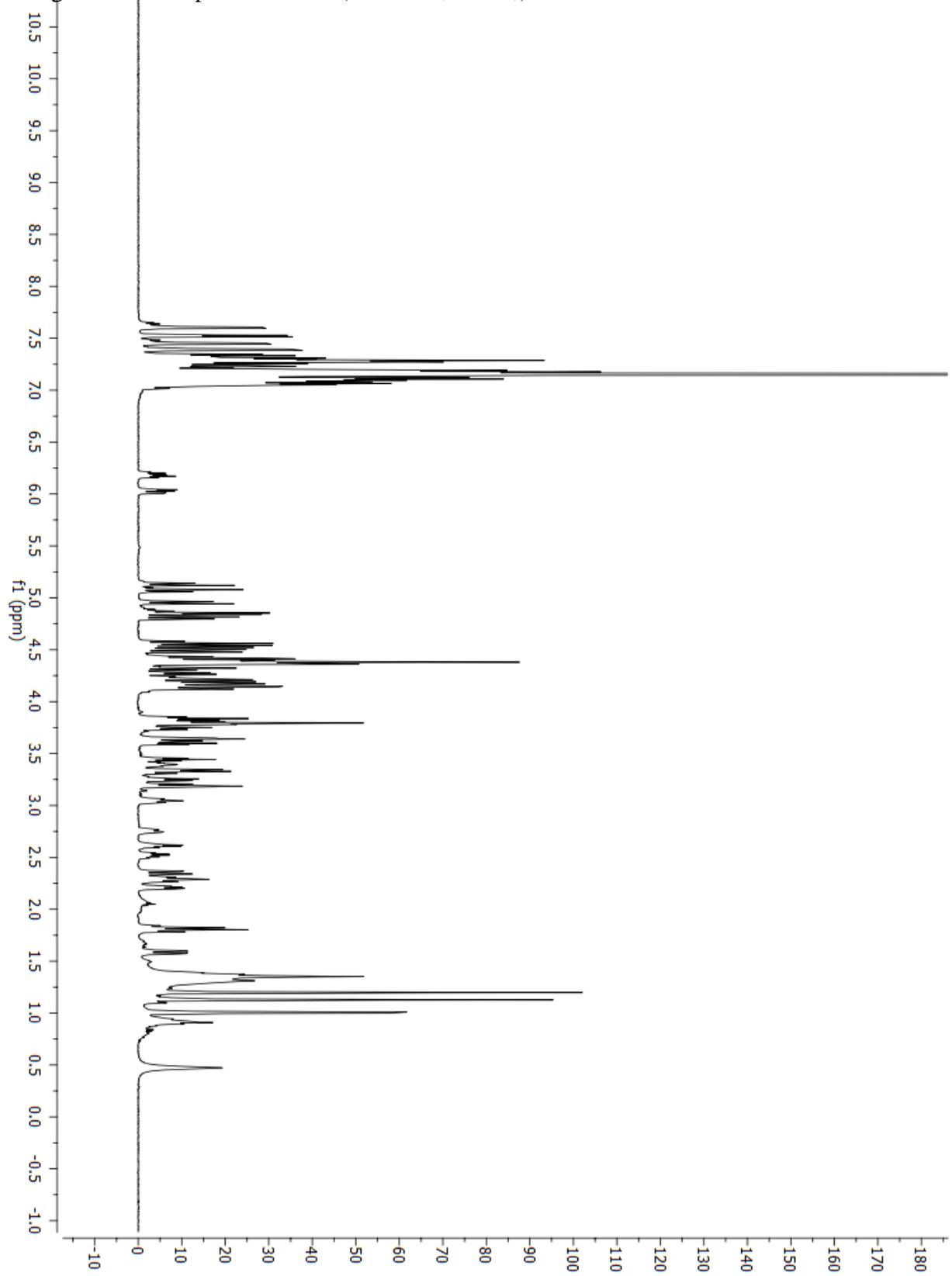
^1H NMR spectrum of **43** (600 MHz, CDCl_3)



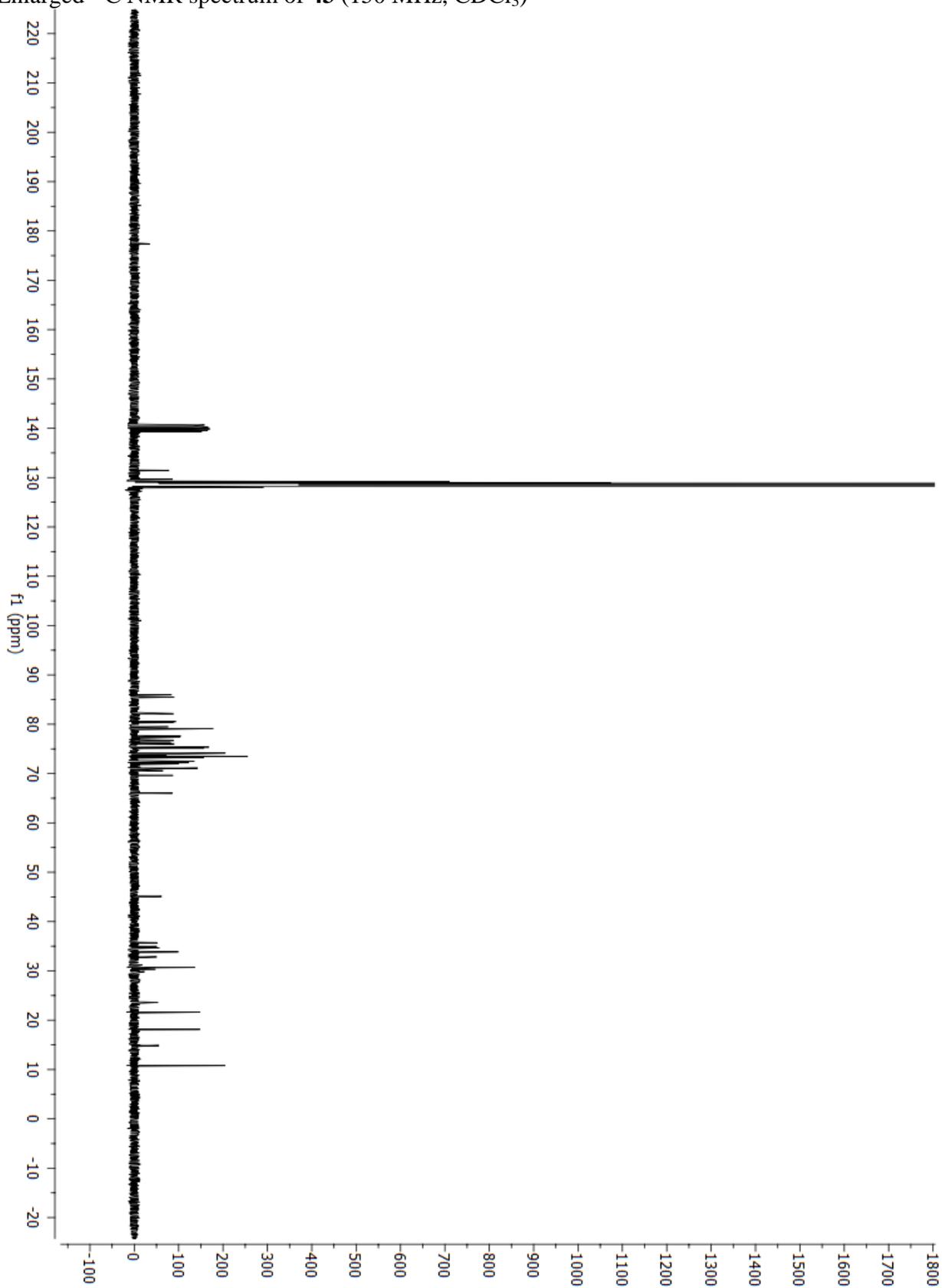
^{13}C NMR spectrum of **43** (150 MHz, CDCl_3)



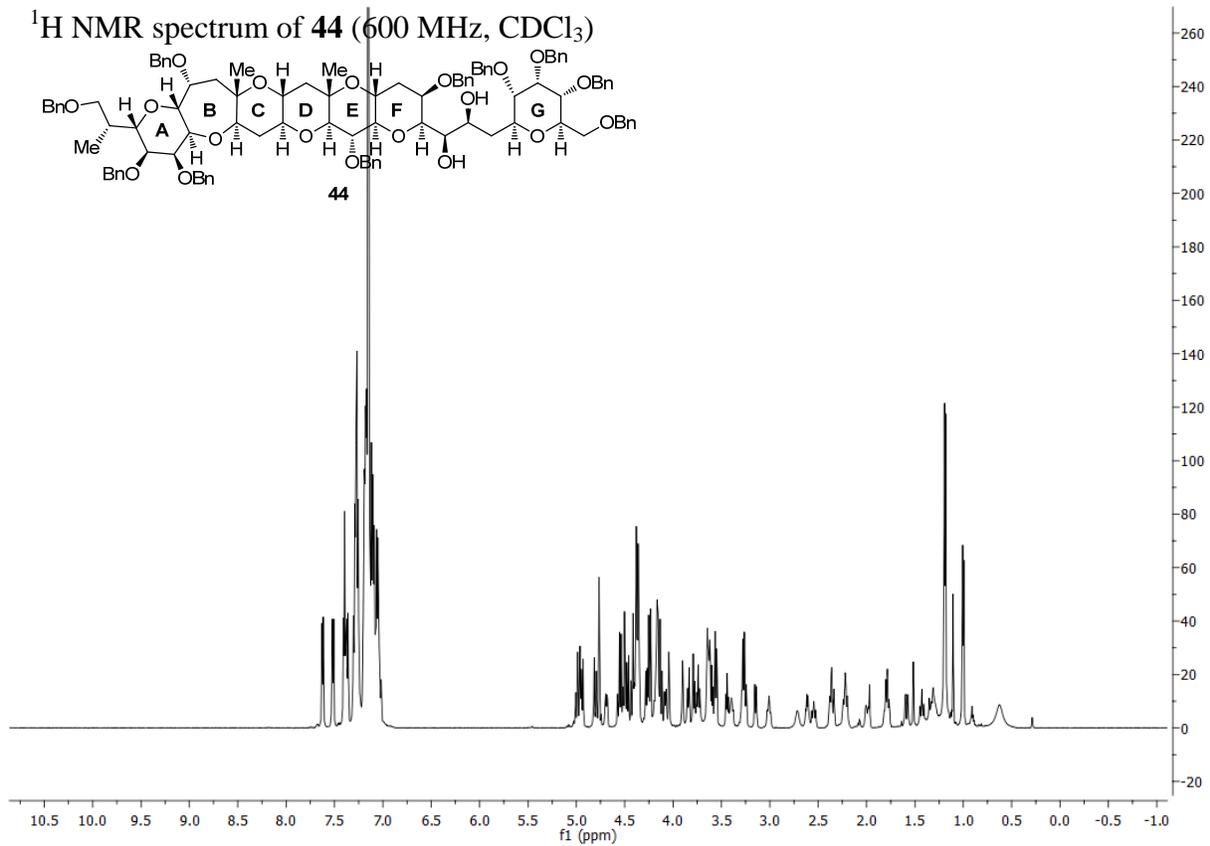
Enlarged ^1H NMR spectrum of **43** (600 MHz, CDCl_3)



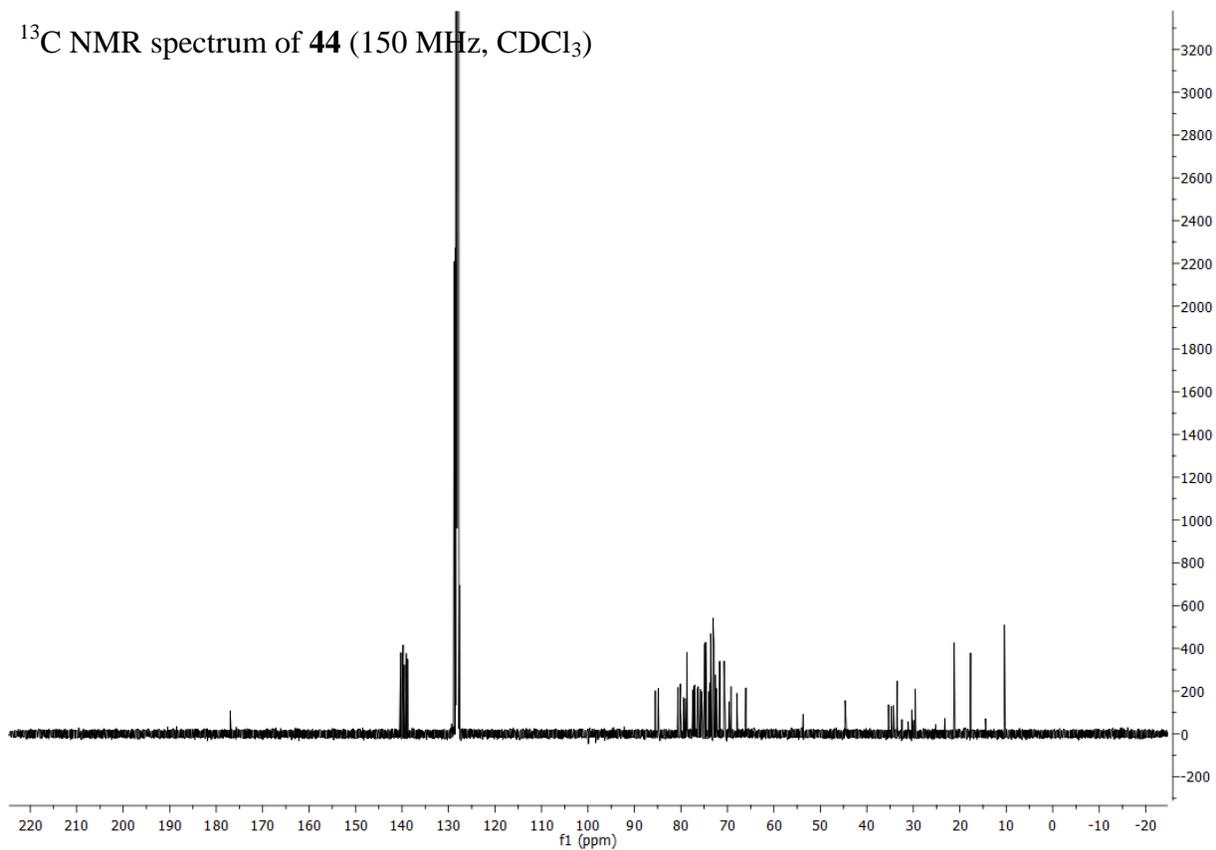
Enlarged ^{13}C NMR spectrum of **43** (150 MHz, CDCl_3)



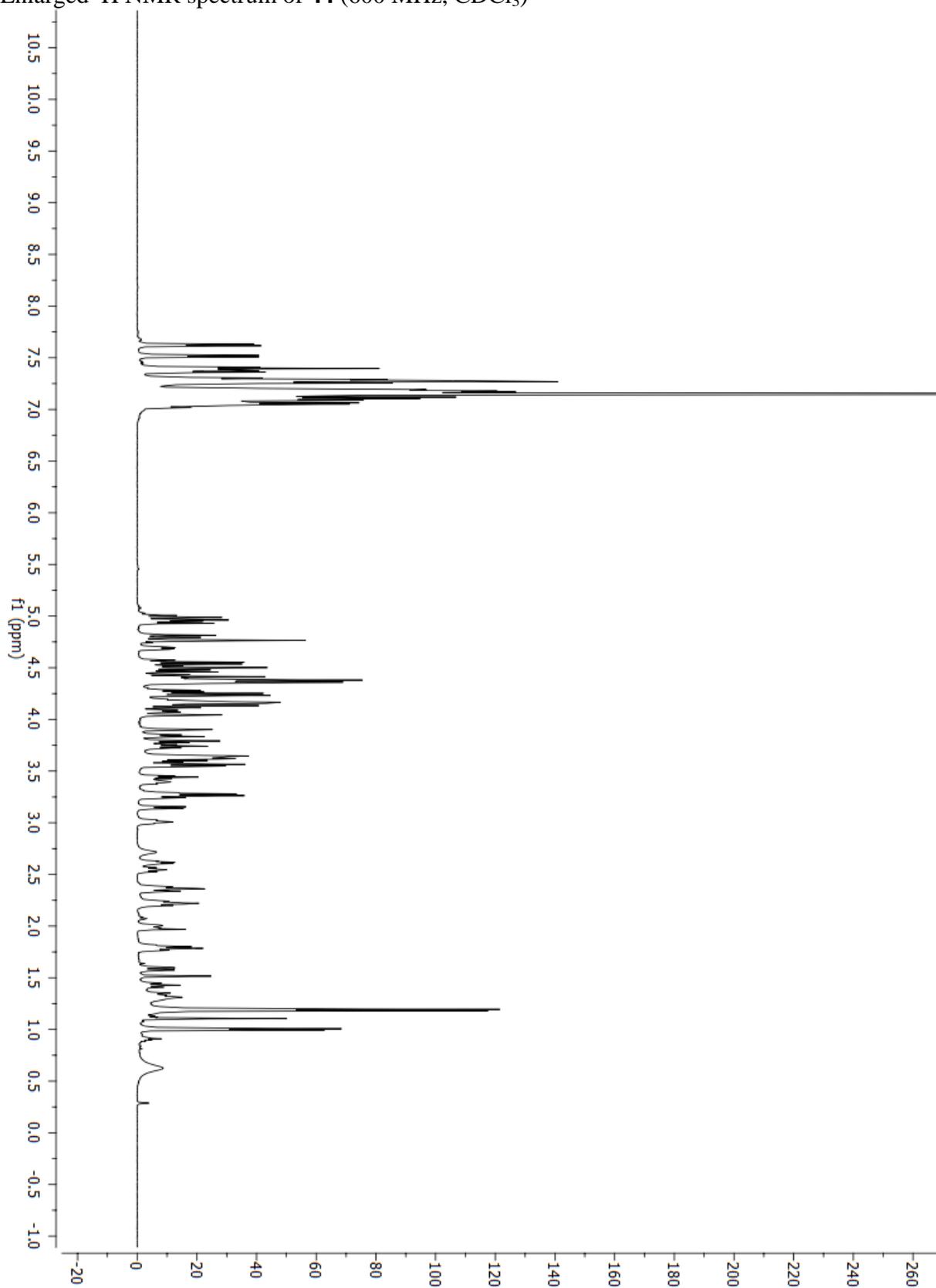
^1H NMR spectrum of **44** (600 MHz, CDCl_3)



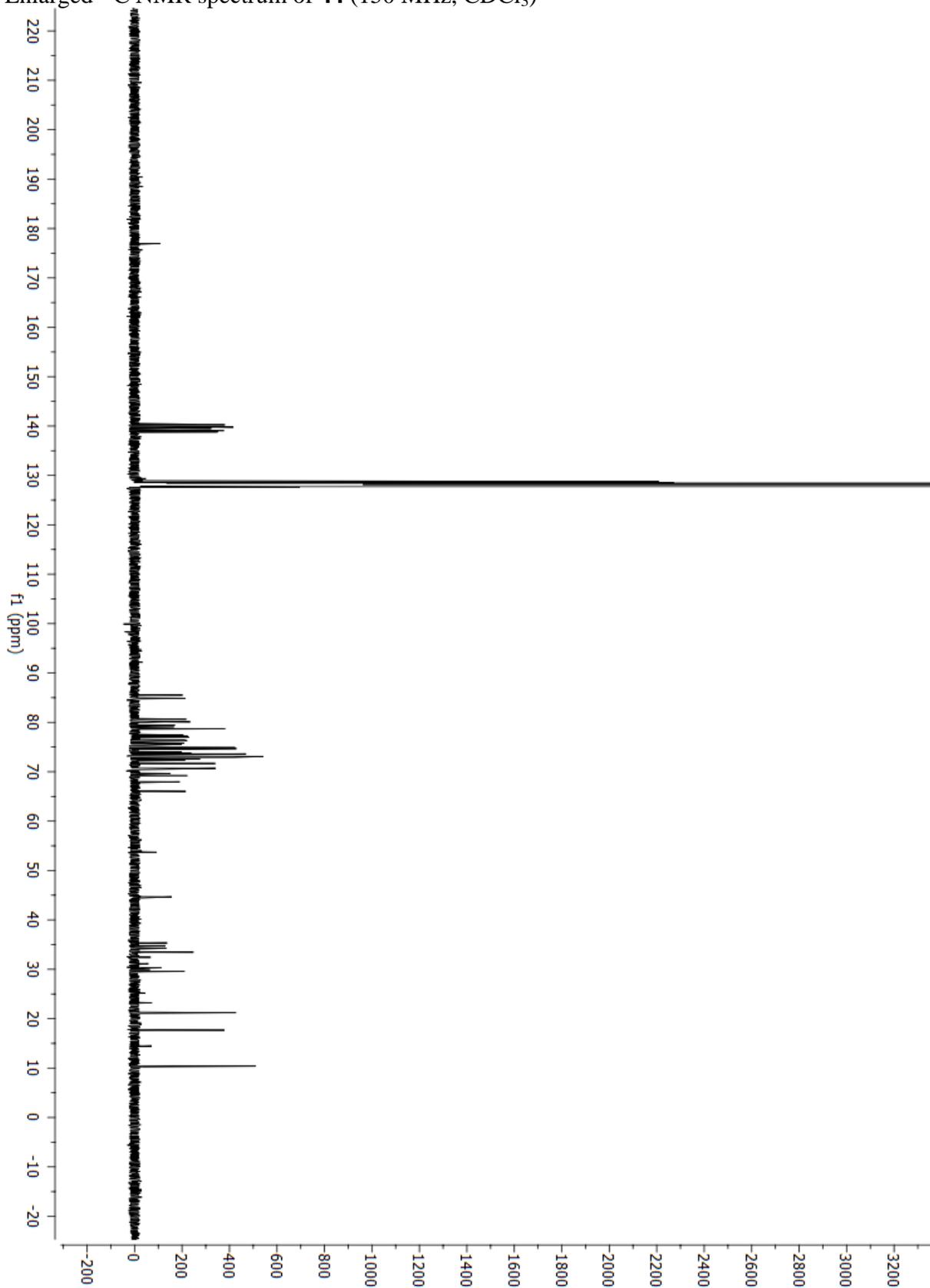
^{13}C NMR spectrum of **44** (150 MHz, CDCl_3)



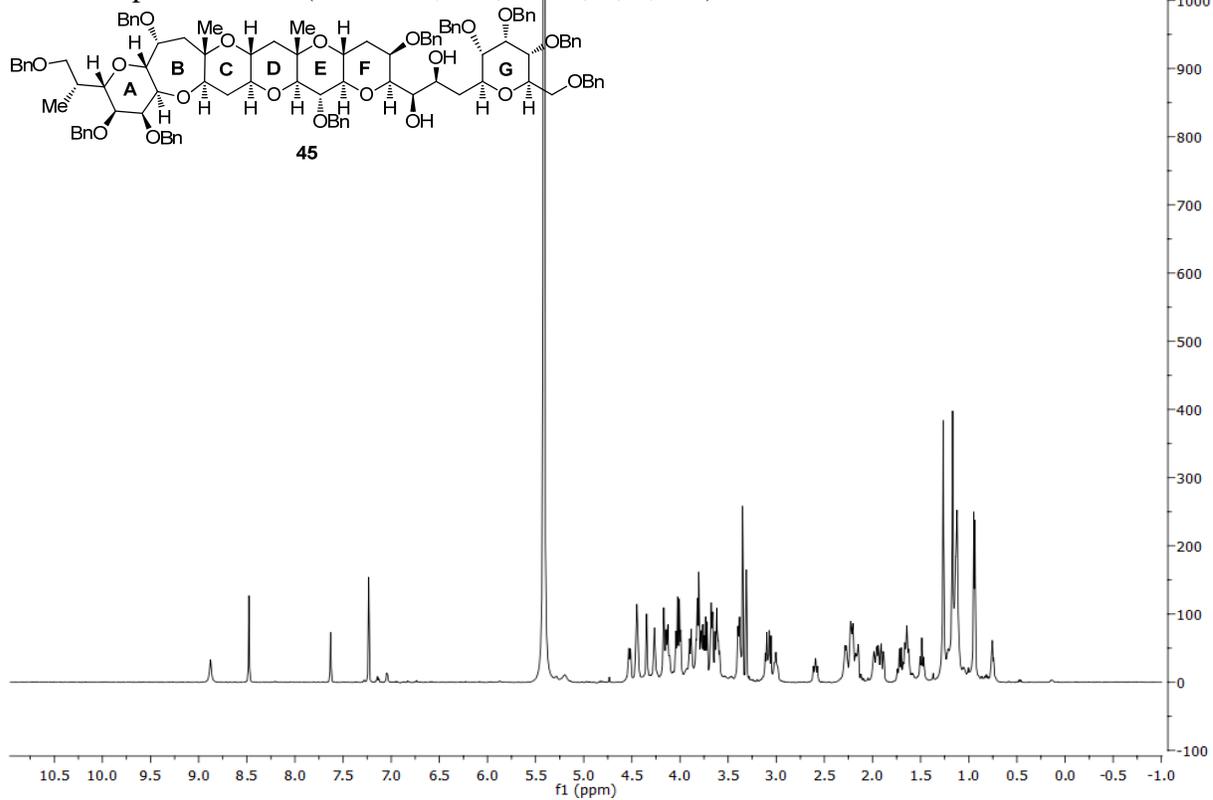
Enlarged ^1H NMR spectrum of **44** (600 MHz, CDCl_3)



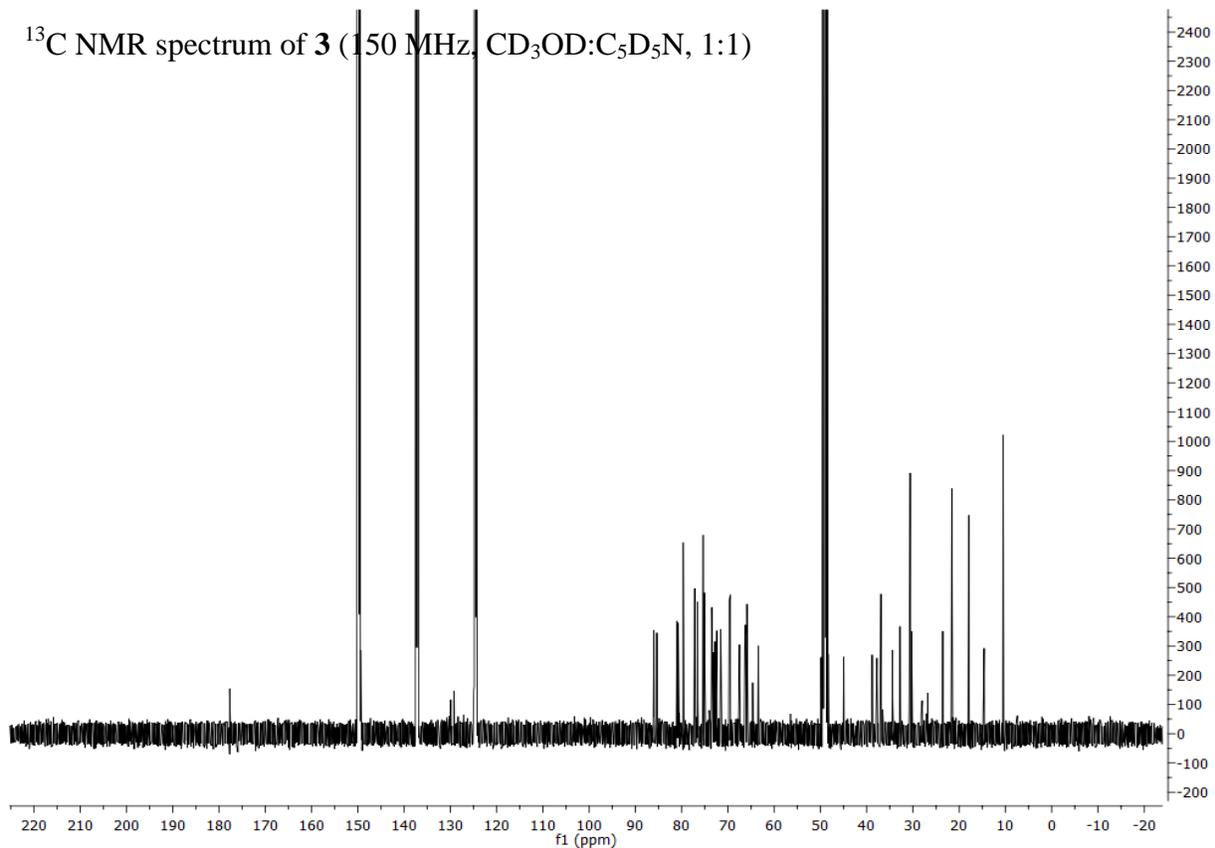
Enlarged ^{13}C NMR spectrum of **44** (150 MHz, CDCl_3)



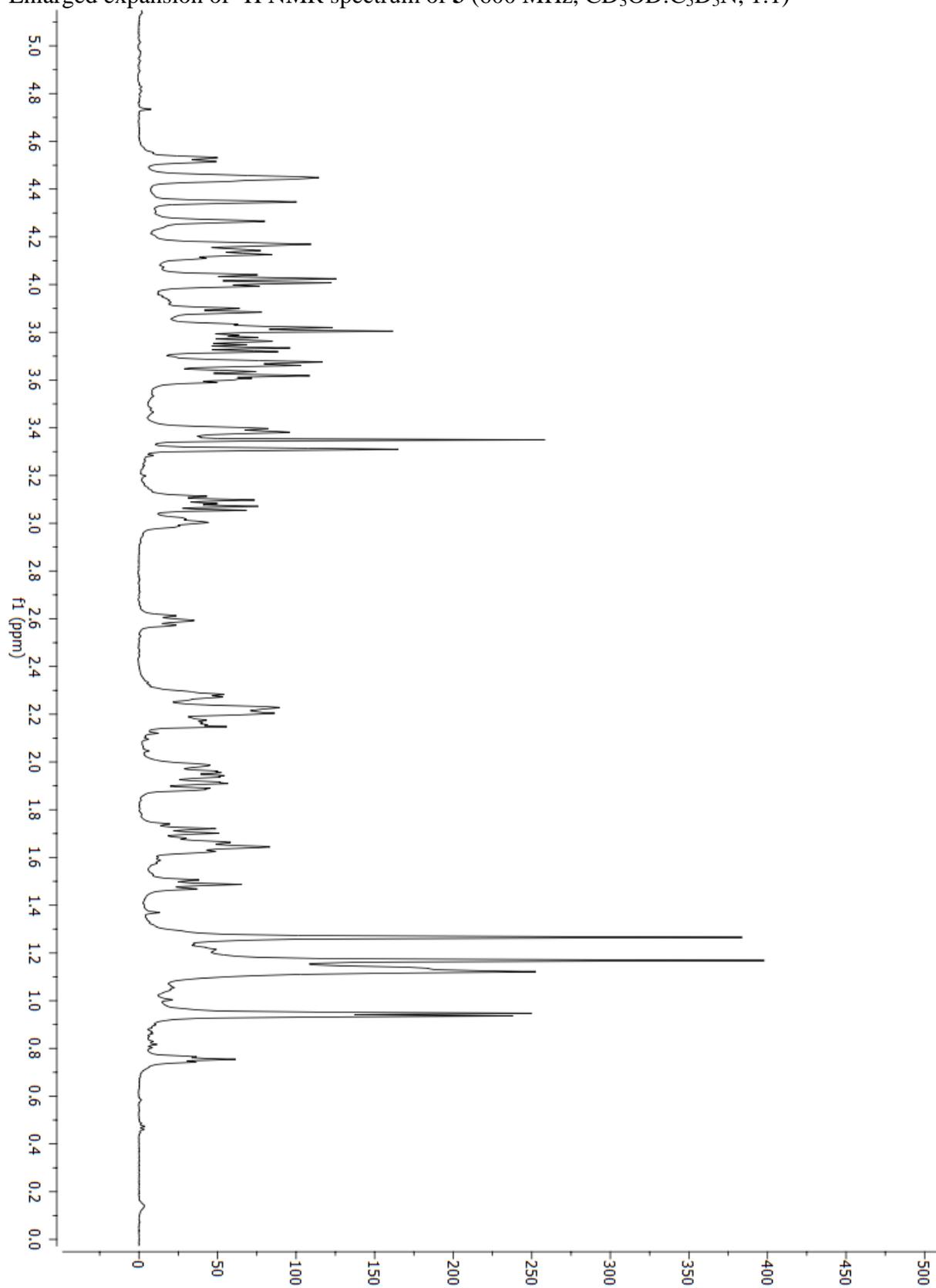
^1H NMR spectrum of **3** (600 MHz, $\text{CD}_3\text{OD}:\text{C}_5\text{D}_5\text{N}$, 1:1)



^{13}C NMR spectrum of **3** (150 MHz, $\text{CD}_3\text{OD}:\text{C}_5\text{D}_5\text{N}$, 1:1)



Enlarged expansion of ^1H NMR spectrum of **3** (600 MHz, $\text{CD}_3\text{OD}:\text{C}_5\text{D}_5\text{N}$, 1:1)



Enlarged expansion of ^{13}C NMR spectrum of **3** (150 MHz, $\text{CD}_3\text{OD}:\text{C}_5\text{D}_5\text{N}$, 1:1)

