Electronic Supplemental Information (ESI)

Lewis acid-catalyzed stereoselective lactonization and subsequent glycosidation of 2-*C*-malonyl carbohydrates

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Contents

General Experimental Techniques

Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. All reactions were performed under argon atmosphere. Removal of solvent *in vacuo* refers to distillation using a rotary evaporator attached to an efficient vacuum pump. Products obtained as solids or syrups were dried under high vacuum. $AuBr_3$ was purchased from multi-national commercial vendors. Analytical thin-layer chromatography was performed on pre-coated silica plates (F_{254}, 0.25 mm thickness); compounds were visualized by UV light or by staining with anisaldehyde spray. Optical rotations were measured on a JASCO P-1020 polarimeter. IR spectra were recorded on a Perkin-Elmer 1600 FT-IR spectrometer. NMR spectra were recorded either on a Bruker AC 300, AV 500 or AV 600 with $CDCl_3$ as the solvent and internal standard. High resolution mass spectroscopy (HRMS) was performed on MALDI-TOF using 2,5-dihydroxybenzoic acid as the solid matrix.

General Experimental Procedures

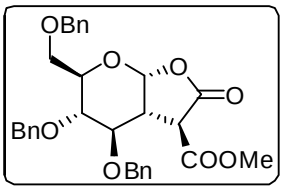
General Procedure for $AuBr_3$-catalyzed lactonizations: To a solution of methyl glycoside **2** (112 mg, 0.2 mmol) in acetonitrile (3 mL) was added water (0.4 mmol) and 8 mol% of $AuBr_3$ at room temperature. The resulting mixture was heated to 70 °C and stirred until TLC showed complete conversion. The reaction mixture was concentrated *in vacuo* to obtain a crude residue which was purified by silica gel column chromatography (ethyl acetate-petroleum ether) to give lactones **1c** in analytically pure form.

General Procedure for lactone openings: To a solution of lactone *gluco*-**1c** (106 mg, 0.2 mmol) in acetonitrile (3 mL) was added nucleophile **5** (0.6 mmol) and TMSOTf (45 mg, 0.2 mmol) at room temperature. The mixture was stirred at this temperature until TLC showed complete conversion. After dilution with water (5 mL), the mixture was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (10 mL) and dried over anhydrous sodium sulphate. After removal of the solvent *in vacuo*, the residue was purified by silica gel column chromatography (ethyl acetate-petroleum ether) to afford the prodducts **6**.

One-pot synthesis of glycoside 6b: To a solution of methyl glycoside *gluco*-**2** (112 mg, 0.2 mmol) in acetonitrile (3 mL) was added water (0.4 mmol) and 8 mol% of $AuBr_3$ at room temperature. The resulting mixture was heated to 70 °C and stirred until TLC showed formation of lactone *gluco*-**1c**. Direct addition of allyl alcohol **5b** (40 μL, 0.6 mmol) and TMSOTf (45 mg, 0.2 mmol) at room temperature gave no conversion after 12 h, due to the presence of water. Thus, powdered 4Å molecular sieves was added prior to the reaction with TMSOTf. Again, the conversion was not complete but the allyl glycoside **6b** could now be isolated in 35% yield. Thus, a one-pot synthesis of glycosides **6** is possible, but in lower yields compared to the two-step procedure.

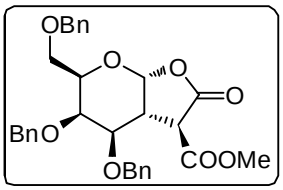
Compound Characterization Data

Gluco-lactone **1c**:



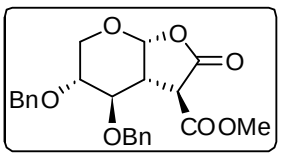
$[\alpha]_D(CHCl_3, c\ 1.3) = +26.4$; ^1H NMR (600,24 MHz, $CDCl_3$): δ 3.10(ddd, 1H, J = 10.0, 5.7, 3.9Hz), 3.54(dd, 1H, J = 6.7, 6.2Hz), 3.48(d, 1H, J = 3.9Hz), 3.69 (dd, 1H, J = 10.4, 2.0Hz), 3.72-3.78(m, 2H), 3.78(s, 3H), 3.84(dd, 1H, J = 10.0, 6.2Hz), 4.55(d, 1H, J = 11.0Hz), 4.57(d, 1H, J = 11.9Hz), 4.61(d, 1H, J = 11.5Hz), 4.66(d, 1H, J = 11.5Hz), 4.67(d, 1H, J = 11.0Hz), 4.79(d, 1H, J = 11.9Hz), 6.08(d, 1H, J = 5.7Hz), 7.15-7.40(m, 15H); ^{13}C NMR (125,06 MHz, $CDCl_3$): δ 43.4, 51.4, 53.2, 68.4, 72.7, 73.5, 73.6, 73.6, 75.7, 76.9, 100.7, 127.8-128.6, 137.4, 137.5, 137.7, 166.9, 168.4; IR ($CHCl_3$) : ν = 3030, 2953, 2920, 2868, 1788, 1736, 1454, 1167, 1141, 1096, 1076, 754, 698 cm^{-1}; Mol. Wt. calculated for $C_{31}H_{32}O_8Na$: 555.5707, Found: 555.5699.

Galacto-lactone **1c**:



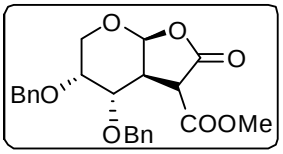
$[\alpha]_D(CHCl_3, c\ 1.6) = +7.6$; ^1H NMR (600,24 MHz, $CDCl_3$): δ 3.05(dd, 1H, J = 10.9, 4.4Hz), 3.21(dd, 1H, J = 10.9, 2.3Hz), 3.51(s, 1H), 3.54 (dd, 1H, J = 8.9, 5.5Hz), 3.59 (dd, 1H, J = 8.9, 7.9Hz), 3.72(s, 3H), 3.88 (dd, 1H, J = 7.9, 5.5Hz), 4.02 (d, 1H, J = 2.3Hz), 4.29(d, 1H, J = 11.6Hz), 4.39(d, 1H, J = 11.6Hz), 4.44(d, 1H, J = 11.9Hz), 4.54(d, 1H, J = 11.3Hz), 4.63(d, 1H, J = 11.9Hz), 4.78(d, 1H, J = 11.3Hz), 6.06(d, 1H, J = 4.4Hz), 7.25-7.40(m, 15H); ^{13}C NMR (55.32 MHz, $CDCl_3$): δ 41.2, 53.2, 53.4, 67.8, 68.9, 71.2, 72.4, 73.5, 74.3, 76.6, 102.6, 126.9-128.7, 136.6, 137.5, 137.8, 166.8, 168.1; IR ($CHCl_3$) : ν = 3030, 2953, 2924, 2870, 1784, 1736, 1454, 1190, 1163, 1113, 1055, 752, 698 cm^{-1}; Mol. Wt. calculated for $C_{31}H_{32}O_8Na$: 555.5707, Found: 555.5699.

Xylo-*l*actone **1c**:



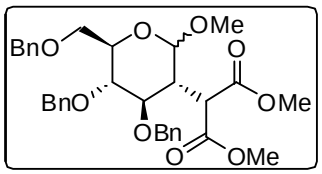
$[\alpha]_D(CHCl_3, c\ 1.7) = -22.0$; ^1H NMR (600,24 MHz, $CDCl_3$): δ 2.91(ddd, 1H, J = 9.8, 4.2, 3.5Hz), 3.43(dd, 1H, J = 3.8, 3.5Hz), 3.65(ddd, 1H, J = 8.8, 3.5, 2.5Hz), 3.72(s, 3H), 3.83(dd, 1H, J = 12.9, 2.5Hz), 3.85(dd, 1H, J = 12.9, 3.5Hz), 4.08(d, 1H, J = 9.8Hz), 4.42(d, 1H, J = 12.0Hz), 4.53(s, 2H), 4.55(d, 1H, J = 12.0Hz), 5.63(d, 1H, J = 4.2Hz), 7.24-7.40(m, 10H) ; ^{13}C NMR (125.06 MHz, $CDCl_3$): δ 42.6, 47.0, 52.9, 62.1, 71.4, 72.2, 72.8, 72.9, 97.6, 127.6-128.6, 137.2, 137.2, 167.2, 169.9; IR ($CHCl_3$) : ν = 3028, 2955, 2926, 2870, 1801, 1736, 1454, 1288, 1265, 1119, 1074, 754, 698cm^{-1}; Mol. Wt. calculated for $C_{23}H_{24}O_7Na$: 435.4222, Found: 435.4231.

Arabino-lactone **1c**:



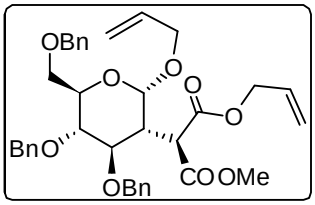
$[\alpha]_D$($CHCl_3$, *c* 1.6) = -34.2; ^{1}H NMR (600.24 MHz, $CDCl_3$): δ 3.02(ddd, 1H, J = 9.5, 4.6, 2.5Hz), 3.29(dd, 1H, J = 9.5, 2.5Hz), 3.47(d, 1H, J = 2.5Hz), 3.62(dd, 1H, J = 12.5, 1.5Hz), 3.68(s, 3H), 3.72-3.78(m, 1H), 3.99(dd, 1H, J = 12.5, 3.8Hz), 4.31(d, 1H, J = 11.7Hz), 4.52(d, 1H, J = 12.1Hz), 4.54(d, 1H, J = 11.7Hz), 4.65(d, 1H, J = 12.1Hz), 6.01(d, 1H, J = 4.6Hz), 7.26-7.41(m, 10H) ; ^{13}C NMR (125.06 MHz, $CDCl_3$): δ 41.8, 52.1, 53.1, 62.3, 68.9, 71.0, 71.3, 77.0, 101.9, 127.3-128.6, 137.0, 137.6, 166.8, 168.5; IR ($CHCl_3$) : ν = 3030, 2955, 2930, 2888, 2874, 1784, 1736, 1454, 1437, 1193, 1163, 1111, 752, 698, 667 cm^{-1}; Mol. Wt. calculated for $C_{23}H_{24}O_7Na$: 435.4222, Found: 435.4231.

Compound **6a**:



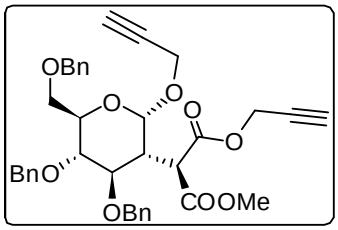
^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.51(ddd, 1H, J = 3.8, 8.8, 12.4 Hz), 2.67(ddd, 1H, J = 3.2, 5.7, 8.8 Hz), 3.27, 3.46, 3.52, 3.58, 3.63, 3.69(6s, 18H), 3.34-3.76(m, 10H), 3.81(d, 1H, J = 2.8Hz), 3.92(d, 1H, J = 3.7Hz), 4.40-4.87(m, 12H), 4.94(d, 1H, J = 4.5Hz), 5.02(d, 1H, J = 3.2Hz), 7.05-7.40(m, 30H); ^{13}C NMR (55.32 MHz, $CDCl_3$): δ 46.1, 48.0, 48.2, 49.8, 52.2, 52.2, 52.3, 52.3, 55.2, 57.3, 68.5, 68.8, 70.9, 72.1, 73.5, 73.5, 74.7, 74.7, 74.8, 74.9, 78.6, 80.0, 80.1, 80.3, 99.2, 101.8, 127.4-128.4, 137.9, 137.9, 138.0, 138.1, 138.2, 138.5, 168.7, 168.9, 169.0, 169.6; IR ($CHCl_3$) : ν = 3030, 3010, 2951, 2928, 2857, 1751, 1736, 1454, 1435, 1146, 1126, 1067, 1051, 754, 698 cm^{-1}; Mol. Wt. calculated for $C_{33}H_{38}O_9Na$: 601.6392, Found: 601.6402.

Compound **6b**:



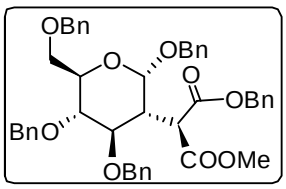
$[\alpha]_D$($CHCl_3$, *c* 1.8) = +69.2; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.71(ddd, 1H, J = 3.2, 6.2, 9.4 Hz), 3.47(s, 3H), 3.59-3.89(m, 7H), 4.04-4.18(m, 2H), 4.50(d, 2H, J = 3.6Hz), 4.55(m, 1H), 4.60(ABq, 2H, J = 13.1Hz), 4.87(ABq, 2H, J = 11.3Hz), 5.11-5.32(m, 4H), 5.29(dd, 1H,J = 1.4, 5.7Hz), 5.70-5.95(m, 2H), 7.05-7.38(m, 15H); ^{13}C NMR (55.32 MHz, $CDCl_3$): δ 46.0, 50.3, 52.2, 65.9, 68.3, 68.5, 71.1, 73.5, 74.6, 74.8, 78.8, 80.2, 97.4, 117.3, 118.5, 127.2-128.4, 131.6, 133.7, 137.9, 137.9, 138.6, 167.8, 168.7; IR ($CHCl_3$) : ν = 3030, 2951, 2918, 2866, 1757, 1736, 1454, 1132, 1041, 1028, 756, 698 cm^{-1}; Mol. Wt. calculated for $C_{37}H_{42}O_9Na$: 653.7138, Found: 653.7137.

Compound **6c**:



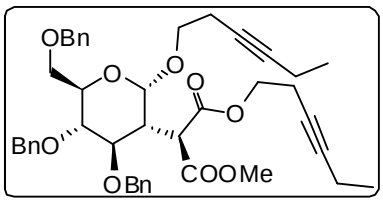
$[\alpha]_D$($CHCl_3$, *c* 1.8) = +64.0; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.40(t, 1H, J = 2.3Hz), 2.48(t, 1H, J = 2.4Hz), 2.73(ddd, 1H, J = 3.1, 6.0, 9.1 Hz), 3.50(s, 3H), 3.62-3.82(m, 6H), 4.14(dd, 2H, J = 2.4, 5.3Hz), 4.60(ABq, 2H, J = 12.1Hz), 4.63(d, 2H, J = 2.2Hz), 4.65(ABq, 2H, J = 10.5Hz), 4.87(ABq, 2H, J = 11.2Hz), 5.28(d, 1H, 3.1Hz), 7.06-7.38(m, 15H) ; ^{13}C NMR (55.32 MHz, $CDCl_3$): δ 45.8, 49.7, 52.4, 52.8, 54.7, 68.3, 71.5, 73.5, 74.5, 74.7, 74.8, 75.3, 77.1, 78.4, 78.8, 80.0, 97.1, 127.3-128.4, 137.8, 137.9, 138.5, 167.3, 168.3; IR ($CHCl_3$) : ν = 3017, 2951, 2926, 1751, 1734, 1454, 1217, 1132, 1053, 1041, 1028, 758, 698, 667 cm^{-1}; Mol. Wt. calculated for $C_{37}H_{38}O_9Na$: 649.6820, Found: 649.6828.

Compound **6d**:



$[\alpha]_D$($CHCl_3$, *c* 1.6) = +55.1; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 2.75(ddd, 1H, J = 3.2, 6.3, 9.6 Hz), 3.38(s, 3H), 3.62-3.92(m, 4H), 4.06(dd, 1H, J = 8.5, 11.2Hz), 4.23(d, 1H, J = 11.3Hz), 4.48-4.96(m, 10H), 5.28(d, 1H J = 3.2Hz), 7.02-7.40(m, 25H) ; ^{13}C NMR (55.32 MHz, $CDCl_3$): δ 46.1, 50.4, 52.2, 67.0, 68.4, 69.6, 71.2, 73.5, 74.5, 74.6, 78.8, 80.2, 97.7, 126.9-128.6, 135.2, 137.2, 137.8, 137.9, 138.6, 167.9, 168.7; IR ($CHCl_3$) : ν = 3064, 3030, 2949, 2924, 2868, 1748, 1732, 1496, 1454, 1435, 1361, 1217, 1132, 1055, 1026, 754, 698, 667 cm^{-1}; Mol. Wt. calculated for $C_{45}H_{46}O_9Na$: 753.8311, Found: 753.8319.

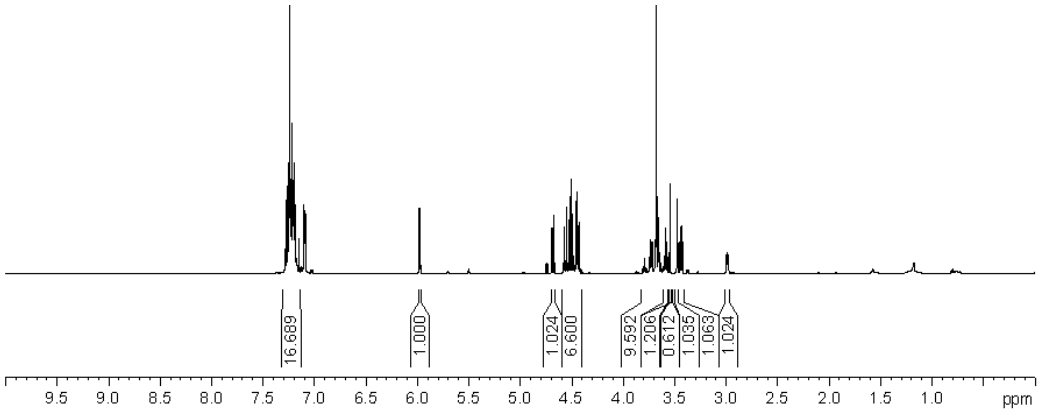
Compound **6e**:



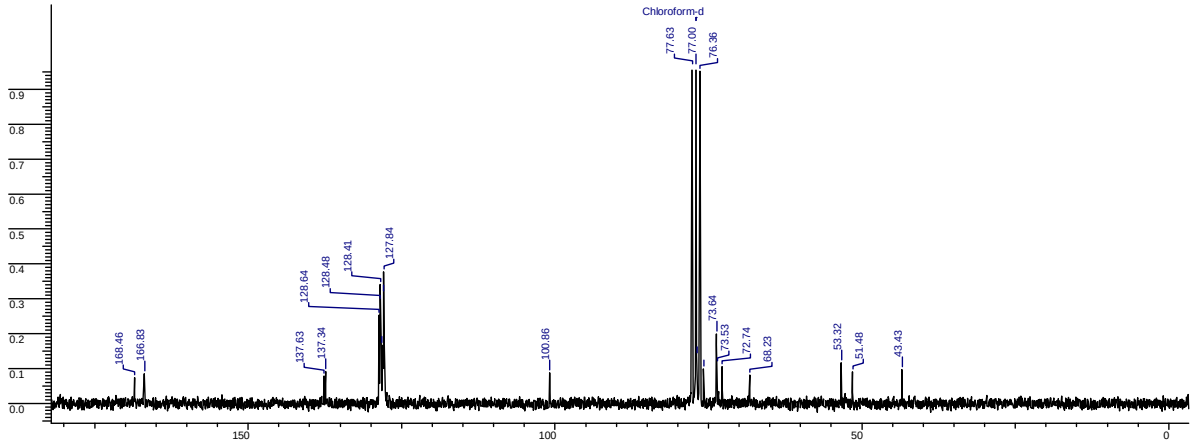
$[\alpha]_D$($CHCl_3$, *c* 1.3) = +53.5; ^{1}H NMR (200.13 MHz, $CDCl_3$): δ 1.04(t, 3H, J = 7.4Hz), 1.10(t, 3H, J = 7.5Hz), 2.01-2.20(m, 4H), 2.32-2.50(m, 4H), 2.65(ddd, 1H, J = 3.2, 5.9, 9.1 Hz), 3.50(s, 3H), 3.55-3.86(m, 8H), 4.10(dd, 2H, J = 4.5, 6.7Hz), 4.60(ABq, 2H, J = 12.1Hz), 4.64(ABq, 2H, J = 10.7Hz), 4.87(ABq, 2H, J = 11.2Hz), 5.22(d, 1H, J = 3.2Hz), 7.05-7.40(m, 15H); ^{13}C NMR (55.32 MHz, $CDCl_3$): δ 12.3, 12.3, 12.3, 14.0, 14.1, 14.1, 19.1, 19.8, 46.0, 49.8, 52.3, 63.8, 66.6, 68.5, 68.7, 71.1, 73.5, 74.7, 75.7, 78.6, 80.2, 83.0, 98.0, 127.2-128.4, 138.0, 138.0, 138.7, 168.1, 168.8; IR ($CHCl_3$) : ν = 3028, 3010, 2974, 2953, 2924, 2875, 2854, 1751, 1736, 1454, 1217, 1134, 1070, 1040, 1028, 756, 698, 667 cm^{-1}; Mol. Wt. calculated for $C_{43}H_{50}O_9Na$: 733.8415, Found: 733.8425.

Spectral charts

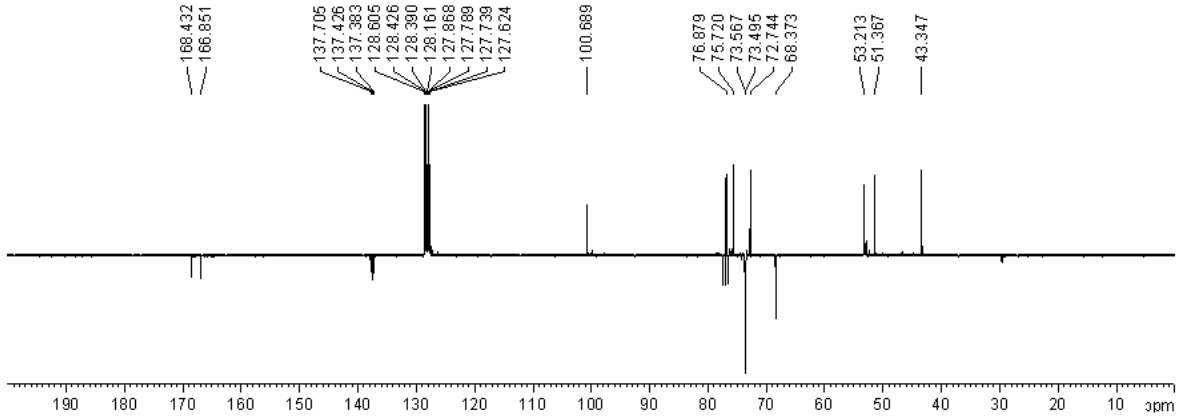
^{1}H NMR Spectrum (500 MHz, $CDCl_3$) of *gluco*-lactone **1c**



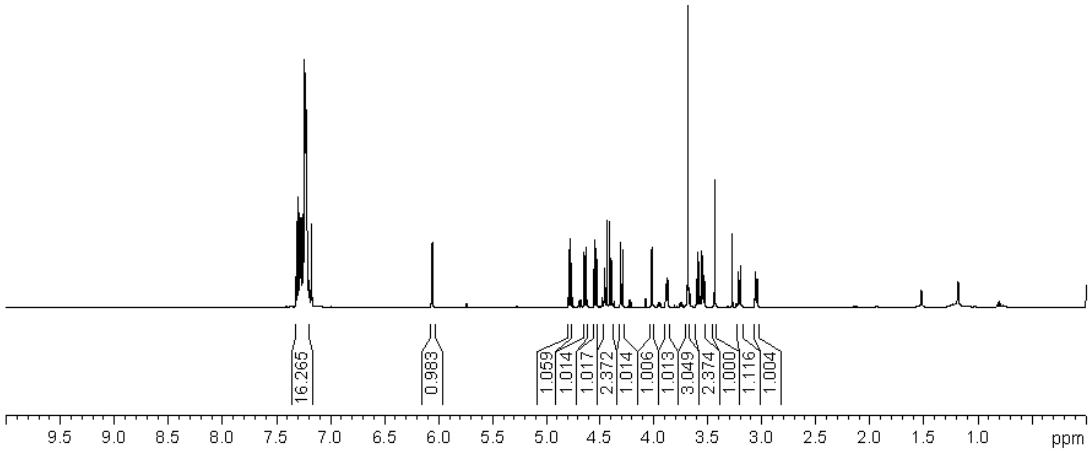
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of *gluco*-lactone **1c**



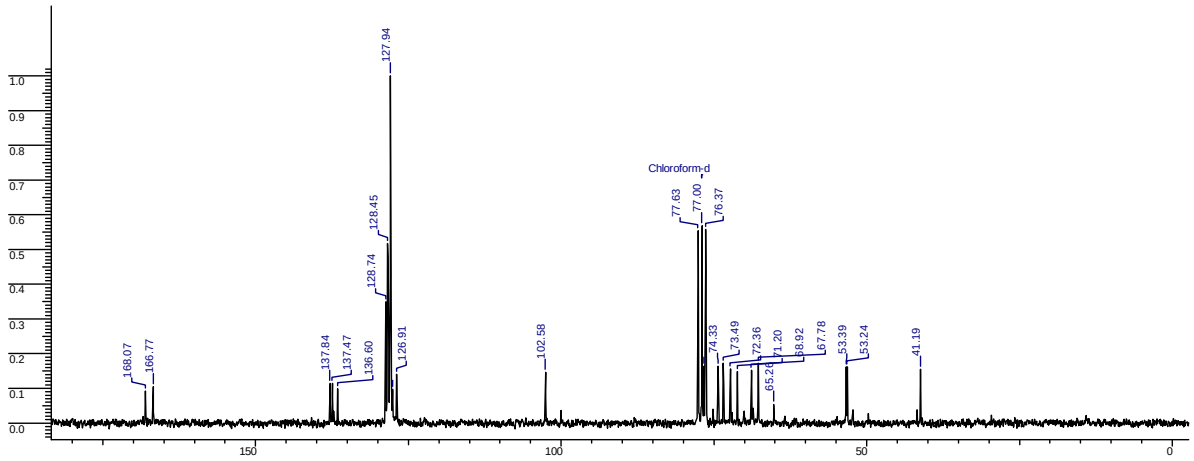
DEPT NMR Spectrum (125 MHz, $CDCl_3$) of *gluco*-lactone **1c**



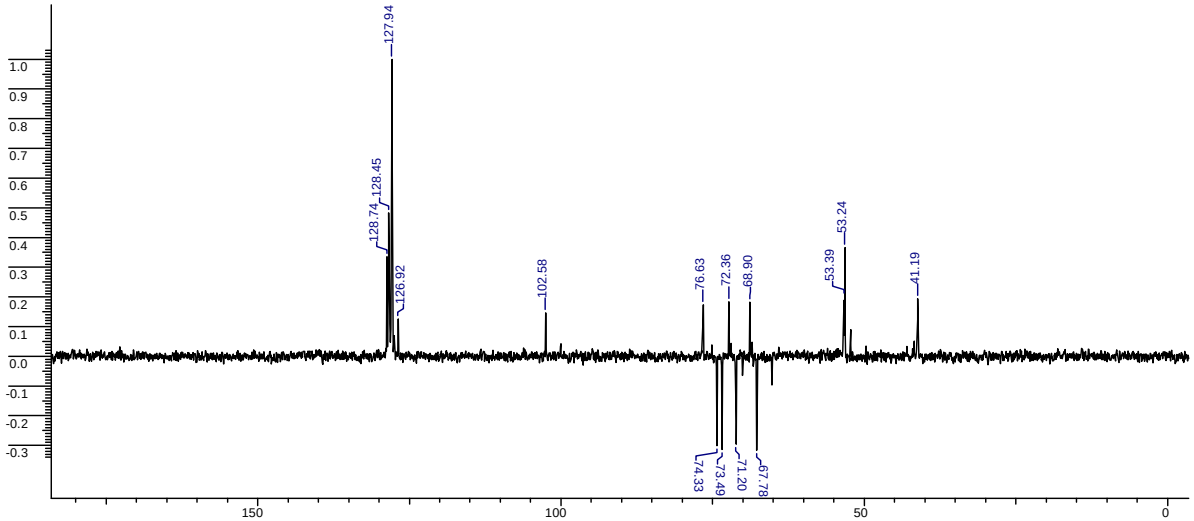
^{1}H NMR Spectrum (500 MHz, $CDCl_3$) of *galacto*-lactone **1c**



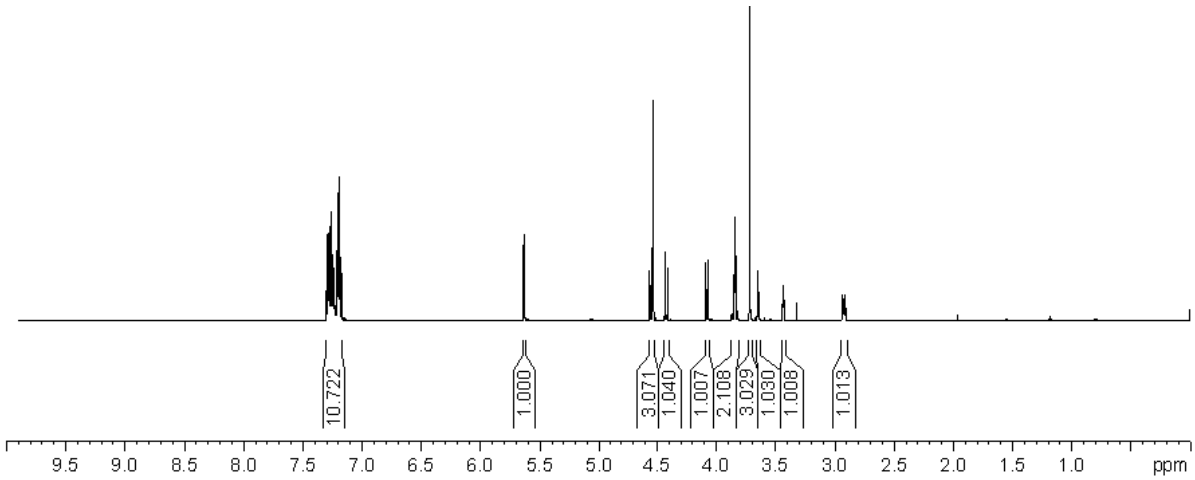
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of *galacto*-lactone **1c**



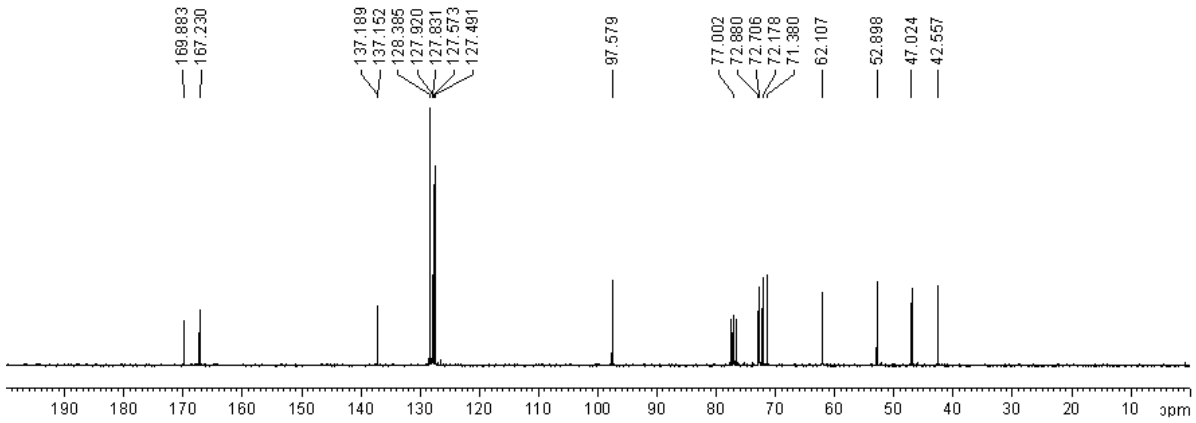
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of *galacto*-lactone **1c**



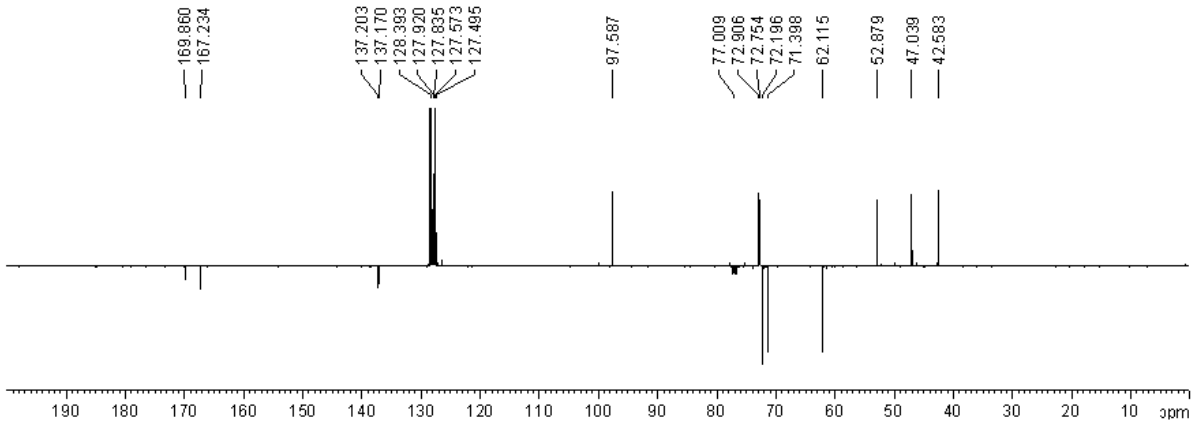
^{1}H NMR Spectrum (500 MHz, $CDCl_3$) of *xylo*-lactone **1c**



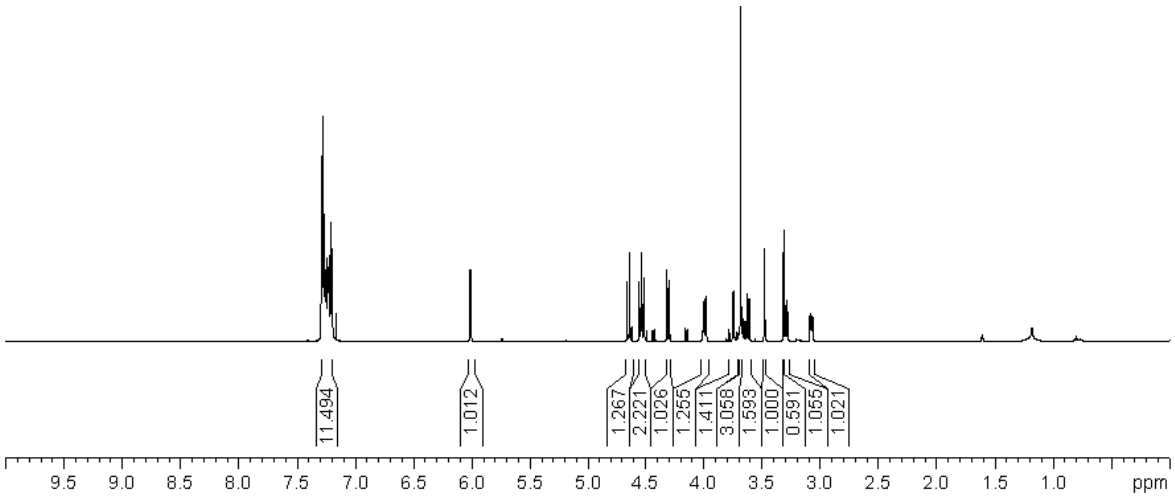
^{13}C NMR Spectrum (125 MHz, $CDCl_3$) of *xylo*-lactone **1c**



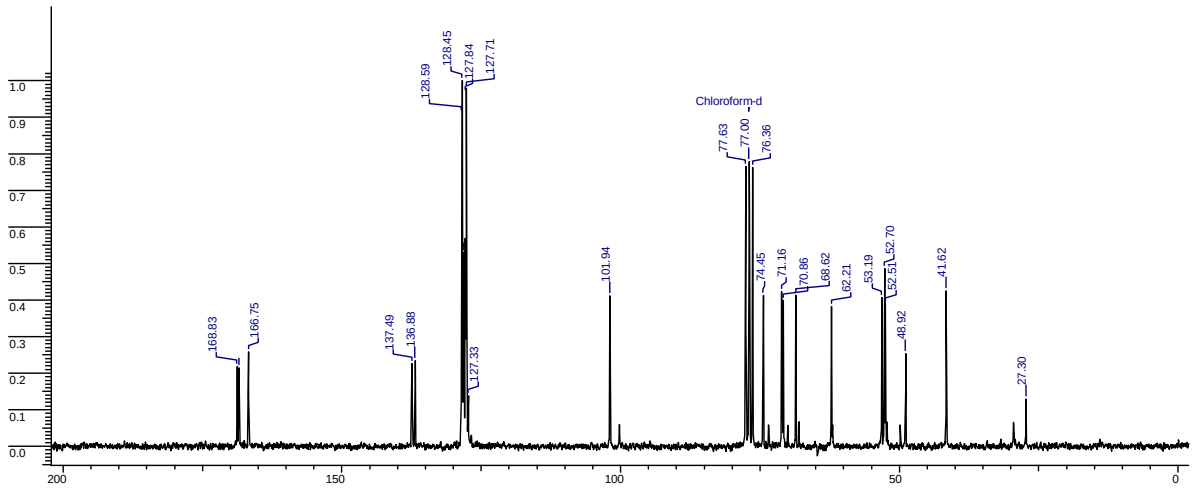
DEPT NMR Spectrum (125 MHz, $CDCl_3$) of *xylo*-lactone **1c**



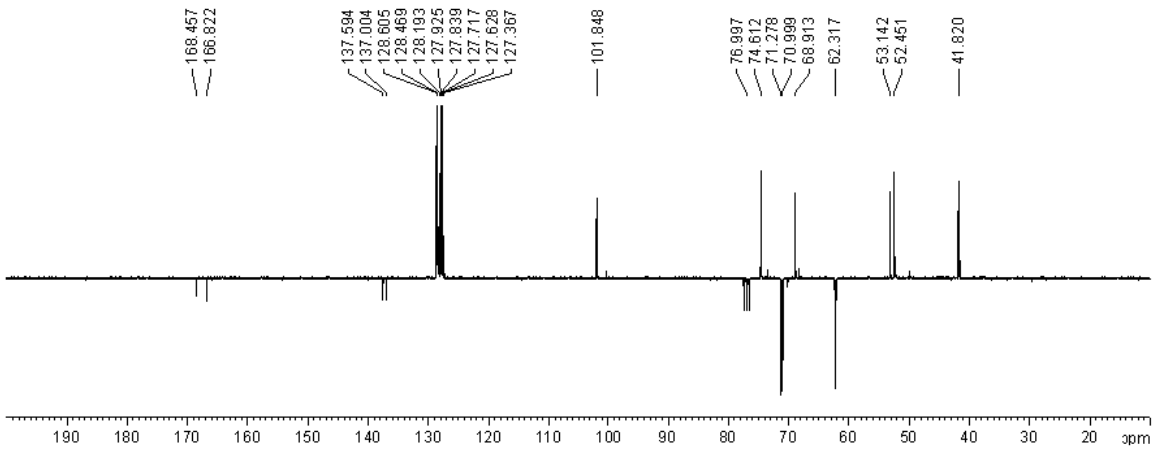
^{1}H NMR Spectrum (500 MHz, $CDCl_3$) of *arabino*-lactone **1c**



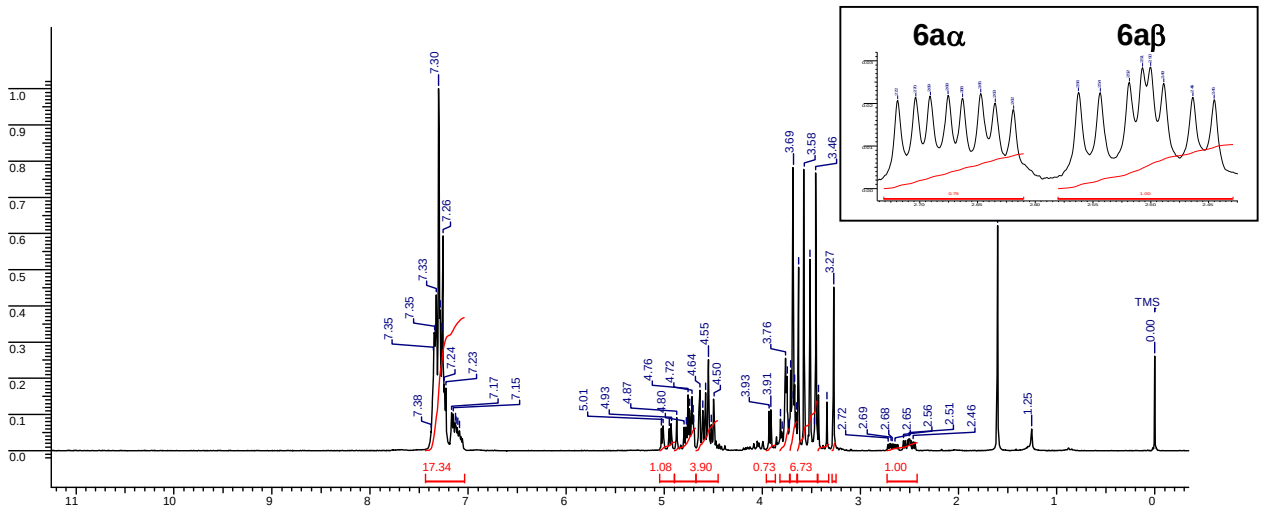
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of *arabino*-lactone **1c**



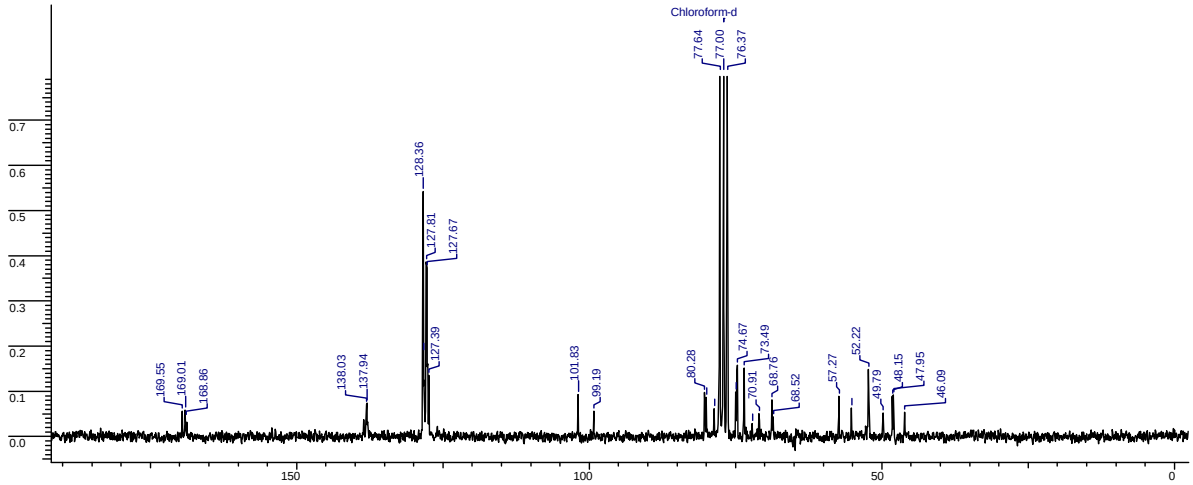
DEPT NMR Spectrum (125 MHz, $CDCl_3$) of *arabino*-lactone **1c**



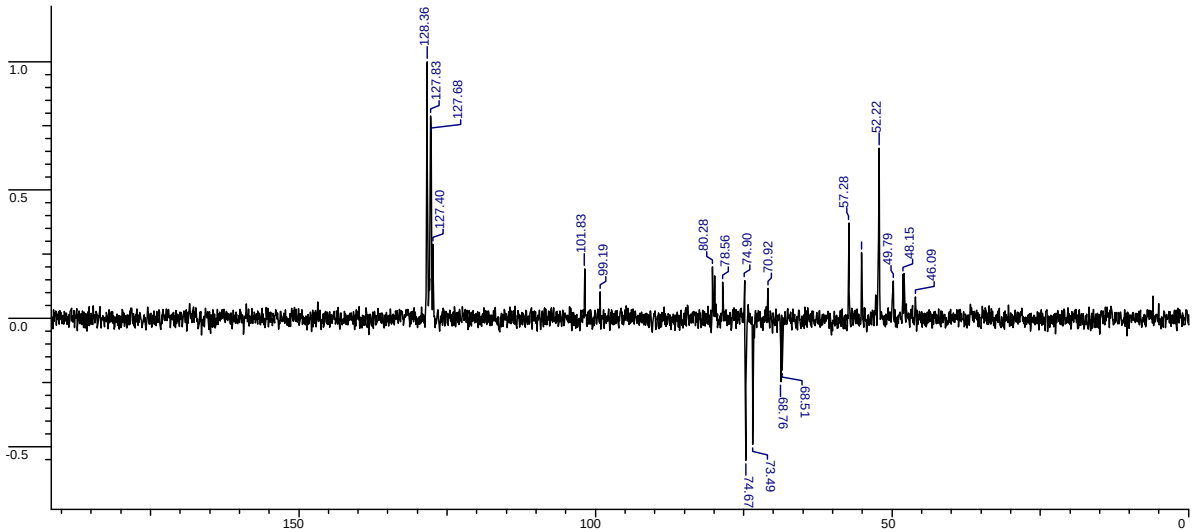
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of compound **6a**



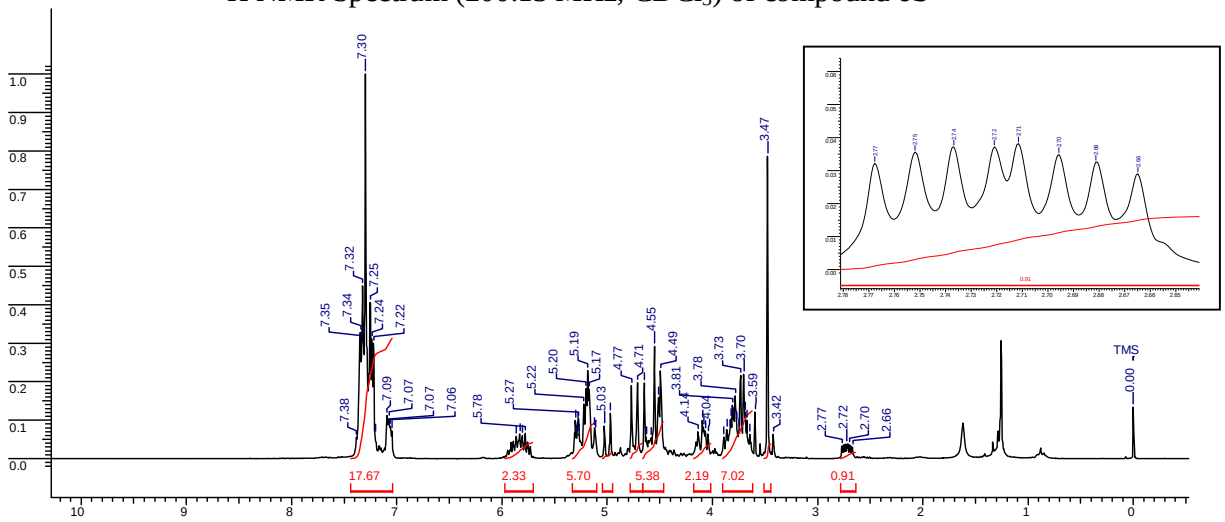
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6a**



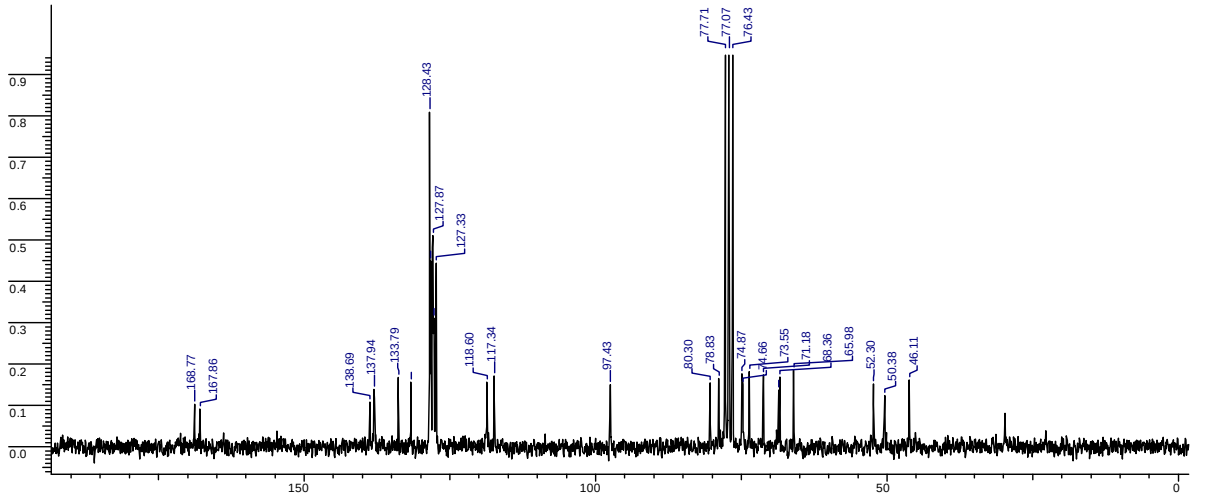
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6a**



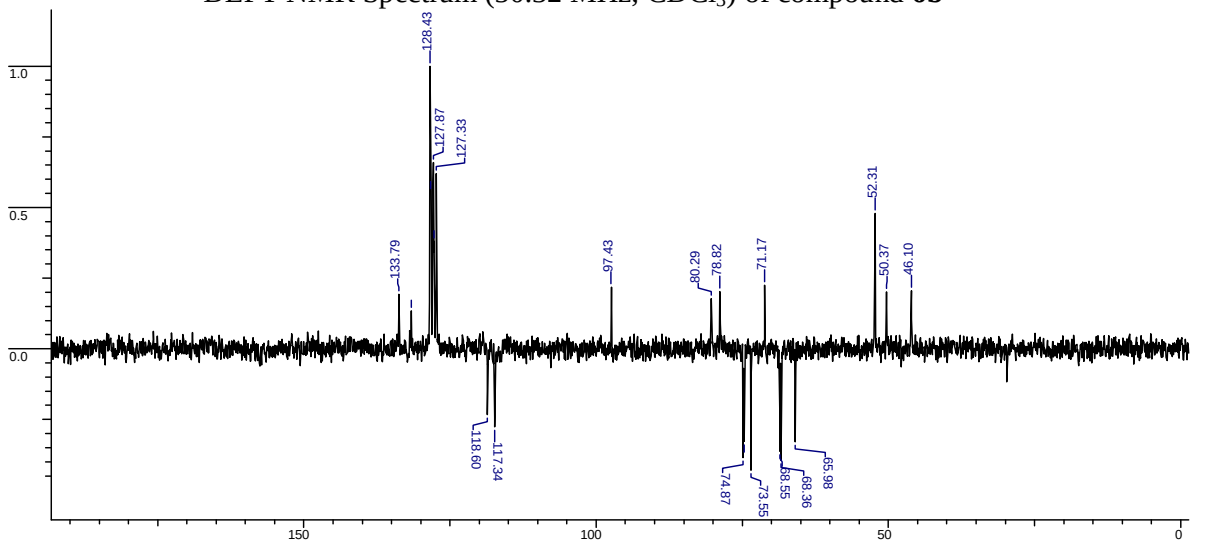
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of compound **6b**



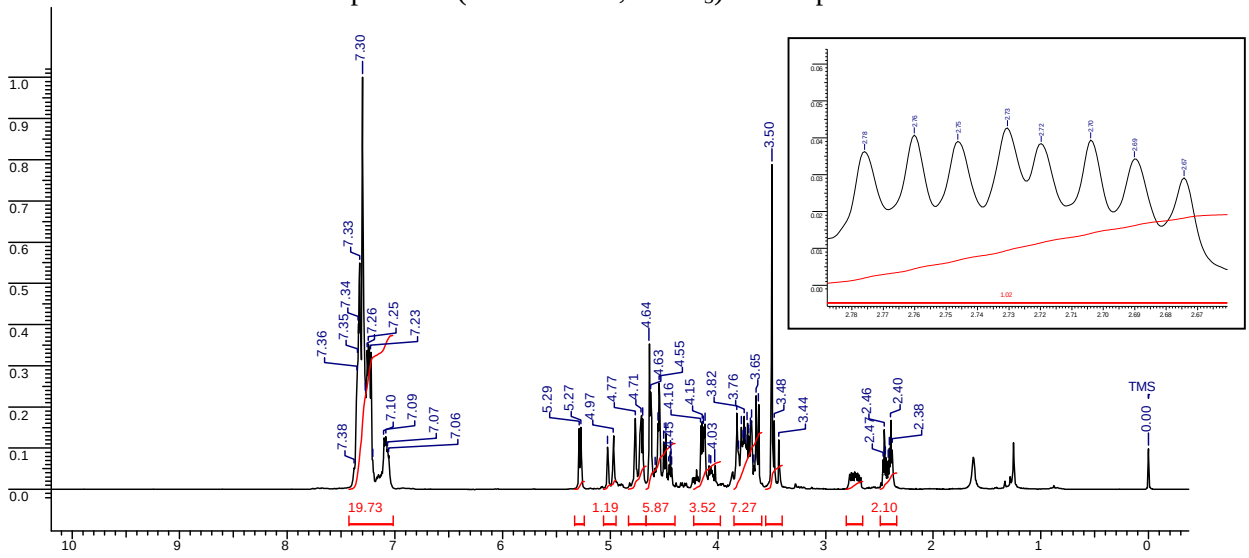
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6b**



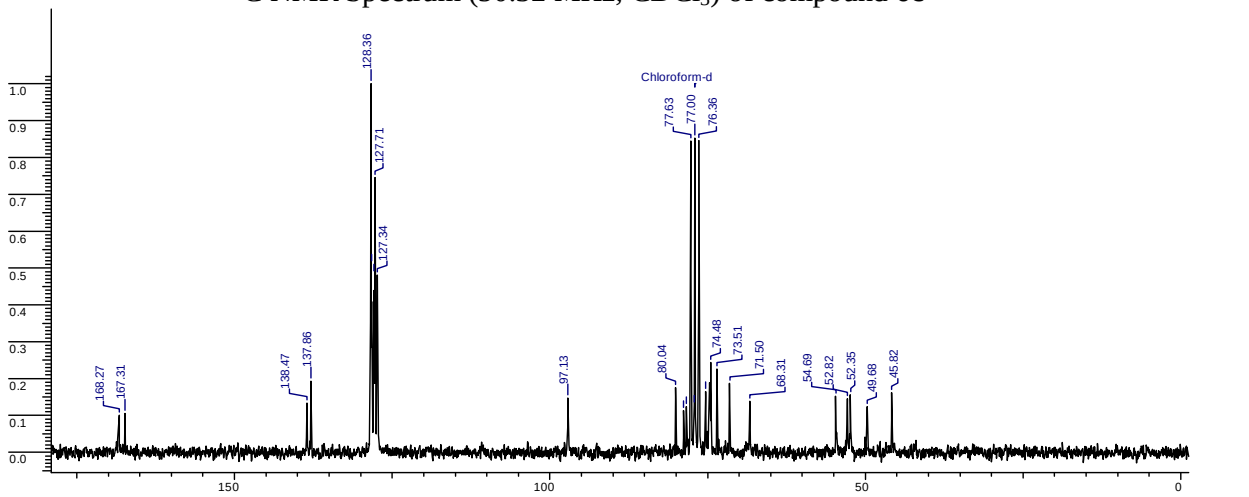
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6b**



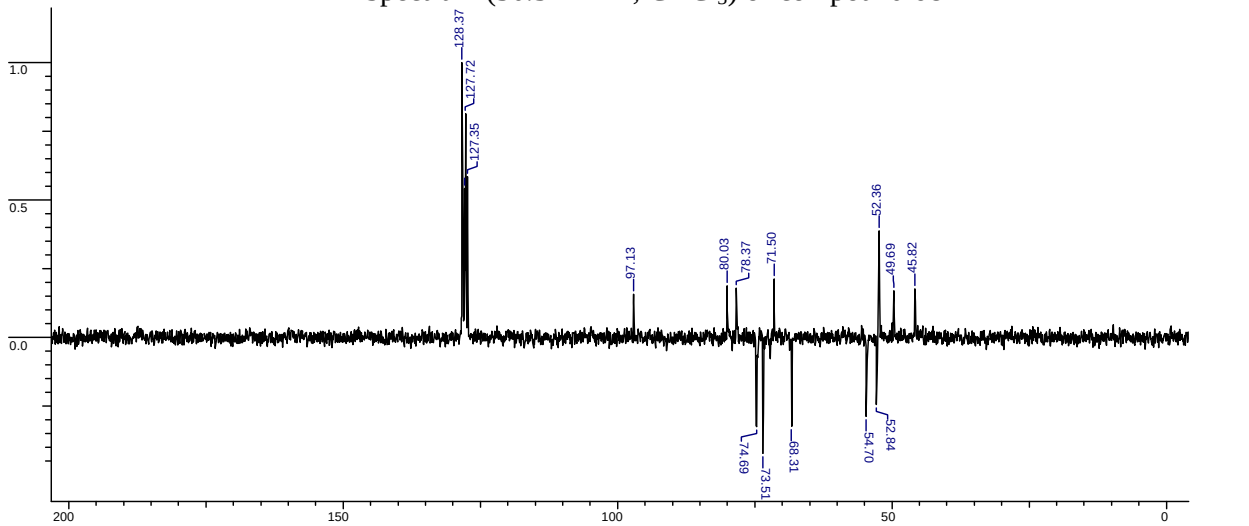
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of compound **6c**



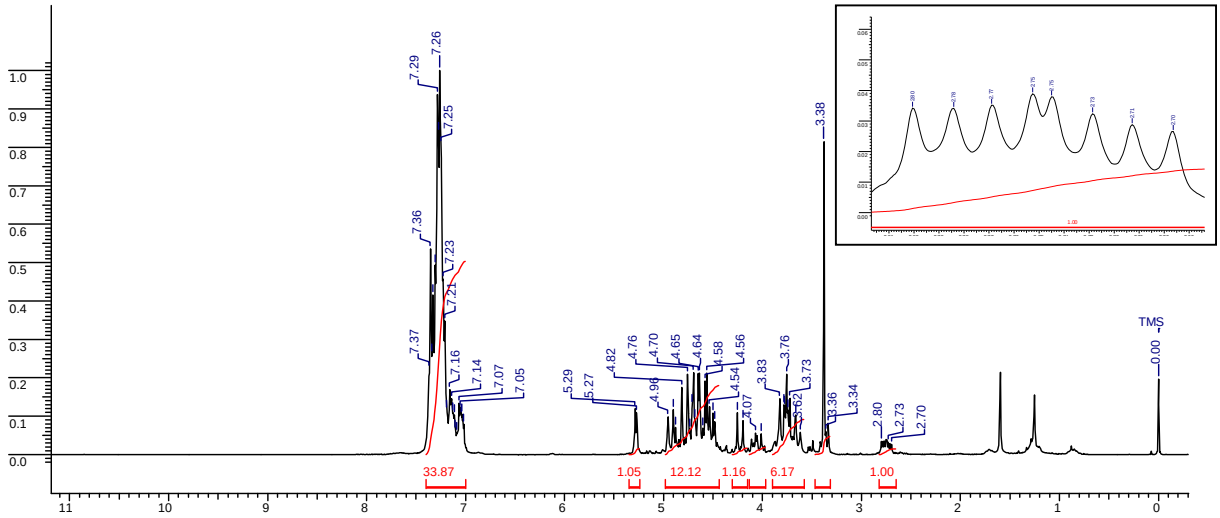
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6c**



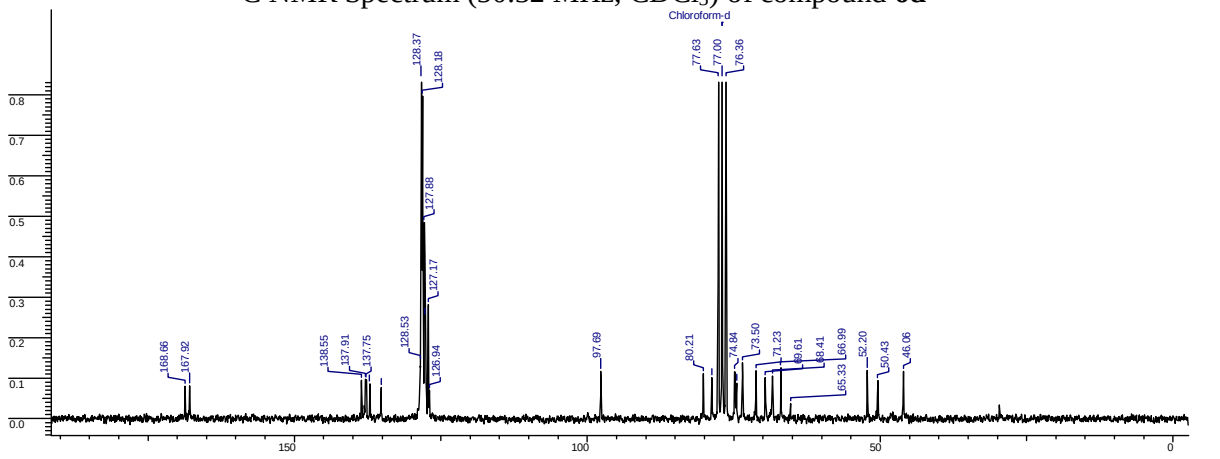
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6c**



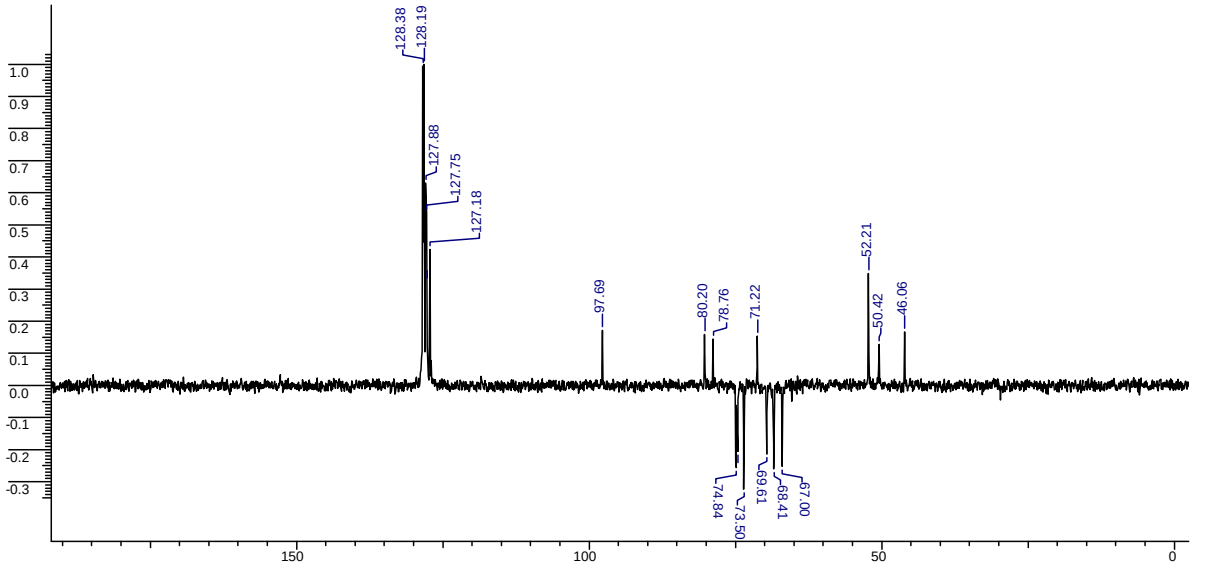
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of compound **6d**



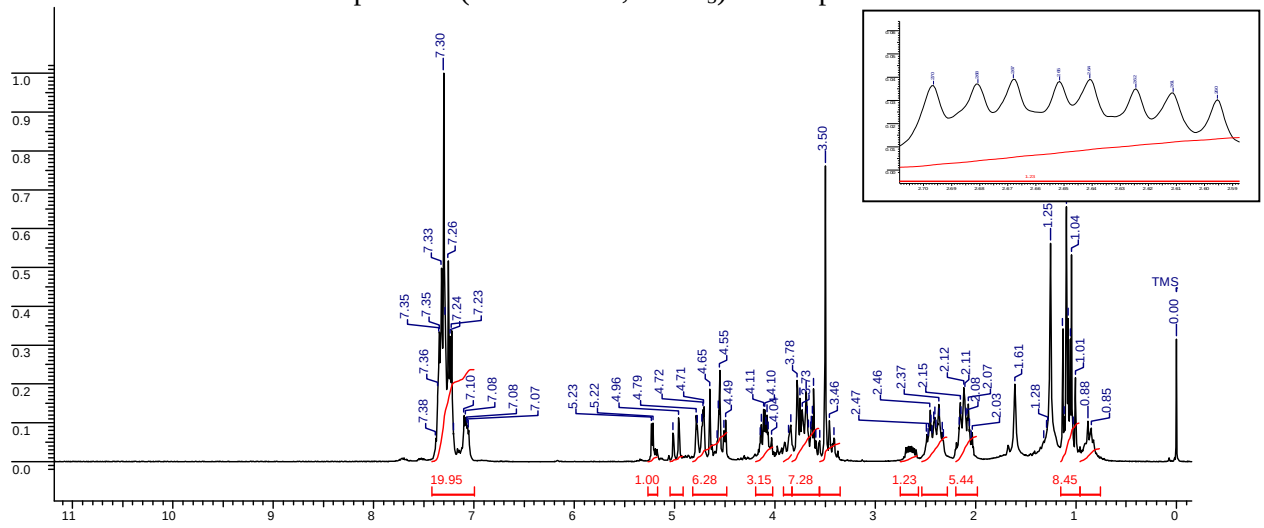
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6d**



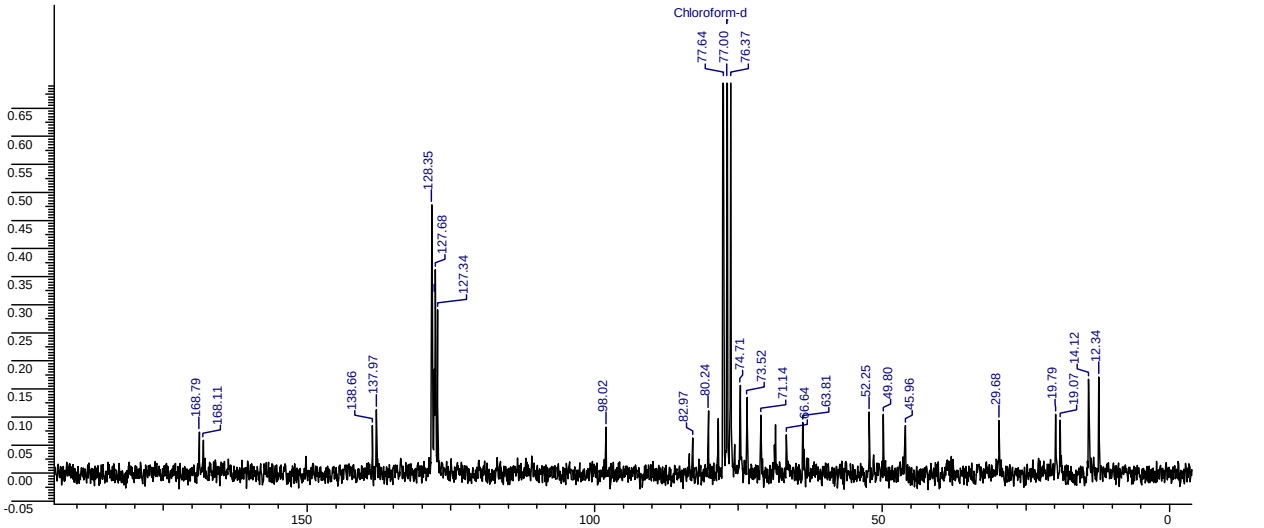
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6d**



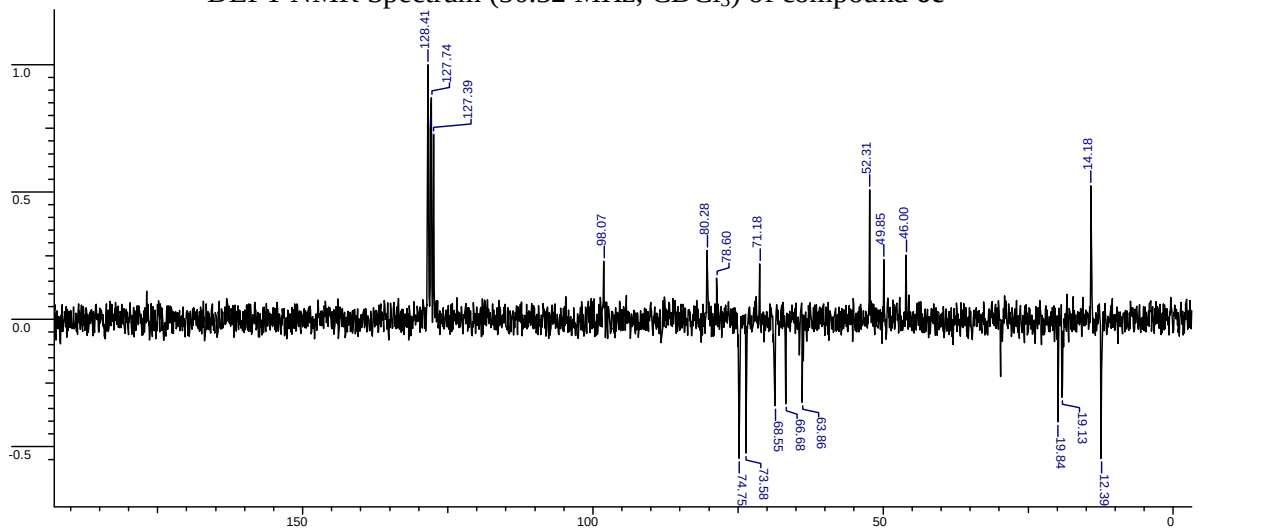
^{1}H NMR Spectrum (200.13 MHz, $CDCl_3$) of compound **6e**



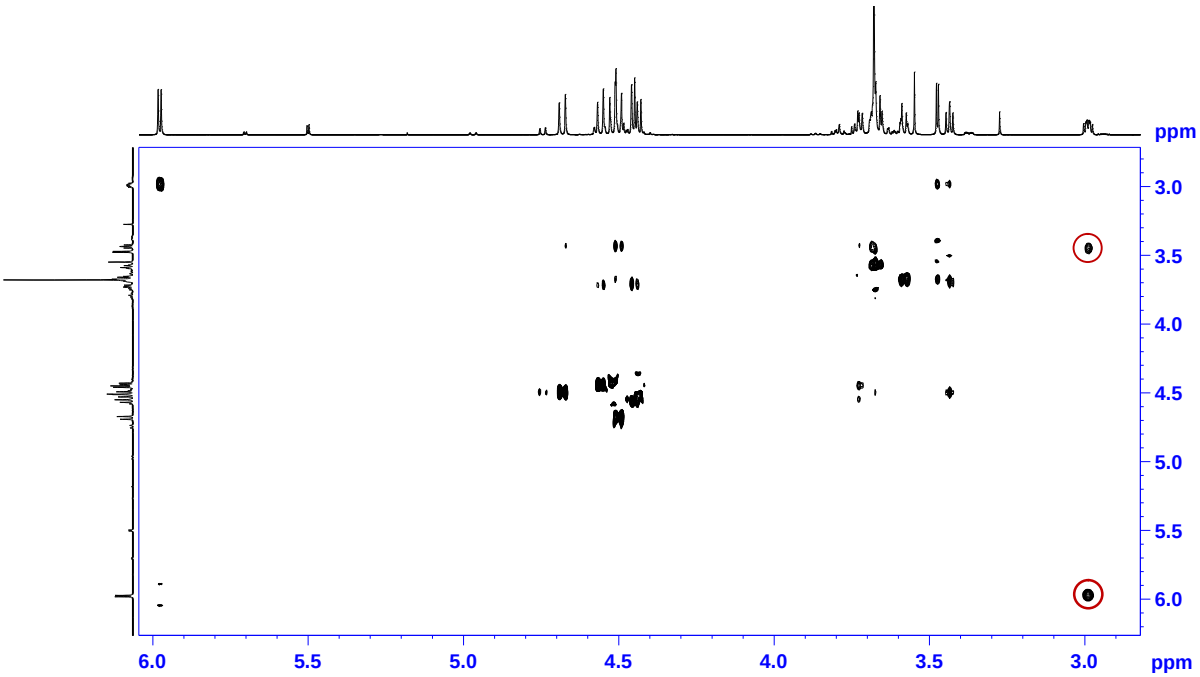
^{13}C NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6e**



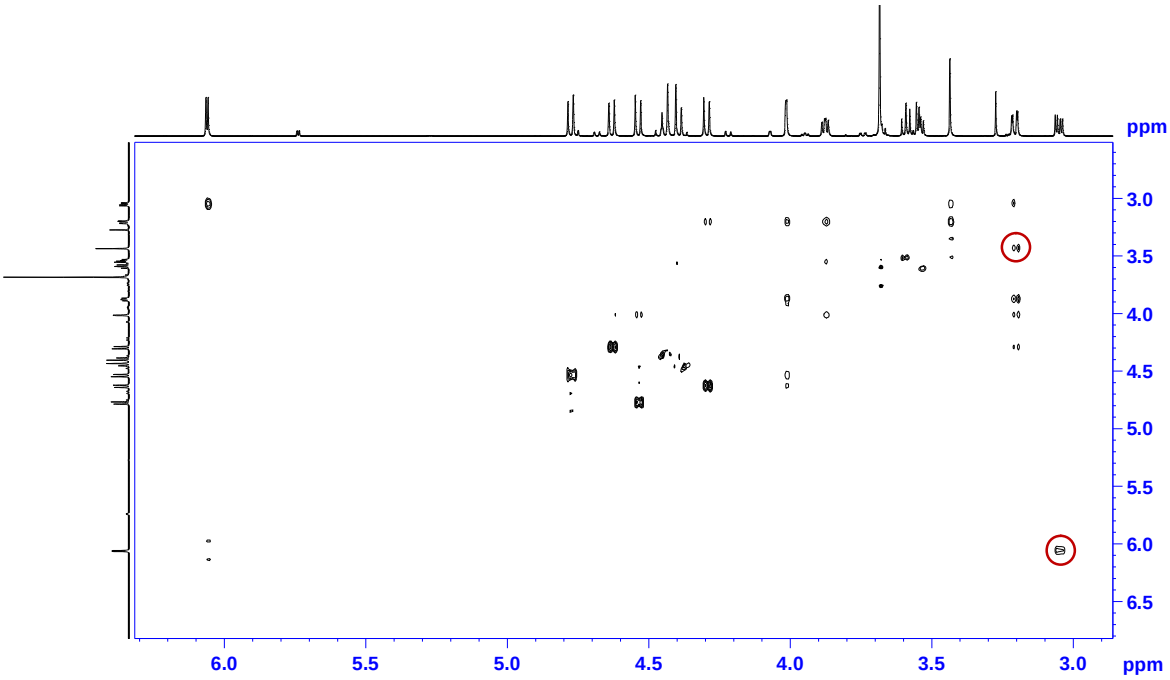
DEPT NMR Spectrum (50.32 MHz, $CDCl_3$) of compound **6e**



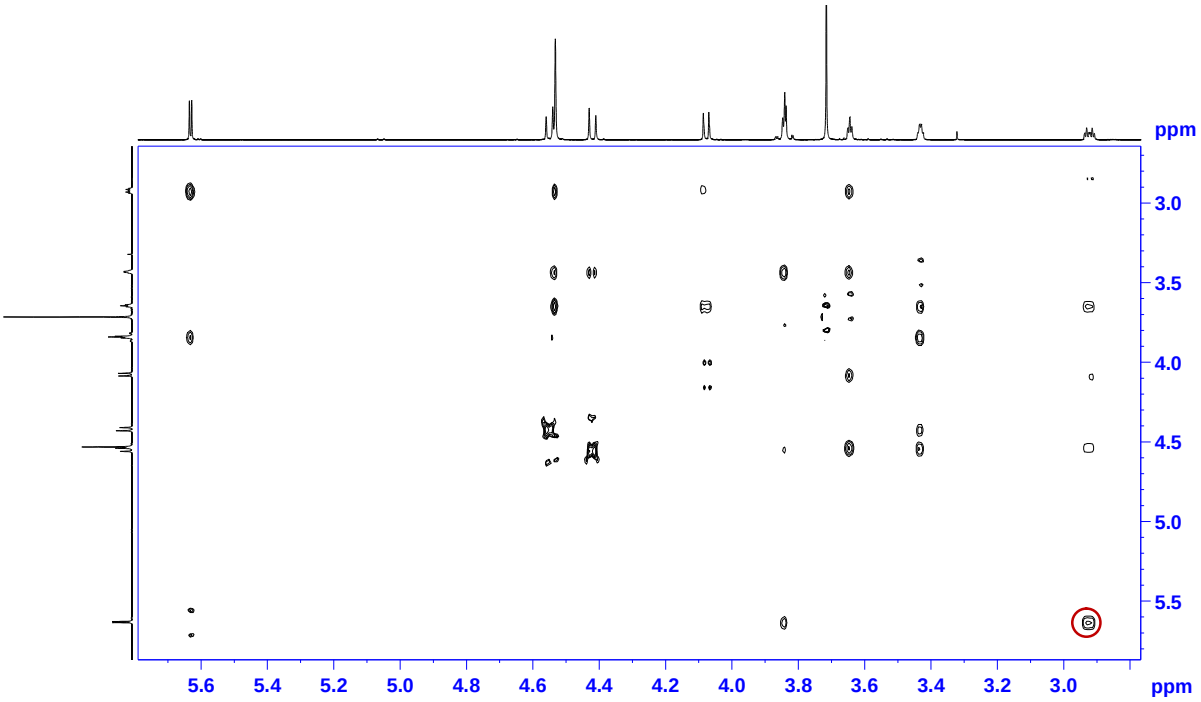
NOESY Spectrum (500 MHz, $CDCl_3$) of *gluco*-lactone **1c**



NOESY Spectrum (500 MHz, $CDCl_3$) of *galacto*-lactone **1c**



NOESY Spectrum (500 MHz, $CDCl_3$) of *xylo*-lactone **1c**



NOESY Spectrum (500 MHz, $CDCl_3$) of *arabino*-lactone **1c**