Supporting Informations

Organocatalyzed Cascade Reactions of Carbohydrates – A Direct Access to C-Glycosides

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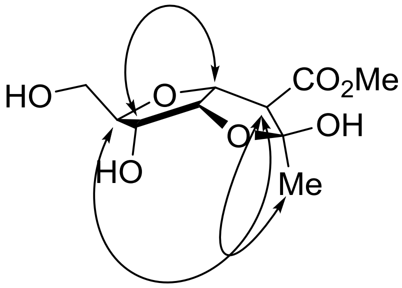
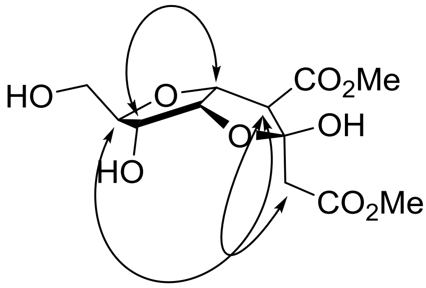
Determination of Configuration

The relative and absolute configuration of the new generated stereocenters was assigned by analysis of nO-interactions of H-Atoms at stereocenters introduced by the employed carbohydrate. The relevant interactions observed in NOESY-experiments are depicted as arrows in the following scheme.

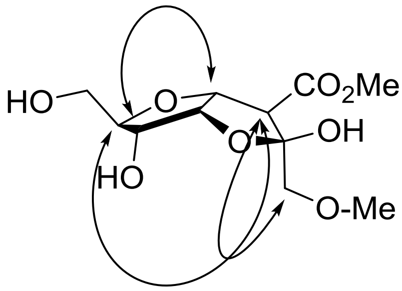
3a



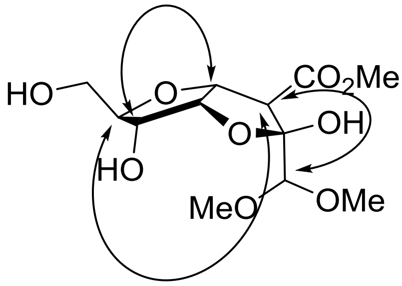
3b



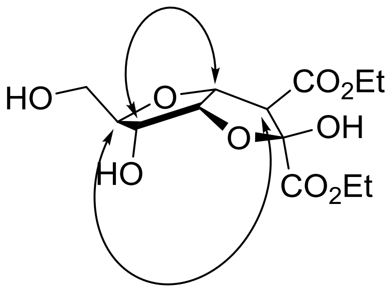
3c



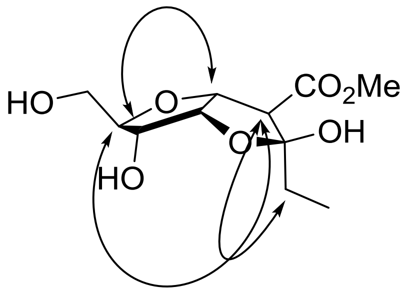
3d



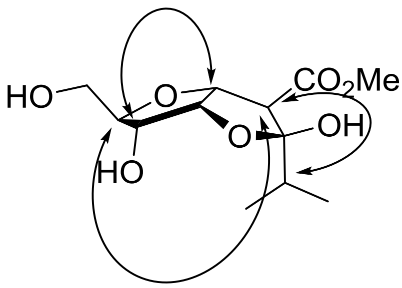
3e



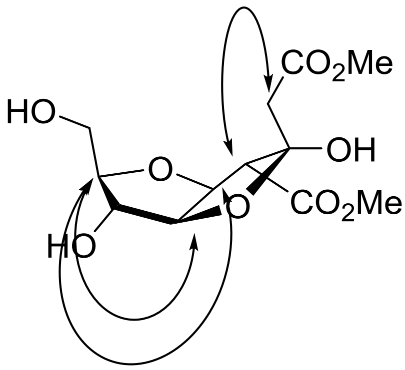
3f



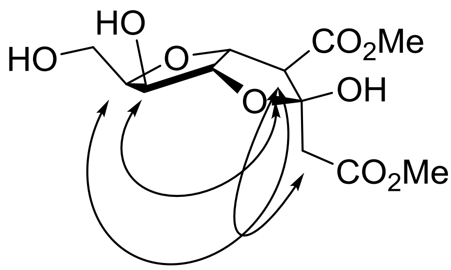
3gi



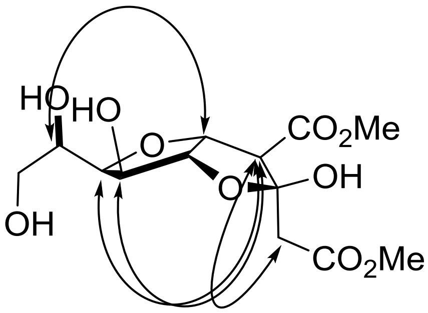
ara-**4b**



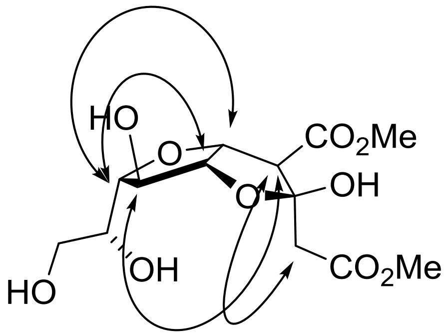
xylo-**5b**



gluco-**6b**



galacto-**7b**



Experimental Procedures

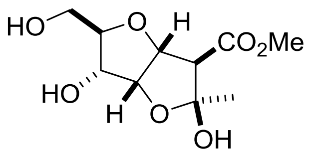
^{1}H – NMR, ^{13}C-NMR and correlation experiments were carried out at 500 MHz and 125 MHz. Chemical shifts are given in ppm. Purification of products was accomplished by flash chromatography using silica (Merck silica gel 60, particle size 0.04 - 0.063 mm) with a solvent mixture of DCM/MeOH 95:5 to 9:1.
Substances were purchased from Aldrich, TCI and ACROS and used without further purification.
Substance **2d** was synthesized according to N.E. Norris[1].

General procedures

150 mg (1 mmol, 1 eq) of the pentoses **1a - c** (180 mg (1 mmol, 1 eq) of the hexoses **1d – e**), (1.2 mmol, 1.2 eq) of the β-keto ester **2**, 23 mg (0.2 mmol, 0.2 eq) of L-proline and 15 mg (0.1 mmol, 0.1 eq) DBU were dissolved in 0.5 ml DMF and the reaction mixture was stirred for 72 h at room temperature. The mixture was purified by silica flash chromatography, using solvent mixtures of dichlormethane/ methanol (95:5 to 9:1). The products were isolated as colourless oils.

Characterization of Products

methyl (2S,3R,3aR,5R,6R,6aR)-2,6-dihydroxy-5-(hydroxymethyl)-2-methylhexahydrofuro[3,2-b]furan-3-carboxylate (**3a**)



Yield: 67%

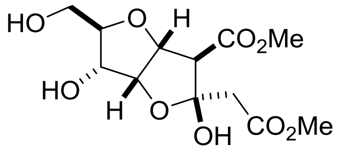
^{1}H NMR (500 MHz, Methanol-d_4) δ 5.26 (dd, J = 5.3, 4.3 Hz, 1H), 4.60 (t, J = 5.3 Hz, 1H), 3.88 (dd, J = 8.9, 5.4 Hz, 1H), 3.80 (dd, J = 12.1, 2.3 Hz, 1H), 3.72 (s, 3H), 3.70 – 3.65 (m, 1H), 3.59 (dd, J = 12.0, 5.1 Hz, 1H), 2.97 (d, J = 4.3 Hz, 1H), 1.68 (s, 3H).

^{13}C NMR (125 MHz, Methanol-d_4) δ 171.16, 107.51, 85.22, 81.65, 80.89, 72.51, 63.01, 62.18, 52.47, 25.95.

HRMS: calcd. for $C_{10}H_{15}O_7^-$: 247.0823, found: 247.0825

$[\alpha]_D^{25°C}$ = +129 (C=1, MeOH)

methyl (2S,3R,3aR,5R,6R,6aR)-2,6-dihydroxy-5-(hydroxymethyl)-2-(2-methoxy-2-oxoethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (**3b**)



Yield: 86%

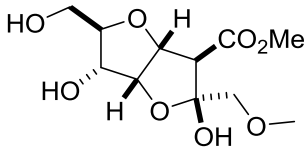
^{1}H NMR (500 MHz, Methanol-d4) δ= 5.30 (dd, J = 5.3, 4.2 Hz, 1H), 4.66 (t, J = 5.4 Hz, 1H), 3.92 (dd, J = 8.9, 5.5 Hz, 1H), 3.83 (dd, J = 12.2, 2.4 Hz, 1H), 3.75 (s, 3H), 3.73 (s, 3H), 3.74 (dd, J = 11.0, 7.5, 1H), 3.62 (ddd, J = 5.8, 2.6, 1.3 Hz, 1H), 3.62 (d, J = 4.0 Hz, 1H), 3.11 (d, J = 15.6 Hz, 1H), 3.02 (d, J = 15.5 Hz, 1H).

^{13}C NMR (125 MHz, Methanol-d_4) δ= 172.03, 170.83, 106.20, 84.47, 81.89, 81.19, 72.44, 62.04, 60.22, 52.58, 52.37, 49.85, 42.58.

HRMS-ESI: calcd. for $C_{12}H_{17}O_9^-$: 305.0878, found: 305.0878

$[\alpha]_D^{25°C}$ = +79 (C=1, MeOH)

methyl (2R,3R,3aR,5R,6R,6aR)-2,6-dihydroxy-5-(hydroxymethyl)-2-(methoxymethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (**3c**)



Yield: 84%

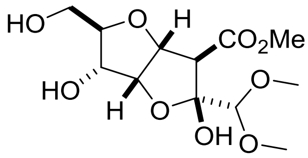
^{1}H NMR (500 MHz, Methanol-d4) δ= 5.28 (dd, J = 5.4, 4.3 Hz, 1H), 4.67 (dd, J = 5.4 Hz, 1H), 3.87 (dd, J = 8.7, 5.3 Hz, 1H), 3.79 (dd J= 12.1, 2.3 Hz, 1H), 3.72 (s, 3H), 3.71 (dd, J = 10.6, 7.5 Hz, 1H), 3.63 (d, J = 10.4 Hz, 1H), 3.60 (d, J = 11.5 Hz, 1H), 3.58 (dd, J= 12.1, 5.0 Hz, 1H), 3.48 (s, 3H), 3.33 (d, J = 4.3 Hz, 1H).

^{13}C NMR (125 MHz, Methanol-d_4) δ= δ 170.95, 107.90, 84.61, 82.02, 82.02, 74.98, 72.89, 62.21, 59.93, 57.97, 52.52.

HRMS-ESI: calcd. for $C_{11}H_{17}O_8^-$: 277.0929, found: 277.0930

$[\alpha]_D^{25°C}$ = +90 (C=1, MeOH)

methyl (2R,3R,3aR,5R,6R,6aR)-2-(dimethoxymethyl)-2,6-dihydroxy-5-(hydroxymethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (**3d**)



Yield: 36%

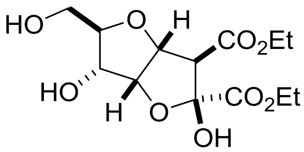
^{1}H NMR (500 MHz, Methanol-d_4) δ= 5.19 (dd, *J* = 5.3, 4.0 Hz, 1H), 4.68 (t, *J* = 5.3 Hz, 1H), 3.87 (dd, *J* = 8.7, 5.3 Hz, 1H), 3.79 (dd, *J* = 12.2, 2.4 Hz, 1H), 3.73 – 3.70 (m, 1H)3.72 (s, 3H), 3.60 (s, 3H), 3.58 (s, 3H), 3.58 (dd, *J* = 12.2, 5.2 Hz, 1H), 3.32 (d, *J* = 4.1 Hz, 1H).

^{13}C NMR (125 MHz, Methanol-d_4) δ 171.18, 108.16, 106.98, 84.61, 82.24, 82.17, 73.03, 62.21, 58.69, 58.12, 52.57.

HRMS-ESI: calcd. for $C_{12}H_{19}O_9$: 307.1035, found: 307.1035

$[\alpha]_D^{25°C}$ = +38 (C=1, MeOH)

diethyl (2R,3R,3aR,5R,6R,6aR)-2,6-dihydroxy-5-(hydroxymethyl)hexahydrofuro[3,2-b]furan-2,3-dicarboxylate (**3e**)



Yield: 37%

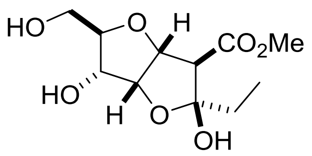
^{1}H NMR (500 MHz, Methanol-d_4) δ= 5.26 (dd, *J* = 5.3, 4.1 Hz, 1H), 4.73 (t, *J* = 5.3 Hz, 1H), 4.20 – 4.11 (m, 4H), 3.93 (dd, *J* = 8.8, 5.2 Hz, 1H), 3.83 (dd, *J* = 12.1, 2.3 Hz, 1H), 3.78 (ddd, *J* = 9.0, 4.9, 2.3 Hz, 1H), 3.67 (d, *J* = 4.1 Hz, 1H), 3.60 (dd, *J* = 12.1, 4.9 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, Methanol-d_4) δ= 169.83, 169.43, 104.67, 83.84, 83.28, 81.81, 72.58, 63.43, 62.15, 61.40, 14.36.

HRMA-ESI: calcd. for $C_{13}H_{24}O_9N^+$: 338.1446, found: 338.1447

$[\alpha]_D^{25°C}$ = -39 (C=1, MeOH)

methyl (2S,3R,3aR,5R,6R,6aR)-2-ethyl-2,6-dihydroxy-5-(hydroxymethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (**3f**)



Yield: 62%

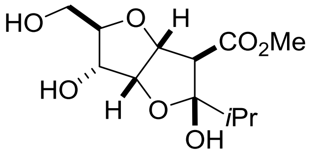
^{1}H NMR (500 MHz, Methanol-d_4) δ 5.23 (dd, J = 5.1, 3.9 Hz, 1H), 4.63 (t, J = 5.2 Hz, 1H), 3.90 (dd, J = 9.0, 5.2 Hz, 1H), 3.81 (dd, J = 12.1, 2.3 Hz, 1H), 3.71 (s, 3H), 3.69 (ddd, J = 9.0, 5.0, 2.3 Hz, 1H), 3.58 (dd, J = 12.1, 5.0 Hz, 1H), 3.08 (d, J = 3.9 Hz, 1H), 1.97 (qd, J = 7.5, 2.4 Hz, 2H), 1.07 (t, J = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, Methanol-d_4) δ 171.34, 109.74, 85.22, 81.88, 81.13, 72.74, 62.22, 60.04, 52.43, 32.41, 8.74.

HRMS-ESI: calcd for $C_{11}H_{17}O_7^-$: 261.0980, found: 261.0981

$[\alpha]_D^{25°C}$ = +113 (C=1, MeOH)

methyl (2S,3R,3aR,5R,6R,6aR)-2,6-dihydroxy-5-(hydroxymethyl)-2-isopropylhexahydrofuro[3,2-b]furan-3-carboxylate (**3g**)

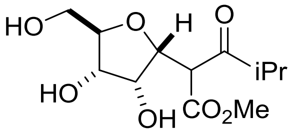


Yield: accumulated **3gi** + **3gii**: 46% (30:70)

^{1}H NMR (500 MHz, Deuterium Oxide) δ= 5.19 (dd, J = 4.7, 3.3 Hz, 1H), 4.72 (t, J = 4.9 Hz, 1H), 4.10 – 4.08 (m, 1H), 3.87 – 3.84 (m, 1H), 3.74 (s, 3H), 3.71 (dd, J = 12.8, 4.4 Hz, 1H), 3.65 (dd, J = 12.8, 5.3 Hz, 1H), 3.37 (d, J = 3.3 Hz, 1H), 2.22 (p, J = 6.9 Hz, 1H), 1.06 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, Deuterium Oxide) δ= 171.85, 110.95, 84.14, 80.26, 80.03, 70.72, 60.09, 57.64, 52.59, 35.55, 16.71, 15.90.

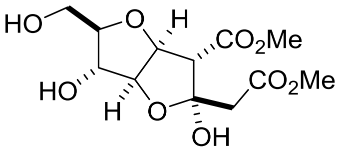
HRMS-ESI: calcd. for $C_{12}H_{19}O_7^-$: 275.1136, found: 275.1136 methyl 2-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-methyl-3-oxopentanoate (*keto*-**3g**)



[1]H NMR (500 MHz, Deuterium Oxide) δ= 4.38 (dd, *J* = 9.4, 5.0 Hz, 1H), 4.34 (dd, *J* = 8.2, 5.4 Hz, 1H), 4.26 (d, *J* = 8.2 Hz, 1H), 4.23 (d, *J* = 9.4 Hz, 1H), 4.11 (t, *J* = 5.2 Hz, 1H), 4.07 – 4.04 (m, 2H), 4.03 (q, *J* = 5.4 Hz, 1H), 3.92 – 3.85 (m, 2H), 3.76 (s, 3H), 3.74 (s, 3H), 3.70 (ddd, *J* = 12.4, 3.5, 1.3 Hz, 2H), 3.60 (ddd, *J* = 12.4, 8.6, 5.0 Hz, 2H), 2.89 (dq, *J* = 13.6, 6.8 Hz, 2H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 6H).

[13]C NMR (126 MHz, Deuterium Oxide) δ= 211.67, 210.97, 169.46, 168.66, 83.58, 83.29, 81.20, 81.00, 73.22, 73.10, 70.79, 61.41, 61.38, 59.40, 59.33, 53.18, 53.13, 42.28, 42.20, 17.08, 16.96, 16.82, 16.76.

methyl (2R,3S,3aS,5R,6R,6aS)-2,6-dihydroxy-5-(hydroxymethyl)-2-(2-methoxy-2-oxoethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (ara-**4b**)



Yield: 81%

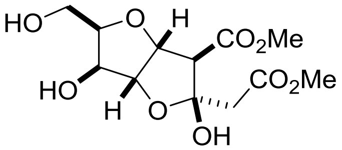
[1]H NMR (500 MHz, Methanol-d_4) δ= 5.22 (dd, *J* = 5.6, 3.7 Hz, 1H), 4.62 (dd, *J* = 5.6, 2.1 Hz, 1H), 4.02 (dd, *J* = 5.4, 2.0 Hz, 1H), 3.85 (ddd, *J* =, 5.8, 5.44, 4.27 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.65 (dd, *J* = 11.7, 4.3 Hz, 1H) 3.56 (dd, *J* = 11.7, 5.8 Hz, 1H), 3.55 (d, *J* = 4.0 Hz, 1H), 3.02 (d, *J* = 15.1 Hz, 1H), 2.93 (d, *J* = 14.6 Hz, 1H).

[13]C NMR (125 MHz, Methanol-d_4) δ= 171.73, 170.82, 107.07, 107.03, 90.32, 89.53, 85.20, 77.22, 63.04, 60.37, 52.47, 52.30, 43.63.

HRMS-ESI: calcd. for $C_{11}H_{17}O_9^-$: 305.0878, found: 305.0878

$[\alpha]_D^{25°C}$ = -36 (C=1, MeOH)

methyl (2S,3R,3aR,5R,6S,6aR)-2,6-dihydroxy-5-(hydroxymethyl)-2-(2-methoxy-2-oxoethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (xylo-**5b**)



Yield: 83%

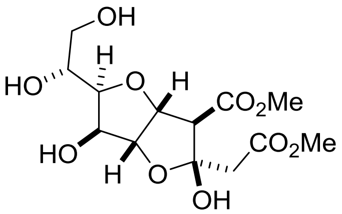
^{1}H NMR (500 MHz, Methanol-d_4) δ= 5.40 (dd, J = 5.6, 4.1 Hz, 1H), 4.54 (d, J = 5.5 Hz, 1H), 4.06 (d, J = 2.9 Hz, 1H), 3.92 (ddd, J = 6.4, 4.9, 2.9 Hz, 1H), 3.81 (dd, J = 11.5, 5.0 Hz, 1H), 3.74 (dd, J = 11.5, 6.3 Hz, 1H), 3.73 (s, 3H), 3.69 (s, 3H), 3.59 (d, J = 4.4 Hz, 1H), 3.06 (d, J = 15.3 Hz, 1H), 2.90 (d, J = 15.2 Hz, 1H).

^{13}C NMR (125 MHz, Methanol-d_4) δ= 171.64, 170.99, 88.16, 84.60, 81.99, 75.96, 60.85, 58.85, 52.57, 52.27, 42.56.

HRMS-ESI: calcd. for $C_{23}H_{18}O_9Cl^-$: 341.0645, found: 341.0645

$[\alpha]_D^{25°C}$ = +49 (C=1, MeOH)

methyl (2S,3R,3aR,5S,6S,6aR)-5-((R)-1,2-dihydroxyethyl)-2,6-dihydroxy-2-(2-methoxy-2-oxoethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (gluco-**6b**)



Yield: 27%

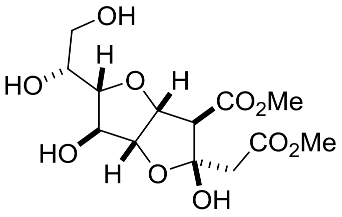
^{1}H NMR (500 MHz, Methanol-d_4) δ= 5.38 (dd, J = 5.3, 4.2 Hz, 1H), 4.54 (d, J = 5.3 Hz, 1H), 4.15 (d, J = 2.7 Hz, 1H), 3.89 (ddd, J = 8.8, 6.0, 3.1 Hz, 1H), 3.75 (dd, J = 4.4, 2.9 Hz, 1H) 3.74 (dd, J = 11.4, 8.8 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.58 (dd, J = 11.4, 6.1 Hz, 1H), 3.05 (d, J = 15.2 Hz, 1H), 2.90 (d, J = 15.0 Hz, 1H).

^{13}C NMR (125 MHz, Methanol-d_4) δ= 171.66, 171.02, 105.75, 105.72, 87.85, 84.78, 81.03, 75.60, 70.38, 65.37, 59.10, 52.53, 52.30, 42.72.

HRMS-ESI: calcd. for $C_{13}H_{20}O_{10}Cl^-$: 371.0750, found: 371.0751

$[\alpha]_D^{25°C}$ = +59 (C=1, MeOH)

methyl (2S,3R,3aR,5R,6S,6aR)-5-((R)-1,2-dihydroxyethyl)-2,6-dihydroxy-2-(2-methoxy-2-oxoethyl)hexahydrofuro[3,2-b]furan-3-carboxylate (galacto-**7b**)



Yield: 67%

^{1}H NMR (500 MHz, Methanol-d_4) δ= 5.18 (dd, *J* = 5.8, 3.9 Hz, 1H), 4.63 (dd, *J* = 5.8, 2.5 Hz, 1H), 4.15 (dd, *J* = 6.8, 2.5 Hz, 1H), 3.78 (dd, *J* = 6.8, 4.0 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.64 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.63 – 3.55 (m, 2H), 3.61 (d, *J* = 3.8 Hz, 1H) 3.04 (d, *J* = 15.1 Hz, 1H), 2.95 (d, *J* = 14.8 Hz, 1H).

^{13}C NMR (125 MHz, Methanol-d_4) δ= 171.98, 170.83, 107.28, 90.54, 88.23, 84.80, 77.35, 72.23, 64.65, 59.90, 52.47, 52.34, 43.54.

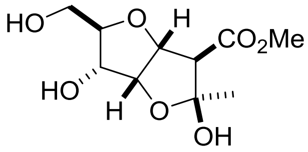
HRMS-ESI: calcd. for $C_{13}H_{19}O_{10}^{-}$: 335.0984, found: 371.0982

$[\alpha]_D^{25°C}$ = +24 (C=1, MeOH)

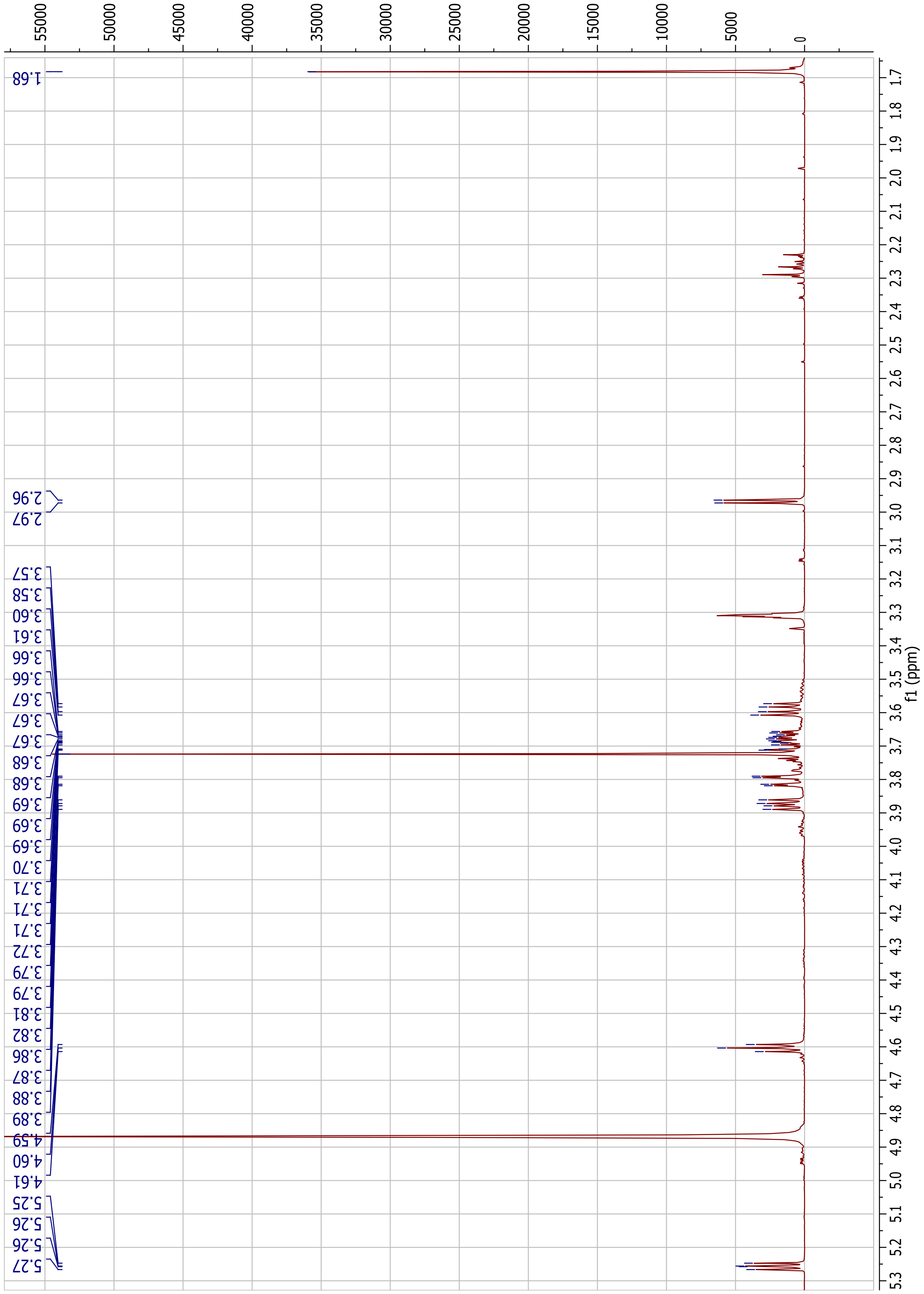
Literature

[1] J. A. Secrist, C. J. Hickey, R. E. Norris, *J. Org. Chem.* **1977**, *42*, 525-527.

3a

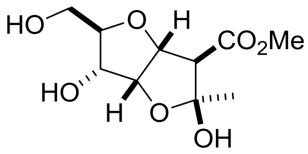


[1]H (500 MHz, Methanol-d_6)

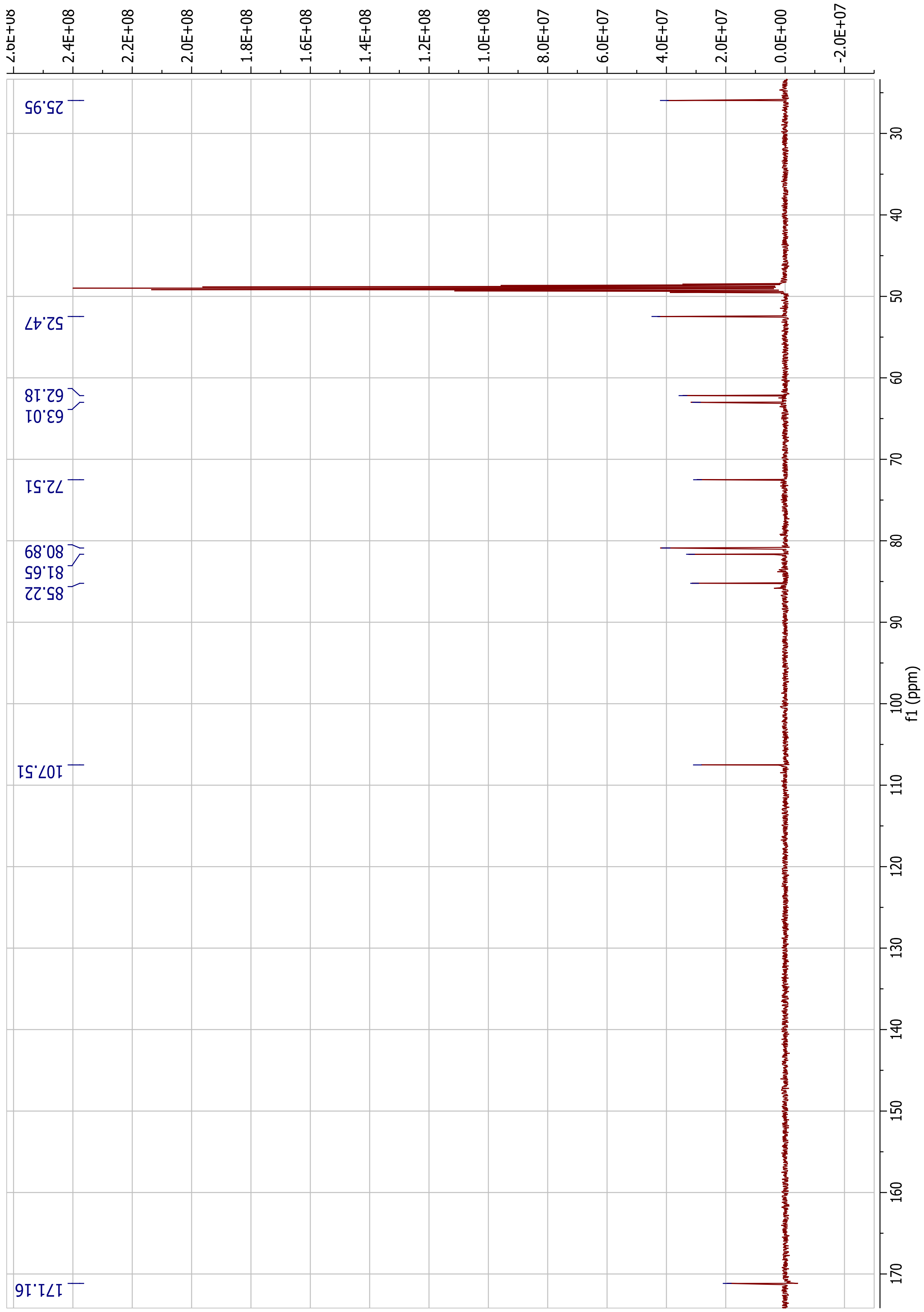


Electronic Supplementary Material (ESI) for Chemical Communications

3a

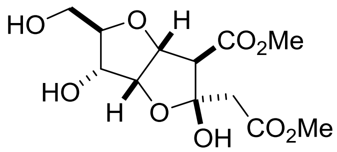


^{13}C (125 MHz, Methanol-d_6)

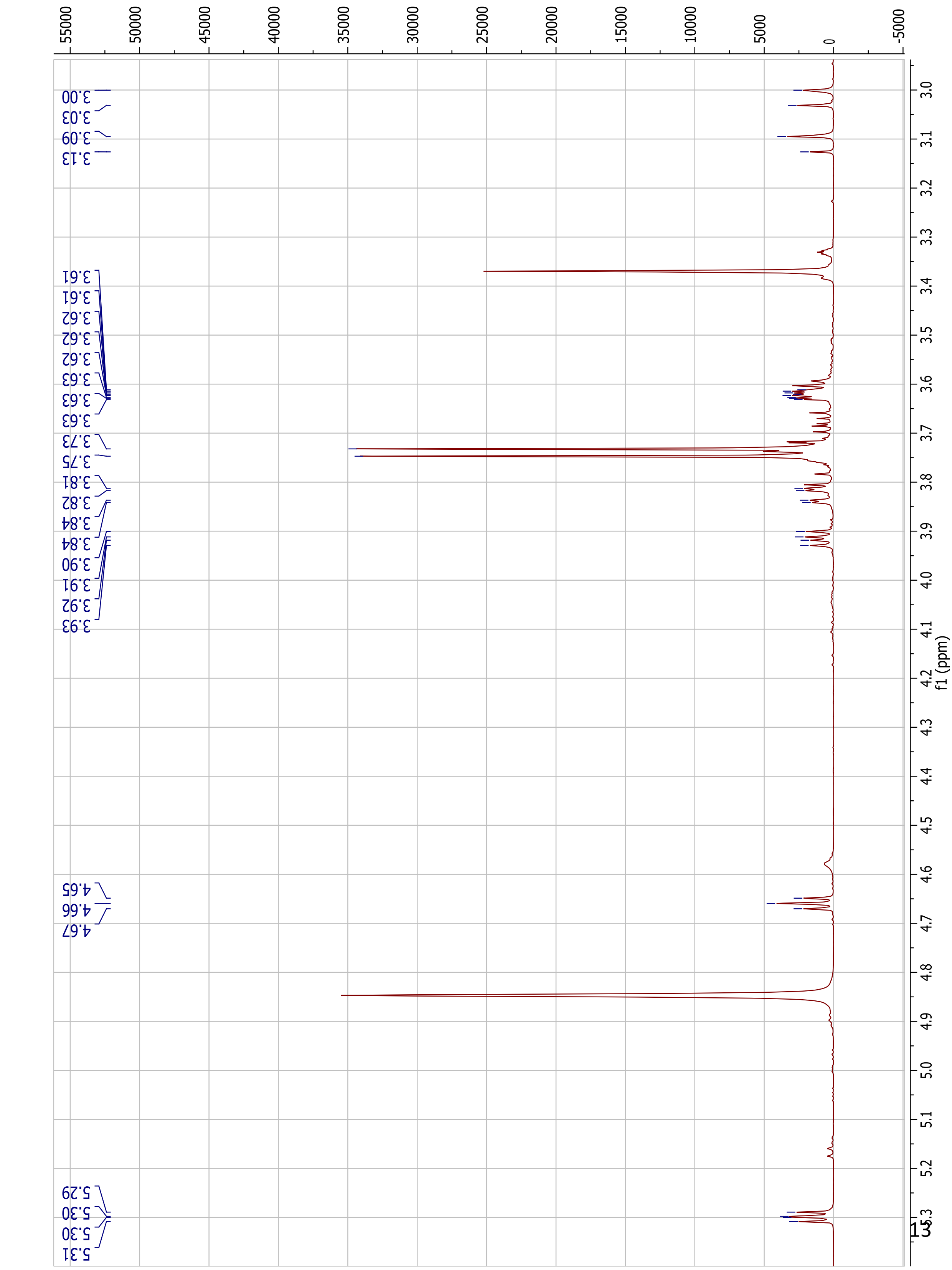


Electronic Supplementary Material (ESI) for Chemical Communications

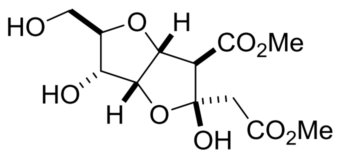
3b



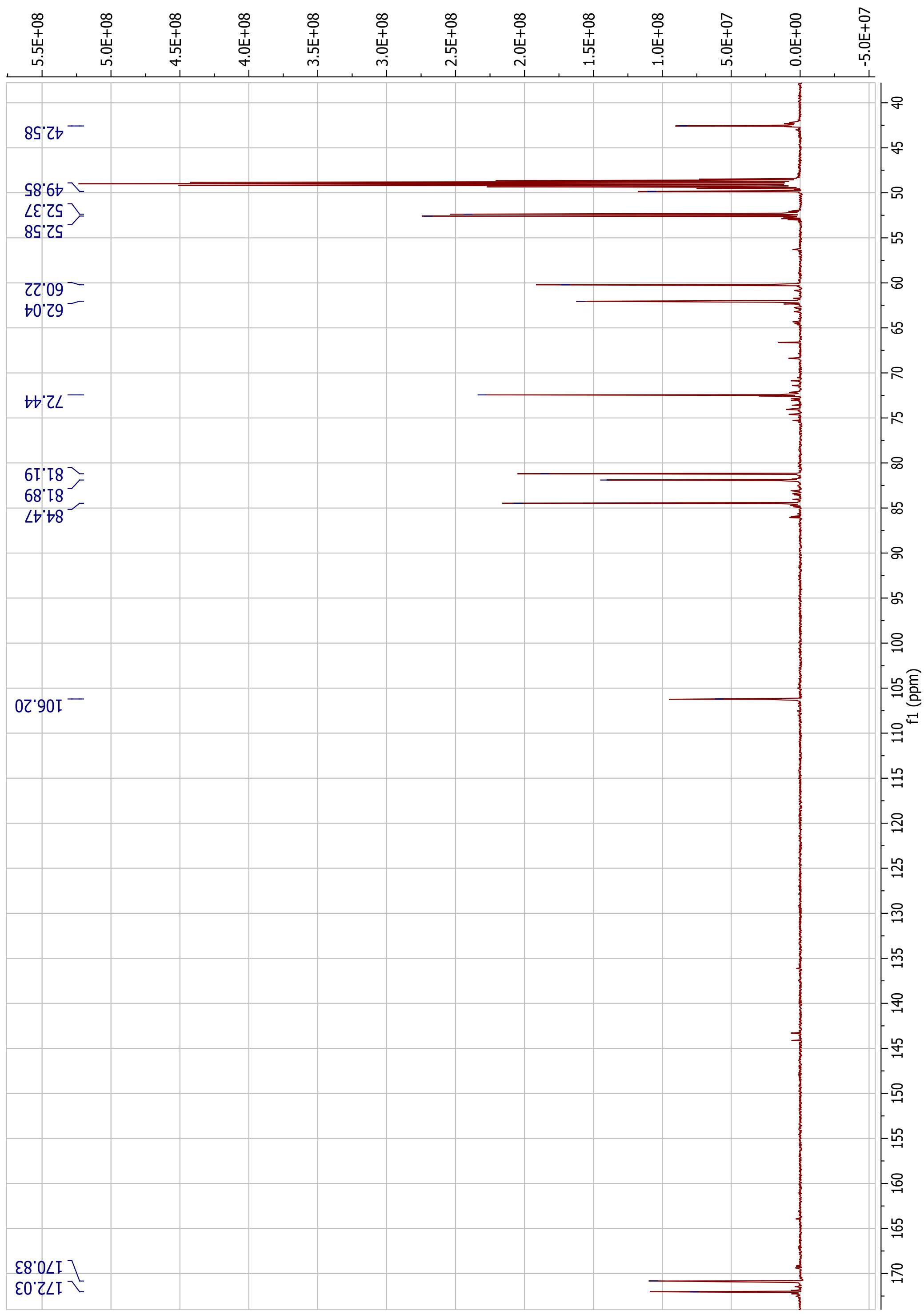
^{1}H (500 MHz, Methanol-d_6)



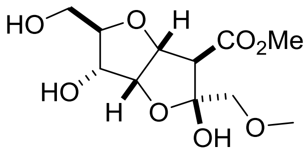
3b



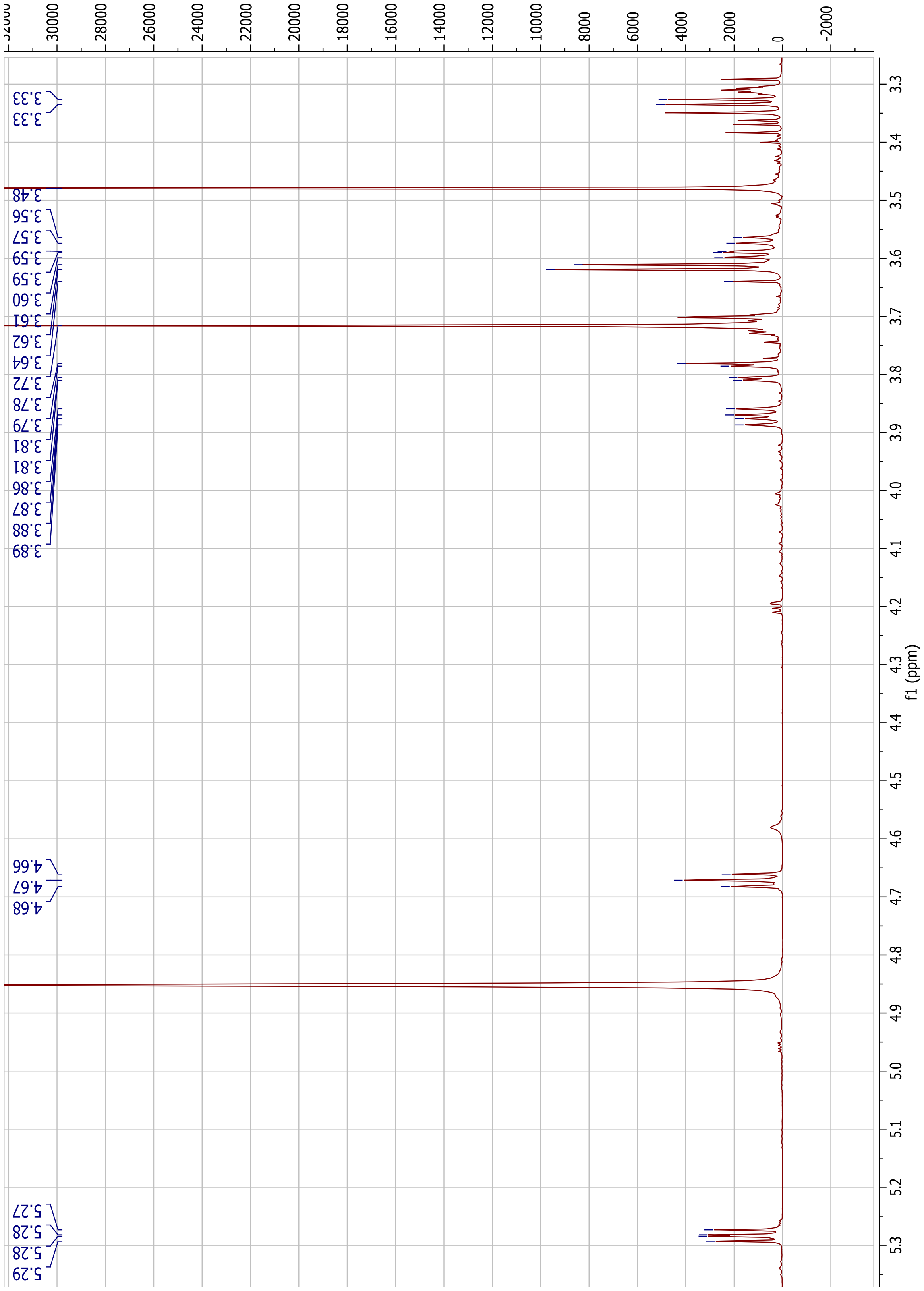
^{13}C (125 MHz, Methonol-d_6)



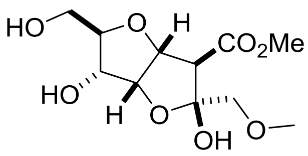
3c



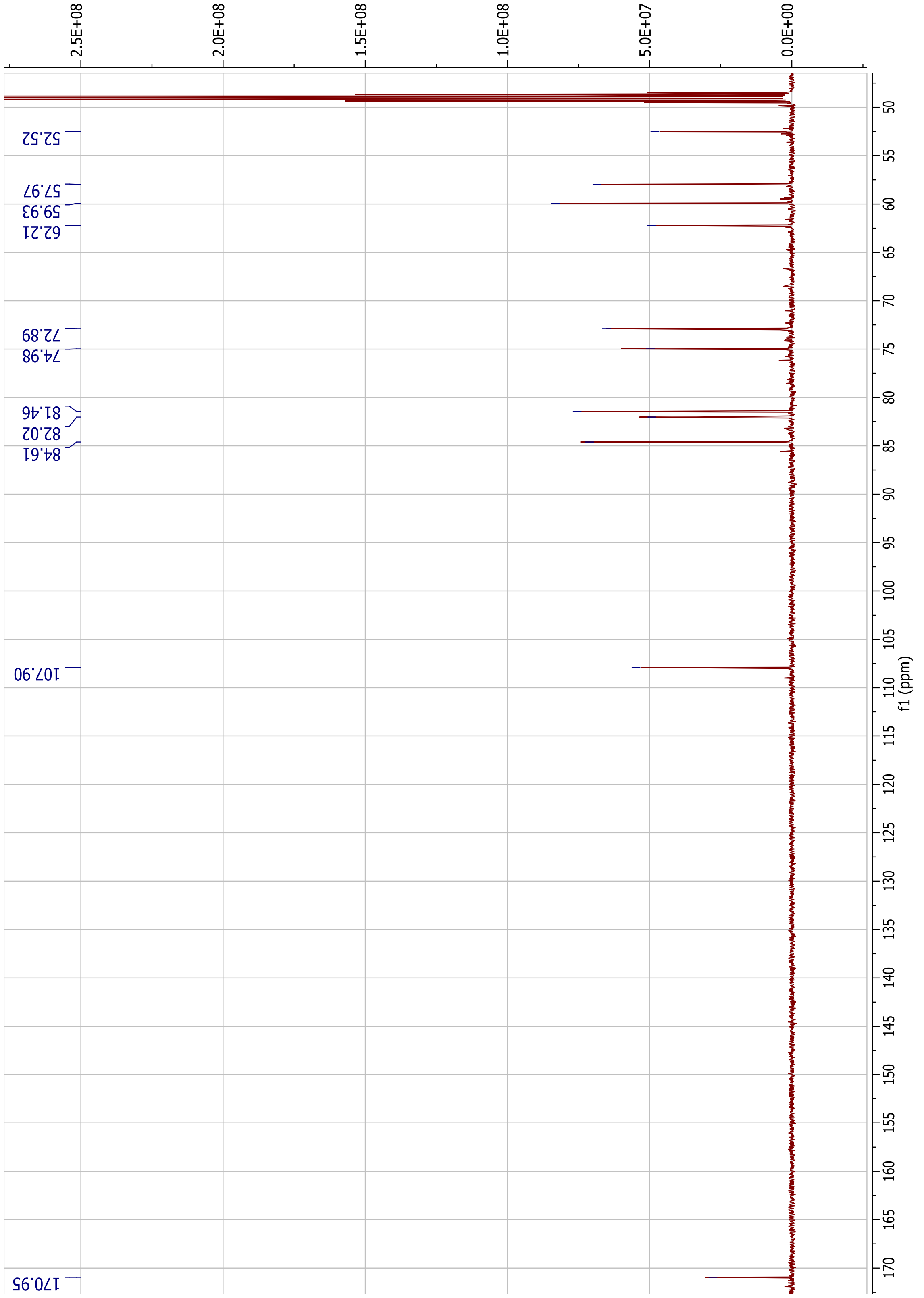
[1]H (500 MHz, Methanol-d_6)



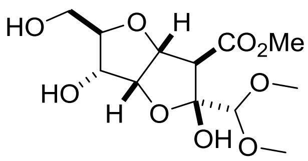
3c



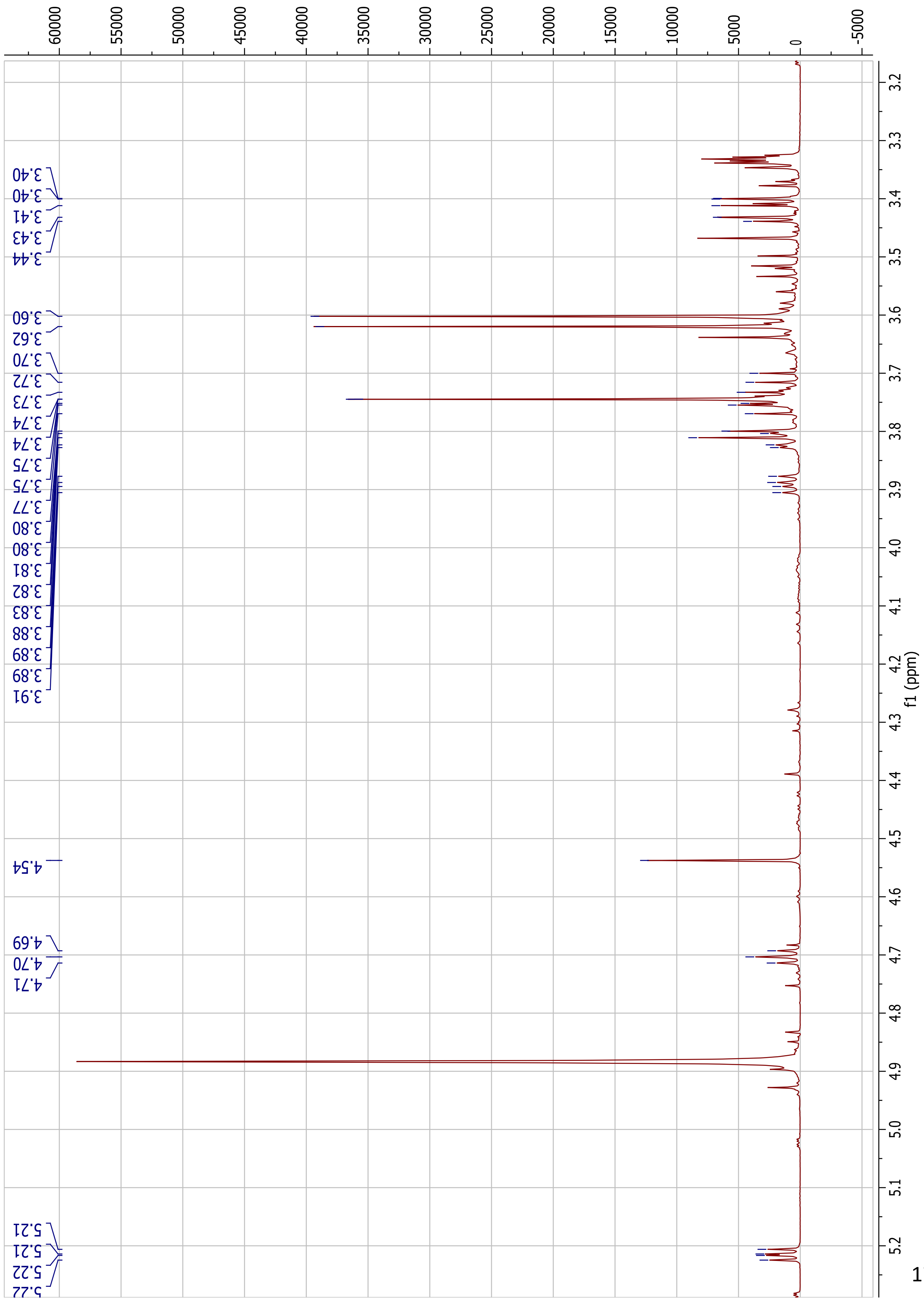
^{13}C (125 MHz, Methanol-d_6)



3d

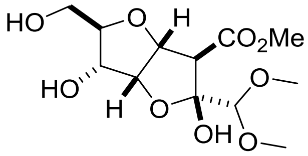


^{1}H (500 MHz, Methanol-d_6)

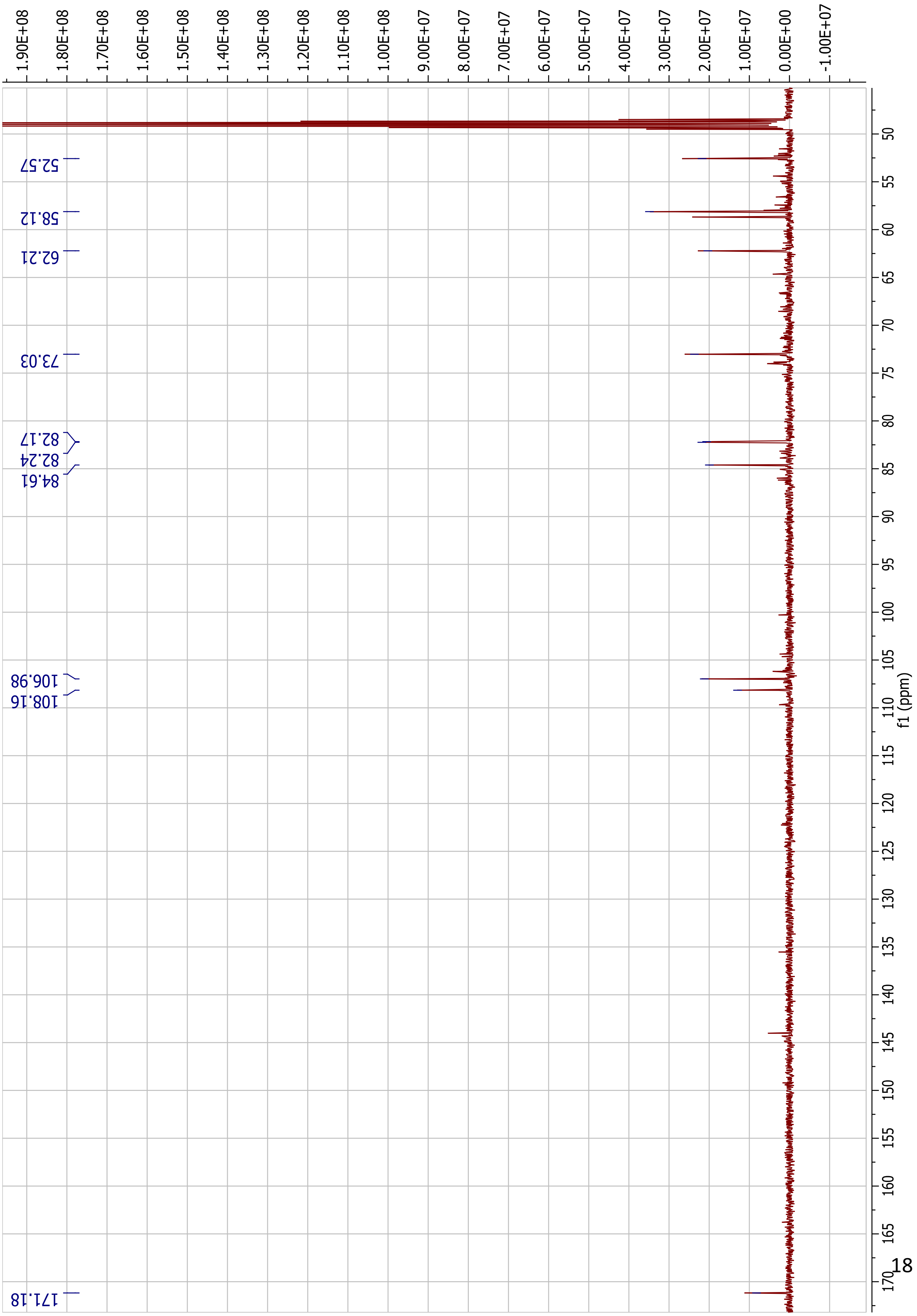


Electronic Supplementary Material (ESI) for Chemical Communications

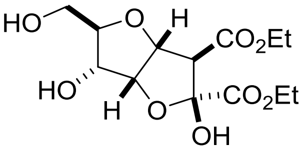
3d



^{13}C (125 MHz, Methanol-d_6)

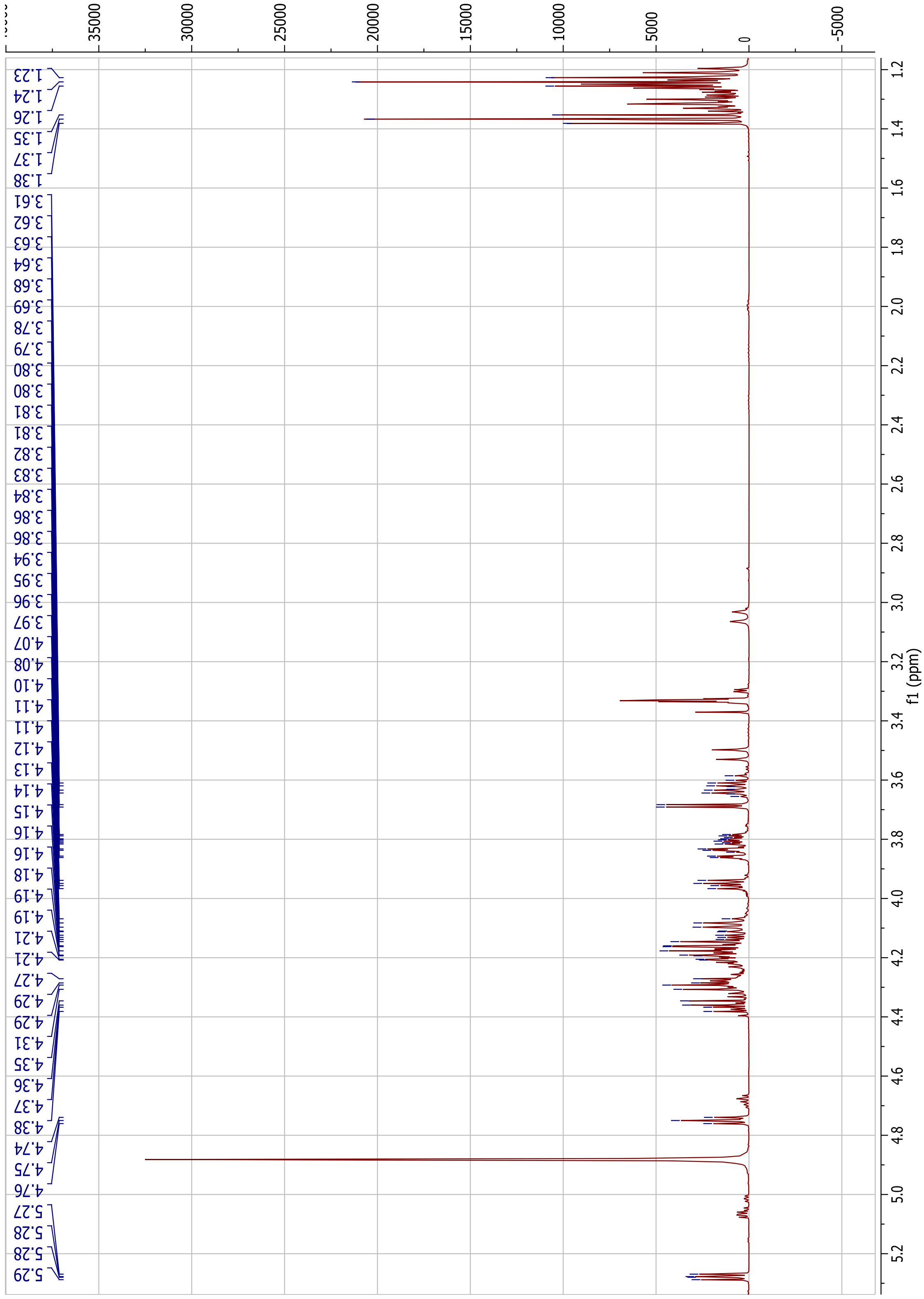


3e

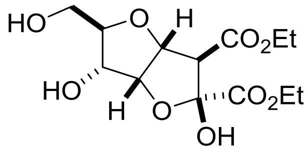


Contains 5% diethyl oxosuccinic ester **2e** as impurity

^{1}H (500 MHz, Methanol-d_6)

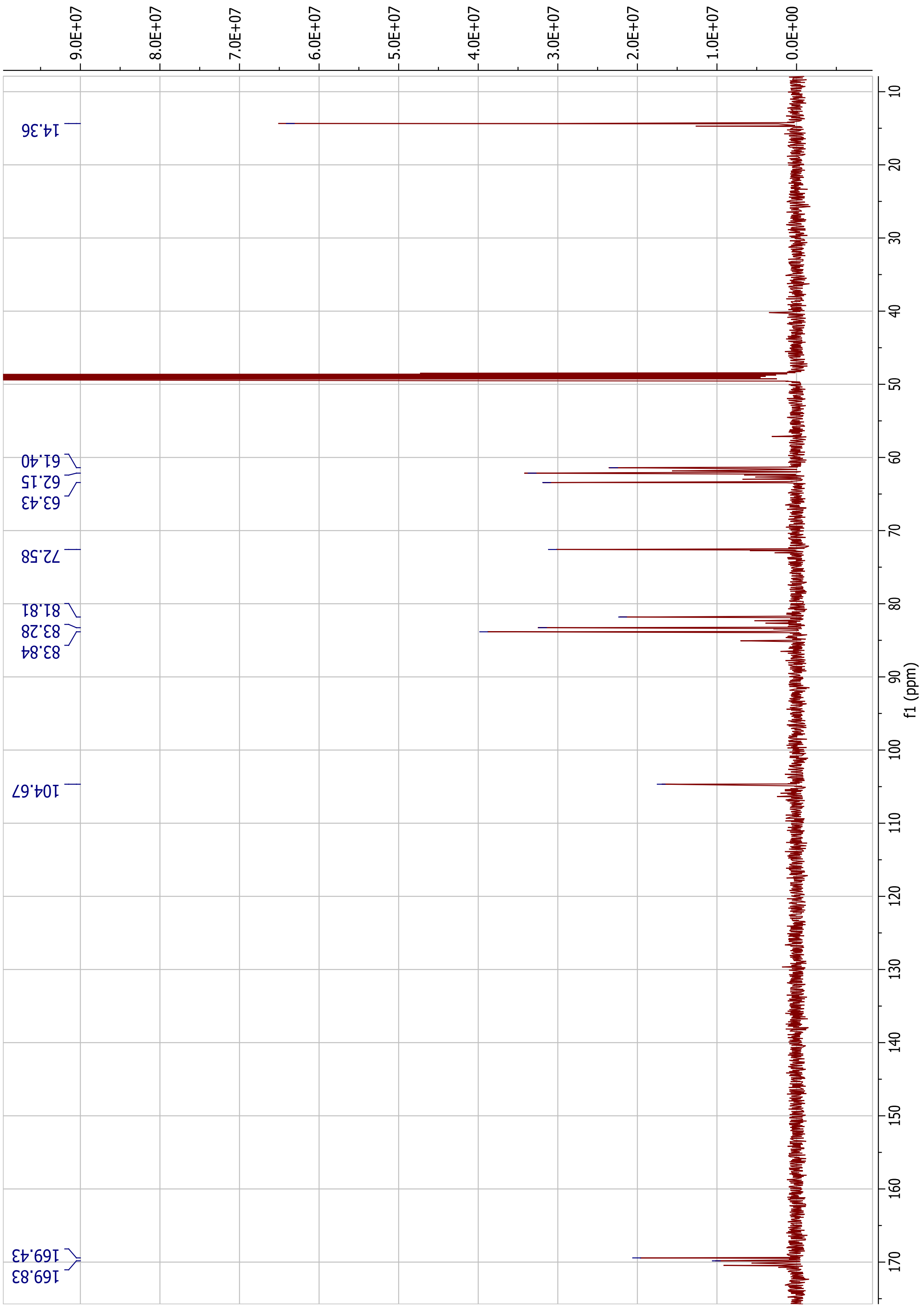


3e

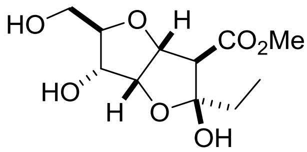


Contains 5% diethyl oxosuccinic ester **2e** as impurity

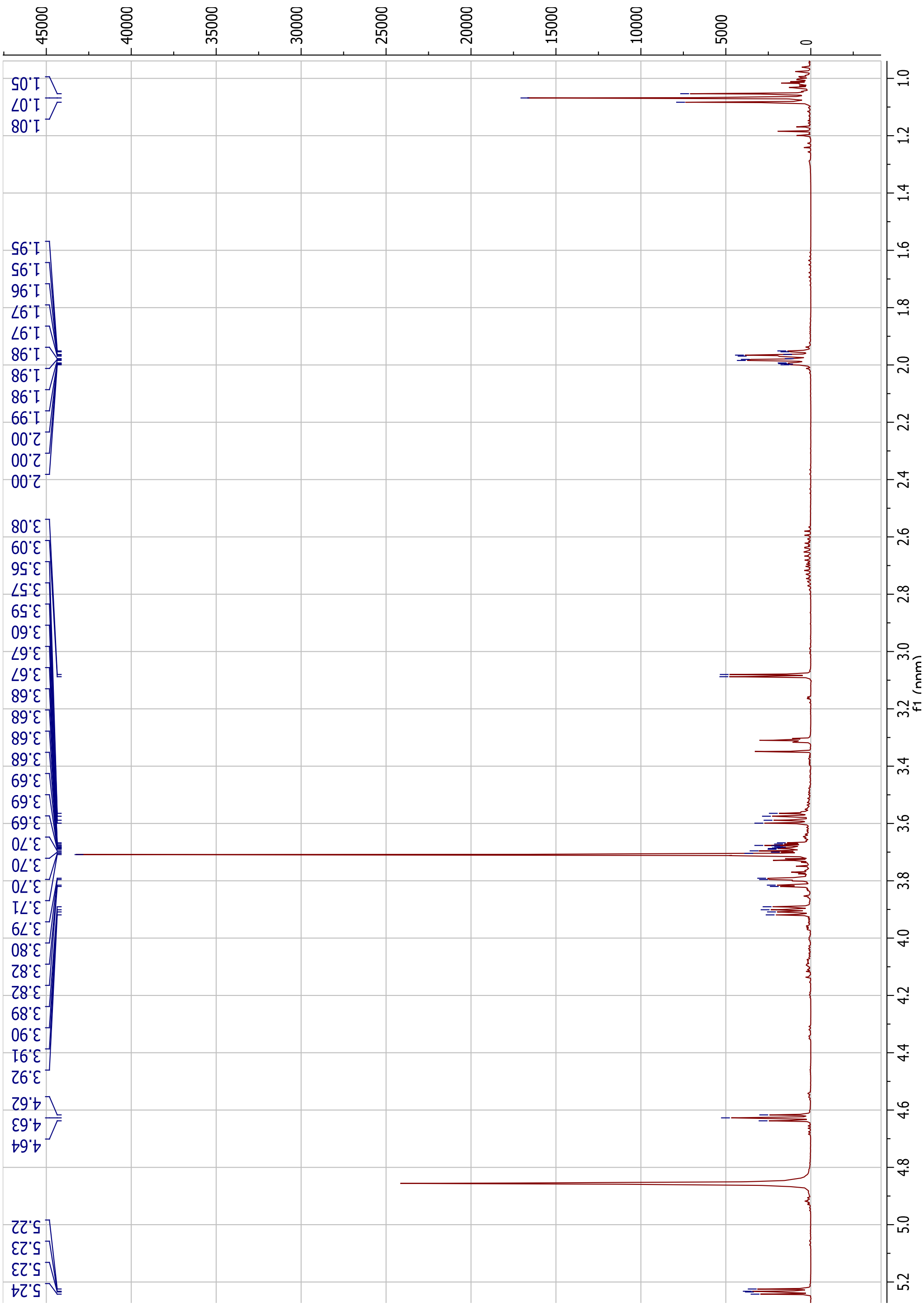
^{13}C (125 MHz, Methanol-d_6)



3f

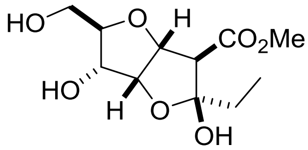


[1]H (500 MHz, Methanol-d_6)

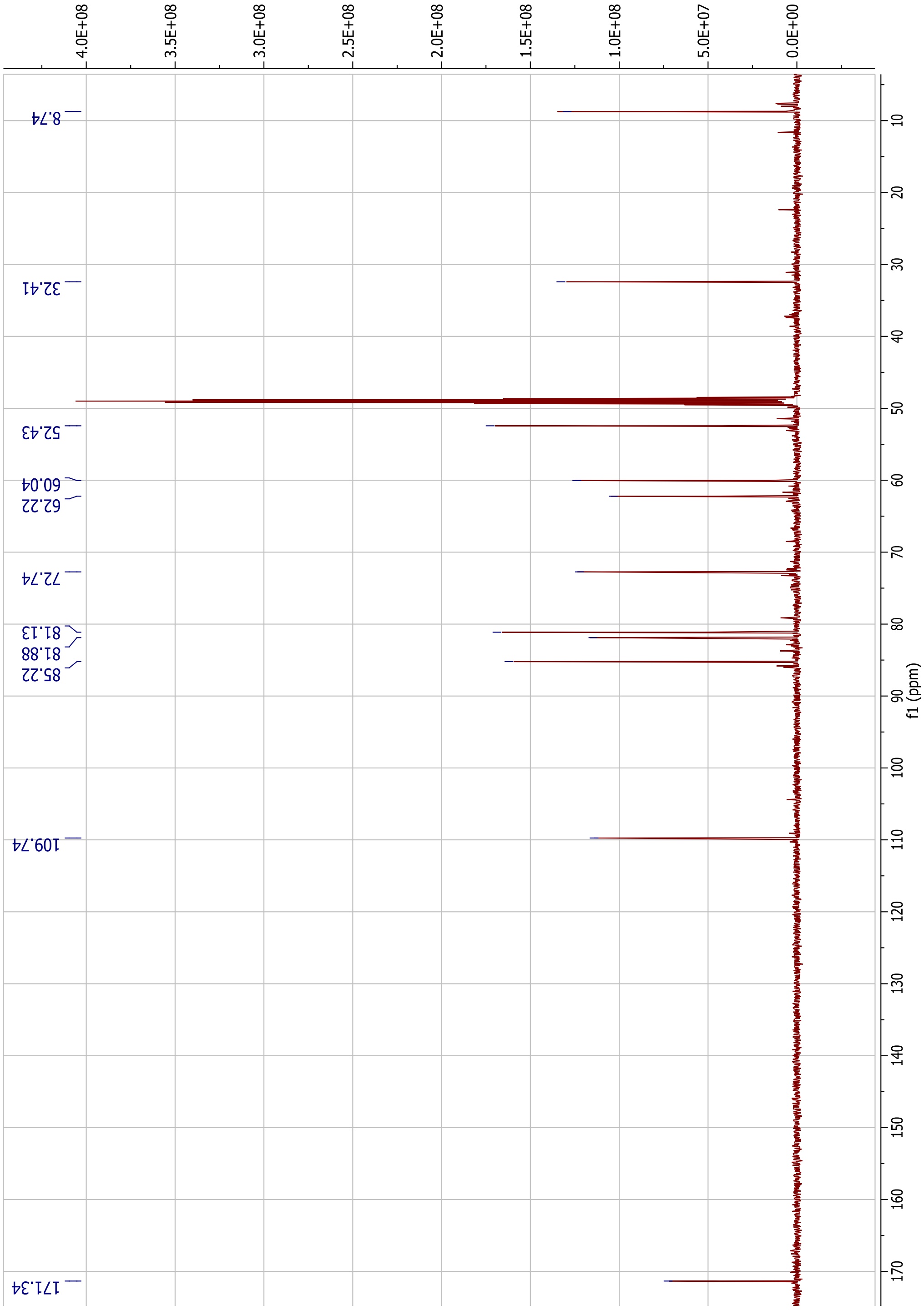


Electronic Supplementary Material (ESI) for Chemical Communications

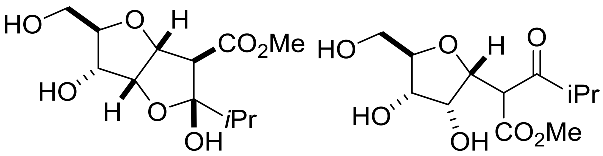
3f



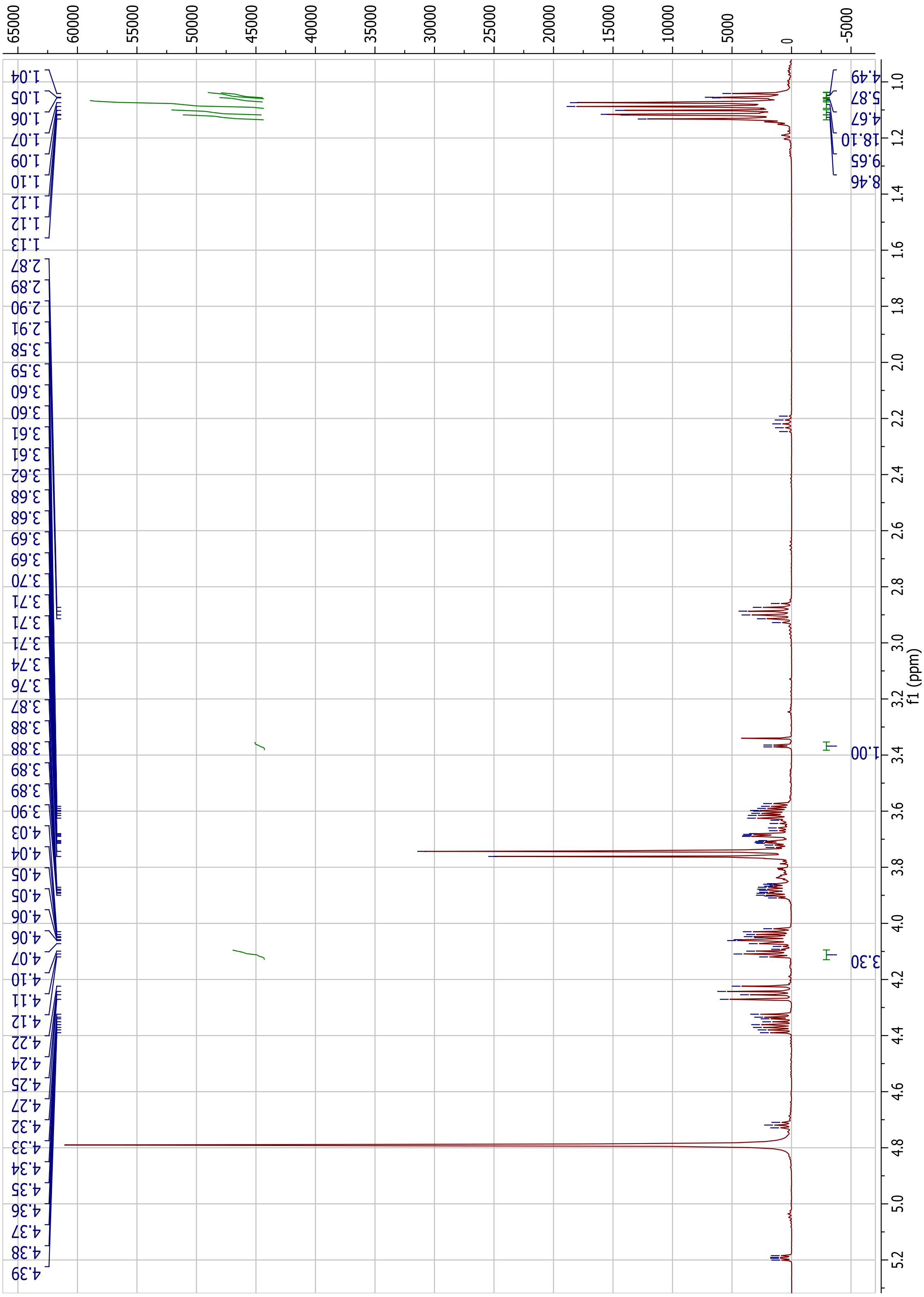
^{13}C (125 MHz, Methanol-d_6)



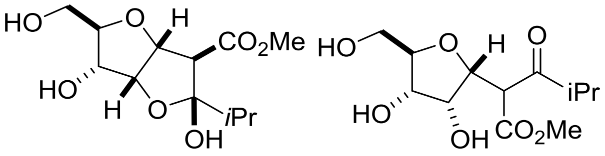
3g + *keto*-**3g**



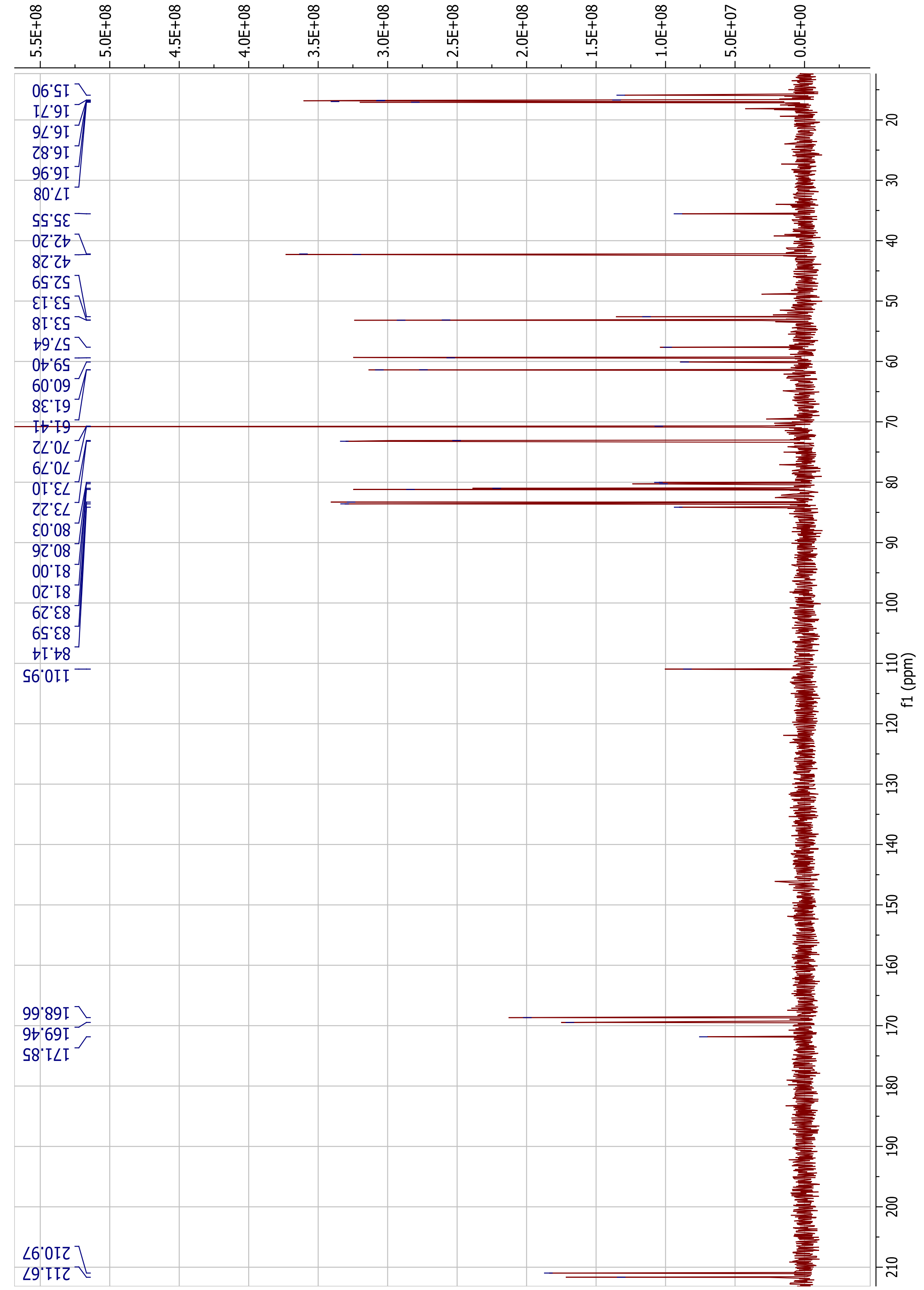
[1]H (500 MHz, Deuterium Oxide)



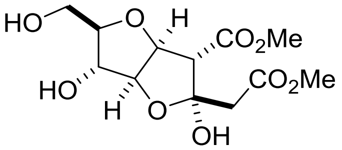
3g + *keto*-**3g**



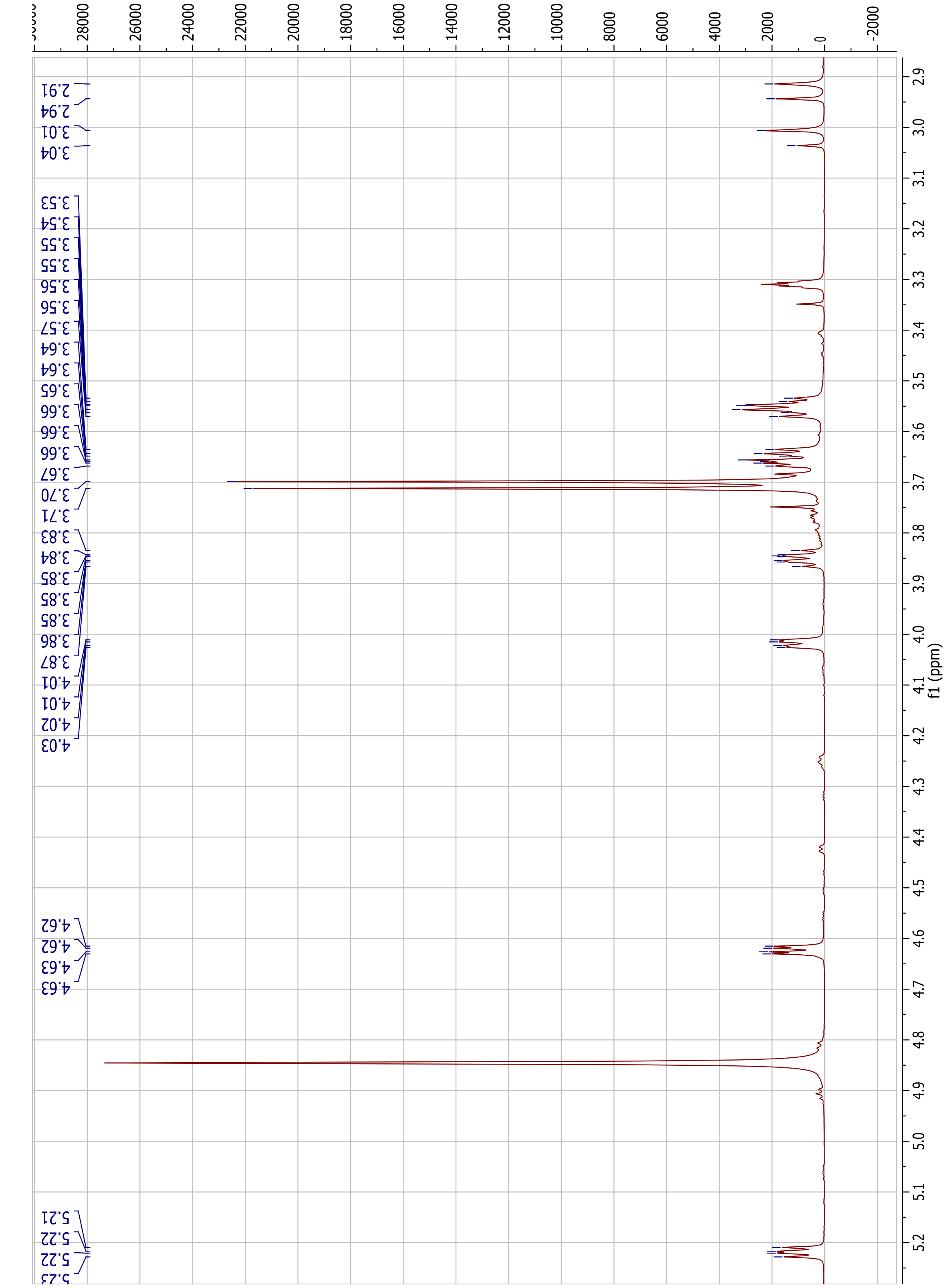
^{13}C (125 MHz, Deuterium Oxide)



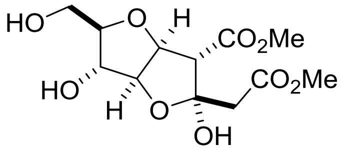
ara-**4b**



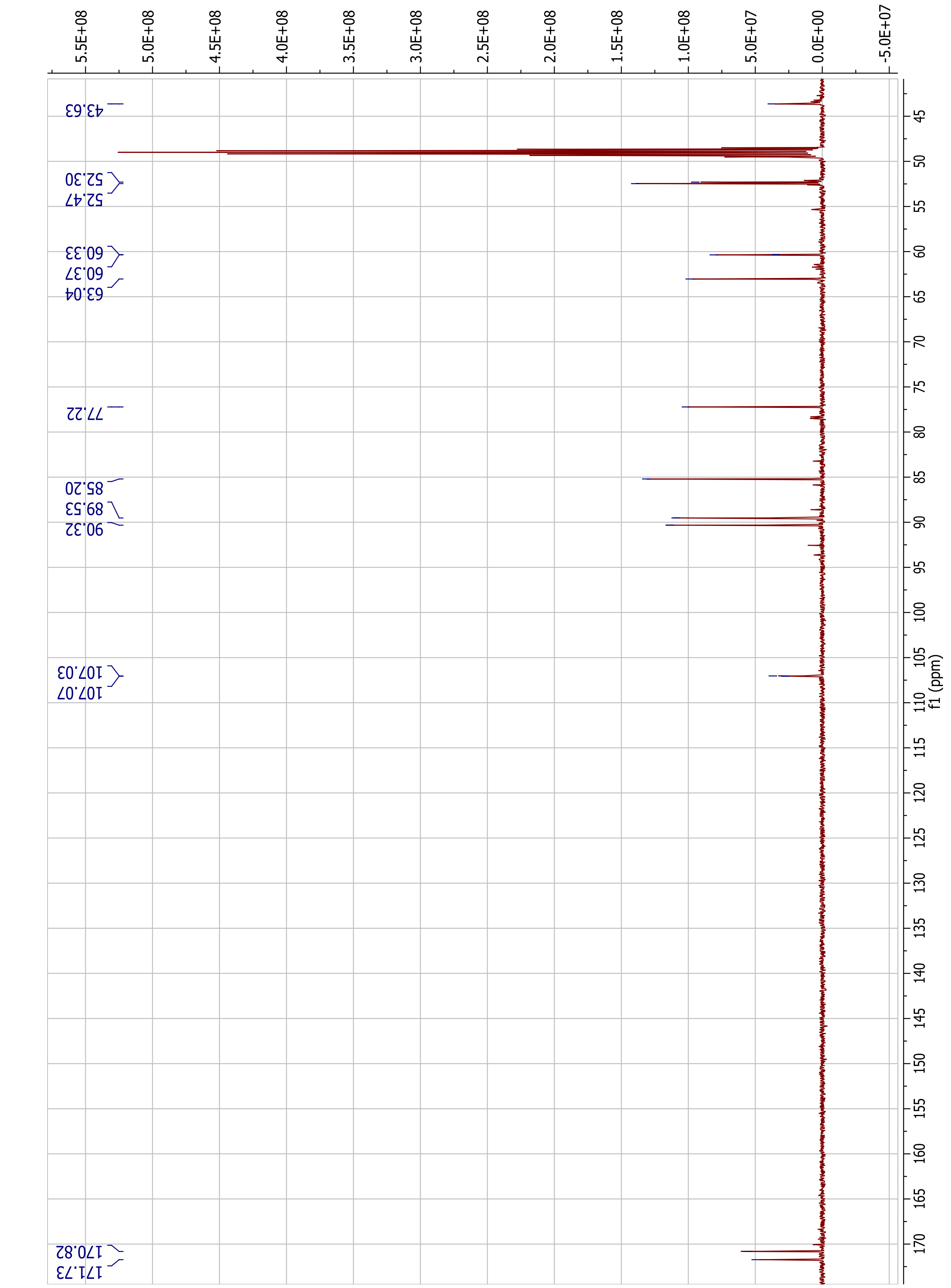
^{1}H (500 MHz, Methanol-d_6)



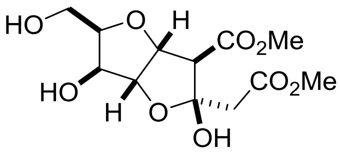
ara-**4b**



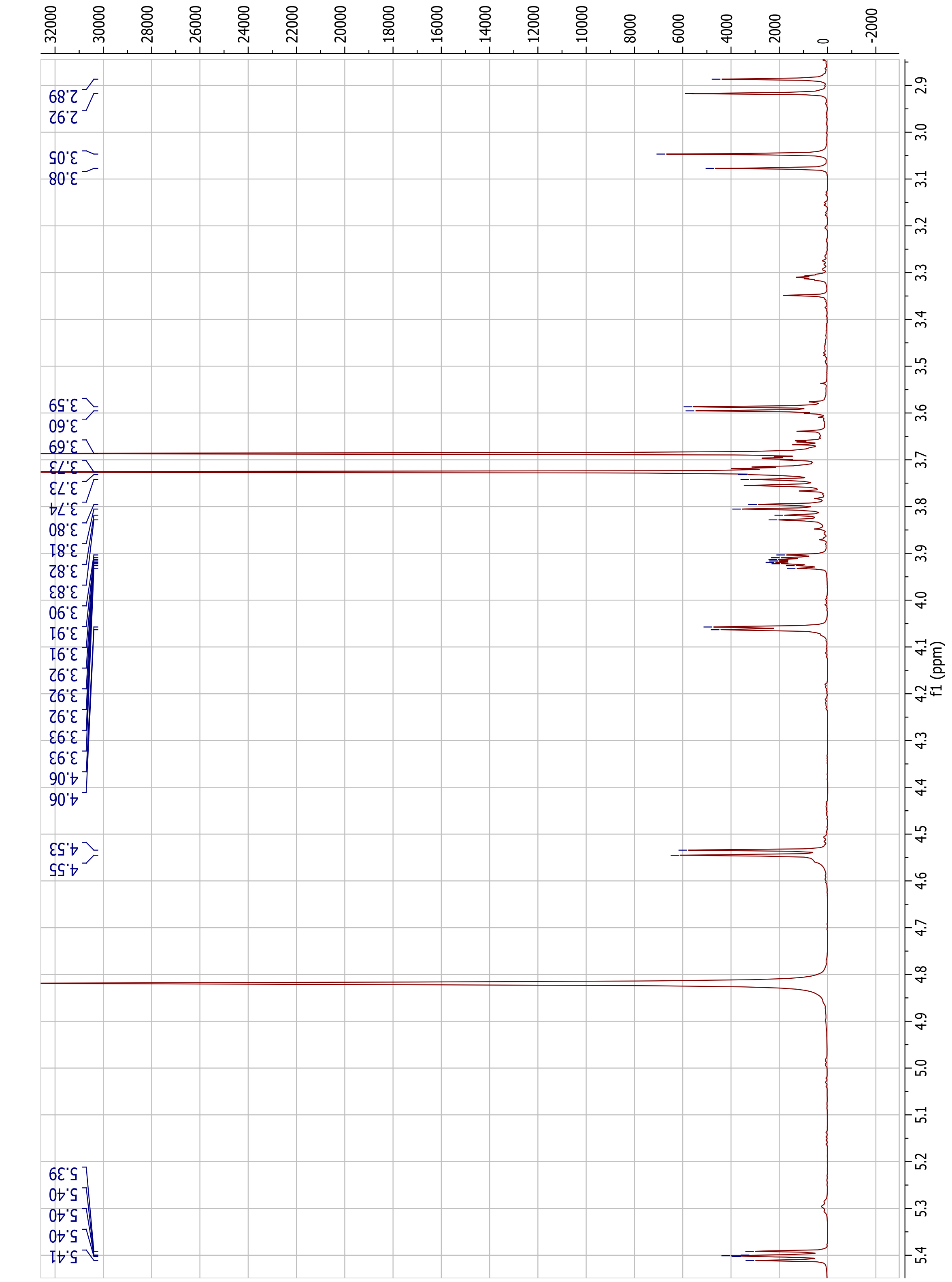
^{13}C (125 MHz, Methanol-d_6)



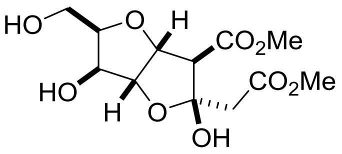
xylo-**5b**



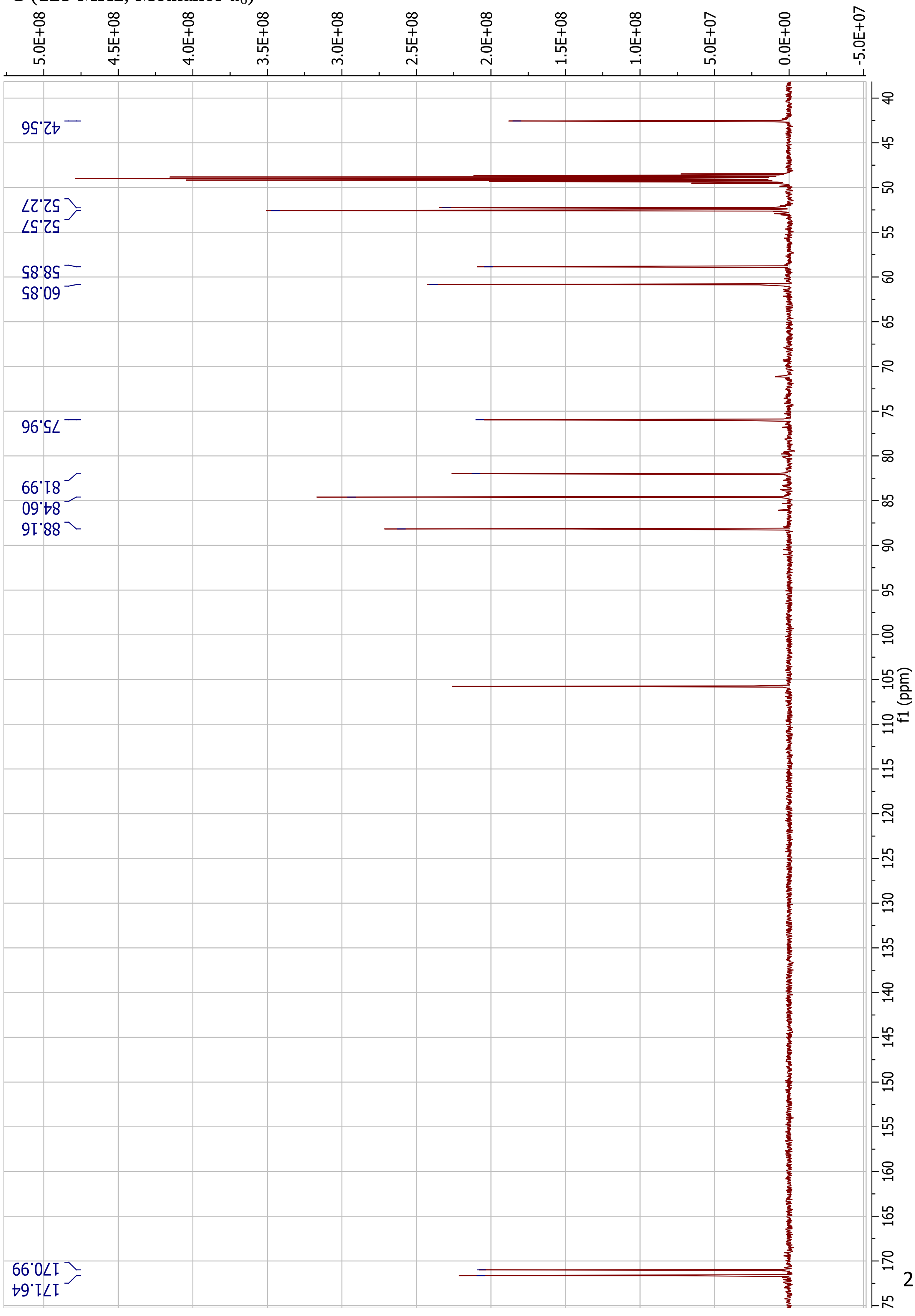
^{1}H (500 MHz, Methanol-d_6)



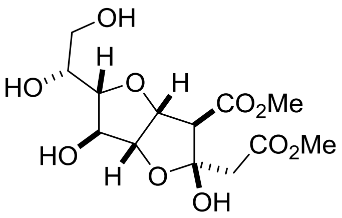
xylo-**5b**



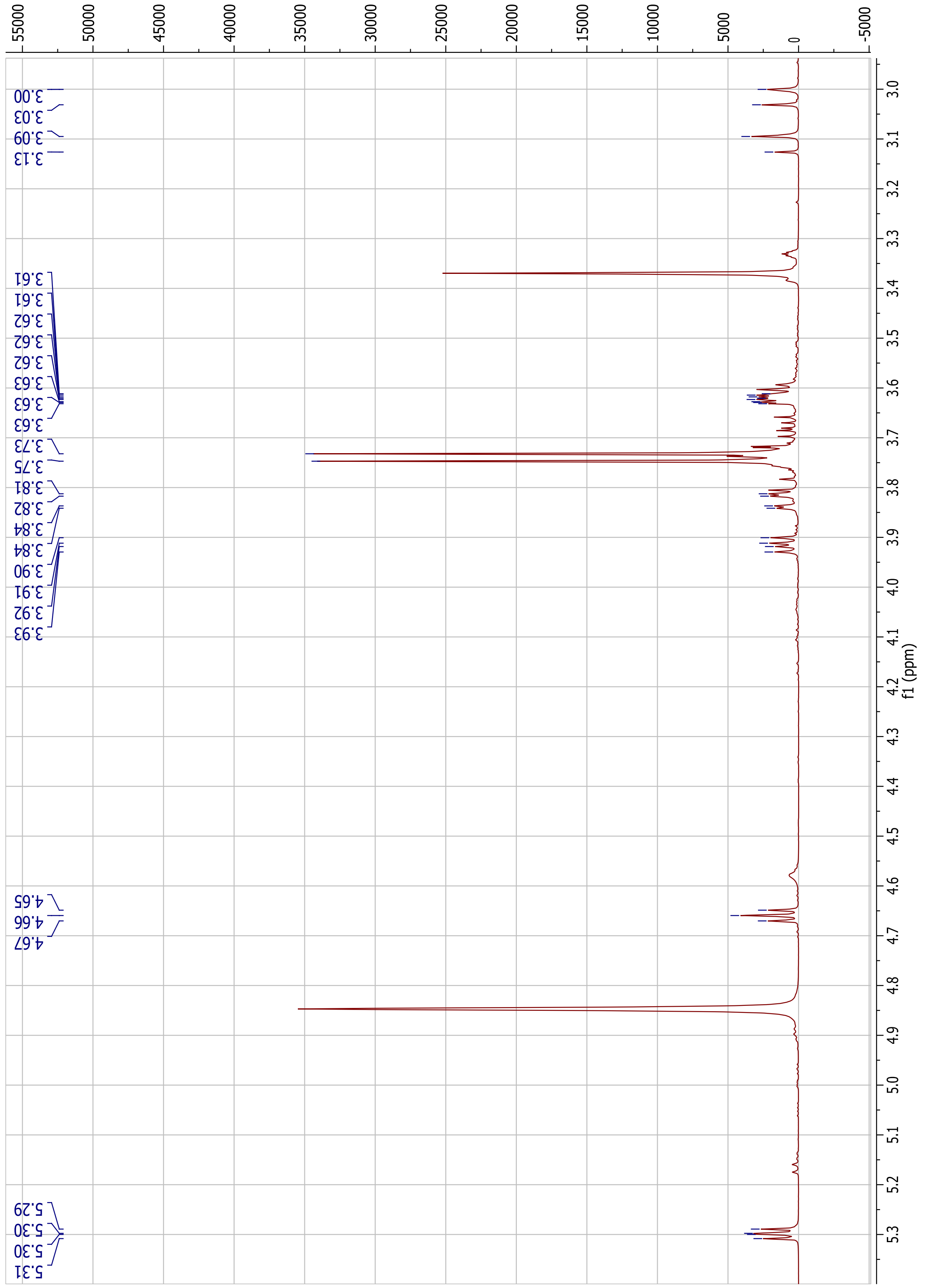
^{13}C (125 MHz, Methanol-d_6)



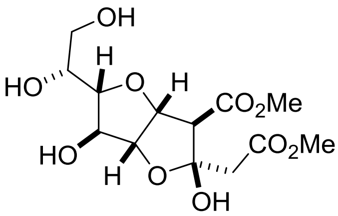
gluco-**6b**



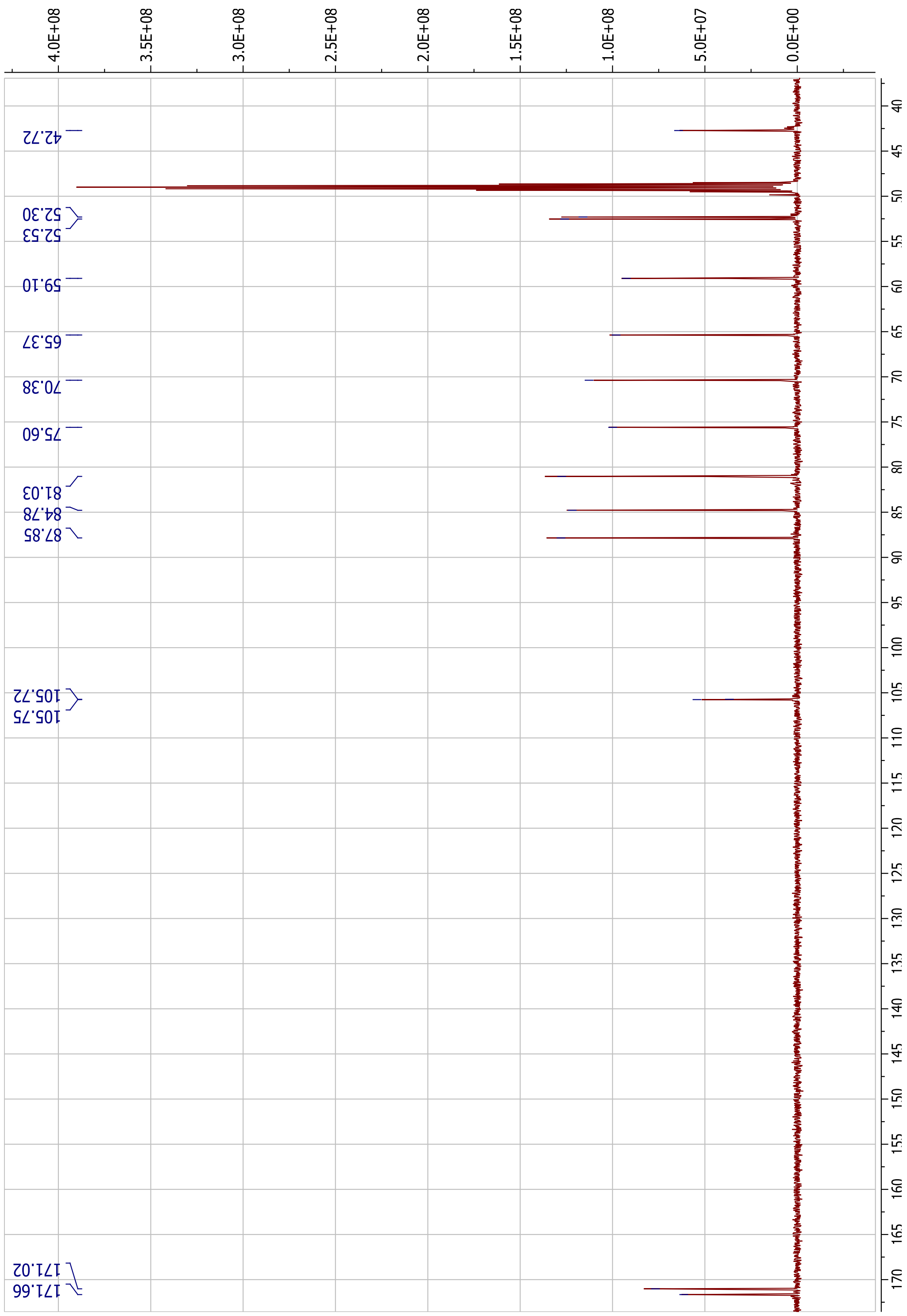
^{1}H (500 MHz, Methanol-d_6)



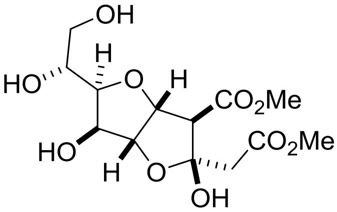
gluco-**6b**



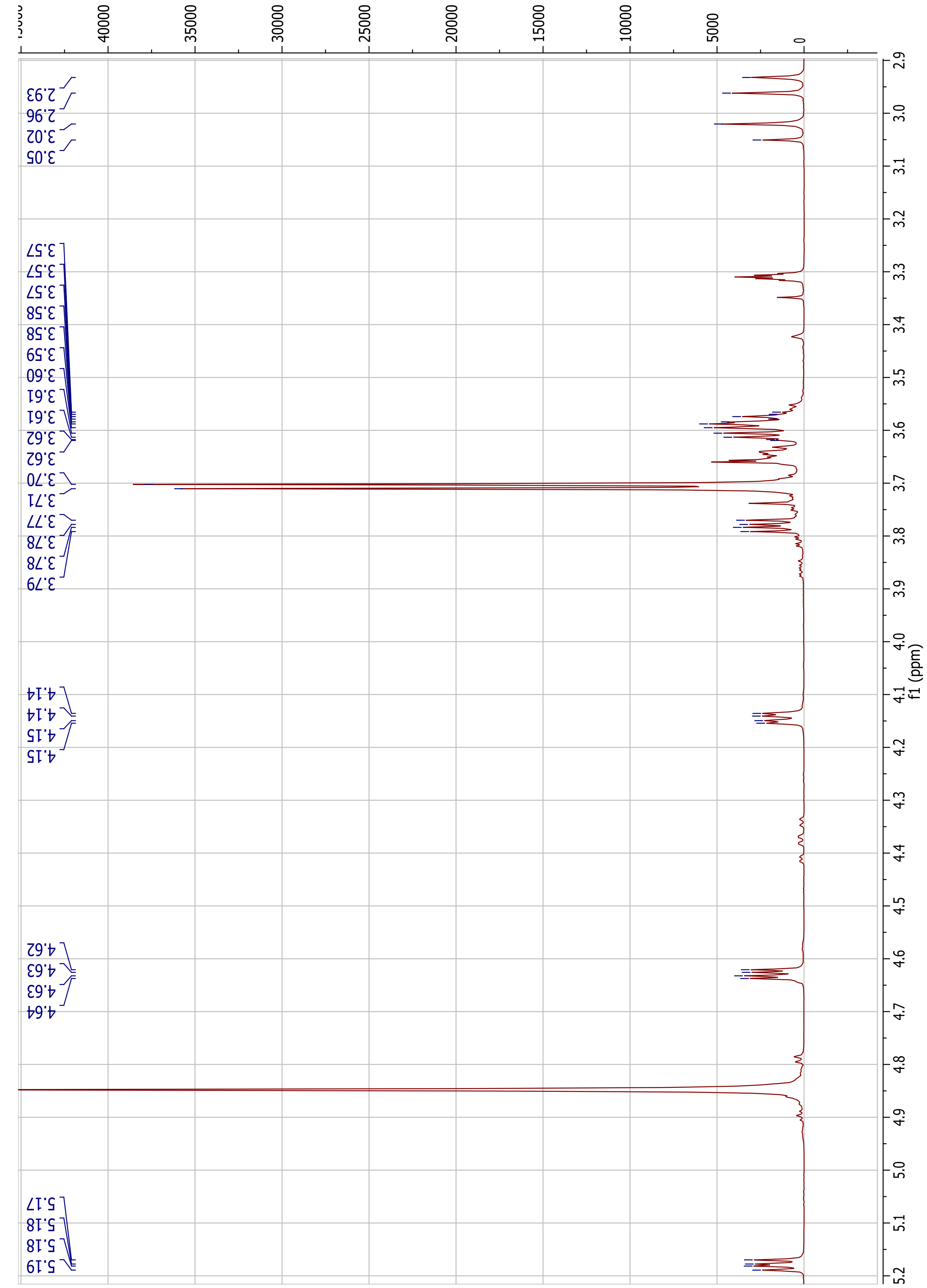
^{13}C (125 MHz, Methanol-d_6)



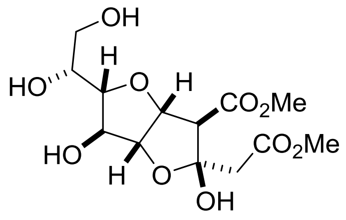
galacto-**7b**



^{1}H (500 MHz, Methanol-d_6)



galacto-**7b**



^{13}C (125 MHz, Methanol-d_6)