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Site-selective carbon-carbon bond formation in unprotected monosaccharides using photoredox catalysis

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General Information

Solvents and Reagents

All solvents used for reactions were of commercial grade, and used without further purification. DMSO (or DMSO-d_6) was degassed using a freeze-pump-thaw procedure for 5 cycles and kept under nitrogen. Reagents were purchased from Sigma-Aldrich, TCI and were used without further purification. Photocatalyst $[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$ was purchased from Strem Chemicals or prepared following a literature procedure.[1] C6-TBS methyl α-D-glucopyranoside and methyl α-D-allopyranoside were prepared according to the literature procedure.[2,3]

Ion Exchange Resin

Dowex 50WX8 (200-400 mesh) was prepared in the Na^+ form by stirring the resin in an excess of saturated NaCl solution overnight, filtered and washed with deionized water until no observable precipitation occurred when a drop of 0.1 M aqueous $AgNO_3$ was added to the fresh mother liquor.

Analysis

^1H-, ^{13}C-, ^{31}P-, APT-, COSY-, HMQC, NOE and NOESY-NMR were recorded on a Varian AMX400 spectrometer (400, 100 and 162 MHz, respectively) using DMSO-*d*$_6$, CD_3OD or a 1:1 mixture of $CDCl_3$ and CD_3OD as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (DMSO-*d*$_6$: δ3.31 for ^1H, δ 49.15 for ^{13}C, CD_3OD: δ3.31 for ^1H, δ 49.15 for ^{13}C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, dd = double doublet, ddd = double double doublet, t = triplet, appt = apparent triplet, q = quartet, m = multiplet), coupling constants J (Hz), and integration. High Resolution Mass measurements were performed using a ThermoScientific LTQ OribitrapXL spectrometer. Optical rotations were measured on a Schmidt + Haensch polarimeter (Polartronic MH8) with a 10 cm cell (c given in g/100 mL).

LED setup

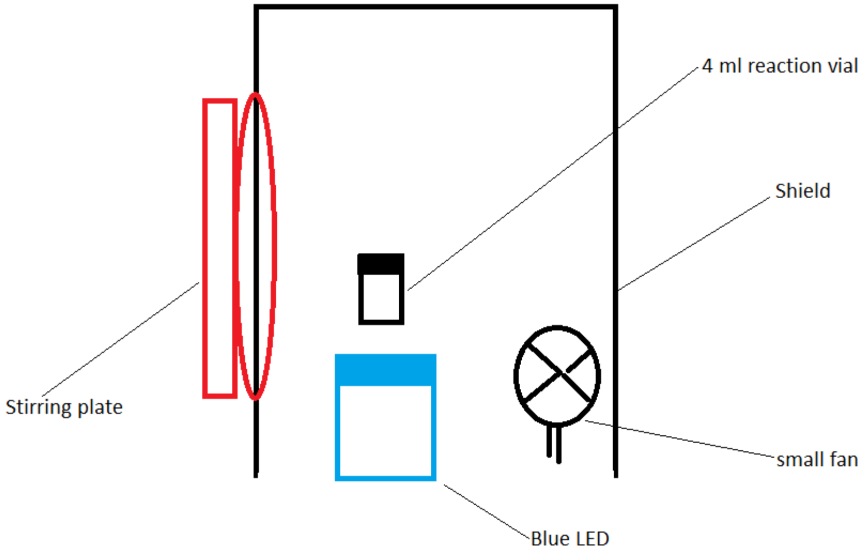
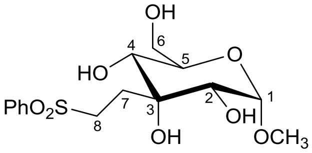


Figure 1 Reaction setup

As shown, the 4 ml reaction vial is secured with a clamp from the back. The blue LED lamp is placed ~5 cm below the vial. The stirring plate is placed ~5 cm to the side of the vial. The small fan is turned on once the blue LED is on to cool down the reaction mixture. The Blue LED source is a Kessil® LED illuminator (model H150 blue, http://www.kessil.com/horticulture/H150.php)

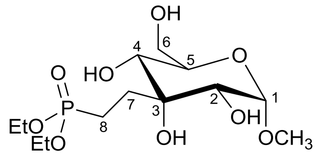
Experimental section



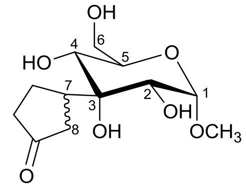
(*2R,3R,4R,5R,6S*)-2-(hydroxymethyl)-6-methoxy-4-(2-(phenylsulfonyl)ethyl)tetrahydro-2H-pyran-3,4,5-triol (2):

From methyl α-D-glucopyranoside 1: A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl α-D-glucopyranoside (48 mg, 0.25 mmol, 1.0 eq), $[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$ (3.2 mg, 0.003 mmol, 0.012 eq), quinuclidine (3.0 mg, 0.027 mmol, 0.11 eq), tetrabutylammonium dihydrogenphosphate (21 mg, 0.062 mmol, 0.25 eq) and degassed DMSO (0.5 mL). The reaction mixture was purged with nitrogen for 5 min, and phenyl vinyl sulfone (62 mg, 0.37 mmol, 1.5 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was then diluted with water (10 mL) and stirred with ~1.0 g Dowex resin for 12 h. The resin was filtered off and washed with water and MeOH (4 mL each × 20). The filtrate was then concentrated *in vacuo* and freeze-dried, and the remaining solid was dissolved in MeOH and coated onto ~0.5 g of celite. The resulting celite was loaded onto a silica column. The flash column was then eluted with 8% MeOH in DCM to obtain **2** as an off-white wax (46 mg, 52% yield adjusted for 15 mol% residual solvent). R_f = 0.3 (8% MeOH in DCM); visualized with *p*-anisaldehyde stain. **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.92 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.76 – 7.69 (m, 1H), 7.64 (dd, *J* = 8.3, 6.9 Hz, 2H), 4.65 (d, *J* = 3.8 Hz, 1H, H1), 3.81 (dd, *J* = 11.7, 2.2 Hz, 1H, H6), 3.70 (dd, *J* = 11.7, 5.3 Hz, 1H, H6), 3.64 (ddd, *J* = 9.9, 5.2, 2.1 Hz, 1H, H5), 3.60 – 3.45 (m, 2H, H8), 3.45 – 3.40 (m, 4H, OMe and H2), 3.27 (d, *J* = 9.9 Hz, 1H, H4), 2.14 (ddd, *J* = 13.3, 12.1, 5.0 Hz, 1H, H7), 2.03 (ddd, *J* = 13.5, 12.0, 5.2 Hz, 1H, H7). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 140.4, 134.9, 130.5, 129.0, 101.7 (C1), 75.8(C3), 71.7(C2), 70.6(C4), 70.3(C5), 62.7(C6), 56.1(OMe), 53.3(C8), 29.7(C7). **HRMS (ESI+)** Calcd. for $C_{15}H_{22}O_8SNa$ ($[M + Na]^+$): 385.093, found: 385.093. **Optical rotation**: $[\alpha]_D^{20}$= + 76.6 (*c* = 0.128 , CH_3OH).

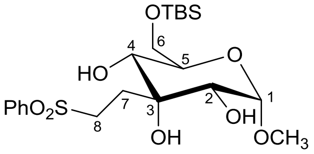
From methyl α-D-allopyranoside 7: A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl α-D-allopyranoside (50 mg, 0.26 mmol, 1.0 eq), $[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$ (2.7 mg, 0.002 mmol, 0.009 eq), quinuclidine (3.5 mg, 0.031 mmol, 0.12 eq), tetrabutylammonium dihydrogenphosphate (23 mg, 0.069 mmol, 0.27 eq) and degassed DMSO (0.5 mL). The reaction mixture was purged with nitrogen for 5 min, and phenyl vinyl sulfone (63 mg, 0.37 mmol, 1.5 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was then diluted with water (10 mL) and stirred with ~1.0 g Dowex resin for 12 h. The resin was filtered off and washed with water and MeOH (4 mL each×20). The filtrate was then concentrated in vacuo and freeze-dried, and the remaining solid was dissolved in MeOH and coated onto ~0.5 g celite. The resulting celite was loaded onto a silica column. The flash column was then eluted with 8% MeOH in DCM to obtain **2** as an off-white wax (46 mg, 52% yield adjusted for 9 mol% residual solvent).



diethyl (2-((*2R,3R,4R,5R,6S*)-3,4,5-trihydroxy-2-(hydroxymethyl)-6-methoxytetrahydro-2H-pyran-4-yl)ethyl)phosphonate (2a): A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl α-D-glucopyranoside (50 mg, 0.26 mmol, 1.0 eq), $[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$ (3.1 mg, 0.003 mmol, 0.011 eq), quinuclidine (3.5 mg, 0.031 mmol, 0.12 eq), tetrabutylammonium dihydrogenphosphate (23 mg, 0.069 mmol, 0.27 eq) and degassed DMSO (0.5 mL). The reaction mixture was purged with nitrogen for 5 min, and diethyl vinylphosphonate (60 µl, 64 mg, 0.39 mmol, 1.5 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was then diluted with water (10 mL) and stirred with ~1.0 g Dowex resin for 12 h. The resin was filtered off and washed with water and MeOH (4 mL each × 20). The filtrate was then concentrated in vacuo and freeze-dried, and the remaining solid was dissolved in MeOH and coated onto ~0.5 g celite. The resulting celite was loaded onto a silica column. The flash column was then eluted with 8% MeOH in DCM to obtain **2a** as an off-white wax (46 mg, 50% yield). R_f = 0.3 (8% MeOH in DCM); visualized with *p*-anisaldehyde stain. **^{1}H NMR** (400 MHz, Methanol-d_4) δ 4.70 (d, *J* = 3.8 Hz, 1H, H1, H1), 4.09 (ddq, *J* = 14.5, 7.2, 3.4 Hz, 4H, CH_2 on OEt), 3.84 (dd, *J* = 11.4, 1.9 Hz, 1H, H6), 3.77 – 3.66 (m, 2H, H6 and H5), 3.49 (d, *J* = 3.9 Hz, 1H, H2), 3.45 (s, 3H, OMe), 3.35 (d, *J* = 9.5 Hz, 1H, H4), 2.10 – 1.88 (m, 4H, H7 and H8), 1.33 (t, *J* = 7.1 Hz, 6H, CH_3 on OEt). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 101.8(C1), 76.4 (d, *J* = 17.8 Hz, C3), 70.4 (2 overlapping signals, C2 and C5), 69.1(C4), 63.2 (d, *J* = 6.6 Hz, CH_2 on OEt), 62.8(C6), 56.1(OMe), 27.9 (d, *J* = 4.2 Hz, C7), 21.1 (d, *J* = 140.4 Hz, C8), 16.7 (d, *J* = 5.9 Hz, CH_3 on OEt). **^{31}P NMR** (162 MHz, Methanol-d_4) δ 34.1. **HRMS (ESI+)** Calcd. for $C_{15}H_{27}O_9PNa$ ($[M + Na]^+$): 381.129, found: 385.129. **Optical rotation**: $[\alpha]_D^{20}$= + 79.3 (*c* = 0.082, CH_3OH).



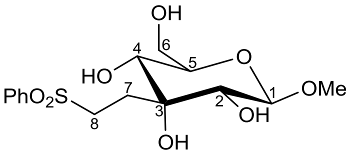
3-((*2R,3R,4R,5R,6S*)-3,4,5-trihydroxy-2-(hydroxymethyl)-6-methoxytetrahydro-2H-pyran-4-yl)cyclopentan-1-one (2b): A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl α-D-glucopyranoside (45 mg, 0.23 mmol, 1.0 eq), $[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$ (3.1 mg, 0.003 mmol, 0.012 eq), quinuclidine (3.1 mg, 0.028 mmol, 0.12 eq), tetrabutylammonium dihydrogenphosphate (20 mg, 0.059 mmol, 0.25 eq) and degassed DMSO (0.5 mL). The whole reaction mixture was purged with nitrogen for 5 min, and cyclopentenone (29 µl, 29 mg, 0.35 mmol, 1.5 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was then diluted with methanol (12 mL) and water (32 mL) and stirred with ~1.0 g Dowex resin for 12 h. The resin was filtered off and washed with water and MeOH (4 mL each × 20). The filtrate was then concentrated in vacuo and freeze-dried, and the remaining solid was dissolved in MeOH and coated onto ~0.5 g celite. The resulting celite was loaded onto a silica column. The flash column was then eluted with 8% MeOH in DCM to obtain **2b** as an off-white wax (38 mg, 59% yield, mixture of diastereomers). R_f = 0.35 (8% MeOH in DCM); visualized with p-anisaldehyde stain. **HRMS (ESI+)** Calcd. for $C_{12}H_{20}O_7Na$ ([M + Na]$^+$): 299.110, found: 299.110. Due to the complexity of the NMR spectra, as the product is a mixture of diastereomers, the reader is referred to the spectra at the end of this section.



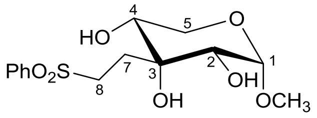
(*2R,3R,4R,5R,6S*)-2-(((tert-butyldimethylsilyl)oxy)methyl)-6-methoxy-4-(2-(phenylsulfonyl)ethyl)tetrahydro-2H-pyran-3,4,5-triol (9):

Method 1: A 4 mL vial equipped with a septum and magnetic stir bar was charged with C6-TBS methyl α-D-glucopyranoside (78 mg, 0.25 mmol, 1.0 eq), [Ir(dF(CF_3)ppy)$_2$(dtbpy)]PF_6 (2.8 mg, 0.002 mmol, 0.010 eq), quinuclidine (3.0 mg, 0.027 mmol, 0.11 eq), tetrabutylammonium dihydrogenphosphate (22 mg, 0.064 mmol, 0.25 eq) and degassed DMSO (0.5 mL). The reaction mixture was purged with nitrogen for 5 minutes, and phenyl vinyl sulfone (128 mg, 0.76 mmol, 3.0 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was transferred to a separatory funnel and diluted to 10 mL with EtOAc. The organic layer was washed with water (1× 5 mL) and brine (1× 5 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The flash column was then eluted with 1:1 EtOAc/toluene to obtain **10** as an off-white wax (63 mg, 52% yield adjusted for residual solvent). **^{1}H NMR** (400 MHz, Methanol-*d*$_4$) δ 7.94 – 7.88 (m, 2H), 7.75 – 7.68 (m, 1H), 7.66 – 7.60 (m, 2H), 4.62 (d, *J* = 3.8 Hz, 1H, H1), 3.92 (dd, *J* = 11.1, 2.1 Hz, 1H, H6), 3.78 (dd, *J* = 11.2, 5.6 Hz, 1H, H6), 3.63 (ddd, *J* = 10.1, 5.6, 2.1 Hz, 1H, H5), 3.59 – 3.44 (m, 2H, H8), 3.42 – 3.37 (m, 4H, OMe and H2), 3.23 (d, *J* = 10.0 Hz, 1H, H4), 2.20 – 1.93 (m, 2H, H7), 0.90 (s, 9H), 0.07 (s, 6H). **^{13}C NMR** (101 MHz, Methanol-*d*$_4$) δ 140.4, 134.9, 130.5, 129.0, 101.6(C1), 75.7(C3), 71.9(C2), 70.7(C4/C5), 70.7(C4/C5), 64.4(C6), 56.0(OMe), 53.3(C8), 29.8(C7), 26.4, 19.2, -5.1, -5.1. **HRMS (ESI+)** Calcd. for $C_{21}H_{36}O_8SSiNa$ ([M + Na]$^+$): 499.179, found: 499.179. **Optical rotation**: $[\alpha]_D^{20}$= + 92.5 (*c* = 0.080, CH_3OH)

Method 2: A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl α-D-glucopyranoside (47 mg, 0.24 mmol, 1.0 eq), [Ir(dF(CF_3)ppy)$_2$(dtbpy)]PF_6 (2.9 mg, 0.003 mmol, 0.011 eq), quinuclidine (2.8 mg, 0.025 mmol, 0.11 eq), tetrabutylammonium dihydrogenphosphate (23 mg, 0.067 mmol, 0.28 eq) and degassed DMF (0.5 mL). The reaction mixture was purged with nitrogen for 5 minutes, and phenyl vinyl sulfone (63 mg, 0.38 mmol, 1.6 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. After switching off the light source, TBDMSCl (94 mg, 0.63 mmol, 2.6 eq) and imidazole (69 mg, 1.0 mmol, 4.2 eq) were added, and the solution was stirred at room temperature for 2.5 h. MeOH (0.5 mL) was subsequently added and stirring was continued for an additional 5 min. The reaction mixture was transferred to a separatory funnel and diluted with 9 mL EtOAc. The organic layer was washed with water (2× 5 mL) and brine (1× 5 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo and loaded onto a silica column. The flash column was then eluted with 1:1 EtOAc/petroleum ether to obtain **10** as an off-white wax (62 mg, 54% yield). **^{1}H NMR** (400 MHz, Methanol-*d*$_4$) δ 7.91 – 7.82 (m, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 2H), 4.63 (d, *J* = 3.8 Hz, 1H, H1), 3.87 (dd, *J* = 11.1, 2.7 Hz, 1H, H6), 3.77 (dd, *J* = 11.1, 5.4 Hz, 1H, H6), 3.61 – 3.41 (m, 3H, H5 and H8), 3.39 (s, 3H, OMe), 3.36 (d, *J* = 3.9 Hz, 1H, H2), 3.21 (d, *J* = 9.9 Hz, 1H, H4), 2.13 (td, *J* = 12.8, 12.1, 4.8 Hz, 1H, H7), 2.00 (td, *J* = 13.5, 12.7, 5.1 Hz, 1H, H7), 0.86 (s, 9H), 0.04 (s, 6H). **^{13}C NMR** (101 MHz, Methanol-*d*$_4$) δ 139.1, 134.1, 129.6, 128.2, 100.4(C1), 74.7(C3), 71.0(C2), 70.3(C4), 69.5(C5), 63.7(C6), 55.8(OMe), 52.5(C8), 28.9(C7), 26.1, -5.2, -5.2. **HRMS (ESI+)** Calcd. for $C_{21}H_{36}O_8SSiNa$ ([M + Na]$^+$): 499.179, found: 499.179. The NMR shifts differ from Method 1 due to added $CDCl_3$.

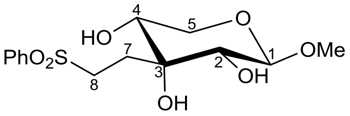


(*2R,3R,4R,5R,6R*)-2-(hydroxymethyl)-6-methoxy-4-(2-(phenylsulfonyl)ethyl)tetrahydro-2H-pyran-3,4,5-triol (10): A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl β-D-glucopyranoside (97 mg, 0.50 mmol, 2.0 eq), [Ir(dF(CF_3)ppy)$_2$(dtbpy)]PF_6 (3.1 mg, 0.003 mmol, 0.011 eq), quinuclidine (3.0 mg, 0.027 mmol, 0.11 eq), tetrabutylammonium dihydrogenphosphate (23 mg, 0.069 mmol, 0.27 eq) and degassed DMSO (0.5 mL). The reaction mixture was purged with nitrogen for 5 min, and phenyl vinyl sulfone (43 mg, 0.25 mmol, 1 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was then diluted with water (10 mL) and stirred with ~1.0 g Dowex resin for 12 h. The resin was filtered off and washed with water and MeOH (4 mL each×20). The filtrate was then concentrated in vacuo and freeze-dried, and the remaining solid was dissolved in MeOH and coated onto ~0.5 g celite. The resulting celite was loaded onto a silica column. The flash column was then eluted with 8% MeOH in DCM to obtain **9** as an off-white wax (27 mg, 30% yield adjusted for 39 mol% residual solvent). R$_f$ = 0.3 (8% MeOH in DCM); visualized with *p*-anisaldehyde stain. **^{1}H NMR** (400 MHz, Methanol-*d*$_4$) δ 8.00 – 7.87 (m, 2H), 7.76 – 7.66 (m, 1H), 7.64 (dd, *J* = 8.3, 6.9 Hz, 3H), 4.43 (d, *J* = 7.7 Hz, 1H, H1), 3.81 (dd, *J* = 11.5, 2.0 Hz, 1H, H6), 3.69 – 3.56 (m, 2H, H6 and H5), 3.52 – 3.41 (m, 5H, H8 and OMe), 3.26 (d, *J* = 9.3 Hz, 1H, H4), 3.07 (d, *J* = 7.7 Hz, 1H, H2), 2.11 (dtt, *J* = 13.0, 10.3, 6.7 Hz, 2H, H7). **^{13}C NMR** (101 MHz, Methanol-*d*$_4$) δ 140.5, 134.9, 130.5, 129.1, 103.4(C1), 76.0(C5), 75.3(C3), 74.1(C2), 70.6(C4), 63.1(C6), 57.2(OMe), 53.1(C8), 29.8(C7). **HRMS (ESI+)** Calcd. for $C_{15}H_{22}O_8SNa$ ([M + Na]$^+$): 385.093, found: 385.093.



(*2S,3R,4R,5R*)-2-methoxy-4-(2-(phenylsulfonyl)ethyl)tetrahydro-2H-pyran-3,4,5-triol (11): A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl α-D-xylopyranoside (42 mg, 0.25 mmol, 1.0 eq), [Ir(dF(CF_3)ppy)$_2$(dtbpy)]PF_6 (2.8 mg, 0.003 mmol, 0.010 eq), quinuclidine (3.2 mg, 0.029 mmol, 0.11 eq), tetrabutylammonium dihydrogenphosphate (22 mg, 0.065 mmol, 0.26 eq) and degassed DMSO (0.5 mL). The whole reaction mixture was purged with nitrogen for 5 min, and phenyl vinyl sulfone (67 mg, 0.40 mmol, 1.6 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was then diluted with MeOH (12 mL) water (32 mL) and stirred with Dowex resin for 12 h. The resin was filtered off and washed with water and MeOH (4 mL each × 20). The filtrate was then concentrated in vacuo and freeze-dried, and the remaining solid was dissolved in MeOH and coated onto ~0.5 g celite. The resulting celite was loaded onto a silica column. The flash column was then eluted with 5% MeOH in

DCM to obtain **(*2S,3R,4R,5R*)-2-methoxy-4-(2-(phenylsulfonyl)ethyl)tetrahydro-2H-pyran-3,4,5-triol** as an off-white wax (45 mg, 55% yield). R_f = 0.3 (5% MeOH in DCM); visualized with p-anisaldehyde stain. **^{1}H NMR** (400 MHz, Methanol-*d*$_4$) δ 7.96 – 7.86 (m, 2H), 7.76 – 7.68 (m, 1H), 7.68 – 7.59 (m, 2H), 4.56 (d, *J* = 3.8 Hz, 1H, H1), 3.63 – 3.48 (m, 3H, H5a and H7), 3.47 – 3.36 (m, 6H, H2, H4, H5b and OMe), 2.18 – 1.97 (m, 2H, H7). Signals on the right (~1.01) correspond to incomplete exchange and coelution of tetrabutylammonium salt. **^{13}C NMR** (101 MHz, Methanol-*d*$_4$) δ 140.4, 134.9, 130.5, 129.1, 101.6(C1), 75.6(C3), 71.9(C4), 70.4(C2), 59.8(C5), 56.2(OMe), 53.3(C8), 29.6(C7). **HRMS (ESI+)** Calcd. for $C_{14}H_{20}O_7SNa$ ([M + Na]$^+$): 355.082, found: 355.082. **Optical rotation**: $[\alpha]_D^{20}$= + 71.0 (*c* = 0.16, CH_3OH)



(*2R,3R,4R,5R*)-2-methoxy-4-(2-(phenylsulfonyl)ethyl)tetrahydro-2H-pyran-3,4,5-triol (12): A 4 mL vial equipped with a septum and magnetic stir bar was charged with methyl β-D-xylopyranoside (41 mg, 0.25 mmol, 1.0 eq), [Ir(dF(CF$_3$)ppy)$_2$(dtbpy)]PF$_6$ (2.8 mg, 0.002 mmol, 0.010 eq), quinuclidine (2.7 mg, 0.025 mmol, 0.10 eq), tetrabutylammonium dihydrogenphosphate (21 mg, 0.062 mmol, 0.25 eq) and degassed DMSO (0.5 mL). The reaction mixture was purged with nitrogen for 5 minutes, and phenyl vinyl sulfone (63 mg, 0.38 mmol, 1.6 equiv) was added. The septum was subsequently replaced with a normal vial cap and tightly sealed. The reaction was irradiated for 18 h at room temperature. The reaction mixture was then diluted with MeOH (12 mL) water (32 mL) and stirred with Dowex resin for 12 h. The resin was filtered off and washed with water and MeOH (4 mL each×20). The filtrate was then concentrated in vacuo and freeze-dried, and the remaining solid was dissolved in MeOH and coated onto ~0.5 g celite. The resulting celite was loaded onto a silica column. The flash column was then eluted with 5% MeOH in DCM to obtain **(*2S,3R,4R,5R*)-2-methoxy-4-(2-(phenylsulfonyl)ethyl)tetrahydro-2H-pyran-3,4,5-triol** as an off-white wax (45 mg, 55% yield). R_f = 0.3 (5% MeOH in DCM); visualized with p-anisaldehyde stain. ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.92 (dd, *J* = 7.5, 1.8 Hz, 2H), 7.77 – 7.69 (m, 1H), 7.64 (dd, *J* = 8.7, 7.0 Hz, 2H), 4.37 (d, *J* = 7.0 Hz, 1H, H1), 3.67 – 3.51 (m, 2H, H5), 3.51 – 3.39 (m, 6H, H4, H8 and OMe), 3.07 (d, *J* = 7.1 Hz, 1H, H2), 2.14 – 2.00 (m, 2H, H8). Signals on the right (~1.01) correspond to incomplete exchange and coelution of tetrabutylammonium salt. ^{13}C NMR (101 MHz, Methanol-*d*$_4$) δ 139.0, 133.5, 129.1, 127.7, 102.4(C1), 73.0(C3), 72.6(C2), 69.3(C4), 63.9(C5), 55.7(OMe), 51.7(C8), 28.4(C7). **HRMS (ESI+)** Calcd. for $C_{14}H_{20}O_7SNa$ ([M + Na]$^+$): 355.082, found: 355.082.

References

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2 E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, 1972, **94**, 6190–6191.

3 V. R. Jumde, N. N. H. M. Eisink, M. D. Witte and A. J. Minnaard, *J. Org. Chem.*, 2016, **81**, 11439–11443.

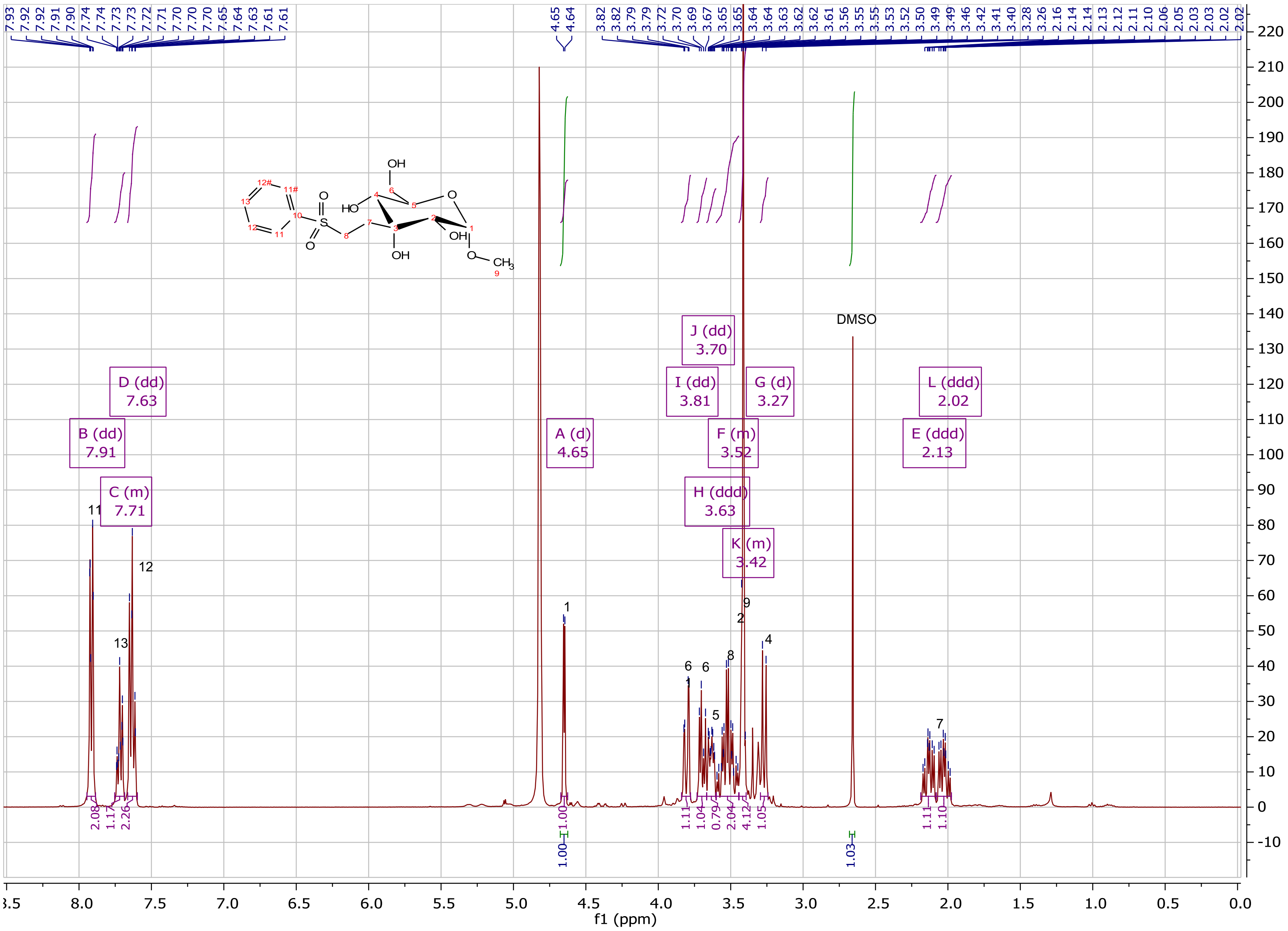

Figure 2 ^{1}H-NMR of **2**, made from **methyl α-D-glucopyranoside 1**

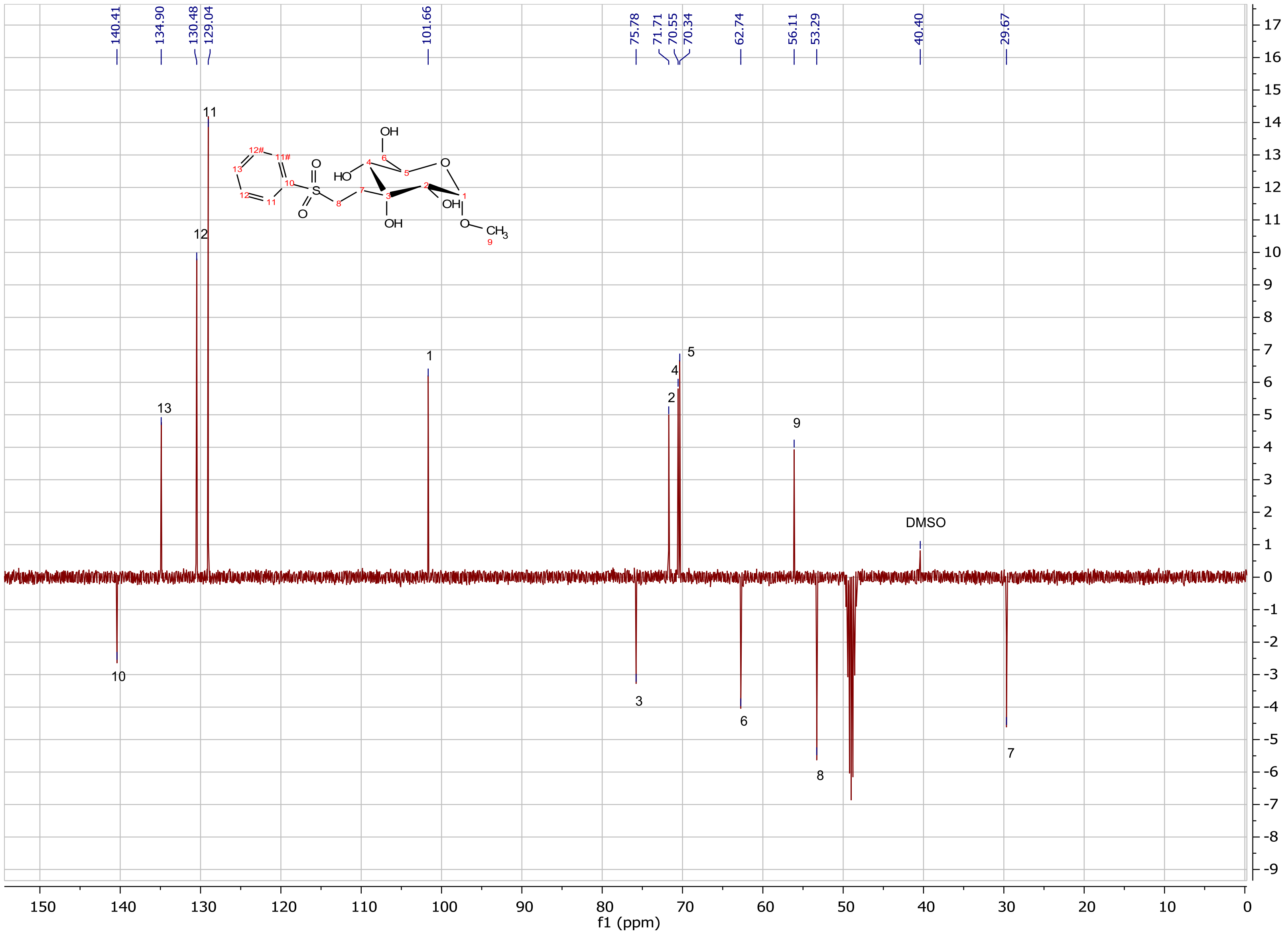

Figure 3 ^{13}C APT-NMR of **2**, made from **methyl α-D-glucopyranoside 1**

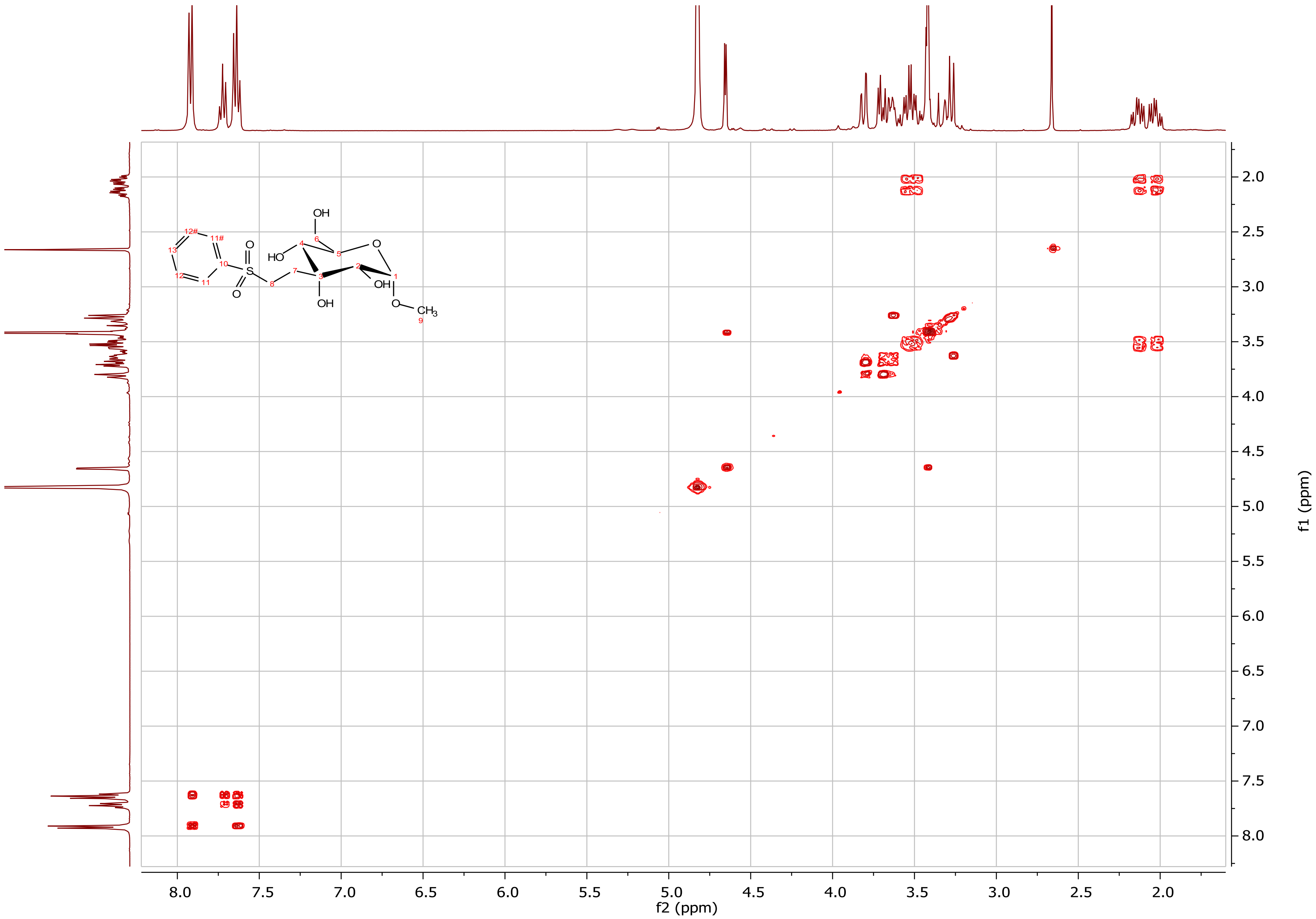

Figure 4 ^{1}H COSY-NMR of **2**, made from **methyl α-D-glucopyranoside 1**

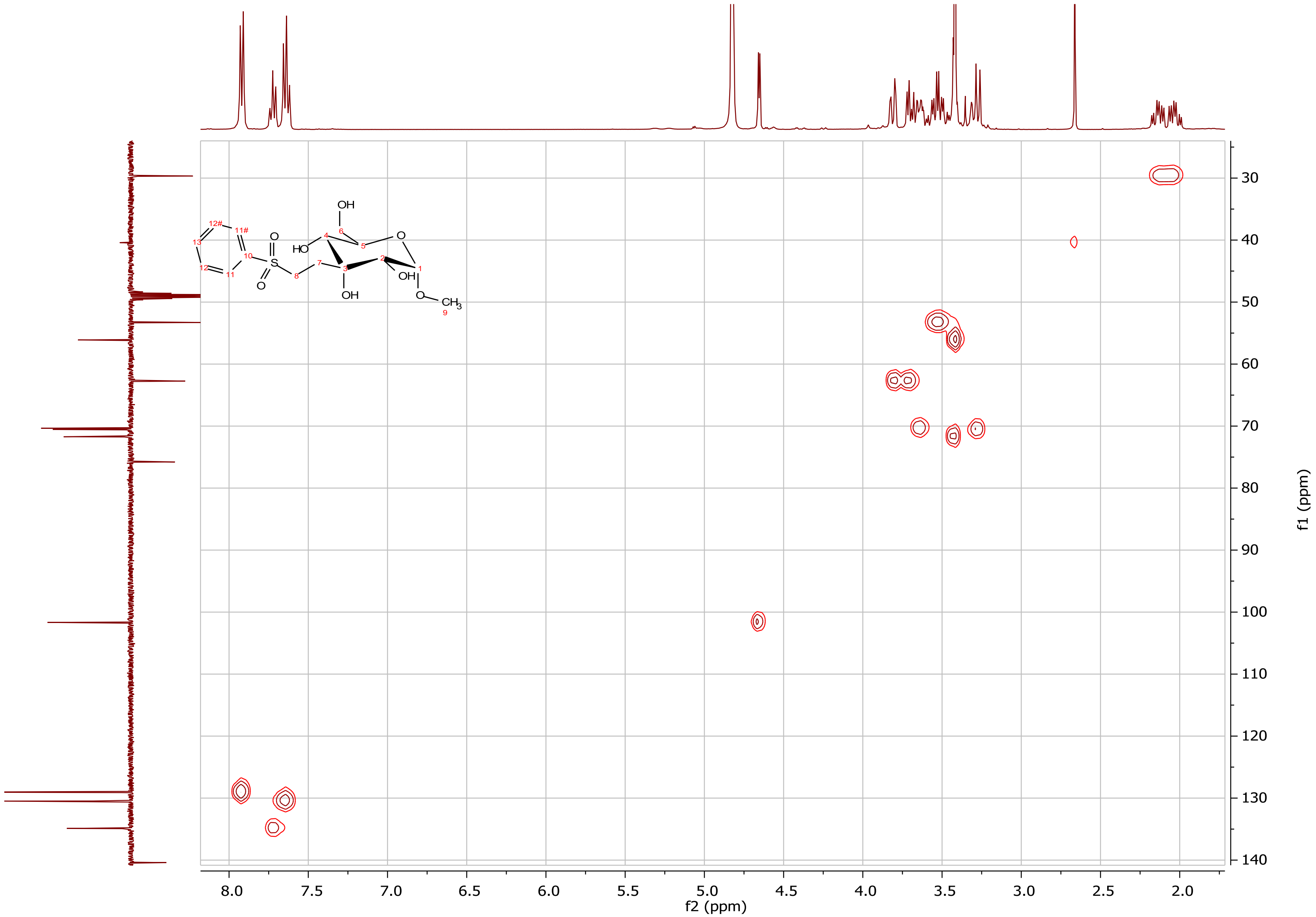

Figure 5 ^{1}H-^{13}C HMQC-NMR of **2**, made from **methyl α-D-glucopyranoside 1**

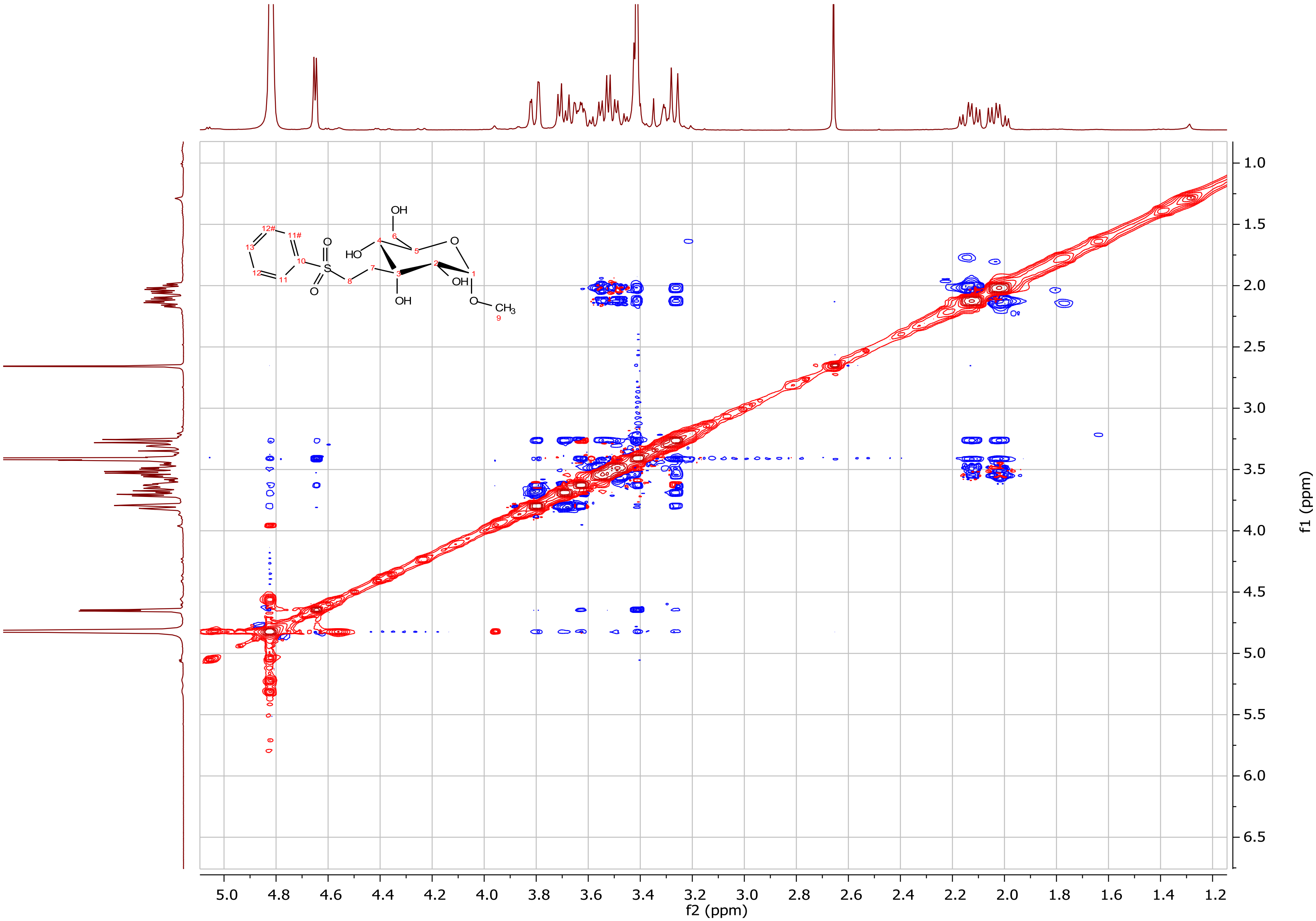

Figure 6 ^{1}H NOESY-NMR of **2**, made from **methyl α-D-glucopyranoside 1**

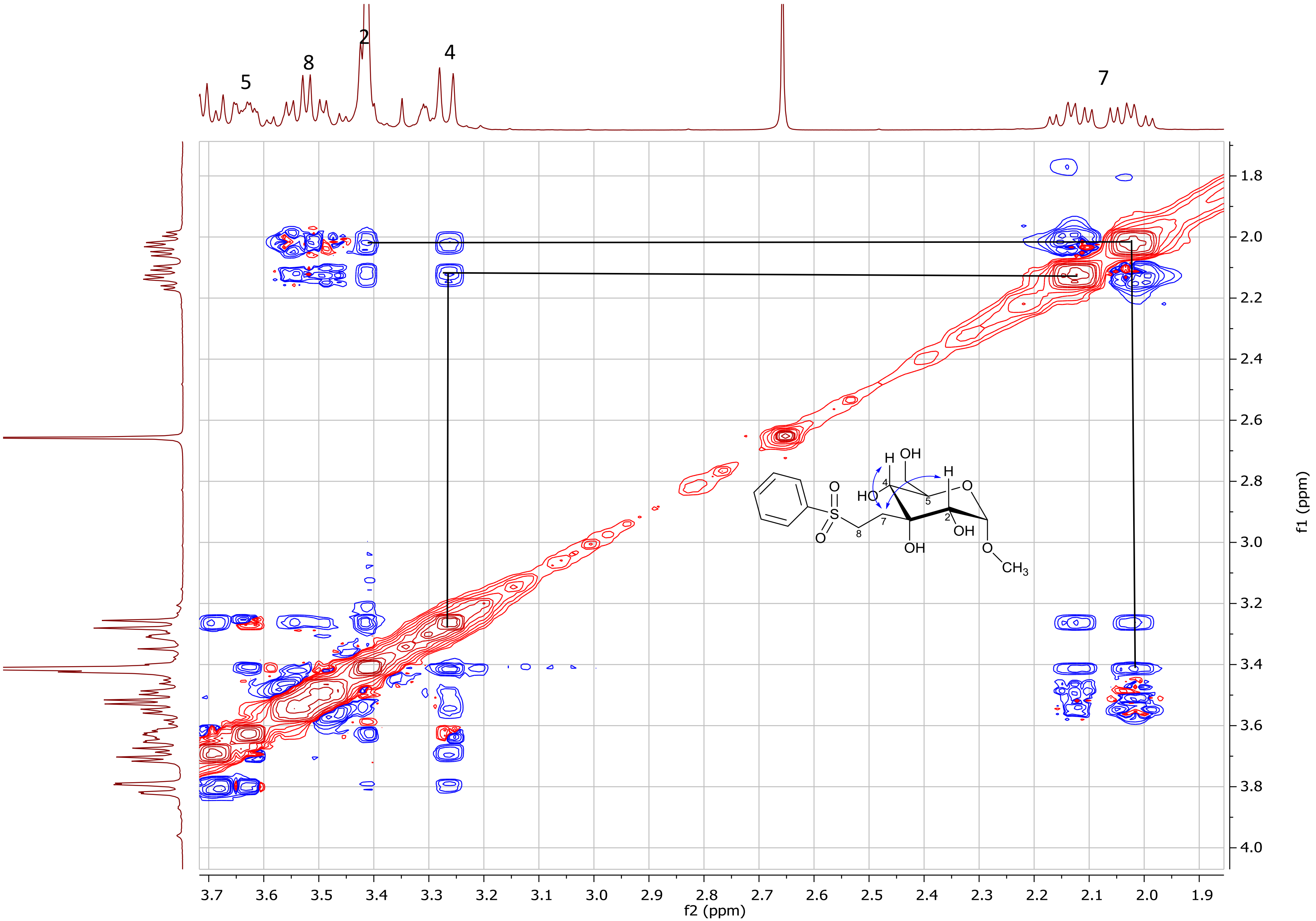

Figure 7 Zoom of ^{1}H NOESY-NMR of **2**, made from **methyl α-D-glucopyranoside 1**

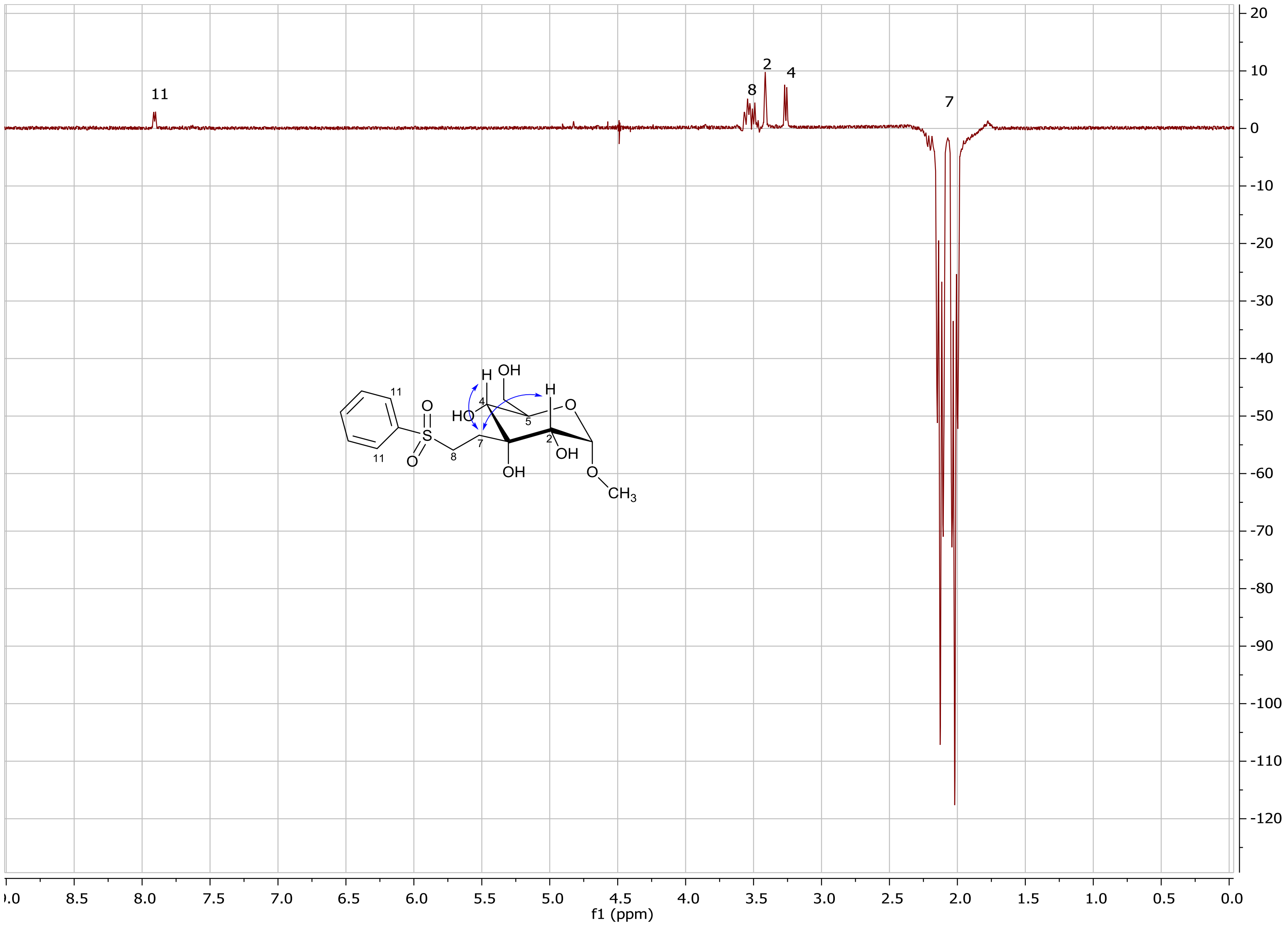

Figure 8 ^{1}H NOE-NMR of **2**, made from **methyl α-D-glucopyranoside 1**. Irradiation at H7.

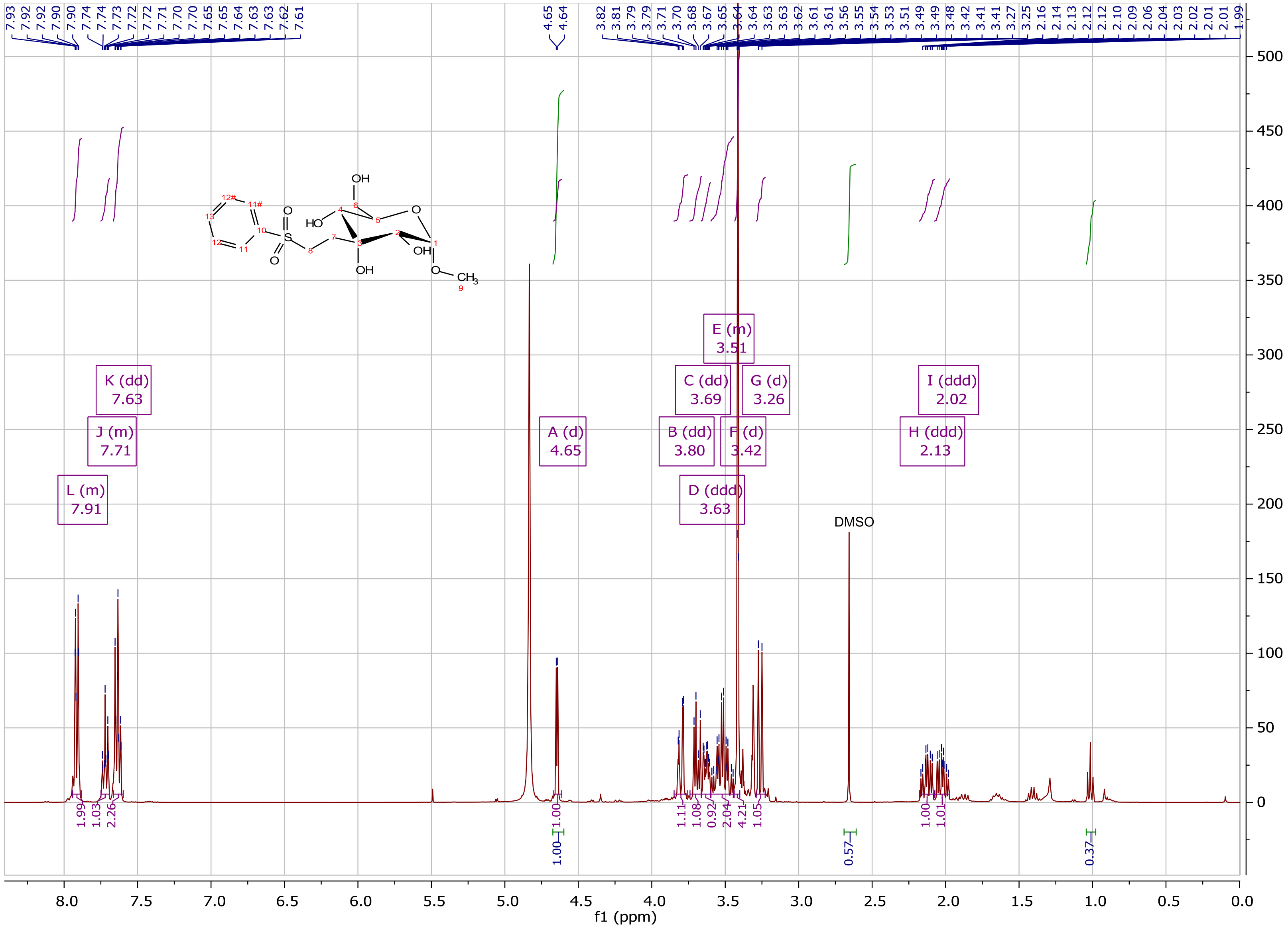

Figure 9 ^{1}H-NMR of **2**, made from **methyl α-D-allopyranoside 7**

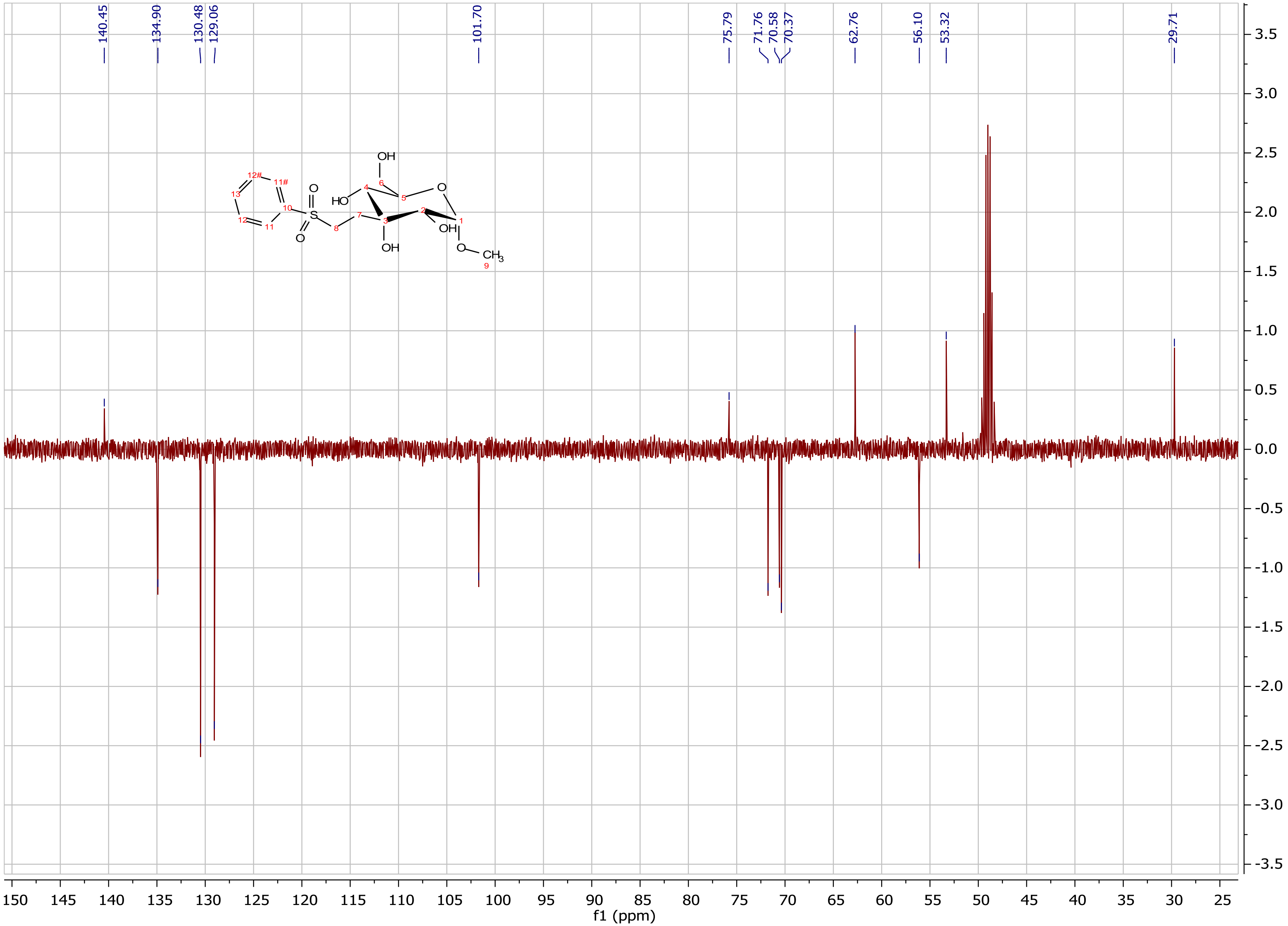

Figure 10 ^{13}C APT-NMR of **2**, made from **methyl α-D-allopyranoside 7**

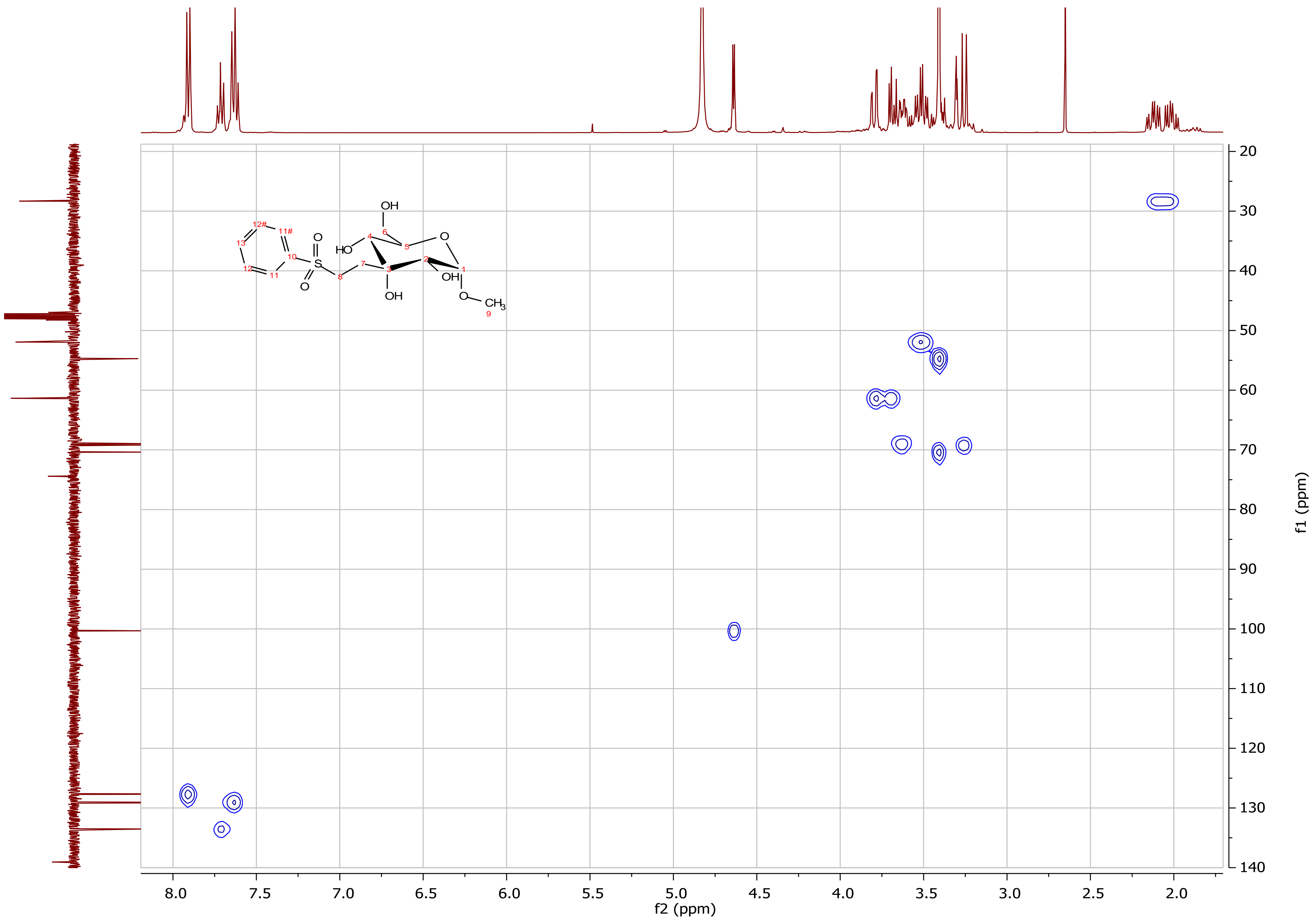

Figure 11 ^{1}H-^{13}C HMQC-NMR of **2**, made from **methyl α-D-allopyranoside 7**

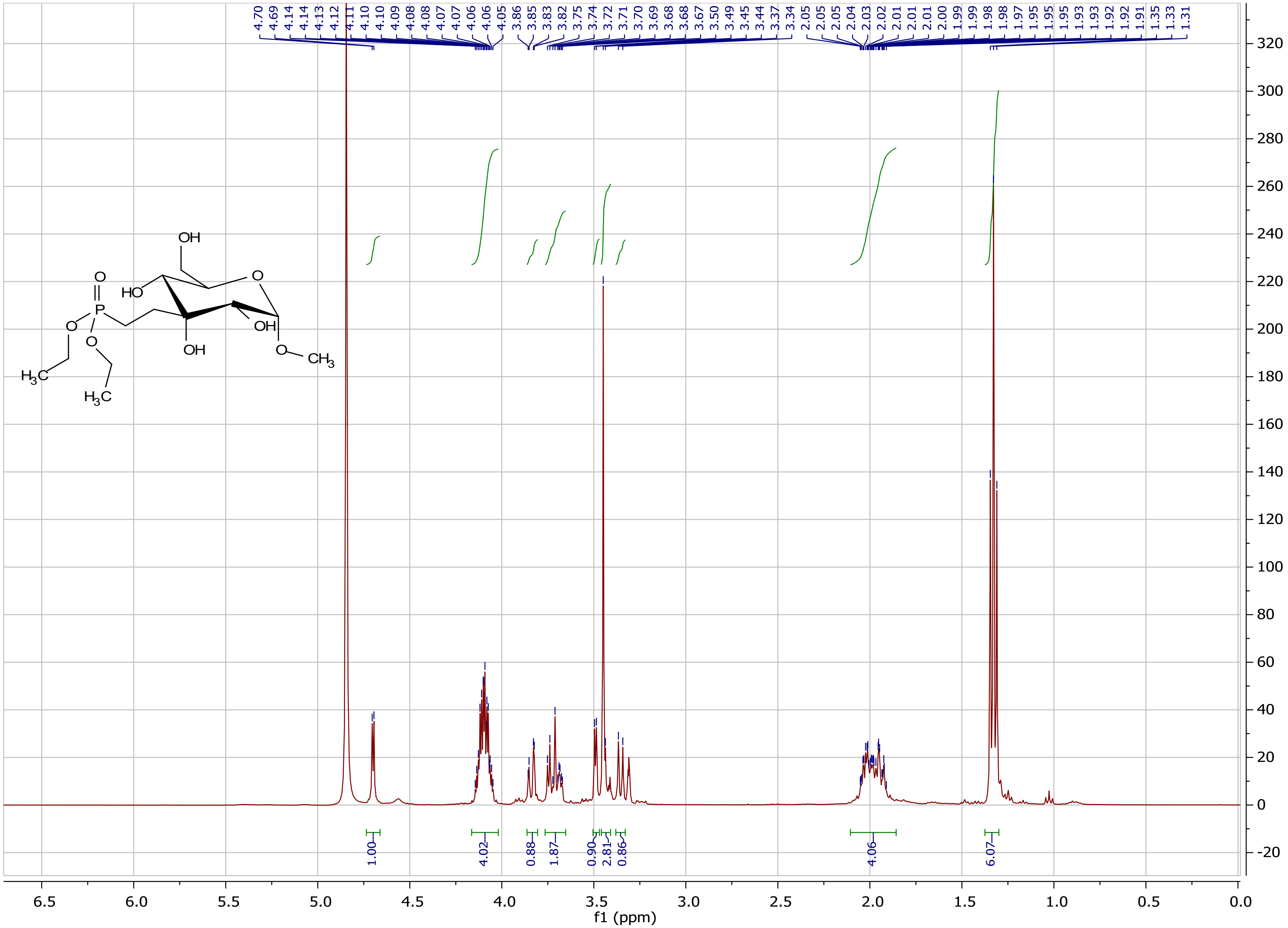

Figure 12 ^{1}H-NMR of **2a**

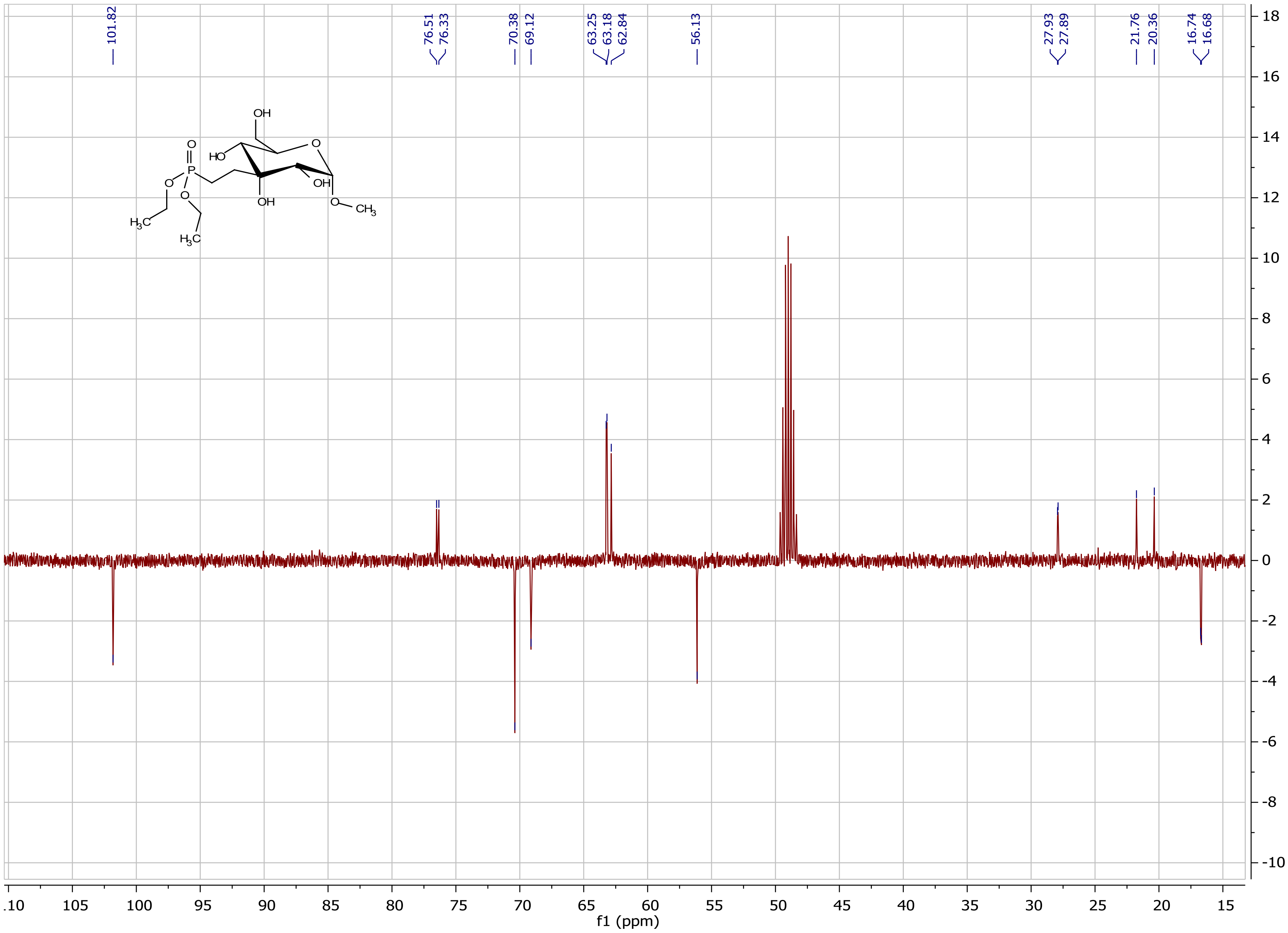

Figure 13 ^{13}C APT-NMR of **2a**

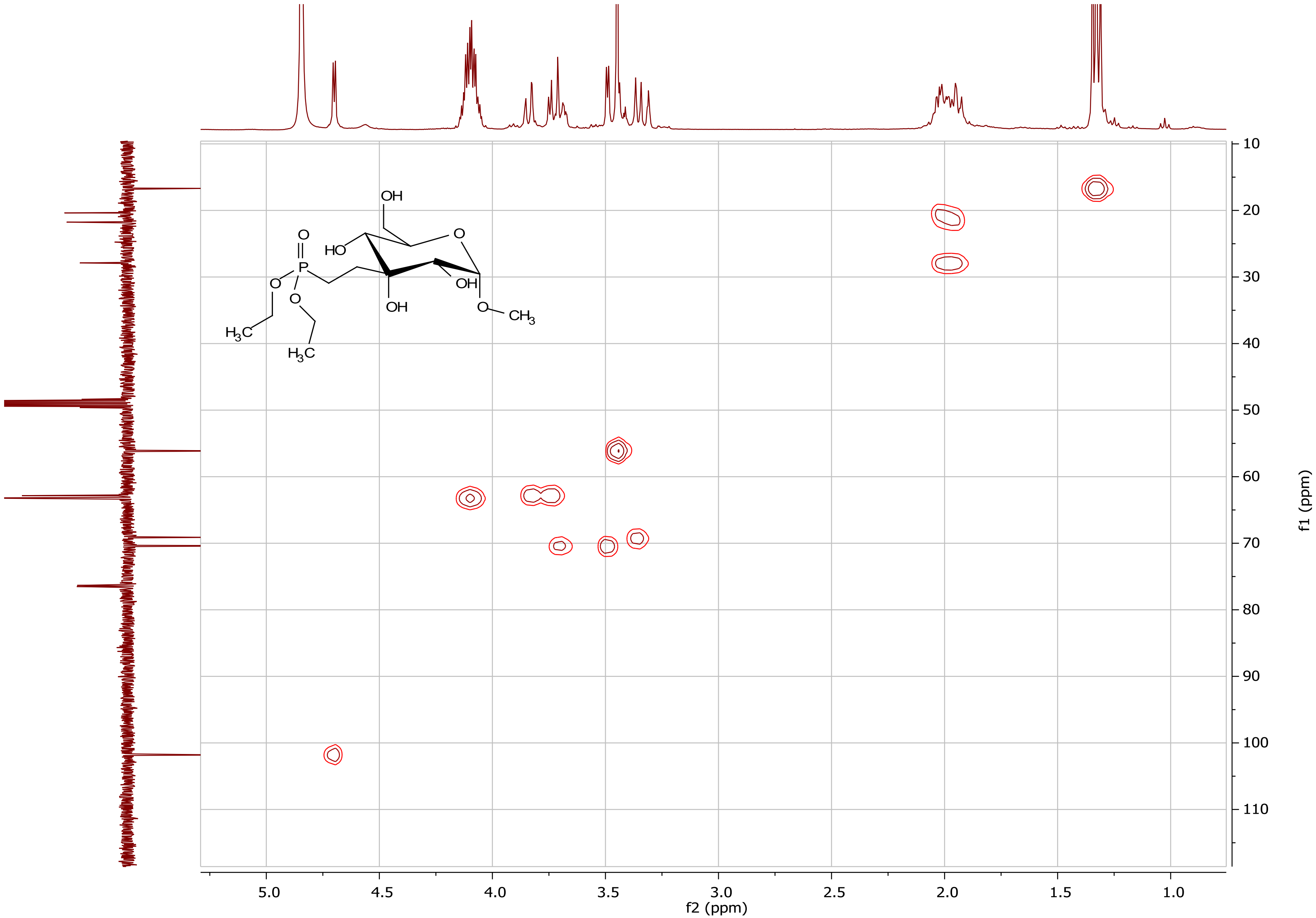

Figure 14 ^{1}H-^{13}C HMQC-NMR of **2a**

Figure 15 ^{31}P-NMR of **2a**

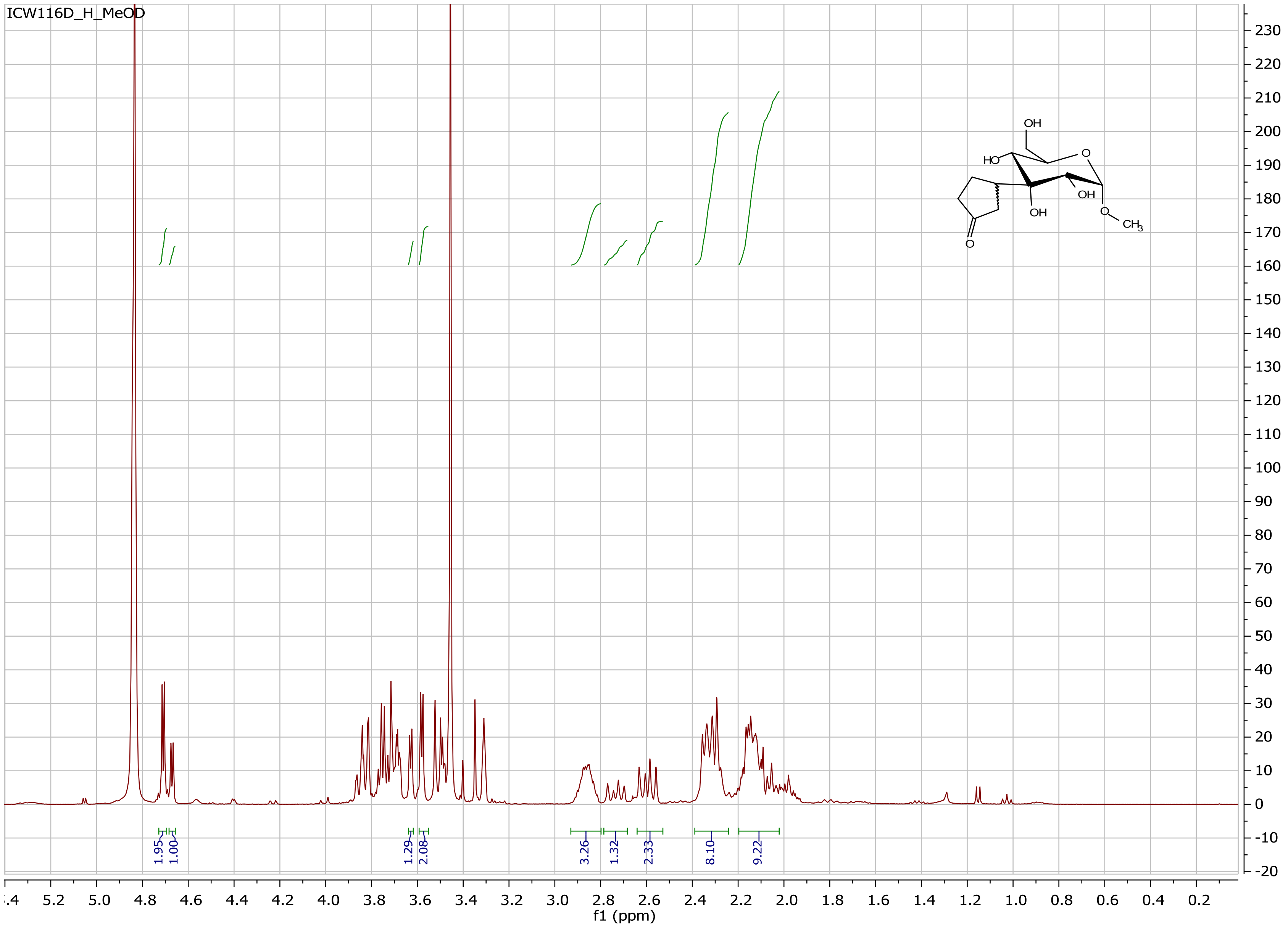

Figure 16 ^{1}H-NMR of **2b**

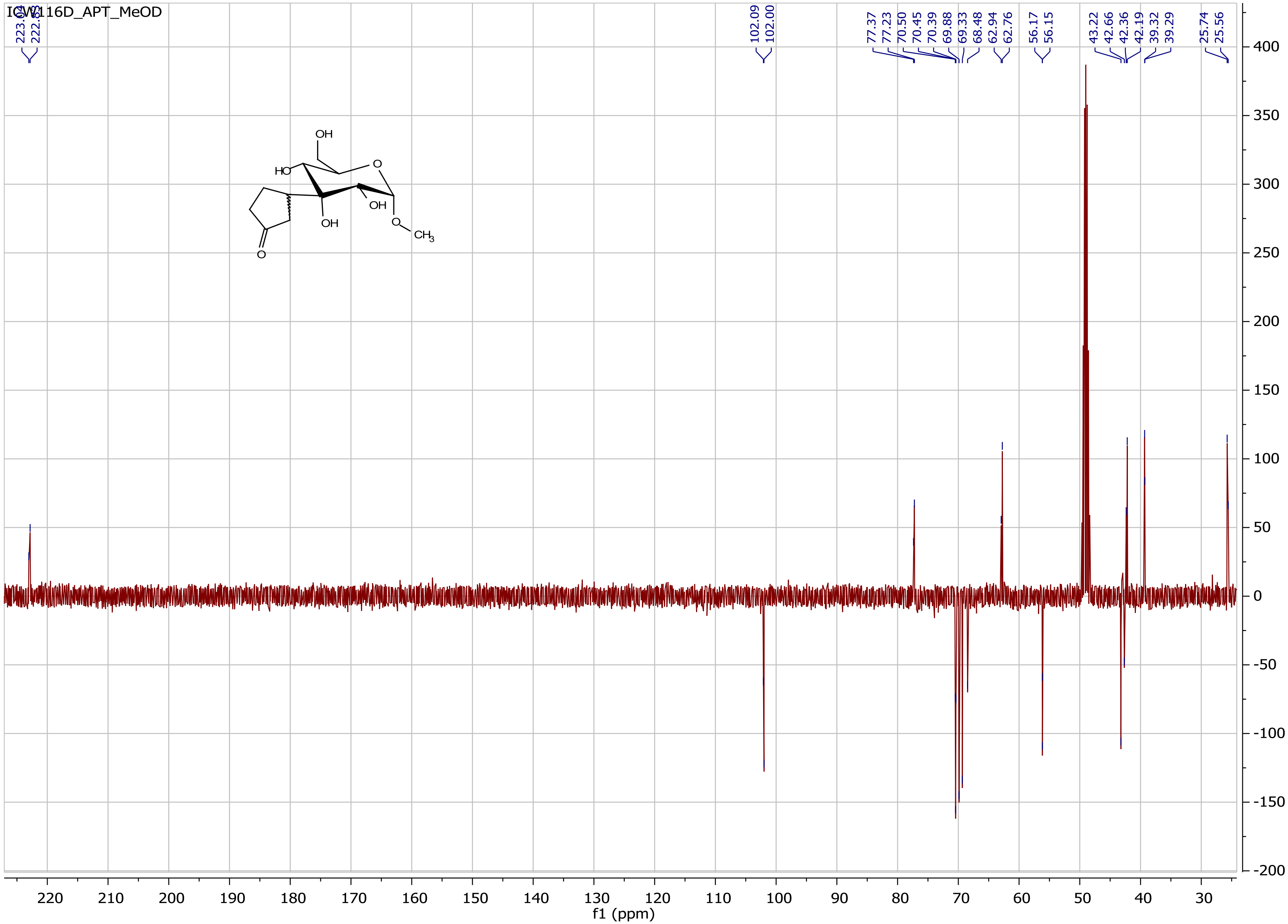

Figure 17 ^{13}C APT-NMR of **2b**

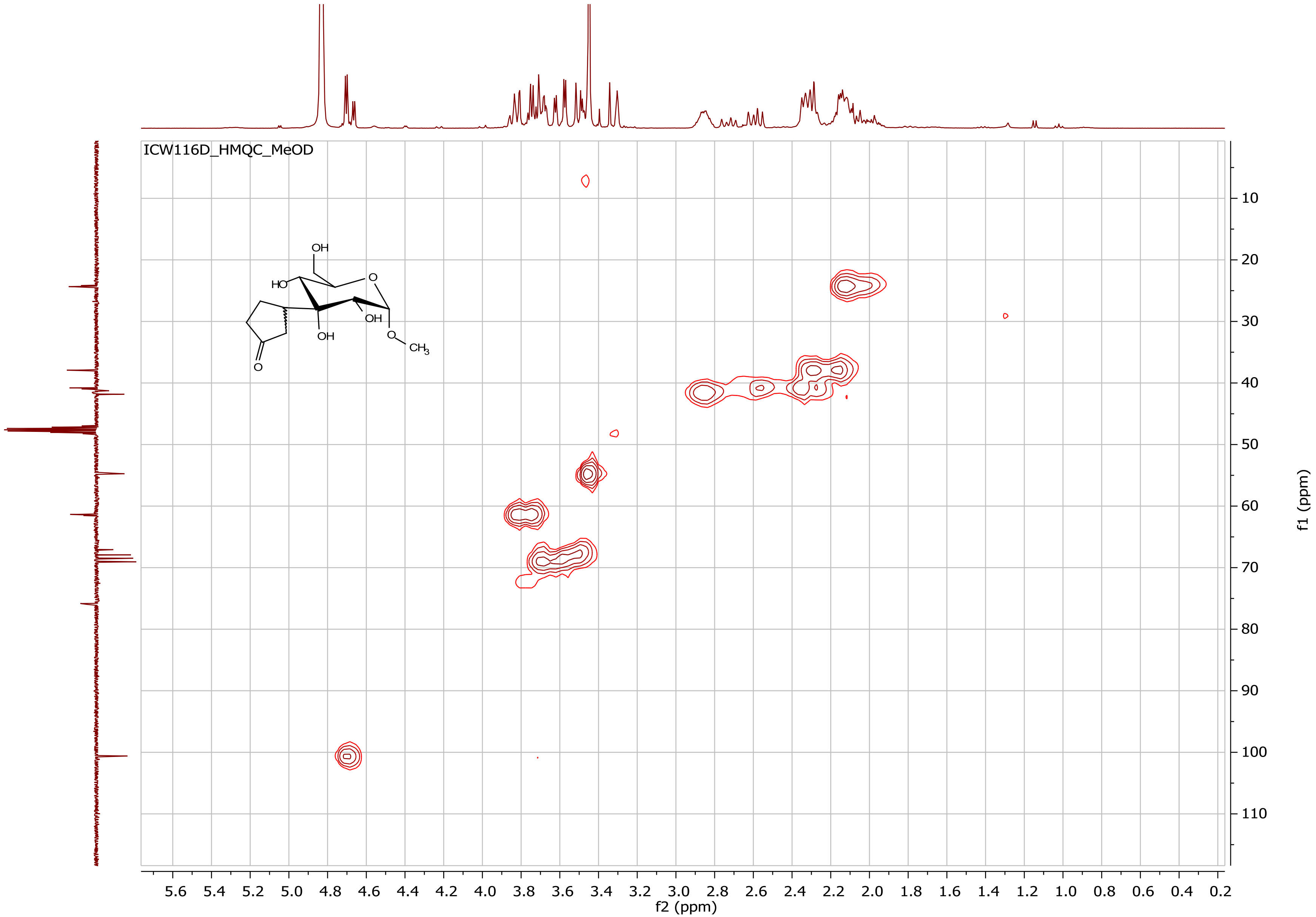

Figure 18 ^{1}H-^{13}C HMQC-NMR of **2b**

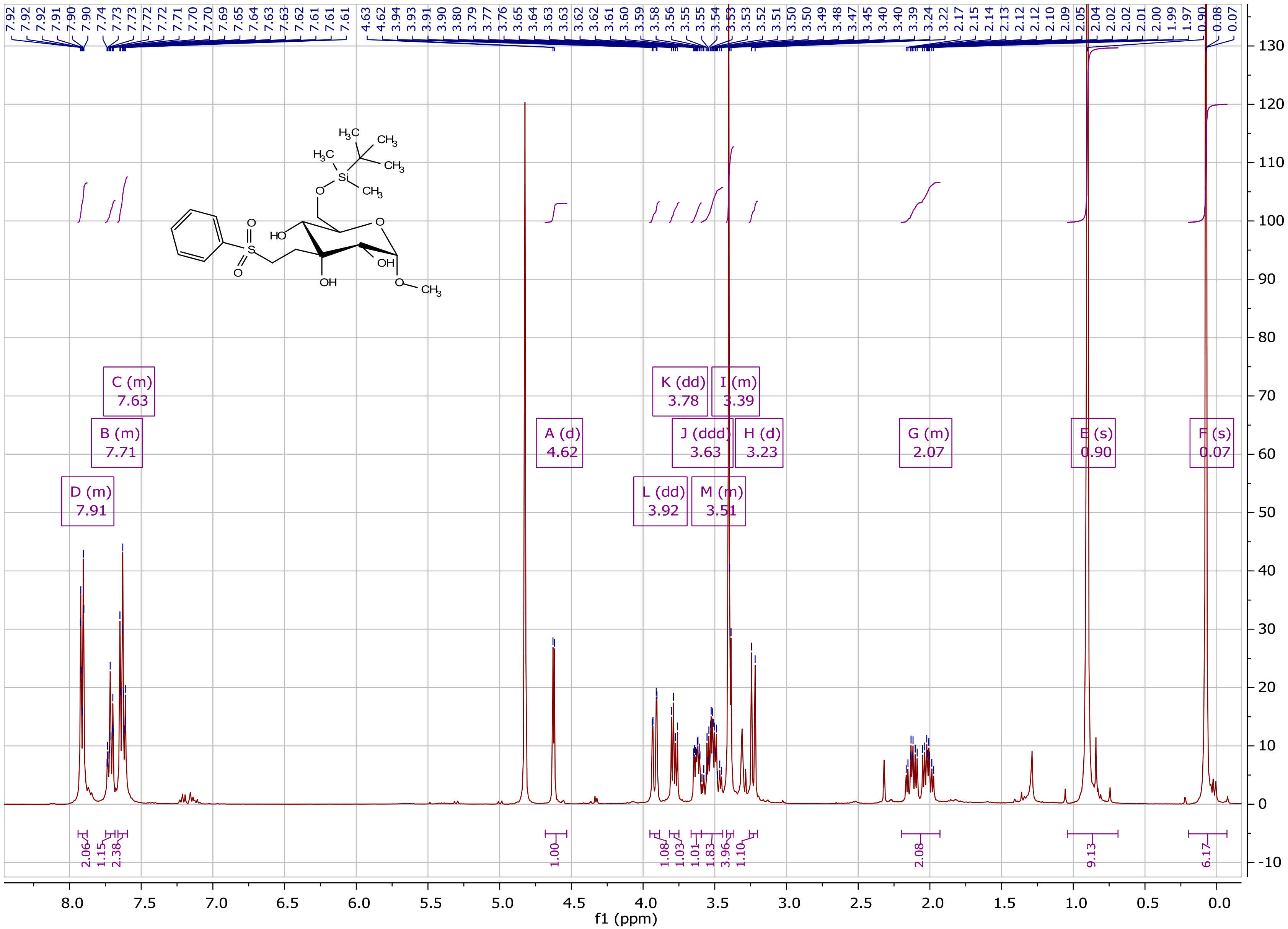

Figure 19 ^{1}H-NMR of **9**, made by method 1

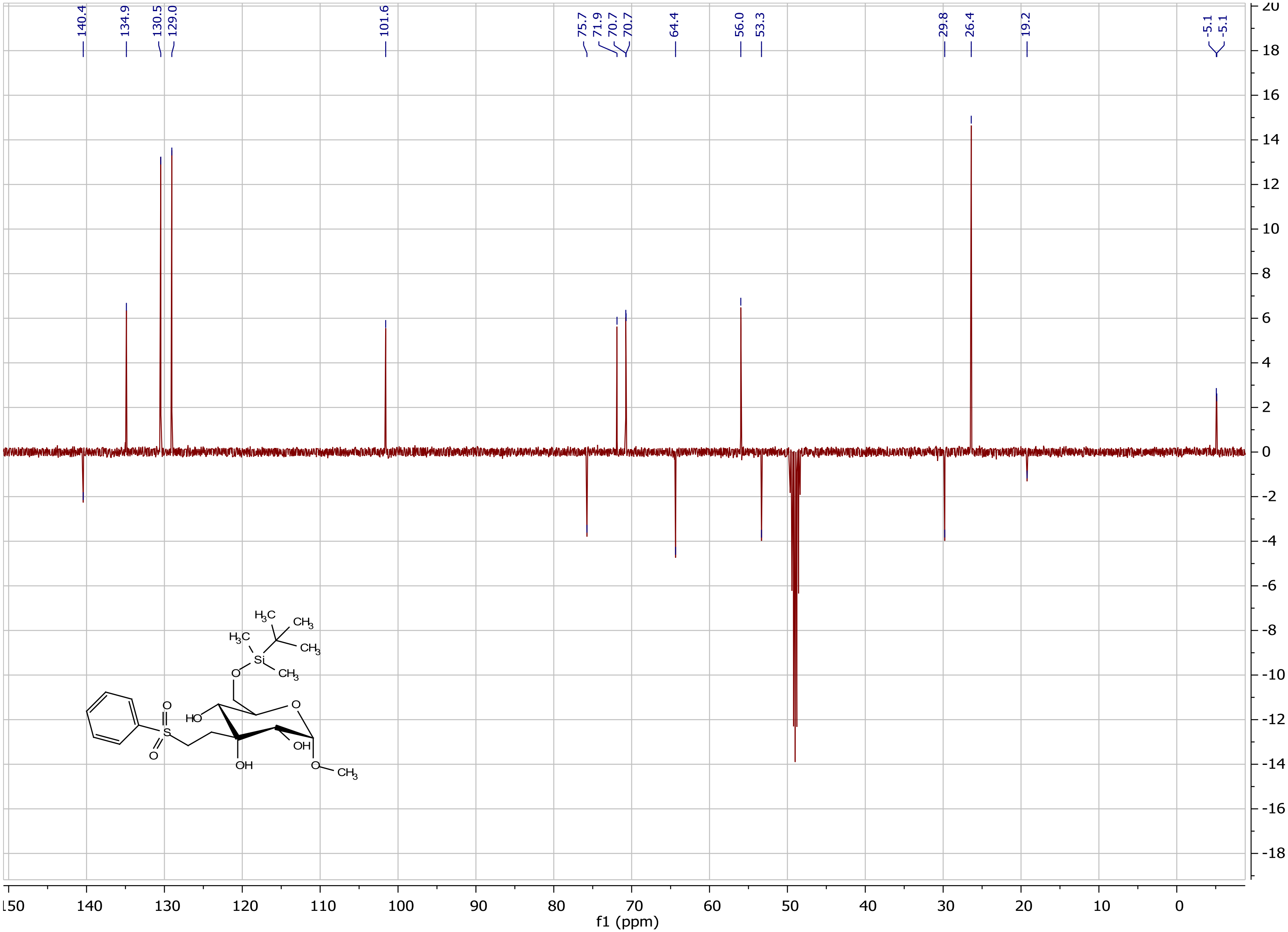

Figure 20 ^{13}C APT-NMR of **9**, made by method 1

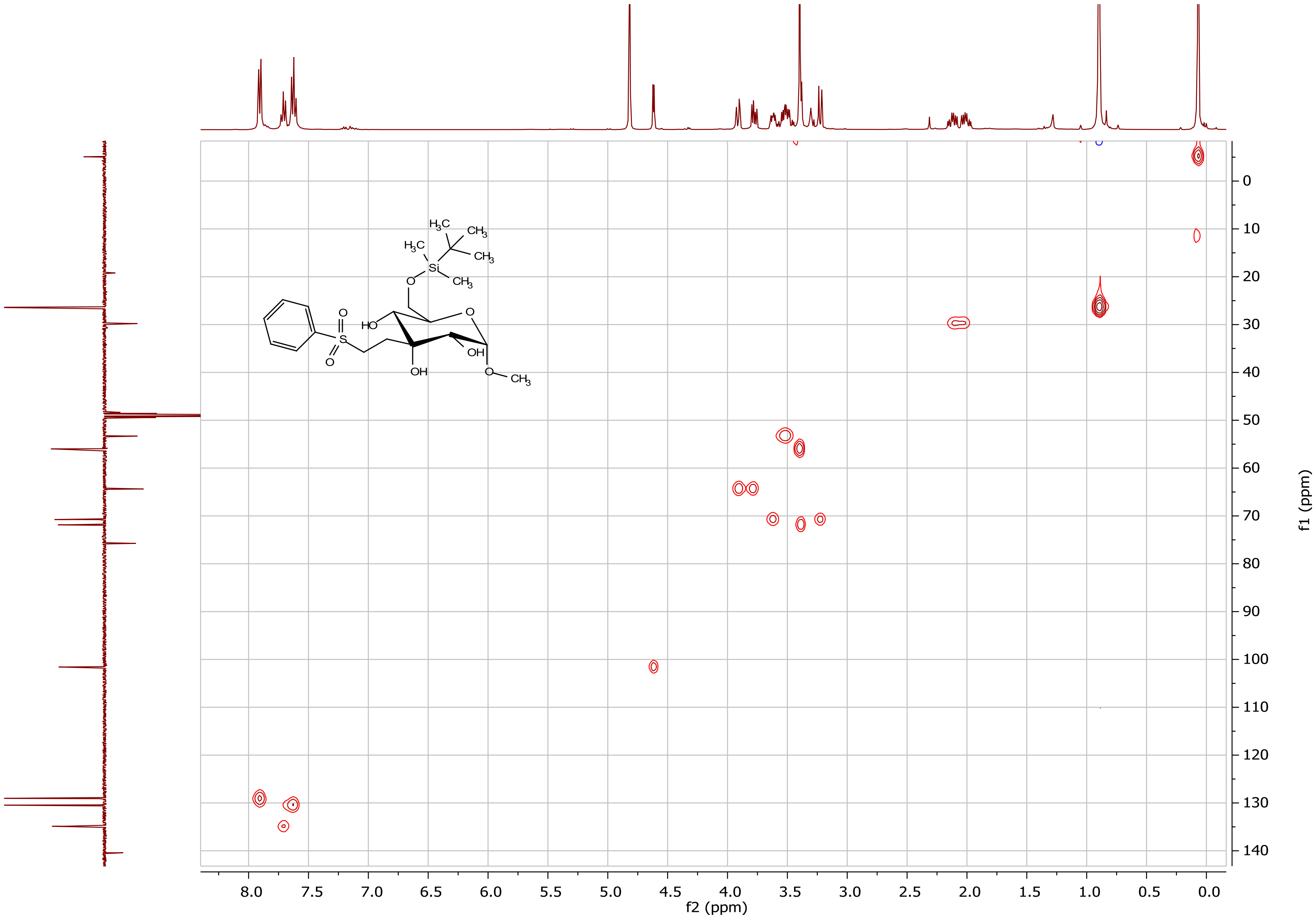

Figure 21 ^{1}H-^{13}C HMQC-NMR of **9**, made by method 1

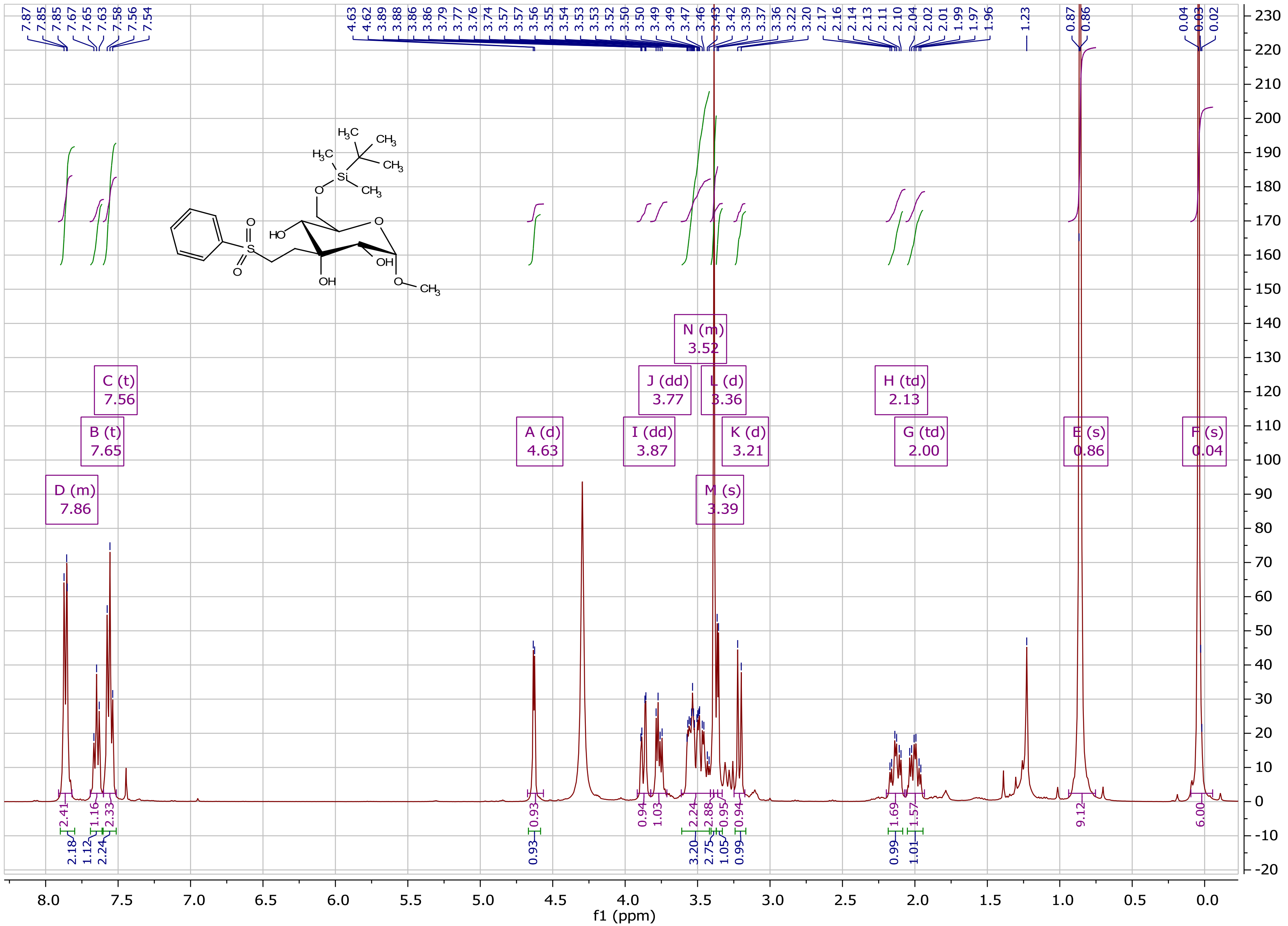

Figure 22 ^{1}H-NMR of **9**, made by method 2

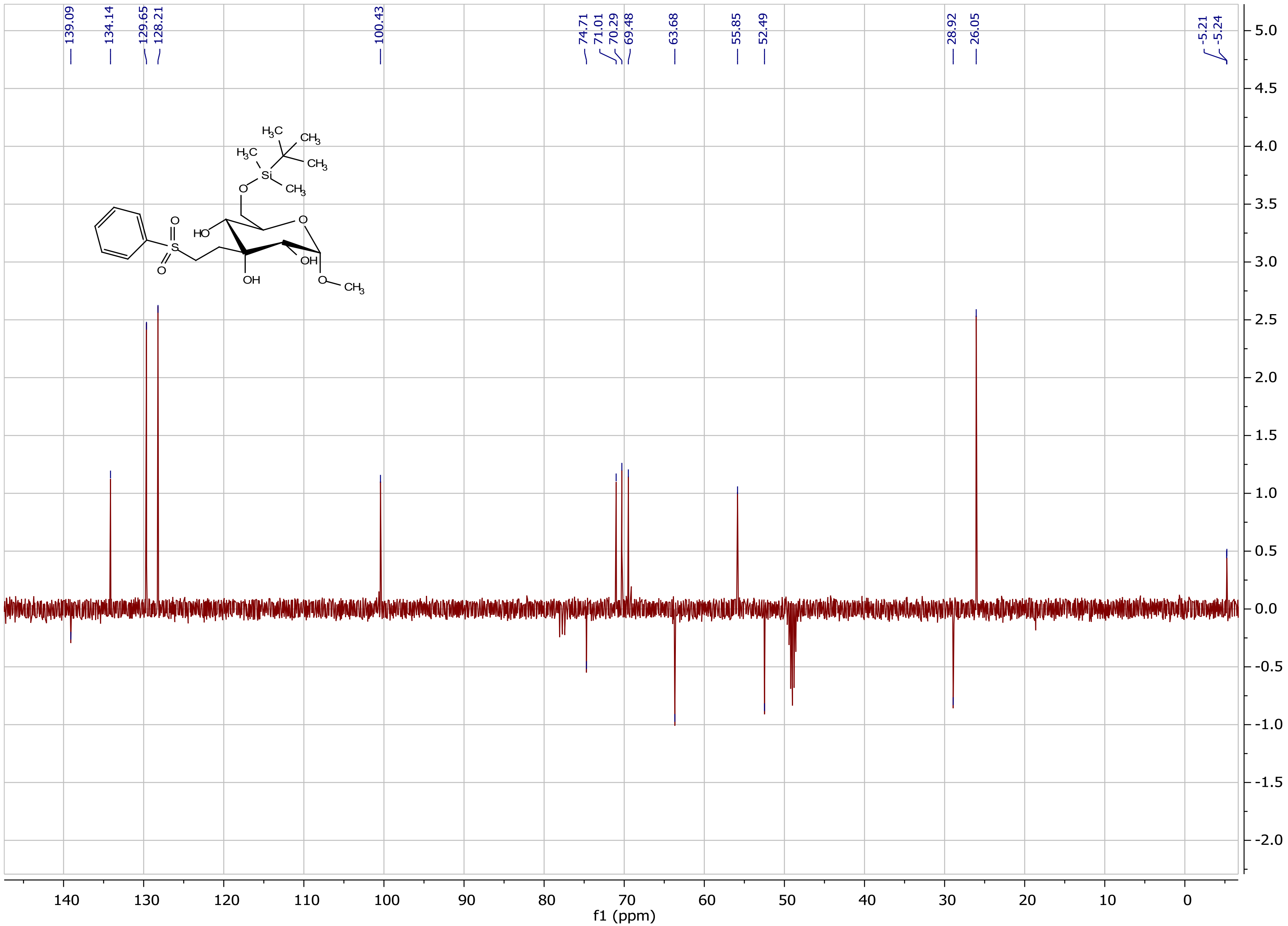

Figure 23 ^{13}C APT-NMR of **9**, made by method 2

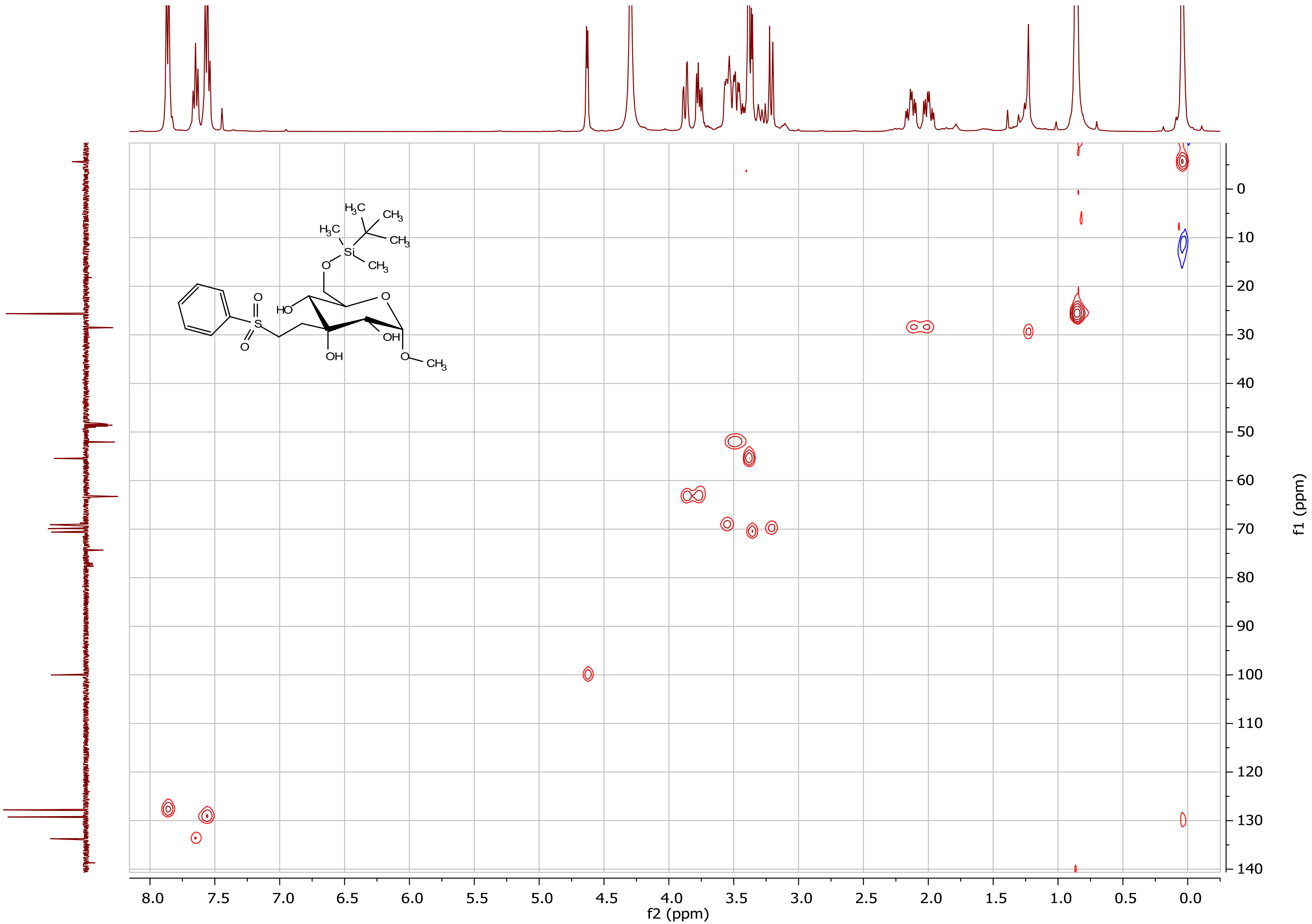

Figure 24 ^{1}H-^{13}C HMQC-NMR of **9**, made by method 2

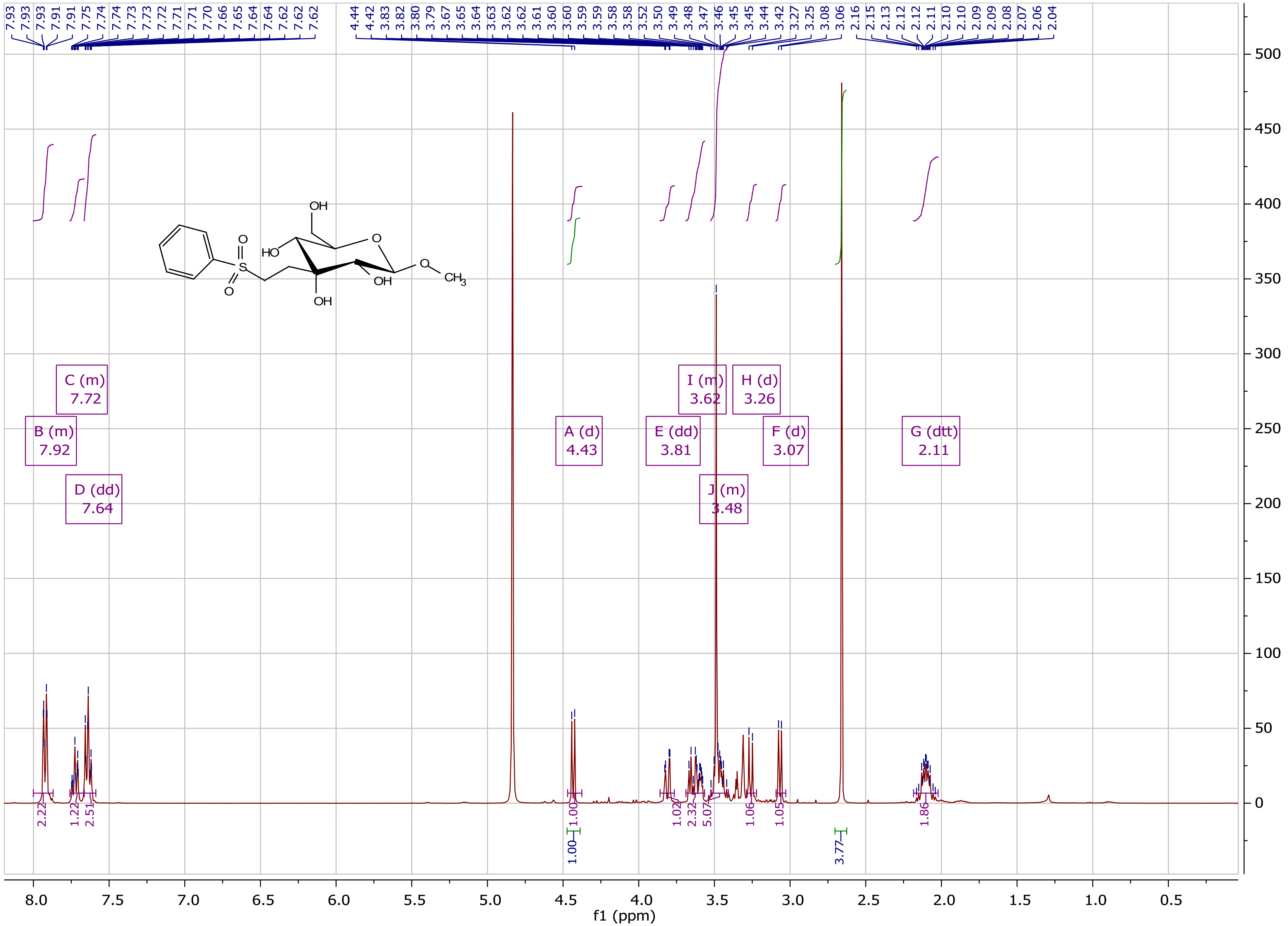

Figure 25 ^{1}H-NMR of **10**

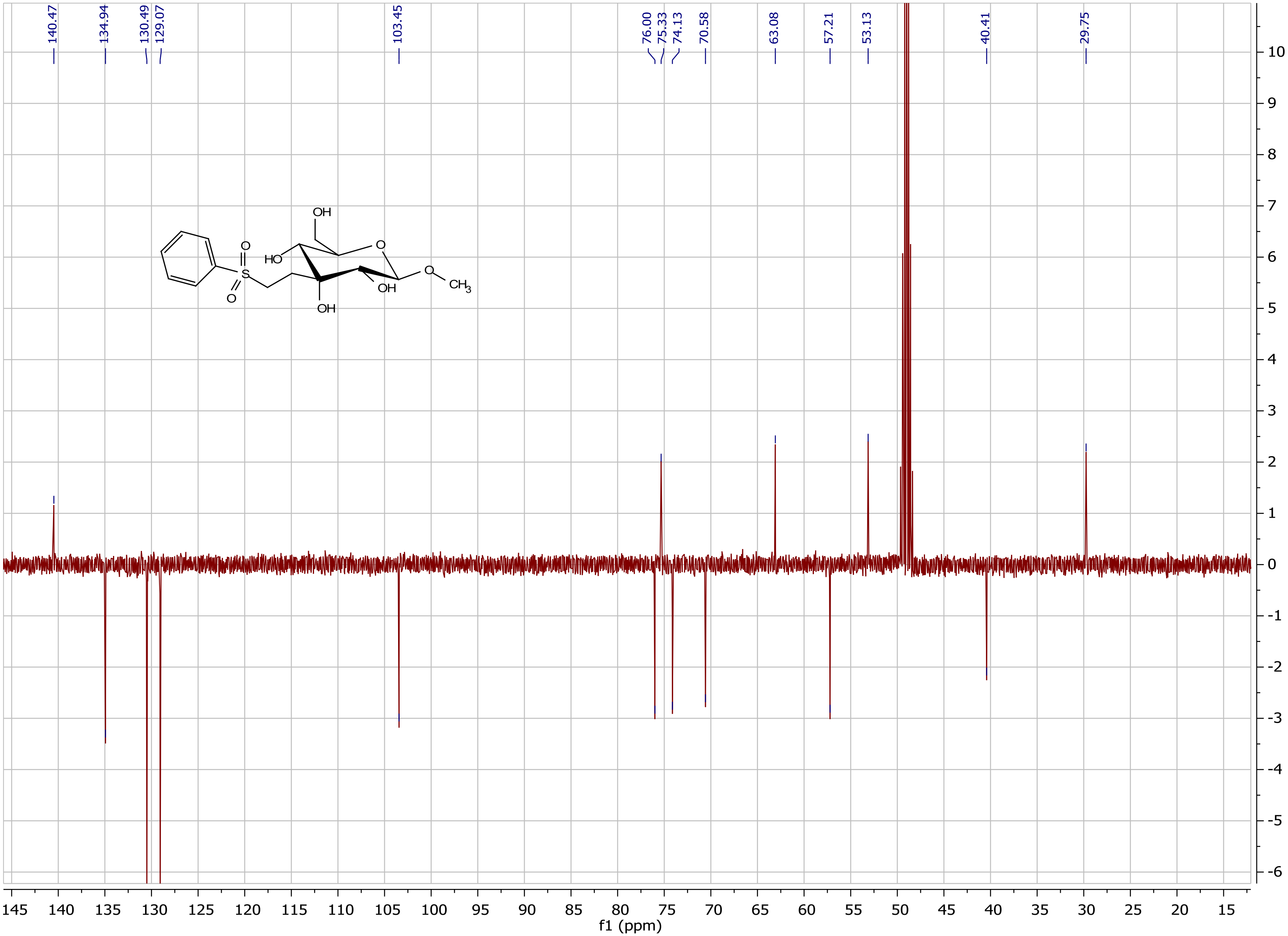

Figure 26 ^{13}C APT-NMR of **10**

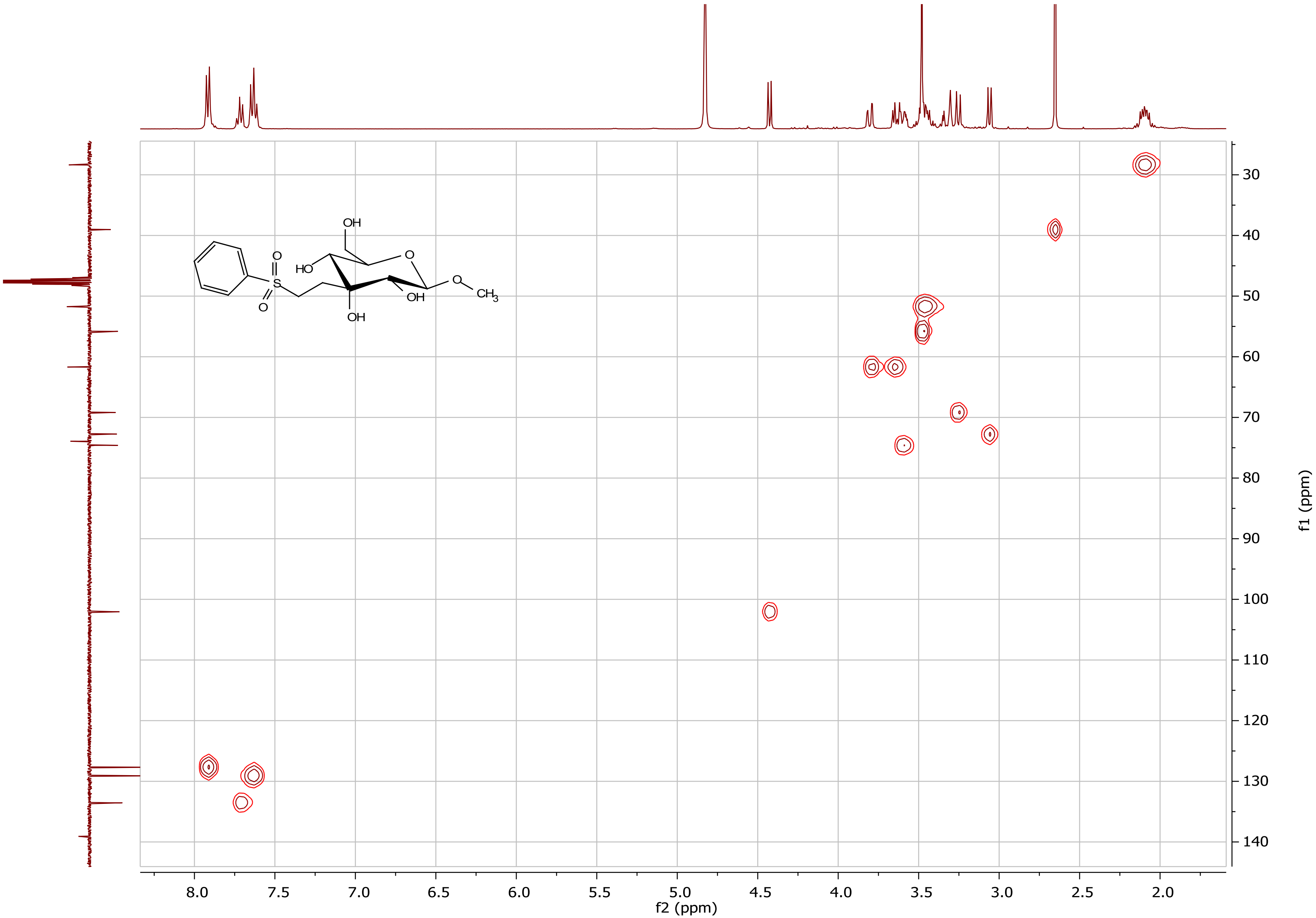

Figure 27 ^{1}H-^{13}C HMQC-NMR of **10**

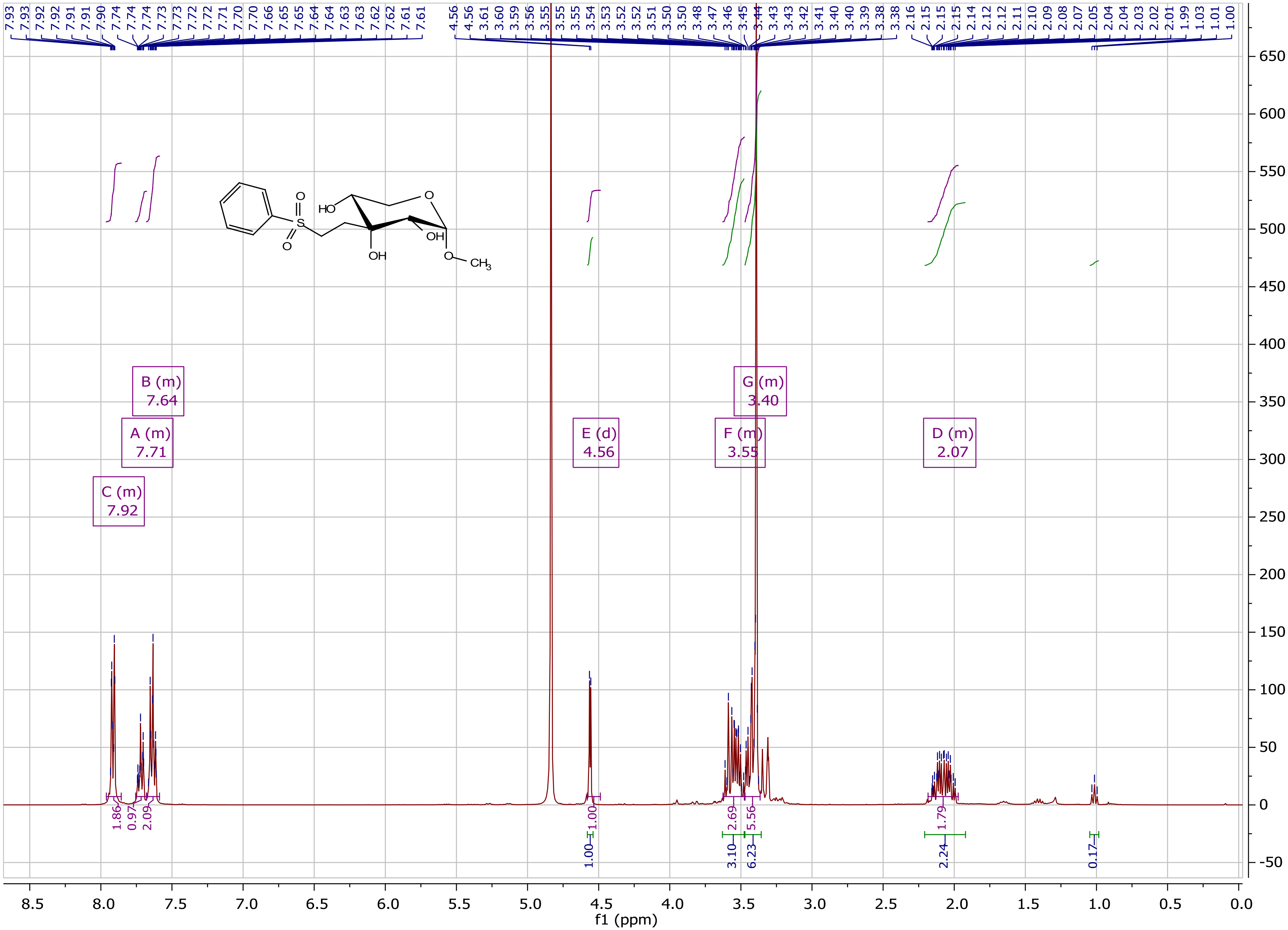

Figure 28 ^{1}H-NMR of **11**

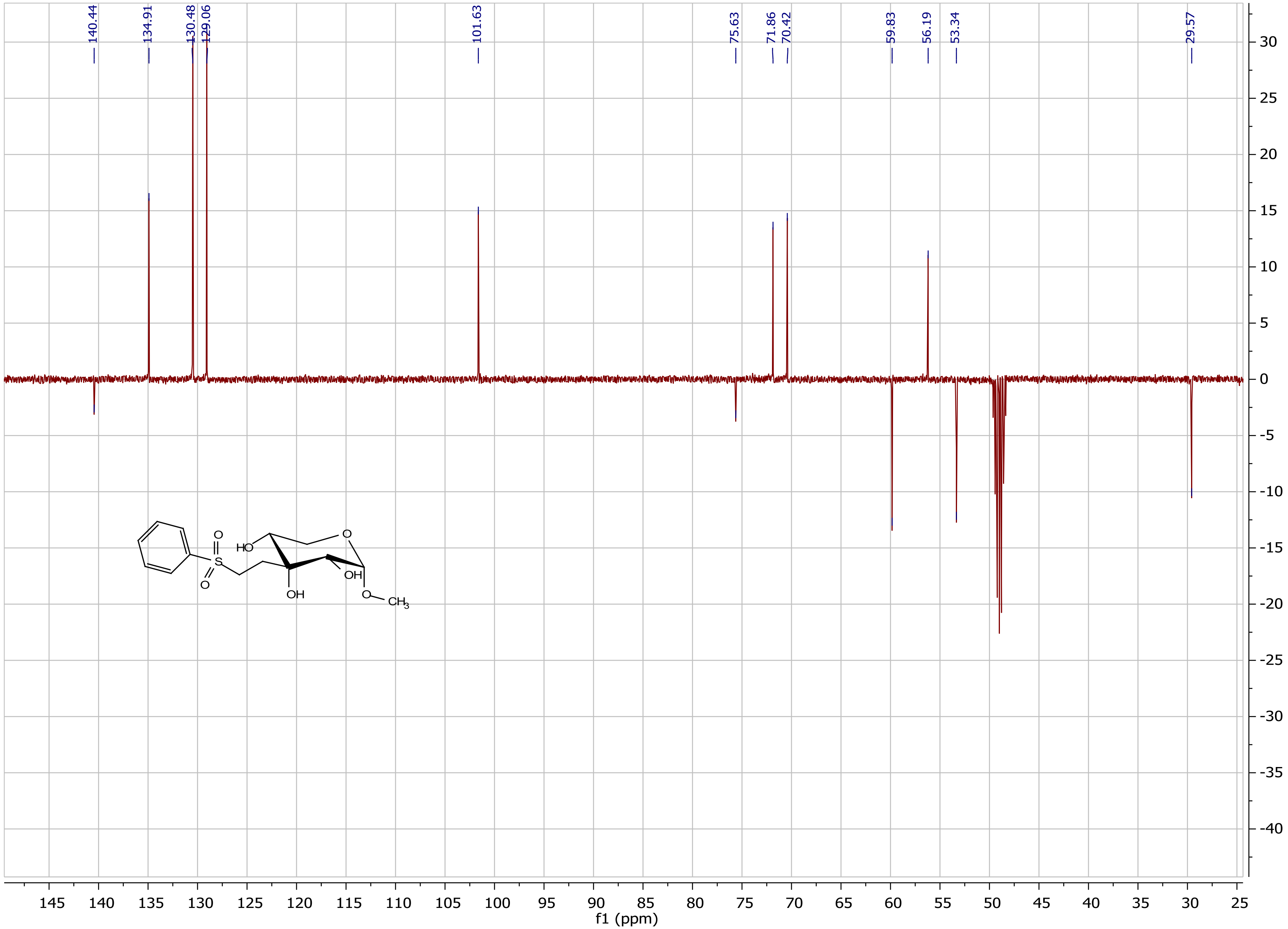

Figure 29 ^{13}C APT-NMR of **11**

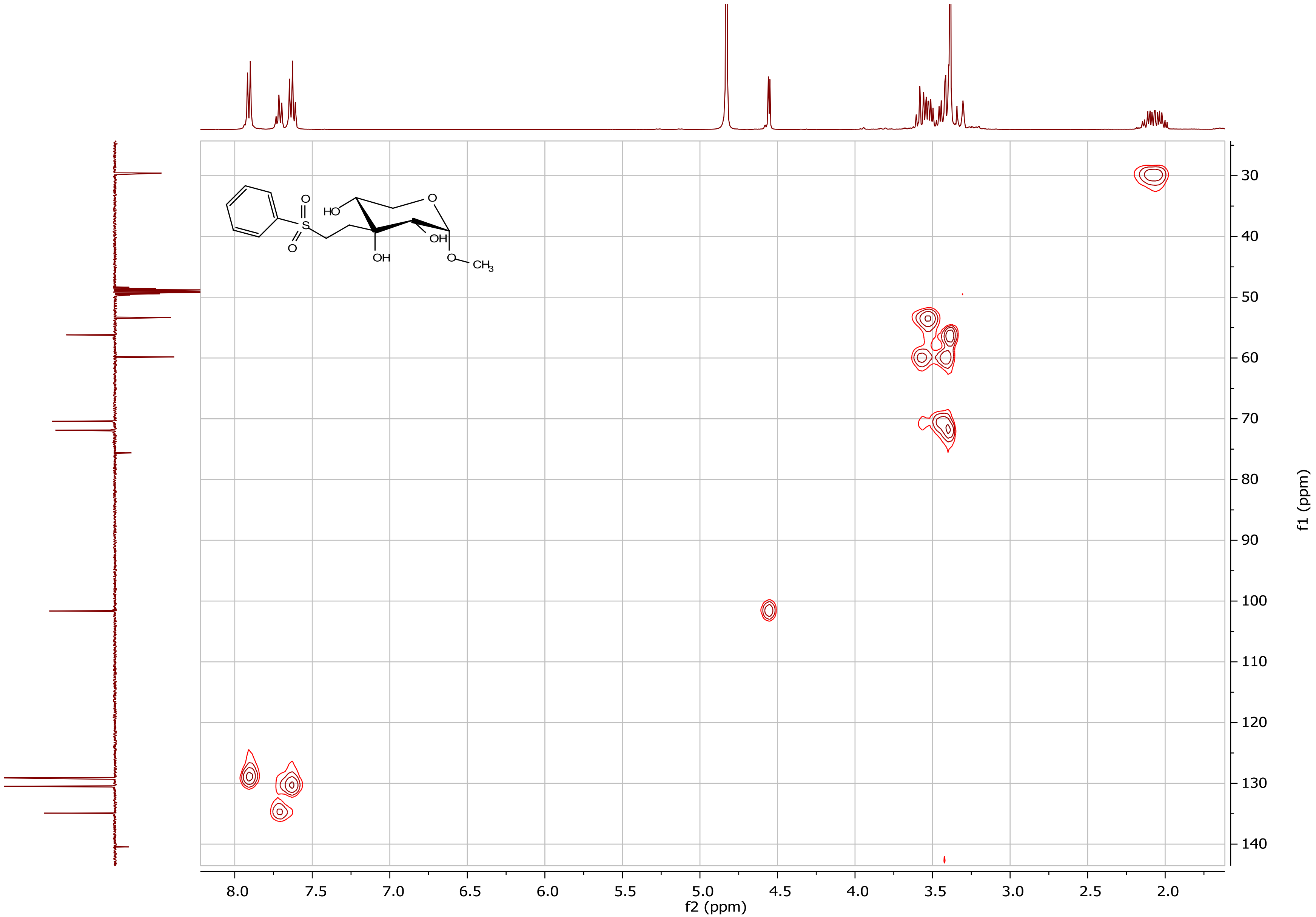

Figure 30 ^{1}H-^{13}C HMQC-NMR of **11**

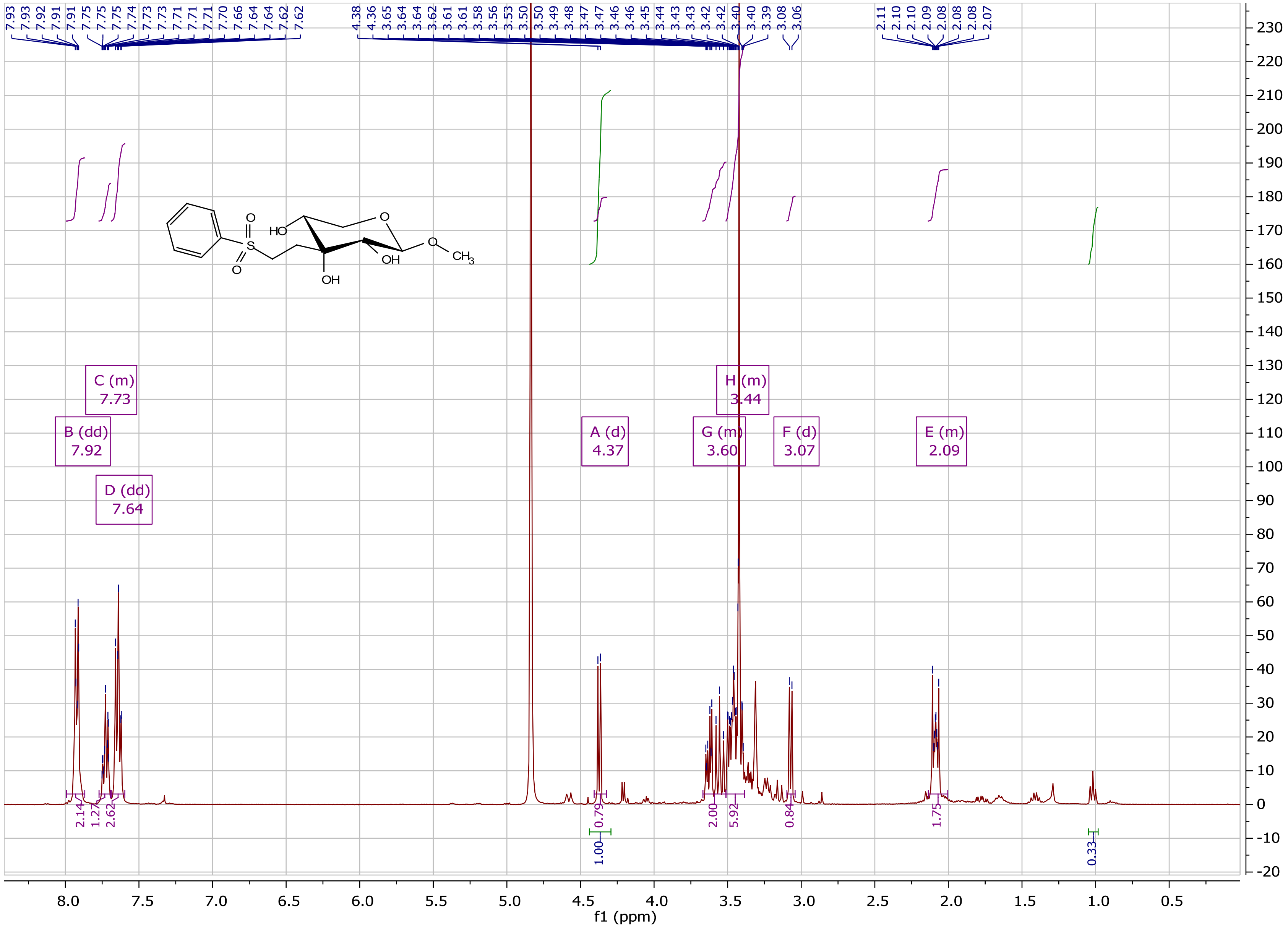

Figure 31 ^{1}H-NMR of **12**

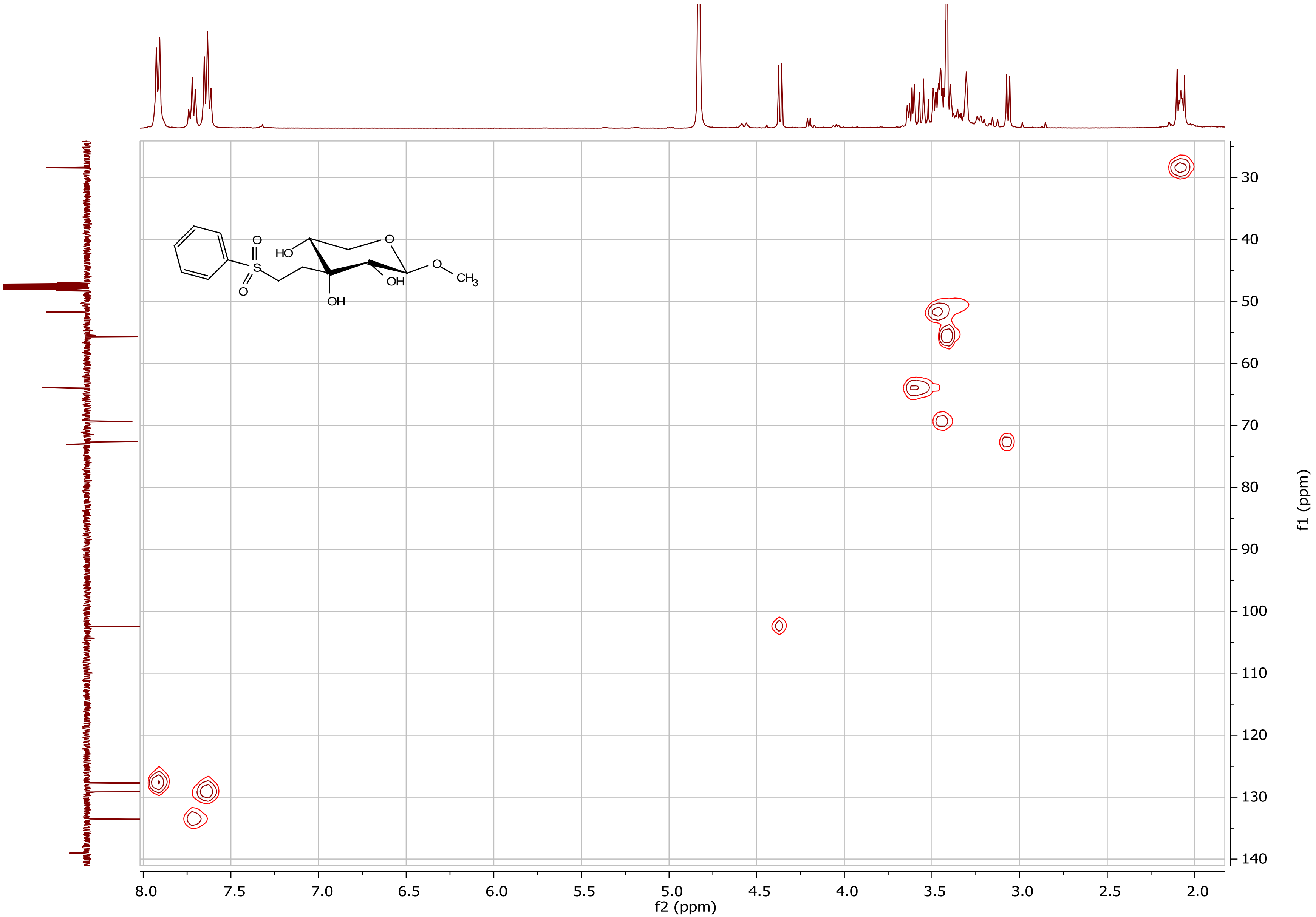

Figure 32 ^{13}C APT-NMR of **12**

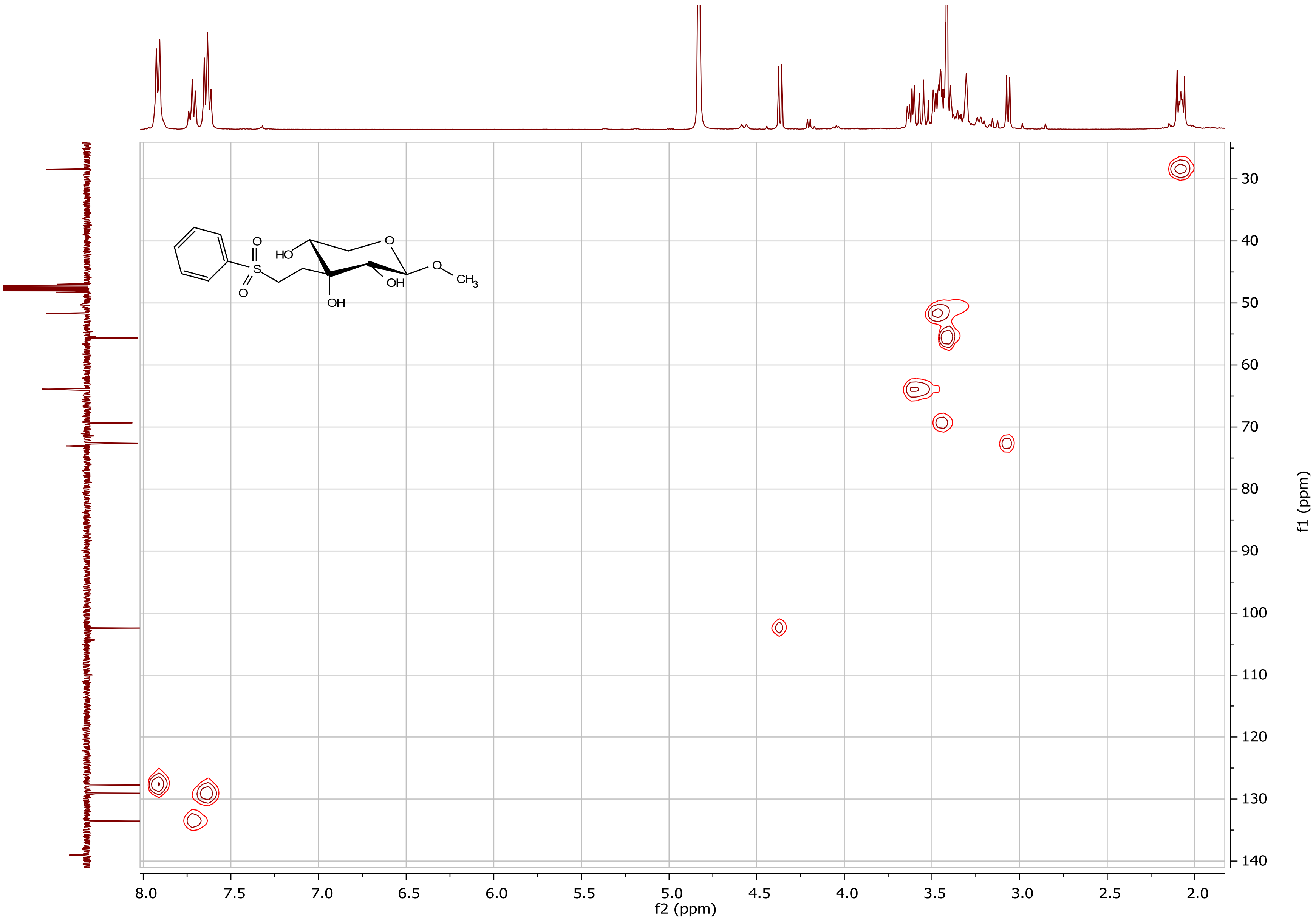

Figure 33 ^{1}H-^{13}C HMQC-NMR of **12**

Crude NMR characterization of reaction mixture (taken in DMSO-d_6)

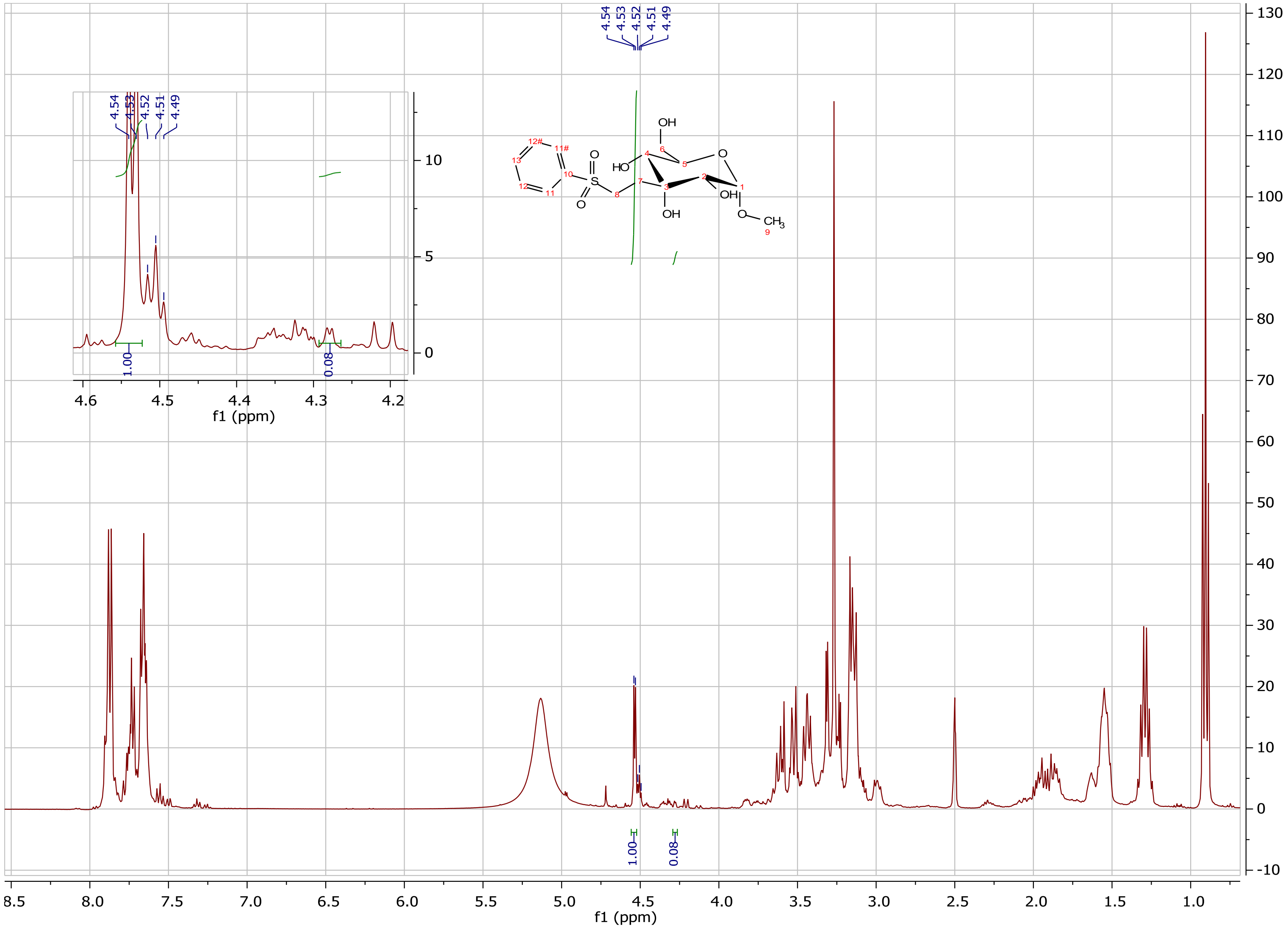

Figure 34 crude ^{1}H-NMR of **2**, made from **methyl α-D-glucopyranoside 1**. The H1 region is zoomed in for easy references.

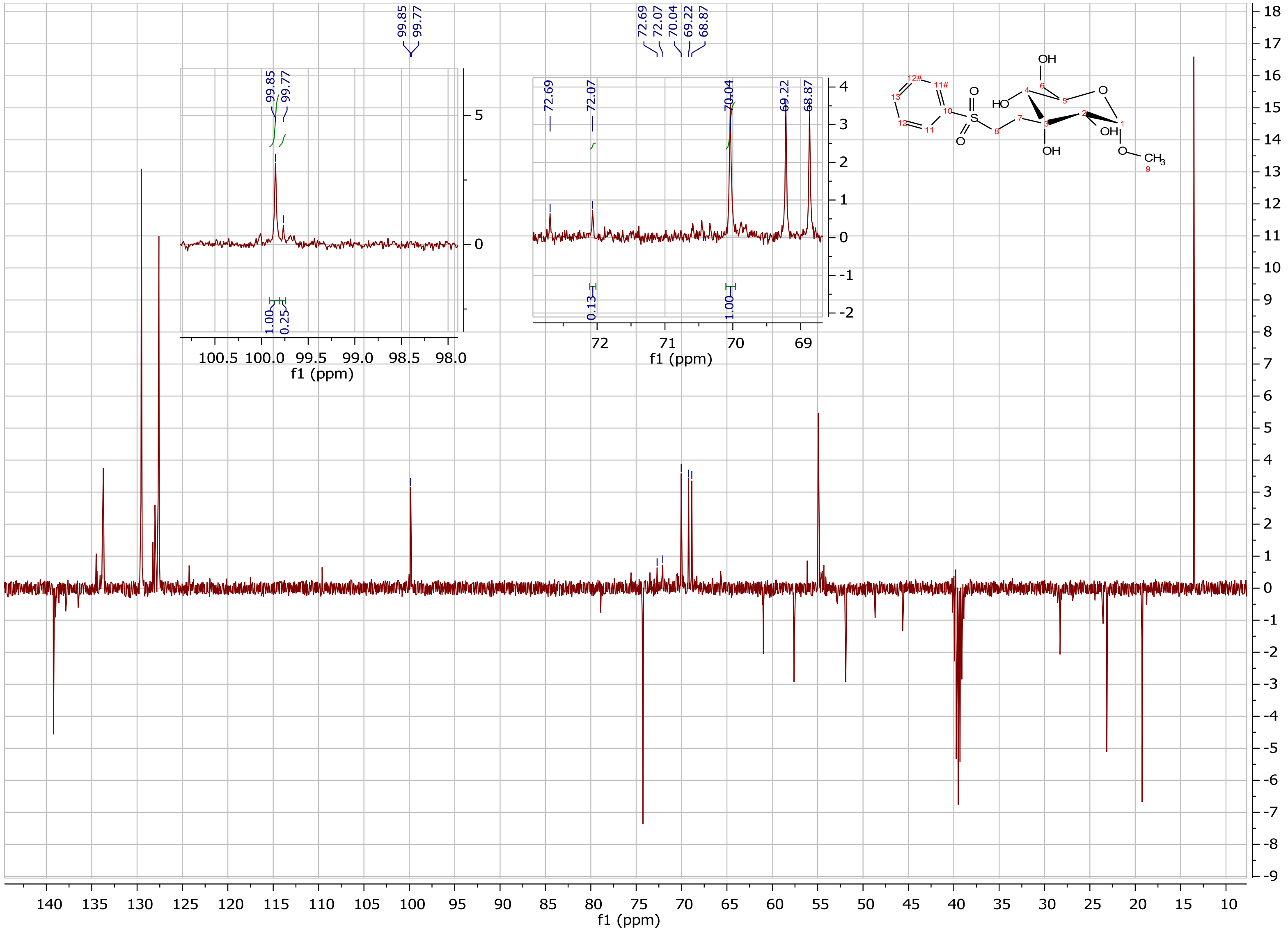

Figure 35 crude ^{13}C APT-NMR of **2**, made from **methyl α-D-glucopyranoside 1.** The C1 region, and the C2-6 region, are zoomed in for easy references.

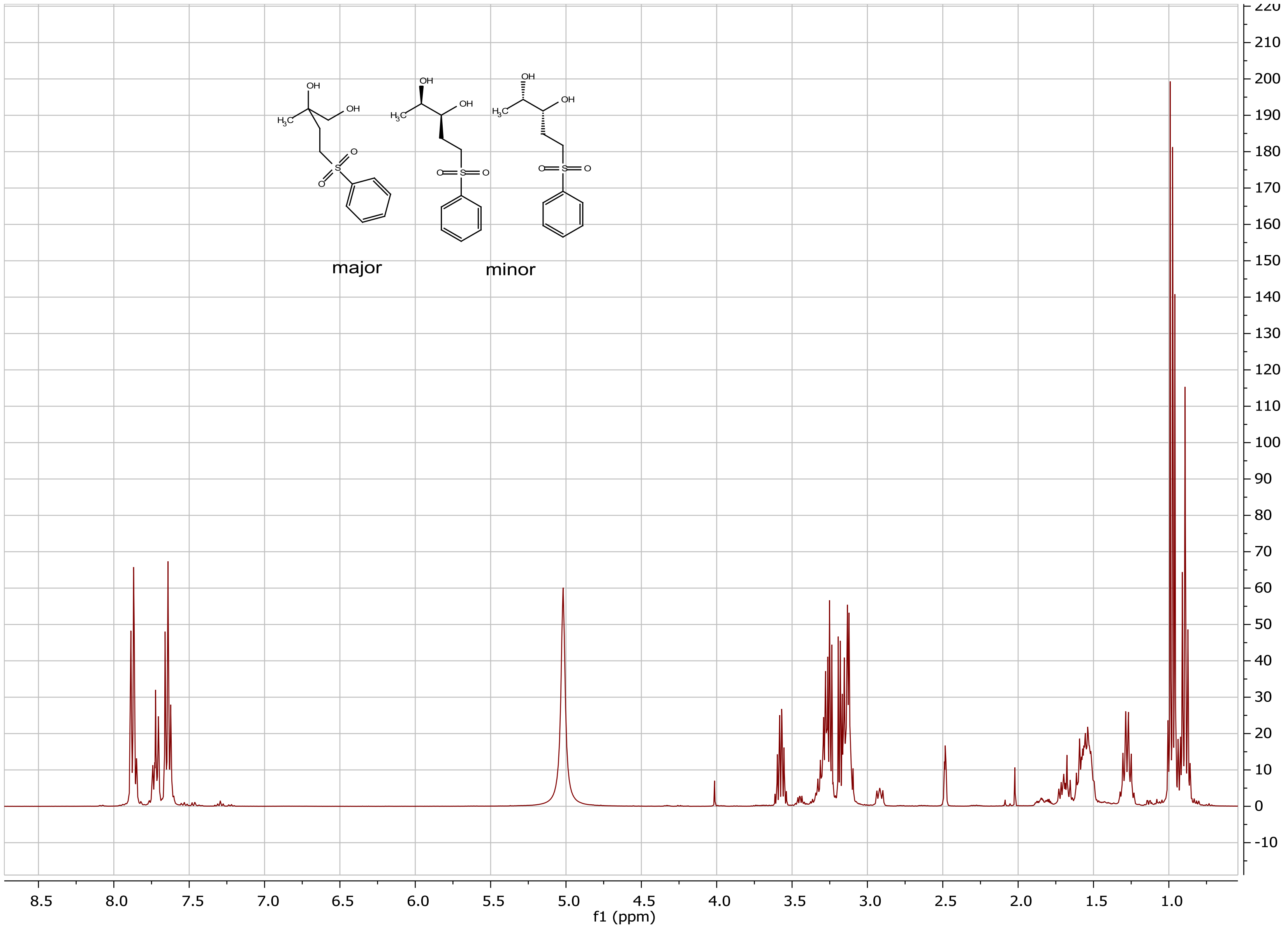

Figure 36 Crude ^{1}H-NMR of **14**

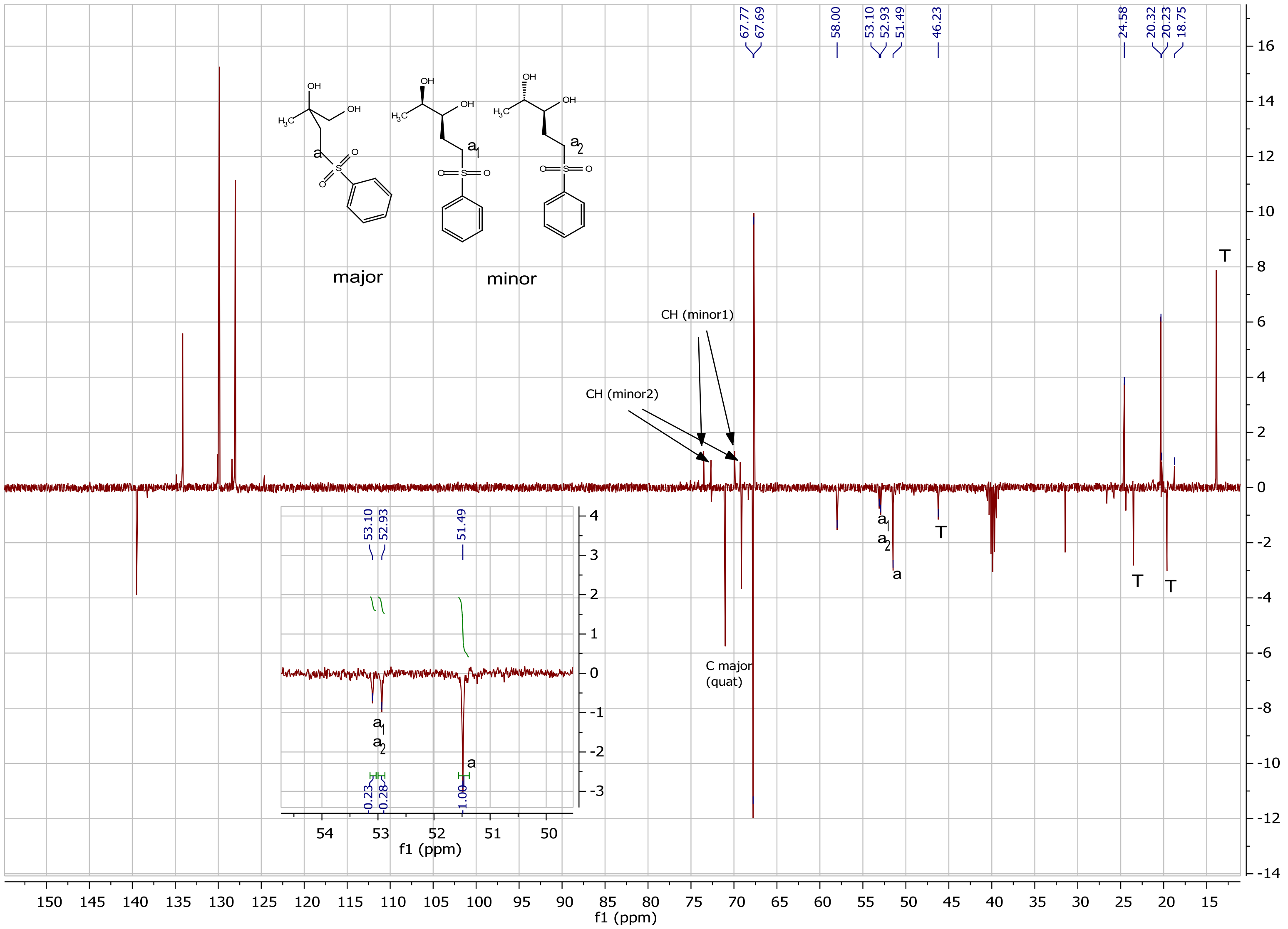

Figure 37 Crude ^{13}C APT-NMR of **14.** T = tetrabutylammonium. The ratio is derived from the integration of the signal of the α-carbon next to the sulfone moiety and by comparing the integral of the signal of the major product to that of the 2 minor products, that are diastereomers of each other. Diagnostic peaks are indicated in the ^{13}C-NMR.

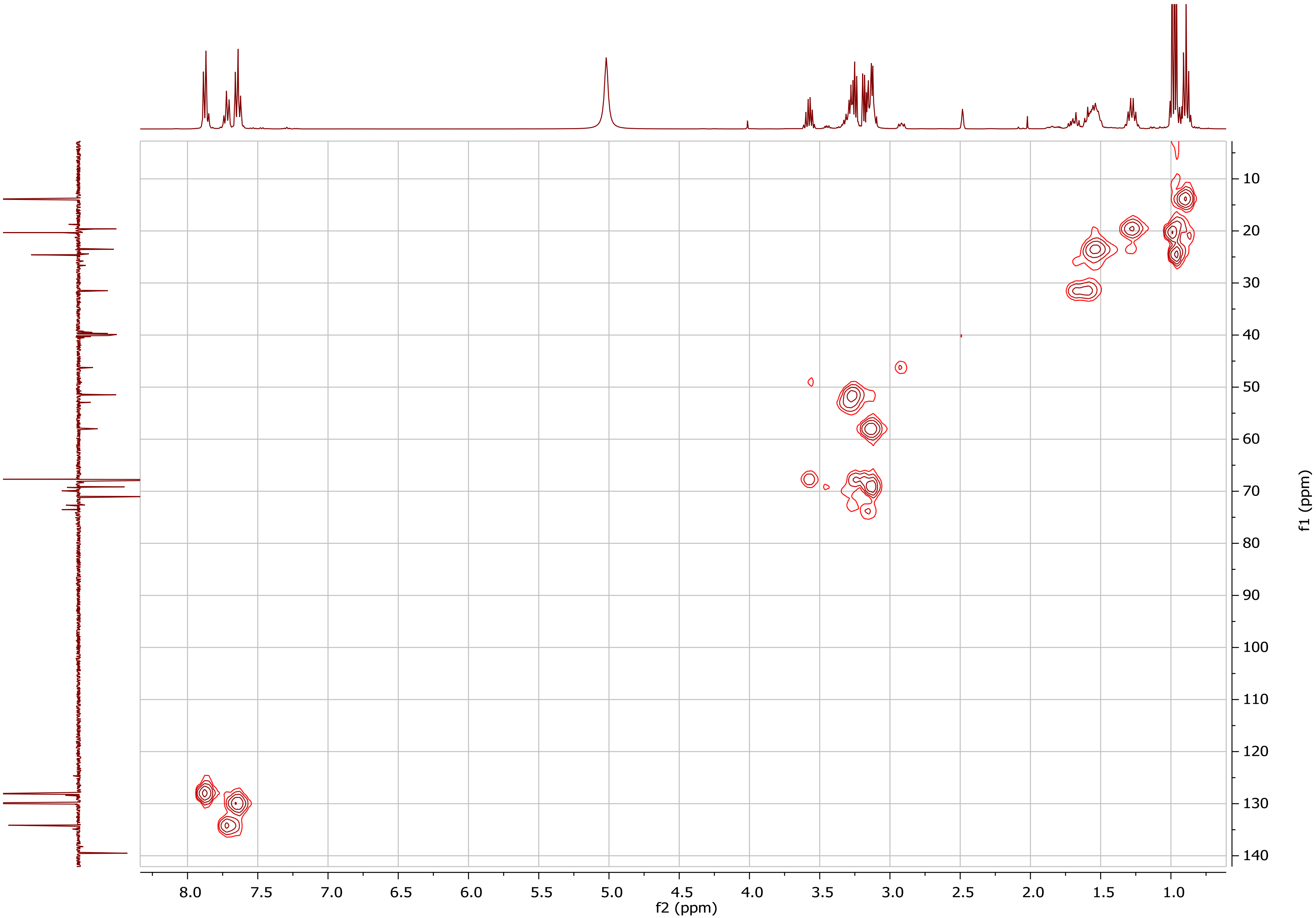

Figure 38 Crude ^1H-^{13}C HMQC-NMR of **14**