The Total Synthesis of Mevashuntin

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SUPPORTING INFORMATION

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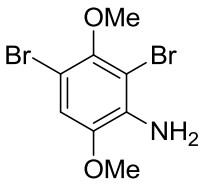
General Experimental Details

Commercially available reagents were used throughout without purification unless otherwise stated. Anhydrous solvents were used as supplied unless otherwise stated. Tetrahydrofuran was distilled from sodium benzophenone ketyl under a nitrogen atmosphere. Dichloromethane was distilled from calcium hydride under a nitrogen atmosphere. Light petroleum refers to the fraction with bp 40-60 °C. Ether refers to diethyl ether. Reactions were routinely carried out under a nitrogen or argon atmosphere. Analytical thin layer chromatography was carried out on aluminum backed plates coated with silica gel, and visualized under UV light at 254 and/or 360 nm and/or potassium permanganate or ethanolic vanillin dip. Chromatography was carried out on silica gel. Fully characterized compounds were chromatographically homogeneous. Infrared spectra were recorded in the range 4000-600 cm^{-1} as solutions in chloroform. NMR spectra were recorded at the frequencies stated. Chemical shifts are quoted in ppm and *J* values in Hz. Chemical shift values are referenced against residual proton in the deuterated solvents. In the ^{13}C NMR spectra, signals corresponding to CH, CH_2, or CH_3 are assigned from DEPT-90 and -135 spectra; all others are quaternary C. High and low resolution mass spectra were recorded on a time-of-flight spectrometer in positive or negative mode.

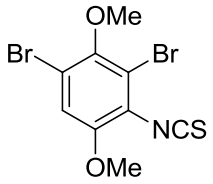
Experimental Procedures

2,4-Dibromo-3,6-dimethoxyaniline



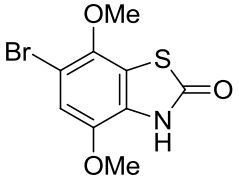
Bromine (32.0 g, 200.0 mmol) was added dropwise to a -40 ºC solution of 2,5-dimethoxyaniline (15.0 g, 97.9 mmol) in dichloromethane (300 mL). After the addition had completed the purple mixture was warmed to rt, concentrated to around one third of its volume and treated with saturated aqueous sodium carbonate solution (100 mL). The layers were separated and the aqueous phase was extracted with dichloromethane (3 × 100 mL). The combined extracts were washed with water (200 mL) and brine (100 mL), dried ($MgSO_4$) and concentrated. Filtration through a short plug of silica gel eluting with ethyl acetate – light petroleum (1 : 9) gave the *title compound* as a brown oil (9.50 g, 31%); (Found: [M + H^+], 311.9041. $C_8H_{10}{}^{79}Br\,{}^{81}BrNO_2{}^+$ requires 311.9058); ν_{max} ($CHCl_3$) 3496, 3397, 3008, 2941, 1606, 1483, 1397, 1039 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 6.89 (1 H, s), 4.31 (2 H, br s), 3.85 (3 H, s), 3.84 (3 H, s); δ_C (75 MHz; $CDCl_3$) 148.1 (C), 143.9 (C), 135.6 (C), 112.9 (CH), 104.1 (C), 102.5 (C), 60.6 (Me), 56.2 (Me).

1,3-Dibromo-4-isothiocyanato-2,5-dimethoxybenzene 6



Thiocarbonyl diimidazole (4.70 g, 26.37 mmol) was added to 2,4-dibromo-3,6-dimethoxyaniline (4.10 g, 13.18 mmol) in 1,2-dichloroethane (25 mL) and the resulting solution heated to 60 ºC and stirred for 50 h. The reaction mixture was adsorbed onto silica gel and purified by flash column chromatography eluting with ethyl acetate – light petroleum (1 : 19 - 1 : 9) to give the *title compound* as a colorless powder (3.38 g, 73%); mp 116 – 117 ºC; (Found: C, 30.5; H, 1.9; N, 3.7. $C_9H_7Br_2NO_2S$ requires C, 30.6; H, 2.0; N, 4.0%); (Found: [M + Na^+], 375.8473. $C_9H_7{}^{79}Br^{81}Br\ NNaO_2S^+$ requires 375.8441); ν_{max} ($CHCl_3$) 3011, 2972, 2940, 2025, 1475, 1434, 1387, 1044, 977 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.06 (1 H, s), 3.91 (3 H, s), 3.84 (3 H, s); δ_C (75 MHz, $CDCl_3$) 153.4 (C), 148.5 (C), 143.1 (C), 121.9 (C), 115.7 (C), 115.6 (C), 114.6 (CH), 60.8 (Me), 56.8 (Me).

6-Bromo-4,7-dimethoxybenzo[*d*]thiazol-2(3*H*)-one 7

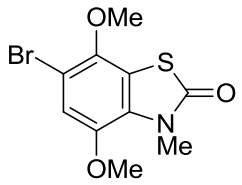


Copper(I) iodide (27 mg, 0.14 mmol) and phenanthroline (51 mg, 0.28 mmol) were added to potassium carbonate (783 mg, 5.66 mmol) and 1,3-dibromo-4-isothiocyanato-2,5-dimethoxybenzene **6** (1.0 g, 2.83 mmol) in ethanol (20 mL) and the suspension heated to reflux and stirred for 14 h. The brown solution was

cooled to rt and the ethanol was removed under reduced pressure. Hydrochloric acid (6 M; 20 mL) was carefully added and the brown solution was heated to 80 ºC. After 1 h a heavy white precipitate had formed. Water (20 mL) was added and the suspension was cooled to rt and filtered to give the *title compound* as a colorless solid that did not require further purification (789 mg, 96%); mp 190 - 191 ºC; (Found: C, 37.0; H, 2.7; N, 4.6. $C_9H_8BrNO_3S$ requires C, 37.3; H, 2.8; N, 4.8%); (Found: [M + Na^+], 311.9281. $C_9H_8{}^{79}BrNNaO_3S^+$ requires 311.9306); ν_{max} ($CHCl_3$) 3416, 3008, 2969, 1700, 1491, 1463, 1383, 1271, 1081 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.65 (1 H, br s, NH), 6.97 (1 H, s), 3.91 (3 H, s), 3.89 (3 H, s); δ_C (75 MHz, $CDCl_3$) 170.2 (C), 144.7 (C), 141.5 (C), 124.5 (C), 118.3 (C), 112.5 (CH), 108.7 (C), 60.5 (Me), 56.5 (Me).

On one occasion the intermediate 6-bromo-2-ethoxy-4,7-dimethoxybenzo[*d*]thiazole was isolated and purified by flash column chromatography (ethyl acetate – light petroleum 1 : 9) but the yield was much lower when this was done (57% before hydrolysis on 100 mg scale); (Found: [M + H^+], 317.9784. $C_{11}H_{13}BrNO_3{}^+$ requires 317.9794); ν_{max} ($CHCl_3$) 3008, 1586, 1537, 1484, 1428, 1318, 1111 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.00 (1 H, s), 4.67 (2 H, q, *J* 6.9), 3.97 (3 H, s), 3.90 (3 H, s), 1.48 (3 H, t, *J* 6.9); δ_c (75 MHz, $CDCl_3$) 172.4 (C), 148.3 (C), 144.3 (C), 139.0 (C), 126.8 (C), 112.1 (CH), 109.3 (C), 68.5 (CH_2), 60.3 (Me), 56.6 (Me), 14.4 (Me).

6-Bromo-4,7-dimethoxy-3-methylbenzo[*d*]thiazol-2(3*H*)-one 8

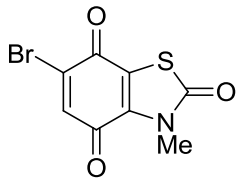


Iodomethane (0.40 mL, 0.69 mmol) was added to 6-bromo-4,7-dimethoxybenzo[*d*]thiazol-2(3*H*)-one **7** (100 mg, 0.34 mmol) and potassium carbonate (95 mg, 0.69 mmol) in DMF (3 mL) and the resulting suspension

was heated to 80 ºC and stirred for 1 h. Water (20 mL) was added was added and the aqueous phase extracted with dichloromethane (3 × 10 mL). The combined extracts were washed with water (3 × 20 mL) and brine (3 × 20 mL), dried ($MgSO_4$) and concentrated to give the *title compound* as an off white solid that did not require further purification (101 mg, 98%); mp > 250 ºC; (Found: [M + H^+], 303.9623. $C_{10}H_{11}{}^{79}BrNO_3S^+$ requires 303.9643); ν_{max} ($CHCl_3$) 2943, 1668, 1487, 1445, 1266, 1002 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.97 (1 H, s), 3.88 (3 H, s), 3.86 (3 H, s), 3.71 (3 H, s); δ_C (75 MHz, $CDCl_3$) 169.6 (C), 144.7 (C), 143.2 (C), 126.7 (C), 118.3 (C), 113.7 (CH), 108.3 (C), 60.4 (Me), 56.7 (Me), 32.6 (Me).

On a larger scale the aqueous workup could be replaced by addition of water and collection of the precipitated solid by filtration.

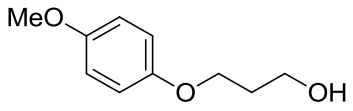
6-Bromo-3-methylbenzo[*d*]thiazole-2,4,7(3*H*)-trione 4



Cerium(IV) ammonium nitrate (15.10 g, 27.57 mmol) in water (100 mL) was added to 6-bromo-4,7-dimethoxy-3-methylbenzo[*d*]thiazol-2(3*H*)-one **8** (3.35 g, 11.03 mmol) in acetonitrile (100 mL), turning the colorless solution deep red. The reaction mixture was stirred for 5 min then acetonitrile was removed under reduced pressure and the remaining aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined extracts were washed with water (3 × 50 mL) and brine (50 mL), dried ($MgSO_4$) and concentrated to give the *title compound* as a dark red solid that did not require further purification (2.21 g, 82%); mp 150 - 152 ºC; (Found: C, 34.8; H, 1.5; N, 4.9. $C_8H_4BrNO_3S$ requires C, 35.1; H, 1.5; N, 5.1%); (Found: [M + Na^+], 295.8974. $C_8H_4{}^{79}BrNNaO_3S^+$ requires 295.8993); λ_{max} (CH_2Cl_2)/nm 226 (4.09), 306 (4.00), 306 (2.95); ν_{max}

($CHCl_3$) 3065, 3007, 1693, 1667, 1556, 1507, 1299, 1086 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.23 (1 H, s), 3.70 (3 H, s); δ_C (75 MHz, $CDCl_3$) 174.3 (C), 170.9 (C), 169.4 (C), 137.4 (C), 136.4 (CH), 135.7 (C), 122.3 (C), 11.8 (Me).

3-(4-Methoxyphenoxy)propan-1-ol 9



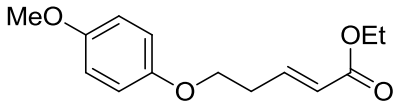
For gram-scale preparation of the *title compound* the procedure of Murphy *et al.*, using 3-bromopropanol and K_2CO_3 in DMF,[1] was successfully employed. However, this method was found to be unsuitable for the preparation of large quantities of material so the following, more scalable, procedure was developed:

A solution of sodium ethoxide was freshly prepared by the addition of sodium (10.0 g, 435 mmol) to ethanol (500 mL) followed by stirring overnight at rt. 4-Methoxyphenol (54.4 g. 414 mmol) was added, and the solution stirred for 30 min, after which time the phenol had dissolved to give a clear solution. 3-Chloropropanol (40 mL, 479 mmol) was added and the reaction mixture heated to reflux and stirred for 9 h. The solution was cooled to rt and water (200 mL) was added. Ethanol was removed under reduced pressure and the remaining aqueous phase was extracted with ether (3 × 150 mL). The combined ethereal extracts were washed with aqueous sodium hydroxide solution (2 M; 2 × 100 mL), water (200 mL) and brine (300 mL), dried (K_2CO_3) and concentrated to a give a brown solid. Recrystallization from toluene - light petroleum (ca. 1:1) gave the *title compound* as large colorless flakes (50.75 g, 67%); mp 58 - 60 ºC (lit.,[1] mp 54 - 56 ºC); (Found: $[M + Na^+]$, 205.0840. $C_{10}H_{14}NaO_3^+$ requires 205.0835); ν_{max} ($CHCl_3$) 3625, 3009, 2955, 2837, 1509, 1468, 1240, 1053 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 6.85 (4 H, s), 4.10 (2 H, t, *J* 5.9), 3.87 (2 H, app.

q, *J* 5.7), 2.04 (2 H, app. quin., *J* 5.9), 1.95 (1 H, t, *J* 5.4); δ_C (75 MHz; $CDCl_3$) 154.0 (C), 152.9 (C), 115.5 (CH) 114.6 (CH), 66.6 (CH_2), 60.7 (CH_2), 55.8 (Me), 32.1 (CH_2).

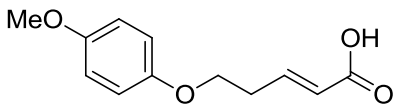
The ^1H and ^{13}C data obtained matched those reported.[1]

(*E*)-Ethyl 5-(4-methoxyphenoxy)pent-2-enoate



Activated manganese dioxide (4.77 g, 54.9 mmol) was added in three portions over 1 h to a solution of ethyl (triphenylphosphoranylidene)acetate (2.29 g, 6.58 mmol) and 3-(4-methoxyphenoxy)propan-1-ol (1.0 g, 5.49 mmol) in dichloromethane (140 mL). The resulting black suspension was heated to reflux and stirred for 3 d, cooled to rt, filtered through a short pad of Celite and concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with ethyl acetate - light petroleum (1:19 - 1:9) to give the *title compound* as a pale yellow oil (960 mg, 70%); (Found: [M + Na^+], 273.1094. $C_{14}H_{18}NaO_4^+$ requires 273.1097); ν_{max} ($CHCl_3$) 3007, 2956, 1711, 1509, 1240, 1181, 1043 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.04 (1 H, dt, *J* 15.7, 6.5), 6.84 (4 H, s), 5.96 (1 H, dt, *J* 15.7, 1.6), 4.21 (2 H, q, *J* 7.2), 4.04 (2 H, t, *J* 6.5), 3.78 (3 H, s), 2.67 (2 H, app. qd, *J* 6.5, 1.6), 1.30 (3 H, t, *J* 7.2); δ_C (75 MHz; $CDCl_3$) 166.4 (C), 154.0 (C), 152.7 (C), 144.7 (CH), 123.4 (CH), 115.6 (CH), 114.7 (CH), 66.7 (CH_2), 60.3 (CH_2), 55.7 (Me), 32.2 (CH_2), 14.3 (Me).

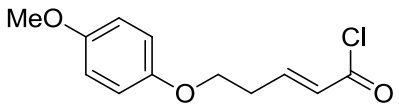
(*E*)-5-(4-Methoxyphenoxy)pent-2-enoic acid



Aqueous sodium hydroxide solution (5 M; 14 mL, 69.9 mmol) was added to a 0 ºC solution of (*E*)-ethyl 5-(4-methoxyphenoxy)pent-2-enoate (3.5 g, 13.98 mmol) in dioxane (61 mL) - water (61 mL). The pale brown solution was warmed to rt and stirred for 19 h, diluted with water (100 mL) and extracted with toluene (100

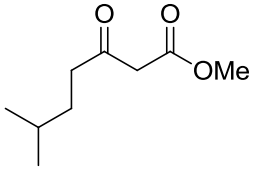
mL). The toluene was then extracted with water (2 × 50 mL) and these aqueous extracts were combined with the remaining aqueous phase from the previous step, then acidified to pH 2 using hydrochloric acid (6 M). The acidified aqueous phase was then extracted with ether (3 × 100 mL) and the combined extracts were dried (Na_2SO_4) and concentrated. The brown solid residue obtained was recrystallized from toluene - light petroleum (ca. 3:1) to give the *title compound* as an off-white powder (2.23 g, 72%); mp 84 - 85 ºC; (Found: [M + Na^+], 245.0781. $C_{12}H_{14}NaO_4^+$ requires 245.0784); ν_{max} ($CHCl_3$) 3524, 3011, 2955, 2837, 1726, 1699, 1656, 1509, 1240, 1044, 980 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.17 (1 H, dt, *J* 15.6, 6.6), 6.84 (4 H, s), 5.98 (1 H, dt, *J* 15.7, 1.6), 4.06 (1 H, t, *J* 6.3), 3.78 (3 H, s), 2.70 (2 H, app. qd, *J* 6.6, 1.6); δ_C (75 MHz; $CDCl_3$) 171.5 (C), 154.1 (C), 152.7 (C), 147.9 (CH), 122.6 (CH), 115.6 (CH), 114.7 (CH), 66.5 (CH_2), 55.7 (CH), 32.3 (CH_2).

(*E*)-5-(4-Methoxyphenoxy)pent-2-enoyl chloride 10



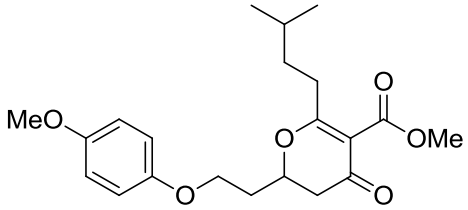
Oxalyl chloride (0.72 mL, 8.41 mmol) was added dropwise to a 0 ºC solution of (*E*)-5-(4-methoxyphenoxy)pent-2-enoic acid (1.70 g, 7.65 mmol) in dichloromethane (100 mL). After 5 min DMF (2 drops) was added and the reaction mixture was slowly warmed to rt and stirred until gas evolution ceased (ca. 2 h). The yellow solution was concentrated *in vacuo* to give the *title compound* as a brown oil that was used without further purification (1.81 g, 98%); ν_{max} ($CHCl_3$) 3009, 2955, 2837, 1785, 1756, 1740, 1647, 1509, 1467, 1240 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 7.31 (1 H, dt, *J* 15.3, 6.9), 6.85 (4 H, s), 6.22 (1 H, dt, *J* 15.3, 1.5), 4.09 (1 H, t, *J* 6.1), 3.78 (3 H, s), 2.76 (2 H, dtd, *J* 6.9, 6.1, 1.5); δ_C (75 MHz; $CDCl_3$) 165.7 (C), 154.2 (C), 152.7 (C), 152.4 (C), 128.2 (CH), 115.7 (CH), 114.7 (CH), 66.0 (CH_2), 55.7 (Me), 32.4 (CH_2).

Methyl 6-methyl-3-oxoheptanoate 11



Methyl acetoacetate was added dropwise over 10 mins to a suspension of sodium hydride (3.79 g of a 60% dispersion in mineral oil, 94.7 mmol) in THF (300 mL) at 0 ºC. The mixture was stirred for 30 min at the same temperature then *n*-butyllithium was slowly added to give a deep orange-red solution. After 30 min, 1-iodo-2-methyl-propane (10.9 mL, 94.7 mmol) was added and the mixture stirred for 23 h at rt, then quenched by addition of saturated aqueous ammonium chloride solution (200 mL). The layers were separated and the aqueous phase was extracted with ether (3 × 200 mL). The combined extracts were washed with brine (500 mL), dried ($MgSO_4$) and concentrated. The residual brown oil was purified by fractional distillation under reduced pressure (water aspirator) to give the *title compound* as a pale brown liquid (9.02 g, 61%); bp 112 - 115 ºC at ca. 20 mmHg; (Found: [M + Na^+], 195.0997. $C_9H_{16}NaO_3^+$ requires 195.0992); ν_{max} ($CHCl_3$) 3012, 2959, 2935, 2872, 1746, 1716, 1652, 1627, 1438, 1319, 1240, 1156, 1011 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 3.75 (3 H, s), 3.46 (2 H, s), 2.54 (2 H, t, *J* 7.5), 1.56 - 1.48 (3 H, m), 0.90 (6 H, d, *J* 6.3); δ_C (75 MHz; $CDCl_3$) 203.0 (C), 167.7 (C), 52.3 (Me), 49.0 (CH_2), 41.1 (CH_2), 32.2 (CH_2), 27.6 (CH), 22.3 (Me).

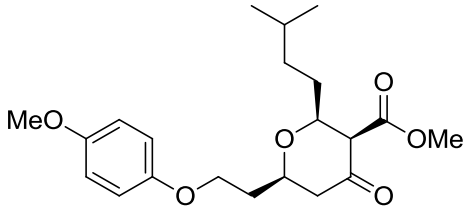
Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-oxo-5,6-dihydro-2*H*-pyran-3-carboxylate 12



Methanol (1.4 mL, 34.9 mmol) was added to a stirred suspension of magnesium turnings (296 mg, 12.19 mmol) in toluene (6 mL) that had been activated by addition of a drop of 1,2-dibromoethane and gentle warming. The reaction mixture was heated to 50 ºC for 5 h, then additional methanol (0.5 mL) was added and

heating was continued for 3 h, after which time all the magnesium turnings had disappeared and a white suspension of magnesium methoxide had formed. The reaction mixture was cooled to 0 ºC and methyl 6-methyl-3-oxoheptanoate **11** (2.00 g, 11.61 mmol) was added. After stirring for 30 min a clear brown solution had formed and (*E*)-5-(4-methoxyphenoxy)pent-2-enoyl chloride **12** (3.07 g, 12.77 mmol) in toluene (5 mL) was added. The reaction mixture was allowed to warm to rt and stirred for 16 h then poured into ice cold hydrochloric acid (0.5 M; 25 mL). The layers were separated and the aqueous phase was extracted with ether (3 × 20 mL). The combined ethereal extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography on silica gel eluting with ethyl acetate - light petroleum (1:20 - 1:2) to give two major products. Eluted first was the intermediate acylated β-ketoester (1.79 g 46%) intermediate that cyclized to the *title compound* upon standing neat at room temperature for ca. 1 week or heating in toluene in the presence of SiO_2. Eluted second was the *title compound* as a yellow oil (1.32 g, 30%); (Found: [M + Na^+], 399.1777. $C_{21}H_{30}NaO_6^+$ requires 399.1778); ν_{max} ($CHCl_3$) 3692, 3607, 3012, 2958, 1726, 1672, 1602, 1509, 1436, 1388, 1348, 1240, 1071 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 6.84 (4 H, s), 4.72 (1 H, dddd, *J* 8.3, 8.3, 8.3, 4.7), 4.16 - 4.01 (2 H, m), 3.82 (3 H, s), 3.77 (3 H, s), 2.59 - 2.56 (2 H, m), 2.51 - 2.45 (2 H, m), 2.30 - 2.09 (2 H, m), 1.60 - 1.43 (3 H, m), 0.87 (3 H, d, *J* 6.5), 0.86 (3 H, d, *J* 6.5); δ_C (75 MHz; $CDCl_3$) 188.3 (C), 180.1 (C), 166.1 (C), 154.1 (C), 152.6 (C), 115.4 (CH), 114.7 (CH), 112.3 (C), 76.2 (CH), 63.5 (CH_2), 55.7 (Me), 52.2 (Me), 40.9 (CH_2), 35.9 (CH_2), 34.1 (CH_2), 31.7 (CH_2), 27.9 (CH), 22.20 (Me), 22.19 (Me).

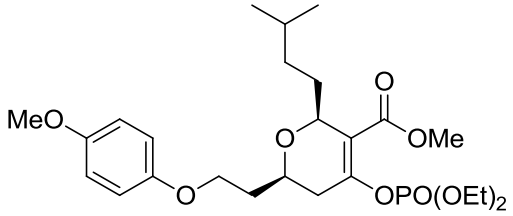
***cis*-Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-oxotetrahydro-2*H*-pyran-3-carboxylate**



Palladium-on-carbon (5wt% Pd; 125 mg) was added to a solution of methyl 6-isopentyl-2-(2-(4-methoxyphenoxy)ethyl)-4-oxo-3,4-dihydro-2*H*-pyran-5-carboxylate **12** (1.25 g, 3.32 mmol) in methanol (20

mL) and the resulting suspension was stirred under hydrogen (100 psi) for 12 h. The reaction mixture was then filtered through a pad of Celite, washing with methanol, and concentrated to give the *title compound* as a pale brown oil that was not purified further (1.24 g, 99%); (Found: [M + Na^+], 401.1931. $C_{21}H_{30}NaO_6^+$ requires 401.1935); ν_{max} ($CHCl_3$) 3011, 2957, 2872, 1744, 1715, 1509, 1468, 1439, 1341, 1240, 1130, 1038 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 6.83 (4 H, s), 4.13 - 4.02 (2 H, m), 3.98 - 3.92 (1 H, m), 3.86 (1 H, ddd, *J* 10.7, 8.2, 3.2), 3.77 (6 H, s), 3.26 (1 H, d, *J* 10.7), 2.53 (1 H, dd, *J* 14.3, 1.8), 2.34 (1 H, dd, *J* 14.0, 12.0), 2.05 - 1.97 (2 H, m), 1.58 - 1.47 (3 H, m), 1.41 - 1.21 (2 H, m), 0.84 (3 H, d *J* 6.4), 0.83 (3 H, d, *J* 6.4); δ_C (75 MHz; $CDCl_3$) 202.1 (C), 168.6 (C), 153.9 (C), 152.9 (C), 115.5 (CH), 114.7 (CH), 78.6 (CH), 73.7 (CH), 64.4 (CH_2), 63.2 (CH), 55.7 (Me), 52.2 (Me), 47.1 (CH_2), 35.9 (CH_2), 34.3 (CH_2), 32.9 (CH_2), 27.6 (CH), 22.7 (Me), 22.1 (Me).

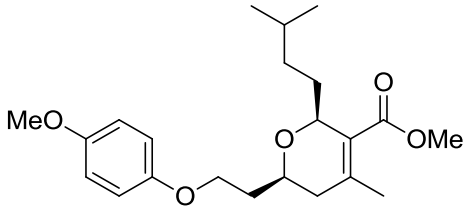
cis-Methyl 4-((diethoxyphosphoryl)oxy)-2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-5,6-dihydro-2*H*-pyran-3-carboxylate 13



cis-Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-oxotetrahydro-2*H*-pyran-3-carboxylate (1.10 g, 2.91 mmol) in ether (5 mL) was added to a 0 ºC suspension of sodium hydride (60% in mineral oil; 128 mg, 3.20 mmol) in ether (30 mL). The reaction mixture was stirred for 5 min, diethyl chlorophosphate (0.46 mL, 3.20 mmol) was added and the solution warmed to rt and stirred for 5 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (30 mL) and the layers were separated. The aqueous phase was extracted with ether (3 × 30 mL) and the combined ethereal extracts were then washed with water (50 mL) and brine (50mL), dried (Na_2SO_4) and concentrated. Filtration through a short plug of silica gel eluting with ethyl acetate - light petroleum (1:2) gave the *title compound* as a pale brown oil (1.18

g, 79%); (Found: [M + Na^+], 537.2220. $C_{25}H_{39}NaO_9P^+$ requires 537.2248); ν_{max} ($CHCl_3$) 3007, 2956, 1724, 1509, 1468, 1437, 1276, 1240, 1108, 1037 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 6.84 (4 H, s), 4.47 (1 H, m), 4.23 - 4.14 (4 H, m), 4.11 - 4.00 (2 H, m), 3.86 - 3.78 (1 H, m), 3.78 (3 H, s), 3.75 (3 H, s), 2.50 - 2.44 (2 H, m), 2.04 - 1.94 (2 H, m), 1.69 - 1.58 (1 H, m), 1.55 - 1.45 (2 H, m), 1.36 (3 H, dt, *J* 7.1, 1.1), 1.35 (3 H, dt, *J* 7.1, 1.1), 1.31 - 1.23 (2 H, m), 0.86 (3 H, d, *J* 6.6), 0.84 (3 H, d, *J* 6.6); δ_C (75 MHz; $CDCl_3$) 165.5 (C), 153.8 (C), 153.1 (C), 148.6 (C), 119.1 (C), 115.5 (CH), 114.7 (CH), 74.4 (CH), 70.0 (CH), 64.6 (CH_2), 64.7 (CH_2), 55.8 (Me), 51.5 (Me), 35.1 (CH_2), 34.3 (CH_2), 33.7 (CH_2), 31.6 (CH_2), 27.8 (CH), 22.9 (Me), 22.2 (Me), 16.1 (Me); δ_P (121 MHz; $CDCl_3$) 7.77 (1 P, s).

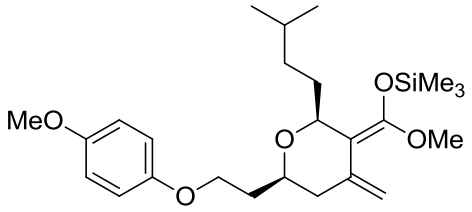
***cis*-Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-methyl-5,6-dihydro-2*H*-pyran-3-carboxylate 14**



Methyllithium solution (1.6 M in ether; 5.48 mL, 8.76 mmol) was added dropwise to a 0 ºC suspension of freshly purified copper(I) iodide (833 mg, 4.37 mmol) in ether (10 mL), initially forming a bright yellow solution that faded to colorless as the addition completed. The resulting solution was cooled to -78 ºC and a solution of *cis*-methyl 4-((diethoxyphosphoryl)oxy)-2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-5,6-dihydro-2*H*-pyran-3-carboxylate **13** (1.50 g, 2.92 mmol) in ether (20 mL) was added dropwise. The brown solution was then stirred at this temperature for 1 h, followed by 1 h at 0 ºC and 2 h at rt before quenching with saturated aqueous ammonium chloride solution (50 mL). The aqueous phase was extracted with ether (3 × 50 mL) and the combined aqueous extracts were washed with saturated aqueous ammonium chloride solution (100 mL), water (100 mL) and brine (100 mL), then dried (Na_2SO_4) and concentrated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate - light petroleum (1:19

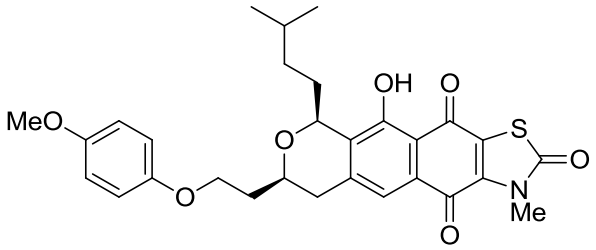
- 1:9) to give the *title compound* as a colorless oil (712 mg, 65%); (Found: [M + Na^+], 399.2143. $C_{22}H_{32}NaO_5^+$ requires 399.2142); ν_{max} ($CHCl_3$) 3011, 2955, 2871, 1714, 1509, 1468, 1435, 1240, 1071, 1040 cm^{-1}; δ_H (300 MHz; $CDCl_3$) 6.85 (4 H, s), 4.39 (1 H, m), 4.14 - 4.01 (2 H, m), 3.78 (3 H, s), 3.74 (3 H, s), 3.72 - 3.66 (1 H, m), 2.23 (1 H, m), 1.99 - 1.91 (5 H, m), 1.65 - 1.53 (2 H, m), 1.50 - 1.38 (2 H, m), 1.32 - 1.24 (2 H, m), 0.86 (3 H, d, *J* 6.6), 0.84 (3 H, d, *J* 6.6); δ_C (75 MHz; $CDCl_3$) 168.4 (C), 153.8 (C), 153.2 (C), 140.3 (C), 128.6 (C), 115.5 (CH), 114.6 (CH), 75.2 (CH), 69.5 (CH), 64.9 (CH_2), 55.8 (Me), 51.1 (Me), 37.8 (CH_2), 35.3 (CH_2), 34.0 (CH_2), 32.0 (CH_2), 27.8 (CH), 22.9 (Me), 22.2 (Me), 21.0 (Me).

(*cis*-2-Isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-methylenedihydro-2*H*-pyran-3(4*H*)-ylidene)(methoxy)methoxy)trimethylsilane 3



cis-Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-methyl-5,6-dihydro-2*H*-pyran-3-carboxylate **14** (700 mg, 1.86 mmol) in THF (5 mL) was added to a -78 ºC solution of LDA (2.79 mmol) and TMSCl (710 µL, 5.58 mmol) in THF (5 mL) and the resulting solution was stirred at the same temperature for 1 h then warmed to rt and concentrated without heating. The resulting turbid oil was diluted with dry *n*-pentane (10 mL) and filtered quickly under nitrogen then again concentrated to give the *title compound* as a colorless oil that was used without further purification (1.0 g, 100%); δ_H (300 MHz; $CDCl_3$) 6.84 (4 H, s), 5.15 (1 H, q, *J* 2.1), 5.02 (1 H, q, *J* 2.1), 4.46 - 4.42 (1 H, m), 4.12 - 4.00 (2 H, m), 3.77 (3 H, s), 3.55 (3 H, s), 2.53 - 2.45 (1 H, m), 2.36 - 2.26 (1 H, m), 1.99 - 1.91 (4 H, m), 1.63 - 1.44 (4 H, m), 1.35 - 1.22 (2 H, m), 0.88 (3 H, d, *J* 6.4), 0.85 (3 H, d, *J* 6.4); δ_C 300 MHz; $CDCl_3$) 153.7 (C), 153.3 (C), 149.9 (C), 138.7 (C), 115.5 (CH), 114.7 (CH), 112.8 (CH_2), 100.0 (C), 75.6 (CH), 69.8 (CH), 65.4 (CH_2), 55.6 (Me), 51.1 (Me), 39.0 (CH_2), 35.6 (CH_2), 34.6 (CH_2), 34.3 (CH_2), 28.0 (CH), 22.5 (Me), 22.3 (Me), 0.17 (Me).

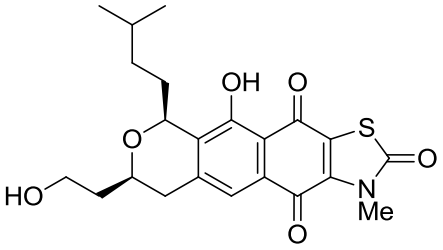
***cis*-5-Hydroxy-6-isopentyl-8-(2-(4-methoxyphenoxy)ethyl)-1-methyl-8,9-dihydro-1*H*-pyrano[3',4':6,7]naphtho[2,3-*d*]thiazole-2,4,11(6*H*)-trione 15**



Diene **3** (700 mg, 1.56 mmol) in dichloromethane (10 mL) was added dropwise to a solution of the quinone **4** (306 mg, 1.12 mmol) and triethylamine (163 µL, 1.18 mmol) in dichloromethane (10 mL) at 0 ºC. The dark purple solution was stirred for 1 h then poured into hydrochloric acid (1 M; 30 mL). The layers were separated and the organic phase was extracted with dichloromethane (3 x 20 mL). The combined extracts were then stood over magnesium sulfate for 1 h, filtered and concentrated to give a red oil that was purified by flash column chromatography on silica gel eluting with ethyl acetate - light petroleum (7:93) to give the *title compound* as a red tar that solidified on standing (410 mg, 68%); mp 138 – 140 ºC; (Found: [M - H^+], 536.1780. $C_{29}H_{30}NO_7S^-$ requires 536.1748); ν_{max} ($CHCl_3$) 3008, 2957, 2932, 2871, 1683, 1584, 1509, 1445, 1340, 1249 cm^{-1}, λ_{max} (CH_2Cl_2)/nm 210 (4.34), 265 (4.10), 297 (3.72), 313 (3.70), 434 (3.21); δ_H (400 MHz; $CDCl_3$) 12.33 (1 H, s), 7.40 (1 H, s), 6.83 (4 H, m), 4.99 (1 H, br d, *J* 4.5), 4.12 (2 H, m), 3.762 (3 H, s), 3.759 (3 H, s), 2.750 (1 H, m), 2.82 (1 H, ddd, *J* 16.6, 10.2, 1.2), 2.17 (1 H, dddd, *J* 13.8, 11.3, 5.2, 2.9), 2.11 - 2.05 (2 H, m), 1.90 (1 H, dddd, *J* 13.8, 11.5, 6.9, 4.7), 1.54 (1 H, tt, *J* 6.7, 13.4), 1.39 - 1.30 (1 H, m), 1.17 - 1.08 (1 H, m), 0.87 (3 H, d, *J* 6.9), 0.85 (3 H, d, *J* 6.9); δ_C (100 MHz; $CDCl_3$) 181.9 (C), 174.1 (C), 169.8 (C), 158.9 (C), 153.8 (C), 153.1 (C), 145.2 (C), 137.9 (C), 135.8 (C), 129.0 (C), 125.8 (C), 121.2 (CH), 115.5 (CH), 114.7 (CH), 111.5 (C), 74.4 (CH), 69.6 (CH), 64.7 (CH_2), 55.7 (Me), 36.5 (CH_2), 35.4 (CH_2), 34.0 (CH_2), 32.2 (Me), 31.9 (CH_2), 28.0 (CH), 22.9 (Me), 22.4 (Me).

Eluted second was a small amount of the corresponding *5*-methyl ether, obtained as a yellow solid (84 mg, 14%); 158-160 ºC; (Found: [M + H^+], 552.2038. $C_{30}H_{34}NO_7S^+$ requires 552.2050); ν_{max} ($CHCl_3$) 3008, 2957, 2932, 2871, 1683, 1584, 1509, 1445, 1340, 1249 cm^{-1}, λ_{max} (MeOH)/nm 267 (4.49), 301 (3.90), 317 (3.91), 376 (3.68); δ_H (400 MHz; $CDCl_3$) 7.71 (1 H, s), 6.87 - 6.85 (4 H, m), 5.01 (1 H, m), 4.21 - 4.09 (2 H, m), 3.86 (3 H, s), 3.79 - 3.76 (1 H, m), 3.78 (3 H, s), 3.77 (3 H, s), 2.85 (1 H, dd, *J* 16.4, 10.0), 2.79 (1 H, dd, *J* 15.5, 2.5), 2.18 - 2.06 (3 H, m), 1.81 (1 H, dddd *J* 13.6, 11.0, 7.0, 4.8), 1.53 (1 H, m), 1.37 - 1.26 (1 H, m), 1.17 - 1.08 (1 H, m), 0.87 (3 H, d, *J* 6.7), 0.84 (3 H, d, *J* 6.7); δ_C (100 MHz; $CDCl_3$) 175.9 (C), 174.4 (C), 170.0 (C), 158.2 (C), 153.9 (C), 153.1 (C), 144.2 (C), 141.5 (C), 136.1 (C), 131.6 (C), 129.3 (C), 124.1 (CH), 121.0 (C), 114.7 (CH), 115.5 (CH), 74.7 (CH), 69.7 (CH), 64.7 (CH_2), 62.0 (Me), 55.8 (Me), 36.5 (CH_2), 35.4 (CH_2), 34.3 (CH_2), 33.3 (CH_2), 32.0 (Me), 27.9 (CH), 22.9 (Me), 22.4 (Me)

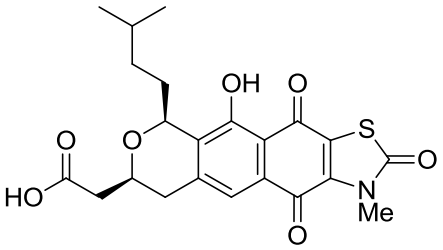
cis-5-Hydroxy-8-(2-hydroxyethyl)-6-isopentyl-1-methyl-8,9-dihydro-1*H*-pyrano[3',4':6,7]naphtho[2,3-*d*]thiazole-2,4,11(6*H*)-trione



Silver(II) oxide (115 mg, 0.93 mmol) and nitric acid (6 M; 186 μL, 1.12 mmol) were added to a solution of *cis*-5-hydroxy-6-isopentyl-8-(2-(4-methoxyphenoxy)ethyl)-1-methyl-8,9-dihydro-1*H*-pyrano[3',4':6,7]naphtho[2,3-*d*]thiazole-2,4,11(6*H*)-trione **15** (100 mg, 0.186 mmol) in dioxane (2 mL) and the suspension was stirred for 30 min, after which time almost all of the silver(II) oxide had dissolved. The reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated and the residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate - light petroleum (2:8 - 2:3) to give the *title compound* as a red solid (67 mg, 84%); 140 – 142 ºC (Found: [M + Na^+], 454.1292. $C_{22}H_{25}NNaO_6S^+$ requires 454.1295); ν_{max}

($CHCl_3$) 3627, 3524, 3013, 2960, 2931, 2872, 1690, 1624, 1565, 1444, 1383, 1276, 1039 cm^{-1}; λ_{max} (MeOH)/nm 215 (4.74), 246 (4.60), 266 (4.78), 327 (4.22), 437 (4.05); δ_H (400 MHz; $CDCl_3$) 12.37 (1 H, s), 7.43 (1 H, s), 5.07 (1 H, dd, *J* 6.4, 1.7). 3.89 (2 H, t, *J* 5.7), 3.82 - 3.77 (1 H, m), 3.79 (3 H, s), 2.87 (1 H, ddd, *J* 16.6, 10.6, 1.2), 2.68 (1 H, dt, *J* 16.4, 1.6), 2.61 (1 H, br s), 2.17 (1 H, dddd, *J* 13.9, 11.3, 5.1, 2.7), 1.96 - 1.85 (3 H, m), 1.57 - 1.49 (1 H, m), 1.40 - 1.30 (1 H, m), 1.15 - 1.05 (1 H, m), 0.88 (3 H, d, *J* 6.6), 0.86 (3 H, d, *J* 6.6); δ_C (100 MHz; $CDCl_3$) 182.0 (C), 174.1 (C), 169.8 (C), 158.8 (C), 144.6 (C). 137.9 (C), 135.1 (C), 129.1 (C), 125.9 (C), 125.9 (C), 121.1 (CH), 111.7 (C), 74.5 (CH), 73.0 (CH), 61.1 (CH_2), 37.2 (CH_2), 36.3 (CH_2), 34.1 (CH_2), 32.2 (Me), 32.0 (CH_2), 28.0 (CH), 22.8 (Me), 22.3 (Me).

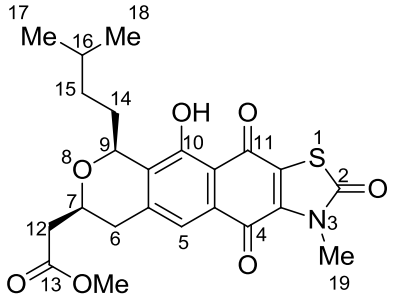
Mevashuntin 1



Jones reagent was added to a solution of *cis*-5-hydroxy-8-(2-hydroxyethyl)-6-isopentyl-1-methyl-8,9-dihydro-1*H*-pyrano[3',4':6,7]naphtho[2,3-*d*]thiazole-2,4,11(6*H*)-trione (5 mg, 11.6 μmol) in acetone (3 mL) until a deep orange color persisted (2 drops). The mixture was stirred for 15 min, diluted with water (10 mL) and extracted with ethyl acetate (3 x 8 mL). The combined extracts were washed with water (20 mL) and brine (20 mL), dried (Na_2SO_4) and concentrated. The residue was purified by flash column chromatography through a short plug of silica gel eluting with ethyl acetate – light petroleum (2:3) to give the *title compound* as an orange-red solid (3.5 mg, 68%); mp 169 - 170 ºC (lit.,[2] mp 166 – 167 ºC); (Found: [M - H^+], 444.1143. $C_{22}H_{22}NO_7S^-$ requires 444.1122), ν_{max} ($CHCl_3$) 3690, 3513, 2958, 2929, 2871, 1749, 1689, 1622, 1563, 1381, 1273 cm^{-1}; λ_{max} (MeOH)/nm 215 (4.12), 246 (3.98), 266 (3.64), 330 (3.64), 429 (3.45); δ_H (400 MHz; $CDCl_3$; 30 mg/mL) 12.33 (1 H, s, 10-OH), 7.30 (1 H, H-5), 5.07 (1 H, br d, *J* 4.2, H-9), 4.00 (1 H, m, H-7), 3.77 (3 H, s, H-19), 2.81 (3 H, dd, *J* 13.5, 7.0, H-12a), 2.69 (1 H, dd, *J* 15.7, 5.8, H-12b), 2.13 (1 H, dddd, *J*

16.6, 8.2, 5.2, 3.2, H-14a), 1.92 (1 H, dddd, *J* 13.8, 11.2, 6.3, 4.8, H-14b), 1.57 - 1.47 (1 H, m, H-16), 1.36 - 1.24 (1 H, m, H-15a), 1.06 (1 H, dddd, *J* 12.5, 11.9, 7.2, 4.8, H-15b), 0.86 (3 H, d *J* 6.7), 0.84 (3 H, d, *J* 6.7); δ_C (100 MHz; $CDCl_3$; 30 mg/mL) 181.9 (C), 176.0 (C), 174.0 (C), 169.8 (C), 158.7 (C), 144.1 (C), 137.9 (C), 135.2 (C), 129.1 (C), 125.9 (C), 121.1 (CH), 111.7 (C), 74.6 (CH), 69.0 (CH), 40.3 (CH_2), 35.8 (CH_2), 33.8 (CH_2), 32.2 (Me), 31.7 (CH_2), 28.0 (CH), 22.8 (Me), 22.4 (Me).

Mevashuntin methyl ester 16



Trimethylsilyldiazomethane solution (2 M in ether; 5 drops) was added to a solution of mevashuntin (9 mg, 0.0021 mmol) in toluene (0.8 mL) - MeOH (0.2 mL). The mixture was stirred at rt for 1 h then acetic acid (5 drops) was added and the solution stirred until nitrogen was no longer evolved. The reaction mixture was concentrated *in vacuo* and the residue purified by flash column chromatography on silica gel eluting with ethyl acetate - light petroleum (1:99 - 1:9) to give the *title compound* as an orange powder (8 mg, 83%); 158-160 ºC, (Found: [M + Na^+], 482.1231. $C_{23}H_{25}NNaO_7S^+$ requires 482.1244); ν_{max} ($CHCl_3$) 3693, 3013, 2958, 2872, 1737, 1690, 1624, 1565, 1442, 1383, 1275 cm^{-1}; λ_{max} (CH_2Cl_2)/nm 214 (4.59), 246 (4.42), 266 (4.61), 326 (1.01), 432 (3.90); δ_H (400 MHz; $CDCl_3$) 12.35 (1 H, s, OH), 7.43 (1 H, s, H-5), 5.06 - 5.04 (1 H, m, H-9), 4.01 - 3.95 (1 H, m, H-9), 3.79 (3 H, s, H-19), 3.74 (3 H, s, H-13), 2.80 (2 H, dd, *J* 5.4, 1.4, H-6), 2.75 (1 H, dd, *J* 15.7, 6.9, H-12a), 2.62 (1 H, dd, *J* 15.7, 5.6, H-12b), 2.14 (1 H, dddd, *J* 13.7, 11.4, 5.2, 2.9, H-14a), 1.91 (1 H, dddd *J* 13.7, 11.2, 6.7, 4.7, H-14b), 1.56 - 1.47 (1 H, m, H-16), 1.31 (1 H, dddd, *J* 12.8, 11.2, 7.3, 5.5, H-15a), 1.06 (1 H, dddd, *J* 12.8, 11.7, 7.3, 4.7, H-15b), 0.86 (3 H, d, *J* 6.7), 0.84 (3 H, d, *J* 6.7); δ_C (100 MHz; $CDCl_3$) 182.0 (C), 174.1 (C), 171.2 (C), 169.8 (C), 158.8 (C), 144.4 (C), 137.9 (C), 135.4 (C), 128.8

(C), 125.9 (C), 121.1 (CH), 111.7 (C), 74.5 (CH), 69.2 (CH), 51.8 (Me), 40.4 (CH_2), 35.8 (CH_2), 33.8 (CH_2), 32.2 (Me), 31.8 (CH_2), 28.0 (CH), 22.9 (Me), 22.3 (Me);

Comparison of Natural and Synthetic Mevashuntin 1

^{13}C NMR data for natural *vs.* synthetic mevashuntin					
Atom	Natural	Synthetic (3mg/mL)	Synthetic (30mg/mL)	δC (3mg/mL)	δC (30 mg/mL)
2	169.8	169.8	169.8	0.0	0.0
3a	137.9	138.0	137.9	0.1	0.0
4	174.1	173.8	174.0	-0.3	-0.1
4a	129.3	129.2	129.1	-0.1	-0.2
5	121	121.0	121.1	0.0	0.0
5a	144	143.9	144.1	-0.1	0.1
6	35.7	35.7	35.8	0.0	0.1
7	69	69.1	69.0	0.1	0.0
9	74.6	74.7	74.6	0.1	0.0
9a	135	134.9	135.2	-0.1	0.2
10	158.7	158.8	158.7	0.1	0.0
10a	111.7	111.8	111.7	0.1	0.0
11	182	182.0	181.9	0.0	-0.1
11a	125.9	125.9	125.9	0.0	0.0
12	40.1	40.0	40.3	-0.1	0.2
13	175	174.1	176.0	-0.9	1.0
14	31.7	31.8	31.7	0.1	0.0
15	33.7	33.8	33.8	0.1	0.1
16	27.9	28.0	28.0	0.1	0.1
17	22.8	22.8	22.8	0.0	0.0
18	22.3	22.4	22.4	0.1	0.1
19	32	32.2	32.2	0.2	0.2

^{1}H NMR data for natural *vs.* synthetic mevashuntin					
Atom	Natural	Synthetic (30mg/mL)	Synthetic (30mg/mL)	δH (3mg/mL)	δH (30 mg/mL)
5	7.4	7.44	7.39	0.04	0.01
6	2.81	2.83	2.81	0.02	0.00
7	3.97	3.8	4.00	-0.17	0.03
9	5.07	5.11	5.07	0.04	0.00
12a	2.78	2.8	2.81	0.02	0.03
12b	2.67	2.71	2.69	0.04	0.02
14a	1.91	1.93	1.92	0.02	0.01
14b	2.12	2.16	2.13	0.04	0.03
15a	1.3	1.32	1.30	0.02	0.00
15b	1.05	1.08	1.06	0.03	0.01
16	1.51	1.54	1.52	0.03	0.01
17	0.85	0.87	0.86	0.02	0.01
18	0.83	0.85	0.84	0.02	0.01
19	3.77	3.79	3.77	0.02	0.00
10-OH	12.33	12.37	12.33	0.04	0

Comparison of Natural and Synthetic Mevashuntin Methyl Ester 16

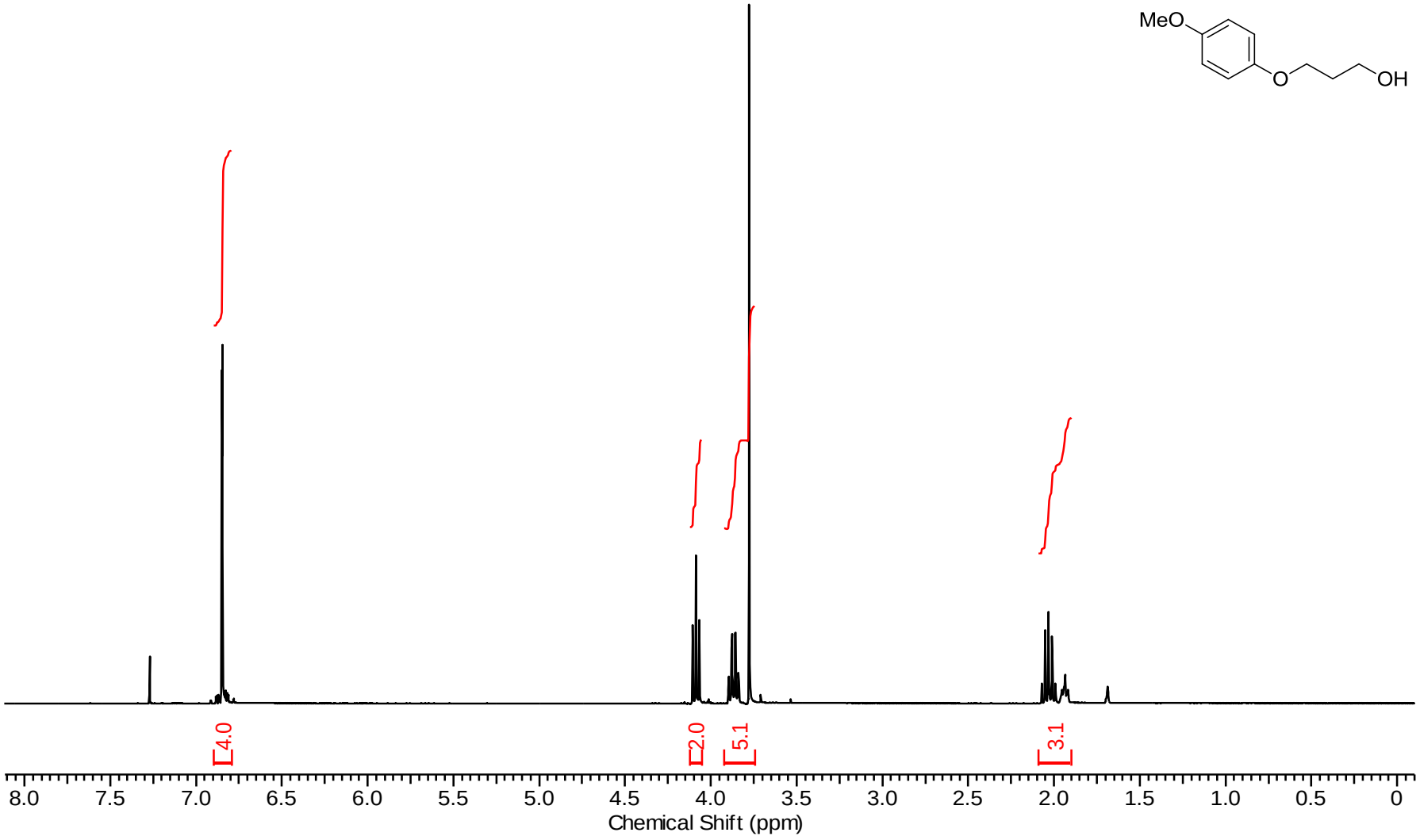
^{13}C NMR data for synthetic mevashuntin methyl ester *vs.* reported			
Atom	Reported	Synthetic	δC
2	169.8	169.80	0.00
3a	137.9	137.91	0.01
4	174.2	174.14	-0.06
4a	129.1	129.07	-0.03
5	121.1	121.10	0.00
5a	144.4	144.35	-0.05
6	35.9	35.84	-0.06
7	69.3	69.24	-0.06
9	74.5	74.46	-0.04
9a	135.4	135.40	0.00
10	158.8	158.78	-0.02
10a	111.7	111.65	-0.05
11	182	181.97	-0.03
11a	125.9	125.88	-0.02
12	40.4	40.38	-0.02
13	171.2	171.20	0.00
14	31.7	31.71	0.01
15	33.8	33.76	-0.04
16	27.9	27.92	0.02
17	22.8	22.92	0.12
18	22.4	22.34	-0.06
19	32.2	32.17	-0.03
13-OMe	51.8	51.78	-0.02

^{1}H NMR data for synthetic mevashuntin methyl ester *vs.* reported			
Atom	Reported	Synthetic	δH
5	7.41	7.43	0.02
6	2.78	2.8	0.02
7	3.96	3.98	0.02
9	5.03	5.05	0.02
12a	2.73	2.75	0.02
12b	2.6	2.62	0.02
14a	1.89	1.91	0.02
14b	1.29	1.31	0.02
16	1.5	1.52	0.02
17	0.84	0.86	0.02
18	0.82	0.84	0.02
19	3.77	3.79	0.02
10-OH	12.34	12.35	0.01
13-OMe	3.72	3.74	0.02

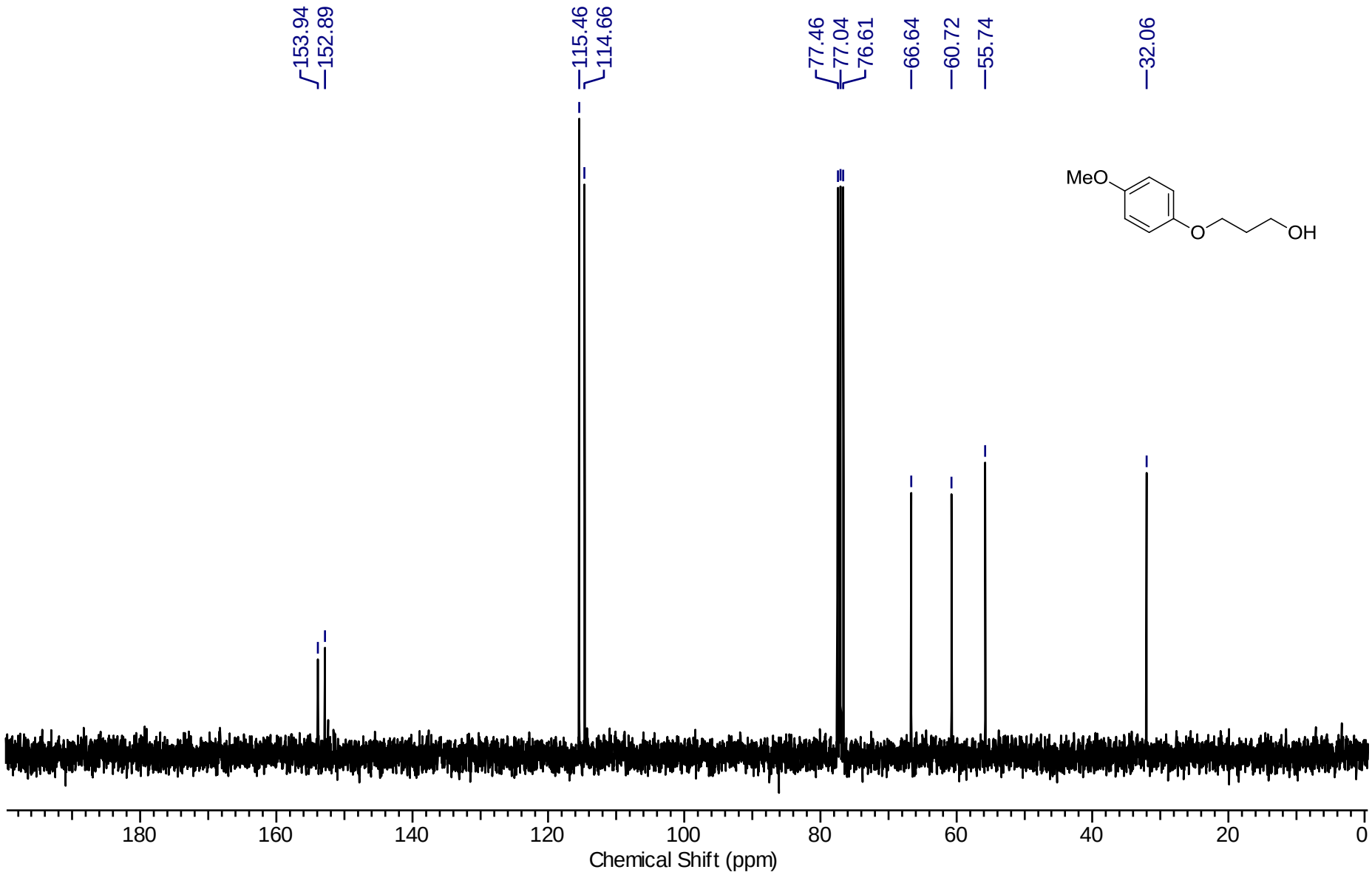
Copies of ^{1}H and ^{13}C NMR Spectra

3-(4-Methoxyphenoxy)propan-1-ol 9

^{1}H NMR at 300MHz in $CDCl_3$

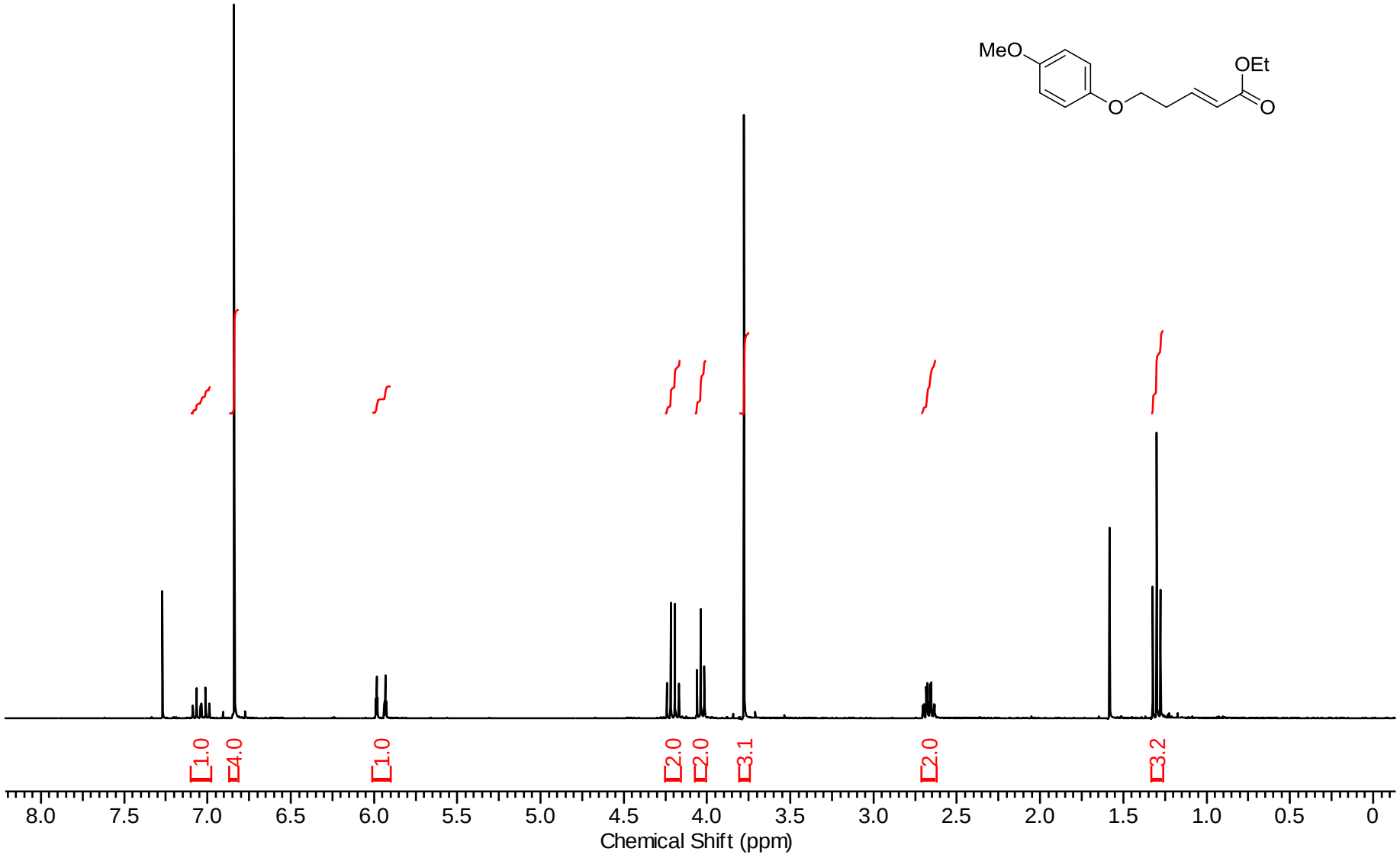


^{13}C NMR at 75MHz in $CDCl_3$

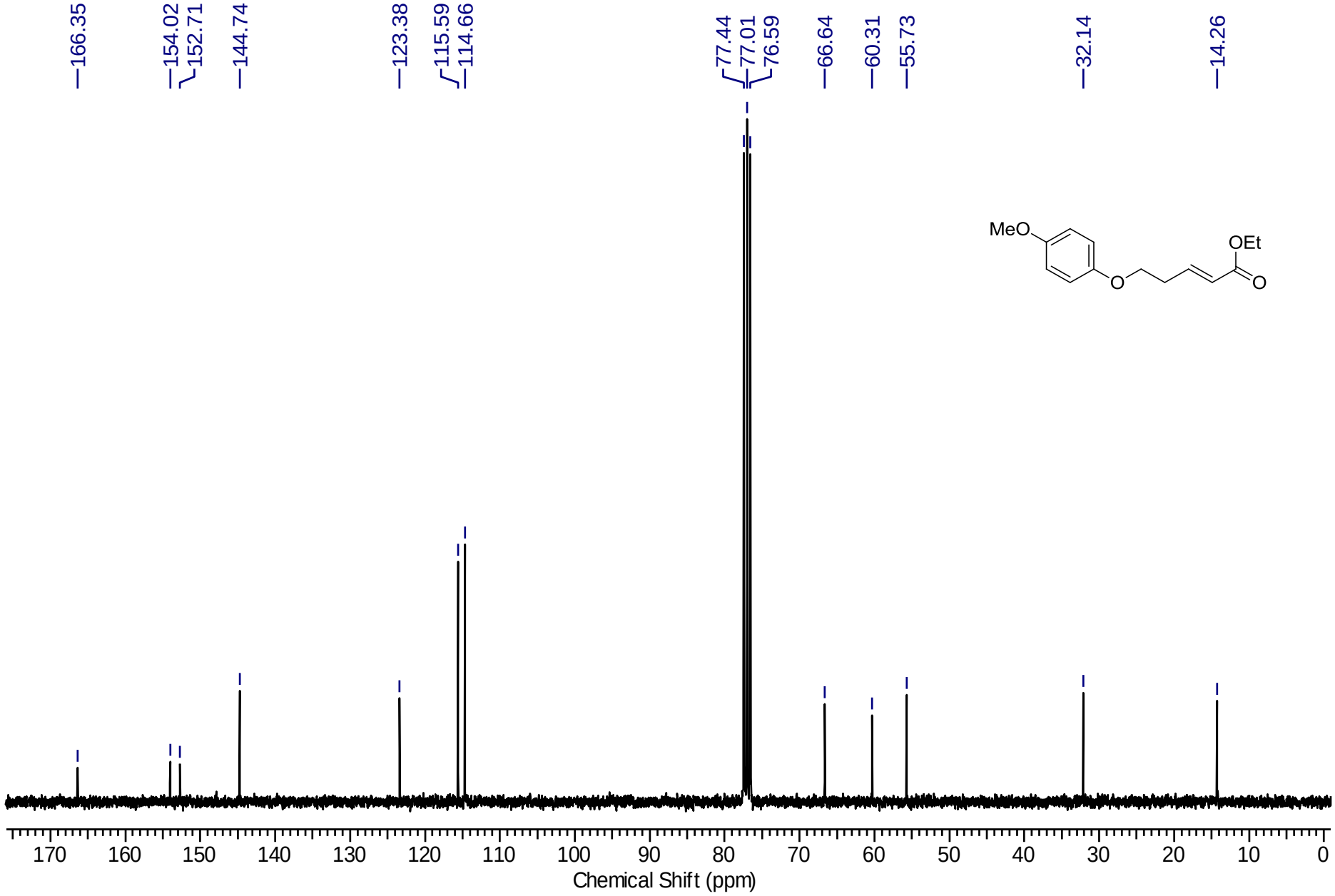


(*E*)-Ethyl 5-(4-methoxyphenoxy)pent-2-enoate

^{1}H NMR at 300MHz in $CDCl_3$

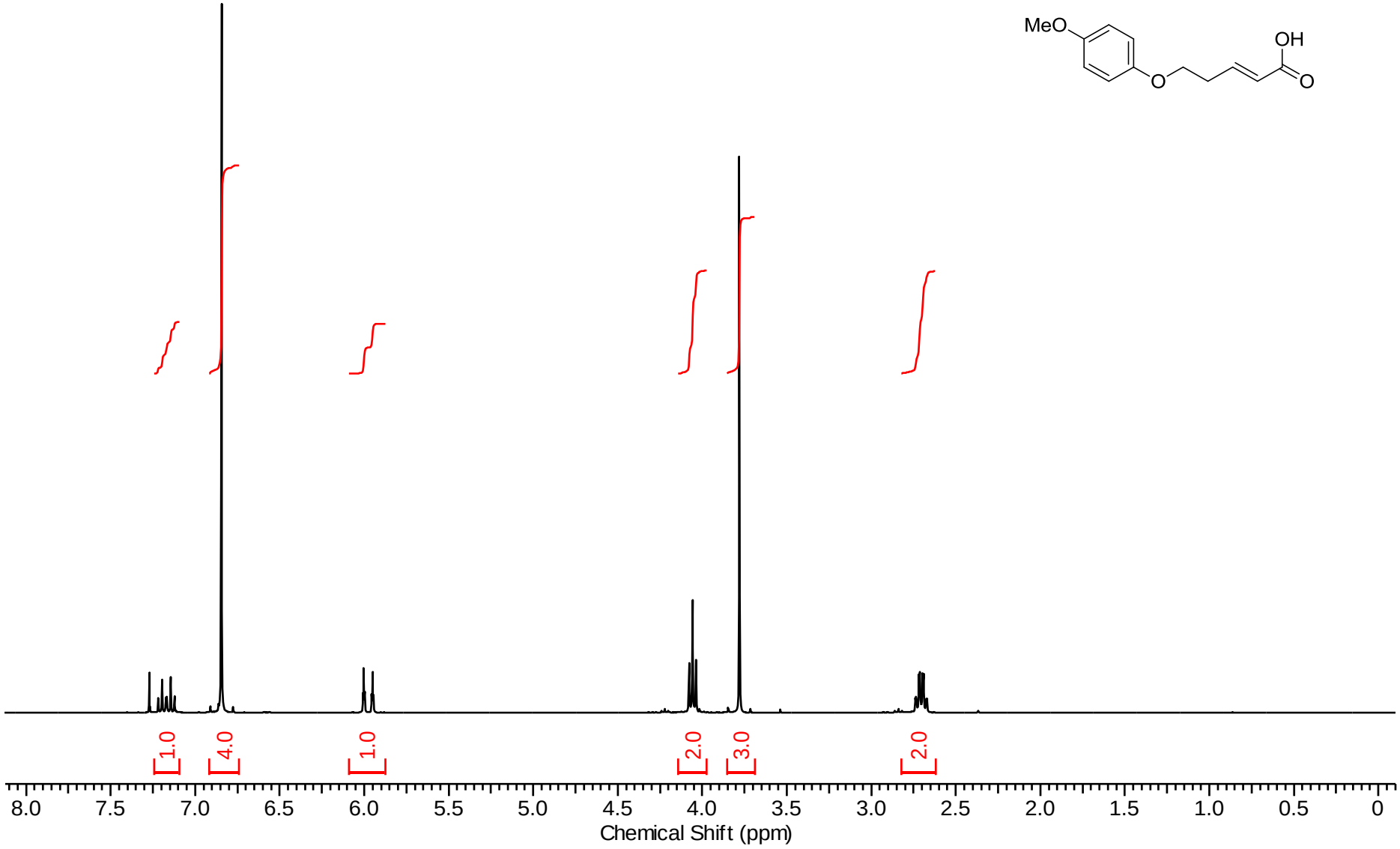


^{13}C NMR at 75MHz in $CDCl_3$

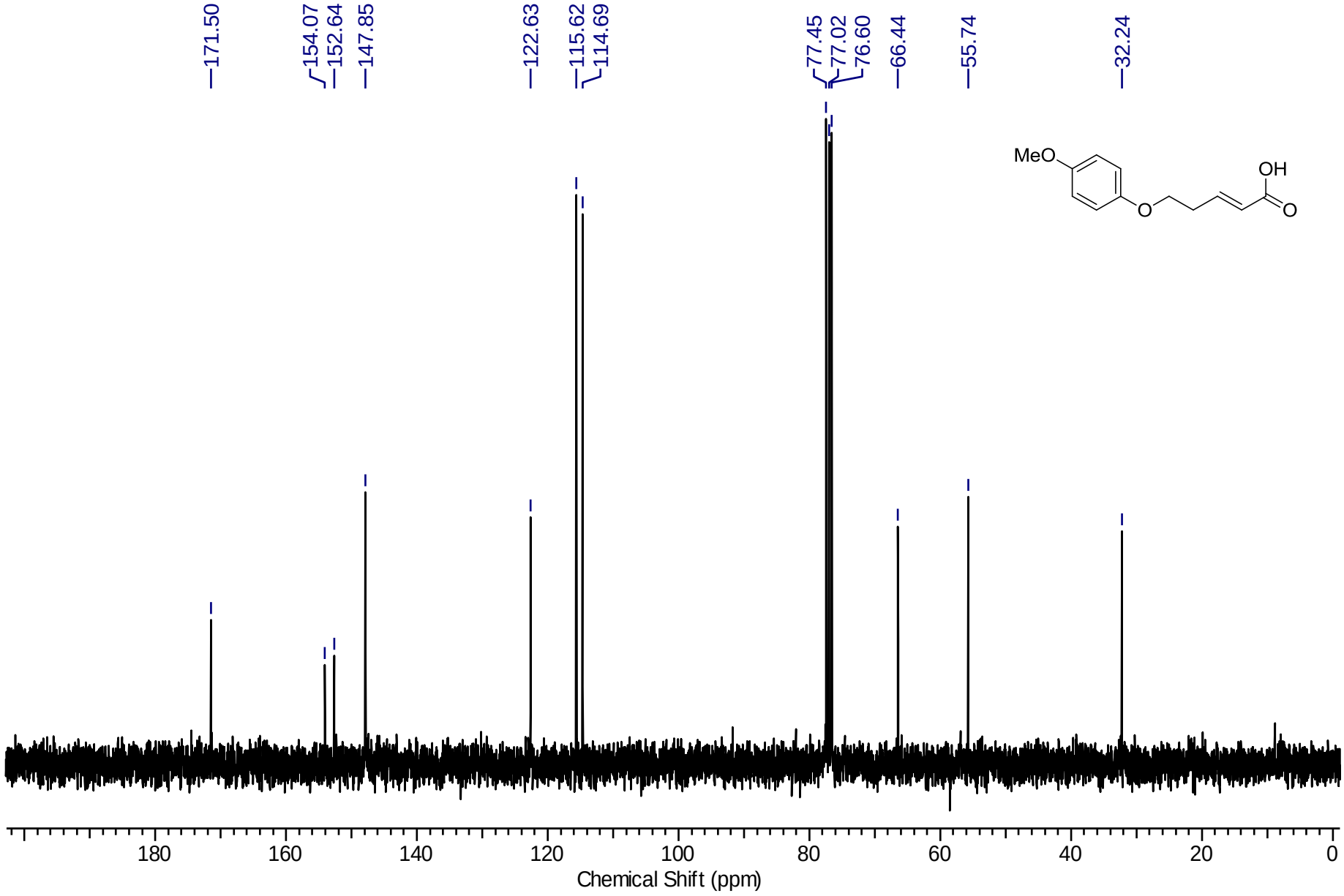


(*E*)-5-(4-Methoxyphenoxy)pent-2-enoic acid

^{1}H NMR at 300MHz in $CDCl_3$

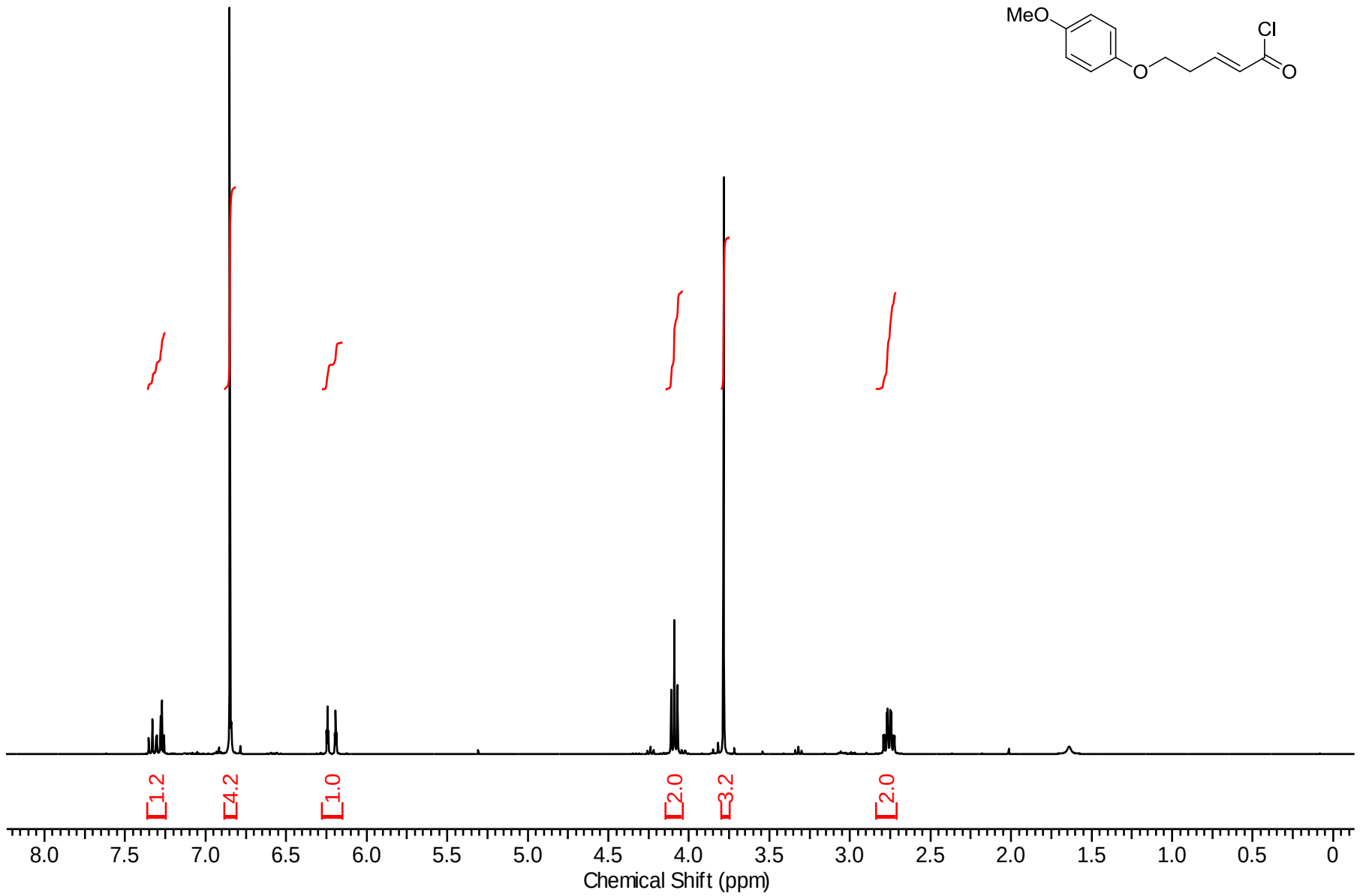


^{13}C NMR at 75MHz in $CDCl_3$

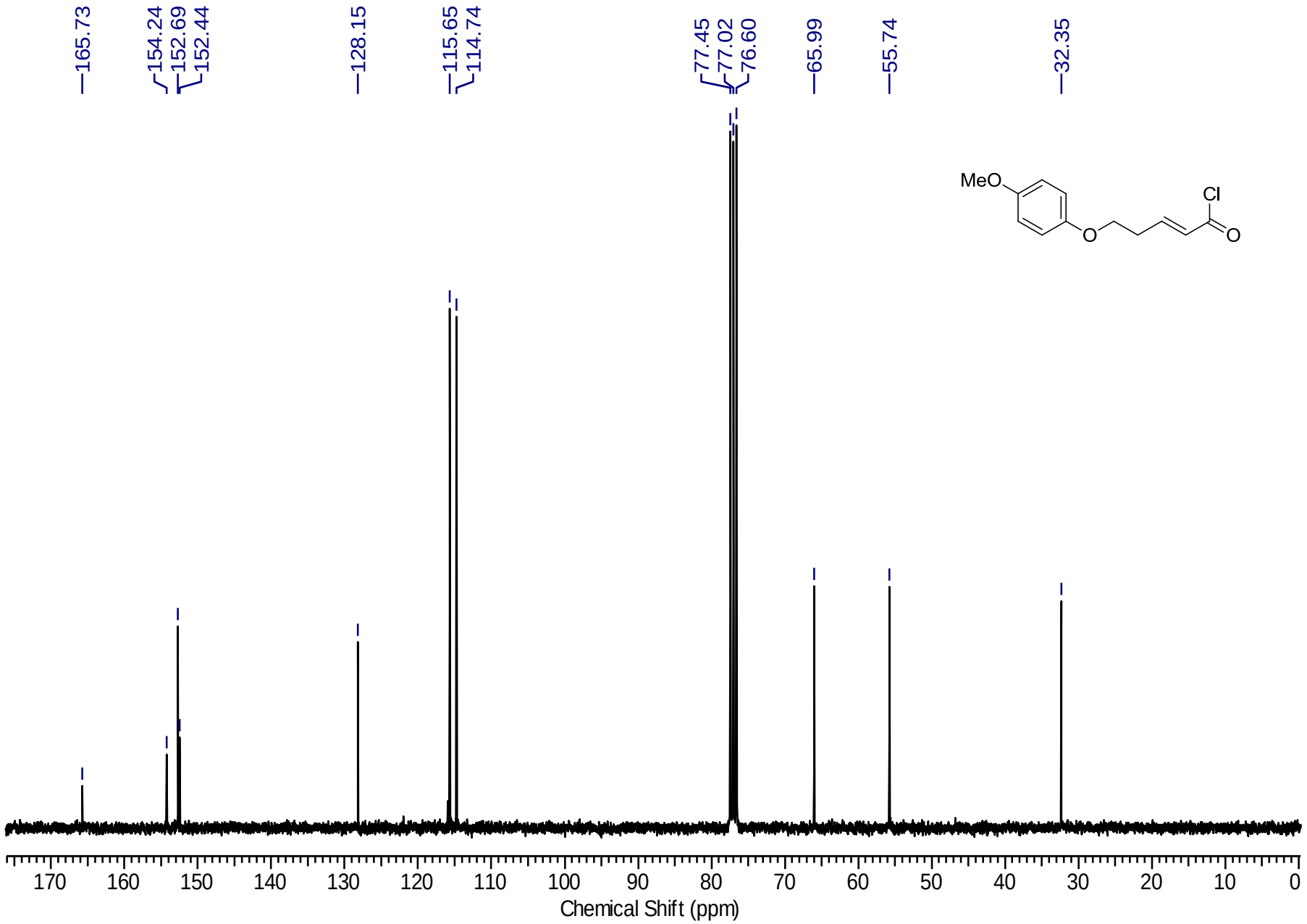


(*E*)-5-(4-Methoxyphenoxy)pent-2-enoyl chloride 10

^{1}H NMR at 300MHz in $CDCl_3$

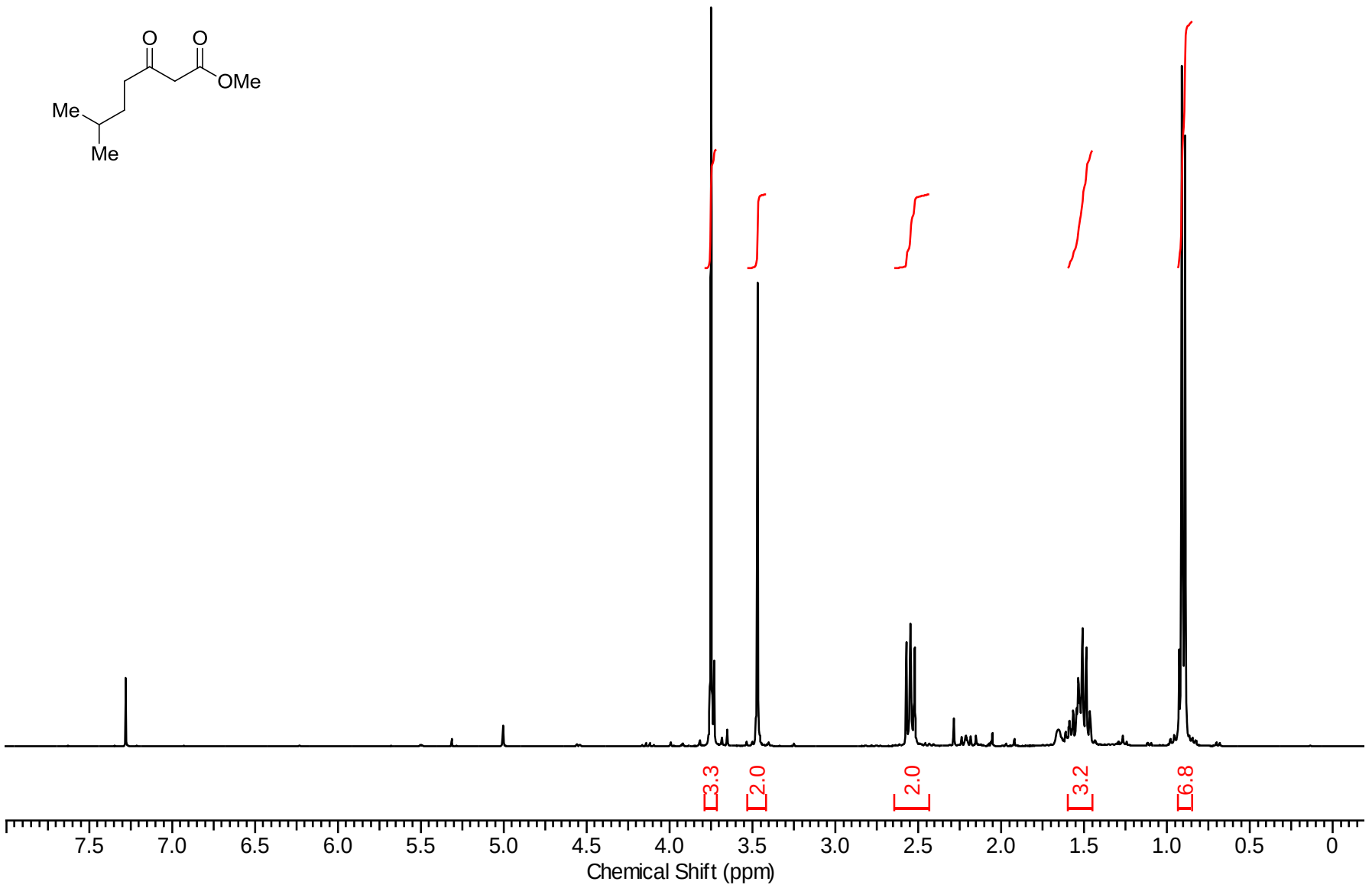


^{13}C NMR at 75MHz in $CDCl_3$

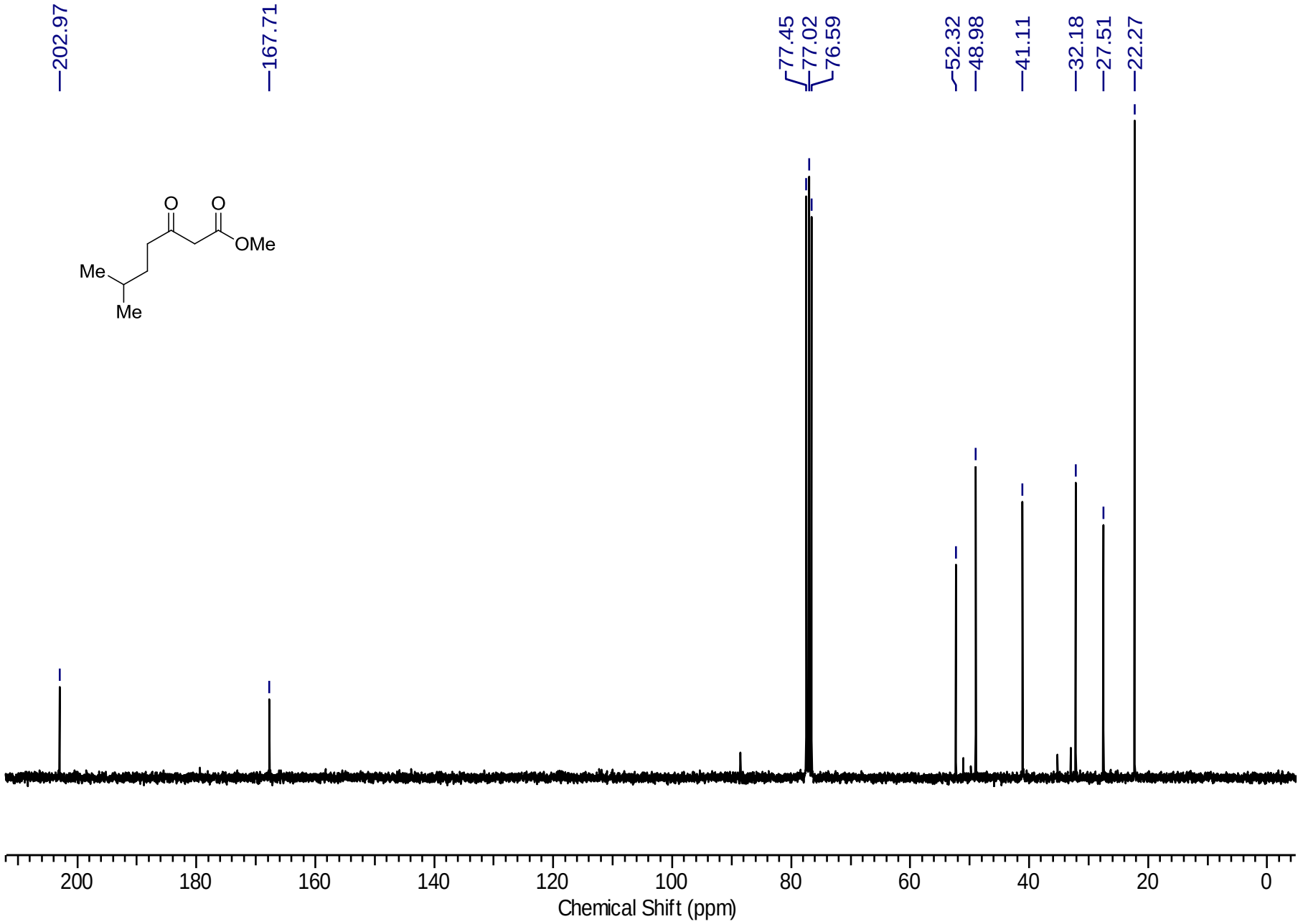


Methyl 6-methyl-3-oxoheptanoate 11

^{1}H NMR at 300MHz in $CDCl_3$

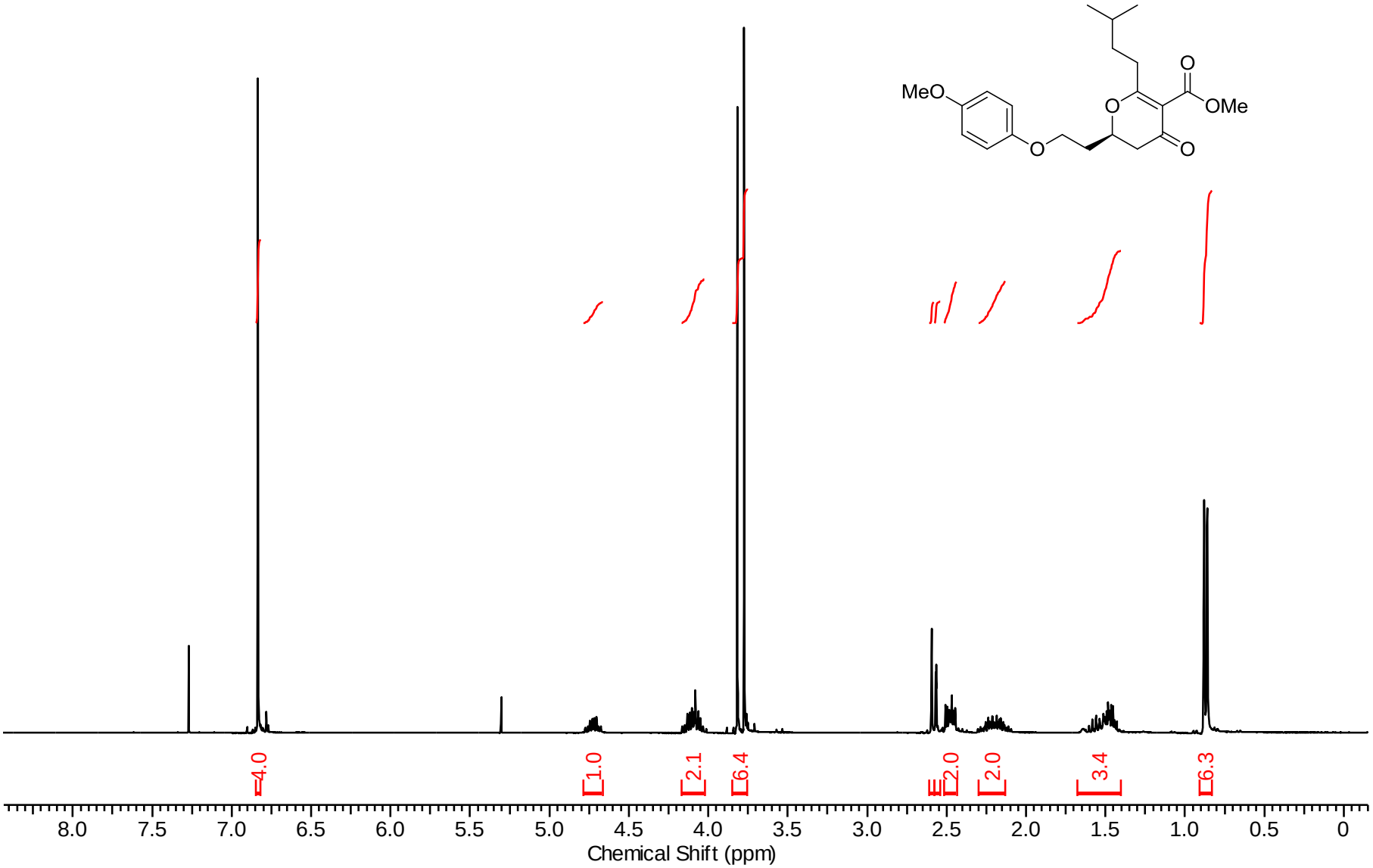


^{13}C NMR at 75MHz in $CDCl_3$

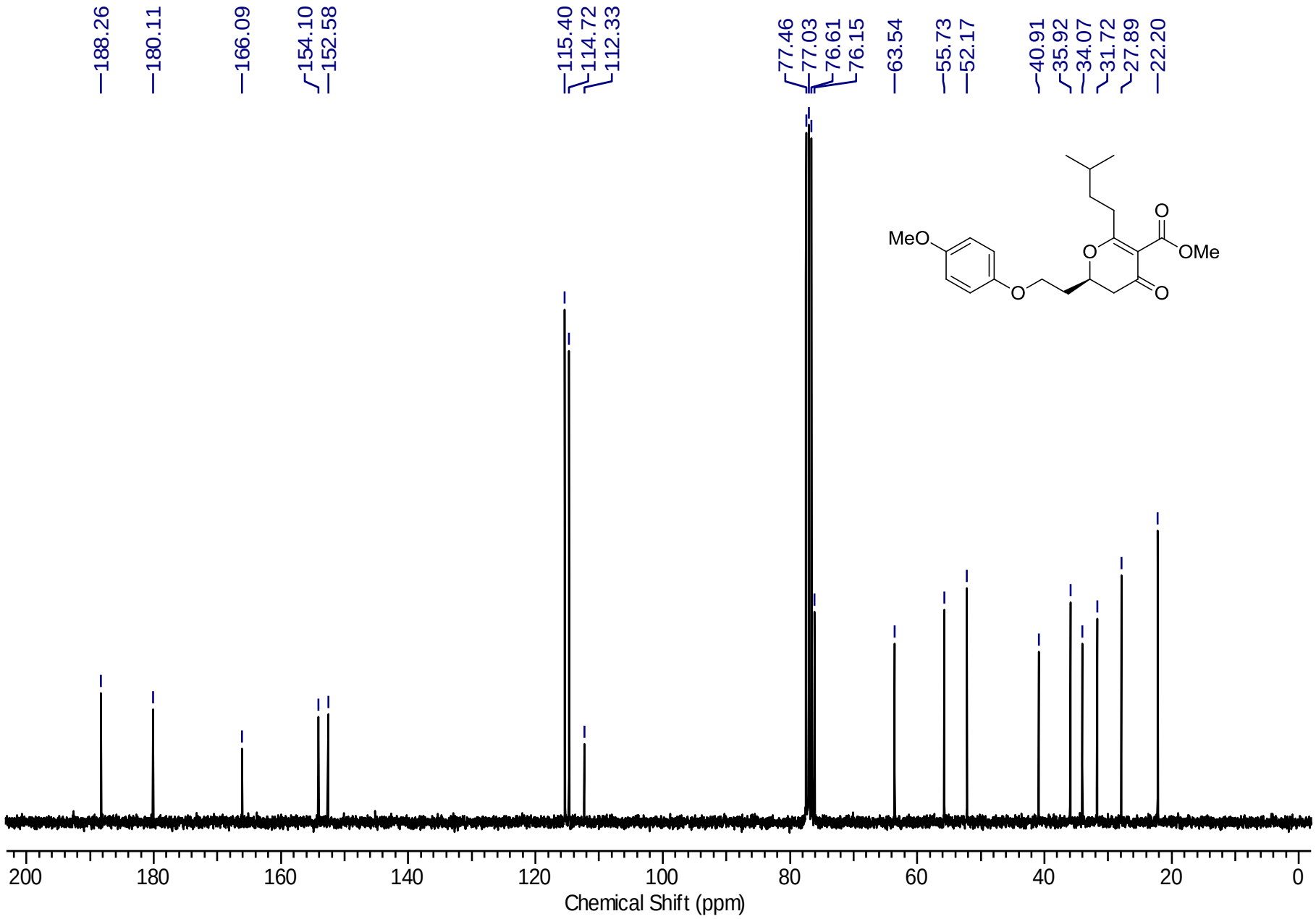


Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-oxo-5,6-dihydro-2H-pyran-3-carboxylate 12

^{1}H NMR at 300MHz in $CDCl_3$

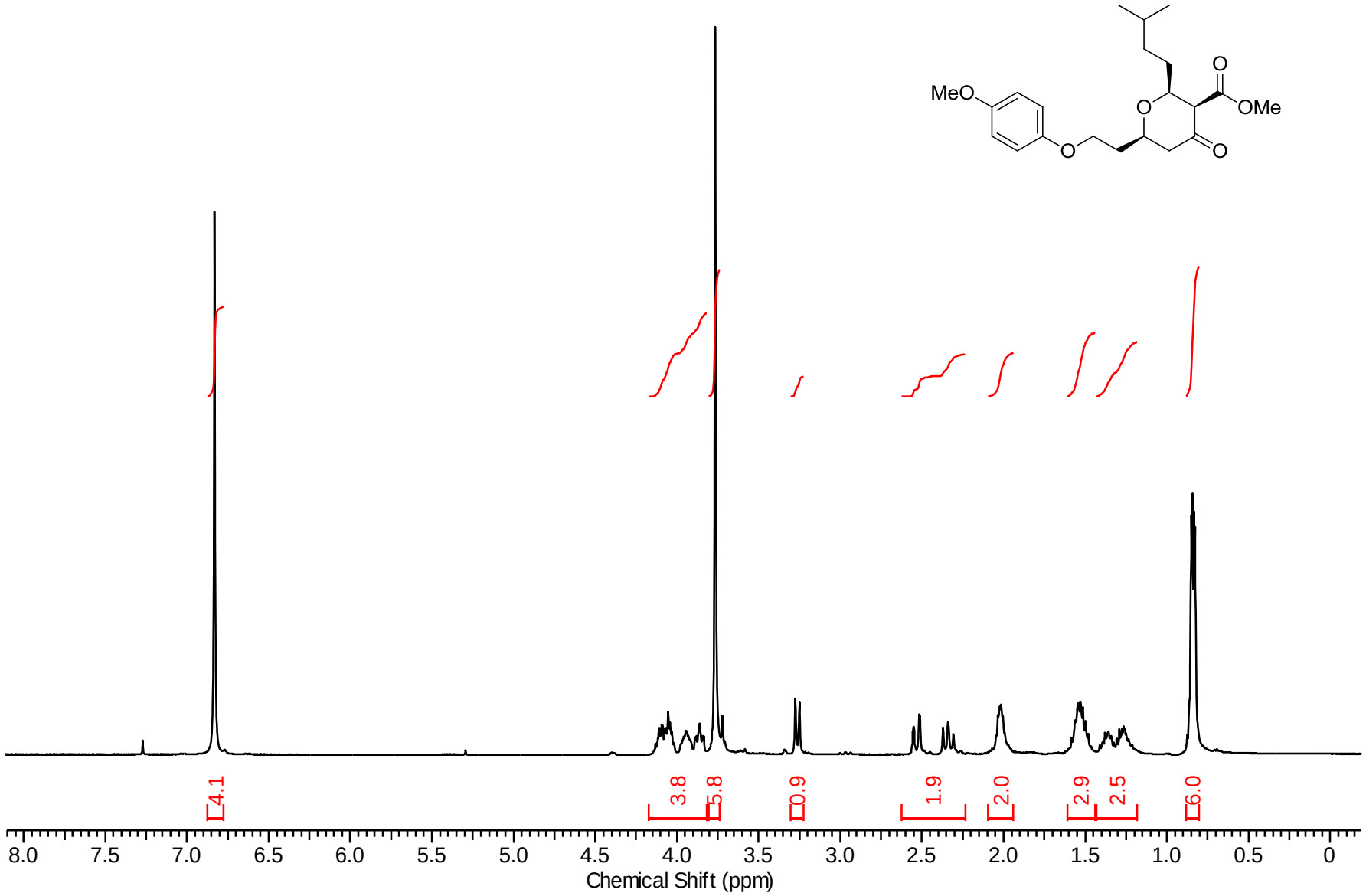


^{13}C NMR at 75MHz in $CDCl_3$

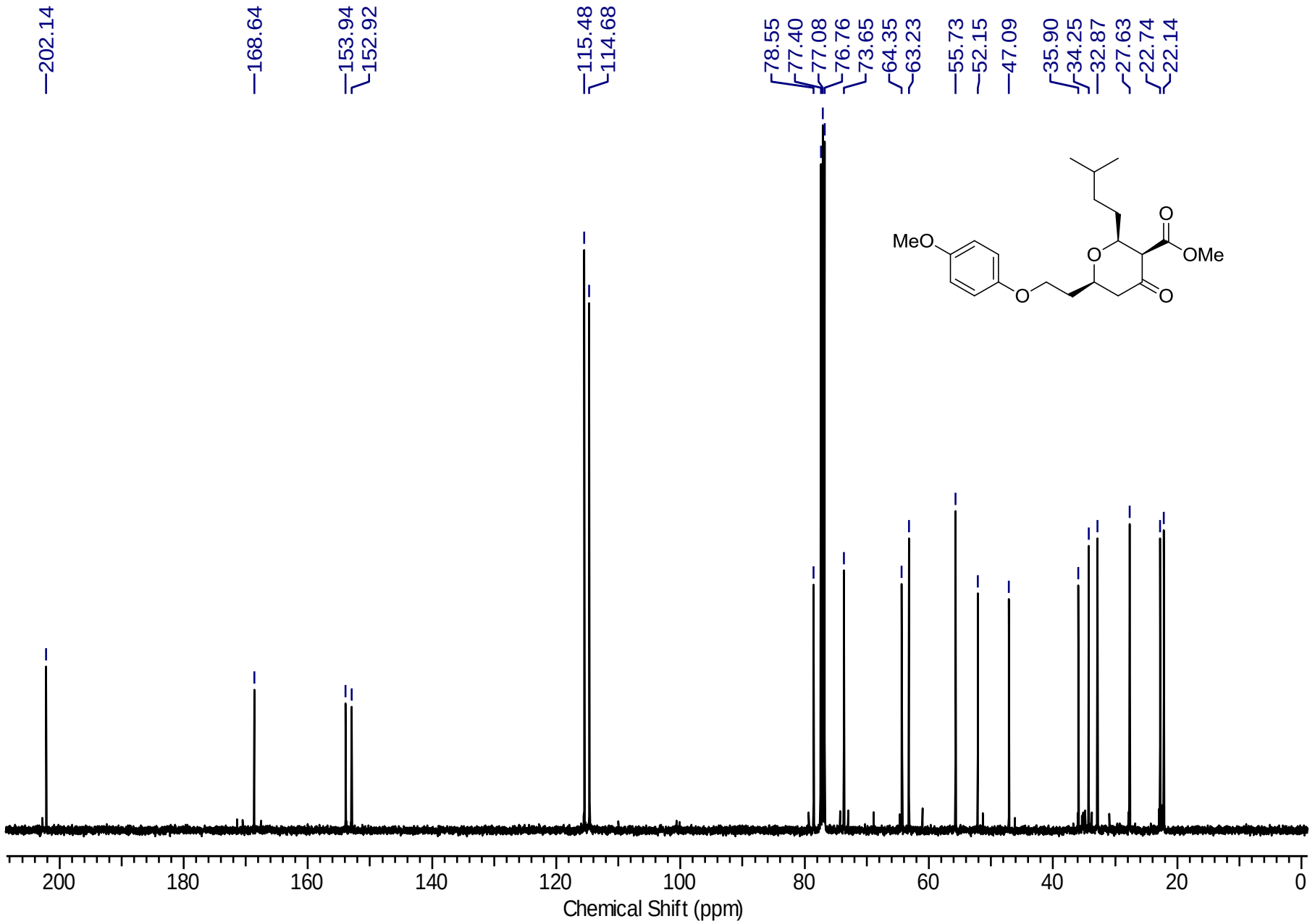


***cis*-Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-oxotetrahydro-2*H*-pyran-3-carboxylate**

^{1}H NMR at 400MHz in $CDCl_3$

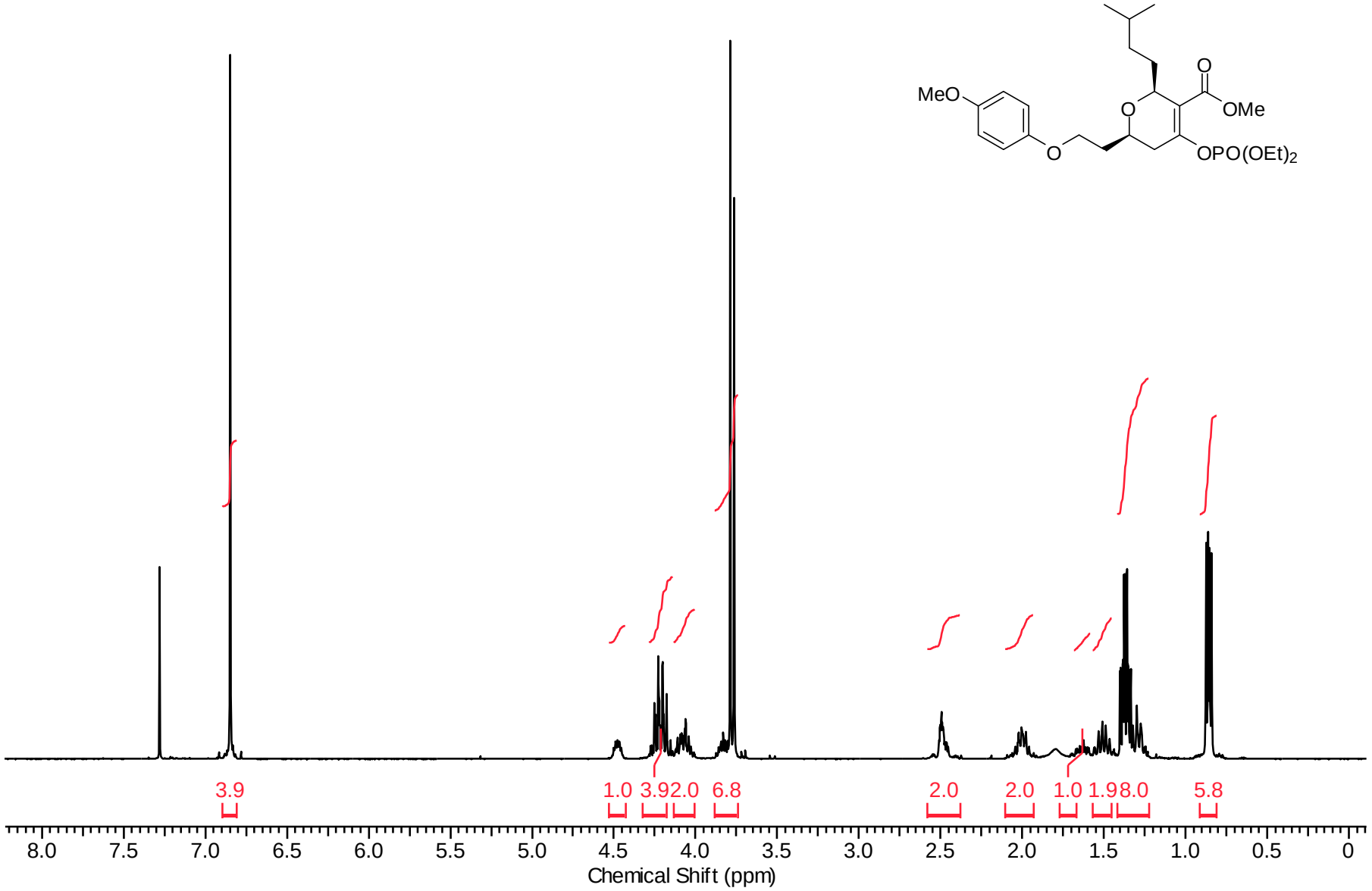


^{13}C NMR at 100MHz in $CDCl_3$

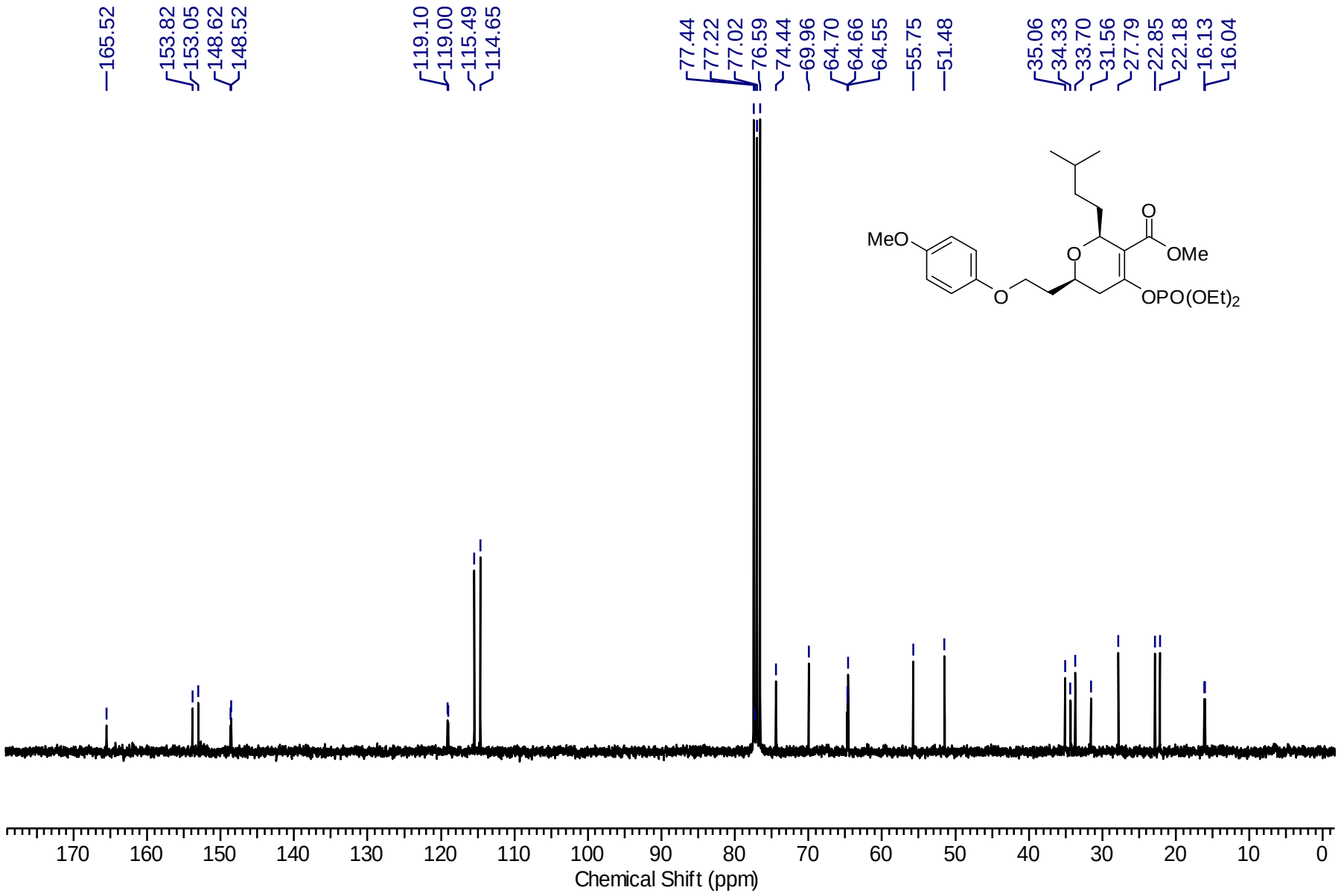


cis-Methyl 4-((diethoxyphosphoryl)oxy)-2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-5,6-dihydro-2_H_-pyran-3-carboxylate 13

^{1}H NMR at 300MHz in $CDCl_3$

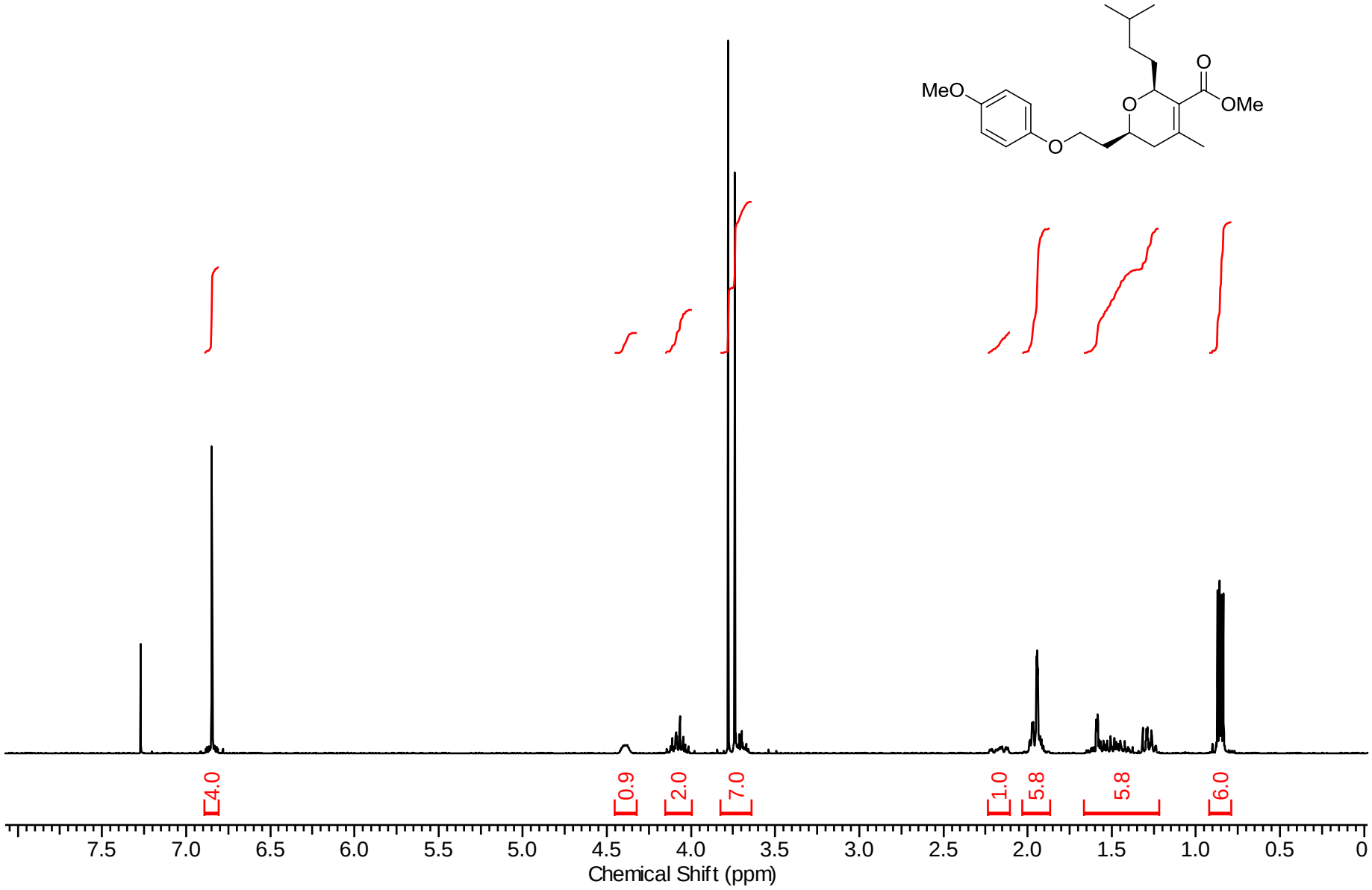


^{13}C NMR at 75MHz in $CDCl_3$

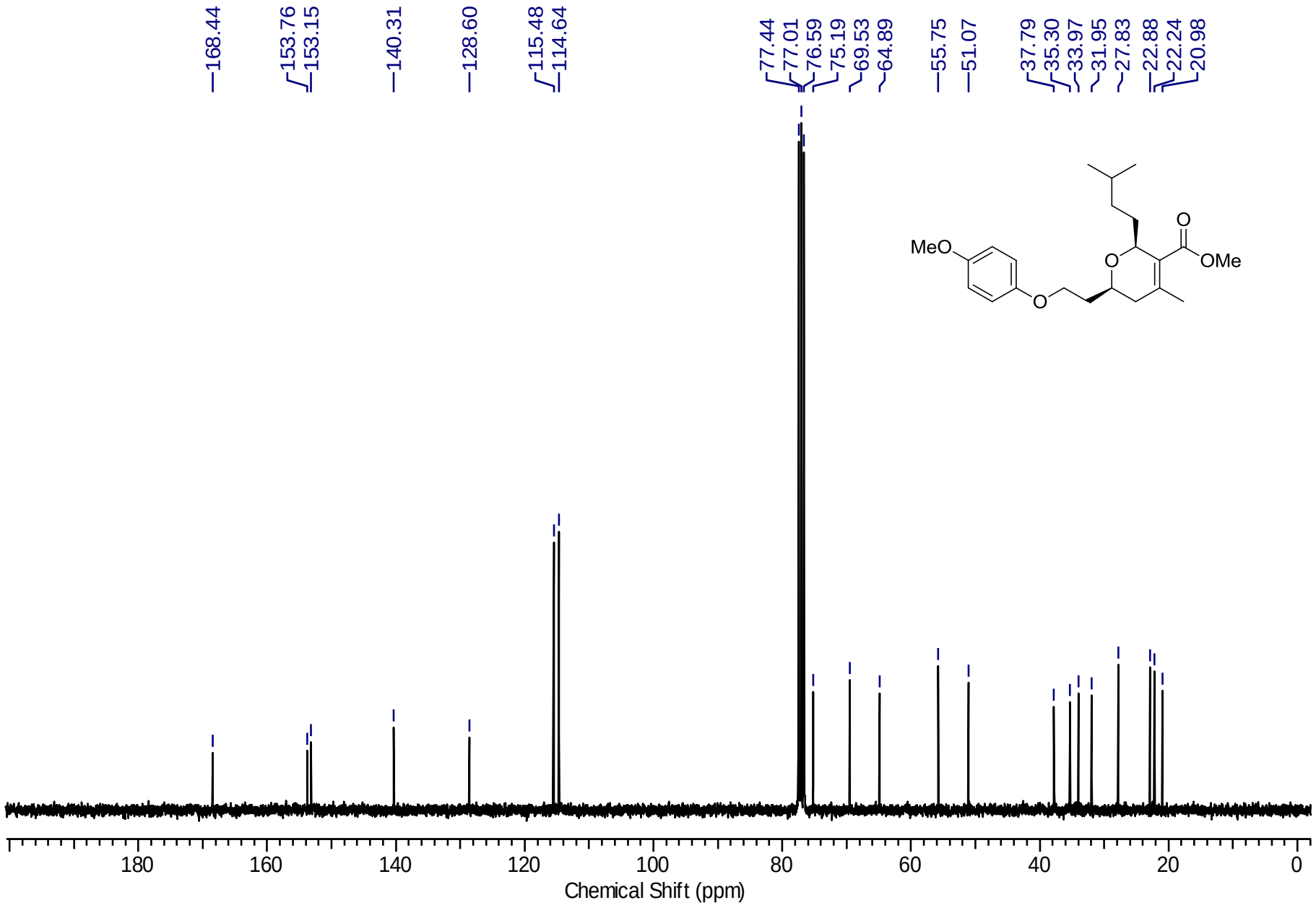


***cis*-Methyl 2-isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-methyl-5,6-dihydro-2*H*-pyran-3-carboxylate 14**

^{1}H NMR at 300MHz in $CDCl_3$

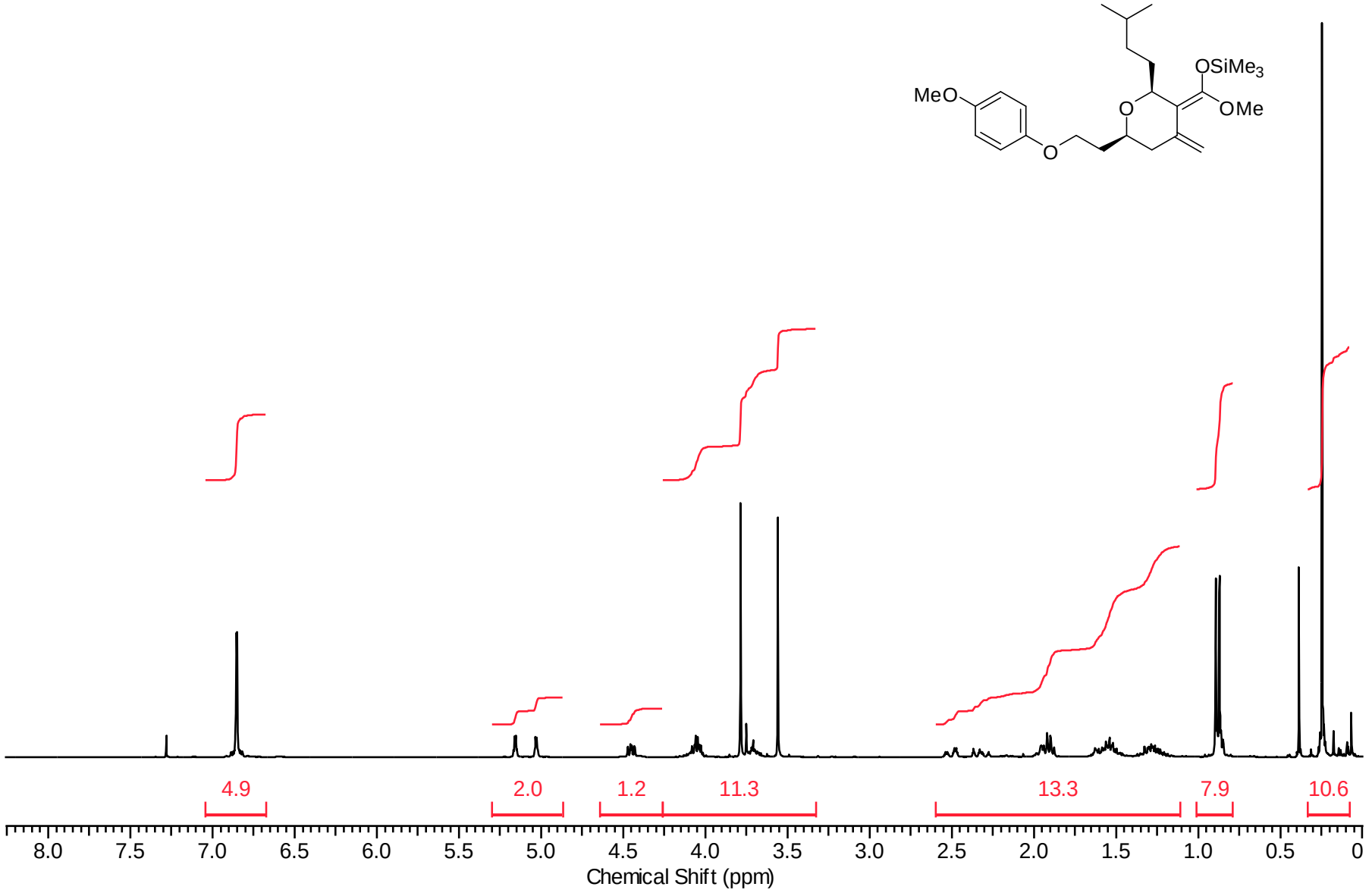


^{13}C NMR at 75MHz in $CDCl_3$

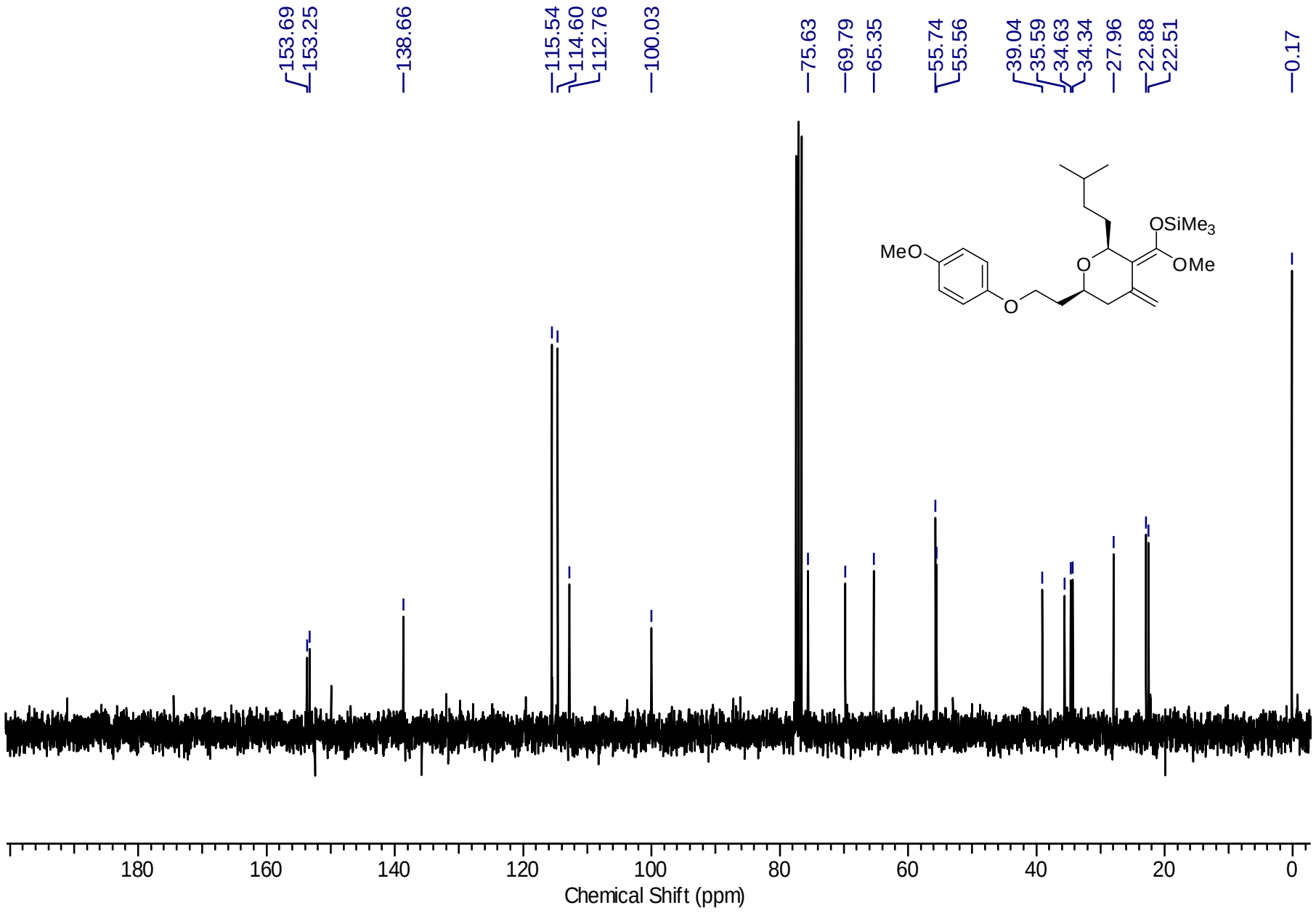


(*cis*-2-Isopentyl-6-(2-(4-methoxyphenoxy)ethyl)-4-methylenedihydro-2*H*-pyran-3(4*H*)-ylidene)(methoxy)methoxy)trimethylsilane 3

^{1}H NMR at 300MHz in $CDCl_3$

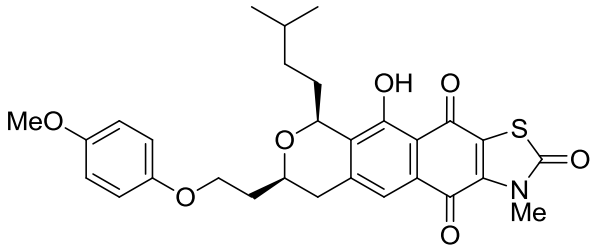


^{13}C NMR at 75MHz in $CDCl_3$

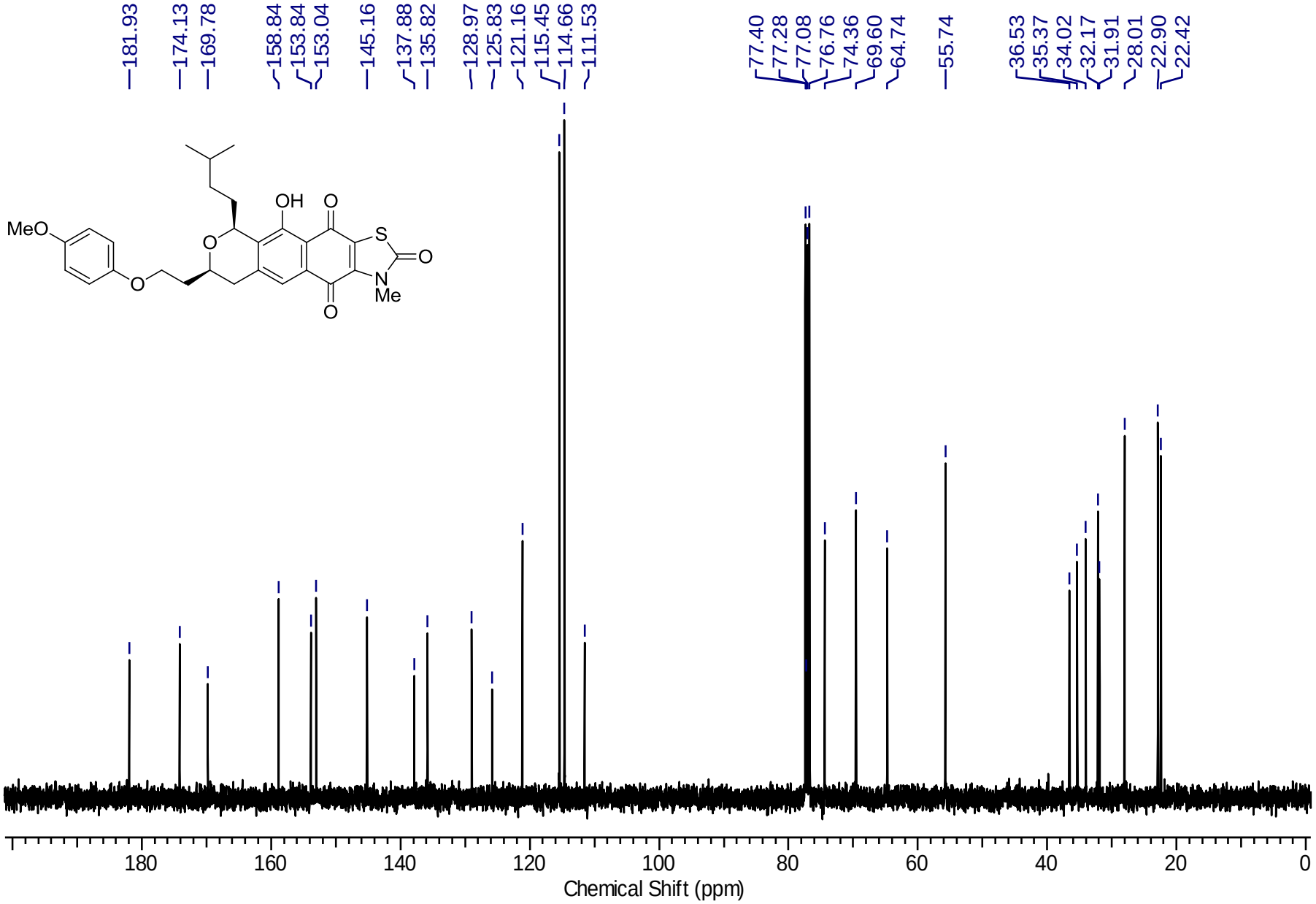


cis-5-Hydroxy-6-isopentyl-8-(2-(4-methoxyphenoxy)ethyl)-1-methyl-8,9-dihydro-1_H_-pyrano[3',4':6,7]naphtho[2,3-_d_]thiazole-2,4,11(6_H_)-trione 15

^{1}H NMR at 400MHz in $CDCl_3$

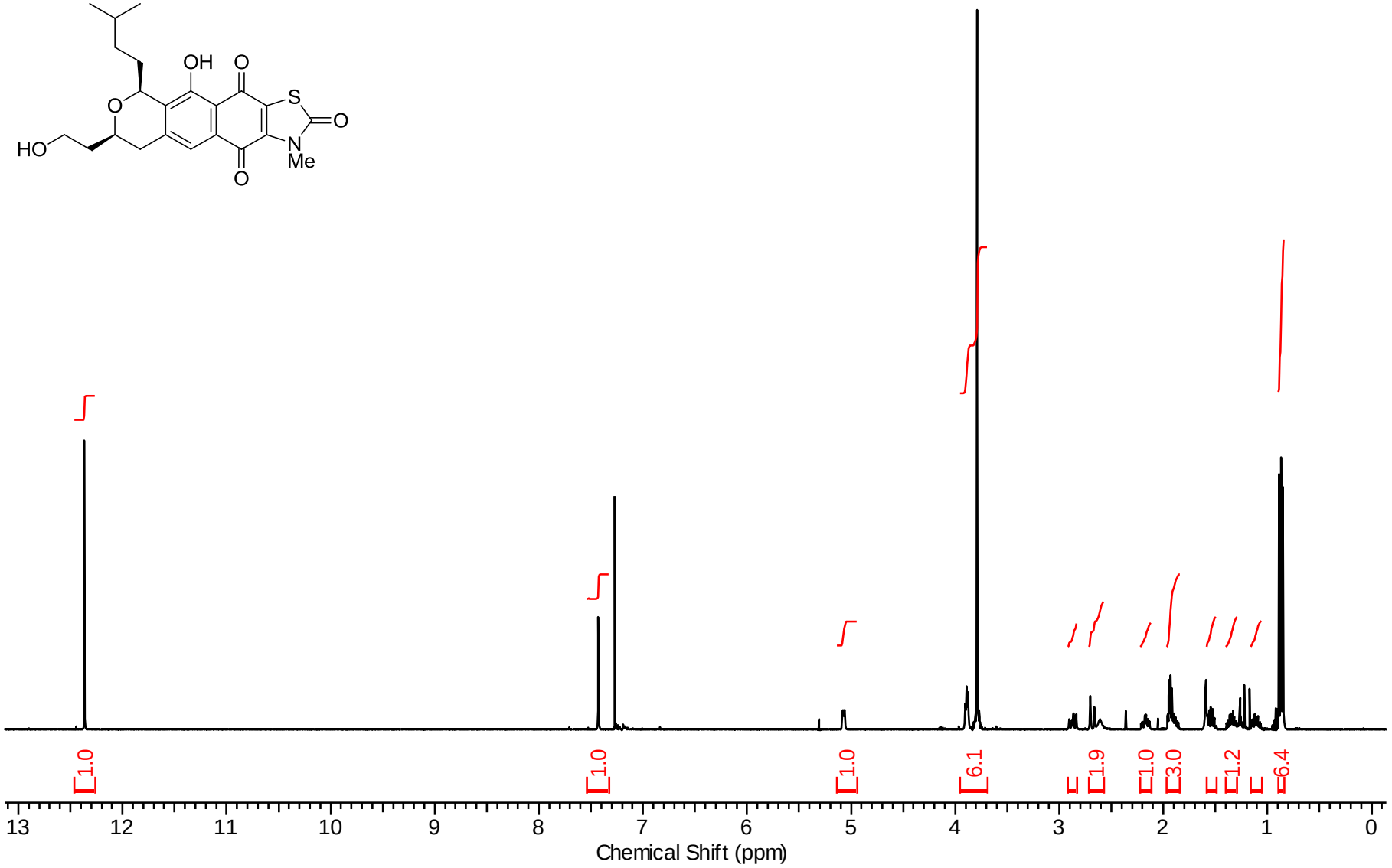


^{13}C NMR at 100MHz in $CDCl_3$

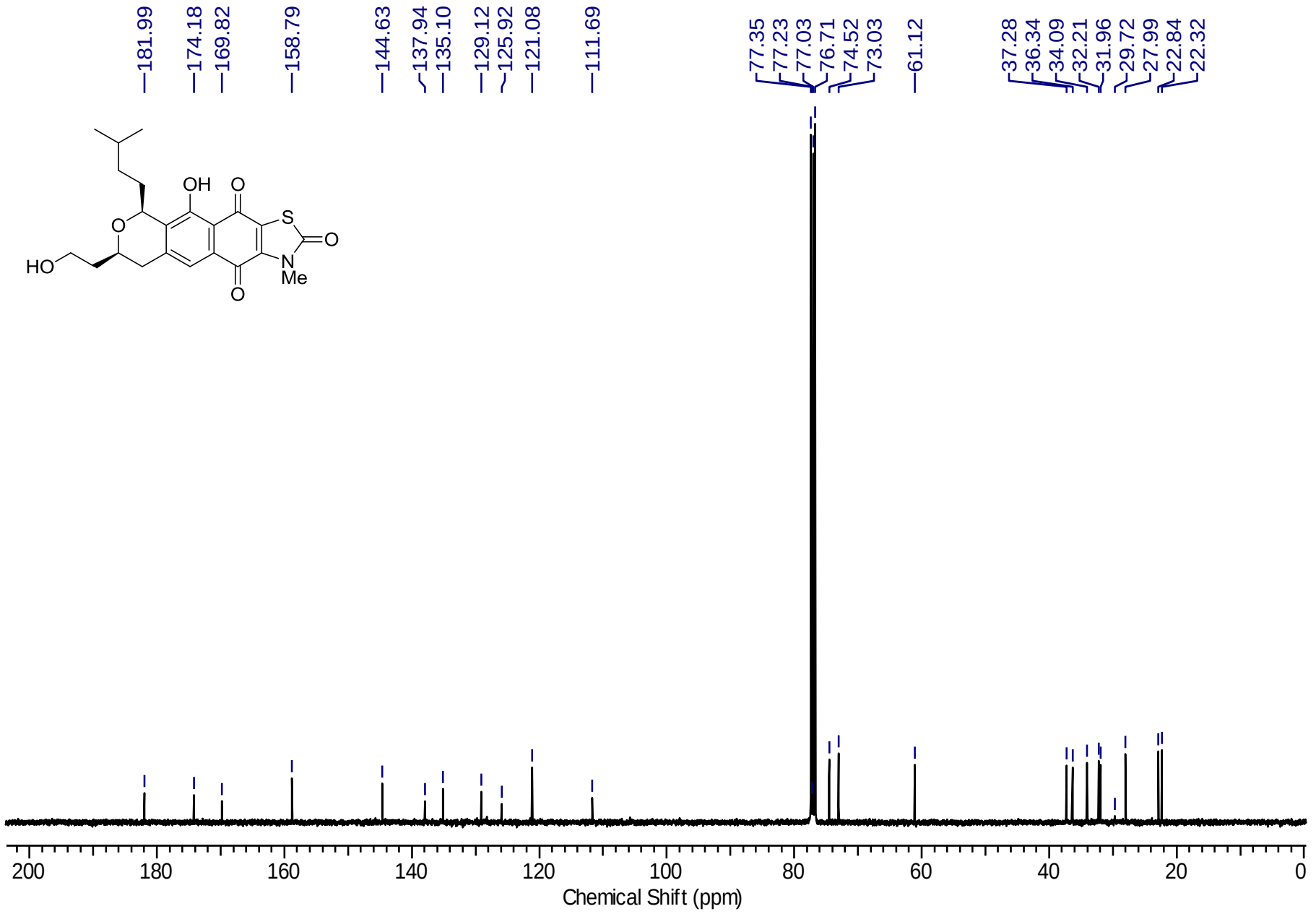


cis-5-Hydroxy-8-(2-hydroxyethyl)-6-isopentyl-1-methyl-8,9-dihydro-1_H_-pyrano[3',4':6,7]naphtho[2,3-_d_]thiazole-2,4,11(6_H_)-trione

^{1}H NMR at 400MHz in $CDCl_3$

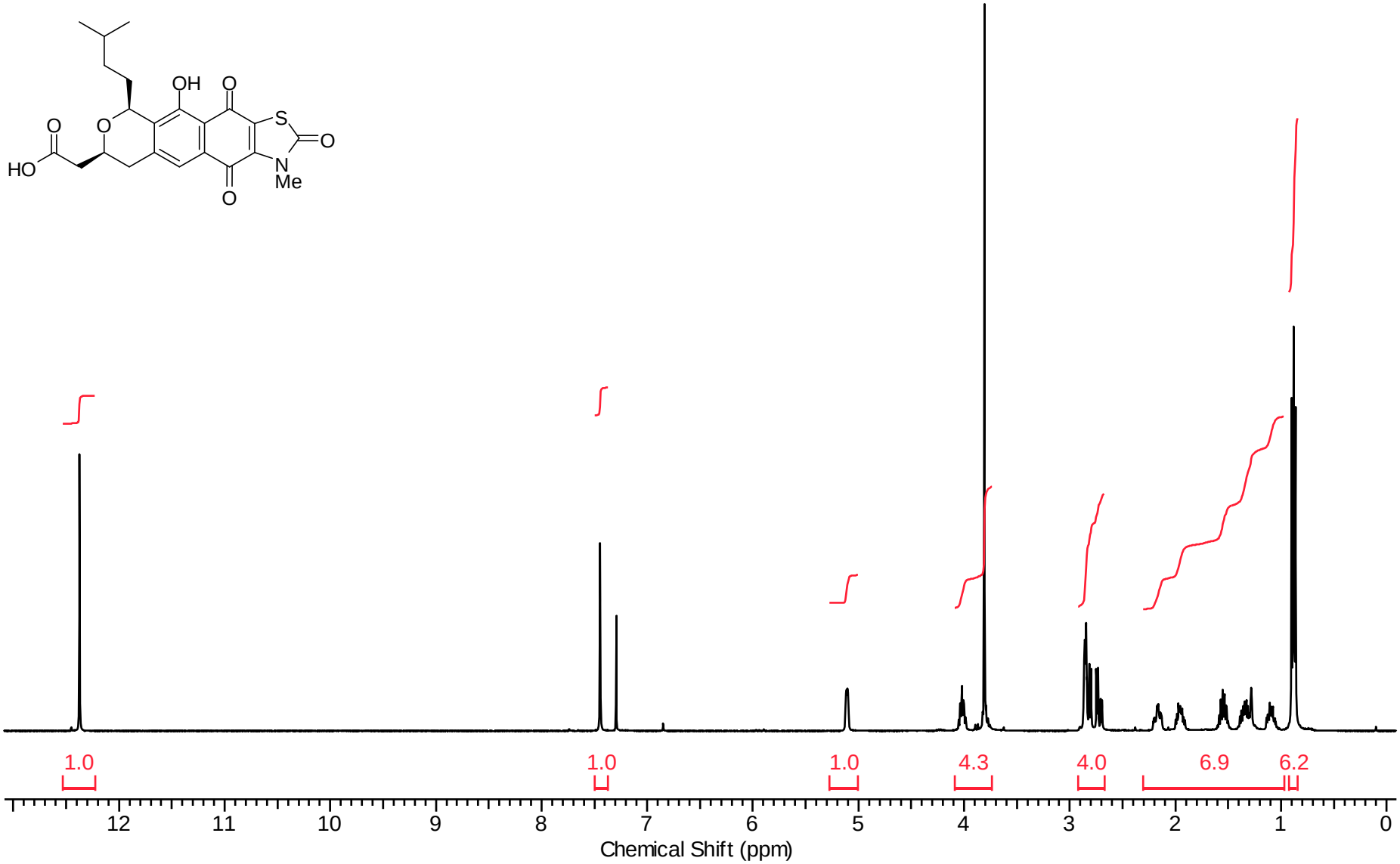


^{13}C NMR at 100MHz in $CDCl_3$

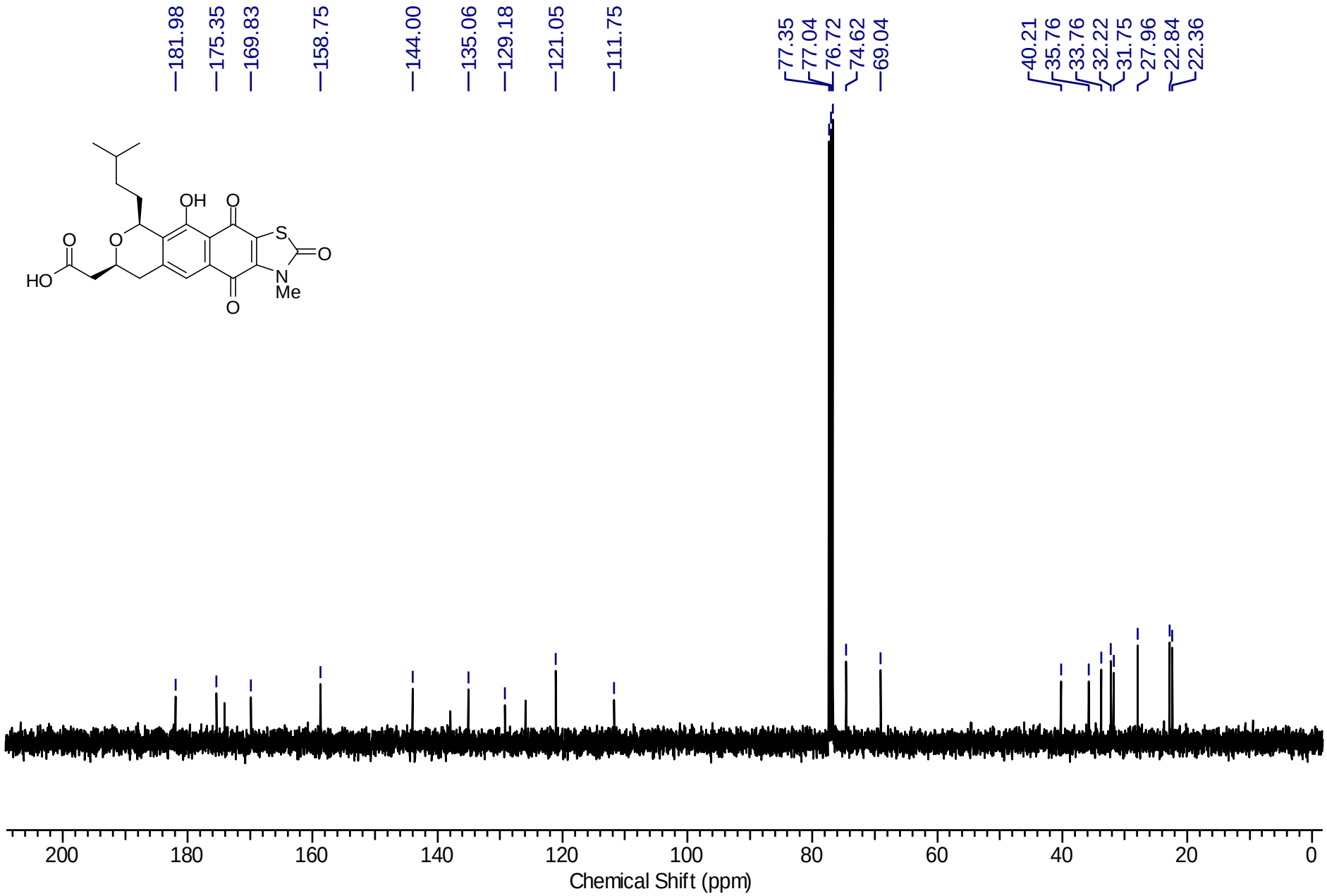


Mevashuntin 1

^{1}H NMR at 400MHz in $CDCl_3$

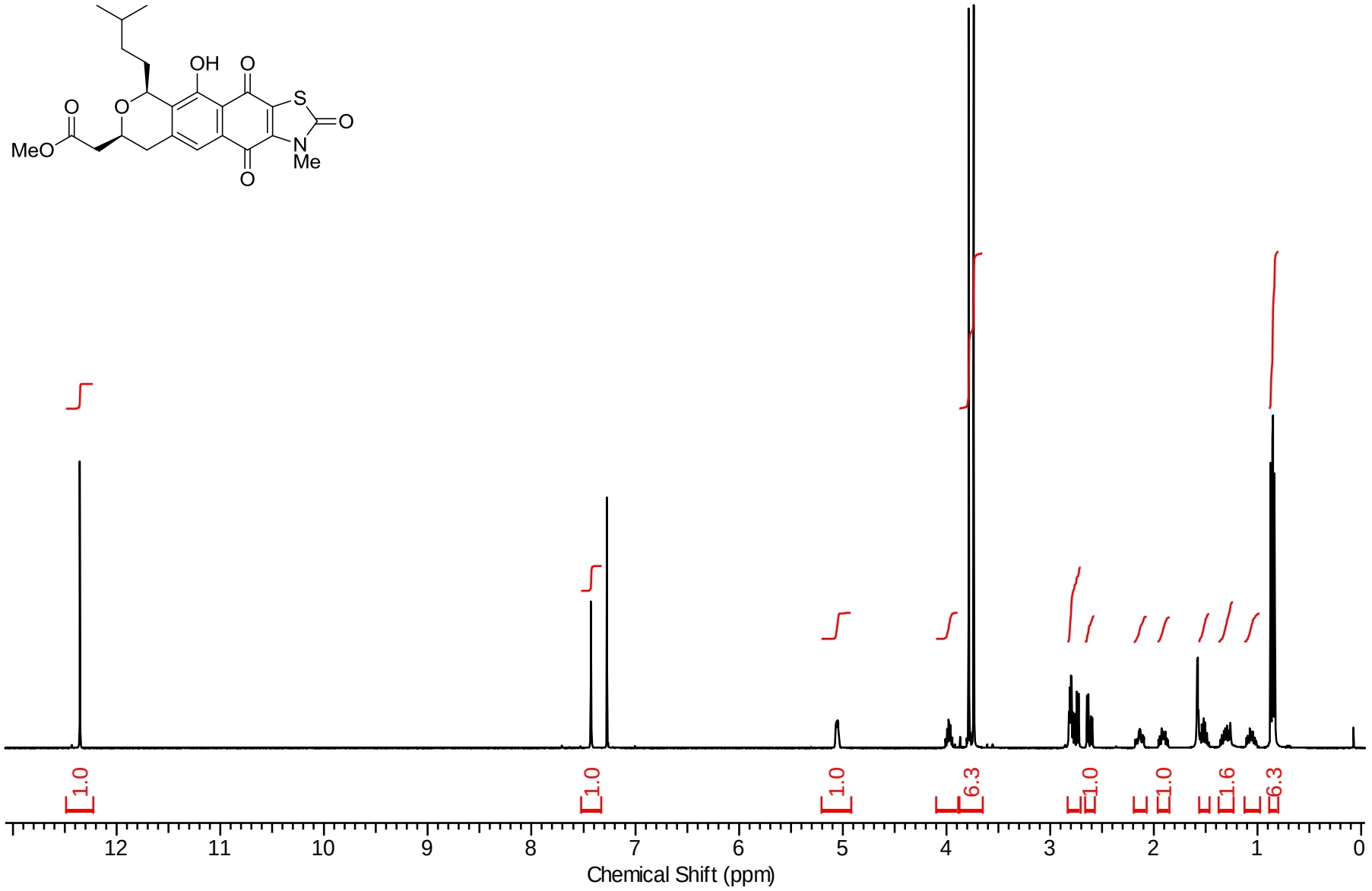


^{13}C NMR at 100MHz in $CDCl_3$

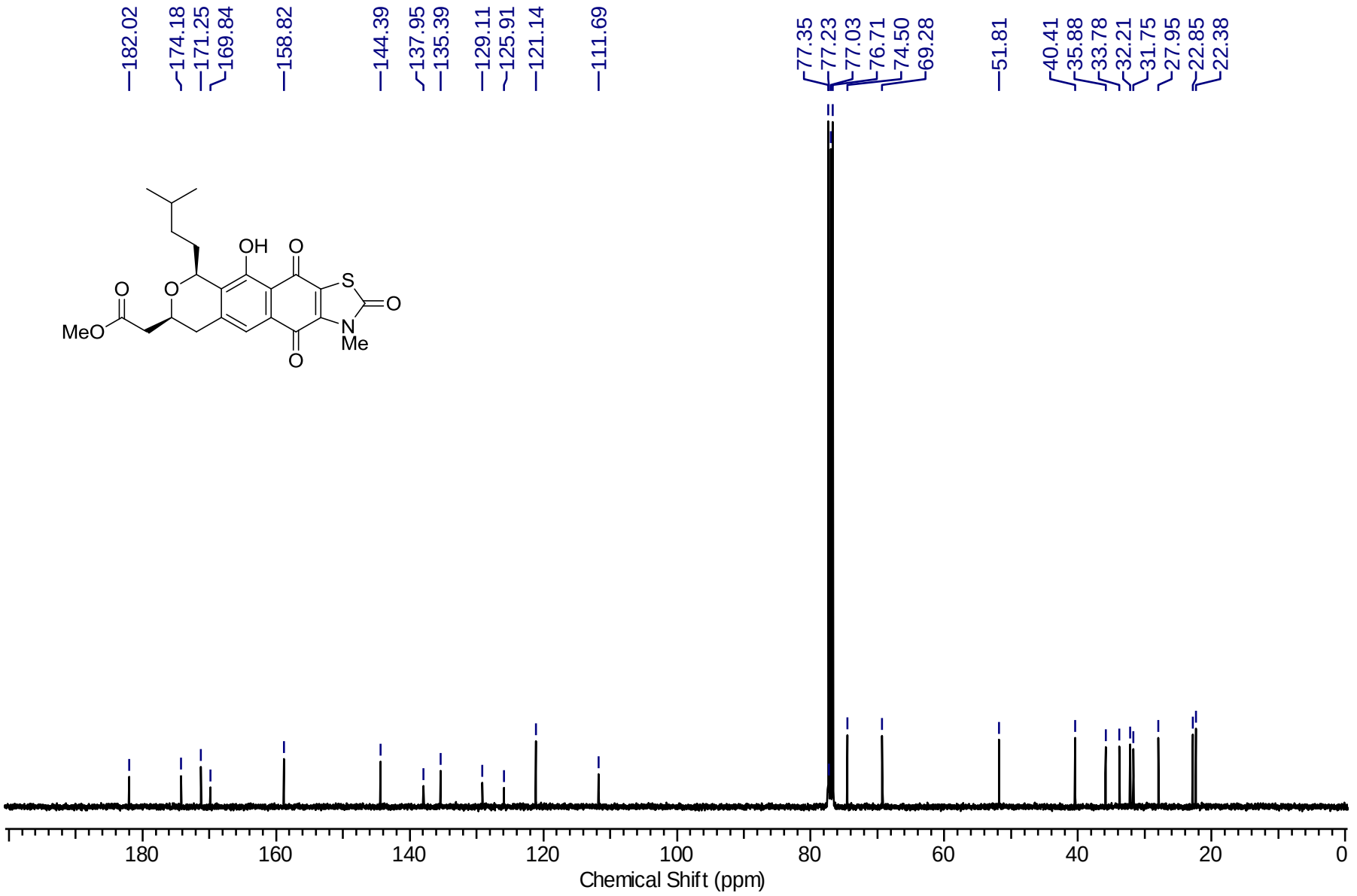


Mevashuntin methyl ester 16

^{1}H NMR at 400MHz in $CDCl_3$



^{13}C NMR at 100MHz in $CDCl_3$



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(1) Murphy, J. A.; Schoenebeck, F.; Findlay, N. J.; Thomson, D. W.; Zhou, S.-z.; Garnier, J. *J. Am. Chem. Soc.* **2009**, *131*, 6475.

(2) Shin-ya, K.; Umeda, K.; Chijiwa, S.; Furihata, K.; Hayakawa, Y.; Seto, H. *Tetrahedron Lett.* **2005**, *46*, 1273.