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A Synthetic Approach to Chrysophaentin F.

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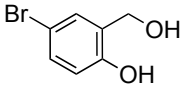
Supporting Information

1. General Remarks

All solvents were distilled prior to use. Tetrahydrofuran, diethyl ether, hexane and pentane were all distilled from sodium benzophenone ketyl under argon. Dichloromethane was distilled from calcium hydride under argon. All air sensitive reactions were carried out under argon using flame or oven dried apparatus. All reactions were monitored by TLC on Merck Silica Gel 60 Å F TLC plates. Plates were visualised with 254 nm UV followed by aqueous 1% $KMnO_4$, ethanolic PMA, DNPH or iodine. Flash chromatography was performed under slight positive pressure on davisil 35-70 µm 60 Å silica. Reaction and chromatography solvents were removed using a rotary evaporator equipped with a diaphragm pump. ^1H and ^{13}C NMR spectroscopy was performed on a Bruker AVX300 (300/75 MHz) or AV400 (400/100 MHz) spectrometer at 298 K in $CDCl_3$ (that had been stored over dried K_2CO_3 to neutralise trace acidity) unless otherwise stated. Chemical shifts are quoted as δ values in ppm. Residual solvent peaks are used as the reference. Coupling constants *J* are given in Hz and multiplicity is described as follows: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; m, multiplet; br, broad. HRMS were obtained using a Bruker APEX III FT-ICR-MS with samples run in HPLC grade methanol or MeCN. Electrospray mass spectrometry was performed on a directly injected Waters quadrupole MSD using ESI+ or ESI- ionisation with MeOH as solvent. Electron ionisation and chemical ionisation mass spectrometry were carried out using a Finnigan 2000 Series GC/MS using a Zebron ZB5 30 m × 0.25 mm × 0.25 µm column run from 40 °C to 200 °C over 18 min. Infrared spectroscopy was performed on a Bio-Rad FTIR instrument using a golden gate window. Spectra were acquired from pure samples directly or from evaporated $CDCl_3$ solutions. Absorption maxima (ν_{max}) are quoted in wavenumbers (cm^{-1}) with the following abbreviations used to describe their intensity: s, strong; m, medium; w, weak; br, broad.

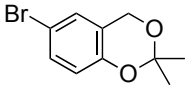
2. Procedures

4-Bromo-2-(hydroxymethyl)phenol (12)



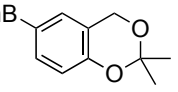
Following a procedure by Gisch *et al.*[1] To a solution of 5-bromosalicylaldehyde **12** (2.02 g, 10.0 mmol) in MeOH (60 mL) at 0 °C was added portionwise $NaBH_4$ (770 mg, 20.1 mmol) over 5 min. After 2 h, water (10 mL) was added then the reaction mixture was filtered through a pad of silica, concentrated *in vacuo* and purified by column chromatography (silica, 50–65% EtOAc in petroleum ether) to give the title compound **12** (1.61 g, 7.93 mmol, 79%) as a white solid. Physical and spectroscopic characteristics were consistent with reported values.[1,2] **MP**: 107–109 °C (EtOAc) [Lit. 109 °C[2]]. **IR** ν_{max} (neat, cm^{-1}): 3401 br, 3130 br, 2908 w, 1604 m, 1479 m, 1403 s, 1353 m, 1260 s, 1175 s, 1121 s, 998 s, 817 s. **^{1}H NMR** (300 MHz; DMSO-d_6): δ ppm 9.67 (1H, s, O**H**), 7.39 (1H, d, *J* = 2.6 Hz, Ar**H**), 7.19 (1H, dd, *J* = 8.4, 2.6 Hz, Ar**H**), 6.72 (1 H, d, *J* = 8.8 Hz, Ar**H**), 4.45 (2 H, s, C**H$_2$**), with one OH not observed. **^{13}C NMR** (75 MHz; DMSO-d_6): δ ppm 153.3 (**C**), 131.6 (**C**), 129.6 (**C**H), 129.4 (**C**H), 116.6 (**C**H), 110.0 (**C**), 57.6 (**C**H_2). **LRMS** (HPLC–MS; ESI^-): 203 ([M(^{81}Br)–H]$^-$, 84%), 201 ([M(^{79}Br)–H]$^-$, 100%). **HRMS** (ESI^-): Calculated for $C_7H_6BrO_2^-$ [M-H]$^-$: 200.9551, found: 200.9557.

6-Bromo-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxine (13)



Following a procedure by Gisch *et al.*[1] To a solution of benzyl alcohol **12** (1.55 g, 7.63 mmol) in acetone (25 mL) was added 2,2-dimethoxypropane (4.8 mL, 39.0 mmol), Na_2SO_4 (4.00 g, 28.2 mmol) and *p*-TSA (177 mg, 0.93 mmol). The reaction mixture was heated at 40 °C for 90 min then concentrated *in vacuo* and partitioned between EtOAc (20 mL) and water (20 mL). The aqueous phase was separated and extracted with EtOAc (3 × 15 mL) then the organic phases were combined, washed with brine (15 mL), dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (silica, 100% petroleum ether) to give the title compound **13** (1.81 g, 7.45 mmol, 98%) as a colourless oil. Physical and spectroscopic characteristics were consistent with reported values.[3] **IR** ν_{max} (neat, cm^{-1}): 3426 br, 3149 br, 1481 s, 1265 s, 1118 s, 817 s, 733 s. **^{1}H NMR** (300 MHz; $CDCl_3$): δ ppm 7.29–7.22 (1H, m, Ar**H**), 7.11 (1H, d, *J* = 2.0 Hz, Ar**H**), 6.71 (1H, d, *J* = 8.8 Hz, Ar**H**), 4.81 (2H, s, C**H$_2$**), 1.54 (6H, s, 2 × C**H$_3$**). **^{13}C NMR** (75 MHz; $CDCl_3$): δ ppm 150.3 (**C**), 131.0 (**C**H), 127.4 (**C**H), 121.4 (**C**), 118.9 (**C**H), 112.4 (**C**), 99.8 (**C**), 60.4 (**C**H_2), 24.6 (2 × **C**H_3). **LRMS** (GC–MS; EI): 244 ([M(^{81}Br)]$^+$, 12%), 242 ([M(^{79}Br)]$^+$, 12%), 186 ([M(^{81}Br)-C_3H_6O]$^+$, 75%), 184 ([M(^{79}Br)-C_3H_6O]$^+$, 70%), 43 ([C_3H_7]$^+$, 100%).

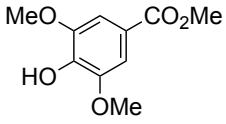
2-(2,2-Dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (15)



A flask charged with bromoarene **13** (734 mg, 3.00 mmol), *bis*(pinacolato)diboron (660 mg, 2.60 mmol) and KOAc (629 mg, 6.40 mmol) was evacuated then filled with Ar in three cycles. THF (7 mL) was added followed by $PdCl_2(dppf)\cdot CH_2Cl_2$ (165 mg, 0.22 mmol). The reaction was degassed with argon for 5 min, heated at 65 °C for 20 h then cooled to RT and filtered through a plug of silica. Concentration *in vacuo* and purification by column chromatography (silica, 0 to 10% Et_2O in petroleum ether) yielded the title compound **15** (870 mg, 3.00 mmol, 100%) as a pale yellow oil. Physical and spectroscopic

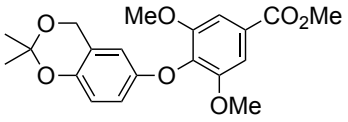
characteristics were consistent with reported values.[4] **^{1}H NMR** (300 MHz; $CDCl_3$): δ ppm 7.61 (1H, d, *J* = 8.2 Hz, Ar**H**), 7.45 (1H, s, Ar**H**), 6.81 (1H, d, *J* = 8.2 Hz, Ar**H**), 4.85 (2H, s, C**H$_2$**), 1.54 (6H, s, 2 × C**H$_3$**), 1.33 (12H, s, 4 × C**H$_3$**). **^{13}C NMR** (75 MHz; $CDCl_3$): δ ppm 154.2 (**C**), 135.0 (**C**H), 131.8 (**C**H), 119.0 (**C**), 116.7 (**C**H), 100.0 (**C**), 83.8 (**C**), 61.0 (**C**H$_2$), 25.0 (**C**H$_3$), 24.9 (**C**H$_3$) with one C coincident or not observed.

Methyl 4-hydroxy-3,5-dimethoxybenzoate (16)

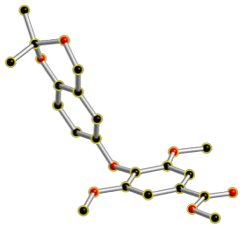


Adapted from a procedure by Bao *et al.*[5] To a suspension of magnesium turnings (3.65 g, 0.15 g-atom) in diethyl ether (100 mL) at 0 °C was added iodine (19.2 g, 75.6 mmol). After 2 h at reflux, a solution of methyl 3,4,5-trimethoxybenzoate **14** (7.92 g, 35.0 mmol) in DCM (50 mL) was added, then the solvent was removed by distillation and the temperature raised to 80 °C. After 1 h, H_2O (100 mL), sodium thiosulfate (10% aqueous solution, 20 mL) and EtOAc (40 mL) were added. The aqueous phase was separated and extracted with EtOAc (3 x 40 mL) then the organic phases were combined, washed with water (40 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the title compound **16** (7.42 g, 35.0 mmol, 100%) as a pale yellow solid with physical and spectroscopic data consistent with reported values.[6] **MP**: 105–107 °C (EtOAc) (lit. 105–107 °C).[6] **IR** ν_{max} (neat, cm^{-1}): 3303 br s, 2944 w, 2840 w, 1694 s, 1611 m, 1594 m, 1518 m, 1459 m, 1371 w, 1333 s, 1232 s, 1180 s, 1103 s, 845 w, 755 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.31 (2H, s, 2 x Ar**H**), 5.95 (1H, br s, O**H**), 3.93 (6H, s, 2 x C**H$_3$**), 3.89 (3H, s, C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 167.0 (**C**), 146.8 (**C**), 139.3 (**C**), 121.2 (**C**), 106.8 (**C**H), 56.5 (**C**H$_3$), 52.2 (**C**H$_3$). **LRMS** (HPLC-MS; ESI$^-$): 249 (100%), 211 ([M–H]$^-$, 51%). **HRMS** (HPLC-MS, ESI$^-$): Calculated for $C_{10}H_{11}O_5^-$ [M+Na]$^-$: 211.0606, found: 211.0613

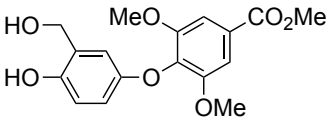
Methyl 4-((2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)oxy)-3,5-dimethoxybenzoate (18)



To solution of phenol **16** (380 mg, 1.80 mmol), borolane **15** (520 mg, 1.80 mmol) and copper triflate (196 mg, 0.50 mmol) in EtOH (18 mL) containing activated powdered 4 Å molecular sieves under a slight positive pressure of oxygen was added pyridine (1 mL, 12 mmol). After heating at 65 °C for 20 h the reaction mixture was cooled to RT, filtered through a pad of silica, concentrated *in vacuo* and purified by column chromatography (silica, 25% EtOAc in petroleum ether) to afford the title compound **18** (513 mg, 1.37 mmol, 76%) as an off-white solid. **MP**: 138–140 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 2946 w, 1716 m, 1491 m, 1435 m, 1415 m, 1338 s, 1214 s, 1182 s, 1123 s, 729 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.36 (2H, s, 2 × Ar**H**), 6.69–6.64 (2H, m, 2 × Ar**H**), 6.47 (1H, d, *J* = 2.0 Hz, Ar**H**), 4.75 (2H, s, C**H$_2$**), 3.93 (3H, s, C**H$_3$**), 3.83 (6H, s, 2 × C**H$_3$**), 1.51 (6H, s, 2 × C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 166.7 (**C**), 153.4 (**C**), 151.9 (**C**), 146.1 (**C**), 136.8 (**C**), 127.1 (**C**), 120.0 (**C**), 117.7 (**C**H), 115.0 (**C**H), 110.8 (**C**H), 107.1 (**C**H), 99.4 (**C**), 61.1 (**C**H$_2$), 56.5 (**C**H$_3$), 52.5 (**C**H$_3$), 24.8 (**C**H$_3$). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{20}H_{22}NaO_7^+$ [M+Na]$^+$: 397.1263, found: 397.1261. **X-ray**: see insert.

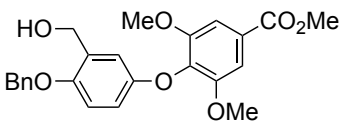


Methyl 4-(4-hydroxy-3-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (17)



A suspension of acetal **18** (377 mg, 1.00 mmol) in water (3 mL) and AcOH (7 mL) was heated at 70 °C for 30 min then cooled to RT and partitioned between sat. $NaHCO_3$ (20 mL) and EtOAc (10 mL). The aqueous phase was separated and extracted with EtOAc (2 × 10 mL) then the organic phases were combined, washed with brine (10 mL), dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (silica, 40% EtOAc in petroleum ether) to give the title compound **17** (298 mg, 0.89 mmol, 89%) as a white solid. **MP**: 113–114 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 3376 br, 2951 w, 2849 w, 1717 m, 1497 m, 1463 m, 1436 m, 1417 m, 1341 s, 1219 s, 1185 m, 1128 s, 764 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.36 (2H, s, 2 × Ar**H**), 6.75 (1H, d, *J* = 8.7 Hz, Ar**H**), 6.68 (1H, dd, *J* = 8.8, 3.0 Hz, Ar**H**), 6.59 (1H, d, *J* = 3.0 Hz, Ar**H**), 4.76 (2H, s, C**H$_2$**), 3.94 (3H, s, C**H$_3$**), 3.82 (3H, s, C**H$_3$**), with one OH not observed. **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 166.7 (**C**), 153.5 (**C**), 151.5 (**C**), 151.0 (**C**), 136.9 (**C**), 127.1 (**C**), 125.5 (**C**), 117.1 (**C**H), 115.5 (**C**H), 114.4 (**C**H), 107.1 (**C**H), 64.6 (**C**H$_2$), 56.6 (**C**H$_3$), 52.5 (**C**H$_3$). **LRMS** (HPLC-MS; ESI$^-$): 333 ([M–H]$^-$, 100%). **HRMS** (HPLC-MS, ESI+): Calculated for $C_{17}H_{18}NaO_7^+$ [M+Na]$^+$: 357.0950, found: 357.0958.

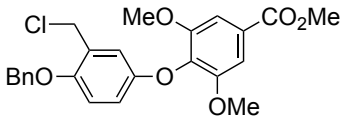
Methyl 4-(4-(benzyloxy)-3-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (19)



To a solution of biaryl ether **17** (287 mg, 0.86 mmol) in acetone (10 mL) was added K_2CO_3 (186 mg, 1.34 mmol) then BnBr (0.1 mL, 0.88 mmol). The reaction mixture was heated at reflux for 18 h then cooled to RT and partitioned between EtOAc (10 mL) and water (10 mL). The aqueous phase was separated and extracted with EtOAc (3 × 10 mL) then the organic phases were combined, washed with brine (10 mL), dried over $MgSO_4$ and concentrated

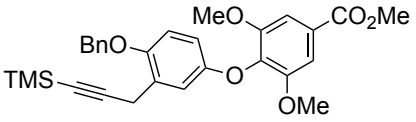
in vacuo. Purification by column chromatography column (40% EtOAc in petroleum ether) afforded the title compound **19** (285 mg, 0.67 mmol, 78%) as a white solid. **MP**: 119–120 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 3454 br, 2948 w, 1718 m, 1492 s, 1462 m, 1434 m, 1416 m, 1340 s, 1217 s, 1128 s, 1025 w, 998 m, 759 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.44–7.28 (7H, m, 7 × Ar**H**), 6.85 (1H, d, *J* = 3.1 Hz, Ar**H**), 6.82 (1H, d, *J* = 8.9 Hz, Ar**H**), 6.72 (1H, dd, *J* = 8.8, 3.1 Hz, Ar**H**), 5.05 (2H, s, C**H$_2$**), 4.65 (2H, d, *J* = 6.3 Hz, C**H$_2$**), 3.94 (3H, s, C**H$_3$**), 3.83 (3H, s, C**H$_3$**), 2.26 (1H, t, *J* = 6.6 Hz, O**H**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 166.7 (**C**), 153.5 (**C**), 152.3 (**C**), 151.7 (**C**), 137.1 (**C**), 136.8 (**C**), 130.7 (**C**), 128.8 (**C**H), 128.2 (**C**H), 127.5 (**C**), 127.2 (**C**H), 115.7 (**C**H), 114.4 (**C**H), 112.7 (**C**H), 107.1 (**C**H), 70.9 (**C**H_2), 62.2 (**C**H_2), 56.6 (C**H$_3$**), 52.5 (C**H$_3$**). **LRMS** (HPLC-MS; ESI$^+$): 463 $[M+K]^+$, 447 $[M+Na]^+$. **HRMS** (HPLC-MS, ESI+): Calculated for $C_{24}H_{24}NaO_7^+$ $[M+Na]^+$: 447.1419, found: 447.1435.

Methyl 4-(4-(benzyloxy)-3-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (20)



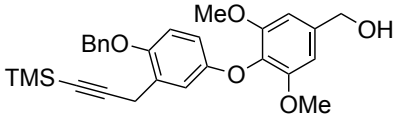
To a solution of benzyl alcohol **19** (412 mg, 0.97 mmol) in THF (4 mL) at 0 °C were added sequentially PPh_3 (305 mg, 1.16 mmol) and NCS (154 mg, 1.16 mmol). The reaction mixture was allowed to warm to RT and after 25 min sat. $NaHCO_3$ (4 mL) and sat. $Na_2S_2O_3$ (4 mL) were added. The aqueous phase was separated and extracted with Et_2O (3 × 6 mL) then the organic phases were combined, washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 20% Et_2O in petroleum ether) gave the title compound **20** (340 mg, 0.77 mmol, 79%) as an off-white solid. **MP**: 125–126 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 2949 w, 1719 m, 1497 s, 1461 m, 1416 m, 1341 s, 1217 s, 1184 m, 1129 s, 999 w, 758 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.49–7.28 (7H, m, 7 × Ar**H**), 6.92 (1H, d, *J* = 3.0 Hz, Ar**H**), 6.81 (1H, d, *J* = 8.9 Hz, Ar**H**), 6.75 (1H, dd, *J* = 8.9, 3.0 Hz, Ar**H**), 5.08 (2H, s, C**H$_2$**), 4.62 (2H, s, C**H$_2$**), 3.94 (3H, s, C**H$_3$**), 3.83 (6H, s, 2 × C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 166.8 (**C**O), 153.5 (**C**), 152.2 (**C**), 151.8 (**C**), 137.3 (**C**), 136.8 (**C**), 128.8 (**C**H), 128.2 (**C**H), 127.5 (**C**H), 127.4 (**C**), 127.3 (**C**), 117.5 (**C**H), 116.0 (**C**H), 113.5 (**C**H), 107.2 (**C**H), 71.1 (**C**H_2), 56.7 (**C**H_3), 52.6 (**C**H_3), 41.8 (**C**H_2). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{24}H_{23}ClNaO_6^+$ $[M+Na]^+$: 465.1080, found: 465.1067.

Methyl 4-(4-(benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (21)



A flask charged with benzyl chloride **20** (750 mg, 1.70 mmol), $PdCl_2(CH_3CN)_2$ (26 mg, 0.1 mmol), XPhos (146 mg, 0.31 mmol) and Cs_2CO_3 (609 mg, 1.87 mmol) was evacuated then filled with Ar in three cycles. TMSacetylene (0.38 mL, 2.70 mmol) and CH_3CN (5 mL) were added sequentially then the reaction mixture was heated at 70 °C for 18 h, cooled to RT, filtered through a plug of silica and concentrated *in vacuo*. Purification by column chromatography (silica, 30% Et_2O in petroleum ether) afforded the title compound **21** (858 mg, 1.70 mmol, quant.) as a wax. **IR** ν_{max} (neat, cm^{-1}): 2956 w, 2177 w, 1720 s, 1493 s, 1463 m, 1433 m, 1416 m, 1340 s, 1216 s, 1130 s, 1027 w, 999 w, 844 s, 758 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7. 45–7. 29 (7H, m, 7 × Ar**H**), 7.05 (1H, d, *J* = 2.8 Hz, Ar**H**), 6.77 (1H, d, *J* = 9.1 Hz, Ar**H**), 6.73 (1H, dd, *J* = 8.9, 3.0 Hz, Ar**H**), 5.02 (2H, s, C**H$_2$**), 3.94 (3H, s, C**H$_3$**), 3.84 (6H, s, 2 × C**H$_3$**), 3.63 (2H, s, C**H$_2$**), 0.09 (9H, s, 3 × C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 166.7 (**C**O), 153.5 (**C**), 152.3 (**C**), 151.1 (**C**), 137.5 (**C**),136.9 (**C**), 128.6 (**C**H), 127.9 (**C**H), 127.3 (**C**H), 127.1 (**C**), 126.4 (**C**), 115.7 (**C**H), 113.6 (**C**H), 112.4 (**C**H), 107.2 (**C**H), 104.1 (**C**), 87.3 (**C**), 70.7 (**C**H_2), 56.6 (**C**H_3), 52.4 (**C**H_3), 21.2 (**C**H_2), 0.2 (**C**H_3), with one **C** coincident or not observed. **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{29}H_{32}NaO_6Si^+$ $[M+Na]^+$: 527.1865, found: 527.1845.

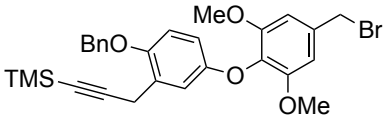
(4-(4-(Benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5- dimethoxyphenyl)methanol (23)



To a solution of benzyl ester **21** (192 mg, 0.38 mmol) in THF (9 mL) at 0 °C was added a solution of $LiAlH_4$ (1.0 M in THF, 0.38 mL, 0.38 mmol) dropwise over 5 min. The resulting mixture was allowed to warm to RT over 20 min then MeOH (0.3 mL) and sat. Rochelle salt (1 mL) were added. The aqueous phase was separated and extracted with EtOAc (3 × 3 mL) then the organic phases were combined, washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 50% EtOAc in petroleum ether) gave the title compound **23** (161 mg, 0.34 mmol, 89%) as a pale yellow oil. **IR** ν_{max} (neat, cm^{-1}): 3416 br, 2958 w, 2177 m, 1493 s, 1463 m, 1423 m, 1335 m, 1248 s, 1219 s, 1129 s, 1027 m, 955 w, 843 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.45–7.28 (5H, m, 5 × Ar**H**), 7.07 (1H, d, *J* = 3.0 Hz, Ar**H**), 6.77 (1H, d, *J* = 8.8 Hz, Ar**H**), 6.72 (1H, dd, *J* = 8.8, 3.0 Hz, Ar**H**), 6.68 (2H, s, 2 × Ar**H**), 5.01 (2H, s, C**H$_2$**), 4.69 (2H, d, *J* = 5.0 Hz, C**H$_2$**), 3.80 (6H, s, 2 × C**H$_3$**), 3.63 (2H, br s, C**H$_2$**), 1.72 (1H, br t, *J* = 5.9 Hz, O**H**), 0.11 (9H, s, 3 × C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.8 (**C**), 152.8 (**C**), 150.8 (**C**), 138.4 (**C**), 137.6 (**C**), 132.2 (**C**), 128.6 (**C**H), 127.9 (**C**H), 127.3 (**C**H), 126.3 (**C**), 115.7 (**C**H), 113.5

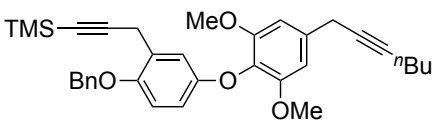
(**C**H), 112.5 (**C**H), 104.32 (**C**), 104.27 (**C**H), 87.0 (**C**), 70.8 (**C**H_2), 65.7 (**C**H_2), 56.5 (**C**H_3), 21.2 (**C**H_2), 0.24 (**C**H_3). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{28}H_{32}NaO_5Si^+$ $[M+Na]^+$: 499.1916 found: 499.1887.

(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (25)



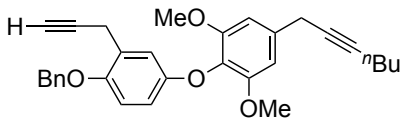
To a solution of benzyl alcohol **23** (136 mg, 0.29 mmol) in THF (1 mL) at 0 °C were added PPh_3 (94.0 mg, 0.36 mmol) and NBS (70.0 mg, 0.39 mmol). The reaction was warmed to RT and after 1 h sat. $NaHCO_3$ (1 mL) and sat. $Na_2S_2O_3$ (1 mL) were added. The aqueous phase was separated and extracted with Et_2O (3 × 2 mL) then the combined organic phases were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 20% Et_2O in petroleum ether) afforded the title compound **25** (160 mg, 0.29 mmol, quant.) as a pale yellow oil. **IR** ν_{max} (neat, cm^{-1}): 2959 w, 2177 m, 1493 s, 1463 s, 1421 m, 1339 m, 1246 s, 1212 s, 1133 s, 1027 m, 844 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.44–7.28 (5H, m, 5 × Ar**H**), 7.07 (1H, d, *J* = 3.0 Hz, Ar**H**), 6.77 (1H, d, *J* = 8.8 Hz, Ar**H**), 6.74–6.67 (3H, m, 3 × Ar**H**), 5.02 (2H, s, C**H$_2$**), 4.49 (2H, s, C**H$_2$**), 3.80 (6H, s, 2 × C**H$_3$**), 3.64 (2H, s, C**H$_2$**), 0.12 (9H, s, 3 × C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.7 (**C**), 152.7 (**C**), 150.9 (**C**), 137.6 (**C**), 134.9 (**C**), 133.0 (**C**), 128.6 (**C**H), 127.9 (**C**H), 127.3 (**C**), 126.4 (**C**H), 115.8 (**C**H), 113.6 (**C**H), 112.5 (**C**H), 106.7 (**C**H), 104.3 (**C**), 87.0 (**C**), 70.8 (**C**H_2), 56.6 (**C**H_3), 34.0 (**C**H_2), 21.2 (**C**H_2), 0.3 (**C**H_3). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{28}H_{31}BrNaO_4Si^+$ $[M+Na]^+$: 561.1072 found: 561.1094.

(3-(2-(Benzyloxy)-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (27)



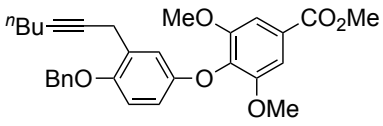
Adapted from a procedure by Gau *et al.*[7] To a solution of hex-1-yne (0.07 mL, 0.58 mmol) in pentane (2 mL) at 0 °C was added *n*-BuLi (1.98 M in hexane, 0.29 mL, 0.58 mmol) over 5 min. After 30 min Et_2AlCl (1.0 M in hexane, 0.58 mL, 0.58 mmol) was added over 5 min. The solution was warmed to RT after 20 min and after a further 2 h Et_2O (4 mL) and $NiCl_2(PPh_3)_2$ (13.0 mg, 0.02 mmol) were added. After a further 15 min benzyl bromide **25** (115 mg, 0.21 mmol) was added followed after 90 min by sat. NH_4Cl (1 mL). The aqueous phase was separated and extracted with Et_2O (3 × 5 mL) then the organic phases were combined, washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 10% Et_2O in petroleum ether) afforded the title compound **27** (192 mg, 0.34 mmol, 72%) as a yellow oil. **IR** ν_{max} (neat, cm^{-1}): 2958 br, 2933 w, 2177 w, 1493 s, 1463 s, 1423 m, 1336 m, 1219 s, 1128 s, 1027 w, 844 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.45–7.33 (5H, m, 5 × Ar**H**), 7.31 (1H, d, *J* = 6.6 Hz, Ar**H**), 7.07 (1H, d, *J* = 2.4 Hz, Ar**H**), 6.77 (1H, d, *J* = 8.7 Hz, Ar**H**), 6.67 (2H, d, *J* = 0.8 Hz, 2 × Ar**H**), 5.01 (2H, s, C**H$_2$**), 3.79 (6H, s, 2 × C**H$_3$**), 3.65–3.62 (2H, m, C**H$_2$**), 3.58 (2H, t, *J* = 2.5 Hz, C**H$_2$**), 2.26 (2H, tt, *J* = 6.9, 2.4 Hz, C**H$_2$**), 1.61–1.42 (4H, m, 2 × C**H$_2$**), 0.93 (3H, t, *J* = 7.2 Hz, C**H$_3$**), 0.11 (9H, s, 3 × C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.5 (**C**), 152.9 (**C**), 150.8 (**C**), 137.6 (**C**), 135.0 (**C**), 131.1 (**C**) 128.6 (**C**H), 127.9 (**C**H), 127.3 (**C**H), 126.3 (**C**), 115.6 (**C**H), 113.5 (**C**H), 112.5 (**C**H), 105.4 (**C**H), 87.0 (**C**), 83.3 (**C**), 70.8 (**C**H_2), 56.5 (**C**H_3), 31.3 (**C**H_2), 25.6 (**C**H_2), 22.1 (**C**H_2), 21.2 (**C**H_2), 18.7 (**C**H_2), 13.8 (**C**H_3), 0.23 (**C**H_3) with one **C** coincident or not observed. **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{34}H_{40}NaO_4Si^+$ $[M+Na]^+$: 563.2593 found: 563.2601.

2-(4-(Benzyloxy)-3-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (28)



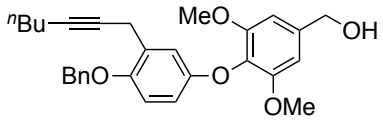
To diyne **27** (379 mg, 0.70 mmol) in MeOH/H_2O/DCM (4.5 mL/1 mL/7 mL) was added AgOTf (59 mg, 0.21 mmol). After 20 h further AgOTf (18 mg, 0.07 mmol) was added followed after 7 h by sat. NH_4Cl (10 mL). The aqueous phase was separated and extracted with Et_2O (3 × 10 mL) then the organic phases were combined, washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 20% Et_2O in petroleum ether) afforded the title compound **28** (272 mg, 0.58 mmol, 83%) as a yellow oil. **IR** ν_{max} (neat, cm^{-1}): 3288 w, 2957 br, 2933 w, 1493 s, 1461 m, 1423 m, 1337 w, 1219 s, 1127 s, 1026 w, 969 w, 737 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.45–7.28 (5H, m, 5 × Ar**H**), 7.20 (1H, d, *J* = 3.1 Hz, Ar**H**), 6.74 (1H, d, *J* = 8.9 Hz, Ar**H**), 6.66 (2H, s, 2 × Ar**H**), 6.61 (1H, dd, *J* = 8.8, 3.1 Hz Ar**H**), 5.02 (2H, s, C**H$_2$**), 3.78 (6H, s, 2 × C**H$_3$**), 3.59 (4H, m, 2 × C**H$_2$**), 2.26 (2H, tt, *J* = 7.0, 2.6 Hz, C**H$_2$**), 2.11 (1H, t, *J* = 2.7 Hz, C**H**), 1.61–1.40 (4H, m, 2 × C**H$_2$**), 0.93 (3H, t, *J* = 7.2 Hz, C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.5 (**C**), 152.9 (**C**), 150.8 (**C**), 137.6 (**C**), 135.1 (**C**), 131.3 (**C**), 128.6 (**C**H), 127.9 (**C**H), 127.4 (**C**H), 126.2 (**C**), 116.7 (**C**H), 113.0 (**C**H), 112.4 (**C**H), 105.3 (**C**H), 83.3 (**C**), 82.0 (**C**), 70.8 (**C**H_2), 70.5 (**C**), 56.4 (**C**H_3), 31.3 (**C**H_2), 25.7 (**C**H_2), 22.1 (**C**H_2), 19.8 (**C**H_2), 18.7 (**C**H_2), 13.8 (**C**H_3) with one **C** coincident or not observed. **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{31}H_{32}NaO_4^+$ $[M+Na]^+$: 491.2198 found: 491.2203.

Methyl 4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (22)



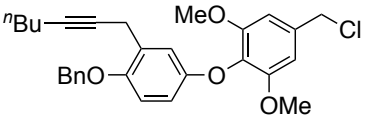
A flask charged with benzyl chloride **20** (200 mg, 0.50 mmol), $PdCl_2(CH_3CN)_2$ (8 mg, 0.03 mmol), XPhos (43 mg, 0.09 mmol) and Cs_2CO_3 (163 mg, 0.50 mmol) was evacuated then filled with Ar in three cycles. Hex-1-yne (0.08 mL, 0.72 mmol) and CH_3CN (1.3 mL) were then added sequentially and the reaction was heated at 65 °C for 18 h then cooled to RT, filtered through a plug of silica and concentrated *in vacuo*. Purification by column chromatography (silica, 20% Et_2O in petroleum ether) gave the title compound **22** (206 mg, 0.42 mmol, 94%) as a yellow wax. **IR** ν_{max} (neat, cm^{-1}): 2956 w, 2934 w, 1720 m, 1492 s, 1463 m, 1434 m, 1416 m, 1340 s, 1216 s, 1130 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.44–7.27 (7H, m, 7 × Ar**H**), 7.15 (1H, dd, *J* = 3.1, 0.9 Hz, Ar**H**), 6.74 (1H, d, *J* = 8.8 Hz, Ar**H**), 6.63 (1H, m, Ar**H**), 5.02 (2H, s, CH2), 3.94 (3H, s, C**H$_3$**), 3.83 (6H, s, 2 × C**H$_3$**), 3.56 (2H, t, *J* = 2.4 Hz, C**H$_2$**), 2.15 (2H, tt, *J* = 7.1, 2.4 Hz, C**H$_2$**), 1.47–1.32 (4H, m, 2 × C**H$_2$**), 0.88 (3H, t, *J* = 7.5 Hz, C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 166.8 (**C**O), 153.6 (**C**), 152.3 (**C**), 151.1 (**C**), 137.6 (**C**), 137.1 (**C**), 128.6 (**C**H), 127.91 (**C**), 127.85 (**C**H), 127.3 (**C**H), 127.0 (**C**), 116.3 (**C**H), 112.9 (**C**H), 112.3 (**C**H), 107.2 (**C**H), 83.1 (**C**), 70.7 (**C**H_2), 56.6 (**C**H_3), 52.4 (**C**H_3), 31.3 (**C**H_2), 22.8 (**C**H_2), 20.1 (**C**H_2), 18.7 (**C**H_2), 13.7 (**C**H_3), with one **C** coincident or not observed. **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{30}H_{32}NaO_6^+$ $[M+Na]^+$: 511.2096 found: 511.2100.

(4-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (24)



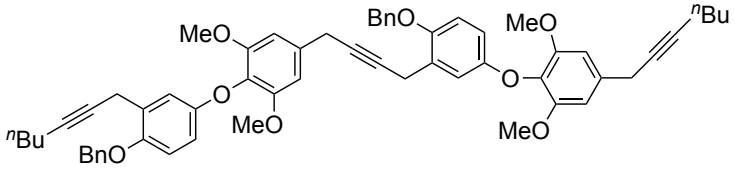
To a solution of benzyl ester **22** (586 mg, 1.20 mmol) in THF (6 mL) at 0 °C was added a solution of $LiAlH_4$ (1.0 M in THF, 1.2 mL, 1.20 mmol) dropwise over 5 min. The resulting mixture was allowed to warm to RT over 20 min then MeOH (1 mL) and sat. Rochelle salt (10 mL) were added. The aqueous phase was separated and extracted with EtOAc (3 × 10 mL) then the organic phases were combined, washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 50% EtOAc in petroleum ether) afforded the title compound **24** (533 mg, 1.16 mmol, 96%) as a pale yellow oil. **IR** ν_{max} (neat, cm^{-1}): 3411 br, 2957 w, 2933 m, 1492 s, 1462 s, 1422 m, 1335 m, 1220 s, 1129 s, 1025 w, 957 w. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.45–7.27 (5H, m, 5 × Ar**H**), 7.19 (1H, d, *J* = 3.1 Hz, Ar**H**), 6.73 (1H, d, *J* = 8.8 Hz, Ar**H**), 6.68 (2H, s, 2 × Ar**H**), 6.60 (1H, dd, *J* = 8.8, 3.1 Hz, Ar**H**), 5.01 (2H, s, C**H$_2$**), 4.70 (2H, d, *J* = 2.3 Hz, C**H$_2$**), 3.79 (6H, s, 2 × C**H$_3$**), 3.56 (2H, t, *J* = 2.4 Hz, C**H$_2$**), 2.17 (2H, tt, *J* = 7.1, 2.4 Hz, C**H$_2$**), 1.74 (1H, br t, *J* = 2.3 Hz, **OH**), 1.51–1.33 (4H, m, C**H$_2$**), 0.90 (3H, t, *J* = 7.2 Hz, C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.9 (**C**), 152.8 (**C**), 150.9 (**C**), 138.3 (**C**), 137.7 (**C**), 132.3 (**C**), 128.6 (**C**H), 127.9 (**C**H), 127.8 (**C**), 127.3 (**C**H), 116.4 (**C**H), 112.6 (**C**H), 112.3 (**C**H), 104.2 (**C**H), 82.9 (C), 70.7 (**C**H_2), 65.7 (**C**H_2), 56.5 (**C**H_3), 31.3 (**C**H_2), 22.1 (**C**H_2), 20.1 (**C**H_2), 18.7 (**C**H_2), 13.8 (**C**H_3) with one **C** coincident or not observed. **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{29}H_{32}NaO_5^+$ $[M+Na]^+$: 483.2147 found: 483.2128.

2-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (26)



To a solution of benzyl alcohol **24** (125 mg, 0.27 mmol) in THF (1 mL) at 0 °C were added PPh_3 (87 mg, 0.33 mmol) and NCS (47 mg, 0.33 mmol). The reaction was warmed to RT and after 1 h sat. $NaHCO_3$ (1 mL) and sat. $Na_2S_2O_3$ (1 mL) were added. The aqueous phase was separated and extracted with Et_2O (3 × 2 mL) then the organic phases were combined, washed with brine (10 mL), dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (silica, 20% Et_2O in petroleum ether) to afford the title compound **26** (124 mg, 0.26 mmol, 96%) as a pale yellow oil. **IR** ν_{max} (neat, cm^{-1}): 2958 w, 2936 w, 1493 s, 1464 m, 1433 m, 1421 m, 1340 m, 1243 m, 1223 s, 1130 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.45–7.28 (5H, m, 5 × Ar**H**), 7.17 (1H, d, *J* = 3.1 Hz, Ar**H**), 6.74 (1H, d, *J* = 8.9 Hz, Ar**H**), 6.69 (2H, s, 2 × Ar**H**), 6.62 (1H, dd, *J* = 8.8, 3.1 Hz, Ar**H**), 5.01 (2H, s, C**H$_2$**), 4.58 (2H, s, C**H$_2$**), 3.80 (6H, s, 2 × C**H$_3$**), 3.56 (2H, t, *J* = 2.3 Hz, C**H$_2$**), 2.17 (2H, tt, *J* = 7.0, 2.4 Hz, C**H$_2$**CH_3), 1.51–1.32 (4H, m, 2 × C**H$_2$**), 0.90 (3H, t, *J* = 7.2 Hz, C**H$_3$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.6 (**C**), 152.5 (**C**), 150.8 (**C**), 137.5 (**C**), 134.5 (**C**), 132.8 (**C**), 128.4 (**C**H), 127.7 (**C**H), 127.6 (**C**), 127.1 (**C**H), 116.1 (**C**H), 112.6 (**C**H), 112.1 (**C**H), 106.0 (**C**H), 82.9 (**C**), 70.6 (**C**H_2), 56.4 (**C**H_3), 46.6 (**C**H_2), 31.1 (**C**H_2), 22.0 (**C**H_2), 19.9 (**C**H_2), 18.5 (**C**H_2), 13.6 (**C**H_3) with one **C** coincident or not observed. **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{29}H_{31}ClNaO_4^+$ $[M+Na]^+$: 501.1808 found: 501.1819.

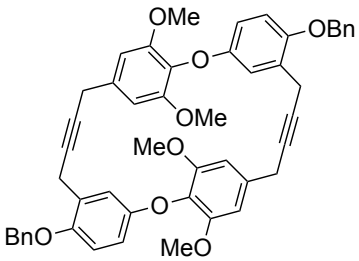
2-(4-(Benzyloxy)-3-(4-(4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)but-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (29)



A flask charged with benzyl chloride **26** (72.0 mg, 0.140 mmol), $PdCl_2(CH_3CN)_2$ (2.0 mg, 0.008 mmol), XPhos (11.0 mg, 0.023 mmol) and Cs_2CO_3 (44.0 mg, 0.130 mmol) was evacuated then filled with Ar in

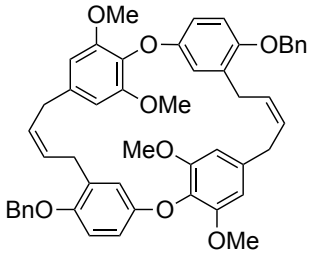
three cycles. Alkyne **28** (0.56 mL, 0.120 mmol) and CH_3CN (1 mL) were then added sequentially. The reaction was heated at 70 °C for 18 h then cooled to RT, filtered through a plug of silica, concentrated *in vacuo* and purified by column chromatography (silica, 20% Et_2O in petroleum ether) to afford the title compound **29** (54.0 mg, 0.060 mmol, 50%) as a pale yellow oil. **IR** ν_{max} (neat, cm^{-1}): 2957 br, 2930 m, 1493 s, 1462 s, 1423 m, 1337 m, 1220 s, 1128 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.44–7.28 (11H, m, 11 × Ar**H**), 7.19 (1H, d, *J* = 3.1 Hz, Ar**H**), 6.72 (1H, d, *J* = 4.4 Hz, Ar**H**), 6.70 (1H, d, *J* = 4.4 Hz, Ar**H**), 6.68 (2H, s, 2 × Ar**H**), 6.64 (2H, s, 2 × Ar**H**), 6.59 (1H, dd, *J* = 8.8, 3.1 Hz, Ar**H**), 6.51 (1H, dd, *J* = 8.8, 3.1 Hz, Ar**H**), 5.01 (2H, s, C**H$_2$**), 4.99 (2H, s, C**H$_2$**), 3.75 (6H, s, 2 × C**H$_3$**) 3.74 (6H, s, 2 × C**H$_3$**), 3.67 (2H, d, *J* = 2.4 Hz, C**H$_2$**), 3.64 (2H, d, *J* = 2.5 Hz, C**H$_2$**), 3.57 (2H, t, *J* = 2.5 Hz, C**H$_2$**), 3.55 (2H, d, *J* = 2.4 Hz, C**H$_2$**), 2.26 (2H, tt, *J* = 6.9, 2.5 Hz, C**H$_2$**), 2.17 (2H, tt, *J* = 7.0, 2.4 Hz, C**H$_2$**), 1.52–1.33 (8H, m, 4 × C**H$_2$**), 0.92 (3H, t, *J* = 7.5 Hz, CH_3), 0.89 (3H, t, *J* = 7.1 Hz, CH_3). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.63 (**C**), 153.56 (**C**), 153.0 (**C**), 150.89 (**C**), 150.87 (**C**), 137.8 (**C**), 137.7 (**C**), 135.2 (**C**), 134.8 (**C**), 131.3 (**C**), 131.2 (**C**), 128.7 (**C**H), 128.6 (**C**H), 128.0 (**C**H), 127.9 (**C**H), 127.8 (**C**), 127.5 (**C**), 127.4 (**C**H), 127.3 (**C**H), 117.0 (**C**H), 116.5 (**C**H), 112.6 (**C**H), 112.33 (**C**H), 112.31 (**C**H), 112.2 (**C**H) 105.4 (**C**H), 105.3 (**C**H), 83.4 (**C**), 83.0 (**C**), 80.5 (**C**), 79.9 (**C**), 70.84 (**C**H_2), 70.78 (**C**H_2), 56.5 (**C**H_3), 56.4 (**C**H_3), 31.33 (**C**H_2), 31.30 (**C**H_2), 29.9 (**C**H_2), 25.8 (**C**H_2), 25.7 (**C**H_2), 22.2 (**C**H_2), 20.3 (**C**H_2), 20.1 (**C**H_2), 18.7 (**C**H_2), 13.8 (**C**H_3). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{60}H_{62}NaO_8^+$ $[M+Na]^+$: 933.4342 found: 933.4346.

6,20-Dibenzyloxy-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo-[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-3,5,7(34),12,14,17,19,21(31),26,28,29,32-dodecaene-9,23-diyne (30)



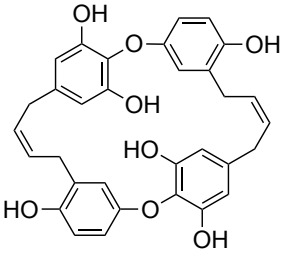
To a solution of triyne **29** (20 mg, 0.022 mmol) in toluene (5 mL) in a glove box was added the Schrock catalyst (2 mg, 0.008 mmol). The reaction was heated at 80 °C for 16 h then filtered through a plug of silica and concentrated *in vacuo*. Purification by column chromatography (silica, 10 to 30% EtOAc in petroleum ether) afforded the title compound **30** (18 mg, 0.022 mmol, quant.) as a yellow oil. **IR** ν_{max} (neat, cm^{-1}): 2957 s, 2917 m, 1731br, 1496 s, 1462 m, 1423 m, 1337 w, 1239 m, 1218 s, 1195 m, 1128 s, 1026 w, 963 w, 913 w. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.47–7.28 (10H, m, 10 × Ar**H**), 7.10 (2H, dd, *J* = 8.8, 3.0 Hz, 2 × Ar**H**), 6.98 (2H, d, *J* = 3.0 Hz, 2 × Ar**H**), 6.89 (2H, d, *J* = 8.8 Hz, 2 × Ar**H**), 6.54 (4H, s, 4 × Ar**H**), 5.06 (4H, s, 2 × C**H$_2$**), 3.69 (12H, s, 4 × C**H$_3$**), 3.63 (4H, br s, 2 × C**H$_2$**), 3.51 (4H, br s, 2 × C**H$_2$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.4 (**C**), 152.8 (**C**), 150.7 (**C**), 137.6 (**C**), 134.1 (**C**), 131.3 (**C**), 128.7 (**C**H), 128.0 (**C**H), 127.4 (**C**H), 126.4 (**C**), 114.9 (**C**H), 113.3 (**C**H), 112.6 (**C**H), 105.0 (**C**H), 80.9 (**C**), 80.6 (**C**), 70.7 (**C**H_2), 56.6 (**C**H_3), 25.1 (**C**H_2), 20.2 (**C**H_2). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{50}H_{44}NaO_8^+$ $[M+Na]^+$: 795.2933 found: 795.2917. **X-ray**: see Figure 2 in paper (crystal attained from an EtOAc solution at –20 °C for 7 days).

6,20-Dibenzyloxy-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo-[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-3,5,7(34),12,14,17,19,21(31),23,26,28,29,32-tetradecaene (31)



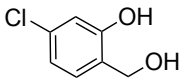
To a solution of diyne **30** (15.0 mg, 0.019 mmol) in MeOH (2 mL) and EtOAc (0.5 mL) was added Lindlar catalyst (1.0 mg) and quinoline (30 µL, 0.25 mmol). The reaction was placed under an atmosphere of hydrogen for 4 h then filtered through a plug of silica and concentrated *in vacuo*. Purification by column chromatography (silica, 10 to 20% EtOAc in petroleum ether) afforded the title compound **31** (10.0 mg, 0.013 mmol, 68%) as a pale yellow oil. **IR** ν_{max} (neat, cm^{-1}): 2916 br, 2849 m, 1492 m, 1462 m, 1423 w, 1217 m, 1127 s, 1026 w, 805 w, 754 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.50–7.29 (10H, m, 10 × Ar**H**), 7.07 (2H, dd, *J* = 8.8, 3.1 Hz, 2 × Ar**H**), 6.91 (2H, d, *J* = 8.9 Hz, 2 × Ar**H**), 6.33 (2H, d, *J* = 3.1 Hz, 2 × Ar**H**), 6.27 (4H, s, 4 × Ar**H**), 5.74 (2H, dt, *J* = 10.7, 7.6 Hz, 2 × =CH), 5.57 (2H, dt, *J* = 10.7, 7.6 Hz, 2 × =CH), 5.10 (4H, s, 2 × C**H$_2$**), 3.60 (12H, s, 4 × C**H$_3$**), 3.47 (4H, d, *J* = 7.6 Hz, 2 × C**H$_2$**), 3.36 (4H, d, *J* = 7.6 Hz, 2 × C**H$_2$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.3 (**C**), 152.9 (**C**), 151.3 (**C**), 138.1 (**C**), 137.8 (**C**), 130.9 (**C**), 130.0 (**C**), 128.7 (**C**H), 128.6 (**C**H), 128.5 (**C**H), 127.9 (**C**H), 127.4 (**C**H), 115.1 (**C**H), 114.2 (**C**H), 113.1 (**C**H), 105.9 (**C**H), 70.8 (**C**H_2), 56.4 (**C**H_3), 33.8 (**C**H_2), 28.8 (**C**H_2). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{50}H_{48}NaO_8^+$ $[M+Na]^+$: 799.3246 found: 799.3236.

(9*E*,23*E*)-2,16-Dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-3,5,7(34),9,12,14,17,19,21(31),23,26,28,29,32-tetradecaene-6,14,20,28,29,32-hexol (11)



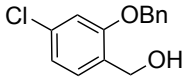
Adapted from a protocol by Coe *et al.* To a solution of macrocycle **31** (5 mg, 0.064 mmol) and TBAI (138 mg, 0.05mmol) in DCM (1 mL) at –78 °C was added BCl_3 (0.16 mL, 0.080 mmol) dropwise. The reaction mixture was warmed to 0 °C for 3 h then ice (1.0 g) and sat. $NaHCO_3$ (2 mL) were added. The aqueous phase was separated and extracted with DCM (3 × 3 mL) then the organic phases were combined, washed with 1 M HCl (3 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The resulting mixture was twice passed through an amberlyst® 15 hydrogen form column then purified by preparative HPLC (C-18, Luna, 30 to 80% acetonitrile in water, 0.01% TFA, 22 min) to afford the chrysophaentin analogue **11** (3.2 mg, 0.0060 mmol, 92%) as a white solid. **IR** ν_{max} (neat, cm^{-1}): 3431 br, 1686 s, 1439 m, 1210 s, 1146 s, 848 w, 805 w, 726 m. **^{1}H NMR** (400 MHz; CD_3OD): δ ppm 6.93 (2H, dd, *J* = 8.7, 2.9 Hz, 2 × Ar**H**), 6.77 (2H, d, *J* = 8.7 Hz, 2 × Ar**H**), 6.41 (2H, d, *J* = 3.1 Hz, 2 × Ar**H**), 6.22 (4H, s, 4 × Ar**H**), 5.56 (2H, dt, *J* = 10.8, 7.9 Hz, 2 × =C**H**), 5.37 (2H, dt, *J* = 10.8, 7.7 Hz, 2 × =C**H**), 3.34 (4H, br d, *J* = 7.3 Hz, 2 × C**H$_2$**), 3.22 (4H, br d, *J* = 7.3 Hz, 2 × C**H$_2$**). **^{13}C NMR** (100 MHz; $CDCl_3$): δ ppm 153.0 (**C**), 151,6 (**C**), 150.4 (**C**), 139.9 (**C**), 130.2 (**C**H), 128.8 (**C**), 127.9 (**C**H), 119.7 (**C**), 116.8 (**C**H), 116.1 (**C**H), 114.0 (**C**H), 109.7 (**C**H), 34.5 (**C**H$_2$), 28.8 (**C**H$_2$). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{32}H_{28}NaO_8^+$ [M+Na]$^+$: 563.1681 found: 563.1666.

5-Chloro-2-(hydroxymethyl)phenol (33)



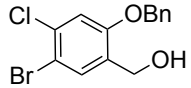
To a solution of 4-chloro-2-hydroxybenzoic acid **32** (5.18 g, 0.30 mmol) in THF (100 mL) at 0 °C was added a solution of $LiAlH_4$ (1 M in THF, 45 mL, 45.0 mmol) dropwise over 10 minutes. After 4 h at 40 °C, MeOH (20 mL) and saturated Rochelle's salt (30 mL) were added. After a further 2 h the aqueous phase was separated and extracted with EtOAc (3 x 50 mL). The organic phases were combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (silica, EtOAc) to afford compound **33** as an off-white solid (4.50 g, 28.3 mmol, 95%) with physical and spectroscopic data consistent with reported values.[8] **MP**: 118–119.5 °C (EtOAc) (lit. 119–120 °C).[9] **IR** ν_{max} (neat, cm^{-1}): 3714 br, 2921 w, 2154 w, 2055 m, 1981 m, 1953 m, 1608 w, 1570 w, 1471 w, 1209 w, 1076 w, 1007 w, 810 w. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.48 (1H, s, O**H**), 6.94 (1H, d, *J* = 8.1 Hz, Ar**H**), 6.91 (1H, d, *J* = 2.0 Hz, Ar**H**), 6.83 (1H, dd, *J* = 8.1, 2.0 Hz, Ar**H**), 4.86 (2H, s, C**H$_2$**), 2.11 (1H, br s, O**H**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 157.2 (**C**), 134.9 (**C**), 128.6 (**C**H), 123.1 (**C**), 120.3 (**C**H), 117.2 (**C**H), 64.5 (**C**H$_2$). **LRMS** (HPLC–MS; ESI$^-$): 159 ([M{^{37}Cl}–H]$^-$, 36%), 157 ([M{^{35}Cl}–H]$^-$, 100%).

(2-(Benzyloxy)-4-chlorophenyl)methanol (34)



To a solution of phenol **33** (5.00 g, 31.5 mmol) in acetone (210 mL) was added K_2CO_3 (12.6 g, 91.4 mmol) and benzyl bromide (5.93 g, 4.12 mL, 34.7 mmol). After 18 h at 40 °C, the reaction mixture was cooled and concentrated *in vacuo*. The resulting residue was partitioned between EtOAc (100 mL) and water (100 mL) then the aqueous phase was separated and extracted with EtOAc (3 x 50 mL). The organic phases were combined, washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 30-40% EtOAc in petroleum ether) afforded compound **34** as a white solid (7.06 g, 28.4 mmol, 90%) with physical and spectroscopic data consistent with reported values. **MP**: 58–59 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 3289 br s, 2919 w, 2862 w, 1597 m, 1585 m, 1489 m, 1450 m, 1404 m, 1365 m, 1241 s, 1225 s, 1053 s, 1043 s, 1026 s, 903 s, 835 m, 725 s, 690 s. **^{1}H NMR** (400 MHz; MeCN-*d$_3$*): δ ppm 7.48–7.30 (6H, m, 6 x Ar**H**), 7.02 (1H, d, *J* = 2.0 Hz, Ar**H**), 6.98 (1H, dd, *J* = 8.1, 2.0 Hz, Ar**H**), 5.12 (2H, s, C**H$_2$**), 4.59 (2H, d, *J* = 6.0 Hz, C**H$_2$**), 3.11 (1H, t, *J* = 6.0 Hz, O**H**). **^{13}C NMR** (101 MHz; MeCN-*d$_3$*): δ ppm 157.4 (**C**), 137.9 (**C**), 133.7 (**C**), 130.5 (**C**), 129.7 (**C**H), 129.6 (**C**H), 129.0 (**C**H), 128.5 (**C**H), 121.4 (**C**H), 113.2 (**C**H), 70.9 (**C**H$_2$), 59.7 (**C**H$_2$). **LRMS** (HPLC–MS; ESI$^+$): 233 ([M{^{37}Cl}–OH]$^+$, 36%), 231 ([M{^{35}Cl}–OH]$^+$, 100%). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{14}H_{13}ClNaO_2^+$ [M+Na]$^+$: 271.0501 found: 271.0486.

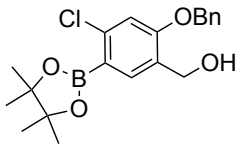
(2-(Benzyloxy)-5-bromo-4-chlorophenyl)methanol (35)



To a solution of benzyl alcohol **34** (6.50 mg, 26.1 mmol) in DMF (52 mL) was added *N*-bromosuccinimide (4.88 g, 27.4 mmol). After 24 h at RT, EtOAc (200 mL) and H_2O (700 mL) were added. The organic phase was separated, washed with H_2O (3 x 150 mL) and brine (150 mL) then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 10% EtOAc in petroleum ether) afforded the title compound **35** (8.01 g, 24.4 mmol, 94%) as an off-white solid. **MP**: 89–91.5 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 3260 br s, 2917 w, 2864 w, 1596 m, 1585 m, 1488 m, 1450 m, 1242 s, 1041 m, 1001 m, 900 m, 835 m, 725 m, 690 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.57 (1H, br s), 7.45–7.33 (5H, m, Ar**H**), 7.04 (1H,

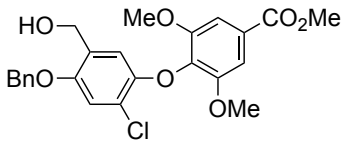
s, Ar**H**), 5.07 (2H, s, C**H**$_2$), 4.67 (2H, br s, C**H**$_2$). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 155.9 (**C**), 135.9 (**C**), 133.9 (**C**), 132.9 (**C**H), 130.4 (**C**), 129.0 (**C**H), 128.6 (**C**H), 127.5 (**C**H), 114.0 (**C**), 113.4 (**C**H), 70.9 (**C**H$_2$), 60.7 (**C**H$_2$). **HRMS** (ESI$^+$): Calculated for $C_{14}H_{12}BrClNaO_2^+$ $[M+Na]^+$ 348.9606, found 348.9603.

(2-(Benzyloxy)-4-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl)-methanol (37)



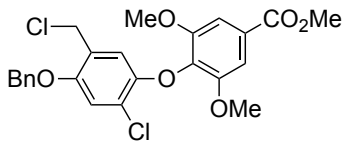
A flask charged with arylbromide **35** (5.00 g, 15.3 mmol), *bis*(pinacolato)diboron (4.65 g, 18.3 mmol) and KOAc (4.20 g, 42.8 mmol) was evacuated and filled with argon in 3 cycles. 1,4-dioxane (80 mL) was then added, followed by Pd(dppf)Cl_2 (1.87 g, 2.30 mmol) and the reaction mixture was degassed with argon for 5 min. After 48 h at 80 °C, the reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica, 10% EtOAc in petroleum ether) to afford the title compound **37** as an off-white solid (4.65 g, 12.4 mmol, 81%). **MP**: 101–102 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 3408 br s, 2974 w, 2925 w, 1600 m, 1371 m, 1324 s, 1232 w, 1140 s, 1120 m, 1052 w, 968 w, 851 m, 731 m, 697 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.67 (1H, s, Ar**H**), 7.42-7.35 (5H, m, 5 x Ar**H**), 6.96 (1H, s, Ar**H**), 5.11 (2H, s, C**H**$_2$), 4.69 (2H, d, *J* = 6.7 Hz, C**H**$_2$), 2.05 (1H, t, *J* = 6.7 Hz, O**H**), 1.35 (12H, s, 4 x C**H**$_3$). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 159.1 (**C**), 140.7 (**C**), 137.1 (**C**H), 136.1 (**C**), 129.0 (**C**H), 128.5 (**C**H), 127. (**C**), 127.5 (**C**H), 113.4 (**C**H), 84.1 (**C**), 70.5 (**C**H$_2$), 61.5 (**C**H$_2$), 25.0 (**C**H$_3$) with one **C** coincident or not observed. **LRMS** (HPLC-MS; ESI$^+$): 399 ([M{^{37}Cl}+Na]$^+$, 1%), 397 ([M{^{35}Cl}+Na]$^+$, 5%), 357 ([M{^{37}Cl}–H_2O+H]$^+$, 23%), 397 [M{^{35}Cl}–H_2O+H]$^+$, 68%). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{20}H_{24}BClNaO_4^+$ $[M+Na]^+$ 397.1353, found: 397.1352.

Methyl 4-(4-(benzyloxy)-2-chloro-5-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (36)



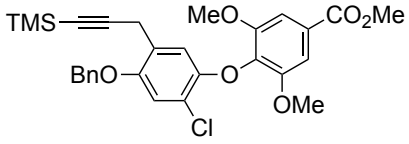
To a solution of phenol **16** (991 mg, 4.67 mmol), borolane **37** (1.75 g, 4.67 mmol) and copper triflate (338 mg, 0.93 mmol) in EtOH (70 mL) was added powdered molecular sieves (1:1 phenol; 991 mg). The reaction mixture was placed under a slight positive pressure of oxygen then pyridine (2.83 mL, 35.0 mmol) was added. After 18 h at 65 °C the reaction mixture was filtered through a pad of silica and concentrated *in vacuo*. Purification by column chromatography (silica, 30% EtOAc in petroleum ether) afforded the title compound **36** (1.71 g, 3.73 mmol, 80%) as a pale orange solid. **MP**: 145–146.5 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 3497 br, 2929 w, 2839 w, 1699 m, 1597 m, 1491 m, 1462 w, 1337 s, 1215 s, 1184 s, 1126 s, 1113 s, 993 m, 864 m, 760 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.43–7.34 (5H, m, 5 x Ar**H**), 7.03 (1H, s, Ar**H**), 6.51 (1H, s, Ar**H**), 5.06 (2H, s, Ar**H**), 4.53 (2H, d, *J* = 6.2 Hz, C**H**$_2$), 3.94 (3H, s, C**H**$_3$), 3.83 (6H, s, 2 x C**H**$_3$), 2.04 (1H, t, *J* = 6.5 Hz, O**H**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 166.7 (**C**), 153.2 (**C**), 151.4 (**C**), 148.1 (**C**), 136.9 (**C**), 136.5 (**C**), 129.1 (**C**), 128.9 (**C**H), 128.4 (**C**H), 127.6 (**C**H), 127.4 (**C**), 121.6 (**C**), 115.1 (**C**H), 114.3 (**C**H), 107.2 (**C**H), 71.2 (**C**H$_2$), 61.4 (**C**H$_3$), 56.7 (**C**H$_3$), 52.5 (**C**H$_2$). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{24}H_{23}ClNaO_7^+$ $[M+Na]^+$ 481.1030, found 481.1019.

Methyl 4-(4-(benzyloxy)-2-chloro-5-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (38)



To a solution of benzyl alcohol **36** (8.53 g, 18.6 mmol) in THF (100 mL) at 0 °C was added PPh_3 (5.85 g, 22.3 mmol) and *N*-chlorosuccinimide (2.97 g, 22.3 mmol). After 4 h at RT, the reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica, 60–70% $CHCl_3$ in petroleum ether) to afford the title compound **38** (8.50 g, 17.8 mmol, 96%) as an off-white solid. **MP**: 175–176 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 2942 w, 2838 w, 1728 m, 1599 m, 1500 s, 1340 m, 1257 m, 1221 s, 1132 s, 997 m, 866 m, 760 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.46-7.36 (7H, m, 7 x Ar**H**), 7.03 (1H, s, Ar**H**), 6.56 (1H, s, Ar**H**), 5.09 (2H, s, C**H**$_2$), 4.49 (2H, s, C**H**$_2$), 3.95 (3H, s, C**H**$_3$), 3.83 (6H, s, 2 x C**H**$_3$). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 166.6 (**C**), 153.1 (**C**), 151.5 (**C**), 147.9 (**C**), 136.7 (**C**), 136.6 (**C**), 128.8 (**C**H), 128.3 (**C**H), 127.5 (**C**), 127.4 (**C**H), 125.7 (**C**), 123.1 (**C**), 116.8 (**C**H), 114.9 (**C**H), 107.3 (**C**H), 71.3 (**C**H$_2$), 56.7 (**C**H$_3$), 52.5 (**C**H$_3$), 41.0 (**C**H$_2$). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{24}H_{22}Cl_2NaO_6^+$ $[M+Na]^+$ 499.0691, found 499.0693.

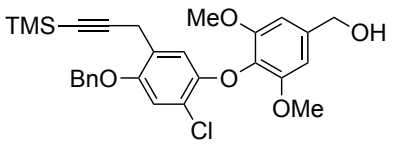
Methyl 4-(4-(benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (39)



A flask charged with Pd(dppf)Cl_2.DCM (49 mg, 0.06 mmol) and KF (351 mg, 6.04 mmol) was evacuated and filled with argon in 3 cycles. Tributyl(trimethylsilyl-ethynyl)tin (876 mg, 2.26 mmol), benzyl chloride **38** (720 mg, 1.51 mmol) and 1,4-dioxane (10 mL) were then added, the reaction mixture was degassed with argon for 5 min, heated to 80 °C for 3 h then concentrated *in vacuo*. Purification by column chromatography (9:1 silica:K_2CO_3,[10] 20% EtOAc in petroleum ether) afforded the title compound **39** as an off white solid (802 mg, 1.49 mmol, 99%). **MP**: 133–135 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 2956 m, 2922 m, 2852 m, 1716 s, 1595 m, 1488 m, 1465 m, 1414 m, 1337 m, 1234 m, 1209 s, 1186 s, 1122 s, 841 s, 758 s. **^{1}H NMR** (400 MHz;

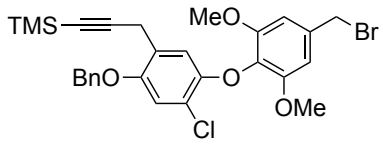
$CDCl_3$): δ ppm 7.42–7.31 (7H, m, 7 x Ar**H**), 6.97 (1H, s, Ar**H**), 6.79 (1H, s, Ar**H**), 5.03 (2H, s, C**H₂**), 3.94 (3H, s, C**H₃**), 3.84 (6H, s, 2 x C**H₃**), 3.53 (2H, s, C**H₂**), 0.01 (9H, s, 3 x C**H₃**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 166.6 (**C**), 153.2 (**C**), 150.8 (**C**), 148.0 (**C**), 136.9 (**C**), 136.8 (**C**), 128.7 (**C**H), 128.2 (**C**H), 127.4 (**C**), 127.3 (**C**H), 124.8 (**C**), 120.3 (**C**), 115.3 (**C**H), 113.8 (**C**H), 107.4 (**C**H), 103.4 (**C**), 87.7 (**C**), 70.9 (**C**H_2), 56.7 (**C**H_3), 52.4 (**C**H_3), 20.8 (**C**H_2), 0.0 (**C**H_3). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{29}H_{32}ClO_6Si^+$ $[M+Na]^+$ 539.1656, found 539.1654.

(4-(4-(Benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (41)



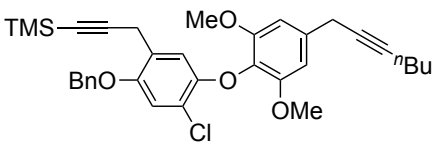
To a solution of benzyl ester **39** (6.21 g, 11.5 mmol) in THF (175 mL) at 0 °C was added a solution of $LiAlH_4$ (1M in THF, 12.7 mL, 12.7 mmol) over 5 min. After 4 h at RT, MeOH (30 mL) and sat. Rochelle's salt (60 mL) was added. After a further 1 h the aqueous phase was separated and extracted with EtOAc (3 x 50 mL) then the organic phases were combined, washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 35-40% EtOAc in petroleum ether) afforded the title compound **41** as an off-white solid (5.22 g, 10.2 mmol, 89%). **MP**: 108.5–110 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 3587 br, 2955 w, 2941 w, 2912 w, 2355 w, 2340 w, 2156 m, 2015 m, 1601 m, 1495 s, 1387 s, 1219 s, 1126 s, 1037 m, 841 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.42–7.30 (5H, m, 5 x Ar**H**), 6.96 (1H, s, Ar**H**), 6.79 (1H, s, Ar**H**), 6.68 (2H, s, 2 x Ar**H**), 5.02 (2H, s, C**H₂**), 4.69 (2H, d, *J* = 5.9 Hz, C**H₂**), 3.80 (6H, s, 2 x C**H₃**), 3.52 (2H, s, C**H₂**), 1.66 (1H, t, *J* = 6.1 Hz, O**H**), 0.04 (9H, s, 3 x C**H₃**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 153.5 (**C**), 150.5 (**C**), 148.4 (**C**), 138.7 (**C**), 136.9 (**C**), 131.9 (**C**), 128.7 (**C**H), 128.1 (**C**H), 127.3 (**C**H), 124.7 (**C**), 120.1 (**C**), 114.7 (**C**H), 113.7 (**C**H), 104.1 (**C**H), 103.7 (**C**), 87.3 (**C**), 70.9 (**C**H_2), 65.6 (**C**H_2), 56.6 (**C**H_3), 20.8 (**C**H_2), 0.1 (**C**H_3). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{28}H_{31}ClNaO_5Si^+$ $[M+Na]^+$ 533.1527; found 533.1536.

(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)-4-chlorophenyl)prop-1-yn-1-yl)trimethylsilane (43)



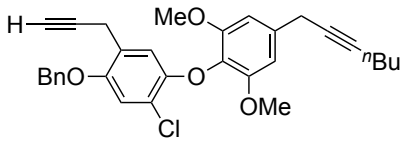
To a solution of benzyl alcohol **41** (5.22, 10.2 mmol) in THF (150 mL) at 0 °C was added PPh_3 (3.21 g, 12.2 mmol) and *N*-bromosuccinimide (2.18 g, 12.2 mmol). After 3 h at RT, the reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica, 0–15% EtOAc in petroleum ether) to afford the title compound **43** as a cream solid (5.82 g, 10.1 mmol, 99%). **MP**: 124.5–126.5 °C ($CHCl_3$). **IR** ν_{max} (neat, cm^{-1}): 2943 w, 2916 w, 2172 w, 1597 m, 1491 m, 1466 m, 1392 m, 1337 m, 1246 m, 1203 m, 1113 s, 1022 m, 841 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.47–7.31 (5H, m, 5 x Ar**H**), 6.95 (1H, s, Ar**H**), 6.79 (1H, s, Ar**H**), 6.69 (2H, s, 2 x Ar**H**), 5.02 (2H, s, C**H₂**), 4.47 (2H, s, C**H₂**), 3.80 (6H, s, 2 x C**H₃**), 3.53 (2H, s, C**H₂**), 0.05 (9H, s, 3 x C**H₃**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 153.4 (**C**), 150.6 (**C**), 148.2 (**C**), 136.9 (**C**), 135.2 (**C**), 131.8 (**C**), 128.7 (**C**H), 128.1 (**C**H), 127.3 (**C**H), 124.7 (**C**), 120.3 (**C**), 115.2 (**C**H), 113.7 (**C**H), 106.7 (**C**H), 103.6 (**C**), 87.4 (**C**), 70.9 (**C**H_2), 56.6 (**C**H_3), 33.9 (**C**H_2), 20.8 (**C**H_2), 0.2 (**C**H_3). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{28}H_{31}BrClO_4Si$ $[M+H]^+$ 573.0863; found 573.0874.

(3-(2-(Benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (45)



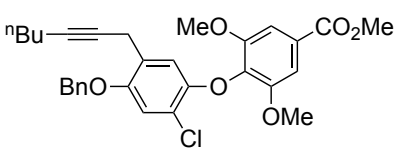
To a solution of hex-1-yne (0.98 mL, 0.85 mmol) in Et_2O (15 mL) at 0 °C was added ^{n}BuLi (2.5M in hexane, 0.34 mL, 0.85 mmol) over 5 min. After 1 h at 0 °C, Et_2AlCl (1M in hexane, 0.85 mL, 0.85 mmol) was added over 5 min. After 20 min at 0 °C and 2 h at RT, $NiCl_2(PPh_3)_2$ (20 mg, 0.03 mmol) was added followed after 15 min by benzyl bromide **43** (245 mg, 0.43 mmol). After a further 2 h at RT, sat. NH_4Cl (5 mL) was added, then the aqueous phase was separated and extracted with Et_2O (3 x 5 mL). The organic phases were combined, washed with brine (8 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 5–10% EtOAc in petroleum ether) afforded the title compound **45** as a yellow oil (204 mg, 0.35 mmol, 82%). **IR** ν_{max} (neat, cm^{-1}): 2958 w, 2935 w, 2871 w, 2177 w, 1699 w, 1597 m, 1491 m, 1462 m, 1215 s, 1126 s, 841 s. **^{1}H NMR** (400 MHz; acetone-d_6): δ ppm 7.53 (2H, d, *J* = 7.0 Hz, 2 x Ar**H**), 7.41–7.33 (3H, m, 3 x Ar**H**), 7.13 (1H, s, Ar**H**), 6.84 (2H, s, 2 x Ar**H**), 6.83 (1H, s, Ar**H**), 5.17 (2H, s, C**H₂**), 3.77 (6H, s, 2 x C**H₃**), 3.63 (2H, t, *J* = 2.4 Hz, C**H₂**), 3.53 (2H, d, *J* = 0.7 Hz, C**H₂**), 2.34–2.19 (2H, m, C**H₂**), 1.60–1.39 (4H, m, 2 x C**H₂**), 0.92 (3H, t, *J* = 7.2 Hz, C**H₃**), 0.04 (9H, s, 3 x C**H₃**). **^{13}C NMR** (101 MHz; acetone-d_6): δ ppm 154.1 (**C**), 151.2 (**C**), 149.3 (**C**), 138.3 (**C**), 136.7 (**C**), 129.4 (**C**H), 128.8 (**C**H), 128.4 (**C**H), 125.5 (**C**), 123.7 (**C**), 120.1 (**C**), 115.2 (**C**H), 114.7 (**C**H), 106.1 (**C**H), 104.2 (**C**), 88.1 (**C**), 83.7 (**C**), 78.1 (**C**), 71.5 (**C**H_2), 56.6 (**C**H_3), 32.0 (**C**H_2), 25.7 (**C**H_2), 22.7 (**C**H_2), 21.0 (**C**H_2), 19.0 (**C**H_2), 14.0 (**C**H_3), 0.18 (**C**H_3). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{34}H_{40}ClO_4Si^+$ $[M+H]^+$ 575.2384; found 575.2360; Calculated for $C_{34}H_{39}ClNaO_4Si^+$ $[M+Na]^+$ 597.2203; found 597.2184.

2-(4-(Benzyloxy)-2-chloro-5-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (46)



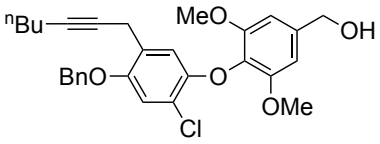
To a solution of TMS-alkyne **45** (100 mg, 0.17 mmol) in MeOH/H_2O/DCM (4:1:7; 1.2 mL: 0.3 mL: 2.0 mL) was added AgOTf (13 mg, 0.05 mmol). After 20 h in the dark, NH_4Cl (3 mL) was added then the aqueous phase was separated and extracted with DCM (3 x 5 mL). The organic phases were combined, washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (5–15% Et_2O in petroleum ether) afforded the title compound **46** as a pale yellow gelatinous solid (74 mg, 0.15 mmol, 87%). **IR** ν_{max} (neat, cm^{-1}): 3302 w, 2957 m, 2927 m, 2856 w, 1597 m, 1493 m, 1460 m, 1395 w, 1238 w, 1217 m, 1124 s. **^{1}H NMR** (400 MHz; MeCN-d_3): δ ppm 7.48–7.32 (5H, m, 5 x Ar**H**), 7.10 (1H, s, Ar**H**), 6.78 (2H, s, 2 x Ar**H**), 6.65 (1H, s, Ar**H**), 5.09 (2H, s, C**H$_2$**), 3.75 (6H, s, 2 x C**H$_3$**), 3.60 (2H, s, C**H$_2$**), 3.44 (2H, d, *J* = 2.6 Hz, C**H$_2$**), 2.28-2.24 (2H, br d, *J* = 10.8 Hz, C**H$_2$**), 2.33 (1H, s, C**H**), 1.53–1.44 (4H, m, 2 x C**H$_2$**), 0.92 (3H, t, *J* = 7.0 Hz, C**H$_3$**). **^{13}C NMR** (101 MHz; MeCN-d_3): δ ppm 154.0 (**C**), 151.4 (**C**), 148.9 (**C**), 138.1 (**C**), 137.2 (**C**), 131.0 (**C**), 129.6 (**C**H), 129.0 (**C**H), 128.6 (**C**H), 126.0 (**C**), 120.3 (**C**), 115.8 (**C**H), 115.3 (**C**H), 106.1 (**C**H), 84.0 (**C**), 82.2 (**C**H), 78.3 (**C**), 71.84 (**C**H_2), 71.76 (**C**), 56.8 (**C**H_3), 31.9 (**C**H_2), 25.7 (**C**H_2), 22.7 (**C**H_2), 19.7 (**C**H_2), 18.9 (**C**H_2), 13.9 (**C**H_3). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{31}H_{31}ClNaO_4^+$ $[M+Na]^+$ 525.1808, found 525.1791.

Methyl 4-(4-(benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (40)



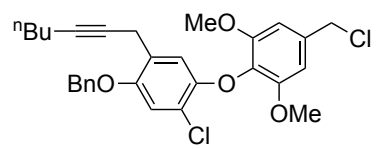
A flask charged with benzyl chloride **38** (200 mg, 0.42 mmol), $PdCl_2(MeCN)_2$ (7 mg, 0.03 mmol), XPhos (36 mg, 0.08 mmol) and Cs_2CO_3 (151 mg, 0.46 mmol) was evacuated and filled with argon in 3 cycles. Hex-1-yne (0.75 mL, 0.67 mmol) and MeCN (2 mL) were then added sequentially, the reaction mixture was degassed with argon for 5 min, heated to 65 °C for 18 h then filtered through a pad of silica and concentrated *in vacuo*. Purification by column chromatography (silica, 10% EtOAc in petroleum ether) afford the title compound **40** as a pale brown solid (164 mg, 0.31 mmol, 75%). **MP**: 138.5–140 °C (EtOAc). **IR** ν_{max} (neat, cm^{-1}): 2954 w, 1712 m, 1458 m, 1422 m, 1336 s, 1213 m, 1128 m, 997 m, 866 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.42–7.34 (7H, m, 7 x Ar**H**), 6.95 (1H, s, Ar**H**), 6.78 (1H, s, Ar**H**), 5.03 (2H, s, C**H$_2$**), 3.93 (3H, s, C**H$_3$**), 3.84 (6H, s, 2 x C**H$_3$**), 3.43 (2H, s, C**H$_2$**), 2.06–1.99 (2H, m, C**H$_2$**), 1.29–1.25 (4H, m, 2 x C**H$_2$**), 0.84 (3H, t, *J* = 7.1 Hz, C**H$_3$**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 166.7 (**C**), 153.3 (**C**), 150.9 (**C**), 147.9 (**C**), 137.1 (**C**), 137.0 (**C**), 128.7 (**C**H), 128.1 (**C**H), 127.4 (**C**), 127.2 (**C**H), 126.2 (**C**), 120.1 (**C**), 115.6 (**C**H), 113.7 (**C**H), 107.3 (**C**H), 83.4 (**C**), 76.6 (**C**), 70.9 (**C**H_2), 56.7 (**C**H_3), 52.4 (**C**H_3), 31.2 (**C**H_2), 22.0 (**C**H_2), 19.7 (**C**H_2), 18.4 (**C**H_2), 13.6 (**C**H_3). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{30}H_{31}ClNaO_6^+$ $[M+Na]^+$ 545.1706, found 545.1704.

(4-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (42)



To a solution of benzyl ester **40** (292 mg, 0.56 mmol) in THF (4.5 mL) at 0 °C was added a solution of $LiAlH_4$ (1 M in THF, 0.56 mL, 0.56 mmol) over 5 min. After 1 h at RT, MeOH (1 mL) and sat. Rochelle's salt (2 mL) were added. After a further 30 min the aqueous phase was separated and extracted with Et_2O (3 x 5 mL). The organic phases were combined, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 40% EtOAc in petroleum ether) afforded the title compound **42** as a pale yellow oil (236 mg, 0.48 mmol, 85%). **IR** ν_{max} (neat, cm^{-1}): 3384 w, 2956 w, 2926 m, 2858 m, 2361 w, 2332 w, 1597 m, 1491 m, 1459 m, 1215 m, 1187 m, 1126 s, 696 m. **^{1}H NMR** (400 MHz; DMSO-d_6): δ ppm 7.48–7.30 (5H, m, 5 x Ar**H**), 7.15 (1H, s, Ar**H**), 6.77 (2H, s, 2 x Ar**H**), 6.64 (1H, s, Ar**H**), 5.28 (1H, t, *J* = 5.7 Hz, O**H**), 5.12 (2H, s, C**H$_2$**), 4.52 (2H, d, *J* = 5.6 Hz, C**H$_2$**), 3.71 (6H, s, 2 x C**H$_3$**), 3.38 (2H, br s, C**H$_2$**), 2.06–1.96 (2H, m, C**H$_2$**), 1.29–1.20 (4H, m, 2 x C**H$_2$**), 0.82 (3H, t, *J* = 7.1 Hz, C**H$_3$**). **^{13}C NMR** (101 MHz; DMSO-d_6): δ ppm 152.4 (**C**), 149.8 (**C**), 147.5 (**C**), 146.6 (**C**), 140.8 (**C**), 137.0 (**C**), 128.4 (**C**H), 127.8 (**C**H), 127.3 (**C**H), 125.5 (**C**), 118.1 (**C**), 114.1 (**C**H), 113.8 (**C**H), 103.2 (**C**H), 83.2 (**C**), 76.6 (**C**), 70.0 (**C**H_2), 62.9 (**C**H_2), 55.9 (**C**H_3), 30.3 (**C**H_2), 21.3 (**C**H_2), 18.9 (**C**H_2), 17.5 (**C**H_2), 13.3 (**C**H_3). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{29}H_{31}ClNaO_5^+$ $[M+Na]^+$ 517.1757, found 517.1750.

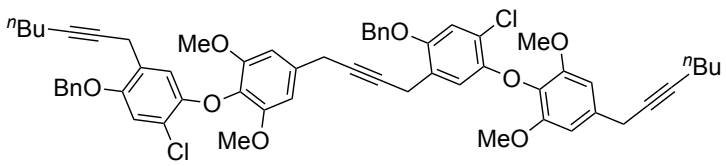
2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (44)



To a solution of benzyl alcohol **42** (200 mg, 0.40 mmol) in THF (4 mL) at 0 °C was added PPh_3 (115 mg, 0.44 mmol) and *N*-chlorosuccinimide (59 mg, 0.44 mmol). After 4 h at RT, sat. $NaHCO_3$ (2 mL) and sat. $Na_2S_2O_3$ (2 mL) were added, the aqueous phase was separated and extracted with Et_2O (3 x 3 mL). The organic phases were combined, washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 10% EtOAc in petroleum ether) afforded the title compound **44** as a pale yellow solid (183 mg, 0.36 mmol, 89%). **MP**: 104.5–105.5 °C ($CHCl_3$). **IR** ν_{max} (neat, cm^{-}

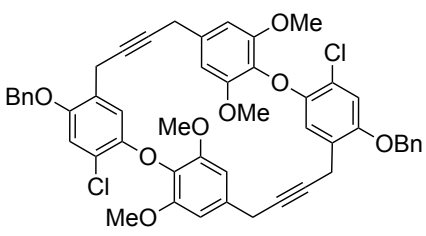
^{1}): 2964 w, 2933 w, 1601 m, 1491 m, 1460 m, 1423 m, 1389 m, 1338 m, 1247 m, 1219 m, 1190 m, 1124 s, 991 w, 700 s, 640 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.51–7.28 (5H, m, 5 x Ar**H**), 6.95 (1H, s, Ar**H**), 6.80 (1H, s, Ar**H**), 6.69 (2H, s, 2 x Ar**H**), 5.02 (2H, s, C**H$_2$**), 4.58 (2H, s, C**H$_2$**), 3.80 (6H, s, 2 x C**H$_3$**), 3.44 (2H, t, *J* = 1.9 Hz, C**H$_2$**), 2.06 (2H, tt, *J* = 6.7, 2.2 Hz, C**H$_2$**), 1.37–1.24 (4H, m, 2 x C**H$_2$**), 0.87 (3H, br t, *J* = 7.0 Hz, C**H$_3$**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 153.5 (**C**), 150.7 (**C**), 148.1 (**C**), 137.0 (**C**), 135.0 (**C**), 132.8 (**C**), 128.7 (**C**H), 128.1 (**C**H), 127.3 (**C**H), 126.0 (**C**), 119.8 (**C**), 115.4 (**C**H), 113.6 (**C**H), 106.1 (**C**H), 83.3 (**C**), 76.7 (**C**), 70.8 (**C**H$_2$), 56.6 (**C**H$_3$), 46.7 (**C**H$_2$), 31.1 (**C**H$_2$), 22.0 (**C**H$_2$), 19.8 (**C**H$_2$), 18.4 (**C**H$_2$), 13.7 (**C**H$_3$). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{29}H_{30}Cl_2NaO_4^+$ [M+Na]$^+$ 535.1418; found 535.1412.

2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(4-(2-(benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)but-2-yn-1-yl)-1,3-dimethoxybenzene (47)



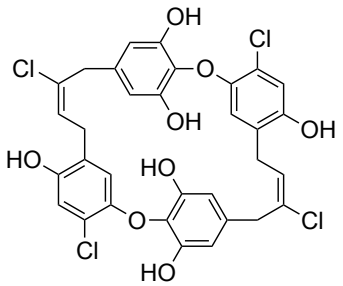
A flask containing alkyne **46** (1.00 g, 1.99 mmol), benzyl chloride **44** (1.22 g, 2.39 mmol), $Pd(MeCN)Cl_2$ (31 mg, 0.12 mmol), XPhos (171 mg, 0.36 mmol) and Cs_2CO_3 (713 mg, 2.19 mmol) was evacuated and filled with argon in 3 cycles. MeCN (10 mL) was added, then the reaction mixture was degassed with argon for 5 min, heated at 65 °C for 12 h and filtered through a pad of silica. Purification by column chromatography (silica, 10–25% Et_2O in petroleum ether) provided the title compound **47** as a pale yellow solid (900 mg, 0.92 mmol, 46%). **MP**: 62–63.5 °C ($CHCl_3$). **IR** ν_{max} (neat, cm^{-1}): 2956 w, 2929 w, 2870 w, 2858 w, 1695 w, 1597 s, 1491 s, 1461 s, 1419 m, 1215 s, 1124 s, 997 m, 750 s, 696 s. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.48–7.28 (10H, m, 10 x Ar**H**), 7.08 (1H, s, Ar**H**), 7.05 (1H, s, Ar**H**), 6.72 (2H, s, 2 x Ar**H**), 6.70 (1H, s, Ar**H**), 6.68 (1H, s, Ar**H**), 6.65 (2H, s, 2 x Ar**H**), 5.08 (2H, s, C**H$_2$**), 5.06 (2H, s, C**H$_2$**), 3.82 (2 H, s, C**H$_2$**), 3.69 (6H, s, 2 x C**H$_3$**), 3.64 (6H, s, 2 x C**H$_3$**), 3.54 (2H, br s, C**H$_2$**), 3.51 (2H, br s, C**H$_2$**), 3.48 (2H, br s, C**H$_2$**), 3.37 (2H, br s, C**H$_2$**), 2.01–1.96 (2H, m, C**H$_2$**), 1.52–1.40 (4H, m, 2 x C**H$_2$**), 1.24–1.18 (4H, m, 2 x C**H$_2$**), 0.88 (3H, br t, *J* = 7.0 Hz, C**H$_3$**), 0.78 (3 H, br t, *J* = 7.0 Hz, C**H$_3$**). **^{13}C NMR** (101 MHz; CD_3CN): δ ppm 153.9 (**C**), 151.4 (**C**), 151.3 (**C**), 148.9 (**C**), 148.8 (**C**), 138.09 (**C**), 138.07 (**C**), 137.2 (**C**), 136.4 (**C**), 130.9 (**C**), 129.5 (**C**H), 129.0 (**C**H), 128.5 (**C**H), 127.2 (**C**), 127.0 (**C**), 119.8 (**C**), 119.6 (**C**), 115.8 (**C**H), 115.3 (**C**H), 115.2 (**C**H), 115.0 (**C**H), 105.95 (**C**H), 105.93 (**C**H), 84.4 (**C**), 84.0 (**C**), 81.0 (**C**), 80.9 (**C**), 78.3 (**C**), 77.3 (**C**), 71.7 (**C**H$_2$), 71.6 (**C**H$_2$), 56.7 (**C**H$_3$), 31.9 (**C**H$_2$), 31.7 (**C**H$_2$), 25.7 (**C**H$_2$), 25.6 (**C**H$_2$), 22.7 (**C**H$_2$), 22.6 (**C**H$_2$), 20.2 (**C**H$_2$), 20.1 (**C**H$_2$) 19.0 (**C**H$_2$), 18.7 (**C**H$_2$), 13.90 (**C**H$_3$), 13.88 (**C**H$_3$) with various signals coincident or not observed. **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{60}H_{60}Cl_2NaO_8^+$ [M+Na]$^+$, 1001.3562; found 1001.3565.

6,20-Bis(benzyloxy)-4,18-dichloro-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-1(28),3(34),4,6,12,14,17(31),18,20,26,29,32-dodecaen-9,23-diyne (48)



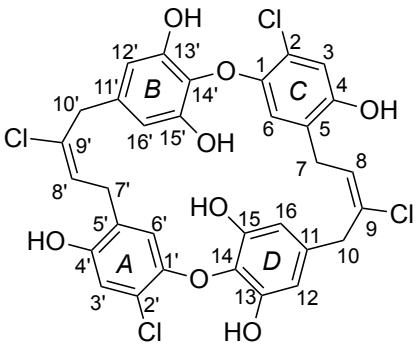
A solution of Mo·phen catalyst (125 mg, 0.1 mmol) and $MnCl_2$ (13 mg, 0.1 mol) in toluene (4 mL) was heated to 80 °C for 1 h, then cooled to RT. A solution of triyne **47** (400 mg, 0.41 mmol) in toluene (2 mL) was then added and the reaction mixture heated to 40 °C for 12 h then filtered through a pad of silica. Purification by column chromatography (silica, 15–25% EtOAc in petroleum ether) afforded the title compound **48** as a pale yellow solid (227 mg, 0.27 mmol, 66%). **MP**: 89.5–90.5 °C ($CHCl_3$). **IR** ν_{max} (neat, cm^{-1}): 2963 w, 2938 w, 1718 m, 1600 m, 1492 s, 1457 s, 1339 w, 1209 s, 1188 s, 1120 s, 994 m, 754 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.45–7.37 (10H, m, 10 x Ar**H**), 7.00 (2H, s, 2 x Ar**H**), 6.97 (2H, s, 2 x Ar**H**), 6.51 (4H, s, 4 x Ar**H**), 5.04 (4H, s, 2 x C**H$_2$**), 3.71 (12H, s, 4 x C**H$_3$**), 3.58 (4H, br s, 2 x C**H$_2$**), 3.49 (4H, br s, 2 x C**H$_2$**). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 153.3 (**C**), 150.4 (**C**), 148.2 (**C**), 136.9 (**C**), 135.1 (**C**), 134.4 (**C**), 128.8 (**C**H), 128.2 (**C**H), 127.4 (**C**H), 125.2 (**C**), 119.1 (**C**), 114.3 (**C**H), 113.4 (**C**H), 105.1 (**C**H), 80.9 (**C**), 80.4 (**C**), 70.8 (**C**H$_2$), 56.7 (**C**H$_3$), 25.0 (**C**H$_2$), 20.0 (**C**H$_2$). **HRMS** (HPLC-MS, ESI$^+$): Calculated for $C_{50}H_{42}Cl_2NaO_8^+$ [M+Na]$^+$ 863.2154; found 863.2146.

Sequence tentatively leading to an impure sample of Chrysophaentin F (8).[11]



To a flask containing $ZrCp_2Cl_2$ (69 mg, 0.24 mmol) in THF (1 mL) at 0 °C was added DiBAlH (1.0 M in hexane, 0.24 mL, 0.24 mmol). After 1 h the reaction mixture was warmed to RT and macrocycle **48** (50 mg, 0.06 mmol) was added. The reaction mixture was then heated to 40 °C for 2 h, cooled to RT and a solution of *N*-chlorosuccinimide (16 mg, 0.12 mmol) in DCM (0.5 mL) was added. After 16 h the reaction mixture was concentrated *in vacuo* and purified by column chromatography (silica, 20–30% EtOAc in petroleum ether) to afford a major fraction (40 mg) exhibiting complex spectral data. This was taken up into DCM (4 mL) and

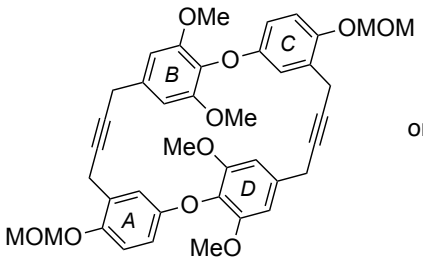
cooled to –78 °C. TBAI (126 mg, 0.34 mmol) and BCl_3 (1.0 M in DCM, 0.53 mL, 0.53 mmol) were added and after 5 min the solution was warmed to 0 °C. After 4 h, ice (1.0 g) and sat. $NaHCO_3$ (1 mL) were added then the reaction mixture was concentrated *in vacuo* and partitioned between Et_2O (5 mL) and H_2O (5 mL). The aqueous phase was separated and extracted with Et_2O (3 x 5 mL) then the organic phases were combined, washed with brine (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (silica, 20-50% EtOAc in petroleum ether) provided an impure fraction (15 mg) containing the title compound **8** as the major component. **^{1}H NMR** (400 MHz; CD_3OD): δ ppm attributed to major isomer 6.90 (2H, s, 2 x Ar**H**), 6.42 (2H, s, 2 x Ar**H**), 6.23 (4H, s, 4 x Ar**H**), 5.89 (2H, t, *J* = 8.3 Hz, 2 x =C**H**), 3.53 (4H, br s, 2 x C$\mathbf{H_2}$), 3.36 (4H, d, *J* = 8.7 Hz, 2 x C$\mathbf{H_2}$). **^{13}C NMR** (101 MHz; CD_3OD): δ ppm attributed to major isomer 151.3 (**C**), 150.7 (**C**), 148.2 (**C**), 137.0 (**C**), 134.3 (**C**), 130.0 (**C**), 127.2 (**C**H), 126.7 (**C**), 120.4 (**C**), 117.4 (**C**H), 115.4 (**C**H), 110.0 (**C**H), 39.8 (**C**H_2), 30.7 (**C**H_2). **LRMS** (HPLC–MS, ESI^-): 681 $[M\{^{35}Cl^{37}Cl_3\}–H]^-$ (15%), 679 $[M\{^{35}Cl_2{}^{37}Cl_2\}–H]^-$ (15%), 677 $[M\{^{35}Cl_3{}^{37}Cl\}–H]^-$ (100%), 675 $[M\{^{35}Cl_4\}-H]^-$ (76%). An attempted separation of these isomers by HPLC in silica led to loss of material. The data attained showed excellent agreement with literature values.[11]



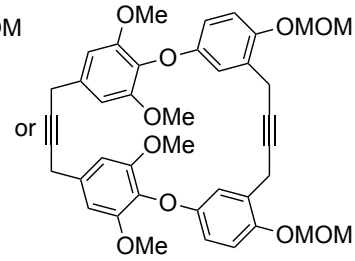
	^{1}H NMR signals literature (CD_3OD)	^{1}H NMR signals observed (CD_3OD)	^{13}C NMR signals literature (observed)
1	-	-	148.2 (148.2)
2	-	-	120.4 (120.4)
3	6.90 (2H, s)	6.90 (2H, s)	117.3 (117.4)
4	-	-	150.7 (150.7)
5	-	-	126.5 (126.7)
6	6.42 (2H, s)	6.42 (2H, s)	115.1 (115.1)
7	3.35 (4H, d, 8.3 Hz)	3.36 (4H, d, 8.4 Hz)	31.0 (30.9)
8	5.89 (2H, t, 8.3 Hz)	5.89 (2H, t, 8.2 Hz)	127.2 (127.2)
9	-	-	134.3 (134.3)
10	3.54 (4H, br s)	3.53 (4H, br s)	39.8 (39.8)
11	-	-	137.0 (137.0)
12, 16	6.23 (2H, s)	6.23 (4H, s)	110.0 (110.0)
13, 15	-	-	151.3 (151.3)
14	-	-	130.0 (130.0)

Macrocycle 50 or 51.

To a solution of alkyne **49** (37.0 mg, 0.09 mmol) in toluene (12 mL) in a nitrogen filled glove box was added the Schrock catalyst, ^{t}BuC≡W(O^{t}Bu)$_3$ (7.0 mg, 0.03 mmol). The reaction was heated at 80 °C for 20 h then filtered through a plug of silica and concentrated *in vacuo*. Purification by HPLC (C-18, Luna, 60 to 90% MeCN in water + 0.01% TFA, 9 min) afforded either macrocycle **50** or macrocycle **51** (2.0 mg, 0.003 mmol, 6%) as a white solid.



50



51

IR ν_{max} (neat, cm^{-1}): 2935 w, 2853 w, 1579 w, 1495 m, 1401m, 1341 m, 1263 s, 1190 m, 1110 s, 1019 s, 914 m, 812 m, 738 m. **^{1}H NMR** (400 MHz; $CDCl_3$): δ ppm 7.08–7.05 (6H, m, 6 × Ar**H**), 6.93 (2H, d, *J* = 0.9 Hz, 2 × Ar**H**), 6.91–6.88 (2H, m, 2 × Ar**H**), 5.16 (4H, s, 2 × C$\mathbf{H_2}$), 3.79 (6H, s, 2 × C$\mathbf{H_3}$), 3.61 (4H, s, 2 × C$\mathbf{H_2}$), 3.59 (6H, s, 2 × C$\mathbf{H_3}$), 3.54 (4H, d, *J* = 0.8 Hz, 2 × C$\mathbf{H_2}$), 3.49 (6H, s, 2 × C$\mathbf{H_3}$). **^{13}C NMR** (101 MHz; $CDCl_3$): δ ppm 152.9 (**C**), 152.0 (**C**), 150.1 (**C**), 149.7 (**C**), 136.3 (**C**), 132.0 (**C**), 127.1 (**C**), 118.9 (**C**), 115.3 (**C**H), 115.2 (**C**H), 113.5 (**C**H), 108.0 (**C**H), 95.3 (**C**H_2), 81.8 (**C**), 79.8 (**C**), 61.1 (**C**H_3), 56.6 (**C**H_3), 56.2 (**C**H_3), 23.5 (**C**H_2), 20.2 (**C**H_2). **HRMS** (HPLC-MS, ESI^+): Calculated for $C_{40}H_{40}NaO_{10}^+$ $[M+Na]^+$ 703.2519; found 703.2547.

3. Reference for Supporting Information

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4-Bromo-2-(hydroxymethyl)phenol (12)

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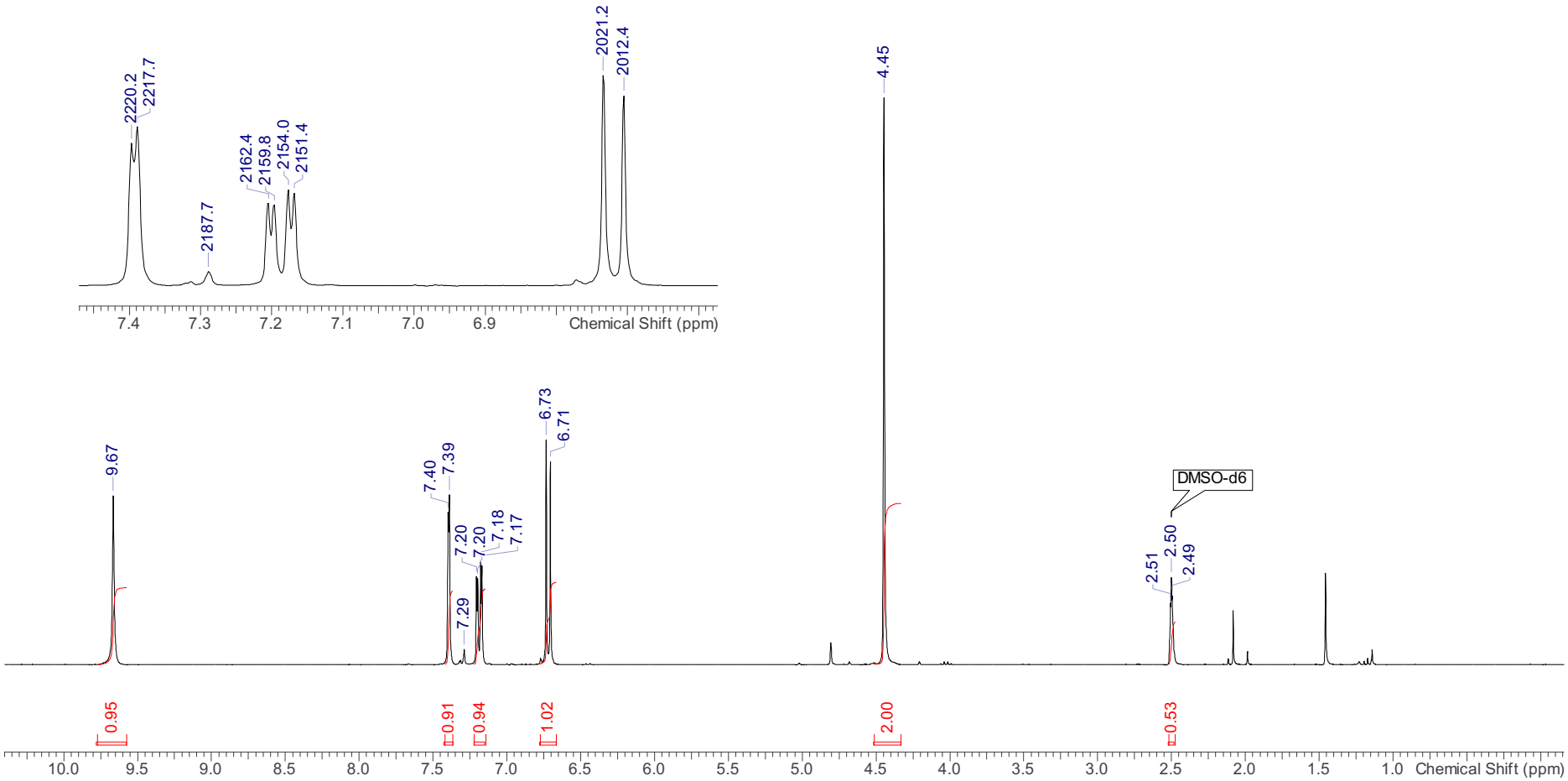
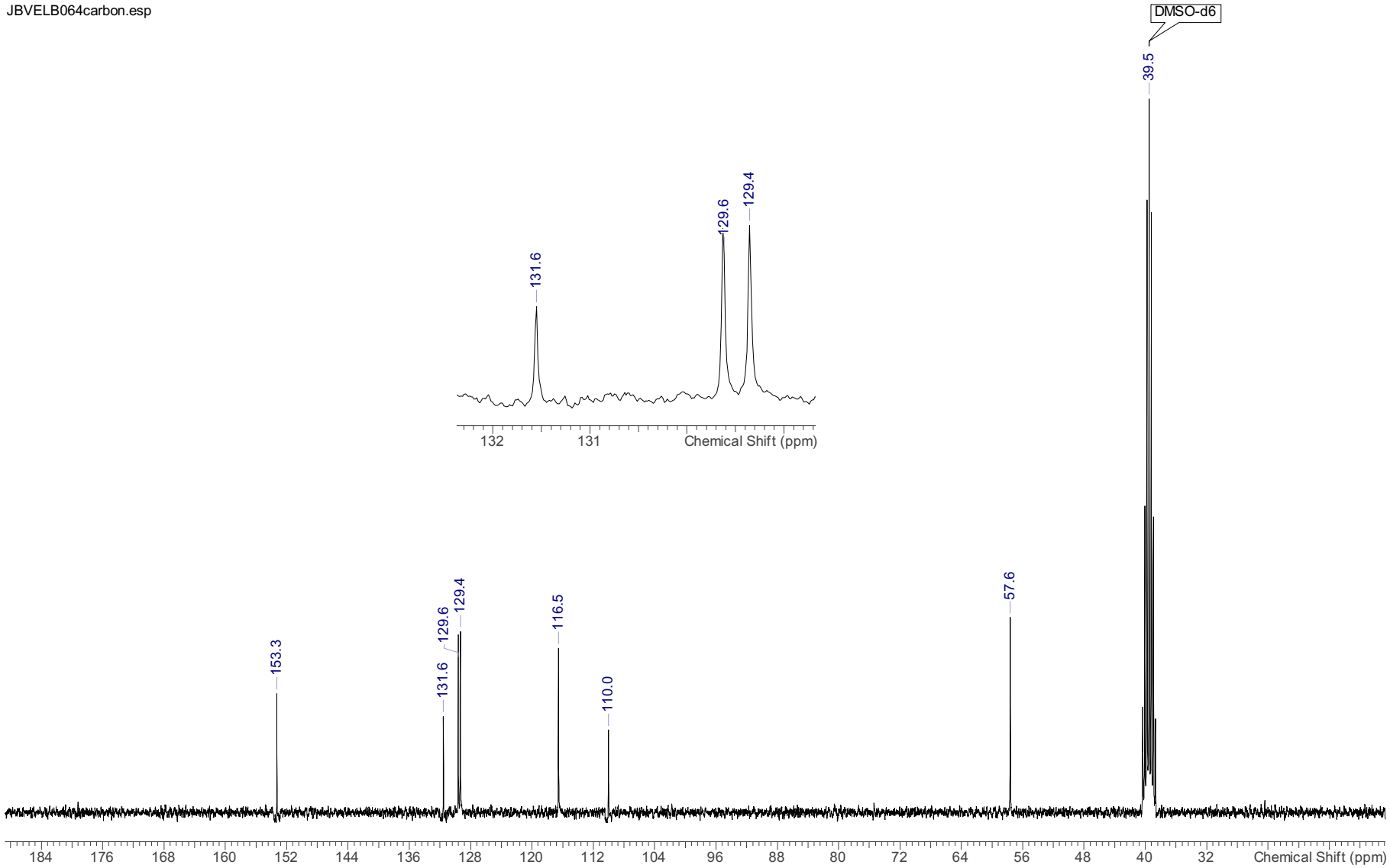


4-Bromo-2-(hydroxymethyl)phenol (12)



4-Bromo-2-(hydroxymethyl)phenol (12)

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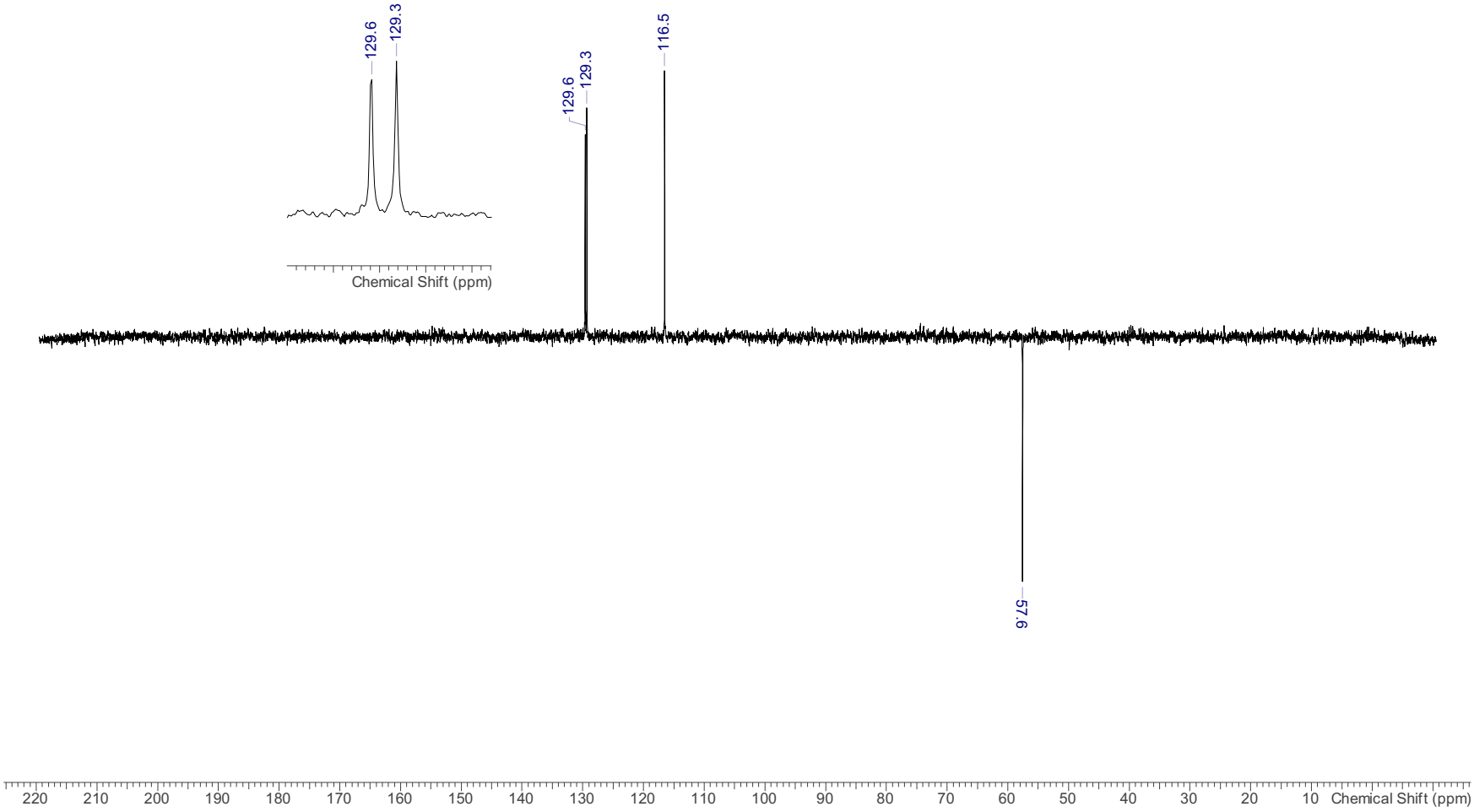
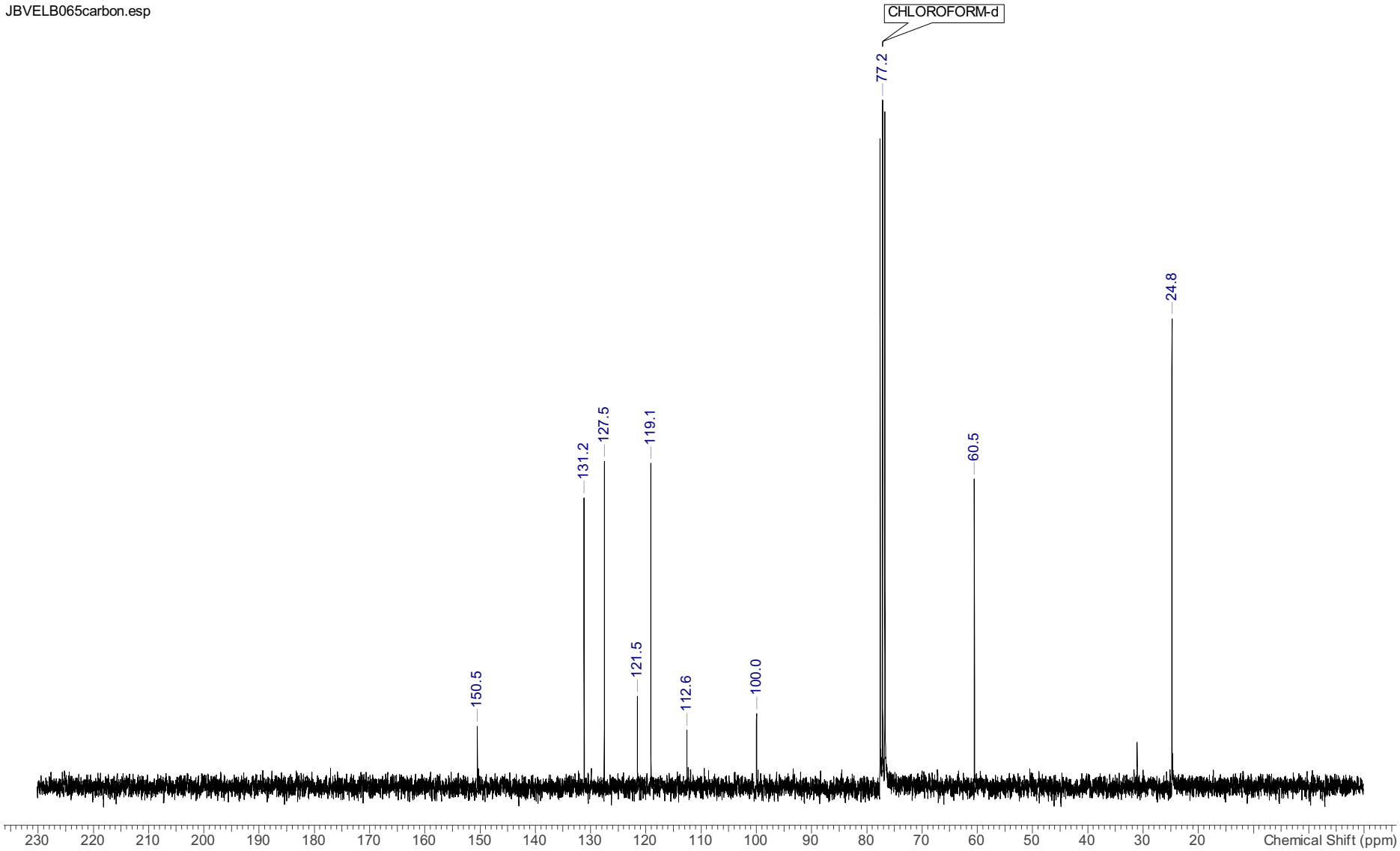
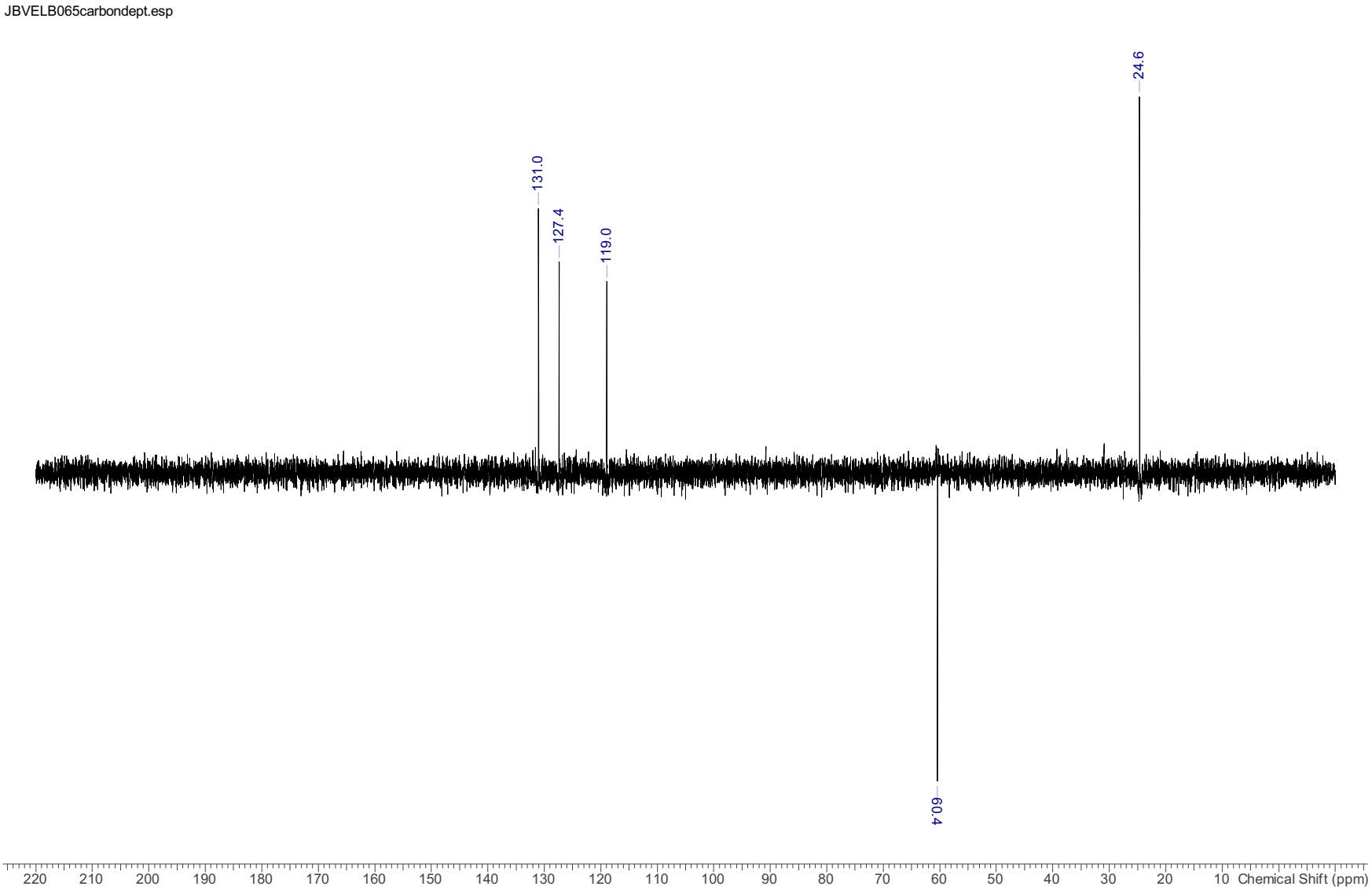


6-Bromo-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxine (13)

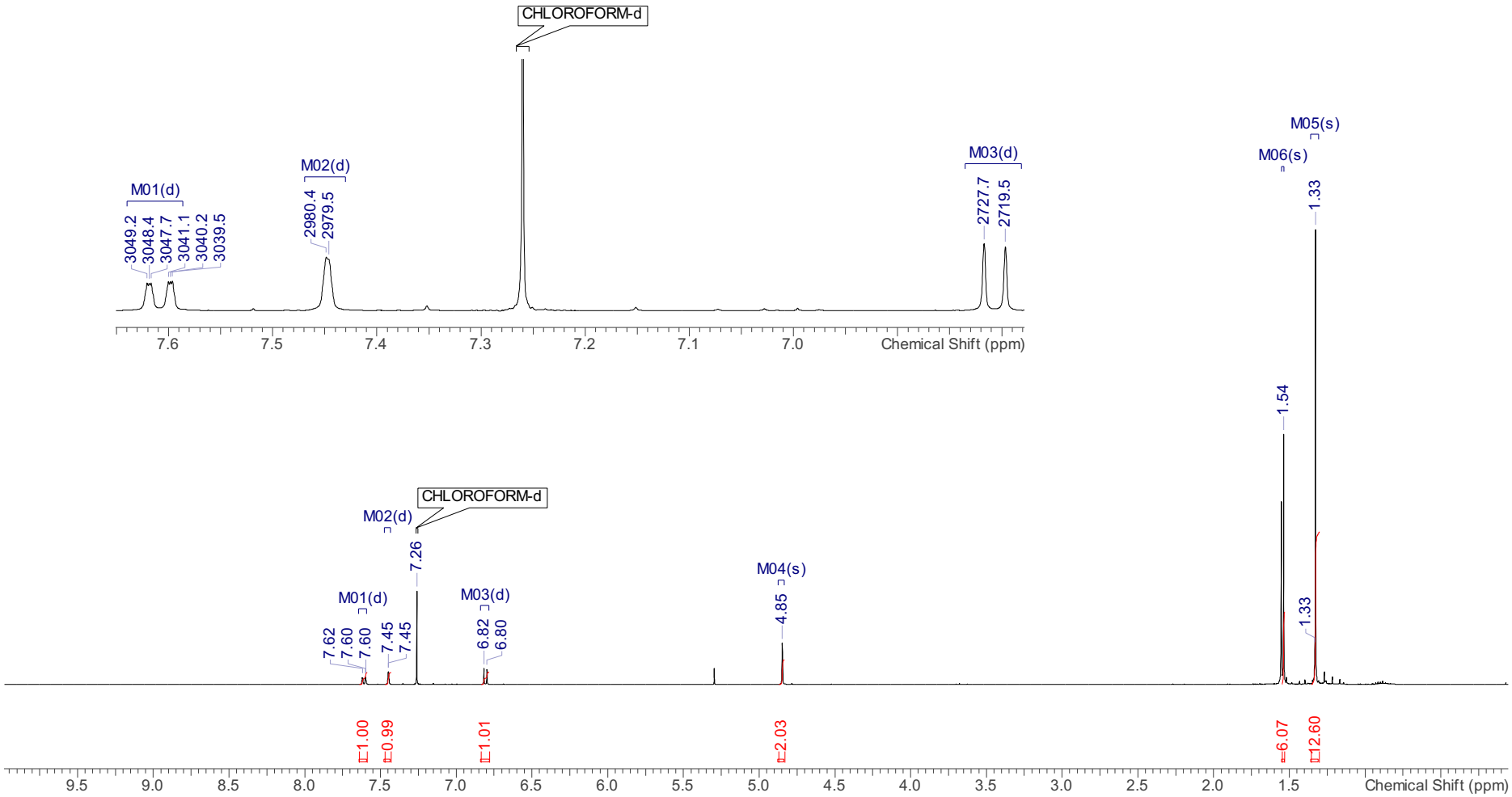


6-Bromo-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxine (13)

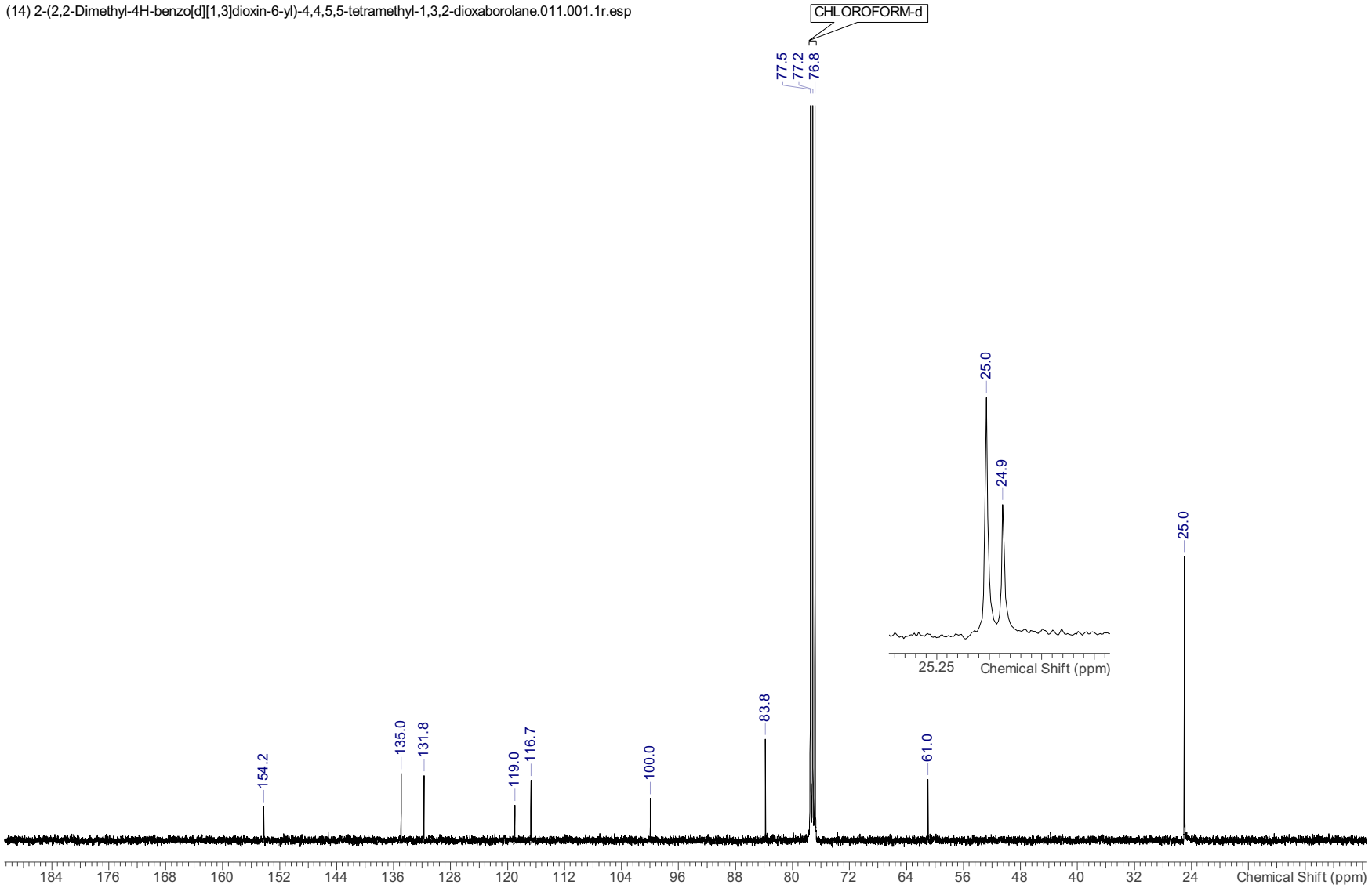


2-(2,2-Dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (15)

(14) 2-(2,2-Dimethyl-4H-benzo[d][1,3]dioxin-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.010.001.1r.esp

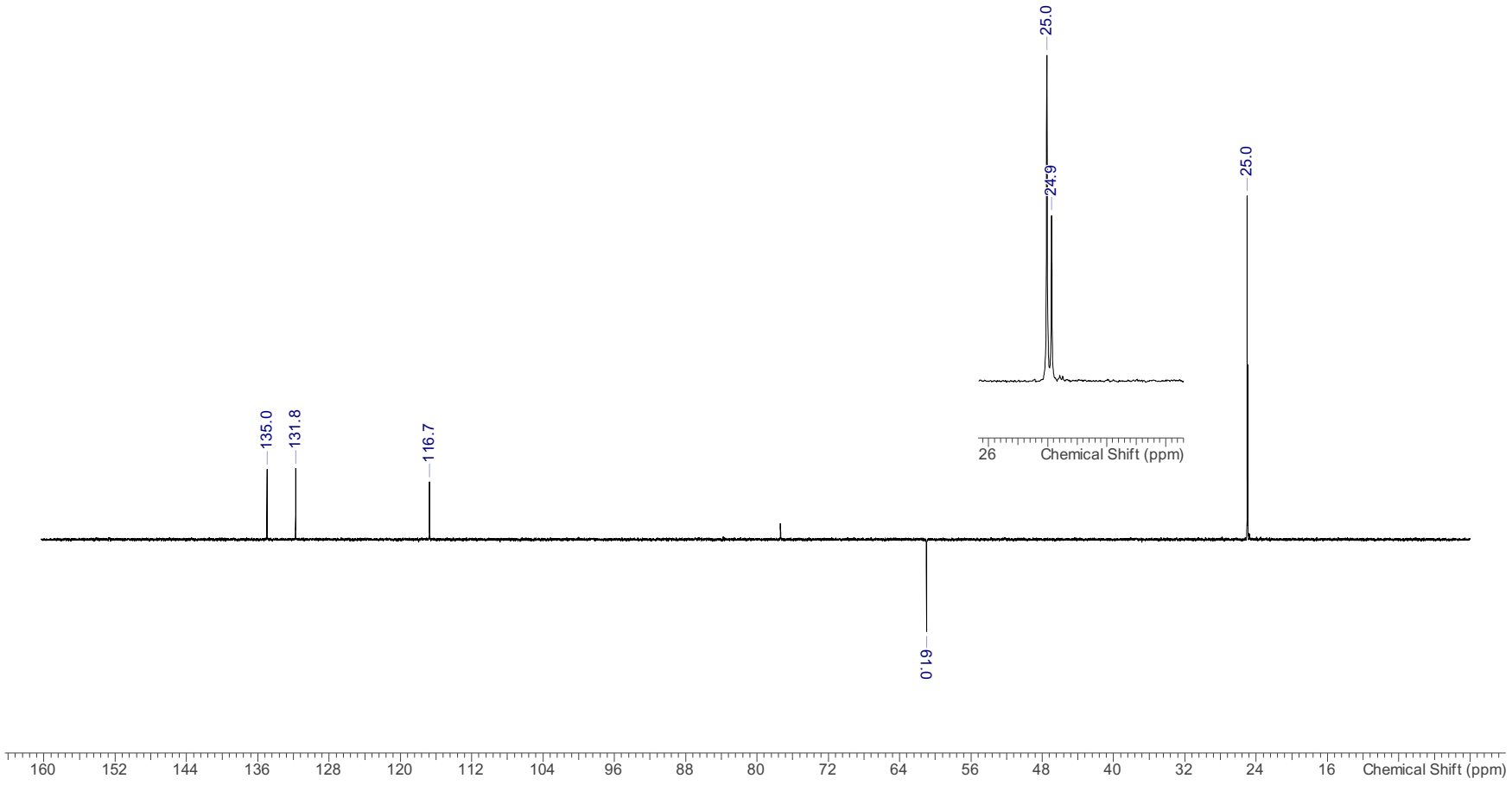


2-(2,2-Dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (15)



2-(2,2-Dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (15)

(14) 2-(2,2-Dimethyl-4H-benzo[d][1,3]dioxin-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.012.001.1r.esp



Methyl 4-hydroxy-3,5-dimethoxybenzoate (16)

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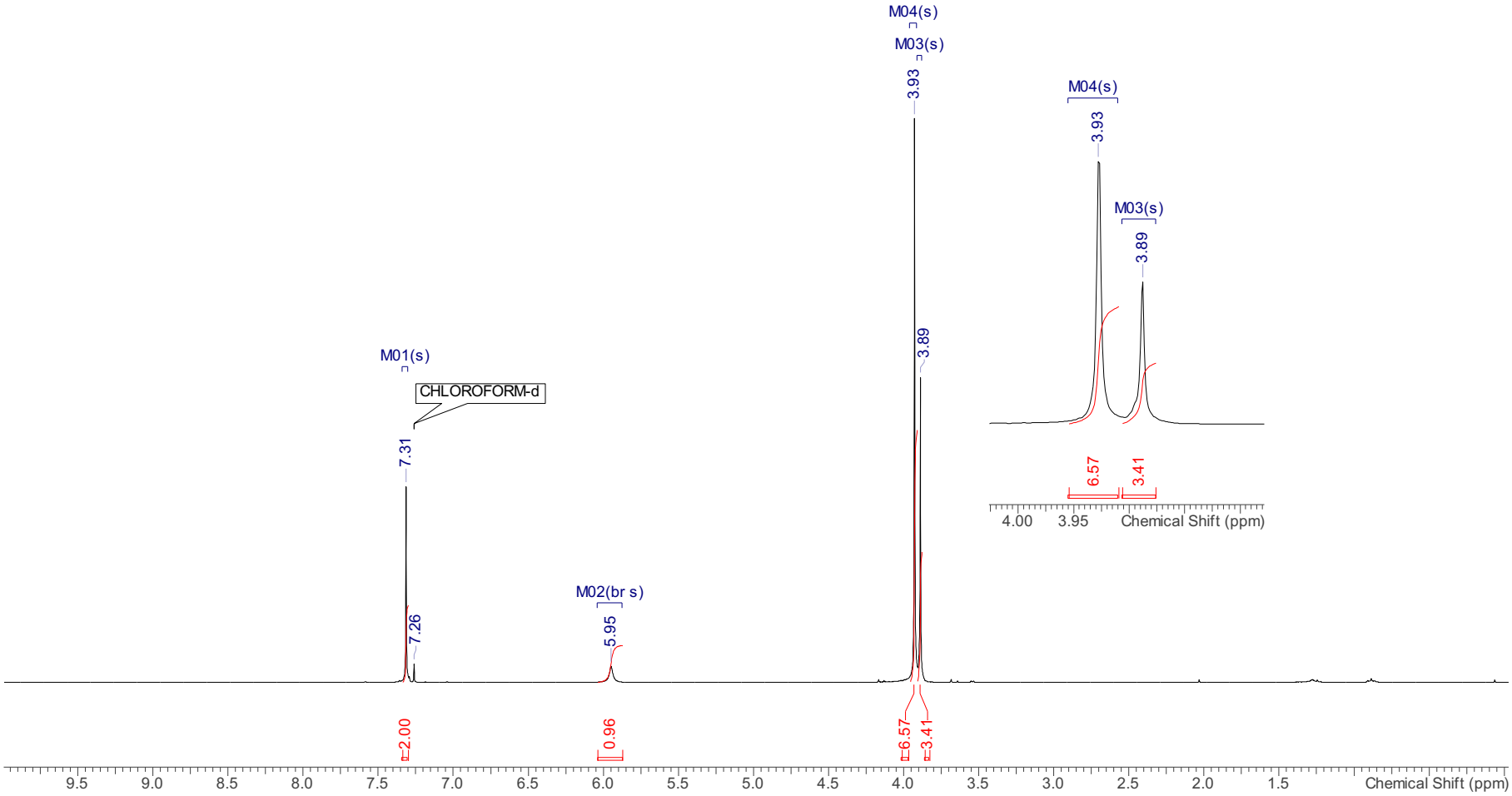

Methyl 4-hydroxy-3,5-dimethoxybenzoate (16)

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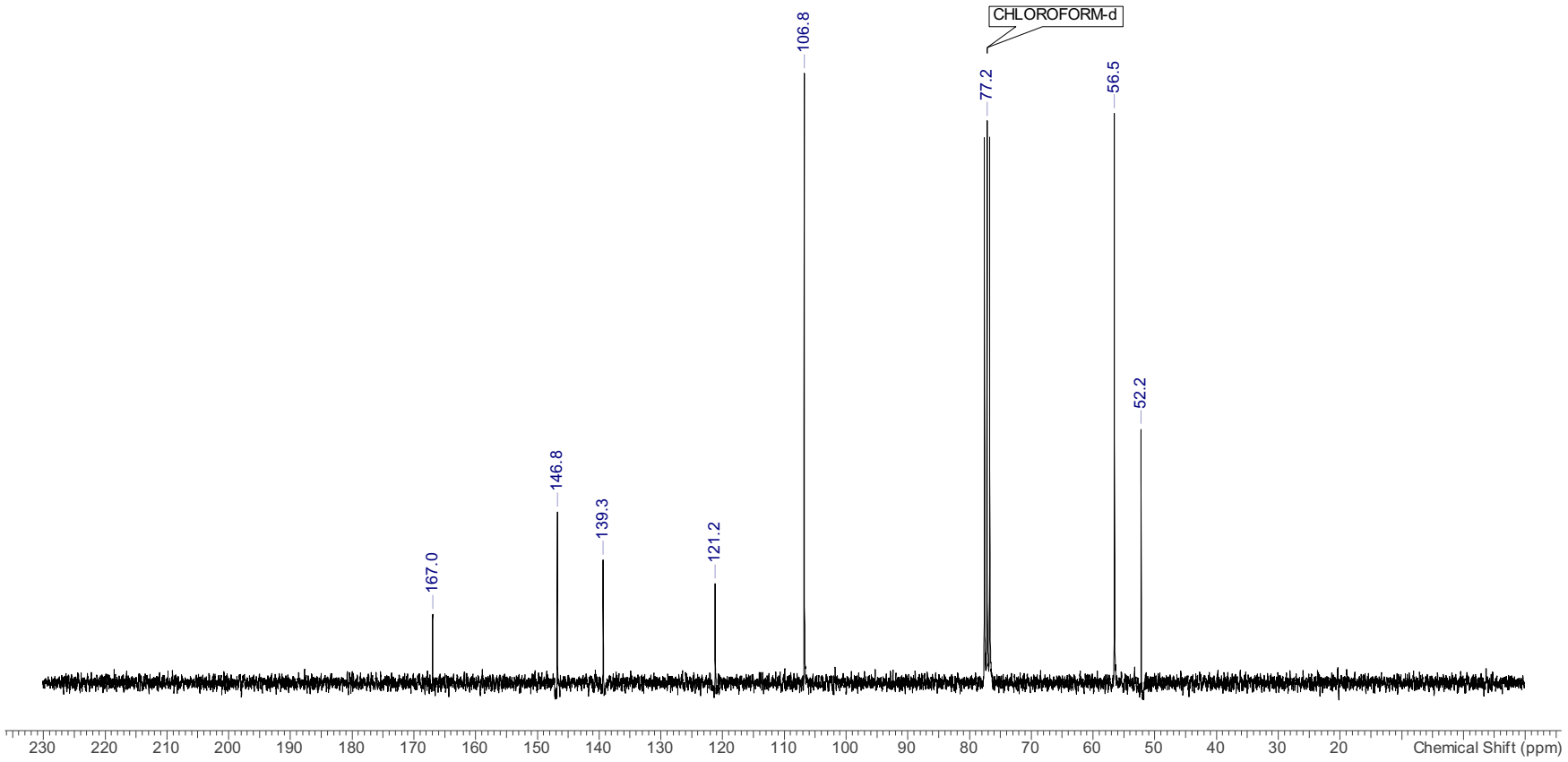

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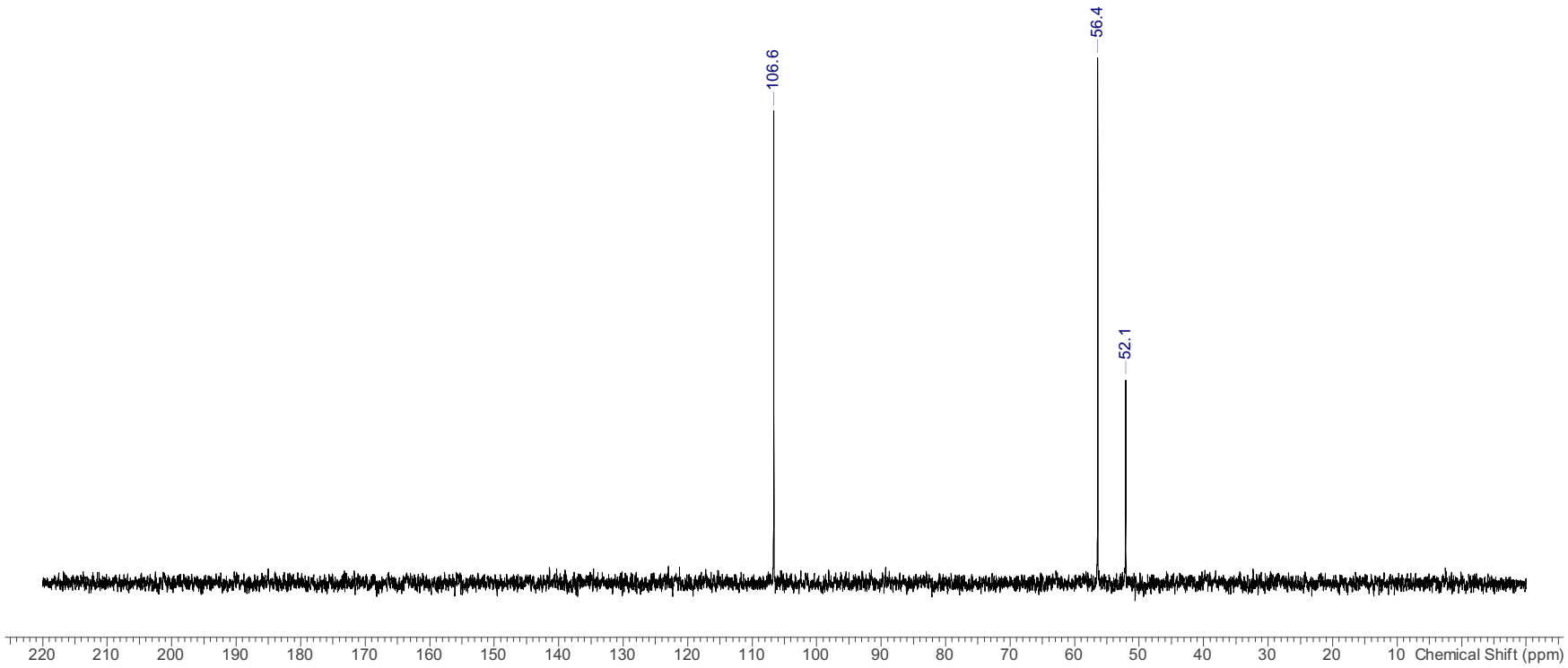

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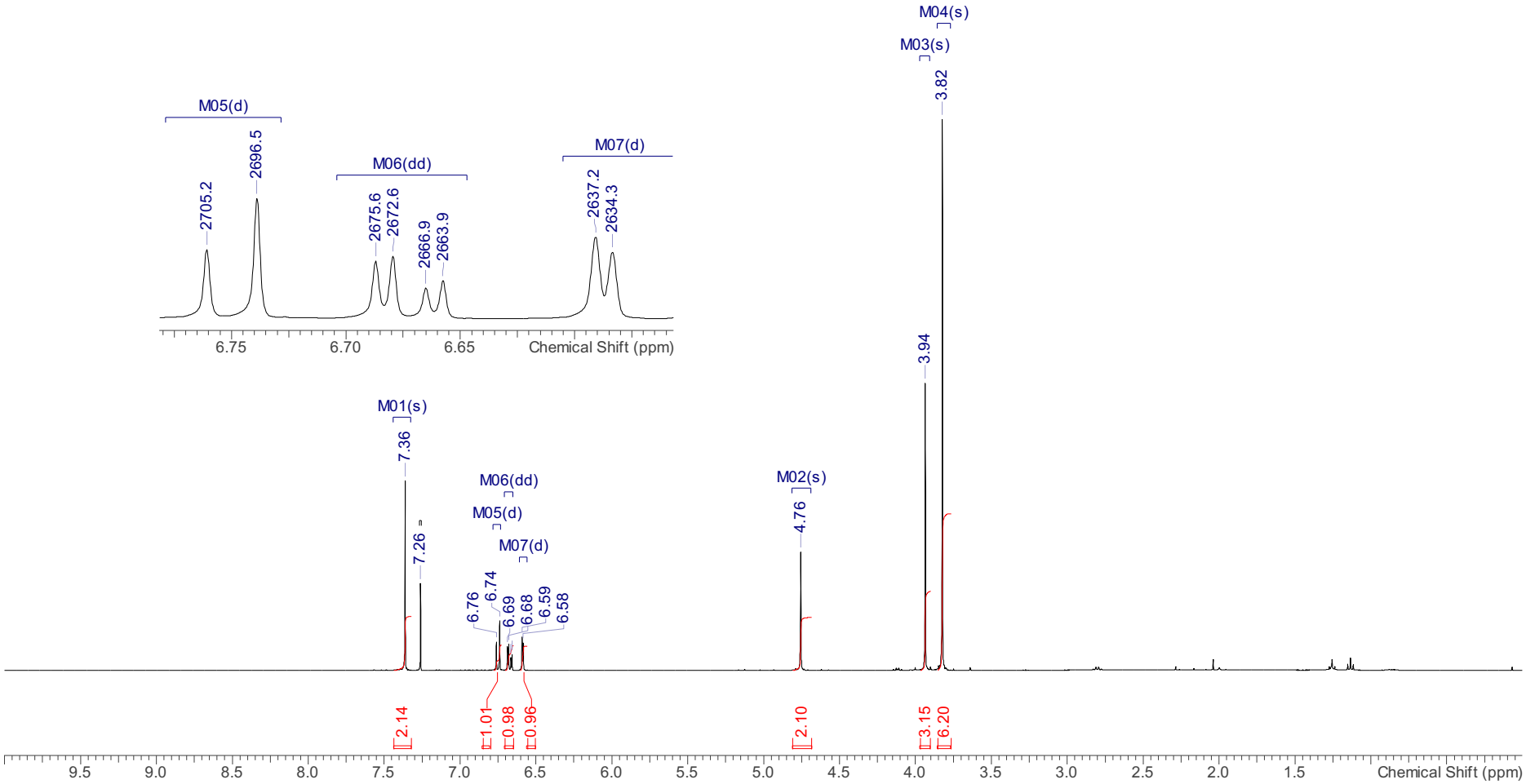
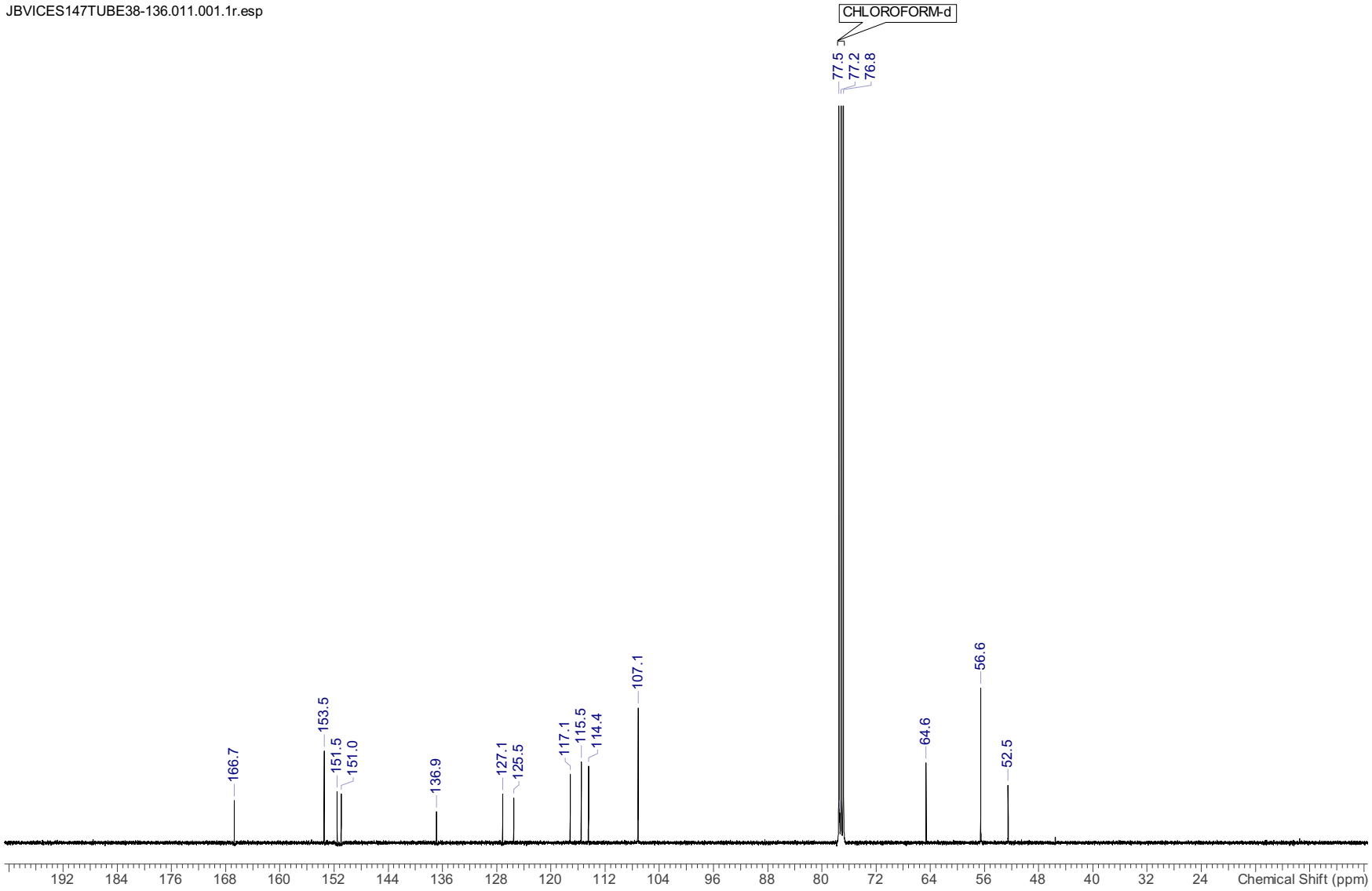
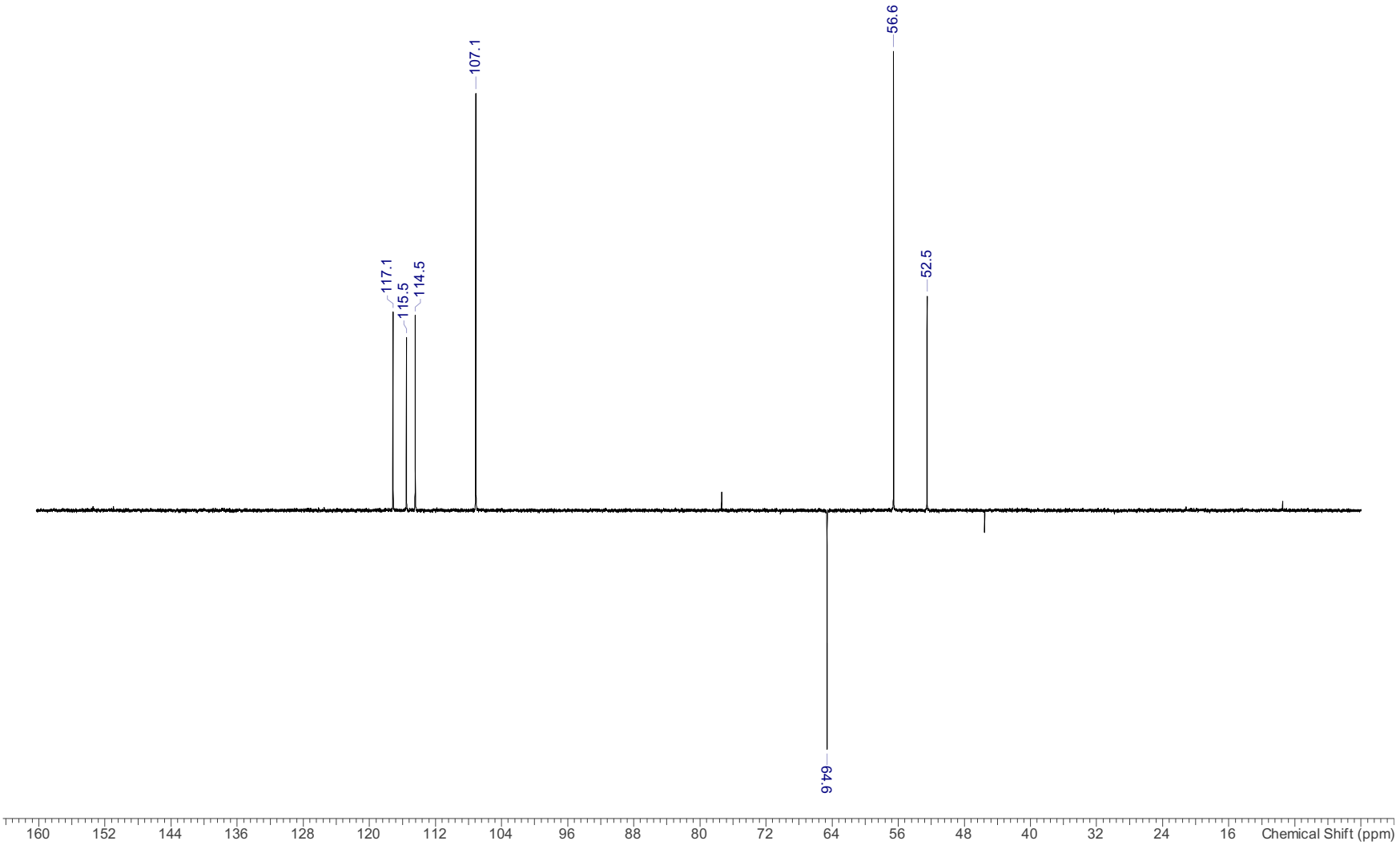


Methyl 4-(4-hydroxy-3-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (17)



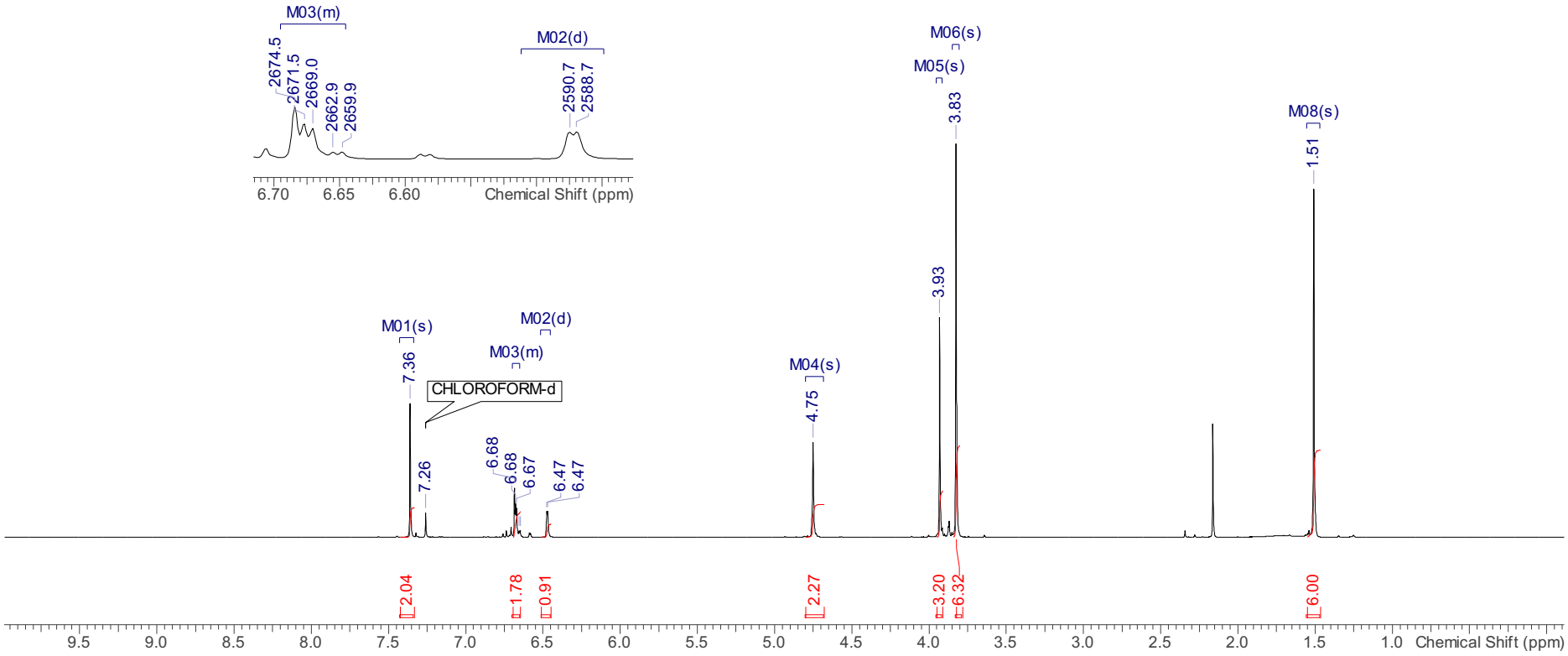
Methyl 4-(4-hydroxy-3-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (17)

JBVICES147TUBE38-136.012.001.1r.esp



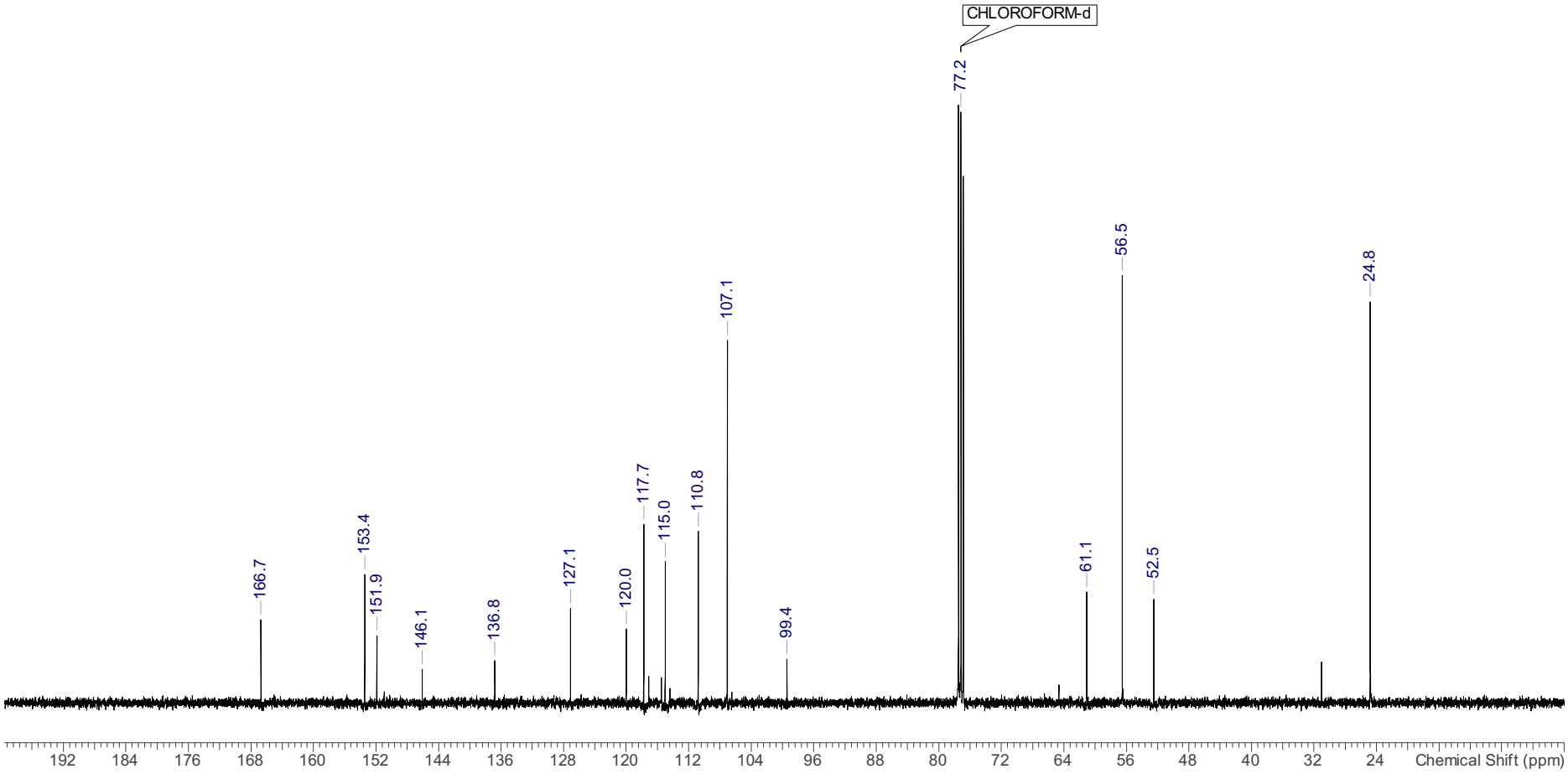
Methyl 4-((2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)oxy)-3,5-dimethoxybenzoate (18)

JBVELB067proton.esp



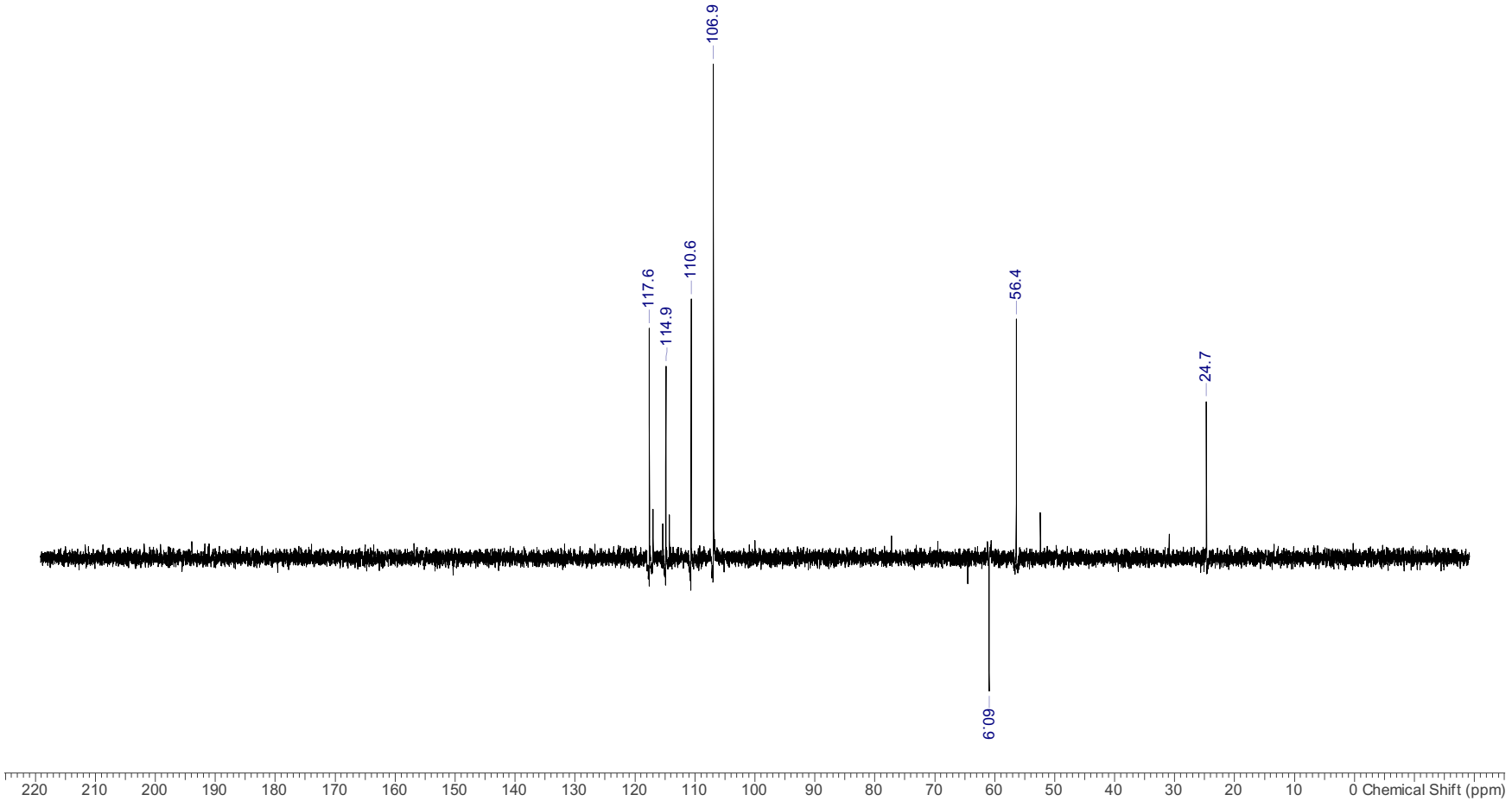
Methyl 4-((2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)oxy)-3,5-dimethoxybenzoate (18)

JBVELB067carbon.esp



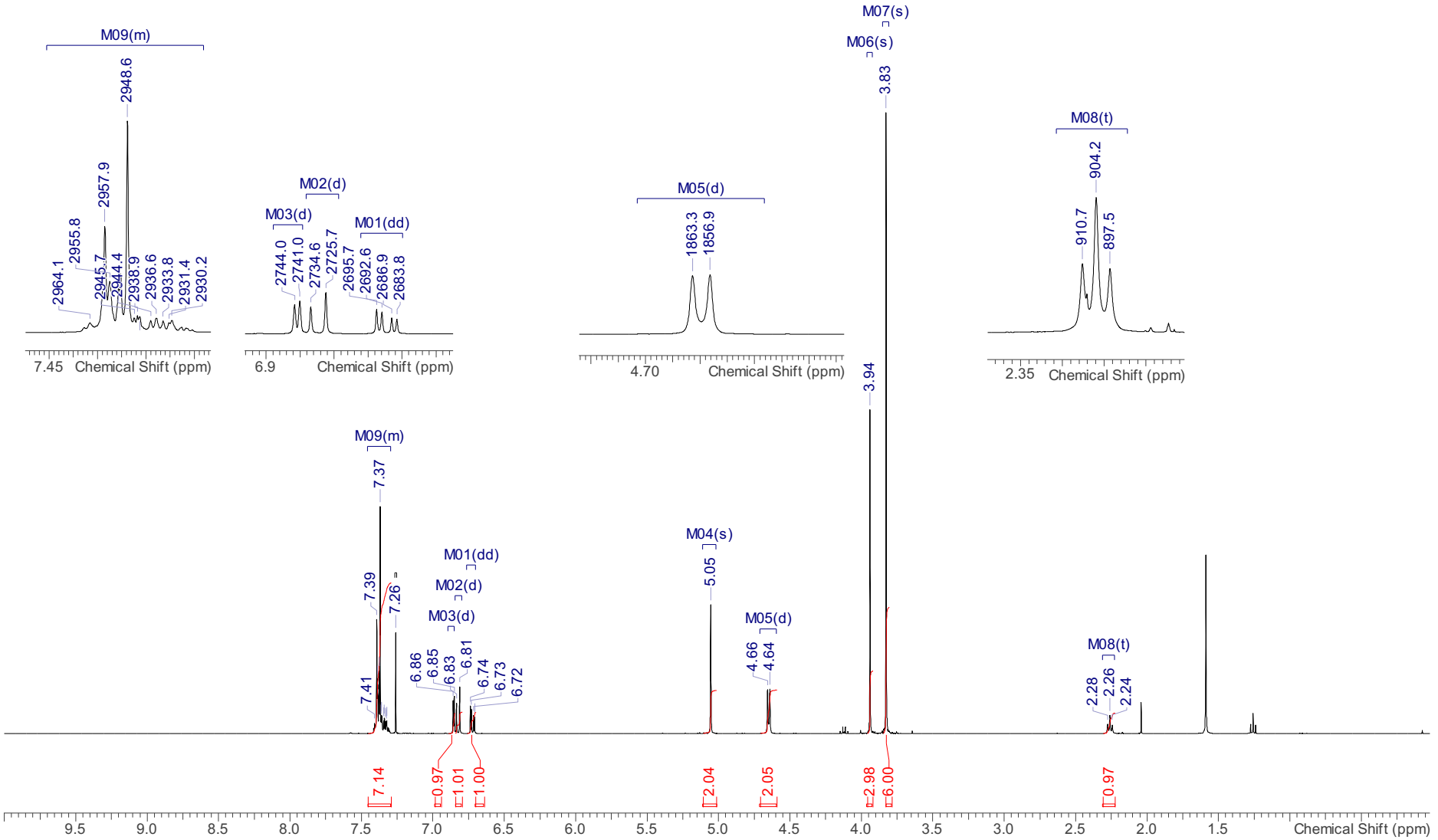
Methyl 4-((2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-6-yl)oxy)-3,5-dimethoxybenzoate (18)

JBVELB067carbondept.esp



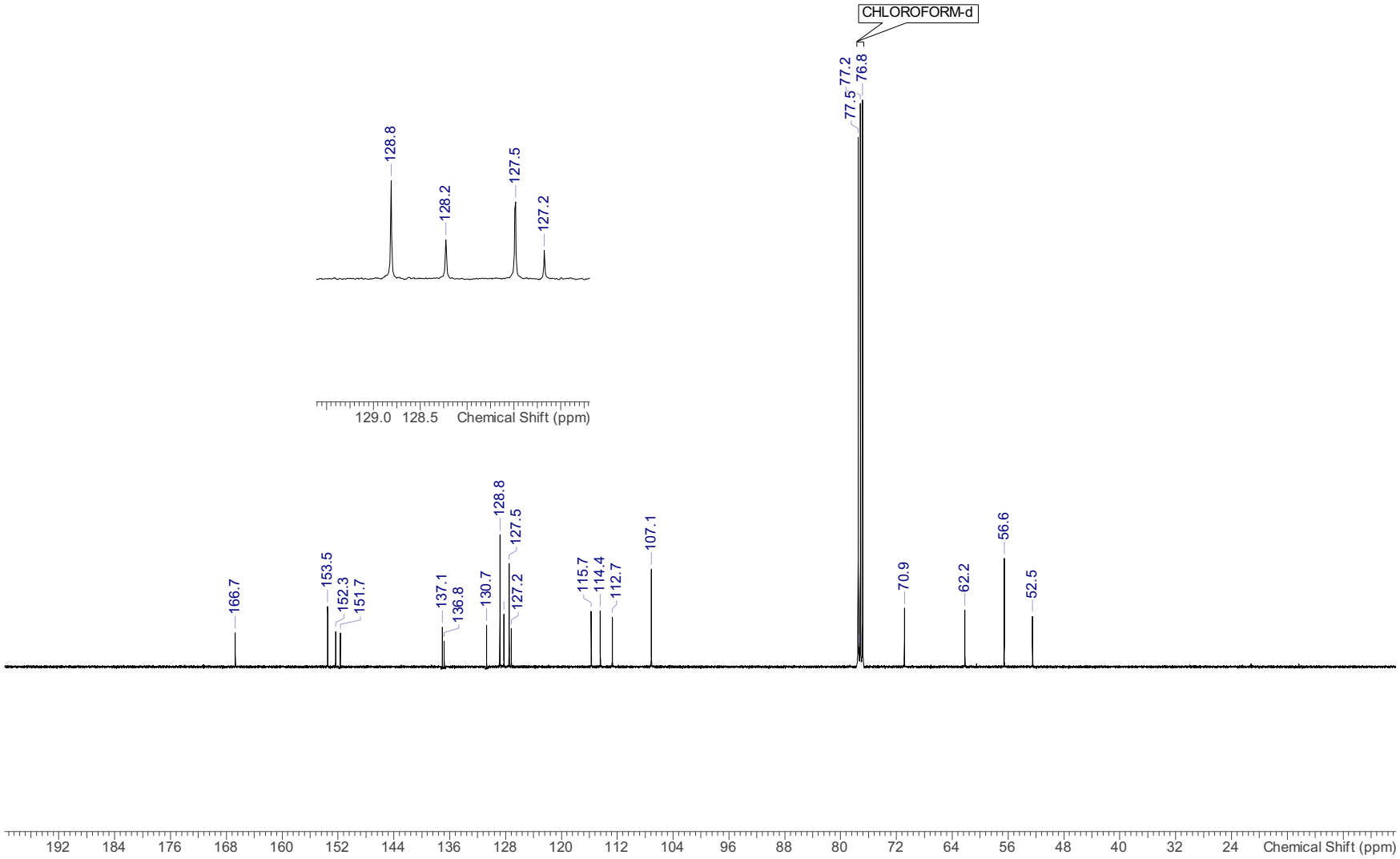
Methyl 4-(4-(benzyloxy)-3-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (19)

jbvices149tube8-19.010.001.1r.esp



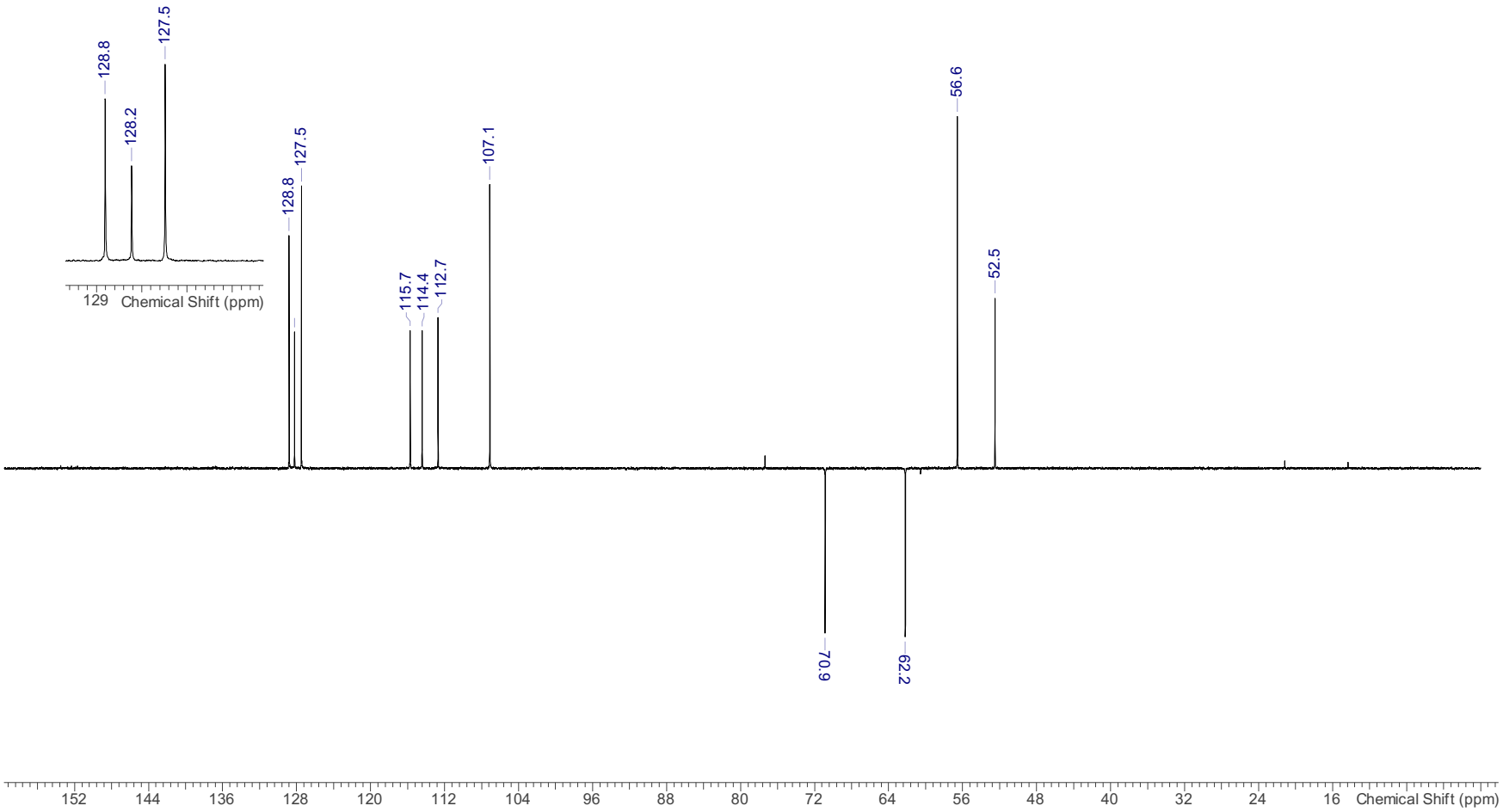
Methyl 4-(4-(benzyloxy)-3-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (19)

jbvices149tube8-19.011.001.1r.esp



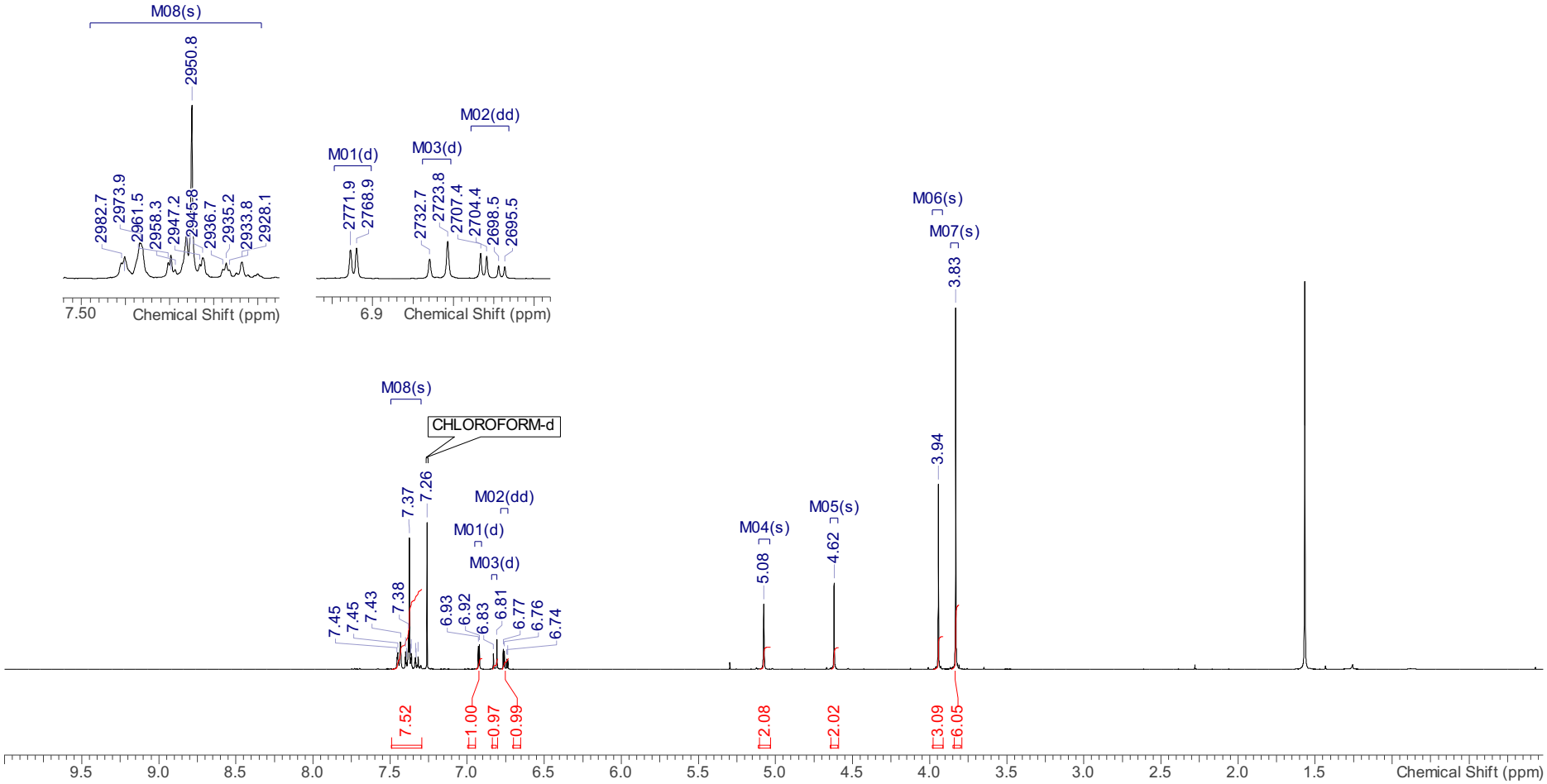
Methyl 4-(4-(benzyloxy)-3-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (19)

jbvices149tube8-19.012.001.1r.esp

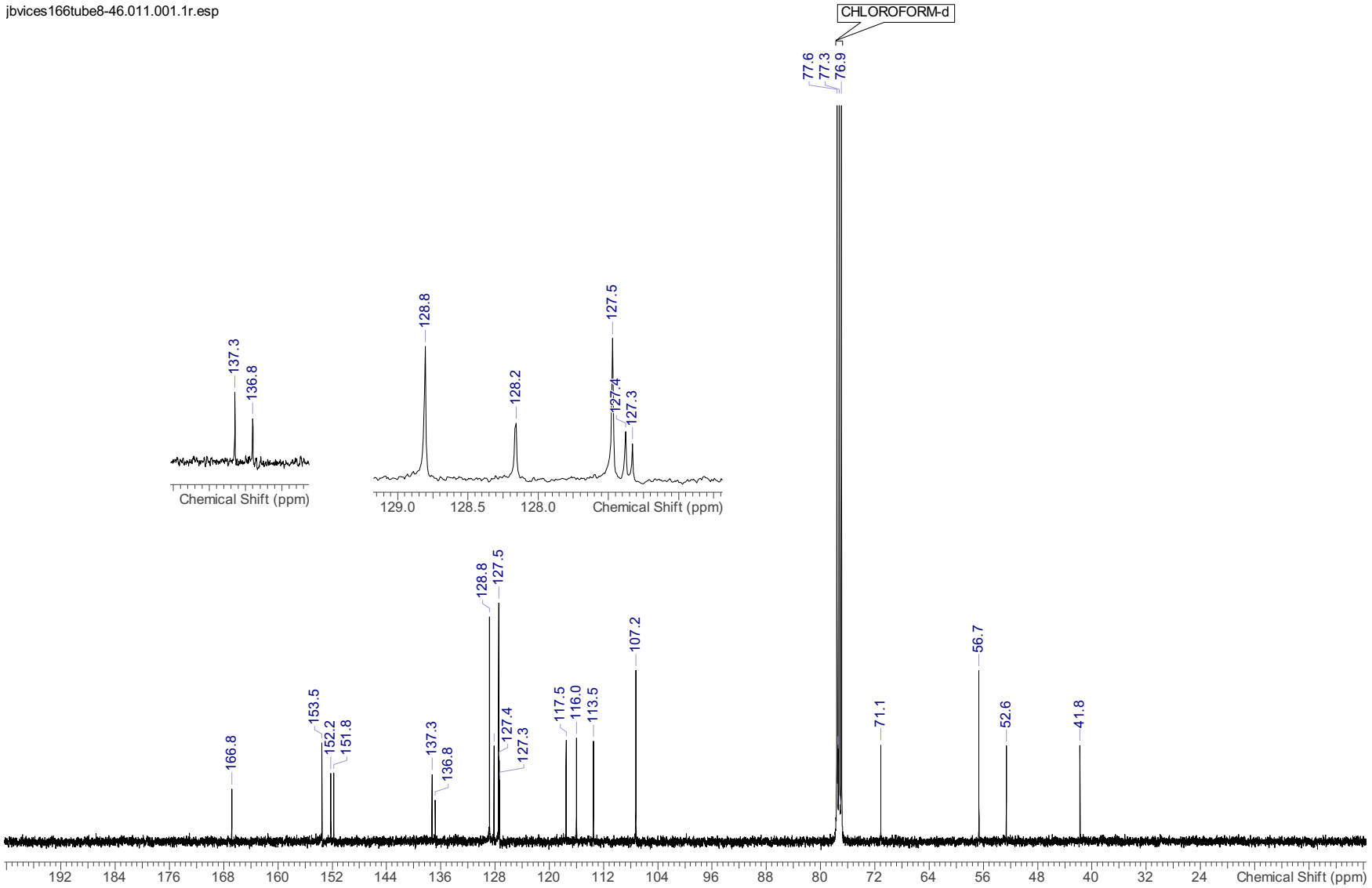


Methyl 4-(4-(benzyloxy)-3-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (20)

jbvices166tube8-46.010.001.1r.esp

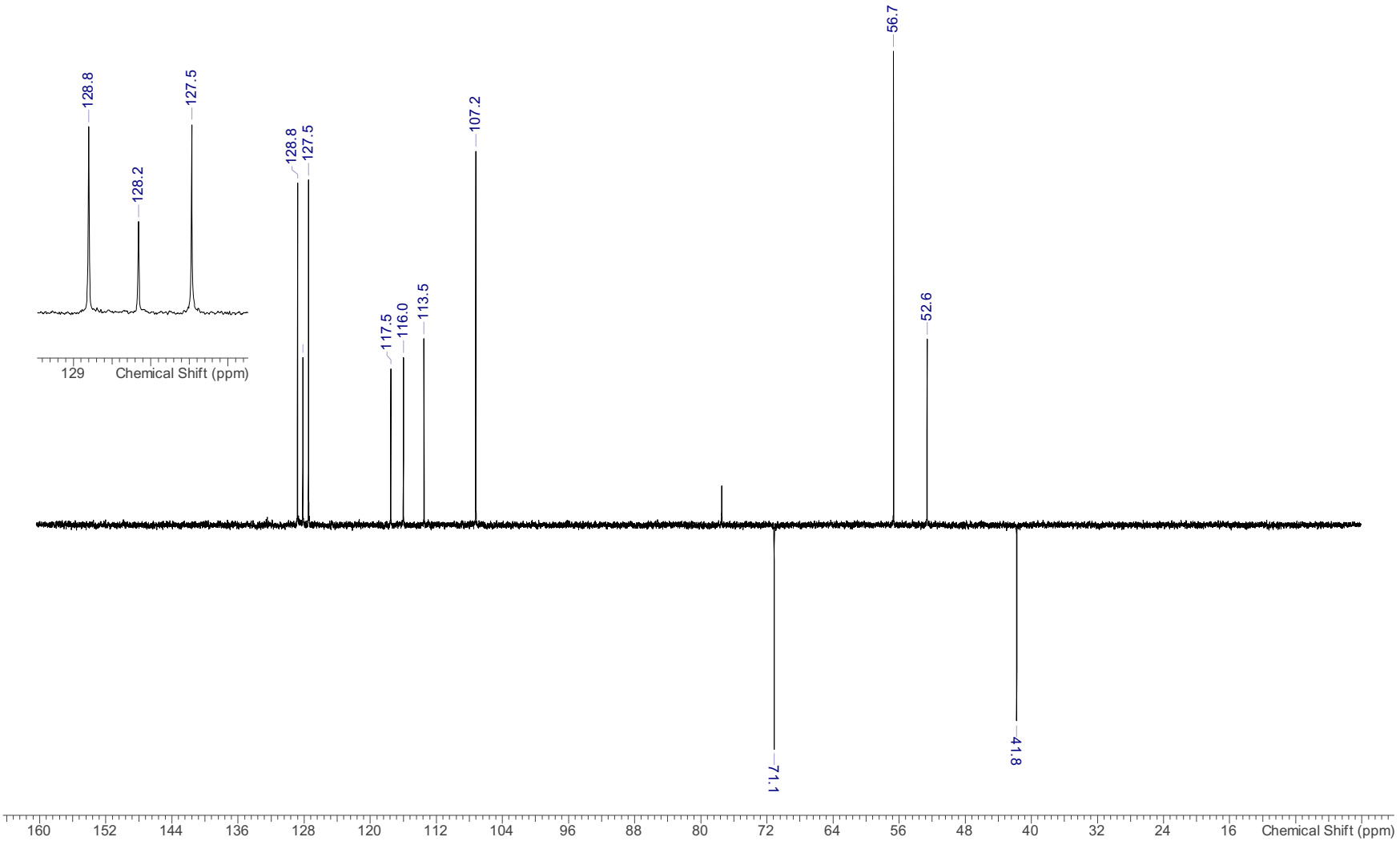


Methyl 4-(4-(benzyloxy)-3-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (20)

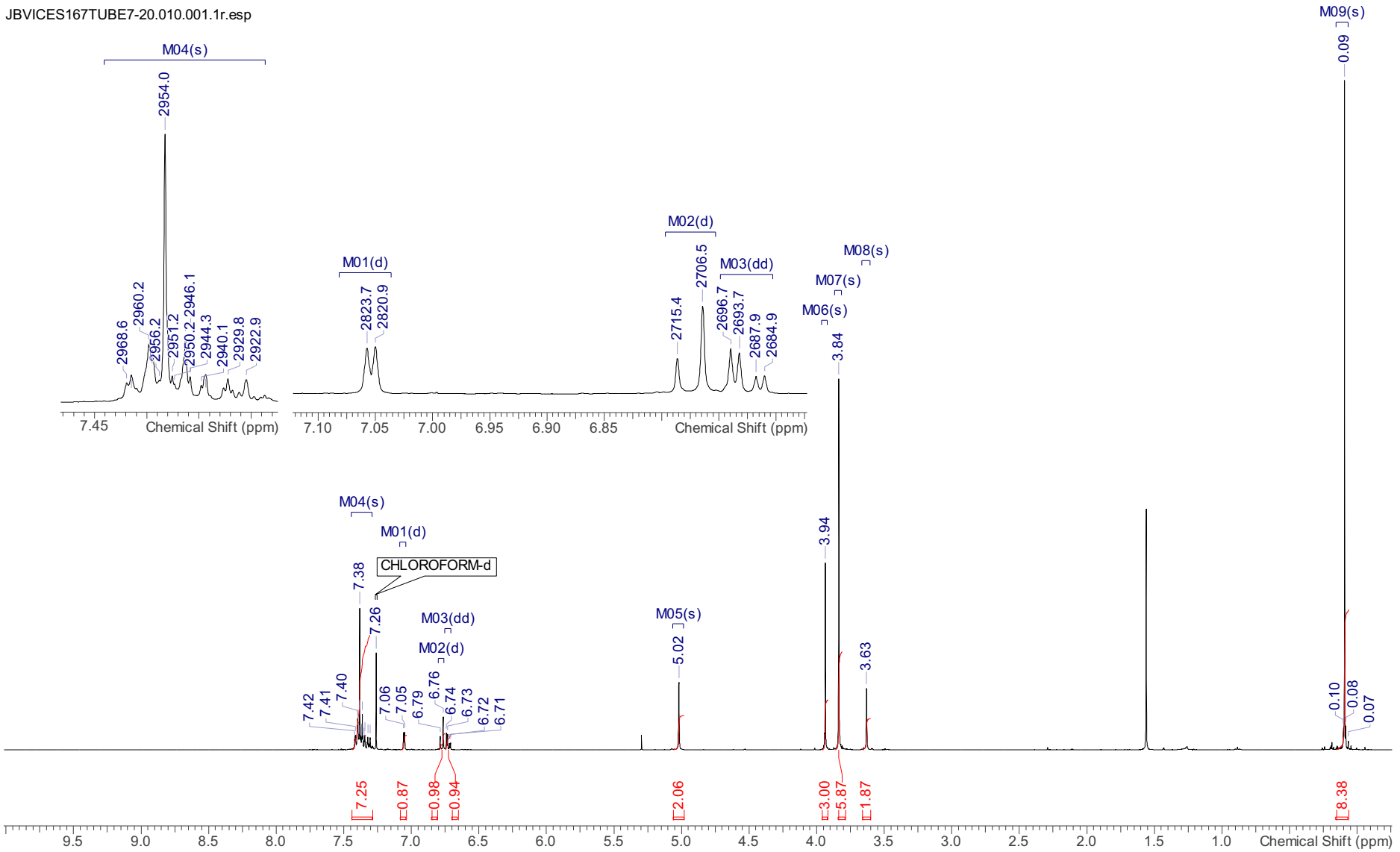


Methyl 4-(4-(benzyloxy)-3-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (20)

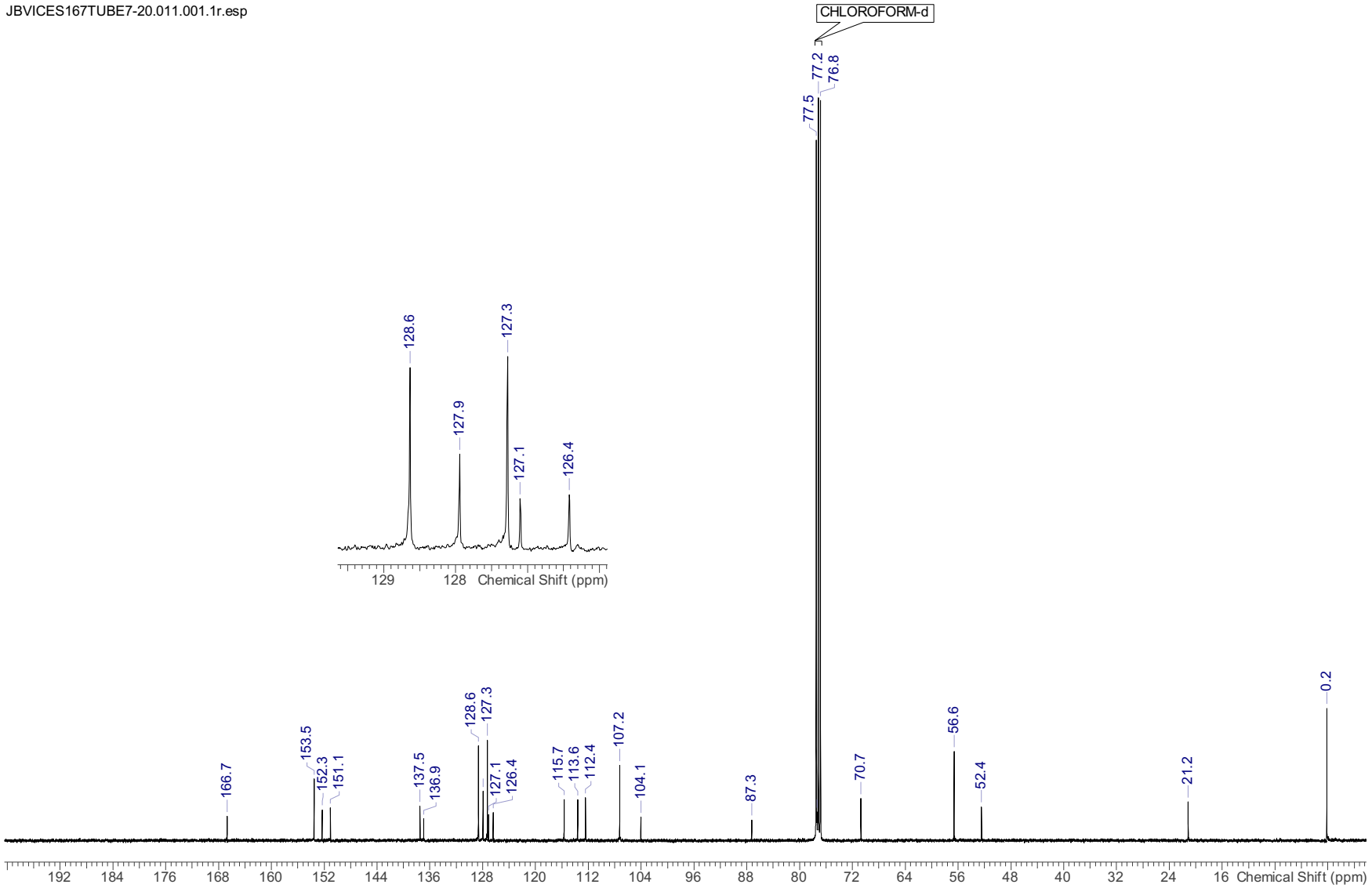
jbvices166tube8-46.012.001.1r.esp



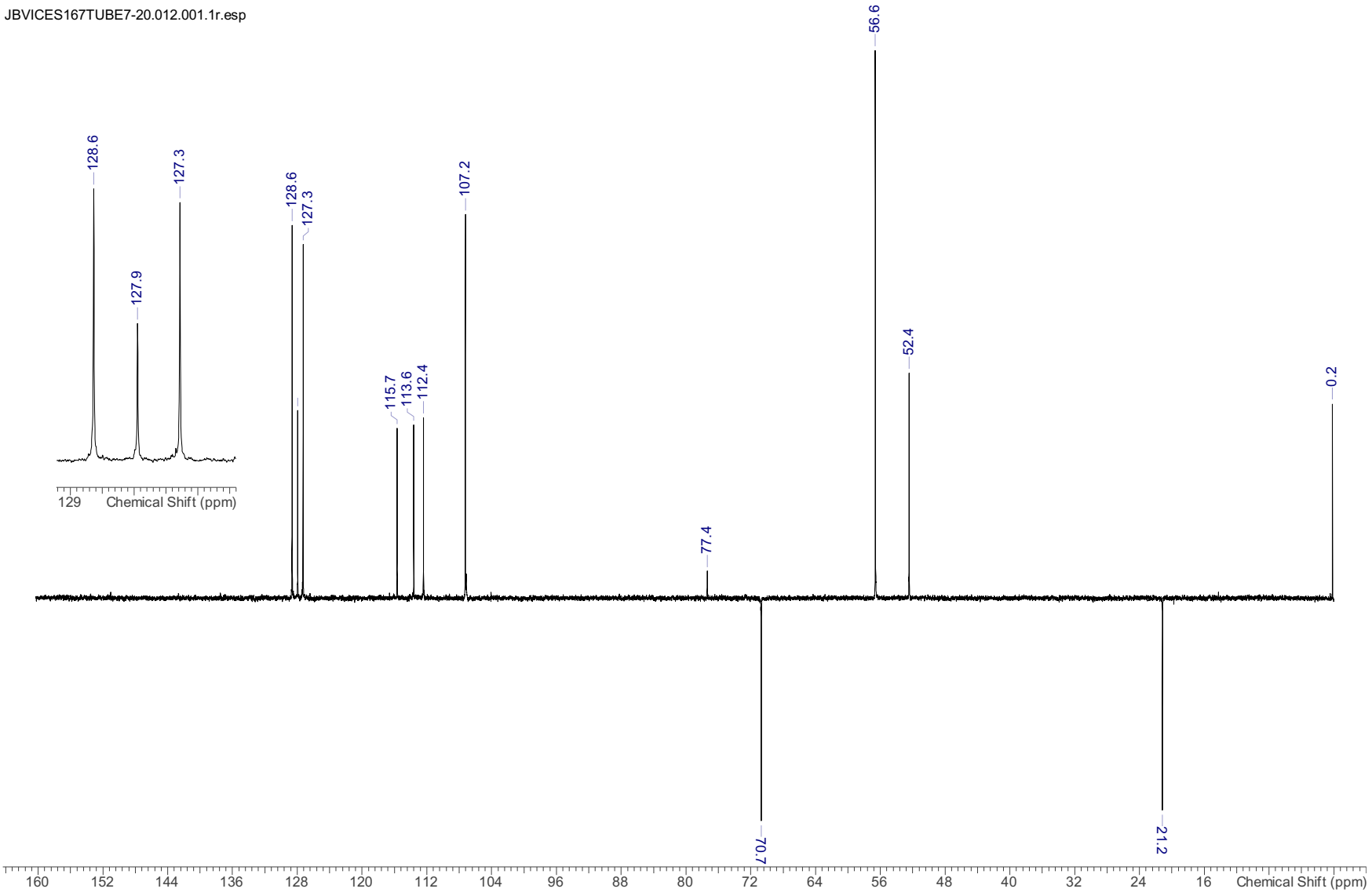
Methyl 4-(4-(benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (21)



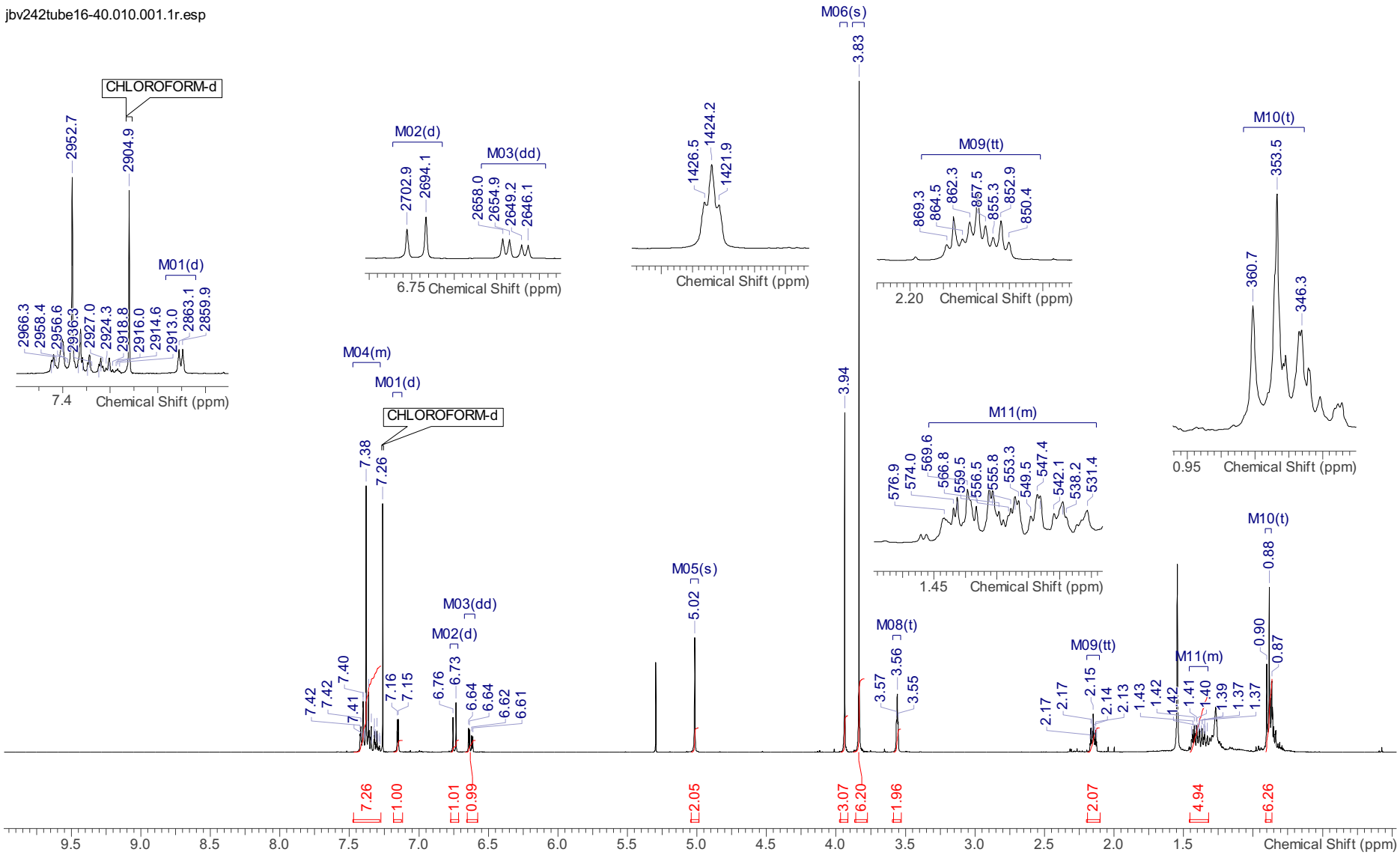
Methyl 4-(4-(benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (21)



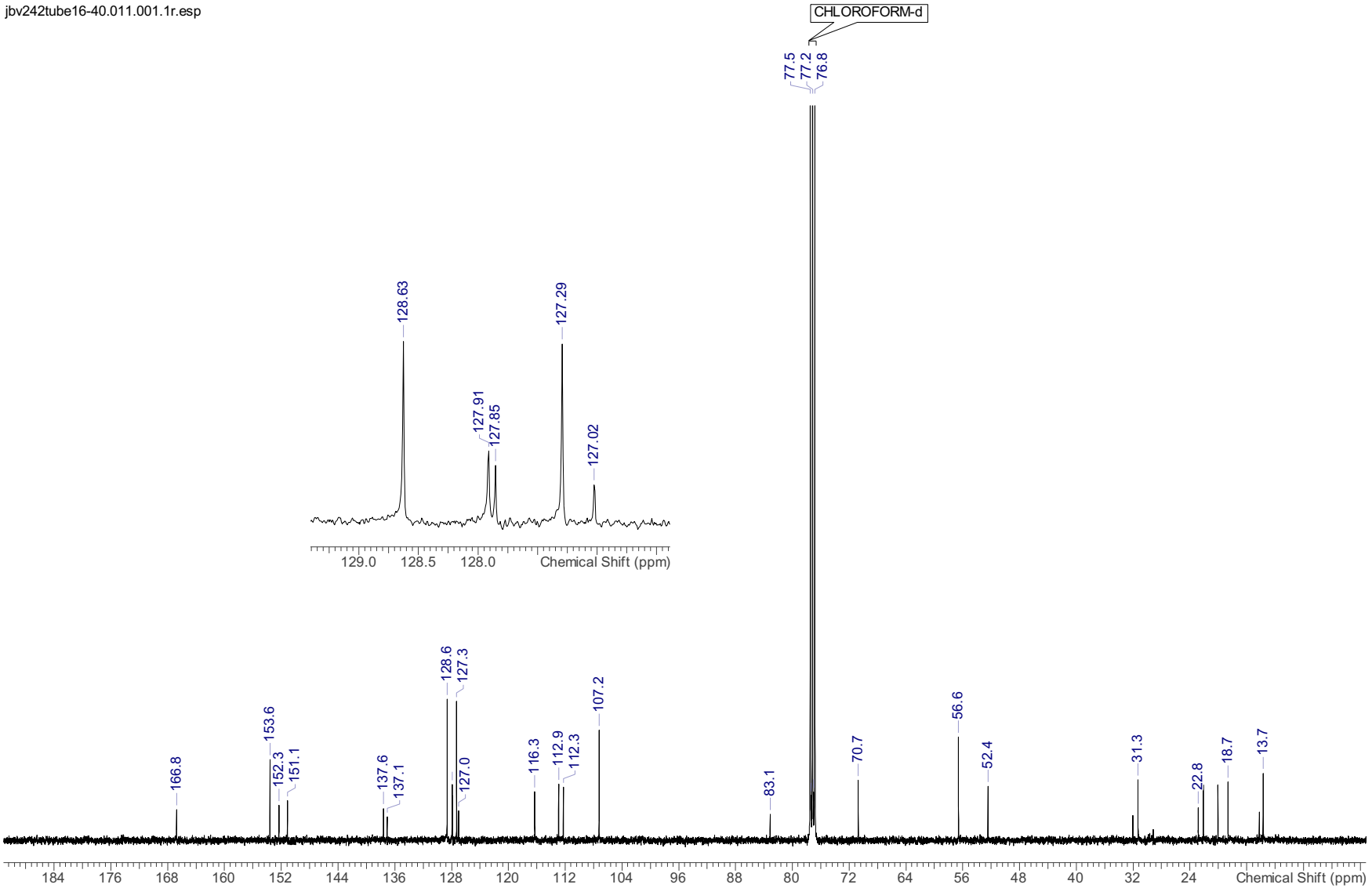
Methyl 4-(4-(benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (21)



Methyl 4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (22)

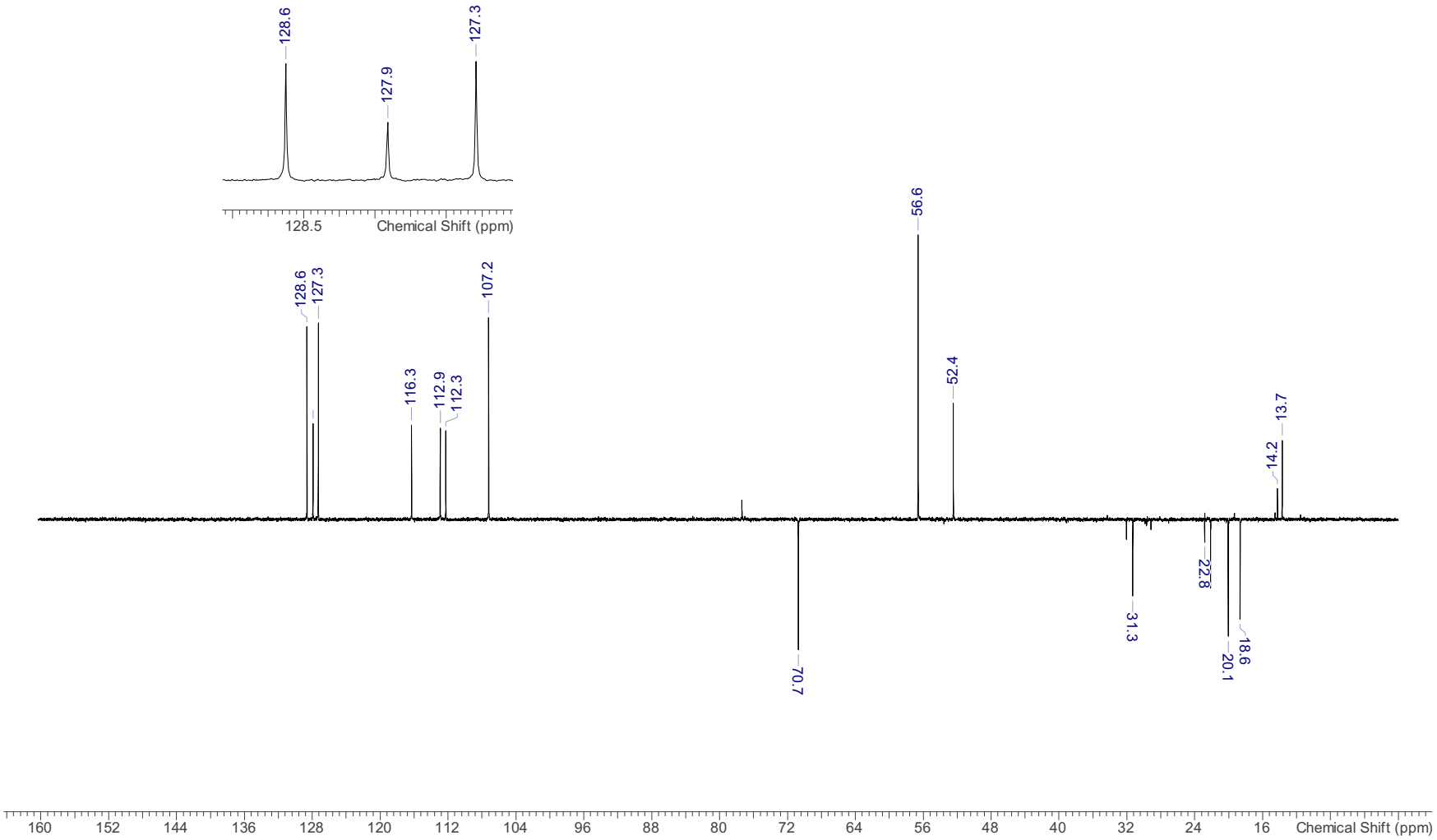


Methyl 4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (22)

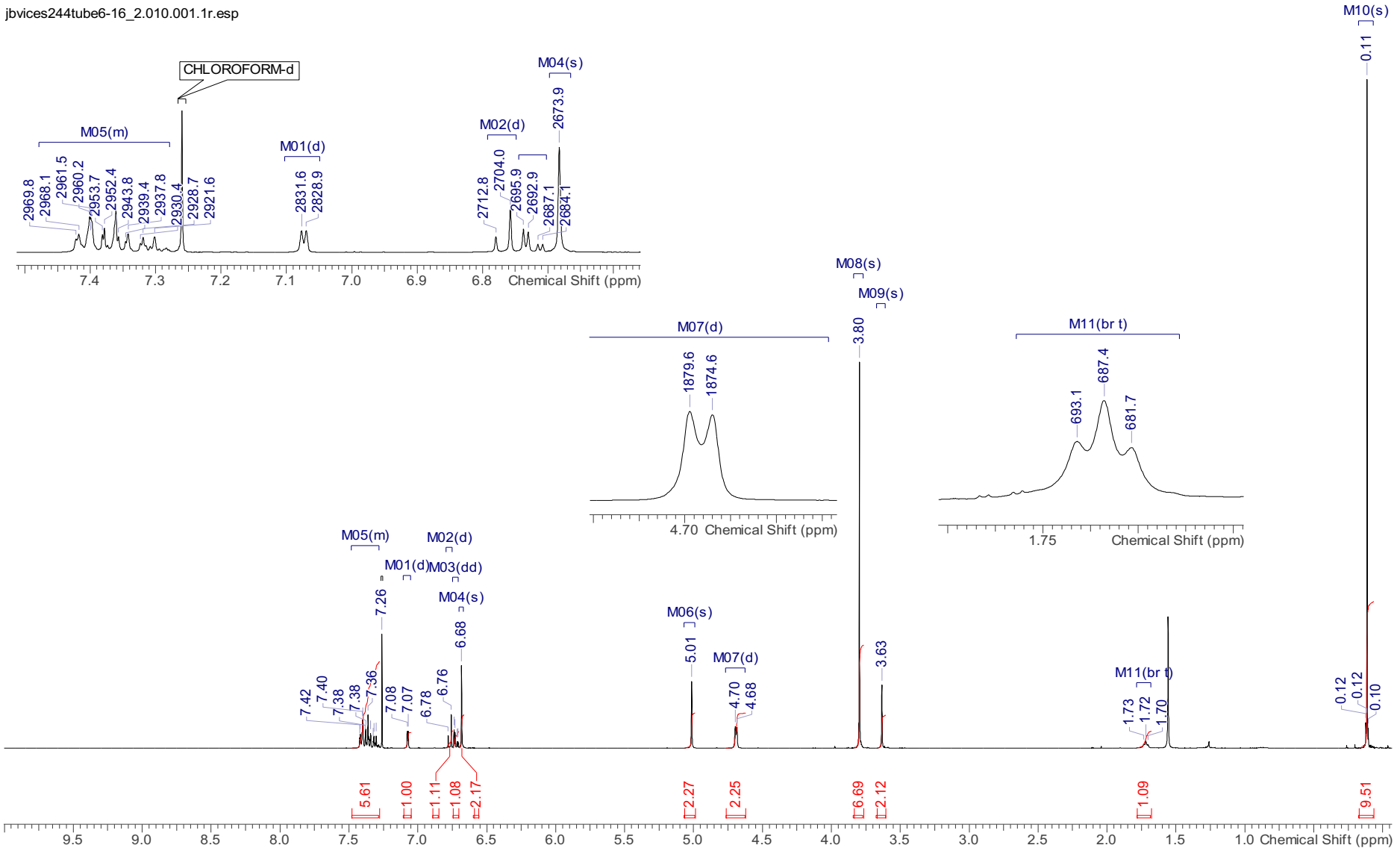


Methyl 4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (22)

jbv242tube16-40.012.001.1r.esp

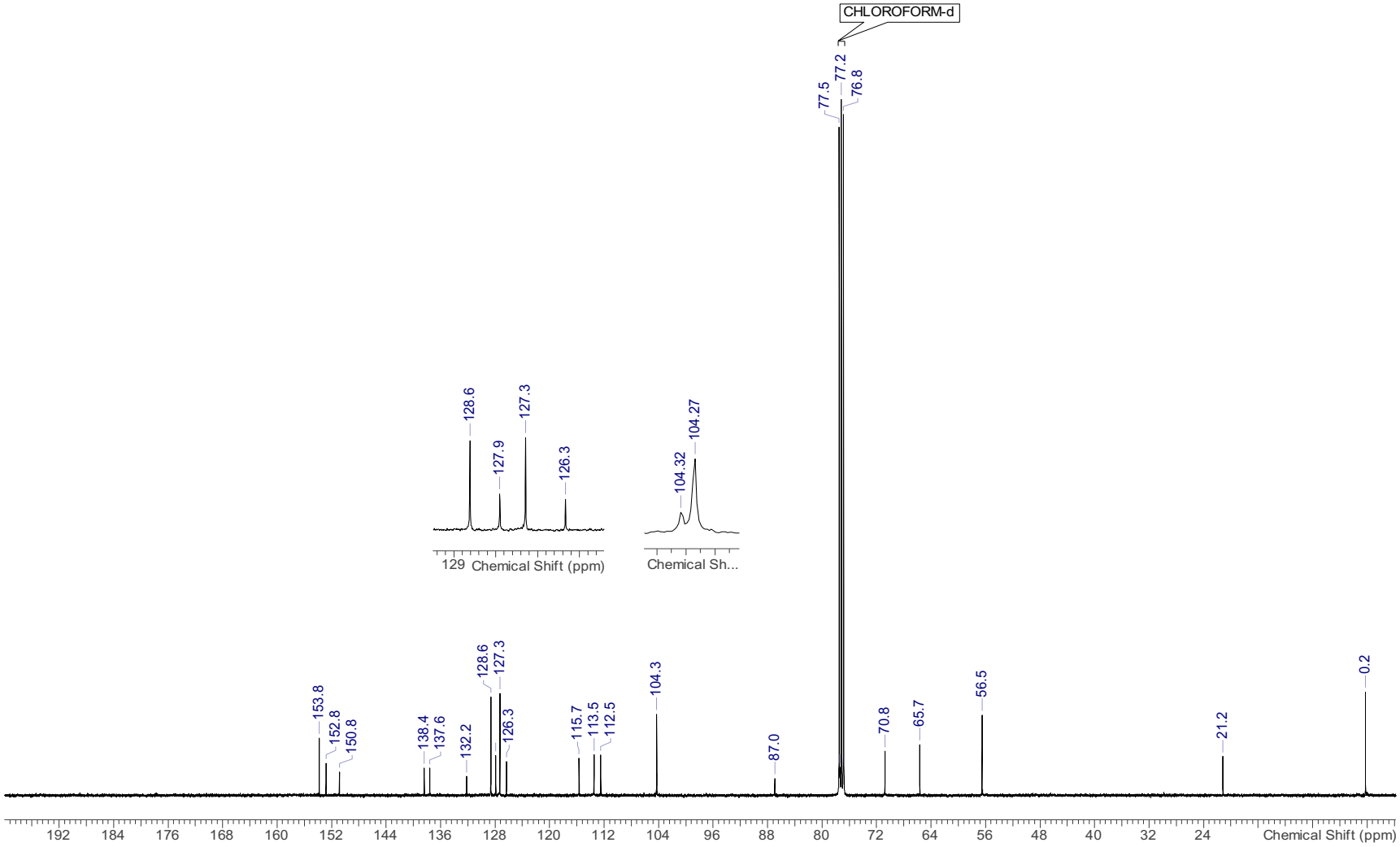


(4-(4-(Benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (23)

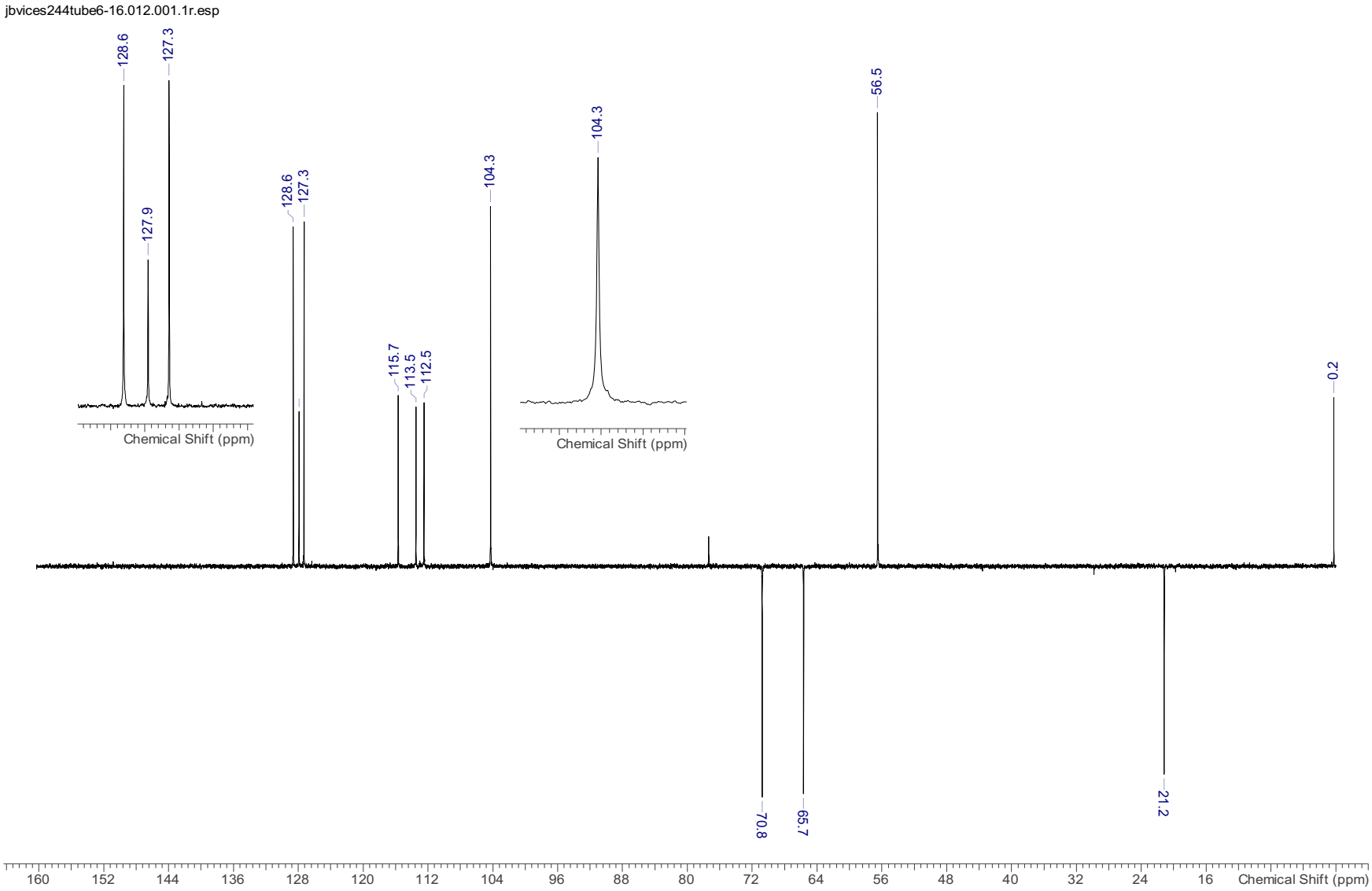


(4-(4-(Benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (23)

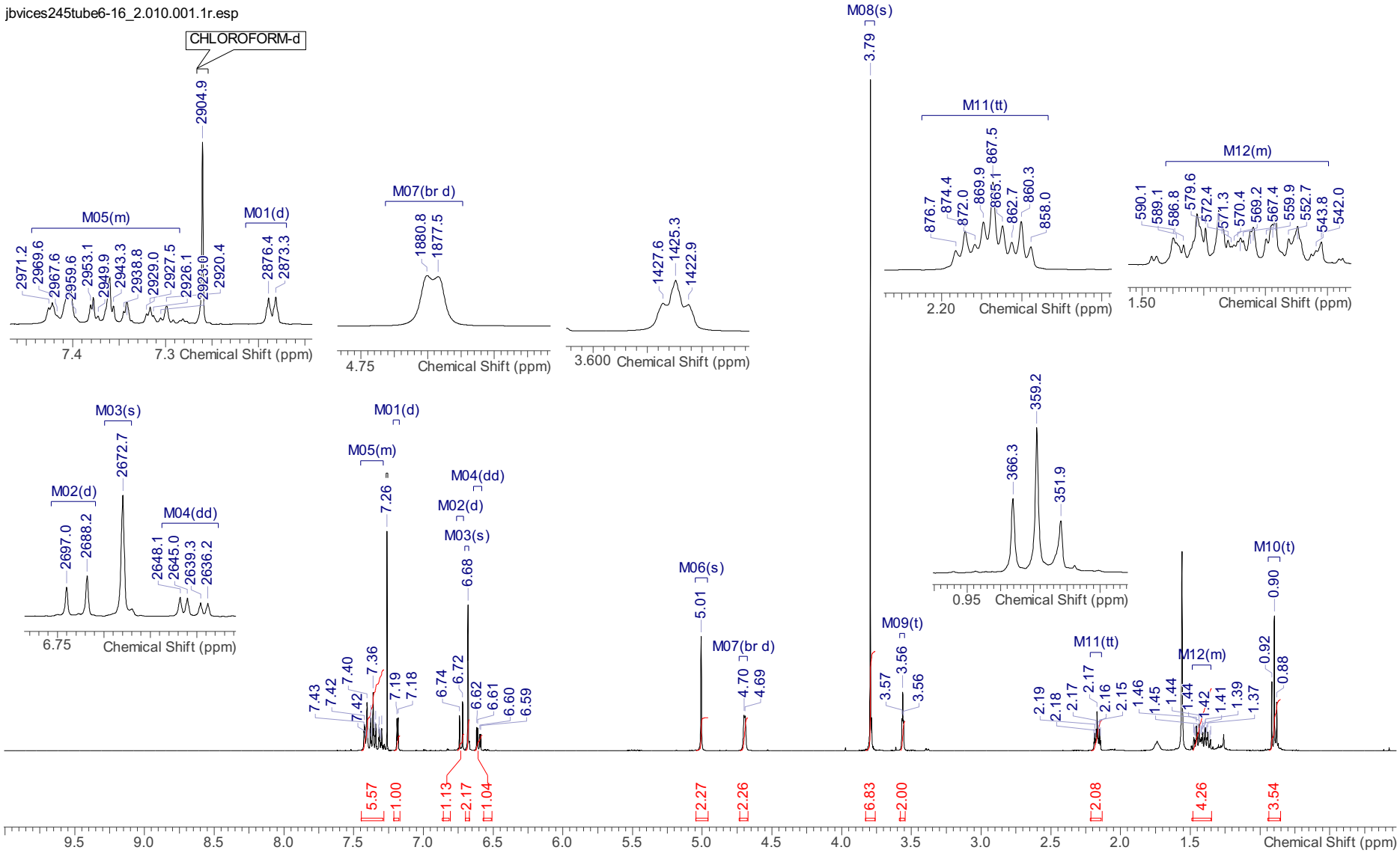
jbvices244tube6-16.011.001.1r.esp



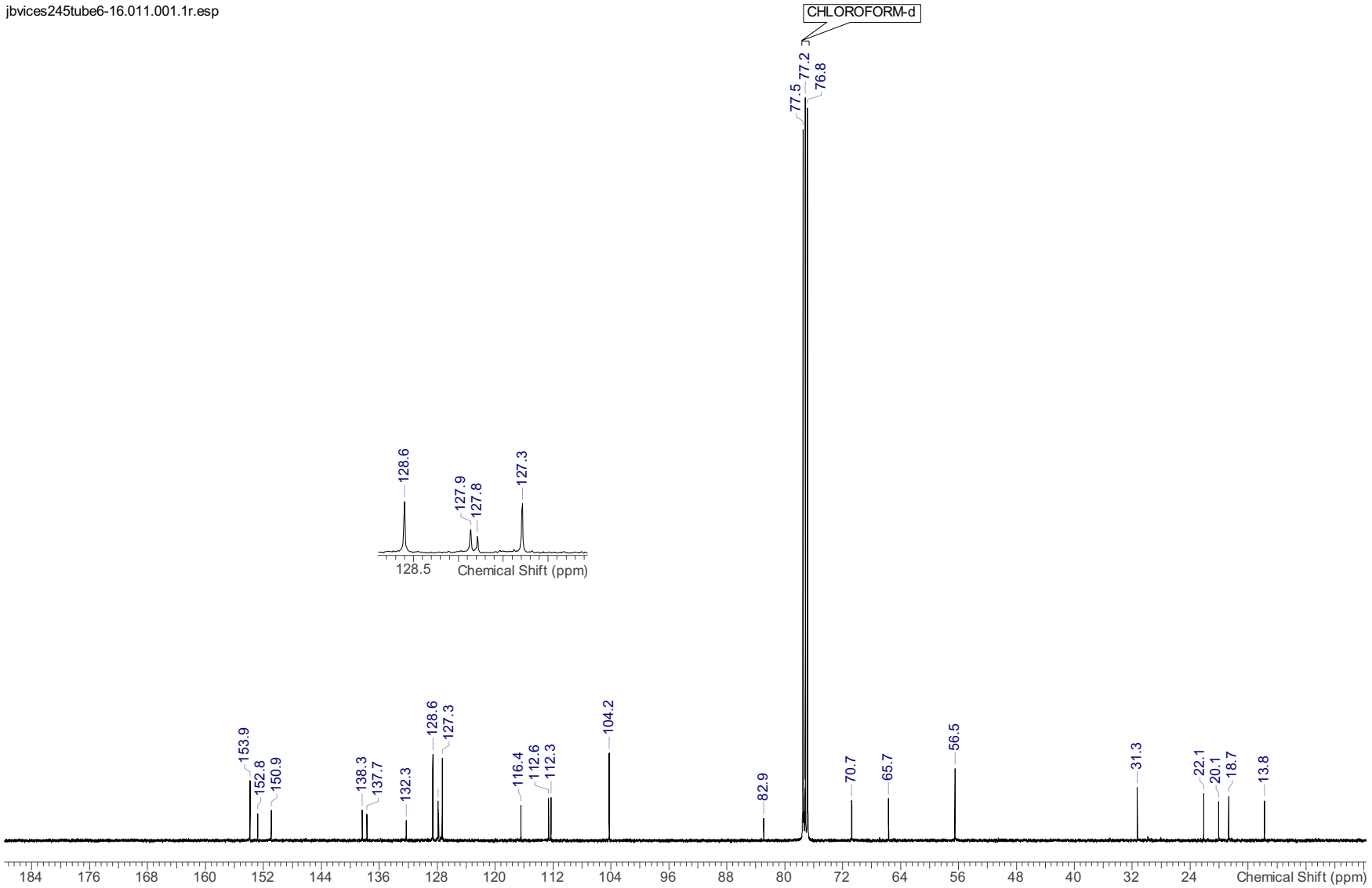
(4-(4-(Benzyloxy)-3-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (23)



(4-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (24)

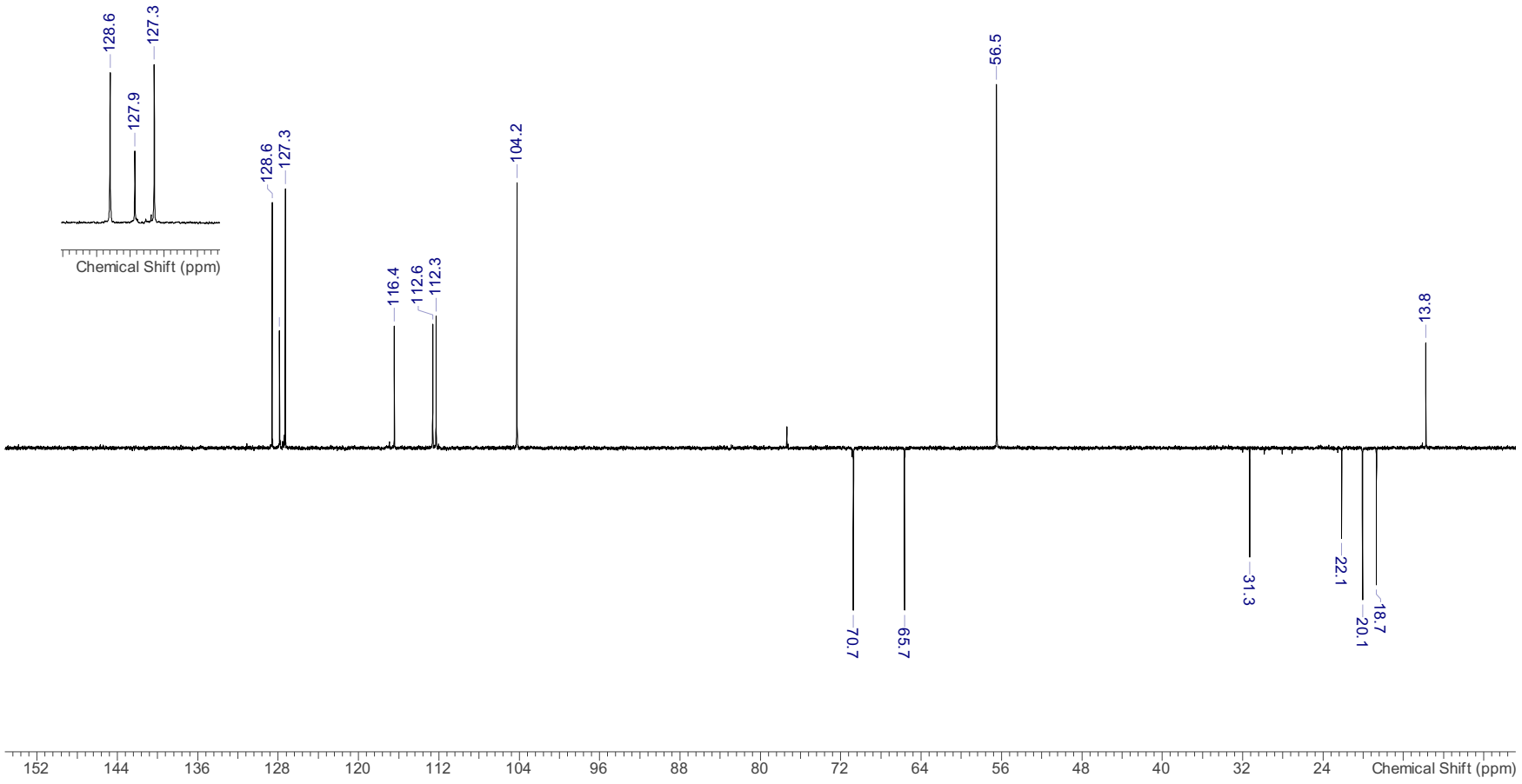


(4-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (24)

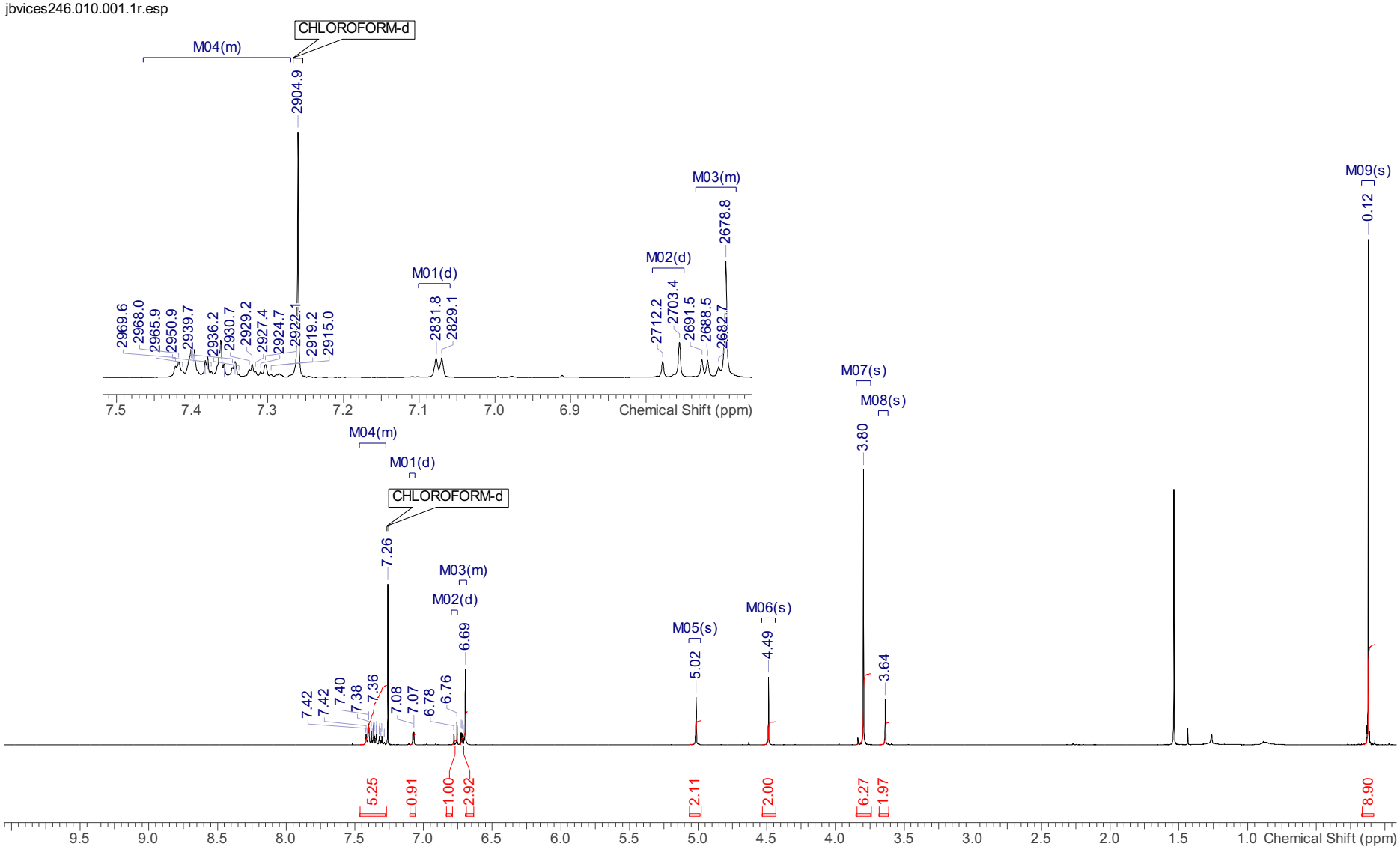


(4-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (24)

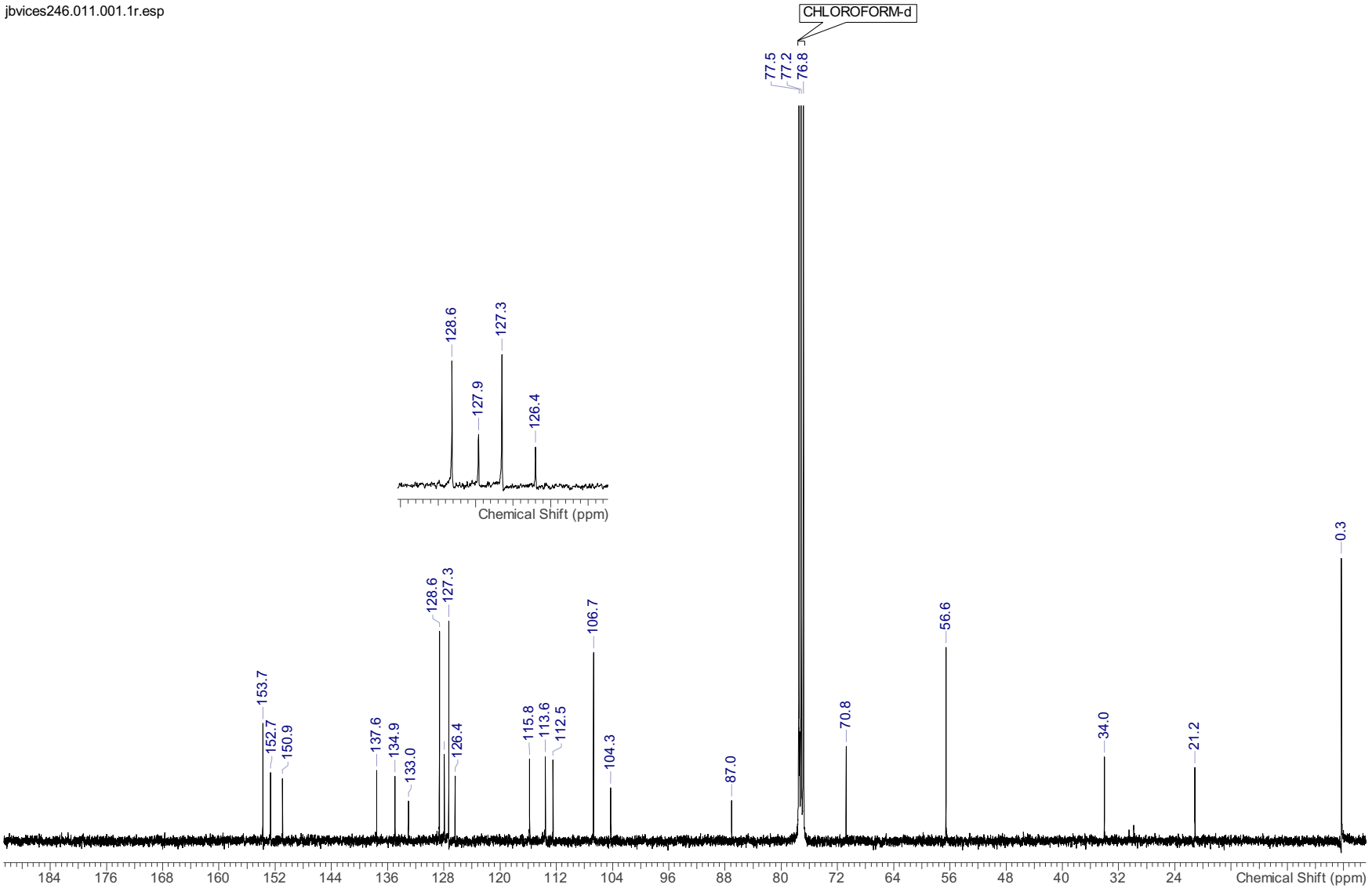
jbvices245tube6-16.012.001.1r.esp



(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (25)

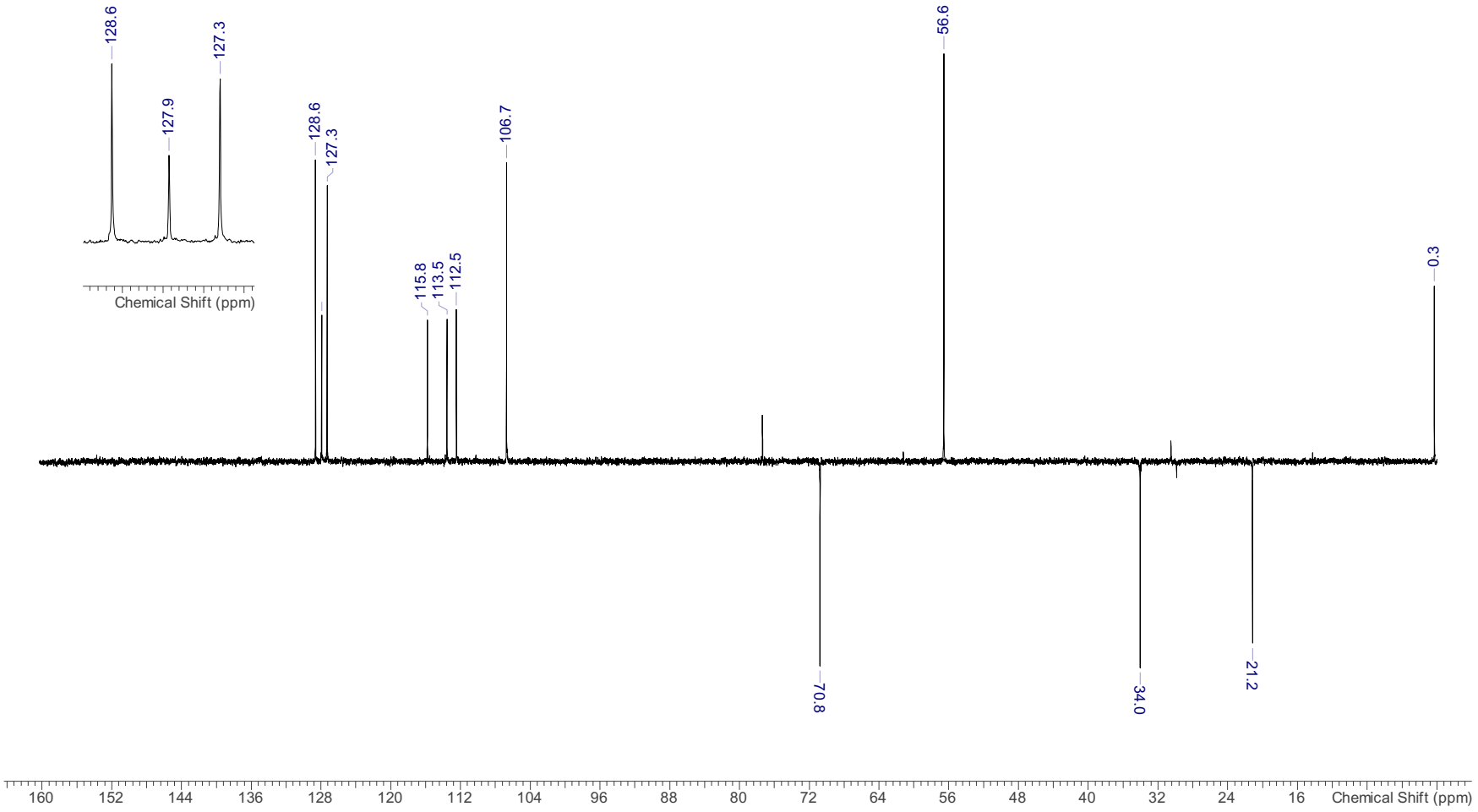


(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (25)



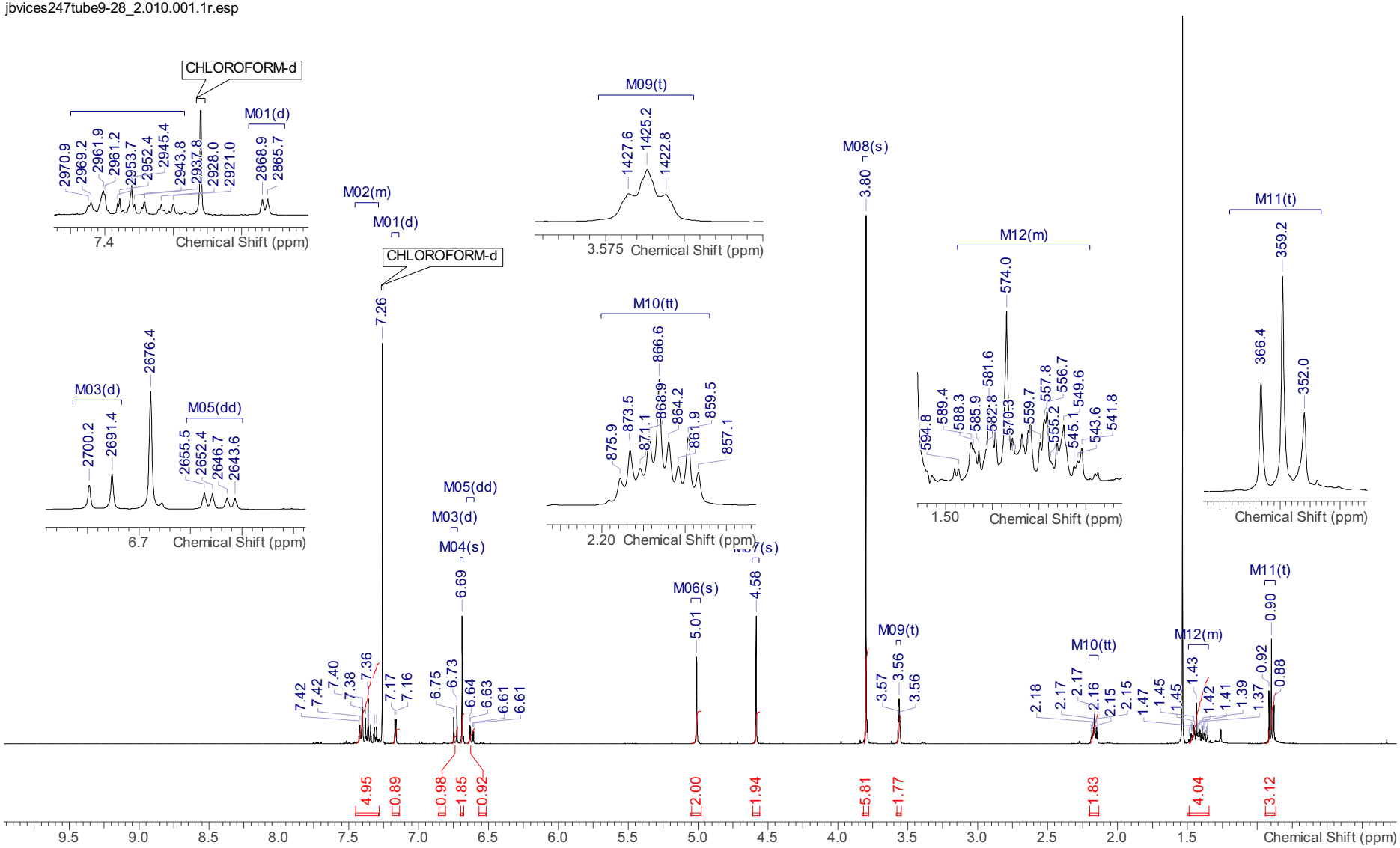
(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (25)

jbvices246.012.001.1r.esp

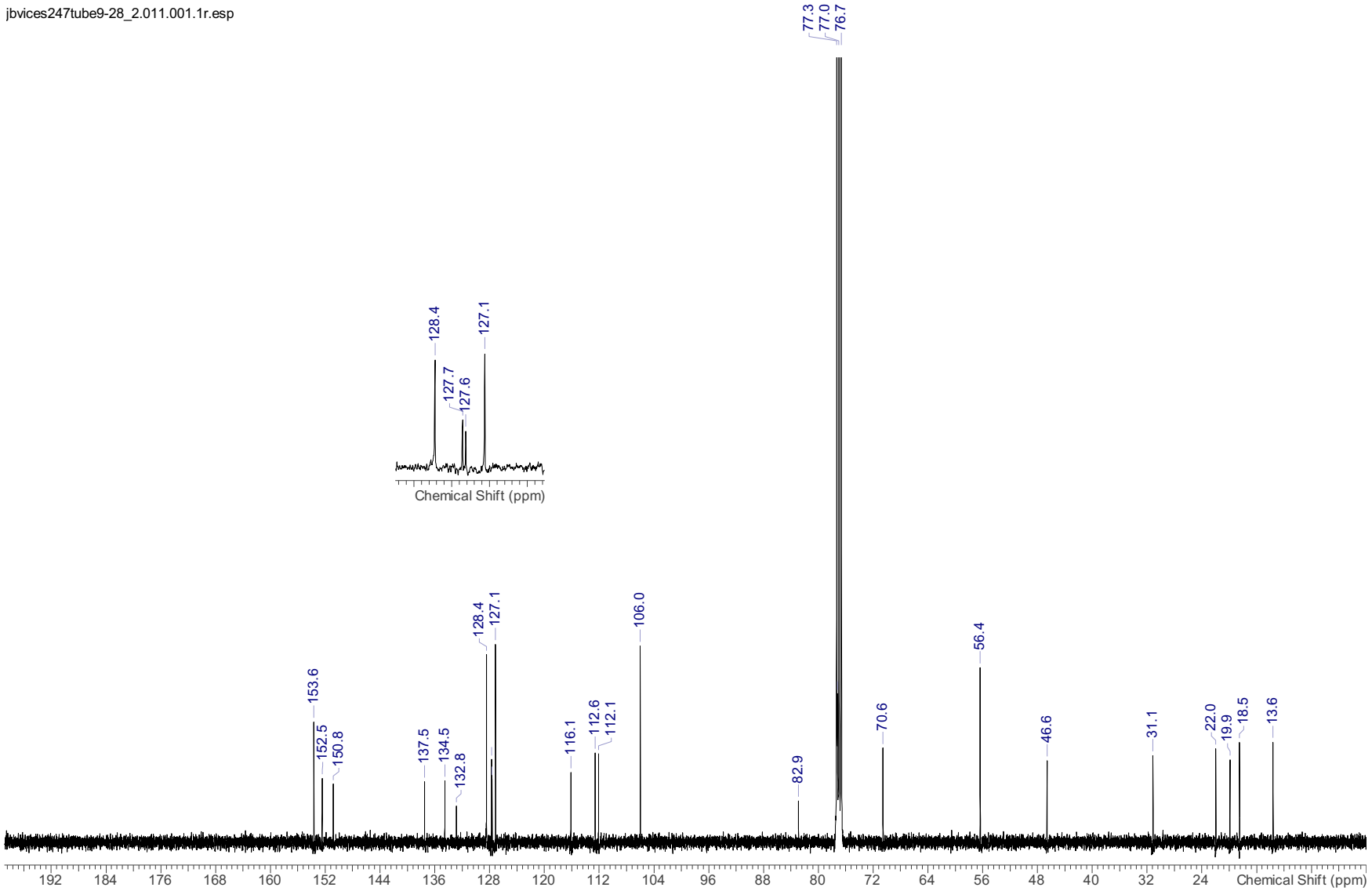


2-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (26)

jbvices247tube9-28_2.010.001.1r.esp

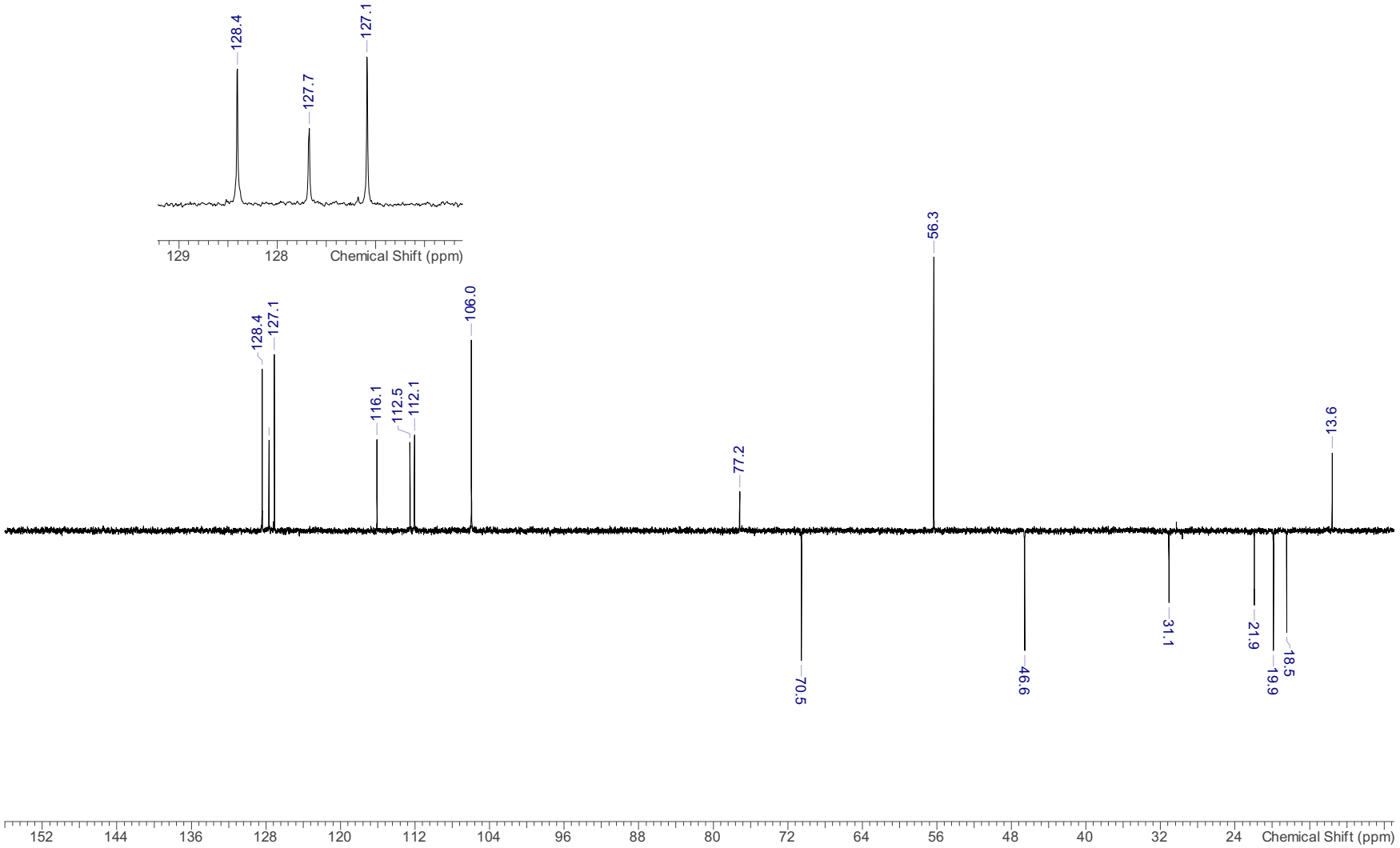


2-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (26)

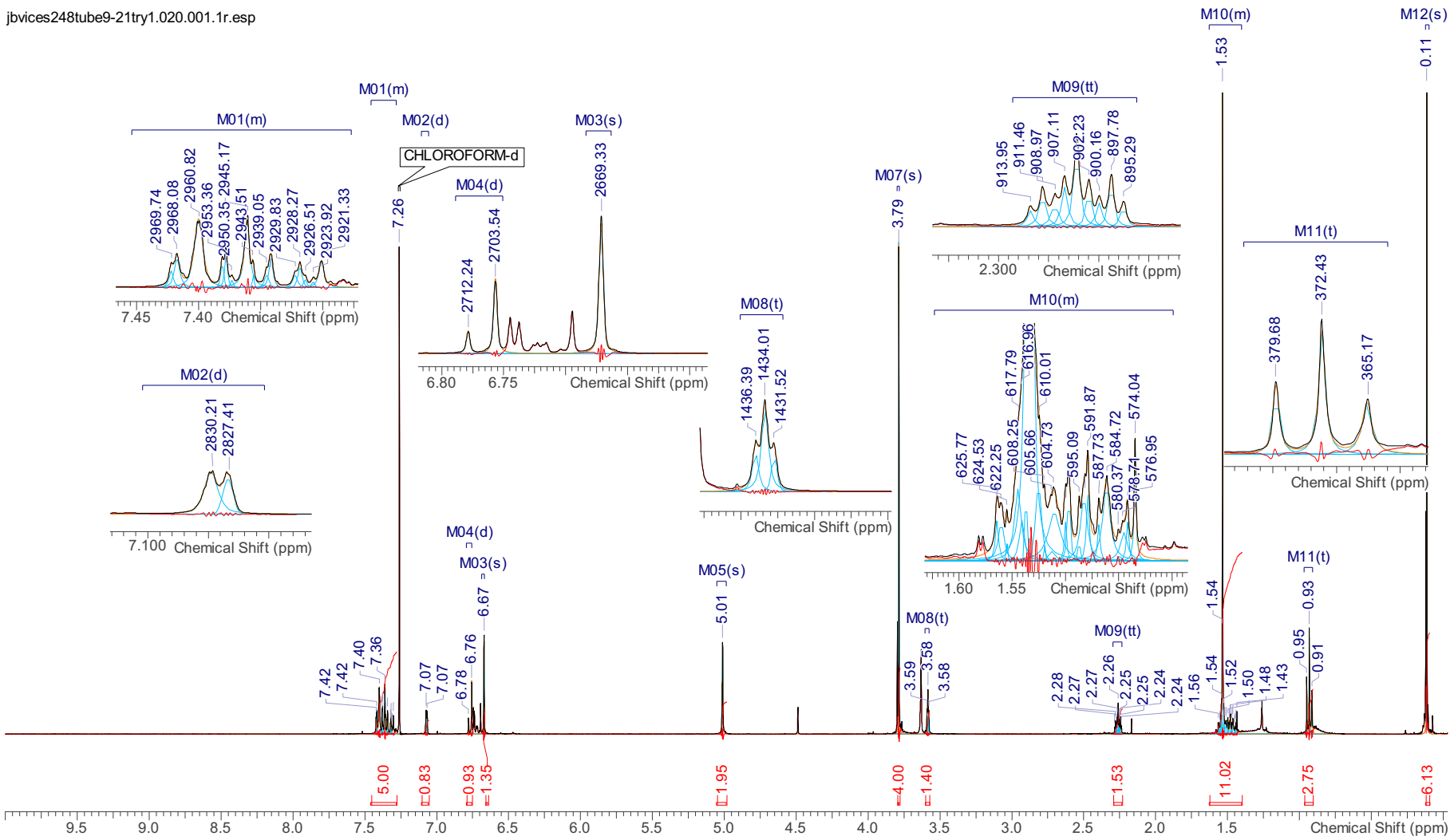


2-(4-(Benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (26)

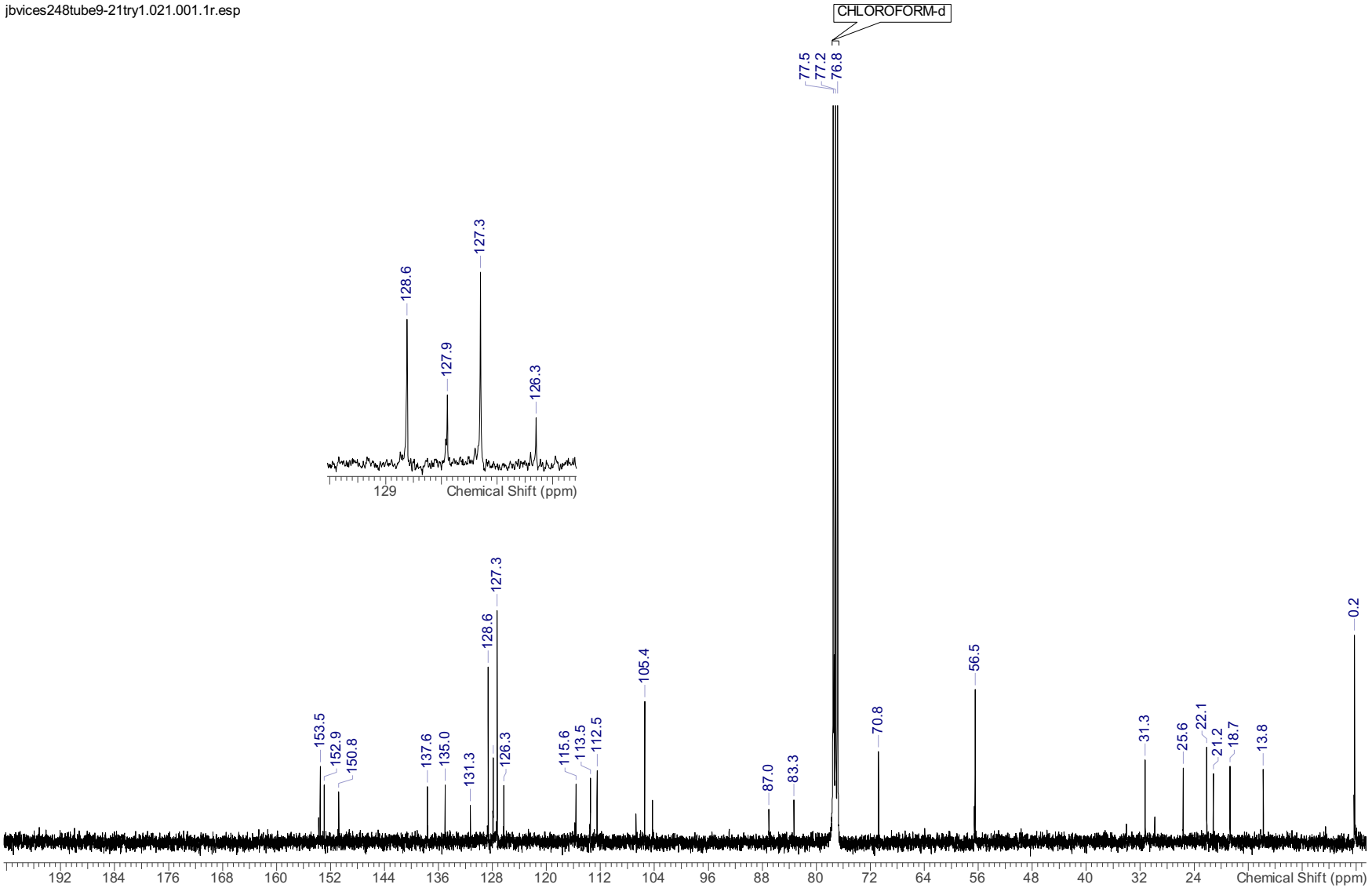
jbvices247tube9-28.012.001.1r.esp



(3-(2-(Benzyloxy)-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (27)

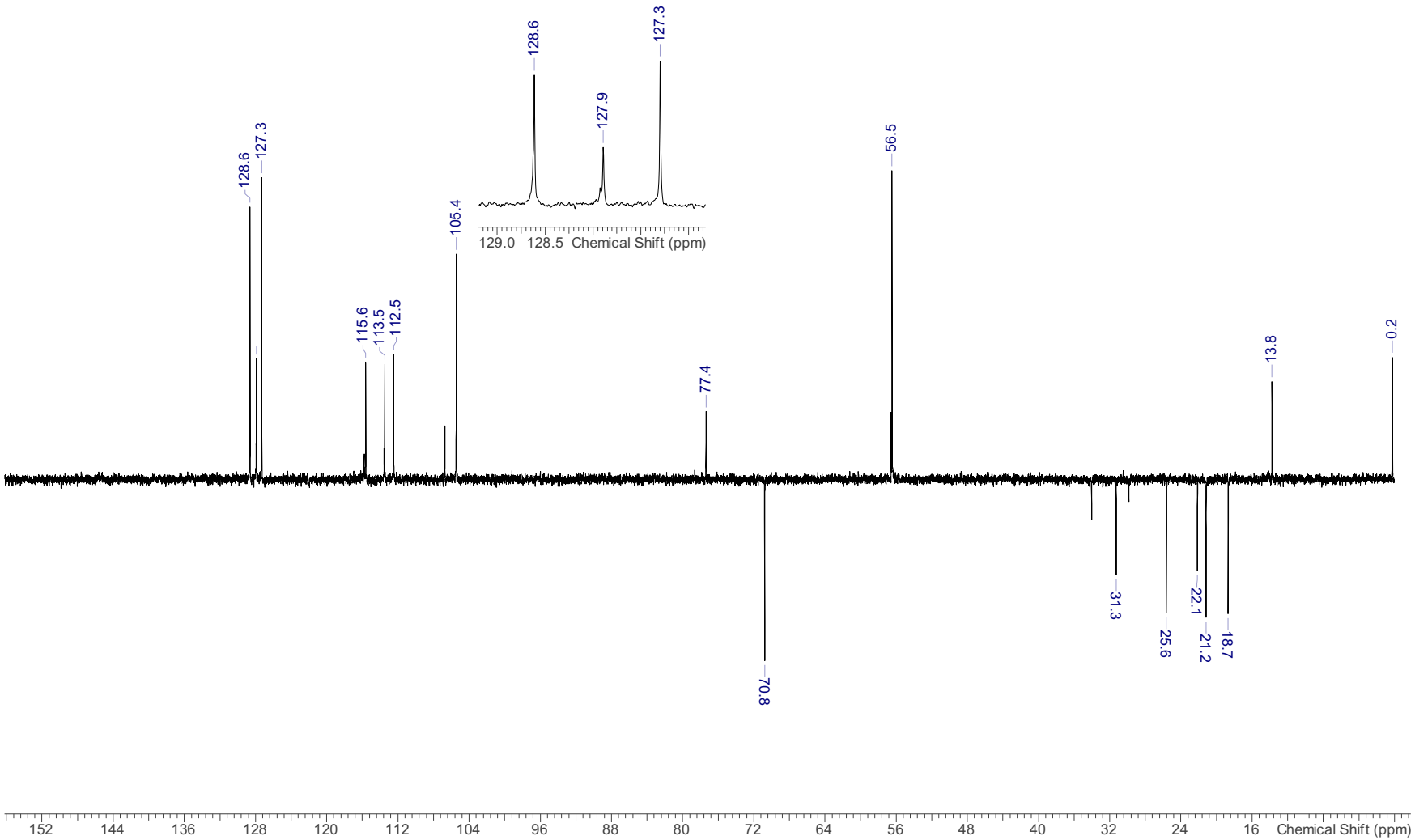


(3-(2-(Benzyloxy)-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (27)



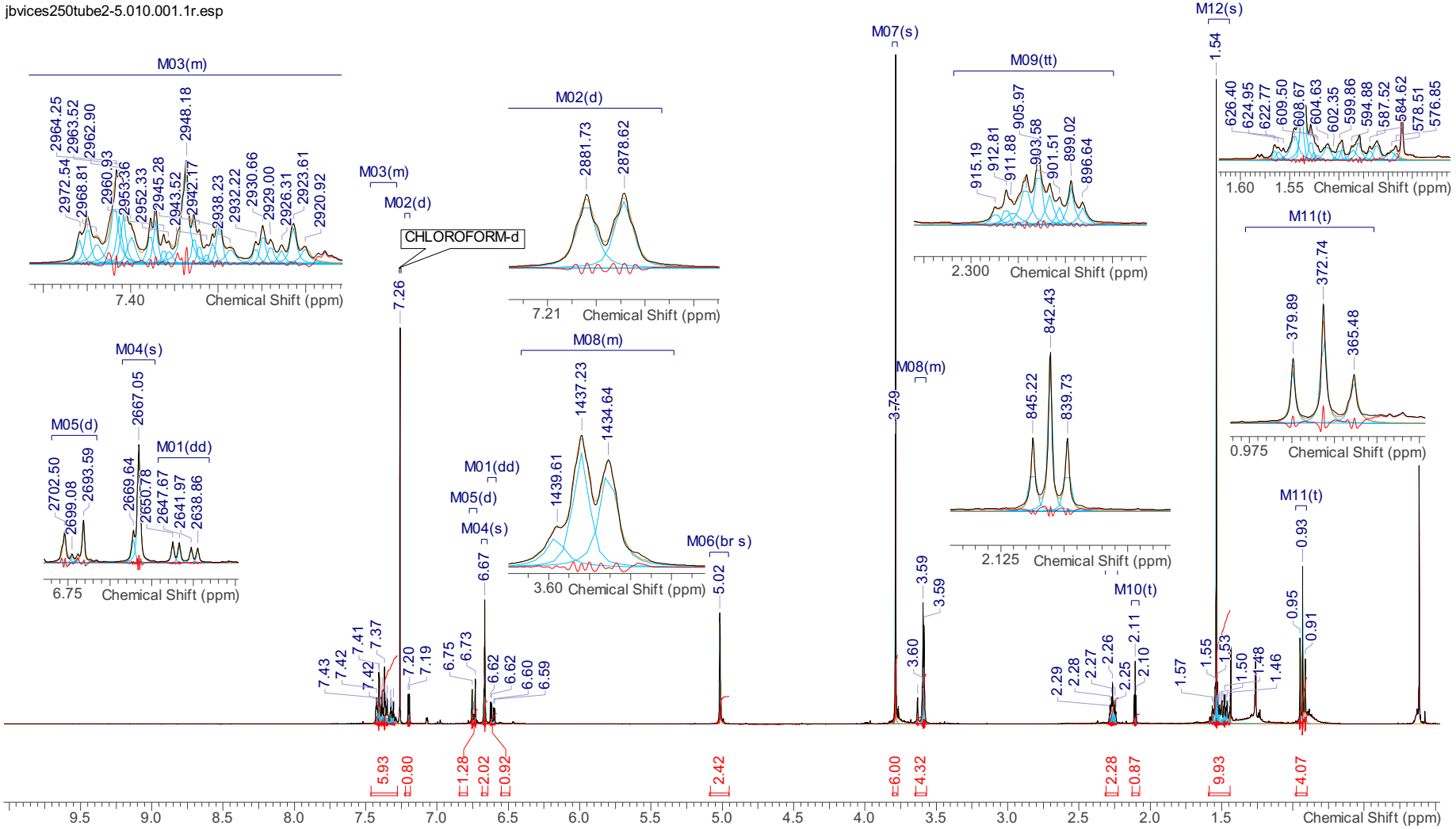
(3-(2-(Benzyloxy)-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (27)

jbvices248tube9-21try1.022.001.1r.esp



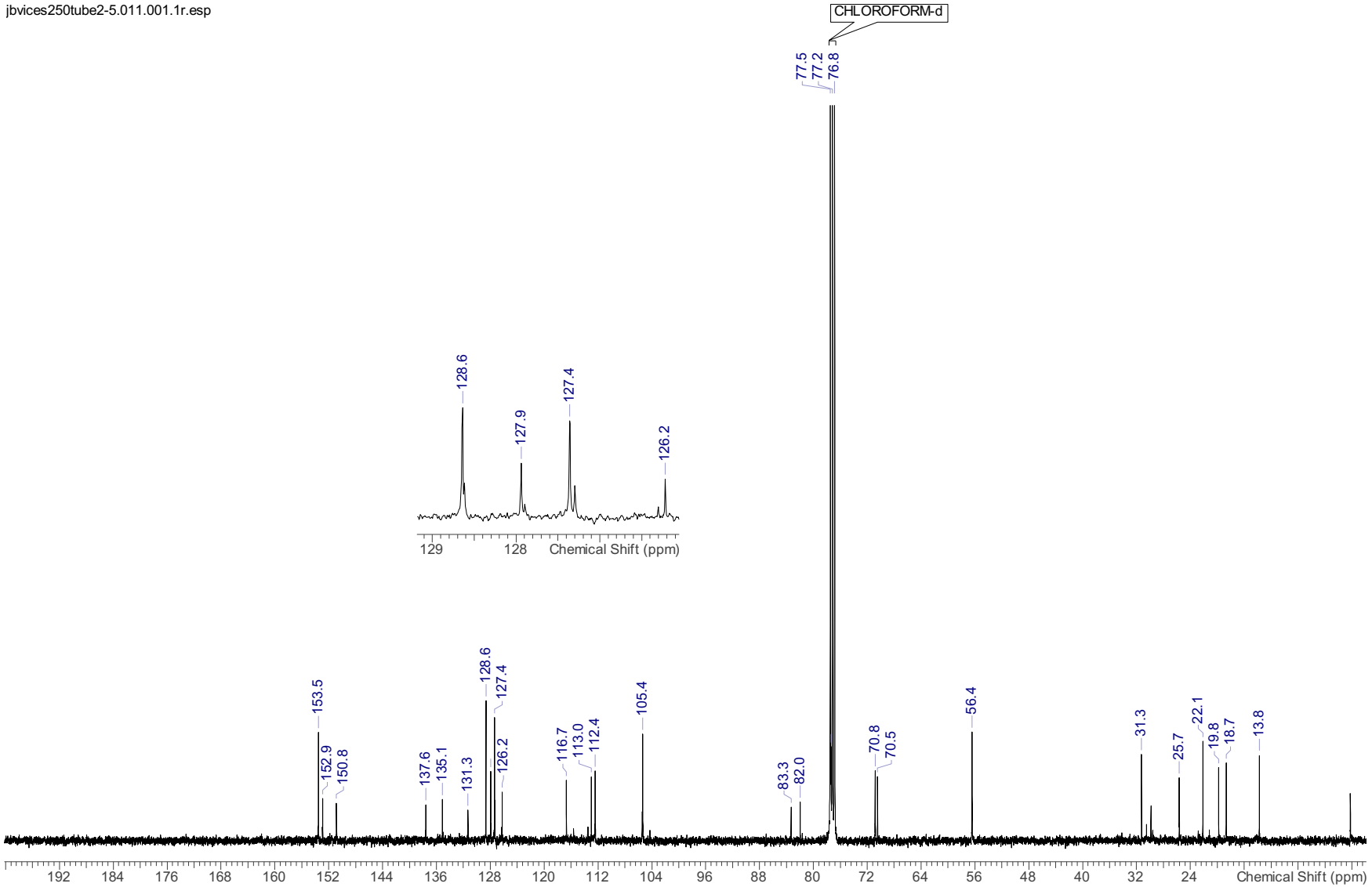
2-(4-(Benzyloxy)-3-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (28)

jbvices250tube2-5.010.001.1r.esp



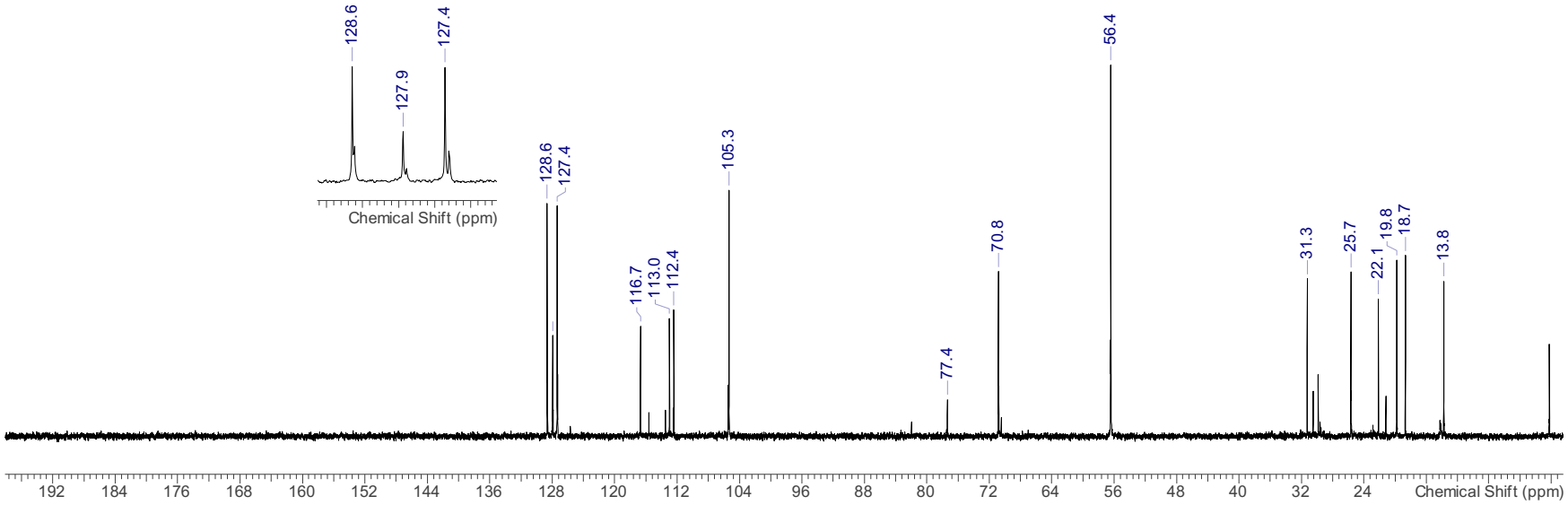
2-(4-(Benzyloxy)-3-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (28)

jbvices250tube2-5.011.001.1r.esp



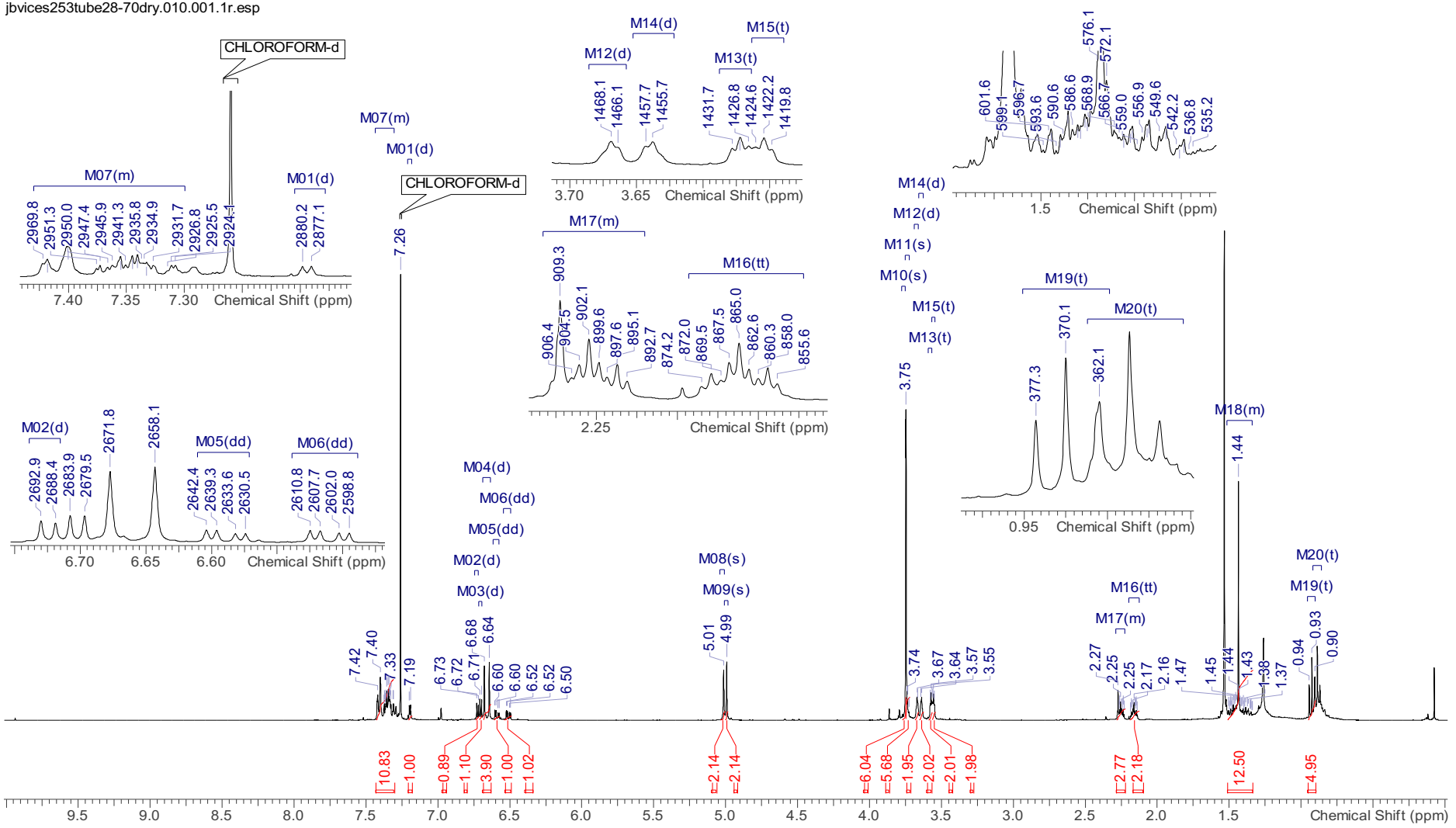
2-(4-(Benzyloxy)-3-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (28)

jbvices250tube2-5.012.001.1r.esp

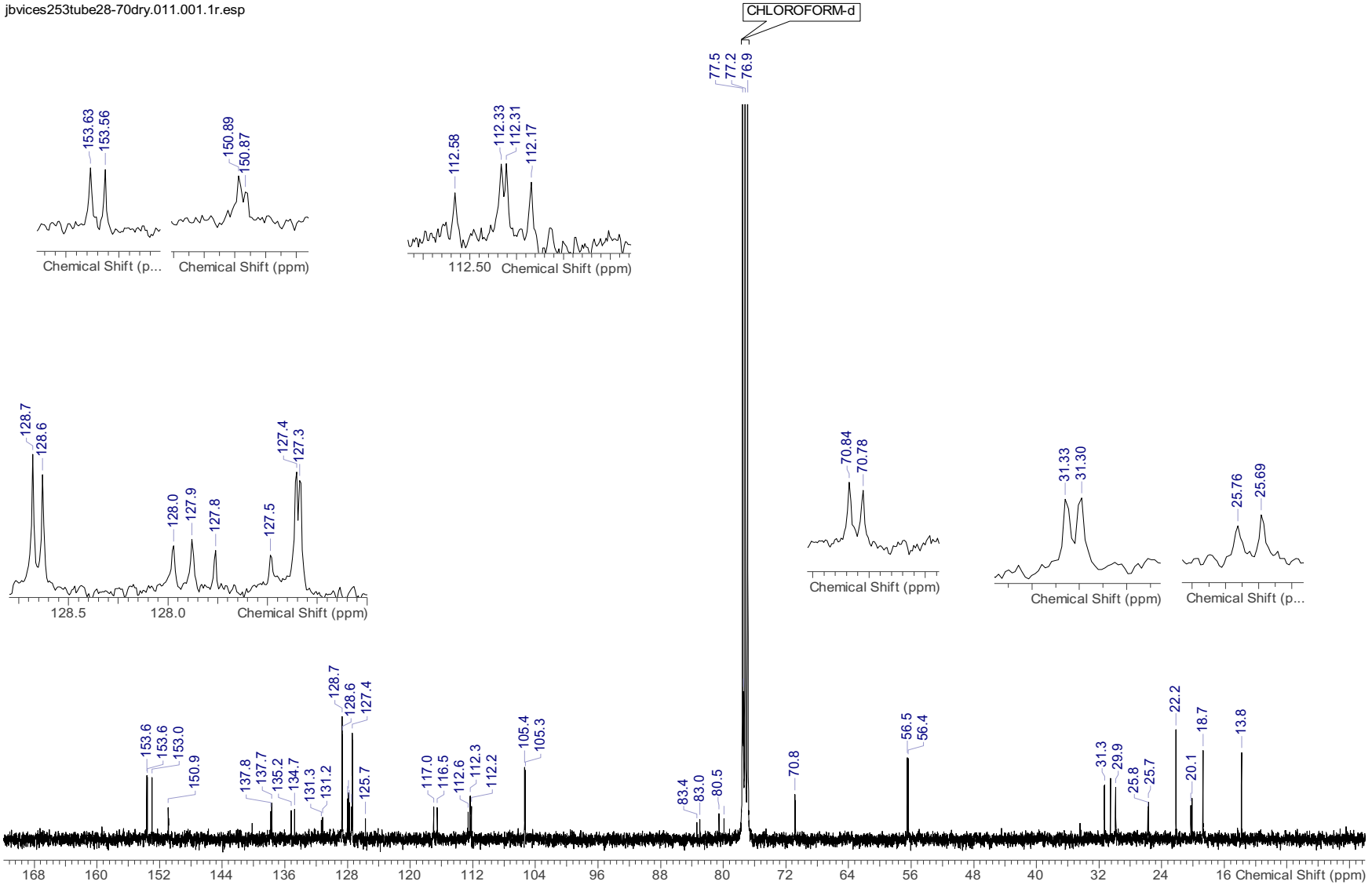


2-(4-(Benzyloxy)-3-(4-(4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)but-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (29)

jbvices253tube28-70dry.010.001.1r.esp

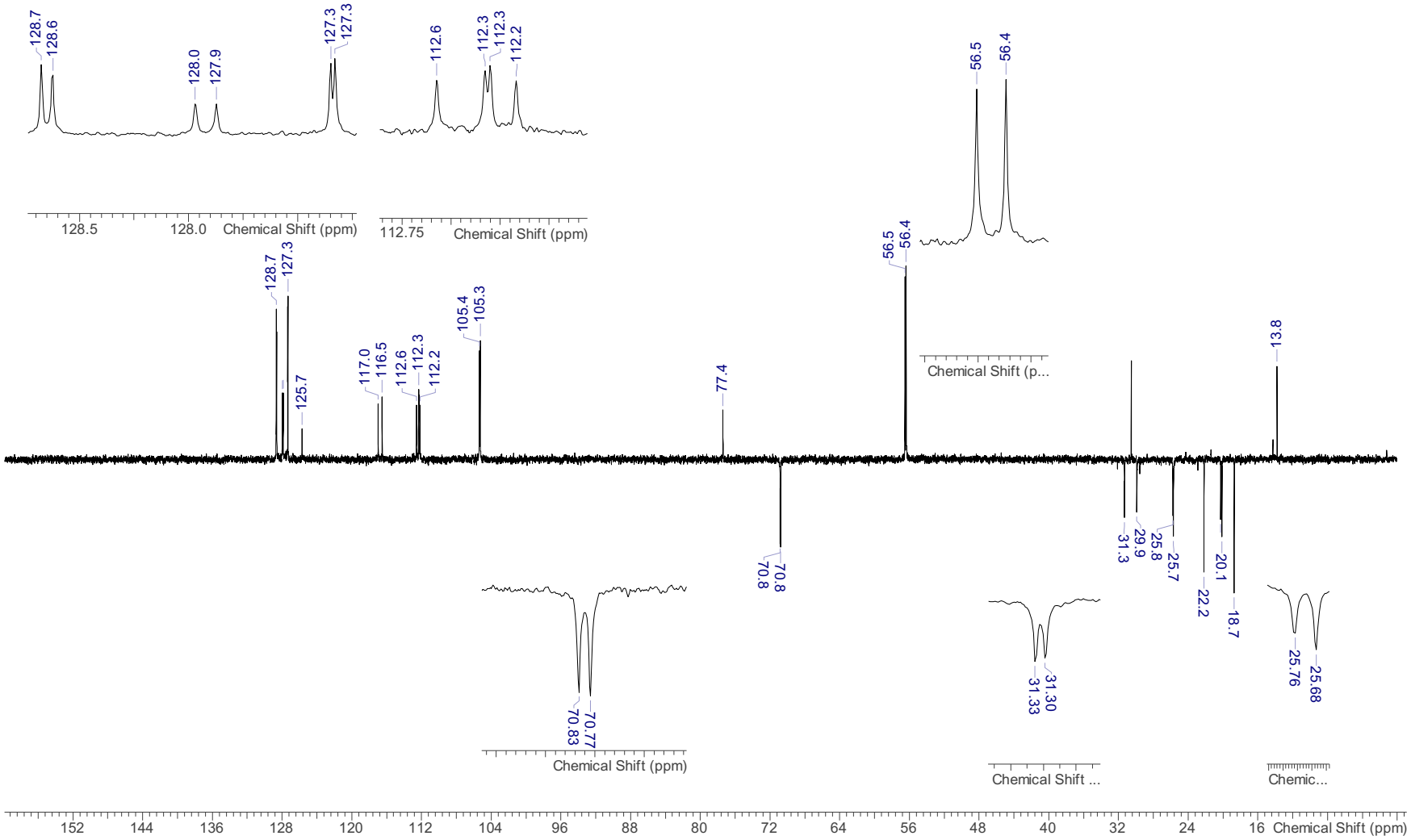


2-(4-(Benzyloxy)-3-(4-(4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)but-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (29)

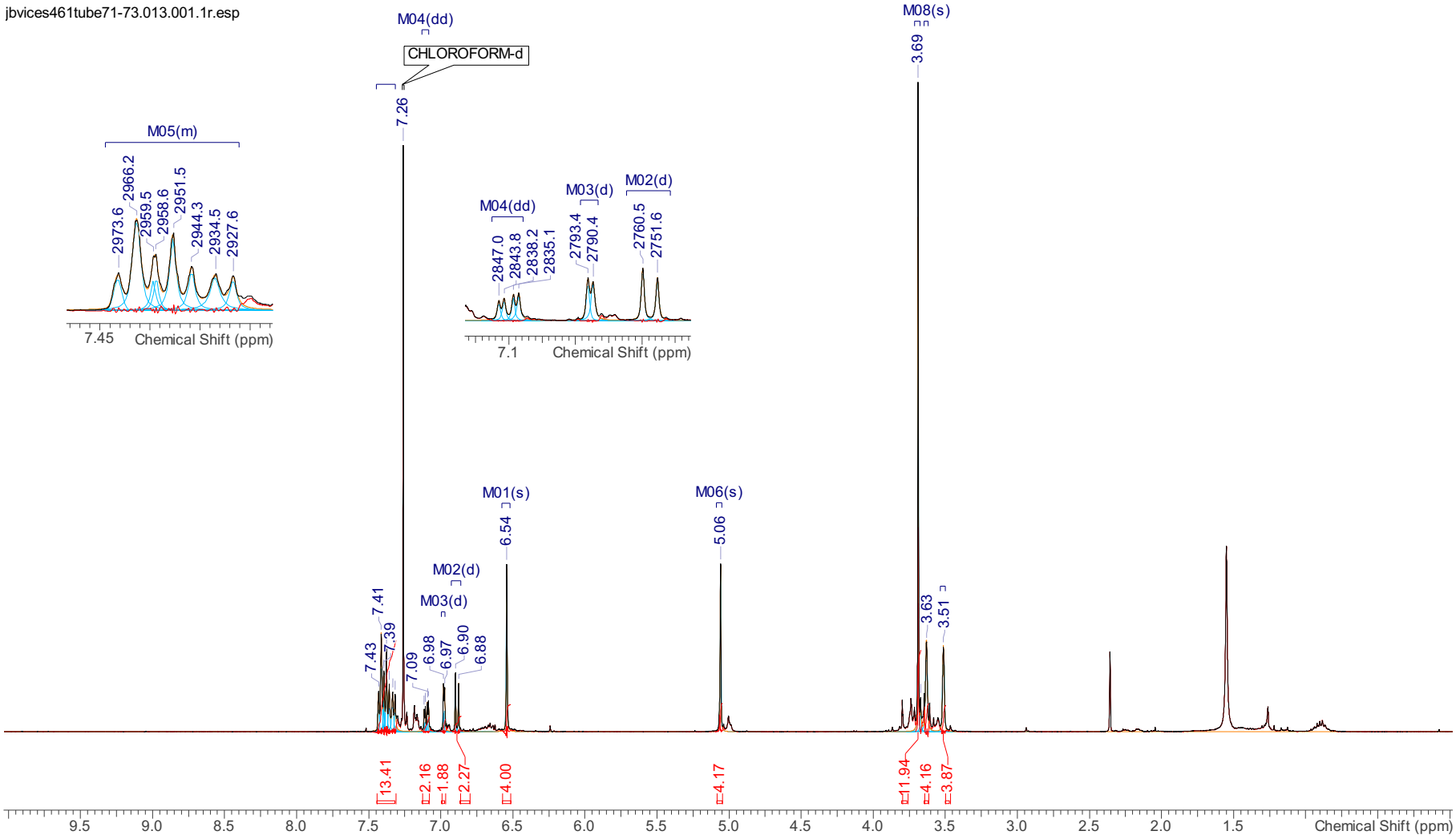


2-(4-(Benzyloxy)-3-(4-(4-(4-(benzyloxy)-3-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)but-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (29)

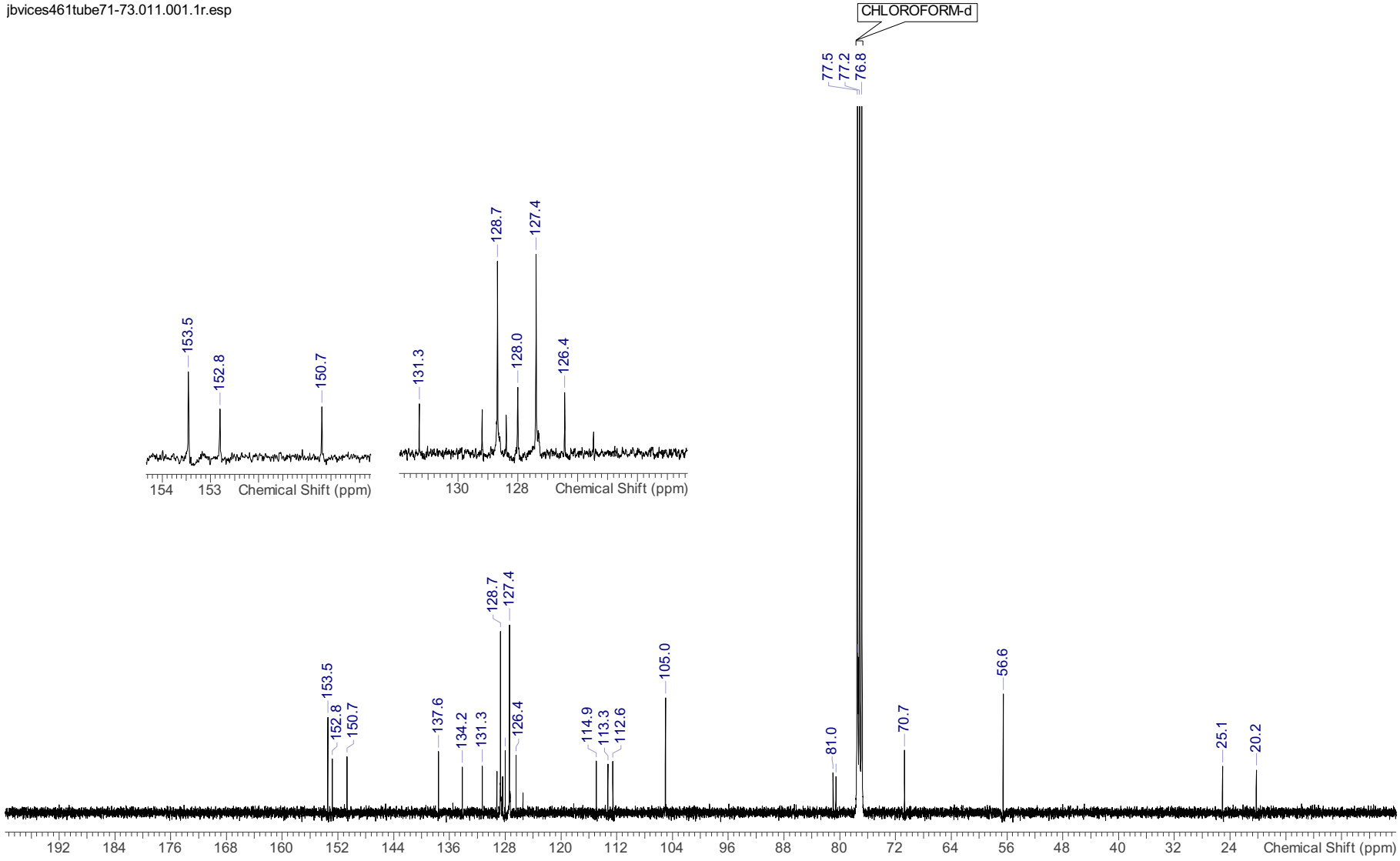
jbvices253tube28-70dry.012.001.1r.esp



6,20-Dibenzyloxy-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-,5,7(34),12,14,17,19,21(31),26,28,29,32-dodecaene-9,23-diyne (30)

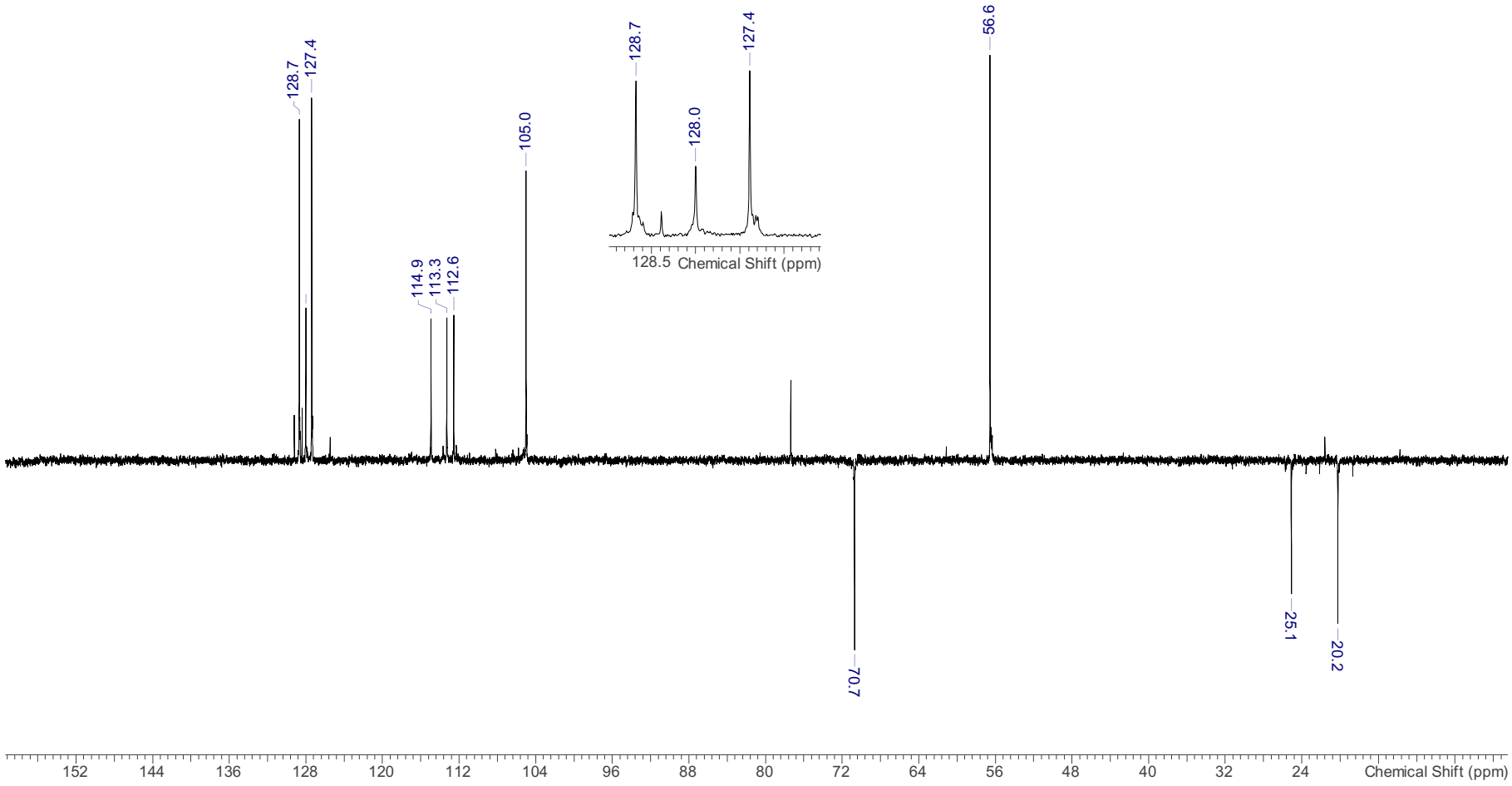


6,20-Dibenzyloxy-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-,5,7(34),12,14,17,19,21(31),26,28,29,32-dodecaene-9,23-diyne (30)

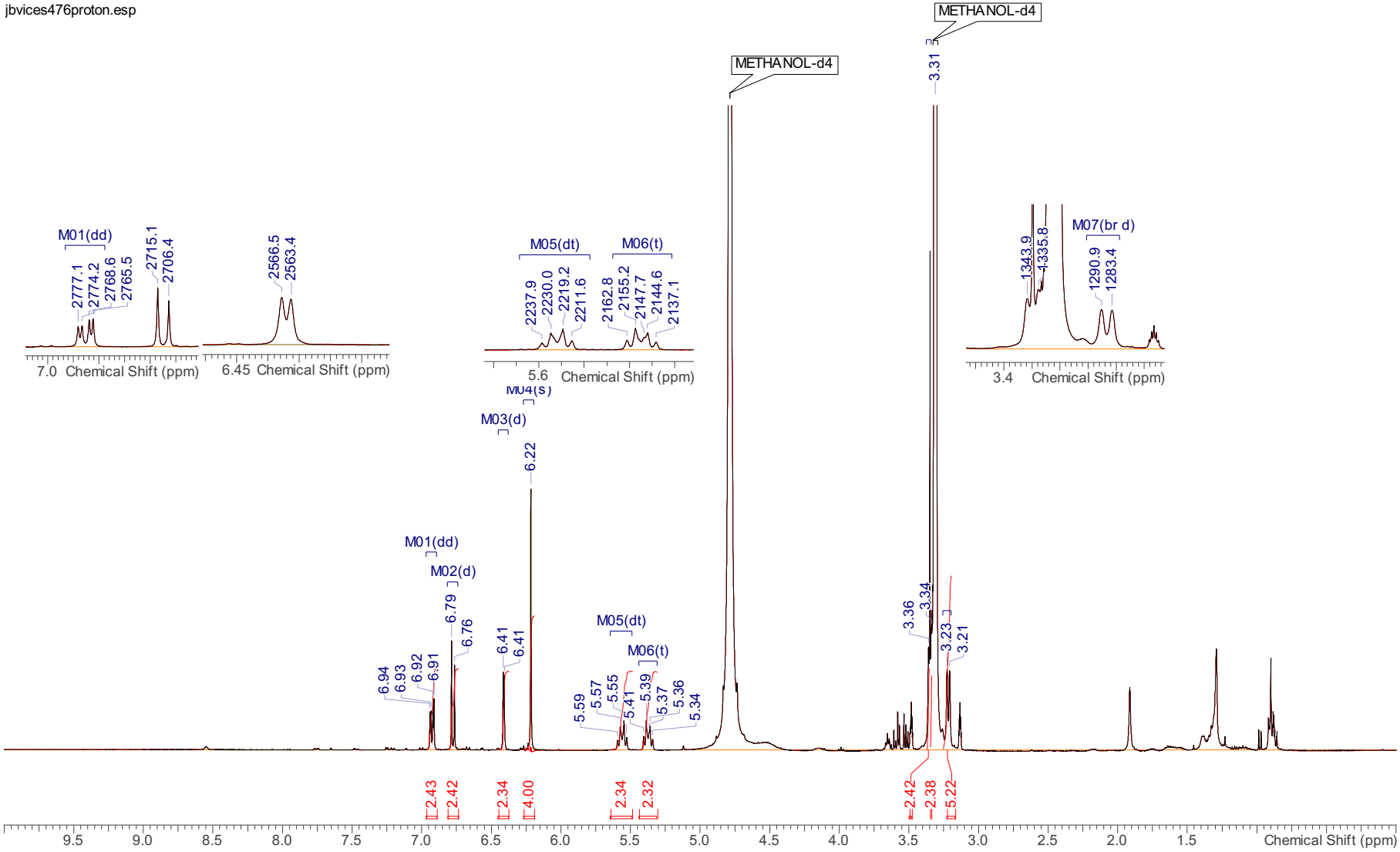


6,20-Dibenzyloxy-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-,5,7(34),12,14,17,19,21(31),26,28,29,32-dodecaene-9,23-diyne (30)

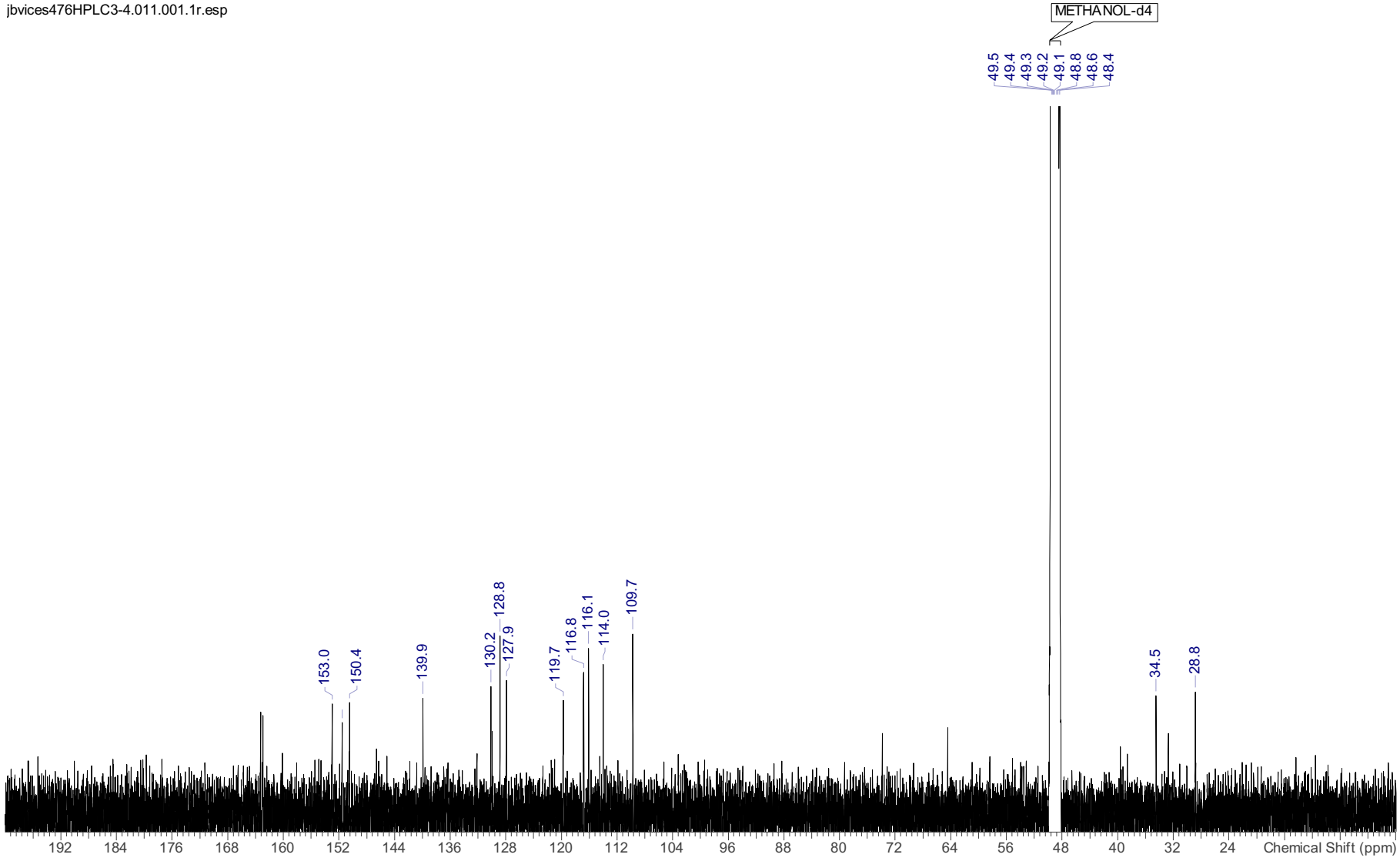
jbvices461tube71-73.012.001.1r.esp



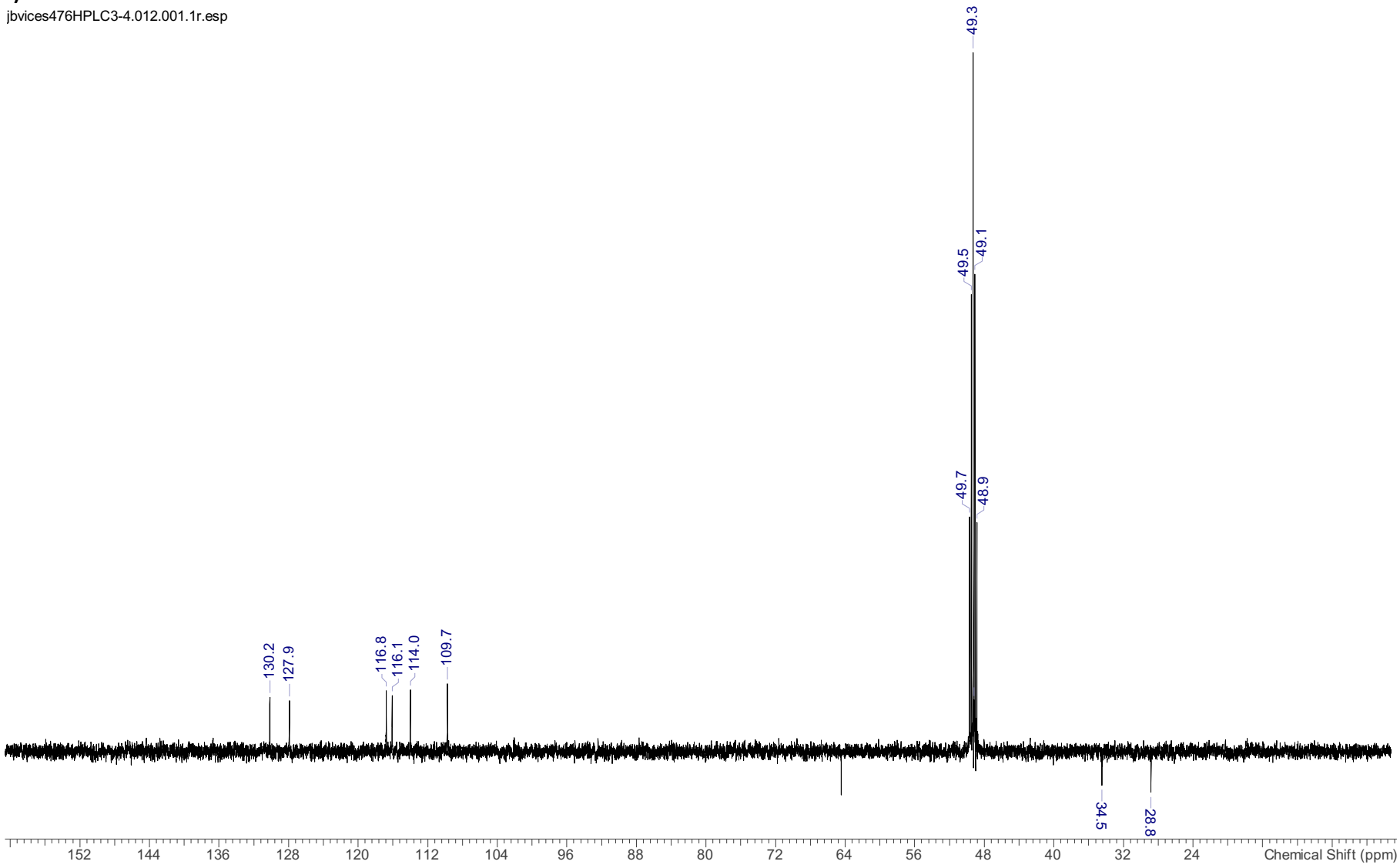
(9*E*,23*E*)-2,16-Dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-3,5,7(34),9,12,14,17,19,21(31),23,26,28,29,32-tetradecaene-6,14,20,28,29,32-hexol (11)



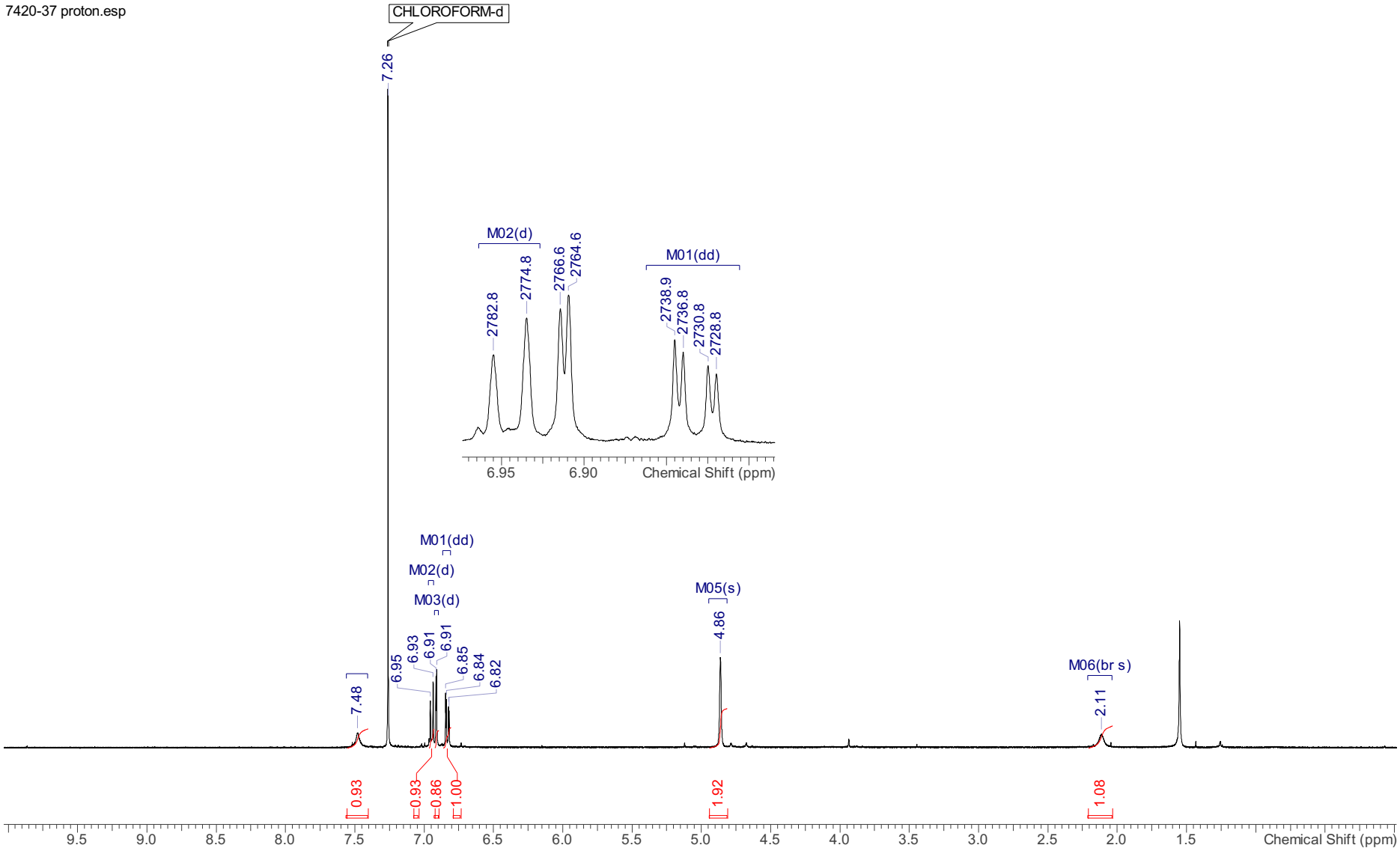
(9*E*,23*E*)-2,16-Dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-3,5,7(34),9,12,14,17,19,21(31),23,26,28,29,32-tetradecaene-6,14,20,28,29,32-hexol (11)



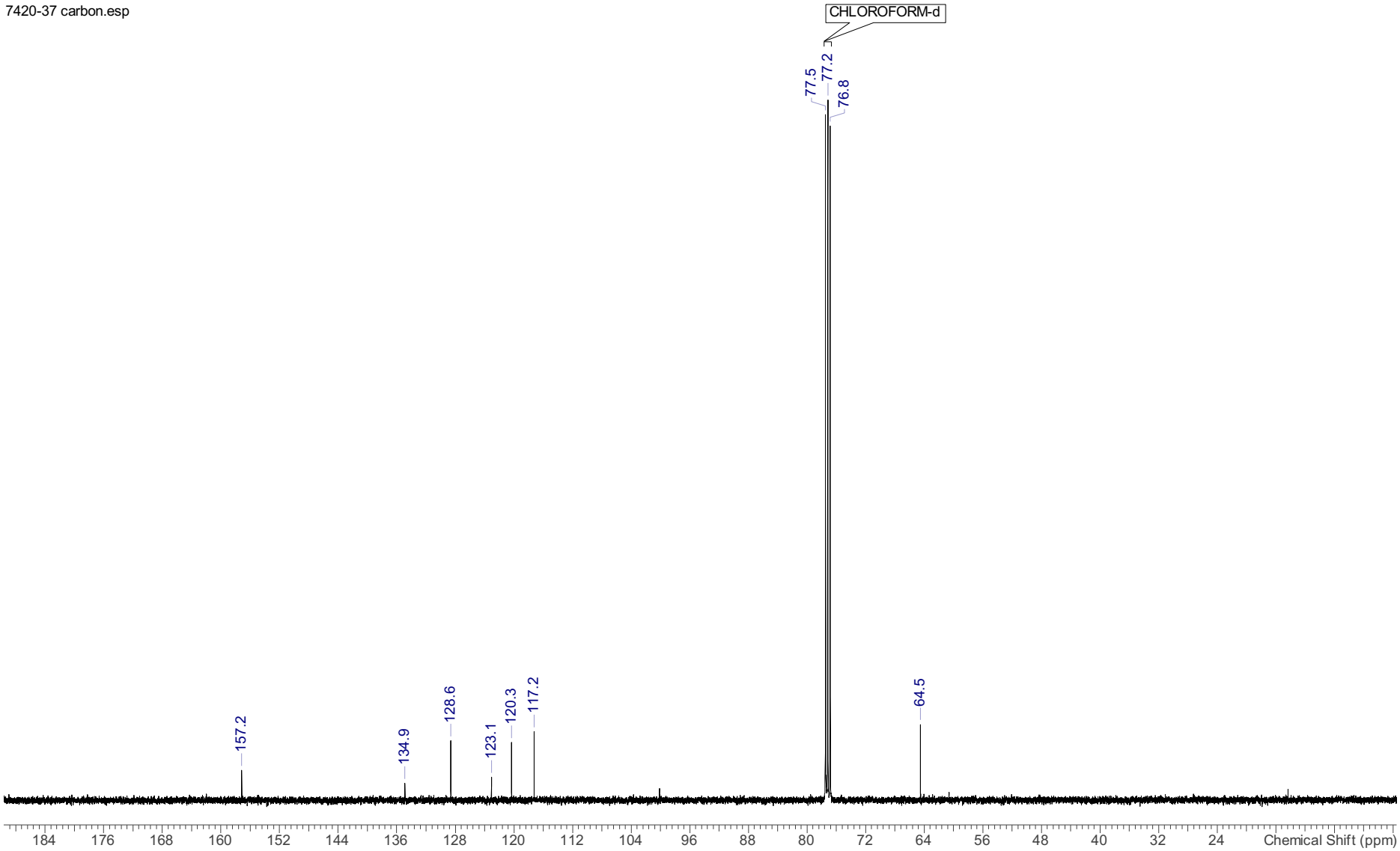
(9*E*,23*E*)-2,16-Dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-3,5,7(34),9,12,14,17,19,21(31),23,26,28,29,32-tetradecaene-6,14,20,28,29,32-hexol (11)



5-Chloro-2-(hydroxymethyl)phenol (33)

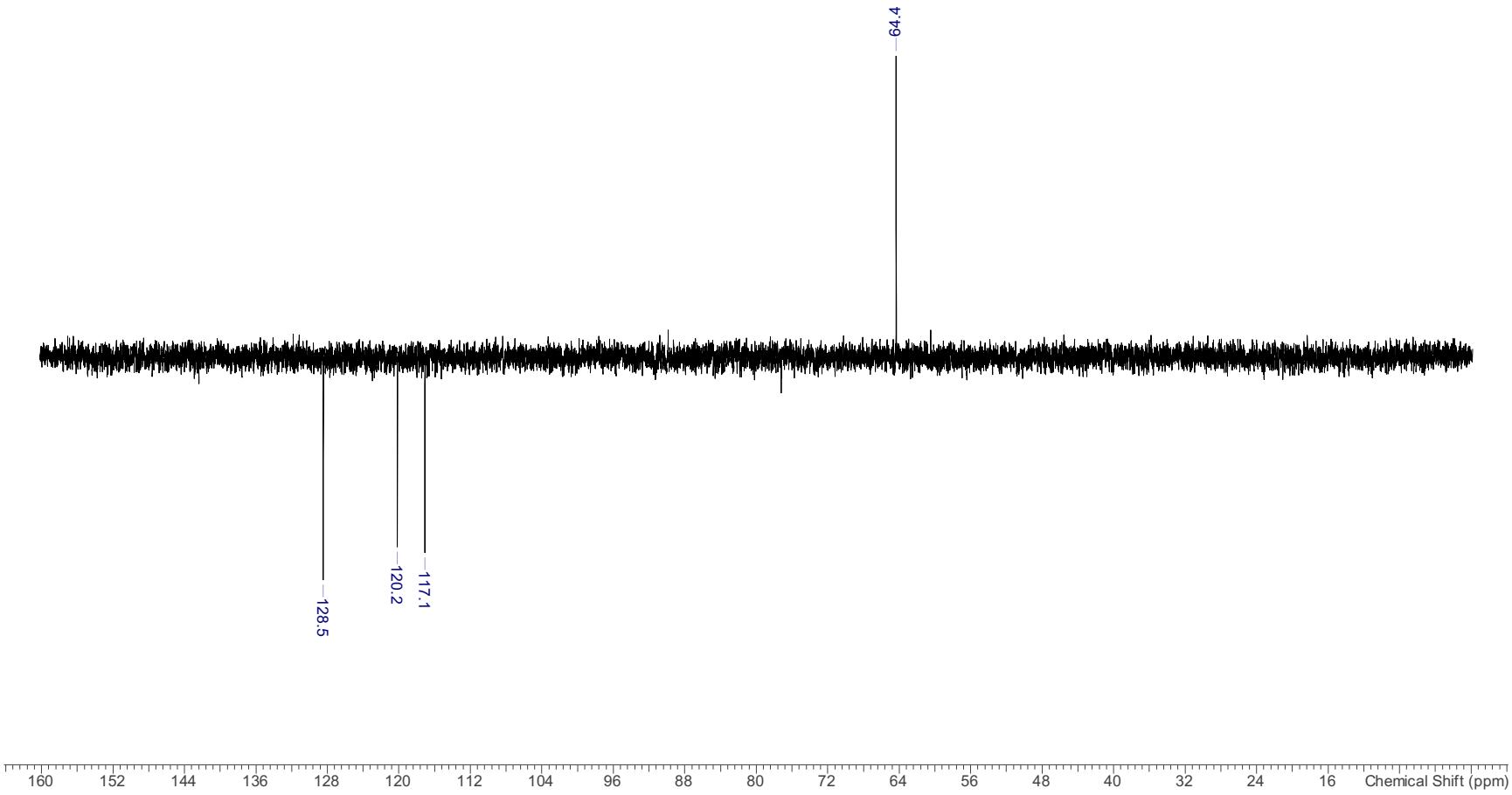


5-Chloro-2-(hydroxymethyl)phenol (33)



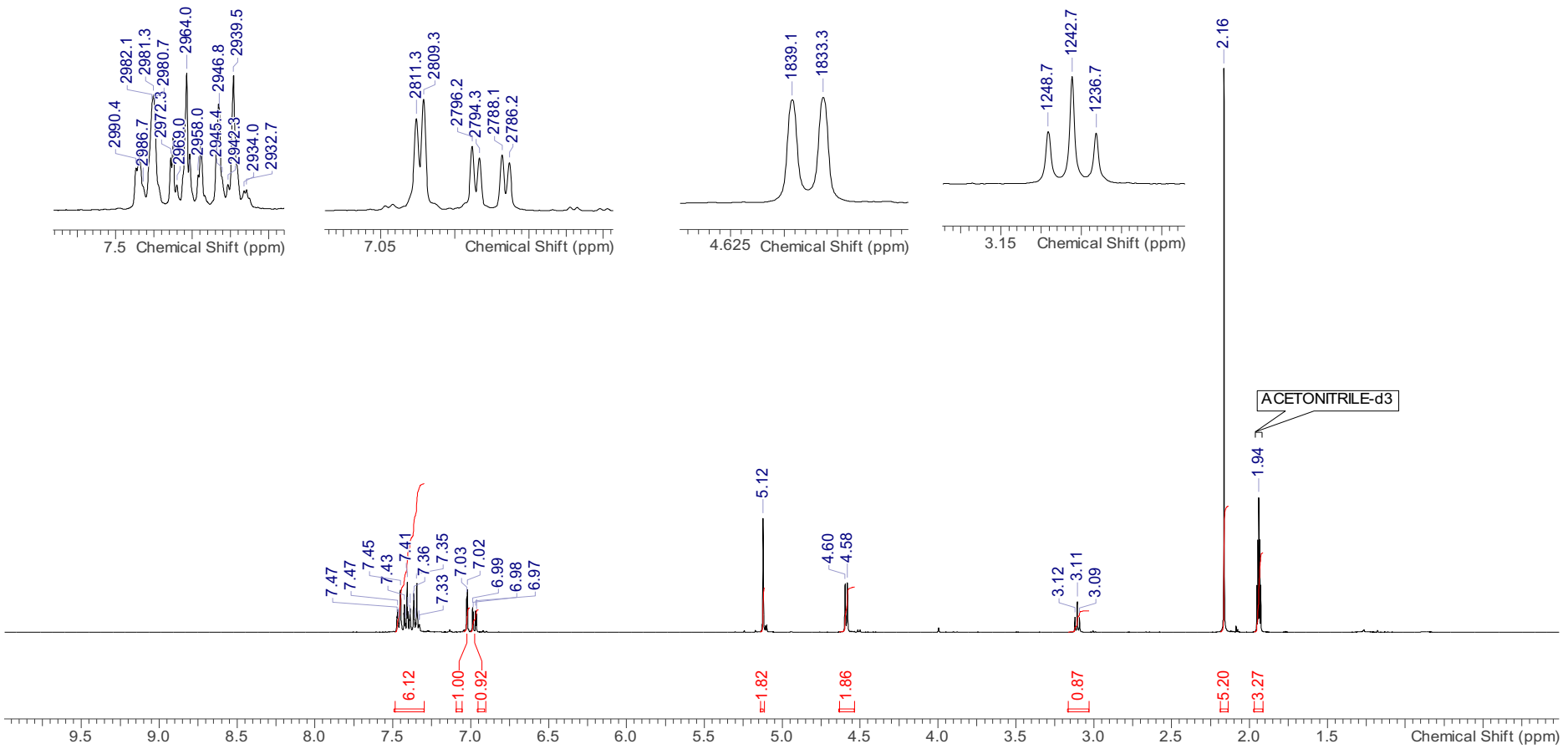
5-Chloro-2-(hydroxymethyl)phenol (33)

7420-37 dept.esp



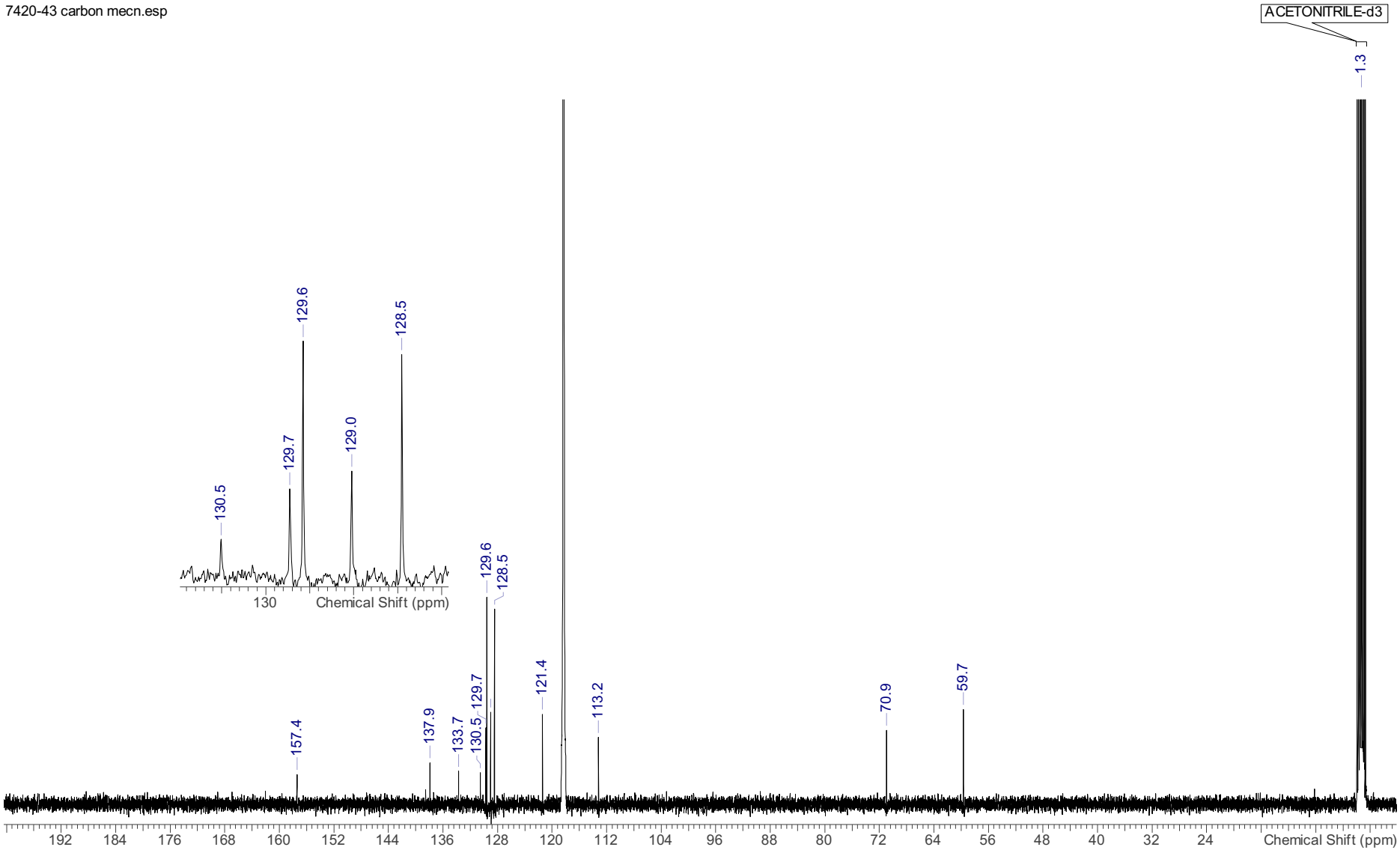
(2-(Benzyloxy)-4-chlorophenyl)methanol (34)

7420-43 proton mecn.esp

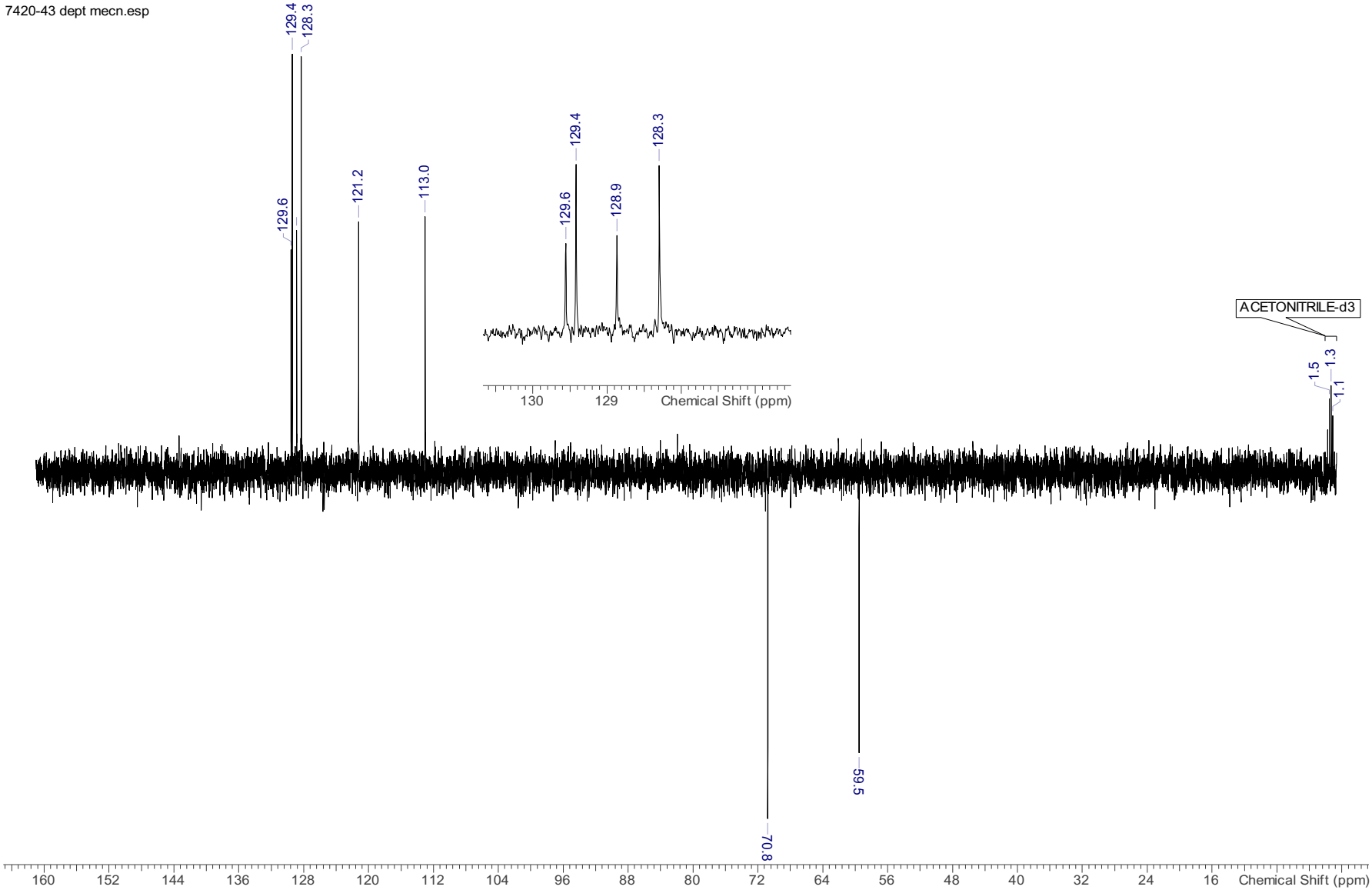


(2-(Benzyloxy)-4-chlorophenyl)methanol (34)

7420-43 carbon mecn.esp

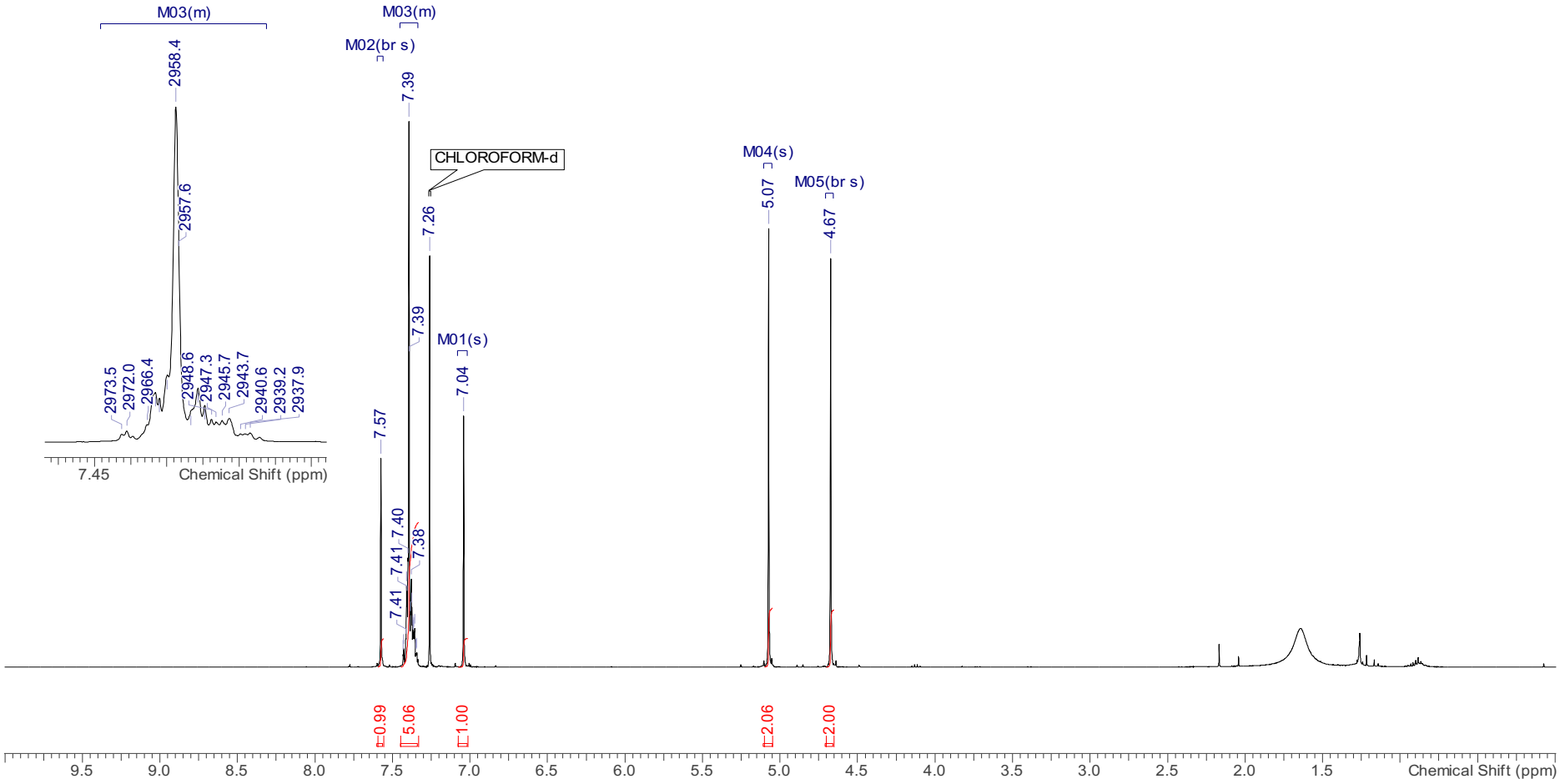


(2-(Benzyloxy)-4-chlorophenyl)methanol (34)



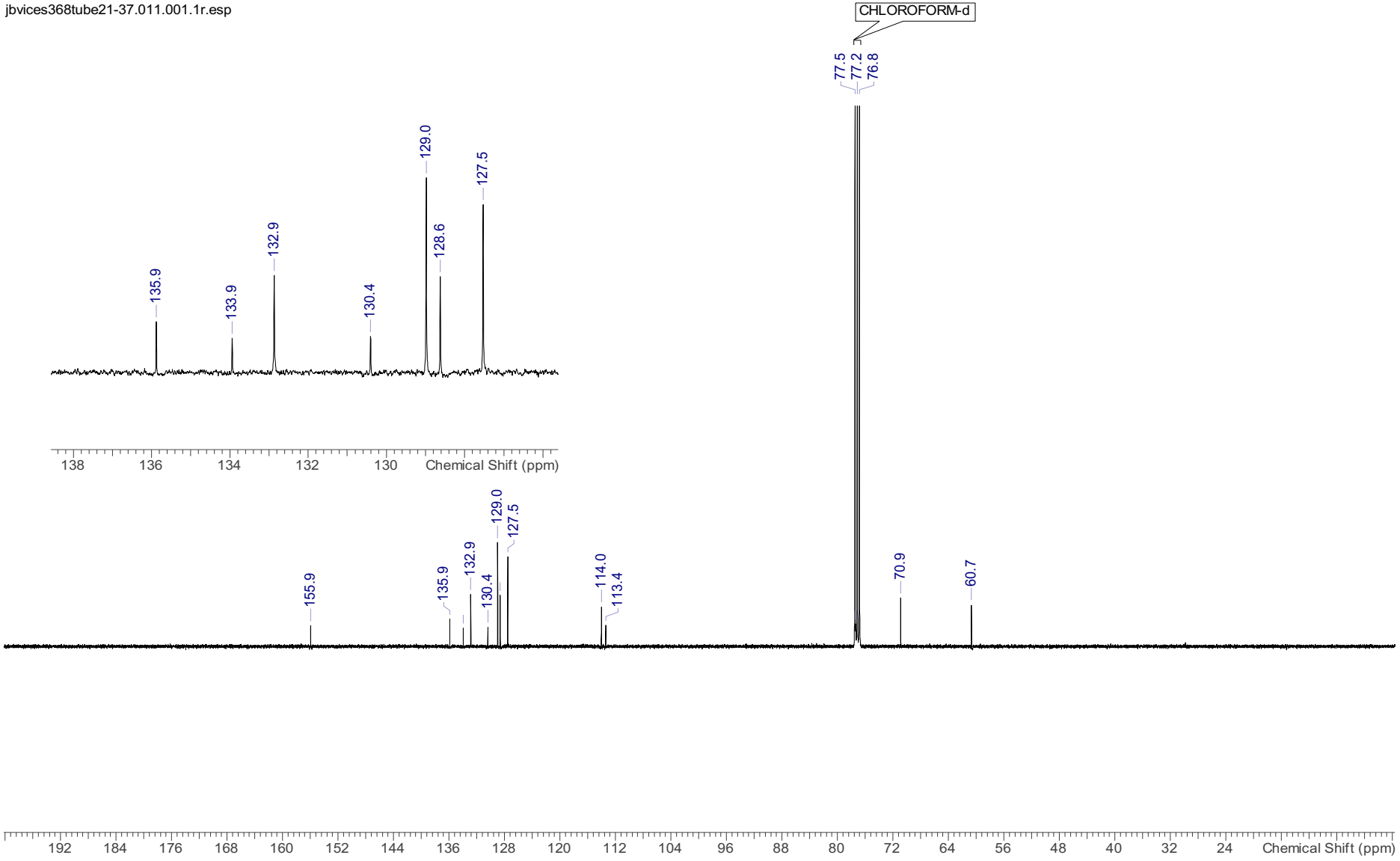
(2-(Benzyloxy)-5-bromo-4-chlorophenyl)methanol (35)

jbvices368tube21-37.010.001.1r.esp



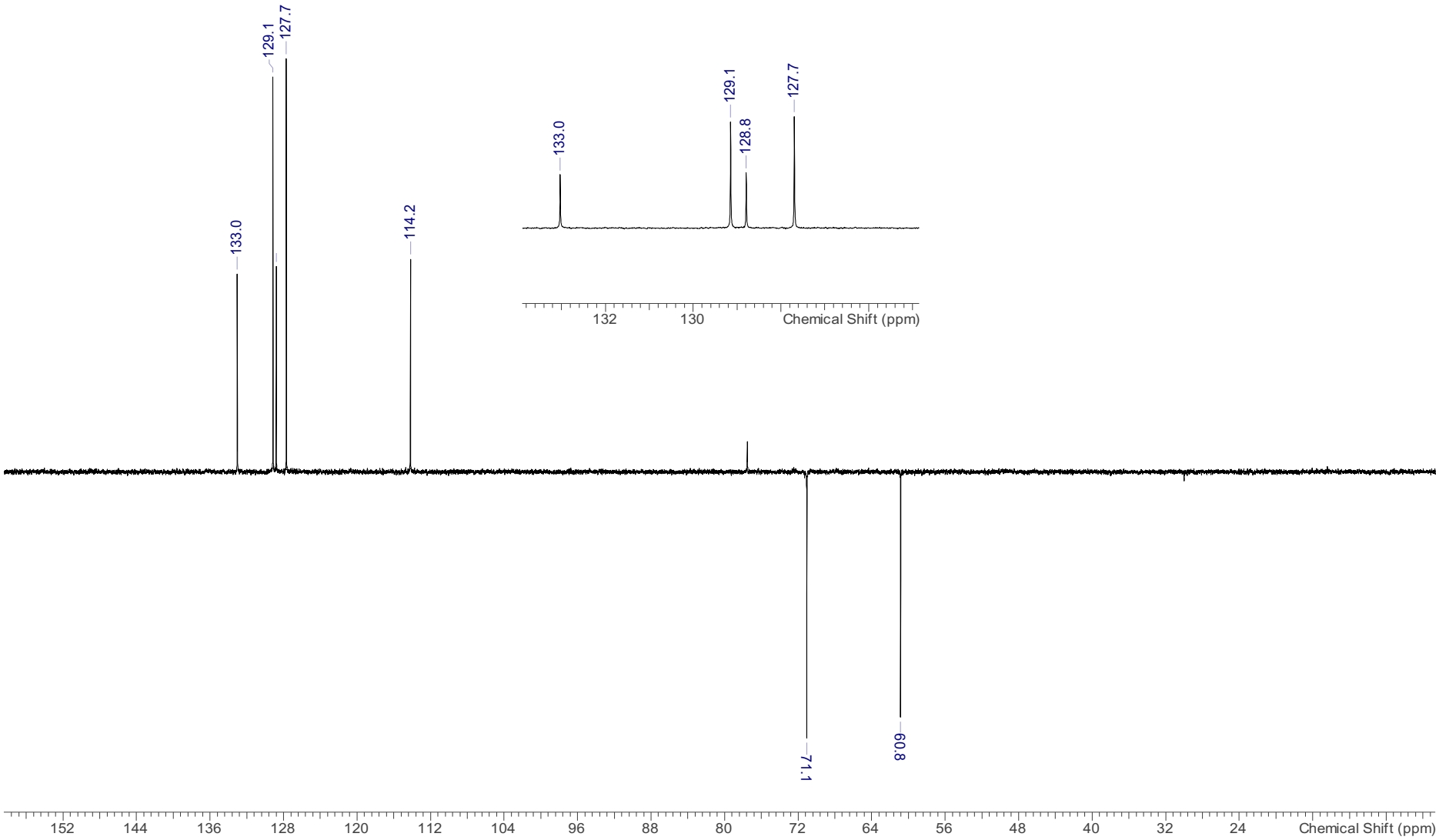
(2-(Benzyloxy)-5-bromo-4-chlorophenyl)methanol (35)

jbvices368tube21-37.011.001.1r.esp



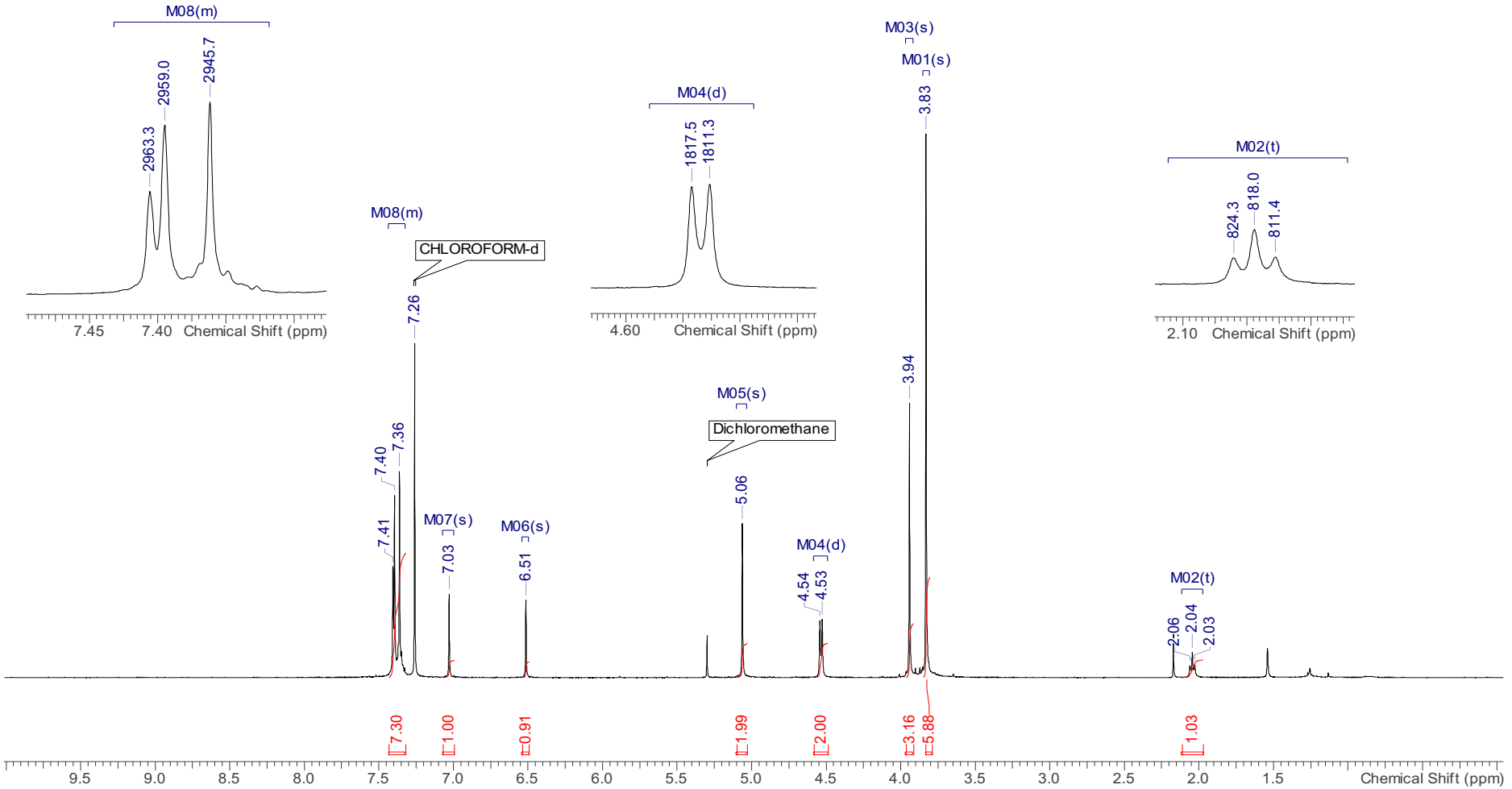
(2-(Benzyloxy)-5-bromo-4-chlorophenyl)methanol (35)

jbvices368tube21-37.012.001.1r.esp

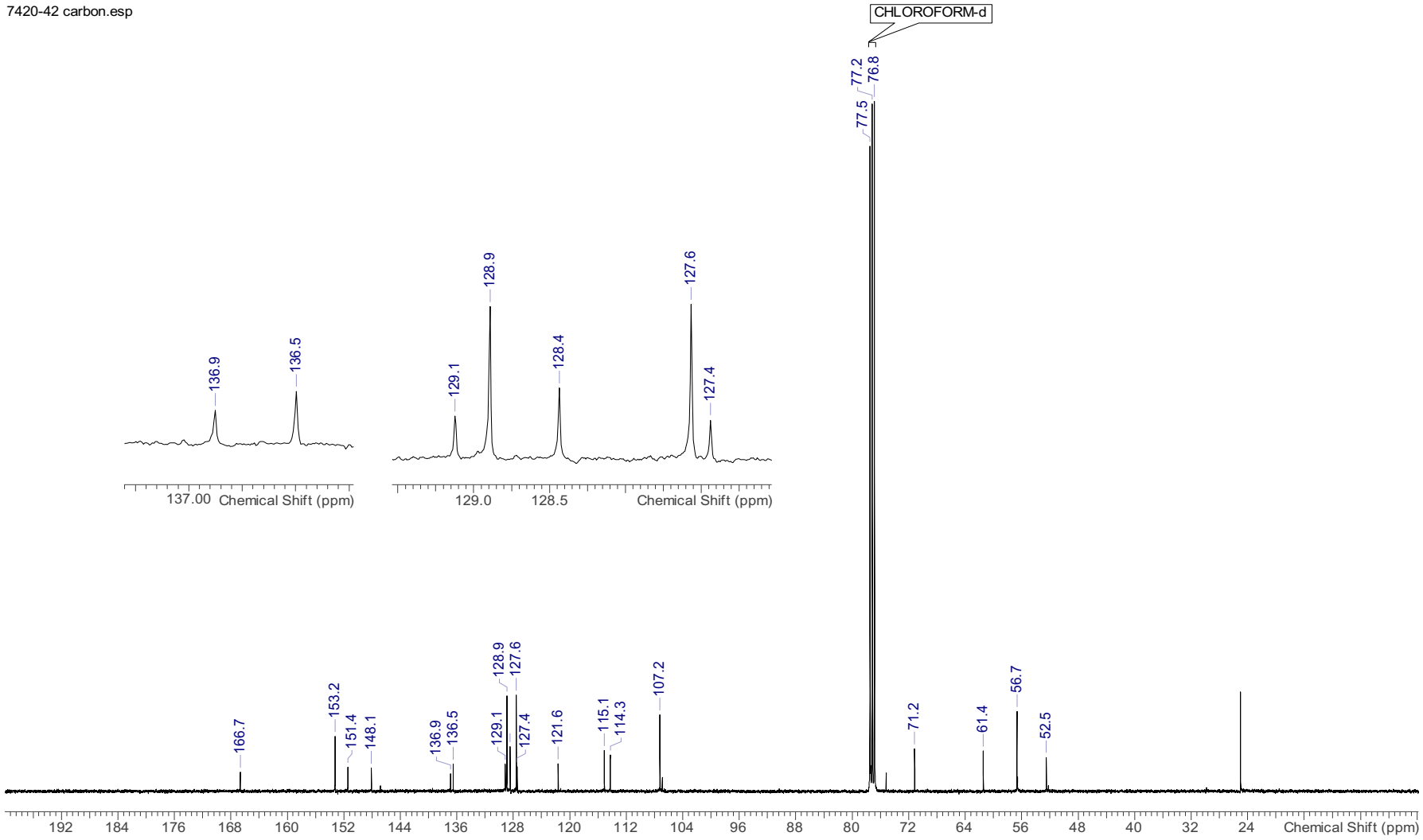


Methyl 4-(4-(benzyloxy)-2-chloro-5-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (36)

7420-42 proton.esp

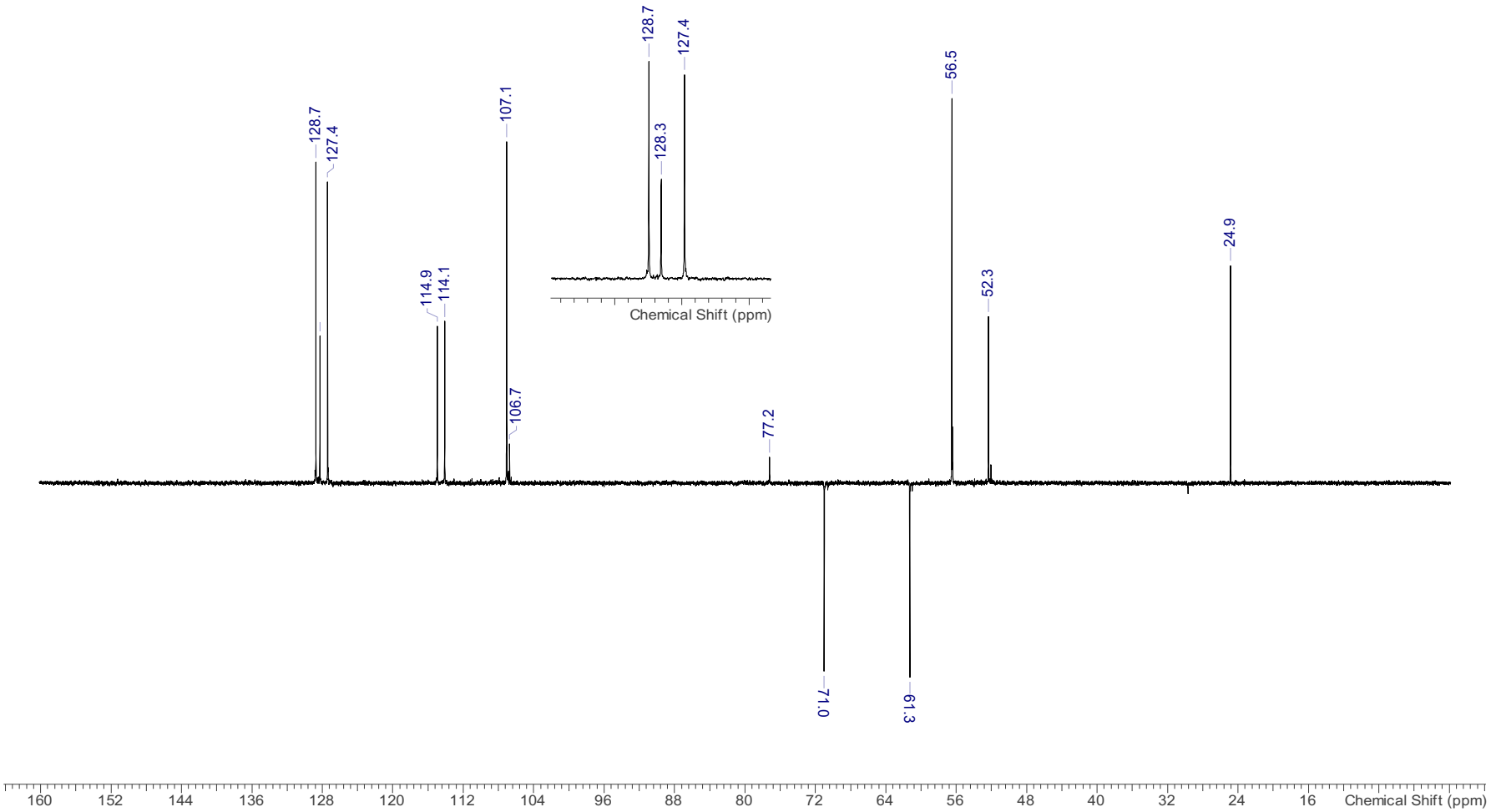


Methyl 4-(4-(benzyloxy)-2-chloro-5-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (36)

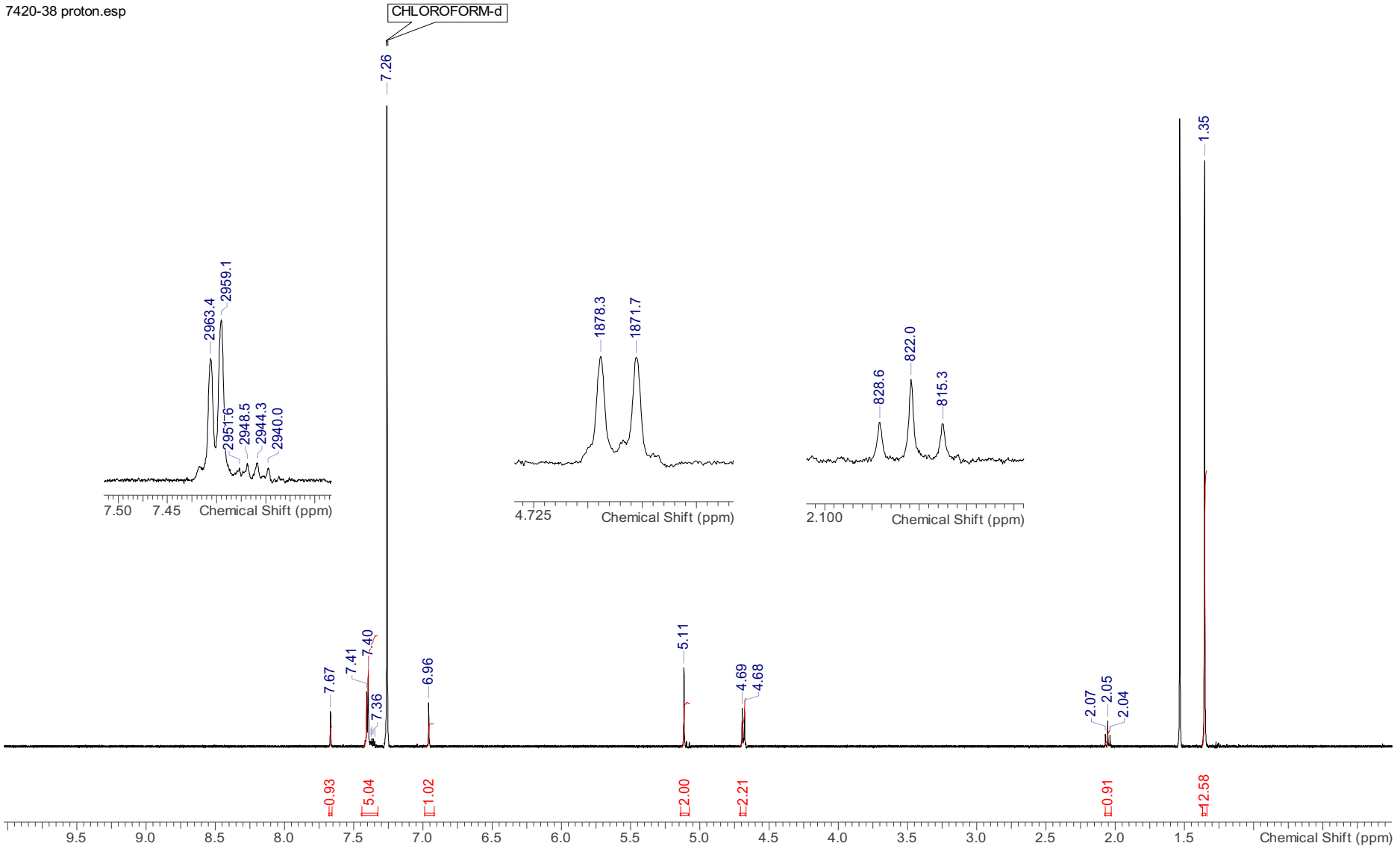


Methyl 4-(4-(benzyloxy)-2-chloro-5-(hydroxymethyl)phenoxy)-3,5-dimethoxybenzoate (36)

7420-42 dept.esp

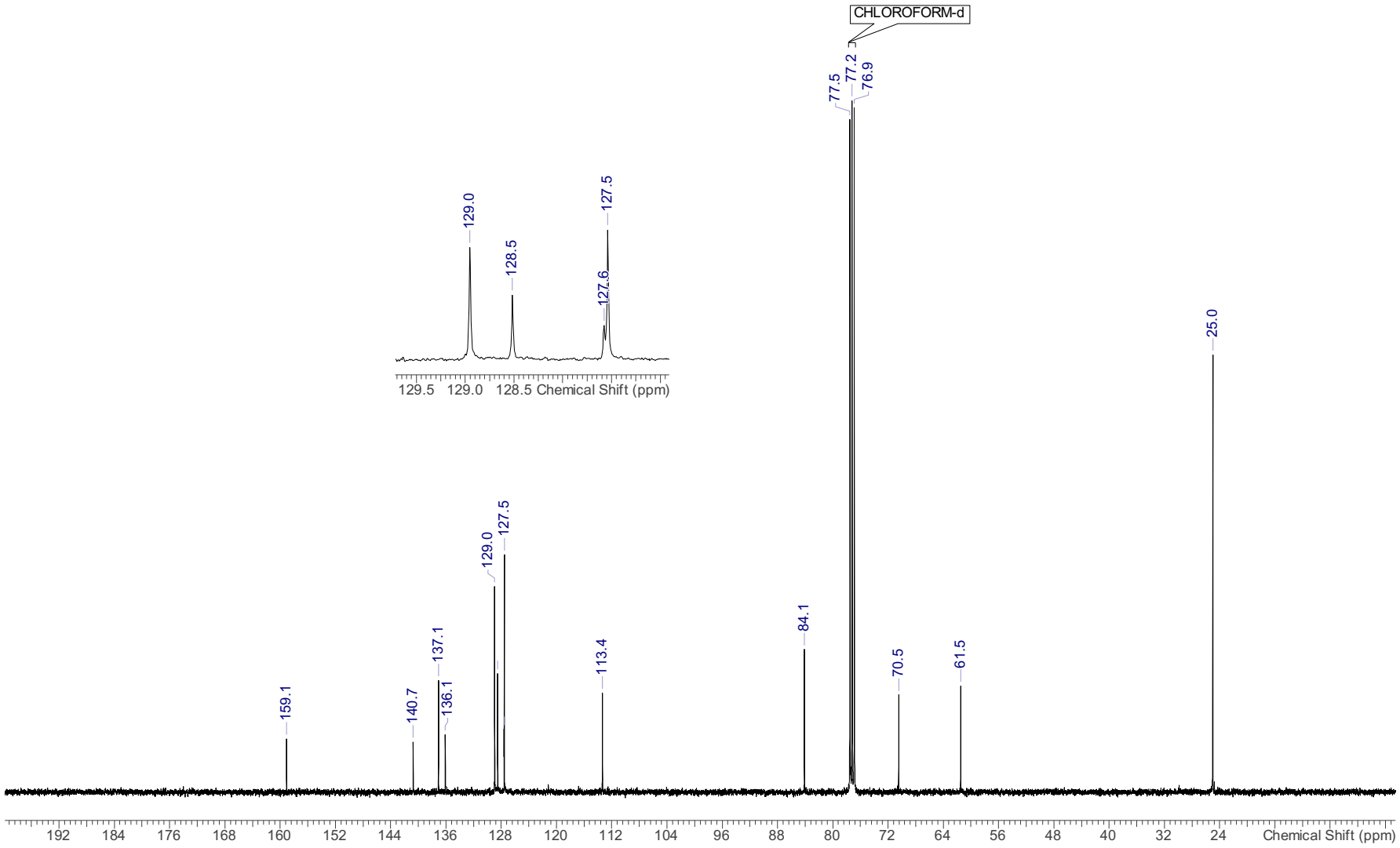


(2-(Benzyloxy)-4-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl)-methanol (37)



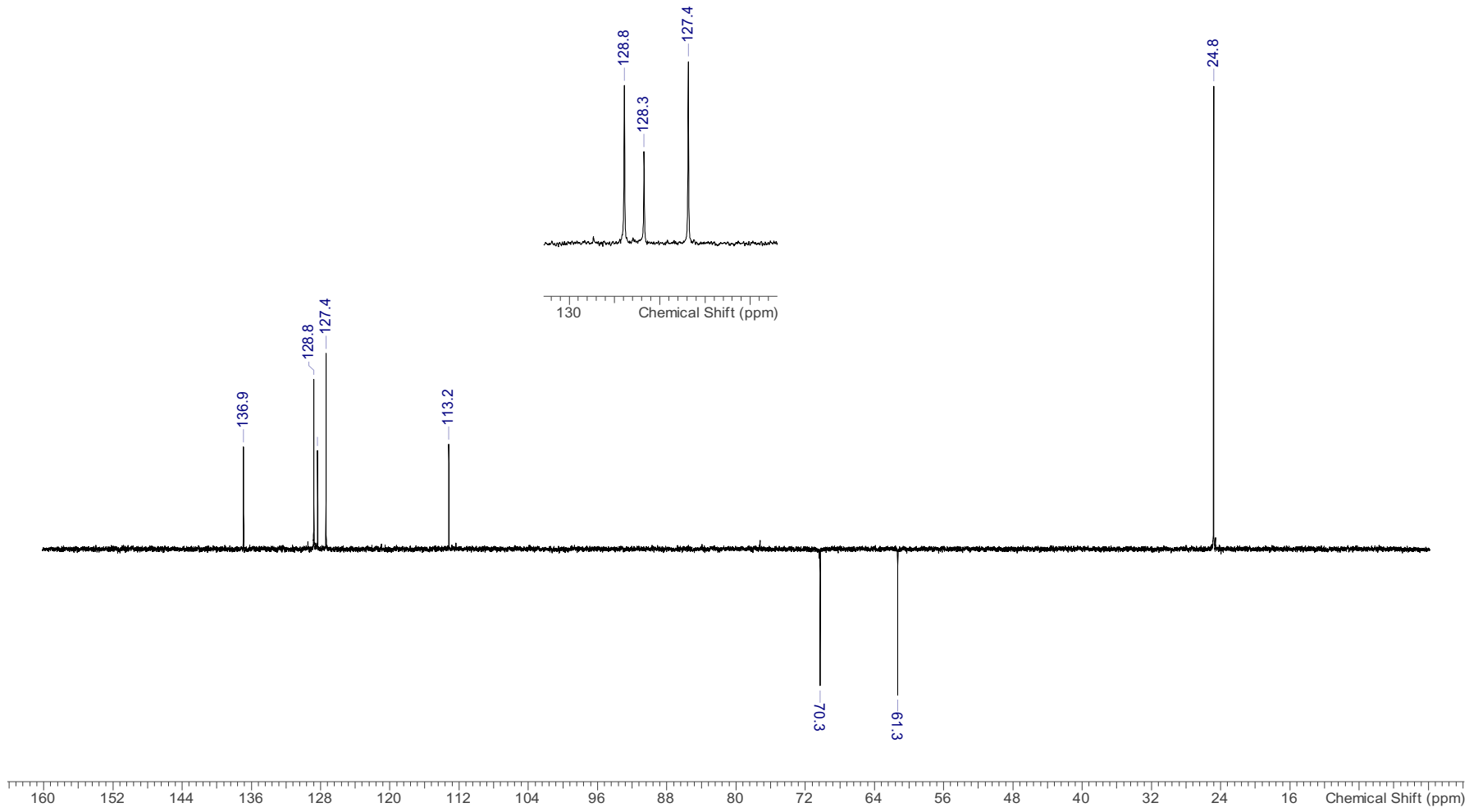
(2-(Benzyloxy)-4-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl)-methanol (37)

7420-38 carbon.esp

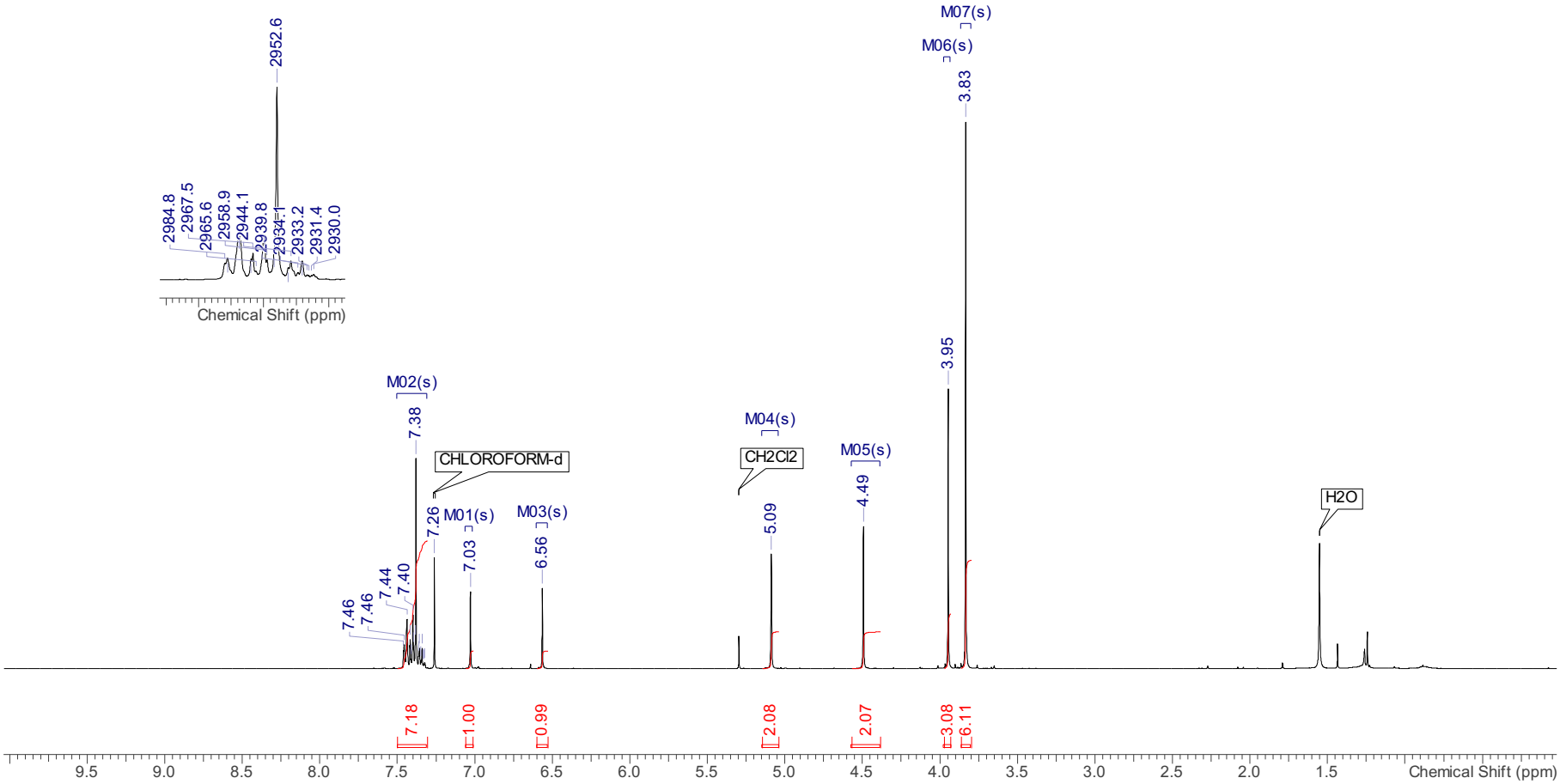


(2-(Benzyloxy)-4-chloro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl)-methanol (37)

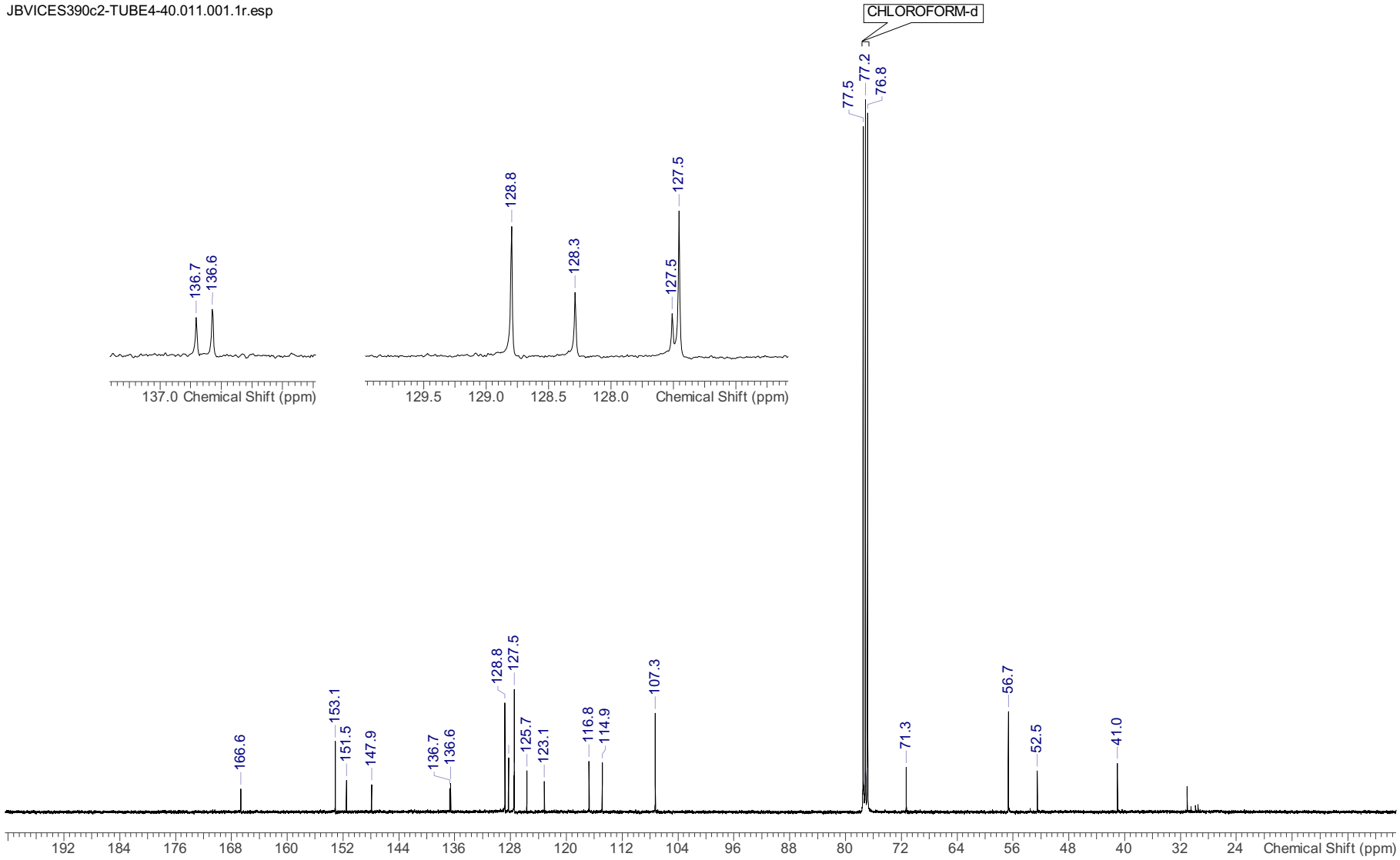
7420-38 dept.esp



Methyl 4-(4-(benzyloxy)-2-chloro-5-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (38)

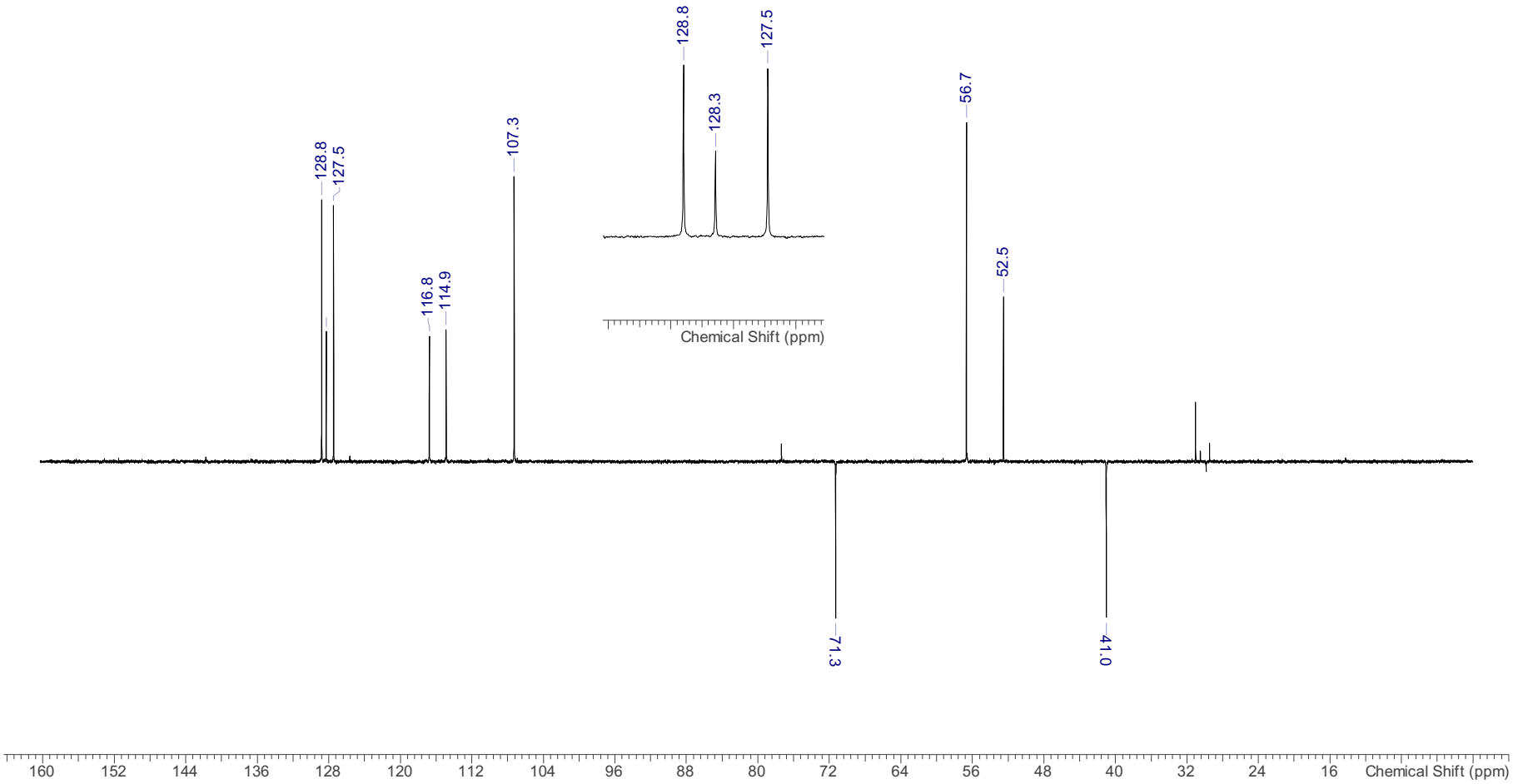


Methyl 4-(4-(benzyloxy)-2-chloro-5-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (38)



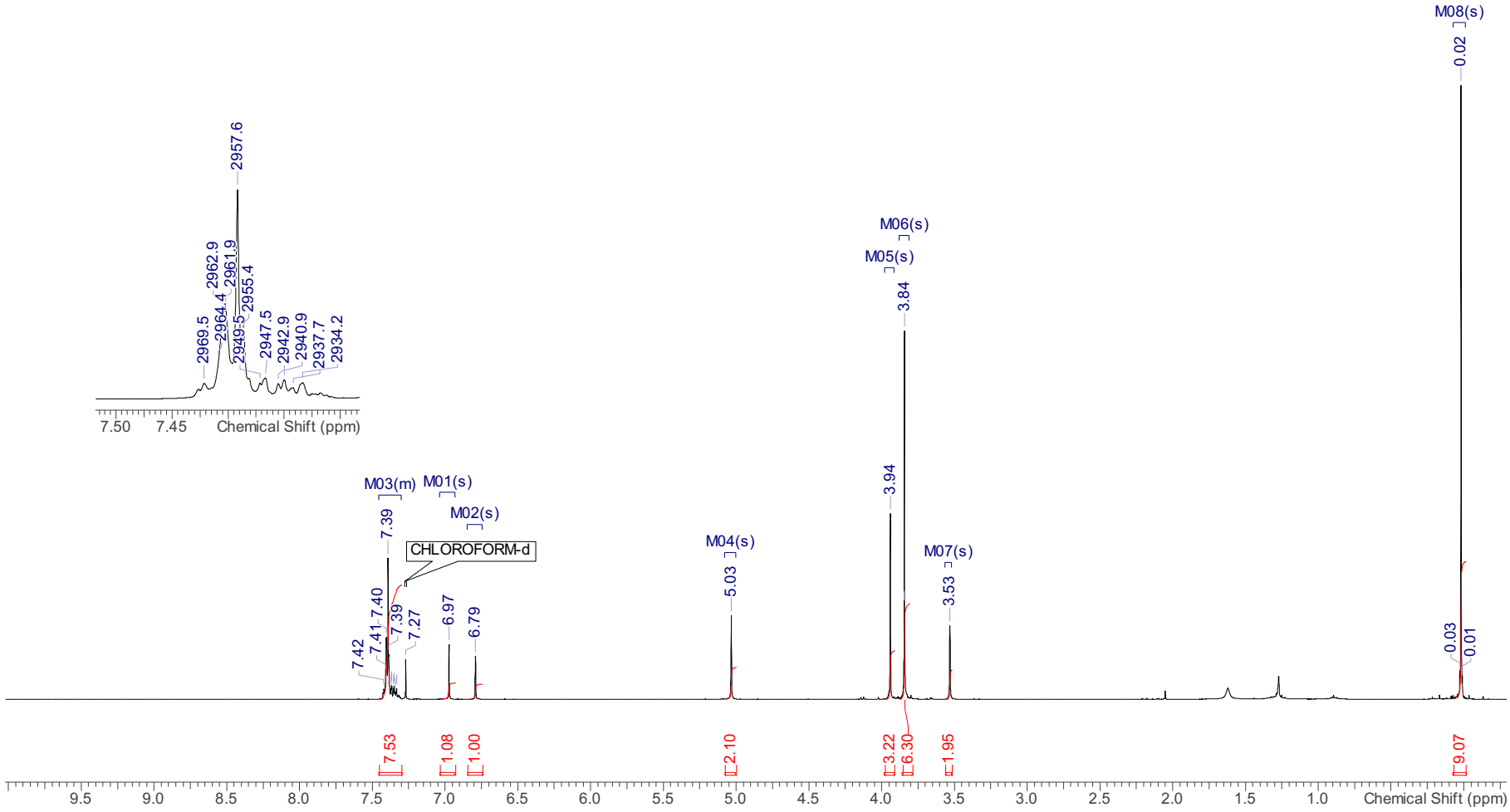
Methyl 4-(4-(benzyloxy)-2-chloro-5-(chloromethyl)phenoxy)-3,5-dimethoxybenzoate (38)

JBVICES390c2-TUBE4-40.012.001.1r.esp



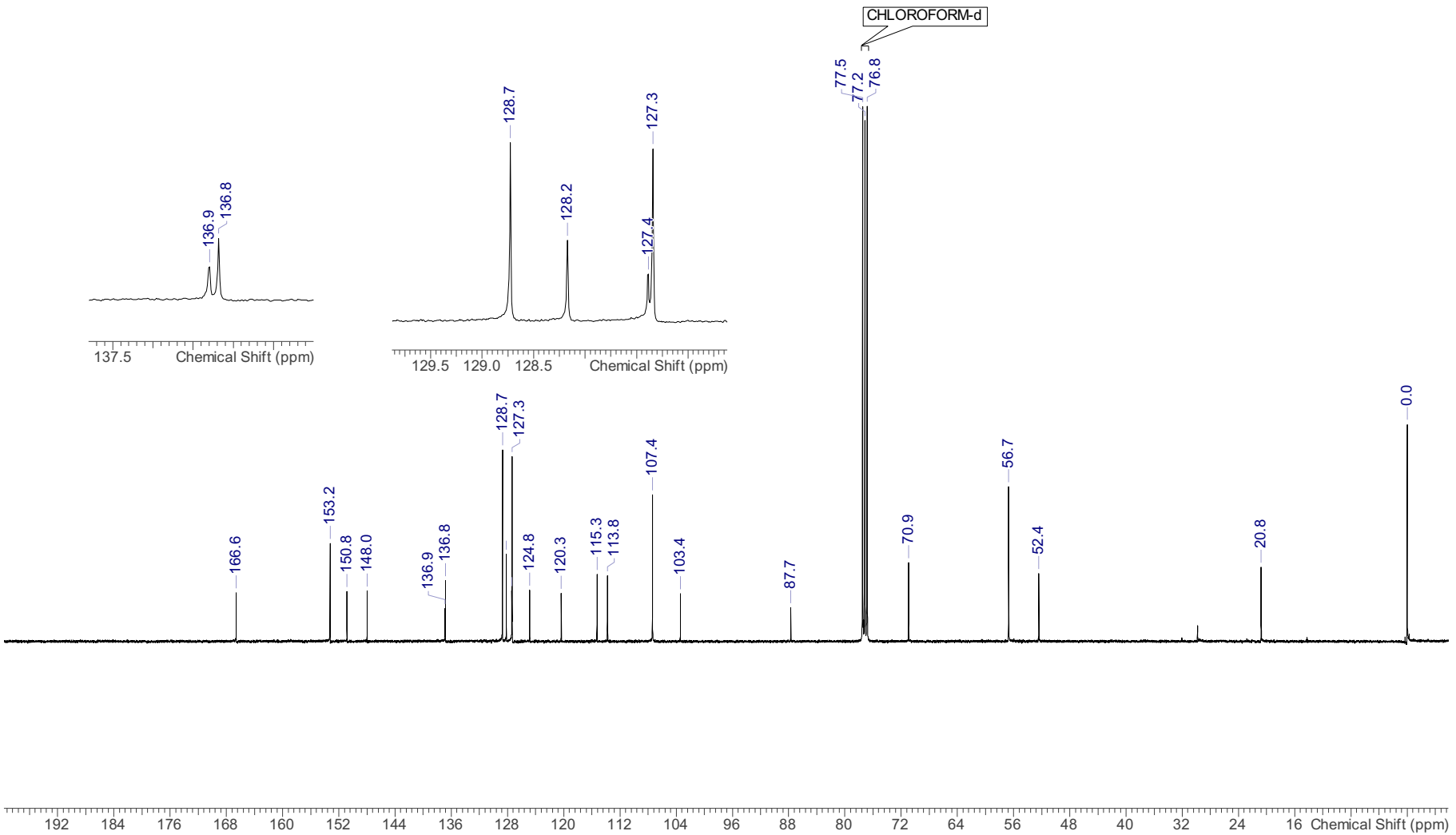
Methyl 4-(4-(benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (39)

jbvices429C2tube10to18.013.001.1r.esp



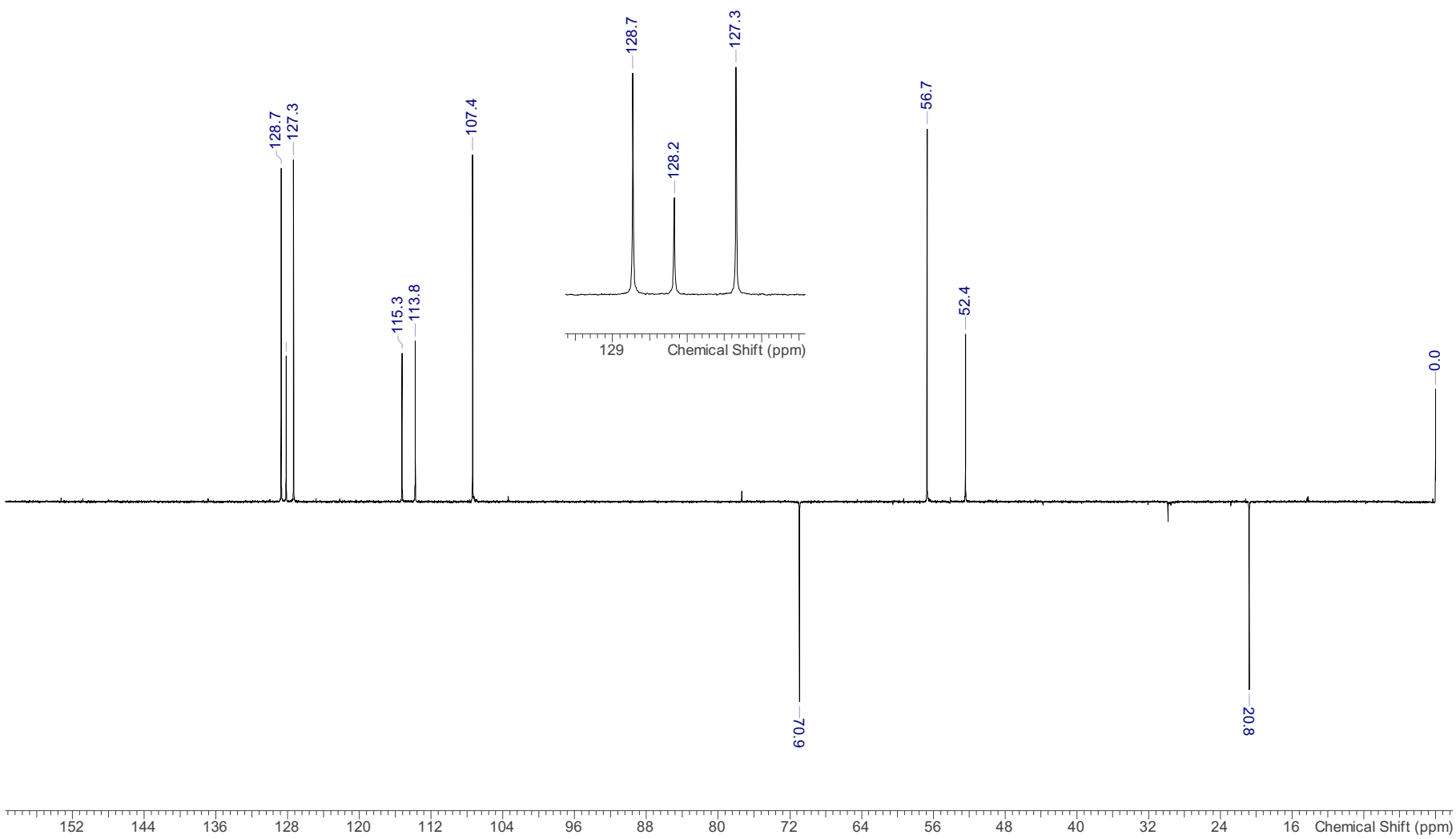
Methyl 4-(4-(benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (39)

jbvices429C2tube10to18.011.001.1r.esp

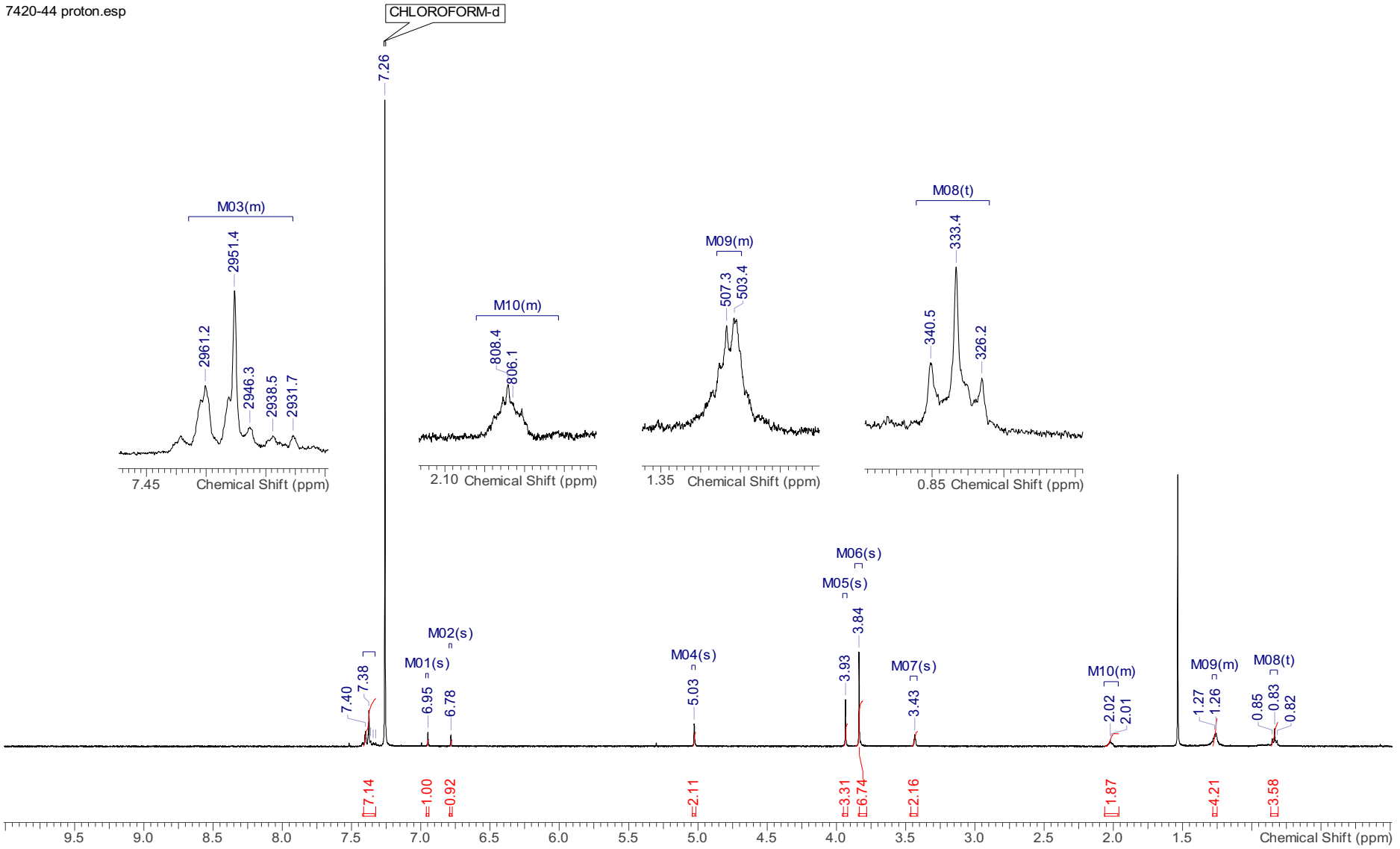


Methyl 4-(4-(benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (39)

jbvices429C2tube10to18.012.001.1r.esp

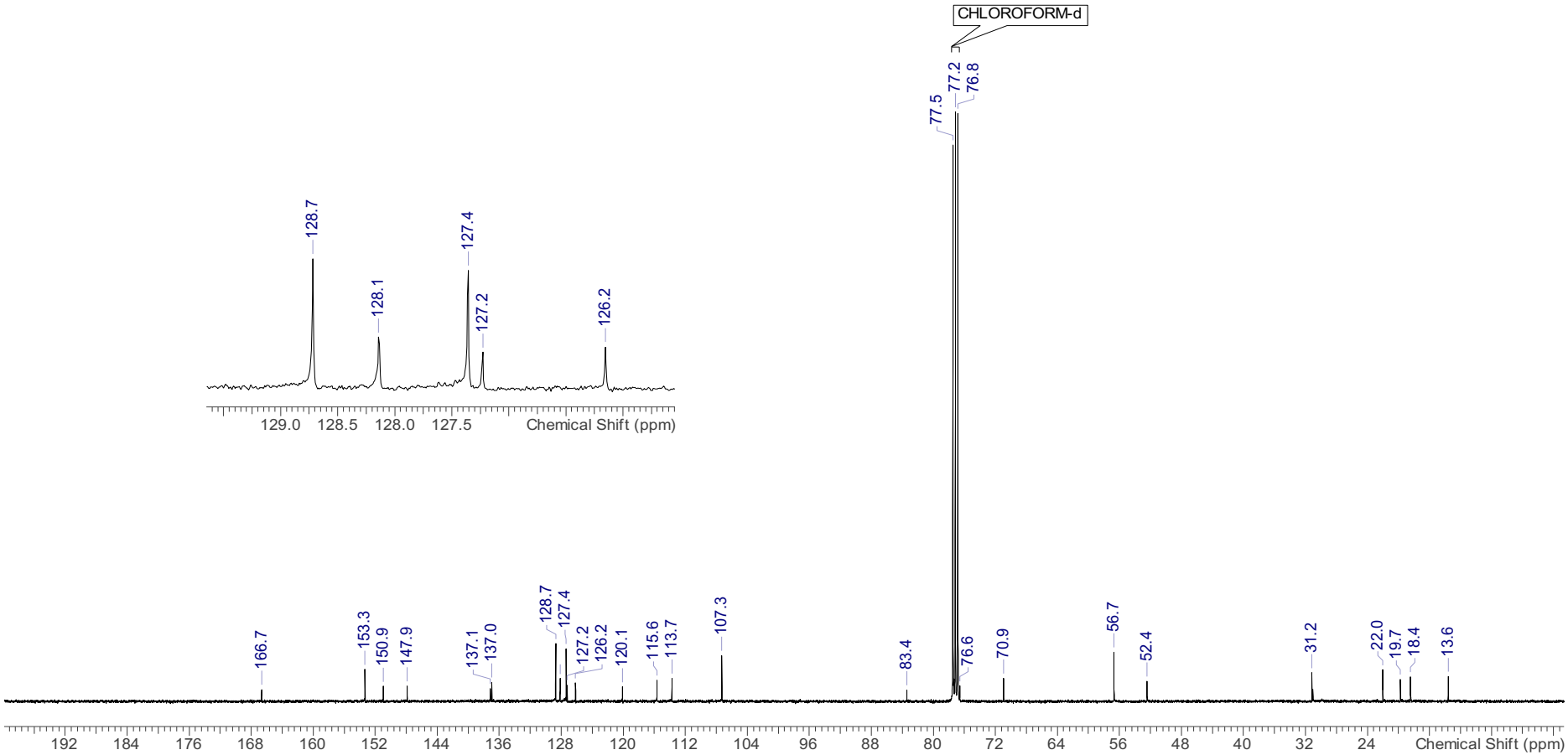


Methyl 4-(4-(benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (40)



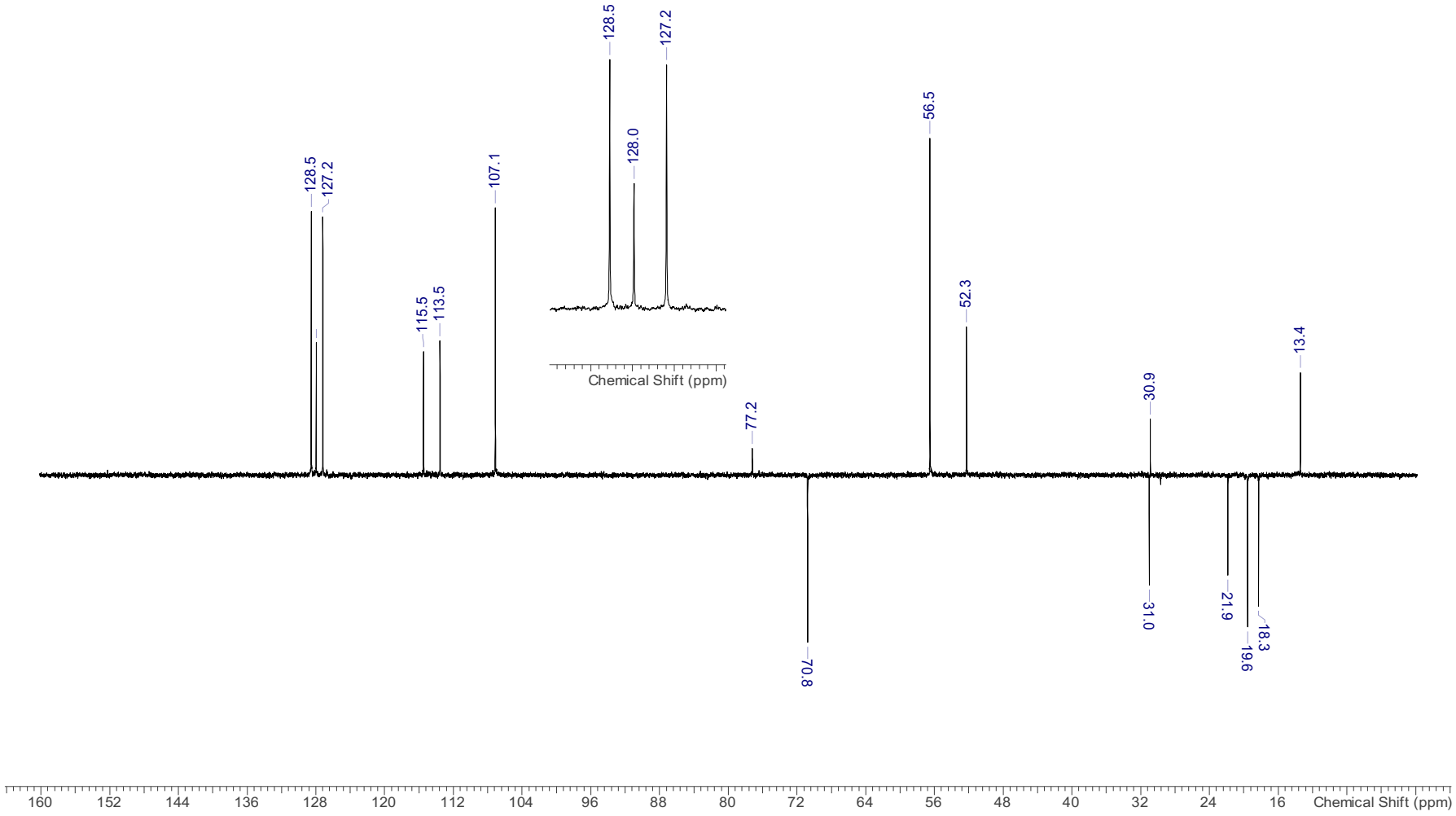
Methyl 4-(4-(benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (40)

7420-44 carbon.esp



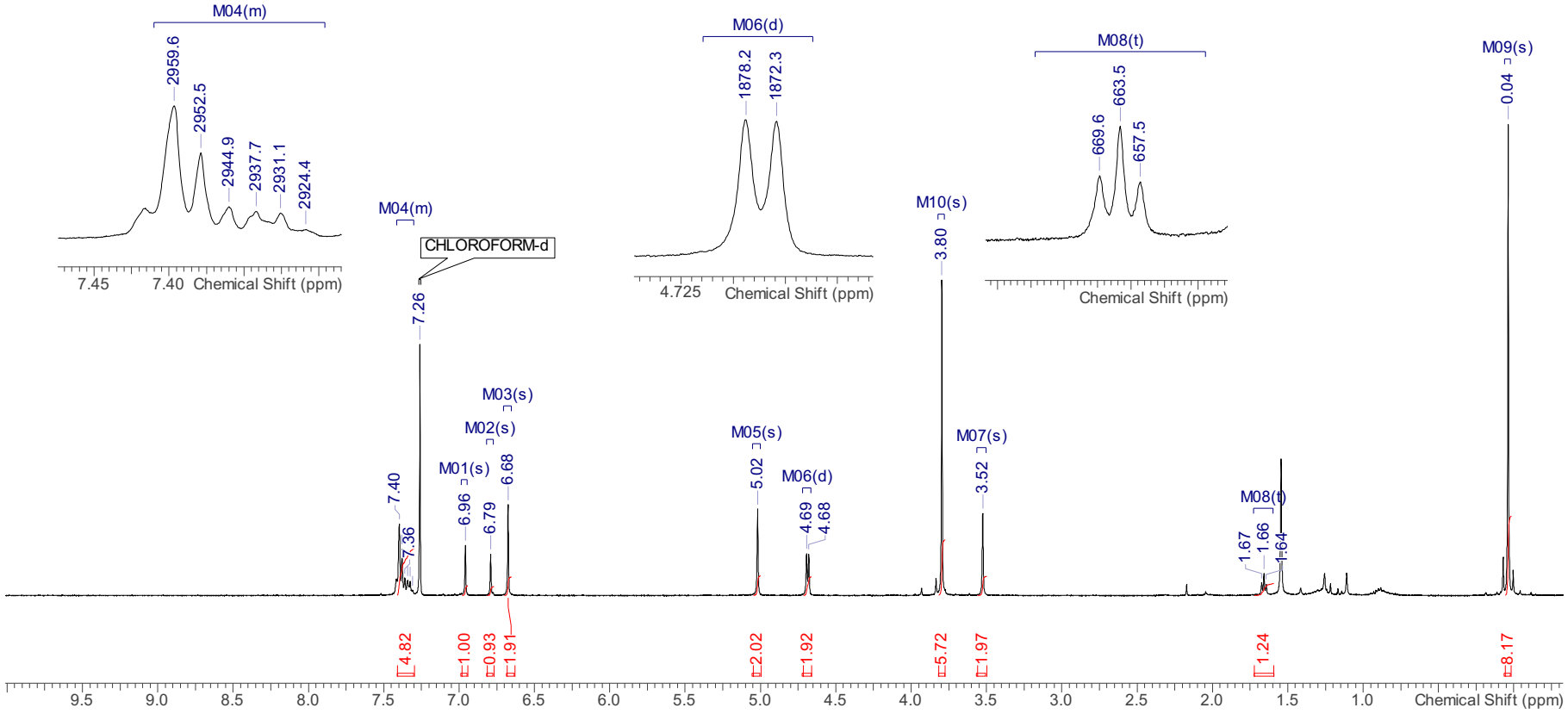
Methyl 4-(4-(benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxybenzoate (40)

7420-44 dept.esp

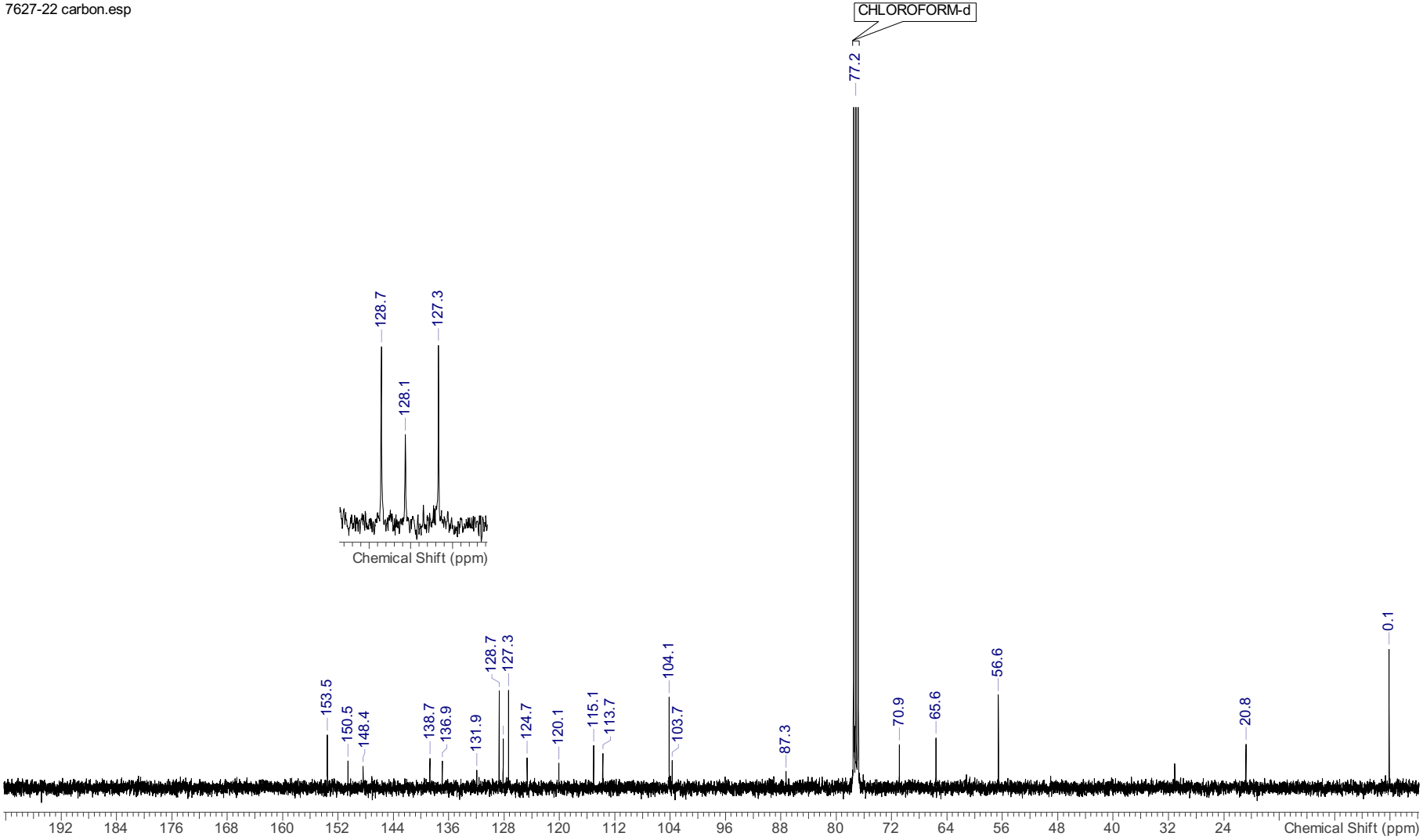


(4-(4-(Benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (41)

7627-22 proton.esp

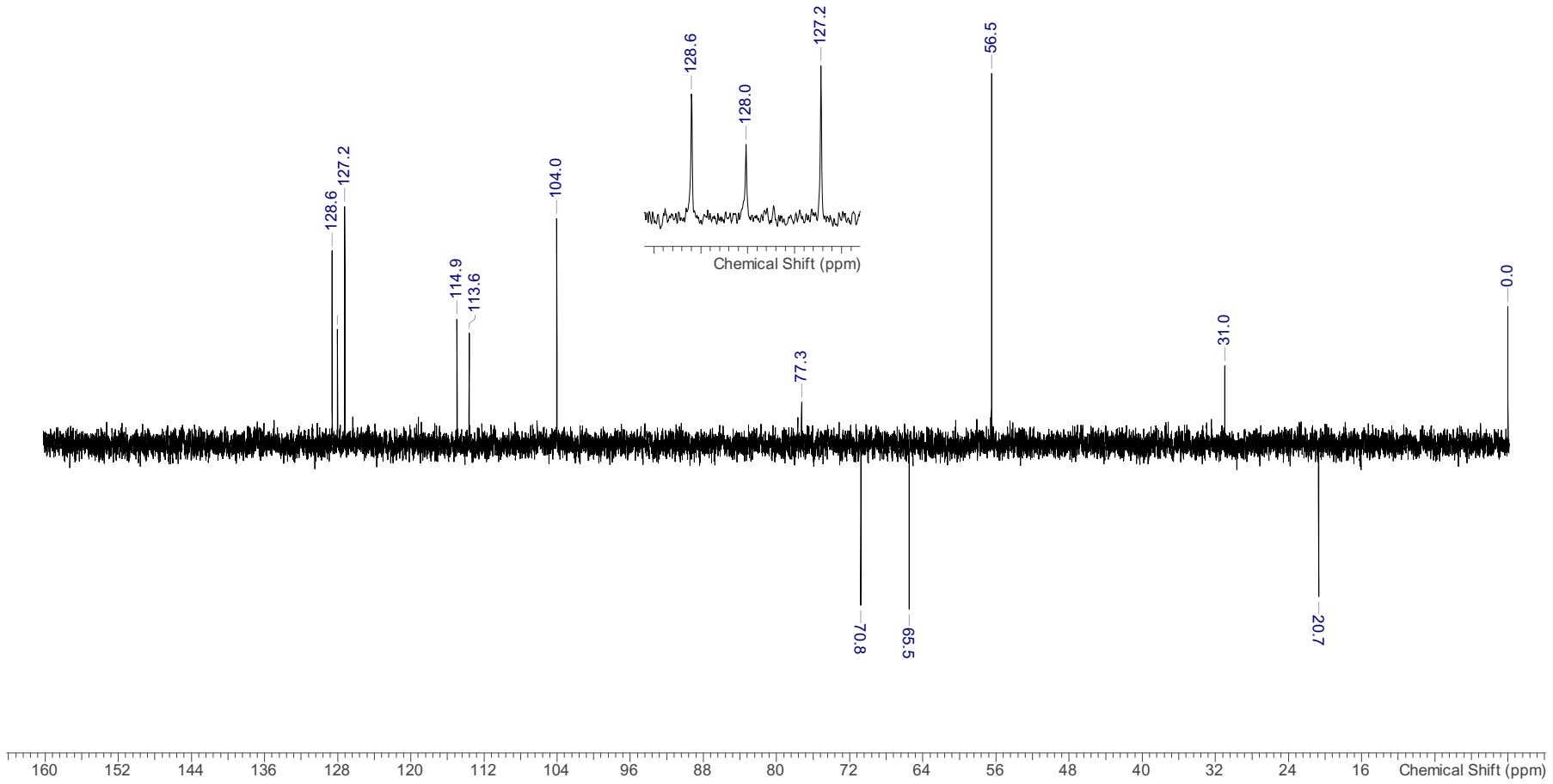


(4-(4-(Benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (41)



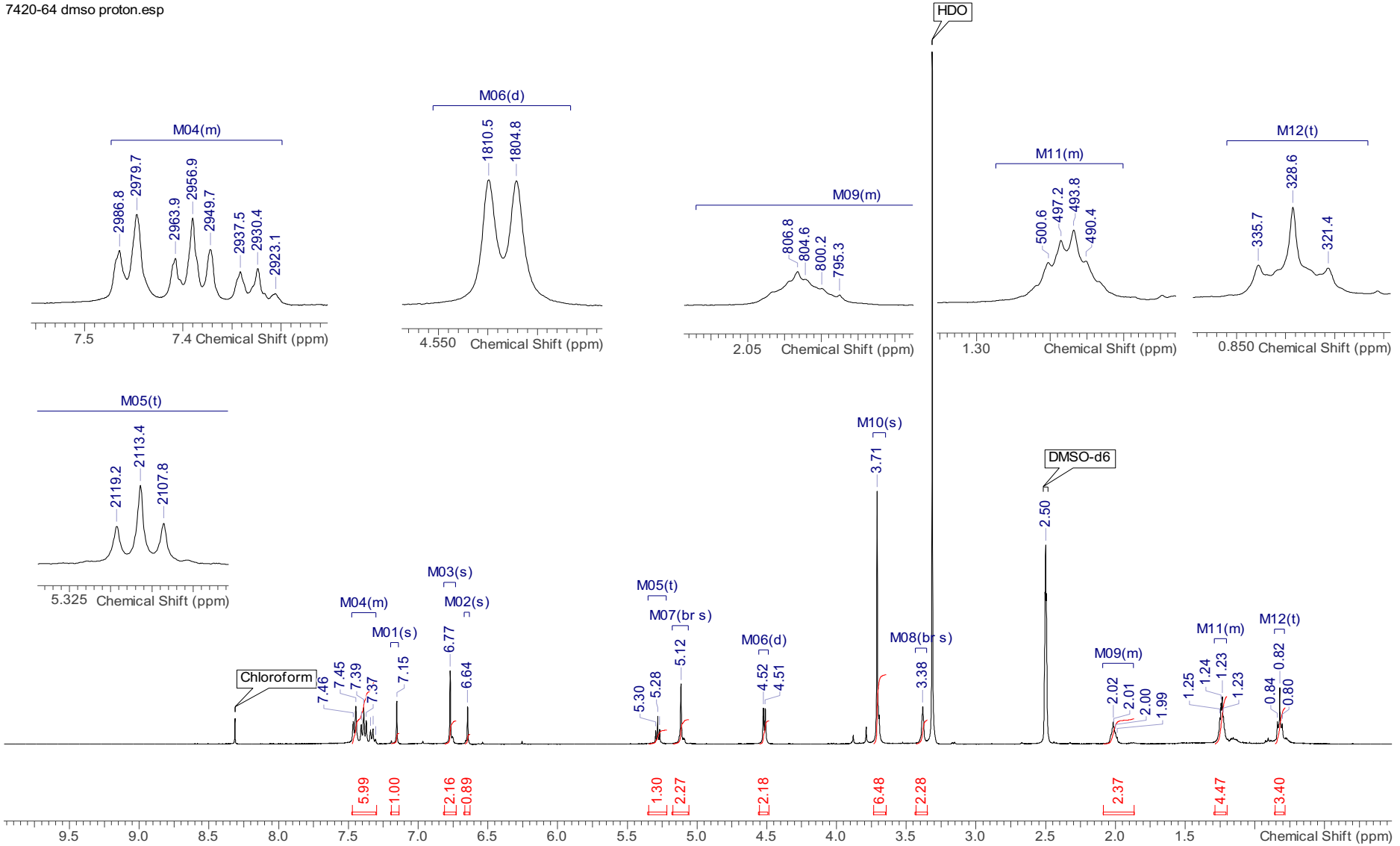
(4-(4-(Benzyloxy)-2-chloro-5-(3-(trimethylsilyl)prop-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (41)

7627-22 dept.esp



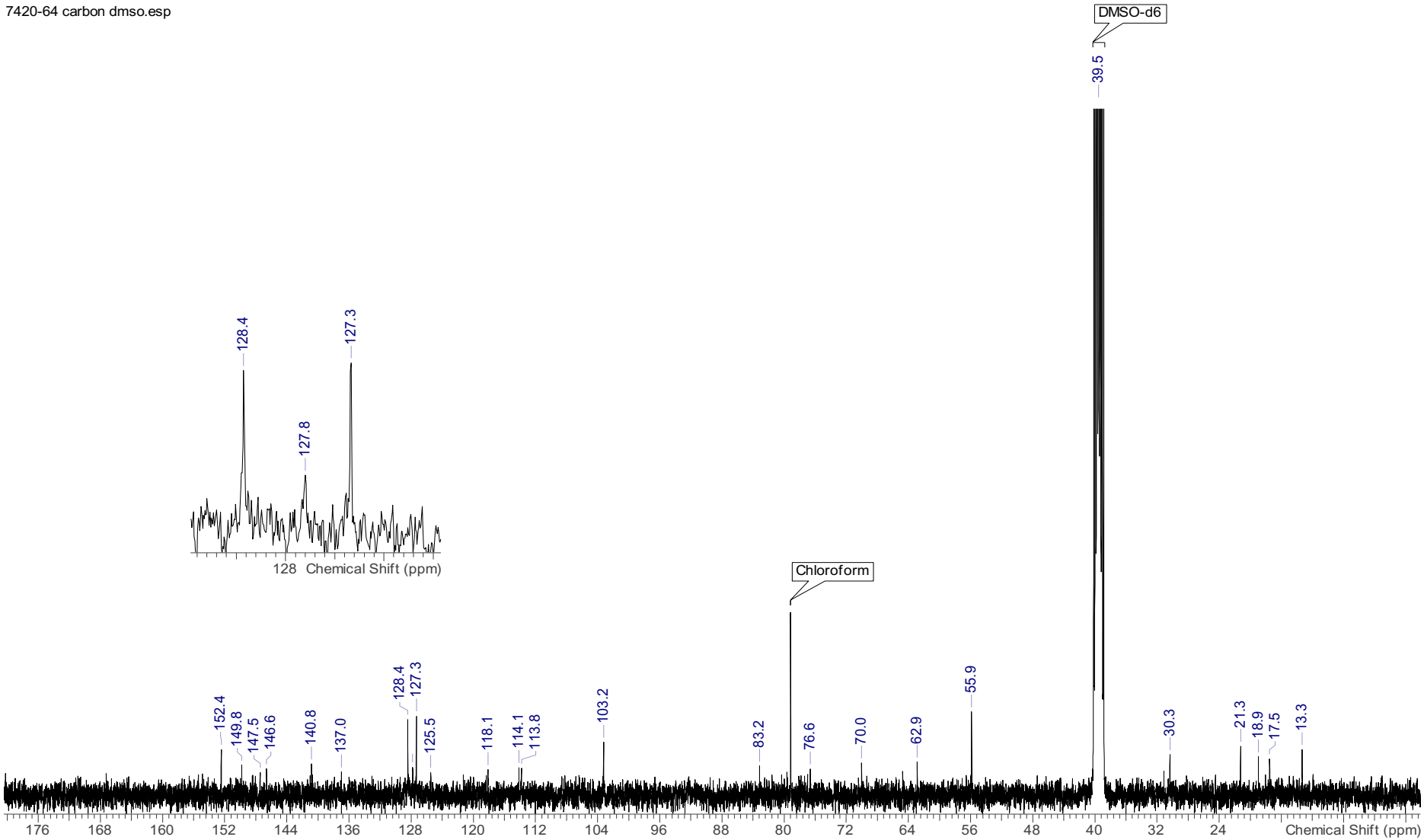
(4-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (42)

7420-64 dmso proton.esp



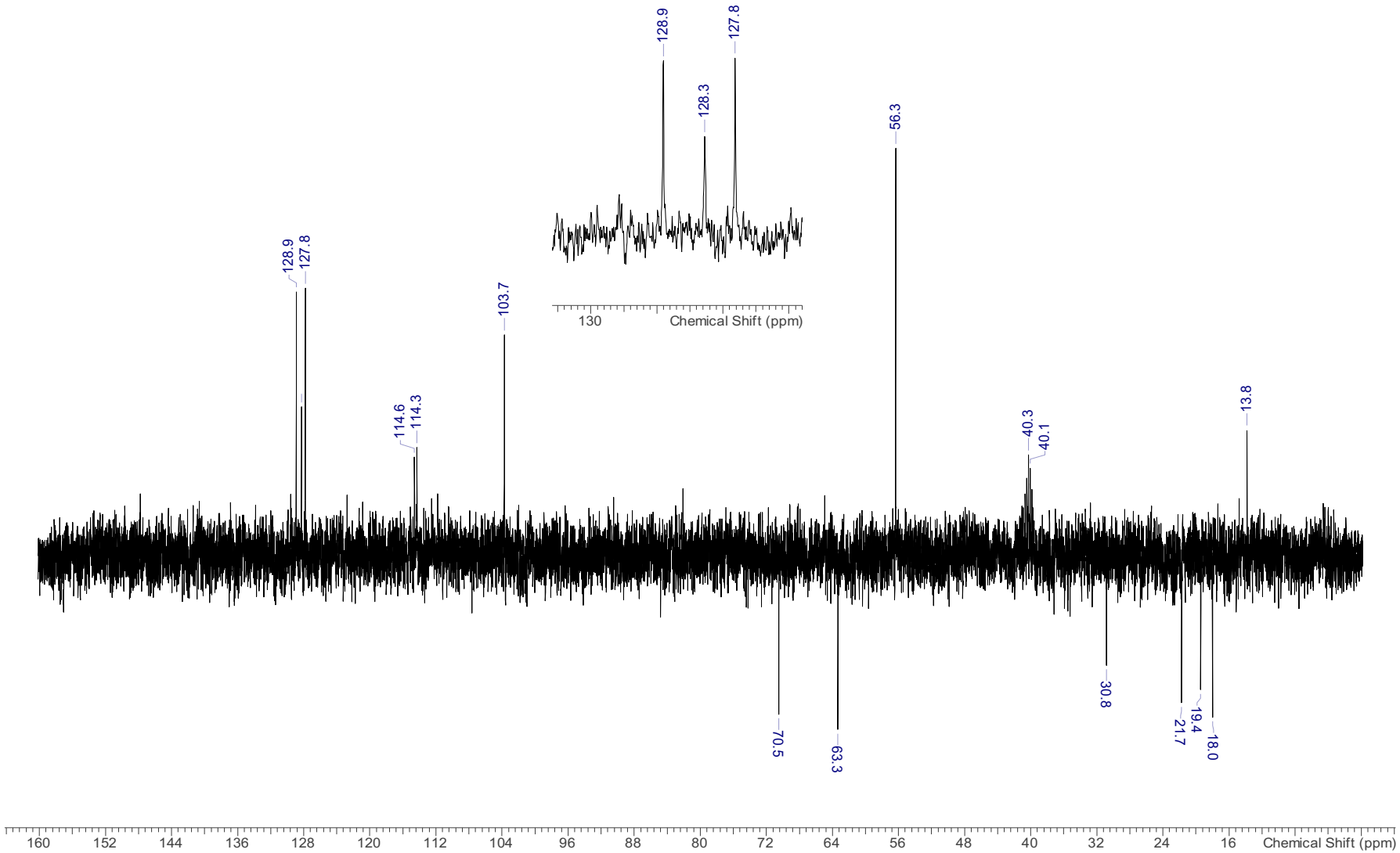
(4-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (42)

7420-64 carbon dmso.esp



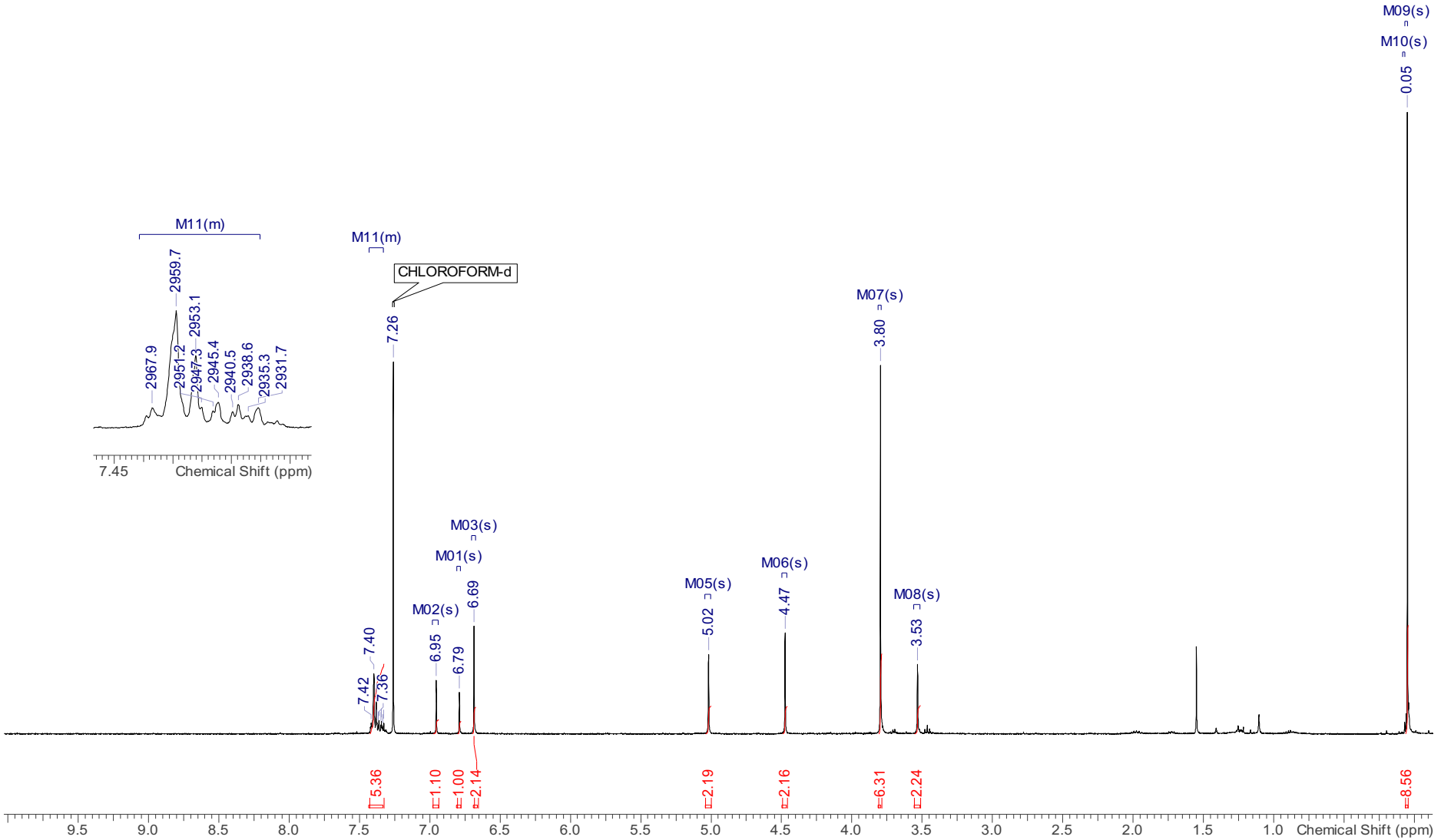
(4-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-3,5-dimethoxyphenyl)methanol (42)

7420-64 dmso dept.esp

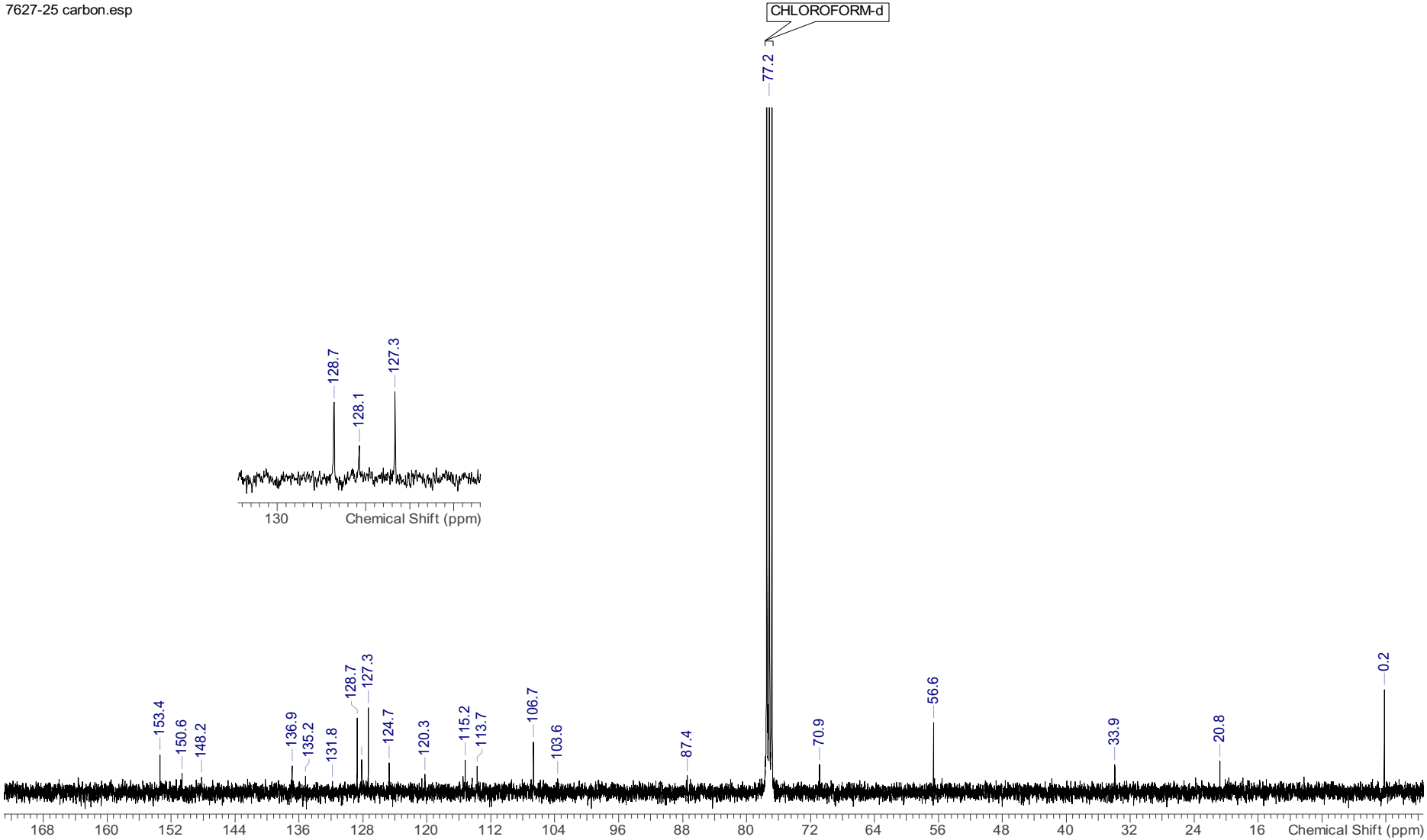


(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)-4-chlorophenyl)prop-1-yn-1-yl)trimethylsilane (43)

7627-25 proton.esp

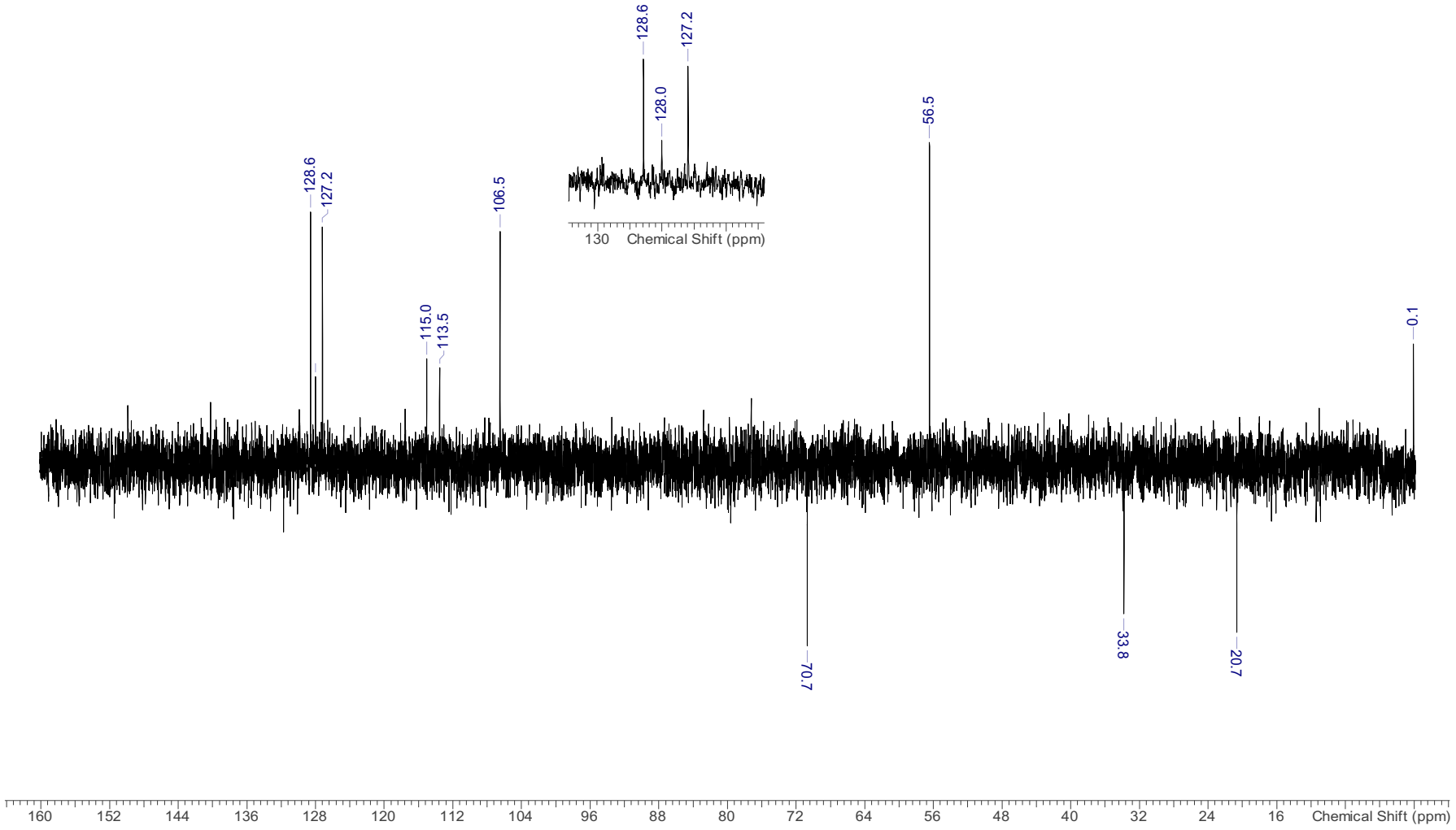


(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)-4-chlorophenyl)prop-1-yn-1-yl)trimethylsilane (43)



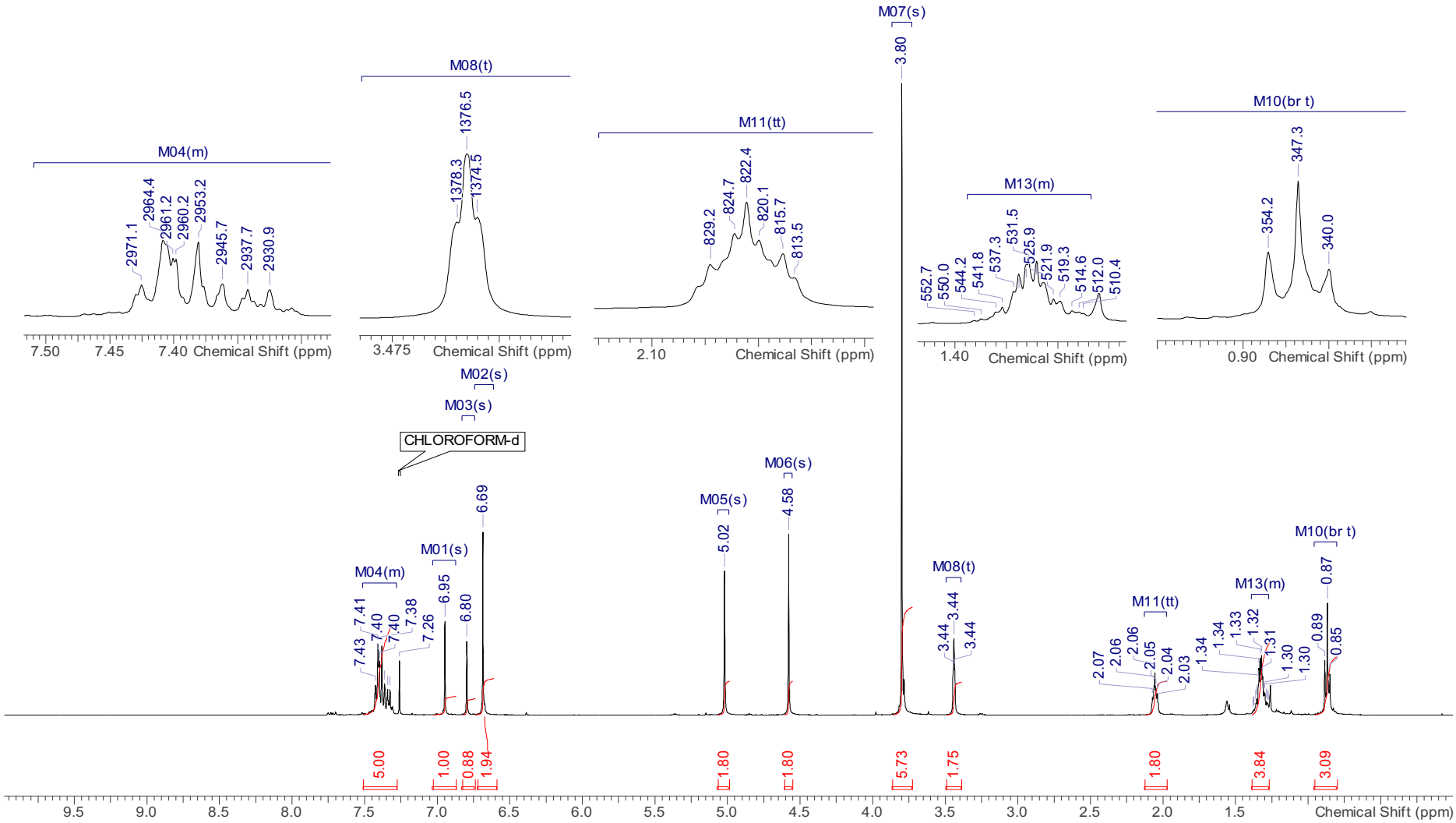
(3-(2-(Benzyloxy)-5-(4-(bromomethyl)-2,6-dimethoxyphenoxy)-4-chlorophenyl)prop-1-yn-1-yl)trimethylsilane (43)

7627-25 dept.esp



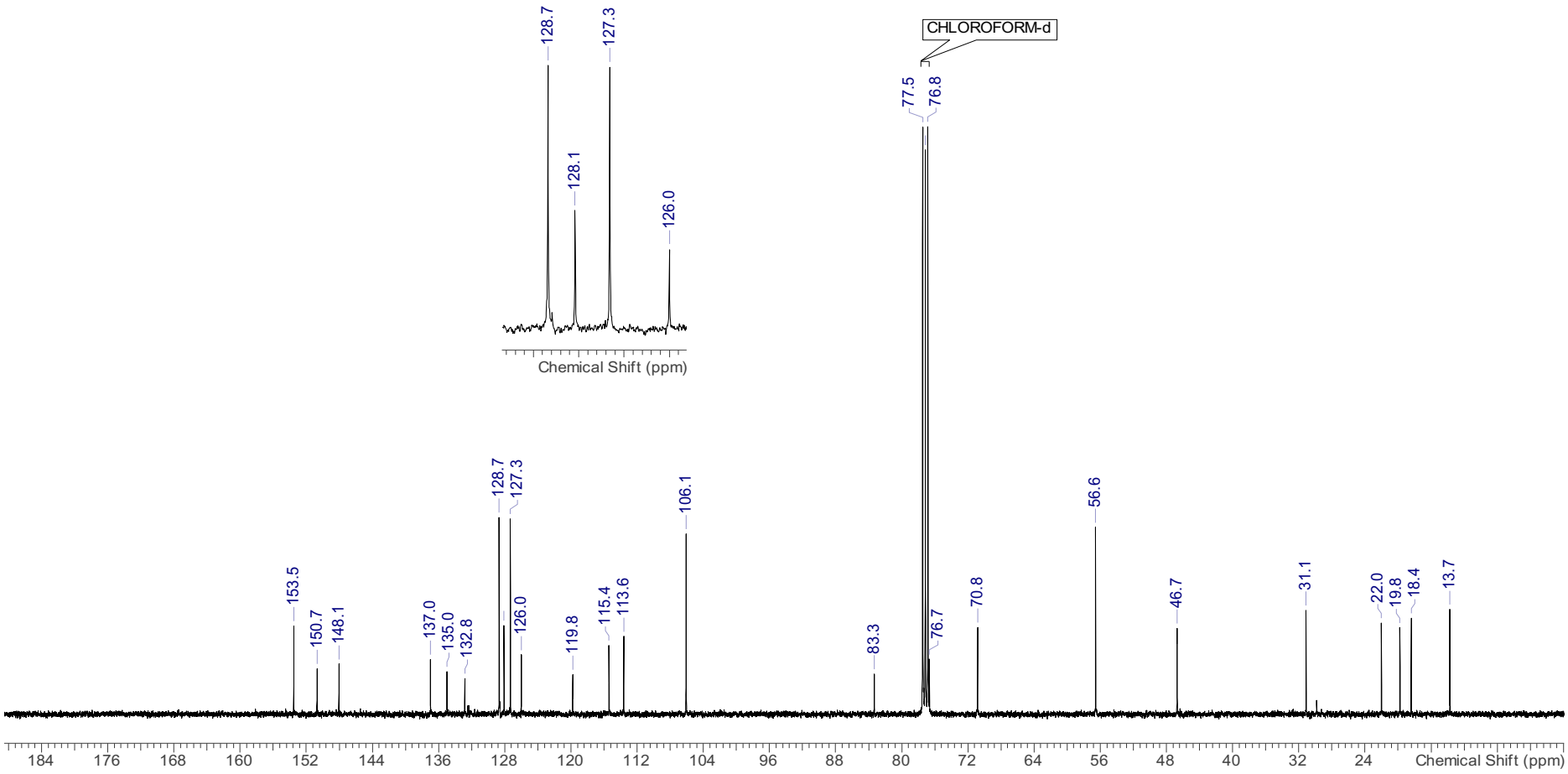
2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (44)

7420-65 proton cdl3.esp



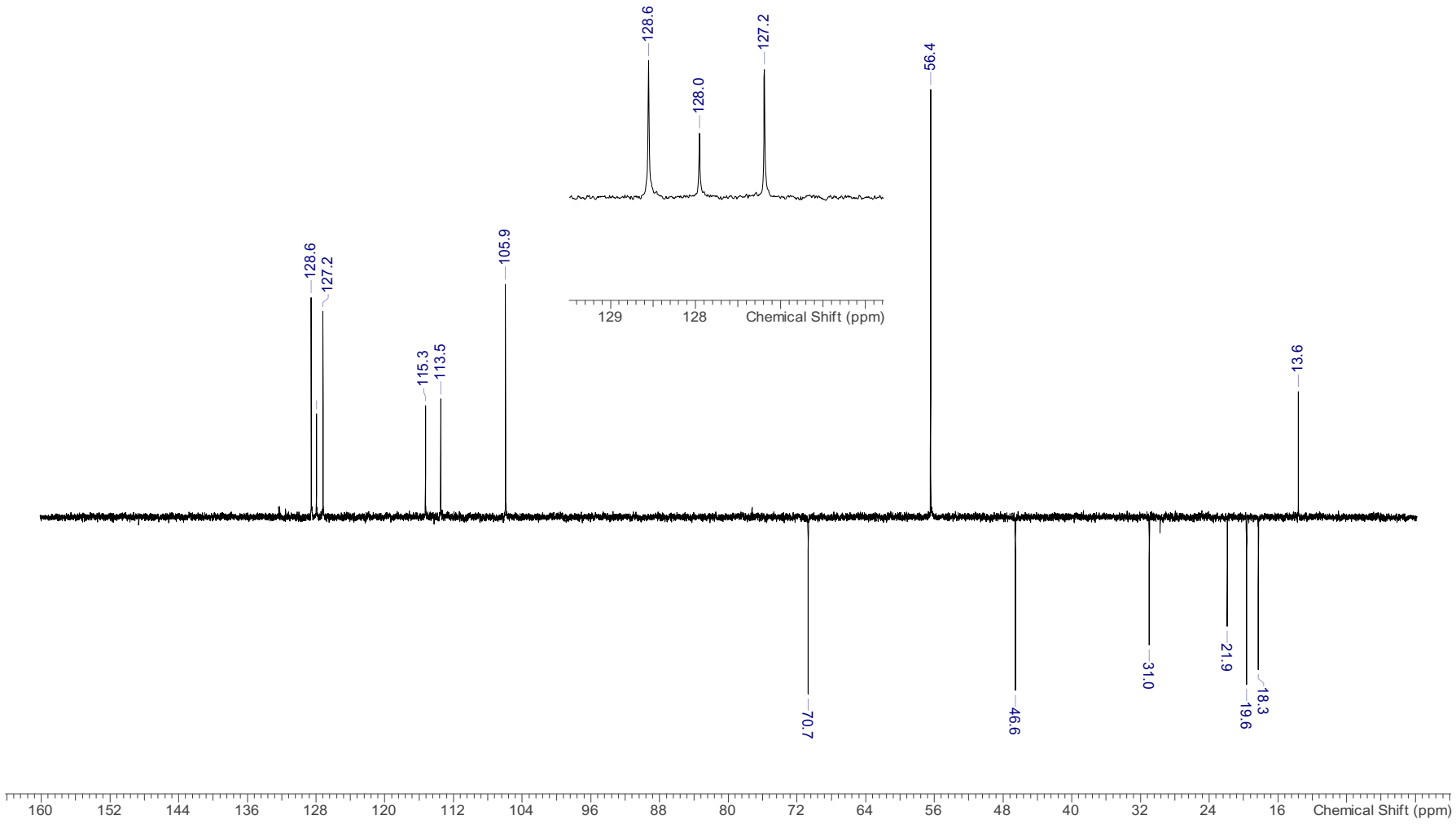
2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (44)

7420-65 carbon cdl3 .esp



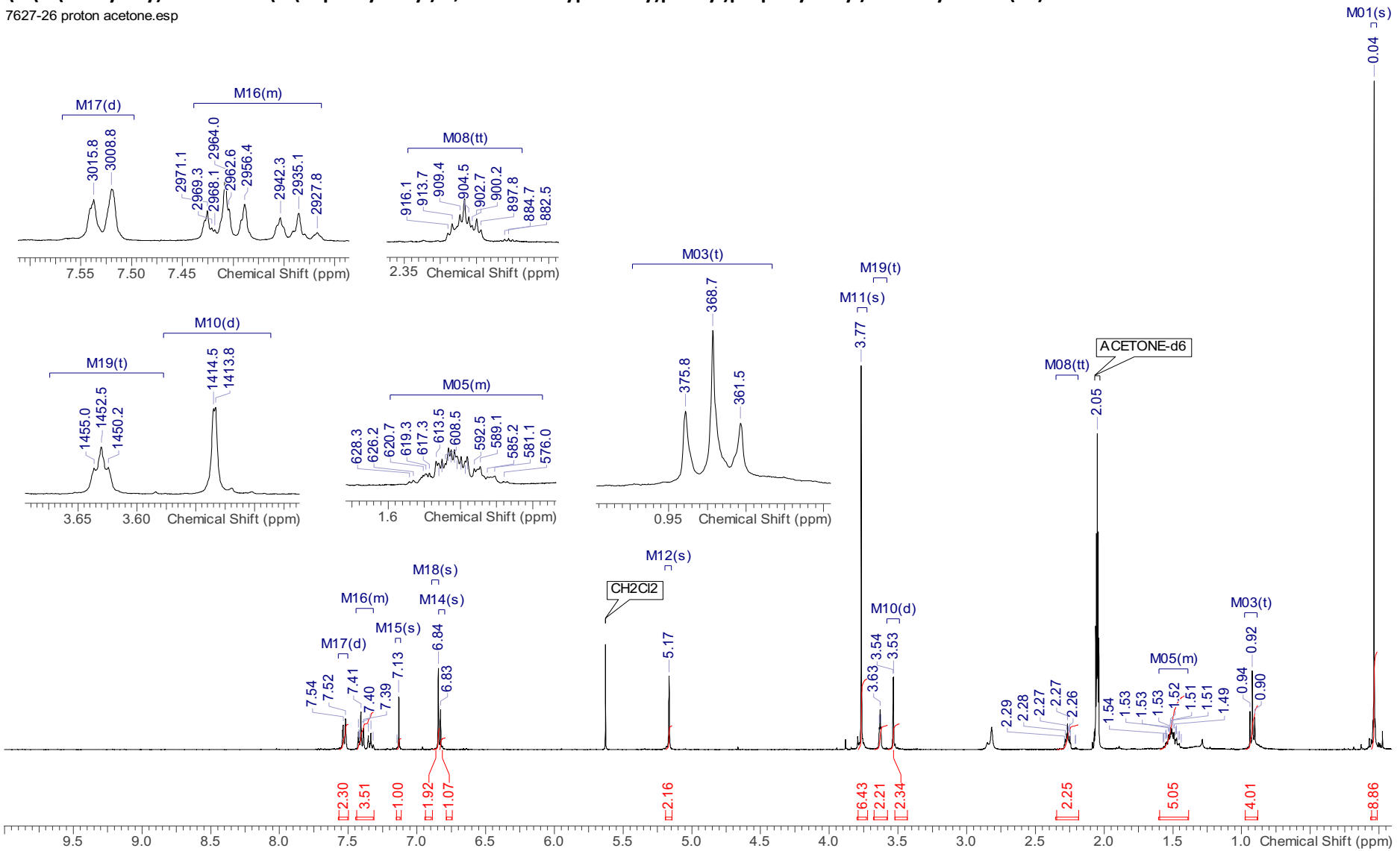
2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(chloromethyl)-1,3-dimethoxybenzene (44)

7420-65 dept cdl3.esp



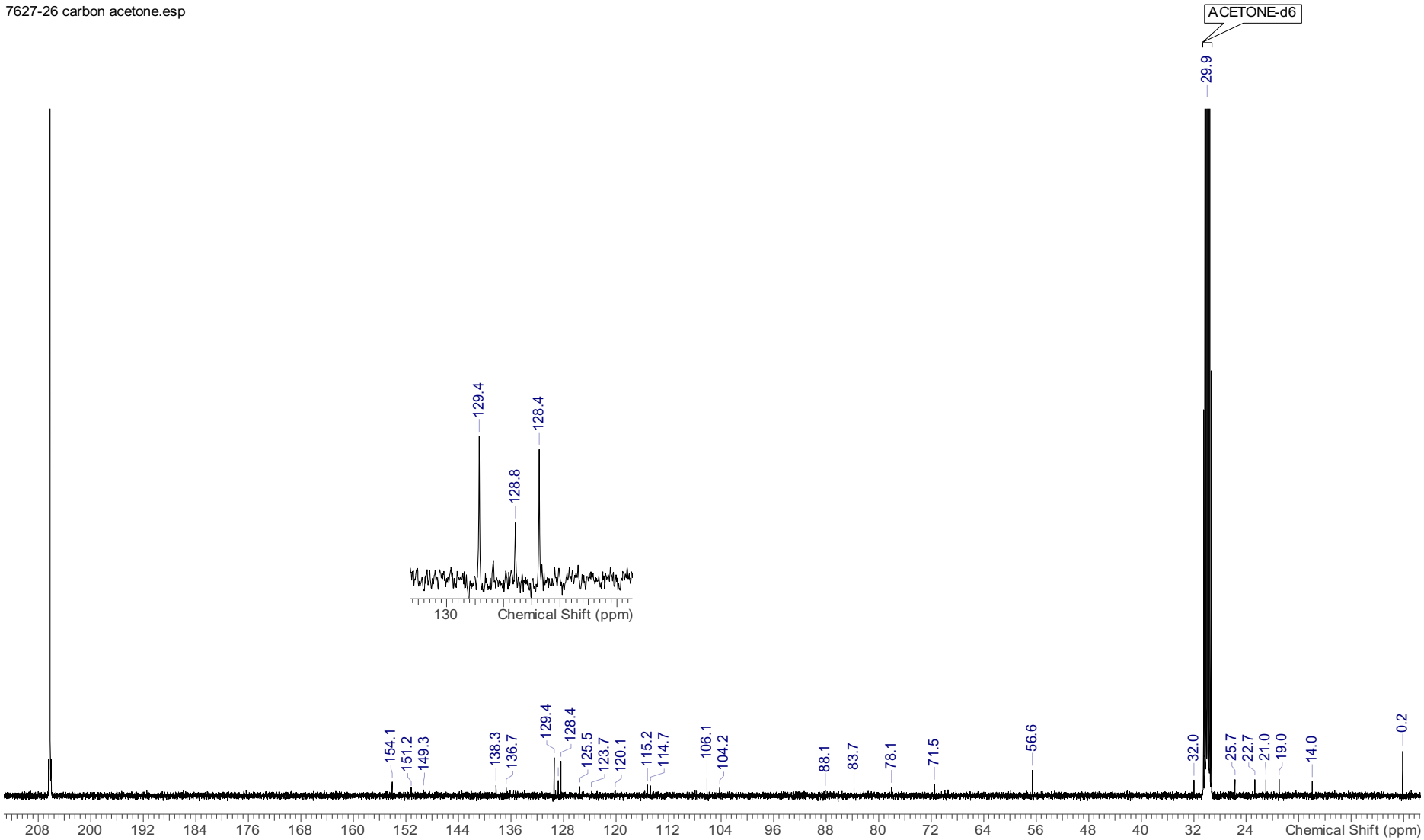
(3-(2-(Benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (45)

7627-26 proton acetone.esp



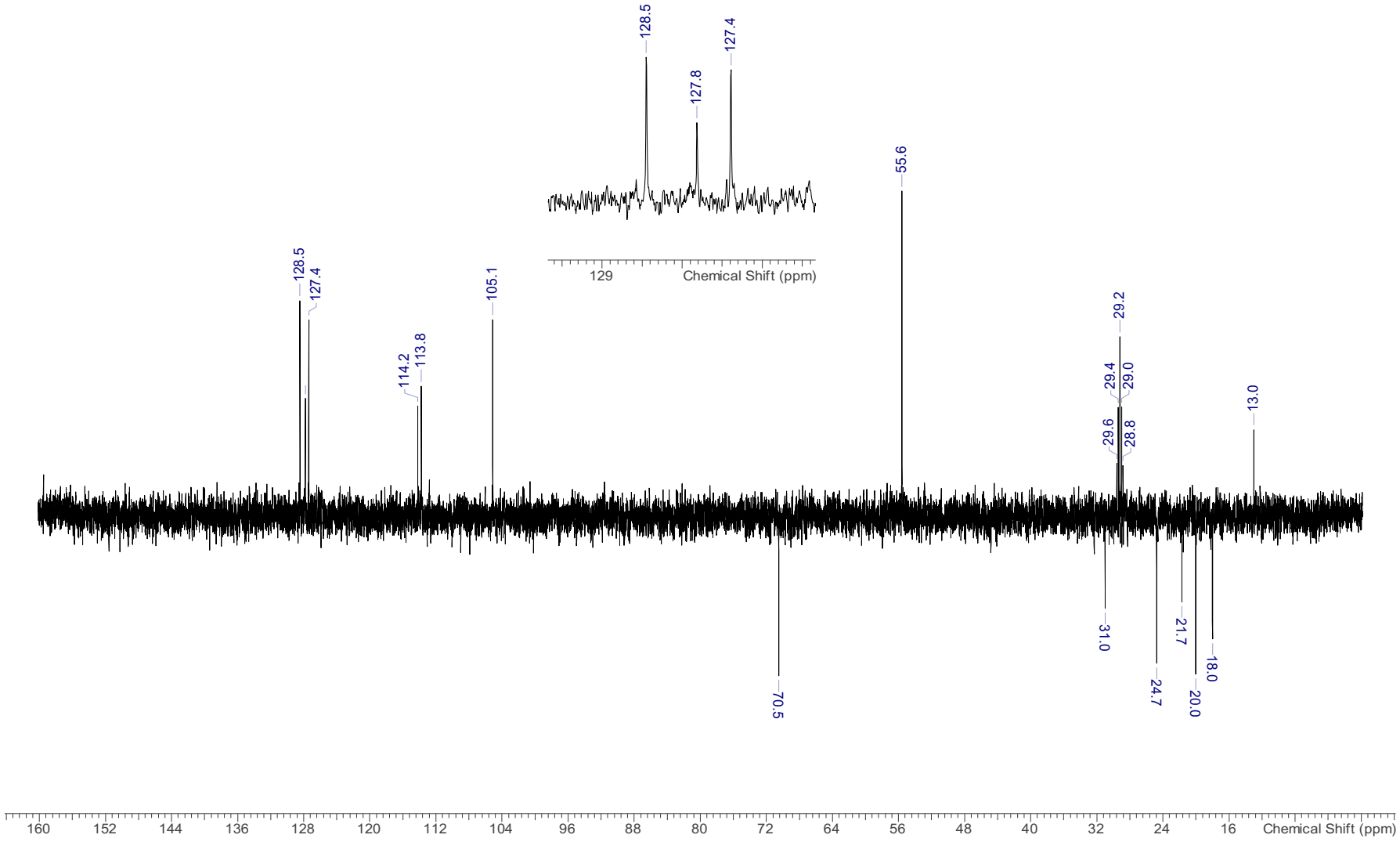
(3-(2-(Benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (45)

7627-26 carbon acetone.esp



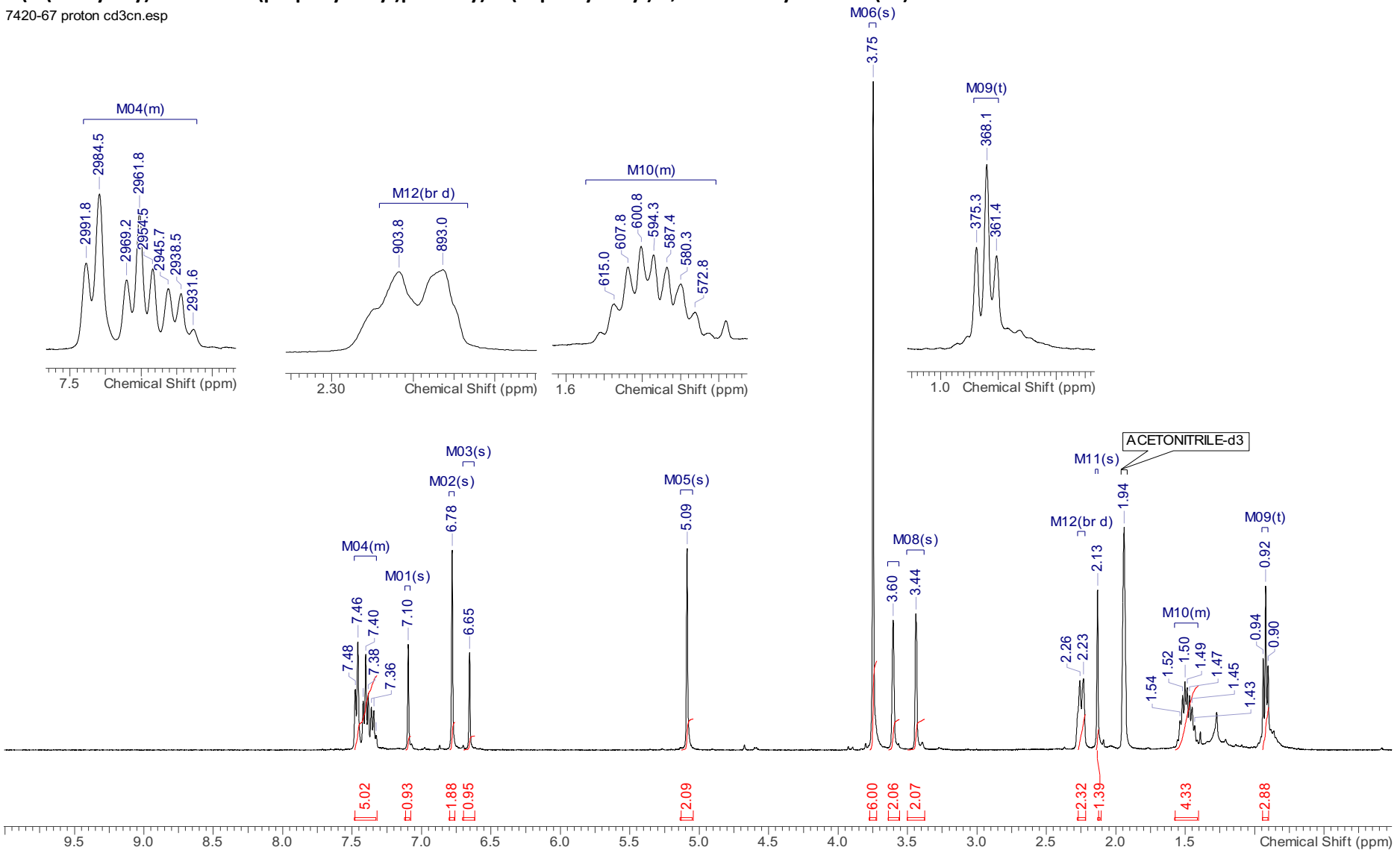
(3-(2-(Benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)prop-1-yn-1-yl)trimethylsilane (45)

7627-26 dept acetone.esp



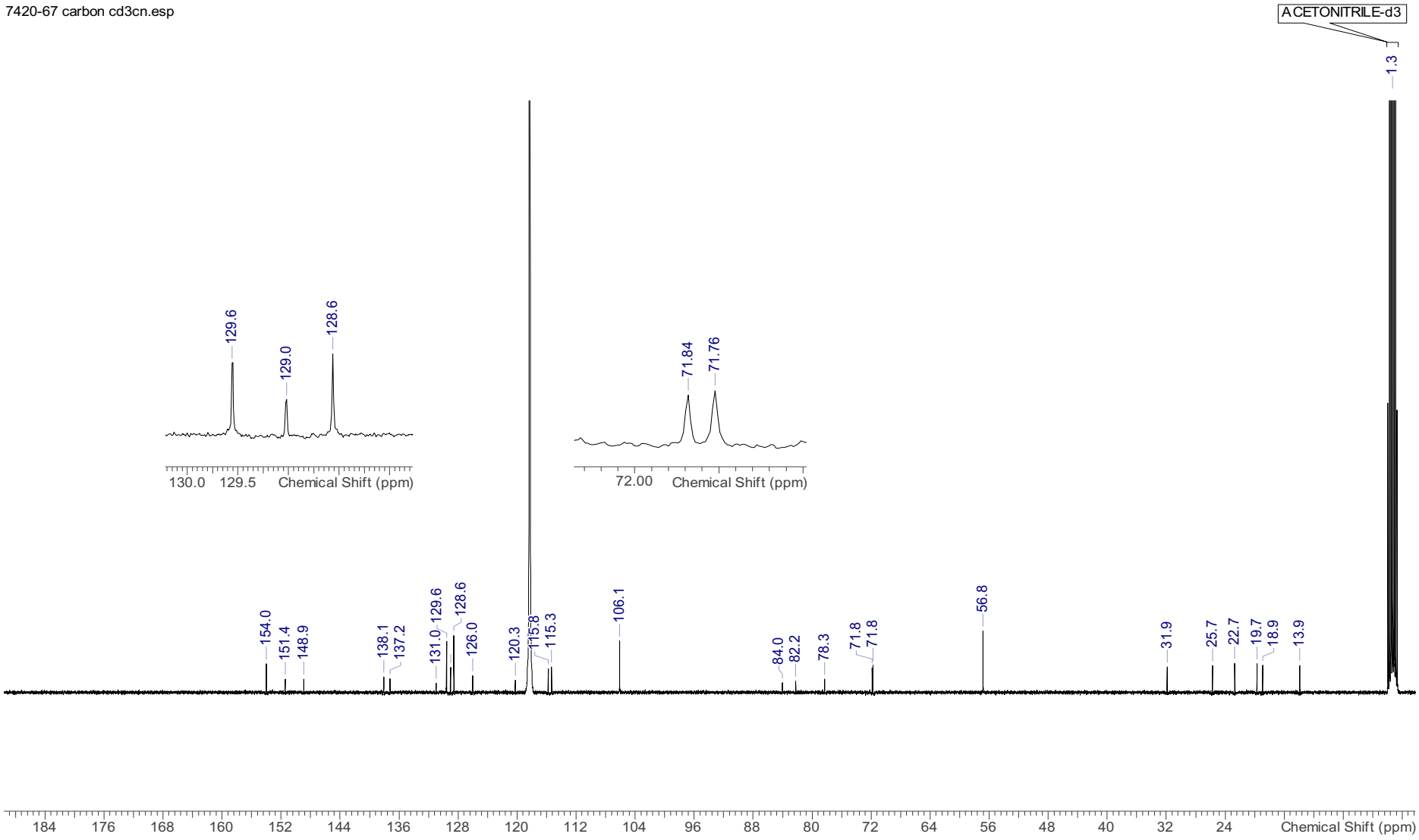
2-(4-(Benzyloxy)-2-chloro-5-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (46)

7420-67 proton cd3cn.esp



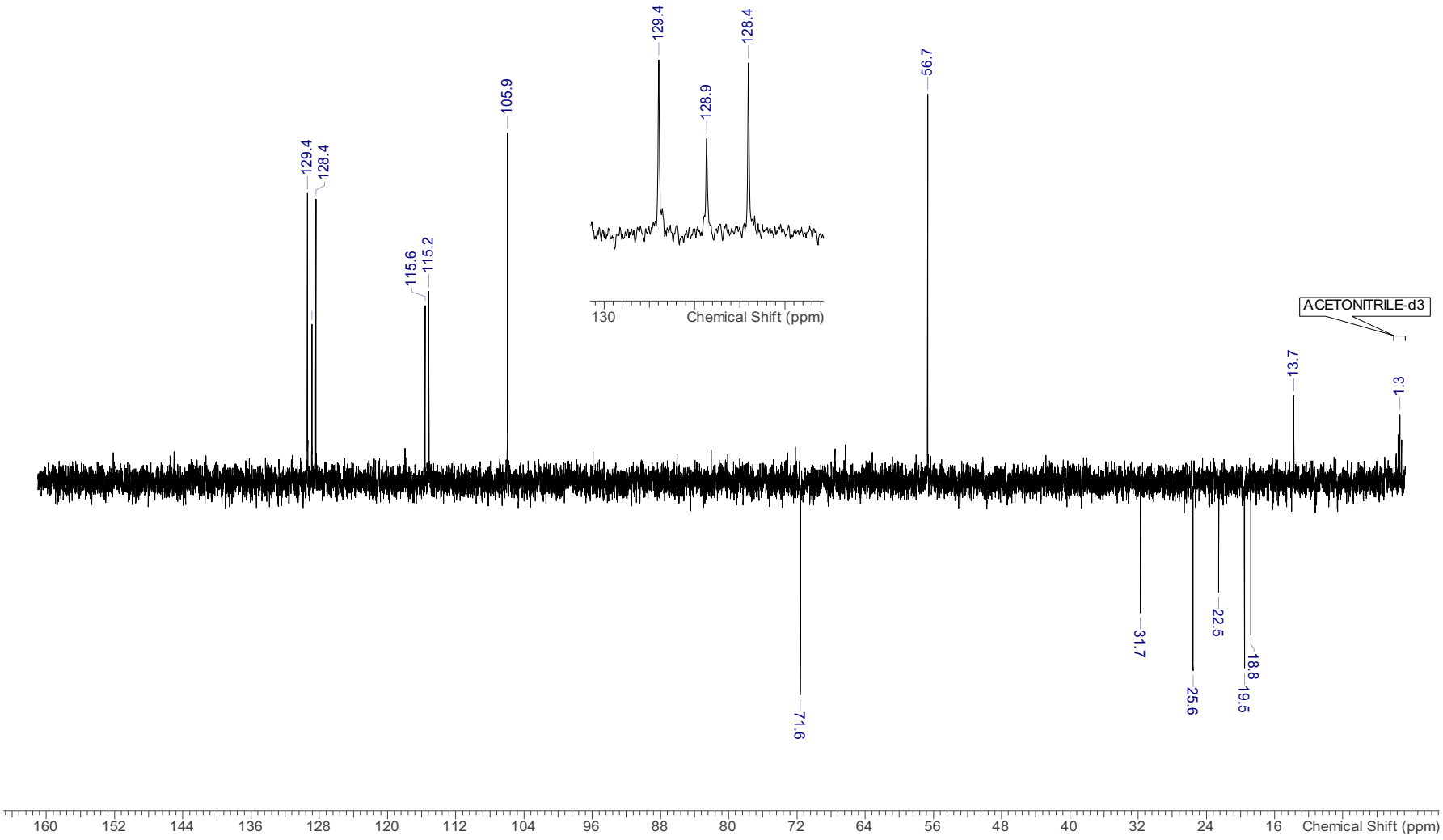
2-(4-(Benzyloxy)-2-chloro-5-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (46)

7420-67 carbon cd3cn.esp



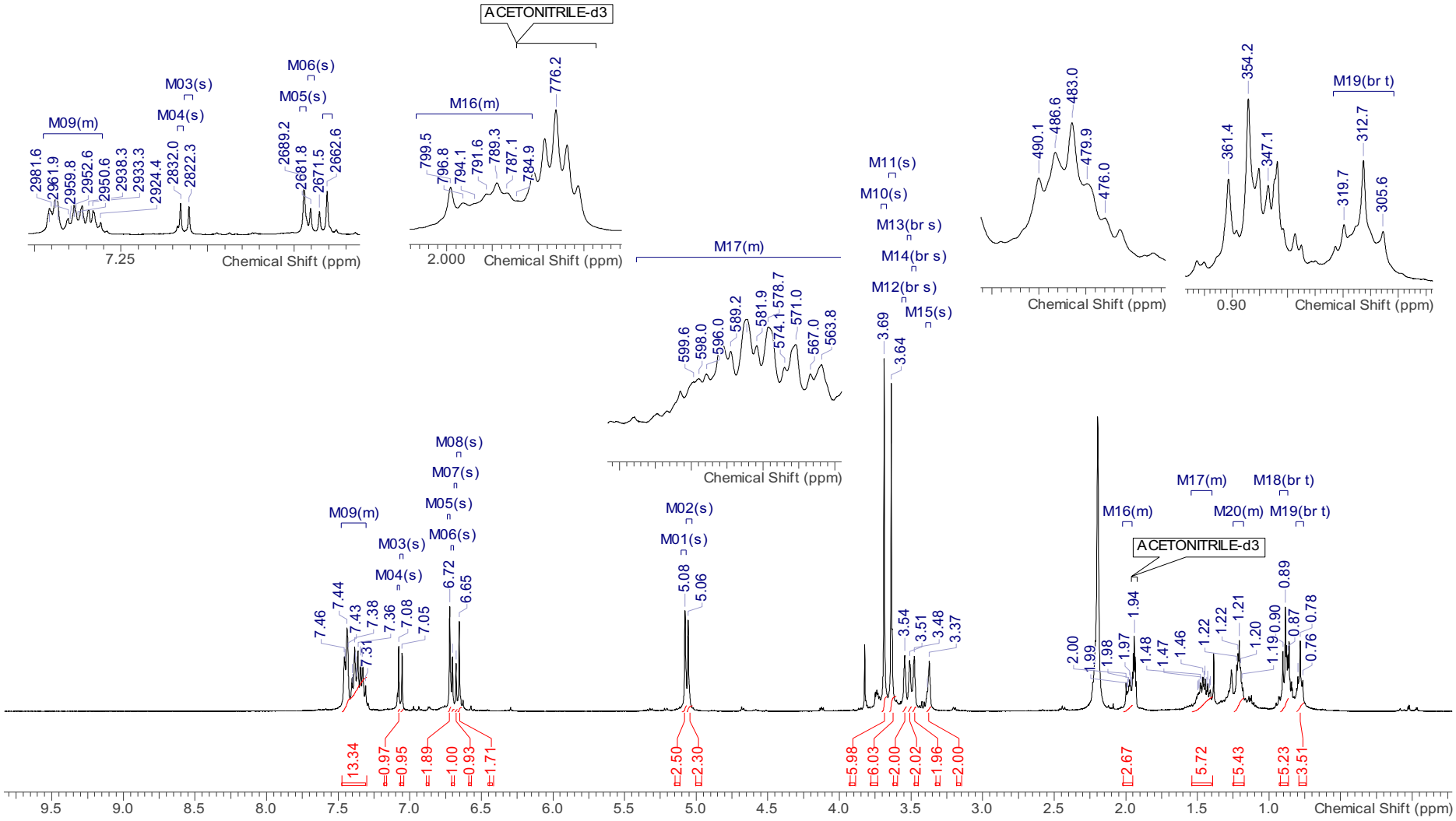
2-(4-(Benzyloxy)-2-chloro-5-(prop-2-yn-1-yl)phenoxy)-5-(hept-2-yn-1-yl)-1,3-dimethoxybenzene (46)

7420-67 dept cd3cn.esp

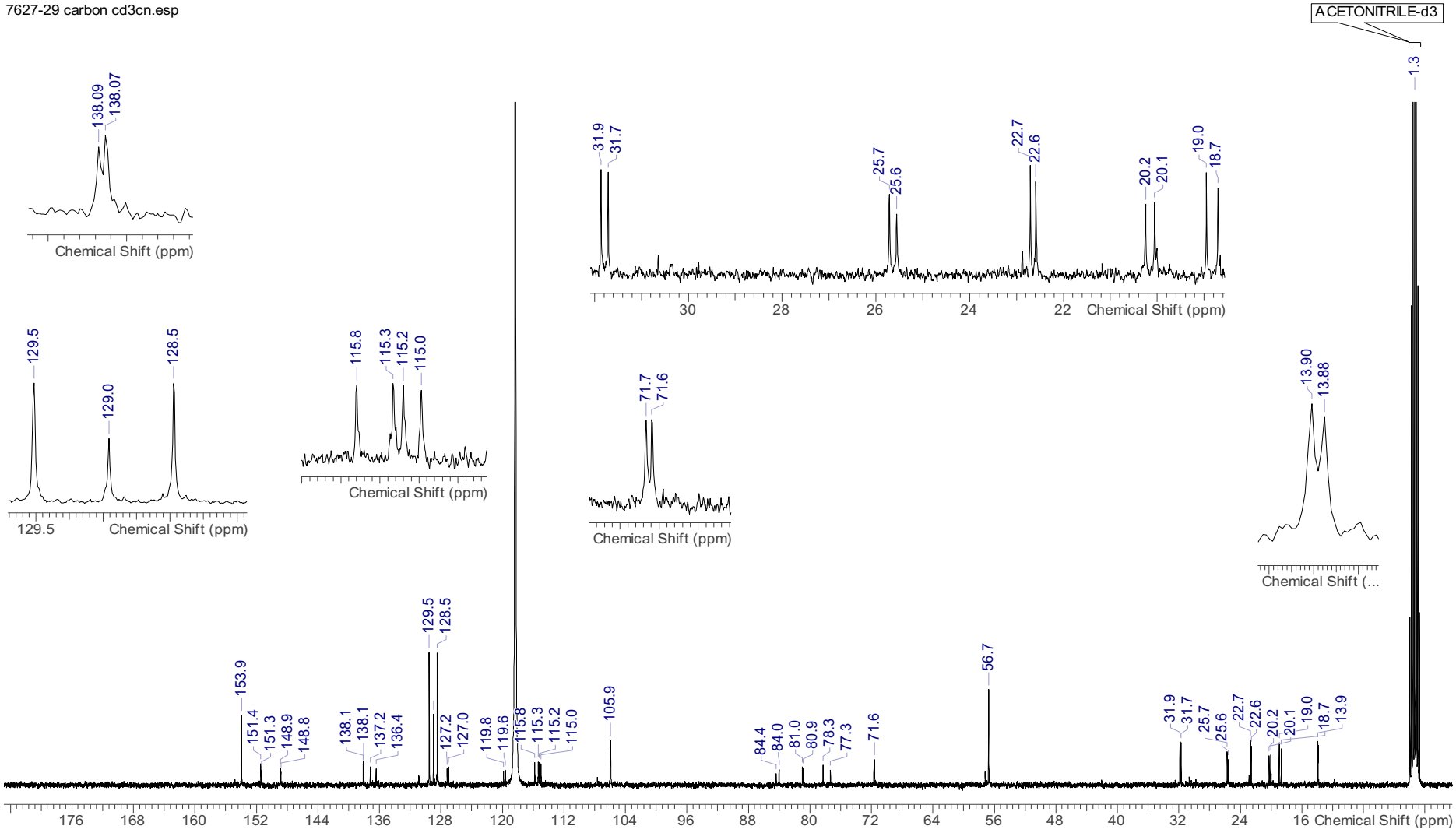


2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(4-(2-(benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)but-2-yn-1-yl)-1,3-dimethoxybenzene (47)

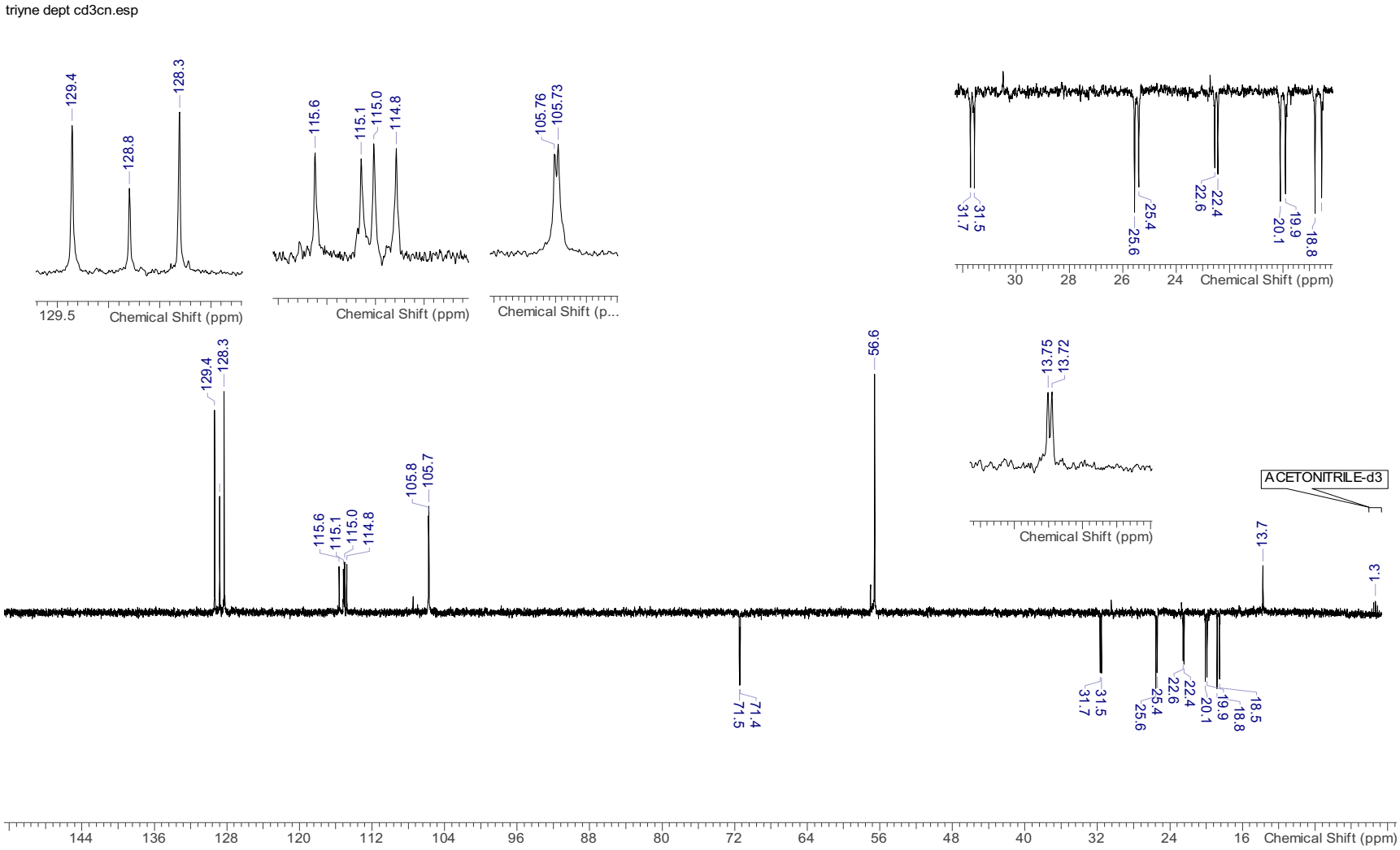
7627-29 proton.esp



2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(4-(2-(benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)but-2-yn-1-yl)-1,3-dimethoxybenzene (47)

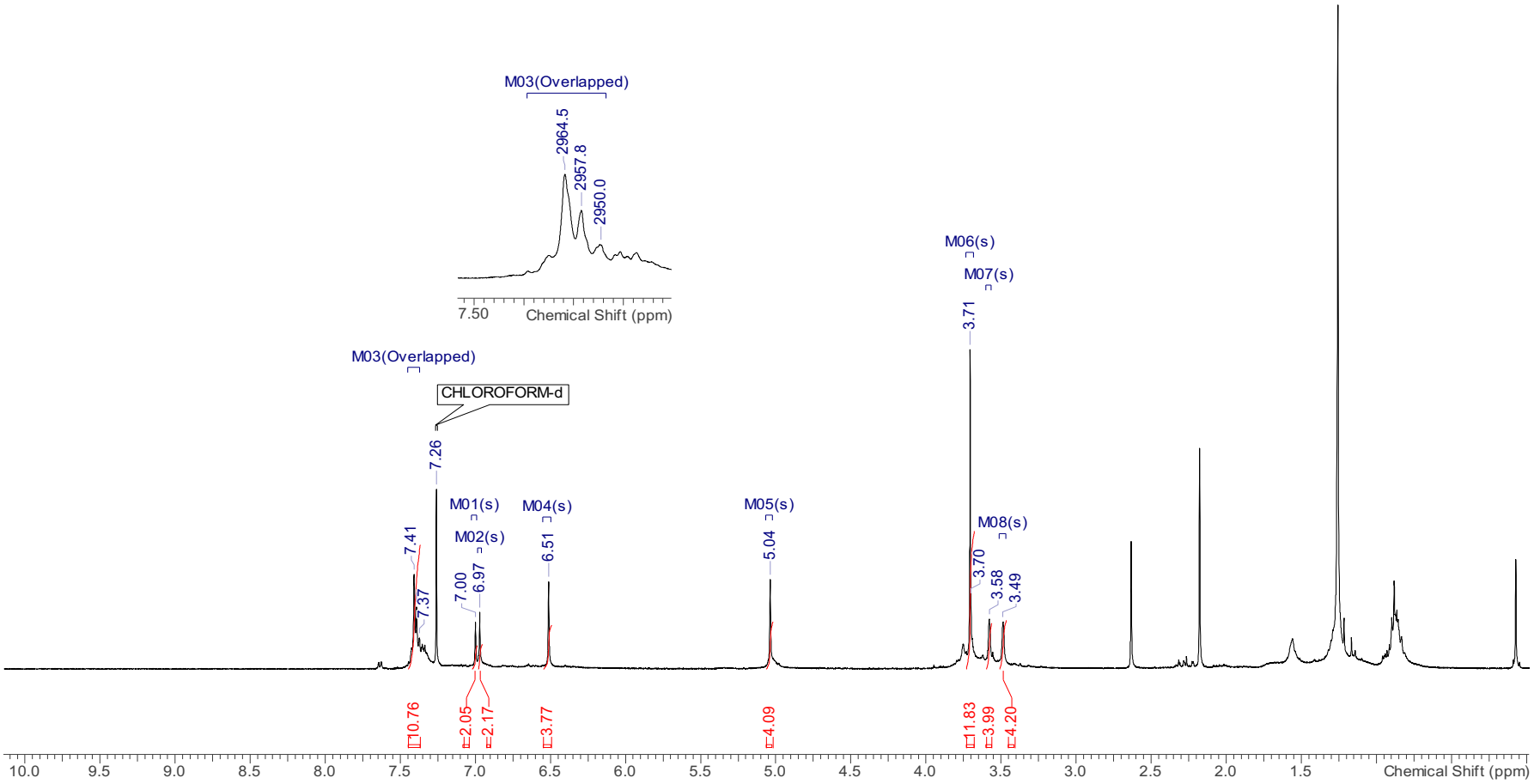


2-(4-(Benzyloxy)-2-chloro-5-(hept-2-yn-1-yl)phenoxy)-5-(4-(2-(benzyloxy)-4-chloro-5-(4-(hept-2-yn-1-yl)-2,6-dimethoxyphenoxy)phenyl)but-2-yn-1-yl)-1,3-dimethoxybenzene (47)



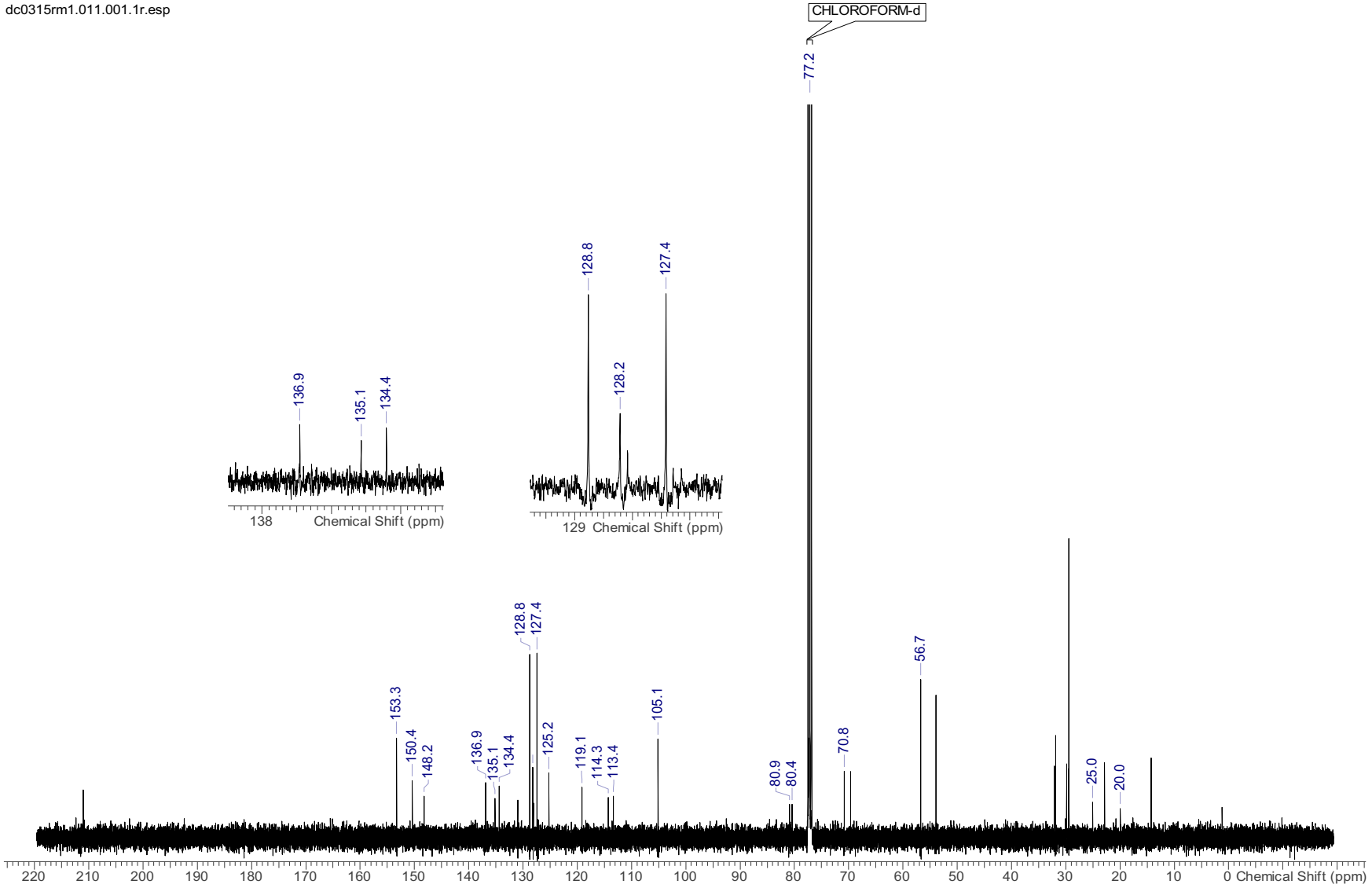
6,20-Bis(benzyloxy)-4,18-dichloro-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-1(28),3(34),4,6,12,14,17(31),18,20,26,29,32-dodecaen-9,23-diyne (48)

dc0315rm1.010.001.1r.esp



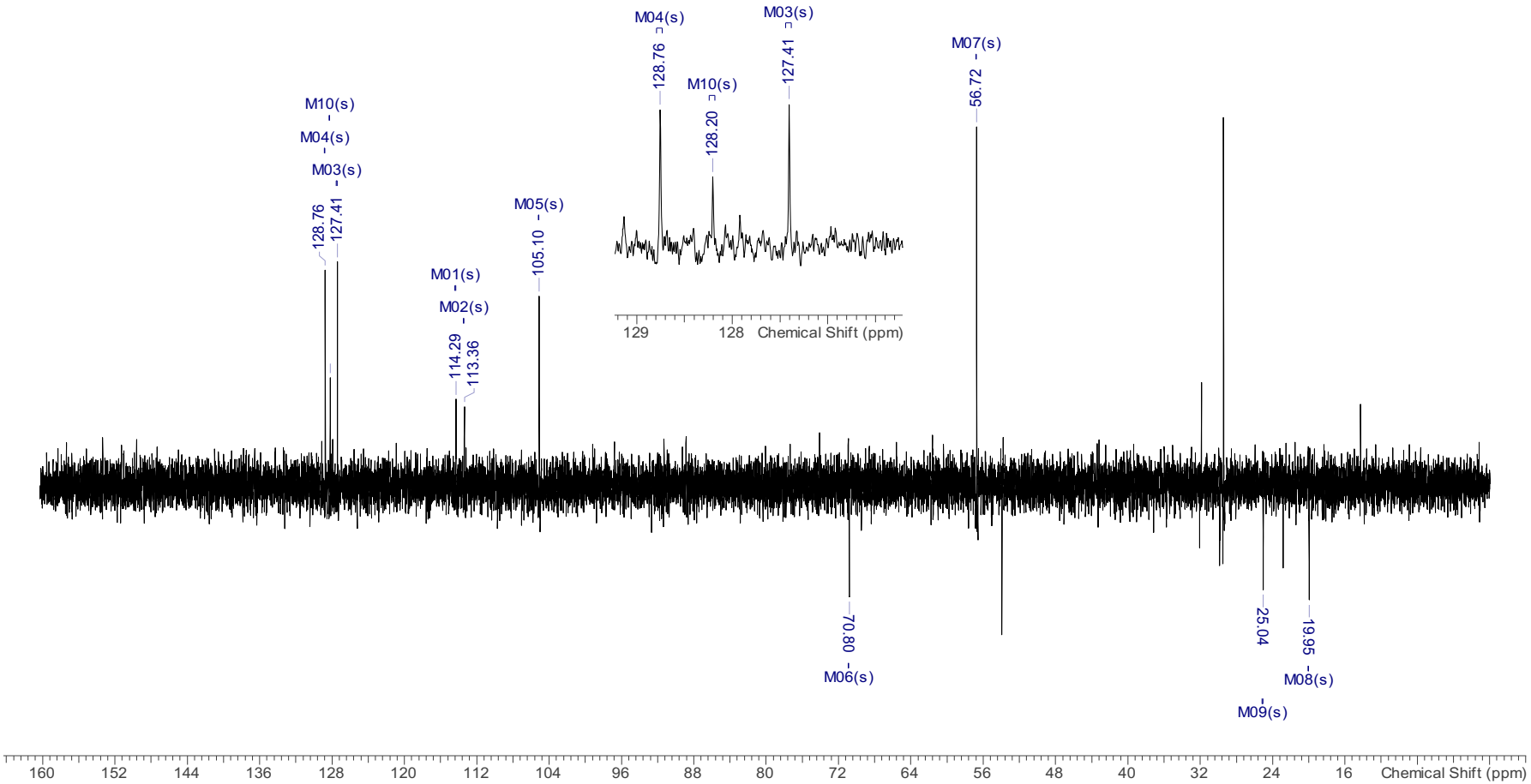
6,20-Bis(benzyloxy)-4,18-dichloro-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-1(28),3(34),4,6,12,14,17(31),18,20,26,29,32-dodecaen-9,23-diyne (48)

dc0315rm1.011.001.1r.esp



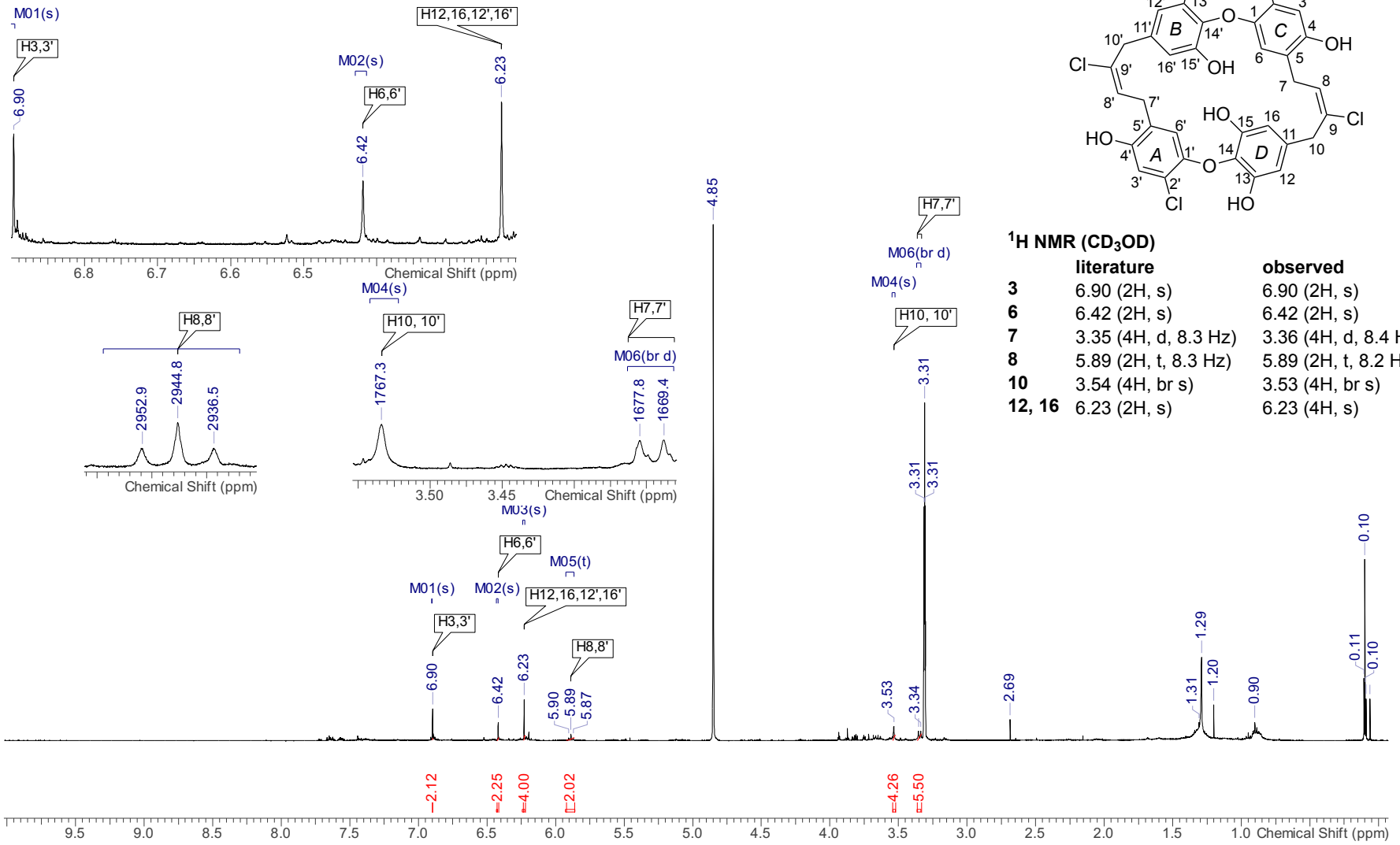
6,20-Bis(benzyloxy)-4,18-dichloro-14,28,29,32-tetramethoxy-2,16-dioxapentacyclo[24.2.2.2^{12,15}.1^{3,7}.1^{17,21}]tetratriaconta-1(28),3(34),4,6,12,14,17(31),18,20,26,29,32-dodecaen-9,23-diyne (48)

dc0315rm1.012.001.1r.esp



Tentatively assigned as an impure sample of Chrysophaentin F (8)

fe2316njwrm1.001.001.1r.esp

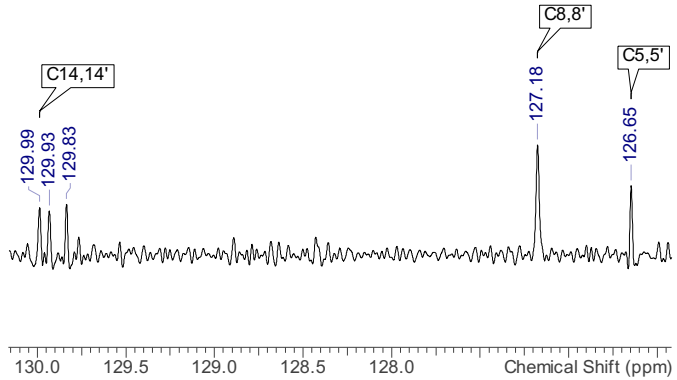


^{1}H NMR (CD_3OD)

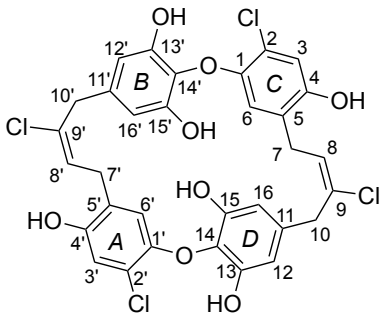
	literature	observed
3	6.90 (2H, s)	6.90 (2H, s)
6	6.42 (2H, s)	6.42 (2H, s)
7	3.35 (4H, d, 8.3 Hz)	3.36 (4H, d, 8.4 Hz)
8	5.89 (2H, t, 8.3 Hz)	5.89 (2H, t, 8.2 Hz)
10	3.54 (4H, br s)	3.53 (4H, br s)
12, 16	6.23 (2H, s)	6.23 (4H, s)

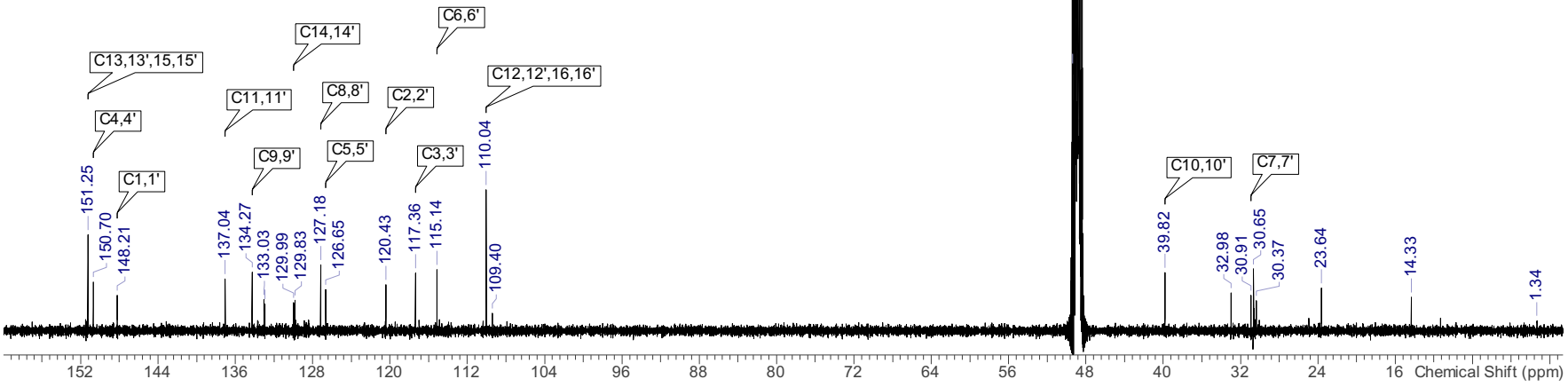
Tentatively assigned as an impure sample of Chrysophaentin F (8)

fe2316njwrm1.002.001.1r.esp



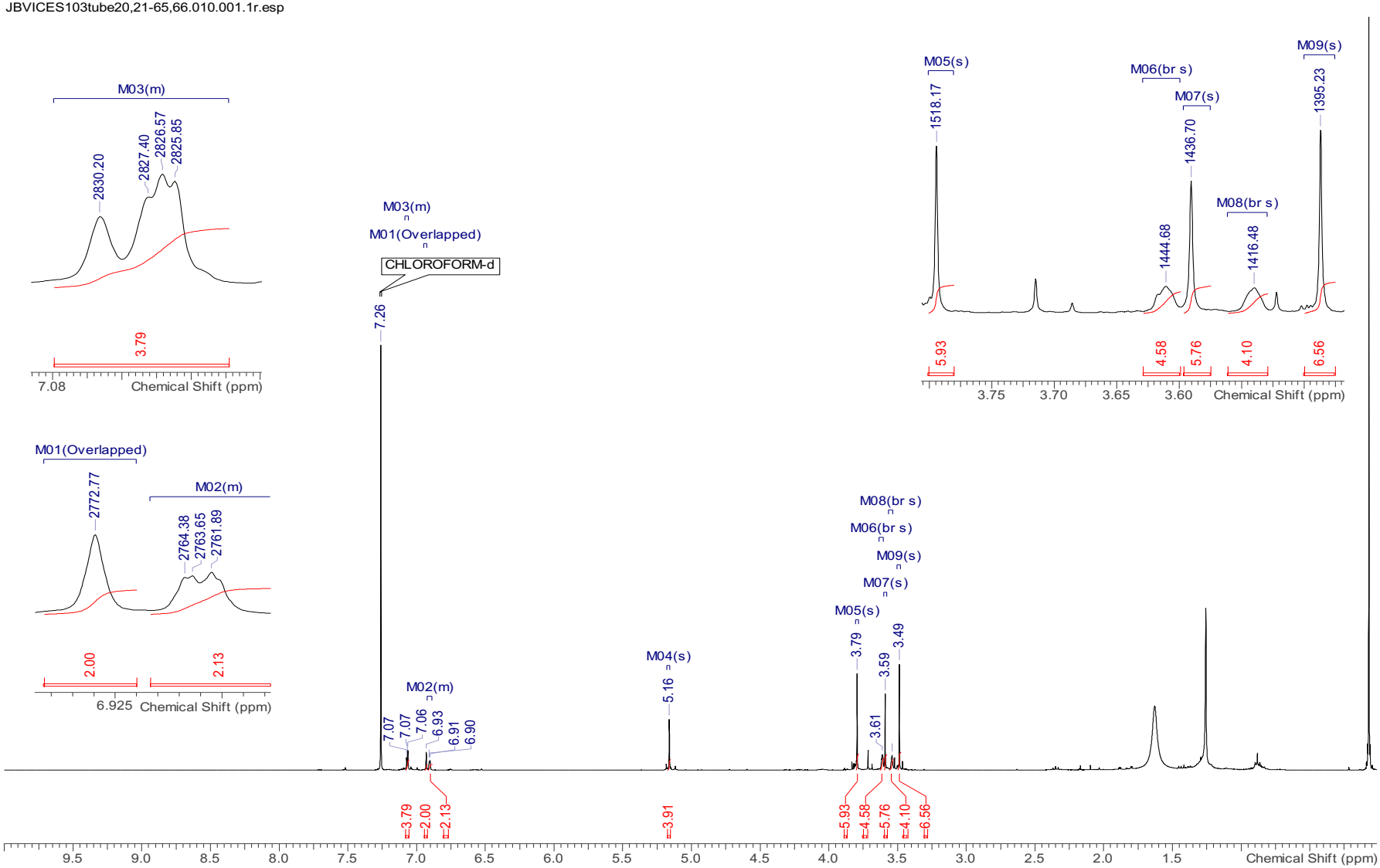
	^{13}C NMR signals literature (observed)
1	148.2 (148.2)
2	120.4 (120.4)
3	117.3 (117.4)
4	150.7 (150.7)
5	126.5 (126.7)
6	115.1 (115.1)
7	31.0 (30.9)
8	127.2 (127.2)
9	134.3 (134.3)
10	39.8 (39.8)
11	137.0 (137.0)
12, 16	110.0 (110.0)
13, 15	151.3 (151.3)
14	130.0 (130.0)





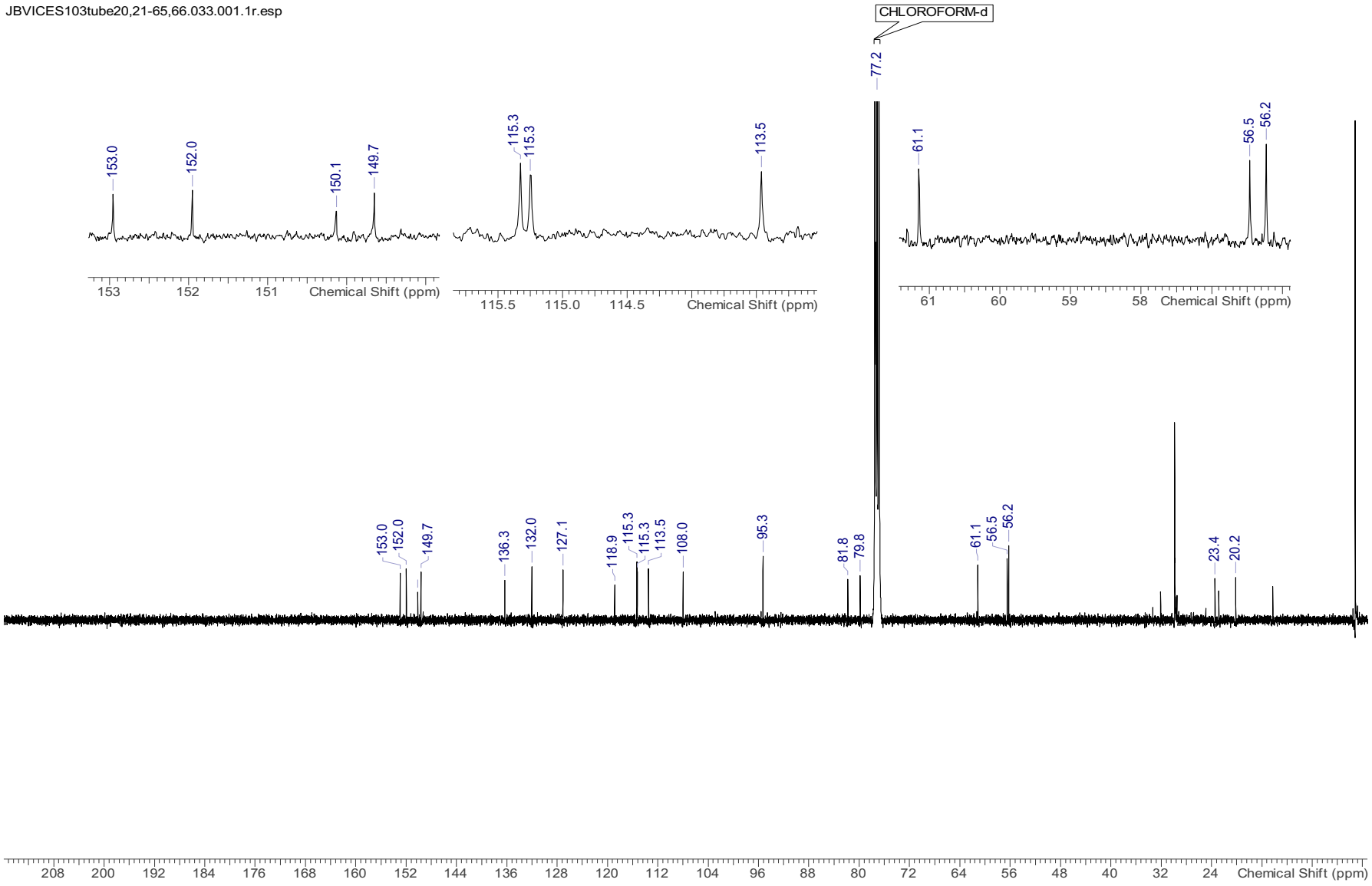
Macrocycle 50 or 51

JBVICES103tube20,21-65,66.010.001.1r.esp



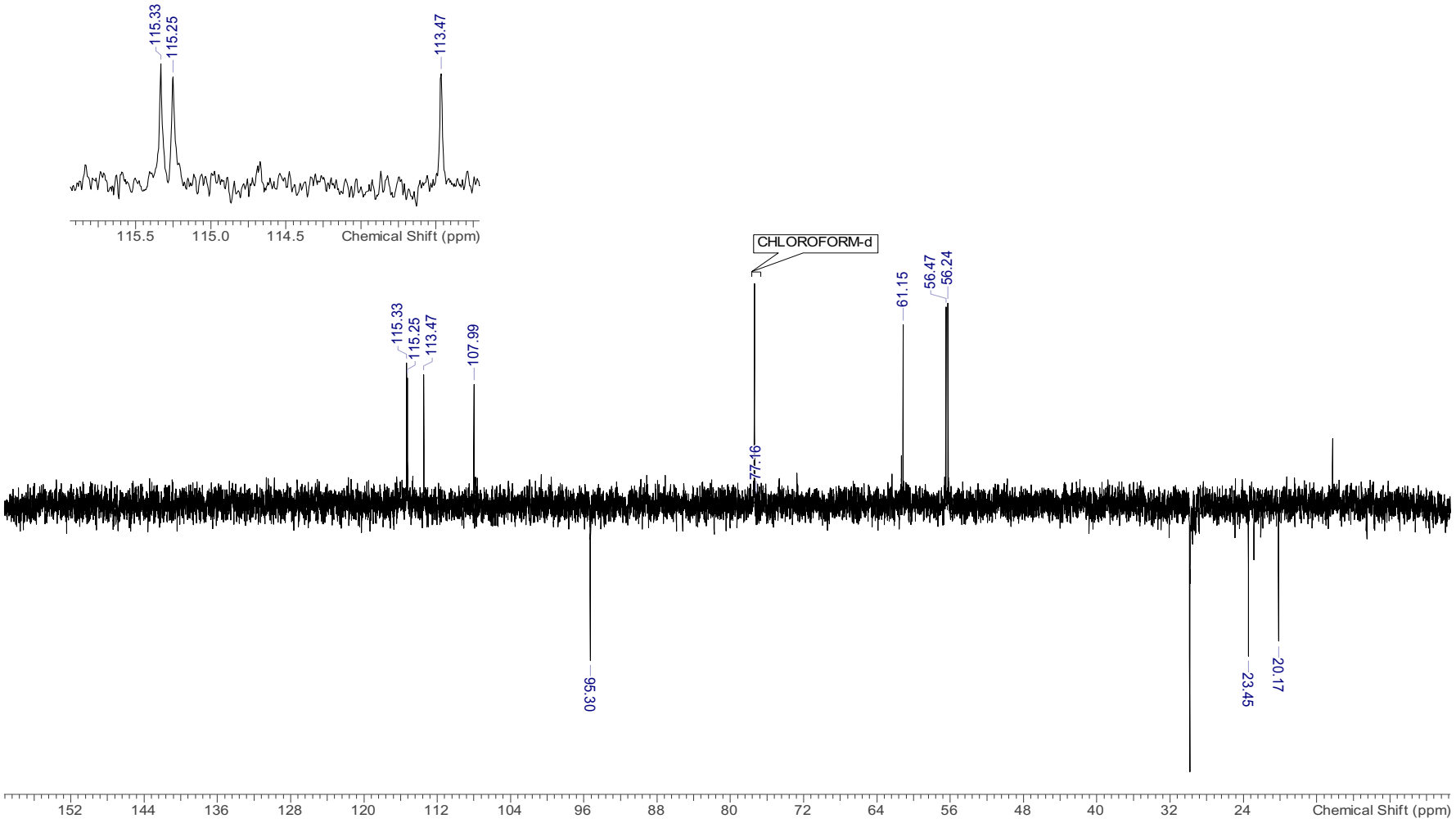
Macrocycle 50 or 51

JBVICES103tube20,21-65,66.033.001.1r.esp

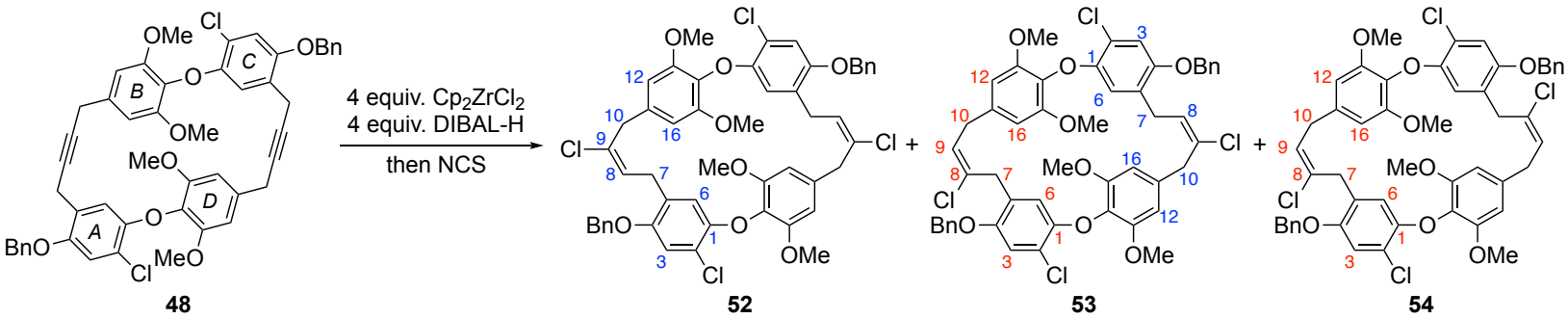


Macrocycle 50 or 51

JBVICES103tube20,21-65,66.014.001.1r.esp



The hydrozirconation and chlorination sequence with diyne **48** gave, after column chromatography, a major fraction exhibiting spectral data consistent with the formation of an isomeric mixture of tetrachlorides **52**–**54**. We tentatively assigned the primary component of that mixture as **52** (blue numbering) and the secondary component as **53** or **54** (red numbering) based on NMR correlation experiments.



48 **52** **53** **54**

Heteronuclear Multiple Bond Correlation (^{1}H-^{13}C)