Supporting Information (SI)

Total Synthesis of Integrastatin B Enabled by a Benzofuran Oxidative Dearomatization Cascade

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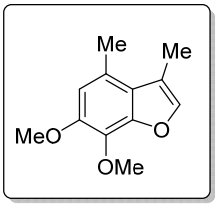
General Experimental Details

Experimental procedures: Standard inert atmosphere techniques were used in handling all air and moisture sensitive reagents. Reactions were carried out under a N_2 atmosphere in oven-dried glassware (temp of oven kept at 100–120 °C). All required solvents were dried according to standard procedures and techniques before use. Room temperature refers to 28–30 °C and the actual temperature of the reaction is mention in synthetic procedure. Oxone was purchased from Aldrich and identified as a triple salt of pottasium peroxy monosulphate (47%). Pet. ether refers to distilled light petroleum of fraction (40–60 °C). Bulk solutions were evaporated under reduced pressure using a rotary evaporator. Reactions were monitored by **thin–layer chromatography** (TLC Silica gel 60 F_{254} from Merck), visualized under dual short/long wave UV fluorescence (λ_{max} = 254 and 365 nm) and developed with *p*–anisaldehyde stains, followed by heating. **Column chromatography** was performed on silica (60–120, 100–200 and 230–400 mesh size). **Melting Points** were measured on a Stuart melting point instrument and are uncorrected. **Fourier transform infrared** (FT–IR) spectra were taken on a Bruker Optics ALPHA–E spectrometer with a universal Zn–Se ATR (attenuated total reflection) accessory in the 600–4000 cm^{-1} region. **NMR spectroscopy**: ^1H NMR spectroscopy measurements were carried out on Bruker DRX 200, 400, 500, 700 and JEOL 400 MHz NMR spectrometers with $CDCl_3$ (δ 7.26) as an internal standard unless otherwise stated. The ^{13}C NMR spectra were recorded on 200 (50 MHz), 400 (100 MHz), 500 (125 MHz) and 700 (175 MHz) NMR spectrometer with $CDCl_3$ (δ 77.0) as an internal standard unless otherwise stated. Chemical shifts (δ) are given in ppm downfield from TMS, and coupling constants (J) are in Hertz (Hz). The ^1H NMR spectra are reported as follows: δ/ppm (multiplicity, coupling constant followed by a number of protons). Multiplicity of ^1H NMR is abbreviated as follows: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplet, q = quartet, dq = doublet of quartet, m = multiplet. The multiplicity of ^{13}C NMR signals was assigned with the help of DEPT spectra and the abbreviations used: s = singlet, d = doublet, t = triplet, q = quartet represent C (quaternary), CH, CH_2 and CH_3 respectively. **HR Mass Spectrometry** were recorded on a Thermo Scientific Q–Exactive, Accela 1250 pump.

***6,7-dimethoxy-3,4-dimethylbenzofuran* (8-Me)**:



Benzofurans **8-Me** was synthesized from compound **9** according to reported procedure (Dawood, K. M.; Fuchigami, T. *J. Org. Chem.*, **2004**, *69*, 5302). **Yield**: 76% over three steps and obtained as yellow syrup.

TLC: R_f 0.4 (2:7 v/v EtOAc/pet. ether, UV active).

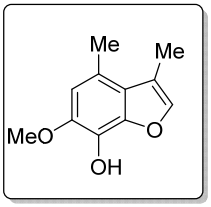
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 2920, 1690, 1615, 1551, 1461, 1211, 750, 668 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.28 (q, J = 1.3 Hz, 1H), 6.63 (d, J = 0.5 Hz, 1H), 4.08 (s, 3 H), 3.91 (s, 3H), 2.58 (d, J = 0.8 Hz, 3H), 2.34 (d, J = 1.4 Hz, 3H) ppm.

^{13}C NMR (50 MHz, $CDCl_3$): δ 148.5 (s), 148.2 (s), 141.0 (d), 132.9 (s), 125.2 (s), 122.9 (s), 116.4 (s), 111.0 (d), 61.0 (q), 57.3 (q), 18.8 (q), 10.4 (q) ppm.

HRMS (m/z): $[M+H]^+$ Calcd. for $C_{12}H_{14}O_3$, 207.1016; found 207.1015.

***6-Methoxy-3,4-dimethylbenzofuran-7-ol* (8-H)**:



To a solution of **8-Me** (3.0 g, 14.5 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added $AlCl_3$ (2.33 g, 17.5 mmol). The resulting mixture was stirred at room temperature for 8 h before it was quenched with sat. NH_4Cl (10 mL). The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (3×100 mL). The combined organic layer was washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (20→50% EtOAc in pet. ether) gave phenol **8-H** (1.91 g, 68%) as a yellow crystalline solid (**mp**: 190–192 °C).

TLC: R_f 0.2 (2:3 v/v EtOAc/pet. ether, UV active).

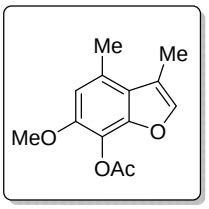
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3015, 2921, 1553, 1469, 1214, 1237, 749, 666 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.28 (q, J = 1.3 Hz, 1H), 6.60 (d, J = 0.6 Hz, 1H), 5.44 (s, 1H), 3.90 (s, 3H), 2.55 (d, J = 0.6 Hz, 3H), 2.33 (d, J = 1.4 Hz, 3H) ppm.

^{13}C NMR (50 MHz, $CDCl_3$): δ 143.8 (s), 143.3 (s), 141.4 (d), 129.3 (s), 122.8 (s), 121.6 (s), 116.4 (s), 109.4 (d), 57.3 (q), 18.7 (q), 10.4 (q) ppm.

HRMS (m/z): $[M+Na]^+$ Calcd. for $C_{11}H_{12}O_3$, 215.0679; found 215.0678.

***6-Methoxy-3,4-dimethylbenzofuran-7-yl acetate* (8-Ac)**:



A solution of phenol **8-H** (1.0 g, 5.2 mmol), Et_3N (1.1 mL, 7.8 mmol), and DMAP (60 mg, 0.52 mmol) in anhydrous CH_2Cl_2 (20 mL) was treated with Ac_2O (0.60 mL, 6.2 mmol) and stirred at room temperature for 4 h. The reaction mixture was quenched with a saturated solution of $NaHCO_3$ (50 mL) and filtered through *celite*. The organic layer was separated and aqueous layer was extracted with EtOAc (4×75 mL). The combined organic layer was washed with brine (2×100 mL), dried over Na_2SO_4 and concentrated in *vacuo*. Purfication of residue by silica gel column chromatography (5→15% EtOAc in pet. ether) gave ester **8-Ac** (1.20 g, 98%) as a white solid. (**mp**: 189–187 °C).

TLC: R_f 0.3 (2:3 v/v EtOAc/pet. ether, UV active).

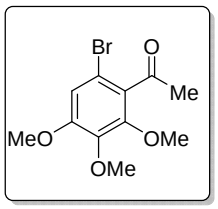
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3017, 2920, 1668, 1553, 1214, 1237, 750, 665 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.28 (d, J = 1.5 Hz, 1H), 6.70 (s, 1H), 3.89 (s, 3H), 2.62 (d, J = 0.6 Hz, 3H), 2.42 (s, 3H), 2.35 (d, J = 1.3 Hz, 3H) ppm.

^{13}C NMR (50 MHz, $CDCl_3$): δ 168.6 (s), 148.4 (s), 141.3 (d, 2C), 129.0 (s), 122.5 (s), 116.6 (s), 110.2 (d, 2C), 57.0 (q), 20.4 (q), 19.1 (q), 10.3 (q) ppm.

HRMS (m/z): $[M+Na]^+$ Calcd. for $C_{13}H_{14}O_4Na$, 257.0784; found 257.0782.

***1-(6-Bromo-2,3,4-trimethoxyphenyl)ethan-1-one* (7-Me)**:



To a solution of 5-bromo-1,2,3-trimethoxybenzene (5.0 g, 20.2 mmol) in Ac_2O (5 mL) was added *p*-TSA·H_2O (1.75 g, 10.1 mmol) at room temperature. The solution was heated at 50 °C for 13 h. After completion of the reaction as indicated by TLC, water was added to the reaction mixture and extracted with CH_2Cl_2 (5 x 100 mL). The combined organic layer was washed with brine (3×50 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (10→50% EtOAc in pet. ether) gave **7-Me** (3.68 g, 63%) as a yellow syrup.

TLC: R_f 0.3 (2:8 v/v EtOAc/pet. ether, UV active).

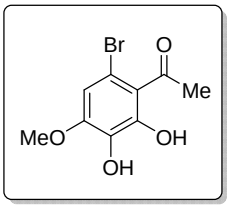
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3020, 2926, 1618, 1557, 1461, 1214, 1230, 750, 668 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 6.82 (s, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 2.49 (s, 3H) ppm.

^{13}C NMR (50 MHz, $CDCl_3$): δ 154.7 (s), 150.8 (s), 150.0 (s), 119.3 (s), 112.0 (d, 2C), 110.9 (s), 62.0 (q), 60.9 (q), 56.3 (q), 31.8 (q) ppm.

HRMS (m/z): $[M+H]^+$ Calcd. for $C_{11}H_{14}BrO_4$, 289.0070; found 289.0067.

1-(6-bromo-2,3-dihydroxy-4-methoxyphenyl)ethan-1-one **(7-H)**:



To a solution of **7-Me** (2.0 g, 6.9 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added BCl_3 (20.8 mL, 1M in CH_2Cl_2, 20.8 mmol). The resulting mixture was stirred at room temperature for 15 h before it was quenched with sat. NH_4Cl (20 mL). The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (4×50 mL). The combined organic layer was washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (20→50% EtOAc in pet. ether) gave catechol **7-H** (1.37 g, 76%) as a yellow crystals (**mp**: 210–212 °C).

TLC: R_f 0.3 (3:8 v/v EtOAc/pet. ether, UV active).

FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3020, 2920, 1635, 1461, 1218, 1230, 750, 670 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 12.88 (s, 1 H), 6.82 (s, 1 H), 5.67 (br. s., 1 H), 3.94 (s, 3 H), 2.85 (s, 3 H) ppm.

^{13}C NMR (50 MHz, $CDCl_3$): δ 204.6 (s), 151.5 (s), 150.1 (s), 133.1 (s), 116.0 (s), 113.7 (s), 110.4 (d), 56.3 (q), 32.9 (q) ppm.

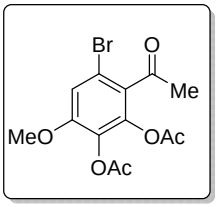
HRMS (m/z): $[M+Na]^+$ Calcd. for $C_9H_{19}BrO_4Na$, 282.9576; found 282.9575.

3-Acetyl-4-bromo-6-methoxy-1,2-phenylene diacetate **(7-Ac)**:

Yield: 97% colorless syrup.

TLC: R_f 0.5 (3:8 v/v EtOAc/pet. ether, UV active).

FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3020, 2926, 1760, 1618, 1557, 1461, 1214, 1230, 668 cm^{-1}.

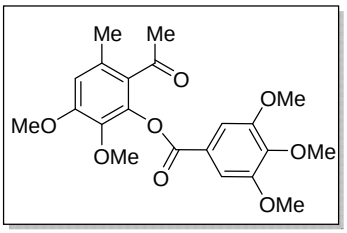


^{1}H NMR (200 MHz, $CDCl_3$): δ 7.05 (s, 1H), 3.83 (s, 3H), 2.51 (s, 3H), 2.27 (s, 3H), 2.23 (s, 3H) ppm.

^{13}C NMR (50 MHz, $CDCl_3$): δ 198.8 (s), 167.4 (s), 167.0 (s), 153.0 (s), 140.6 (s), 132.0 (s), 129.6 (s), 114.7 (s), 114.3 (d), 56.5 (q), 31.1 (q), 20.1 (q), 20.0 (q) ppm.

HRMS (m/z): $[M+Na]^+$ Calcd. for $C_{13}H_{13}NaBrO_4$, 366.9788; found 366.9785.

***2-Acetyl-5,6-dimethoxy-3-methylphenyl 3,4,5-trimethoxybenzoate* (11)**:



To a solution of phenol **9** (5.0 g, 2.4 mmol), eudesmic acid (7.6 g, 3.60 mmol), DCC (5.9 g, 2.9 mmol) and DMAP (140 mg, 0.12 mmol) in CH_2Cl_2 (50 mL) was added Et_3N (5.0 mL, 3.6 mmol) at room temperature. After 4 h, water was added to the reaction mixture and extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layer was washed with brine (3×50 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (20→40% EtOAc in pet. ether) gave ester **11** (8.9 g, 92%) as a white solid (**mp** 133–134 °C).

TLC: R_f 0.3 (1:4 v/v EtOAc/pet. ether, UV active).

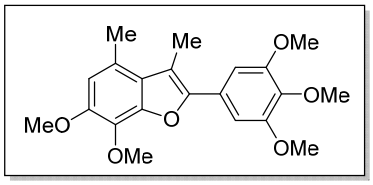
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3020, 1740, 1213, 750, 669 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.43 (s, 2H), 6.69 (s, 1H), 3.95 (s, 3H), 3.93 (s, 6H), 3.90 (s, 3H), 3.80 (s, 3H), 2.41 (s, 3H), 2.32 (s, 3H) ppm.

^{13}C NMR (50 MHz, $CDCl_3$): δ 201.9 (s), 164.1 (s), 153.9 (s), 153.1 (s, 2C), 143.0 (s), 141.7 (s), 138.8 (s), 131.2 (s), 127.9 (s), 123.6 (s), 112.4 (d), 107.6 (d, 2C), 60.9 (q), 60.7 (q), 56.3 (q, 2C), 56.0 (q), 31.9 (q), 19.8 (q) ppm.

HRMS (m/z): $[M+Na]^+$ Calcd. for $C_{21}H_{24}NaO_8$, 427.1363; found, 427.1360.

***6,7-Dimethoxy-3,4-dimethyl-2-(3,4,5-trimethoxyphenyl)benzofuran* (10)**:



(a) **Through palladium catalysed C-H arylation**: Benzofuran **8-Me** was treated under reported procedure for palladium catalyzed direct arylation reaction (Ionita. M.; Roger, J.; Doucet, H. *ChemSusChem*, **2010**, *3*, 367) with 5-Bromo-1,2,3-trimethoxybenzene to gave compound **10** in 56% yield. (b) **Through intramolecular McMurry type coupling of 11**: To an ice cooled solution of ester **11** (5.0 g, 12.4 mmol) in THF (100 mL) was added $TiCl_3.1\backslash 3AlCl_3$ (7.4 g, 36.8 mmol) and Zn (1.62 g, 24.7 mmol). Then ice bath was removed and slowly heated to 70 °C. After 6 h, the reaction mixture was quenched with sat. $NaHCO_3$ (30 mL) and diluted with EtOAc (200 mL). The organic layer was separated and aqueous layer was extracted with EtOAc (2×100 mL). The combined organic layer was washed with brine (3×10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (10→30% EtOAc in pet. ether) gave **10** (3.3 g, 71%) as a white solid (**mp** 131–132 °C).

TLC: R_f 0.5 (1:4 v/v EtOAc/pet. ether, UV active).

FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3020, 2927, 1460, 1398, 1241, 1162, 1001, 950, 669 cm^{-1}.

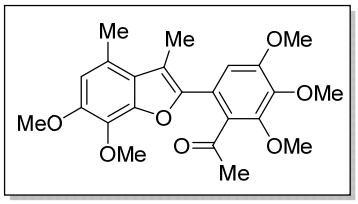
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.90 (s, 2H), 6.62 (s, 1H), 4.10 (s, 3H), 3.93 (s, 6H), 3.91 (s, 3H), 3.89 (s, 3H), 2.62 (s, 3H), 2.56 (s, 3H) ppm.

^{13}C NMR (125 MHz,$CDCl_3$): δ 153.3 (s, 2C), 150.6 (s), 148.5 (s), 146.4 (s), 138.1 (s), 132.5 (s), 126.7 (s), 125.3 (s), 124.6 (s), 111.9 (s), 111.2 (d), 104.9 (d, 2C), 61.1 (q), 60.9 (q), 57.2 (q), 56.3 (q, 2 C), 19.3 (q), 11.6 (q) ppm.

HRMS (m/z): $[M+H]^+$ Calcd. for $C_{21}H_{25}O_6$, 373.1646; found, 373.1643.

***1-(6-(6,7-Dimethoxy-3,4-dimethylbenzofuran-2-yl)-2,3,4-trimethoxyphenyl)ethanone* (6-Me)**:

To a solution of benzofuran **10** (2.0 g, 5.4 mmol) in Ac_2O (5 mL) was added *p*-TSA·H_2O (510 mg, 2.7 mmol) at room temperature. The solution was heated at 50 °C for 6 h. After completion of the reaction as indicated by TLC, water was added to the reaction mixture and extracted with



CH_2Cl_2 (2×100 mL). The combined organic layer was washed with brine (3×20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (10→25% EtOAc in pet. ether) gave **6-Me** (1.83 g, 82%) as a white powder (**mp** 115–116 °C).

TLC: R_f 0.6 (1:4 v/v EtOAc/pet. ether, UV active).

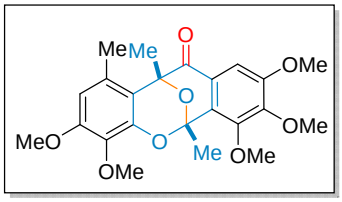
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3020, 1700, 1520, 1214, 750, 669 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.79 (s, 1H), 6.64 (s, 1H), 4.04 (s, 3H), 3.94 (s, 6H), 3.92 (s, 3H), 3.91 (s, 3H), 2.61 (s, 3H), 2.44 (s, 3H), 2.40 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 202.2 (s), 153.8 (s), 150.8 (s), 148.8 (s), 148.7 (s), 146.7 (s), 142.4 (s), 132.6 (s), 130.2 (s), 125.4 (s), 124.0 (s), 123.3 (s), 113.8 (s), 111.3 (d), 109.2 (d), 62.0 (q), 61.1 (q), 61.0 (q), 57.2 (q), 56.2 (q), 31.9 (q), 19.1 (q), 11.4 (q) ppm.

HRMS (m/z): $[M+H]^+$ Calcd. for $C_{23}H_{27}O_7$, 415.1751; found, 415.1749.

***3,4,7,8,9-pentamethoxy-1,6,12-trimethyl-6H-6,12-epoxydibenzo[b,f]oxocin-11(12H)-one* (5-Me)**



To a solution of **6-Me** (100 mg, 0.24 mmol) in acetone (5 mL) and water (2 mL) was added Oxone (47%, 296 mg, 0.48 mmol) and $NaHCO_3$ (80 mg, 0.96 mmol). The reaction mixture was stirred at room temperature for 8 h. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with EtOAc and washed with water (2–3 times) and then with brine. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. Purification of residue by silica gel column chromatography (20→50% EtOAc in pet. ether) gave **5-Me** (88 mg, 84%) as a colorless liquid.

TLC: R_f 0.5 (1:4 v/v EtOAc/pet. ether, UV active).

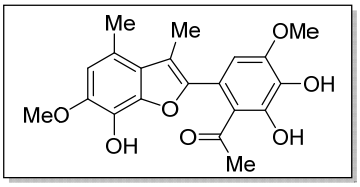
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 2929, 2851, 2648, 2049, 1611, 1513, 1457, 1363, 1248, 1176, 1077, 1034, 836, 775 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24 (s, 1H), 6.28 (s, 1H), 3.91 (s, 6H), 3.87 (s, 3H), 3.84 (s, 3H), 3.77 (s, 3H), 2.32 (s, 3H), 2.15 (s, 3H), 1.89 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 192.6 (s), 154.0 (s), 151.9 (s), 150.5 (s), 148.3 (s), 145.7 (s), 135.5 (s), 130.9 (s), 127.2 (s), 124.2 (s), 114.2 (s), 108.3 (d), 104.6 (d), 95.9 (s), 77.2 (s), 61.6 (q), 60.9 (q), 60.8 (q), 56.0 (q), 55.7 (q), 26.9 (q), 20.7 (s), 20.5 (q) ppm.

HRMS (m/z): $[M+H]^+$ Calcd. for $C_{23}H_{27}NaO_8$, 431.1706; found, 431.1703.

***1-(2,3-Dihydroxy-6-(7-hydroxy-6-methoxy-3,4-dimethylbenzofuran-2-yl)-4-methoxyphenyl) ethanone* (6-H)**:



To a solution of ketone **6-Me** (1.2 g, 2.9 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added BCl_3 (14.5 mL, 1.0 M in CH_2Cl_2, 14.5 mmol) dropwise. The resulting mixture was stirred at room temperature for 8 h before it was quenched with sat. NH_4Cl (20 mL). The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic layer was washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (20→50% EtOAc in pet. ether) gave phenol **6-H** (800 mg, 74%) as a yellow crystalline solid (**mp** 206–207 °C).

TLC: R_f 0.3 (2:3 v/v EtOAc/pet. ether, UV active).

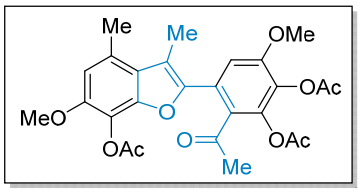
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3565, 3020, 2400, 1700, 1214, 750, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 12.96 (s, 1H), 6.68 (s, 1H), 6.59 (s, 1H), 5.76 (s, 1H), 5.49 (s, 1H), 3.97 (s, 3H), 3.95 (s, 3H), 2.62 (s, 3H), 2.36 (s, 3H), 2.07 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 205.2 (s), 150.9 (s), 150.4 (s), 149.7 (s), 143.7 (s), 142.3 (s), 134.2 (s), 129.2 (s), 124.1 (s), 123.6 (s), 121.9 (s), 115.6 (s), 114.3 (s), 109.9 (d), 108.0 (d), 57.2 (q), 56.3 (q), 28.7 (q), 18.8 (q), 11.0 (q) ppm.

HRMS (m/z): $[M+H]^+$ Calcd. for $C_{20}H_{21}O_7$, 373.1282; found, 373.1279.

***4-(7-Acetoxy-6-methoxy-3,4-dimethylbenzofuran-2-yl)-3-acetyl-6-methoxy-1,2-phenylene diacetate* (6-Ac)**:



To a solution of phenol **6-H** (600 mg, 1.6 mmol), Et_3N (2.3 mL, 16.1 mmol) and DMAP (20 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) was added Ac_2O (0.8 mL, 8.1 mmol) at room temperature. After 6 h, water was added to the reaction mixture and extracted with CH_2Cl_2 (2×50 mL). The combined organic layer was washed with brine (3×20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Purification of residue by silica gel column chromatography (20→50% EtOAc in pet. ether) gave **6-Ac** (0.74g, 93%) as a white powder (**mp** 214–215 °C).

TLC: R_f 0.4 (2:3 v/v EtOAc/pet. ether, UV active).

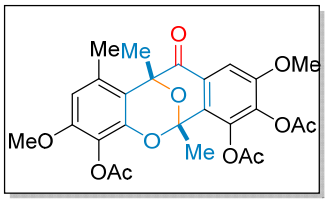
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3020, 1773, 1699, 1458, 1213, 1097, 750, 669 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.97 (s, 1H), 6.72 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 2.66 (s, 3H), 2.45 (s, 3H), 2.39 (s, 3H), 2.34 (s, 3H), 2.28 (s, 3H), 2.02 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6 (s), 168.6 (s), 168.2 (s), 167.5 (s), 152.7 (s), 149.1 (s), 148.1 (s), 146.9 (s), 140.9 (s), 132.8 (s), 129.5 (s), 128.3 (s), 126.8 (s), 123.3 (s), 122.7 (s), 115.4 (s), 110.9 (d), 110.8 (d), 56.9 (q), 56.4 (q), 30.1 (q), 20.4 (q), 20.4 (q), 20.3 (q), 19.3 (q), 11.3 (q) ppm.

HRMS (m/z): $[M+H]^+$ Calcd. for $C_{26}H_{27}O_{10}$, 499.1599; found, 499.1599.

***3,9-Dimethoxy-1,6,12-trimethyl-11-oxo-11,12-dihydro-6H-6,12-epoxydibenzo[b,f]oxocine-4,7,8-triyl triacetate* (5-Ac)**



To a solution of **6-Ac** (300 mg, 0.6 mmol) in acetone (5 mL) and water (2 mL) was added Oxone (47%, 1.57 g, 1.2 mmol) and $NaHCO_3$ (253 mg, 3.01 mmol). The reaction mixture was stirred at room temperature for 8 h. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with EtOAc and washed with water (2–3 times) and then with brine. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. Purification of residue by silica gel column chromatography (20→50% EtOAc in pet. ether) gave **5-Ac** (245 mg, 77%) as a colorless solid (**mp** 193–194 °C).

TLC: R_f 0.4 (2:3 v/v EtOAc/pet. ether, UV active).

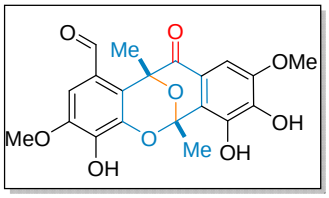
FT–IR ($CHCl_3$): $\bar{\nu}_{max}$ 3565, 3020, 1772, 1520, 1214 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (s, 1H), 6.33 (s, 1H), 3.86 (s, 3H), 3.71 (s, 3H), 2.38 (s, 3H), 2.31 (s, 6H), 2.28 (s, 3H), 2.02 (s, 3H), 1.89 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$): δ 191.6 (s), 168.2 (s), 166.8 (s), 166.5 (s), 152.9 (s), 151.1 (s), 144.1 (s), 140.2 (s), 138.0 (s), 133.8 (s), 126.7 (s), 126.4 (s), 125.7 (s), 113.4 (s), 108.5 (d), 107.0 (d), 95.3 (s), 76.9 (s), 56.3 (q), 55.7 (q), 26.6 (q), 20.6 (q), 20.4 (q), 20.4 (q), 20.3 (q), 20.3 (q) ppm.

HRMS (m/z): $[M+Na]^+$ Calcd. for $C_{26}H_{26}NaO_{11}$, 537.1367; found, 537.1362.

***Integrastatin B* (2)**



To a solution of **5-Ac** (40 mg, 0.08 mmol) in $CHCl_3$ was added *N*-bromosuccinimide (16 mg, 0.09 mmol) and $[C_6H_5C(O)]_2O_2$ (2 mg, 8.0 µmol). The reaction mixture was stirred under sunlight for 25–30 min. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with CH_2Cl_2 and washed with water (2–3 times) and then with brine. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was subjected to hydrolysis in the presence of K_2CO_3 (50 mg, 0.4 mmol) in dioxane (2 mL) and H_2O (1 mL) at 50–60 °C. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with EtOAc. The aqueous layer was neutralized with 1N HCl (2.0 mL) and again extracted with EtOAc (2–3 times). The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. Purification of the residue by silica gel column chromatography (40→80% EtOAc in pet. ether) gave **2** (19 mg, 63%) as a brown solid.

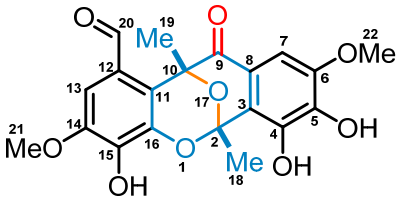
TLC: R_f 0.4 (7:3 v/v EtOAc/pet. ether, UV active).

^{1}H NMR (700 MHz, $CDCl_3$): (*NMR was recorded in 1:1 CD_3Cl:CD_3CN and reference was assigned to **H_{13}** of natural product with δ 7.14 ppm*) δ 10.22 (s, 1H), 7.14 (s, 1H), 7.06 (s, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 2.91 (s, 1H), 2.80 (s, 1H), 2.16 (s, 3H), 1.87 (s, 3H) ppm.

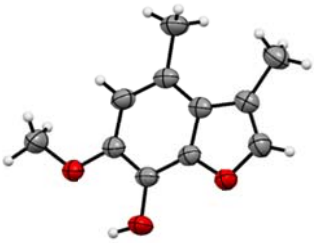
^{13}C NMR (175 MHz, $CDCl_3$): (*NMR was recorded in 1:1 CD_3Cl:CD_3CN and reference was assigned to **C_{10}** of natural product with δ 77.1 ppm*) δ 193.7 (s), 190.3 (d), 148.6 (s), 147.7 (s), 142.0 (s),

140.9 (s), 140.7 (s), 140.1 (s), 126.0 (s), 121.3 (s), 120.5 (s), 120.4 (s), 105.8 (d), 101.9 (d), 97.5 (s), 77.1 (s), 56.9 (q), 56.7 (q), 26.6 (q), 25.9 (q) ppm.

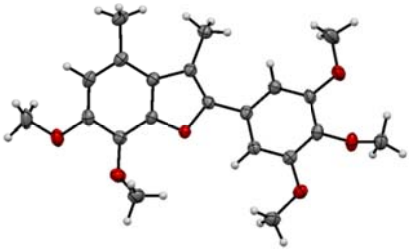
HRMS (m/z): $[M+H]^+$ Calcd. for $C_{20}H_{19}O_9$, 403.1024; found, 403.1021 and $[M+Na]^+$ for $C_{20}H_{18}NaO_9$, 425.0843; found, 425.0838.

Position	^{1}H of Natural 2	^{1}H of Synthetic 2	^{13}C of Natural 2	^{13}C of Synthetic 2
2			97.8 (s)	97.5 (s)
3			120.7 (s)	120.5 (s)
4			140.1 (s)	140.1 (s)
5			142.2 (s)	142.0 (s)
6			148.7 (s)	148.6 (s)
7	7.06 (s, 1 H)	7.06 (s, 1 H)	101.8 (d)	101.9 (d)
8			120.4 (s)	120.4 (s)
9			193.7 (s)	193.7 (s)
10			77.1 (s)	77.1 (s)
11			121.3 (s)	121.3 (s)
12			126.0 (s)	126.0 (s)
13	7.14 (s, 1 H)	7.14 (s, 1 H)	105.7 (d)	105.8 (d)
14			147.8 (s)	147.7 (s)
15			140.9 (s)	140.9 (s)
16			140.8 (s)	140.7 (s)
18	2.15 (s, 3 H)	2.16 (s, 3 H)	26.5 (q)	26.6 (q)
19	1.87 (s, 3 H)	1.87 (s, 3 H)	25.8 (q)	25.9 (q)
20	10.21 (s, 1 H)	10.22 (s, 1 H)	190.6 (d)	190.3 (d)
21	3.75 (s, 3 H)	3.81 (s, 3 H)	56.6 (q)	56.8 (q)
22	3.85 (s, 3 H)	3.84 (s, 3 H)	56.7 (q)	56.7 (q)

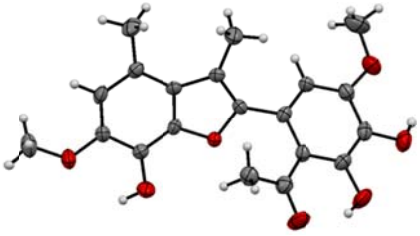
ORTEP of structures 8-H, 10 and 6-H:



8-H; CCDC 1450408



10; CCDC 1407994



6-H; CCDC 1407996

X–ray crystallographic data of compound **8-H**, **10** and **6-H** were carried out on a Bruker SMART APEX II CCD diffractometer with graphite–monochromatized (MoK_{α}= 0.71073Å) radiation. The X–ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from three sets of 36 frames. Data were collected with ω scan width of 0.5° at different settings of φ and 2θ with a frame time of 10 sec each for **8-H**, **10** and **6-H** keeping the sample–to–detector distance fixed at 5.00 cm. The X–ray data collection was monitored by APEX2 program (Bruker, 2006). All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2006). SHELX–97 was used for structure solution and full matrix least–squares refinement on F^2. All the hydrogen atoms were placed in geometrically idealized position and constrained to ride on their parent atoms. ORTEP views of seven compounds were drawn with 30% probability displacement ellipsoids, and H atoms are shown as small spheres of arbitrary radii.

References for X–ray crystallography

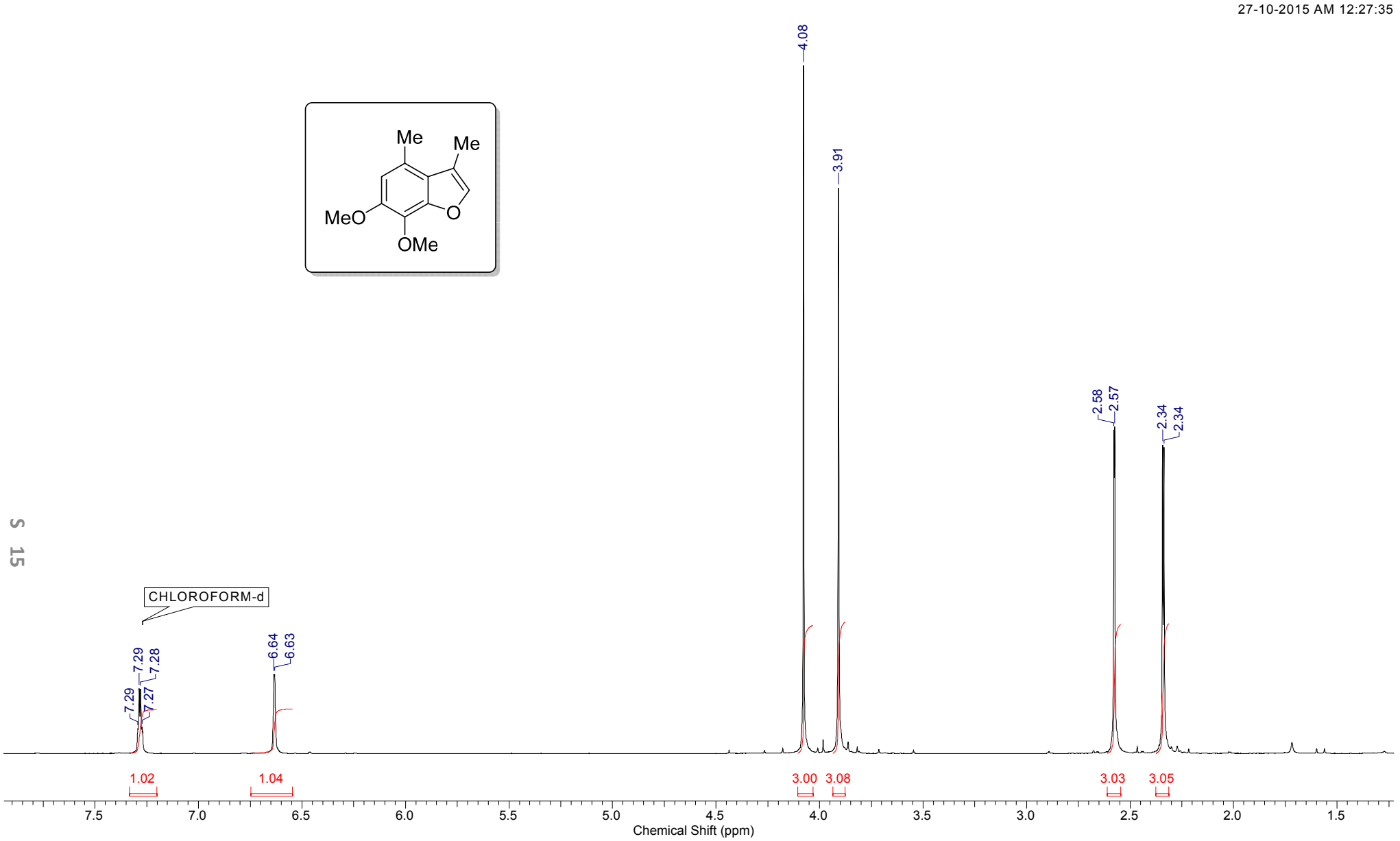
(1) Bruker (2006). *APEX2*, *SAINT* and *SADABS*. Bruker AXS Inc., Madison, Wisconsin, USA.

(2) Sheldrick, G. M.; *Acta Crystallogr*. **2008**, A *64*, 112. (3) Farrugia, L. J.. *J. Appl. Cryst.,* **1997**, *30*, 565–565.

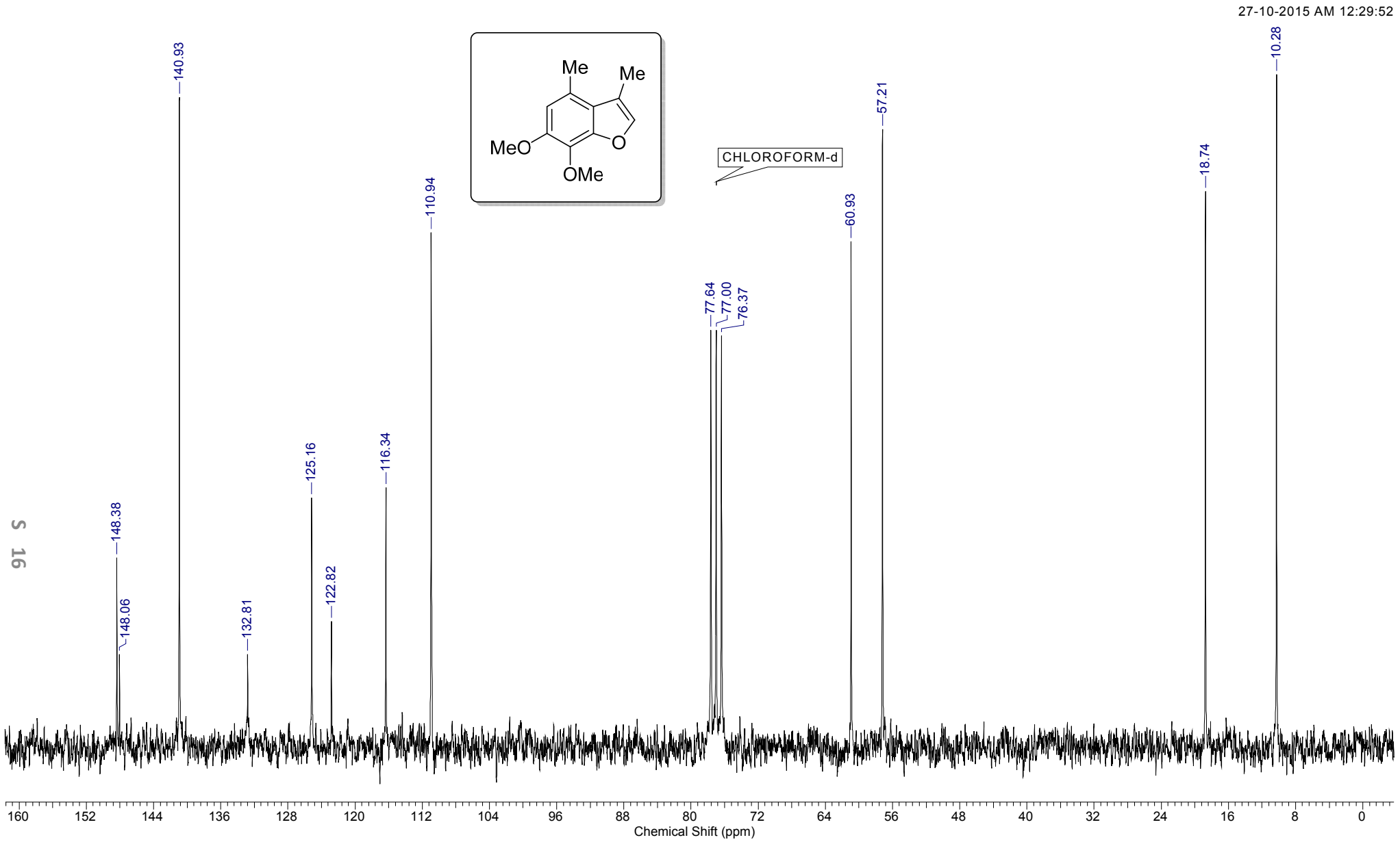
CCDC for all three compounds contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from by contacting the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Tel: +44 (0)1223 336408; Fax: +44 (0)1223 336033 or by linking to http://www.ccdc.cam.ac.uk/pages/Home.aspx

↓	**10**	**8-H**	**6-H**
Structure Code.	ATUL280315	Int-3	ABC
CCDC No.	1407994	1450408	1407996
Mol. Formula	$C_{21}H_{24}O_6$	$C_{11}H_{12}O_3$	$C_{20}H_{20}O_7$
Mr	372.40	192.21	372.36
Temp. (K)	200(2)	296(2)	293(2)
Crystal System	Monoclinic	Triclinic	Monoclinic
Space group	*$P2_1/c$*	*P-1*	*P21/c*
a/Å	11.9383(8)	7.2646(7)	13.364(4)
b/Å	10.2634(6)	8.0955(8)	7.917(3)
c/Å	15.2907(9)	8.0955(8)	21.513(6)
α/°	90	90.831	90
β/°	97.621(3)	97.639(6)	127.540(18)
γ/°	90	93.425(6)	90
V/Å^3	1857.0(2)	476.06(8)	1804.8(10)
Z,D_{calc}/g cm^{-3}	4, 1.332	2, 1.341	4, 1.370
μ/mm^{-1}	0.097	0.097	0.104
F (000)	792	204	784
θ max/°	25.00	24.99	24.99
Absor.correction	multi-scan	multi-scan	multi-scan
Refln. collected	28576	8060	13682
Unique Refln.	3272	1681	3173
Observed Refln.	3010	1515	2115
R_{int}	0.0247	0.0149	0.1291
No. of Parameter	251	131	250
R_1_obs, R_1 _*all*	0.0348, 0.0377	0.03753, 0.0409	0.0940, 0.1387
wR_2_obs, wR_2_*all*	0.0935, 0.0965	0.1039, 0.1078	0.1863, 0.2077
GoF	1.045	1.070	1.110
$\Delta\rho_{max}$,$\Delta\rho_{min}$/eÅ^{-3}	0.176, -0.209	0.150, -0.165	0.362, -0.279

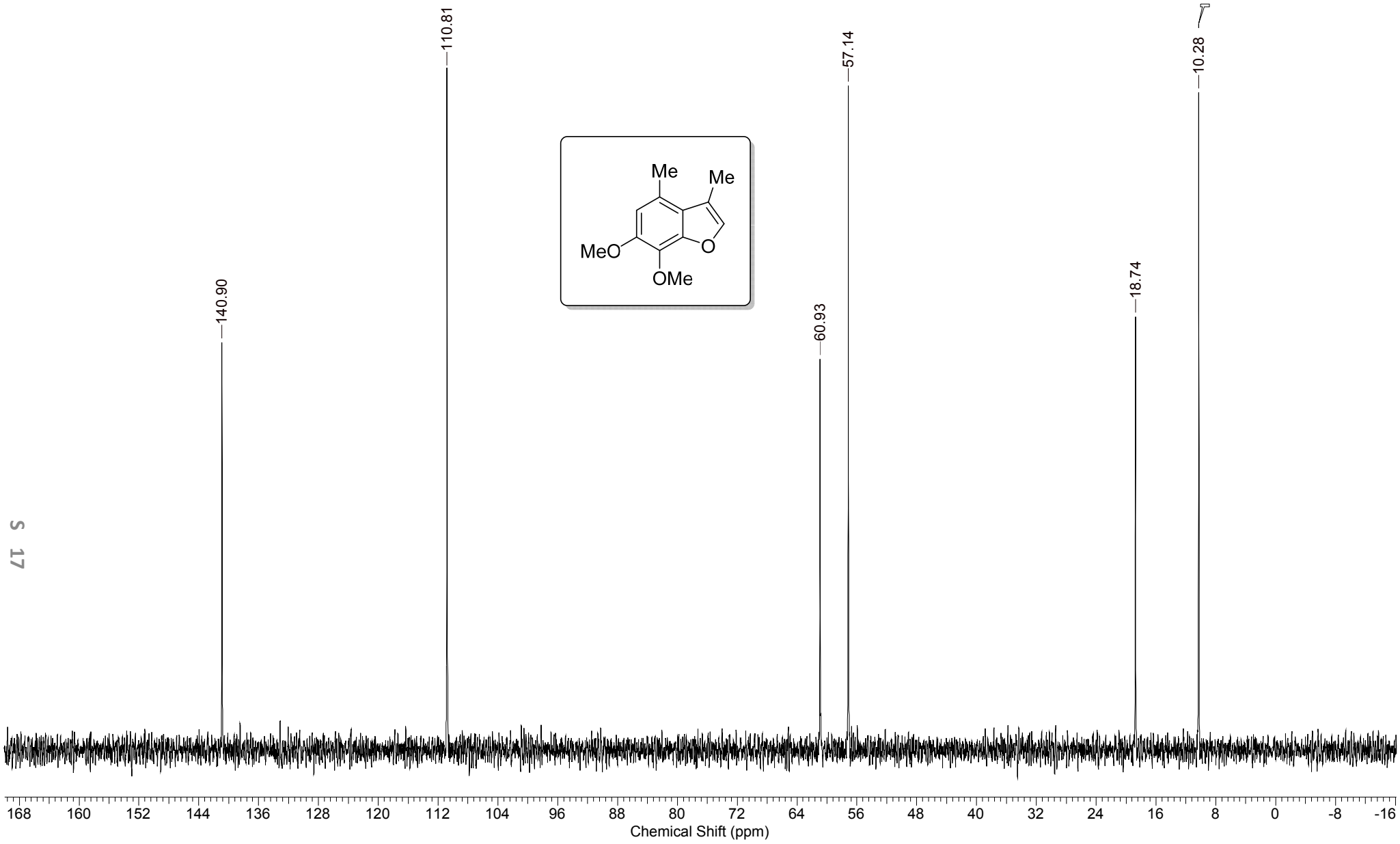
Crystallographic Data for 10, 8-H and 6-H



^{1}H NMR of compound 8-Me

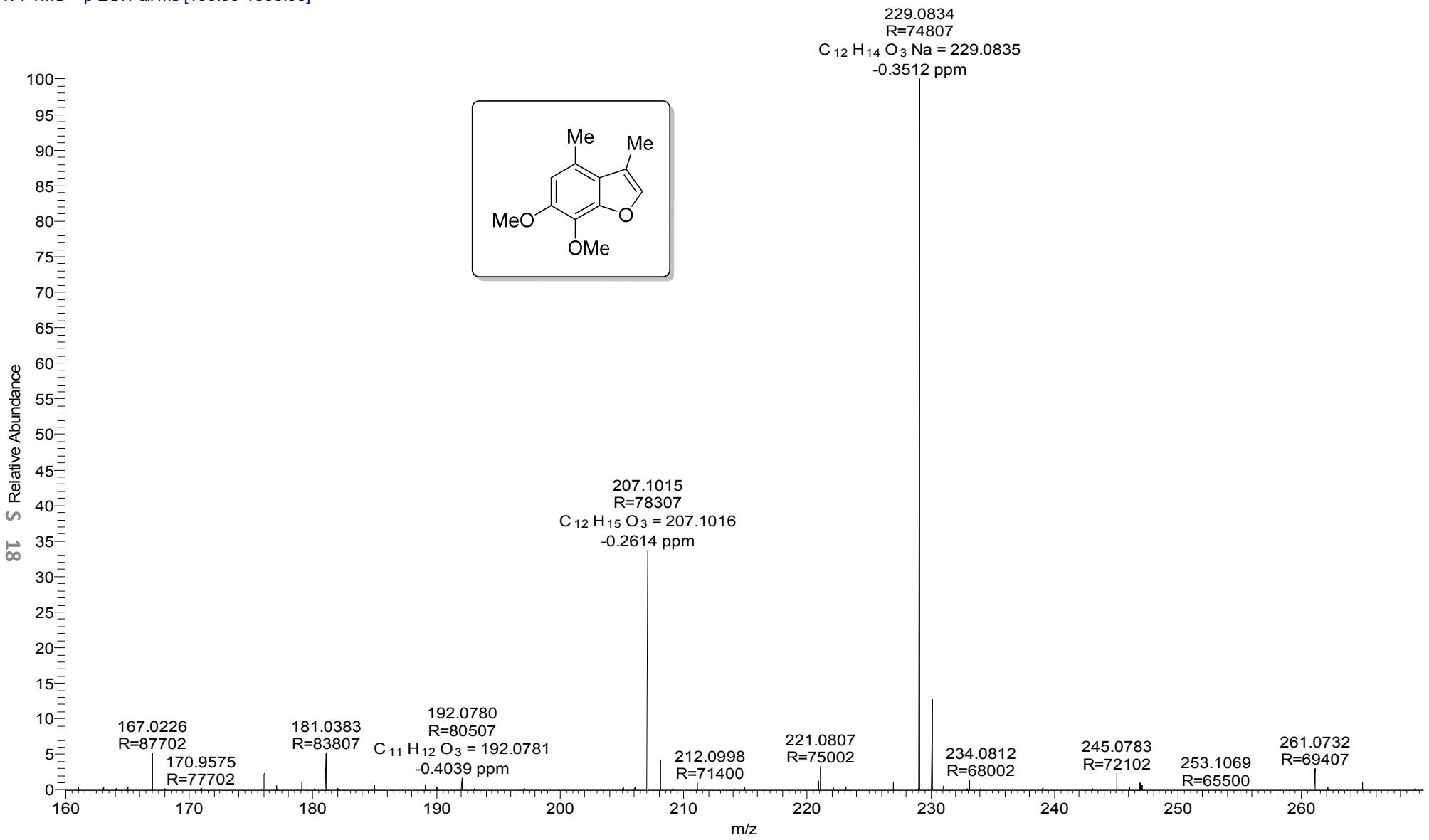


^{13}C NMR of compound 8-Me

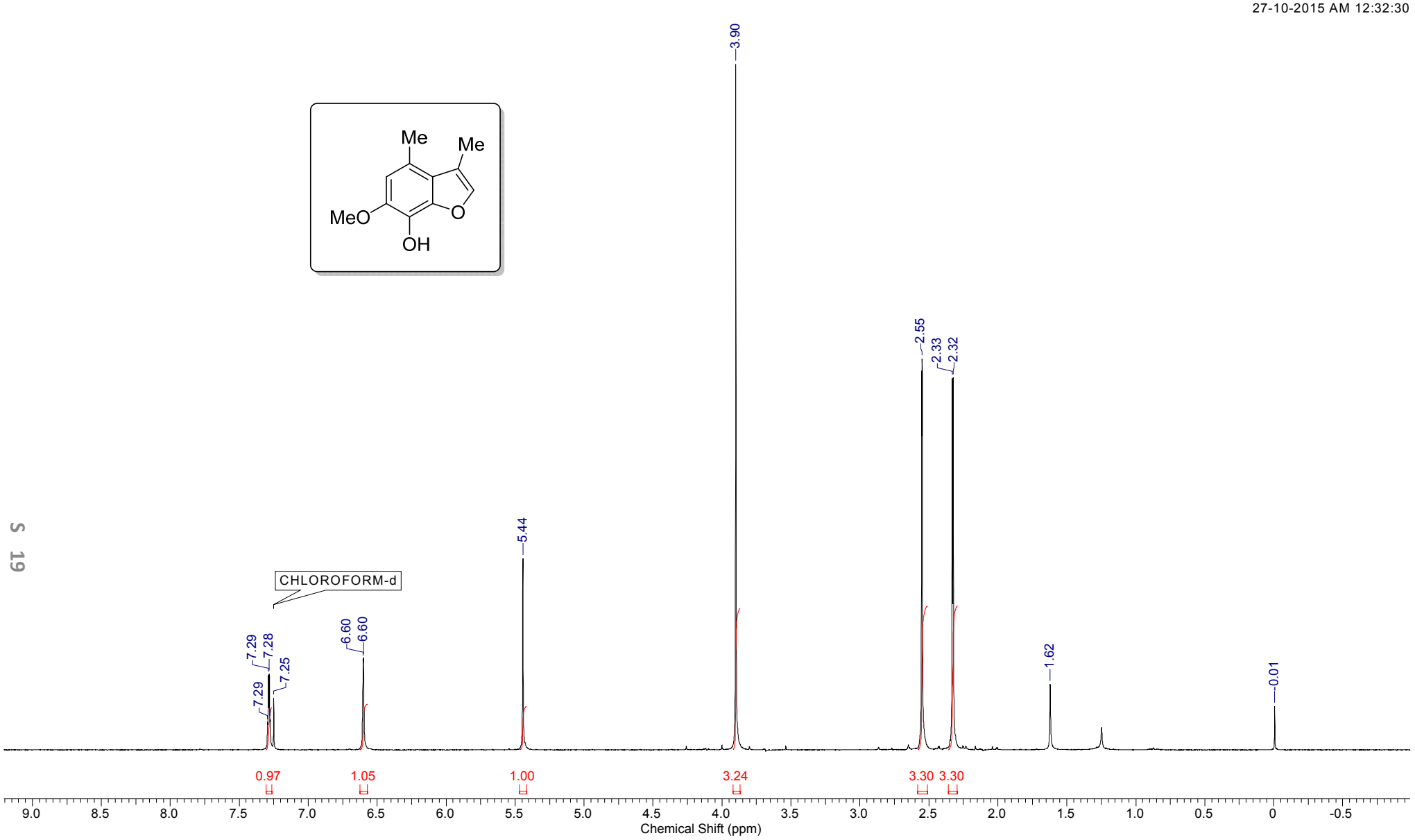


DEPT of compound 8-Me

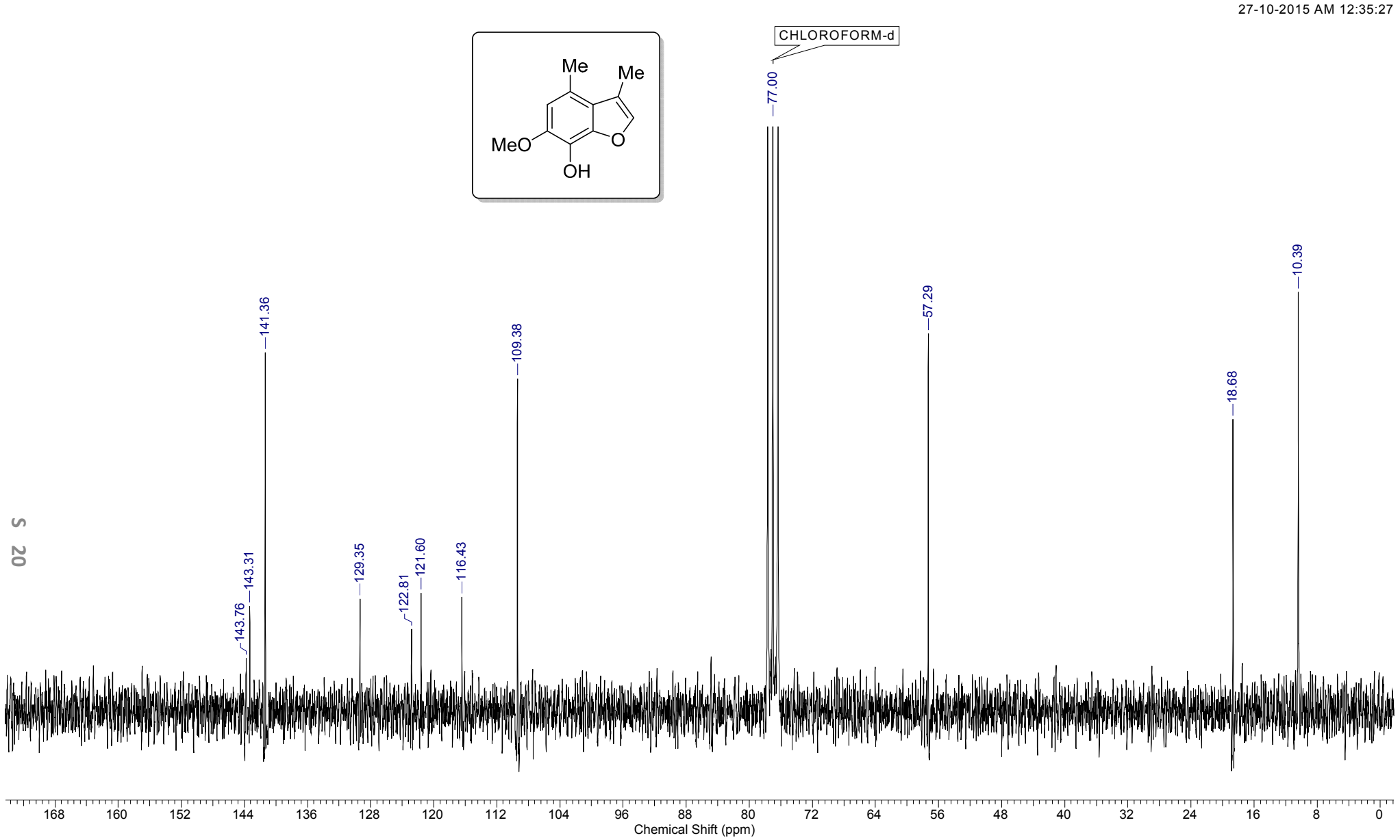
AMI-1_160128154751 #121 RT: 0.54 AV: 1 NL: 4.28E8
T: FTMS + p ESI Full ms [100.00-1500.00]



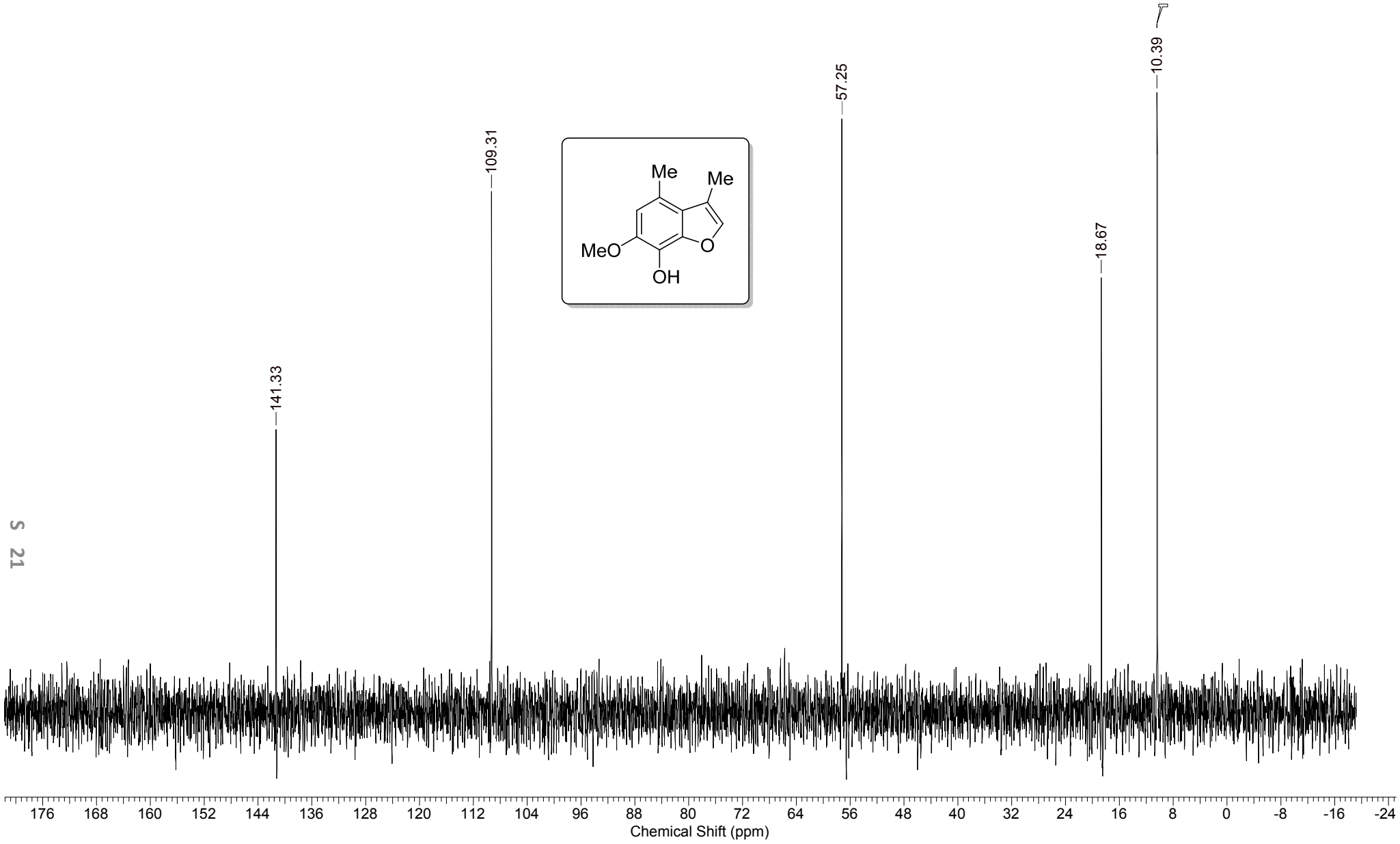
HRMS of compound 8-Me



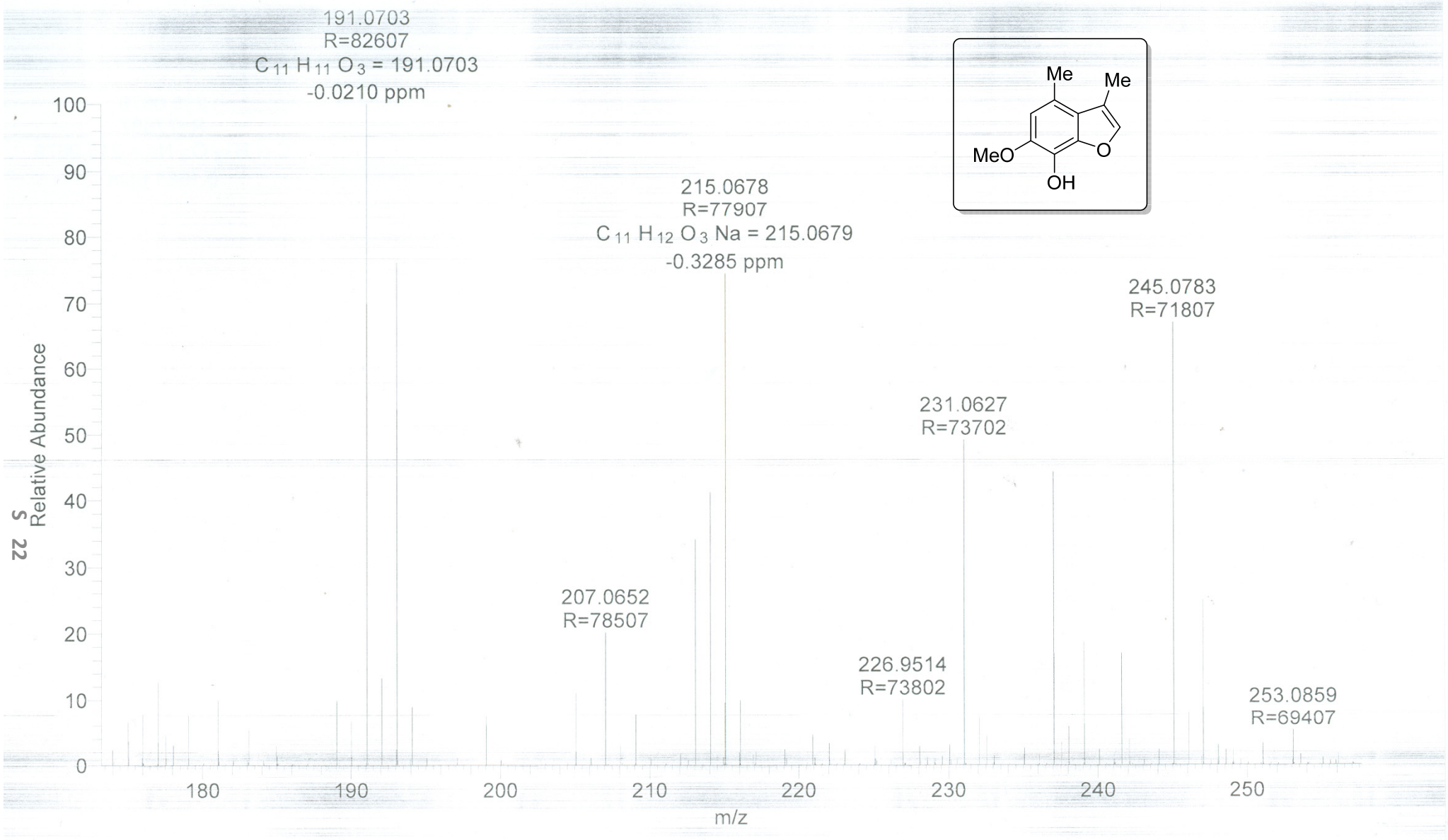
^{1}H NMR of compound 8-H



^{13}C NMR of compound 8-H

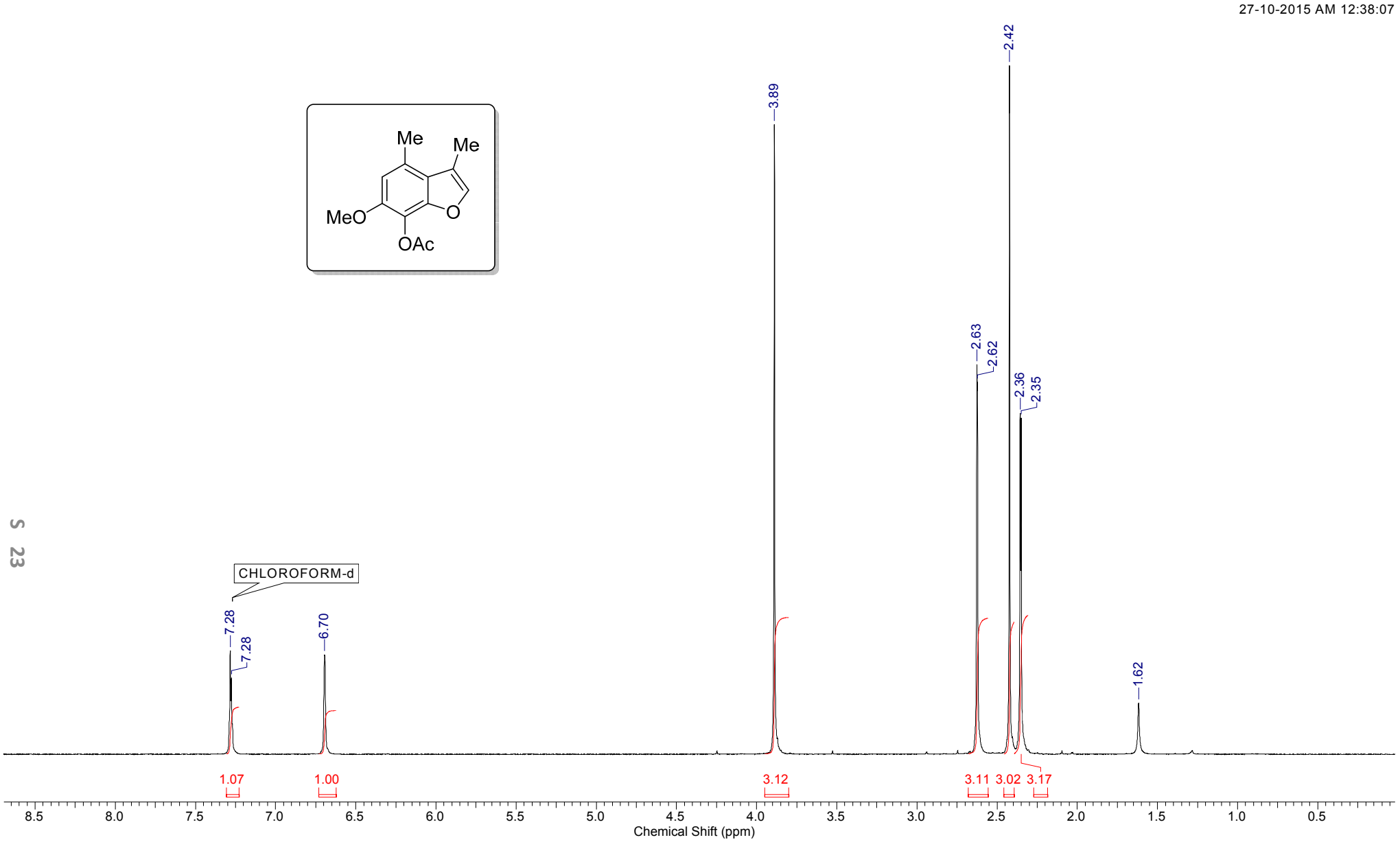


DEPT of compound 8-H

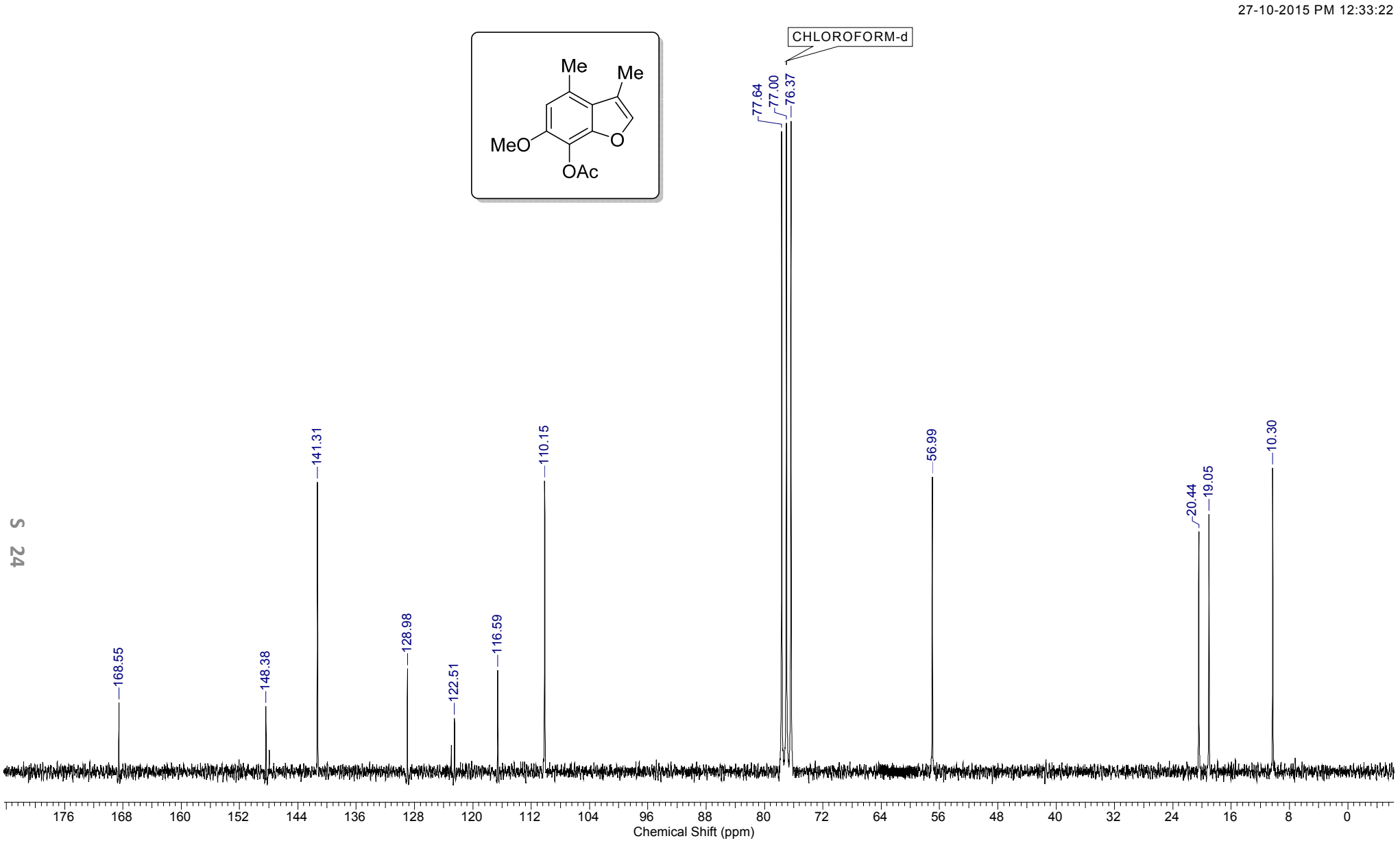


S 22

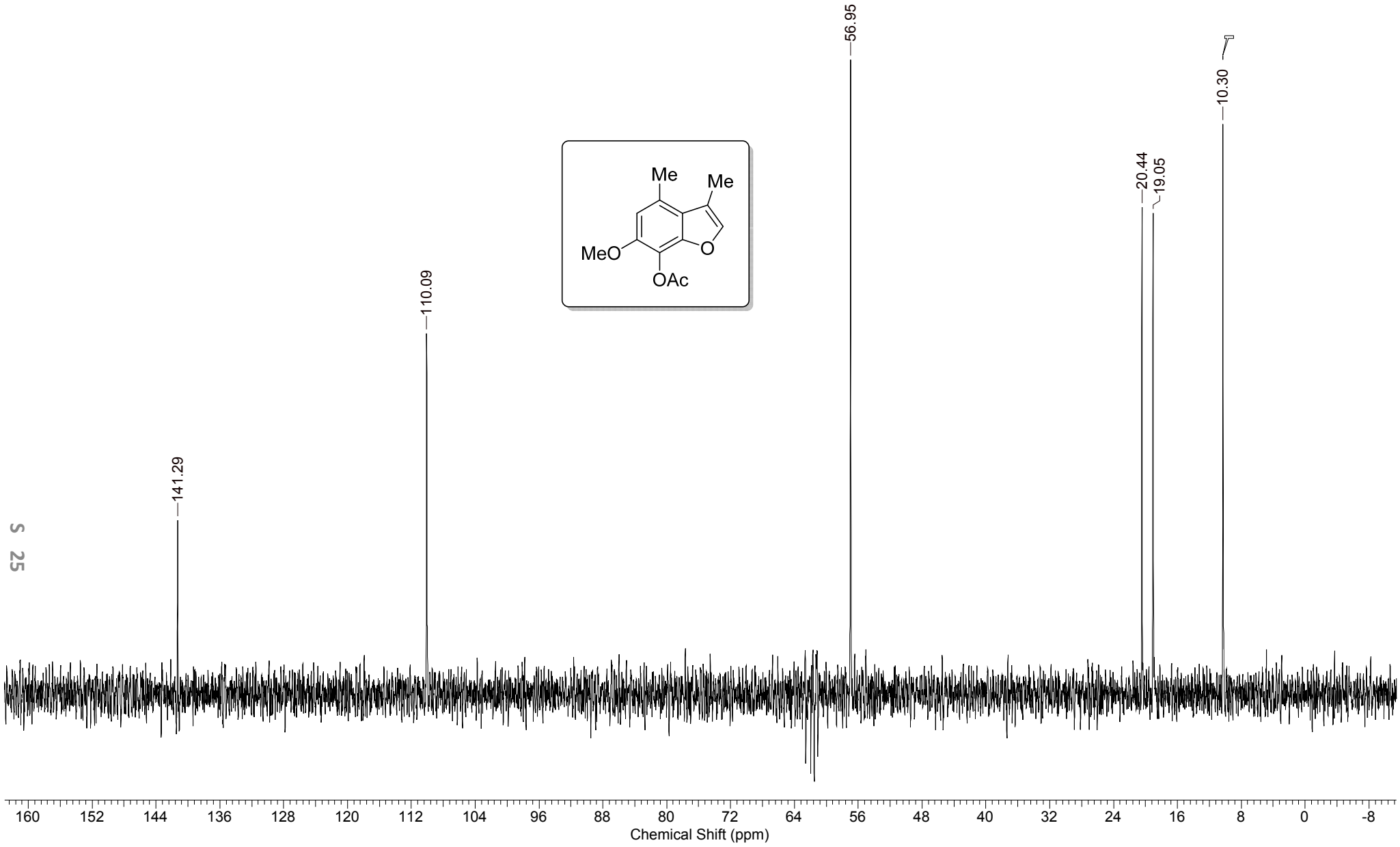
HRMS of compound 8-H



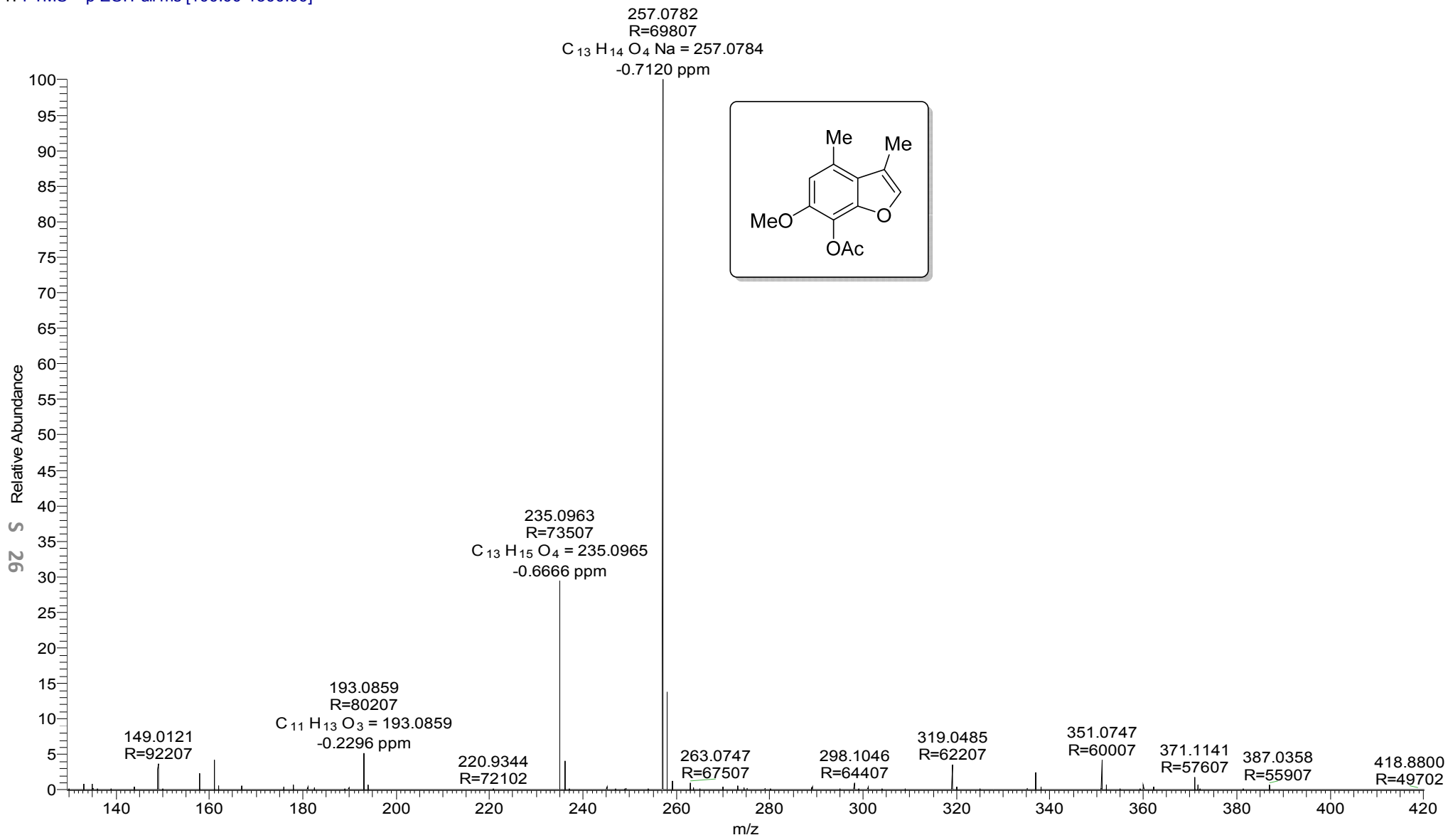
^{1}H NMR of compound 8-Ac



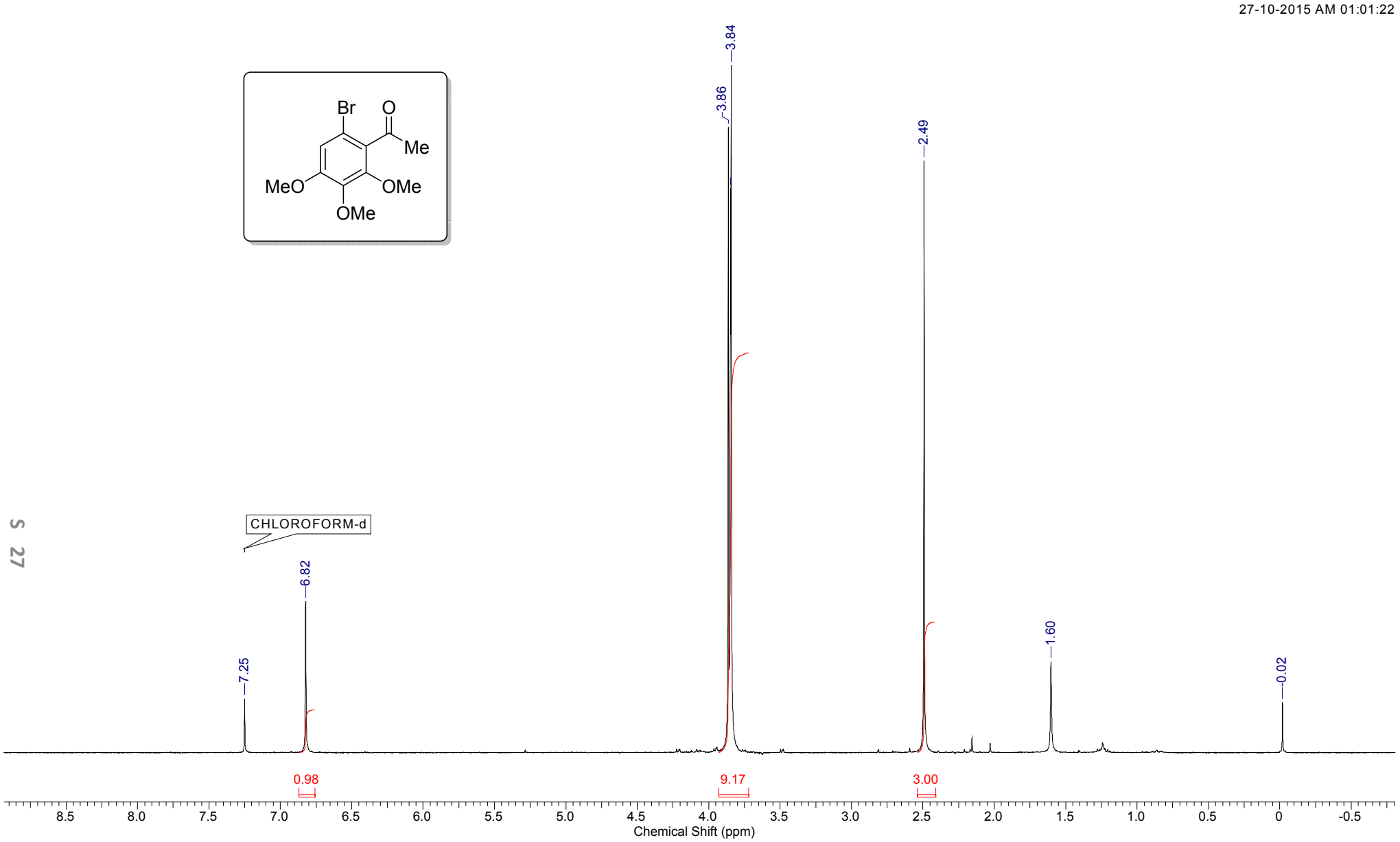
^{13}C NMR of compound 8-Ac



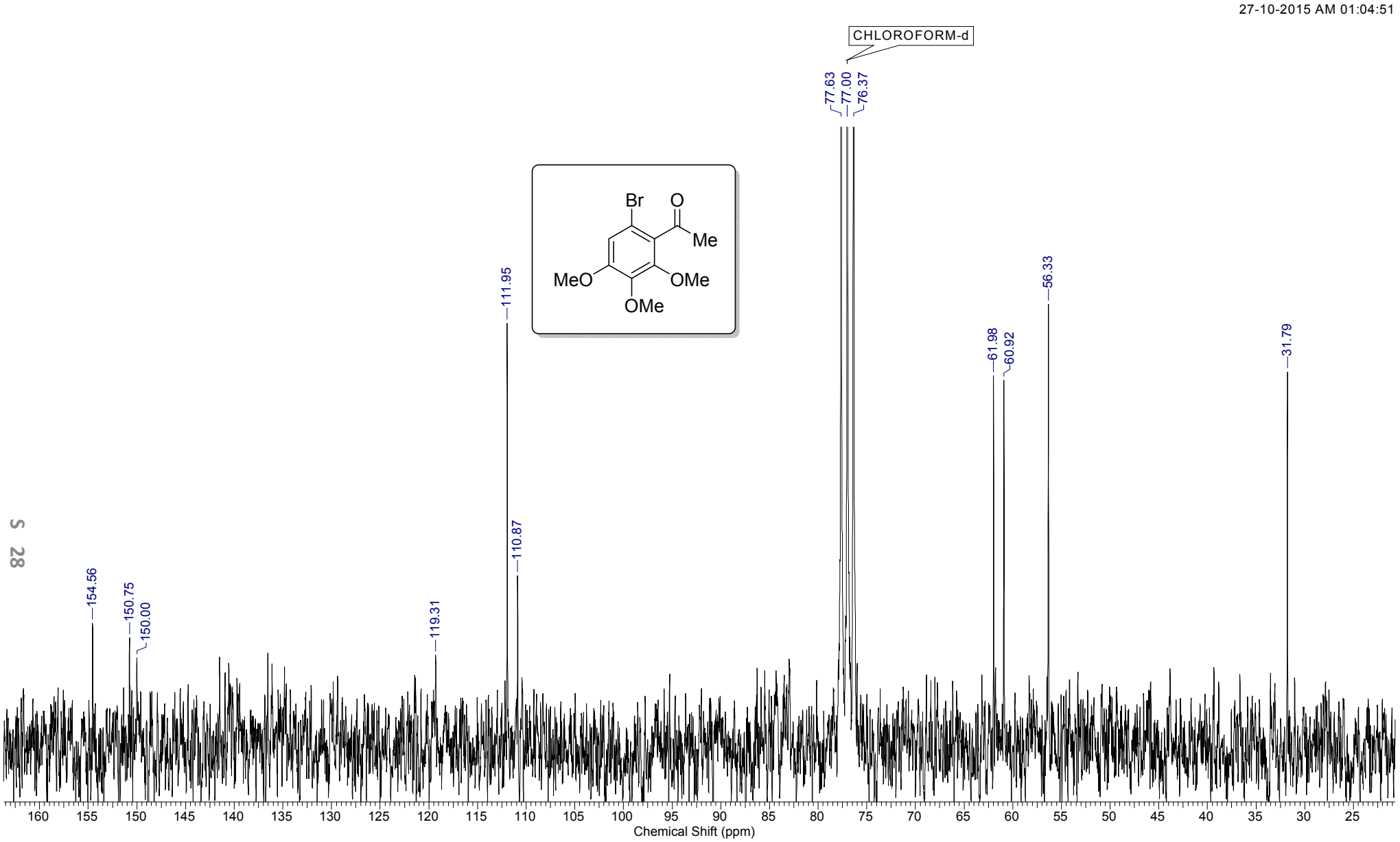
DEPT of compound 8-Ac



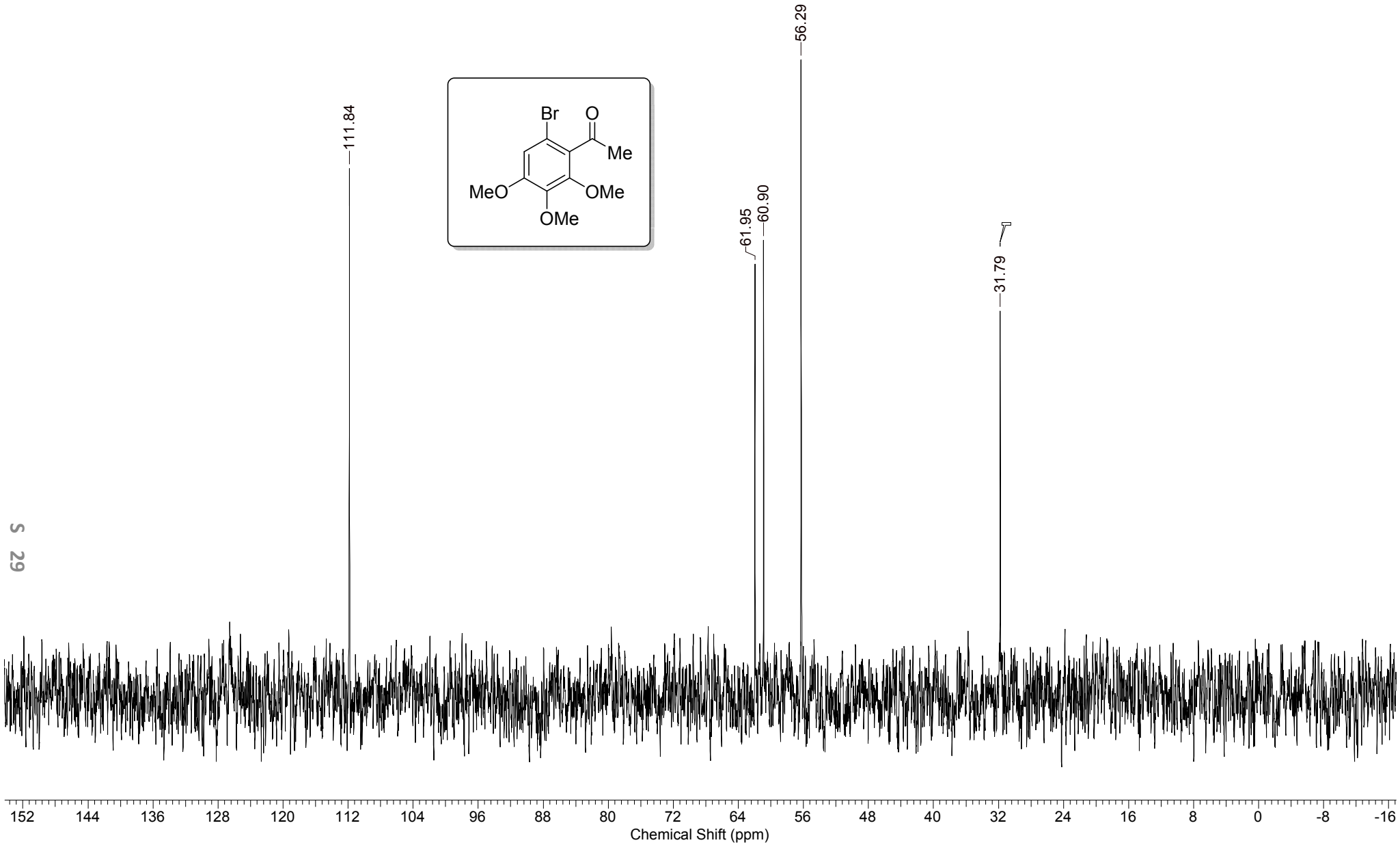
HRMS of compound 8-Ac



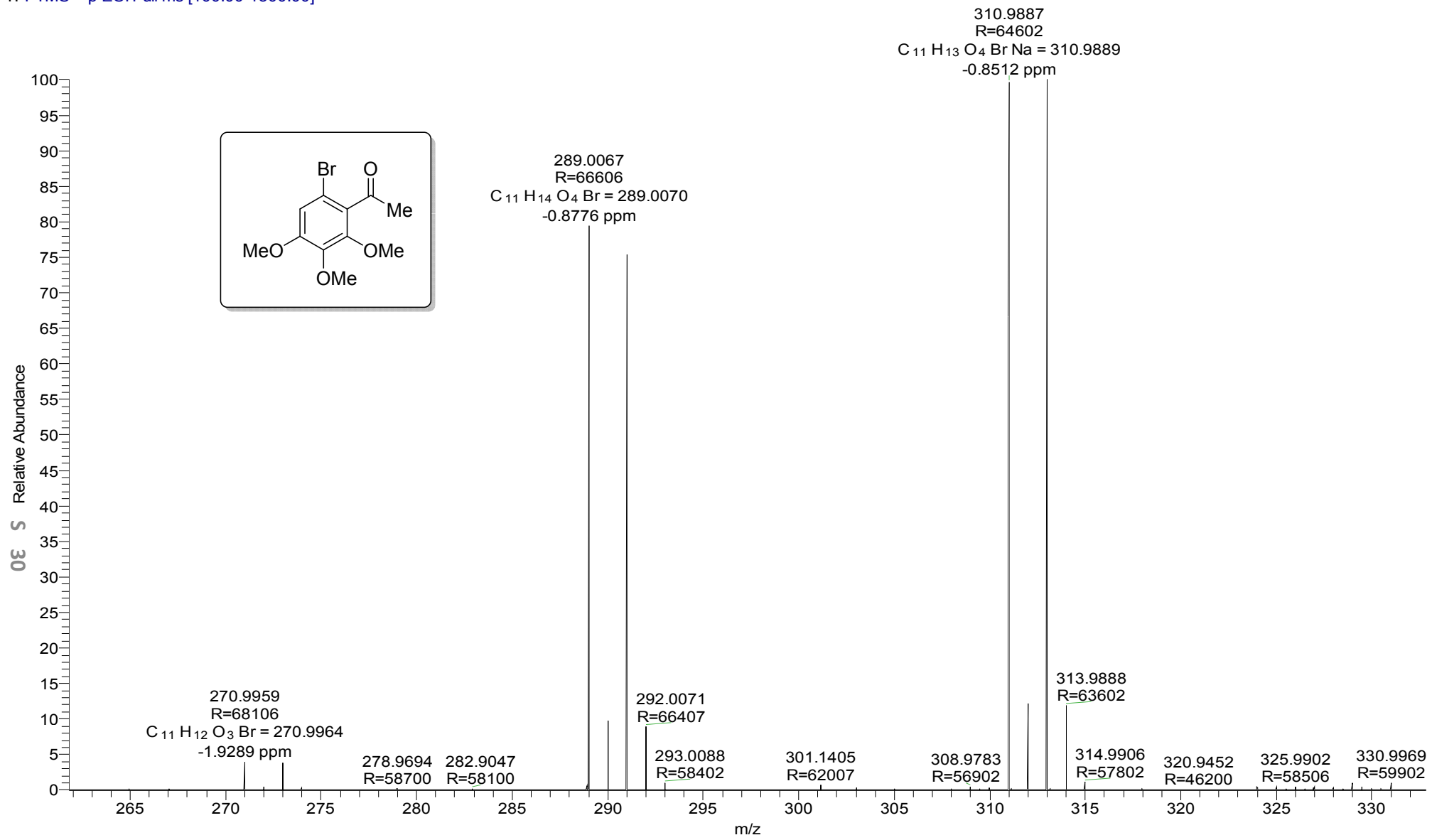
^{1}H NMR of compound 7-Me



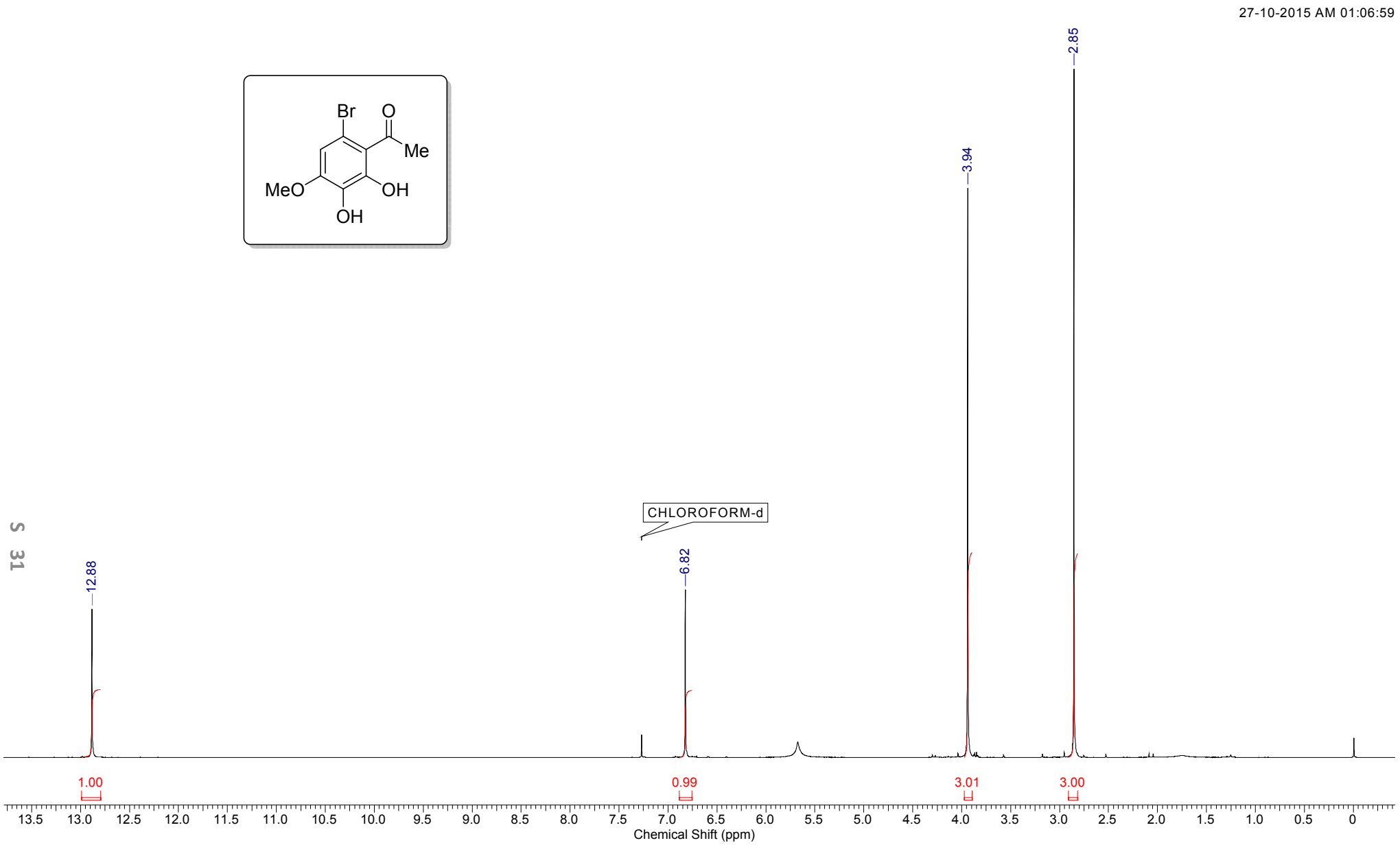
^{13}C NMR of compound 7-Me



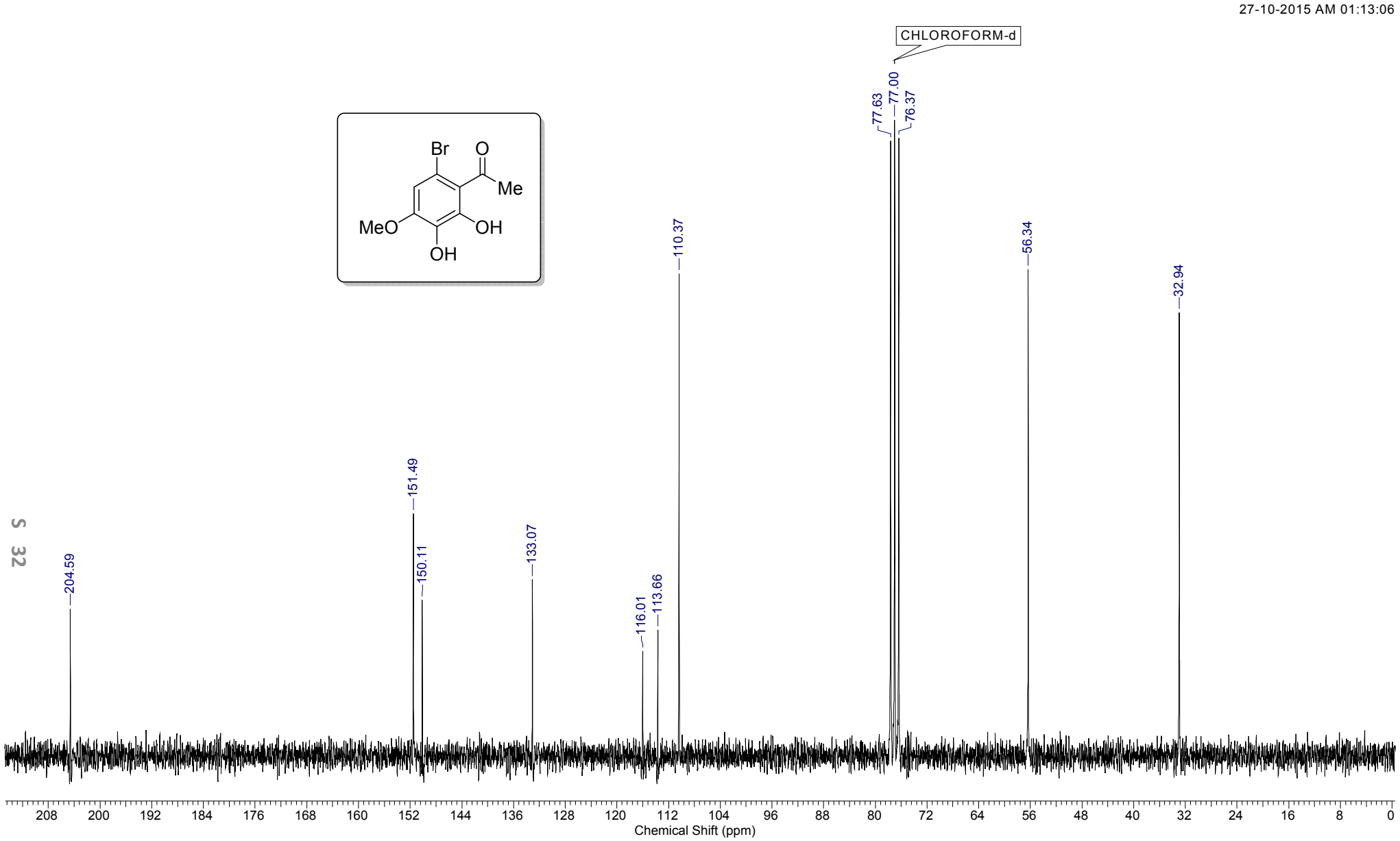
DEPT of compound 7-Me



HRMS of compound 7-Me



^{1}H NMR of compound 7-H



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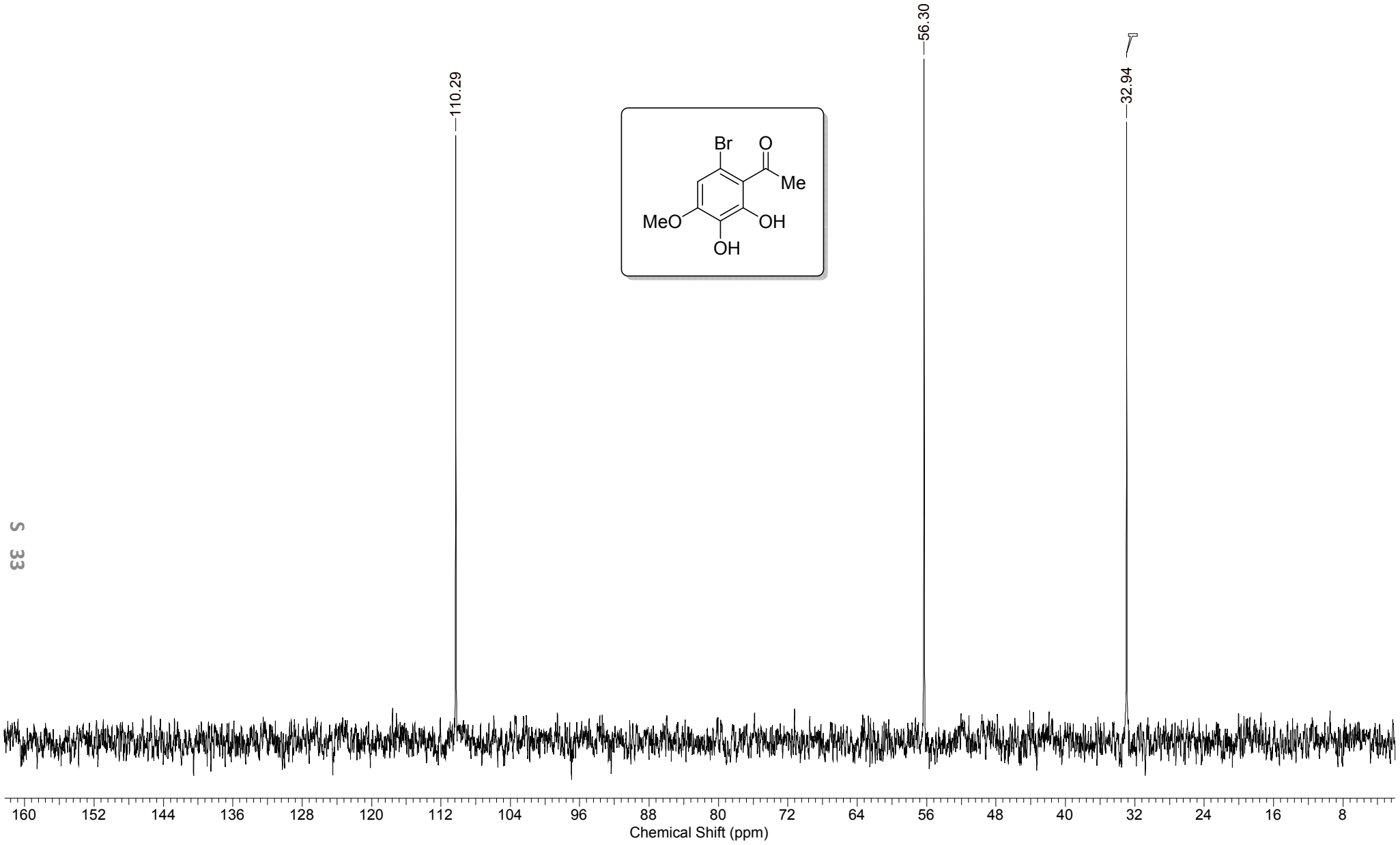
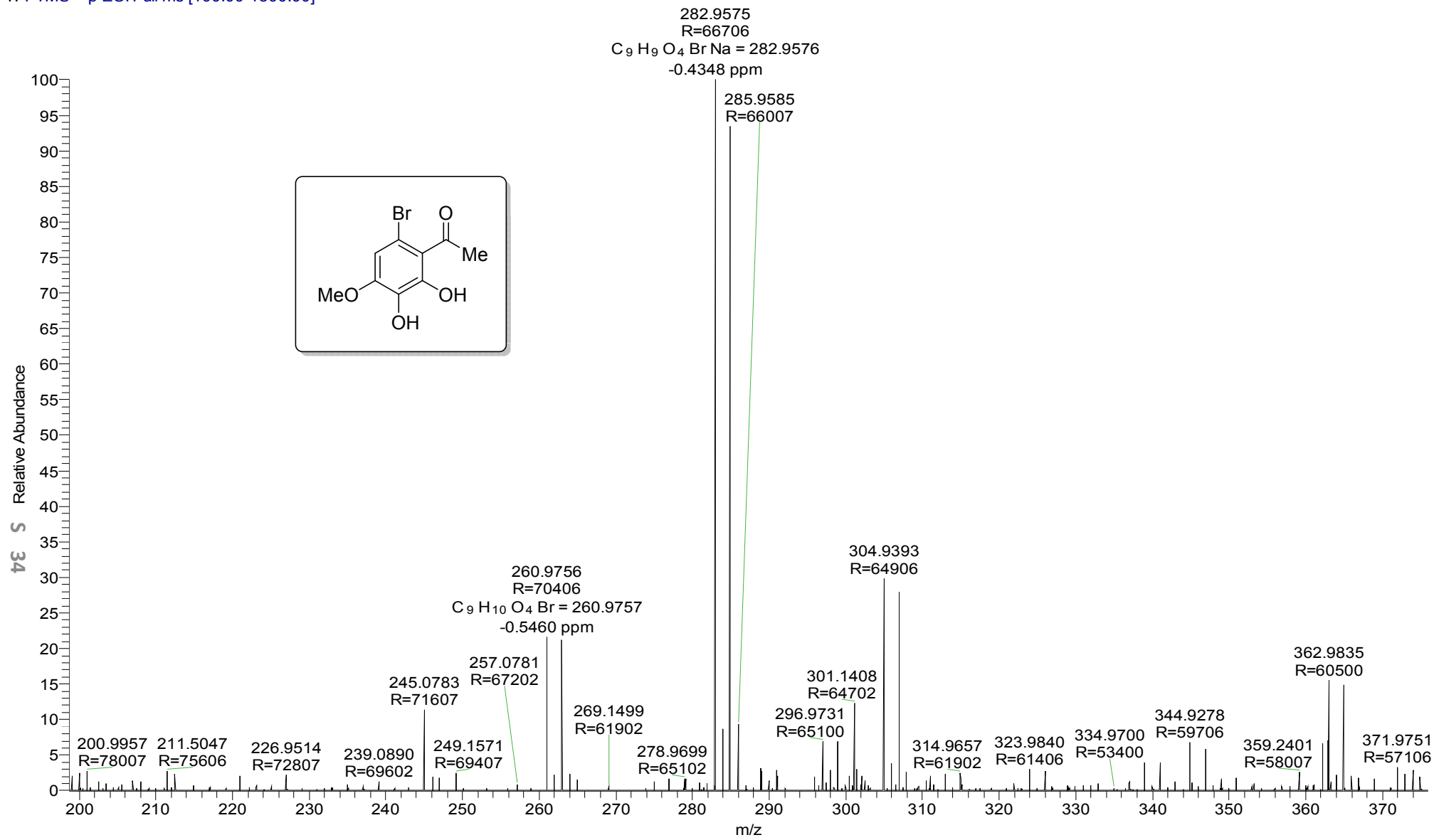
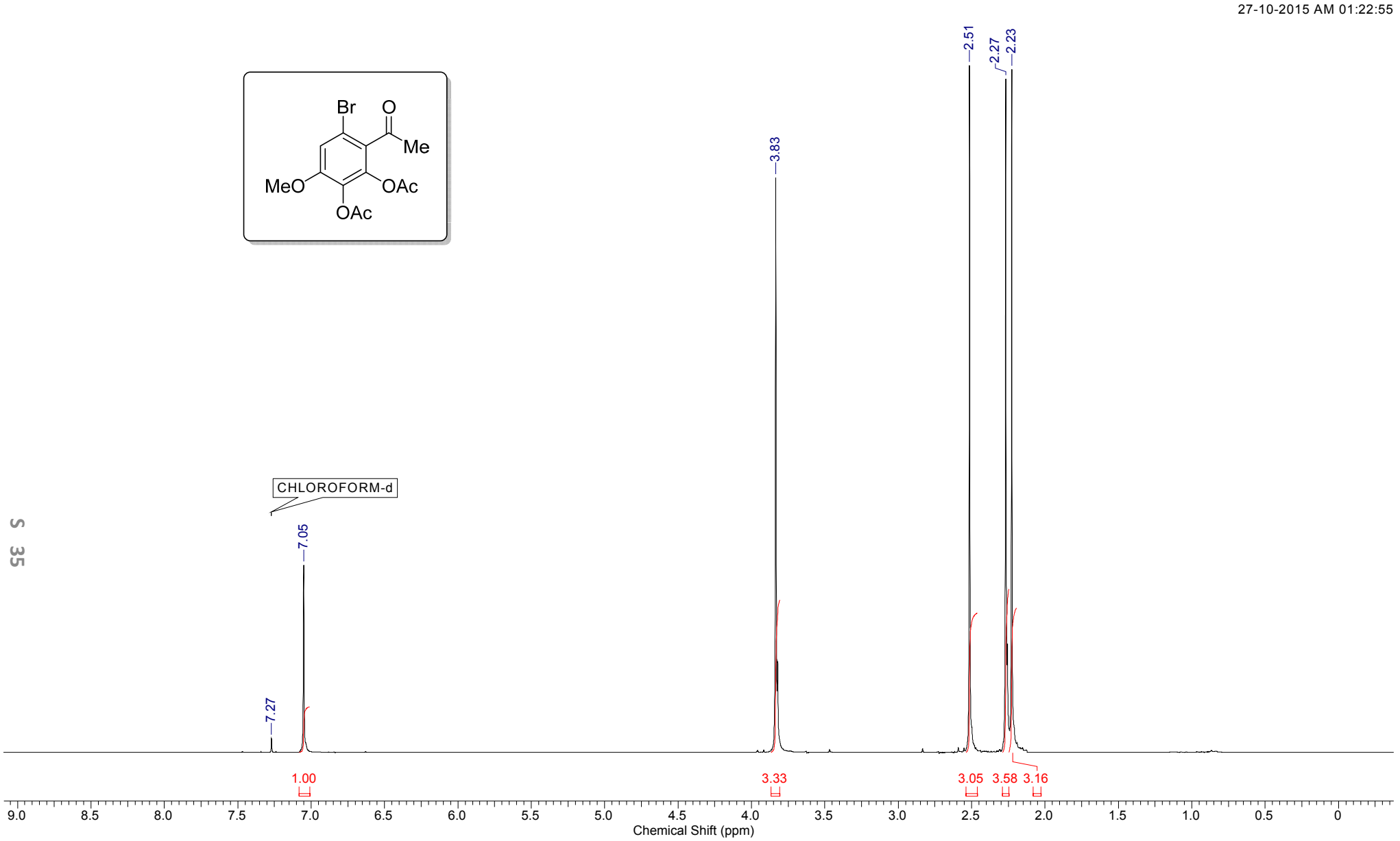


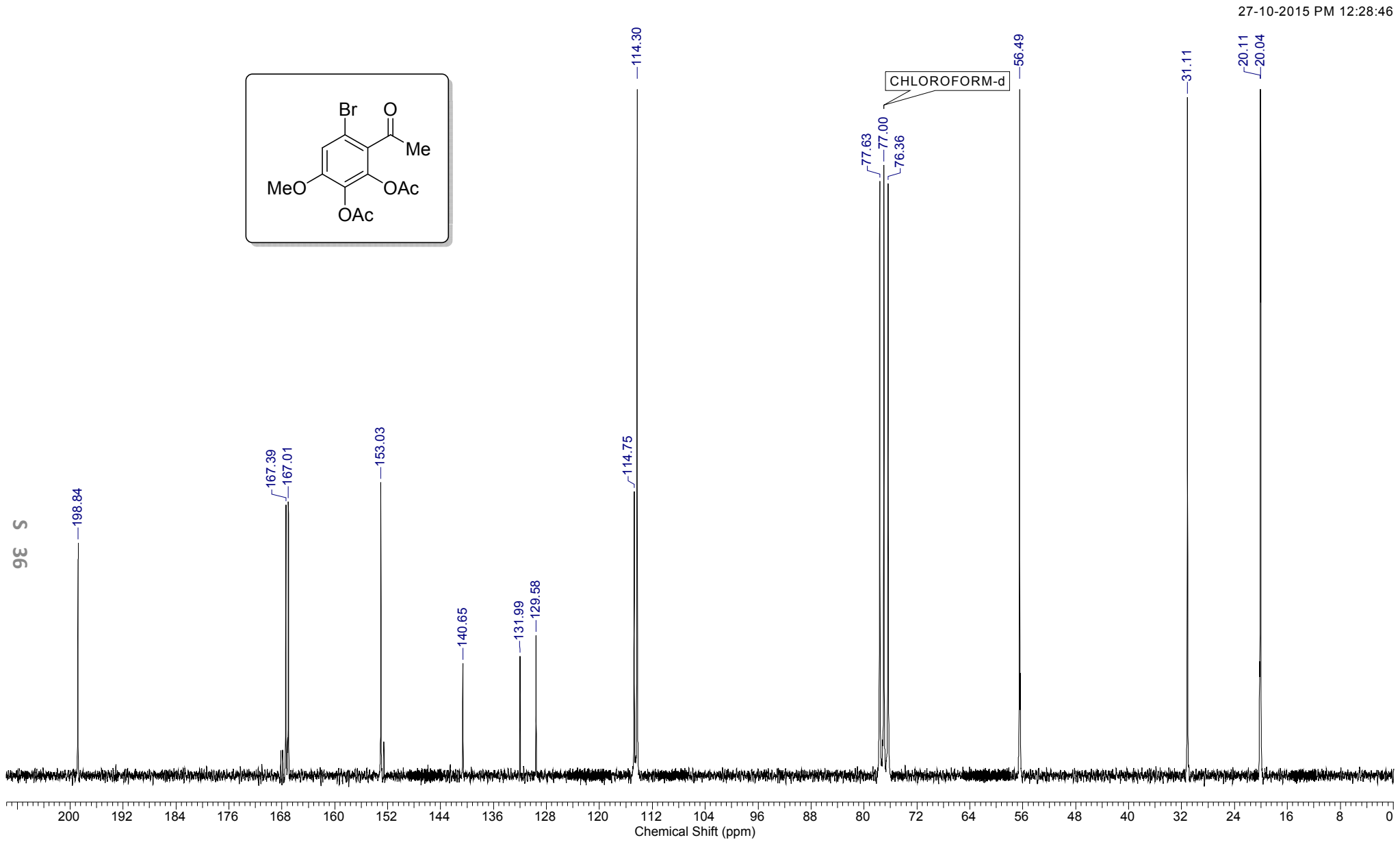
DEPT of compound 7-H



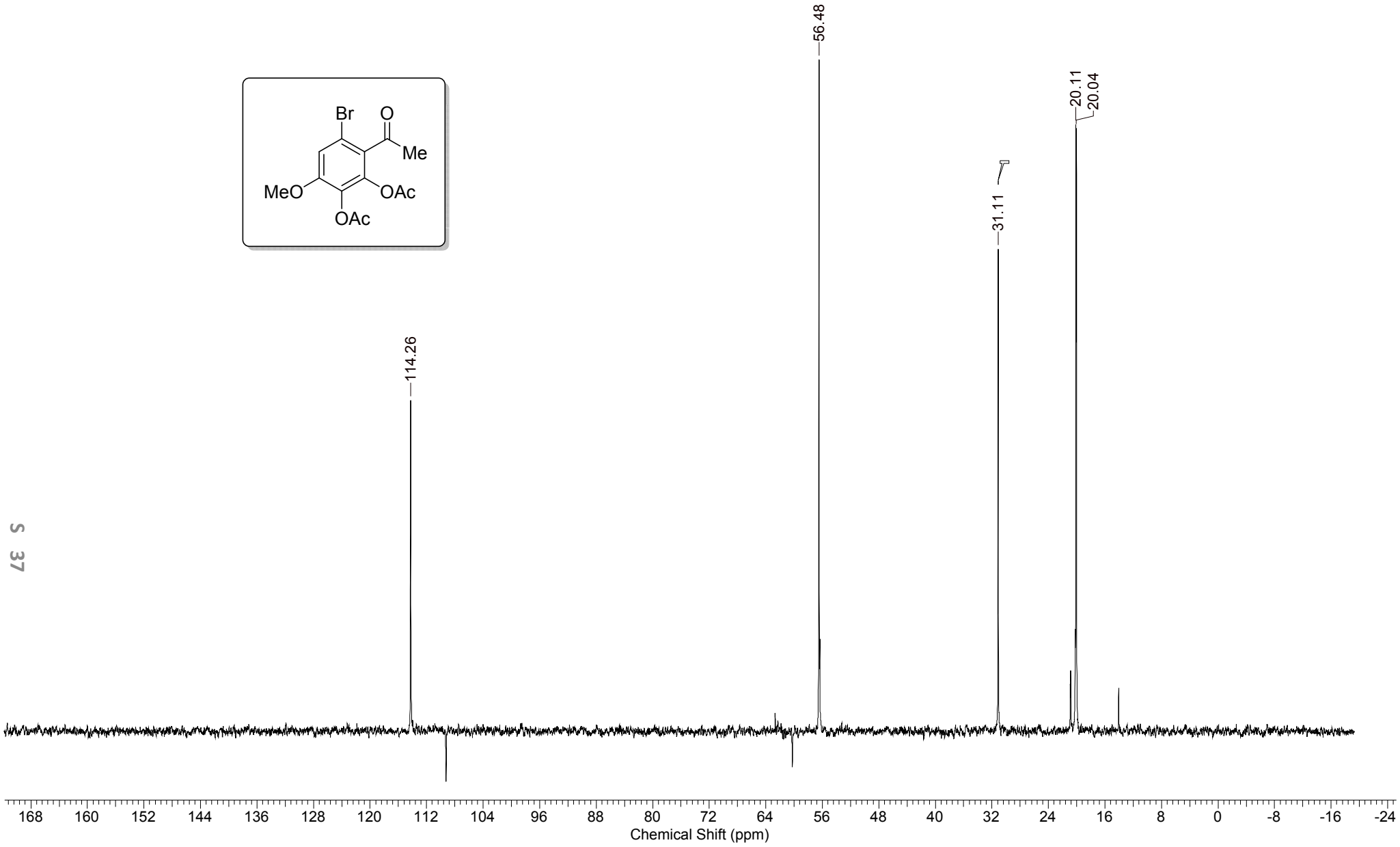
HRMS of compound 7-H



^{1}H NMR of compound 7-Ac



^{13}C NMR of compound 7-Ac



DEPT of compound 7-Ac

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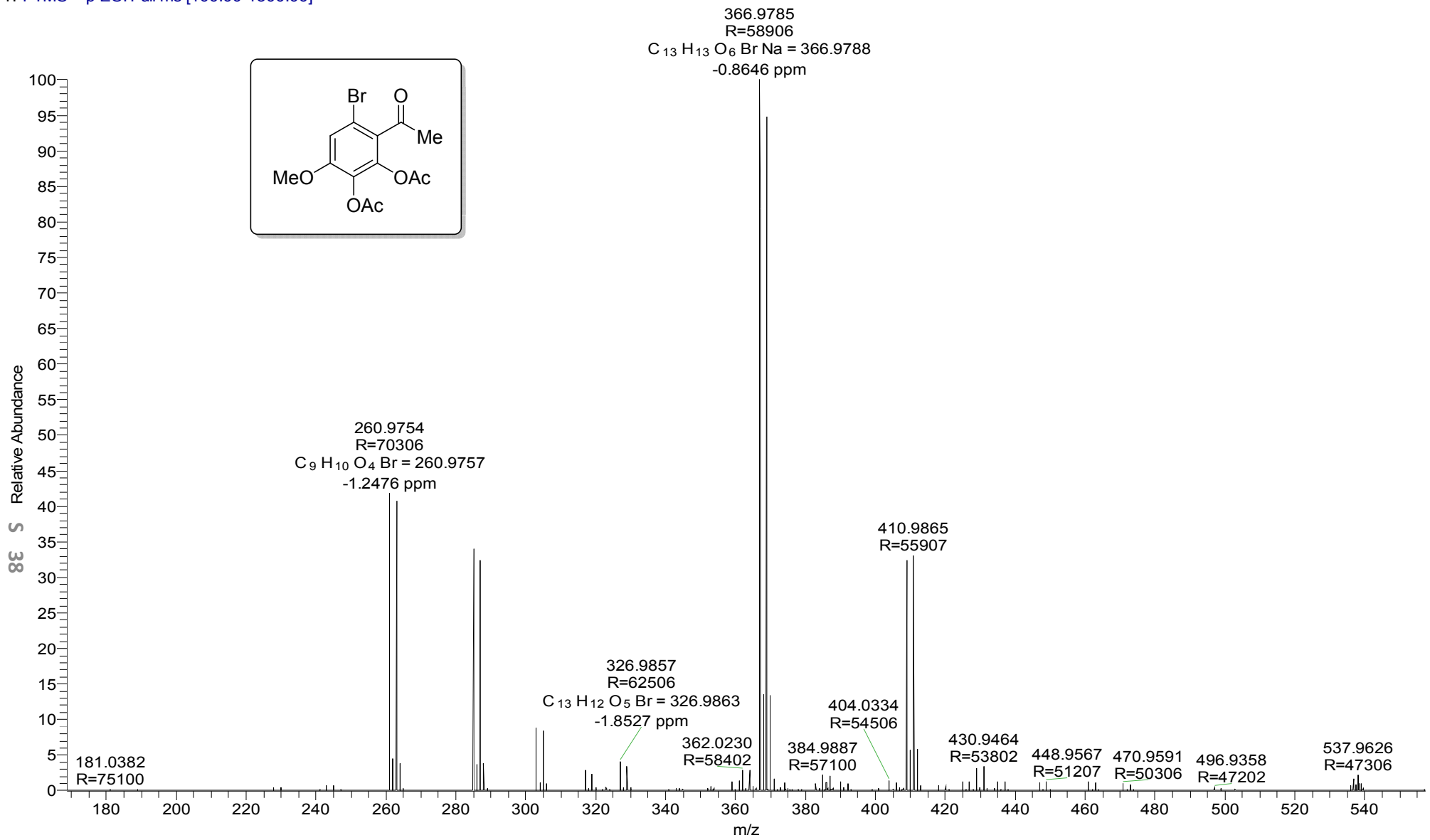
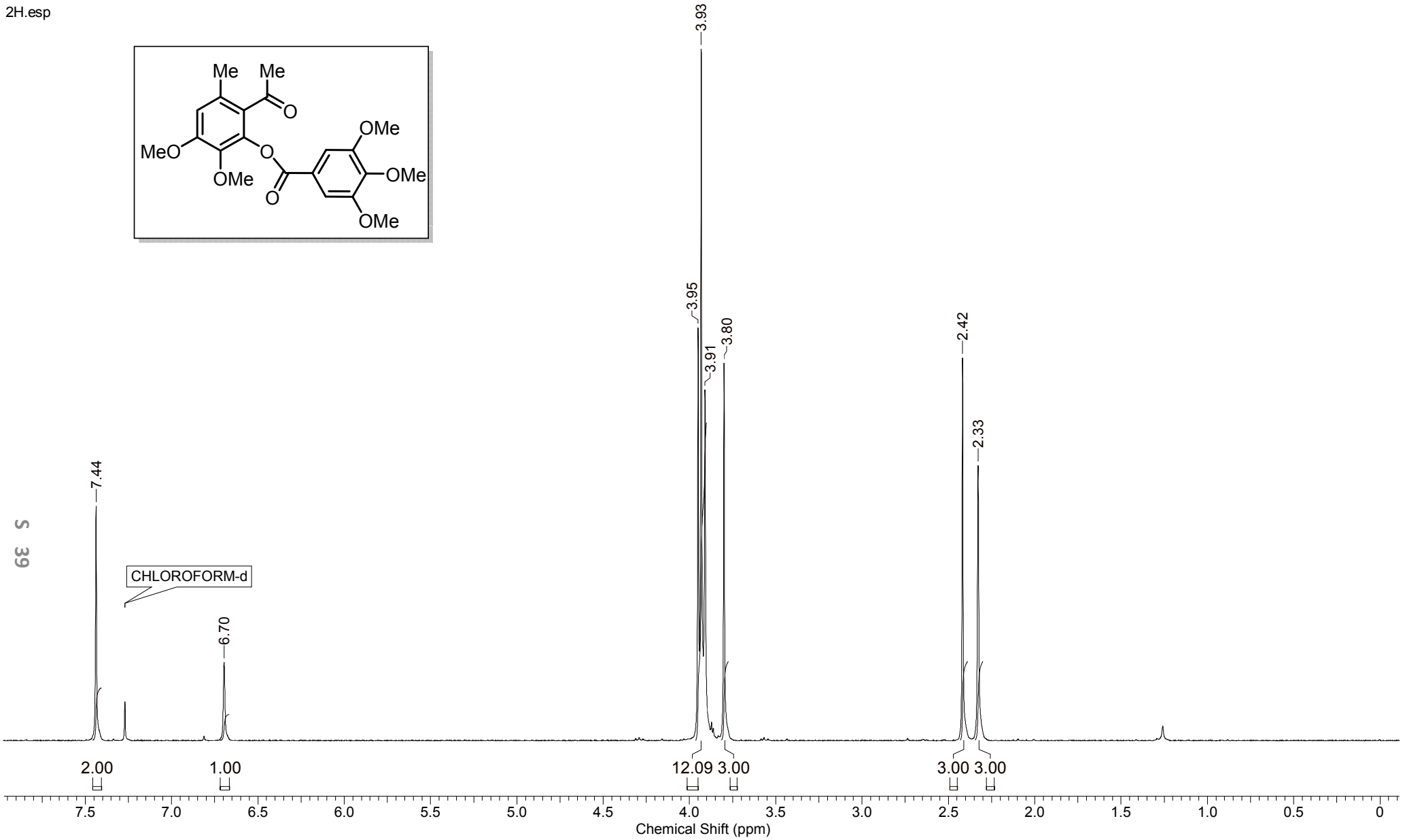
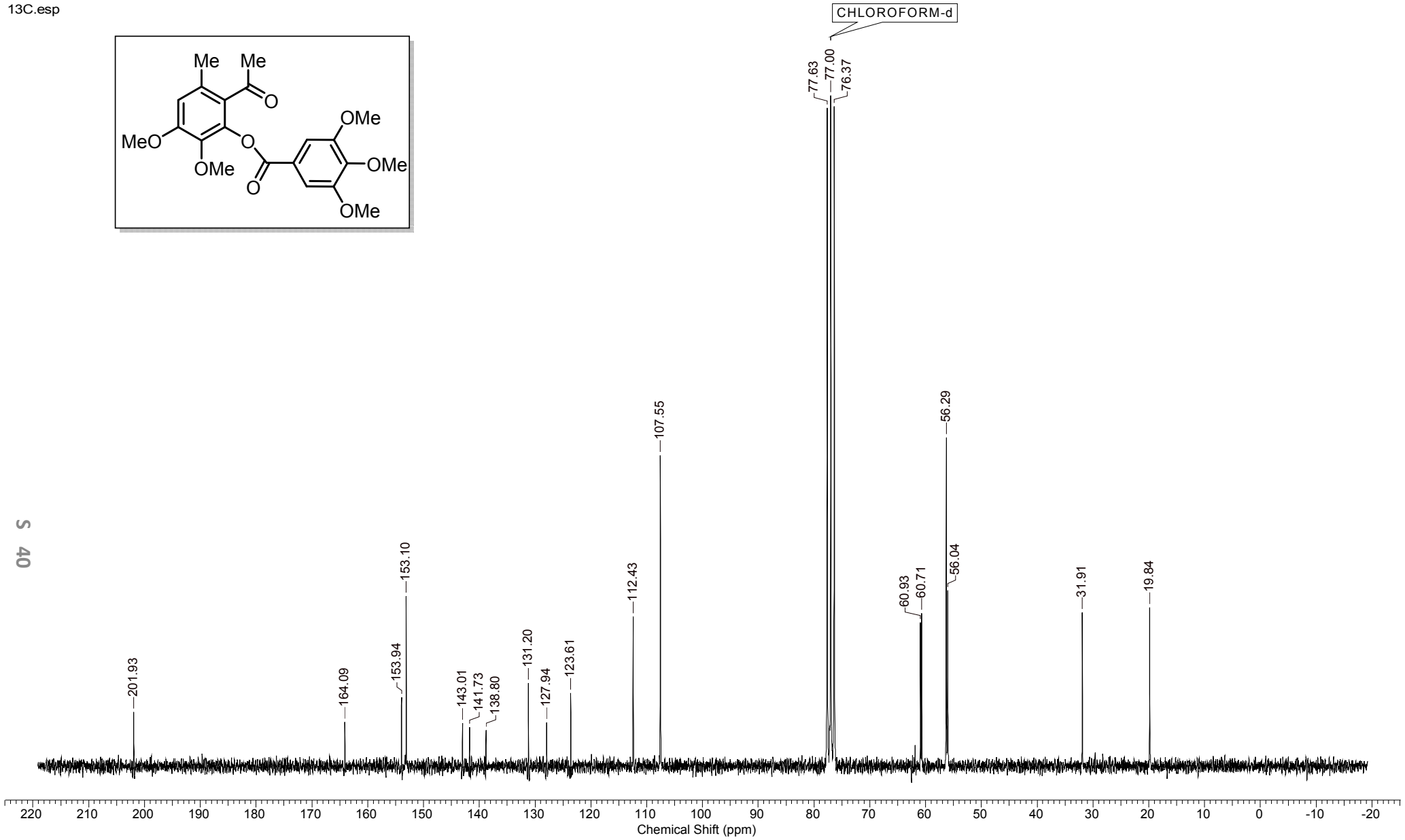
T: FTMS + p ESI Full ms [100.00-1500.00]



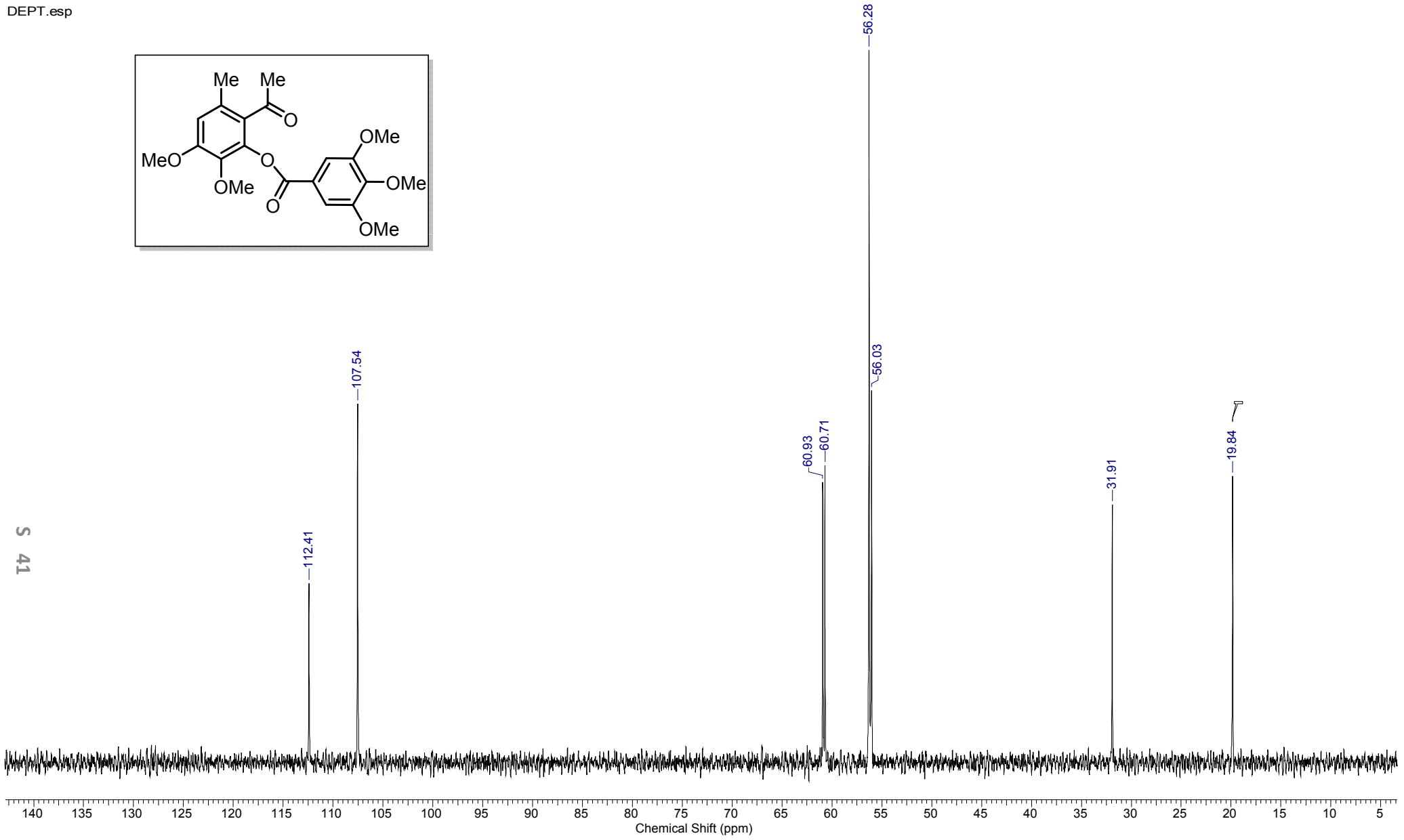
HRMS of compound 7-Ac



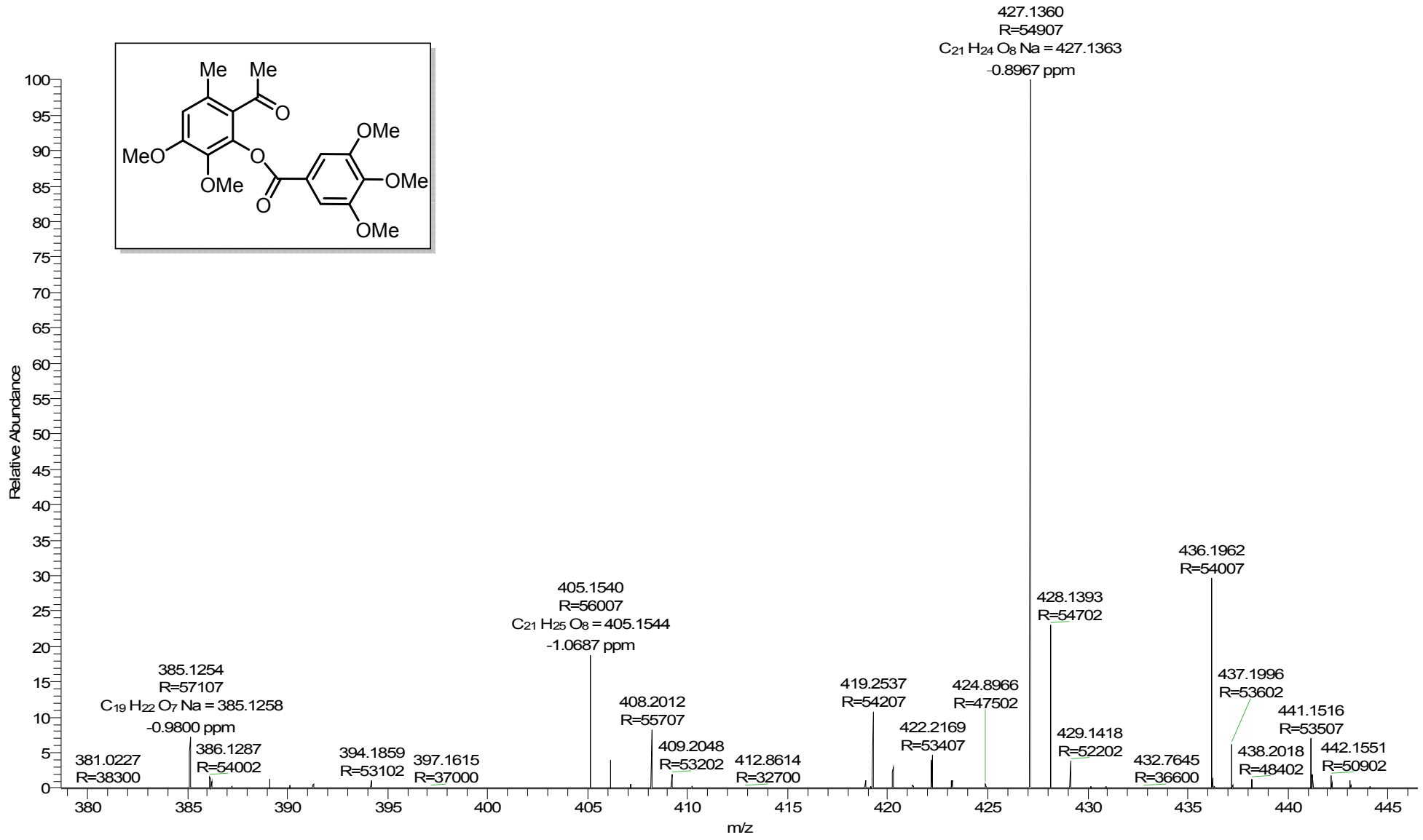
^{1}H NMR of compound 11



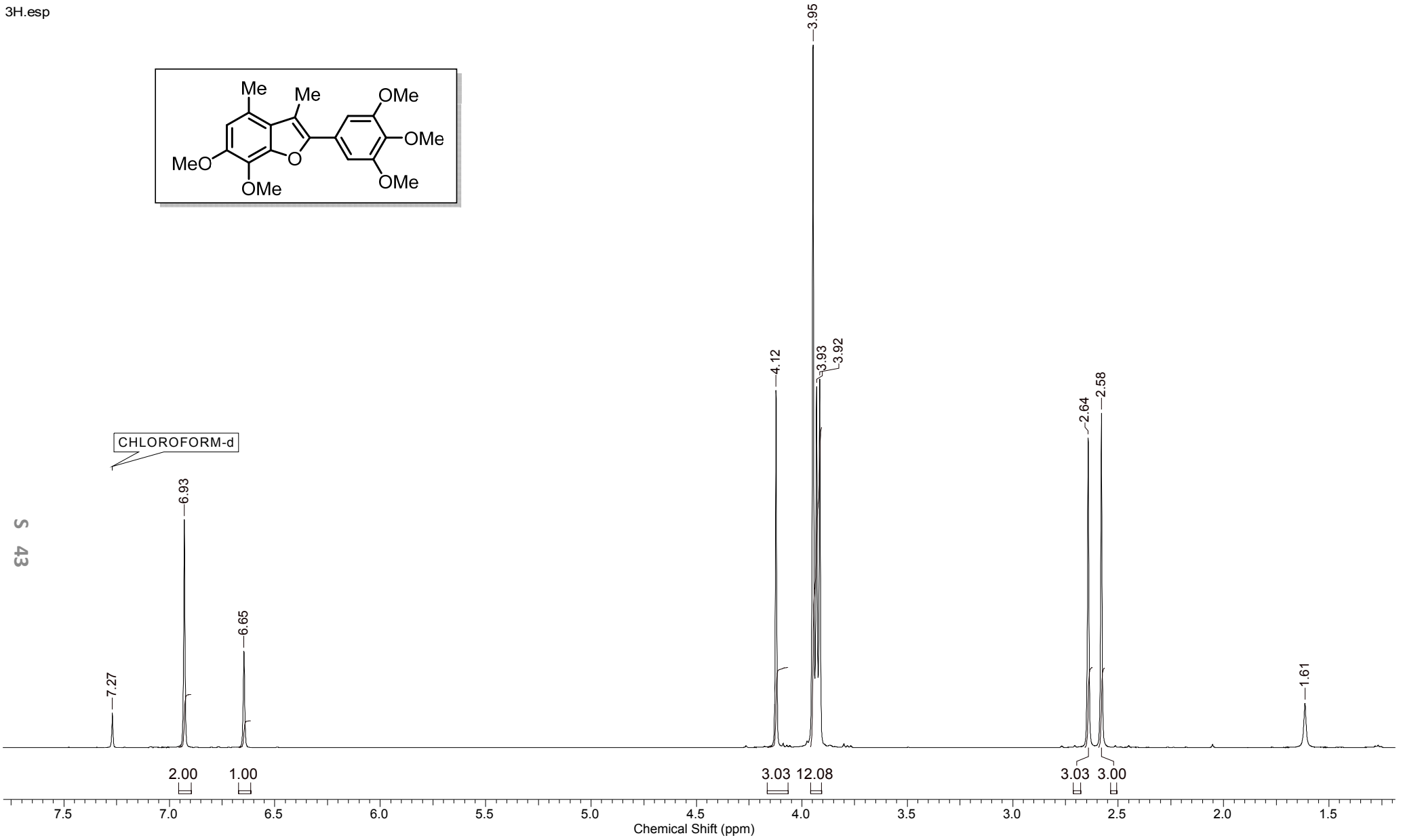
^{13}C NMR of compound 11



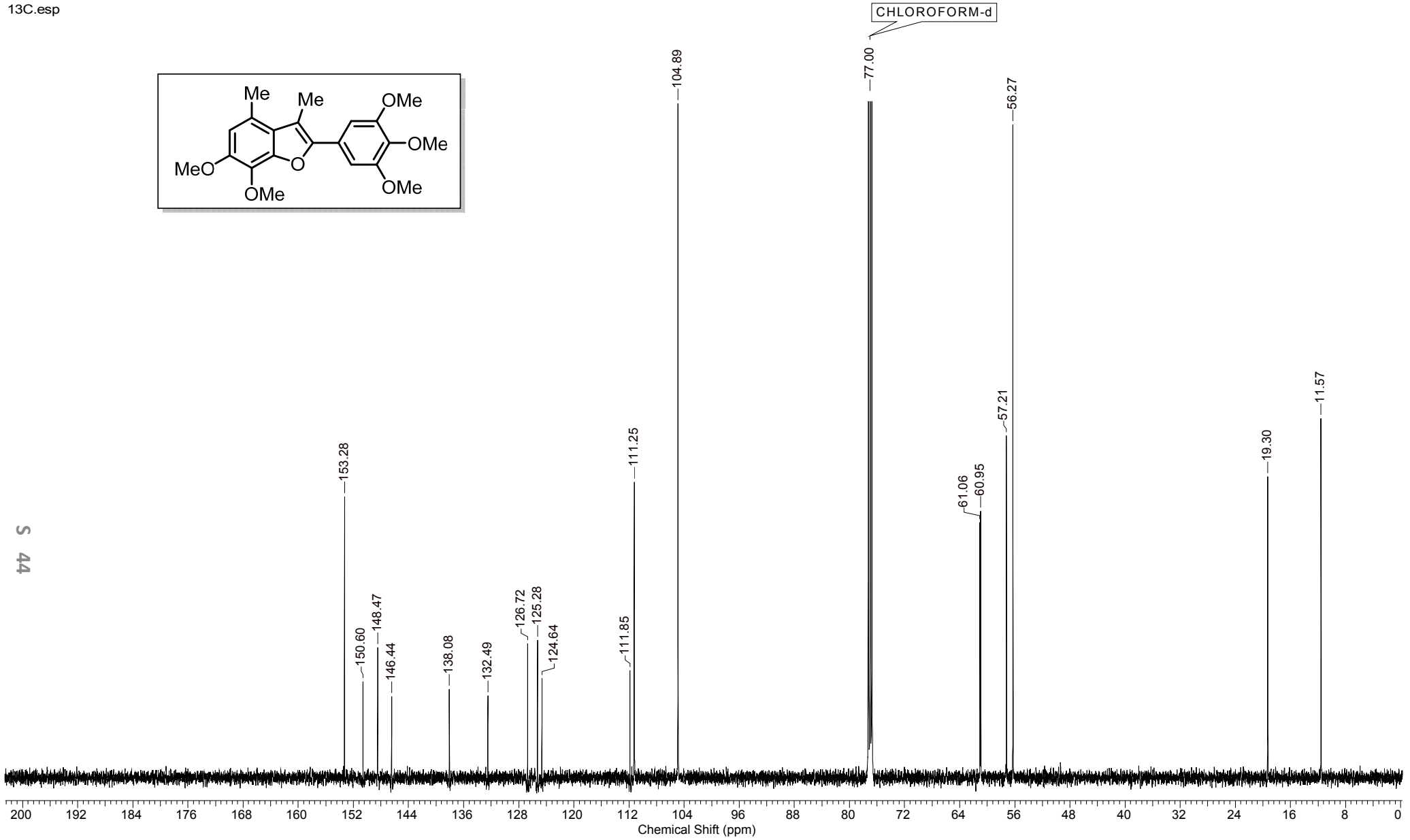
DEPT of compound 11



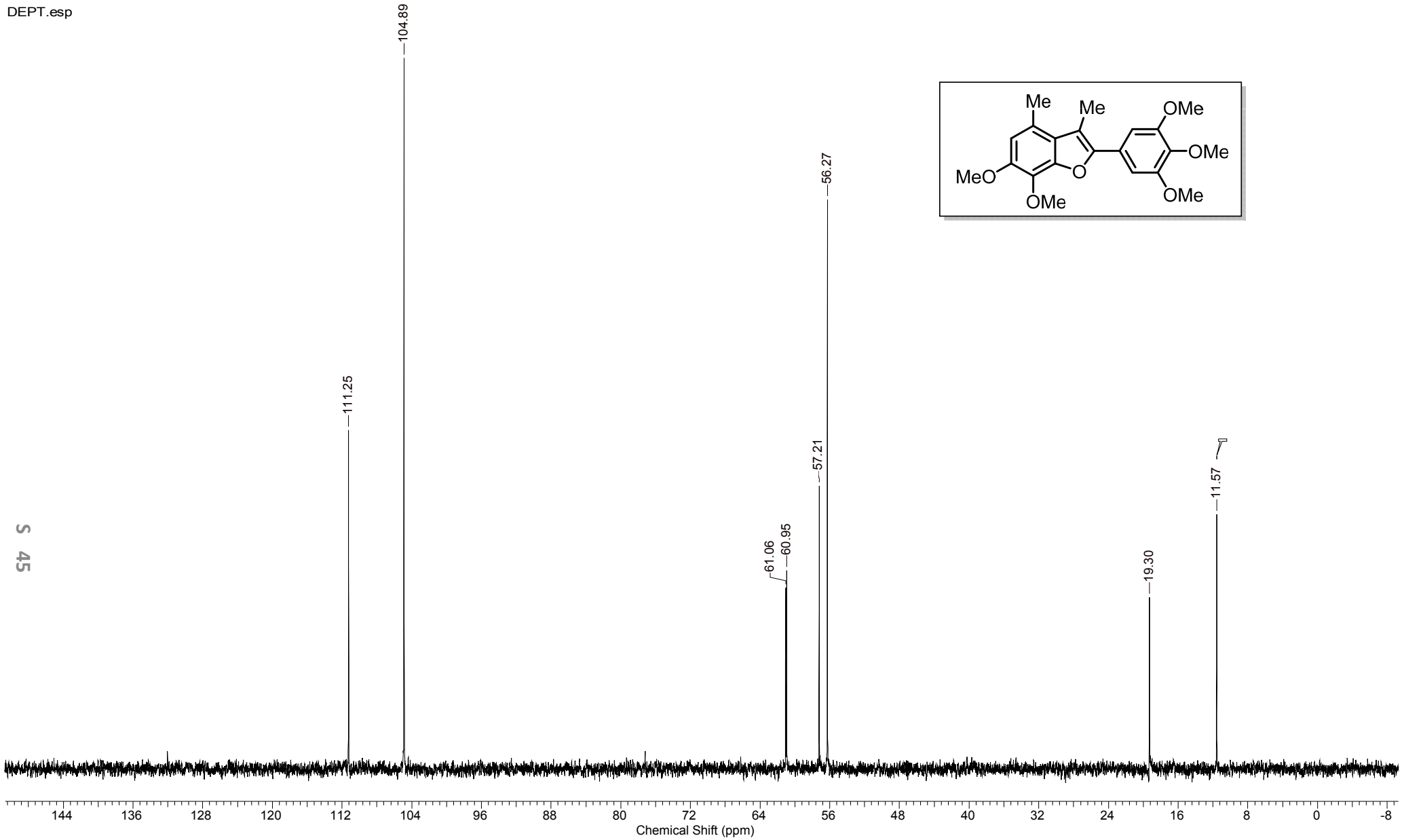
HRMS of compound 11



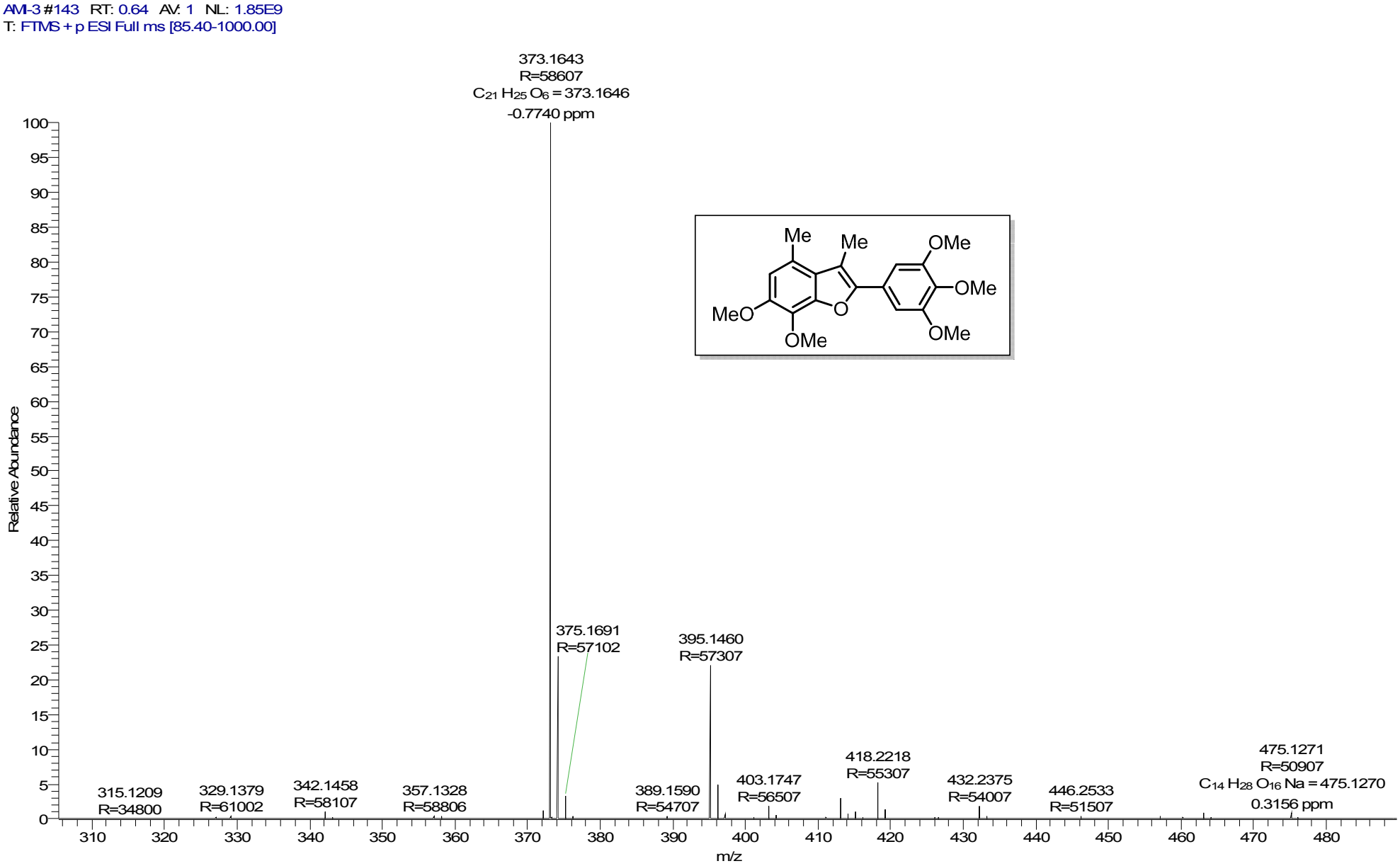
^{1}H NMR of compound 10



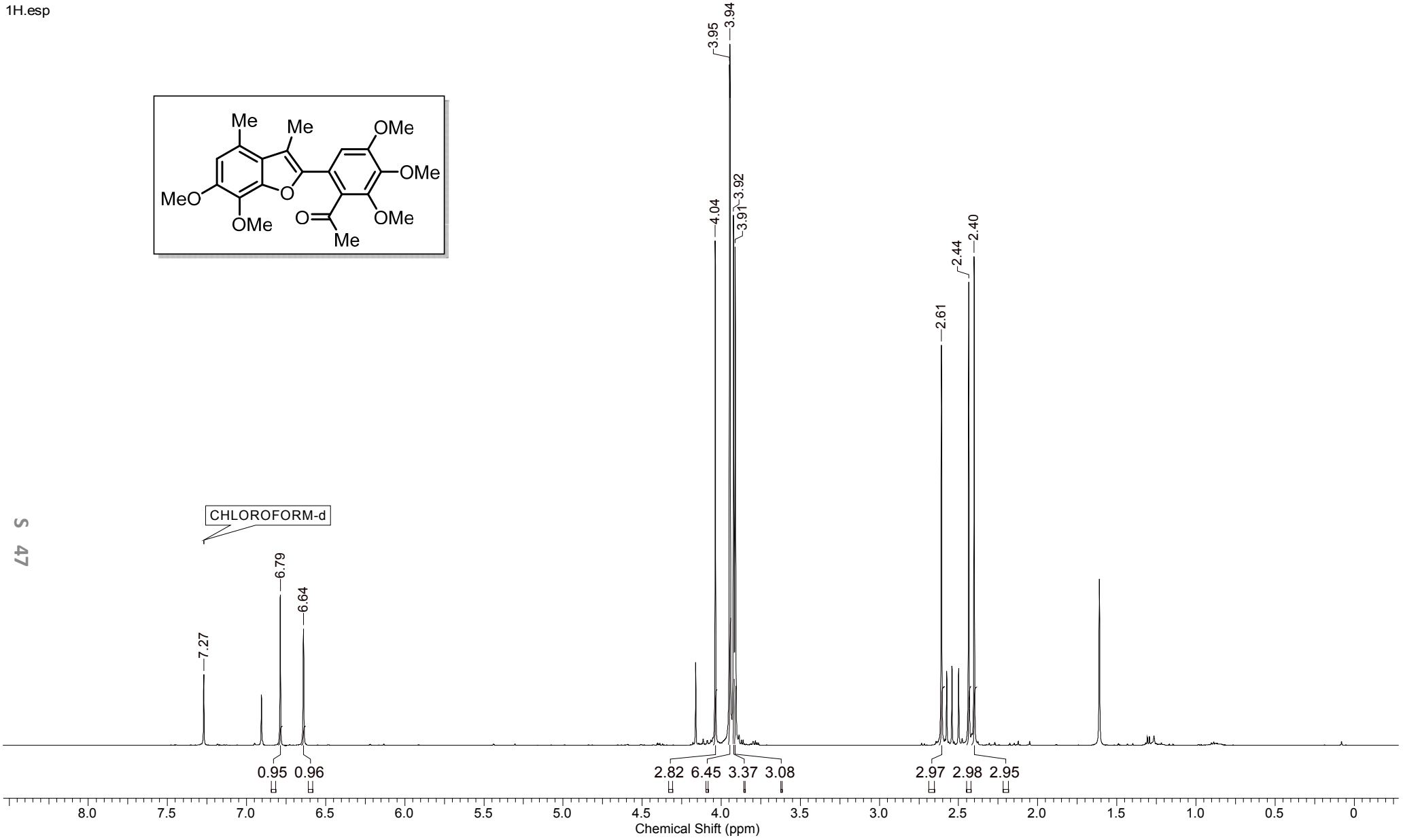
^{13}C NMR of compound 10



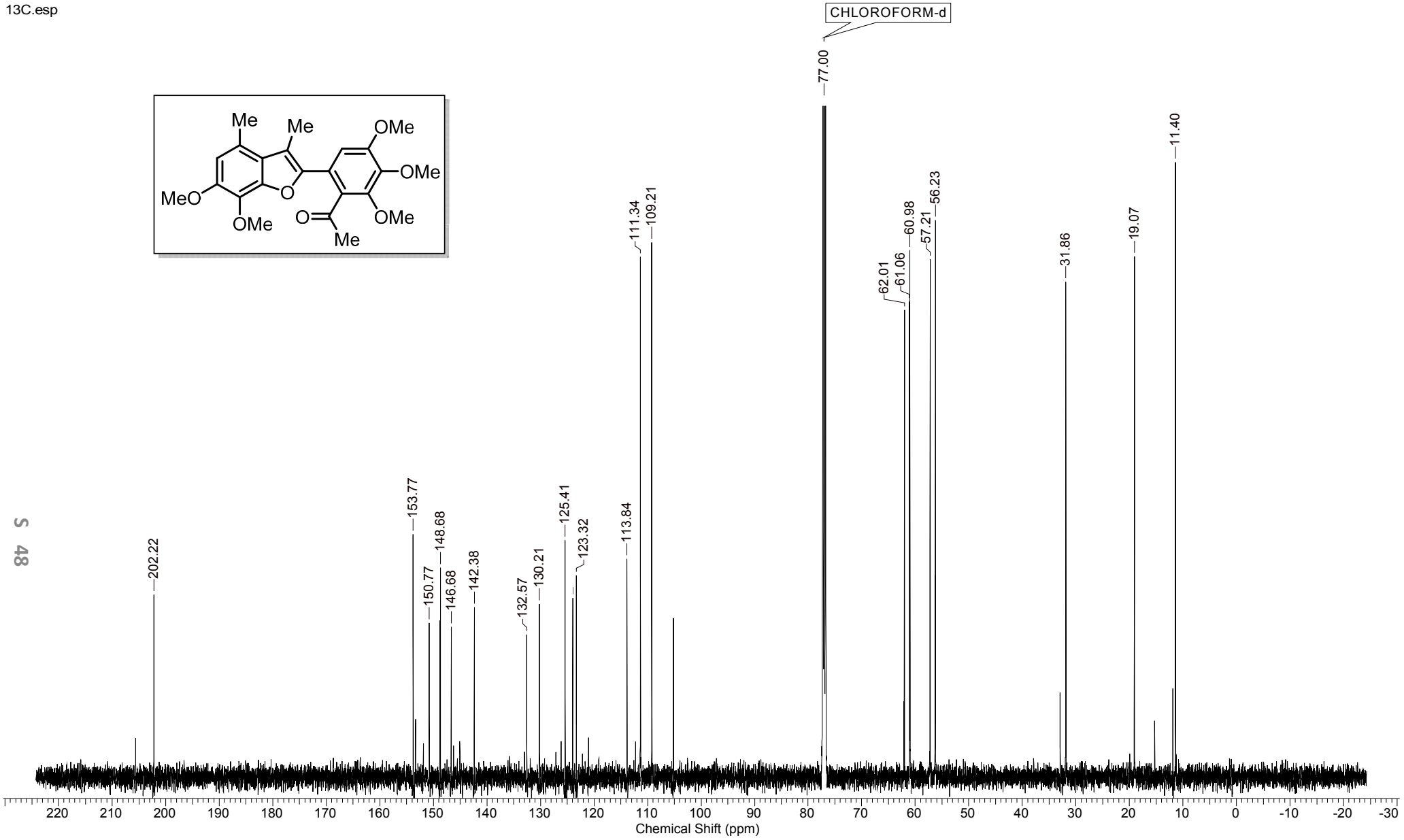
DEPT of compound 10



HRMS of compound 10



^{1}H NMR of compound 6-Me



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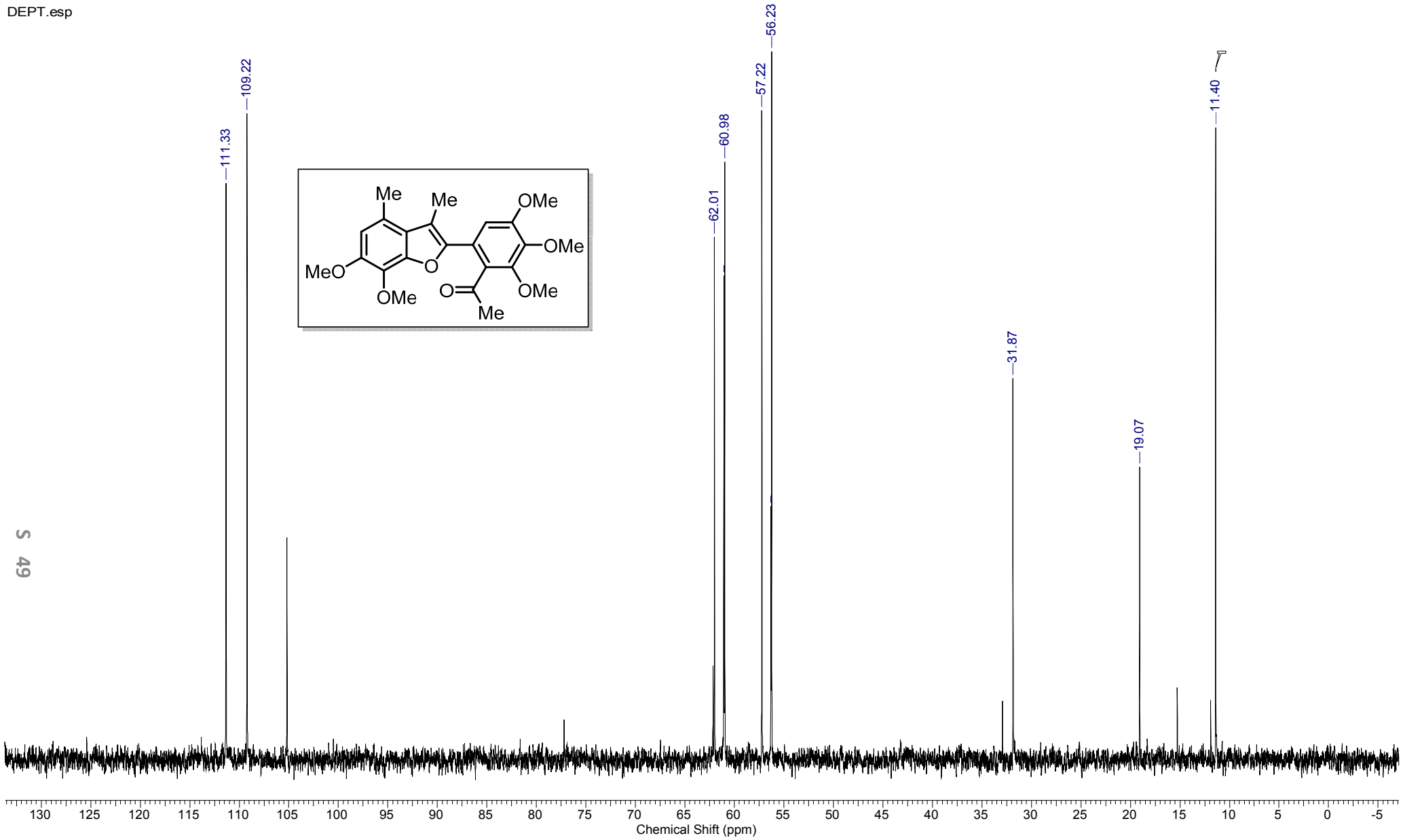
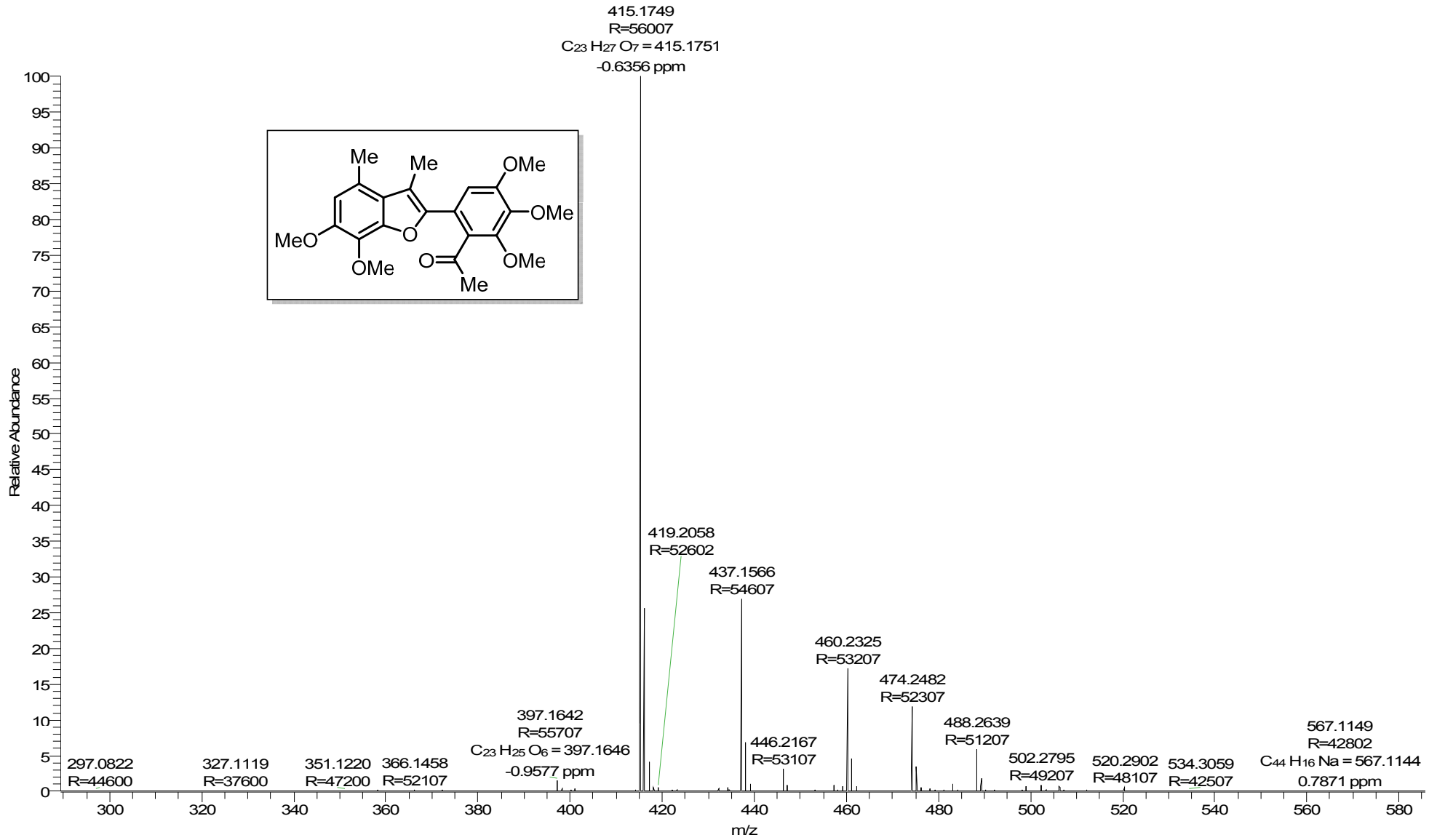
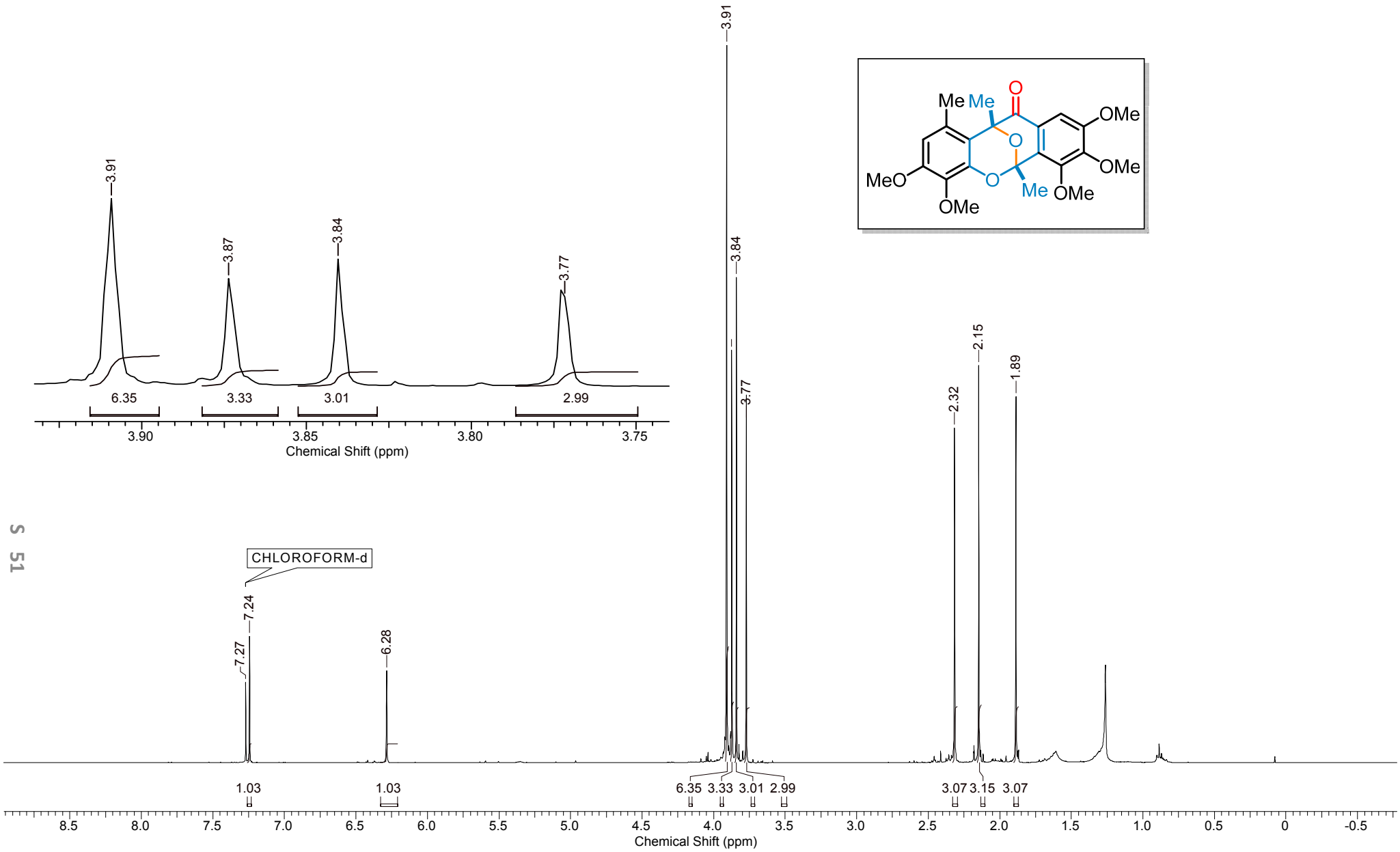


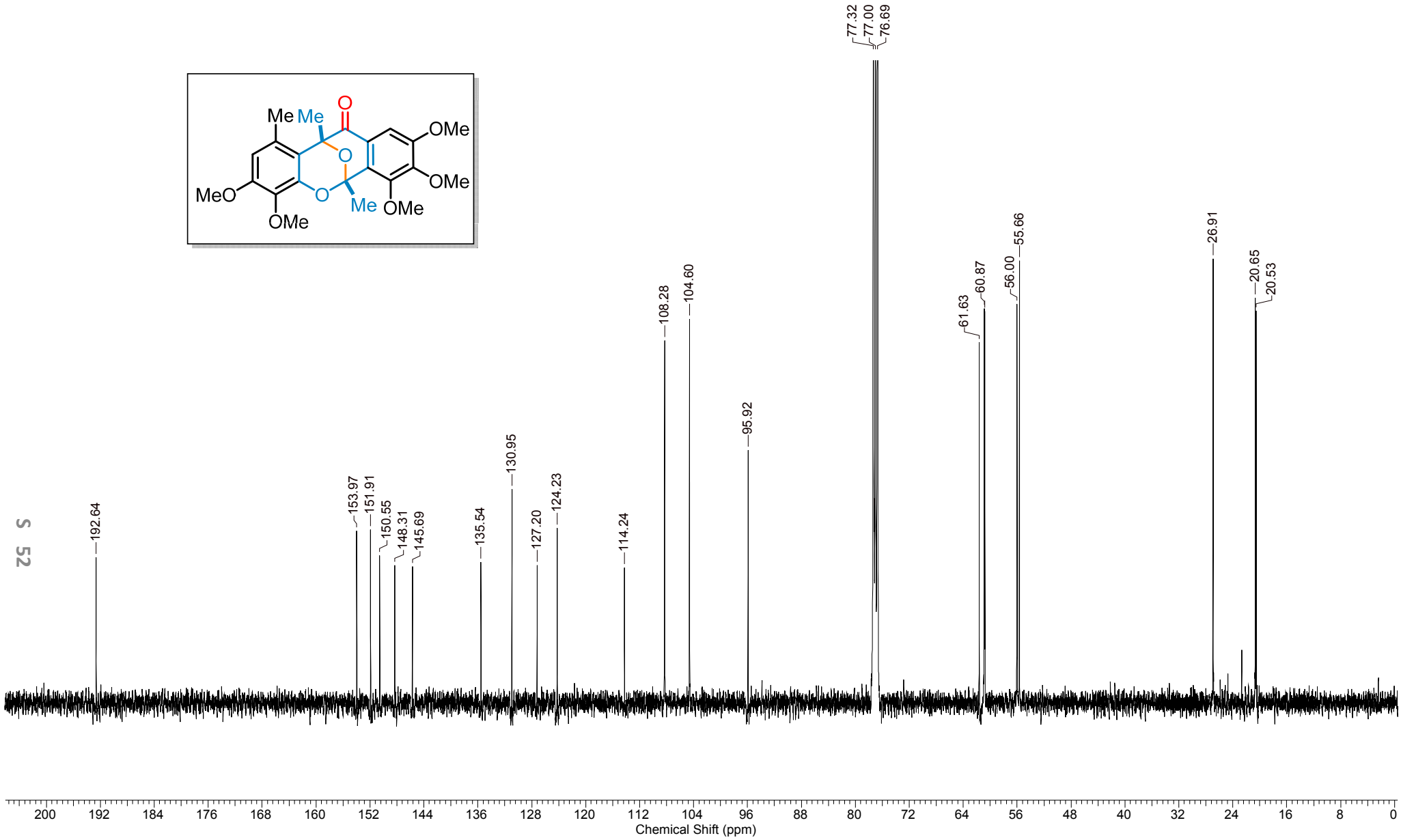
DEPT of compound 6-Me



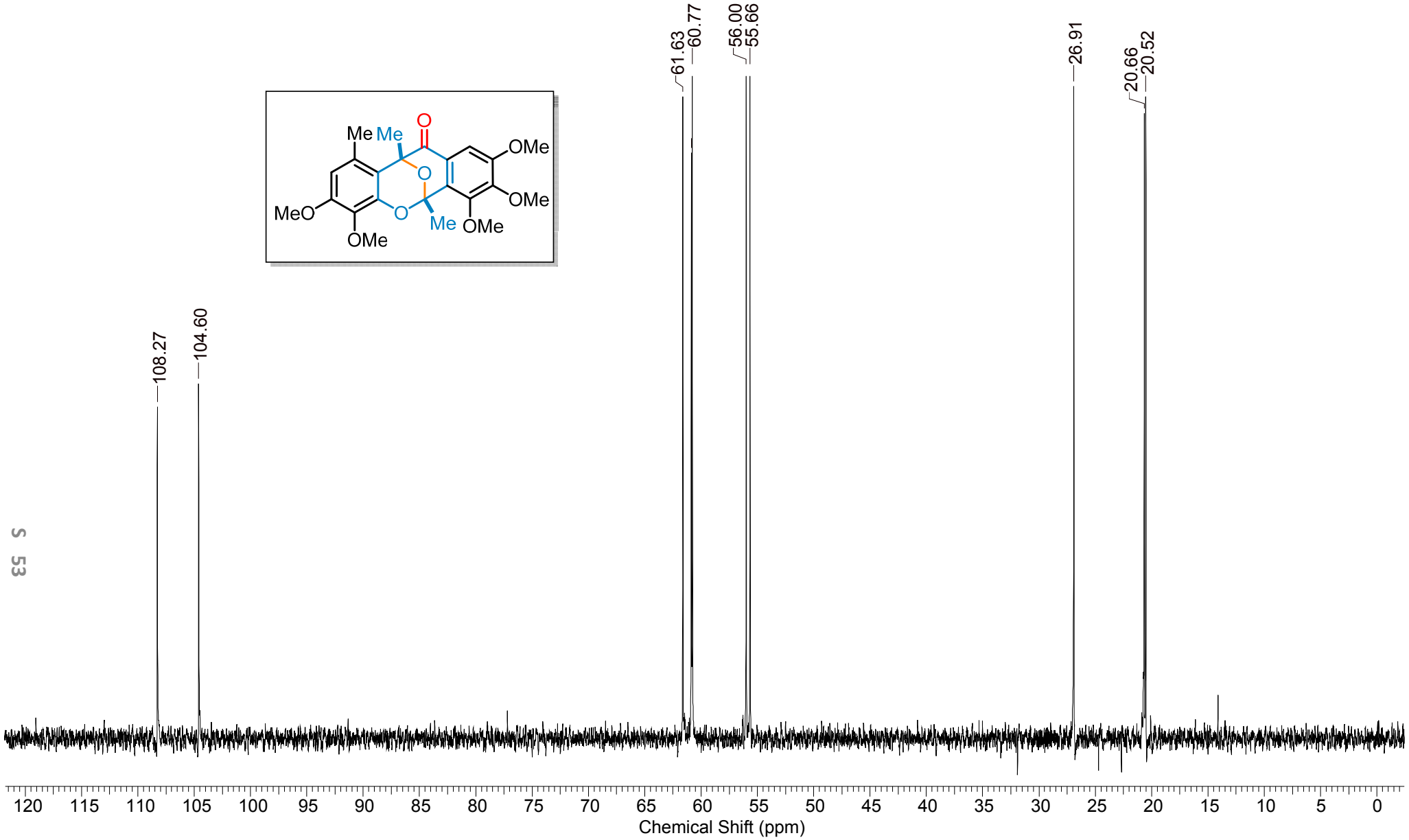
HRMS of compound 6-Me



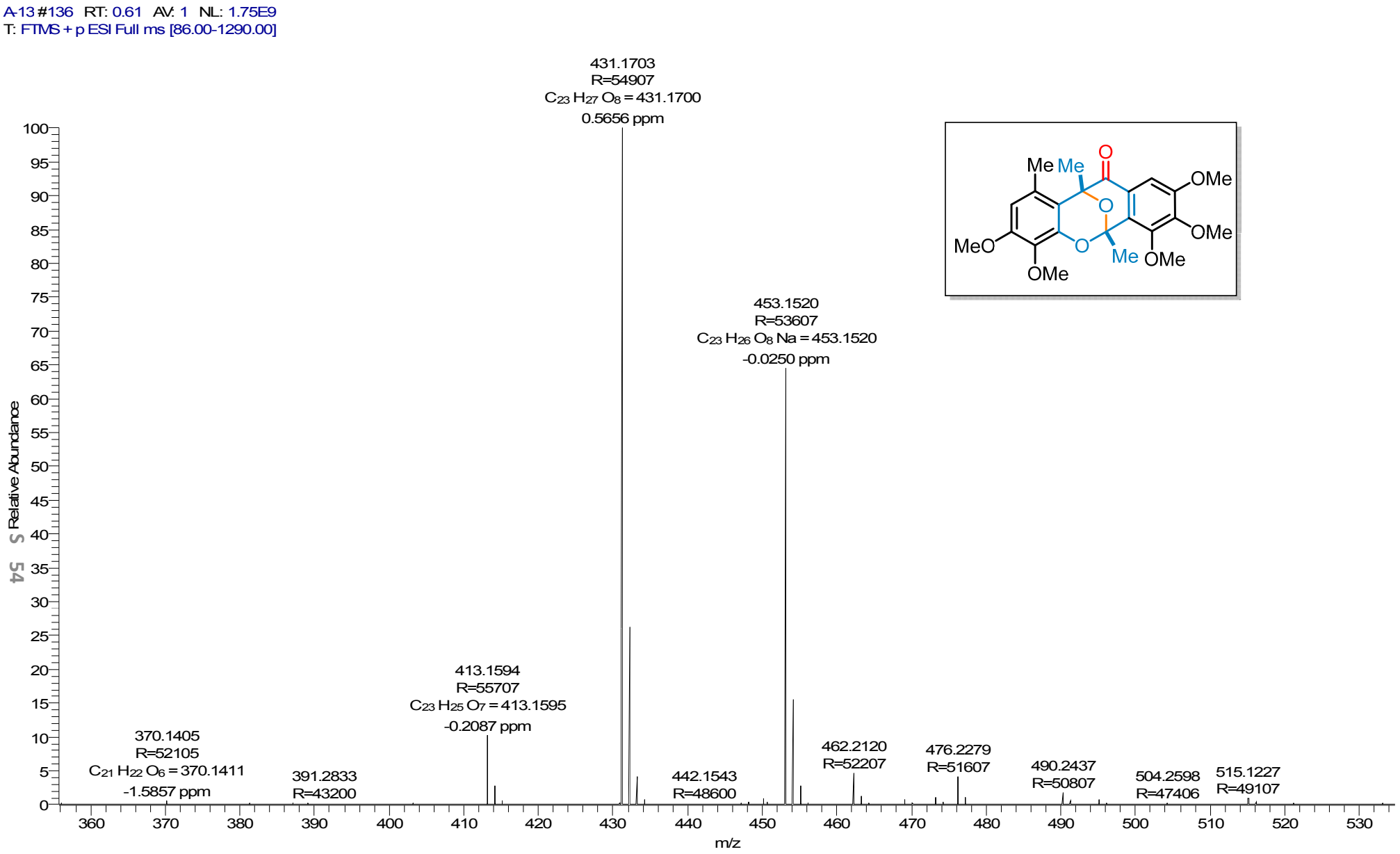
^{1}H NMR of compound 5-Me



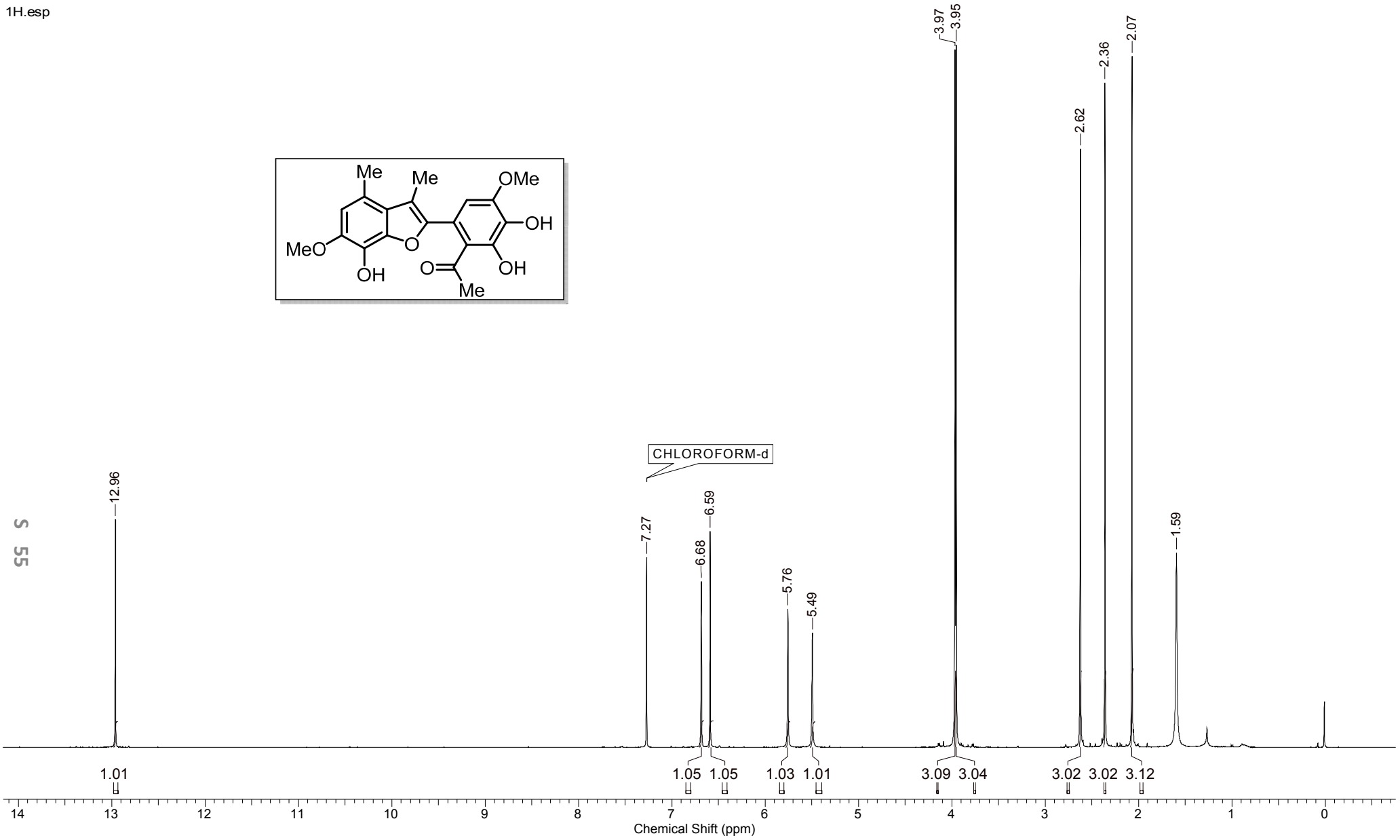
^{13}C NMR of compound 5-Me



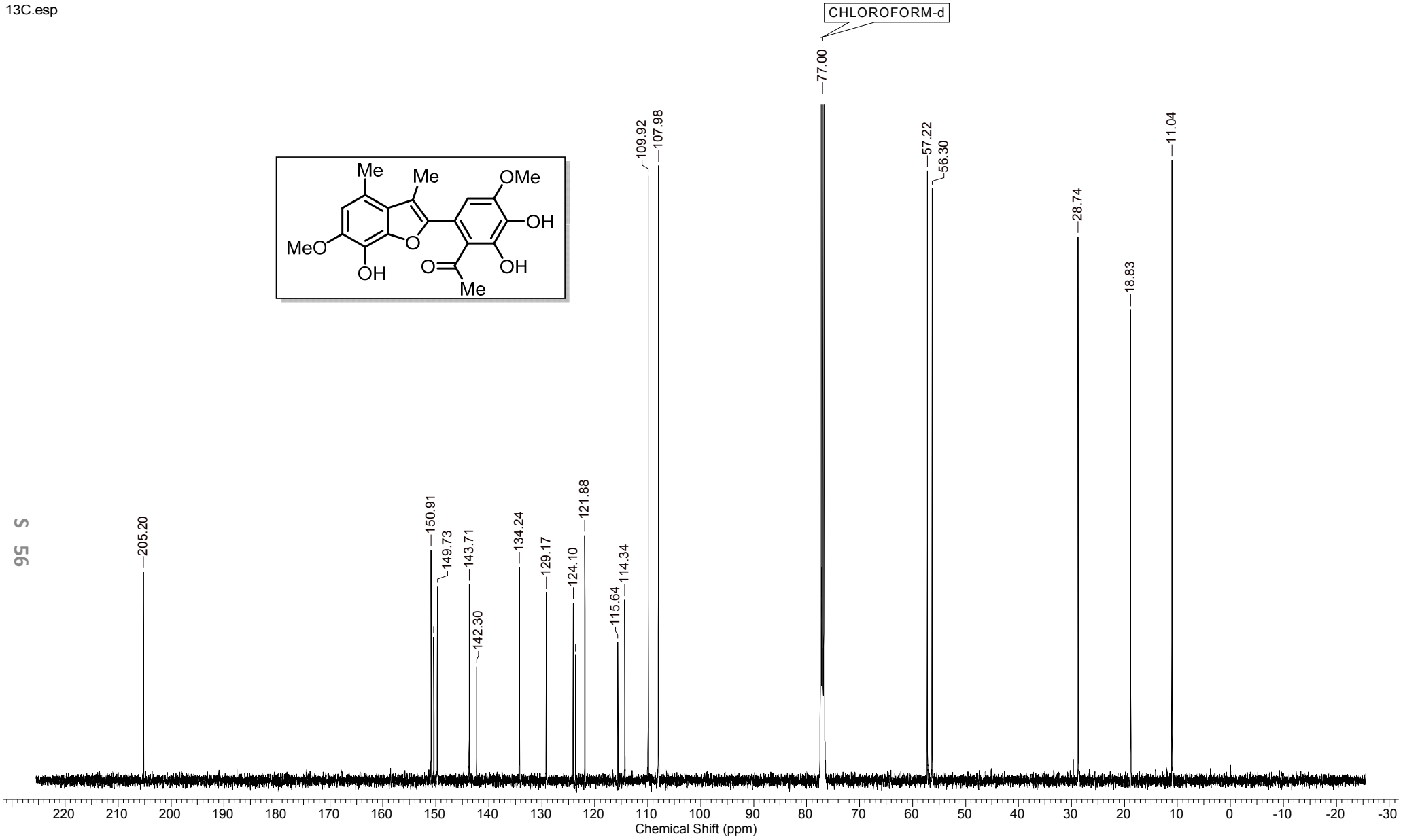
DEPT of compound 5-Me



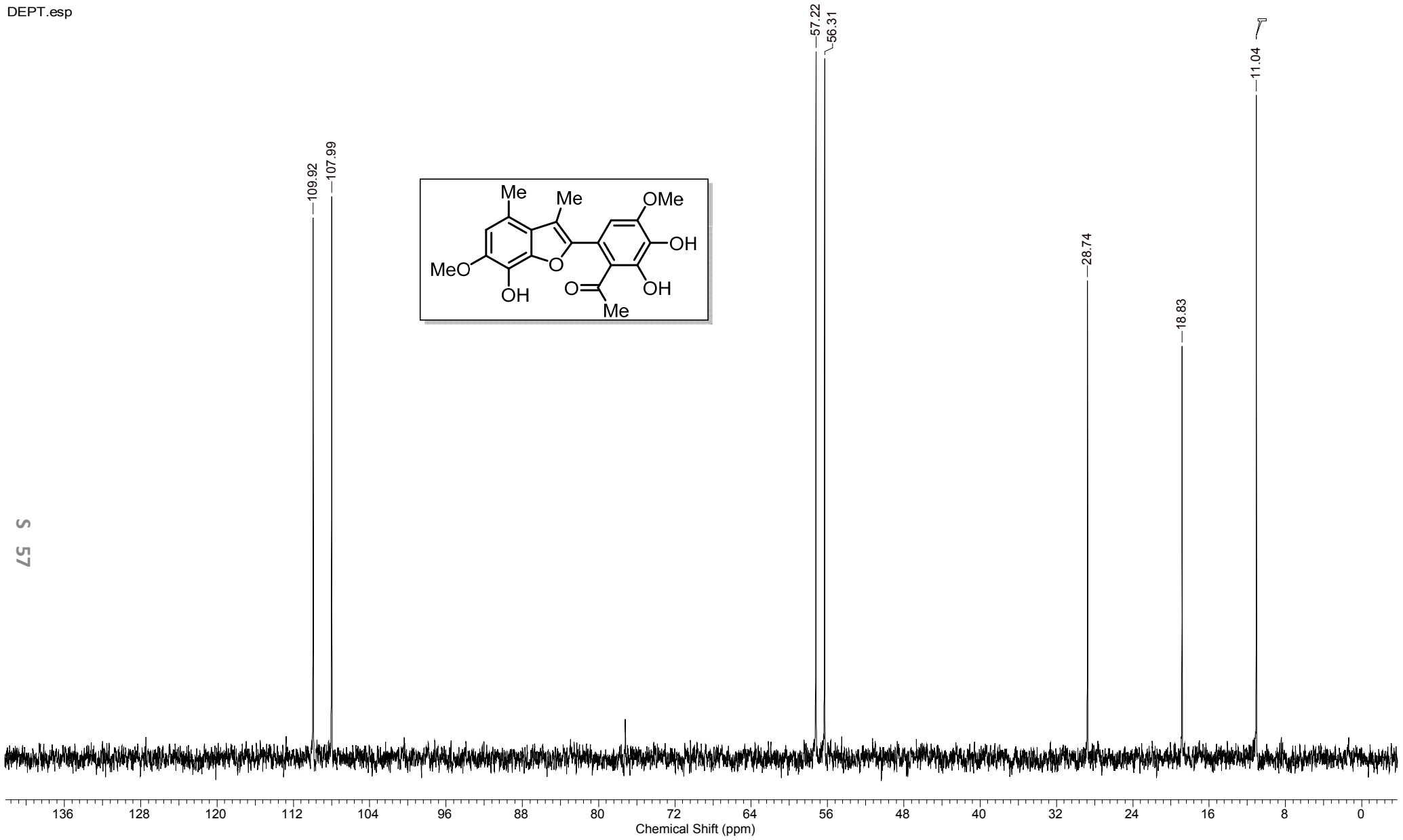
HRMS of compound 5-Me



^{1}H NMR of compound 6-H



^{13}C NMR of compound 6-H



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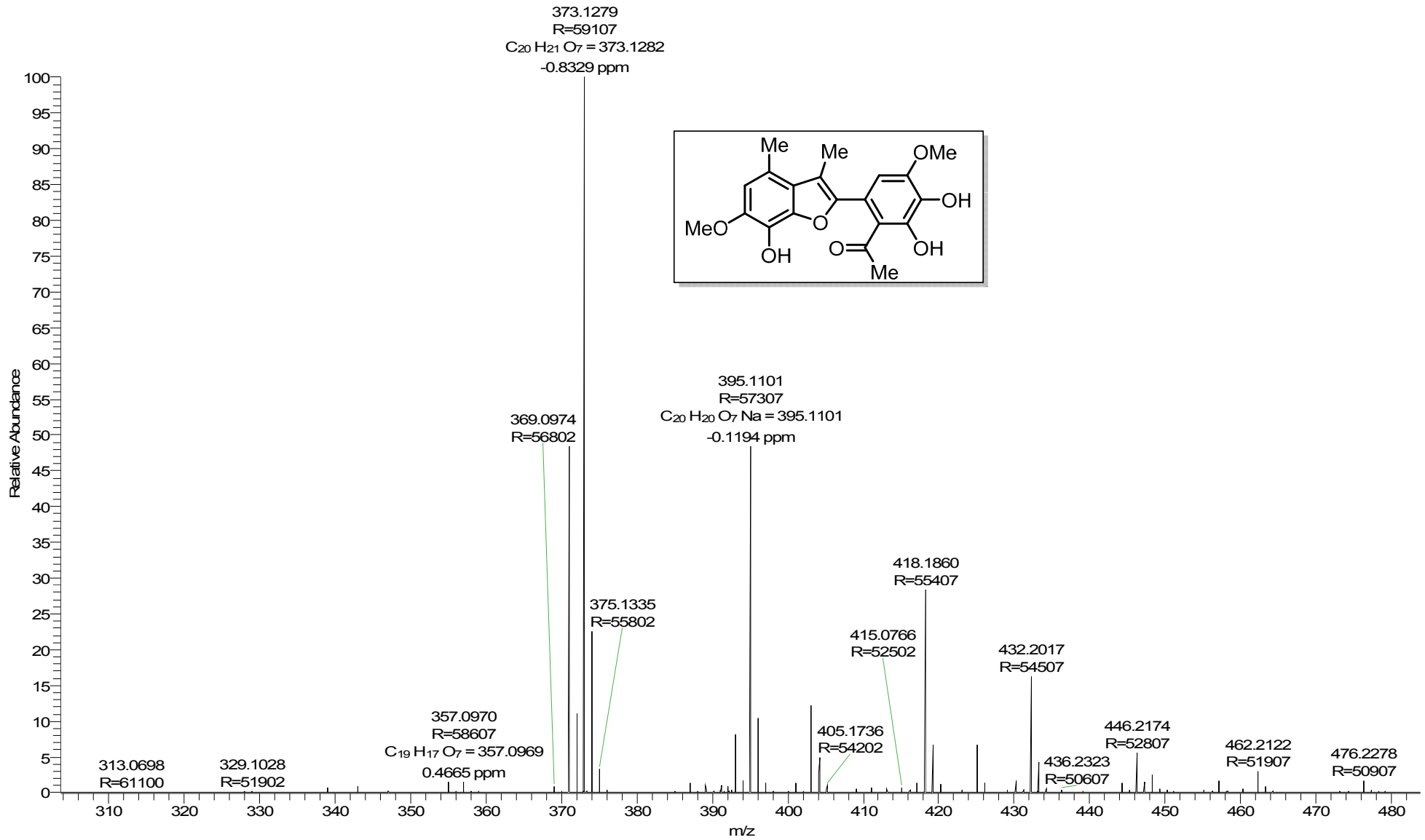
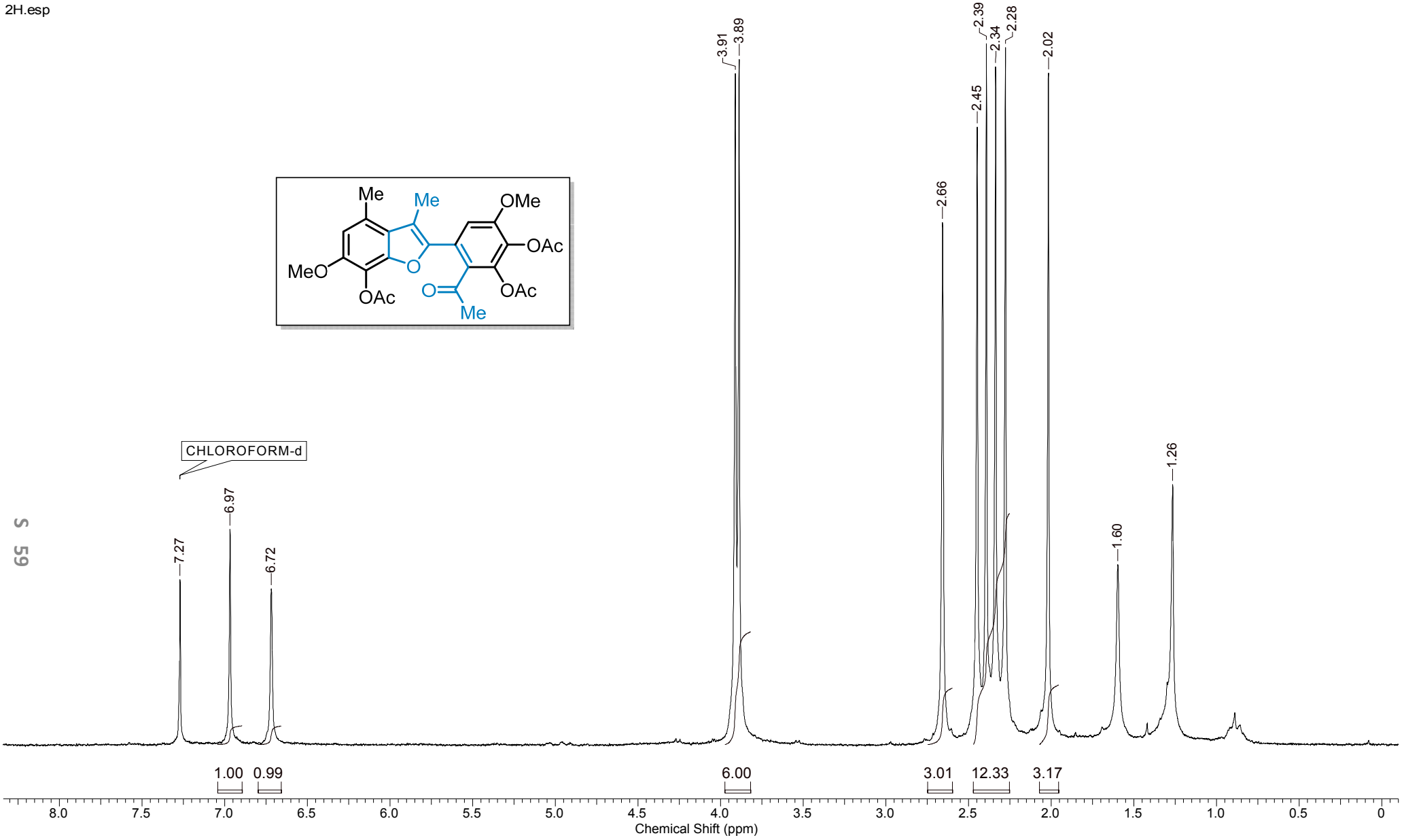
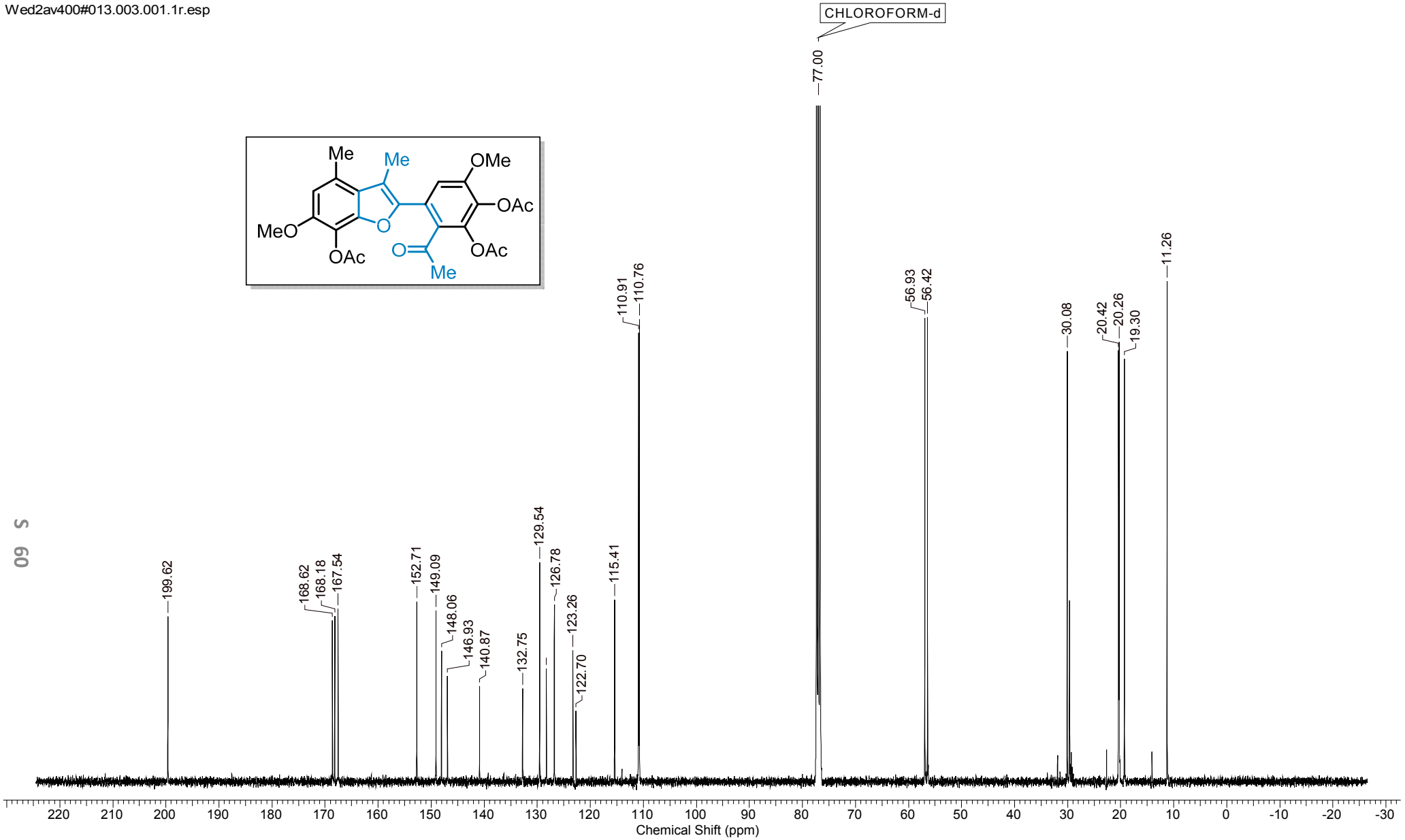


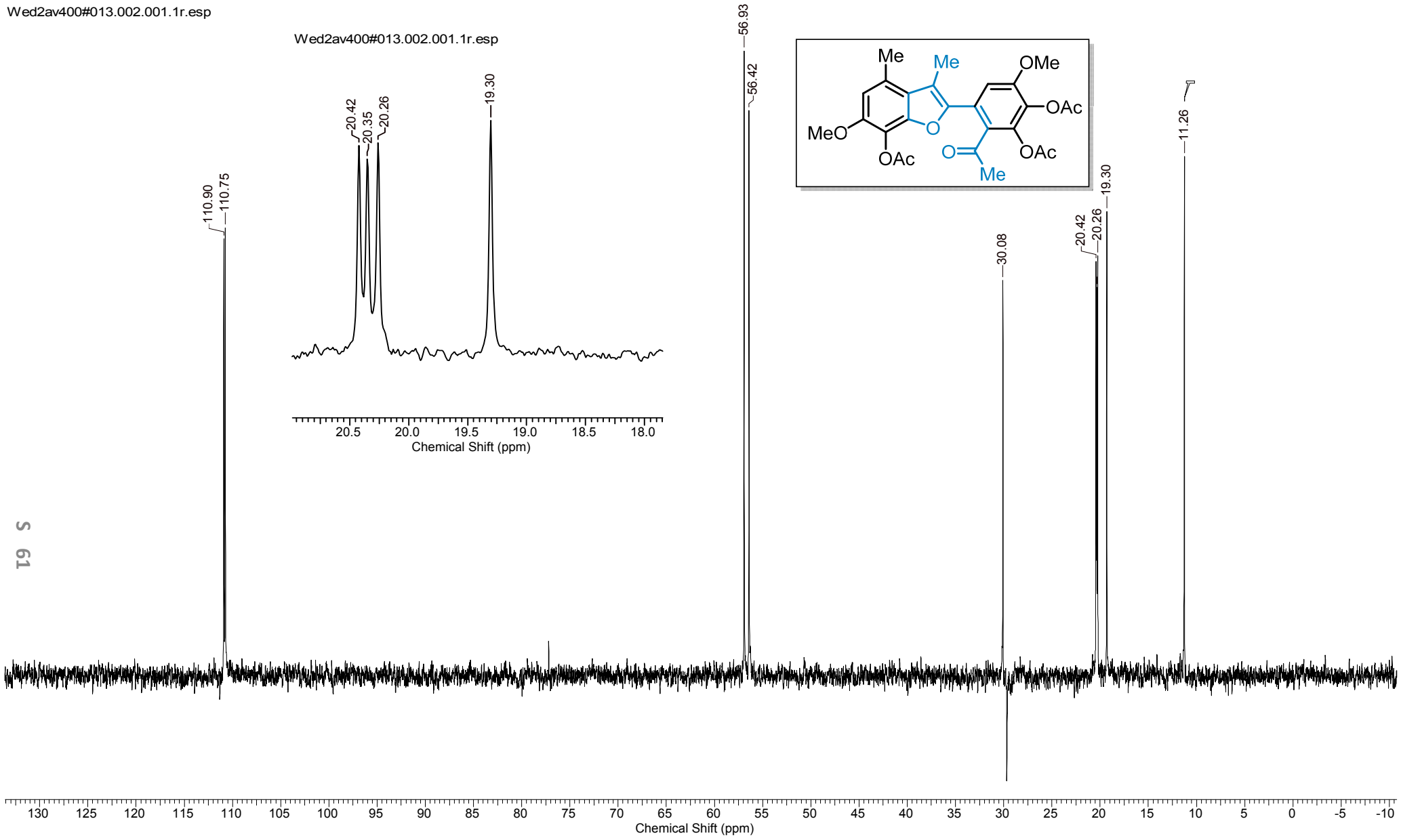
HRMS of compound 6-H



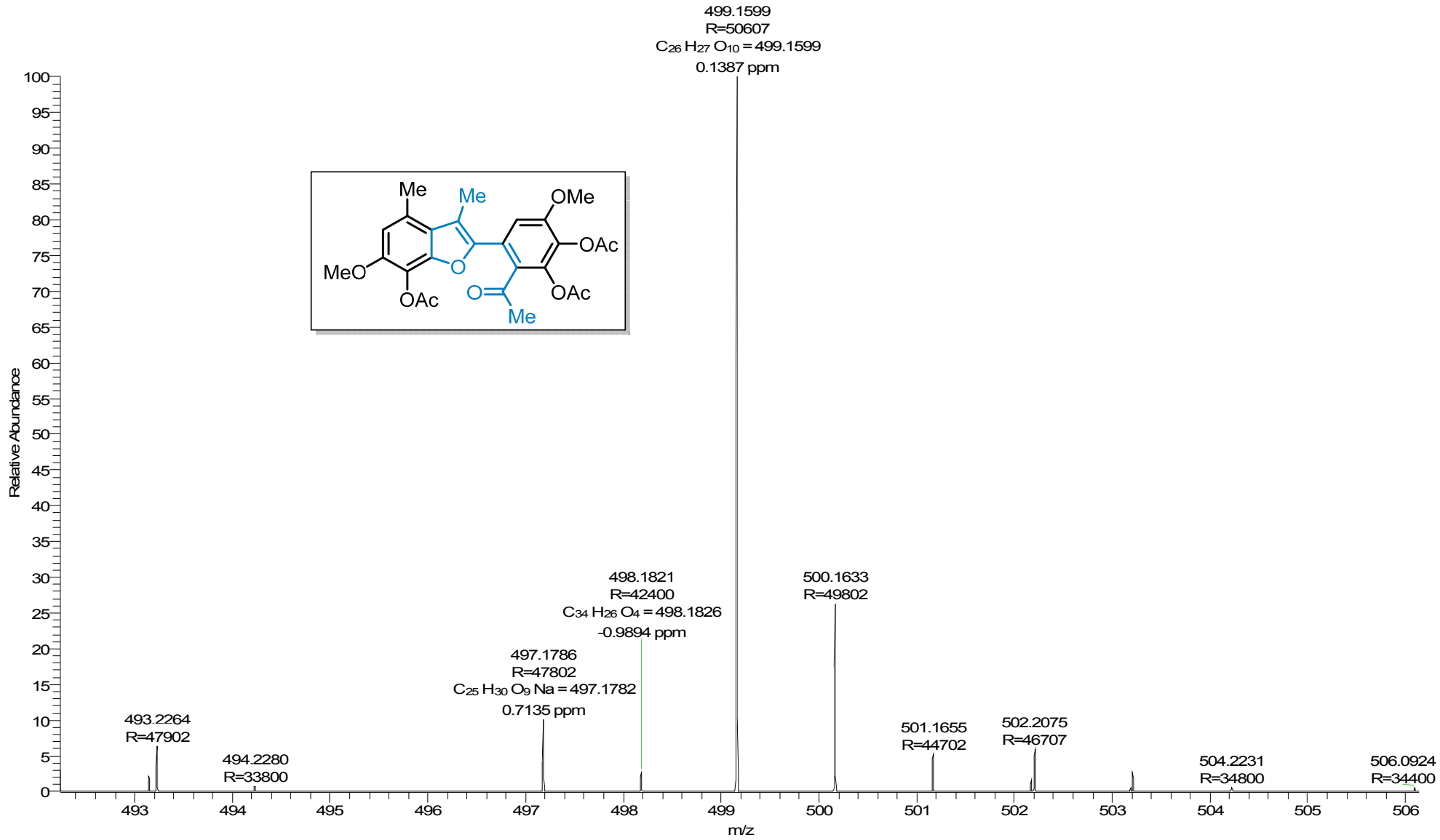
^{1}H NMR of compound 6-Ac



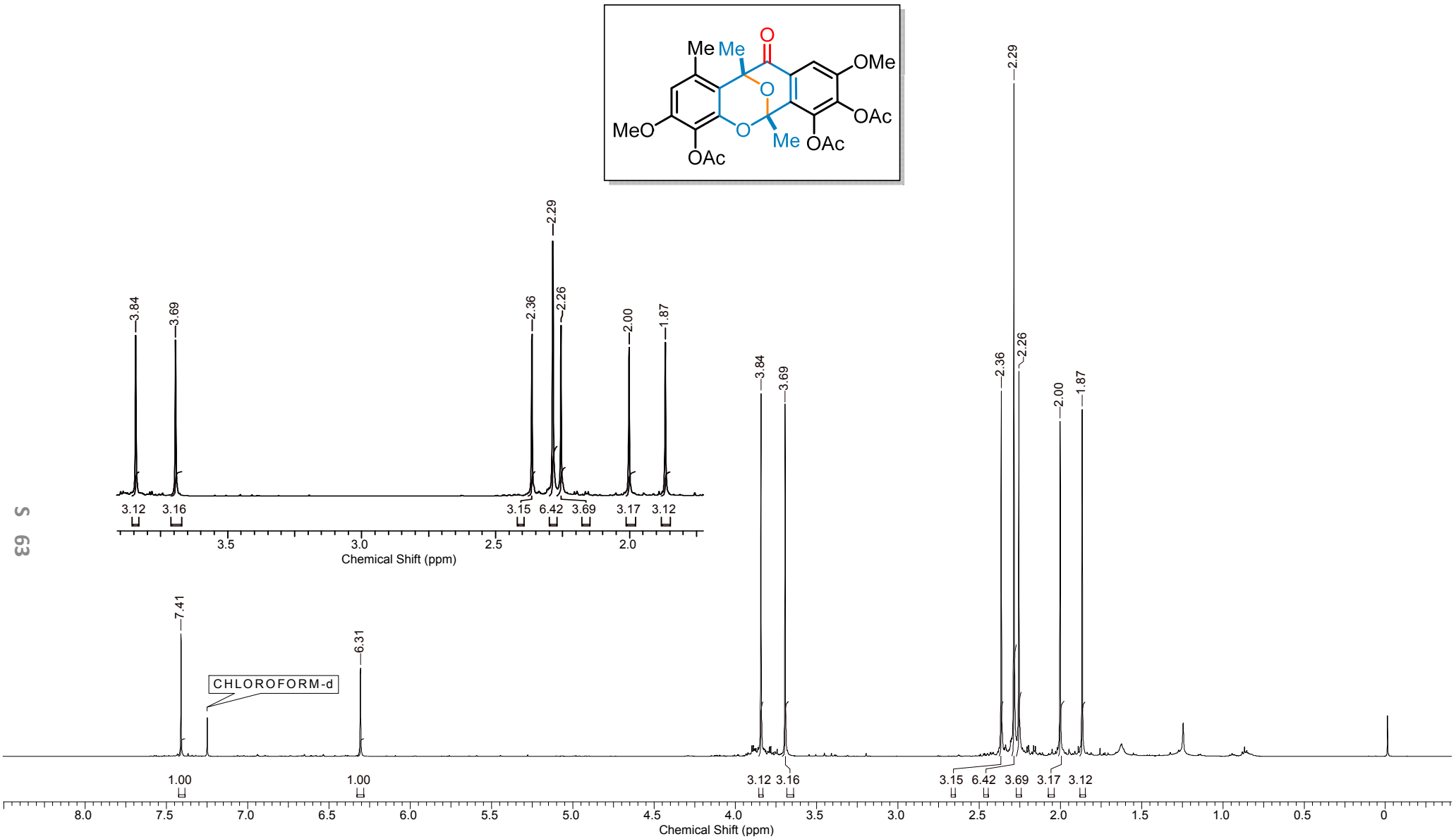
^{13}C NMR of compound 6-Ac



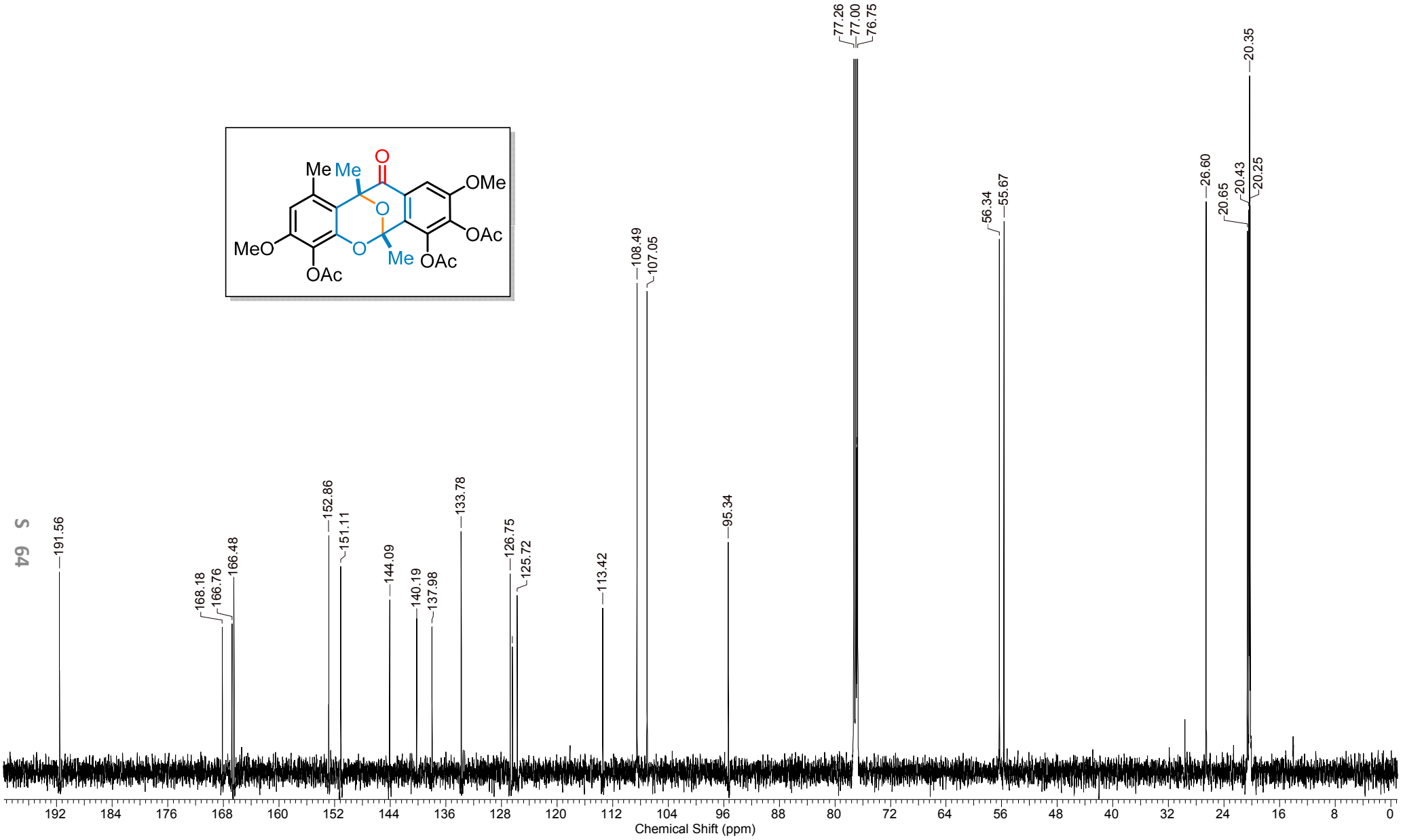
DEPT of compound 6-Ac



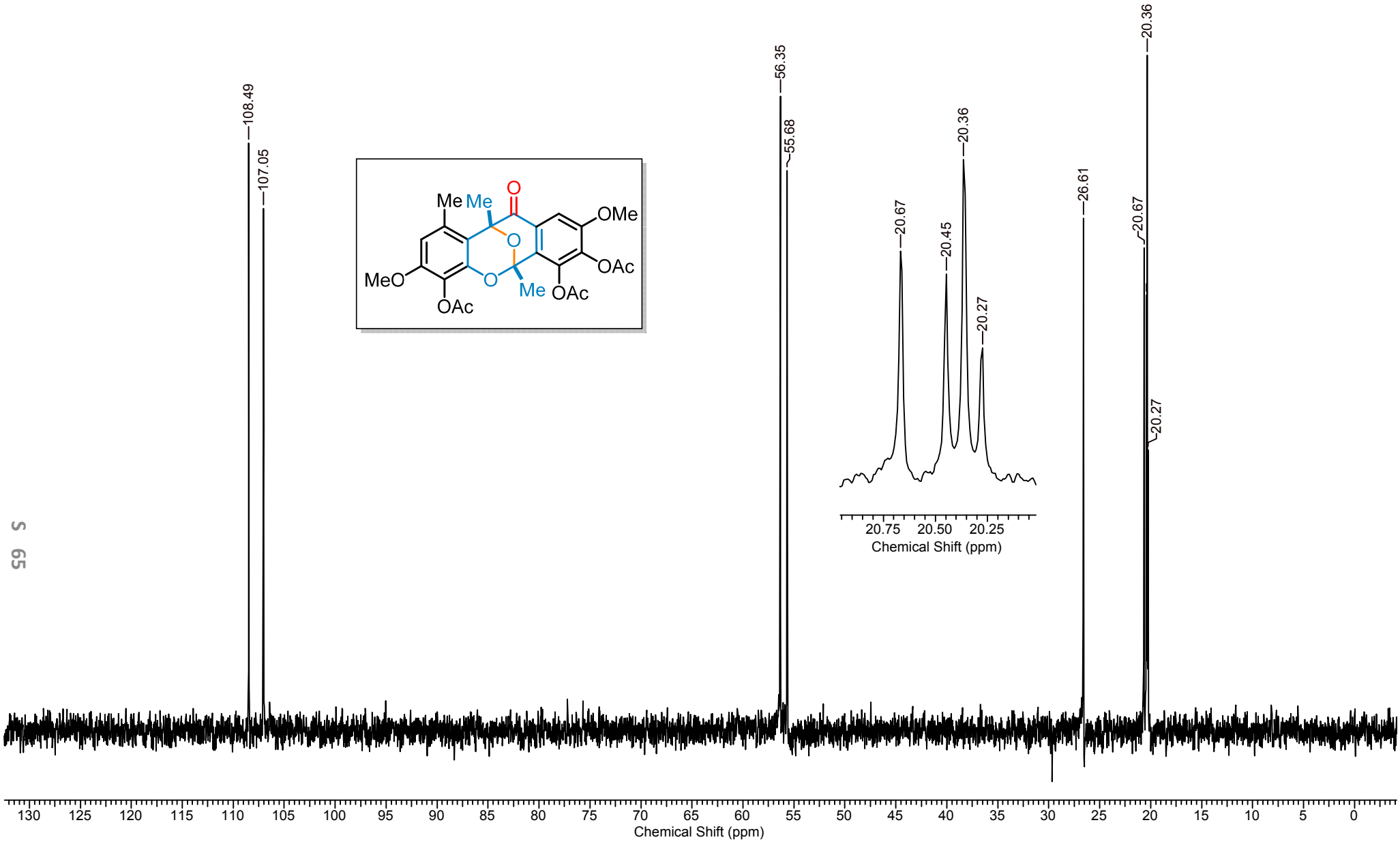
HRMS of compound 6-Ac



^{1}H NMR of compound 5-Ac

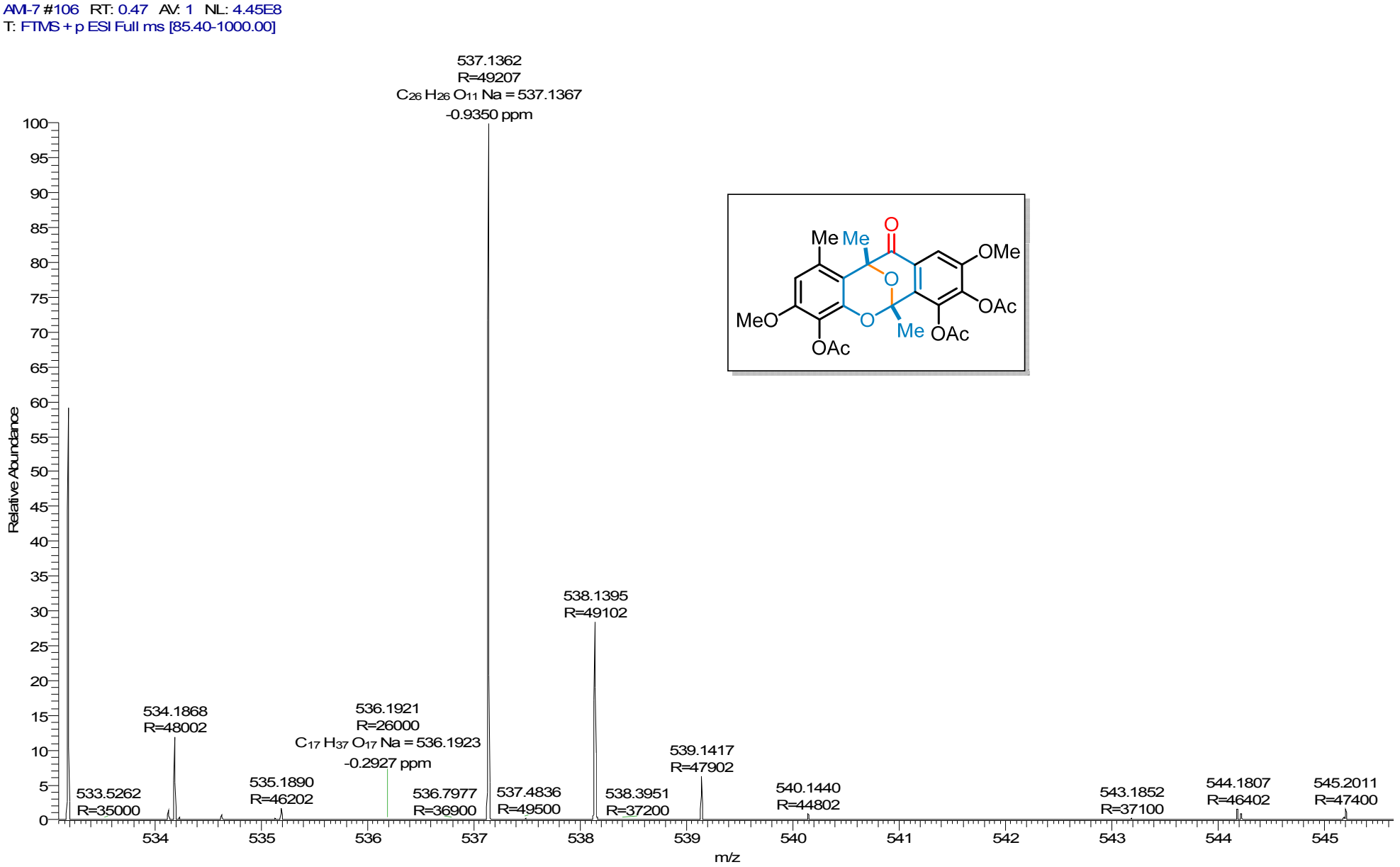


^{13}C NMR of compound 5-Ac

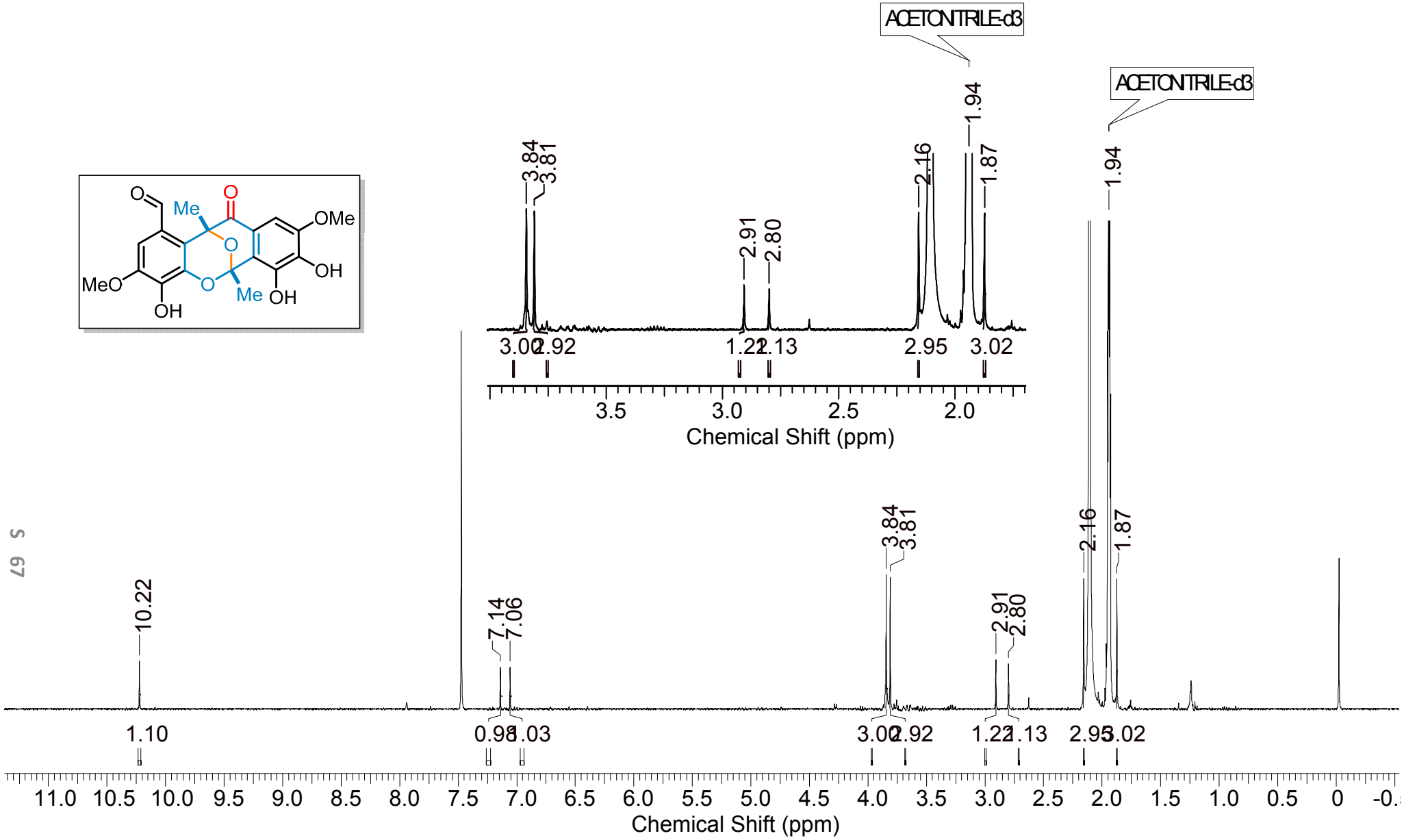


S 65

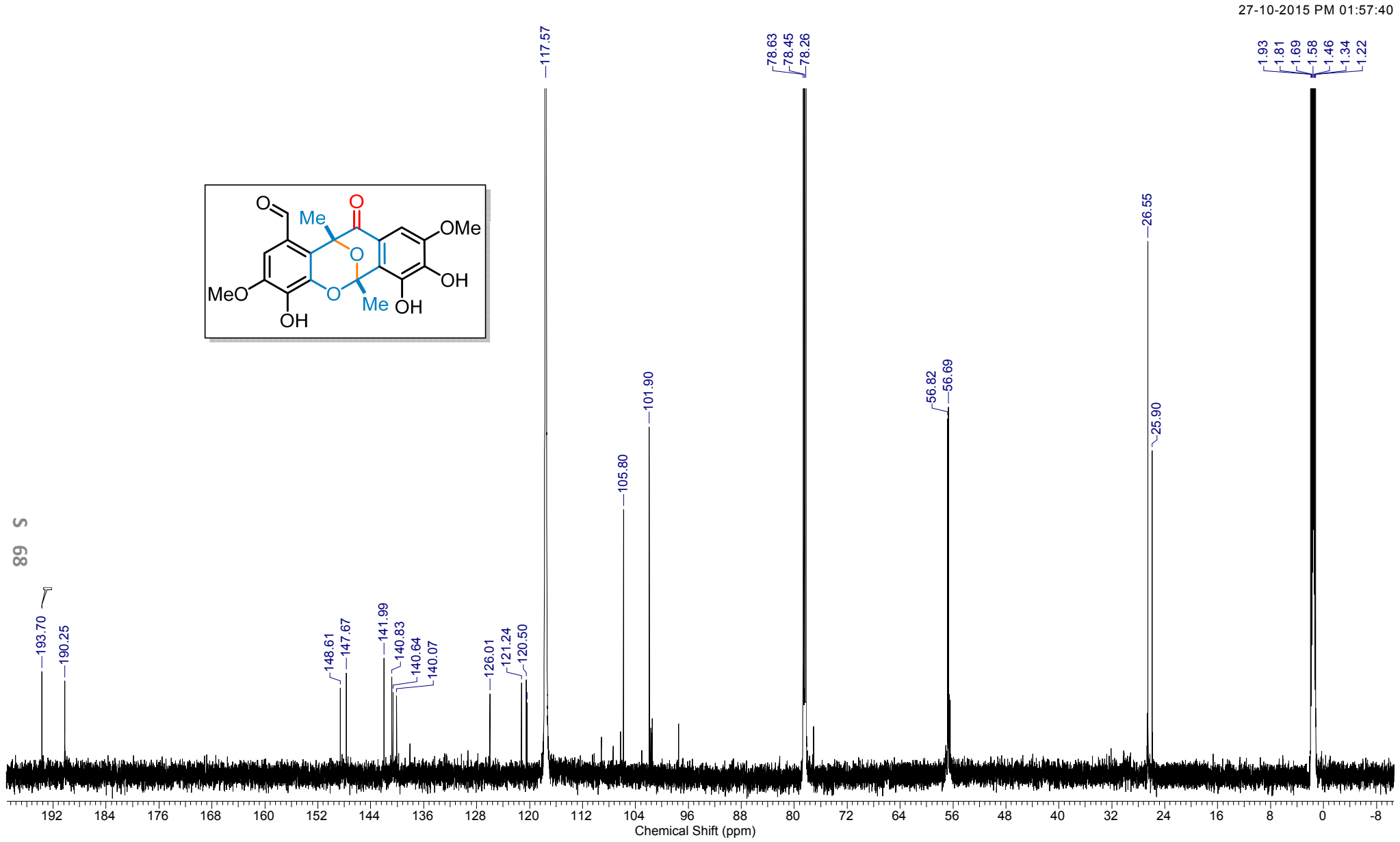
DEPT of compound 5-Ac



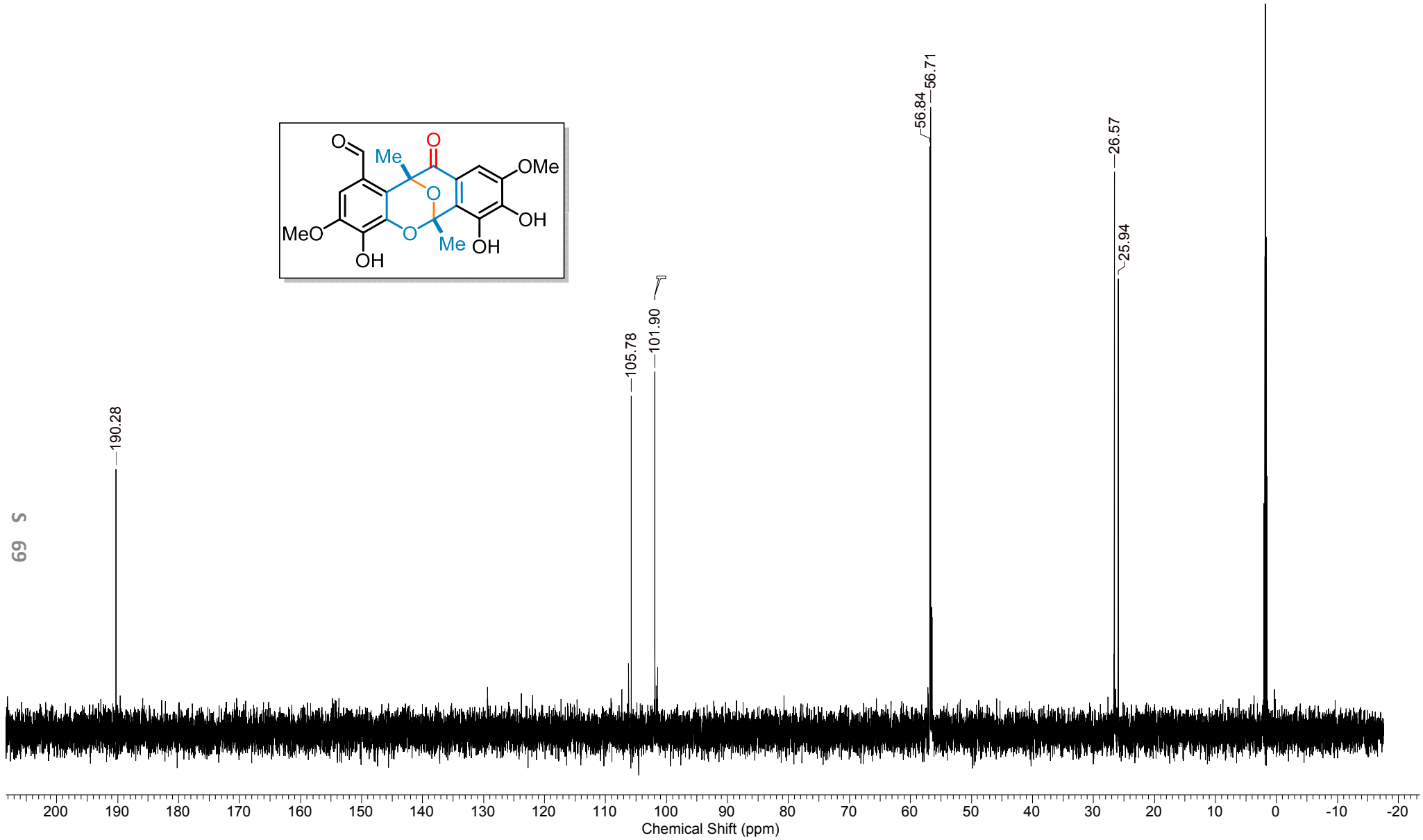
HRMS of compound 5-Ac



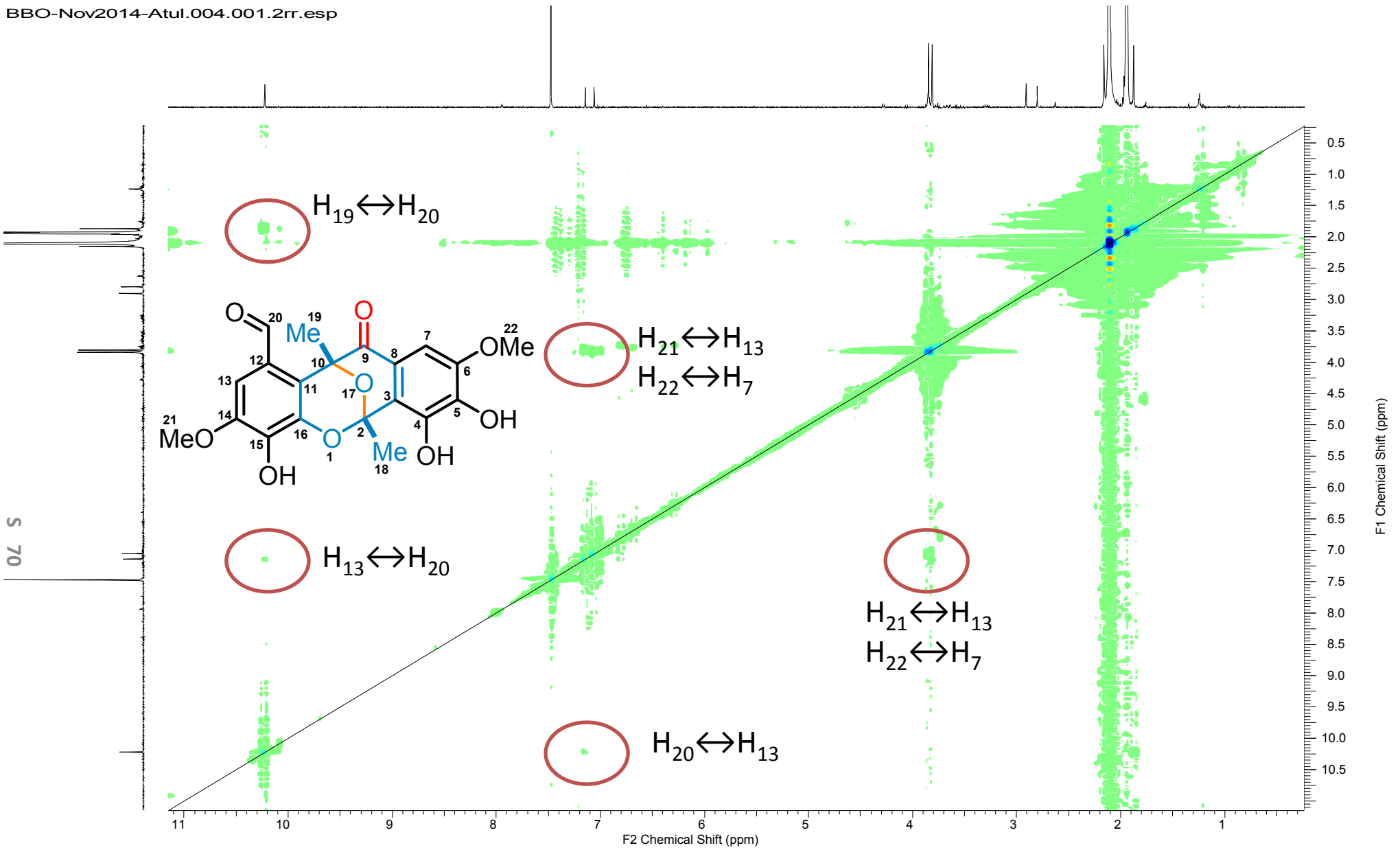
^{1}H NMR of compound 2 (700 MHz, $CDCl_3/CD_3CN$ = 1/1, v/v**)**



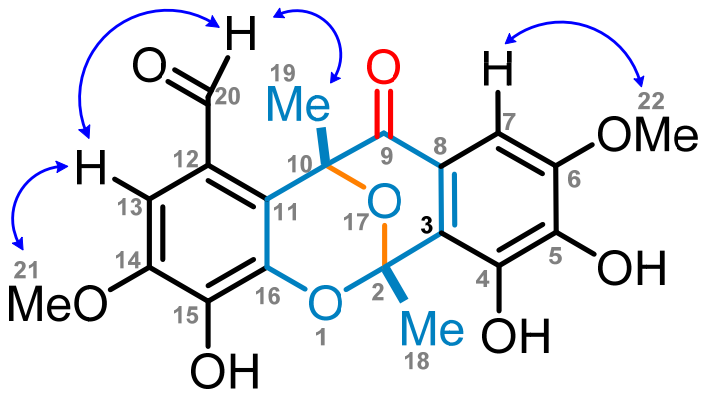
^{13}C NMR of compound 2 (700 MHz, $CDCl_3/CD_3CN$ = 1/1, v/v**)**

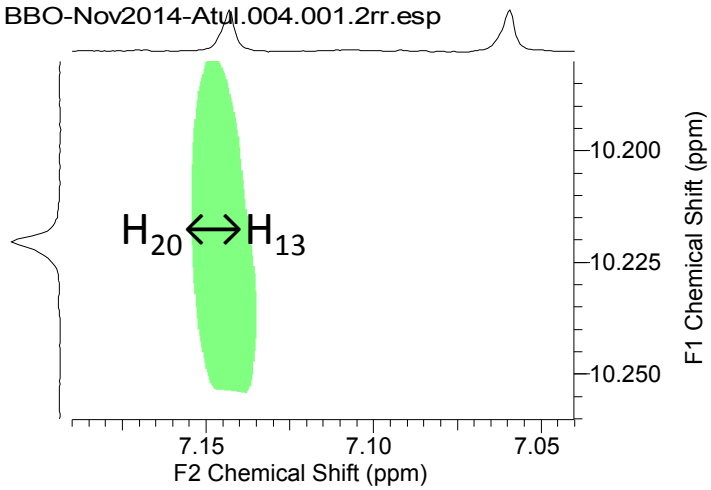


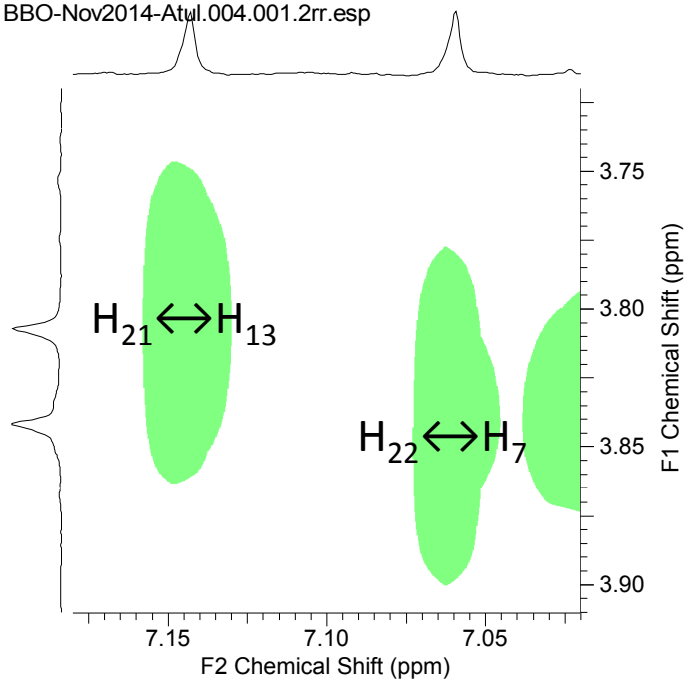
DEPT of compound 2 (700 MHz, $CDCl_3/CD_3CN$ = 1/1, v/v**)**

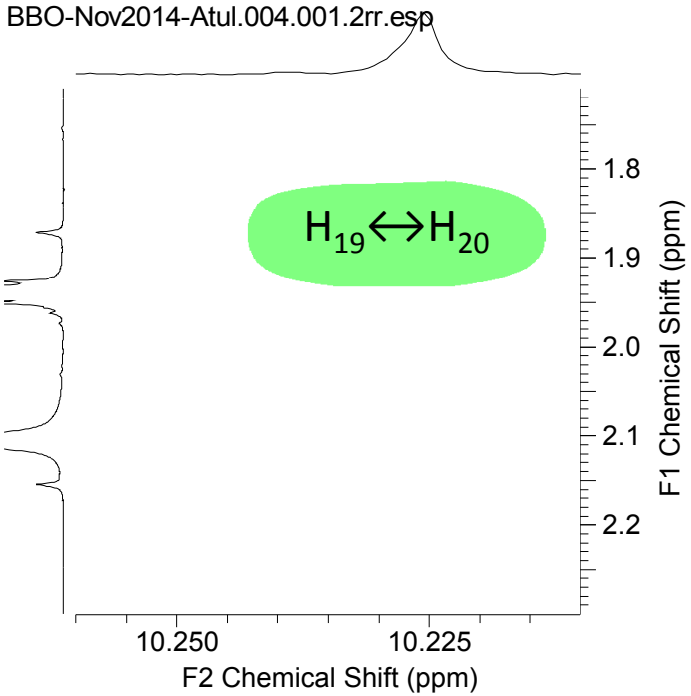


NOSEY NMR of compound 2 (700 MHz, $CDCl_3/CD_3CN$ = 1/1, v/v**)**

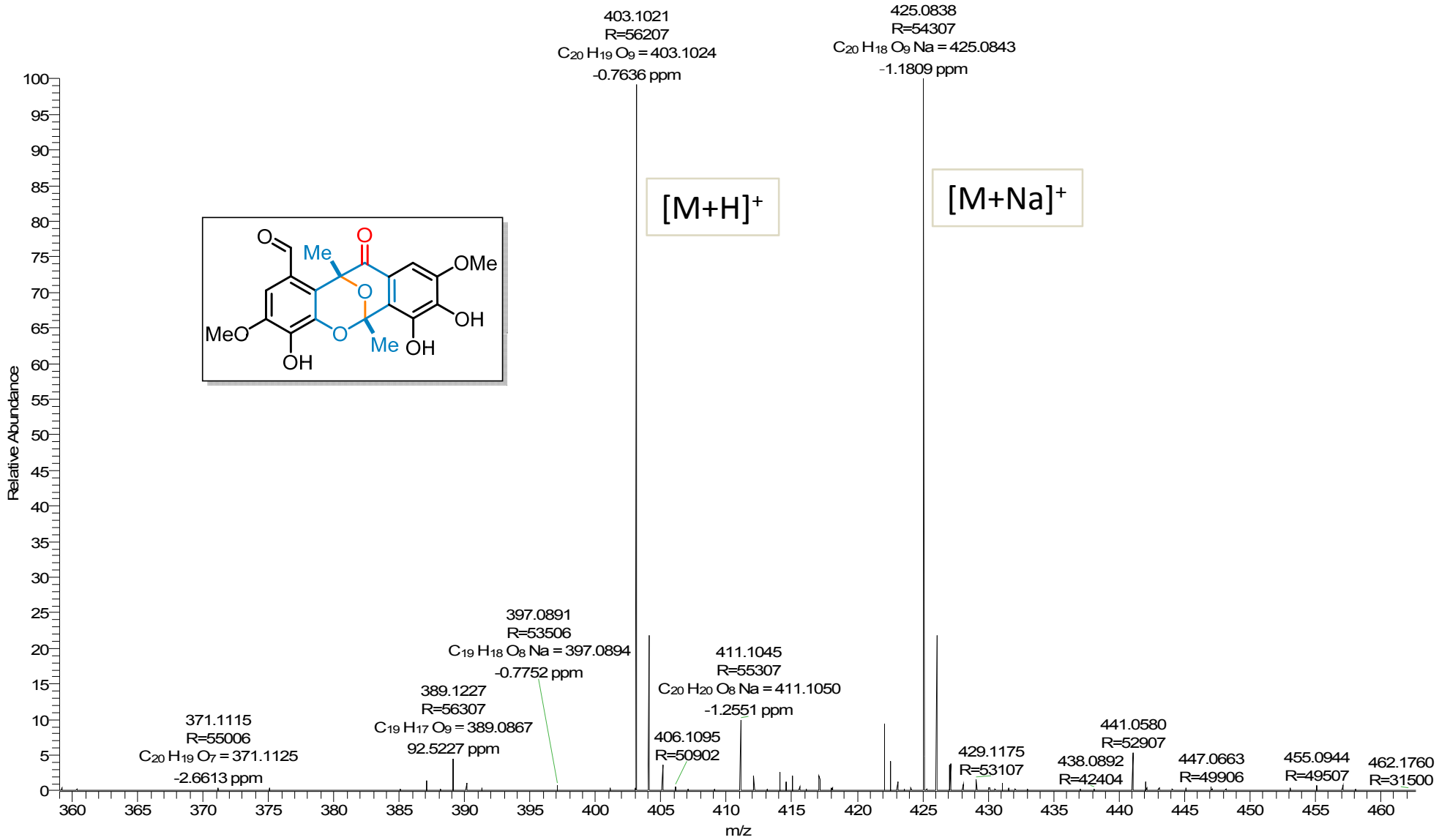








Expansion of NOSEY spectrum of compound 2 (700 MHz, $CDCl_3/CD_3CN$ = 1/1, v/v**)**



HRMS of compound 2