Electronic Supporting Information

Brønsted Acid and Ni(II)-catalyzed C-H Oxidation/Rearrangement of Cyclotriveratrylenes (CTVs) to Cyclic and Acyclic Quinones as potential anti-cancer agents.

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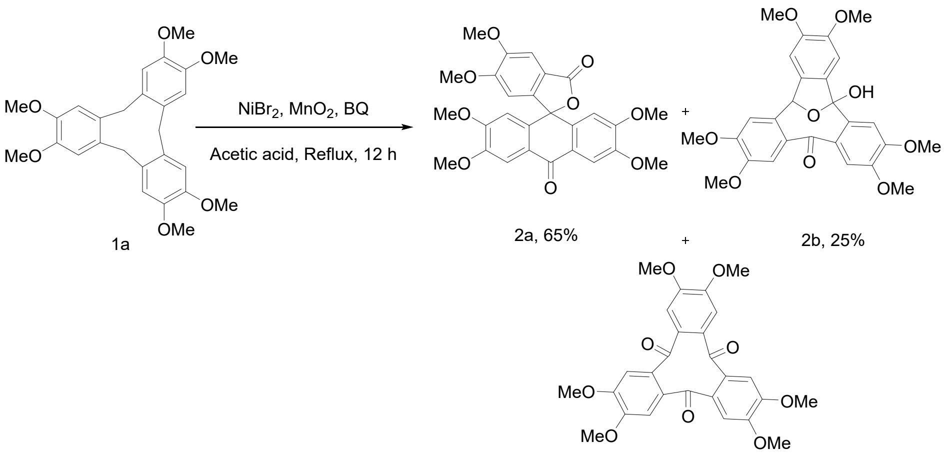
1. General information:-

Reactions were carried out using commercial reagents and solvents were used without purification. Column chromatography was carried out by using Spectrochem silica gel (100–200, 230–400 mesh). The purity of the compounds was checked on Merck precoated silica gel 60 F-254. Melting points were determined using Buchi B-540 melting point apparatus and uncorrected.^{1}H and ^{13}C-NMR spectra were recorded on a Bruker Avance NMR spectrometer operating at 500 or 400 MHz for 1H-NMR and 125 or 100 MHz for ^{13}C-NMR at room temperature using $CDCl_3$ as a solvent. the chemical shifts (δ) are reported in ppm and coupling constants (*J*) are given in Hz. Signal multiplicities are represented by s (singlet), d (doublet), t (triplet), dd (double doublet), m (multiplet) and bs (broad singlet). IR spectra were recorded in $CHCl_3$ or Neat on an IR Pristige-21 spectrometer (Shimadzu Corporation, Japan). Mass spectra were recorded on a Agilent ESI mass spectrometer. HR MS were performed on a Thermo fisher Q Exactive Mass spectometry analyzer.

2. Experimental Procedures

Experimental Procedure for Metal Catalyzed C-H Oxidation of Cyclotriveratrylene 1a:



$NiBr_2$ (0.044 mmol), benzoquinone (0.11 mmol) and manganese dioxide (4.44 mmol) (a dark black fine powder from Aldrich) were added to a 50-mL round-bottomed flask containing CTV **1a** (0.100gm, 0.22 mmol) in 10 mL of acetic acid and stirred to reflux for 12 h. The reaction progress was monitored using TLC (ethyl acetate in pet ether) (4:6), run for 3 times. The crude reaction mixture was cooled and diluted with 50 mL of EtOAc and stirred for 10 min. The content was filtrated over Celite pad and the Celite pad was washed successively with 50 mL of EtOAc. The washed filtrate was evaporated under reduced pressure and further extracted with EtOAc and water. The organic phase was dried over sodium sulphate and crude product was purified by column chromatography using a mixture of ethyl acetate-petroleum ether as eluent to give corresponding products **2a**, **2b** and **2c**.

2,3,5',6,6',7-hexamethoxy-3'H,10H-spiro[anthracene-9,1'-isobenzofuran]-3',10-dione (**2a**):
White solid, (0.071 gm., 65 % yield); $\boldsymbol{R_f}$ = 0.50 (pet ether/ethyl acetate = 60/40); **M.P**: 273–275° C; **FTIR** ($CHCl_3$): ν 3023, 1759, 1654, 1596, 1509, 1462, 1366, 1297, 1216, 739 (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$): 7.80 (s, 2H), 7.38 (s, 1H), 6.20 (s, 1H), 4.01 (s, 6H), 3.98 (s, 3H), 3.81 (s, 6H), 3.72 (s, 3H) δ ppm; **^{13}C NMR** (400 MHz, $CDCl_3$): 180.9, 171.0, 155.9, 153.8 (2C), 150.8, 150.0 (2C), 149.0, 134.2 (2C), 124.3 (2C), 117.3, 115.4, 108.8, 107.2 (2C),105.9, 103.1, 82.5, 56.3(2C), 56.2 (2C), 56.17 (2C) δ ppm; **HR MS (ESI)** Calculated for $C_{27}H_{25}O_9$ $[M+H]^+$: 493.1454 m/z, found: 493.1488 m/z.

5-hydroxy-2, 3, 7, 8, 12, 13-hexamethoxy-5, 10-dihydro-15H-5, 10-epoxytribenzo [a, d, g][9] annulen-15-one (2b):
Yellow solid, (0.027gm, 25% yield); $\boldsymbol{R_f}$ = 0.30 (pet ether/ethyl acetate = 60/40); **M.P**; 156–158 ˚ C; **FTIR** ($CHCl_3$): ν 3432 (br), 3020, 1598, 1508, 1465, 1421, 1292, 1117, 1019 (cm^{-1}); **^{1}H NMR** (400MHz, $CDCl_3$): 7.75 (s, 1H), 7.72 (s, 1H), 7.43 (s, 1H), 7.07 (s, 1H), 6.94 (s, 1H), 6.58 (s, 1H), 5.98 (s, 1H), 3.98 (s, 6H), 3.89 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.59

(s, 3H) δ ppm; **^{13}C NMR** (100 MHz, $CDCl_3$): 181.82, 153.70, 153.55, 151.42, 149.81, 149.22, 149.13, 140.03, 139.84, 138.81, 128.10, 124.11, 123.45, 110.64, 108.34, 108.31, 107.97(2C), 105.06, 103.42, 102.05, 87.23, 56.16, 56.14, 56.08, 55.99, 55.95 δ ppm; **HRMS** (ESI) calculated for $C_{27}H_{26}O_9$ is $[M+H]^+$ 495.1642m/z and $C_{27}H_{25}O_8$ ($M-H_2O$) 477.1577 m/z is calculated and found 477.1537 m/z.

2,3,7,8,12,13-hexamethoxy-5H-tribenzo[a,d,g][9]annulene-5,10,15-trione(2c):

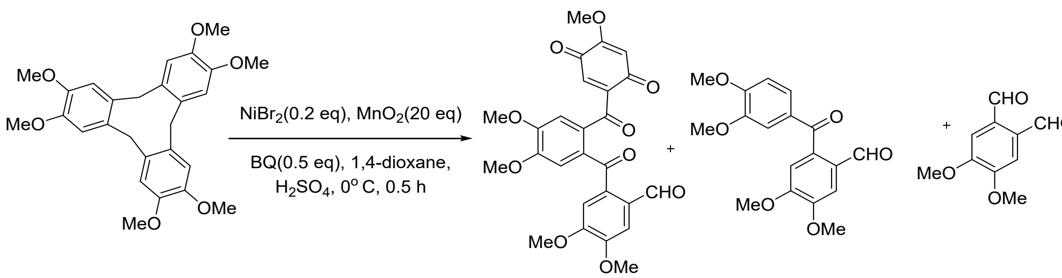
White solid, (0.011gm, 10% yield); ***R$_f$*** = 0.60 (pet ether/ethyl acetate = 60/40); **M.P.** 273–275°C; **FTIR** ($CHCl_3$): ν 3024, 2937, 2404, 1784, 1602, 1507, 1468, 1323, 1152, 1093, 1018, 974, 867 (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$): 7.30 (s, 3 H), 6.56 (s, 3 H), 3.92 (s, 9 H), 3.81 (s, 9 H), δ ppm; **^{13}C NMR** (100 MHz, $CDCl_3$): 167.07 (3C), 155.81 (3C), 152.49 (3C), 138.65 (3C), 118.51 (3C), 106.14 (3C), 103.98 (3C), 56.64 (3C), 56.55 (3C) δ ppm; **HRMS** (ESI):$C_{27}H_{25}O_9$ $[M+H]^+$: 493.1454 m/z found : 493.1487 m/z.

General Experimental Procedure for Acid mediated C-H Oxidation of Cyclotriveratrylenes (CTVs) (3a-4e).

The starting material (**1a-1d**) was prepared using the reported procedure [44] in gram scale and further, used for acid mediated C-H oxidation approach, where CTVs (0.88mmol, 0.400gm) were placed in 50ml two neck round bottom flask in 15 ml 1, 4-Dioxane solvent and MnO_2 (17mmol), BQ (0.44mmol) and $NiBr_2$ (0.17mmol) were added subsequently followed by the slow addition of H_2SO_4 (0.3ml) carried out at zero degree Celsius. The reaction progress was monitored using TLC (ethyl acetate in pet ether)(4:6) found **1a** was completely consumed within half an hour, the reaction mixture was diluted with 50 mL of EtOAc and stirred for 10 min. The content was filtrated over Celite pad and the Celite pad was washed successively with 50 mL EtOAc. The organic phase was evaporated under reduced pressure and further was extracted EtOAc and water. The crude product was purified by column chromatography using a mixture of ethyl acetate-petroleum ether as eluent to give corresponding acyclic and cyclic quinones products.

Experimental Procedure (A) for Acid mediated C-H Oxidation of Cyclotriveratrylene 1a to the synthesis of (3a-3c).

CTV **1a** (1.11mmol, 0.500gm) was placed in 50ml two neck round bottom flask containing 19 ml of 1, 4-Dioxane solvent, MnO_2 (22.2mmol, 1.93gm), BQ (0.5mmol, 0.058gm) and $NiBr_2$ (0.22mmol, 0.0484gm) were added subsequently followed by the slow addition of H_2SO_4 (0.4ml) carried out at zero degree. The reaction progress was monitored using TLC (ethyl acetate in pet ether) (4:6) run 2-3 times to see the all spots well separated. Where, the starting material **1a** was completely consumed within half an hour. The content was filtrated over Celite pad and the Celite pad was washed successively with 50 mL EtOAc. The organic phase was evaporated under reduced pressure and further was extracted EtOAc and 100 ml water. The product was purified by column chromatography using ethyl acetate- petroleum ether (2:8) as the eluent to give **3a** as acyclic aldehyde quinone analogues of **1a** and **3b** and **3c** as decomposed products of **3a** respectively.



1a 3a, 46% 3b, 21% 3c, 23%

Experimental data:-(2-(4,5-dimethoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-diene-1-carbonyl)benzoyl)-4,5-dimethoxybenzaldehyde (3a):

Yellow solid, (0.350 gm, 46% yield); ***R$_f$*** = 0.20 (pet ether/ethyl acetate = 60/40); **M.P**:190-192 °C; **FTIR**($CHCl_3$): ν 3021, 2957, 2854, 2098, 1648, 1641, 1510, 1462, 1377, 1265, 1123, 1017(cm^{-1}); **^{1}H NMR** (500 MHz, $CDCl_3$): 9.34 (s, 1H), 8.61 (s, 1H), 7.63 (s, 1H), 7.35 (s, 1H), 6.63 (d, 2H), 6.21 (s, 1H), 4.07 (s, 3H), 4.06 (s, 3H), 3.89 (s, 3H), 3.84 (s, 3H), 3.70 (s, 3H) δ ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): 189.33, 184.49, 179.53 , 161.51, 154.47, 152.46, 152.37, 148.99, 138.22, 137.66, 132.22, 131.28 , 127.86, 127.44, 127.36, 124.11, 111.50 , 109.76, 109.29, 108.16, 106.55, 56.39, 56.30, 56.27, 56.15, 55.91 δ ppm ; **HRMS** (ESI): Calculated for $C_{26}H_{23}O_{10}$ [M-H] :495.1247 m/z, found : 495.1289 m/z.

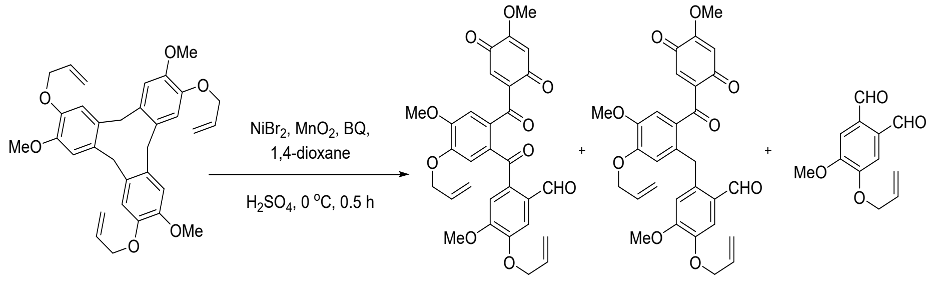
2-(3, 4-dimethoxybenzoyl)-4, 5-dimethoxybenzaldehyde (3b):

Pale yellow solid, (0.080gm, 21% yield); ***R_f*** = 0.40 (pet ether/ethyl acetate = 60/40); **M.P**:161–163 ° C; **FTIR**($CHCl_3$): ν 3020, 2960, 2928, 1683, 1648, 1590, 1513, 1463, 1419, 1349, 1292, 1275, 1157, 1142, 1094, 1021 (cm^{-1}); **^{1}H NMR** (500 MHz, $CDCl_3$): 9.80 (s, 1H), 7.50 (d, 1H, J = 1.8 Hz), 7.48(s, 1H), 7.17–7.15 (dd, 1H, J = 2 Hz, J = 8.3 Hz), 6.92 (s,1H), 6.78 (d, 1H, J = 8.5 Hz), 3.94 (s, 3H), 3.88 (s, 6H), 3.87(s, 3H) δ ppm;**^{13}C NMR** (125 MHz, $CDCl_3$): 194.25, 189.09, 154.02, 152.87, 150.57, 149.38, 136.97, 130.94, 129.15, 126.23, 111.20, 111.05, 110.01, 109.47, 56.41, 56.30, 56.18, 56.10 δ ppm **HRMS** (ESI): Calculated for $C_{18}H_{17}O_6$ [M-H] :329.1020 m/z, found : 329.1017 m/z..

4, 5-dimethoxyphthalaldehyde (3c):

White solid, (0.080gm, 23% yield); ***R_f*** = 0.70 (pet ether/ethyl acetate = 60/40); **M.P**: 202–204°C; **FTIR**($CHCl_3$): ν 3020, 2927, 2855, 2400, 2957, 1657, 1641, 1632, 1513, 1462, 1378, 1122, 1018 (cm^{-1}); **^{1}H NMR** (500 MHz, $CDCl_3$): 10.53 (s, 2H), 7.41 (s, 2H), 3.97 (s, 6H) δ ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) : 190.18 (2C), 153.19 (2C), 131.03 (2 C), 111.60 (2C), 56.53 (2C) δ ppm; **HRMS** (ESI): Calculated for $C_{10}H_{11}O_4$ $[M+H]^+$:195.0652 m/z, found : 195.0659 m/z.

Procedure: (B) Acid mediated C-H Oxidation of Methoxy Allyloxy Cyclotriveratrylene (1b):



1b **3d, 25%** **3e, 20%** **3f, 10%**

Following the Procedure **A**, allyloxy methoxy CTV **1b** (3.788mmol, 2gm), MnO_2 (80mmol, 6.59gm), BQ (1.8mmol, 0.200gm) and $NiBr_2$ (0.8 mmol, 0.165gm) was added to round bottom flask containing 1,4-dioxane followed by dropwise addition of H_2SO_4 at zero degree Celsius. The reaction progress was monitored using TLC (ethyl acetate in pet ether) (4:6), resulted in complete consumption of starting material in half an hour. The product was purified by column chromatography using ethyl acetate- petroleum ether (2:8) system as the eluent, offers **3d, 3e** and **3f** as acyclic aldehyde quinone analogues of **1b** and decomposed product of **3d** respectively.

5-(allyloxy)-2-(5-(allyloxy)-4-methoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-diene-1 carbonyl) benzoyl) - 4-methoxybenzaldehyde (3d) :

yellow solid, (0.530gm, 25% yield); ***R_f*** = 0.3 (pet ether/ethyl acetate = 60/40); **M.P**:191–193 ° C; **FTIR**($CHCl_3$): ν 3020, 2927, 2855, 1656, 1641, 1632, 1536, 1529, 1512, 1466, 1423, 1378, 1366, 1261, 1121, 1018 (cm^{-1}); **^{1}H NMR** (500 MHz, $CDCl_3$): 9.31 (s, 1H), 8.59 (s, 1H), 7.63 (s, 1H), 7.34 (s, 1H), 6.65 (s, 1H), 6.62 (s, 1H), 6.21 (s, 1H), 6.12–6.20 (m, 1H) 5.80–5.92 (m, 1H), 5.52 (dd, *J* = 17.26, 1.38 Hz, 1 H), 5.38 (dd, *J* = 10.51, 1.13 Hz, 1H), 5.19–5.24 (dd, *J* = 10.51, 1.13 Hz, 1H), 5.10–5.17 (dd, *J* = 17.26, 1.38 Hz, 1H), 4.79 (d, *J* = 5.50 Hz, 2H), 4.43 (d, *J* = 5.75 Hz, 2H), 4.06 (s, 3H), 3.87 (s, 3H), 3.84 (s, 3H) δ ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) : 189.27 (2C), 184.52, 179.50, 161.49, 154.76, 152.64, 151.08, 147.87, 138.40, 137.66, 132.63 (2C), 132.10, 131.92, 131.15, 127.80, 127.30, 123.99, 119.48 (2C), 118.75, 111.73, 110.95, 109.79, 108.44, 108.24, 69.95, 69.76, 56.39, 56.28, 56.22 δ ppm.; **HRMS** (ESI): Calculated for $C_{30}H_{25}O_{10}$[M-H] :545.1560 m/z, found : 545.1595 m/z.

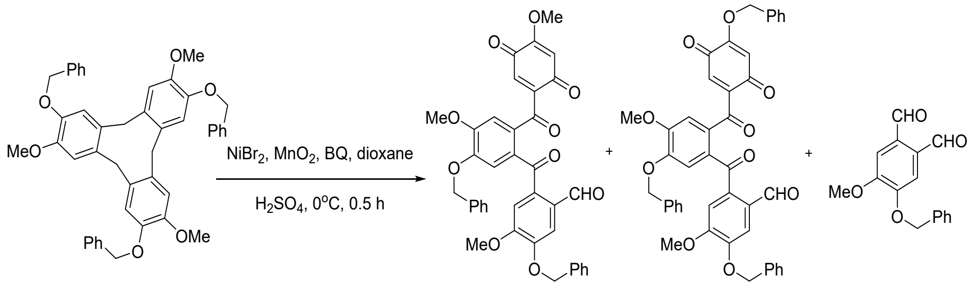
5-(allyloxy)-2-(5-(allyloxy)-4-methoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-diene-1-carbonyl)benzyl)-4-methoxybenzaldehyde (3e):

Yellow solid, (0.410gm, 20% yield); ***R$_f$*** = 0.5 (pet ether/ethyl acetate = 60/40); **M.P**: 163–165 ^{o} C; **FTIR**($CHCl_3$): ν 3020, 2927, 2855, 2400, 1676, 1644, 1612, 1597, 1585, 1506, 1467,1423, 1263, 1124,1018 (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$) : 9.84 (s, 1H), 7.49 (s, 1H), 6.90 (s, 1H,) 6.88 (s, 1H), 6.81 (s, 1H), 6.19 (s, 1H), 6.04–6.15 (m, 1H), 5.97 (s, 1 H), 5.83–5.94 (m, 1H), 5.48 (dd, *J* = 17.36, 1.34 Hz, 1H), 5.36 (dd, *J* = 10.49, 0.95 Hz, 1H), 5.15–5.23 (m, 2H), 4.74 (d, *J* = 5.34 Hz, 2H), 4.43 (d, *J* = 5.72 Hz, 2H), 4.08 (s, 2H), 3.95 (s, 3H), 3.90 (s, 3H), 3.80–3.85 (m, 3H) δ ppm; **^{13}C NMR** (100 MHz, $CDCl_3$): 195.16, 189.14, 187.04, 182.50, 158.56, 153.00 , 152.95, 150.17, 149.80, 145.91, 137.14, 132.76, 132.64, 132.02, 130.57, 129.51, 129.43, 119.09, 118.64, 118.01, 115.31, 111.97, 111.48, 107.62, 70.08, 69.93, 56.42, 56.29, 56.19, 33.13 δ ppm.; **HRMS** (ESI): Calculated for $C_{30}H_{27}O_9$[M-H] : 531.1767 m/z, found : 531.1783 m/z.

4-(allyloxy)-5-methoxyphthalaldehyde (3f):

White solid, (0.090gm, 10% yield); ***R$_f$*** = 0.8 (pet ether/ethyl acetate = 60/40); **M.P**: 115–117 ^{o} C; **FTIR**($CHCl_3$): ν 3019, 2957, 2927, 2855, 2400, 1726, 1676, 1598, 1506, 1464, 1377,1261, 1096, 1019 (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$): 10.59 (s, 1H), 10.56 (s, 1H), 7.48 (s, 1H), 7.46 (s, 1H), 6.03–6.16 (m, 1H), 5.48 (dd, *J* = 17.20, 1.31 Hz, 2H), 5.38 (dd, *J* = 10.51, 1.25 Hz, 1H), 4.76 (dt, *J* = 5.47, 1.39 Hz, 2H), 4.03 (s, 3H) δ ppm ; **^{13}C NMR** (100 MHz, $CDCl_3$) : 190.16, 190.14, 153.48, 152.17, 131.71, 131.06, 130.88, 119.32, 113.18, 111.86, 70.07, 56.49 δ ppm; **HRMS** (ESI): calculated for $C_{12}H_{13}O_4$$[M+H]^+$: 221.0808 m/z found 221.0805 m/z.

Procedure: Acid mediated C-H Oxidation of Benzyloxy Methoxy Cyclotriveratrylene (1c):-



1c 3g, 30% 3h, 25% 3i, 12%

The Procedure **A** was followed, with the quantities of benzyloxy methoxy CTV **1c** (0.589mmol, 0.400gm), MnO_2 (12mmol, 1gm), BQ (0.294mmol, 0.0312gm) and $NiBr_2$ (0.1179 mmol, 0.025gm) in 15ml 1,4-Dioxane for half hour, yields **3g, 3h** and **3i** a acyclic aldehyde quinone analogues of benzyloxy methoxy CTV **1c** and decomposed product of **3g/3h** respectively.

5-(benzyloxy)-2-(5-(benzyloxy)-4-methoxy-2-(4-methoxy-3,6-dioxocyclohexa-1,4-diene-1-carbonyl)benzoyl)-4-methoxybenzaldehyde (3g).

Pale yellow solid, (0.116gm, 30% yield); ***R$_f$*** = 0.3 (pet ether/ethyl acetate = 60/40); **M.P**: 205–207 ^{o} C; **FTIR**($CHCl_3$): ν 3020, 2854, 2927, 1673, 1617, 1643, 1504, 1467, 1437, 1342, 1264, 1124, 1159, 1075, 1029 (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$): 9.22 (s, 1H), 8.59 (s, 1H), 7.70 (s, 1H), 7.61 (d, *J* = 7.32 Hz, 2H), 7.46 (t, *J* = 7.48 Hz, 2H), 7.38 (d, *J* = 7.63 Hz, 1H) 7.36 (s, 1H), 7.23–7.26 (m, 3H), 7.05–7.09 (m, 2H), 6.61 (s, 1H), 6.42 (s, 1H), 6.21 (s, 1H), 5.38 (d, *J* = 2.14 Hz, 2H), 5.11 (d, *J* = 13.12 Hz, 1H), 4.92 (d, *J* = 13.12 Hz, 1H), 4.10 (s, 3H), 3.84 (s, 3H), 3.77 (s, 3H) δ ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) : 189.06 (2C), 184.54, 179.46, 161.45, 154.93, 152.72, 150.89, 148.04, 138.43, 137.81, 136.55, 135.49, 131.97, 131.10, 128.78 (2C), 128.67 (2C), 128.24, 128.09, 127.78, 127.65 (2C), 127.24, 127.07 (2C), 123.86, 111.55, 111.27, 109.79, 109.20, 108.22, 71.06, 70.82, 56.38, 56.33, 56.04 δ ppm. **HRMS** (ESI): calculated for $C_{38}H_{31}O_{10}$ $[M+H]^+$: 647.1917 m/z found 647.1937 m/z; $C_{38}H_{29}O_{10}$ [M-H]: 646.1873 m/z found 646.1895 m/z.

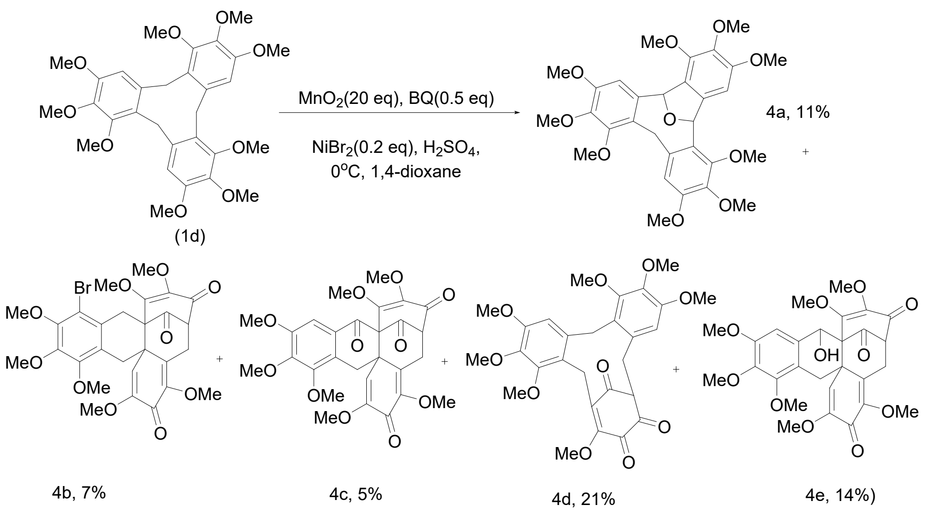
5-(benzyloxy)-2-(5-(benzyloxy)-2-(4-(benzyloxy)-3,6-dioxocyclohexa-1,4-diene-1-carbonyl)-4-methoxybenzoyl)-4-methoxybenzaldehyde (3h):

Yellow solid, (0.110gm, 25% yield); $\boldsymbol{R_f}$ = 0.6 (pet ether/ethyl acetate = 60/40); **M.P:** 183–185^{o}C; **FTIR**($CHCl_3$): ν 3020, 2928, 2855, 2400, 2097, 1656, 1640, 1631, 1467, 1422, 1122, 1018, (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$): 9.24 (s, 1H), 8.44 (s, 1H), 7.56 (s, 1H), 7.39–7.43 (m, 2H), 7.21–7.36 (m, 13H), 7.19 (s, 1H), 6.61 (s, 1H), 6.44 (s, 1H), 6.20 (s, 1H) 5.27 (s, 2H) 5.08 (s, 1H) 4.93–5.03 (m, 3H) 3.96 (s, 3H) 3.53 (s, 3H) δ ppm; **^{13}C NMR** (100 MHz, $CDCl_3$): 189.52 (2C), 184.71, 179.31, 160.45, 153.46, 152.62, 151.35, 149.31, 138.08, 137.36, 135.73, 135.66, 134.01, 132.31, 130.97, 128.89 (2C), 128.85 (2C), 128.63 (2C), 128.41, 128.23, 127.99 (2C), 127.59, 127.54 (2C), 127.46, 127.30 (2C), 124.14, 113.19, 110.89, 109.92, 109.47 (2C), 106.67, 71.33, 70.97, 70.74, 56.11, 55.89 δ ppm. **HRMS** (ESI): calculated for $C_{44}H_{35}O_{10}$ $[M+H]^+$: 723.2230 m/z found 723.2527m/z (We could not get the HRMS value within 0.003 m/z after several attempts with +ve/-ve ionization methods).

4-(benzyloxy)-5-methoxyphthalaldehyde (3i):

White solid, (0.020gm, 12% yield); $\boldsymbol{R_f}$ = 0.8 (pet ether/ethyl acetate = 60/40); **M.P:** 110–112^{o} C; **FTIR**($CHCl_3$): ν 3022**,** 2929, 2403, 1758, 1684, 1592, 1511, 1460, 1273, 1141,1022 (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$): 10.59 (s, 1 H), 10.52 (s, 1H), 7.51 (s, 1H), 7.49 (s, 1H), 7.45 (d, *J* = 7.25 Hz, 2H), 7.39 (t, *J* = 7.63 Hz, 3H), 5.29 (s, 2H), 4.03 (s, 3H) δ ppm; **^{13}C NMR** (100 MHz, $CDCl_3$): 190.20, 190.15, 153.68, 152.31, 135.43, 131.17, 130.84, 128.83 (2C), 128.50, 127.50 (2C), 113.64, 111.89, 71.18, 56.50 δ ppm; **HRMS** (ESI): calculated for $C_{16}H_{15}O_4$ $[M+H]^+$:271.0965 m/z, found :271.0972 m/z.

Procedure: Acid mediated C-H Oxidation of Trimethoxy Cyclotriveratrylene (TCTV) (1d):



CTV **1d** (0.833mmol, 0.450gm) were placed in 50ml two neck round bottom flask in 17 ml 1, 4-dioxane solvent, MnO_2 (17mmol, 1.44gm), BQ (0.42mmol, 0.044gm) and $NiBr_2$ (0.166mmol, 0.036gm) were added subsequently followed by the slow addition of H_2SO_4 (0.337ml) carried out at zero degree celsius. The reaction progress was monitored using TLC (ethyl acetate in pet ether) (4:6) run 2-3 times to see the all spots well separated. Where, the starting material **1d** was completely consumed within half an hour. The product was purified by column chromatography using ethyl acetate-petroleum ether (2:8) as the eluent to give **4a, 4b, 4c, 4d** and **4e** as cyclic quinone analogues of Trimethoxy Cyclotriveratrylene (TCTV) **1d**.

Procedure: Acid mediated C-H Oxidation of Trimethoxy Cyclotriveratrylene (TCTV) (1d). A control experiment:

CTV **1d** (0.0925mmol, 0.05gm) were placed in 25ml two neck round bottom flask in 2ml 1, 4-dioxane solvent, TEMPO(0.185mmol, 0.028gm), MnO_2 (1.85mmol, 0.160gm), BQ (0.05mmol, 0.005gm) and $NiBr_2$ (0.019mmol, 0.004gm) were added subsequently, slow addition of H_2SO_4 (0.04ml) carried out at zero degree. The reaction progress was monitored using TLC (ethyl acetate in pet ether) (4:6). Where, the starting material **1d** was completely consumed within half an hour. The product was purified by column chromatography using ethyl acetate- petroleum ether (2:8) as the eluent to give **4a, 4b,4d** and **4e** in **20%, 32%, 24%** and **15%** yields respectively as a cyclic quinone analogues of Trimethoxy Cyclotriveratrylene(TCTV) **1d**.

1,2,3,6,7,8,11,12,13-nonamethoxy-10,15-dihydro-5H-5,10-epoxytribenzo[a,d,g][9]annulene (4a):
White solid, (0.0495gm, 11% yield); R_f = 0.9 (pet ether/ethyl acetate = 60/40); **M.P**: 98–99° C; **FTIR**($CHCl_3$): ν 3019, 2934, 2854, 2400, 1654, 1636, 1596, 1527, 1491, 1466, 1410, 1341, 1313, 1118,1016 (cm^{-1}); **^{1}H NMR** (500 MHz, $CDCl_3$): 6.83 (s, 1H), 6.78 (s, 1H), 6.75 (s, 1H), 6.44 (s, 1H), 6.18 (s, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.87 (d, *J* = 2.29 Hz, 6H) 3.85 (s, 6H) 3.83 (s, 3H) 3.81 (s, 3H) 3.71 (d, *J* = 14.50 Hz, 1H) 3.56 (s, 3H) 2.98 (d, *J* = 14.50 Hz, 1H) δ ppm ; **^{13}C NMR** (125 MHz, $CDCl_3$): 155.30, 152.85, 152.59, 152.23, 151.26, 147.26, 142.05, 141.98, 140.24, 138.01, 137.02, 136.77, 127.41, 126.29, 126.08, 112.60, 109.97, 99.84, 87.71, 79.77, 62.30, 61.19(2C), 60.91, 60.68, 60.49, 56.35, 56.18, 56.01, 27.61 δ ppm ; **HRMS** (ESI): calculated for $C_{30}H_{34}O_{10}$ $[M+Na]^+$:577.2044 m/z, found: 577.2036 m/z.

11-bromo-2,4, 8, 9, 12, 13,14-heptamethoxy-5, 6, 10, 15-tetrahydro-6, 9a-methanobenzo[1,8] cycloocta[1, 2-b]naphthalene-3, 7, 16-trione(4b):
Yellow solid, (0.0359 gm, 07% yield); R_f = 0.7 (pet ether/ethyl acetate = 60/40); **M.P**: 230–232°C; **FTIR**($CHCl_3$): ν 3020, 2400, 1734, 1662, 1645, 1602, 1528, 1494, 1465, 1412, 1329, 1121, 1088, 1070, 1018(cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$) : 5.68 (s, 1H), 3.99 (s, 3H), 3.94 (s, 3H), 3.90 (s, 3H), 3.79 (s, 3H), 3.76 (s, 3H), 3.61–3.69 (m, 4H), 3.57–3.61 (m, 4H), 3.34 (s, 2H), 2.94 (dd, *J* = 15.38, 5.75 Hz, 1H), 2.76–2.90 (dd, *J* = 17.36, *J* = 17.26 2H) δ ppm ; **^{13}C NMR** (100 MHz, $CDCl_3$): 200.90, 189.43, 176.10, 162.44, 152.12, 151.11, 150.35, 150.32, 144.96, 140.50, 139.06, 127.91, 120.95, 115.58, 113.90, 61.91, 61.19, 61.00, 60.91, 60.76, 60.60, 60.56, 59.81, 55.58, 46.20, 33.13, 29.54, 28.12 δ ppm; **HRMS** (ESI): calculated for $C_{28}H_{30}BrO_{10.}$ $[M+H]^+$: 605.1017 m/z, found: 605.1039 m/z.

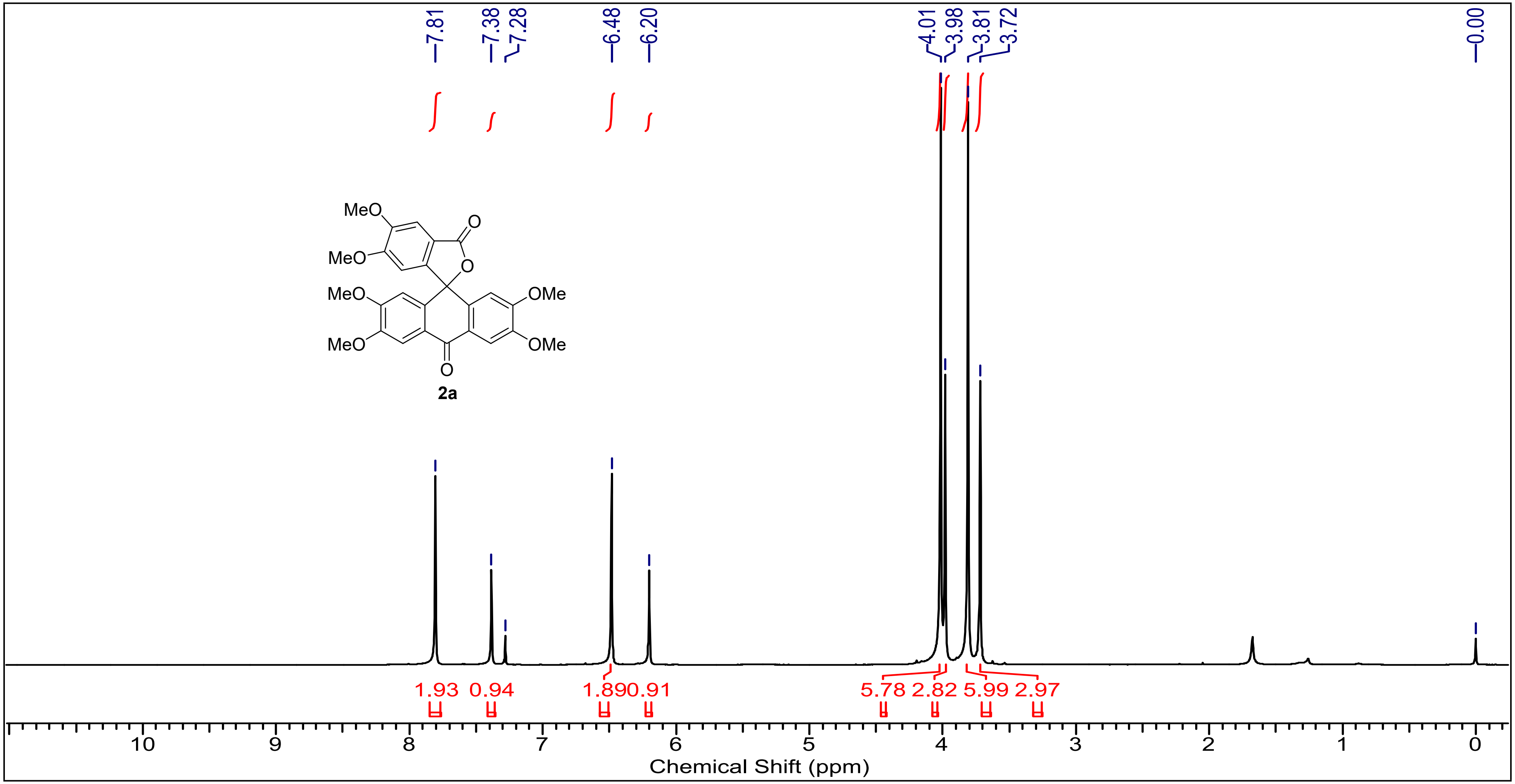
2, 4, 8, 9, 12, 13, 14 heptamethoxy5, 6dihydro6, 9a-methanobenzo [1, 8]cycloocta[1,2b] Naphthalene-3, 7, 10, 16 (15H)-tetraone (4c):
Dark brown solid, (0.0201gm, 05% yield); R_f = 0.4 (pet ether/ethyl acetate = 60/40); **M.P:** 149–151°C; **FTIR** ($CHCl_3$): ν 3020, 2940, 2854, 2400, 2106, 1775, 1649, 1641, 1483, 1463, 1416, 1353, 1315, 1101, 1018 (cm^{-1}). **^{1}H NMR** (400 MHz, $CDCl_3$) : 7.55 (s, 1H), 5.78 (s, 1H), 4.01 (s, 3H), 3.95–4.00 (m, 6H), 3.80 (s, 3H), 3.76 (s, 3H), 3.66 (s, 3H), 3.58 (d, *J* = 2.63 Hz, 1H), 3.47 (s, 3H), 3.43 (d, *J* = 16.13 Hz, 1H), 3.19 (d, *J* = 16.63 Hz, 1H), 2.91–3.01 (m, 2H) δ ppm ; **^{13}C NMR** (100 MHz, $CDCl_3$): 200.77, 189.00, 187.87, 175.70, 161.33, 153.05, 152.02, 150.96, 150.45, 148.30, 142.63, 136.71, 126.38, 125.28, 115.97, 105.87, 71.10, 61.88, 61.12, 61.06, 60.98, 60.80, 59.19, 56.08, 55.32, 51.01, 32.25, 30.01 δ ppm ; **HRMS** (ESI): calculated for $C_{28}H_{28}O_{11}$ [M+Na]: 563.1524 m/z; found: 563.1547 m/z.

1,2,3,9,12,13,14-heptamethoxy-5,6,11,16-tetrahydro-6,10methanodibenzo[a,d][12]annulene-7,8,17-trione (4d):
White solid, (0.090gm, 21% yield); R_f = 0.3 (pet ether/ethyl acetate = 60/40); **M.P:** 186–188°C; **FTIR**($CHCl_3$): ν 3020, 2937, 2850, 2400, 1736, 1666, 1620, 1590, 1497, 1458, 1432, 1414, 1298, 1122, 1107,1066 (cm^{-1}); **^{1}H NMR** (400 MHz, $CDCl_3$): 6.57 (s, 1 H), 5.80 (s, 1 H), 3.97 (s, 3 H), 3.89 (s, 3H), 3.85 (s, 3 H), 3.80 (s, 3 H), 3.77 (s, 3 H), 3.57–3.66 (m, 9 H), 3.22 (d, *J* = 17.70 Hz, 1 H), 2.98 (dd, *J* = 15.26, 5.80 Hz, 1 H), 2.87 (d, *J* = 17.09 Hz, 1 H), 2.75 (d, *J* = 17.09 Hz, 1 H) δ ppm; **^{13}C NMR** (100 MHz, $CDCl_3$): 201.20, 189.67, 176.27, 162.86, 152.71, 152.05, 151.01 (2C), 140.47, 140.15, 139.77, 127.79, 116.30, 115.90, 106.67, 61.90, 61.25, 60.91, 60.82, 60.67, 60.38, 60.06, 55.90, 55.50, 46.69, 32.71, 29.59, 26.58 δ ppm; **HRMS**(ESI): calculated for $C_{28}H_{30}O_{10}$$[M+H]^+$: 527.1912 m/z; found: 527.1924 m/z.

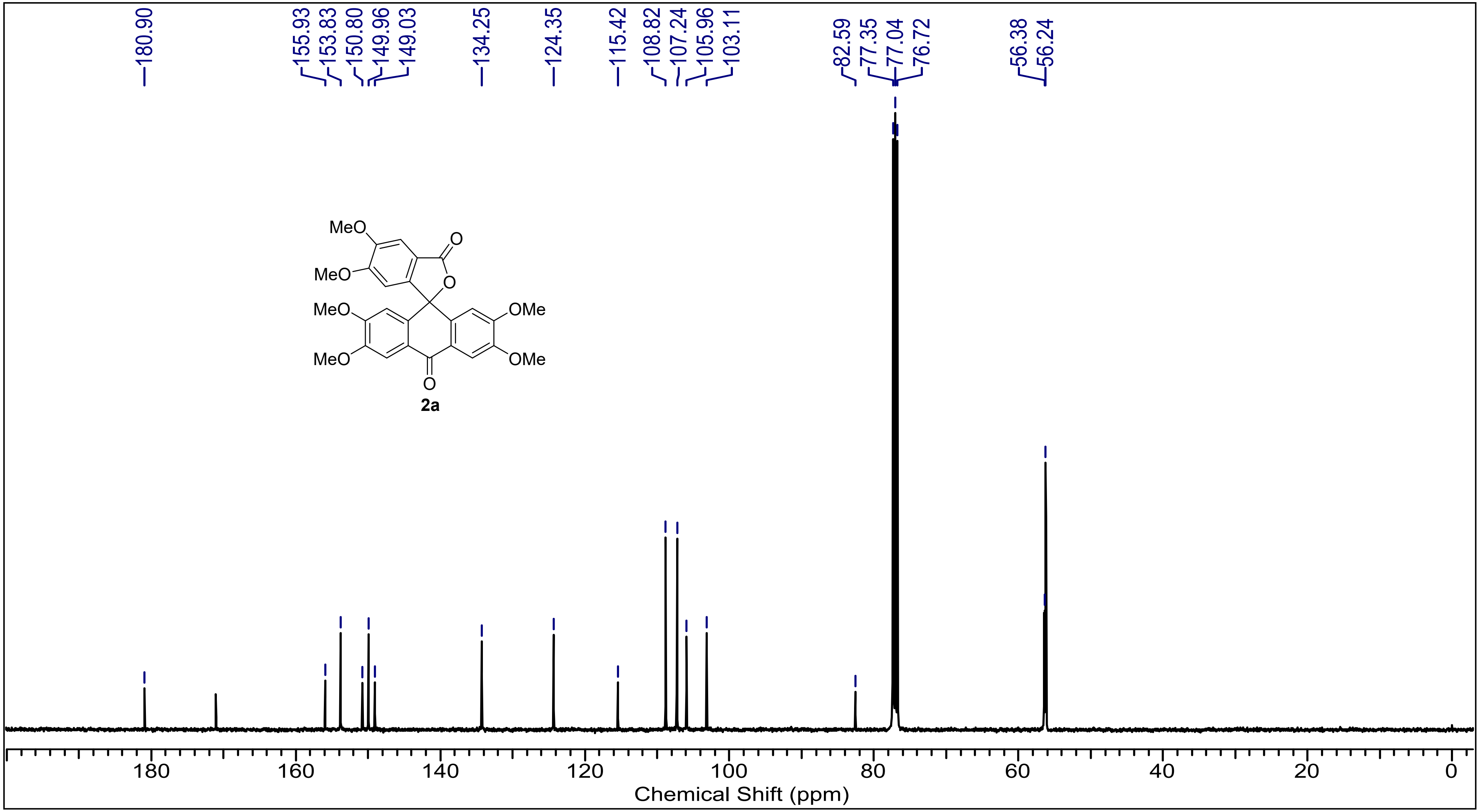
10-hydroxy-2,4,8,9,12,13,14-heptamethoxy-5,6,10,15-tetrahydro-6,9a-methanobenzo[1,8] cycloocta[1,2-b]naphthalene-3,7,16-trione (4e):
Pale yellow solid,(0.065gm, 14% yield); R_f = 0.1 (pet ether/ethyl acetate = 60/40); **M.P**: 163–164° C; **FTIR**($CHCl_3$): ν 3397, 3020, 2939, 2850, 1726, 1701, 1596, 1524, 1494, 1431, 1327, 1300, 1122, 1047,1019 (cm^{-1}); **^{1}H NMR** (400 MHz,

$CDCl_3$): 7.12 (s, 1 H), 5.72 (s, 1 H), 5.48 (d, *J* = 11.29 Hz, 1H), 4.07 (s, 3 H), 3.94 (s, 3 H), 3.89 (s, 3 H), 3.84 (s, 3H), 3.78 (s, 3 H), 3.66 (s, 3 H), 3.61–3.63 (m, 4 H), 3.58 (dd, *J* = 5.65, 1.68 Hz, 1 H), 3.20 (d, *J* = 11.90 Hz, 1 H, OH), 3.00–3.05 (m, 2 H), 2.75 (d, *J* = 17.40 Hz, 1 H) δ ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): 203.48, 188.80, 175.98, 162.70, 153.25, 151.93, 151.31, 150.53, 141.96, 141.07, 138.38, 131.92, 115.97, 114.74, 104.56, 67.43, 64.05, 62.18, 61.13, 60.94, 60.80, 60.75, 60.59, 55.95, 55.51, 48.78, 32.65, 29.70 δ ppm; **HRMS** (ESI): calculated $C_{28}H_{30}O_{11}$ $[M+H]^+$: 543.1861 m/z; found: 543.1880 m/z.

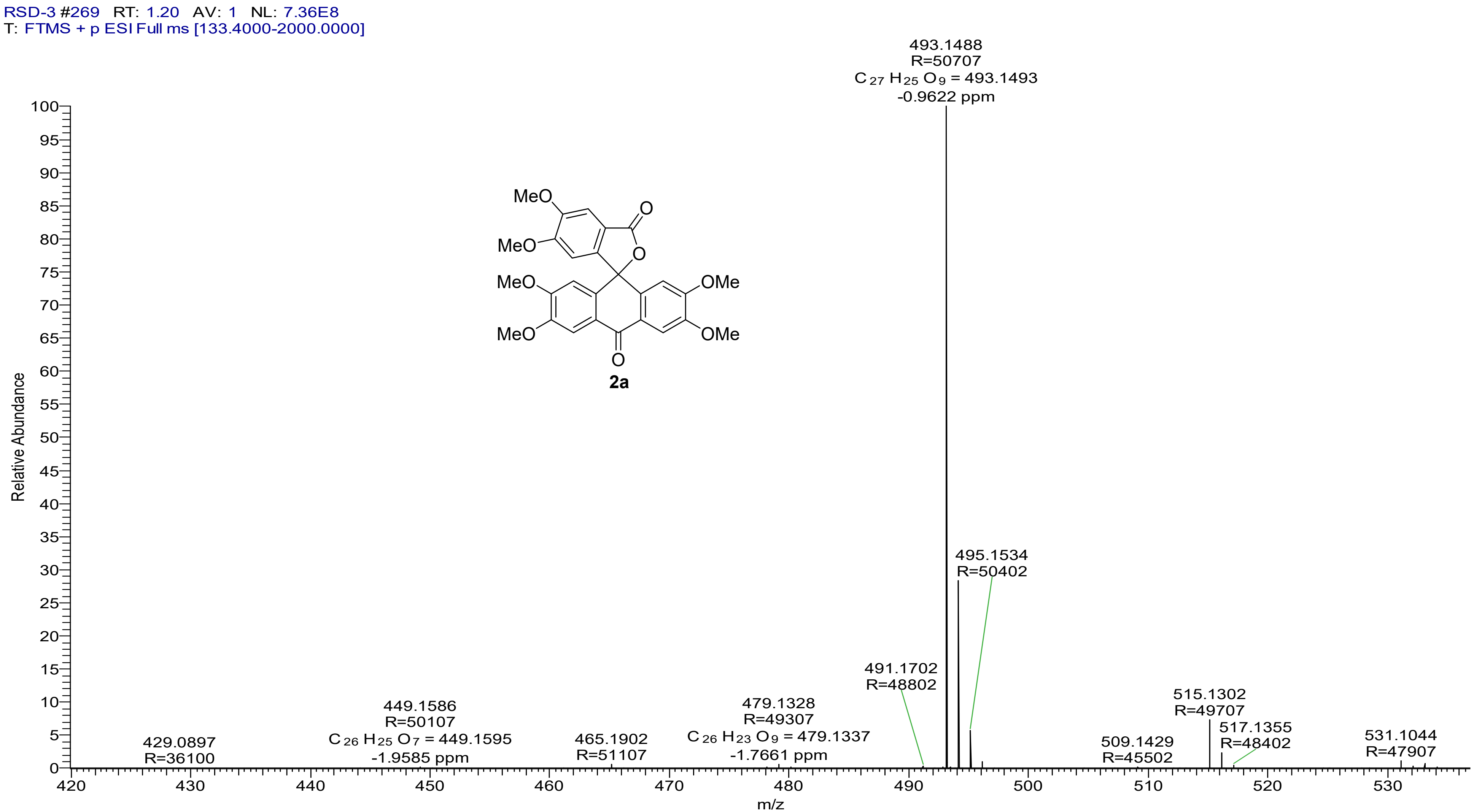
3. NMR Spectra's:



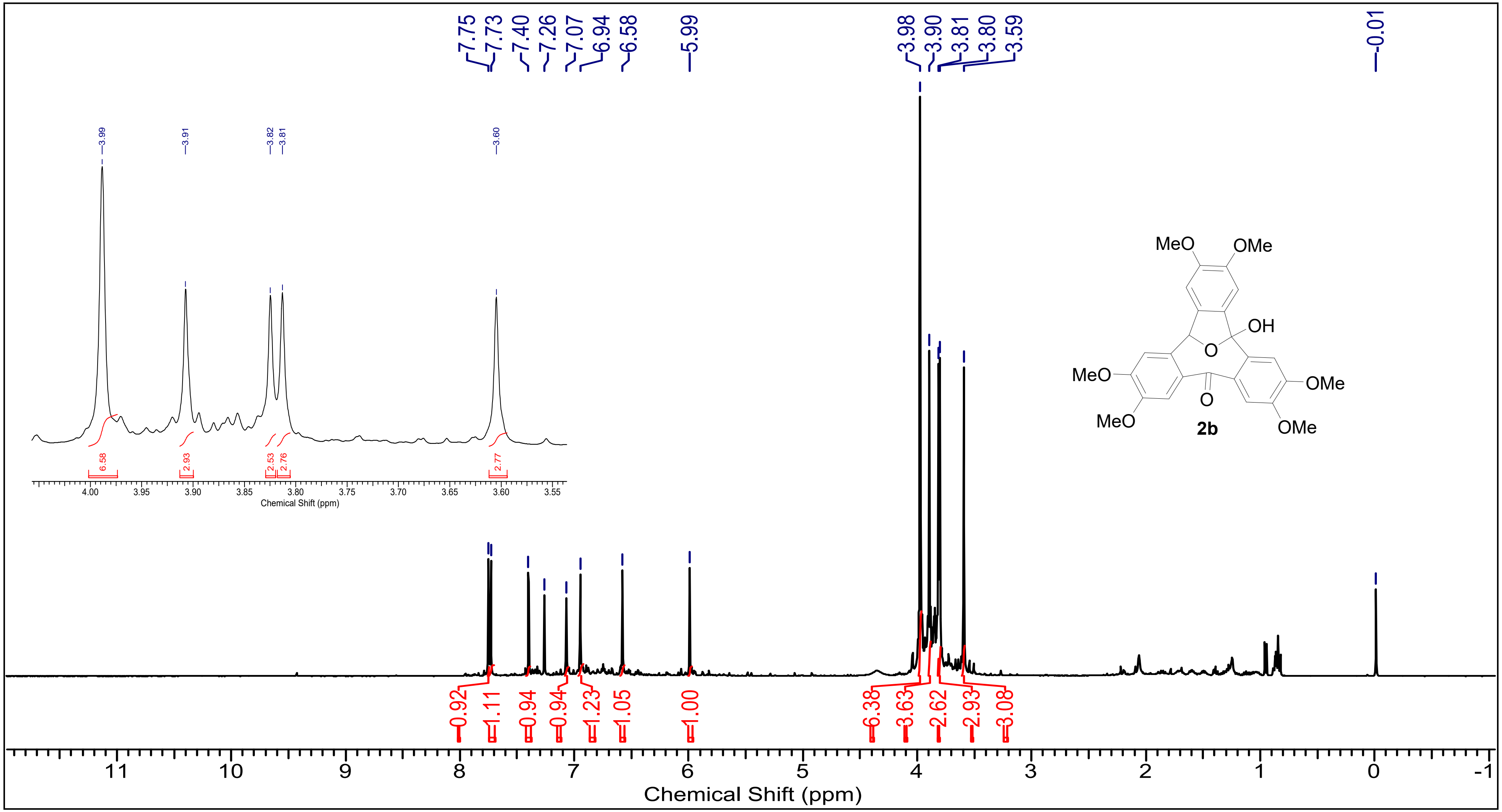
^{1}H NMR of compound (**2a**) in $CDCl_3$ (400 MHz)



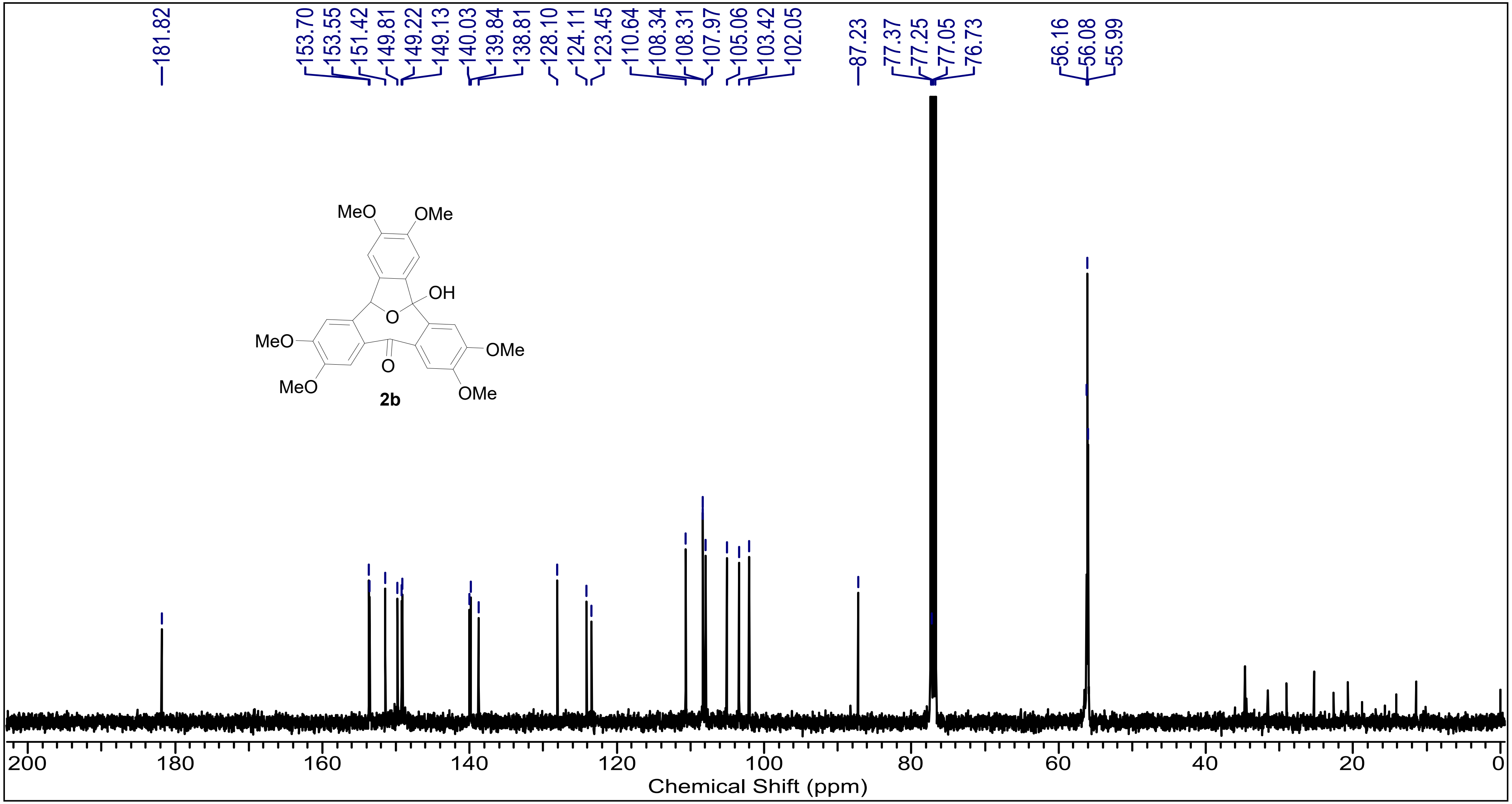
^{13}C NMR of compound (**2a**) in $CDCl_3$ (100 MHz)



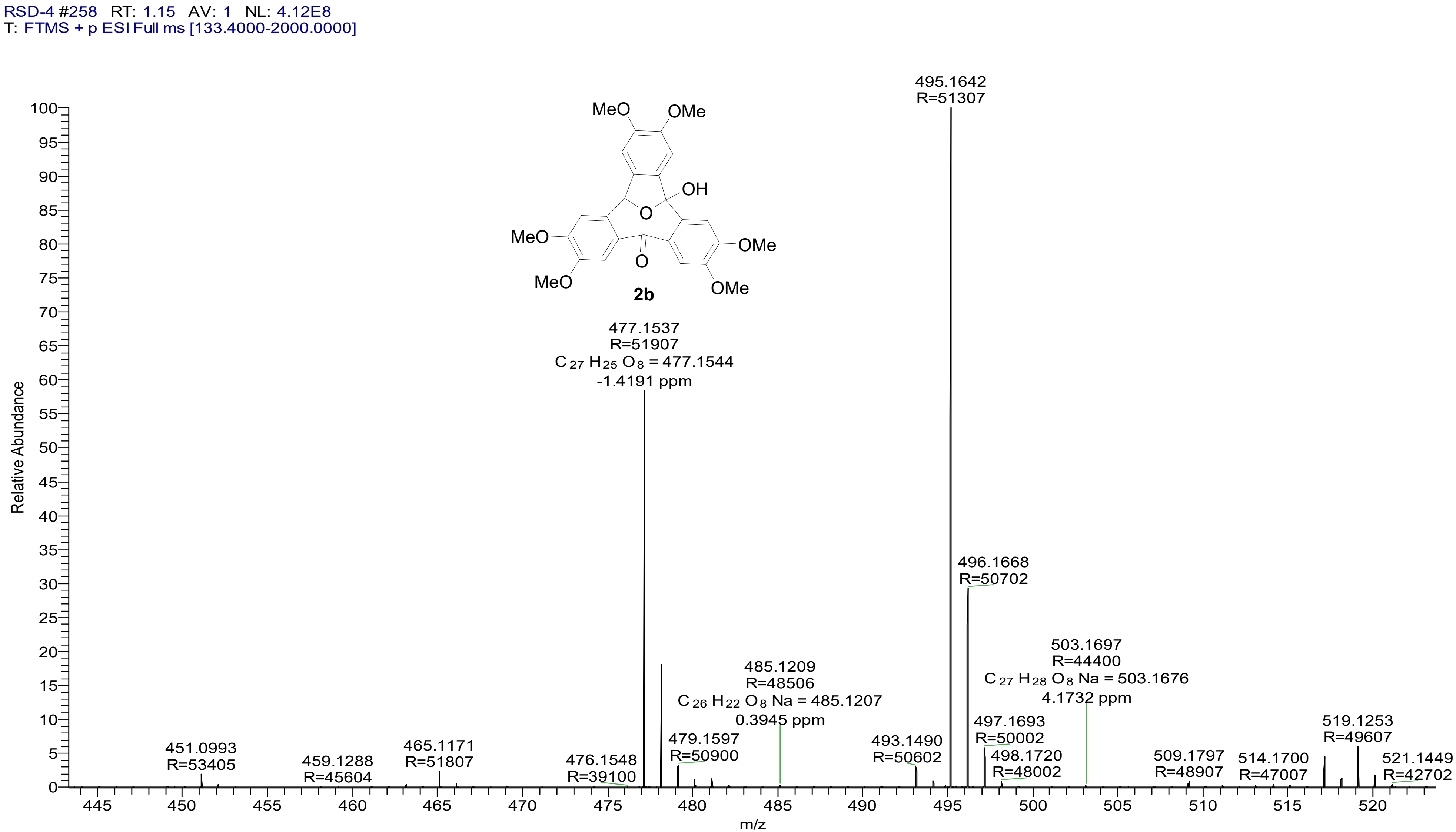
HRMS (ESI) of compound (**2a**)



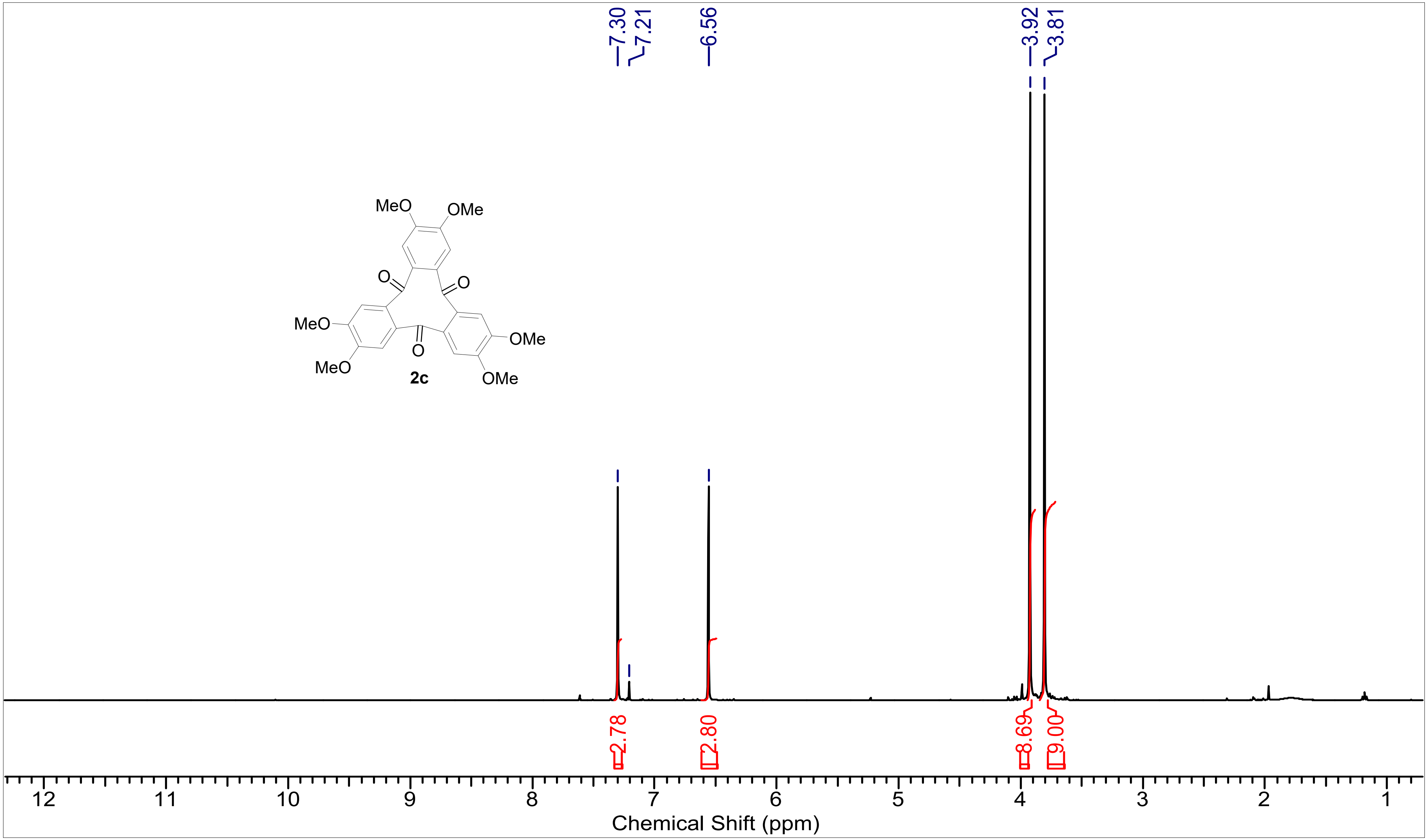
^{1}H NMR of (**2b**) compound in $CDCl_3$ (400 MHz)



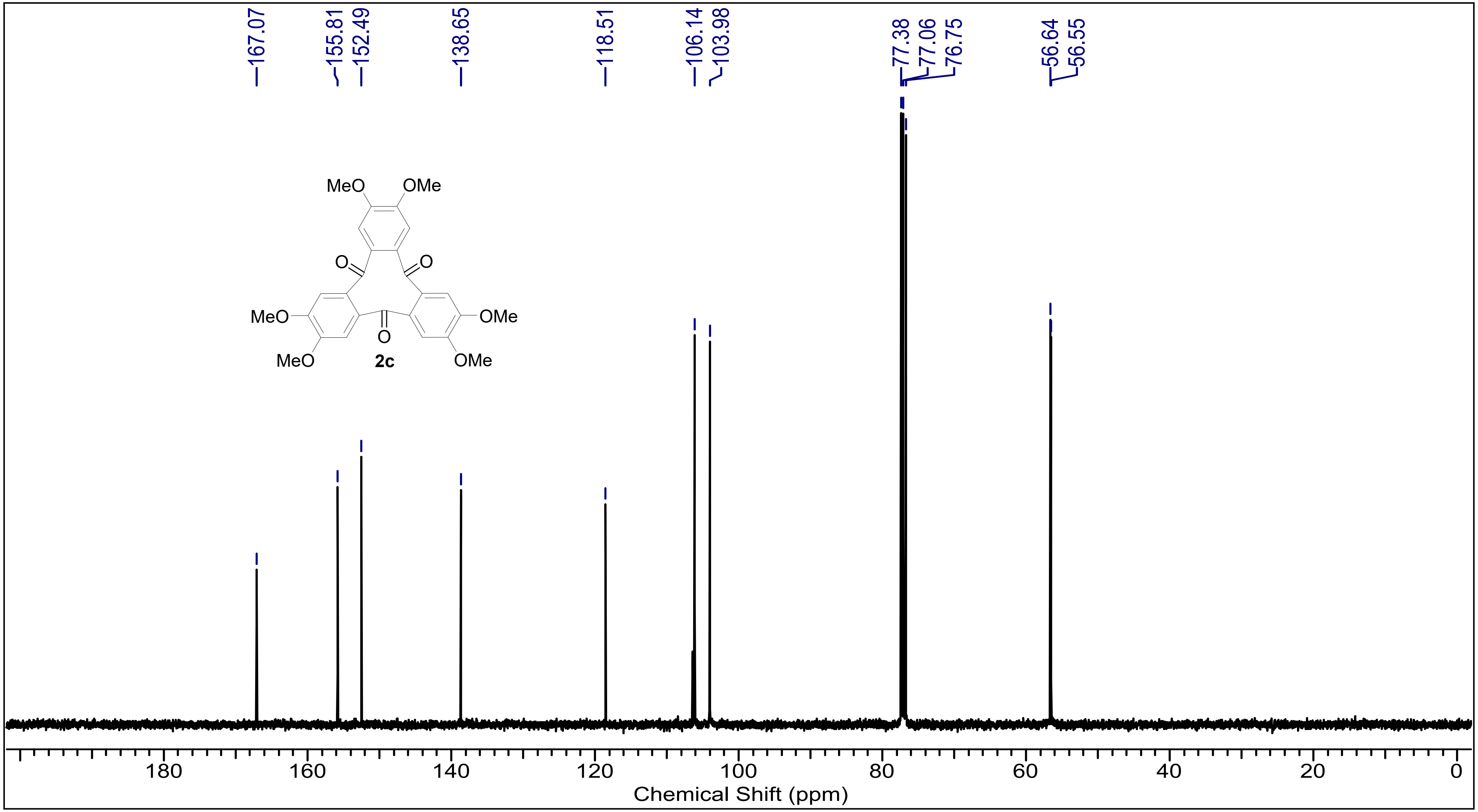
^{13}C NMR of compound (**2b**) in $CDCl_3$ (100 MHz)



HRMS(ESI) of compound (2b)

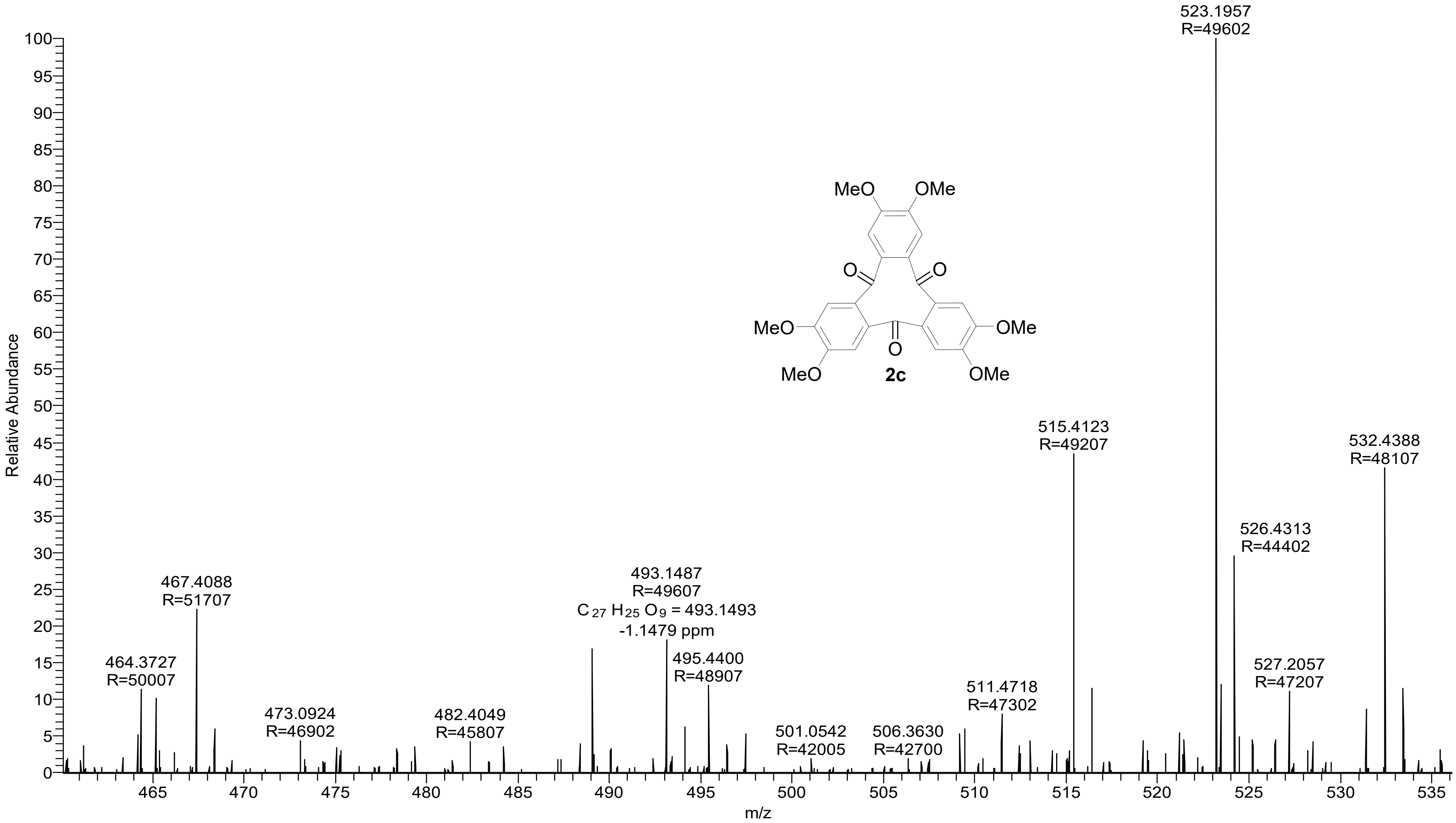


^{1}H NMR of compound (**2c**) in $CDCl_3$ (400 MHz)

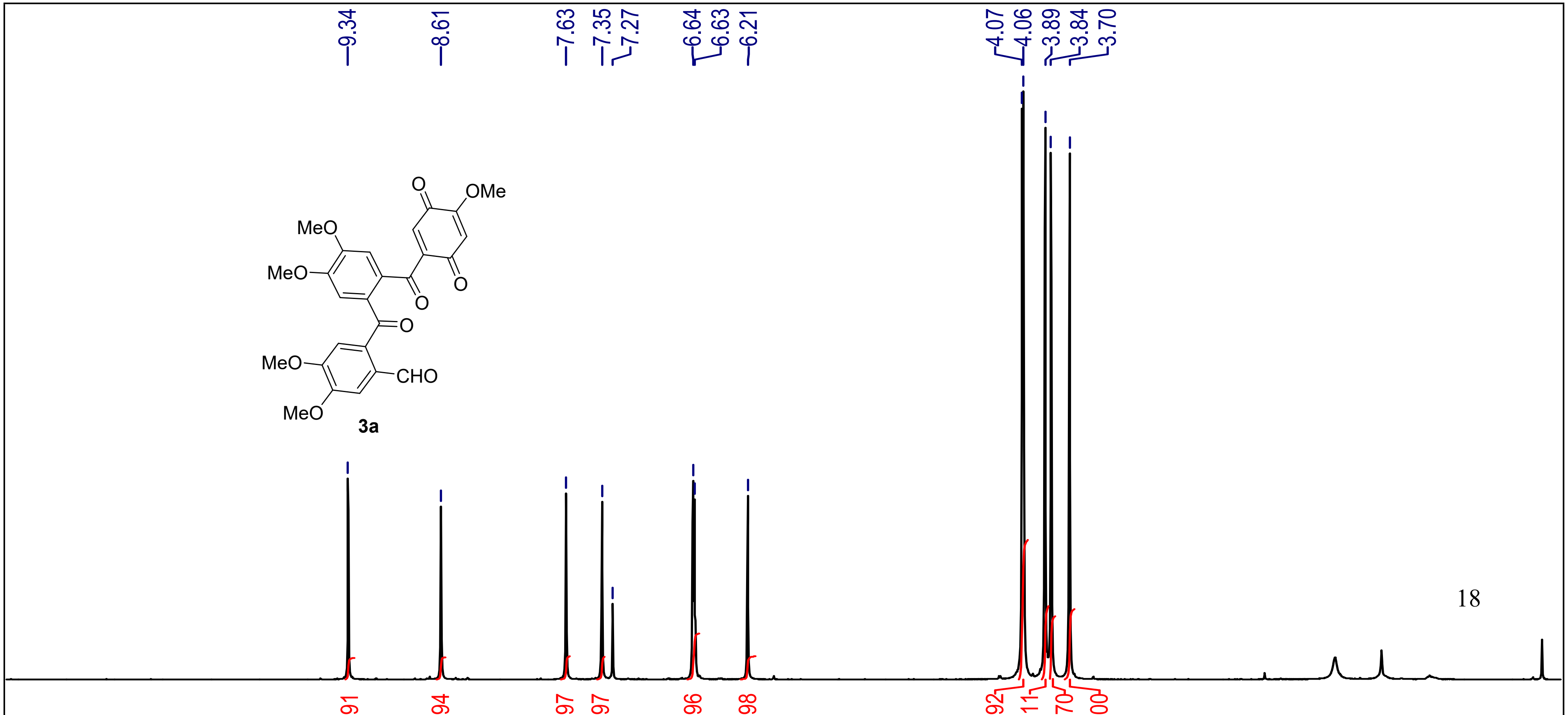


^{13}C NMR of compound (**2c**) in $CDCl_3$ (100 MHz)

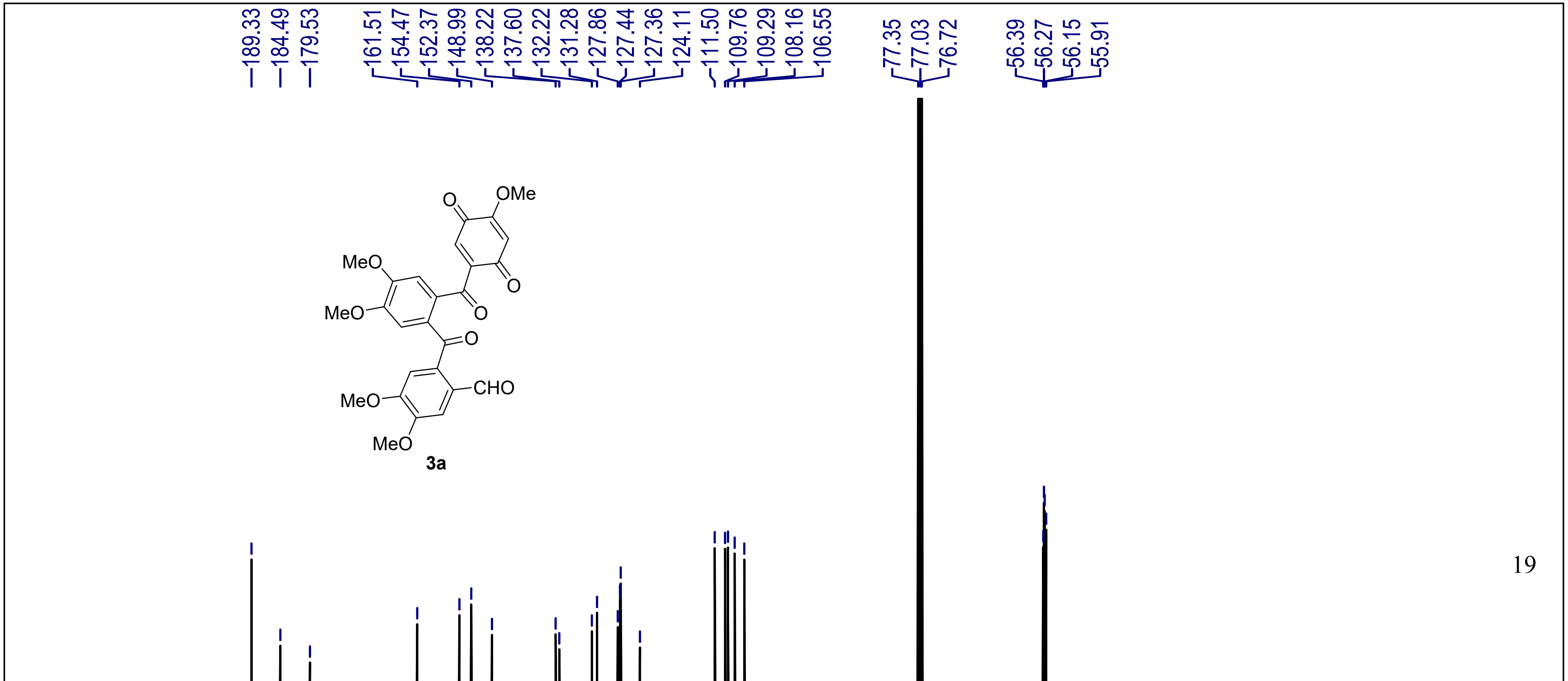
RSDOTRIK #377 RT: 1.68 AV: 1 NL: 1.04E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]



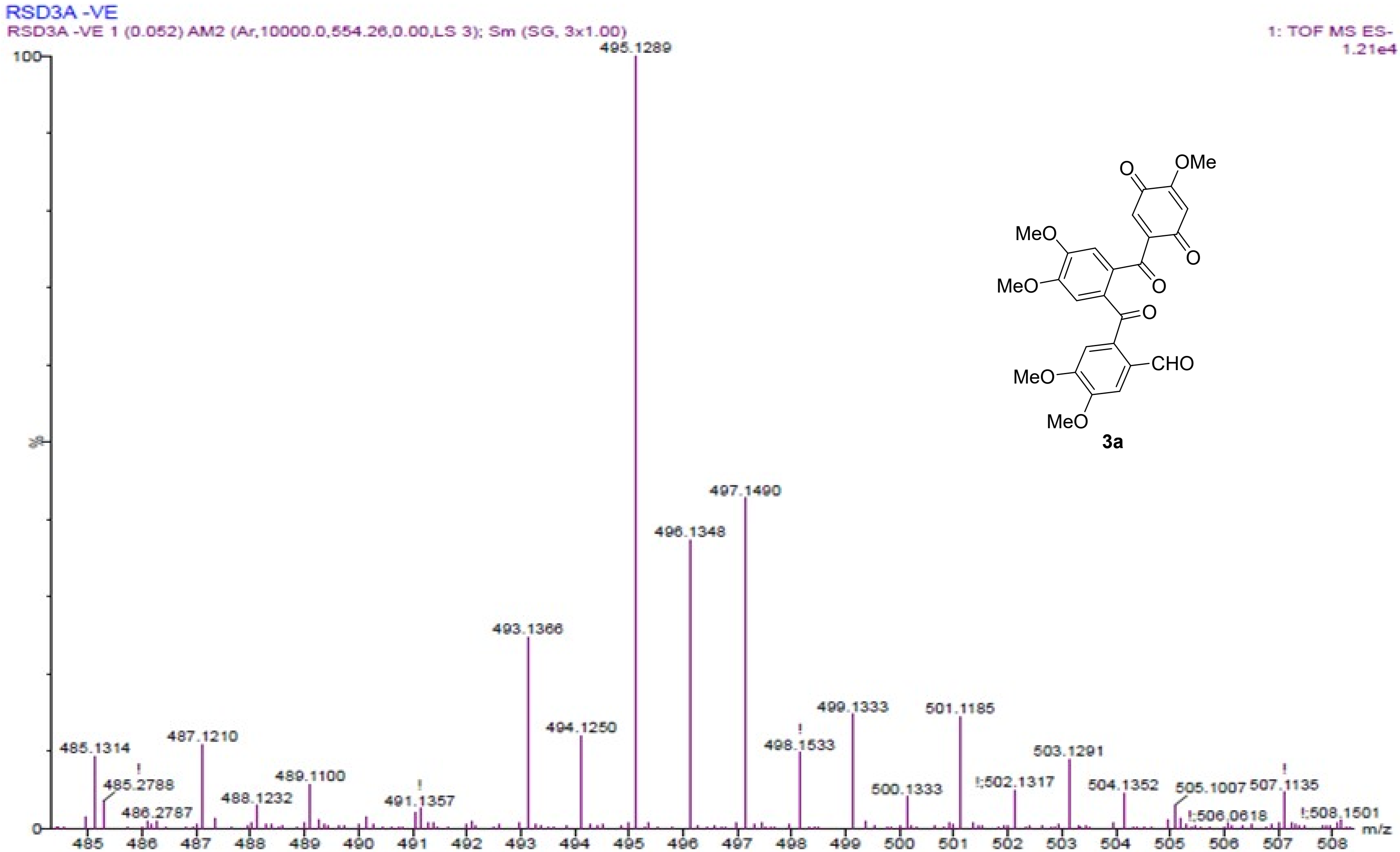
HRMS (ESI) of compound (**2c)**



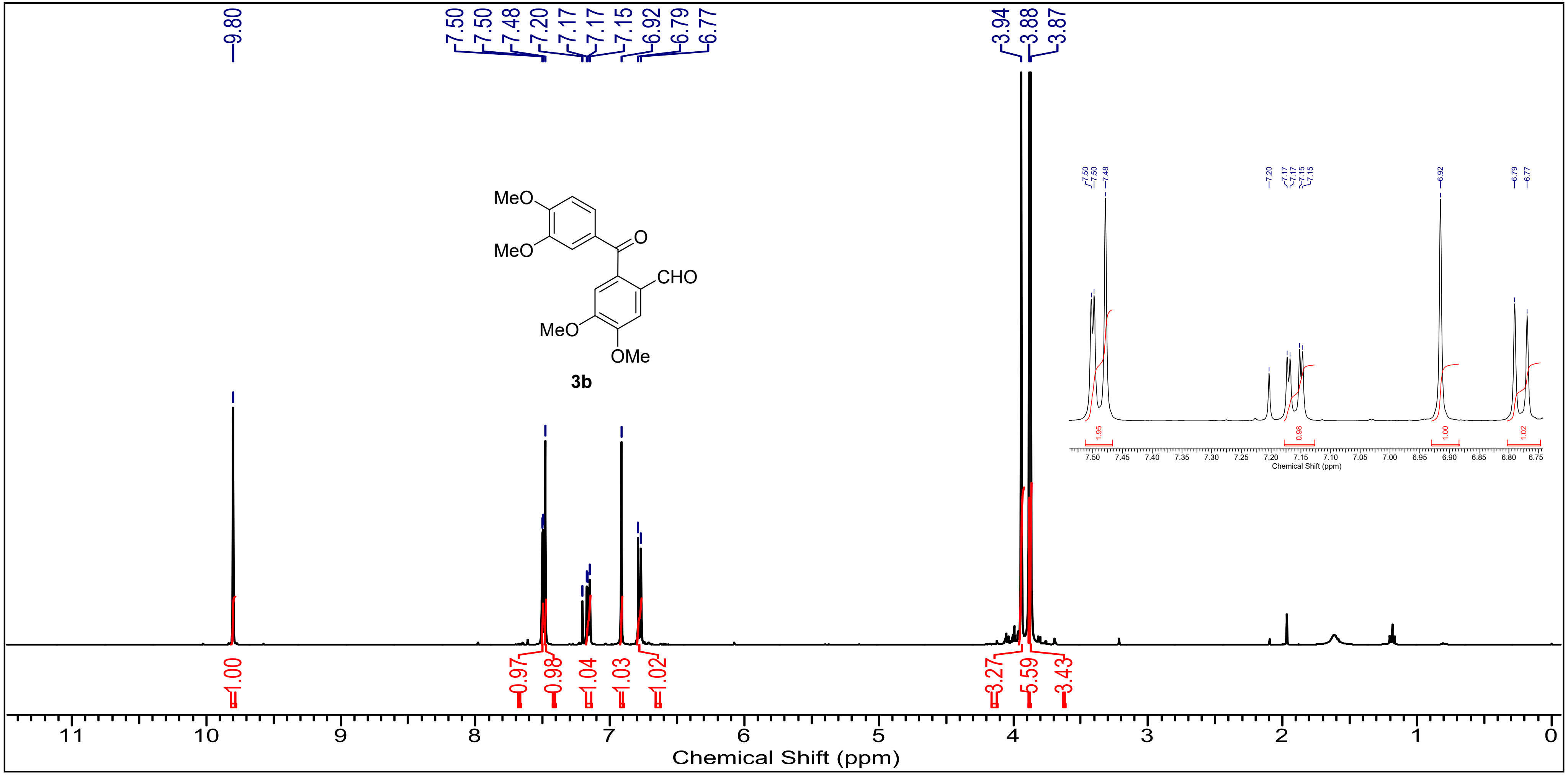
^{1}H NMR of compound (**3a**) in $CDCl_3$ (400 MHz)



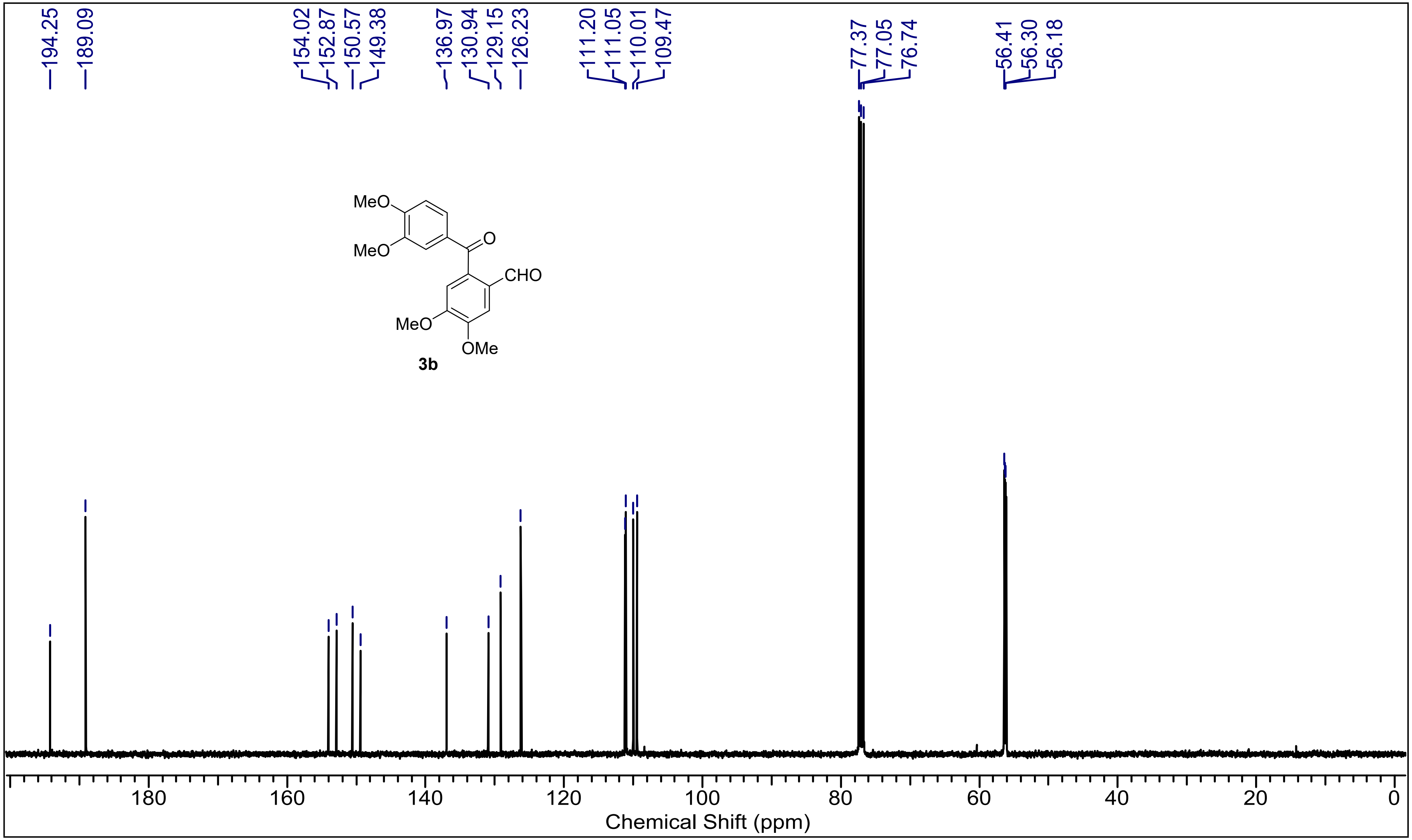
^{13}C NMR compound (**3a**) in $CDCl_3$ (100 MHz)



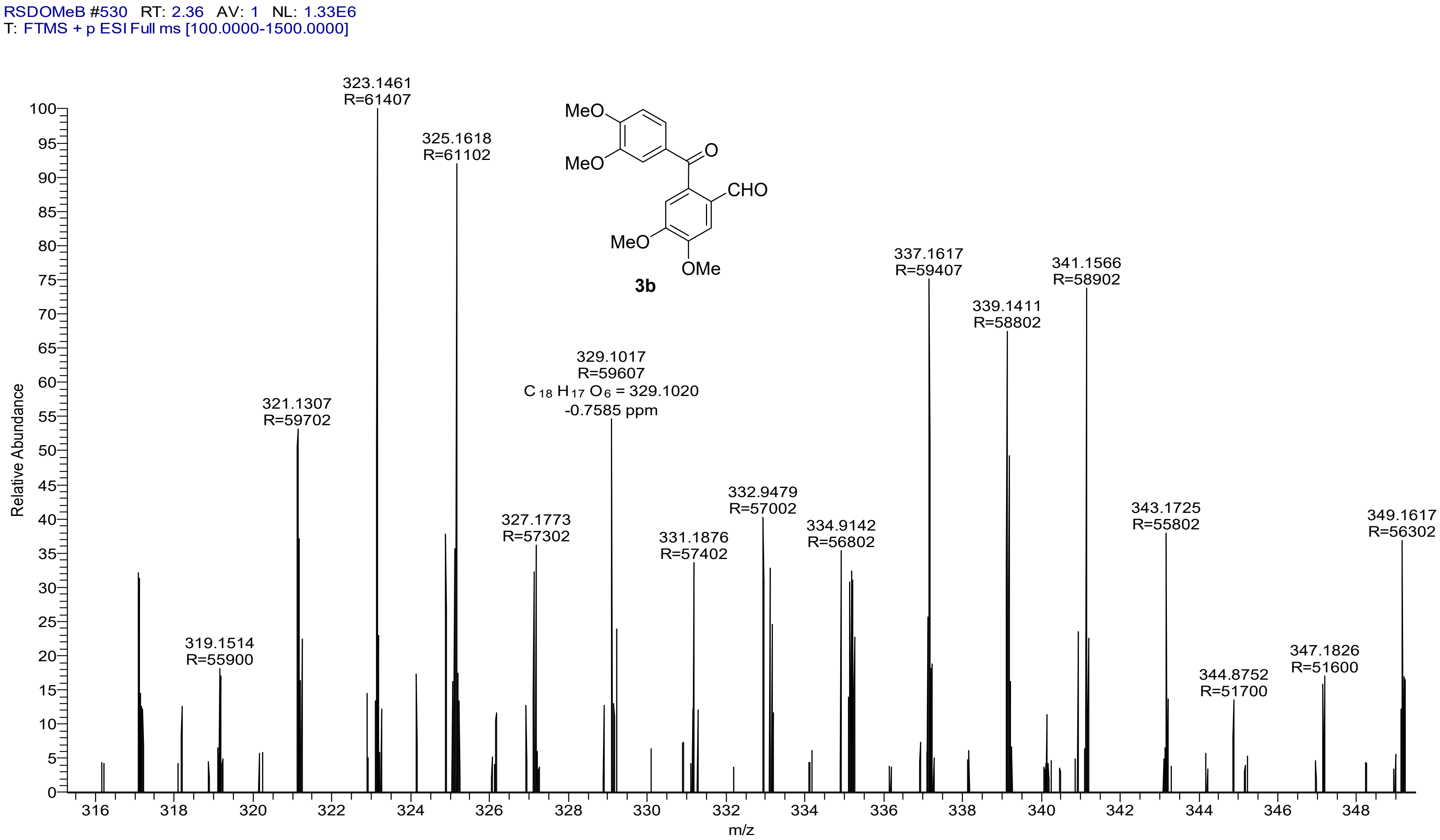
HRMS (ESI) of compound (**3a)**



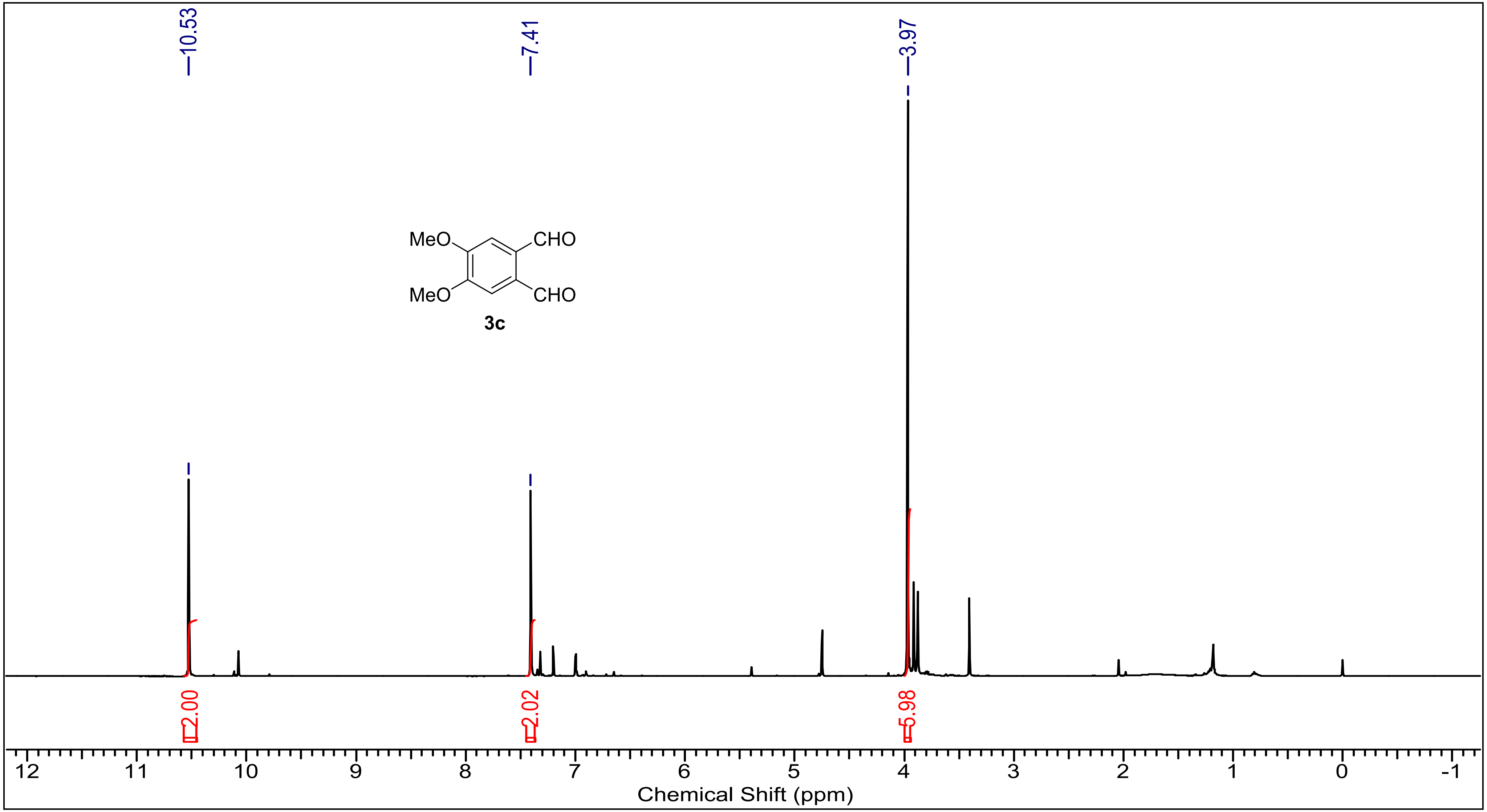
[1]H NMR of compound (**3b**) in $CDCl_3$ (400 MHz)



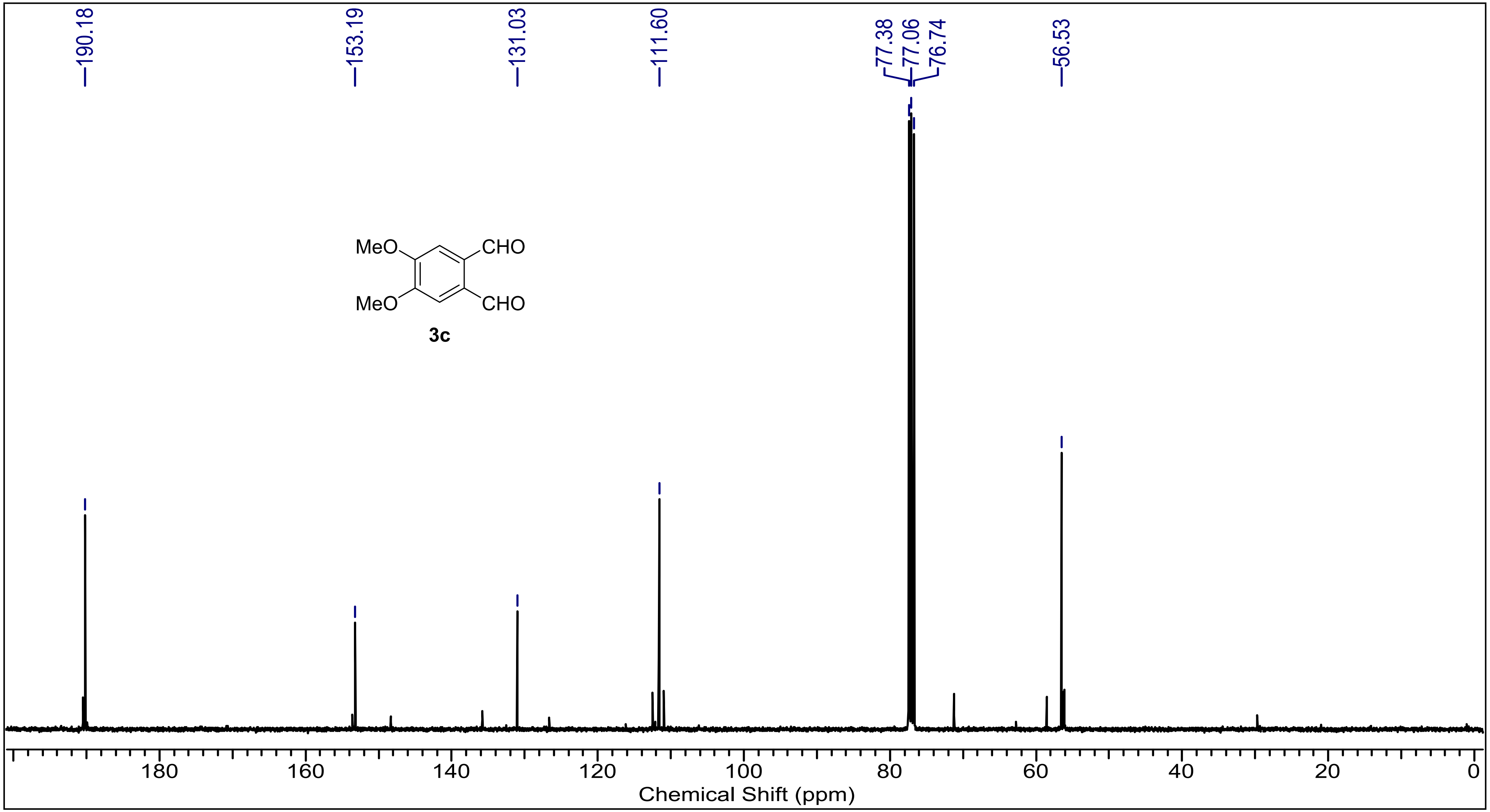
^{13}C NMR of compound (**3b**) in $CDCl_3$ (100 MHz)



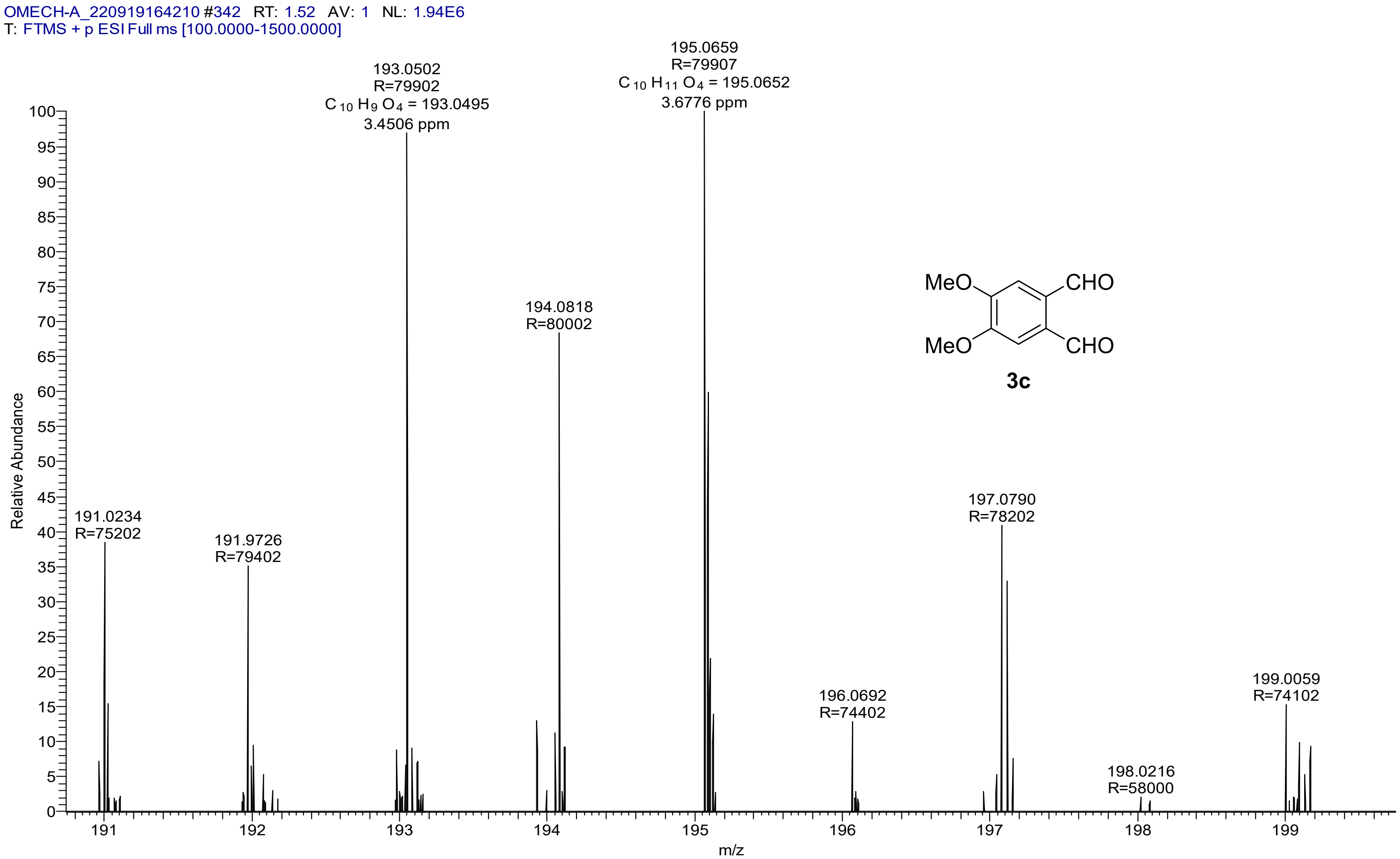
HRMS (ESI) of compound (**3b)**



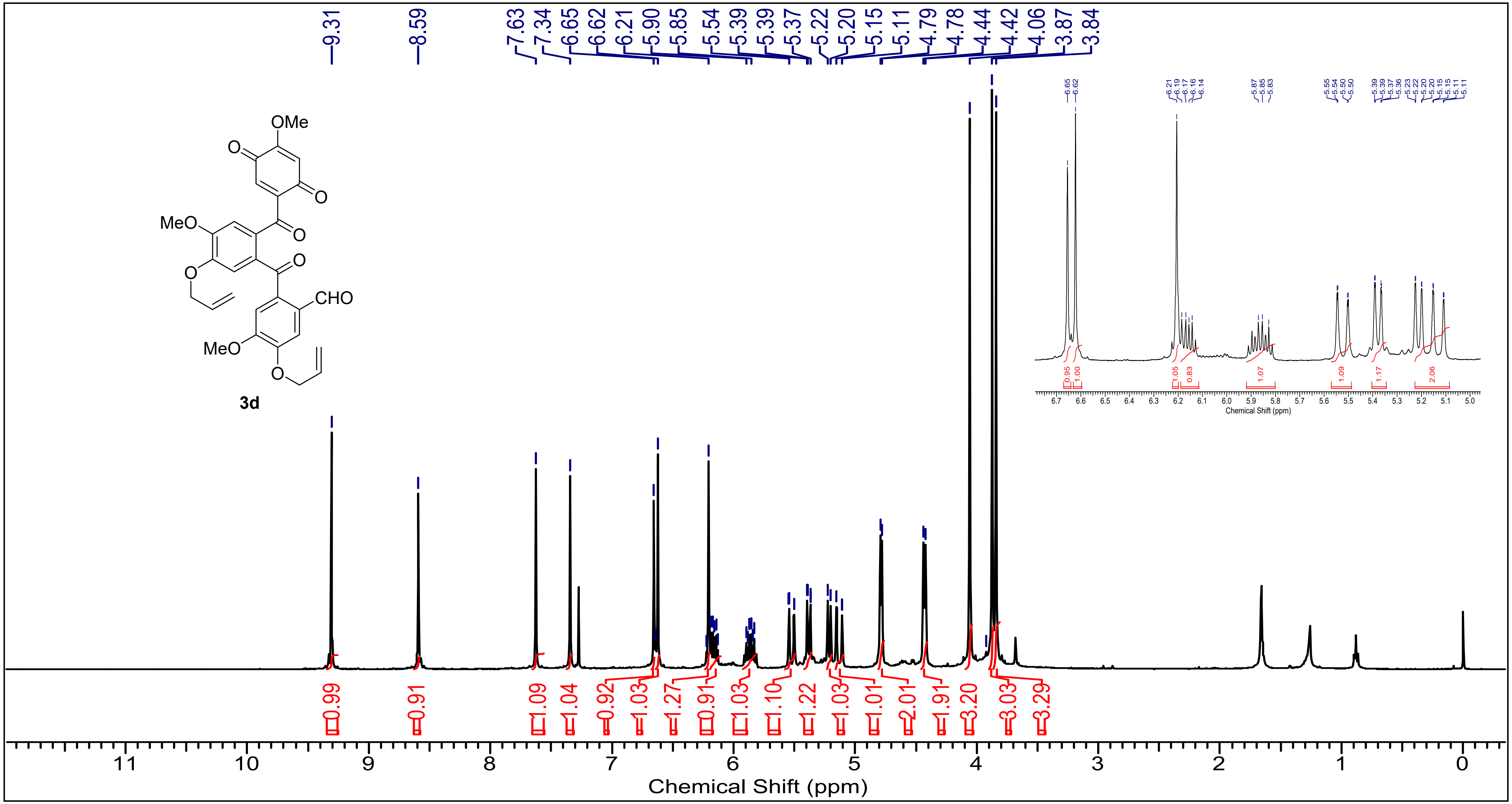
^{1}H NMR of compound (**3c**) in $CDCl_3$ (400 MHz)



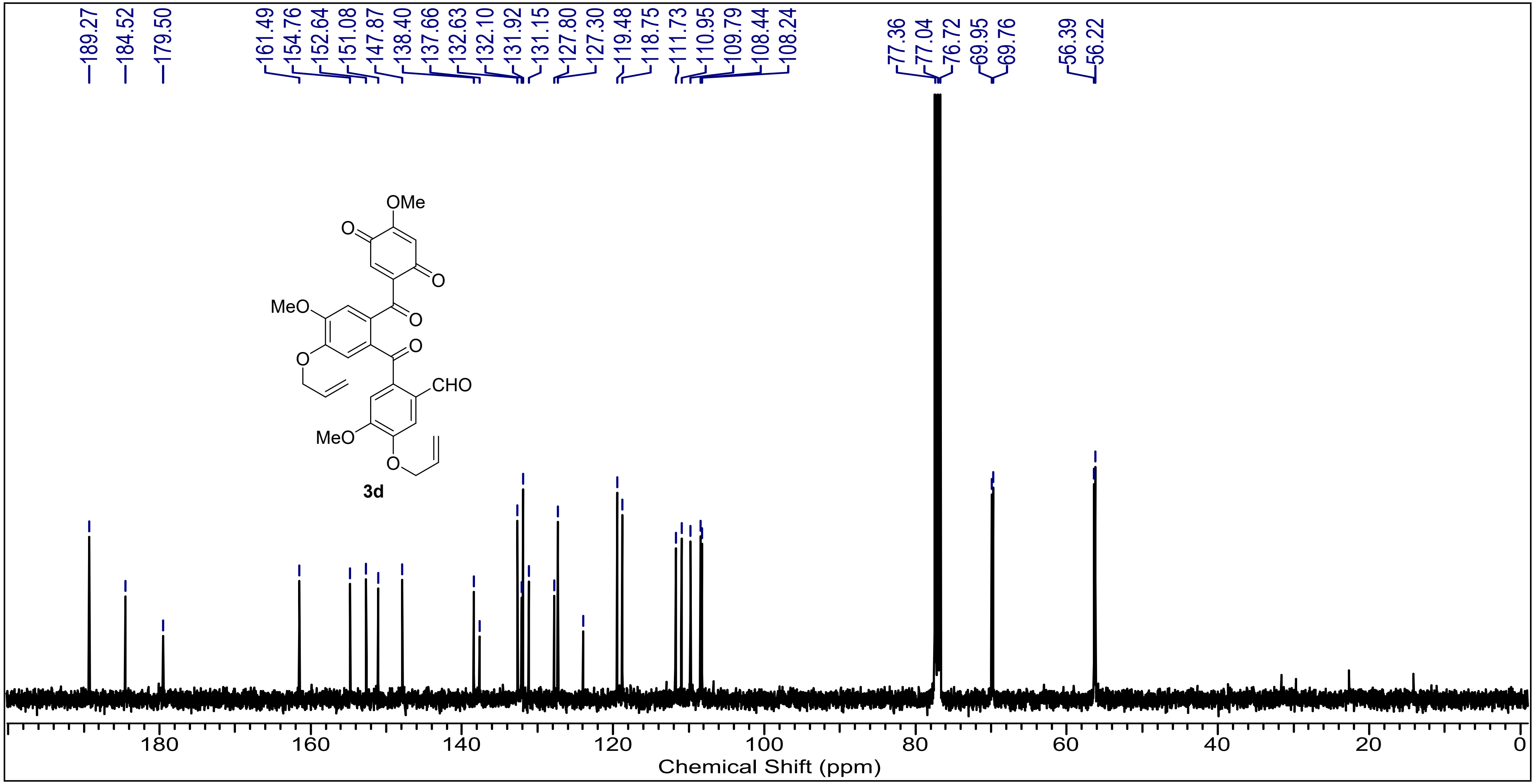
^{13}C NMR of compound (**3c**) in $CDCl_3$ (100 MHz)



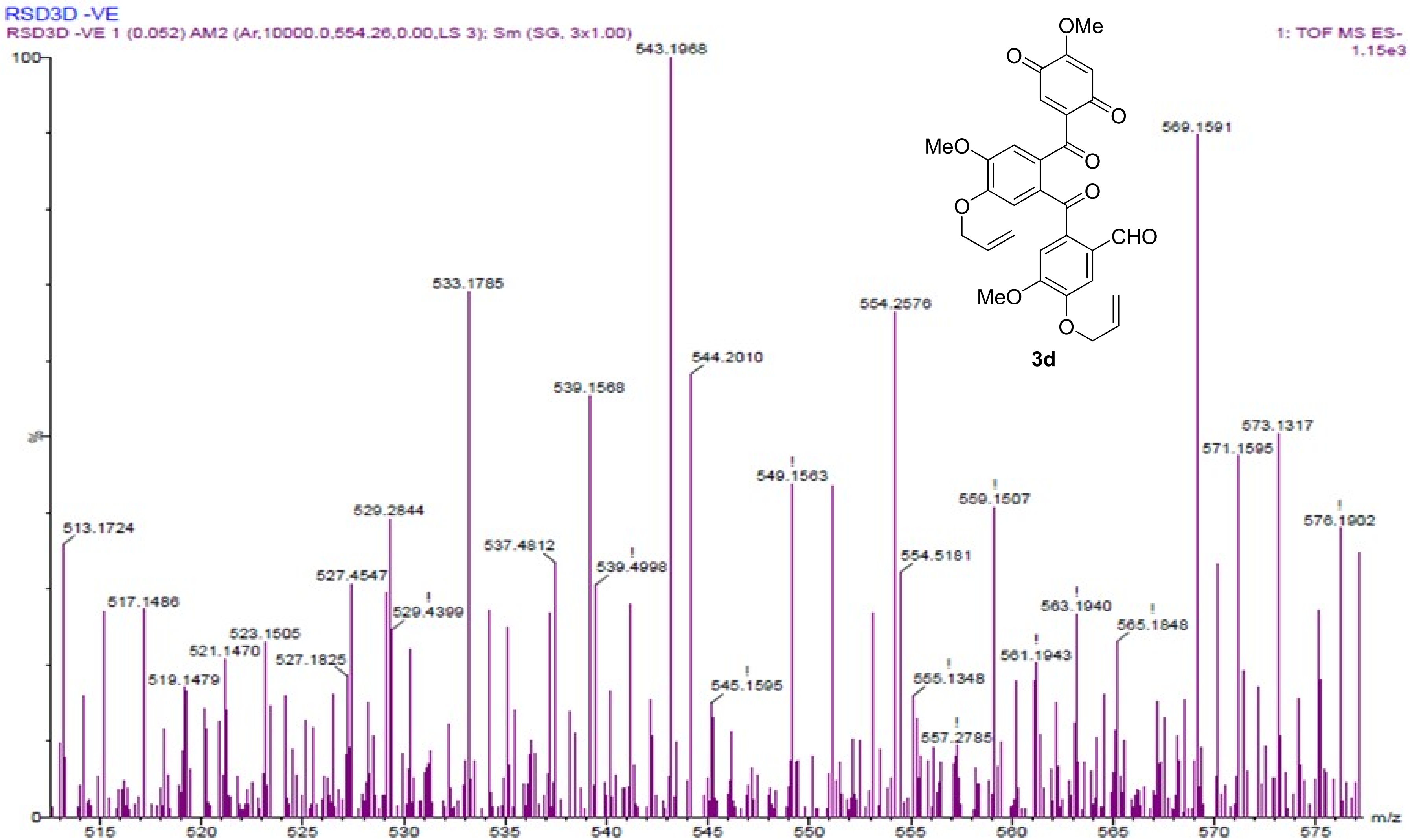
HRMS (ESI) of compound (**3c**)



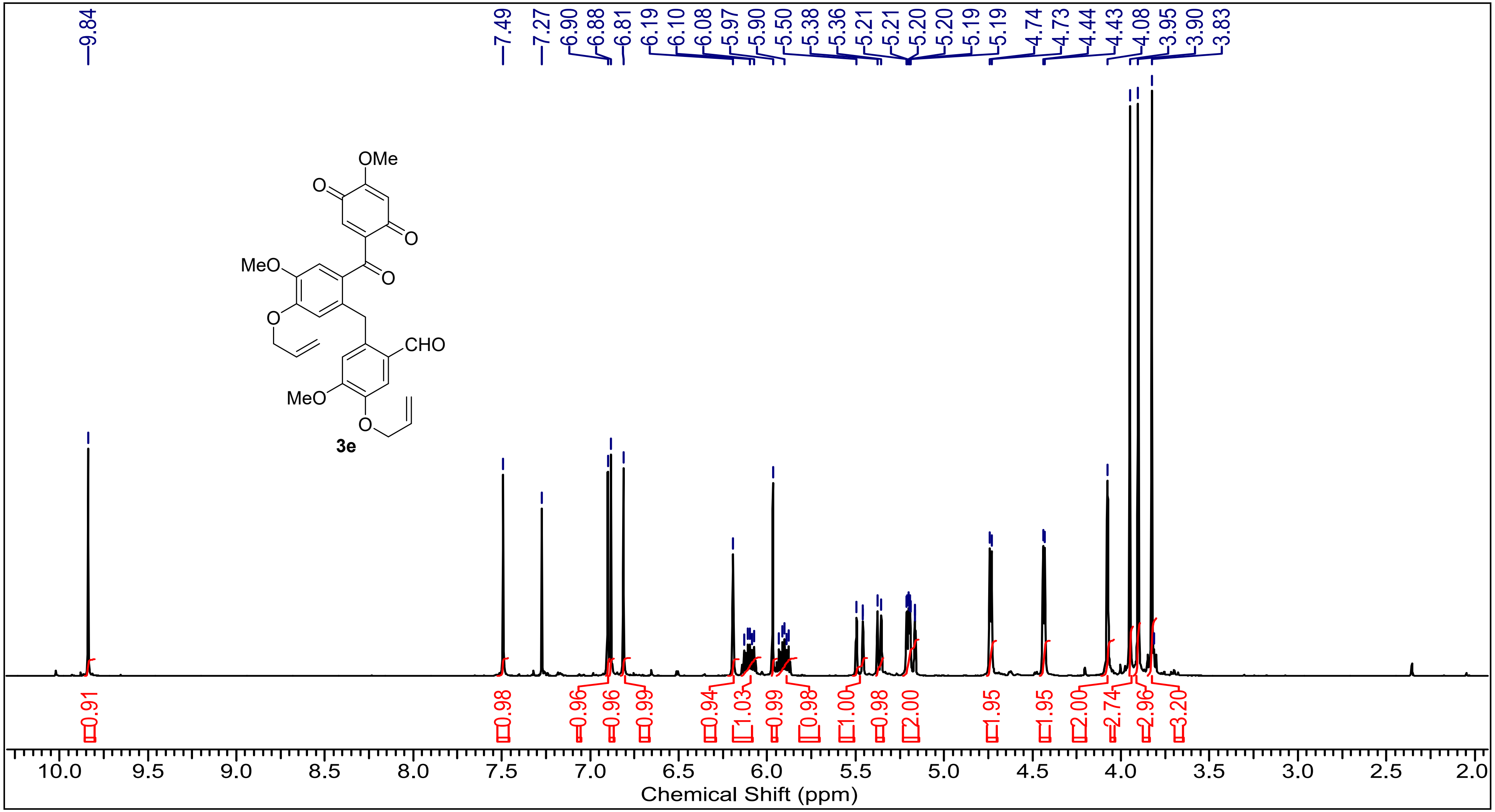
^{1}H NMR of compound (**3d**) in $CDCl_3$ (400 MHz)



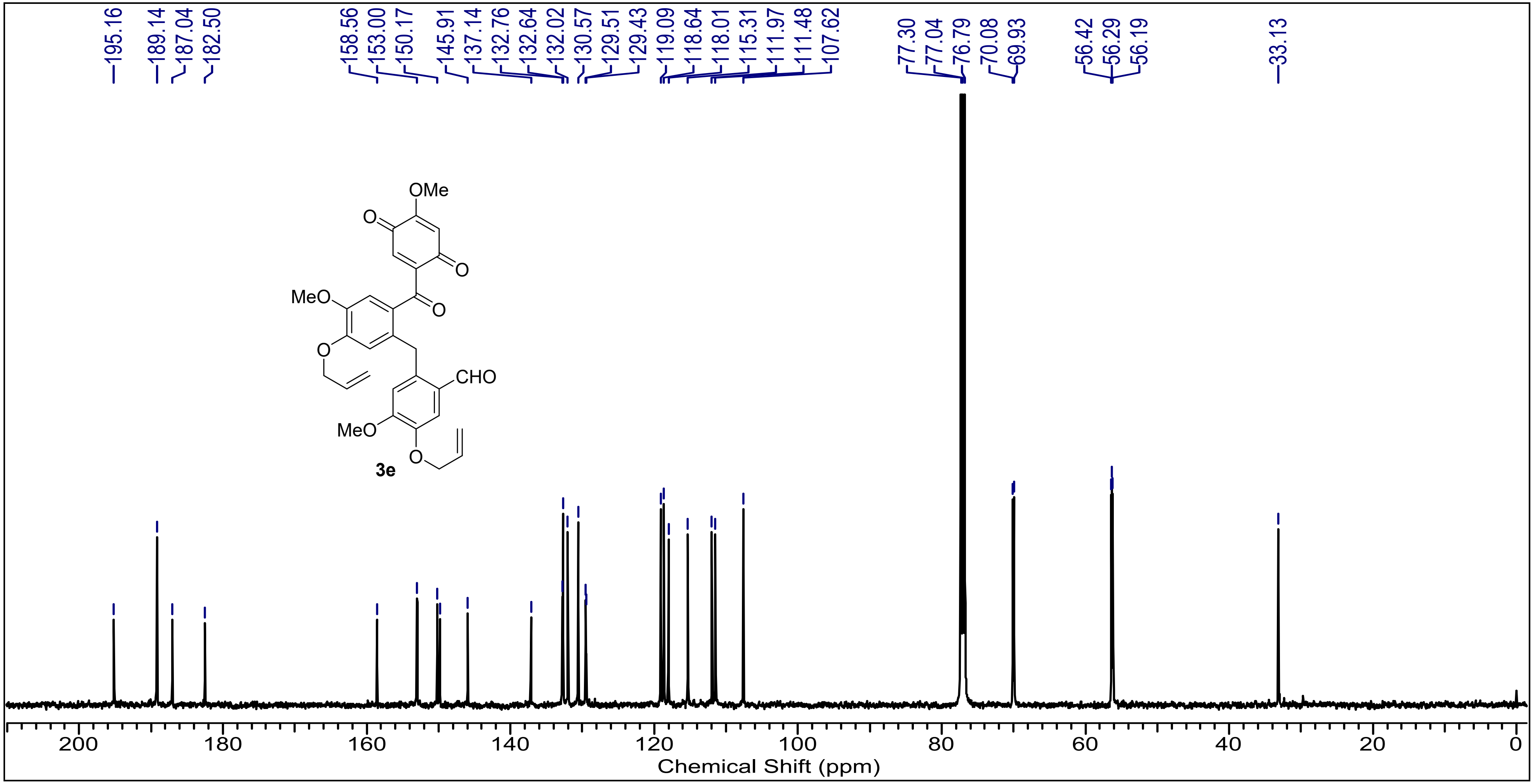
^{13}C NMR of compound (**3d**) in $CDCl_3$ (100 MHz)



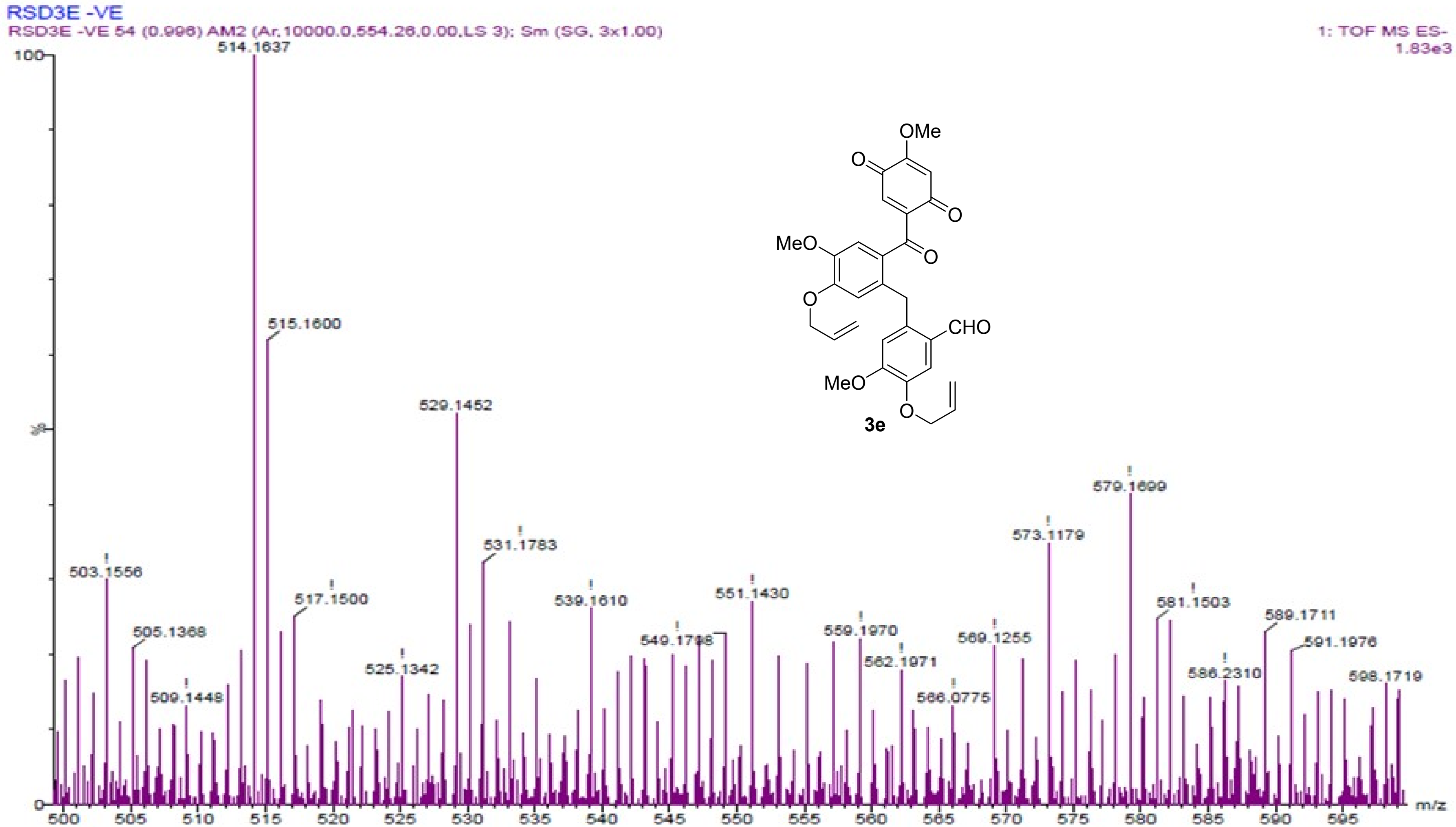
HRMS (ESI) of compound (**3d**)



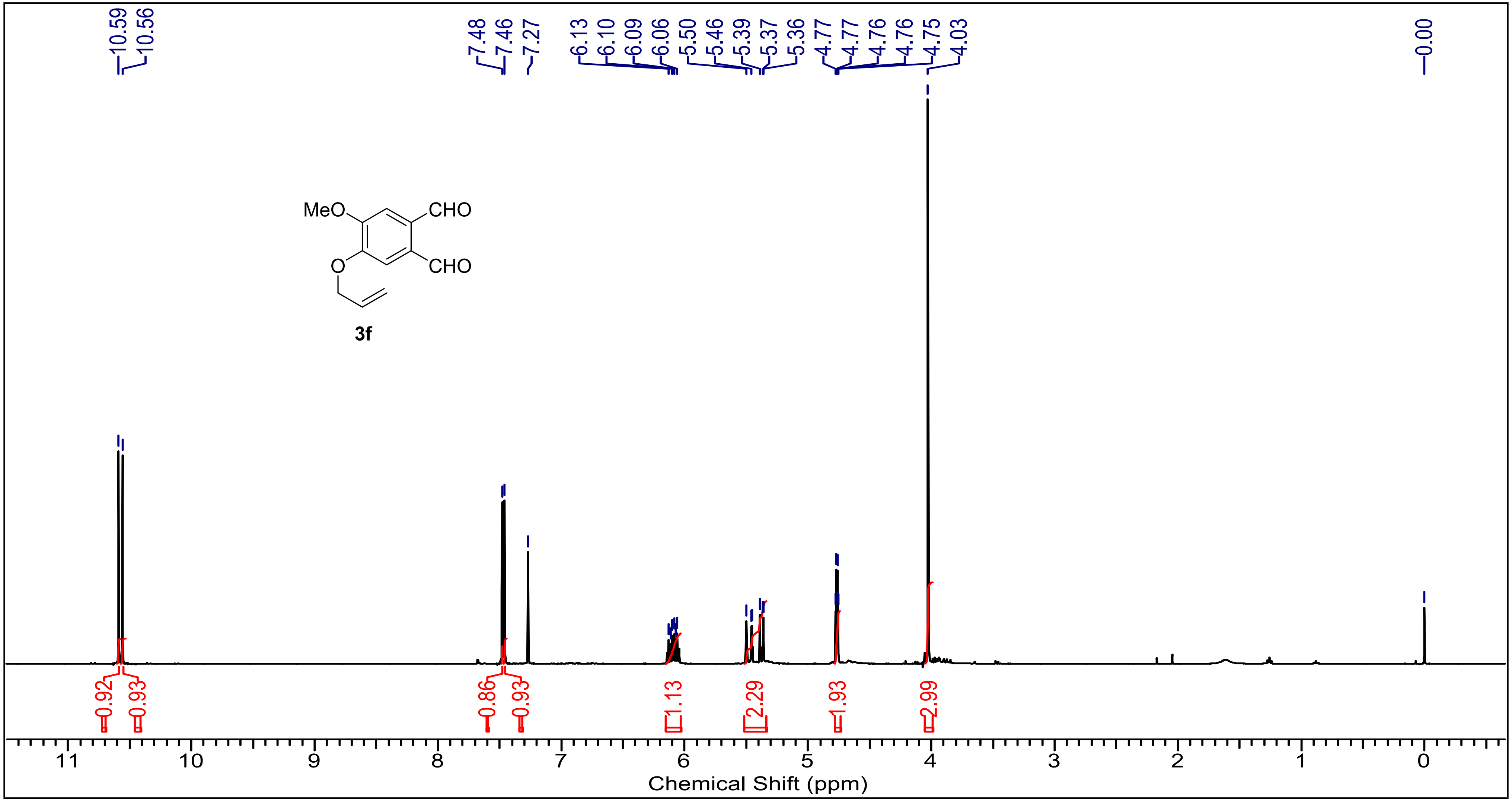
^{1}H NMR of compound (**3e**) in $CDCl_3$ (400 MHz)



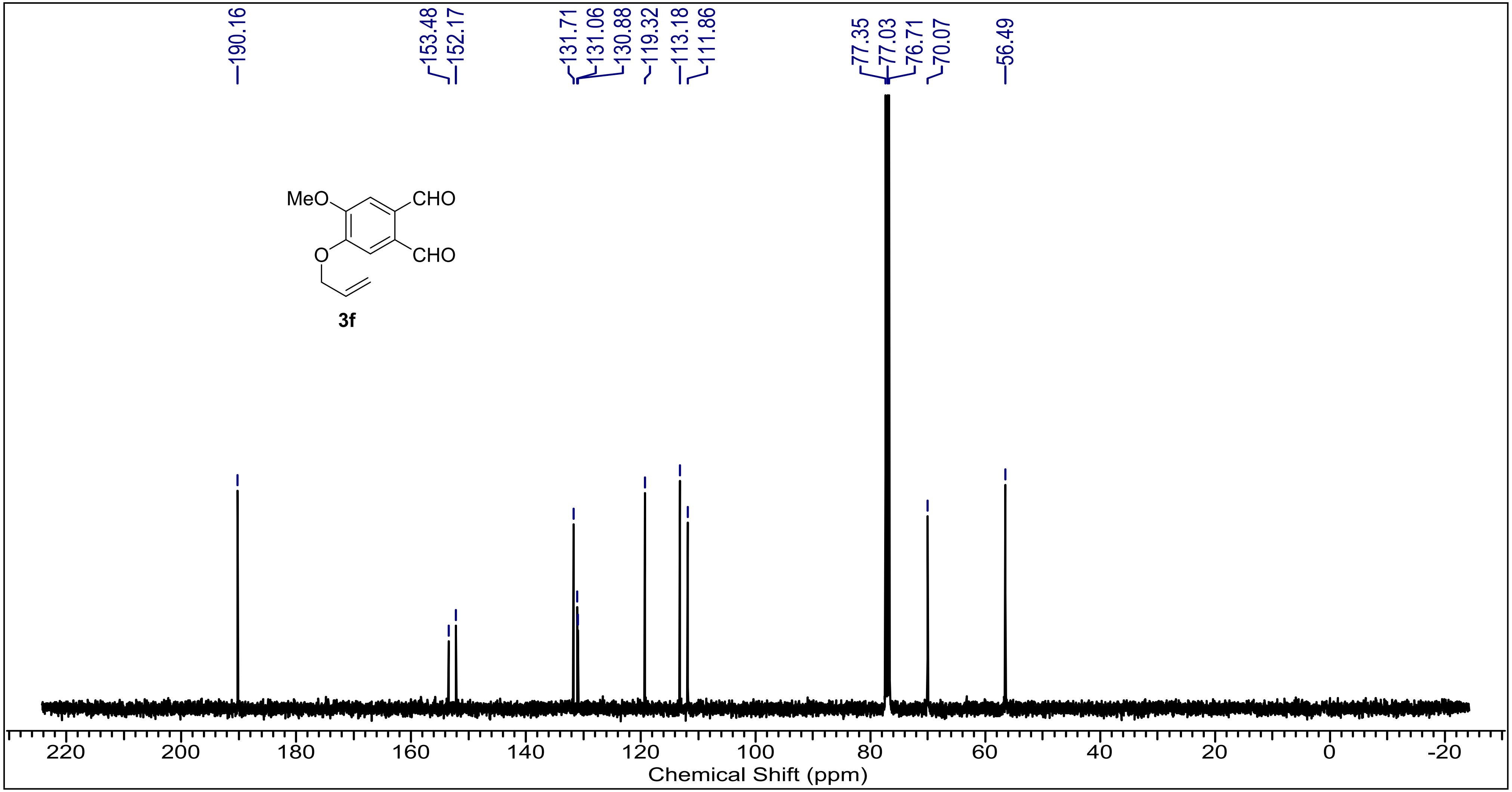
^{13}C NMR of compound (**3e**) in $CDCl_3$ (100 MHz)



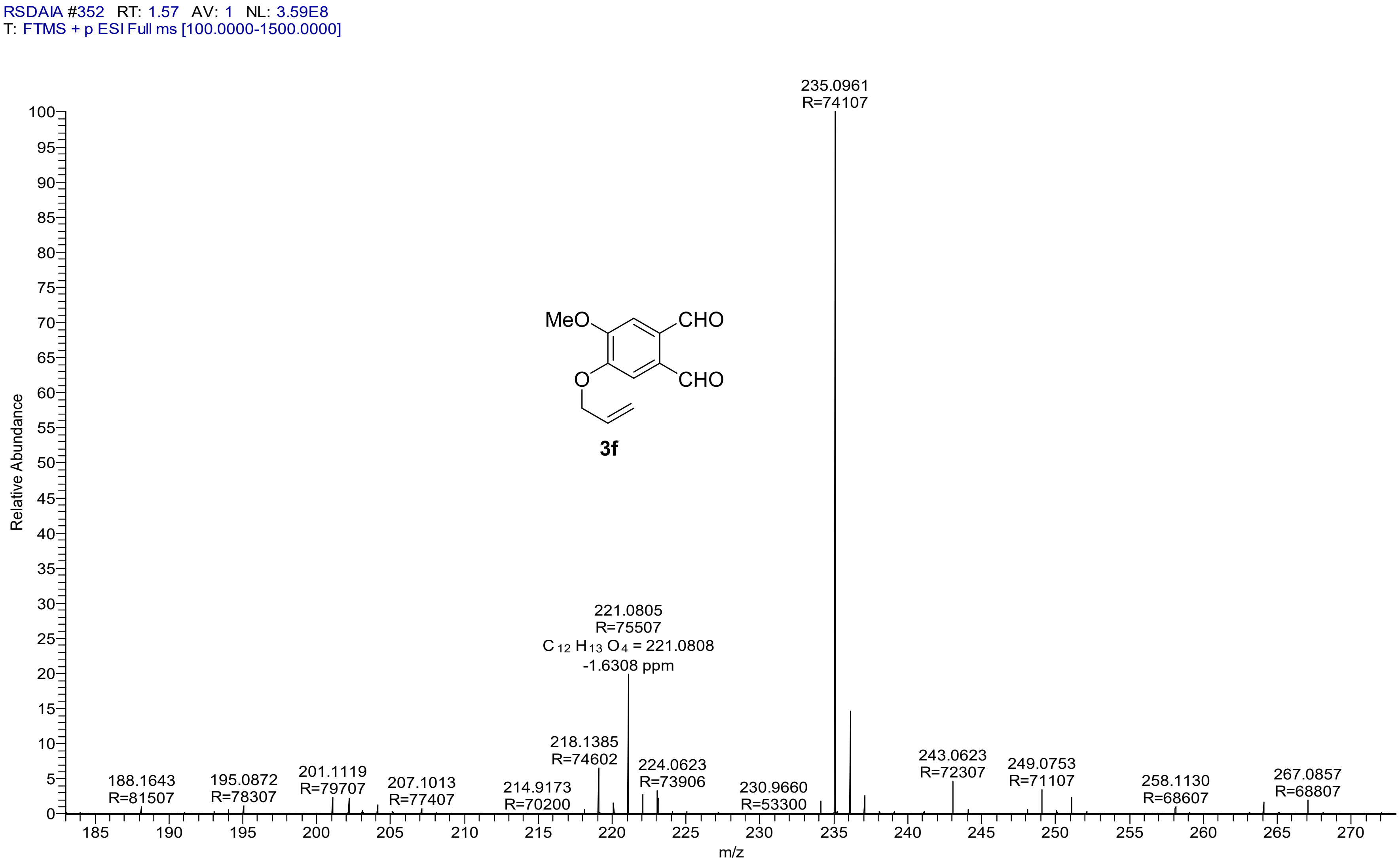
HRMS (ESI) of Compound (**3e**)



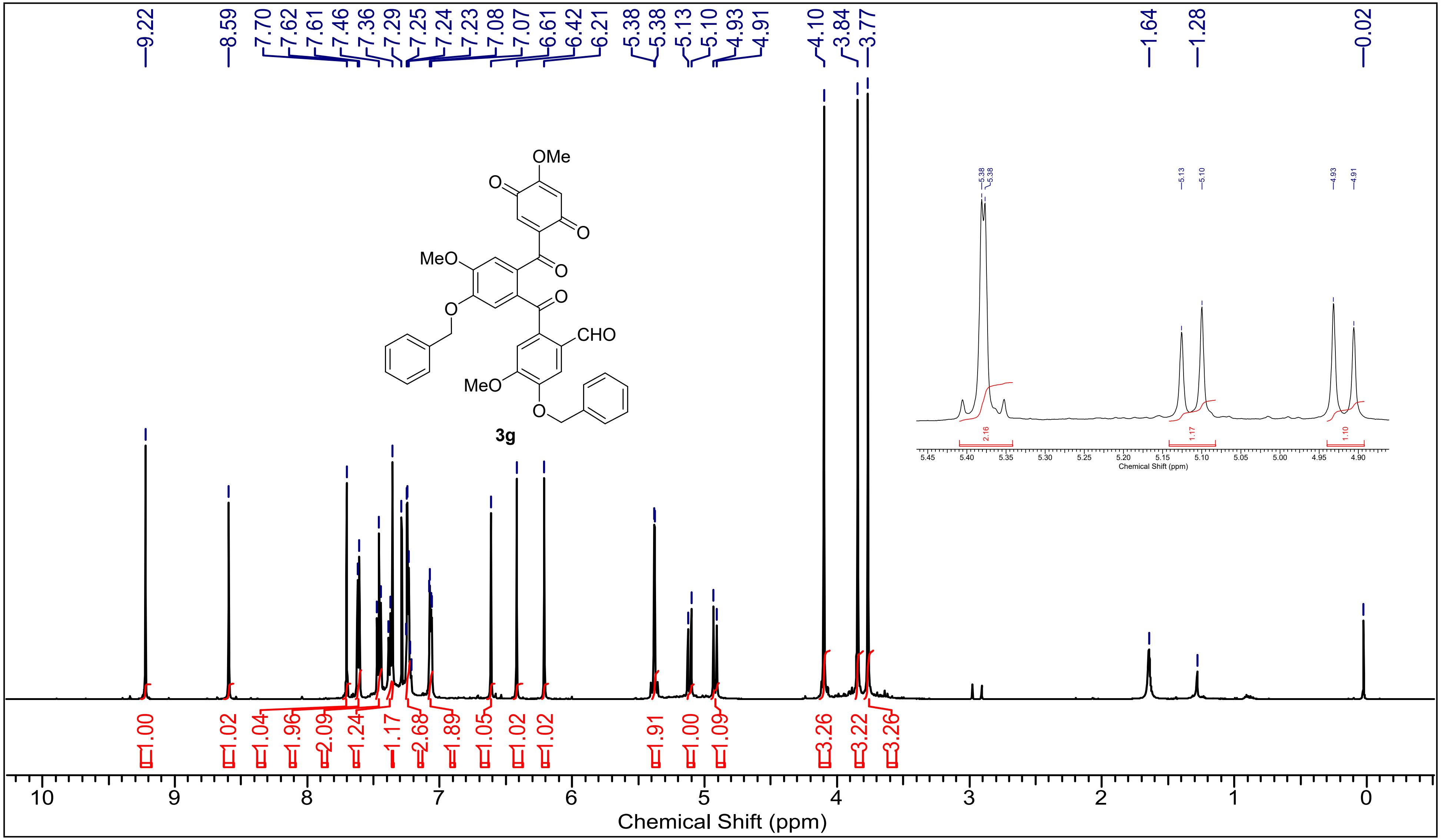
^{1}H NMR of compound (**3f**) in $CDCl_3$ (400 MHz)



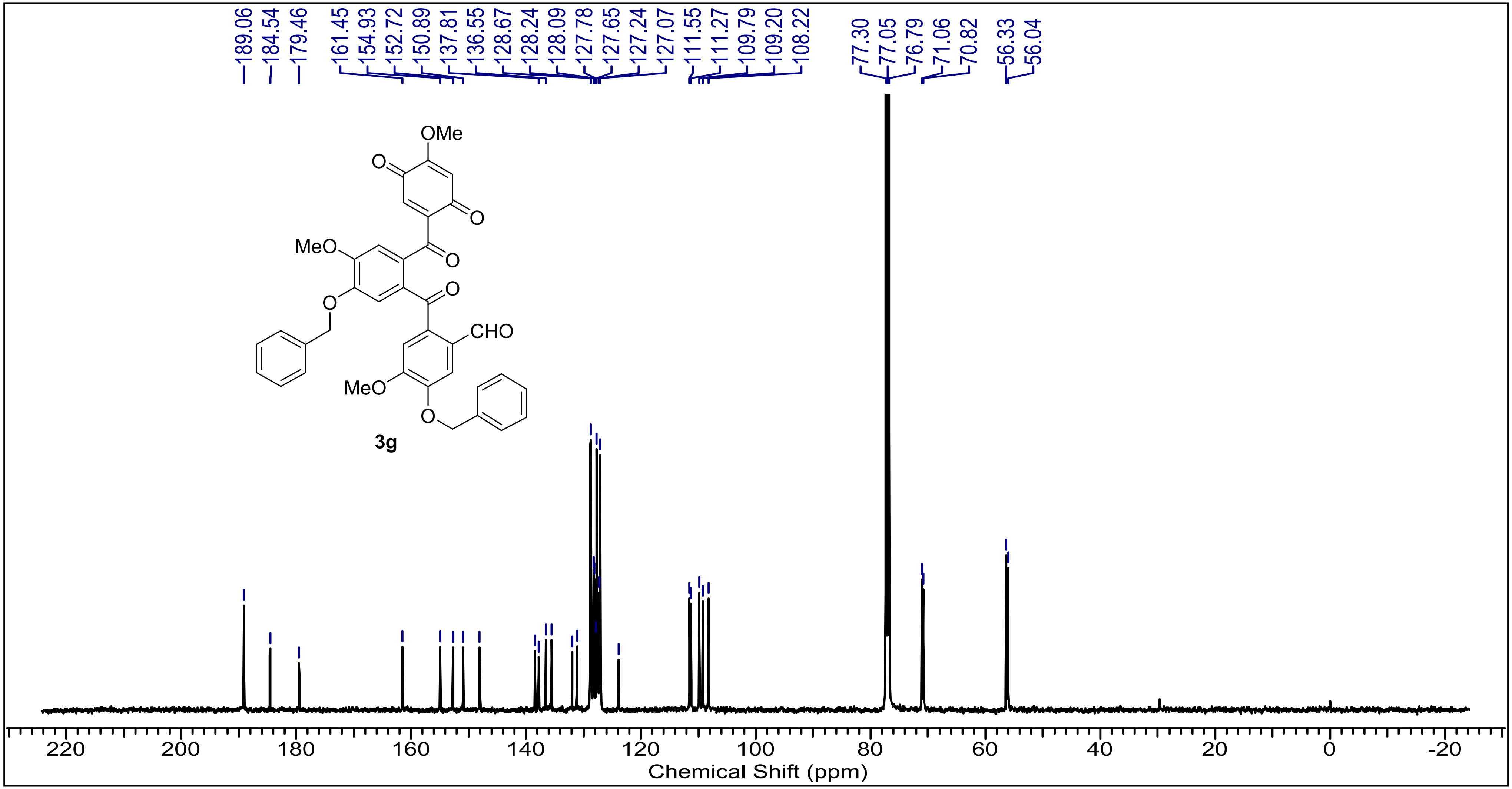
^{13}C NMR of compound (**3f**) in $CDCl_3$ (100 MHz)



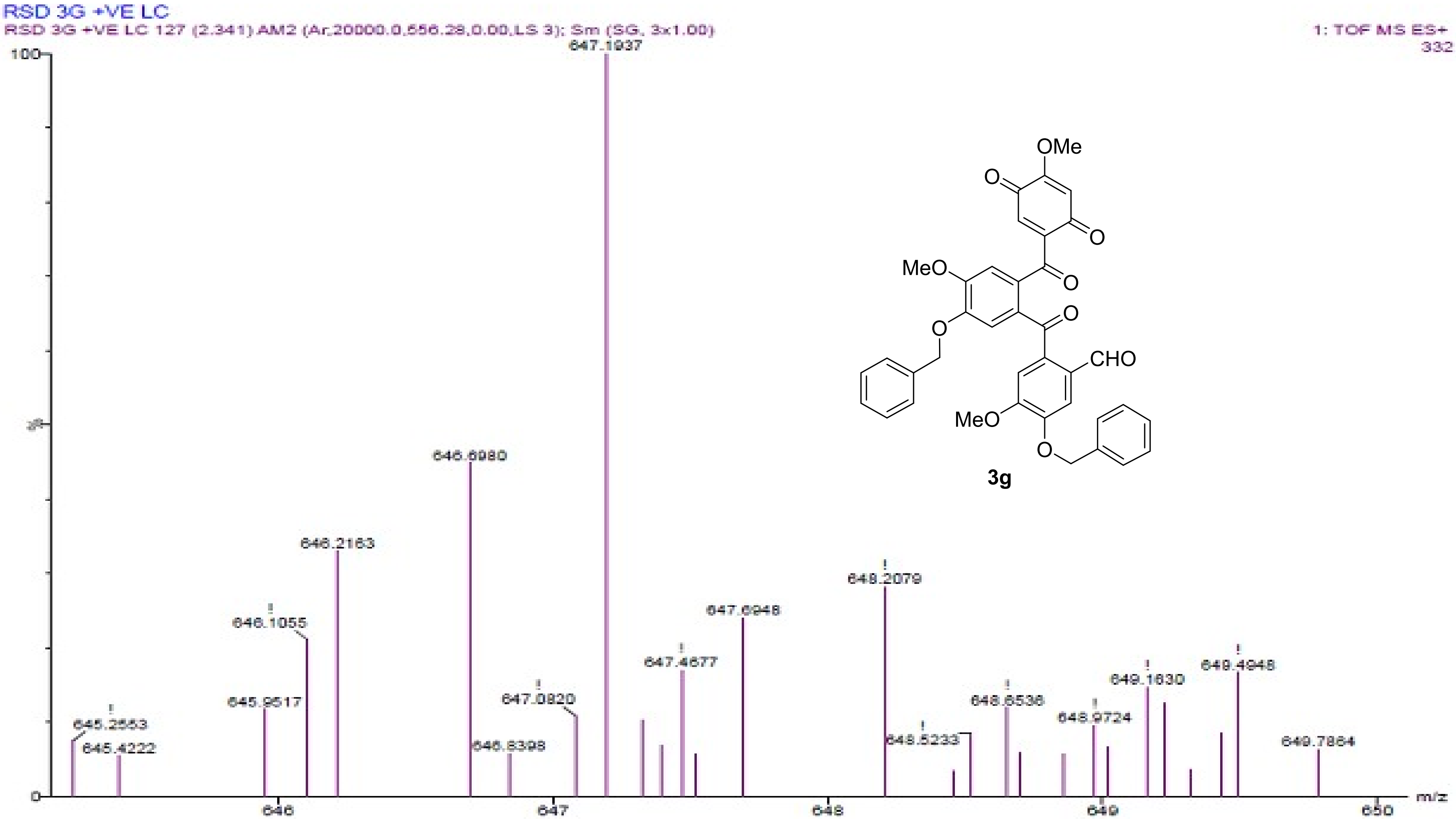
HRMS (ESI) of compound (**3f**)



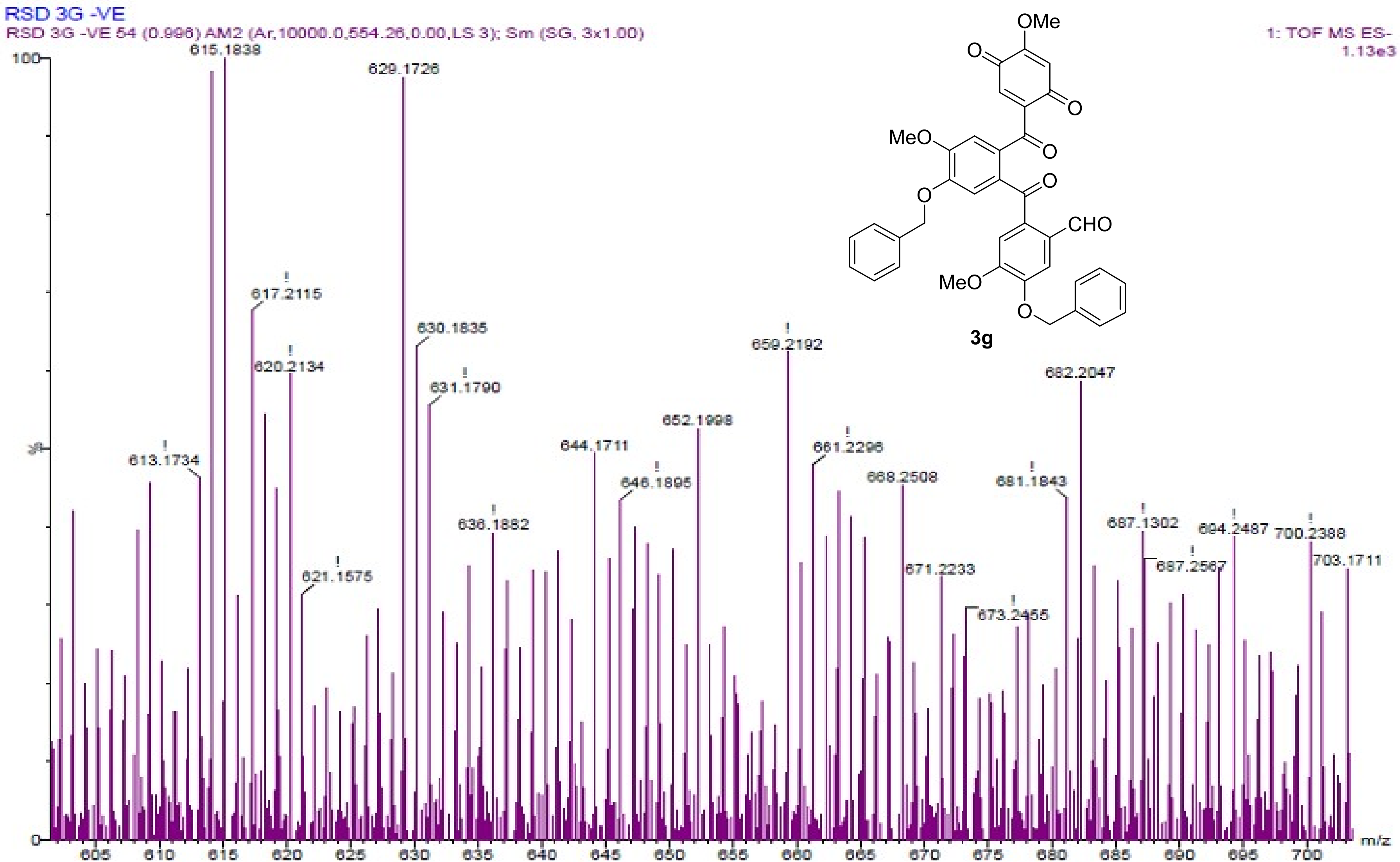
[1]H NMR of compound (**3g**) in $CDCl_3$ (400 MHz)



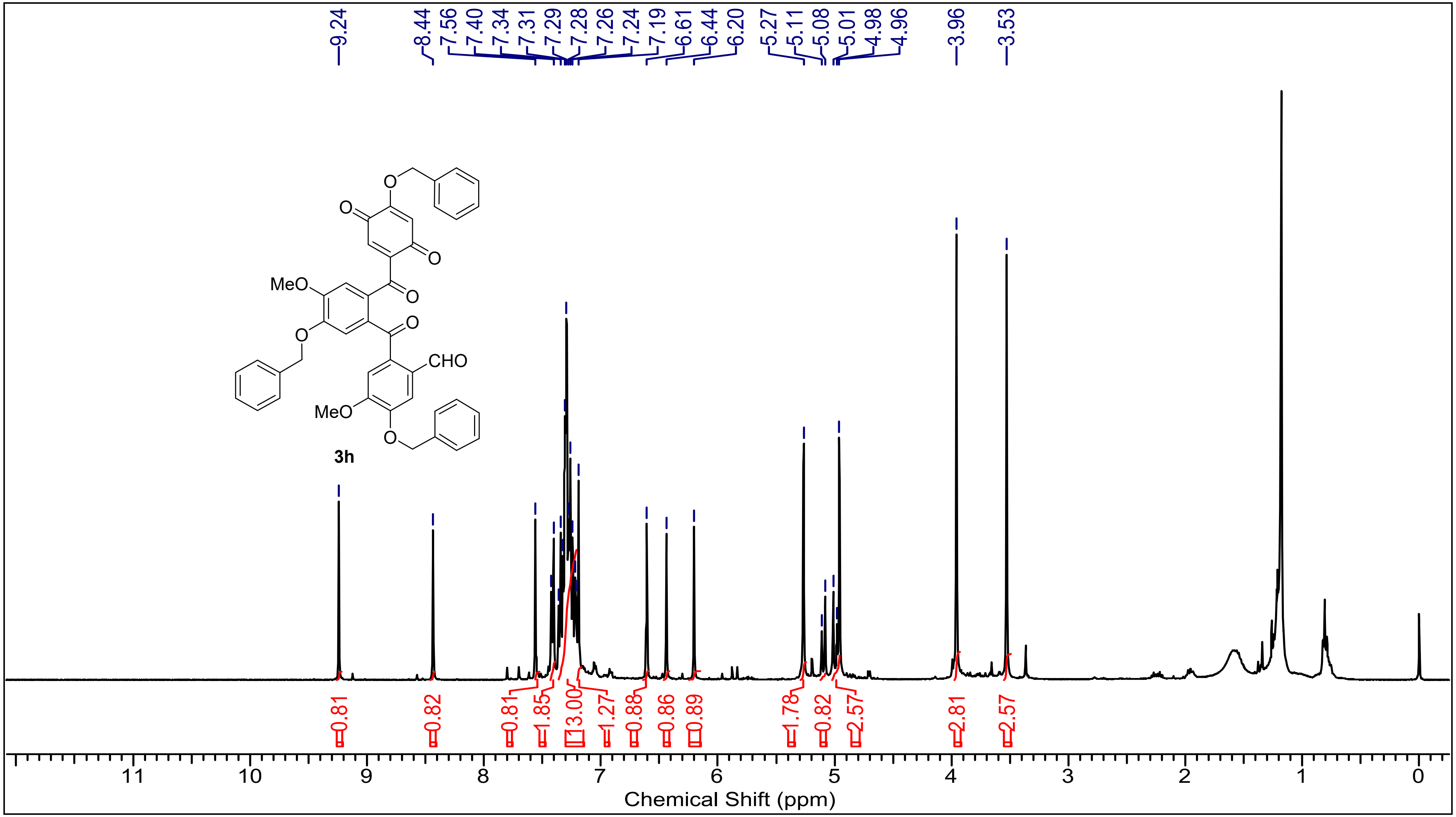
^{13}C NMR of compound (**3g**) in $CDCl_3$ (100 MHz)



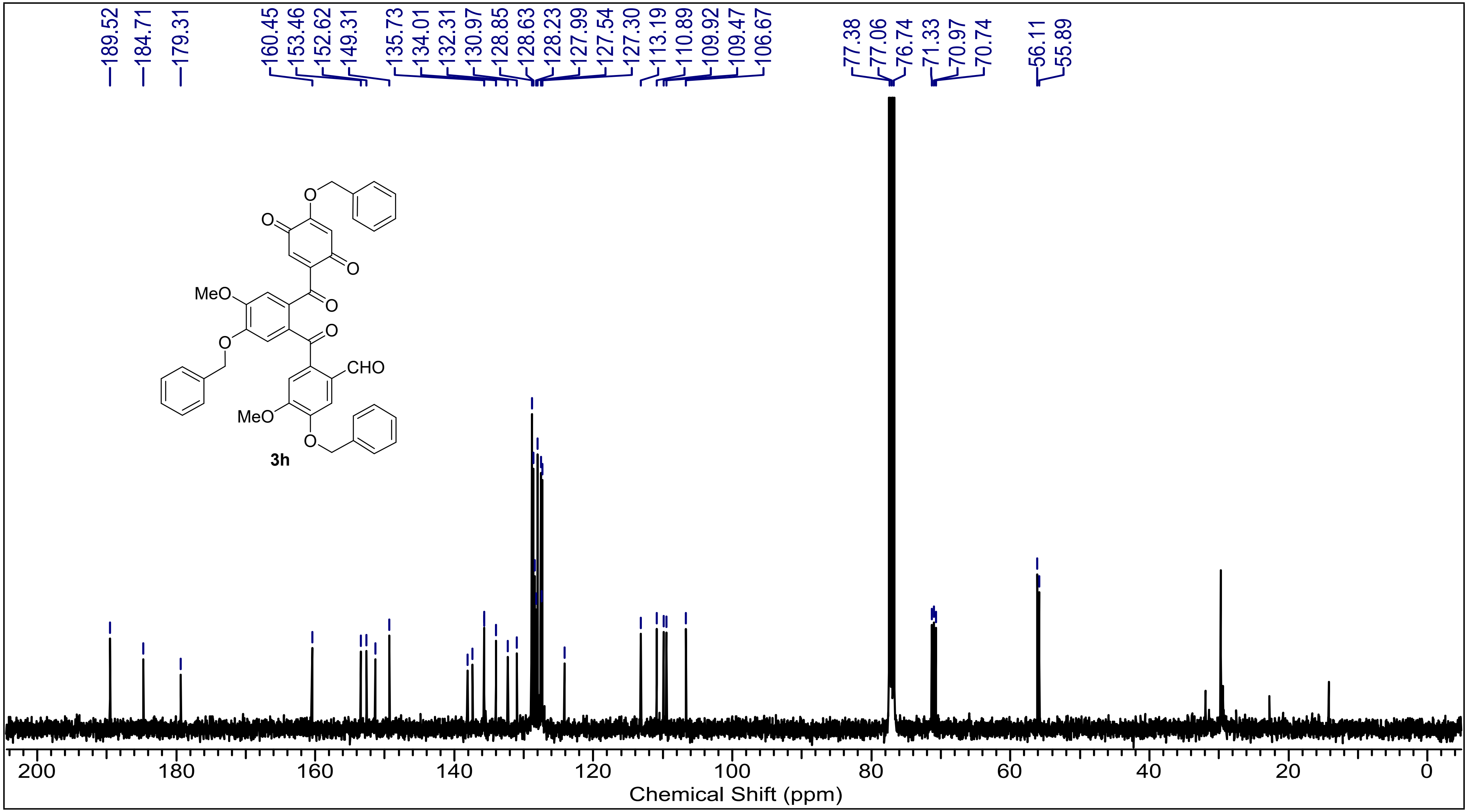
HRMS (ESI) of Compound (**3g**)



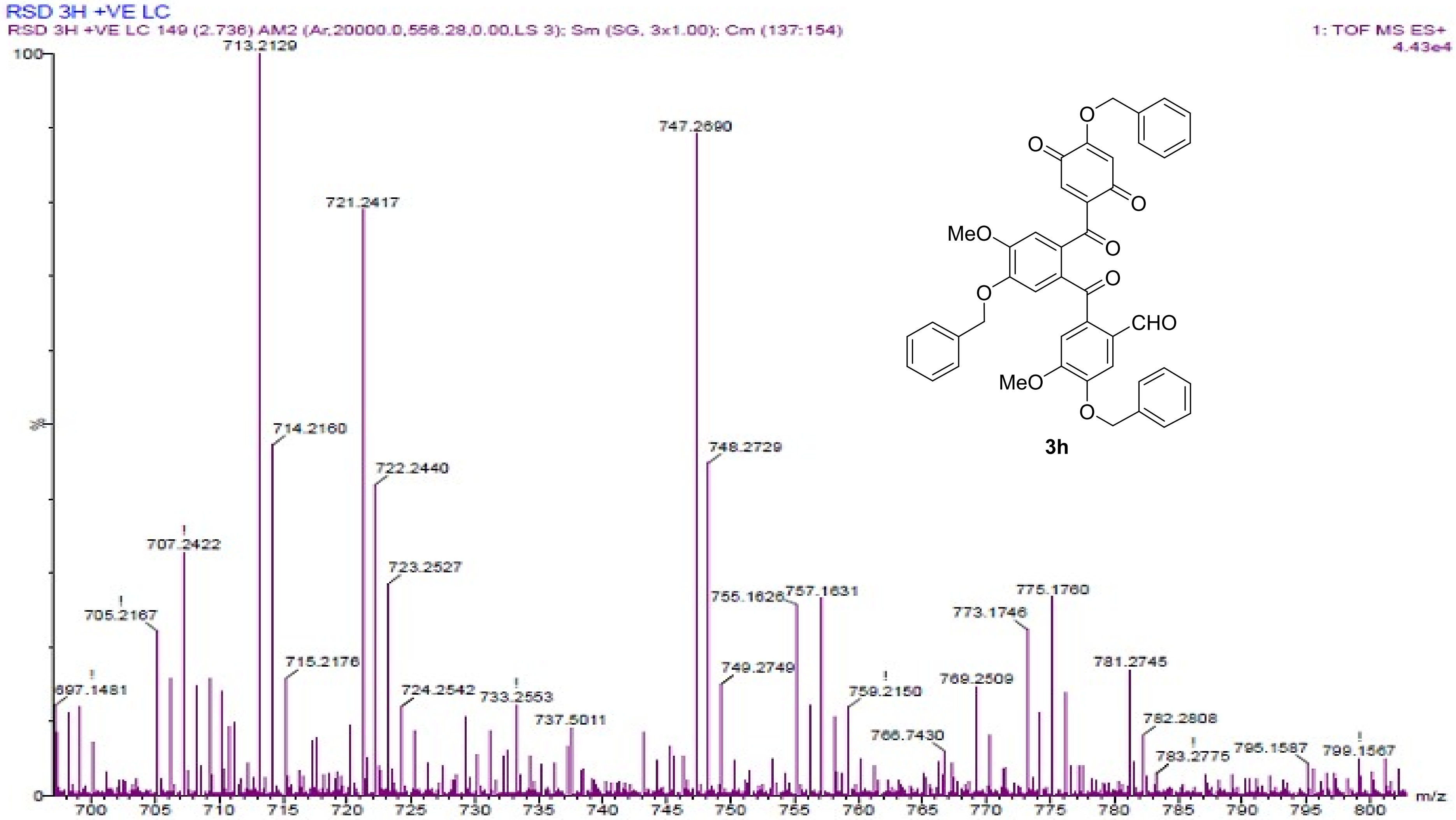
HRMS (ESI) of Compound (**3g**)



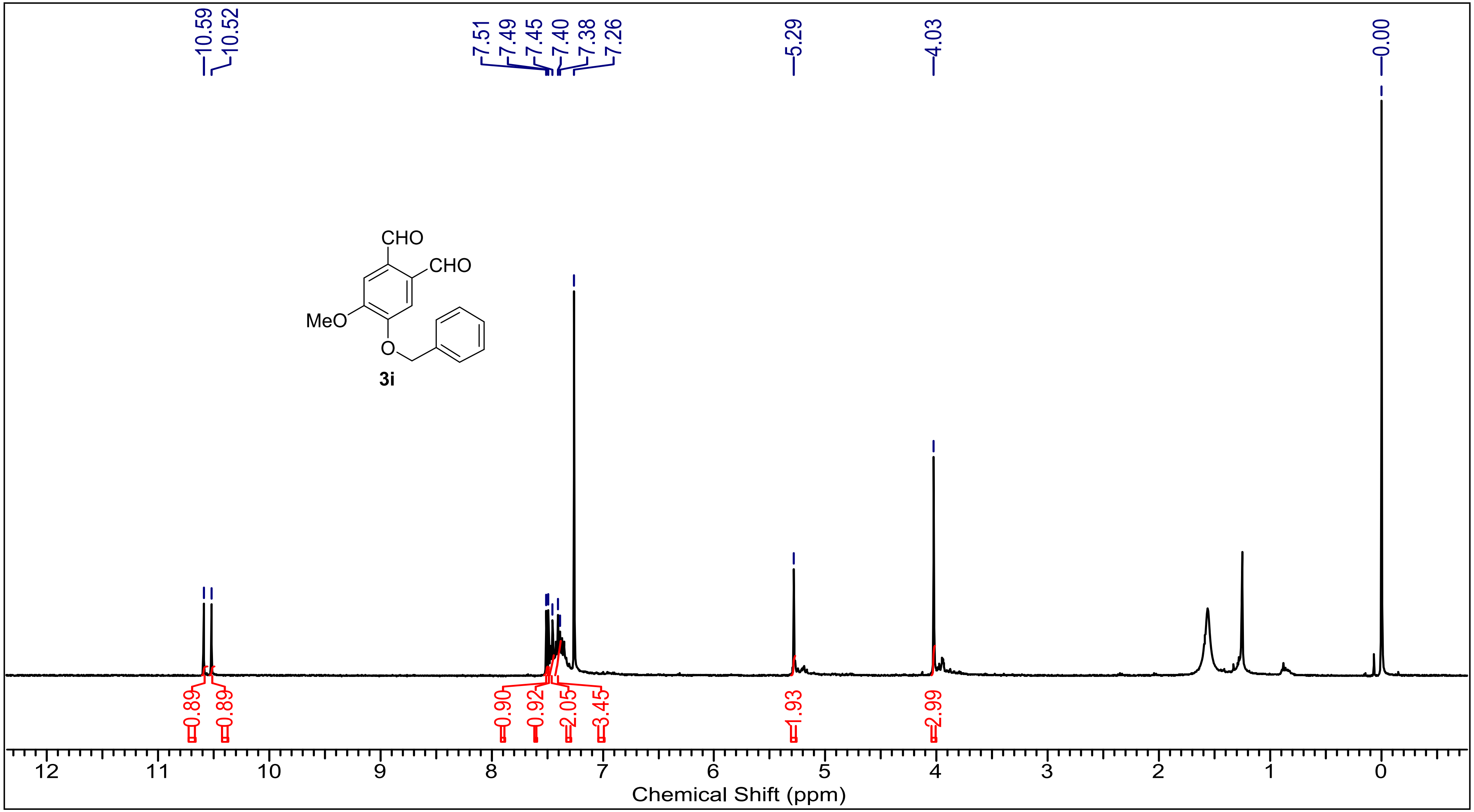
^{1}H NMR of compound (**3h**) in $CDCl_3$ (400 MHz)



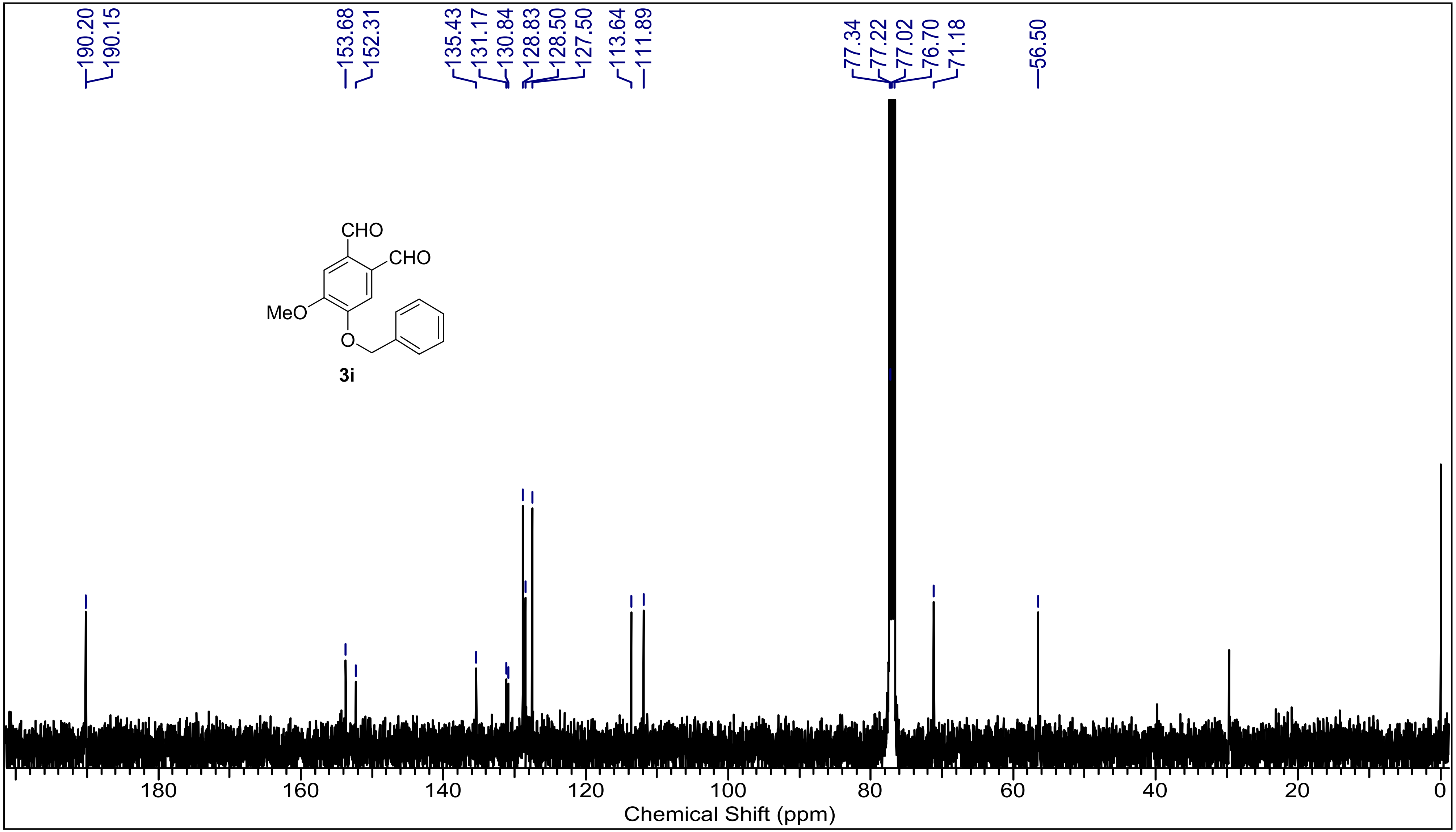
^{13}C NMR of compound (**3h**) in $CDCl_3$ (100 MHz)



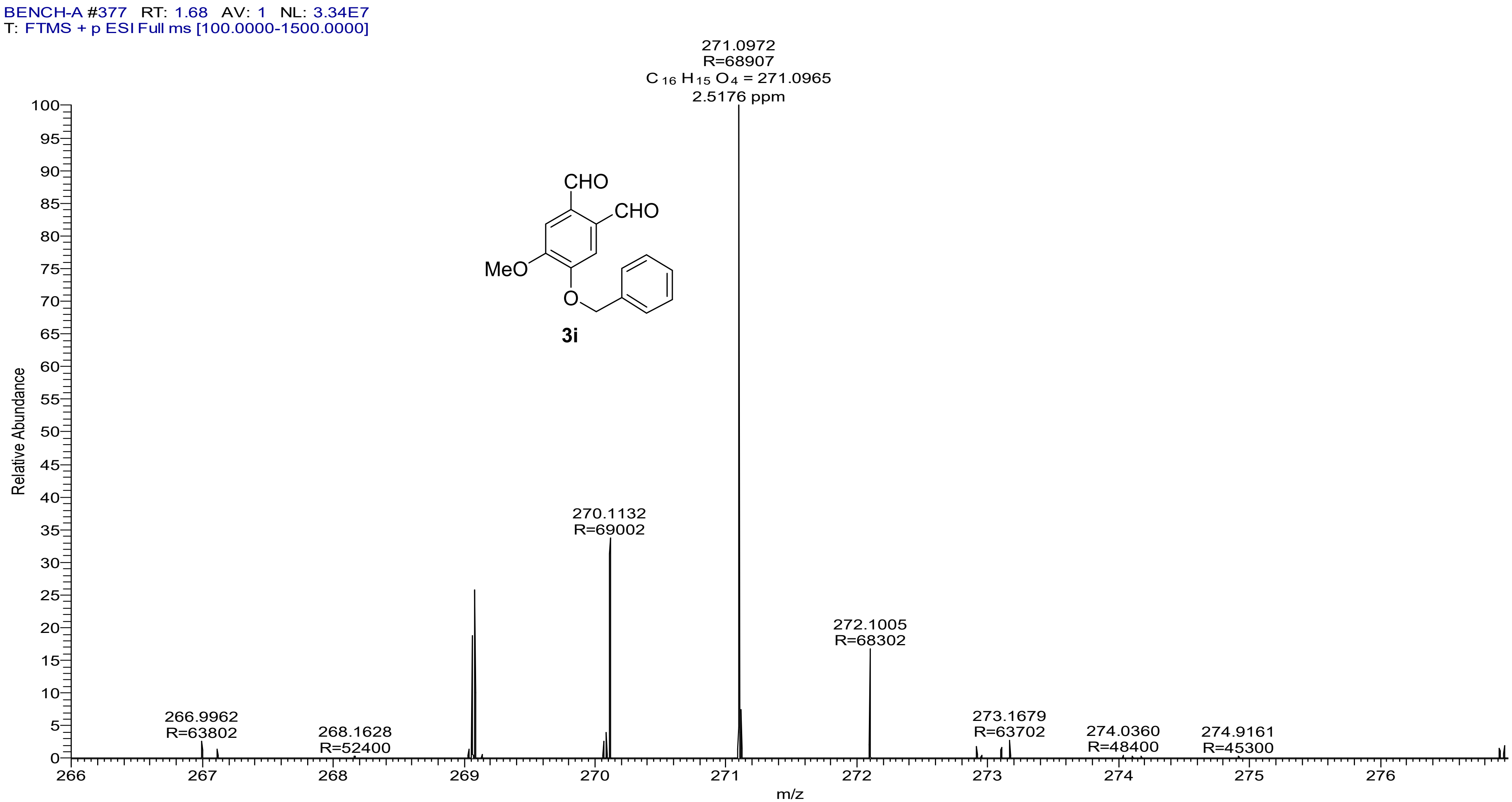
HRMS (ESI) of compound (**3h**)



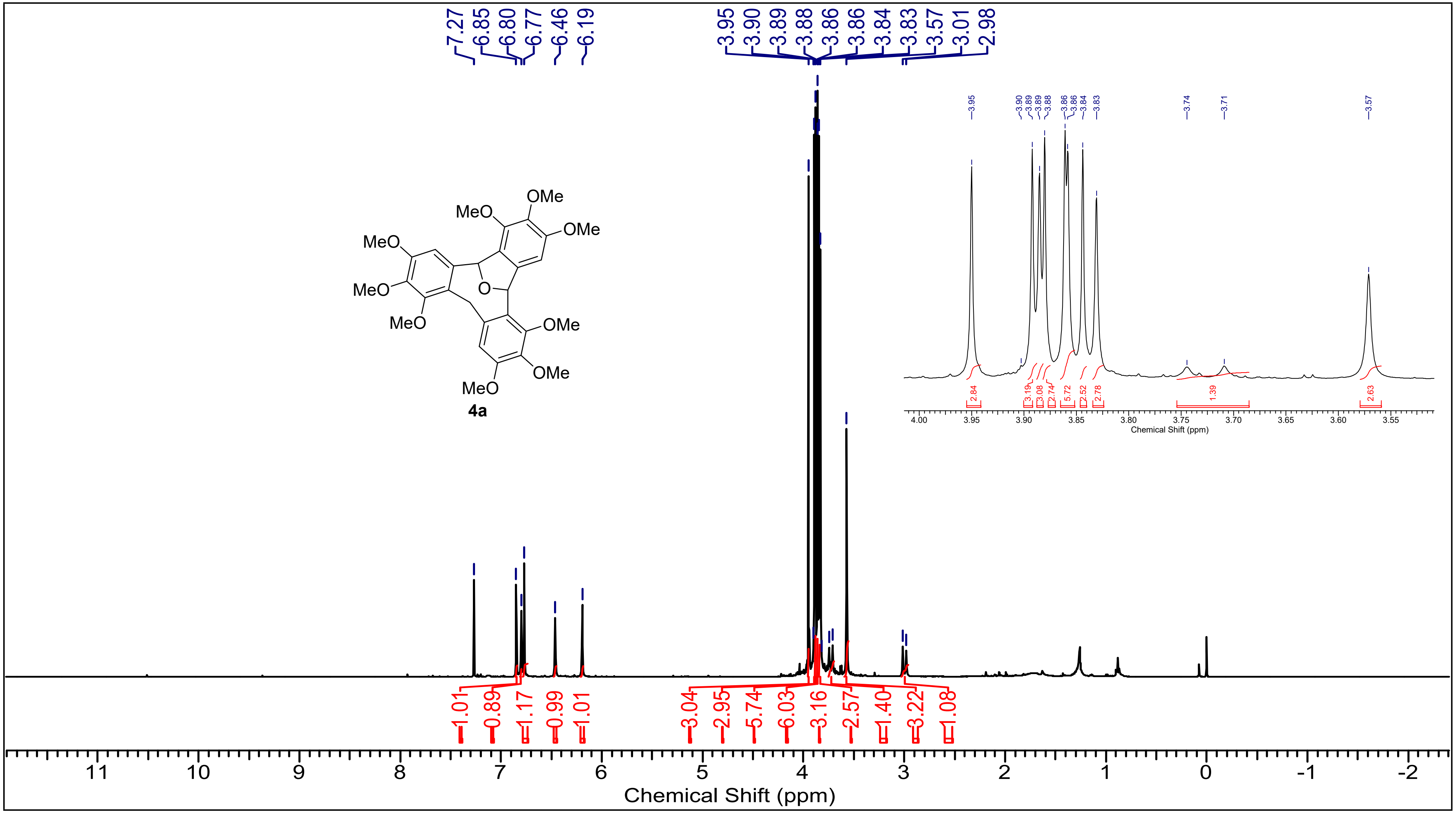
^{1}H NMR of compound (**3i**) in $CDCl_3$ (400 MHz)



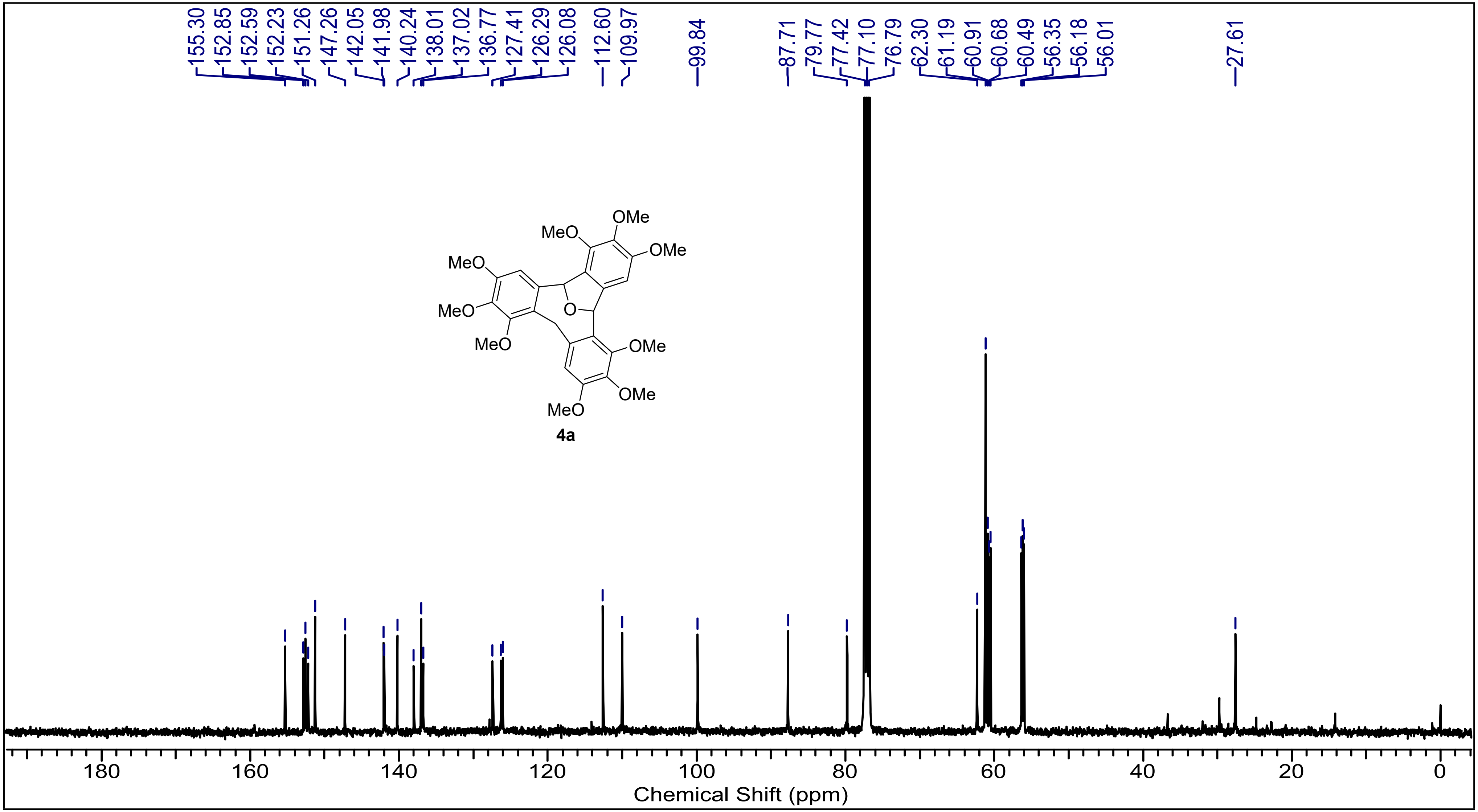
^{13}C NMR of compound (**3i**) in $CDCl_3$ (100 MHz)



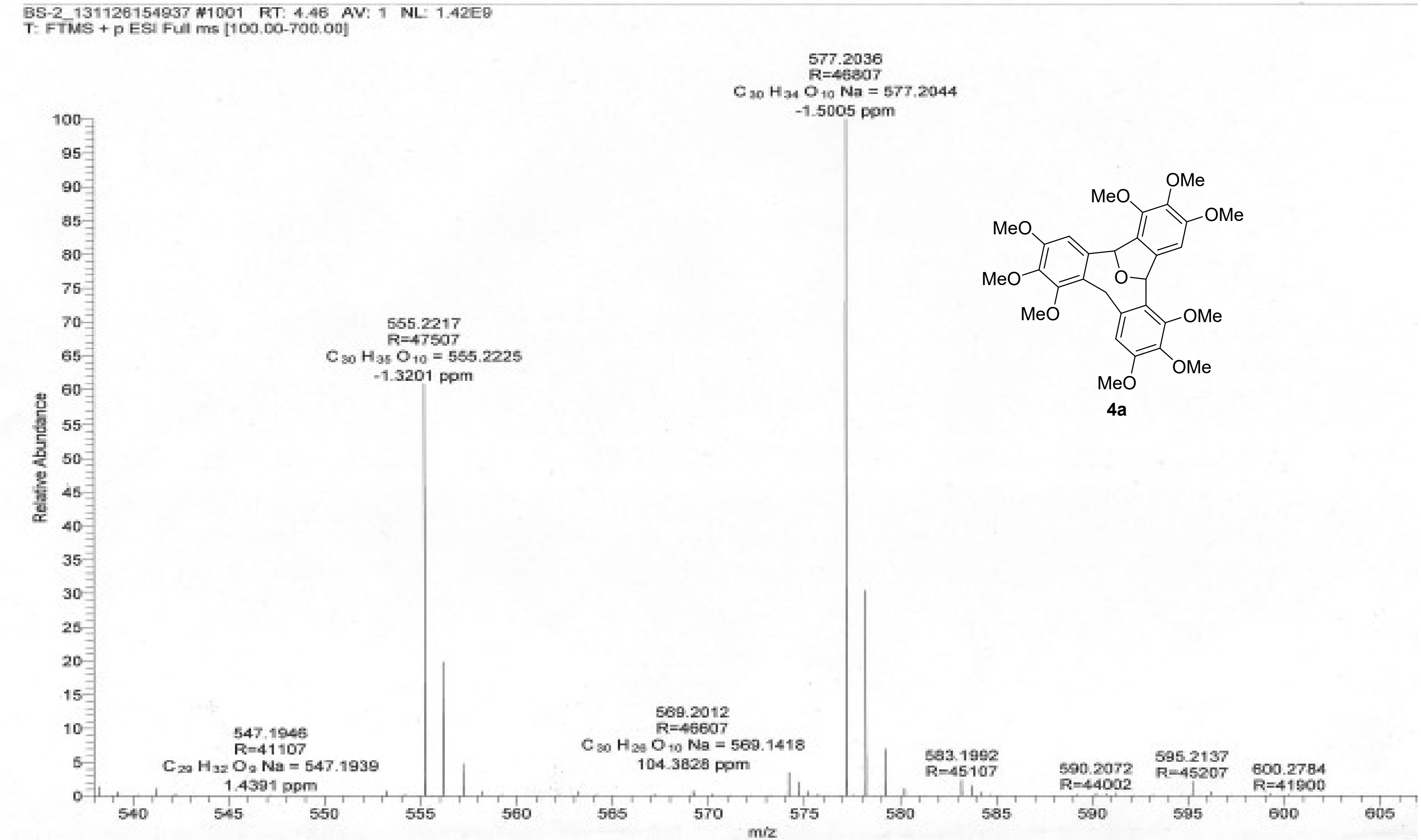
HRMS (ESI) of compound (**3i**)



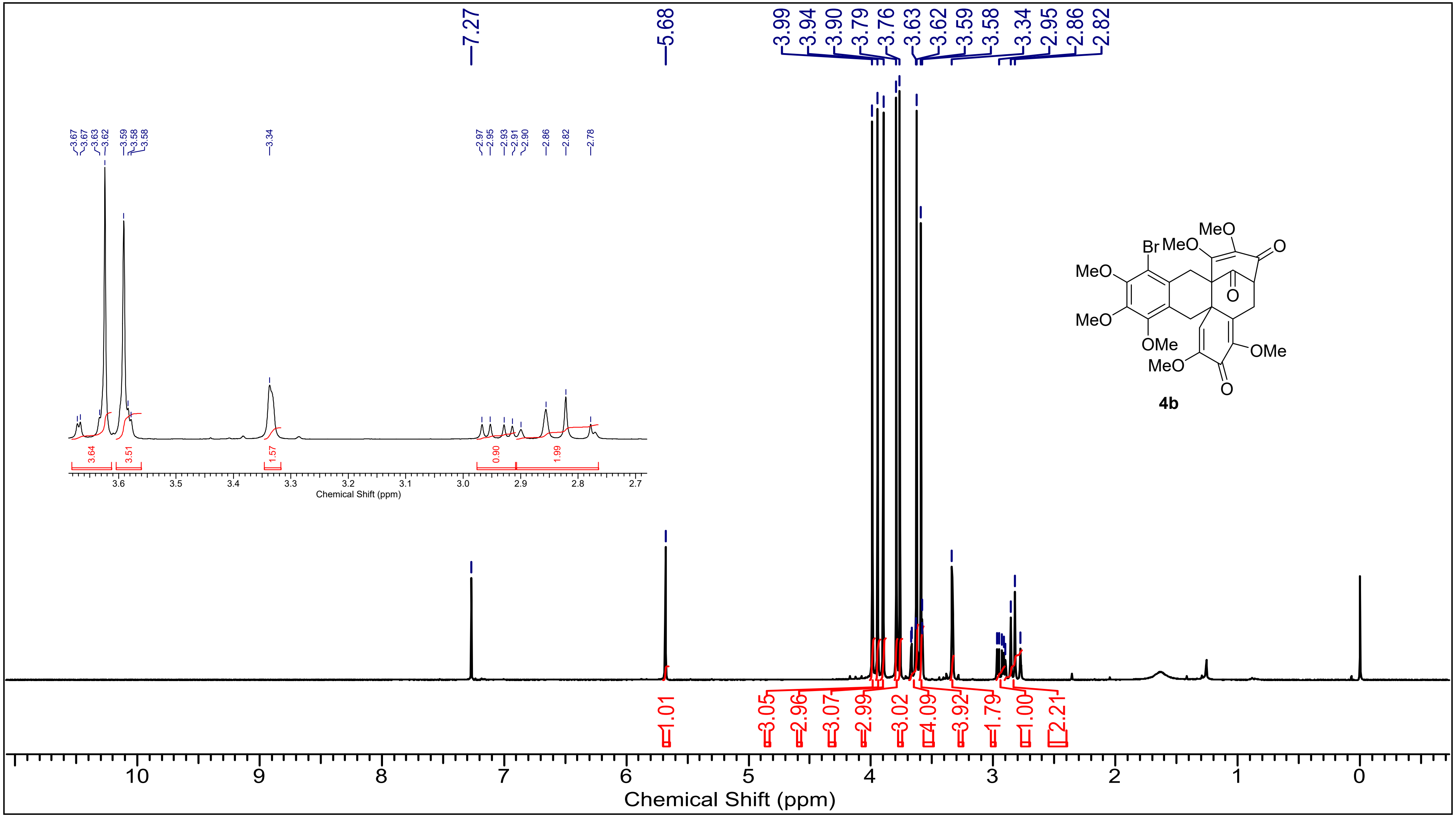
^{1}H NMR of compound (**4a**) in $CDCl_3$ (400 MHz)



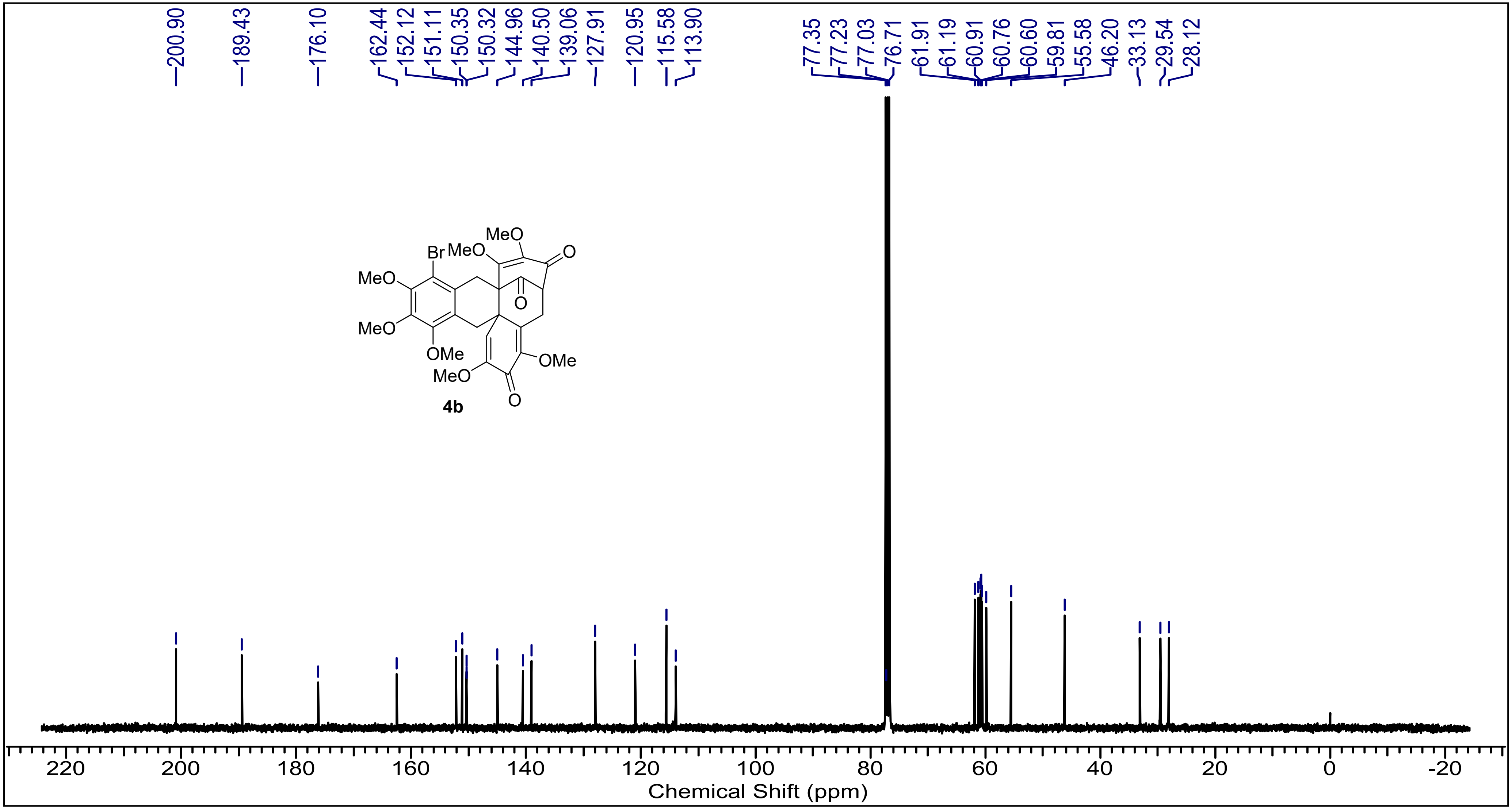
^{13}C NMR of compound (**4a**) in $CDCl_3$ (100 MHz)



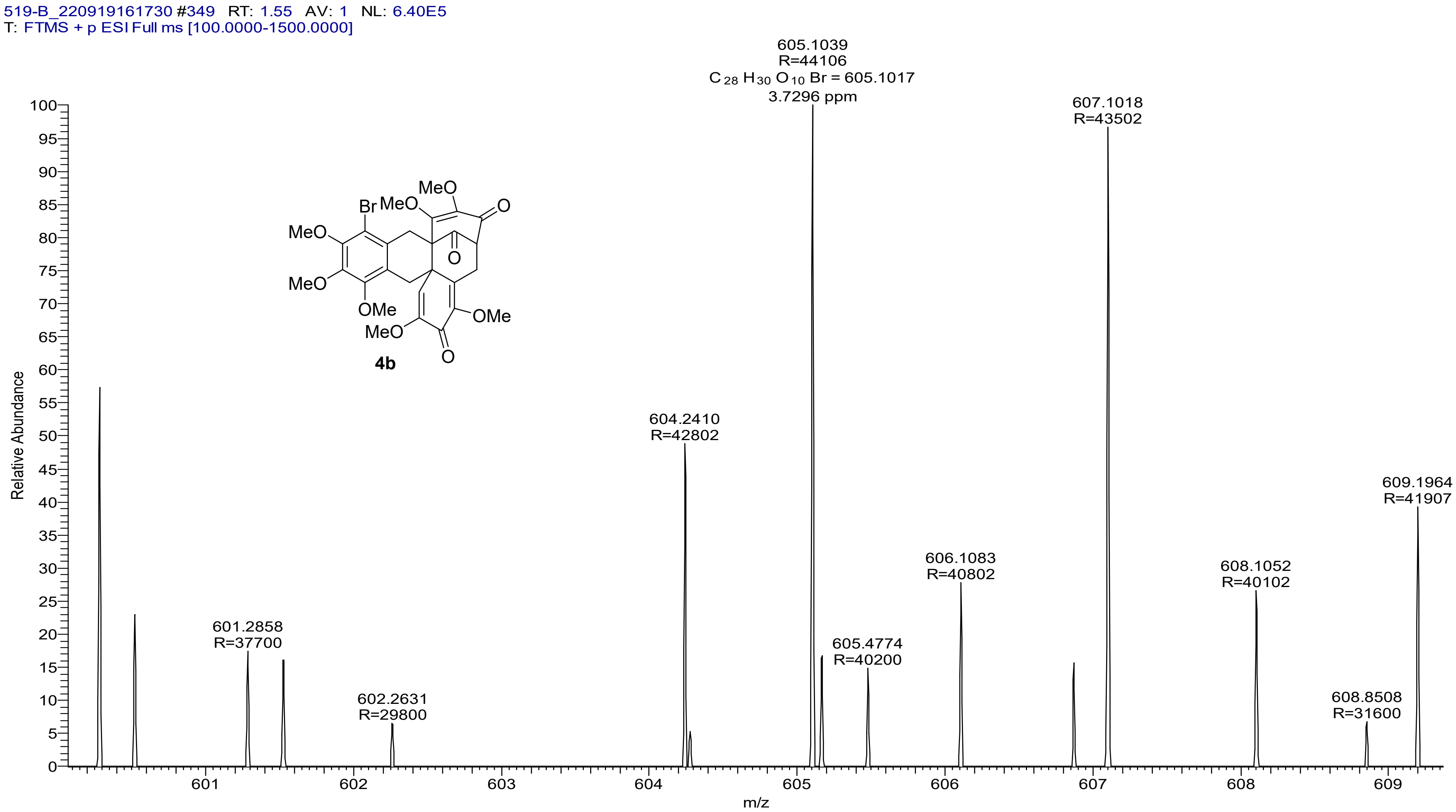
HRMS (ESI) of compound (**4a)**



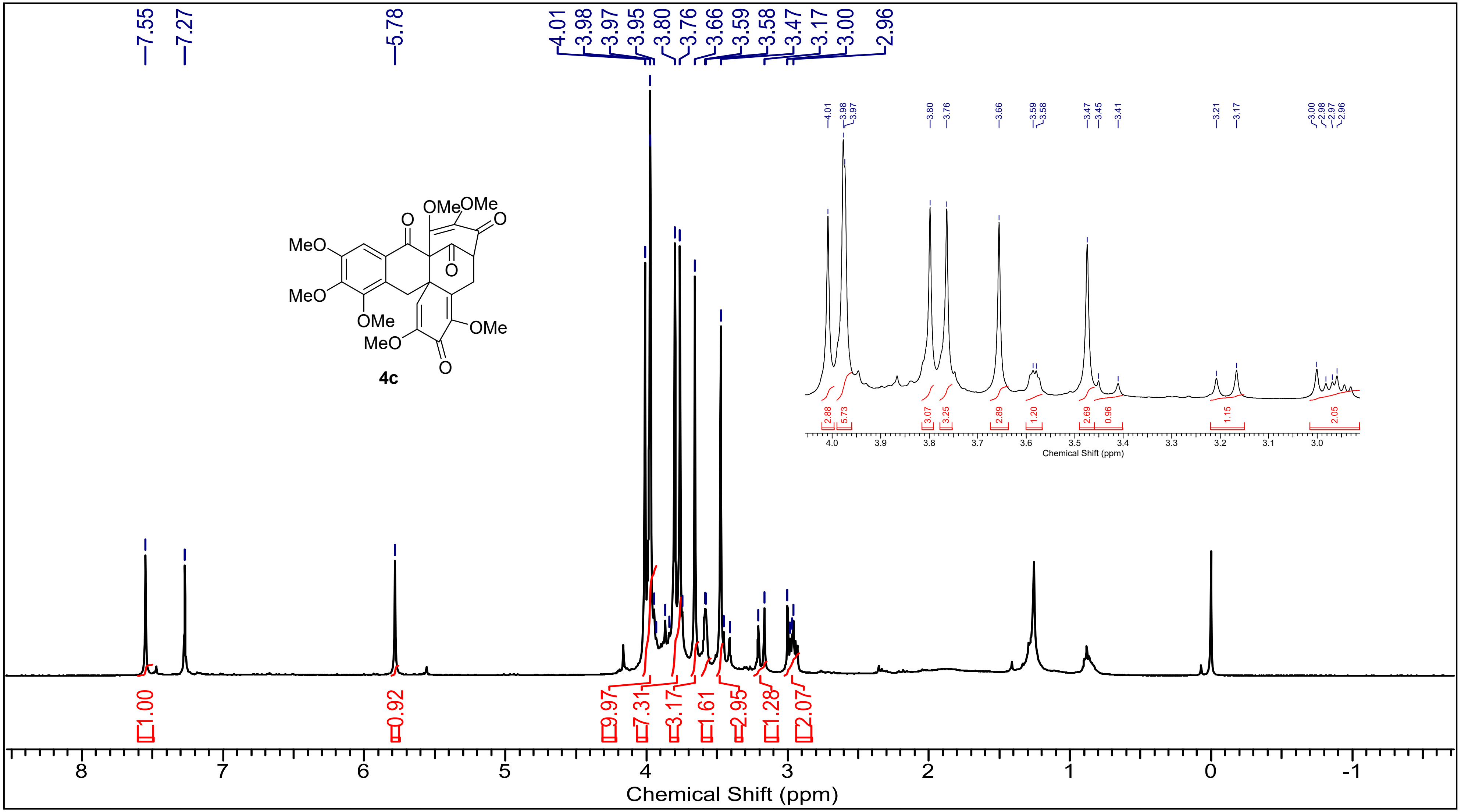
^{1}H NMR of compound (**4b**) in $CDCl_3$ (400 MHz)



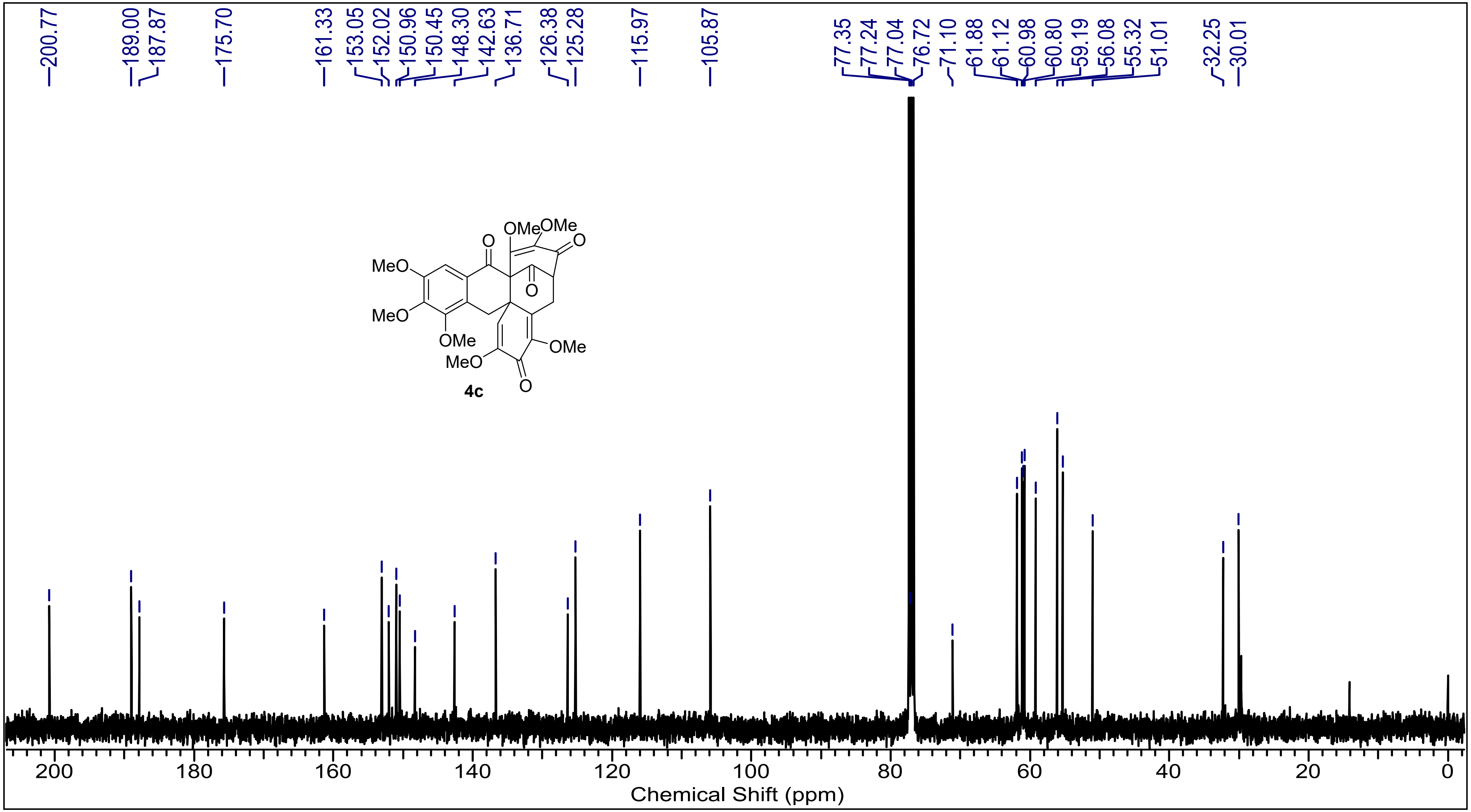
^{13}C NMR of compound (**4b**) in $CDCl_3$ (100 MHz)



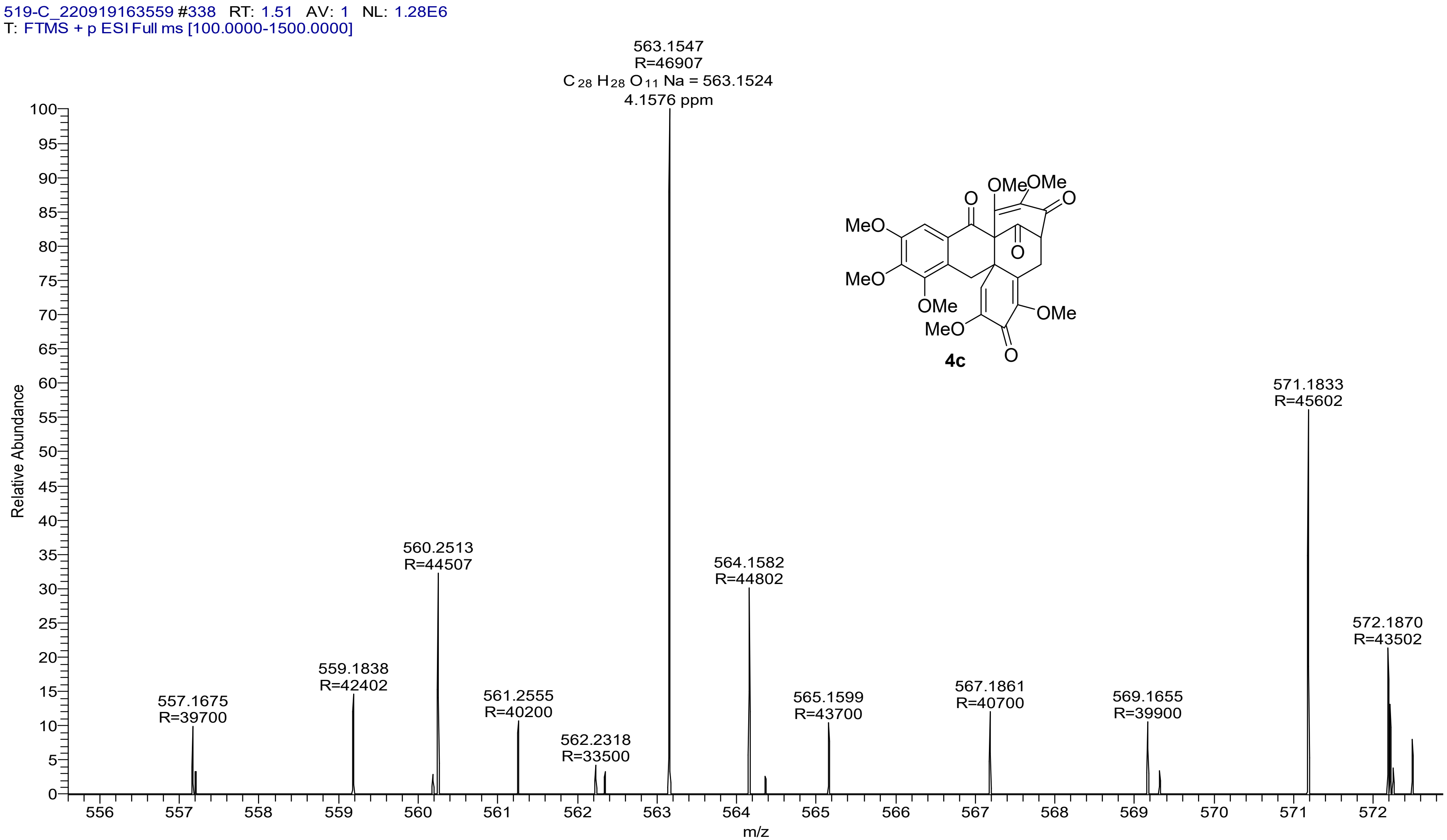
HRMS (ESI) of compound (**4b)**



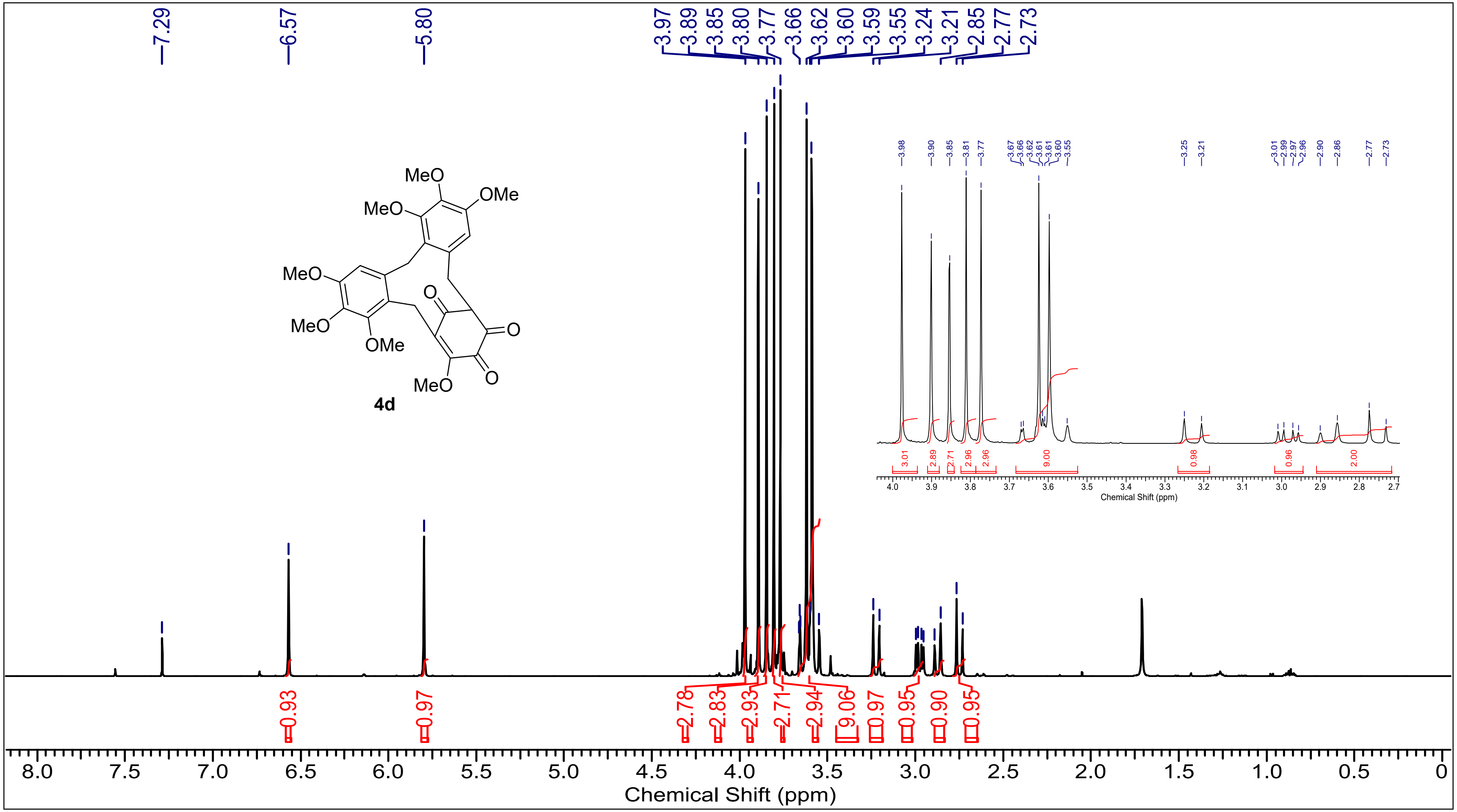
^{1}H NMR of compound (**4c**) in $CDCl_3$ (400 MHz)



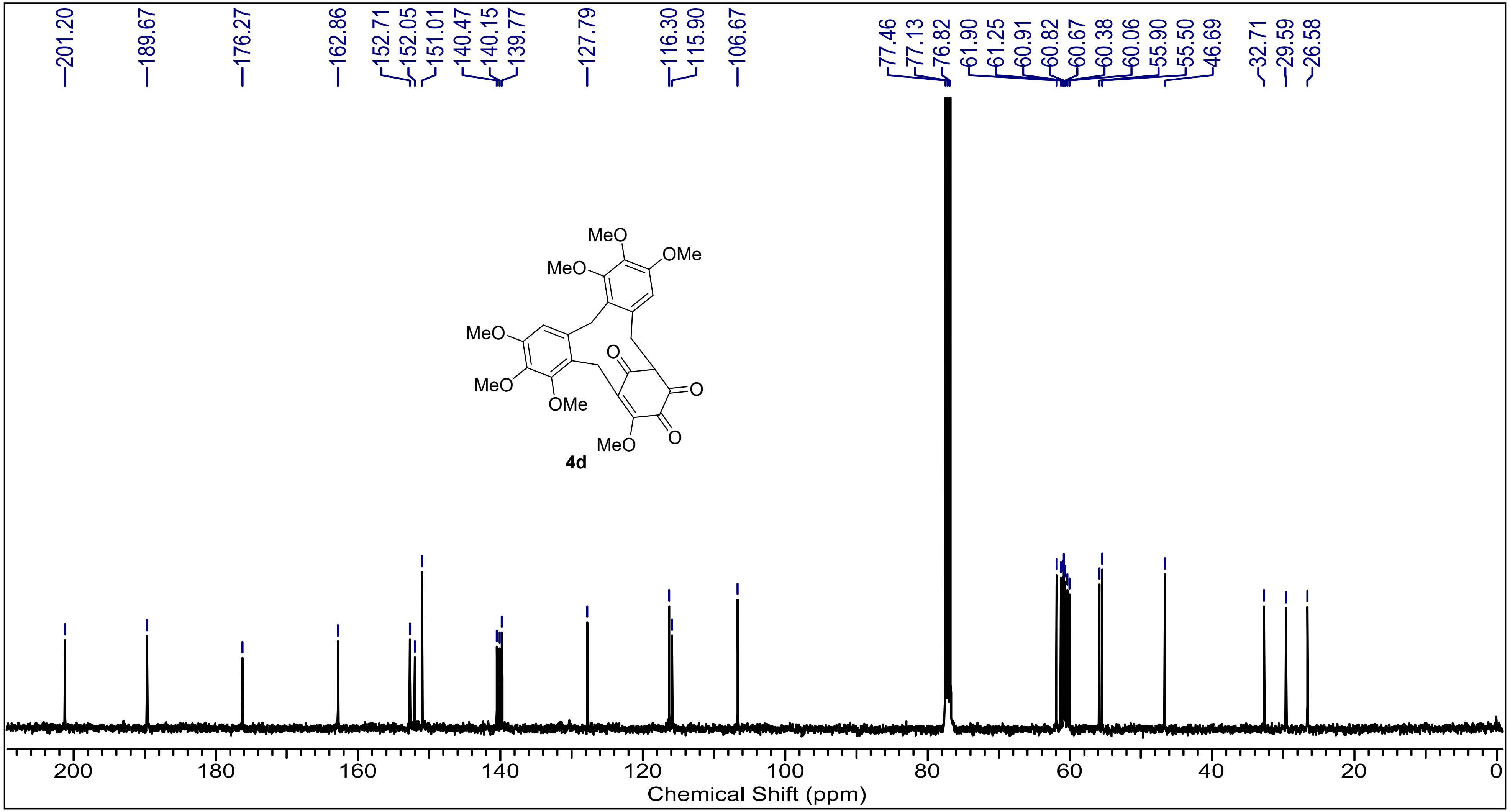
^{13}C NMR of compound (**4c**) in $CDCl_3$ (400 MHz)



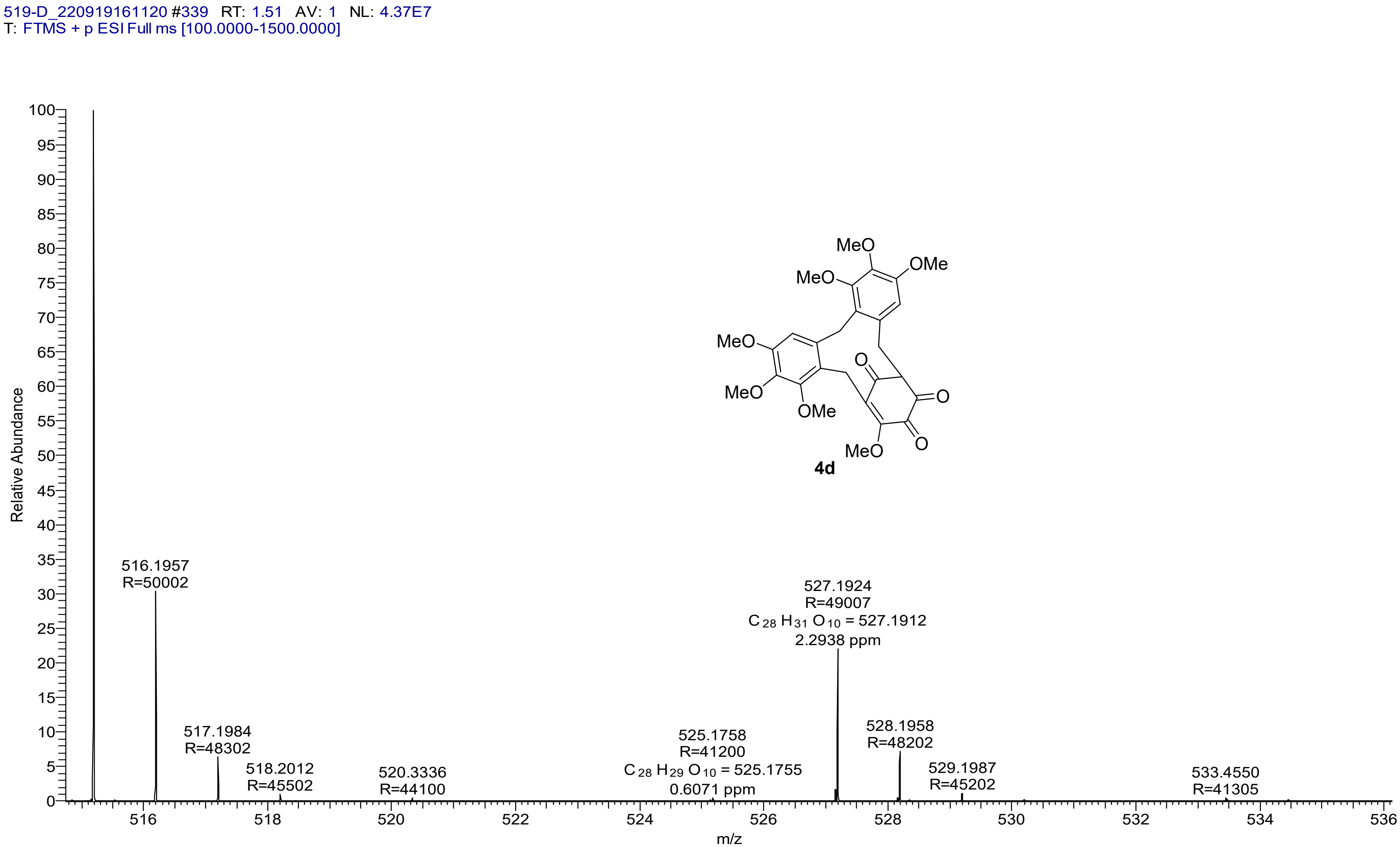
HRMS (ESI) of compound (**4c)**



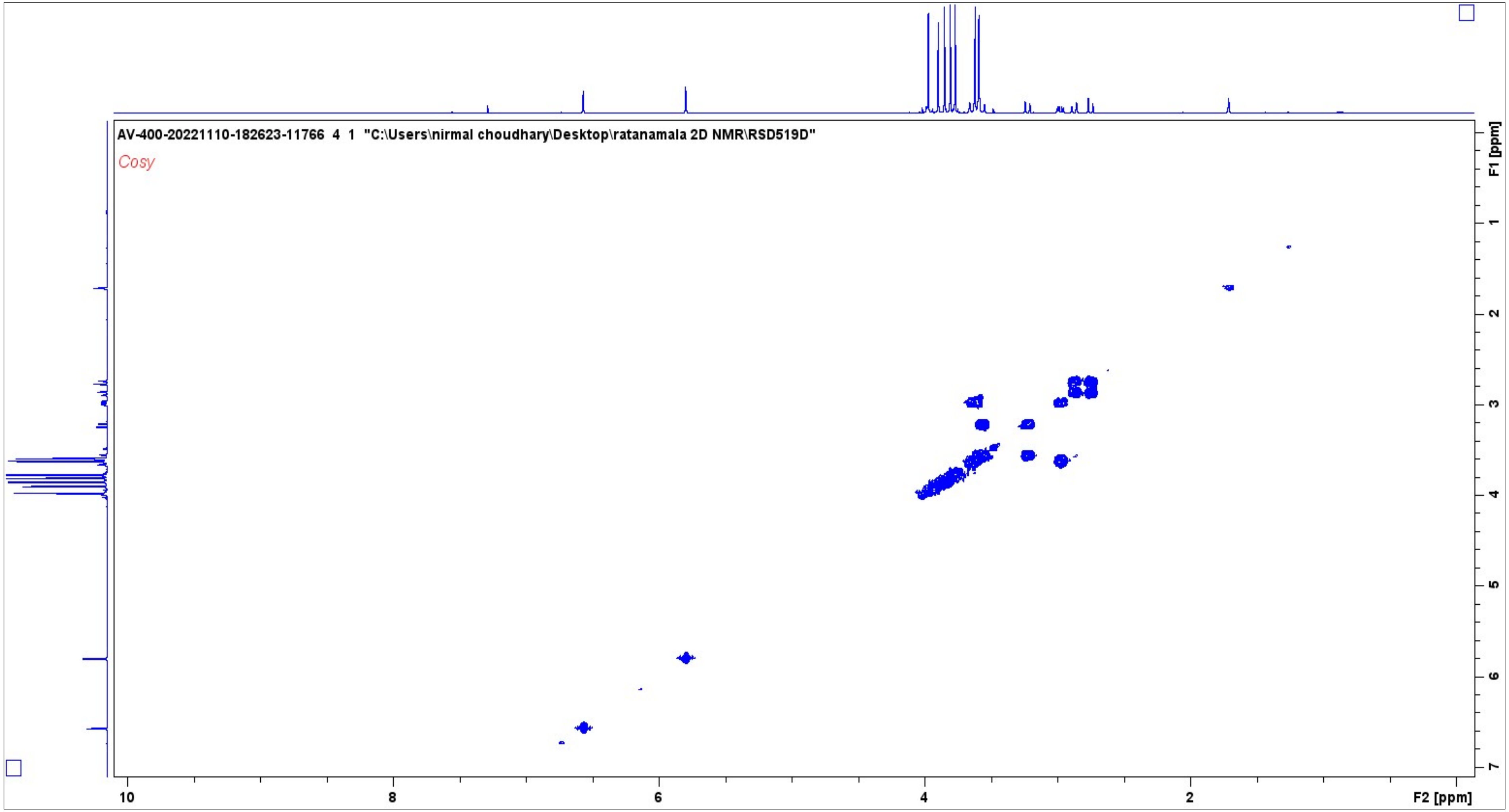
[1]H NMR of compound (**4d**) in $CDCl_3$ (400 MHz)



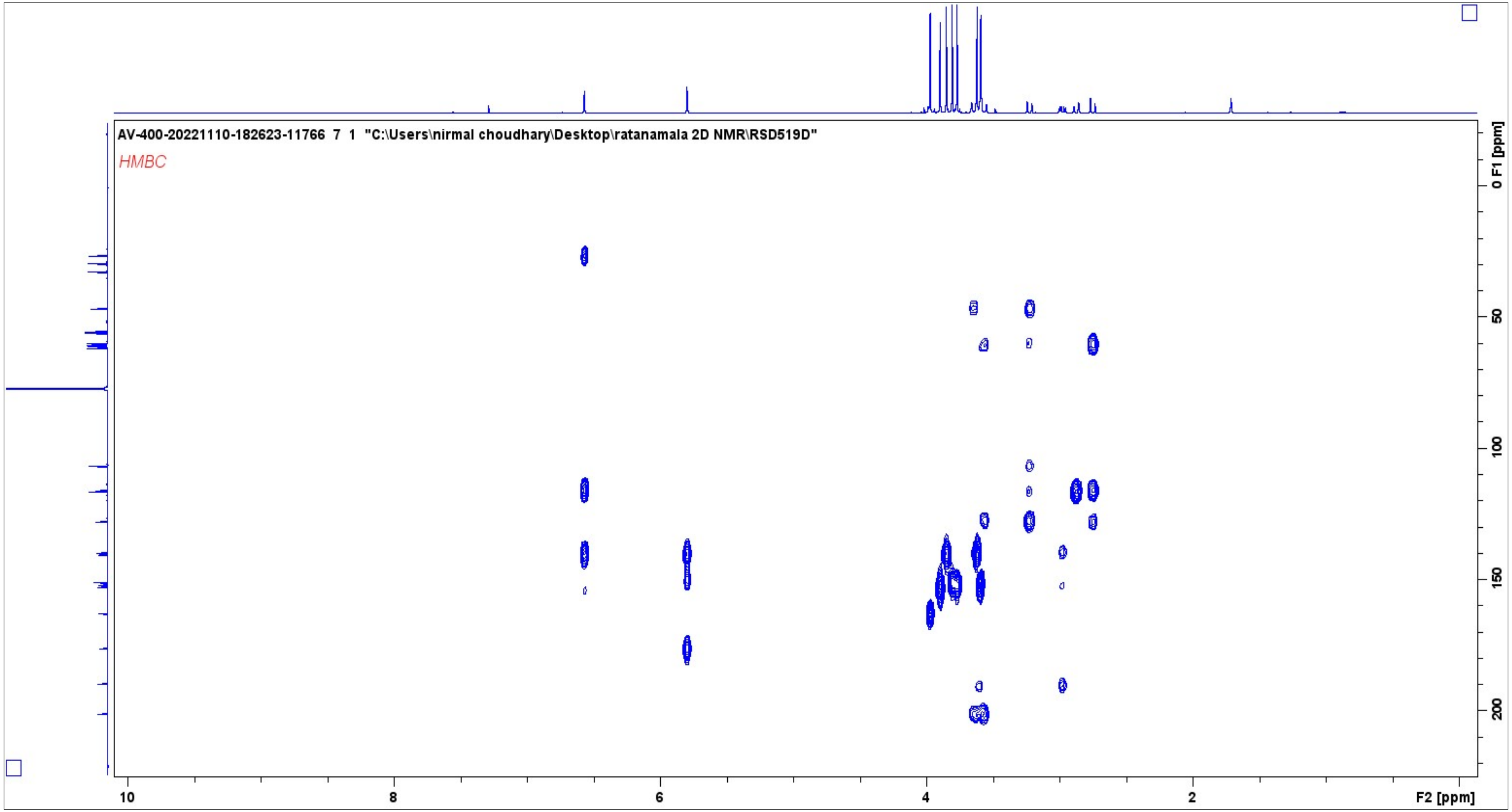
^{13}C NMR of compound (**4d**) in $CDCl_3$ (100 MHz)



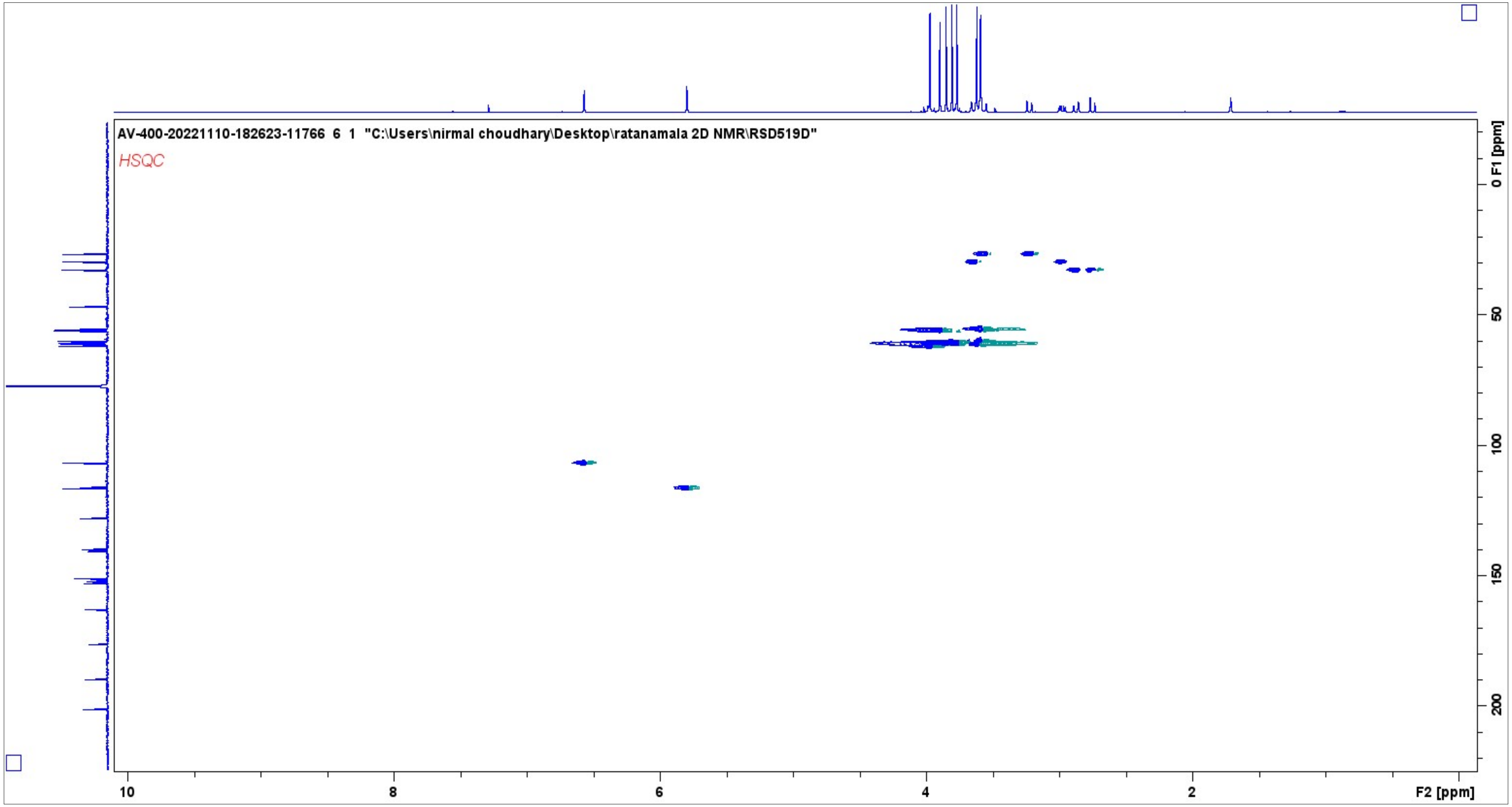
HRMS (ESI) of compound (**4d**)



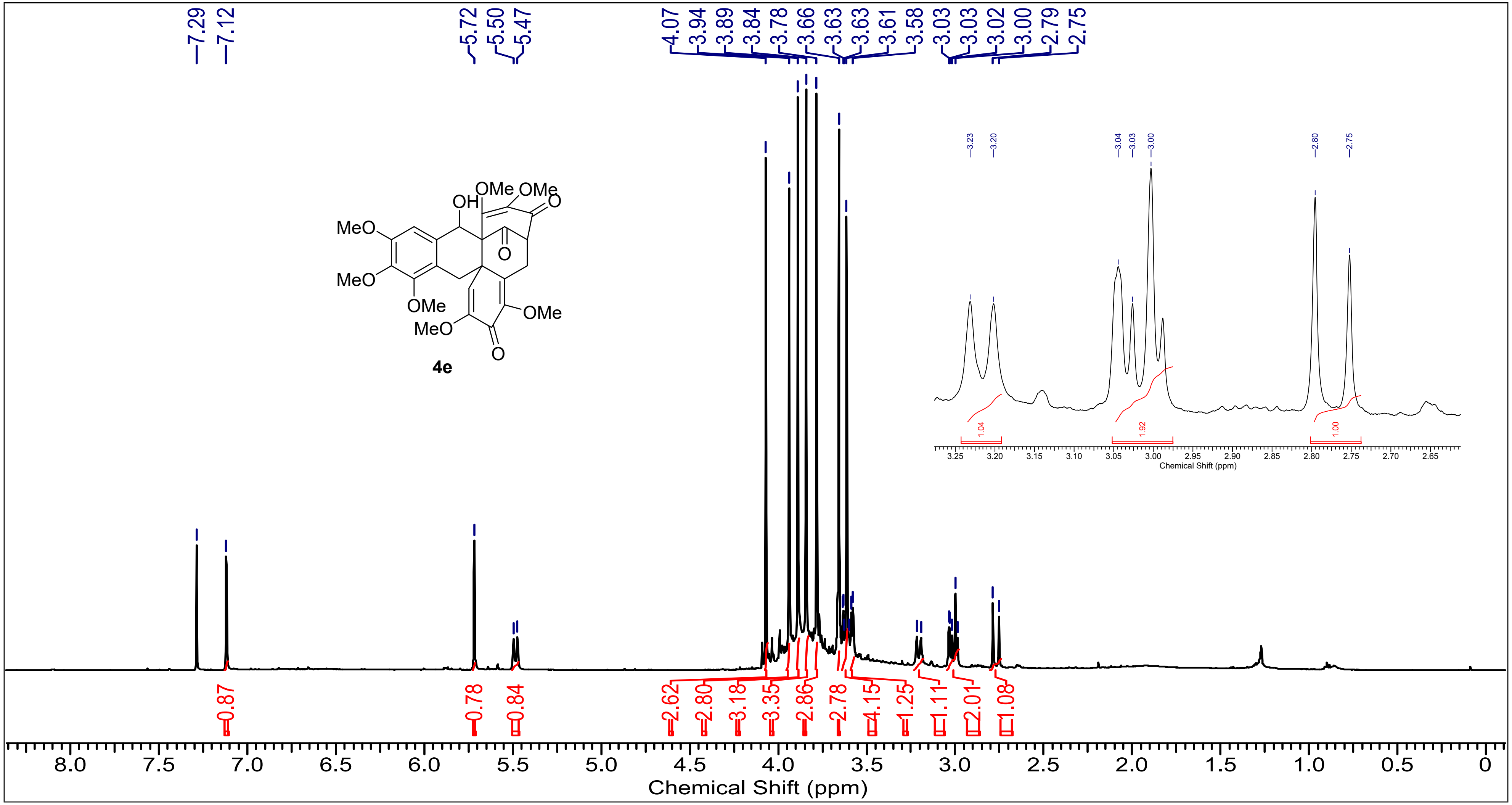
COSY (^1H-^1H) correlation NMR of compound (**4d**) in $CDCl_3$ (400 MHz)



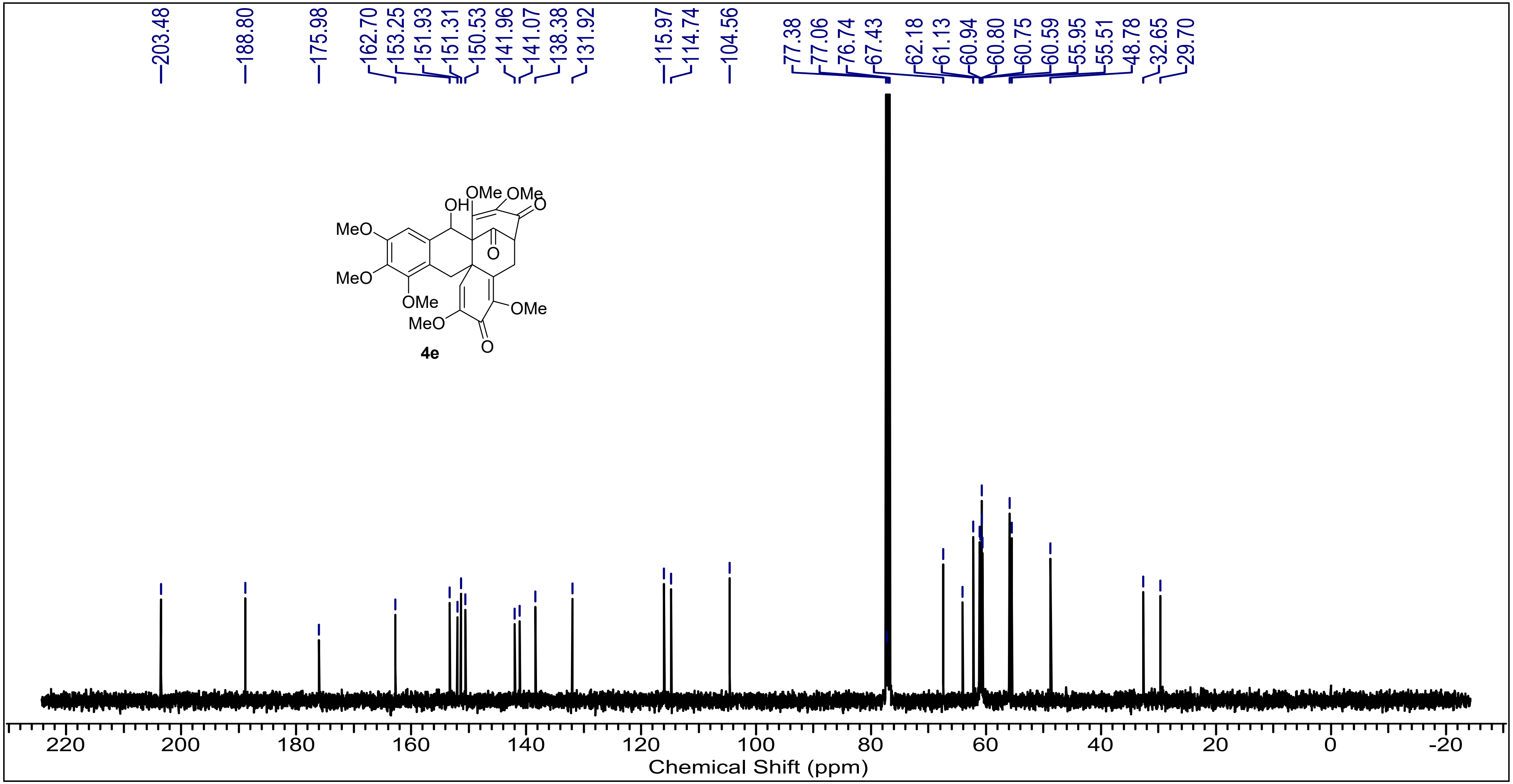
HMBC (^{1}H -^{13}C) correlation NMR of compound (**4d**) in $CDCl_3$ (400 MHz)



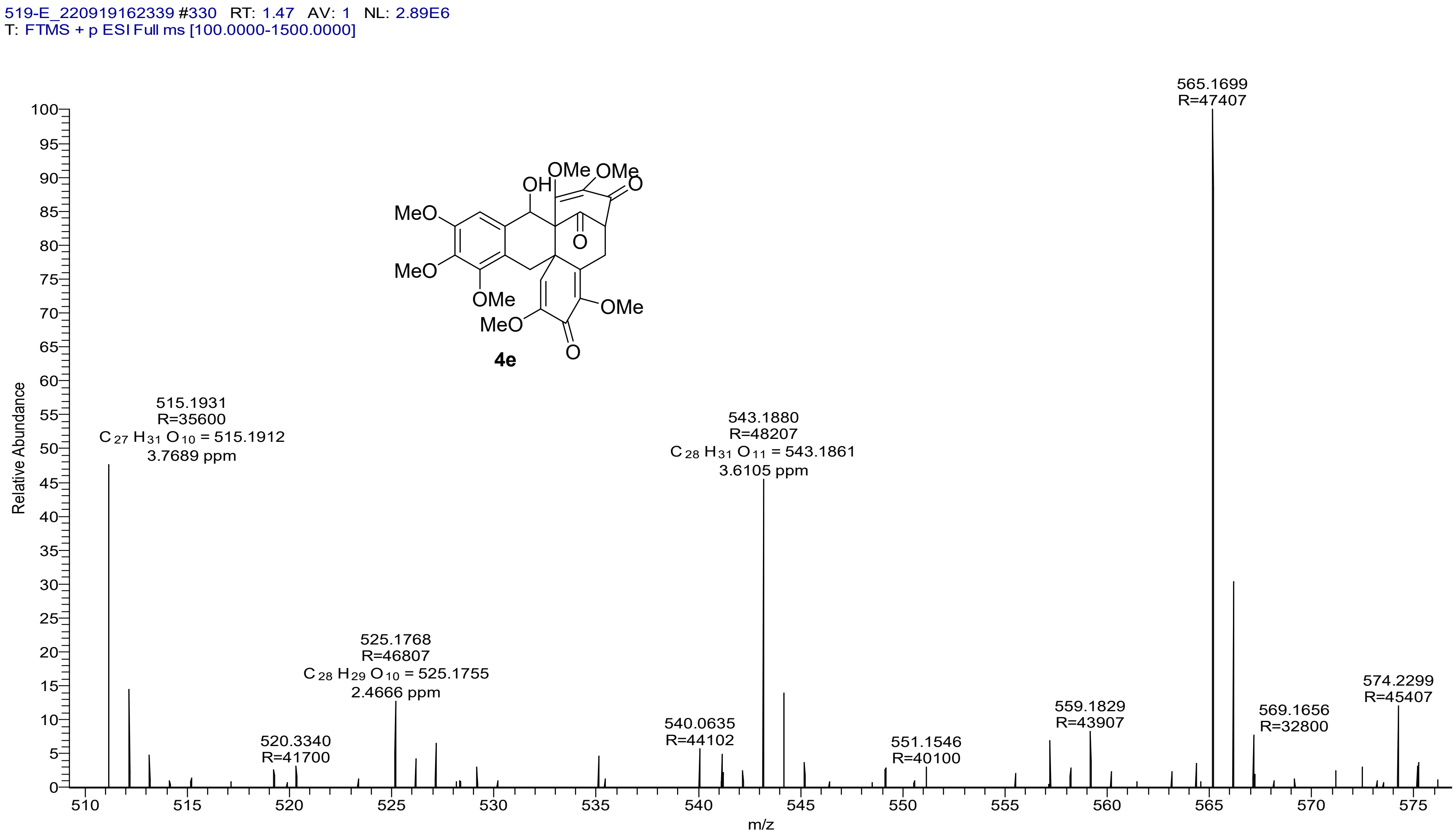
HSQC (^{1}H -^{13}C) correlation NMR of compound (**4d**) in $CDCl_3$ (400 MHz)



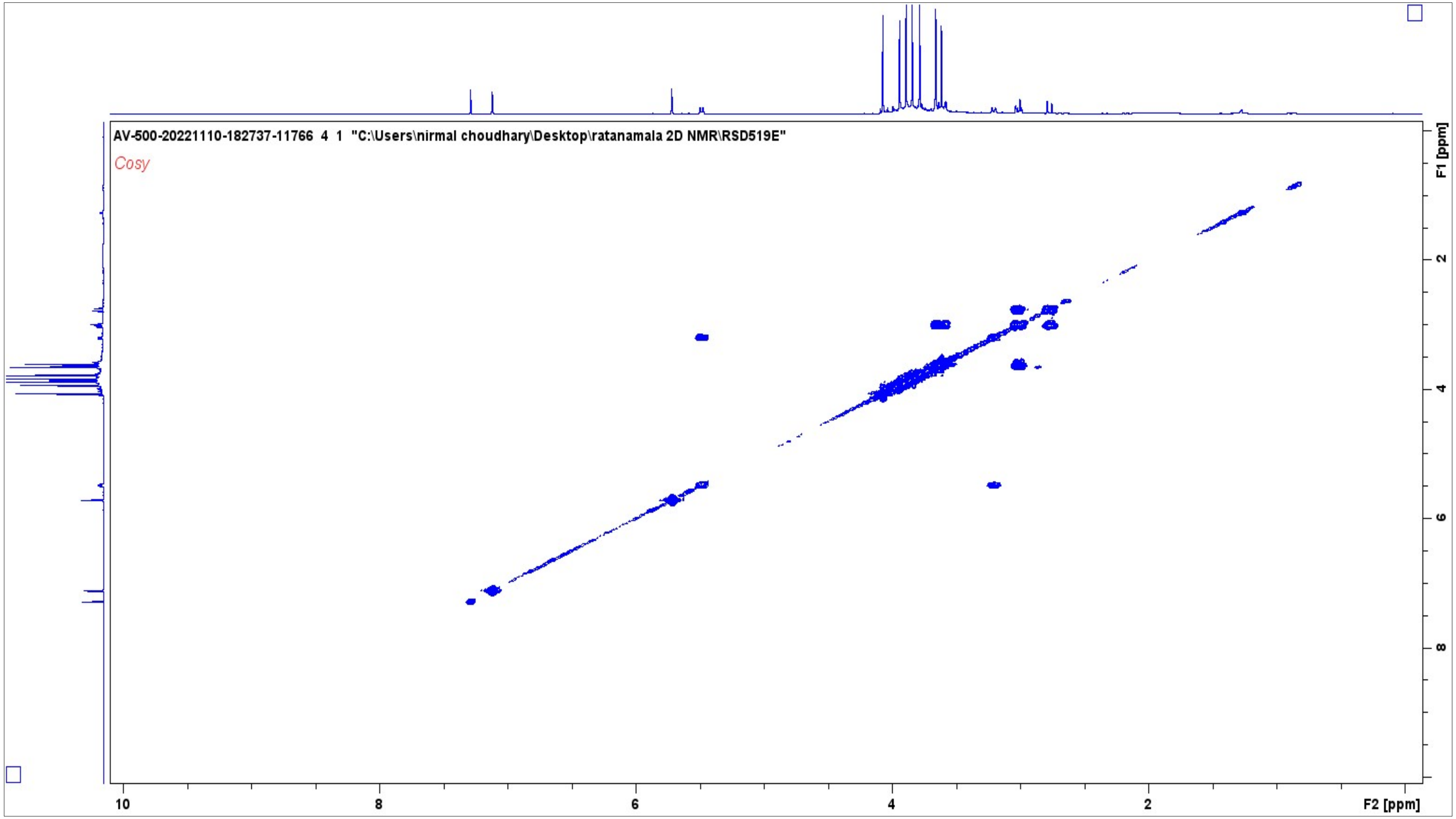
^{1}H NMR of compound (**4e**) in $CDCl_3$ (400 MHz)



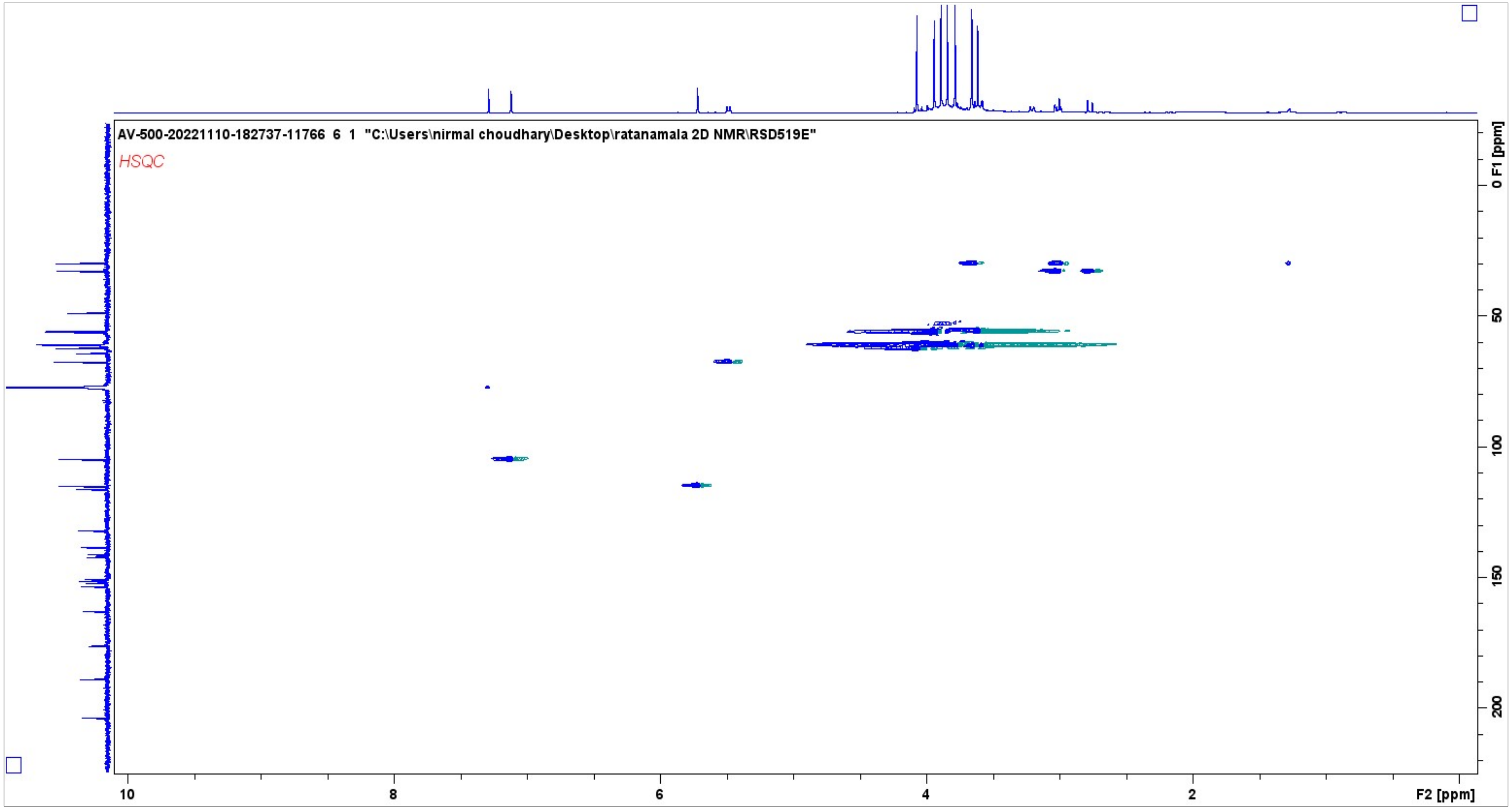
^{13}C NMR of compound (**4e**) in $CDCl_3$ (100 MHz)



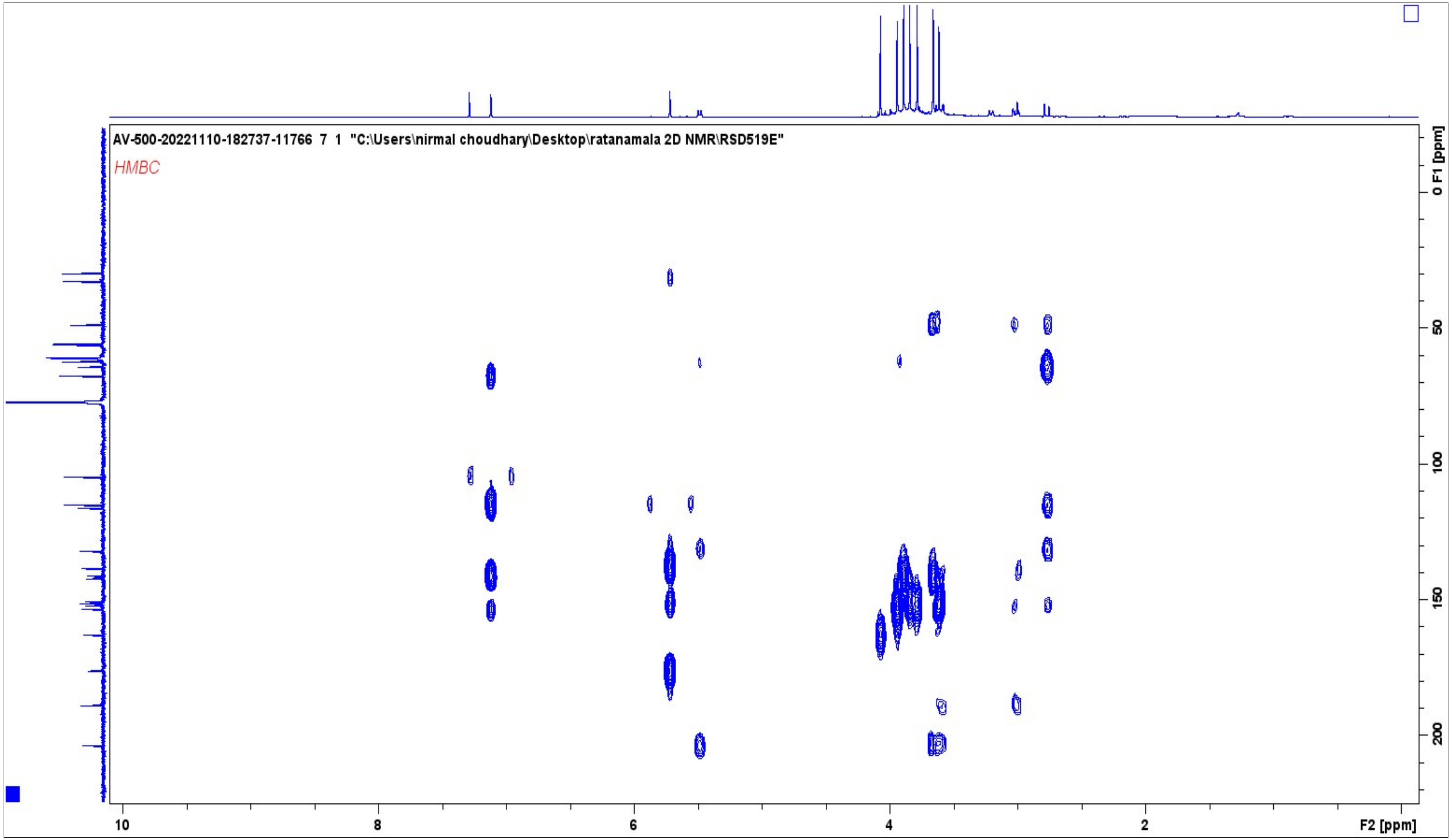
HRMS (ESI) of compound (**4e**)



COSY (^1H-^1H) correlation NMR of compound (**4e**) in $CDCl_3$ (500 MHz)



HSQC (^{1}H -^{13}C) correlation NMR of compound (**4e**) in $CDCl_3$ (500 MHz)



HMBC (^1H -^{13}C) correlation NMR of compound (**4e**) in $CDCl_3$ (500 MHz)

4. SINGLE CRYSTAL X-RAY DIFFRACTION STUDIES

The good quality single crystals of each compound suitable for single-crystal X-ray diffraction analysis were selected using Leica polarizing microscope (S8APO). The X-ray intensity data for all compounds were measured on a Bruker D8 VENTURE Kappa Duo PHOTON II CPAD diffractometer equipped with Incoatech multilayer mirrors optics with X-ray generator power setting at 50 kV and 1.4 mA. The intensity measurements were carried out with Mo micro-focus sealed tube diffraction source (Mo Kα = 0.71073 Å) at 100(2) K temperature. A preliminary set of cell constants and an orientation matrix were calculated from 36 and 40 frames for Mo and Cu radiations, respectively. The complete intensity data were collected using an optimized strategy that consisted of different sets of ω, φ and 2θ with 0.5° width keeping the sample-to-detector distance fixed at 5.00 cm with varying exposure time (10-20 sec) depending on the diffraction power of the crystals. The whole process of X-ray data acquisition (unit–cell measurements and data collection) was controlled and monitored by the APEX3 program suite of Bruker-AXS (Bruker, 2016).[1] The complete data sets were corrected for Lorentz-polarization and absorption effects (multi-scan method) using SAINT and SADABS programs with the transmission coefficients. Using the APEX3 (Bruker, 2016) program suite,[1] the structure was solved using direct methods with the ShelXS-97 (Sheldrick, 2008) structure solution program.[2] The model was refined with ShelXL-2013 (Sheldrick, 2015) using Least Squares minimization based on F^2.[3] All non-hydrogen atoms were refined anisotropically. Conversely, hydrogen atoms were refined isotropically by placing them in a geometrically idealized position (C-H = 0.95 Å for sp2 hybridized C-atoms including H atoms in phenyl and ethyne groups, C-H = 0.98 Å for the methyl H-atoms) and constrained to ride on their parent atoms [Uiso(H) = 1.2 Ueq(C) or 1.5 Ueq(methyl C)]. ORTEPs for all the compounds were plotted at the 50% probability displacement ellipsoids, and H atoms are shown as small spheres of arbitrary radii.[4] The molecular packing diagrams were generated using the Mercury program.[5] Geometrical calculations were performed using SHELXTL (Bruker, 2016)[1] and PLATON.[6] Experiment details of the single crystal X-ray diffraction analysis, including crystal data, data collection and structure refinement for all the compounds, are summarized in Tables.

Compound 4b

A compound **4b** having molecular formula $C_{28}H_{29}BrO_{10}$, approximate dimensions 0.130 mm x 0.160 mm x 0.180 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 0.71073 Å). The total exposure time was 12.43 hours. The frames were integrated with the Bruker SAINT Software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 48761 reflections to a maximum θ angle of 28.74° (0.74 Å resolution), of which 6531 were independent (average redundancy 7.466, completeness = 99.1%, R_{int} = 7.76%, R_{sig} = 4.61%) and 5758 (88.16%) were greater than $2\sigma(F^2)$. The final cell constants of <u>a</u> = 8.6985(11) Å, <u>b</u> = 9.1415(10) Å, <u>c</u> = 32.062(4) Å, β = 94.221(5)°, volume = 2542.6(5) Å^3, are based upon the refinement of the XYZ-centroids of 9469 reflections above 20 σ(I) with 4.643° < 2θ < 52.90°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.800. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.7520 and 0.8110. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/c 1, with Z = 4 for the formula unit, $C_{28}H_{29}BrO_{10}$. The final anisotropic full-matrix least-squares refinement on F^2 with360 variables converged at R1 = 6.57%, for the observed data and wR2 = 14.98% for all data. The goodness-of-fit was 1.130. The largest peak in the final difference electron density synthesis was 2.283 e$^-$/Å^3 and the largest hole was -1.842 e$^-$/Å^3 with an RMS deviation of 0.128 e$^-$/Å^3. On the basis of the final model, the calculated density was 1.582 g/cm^3 and F(000), 1248 e$^-$.

Table 1SI: Sample and crystal data for 4b

Identification code	4b
Chemical formula	$C_{28}H_{29}BrO_{10}$

CCDC	2225873	
Formula weight	604.09 g/mol	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal size	0.130 x 0.160 x 0.180 mm	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 8.6985(11) Å	α = 90°
	b = 9.1415(10) Å	β = 94.221(5)°
	c = 32.062(4) Å	γ = 90°
Volume	2542.6(5) $Å^3$	
Z	4	
Density (calculated)	1.582 g/cm^3	
Absorption coefficient	1.678 mm^{-1}	
F(000)	1248	

Table 2SI : Data collection and structure refinement for 4b

Theta range for data collection	1.91 to 28.74°	
Index ranges	-11<=h<=11, -12<=k<=12, -43<=l<=43	
Reflections collected	48761	
Independent reflections	6531 [R(int) = 0.0776]	
Coverage of independent reflections	99.1%	
Absorption correction	Multi-Scan	
Max. and min. transmission	0.8110 and 0.7520	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	6531 / 0 / 360	
Goodness-of-fit on F^2	1.130	
Δ/σ_{max}	0.001	
Final R indices	5758 data; I>2σ(I)	R1 = 0.0657, wR2 = 0.1458
	all data	R1 = 0.0743, wR2 = 0.1498
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0152P)^2+19.4909P]$ where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	2.283 and -1.842 $eÅ^{-3}$	
R.M.S. deviation from mean	0.128 $eÅ^{-3}$	

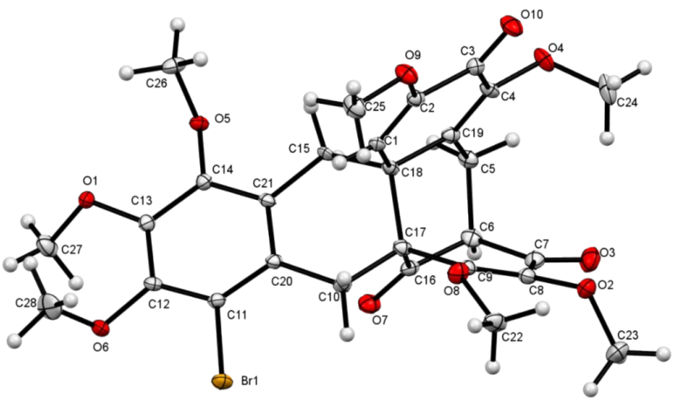


Figure 1SI. ORTEP view of compound **4b** showing the atom-numbering scheme: The displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres with arbitrary radii

Compound 4e

A compound **4e** having molecular formula $C_{28}H_{30}O_{11}$, approximate dimensions 0.100 mm x 0.120 mm x 0.130 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 0.71073 Å). The total exposure time was 12.43 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 150943 reflections to a maximum θ angle of 30.57° (0.70 Å resolution), of which 7679 were independent (average redundancy 19.657, completeness = 99.7%, R_{int} = 5.26%, R_{sig} = 1.98%) and 6998 (91.13%) were greater than 2σ(F^2). The final cell constants of a = 10.229(2) Å, b = 12.381(3) Å, c = 20.060(4) Å, β = 98.934(7)°, volume = 2509.7(9) $Å^3$, are based upon the refinement of the XYZ-centroids of 9469 reflections above 20 σ(I) with 4.643° < 2θ < 52.90°.Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.800. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9860 and 0.9890. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/c 1, with Z = 50 for the formula unit, $C_{28}H_{30}O_{11}$. The final anisotropic full-matrix least-squares refinement on F^2 with 362 variables converged at R1 = 3.61%, for the observed data and wR2 = 10.11% for all data. The goodness-of-fit was 1.044. The largest peak in the final difference electron density synthesis was 0.476 $e^-/Å^3$ and the largest hole was -0.231 $e^-/Å^3$ with an RMS deviation of 0.053 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.436 g/cm^3 and F(000), 1144 e^-.

Table 3SI: Sample and crystal data for **4e**.

Identification code	**4e**	
Chemical formula	$C_{28}H_{30}O_{11}$	
CCDC	2225874	
Formula weight	542.18 g/mol	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal size	0.100 x 0.120 x 0.130 mm	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 10.229(2) Å	α = 90°
	b = 12.381(3) Å	β = 98.934(7)°
	c = 20.060(4) Å	γ = 90°
Volume	2509.7(9) $Å^3$	
Z	50	
Density (calculated)	1.436 g/cm^3	
Absorption coefficient	0.111 mm^{-1}	
F(000)	1144	

Table 4SI: Data collection and structure refinement for **4e**

Theta range for data collection	2.60 to 30.57°
Index ranges	-14<=h<=14, -17<=k<=17, -28<=l<=28
Reflections collected	150943
Independent reflections	7679 [R(int) = 0.0526]
Coverage of independent reflections	99.7%
Absorption correction	Multi-Scan
Max. and min. transmission	0.9890 and 0.9860
Structure solution technique	direct methods
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$

Data / restraints / parameters	7679 / 0 / 362	
Goodness-of-fit on F^2	1.044	
Δ/σ_{max}	0.001	
Final R indices	6998 data; I>2σ(I)	R1 = 0.0361, wR2 = 0.0977
	all data	R1 = 0.0400, wR2 = 0.1011
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0540P)^2+0.9540P]$ where $P=(F_o^2+2F_c^2)/3$	
Extinction coefficient	0.0037(9)	
Largest diff. peak and hole	0.476 and -0.231 eÅ^{-3}	
R.M.S. deviation from mean	0.053 eÅ^{-3}	

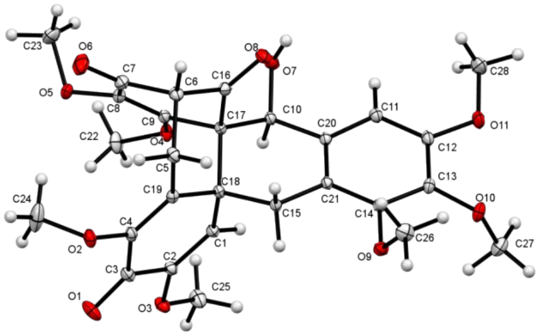


Figure 2SI. ORTEP view of compound 4e showing the atom-numbering scheme: The displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres with arbitrary radii.

Compound 3c

A compound **3c** having molecular formula $C_{10}H_{10}O_4$, approximate dimensions 0.110 mm x 0.120 mm x 0.140 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 0.71073 Å). The total exposure time was 12.43 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 13752 reflections to a maximum θ angle of 31.59° (0.68 Å resolution), of which 1518 were independent (average redundancy 9.059, completeness = 99.9%, R_{int} = 4.32%, R_{sig} = 2.33%) and 1406 (92.62%) were greater than $2\sigma(F^2)$. The final cell constants of a = 6.3968(5) Å, b = 15.9612(14) Å, c = 4.3338(4) Å, β = 100.453(3)°, volume = 435.14(7) Å^3, are based upon the refinement of the XYZ-centroids of 9469 reflections above 20 σ(I) with 4.643° < 2θ < 52.90°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.800. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9840 and 0.9870. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group C 1 m 1, with Z = 4 for the formula unit, $C_{10}H_{10}O_4$. The final anisotropic full-matrix least-squares refinement on F^2 with 65variables converged at R1 = 3.06%, for the observed data and wR2 = 8.58% for all data. The goodness-of-fit was 1.101. The largest peak in the final difference electron density synthesis was 0.400 e$^-$/Å^3 and the largest hole was-0.331 e$^-$/Å^3 with an RMS deviation of 0.048 e$^-$/Å^3. On the basis of the final model, the calculated density was 1.482 g/cm^3 and F(000), 204 e$^-$.

Table 5SI: Sample and crystal data for **3c**

Identification code	**3c**
Chemical formula	$C_{10}H_{10}O_4$
CCDC	2225872
Formula weight	194.06 g/mol
Temperature	100(2) K

Wavelength	0.71073 Å	
Crystal size	0.110 x 0.120 x 0.140 mm	
Crystal system	Monoclinic	
Space group	C 1 m 1	
Unit cell dimensions	a = 6.3968(5) Å	α = 90°
	b = 15.9612(14) Å	β = 100.453(3)°
	c = 4.3338(4) Å	γ = 90°
Volume	435.14(7) $Å^3$	
Z	4	
Density (calculated)	1.482 g/cm^3	
Absorption coefficient	0.115 mm^{-1}	
F(000)	204	

Table 6SI: Data collection and structure refinement for **3c**

Theta range for data collection	2.55 to 31.59°	
Index ranges	-9<=h<=9, -23<=k<=23, -6<=l<=6	
Reflections collected	13752	
Independent reflections	1518 [R(int) = 0.0432]	
Coverage of independent reflections	99.9%	
Absorption correction	Multi-Scan	
Max. and min. transmission	0.9870 and 0.9840	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)	
Function minimized	Σ w(F_o^2 - F_c^2)^2	
Data / restraints / parameters	1518 / 2 / 65	
Goodness-of-fit on F^2	1.101	
Final R indices	1406 data; I>2σ(I)	R1 = 0.0306, wR2 = 0.0820
	all data	R1 = 0.0350, wR2 = 0.0858
Weighting scheme	w=1/[σ^2(F_o^2)+(0.0493P)^2+0.0820P] where P=(F_o^2+2F_c^2)/3	
Absolute structure parameter	0.4(3)	
Largest diff. peak and hole	0.400 and -0.331 $eÅ^{-3}$	
R.M.S. deviation from mean	0.048 $eÅ^{-3}$	

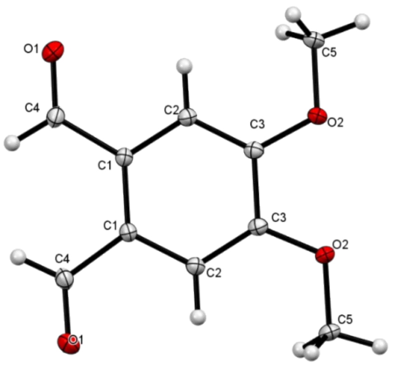


Figure 3SI: ORTEP view of compound **3c** showing the atom-numbering scheme. The displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres with arbitrary radii.

Compound 4d

A compound **4d** having molecular formula $C_{28}H_{30}O_{10}$, approximate dimensions 0.120 mm x 0.140 mm x 0.170 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 0.71073 Å). The total exposure time was 12.43 hours. The frames were integrated with the Bruker SAINT Software package using a narrow-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 104204 reflections to a maximum θ angle of 26.49° (0.80 Å resolution), of which 10062 were independent (average redundancy 10.356, completeness = 99.0%, R_{int} = 6.99%, R_{sig} = 3.42%) and 8643 (85.90%) were greater than 2σ (F^2). The final cell constants of a = 12.153(2) Å, b = 12.656(2) Å, c = 16.822(3) Å, α = 103.366(6)°, β = 102.402(6)°, γ = 90.075(6)°, volume = 2455.0(8) $Å^3$, are based upon the refinement of the XYZ-centroids of 9469 reflections above 20 σ(I) with 4.643° < 2θ < 52.90°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.800. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9820 and 0.9870. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P -1, with Z = 2 for the formula unit, $C_{28}H_{30}O_{10}$. The final anisotropic full-matrix least-squares refinement on F^2 with 701variables converged at R1 = 9.74%, for the observed data and wR2 = 25.79% for all data. The goodness-of-fit was 1.061. The largest peak in the final difference electron density synthesis was 1.285 $e^-/Å^3$ and the largest hole was-0.378 $e^-/Å^3$ with an RMS deviation of 0.121 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.425 g/cm^3 and F(000), 1112 e^-.

Table 7SI. Sample and crystal data for **4d**

Identification code	**4d**	
Chemical formula	$C_{28}H_{30}O_{10}$	
CCDC	2225875	
Formula weight	526.18 g/mol	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal size	0.120 x 0.140 x 0.170 mm	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 12.153(2) Å	α = 103.366(6)°
	b = 12.656(2) Å	β = 102.402(6)°
	c = 16.822(3) Å	γ = 90.075(6)°
Volume	2455.0(8) $Å^3$	
Z	2	
Density (calculated)	1.425 g/cm^3	
Absorption coefficient	0.108 mm^{-1}	
F(000)	1112	

Table 8SI: Data collection and structure refinement for **4d**.

Theta range for data collection	2.32 to 26.49°	
Index ranges	-15<=h<=15, -15<=k<=15, -21<=l<=21	
Reflections collected	104204	
Independent reflections	10062 [R(int) = 0.0699]	
Coverage of independent reflections	99.0%	
Absorption correction	Multi-Scan	
Max. and min. transmission	0.9870 and 0.9820	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)	
Function minimized	Σ w$(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	10062 / 0 / 701	
Goodness-of-fit on F^2	1.061	
Final R indices	8643 data; I>2σ(I)	R1 = 0.0974, wR2 = 0.2482

	all data	R1 = 0.1088, wR2 = 0.2579
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.1132P)^2+11.7285P]$ where $P=(F_o^2+2F_c^2)/3$	
Absolute structure parameter	0.0(3)	
Extinction coefficient	0.0190(20)	
Largest diff. peak and hole	1.285 and -0.378 eÅ^{-3}	
R.M.S. deviation from mean	0.121 eÅ^{-3}	

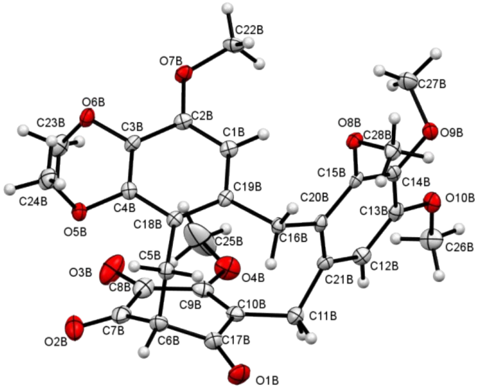


Figure 4SI. ORTEP view of compound **4d** showing the atom-numbering scheme: The displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres with arbitrary radii.

5. Biological Activity Data:

Cancer treatment requires a new class of drug compounds to overcome drug resistance. A series of NCLBSK-22 to 30 compounds were synthesized and investigated against various cancer cell lines named as Colon (SW-620 and HCT-116), Breast (MDA-MB-231), Lung (A549), and Prostate (PC-3) using Sulforhodamine (SRB) assay. Among all the compounds in the series, compound 23 showed good cytotoxicity on all cancer cell lines tested. Further, the mechanistic study may elucidate the mechanism behind the cytotoxic effect of these compounds.

Determination of cytotoxicity

Cell culture and chemicals

Human cancer cell lines: Colon (SW-620 and HCT-116), Breast (MDA-MB-231), Lung (A549), and Prostate (PC-3) were obtained from NCCS, Pune. Cells were cultured in RPMI/DMEM medium, which consists of 10% FBS and supplemented with Penicillin (100U/ml) and Streptomycin (100µg/ml) for the growth of the cells and control of bacterial growth. All cell lines were then maintained in a CO_2 incubator at 37ºC with 95% humidity and 5% CO_2.

Sulforhodamine B assay

Sulforhodamine B dye is a pH-dependent staining of proteins assay performed on the treated plates to evaluate the anticancer potential of the novel compounds. The cells were grown in a 75 cm^2 flask and were allowed to grow till 90-95% confluency and were trypsinized using 0.5% trypsin. Then, the cells were seeded in 96-well plates at the required density based on the cell lines (SW-620- 8000/well and HCT-116- 8000/well, MDA-MB-231- 8000/well, A549-9000/well, and PC-3- 8000/well), and their colony morphology was observed under a bright field microscope. After 24 hours of CO_2 incubation, cells were treated with the compounds (NCLBSK-22 to 30) dissolved in DMSO along with camptothecin at the concentrations of 1µM, 5µM, 10µM and 50µM in triplets. Camptothecin was used as the positive control. The plates were then incubated for 48 hours.

After completion of 48 hours, the cells were fixed using 50% (w/v) ice-cold TCA (Trichloro acetic acid) (100µl/well) and kept for 1 hour at 4ºC. Plates were then washed with water thrice and kept overnight for air drying. Then plates were stained with 100µl/well of SRB dye (0.4% w/v in 1% acetic acid) at room temperature for 1 hour, and plates were washed with 1% (v/v) glacial acetic acid twice or thrice to remove the unbound SRB dye and were kept overnight for air drying. Furthermore, 100µl of 10mM Tris base solution of pH 10.5 was added to each well of the plate to solubilize the protein-bound SRB, plates were then subjected to a shaker for 10 min, and the optical density was measured at 540 nm using a multimode plate reader. The cell growth inhibition (%) and IC_{50} were calculated with reference to untreated control cells.

Statistics

Each compound's median inhibition concentration (IC_{50}) was calculated using non-linear regression analysis in GraphPad PRISM™ 8 software.

Cell growth inhibition using SRB assay The compounds NCLBSK-22 to 30 (3d ,3a, 3g, 3h, 4a, 4b, 4c, 4d and 4e) inhibited cancer cell growth at various concentrations. The broad spectrum of lethality was observed on all compounds against all cancer cell lines. Among 9 compounds, compound 23 (3a) exhibited the maximum cytotoxic effect on all cell lines at ~18 to 49 µM after 48 hours of the treatment (**Fig.5SI**). At 50 µM, compound 23 (3a) showed moderate growth inhibition activity against all cancer cell lines and the most growth-inhibitory effect was observed on colon cancer cell lines, SW-620 (96.25%)and HCT116 (91.30 %). Compound 23 (3a) exhibited cancer cell growth on A549 cell lines at 18.07 µM (**Fig.5SI**).

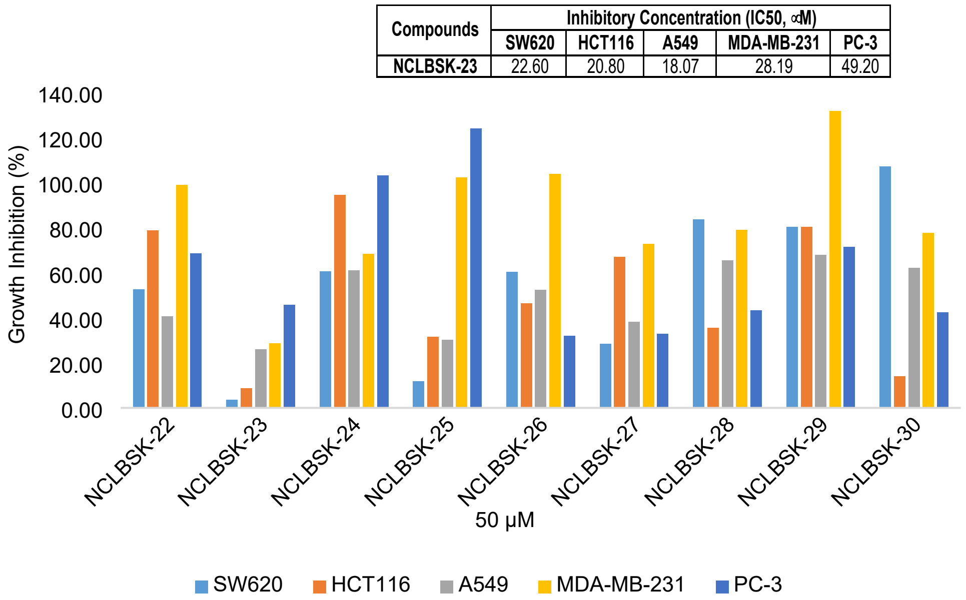


Fig. 5SI. Growth inhibition screening of the cancer cells treated with NCLBSK-22 to 30 (50 µM) for 48 h using SRB. Table inside the graph - IC_{50} values of NCLBSK-23(**3a**) against various cancer cell lines.

Molecular Docking Studies

Table 9SI. Docking affinity of given compounds with respective proteins.

Sr. No	Compound name	BAX (4S0O)	Bcl 2 (1G5M)	Caspase 3 (5I9B)	Caspase 9 (2AR9)
1	Comp **4b**	13.2	-4.8	-7.1	-5.8
2	Comp **3a**	1.5	-7.2	-6.0	-5.8

Table 10SI. Interacting atoms of respective proteins with given compounds.

S. No	Compound name	Best interaction	Binding affinity	Interacting Amino acids	Bonds and interactions
1	Comp **4b**	Caspase-3	-7.1	HIS 121, GLY 122, THR 62, ARGG 207, SER 205, GLU 123	One pi-alkyl bond, three H-bonds, And four C-H bonds.
2	Comp **3a**	Bcl-2	-7.2	HIS 3, ASN 11, TYR 9, TRP 195, ILE 189, GLY 194	Two pi-alkyl bonds and three H-bonds.

6. Computational Details:

The calculations for geometry optimizations and transition states were performed using density functional theory (DFT) with the Turbomole 7.0 software package[7]. The def2-TZVPD basis set[8] was used for Ni and Br atoms, while the rest of the atoms utilized the def2-SVP basis set[8]. The B3LYP[9] hybrid density functional was employed throughout the calculations. To account for long-range interactions, Grimme's dispersion corrections (D3)[10] was applied in all the calculations. For an accurate and efficient treatment of the electronic Coulomb term in the DFT calculations, the resolution of identity (RI)[11] along with the multipole accelerated resolution of identity (marij)[12] approximations were employed. Frequency calculations were conducted for all the stationary points to confirm their classification as local minima or transition state structures at room temperature 298.15K. In addition, intrinsic reaction coordinate (IRC)[13] calculations were performed to verify that the obtained transition states connect with the correct reactants and products. Solvent corrections were included using the COSMO[14] dielectric continuum solvent model, with a dielectric constant (ε) of 6.15.[15]

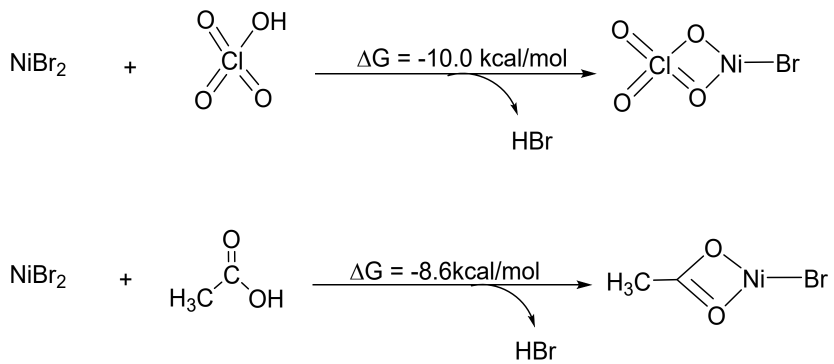


Figure 6SI. The Gibbs free energy for the formation of active complexes **NiBr(OCOCH$_3$)** and **NiBr(ClO$_4$)**, at B3LYP-D3/ def2-TZVPD for Fe and Br and def2-SVP for rest atoms, level of theory has been shown here. All values are in kcal/mol.

XYZ Coordinate

CTV(1a)

Energy = -1496.317094 Hartree

C	-1.3362777	2.1016824	0.1339118
C	-1.5575554	0.9103265	0.8386713
C	0.0004545	2.8271389	0.0018171
C	1.3367954	2.1011818	-0.1319980
C	1.5571956	0.9101069	-0.8375043
C	0.4563182	0.0659765	-1.4592892
C	0.1960184	-1.2142020	-0.6759462
C	-0.1971220	-1.2143952	0.6768791
C	-0.4572890	0.0655613	1.4606155
C	-2.8697573	0.3943418	0.9208594
C	-3.9623047	1.0321318	0.3417942
C	-3.7441734	2.2430831	-0.3688321
C	-2.4483320	2.7456728	-0.4587639
C	2.4495848	2.7445228	0.4601331
C	3.7451926	2.2415724	0.3690232
C	3.9623358	1.0307962	-0.3422665
C	2.8691594	0.3936724	-0.9208663
C	0.3868609	-2.4487272	-1.3272830
C	0.1960135	-3.6719089	-0.6808886
C	-0.1973343	-3.6721207	0.6810212
C	-0.3880511	-2.4491208	1.3278200
O	-0.3618260	-4.8929329	1.2556946
C	-0.7415576	-4.9620363	2.6168920
O	0.3603871	-4.8925405	-1.2559558
C	0.7404906	-4.9611986	-2.6170779
O	-5.2462627	0.5912296	0.3916721
C	-5.5224818	-0.6233159	1.0635894
O	-4.8458437	2.8177963	-0.9175046
C	-4.6986888	4.0238195	-1.6430212
O	4.8474651	2.8156001	0.9171142
C	4.7013173	4.0215609	1.6429765
O	5.2460803	0.5893780	-0.3931650
C	5.5213405	-0.6249828	-1.0658164
H	-3.0139774	-0.5474074	1.4521207
H	-2.2747106	3.6711969	-1.0089754
H	2.2766963	3.6698479	1.0109576
H	3.0126629	-0.5478715	-1.4526329
H	0.6945878	-2.4387647	-2.3734010
H	-0.6957441	-2.4395128	2.3739577
H	-1.7259953	-4.4913703	2.7935099
H	-0.8054731	-6.0291995	2.8699159
H	0.0041080	-4.4809132	3.2759252
H	1.7249871	-4.4905141	-2.7932566
H	0.8044765	-6.0282902	-2.8703775
H	-0.0049737	-4.4798740	-3.2761845
H	-4.9897761	-1.4755749	0.6036623
H	-5.2507989	-0.5706155	2.1336992
H	-6.6050130	-0.7894216	0.9773644
H	-4.2944926	4.8356059	-1.0110129
H	-4.0393219	3.8964004	-2.5209723
H	-5.7030445	4.3055178	-1.9876017
H	5.7060613	4.3028348	1.9868398
H	4.2969518	4.8335770	1.0113865
H	4.0425734	3.8942607	2.5214066
H	5.2489779	-0.5716784	-2.1357090
H	6.6038696	-0.7915215	-0.9803887
H	4.9886493	-1.4772643	-0.6059176
H	-0.4697767	0.6465996	-1.5605248
H	0.7582282	-0.2090239	-2.4822594
H	-0.0880574	3.5053820	-0.8655469
H	0.0893744	3.5032345	0.8708154
H	0.4690159	0.6457763	1.5624314
H	-0.7596912	-0.2097355	2.4833592

NiBr(OCOCH$_3$)

Energy = -4310.588343 Hartree

Ni	0.2537377	0.8979758	0.0632768
Br	2.3656696	1.3376242	0.6807647
C	-1.5630216	-0.4435505	0.0123731
O	-0.4661575	-0.7341780	0.6099436
O	-1.5376339	0.6986297	-0.5563845
C	-2.7362303	-1.3502436	-0.0155643
H	-3.6050858	-0.8209736	0.4056204
H	-2.9675698	-1.5938668	-1.0645048
H	-2.5325219	-2.2663255	0.5525844

NiBr(ClO$_4$)

Energy = -4842.522859 Hartree

Ni	0.3127433	0.2010946	0.0019131
Br	-1.3596538	-1.2565296	-0.0016710
O	-0.2585488	1.9829373	0.0006531
Cl	1.2213209	2.5989748	0.0028079
O	1.4724554	3.3337804	1.2240384
O	1.4766085	3.3325457	-1.2183600
O	1.9527038	1.1995797	0.0046411

Int1'

Energy = -5806.889905 Hartree

C	-1.6472735	0.2935143	2.2263173
C	-0.9260525	1.5006488	2.1437381
C	-1.0007910	-1.0498384	2.5329615
C	-0.9526047	-1.9850855	1.3242000
C	-0.3650085	-1.6102792	0.0939743
C	0.2132249	-0.2293604	0.0403930
C	1.4982443	-0.0138662	0.6957132
C	1.6517518	0.9086780	1.7586126
C	0.5384304	1.6292844	2.5293266
C	-1.5789805	2.6468461	1.6496269
C	-2.9103439	2.6223234	1.2379032
C	-3.6466886	1.4152885	1.3587650
C	-3.0006945	0.2778961	1.8406802
C	-1.4781494	-3.2853088	1.4439629
C	-1.4300537	-4.2078230	0.3960987
C	-0.8326405	-3.8238121	-0.8328842
C	-0.3117894	-2.5361723	-0.9589104
C	2.6118476	-0.7865069	0.2704530
C	3.8796836	-0.5851758	0.7765025
C	4.0557297	0.3990880	1.8017971
C	2.9440823	1.0909991	2.2851813
O	5.3127262	0.5576191	2.2441637
C	5.5876181	1.5260319	3.2483961
O	4.9989971	-1.2295686	0.3795994
C	4.8929361	-2.1895556	-0.6597882
O	-3.5692204	3.6675488	0.6784869
C	-2.8167093	4.7989076	0.2618501
O	-4.9365765	1.4604219	0.9394094
C	-5.6810390	0.2560173	0.8889229
O	-1.9203576	-5.4711310	0.4490344
C	-2.5492388	-5.9141062	1.6380331
O	-0.8243115	-4.7603264	-1.8138794
C	-0.2457661	-4.4315095	-3.0644605
H	-1.0042732	3.5664048	1.5432023
H	-3.5356715	-0.6711880	1.8829934
H	-1.9318140	-3.5731233	2.3928560
H	0.1232478	-2.2120480	-1.9027837
H	2.4483057	-1.5033297	-0.5320375
H	3.0701305	1.7848382	3.1169483
H	5.3022518	2.5392103	2.9170121
H	5.0618828	1.2888446	4.1895606
H	6.6709989	1.4910111	3.4207393
H	5.9049819	-2.5807426	-0.8271065
H	4.2255865	-3.0223557	-0.3747984
H	4.5208722	-1.7327091	-1.5940639
H	-3.5221722	5.4672065	-0.2500970
H	-2.3765847	5.3352038	1.1210472
H	-2.0167685	4.4993869	-0.4366172
H	-5.2048045	-0.4868789	0.2234235
H	-5.8054316	-0.1902459	1.8914751
H	-6.6695317	0.5171296	0.4877901
H	-3.4344455	-5.3004063	1.8849729
H	-2.8705166	-6.9481980	1.4539944
H	-1.8550338	-5.9005161	2.4976893

H	-0.7684861	-3.5862727	-3.5473260
H	0.8252454	-4.1774692	-2.9648388
H	-0.3440727	-5.3230804	-3.6980850
H	-0.5251156	0.5246187	0.3043964
H	0.0187228	-0.9085901	2.9236703
H	-1.5656717	-1.5516218	3.3337894
H	0.7931837	2.7013788	2.5413511
H	0.6488805	1.3042101	3.5797434
Ni	0.2382835	0.6939428	-1.8095596
H	0.9522208	-0.4716856	-2.1779571
Br	2.2352011	1.7878890	-2.1528607
C	-2.0388148	1.3083265	-1.9360630
O	-1.5667846	0.1185908	-2.0889689
O	-1.2167742	2.2112577	-1.6229383
C	-3.4956810	1.5774516	-2.1488212
H	-3.6081066	2.1870360	-3.0597054
H	-4.0557187	0.6406082	-2.2628148
H	-3.8913583	2.1581875	-1.3039023

Int1

Energy = -5806.957432 Hartree

C	1.8649939	-1.7587159	0.7341151
C	1.8249158	-1.2313234	-0.5680602
C	1.1705972	-1.0766145	1.9011829
C	-0.3459424	-1.0226975	1.7922354
C	-1.0898247	0.1927375	1.6896276
C	-0.6531663	1.5166197	1.2487488
C	0.7189362	1.9228294	0.8430629
C	1.5119132	1.2634404	-0.1158174
C	1.0642069	0.0394548	-0.8951183
C	2.4953428	-1.9133728	-1.6015003
C	3.1899543	-3.1040483	-1.3755288
C	3.2198764	-3.6431039	-0.0637222
C	2.5610279	-2.9615158	0.9624447
C	-1.0492581	-2.2230237	1.8710619
C	-2.4553408	-2.3032849	1.8587795
C	-3.2084548	-1.1159036	1.8567070
C	-2.5291520	0.1182096	1.7854043
C	1.2401909	3.0876729	1.4595563
C	2.5135644	3.5753880	1.1797685
C	3.3213974	2.8853738	0.2349802
C	2.8020677	1.7536101	-0.3914574
O	4.5533162	3.4056159	0.0110242
C	5.4076072	2.7627978	-0.9179382
O	3.0707272	4.6773373	1.7447963
C	2.3129328	5.4235250	2.6791489
O	3.8559706	-3.8099760	-2.3259348
C	3.8628589	-3.3271266	-3.6565737
O	3.9060803	-4.8061222	0.0877515
C	3.9589982	-5.4070463	1.3677713
O	-3.1576123	-3.4604852	1.8833626
C	-2.4615376	-4.6957609	1.8929637
O	-4.5521177	-1.2368810	1.8883640
C	-5.3482905	-0.0750185	1.7032837
H	2.4627899	-1.4911300	-2.6064720
H	2.5838905	-3.3637689	1.9759342
H	-0.4688145	-3.1445484	1.9365060
H	-3.0882803	1.0349065	1.9937953
H	0.6172406	3.6067859	2.1879402
H	3.4039903	1.2195631	-1.1274665
H	6.3410717	3.3414518	-0.9357972
H	5.6327262	1.7241497	-0.6145715
H	4.9716798	2.7506953	-1.9333577
H	2.9457622	6.2643735	2.9943282
H	1.3844751	5.8199355	2.2294118
H	2.0482833	4.8205898	3.5669112
H	4.3332709	-2.3295495	-3.7281443
H	4.4521455	-4.0428765	-4.2458278
H	2.8422179	-3.2696716	-4.0771731
H	4.4522900	-4.7521731	2.1090473
H	2.9512140	-5.6682685	1.7396537
H	4.5482245	-6.3275595	1.2570093

H	-3.2277105	-5.4826071	1.8843338
H	-1.8191291	-4.8090821	1.0015667
H	-1.8415872	-4.8084293	2.8001514
H	-5.2498493	0.6255735	2.5509213
H	-5.0797166	0.4443509	0.7673004
H	-6.3895273	-0.4188232	1.6463887
H	-1.1794407	2.3359698	1.7599999
H	1.4157130	-1.6306572	2.8213561
H	1.5700688	-0.0645615	2.0413267
H	1.1705610	0.2553622	-1.9696826
H	-0.0135851	-0.1327543	-0.7458560
Ni	-1.9602364	0.8963465	-0.0894004
Br	-1.6196157	2.5594658	-1.7415913
C	-3.7582846	-0.3854710	-2.1666882
O	-3.2692188	-0.2895537	-1.0375696
O	-3.5420308	0.4827301	-3.1267527
H	-2.9310020	1.2081302	-2.8026832
C	-4.6371789	-1.5376812	-2.5474983
H	-4.0579796	-2.2183763	-3.1934277
H	-4.9589346	-2.0755275	-1.6475571
H	-5.5012951	-1.1832772	-3.1276042

Int2'

Energy = -6338.842718 Hartree

C	-1.2129226	-0.9693122	-2.3526814
C	0.1165294	-1.4375549	-2.3330114
C	-1.5954990	0.4363633	-2.7759655
C	-1.3844476	1.6184033	-1.8199575
C	-0.4631961	1.6747953	-0.7391208
C	0.1792869	0.4784942	-0.2276699
C	1.6603823	0.3557030	-0.2738768
C	2.1896002	-0.1890552	-1.4667736
C	1.3159103	-0.5634367	-2.6665622
C	0.3818852	-2.7117077	-1.7940343
C	-0.6235831	-3.5086268	-1.2496309
C	-1.9647024	-3.0369713	-1.2719036
C	-2.2331593	-1.7926776	-1.8383454
C	-2.0218333	2.8124463	-2.1932208
C	-1.7809430	4.0276503	-1.5473326
C	-0.7975977	4.0914834	-0.5069806
C	-0.1470952	2.9288939	-0.1463372
C	2.5279301	0.8014635	0.7364851
C	3.9111676	0.6936451	0.6127591
C	4.4542052	0.1269705	-0.5728653
C	3.5882285	-0.2936903	-1.5846399
O	5.8039889	0.0382549	-0.6197696
C	6.4160083	-0.5560727	-1.7515563
O	4.8047772	1.0734521	1.5570445
C	4.3218687	1.6235852	2.7707157
O	-0.4260893	-4.7081140	-0.6541466
C	0.9022939	-5.1686976	-0.4685561
O	-2.8886780	-3.8410424	-0.6978801
C	-4.2348355	-3.3968404	-0.6275978
O	-2.3873338	5.1846997	-1.8399767
C	-3.3997612	5.2192854	-2.8398196
O	-0.6034087	5.3069098	0.0450877
C	0.3407734	5.4303779	1.0972527
H	1.4193091	-3.0435162	-1.7470402
H	-3.2490897	-1.4015282	-1.8178108
H	-2.7161551	2.7859197	-3.0333449
H	0.5832602	2.9376399	0.6605734
H	2.0931518	1.1888957	1.6560060
H	3.9989383	-0.7125473	-2.5036707
H	6.0895337	-1.6028328	-1.8876489
H	6.2005071	0.0097841	-2.6757960
H	7.4981029	-0.5387159	-1.5650184
H	3.7537169	2.5557251	2.5974797
H	3.6796858	0.9089753	3.3160166
H	5.2046803	1.8520485	3.3823434
H	1.4153512	-5.3351000	-1.4327520
H	1.4926458	-4.4583917	0.1374836
H	0.8280656	-6.1245400	0.0670623

H	-4.7931854	-4.1829285	-0.1021342
H	-4.3165932	-2.4538523	-0.0628657
H	-4.6686867	-3.2577434	-1.6343204
H	-2.9950139	4.9437689	-3.8286332
H	-4.2350051	4.5449272	-2.5855057
H	-3.7628304	6.2542862	-2.8718553
H	0.0611327	4.8057899	1.9646166
H	1.3564855	5.1524437	0.7633770
H	0.3365617	6.4862107	1.3974298
H	-0.3065040	-0.4408668	-0.5408841
H	-1.0604276	0.7039727	-3.7043047
H	-2.6606268	0.4332877	-3.0531801
H	1.9505972	-1.0827332	-3.4021385
H	0.9865447	0.3667720	-3.1557274
Ni	-0.8311239	0.0583765	1.5774802
H	0.1595354	0.9147511	2.1060650
Br	0.4443706	-1.6829198	2.2552758
O	-2.3199517	1.3922417	1.4937088
O	-2.6752017	-0.9472439	1.1917040
Cl	-3.4554378	0.3750792	1.1384988
O	-4.5055864	0.4178874	2.1526314
O	-3.9631007	0.6317459	-0.2113450

Int2

Energy = -6338.887543Hartree

C	1.8940897	-1.7700103	0.7573753
C	1.8550564	-1.2509148	-0.5479617
C	1.1908004	-1.0871084	1.9185848
C	-0.3244171	-1.0512938	1.7981564
C	-1.0801659	0.1550241	1.6837808
C	-0.6475979	1.4833141	1.2503400
C	0.7162629	1.9047611	0.8414723
C	1.5207081	1.2472524	-0.1102364
C	1.0917910	0.0150376	-0.8871040
C	2.5244271	-1.9405953	-1.5772509
C	3.2181431	-3.1300459	-1.3434748
C	3.2494517	-3.6592743	-0.0270215
C	2.5905291	-2.9708841	0.9943002
C	-1.0158951	-2.2586968	1.8691668
C	-2.4206642	-2.3523326	1.8412958
C	-3.1886435	-1.1706285	1.8301500
C	-2.5222513	0.0695859	1.7588574
C	1.2141271	3.0873357	1.4449823
C	2.4799560	3.5916456	1.1639361
C	3.3018248	2.9024622	0.2291683
C	2.8026361	1.7561187	-0.3877055
O	4.5236784	3.4391319	0.0029213
C	5.3907603	2.8041564	-0.9211780
O	3.0175974	4.7084686	1.7150896
C	2.2451542	5.4575437	2.6360136
O	3.8812954	-3.8434370	-2.2891579
C	3.8768946	-3.3781502	-3.6265876
O	3.9355266	-4.8202731	0.1329344
C	3.9903972	-5.4117048	1.4177077
O	-3.1105553	-3.5118760	1.8645219
C	-2.4066479	-4.7448420	1.8927990
O	-4.5291467	-1.3111704	1.8590515
C	-5.3481015	-0.1523108	1.7695904
H	2.4905141	-1.5261061	-2.5853650
H	2.6131084	-3.3663083	2.0104400
H	-0.4277391	-3.1744194	1.9430784
H	-3.0924404	0.9820558	1.9542269
H	0.5797335	3.6053074	2.1641454
H	3.4145221	1.2264888	-1.1185245
H	6.3130543	3.3998944	-0.9425003
H	5.6340128	1.7725585	-0.6089123
H	4.9551223	2.7771394	-1.9361728
H	2.8640527	6.3129659	2.9389725
H	1.3122811	5.8320132	2.1770216
H	1.9881743	4.8642600	3.5323710
H	4.3470567	-2.3818722	-3.7160455
H	4.4611644	-4.1020268	-4.2106491
H	2.8527318	-3.3267193	-4.0391012
H	4.4837329	-4.7505633	2.1533112
H	2.9832246	-5.6716421	1.7920556
H	4.5807413	-6.3321214	1.3132106
H	-3.1691687	-5.5347299	1.8809523
H	-1.7540898	-4.8598661	1.0097349
H	-1.7984729	-4.8440970	2.8089439
H	-5.2181611	0.5042575	2.6471478
H	-5.1362462	0.4200117	0.8505694
H	-6.3853817	-0.5101910	1.7405932
H	-1.1934557	2.2993388	1.7450815
H	1.4345464	-1.6345942	2.8428811
H	1.5781744	-0.0702570	2.0564448
H	1.2081163	0.2274875	-1.9611523
H	0.0123504	-0.1651616	-0.7528545
Ni	-1.8954382	0.8218547	-0.1079534
Br	-1.6588618	2.4846446	-1.7687761
O	-3.0021713	-0.5823499	-1.1647142
O	-3.2554169	0.4663801	-3.4346166
H	-2.7113510	1.2314673	-2.9910498
Cl	-4.0534919	-0.2703969	-2.1985037
O	-4.5901859	-1.4712540	-2.8045404
O	-5.0439843	0.6773300	-1.6957982

TS1

Energy = -5806.889264 Hartree

C	-0.9246069	-0.1665728	1.8876979
C	-0.9135761	1.2414979	1.8842039
C	0.3400172	-1.0112480	1.8479311
C	0.5546081	-1.7036266	0.5005747
C	0.5598783	-1.0052928	-0.7288294
C	0.3547568	0.4781480	-0.6539668
C	1.4993621	1.2762953	-0.2082208
C	1.4665876	2.0353844	0.9831184
C	0.3550294	2.0628264	2.0395566
C	-2.1263323	1.9281472	1.6774002
C	-3.3323089	1.2577146	1.4741137
C	-3.3491502	-0.1603867	1.5312416
C	-2.1488032	-0.8410644	1.7260207
C	0.7959777	-3.0904012	0.4801505
C	1.0437088	-3.7875243	-0.7047311
C	1.0497798	-3.0767781	-1.9332063
C	0.8106474	-1.7033513	-1.9199835
C	2.6925962	1.2231668	-0.9739476
C	3.8099885	1.9650991	-0.6467669
C	3.7714283	2.7688805	0.5364758
C	2.6222046	2.7659712	1.3263379
O	4.8914674	3.4621936	0.8044733
C	4.9468176	4.2832728	1.9626054
O	4.9587417	2.0127375	-1.3579492
C	5.0414301	1.2604153	-2.5578658
O	-4.5131324	1.8562605	1.1837181
C	-4.5055310	3.2285994	0.8112703
O	-4.5559655	-0.7510194	1.3353830
C	-4.6107032	-2.1602279	1.1950634
O	1.2803653	-5.1201895	-0.7885033
C	1.2861643	-5.8928132	0.3985750
O	1.2858811	-3.8095134	-3.0498552
C	1.2935879	-3.1525612	-4.3049901
H	-2.1048413	3.0164393	1.6245523
H	-2.1357242	-1.9311119	1.7038344
H	0.7909749	-3.6282126	1.4287649
H	0.7842709	-1.1450170	-2.8548074
H	2.6845614	0.6161264	-1.8772765
H	2.6142749	3.3341793	2.2570702
H	4.1722168	5.0693626	1.9369791
H	4.8284869	3.6867271	2.8840693
H	5.9394126	4.7518580	1.9605351
H	6.0389308	1.4489903	-2.9760664
H	4.9284833	0.1781696	-2.3662387
H	4.2758103	1.5789399	-3.2878093
H	-5.5334206	3.4716725	0.5098652

H	-4.2187235	3.8789654	1.6563217
H	-3.8222043	3.3971073	-0.0380307
H	-3.9829735	-2.5072891	0.3544074
H	-4.2900082	-2.6757328	2.1177091
H	-5.6595650	-2.4125548	0.9897041
H	0.3089924	-5.8584182	0.9132804
H	1.4951868	-6.9276670	0.0955093
H	2.0712952	-5.5578504	1.1003719
H	0.3188246	-2.6813082	-4.5262112
H	2.0824150	-2.3798737	-4.3570372
H	1.4983284	-3.9232208	-5.0599340
H	-0.5616283	0.7244404	-0.1209032
H	1.2228647	-0.3987800	2.0863007
H	0.2879642	-1.7868523	2.6283491
H	0.0632575	3.1170632	2.1756212
H	0.8373609	1.7801169	2.9926007
Ni	-0.6362418	1.3665134	-2.2278513
H	0.5060045	0.7704444	-2.8176764
Br	0.3891182	3.3752659	-2.6769661
C	-2.8713896	0.6866281	-1.9576487
O	-1.8886163	-0.0882923	-2.2587036
O	-2.5881696	1.8975509	-1.7366091
C	-4.2687132	0.1610765	-1.8830216
H	-4.8986558	0.7276287	-2.5860884
H	-4.3018776	-0.9088378	-2.1251579
H	-4.6613832	0.3317934	-0.8694504

TS2

Energy = -6338.837919 Hartree

C	-1.5261202	-0.0077031	1.6165515
C	-1.2683707	1.3780284	1.6492732
C	-0.4389353	-1.0562168	1.7876378
C	0.0456896	-1.7348973	0.5006435
C	0.4512480	-1.0238472	-0.6545371
C	0.2611429	0.4450510	-0.6388793
C	1.3461583	1.3224102	-0.1972114
C	1.2096130	2.0779702	0.9916259
C	0.0798153	1.9670181	2.0245673
C	-2.2828348	2.2661487	1.2383882
C	-3.5341839	1.8175811	0.8188001
C	-3.8197546	0.4250860	0.8659421
C	-2.8094113	-0.4560298	1.2473220
C	0.2515707	-3.1267904	0.5212452
C	0.8274947	-3.8136333	-0.5502443
C	1.2512798	-3.0842027	-1.6970666
C	1.0683714	-1.7060238	-1.7202018
C	2.5584326	1.3751607	-0.9286602
C	3.6006512	2.2084457	-0.5632372
C	3.4562152	3.0056566	0.6158233
C	2.2859915	2.9050610	1.3686153
O	4.4998965	3.7985030	0.9125663
C	4.4338511	4.6472973	2.0504126
O	4.7627545	2.3535587	-1.2358410
C	4.9518039	1.6143862	-2.4315590
O	-4.5261747	2.6128183	0.3589388
C	-4.2392930	3.9776533	0.0982407
O	-5.0714316	0.0646589	0.5052130
C	-5.4726360	-1.2856493	0.6684680
O	1.0264944	-5.1486057	-0.5964728
C	0.5936682	-5.9520989	0.4894113
O	1.7925902	-3.8124611	-2.7006783
C	2.1847990	-3.1469177	-3.8896280
H	-2.0614553	3.3331919	1.2234190
H	-2.9929839	-1.5301855	1.2149282
H	-0.0413324	-3.6785314	1.4148640
H	1.3400303	-1.1364537	-2.6075087
H	2.6369532	0.7754531	-1.8331764
H	2.1982780	3.4754668	2.2936179
H	3.5877130	5.3522105	1.9772532
H	4.3409009	4.0637698	2.9829080
H	5.3754964	5.2109598	2.0690147
H	5.9431018	1.8892596	-2.8148416
H	4.9260887	0.5260286	-2.2429683
H	4.1877100	1.8677376	-3.1882736
H	-5.1432826	4.4036708	-0.3570227
H	-4.0103043	4.5325826	1.0258428
H	-3.3925727	4.0818286	-0.6036931
H	-4.8955970	-1.9638791	0.0200334
H	-5.3674494	-1.6107612	1.7193106
H	-6.5315902	-1.3308091	0.3802797
H	-0.4951577	-5.8621819	0.6510295
H	0.8342636	-6.9896164	0.2222816
H	1.1193135	-5.6889782	1.4245898
H	1.3293618	-2.6424875	-4.3734727
H	2.9774172	-2.4018802	-3.6960793
H	2.5763488	-3.9193480	-4.5646014
H	-0.6870014	0.7191568	-0.1827657
H	0.4412742	-0.6161342	2.2826709
H	-0.8012661	-1.8439933	2.4661441
H	-0.0952795	2.9812137	2.4170717
H	0.4983245	1.4043696	2.8769376
Ni	-0.8432092	1.0637275	-2.3389251
H	0.5152614	0.9237584	-2.7078709
Br	-0.4848422	3.3056276	-2.2770638
O	-1.4384215	-0.7250375	-2.8743274
O	-2.9613397	1.0269216	-2.3326677
Cl	-2.9834088	-0.4187387	-2.8568545
O	-3.5226735	-0.4844788	-4.2127977
O	-3.6526397	-1.3274294	-1.93223747

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