Supporting Information

One-pot Synthesis of Sulfonylmethyl Phthalides via $K_2S_2O_8$/DMSO-Mediated Methylenylation/Sulfonylation of Eudesmic Acid with Sulfinates

Meng-Yang Chang*[a,b,c] and Chen-Yo Ou[a]

[a]*Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung 807, Taiwan* [b]*Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung 807, Taiwan.* [c]*NPUST College of Professional Studies, National Pingtung University of Science and Technology, Pingtung 912, Taiwan.*

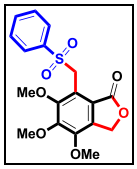
*Corresponding author, email: mychang@kmu.edu.tw

Table of Contents

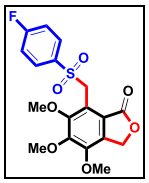
Experimental section

General. All reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Melting points were determined with a SMP3 melting apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer operating at 400 and at 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (*J*) are given in Hertz. High resolution mass spectra (HRMS) were measured with a mass spectrometer Finnigan/Thermo Quest MAT 95XL. X-ray crystal structures were obtained with an Enraf-Nonius FR-590 diffractometer (CAD4, Kappa CCD).

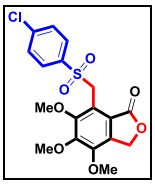
A representative synthetic procedure of skeleton 4 is as follows: $K_2S_2O_8$ (120 mg, 0.44 mmol) was added to a solution of **3** (0.2 mmol) in DMSO (5 mL) at 25 ^{o}C. The reaction mixture was stirred at 25 ^{o}C for 5 min. RSO_2Na (0.24 mmol) was added to the reaction mixture at 25 ^{o}C. The reaction mixture was stirred at 100 ^{o}C for 10 h. The reaction mixture was cooled to 25 ^{o}C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 20/1~4/1) afforded **4**.



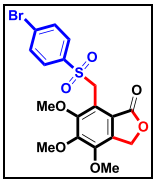
4,5,6-Trimethoxy-7-((phenylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4a). Yield = 81% (61 mg); White solid; mp = 97-99 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{18}H_{19}O_7S$ 379.0852, found 379.0855; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91-7.89 (m, 2H), 7.64-7.60 (m, 1H), 7.53-7.49 (m, 2H), 5.18 (s, 2H), 4.96 (s, 2H), 4.01 (s, 3H), 4.00 (s, 3H), 3.91 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 155.2, 149.7, 148.2, 139.5, 133.6, 133.5, 128.9 (2x), 128.5 (2x), 120.0, 115.5, 66.9, 61.7, 60.8, 60.3, 51.2. Single-crystal X-Ray diagram: crystal of compound **4a** was grown by slow diffusion of EtOAc into a solution of compound **4a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group P-1, *a* = 10.5691(4) Å, *b* = 12.9071(5) Å, *c* = 14.2075(4) Å, *V* = 1737.72(12) $Å^3$, *Z* = 4, d_{calcd} = 1.446 g/cm^3, *F*(000) = 792.0, 2*θ* range 6.696~134.156^{o}, R indices (all data) R1 = 0.0520, wR2 = 0.1163.



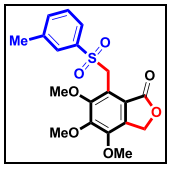
7-(((4-Fluorophenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4b). Yield = 76% (60 mg); White solid; mp = 125-127 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ calcd for $C_{18}H_{19}FO_7S$ 397.0757, found 397.0759; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.90 (m, 2H), 7.22-7.16 (m, 2H), 5.20 (s, 2H), 4.97 (s, 2H), 4.03 (s, 3H), 4.02 (s, 3H), 3.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 165.9 (d, *J* = 254.7 Hz), 155.3, 149.8, 148.3, 135.6 (d, *J* = 3.0 Hz), 133.6, 131.4 (d, *J* = 9.9 Hz, 2x), 120.0, 116.2 (d, *J* = 22.0 Hz, 2x), 115.4, 66.9, 61.8, 60.9, 60.4, 51.4; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ -103.65~-103.72 (m, 1F).



7-(((4-Chlorophenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4c). Yield = 73% (60 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ calcd for $C_{18}H_{18}ClO_7S$ 413.0462, found 413.0460; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 2H), 5.21 (s, 2H), 4.97 (s, 2H), 4.03 (s, 3H), 4.02 (s, 3H), 3.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.6, 155.3, 149.8, 148.3, 140.4, 138.1, 133.7, 130.0 (2x), 129.2 (2x), 120.0, 115.3, 67.0, 61.8, 60.9, 60.4, 51.3.

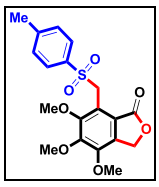


7-(((4-Bromophenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4d). Yield = 72% (66 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ calcd for $C_{18}H_{18}BrO_7S$ 456.9957, found 456.9961; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 5.22 (s, 2H), 4.97 (s, 2H), 4.03 (s, 3H), 4.02 (s, 3H), 3.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.6, 155.3, 149.8, 148.4, 138.7, 133.7, 132.2 (2x), 130.1 (2x), 129.0, 120.1, 115.2, 67.0, 61.8, 60.9, 60.4, 51.3.

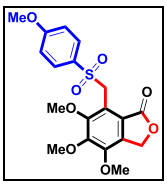


4,5,6-Trimethoxy-7-((*m*-tolylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4e). Yield = 77%

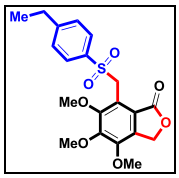
(60 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{19}H_{21}O_7S$ 393.1008, found 393.1010; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.74 (dd, *J* = 1.6, 8.8 Hz, 1H), 7.45-7.39 (m, 2H), 5.20 (s, 2H), 4.96 (s, 2H), 4.04 (s, 3H), 4.02 (s, 3H), 3.93 (s, 3H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 155.3, 149.8, 148.2, 139.5, 139.2, 134.4, 133.6, 128.82, 128.80, 125.6, 120.2, 115.7, 66.9, 61.8, 60.9, 60.4, 51.3, 21.3.



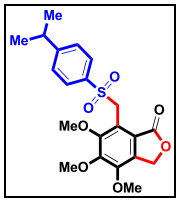
4,5,6-Trimethoxy-7-((*p*-tolylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4f). Yield = 80% (63 mg); White solid; mp = 117-119 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{19}H_{21}O_7S$ 393.1008, found 393.1007; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.19 (s, 2H), 4.95 (s, 2H), 4.03 (s, 3H), 4.01 (s, 3H), 3.92 (s, 3H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 155.2, 149.7, 148.1, 144.6, 136.7, 133.6, 129.5 (2x), 128.5 (2x), 120.1, 115.8, 66.8, 61.8, 60.8, 60.3, 51.3, 21.6.



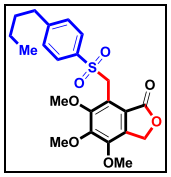
4,5,6-Trimethoxy-7-(((4-methoxyphenyl)sulfonyl)methyl)isobenzofuran-1(3*H*)-one (4g). Yield = 76% (62 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{19}H_{21}O_8S$ 409.0957, found 409.0962; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 9.2 Hz, 2H), 5.19 (s, 2H), 4.96 (s, 2H), 4.05 (s, 3H), 4.02 (s, 3H), 3.94 (s, 3H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 163.7, 155.3, 149.8, 148.1, 133.6, 131.3, 130.7 (2x), 120.1, 116.1, 114.1 (2x), 66.9, 61.9, 60.9, 60.4, 55.7, 51.5.



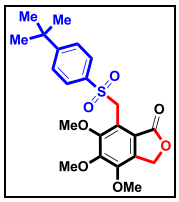
7-(((4-Ethylphenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4h). Yield = 70% (57 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{20}H_{23}O_7S$ 407.1165, found 407.1168; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.18 (s, 2H), 4.95 (s, 2H), 4.02 (s, 3H), 4.00 (s, 3H), 3.91 (s, 3H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 155.2, 150.7, 149.7, 148.1, 136.8, 133.6, 128.6 (2x), 128.4 (2x), 120.1, 115.8, 66.8, 61.8, 60.8, 60.3, 51.3, 28.9, 15.2.



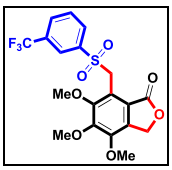
7-(((4-Isopropylphenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4i). Yield = 73% (61 mg); White solid; mp = 84-86 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ calcd for $C_{21}H_{25}O_7S$ 421.1321, found 421.1325; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 5.19 (s, 2H), 4.96 (s, 2H), 4.03 (s, 3H), 4.01 (s, 3H), 3.92 (s, 3H), 3.02-2.95 (m, 1H), 1.27 (d, *J* = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 155.3, 155.2, 149.7, 148.2, 136.9, 133.6, 128.7 (2x), 127.0 (2x), 120.2, 115.8, 66.8, 61.8, 60.9, 60.4, 51.3, 34.3, 23.6 (2x).



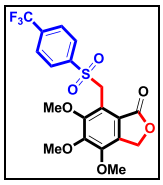
7-(((4-*n*-Butylphenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4j). Yield = 72% (62 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ calcd for $C_{22}H_{27}O_7S$ 435.1478, found 435.1481; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.18 (s, 2H), 4.96 (s, 2H), 4.03 (s, 3H), 4.01 (s, 3H), 3.92 (s, 3H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.64-1.57 (m, 2H), 1.37-1.32 (m, 2H), 0.93 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 155.2, 149.7, 149.5, 148.1, 136.8, 133.6, 128.9 (2x), 128.5 (2x), 120.2, 115.8, 66.8, 61.8, 60.8, 60.4, 51.3, 35.6, 33.2, 22.1, 13.8.



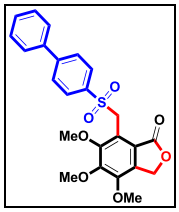
7-(((4-*t*-Butylphenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4k). Yield = 71% (62 mg); White solid; mp = 118-120 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: [M + H]$^{+}$ calcd for $C_{22}H_{27}O_7S$ 435.1478, found 435.1477; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 5.18 (s, 2H), 4.95 (s, 2H), 4.01 (s, 3H), 4.00 (s, 3H), 3.91 (s, 3H), 1.33 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.4, 157.5, 155.1, 149.7, 148.1, 136.5, 133.5, 128.4 (2x), 125.9 (2x), 120.2, 115.8, 66.8, 61.7, 60.8, 60.3, 51.3, 35.2, 31.0 (3x).



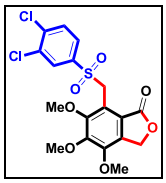
4,5,6-Trimethoxy-7-(((3-(trifluoromethyl)phenyl)sulfonyl)methyl)isobenzofuran-1(3*H*)-one (4m). Yield = 63% (56 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{19}H_{18}F_3O_7S$ 447.0725, found 447.0728; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, *J* = 7.6 Hz, 1H), 7.90 s, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 5.16 (s, 2H), 5.01 (s, 2H), 4.04 (s, 3H), 4.02 (s, 3H), 3.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.3, 155.3, 149.8, 148.5, 140.2, 133.6, 132.2, 131.1 (q, *J* = 33.4 Hz), 130.3 (q, *J* = 3.8 Hz), 130.0, 125.9 (q, *J* = 271.4 Hz), 125.8 (q, *J* = 3.8 Hz), 119.7, 115.2, 66.9, 61.8, 60.9, 60.4, 51.3; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ -62.77 (s, 3F).



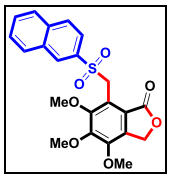
4,5,6-Trimethoxy-7-(((4-(trifluoromethyl)phenyl)sulfonyl)methyl)isobenzofuran-1(3*H*)-one (4n). Yield = 68% (61 mg); White solid; mp = 104-106 ºC (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{19}H_{18}F_3O_7S$ 447.0725, found 447.0724; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 5.21 (s, 2H), 5.00 (s, 2H), 4.020 (s, 3H), 4.018 (s, 3H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.6, 155.2, 149.7, 148.5, 143.1, 135.3 (q, *J* = 33.3 Hz), 133.7, 129.2 (2x), 126.0 (q, *J* = 3.8 Hz, 2x), 123.2 (q, *J* = 271.4 Hz), 120.1, 114.8, 67.0, 61.8, 60.9, 60.3, 51.3; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$): δ -63.23 (s, 3F).



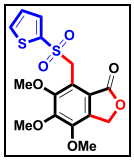
7-(([1,1'-Biphenyl]-4-ylsulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4o). Yield = 70% (64 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: [M + H]$^+$ calcd for $C_{24}H_{23}O_7S$ 455.1165, found 455.1168; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.63-7.60 (m, 2H), 7.51-7.41 (m, 3H), 5.21 (s, 2H), 5.03 (s, 2H), 4.06 (s, 3H), 4.02 (s, 3H), 3.94 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.6, 155.3, 149.8, 148.3, 146.6, 139.3, 138.3, 133.7, 129.1 (2x), 129.0 (2x), 128.5, 127.6 (2x), 127.4 (2x), 120.3, 115.7, 66.9, 61.9, 60.9, 60.4, 51.4.



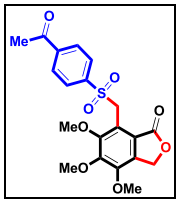
7-(((3,4-Dichlorophenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4p). Yield = 73% (65 mg); White solid; mp = 108-110 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{18}H_{17}Cl_2O_7S$ 447.0072, found 447.0070; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 2.0 Hz, 1H), 7.76 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 5.21 (s, 2H), 4.97 (s, 2H), 4.01 (s, 3H), 4.00 (s, 3H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 155.2, 149.7, 148.5, 139.1, 138.6, 133.6, 133.3, 131.1, 130.5, 137.7, 119.9, 114.8, 67.0, 61.7, 60.9, 60.3, 51.3.



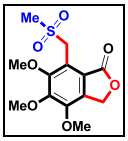
4,5,6-Trimethoxy-7-((naphthalen-2-ylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4q). Yield = 70% (60 mg); White solid; mp = 165-167 ^{o}C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{22}H_{21}O_7S$ 429.1008, found 429.1002; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.99-7.90 (m, 4H), 7.65 (dt, *J* = 0.8, 7.2 Hz, 1H), 7.59 (dt, *J* = 1.2, 8.0 Hz, 1H), 5.16 (s, 2H), 5.04 (s, 2H), 4.01 (s, 3H), 4.00 (s, 3H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.5, 155.2, 149.7, 148.2, 136.5, 135.2, 133.6, 132.0, 130.2, 129.3, 129.2, 129.1, 127.9, 127.4, 123.2, 120.2, 115.5, 66.8, 61.7, 60.8, 60.3, 51.3.



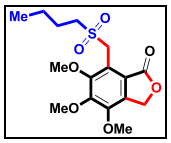
4,5,6-Trimethoxy-7-((thiophen-2-ylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4r). Yield = 67% (51 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{17}O_7S_2$ 385.0416, found 385.0421; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, *J* = 0.8, 4.4 Hz, 1H), 7.63 (dd, *J* = 0.8, 4.0 Hz, 1H), 7.12 (t, *J* = 4.0, 4.4 Hz, 1H), 5.19 (s, 2H), 5.10 (s, 2H), 4.01 (s, 3H), 4.00 (s, 3H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.4, 155.3, 149.7, 148.3, 140.2, 134.7, 134.2, 133.5, 127.8, 120.0, 115.7, 66.9, 61.7, 60.9, 60.4, 52.5.



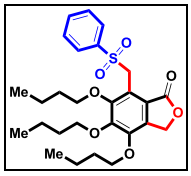
7-(((4-Acetylphenyl)sulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4s). Yield = 65% (55 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{20}H_{21}O_8S$ 421.0957, found 421.0961; ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.8 Hz, 2H), 5.20 (s, 2H), 5.01 (s, 2H), 4.05 (s, 3H), 4.03 (s, 3H), 3.94 (s, 3H), 2.67 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 196.9, 169.6, 155.4, 149.8, 148.4, 143.5, 140.8, 133.7, 129.0 (2x), 128.7 (2x), 120.0, 115.0, 67.0, 61.9, 60.9, 60.4, 51.3, 27.0.



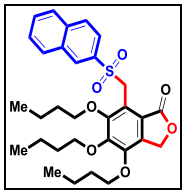
4,5,6-Trimethoxy-7-((methylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4t). Yield = 76% (48 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{13}H_{17}O_7S$ 317.0695, found 317.0700; ^1H NMR (400 MHz, $CDCl_3$): δ 5.26 (s, 2H), 4.89 (s, 2H), 4.01 (s, 6H), 3.94 (s, 3H), 2.93 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.2, 155.3, 150.1, 148.3, 133.9, 119.1, 116.5, 67.2, 61.7, 60.9, 60.4, 49.9, 41.2.



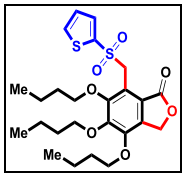
7-((*n*-Butylsulfonyl)methyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (4u). Yield = 77% (55 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{23}O_7S$ 359.1165, found 359.1169; ^1H NMR (400 MHz, $CDCl_3$): δ 5.25 (s, 2H), 4.87 (s, 2H), 4.03 (s, 3H), 4.01 (s, 3H), 3.94 (s, 3H), 3.10-3.06 (m, 2H), 1.91-1.83 (m, 2H), 1.52-1.42 (m, 2H), 0.95 (t, *J* =7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.2, 155.4, 150.1, 148.2, 133.9, 119.3, 116.5, 67.2, 61.8, 60.9, 60.4, 53.6, 48.5, 28.9, 21.7, 13.6.



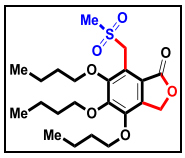
4,5,6-Tri-*n*-butoxy-7-((phenylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4v). Yield = 70% (71 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{27}H_{37}O_7S$ 505.2260, found 505.2263; ^1H NMR (400 MHz, $CDCl_3$): δ 7.88-7.86 (m, 2H), 7.63-7.60 (m, 1H), 7.52-7.48 (m, 2H), 5.16 (s, 2H), 4.97 (s, 2H), 4.16-4.13 (m, 4H), 3.99 (t, *J* = 6.8 Hz, 2H), 1.78-1.68 (m, 6H), 1.53-1.42 (m, 6H), 1.00-0.96 (m, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.7, 154.7, 149.8, 147.8, 139.6, 134.4, 133.5, 128.8 (2x), 128.6 (2x), 120.0, 115.9, 73.9, 73.7, 73.2, 66.9, 51.5, 32.24, 32.22, 32.17, 19.1 (2x), 19.0, 14.0, 13.84, 13.78.



4,5,6-Tri-*n*-butoxy-7-((naphthalen-2-ylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4w). Yield = 73% (81 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{31}H_{39}O_7S$ 555.2417, found 555.2421; ^1H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.97-7.89 (m, 4H), 7.66 (dt, *J* = 0.8, 7.2 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 5.15 (s, 2H), 5.04 (s, 2H), 4.13 (t, *J* = 6.4 Hz, 2H), 4.08 (t, *J* = 6.4 Hz, 2H), 3.84 (t, *J* = 6.8 Hz, 2H), 1.75-1.62 (m, 6H), 1.50-1.37 (m, 6H), 1.01-0.92 (m, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 154.6, 149.7, 147.8, 136.6, 135.3, 134.5, 132.0, 130.4, 129.3, 129.0 (2x), 127.9, 127.4, 123.4, 120.1, 116.0, 73.9, 73.7, 73.0, 66.9, 51.6, 32.2 (2x), 32.1, 19.1, 19.0 (2x), 14.0, 13.83, 13.79.



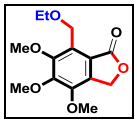
4,5,6-Tri-*n*-butoxy-7-((thiophen-2-ylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4x). Yield = 68% (69 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{25}H_{35}O_7S_2$ 511.1824, found 511.1830; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.59 (dd, *J* = 1.2, 4.0 Hz, 1H), 7.10 (dd, *J* = 3.6, 4.8 Hz, 1H), 5.17 (s, 2H), 5.09 (s, 2H), 4.16-4.10 (m, 4H), 4.00 (t, *J* = 6.8 Hz, 2H), 1.77-1.68 (m, 6H), 1.51-1.44 (m, 6H), 1.00-0.96 (m, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.6, 154.8, 149.7, 147.9, 140.4, 134.6, 134.3, 134.0, 127.7, 119.9, 116.0, 77.9, 73.7, 73.0, 66.9, 52.8, 32.24, 32.22, 32.16, 19.1 (2x), 19.0, 14.0, 13.9, 13.8.



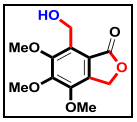
4,5,6-Tri-*n*-butoxy-7-((methylsulfonyl)methyl)isobenzofuran-1(3*H*)-one (4y). Yield = 67% (59 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{22}H_{35}O_7S$ 443.2104, found 443.2108; ^1H NMR (400 MHz, $CDCl_3$): δ 5.23 (s, 2H), 4.89 (s, 2H), 4.18-4.13 (m, 4H), 4.05 (t, *J* = 6.8 Hz, 2H), 2.93 (s, 3H), 1.83-1.69 (m, 6H), 1.54-1.42 (m, 6H), 1.00-0.95 (m, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.3, 154.8, 150.2, 147.9, 134.7, 119.0, 116.8, 74.1, 73.8, 73.1, 67.3, 50.2, 41.4, 32.21 (2x), 32.19, 19.14, 19.10, 19.0, 13.9, 13.83, 13.77.

A representative synthetic procedure of skeleton 5 is as follows: $K_2S_2O_8$ (120 mg, 0.44 mmol) was added to a solution of **3** (0.2 mmol) in DMSO (5 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. NaOEt, NaOH KCl or NaSPh (0.66 mmol) was added to the reaction mixture at 25 °C. The reaction mixture was stirred at 100 °C for 10 h. The reaction

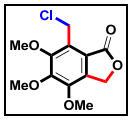
mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 10/1~4/1) afforded **5**.



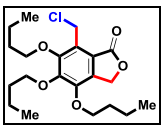
7-(Ethoxymethyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (5a). Yield = 66% (37 mg); White solid; mp = 67-69 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{19}O_6$ 283.1182, found 283.1180; ^1H NMR (400 MHz, $CDCl_3$): δ 5.18 (s, 2H), 4.84 (s, 2H), 3.944 (s, 3H), 3.938 (s, 3H), 3.90 (s, 3H), 3.63 (q, *J* = 7.2 Hz, 2H), 1.19 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.8, 154.8, 150.2, 147.3, 134.2, 126.8, 119.3, 66.7, 66.1, 62.0, 60.9, 60.30, 60.26, 15.2.



7-(Hydroxymethyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (5b). Yield = 69% (35 mg); White solid; mp = 89-91 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{12}H_{15}O_6$ 255.0869, found 255.0871; ^1H NMR (400 MHz, $CDCl_3$): δ 5.30 (s, 2H), 4.93 (s, 2H), 3.97 (s, 3H), 3.96 (s, 3H), 3.87 (s, 3H), 3.40 (br s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.0, 152.8, 150.4, 146.6, 135.0, 130.4, 119.2, 68.3, 62.0, 61.1, 60.4, 55.4.

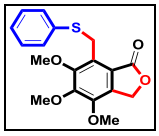


7-(Chloromethyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (5c). Yield = 40% (22 mg); White solid; mp = 83-85 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{12}H_{14}ClO_5$ 273.0530, found 273.0533; ^1H NMR (400 MHz, $CDCl_3$): δ 5.21 (s, 2H), 5.00 (s, 2H), 3.97 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.3, 154.1, 149.8, 147.8, 134.0, 125.7, 118.1, 67.0, 61.7, 60.9, 60.2, 33.9.

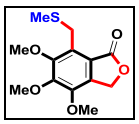


4,5,6-Tri-*n*-butoxy-7-(chloromethyl)isobenzofuran-1(3*H*)-one (5d). Yield = 33% (26 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{21}H_{32}ClO_5$ 399.1938, found 399.1942; ^1H NMR (400 MHz, $CDCl_3$): δ 5.21 (s, 2H), 5.07 (s, 2H), 4.14 (t, *J* = 6.8 Hz, 2H), 4.12 (t, *J* = 6.8 Hz, 2H), 4.07 (t, *J* = 6.4 Hz, 2H), 1.86-1.68 (m, 6H), 1.59-1.43 (m, 6H), 1.00 (t, *J* = 7.6 Hz, 3H), 0.99 (t, *J* = 7.2 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.7,

153.8, 150.0, 147.6, 134.9, 126.2, 118.3, 103.2, 74.4, 73.8, 73.0, 67.1, 34.2, 32.3, 32.2, 19.2, 19.12, 19.06, 13.95, 13.85, 13.79.

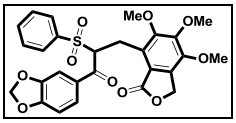


4,5,6-Trimethoxy-7-((phenylthio)methyl)isobenzofuran-1(3*H*)-one (5g). Yield = 76% (55 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{18}H_{19}O_5S$ 365.0953, found 365.0955; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93-7.91 (m, 2H), 7.65-7.61 (m, 1H), 7.54-7.50 (m, 2H), 5.19 (s, 2H), 4.98 (s, 2H), 4.03 (s, 3H), 4.01 (s, 3H), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.5, 155.2, 149.7, 148.2, 139.6, 133.7, 133.6, 128.9 (2x), 128.5 (2x), 120.1, 115.6, 66.9, 61.8, 60.9, 60.4, 51.2.

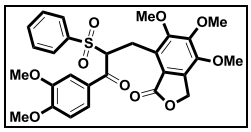


4,5,6-Trimethoxy-7-((methylthio)methyl)isobenzofuran-1(3*H*)-one (intermediate C). $K_2S_2O_8$ (120 mg, 0.44 mmol) was added to a solution of **3a** (0.2 mmol) in DMSO (5 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. The reaction mixture was stirred at 100 °C for 10 h. The reaction mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 10/1~4/1) afforded **C**. Yield = 76% (43 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{13}H_{17}O_5S$ 285.0797, found 285.0802; ^1H NMR (400 MHz, $CDCl_3$): δ 5.21 (s, 2H), 4.13 (s, 2H), 3.97 (s, 3H), 3.96 (s, 3H), 3.94 (s, 3H), 2.11 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.2, 153.5, 150.3, 146.3, 133.9, 128.8, 118.1, 66.8, 61.5, 60.9, 60.4, 25.8, 15.6.

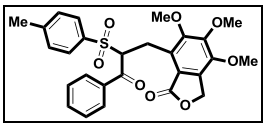
A representative synthetic procedure of skeleton 6 is as follows: $K_2S_2O_8$ (120 mg, 0.44 mmol) was added to a solution of **3a** (42 mg, 0.2 mmol) in DMSO (5 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. β-Ketosulfones (0.3 mmol) and K_2CO_3 (70 mg, 0.5 mmol) were added to the reaction mixture at 25 °C. The reaction mixture was stirred at 100 °C for 10 h.The reaction mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 10/1~4/1) afforded **6**.



7-(3-(Benzo[*d*][1,3]dioxol-5-yl)-3-oxo-2-(phenylsulfonyl)propyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (6a). Yield = 45% (49 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{27}H_{25}O_{10}S$ 541.1169, found 541.1174; ^1H NMR (400 MHz, $CDCl_3$): δ 7.87-7.85 (m, 2H), 7.63-7.60 (m, 1H), 7.52-7.48 (m, 2H), 7.47 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.29 (d, *J* = 1.6 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.03 (dd, *J* = 6.0, 8.4 Hz, 1H), 6.00 (d, *J* = 1.2 Hz, 1H), 5.99 (d, *J* = 1.2 Hz, 1H), 5.10 (s, 2H), 3.91 (s, 3H), 3.87 (s, 6H), 3.82 (dd, *J* = 8.4, 14.0 Hz, 1H), 3.68 (dd, *J* = 6.0, 14.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.8, 170.3, 154.1, 152.4, 150.2, 148.1, 146.4, 137.2, 134.4, 133.9, 131.9, 129.6 (2x), 128.7 (2x), 126.0, 125.4, 118.5, 108.3, 107.8, 102.0, 68.3, 67.0, 61.2, 60.8, 60.3, 23.1.



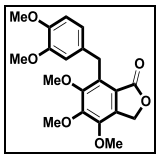
7-(3-(3,4-Dimethoxyphenyl)-3-oxo-2-(phenylsulfonyl)propyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (6b). Yield = 42% (47 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{28}H_{29}O_{10}S$ 557.1482, found 557.1485; ^1H NMR (400 MHz, $CDCl_3$): δ 7.88-7.85 (m, 2H), 7.63-7.58 (m, 1H), 7.52-7.47 (m, 3H), 7.37 (d, *J* = 2.0 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.15 (dd, *J* = 6.4, 8.8 Hz, 1H), 5.09 (s, 2H), 3.899 (s, 3H), 3.896 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 3.86 (s, 3H), 3.84 (dd, *J* = 8.8, 14.0 Hz, 1H), 3.68 (dd, *J* = 6.0, 14.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 190.1, 170.4, 154.1, 153.8, 150.2, 148.8, 146.3, 137.3, 134.4, 133.8, 130.2, 129.5 (2x), 128.7 (2x), 125.4, 124.3, 118.6, 110.5, 110.0, 67.9, 67.0, 61.3, 60.8, 60.3, 56.1, 55.9, 23.1.



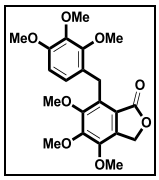
4,5,6-Trimethoxy-7-(3-oxo-3-phenyl-2-tosylpropyl)isobenzofuran-1(3*H*)-one (6c). Yield = 51% (52 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{27}H_{27}O_8S$ 511.1427, found 511.1432; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83-7.72 (m, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.51-7.47 (m, 1H), 7.37-7.33 (m, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 6.09 (dd, *J* = 6.0, 8.8 Hz, 1H), 5.09 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.87-3.85 (m, 1H), 3.71 (dd, *J* = 2.0, 13.6 Hz, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.2, 170.3, 154.1, 150.2, 146.4, 145.0, 137.1, 134.4, 134.1, 133.5, 129.6 (2x), 129.4 (2x), 128.8 (2x), 128.4 (2x), 125.5, 118.5, 66.5, 67.0, 61.2, 60.8, 60.3, 22.9, 21.6.

A representative synthetic procedure of skeleton 7 is as follows: Oxygenated benzenes (0.12 mmol) was added to a solution of **4a** o **4v** (0.1 mmol) in $CHCl_3$ (10 mL) at 25 °C. The

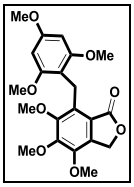
reaction mixture was stirred at 25 °C for 5 min. BF_3-OEt_2 (22 mg, 0.15 mmol) was added to the reaction mixture at 25 °C. The reaction mixture was stirred at 61 °C (reflux) for 10 h. The reaction mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 20/1~4/1) afforded **7**.



7-(3,4-Dimethoxybenzyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (7a). Yield = 68% (25 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{20}H_{23}O_7$ 375.1444, found 375.1438; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03 (d, *J* = 2.0 Hz, 1H), 6.89 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 5.19 (s, 2H), 4.34 (s, 2H), 3.95 (s, 3H), 3.93 (s, 3H), 3.83 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.5, 153.2, 150.4, 148.5, 147.1, 145.7, 134.2, 133.4, 131.2, 120.8, 118.0, 112.5, 110.9, 66.6, 61.0, 60.8, 60.3, 55.7 (2x), 29.1.

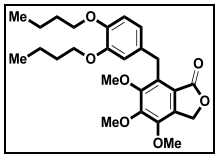


4,5,6-Trimethoxy-7-(2,3,4-trimethoxybenzyl)isobenzofuran-1(3*H*)-one (7b). Yield = 70% (28 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{21}H_{25}O_8$ 405.1550, found 405.1555; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.49 (d, *J* = 8.8 Hz, 1H), 6.44 (d, *J* = 8.4 Hz, 1H), 5.24 (s, 2H), 4.39 (s, 2H), 3.97 (s, 3H), 3.94 (s, 3H), 3.92 (s, 3H), 3.88 (s, 3H), 3.78 (s, 3H), 3.56 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.3, 153.9, 151.8, 151.7, 150.4, 145.9, 142.2, 134.0, 130.6, 126.6, 123.1, 118.8, 106.9, 66.6, 60.9, 60.8 (2x), 60.7, 60.4, 55.9, 23.4.

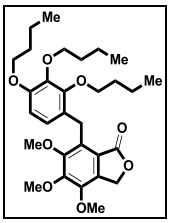


4,5,6-Trimethoxy-7-(2,4,6-trimethoxybenzyl)isobenzofuran-1(3*H*)-one (7c). Yield = 72% (29 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{21}H_{25}O_8$ 405.1550, found 405.1548; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.08 (s, 2H), 5.19 (s, 2H), 4.41 (s, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 3.76 (s, 3H), 3.70 (s, 6H), 3.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.5, 159.3, 159.1 (2x), 153.6, 150.2, 144.8, 133.3, 132.9, 118.8, 110.2, 90.8 (2x), 66.1, 60.7, 60.3,

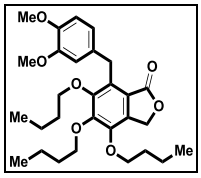
60.1, 55.8 (2x), 55.1, 18.2.



7-(3,4-Di-*n*-butoxybenzyl)-4,5,6-trimethoxyisobenzofuran-1(3*H*)-one (7d). Yield = 66% (30 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{26}H_{35}O_7$ 459.2383, found 459.2385; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (d, *J* = 2.0 Hz, 1H), 6.85 (dd, *J* = 2.0, 8.0 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.20 (s, 2H), 4.33 (s, 2H), 3.97 (t, *J* = 6.4 Hz, 2H), 3.95 (s, 3H), 3.94 (s, 3H), 3.92 (t, *J* = 6.4 Hz, 2H), 3.75 (s, 3H), 1.79-1.71 (m, 4H), 1.50-1.42 (m, 4H), 0.95 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.6, 153.3, 150.5, 148.8, 147.4, 145.8, 134.2, 133.6, 131.5, 121.1, 118.1, 115.2, 113.9, 69.0, 68.9, 66.6, 61.0, 60.8, 60.4, 31.34, 31.31, 29.1, 19.18, 19.16, 13.84, 13.81.



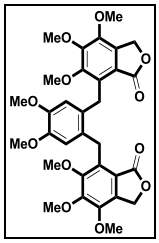
4,5,6-Trimethoxy-7-(2,3,4-tri-*n*-butoxybenzyl)isobenzofuran-1(3*H*)-one (7e). Yield = 65% (34 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{30}H_{43}O_8$ 531.2958, found 531.2962; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.33 (d, *J* = 8.8 Hz, 1H), 6.29 (d, *J* = 8.8 Hz, 1H), 5.23 (s, 2H), 4.40 (s, 2H), 4.10 (t, *J* = 6.8 Hz, 2H), 3.98 (t, *J* = 6.8 Hz, 2H), 3.97 (s, 3H), 3.94 (s, 3H), 3.87 (t, *J* = 6.8 Hz, 2H), 3.53 (s, 3H), 1.80-1.71 (m, 6H), 1.54-1.45 (m, 6H), 0.971 (t, *J* = 7.2 Hz, 3H), 0.965 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.3, 153.9, 151.6, 151.1, 150.5, 145.8, 141.8, 133.9, 130.9, 126.6, 122.4, 118.9, 107.8, 73.10, 73.06, 68.3, 66.5, 60.9, 60.7, 60.4, 32.5, 32.4, 31.4, 23.4, 19.32, 19.25, 19.22, 14.0, 13.9, 13.8.



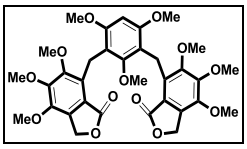
4,5,6-Tri-*n*-butoxy-7-(3,4-dimethoxybenzyl)isobenzofuran-1(3*H*)-one (7f). Yield = 71% (36 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{29}H_{41}O_7$ 501.2852, found 501.2856; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (d, *J* = 2.0 Hz, 1H), 6.93 (dd, *J* = 2.0, 8.4 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 5.16 (s, 2H), 4.34 (s, 2H), 4.07 (t, *J* = 6.8 Hz, 2H), 4.06 (t, *J* = 6.8 Hz, 2H), 3.93 (t, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 3H), 1.81-1.67 (m, 6H), 1.55-1.42 (m, 6H), 0.97 (t, *J* = 7.2 Hz, 6H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.7,

152.7, 150.4, 148.4, 147.1, 145.4, 134.9, 133.7, 131.4, 120.8, 117.9, 112.5, 110.9, 73.6, 73.5, 72.9, 66.7, 55.7, 55.6, 32.4, 32.2 (2x), 29.2, 19.3, 19.1, 19.0, 13.9, 13.80, 13.76.

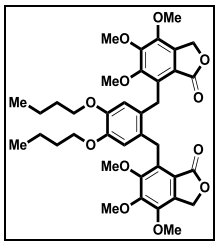
A representative synthetic procedure of skeleton 8 is as follows: Oxygenated benzenes (0.05 mmol) was added to a solution of **4a** o **4v** (0.1 mmol) in $CHCl_3$ (10 mL) at 25 ^oC. The reaction mixture was stirred at 25 ^oC for 5 min. BF_3-OEt_2 (45 mg, 0.3 mmol) was added to the reaction mixture at 25 ^oC. The reaction mixture was stirred at 61 ^oC (reflux) for 10 h. The reaction mixture was cooled to 25 ^oC and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 20/1~4/1) afforded **8**.



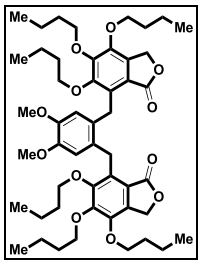
7,7'-((4,5-Dimethoxy-1,2-phenylene)bis(methylene))bis(4,5,6-trimethoxyisobenzofuran-1(3*H*)-one) (8a). Yield = 66% (20 mg); White solid; mp = 169-171 ^oC (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{32}H_{35}O_{12}$ 611.2129, found 611.2133; ^1H NMR (400 MHz, $CDCl_3$): δ 6.46 (s, 2H), 5.25 (s, 4H), 4.56 (s, 4H), 3.98 (s, 6H), 3.95 (s, 6H), 3.64 (s, 6H), 3.61 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.6 (2x), 154.2 (2x), 150.6 (2x), 146.9 (2x), 146.0 (2x), 134.0 (2x), 131.2 (2x), 130.9 (2x), 118.6 (2x), 112.8 (2x), 66.6 (2x), 60.9 (2x), 60.8 (2x), 60.5 (2x), 56.0 (2x), 26.5 (2x).



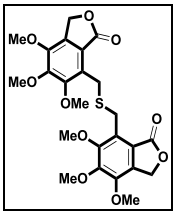
7,7'-((2,4,6-Trimethoxy-1,3-phenylene)bis(methylene))bis(4,5,6-trimethoxyisobenzofuran-1(3*H*)-one) (8b). Yield = 56% (18 mg); White solid; mp = 177-179 ^oC (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{33}H_{37}O_{13}$ 641.2234, found 641.2236; ^1H NMR (400 MHz, $CDCl_3$): δ 6.19 (s, 1H), 5.20 (s, 4H), 4.45 (s, 4H), 3.92 (s, 6H), 3.82 (s, 6H), 3.68 (s, 3H), 3.64 (s, 6H), 3.24 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7 (2x), 158.5, 157.5 (2x), 153.7 (2x), 150.2 (2x), 145.1 (2x), 133.3 (2x), 132.7 (2x), 118.8, 115.0 (2x), 92.5 (2x), 66.3 (2x), 61.9, 60.6 (2x), 60.4 (2x), 60.0 (2x), 55.9 (2x), 19.0 (2x).



7,7'-((4,5-Di-*n*-butoxy-1,2-phenylene)bis(methylene))bis(4,5,6-trimethoxyisobenzofuran-1(3*H*)-one) (8c). Yield = 54% (19 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{38}H_{47}O_{12}$ 695.3068, found 695.3071; ^1H NMR (400 MHz, $CDCl_3$): δ 6.40 (s, 2H), 5.24 (s, 4H), 4.53 (s, 4H), 3.98 (s, 6H), 3.95 (s, 6H), 3.77 (t, *J* = 6.4 Hz, 4H), 3.57 (s, 6H), 1.65-1.58 (m, 4H), 1.42-1.33 (m, 4H), 0.87 (t, *J* = 7.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.5 (2x), 154.2 (2x), 150.6 (2x), 147.0 (2x), 145.9 (2x), 133.9 (2x), 131.4 (2x), 131.2 (2x), 118.6 (2x), 116.0 (2x), 69.5 (2x), 66.6 (2x), 60.9 (2x), 60.8 (2x), 60.5 (2x), 31.3 (2x), 26.4 (2x), 19.1 (2x), 13.8 (2x).

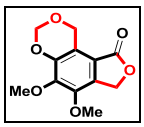


7,7'-((4,5-Dimethoxy-1,2-phenylene)bis(methylene))bis(4,5,6-tri-*n*-butoxyisobenzofuran-1(3*H*)-one) (8d). Yield = 40% (17 mg); White solid; mp = 120-122 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{50}H_{71}O_{12}$ 863.4946, found 863.4951; ^1H NMR (400 MHz, $CDCl_3$): δ 6.42 (s, 2H), 5.19 (s, 4H), 4.55 (s, 4H), 4.13 (t, *J* = 6.8 Hz, 4H), 4.08 (t, *J* = 6.8 Hz, 4H), 3.77 (t, *J* = 6.8 Hz, 4H), 3.62 (s, 6H), 1.77-1.69 (m, 8H), 1.64-1.57 (m, 4H), 1.52-1.46 (m, 8H), 1.35-1.30 (m, 4H), 0.98 (t, *J* = 7.2 Hz, 6H), 0.96 (t, *J* = 7.2 Hz, 6H), 0.86 (t, *J* = 7.2 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.3 (2x), 153.7 (2x), 150.4 (2x), 146.7 (2x), 145.5 (2x), 134.6 (2x), 131.3 (2x), 130.9 (2x), 118.8 (2x), 112.7 (2x), 73.8 (2x), 73.6 (2x), 73.0 (2x), 66.6 (2x), 56.0 (2x), 32.33 (2x), 32.30 (2x), 32.1 (2x), 26.8 (2x), 19.2 (2x), 19.12 (2x), 19.06 (2x), 13.89 (2x), 13.86 (2x), 13.8 (2x).

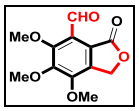


7,7'-(Thiobis(methylene))bis(4,5,6-trimethoxyisobenzofuran-1(3*H*)-one) (9a). BF_3-OEt_2 (14 mg, 0.1 mmol) was added to a solution of intermediate **C** (28 mg, 0.1 mmol) in $CHCl_3$ (10 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 10 h. The reaction mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL)

and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 20/1~4/1) afforded **9a**. Yield = 56% (14 mg); Colorless oil; HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{24}H_{27}O_{10}S$ 507.1325, found 507.1331; ^1H NMR (400 MHz, $CDCl_3$): δ 5.18 (s, 4H), 4.30 (s, 4H), 3.95 (s, 6H), 3.94 (s, 6H), 3.92 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.9 (2x), 153.7 (2x), 150.2 (2x), 146.4 (2x), 134.0 (2x), 128.3 (2x), 118.2 (2x), 66.7 (2x), 61.7 (2x), 60.9 (2x), 60.4 (2x), 25.4 (2x).

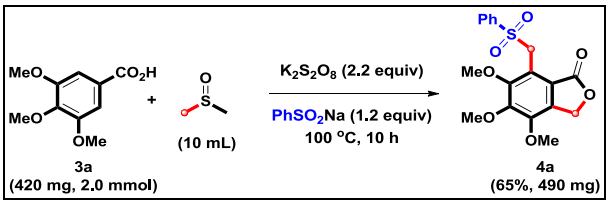


5,6-Dimethoxy-1*H*-[1,3]dioxino[5,4-*e*]isobenzofuran-9(7*H*)-one (10a). DDQ (90 mg, 0.4 mmol) was added to a solution of **5b** (50 mg, 0.2 mmol) in $MeNO_2$ (5 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 6 h and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 10/1~4/1) afforded **10a**. Yield = 45% (23 mg); White solid; mp = 152-154 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{12}H_{13}O_6$ 253.0712, found 253.0718; ^1H NMR (400 MHz, $CDCl_3$): δ 5.32 (s, 2H), 5.27 (s, 2H), 5.22 (s, 2H), 3.97 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.1, 147.9, 145.8, 145.0, 131.5, 116.5, 116.4, 91.6, 68.0, 64.1, 61.3, 60.4. Single-crystal X-Ray diagram: crystal of compound **10a** was grown by slow diffusion of EtOAc into a solution of compound **10a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P2_1/c$, *a* = 3.8823(2) Å, *b* = 30.4422(18) Å, *c* = 9.0099(6) Å, *V* = 1061.18(11) $Å^3$, *Z* = 4, d_{calcd} = 1.579 g/cm^3, *F*(000) = 528.0, 2*θ* range 10.272~146.476°, R indices (all data) R1 = 0.0781, wR2 = 0.1881.



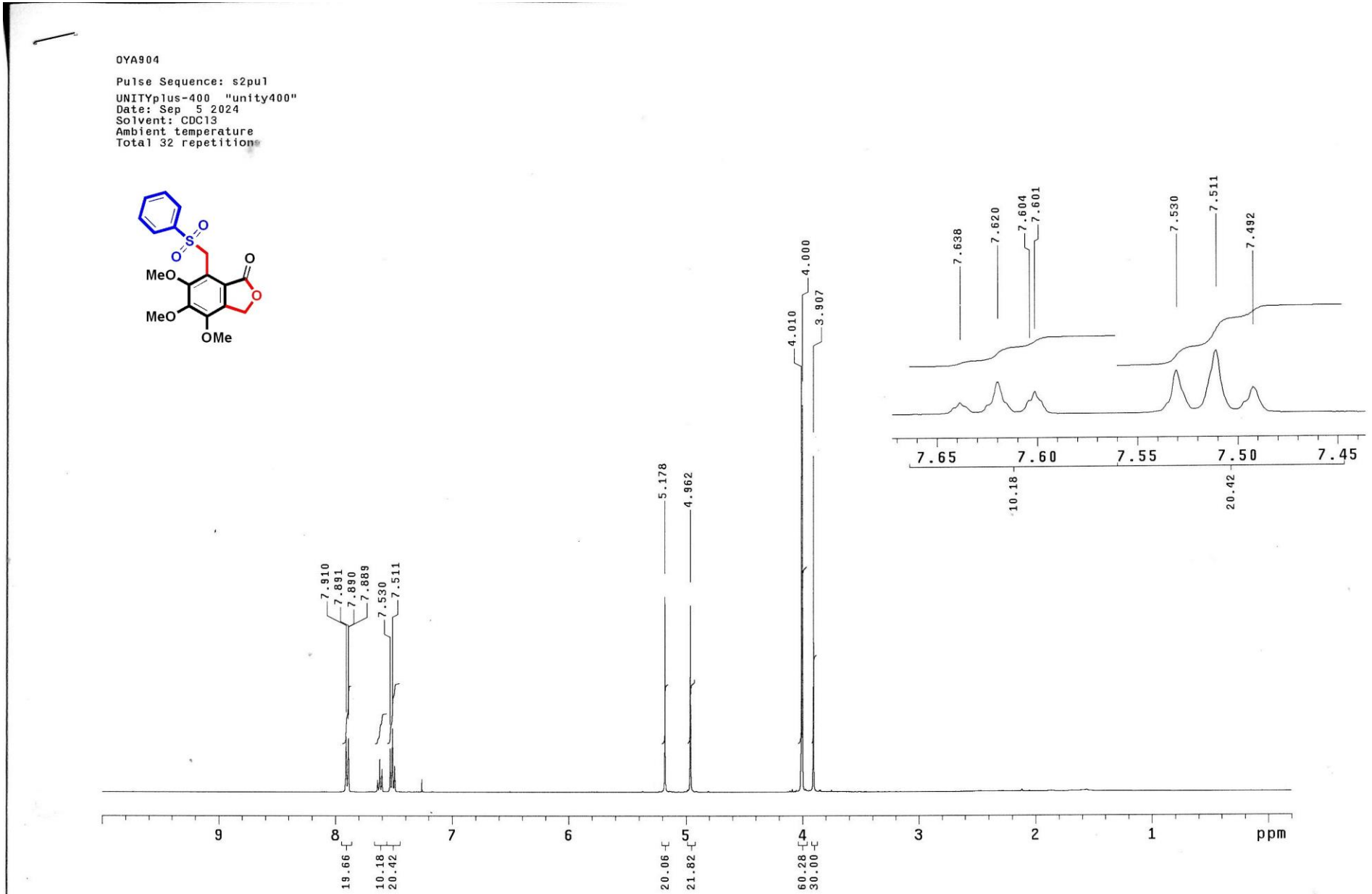
5,6,7-Trimethoxy-3-oxo-1,3-dihydroisobenzofuran-4-carbaldehyde (10b). DMP (90 mg, 0.21 mmol) was added to a solution of **5b** (50 mg, 0.2 mmol) in CH_2Cl_2 (5 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 6 h and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 15/1~8/1) afforded **10b**. Yield = 75% (38 mg); White solid; mp = 131-133 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{12}H_{13}O_6$ 253.0712, found 253.0718; ^1H NMR (400 MHz, $CDCl_3$): δ 10.88 (s, 1H), 5.29 (s, 2H), 4.12 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 187.6, 169.2, 156.4, 151.0, 149.2, 134.4,

123.4, 121.8, 67.8, 62.3, 61.6, 60.4.

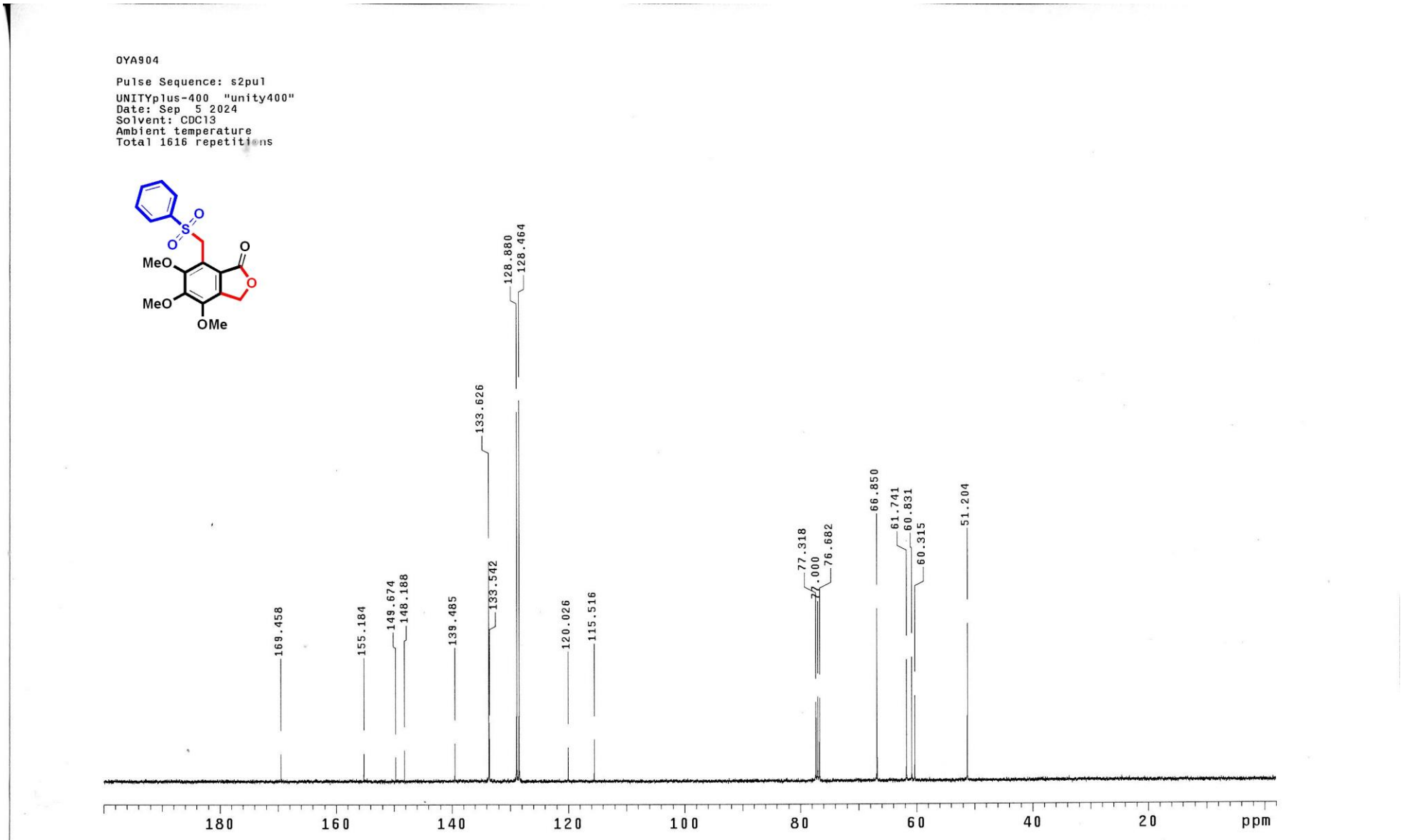


Large-scale synthesis of compound 4a. $K_2S_2O_8$ (1.2 g, 4.4 mmol) was added to a solution of eudesmic acid (**3a**, 420 mg, 2.0 mmol) in DMSO (10 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. $PhSO_2Na$ (400 mg, 2.4 mmol) was added to the reaction mixture at 25 °C. The reaction mixture was stirred at 100 °C for 10 h. The reaction mixture was cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 20/1~4/1) afforded **4a** (65%, 490 mg).

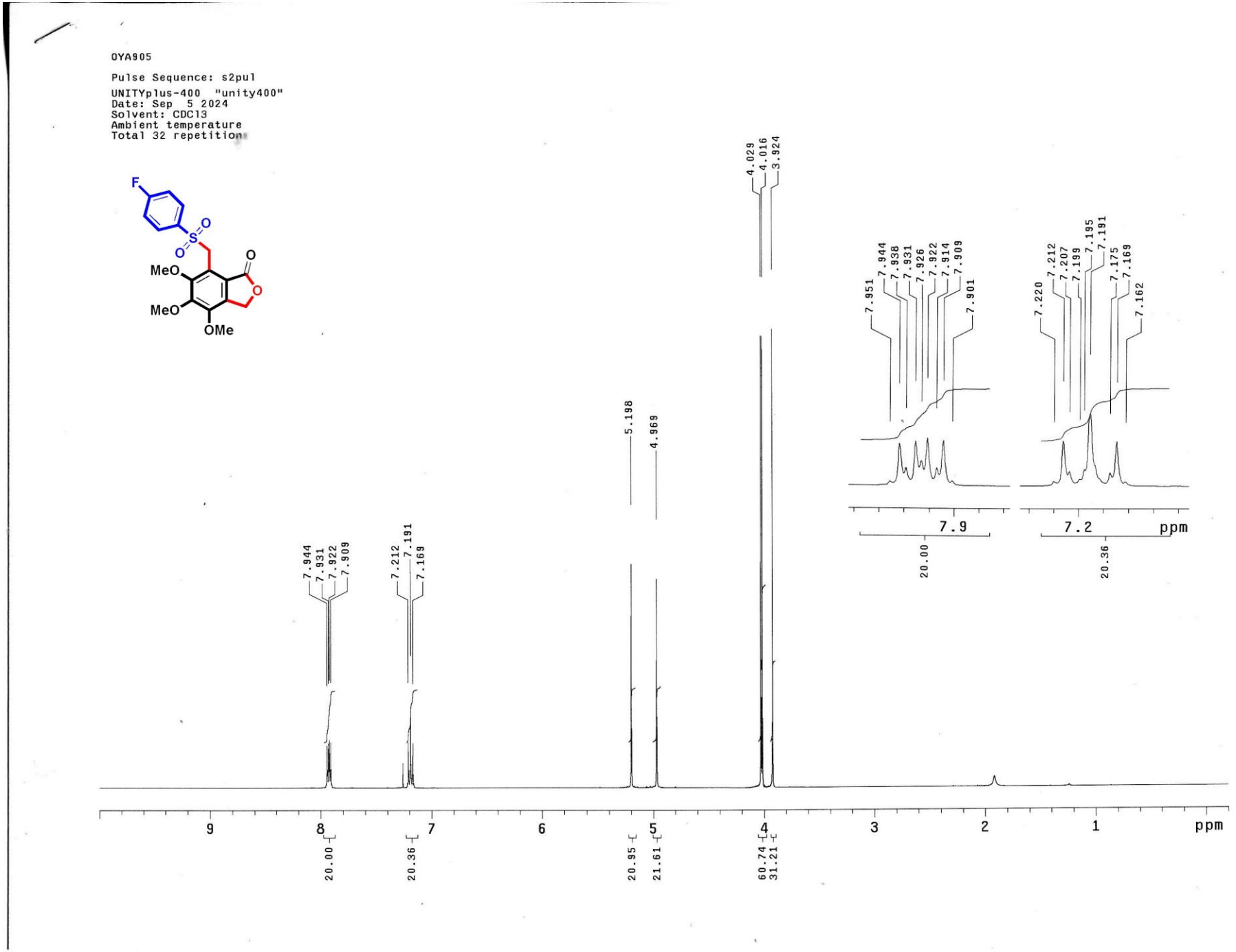
Compound 4a (^{1}H-NMR spectral data)



Compound 4a (^{13}C-NMR spectral data)



Compound 4b (^{1}H-NMR spectral data)

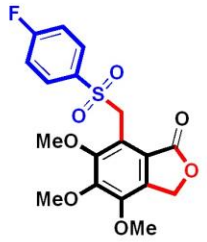


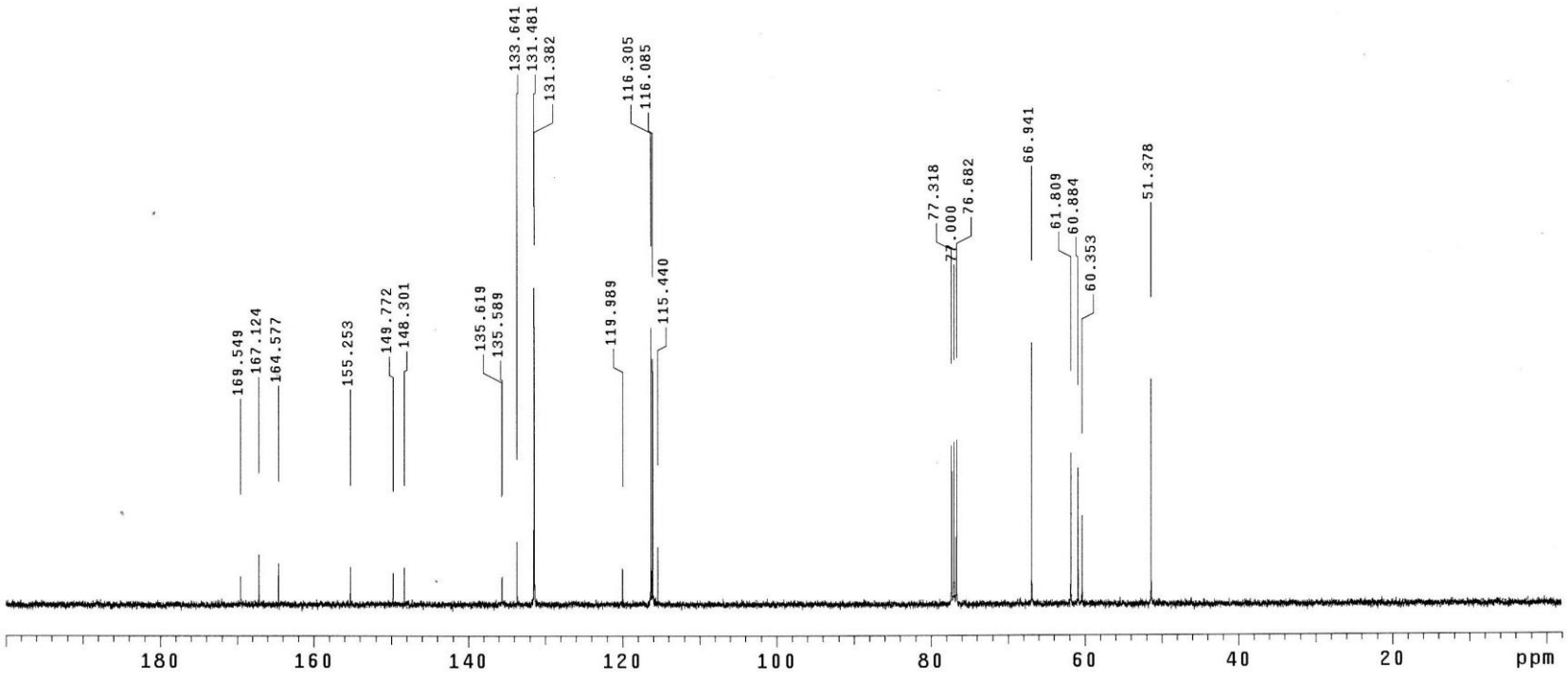
Compound 4b (^{13}C-NMR spectral data)

OYA905

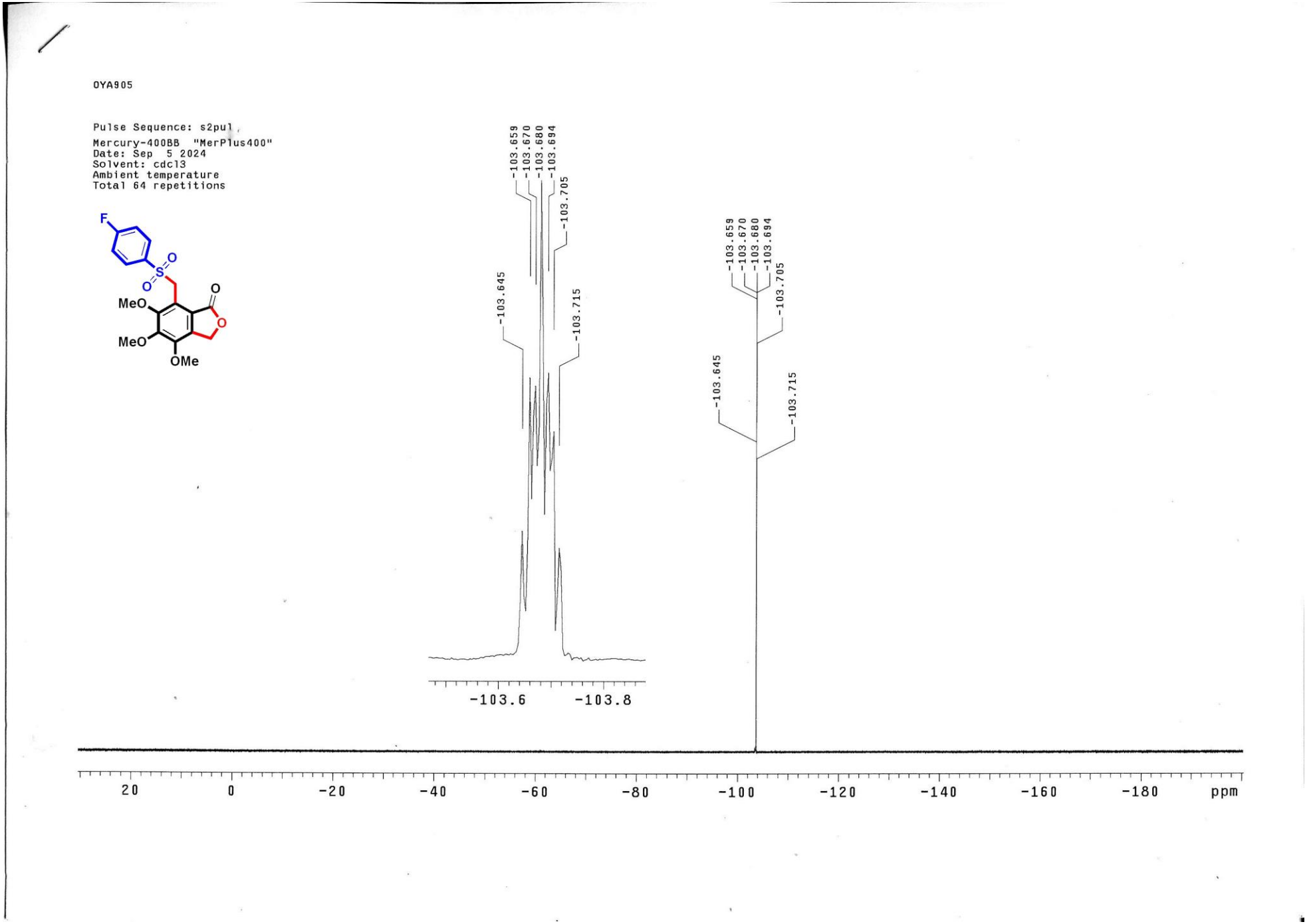
Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: Sep 5 2024
Solvent: CDCl3
Ambient temperature
Total 2016 repetitions

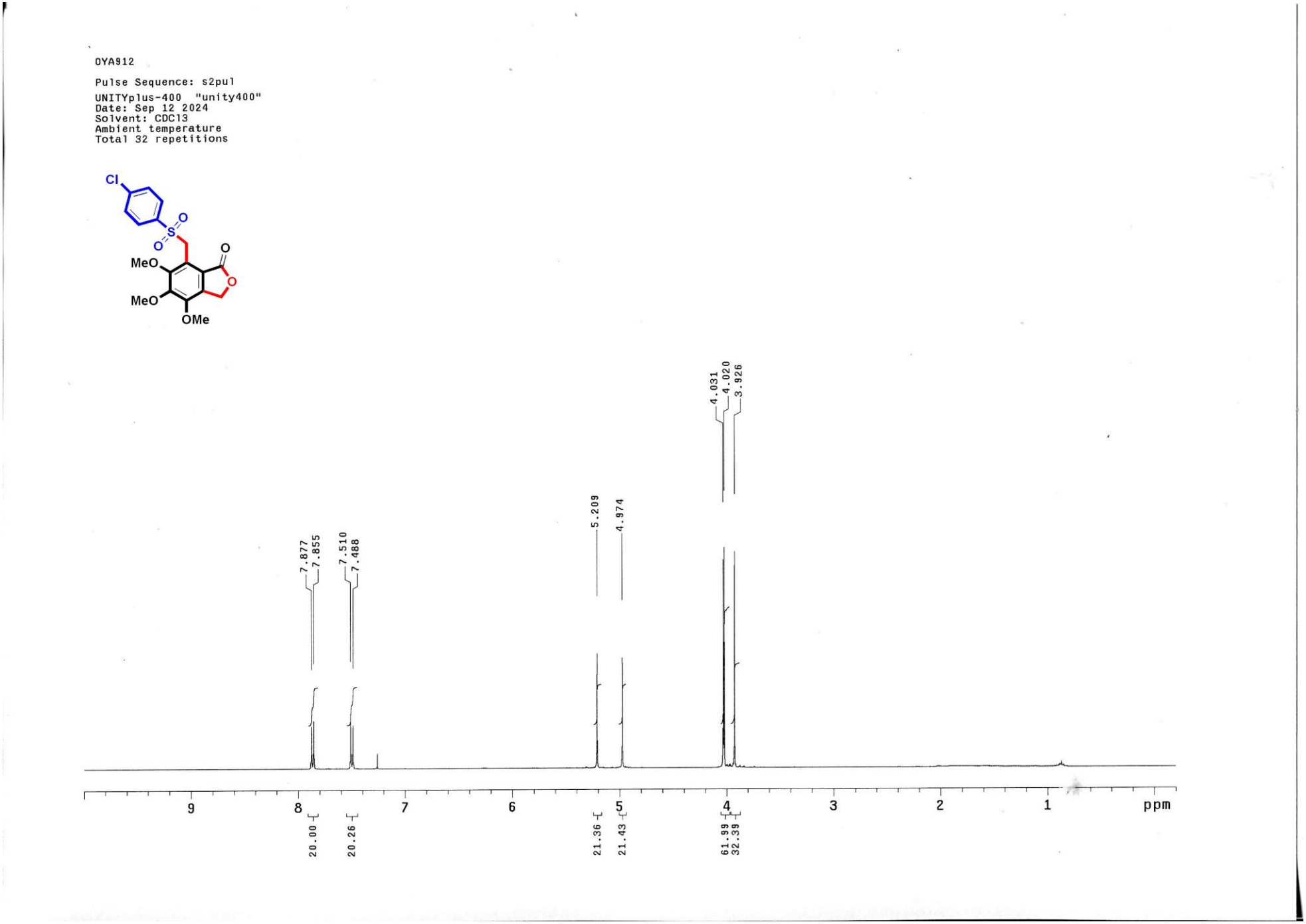




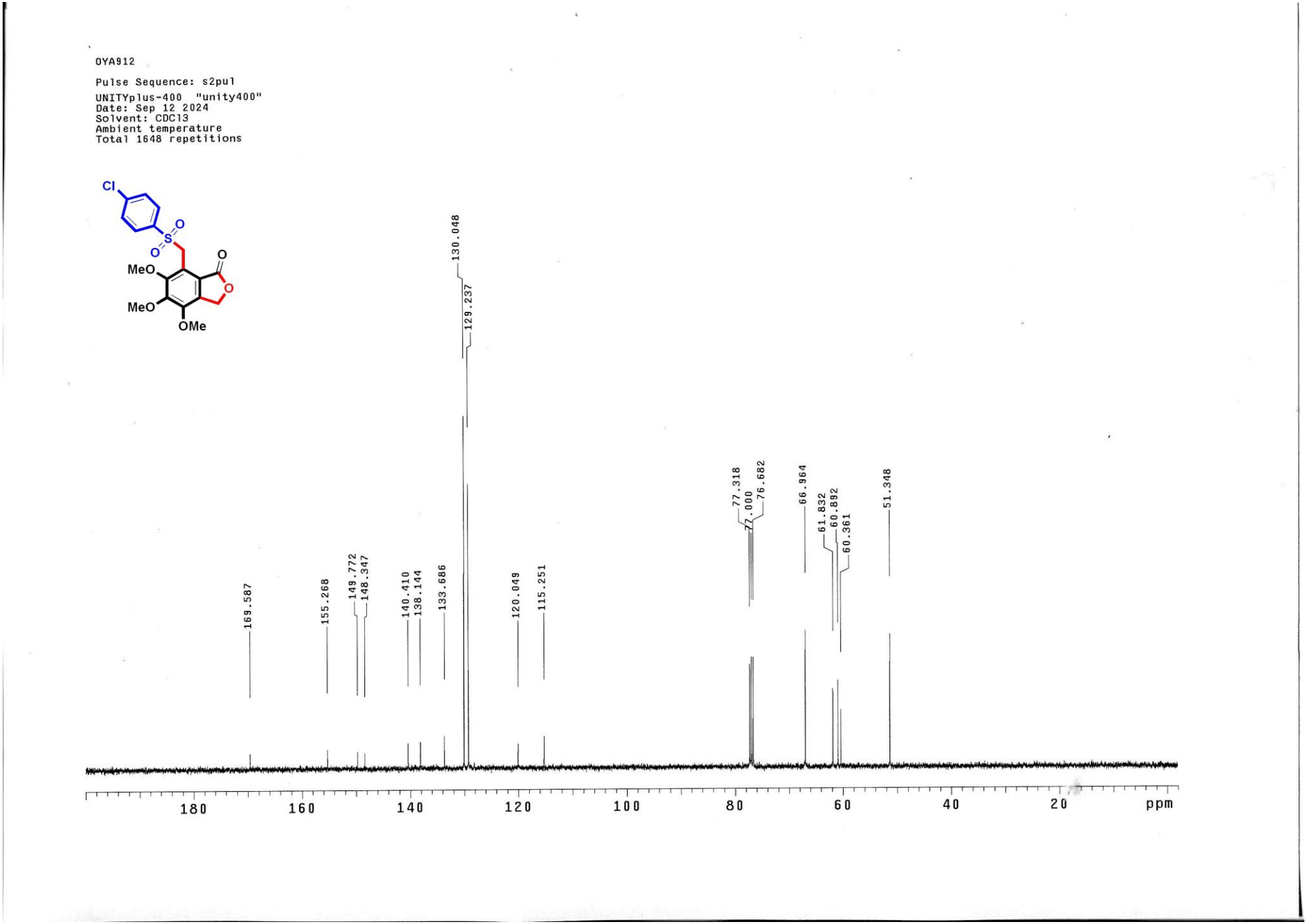
Compound 4b (^{19}F-NMR spectral data)



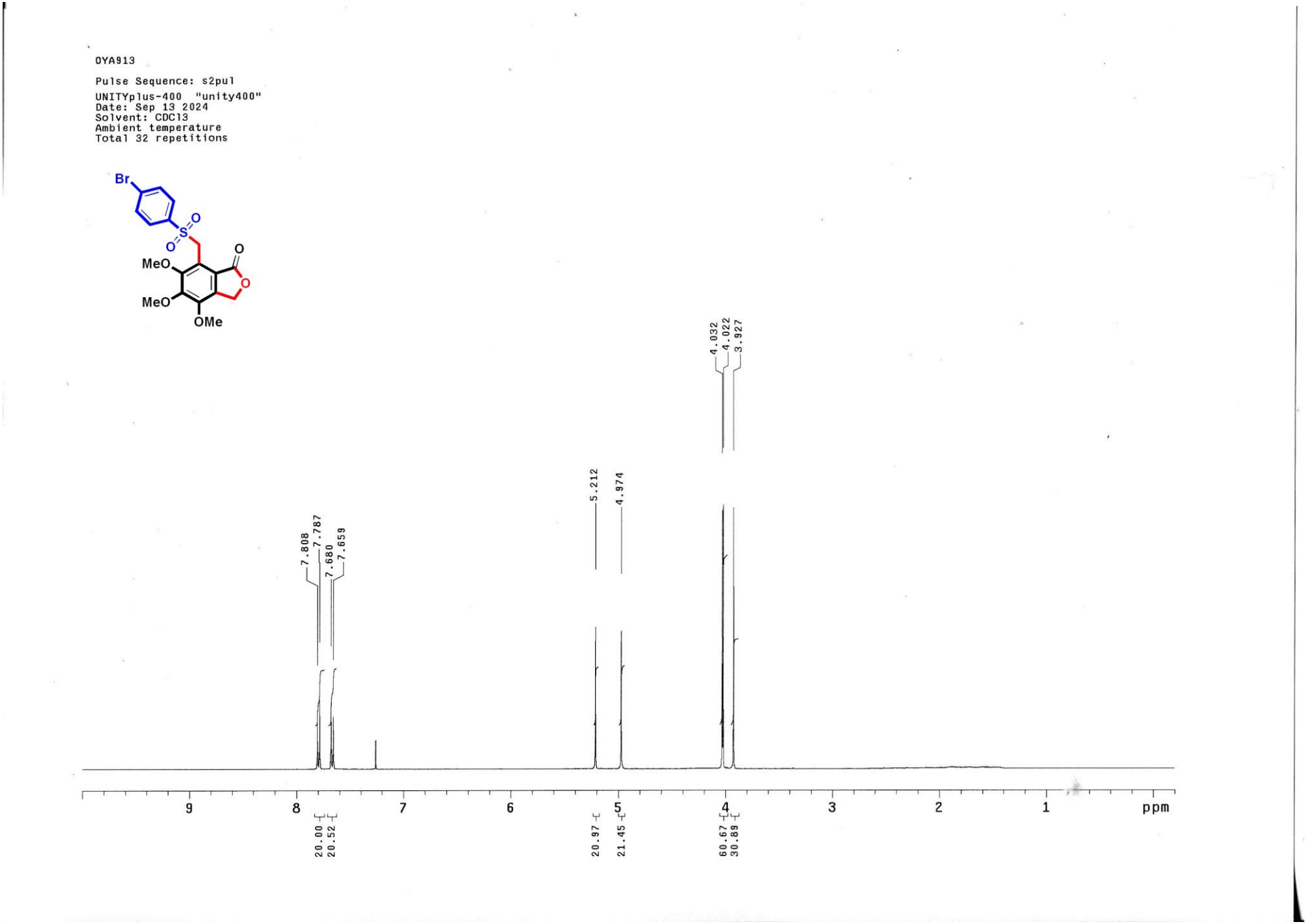
Compound 4c (^{1}H-NMR spectral data)



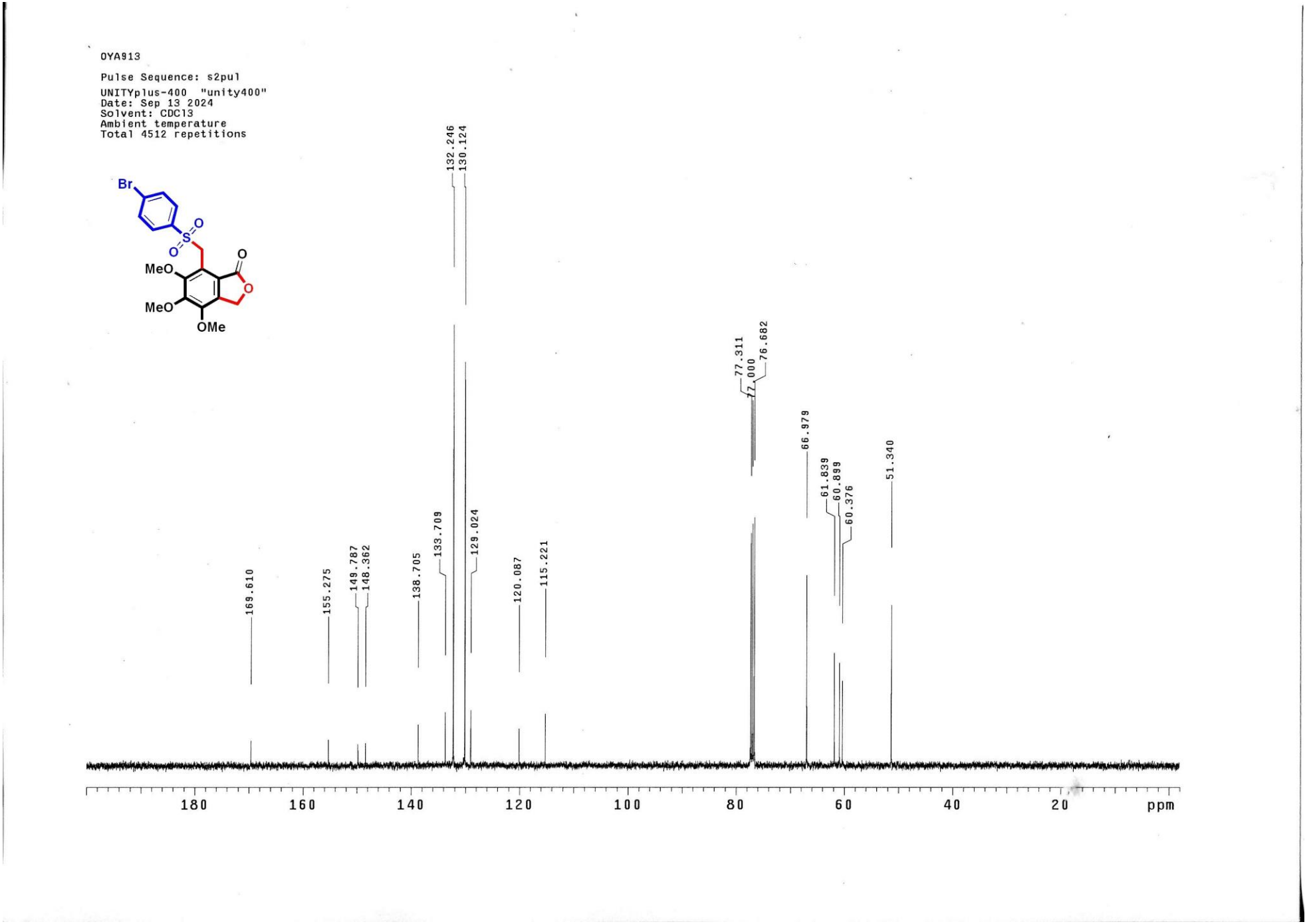
Compound 4c (^{13}C-NMR spectral data)



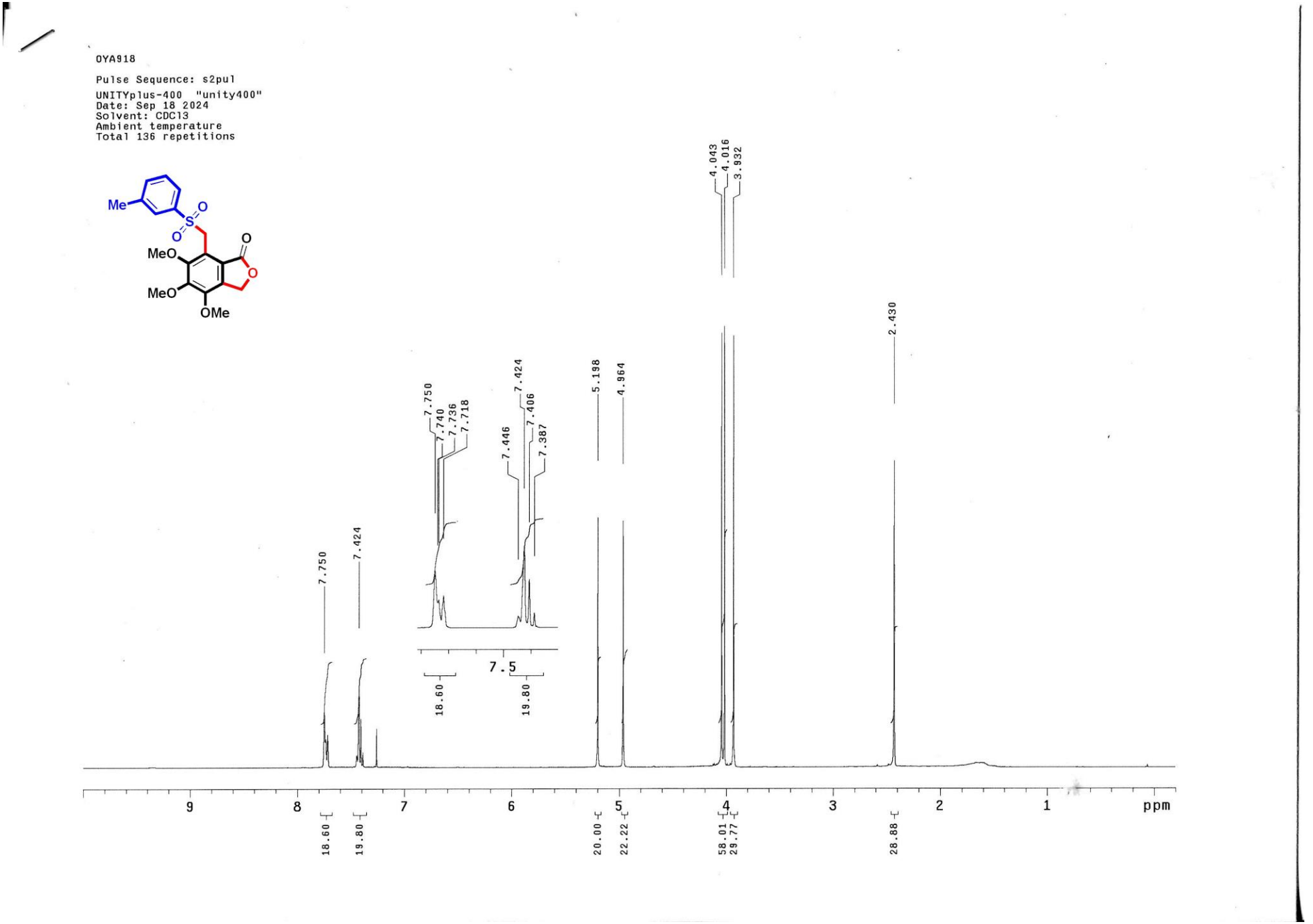
Compound 4d (^{1}H-NMR spectral data)



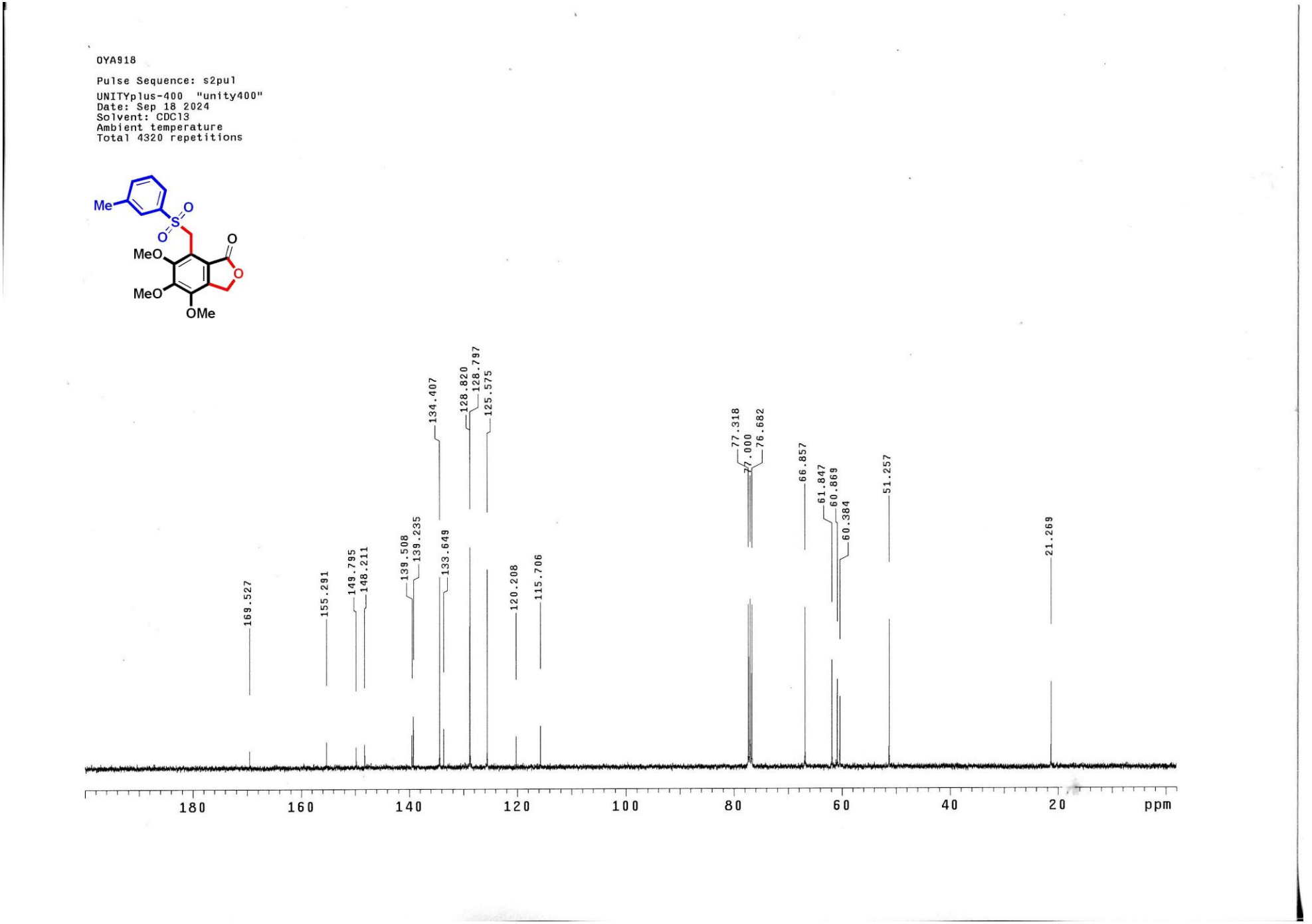
Compound 4d (^{13}C-NMR spectral data)



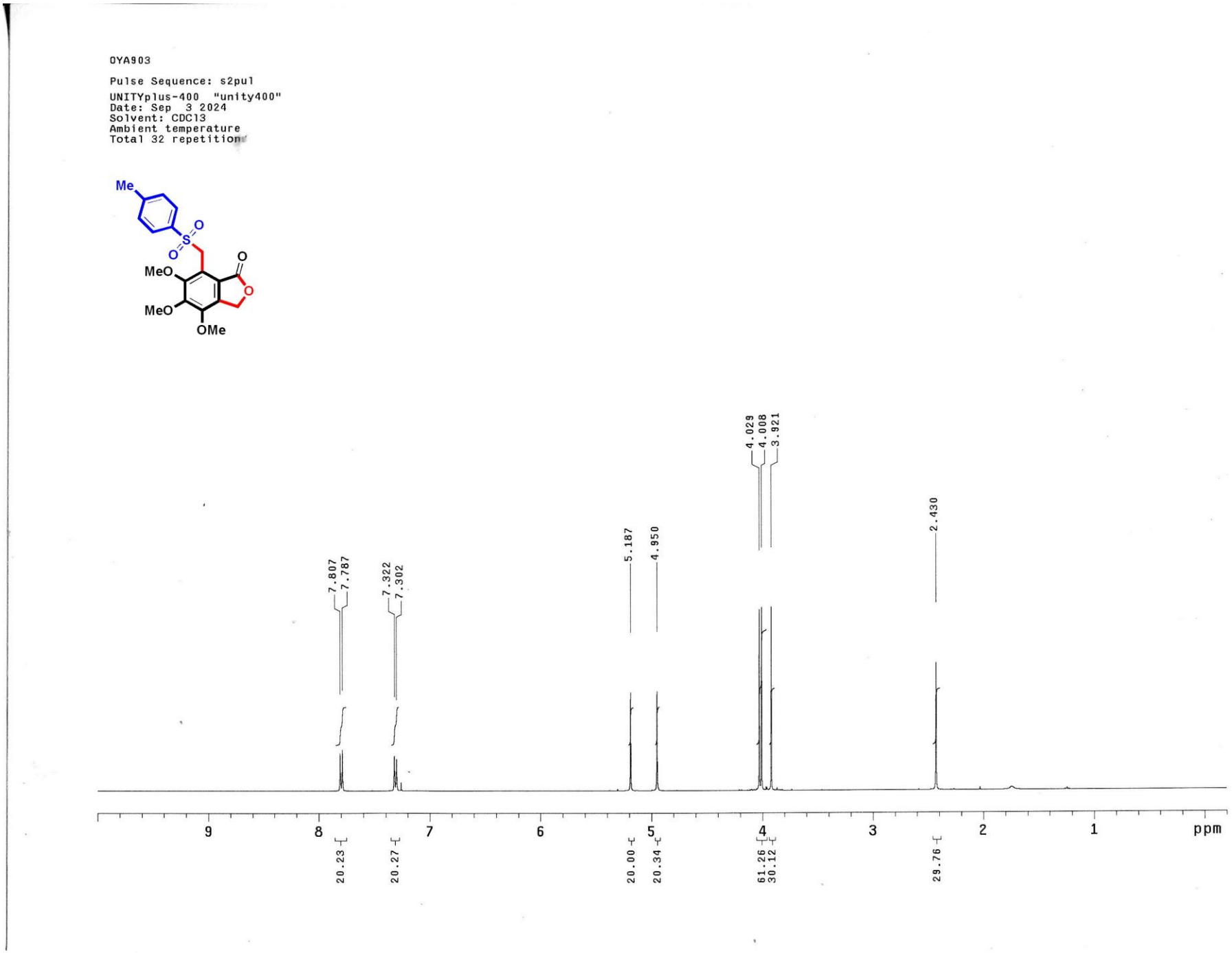
Compound 4e (^{1}H-NMR spectral data)



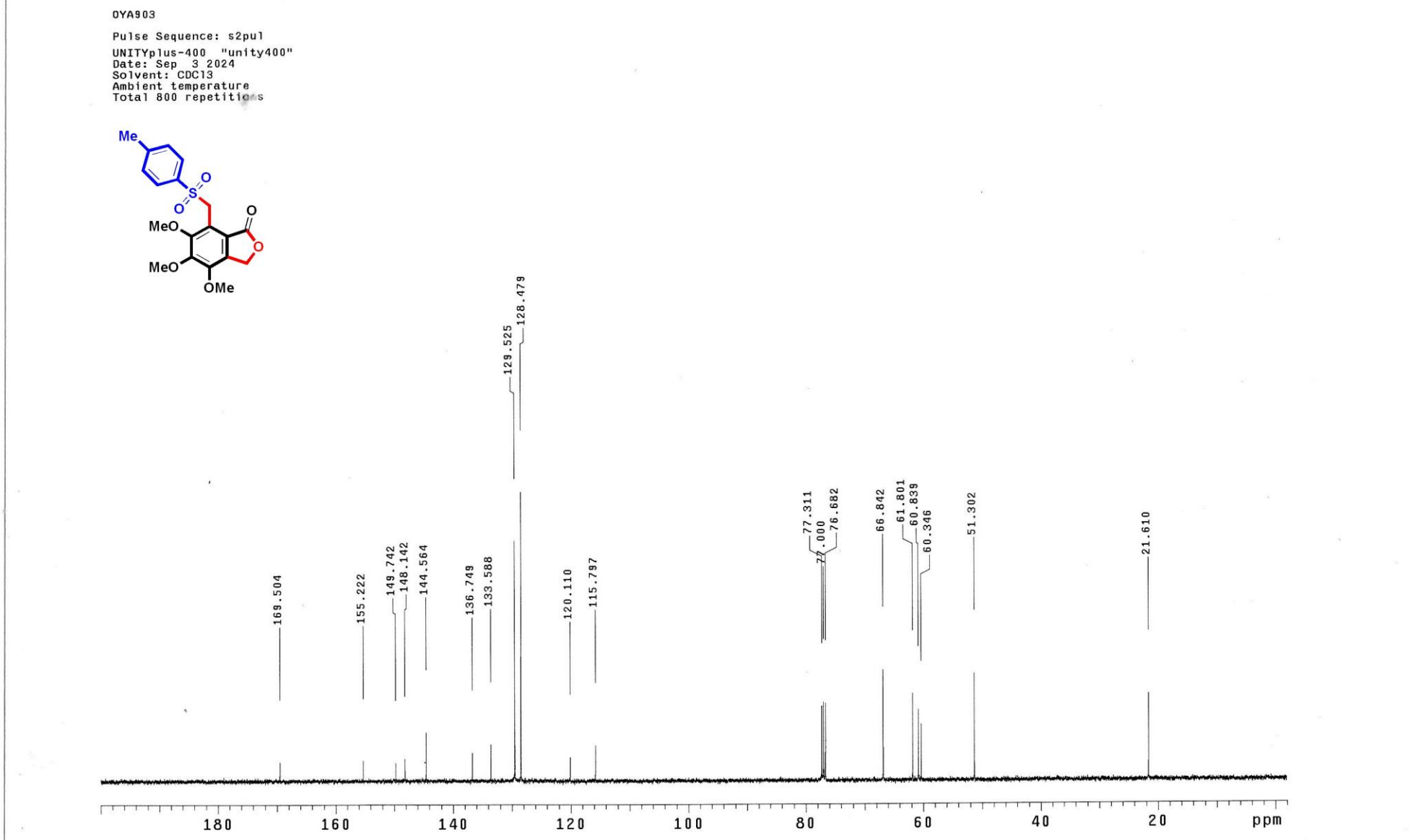
Compound 4e (^{13}C-NMR spectral data)



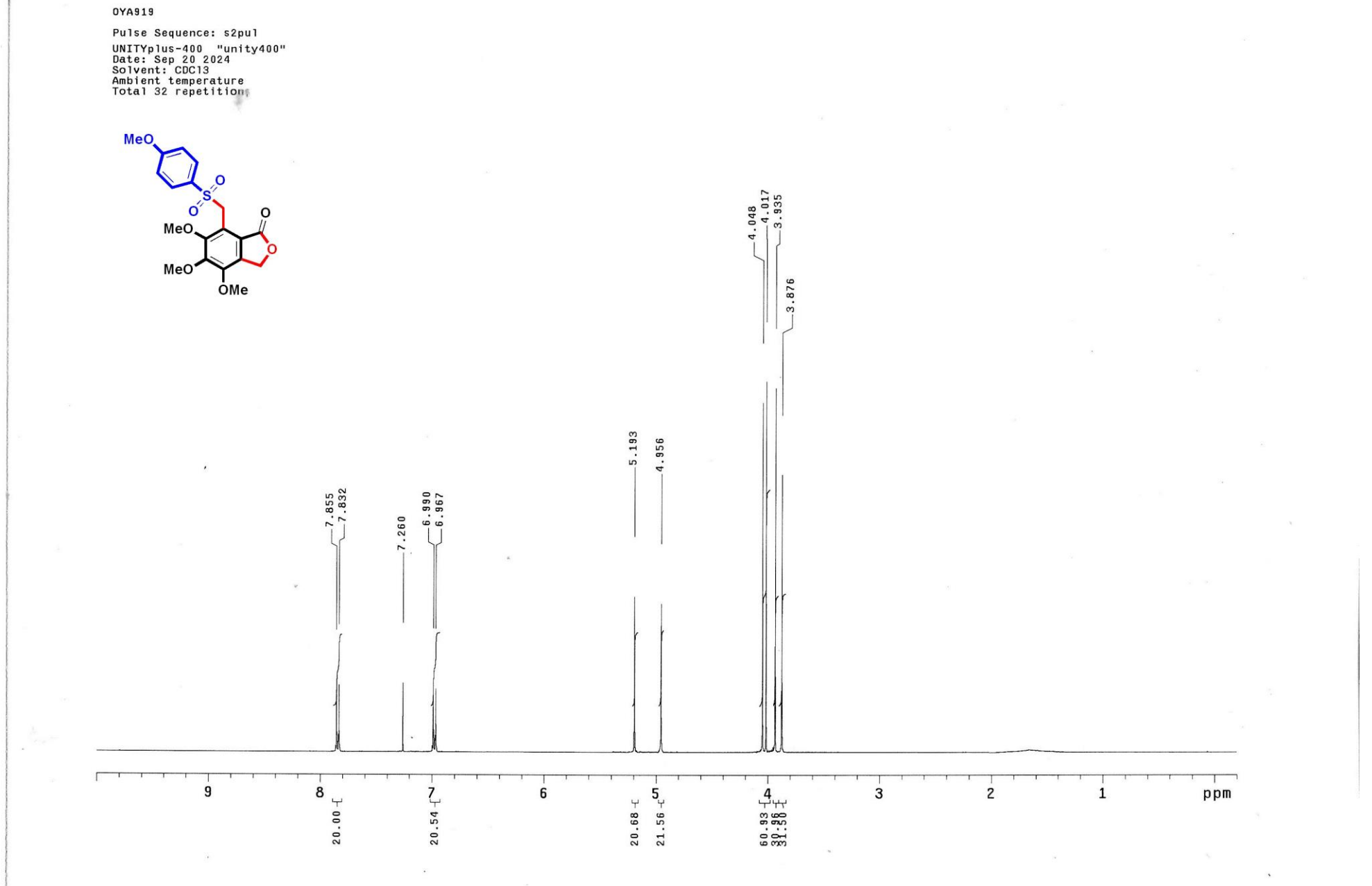
Compound 4f (^{1}H-NMR spectral data)



Compound 4f (^{13}C-NMR spectral data)



Compound 4g (^{1}H-NMR spectral data)

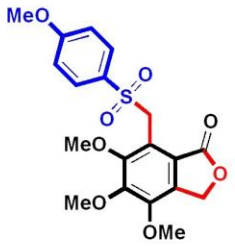


Compound 4g (^{13}C-NMR spectral data)

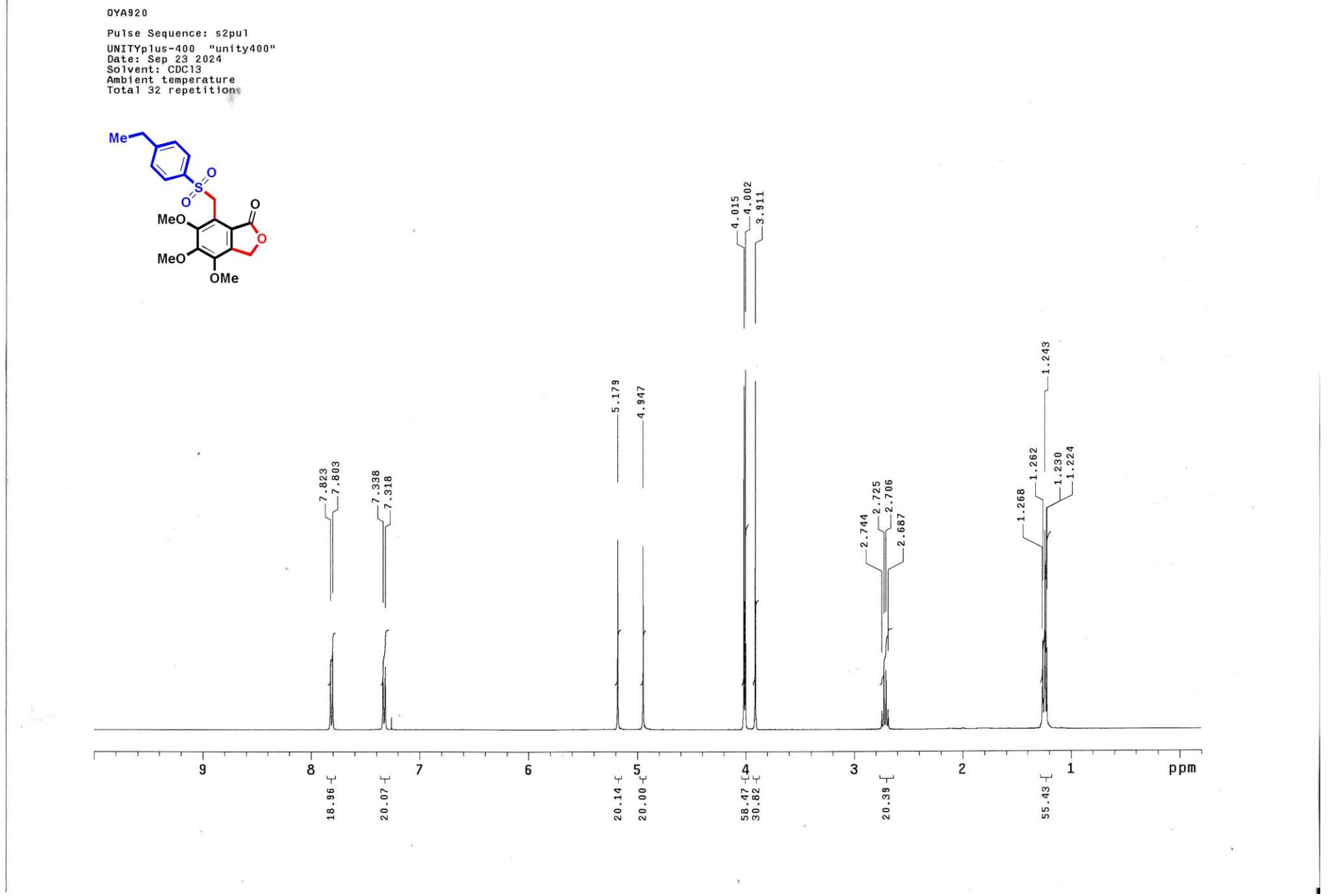
OYA919

Pulse Sequence: s2pul

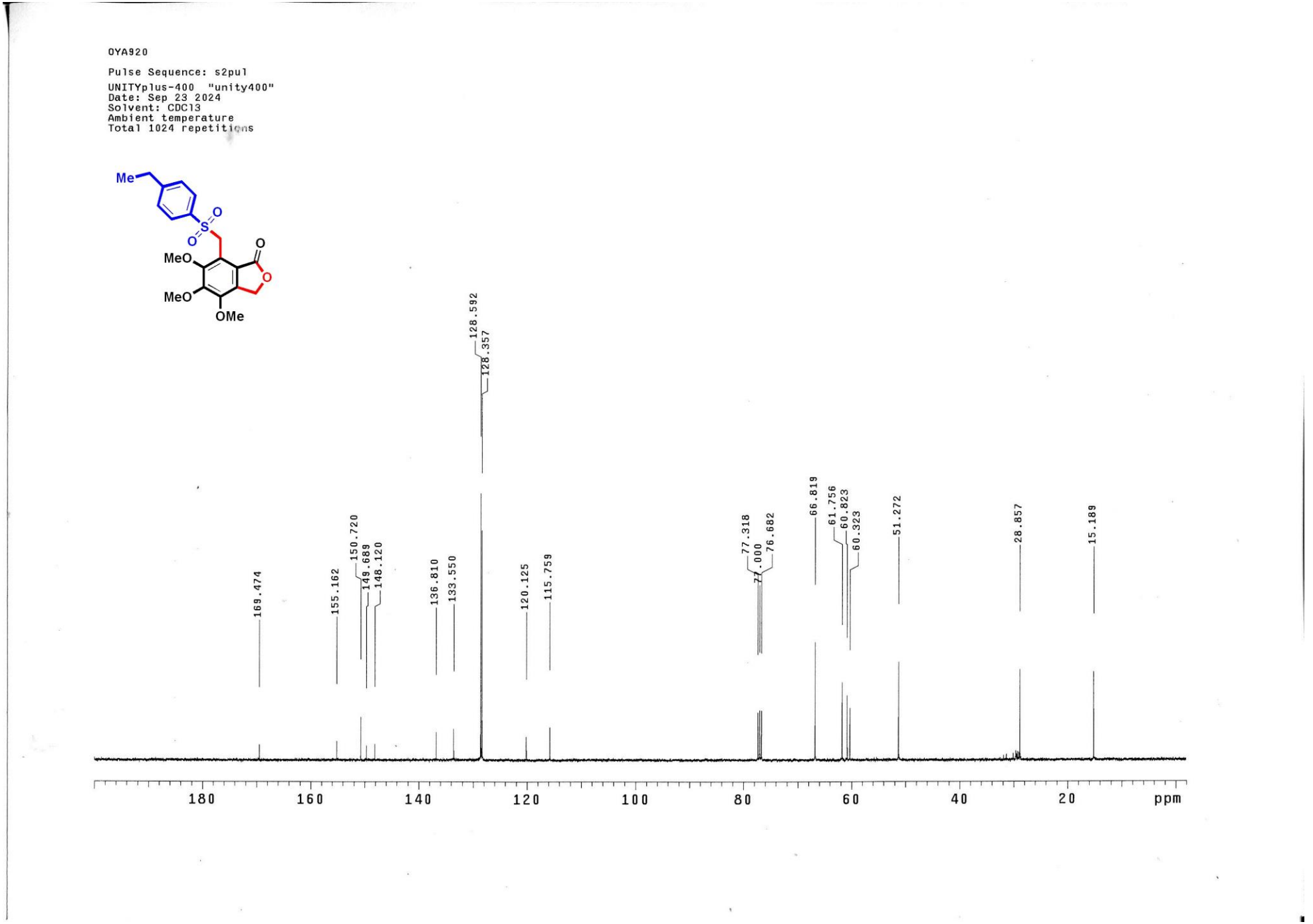
UNITYplus-400 "unity400"
Date: Sep 20 2024
Solvent: CDCl3
Ambient temperature
Total 6480 repetitions



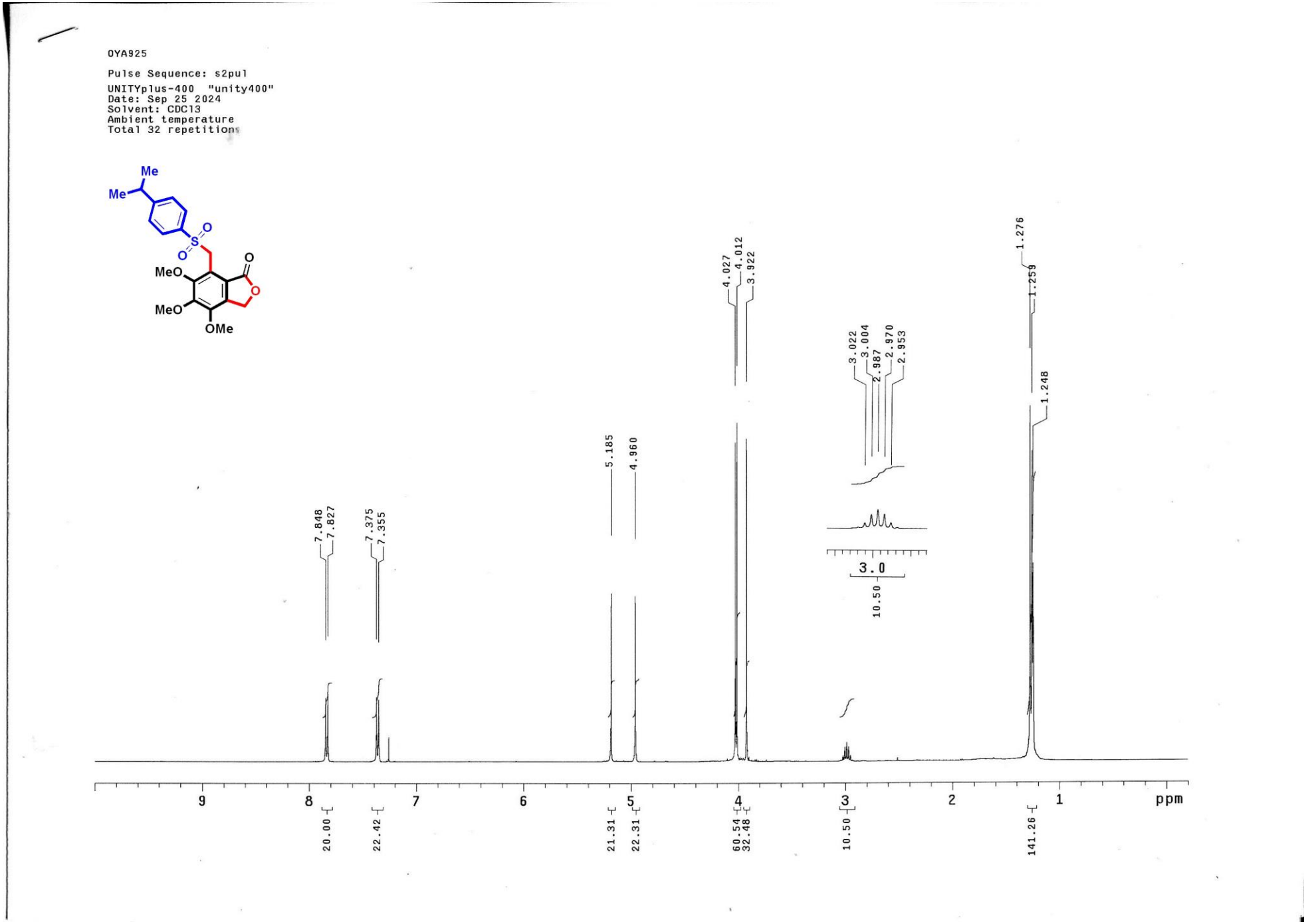
Compound 4h (^{1}H-NMR spectral data)



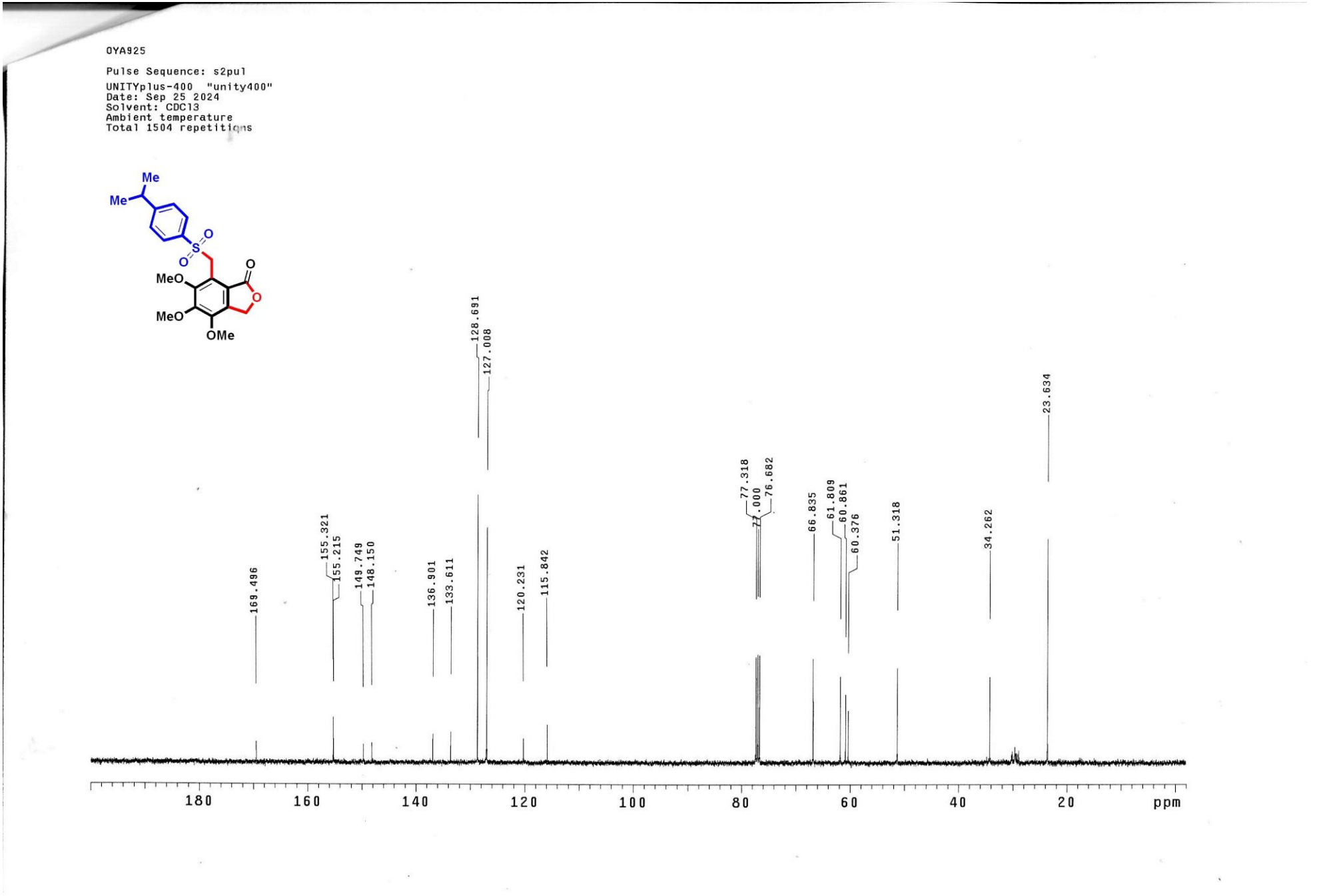
Compound 4h (^{13}C-NMR spectral data)



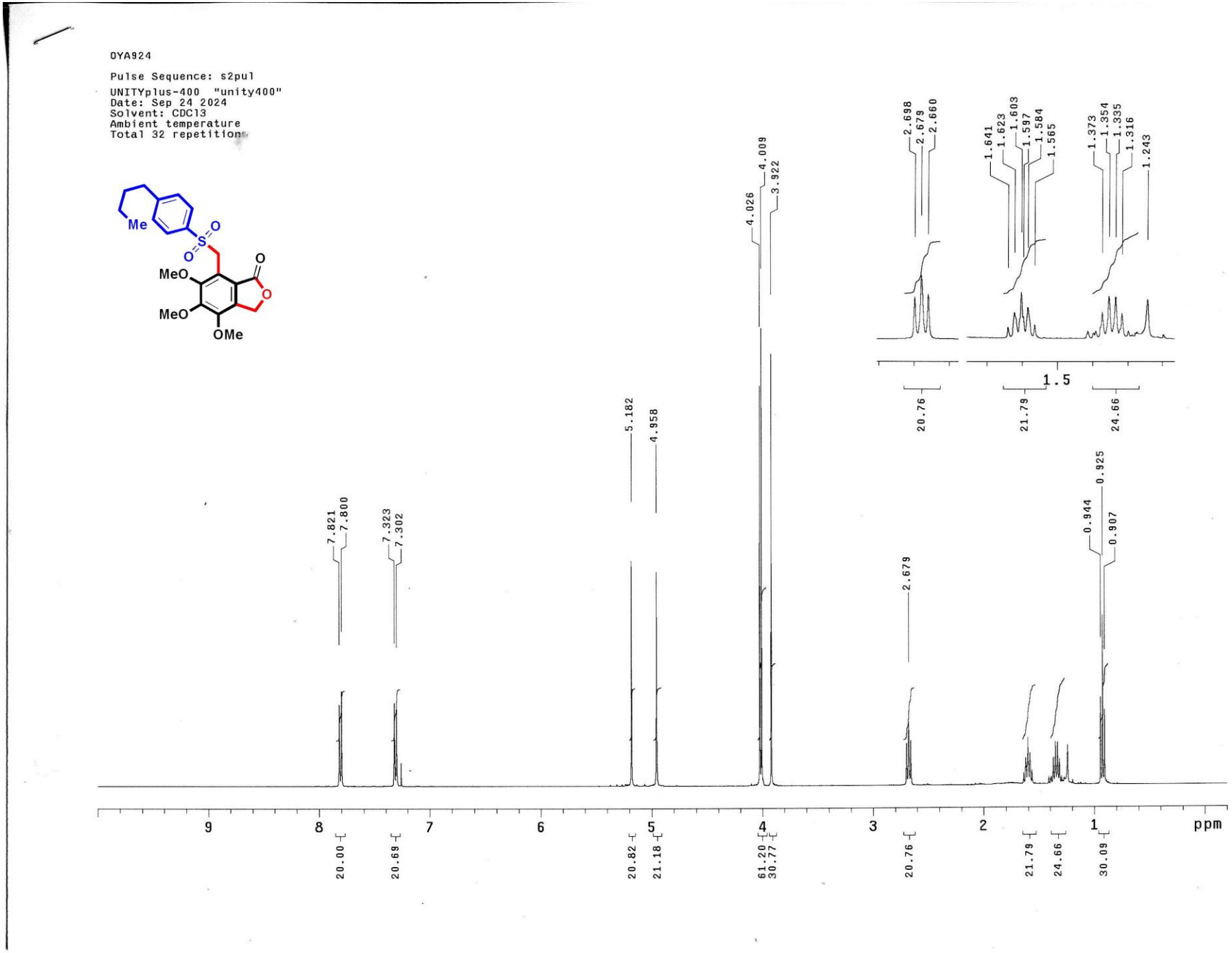
Compound 4i (^{1}H-NMR spectral data)



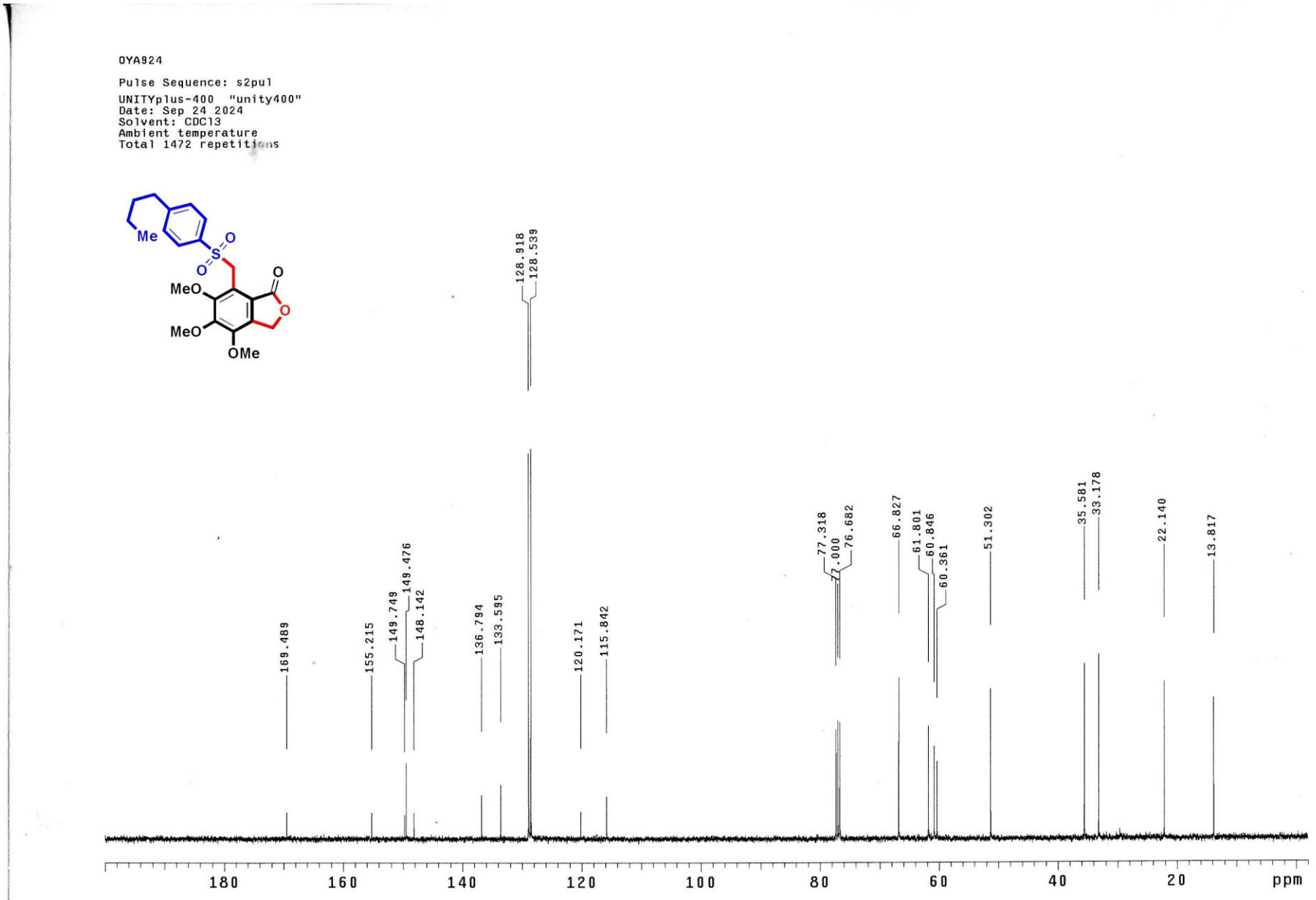
Compound 4i (^{13}C-NMR spectral data)



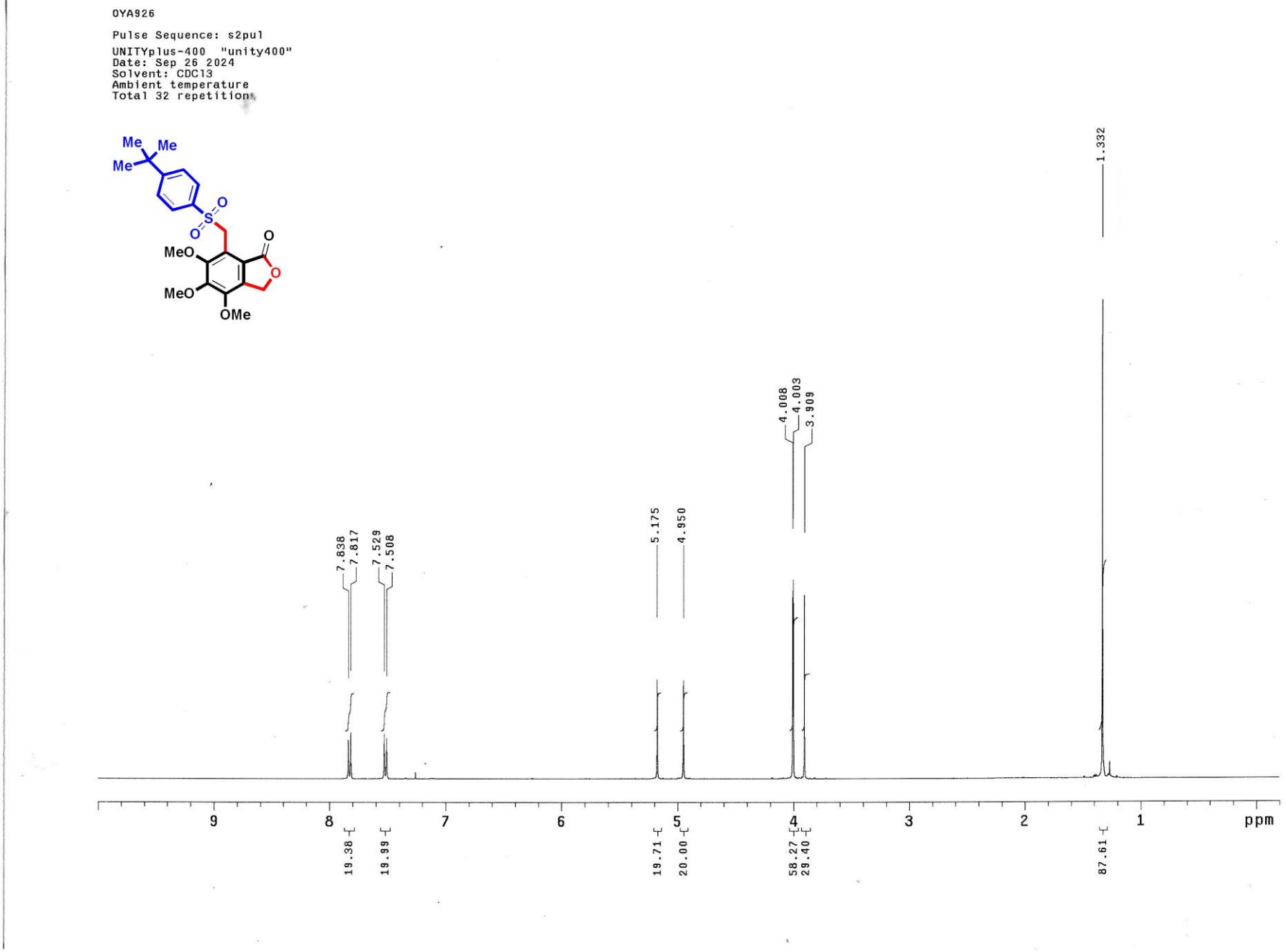
Compound 4j (^{1}H-NMR spectral data)



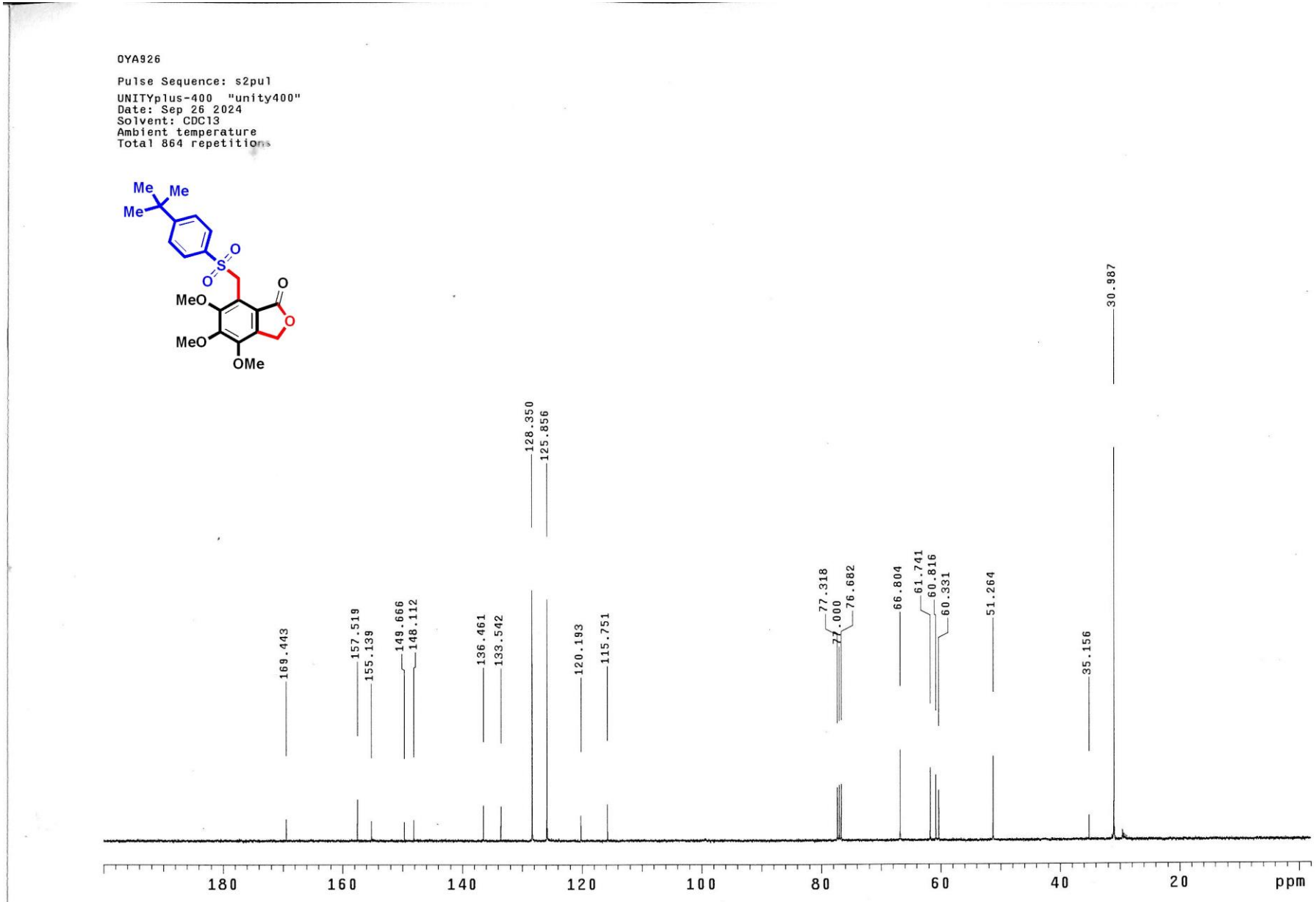
Compound 4j (^{13}C-NMR spectral data)



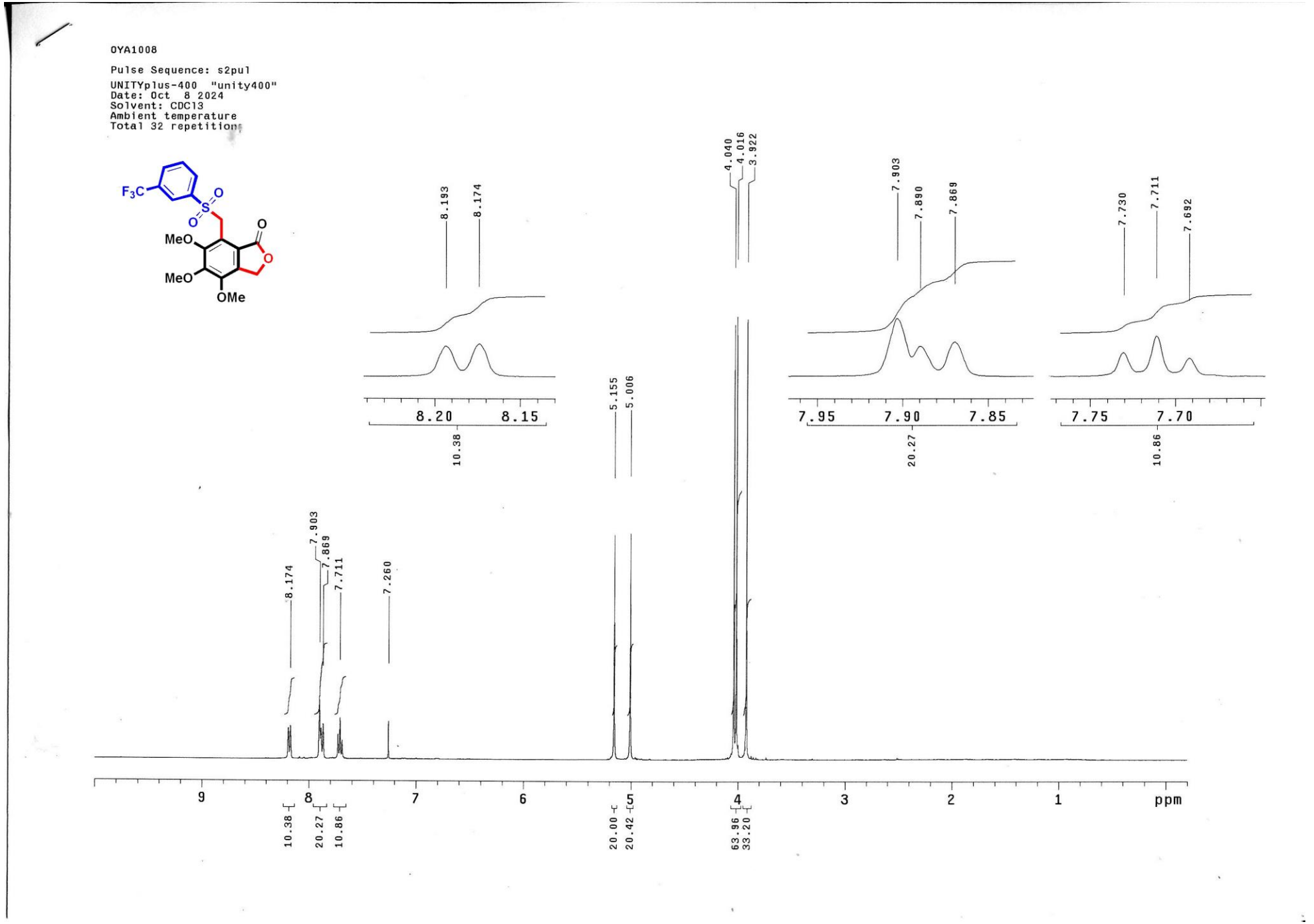
Compound 4k (^{1}H-NMR spectral data)



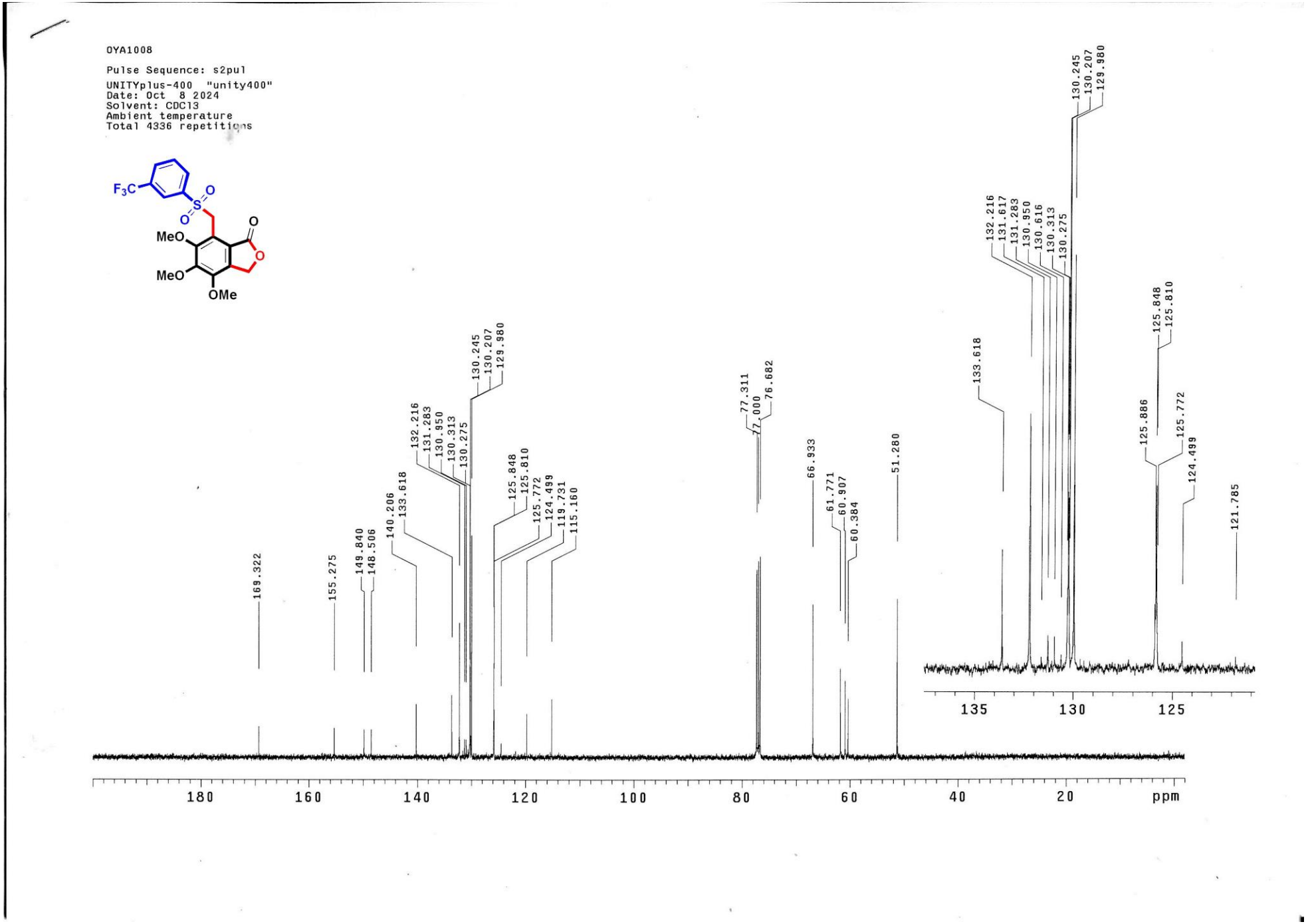
Compound 4k (^{13}C-NMR spectral data)



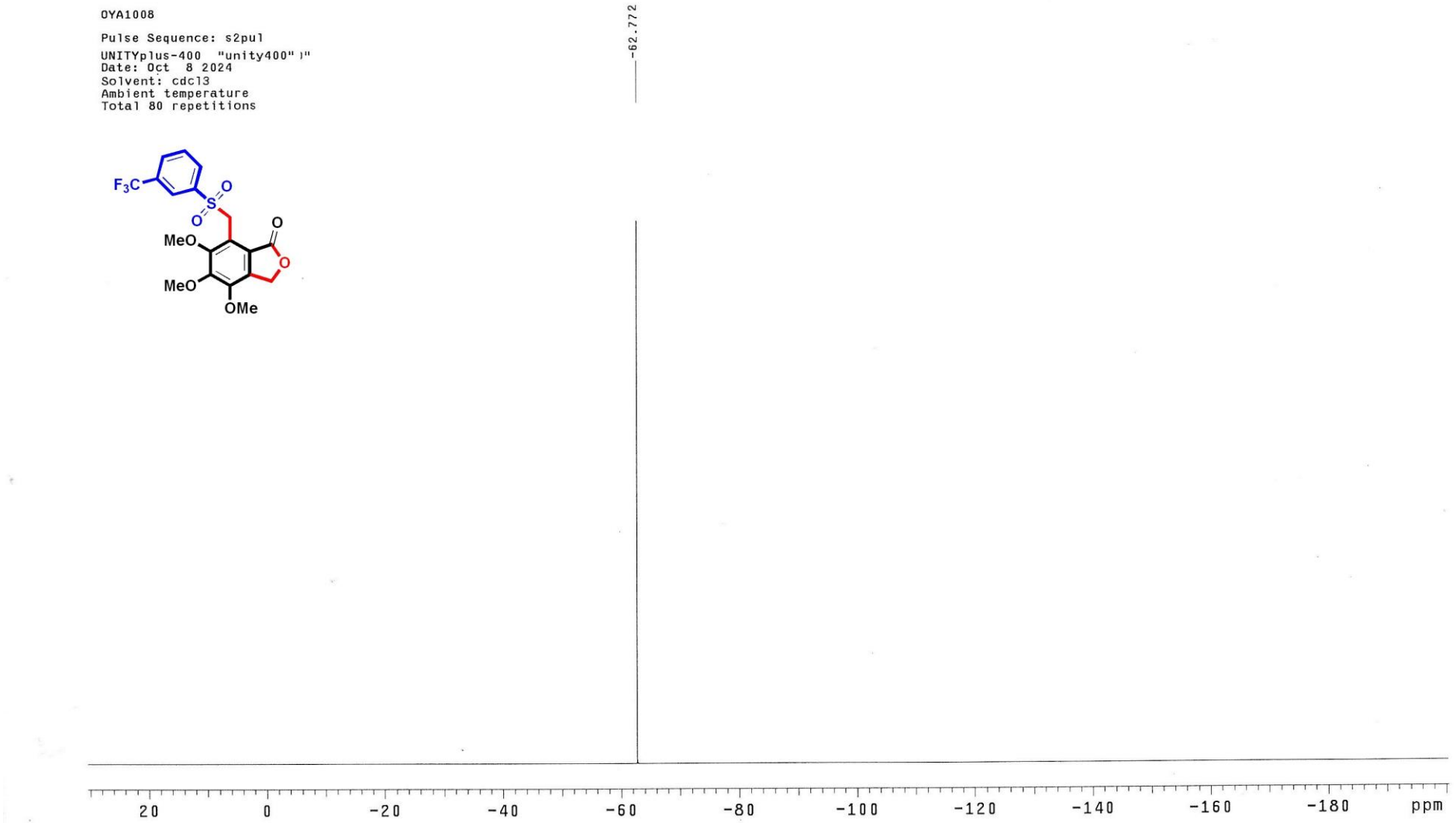
Compound 4m (^{1}H-NMR spectral data)



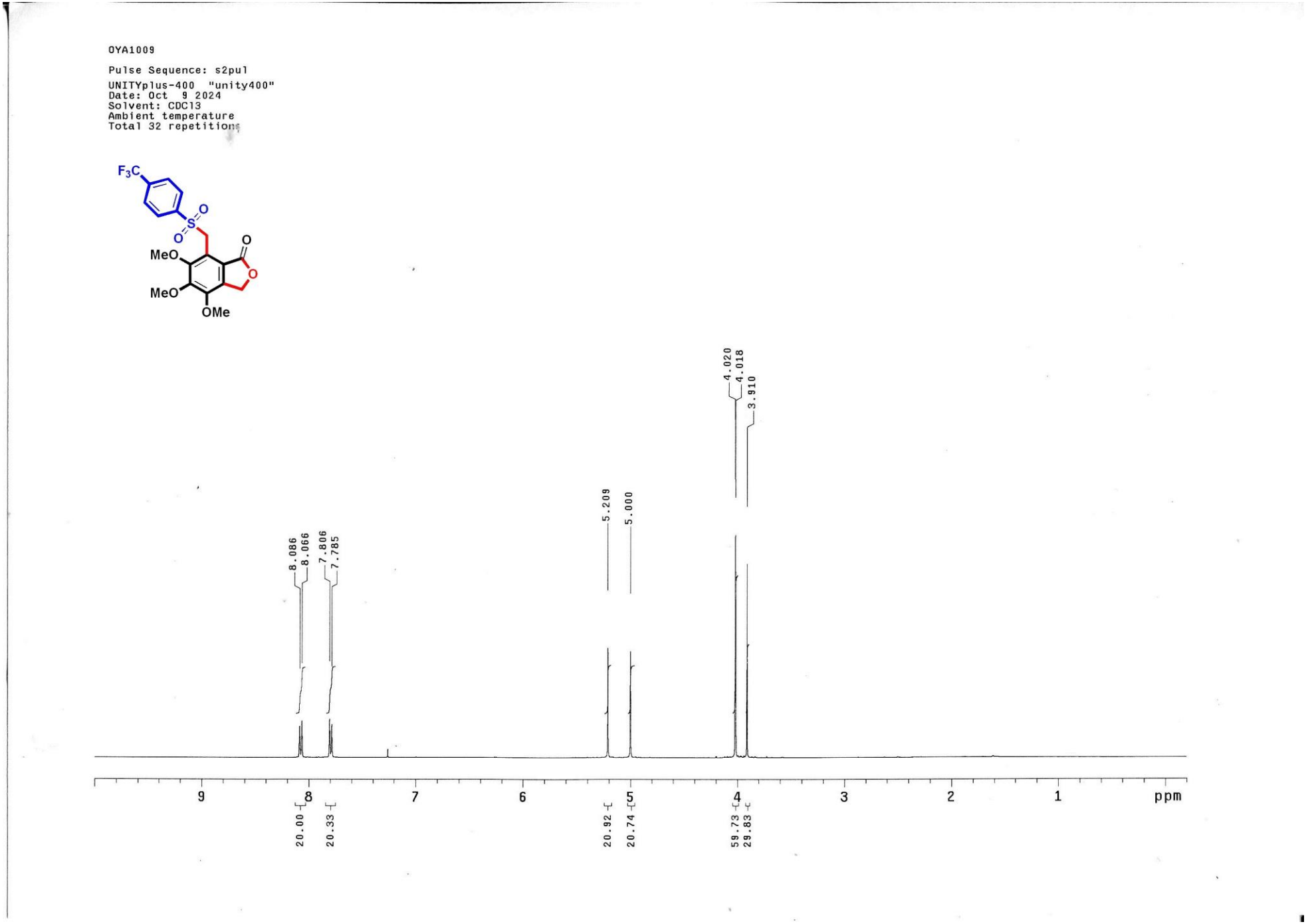
Compound 4m (^{13}C-NMR spectral data)



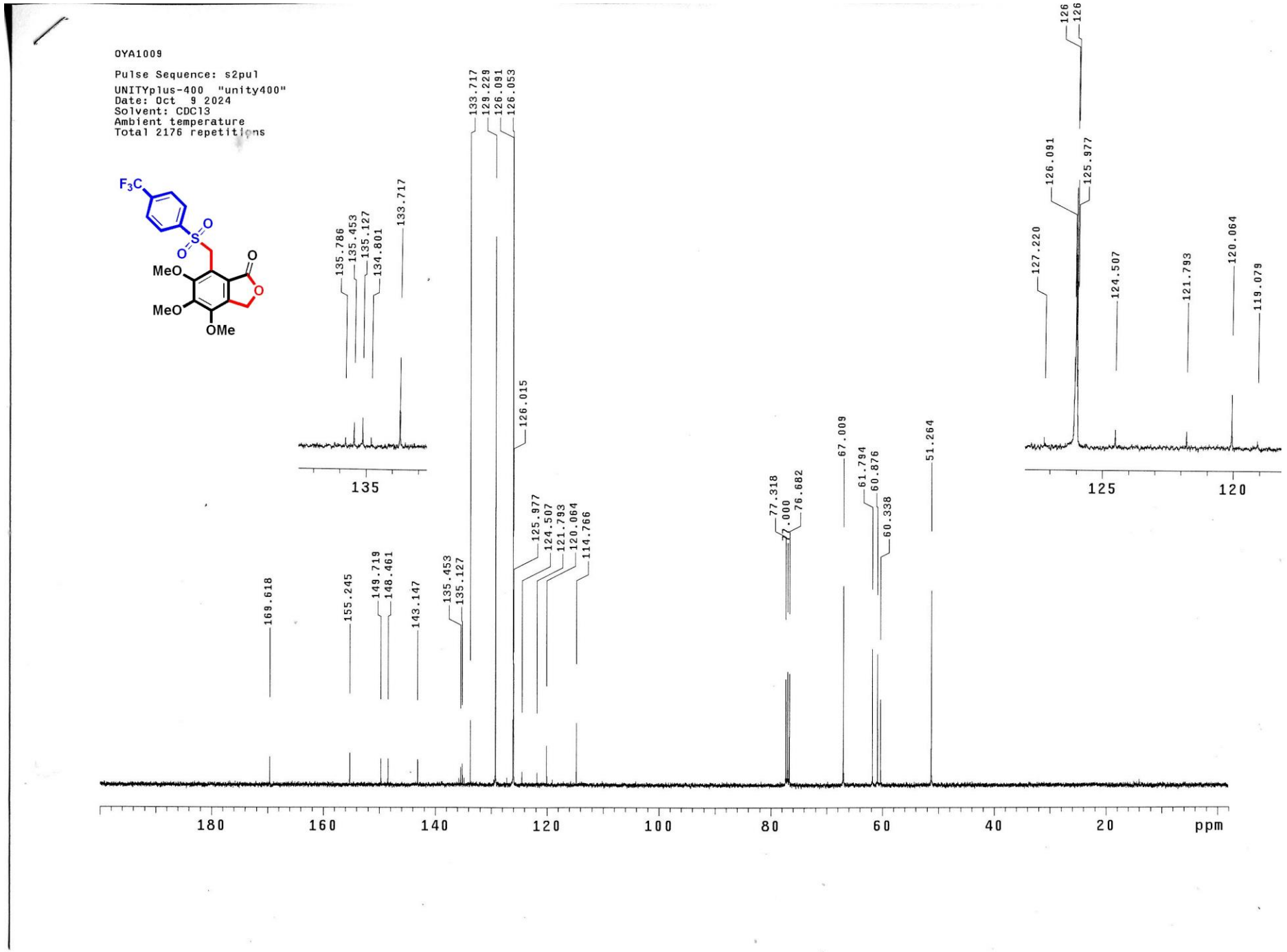
Compound 4m (^{19}F-NMR spectral data)



Compound 4n (^{1}H-NMR spectral data)



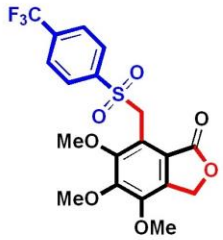
Compound 4n (^{13}C-NMR spectral data)



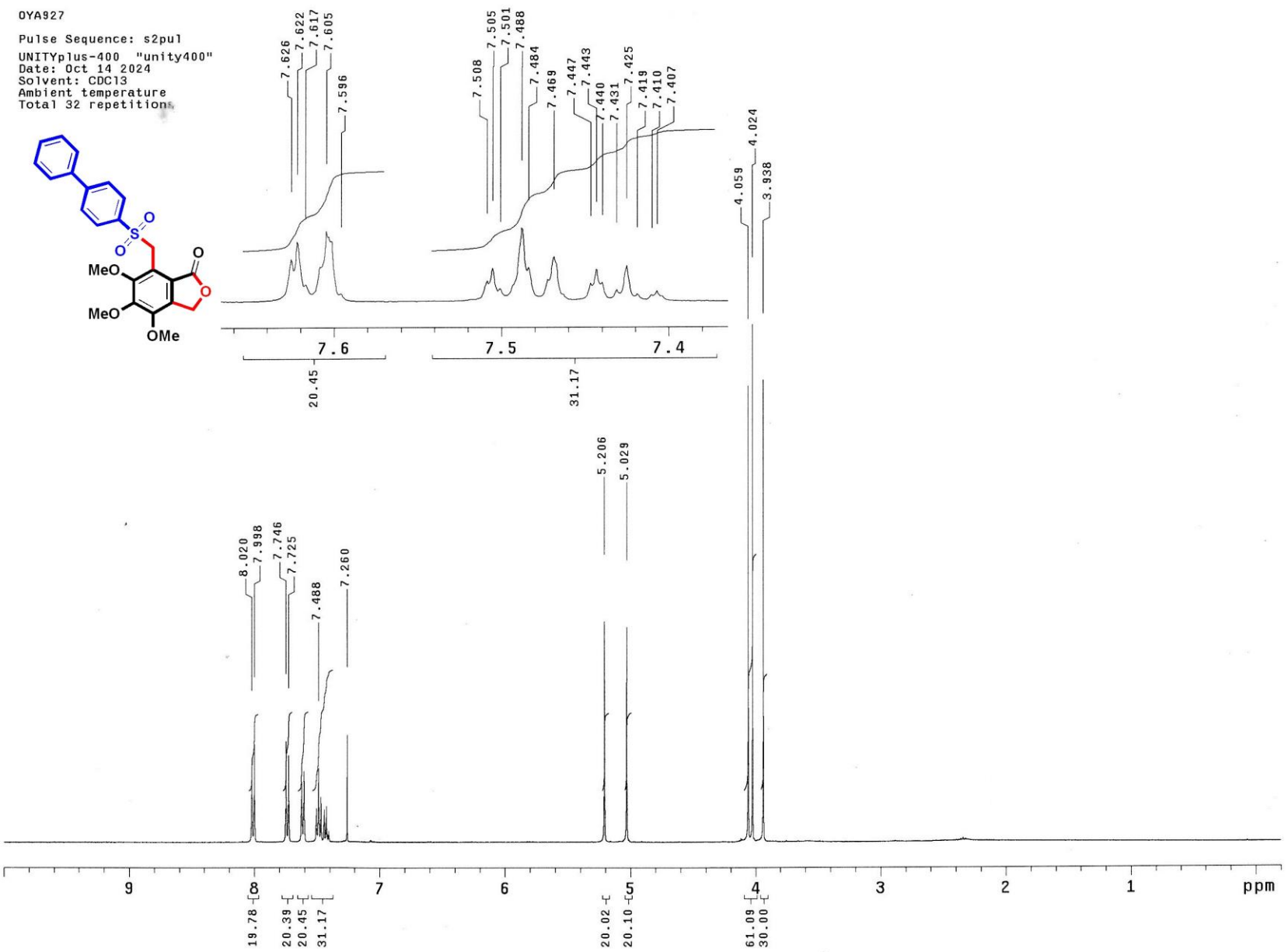
Compound 4n (^{19}F-NMR spectral data)

OYA1009

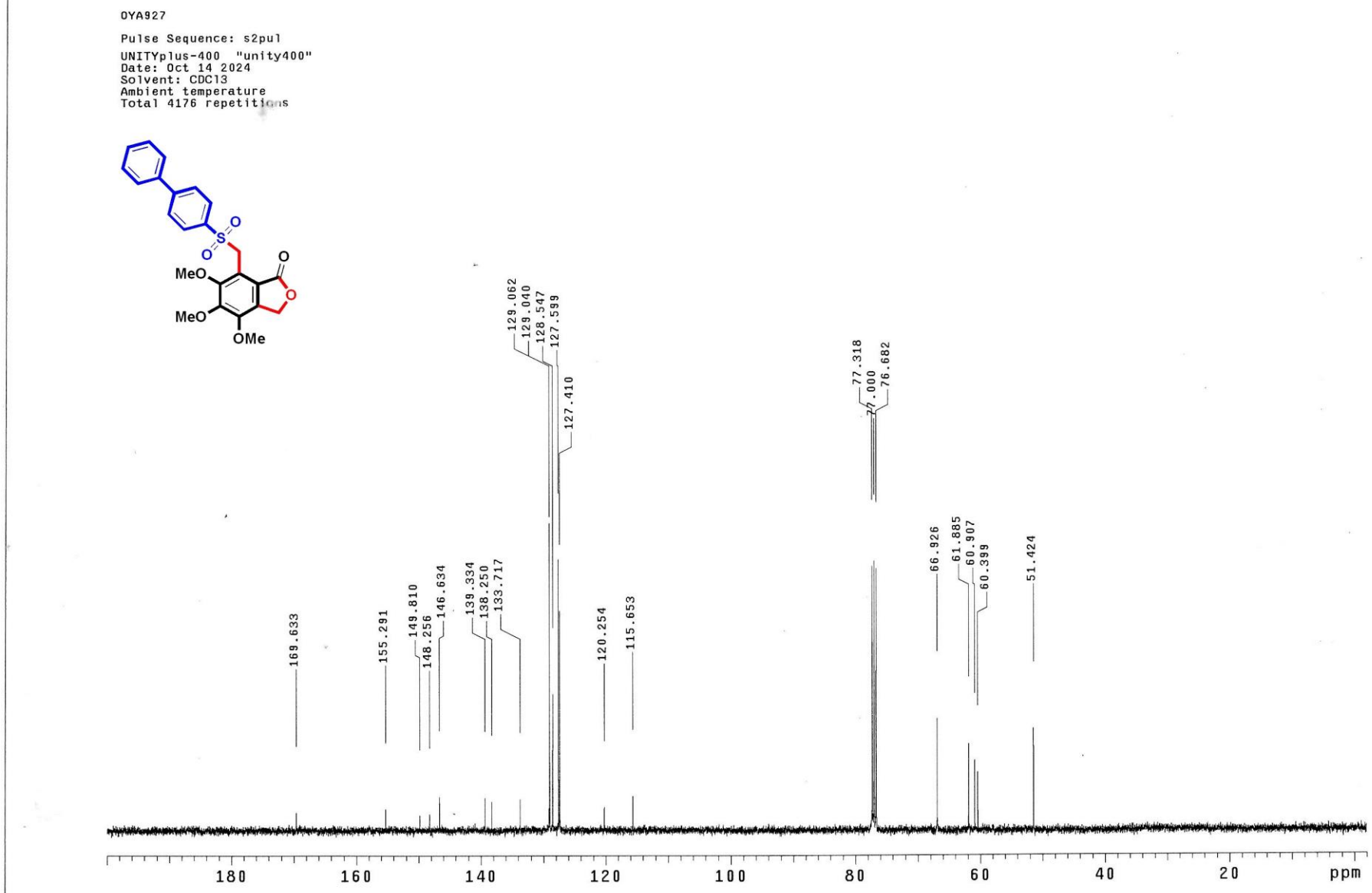
Pulse Sequence: s2pul
UNITYplus-400 "unity400" "
Date: Oct 9 2024
Solvent: CDCl3
Ambient temperature
Total 40 repetitions



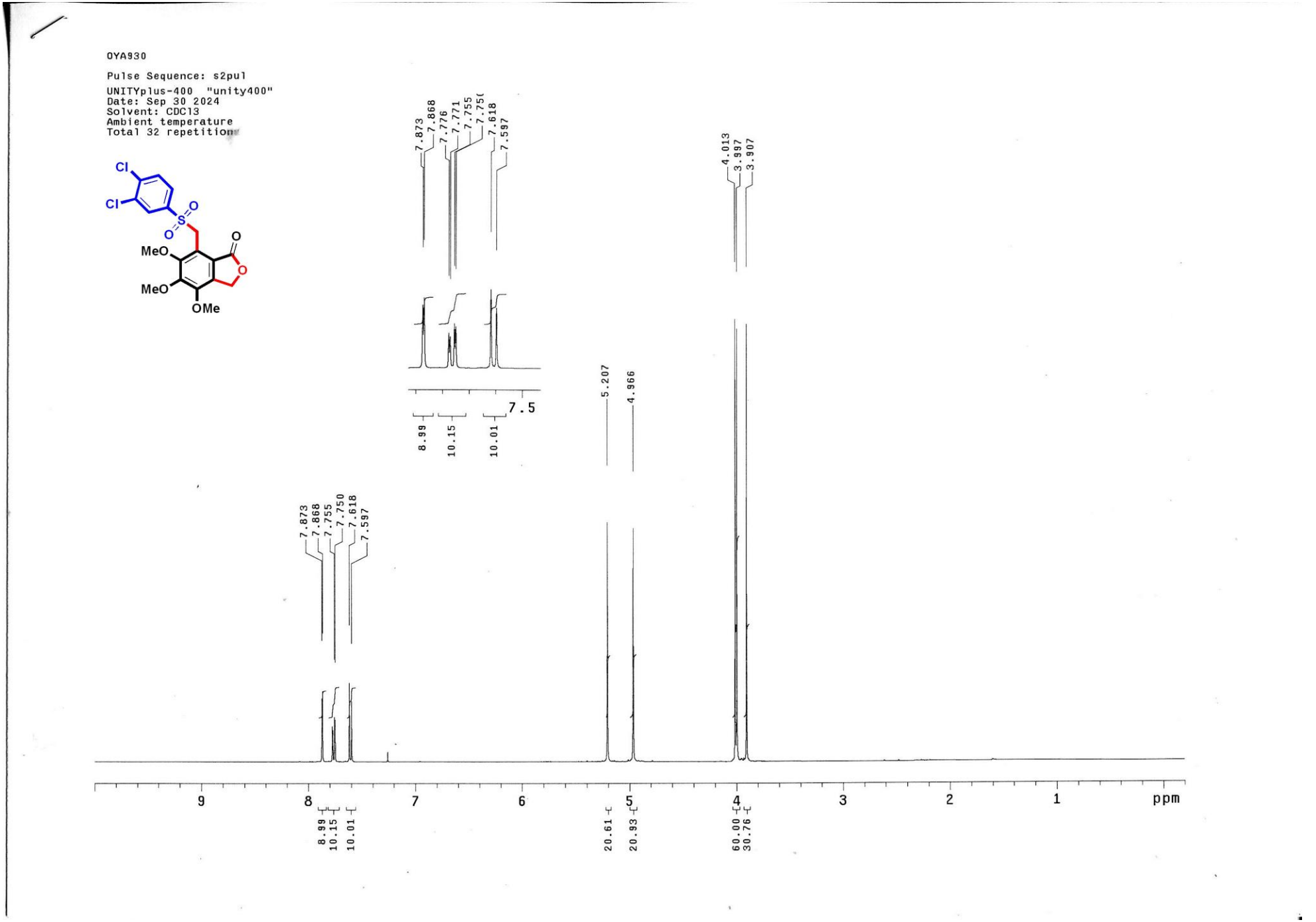
Compound 4o (^{1}H-NMR spectral data)



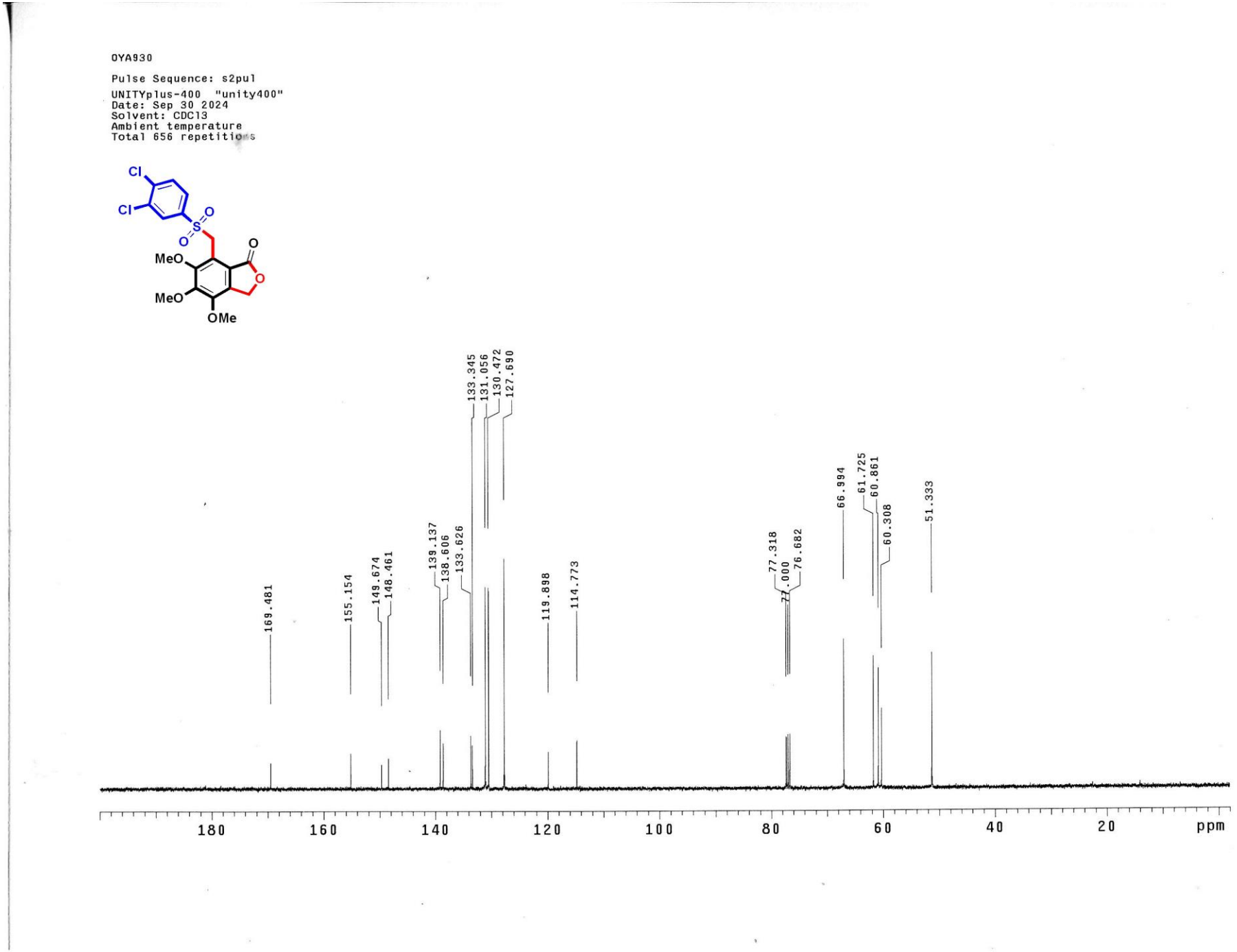
Compound 4o (^{13}C-NMR spectral data)



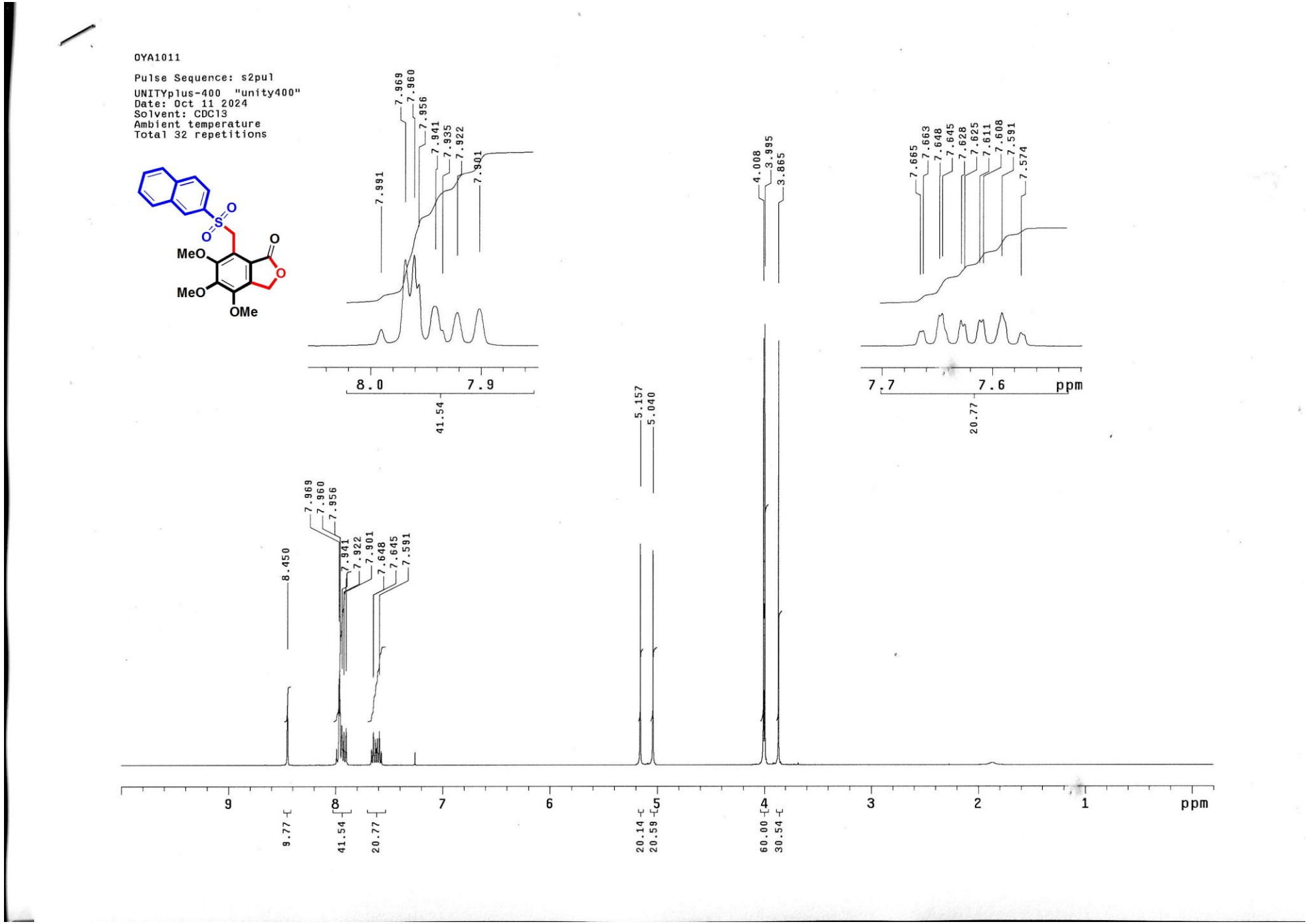
Compound 4p (^{1}H-NMR spectral data)



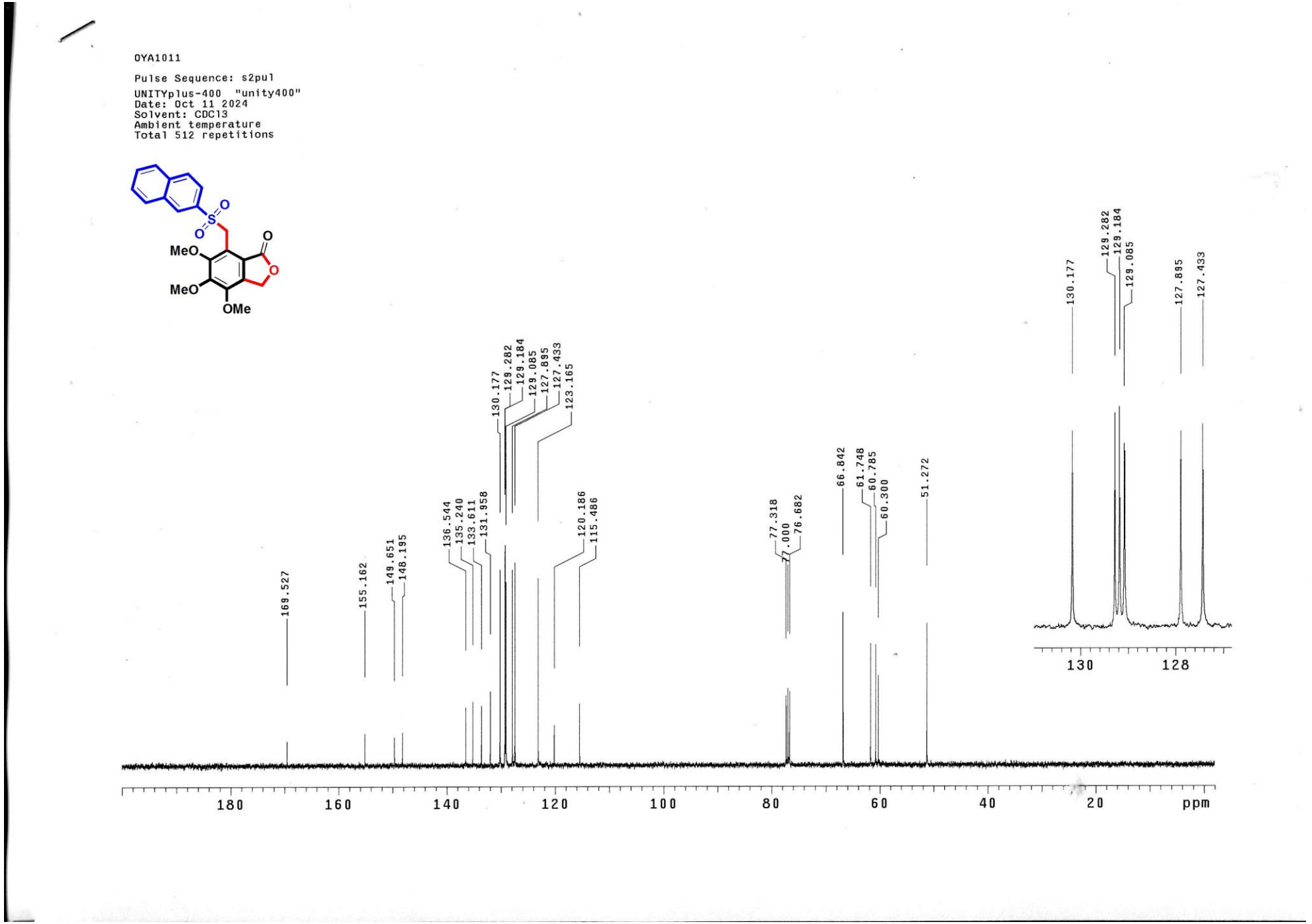
Compound 4p (^{13}C-NMR spectral data)



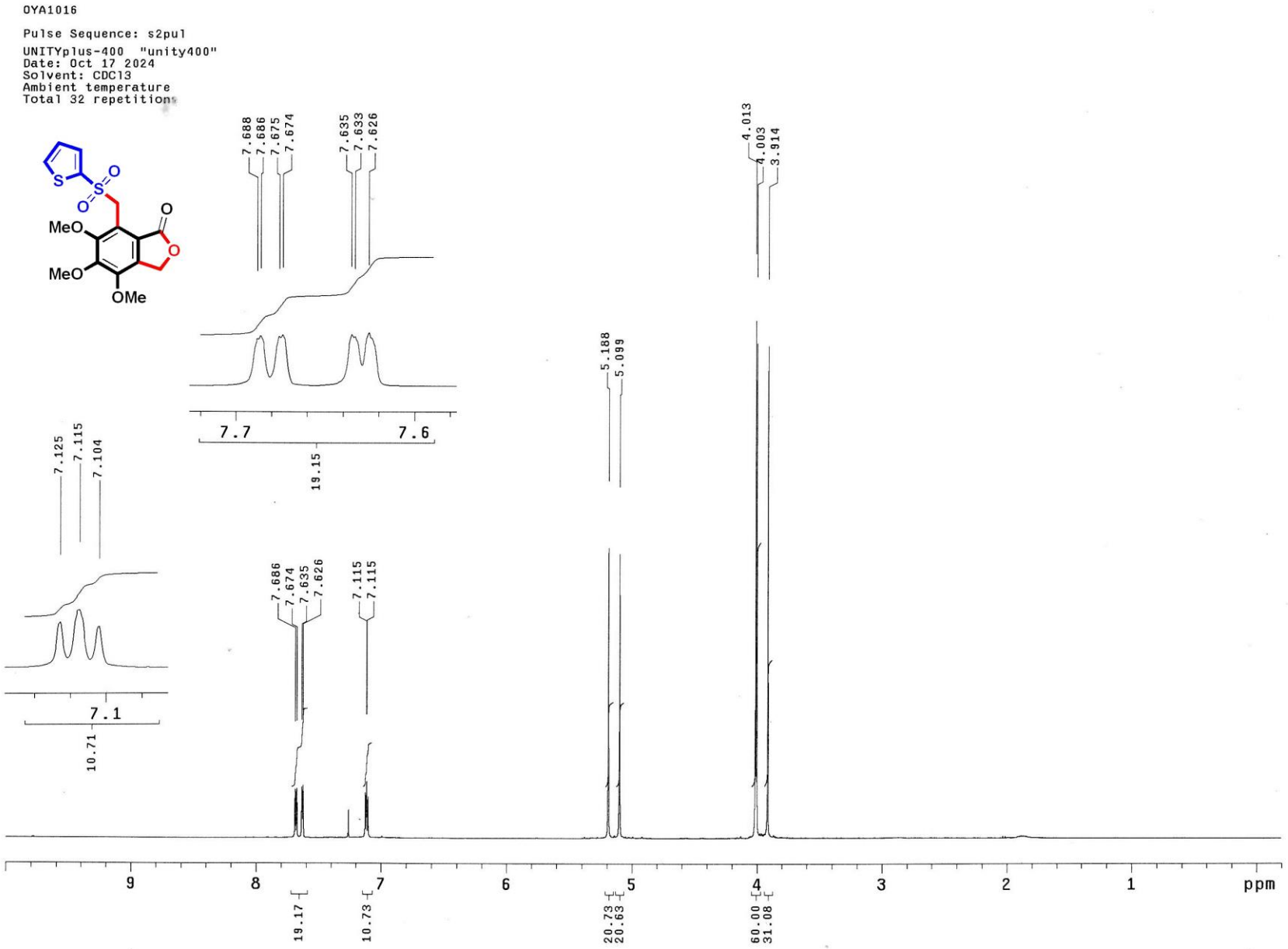
Compound 4q (^{1}H-NMR spectral data)



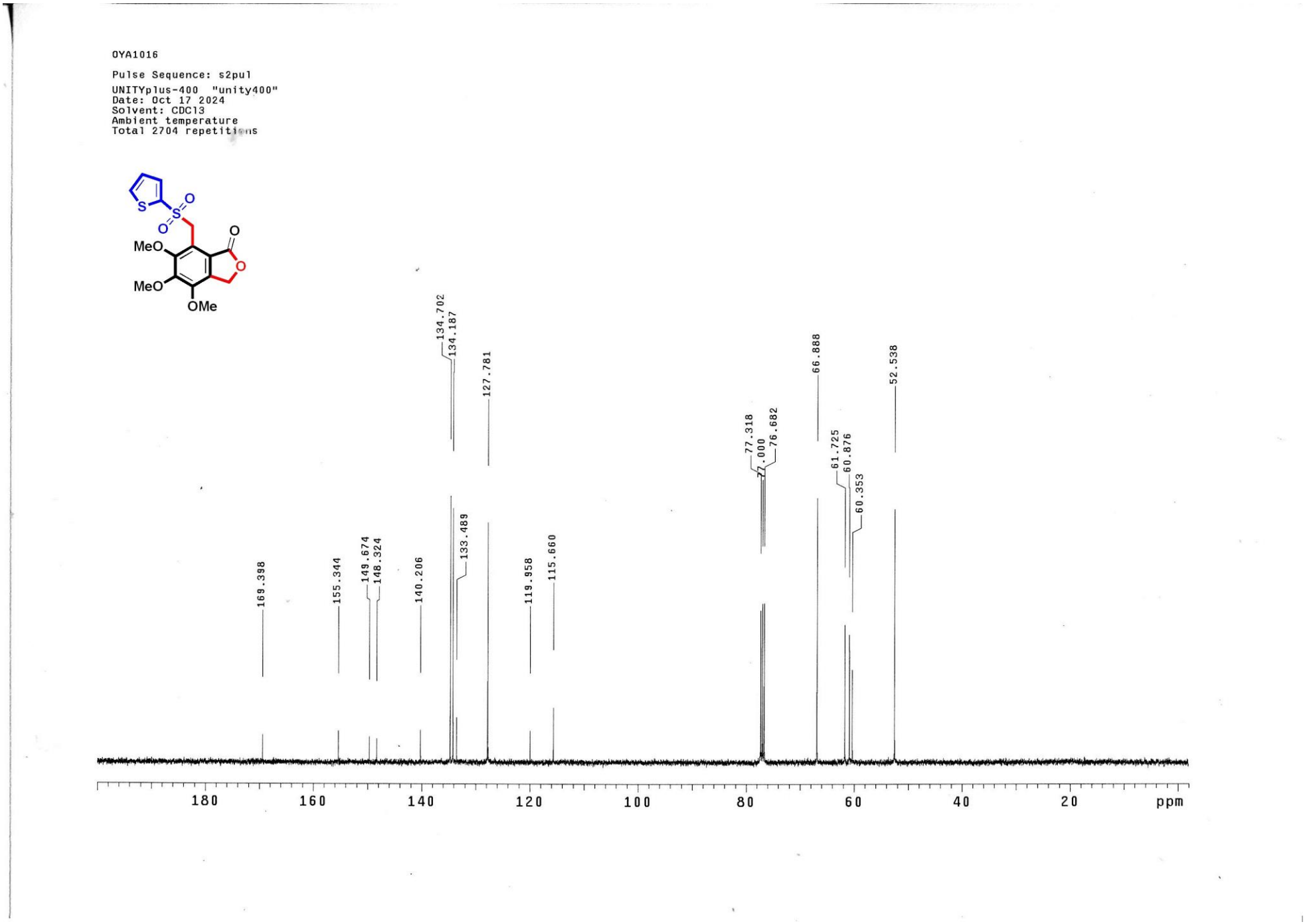
Compound 4q (^{13}C-NMR spectral data)



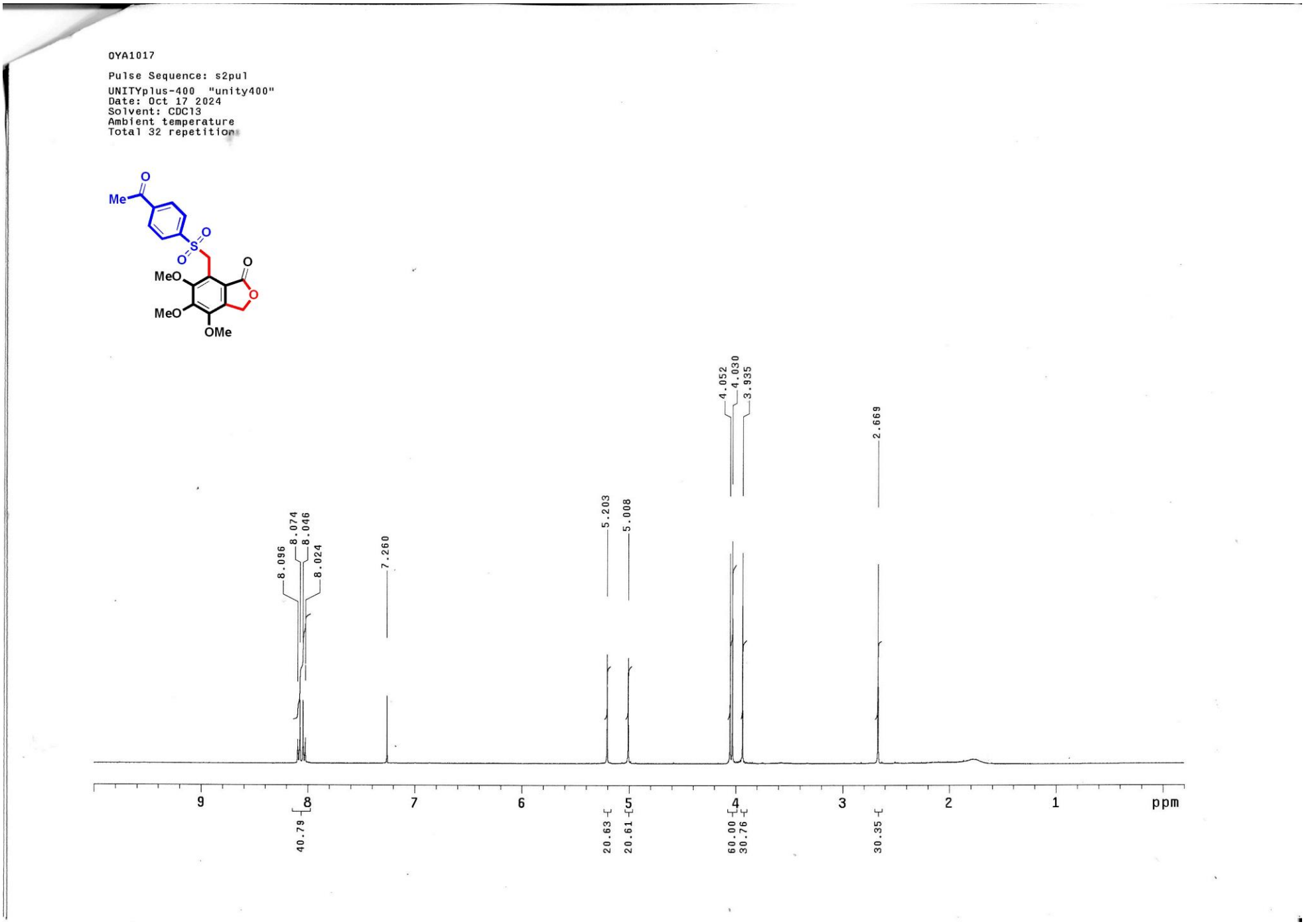
Compound 4r (^{1}H-NMR spectral data)



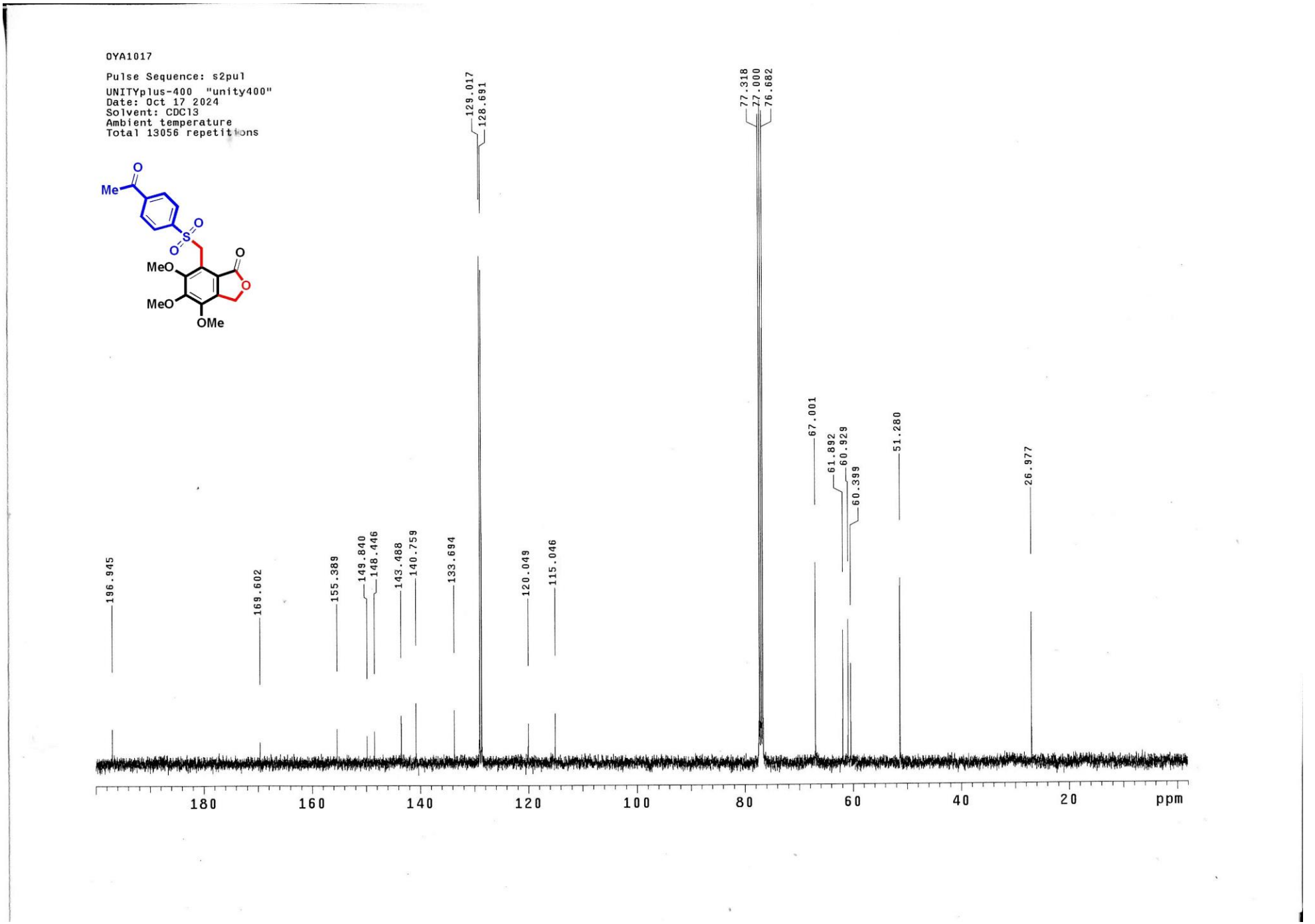
Compound 4r (^{13}C-NMR spectral data)



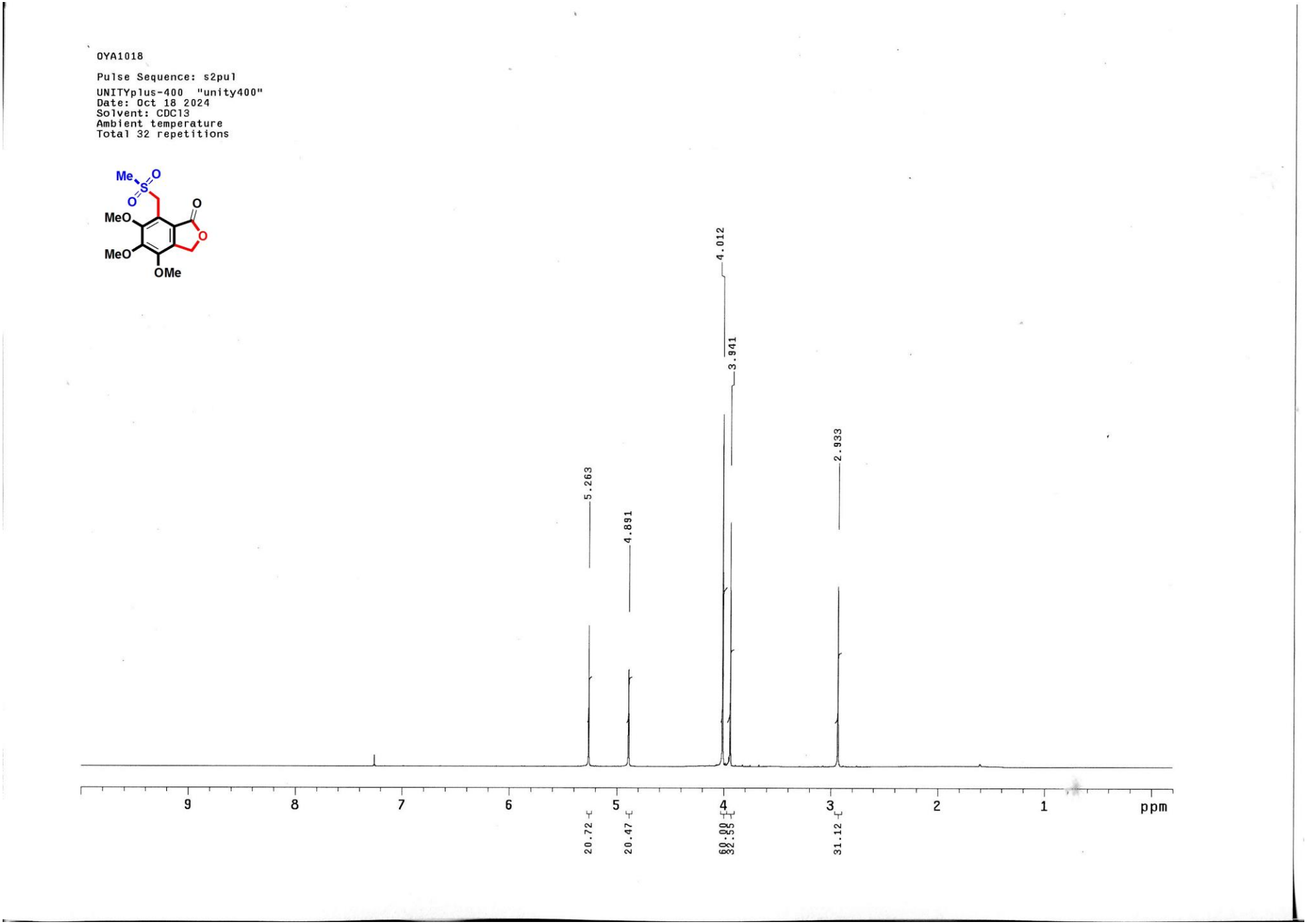
Compound 4s (^{1}H-NMR spectral data)



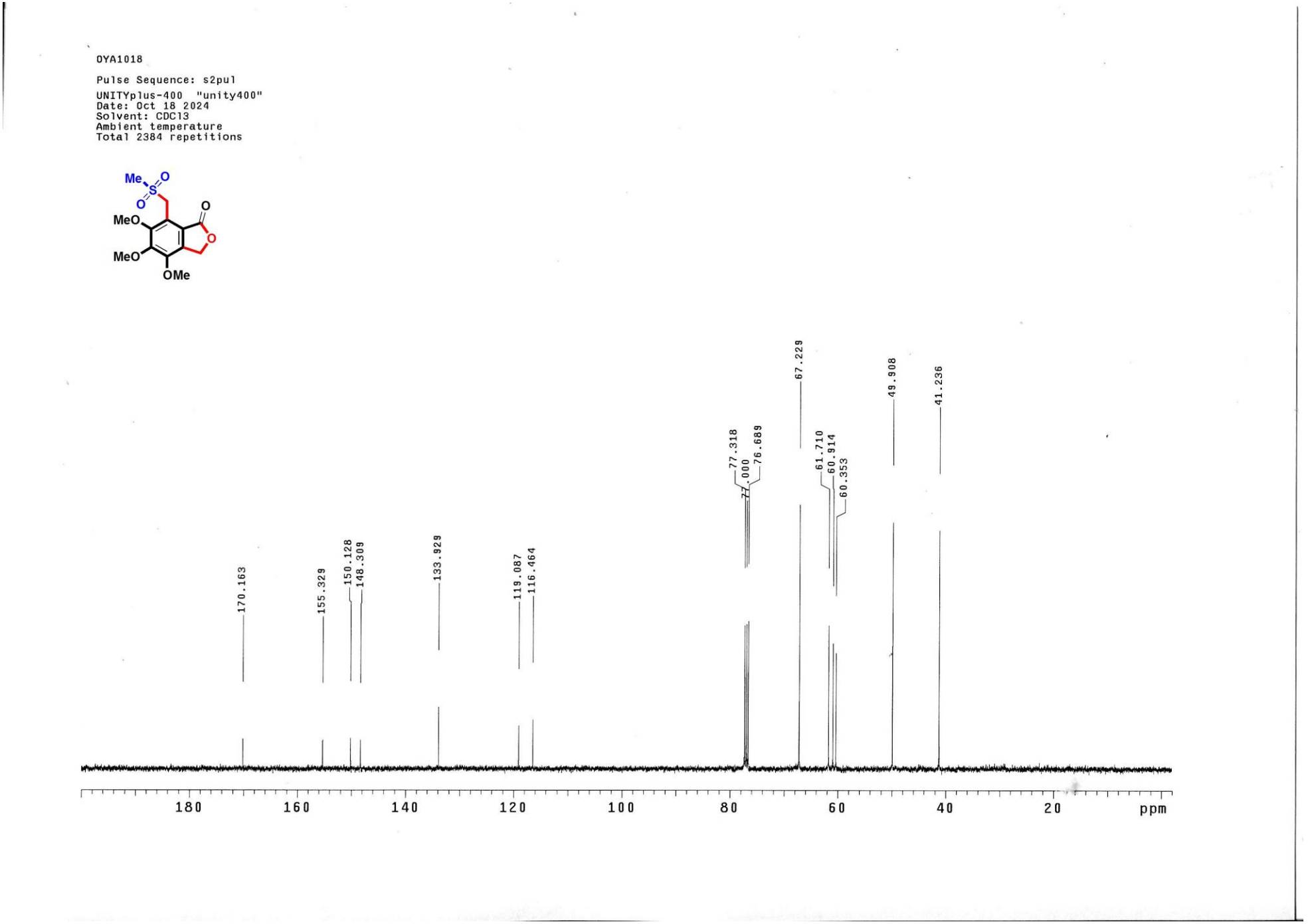
Compound 4s (^{13}C-NMR spectral data)



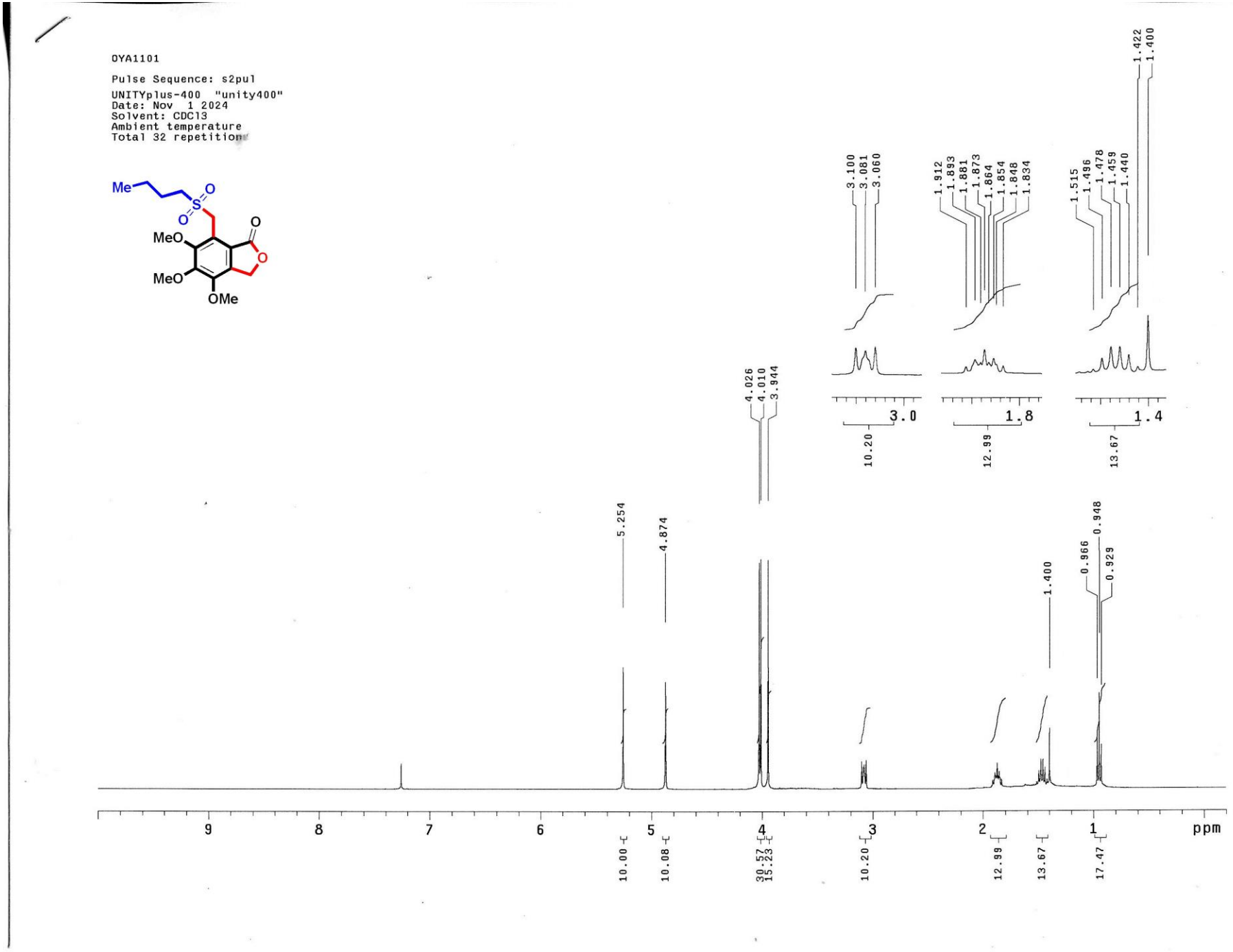
Compound 4t (^{1}H-NMR spectral data)



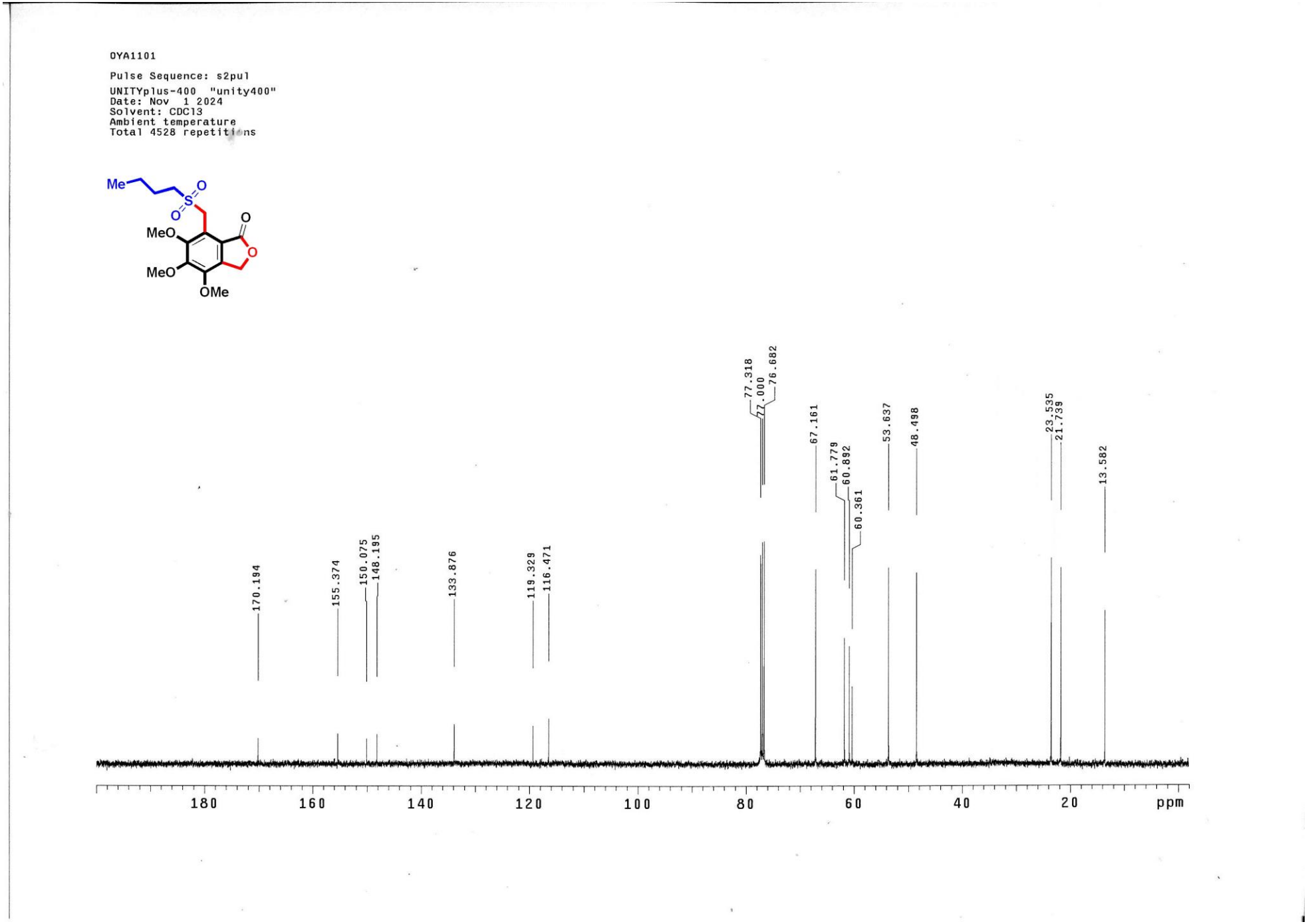
Compound 4t (^{13}C-NMR spectral data)



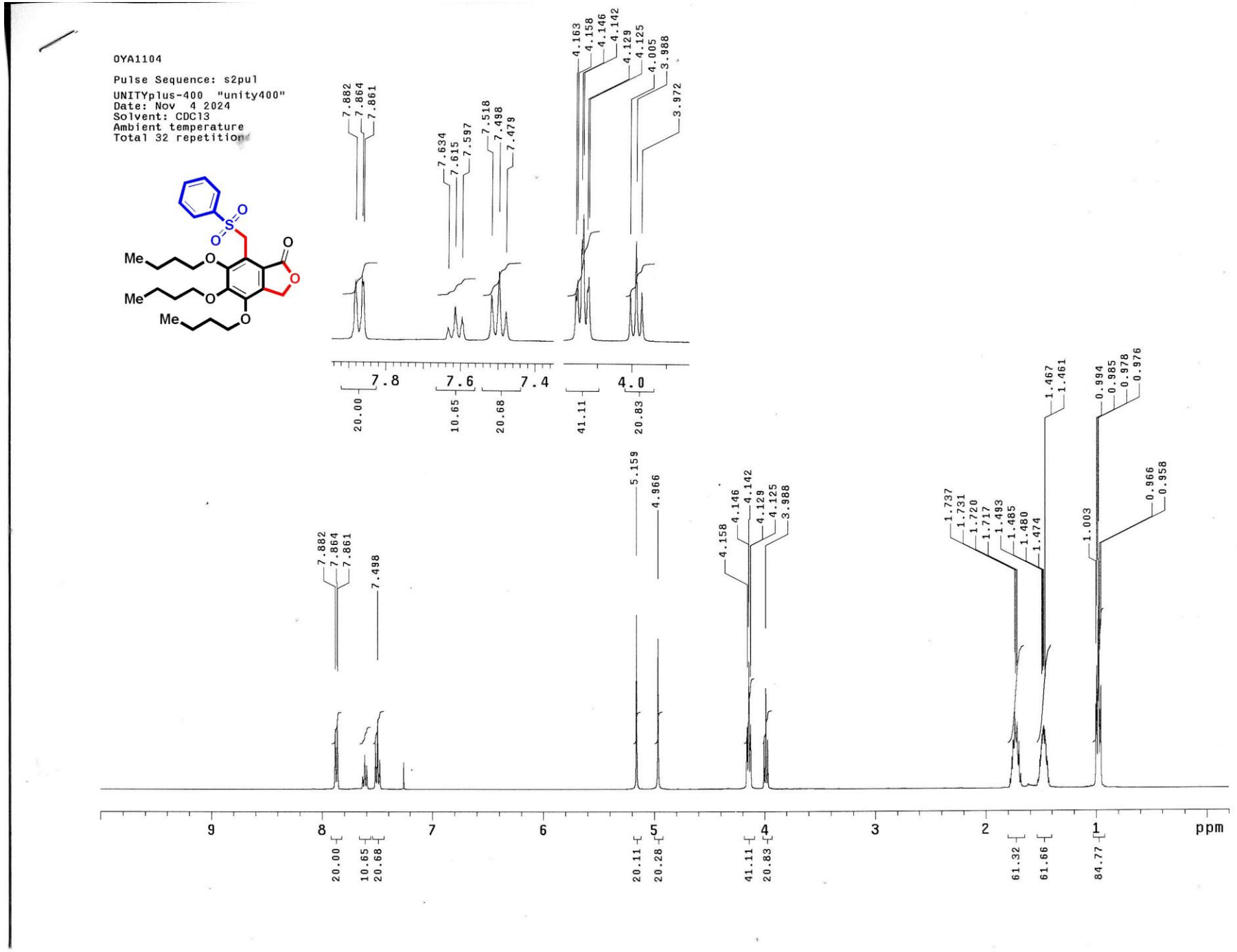
Compound 4u (^{1}H-NMR spectral data)



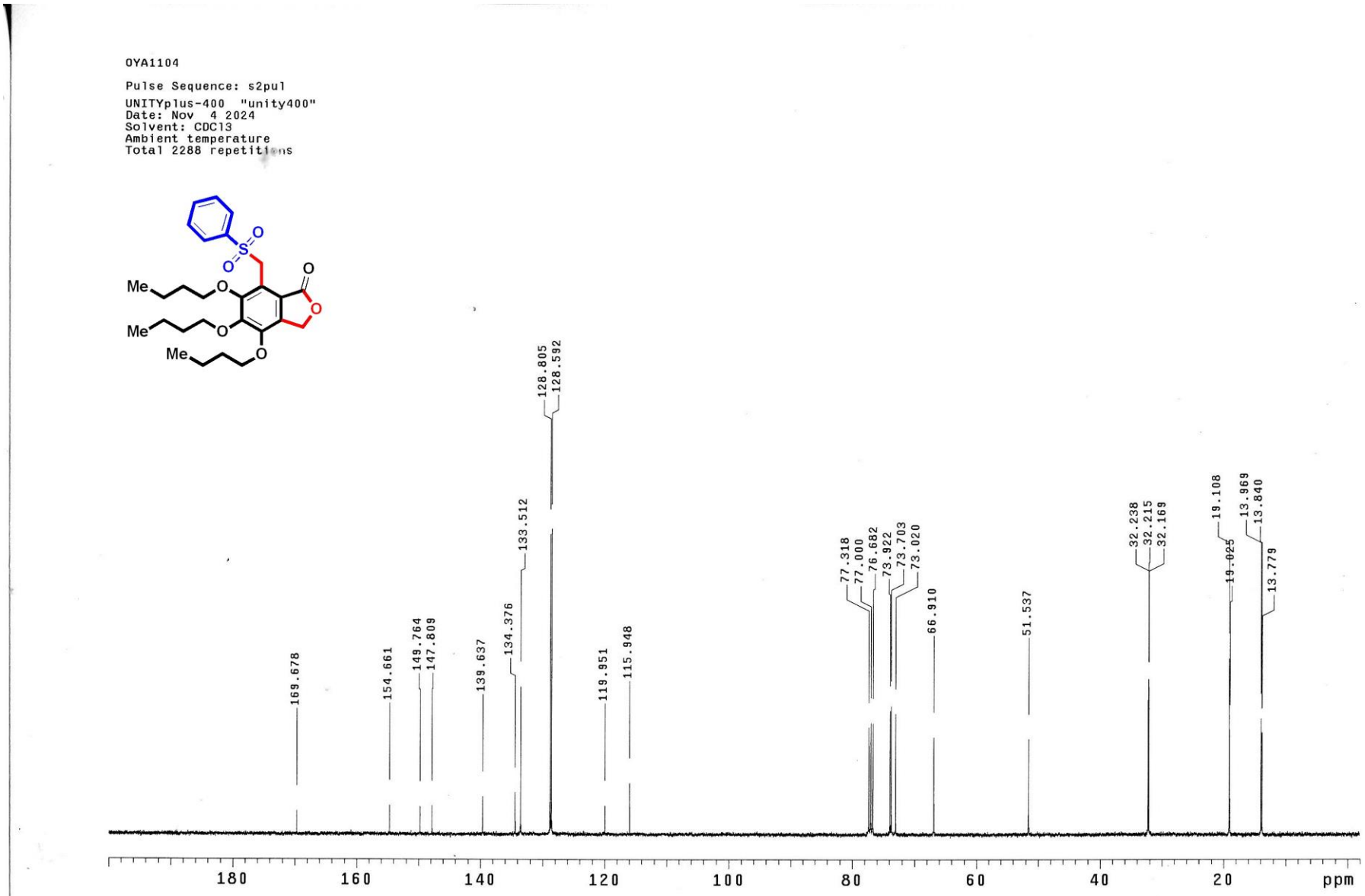
Compound 4u (^{13}C-NMR spectral data)



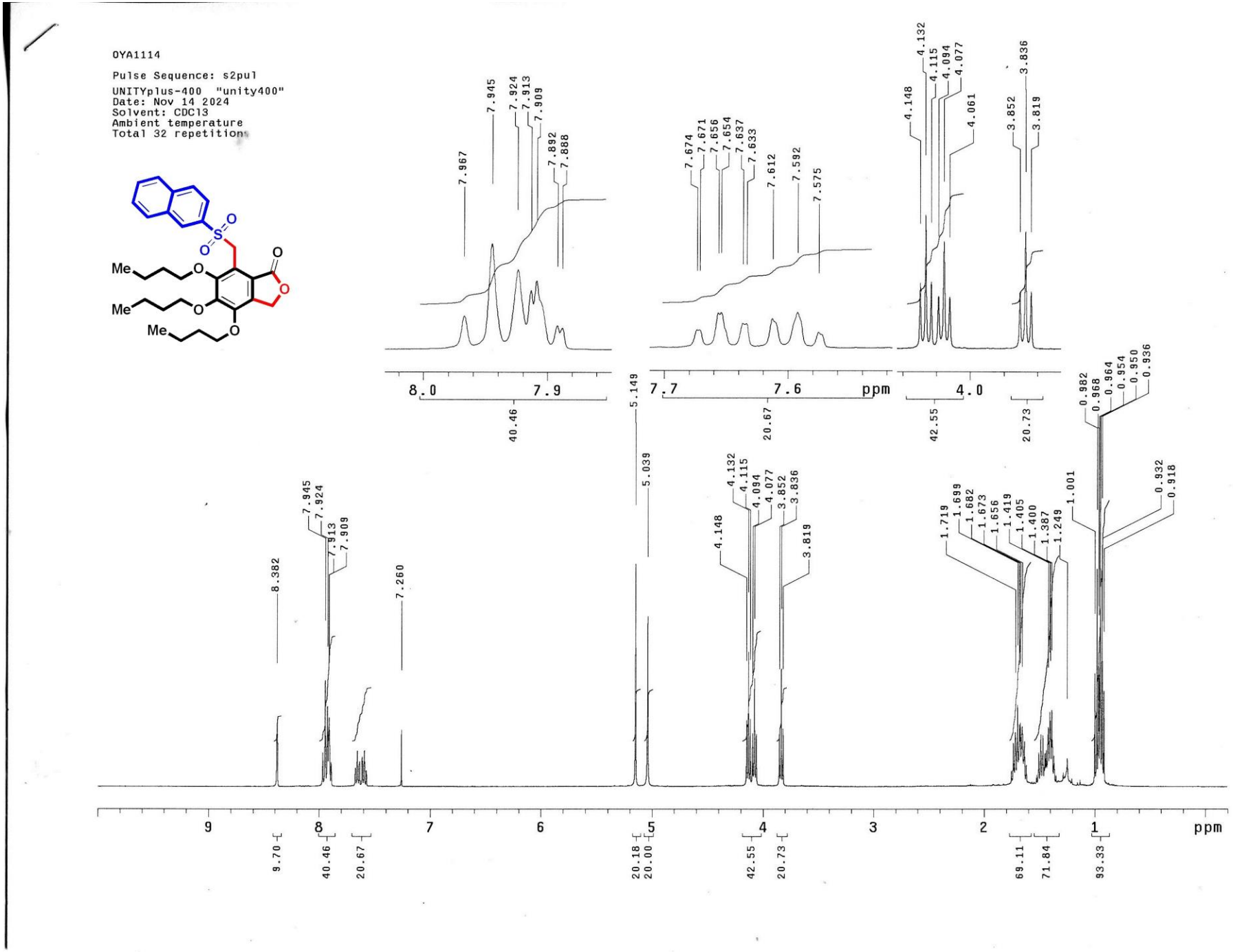
Compound 4v (^{1}H-NMR spectral data)



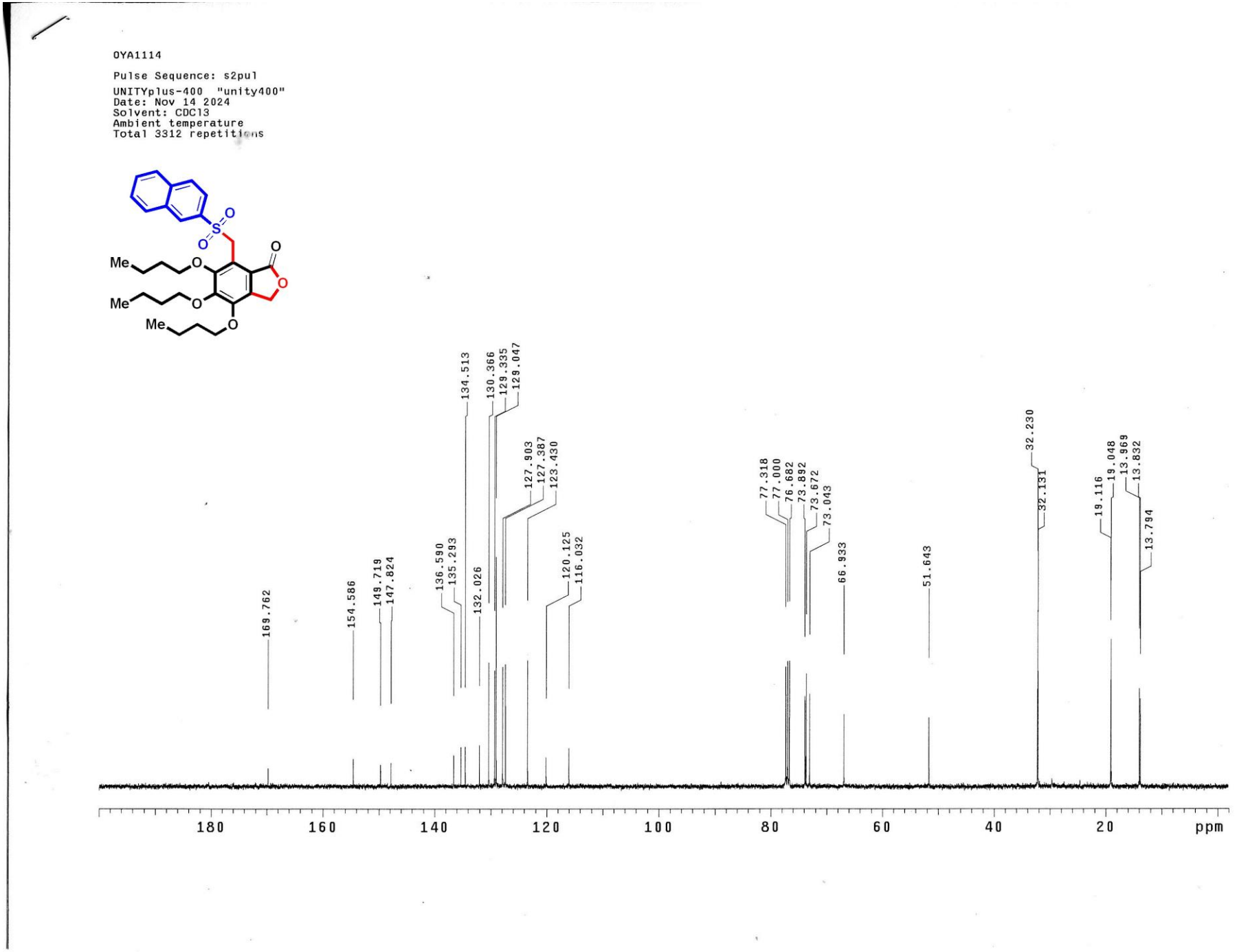
Compound 4v (^{13}C-NMR spectral data)



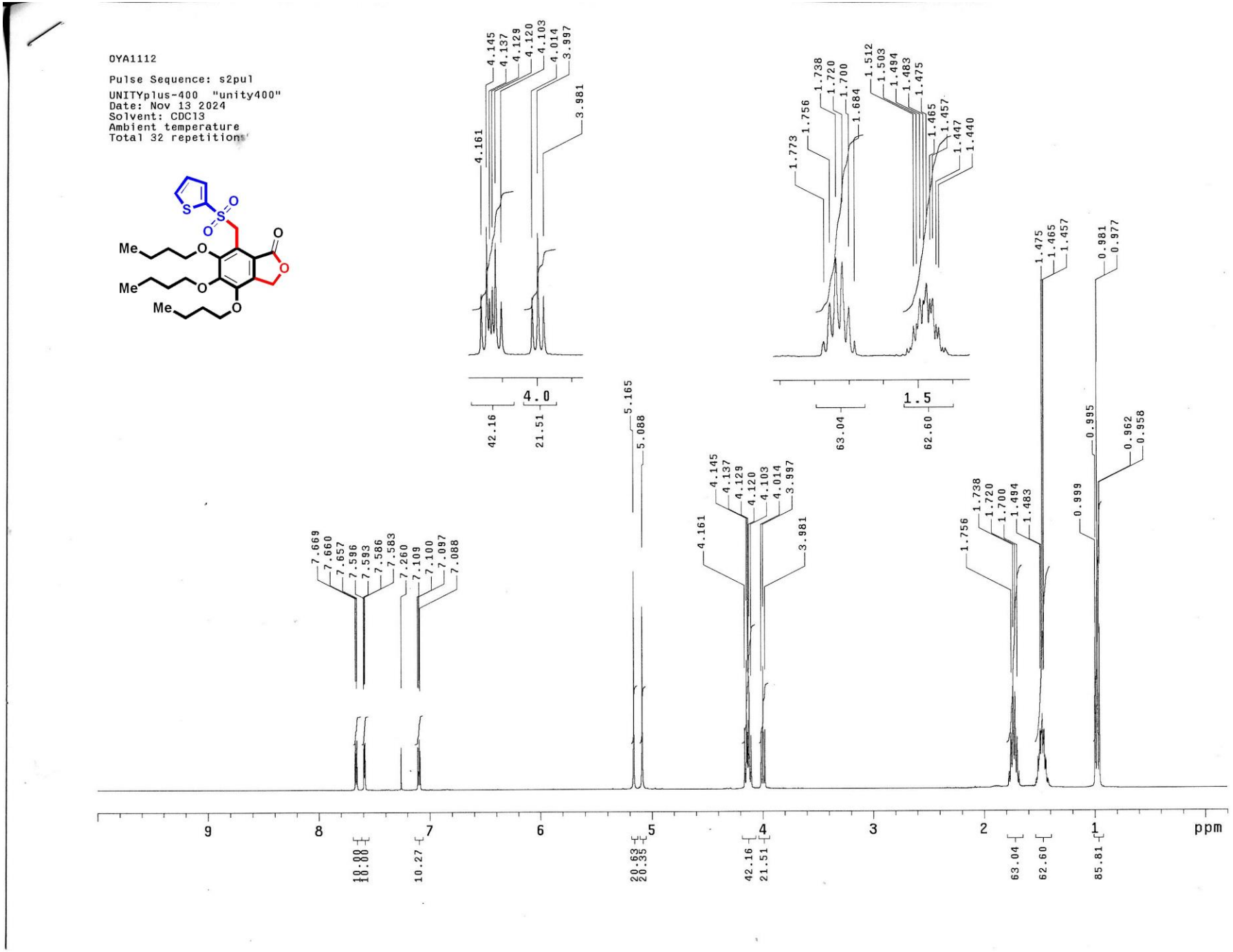
Compound 4w (^{1}H-NMR spectral data)



Compound 4w (^{13}C-NMR spectral data)



Compound 4x (^{1}H-NMR spectral data)

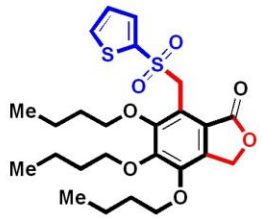


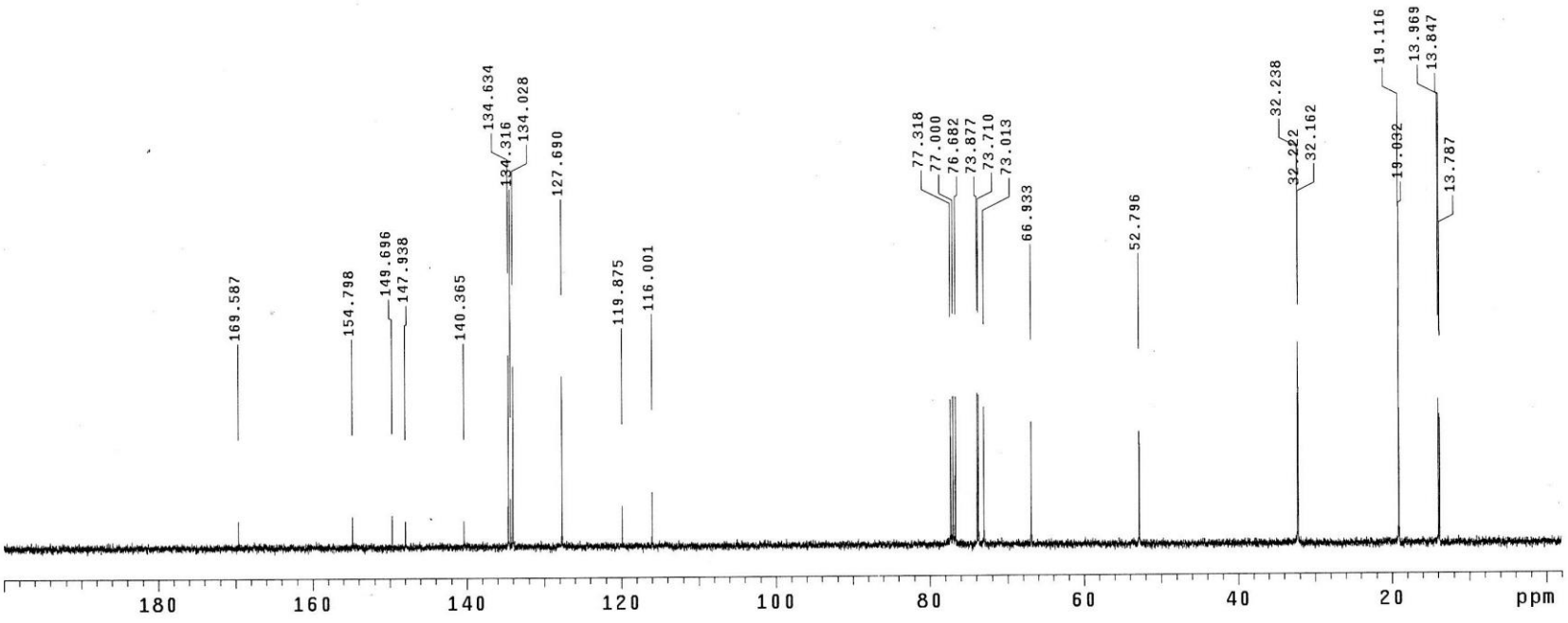
Compound 4x (^{13}C-NMR spectral data)

OYA1112

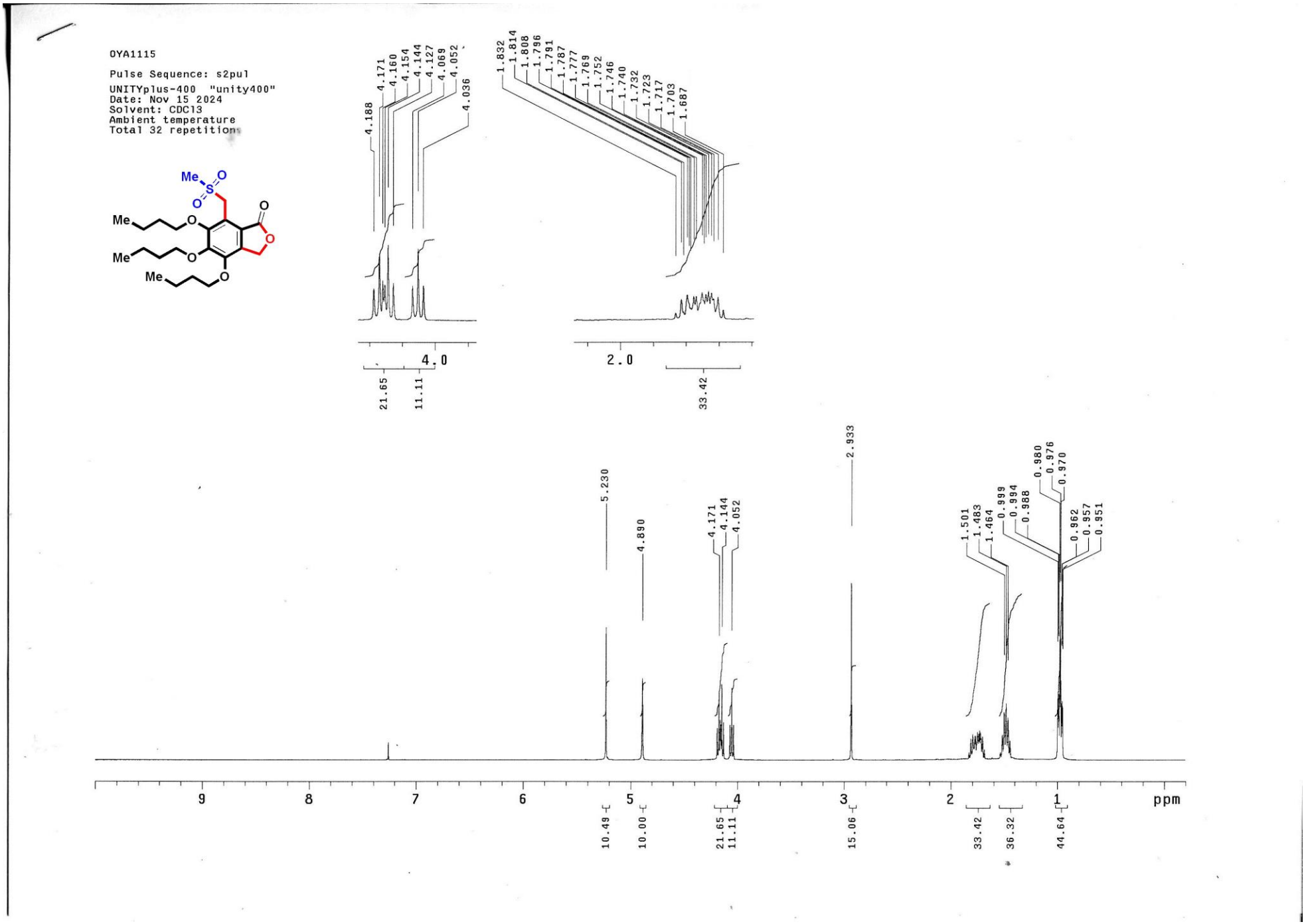
Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: Nov 13 2024
Solvent: CDCl3
Ambient temperature
Total 1024 repetitions





Compound 4y (^{1}H-NMR spectral data)

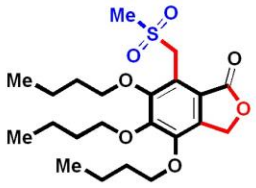


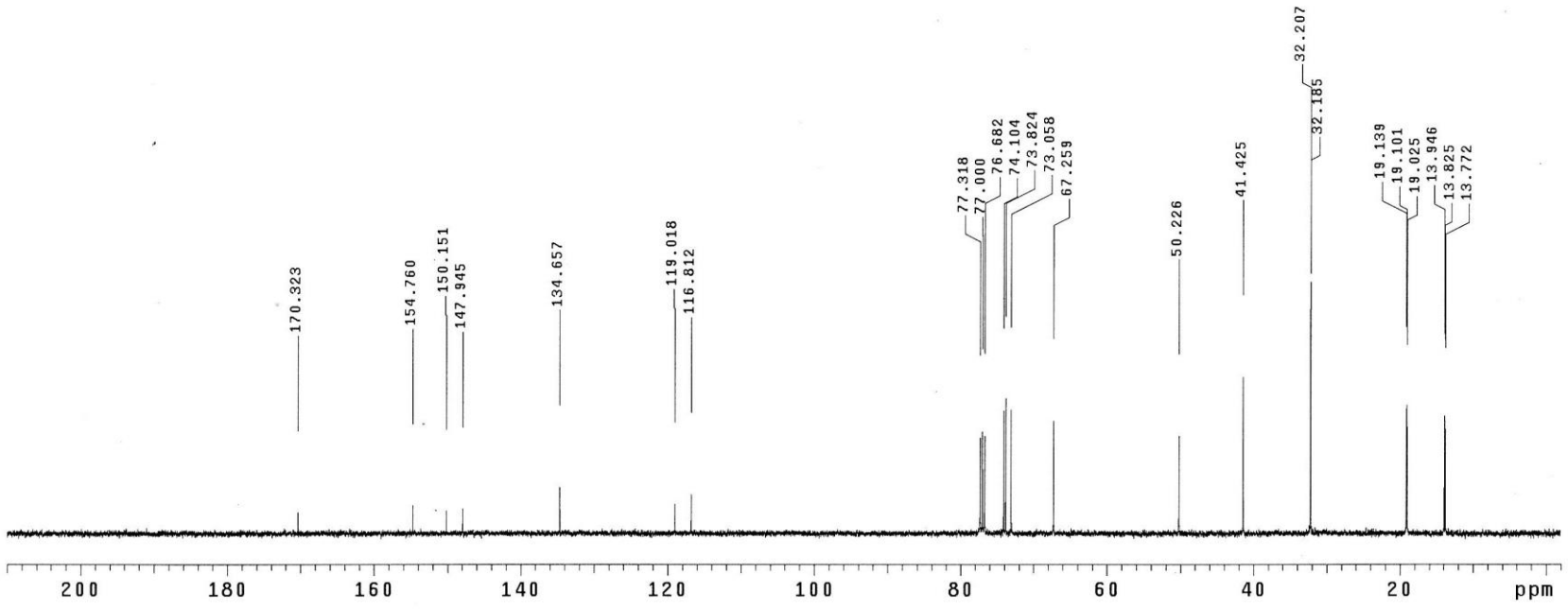
Compound 4y (^{13}C-NMR spectral data)

OYA1115

Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: Nov 15 2024
Solvent: CDCl3
Ambient temperature
Total 1407 repetitions

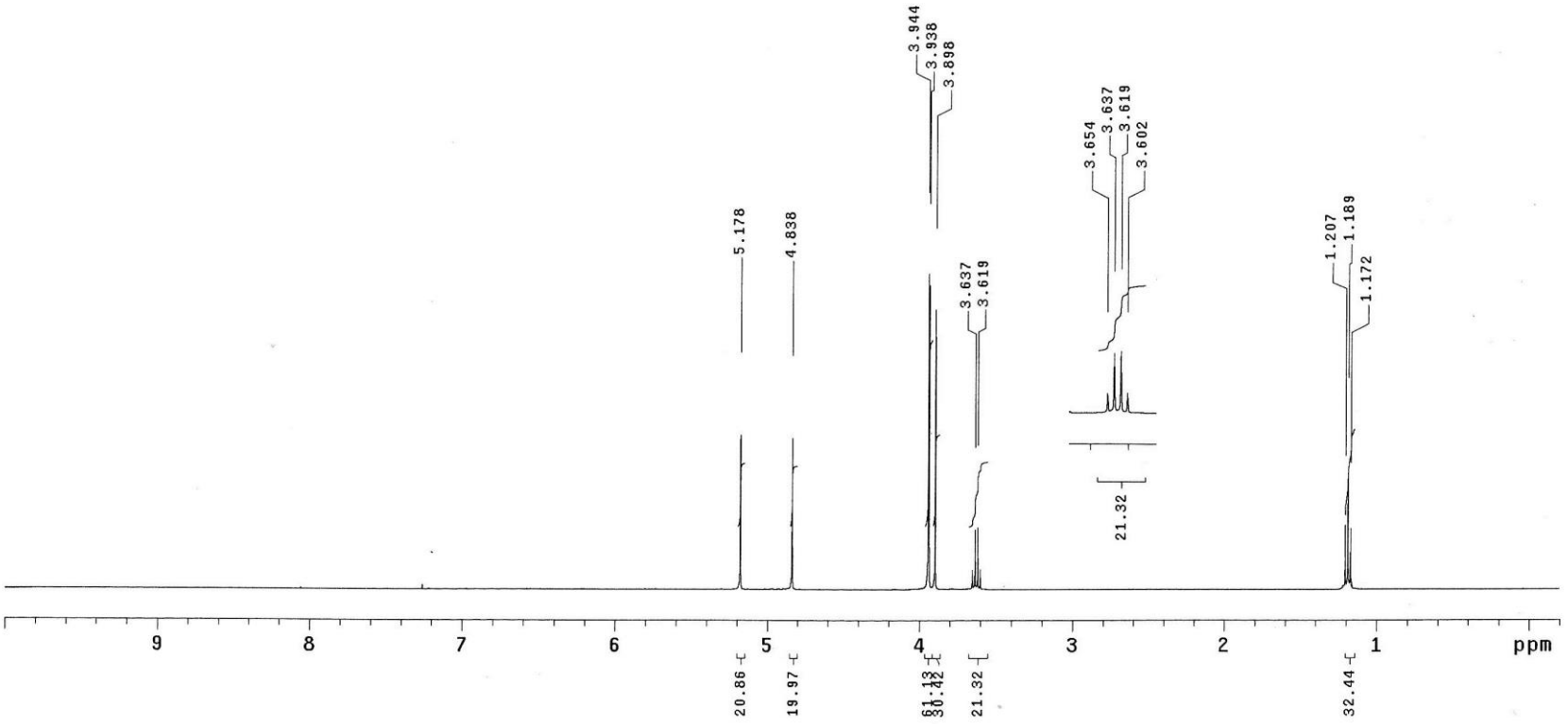




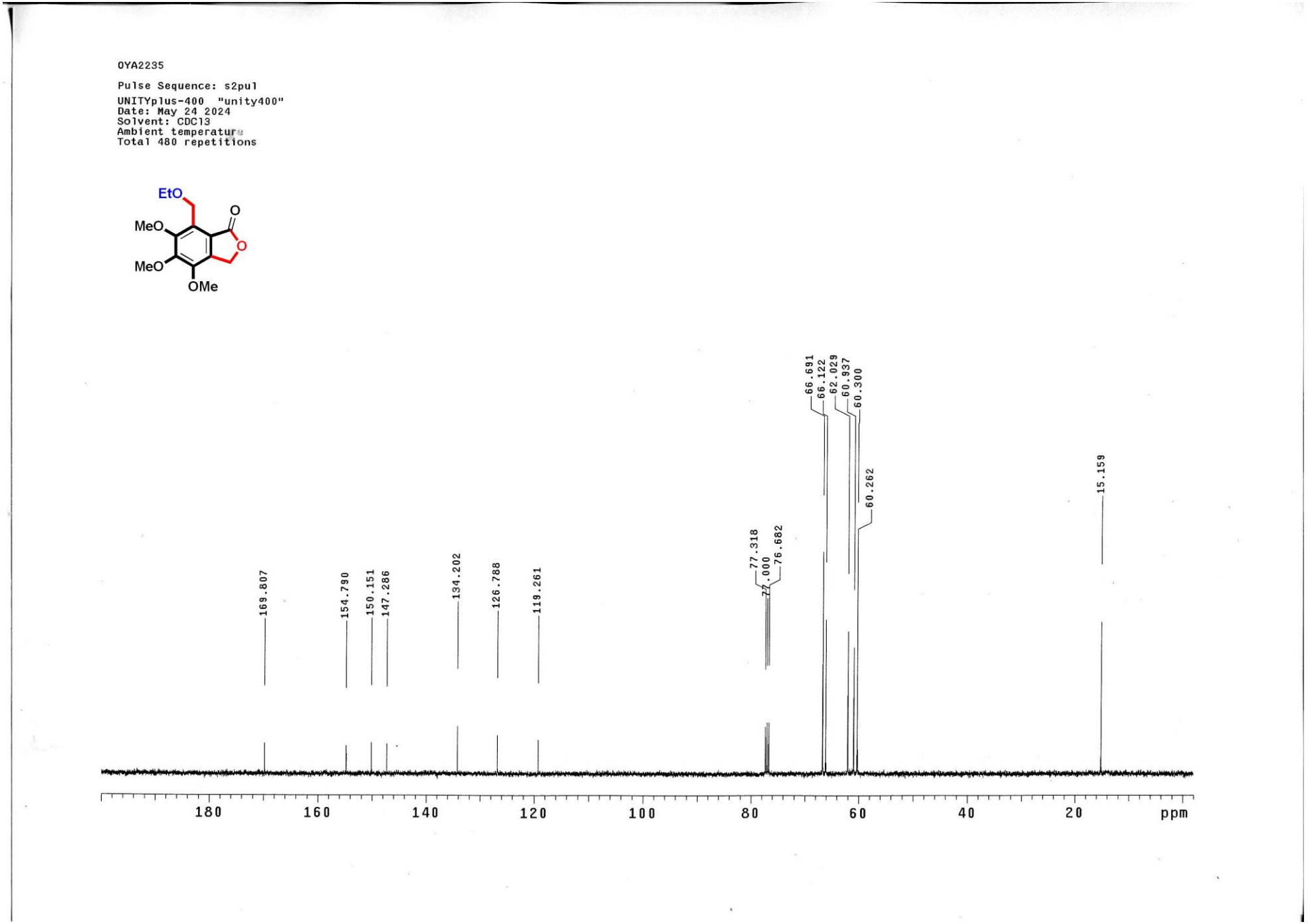
Compound 5a (^{1}H-NMR spectral data)

OYA2235

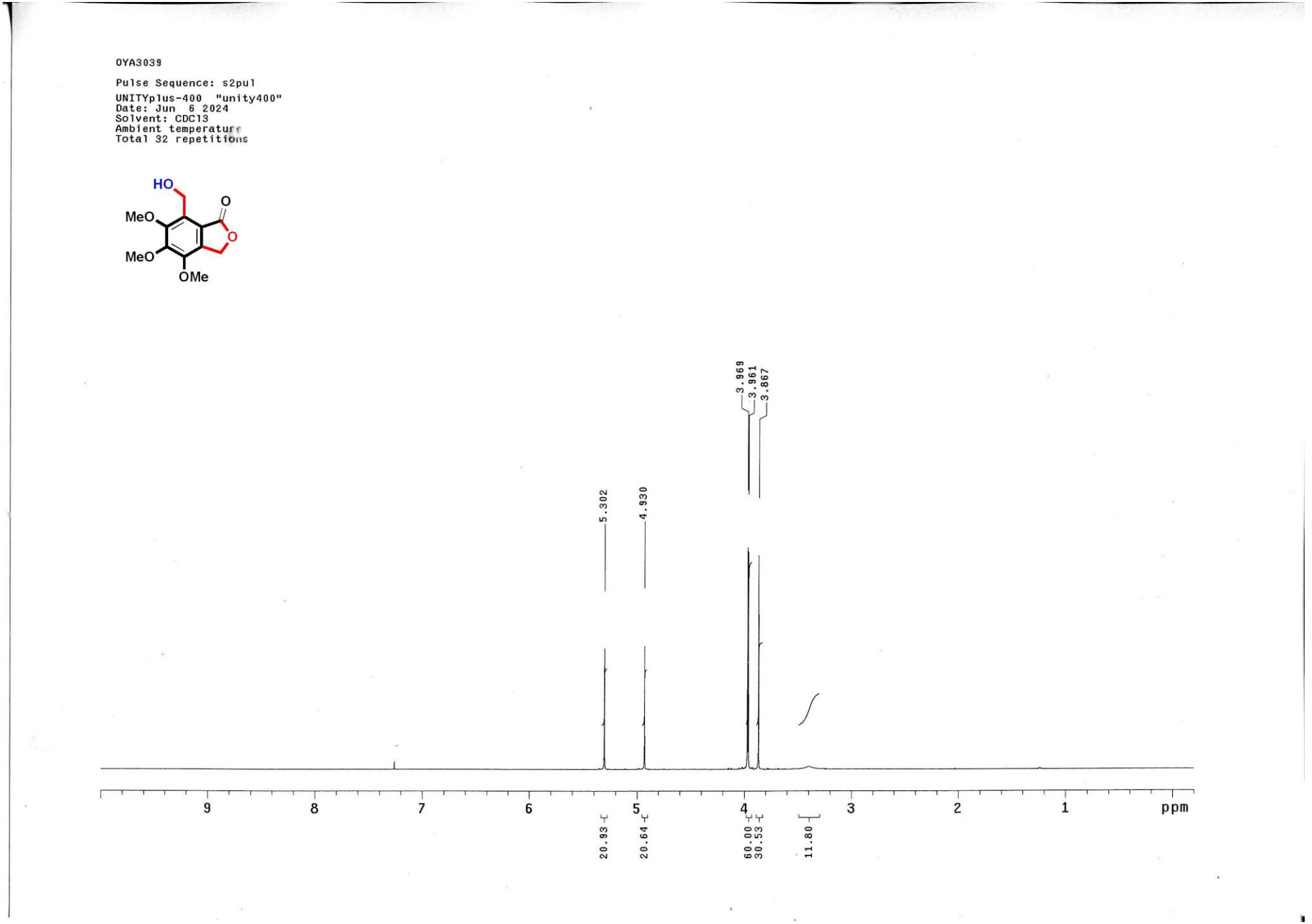
Pulse Sequence: s2pul
UNITYplus-400 "unity400"
Date: May 24 2024
Solvent: CDCl3
Ambient temperature
Total 32 repetitions



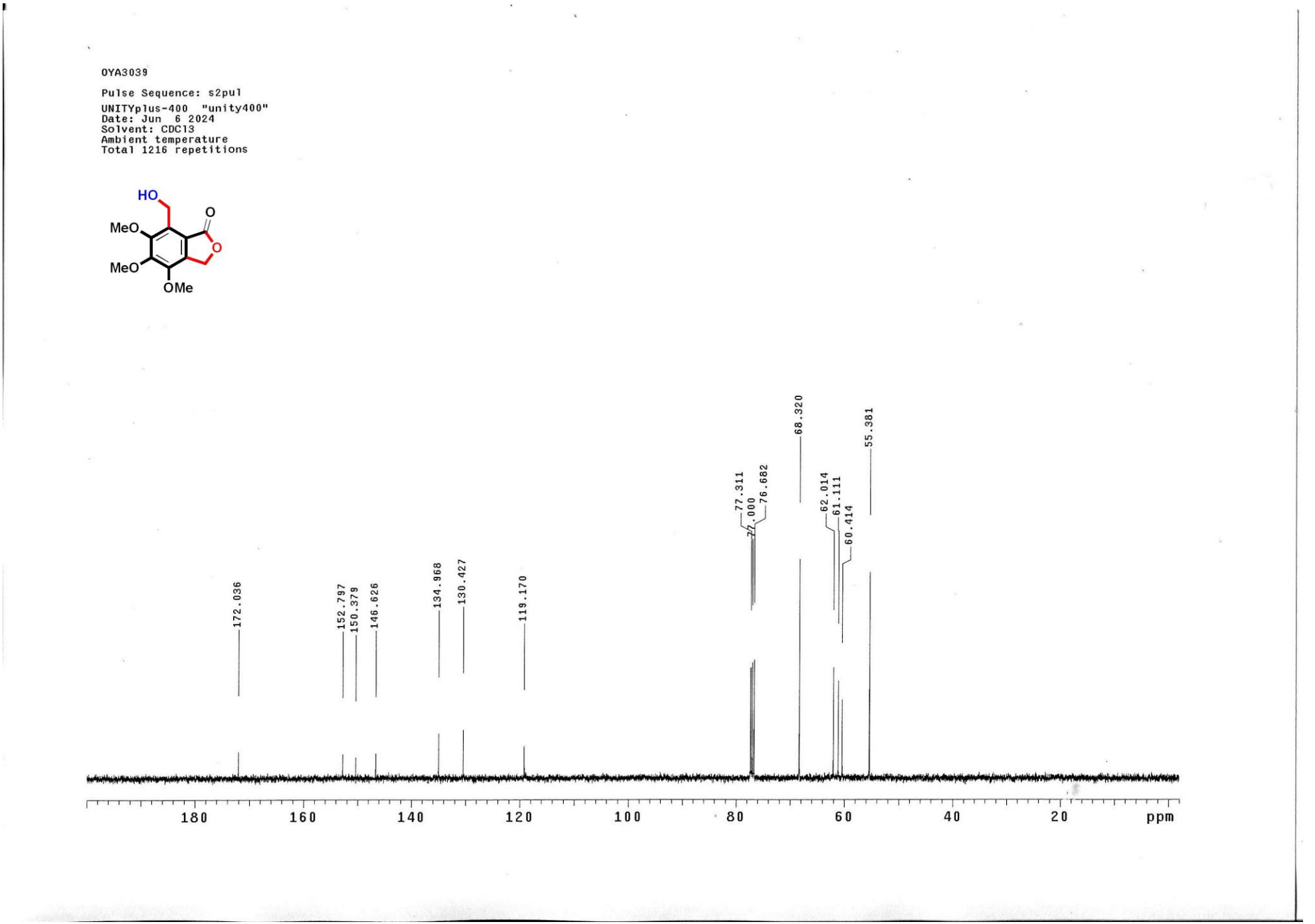
Compound 5a (^{13}C-NMR spectral data)



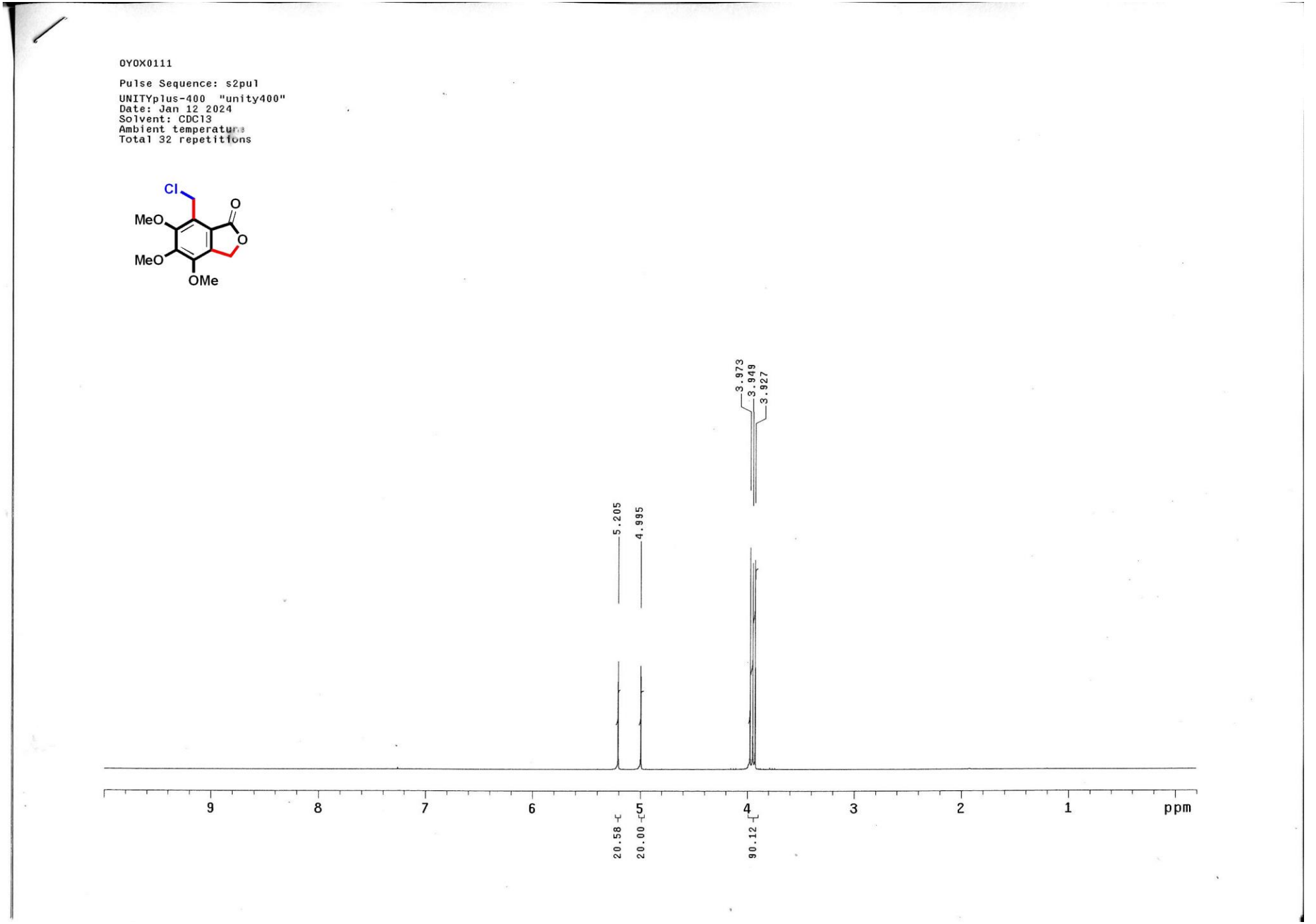
Compound 5b (^{1}H-NMR spectral data)



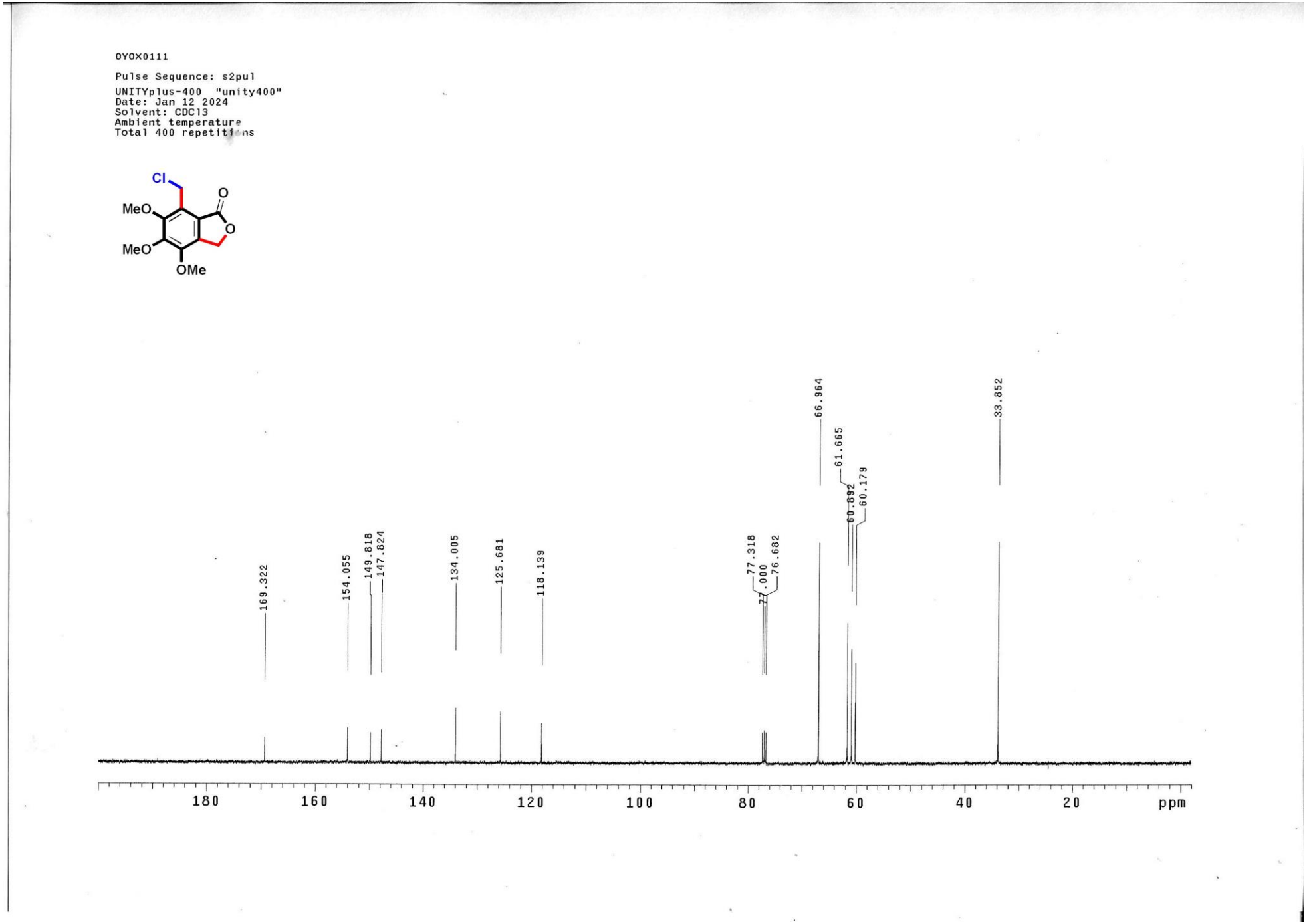
Compound 5b (^{13}C-NMR spectral data)



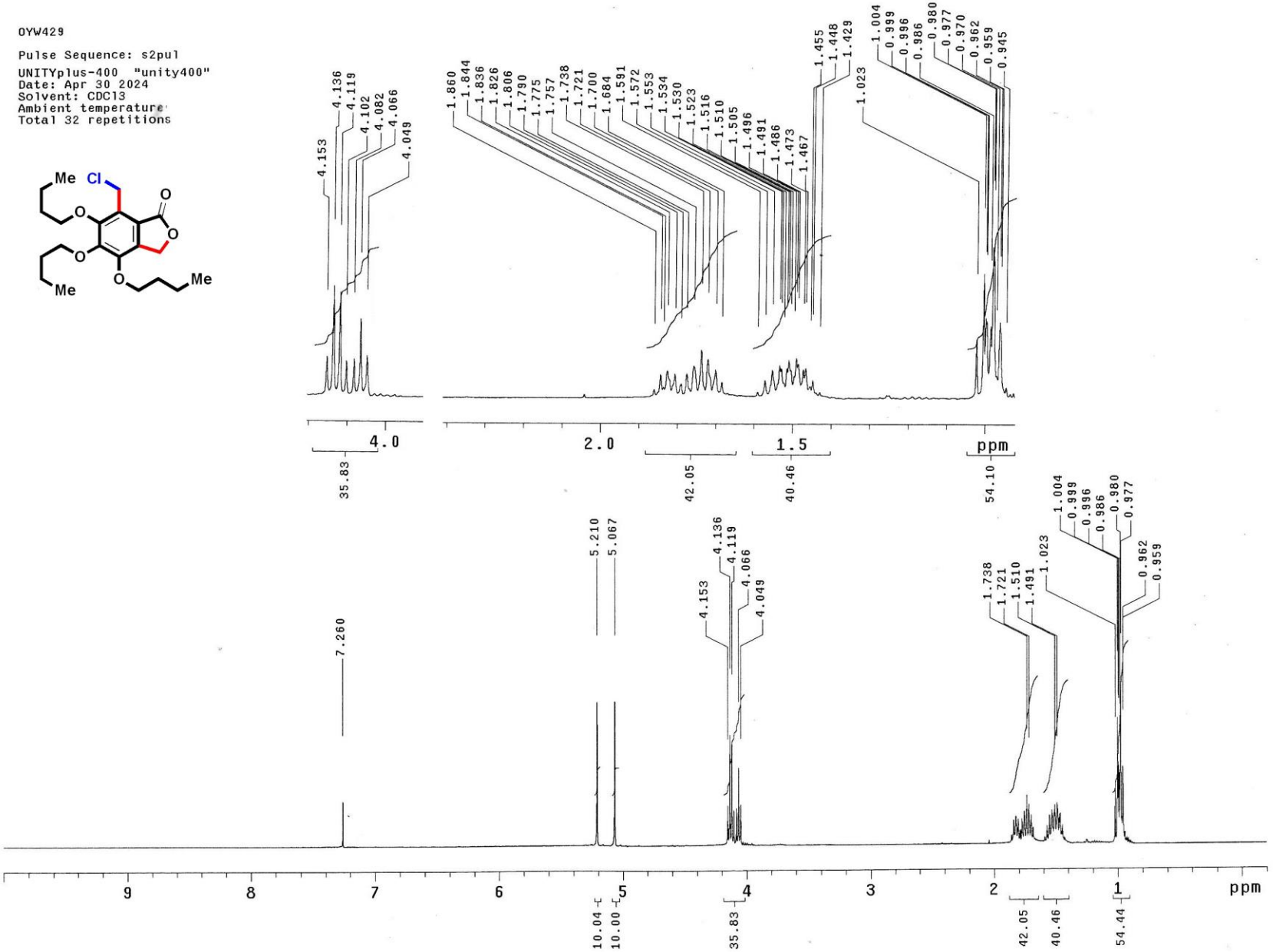
Compound 5c (^{1}H-NMR spectral data)



Compound 5c (^{13}C-NMR spectral data)



Compound 5d (^{1}H-NMR spectral data)

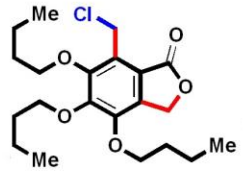


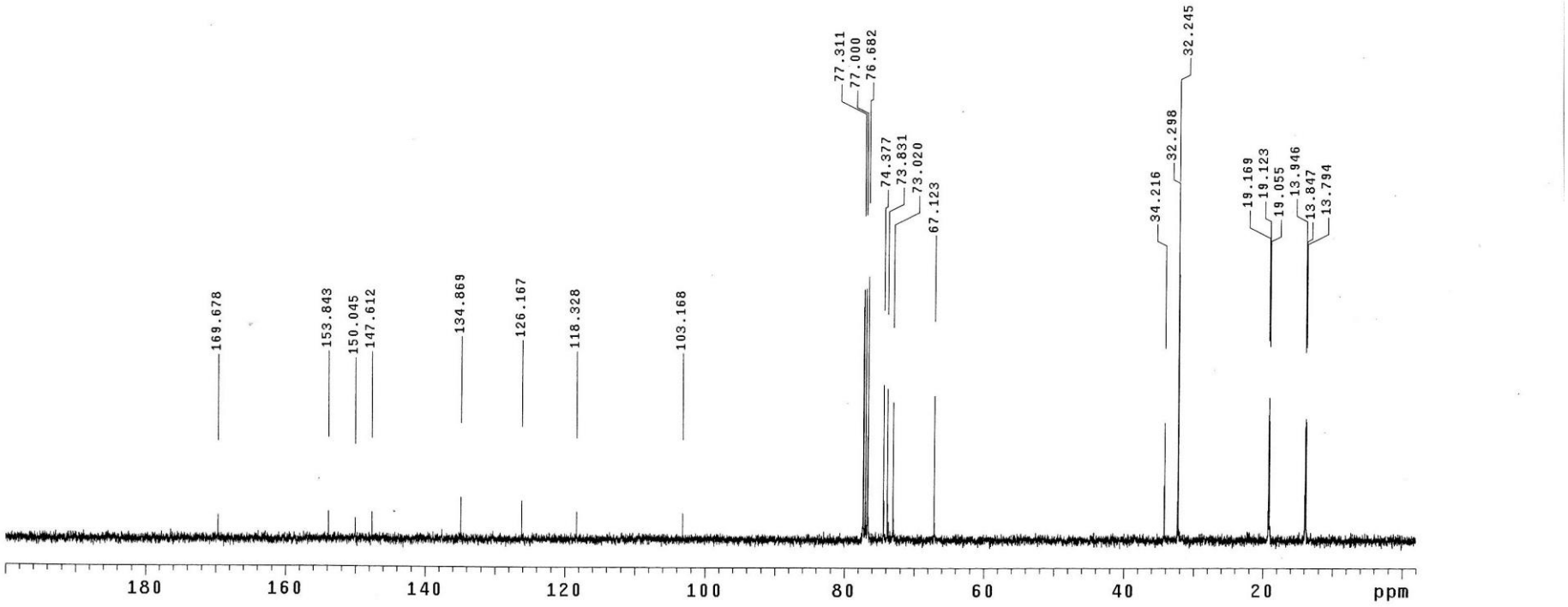
Compound 5d (^{13}C-NMR spectral data)

OYW429

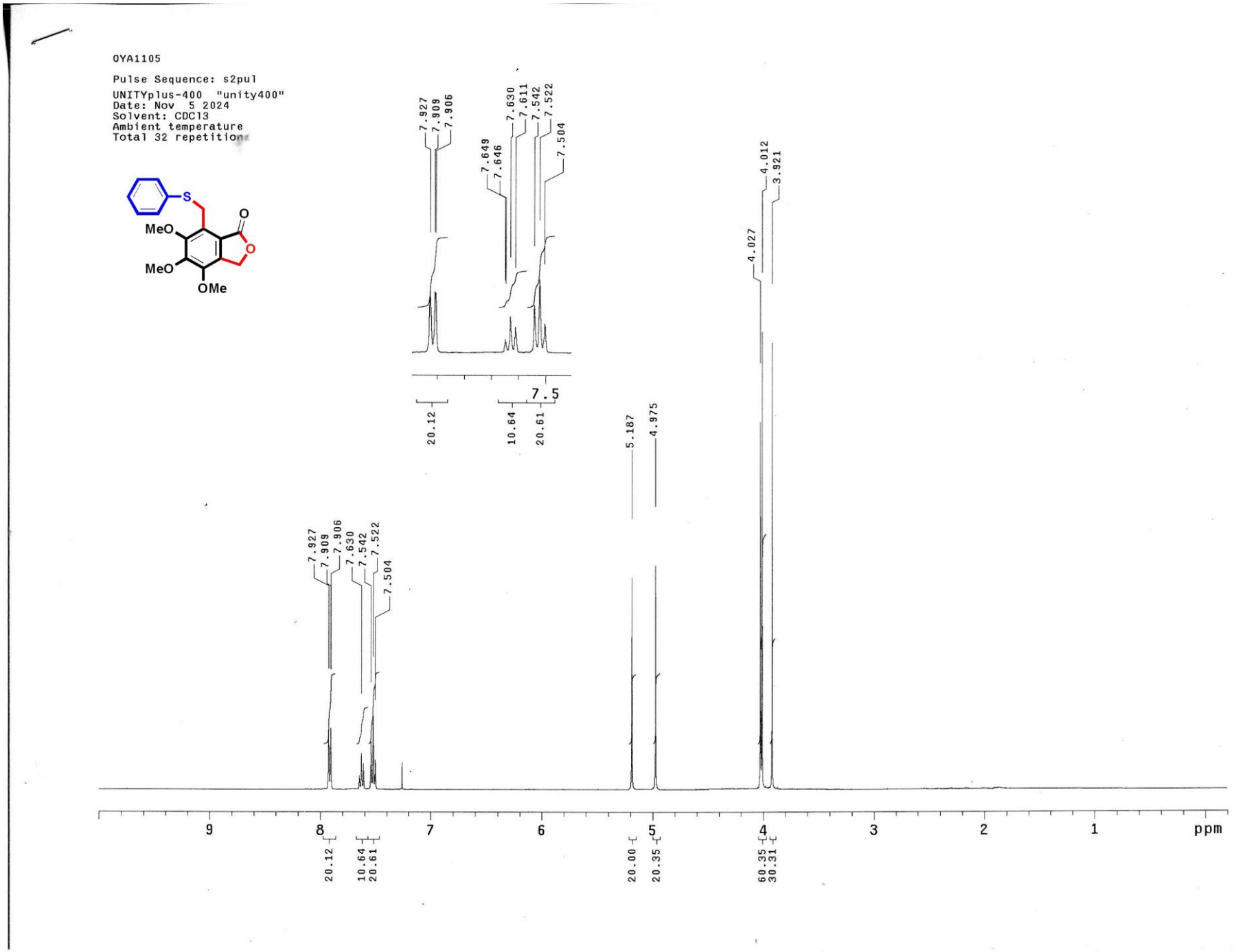
Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: Apr 30 2024
Solvent: CDCl3
Ambient temperature
Total 4096 repetitions

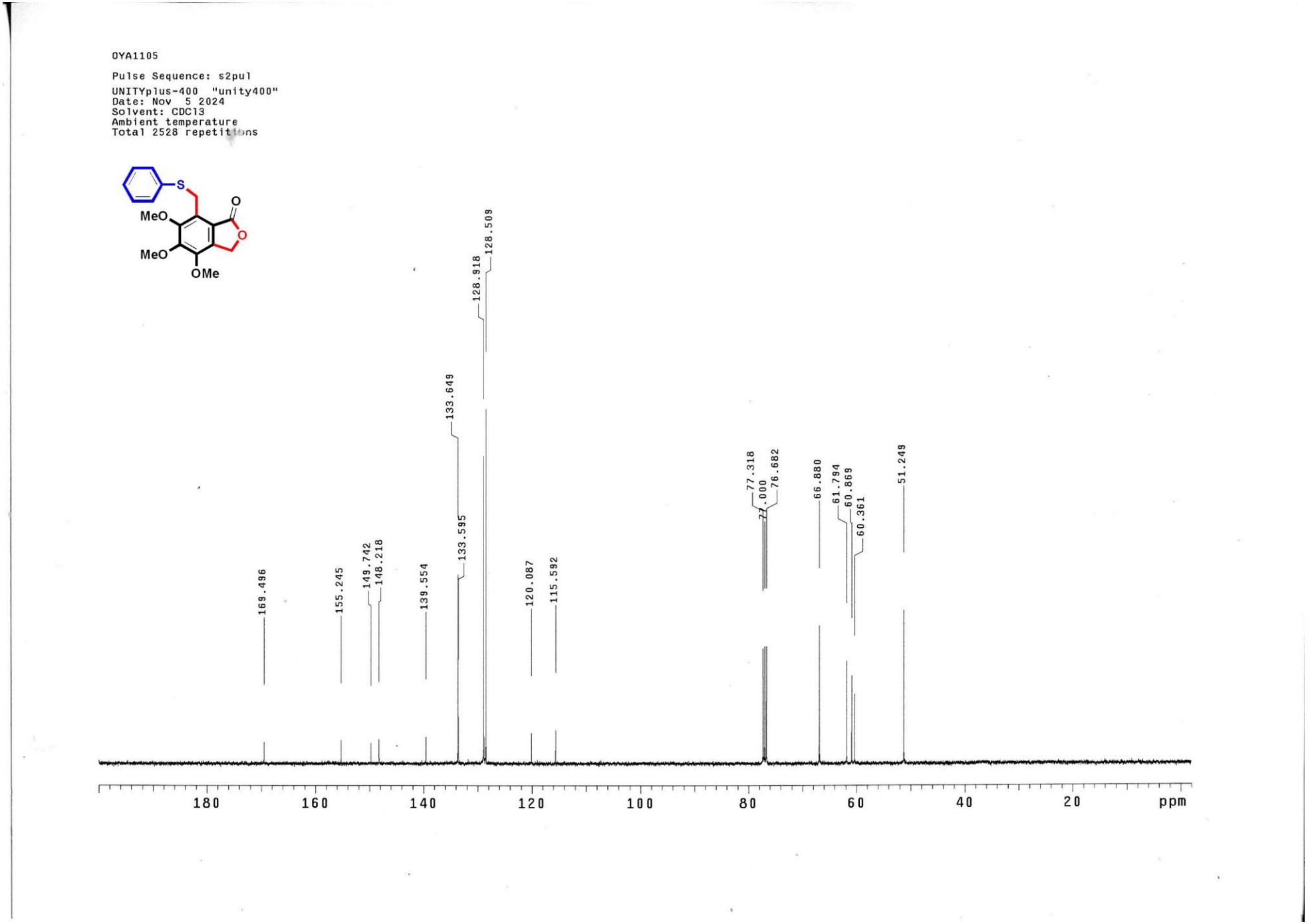




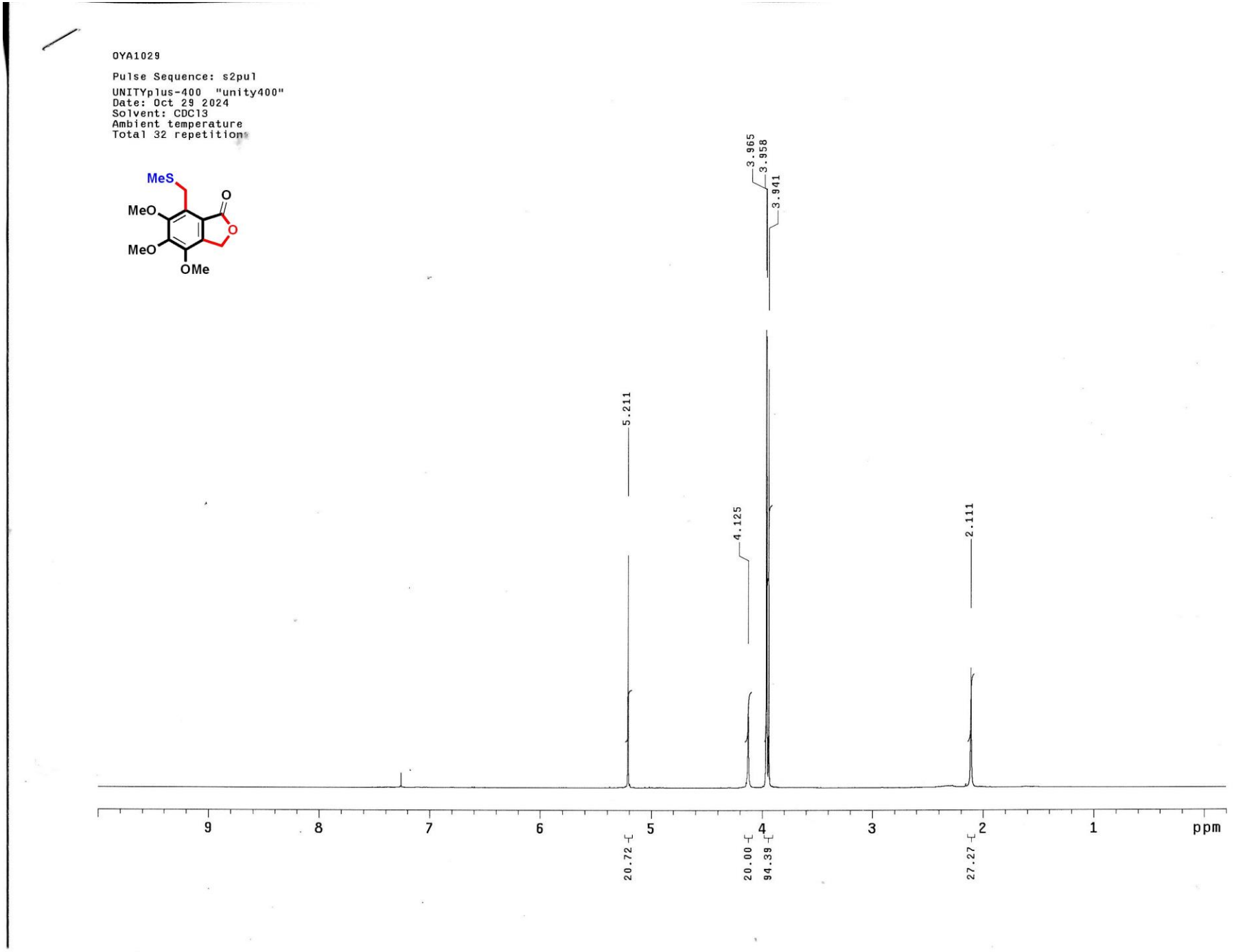
Compound 5g (^{1}H-NMR spectral data)



Compound 5g (^{13}C-NMR spectral data)



Intermediate C (^{1}H-NMR spectral data)

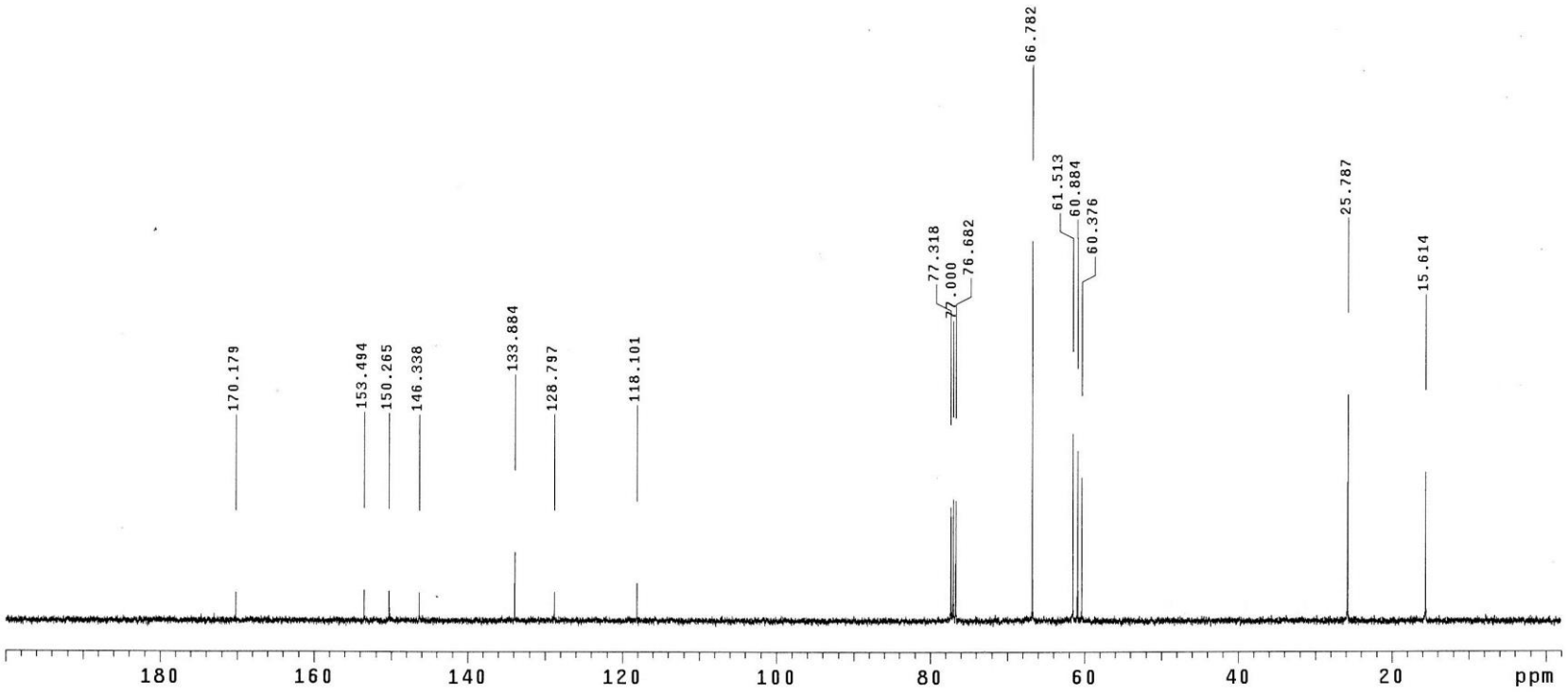


Intermediate C (^{13}C-NMR spectral data)

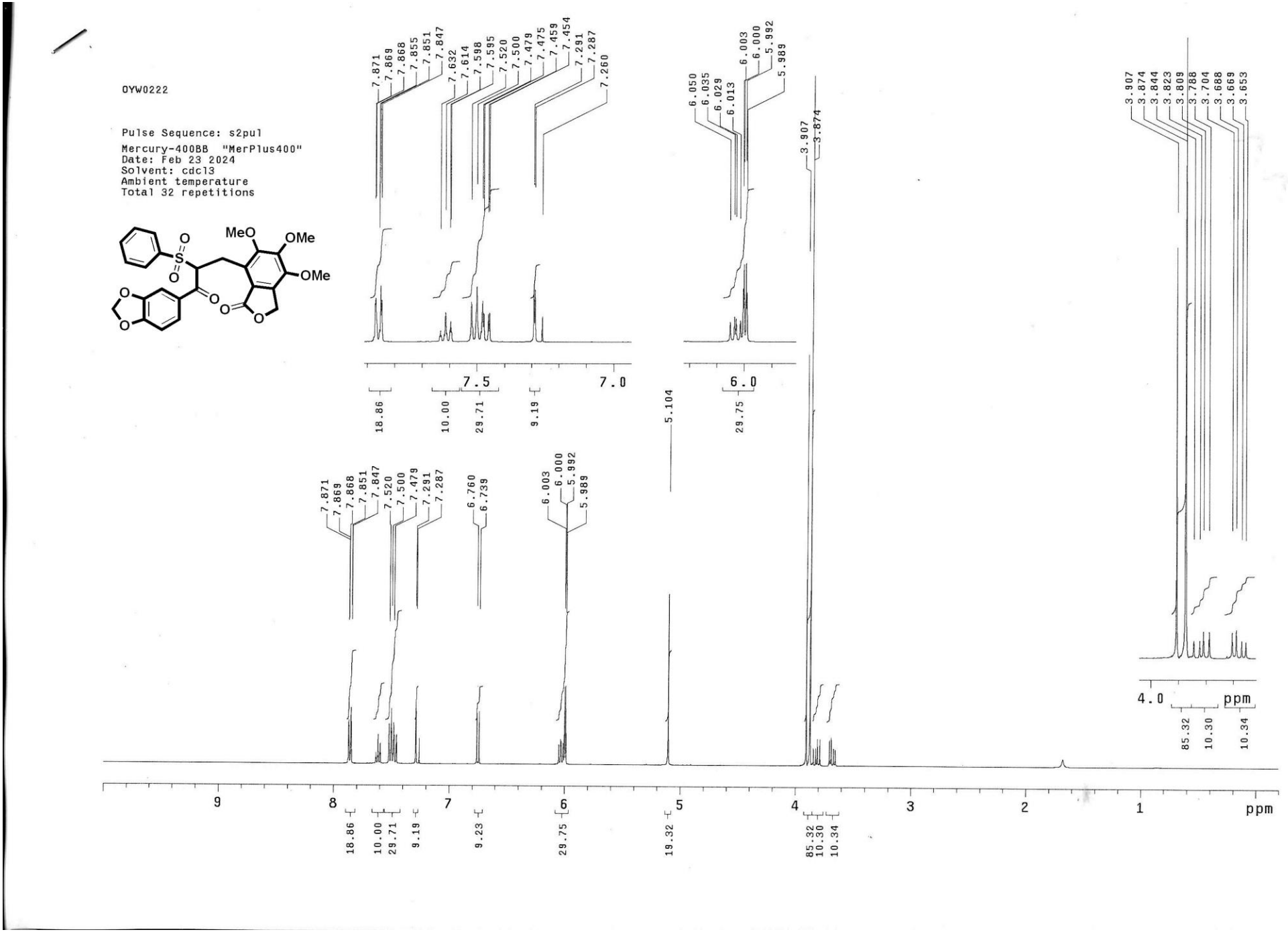
OYA1029

Pulse Sequence: s2pul

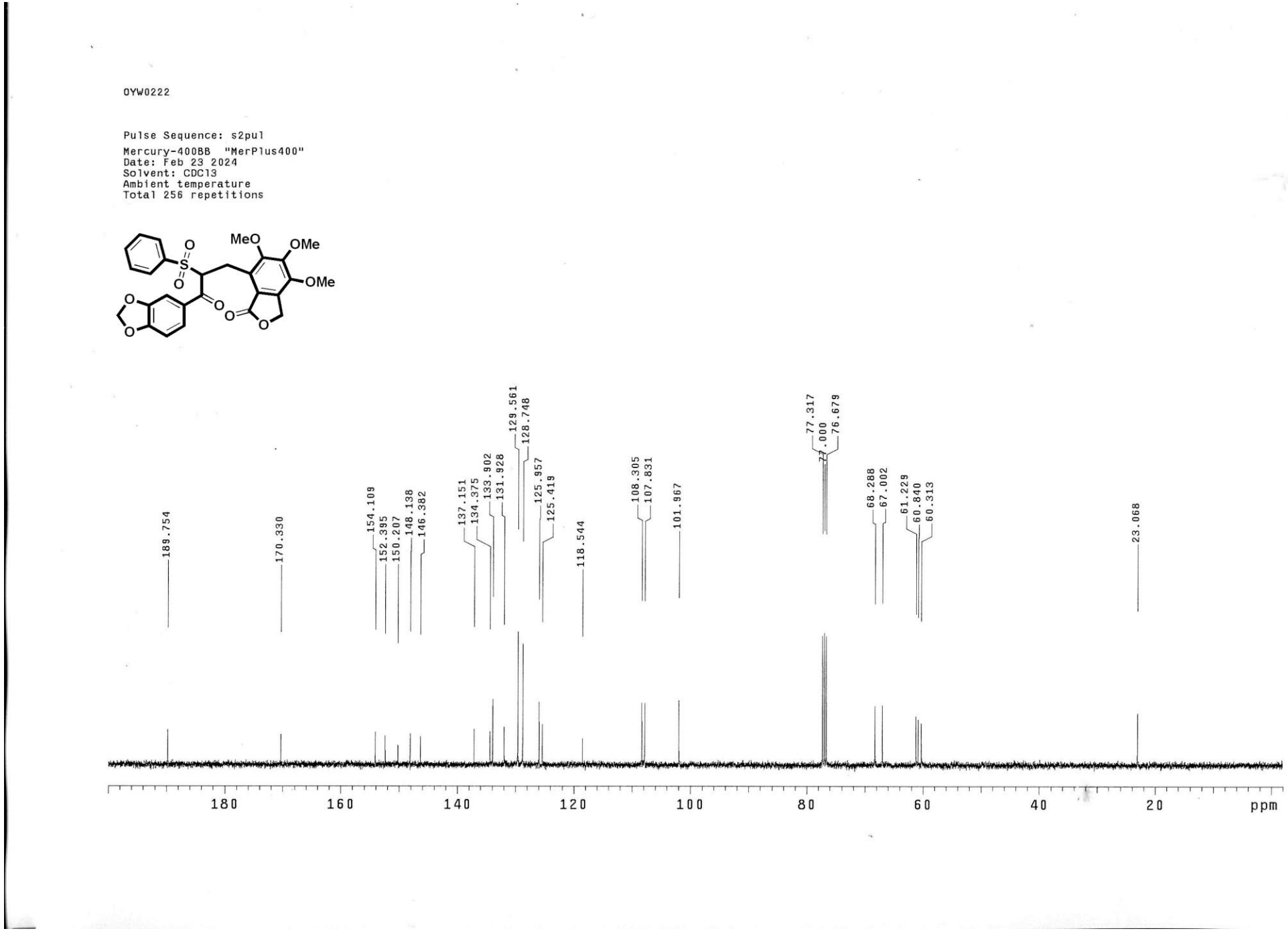
UNITYplus-400 "unity400"
Date: Oct 29 2024
Solvent: CDCl3
Ambient temperature
Total 2608 repetitions



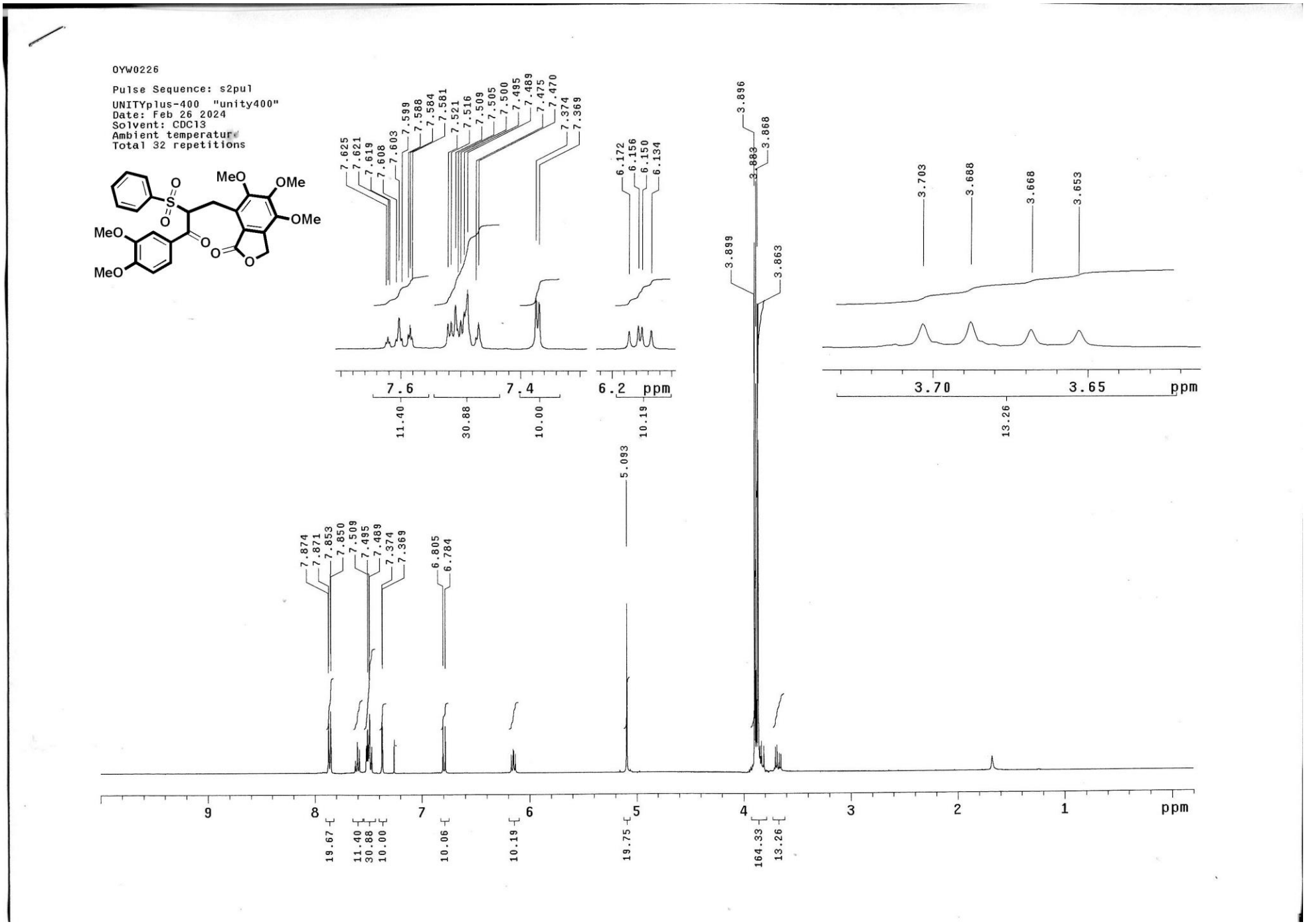
Compound 6a (^{1}H-NMR spectral data)



Compound 6a (^{13}C-NMR spectral data)



Compound 6b (^{1}H-NMR spectral data)

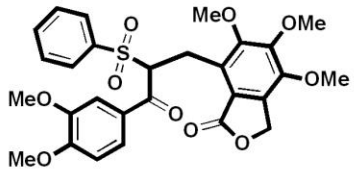


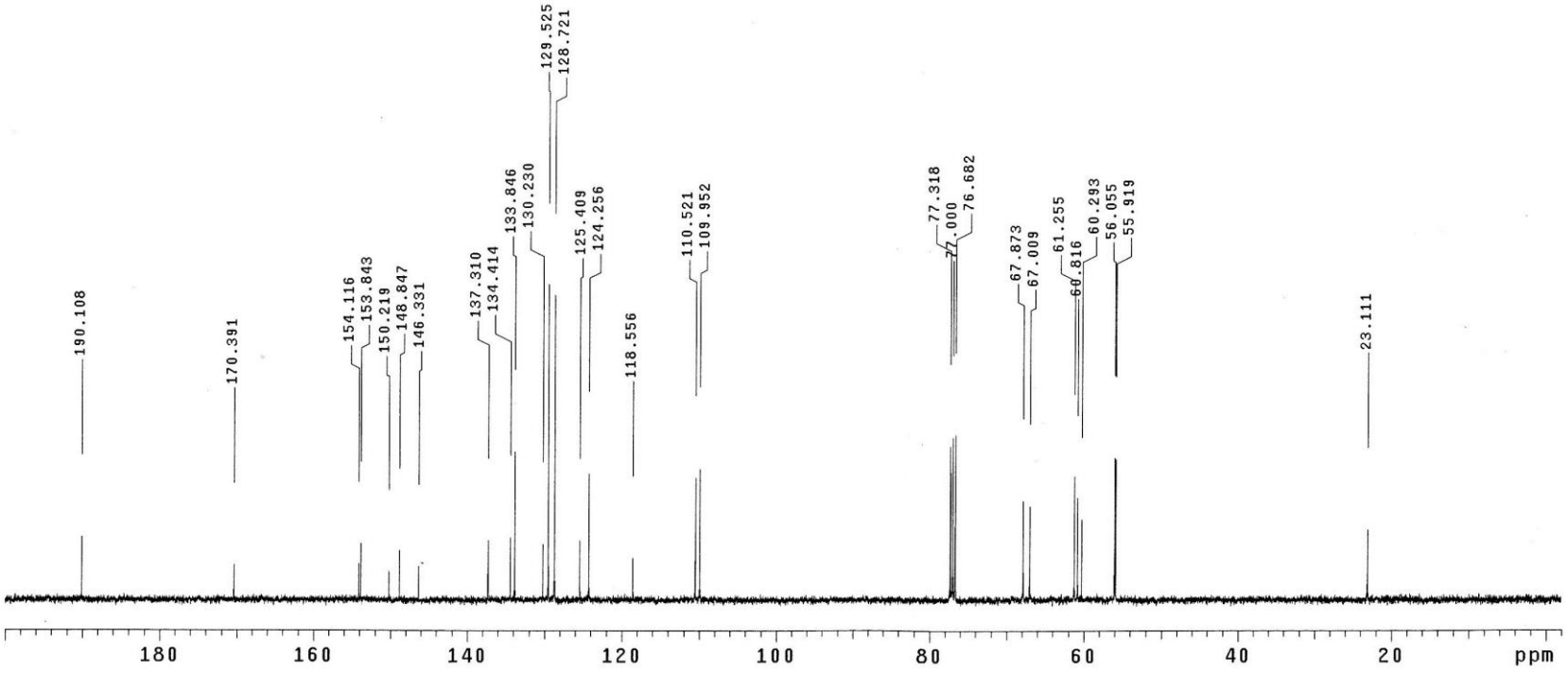
Compound 6b (^{13}C-NMR spectral data)

OYW0226

Pulse Sequence: s2pul

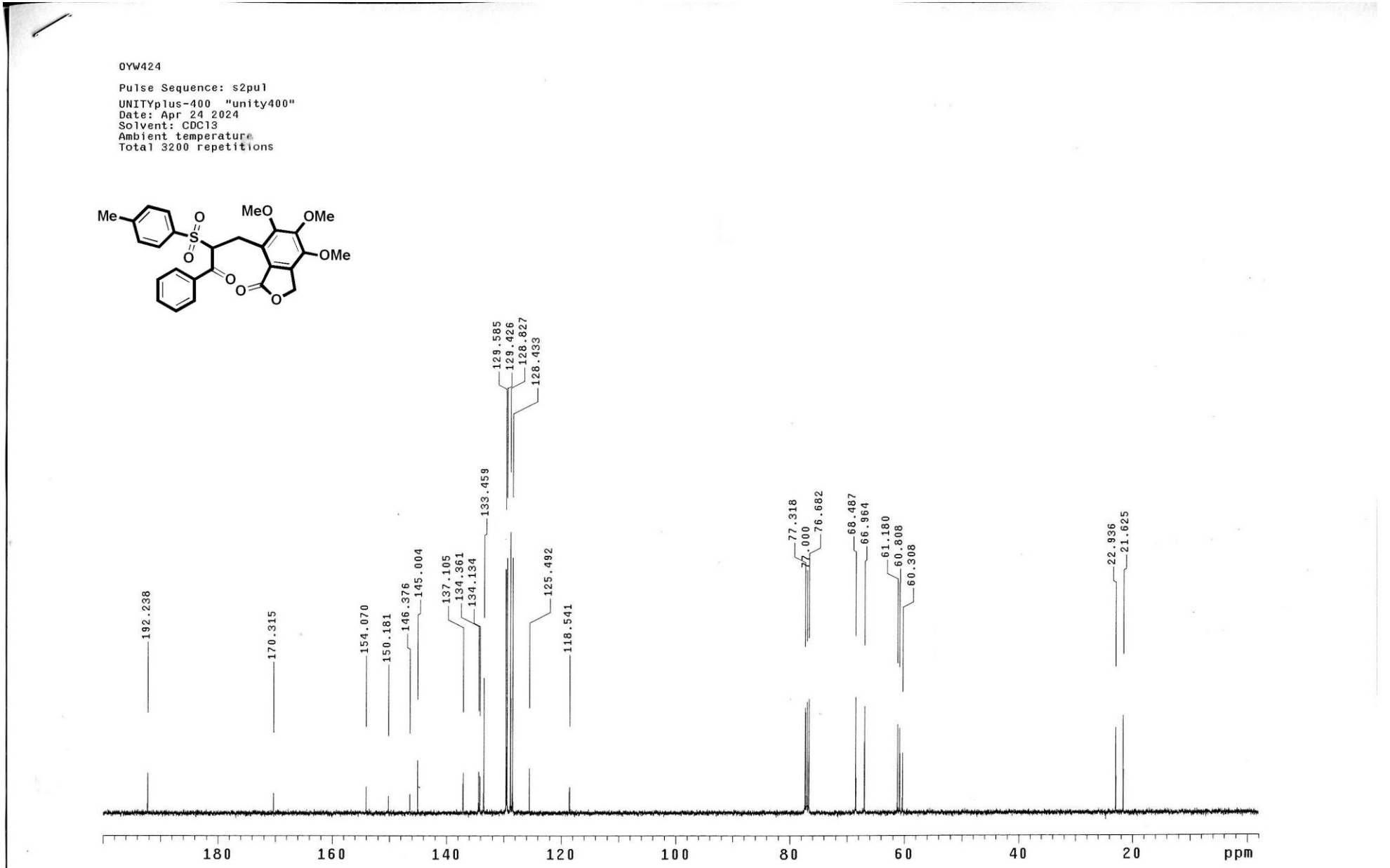
UNITYplus-400 "unity400"
Date: Feb 26 2024
Solvent: CDCl3
Ambient temperature
Total 2112 repetitions



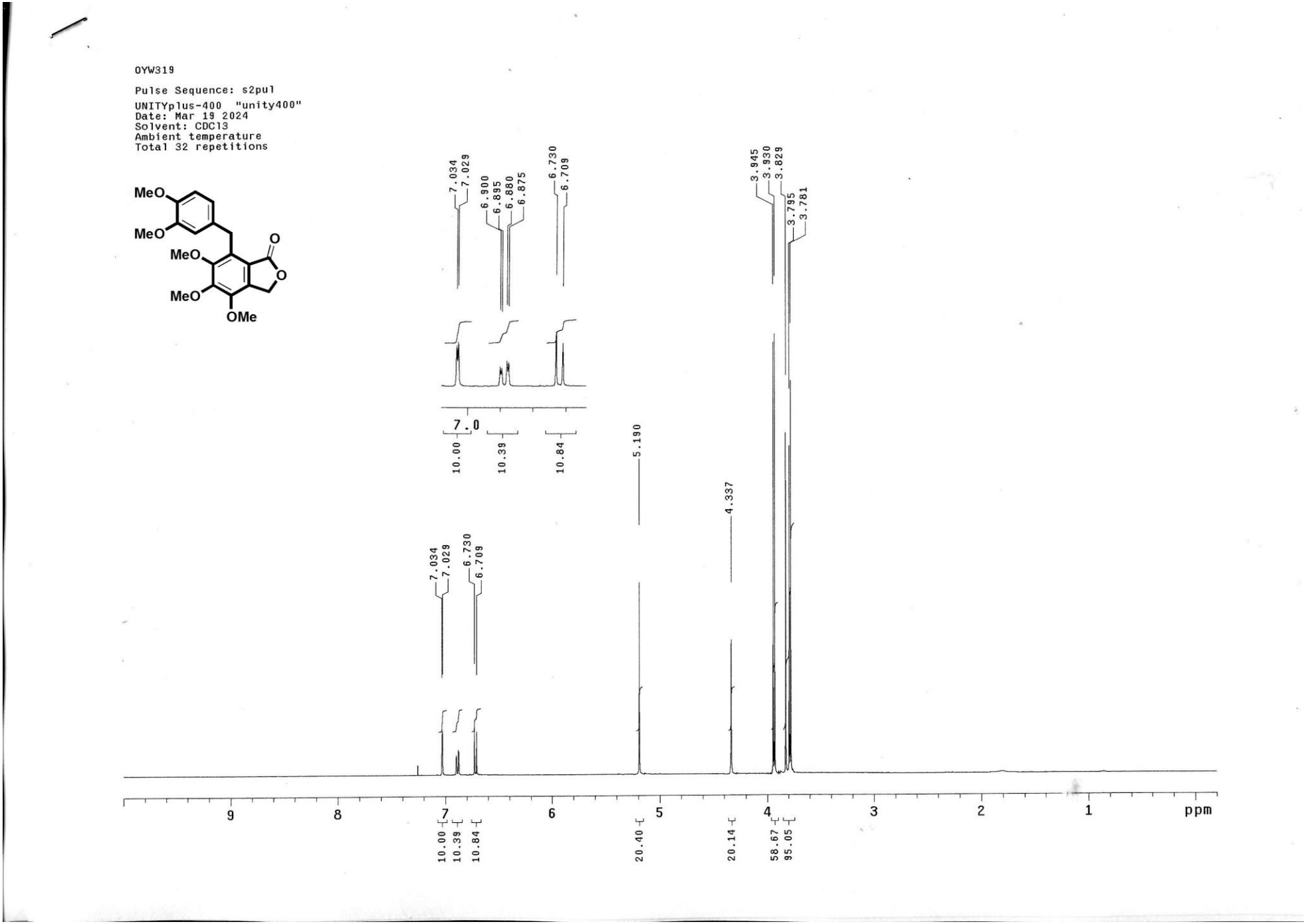


Compound 6c (^{1}H-NMR spectral data)

Compound 6c (^{13}C-NMR spectral data)



Compound 7a (^{1}H-NMR spectral data)

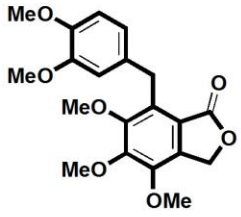


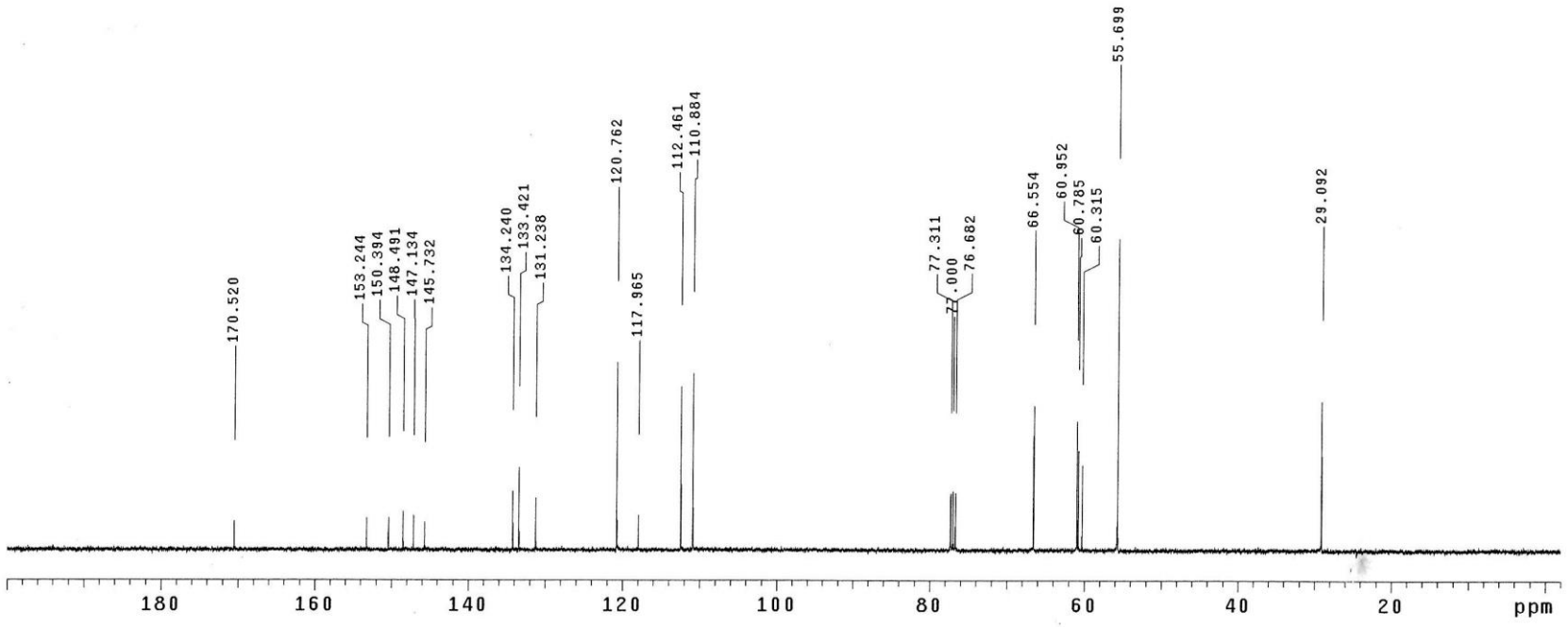
Compound 7a (^{13}C-NMR spectral data)

OYW319

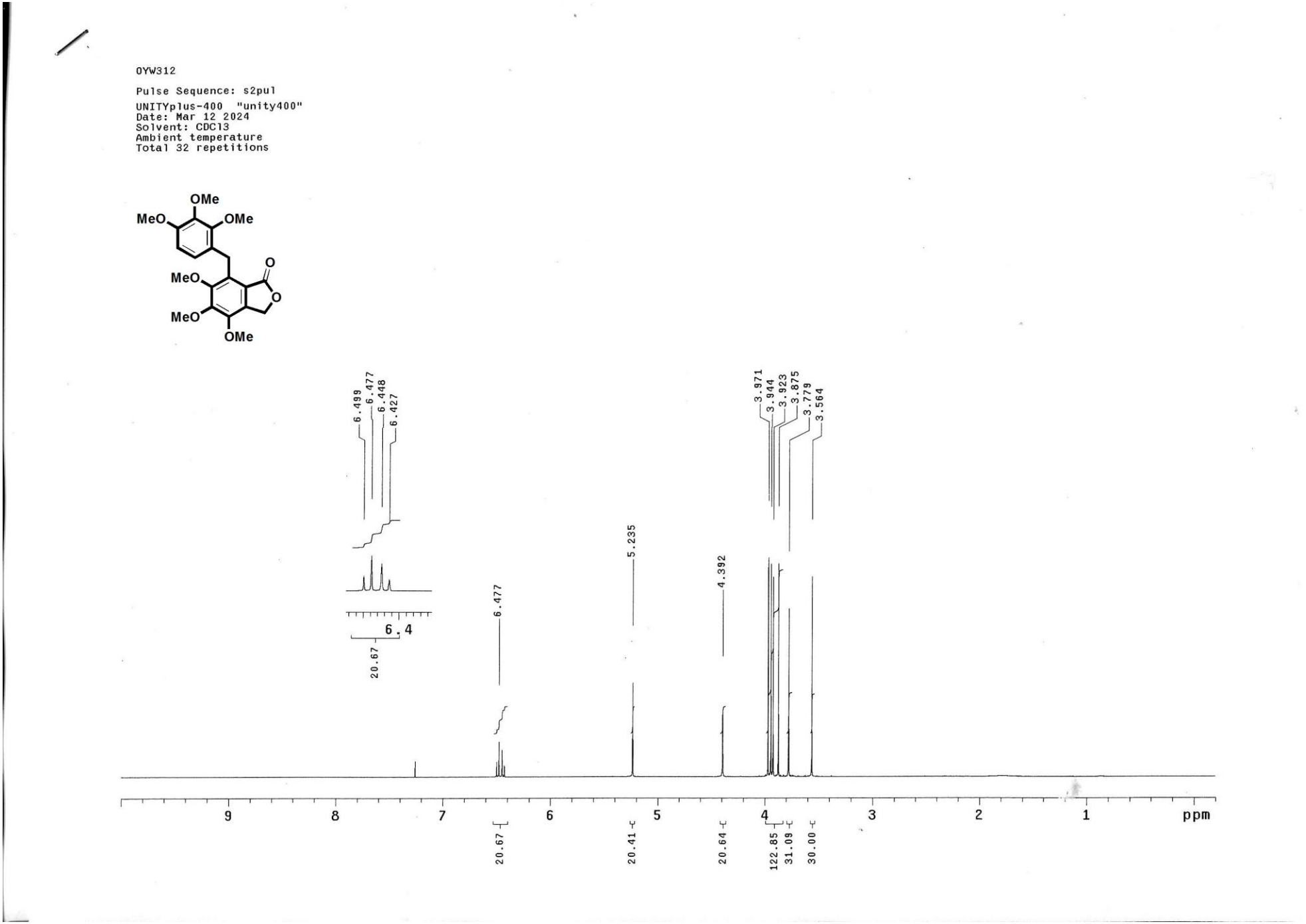
Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: Mar 19 2024
Solvent: CDCl3
Ambient temperature
Total 768 repetitions

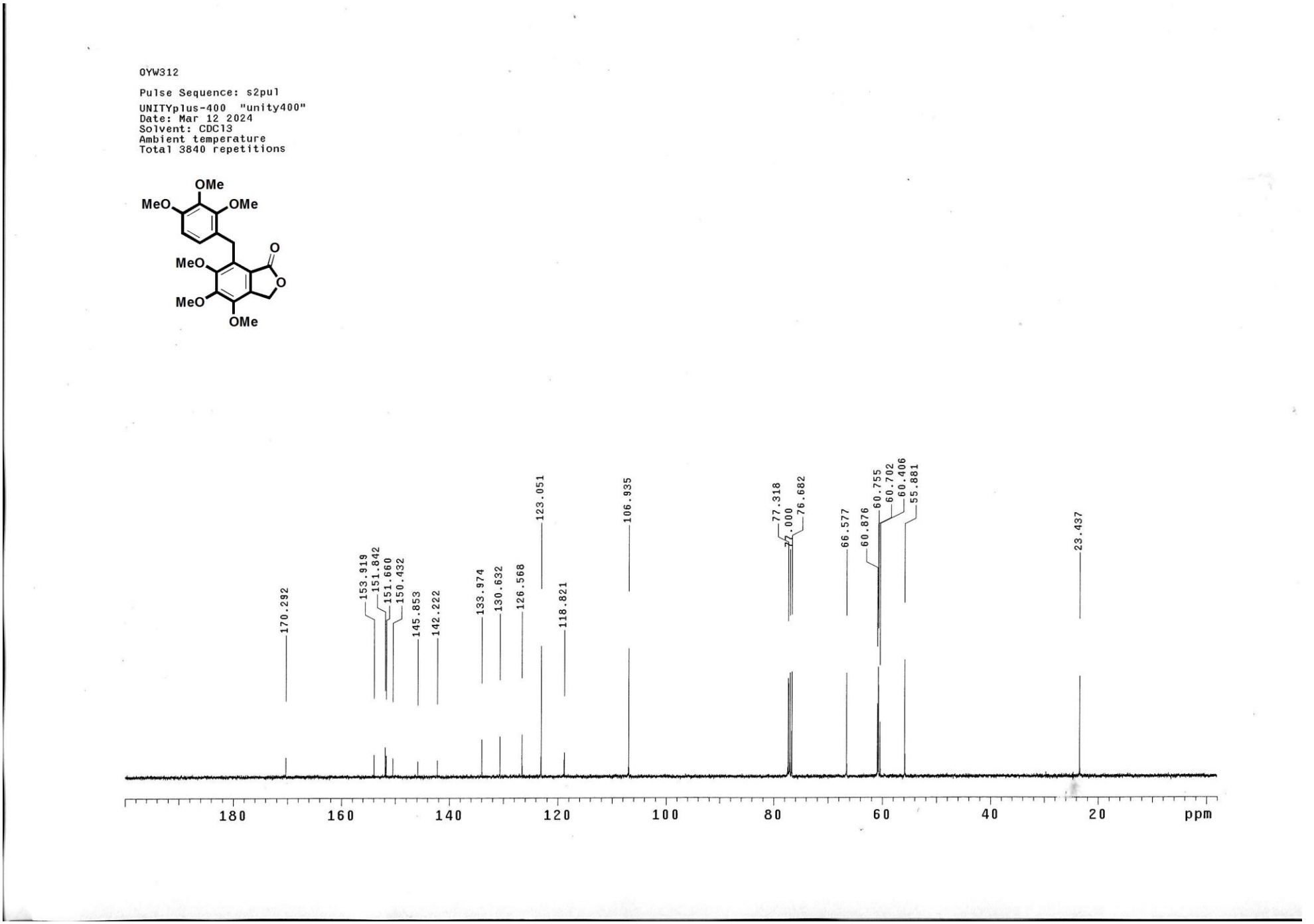




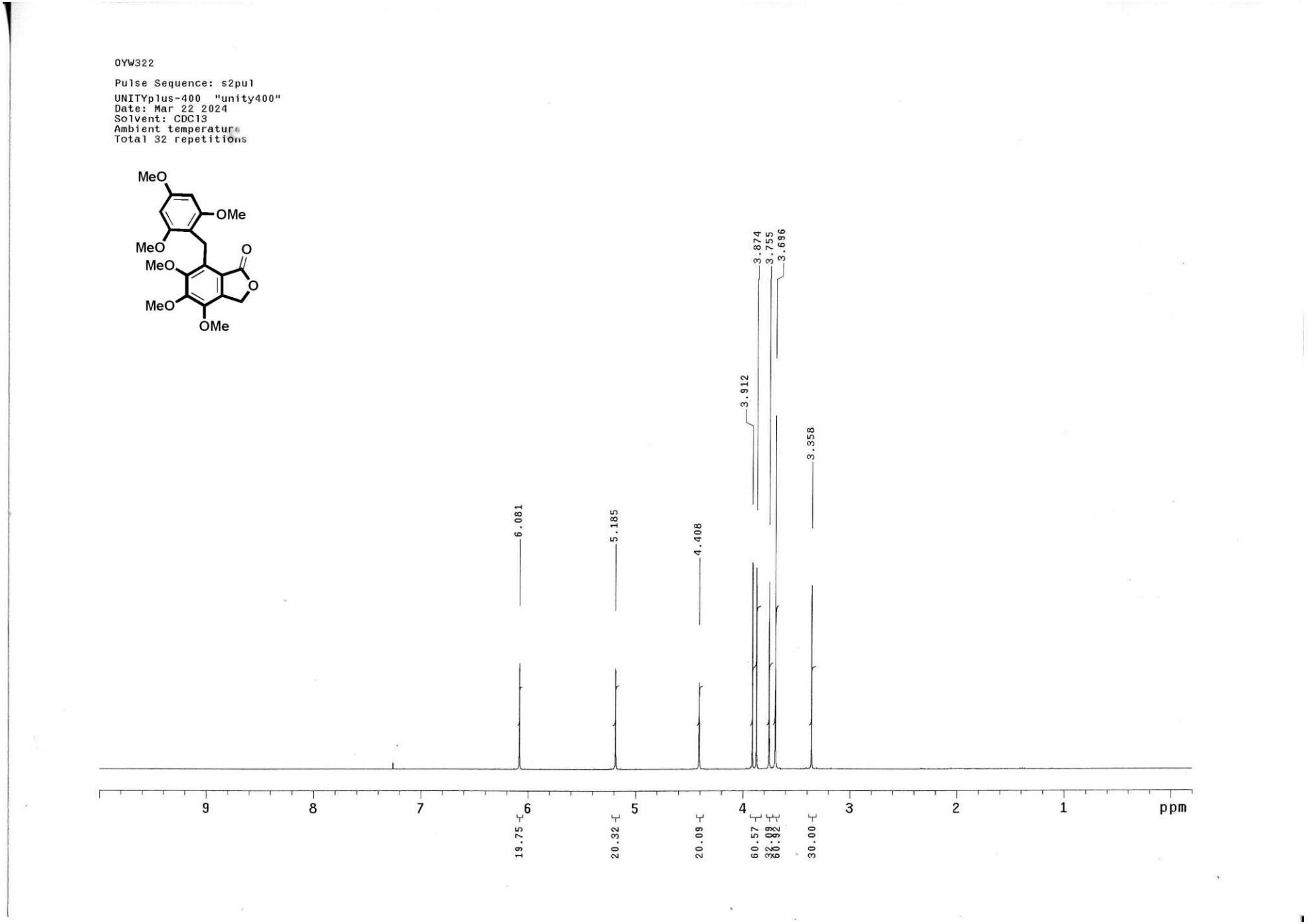
Compound 7b (^{1}H-NMR spectral data)



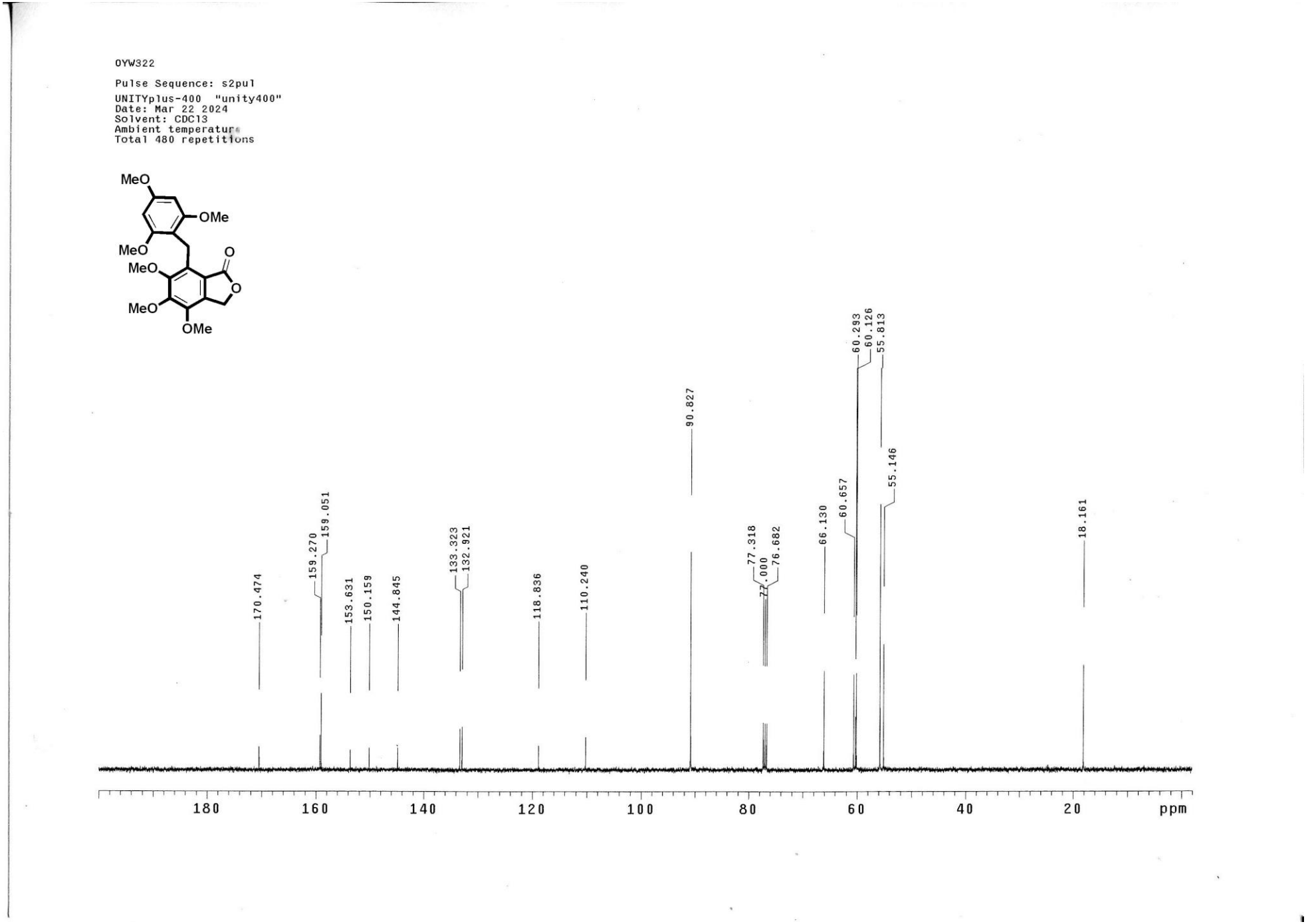
Compound 7b (^{13}C-NMR spectral data)



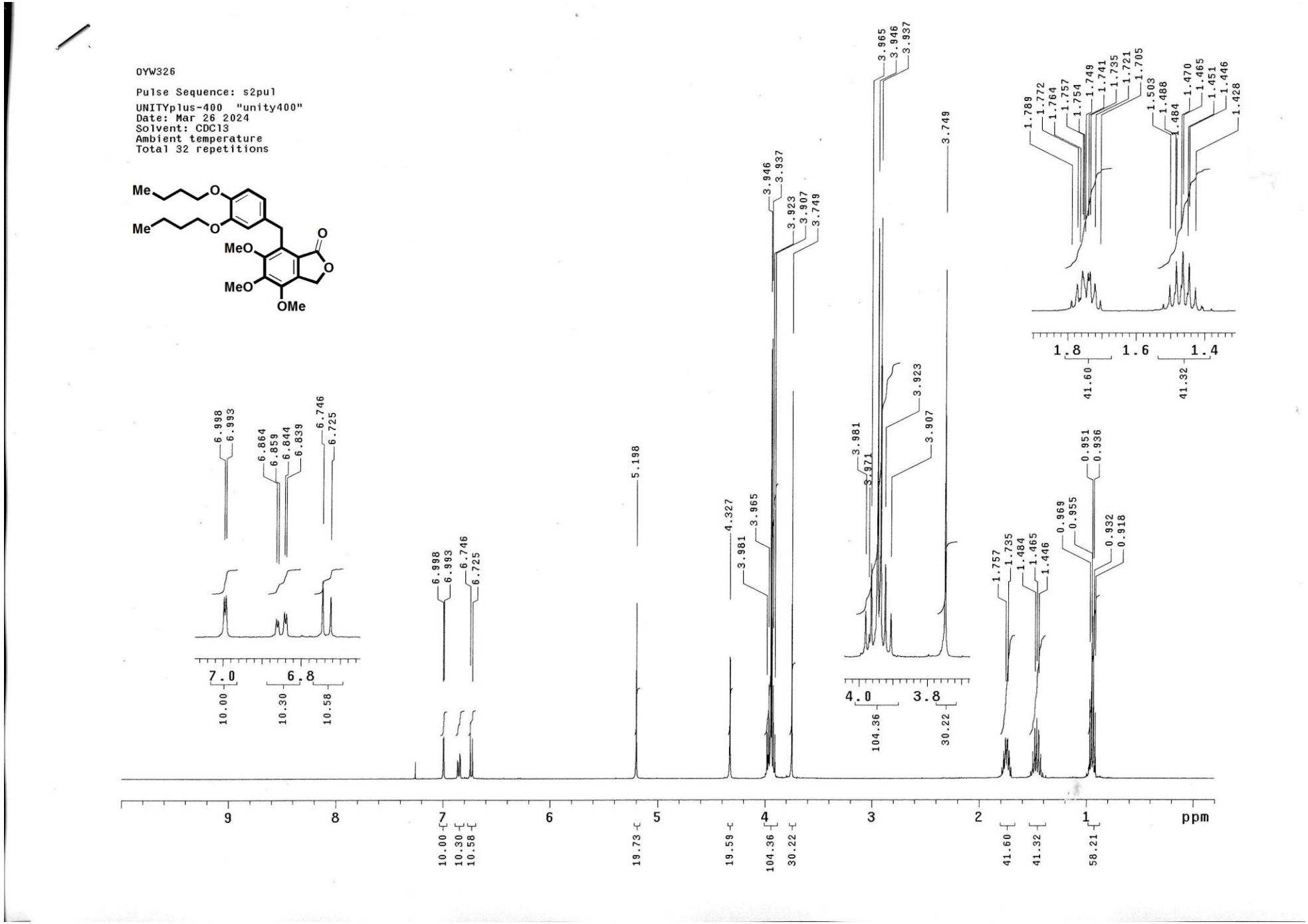
Compound 7c (^{1}H-NMR spectral data)



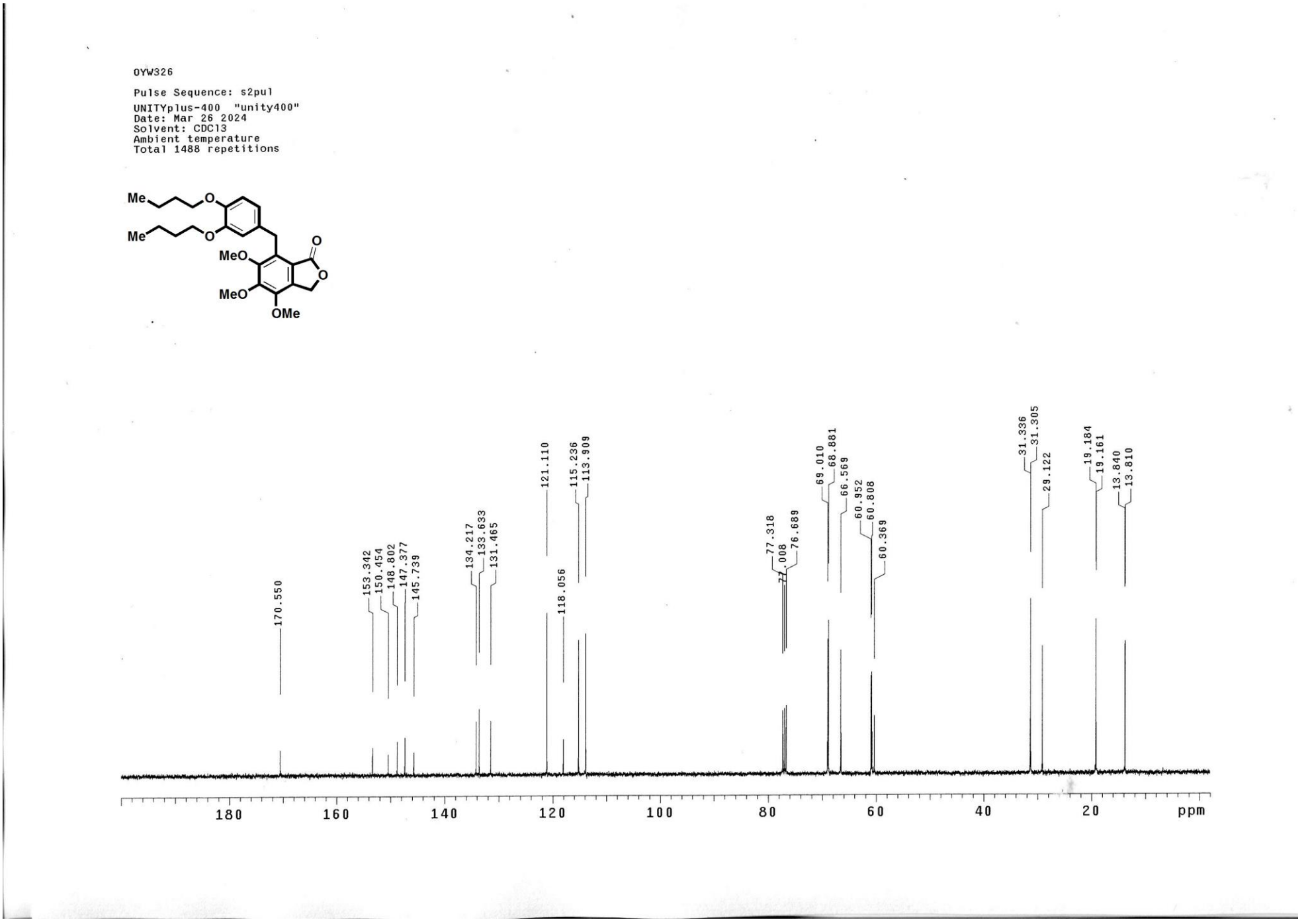
Compound 7c (^{13}C-NMR spectral data)



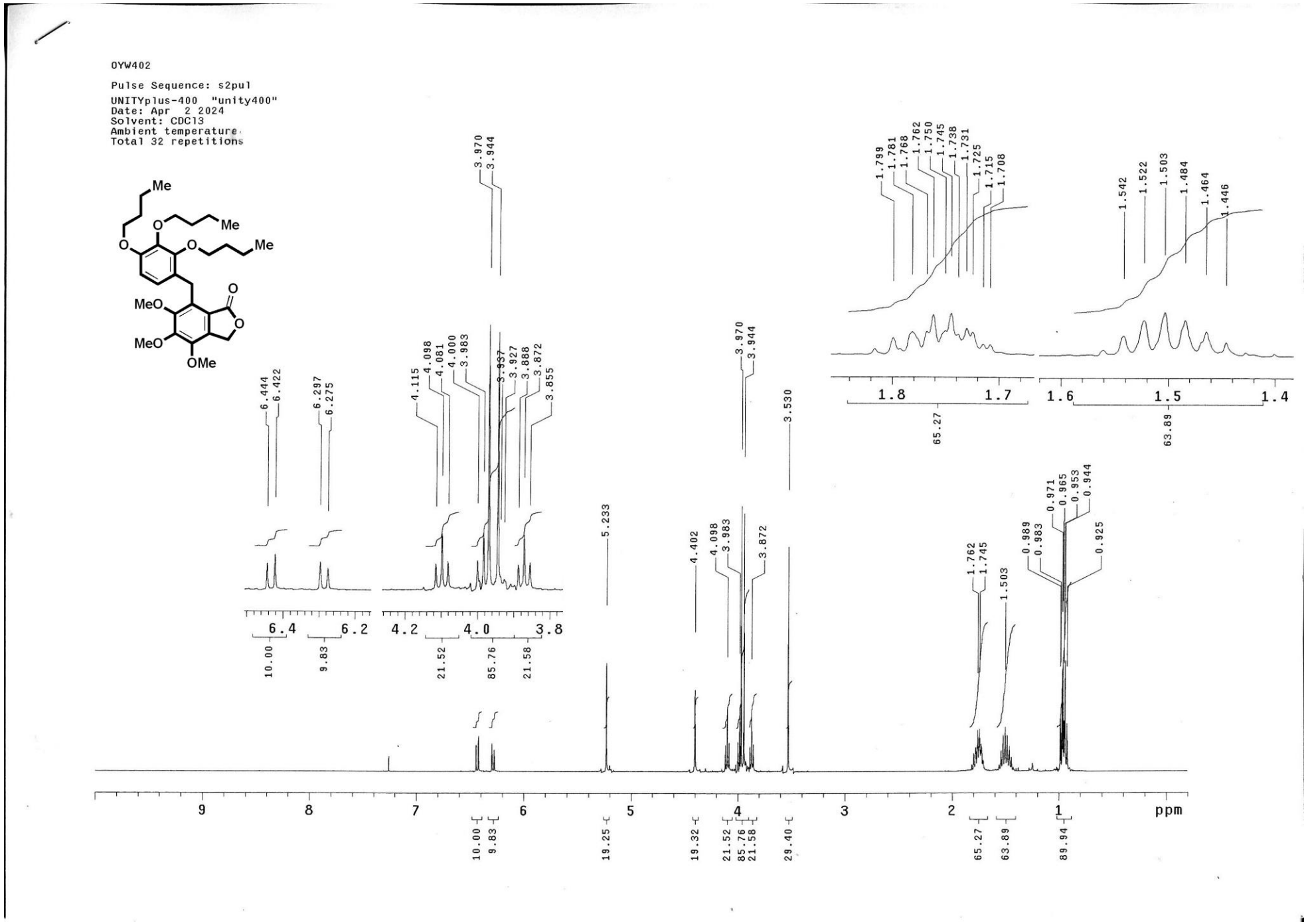
Compound 7d (^{1}H-NMR spectral data)



Compound 7d (^{13}C-NMR spectral data)



Compound 7e (^{1}H-NMR spectral data)

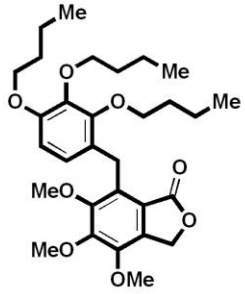


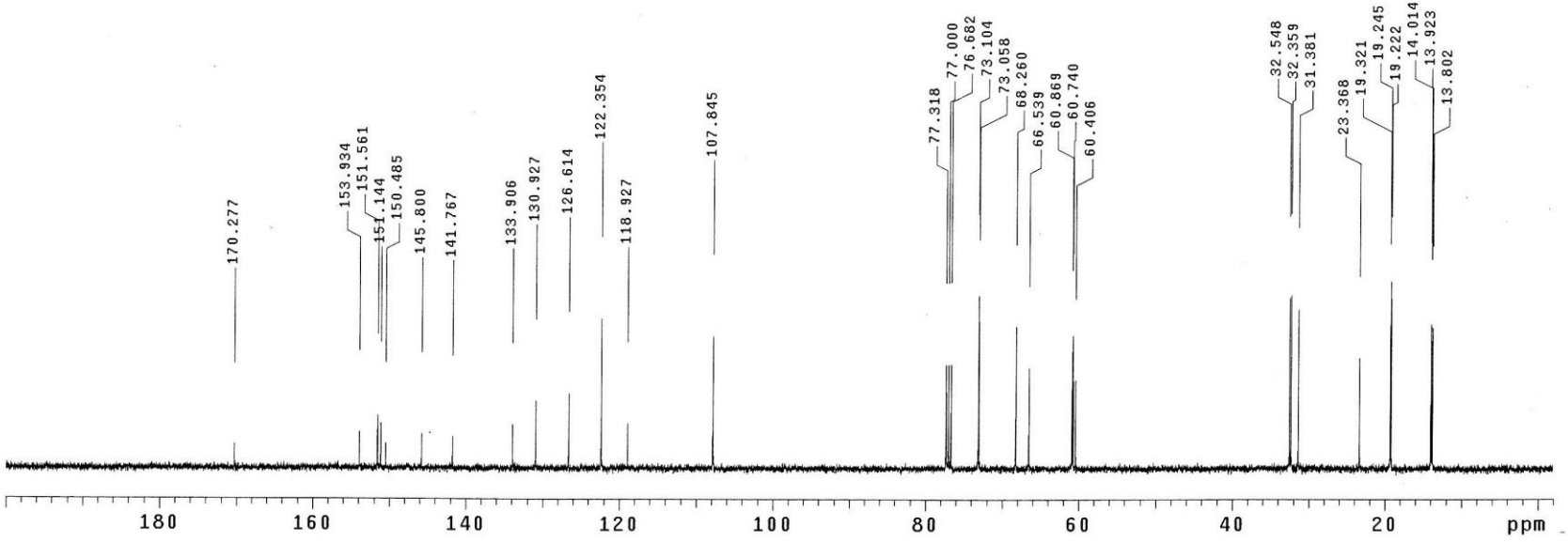
Compound 7e (^{13}C-NMR spectral data)

OYW402

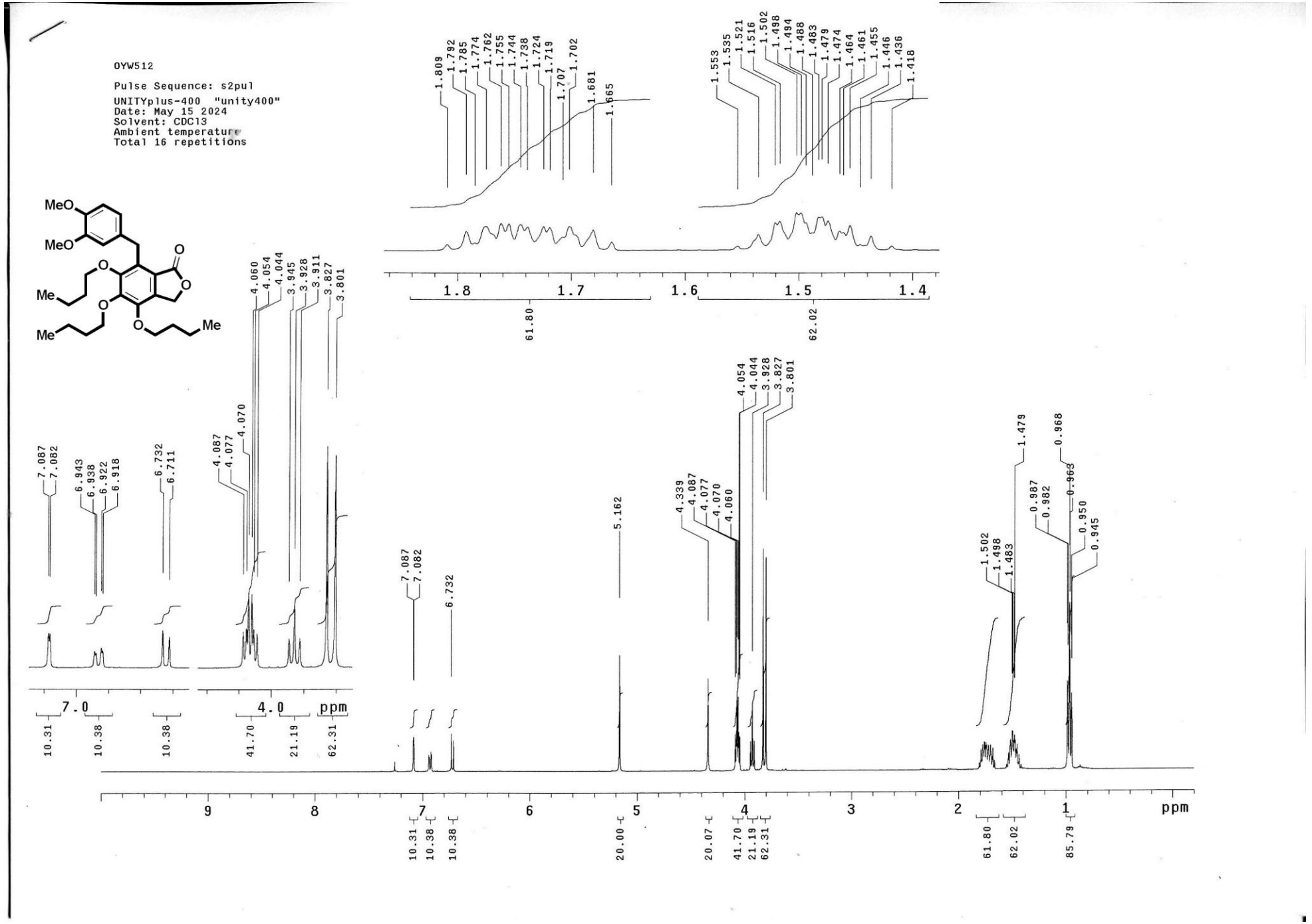
Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: Apr 2 2024
Solvent: CDCl3
Ambient temperature
Total 1328 repetitions





Compound 7f (^{1}H-NMR spectral data)

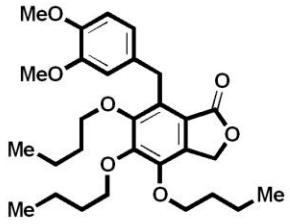


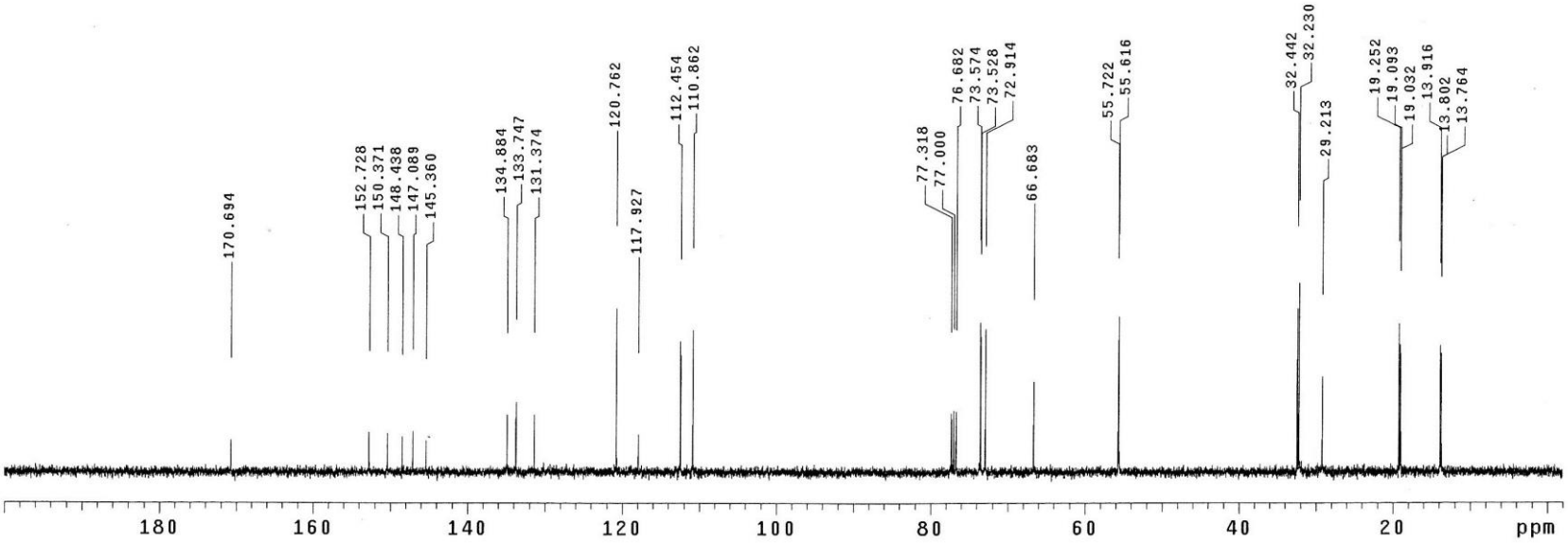
Compound 7f (^{13}C-NMR spectral data)

OYW512

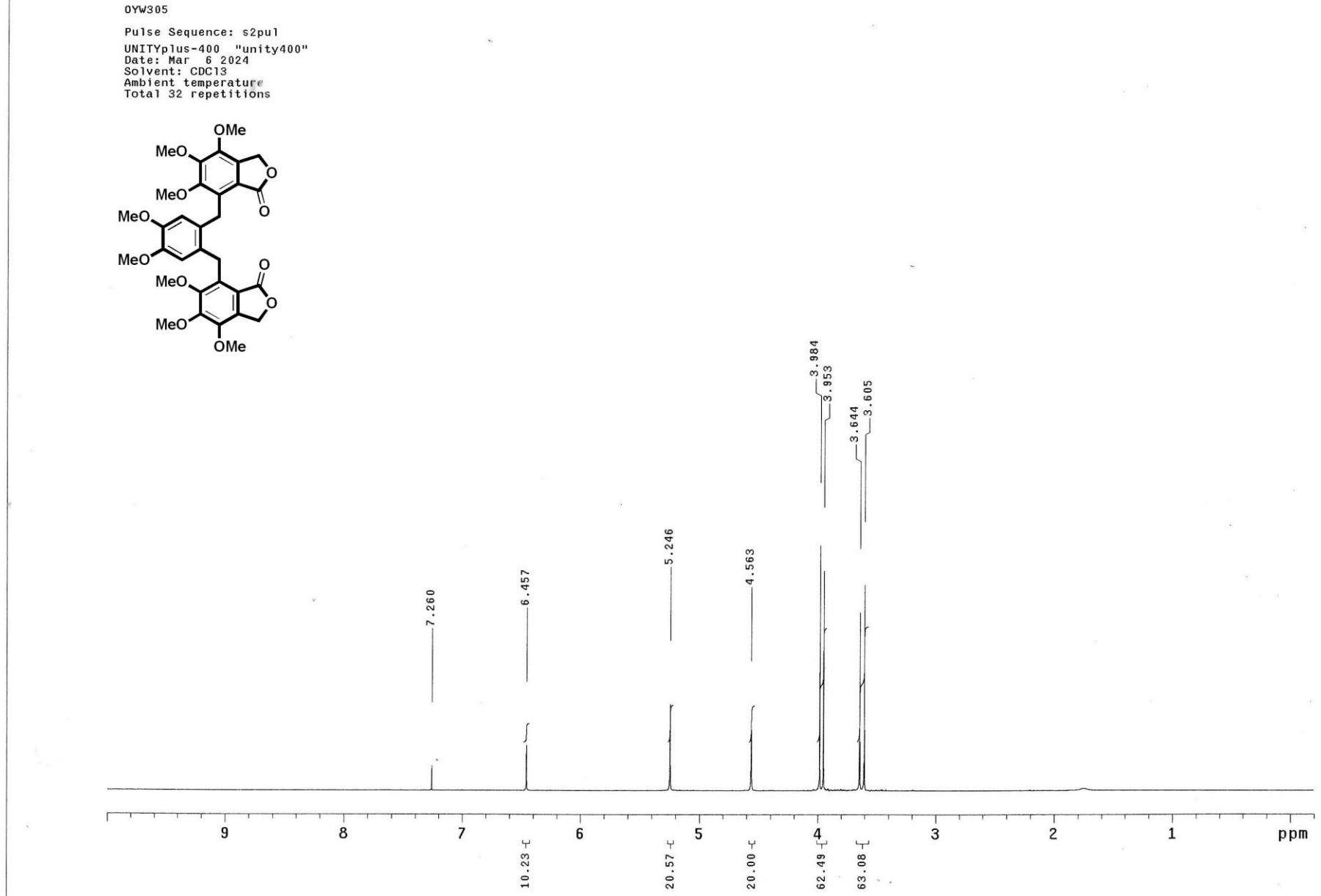
Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: May 15 2024
Solvent: CDCl3
Ambient temperature
Total 224 repetitions

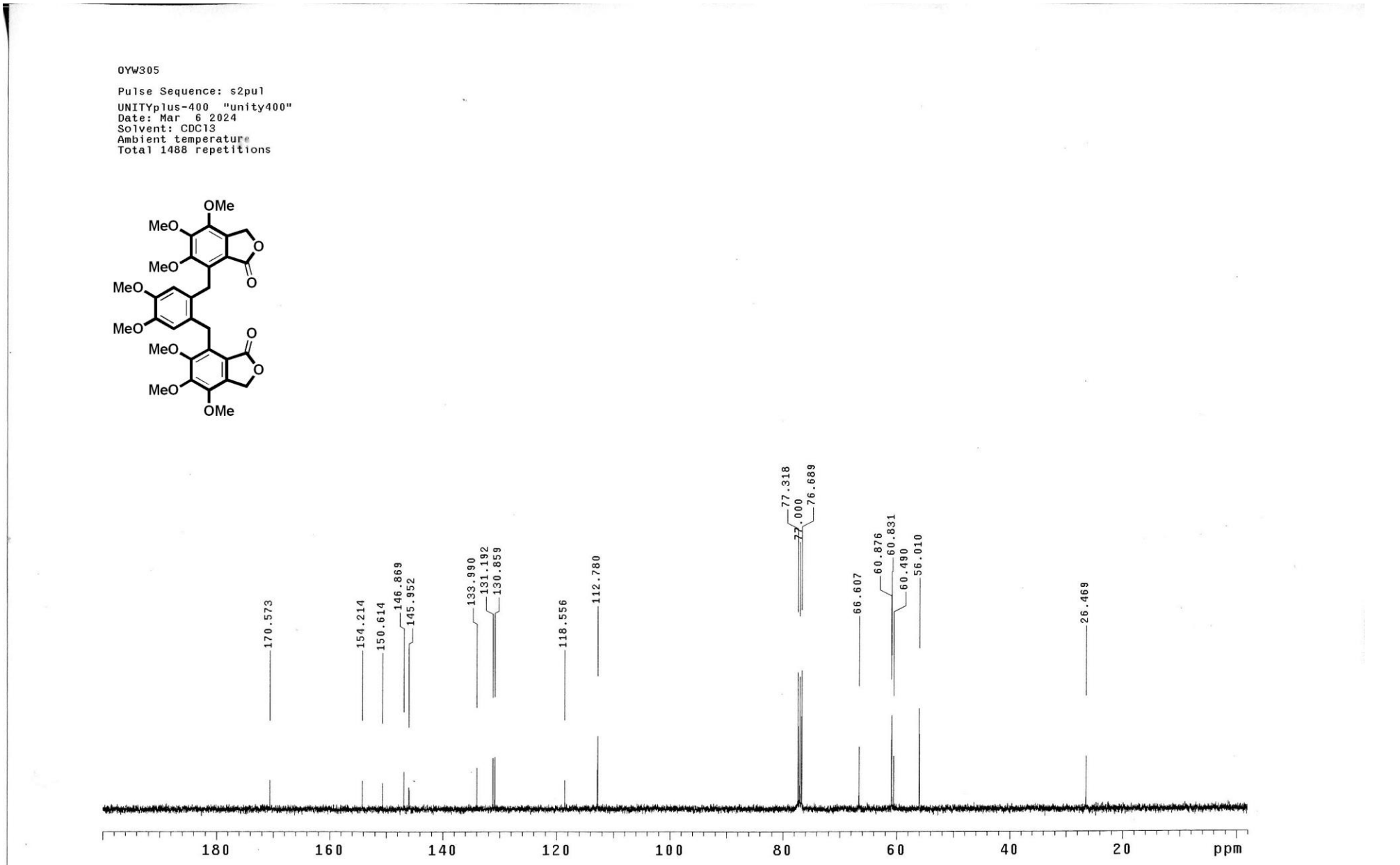




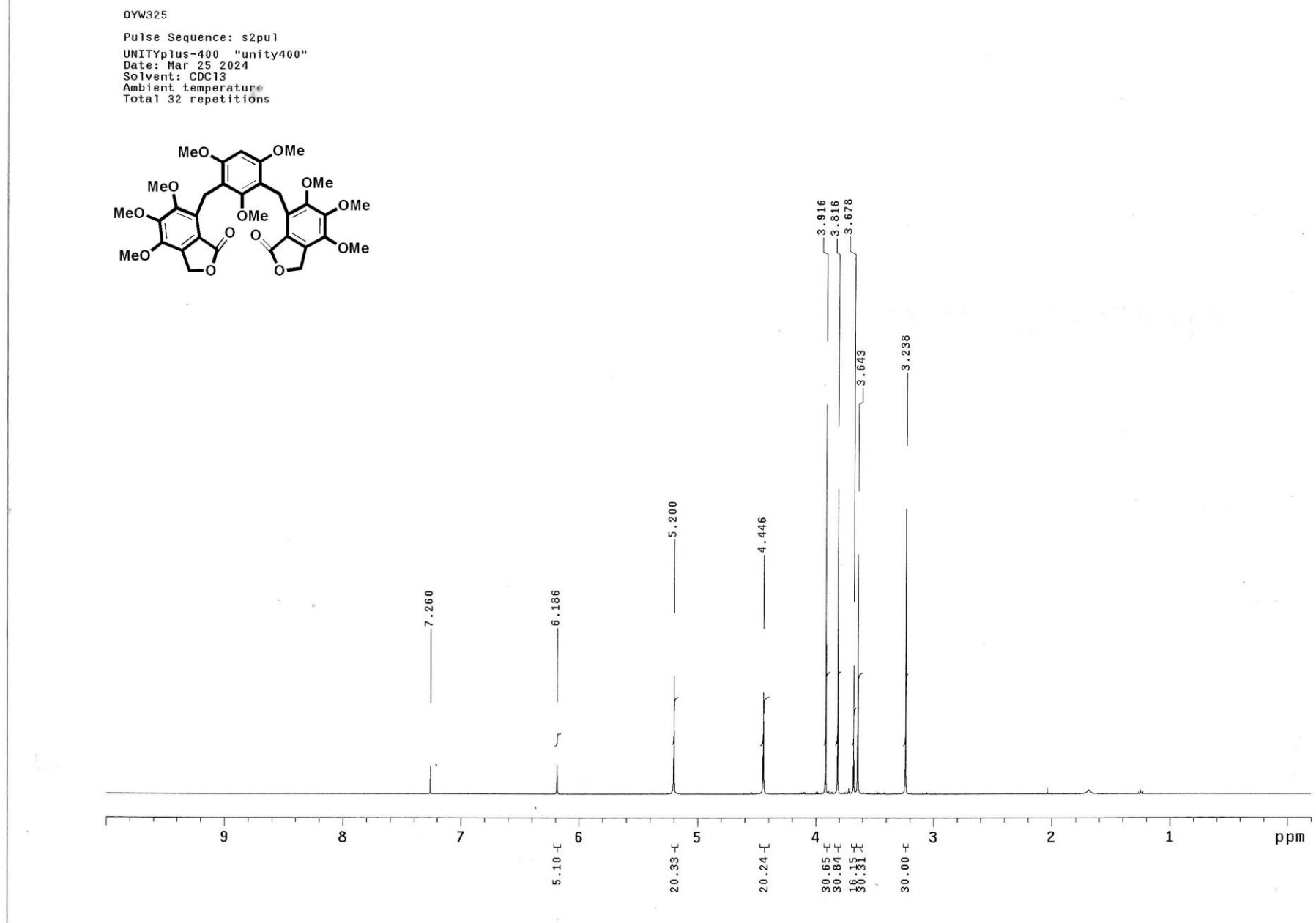
Compound 8a (^{1}H-NMR spectral data)



Compound 8a (^{13}C-NMR spectral data)



Compound 8b (^{1}H-NMR spectral data)

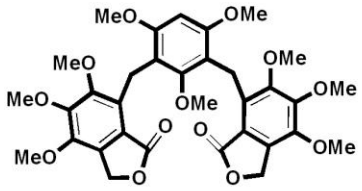


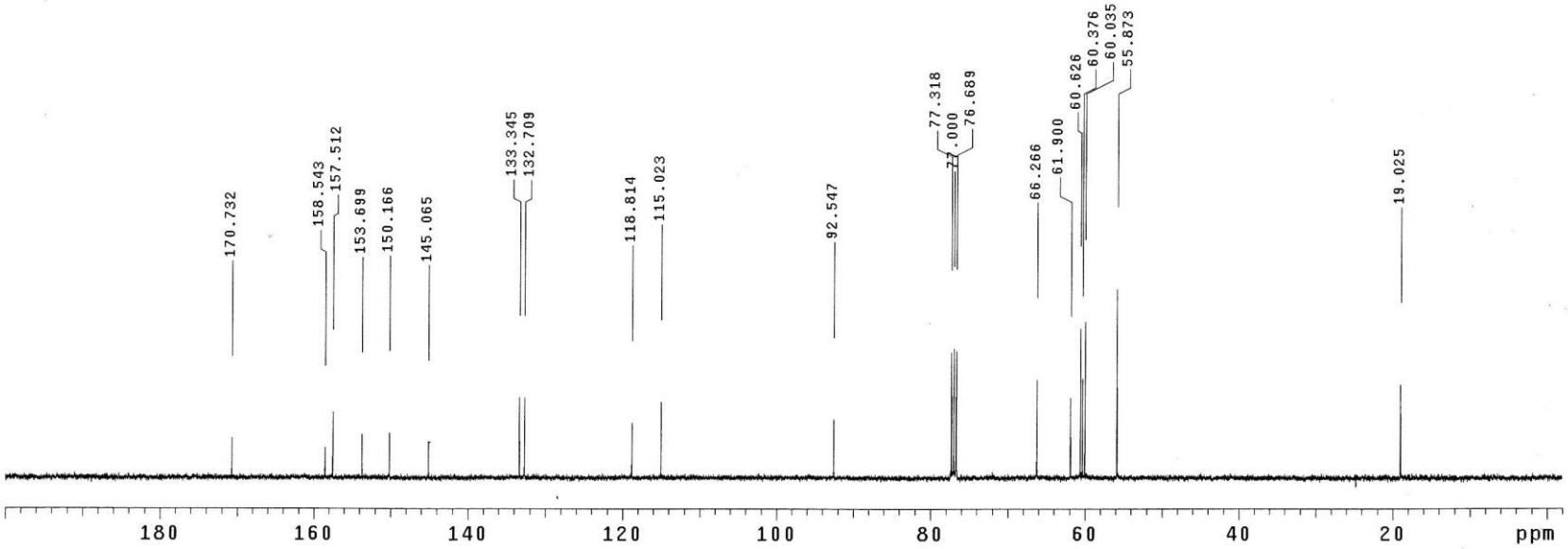
Compound 8b (^{13}C-NMR spectral data)

OYW325

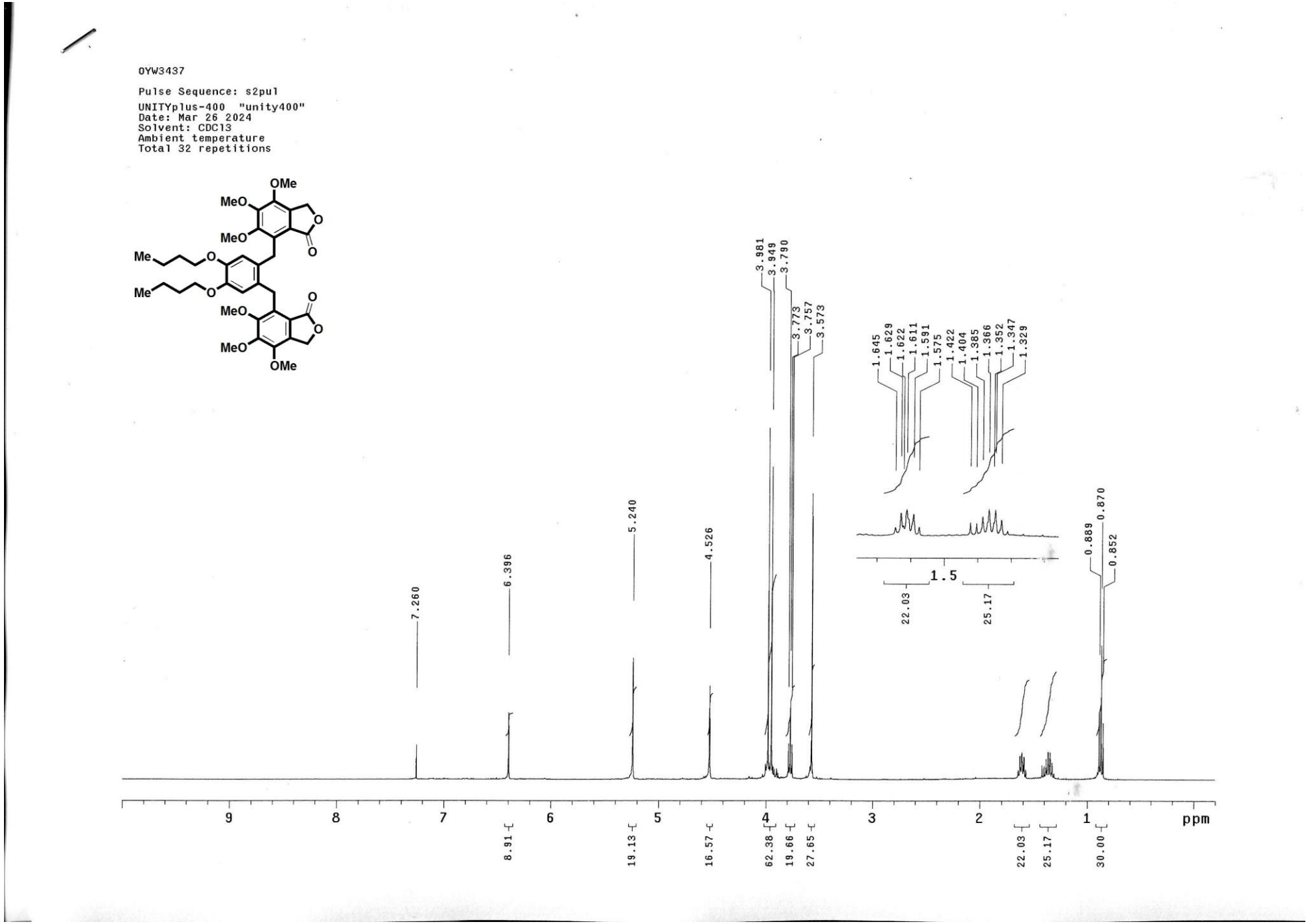
Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: Mar 25 2024
Solvent: CDCl3
Ambient temperature
Total 2688 repetitions

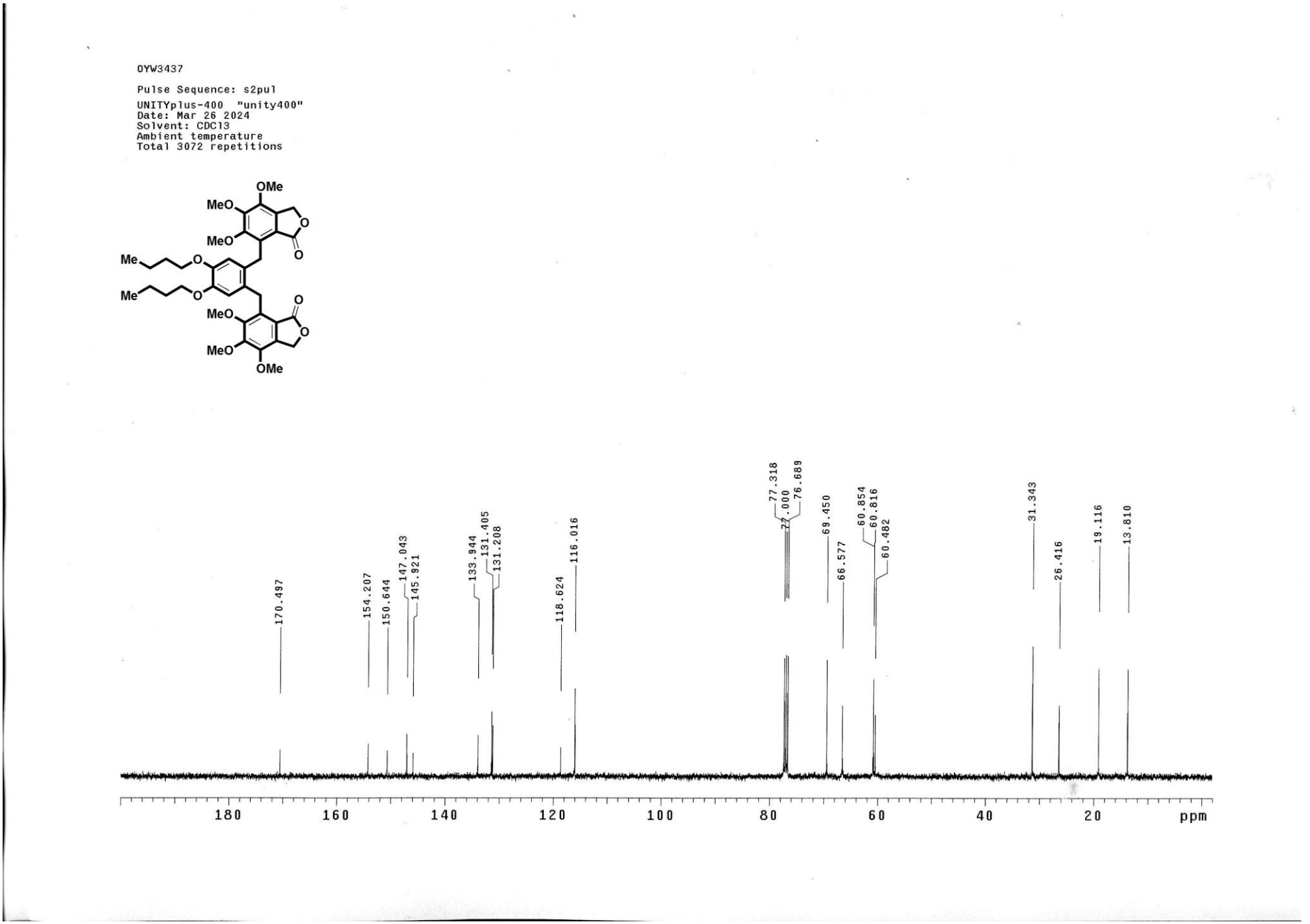




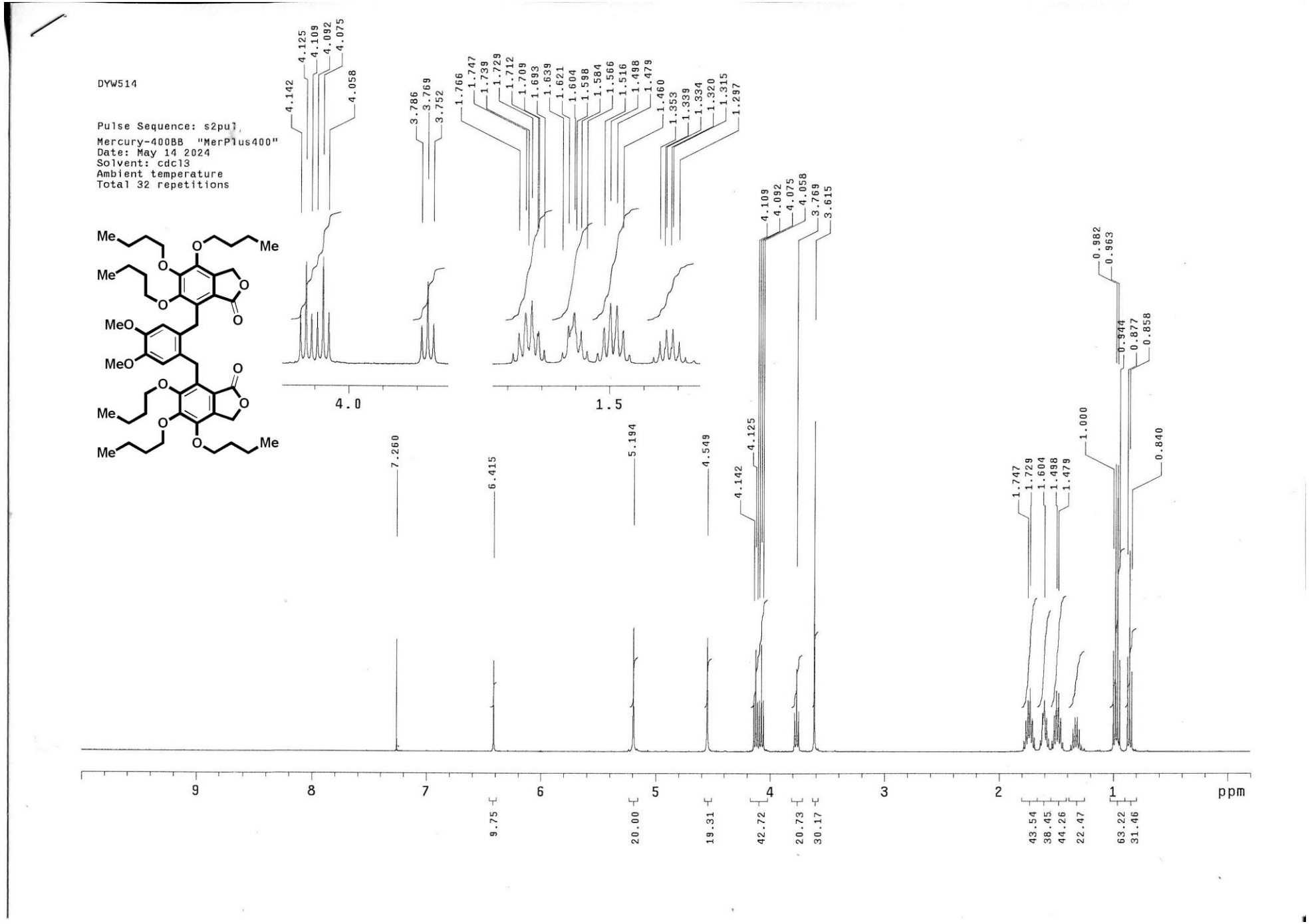
Compound 8c (^{1}H-NMR spectral data)



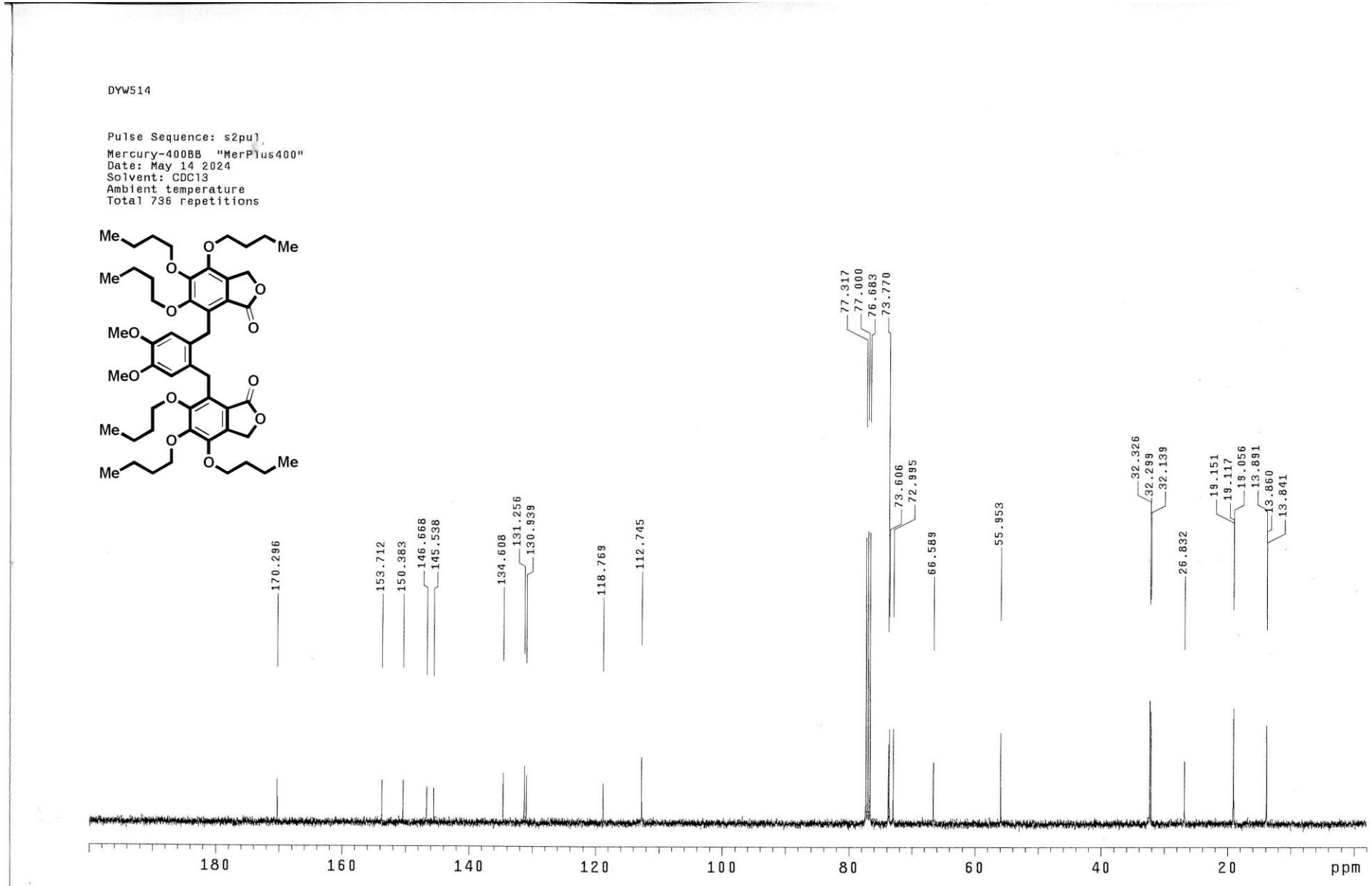
Compound 8c (^{13}C-NMR spectral data)



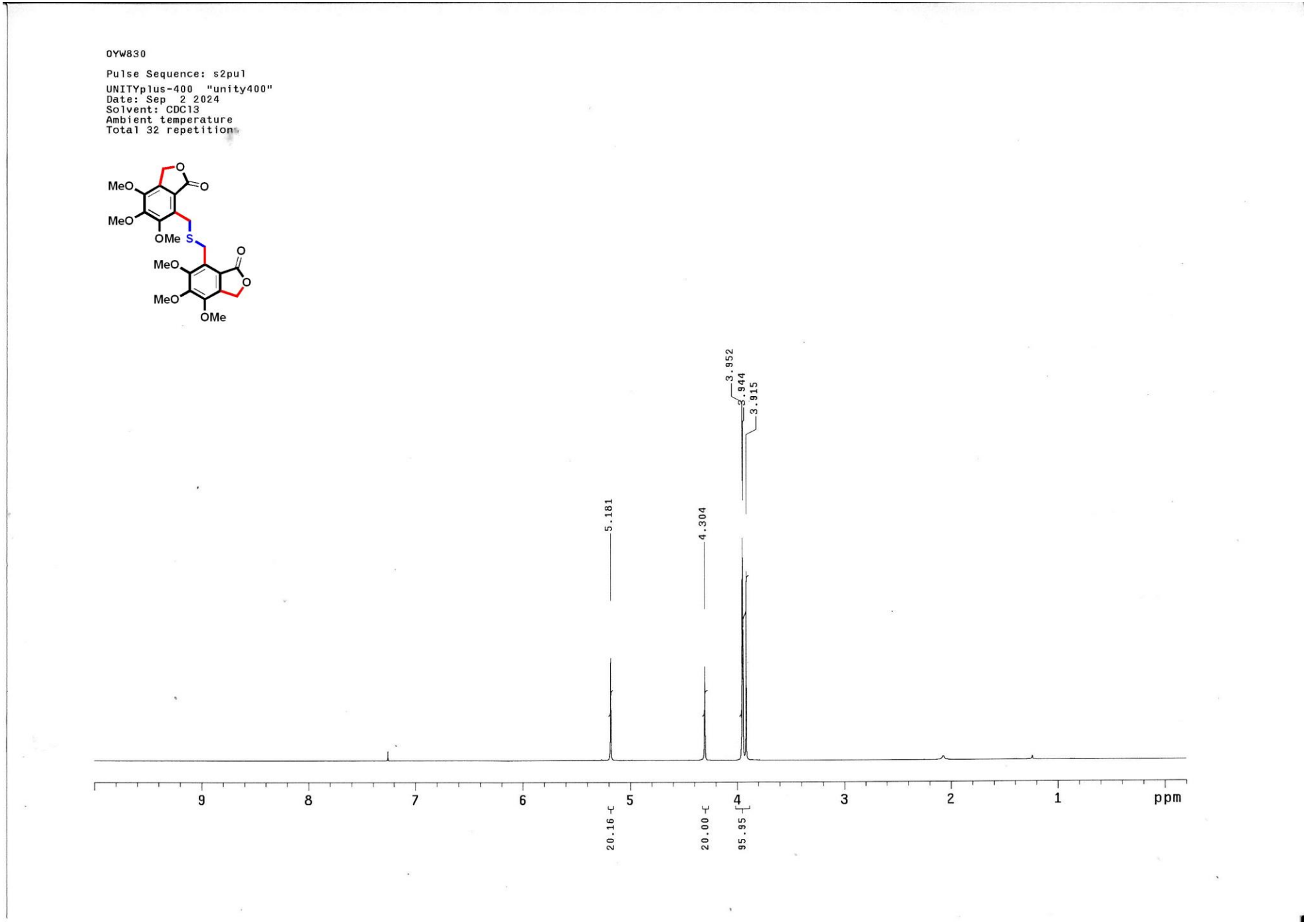
Compound 8d (^{1}H-NMR spectral data)



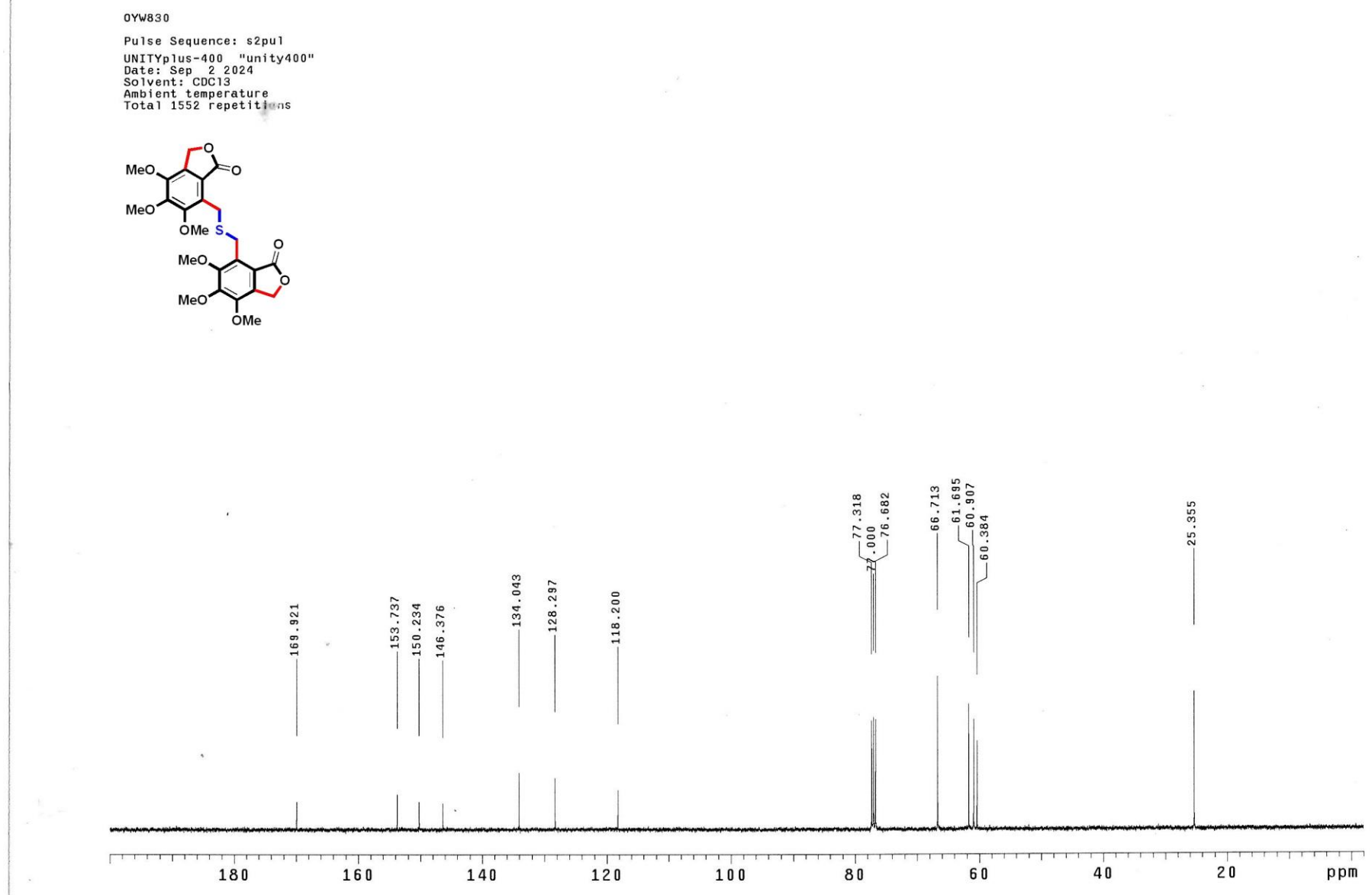
Compound 8d (^{13}C-NMR spectral data)



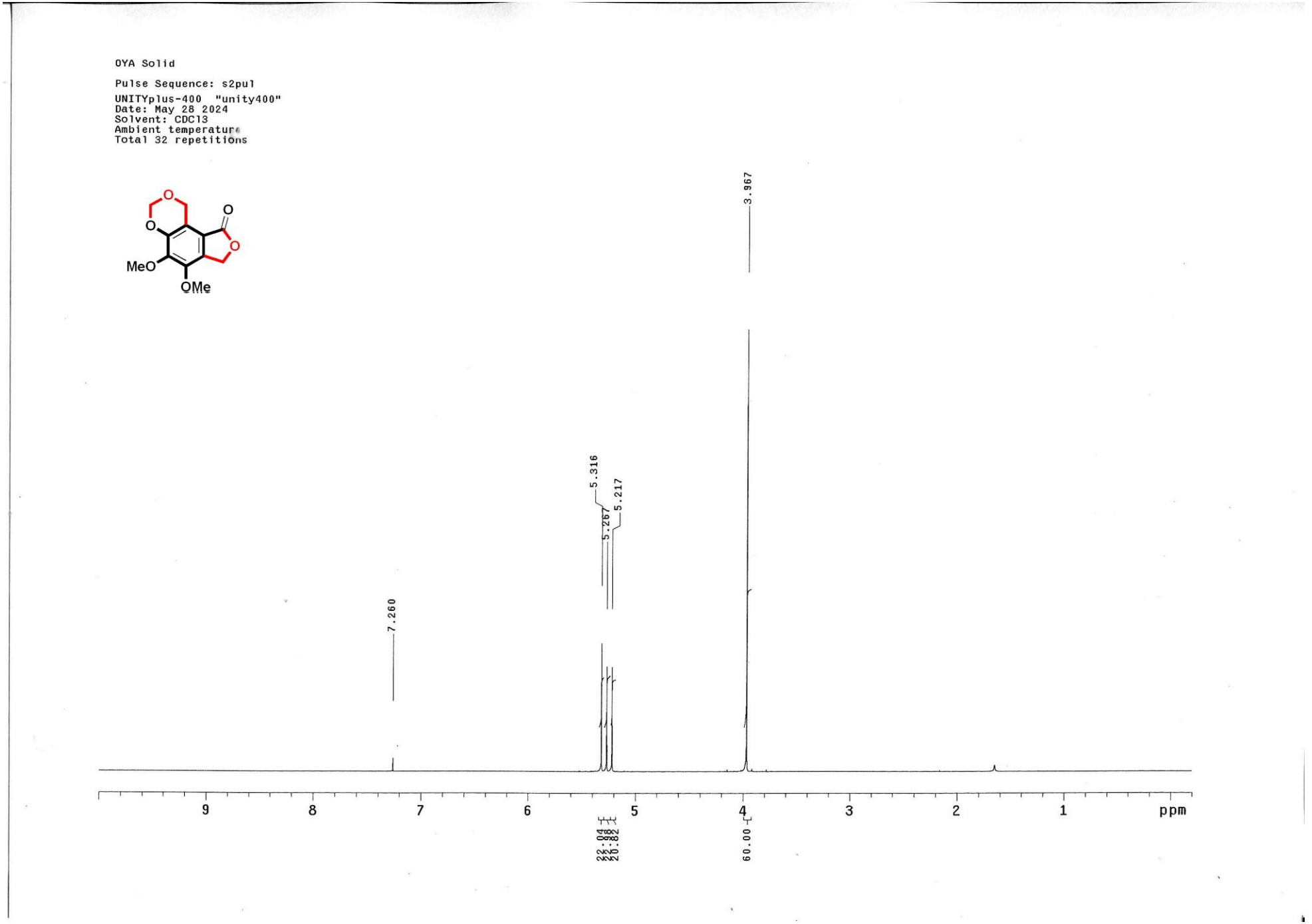
Compound 9a (^{1}H-NMR spectral data)



Compound 9a (^{13}C-NMR spectral data)



Compound 10a (^{1}H-NMR spectral data)

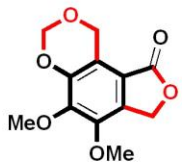


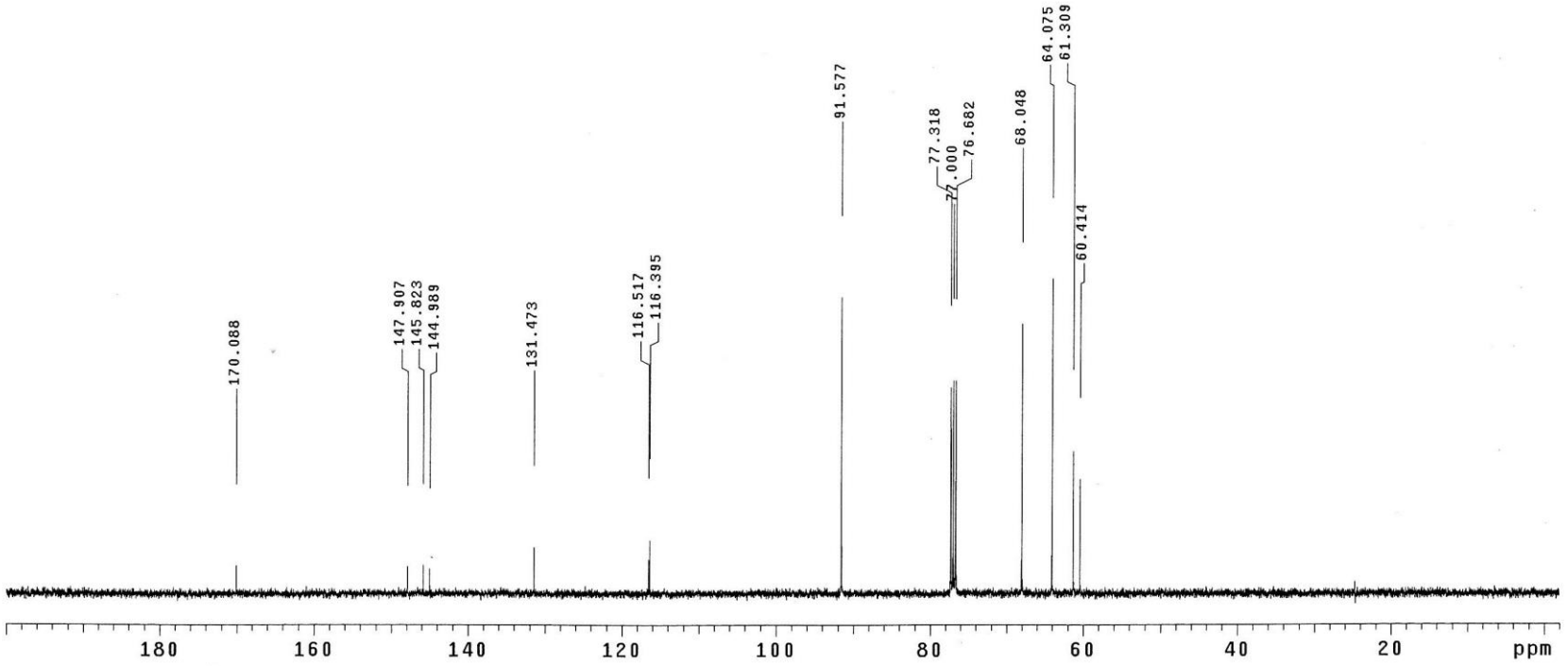
Compound 10a (^{13}C-NMR spectral data)

OYA Solid

Pulse Sequence: s2pul

UNITYplus-400 "unity400"
Date: May 28 2024
Solvent: CDCl3
Ambient temperature
Total 3120 repetitions



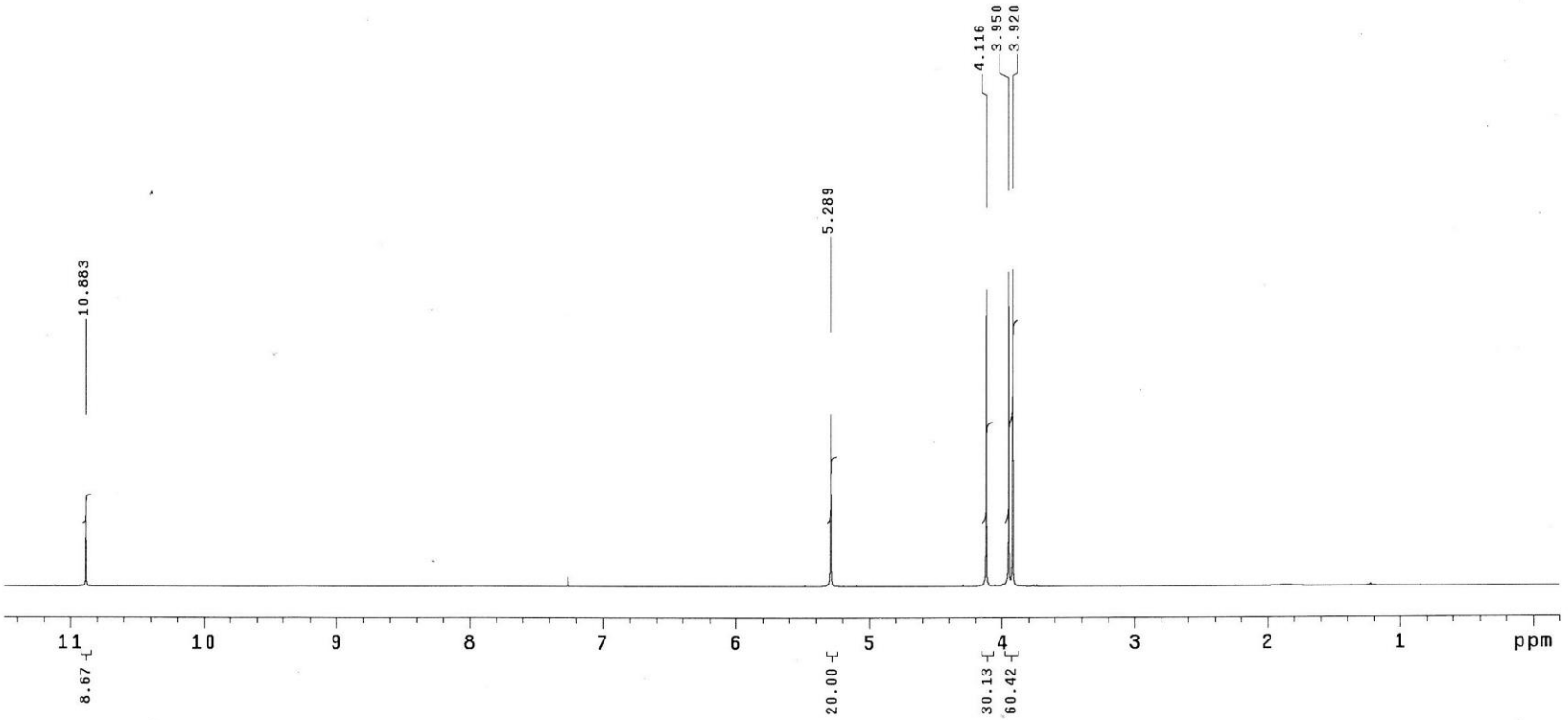


Compound 10b (^{1}H-NMR spectral data)

OYA1103

Pulse Sequence: s2pul

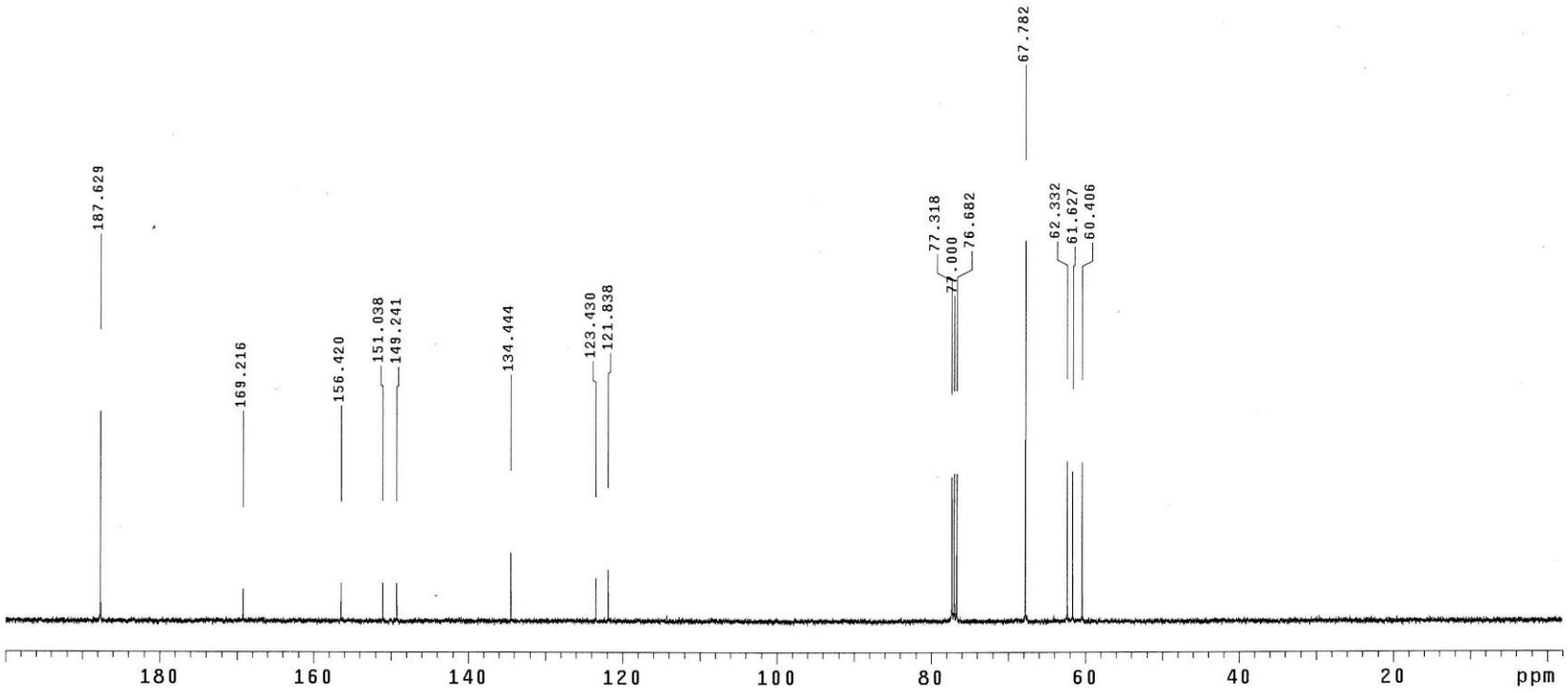
UNITYplus-400 "unity400"
Date: Nov 5 2024
Solvent: CDCl3
Ambient temperature
Total 32 repetitions



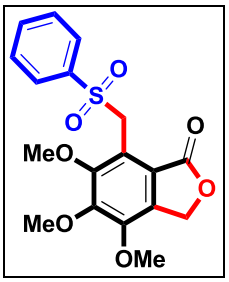
Compound 10b (^{13}C-NMR spectral data)

OYA1103

Pulse Sequence: s2pul
UNITYplus-400 "unity400"
Date: Nov 5 2024
Solvent: CDCl3
Ambient temperature
Total 1488 repetitions

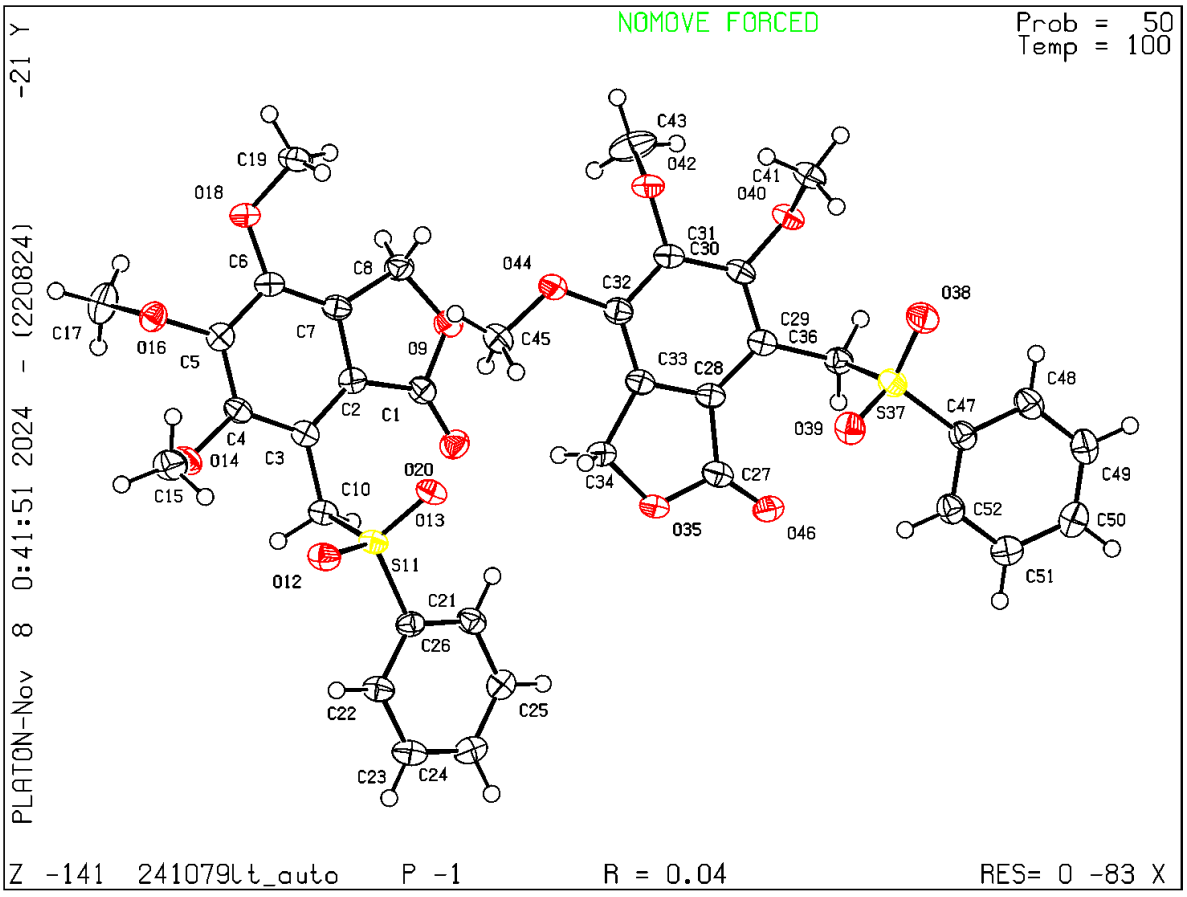


X-ray crystal data of compound 4a



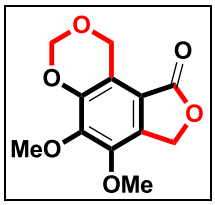
Sample preparation : A solution of compound **4a** (30 mg) in CH_2Cl_2 (10 mL) was placed in a tube (10 mL). EtOAc (2 mL) was added slowly to the vial with a dropper. The vial was closed with little cotton and kept at room temperature for 2 days. Then, colorless prisms were observed.

Crystal measurement : X-ray crystal structures were determined with a Bruker Enraf-Nonius single-crystal diffractometer (CAD4, Kappa CCD). Thermal ellipsoids are drawn at 50% probability level.



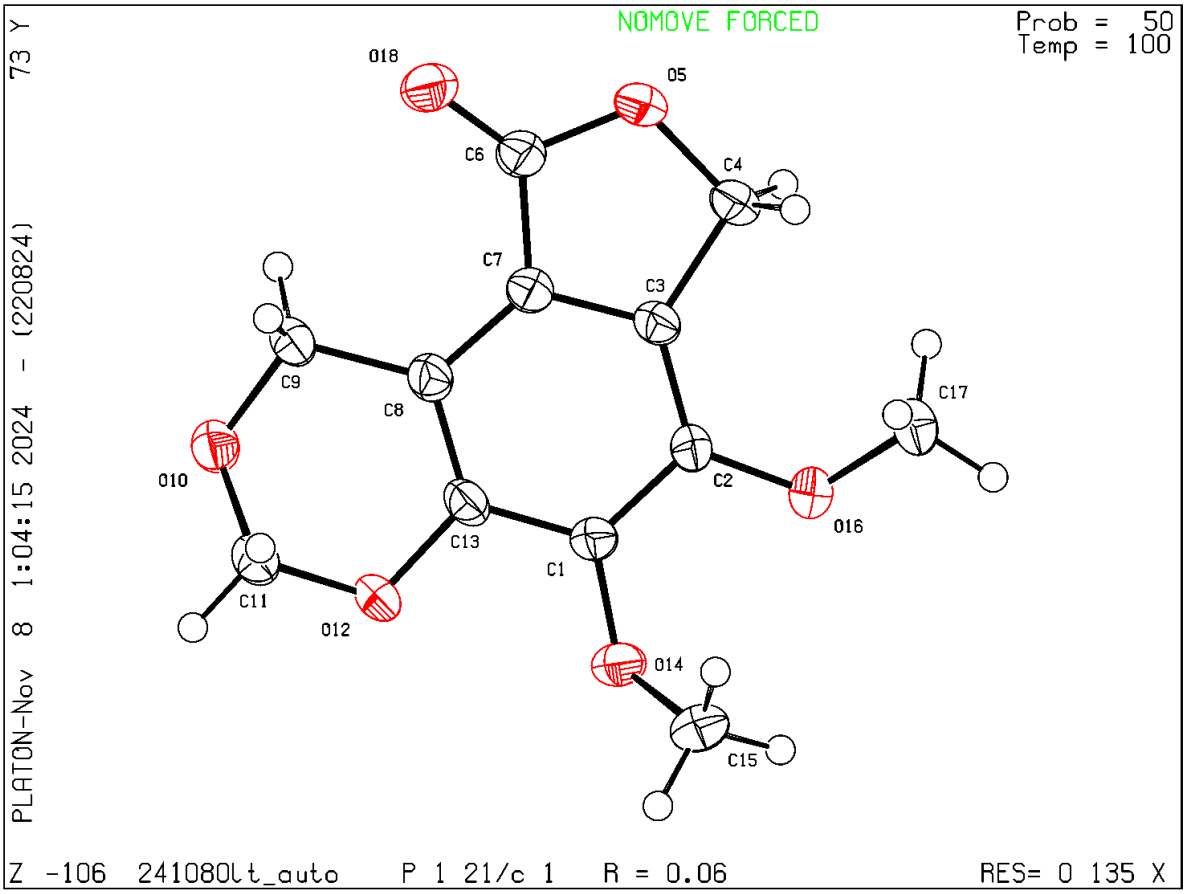
Empirical formula	$C_{18}H_{18}O_7S$
Formula weight	378.38
Temperature/K	99.99(10)
Crystal system	triclinic
Space group	P-1
a/Å	10.5691(4)
b/Å	12.9071(5)
c/Å	14.2075(4)
α/°	109.751(3)
β/°	93.260(3)
γ/°	105.188(4)
Volume/Å ^{3}	1737.72(12)
Z	4
ρ_{calc}g/cm^3	1.446
μ/mm^{-1}	2.009
F(000)	792.0
Crystal size/mm^3	0.16 × 0.14 × 0.13
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.696 to 134.156
Index ranges	$-12 \leq h \leq 12$, $-15 \leq k \leq 15$, $-16 \leq l \leq 16$
Reflections collected	18448
Independent reflections	6117 [R_{int} = 0.0285, R_{sigma} = 0.0359]
Data/restraints/parameters	6117/0/476
Goodness-of-fit on F^2	1.077
Final R indexes [I>=2σ (I)]	R_1 = 0.0416, wR_2 = 0.1108
Final R indexes [all data]	R_1 = 0.0520, wR_2 = 0.1163

X-ray crystal data of compound 10a



Sample preparation : A solution of compound **11a** (30 mg) in CH_2Cl_2 (10 mL) was placed in a tube (10 mL). EtOAc (2 mL) was added slowly to the vial with a dropper. The vial was closed with little cotton and kept at room temperature for 2 days. Then, colorless prisms were observed.

Crystal measurement : X-ray crystal structures were determined with a Bruker Enraf-Nonius single-crystal diffractometer (CAD4, Kappa CCD). Thermal ellipsoids are drawn at 50% probability level.



Empirical formula	$C_{12}H_{12}O_6$
Formula weight	252.22
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	3.8823(2)
b/Å	30.4422(18)
c/Å	9.0099(6)
α/°	90
β/°	94.758(5)
γ/°	90
Volume/Å ^{3}	1061.18(11)
Z	4
ρ_{calc}g/cm^3	1.579
μ/mm^{-1}	1.097
F(000)	528.0
Crystal size/mm^3	0.23 × 0.03 × 0.03
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	10.272 to 146.476
Index ranges	$-4 \leq h \leq 3$, $-33 \leq k \leq 37$, $-10 \leq l \leq 10$
Reflections collected	5492
Independent reflections	2010 [R_{int} = 0.0392, R_{sigma} = 0.0532]
Data/restraints/parameters	2010/0/166
Goodness-of-fit on F^2	1.081
Final R indexes [I>=2σ (I)]	R_1 = 0.0622, wR_2 = 0.1719
Final R indexes [all data]	R_1 = 0.0781, wR_2 = 0.1881
Largest diff. peak/hole / e Å $^{-3}$	0.33/-0.40