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Electronic Supplementary Information

Iridium-catalyzed reductive γ-lactonization of *ortho*-acylbenzoic acids in water: sustainable access to phthalides

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Contents

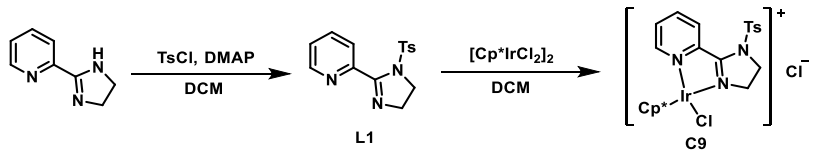
1. General Information

Except for specially stated, all the chemicals were used directly as commercially received. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer, in trichloromethane-*d* with tetramethylsilane as internal standard, and the chemical shifts were recorded in part(s) per million (ppm). Column chromatography was performed on silica gel (200–300 mesh) from Anhui Liangchen silicon source material Co., Ltd, and petroleum ether (PE, b.p. 60–90 °C) and ethyl acetate (EA, commercially received) were used as eluents. The high-resolution mass analyses were performed under ESI ionization using an Agilent LC/MSD TOF mass spectrometer in positive or negative modes. TLC analyses were performed on silica gel plates, and the plates were visualized with UV light. Microwave irradiation was performed in a commercial DISCOVER SP microwave reactor with an external IR sensor and in a closed reaction vessel.

2. Synthesis and Characterization of Catalysts.

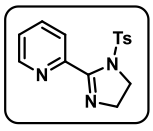
The catalysts (**C1-C12**, **C18**, and **C19**) were synthesized according to our previous publications, [1] and their solution in water at different concentrations were also prepared according to our previous publication.[1] The **C13** catalyst were synthesized according to reported stratagy.[2]

1.1 The synthesis of C9.



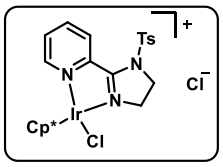
To the solution of 2-(4,5-dihydro-1*H*-imidazol-2-yl)pyridine (147 mg, 1 mmol) and DMAP (220 mg, 1.8 mmol) in dichloromethane (10 mL) was dropwise added the solution of TsCl (229 mg, 1.2 mmol) in 5 mL of dichloromethane at 0 °C. The mixture was stirred for 5 h at room temperature. Removal of the dichloromethane under vacuum directly gave the desired substituted 2-(4,5-dihydro-1*H*-imidazol-2-yl)pyridine crude products, which was purified by silica gel column chromatography to give a white solid.

2-(1-tosyl-4,5-dihydro-1*H*-imidazol-2-yl)pyridine (L1).



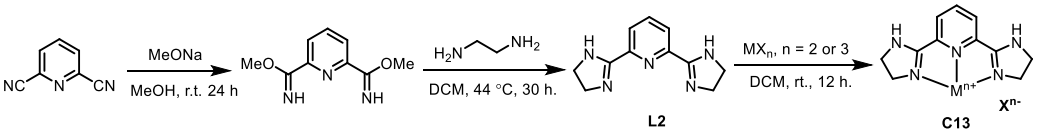
White solid, 245 mg, yield 80%, m.p. 112–114 °C, R_f = 0.40 (DCM/MeOH/ = 10:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.61 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 7.77 (ddd, *J* = 15.2, 7.6, 1.7 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.37 (ddd, *J* = 7.4, 4.8, 1.5 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.03 – 3.96 (m, 2H), 3.89 – 3.81 (m, 2H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 158.4, 149.8, 148.9, 144.5, 136.3, 135.6, 129.8, 127.7, 125.0, 124.7, 54.4, 48.9, 21.7. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{16}N_3O_2S^+$, 302.0958; found, 302.0968.

To a suspension of $[Cp^*IrCl_2]_2$ (40 mg, 0.05 mmol) in 5 ml of DCM was dropwise added the solution of 2-(1-tosyl-4,5-dihydro-1*H*-imidazol-2-yl)pyridine (33 mg, 0.11 mmol, in 3 ml of DCM). The resultant orange solution was stirred overnight. DCM was removed under reduced pressure, and the resultant yellow solid was dissolved in minimum amount of DCM. Then a large amount of EtOAc slowly was added to precipitate an orange solid as desired product, which was isolated by reduced-pressure filtration and further dried under vacuum at room temperature.



Light yellow solid, 67 mg, yield 95%, m.p. > 300 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.04 (d, J = 5.4 Hz, 1H), 8.80 (d, J = 8.0 Hz, 1H), 8.20 (td, J = 7.9, 1.4 Hz, 1H), 8.04 (ddd, J = 7.5, 5.6, 1.4 Hz, 1H), 7.73 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 4.83 (dt, J = 12.1, 9.6 Hz, 1H), 4.59 (ddd, J = 15.3, 9.6, 5.8 Hz, 1H), 4.30 (ddd, J = 12.0, 9.4, 5.7 Hz, 1H), 3.63 (dt, J = 15.4, 9.6 Hz, 1H), 2.43 (s, 3H), 1.76 (s, 15H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 166.4, 153.0, 146.7, 146.2, 139.6, 133.4, 131.0, 130.83, 130.79, 128.2, 90.4, 54.0, 52.9, 21.9, 9.4. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{25}H_{30}ClIrN_3O_2S^+$, 664.1371; found, 664.1362.

1.2 The synthesis of C13.

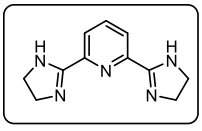


To an anhydrous round-bottomed flask was added 2,6-dicyanopyridine (1.03 g, 8 mmol), 25 mL of anhydrous methanol and sodium methanolate (54 mg, 1.0 mmol, 0.125 equiv.) under nitrogen condition. The reaction mixture was stirred for 24 h at room temperature to obtain a clarified, slightly yellowish liquid. Then the reaction system was quenched by the addition of glacial acetic acid (1.0 mmol, 0.125 equiv.), and the solvent was removed under vacuum to give a white, slightly yellow solid, which could be used in the next step without purification.

To a dry round-bottomed flask fitted with a reflux condenser tube were added successively dimethylpyridine-2,6-bis(methimidate) (768 mg, 4 mmol), 20 mL of dichloromethane solution, and ethylenediamine (480 μL, 7.2 mmol, 1.8 equiv.) under N_2 condition. The reaction mixture was refluxed for 30 h to obtain a slightly clarified solution. The reaction system was washed with water (20 mL) and the washings were extracted with dichloromethane (3 x 20 mL). The organic phases were combined and solvent was removed under vacuum and purified by column chromatography to obtain the crude product. The obtained crude product was recrystallized to give pure ligand.

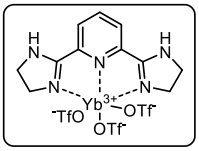
To a dried round-bottomed flask under nitrogen atmosphere were added pyridine-2,6-diimidazoline ligand (120 mg, 0.55 mmol) and metal salt (0.5 mmol), followed by addition of about 10 mL of anhydrous dichloromethane. The reaction solution was stirred at room temperature for 12-18 h. The obtained reaction solution was filtered and then the solid was washed with anhydrous ether to obtain the metal complex.

2,6-bis(4,5-Dihydro-1H-imidazol-2-yl)pyridine (L2).[3] [CAS No:138150-34-2]



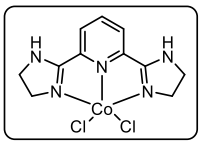
White solid, 562 mg, yield 65%, m.p. 205–207 °C, R_f = 0.30 (DCM/MeOH = 40:1, *v*/*v*). **^{1}H NMR** (400 MHz, DMSO-d_6): δ 8.07 (d, J = 7.5 Hz, 2H), 8.00 – 7.92 (m, 1H), 7.34 (s, br, 2H), 3.70 (s, 8H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ 162.9, 147.3, 137.6, 122.9, 49.8.

The catalyst of C13.[2]



White solid, 383 mg, yield 95%, m.p. 194–196 °C. **^{1}H NMR** (400 MHz, DMSO-d_6): δ 8.46 (t, J = 8.0 Hz, 1H), 8.37 (d, J = 7.8 Hz, 2H), 4.07 (s, 8H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ 162.5, 141.2, 141.0, 128.0, 120.8 (q, J = 323.1 Hz), 45.0.

The catalyst of C17.[2]

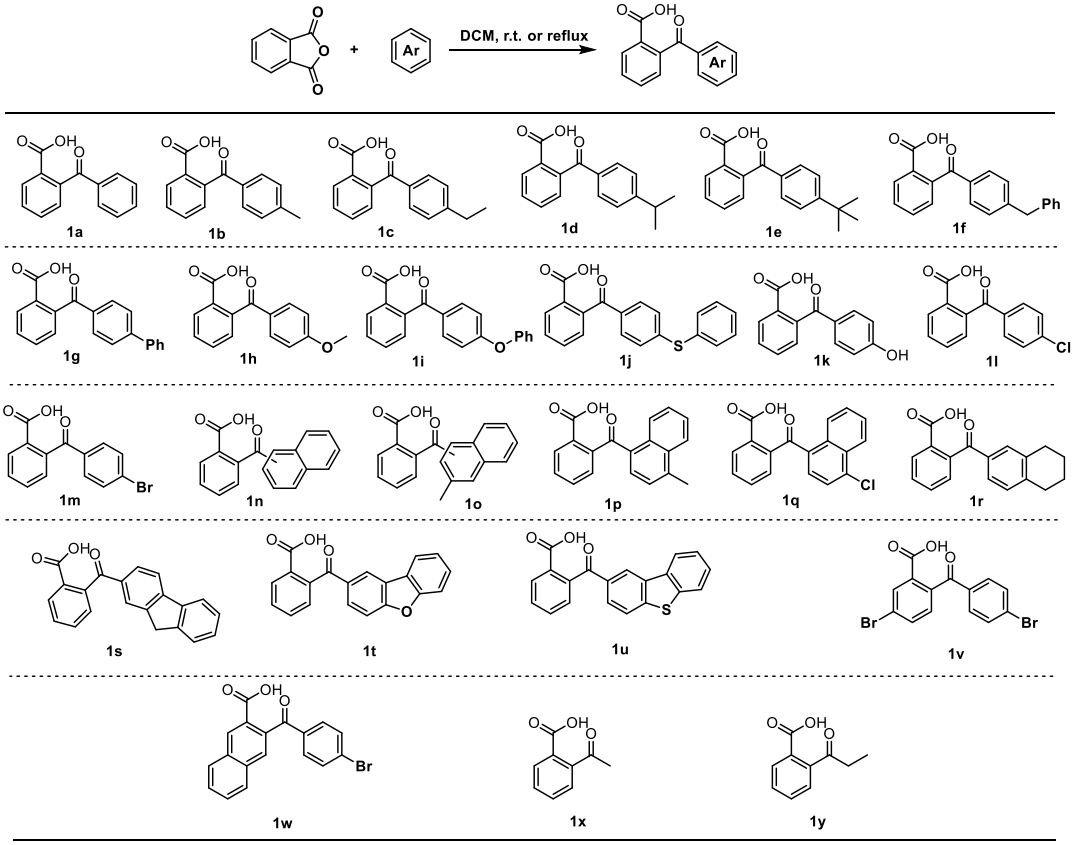


Paramagnetic substance without NMR test. Blue powder,155 mg, yield, 90%. m.p. > 300 °C. HRMS (ESI) m/z: $[M\text{-}Cl^-]^+$ calcd for $C_{11}H_{13}ClCoN_5^+$, 309.0186; found: 309.0194.

Note: **C14-C16** were prepared in situ by pre-mixing the metal salts with ligands, and was used directly.

3. Synthesis and Characterization of Substrates.

Table S1. The synthesis of 2-Acylbenzoic acids via acylation of arenes with phthalic anhydride.



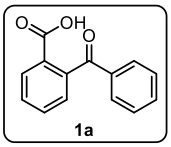
General procedure.

Most of substrates were synthesized following a modified reported procedure.[4a] **1x** was commercially available. **1y** was synthesized according to reported strategy[4b]. **1k** was synthesized according to a modified reported procedure.[4c] The NMR spectra of the known compounds **1a**, **1d**, **1g**, **1k**, **1m**, **1q**, **1r**, **1t**, **1u**, and **1y** were identical with those reported.[4-9]

To an oven-dried two-necked round-bottomed flask, equipped with a magnetic stirrer and a reflux condenser, were added Phthalic anhydride (1.48 g; 10.0 mmol) and anhydrous DCE (1,2-dichloroethane) (20 mL). Anhydrous $AlCl_3$ (3.33 g; 25.0 mmol) was added in portions over 10 minutes and stirred half an hour at rt. An arene (10.0 mmol) in anhydrous DCE(10 mL) was then added dropwise to the system over 30 minutes and the resulting mixture was heated at 85 ºC for 4 h. After this, the resulting suspension was stirred overnight at room temperature. Then the mixture was poured into the mixture of ice water (50 mL) and conc. HCl (2 mL), and extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were treated with NaOH 1M (20 mL). The aqueous layer was acidified with

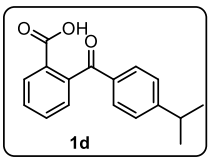
concentrated HCl (37% w/w) until pH= 1, resulting in a milky white suspension. (***Note**: When the system precipitates a large amount of solid, it is filtered directly. The filter cake was washed with water and dried to obtain the product.*). White suspension was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The resulting product was used in the next step either directly or after recrystallization.

2-Benzoylbenzoic acid (1a).[5] [CAS No: 85-52-9]



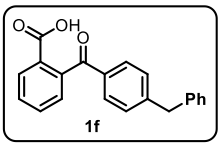
White solid, 2.04 g, yield 90%, m.p.: 124–126 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.23 (s, br, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 2H), 7.66 (td, *J* = 7.6 Hz, 0.8 Hz, 1H), 7.60 – 7.50 (m, 2H), 7.44 – 7.35 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 197.2, 170.9, 142.7, 137.1, 133.33, 133.30, 131.0, 129.7, 129.6, 128.6, 128.0, 127.8.

2-(4-isopropylbenzoyl)benzoic acid (1d).[6] [CAS No: 7471-33-2]



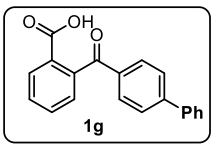
White solid, 1.70 g, yield 63%, m.p.: 115–117 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 11.29 (s, br, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.67 – 7.61 (m, 3H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 2H), 2.95 (hept, *J* = 6.9 Hz, 1H), 1.26 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 196.8, 171.1, 154.9, 142.9, 134.9, 133.2, 131.0, 129.9, 129.5, 128.0, 127.8, 126.7, 34.4, 23.7.

2-(4-benzylbenzoyl)benzoic acid (1f).



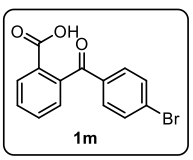
White solid, 1.32 g, yield 42%, m.p.: 195–197 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR (**400 MHz, $CDCl_3$**)**: δ 9.61 (s, br, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 3H), 7.55 (td, *J* = 7.7, 1.2 Hz, 1H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 7.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 3H), 7.20 – 7.15 (m, 2H), 4.02 (s, 2H). **^{13}C NMR (**400 MHz, $CDCl_3$**)**: δ 196.7, 170.7, 147.1, 142.8, 140.0, 135.2, 133.2, 131.0, 129.9, 129.6, 129.1, 128.7, 128.0, 127.8, 126.5, 42.1. HRMS (ESI) *m/z*: $[M - H]^-$ calcd for $C_{21}H_{15}O_3^-$, 315.1027; found, 315.1018.

2-([1,1'-biphenyl]-4-carbonyl)benzoic acid (1g).[7a] [CAS No: 42797-18-2]



White solid, 2.1 g, yield 66%, m.p.: 218–220 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR (400 MHz, DMSO-*d*$_6$)**: δ 7.99 (dd, *J* = 5.9, 2.8 Hz, 1H), 7.71 (t, *J* = 8.4 Hz, 4H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.54 – 7.46 (m, 4H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.22 (dd, *J* = 5.7, 2.8 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-*d*$_6$)**: δ 196.6, 168.3, 143.4, 141.6, 139.3, 137.1, 136.5, 129.8, 129.5, 129.2, 129.0, 128.5, 128.1, 126.9, 126.5, 126.0.

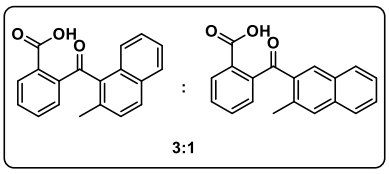
2-(4-bromobenzoyl)benzoic acid (1m).[7b] [CAS No: 2159-40-2]



White solid, 2.29 g, yield 75%, m.p.: 155–157 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR (400 MHz, DMSO-*d*$_6$)**: δ 8.00 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.66 (td, *J* = 7.6, 1.3 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.43 (dd, *J* = 7.6, 0.8 Hz, 1H). **^{13}C NMR (101 MHz, DMSO-*d*$_6$)**: δ 166.8, 136.2, 131.8, 130.6, 130.0, 129.84, 129.81, 129.7, 127.2, 127.0. (Carbon signal of

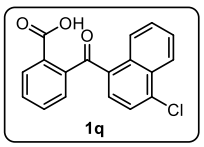
ketocarbonyl groups were not scanned)

2-(2-methyl-1-naphthoyl)benzoic acid (1o).



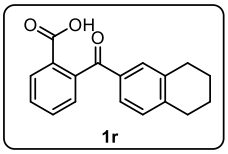
White solid, 1.39 g, yield 48%, R_f = 0.60 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). Major isomer: **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.24 (s, 1H), 8.76 (s, 1H), 7.94 (d, *J* = 7.1 Hz,1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.73 – 7.59 (m, 1H), 7.54 (t, *J* = 8.1 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 1H), 7.40 – 7.28 (m, 2H), 7.27 – 7.18 (m, 1H), 2.55 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 198.7, 171.2, 144.0, 138.5, 133.9, 133.4, 132.8, 132.3, 131.7, 131.5, 130.8, 129.9, 128.9, 128.7, 128.1, 127.9, 125.5, 123.1, 22.4. HRMS (ESI) *m/z*: $[M - H]^-$ calcd for $C_{19}H_{13}O_3^-$, 289.0870; found, 289.0868.

2-(4-chloro-1-naphthoyl)benzoic acid (1q).[8a] [CAS No: 93657-54-6]



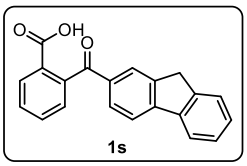
White solid, 2.64 g, yield 85%, mp 170–172 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.05 (s, 1H), 9.10 – 8.74 (m, 1H), 8.48 – 8.21 (m, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.67 – 7.61(m, 3H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 197.8, 171.2, 143.6, 137.5, 133.9, 133.1, 132.3, 131.2, 131.0, 130.8, 130.1, 129.0, 128.6, 128.4, 127.8, 127.0, 124.63, 124.55.

2-(5,6,7,8-tetrahydronaphthalene-2-carbonyl)benzoic acid (1r).[8b] [CAS No: 61959-33-9]



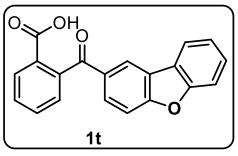
White solid, 1.82 g, yield 65%, mp 136–138 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.83 (s, br, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.45 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 2.78 (d, *J* = 16.9 Hz, 4H), 1.80 (s, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 197.1, 171.0, 143.7, 143.1, 137.5, 134.5, 133.1, 131.0, 130.5, 129.4, 128.0, 127.8, 126.9, 29.9, 29.4, 23.0, 22.9. (There is one carbon signal overlapping)

2-(9*H*-fluorene-2-carbonyl)benzoic acid (1s).[9] [CAS No: 77308-57-7]



Light yellow, 1.82 g, yield 58%, mp 218–220 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR (400 MHz, DMSO-*d*$_6$)**: δ 13.14 (s, br, 1H), 8.03 (dd, *J* = 7.6, 0.8 Hz 1H), 7.99 (t, *J* = 7.3 Hz, 2H), 7.86 (s, 1H), 7.75 (td, *J* = 7.5, 1.3 Hz, 1H), 7.68 (m, 2H), 7.63 (d, *J* = 6.6 Hz, 1H), 7.45 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.44 – 7.37(m, 2H), 3.97 (s, 2H). **^{13}C NMR (101 MHz, DMSO-*d*$_6$)**: δ 196.6, 167.4, 146.2, 145.0, 143.7, 142.3, 140.3, 135.9, 132.9, 130.34, 130.32, 130.1, 128.9, 128.6, 127.9, 127.5, 126.1, 125.8, 121.6, 120.4, 36.9. HRMS (ESI) *m/z*: $[M - H]^-$ calcd for $C_{21}H_{13}O_3^-$, 313.0870; found, 313.0867.

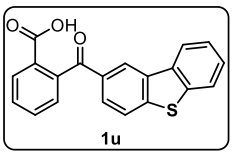
2-(dibenzo[b,d]furan-2-carbonyl)benzoic acid (1t).[9] [CAS No: 56260-28-7]



Light yellow solid, 1.55 g, yield 49%, mp 178–180 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.18 (s, br, 1H), 8.33 (s, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 8.7 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.60 – 7.52 (m, 2H), 7.50 – 7.45 (m,

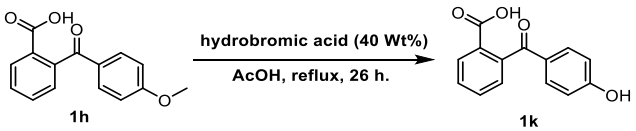
2H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 196.4, 170.7, 159.1, 157.0, 142.9, 133.3, 132.4, 131.2, 129.6, 129.4, 128.1, 128.0, 127.8, 124.7, 123.8, 123.5, 122.9, 121.3, 112.0, 111.7.

2-(Dibenzo[*b*,*d*]thiophene-2-carbonyl)benzoic acid (1u).[9] [CAS No: 31123-60-1]



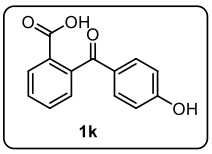
Yellow solid, 2.06 g, yield 62%, mp 162–164 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 10.07 (s, 1H), 8.51 (s, 1H), 8.08 (dd, *J* = 14.8, 7.7 Hz, 2H), 7.84 (d, *J* = 7.3 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.46 (quint, *J* = 7.2 Hz, 2H), 7.40 (d, *J* = 7.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 196.8, 170.7, 144.9, 142.8, 139.8, 135.7, 135.3, 133.7, 133.4, 131.2, 129.7, 128.0, 127.8, 127.6, 127.5, 125.0, 123.0, 122.9, 122.8, 122.2.

The synthesis of 1k.



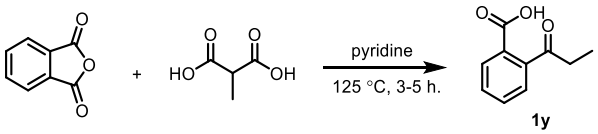
To a round-bottomed flask equipped with a magnetic stirrer and a reflux condenser were added **1h** (1.53 g, 6 mmol), glacial aceticacid (7.5 mL) and 48% aqueous HBr (7.5 mL). The mixture was refluxed (115-125 °C) overnight (26 h). The reaction mixture was cooled to room temperature and the pH of the system was adjusted to 2-3 with Na_2CO_3 (aq). The aqueous layer was extracted with EtOAc. The combined organic layer was dried (Na_2SO_4), and concentrated. The crude residue was purified by silica gel column chromatography to give desired product **1k**.

2-(4-hydroxybenzoyl)benzoic acid (1k).[4c] [CAS No: 85-57-4]



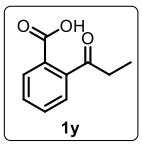
White solid, 1.13 g, yield 78%, m.p.: 197–199 °C, R_f = 0.30 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR (400 MHz, DMSO-d_6)**: δ 13.01 (s, br, 1H), 10.40 (s, br, 1H), 7.96 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.68 (td, *J* = 7.5, 1.3 Hz, 1H), 7.61 (td, *J* = 7.6, 1.3 Hz, 1H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.34 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H). **^{13}C NMR (101 MHz, DMSO-d_6)**: δ 194.8, 167.0, 162.1, 141.9, 132.1, 131.6, 129.9, 129.7, 129.3, 128.5, 127.4, 115.3.

The synthesis of 1y.



A mixture of phthalic anhydride (12 mmol), malonic acid (10 mmol) and pyridine (0.79 g, 10 mol) was refluxed for 3 h to 5 h. Upon completion, the resulting mixture was cooled to room temperature, and then water (9 mL) was added and the mixture was stirred for 30 min. The solution was treated with concentrated HCl to pH 3-4, extracted with ethyl acetate (2×10 mL). The organic layers were combined, dried over Na_2SO_4 and evaporated under reduced pressure toobtain the crude product without further purification.

2-propionylbenzoic acid (1y). [CAS No: 2360-45-4]



White solid, 0.80 g, yield 45%, m.p. 88–90 °C, R_f = 0.60 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 7.4 Hz, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.56 – 7.44 (m, 2H), 5.54 (br, 1H), 2.22 (br, 2H), 0.86 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 196.8, 169.4, 148.2, 134.5, 130.4, 126.9, 125.8, 122.7, 32.5, 7.9.

4. Procedure for optimization of reaction conditions.

3.1 Optimization of catalysts in entries 1-17, Table 1.

To a 10-mL reaction tube was sequentially added 2-benzoylbenzoic acid (**1a**, 45 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (0.0002 mol/L for *S/C* = 1000; 0.00004 mol/L for *S/C* = 5000, **C1**-**C17** dissolved in deionized water). The mixture was stirred for 3 minutes at 80 °C, followed by addition of formic acid (120 μL, 3.2 mmol, 16 equiv) in one portion. After stirring for 6 h, the reaction mixture was cooled to room temperature and diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The ^{1}H NMR yields of the crude residues were determined using 1,3,5- trimethoxybenzene as internal standard. (Note: **C14-C17** were mixed in situ by metal salts with ligands, respectively, and no NMR spectra were obtained)

3.2 Optimization of equivalents of formic acid in entries 18-21, Table 1.

To a 10-mL reaction tube was sequentially added 2-benzoylbenzoic acid (**1a**, 45 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (0.0002 mol/L for *S/C* = 1000, **C2** dissolved in deionized water). The mixture was stirred for 3 minutes at 80 °C, followed by addition of formic acid (60 μL, 1.6 mmol, 8 equiv; 90 μL, 2.4 mmol, 12 equiv; 120 μL, 3.2 mmol, 24 equiv; 226 μL, 6.0 mmol, 30 equiv) in one portion. After stirring for 6 h, the reaction mixture was cooled to room temperature and diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The ^{1}H NMR yields of the crude residues were determined using 1,3,5- trimethoxybenzene as internal standard.

3.3 Optimization of equivalents of formic acid in entries 23-25, Table 1.

To a 10-mL reaction tube was sequentially added 2-benzoylbenzoic acid (**1a**, 45 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (0.0002 mol/L for *S/C* = 1000, **C2** dissolved in deionized water). The mixture was stirred for 3 minutes at 80 °C, followed by addition of formic acid (180 μL, 4.8 mmol, 24 equiv; 226 μL, 6.0 mmol, 30 equiv) in two portions at interval of 4.5 h or in three portions at interval of 3 h (total reaction time is 9 h). The reaction mixture was then cooled to room temperature and diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The crude residue was submitted to ^{1}H NMR yield determination with 1,3,5-trimethoxybenzene as an internal standard.

3.4 Optimization of catalyst loading in entries 26, Table 1.

To a 10-mL reaction tube was sequentially added 2-benzoylbenzoic acid (**1a**, 45 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (0.00004 mol/L for *S/C* = 5000, **C2** dissolved in deionized water). The mixture was stirred for 3 minutes at 80 °C, followed by addition of formic acid (226 μL, 6.0 mmol, 30 equiv) in three portions at interval of 3 h (total reaction time is 9 h). The reaction mixture was then cooled to room temperature. The mixture was diluted with saturated brine (2

mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The ^{1}H NMR yields of the crude residues were determined using 1,3,5- trimethoxybenzene as internal standard.

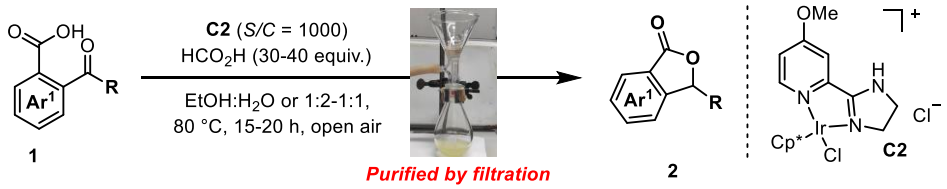
3.5 Optimization of solvent proportion in entries 27, Table 1.

To a 10-mL reaction tube was sequentially added 2-benzoylbenzoic acid (**1a**, 45 mg, 0.2 mmol), absolute ethanol (1 mL), 1 mL of catalyst solution (0.0002 mol/L for *S/C* = 1000, **C2** dissolved in deionized water).The mixture was stirred for 3 minutes at 80 °C, followed by addition of formic acid (226 μL, 6.0 mmol, 30 equiv) in three portions at interval of 3 h (total reaction time is 9 h). The reaction mixture was then cooled to room temperature. The mixture was diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The ^{1}H NMR yields of the crude residues were determined using 1,3,5- trimethoxybenzene as internal standard.

3.6 Gram-scale reaction attempts under optimal conditions in entries 28, Table 1.

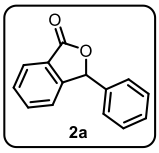
To a 50-mL reaction tube was sequentially added 2-benzoylbenzoic acid **1a** (2.49 g, 11.0 mmol), absolute ethanol (10 mL), **C2** (6.3 mg for *S/C* = 1000) in 20 mL of deionized water. The mixture was stirred for 3 minutes at 80 °C, followed by addition of formic acid (12.4 mL, 0.33 mol, 30 equiv) in three portions at interval of 5 h (total reaction time is 15 h). After TLC showed full consumption of substrates, the system was cooled to room temperature and ethanol was removed under reduced pressure to decrease loss of product. The residual solid-liquid mixture was filtered and the filter cake was washed with water (3 × 15 mL) and then dried to obtain **2a**. (White solid, 2.10 g, yield 90%)

5. Iridium-catalyzed Reductive Lactonization.



To a 50-mL round-bottom flask charged with a magnetic stirring bar were added substrate (4.0, 5.0, 1.0 or 11.0 mmol), **C2** (*S/C* = 1000), solvent (20-30 mL, H_2O/EtOH = 2/1 or 1/1, *v*/*v*). Then formic acid (32 equiv) was added to the reaction flask in three portions over a period of 15-20 hours at 80°C in the oil bath. After TLC showed full consumption of substrates, the system was cooled to room temperature and ethanol was removed under reduced pressure to decrease loss of product. The residual solid-liquid mixture was filtered and the filter cake was washed with water (3 × 15 mL) and then dried to obtain the corresponding NMR-pure phthalides. (Note: The purpose of adding ethanol is to increase the solubility of the substrate in the solvent mixture)

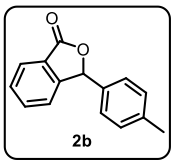
3-phenylisobenzofuran-1(3*H*)-one (2a).[10] [CAS No:5398-11-8]



Prepared on 11 mmol-scale, 6.3 mg of **C2**, *S/C* = 1000. White solid, 2.10 g, yield 90%, mp 100–102 °C, R_f = 0.50 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.65 (td, *J* = 7.6, 0.9 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.40 – 7.45 (m, 3H), 7.33 (dd, *J* = 7.6, 0.4 Hz, 1H), 7.28 (d, *J* = 3.7 Hz, 1H), 7.26 (d, *J* = 2.1 Hz, 1H), 6.40 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.6, 149.8, 136.5, 134.4, 129.5, 129.4, 129.1, 127.1,

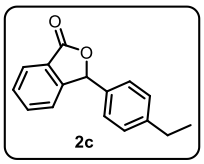
125.8, 125.7, 123.0, 82.8.

3-(*p*-tolyl)isobenzofuran-1(3*H*)-one (2b).[10] [CAS No: 21615-75-8]



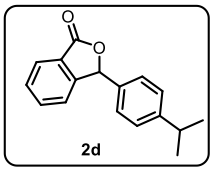
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 0.85 g, yield 94%, mp 92–93 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.1 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.37 (s, 1H), 2.35 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 149.9, 139.4, 134.4, 133.5, 129.7, 129.4, 127.2, 125.8, 125.7, 123.0, 82.9, 21.3.

3-(4-ethylphenyl)isobenzofuran-1(3*H*)-one (2c).[11] [CAS No: 36778-41-3]



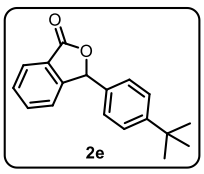
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000.White solid, 0.85 g, yield 89%, mp 77–79 °C, R_f = 0.60 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.2 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.33 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.39 (s, 1H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 149.9, 145.7, 134.4, 133.7, 129.4, 128.6, 127.2, 125.9, 125.7, 123.0, 82.9, 28.7, 15.5.

3-(4-isopropylphenyl)isobenzofuran-1(3*H*)-one (2d). [CAS No: 15836-65-4]



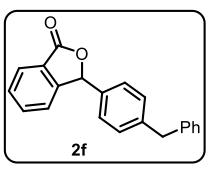
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 0.96 g, yield 94%, mp 57–59 °C, R_f = 0.60 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.2 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 6.39 (s, 1H), 2.91 (hept, *J* = 6.9 Hz, 1H), 1.23 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 150.3, 149.9, 134.4, 133.8, 129.4, 127.3, 127.2, 125.9, 125.7, 123.1, 82.9, 34.0, 24.0. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{17}O_2^+$, 253.1223; found, 253.1242.

3-(4-(tert-butyl)phenyl)isobenzofuran-1(3*H*)-one (2e).[10] [CAS No: 337966-40-2]



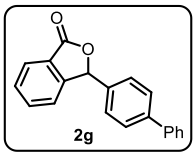
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.03 g, yield 96%, mp 109–111 °C, R_f = 0.60 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.67 (td, *J* = 7.5, 1.1 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.39 – 7.35 (m, 1H), 7.22 (d, *J* = 8.3 Hz, 2H), 6.42 (s, 1H), 1.33 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 152.6, 149.9, 134.3, 133.4, 129.4, 127.0, 126.0, 125.9, 125.7, 123.1, 82.8, 34.8, 31.4.

3-(4-benzylphenyl)isobenzofuran-1(3*H*)-one (2f).[11b] [CAS No: 1401235-71-9]



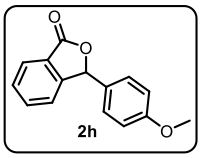
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 0.86 g, yield 30%, mp 104–106 °C, R_f = 0.60 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.2 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.33 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.13 (m, 7H), 6.38 (s, 1H), 3.99 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.6, 149.8, 142.6, 140.6, 134.4, 134.2, 129.6, 129.4, 129.0, 128.6, 127.3, 126.4, 125.8, 125.7, 123.0, 82.7, 41.7. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{17}O_2^+$, 301.1223; found, 301.1225.

3-([1,1'-biphenyl]-4-yl)isobenzofuran-1(3*H*)-one (2g).[10] [CAS No: 135381-46-3]



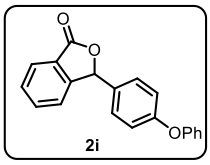
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.03 g, yield 90%, mp 204–206 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.6 Hz, 1H), 7.67 (td, *J* = 7.5, 0.9 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.59 – 7.53 (m, 3H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.39 (d, *J* = 7.4 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 6.46 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.6, 149.7, 142.4, 140.4, 135.4, 134.5, 129.5, 129.0, 127.8, 127.6, 127.3, 125.8, 123.0, 82.6.

3-(4-methoxyphenyl)isobenzofuran-1(3*H*)-one (2h).[10] [CAS No: 21615-74-7]



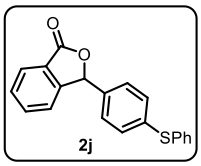
Prepared on 5 mmol-scale, 2.8 mg of **C2**, *S/C* = 1000. White solid, 1.02 g, yield 85%, mp 111–113 °C, R_f = 0.30 (PE/EA = 1:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.37 (s, 1H), 3.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.6, 160.5, 149.9, 134.4, 129.4, 128.9, 128.4, 126.0, 125.7, 123.1, 114.4, 82.8, 55.5.

3-(4-phenoxyphenyl)isobenzofuran-1(3*H*)-one (2i). [CAS No: 1136308-83-2]



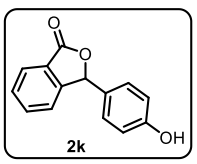
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.17 mg, yield 97%, mp 80–82 °C, R_f = 0.40 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 7.6 Hz, 1H), 7.67 (td, *J* = 7.5, 1.2 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.01 (dd, *J* = 8.5, 1.0 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.40 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.5, 158.6, 156.6, 149.7, 134.4, 130.9, 130.0, 129.5, 129.0, 125.9, 125.8, 124.0, 123.1, 119.5, 118.9, 82.6. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{15}O_3^+$, 303.1016; found, 303.1017.

3-(4-(phenylthio)phenyl)isobenzofuran-1(3*H*)-one (2j).



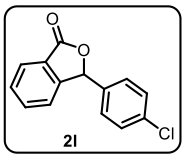
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.00 g, yield 78%, mp 84–86 °C, R_f = 0.40 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.7 Hz, 1H), 7.65 (td, *J* = 7.5, 1.2 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.36 – 7.30 (m, 4H), 7.26 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.37 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.5, 149.4, 138.6, 134.7, 134.5, 134.2, 132.4, 130.2, 129.6, 129.5, 128.0, 127.9, 125.83, 125.75, 123.0, 82.4. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{15}O_2S^+$, 319.0787; found, 319.0793.

3-(4-hydroxyphenyl)isobenzofuran-1(3*H*)-one (2k).[12] [CAS No: 7468-76-0]



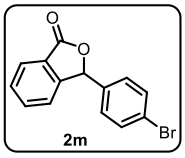
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 0.80 g, yield 88%, mp 144–146 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.36 (s, 1H), 5.58 (s, br, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 171.1, 156.9, 149.9, 134.5, 129.5, 129.2, 128.3, 126.0, 125.7, 123.1, 116.0, 83.1.

3-(4-chlorophenyl)isobenzofuran-1(3*H*)-one (2l).[10] [CAS No: 4889-69-4]



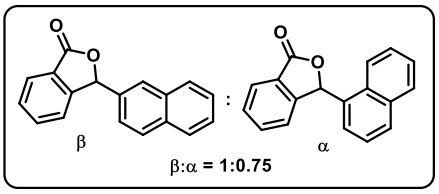
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 0.93 g, yield 95%, mp 118–120 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.66 (td, *J* = 7.5, 1.0 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.31 (dd, *J* = 7.6, 0.4 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.37 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.3, 149.3, 135.4, 135.1, 134.6, 129.7, 129.4, 128.5, 125.9, 125.6, 122.9, 82.0.

3-(4-bromophenyl)isobenzofuran-1(3*H*)-one (2m).[11] [CAS No: 25933-36-2]



Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.02 g, yield 88%, mp 117–119 °C, R_f = 0.50 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.1 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.36 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.3, 149.3, 135.6, 134.6, 132.3, 129.7, 128.7, 125.9, 125.6, 123.6, 122.9, 82.0.

The mixture of 3-(naphthalen-2-yl)isobenzofuran-1(3*H*)-one and 3-(naphthalen-1-yl)isobenzofuran-1(3*H*)-one (2n).[13]



Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.0 g, total yield 96%, mp 145–149 °C, R_f = 0.50-0.6 (PE/EA = 5:1, *v*/*v*). The ratio of α- and β-isomers is 0.75:1.

The proton signal of C*H*O of α-isomer appears at 7.27 ppm, while that of β-isomer at 6.56.

β-**Isomer**: **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (t, *J* = 7.1 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.86 – 7.82 (m, 2H), 7.64 (t, *J* = 7.4 Hz, 2H), 7.61 – 7.54 (m, 2H), 7.52 (dd, *J* = 6.3, 3.2 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.22 (m, 1H), 6.56 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 149.8, 134.5, 134.1, 133.8, 133.2, 130.1, 129.6, 129.2, 128.2, 127.0, 126.8, 126.4, 125.8, 125.4, 123.9, 123.1, 83.0.

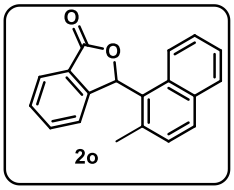
α-**Isomer**: **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.4 Hz, 0.75H), 8.01 (t, *J* = 7.1 Hz, 0.75H), 7.94 (d, *J* = 8.0 Hz, 0.75H), 7.86 – 7.82 (m, 1.5H), 7.64 (t, *J* = 7.4 Hz, 0.75H), 7.61 – 7.56 (m, 0.75H), 7.52 (dd, *J* = 6.3, 3.2 Hz, 0.75H), 7.46 – 7.41 (m, 0.75H), 7.39 (d, *J* = 7.9 Hz, 0.75H), 7.27 (d, *J* = 8.2 Hz, 0.75H), 7.26 – 7.22 (m, *J* = 8.5 Hz, 0.75H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.6, 149.4, 134.1, 133.7, 133.2, 131.4, 130.1, 129.6, 129.2, 128.2, 127.2, 126.8, 126.2, 125.8, 125.4, 124.7, 123.3, 79.8.

3-(2-methylnaphthalen-1-yl)isobenzofuran-1(3H)-one (2o) (α-isomer**) and 3-(2-methylnaphthalen-1-yl)isobenzofuran-1(3H)-one (2o) (**β-isomer**)**

Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 0.99 g, total yield 90%, R_f = 0.40 and 0.45 (PE/EA = 5:1, *v*/*v*). The proton signal of C*H*O of α-isomer appears at 7.24 ppm, while that of β-isomers at 6.53. The ratio of α- and β- isomers is 3:1.

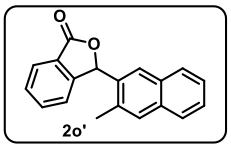
These two isomers were separated by column chromatography.

3-(2-methylnaphthalen-1-yl)isobenzofuran-1(3H)-one (α-isomer**)**



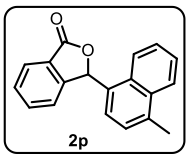
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 8.01 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.65 (td, *J* = 7.5, 1.3 Hz, 1H), 7.58 (tt, *J* = 7.5, 0.8 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.24 (s, 1H), 7.20 (d, *J* = 7.1 Hz, 1H), 2.60 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 149.4, 137.0, 134.2, 132.3, 131.7, 131.2, 129.8, 129.5, 128.9, 128.5, 126.3, 126.0, 124.6, 124.4, 123.4, 122.1, 79.7, 22.4. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{15}O_2^+$, 275.1067; found, 275.1071.

3-(3-methylnaphthalen-2-yl)isobenzofuran-1(3H)-one (β-isomer**)**



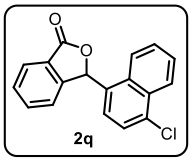
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.6 Hz, 1H), 7.79 (s, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.64 (td, *J* = 7.6, 0.8 Hz, 1H), 7.60 (s, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.0 Hz, 2H), 7.19 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.53 (s, 1H), 2.51 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 149.9, 136.8, 134.4, 133.9, 132.8, 131.4, 129.5, 129.1, 128.5, 128.0, 126.9, 126.6, 125.8, 125.7, 124.0, 123.1, 83.2, 21.8. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{15}O_2^+$, 275.1067; found, 275.1075.

3-(4-methylnaphthalen-1-yl)isobenzofuran-1(3*H*)-one (2p).[15] [CAS No: 903631-55-0]



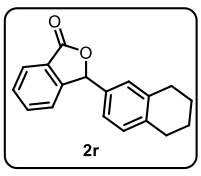
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.07 mg, yield 97%, mp 145–147 °C, R_f = 0.50 (PE/EA/AcOH = 1:1:0.02, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.26 (dd, *J* = 7.3, 2.1 Hz, 1H), 8.10 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.67 – 7.61 (m, 3H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.43 (dd, *J* = 7.6, 0.4 Hz, 1H), 7.23 (d, *J* = 6.7 Hz, 1H), 7.22 (s, 1H),7.14 (d, *J* = 7.3 Hz, 1H), 2.70 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 149.5, 136.6, 134.2, 133.2, 131.5, 130.2, 129.5, 126.8, 126.4, 126.2, 126.14, 126.06, 125.3, 124.5, 123.6, 123.4, 80.0, 19.8.

3-(4-chloronaphthalen-1-yl)isobenzofuran-1(3*H*)-one (2q). [CAS No: 908807-29-4]



Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.10 g, yield 94%, mp 184–186 °C, R_f = 0.40 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.45 – 8.37 (m, 1H), 8.31 – 8.23 (m, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.71 (t, *J* = 4.5 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.21 (s, 1H), 7.18 (d, *J* = 7.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.3, 148.8, 134.3, 133.8, 132.4, 131.3, 131.2, 129.7, 127.9, 127.4, 126.1, 125.64, 125.59, 124.5, 123.4, 123.2, 79.2. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for 295.0520, 299.1067; found, 295.0524. (There is one carbon signal overlapping)

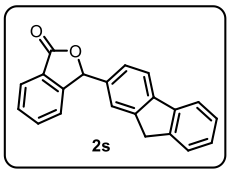
3-(5,6,7,8-tetrahydronaphthalen-2-yl)isobenzofuran-1(3*H*)-one (2r).[16] [CAS No: 351328-32-0]



Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.01 g, yield 95%, mp 127–129 °C, R_f = 0.50 (PE/EA = 1:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.2 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H),

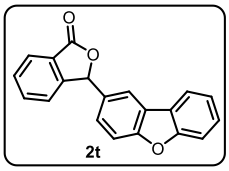
7.34 (d, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 1H), 6.96 (d, *J* = 6.5 Hz, 1H), 6.95 (s, 1H), 6.34 (s, 1H), 2.73 (m, 4H), 1.78 (hept, *J* = 5.0 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* 170.8, 150.0, 138.7, 138.0, 134.3, 133.5, 129.8, 129.3, 127.8, 125.8, 125.7, 124.2, 123.0, 83.0, 29.5, 29.3, 23.1. (There is one carbon signal overlapping)

3-(9H-fluoren-2-yl)isobenzofuran-1(3*H*)-one (2s).[17] [CAS No: 246525-87-1]



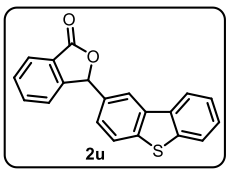
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.07 g, yield 90%, mp 226–228 °C, R_f = 0.40 (PE/EA = 1:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.00 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.43 – 7.35 (m, 3H), 7.31 (t, *J* = 8.0 Hz, 2H), 6.49 (s, 1H), 3.87 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* 170.7, 150.0, 144.1, 143.6, 143.1, 141.0, 134.8, 134.5, 129.5, 127.4, 127.0, 126.2, 125.9, 125.8, 125.2, 123.8, 123.1, 120.3, 83.3, 37.0. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{15}O_2^+$, 299.1067; found, 299.1065. (There is one carbon signal overlapping)

3-(dibenzo[b,d]furan-2-yl)isobenzofuran-1(3H)-one (2t).[14] [CAS No: 1115589-12-2]



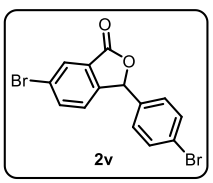
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.15 g, yield 96%, mp 167–169 °C, R_f = 0.40 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.01 (d, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 7.7 Hz, 1H), 7.85 (d, *J* = 1.2 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.61 – 7.53 (m, 3H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.34 ((m, 3H), 6.57 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* 170.6, 156.8, 156.6, 150.0, 134.5, 131.1, 129.6, 127.8, 126.3, 125.8, 125.0, 123.7, 123.14, 123.08, 120.9, 119.7, 112.3, 111.9, 83.1. (There is one carbon signal overlapping)

3-(dibenzo[b,d]thiophen-2-yl)isobenzofuran-1(3*H*)-one (2u).[14] [CAS No: 1115589-13-3]



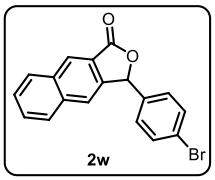
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.20 g, yield 95%, mp 120–122 °C, R_f = 0.40 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.15 – 8.09 (m, 1H), 8.07 (d, *J* = 1.4 Hz, 1H), 8.01 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 7.6, 0.8 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.51 – 7.41 (m, 2H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.31 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.58 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* 170.7, 149.9, 140.6, 140.0, 136.1, 135.0, 134.6, 132.9, 129.6, 127.3, 125.9, 125.8, 125.4, 124.7, 123.5, 123.05, 123.01, 121.9, 120.4, 83.0.

6-Bromo-3-(4-bromophenyl)isobenzofuran-1(3H)-one (2v).[18] [CAS No: 38917-90-7]



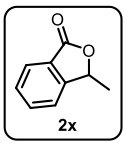
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 1.26 g, yield 85%, 145–147 °C, R_f = 0.30 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.09 (d, *J* = 1.2 Hz, 1H), 7.77 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 1H), 7.13 (d, *J* = 8.3 Hz, 2H), 6.31 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* 168.7, 147.9, 137.7, 134.9, 132.5, 128.9, 128.7, 127.7, 124.5, 123.93, 123.86, 81.9. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_9Br_2O_2^+$, 366.8964; found, 366.8964.

3-(4-bromophenyl)naphtho[2,3-c]furan-1(3*H*)-one (2w).



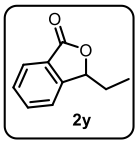
Prepared on 4 mmol-scale, 2.3 mg of **C2**, *S/C* = 1000. White solid, 0.77 g, yield 56%, mp 148–150 °C, R_f = 0.40 (PE/EA = 1:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.72 (s, 1H), 7.63 (dddd, *J* =1 4.8, 6.8, 2.0, 1.2 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.52 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.2, 143.0, 136.5, 136.4, 133.4, 132.3, 130.1, 129.3, 128.8, 128.4, 127.4, 127.3, 123.6, 123.3, 122.0, 82.0. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{12}BrO_2^+$, 339.0015; found, 339.0015.

3-methylisobenzofuran-1(3*H*)-one (2x).[11] [CAS No: 3453-64-3]



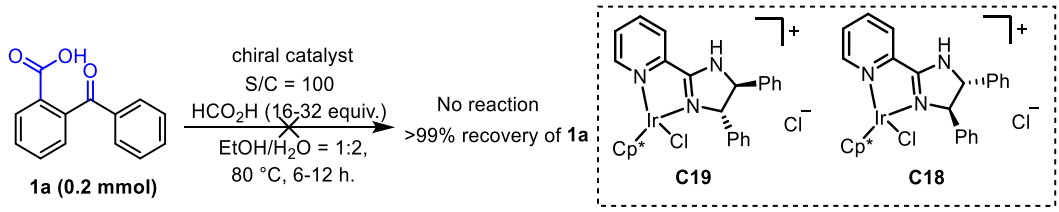
Prepared on 10 mmol-scale, 1.2 mg of **C2**, *S/C* = 5000. Colorless oil, 1.18 g, yield 99%, R_f = 0.50 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 7.6 Hz, 1H), 7.66 (td, *J* = 7.5, 1.1 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 7.6, 0.8 Hz, 1H), 5.54 (q, *J* = 6.7 Hz, 1H), 1.61 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.5, 151.2, 134.1, 129.1, 125.7, 121.6, 77.8, 20.4.

3-Ethylisobenzofuran-1(3H)-one (2y).[11] [CAS No: 17475-41-1]



Prepared on 4 mmol-scale, 0.5 mg of **C2**, *S/C* = 5000. Colorless oil, 0.62 g, yield 95%, R_f = 0.50 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 7.7 Hz, 1H), 7.66 (td, *J* = 7.5, 1.0 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.43 (dd, *J* = 7.6, 0.8 Hz,, 1H), 5.44 (dd, *J* = 7.1, 4.4 Hz, 1H), 2.11 (dqd, *J* = 14.8, 7.4, 4.3 Hz, 1H), 1.81 (dp, *J* = 14.5, 7.3 Hz, 1H), 0.98 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.8, 149.8, 134.1, 129.1, 126.4, 125.7, 121.8, 82.4, 27.7, 8.9.

6. Exploration of asymmetric reductive γ-lactonization



To a 10-mL reaction tube was sequentially added **1a** (46 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (chiral catalyst **C18** or **C19** in deionized water, 0.002 mol/L for *S/C* = 100). The mixture was stirred for 3 minutes at 80 °C, and then formic acid (120 μL, 3.2 mmol, 16 equiv or 240 μL, 6.4 mmol, 32 equiv) was added. After stirring for 6-12 h, the reaction mixture was cooled to room temperature. No reaction was observed by TLC, and **1a** was completely recovered.

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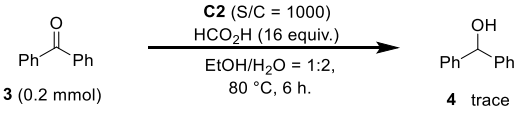
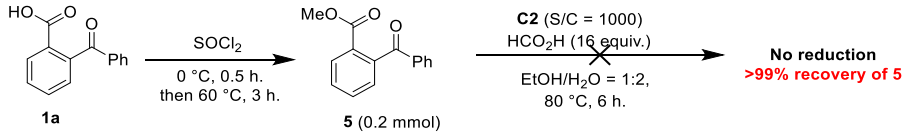
7. Control experiments.

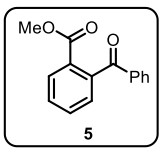


To a 10-mL reaction tube was sequentially added benzophenone **3** (36 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (**C2** in deionized water, 0.0002 mol/L for S/C = 1000). The mixture was stirred for 3 minutes at 80 °C, and then formic acid (120 μL, 3.2 mmol, 16 equiv) was added. After stirring for 6 h, the reaction mixture was cooled to room temperature. The mixture was diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The ^{1}H NMR yields of the crude residues were determined using 1,3,5-trimethoxybenzene as internal standard.



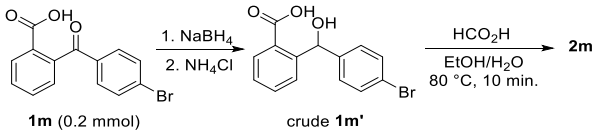
To a 10-mL reaction tube was sequentially added 2-benzoylbenzoic acid (**1a**, 226 mg, 1.0 mmol), absolute methanol (2 mL) at a nitrogen atmosphere. Thionyl chloride (87 μL, 1.2 mmol) was added to tube dropwise and the reaction mixture was stirred for 30 minutes at 0 °C. The system was then heated to 60 °C and stirred for 3 h. The solvent was evaporated under reduced pressure. The residue was partitioned between ethyl acetate (5 mL) and water (5 mL). The separated aqueous layer was extracted with ethyl acetate (5 mL) twice. The combined organic layers were washed with an aqueous solution of sodium chloride and dried over Na_2SO_4. The organic solvent was evaporated under reduced pressure and colorless oil was obtained.

Methyl 2-benzoylbenzoate (5). [19] [CAS No: 606-28-0]



Colorless oil, 224 mg, yield 93%, R_f = 0.60 (PE/EA = 5:1, *v/v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 7.7 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.57 (q, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 8.0 Hz, 3H), 3.62 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 197.1, 166.4, 141.7, 137.2, 133.1, 132.5, 130.2, 129.7, 129.3, 128.6, 127.9, 52.2. (There is one carbon signal overlapping)

To a 10-mL reaction tube was sequentially added 2-benzoylbenzoic acid (**5**, 48 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (**C2** in deionized water, 0.0002 mol/L for *S/C* = 1000). The mixture was stirred for 3 minutes at 80 °C, and then formic acid (120 μL, 3.2 mmol, 16 equiv) was added to the tube. After stirring for 6 h, the reaction mixture was cooled to room temperature. No reaction was observed by TLC, and **5** was completely recovered.



1m (60 mg, 0.2 mmol) was dissolved in 1 mL of ethanol in a 10-mL reaction tube equipped with a stirrer. $NaBH_4$ (23 mg, 0.6 mmol) was added to the tube in portion within 3 minutes at 0 °C. The tube was then allowed to warm to room temperature and stirred for 4-5 h. The reaction was complete as detected by TLC. 2 mL of saturated ammonium chloride was added to the tube to quench the reaction. The aqueous layer was extracted with EA (3 mL) three times. The combined organic layers were dried over Na_2SO_4 and removed under reduced pressure below 25 °C to avoid lactonization of **1m'**. Crude **1m'** was obtained and comfirmed by ^1H NMR. Further purification of **1m'** failed, due to its fast lactonization, even at room temperature.

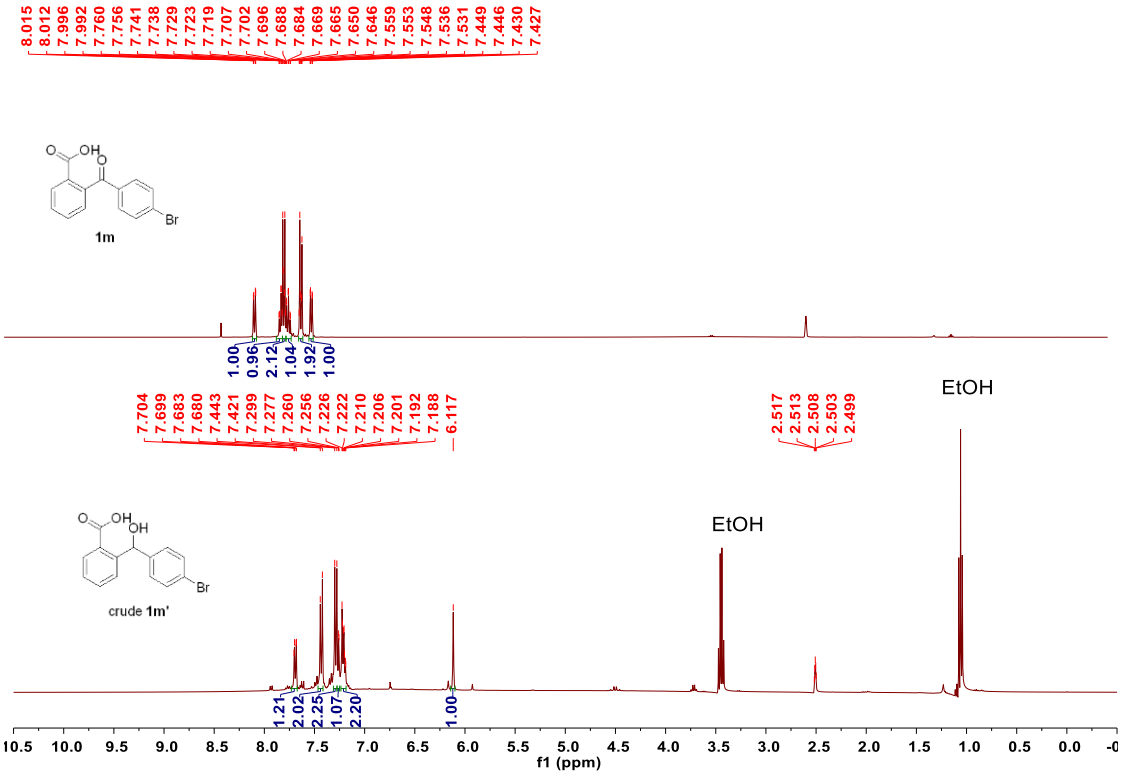


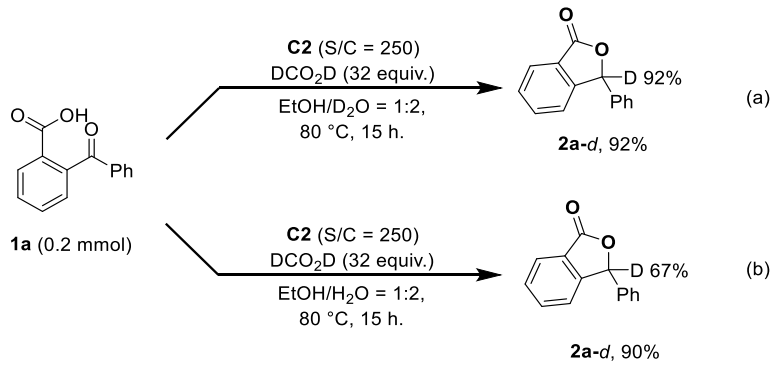
Figure S1. ^1H NMR Spectrum of **1m** and **1m'**.

To a 10-mL reaction tube was sequentially added **1m'** (45 mg, 0.2 mmol), absolute ethanol (0.5 mL), and deionized water (1 mL). The mixture was stirred for 3 minutes at 80 °C, and then formic acid (120 μL, 3.2 mmol, 16 equiv) was added. After stirring for 10 minutes, the reaction mixture was cooled to room temperature and diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3).

The organic solvent was dried over Na_2SO_4 and evaporated under reduced pressure. The ^1H NMR spectrum of product is consistent with **2m**.

8. Isotope tracing.

To a 10 mL reaction tube was sequentially added 2-benzoylbenzoic acid (45 mg, 0.2 mmol), absolute ethanol (0.5 mL), 1 mL of catalyst solution (**C2**, 0.008 mol/L for *S/C* = 250) in deuteroxide (a) or deionized water (b). DCO_2D (32 equiv, 122 μL) was added to the tube in three portions at interval of 5 h (total reaction time is 15 h) at 80 °C. The system was monitored by TLC analysis. Then saturated NaCl (2 mL) and H_2O (2 mL) were added to the tube, and reaction mixture was extracted with EA (2 mL × 3). After that the combined organic phases was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The organic solvent was evaporated under reduced pressure. The ^1H NMR yields of the crude residues were determined using 1,3,5- trimethoxybenzene as internal standard.



Scheme S1. Isotopic labeling of 1a.

9. Kinetic isotope effect studies.

Kinetic isotope effect studies were carried out according to the following experimental steps.

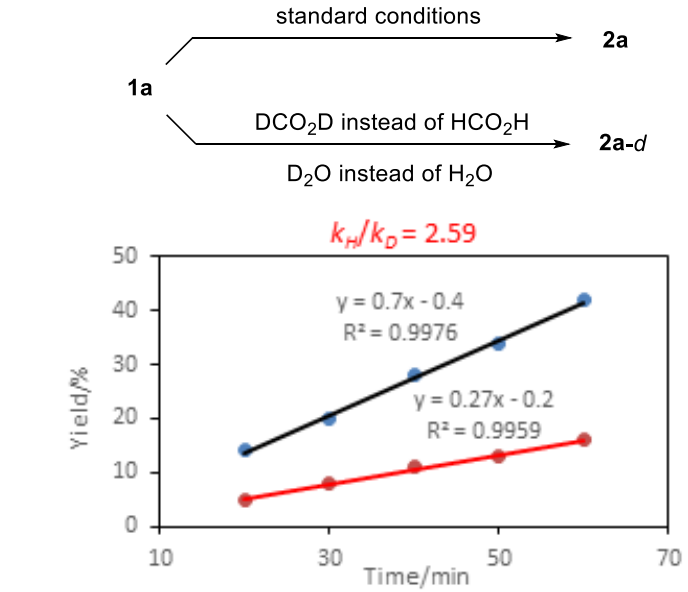
For **2a**: To each of five 10-mL reaction tubes were sequentially added 2-benzoylbenzoic acid **1a** (23 mg, 0.1 mmol), absolute ethanol (0.25 mL), 0.5 mL of catalyst solution (0.0002 mol/L for *S/C* = 1000, **C2** in deionized water) respectively. The mixtures were stirred for 3 minutes at 80 °C, and then formic acid (60 μL, 1.6 mmol, 16 equiv) was added to each tube. After stirring for corresponding time (20 min-60min), the reaction mixture was cooled to room temperature. The mixture was diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The ^1H NMR yield of the each crude residue was determined using 1,3,5-trimethoxybenzene as internal standard.

For **2a**-*d*: To each of five 10-mL reaction tubes were sequentially added 2-benzoylbenzoic acid **1a** (23 mg, 0.1 mmol), absolute ethanol (0.25 mL), 0.5 mL of catalyst solution (0.0002 mol/L for *S/C* = 1000, **C2** in deuterated water) respectively. The mixtures were stirred for 3 minutes at 80 °C, and then formic acid (60 μL, 1.6 mmol, 16 equiv) was added to each tube. After stirring for corresponding time (20 min-60min), the reaction mixture was cooled to room temperature. The mixture was diluted with saturated brine (2 mL) and extracted with ethyl acetate (2 mL × 3). The organic solvent was evaporated under reduced pressure. The ^1H NMR yield of each crude residue was determined using 1,3,5-trimethoxybenzene as internal standard.

Table S2. Kinetic isotope effeft studies of reductive lactonization of **1a**.

Entry	Time (min)	2a yield (%)[b]	2a-$_{d1}$ yield (%)[b,c]
1	20	14	5
2	30	20	8
3	40	28	11
4	50	34	13
5	60	42	16

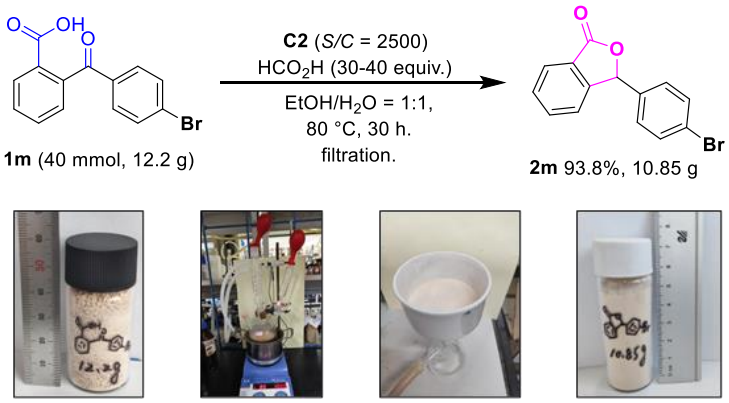
Kinetic isopote effect



Scheme S2. Kinetic isotope effeft studies of reductive lactonization of 1a.

10. Decagram-scale preparation of 2m.

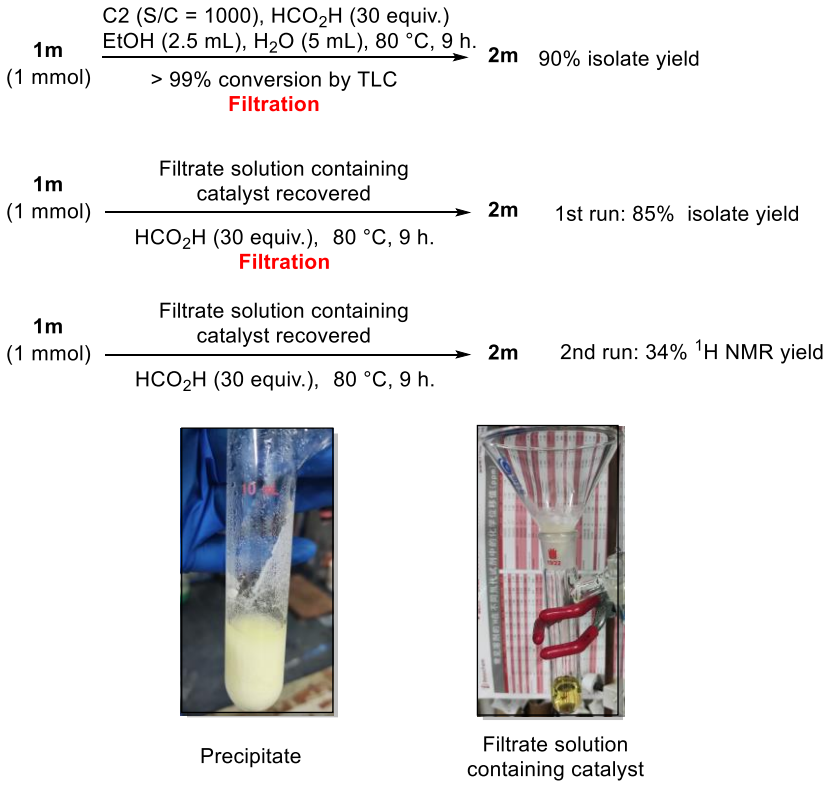
To a 500-mL three-necked flask charged with a magnetic stirring bar were added **1m** (12.2 g, 40.0 mmol), **C2** (0.016 mmol, 9.2 mg, *S/C* = 2500), ethanol (100 mL) and deionized water (100 mL). Then anhydrous formic acid (32 equiv, 48 mL) was added to the reaction flask in three or five portions over a period of 30 hours at 80°C in the oil bath. Until TLC showed full consumption of substrates, the system was cooled to room temperature and ethanol was removed under reduced pressure to decrease loss of product. The residual solid-liquid mixture was filtered and the filter cake was washed with water (3 × 15 mL) and then dried to obtain the corresponding NMR-pure lactone **2m** (10.85 g, 93.8%).



Scheme S3. Decagram-scale preparation of **2m**.

11. Catalyst recycling experiments.

To a 10-mL reaction tube was sequentially added **1m** (300 mg, 1.0 mmol), absolute ethanol (2.5 mL), 5 mL of catalyst solution (**C2** in deionized water, 0.0002 mol/L for S/C = 1000). The mixture was stirred for 3 minutes at 80 °C, and then formic acid (1.1 mL, 30.0 mmol, 30 equiv) was added to the reaction tube in three portions at interval of 3 h (total reaction time is 9 h). After **1m** was consumed completely as detected by TLC, the mixture was allowed to cool to room temperature. A large number of solid precipitated out of solution. The precipitate was filtered off and dried. The filtrate is collected in another reaction tube for recycling.



Scheme S4. Catalyst recycling experiments of reductive lactonization of **1m**.

1st run: To the 10-mL reaction tube containing filtrate recovered charged with a magnetic stirring bar were added **1m** (300 mg, 1.0 mmol). 1 mL of ethanol was added to the tube, due to the loss of ethanol in previous isolation process. Formic acid (1.1 mL, 30.0 mmol, 30 equiv) was added in three portions

at interval of 3 h (total reaction time is 9 h). Until **1m** was consumed completely as detected by TLC, the mixture was allowed to cool to room temperature. A large number of solid precipitated out of the solution. The solid was filtered and the filtrate is collected in another reaction tube for recycling.

2nd run: To the 10-mL reaction tube containing filtrate recovered charged with a magnetic stirring bar were added **1m** (300 mg, 1.0 mmol). 1 mL of ethanol was added to the tube, due to the loss of ethanol in previous isolation process. Formic acid (1.1 mL, 30.0 mmol, 30 equiv) was added in three portions at interval of 3 h (total reaction time is 9 h). But, **1m** was not consumed completely as detected by TLC. The ^{1}H NMR yield of the crude residue was determined using 1,3,5- trimethoxybenzene as internal standard.

12. Robustness demonstration.

Five Chinese liquors with different alcoholic strengths were used as solvents in the following reactions.

To five 10-mL reaction tube were sequentially added 2-benzoylbenzoic acid (**1a**, 225 mg, 1 mmol) and **C2** (0.6 mg, 0.001 mmol). 5 mL of **CL1** (Hengshui Laobaigan), **CL2** (Fenjiu), **CL3** (Langjiu), **CL4** (Niulanshan Erguotou), **CL5** (Red-star Erguotou) were added to these reaction tubes, respectively. The mixture was stirred for 3 minutes at 80 °C, and then formic acid (1.1 mL, 30 mmol, 30 equiv) was added in three portions at interval of 3 h (total reaction time 9 h). The reaction mixture was cooled to room temperature. Ethanol in the reaction mixture was removed under reduced pressure as much as possible. The precipitate was filtered and dried, giving ^{1}H NMR-pure **2m** in different yields.

1m (1 mmol) → **2m**: **C2** (*S/C* = 1000), HCO_2H (30 equiv.), 80 °C, **commercial liquors as solvent**

	CL-1	CL-2	CL-3	CL-4	CL-5
alc / vol (%vol)	41	42	45	46	56
time (h)	12	12	12	12	16
conv. (%)[a]	>99	>99	>99	>99	>99
yield (%)[b]	89	92	93 (99)[c]	91	90

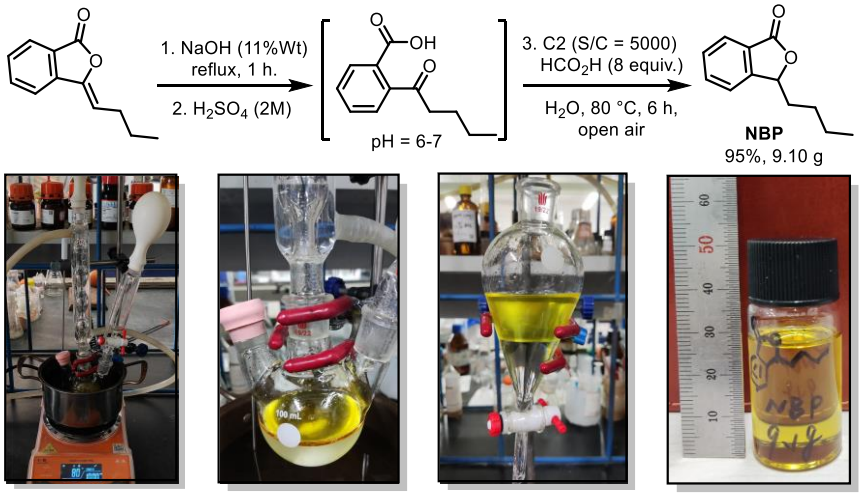
CL-1 Hengshui Laobaigan | **CL-2** Fenjiu | **CL-3** Langjiu | **CL-4** Niulanshan Erguotou | **CL-5** Red-star Erguotou

Scheme S5. Reductive lactonization reaction of 1m in Five Chinese liquors.

13. One-pot and large-scale preparation of medicinally relevant (±)-NBP from *n*-butylenephthalein.

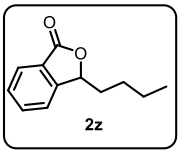
To a 100-mL three-necked flask were added *n*-butylenephthalein (9.40 g, 50 mmol), 20 ml of sodium

hydroxide aqueous solution (11 wt%, in deionized water). The system was stirred for 1 h at 100 °C and cooled to room temperature. After that, dilute sulphuric acid (2M) was added to flask to adjust pH to 6-7, followed by the addition of the **C2** (5.7 mg, 0.02 mol%, *S/C* = 5000) and an additional 10 ml of deionized water. The mixture was stirred for 3 minutes at 80 °C, followed by addition of formic acid (15 mL, 0.4 mol, 8 equiv) via the dropping funnel in one portion and stirred for 6 h. After completion of the reaction, the above system was diluted with water (10 mL) and extracted with ethyl acetate (30 mL × 3). The organic phase was dried with anhydrous sodium sulfate and solvent was removed under reduced pressure. NMR-pure NBP (**2z**) was obtained as a yellow oily liquid (9.10 g, 95% yield).



Scheme S6. One-pot and large-scale preparation of medicinally revelant (±)-NBP.

3-butylisobenzofuran-1(3*H*)-one (2z).[20] [CAS No: 6066-49-5]

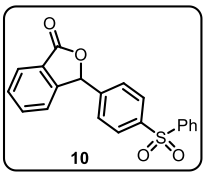


Yellow liquid, 9.10 g, yield 95%, R_f = 0.60 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 7.7 Hz, 1H), 7.65 (td, *J* = 7.6, 0.9 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 5.46 (dd, *J* = 7.9, 4.1 Hz, 1H), 2.03 (dddd, *J* = 14.2, 10.0, 5.9, 4.2 Hz, 1H), 1.74 (dddd, *J* = 14.5, 10.0, 7.9, 4.9 Hz, 1H), 1.52 – 1.31 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* 170.8, 150.2, 134.0, 129.1, 126.2, 125.7, 121.8, 81.5, 34.5, 27.0, 22.5, 13.9.

14. The synthesis of 10 via oxidation of 2j.

To a dried round bottom flask charged with a magnetic stirring bar were added compound **2j** (64 mg, 0.2 mmol) and DCM (4 mL). Then 3-chloroperbenzoic acid (138 mg, 0.6 mmol, 85 wt%) dissolved in DCM was added dropwise at 0 °C. After stirring for 4 hours at room temperature, the mixture was diluted with DCM (5 mL) and washed with saturated aq. $NaHCO_3$ (10 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated to dryness. Purification by gradient column chromatography (PE:EA from 10:1 to 1:1) afforded **10**.

3-(4-(phenylsulfonyl)phenyl)isobenzofuran-1(3H)-one (10).

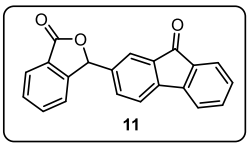


White solid, 49 mg, yield 70%, mp 194–196 °C, R_f = 0.20 (PE/EA = 2:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 8.09 – 7.85 (m, 5H), 7.71 – 7.41 (m, 7H), 7.31 (d, *J* = 6.6 Hz, 1H), 6.42 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* 170.1, 148.7, 142.6, 142.1, 141.1, 134.8, 133.6, 130.0, 129.5, 128.5, 127.8, 127.6, 126.1, 125.2, 122.8, 81.3. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{15}O_4S^+$, 351.0686; found, 351.0686.

15. The synthesis of 11 via oxidation of 2s.

Compound **2s** (60 mg, 0.2 mmol) and KI (7 mg, 20 mol%) were suspended in MeCN (2 mL). Then *tert*-butyl hydroperoxide (83 μL, 0.6 mmol, 70% in H_2O) was added and the reaction mixture was stirred overnight. Remaining peroxide was quenched by addition of sat. aqueous $Na_2S_2O_3$ solution. The product was extracted into CH_2Cl_2 and the combined organic phases were dried over anhydrous Na_2SO_4. The solvents were removed under reduced pressure and the crude product were purified on column chromatography (PE/EA = 10:1). The product was isolated as white solid.

3-(9-oxo-9H-fluoren-3-yl)isobenzofuran-1(3*H*)-one (11).

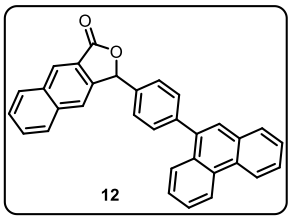


White solid, 37 mg, yield 60%, mp 183–185 °C, R_f = 0.40 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.6 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.55 – 7.47 (m, 4H), 7.44 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.32 (td, *J* = 7.2, 1.4 Hz, 1H), 6.42 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 193.1, 170.3, 149.1, 145.5, 143.8, 137.8, 135.1, 135.0, 134.7, 134.4, 133.6, 129.8, 129.7, 126.1, 125.8, 124.7, 122.94, 122.88, 121.0, 120.8, 82.1. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{13}O_3^+$, 313.0859; found, 313.0862.

16. The synthesis of 12 via Suzuki coupling of 2w.

To a dried reaction tube charged with a magnetic stirring bar was sequentially added **2w** (33.8 mg, 0.1 mmol), phenanthren-9-ylboronic acid (0.15 mmol), K_3PO_4 (42.5 mg, 0.2 mmol), $Pd(PPh_3)_4$ (7 mg, 0.006 mmol, 6 mol%). The tube was then sealed with a rubber cap and a metal sealing ring. The air in the tube was evacuated, and then filled with nitrogen through a needle. This operation was repeated three times. Then dry toluene was added to reaction tube via a syringe. The reaction was stirred for 9 h at 100 °C. The solvent was removed by distillation under reduced pressure and crude residue was purified by silica gel column chromatography to give desired product **12**.

3-(4-(Phenanthren-9-yl)phenyl)naphtho[2,3-c]furan-1(3H)-one (12).



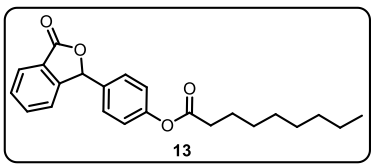
White solid, 40 mg, yield 91%, mp 200–202 °C, R_f = 0.50 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.77 (d, *J* = 8.2 Hz, 1H), 8.71 (d, *J* = 8.2 Hz, 1H), 8.59 (s, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.89 (s, 1H), 7.87 (s, 2H), 7.70 – 7.60 (m, 6H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.56 – 7.51 (m, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 6.68 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.5, 143.5, 142.0, 138.0, 136.5, 136.4, 133.4, 131.5, 130.9, 130.8, 130.7, 130.13, 130.09, 129.2, 128.8, 128.5, 127.8, 127.3, 127.2, 127.0, 126.9, 126.8, 126.72, 126.71, 123.6, 123.1, 122.7, 122.2, 82.8. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{21}O_2^+$, 437.1536; found, 437.1533. (There is one carbon signal overlapping)

17. Derivatization of product 2k.

Compound **2k** (45 mg, 0.2 mmol) and triethylamine (56 uL, 0.4 mmol) were dissolved in dry DCM (2 mL). Nonanoyl chloride (54 uL, 0.3 mmol) was added dropwise to the reaction system under nitrogen atomsphere at 0 °C. The reaction mixture was stirred at room temperature for 3 hours. Then 2 ml of H_2O was added to the reaction mixture. Organic layer was washed with water (2 × 3 mL) and the

remaining organic layer was dried over Na_2SO_4 and removed by distillation under reduced pressure. The crude residue was purified by silica gel column chromatography to give desired product **13**.

4-(3-oxo-1,3-dihydroisobenzofuran-1-yl)phenyl nonanoate (13).

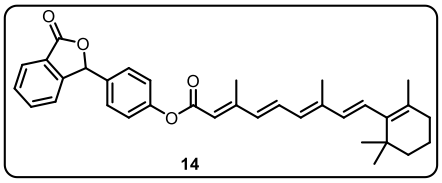


White solid, 34 mg, yield 93%, mp 77–79 °C, R_f = 0.30 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.65 (td, *J* = 7.2, 0.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.40 (s, 1H), 2.54 (t, *J* = 7.5 Hz, 2H), 1.74 (p, *J* = 7.5 Hz, 2H), 1.45 – 1.23 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 172.2, 170.4, 151.5, 149.5, 134.5, 133.9, 129.6, 128.3, 125.8, 125.7, 123.1, 122.3, 82.2, 34.5, 31.9, 29.3, 29.22, 29.20, 25.0, 22.7, 14.2. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{27}O_4^+$, 367.1904; found, 367.1914.

The synthesis of 14 via condensation 2k and Retinoic acid.

To a dried reaction tube charged with a magnetic stirring bar were sequentially added **2k** (46 mg, 0.2 mmol), retinoic acid (0.2 mmol, 60 mg), DMAP (20 mol%, 5.0 mg), and DMAP·HCl (20 mol%, 6.0 mg). The tube was then sealed with a rubber cap and a metal sealing ring. The air in the tube was evacuated, and then filled with nitrogen through a needle. This operation was repeated three times. Then dry DCM (3 ml) was added to the reaction tube under dark condition. DCC (0.22 mmol, 45 mg, dissolved in 2 ml of DCM) was injected dropwise into the reaction tube via a syringes at 0 ºC. Then the mixture was stirred for 8 h at room temperature under dark condition. When substrate was consumed completely, as detected by TLC, the reaction tube was kept in the refrigerator for 5 hours. The precipitate was filtered off, and then the filtrate evaporated under reduced pressure. The product was purified by column chromatography on silica gel to afford the pure products.

4-(3-oxo-1,3-dihydroisobenzofuran-1-yl)phenyl (2*E*,4*E*,6*E*,8*E*)-3,7-dimethyl-9-(2,6,6-trimethylcyclohex-1-en-1-yl)nona-2,4,6,8-tetraenoate (14).



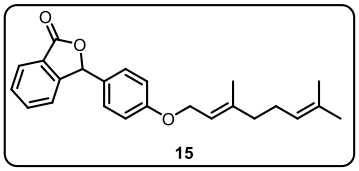
White solid, 76 mg, yield 75%, mp 107–109 °C, R_f = 0.30 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.3 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.09 (dd, *J* = 15.1, 11.6 Hz, 1H), 6.41 (s, 1H), 6.39 – 6.29 (m, 2H), 6.18 (d, *J* = 11.6 Hz, 1H), 6.16 (d, *J* = 16.2 Hz, 1H), 5.97 (s, 1H), 2.40 (s, 3H), 2.05 – 2.02 (m, 5H), 1.72 (s, 3H), 1.68 – 1.57 (m, 2H), 1.52 – 1.43 (m, 2H), 1.04 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.5, 165.3, 156.2, 151.7, 149.6, 140.8, 137.8, 137.3, 134.7, 134.5, 133.6, 132.4, 130.4, 129.6, 129.5, 129.4, 128.3, 125.80, 125.76, 123.1, 122.6, 116.9, 82.3, 39.7, 34.4, 33.3, 29.1, 21.9, 19.3, 14.2, 13.1. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{37}O_4^+$, 509.2686; found, 509.2682.

The synthesis of 15 via Mitsunobu reaction of 2k.

To a dried reaction tube charged with a magnetic stirring bar were sequentially added **2k** (50.6 mg, 0.22 mmol) and PPh_3 (0.22 mmol, 58 mg). The tube was then sealed with a rubber cap and a metal sealing ring. The air in the tube was evacuated, and then filled with nitrogen through a needle. This operation was repeated three times. Then dry THF (3 ml) and geraniol (0.2 mmol, 35 μL) were added to the reaction tube, respectively. Thereafter DIAD (0.22 mmol, 43 μL) was injected dropwise into the

reaction tube via a microsyringe. Then the reaction was stirred for 12 h at room temperature. The solvent was evaporated, and the residue was dissolved in ether. Then triphenylphosphane oxide precipitated and was filtered off. The filtrate was evaporated under reduced pressure. Purification by column chromatography on silica gel to afford the pure products.

(*E*)-3-(4-((3,7-dimethylocta-2,6-dien-1-yl)oxy)phenyl)isobenzofuran-1(3H)-one (15).

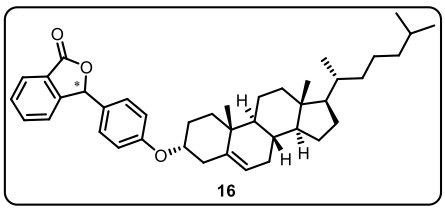


White solid, 47 mg, yield 64%, mp 68–79 °C, R_f = 0.50 (PE/EA = 5:1, *v*/*v*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.37 (s, 1H), 5.46 (t, *J* = 6.4 Hz, 1H), 5.08 (t, *J* = 6.2 Hz, 1H), 4.53 (d, *J* = 6.5 Hz, 2H), 2.09 (m, 4H), 1.72 (s, 3H), 1.66 (s, 3H), 1.60 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 159.9, 149.9, 141.7, 134.3, 132.0, 129.4, 128.9, 128.2, 126.1, 125.7, 123.9, 123.1, 119.3, 115.2, 82.9, 65.1, 39.7, 26.4, 25.8, 17.8, 16.8. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{27}O_3^+$, 363.1955; found, 363.1951.

The synthesis of 16 via Mitsunobu reaction of 2k.

To a dried reaction tube charged with a magnetic stirring bar were sequentially added **2k** (50.6 mg, 0.22 mmol), PPh_3 (0.22 mmol, 58 mg), Cholesterol (0.2 mmol, 77 mg). The tube was then sealed with a rubber cap and a metal sealing ring. The air in the tube was evacuated, and then filled with nitrogen through a needle. This operation was repeated three times. Then dry THF (3 ml) was added to the reaction tube. DIAD (0.22 mmol, 43 μL) was injected dropwise into the reaction tube via a microsyringe. Similar operations as described above gave pure product **16**.

3-(4-(((3R,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)phenyl)isobenzofuran-1(3*H*)-one (16).



White solid, 48 mg, yield 40%, mp 92–93 °C, R_f = 0.60 (PE/EA = 5:1, *v*/*v*). *dr.* = 1:0.6. Only one pure isomer was isolated. **Isomer 1**: **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.65 (td, *J* = 7.6, 0.8 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.36 (s, 1H), 5.28 – 5.20 (m, 1H), 4.55 – 4.51 (m, 1H), 2.52 (dt, *J* = 14.8, 2.8 Hz, 1H), 2.32 (dt, *J* = 15.2, 2.4 Hz, 1H), 2.06 – 1.87 (m, 4H), 1.87 – 1.70 (m, 3H), 1.55 – 1.43 (m, 5H), 1.39 – 1.30 (m, 4H), 1.28 – 1.23 (m, 2H), 1.18 – 1.06 (m, 8H), 1.03 (s, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.87 (dd, *J* = 6.6, 1.9 Hz, 6H), 0.68 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 170.7, 158.8, 149.9, 138.5, 134.3, 129.4, 128.8, 128.1, 126.2, 125.7, 123.1, 122.5, 117.0, 83.0, 73.2, 56.9, 56.3, 50.0, 42.5, 39.9, 39.7, 37.1, 36.3, 36.0, 33.2, 32.0, 28.4, 28.2, 25.9, 24.4, 24.0, 23.0, 22.7, 20.9, 19.2, 18.9, 12.0. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{41}H_{55}O_3^+$, 595.4146; found, 595.4143.

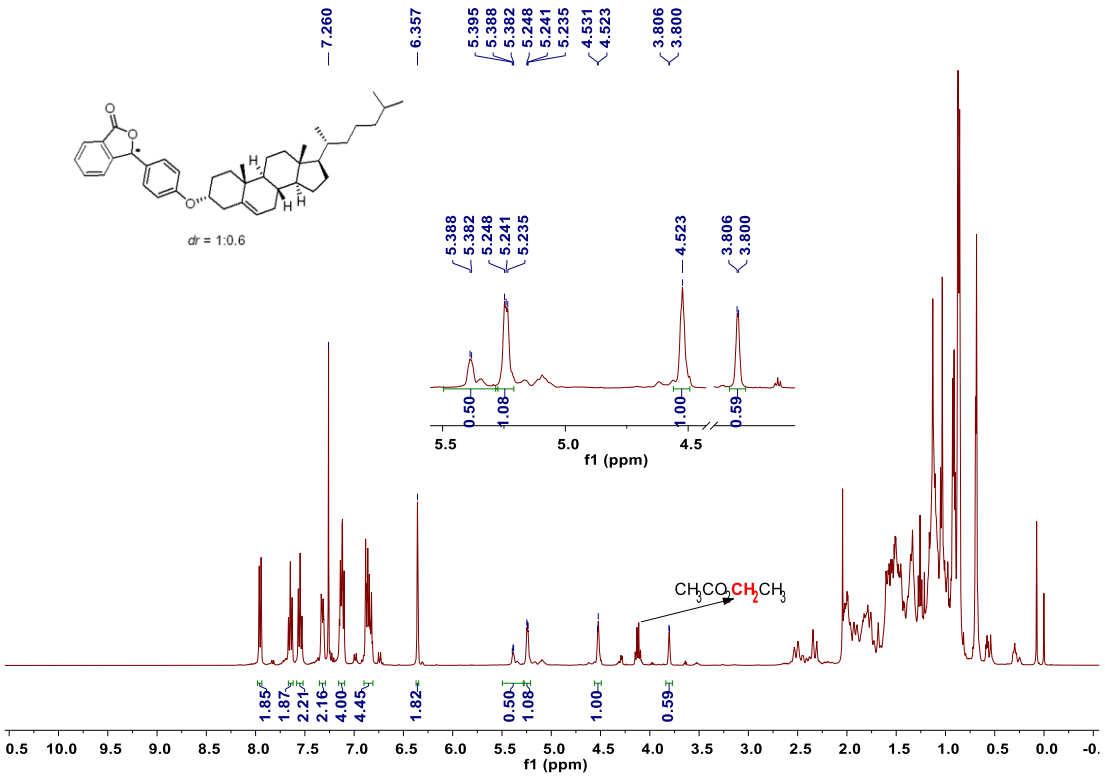


Figure S2. ^{1}H NMR spectrum of reaction mixture of compound **16**.

18. Using product 2k as acid-base indicator.

Phenolphthalein is a commonly used acid-base indicator, which turns colorless in acidic solutions (pH < 8.3) and pink in basic solutions (8.3 < pH < 10.0). As an analog of phenolphthalein, **2k** (c = 5 g/L in absolute ethanol) shows different a color change at different pH values in our titration experiments. Under acidic conditions (pH = 1), it is colorless. It turned to light pink at pH = 9.0-11.2, deep pink at 11.2, and again light pink at 11.2-12.5. At pH > 13.0, the color disappered.

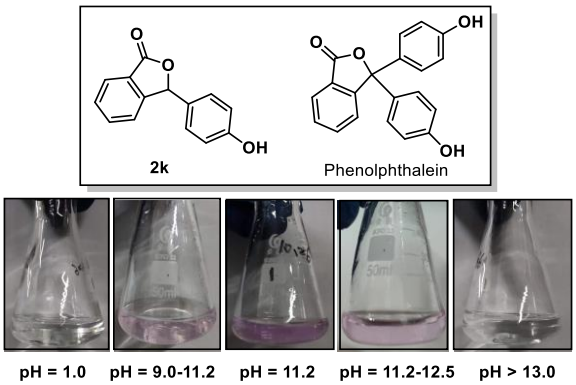


Figure S3. Colors of 2k in aqueous solutions at different pH values.

2k (5 mg) was dissolved in 1 mL of absolute ethanol, and was used as a kind of acid-base indicator. 100 ml of sodium hydroxide solution (0.1 M, pH = 1) and hydrochloric acid solution (0.1 M, pH = 13) were prepared respectively. 5.00 mL of hydrochloric acid solution (0.1 M, pH = 1), measured by a pipette gun, was added into a conical flask. Then, 2 drops of the ethanol solution of **2k** were added to the conical flask. Sodium hydroxide solution was added drop by drop with a pipette gun to the hydrochloric acid solution containing **2k**, continuously shaking the conical flask. When the color

of the solution in the conical flask changed and did not fade for more than 30 seconds, the pH value of the solution was recorded by using a calibrated pH meter. The above experiment was repeated three times and the average value of the ph value was taken.

19. References

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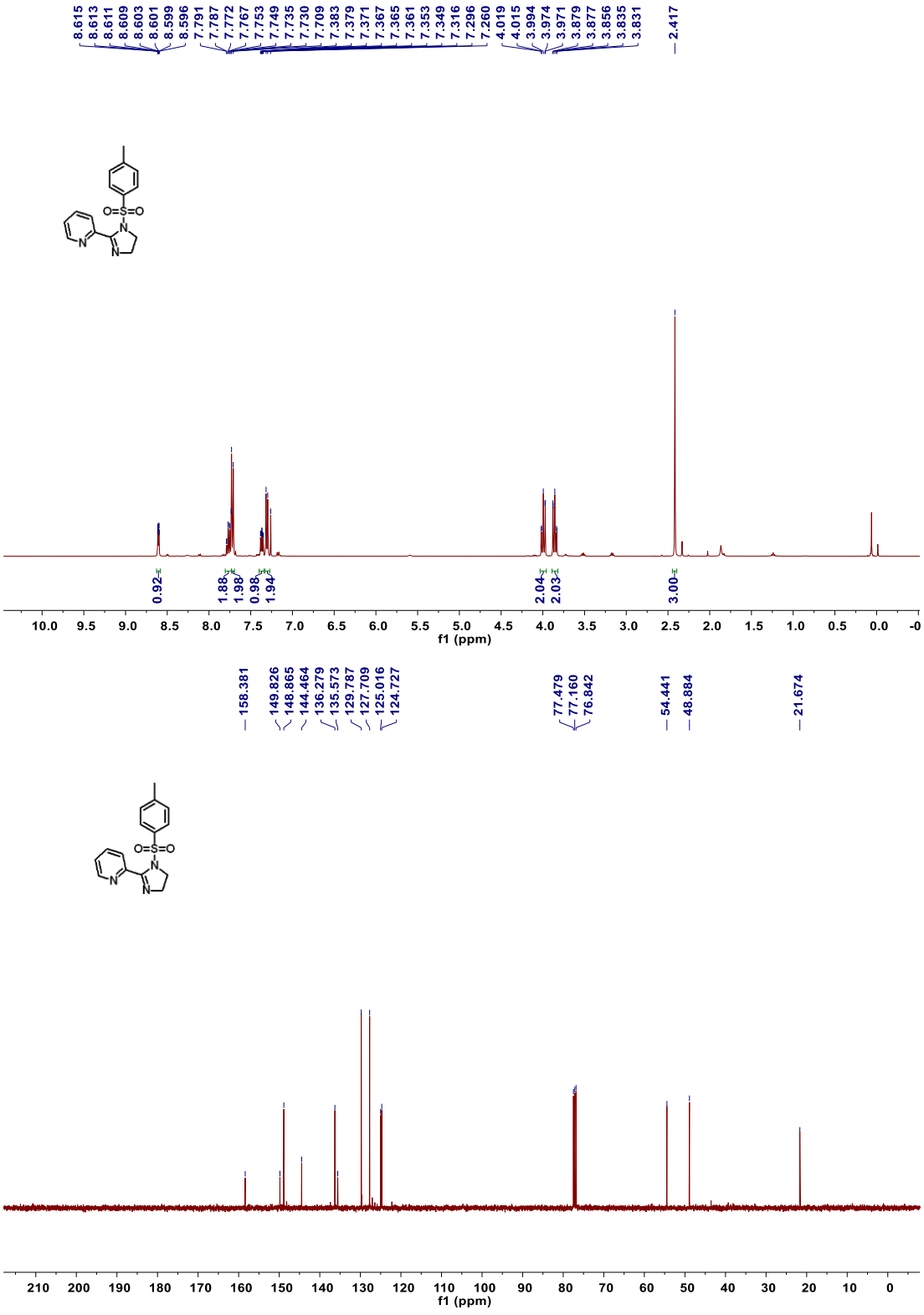
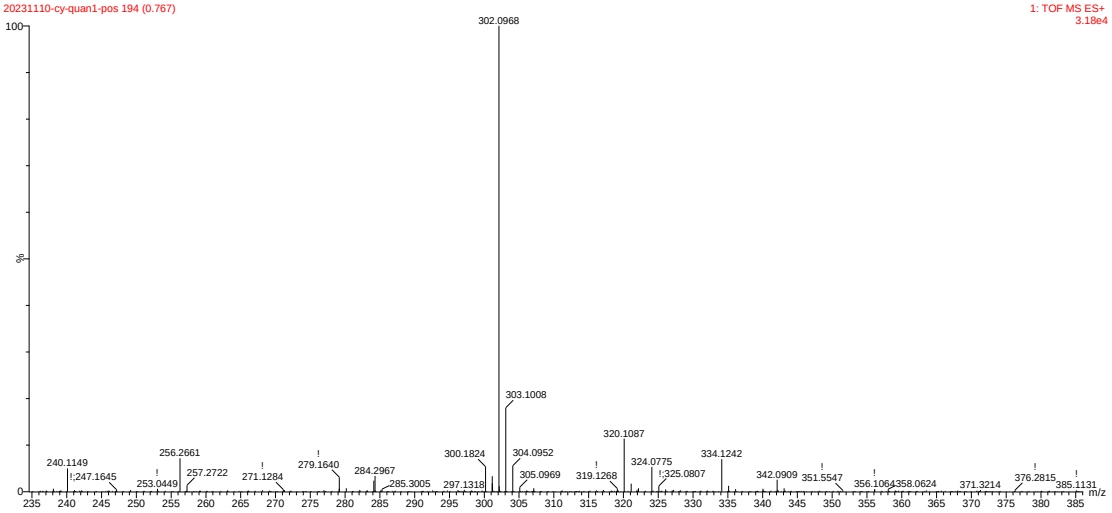
20. The NMR and HRMS spectrum of substrates and products.

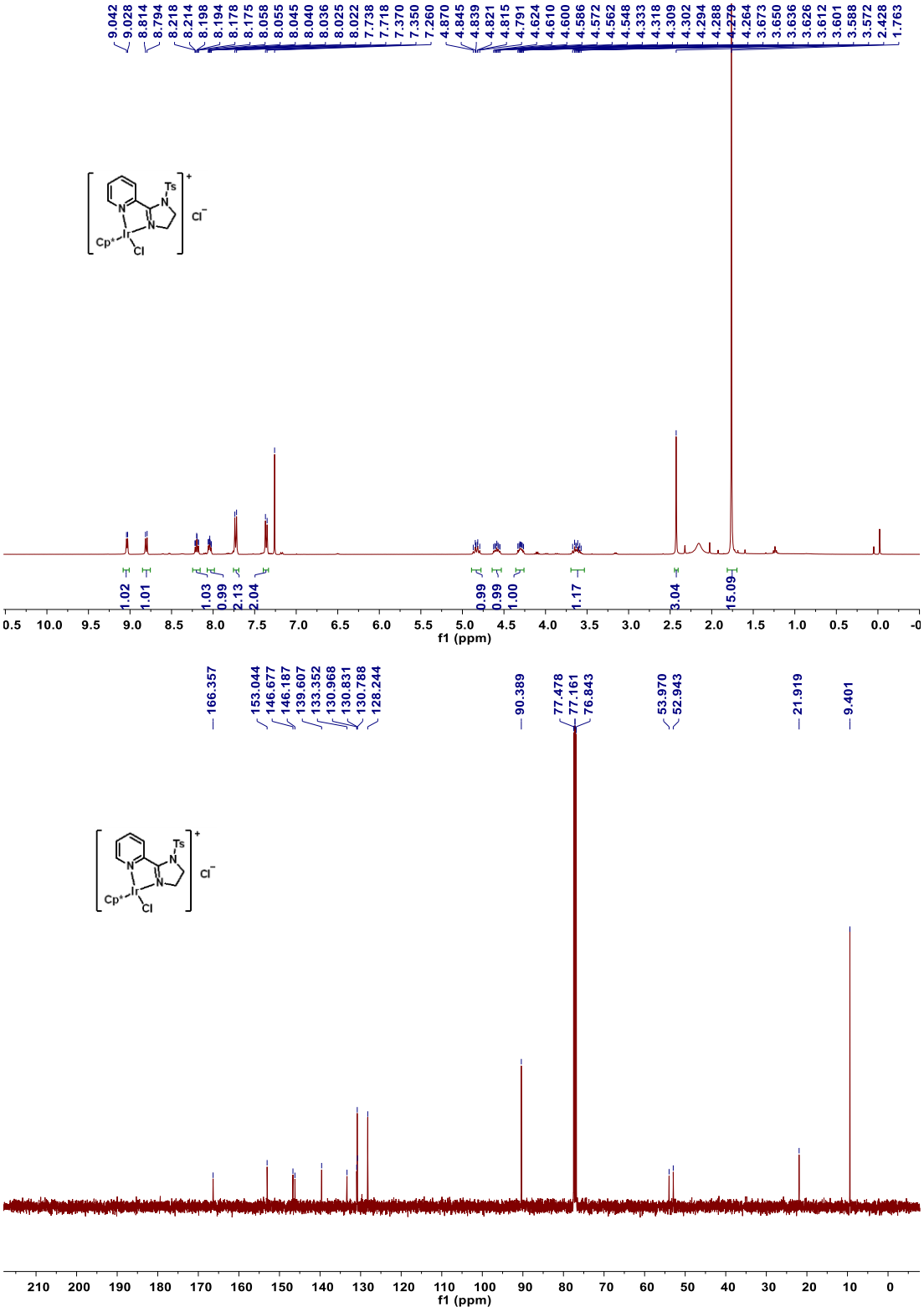
The ^{1}H and ^{13}C NMR spectrum of 2-(1-tosyl-4,5-dihydro-1H-imidazol-2-yl)pyridine.



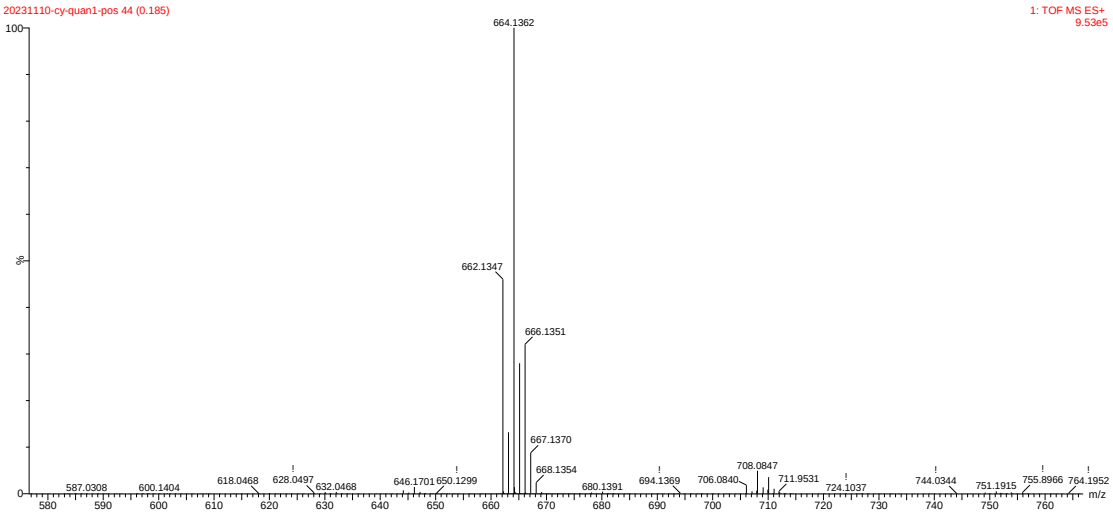
The HRMS spectrum of 2-(1-tosyl-4,5-dihydro-1H-imidazol-2-yl)pyridine.



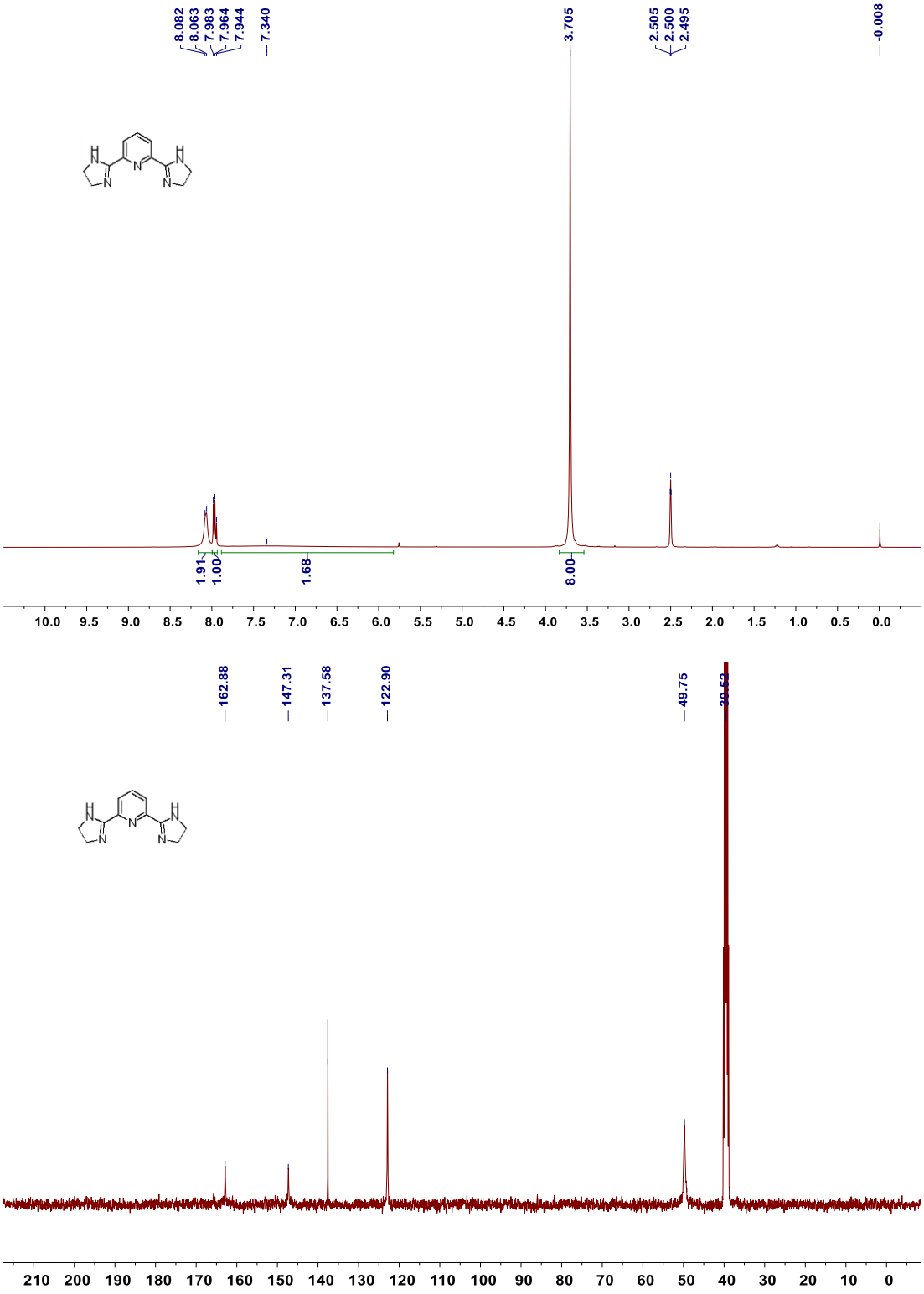
The ^{1}H and ^{13}C NMR spectrum of C9.



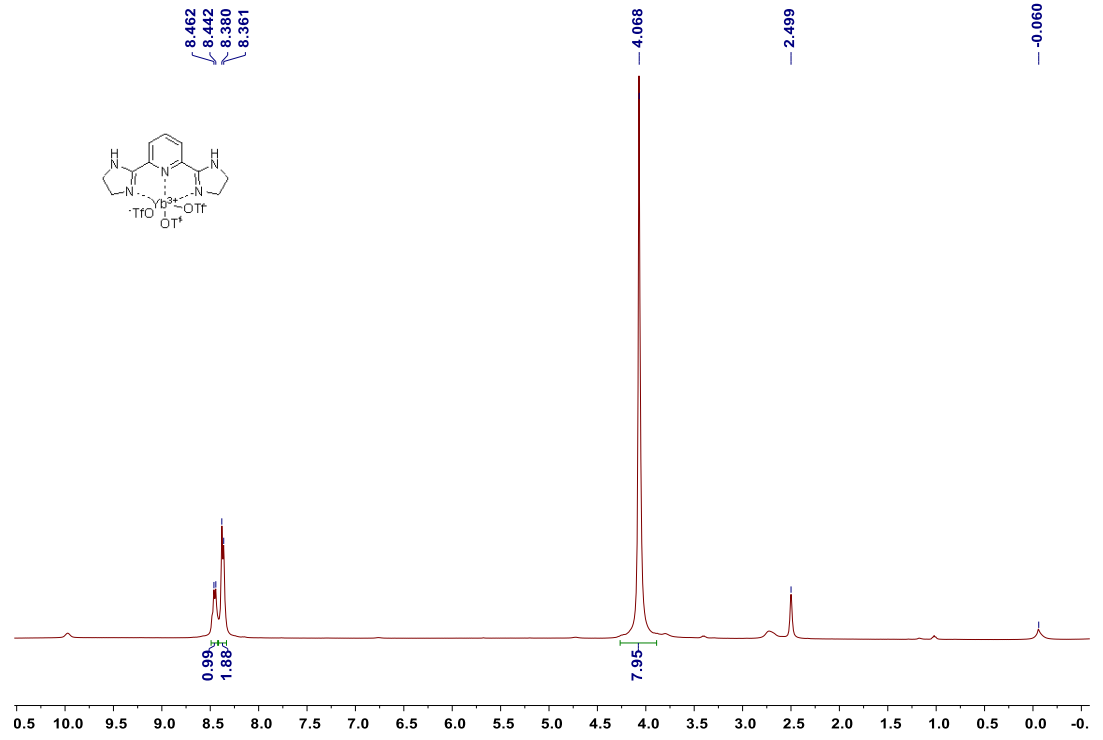
The ^{1}H and ^{13}C NMR spectrum of C9.

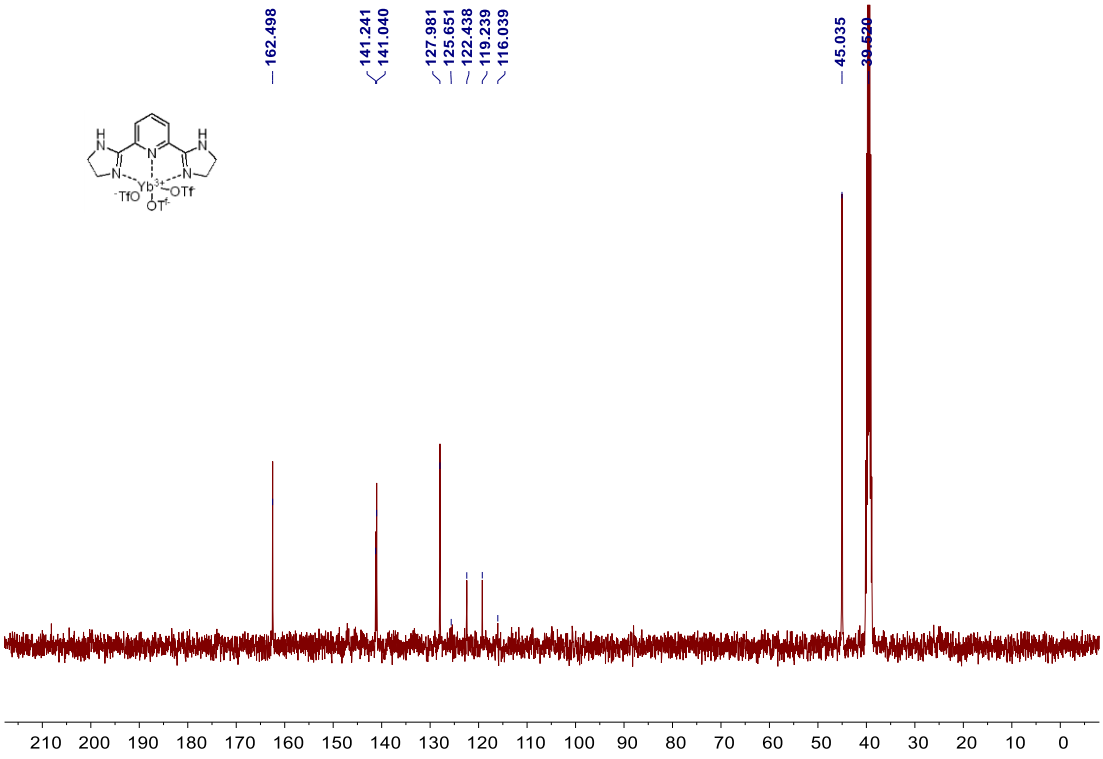


The ^{1}H and ^{13}C NMR spectrum of 2,6-bis(4,5-dihydro-1H-imidazol-2-yl)pyridine.

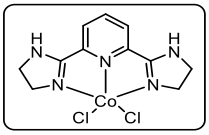


The ^{1}H and ^{13}C NMR spectrum of C13.

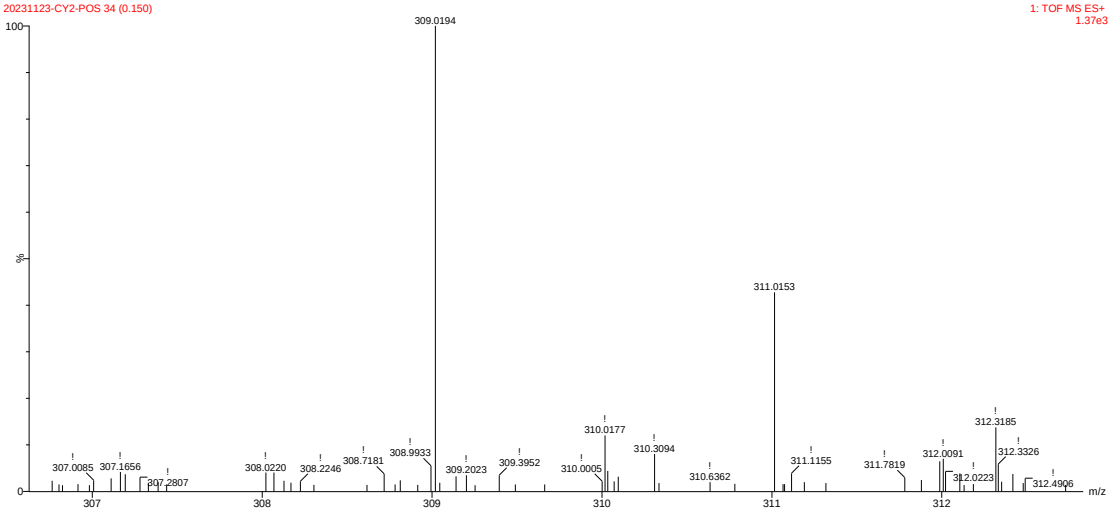




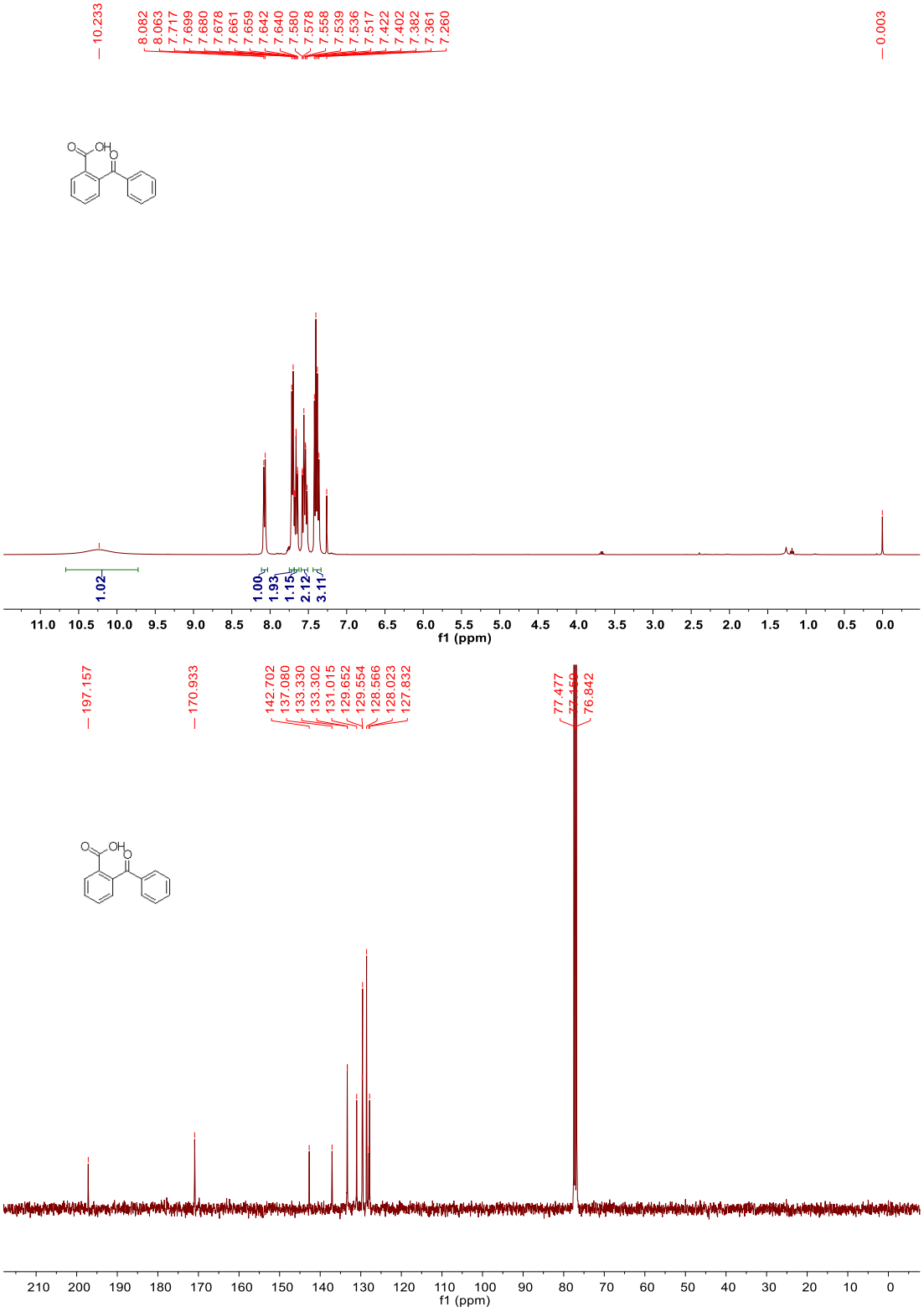
The HRNS spectrum of C17.



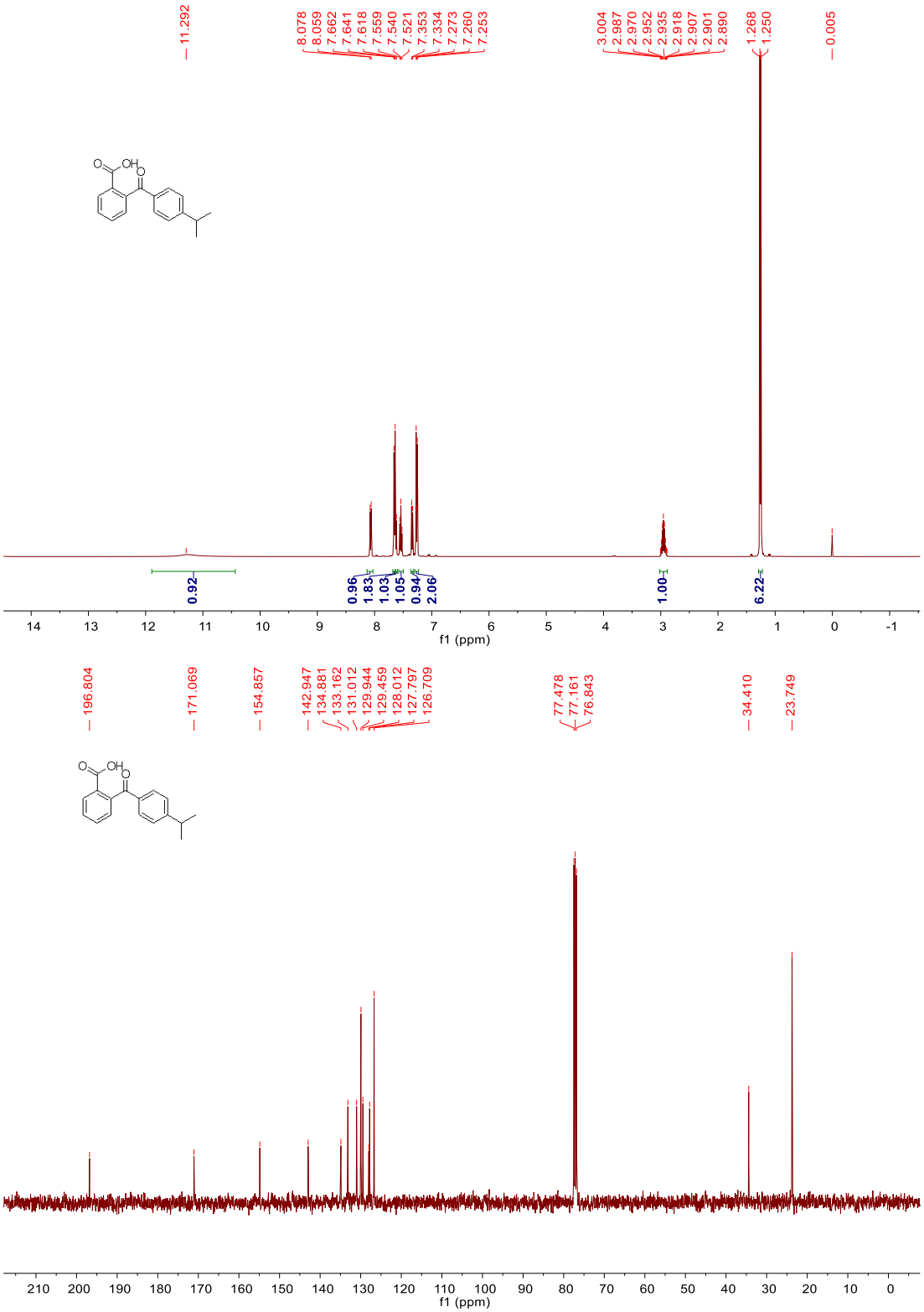
HRMS (ESI) m/z: $[M\text{-}Cl^-]^+$ calcd for $C_{11}H_{13}ClCoN_5^+$, 309.0186; found: 309.0194.



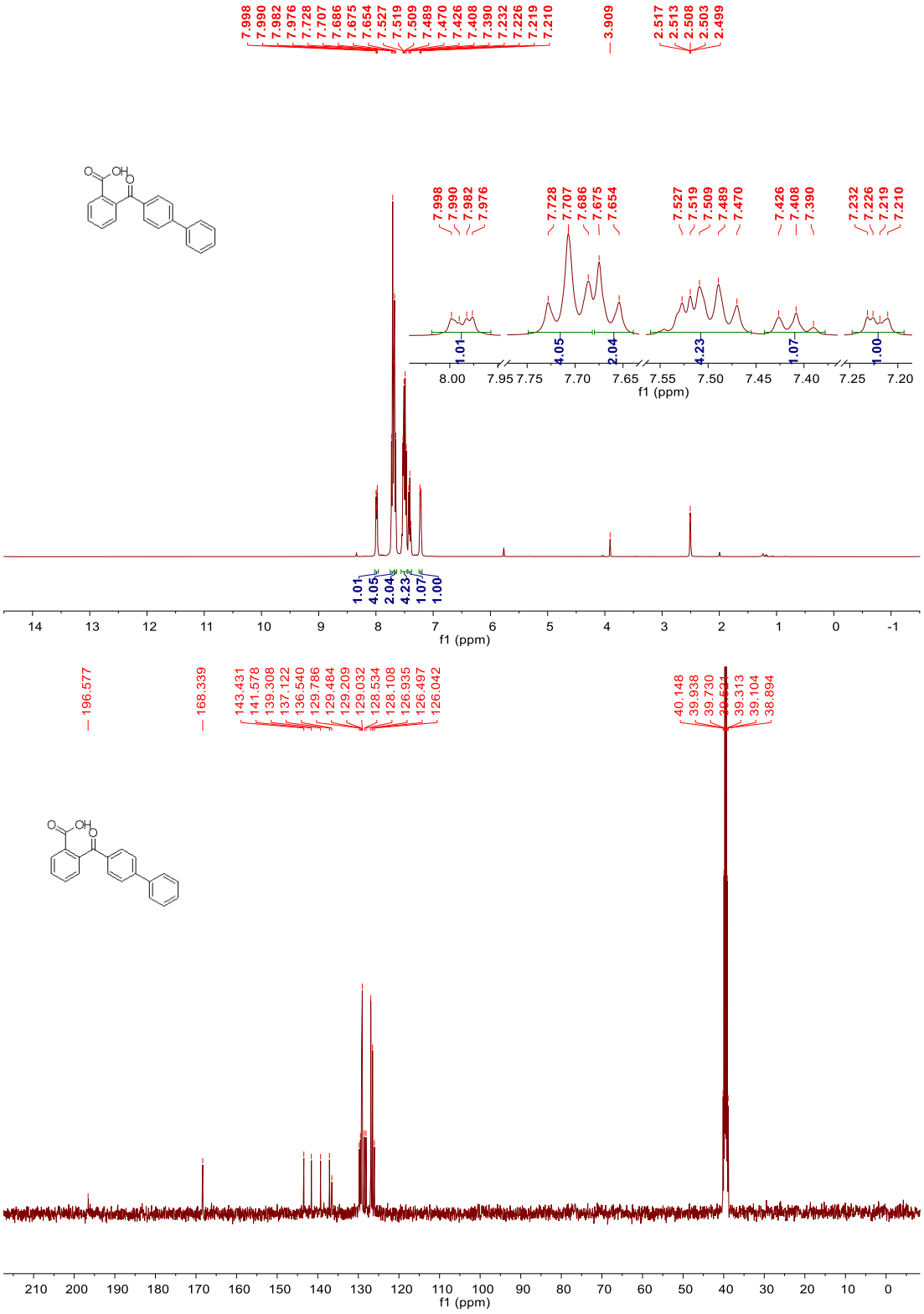
The ^{1}H and ^{13}C NMR spectrum of 2-Benzoylbenzoic acid (1a).



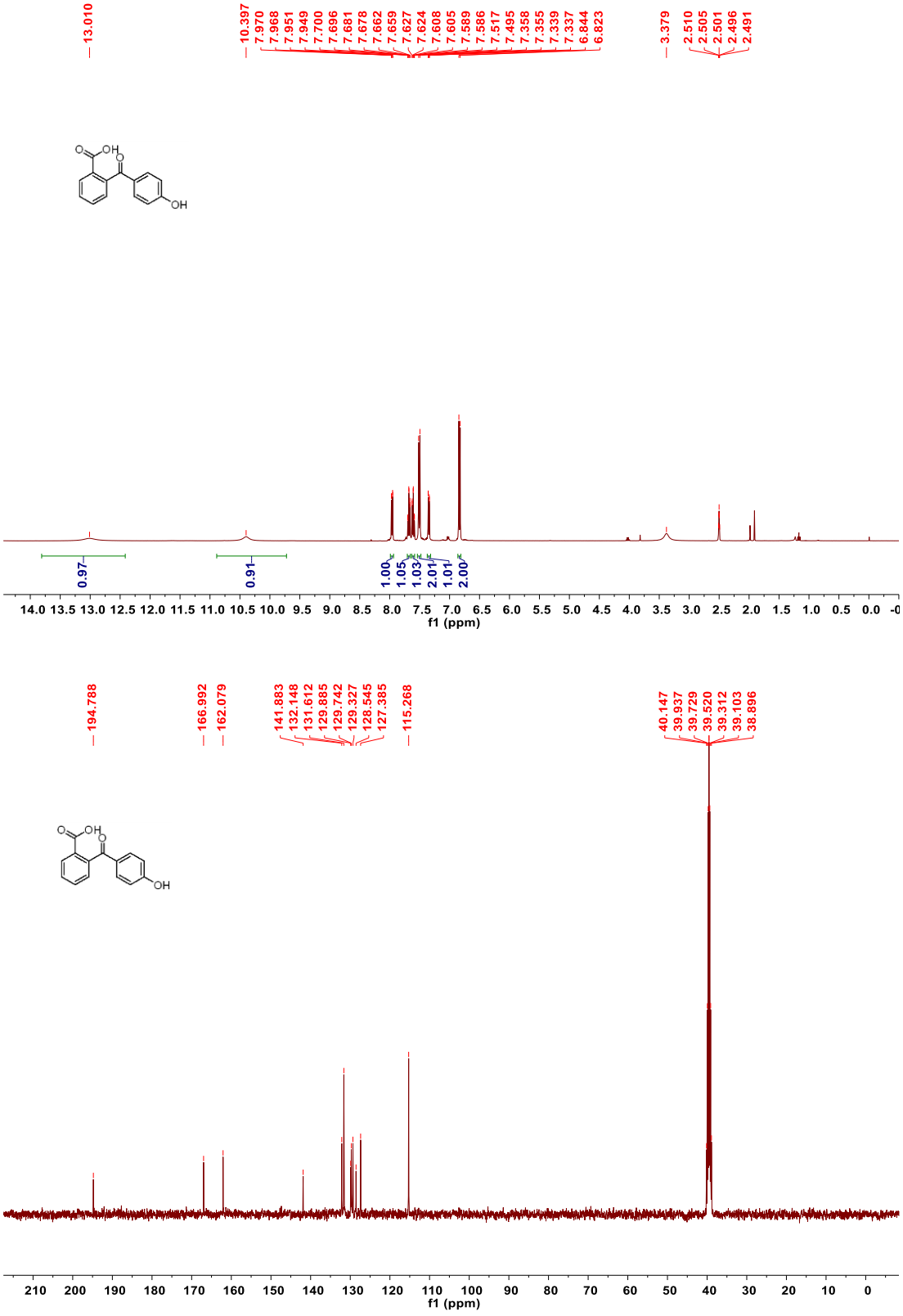
The ^{1}H and ^{13}C NMR spectrum of 2-(4-isopropylbenzoyl)benzoic acid (1d).



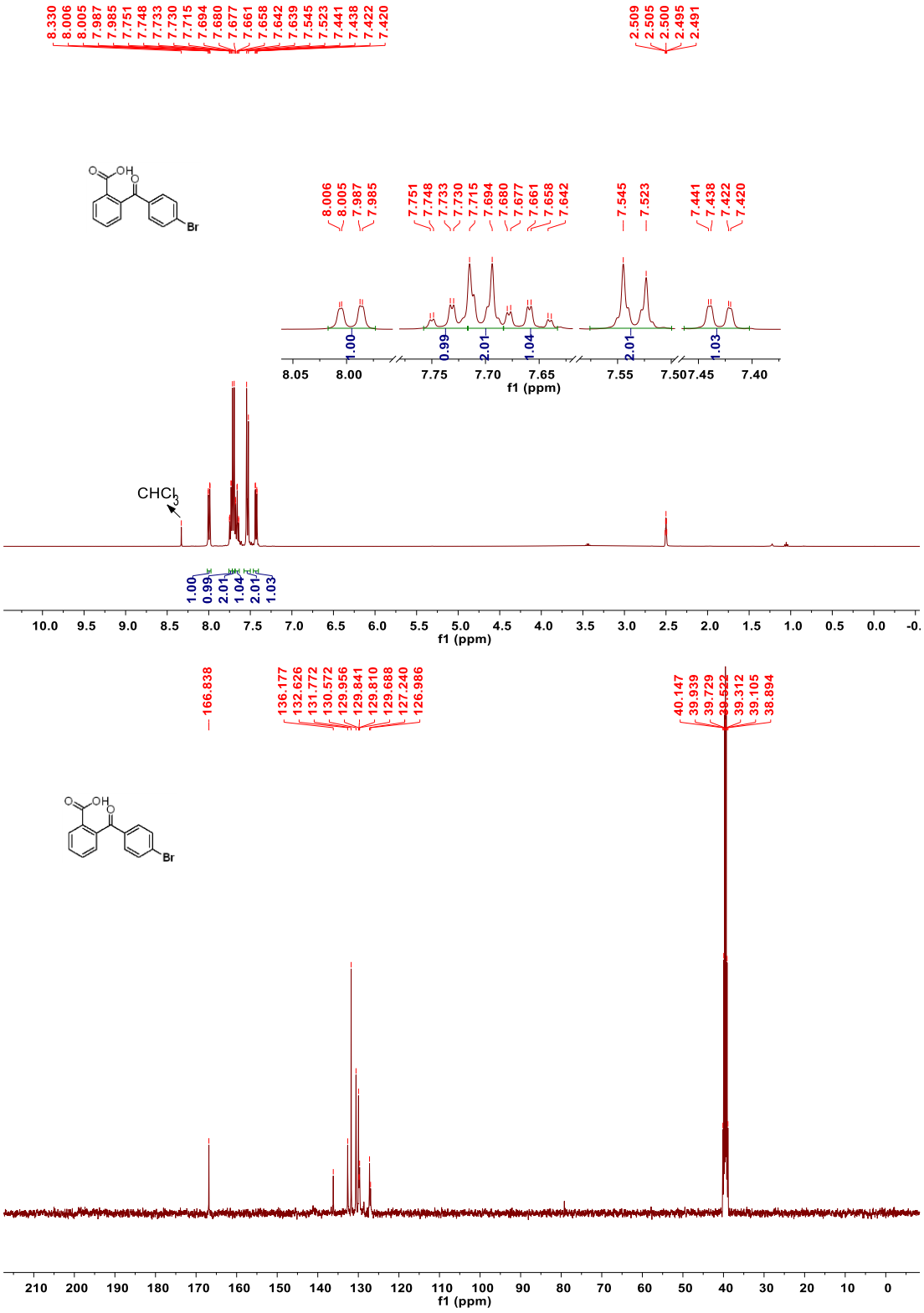
The ^{1}H and ^{13}C NMR spectrum of 2-([1,1'-biphenyl]-4-carbonyl)benzoic acid (1g).



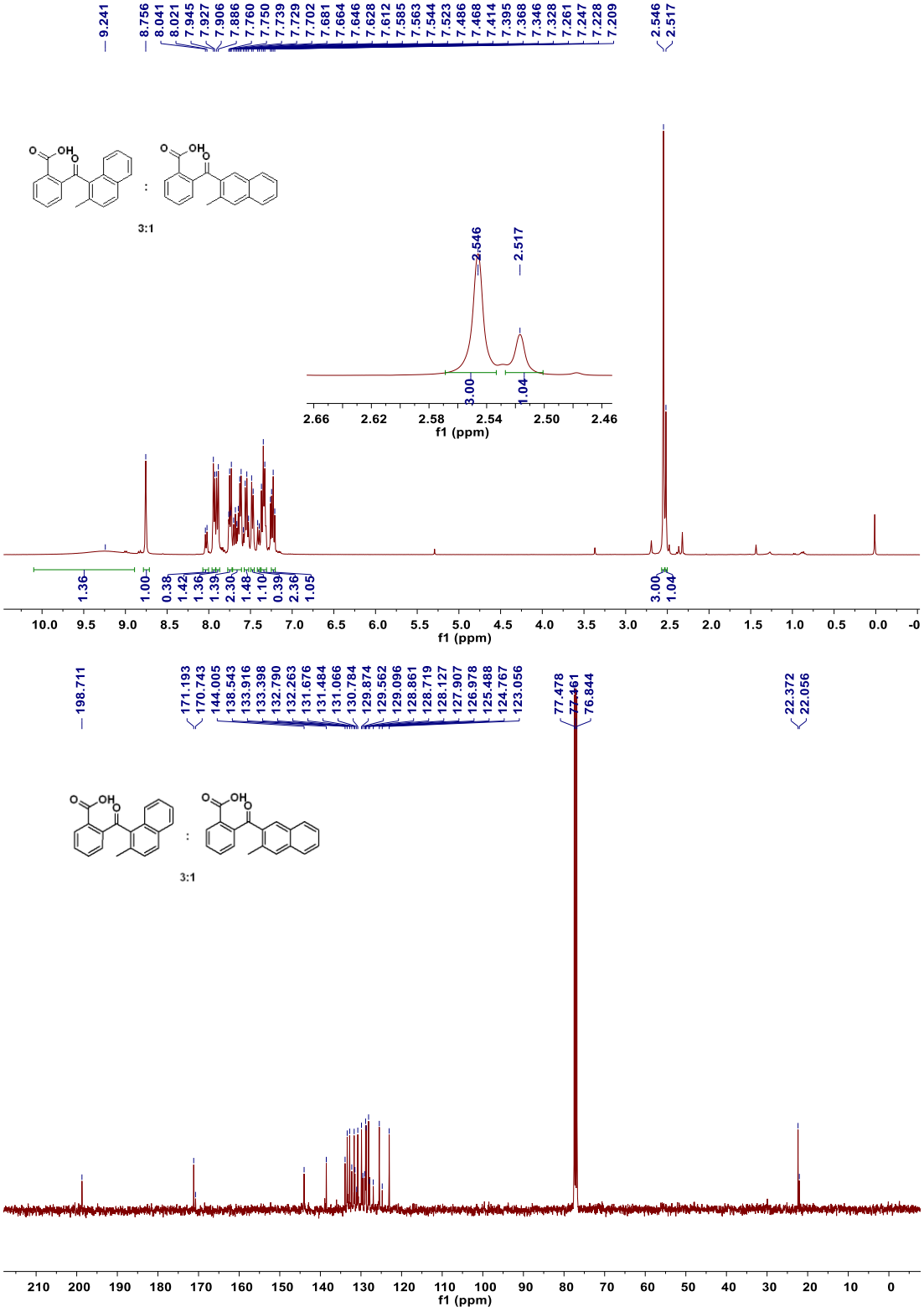
The ^{1}H and ^{13}C NMR spectrum of 2-(4-hydroxybenzoyl)benzoic acid (1k).



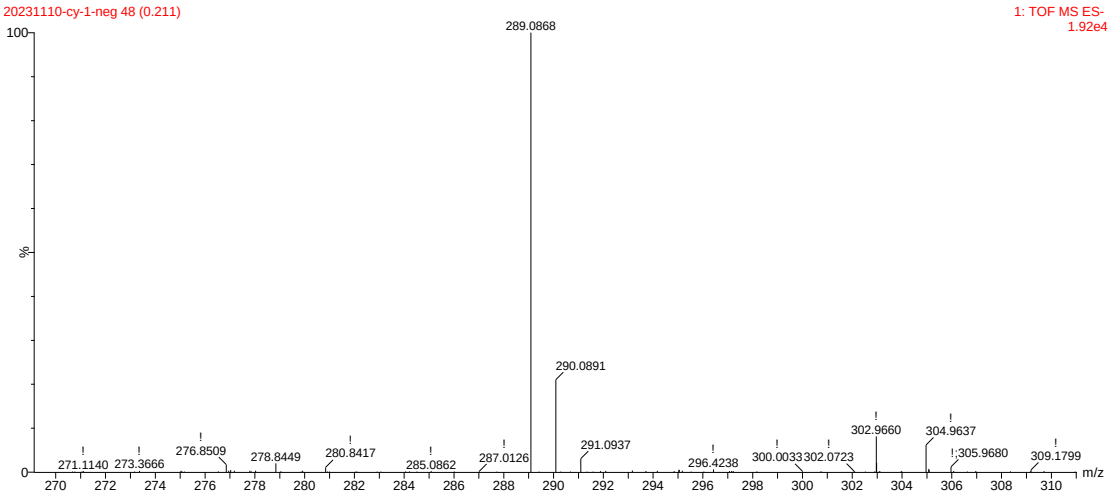
The ^{1}H and ^{13}C NMR spectrum of 2-(4-bromobenzoyl)benzoic acid (1m).



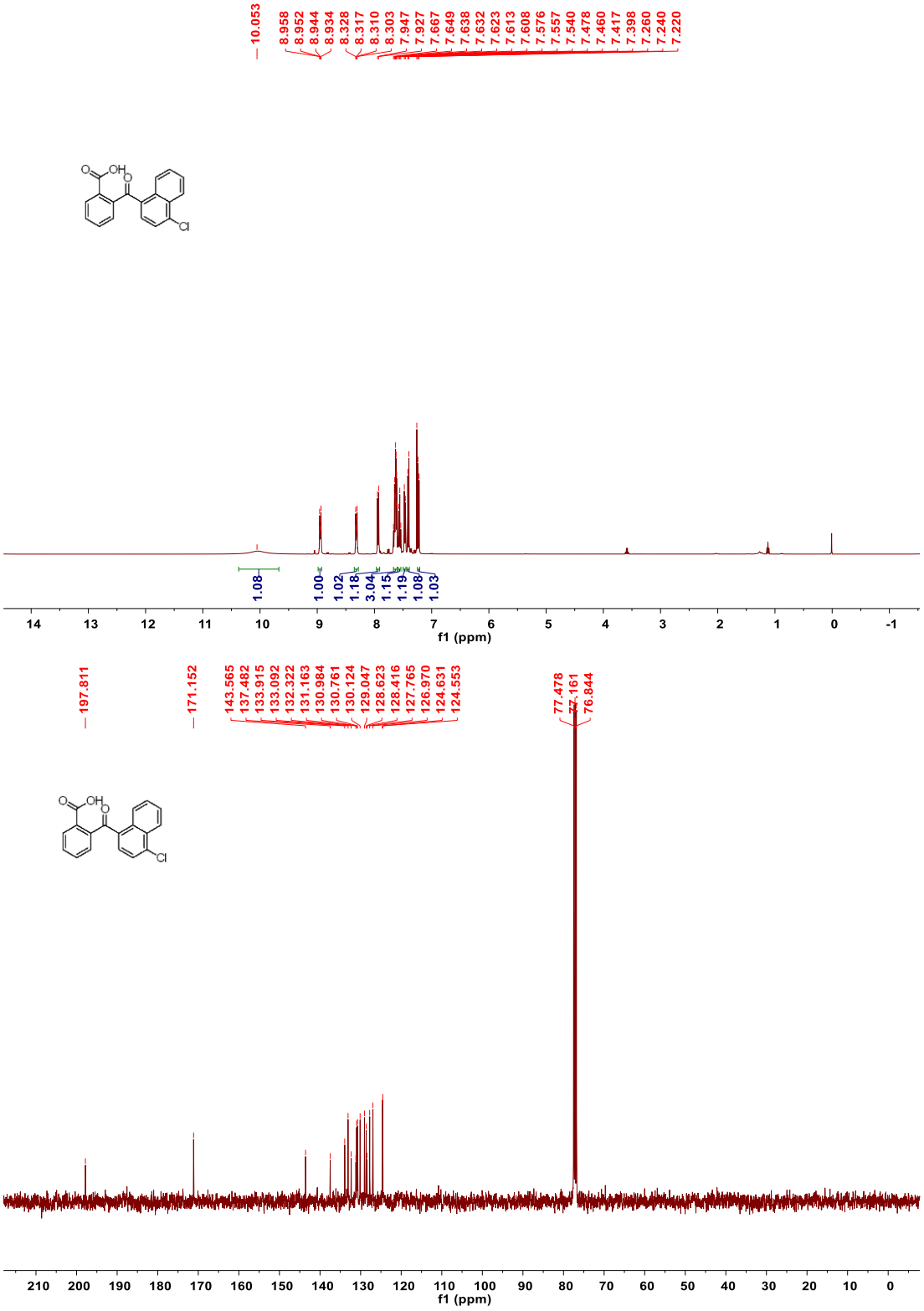
The ^{1}H and ^{13}C NMR spectrum of the mixture of (1o).



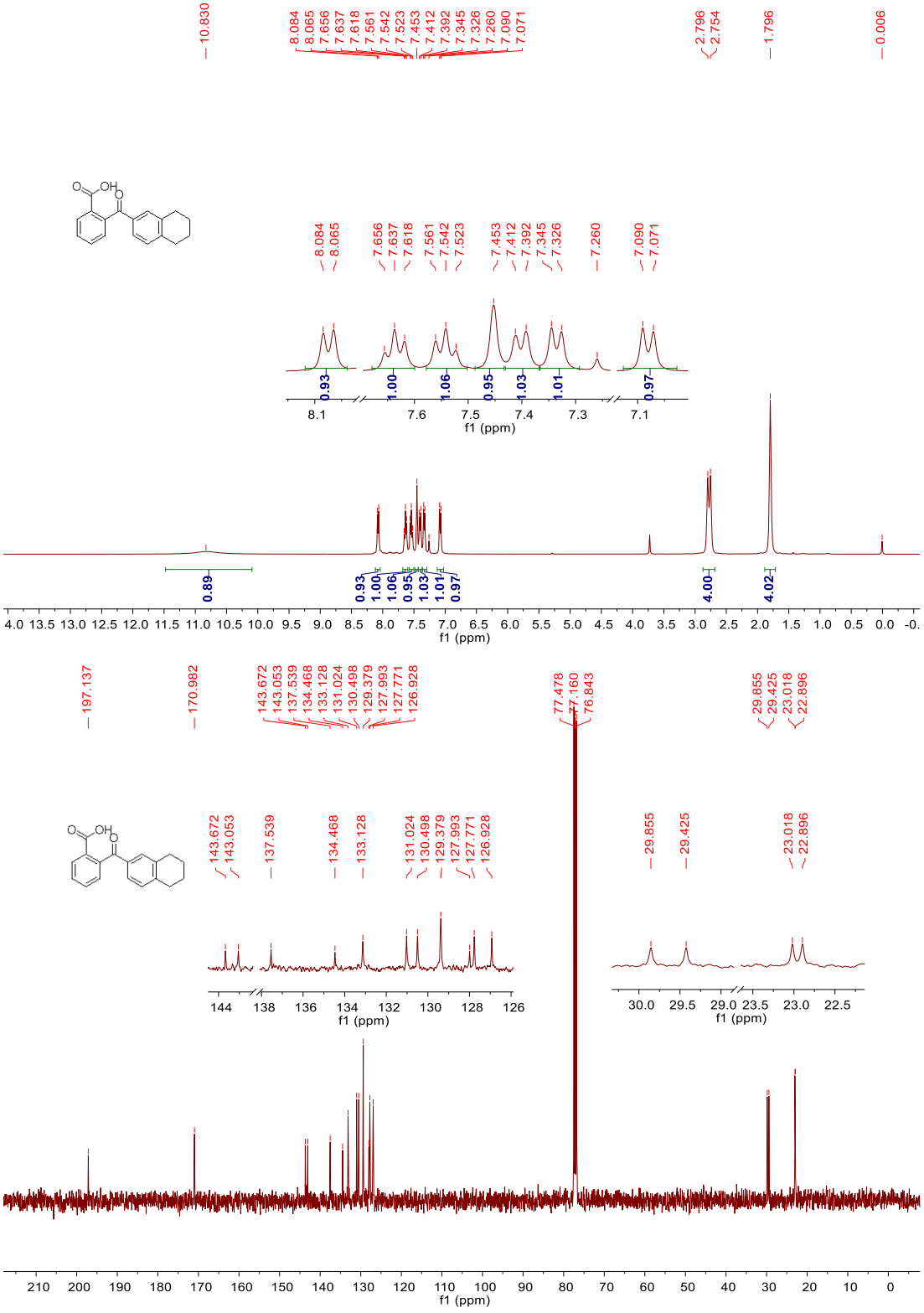
The HRMS spectrum of 2-(2-methyl-1-naphthoyl)benzoic acid (1o).



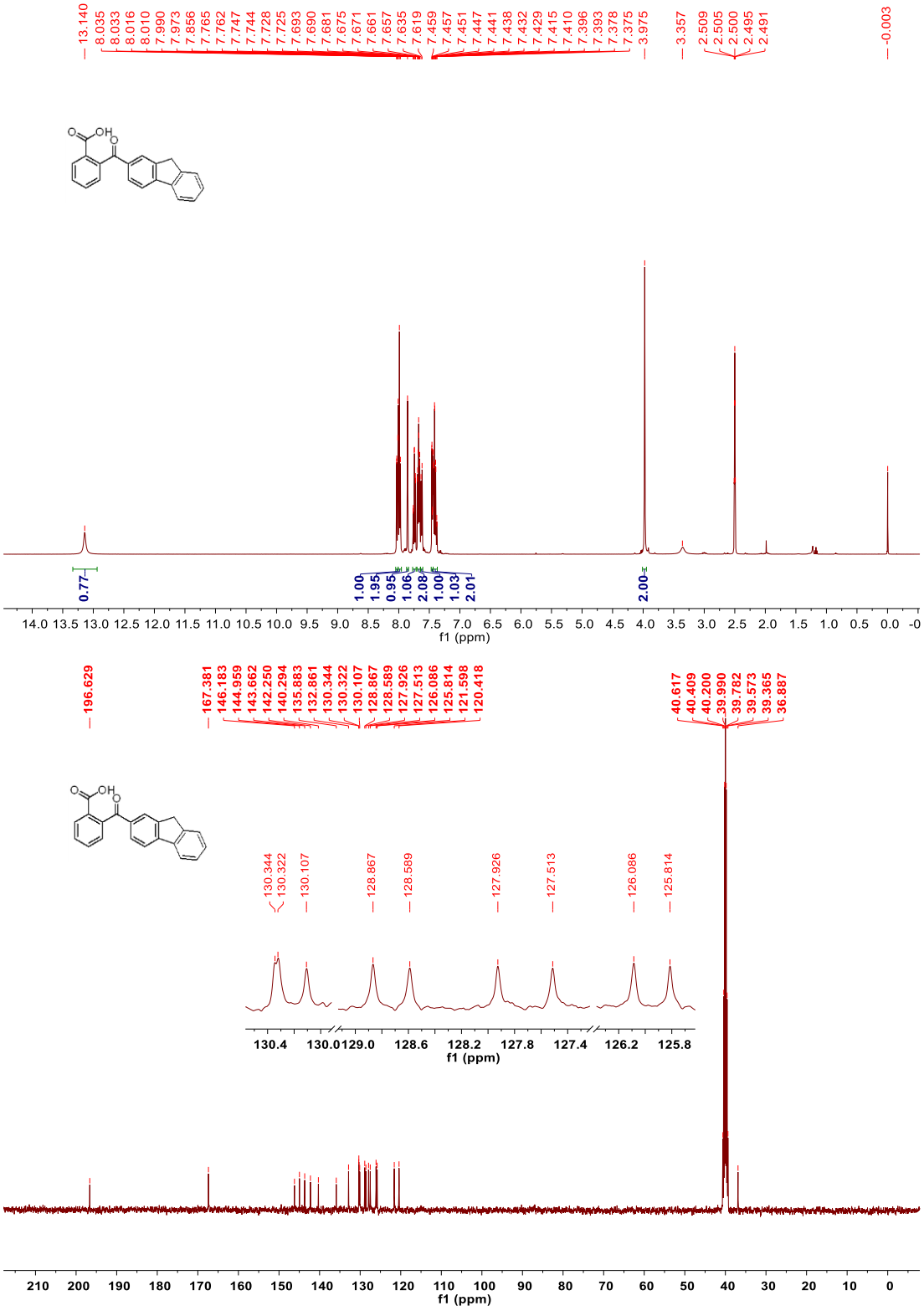
The ^{1}H and ^{13}C NMR spectrum of 2-(4-chloro-1-naphthoyl)benzoic acid (1q).



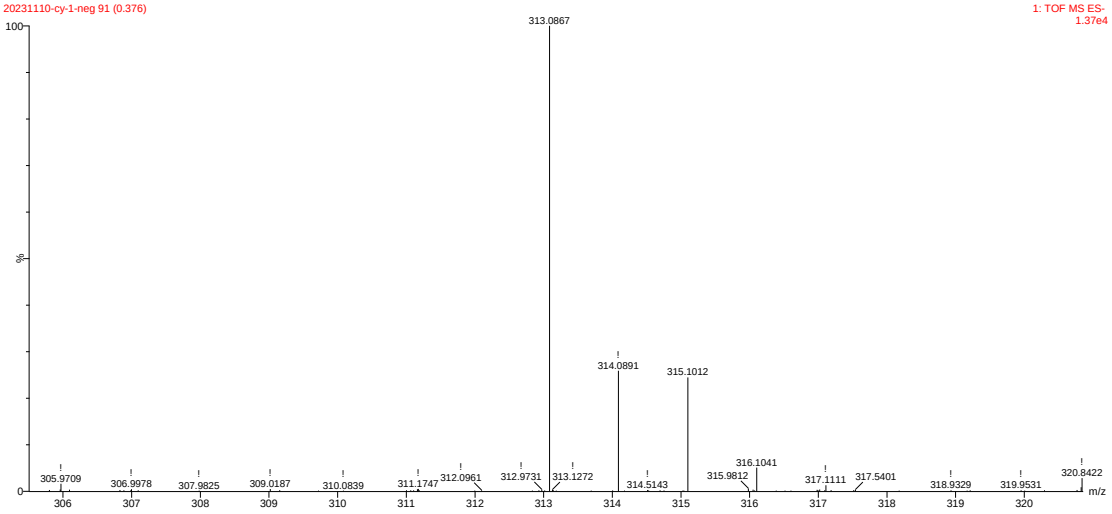
The ^{1}H and ^{13}C NMR spectrum of 2-(5,6,7,8-tetrahydronaphthalene-2-carbonyl)benzoic acid (1r).



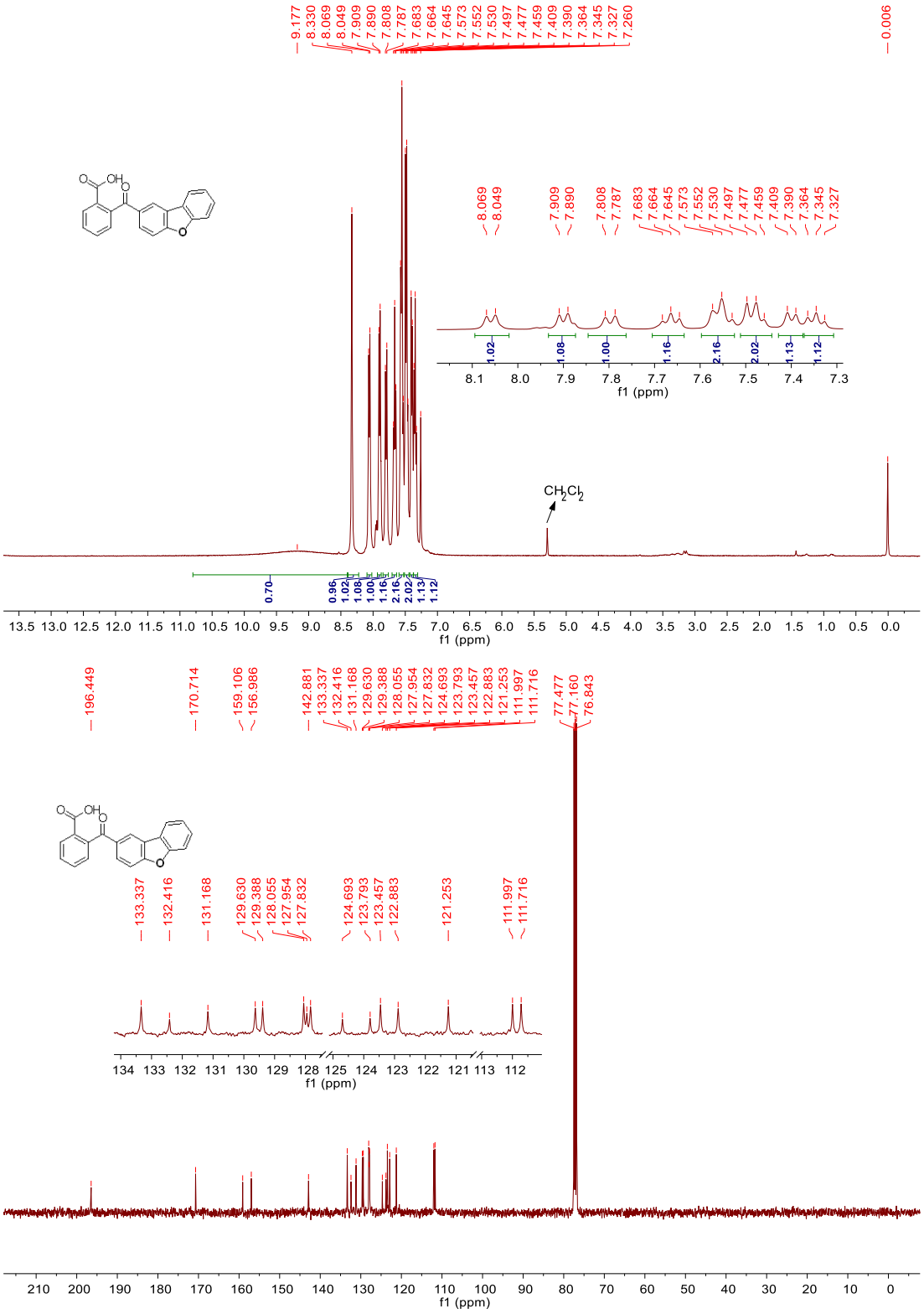
The ^{1}H and ^{13}C NMR spectrum of 2-(9H-fluorene-2-carbonyl)benzoic acid (1s).



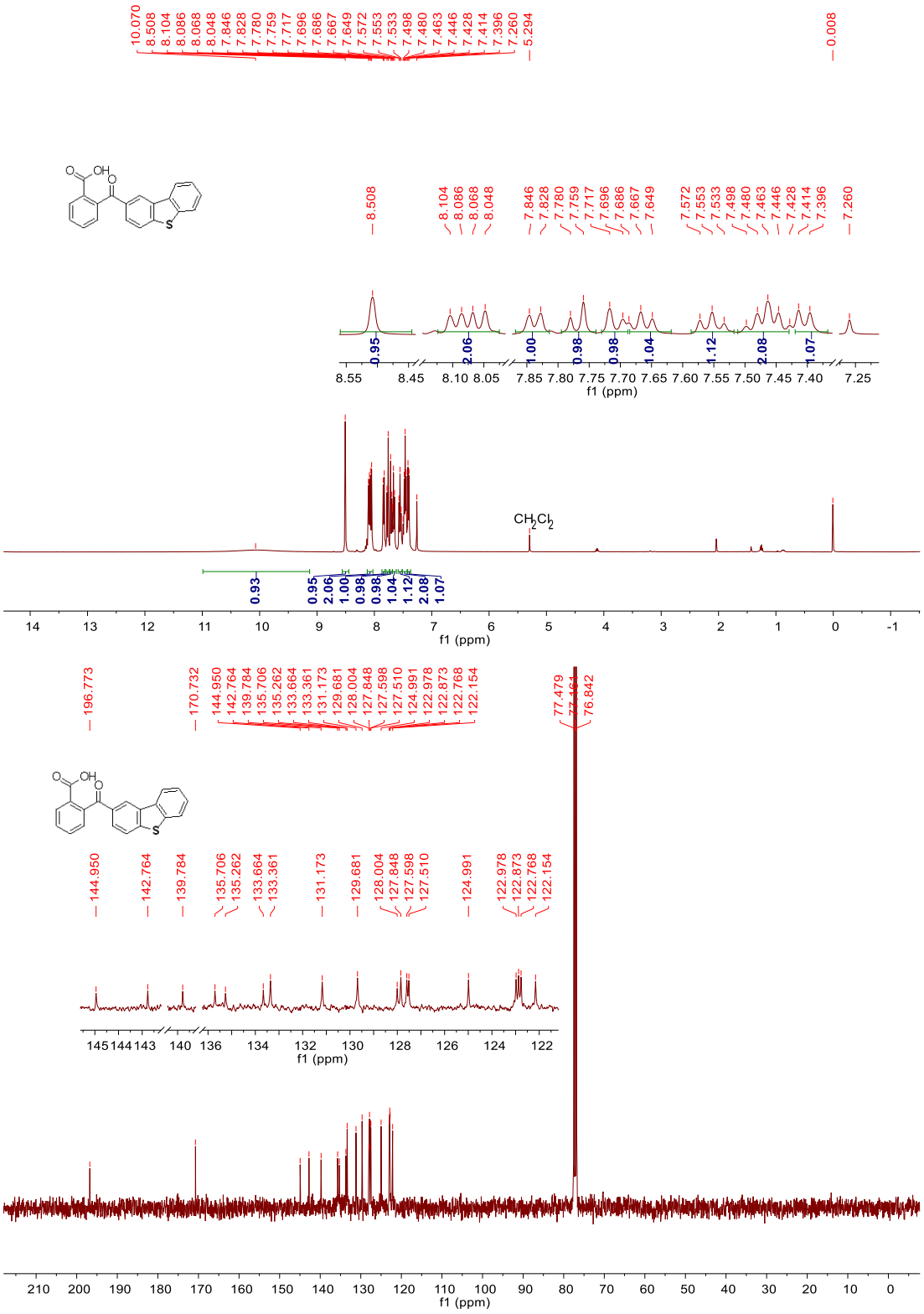
The HRMS spectrum of 2-(9H-fluorene-2-carbonyl)benzoic acid (1s).



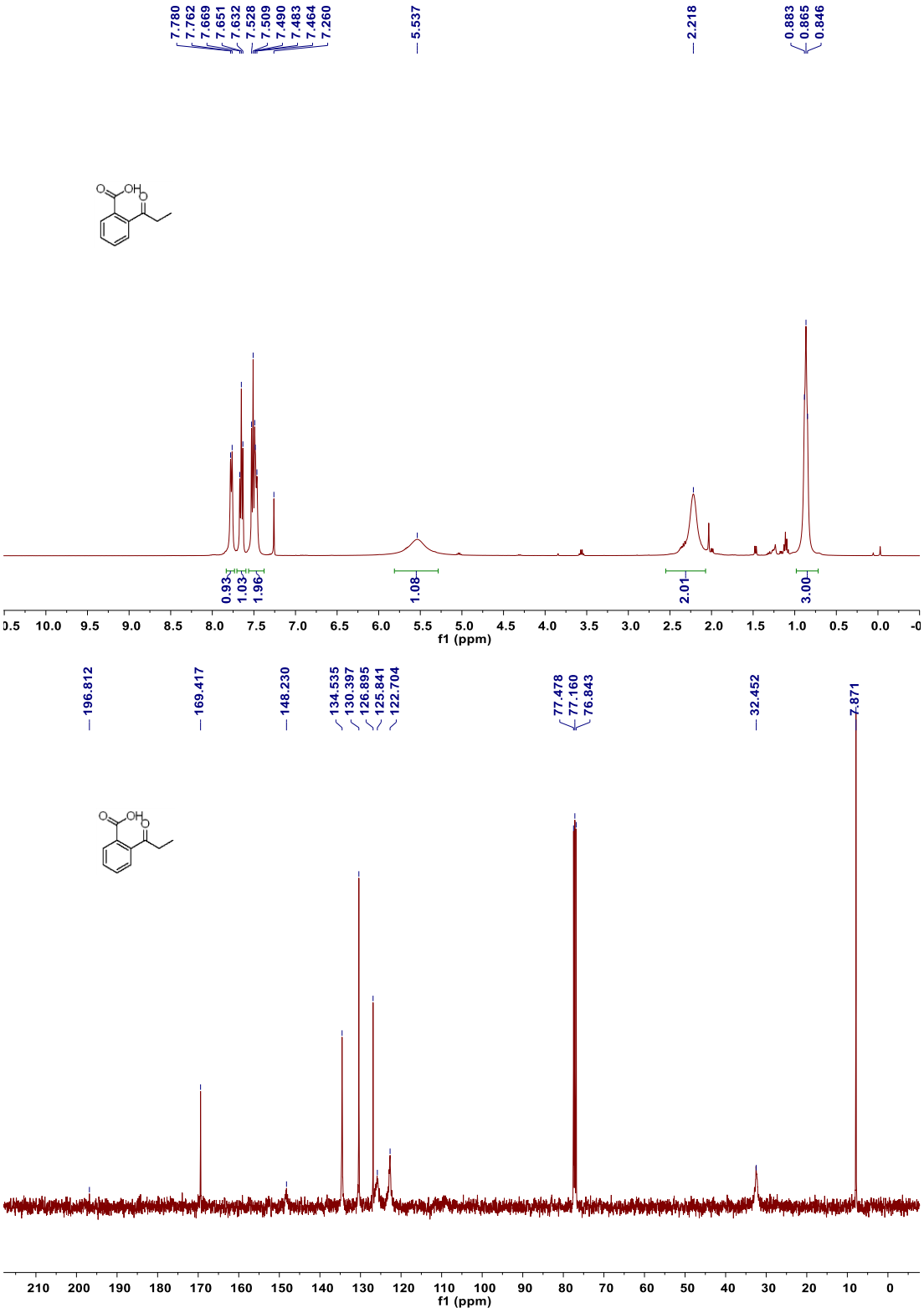
The ^{1}H and ^{13}C NMR spectrum of 2-(dibenzo[*b*,*d*]furan-2-carbonyl)benzoic acid (1t).



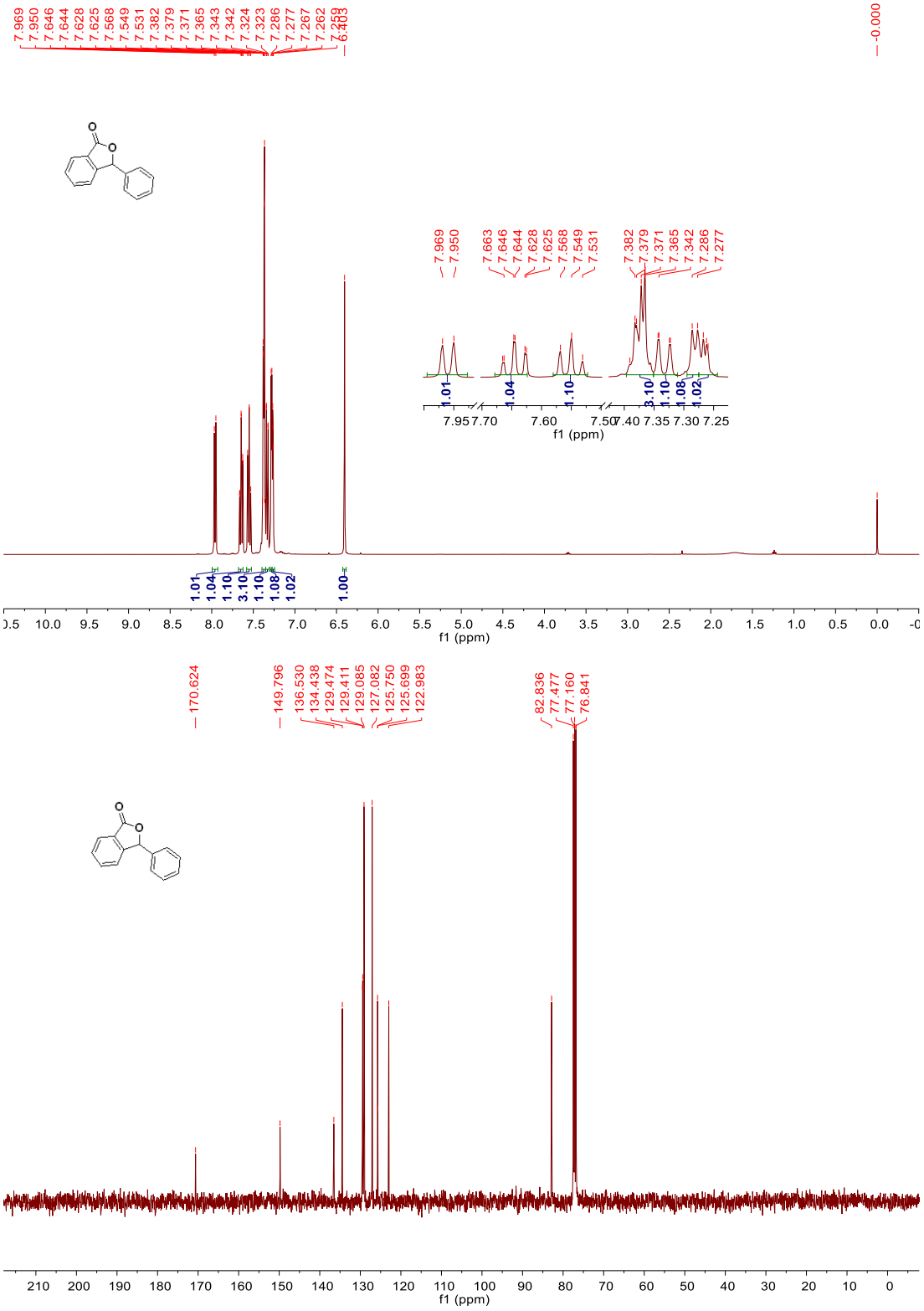
The ^{1}H and ^{13}C NMR spectrum of 2-(dibenzo[*b*,*d*]thiophene-2-carbonyl)benzoic acid (1u).



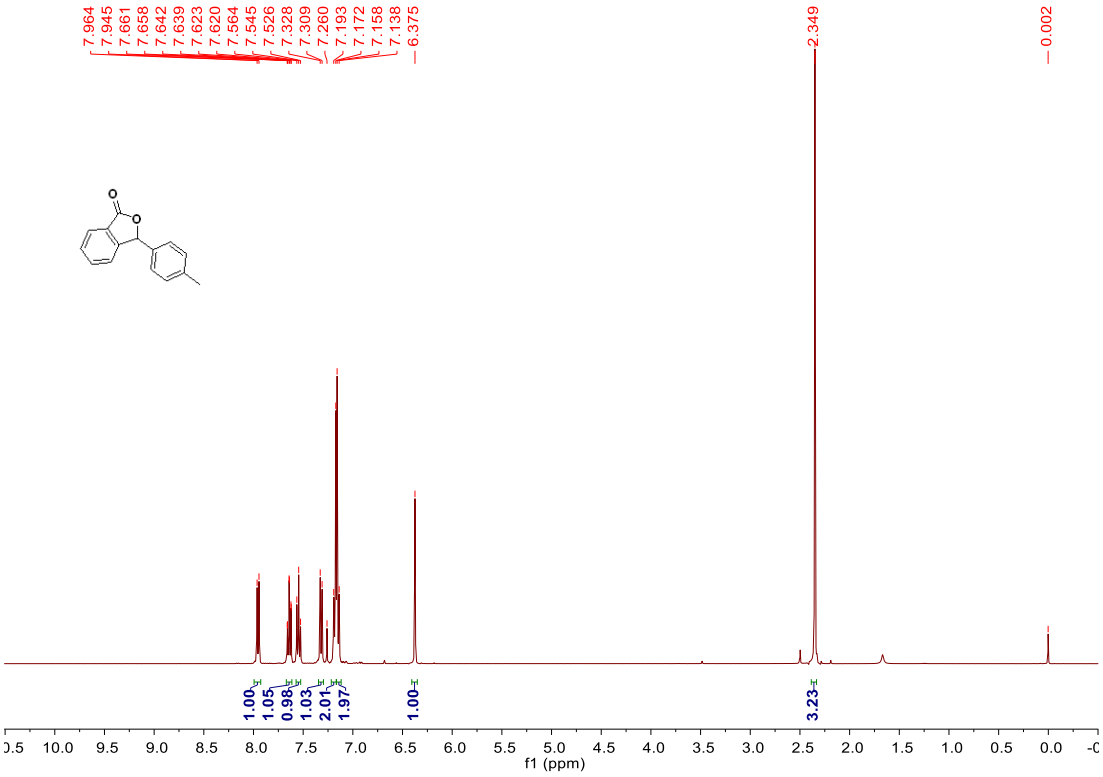
The ^{1}H and ^{13}C NMR spectrum of 2-propionylbenzoic acid (1y).

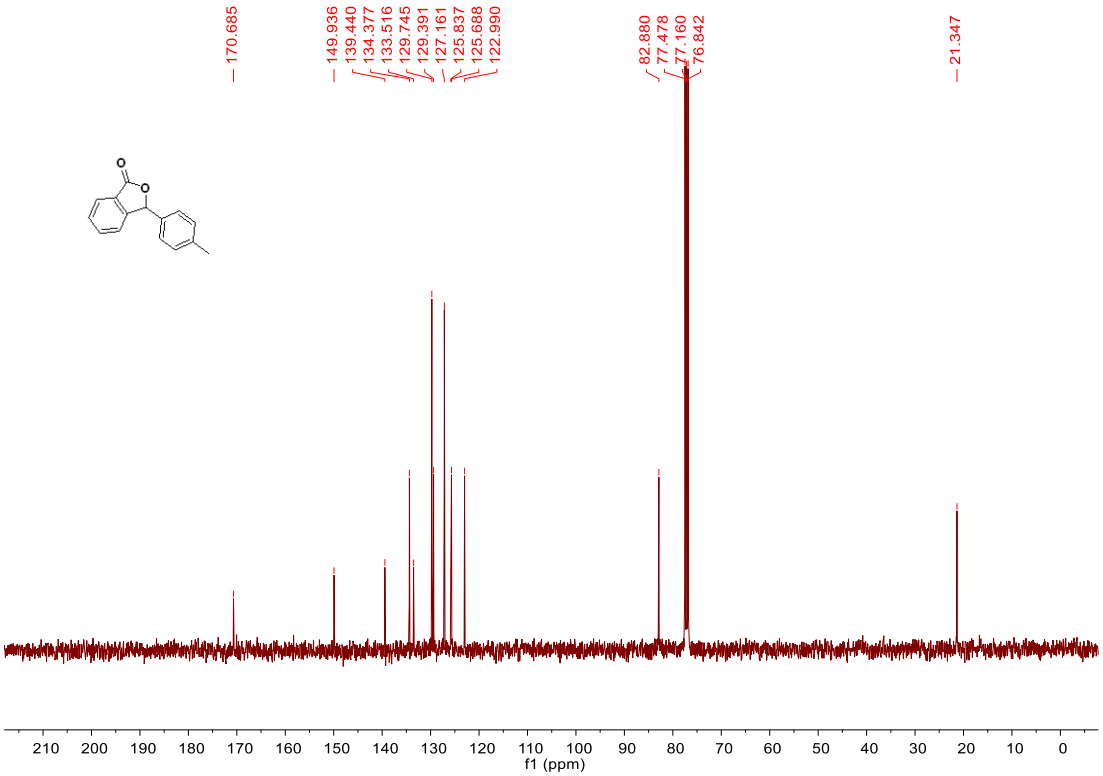


The ^{1}H and ^{13}C NMR spectrum of 3-phenylisobenzofuran-1(3*H*)-one (2a).

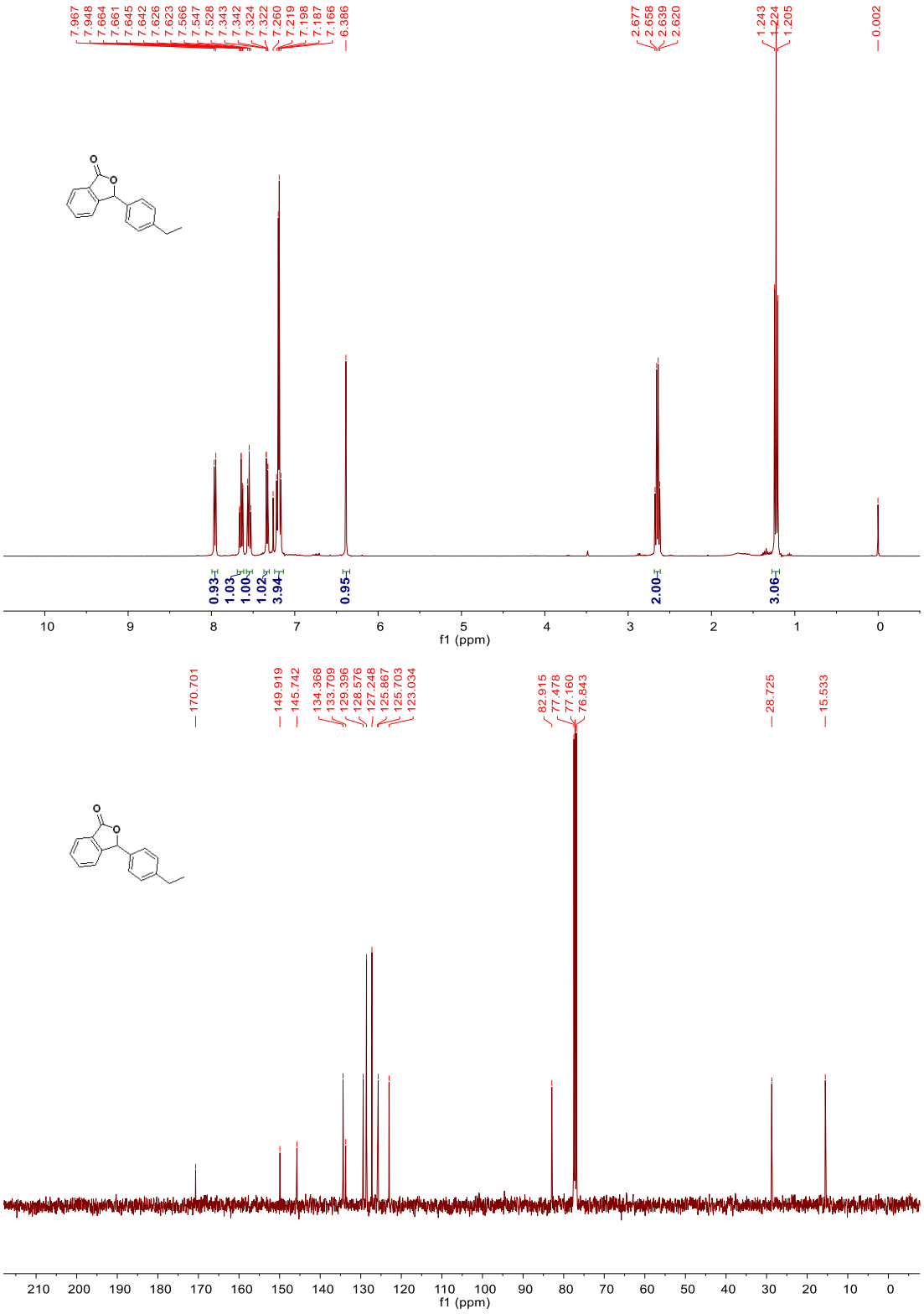


The ^{1}H and ^{13}C NMR spectrum of 3-(p-tolyl)isobenzofuran-1(3*H*)-one (2b).

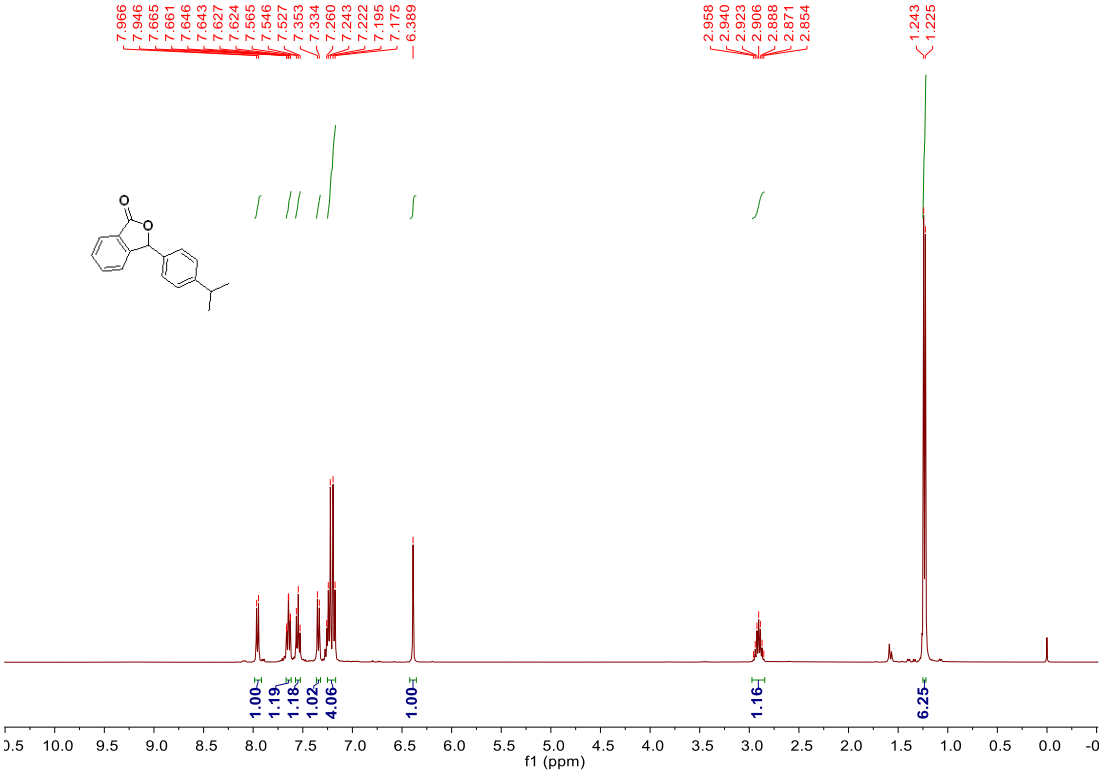


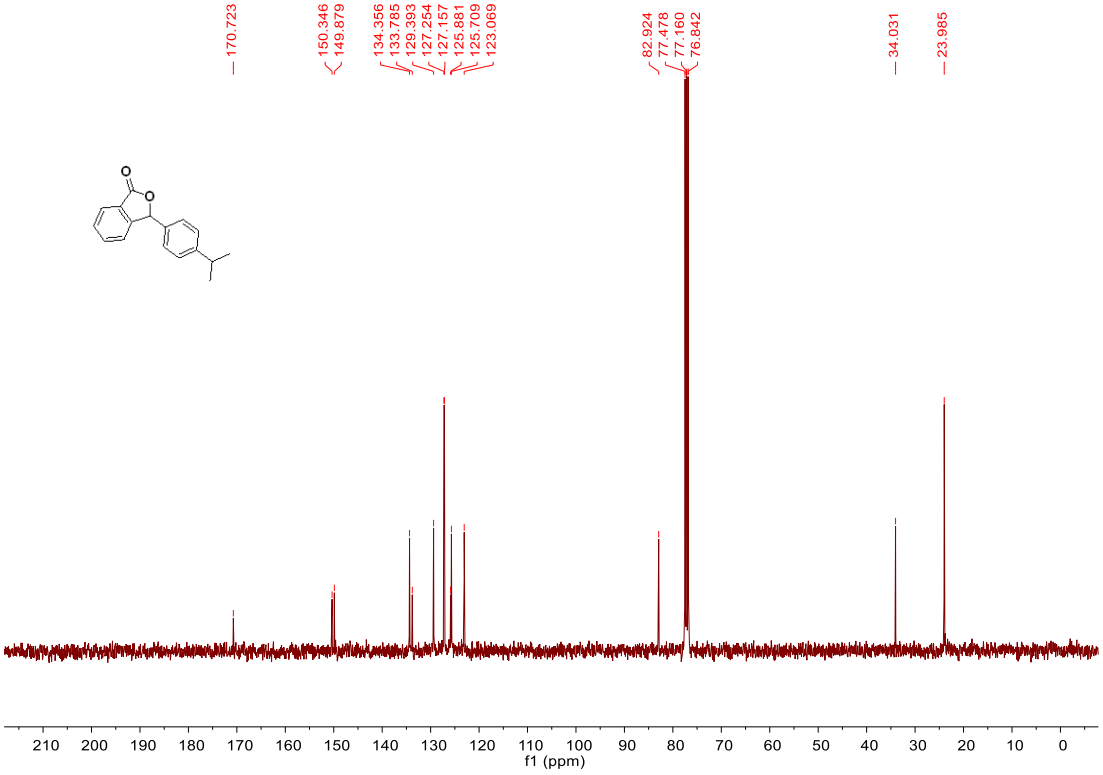


The ^{1}H and ^{13}C NMR spectrum of 3-(4-ethylphenyl)isobenzofuran-1(3*H*)-one (2c).

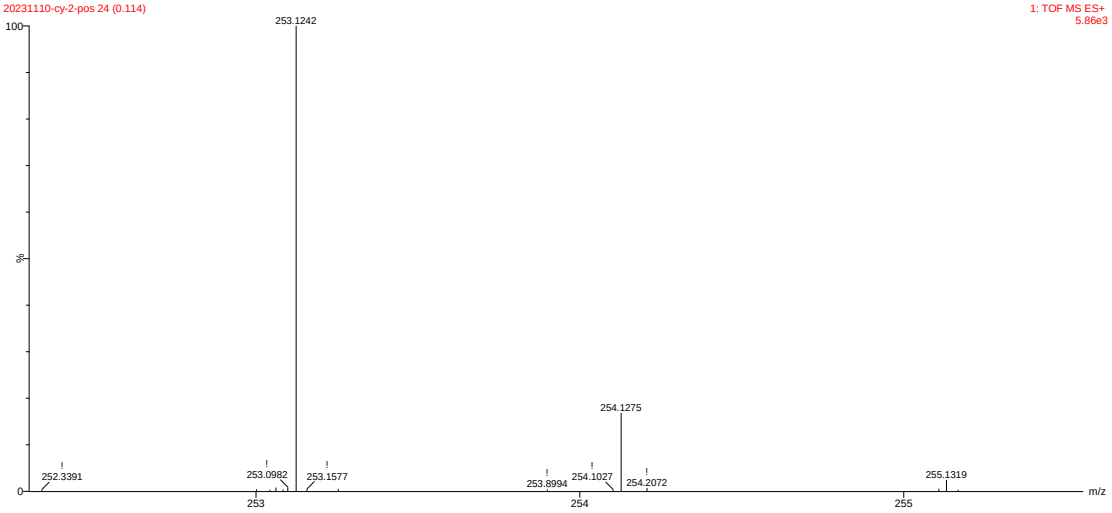


The ^{1}H and ^{13}C NMR spectrum of 3-(4-isopropylphenyl)isobenzofuran-1(3*H*)-one (2d).

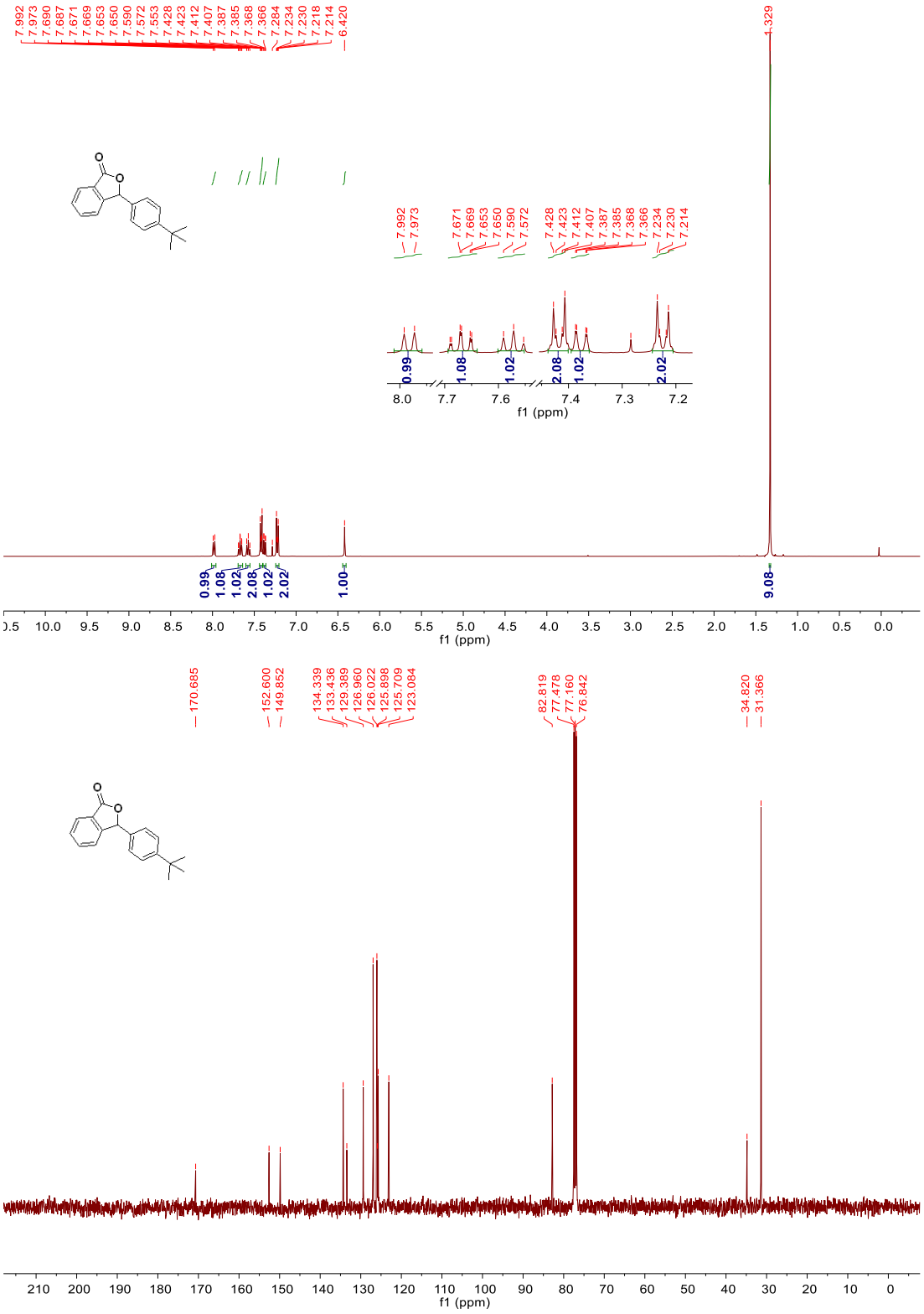




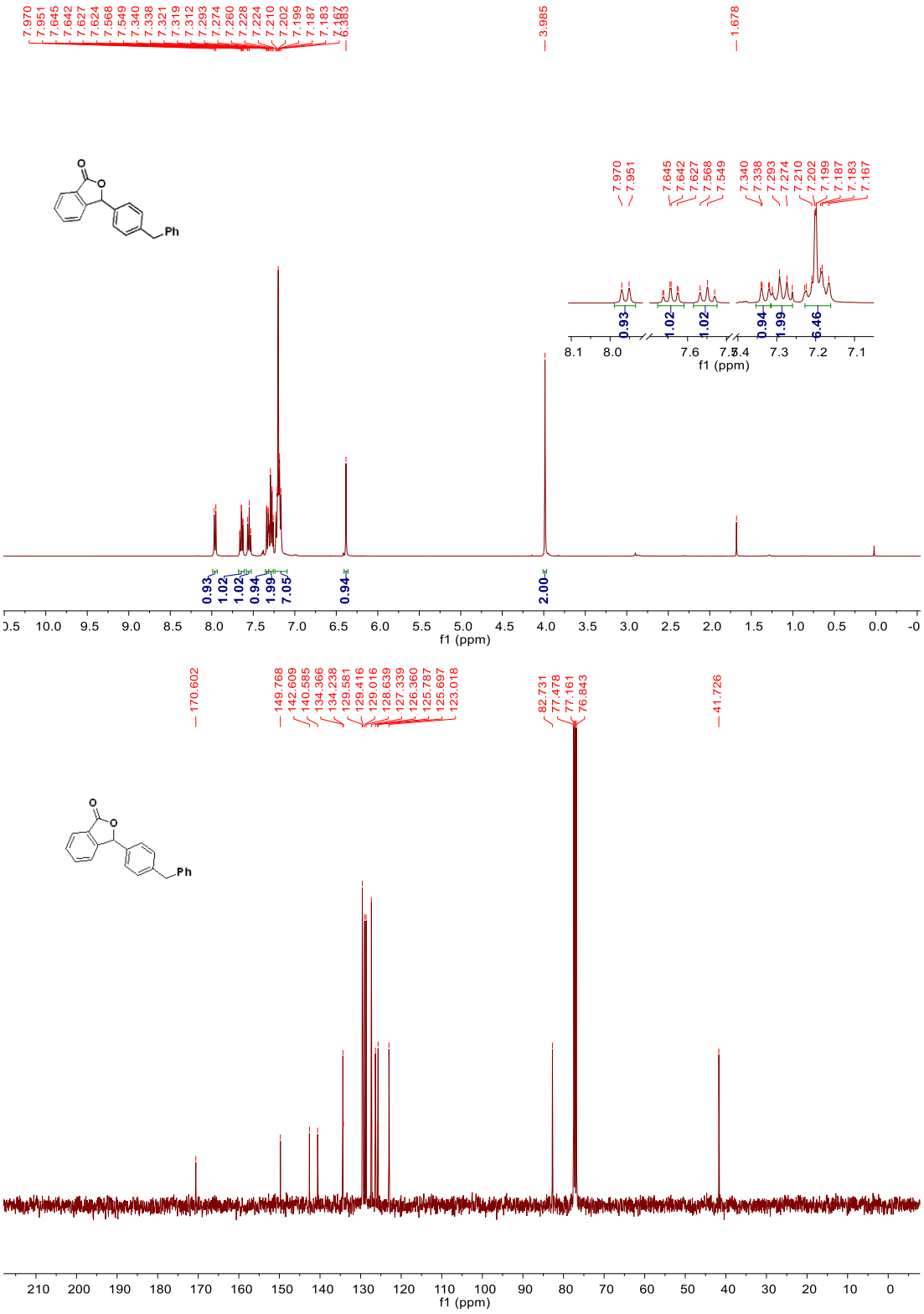
The HRMS spectrum of 3-(4-isopropylphenyl)isobenzofuran-1(3*H*)-one (2d).



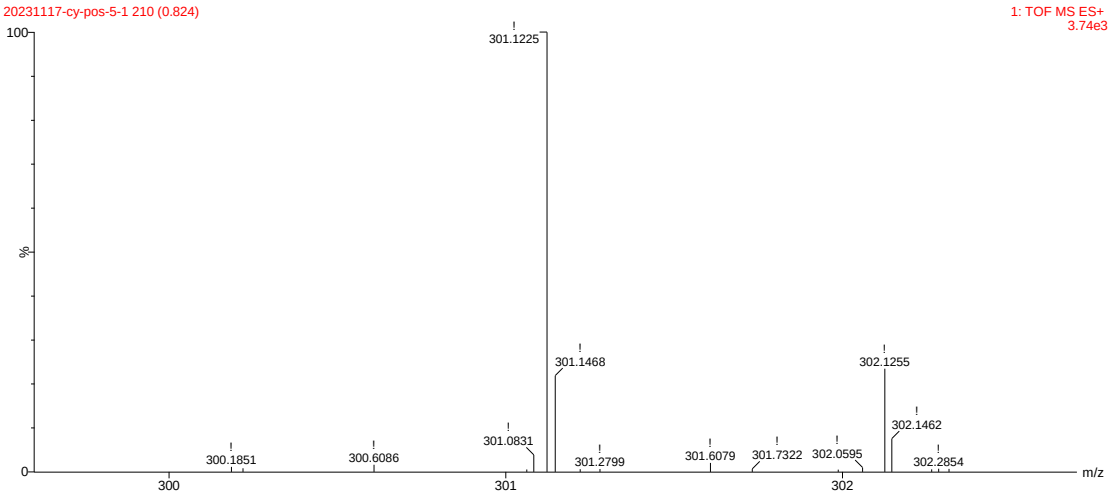
The ^{1}H and ^{13}C NMR spectrum of 3-(4-(tert-butyl)phenyl)isobenzofuran-1(3*H*)-one (2e).



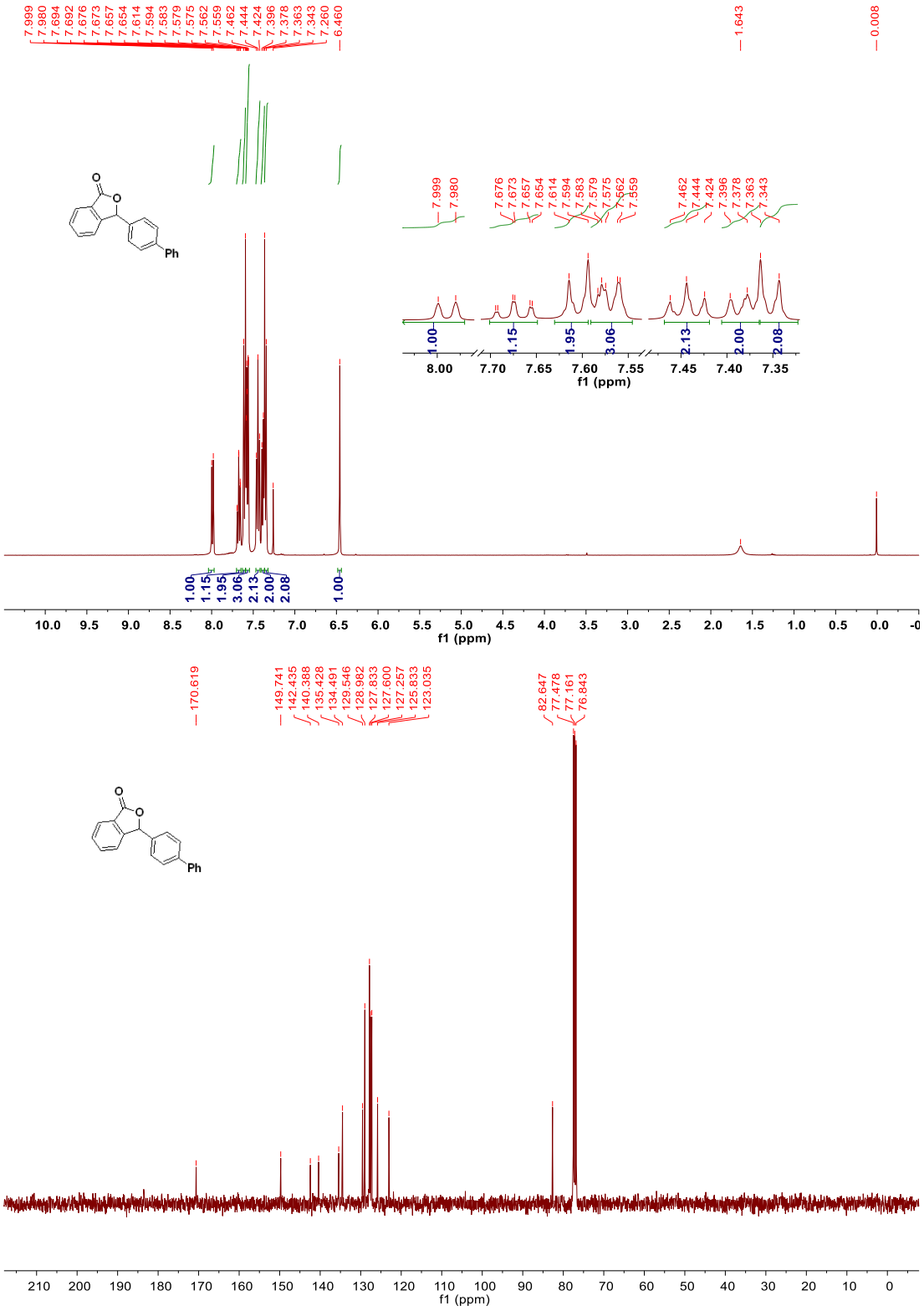
The ^{1}H and ^{13}C NMR spectrum of 3-(4-benzylphenyl)isobenzofuran-1(3*H*)-one (2f).



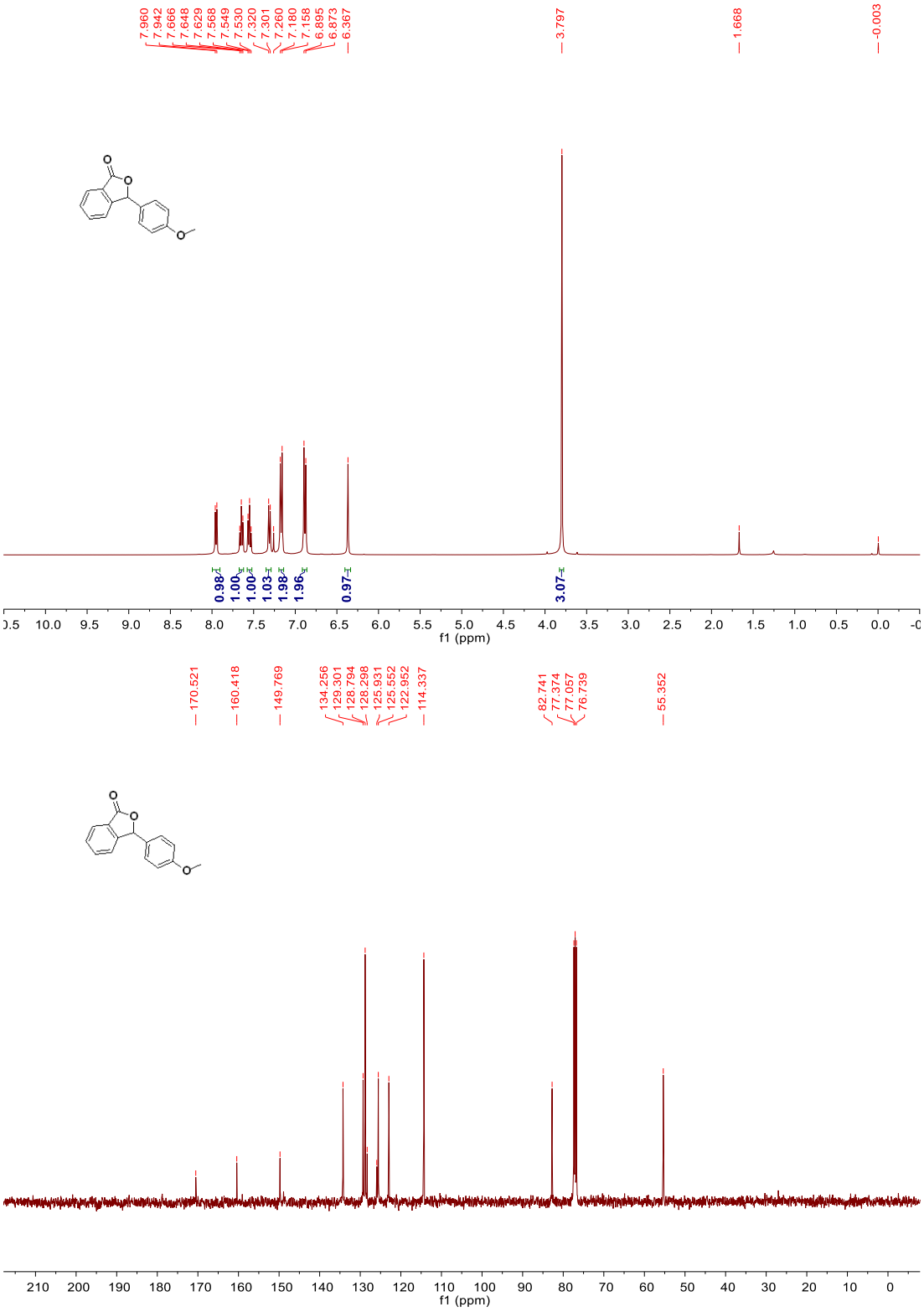
The HRMS spectrum of 3-(4-benzylphenyl)isobenzofuran-1(3*H*)-one (2f).



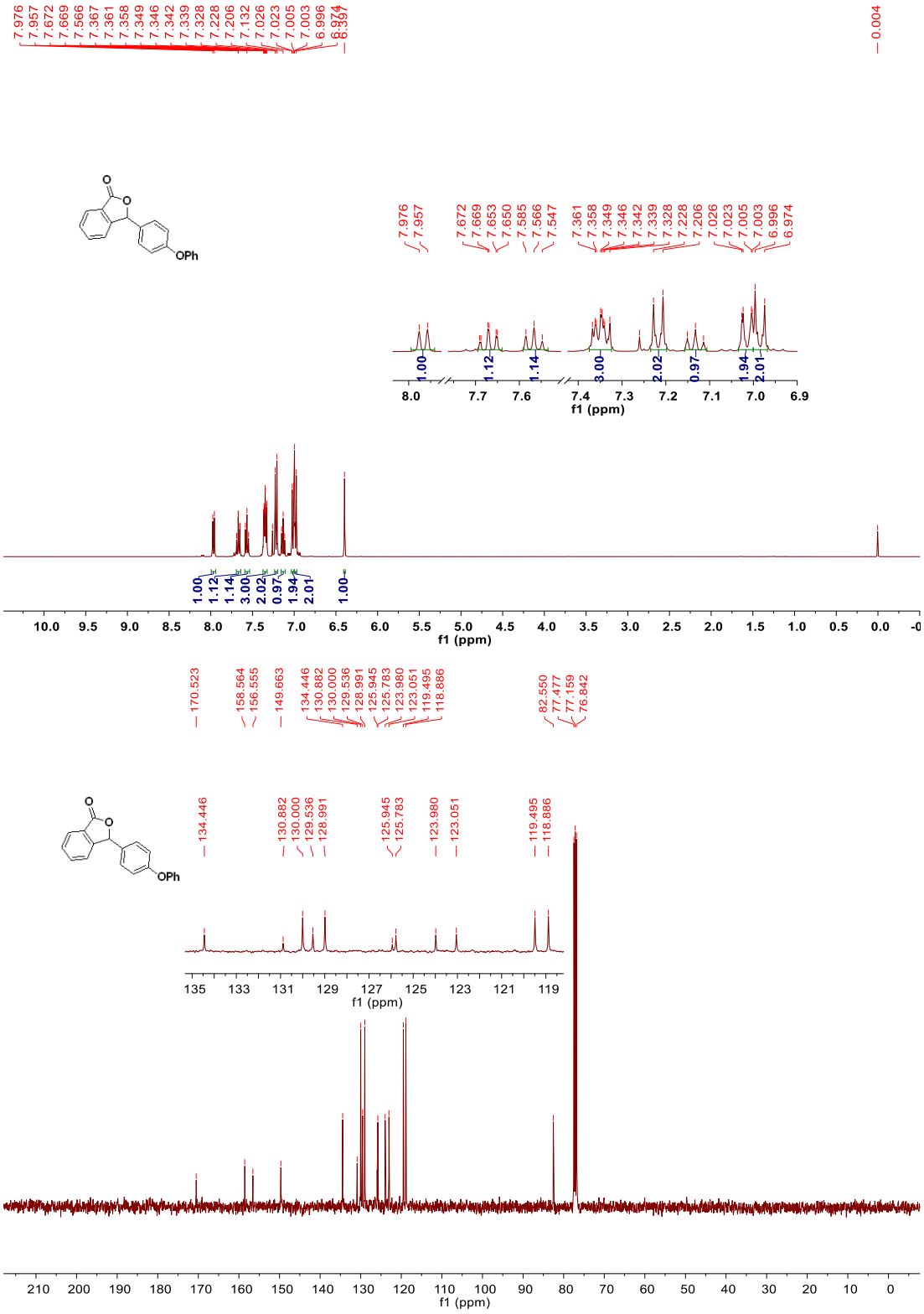
The ^{1}H and ^{13}C NMR spectrum of 3-([1,1'-biphenyl]-4-yl)isobenzofuran-1(3*H*)-one (2g).



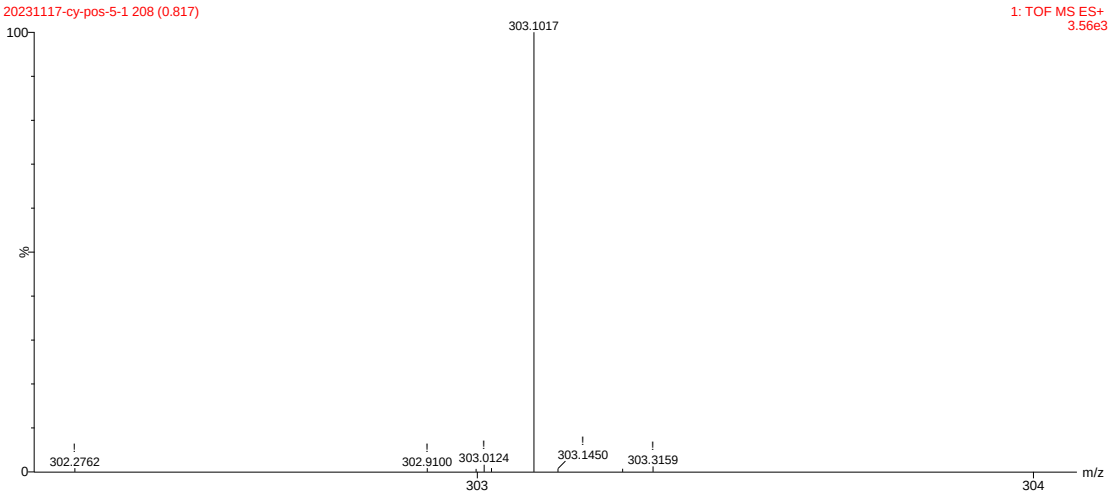
The ^{1}H and ^{13}C NMR spectrum of 3-(4-methoxyphenyl)isobenzofuran-1(3*H*)-one (2h).



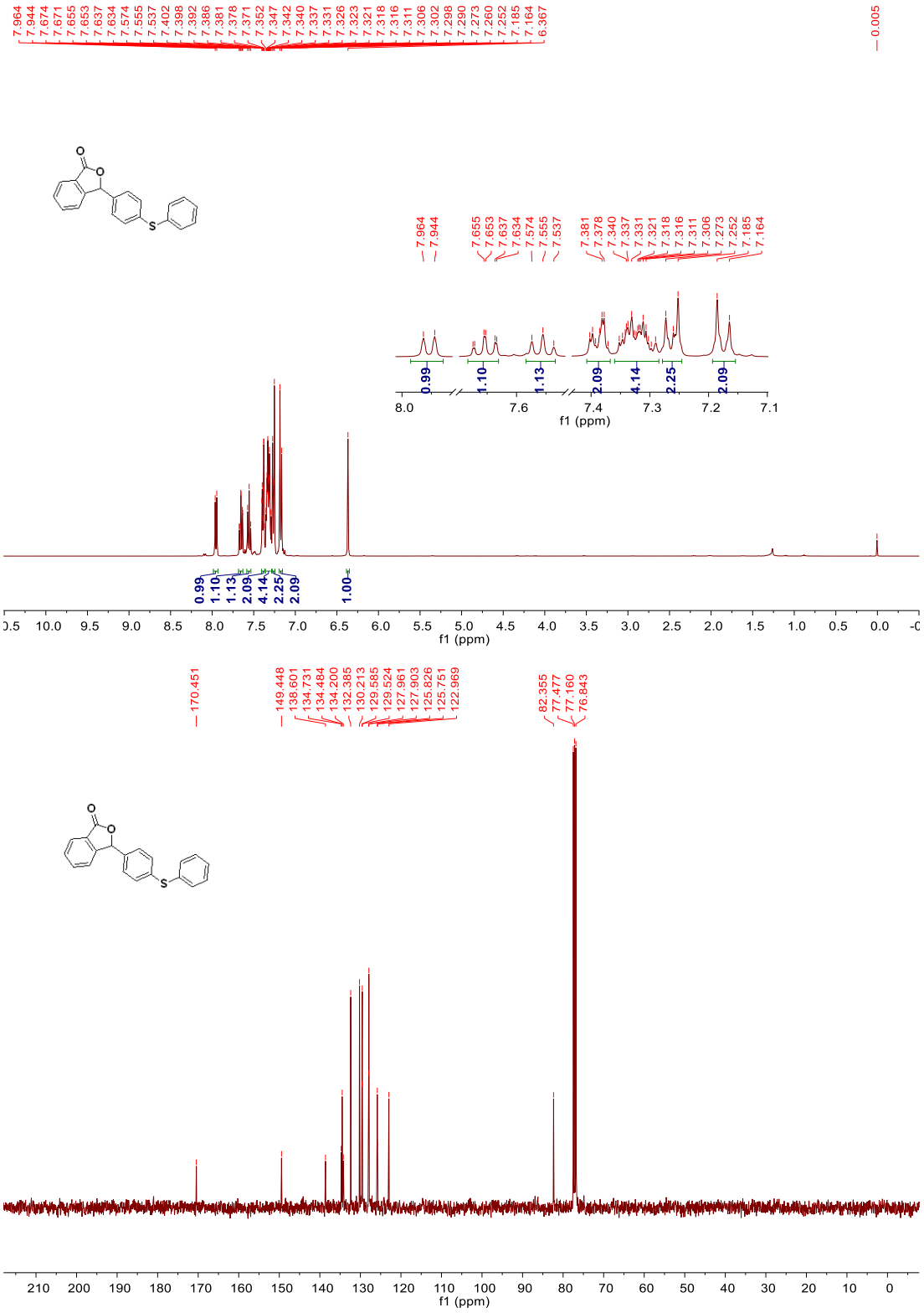
The ^{1}H and ^{13}C NMR spectrum of 3-(4-phenoxyphenyl)isobenzofuran-1(3*H*)-one (2i).



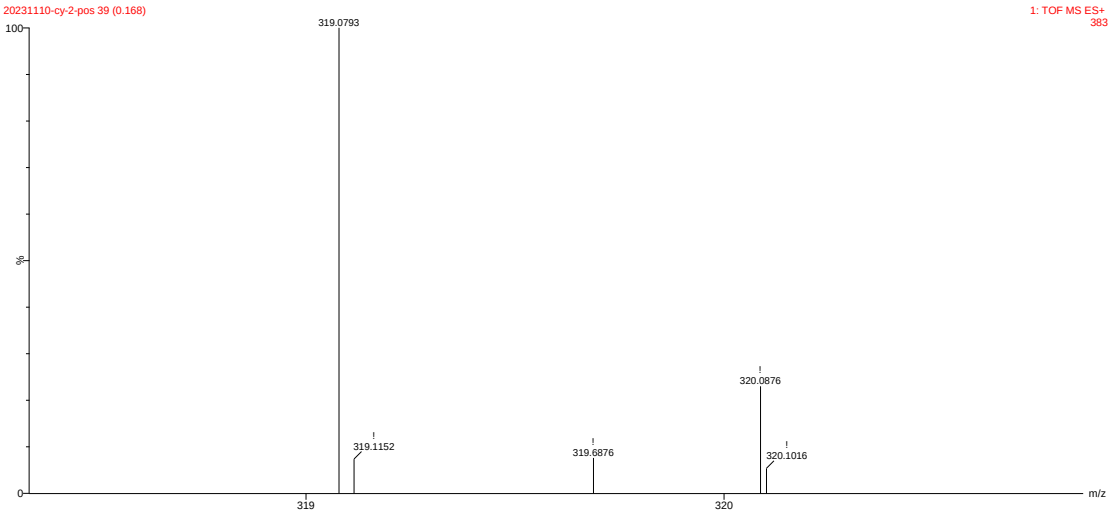
The HRMS spectrum of 3-(4-phenoxyphenyl)isobenzofuran-1(3*H*)-one (2i).



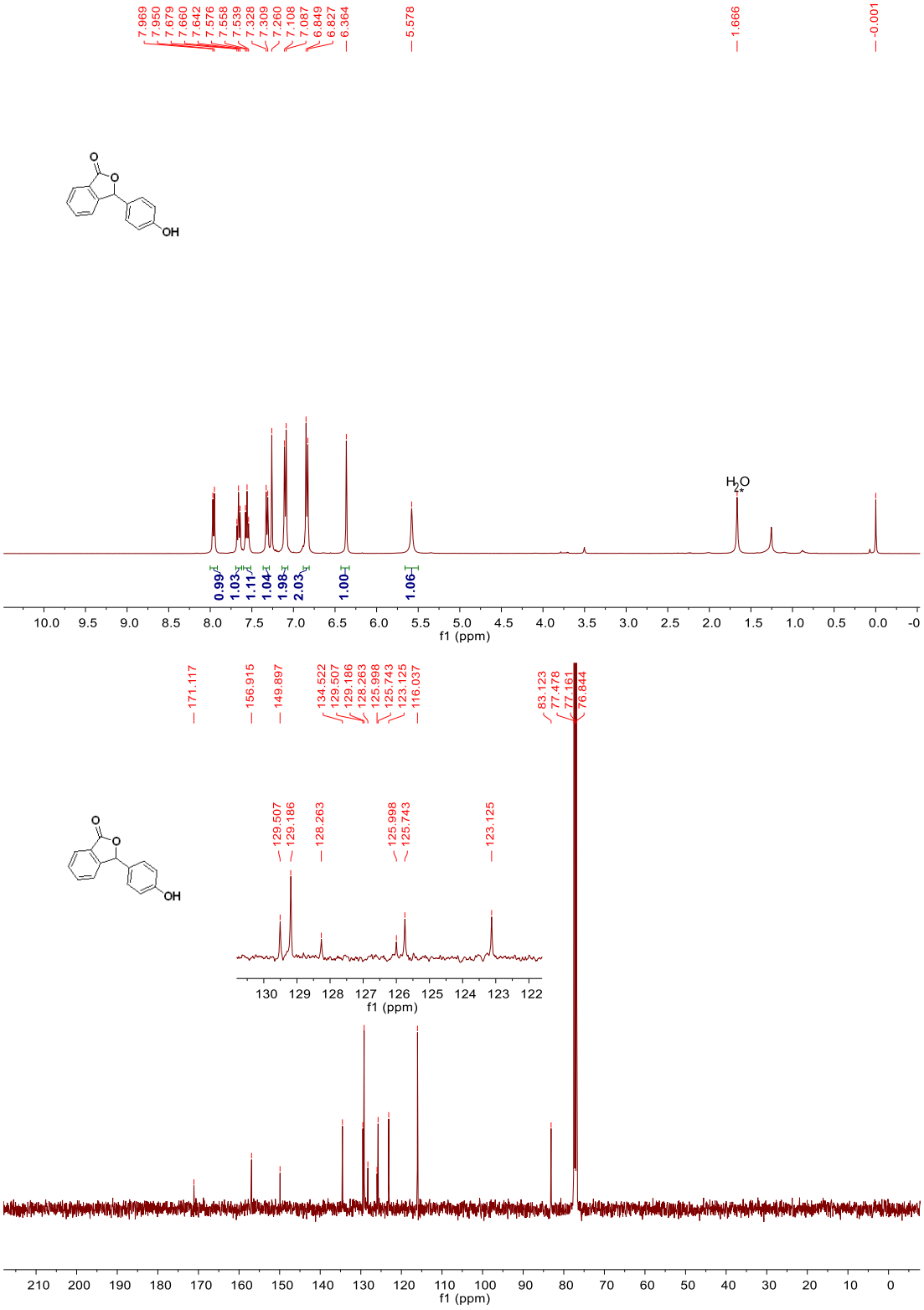
The ^{1}H and ^{13}C NMR spectrum of 3-(4-(phenylthio)phenyl)isobenzofuran-1(3*H*)-one (2j).



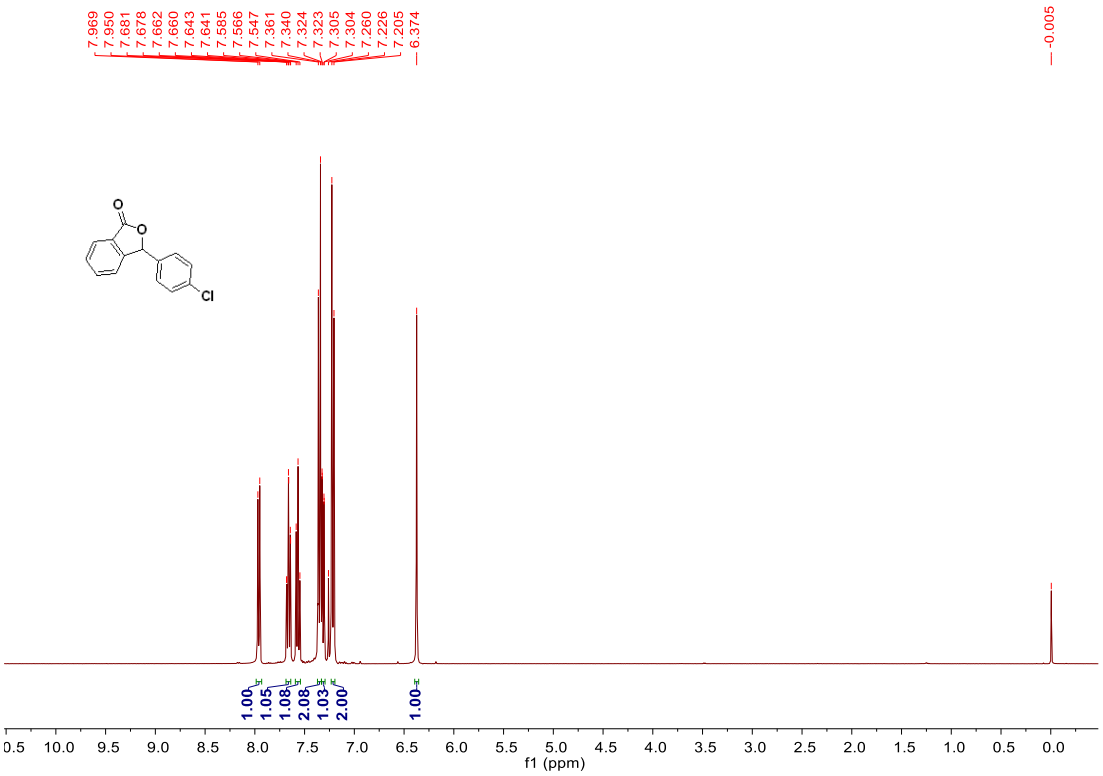
HRMS spectrum of 2j.

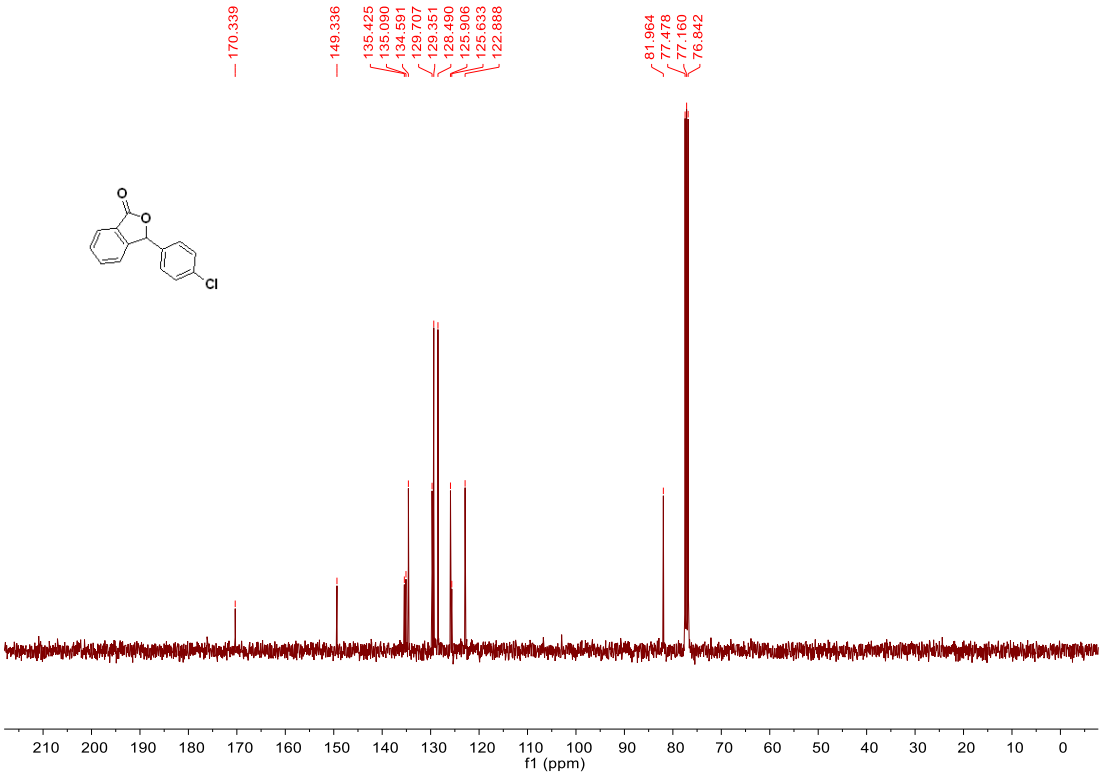


The ^{1}H and ^{13}C NMR spectrum of 3-(4-hydroxyphenyl)isobenzofuran-1(3*H*)-one (2k).

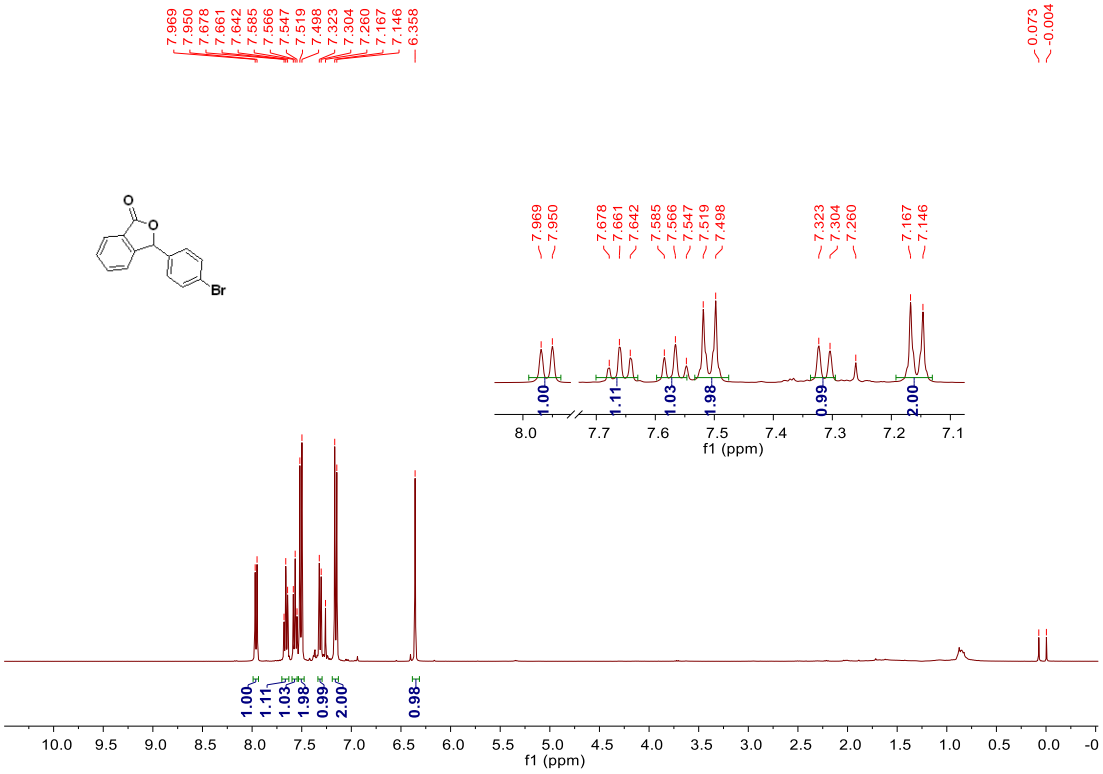


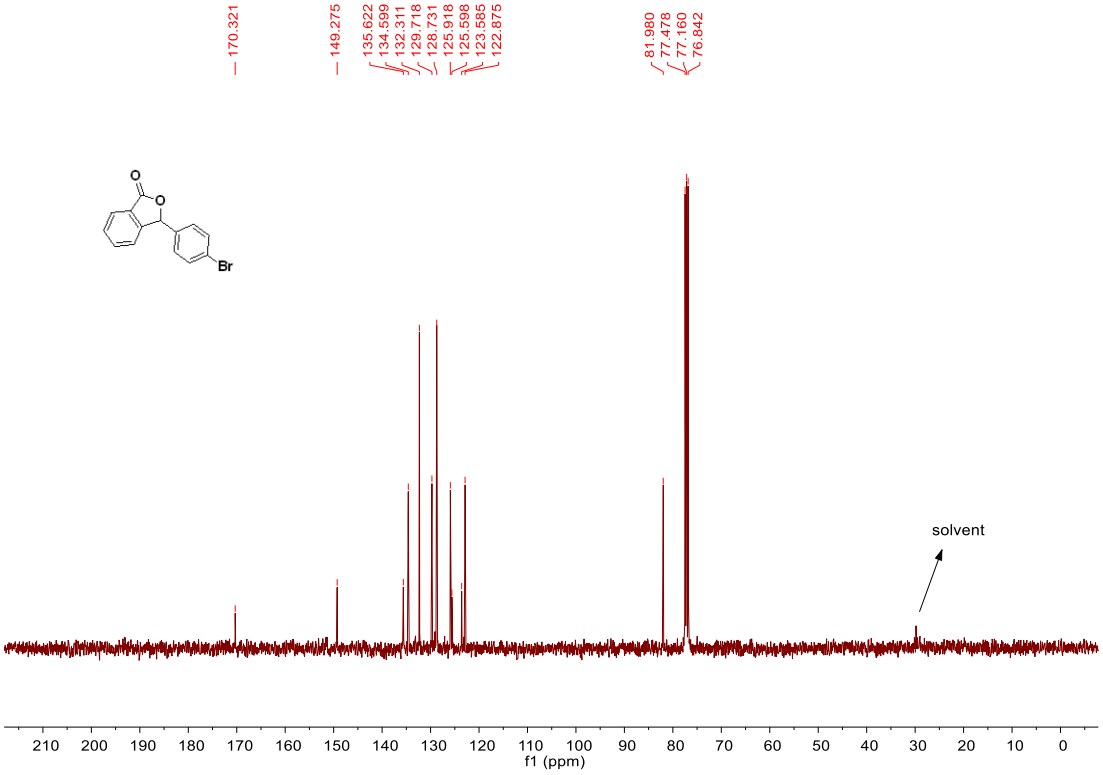
The ^{1}H and ^{13}C NMR spectrum of 3-(4-chlorophenyl)isobenzofuran-1(3*H*)-one (2l).



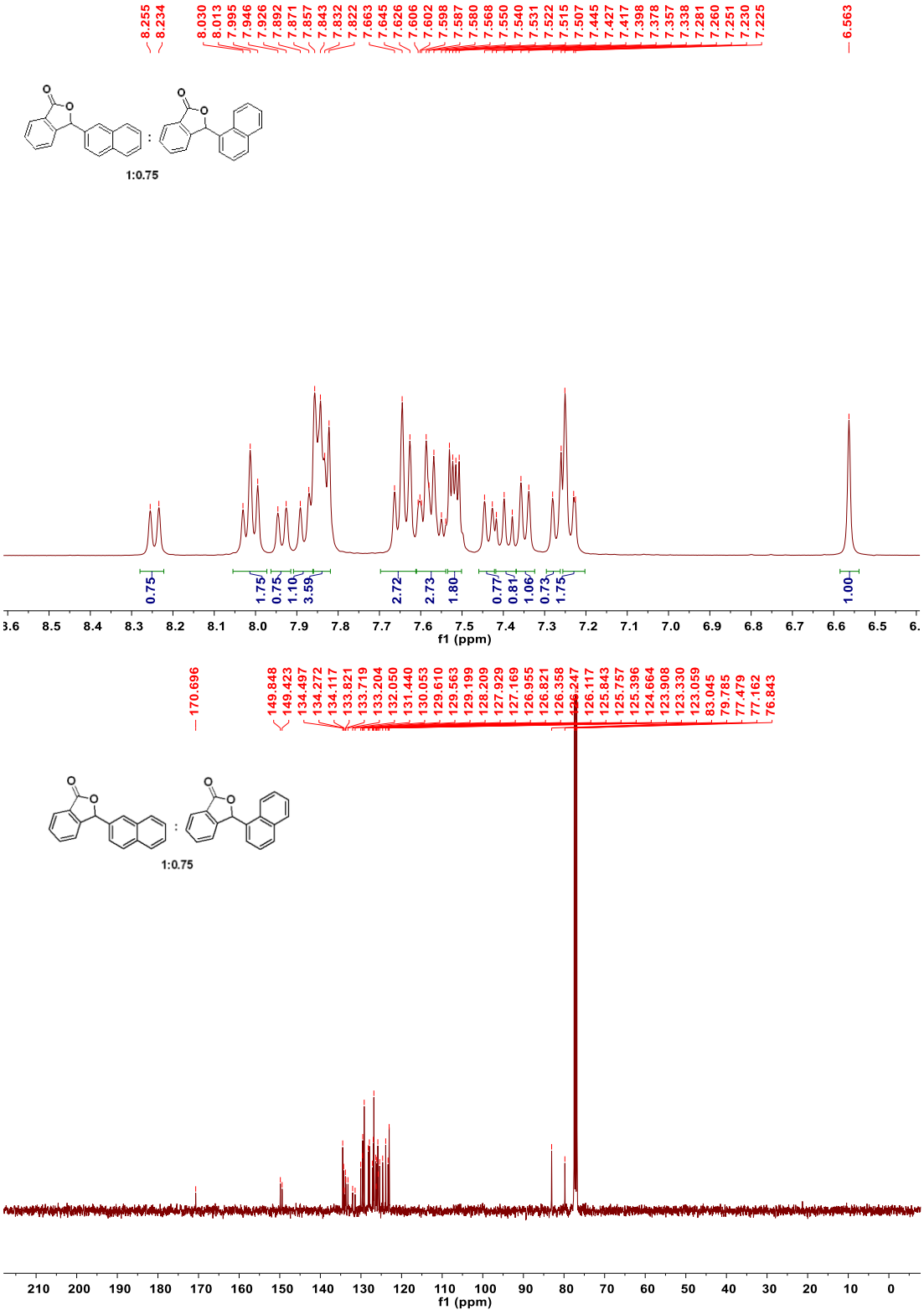


The ^{1}H and ^{13}C NMR spectrum of 3-(4-bromophenyl)isobenzofuran-1(3*H*)-one (2m).

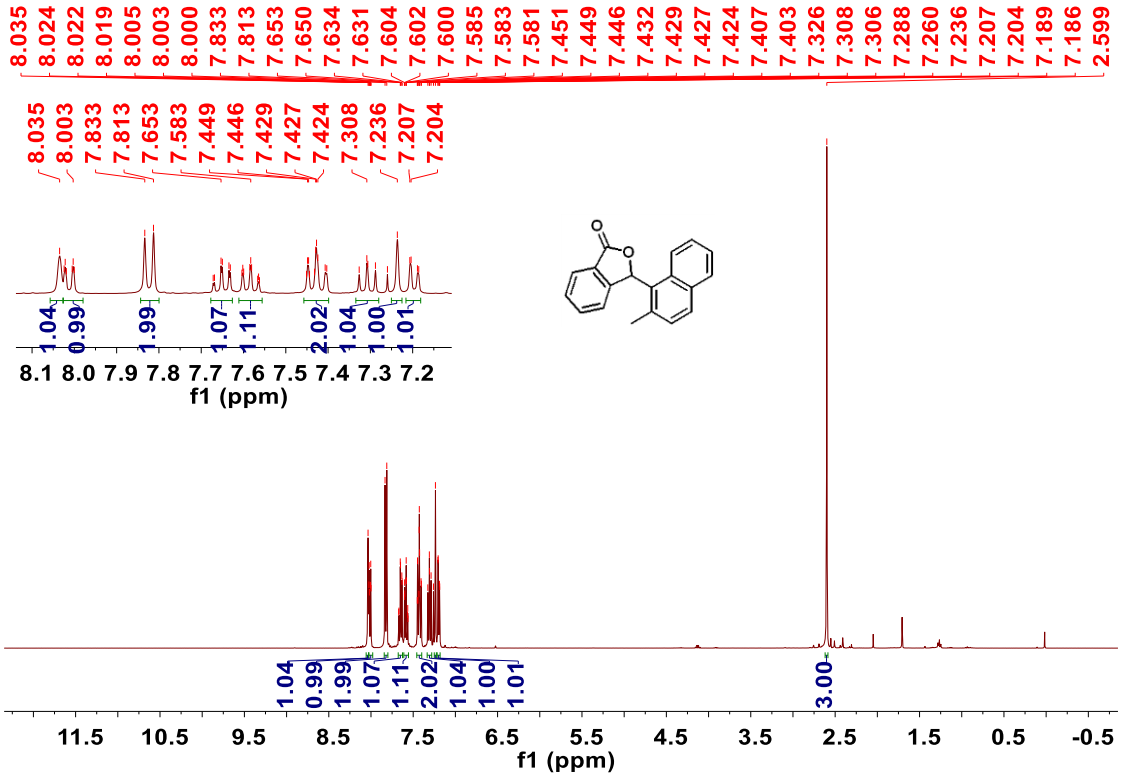


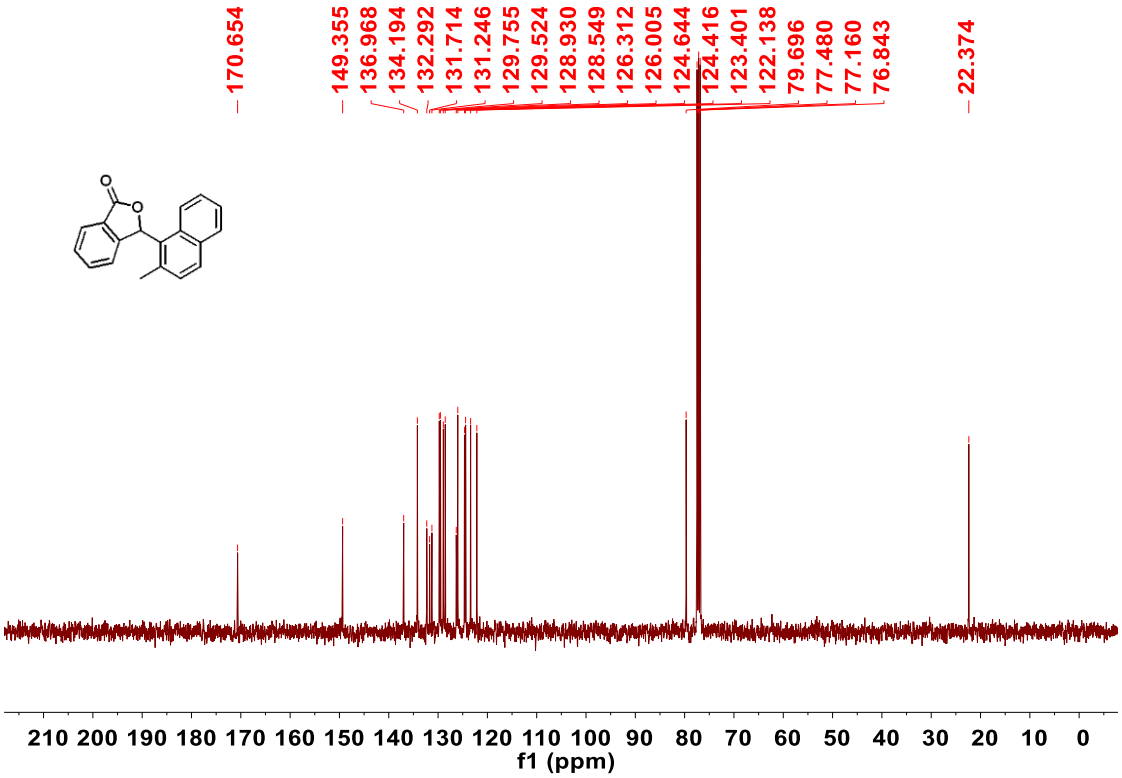


The ^{1}H and ^{13}C NMR spectrum of the mixture of 3-(naphthalen-2-yl)isobenzofuran-1(3H)-one and 3-(naphthalen-1-yl)isobenzofuran-1(3H)-one (2n).

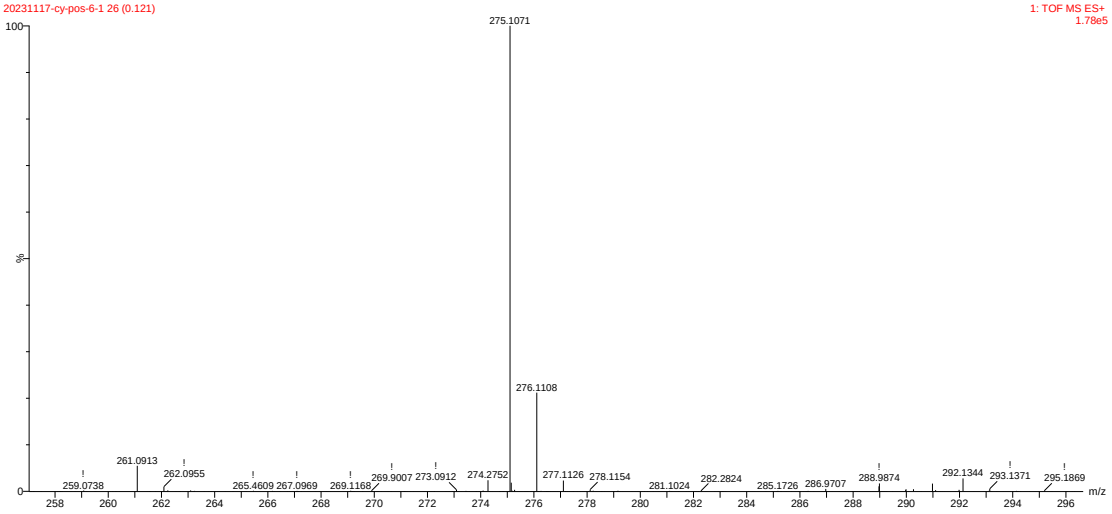


The ^{1}H and ^{13}C NMR spectrum of 3-(2-methylnaphthalen-1-yl)isobenzofuran-1(3H)-one (2o).

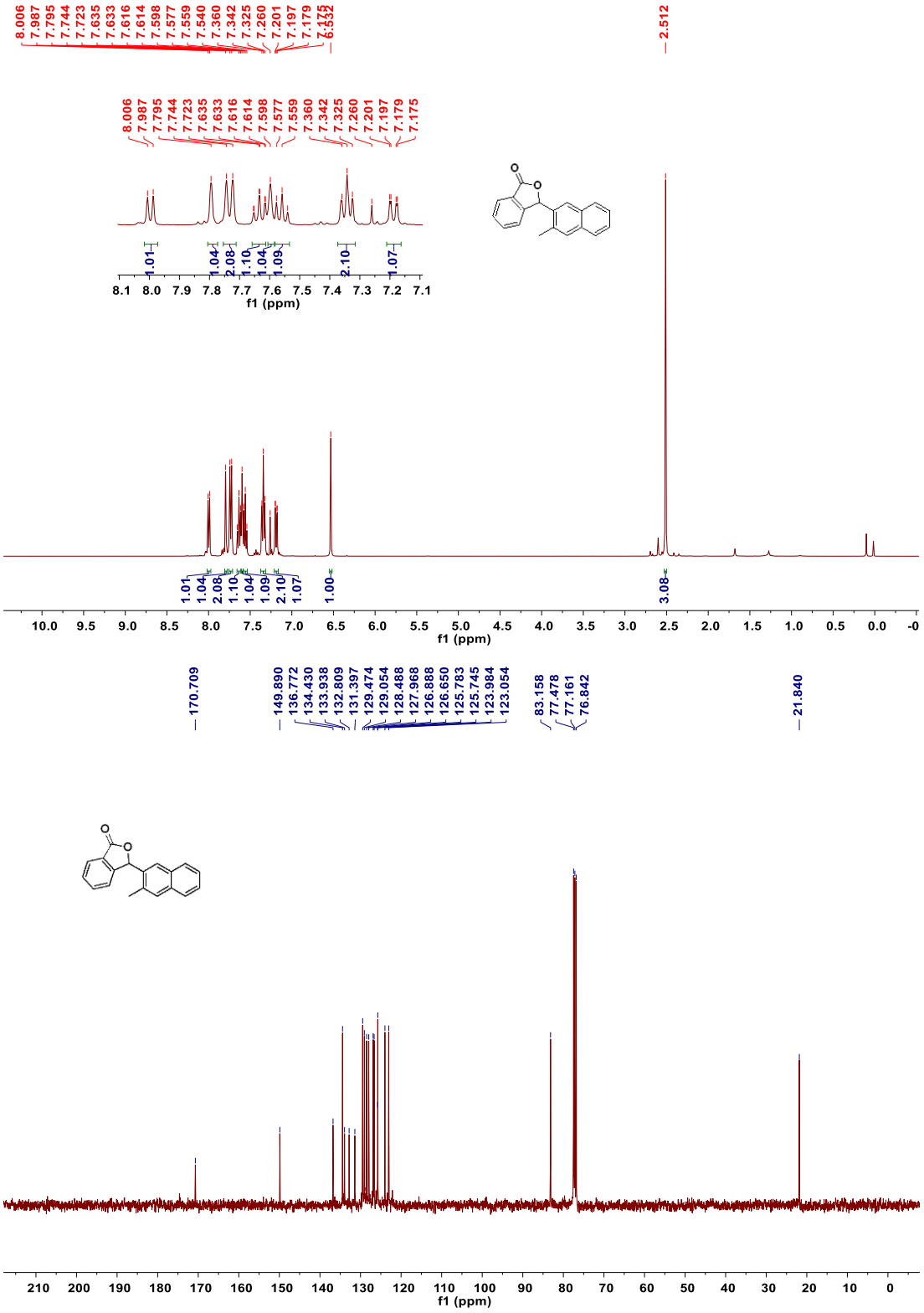




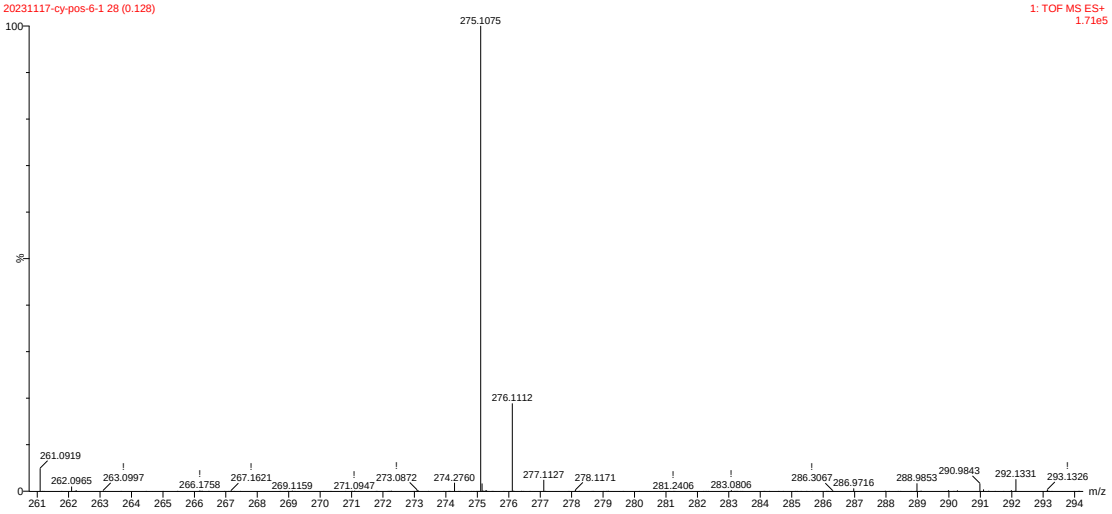
The HRMS spectrum of 3-(2-methylnaphthalen-1-yl)isobenzofuran-1(3H)-one (2o).



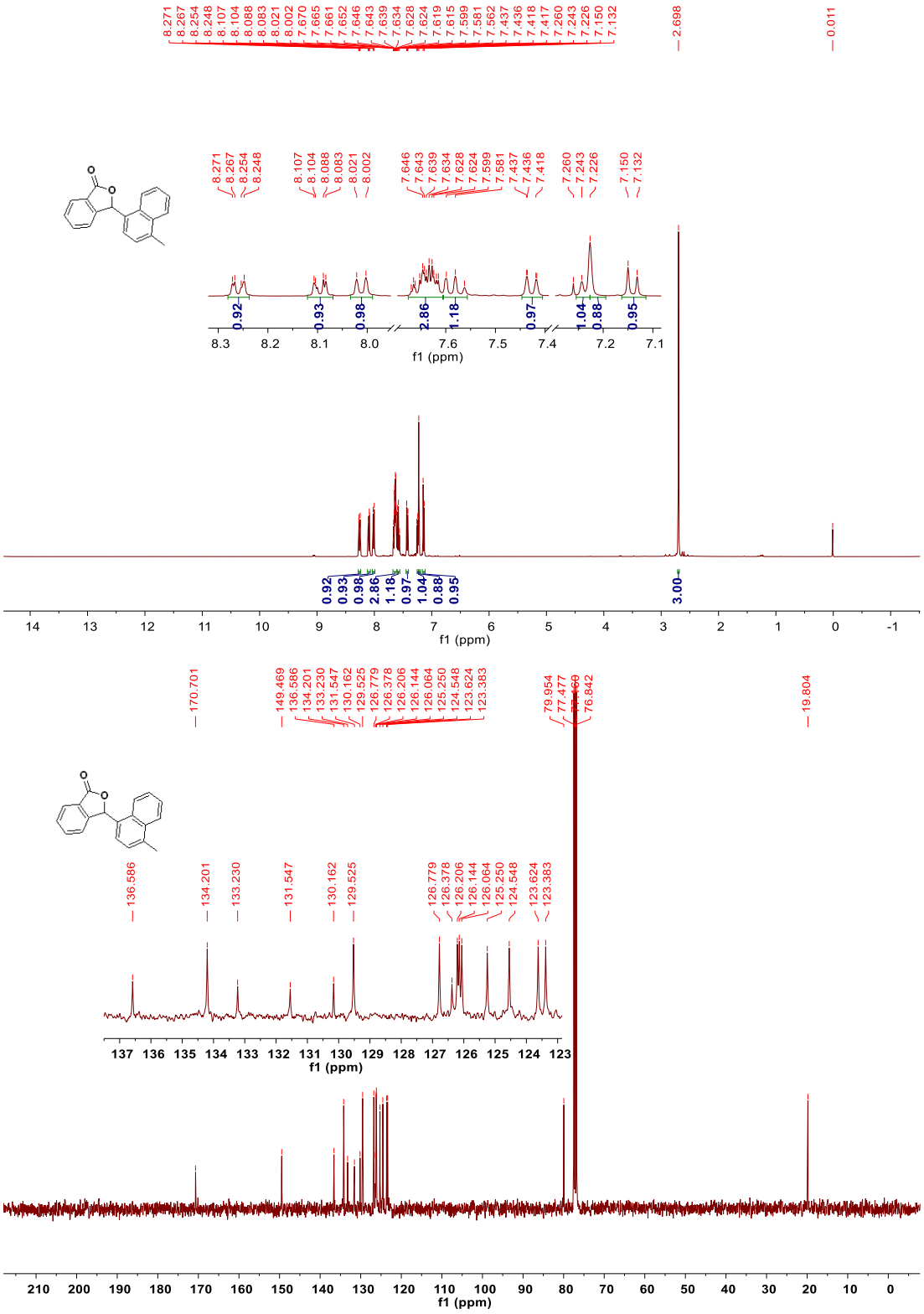
The ^{1}H and ^{13}C NMR spectrum of 3-(3-methylnaphthalen-2-yl)isobenzofuran-1(3H)-one (2o').



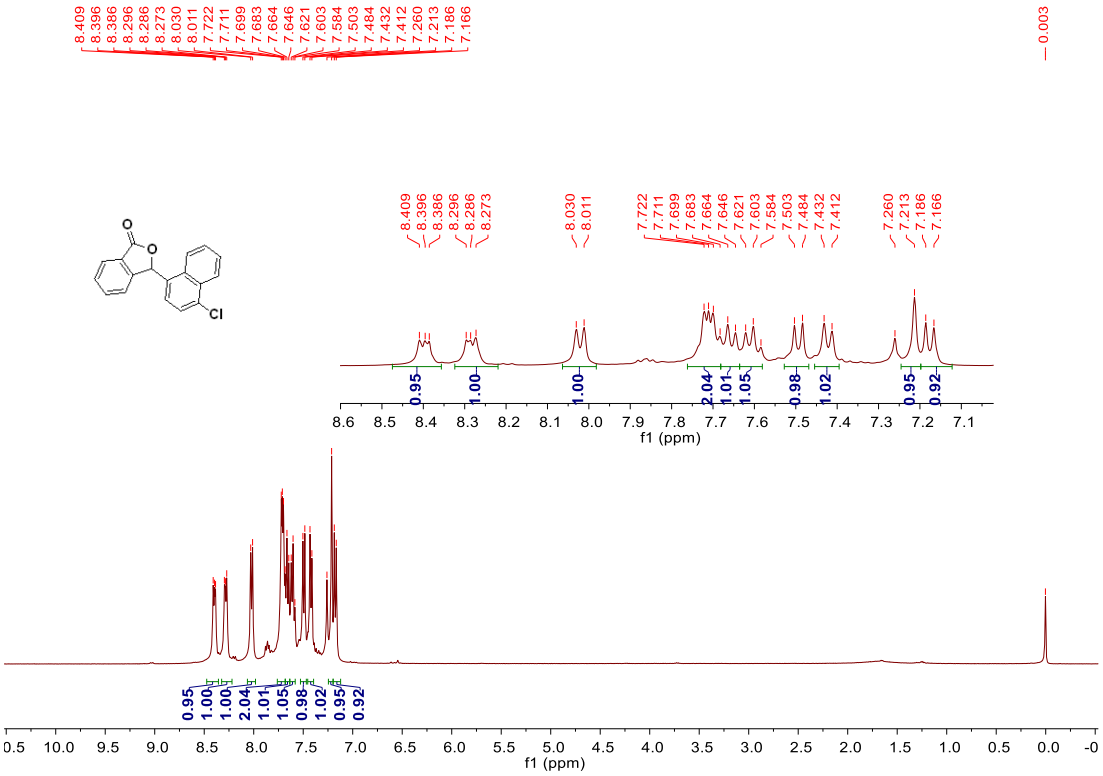
The HRMS spectrum of 3-(3-methylnaphthalen-2-yl)isobenzofuran-1(3H)-one (2o').

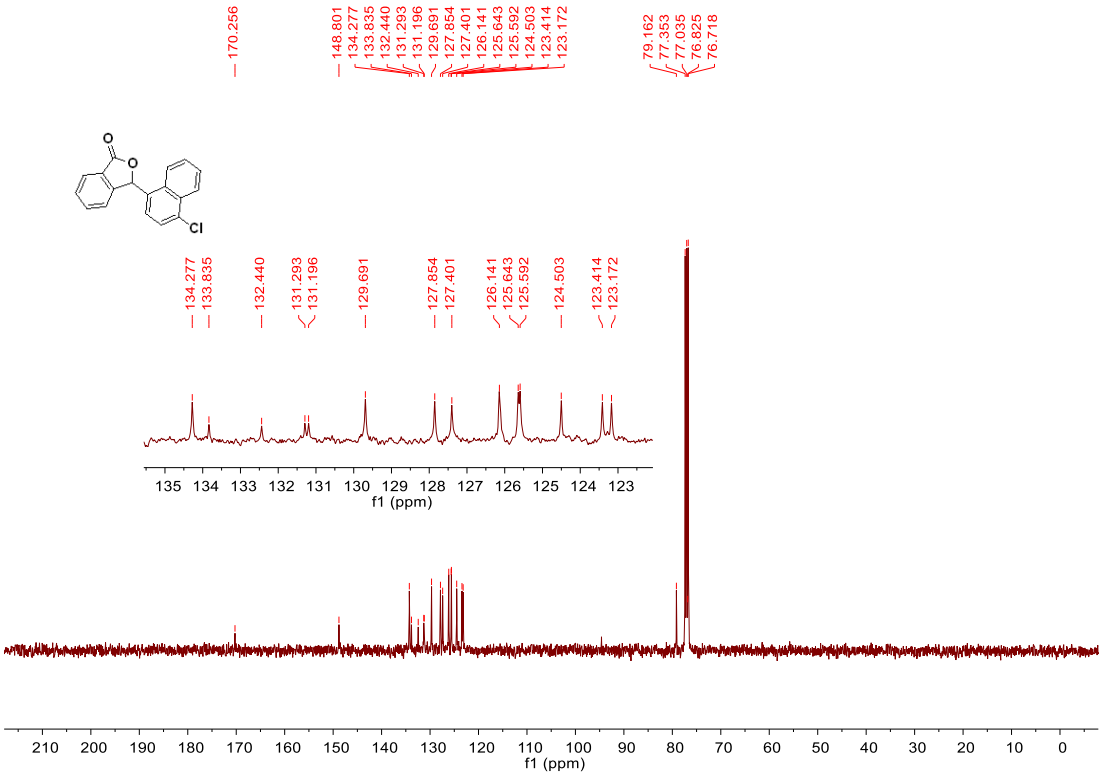


The ^{1}H and ^{13}C NMR spectrum of 3-(4-methylnaphthalen-1-yl)isobenzofuran-1(3*H*)-one (2p).

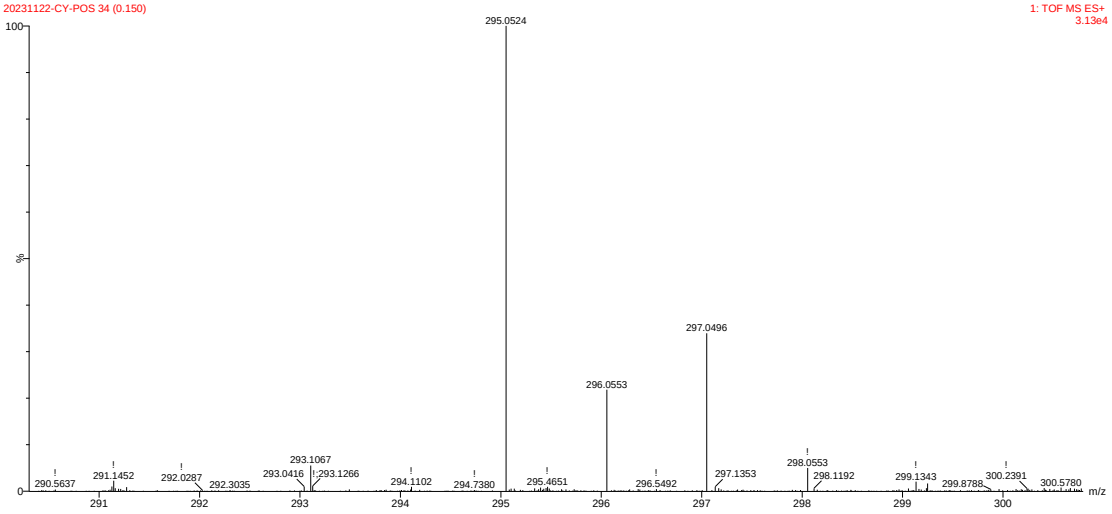


The ^{1}H and ^{13}C NMR spectrum of 3-(4-chloronaphthalen-1-yl)isobenzofuran-1(3*H*)-one (2q).

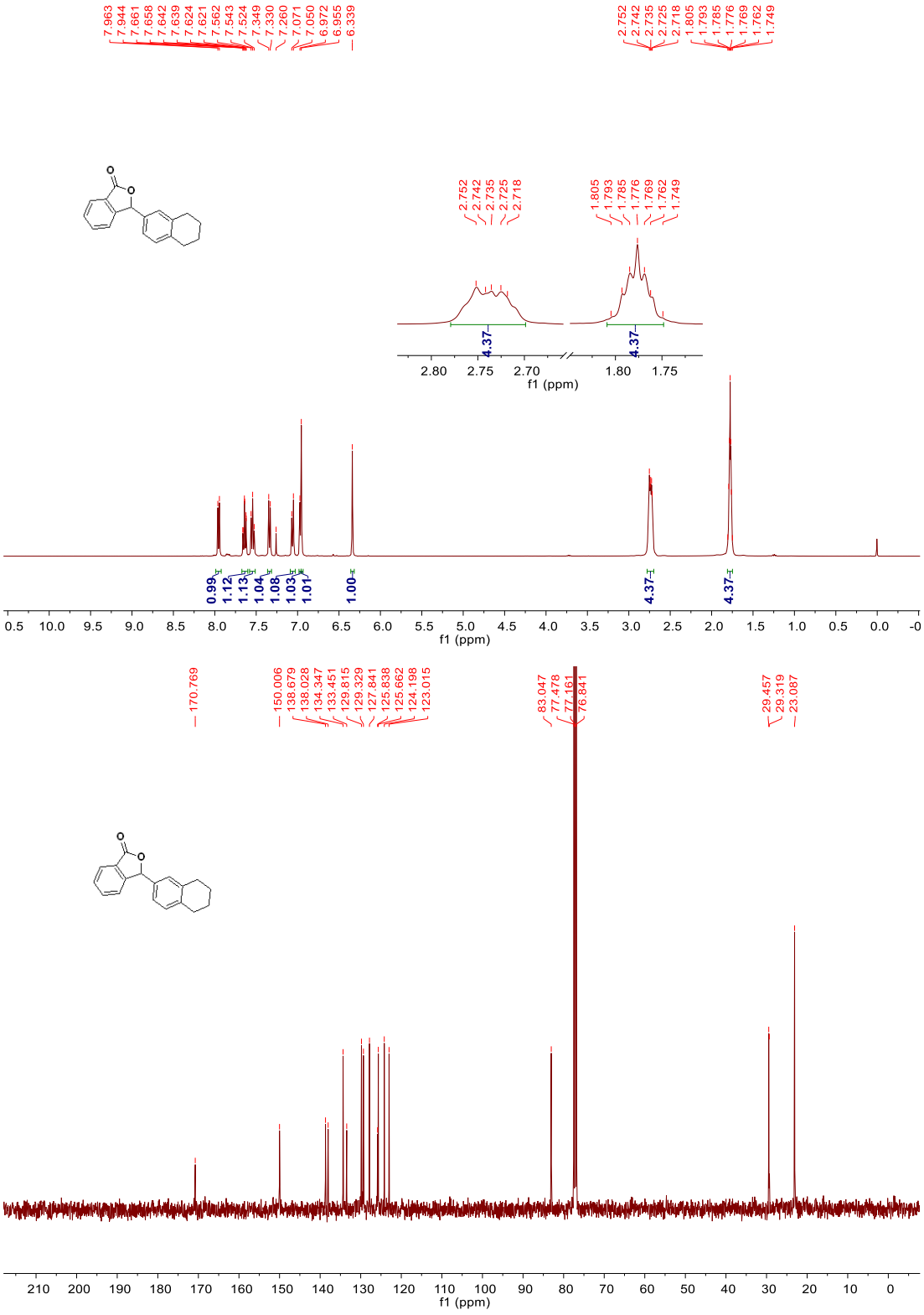




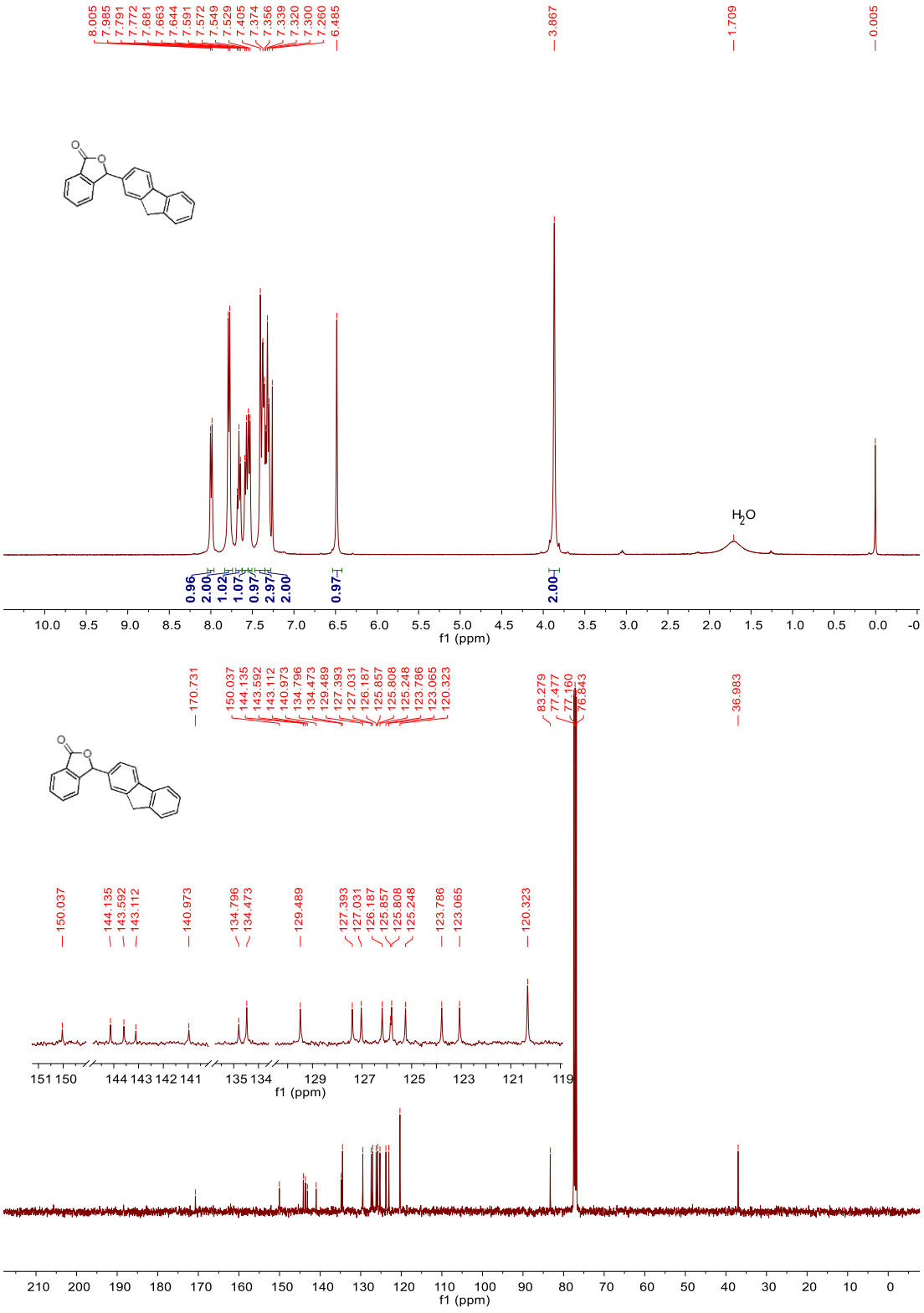
The HRMS spectrum of 3-(4-chloronaphthalen-1-yl)isobenzofuran-1(3*H*)-one (2q).



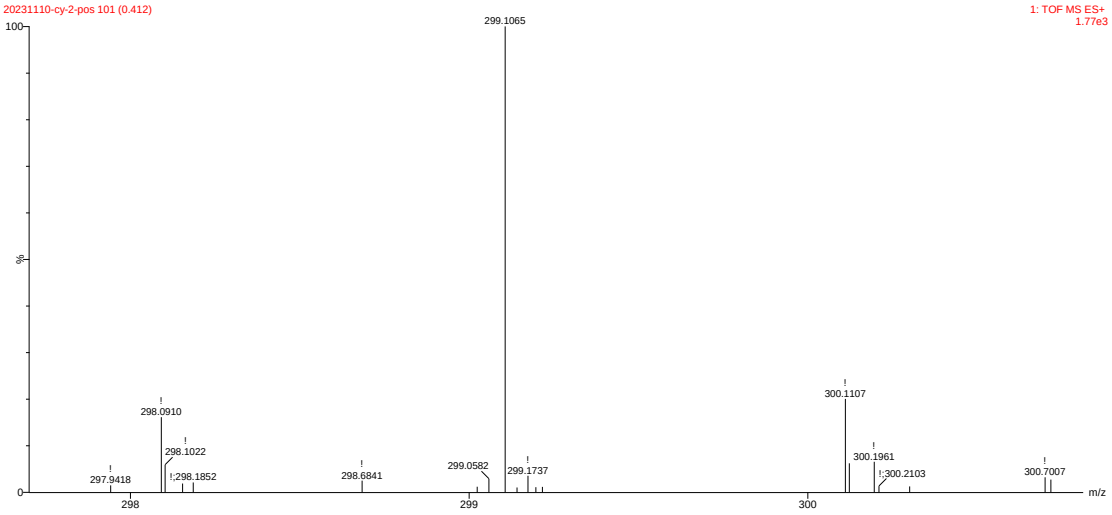
The ^{1}H and ^{13}C NMR spectrum of 3-(5,6,7,8-tetrahydronaphthalen-2-yl)isobenzofuran-1(3*H*)-one (2r).



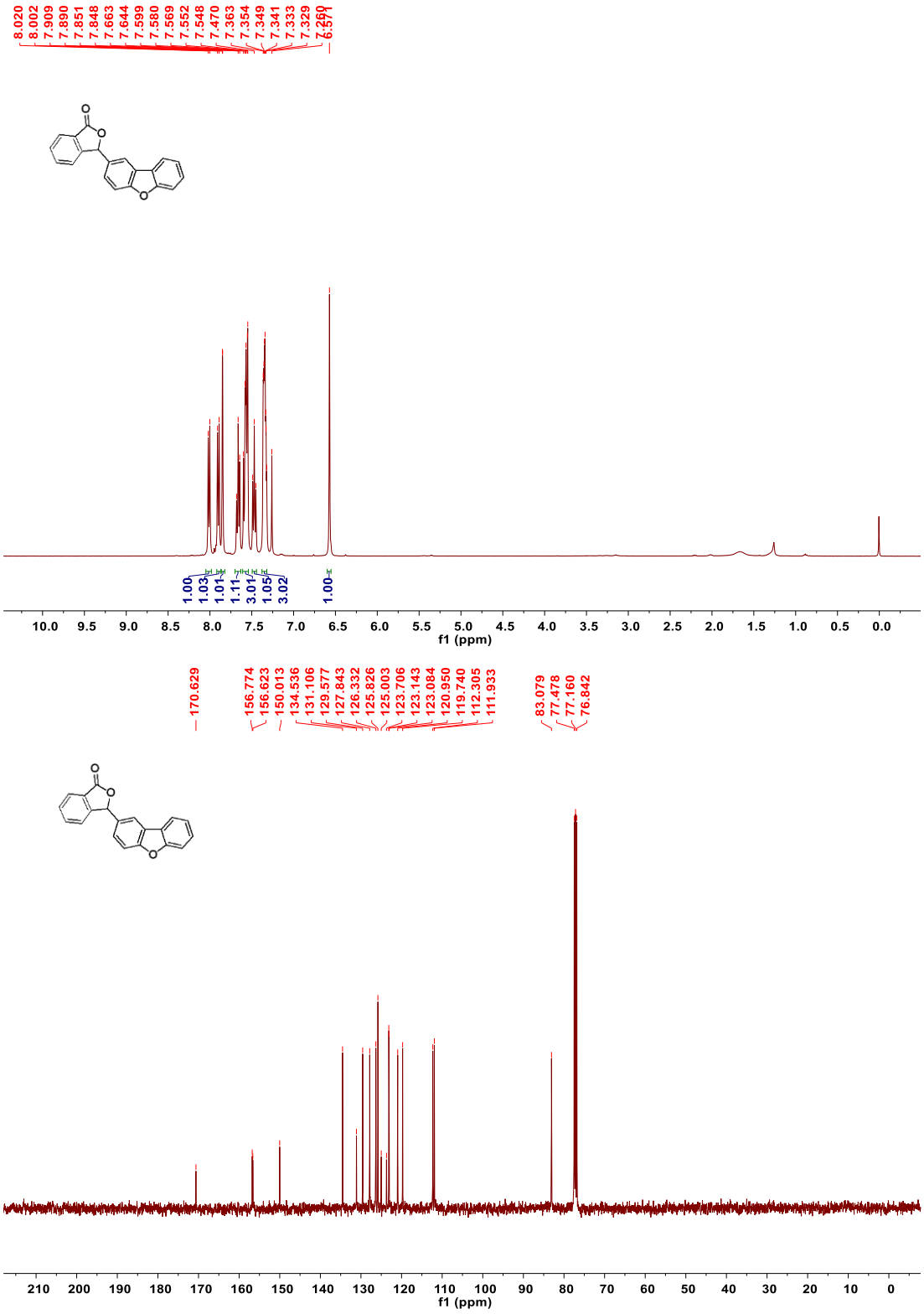
The ^{1}H and ^{13}C NMR spectrum of 3-(9H-fluoren-2-yl)isobenzofuran-1(3*H*)-one (2s).



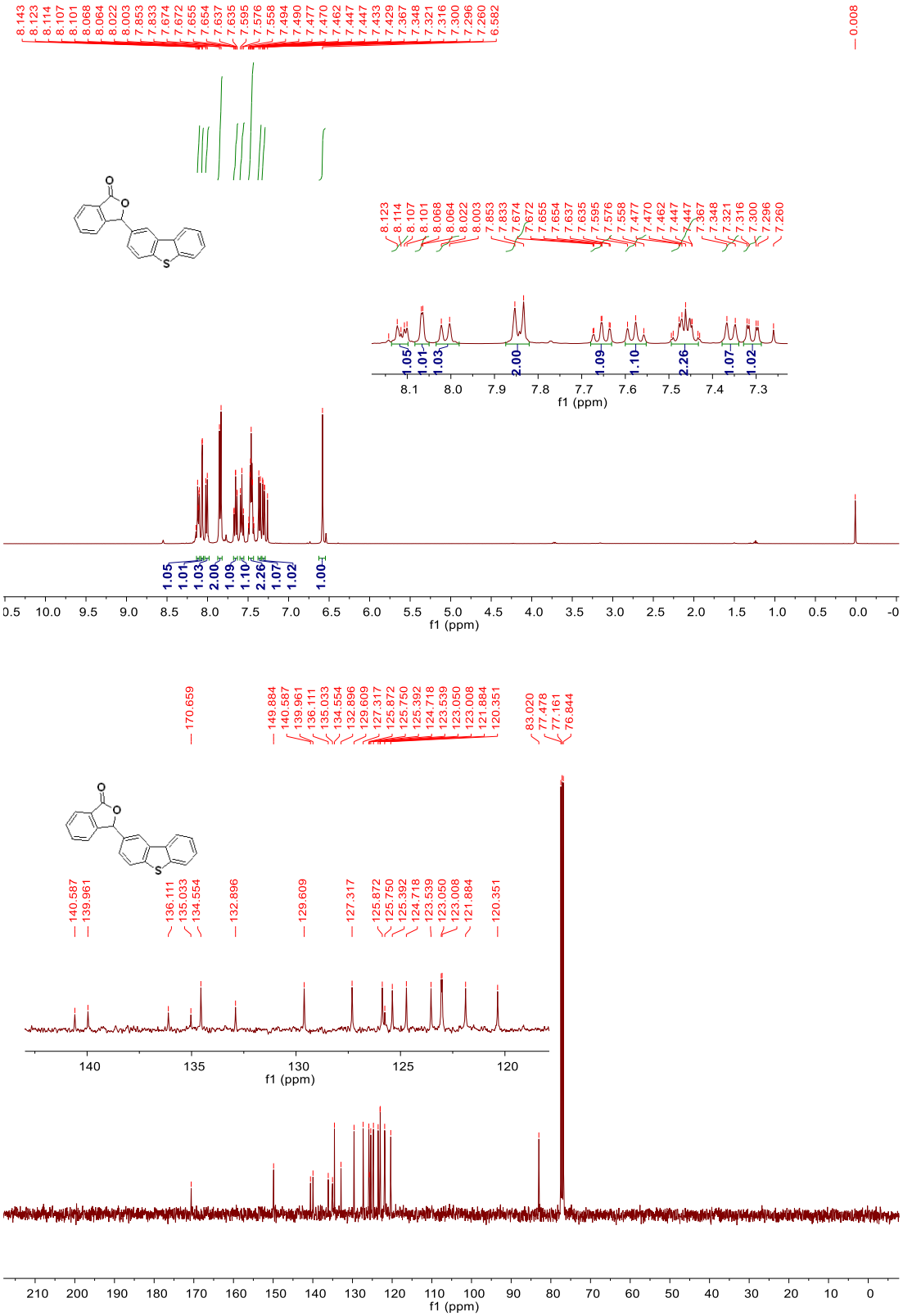
The HRMS spectrum of 3-(9H-fluoren-3-yl)isobenzofuran-1(3*H*)-one (2s).



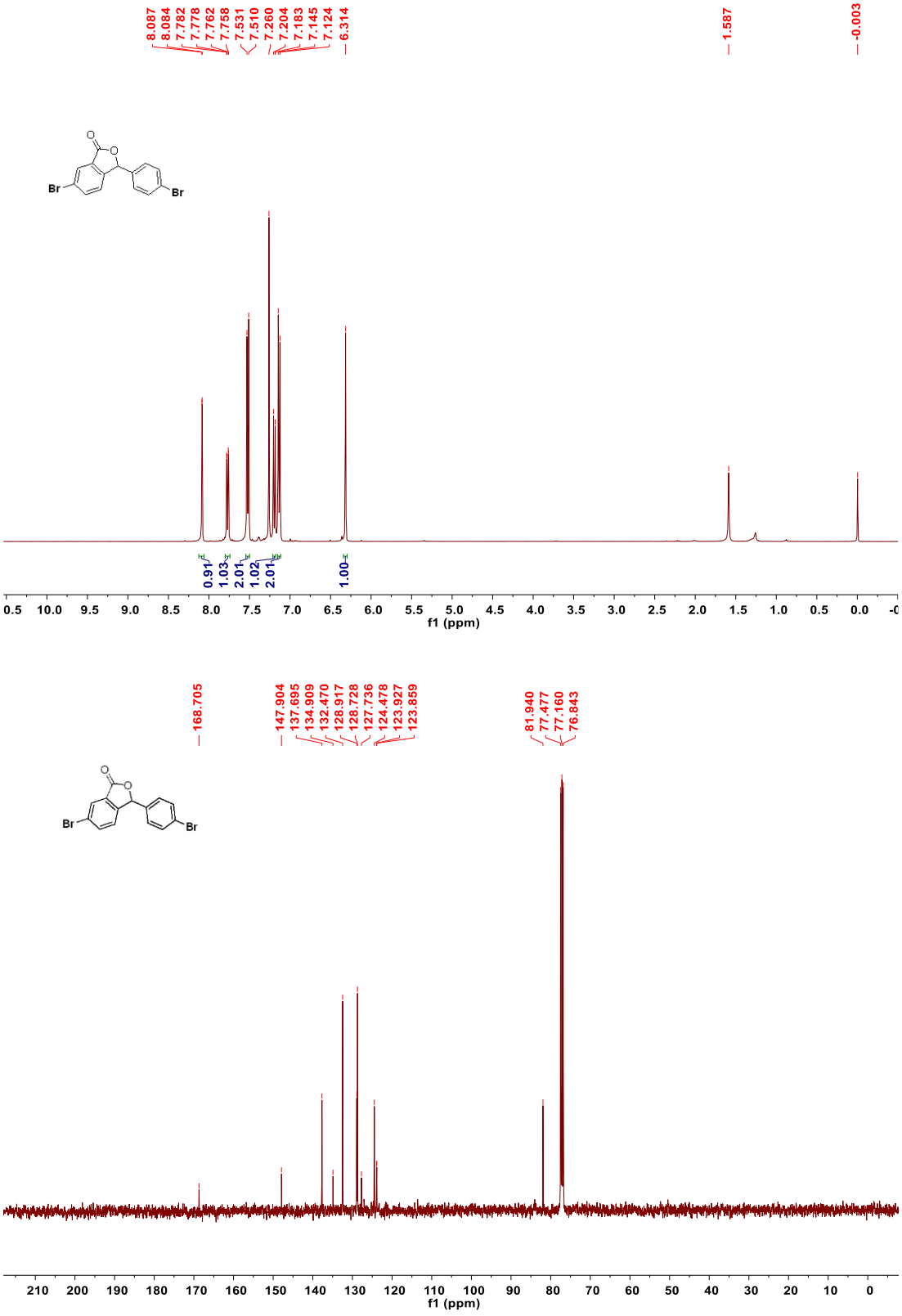
The ^{1}H and ^{13}C NMR spectrum of 3-(dibenzo[b,d]furan-2-yl)isobenzofuran-1(3H)-one (2t).



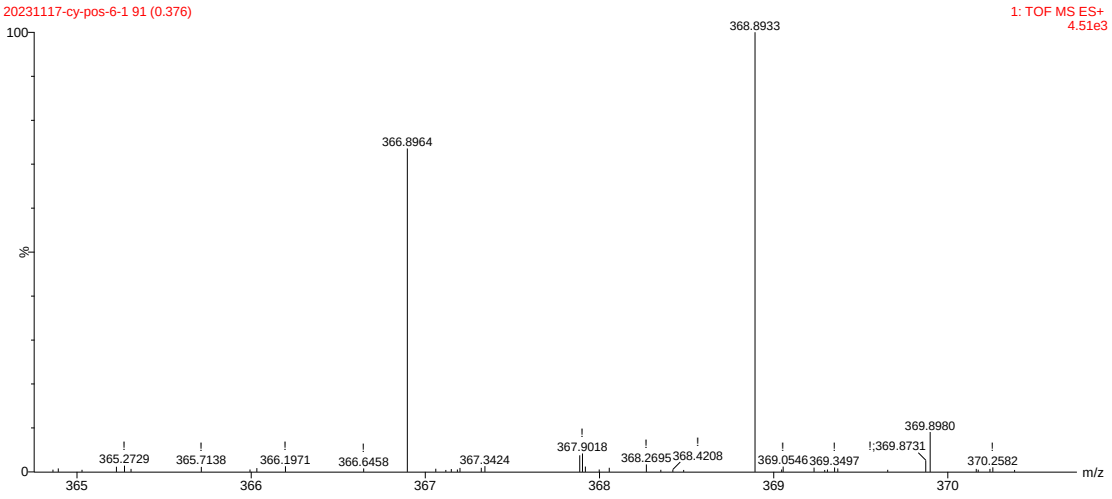
The ^{1}H and ^{13}C NMR spectrum of 3-(dibenzo[*b*,*d*]thiophen-2-yl)isobenzofuran-1(3*H*)-one (2u).



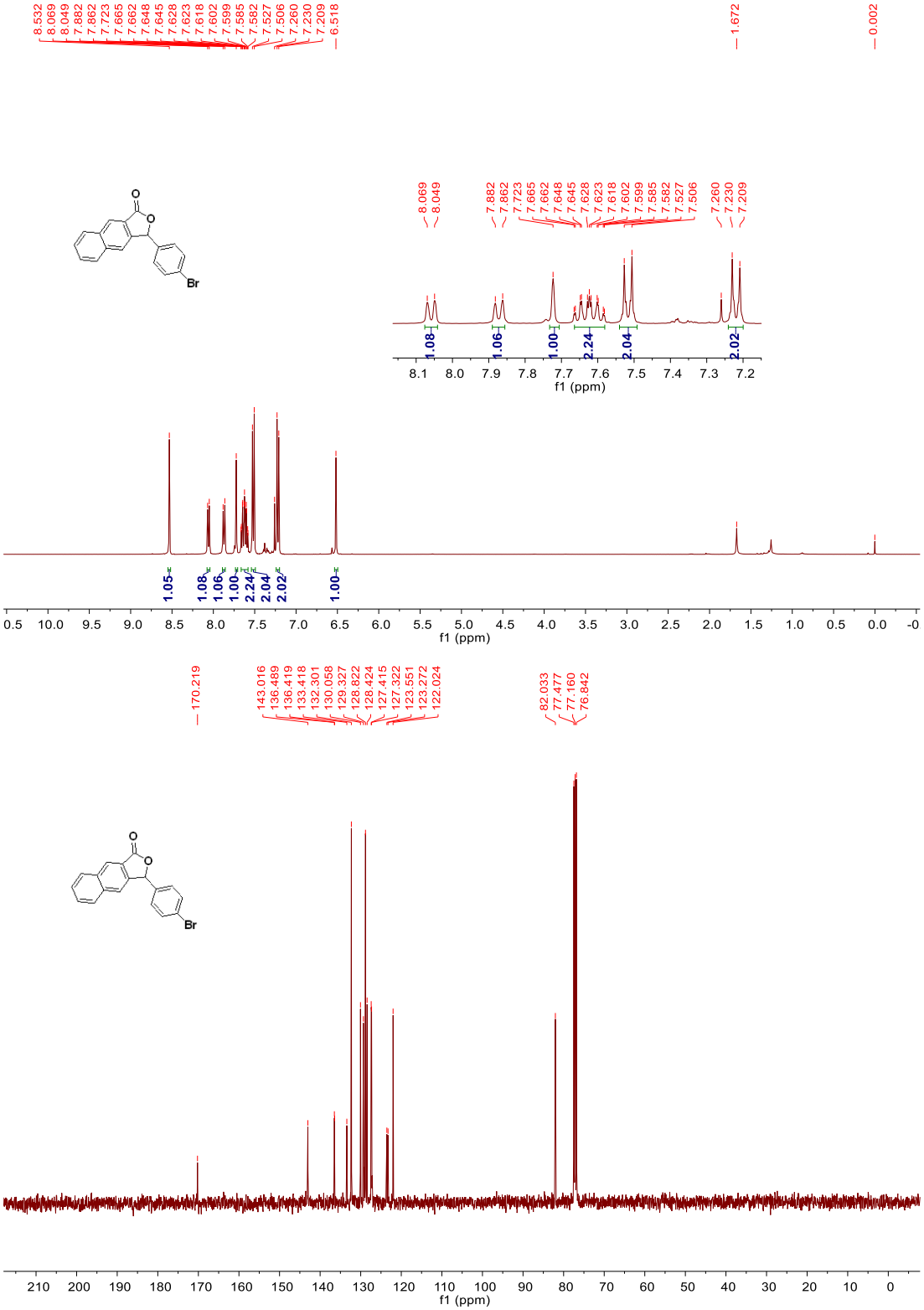
The ^{1}H and ^{13}C NMR spectrum of 6-bromo-3-(4-bromophenyl)isobenzofuran-1(3H)-one (2v).



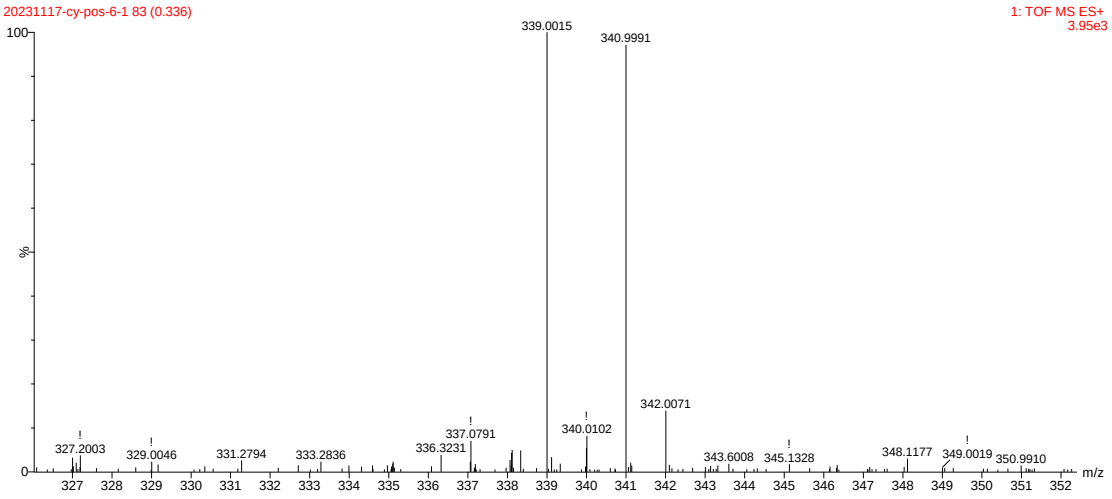
The ^{1}H and ^{13}C NMR spectrum of 6-bromo-3-(4-bromophenyl)isobenzofuran-1(3H)-one (2v).



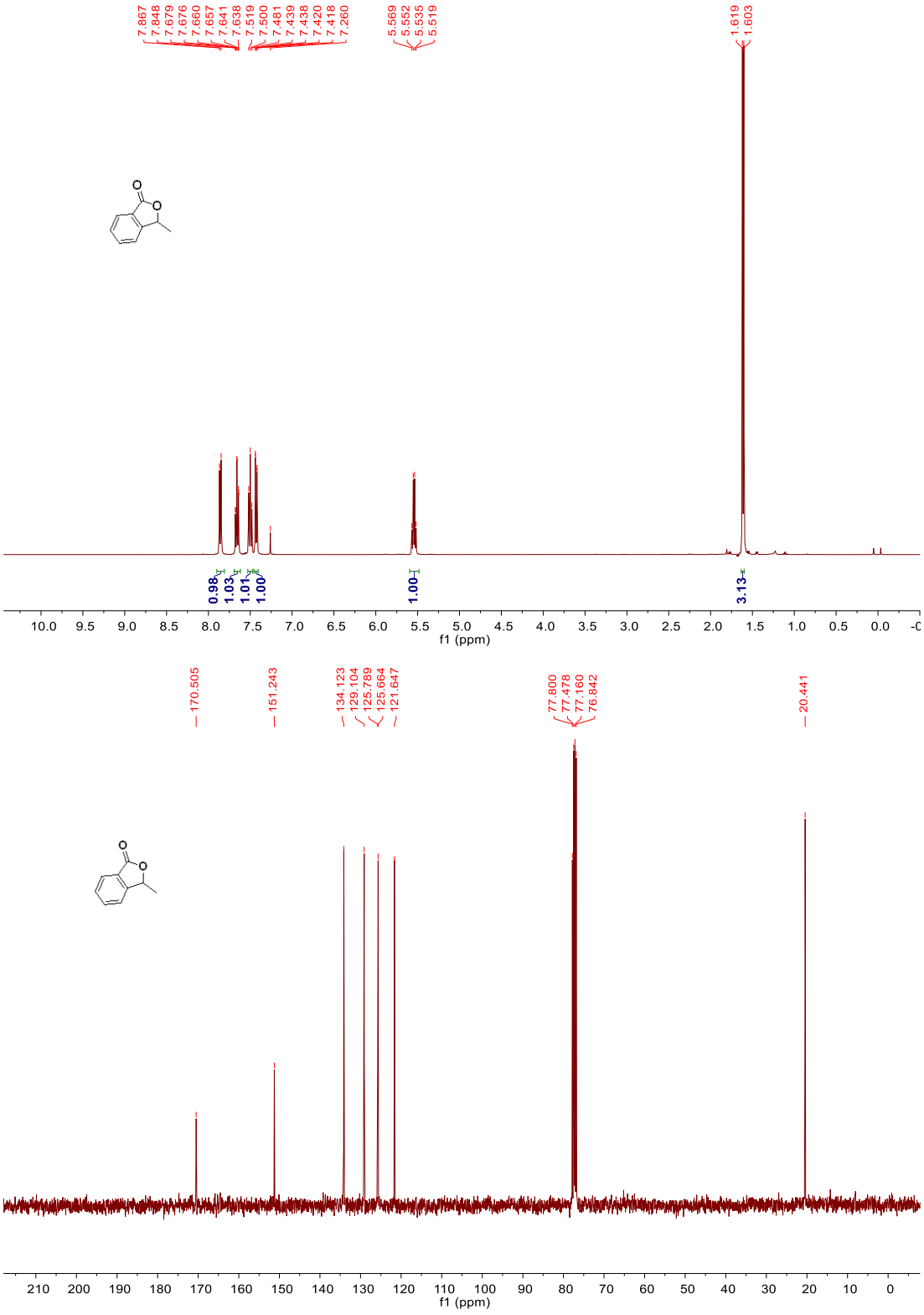
The ^{1}H and ^{13}C NMR spectrum of 3-(4-bromophenyl)naphtho[2,3-c]furan-1(3*H*)-one (2w).



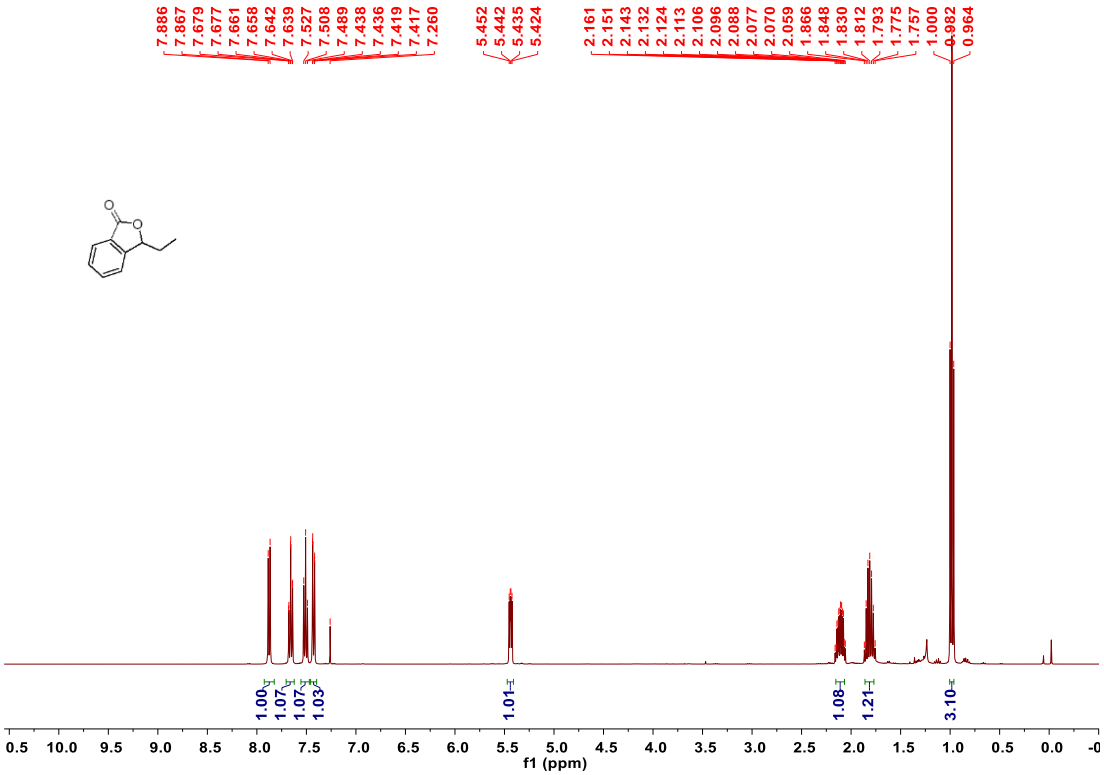
The HRMS spectrum of 3-(4-bromophenyl)naphtho[2,3-c]furan-1(3*H*)-one (2w).

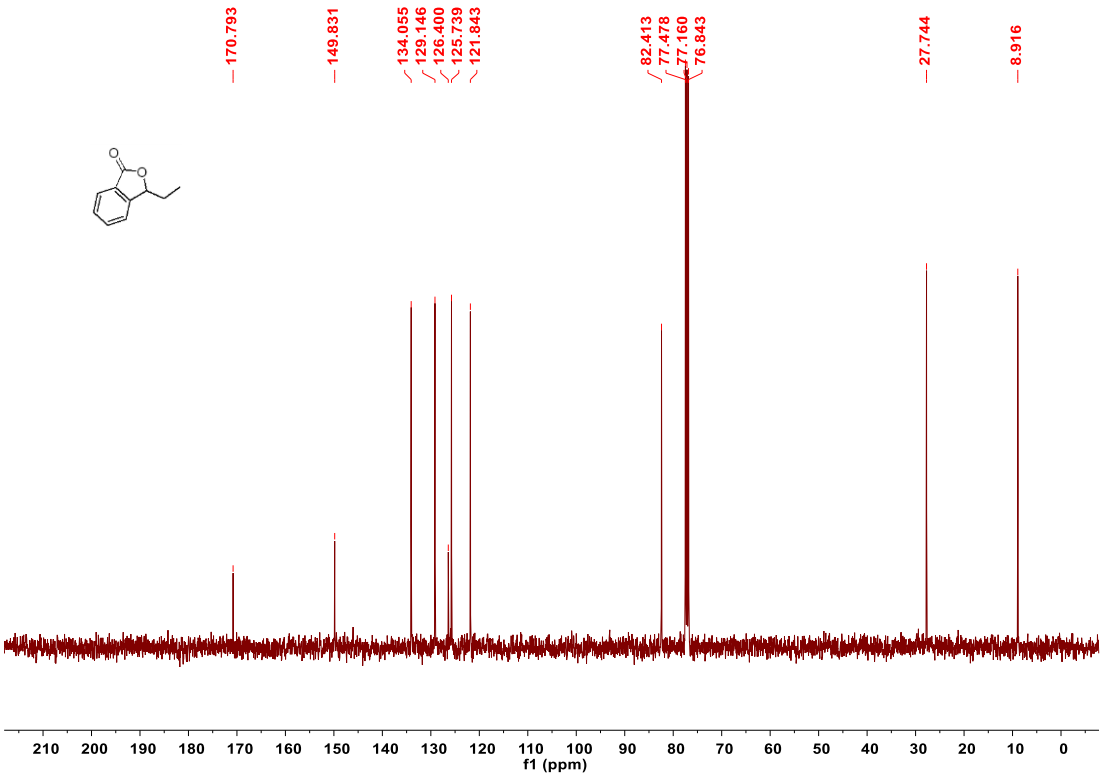


The ^{1}H and ^{13}C NMR spectrum of 3-methylisobenzofuran-1(3*H*)-one (2x).

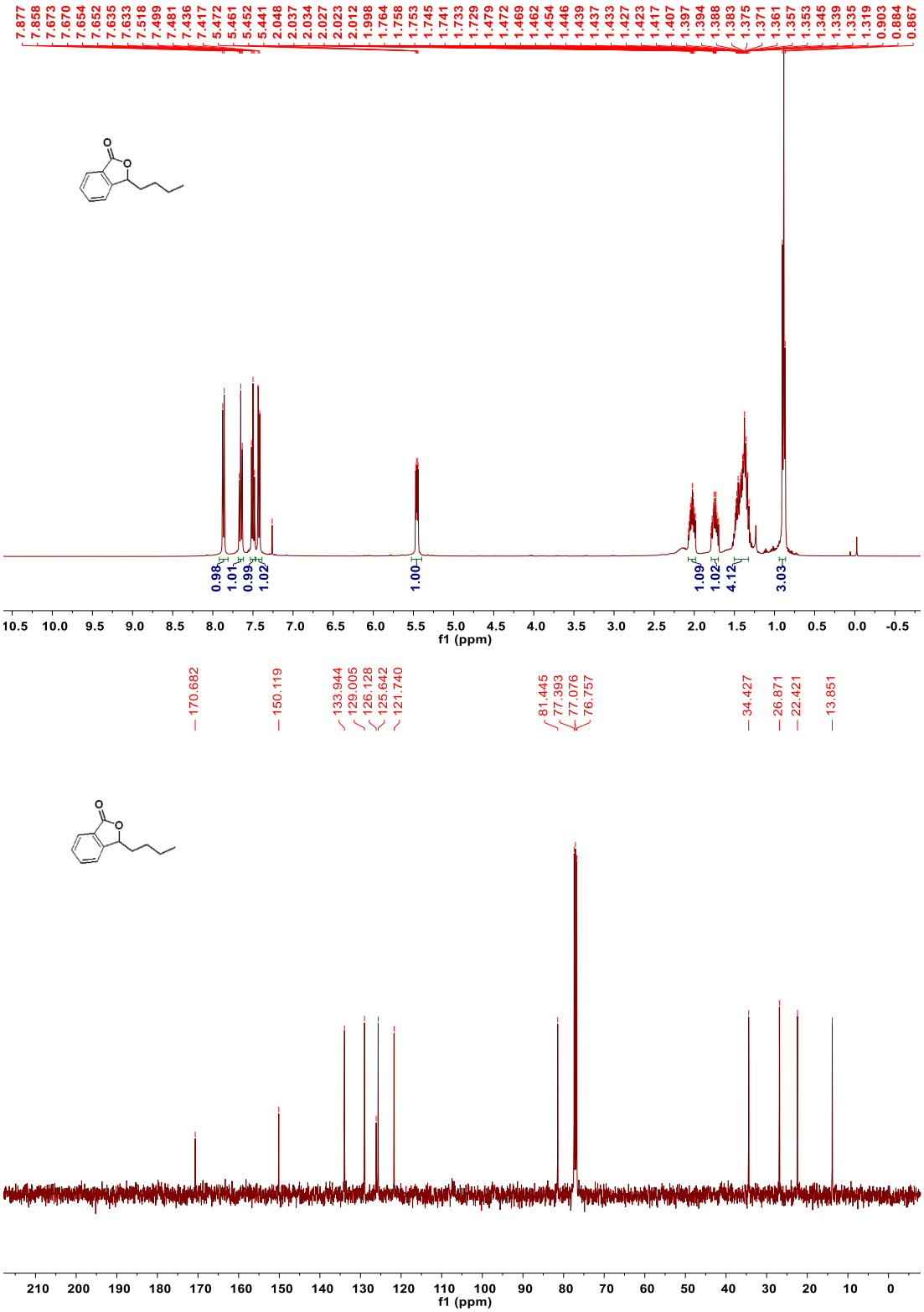


The ^{1}H and ^{13}C NMR spectrum of 3-ethylisobenzofuran-1(3H)-one (2y).

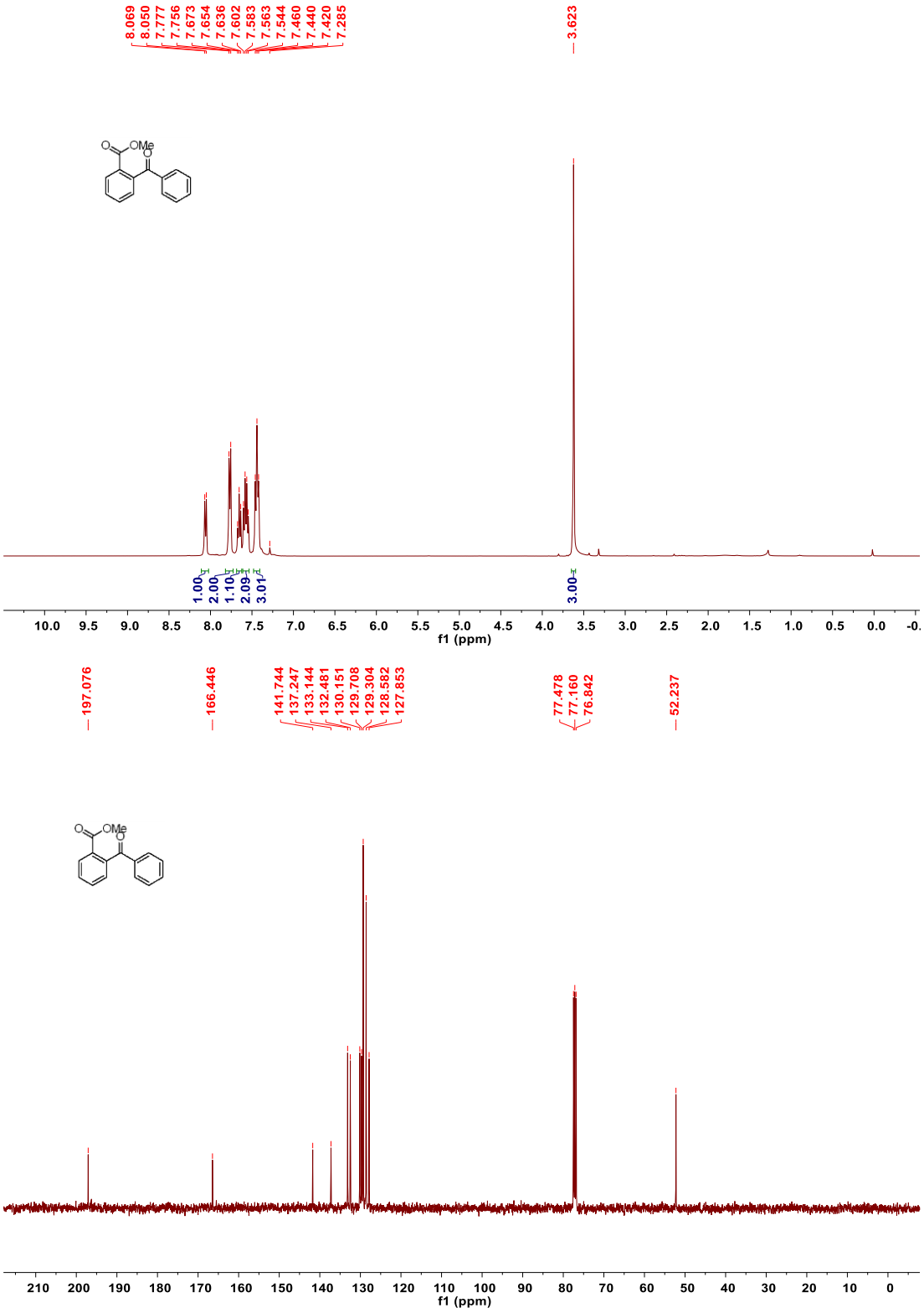




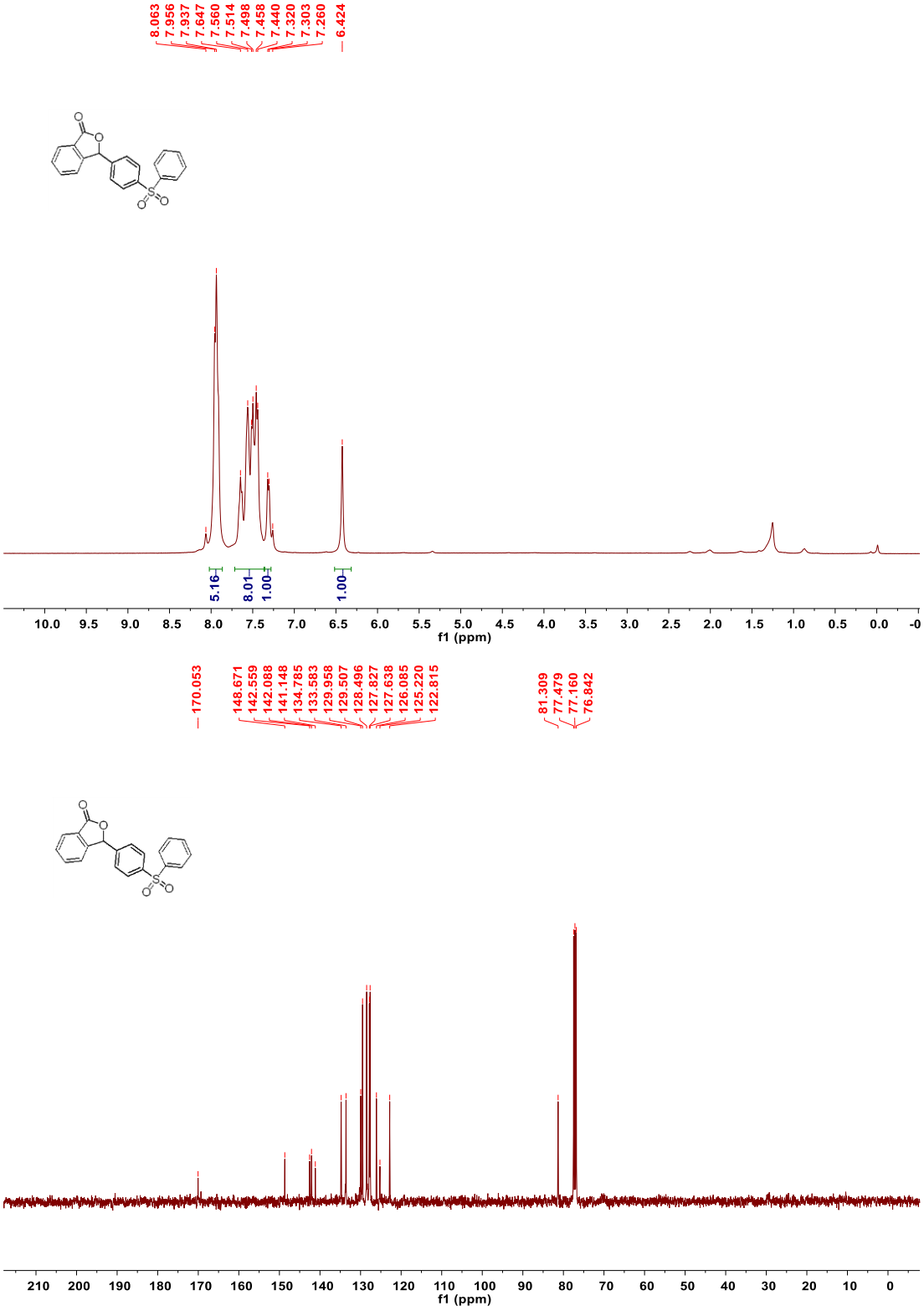
The ^{1}H and ^{13}C NMR spectrum of 3-butylisobenzofuran-1(3*H*)-one (2z).



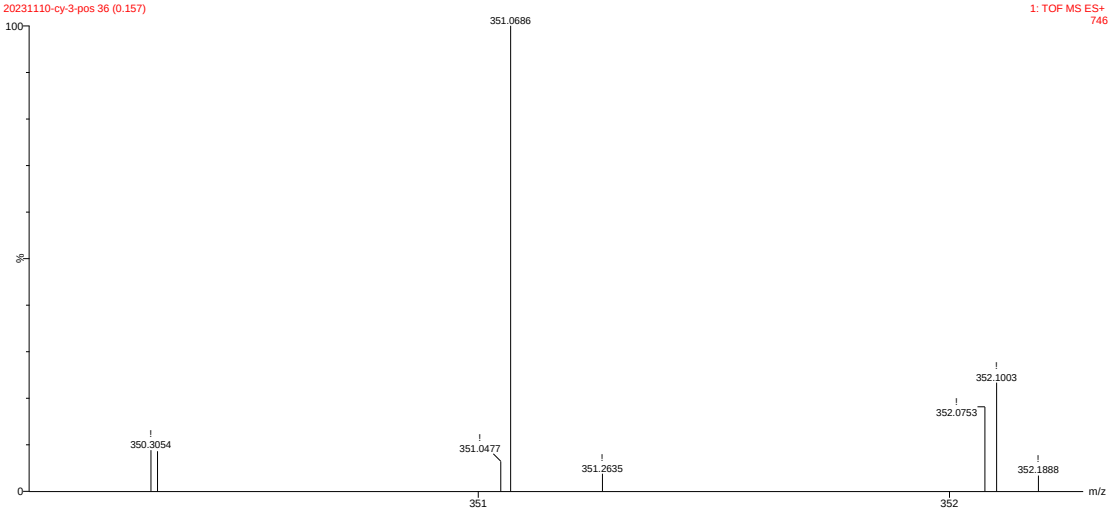
The ^{1}H and ^{13}C NMR spectrum of methyl 2-benzoylbenzoate (5).



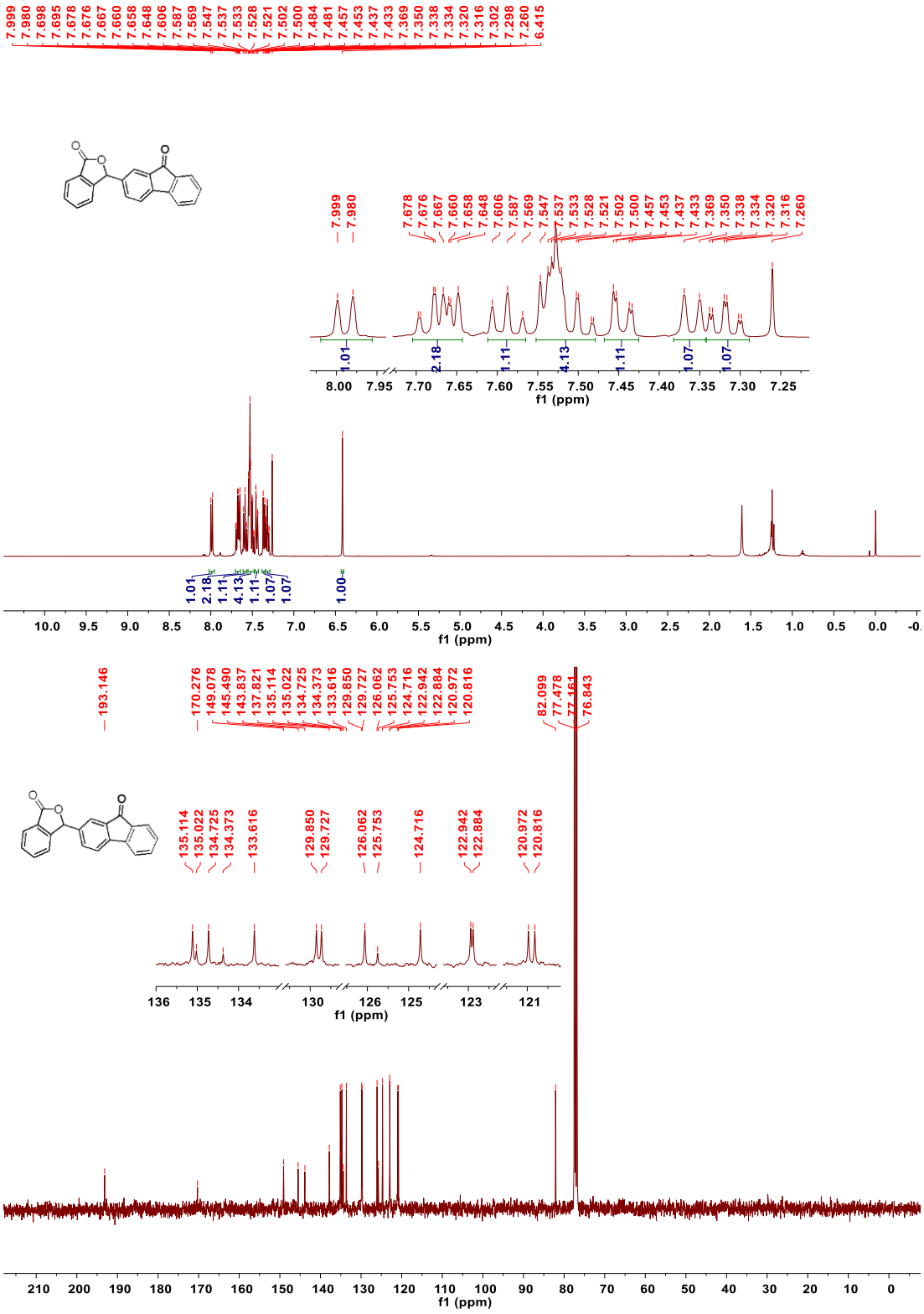
The ^{1}H and ^{13}C NMR spectrum of 3-(4-(phenylsulfonyl)phenyl)isobenzofuran-1(3H)-one (10).



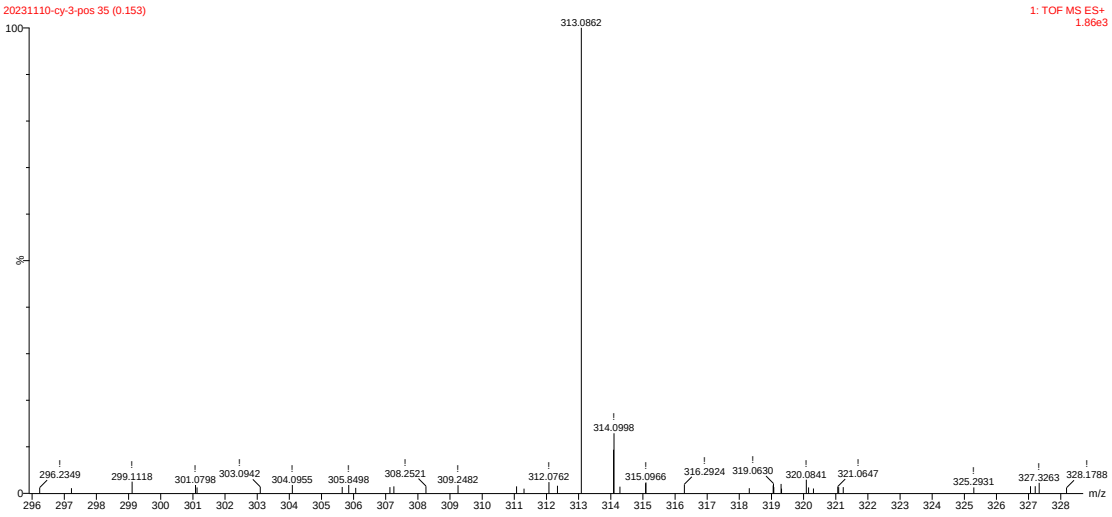
The HRMS spectrum of 3-(4-(phenylsulfonyl)phenyl)isobenzofuran-1(3H)-one (10).



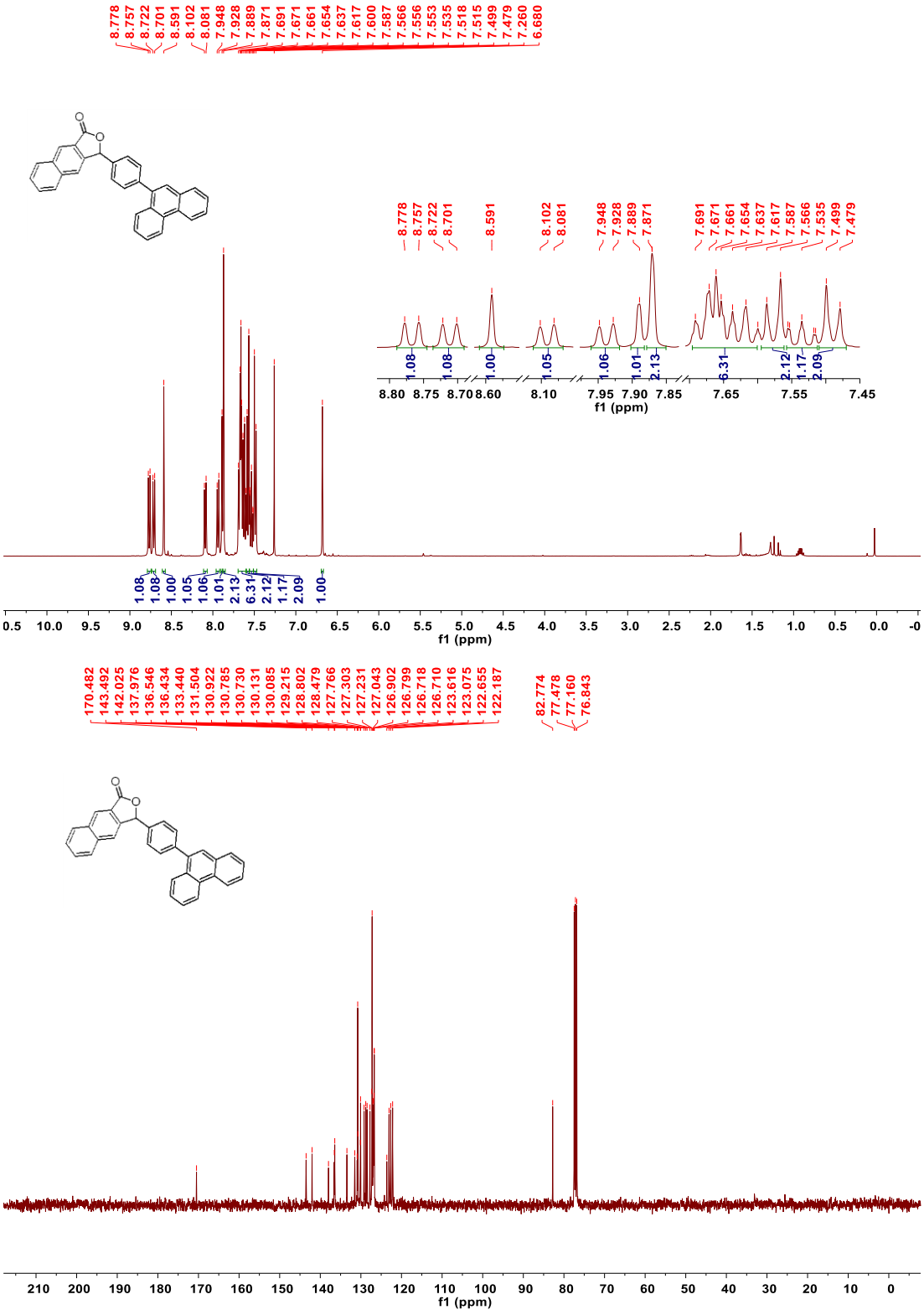
The ^{1}H and ^{13}C NMR spectrum of 3-(9-oxo-9H-fluoren-2-yl)isobenzofuran-1(3H)-one (11).



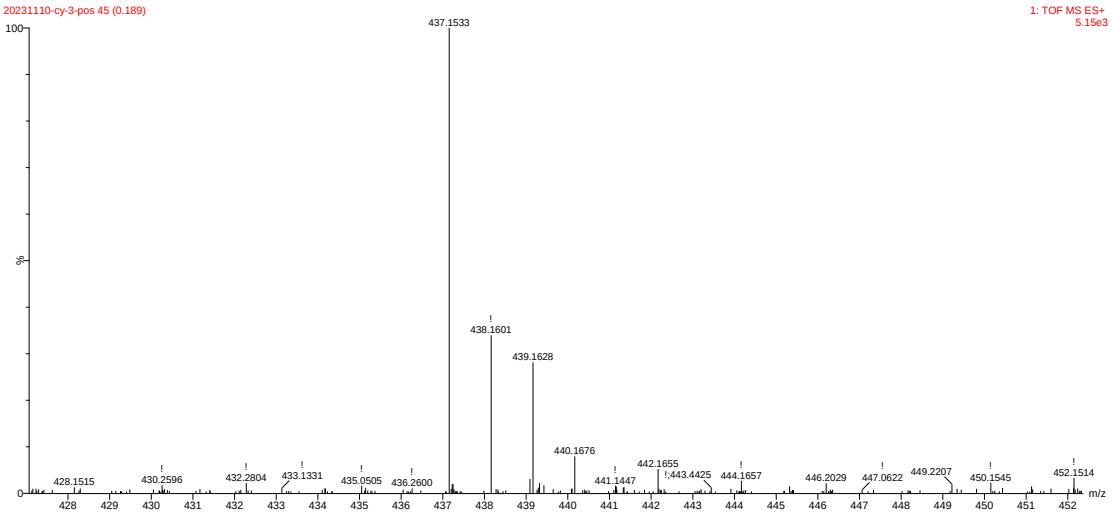
The HRMS spectrum of 3-(9-oxo-9H-fluoren-2-yl)isobenzofuran-1(3H)-one (11).



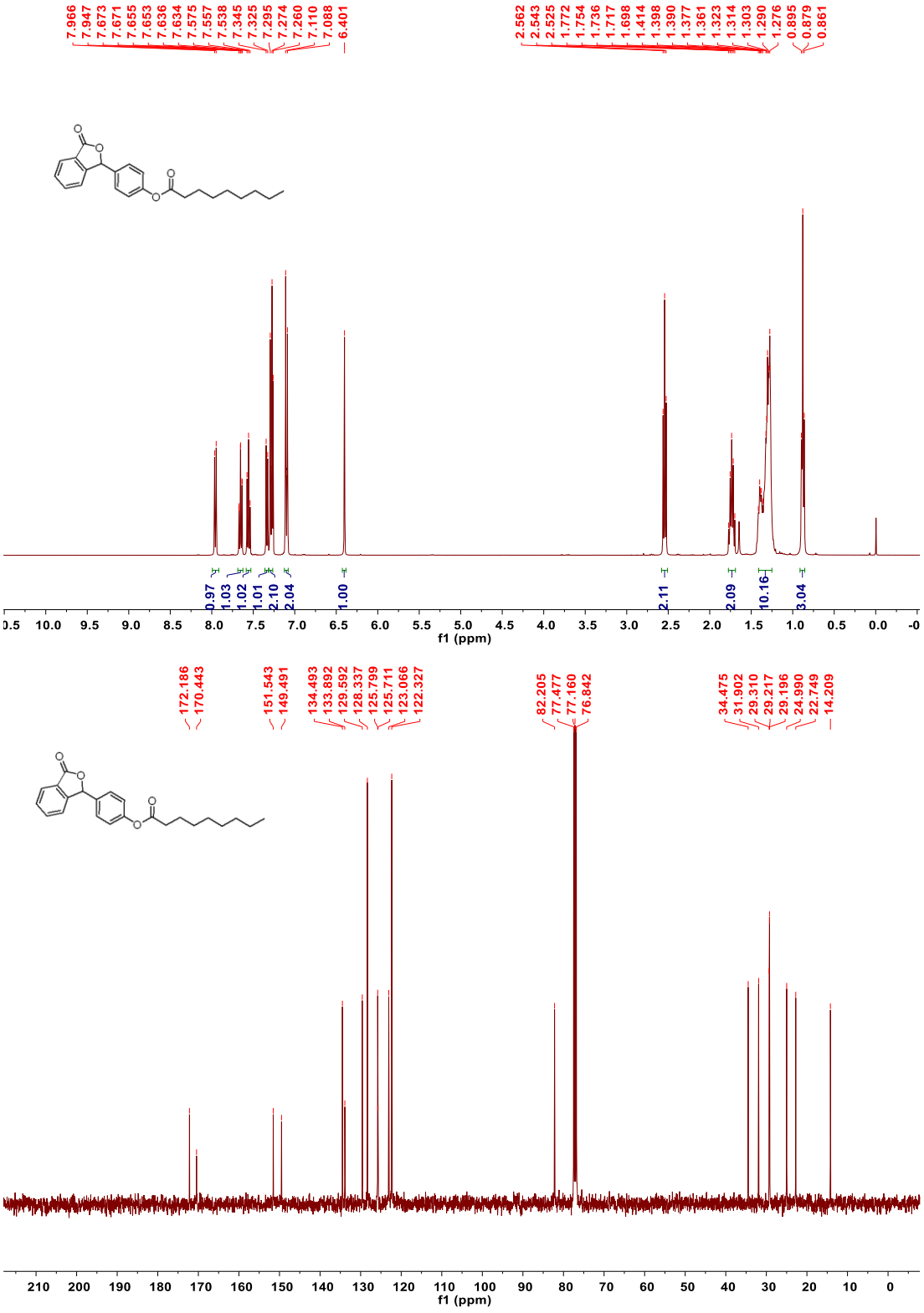
The ^{1}H and ^{13}C NMR spectrum of 3-(4-(Phenanthren-9-yl)phenyl)naphtho[2,3-c]furan-1(3H)-one (12).



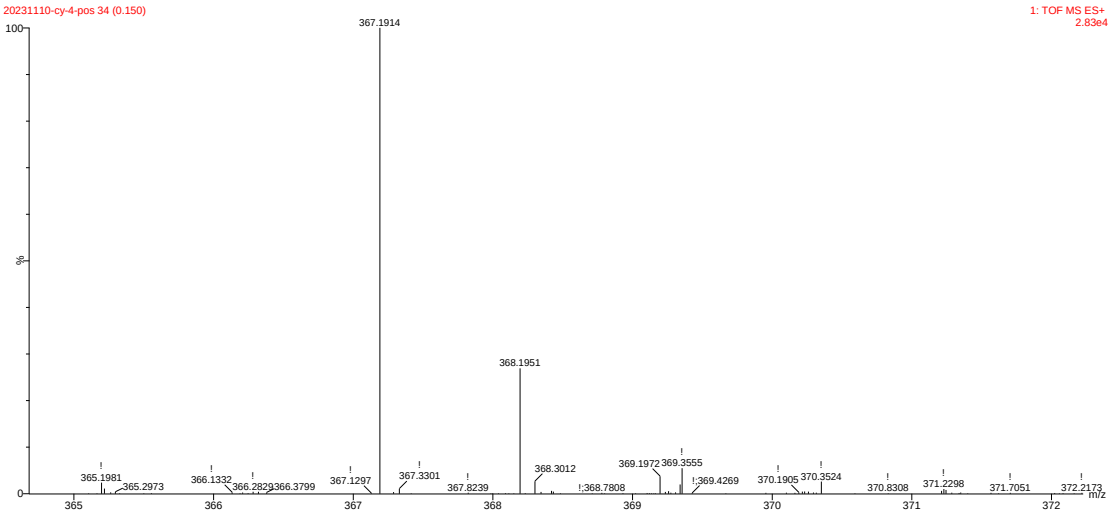
The HRMS spectrum of 3-(4-(Phenanthren-9-yl)phenyl)naphtho[2,3-c]furan-1(3H)-one (12).



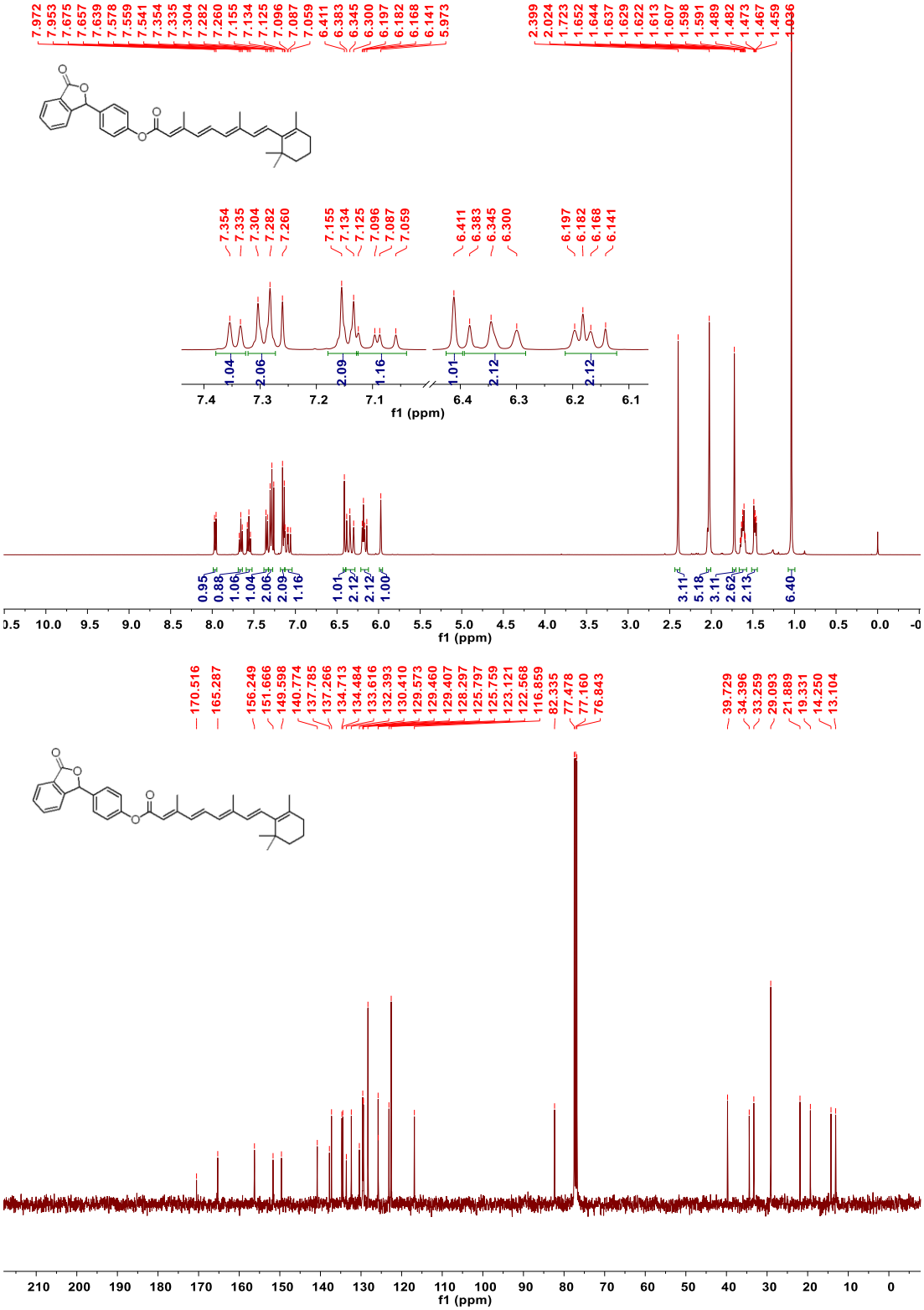
The ^{1}H and ^{13}C NMR spectrum of 4-(3-oxo-1,3-dihydroisobenzofuran-1-yl)phenyl nonanoate (13).



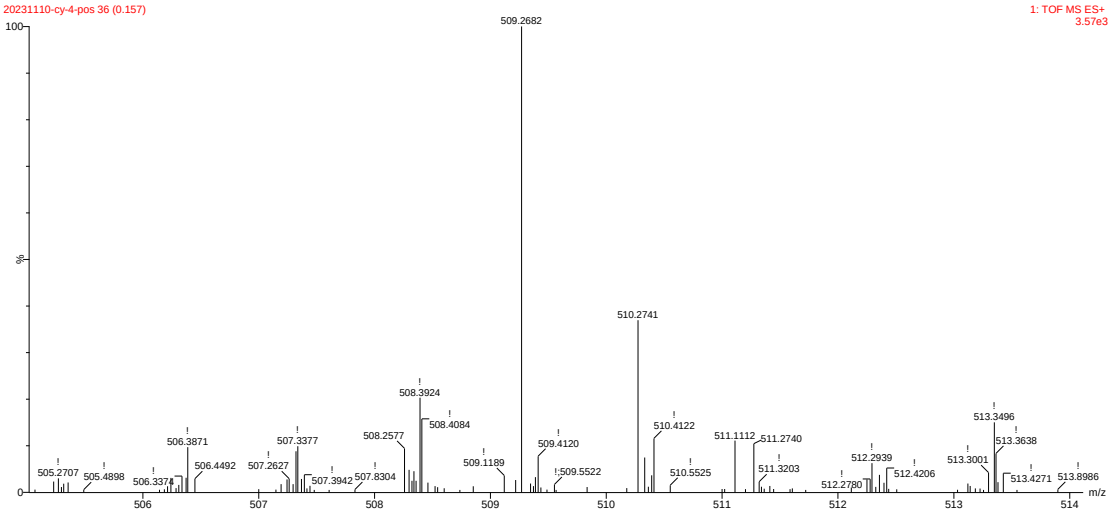
The HRMS spectrum of 4-(3-oxo-1,3-dihydroisobenzofuran-1-yl)phenyl nonanoate (13).



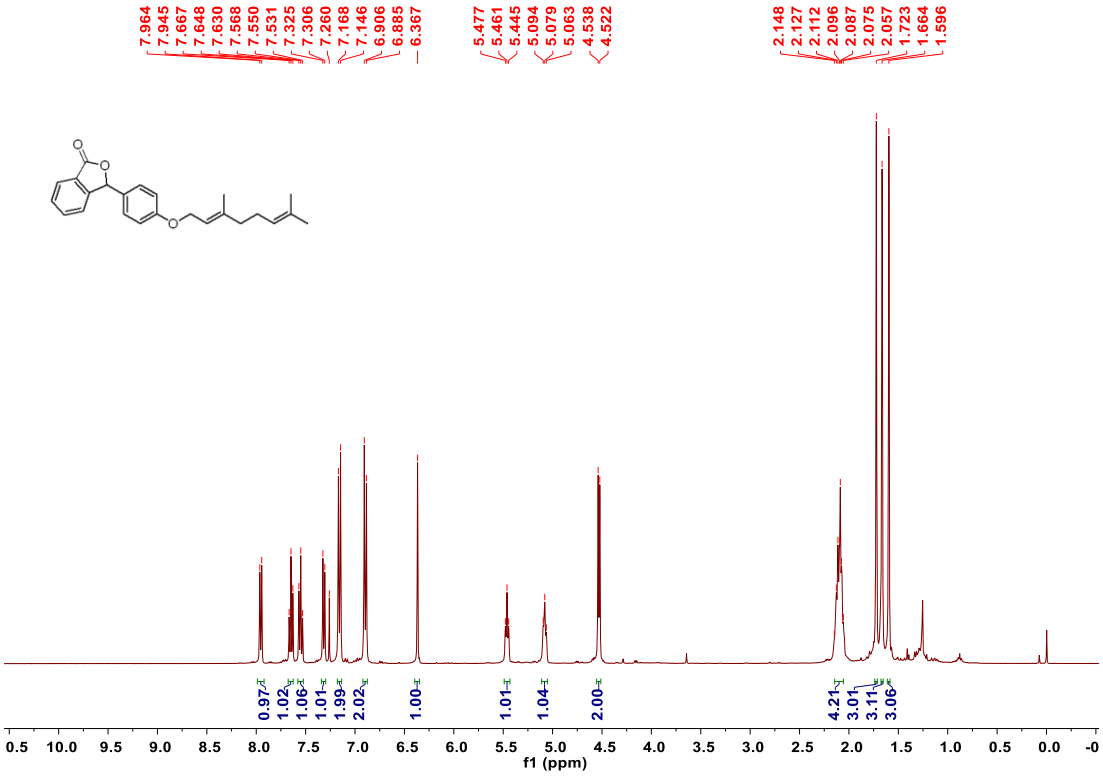
The ^{1}H and ^{13}C NMR spectrum of 4-(3-oxo-1,3-dihydroisobenzofuran-1-yl)phenyl (2*E*,4*E*,6*E*,8*E*)-3,7-dimethyl-9-(2,6,6-trimethylcyclohex-1-en-1-yl)nona-2,4,6,8-tetraenoate (14).

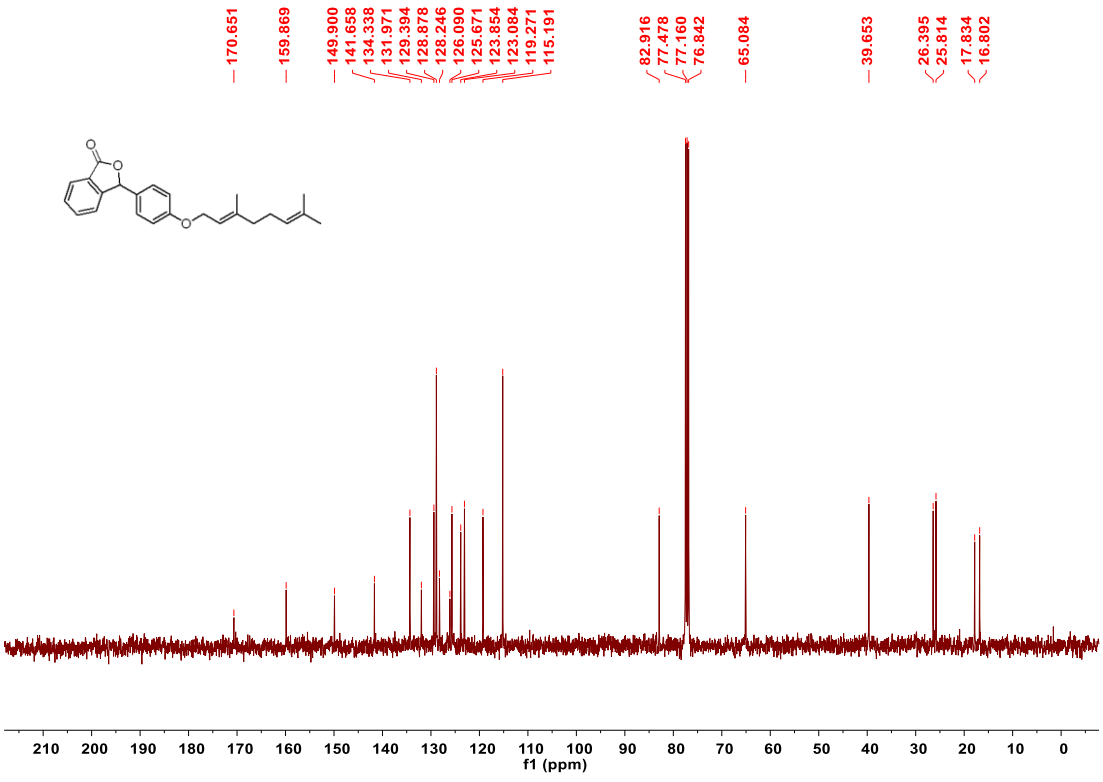


The HRMS spectrum of 4-(3-oxo-1,3-dihydroisobenzofuran-1-yl)phenyl (2*E*,4*E*,6*E*,8*E*)-3,7-dimethyl-9-(2,6,6-trimethylcyclohex-1-en-1-yl)nona-2,4,6,8-tetraenoate (14).

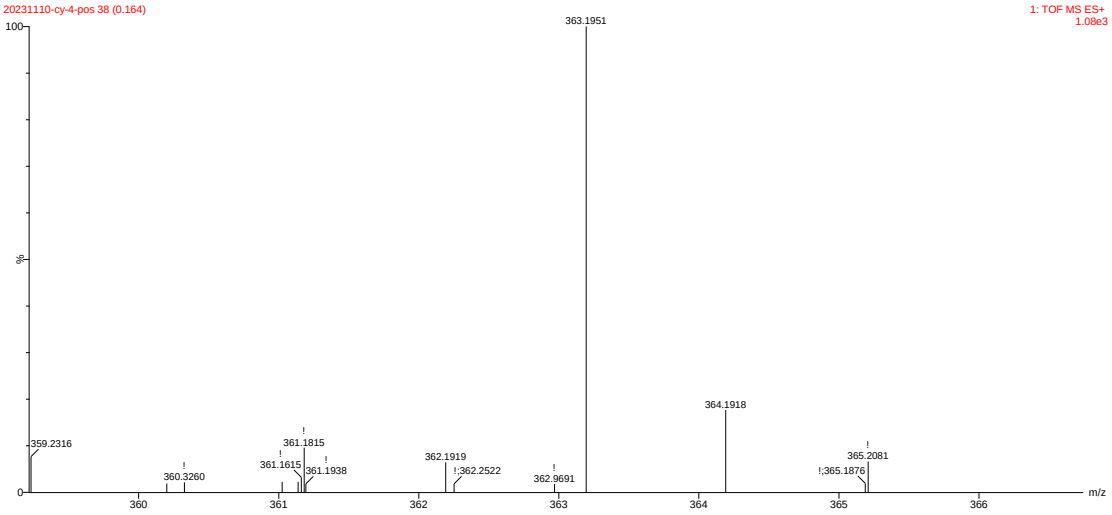


The ^{1}H and ^{13}C NMR spectrum of (E)-3-(4-((3,7-dimethylocta-2,6-dien-1-yl)oxy)phenyl)isobenzofuran-1(3H)-one (15).

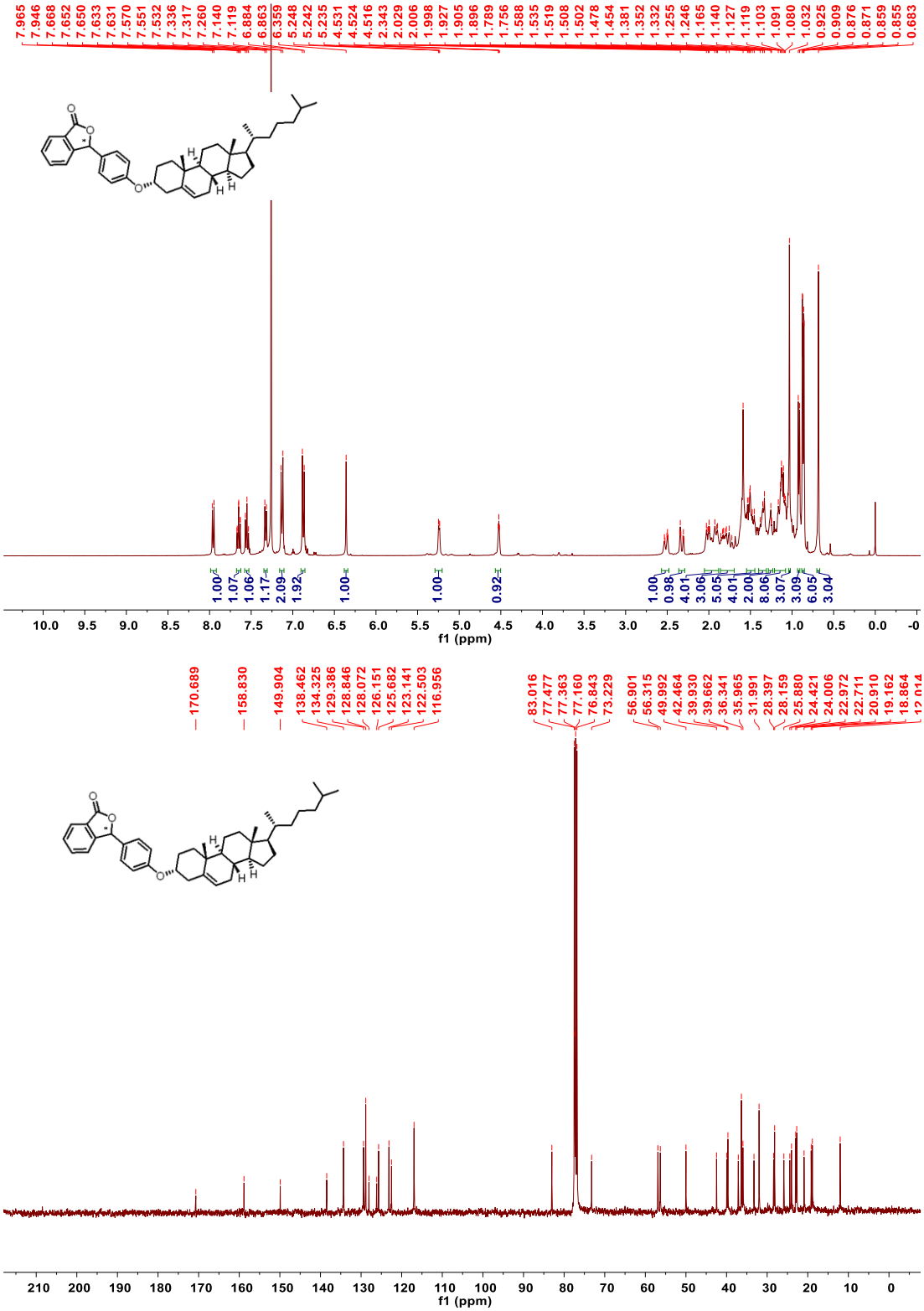




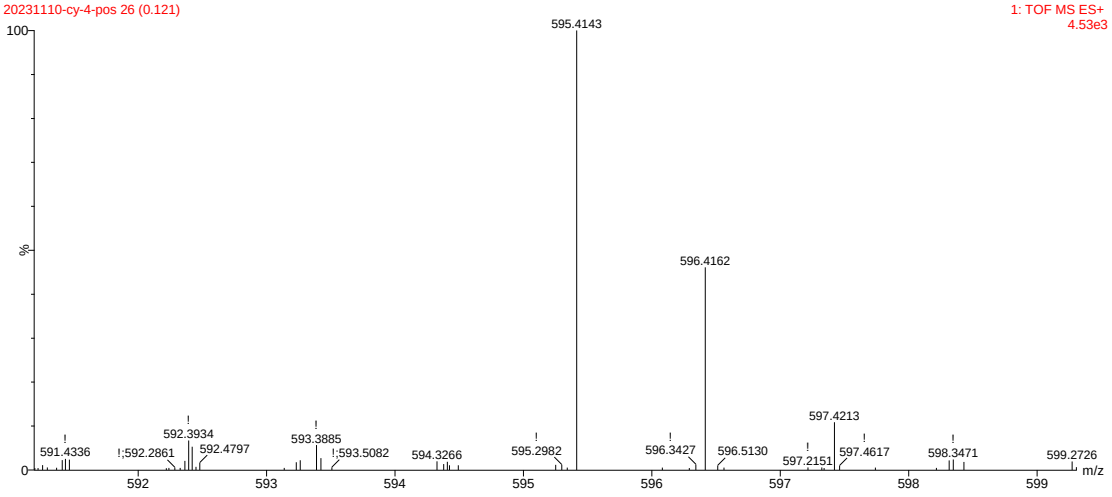
The HRMS spectrum of (E)-3-(4-((3,7-dimethylocta-2,6-dien-1-yl)oxy)phenyl)isobenzofuran-1(3H)-one (15).



The ^{1}H and ^{13}C NMR spectrum of 3-(4-(((3R,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)phenyl)-3l3-isobenzofuran-1(3*H*)-one (16).



The HRMS spectrum of 3-(4-(((3R,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)phenyl)-3l3-isobenzofuran-1(3H)-one (16).



21. The ^{1}H NMR of crude reaction mixtures for the KIE studies.

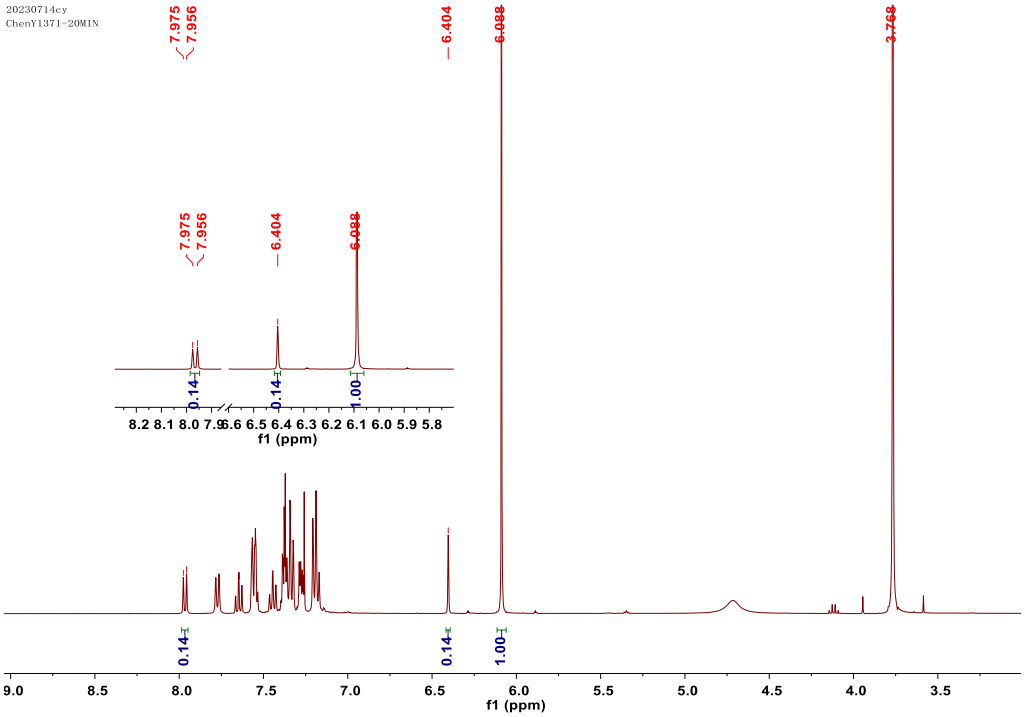


Figure S4. The ^{1}H NMR yield of the crude residues **2a** for 20-minute reaction.

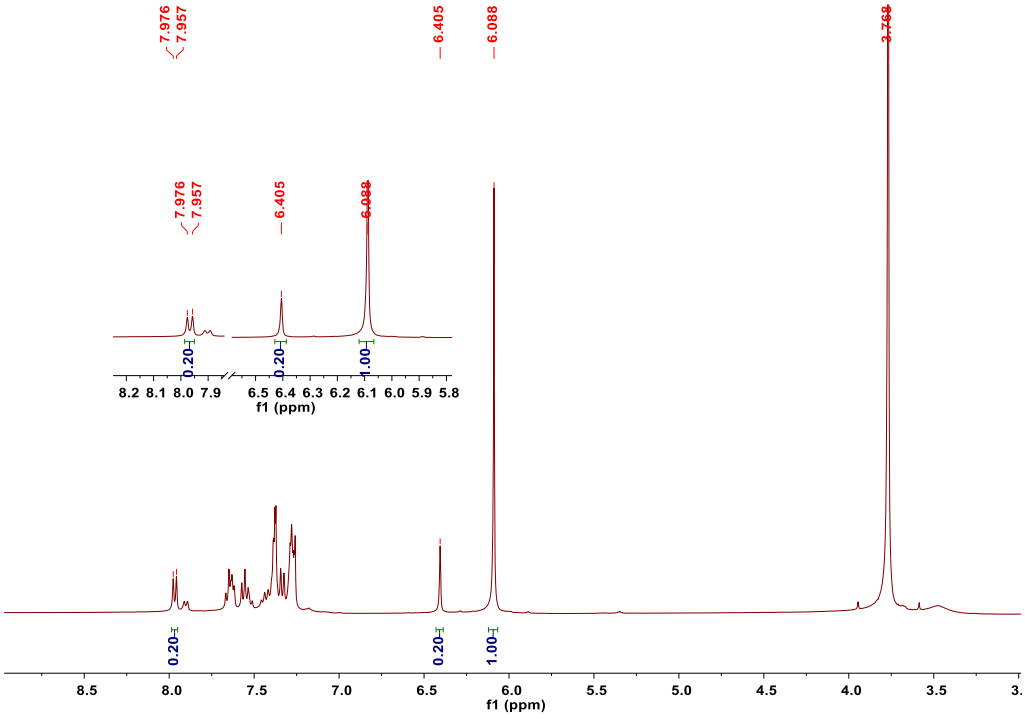


Figure S5. The ^{1}H NMR yield of the crude residues **2a** for 30-minute reaction.

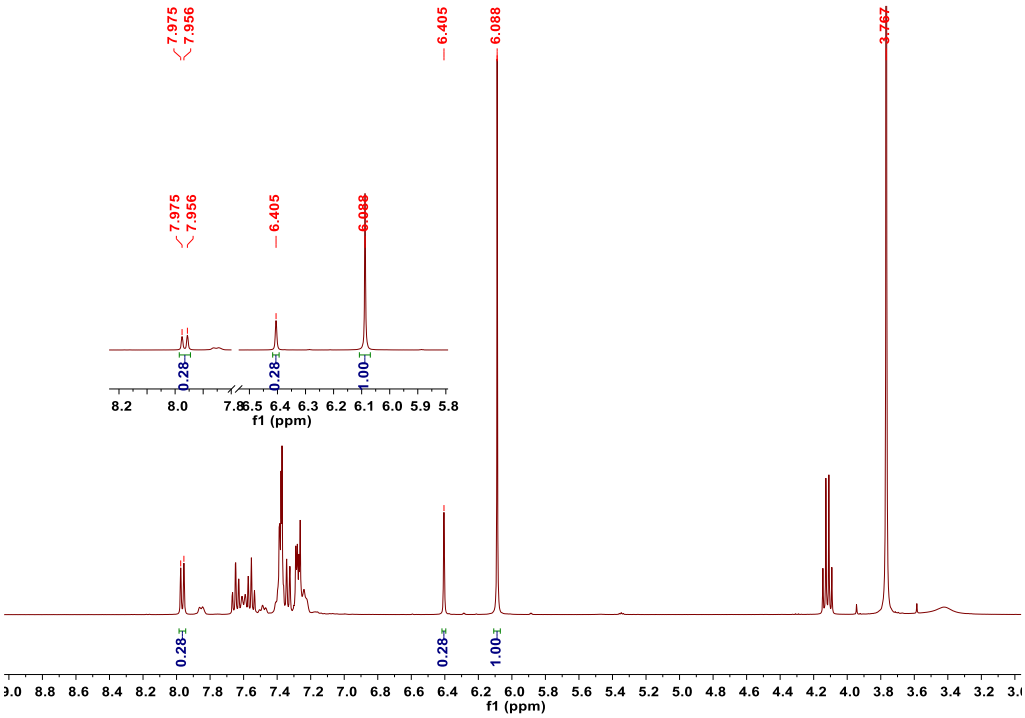


Figure S6. The ^{1}H NMR yield of the crude residues **2a** for 40-minute reaction.

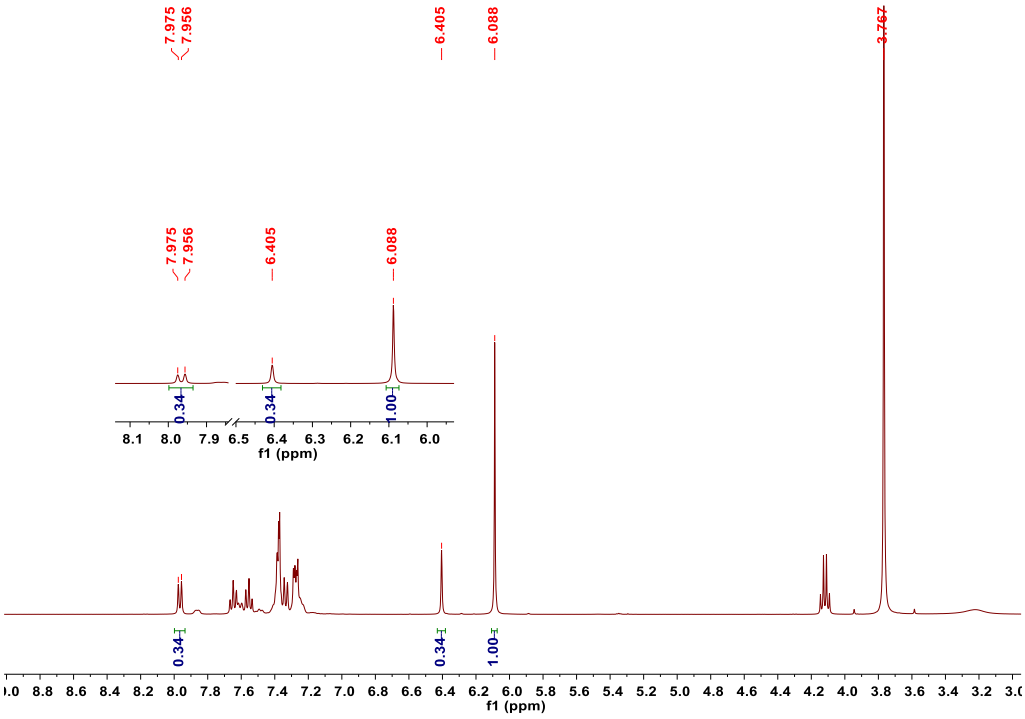


Figure S7. The ^{1}H NMR yield of the crude residues **2a** for 50-minute reaction.

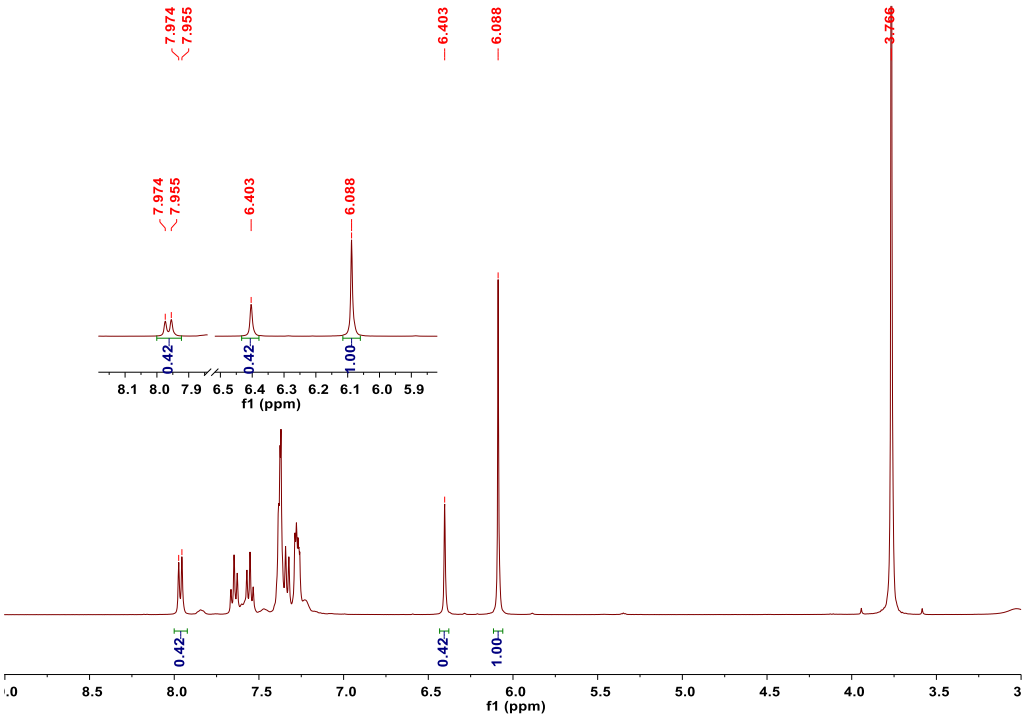


Figure S8. The ^{1}H NMR yield of the crude residues **2a** for 60-minute reaction.

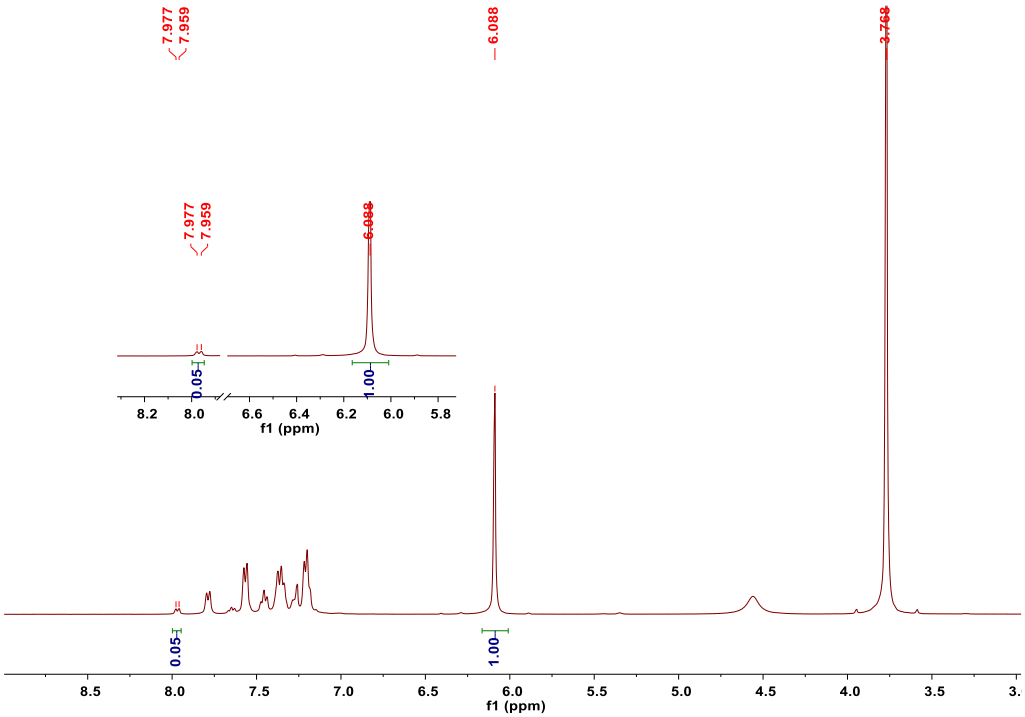


Figure S9. The ^{1}H NMR yield of the crude residues **2a**-*d* for 20-minute reaction.

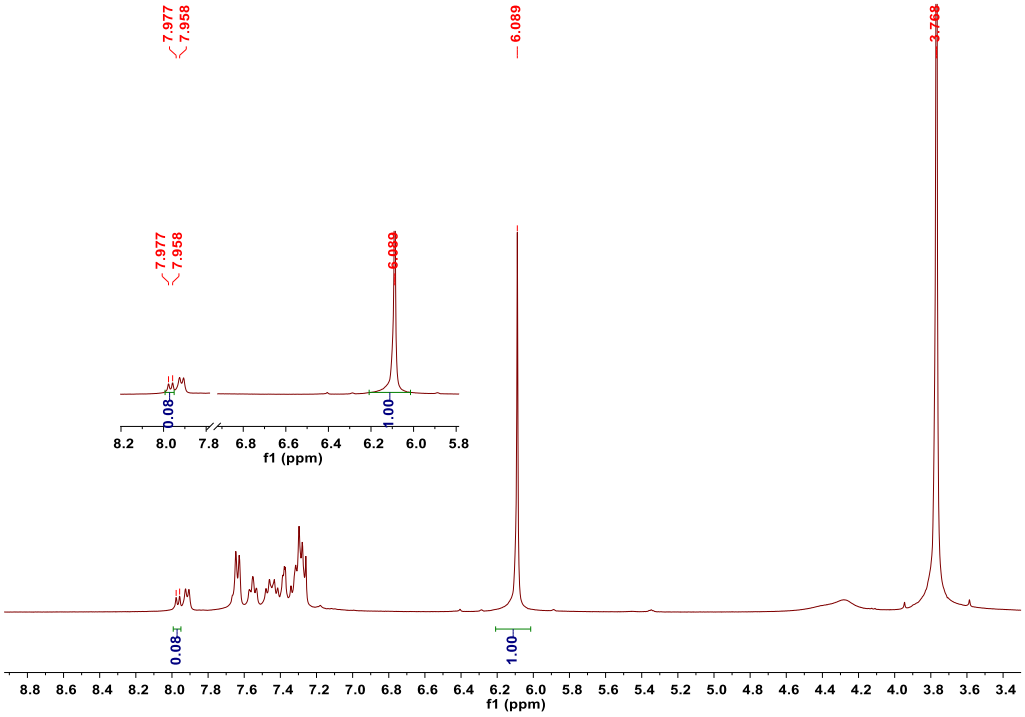


Figure S10. The ^{1}H NMR yield of the crude residues **2a**-*d* for 30-minute reaction.

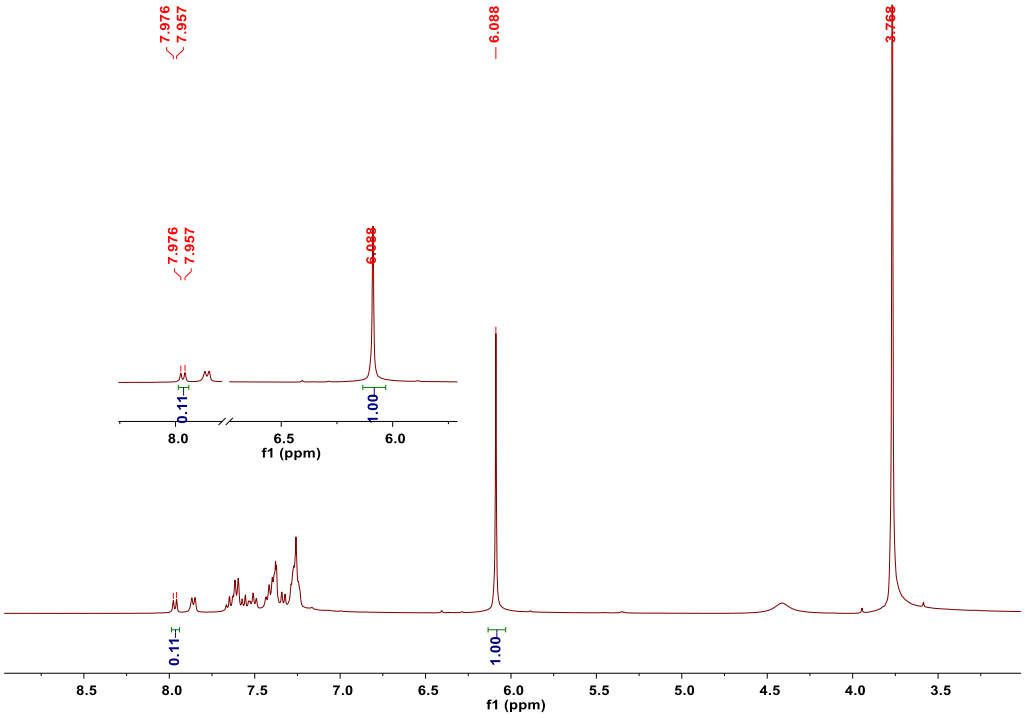


Figure S11. The ^{1}H NMR yield of the crude residues **2a**-*d* for 40-minute reaction.

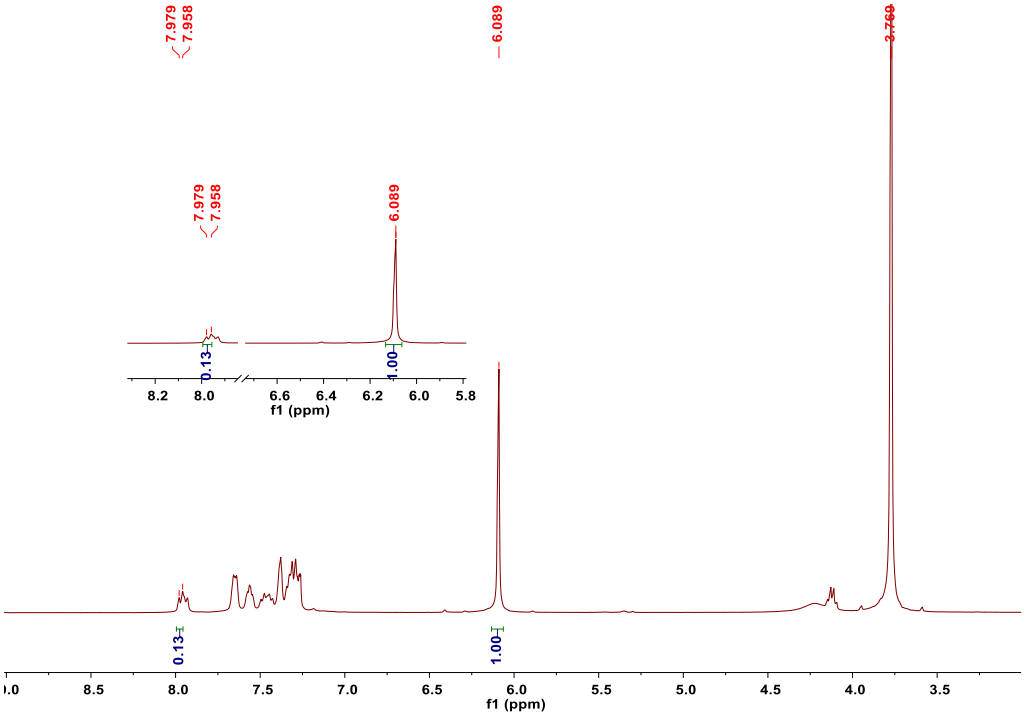


Figure S12. The ^{1}H NMR yield of the crude residues **2a**-*d* for 50-minute reaction.

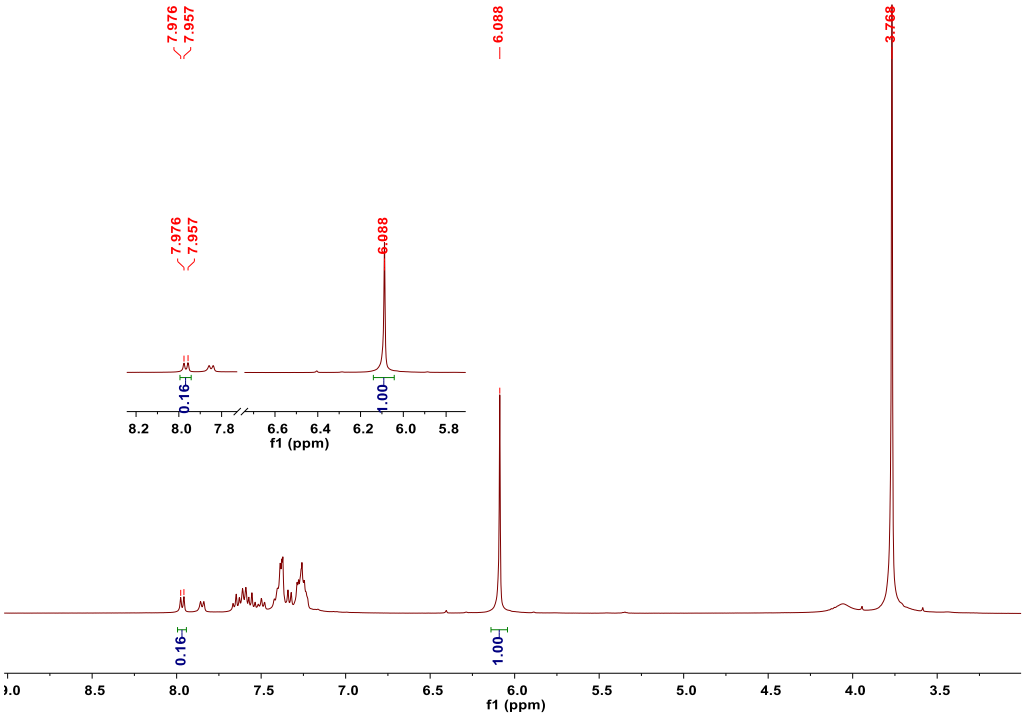


Figure S13. The ^{1}H NMR yield of the crude residues **2a**-*d* for 60-minute reaction.